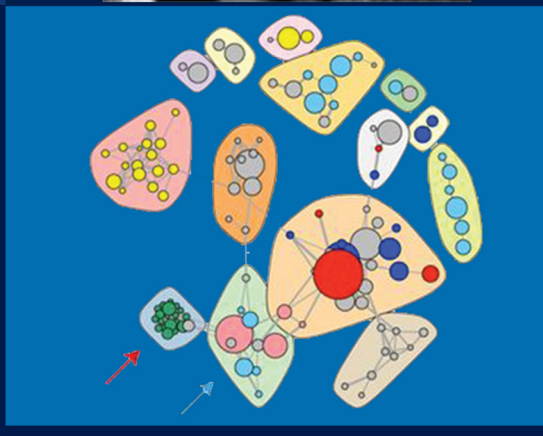
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ABSTRACT OPENING PLENARY

OP0001 DECONVOLUTING IMMUNOLOGICAL AND CLINICAL HETEROGENEITY ACROSS AUTOIMMUNE RHEUMATIC DISEASES BY COHORT-WIDE IMMUNO-PHENOTYPING

Keywords: Systemic lupus erythematosus, Genetics/Epigenetics, Rheumatoid arthritis

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Background: Autoimmune rheumatic diseases (AIRDs) are systemic but heterogeneous diseases characterized by orchestration of disrupted self-tolerance of immune systems. We face a challenge in characterizing clinical immune features and selecting best treatment strategy of the AIRD patients.
Objectives: Deconvolution of immunological and clinical heterogeneity within and across AIRDs is an essential step towards implementation of personalized medicine. Immuno-phenotypes, immune-related cell types in peripheral blood mononuclear cells quantified by flow-cytometry analysis, can less invasively describe immune profiles of individuals and is considered as a promising technique.
Methods: We conducted large-scale and cohort-wide immuno-phenotyping of 46 peripheral immune cells using the Human Immunology Protocol of comprehensive 8-color flow cytometric analysis. The dataset consisted of >1,000 Japanese patients of 11 AIRDs and controls with deep clinical information registered at the FLOW study, including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc), ANCA related vasculitis (AAV), idiopathic inflammatory myopathy (IIM), psoriasis, IgG4 related disease (IgG4RD), mixed connective tissue disease (MCTD), ankylosing spondylitis (AS), Sjogren's syndrome (SjS), and giant cell aortitis (GCA). In depth and longitudinal clinical analysis was conducted for the identified RA patient clusters registered at the FIRST registry. Inborn human genetics represented by genome-wide polygenic risk score (PRS) were estimated for the RA patients.
Results: Multimodal clustering of immuno-phenotypes deciphered underlying disease-cell type network, providing immune cell type specificity shared or distinct across AIRDs, such as close immunological network of MCTD with SLE rather than with SSc. Individual patient-level clustering deconvoluted the AIRD patients into several clusters with different immunological features (**Figure 1A**). Of these, RA- or SLE-like clusters were exclusively dominant, showing immunological polarization between RA and SLE across AIRDs (the patient clusters 4-6 and 1-3 for RA and SLE, respectively; **Figure 1B**). In depth and longitudinal clinical analysis of RA revealed that such patient clusters differentially defined clinical heterogeneity in disease activity and treatment responses, which were supported by immune cell-type specificity (e.g., decreased regulatory T cells associated with treatment resistance in the RA patients with SLE-like immuno-phenotypes). PRS based on RA case-control genome-wide association study (GWAS) and within-case stratified RA GWAS were associated with patient characteristics, disease activity, and immuno-phenotypes of the RA patients, such as dendritic cells for RA-interstitial lung disease.
Conclusion: Our study demonstrated a value of cohort-wide and cross-disease immuno-phenotyping to elucidate clinically heterogenous patient subtypes existing within the single disease in an immune cell type-specific manner.

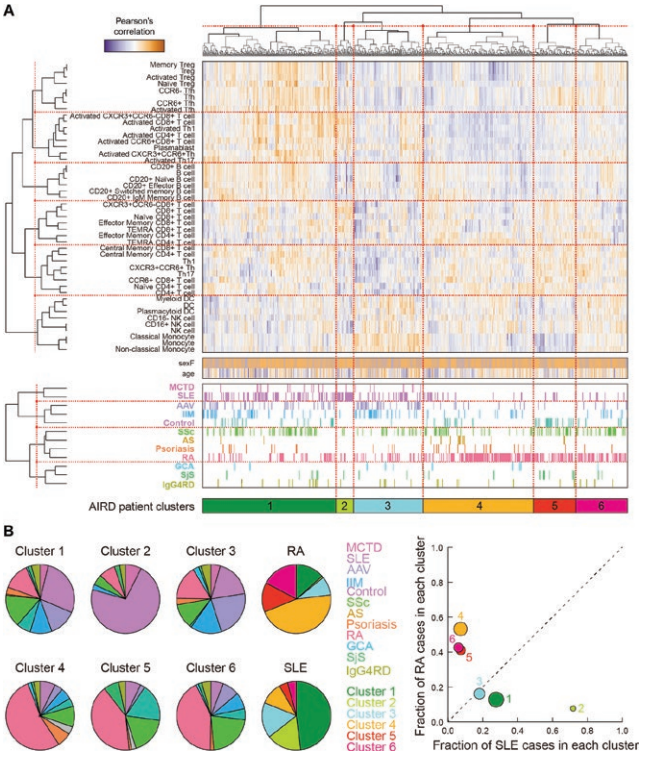


Figure 1. Patient-level clustering of the 11 AIRDs based on the cohort-wide immuno-phenotypes

(A) Unsupervised clustering of individual AIRD patients according to the immuno-phenotypes of the 46 peripheral immune cells. (B) Pie charts showing proportions of the AIRDs within each cluster, and those of the clusters within RA and SLE (left). A co-plot of the fractions of the RA and SLE patients within each cluster (right).

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OP0002 EXPLORING THE USE OF ARTIFICIAL INTELLIGENCE IN PREDICTING RHEUMATOID ARTHRITIS, BASED ON EXTREMITY MR SCANS IN EARLY ARTHRITIS AND CLINICALLY SUSPECT ARTHRALGIA PATIENTS

Keywords: Imaging, Rheumatoid arthritis, Artificial Intelligence

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Background: Predicting early rheumatoid arthritis (RA) from extremity MRI facilitates timely treatment, possibly preventing chronicity. Image interpretation by Artificial Intelligence (AI) may provide more accurate predictions than visual scoring.
Objectives: We developed a deep learning AI-method that automatically analyzes extremity MR scans by pre- and post-processing images, in order to predict RA at an early stage.
Methods: MR scans of the hands and feet from a total of 1974 patients were collected, consisting of 1247 early onset arthritis (EAC) patients, of whom 538 developed RA in two years, and 727 clinically suspect arthralgia (CSA) patients, of whom 113 developed RA. MRI scans were preprocessed automatically through background removal, slice-by-slice normalization and central slice selection. Subsequently, a self-supervised deep learning model was pre-trained to fill-in parts of the image that have been blinded by square patches (Figure 1(a), top row). Finally, after transferring the resulting weights, the model was fine-tuned to predict RA development (see Figure 1 (a) bottom row). The model was evaluated through 5-fold cross-validation and in a held-out test set (n=312 for EAC and n=146 for CSA). The model's accuracy was evaluated with the area under the receiver operator curve (AUC). An improved class activation map was developed and applied to indicate, which areas were most important to the AI decision.
Results: On the test set, the proposed model obtained a mean AUC of 0.683 in the EAC group, and 0.727 in the CSA group, using MR scans of the hands (wrist and metacarpophalangeal joints). Models trained separately on the wrists, MCPs and feet, received a mean AUC of 0.679, 0.647, 0.664, and 0.688, 0.669, 0.715, for the EAC and CSA group, respectively (see Table 1). These accuracies were close to the expert-level using RAMRIS, with reported AUCs of 0.74 and 0.69 in predicting RA in CSA [1]. According to the proposed visualization method,

the deep learning models predict RA, based on very similar patterns of known (teno-)synovial inflammation and bone marrow edema (see Figure 1 (b)).

Table 1. The overall performance, mean AUC (±SD)

Method:	Input			AUC RA in EAC	AUC RA in CSA
	Wrist	MCP	Foot		
MR scans + AI models	√			0.679 (±0.021)	0.688 (±0.039)
		√		0.647 (±0.015)	0.669 (±0.024)
			√	0.664 (±0.009)	0.715 (±0.026)
	√	√		0.683 (±0.025)	**0.727 (±0.037)**
	√	√	√	**0.707 (±0.016)**	0.708 (±0.068)

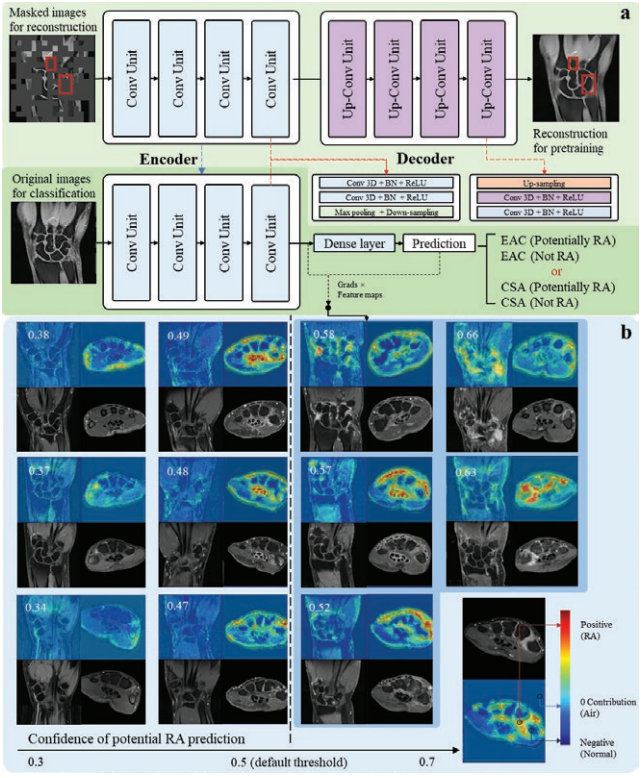


Figure 1. The overall workflow of the AI model and visualization examples from correctly-predicted samples.

Conclusion: Automatic RA prediction is feasible, using AI interpretation of MRI scans. AI performed close to the level of human experts. Including MRI data from healthy controls, as used in RAMRIS-based prediction [1], will probably improve the AI prediction further. The new visualization method not only confirms the significance of known inflammatory features but may also point to new imaging biomarkers, giving a different perspective of understanding RA.

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Disclosure of Interests: None Declared.

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OP0003 TASK-SHIFTING IN HAND-OSTEOARTHRITIS CARE

Keywords: Randomized control trial, Osteoarthritis, Health Services Research

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Background: Hand-osteoarthritis (HOA) is a prevalent rheumatic joint disease that significantly reduces quality of life. In Norway, HOA should mainly be managed in primary care, but patients often have insufficient access to recommended treatment options there and are instead frequently referred to rheumatologists. This leads to high healthcare costs and reduces the access to rheumatologists for patients with inflammatory rheumatic diseases, for whom early diagnosis, disease modifying medication and tight controls may induce remission and prevent irreversible joint damage and long-term disability. Delegating the healthcare management and treatment of HOA to allied health professions such as occupational therapists may therefore free scarce healthcare resources and improve overall health economics.

Objectives: In this study we evaluated a new model of care in specialist healthcare, where HOA patients receive their first consultation by occupational therapists instead of rheumatologists. The objective was to test the non-inferiority of occupational therapist-led care (OTC) compared to rheumatologist-led care (RC) with regards to effectiveness defined as proportion of responders (based on OMERACT/OARSI criteria) and safety. In addition, we conducted a health economics evaluation comparing Quality-adjusted life years (QUALYs) and treatment costs between the treatment groups and conducted a cost-economics analysis.

Methods: We conducted a randomized controlled multicentre parallel group trial in which we recruited 400 patients with symptomatic HOA and no signs of possible inflammatory rheumatic disease at two Norwegian hospitals. Participants were randomized (1:1, computer-based) to either OTC (n=200) or RC (n=200). Various demographic and clinical parameters were registered at baseline. Disease activity (numeric rating scale, NRS, 0-10, 0=no disease activity), pain (NRS, 0-10, 0=no pain) and function (using the MAP-hand questionnaire, 18 items averaged to a 1-4 score, 1=no problems) were registered at baseline and 6 months post-intervention, and the delta was used to determine if patients were responders/non-responders based on OMERACT/OARSI criteria. Chi2-test and logistic regression were used to compare the proportion of responders/non-responder per treatment arm, and to analyse the relationship between response status (as dependent variable) and treatment arm (as independent variables). Results of the logistic regression are presented as odds ratio (OR) with 95% confidence interval (CI). Safety analysis was conducted by screening healthcare journals 12 months post-baseline for new diagnoses and adverse events related to musculoskeletal diseases. QUALYs were calculated using data from EQ-5D weighted with preference weights from the general population. To evaluate cost-effectiveness, we calculated and compared the incremental cost-effectiveness ratio (ICER).

Results: Mean age was 63.6 years (SD=10.01), 80.8 % were female. No statistical difference between the treatment arms was found in any baseline variables. In the RC group, 48 patients (25.8%) met the primary outcome criteria for treatment response. In the OTC group, also 48 (25.4%) were classified as responders. The proportion of responders did not differ by treatment group (X2 (1, N = 337) = 0.0012, p =.97). Treatment group did not significantly predict response status (OR=0.99, CI=0.62-1.59, p = 0.97). No notable safety-related events were found in either group. No statistically significant differences were found regarding QUALYs and overall treatment costs, and cost-effectiveness was marginal.

Conclusion: We found no statistically significant difference regarding proportion of treatment responders between the two treatment arms, suggesting non-inferiority of OTC compared to RC with regards to effectiveness and safety. While the cost-effectiveness analysis showed no clear benefit for either of the treatment options, delegating HOA treatment to OTs may free RT time and improve healthcare accessibility for urgent diagnoses, and thus prove a valuable opportunity to optimize future healthcare allocation.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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OP0004 LUPUS100.ORG – A STEP CHANGE IN ACCESS TO QUALITY INFORMATION FOR EUROPEAN LUPUS PATIENTS

Keywords: Patient information and education, Systemic lupus erythematosus, Self-management

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Background: Quality of information on lupus on the internet is a real issue. ''Word of mouth'', rumours, unchecked data, or unconfirmed research increase

confusion, create anxiety and can lead to incorrect actions. Patients need access to quality information about lupus. Therapeutic Patient Education (TPE) is a key part of the self-management of chronic conditions; an essential component of TPE is access to valid information. Most patients in Europe don't speak English.
Objectives: To provide access to quality information on lupus online, in the native language of 95%+ of the European population.
Methods: The first step was to get the project endorsed by specialised lupus doctors, ERN ReCONNET. The French book "lupus en 100 questions" (initiated by FAI2R) was used as a starting point. Patients from the Lupus Europe Patient Advisory Network (PAN) and doctors worked together to create the English version. The least internationally relevant questions were removed to make space for new questions suggested by Lupus Europe's PAN. Answers for the new questions were constructed collaboratively between patients and doctors. The other questions were translated to English, updated where needed and adapted for international use. The resulting English document was distributed to ERN ReCONNET SLE working group doctors and to all PAN members, and feedback was incorporated. This master version was then put online and served as starting point for an ambitious multilingual translation. The translation process included generating an initial draft translation through Deepl Pro, and then upgrading this by a Doctor-Patient native speaker team. In parallel, a process has been established to collect comments and suggestions so that content can be maintained and upgraded on a continuous basis while keeping all language versions synchronised.
Results: lupus100.org in English was launched at the European Lupus Meeting in October 2022 and has to date received 8,900 visits. 18 translations have been completed and 10 of them are under final validation. The international launch of the multilingual website will take place on May 10, World Lupus day.
Conclusion: This effort will provide access to quality information about lupus to 95% of European lupus patients in their own language, eliminating a big barrier to quality information. Thanks to the effective collaboration between patients and doctors, quality of information can be guaranteed and information truly answers the patient concerns. Both national groups and the ERN network of doctors will ensure effective dissemination, so patients in all European countries are aware of the initiative.
REFERENCE:
[1] Zangi, H.A.; Ndosi, M.; Adams, J.; Andersen, L; Bode, C.; Bostrom, C.; van Eijk-Hustings, Y.; Gossec, L.; Korandova, J.; Mendes, G.; Niedermann, K.; Primdahl, J.; Stoffer, M.; Voshaar, M.; van Tubergen, A. EULAR recommendations for patient education for people with inflammatory arthritis. Ann Rheum Dis. 2015; 74 (6): 945-62 DOI: 10.1136/annrheumdis-2014- 206807
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OP0005

CAN AXIAL SPONDYLOARTHRITIS UNEQUIVOCALLY BE DIAGNOSED BY RHEUMATOLOGISTS IN PATIENTS WITH CHRONIC BACK PAIN OF LESS THAN TWO YEARS DURATION? MAIN RESULT OF THE SPONDYLOARTHRITIS CAUGHT EARLY (SPACE) COHORT

Keywords: Diagnostic Tests, Spondyloarthritis, Epidemiology

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Background: Unacceptable diagnostic delay in axial Spondyloarthritis (axSpA) remains an issue. In 2009, the longitudinal SPondyloArthritis Caught Early (SPACE)-cohort started to assess the prevalence of axSpA and the reliability of an early diagnosis in patients with chronic back (CBP) of unknown origin. Here we present one of the main outcomes of SPACE.
Objectives: To assess the two-year (2y) prevalence of an axSpA diagnosis among patients with recent onset CBP referred to the rheumatologist; To investigate the sustainability of a baseline (BL) diagnosis of axSpA when reviewed after 2y; And to explore patient-differences between BL and 2y, in those with and without an axSpA diagnosis.
Methods: We analysed the 2y data from SPACE, a European inception cohort of patients (age <45y) with CBP of recent onset (≥3 months, ≤2y) and unknown origin. The full diagnostic work-up included all clinical SpA-features, acute phase reactants, HLA-B27, radiographs and MRI of the sacroiliac joints (SI-CR and SI-MRI) and spine (data not shown). Patients with increased likelihood of having axSpA (≥1 major or ≥2 minor prespecified SpA-features) were eligible for follow-up with the remaining patients excluded per protocol. The clinical diagnosis at 2y was the main outcome of this study. At each visit, the treating rheumatologist judged on the presence or absence of axSpA (axSpA or no-axSpA) with a level of confidence (LoC) on a numeric rating scale (0: *not confident at all* to 10: *very confident)*. The main outcome was the presence of 'definite axSpA' at 2y, defined as a clinical diagnosis of axSpA with a LoC ≥7 (complete follow-up) or at the two last available visits if 2y visit was missing. 'No axSpA' was defined as not having axSpA at 2y (with LoC ≥7; or if LoC <7, plus an alternative diagnosis for CBP reported). All other patients were considered having an 'uncertain' diagnosis. The ASAS classification criteria were computed using sacroiliitis central reading results in definite axSpA patients. We assessed the prevalence of definite axSpA at 2y as well as changes in diagnosis over time, and descriptively summarised BL characteristics.
Results: A total of 555 CBP patients were included (Leiden n=383, Oslo n=97, Amsterdam n=48, and Gouda n=27). A diagnosis of definite axSpA was given to 175 (32%) patients at BL and 166 (30%) at 2y (***Figure 1***). The mean (SD) LoC's were 8.1 (2.0) and 8.7 (1.0), with 155/175 (89%) and 145/166 (87%) fulfilling ASAS classification criteria, respectively. BL diagnostic judgments were relatively unequivocal and remained rather stable: At 2y, 6% of the BL diagnoses of definite axSpA were refuted; and -*vice versa*: 9% of those who did not obtain a BL diagnosis of axSpA 'gained' one at 2y. Residual diagnostic uncertainty remained in 14% of CBP-patients. Expectedly, BL SpA-related features were more prevalent in the 2y definite axSpA group (***Table 1***). (The presence or absence of) imaging-detected sacroiliitis at BL appeared the best discriminator between axSpA and no axSpA at 2y.
Conclusion: One third of patients with CBP of recent onset referred to the rheumatologist has definite axSpA. Most of these patients can be unequivocally and reliably diagnosed at their first assessment. None of the many SpA-features suffices alone, but imaging discriminates best.

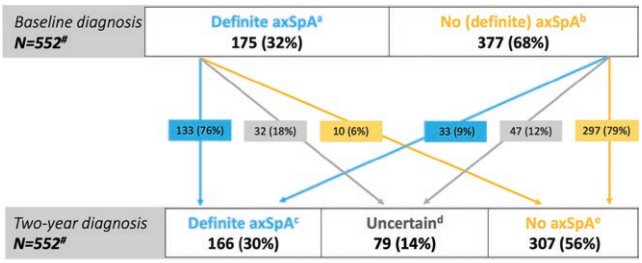


Figure 1. Diagnosis course from baseline (BL) to the two-year (2y) anchor visit.
axSpA: axial Spondyloarthritis; [a] patients diagnosed at BL with axSpA with a Level of Confidence (LoC) ≥7; [b] patients diagnosed at BL with axSpA (LoC <7) or with no axSpA (any LoC); [c] patients diagnosed with axSpA with a LoC ≥7 at 2y (if complete follow-up) or at the last two available visits (if missing the 2y visit); [d] patients diagnosed with axSpA with a LoC <7 at 2y (or LoC ≥7, if only baseline observation available), and patients with axSpA with LoC <7 at the last available observation and no consistent diagnosis at the last two observations nor alternative no axSpA diagnosis given at the last observation; [e] patients with no axSpA at the last observation over 2y with LoC ≥7 (or if <7, plus an alternative no axSpA diagnosis reported, e.g. fibromyalgia or aspecific back pain).

Table 1. Baseline characteristics by 2y diagnosis of patients with chronic back pain duration of ≥3 months but ≤2y, < 45y of age

	Definite axSpA N=166	Uncertain N=79	No axSpA N=307
Mean age at inclusion, y (SD)	29.8 (7.6)	30.8 (8.3)	31.0 (8.4)
Male	52%	65%	26%
Mean symptom duration, months (SD)	12.8 (7.0)	13.4 (7.2)	13.4 (7.2)
HLA-B27 +	81%	61%	15%
Family history of SpA	48%	61%	39%
Inflammatory back pain§	76%	65%	55%
Good response to NSAIDs	43%	42%	23%
Peripheral arthritis	16%	15%	8%
Dactylitis	7%	8%	3%
Heel enthesitis	19%	14%	8%
Anterior uveitis	14%	11%	3%
Inflammatory bowel disease	7%	6%	7%
Psoriasis	11%	8%	8%
Increased acute phase reactants§	36%	19%	20%
SI-CR§	23%	8%	1%
SI-MRI§	67%	24%	7%

§ local data; SI-CR/MRI: sacroiliitis on radiographs/MRI

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OP0006

INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID OR PSORIATIC ARTHRITIS STARTING BDMARDS: INCIDENCE VS. GENERAL POPULATION, AND THE ROLE OF METHOTHREXATE CO-MEDICATION

Keywords: Comorbidities, Lungs

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Background: Interstitial lung disease (ILD) is a common (extra-articular) pulmonary manifestation of rheumatoid arthritis (RA). In RA, use of biologic or targeted synthetic disease-modifying drugs (b/tsDMARDs) have been linked to ILD, whereas the risk attributable to MTX use remains unclear. In psoriatic arthritis (PsA), few studies have investigated the risk of ILD, let alone in relation to use of MTX and b/tsDMARDs.
Objectives: To assess the incidence of ILD in patients with RA or PsA initiating a b/tsDMARD (vs. the general population), compare the risk of ILDs across b/tsDMARDS and investigate the role of MTX co-medication.
Methods: Patients with RA or PsA initiating a b/tsDMARD were identified in rheumatology registers from Denmark, Finland, Iceland, Norway and Sweden. Details of b/tsDMARD treatment, MTX co-medication, and disease activity at treatment initiation were retrieved. Gender and age-matched general population subjects were available from four countries. The incidence of ILD was assessed through linkages to national hospital and death registers with cases defined as patients who had been given an ILD diagnoses on more than one occasions. Subjects with a history of ILD prior to b/tsDMARD initiation were excluded. In multivariable models, we calculated the hazard ratios (HR) for ILD in individual patients starting b/tsDMARDs vs. population subjects, following each patient from treatment start until the first of ILD event, end of, death, or five years of follow-up. In separate on-treatment analyses we compared the risk of ILD between b/tsDMARDS initiators using etanercept treatment as a reference, and between those using vs. not using MTX (reference) as co-medication. Follow-up in on-treatment analyses was defined as time to first of ILD event, end of treatment plus 29 days, death or five years. For these analyses one patient could have several treatment courses in a time-split cox-regression analyses.
Results: 37.010 patients with RA, 12.341 patients with PsA and 569.451 population subjects, were identified, contributing 300, 30 and 400 ILD cases during follow-up, respectively. HR for ILD (vs. the general population) was 10.1 (95% CI 8.6 to 11.9) in RA and 5.0 (3.4 to 7.4) in PsA patients initiating a b/tsDMARD. In on-treatment analyses 69 608/21 340 b/ts DMARD treatment-courses were identified in RA/PsA patients with 558 and 46 ILD events during follow-up, respectively Among patients with RA a significantly increased HR (vs. etanercept) was only noted for rituximab 1.7 (1.2 to 2.4). No b/tsDMARD increased the risk of ILD in patients with PsA. MTX co-medication was used in 51.3%/42.2% of RA/PsA patients but did not give an increased risk of ILD compared to no use of MTX-co-medication (Figure 1 shows details of results for RA populations).
Conclusion: Among RA and PsA patients initiating b/tsDMARDs, the risk of ILD was higher than in the general population, and the risk of ILD in RA was approximately twice that of PsA patients. In these preliminary analyses, the increased risk of ILD in RA patients initiating treatment with rituximab may indicated a channeling bias. When used in clinical practice, MTX co-medication is not a risk factor for ILD in RA/PsA patients initiating b/tsDMARD therapy.

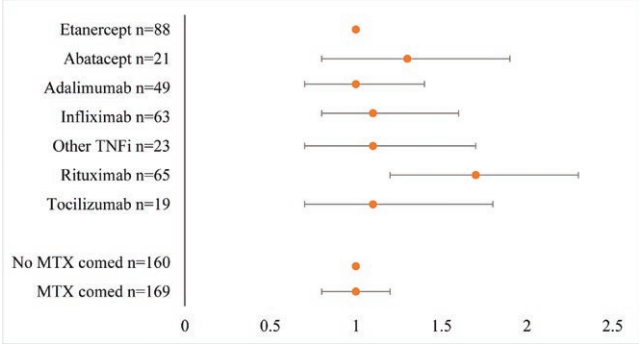


Figure 1. Risk of ILD across b/tsDMARD treatment and methotrexate co-medication in patients with rheumatoid arthritis. (Hazard ratios (95% CI). Etanercept 21 079 patients, adalimumab 12 018, abatacept 4 973, infliximab 12 636, Other TNFis 5 424, other bDMARDs 244 (not shown, no events) Rituximab 6 917, tsDMARDs 1 248 (not shown, no events), Tocilizumab 5 067

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OP0007

INCIDENCE, PREVALENCE AND CO-OCCURRENCE OF AUTOIMMUNE DISORDERS, TRENDS OVER TIME AND BY AGE, SEX AND SOCIOECONOMIC STATUS. A POPULATION-BASED STUDY IN 22 MILLION INDIVIDUALS.

Keywords: Real-world evidence, Gender/diversity issues, Epidemiology

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Background: A rise in the incidence of selected autoimmune disorders has been described, raising the question as to whether the overall incidence of autoimmune disorders might be on the rise due to environmental factors. However, reliable estimates of disease incidence and trends over time, particularly as pertains to autoimmune diseases as a group, are not available. Commonalities and differences between individual diseases also remain poorly understood.

Objectives: To investigate the incidence and prevalence for 19 of the most common autoimmune diseases, to assess trends over time, by sex, age, socioeconomic status, season and region, and to examine rates of co-occurrence among autoimmune diseases.

Methods: We used linked primary and secondary electronic health records of 22 million individuals from the Clinical Practice Research Datalink (CPRD), a cohort that is representative of the UK population in terms of age and sex. We calculated incidence and prevalence of 19 autoimmune disorders from 2000 to 2019 and used negative binomial regression models to investigate temporal trends and variation by age, sex, socioeconomic status, season of onset and region. To characterise co-occurrence of autoimmune diseases, we calculated incidence rate ratios, comparing incidence rates of comorbid autoimmune disease among patients with a first autoimmune disease with incidence rates in the general population, using negative binomial regression models, adjusted for age and sex.

Results: Among the 22,009,375 individuals included in the study, we identified a total of 978 872patients with a new diagnosis of at least one autoimmune disease between 2000 and 2019 (mean (SD) age: 54.0 (21.4) years, 64% women). Over the study period, age-standardised incidence rates of autoimmune diseases increased by 4%, similarly for men and women. The largest increases were seen in Graves' disease, coeliac disease and Sjogren's syndrome, for which incidences have doubled over the past two decades. Two conditions exhibited a significant decrease in incidence (Hashimoto's thyroiditis and pernicious anaemia). Taken together the 19 autoimmune disorders examined affected 10.2% of the population over the study period (13.1% of women, 7.4% of men). A socioeconomic gradient was evident across several diseases, including Graves' disease, pernicious anaemia, rheumatoid arthritis, and systemic lupus erythematosus. Seasonal variations were observed for type 1 diabetes (more commonly diagnosed in winter) and vitiligo (more commonly diagnosed in summer), and regional variations were observed for a range of conditions. Autoimmune disorders were commonly associated with each other, particularly Sjogren's, systemic lupus erythematosus and systemic sclerosis. Patients with type 1 diabetes also had significantly higher rates of Addison's, coeliac, and thyroid diseases, and multiple sclerosis stood out as having low rates of co-occurrence with other autoimmune diseases.

Conclusion: Autoimmune diseases affect about one in ten individuals. Their burden continues to increase over time, albeit at varying rates across individual diseases. The socioeconomic, seasonal, and regional disparities observed among several autoimmune disorders, implicate environmental factors in disease pathogenesis. The interrelations between autoimmune diseases are commensurate with shared pathogenetic mechanisms or predisposing factors, particularly among connective tissue diseases and among endocrine diseases.

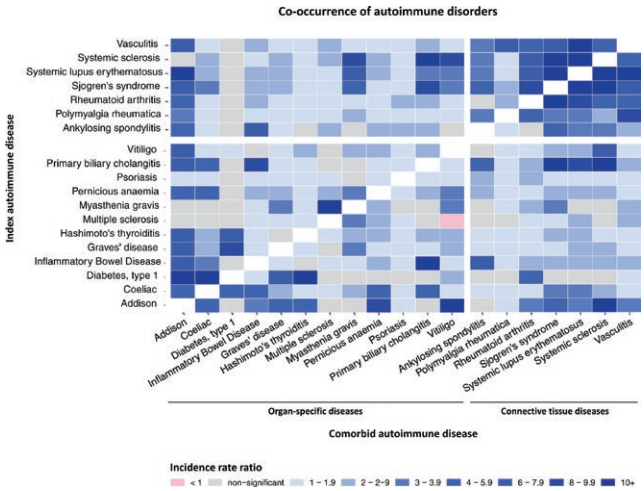


Figure 1. Incidence rate ratios for development of comorbid autoimmune disease among index populations with autoimmune disease compared with the general population

Incidence rate ratios were calculated for development of a second (comorbid) autoimmune disease among index populations with pre-existing autoimmune disease compared with the general population using negative binomial regression models adjusted for age and sex. Diabetes refers to childhood-onset type 1 diabetes (people aged <20 years at diagnosis).

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OP0008

EULAR RECOMMENDATIONS FOR THE USE OF IMAGING IN THE DIAGNOSIS AND MANAGEMENT OF CRYSTAL-INDUCED ARTHROPATHIES IN CLINICAL PRACTICE

Keywords: Imaging, Quality of care, Crystal Arthritis

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Background: The multifaceted clinical presentation in crystal-induced arthropathies (CiA) poses challenges to imaging.
Objectives: To formulate evidence-based recommendations on the use of imaging in the diagnosis and management of CiA.
Methods: Following EULAR standard operating procedures a task force of 25 stakeholders from 11 countries was created. Four systematic literature searches were performed in MEDLINE, EMBASE and CENTRAL to guide task force decisions, answering 14 research questions on the role of imaging in gout, calcium pyrophosphate and basic calcium phosphate deposition disease. Level of agreement (LoA) with each overarching principle and recommendation was assessed by numerical rating scale (0-10).
Results: Five overarching principles and 10 recommendations were produced on the role of imaging in making a diagnosis, monitoring, predicting, guiding intervention, and patient education in CiA (Table 1). Overall, the LoA for the recommendations was very high (8.5-9.9).
Conclusion: These are the first recommendations that encompass all common forms of CiA and guide the use of established imaging modalities in this disease group.

Table 1. EULAR recommendations for the use of imaging in CiA in clinical practice

Overarching principles	Level of agreement Mean (standard deviation)
A. CiA are typically characterized by intermittent, acute episodes of inflammation, but may also exhibit a persistent disease course with or without superimposed flares.	9.8 (0.5)
B. Imaging in CiA provides useful information on crystal deposition, inflammation, and structural damage.	9.8 (0.5)
C. The presence of imaging abnormalities, in particular those related to crystal deposition, may not always be related to clinical manifestations.	9.8 (0.5)
D. Patient information (medical history, physical/laboratory examination, synovial fluid/tissue analysis) should be taken into account when imaging is considered in CiA.	9.7 (0.7)
E. Imaging in CiA should be performed and interpreted by trained health care professionals.	9.9 (0.4)
Recommendations	
1. When performing imaging in CiA, both symptomatic areas and disease-specific target sites (i.e. MTP1 in gout, wrist and knee in CPPD, shoulder in BCPD) should be considered.	9.7 (0.5)
2. In the diagnostic assessment of gout, US and DECT are both recommended imaging modalities.	9.7 (0.6)
3. When characteristic features of MSU crystal deposition on US (i.e. double contour sign or tophi) or on DECT are identified, synovial fluid analysis is not needed to confirm a diagnosis of gout.	8.8 (1.8)
4. In the diagnostic assessment of CPPD, CR and US (or CT if axial involvement is suspected) are recommended imaging modalities.	9.6 (0.9)
5. In the diagnostic assessment of BCPD, imaging is necessary; CR or US are the recommended modalities.	9.1 (1.7)
6. In gout, US and DECT can be used to monitor crystal deposition and in case of US, also inflammation. Both modalities provide additional information on top of clinical and biochemical assessment. In case US/DECT are not available, CR can be used to assess structural damage due to gout. The decision on when to repeat imaging depends on the clinical circumstances.	9.3 (1.2)
7. In CPPD and BCPD serial imaging is not recommended, unless there is an unexpected change in clinical characteristics.	9.4 (1.2)
8. In gout, assessing the amount of MSU crystal deposition by US or DECT may be used to predict future flares.	8.5 (1.7)
9. If synovial fluid analysis is required in the assessment of CiA, US-guidance should be used in cases where aspiration based on anatomical landmarks is challenging.	9.7 (0.5)
10. Showing and explaining imaging findings of CiA to people with such conditions may help them understand their condition and improve treatment adherence in gout.	9.4 (0.9)

BCPD: basic calcium phosphate deposition disease; CiA: crystal-induced arthropathies; CPPD: calcium pyrophosphate deposition disease; CR: conventional radiography; CT: computed tomography; DECT: dual-energy computed tomography; MSU: monosodium urate; MTP: metatarsophalangeal joint; US: ultrasound

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"Buy one - get 4 free" - RMDs and comorbidities

OP0009-PARE **CREATIVITY AND CO-PRODUCTION TO SUPPORT PEOPLE LIVING WITH CHRONIC PAIN WITH THEIR MENTAL HEALTH**

Keywords: Mental health, Pain, Patient information and education

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Background: As many as 1-in-5 people are living with chronic pain (pain for three or more months) in the UK. Living with a long-term health condition can increase the likelihood of experiencing poor mental health. Having access to high-quality resources to raise mental health awareness and support good mental health among this population is crucial. Co-production of patient-facing resources with people with lived experience of health conditions (experts by experience) has been acknowledged as an important way of achieving impact and engagement.
Objectives: To describe how branding and design expertise was used to co-produce with experts by experience evidence-based, patient-facing animations to support the mental health needs of people with chronic pain.
Methods: A task and finish group (n=10) met virtually six times over 12 months from March 2020. The group included patients, public, representatives of charities, hospital volunteers, researchers and design experts. The group started with a blank canvas and worked together to decide which evidence-based messages to include in the resources, their format and style, and where and how they would be implemented. The group decided to create one website to host branded resources:

- A positive and informative animation and social media content
- Free online training for healthcare professionals, public and volunteers to improve awareness of the links between pain and mental health
- A library of local support resources

The marketing and design experts facilitated collaborative working to develop clinical (physiotherapist, general practitioner) and patient (retired, volunteer, carer) 'personas' to better understand the intended resource end-users. The group explored in-depth the emotions, thoughts and actions conveyed by the resources through word clouds and brainstorming. This helped the group to create a brand, the central character and provided vision for the style of the resources. Through facilitated discussion with design experts, the group co-produced animation storyboards, the plain language text on the website, training package, animation and local support library, and the final overall brand by choosing logos, colour schemes, fonts and images.
Results: The group chose Support, Progression and Freedom through 'Mind and Movement' as the key words on which to base the resources. Patients and the public suggested that a human character would not represent all people living with chronic pain; so, a bee was chosen to be the central character. It was agreed that the bee personified the key words whilst generating an engaging theme. The group agreed to name the resource package 'BeeFree' with the website slogan 'a support hive for mind and movement'. All resources were based around five evidence-based messages (Get Active, Get Talking, Get Creative, Eat Well and Sleep Well) called 'The Hive Five' and were housed on a new branded website - www.beefree.org.uk BeeFree was successfully launched online via regional NHS Trusts, charity and voluntary groups, First Contact Physiotherapy networks and social media in 2021. Patients and the public championed the resources and facilitated the launch. Challenges for the clinical group members included negotiating time and commitment to the work amidst multiple pandemic-related NHS pressures, and for the public group members there were difficulties adapting to working collaboratively online.



Figure 1.

Conclusion: Co-creating a positive, recognisable brand with patients and the public can facilitate the promotion and impact of evidence-based messages into healthcare. In the pandemic online co-production approaches offered creative adaptations to bring together stakeholders. Utilising design expertise and taking time to build and nurture relationships with patients and the public resulted in valuable and insightful co-production and consequently highly accessible and engaging resources.
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OP0010-PARE **PRELIMINARY FINDINGS OF QUALITATIVE EXPLORATION OF THE EFFECTIVENESS OF AN ONLINE "FATIGUE AND ACTIVITY MANAGEMENT EDUCATION IN WORK" (FAME-W) INTERVENTION FOR INDIVIDUALS WITH INFLAMMATORY ARTHRITIS**

Keywords: Self-management, Work-related issues, Telemedicine

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Background: A Fatigue and Activity Management Education in Work (FAME-W) programme was developed for individuals with inflammatory arthritis to manage fatigue in work (McCormick, 2018). FAME-W was designed as an in-person programme; however, due to COVID-19 pandemic it was modified to be an online group-based self-management intervention.
Objectives: This study tested the effectiveness of an online format of FAME-W for future use by occupational therapist to help individuals with inflammatory arthritis to stay in work.
Methods: Participants were randomly allocated to intervention or control groups. Participants in the intervention group received the online four-week FAME-W and the control group participants received a FAME-W handbook. Participants in the intervention group attended a focus group immediately after the completion of the online FAME-W programme. A qualitative descriptive design was used with semi-structured focus groups. Data were analysed by thematic analysis (Braun and Clark, 2021).
Results: Twenty-six individuals took part in five separate focus groups. The average number of participants per group was 5 individuals with the largest group having 8 and smallest having 3 participants. The majority of participants were female, working full time and had Rheumatoid Arthritis. The four themes emerging from the focus groups were: "content and delivery of the programme" where participants discussed the relevance of the content to their symptoms and the online delivery format of FAME-W. In the second theme, participants discussed "understanding the effects of symptoms on their own and combined" and how symptoms effect mood, work, cognitive and physical abilities. In the third theme, "implementing the knowledge gained from the programme" through goal setting and practicality of the self-management strategies provided were discussed. Final theme "impact of the FAME-W on symptoms and work" including reassurance of normalising symptoms, change in mindset and approach to their condition were discussed.

Table 1.

Themes	Quotes
Content and delivery of the programme	"Each of the four sections were all very relevant" "I am quite happy that it is online because face to face would depend on location if I had the choice"
Understanding the effects of symptoms on their own and combined	"Now I know that I can sleep better when I manage my pain, and I can manage my pain by managing fatigue" "When you have a long-term illness, you don't look at the symptoms individually, you need to break it and look at it individually to know how to manage it"
Implementing the knowledge gained from the programme	"I'm in a different place today than I was four weeks ago. I am doing well now. So, for me the goal setting is excellent" "Helps you implement the knowledge into your regular routine and check in with yourself"
Impact of the FAME-W on symptoms and work	"Just a lightbulb moment to say, great, this is not my fault, because you can blame yourself for all the symptoms"

Conclusion: Preliminary results show that participants found the online FAME-W to be effective, relevant, reassuring, and helpful. These results suggest that work-related self-management skills are essential in assisting participants with symptom management in the workplace. Furthermore, these preliminary results suggest that the online format of FAME-W may be helpful for individuals with inflammatory arthritis to stay in work and it may become a standard part of clinical care for occupational therapists.

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Epigenetics in chronic inflammation

OP0011 EPITRANSCRIPTOME EDITING REPRESENTS AN ADDITIONAL LAYER OF IMMUNE-RELATED EPIGENETIC MEMORY OF MONOCYTES IN HUMAN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Keywords: Systemic lupus erythematosus, Genetics/Epigenetics, Innate immunity

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Background: Monocytes are key effector cells in human systemic lupus erythematosus (SLE). Cytokine production, antigen presentation and initiation/amplification of tissue inflammation[1] represent some of output functions of transcriptional rewiring within the inflammatory milieu of the disease. Epitranscriptome includes all functionally relevant changes to the RNA level (transcriptome), reforming RNA metabolism and fine-tuning gene expression[2].

Objectives: To construct the transcriptional map of monocytes in lupus patients and impose the A-to-I base editing events as co-factor of the disease pathogenesis.

Methods: A cohort of 8 SLE patients (SLEDAI≥8) and 5 age/sex matched healthy volunteers was used for this study. PBMCs were obtained through Ficoll centrifugation and monocytes were isolated with $CD14^+$ magnetic bead selection. Total RNA was extracted and mRNA libraries were generated. Single-end 75-bp mRNA sequencing was performed on Illumina NextSeq 500. Differential expression analysis was performed using edgeR package. Genes with a false discovery rate of ≤0.05 and a fold change of >1.5 were considered statistically significantly deregulated. Significant differentially expressed genes (DEGs) were used for pathway and gene ontology (GO) analysis using g:Profiler webserver[3]. For base editing events, JACUSA2 was utilized for base calling and list refinement was performed by the following criteria: (a) known editing sites based on REDIportal, (b) the number of reads with "G" at the putative editing site is at least 10 and (b) the editing level per sample, defined as 100 n(G)/[n(A)+n(G)], is at least 20%, (c) JACUSA2 call-2 score for differential editing between SLE and healthy was 1.5.

Results: Differential gene expression analysis produced a list of 764 statistically significant genes, 492 of which are upregulated and 272 downregulated. Gene enrichment analysis concluded that DEGs are participating in transcription regulation, signal transduction, regulation of immune processes and apoptosis/cell death. IL-17 signaling pathway and RNA metabolic process are part of the pathogenetic profile of lupus monocytes. Interestingly, *ADARB1*, key regulator of RNA editing, is upregulated (logFC=0.76, pval=0.018). A-to-I editing events found to be significant, contain among others *GDI2* (UTR3 region/signaling mediator), *ARPC2* (Alu region/actin polymerization) and *CERK* (UTR3 region/ inflammation) regulatory regions. A complex network of transcriptomic and epitranscriptomic alterations embeds immune-related genes and affects multiple cellular processes.

Conclusion: Transcriptional machinery and signal transduction molecules exhibit abnormal expression during transcriptional rewiring in monocytes of lupus patients. Our data support RNA editing as an additional player of immune-related epigenetic memory of monocytes, further integrating inflammatory cues and enhancing autoimmune identity of the disease.

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How to treat older people with RMD

OP0012-HPR CENTRAL SENSITIZATION HAS MAJOR IMPACT ON DISEASE ACTIVITY, FUNCTIONAL DISABILITY AND FRAILTY IN PATIENTS WITH RA

Keywords: Patient reported outcomes, Rheumatoid arthritis, Outcome measures

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Background: Central sensitization (CS) assessed with Central sensitization Inventory (CSI) is significantly associated with functional disability and frailty in patients with rheumatoid arthritis (RA). Frailty is common in RA and associated with hospitalization and mortality. Frailty in RA is dynamic and, for some, may be ameliorated through controlling disease activity and functional disability.

Objectives: Our aim was to investigate the prevalence of CS in patients with RA and its association with measures of disease activity, functional disability, and frailty.

Methods: We administered to all the subjects in the study the CS inventory (CSI), a questionnaire that has been used for the diagnosis of CS. Demographic and clinical characteristics were collected as well as measures of disease activity [RAID), functional disability (ROAD) and Kihon Checklist (KCL) screening tool to identify community-dwelling adults vulnerable to frailty potentially at risk of becoming dependent. Patients with fibromyalgia were excluded from the study.

Results: Of the 192 included RA patients, mean CSI score was 36.7 ±15.5 and 36.5% scored >40, which indicates a high probability of CS. Mean CDAI score was 16.8 ± 12.4 and mean RAID 5.0 ± 2.0. A CSI score >40 was significantly associated with higher RAID (mean 5.7 vs. 4.6; F-ratio 12.28; p=0.001), higher

ROAD (mean 4.3 vs. 3.0; F-ratio 17.37; p<0.001) and higher Kihon score (mean 9.1 vs. 5.7; F-ratio 29.88; p<0.001).

Conclusion: CS is strongly related to patient-reported disease activity, functional disability and frailty in patients with RA independently from other patient-and disease-related aspects. CS is an important determinant of functional disability in patients with chronic inflammatory arthritides. Therefore, special attention should be paid to RA patients, in whom the concomitant diagnosis of CS should be routinely ruled out.

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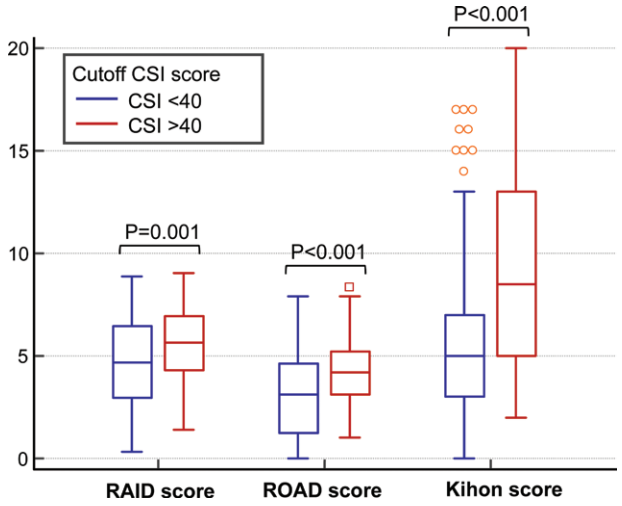


Figure 1. Disease activity (RAID score), functional disability (ROAD score) and frailty (Kihon score) in patient with CSI < 40 (n° 122) and CSI > 40 (n° 70).

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Disclosure of Interests: None Declared.
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Precision medicine in SLE: where are we?

OP0013

APPLYING STANDARD CLASSIFICATION CRITERIA EXCLUDES UP TO A HALF OF ALL PATIENTS FROM CONNECTIVE TISSUE DISEASES (CTD) CLINICAL TRIALS

Keywords: Sjögren syndrome, Systemic sclerosis, Systemic lupus erythematosus

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Background: Classification criteria aim to identify a homogenous population of patients with a high specificity for clinical research.

Objectives: To determine how connective tissue disease (CTD) phase III trials utilise classification criteria within their inclusion and exclusion criteria. We then applied the most commonly used classification criteria to a large cohort of patients with an existing CTD diagnosis to explore which patients would be included and excluded from trials.

Methods: A comprehensive review of all major published phase III trials in CTDs was performed using clinicaltrials.gov (Nov 22). We included trials of biological or DMARD therapy, and excluded open label trials and long-term extensions. Adult patients (May 14 - July 22) were recruited from five rheumatology centres in North West England into the LEAP cohort. Patients were eligible for inclusion if they had ≥1 clinical feature of a CTD and ≥1 antibody within the ANA spectrum. The physician (rheumatologist) diagnosis at time of recruitment was used as the primary classifier of patients. Classification criteria utilised in the majority of clinical trials were systematically applied to this cohort, irrespective of clinical diagnosis.

Results: There were 49 trials in CTDs identified from 1909 records: systemic lupus erythematosus (SLE)=29, systemic sclerosis (SSc)=7, idiopathic inflammatory myopathy (IIM)=7 and primary Sjögren's syndrome (pSS)=6. There were no trials in MCTD or UCTD. The majority of trials (N=47, 95.9%) required patients to meet classification criteria for their respective disease. The ACR-1997 for SLE, 2002 American European Consensus Criteria (AECG) criteria for pSS, ACR criteria for SSc 1980, and Bohan and Peter for IIM were the most commonly employed criteria. The majority of pSS (N=5, 83.3%) and SSc (N=4, 57.1%) trials excluded patients with other overlapping CTDs, whereas only a minority of IIM (N=1, 14.3%) and SLE (N=2, 6.9%) trials mandated this. A further 2 (28.6%) IIM and 2 (6.9%) SLE trials excluded CTD patients with specific overlapping features, e.g. SSc with significant pulmonary hypertension. 15 trials (30.6%) allowed exclusion of significant coexisting diseases at the investigators' discretion and 18 (36.7%) made no reference. 391 patients were recruited to the LEAP cohort (Female: 352 [90.0%], median [IQR] age: 52 [40-59] years, median [IQR] disease duration: 6.1 [2.9-13.2] years). 254 (65.0%) patients met classification criteria for at least one CTD (Table 1). 222 (74.0%) patients with pSS, SLE, SSc or IIM, met the classification criteria for their respective diagnosis. Of these, 26/222 (6.7%) met criteria for >1 CTD. In total, 196/391 (50.1%) would be eligible, and 195/391 (49.9%) ineligible for recruitment to a phase III trial, based upon their physician diagnosis, and trial eligibility criteria. Patients eligible to participate were similar in age (*p= 0.882*), gender (*p=0.601*) and ethnic background (*p= 0.822*) but had longer median disease duration (7.5 vs 5.2 years, *p=0.024*) to those ineligible.

Table 1. The proportion of patients meeting classification criteria utilised in clinical trials, by physician diagnosis

	SLE	pSS	UCTD	SSc	MCTD	IIM	Overall
	N=164	N=77	N=61	N=37	N=30	N=22	N=391
Bohan and Peter for IIM	2 (1.2)	0 (0)	0 (0)	3 (8.1)	2 (6.7)	9 (40.9)	16 (4.1)
ACR/EULAR Systemic sclerosis 2013	1 (0.6)	0 (0)	0 (0)	30 (81.1)	8 (26.7)	4 (18.2)	43 (11.0)
AECG Sjögren's	10 (6.1)	45 (58.4)	0 (0)	0 (0)	1 (3.3)	1 (4.5)	57 (14.6)
ACR SLE 1997	138 (84.1)	14 (18.2)	0 (0)	2 (5.4)	14 (46.7)	5 (22.7)	173 (44.2)

Conclusion: Clinical trial recruitment is challenging, in part due to due to strict eligibility criteria. In an unselected, real-world cohort of CTD patients, up to a half would be excluded due to classification criteria, overlapping features or a lack of trials within their disease. Directly targeting molecular pathology in biomarker driven basket trials could potentially revolutionise drug development by benefitting those with an undifferentiated or overlap condition who would be traditionally excluded from clinical trials.

REFERENCES: NIL.

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Disclosure of Interests: Sarah Dyball: None declared, Mia Rodziewicz: None declared, Anastasia- Vasiliki Madenidou: None declared, John Reynolds: None declared, Ariane Herrick: None declared, Sahena Haque: None declared, Hector Chinoy: None declared, Ellen Bruce: None declared, Ben Parker: None declared, Ian N. Bruce Speakers bureau: GSK, Astra Zeneca, Janssen, Consultant of: GSK, Astra Zeneca, Aurinia, Lilly, Grant/research support from: GSK, Astra Zeneca, Janssen.

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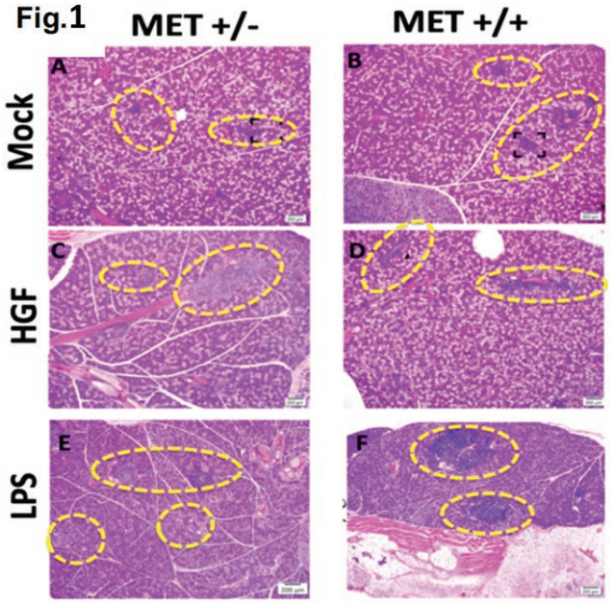
Adaptive immunity (T cells and B cells) in rheumatic diseases

OP0014 SHARED MOLECULAR TARGETS OF APOPTOSIS IN CHRONIC INFLAMMATION AND AUTOIMMUNITY: HOW TO BLOCK AUTOIMMUNE ARTHRITIS

Keywords: Autoantibodies, Animal Models, Cell biology

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Background: Aging is associated with an increased incidence of cancers and autoimmune diseases, which share pathophysiological mechanisms. Understanding these common pathways would make it possible to better define a certain risk linked to the disease or their treatment and to decipher new therapeutic targets in autoimmunity. Using an original individual approach to constitutional genetics at low penetrance, our team identified a constitutional mutation pR988C, c2962C> T of MET gene (tyrosine kinase receptor MET) in a patient with autoimmune diseases and malignant tumors. This mutation results in the constitutive activation of MET receptor and to the expression of an autoimmune phenotype associating a diffuse Sjögren disease with histological synovitis in transgenic MET mice [1]. The MET receptor (hepatocyte growth factor, HGF) participates in the regulation of physiological defensive responses following organs failure and its role has been proposed in several inflammatory diseases. In addition, the MET pathway has been implicated in the modification of the dendritic cells phenotype and the response of T cells with cancerous diseases.
Objectives: The objective of our work is to study the histological and cellular phenomenon of transition between self-reactivity and aggressive auto-immunity. Our new genetic model appears to be a good candidate to study the mechanisms involved in autoimmunity transition. To this purpose, we have three objectives i) to describe the effects of the genetic pressure in our model of MET mutated mice, ii) to induce in vivo inflammation with LPS or HGF in heterozygous/homozygous MET mice to assess the autoimmunity induced by external factors, iii) to study the function of immune cells of mutated MET mice.
Methods: Using heterozygous or homozygous mutated MET mice, we *in vivo* stimulated them for 6 months with LPS or HGF, to add an environmental pressure. Mice were systematically assessed for clinical symptoms, autoantibodies production, histological phenotypes, immune cells phenotyping, bone marrow at euthanasia. We focused on the functional phenotype of bone marrow dendritic cells (BMDC) with assessment of co-stimulatory molecular surface expression, cytokine production, endocytosis, allogeneic reactivity.
Results: We confirmed that heterozygous MET mice develop systemic autoimmune diseases and observed that homozygous mice have a more severe clinical phenotype (Figure 1). Homozygous MET mice have severe inflammatory infiltrates and higher circulating autoantibody levels. We observed an increase in monomacrophagic pro-inflammatory subpopulations in the bone marrow parallel to the MET gene expression, higher with homozygotous mice as compared to heterozygotous and to non-transgenic mice. Stimulation with HGF or LPS increased the inflammatory status, with a maximum peaking in LPS treated MET homozygotous mice. We confirmed that, *in vitro* stimulation of BMDC with HGF induces an intermediate phenotype of maturation dendritic cells whatever the status of transgenic mice. Furthermore, dendritic cells obtained from mice exposed to LPS have an exhausted phenotype, in parallel with the high level of inflammation in tissues. Studying apoptosis phenotype, we observed a shift in cell death pathways that could be the relying mechanism of autoimmune prone phenotype linked to the MET mutation.
Conclusion: The model of transgenic mice appears ideal for studying the transition phenomena of autoreactivity versus autoimmune disease and the functional involvement of dendritic cells. We confirmed the direct involvement of the MET gene in autoimmunity. For the first time, we showed that the change in cell death pathways could be the direct origin of the emergence of autoimmunity. These preliminary results, for which additional experiments are underway, open up physiopathological and therapeutic perspectives.



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Disclosure of Interests: None Declared.
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OP0015 CD38HI CYTOTOXIC CD8 T CELLS ARE EXPANDED FOLLOWING CHECKPOINT BLOCKADE AND CHARACTERIZE THE T CELL INFILTRATE IN CHECKPOINT INHIBITOR-ASSOCIATED ARTHRITIS

Keywords: Synovium, Inflammatory arthritides, Malignancy

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Background: Immune checkpoint inhibitor (ICI) therapies used to treat cancer, such as anti-PD1 antibodies, can induce autoimmune conditions. The T cells responsible for mediating such iatrogenic autoimmunity, their activation profiles and characteristics remain unclear.
Objectives: To investigate the transcriptomic and clonotypic features, activation, and role of infiltrating T cells in patient joints affected by ICI-induced inflammatory arthritis (ICI-arthritis).
Methods: Paired TCR and scRNA-seq was performed on synovial fluid (SF) CD8 T cells from ICI-arthritis (ICI-A) to determine their transcriptomic and clonotypic features. Detailed immunophenotyping was performed on SF mononuclear cells using mass cytometry and flow cytometry to identify significantly altered populations in ICI-A compared to seropositive rheumatoid arthritis (RA) and psoriatic arthritis (PsA). Further, bulk RNA-seq was performed on altered SF CD8 T cell subsets from the three arthritides to investigate differences in activation profiles and immune pathways enriched. *In vitro* cytotoxicity assays were performed by measuring annexin staining in fibroblasts co-cultured with various CD8 subsets from synovial fluid and blood. Mass cytometry was performed on PBMCs from melanoma patients to assess changes before and after checkpoint blockade and bulk TCR-seq of ICI-bound (IgG4+/-) non-naive CD8 T cells was used to analyze TCRs enriched in blood and synovial fluid of ICI-arthritis patients.
Results: Single cell transcriptomic and antigen receptor repertoire analyses highlighted clonal expansion of an activated effector CD8 T cell population in the joints and blood of ICI-arthritis patients (n = 6). These CD8 T cells, identified as $CD38^{hi}CD127^{-}$, were uniquely enriched in ICI-arthritis joints compared to RA and PsA and displayed an elevated interferon signature. *In vitro*, type I interferon induced CD8 T cells to acquire the ICI-associated $CD38^{hi}$ phenotype and boosted cytotoxic function in a novel cytotoxicity assay. In a cohort of patients with advanced melanoma, anti-PD-1 and anti-CTLA-4 therapy dramatically expanded circulating $CD38^{hi}CD127^{-}$ T cells more so than any other T cell

population. CD38^{hi}CD127^{-} T cells were Ki67+ and were frequently bound by the therapeutic anti-PD-1 drug. In ICI-arthritis patients, anti-PD-1 drug-bound CD8 T cells in circulation showed marked clonal overlap with drug-bound CD8 T cells from synovial fluid, but almost no overlap was observed between drug-bound cells in the synovial fluid and non-drug-bound cells in blood (**Figure 1**).
Conclusion: These results suggest that ICI therapy directly targets CD8 T cells in patients with ICI-arthritis to induce a novel autoimmune pathology that is distinct from the prototypical spontaneous autoimmune arthritides.

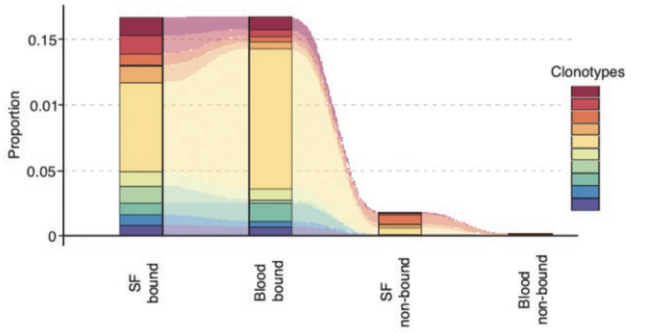


Fig.1: Anti-PD-1 drug-bound CD8 T cells in circulation and synovial fluid are clonally linked in ICI arthritis patients.
CD8 T cells from paired blood and synovial fluid from ICI-arthritis patients on an anti-PD-1 therapy, were sorted into anti-IgG4+ (drug-bound) or anti-IgG4- (non-drug-bound) populations. Alluvial plot representation of one patient showing the 10 most abundant clonotypes in the drug-bound synovial fluid CD8 T cells demonstrating substantial overlap in these large clones between drug-bound cells in synovial fluid and blood, and much less sharing with non-drug-bound cells. Representative plot of 3 patients.

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Disclosure of Interests: None Declared.
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OP0016 ABATACEPT TO SILENCE ANTI-CITRULLINATED PROTEIN ANTIBODY-EXPRESSING B CELLS IN RHEUMATOID ARTHRITIS: THE ASCARA TRIAL

Keywords: Rheumatoid arthritis, Randomized control trial, Biomarkers

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Background: Rheumatoid arthritis (RA) is one of the most prevalent systemic autoimmune diseases. Despite clinically effective drugs, RA remains a chronic disease with frequent disease flares upon drug tapering. Patients harbouring anti-citrullinated protein antibodies (ACPA) most frequently relapse and rarely achieve drug-free remission. We observed that in established RA, ACPA-expressing memory B cells (mBC) are highly activated, proliferate, secrete pro-inflammatory cytokines and differentiate into plasmablasts [1]. This phenotype points to continuous, T helper cell-driven stimulation of the ACPA B cell response and persists in patients in clinical remission induced by conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), suggesting ongoing immunological disease activity (IDA) despite clinically quiescent disease. Persistent IDA may be responsible for disease flares, making immunological remission a potential treatment target required for cure.
Objectives: To test the hypothesis that CTLA4-Ig (abatacept), a biological DMARD that blocks co-stimulatory signals such as those provided by helper T cells to B cells, can impact on IDA, as evidenced by the induction of a silent, non-proliferative phenotype of ACPA-expressing mBC.
Methods: We conducted a single-center, randomized, open-label clinical trial in which patients with newly diagnosed, untreated RA (n=42) were treated with either methotrexate (MTX, n=21) or abatacept/MTX (ABA/MTX) combination therapy (n=21) for 6 months. Frequency and phenotypic characteristics of peripheral blood ACPA-expressing B cells were assessed directly ex-vivo by flow-cytometry at baseline (BL), 3 months (V2) and 6 months (V3). The expression of Ki-67 (primary endpoint), CD80, CD86 and HLA-DR were used to determine the activation state of the B cells in either group, next to B cell lineage and differentiation markers. Tetanus-toxoid (TT) specific B cells served as antigen-specific controls. Clinical disease characteristics as well as serum parameters were assessed in parallel. Differences between treatment groups were statistically analyzed using a mixed effect model with random slope and intercept.

Results: Of patients receiving treatment, n=14 in the ABA/MTX and n=16 in the MTX monotherapy arm harboured ACPA-expressing mBC in the circulation at sufficient frequency for phenotypic analysis. Patients with untreated RA exhibited a highly active ACPA mBC response, in line with previous results [1]. Both MTX and ABA/MTX reduced clinical disease activity at 6 months to a similar extent (p=0.33). The frequency of circulating ACPA-expressing mBC remained unaffected in either group. However, while ACPA-expressing mBC maintained their highly active phenotype in the MTX group, ABA/MTX impacted on the ACPA mBC response by significantly reducing the expression of Ki-67, CD86 and CD80. The expression of HLA-DR did not change upon treatment.

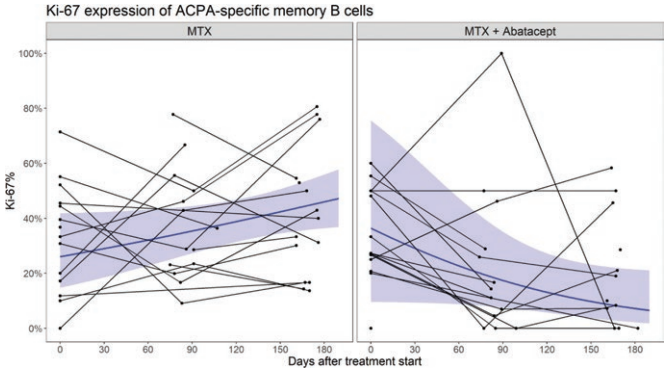


Figure 1.

Conclusion: The ASCARA study provides first evidence that the activation of ACPA-expressing mBC can be therapeutically modulated towards a phenotype compatible with immunological remission. ABA/MTX, but not MTX alone had this modulatory effect, indicating that potentially important immunological drivers of RA disease processes are resistant to MTX-mediated effects. Interestingly, the phenotype induced by ABA/MTX resembles that observed in patients in sustained drug-free remission as well as in individuals with clinically suspect arthralgia that do not convert to RA (long-term non-converters, (1)). Follow-up analysis of the ASCARA study with ABA discontinuation beyond V3 will elucidate the stability of this effect and its relation to clinical disease characteristics.
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Disclosure of Interests: Nienke Blomberg: None declared, Joanneke Kwekkeboom: None declared, Stefan Böhringer: None declared, Thomas Huizinga Speakers bureau: Bristol Myers Squibb, Grant/research support from: Bristol Myers Squibb, Rene Toes Grant/research support from: Bristol Myers Squibb, Hans Ulrich Scherer Speakers bureau: Bristol Myers Squibb, Grant/research support from: Bristol Myers Squibb.
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OP0017 ACTIVE LUPUS NEPHRITIS PATIENTS DISPLAY AN INCREASED PROPORTION OF RECENTLY ACTIVATED NAÏVE DNA-REACTIVE B CELLS

Keywords: Adaptive immunity, Kidneys, Systemic lupus erythematosus

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Background: Altered composition of B cell compartments is known in patients with systemic lupus erythematosus (SLE). However, similar characterisation of the disease-associated autoreactive B cells remains scarce. Elucidating the autoreactive B cell subsets and their association to lupus manifestations may provide tools for monitoring, biomarkers and even identifying possible targets for future therapeutic intervention.
Objectives: To investigate phenotypic characteristics of extrafollicular B cell subsets in a cohort of SLE patients.

Methods: Twelve SLE patients, including nine with positive anti-dsDNA antibodies (75%), and ten healthy controls (HCs) were recruited for this study. Data was represented as median and interquartile range (IQR). To identify DNA-reactive B cells, surrogate peptide (DWEYSVWLSN) that serves as dsDNA mimotope was used, as previously shown (1, 2). The phenotype of peripheral B cell subsets and DNA-reactive B cells was analyzed by spectral flow cytometric analysis. The correlations between different B cell populations and Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) scores, clinical manifestations and laboratory data were assessed.

Results: In SLE patients, median SLEDAI-2K score was 14.5 (4.5-19.5), median age and disease duration were 32 (29-48.5) and 10 (1-13) years, respectively. Eight patients presented with lupus nephritis (LN), with proliferative (class III/IV, n = 2), membranous (class V, n = 1) and mixed histological pattern (class III & V, n = 3 and class IV & V, n = 2). Phenotypic analysis showed an expansion of recently activated, so called activated naïve (aNAV: $CD11c^+CXCR5^-CD21^-CD27^-IgD^+$, p = 0.0005), double negative 2 B cells (DN2: $CD11c^+CXCR5^-CD21^-CD27^-IgD^-$, p = 0.0001) and double negative 3 B cells (DN3: $CD11c^-CXCR5^-CD21^-CD27^-IgD^-$, p = 0.005) in the blood of the total SLE patient group compared to HC, with aNAV B cells frequency being higher in LN patients (Figure 1). DNA-reactive B cells were mostly represented by an aNAV phenotype ($CD11c^+CXCR5^-CD21^-$) which overexpressed CD11c and CD80. Moreover, a significantly increased percentage of such autoreactive B cells was observed in LN patients (median (IQR) 0.13% (0.095-0.160) compared with non-LN patients (median (IQR) 0.056% (0.042-0.070), p = 0.0357). The percentage of aNAV B cells were positively correlated with disease activity measured as SLEDAI-2K index (r = 0.619, p = 0.036). These aNAV B cells also had a positive correlation with DN2 (r = 0.578, p = 0.049) and plasmablasts (r = 0.420, p = 0.041).

Conclusion: Our data show that aNAV B cells are expanded in SLE and display autoreactivity to dsDNA. The association between the frequency of aNAV B cells and disease activity, and with lupus nephritis suggests that these cells may be used as a monitoring biomarker in the disease.

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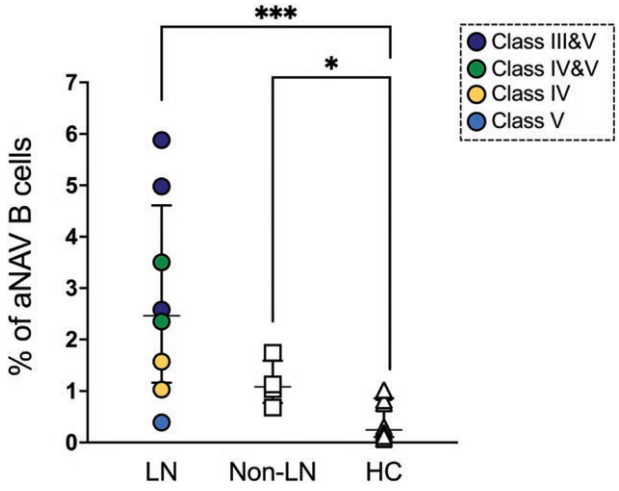


Figure 1. Frequency of aNAV B cells in LN patients with different histological classes with respect to non LN and HC

Disclosure of Interests: None Declared.

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OP0018 **WITHDRAWN**

OP0019 **PREMATURE AGING IN LYMPH NODE STROMAL CELLS OF PATIENTS WITH RHEUMATOID ARTHRITIS PARTY RESTORED BY DASATINIB TREATMENT**

Keywords: Adaptive immunity, Rheumatoid arthritis, Cell biology

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Background: Cellular senescence is a state of proliferation arrest of cells occurring and cleared during normal aging. However, the persistence and accumulation of senescent cells has been implicated in the pathogenesis of age-related diseases like rheumatoid arthritis (RA). Aging is an important risk factor of RA, a chronic autoimmune disease in which loss of immune tolerance and systemic autoimmunity precedes clinical onset of disease. Lymph node stromal cells (LNSCs) are important regulators of peripheral tolerance. Accordingly, accumulating senescent LNSCs may potentially lead to defective peripheral tolerance and the development of systemic autoimmune disease.

Objectives: In this study we investigated the senescence phenotype of LNSCs during health, systemic autoimmunity and RA. Additionally, we examined whether dasatinib treatment could restore their cellular phenotype and function.

Methods: LNSCs were isolated and cultured from inguinal lymph node needle biopsies from autoantibody positive individuals with arthralgia and therefore at risk of developing RA (RA-risk individuals), RA patients and seronegative healthy volunteers. The senescent phenotype and the effect of dasatinib treatment were assessed using quantitative PCR, flow cytometry, microscopy and live-cell analysis.

Results: Cell size, granularity and autofluorescence were significantly higher in RA LNSCs compared with control LNSCs. Stainings indicate more senescence associated β-galactosidase activity, more lipofuscin granules and increased DNA damage in RA-risk and RA LNSCs compared with control LNSCs. Moreover, we found altered gene expression levels of senescence associated genes in LNSCs from RA patients. Functional experiments showed no difference in proliferation and migration capacity between donor groups. Strikingly, the capacity to repair irradiation induced DNA damage was significantly lower in RA-risk and RA LNSCs compared with control LNSCs. Treating LNSCs with dasatinib significantly improved cell size and DNA repair capacity of cultured LNSCs.

Conclusion: We observed premature aging of lymphoid stroma in RA patients and to lesser extent already in individuals at risk of developing RA, which could partly be restored by dasatinib treatment. Premature aging of LNSCs may negatively impact the local niche by inducing inflammation and senescence in nearby cells. However, consequences of prematurely aged lymphoid stroma remain inconclusive providing a rationale for investigating the effect on immune cell responses.

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OP0020 THE CELLULAR METABOLISM OF SLE NK CELLS IS PRIMARILY ALTERED AT THE LEVEL OF MITOCHONDRIAL HOMEOSTASIS

Keywords: Systemic lupus erythematosus, Innate immunity, Cell biology

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Background: Systemic lupus erythematosus (SLE) is a multi-systemic inflammatory disease, of unknown etiology, which involves the development of autoreactive cells and a loss of tolerance to self. Natural Killer (NK) cells represent a group of innate immune cells that play a pivotal role in the interaction between the innate and adaptive immune system. In patients with SLE, NK cells are decreased in the peripheral blood, exhibit reduced cytotoxicity, and impaired cytokine production.(1, 2) To date, few studies have explored the molecular mechanisms underlying NK cell dysfunction in SLE.

Objectives: To characterize the immunometabolic alterations of NK cells from patients with SLE.

Methods: SLE and healthy NK cells were isolated from human PBMCs. Glycolysis and mitochondrial respiration (OXPHOS) were measured using Seahorse real-time metabolic assay. Mitochondrial function (membrane potential, mitochondrial mass), superoxide levels and lysosomes acidification were assessed by flow cytometry. Mitochondrial membrane potential and mass were analyzed by confocal microscopy (CM). Mitochondrial DNA was quantified by qPCR. Mitochondrial structure was examined by transmission electron microscopy (EM). Functional (cytokine production, degranulation) assays were performed in parallel with mitochondrial mass measurement by flow cytometry. Quantitative proteomic analysis was conducted focusing on the expression of proteins involved in mitochondrial homeostasis.

Results: We first examined the cellular metabolism of SLE NK cells in comparison to healthy NK cells. We observed that OXPHOS is significantly increased in SLE NK cells, while glycolysis is similar to healthy controls. Due to this alteration in oxidative phosphorylation, we conducted experiments to examine the mitochondrial fitness of SLE NK cells. We showed that mitochondrial mass is increased, while mitochondrial activity is decreased in SLE NK cells, suggesting an accumulation of dysfunctional mitochondria. SLE NK cell mitochondria displayed increased superoxide levels and elevated lysosomal acidification, compared to healthy NK cells. qPCR analysis showed no significant difference. in mitochondrial DNA between SLE NK cells and healthy controls suggesting that the size of mitochondria is increased but not their number in SLE NK cells. Examination of the mitochondrial structure in SLE NK cells by TEM, showed cristae disorganization. Quantitative proteomic analysis showed that SLE NK cells express high levels of proteins associated with mitochondrial synthesis (mitochondrial import receptor TOM6) and OXPHOS (ATP synthase F(0), NADH deshydrogenase1 C1). In parallel, we observed a reduction in proteins key for mitochondrial clearance such as E3 ubiquitin ligases (RNF181, MARCHF5), as well as lysosomal acidification (Proton-transporting V-Type ATPase), in SLE NK cells.

Conclusion: SLE NK cells exhibit impaired mitochondrial respiration, which is linked to an accumulation of large mitochondria with cristae disorganization. These results suggest an alteration in mitochondrial degradation in SLE NK cells related to dysfunctional mitophagy. Taken together, these data suggest that impaired mitochondrial function and homeostasis represent a major feature of SLE pathogenesis.

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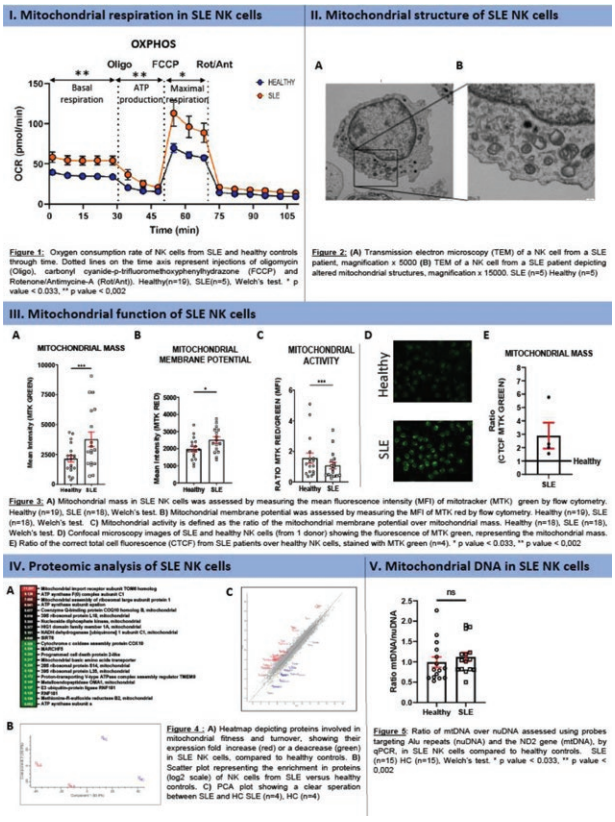


Figure 1: Oxygen consumption rate of NK cells from SLE and healthy controls through time. Dotted lines on the time axis represent injections of oligomycin (Oligo), carbonyl cyanide-p-trifluoromethoxyphenylhydrazone (FCCP) and Rotenone/Antimycine-A (Rot/Ant)). Healthy(n=19), SLE(n=5), Welch's test. * p value < 0.033, ** p value < 0,002

Figure 2: (A) Transmission electron microscopy (TEM) of a NK cell from a SLE patient, magnification x 5000 (B) TEM of a NK cell from a SLE patient depicting altered mitochondrial structures, magnification x 15000. SLE (n=5) Healthy (n=5)

Figure 3: A) Mitochondrial mass in SLE NK cells was assessed by measuring the mean fluorescence intensity (MFI) of mitotracker (MTK) green by flow cytometry. Healthy (n=19), SLE (n=18), Welch's test. B) Mitochondrial membrane potential was assessed by measuring the MFI of MTK red by flow cytometry. Healthy (n=19), SLE (n=18), Welch's test. C) Mitochondrial activity is defined as the ratio of the mitochondrial membrane potential over mitochondrial mass. Healthy (n=18), SLE (n=18), Welch's test. D) Confocal microscopy images of SLE and healthy NK cells (from 1 donor) showing the fluorescence of MTK green, representing the mitochondrial mass. E) Ratio of the correct total cell fluorescence (CTCF) from SLE patients over healthy NK cells, stained with MTK green (n=4). * p value < 0.033, ** p value < 0,002

Figure 4 : A) Heatmap depicting proteins involved in mitochondrial fitness and turnover, showing their expression fold increase (red) or a deacrease (green) in SLE NK cells, compared to healthy controls. B) Scatter plot representing the enrichment in proteins (log2 scale) of NK cells from SLE versus healthy controls. C) PCA plot showing a clear seperation between SLE and HC SLE (n=4), HC (n=4)

Figure 5: Ratio of mtDNA over nuDNA assessed using probes targeting Alu repeats (nuDNA) and the ND2 gene (mtDNA), by qPCR, in SLE NK cells compared to healthy controls. SLE (n=15) HC (n=15), Welch's test. * p value < 0.033, ** p value < 0,002

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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OP0021 STRATIFICATION OF PATIENTS WITH SJÖGREN'S SYNDROME BY JOINT MULTI-MODAL ANALYSIS OF CIRCULATING B CELLS

Keywords: Sjögren syndrome, Adaptive immunity, Autoantibodies

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Background: B cells are important in the pathogenesis of primary Sjögren's syndrome (pSS) with hypergammaglobulinemia, SSA/SSB autoantibodies and an increased risk of B cell lymphoma [1]. Patients with pSS positive for SSA/SSB autoantibodies are more prone to systemic disease manifestations and adverse outcomes. Only few studied have investigated peripheral blood mononuclear cells at single cell resolution and primarily reported differences in the T cell compartment while the B cells were only briefly considered [2,3].

Objectives: We aimed to determine the role of peripheral B cell subtype composition, gene expression and B cell receptor (BCR) usage in patients with pSS stratified for SSA/SSB antibodies.

Methods: Over 230 000 B cells were isolated by negative selection from peripheral blood of 24 pSS patients (n=6 SSA+, n=8 SSA- and n=10 SSA and SSB+ (SSAB)) and four healthy controls. Single cell gene expression and targeted BCR libraries were generated and processed for RNA and VDJ sequencing.

Results: Gene expression-based clustering and cell annotation defined 16 B cell subtypes. We show that pSS patients have a heterogeneous circulating B cell composition, with SSAB patients presenting the highest and lowest proportion of naïve and memory B cells, respectively. Interferon-induced genes were upregulated across all B cell subtypes with the highest levels in the SSAB group. Differential usage of Immunoglobulin Heavy Chain (*IGH*) genes, showed that memory B cells from SSAB patients displayed a higher proportion of *IGHM* expressing cells and cells with unmutated VDJ transcripts, including *IGHV1-69* and *IGHV4-34*, compared to other pSS patient groups and controls, indicating altered somatic hypermutation and class switching processes. Comparison with

previous studies revealed heterogeneous clonotype pools, with little overlap in CDR3 sequences. Joint principal component analysis using scRNA-seq and scVDJ-seq data including B cell subtype composition, IFN-score, *IGH* constant gene usage, *IGHV* usage and VDJ mutation status allowed unsupervised stratification pSS patients that correlated to disease manifestations and antibody status.

Conclusion: Combining single cell gene expression and VDJ sequence data we describe heterogeneity and molecular characteristics in B cells from pSS patients with different autoantibody profiles. Our results may provide clues to intrinsic differences in B cells that affect the phenotype and outcome, and allow stratification of pSS patients at improved resolution.

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Comorbidities in RMD

OP0022

COMPARATIVE EFFECTIVENESS OF BIOLOGIC AND TARGETED SYNTHETIC DMARDS IN PSORIATIC ARTHRITIS ACCORDING TO COMORBIDITIES AT TREATMENT START: A NORDIC COLLABORATIVE STUDY BASED ON ENRICHED CLINICAL REGISTERS

Keywords: Targeted synthetic drugs, Psoriatic arthritis, Comorbidities

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Background: Considering recent safety concerns for JAK-inhibitors (JAKi), clinicians need to make informed treatment decisions balancing expected effectiveness against risk for adverse events (AE). Current guidelines specifically caution that the use of JAKi in patients with pre-existing comorbidities increases risk of AE, but more data are needed regarding expected drug performance in these patients.

Objectives: To compare 1-year treatment retention and 6-month effectiveness in PsA patients with or without comorbidities at treatment start for A) IL17i versus TNFi, and B) JAKi versus TNFi.

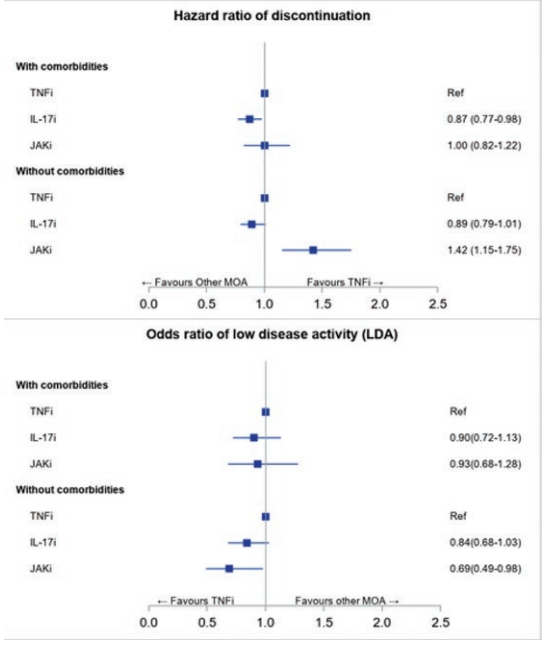
Methods: Patients with PsA starting TNFi, IL17i or JAKi in routine care (years 2012-2020), were included from 5 Nordic rheumatology registries. Due to preferred use of IL17i and JAKi in bDMARD-experienced patients, b/tsDMARD naïve patients were excluded. Baseline patient characteristics were identified, as well as 6- and 12-month follow-up data. Linkage to national patient registries was used to identify comorbidities at treatment start (0-5 years for congestive heart disease, ischemic heart disease, thrombosis, depression/anxiety, chronic obstructive or interstitial pulmonary disease, diabetes, hospitalized infection, and chronic kidney disease; ever for malignancies). Hazard ratios (HR) for discontinuation at 1 year were estimated through Cox regression, while odds ratios (OR) at 6 months for low disease activity (LDA, DAPSA28≤14, LUNDEX adjusted) were estimated using logistic regression (adjusted for baseline variables, see Figure 1 text). Multiple imputation was performed to account for missing baseline data. For sensitivity, analyses limiting the TNFi group to adalimumab-treated patients were performed.

Results: A total of 10 276 treatment starts among 6118 patients with PsA were included. Patients initiating a TNFi were more often men and more often used concomitant csDMARDs, and they were less likely to have any (vs. none) of the above-mentioned comorbidities at treatment start (43%) compared to IL17i (46%) and JAKi (55%). IL17i and JAKi were frequently used in patients having failed >3 b/tsDMARDs (Table 1). Patients with a comorbidity were less likely to discontinue IL17i vs. TNFi (HR=0.87, 95%CI 0.77-0.98), no difference was seen for JAKi vs TNFi. Patients without comorbidities were less likely to discontinue IL17i than TNFi but more likely to discontinue JAKi (HR=1.42, 1.15-1.75) (Figure 1). For LDA, among patients with at least one co-morbidity, there was no difference in the chance of reaching LDA between TNFi (33%), IL17i (30%) and JAKi (29%). Among patients without comorbidities, the odds of reaching LDA were lower for JAKi and for IL17i vs. TNFi (Figure 1). Sensitivity analyses replacing TNFi with adalimumab showed similar estimates for both discontinuation and effectiveness (not shown).

Table 1. Baseline characteristics and outcomes stratified by previous comorbidities and treatment. Numbers are mean (SD) unless otherwise stated

	With comorbidity			Without comorbidity		
	TNFi	IL17i	JAKi	TNFi	IL17i	JAKi
N	3314	929	311	4393	1075	254
Baseline characteristics						
Age, y	52 (13)	53 (12)	55 (12)	49 (12)	50 (12)	52 (12)
Men, %	34	31	27	45	44	37
Number of comorbidities	1.26 (0.5)	1.31 (0.6)	1.32 (0.7)	0	0	0
Line of treatment, %						
2-3	78	53	36	82	59	41
4+	22	47	64	18	41	59
Disease duration, y	9 (9)	10 (9)	12 (10)	9 (9)	10 (9)	11 (9)
csDMARD use, %	59	50	47	61	53	52
C- reactive protein, mg/L	11 (18)	12 (21)	13 (20)	10 (19)	11 (18)	13 (19)
Patient global health, mm	65 (24)	68 (22)	69 (22)	59 (26)	65 (24)	64 (25)
Treatment outcomes, crude						
Retention at 1 y, % (95% CI)	59 (57-60)	63 (60-66)	60 (54-65)	63 (61-64)	66 (63-68)	52 (45-58)
LDA at 6 m	33%	30%	29%	45%	38%	30%

Figure 1
Discontinuation at 1 year with hazard ratio (HR), and effectiveness at 6 months with odds ratio (OR) of low disease activity (LDA).Adjusted for age (and the quadratic term), sex, country, line of treatment, disease duration, csDMARD use, C-reactive protein, patient global score, and treatment start year. MOA=Mode of action



Conclusion: Comorbidities impact treatment outcomes in patients with PsA. The retention and effectiveness of JAKi and TNFi are similar in patients with (but not in patients without) at least one pre-existing comorbidity. Further analyses exploring impact of the number of comorbidities and of specific comorbidities are planned.
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OP0023 UNBIASED HIERARCHICAL CLUSTERING OF CIRCULATING MOLECULAR PROFILES IN RHEUMATOID ARTHRITIS PATIENTS DEFINES PRECISE CV RISK. EFFECTS OF TNFI, IL6RI, AND JAKINIBS

Keywords: Cardiovascular disease, Inflammatory arthritides

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Objectives: This study aimed to: 1) Analyze the circulating inflammatory profile of Rheumatoid Arthritis (RA) patients, in order to recognize distinctive clinical phenotypes associated with CV risk; 2) Evaluate modulatory effects of TNF inhibitors (TNFi), JAK-STAT inhibitors (JAKInibs) and IL-6R inhibitors (IL6Ri); 3) Characterize underlying molecular mechanisms involved in endothelial dysfunction.
Methods: Two hundred and eight RA patients and 45 healthy donors (HD) were recruited. Serum inflammatory profile was assessed by analyzing 27 cytokines/chemokines -Luminex assays-, and biomolecules related to NETosis and oxidative stress -by base-plate kits-. Parallel extensive clinical analyses were performed. TNFi, JAKinibs and IL-6Ri effects were evaluated, respectively, in 45, 20 and 17 RA patients after 6 months. Lastly, mechanistic *in vitro* studies were developed in cultured endothelial cells (ECs) and changes in protein expression were evaluated in cell lysates by proximity extension assay technology, analyzing a panel of 88 proteins related to CV disease.
Results: Unsupervised-clustering identified 3 clusters representing specific molecular profiles. Clinically, even in the presence of similar disease score (DAS28) and positivity for autoantibodies, cluster 1 (C1) identified RA-patients expressing high inflammatory mediators' levels, the highest CV-risk score, and a preponderance of atheroma plaques. Conversely, RA-patients conforming C3 showed the lowest inflammatory profile and the lowest CV-risk score. Lastly, C2 characterized an intermediate phenotype. Comparative analyses with a cohort of 98 RA patients presenting previous CV events, demonstrated that their inflammatory profile mimicked that found in C1, supporting the association of this altered shape with the CV status. *In vivo*, both biological and targeted-synthetic DMARDs' therapy reduced DAS28-score and re-established normal levels of several altered biomolecules, reflecting a key role in the CV-risk control. *In vitro*, RA patients' serum pool from cluster 1 promoted in cultured ECs increased expression of several CV-related proteins, further prevented-albeit in an specific way- by the pre-incubation with TNFi (Etanercept), JAKinibs (Baricitinib) and anti-IL6Ri (Tocilizumab).
CONCLUSION:
1. The systemic inflammatory profile of RA identified patients' subgroups with enhanced CV-risk, not associated with their disease activity status.
2. Both biological and targeted-synthetic DMARDs re-established normal levels of circulating inflammatory biomolecules, reducing the CV-risk in RA.
3. *In vitro* studies revealed that RA-serum inflammatory mediators directly induced endothelial damage which might be prevented by effect of both, biological and targeted-synthetic DMARDs' therapy.

Thus, the analysis of the RA patients circulating molecular profile might contribute to improve the personalized clinical management of these patients and their CV risk.
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Disclosure of Interests: None Declared.
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OP0024 DOES ANTIRHEUMATIC MEDICAL TREATMENT OF RHEUMATOID ARTHRITIS AFFECT SURVIVAL AFTER FIRST ACUTE MYOCARDIAL INFARCTION

Keywords: Comorbidities, Disease-modifying drugs (DMARDs), Cardiovascular disease

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Background: Our previous study showed that rheumatoid arthritis (RA) was associated with higher one-year mortality after first acute myocardial infarction (AMI). Studies have shown increased mortality already within 30 days after cardiovascular events (AMI or stroke) in RA patients compared to non-RA patients.
Objectives: We aimed to study if antirheumatic medical treatment affected survival within 30 days after a first AMI in patients with RA versus non-RA patients.
Methods: Data for 198944 patients with a first AMI were drawn from the Swedish Register of Information and Knowledge about Swedish Heart Intensive Care Admissions for 2006-2017. We used the National Patient Register to identify RA patients with AMI. RA was defined as ≥2 visits to a Rheumatology or Internal Medicine department with a diagnosis of RA, 3725 patients were diagnosed. Antirheumatic medical treatment prescribed during six months prior to the first AMI in RA and non-RA patients was obtained from the National Prescribed Drug Register. The drugs and all their combinations were divided into five groups: Corticosteroids, NSAID (Non-steroidal anti-inflammatory drug), csDMARD (conventional syntethic Disease-modifying antirheumatic drug), anti-TNF (anti Tumor Necrosis Factor), bDMARD (biological Disease-modifying antirheumatic drug). Logistic regression analysis was used to identify variables associated with increased mortality within 30 days after first AMI in each treatment group.
Results: Increased risk of death was found in the corticosteroid group in both non-RA and RA groups (OR 1.61 and 1.66). Treatment with csDMARD and anti-TNF in the RA group were associated with increased survival (OR 0.81 and 0.72), Table 1.
Conclusion: We showed that patients treated with corticosteroids had an increased risk of death after first AMI. RA patients treated with csDMARD and anti-TNF had an increased survival which could imply that high inflammatory activity in RA patients may be part of the explanation of the increased mortality after first AMI.
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Table 1. Odds ratios (OR) for death within 30 days after first AMI from the multivariable logistic regression analyses

	Cortiocosteroids		NSAID		csDMARD		anti-TNF		bDMARD	
	NonRA	RA	NonRA	RA	NonRA	RA	NonRA	RA	NonRA	RA
	n=14908	n=1888	n=22881	n=1227	n=1969	n=1897	n=179	n=312	n=9	n=18
Riskfactor	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR
Age	1.08***	1.06***	1.08***	1.06***	1.08***	1.06***	1.08***	1.06***	1.08***	1.06***
Sex (male)	1.10***	0.98	1.09***	0.97	1.09***	0.98	1.09***	0.97	1.09***	0.97
Medication	1.61***	1.66***	1.07**	1.18	1.24**	0.81*	0.60	0.72*	2.20	-
Smoking	1.32***	1.05	1.33***	1.05	1.33***	1.05	1.33***	1.06	1.33***	1.04
Hypertension	1.02	0.82*	1.04**	0.87	1.04*	0.86	1.04*	0.86	1.04*	0.86
Diabetes	1.60***	1.52***	1.59***	1.48**	1.59***	1.46**	1.59***	1.47**	1.59***	1.48**
Atrial fibrillation	1.58***	1.58**	1.59***	1.66**	1.59***	1.62**	1.59***	1.62**	1.59***	1.63**
CHF	2.48***	2.62***	2.48***	2.65***	2.48***	2.67***	2.48***	2.64***	2.48***	2.64***
STEMI	0.90***	0.80*	0.89***	0.80*	0.89***	0.81*	0.89***	0.81*	0.89***	0.81*
eGFR	0.98***	0.98***	0.98***	0.98***	0.98***	0.98***	0.98***	0.98***	0.98***	0.98***
Anginotensin receptor blockers	0.98	0.85	0.98	0.83*	0.98	0.84*	0.97	0.83*	0.97	0.83*
Statins	0.32***	0.38***	0.31***	0.37***	0.31***	0.37***	0.31***	0.37***	0.31***	0.36***
Aspirin	0.84***	0.75	0.83***	0.74	0.84***	0.75*	0.84***	0.75*	0.84***	0.73*
Betablocker	0.90***	0.80	0.89***	0.79	0.89***	0.78	0.89***	0.78	0.89***	0.78

OR *p<0.05, **p<0.01, ***p<0.001 AMI: Acute Myocardial Infarction; CHF: Congestive heart failure; GFR: estimated glomerular filtration rate (ml/min/1.73m2); STEMI: ST-elevation myocardial infarction

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0025

MORTALITY AND MAJOR ADVERSE CARDIOVASCULAR EVENTS AFTER GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST INITIATION IN PATIENTS WITH AUTOIMMUNE DISEASES AND TYPE 2 DIABETES: A POPULATION-BASED STUDY

Keywords: Cardiovascular disease, Comorbidities, Epidemiology

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Background: Patients with autoimmune rheumatic diseases are at higher risk of cardiovascular complications and premature mortality[1,2], possibly related to chronic inflammation. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are used to treat type 2 diabetes and obesity (two pro-inflammatory states associated with systemic autoimmune diseases) and have anti-inflammatory properties[4], but their clinical effects on cardiovascular outcomes and mortality in patients with autoimmune diseases remain unknown.
Objectives: To assess the risk of all-cause mortality and major adverse cardiovascular events (MACE) in patients with autoimmune diseases and type 2 diabetes initiating GLP-1 RAs versus dipeptidyl peptidase-4 inhibitors (DPP-4is).
Methods: We performed a sequential propensity score (PS) overlap weighted population-based cohort study using administrative health data from British Columbia. Data included diagnostic codes from physician visits and hospitalizations in a universal health care system, all pharmacy-dispensed medications, and vital statistics from January 1, 2010, to December 31, 2021. All patients with an autoimmune disease (i.e., rheumatoid arthritis, psoriatic disease, ankylosing spondylitis, inflammatory bowel disease, or a systemic autoimmune rheumatic disease) and type 2 diabetes who newly initiated a GLP-1 RA or DPP-4i were identified using ICD-9/10 codes. The primary outcome of interest was all-cause mortality. The secondary outcome was MACE (composite of cardiovascular death, myocardial infarction, and ischemic stroke). Herpes zoster reactivation was assessed as a negative control outcome. Cox proportional hazard regression models with PS overlap weighting were used.
Results: We identified 10,855 patients with autoimmune diseases and type 2 diabetes who newly initiated a GLP-1 RA or DPP-4i. All-cause mortality rate was lower among initiators of GLP-1 RAs compared to initiators of DPP-4is, with a weighted hazard ratio (HR) of 0.48 (95% CI, 0.31-0.75) and rate difference (RD) of -9.4 (95% CI, -16.0 to -2.7) per 1000 person-years (Table 1). Rates of MACE were also lower with GLP-1 RA versus DPP-4i exposure (HR 0.66 [CI, 0.50-0.88], RD -10.5 [CI, -20.4 to -0.8]). There was no difference in the risk of herpes zoster reactivation (HR 0.96 [CI, 0.65-1.43).
Conclusion: In patients with autoimmune diseases and type 2 diabetes, GLP-1 RA exposure is associated with a lower risk of all-cause mortality and MACE compared to DPP-4i exposure. Further research is needed to explore potential adiposity-dependent and independent mechanisms through which GLP-1 RAs may reduce cardiovascular risk for patients with autoimmune rheumatic diseases.

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Table 1. All-cause mortality and major adverse cardiovascular events (MACE) among patients with autoimmune diseases and type 2 diabetes initiating GLP-1 receptor agonists or DPP-4 inhibitors, after propensity-score overlap weighting

	GLP-1 receptor agonists (n=3,570)	DPP-4 inhibitors (n=7,285)
All-Cause Mortality		
Event, number	28	446
Mean follow-up (years)	1.46	1.88
IR, per 1000 person-years	8.5	17.9
HR (95% CI)	0.48 (0.31, 0.75)	1.0 (ref)
RD (95% CI)	-9.4 (-16.0, -2.7)	Reference
MACE		
Event, number	83	632
Mean follow-up (years)	1.42	1.81
IR, per 1000 person-years	21.5	32.0
HR (95% CI)	0.66 (0.50, 0.88)	1.0 (ref)
RD (95% CI)	-10.5 (-20.4, -0.8)	Reference

n, number; IR, incidence rate; HR, hazard ratio; RD, risk difference; CI, confidence interval.

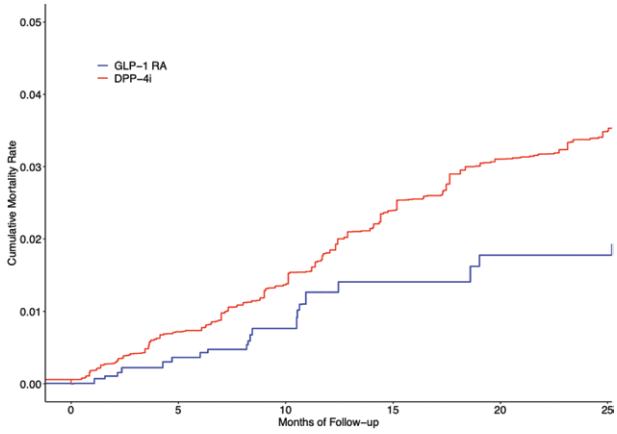


Figure 1. Cumulative all-cause mortality among patients with autoimmune diseases and type 2 diabetes initiating GLP-1 RAs compared with those initiating DPP-4is. GLP-1 RAs, glucagon-like peptide-1 receptor agonists; DDP-4is, dipeptidyl peptidase-4 inhibitors.

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OP0026

INCREASED VASCULAR INFLAMMATION ON PET-CT IN PSORIATIC ARTHRITIS PATIENTS IN COMPARISON WITH HEALTHY CONTROLS

Keywords: Psoriatic arthritis, Cardiovascular disease, Imaging

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Background: Patients with psoriatic arthritis (PsA) have an increased risk of cardiovascular disease, possibly due to a chronic inflammatory state.

Objectives: The main objective of this study was to investigate whether vascular inflammation, measured with 18-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT), is elevated in PsA patients.
Methods: We included 75 PsA patients with active peripheral arthritis (≥2 tender and swollen joints) from an ongoing clinical trial (EudraCT 2017-003900-28), and a retrospective group of 40 controls with melanoma, without distant metastases and not receiving immunotherapy. Both PsA patients and controls were aged 18-75 years. The main outcome measure was aortic vascular inflammation, which was measured using target-to-background-ratios (TBR) on PET/CT. Clinical disease activity in PsA was assessed with joint counts, body surface area and the composite measure Disease Activity index for PsA. Laboratory assessments included the inflammatory parameters C-reactive protein and Erythrocyte Sedimentation Rate. Vascular inflammation was compared between PsA patients and controls in univariate analysis with an unpaired t-test with equal variances. A multiple linear regression analysis was performed to adjust for age, gender, body mass index and mean arterial pressure (MAP). Associations of clinical parameters of disease activity in PsA with vascular inflammation were assessed using Spearman's correlation coefficient.
Results: Vascular inflammation was increased in PsA patients in comparison with controls (mean TBR for entire aorta respectively 1.53±0.15 and 1.42±0.13; P<0.001; Figure 1). This association remained significant after adjusting for gender, age, body mass index and mean arterial pressure (P=0.002). In individuals with PsA, vascular inflammation was not associated with disease-related parameters. There were no significant differences between PsA patients and controls regarding age, mean arterial pressure (MAP) and history of CVD. PsA patients had a higher BMI in comparison with healthy controls (Table 1).
Conclusion: Aortic vascular inflammation was increased in patients with active PsA compared with controls. This evidence suggests that inflammation in PsA is not limited to skin and joints, but also involves the cardiovascular system.

Table 1. Patients' characteristics

Characteristic[a]	PsA (N=75)	Controls (N=40)	p-value
Age, years, median (IQR)	53 (46-59)	52 (42-59)	0.353[b]
Male sex	43 (57.3)	23 (57.5)	1.000[c]
Body Mass Index, kg/m^2, mean±SD	28.4±4.9	25.9±4.0	0.008[d]
Mean Arterial Pressure, mean±SD	102.8±11.6	98.5±13.9	0.090[d]
Current smoking	10 (13.3)	NA	
History of cardiovascular disease:	12 (16.0)	6 (15.0)	1.000[c]
Hypertension	1 (1.3)	2 (5.0)	0.277[c]
Hyperlipidemia	2 (2.7)	0	0.542[c]
Diabetes	2 (2.7)	0	0.542[c]
Myocardial infarction	0	1 (2.5)	0.348[c]
Cerebrovascular event			
PsA duration, months, median (IQR)	10.0 (1.0-123)	NA	
Current csDMARD use	37 (49.3)	NA	
TJC (of 68 joints), median (IQR)	4.0 (6.5-10.0)	NA	
SJC (of 66 joints), median (IQR)	3.0 (5.0-9.0)	NA	
LEI count (1-6), median (IQR)	0 (0.0-1.0)	NA	
BSA, median (IQR)	1.0 (1.0-3.0)	NA	
CRP, median (IQR)	1.0 (4.0-10.3)	NA	
LDL-cholesterol, mean±SD	3.0±0.9	NA	

[a]Values are expressed as n (%) unless stated otherwise.[b]Mann-Whitney test[c]Fisher's exact test[d]Independent Samples t-test*Abbreviations*. CRP = C-reactive protein, BSA = body surface area, LEI = Leeds Enthesitis Index, DMARD = Disease Modifying Anti-Rheumatic Drugs, LEI = Leeds Enthesitis Index, LDL = low-density lipoprotein, NA= not available, PsA = psoriatic arthritis, SD = standard deviation, SJC = swollen joint count, TJC = tender joint count

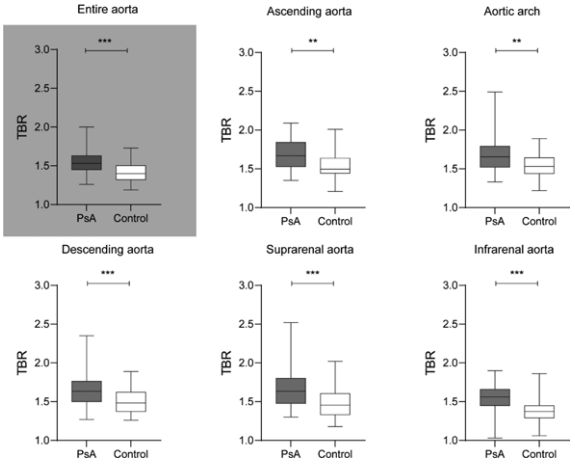


Figure 1. Increased vascular inflammation in the entire aorta and all separate aortic segments, assessed with the TBR, in PsA (n=75) in comparison with controls (n=40).***= P ≤ 0.001, **= P ≤ 0.01. Abbreviations: PsA = psoriatic arthritis.

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Disclosure of Interests: Nienke J. Kleinrensink: None declared, Wouter Foppen Grant/research support from: WF has received research grants from NovoNordisk and Pfizer which were paid to the institution., Negina Seddiqi: None declared, Harald Vonkeman Grant/research support from: Prof. H. Vonkeman reports having received grants, consulting fees or honorarium from AbbVie, Boehringer Ingelheim, Novartis, Pfizer, UCB, Janssen and Galapagos; all outside the submitted work., Karijn Suijkerbuijk Consultant of: Bristol-Myers Squibb, Merck Sharp and Dome, Abbvie, Pierre Fabre, Novartis, Sairopa. All paid to institution and outside the submitted work, Grant/research support from: Novartis, Roche, Merck Sharp and Dome. All paid to institution and outside the submitted work., Mylène Jansen: None declared, Pim de Jong Consultant of: Vifor Pharma and Philips Healthcare, Marloes W. Heijstek: None declared, Julia Spierings: None declared.
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OP0027

APPLICATION OF PREVENTIVE CV RISK STRATEGIES FOR DYSLIPIDEMIA IN RHEUMATOID ARTHRITIS PATIENTS: DATA FROM THE CARDIOVASCULAR OBESITY AND RHEUMATIC DISEASES (CORDIS) STUDY GROUP OF THE ITALIAN SOCIETY OF RHEUMATOLOGY

Keywords: Rheumatoid arthritis, Cardiovascular disease

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Background: Rheumatoid arthritis (RA) patients are at high risk for atherosclerotic cardiovascular disease (CVD) and mortality, and dyslipidemia represents a modifiable CV risk factor significantly contributing to the increased risk. However, dyslipidemia is frequently underestimated and inadequately managed in rheumatologic clinical practice.
Objectives: The aim of the present study was to investigate how dyslipidemia in RA patients is managed in a real-life setting for primary prevention strategies.
Methods: A cross-sectional study of RA patients of the Cardiovascular Obesity and Rheumatic DISeases (CORDIS) cohort [1], with no previous CVD and with available lipid levels was performed. All patients were stratified by the Systematic COronary Risk Evaluation (SCORE) algorithm for CV risk [2] and the application of primary preventive strategy was assessed in accordance with the 2019 European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) guidelines for the management of dyslipidaemias [3].
Results: A total of 1296 RA patients (79% females) with a mean age of 59±12 years were included. According to the SCORE algorithm, 457 (35.5%) patients were at moderate CV risk (1-5%), 455 (35.1%) at high CV risk (5-10%), and 384 (29.6%) at very high (>10%) CV risk. None was at low CV risk (<1%). Eighty percent of the whole cohort was eligible for statin therapy, but only 22.3% was on treatment at inclusion, and 38.2% presented lipid levels on target. Among patients at high and/or very-high SCORE risk, 70% were not on statin treatment even if recommended and 26.7% were not at lipid target even if under statin use. Among patients at moderate SCORE risk, 208 (45.5%) were at lipid target and 31(14.9%) of them were on statin therapy. Globally 565 (43.6%) patients were not on treatment for dyslipidemia even if recommended according to ESC/EAS guidelines (Figure 1). Of note, about 80% of RA patients at high or very high CV risk were on anti-hypertensive and/or antiaggregant treatment.
Conclusion: Statin therapy prescription is suboptimal in RA despite a relevant proportion of patients meeting indications according to LDL thresholds and/or

SCORE algorithm. Preventive CV strategies seem mainly focused on anti-hypertensive or antiplatelet therapy. Rheumatologists should pay close attention to lipid levels and preventive therapeutic interventions to reduce the CV risk of RA patients.

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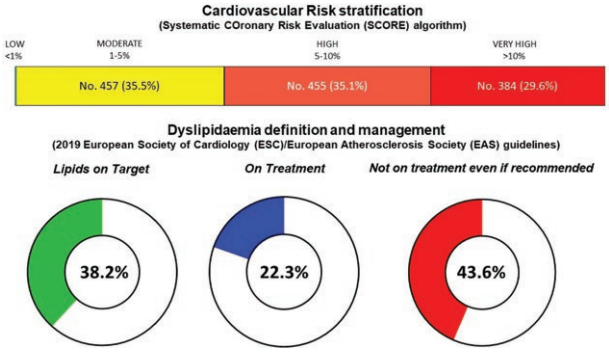


Figure 1.

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Disclosure of Interests: None Declared.
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OP0028

IMMUNOMODULATORY MEDICATIONS AND OUTCOMES OF PATIENTS WITH PRE-EXISTING RHEUMATOID ARTHRITIS USING IMMUNE CHECKPOINT INHIBITORS TO TREAT CANCER

Keywords: Malignancy, Rheumatoid arthritis

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Background: Immune checkpoint inhibitors (ICI) stimulate the immune system to treat cancer but may cause flares of pre-existing immune-mediated diseases such as rheumatoid arthritis (RA). Disease-modifying antirheumatic drugs (DMARDs) used to treat RA may attenuate ICI efficacy. Studies suggest that experiencing flare of a pre-existing disease after ICI may portend a mortality benefit, but no studies have examined whether RA flare after ICI initiation is associated with mortality.
Objectives: To describe the management and outcomes of patients with pre-existing RA after ICI initiation for cancer.
Methods: Retrospective cohort study of patients with pre-existing RA initiating ICI for cancer treatment at Dana-Farber Cancer Institute and Mass General Brigham in Boston, MA, USA (April 2011 to April 2022). Included patients: 1) RA diagnosis code prior to ICI initiation, 2) Met 2010 ACR/EULAR RA criteria by record review. We performed medical record review for data on demographics, cancer, RA disease activity/flares after ICI initiation, DMARDs, ICI disruption, and mortality. We described DMARDs at ICI initiation and for treatment of RA flares. We examined whether RA flare after ICI initiation was associated with mortality using Cox regression in a landmark analysis of those who survived at least 3 months after ICI initiation.
Results: Among 11,901 patients who initiated ICI for cancer treatment, 100 pre-existing RA patients were included (mean age 70.3 years, 63% female, 89% on PD-1 monotherapy, 50% lung cancer). At ICI initiation, 82% had remission/low RA disease activity, 24% were on glucocorticoids (median prednisone dose 10 mg/day), 35% on conventional DMARDs and 10% on biologic DMARDs (**Table 1**). None discontinued glucocorticoids and 3/35 (9%) discontinued DMARDs in anticipation of starting ICI. RA flare after ICI occurred in 46/100 (46%, **Figure 1**) (grade 1 in 16/46 [35%], grade 2 in 25/46 [54%], grade 3 in 5/46 [11%]; 2/46 [4%] required hospitalization for RA flare); 15/46 (33%) that flared had a concomitant immune-related adverse event. RA flares occurred a median of 7 days (IQR 4, 21), usually after the first ICI infusion (ICI cycle IQR 1, 3). RA flares were treated with glucocorticoids (36/46, 78%), often prescribed by oncologists (19/36, 53%), and median initial prednisone dose was 20 mg/day. Treatments of RA flares included DMARDs (19/46, 41%), NSAIDs (12/46, 26%), and intra-articular glucocorticoid injections (5/46, 11%). DMARDs used to treat RA flare included: methotrexate (6/19, 32%), TNF inhibitors (4/19, 21%), hydroxychloroquine (3/19, 16%), sulfasalazine (2/19, 11%), and rituximab (1/19, 5%). ICI was paused or discontinued due to RA flare in 6/46 (13%). Among those who survived at least 3 months, RA flare was not associated with mortality (adjusted hazard ratio 1.24, 95%CI 0.71-2.16).
Conclusion: In this largest study to date of patients with pre-existing RA initiating ICI, 46% flared, often after initial ICI infusion, but were mostly mild and managed with typical therapies. A minority had severe RA flares requiring disruption of ICI, but RA flares were not associated with mortality. These results reiterate that pre-existing RA should not be considered a contraindication to ICI treatment for cancer.

Table 1. Characteristics at index date of immune checkpoint inhibitor initiation.

	Pre-existing RA patients (n=100)
Mean age, years (SD)	70.3 (10.6)
Female sex	63%
PD-1/PD-L1 monotherapy	93%
CTLA-4 and combination	7%
Lung cancer	50%
Melanoma	20%
Genitourinary tract cancer	9%
Median RA duration, years (IQR)	9.4 (4.8, 17.4)
Seropositive	59/83 (71%)
Most recent disease activity	
Remission/low	63/77 (82%)
Moderate/high	14/77 (18%)
Glucocorticoid	24%
Hydroxychloroquine	15%
Sulfasalazine/leflunomide	11%
Methotrexate	9%
Rituximab	5%
IL-6 receptor inhibitors	2%
Tumor necrosis factor inhibitors/tofacitinib	3%

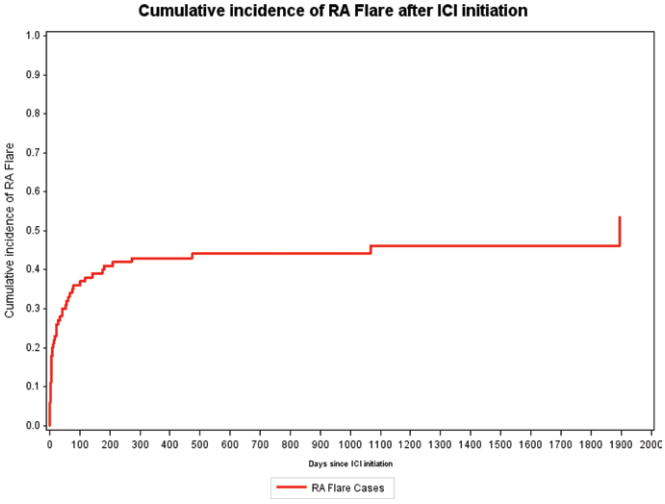


Figure 1. Cumulative incidence curve of rheumatoid arthritis flare after initiation of immune checkpoint inhibitor for cancer treatment among patients with pre-existing rheumatoid arthritis (n=100)

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OP0029

COMPARATIVE SAFETY AND EFFECTIVENESS OF TNF INHIBITORS, IL6R INHIBITORS AND METHOTREXATE FOR THE TREATMENT OF IMMUNE CHECKPOINT INHIBITOR ASSOCIATED ARTHRITIS

Keywords: Malignancy, bDMARD, Inflammatory arthritides

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Background: Immune checkpoint inhibitor associated arthritis (ICI-A) commonly persists for months to years, even after ICI cessation.[1]

Objectives: To compare the safety and effectiveness of biologic and conventional disease modifying anti-rheumatic drugs (DMARDs) for ICI-A.

Methods: Retrospective multicenter observational study. Inclusion: 1) diagnosis of ICI-A and 2) treatment with a tumor necrosis factor inhibitor (TNFi), interleukin-6 receptor inhibitor (IL6Ri) and/or methotrexate (MTX). Exclusion: preexisting autoimmune disease. The primary outcome was time to cancer progression from ICI initiation. Patients whose cancer progressed prior to DMARD initiation were excluded from this analysis. The secondary outcome was time to arthritis control from DMARD initiation, defined as grade 1 arthritis and prednisone ≤10mg/day. Cox proportional hazard models were generated, adjusting for confounders. A sensitivity analysis was performed incorporating a time dependent variable "time from ICI initiation to DMARD initiation."

Results: 147 patients were included, mean (SD) age 60.3 (11.9) years, 66 (45%) females. Sixty percent had received PD1/PDL1 monotherapy, 30% received combination CTLA4/PD1. Eighty percent had stage IV cancer. ICI-A treatment was TNFi in 33 (22%), IL6Ri 42 (29%), MTX 72 (49%) (**Table 1**). A Kaplan-Meier curve showing time to cancer progression by DMARD is shown in **Figure 1**. In an unadjusted Cox model with MTX as the reference, time to cancer progression with a TNFi was HR 2.51 (95% CI 0.91-6.93, p=0.075) and for IL6Ri HR 2.36 (95% CI 0.91-6.12, p=0.078). After adjustment for the time dependent variable, time to cancer progression was significantly shorter for TNFi-treated patients compared to MTX, HR 3.27 (95% CI 1.21-8.84, p=0.019). The result for IL6Ri was HR 2.31 (95% CI 0.98-5.41, p=0.055). Time to arthritis control was significantly faster for TNFi compared to MTX, HR 1.91 (95% CI 1.06-3.45, p=0.032) in an adjusted Cox model. Results for IL6Ri were HR 1.66 (95% CI 0.93-2.97, p=0.089). Results for cancer progression and arthritis control were similar in the subset of patients with melanoma.

Conclusion: Treatment of ICI-A with biologic DMARDs is associated with more rapid arthritis control than with MTX but may be associated with a shorter time to cancer progression. A prospective randomized controlled trial is needed to verify these findings and to identify the optimal approach to managing patients with high grade ICI-A.

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Table 1. Patient characteristics

	Total	TNFi	IL6R	MTX	p-value
N	147 (100%)	33 (22%)	42 (29%)	72 (49%)	
Age, mean (SD)	60.3 (11.9)	56.3 (14.0)	61.5 (12.5)	61.5 (10.1)	0.085
Sex (female)	66 (45%)	13 (39%)	15 (36%)	38 (53%)	0.17
Race (white)	136 (92%)	30 (91%)	40 (95%)	66 (92%)	0.18
Cancer type					0.068
Melanoma	63 (43%)	16 (48%)	21 (50%)	26 (36%)	
Non-small cell lung cancer	15 (10%)	1 (3%)	0 (0%)	14 (19%)	
Renal cell carcinoma	24 (16%)	5 (15%)	12 (29%)	7 (10%)	
Bladder cancer	7 (5%)	1 (3%)	3 (7%)	1 (4%)	
Other	38 (25%)	10 (30%)	6 (14%)	22 (31%)	
Cancer stage					0.34
III	26 (18%)	7 (21%)	6 (14%)	13 (18%)	
IV	118 (80%)	24 (73%)	36 (86%)	58 (81%)	
Checkpoint inhibitor					0.91
PD1/PDL1 monotherapy	101 (69%)	24 (73%)	28 (67%)	49 (68%)	
Combination (CTLA4/PD1)	44 (30%)	9 (27%)	13 (31%)	22 (31%)	
ICI discontinued for arthritis	58 (40%)	12 (36%)	17 (40%)	29 (40%)	0.92
ICI initiation to DMARD start (days), median (IQR)	403 (258,638)	411 (284, 622)	300 (170, 435)	486(258, 675)	0.020
Duration of DMARD treatment, median (IQR)	278 (77, 546)	92 (45, 149)	309 (63, 483)	420 (138, 765)	<0.001
Maximum glucocorticoid dose, mean (SD)	40 (27)	53 (27)	42 (28)	33 (23)	0.002

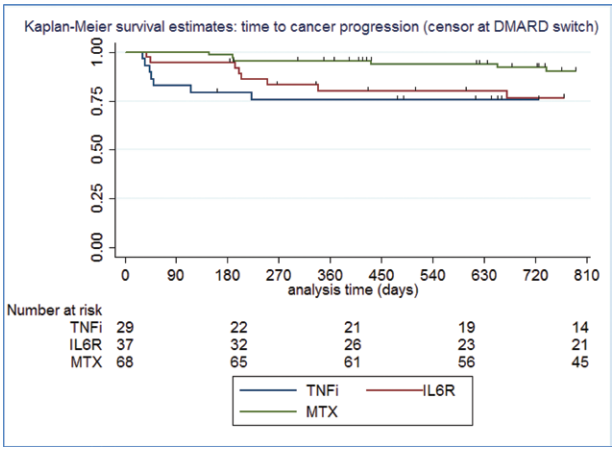


Figure 1. Kaplan-Meier curve showing time to cancer progression from time of immune checkpoint inhibitor initiation

Acknowledgements: NIL.

Disclosure of Interests: Anne Bass: None declared, Noha Abdel-Wahab Speakers bureau: ChemoCentryx, Consultant of: ChemoCentryx, Pankti Reid: None declared, Jeffrey Sparks Consultant of: Bristol Myers Squibb, AbbVie, Amgen, Boehringer Ingelheim, Gilead, Inova Diagnostics, Janssen, Optum, Pfizer, Grant/research support from: Bristol Myers Squibb, cassandra calabrese Speakers bureau: Sanofi, Consultant of: Astazenica, Deanna Jannat-Khah: None declared, Nilasha Ghosh: None declared, Divya Rajesh: None declared, Carlos Aude: None declared, Lydia Gedmintas: None declared, Lindsey MacFarlane: None declared, Senada Arabelovic: None declared, Adewunmi Falohun: None declared, Komal Mushtak: None declared, Farah Al Haj: None declared, Adi Diab: None declared, Ami Shah Grant/research support from: Eicos Sciences, Medpace LLC, Arena Pharmaceuticals, Kadmon Corporation, Clifton Bingham Consultant of: Bristol Myers Squibb,: Abbvie, Janssen, Lilly, Pfizer, Sanofi, Moderna, Grant/research support from: Bristol Myers Squibb, Karmela Kim Chan: None declared, Laura Cappelli Consultant of: Bristol Myers Squibb, Grant/research support from: Bristol Myers Squibb.

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Improving our understanding of RMDs in children and young people

OP0030 DIFFERENTIAL GENE EXPRESSION IN RESPONSE TO TOFACITNIB TREATMENT IN POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

Keywords: bDMARD, -omics, Inflammatory arthritides

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Background: Despite advances in the understanding of juvenile idiopathic arthritis (JIA) pathophysiology, personalized treatments informed by gene transcriptomic profiles remain elusive.
Objectives: To examine the relationship between changes in gene expression and treatment response in patients with JIA treated with tofacitinib.
Methods: Whole blood samples from patients with JIA were collected using Paxgene tubes at baseline (BL) and again at week (wk) 18 of treatment with tofacitinib as part of a clinical trial (NCT02592434) [1]. Patients were classified as treatment responders (TR) if they achieved at least a JIA-American College of Rheumatology score of (JIA-ACR70) or above (N_{BL}=47; N_{WK18}=38); and non-responders (NR) improvement was no more than a JIA-ACR30 response (N_{BL}=20; N_{WK18}=8). Bulk RNA was isolated, subjected to globin/rRNA depletion, and used for generation of cDNA libraries for subsequent sequencing. RNA sequencing via Illumina Nova-seq generated 50 million reads per sample. Gene expression was compared in TR and NR (BL, wk18; change BL to wk18). Kallisto 0.48.0 was used for pseudo-quantification (GRCh38 release 94 index). Differential expression and Gene Ontology (GO) over-representation analyses were performed with dseqr 0.34.0.
Results: Significant differential expression (FDR<0.05) was observed in 10,138 genes between BL and wk18. GO over-representation analysis was performed separately for up- and down-regulated genes with FDR<0.05 and absolute logFC>0.8 (n=231). For genes down-regulated with treatment (BL-wk18), ontologies related to negative regulation of gene expression, type I and type II interferon pathways were significantly over-represented (FDR<0.05), while ontologies for synapse organization and activity were over-represented among up-regulated genes (Figure 1). The latter might reflect the normalization of the immunological synapse leading to improved cytotoxic NK and T cell functions, the impairment of which has been proposed to escalate the production of IFN-γ and other proinflammatory cytokines [2]. There were no significantly differentially expressed genes (FDR < 0.05) between TR vs. NR at BL or wk18. Exploratory GO analysis in NR vs. TR at baseline (FDR<0.13, n=76 genes) suggests up-regulation of genes in ontologies related to the activation of MAP kinase activity.
Conclusion: Tofacitinib treatment in JIA patients leads to widespread changes in whole blood transcriptional profiles. The most significant transcriptional changes observed included the down-regulation of genes associated with type I and type II interferon pathways, and the up-regulation of genes involved in synapse organization and activity. Potential association of MAP-kinase activation in NR at baseline needs to be further explored. MAP-kinase is one of the signalling pathways in inflammatory arthritis that can be targeted by small molecules other than JAK inhibitors. Thus, patients with a predominantly active MAP-kinase pathway could be less likely to respond to tofacitinib. If confirmed, these findings might be useful to personalize JIA treatment in the future.

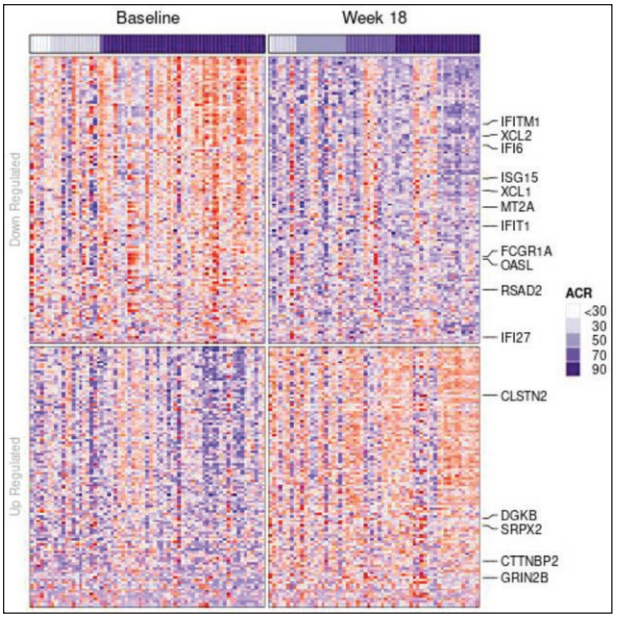


Figure 1. Heatmap showing differentially expressed genes (FDR < 0.05 and |logFC| > 1) at week 18 vs baseline in JIA patients receiving tofacitinib. Annotated genes are from ontologies related to type I and type II interferon activity (down-regulated), as well as from ontologies related to synapse organization (up-regulated).

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OP0031 CHILDREN WITH EXTENDED OLIGOARTICULAR AND POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS HAVE ALTERATIONS IN B AND T FOLLICULAR CELL SUBSETS IN PERIPHERAL BLOOD AND A CYTOKINE PROFILE SUSTAINING B CELL ACTIVATION

Keywords: Adaptive immunity, Cytokines and chemokines

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children. Our group has recently demonstrated that extended oligoarticular and polyarticular JIA mostly evolve to a rheumatoid arthritis (RA)-like phenotype in adulthood. Disturbances in B cells, T follicular helper (Tfh) and T follicular regulatory (Tfr) cell immune responses are associated with RA pathogenesis, but their exact role in JIA development is poorly understood.
Objectives: The main goal of this study was to characterize the frequency and phenotype of B, Tfh and Tfr cells in peripheral blood and the cytokine environment present in circulation in children with with extended oligoarticular JIA (eoJIA) and polyarticular JIA (pJIA) when compared to healthy controls, children with persistent oligoarticular JIA (poJIA) and adult JIA patients.
Methods: Blood samples were collected from 105 JIA patients (children and adults) and 50 age- and gender-matched healthy individuals. Peripheral blood mononuclear

cells were isolated and the frequency and phenotype of B, Tfh and Tfr cells were evaluated by flow cytometry. Serum levels of APRIL, BAFF, IL-1β, IL-2, IL-4, IL-6, IL-10, IL-17A, IL-21, IL-22, IFN-γ, PD-1, PD-L1, sCD40L, CXCL13 and TNF were measured by multiplex bead-based immunoassay and/ or ELISA in all groups included.
Results: The frequency of B, Tfh and Tfr cells was similar between JIA patients and controls. Children with eoJIA and pJIA, but not poJIA, had significantly lower frequencies of plasmablasts, regulatory T cells and higher levels of Th17-like Tfh cells in circulation when compared to controls. Furthermore, APRIL, BAFF, IL-6 and IL-17A serum levels were significantly higher in pediatric eoJIA and pJIA patients when compared to controls. These immunological alterations were not found in adult JIA patients in comparison to controls.
Conclusion: Changes in B and Tfh cell subpopulations, but not in Tfr cells, were found in peripheral blood of children with eoJIA and pJIA when compared to controls. Our results suggest a potential role and/ or activation profile of B and Th17-like Tfh cells in the pathogenesis of eoJIA and pJIA, but not poJIA.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3217

OP0032 MULTI-PARAMETRIC ANALYSIS EVIDENCES TRAFFICKING OF CIRCULATORY CXCR3+CCR6+ CD4+ T CELLS AS A SOURCE OF TH1- AND TH17-MEDIATED INFLAMMATION IN THE ENTHESITIS-RELATED ARTHRITIS (ERA) SYNOVIUM

Keywords: Synovium, Adaptive immunity, Cytokines and chemokines

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Background: Enthesitis-related arthritis (ERA), a common subtype of juvenile idiopathic arthritis (JIA), carries a poor prognosis. Current therapies, including anti-TNF agents, are limited in controlling disease. There is a poor understanding of ERA immunopathogenesis, especially the ontogeny of synovial pro-inflammatory T cells, which limits prognostic and therapeutic targets.
Objectives: We aim to compare, using a high-dimensional approach, the synovial and circulatory immune architectures of active ERA patients. Through this, we aim to identify CD4+ T cell subsets strongly associated with synovial inflammation in active ERA patients. We also aim to assess differentiation, cytokine production and regulation of candidate CD4+ T cell subsets.
Methods: We interrogated, using mass cytometry, CD45+ immune cells from the synovium (n=10) and circulation (n=30) of ERA patients with active joint inflammation, as well from blood of healthy paediatric controls (n=30). FlowSOM clustering were performed with functionally and phenotypically important immune markers. Multiple Mann-Whitney U tests with Holm-Sidak correction identified significantly different cluster frequencies. Significant clusters were validated with supervised gating on FlowJo. To evaluate CXCR3+CCR6+ CD4+ T cells, we sorted CXCR3+CCR6+ Teffs and Tregs from active ERA SFMCs and PBMCs with FACS. We then conducted in-vitro maturation and Treg suppression assays on sorted cells.
Results: The ERA synovium has a deranged immune architecture that is distinct from the circulation, and this involves innate and adaptive immune perturbations. The ERA synovium is enriched with CD4+ T effector memory cells (median: 68.45% vs. 23.85% of total CD4+ T cells; p<0.0001), of which IFNγ+ (44.85% vs. 4.08% of total CD4+ T cells; p<0.0001), IL-17A+ (2.62% vs. 0.66% of total CD4+ T cells; p<0.0001) and TNFa+ (10.64% vs. 2.52% of total CD4+ T cells; p<0.0001) producers dominate. The ERA synovium is also enriched with CXCR3+CCR6+ CD4+ T cells, which are present at lower numbers and activation status in the ERA circulation (6.64% vs. 2.00% of total CD4+ T cells; p<0.0001). Under in-vitro TCR stimulation, synovial CXCR3+CCR6+ CD4+ Teffs mature into IFNγ, IL-17A, and dual IFNγ-IL-17A producers. Synovial CXCR3+CCR6+ CD4+ Tregs are bona fide Tregs that suppress their Teff counterparts. However, CXCR3+CCR6+ CD4+ Tregs are not proportionately expanded relative to CXCR3+CCR6+ CD4+ Teffs in the ERA synovium.
Conclusion: In ERA, the immune architecture of the inflamed synovium is profoundly perturbed, whereby Th1 and Th17 cells are the main CD4+ T cell drivers of disease. CXCR3+CCR6+ CD4+ Teffs are possible precursors of Th1- and Th17-mediated synovial inflammation, and may be inadequately regulated during disease. The results provide mechanistic support for therapeutic targeting of the Th1 and Th17 pathways, as well as CXCR3 and CCR6 signalling to curb T cell-mediated inflammation.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3011

OP0033 ANALYSIS OF B CELL SUBSETS AND B CELL CYTOKINES IN PEDIATRIC SJOGREN'S SYNDROME

Keywords: Sjögren syndrome, Cell biology, Adaptive immunity

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Background: Pediatric Sjögren's syndrome (pSS) is a rare disorder that is often diagnosed late due to the lack of validated diagnostic criteria and validated biomarkers. The pathogenesis is largely unknown, but there is evidence of involvement of both the innate and adaptive branch of the immune system. Immunological overactivity is central in the pathogenesis of pSS. Several studies showed the presence of B cells abnormalities in patients with SS with an expansion of naïve B cells and a decrease in the frequency of memory B cells.
Objectives: We set out to investigate the distribution of B cell subsets and B cell cytokines in patients with pSS at disease onset and at follow up visits.
Methods: A monocentric retrospective cohort study was conducted on 23 patients with pSS enrolled at the department of Rheumatology of Bambino Gesù Children's Hospital. Serum levels of CXCL13 and BAFF were analyzed by ELISA. B cell phenotype was assessed on peripheral blood mononuclear cells (PBMCs) by flow cytometry. Systemic disease activity was evaluated by ESSDAI (EULAR Sjogren's syndrome disease activity index) and Clinical-ESSDAI score (Clin-ESSDAI), according to 2020 EULAR recommendations; active disease was defined by ClinESSDAI ≥1 and remission by ClinESSDAI=0. As controls we selected age-matched people with no diagnosis of pSS or any other systemic autoimmune disease.
Results: Serum levels of CXCL13 and BAFF were significantly higher in patients with pSS than the control group (p<0.05) (Figure 1A). We correlated levels of biomarkers with clinical and laboratory parameters: we observed a positive correlation between hypergammaglobulinemia and BAFF (rho=+0,80). Analysis of B-cell subsets at disease onset revealed the expansion of a population of atypical memory B cells (p=0,00049) and a reduction in IgM memory B cells (p=0,0034) compared to the control group (Figure 1B). We then compared the distribution of B cell subpopulations at disease onset (pre) with samples obtained at follow-up (post) for each patient no significant differences were observed (Figure 1B). We also investigated the distribution of Tfh cells in patients with pSS and we observed a significant expansion of CXCR5$^-$PD1^{hi} T_{fh} (Figure 1B).
Conclusion: Patients with pSS showed high levels of CXCL13 and BAFF at disease onset. Alteration in B cell subsets are present in patients with pSS compared to controls, with an expansion of atypical memory B cells and T_{fh}. The B cell abnormalities are not affected by treatment. Our data confirm an hyperactivation of the humoral immune system in patients with pSS and provide evidence for their development as biomarkers and to develop new therapeutic strategies aimed at controlling B cell hyperactivation in pediatric patients with SS.

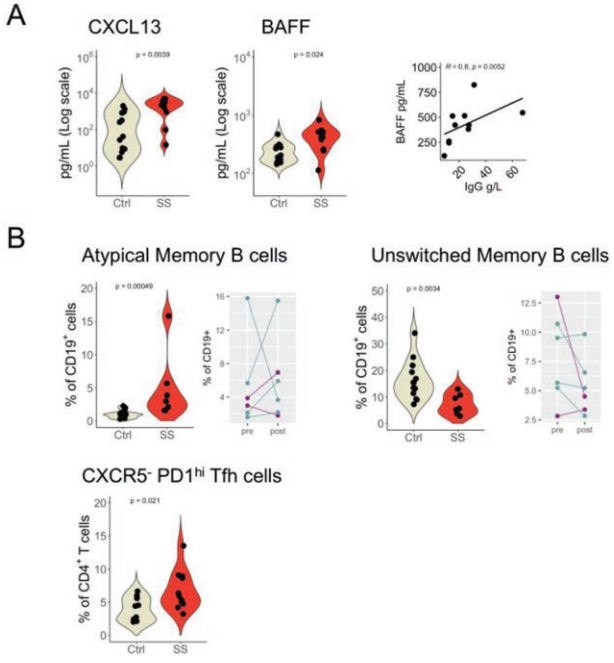


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.

Disclosure of Interests: None Declared.
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OP0034

A NOVEL SERUM CALPROTECTIN (MRP8/14) PARTICLE ENHANCED IMMUNO-TURBIDIMETRIC ASSAY (SCAL TURBO) HELPS TO DIFFERENTIATE SJIA FROM OTHER DISEASES IN ROUTINE CLINICAL LABORATORY SETTINGS

Keywords: Innate immunity, Diagnostic Tests, Biomarkers

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Background: Differential diagnosis in children with signs of unprovoked inflammation can be challenging. In particular, differentiating systemic-onset juvenile idiopathic arthritis (SJIA) from other diagnoses is difficult in individuals presenting with fever of unknown origin. We have recently validated myeloid-related protein 8/14 (MRP8/14, S100A8/A9, calprotectin) serum analyses as a helpful tool supporting the diagnosis of SJIA. The results could be confirmed with a commercial ELISA. However, further optimization of the analytical technology will be important to enable large-scale use in routine laboratory settings.
Objectives: To evaluate the accuracy in identifying children with SJIA, the performance of an immunoturbidimetric assay for measurements of serum-calprotectin (BÜHLMANN sCAL turbo) on an automated laboratory instrument was tested in serum samples of children with various conditions.
Methods: Samples from 650 children were available with diagnoses SJIA (n=99), non-systemic JIA (n=169), infections (n=51), other inflammatory diseases (n=161), and acute lymphatic leukemia (ALL, n=147). In addition, samples from 23 healthy controls were included. The patients with systemic inflammatory diseases were collected at Muenster University as reported before.[1] Patients with non-systemic JIA were from the Nordic JIA cohort as previously described in detail.[2] The ALL cohort included consecutive cases from Aalborg and Aarhus University Hospitals.[3] The BÜHLMANN sCAL turbo test is a particle enhanced immuno-turbidimetric assay (PETIA) and was compared to the established MRP8/14 ELISA from BÜHLMANN (EK-MRP8/14). The sCAL PETIA has a range of 230-15,000 ng/mL (extended range up to 225,000 ng/ml by dilution of 1:15) in sample volumes of only 2-3 µl and was implemented into the automated laboratory setting at the central clinical laboratory of the University Hospital Muenster as a rapid test available on demand.
Results: The sCAL turbo assay showed an excellent correlation to the MRP8/14 ELISA used in the previous validation studies (r=0.99, p<0.001). It could reliably differentiate SJIA from all other diagnoses with significant accuracy (cut-off at 9,100 ng/ml, sensitivity 93%, specificity 87%, ROC area under curve 0.961, p<0.001). Results are shown in Table 1 and Figure 1.

Table 1. Accuracy (ROC analyses) of sCAL turbo measurements in differentiating groups of patients

	SJIA vs all groups	*SJIA vs infections*	*SJIA vs ALL*	*SJIA vs others*
AUC (95%CI)	0.961 (0.943-0.978)	0.908 (0.862-0.953)	0.992 (0.985-0.999)	0.958 (0.934-0.981)
Cut-Off (ng/ml)	9,100	10,500	9,100	9,100
Sensitivity (%)	93	82	99	93
Specificity (%)	87	84	87	86

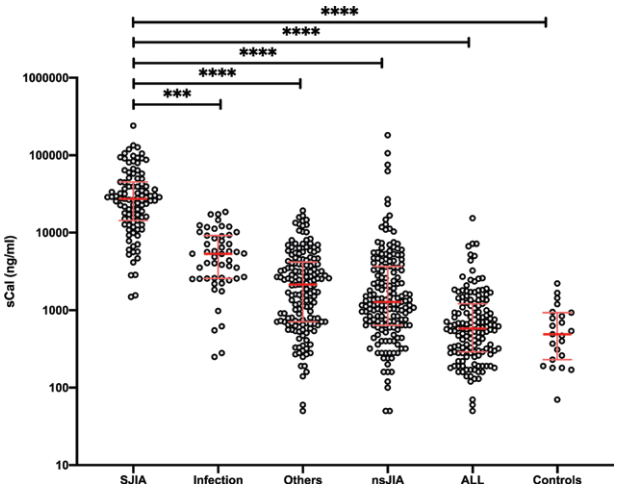


Figure 1. Results of sCAL turbo measurements in different groups of patients (red line showing median, error bars showing interquartile range; *** p<0.001, **** p<0.0001)

Conclusion: MRP8/14 (S100A8/A9, calprotectin) serum analyses have been validated as a helpful tool supporting the diagnosis of SJIA in children with prolonged fever or inflammatory disease. Here we show that an immunoturbidimetric assay for detection of serum-calprotectin on an automated laboratory instrument can be implemented in clinical laboratory settings to facilitate its use as a diagnostic routine test in clinical practice.

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OP0035

THE USE OF CHILDHOOD LLDAS: FIRST RESULTS IN A REAL-LIFE LONGITUDINAL CHILDHOOD LUPUS COHORT SHOW GOOD FEASIBILITY BUT DIFFICULT ATTAINMENT

Keywords: Treat to target, Systemic lupus erythematosus

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Background: Almost half of childhood-onset SLE (cSLE) patients show damage within 5 years after disease onset, which is partially disease- and partially

drug-related [1]. Therefore, the challenge in (c)SLE is not only to lower disease activity, but also to minimalize glucocorticoid toxicity. Treat-to-target (T2T) has been a new type of approach to improve long-term patient outcomes by adapting treatment regimens until the target is met. For T2T, the concept of Lupus-Low-Disease-Activity-State (LLDAS) as a target in SLE has been defined which contains a SLE disease activity index (SLEDAI) ≤ 4 and a maximum prednisolone use of 7.5mg/day [2]. This adult LLDAS (aLLDAS) has been shown to be a feasible target in cSLE patients and attainment leads to lowering risk for severe flare and cumulative damage [3]. Another cSLE cohort study demonstrated that all patients were able to reach aLLDAS (median 186 days) and 72.5% remained in aLLDAS >50% of time [4]. Recently, an international cSLE T2T Task Force has adapted the LLDAS definition specifically for cSLE patients (cLLDAS) by Delphi surveys and consensus meetings, with an addition of a calculated prednisolone dose per body weight in maximum dose of 0.15 mg/kg/day and an absolute maximum of 7,5 mg/day (Smith et al., submitted).

Objectives: The first objective was to investigate if the time to reach first aLLDAS and cLLDAS differs in cSLE. The second objective was to observe if cSLE patients maintain in cLLDAS for 50% of follow-up time (cLLDAS-50).

Methods: Data from a prospective longitudinal cSLE cohort were used, with patient/parent consent. Patients were classified as cSLE by SLICC 2012 criteria with a disease onset < 18 years old. Definitions were: aLLDAS according to Franklyn (2), disease activity score by SLEDAI-2K, cLLDAS by cLSE T2T Task Force (Smith et al. submitted) and damage according to SLICC Damage Index. cLLDAS-50 was defined as attainment of cLLDAS in more than 50% of follow-up. Binary regression analysis was used for testing co-variates for attaining cLLDAS-50 with significance for p<0.05.

Results: 43 cSLE patients were studied, with a median age of symptom onset at 13.6 years, median age at diagnosis of 14.6 years and median follow-up of 4.6 years (range 1-13 years). Mean number of visits was 10.9 per patient. Mean SLEDAI at diagnosis was 15.4 (SD 10.4, range 2-43). Use of MMF was in 62.8%, AZA in 37.2%, and use of HCQ in 100% of patients. 41.9% of patients used a biologic (rituximab or belimumab) at any time point. Each patient reached aLLDAS and cLLDAS at least once during follow-up. Mean time to reach first aLLDAS/cLLDAS was 8.8 months and 9.7 months respectively. Only 58.1% (25/43) of patients were able to maintain cLLDAS-50. The use of biologic(s) had a inversely correlation on reaching cLLDAS-50 (p=0.005), but time to start biologic(s) was not taken into account. Shorter time to cLLDAS was correlated with attaining cLLDAS-50 (p=0.025). SLEDAI at diagnosis, renal/neurological disease and compliance problems were not correlated with attaining cLLDAS-50.

Conclusion: In a longitudinal cSLE cohort, reaching cLLDAS occurred later than aLLDAS, emphasizing the need for an adapted LLDAS definition for cSLE. This study shows that reaching cLLDAS in cSLE is feasible, but attaining cLLDAS-50 is difficult. Earlier starting of glucocorticoid-sparing drugs (such as biologics) seems necessary in a severe subgroup not retaining, or not reaching, cLLDAS.

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OP0036

FREQUENCY AND FACTORS ASSOCIATED WITH DIAGNOSTIC DELAY IN EUROPEAN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: A STUDY ON 960 PATIENTS FROM THE JIR COHORT

Keywords: Innate immunity, Genetics/Epigenetics, Epidemiology

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Background: Familial Mediterranean fever (FMF) is the most common autoinflammatory disease worldwide. It affects mainly population from Mediterranean origin and is associated with *MEFV* exon 10 mutations. FMF is characterized by short and recurrent attacks of fever, abdominal or thoracic pain that lasts less than three days [1]. Several studies reported that FMF diagnosis may be missed or delayed even in countries with a high prevalence of the disease such Turkey and Israel but real causes explaining diagnostic delay in FMF are not totally elucidated.

Objectives: Our aim was to study a large cohort of European FMF patients to identify the frequency and associated factors of diagnosis delay.

Methods: Clinical data were extracted from the Juvenile Inflammatory Rheumatism (JIR)- cohort. All FMF patients fulfilled Livneh Criteria and had a sequencing of *MEFV* exon 10 available [2]. We defined FMF-diagnostic delay (d-FMF) as a duration between the onset of the symptoms and FMF diagnosis of more than 10 years.

Results: We enrolled 960 FMF patients; delayed diagnosis (d-FMF) was noted in 20% of patients (n=200) whereas 80% of other patients (FMF) (n=760) had the diagnosis made within the 10 years from the onset of symptoms. d-FMF patients were significantly older than other FMF with a median age of 46.4 years old versus 15.5 (p < 0.0001). Concerning women, the percentage of d-FMF was higher than other FMF patients (56% versus 47%, p=0.03). Regarding the clinical presentation during FMF attacks, the difference was not statistically significant on abdominal pain, musculoskeletal symptoms and chest pain. Only, erysipelas-like erythema was more frequently observed among d-FMF patients (33% versus 22%, p=0.0003). The percentage of patients with one or two pathogenic *MEFV* mutation was not different between d-FMF and other FMF patients. AA amyloidosis was significantly more frequent in d-FMF than FMF (10 % versus 2.6 %, p< 0.0001). As well, d-FMF patients received significantly more biotherapy compared to other FMF (18% versus 3.8%, p<0.0001).

Conclusion: Twenty percent of FMF patients were misdiagnosed before being officially diagnosed as FMF with significantly more women; this could be linked to the differential diagnosis of abdominal attacks with period pains, as frequently reported be women patients. Another clinical feature is erysipelas-like erythema which seems not be known as a pathognomonic symptom of FMF by all practitioners; this finding was previously reported in Israel and Turkey were the disease is however highly prevalent [4,5]. In conclusion, FMF delay is still significantly high nowadays. To our knowledge, our study is the first cohort study to investigate diagnostic wandering and the factors associated with long diagnostic wandering in a large European cohort. Education and better communication on this disease to patients and practitioners could be fruitful to improve FMF earlier diagnosis.

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OP0037

ADHERENCE TO URATE-LOWERING THERAPY AFFECTS THE RISK OF CARDIOVASCULAR EVENTS IN PATIENTS WITH GOUT

Keywords: Cardiovascular disease, Real-world evidence, Gout

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Background: The benefit of urate-lowering therapy (ULT) on cardiovascular diseases is still controversial. One confounding factor of its association is the adherence to ULT. The impact of adherence to ULT on major adverse cardiovascular events (MACE) has not yet been characterized.
Objectives: We aimed to investigate the patterns of adherence to ULT and their long-term effects on the risk of MACE in patients with gout.
Methods: Using the Korean national health insurance database, we identified 48,600 patients with gout who were 40 years-old or older and started ULT (allopurinol or febuxostat) in 2013-2014. Patient groups were determined based on ULT adherence at 1 and 3 years after its initiation. Non-adherence was defined by the ratio (<80%) of the proportion days covered during the reference period. Patients were divided into 4 groups: persistently adherent (n=11,087), first adherent/later non-adherent (n=4,492), first non-adherent/later adherent (n=5,486), and persistently non-adherent (n=27,535). The primary outcome was the occurrence of MACE (a composite of acute myocardial infarction, revascularization, or acute ischemic stroke) identified in the claims database. The hazard ratio (HR) derived by Cox proportional hazards models was calculated adjusting for age, sex, and comorbidities.
Results: The median follow-up period was 5.2 (interquartile range, 4.6-5.6) years. The persistently non-adherent group had a significantly higher risk of MACE than the persistently adherent group (adjusted HR, 1.14 [95% CI, 1.05-1.24]). The first non-adherent/later adherent group had a significantly lower risk of MACE than the persistently non-adherent group (adjusted HR, 0.85 [95% CI, 0.76-0.96]). The risk of MACE was comparable between the persistently adherent group and the first adherent/later non-adherent group (adjusted HR, 1.03 [95% CI, 0.91-1.17]).
Conclusion: Sustained non-adherent to ULT significantly increases the risk of MACE in patients with gout. Regained adherence to ULT was associated with a lower risk of MACE compared with sustained non-adherence.
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Table 1. Risk for major adverse cardiovascular events (MACE) according to the adherence status of urate lowering therapy

Outcomes	IR per 1000 person-years	Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
MACE					
Persistently adherence	17.5 (16.4, 18.6)	1 (reference)		1 (reference)	
First adherent/later non-adherent	16.2 (14.6, 17.9)	0.926 (0.820, 1.047)	0.220	0.955 (0.845, 1.080)	0.467
First non-adherent/later adherent	14.7 (13.3, 16.2)	0.844 (0.750, 0.949)	**0.005**	0.966 (0.858, 1.086)	0.560
Persistently non-adherence	12.6 (12.0, 13.2)	0.725 (0.669, 0.785)	**<0.001**	1.140 (1.048, 1.240)	**0.002**
Acute myocardial infarction					
Persistently adherence	4.5 (4.0, 5.1)	1 (reference)		1 (reference)	
First adherent/later non-adherent	3.7 (3.0, 4.6)	0.829 (0.648, 1.062)	0.138	0.858 (0.670, 1.099)	0.226
First non-adherent/later adherent	3.6 (3.0, 4.4)	0.813 (0.645, 1.025)	0.080	0.928 (0.736, 1.170)	0.527
Persistently non-adherence	3.3 (3.0, 3.6)	0.746 (0.640, 0.870)	**<0.001**	1.167 (0.990, 1.376)	0.065
Revascularization					
Persistently adherence	9.2 (8.4, 10.0)	1 (reference)		1 (reference)	
First adherent/later non-adherent	8.9 (7.8, 10.3)	0.960 (0.795,1.160)	0.675	1.023 (0.847, 1.236)	0.812
First non-adherent/later adherent	8.4 (7.4, 9.6)	0.722 (0.595,0.877)	**0.001**	0.806 (0.663, 0.978)	**0.029**
Persistently non-adherence	6.5 (6.1, 6.9)	0.747 (0.661,0.846)	**<0.001**	1.111 (0.974, 1.267)	0.117
Acute ischemic stroke					
Persistently adherence	7.0 (6.3, 7.7)	1 (reference)		1 (reference)	
First adherent/later non-adherent	6.7 (5.7, 7.9)	0.972 (0.825, 1.145)	0.732	0.988 (0.838, 1.165)	0.888
First non-adherent/later adherent	5.0 (4.3, 5.9)	0.919 (0.786, 1.074)	0.287	1.061 (0.907, 1.240)	0.460
Persistently non-adherence	5.2 (4.8, 5.6)	0.709 (0.635, 0.790)	**<0.001**	1.136 (1.012, 1.274)	**0.030**

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Disclosure of Interests: None Declared.
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From hearts to lungs: comobidities in RA

OP0038

THE RISK OF ACUTE CORONARY SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ATTAINED REMISSION WITH METHOTREXATE OR A TUMOR NECROSIS FACTOR INHIBITOR.

Keywords: Real-world evidence, bDMARD, Rheumatoid arthritis

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Background: Patients with rheumatoid arthritis (RA) are at higher risk for cardiovascular disease including acute coronary syndromes (ACS) than the general population. Systemic inflammation may mediate some of this increased risk. Treatment with disease modifying anti-rheumatic drugs (DMARDs) may induce remission and thereby lower any increase in ACS risk related to RA inflammation, but the size of this risk reduction vs. rates in the general population, and whether there are, in addition, DMARD-specific beneficial effects on ACS risk, remain unknown.
Objectives: To compare the incidence rates of ACS in patients with RA who attain remission while treated with a tumor necrosis factor inhibitor (TNFi) vs. methotrexate (MTX), and to anchor these incidence rates to those in the general population.
Methods: We defined and pooled treatment cohorts of patients with RA from clinical rheumatology registers in Norway and Sweden who started MTX or a TNFi between January 01, 2012 and December 31, 2021. To be eligible, patients had to start MTX or TNFi while not being in remission (swollen joint count (SJC) >1 or c-reactive protein (CRP) >10 mg/dL or erythrocyte sedimentation rate (ESR) >20), and had to attain remission in a time window of 90 to 548 days after treatment start. They were followed up for one year from the first date at which remission was recorded until any ACS (as assessed through register linkages) or a censoring event (first of: death from other cause than ACS, emigration, treatment discontinuation (+90 days), a new DMARD treatment start, first non-remission date, end of the study). Patients had to be free from a history of ACS in the 5 years before start of follow-up. One patient could contribute several treatment episodes. We compared the incidence rates of ACS between the two DMARD cohorts using Cox regression analyses with robust standard errors and different adjustments: 1. Country; 2. Country, age, sex, calendar year; 3. Country, age, sex, calendar year, RA disease duration, use of oral corticosteroids, comorbidities (hyperlipidemia, hypertension, diabetes), smoking. The main disease activity (DA) metric for defining remission was DAS28 (DAS28-ESR ≤2.6 or DAS28-CRP ≤2.4). Other metrics were used in sensitivity analyses, including SJC=0, CRP≤10 mg/dL, and patient global health assessment (PGA) ≤14. For each of the Swedish RA patients, general population controls were matched on age and sex and similarly followed-up for ACS.
Results: 14,488 treatment courses with MTX and 13,056 with TNFi were included (25,283 from Sweden and 1786 from Norway). DAS28 remission in the allowed time-window was achieved in 5867 (40%) for MTX and 4147 (32%) for TNFi. At start of follow-up, and compared to the TNFi cohort, the MTX cohort included more male patients (35% vs. 27%), was older (mean age 64 years vs. 58), had a lower disease duration (1.3 years vs. 7.5), was more often treated with steroids (62% vs. 43%), and had more often recorded comorbidities. 70% of the patients in the TNFi cohort were treated with concomitant MTX. During the one-year follow-up (7570 person-years) 15 ACS events were recorded in the MTX cohort and 12 in the TNFi cohort, corresponding to crude incidence rates of 3.4 (95% confidence interval (CI) 2.0-5.6) and 3.8 (95% CI 2.2-6.7) per 1000 person-years. Comparing these incidence rates, the fully adjusted Cox regression analysis (model 3) provided a HR (95% CI) of 1.19 (0.48-2.93) for TNFi vs. MTX. Using other DA metrics provided similar and statistically non-significant estimates (Figure 1). In the matched general population subjects (Sweden only), we observed 128 events. The comparison of the treated (MTX or TNFi) patients in remission to the general population provided a HR (95% CI) of 1.08 (0.70-1.64), adjusted for age, sex and calendar year.
Conclusion: Patients with RA who reach remission on MTX have a similar ACS risk as those reaching remission on TNFi. The incidence rates of ACS in patients in remission were comparable to the incidence rate in the general population.

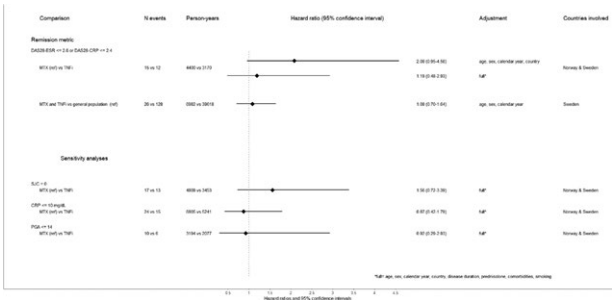


Figure 1. Cox regression analyses results.

REFERENCES: NIL.
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OP0039

TOWARDS UNDERSTANDING THE FAVORABLE EFFECT OF INCREASED BMI ON RADIOGRAPHIC PROGRESSION: A LARGE MRI-STUDY IN AN EARLY ARTHRITIS INCEPTION COHORT

Keywords: Rheumatoid arthritis, Imaging, Comorbidities

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Background: Obesity is considered a risk factor for RA-development. Paradoxically, in RA obesity is associated with less severe radiographic progression. A previous MRI-study suggested that obesity associated with less osteitis and synovitis.
Objectives: To increase our understanding of the favorable association between obesity and radiographic progression, we performed a large MRI-study and aimed to 1) validate the association between BMI and MRI-detected osteitis/synovitis, 2) study whether this is a subgroup-effect in ACPA-positive/-negative RA or a general effect in early arthritides (also in 'non-RA diagnoses') and 3) study whether increased BMI associates with MRI-detected erosive progression, since MRI-detected erosive progression may follow osteitis but precedes radiographic progression.
Methods: We studied 1,029 patients (454 RA, 575 other arthritides), consecutively included in the Leiden Early Arthritis Clinic. At baseline, clinical parameters(including BMI) were measured and patients underwent hand-and-foot MRI that were RAMRIS-scored. 149 RA-patients underwent follow-up MRIs. Associations between baseline BMI and MRI-detected osteitis/synovitis, and baseline BMI and MRI-detected erosive progression were assessed using linear-regression and Poisson mixed-models.
Results: In RA, higher BMI associated with less osteitis(β=0.95; 95%CI=0.93-0.97) but not with synovitis, validating the previously found association with osteitis. The association of BMI with less osteitis was present in ACPA-positive RA(β=0.93; 95%CI=0.91-0.96), ACPA-negative RA(β=0.96; 95%CI=0.94-0.98) and other arthritides(β=0.98; 95%CI=0.96-0.996). During 2-years follow-up overweight and obese RA-patients had less MRI-detected erosive progression than normal-weight RA-patients(IRR=0.989, p-value=0.02 and IRR=0.989, p-value=0.03 respectively). This indicates that the MRI-detected erosive progression was 0.989 times lower per month or 23% lower over 2 years (IRR for one month 0.989, thus 0.989^24=0.77 over 2 years), in both overweight and obese patients, compared to normal weight patients (Figure 1A). Comparable results were found in both ACPA-positive and negative RA (Figure 1B and 1C).
Conclusion: High BMI associated with less osteitis at disease-onset; this was present in all early arthritis patients and not confined to ACPA-positive RA. Moreover, overweight/obesity in RA associated with less severe MRI-detected erosive progression over time. These findings substantiate the previously reported observation of less severe radiographic progression in obese RA-patients and bring us a step forward in unraveling the contradictory association between high BMI and less erosive disease, which is essential in a time where overweight and obesity keep increasing.

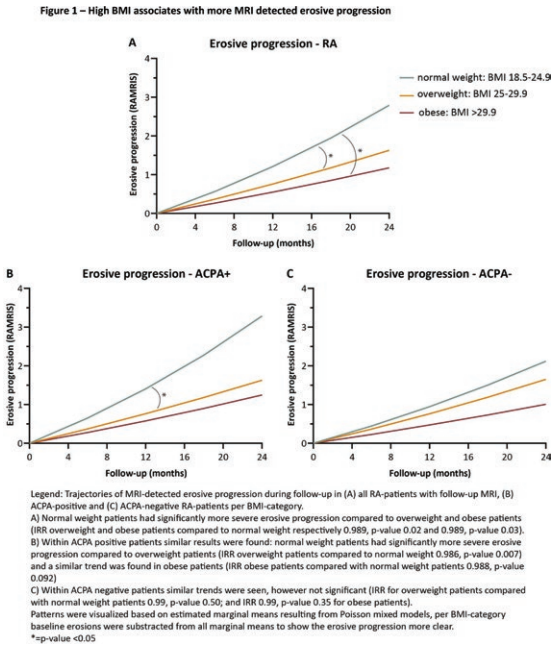


Figure 1. High BMI associates with more MRI detected erosive progression

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OP0040

CHANGES IN BODY WEIGHT AND BODY COMPOSITION IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AGED 65+ TREATED WITH 2-YEAR LOW-DOSE ADD-ON PREDNISOLONE IN THE RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED GLORIA TRIAL

Keywords: Sarcopenia, Rheumatoid arthritis, Randomized control trial

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Background: Weight gain is one of the most feared patient-reported adverse event of glucocorticoids, however the effect of low-dose prednisolone on body weight and composition in RA still has to be unraveled.
Objectives: Current study is a substudy of the GLORIA trial.[1] We report changes in body weight of the whole study population, and relate these to changes in disease activity, and changes in body composition in a subgroup of patients.
Methods: The GLORIA trial, a pragmatic, placebo-controlled, double-blind, randomised controlled trial investigated the balance of benefit and harm of 2 years of prednisolone 5 mg/day added to standard care in 451 patients with active RA aged 65+.[1] In current study 449 patients were included, and body weight and disease activity score of 28 joints (DAS28) were measured at baseline and after 3, 6, 12, 18 and 24 months. In 57 patients body composition was assessed at baseline and after 2 years with dual-energy X-ray absorptiometry. Data were analysed with longitudinal mixed models, and log-ratio analysis to evaluate the mutual changes in body composition, given as the proportions total lean mass, total fat mass, and total bone mass.
Results: Body weight changed by mean (95% CI) 0.9 (0.3;1.6) kg on prednisolone after 2 years, versus –0.4 (–1.1;0.2) kg on placebo, with a difference between treatment groups of 1.3 (0.5;2.2) kg (p<0.01). In multivariable regression analysis, the effect of AUC DAS28 0–2 years was not significantly associated with weight change (p=0.18). The change in body composition after 2 years was different in

prednisolone compared to placebo patients (log-ratio analysis, p=0.02; Table 1). Prednisolone patients showed small but favorable changes in body composition, i.e. lean mass increases exceeding fat mass increases, with trends in differences for total lean mass and lean mass index, and even significant differences for appendicular lean mass (p=0.02), and its corresponding index (p<0.01). No differences in change were seen in total fat mass, nor in fat distribution over the body, i.e. trunk, extremities and head (log-ratio analysis, p=0.93).

Conclusion: Patients with active RA aged 65+ treated with prednisolone 5 mg/day for 2 years gained about 1 kg in weight, compared to non-significant weight loss on placebo. This weight gain is a direct effect of the glucocorticoid treatment, and not significantly dependent of decrease in disease activity. The small increase in weight is mostly (appendicular) lean mass, rather than increase or redistribution of fat mass traditionally associated with glucocorticoid treatment.

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Table 1. Changes in body composition components after 2 years of prednisolone (5 mg/day) or placebo.

	Prednisolone (n=28)		Placebo (n=27)			
	baseline	2-year change	baseline	2-year change	Difference in change	p-value
Body weight (kg)	77.4 (13.3)	0.9(–0.5;2.3)	79.0(12.2)	–0.7(–2.2;0.7)	1.6(–0.4;3.6)	0.12
Body composition						0.02*
Total fat mass (kg)	28.8(8.6)	0.3(–0.7;1.2)	29.4(7.0)	–0.4(–1.4;0.6)	0.7(–0.7;2.1)	
Total lean mass (kg)	46.4(9.0)	0.7(–0.1;1.4)	47.3(10.3)	–0.3(–1.1;0.5)	1.0(–0.1;2.1)	
Total bone mass (kg)	2.2 (0.5)	–0.008 (–0.05;0.03)	2.3 (0.5)	0.03 (–0.008;0.07)	0.04 (–0.02;0.1)	
Body composition in detail						
Fat mass ratio trunk/ appendicular	1.06(0.30)	–0.01(–0.04;0.02)	1.09(0.23)	–0.02(–0.05;0.02)	0.00(–0.04;0.05)	0.85
Lean mass appendicular (kg)	18.5(4.1)	0.4(0.0;0.8)	19.4(5.0)	–0.3(–0.8;0.2)	0.7(0.1;1.4)	0.02
LMI (kg/m^2)	15.8(2.1)	0.3(0.0;0.5)	16.8(2.7)	–0.1(–0.4;0.2)	0.4(0.0;0.7)	0.05
ALMI (kg/m^2)	6.3(1.0)	0.2(0.0;0.3)	6.9(1.4)	–0.1(–0.3;0.0)	0.3(0.1;0.5)	<0.01

Data are presented as mean (SD) or mean (95% CI), unless otherwise specified; LMI=Lean Mass Index; ALMI=Appendicular Lean Mass Index;*overall test (log-ratio analysis).

Acknowledgements: We thank all patients and trial collaborators – listed in previous published main manuscript of the GLORIA trial – for their participation in the trial.21 We thank the nuclear medicine department of the Maasstad hospital, Medical Center Leeuwarden and Groene Hart hospital (all in the Netherlands) for performing the bodyscans.

Disclosure of Interests: None Declared.

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OP0041

LIFETIME MULTIMORBIDITY PROGRESSION IN RHEUMATOID ARTHRITIS: A MULTISTATE MODELLING ANALYSIS OF 20 YEAR DATA FROM THE NORFOLK ARTHRITIS REGISTER

Keywords: Comorbidities, Patient reported outcomes, Rheumatoid arthritis

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Background: The relationship between multiple long term conditions (MLTC) and rheumatoid arthritis (RA) is well known; however the trajectory of accumulation of MLTC and the factors that influence the rate of progression of MLTC following the onset of RA are yet to be fully established. The Norfolk Arthritis Register (NOAR) is a cohort study established in 1989 to record incident cases of early inflammatory arthritis, and is unique in its long follow-up period of up to 20 years. Here we examine the pattern of MLTC progression in the cohort, and apply a multistate model to examine the factors that influence MLTC progression.

Objectives:

- Describe the patten of MLTC progression among newly diagnosed cases with RA over the disease course.
- Develop and apply a multistate model to examine the rate of accumulation of MLTC among people with RA following disease onset.
- Examine predictors that influence the rate of MLTC at different timepoints in the disease course.

Methods: The Norfolk Arthritis Register (NOAR) is an inception cohort of early inflammatory arthritis established in 1989, with over 4500 cases of new onset inflammatory arthritis. Cases were recruited in primary care or from hospital clinics, and inclusion criteria were age >16 years with 2 swollen joints lasting ≥4 weeks. The analysis focused on 13 self-reported chronic diseases involving multiple organ systems ascertained at each follow up point over an interval of 20 years. A multistate model was constructed to examine the accumulation of the number of MLTCs over time ('states') since the onset of disease. Death was included as a separate state. Demographic data at baseline and follow up was included in the model. The multistate model was implemented in the R package *msm,* which provides longitudinal information on the transfer rates from the lower to higher levels of MLTC-M and to death. Multivariate multiple imputation (nburn=1000, 5 datasets) was used to impute missing values using R packages *mice* and *jomo*.

Results: The analysis is based on 4674 patients observed 2 to 15 times; this provided 33,356 records in total. The number of comorbidities increases over time from onset of RA, rho=0.299 (p-value < 2.2e-16). This increase was more pronounced than the increase by age, rho=0.159 (p-value < 2.2e-16), suggesting that inflammation drives number of comorbidities more than age. There were 269 unique combinations of MLTC. The most frequent single morbidities were hypertension, depression and lung disease, with frequencies 0.325, 0.320, and 0.167, respectively (0.812 total probability). The multistate model (Figure 1) considered six defined MLTC states corresponding to total number of MLTC conditions: ranging from State-1 representing RA alone to State-6 representing death. The best fitting model proved to be an additive model including the 5 predictors of gender, age of onset, BMI, smoking status and logDMARDs. Males had significantly higher hazards of accumulation of MLTCs and mortality risk. The total number of MLTCs alone were not associated with the hazard of death. Being overweight significantly increases hazards of progression from State-2 to State-3, and 3 to 4, but also did not affect hazards of death. Ex and non-smokers had significantly lower hazards of accumulation of MLTCs and death, and the number of DMARDs reduced disease progression from State-2 to State-3, and 3 to 4, but did not affect mortality.

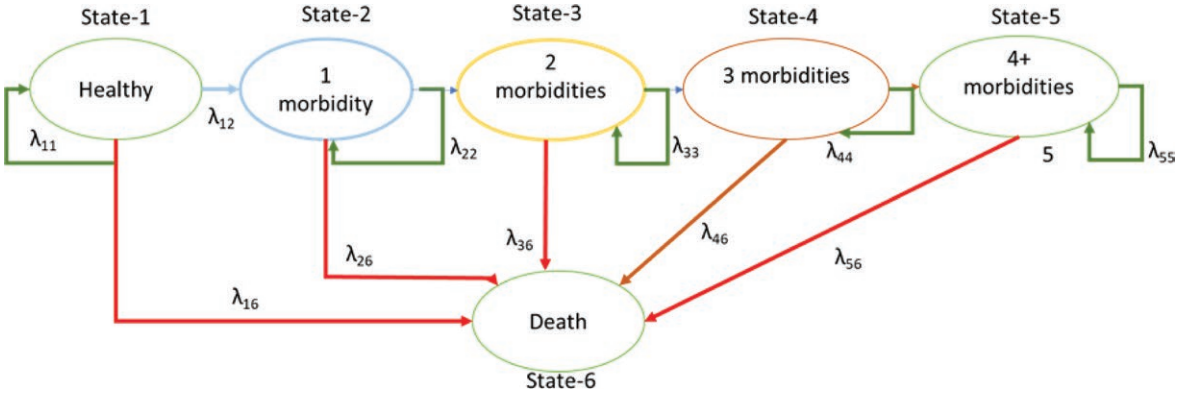


Figure 1. State transitions (arrows) and transition rates (λ) between 6 states in NOAR

Conclusion: This study provides a comprehensive long-term picture of the rate and pattern of accumulation of multimorbidity in RA over the disease course. MLTC involved most patients with RA over time. Smoking, obesity and the use of disease modifying drugs were all found to influence the rate of MLTC accumulation across a range of organ systems. The data suggest that sustained control of inflammation in RA, both through drug interventions and lifestyle management is an important part of limiting the risk of MLTC development throughout the disease course.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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OP0042 VACCINATION RATE, ADVERSE REACTIONS, AND REASONS FOR NONVACCINATION OF COVID-19 VACCINE IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A JAPANESE REAL-WORLD CLINICAL PRACTICE

Keywords: Rheumatoid arthritis, COVID, Vaccination/Immunization

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Background: The first coronavirus infection was confirmed in Wuhan City, People's Republic of China, in December 2019. On January 30, 2020, the World Health Organization declared the novel coronavirus disease a public health emergency of international concern. On March 11, 2020, World Health Organization announced that the new coronavirus infection can be regarded as a pandemic because of the global spread of the infection. The world's first authorization for a coronavirus disease 2019 vaccine (CV) in the UK was in December 2020. The first authorization for a CV in Japan was in February 2021. A maximum of five times of vaccination had been performed in Japanese people until January 2023. Patients with rheumatoid arthritis (RA) are generally immunocompromised because of the drugs used for RA treatment. Patients with RA are recommended to receive a CV in the 2021 update of the EULAR recommendations for the management of rheumatic and musculoskeletal diseases in the context of SARS-CoV-2 [1]. However, some patients with RA rejected CV for various reasons or reports of adverse reactions (ARs) in clinical practice. Real-world clinical information on CV is necessary for better relationships between patients with RA and their physicians.

Objectives: This retrospective study aimed to determine the vaccination rate, ARs, and reasons for nonvaccination of CV in patients with RA in clinical practice.

Methods: The vaccination rate, ARs, and reasons for nonvaccination of CV in patients with RA on clinical records of our institute were investigated up to the third vaccination. Patients were divided into three age groups: 0–64 years old (YG), 65–74 years old (OG), and >75 years old (VOG). The association between age groups and vaccination rates was also investigated. The Cochran–Armitage test was used for statistical analysis.

Results: Regarding patient background (n = 610), the mean age was 67.8 years (YG, n = 207; OG, n = 196; VOG, n = 207; female, 75.1%; mean RA duration, 14.1 years). The vaccination rate among all patients was 8.4% for nonvaccination; 91.6% for the first dose; 91.3%, second dose; and 86.6%, third dose. A significant decrease over time was observed ($p < 0.01$). Nonvaccination was observed in 13.0%, 9.2%, and 2.9% of those in YG, OG, and VOG, respectively. A higher rate of nonvaccination was observed in the YG ($p < 0.01$). The results of the analysis by age group were 87.0%/90.8%/97.1% (first dose), 87.0%/90.3%/96.6% (second dose), and 77.8%/86.7%/95.2% (third dose) among the YG/OG/VOG, respectively (Figure 1). No statistically significant decrease in the vaccination rate was found over time in OG ($p = 0.19$) and VOG ($p = 0.30$) but not in VOG ($p = 0.01$). ARs occurred in 8.2%, 14.5%, and 16.1% of the patients receiving the first, second, and third doses, respectively. Among the reasons for nonvaccination, 35 (68.6%) patients were concerned about ARs to CV and 6 (11.8%) thought that CV was unnecessary.

Conclusion: CV rate in our cohort was higher than that of whole nation in Japan (81.4% for the first dose, 80.4% for the second dose, 67.8% for the third dose). CV rate has been declining steadily in patients with RA, with a stronger trend in younger age groups. Fear of ARs was the most frequent reason for nonvaccination.

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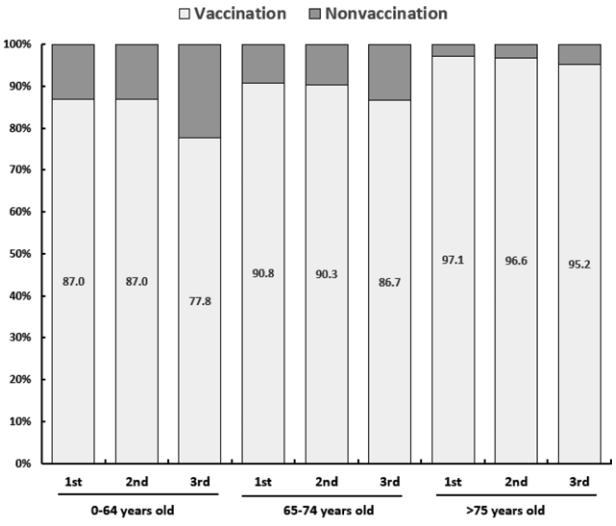


Figure. Vaccination rate in three age groups

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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OP0043 IMPACT OF CARDIOVASCULAR COMORBIDITIES ON EFFICACY OF TOFACITINIB VS TNFI IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Cardiovascular disease, Comorbidities

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Background: Patients (pts) with rheumatoid arthritis (RA) and a history of atherosclerotic cardiovascular (CV) disease (HxASCVD) have a higher risk of major adverse CV events (MACE) with tofacitinib vs tumour necrosis factor inhibitors (TNFi), whereas risk difference is not detected in pts with no HxASCVD.[1]

Objectives: To further explore the benefit/risk profile of tofacitinib by assessing efficacy in pts with RA with and without HxASCVD.

Methods: ORAL Surveillance (NCT02092467) was an open-label, post-authorisation safety study that included pts with active RA despite methotrexate treatment, aged ≥50 years and with ≥1 additional CV risk factor.[2] Pts were randomised 1:1:1 to receive tofacitinib 5 or 10 mg twice daily (BID) or TNFi. In this post hoc analysis, pts were categorised by HxASCVD; for pts with no HxASCVD, 10-year risk of ASCVD was determined using the pooled cohort equations calculator[3] with a 1.5x multiplier applied per EULAR guidelines.[4] Odds ratios (ORs) were presented to compare tofacitinib vs TNFi in achieving remission (Clinical Disease Activity Index [CDAI] ≤2.8) or low disease activity (LDA; CDAI ≤10) at Month 6. ORs and adjusted rates of remission and LDA were obtained from a Generalised Estimating Equation repeated measures model, including baseline (BL) value, visit, treatment, treatment × visit and disease duration.

Results: Of 4362 pts, 640 had a HxASCVD, and 3722 had no HxASCVD, of which 3672 had BL CV scores calculated. Full pt demographics and BL disease characteristics have been published.[1,2] Mean BL CDAI scores across

treatment groups ranged from 37.6–41.0 for pts with a HxASCVD or non-missing BL CV scores. ORs and the percentage of pts achieving remission and LDA with tofacitinib vs TNFi at Month 6 are shown in the Table 1 and Figure 1, respectively. ORs were greater for pts receiving tofacitinib vs TNFi in the Overall population, and in pts with no HxASCVD, and were similar in pts with a HxASCVD. Pts with high or intermediate CV risk scores tended to be more likely to reach remission or LDA with tofacitinib vs TNFi, as were pts with low–borderline risk scores who received tofacitinib 10 mg BID.

Table 1. ORs of tofacitinib vs TNFi for achieving remission or LDA at Month 6

	N	Remission (CDAI ≤2.8)		LDA (CDAI ≤10)	
		OR vs TNFi	(95% CI)	OR vs TNFi	(95% CI)
Overall					
Tofacitinib 5 mg BID	1414	1.32	(1.04, 1.67)	1.31	(1.12, 1.53)
Tofacitinib 10 mg BID	1391	1.48	(1.17, 1.88)	1.43	(1.22, 1.67)
HxASCVD					
Tofacitinib 5 mg BID	196	0.89	(0.46, 1.70)	1.43	(0.94, 2.19)
Tofacitinib 10 mg BID	211	1.48	(0.82, 2.65)	1.22	(0.81, 1.84)
No HxASCVD					
Tofacitinib 5 mg BID	1218	1.40	(1.08, 1.82)	1.29	(1.09, 1.52)
Tofacitinib 10 mg BID	1180	1.48	(1.14, 1.92)	1.47	(1.24, 1.74)
High CV risk (≥20%)					
Tofacitinib 5 mg BID	250	1.80	(1.03, 3.13)	1.35	(0.95, 1.94)
Tofacitinib 10 mg BID	269	1.52	(0.86, 2.68)	1.11	(0.78, 1.58)
Intermediate CV risk (≥7.5–<20%)					
Tofacitinib 5 mg BID	456	1.64	(1.07, 2.54)	1.43	(1.10, 1.88)
Tofacitinib 10 mg BID	474	1.52	(0.98, 2.34)	1.77	(1.35, 2.33)
Low–borderline CV risk (<7.5%)					
Tofacitinib 5 mg BID	496	0.99	(0.66, 1.48)	1.13	(0.87, 1.47)
Tofacitinib 10 mg BID	420	1.46	(0.98, 2.16)	1.49	(1.12, 1.97)

For pts randomised to tofacitinib 10 mg BID who had their dose reduced to 5 mg BID due to a protocol amendment in 2019, data collected after pts were switched to 5 mg BID were counted in the tofacitinib 10 mg BID groupCI, confidence interval; N, number of evaluable pts

Figure. Percentage of pts achieving remission or LDA with tofacitinib[a] vs TNFi at Month 6 for pts overall and by HxASCVD



[a]For pts randomised to the tofacitinib 10 mg BID group who had their dose of tofacitinib reduced to 5 mg BID due to a protocol amendment in 2019, data collected after pts were switched to tofacitinib 5 mg BID were counted in the tofacitinib 10 mg BID group
[b]The darker shaded portion of each bar represents the percentage of pts achieving remission (CDAI ≤2.8); the full bar represents the percentage of pts achieving LDA (CDAI ≤10)
[c]Data for the high, intermediate and low–borderline CV risk categories were derived from pts with no HxASCVD, in whom the 10-year risk of ASCVD was calculated using the pooled cohort equations calculator[3]
N, number of evaluable pts

Conclusion: In pts with no HxASCVD, the efficacy of tofacitinib is at least as good as TNFi, and risk of MACE is comparable.[1] In pts with HxASCVD, clinicians should consider that risk of MACE with tofacitinib is higher vs TNFi,[1] while efficacy is similar. Overall, our findings further characterise the benefit/risk of tofacitinib by risk category, and provide a means to risk-stratify pts such that tofacitinib can be considered an effective treatment option where appropriate.

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OP0044

DOES RHEUMATOID ARTHRITIS PATIENTS' RISK OF OVERALL AND SITE SPECIFIC CANCER DIFFERS FROM THE GENERAL POPULATION? A NATIONAL CLAIMS DATABASE COHORT STUDY IN THE ERA OF BIOLOGICAL TREATMENTS

Keywords: Rheumatoid arthritis, Epidemiology, Comorbidities

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Background: Earlier studies, before the era of biologics, showed that rheumatoid arthritis (RA) patients were at higher risk of overall malignancies, with an excess relative risk of 28% compared to the general population. This risk is mostly carried by specific cancers such as lung cancer, lymphomas along with skin cancers. An update of cancer incidence is warranted in order to explore whether cancer risk has been modified in the era of biological and targeted DMARDs.
Objectives: To estimate the risk of cancer in patients with rheumatoid arthritis compared to the general population.
Methods: We conducted a nationwide population-based study within the French national claim database "Système National des Données de Santé" (SNDS) between January 1st 2010 and December 31st 2020. We estimated the age and sex-standardized incidence ratios (SIR) and [95% CI] of cancer (all sites, site specific and hematologic malignancies) of RA patients, with the French population as reference, by use of the French Network of Population-Based Cancer Registries (FRANCIM). SIR were estimated with Poisson regression models.
Results: During the study period, 257,075 patients met the eligibility criteria, who contributed to a total of 1,906,742 person-years for the main analysis. RA patients had an increased risk of overall malignancy (SIR 1.20 [1.17-1.23]), particularly lung (SIR 1.41 [1.36-1.46], bladder (SIR 2.38 [2.25-2.51]), ears-nose-throat (SIR 1.40 [1.31-1.50]), cervix (SIR 1.80 [1.62-2.01]), prostate (SIR 1.08 [1.04, 1.13]), melanoma (SIR 1.37 [1.29-1.46]) cancers, marginal zone (SIR 1.22 [1.06-1.42]), diffuse large b cell (SIR 1.79 [1.63-1.96]), and Hodgkin (SIR 2.68 [2.23-3.18]) lymphomas, and multiple myeloma (SIR 1.50 [1.36-1.65]). Of note, some cancers were less frequent than in the general population such as pancreatic cancer (SIR 0.90, [0.83-0.97]) as well as breast and uterine body cancers (SIR 0.91 [0.88-0.94] and SIR 0.77 [0.71-0.84] respectively). Subgroup analyses revealed that the risk of overall malignancy was significantly less increased in women (SIR 1.08 [1.06-1.10]) than in men (SIR 1.34 [1.31-1.36]) (between group difference p < 0.001). Whereas, the risk of pancreatic cancer was only decreased in men but not in women (SIR 0.83 [0.75-0.91] vs SIR 1.04 [0.92-1.17] respectively, p < 0.001). Full details are presented in the Figure 1 below. Overall risk of cancer

was increased in patients treated with csDMARD (SIR 1.15 [1.13-1.17]), Tumor Necrosis Factor inhibitors (SIR 1.11, [1.07-1.15]), abatacept (SIR 1.27 [1.16-1.39]) and rituximab (SIR 1.43 [1.31-1.55]) versus the general population, however this association was not found in patients exposed to anti-IL6 (SIR 1.00 [0.90-1.10]) and Janus Kinase inhibitors (SIR 0.97 [0.77-1.21]).
Conclusion: In the era of biologics, RA patients remain at greater risk of overall malignancy and some site-specific cancers, not only lung cancer and lymphoma. This higher incidence of overall malignancy was observed in RA patients treated with almost all type of DMARD or bDMARD. However, no causal relationship between treatments and cancer incidence can be drawn as indication bias was not taken into account. Of note, we observed a lower incidence of breast, pancreatic and uterine body cancers than the general population.
REFERENCES: NIL.

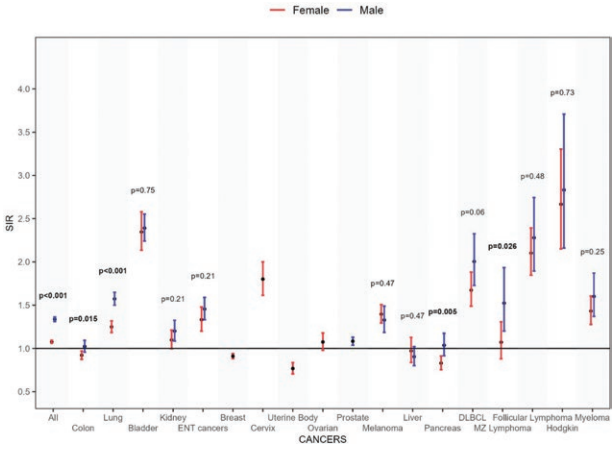


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0045

EULAR POINTS TO CONSIDER ON THE INITIATION OF TARGETED THERAPIES IN PATIENTS WITH INFLAMMATORY ARTHRITIDES AND A HISTORY OF CANCER

Keywords: Comorbidities, Malignancy, bDMARD

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Background: Potential associations between targeted therapies and a new cancer in patients with an inflammatory arthritis (IA) and a history of malignant disease are a frequent concern in daily rheumatology practice. IA and/or immunomodulatory drugs might confer a specific risk of malignancy. No evidence-based framework has been proposed to guide clinicians on the benefit/risk balance when initiating or reinitiating a targeted therapy (bDMARDs/tsDMARDs) in this context.
Objectives: This initiative aimed to develop points to consider (PTC) to assist rheumatologists. when initiating/reinitiating a targeted therapy in the context of a previous malignancy.
Methods: Following EULAR standardised operating procedures, a task force of 2 patient representatives. and 25 experts (comprising 2 methodologists, 2 EMEUNET members, 1 oncologist. and 20 rheumatologists) first met to define the research questions for a systematic literature review concerning patients with IA and a history of cancer and other relevant information for consideration including: incidence of cancer in targeted therapy-treated patients and no history of cancer, translational research in onco-rheumatology, management with targeted therapy of immune-related adverse events of checkpoint inhibitors. In a second meeting, the task force formulated. the overarching principles and the PTC.
Results: The group formulated 5 overarching principles and 8 PTC relevant to the initiation of targeted therapies in patients with IA and a history of cancer. Major themes included a) the need to assess. the individualized risk of cancer recurrence based on the characteristics of the patient, the cancer and the underlying disease; b) the importance of engaging with specialists caring for the cancer and. to define treatment based on a shared decision between the patient and the rheumatologist; c) the possibility to initiate without delay an appropriate targeted therapy for the treatment of. the IA in patients in remission of their cancer; d) the proposal to prefer anti-cytokine bDMARDs. over other treatment options in patients with history of solid cancer and to prefer. B cell depleting therapy in patients with a history of lymphoma; e) the proposal to use JAK inhibitors and abatacept with caution, and only in the absence of therapeutic alternatives, based on. the significant increase in cancer incidence in patients without a history of cancer, with tofacitinib compared to anti-TNF in a randomized clinical trial, and a modest but significant increase. with abatacept compared to other bDMARDs in some observational studies.
Conclusion: The 2023 EULAR Points to Consider provide guidance on the management of targeted therapies. in patients with IA and a history of cancer. The research agenda highlights the need for studies. to evaluate targeted therapies other than TNF inhibitors and anti-CD20 to address the evidence gaps in this setting.
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GC to new therapies

OP0046 REAL-WORLD ORAL GLUCOCORTICOID USE IN SYSTEMIC LUPUS ERYTHEMATOSUS: A NATION-WIDE POPULATION-BASED STUDY USING THE FRENCH NATIONAL MEDICO-ADMINISTRATIVE DATABASE (LUPIN-F STUDY)

Keywords: Systemic lupus erythematosus, Real-world evidence

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Background: The daily dose of oral glucocorticoids (OCS) is associated with damage in Systemic Lupus Erythematosus (SLE), and OCS reduction is a major goal of SLE care. However, evidence regarding the real-world use of OCS in nation-wide populations are currently lacking.

Objectives: The aim of this study was to analyze the use of OCS in French patients with SLE, at the national level, using medico-administrative data.

Methods: This study used the French health-insurance claims database (SNDS), which contains pseudonymized individual data for over 66 million people. SLE patients were identified with the ICD-10 diagnosis code for SLE (M32), documented as a chronic condition or associated to hospital stay. Included SLE patients were defined as patients alive on January 1st 2020 whenever the SLE diagnosis occurred. SLE comorbidities and OCS complications were identified through validated algorithms. Real-world use of treatments was identified through drug deliveries in pharmacies and daily OCS doses (expressed in prednisone-equivalent) were calculated for the year 2019. Comparisons were made to age- and gender-matched controls without SLE from the general population.

Results: A total of 32,173 patients with SLE (mean age 49.9 ± 16.0 years; 86.1% women) were alive on January 1st 2020, with a mean disease duration of 7.1 ± 6.2 years. Among these prevalent SLE patients, 48.2% were treated with OCS. The mean daily dose of OCS was below 5 mg/day in 35.7%, between 5 and 7.5 mg/day in 6.4% and above 7.5 mg/day in 6.1%. OCS use was significantly more frequent in women, in patients with CMUc (specific health coverage for low income patients) and decreased with age (p<0.0001, for all). SLE-specific comorbidities, including glomerular disease, skin involvement, polyarthritis, pleurisy, pericarditis, and thrombocytopenia, were significantly increased in patients with higher doses of OCS (p<0.0001, for all). Use of SLE treatments other than OCS was significantly increased in patients with higher doses of OCS (p<0.0001, for all) (Table 1). Strikingly, 14.6% of patients receiving 5 to 7.5 mg of OCS per day and 14.2% of those receiving more than 7.5 mg per day were not treated with antimalarial drugs, immunosuppressives or other biologic treatments for SLE. Complications of OCS, including cardiovascular diseases, infections, osteoporosis, and obesity, were significantly increased in SLE patients receiving ≥ 5 mg per day of OCS (p<0.0001 for all). The overall annual mean cost of healthcare consumptions from a societal perspective in 2019 was 6,048€ for prevalent SLE patients and 2,601€ for matched controls (p<0.0001). Among prevalent SLE patients, the cost increased significantly according to the OCS daily dose: 4,633€ for patients without OCS, 6,383€ (daily dose of 0-5 mg/day), 9,815€ (5-7.5 mg/day) and 13,861€ (above 7.5 mg/day).

Conclusion: To the best of our knowledge, this is the first nation-wide study reporting on real-life use of OCS in patients with SLE. The proportion of patients treated with high-dose OCS ≥ 7.5mg/day remains unacceptably high and associated with increased comorbidities, OCS complications and significantly increased healthcare costs. Also, over 14% of patients receiving OCS doses ≥ 5 mg/day were not treated with antimalarial drugs, immunosuppressives or other biologic treatments for SLE. These results highlight the need for tight disease control and implementation of robust OCS-sparing strategies in SLE.

Table 1. Proportion of patients treated with SLE treatments other than corticosteroids in 2019

	No OCS	OCS 0-5 mg/day	OCS 5-7.5 mg/day	OCS ≥ 7.5 mg/day	p-value
Antimalarials (Hydroxychloroquine/ Chloroquine)	8,826 (53.0%)	7,286 (63.5%)	1,505 (72.9%)	1,416 (71.9%)	<0.0001
Methotrexate	958 (5.7%)	1,405 (12.2%)	361 (17.5%)	358 (18.2%)	<0.0001
Mycophenolate mofetil	337 (2.0%)	878 (7.6%)	350 (17.0%)	496 (25.2%)	<0.0001
Azathioprine	264 (1.6%)	549 (4.8%)	175 (8.5%)	206 (10.5%)	<0.0001
Cyclophosphamide	207 (1.2%)	367 (3.2%)	147 (7.1%)	266 (13.5%)	<0.0001

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OP0047 WITHDRAWAL OF MAINTENANCE GLUCOCORTICOID VERSUS OTHER IMMUNOSUPPRESSANTS AMONG PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN LONG TERM CLINICAL REMISSION: INTERIM ANALYSIS OF A NON-INFERIORITY RANDOMISED CONTROLLED TRIAL

Keywords: Randomized control trial, Tapering, Systemic lupus erythematosus

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Background: Attempts to stop glucocorticoids (GC) among lupus patients in long term remission have been successful. Continuing other immunosuppressive (IS) agents indefinitely is currently the norm and this approach results in significant infectious, psychological and economic burden on patients. Moreover, there is no pathophysiological basis to withdraw GC over the other IS agents, except for the indirect evidence of higher adverse effects with continued low dose GC use. Hence, there is a need to assess, if the approach to taper steroids first is the right way in lupus.

Objectives: To compare the outcome of glucocorticoid withdrawal versus immunosuppressant withdrawal in patients of SLE in clinical remission.

Methods: This is a single centre, non-inferiority, open-label stratified randomized (1:1) controlled trial. Patients with SLE who were on IS for at least 3 years, in DORIS remission for a minimum of 1-year preceding screening and were on stable prednisolone dose of ≤7.5mg/day plus a maintenance non biological IS were included. Stratification was done based on duration of IS use (<3 years and ≥ 3 years), and presence of proliferative lupus nephritis. All patients continued HCQ during the study. Prednisolone or IS was tapered gradually over 3 months after randomisation. Primary end point was proportion experiencing a flare [SELENA-SLEDAI flare index (SFI)] and BILAG index at 52 weeks. Secondary end points were time to flare and severity of flare. Non-inferiority margin considered was 10%. For this abstract, data of maximum available follow up period for each patient was used.

Results: A total of 117 patients were randomised into steroid withdrawal (n=58) and IS withdrawal (n=59). Overall, 72% of the patients were in prolonged remission (DORIS remission on treatment >5 years). Median duration of available follow up is 46 weeks. There was a total of 23 flares of which 20 were mild-moderate and 3 were severe flares (SFI). Proportion of patients experiencing a flare was numerically higher in the steroid withdrawal group (15 vs 8 patients, RR 1.91 (0.88-4.15), p=0.09). (Table 1). Time to first flare was 27 days and 18 days following intervention in steroid and IS arm respectively. Severity of flare and time of first flare were not significantly different between the two groups (HR=0.49, 95%CI (0.20-1.15), p=0.096) (Figure 1). Severe flares were 2(3.4%) vs 1(1.7%) and mild-moderate flares were 13(22.4%) and 7(11.9%) in the steroid versus IS withdrawal arm respectively. There was one death due to MI secondary to ASCVD in a patient on IS withdrawal.

Conclusion: Immunosuppressant withdrawal is noninferior to steroid withdrawal in patients with SLE in long term clinical remission. Identifying the individuals who are likely to flare is of utmost importance which can pave the way for a more personalised drug withdrawal approach.

Table 1. Results of primary and secondary endpoints at maximum available follow up period (mean:46 weeks)

	Prednisolone withdrawal group (n = 58)	*Immunosuppressant withdrawal group (n = 59)*	*Relative risk (95% CI)*	*P value**
Primary endpoints:				
Any flare according to SFI, n (%)	15 (25.9)	8 (13.6)	1.91 (0.88-4.15)	0.09
Any flare according to BILAG, n (%)	9 (15.5)	7 (11.9)	1.31 (0.52 -3.28)	0.60
Any flare according to PGA, n (%)	15 (25.9)	8 (13.6)	1.91 (0.88-4.15)	0.09
Secondary endpoints				
Details of SFI flares				
No flare, n (%)	43 (74.1)	51 (86.4)	1 (Ref.)	Ref.
Mild/Moderate, n (%)	13 (22.4)	7 (11.9)	1.89 (0.85 – 4.40)	0.13
Severe, n (%)	2 (3.4)	1 (1.7)	2.03 (0.19–21.83)	0.62
Details of BILAG flares				
No flare, n (%)	49 (84.5)	52 (88.1)	1 (Ref.)	Ref.
Mild, n (%)	7 (12.1)	4 (6.8)	1.78 (0.55 – 5.76)	0.33
Moderate, n (%)	1 (1.7)	2 (3.4)	0.51 (0.47 – 5.46)	1.00
Severe, n (%)	1 (1.7)	1 (1.7)	1.02 (0.0 – 15.88)	1.00
Patients experiencing an increase in SDI, n (%)	1 (1.9)	0 (0)	0.96 (0.91 – 1.01)	0.23

p <0.05 is significant; *Using Chi-square test; SFI, SELENA-SLEDAI Flare Index, BILAG, British Isles Lupus Assessment Group; PGA, Physician's Global Assessment; SDI, SLICC/ACR Damage Index

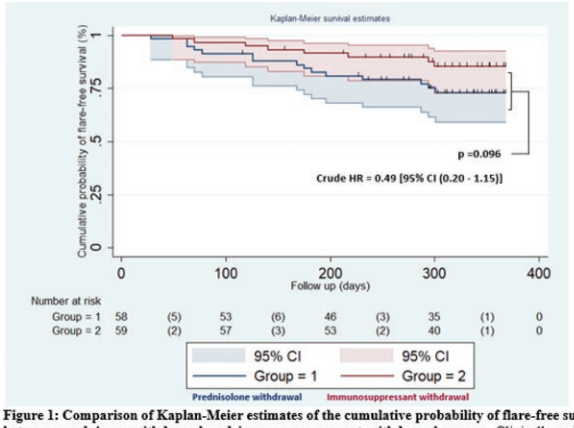


Figure 1: Comparison of Kaplan-Meier estimates of the cumulative probability of flare-free survival between prednisone withdrawal and immunosuppressant withdrawal groups. Clinically quiescent SLE patients were allocated at day 0 to stop prednisolone (blue line) or immunosuppressant (red line) and were followed for 52 weeks. Each corner and the number in parentheses represent a lupus flare, defined by SELENA-SLEDAI flare index. The vertical lines on the curves represent the censored participants. Patients who had a flare in any organ system were recorded. Kaplan-Meier plots show the percentage of patients with flare-free survival in any organ system. Curves were compared using log-rank test. Crude HR was calculated using Cox proportional hazards model. SLE, systemic lupus erythematosus.

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OP0048

RISK OF FLARE AND DAMAGE ACCRUAL AFTER TAPERING GLUCOCORTICOIDS IN SEROLOGICALLY ACTIVE CLINICALLY QUIESCENT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Real-world evidence, Tapering

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Background: Some studies demonstrated that withdrawal of low-dose glucocorticoids in clinically quiescent systemic lupus erythematosus (SLE) patients increased the risk of flare [1]. An international survey of 130 clinicians showed that persistent abnormal serology led to a reluctance to reduce or discontinue medications [2].
Objectives: To assess the risk of flare and damage accrual after tapering glucocorticoids in serologically active clinically quiescent (SACQ) patients with SLE. Association of other medications with flare in SACQ patients was also analyzed.
Methods: We used data from the Asia Pacific Lupus Collaboration cohort, prospectively collected from SLE patients (ACR/SLICC criteria) observed for at least 2 visits between 2013 and 2020. Disease activity and medication details were captured at enrolment and at routine visits. SACQ was defined at any visit as the state with serological activity (increased anti-dsDNA or hypocomplementemia) but without clinical activity as measured by SLEDAI-2K. Patients treated with 0 to 7.5 mg/day of prednisolone at a SACQ visit were analyzed after stratification according to the initial dosages of prednisolone. Cox proportional hazard models were used to assess the time-dependent relationship between decreasing prednisolone in SACQ patients and disease flares captured with the SELENA flare index at each subsequent visit, as well as subsequent damage accrual (≥1-point increase in SLICC/ACR damage index [SDI]). Each patient was observed for up to 2 years or until each outcome event occurred.
Results: From a total of 4,106 patients, 1,850 patients with SACQ and 8,905 visits were analyzed: 742, 271, and 180 patients experienced overall flare, severe flare, and increase in SDI, respectively. Tapering prednisolone was not associated with subsequent overall or severe flare: Each unit decrease in prednisolone dosage (1 mg/day) resulted in adjusted HRs 1.02 (95%CI, 0.99–1.05) and 0.98 (95%CI, 0.96–1.00) for overall and severe flare, respectively, in the group with initial prednisolone dosages of 0–7.5 mg/day. However, among SACQ patients, antimalarial use was significantly associated with reduced overall and severe flare in the groups with initial prednisolone of 0–7.5 or 0–5 mg/day. In addition, immunosuppressive use was significantly associated with reduced severe flare but not overall flare in these groups. Decreasing the dosage of prednisolone was significantly negatively associated with damage accrual in the groups with initial prednisolone dosages of 0–7.5 mg/day (adjusted HR [95%CI], 0.97 [0.96–0.99]) and 5–7.5 mg/day (adjusted HR [95%CI], 0.96 [0.94–0.99]) but not 0–5 mg/day (adjusted HR [95%CI], 0.98 [0.95–1.01]).

Table 1. Summary results of association between decreasing the prednisolone dosages and disease flares or damage accrual in SLE patients with SACQ

Initial prednisolone dosage (mg/day)	Overall disease flare	Severe disease flare	Increase in SDI
0 ≤ prednisolone ≤7.5	1.02 (0.99–1.05), $p = 0.27$	0.98 (0.96–1.00), $p = 0.11$	0.97 (0.96–0.99), $p < 0.01$
0 ≤ prednisolone ≤5	1.02 (0.98–1.06), $p = 0.41$	0.98 (0.96–1.01), $p = 0.28$	0.98 (0.95–1.01), $p = 0.14$
5 < prednisolone ≤7.5	1.01 (0.96–1.06), $p = 0.84$	0.98 (0.92–1.03), $p = 0.41$	0.97 (0.96–0.99), $p < 0.01$

* HRs (95% CIs) per unit decrease in prednisolone dosages (1 mg/day) were calculated using Cox proportional hazard models and adjusted by initial prednisolone dosage, antimalarial, immunosuppressive, disease duration, SLEDAI-2K, age at visit, gender, and ethnicity.

Conclusion: Tapering prednisolone was not significantly associated with subsequent flare in SLE patients who were SACQ. Antimalarial and immunosuppressive use were associated with reduced risk of flares in SACQ patients. Tapering prednisolone was associated with reduced risk of damage accrual in SACQ patients treated with more than 5 mg/day of prednisolone. These findings suggest glucocorticoid tapering is safe and protective in SLE patients in SACQ.

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OP0049 AN IMMUNE TARGETED, NON-TOXIC CORTICOSTEROID FOR THE TREATMENT OF SEVERE AUTOIMMUNE DISEASE

Keywords: Targeted synthetic drugs, Systemic lupus erythematosus, bDMARD

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Background: Glucocorticoids (GC) (aka corticosteroids) are a class of drugs with broad range anti-inflammatory and immunosuppressive activities making them the most potent anti-inflammatory drugs. However, chronic or high dose systemic exposure consistently leads to grievous dose limiting toxicities as in multiple organs including brain, liver and bone.. Altogether, these toxicities prevent GC from being a true panacea in the management of inflammatory diseases particularly in the case of chronic diseases. Targeting GC to immune cells will solve this problem as toxicity mostly occurs in non-immune tissues and cells that are unnecessary for therapeutic efficacy.

Objectives: The objective of INX200 is to give patients a non-toxic glucocorticoid that provides anti-inflammatory efficacy without any glucocorticoid toxicity in a once-per month injection.

Methods: We have achieved specific targeting of GC to the immune system with INX200, an antibody-drug conjugate (ADC). INX200 is a fully humanized immune-targeting monoclonal antibody with silent Fc domain and conjugated through a cleavable linker to budesonide. Validation experiments were conducted using human target knock-in mice, mouse surrogate antibodies and non-human primates in various inflammation and chronic disease models.

Results: We show that INX200 targets both lymphoid and myeloid cells with minimal off-target activity outside the immune compartment. This translates to reduced toxicity when compared to free GC as measured by the lack of impact on the Hypothalamic-Pituitary-Adrenal axis (no changes in corticosterone levels) and bones (no changes in GC- activated transcription) both in mice and non-human primates. INX200 rapidly internalizes allowing for robust and efficient uptake of the ADC thereby providing superior loading of GC into immune cells which results in therapeutic equivalence to free GC at 1/10th of the dose. One dose of INX200 also leads to substantially longer exposure (>3 weeks) when compared to free GC (<24h) both in mice and non-human primates. Additionally, we show that in both acute and chronic inflammation models (Figure 1), INX200 is therapeutically as broadly efficacious as free GC demonstrating that GC targeting to immune cells is sufficient for full GC anti-inflammatory efficacy. Finally, developability studies show that INX200 is stable at high concentration and as such suitable for subcutaneous administration.

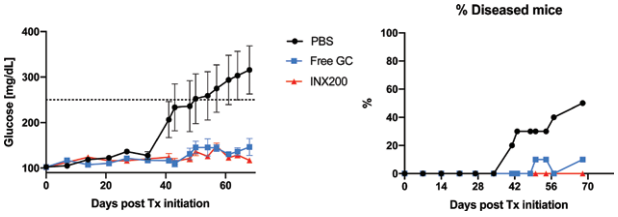


Figure 1. INX200 has equivalent efficacy to free GC at <1/10th of the dose in controlling disease development in the type 1 diabetes NOD mouse model. NOD mice were enrolled at 12-week old; INX200 (red) was dosed once a week at 10 mg/Kg (= 0.2 mg/Kg of GC payload) and free GC (blue) in water at 2 mg/kg per day. Left graph shows blood glucose levels over time of treatment, the dashed line indicating diabetic glucose levels as >250 mg/dL. Right graph shows the % of diseased mice over time (n=10 mice, experiment repeated twice).

Conclusion: INX200 retains all the efficacy/potent therapeutic activities of GC but with little to no side effects. The successful targeting of GC to the immune system with the sparing of non-hematopoietic toxicities, offers a transformative advance in GC-based drugs for the treatment of severe, chronic inflammatory diseases such as IBD, lupus and asthma.

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OP0050 INCREASED IFITM GENE-SIGNATURES IN AGE-ASSOCIATED B AND PLASMA CELLS DEFINE NON-RESPONSE TO MYCOPHENOLATE MOFETIL IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Treat to target, -omics, Systemic lupus erythematosus

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Background: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease that leads to significant worsening of quality of life and mortality. The

enormous molecular heterogeneity of SLE is reflected in different clinical manifestations, disease progression and also in a different drug efficacy across patients[1]. Lupus nephritis (LN) is the most severe SLE manifestation with the potential of rapidly evolving into irreversible chronic kidney disease and kidney failure if not adequately followed and treated. Mycophenolate mofetil (MMF) is the most widely used first-line treatment for LN, being ineffective or partially effective in 15-30 percent of the patients[2]. Reasons for non-response are still unknown and low or moderate drug efficacy may lead to aggravation of the disease. Treat-to-target approaches where personalized molecular patterns guide therapeutic decisions, are rapidly growing in medical fields such as oncology, but remain unmet within clinical rheumatology[3]. In addition, pathological molecular dysregulation behind SLE fluctuates within a non-linear clinical course and unpredictable patterns of flares and remissions, hindering the development of effective and robust predictive biomarkers for both diagnosis and drug responsiveness[4].

Objectives: The development of new, more effective therapies to treat LN is an urgent unmet need. The objective of this work is to define the cellular and molecular immune landscape behind non-response to MMF to finally apply this knowledge within routine clinical practice.

Methods: A longitudinal cohort comprising gene-expression and clinical data of 97 MMF responder and 28 non-responder blood samples was retrospectively analyzed. Differential gene expression and functional analysis were performed. Response rate was measured based on blood cell proportions. Single-cell RNA sequencing data was analyzed to identify the cell subtypes influencing non-response and their contributing genes and regulation mechanisms.

Results: A robust signature comprising 41 differentially expressed genes defined non-response to MMF and cellular profiles that favor the response to the drug in the patients were revealed. The response rate to MMF increases the lower the B cell/T cell ratio. Single-cell RNA sequencing showed that overexpression of the IFITM-family of genes in age-associated B cells, plasma cells, myeloid dendritic cells and macrophages was behind the non-response signature.

Conclusion: Blood cell subtypes and genes mediating non-response to MMF were revealed, opening a new scenario for the development of new therapeutic strategies for LN.

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OP0051 LUPUS LOW DISEASE ACTIVITY STATE ATTAINMENT IN THE PHASE 3 PLACEBO-CONTROLLED TULIP LONG-TERM EXTENSION TRIAL OF ANIFROLUMAB

Keywords: Treat to target, Systemic lupus erythematosus, Clinical Trials

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Background: The Lupus Low Disease Activity State (LLDAS) has been prospectively validated as protective from flares, damage accrual, and mortality and is an important treatment goal in patients with SLE.[1] Recent analysis of pooled data from 2 phase 3 trials (TULIP-1 and TULIP-2) found that LLDAS attainment was achieved earlier, more frequently, and for a more sustained period with anifrolumab vs placebo in patients with moderate to severe SLE.[2]

Objectives: We investigated the long-term impact of anifrolumab compared with placebo on LLDAS attainment over the 1 year TULIP-1/TULIP-2 and 3 year long-term extension (LTE) study periods.[3]

Methods: TULIP-1 and TULIP-2 (NCT02446912, NCT02446899) were randomized, placebo-controlled, 52-week trials of IV anifrolumab (Q4W, 48 weeks) in patients with moderate to severe SLE despite standard therapy. Following the double-blind treatment period of the TULIP trials, patients could reconsent to participate in the 3-year, randomized, blinded, placebo-controlled LTE study (NCT02794285).[3] Here, data were analyzed by timepoint from TULIP baseline through the end of the LTE (Week 208) for patients who were assigned and received the same study drug (anifrolumab 300 mg or placebo) during the TULIP+LTE periods. LLDAS attainment was defined as all of the following: SLEDAI-2K ≤4 without major organ activity, no new disease activity, Physician's Global Assessment [0–3] ≤1, prednisone or equivalent ≤7.5 mg/day, standard immunosuppressant dosing, no use of restricted medications (considered only during the pooled TULIP-1/TULIP-2 period but not during the LTE period), and no investigational product (IP) discontinuation. LLDAS percentages and cumulative time in LLDAS were compared using a Cochran–Mantel–Haenszel approach, and response rates were compared using logistic regression. Last observation carried forward was used to impute missing data for TULIP-1/TULIP-2, but not for data captured in the LTE. All *P*-values are nominal.

Results: Data from 369 patients (anifrolumab 300 mg, n=257; placebo, n=112) were evaluable for the 4-year TULIP+LTE study period. At the last TULIP visit (Week 52), 39.3% of the anifrolumab group and 27.9% of the placebo group were in LLDAS (odds ratio [OR] 1.6, 95% CI 1.0–2.7, *P*=0.049). At the first visit of the LTE (Week 64), 33.5% of the anifrolumab group and 22.8% of the placebo group were in LLDAS (OR 1.7, 95% CI 1.0–2.9, *P*=0.038). LLDAS attainment was relatively stable for the first 3 years (up to Week 156) and declined slightly in Year 4; this decrease likely reflects the proportions of patients who discontinued IP over time (Figure 1). However, attainment of LLDAS favored anifrolumab vs placebo at all timepoints up to Week 208 (OR 2.7, 95% CI 1.3–5.6, *P*=0.007). For the combined 4-year TULIP+LTE period, greater cumulative time (*P*=0.001) and percentage of time (*P*=0.006) was spent in LLDAS by patients receiving anifrolumab compared with placebo. Cumulative time in LLDAS at a threshold of ≥20% also favored anifrolumab (OR 2.2, 95% CI 1.4–3.5, *P*=0.001); a similar trend was seen with a threshold of ≥50%, although this did not reach statistical significance (OR 1.4, 95% CI 0.8–2.4, *P*=0.217). Compared with placebo, patients treated with anifrolumab were more likely to be in sustained LLDAS for ≥3 consecutive visits (49.4% vs 35.1%; OR 1.8, 95% CI 1.1–2.8, *P*=0.018), ≥5 consecutive visits (32.6% vs 20.1%; OR 1.8, 95% CI 1.0–3.1, *P*=0.033), or ≥7 consecutive visits (22.2% vs 11.6%; OR 2.1, 95% CI 1.1–4.1, *P*=0.028).

Conclusion: Anifrolumab 300 mg treatment was associated with more frequent, prolonged, and sustained LLDAS compared with placebo during the 4-year TULIP+LTE period.

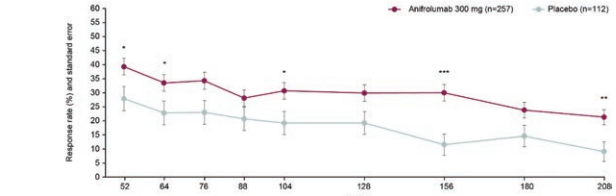
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Figure. Lupus Low Disease Activity State (LLDAS) response rate and percentage of patients with no IP discontinuation by randomized treatment in patients with SLE in the TULIP long-term extension study



No IP discontinuation, %								
Anifrolumab 300 mg (n=257)	98.4	96.1	94.9	92.6	89.5	83.3	77.4	73.5	69.3
Placebo (n=112)	96.4	90.2	87.5	83.0	75.9	66.1	57.1	54.5	46.4

IP, investigational product; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.
Responder rates were calculated using a stratified Cochran–Mantel–Haenszel approach, with stratification factors of SLEDAI-2K at screening, Day 1 glucocorticoid dosage, type I interferon gene signature at screening, and study. Nominal *P*-values: *<0.05; **<0.01; ***<0.001.

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OP0052 PREDICTORS OF RENAL FLARES IN SYSTEMIC LUPUS ERYTHEMATOSUS: A POST-HOC ANALYSIS OF FOUR PHASE III CLINICAL TRIALS OF BELIMUMAB

Keywords: Systemic lupus erythematosus, Kidneys, Biomarkers

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Background: In patients with systemic lupus erythematosus (SLE), renal involvement is associated with high morbidity, and renal flares are major contributors to poor long-term prognosis. Identification of patients at risk of developing renal flares despite immunosuppressant therapy is imperative to optimise management.

Objectives: To identify predictors of renal flares in patients receiving treatment for active extra-renal SLE.

Methods: Data from BLISS-52 (NCT00424476), BLISS-76 (NCT00410384), BLISS Northeast Asia (NEA; NCT01345253), and BLISS-SC (NCT01484496) were used (N=3225). The trials included patients with active, seropositive SLE and excluded active severe renal SLE. Participants were assigned to belimumab or placebo, on top of non-biologic standard therapy. We investigated anti-dsDNA, anti-Sm, anti-ribosomal P, and anti-cardiolipin (aCL) antibodies, low C3 and low C4 levels, B cell activating factor (BAFF), serum albumin, serum creatinine, and proteinuria at baseline as potential predictors of renal flares during a 52-week follow-up. We used Cox regression models to evaluate traditional disease features as predictors of renal flares in the pooled trial population. We also performed subgroup analysis of belimumab and placebo recipients. Covariates in the adjusted models included age, sex, ethnicity, body mass index, organ damage, baseline extra-renal activity (SLEDAI-2K score excluding renal and immunological descriptors), current or former renal SLE history (renal BILAG A–D), baseline use of glucocorticoids, antimalarials, and immunosuppressants, and use of belimumab.

Results: The mean age of the study population was 36.7 years, 94% were women, 54.6% had current or former renal involvement at baseline, and 192 developed a renal flare after a median follow-up time of 197 (IQR: 85–330) days from baseline. Patients with current or former renal involvement at baseline displayed a >9-fold increased hazard to develop a new renal flare (HR: 9.4; 95% CI: 5.0–17.7; P<0.001). In the pooled study population, baseline serum albumin (adjusted HR 0.9; 95% CI: 0.9–0.9; P<0.001), proteinuria (adjusted HR: 1.3; 95% CI: 1.2–1.4; P<0.001), and low C3 levels (adjusted HR: 1.8; 95% CI: 1.3–2.5; P<0.001) were robust determinants of subsequent renal flare occurrence; similar associations were found in the belimumab and placebo subgroups. Furthermore, we observed an association between anti-dsDNA positivity and renal flare development in univariable models (HR: 2.1; 95% CI: 1.4–3.2; P<0.001 in the pooled population), which attenuated in multivariable models (Figure 1). Positive levels of anti-Sm antibodies were associated with renal flare occurrence in the placebo (adjusted HR: 2.9; 95% CI: 1.5–5.6; P=0.002) but not in the belimumab subgroup, whereas anti-ribosomal P antibodies were associated with renal flare development in belimumab-treated (HR: 2.8; 95% CI: 1.5–5.0; P<0.001) but not in placebo-treated patients. Finally, positive levels of aCL antibodies (any isotype) predicted renal flare development in the belimumab group (adjusted HR: 1.8; 95% CI: 1.1–2.8; P=0.020) but yielded a negative association in the placebo group (adjusted HR: 0.4; 95% CI: 0.2–0.9; P=0.028).

Conclusion: Current or former renal involvement, high baseline proteinuria levels, hypoalbuminaemia, and C3 consumption were robust determinants of imminent renal flares. Beyond anti-dsDNA, anti-ribosomal P and aCL antibody positivity may prove valuable early signals of imminent renal flares in patients treated with belimumab. Anti-Sm positivity predicted imminent renal flares in patients treated with non-biological standard therapy, but not in belimumab-treated patients, assumably due to benefit conferred from belimumab in anti-Sm positive individuals, as shown previously [1].

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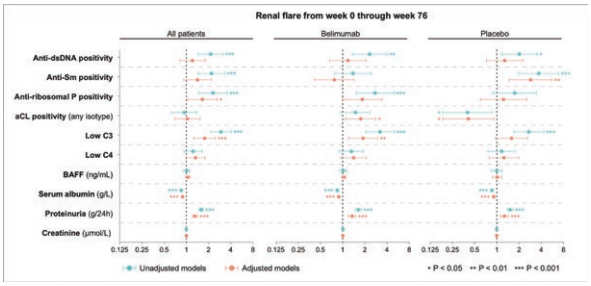


Figure 1. Cox regression models evaluating traditional markers as predictors of renal flares in patients with SLE treated with non-biological standard therapy with or without add-on belimumab.

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OP0053 EFFICACY AND SAFETY OF BARICITINIB IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PHASE 3 TRIAL

Keywords: Systemic lupus erythematosus, Remission, Randomized control trial

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Background: Baricitinib a selective Janus kinase (JAK) inhibitors 1&2 have been recognized as a potential therapeutic option in systemic lupus (SLE), also known Baricitinib, a JAK inhibitor, has demonstrated efficacy and safety in the treatment of dermatitis and arthritis 1; however, no JAK inhibitor studies have been conducted in lupus nephritis (LN) to dat.e.

Objectives: To assess the efficacy and safety of Baricitinib in patients (pts) with active LN.

Methods: The study is a randomized, double-blind, active competitor (cyclophosphamide)-controlled, phase 3 trial registered on clinicaltrials.com (NCT05432531), enrolled adults ≥18 years with a clinical diagnosis of LN (who also fulfilled classification criteria for LN grade III & IV), who had objective signs of active nephritis consistent with persistent proteinuria>0.5 g/day and/or cellular casts at screening, and who had SLEDAI-2K > 4 and patient assessment of anti-ds DNA and C3 serum levels at study entry. Pts were randomized 1:1 to receive Group 1: oral Baricitinib 4mg once daily and PBO saline infusion monthly, Group 2: oral PBO tablet and cyclophosphamide (0.7mg/m2) infusion monthly during a 6-months double-blind treatment period. The primary endpoint was proteinuria, response at week 12 and 24. Multiplicity-controlled secondary endpoints assessed at week 12 &24 included C3, anti-ds-DNA and SLEDAI-2K, and their changes from baseline, Treatment adverse events was recorded.

Results: Of 65 pts randomized at baseline, 60 enrolled in the study (Baricitinib 4mg, n=30; cyclophosphamide, n=30) and 100% received study drug through week 24. Baseline demographic and disease characteristics were balanced across treatment groups and consistent with an active LN population, all were females, 58% LN grade III; mean age 32.4 years; mean SLEDAI-2K 6.9; mean C3 12.1mg/L). A significantly reduction in proteinuria response rate at week 12 was achieved in group 1 vs group 2 (70% vs 43%; P<0.0001). Statistical significance was also achieved in the first 12 of the 24 w multiplicity-controlled secondary endpoints (C3 and SLEDAI-2k) at week 12 in group 1 compared with group 2 (P<0.01). The proportion of pts who experienced adverse events was similar between treatment groups (group 1, 48%; group 2, 46%). Serious adverse events leading to discontinuation were reported in 2 (6.6%) pts treated with Baricitinib and 1 (3.3%) pts treated with cyclophosphamide, respectively (serious infection or herpes zoster), major adverse cardiovascular events, venous thromboembolic events, were not reported in the study.

Conclusion: Baricitinib 4mg once daily demonstrated significantly good improvements in disease activity, proteinuria, C3, anti-ds-DNA, than cyclophosphamide after 12 &24 weeks of treatment in pts with active LN. The safety profile of Baricitinib 4mg was consistent with what has been observed with other inflammatory musculoskeletal diseases, and no new risks were identified. These results support the potential use of Baricitinib 4mg in pts with active LN.

Table 1. Patients showed ≥ 50% reduction in their initial Proteinuria level.

Variable	Group 1 (n=30)	Group 2 (n=30)	P value
4th w	17/30, 56.6%	9/30, 30%	
8th w	20/30, 66.6%	10/30, 33.3%	
12th w	21/30, 70%	13/30, 43.3%	
24th w	23/30, 76.6%	15/30, 50%	

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Clinical aspects and Treatment of axSpA: effects and predictors of effects

OP0054

THE YIELD OF REPEATED ASSESSMENTS IN CHRONIC BACK PAIN PATIENTS SUSPECTED OF EARLY AXIAL SPONDYLOARTHRITIS: TWO-YEAR DATA FROM THE SPONDYLOARTHRITIS CAUGHT EARLY (SPACE) COHORT

Keywords: Real-world evidence, Diagnostic Tests, Spondyloarthritis

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Background: We have shown in the SPACE cohort that a diagnosis of early axial spondyloarthritis (axSpA) can be made in patients with chronic back pain (CBP) of less than two years (2y). However, diagnostic uncertainty can be an obstacle towards initiating disease-modifying treatment. The value of repeated assessments of SpA features for a definite clinical diagnosis is yet to be determined.
Objectives: To assess the yield of repeated assessments of SpA features over 2y to make a *definite axSpA* diagnosis in patients with recent onset CBP referred to the rheumatologist, and to describe the characteristics of patients that change to *definite axSpA* over time.
Methods: We used the 2y data from the SPACE cohort, a European multicentre inception cohort of patients (age <45y) with CBP of recent onset (≥3 months, ≤2y) included from 2009 to 2016. The diagnostic work-up consisted of patient history, physical examination, acute phase reactants (APR) and HLA-B27 testing, radiographs and MRI of the sacroiliac joints (SI-CR and SI-MRI) and spine (not shown). In patients with ≥1 major or ≥2 minor prespecified SpA features, clinical assessments, APR, and imaging were repeated at 1y and 2y visits. At each visit, the rheumatologist reported a clinical diagnosis of *axSpA* or *no axSpA* with level of confidence (LoC; numeric rating scale from 0 (*not confident at all*) to 10 (*very confident*)). Herein, we categorized patients by diagnosis likelihood. At baseline (BL), two categories were defined: 'Definite *axSpA/no axSpA*' when the diagnosis was given with a LoC ≥7 and 'Uncertain *axSpA/no axSpA*' if LOC <7. At 2y, the following categories were defined: 'definite, most likely and possible axSpA' and 'possible, most likely and definite no axSpA' (***Figure 1***). The ASAS classification criteria were applied using central reading. We explored the diagnostic course over 2y. In patients shifting from *no axSpA* (*definite* or *uncertain*) or *uncertain axSpA* at BL to *definite axSpA* at 2y, SpA features were investigated over time.
Results: We included 552 patients. *Definite axSpA* was attributed to 175 (32%) patients at BL and 166 (30%) at 2y (***Figure 1***); 155/175 (89%) and 145/166 (87%) fulfilled ASAS classification criteria, respectively. Of the 175 patients with *definite axSpA* at BL, 133 retained the diagnosis, and only 13 changed to *no axSpA* at 2y. Although still considered as axSpA by the rheumatologist, 29 *definite axSpA* patients at BL were no longer definite axSpA at 2y, due to decrease in LOC to <7 (n=14) or incomplete follow-up (n=15). Overall, the diagnosis changed to *definite axSpA* over 2y in 33 patients (BL: 16 *uncertain axSpA*, 12 *uncertain no axSpA*, and 5 *definite no axSpA*); on average, 3 SpA features were already present at BL and 1 to 2 new SpA features developed over 2y (***Table 1***), with response to NSAIDs and MRI sacroiliitis being the most frequently captured over time.
Conclusion: The yield of repeated assessments of SpA features in patients with CBP suspected of axSpA was modest for the new *definite axSpA* diagnosis at 2y. Most SpA features were already present at BL, with imaging findings and response to NSAIDs appearing as frequent incident SpA features potentially adding to a *definite axSpA* diagnosis over time.

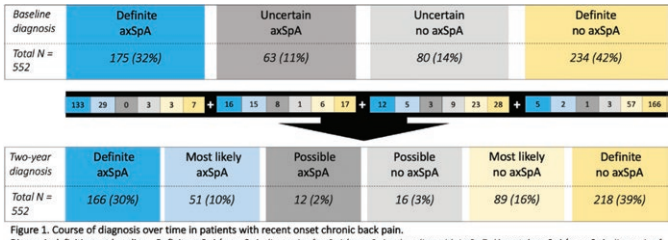


Figure 1. Course of diagnosis over time in patients with recent onset chronic back pain.
Diagnosis definitions at baseline - ***Definite axSpA/no axSpA:*** diagnosis of *axSpA/no axSpA* at baseline with LoC ≥7; ***Uncertain axSpA/no axSpA:*** diagnosis of *axSpA/no axSpA* with LoC <7. **Diagnosis definitions at two years (last observation carried forward approach if two-year visit data was missing)** - ***Definite axSpA:*** diagnosis of *axSpA* with a LoC ≥7 at two years (complete follow-up) or at the two last available visits (missing at the two-year visit); ***Most likely axSpA:*** diagnosis of axSpA with LOC <7 at two years, plus a consistent diagnosis of axSpA in the two last visits (complete follow-up) or diagnosis of *axSpA* with LoC ≥7 at the last visit only (missing at the two-year visit); ***Possible axSpA:*** diagnosis of *axSpA* with LOC <7 at two years, plus no consistent diagnosis of *axSpA* in the last two visits (complete follow-up) or diagnosis of *axSpA* with LoC <7 at the last visit (missing at the two-year visit); ***Possible no axSpA:*** diagnosis of *no axSpA* with LOC <7, plus no consistent diagnosis of *no axSpA* in the last two visits (complete follow-up) or *no axSpA* diagnosis with LoC <7 at the last visit and no alternative diagnosis reported (missing at the two-year visit); ***Most likely no axSpA:*** diagnosis of *no axSpA* with LOC <7, plus a consistent diagnosis of *no axSpA* in the last two available visits (complete follow-up) or diagnosis of *no axSpA* with LoC ≥7 at the last visit only or if LoC <7, plus an alternative diagnosis reported (missing at the two-year visit); ***Definite no axSpA:*** diagnosis of *no axSpA* with a LoC ≥7 at two years (complete follow-up) or at the two last available visits (missing at the two-year visit).

Table 1. Characteristics of 33 patients changing to *definite axSpA* with newly developed SpA features over 2 years

Baseline diagnosis	Uncertain axSpA at BL N=16		Uncertain no axSpA at BL N=12		Definite no axSpA at BL N=5	
	BL	**2Y**	**BL**	**2Y**	**BL**	**2Y**
Age at inclusion, years	30 (9)	-	35 (8)	-	26 (6)	-
Male	50%	-	75%	-	40%	-
Symptom duration, months	13 (7)	-	12 (7)	-	12 (5)	-
HLA-B27 +	81%	-	58%	-	80%	-
Family history of SpA	8	9	4	5	3	4
Inflammatory back pain§	14	15	7	8	5	5
Good response to NSAIDs	4	10	5	7	3	4
Peripheral manifestations	4	8	2	3	1	2
Extra-musculoskeletal manifestations	4	6	4	5	0	1
Increased acute phase reactants§	4	4	1	3	2	2
SI-CR§	0	0	1	2	0	1
SI-MRI§	3	8	3	5	0	1
Nr of SpA features#	3 (1)	5 (2)	3 (1)	4 (2)	3 (1)	5 (1)
ASAS classification criteria at 2y	-	81%	-	58%	-	80%

Data presented as mean (SD), % or n of patients§local data; #including HLA-B27 and imaging; **BL –** baseline; **SI-CR/MRI –** sacroiliitis on radiographs/MRI

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OP0055

ASAS CONSENSUS DEFINITION OF EARLY AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis

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Background: There is a growing interest in understanding the early disease stages of axial and peripheral SpA (axSpA and pSpA). In order to facilitate this, standardized definitions are needed for research purposes.
Objectives: To develop a consensual definition for the terms "early axSpA" and "early pSpA" in the research setting under the auspices of the Assessment of SpondyloArthritis international Society (ASAS).
Methods: The ASAS-SPEAR (SPondyloarthritis EARly definition) steering committee convened an international working group (WG). Five consecutive steps were followed: i) Systematic literature review (SLR) to identify existing definitions of early axSpA/pSpA and to summarize the evidence on the relationship between early treatment and clinical response in SpA[1,2]; ii) Discussion of SLR results within the WG and ASAS community (2022 annual meeting); iii) A three-round Delphi survey (Apr-Nov 2022) inviting all ASAS members to select the items that should be considered for the definition of the terms (using a Likert scale 1-9). In total, 20 items relating to three different aspects (axial symptoms, duration of symptoms and radiographic damage involvement) were voted on. Consensus was defined as acceptance or rejection if ≥70% of responses fell within 7-9 or 1-3 on the Likert scale, respectively; iv) Presentation of Delphi survey results to the WG and later to the ASAS community; v) Final discussion, voting and endorsement by ASAS members (2023 annual meeting).
Results: After discussing the results of the SLR[1,2] (step i) with the ASAS community, consensus was to proceed with an expert-based consensual definition for early axSpA (81% full ASAS members voted in favor) but not for pSpA (54% voted against) (step ii). Importantly, it was decided that the definition should be based on the symptom duration (91% in favor) taking solely axial symptoms into account (77% in favor). A total of 151-164/209 (72-78%) ASAS members participated in the Delphi survey rounds (step iii). Consensus was achieved to define early axSpA as a duration of symptoms of ≤2 years. Relating to axial symptoms, consensus was reached for acceptance of 6 items (axial symptoms should include cervical pain, thoracic pain, back pain, buttock pain and morning stiffness and be defined by a rheumatologist) and rejection of 2 items (should not include shoulder pain and hip pain). In addition, consensus was achieved to define early axSpA regardless of the presence/absence of radiographic damage (Table 1). Following the discussion of the Delphi survey results the WG agreed that in patients with a diagnosis of axSpA **"early axSpA" should be defined as a duration of ≤2 years of axial symptoms. Axial symptoms should include spinal/buttock pain or morning stiffness and should be considered by a rheumatologist as related to axSpA, Figure 1.** The WG proposal was discussed and endorsed by the ASAS community with 88% full ASAS members voting in favor (step v).
Conclusion: Early axSpA has for the first time been defined based on expert consensus. This ASAS definition should be used in research studies addressing early axSpA.
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Funding: The Assessment of Spondyloarthritis international Society (ASAS) supported the ASAS- SPEAR (ASAS-SPondyloarthritis EARly definition) project.

Table 1. Delphi survey final results to select radiographic damage involvement items to define early axial spondyloarthritis.

	Third round (n=151)	
	Level of agreement: Likert scale (1-9)	
	1-3	7-9
A patient with axSpA with axial symptoms ≤2 years has early axSpA regardless of the presence or absence of radiographic damage of the SIJ	13%	76%
A patient with axSpA with axial symptoms ≤2 years has early axSpA regardless of the presence or absence of syndesmophytes on x-rays of the spine	20%	70%

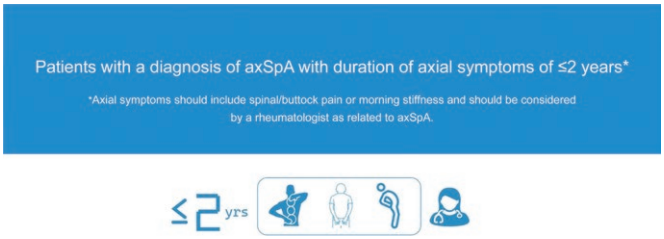


Figure 1. ASAS definition of early axial spondyloarthritis

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OP0056 SENSITIVITY TO CHANGE OF STRUCTURAL LESIONS IN EARLY AXIAL SPONDYLOARTHRITIS AFTER 10 YEARS OF FOLLOW UP. DATA FROM DESIR COHORT

Keywords: Spondyloarthritis, Imaging

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Background: The change over time of the structural damage of axial spondyloarthritis (axSpA) is important to consider since it may reflect the severity of the disease. In axSpA this structural damage can be evaluated either at the sacroiliac joints (SIJ) or spine level, and also either on conventional radiographs or Magnetic Resonance Imaging (MRI).
Objectives: To evaluate the sensitivity to change of different structural imaging outcomes over 10 years of follow-up in patients with early axSpA.
Methods: Patients with early onset (≤3 years) axSpA (according to the treating rheumatologist) from the DESIR cohort were included. Radiographs and MRI of the SIJ and spine were obtained at baseline, 1, 2, 5 and 10 years in 4 separate reading waves. Images were scored by 3 trained central readers (wave 1 only 2 readers with one adjudicator) unaware of chronology. The yearly rate of change (ROC) of each outcome was analyzed using generalized estimation equations (GEEs) including all patients with ≥1 score from ≥1 reader from ≥1 wave and using time (years) as explanatory variable. All outcomes (see the list on Table 1) were standardized (difference between the individual's value and the population mean divided by the population SD). In addition, the relative standardized ROC (i.e., the standardized yearly ROC of an outcome divided by the corresponding rate of a reference imaging outcome) was calculated, with a value >1 reflecting larger sensitivity, and <1 lower sensitivity compared to the reference. Finally, the relative standardized ROC per anatomic site was calculated.
Results: Among all locations and modalities, the change in ≥3 fatty lesions was the outcome with the highest sensitivity to change (standardized ROC 0.073 per year). Considering as reference the modified New York criteria (mNY), the two most sensitive to change outcomes in SIJ (taking into account both MRI and radiographs) were ≥3 fatty lesions and the absolute number of fatty lesions on MRI (relative standardized ROC per year 4.867 and 4.130, respectively). Similarly, the most sensitive to change lesion in the spine (both MRI and radiographs) was the mSASSS score (relative standardized ROC per year 1.778) considering ≥1 syndesmophyte as the reference.
Conclusion: MRI structural outcomes in the SIJ, in particular fatty lesions, are more sensitive to change than radiographic outcomes. On the other hand, mSASSS remains the most sensitive method, even if compared to MRI of the spine.

Table 1. Sensitivity of change of the structural lesions.

	Standardized ROC per year	Relative standardized ROC	Relative standardized ROC per anatomic site
Pelvic radiographs			
mNY dichotomous	0.015	1 (reference)	1 (reference)
mNY 1-grade change	0.017	1.133	1.133
mNY 1-grade change and value >=2	0.011	0.733	0.733
mNY continuous grade (range 0-8)	0.016	1.067	1.067
MRI of the SIJ			
≥5 fatty lesions and/or erosions	0.053*	3.533	3.533
≥3 erosions	0.010	0.667	0.667
≥3 fatty lesions	0.073*	4.867	4.867
No. of erosions (range 0-40)	0.012	0.800	0.800
No. of fatty lesions (range 0-40)	0.062*	4.130	4.130
Total structural lesions without sclerosis (range 0-104)	0.031	2.067	2.067
Spine radiographs			
≥ 1 syndesmophyte	0.027	1.800	1 (reference)
mSASSS score (range 0-72)	0.048	3.200	1.778
MRI of the spine			
≥5 fatty lesions	-0.036*	2.400	1.333
Total structural lesions (range 0-322)	0.037	2.460	1.370
No. of fatty lesions (range 0-92)	0.035	2.330	1.296
No. of corner erosions (range 0-92)	0.018	1.200	0.667

*Quadratic distribution

REFERENCES: NIL.
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OP0057

FACTORS ASSOCIATED WITH ACHIEVING REMISSION IN PATIENTS WITH EARLY PERIPHERAL SPONDYLOARTHRITIS: 10-YEAR RESULTS FROM THE GERMAN SPONDYLOARTHRITIS INCEPTION COHORT (GESPIC)

Keywords: Epidemiology, Registries, Spondyloarthritis

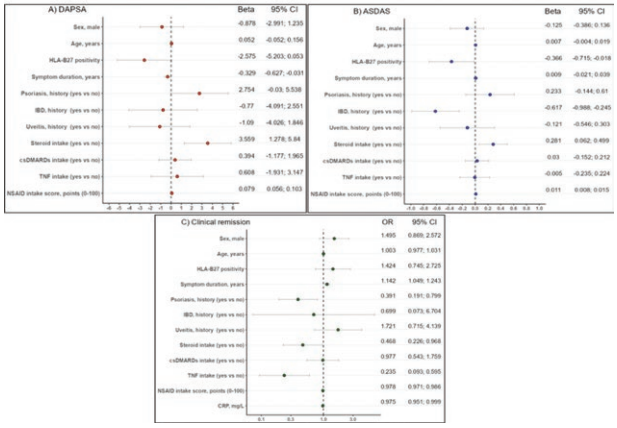
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Background: Depending on leading manifestation, Spondyloarthritis (SpA) is classified as axial (axSpA) or peripheral SpA (pSpA). Achieving of remission/inactive disease is key goal in treatment of SpA, including pSpA. Results from recent worldwide ASAS PerSpA study showed that nearly 10% of SpA patients were identified as having pSpA (as opposed to other forms of SpA) by rheumatologist, but there are still no long-term observational studies focusing on outcomes including disease activity/remission in pSpA.
Objectives: To investigate factors associated with disease activity and achievement of remission over a period of up to 10 years of clinical observation in early pSpA patients.
Methods: Data from patients diagnosed with pSpA in GESPIC (with predominant peripheral manifestations, symptom duration of up to 5 years and not classified as axSpA) according to rheumatologist were used for this study. Visits were scheduled every 6 months for 2 years, then annually up to year 10. Clinical characteristics, examination (arthritis, enthesitis), and activity (questionnaires and laboratory) were collected at visits. Association between parameters and disease activity/remission [defined by Disease Activity in Psoriatic Arthritis (DAPSA), Axial SpA Disease Activity Score (ASDAS), and clinical remission (complete absence of arthritis or enthesitis)], was analysed by generalized estimating equations (GEE).
Results: The mean age of 115 pSpA patients (51.3% male) was 37.3 ± 12.2 years, and 71 (61.7%) patients were HLA-B27 positive. Baseline DAPSA and ASDAS were 13.3 ± 8.1 and 2.4 ± 0.9. During follow up 48 (41.7%), 46 (41.7%), and 94 (81.9%) patients reached at least once DAPSA remission (DAPSA <4), ASDAS-Inactive disease (ASDAS<1.3), and clinical remission, respectively. In univariable analyses, female sex, older age, HLA-B27 negativity, current and history of psoriasis, steroid, csDMARDs and higher NSAID intake were associated with higher DAPSA and lower odds of remission. Similar results were observed regarding ASDAS and clinical remission (Table 1). Multivariable analyses showed that history of psoriasis, HLA-B27 negativity, steroid intake, and higher NSAID intake were associated with higher DAPSA and ASDAS scores (Figure 1A,B), while longer symptom duration, psoriasis history, steroid, TNFi and higher NSAID intake, and higher CRP were associated with lower odds of remission (Figure 1C).
Conclusion: Several parameters associated with higher disease activity and absence of remission were identified. Psoriasis and higher CRP were associated with lower odds of achieving clinical remission, while an association with drug usage is likely a consequence of high disease activity.

Table 1. Univariable GEE analysis of association between clinical parameters and disease activity/remission.

	DAPSA	ASDAS	Clinical Remission
	B (95% CI)	**β (95% CI)**	**OR (95% CI)**
Male Sex	-2.12(-4.69;0.46)	-0.29(-0.63;0.05)	1.54(0.96;2.47)
Age	**0.12(0.03;0.21)**	**0.02(0.01;0.03)**	1.00(0.98;1.02)
HLA-B27 Positivity	**-3.95(-6.46;-1.45)**	**-0.56(-0.90;-0.23)**	**1.63(1.01;2.62)**
Symptom duration	-0.27(-0.60;0.05)	0.01(-0.03;0.05)	**1.14(1.03;1.26)**
Current psoriasis	**4.29(1.34;7.23)**	**0.39(0.05;0.73)**	**0.27(0.13;0.53)**
Ever psoriasis	**3.13(-0.01;6.26)**	0.38(-0.03;0.79)	0.67(0.38;1.18)
Current IBD	-0.79(-2.66;1.08)	**-0.73(-1.01;-0.46)**	0.26(0.03;2.01)
Ever IBD	-0.94(-5.31;3.43)	**-0.67(-1.00;-0.34)**	0.65(0.11;3.93)
Current Uveitis	3.68(-4.64;12.00)	0.54(-0.61;1.70)	0.28(0.05;1.59)
Ever uveitis	-2.81(-6.62;1.00)	-0.31(-0.86;0.24)	**1.74(0.99;3.07)**
CRP, mg/L	**0.15(0.12;0.19)**	**0.03(0.02;0.03)**	**0.96(0.93;0.99)**
Steroid intake	**3.96(1.62;6.30)**	0.25(-0.02;0.52)	**0.35(0.19;0.66)**
csDMARDs intake	1.52(-0.25;3.29)	0.05(-0.17;0.27)	**0.48(0.31;0.75)**
TNF intake	-0.50(-3.17;2.18)	-0.13(-0.48;0.22)	**0.37(0.16;0.82)**
NSAID intake score, (0-100)	**0.08(0.06;0.11)**	**0.01(0.01;0.01)**	**0.97(0.97;0.98)**

Figure. Multivariable GEE analyses show associations between parameters and outcomes A) DAPSA, B) ASDAS, and C) Clinical remission.



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OP0058 PREDICTION OF LOW DISEASE ACTIVITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH SECUKINUMAB IN REAL WORLD – DATA FROM THE GERMAN AQUILA STUDY

Keywords: Real-world evidence, Spondyloarthritis, Artificial Intelligence

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Background: Secukinumab (SEC) proved to be an effective treatment for patients suffering from ankylosing spondylitis (AS) in randomized clinical trials [1]. There is only limited knowledge on prediction of low disease activity (LDA) and treatment strategy in AS patients under SEC treatment in routine clinical care.
Objectives: Using real-world data from the German non-interventional study AQUILA [2], the main objectives were (1) to predict LDA in individual AS patients treated with SEC through machine learning methods and (2) to identify the most important predictors and their influence on the prediction using explainable artificial intelligence (XAI).
Methods: Data of 580 AS patients from the AQUILA study were used. Thirty-two demographic, clinical and treatment parameters at baseline (BL) served as input data to develop prediction models. LDA was defined as Bath ankylosing spondylitis disease activity index (BASDAI) ≤ 2.0 at week (w) 16 (+/- 6 w). Samples were divided into training (70%) and validation (30%) cohorts. Ten different prediction models were applied and compared. Model performance was measured using area under the receiver operating characteristic curve (AUROC) which represents the probability that a randomly selected patient with LDA will have higher prediction to achieve LDA than a patient with moderate/high disease activity. Additionally, sensitivity and specificity of the prediction model were computed and express the proportion of correctly identified patients who reach or don't reach LDA at w16, respectively. Shapley XAI estimated importance and impact of each predictor based on how it affected the change in individual prediction [3].
Results: The most influencing predictor was BASDAI at BL, followed by the number of pretreatments with biologics, C-reactive protein (CRP), assessment of spondyloarthritis international society health index (ASAS-HI) and patient height (**Figure 1 A**). AUROC of the best performing prediction model was 0.84. Sensitivity and specificity were 0.87 and 0.67, respectively. Applied XAI approach showed that the lower the BL values of BASDAI, ASAS-HI and number of pretreatments with biologics were, the higher the probability of reaching LDA at w16 was. The opposite was the case for BL values of CRP and body height (**Figure 1 A**). The approach also provided visual explanations of patient-individual predictions: Variables with values shown in green color increased probability of reaching LDA at w16, whereas red ones showed the opposite effect (**Figure 1 B**).
Conclusion: A promising prediction model accuracy of LDA in AS patients treated with SEC could be reached and validated. Identified main predictors at BL, such as BASDAI and number of pretreatments with biologics, and their direction of influence on the prediction of LDA mostly match the existing clinical knowledge [4]. The analysis showed that XAI can provide useful clinical insights into patient-individual predictions, potentially guiding AS treatment decisions in future.
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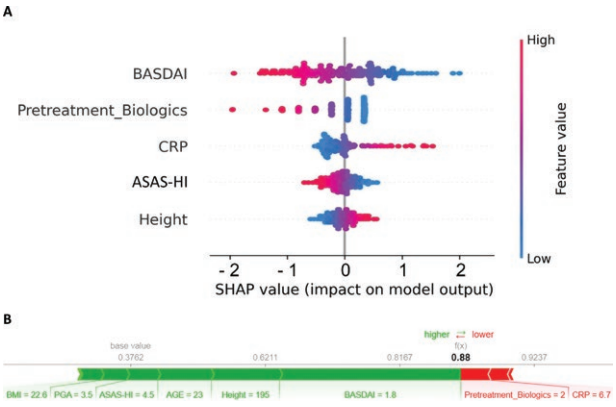


Figure 1. Main results

A: Main predictors at baseline and their direction of influence based on Shapley values [3]

B: Explanation of patient-individual prediction of 88% using baseline data

Assessment of spondyloarthritis international society health index (ASAS-HI), Bath ankylosing spondylitis disease activity index (BASDAI), body mass index (BMI), C-reactive protein (CRP), patient global assessment (PGA), Shapley Additive exPlanations (SHAP)
Acknowledgements: NIL.
Disclosure of Interests: Asmir Vodencarevic Employee of: Novartis Pharma GmbH, Jan Brandt-Juergens Consultant of: Abbvie, Affibody, BMS, Gilead, Janssen, Lilly, Medac, MSD, Novartis, Pfizer, Roche, Sanofi-Aventis, UCB, Daniel Peterlik Employee of: Novartis Pharma GmbH, Benjamin Gmeiner Employee of: Novartis Pharma GmbH, Uta Kiltz Consultant of: AbbVie, Amgen, Biogen, Chugai, Eli Lilly, Gilead, GSK, Grünenthal, Hexal, Janssen, MSD, Novartis, Pfizer, Roche, UCB, Grant/research support from: AbbVie, Amgen, Biogen, Chugai, Eli Lilly, Gilead, GSK, Grünenthal, Hexal, Janssen, MSD, Novartis, Pfizer, Roche, UCB.
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OP0059 EFFECT OF SECUKINUMAB VERSUS ADALIMUMAB BIOSIMILAR ON RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: A RANDOMISED PHASE IIIB STUDY

Keywords: Randomized control trial, Spondyloarthritis, Clinical Trials

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Background: Limited data exist on the effect of biologics in slowing radiographic progression in patients (pts) with radiographic axial spondyloarthritis (r-axSpA). Two-year data from MEASURE 1 showed low radiographic progression with secukinumab (SEC).[1]

Objectives: To compare the effect of SEC vs adalimumab biosimilar (SDZ-ADL) on spinal radiographic progression from SURPASS,[2,3] the first head-to-head study in r-axSpA.

Methods: In this phase IIIb study, bio-naïve pts with active r-axSpA with a BASDAI ≥4, spinal pain score ≥4 (range 0–10), total back pain score ≥40 mm (range 0–100 mm), and with hs-CRP ≥5 mg/L or ≥1 syndesmophyte(s) on spinal radiograph were randomised (1:1:1) to SEC (150/300 mg; dose-blinded) or SDZ-ADL (40 mg; open label). Radiographs and MRIs were reviewed by 3 independent central readers (no adjudication performed) blinded to treatment and chronology of images. Primary endpoint was the proportion of pts with no radiographic progression (change from baseline [CFB] in modified Stoke AS Spinal Score [mSASSS] ≤0.5) on SEC vs SDZ-ADL at week (wk) 104 (superiority testing). Secondary endpoints included CFB-mSASSS at wk 104, proportion of pts with ≥1 syndesmophyte(s) at baseline (BSL) with no new syndesmophytes(s) at wk 104, CFB-MRI Berlin sacroiliac joint (SIJ) inflammation score, CFB-AS Spine MRI-activity (ASspiMRI-a) Berlin modification score, and safety.

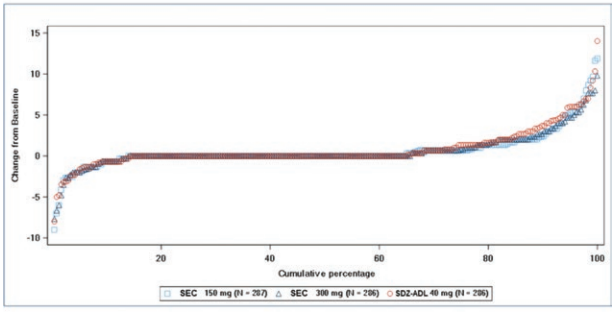
Results: Overall, 859 pts received SEC 150 mg (n=287), 300 mg (n=286), or SDZ-ADL (n=286). With 78.5% male, mean age 42.1 years, mSASSS 16.6, BASDAI 7.1, hsCRP 20.4 mg/L, and 73% with ≥1 syndesmophyte(s), this population had high risk of radiographic progression. At wk 104, cumulative distribution of CFB-mSASSS was similar across arms (**Figure 1**). Proportion of pts with no radiographic progression was 66.1%, 66.9%, and 65.6% (*P*=ns, both SEC doses) while mean CFB-mSASSS was 0.54, 0.55, and 0.72 with SEC 150 mg, 300 mg, and SDZ-ADL. Overall, 56.9%, 53.8%, and 53.3% of pts in SEC 150 mg, 300 mg, and SDZ-ADL arms, with a BSL ≥1 syndesmophyte(s) did not develop new syndesmophyte(s) by wk 104 (**Table 1**). In the MRI sub-set (N=418), mean SIJ scores at BSL and wk 16 were 2.54 and 0.98 (SEC 150 mg), 1.96 and 0.92 (SEC 300 mg), and 1.59 and 0.38 (SDZ-ADL); corresponding spine scores were 3.50 and 1.79, 2.56 and 1.25, and 3.00 and 0.71.

Conclusion: Spinal radiographic progression over 2 years was low with no significant difference between SEC and SDZ-ADL arms. No new safety signals were identified.

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Figure 1. Probability plot of change from BSL in mSASSS at wk 104



mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; SDZ-ADL, adalimumab biosimilar; SEC, secukinumab

Table 1. Radiographic assessments at wk 104

No radiographic progression*	Treatment group	n	No progression rate (%)	Estimated mean (95% CI)	Marginal difference (95% CI)†	Nominal *P*-value
	SEC 150 mg	283	66.1	66.63 (60.73, 72.54)	1.51 (–6.63, 9.64)	0.716
	SEC 300 mg	280	66.9	66.80 (60.45, 73.14)	1.67 (–6.61, 9.95)	0.693
	SDZ-ADL 40 mg	283	65.6	65.13 (58.77, 71.49)	-	-
Change from BSL in mSASSS#	**Treatment group**	**n**	**Within treatment**		**Treatment contrast in LS mean†**	
			LS mean (SE)		**LS mean (SE)**	**95% CI**
	SEC 150 mg	283	0.54 (0.18)		–0.18 (0.24)	–0.65, 0.29
	SEC 300 mg	280	0.55 (0.18)		–0.16 (0.24)	–0.64, 0.32
	SDZ-ADL 40 mg	283	0.72 (0.18)		-	-
No new syndesmophytes*‡	**Treatment group**	**n (%)‡**	**Pts with no new syndesmophyte(s) (%)**		**Estimated mean (95% CI)**	**Marginal difference (95% CI)†**
	SEC 150 mg	211 (73.5)	56.9		57.22 (50.16, 64.28)	4.32 (–5.62, 14.27)
	SEC 300 mg	204 (71.3)	53.8		53.98 (46.19, 61.78)	1.09 (–9.13, 11.31)
	SDZ-ADL 40 mg	212 (74.1)	53.3		52.89 (45.54, 60.24)	-

SEC 150 mg, N=287; SEC 300 mg, N=286; SDZ-ADL 40 mg, N=286.
*Estimated mean, marginal difference, 95% CI, and p-value are from logistic regression model with treatment as a factor and BSL mSASSS score/count of vertebral corners with syndesmophyte as covariate using marginal standardisation method.
#LS Mean and 95% CI are from ANCOVA model with treatment as a factor and BSL mSASSS score as covariate.
†Comparison vs SDZ-ADL 40 mg.
‡pts with syndesmophyte(s) at BSL

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and UCB, Grant/research support from: AbbVie, Biocad, Biogen, Chugai, Eli Lilly, Fresenius, GSK, Grünenthal, Hexal, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Marco Eigenmann Shareholder of: Novartis, Employee of: Novartis, Patricia Pertel Shareholder of: Novartis, Employee of: Novartis, Aimee Readie Shareholder of: Novartis, Employee of: Novartis, Hanno Richards Shareholder of: Novartis, Employee of: Novartis, Brian Porter Shareholder of: Novartis, Employee of: Novartis, Juergen Braun Consultant of: Personal fees from: Abbvie, Amgen, Boehringer, Celltrion, MSD, Novartis, UCB, and Eli Lilly.
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OP0060 CLINICAL CONSEQUENCES OF INFLIXIMAB IMMUNOGENICITY AND THE IMPACT OF THERAPEUTIC DRUG MONITORING: SECONDARY ANALYSES OF A RANDOMISED CLINICAL TRIAL

Keywords: Rheumatoid arthritis, bDMARD, Spondyloarthritis

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Background: Neutralising anti-drug antibodies (ADAb) are a problem in treatment with TNF-inhibitors (TNFi). Prospective data are needed to better understand how ADAb formation impacts safety and treatment outcomes of TNFi. Proactive therapeutic drug monitoring (TDM) allows for timely detection of ADAb and this strategy may have a role in reducing the negative clinical consequences of ADAb.
Objectives: To explore the temporal relation between anti-infliximab antibody formation and treatment outcomes and adverse events, and to assess the impact of TDM as a strategy to reduce these consequences.
Methods: Patients with immune mediated inflammatory diseases on infliximab therapy (n=615; 181 spondyloarthritis, 120 rheumatoid arthritis, 72 psoriatic arthritis, 114 ulcerative colitis, 83 Crohns disease and 45 psoriasis) were included in the Norwegian Drug Monitoring (NOR-DRUM) trials (1, 2) and randomised to TDM or standard infliximab therapy. Patients were followed for 30 and 52 weeks in the NOR-DRUM A (induction therapy) and NOR-DRUM B (maintenance therapy) trials, respectively. Neutralising ADAb were assessed with a drug sensitive automated fluorescence assay at each infusion. In this sub-study, we assessed the risk of; failure to achieve remission (analysis A), disease worsening during maintenance therapy (analysis B), treatment discontinuation (analysis C) and adverse events (analysis D) in patients developing ADAb compared to patients without ADAb using logistic- or cox regression and Kaplan-Meier survival analyses, stratified by TDM or standard therapy. Regression analyses were adjusted for potential confounders (Table 1). Remission and disease worsening were defined by disease specific composite scores (1, 2).
Results: ADAb were detected in 147/615 (24 %) patients. Patients with ADAb had higher risk of not achieving remission 30 weeks after initiating infliximab therapy (odds ratio (OR) 2.4, 95 % confidence interval (CI) 1.3-4.2, P<0.01) (Table 1, Figure 1A) and of having a disease worsening during 52 weeks of infliximab maintenance therapy (hazard ratio (HR) 2.1, CI 1.4-3.3, P<0.001) (Figure 1B). ADAb formation was not significantly associated with adverse events in general, but the risk of infusion reactions was highly increased in patients with ADAb (HR 29, CI 11-78, P<0.001). The risk of infliximab treatment discontinuation was increased in ADAb positive patients (HR 6.5, CI 4.7-8.9, P<0.001). Patients developing ADAb in the TDM group had lower risk of disease worsening or an infusion reaction than patients with ADAb in the standard infliximab therapy group (Table 1, Figure 1B and C). Patients with ADAb discontinued infliximab treatment more often in the TDM group than in the control group (Table 1, Figure 1D).
Conclusion: Formation of ADAb led to poorer clinical outcomes both during induction and maintenance therapy with infliximab and increased the risk of infusion reactions. Early detection of ADAb by proactive TDM reduced the negative consequences of ADAb, both on infliximab effectiveness and safety, highlighting the role of proactive TDM in optimising TNFi therapy.
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Table 1. Treatment and safety outcomes related to ADAb formation and TDM

Analysis A) Non-remission	**OR (CI)**	**P**
ADAb	2.4 (1.3-4.2)	<0.01
TDM	1.0 (0.7-1.5)	0.9
Analysis B) Disease worsening	**HR (CI)**	**P**
ADAb	2.1 (1.4,3.2)	<0.01
TDM	0.4 (0.3-0.6)	<0.001
Analysis C) Infusion reaction	**HR (CI)**	**P**
ADAb	29 (11-78)	<0.001
TDM	0.3 (0.1-0.7)	<0.01
Analysis D) Treatment discontinuation	**HR (CI)**	**P**
ADAb	6.5 (4.7-8.9)	<0.001
TDM	1.4 (1.0-1.8)	0.03

Results from multivariable logistic (A)- or cox (B-D) regression models including the covariates: ADAb, TDM, age, sex, diagnosis, comedication. Results shown in table are risk of A) non-remission week 30, B) disease worsening during 52 weeks of maintenance therapy, C) infusion reactions and D) infliximab treatment discontinuation for patients developing ADAb and for patents in the TDM group.

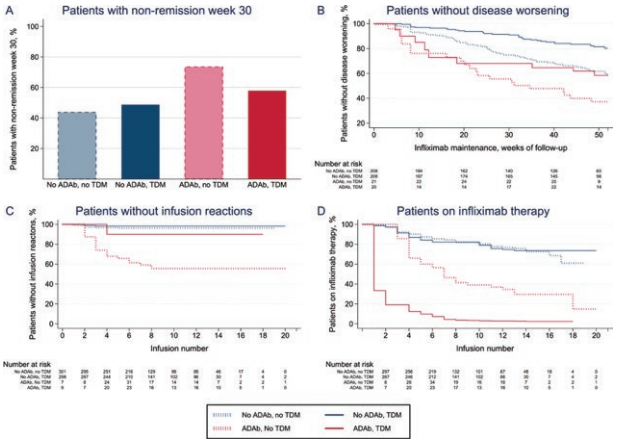


Figure 1.

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OP0061 DEVELOPMENT OF EXTRA-MUSCULOSKELETAL MANIFESTATIONS IN UPADACITINIB-TREATED PATIENTS WITH PSORIATIC ARTHRITIS, ANKYLOSING SPONDYLITIS, OR NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

Keywords: Uveitis, Safety, Spondyloarthritis

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Background: Extra-musculoskeletal manifestations (EMMs) are common in patients with spondyloarthritis (SpA), but there are limited data on the impact of upadacitinib (UPA), an oral JAK inhibitor, on EMMs in SpA patients.
Objectives: To assess the development of EMMs among patients with PsA, AS, or non-radiographic axial spondyloarthritis (nr-axSpA) treated with UPA 15 mg (UPA15) or placebo (PBO) in the SELECT clinical trial program.
Methods: This analysis includes safety data from UPA trials in PsA (2 trials),[1,2] AS (2 trials),[3,4] and nr-axSpA (1 trial).[5] All trials were designed with initial randomization to UPA or PBO for a pre-specified number of weeks, followed by a second open-label extension where PBO-treated patients were switched to UPA. Treatment-emergent adverse events (TEAEs) of EMMs, including uveitis, inflammatory bowel disease (IBD), and psoriasis, were assessed; as psoriasis is considered a core manifestation of PsA, it was only evaluated as an EMM in AS and nr-axSpA.[6] TEAEs were defined as an AE with onset on or after first dose of study drug and ≤30 days after last dose and summarized for PsA (pooled PBO to week 24 and pooled UPA15 to data cut-off [15 Aug 2022]), AS (pooled PBO to week 14 and pooled UPA15 to data cut-off), and nr-axSpA (PBO to week 52 and UPA15 to data cut-off). EMMs are reported as exposure-adjusted event rates (EAERs; events/100 patient years [E/100 PY]) and are stratified by patients with a reported history (flare) of the respective EMM vs those without a history (new onset).
Results: The vast majority (92-99%) of patients across PsA, AS, and nr-axSpA did not have a prior history of EMMs at baseline (**Table 1**). In PsA, development of uveitis and IBD were low regardless of treatment or prior history (**Figure 1**). In AS, development of uveitis was numerically higher (E/100 PY [95% CI]) in patients treated with PBO (total: 7.5 [2.7, 16.3]) vs UPA15 (total: 2.8 [1.8, 4.1]) and in patients with a prior history of uveitis (PBO: 6.2 [2.0, 14.5], UPA15: 2.1 [1.3, 3.3]) vs no prior history (PBO: 1.2 [0.0, 6.9]; UPA15: 0.6 [0.2, 1.4]); occurrence of IBD and psoriasis were low regardless of treatment or prior history. In nr-axSpA, development of uveitis was low regardless of prior history, while the total rate was numerically higher in patients treated with PBO (2.1 [0.4, 6.3]) vs UPA15 (0.9 [0.2, 2.7]); occurrence of IBD and psoriasis were low or absent.
Conclusion: Data from this post-hoc analysis describe adverse events of relevant EMMs in the SELECT program and should be interpretated with caution as the efficacy of UPA in patients with specific EMMs was not systematically evaluated, as well as the overall low number of events observed. Development of EMMs in patients treated with UPA15 was generally low across PsA, AS, and nr-axSpA. Uveitis was numerically higher in patients treated with PBO vs UPA, and particularly in patients with AS. A better understanding of the impact of UPA across EMMs in SpA, and subsequent follow-up analyses, may help clinicians make informed treatment decisions and guide future treatment recommendations.

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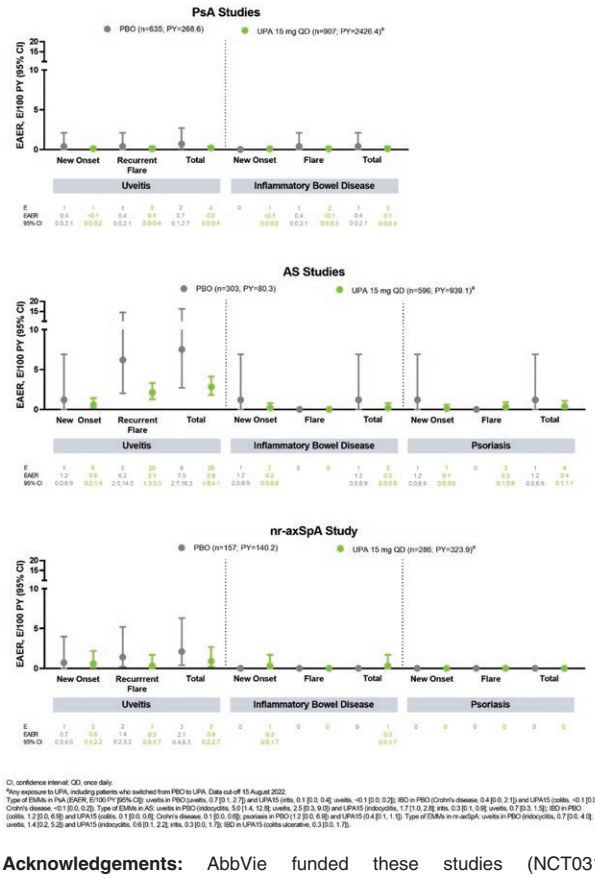
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Table 1. Prior History of EMMs Reported at Baseline in Patients Treated With UPA Across PsA, AS, and nr-axSpA

	PsA		AS		nr-axSpA	
EMM, n (%)	**PBO n=635**	**UPA 15 mg QD[a] n=907**	**PBO n=303**	**UPA 15 mg QD[a] n=596**	**PBO n=157**	**UPA 15 mg QD[a] n=286**
Uveitis	5 (0.8)	8 (0.9)	23 (7.6)	49 (8.2)	11 (7.0)	21 (7.3)
Inflammatory bowel disease	10 (1.6)	13 (1.4)	7 (2.3)	16 (2.7)	6 (3.8)	8 (2.8)
Psoriasis	N/A[b]	N/A[b]	10 (3.3)	19 (3.2)	4 (2.5)	7 (2.4)

N/A, not applicable; QD, once daily; UPA.
[a]Any UPA exposure, including patients who switched from PBO to UPA.
[b]As psoriasis is considered a core manifestation of PsA, it was only evaluated as an EMM in AS and nr-axSpA.

Figure. Development of EMMs by Prior History in Patients Treated With UPA Across PsA, AS, and nr-axSpA



CI, confidence interval; QD, once daily.
[a]Any exposure to UPA, including patients who switched from PBO to UPA. Data cut-off 15 August 2022.
Type of EMMs in PsA (EAER, E/100 PY [95% CI]): uveitis in PBO (uveitis, 0.7 [0.1, 2.7]) and UPA15 (uveitis, 0.1 [0.0, 0.4]; uveitis, <0.1 [0.0, 0.2]); IBD in PBO (Crohn's disease, 0.4 [0.0, 2.1]) and UPA15 (colitis, <0.1 [0.0, 0.3]; Crohn's disease, <0.1 [0.0, 0.2]). Type of EMMs in AS: uveitis in PBO (iridocyclitis, 5.0 [1.4, 12.8]; uveitis, 2.5 [0.3, 9.0]) and UPA15 (iridocyclitis, 1.7 [1.0, 2.8]; iritis, 0.3 [0.1, 0.9]; uveitis, 0.7 [0.3, 1.5]); IBD in PBO (colitis, 1.2 [0.0, 6.9]) and UPA15 (colitis, 0.1 [0.0, 0.6]). Crohn's disease, 0.1 [0.0, 0.6]); psoriasis in PBO (1.2 [0.0, 6.9]) and UPA15 (0.4 [0.1, 1.1]). Type of EMMs in nr-axSpA: uveitis in PBO (iridocyclitis, 0.7 [0.0, 4.0]; uveitis, 1.4 [0.2, 5.2]) and UPA15 (iridocyclitis, 0.6 [0.1, 2.2]; iritis, 0.3 [0.0, 1.7]); IBD in UPA15 (colitis ulcerative, 0.3 [0.0, 1.7]).

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Disclosure of Interests: Denis Poddubnyy Speakers bureau: AbbVie, Biocad, BMS, Galapagos, Gilead, GSK, Janssen, Lilly, MSD, Medscape, MoonLake, Novartis, Peervoice, Pfizer, Roche, Samsung Bioepis, and UCB, Consultant of: AbbVie, Biocad, BMS, Galapagos, Gilead, GSK, Janssen, Lilly, MSD, Medscape, MoonLake, Novartis, Peervoice, Pfizer, Roche, Samsung Bioepis, and UCB, Grant/research support from: AbbVie, Lilly, MSD, Novartis, and Pfizer, Bhumik Parikh Shareholder of: Employee of AbbVie and may hold stock or options, Employee of: AbbVie, Dirk Elewaut Speakers bureau: AbbVie, Consultant of: AbbVie, Victoria Navarro-Compán Speakers bureau: AbbVie, BMS, Galapagos, Janssen, Lilly, MoonLake, MSD, Novartis, Pfizer, Roche, and UCB, Consultant of: AbbVie, BMS, Galapagos, Janssen, Lilly, MoonLake, MSD, Novartis, Pfizer, Roche, and UCB, Grant/research support from: AbbVie, BMS, Galapagos, Janssen, Lilly, MoonLake, MSD, Novartis, Pfizer, Roche, and UCB, Stefan Siebert Speakers bureau: AbbVie, Amgen, Eli Lilly, GSK, Janssen, and UCB, Consultant of: AbbVie, Amgen, Eli Lilly, GSK, Janssen, and UCB, Grant/research support from: Amgen, Boehringer-Ingelheim, BMS, Eli Lilly, GSK, Janssen and UCB, Michael Paley Consultant of: AbbVie and Priovant Therapeutics, Grant/research support from: Lilly, Derek Coombs Shareholder of: Employee of AbbVie and may hold stock or options, Employee of: AbbVie, Reva McCaskill Shareholder of: Employee of AbbVie and may hold stock or options, Employee of: AbbVie, Ana Biljan Shareholder of: Employee of AbbVie and may hold stock or options, Employee of: AbbVie, Peter Wung Shareholder of: Employee of AbbVie and may hold stock or options, Employee of: AbbVie, Ennio Lubrano Speakers bureau: AbbVie, Celgene, Galapagos, Janssen, MSD, Novartis, and Pfizer, Consultant of: AbbVie, Celgene, Galapagos, Janssen, MSD, Novartis, and Pfizer, Grant/research support from: AbbVie, Celgene, Galapagos, Janssen, MSD, Novartis, and Pfizer.
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New clinical aspects in psoriatic arthritis

OP0062

EULAR POINTS TO CONSIDER FOR THE DEFINITION OF CLINICAL AND IMAGING FEATURES SUSPICIOUS FOR PROGRESSION TO PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Clinical Trials, Skin

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Background: The transition from psoriasis (PsO) to PsA is of considerable interest for potential prevention and interception of PsA[1].
Objectives: To formulate EULAR points to consider (PtC) for the development of data-driven guidance and consensus for clinical trials and clinical practice in the field of prevention/interception of PsA.
Methods: A multidisciplinary EULAR task force of 30 European members was established and the EULAR standardized operating procedures were followed.
Results: Nomenclature was proposed for 3 stages towards PsA development: i) PsO patients at higher risk of PsA (i.e., nail disease, obesity, severe PsO); ii) subclinical PsA (those at more imminent risk of PsA for arthralgia and imaging abnormalities) and iii) clinical PsA that most typically manifests as synovitis *(Figure 1)*. For the purpose of prevention, our SLR showed that the vast majority of new PsA presented with synovitis. Thus, the presence of synovitis in PsO could be used as an outcome for prevention trials. Five overarching principles (OAPs) addressed the nature of PsA at its onset and underline the importance of collaboration between rheumatologists and dermatologists *(Table 1)*.The 10 PtC highlight arthralgia plus imaging abnormalities as key elements of subclinical PsA that can be used as potential short-term predictors of PsA development and useful criteria to design trials for PsA interception *(Table 1)*.
Conclusion: These PtC are helpful to define the features of PsO patients suspicious for progression to PsA. This information may ultimately facilitate identification of those who could benefit from a therapeutic intervention to attenuate, delay, or prevent PsA development.
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Table 1.

Overarching Principles	Level of Evidence	Level of Agreement
A.PsO patients may develop PsA at different time-points.		9.7± 0.7
B.Close collaboration between dermatologists and rheumatologists is important to understand and optimize PsA prevention, interception and early diagnosis.		9.7± 0.6
C.The identification of risk factors for PsA development in PsO patients may influence therapy choices for PsO.		8.9± 1.3
D.The rheumatologist has a key role in the diagnosis and management of PsA.		9.7± 0.6
E.Certain systemic treatments of PsO may reduce the risk of transition to PsA.		8.4± 1.8
Points to Consider		
1.Arthralgia in PsO patients should be considered as a risk factor for PsA, taking into account alternative diagnoses such as osteoarthritis and fibromyalgia.	3a	9.2± 1.3
2.In PsO patients, joint and entheseal pain and functional limitation should be enquired about regularly and, if present, referral to a rheumatologist should be considered	3b	9.3± 0.9
3.Imaging in PsO could be used to help identify those at risk for PsA; in particular to detect synovio-entheseal involvement/abnormalities	3b	9.1± 1.2
4.Imaging abnormalities in the absence of musculoskeletal symptoms should be considered carefully in order to avoid the risk of inappropriate treatment	3b	9.5± 0.9
5.The combination of musculoskeletal symptoms and imaging abnormalities in PsO, without a diagnosis of PsA, should be considered as an entry criterion for clinical trials to prevent the transition to PsA	5	8.8± 1.2
6.In the context of clinical trials, patients with PsO and clinically evident synovitis should be considered to have PsA, when alternative diagnoses have been excluded	5	9.3± 0.8
7.In PsO patients that require systemic treatment, the risk of transition to PsA should be taken into account in the choice of treatment	5	9.1± 1.3
8.PsO patients with obesity, nail disease and/or extensive PsO should be considered at increased risk for PsA over the longer term	3a	9.3± 0.9
9.PsO patients should be informed about the risk of developing PsA and prompted to report their symptoms to facilitate early PsA recognition	5	9.5± 0.8
10.In PsO patients, risk factors for PsA development should be regularly assessed over time	5	9.5± 0.8

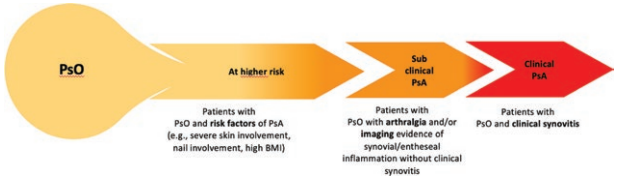


Figure 1.

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OP0063

PSA PATIENTS RECEIVING MONOTHERAPY WITH BDMARD/TSDMARD DO NOT DIFFER IN CLINICAL PARAMETERS FROM PATIENTS RECEIVING BDMARD/TSDMARD IN COMBINATION WITH MTX - DATA FROM RABBIT-SPA

Keywords: Registries, Psoriatic arthritis

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Background: While in RA, methotrexate (MTX) increases the efficacy of most biologic (b) and targeted synthetic (ts) disease modifying anti-rheumatic drugs (DMARDs), the situation in PSA may be substantially different.

Objectives: To compare clinical and patient reported baseline parameters of PsA patients starting bDMARD/tsDMARD monotherapy with those starting these treatments in combination with MTX as well as to assess the drug retention rates in the two groups.

Methods: RABBIT-SpA is a prospective longitudinal cohort study including axSpA and PsA patients enrolled at initiation of a new conventional or bDMARD/tsDMARD treatment. In this analysis, PsA patients newly enrolled at initiation of bDMARD/tsDMARD treatment were stratified into two groups: as monotherapy or in combination with MTX. Treatment retention was compared by drug survival analysis.

Results: 69% of the patients (n=833) started bDMARD/tsDMARD as monotherapy. Combination treatment with MTX was started in 31% of the patients (n=369). In 85% of the patients in the combination group, MTX had previously been given as monotherapy and treatment was then escalated with the addition of a bDMARD/tsDMARD. Baseline clinical parameters were very similar between the two groups (Table 1). No difference between the groups was found in the six different PsA domains skin, joints, dactylitis, enthesitis, nail psoriasis, and axial involvement. Only the patients´ satisfaction with tolerability of the current treatment (4 point Likert scale) was significantly better in the combination group.

Table 1. Patient characteristics by the two treatment groups

	b/tsDMARD mono	b/tsDMARD +MTX	Total
n	833	369	1202
Females, n (%)	486 (58)	213 (58)	699 (58)
Age, mean (SD)	51.9 (12.6)	52.2 (12.1)	52 (12.4)
BMI, mean (SD)	29.1 (6)	28.7 (5.9)	29 (6)
CRP mg/l, mean (SD)	7.2 (11.5)	7.6 (13.7)	7.3 (12.2)
TJC (0-68), mean (SD)	7 (8.2)	6.9 (7.6)	7 (8)
SJC (0-66), mean (SD)	3.5 (5.1)	2.8 (3.8)	3.3 (4.8)
Number of sites with enthesitis, mean (SD)	0.6 (1.6)	0.7 (1.8)	0.6 (1.7)
Dactylitis, n (%)	161 (20)	60 (16)	221 (19)
Axial manifestation, n (%)	180 (22)	76 (21)	256 (22)
Affected body surface area in %, mean (SD)	8.7 (15.8)	7.9 (13.2)	8.5 (15)
Nail psoriasis, n (%)	345 (42)	148 (40)	493 (41)
Uveitis, n (%)	18 (2)	3 (1)	21 (2)
IBD, n (%)	18 (2)	3 (1)	21 (2)
Number of comorbidities, mean (SD)	2.2 (2.3)	2.1 (2.2)	2.2 (2.3)
Physician global disease activity, mean (SD)	5.1 (1.9)	5.3 (1.9)	5.2 (1.9)
Physician skin disease activity, mean (SD)	3.3 (2.5)	3.1 (2.6)	3.2 (2.5)
DAPSA, mean (SD)	22.9 (14)	22.4 (12.9)	22.7 (13.7)
Patient global disease activity, mean (SD)	5.7 (2.4)	5.7 (2.4)	5.7 (2.4)
Patient pain, mean (SD)	5.6 (2.4)	5.6 (2.4)	5.6 (2.4)
DLQI, mean (SD)	6.4 (6.4)	4.8 (5.9)	5.9 (6.3)
HAQ, mean (SD)	1 (0.7)	0.9 (0.7)	1 (0.7)
bDMARDs before, n (%)	380 (46)	122 (33)	502 (42)
csDMARDs before, n (%)	647 (78)	332 (90)	979 (81)
MTX before, n (%)	598 (72)	325 (88)	923 (77)
Glucocorticoids, n (%)	234 (29)	125 (36)	359 (31)
Patient satisfaction with the current treatment, n (%)	260 (43)	149 (52)	409 (46)
Patient satisfaction with the tolerability of the current treatment, n (%)	349 (60)	217 (76)	566 (66)

Drug retention rates did not differ between the two groups (p=0.19; Figure 1). After 6 months, 62% of patients with combination and 58% of those receiving bDMARD/tsDMARD as monotherapy were still on their respective treatment.

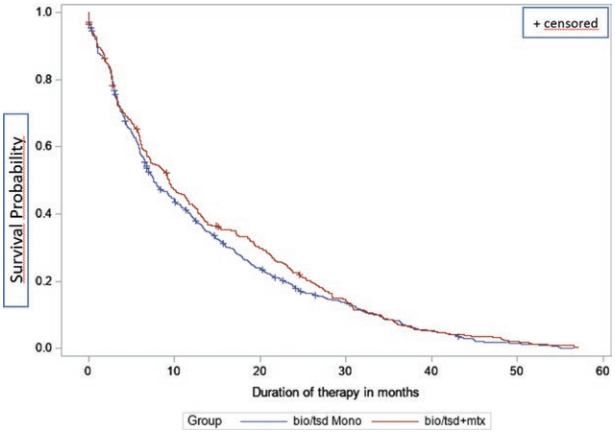


Figure 1. Drug retention rates

Conclusion: Baseline clinical parameters did not differ whether a PsA patient was started on bDMARD/tsDMARDs monotherapy or MTX-bDMARD/tsDMARDs combination. Especially parameters usually taken into account for GRAPPA or EULAR treatment recommendations, such as the number of swollen or tender joints, the number of involved enthesial sites and the severity of affected skin did not differ between the two treatment groups. Also drug retention rates were very similar. It seems that in routine care, the decision to continue or stop MTX at escalation to bDMARD/tsDMARD treatment mostly depends on the subjective tolerability of the ongoing MTX treatment.

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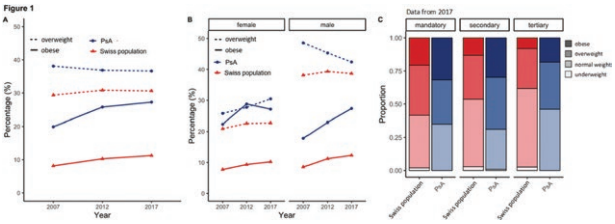
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OP0064 OBESITY IN PSORIATIC ARTHRITIS IS INCREASINGLY AFFECTING MEN AND APPEARS LESS DEPENDENT OF SOCIOECONOMIC STATUS THAN IN THE GENERAL POPULATION

Keywords: Epidemiology, Psoriatic arthritis, Comorbidities

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Background: Obesity in psoriatic arthritis (PsA) is associated with an elevated cardiovascular risk and higher disease activity. It represents a negative prognostic marker with a lower probability of remission on biologic therapy. Furthermore, obese patients with psoriasis have an increased risk of developing PsA. However, the prevalence of obesity in PsA compared with the general population and associated socioeconomic factors that would allow interventions targeted at these individuals are unknown.
Objectives: This study aimed to compare the prevalence of obesity in PsA patients and individuals from the general population at several time points and within those time points and find socioeconomic characteristics for obesity in PsA patients.
Methods: We compared the distribution of different body mass index (BMI) groups between patients with PsA from the Swiss Clinical Quality Management (SCQM) cohort and individuals from the general Swiss population using publicly available data from the Federal Statistical Office collected in 2007, 2012, and 2017. Patients were grouped into four BMI categories: underweight (BMI <18.5), normal weight (BMI 18.5 to <25), overweight (BMI 25 to <30) and obese (BMI ≥30). A comparison of BMI categories between the general Swiss population and PsA patients was performed by sex and level of education using the Chi-Squared Goodness of Fit test. Patient characteristics were compared using Fisher's exact test for categorical variables.
Results: The PsA population recruited to the SCQM registry increased from 517 patients in 2007 (54.5% male, mean (SD) age 47.9 (22.7) years) to 1245 patients in 2017 (51.7% male, mean (SD) age 53.1 (23.9) years). Within this timeline the mean (SD) BMI of 26.6 (10.0) in 2007 raised to 27.5 (10.6) in 2017, representing a significant change (p<0.001). Compared to the general Swiss population, the proportions of obese and overweight individuals were significantly higher in PsA patients at all collected time points (e.g., in 2017: 27.2% being obese and 36.6% being overweight in PsA patients compared to 11.3% being obese and 30.6% being overweight in the general Swiss population) (Figure 1A). In male PsA patients, the proportion of obesity increased, while female PsA patients had a slightly lower proportion of obese patients in 2017 than in 2012 (proportions of obese PsA patients in 2007, 2012 and 2017: 17.9%, 23.0%, and 27.3% in males compared to 22.4%, 28.8%, and 27.1% in females, respectively) (Figure 1B). Compared to the general Swiss population, the proportion of obese and overweight PsA patients was higher in both sexes at all three time points. Higher socioeconomic status represented by a higher level of education was associated with lower proportions of obesity and overweight in the general Swiss population at all three time points. However, patients with PsA lacked those differences in 2007. A decrease of obesity and overweight proportions in PsA patients exists only between secondary to tertiary education in 2012 and 2017. Between mandatory and secondary education, the proportions stay similar (Figure 1C shows the distribution of the BMI groups within education levels using data from 2017). In addition, PsA patients who worked in physically demanding occupations (e.g., transport, manufacturing or agriculture) had a comparable proportion of overweight and obesity as patients who worked in less physically demanding occupations (e.g., office workers, homemakers, teachers) (p=0.13).
Conclusion: Overweight and obesity are much more prevalent in patients with PsA than in the general population. Men have shown an increasing trend of obesity in recent years, and our data suggest that it is not only the socially disadvantaged who are at risk. There is an urgent need to address the expanding obesity epidemic in PsA with future public health incentives that should consider our findings.



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OP0065 THE DETERMINANTS OF RADIOGRAPHIC PROGRESSION IN EARLY PSA PATIENTS

Keywords: Outcome measures, Imaging, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is inflammatory arthritis associated with a progressive erosive disease which had been reported in more than one-half of patients with PsA and is often associated with functional impairment [1]. Despite advances in diagnosis and therapy, radiographic structural damage is still prevalent in PsA. To shed light on this topic, we studied which clinical characteristics determine radiographic progression using conventional radiography.
Objectives: Our aim is to assess baseline clinical parameters as determinants for radiographic progression in early PsA patients at 2-year follow-up.
Methods: The study population consisted of 358 PsA patients from the DEPAR study which consists of PsA patients who were newly diagnosed from 11 centers in the Netherlands. Radiographic progression was measured with the modified Total Sharp Score(mTSS). The proportion of patients with radiographic progression was defined as a change in(ΔmTSS)>1.97(the smallest detectable change) over 2 years of follow-up. Baseline clinical parameters comparisons between groups at diagnosis were made by Student's t-test, chi-squared test, ANCOVA(age, gender baseline CRP and baseline mTSS were used as confounders). All clinical data are observed, without imputation; except for the mTSS values, which were imputed using the linear interpolation approach.
Results: Of the 358 early PsA patients, change in mTSS(mean(S.D.) was found 1.23(5.21), and 42 were in the radiographic progression group at follow-up 2-year(12%). At diagnosis, the mean age of the progression group was older than the non-progression group(57 ± 14 vs 50 ± 14). Patients who had a radiographic progression in 2 years had significantly higher median scores in mTSS(22, IQR =4-48 vs 0, IQR =0-2) and in joint space narrowing score(JSN)(13, IQR =1-23 vs 0, IQR = 0-1) at diagnosis. The erosion score in progressors followed poorer results compared to non-progressors but there was no significance. In addition, the patients with progressive mTSS had a significantly higher prevalence of erosive disease at baseline(57% versus 18%). The progression group had higher swollen joint counts (median(IQR)) but was no difference in statistics. However, the percentage of the presence of swollen joints was significantly greater in the progression group at baseline(93% vs 78%)(Figure 1). Baseline CRP levels were higher in progressions than non-progressions, but there was no difference between groups as a continuous measure(12.3(18.4) vs 8.5(13.6)). Furthermore, the progression group had a significantly higher percentage of patients with CRP levels of more than 1 mg/dl(88% vs. 74%). Meanwhile, DAPSA, ESR, and the baseline presence of dactylitis/enthesitis did not differ between the groups. We also observed a difference in initial treatments between progressors and non-progressors.
Conclusion: According to this real-world longitudinal cohort, early PsA patients have low radiographic progressions with the current treatment protocols. Baseline clinical determinants for radiographic progression at follow-up 2 years are older age, swollen joints, erosive disease, JSN score, and baseline CRP levels (>1 mg/dl).

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Table 1. Baseline clinical parameters for radiographic progression

	Non-progression (n=316)	Progression (n=42)
Age [a]	50 (14)	57 (11)
Gender (Female)(%)	50%	52%
Symptom duration [b]	10 (4-27)	11 (4-35)
Swollen joint count [b]	2 (1-5)	3 (2-5)
Swollen joint count (y/n)(%)	78%	93%
Tender joint count [b]	4 (2-8)	4 (1-8)
Tender joint count (y/n) (%)	89%	83%
CRP [a]	8.50 (13.61)	12.28 (18.4)
CRP* (%)	74%	88%
ESR [b]	10 (5-26)	16 (8-40)
DAPSA [a]	19.3 (10.57)	18.81 (9.55)
Enthesitis (y/n)(%)	44%	50%
ΔmTSS [b]	0 (0-0)	3 (2-5)
mTSS [b]	0 (0-2)	22 (4-48)
JSN [b]	0 (0-1)	13 (1-23)
Erosion score [b]	0 (0-1)	11 (1-21)
Erosive disease (y/n) ° (%)	18%	57%

[a]mean (S.D)[b]*median(IQR) *CRP level >1mg/dl at baseline °Erosion score >1 in three separate joints*

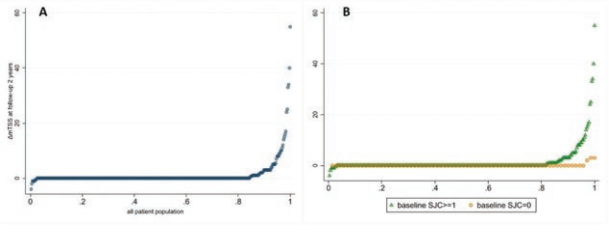


Figure 1. Cumulative probability plots for radiographic progression A: All study population B: Stratified according to the presence of SJC

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OP0066

HIGHER COMORBIDITY BURDEN IN EARLY PSORIATIC ARTHRITIS AS COMPARED TO EARLY RHEUMATOID ARTHRITIS: CLUES FOR PATHOGENESIS OF PSORIATIC DISEASE

Keywords: Rheumatoid arthritis, Psoriatic arthritis, Comorbidities

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Background: Prevalence of comorbidities and cardiovascular risk factors in rheumatoid arthritis (RA) and psoriatic arthritis (PsA) is higher than in general population. Chronic systemic inflammation is perceived as a major cause of increased comorbid conditions. Obesity and certain metabolic disturbances are present at early stages of the PsA suggesting a link between certain comorbidities and PsA at a pathophysiological level.
Objectives: The aim of the study was to investigate which comorbidities contribute to metabolic burden and cardiovascular morbidity in early PsA and to compare the rate of comorbidities to sex and age matched healthy volunteers and early RA patients.
Methods: Clinical, demographic data and comorbidities were collected from patients with PsA (all CASPAR positive), RA (all 2010 ACR positive) from two prospective multicenter cohorts (METAPSA&CARRERA) and from healthy volunteers (matched by sex and age). Patients were naïve to DMARD treatment and had symptom duration of < 2 years.
Results: Patients with PsA (67) and RA (50) were compared to healthy volunteers (61) (Table 1). The overall number of comorbidities was high in PsA (74.6%), RA (66.7%) and control group (60.7%) (p=0.238). However, more PsA patients had multiple comorbidities than RA patients and controls (p=0.007). PsA and RA patients had above normal BMI, higher than matched controls. RA group had a higher proportion of smokers than PsA group and controls. Number of patients having cardiovascular risk factors was higher in PsA (82.1%) and in RA (88.9%) as compared to controls (62.3%) (p=0.003). The most frequent comorbidity was dyslipidemia in both RA and PsA. The rate of hyperuricemia and depression were significantly higher in PsA than in RA and controls. The rate of obesity, type 2 diabetes mellitus, arterial hypertension, COPD, gout, malignancy was similar in PsA and RA but higher than in controls. Patients with PsA had higher Charlson comorbidity index and higher rate of cardiovascular disease as compared to RA and control group (p=0.005).
Conclusion: In conclusion, patients with PsA have a high cardiovascular and metabolic burden already at early stages of the disease. They have higher rate of multiple comorbidities and higher of cardiovascular morbidity as compared to age-matched early RA patients despite comparable BMI and similar rates of obesity. This suggests that metabolic disturbances, present at early stages of PsA might be linked to PsA at a pathophysiological level.

Table 1.

	early PsA (n=67)	early RA (n=50)	2-sided significance (PsA vs RA)	healthy controls, (n=61)	F-value/ chi-square	2-sided significance PsA vs RA vs controls)
age, years, mean (±SD)	47.9 (±14.3)	51.4 (±14.6)	0.905	45 (±14.2)	2.8	0.063
BMI, mean (±SD)	28.2 (±4.5)	27 (±4.7)	0.535	25.8 (±5.2)	4.5	**0.013**
sex, male, n (%)	47 (70.1)	14 (28)	**<0.001**	35 (57.4)	20.9	**<0.001**
TJC68, median (IQR)	2 (1-5)	12 (0)	**<0.001**			
SJC66, median (IQR)	2 (1-4)	9 (7)	**<0.001**			
CRP, mg/l, median (±IQL)	3.6 (8.6)	4.8 (11.1)	0.371	0.9 (1.7)	5.9	**0.003**
comorbidities ≥2, n patients (%)	35 (52.2)	13 (28.9)	**0.019**	17 (27.9)	10	**0.007**
number (%) of patients with ≥2 CV RF	38 (56.7)	21 (46.7)	0.338	16 (26.2)	12.4	**0.002**
Smoking, n (%)	16 (23.9)	30 (60)	**<0.001**	4 (6.6)	39.8	**<0.001**
dyslipidemia, n patients (%)	45 (67.2)	19 (67.9)[£]	1.0	25 (41)	10.6	**0.005**
obesity	27 (40.3)	14 (28)	0.178	11 (18.3)	7.4	**0.024**
type 2 diabetes mellitus, n patients (%)	8 (11.9)	4 (8.9)	0.759	1 (1.6)	5.0	**0.08**
arterial hypertension	19 (28.4)	7 (15.6)	0.17	12 (19.7)	2.9	0.239
Abnormal liver tests	8 (11.9)	4 (8)	0.553	2 (3.3)	3.3	0.191
Hyperuricemia, n patients (%)	8 (11.9)	0	**0.021**	5 (8.2)	5.6	0.061
COPD	2 (3)	0	0.515	1 (1.6)	1.4	0.493
Depression	8 (11.9)	0	**0.021**	2 (3.3)	8.1	**0.017**
cardiovascular disease, n patients (%)	14 (20.9)	1 (2.2)	**0.042**	4 (6.6)	16	**0.043**
Charlson Comorbidity Index≥1, n patients (%)	21 (31.3)	8 (17.8)	**0.042**	4 (6.6)	12.9	**0.005**
CCI ≥2, n patients (%)	11 (16.4)	0	**0.004**	2 (3.3)	26	**<0.001**

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0067

SEX DIFFERENCES IN PERCEPTIONS OF PSORIATIC ARTHRITIS DISEASE IMPACT, MANAGEMENT AND PHYSICIAN INTERACTIONS: RESULTS FROM A GLOBAL PATIENT SURVEY

Keywords: Gender/diversity issues, Quality of life, Psoriatic arthritis

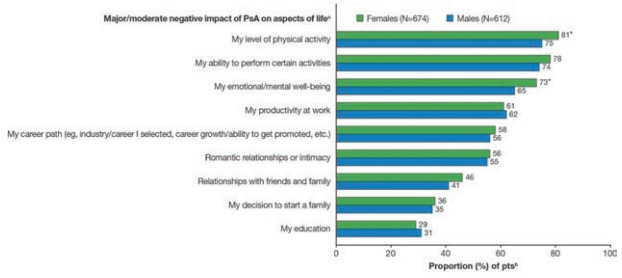
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Background: Women with psoriatic arthritis (PsA) have more severe disease activity and lower health-related quality of life vs men.[1]
Objectives: To assess sex differences in disease impact perceptions and physician interactions with patients (pts) with PsA using global survey data.
Methods: An online survey by The Harris Poll (2 Nov 2017–12 Mar 2018) included 1286 pts from 8 countries, aged ≥18 years, who had PsA for >1 year, visited a rheumatologist/dermatologist in the past 12 months and had used ≥1 disease-modifying antirheumatic drug (DMARD) for PsA.[2] Results were stratified post hoc by sex; analysed descriptively and by binomial (chi-squared) tests.

Percentages/binomial tests of the final global data were adjusted for size of each country's adult population. Statistically significant differences (p<0.05) were described as more/higher.

Results: 52% of pts were female; 24% from Europe (France/Spain/UK). Mean age of females/males (41.3/41.0 years) and time since diagnosis (9.2/8.8 years) were similar. More females had anxiety (32% vs 24%), osteoarthritis (17% vs 9%), had taken a steroid (57% vs 43%) and were taking any DMARD (biologic and oral DMARDs; 20% vs 15%). More females vs males reported a major/moderate negative PsA impact on physical activity (81% vs 75%) and emotional/mental well-being (73% vs 65%); major/moderate impact on other life aspects, such as work productivity, was similar between sexes (Figure 1). More females vs males reported the following because of PsA: emotional distress (65% vs 50%), stopped social activities (49% vs 41%) and went on permanent work disability (14% vs 9%); more males vs females reported lower work productivity (47% vs 38%) because of PsA. Switching treatment due to joint symptoms (41% vs 28%) and side effects (35% vs 22%) were higher in females vs males; switching due to potential serious side effect concerns (29% vs 16%) and symptoms being under control (18% vs 9%) were higher in males vs females. More females vs males were very satisfied with their rheumatologist's communication (60% vs 51%), and discussed treatment goals (83% vs 78%), impact on ability to conduct daily activities (82% vs 73%) and response to and/or satisfaction with treatment regimen (81% vs 72%; Table 1). Pt ability to describe their PsA diagnosis/recall symptoms may limit the study.

Figure. Major/moderate negative impacts of PsA for female vs male pts



*p<0.05 for females vs males
[a]How much of a negative impact, if any, has PsA had on each of the following aspects of your life?
[b]% based on weighted n (adjusted for size of each country's adult population)
N, number of pts that answered question

Table 1. Communication satisfaction[a] with rheumatologist, and discussion topics[b] between pts and their rheumatologist

n, yes, (%)[c]	Female (N=620)	Male (N=552)
Satisfaction[a]		
Very satisfied	371 (60)*	281 (51)
Somewhat satisfied	174 (28)*	214 (39)
Somewhat dissatisfied	40 (6)	33 (6)
Very dissatisfied	36 (6)	24 (4)
Discussion topics[b]		
Treatment goals	515 (83)*	428 (78)
Overall health	507 (82)	444 (80)
Physical exam of musculoskeletal symptoms	509 (82)	432 (78)
Impact on ability to conduct daily activities	510 (82)*	403 (73)
Response to and/or satisfaction with treatment regimen	500 (81)*	396 (72)
Impact on physical activity	491 (79)	413 (75)
Physical exam of skin/nail symptoms	469 (76)	406 (74)
Back pain (pain/stiffness)	467 (75)	411 (74)
Disease management plan	448 (72)	411 (74)
Unusual fatigue	430 (69)	370 (67)

*p<0.05 for females vs males. [a]How satisfied are you with the communication you currently have with your rheumatologist regarding PsA? (Among pts who visited a rheumatologist in the past 12 months). [b]In the last 12 months, have you discussed/conducted the following with your rheumatologist regarding PsA?. [c]% and binomial tests based on weighted data (adjusted for size of each country's adult population). N, number of pts that answered question; n, number of pts with satisfaction level or who participated in each discussion topic

Conclusion: More women vs men reported a major/moderate PsA impact on physical and emotional/mental well-being. More women were very satisfied with communication and discussed treatment goals with their rheumatologist. It is important to consider how sex impacts a pt's experience with PsA.

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OP0068

BARRIERS TO OVERCOME IN THE ACHIEVEMENT TO THE TREATMENT GOAL IN PSORIATIC ARTHRITIS; CENTRAL SENSITIZATION AND NEUROPATHIC PAIN

Keywords: Fibromyalgia, Pain, Psoriatic arthritis

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Background: Chronic inflammation in inflammatory arthritis can trigger both peripheral and central sensitization (CS) through central modifications of pain pathways. CS is an abnormal pain management mechanism involving the central nervous system.

Objectives: To evaluate the frequency of CS and neuropathic pain (NP) in patients with psoriatic arthritis (PsA) and its relationship with disease activity and functional status.

Methods: Patients classified as PsA according to CASPAR classification criteria were included in this cross-sectional study. Disease activity was evaluated with DAPSA, VAS, pain and fatigue level (0-100 mm), quality of life with HAQ, CS with CS inventory (CSI). A score of 40 point was used to predict the presence of CS. CS score of <30 was also categorized as subclinical, 30 -39 as mild, 40-49 as moderate, 50-59 as severe and ≥60 as extreme. NP was evaluated with the DN4 (Douleur Neuropathique en 4 questions) scale. The presence of anxiety and depression were evaluated by using the Hospital Anxiety and Depression questionnaire (HADS) and fibromyalgia syndrome (FMS) by ACR 2016 criteria.

Results: İn total 114 PsA patients (78 [68.4%] female, mean age: 48.8 ±11.6 years, median disease duration was 4 [9] years) were included in the study. The median DAPSA score was 15.2(16), with approximately half of the patients were in remission or low disease activity. The proportion of patients with LEI≥1 was 28.9%, median BSA was 1(2), BASDAI was 3.8(3.6), BASFI was 2[4]. Of our patients 39.8% were receiving biological treatment. 61.4% of the patients had at least one comorbidity. CS was detected in 49 (42.9%) and NP in 24 (23.7%) patients. The median CSI score was 35.5 (IQR 29) Among patients with CS and NP the percentage of female was higher. DAPSA, PGA, PhGA, Pain VAS, TJC were found to be significantly higher and HAQ scores were found to be worse in patients with CS and NP. In addition,the percentage of patients with a LEI ≥1 was found 44.9% in patients with CS, and body mass index was found to be higher in patients with NP **(Table 1).** Duration of disease, CRP, ESR, BSA, usage of biological therapy, treatment with GCs, comorbidities were similar between the groups. Anxiety were higher in patıent with CS and NP, and depression was higher in only CS patients. While all 11 patients with FMS had NP, only 8 had CS. Sixteen (%32.7) patients with CS also had NP and 16 (66.7%) patients with NP had also CS. The positive correlation between PGA, PhGA, DAPSA, HAQ and CS severity in PsA patients **(Figure 1)**.

Conclusion: The results of the present study revealed that both CS and NP are common in PsA, and FMS accompanies 22.4% of those patients. CS and NP affect quality of life and functionality. In PsA patients, especially in cases where treatment goals cannot be achieved, it may be useful to evaluate the presence of concomitant CS and NP.

Table 1. Comparison of characteristics of PsA patients with and without central sensitization and neuropathic pain

Variables	Patient with CS n:49	Patient without CS n:65	p	Patient with NP n:24	Patient without NP n:77	p
Female gender,n(%)	38(81.6)	40(58.5)	**0.008**	19(90.5)	45(60)	**0.009**
Age,y,mean(SD)	51(11)	47.7(11)	0.439	50.1(10)	48.2(11.6)	0.487
BMI,kg/m^2, median(IQR)	29.3(8)	28.2(7.7)	0.749	32.3(9.6)	26.9(5.9)	**0.011**
TJC, median(IQR)	2(4)	0(1)	**0.003**	1(11)	0(2)	**0.021**
SJC, median(IQR)	0(0)	0(0)	0.996	0(0)	0(0)	0.533
PGA, median(IQR)	50(48)	30(20)	**<0.001**	60(60)	30(25)	**<0.001**
PhGA, median(IQR)	20(30)	20(10)	**0.001**	30(20)	20(20)	**0.001**
Pain VAS, median(IQR)	50(38)	20(30)	**<0.001**	60(60)	30(50)	**<0.001**
LEI≥1,n(%)	22(44.9)	11(16.9)	**0.001**	10(41.7)	19(24.4)	0.100
DAPSA, n(%)	17.9(11)	9.7(11.9)	**<0.001**	20.2(13)	11.7(11)	**0.003**
Biological therapy, n(%)	18(37.5)	27(41.5)	0.712	10(41.7)	27(35.1)	0.558
HAQ median(IQR)	1(0.85)	0.38(0.75)	**<0.001**	1.38(1.3)	0.5(0.8)	**<0.001**
Anxiety, n(%)	18(40)	5(8.1)	**<0.001**	9(40.9)	12(16.2)	**0.020**
Depression, n(%)	15(33.3)	4(6.5)	**<0.001**	5(22.7)	11(14.9)	0.514
FMS, n(%)	13(35.6)	8(12.9)	0.006	11(45.8)	10(13)	**0.001**

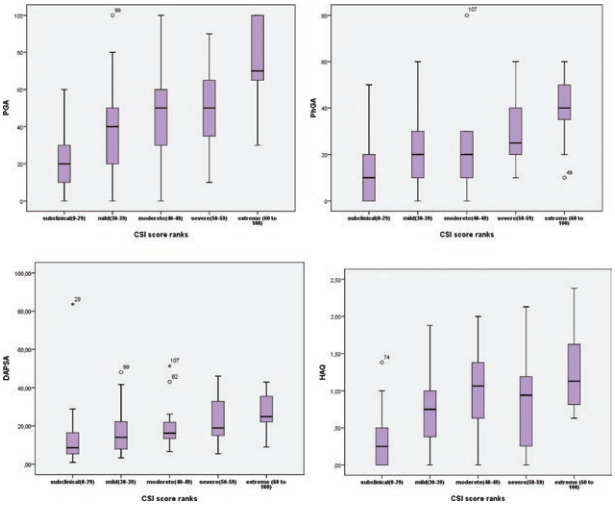


Figure 1. The positive correlation between PGA, PhGA, DAPSA, HAQ and CS severity in PsA patients

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OP0069

CHRONIC TENOSYNOVITIS IS ASSOCIATED WITH LOSS OF GRIP STRENGTH IN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Ultrasound, Diagnostic Tests

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Background: Rheumatic diseases result in joint destruction and impaired physical function [1]. We recently showed, that hand function based on objective tests may serve as a biomarker representing subclinical inflammation in psoriasis (Pso) patients and thus could support the early detection of psoriatic arthritis (PsA) onset [2]. Hand function tests are relevant for objective assessment of musculoskeletal function in relation to disease activity in PsA [3], However, the relationship of hand function with the synovitis and tenosynovitis detected by ultrasound (US) in PsA and Pso patients has not been well studied.

Objectives: To investigate the association of synovitis and tenosynovitis detected by US in greyscale (GS) and power doppler (PD) activity with grip strength and fine motor skills in patients with PsA and Pso.

Methods: PsA and Pso patients were recruited from the Rheumatology Department at the University Hospital erlangen, for this cross-sectional study. After giving written informed consent, subject characteristics were recorded and study participants underwent bilateral US of the wrists, metacarpophalangeal (MCP) joints, and flexor tendons of all fingers. Each joint was examined by GS (0-3), PD (0-3) and finally a combined score (PDUS: PD + GS) was calculated (0-3) [4]. The flexor tendon was scanned in GS (0/1) and with PD [0-3]. US activity considered either a synovitis or tenosynovitis score ≥1. Activity in tender joint count (TJC) and swollen joint count (SJC) 68/66 was considered ≥1 tender or ≥1 swollen joint. Hand function was assessed by vigorimetric grip strength (lbf) and the fine motor skill MPUT (Moberg pick-up test). For the analysis, patients' hands were either divided in dominant/non-dominant or patient reported affected/non-affected hand. A correlation matrix was applied to measure the linear relation between the pairs of synovitis and tenosynovitis scores, grip strength and MPUT for both hands, using the Spearman correlation method.

Results: 106 patients (40 PsA, 66 Pso) participated in this study. Subject characteristics and general outcomes are summarized in Table 1. While grip strength was higher in the dominant hand ($p<0.001$), MPUT times are comparable between the dominant vs. non-dominant hands ($p=0.056$) but was faster in the non-affected hand ($p=0.008$). Low to moderate positive correlations were observed between both, overall GS synovitis score (MCP 2-5 + wrist) ($r=0.24$, $p<0.05$), and PDUS ($r=0.23$, $p<0.05$) with MPUT. In US active patients, a high correlation between grip strength and GS tenosynovitis score in digit 2 ($r=-0.566$, $p=0.028$) was detected. When considering patients with US in addition to SJC/TJC activity, imaging modalities did not correlate with hand function.

Conclusion: These findings indicate that the synovitis detected by greyscale is related with fine motor skills and tenosynovitis in greyscale with grip strength. This suggests, that chronic tenosynovitis has a greater impact on hand function than the acute inflammatory phase. When considering patients with TJC68/SJC66 ≥1 this relation is not present, suggesting that clinically assessed joint count, unlike ultrasonography, does not correlate with hand function impairment.

Table 1. Participants characteristics, clinical scores, functional tests and ultrasound scores by group.

	PsA	Pso
Characteristics, Mean (SD)		
Age (years)	47.5(12.3)	43.6(14.1)
Sex (Woman/Man)	15/25	26/40
Clinical Scores, Mean (SD)		
TJC 68/SJC 66	3.4(5.1)/ 0.4(1)	0.5(0.9)/ 0.2(1.3)
Visual Analogue Scale Global	43.7(30.6)	25.0(23.6)
Functional tests, Mean (SD)		
Grip strength (lbs)	84.3(32.9)	98.1(33.2)
MPUT (sec)	13.3(3.2)	10.9(2.6)
US Scores, active (score≥1)/non-active		
GS Synovitis	20/20	13/53
PD Synovits	7/33	1/65
GS Tenosynovitis	14/26	7/59
PD Tenosynovitis	11/29	1/65

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Emerging a New Era in Osteoarthritis Therapies

OP0070 METHODS - A RANDOMIZED CONTROLLED TRIAL OF METHOTREXATE TO TREAT HAND OSTEOARTHRITIS WITH SYNOVITIS

Keywords: Disease-modifying drugs (DMARDs), Randomized control trial, Osteoarthritis

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Background: Hand osteoarthritis (OA) with synovitis is a common clinically identifiable phenotype which is associated with pain and disease progression. Methotrexate is a low-cost, well-established and effective treatment for inflammatory arthritis with a well-described safety profile. A previous randomized controlled trial showed no superiority of 10 mg methotrexate over placebo in pain relief at 3 or 12 months in patients with erosive hand OA[1]. No study has examined methotrexate in hand OA with inflammatory phenotype.

Objectives: To examine whether methotrexate reduced pain and improved function over 6 months in patients with hand OA and synovitis.

Methods: In a multicentre, randomized, double-blind, placebo-controlled trial, patients with symptomatic hand OA and MRI-detected synovitis were recruited and randomly assigned in a 1:1 ratio to receive methotrexate 20 mg (n=50) or identical placebo (n=47) once weekly for 6 months. The primary outcome was pain reduction (assessed by 100mm visual analogue scale, VAS) at 6 months. Secondary outcomes included changes in physical function and quality of life assessed using Australian Canadian Osteoarthritis Hand Index (AUSCAN), Functional Index for Hand Osteoarthritis (FIHOA), Health Assessment Questionnaire (HAQ), and Michigan Hand Outcomes Questionnaire (MHQ). Adverse events were recorded. The primary analysis was by intention to treat, including all participants in their randomized groups. Mixed linear regression models were fit to continuous outcomes, adjusting for baseline values of outcome, sex and site, and the clustering of measurements within participants.

Results: Of 97 patients [mean age 61.4 (SD 6.7) years, 68 (70.1%) female], 82 (84.5%) provided the 6-month primary outcome. At 6 months, the methotrexate group had greater reduction in VAS pain (-15.2 vs -7.7, difference -9.9, 95% CI -19.3 to -0.6) (Figure 1), AUSCAN pain (-55.3 vs -13.5, diff -47.0, 95% CI -91.5 to -2.5) and stiffness (-14.5 vs -2.9, diff -11.4, 95% CI -20.8 to -2.0) than the placebo group (Table 1). The between-group differences were not clinically meaningful for change in AUSCAN function [-52.7 (-127.3 to 21.9)], FIHOA [-0.9 (-3.4 to 1.7)], HAQ [-0.0 (-0.2 to 0.2)], or MHQ [5.5 (-0.3 to 11.3)]. Incidence of adverse events was 62.0% in methotrexate and 59.6% in placebo group.

Conclusion: This study provides high-quality evidence for the effect of methotrexate (20 mg once weekly) on reducing pain and stiffness over 6 months in patients with hand OA and synovitis. The results have the potential to inform clinical practice guidelines for the management of hand OA with the inflammatory phenotype.

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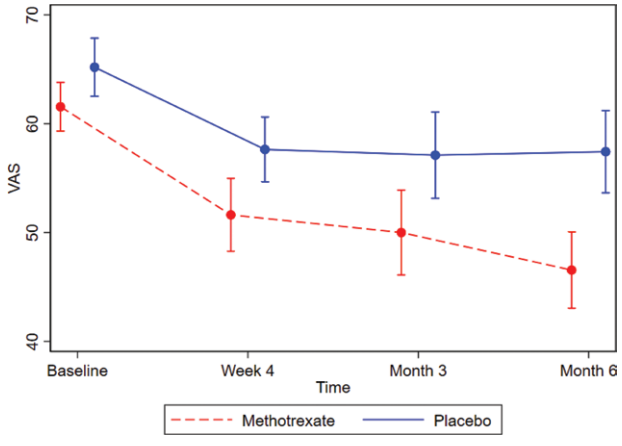


Figure 1. Pain at each time point over the study period (mean with standard error)

Table 1. Primary and secondary outcomes at 6 months, using a multiply imputed dataset

	Baseline Mean (SD)		Change between baseline and 6 months Mean (SD)		Between group difference Mean (95% CI)*	P*
	Methotrexate (N=50)	Placebo (N=47)	Methotrexate (N=50)	Placebo (N=47)		
Primary endpoint						
VAS	61.6 (15.7)	65.2 (18.1)	-15.2 (24.0)	-7.7 (25.3)	-9.9 (-19.3, -0.6)	0.037
Secondary endpoints						
AUSCAN pain	233.6 (84.1)	242.7 (107.4)	-55.3 (102.6)	-13.5 (121.0)	-47.0 (-91.5, -2.5)	0.038
AUSCAN stiffness	47.4 (23.1)	46.8 (25.6)	-14.5 (24.1)	-2.9 (28.7)	-11.4 (-20.8, -2.0)	0.018
AUSCAN function	452.4 (198.1)	462.3 (196.3)	-79.4 (170.8)	-31.9 (202.5)	-52.7 (-127.3, 21.9)	0.17
FIHOA	9.4 (6.0)	9.6 (5.5)	0.0 (5.1)	0.7 (5.9)	-0.9 (-3.4, 1.7)	0.50
HAQ	0.7 (0.6)	0.6 (0.4)	-0.0 (0.4)	-0.0 (0.4)	-0.0 (-0.2, 0.2)	0.89
MHQ	57.8 (11.8)	56.1 (12.9)	8.5 (11.7)	3.9 (16.1)	5.5 (-0.3, 11.3)	0.065

*Adjusted for baseline measure of outcome, sex, and study site

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OP0071 EFFECT OF DENOSUMAB ON STRUCTURE MODIFICATION IN EROSIVE HAND OSTEOARTHRITIS: RESULTS OF A 48-WEEKS, MONOCENTRIC, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND PHASE 2 STUDY AND OPEN LABEL EXTENSION PHASE

Keywords: Clinical Trials, Osteoarthritis

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Background: Erosive hand osteoarthritis (OA) is a disabling disease with limited therapeutic options. Denosumab, a Receptor Activator of Nuclear Factor kappa-β Ligand inhibitor affects bone resorption and osteoclast activity.

Objectives: The purpose of this clinical trial was to study the structure modifying effect of denosumab in patients with erosive hand OA, and to explore the clinical benefits and safety of subcutaneous denosumab 60 mg every 3 months versus placebo.

Methods: One hundred patients with erosive hand OA were randomly allocated to placebo or denosumab in a monocentric clinical trial during 48 weeks, followed by an open-label extension phase through week 96. The primary radiographic endpoint was change in total Ghent University Scoring System (GUSS) score at week 24. GUSS (0-300) is a semi-quantitative scoring system specifically developed to combine scoring of both aspects of radiographic changes in erosive hand OA, being erosive progression (decrease of score) and signs of repair (increase of score) (1) and able to detect changes on short term [2]. The secondary endpoint was the percentage of new erosive joints at week 48. Exploratory clinical outcomes (e.g., pain, tender joint count, swollen joint count, grip strength, the Australian-Canadian Hand Osteoarthritis Index and the Functional Index for Hand Osteoarthritis) were assessed. Radiographic and clinical changes after 96 weeks of treatments were measured. Safety outcomes including (serious) adverse events, laboratory changes and changes in bone mineral density by dual-energy X-ray absorptiometry were registered. Primary efficacy analyses were performed in an intention-to-treat approach. Changes in GUSS were analysed at joint level with generalized estimating equations, accounting for within-patient clustering. Robust standard errors were used and the working correlation structure specified exchangeable. Trial registration number: EUDRACT CT 2015-003223-53.

Results: 51 and 49 patients received subcutaneous administration of denosumab and placebo respectively. Total change GUSS was found statistically higher in denosumab compared to placebo at week 24 (mean change GUSS = 8.9 (95% CI: 1.0 - 16.9; p = 0.024))(Figure 1A). This difference further increased at week 48 (ΔGUSS = 14.3 (95% CI: 4.6 – 24.0; p = 0.003)). Development of new erosive joints was significantly lower in denosumab (1.8%) compared to placebo (7.0%) at week 48 (OR = 0.23 (95% CI: 0.10 to 0.50); p < 0.001)(Figure 1B). After open-label treatment through week 96, both groups continued remodelling and both pain and function significantly improved compared to baseline. Equal numbers of adverse events occurred in both groups.

Conclusion: Denosumab has clear structure modifying effects in erosive hand OA compared to placebo: significantly less erosive progression occurs after 24 weeks treatment, and the treatment effect enhances after 48 weeks. Symptom improvement was observed after sustained treatment.

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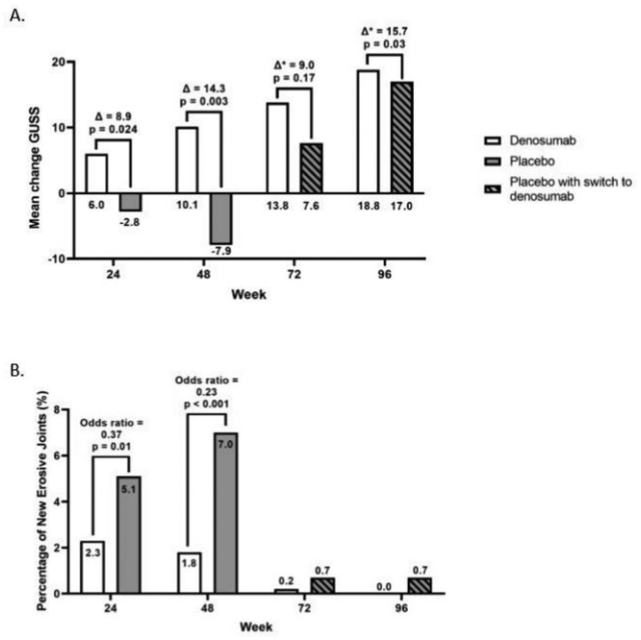


Figure 1. Radiographic changes after 48-weeks placebo-controlled phase and extension phase through 96 weeks. Panel A is showing the primary endpoint GUSS; panel B is showing the percentage of new erosive joints (secondary endpoint)

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OP0072

LOW-DOSE COLCHICINE IS ASSOCIATED WITH LOWER INCIDENCE OF KNEE AND HIP REPLACEMENTS: A POST-HOC ANALYSIS FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Keywords: Osteoarthritis, Cartilage

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Background: Osteoarthritis is a major contributor to pain and disability worldwide [1]. Considering that inflammation plays an important role in the development of osteoarthritis, anti-inflammatory drugs may slow the progression of the disease [2].
Objectives: To examine whether years-long use of colchicine 0.5 mg daily reduces incident total knee replacements (TKRs) and total hip replacements (THRs).
Methods: We performed a post-hoc analysis of data collected in the LoDoCo2 trial to determine the time to first knee or hip replacement. A Cox proportional hazard model was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for colchicine 0.5 mg once daily as compared to placebo. Sensitivity analyses were performed by excluding patients known with gout at baseline (to avoid possible carry-over effects as colchicine is used to prevent gout attacks) or by excluding the patients who had joint surgery within the first 3 months after randomization (to avoid any bias related to planned joint surgery prior to randomization). All analyses were performed on an intention-to-treat basis.
Results: Among the 5522 randomized LoDoCo2 trial participants, 2762 received colchicine and 2760 placebo during a median duration of follow-up of 28.6 months (interquartile range, 20.5 to 44.4). The mean (SD) age was 66 (8.6) years and 846 (15.3%) were female. During the trial, TKR/ THR was performed in 68 patients (2.5%) in the colchicine group and in 97 patients (3.5%) in the placebo group (HR, 0.69; 95% CI, 0.51-0.95; p = 0.02) (Table 1 and Figure 1). In a sensitivity analysis that excluded patients with gout similar results were obtained, while omitting joint replacements that took place in the first three months of follow-up yielded in an even larger rate reduction of TKR/ THR (Table 1).

Table 1. Incidence rates and hazard ratios for hip and knee replacements according to treatment.

Trial cohort/ subgroup	Placebo (n=2760)		Colchicine (n=2762)		Hazard ratio (95% CI)
	No. of patients/ total no. (%)	*No. of events/100 person-yrs*	*No. of patients/ total no. (%)*	*No. of events/100 person-yrs*	
Full trial population					
TKR/ THR events	97/2760 (3.5)	1.30	68/2762 (2.5)	0.90	0.69 (0.51-0.95)
Participants with gout at baseline excluded					
TKR/ THR events	89/2534 (3.5)	1.30	61/2542 (2.4)	0.88	0.68 (0.49-0.94)
TKR/ THR in the first three months excluded					
TKR/ THR events	96/2760 (3.5)	1.29	59/2762 (2.1)	0.78	0.61 (0.44-0.84)

TKR/ THR= total knee replacement/ total hip replacement

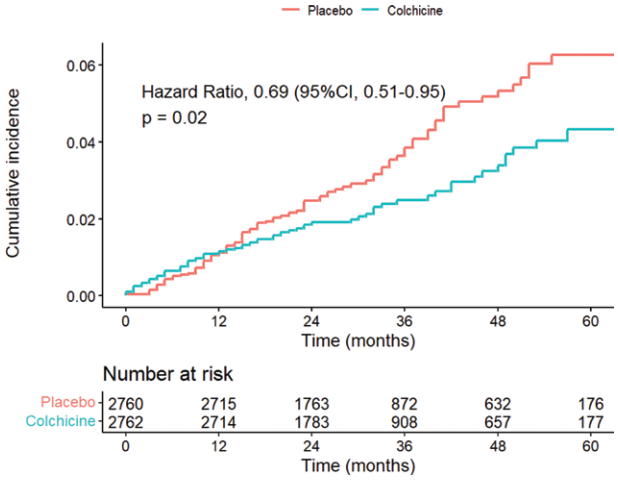


Figure 1. Cumulative incidence rates for time to first total knee/hip replacement in the full trial population.Cumulative incidence of time to first total knee/hip replacement in participants receiving colchicine in comparison with placebo once daily. Data are shown on an enlarged y-axis.

Conclusion: In this post-hoc analysis of the LoDoCo2 trial, use of colchicine 0.5 mg daily was associated with a reduced risk of TKR/ THR. Further investigation of long-term therapy with colchicine to slow disease progression in osteoarthritis is warranted.

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Disclosure of Interests: None Declared.
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OP0073

COLCHICINE TWICE DAILY FOR HAND OSTEOARTHRITIS: RESULTS FROM THE DOUBLE-BLIND, RANDOMISED, PLACEBO-CONTROLLED COLOR TRIAL

Keywords: Osteoarthritis, Randomized control trial, Pain

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Background: Colchicine has been suggested as a treatment for osteoarthritis symptoms, but evidence is contradictory.[1]
Objectives: To investigate the clinical efficacy and safety of colchicine compared with placebo in people with hand osteoarthritis.
Methods: In this double-blind, randomised, placebo-controlled trial we recruited adults from a dedicated outpatient clinic in Denmark. Eligibility criteria included symptomatic hand osteoarthritis and finger pain of at least 40 mm on a 100-mm visual analogue scale (VAS). The hand with the most severe finger pain at inclusion was considered the target hand. Participants were randomly assigned to 0.5 mg colchicine or placebo taken orally twice daily for 12 weeks. The primary endpoint was change from baseline to week 12 in target hand finger pain, assessed on a 100-mm VAS with a pre-specified minimal clinically important difference of 15 mm, in the intention-to-treat population. The study was registered prospectively at ClinicalTrials.gov, NCT04601883.
Results: We screened 186 people for eligibility between January 15, 2021 and March 3, 2022 and randomly assigned 100 participants: 50 (50%) to colchicine and 50 (50%) to placebo. All participants completed the study. The mean changes from baseline to week 12 in finger pain were -13.9 mm (SE 2.8) in the colchicine group, and -13.5 mm (2.8) in the placebo group with a between-group difference (colchicine versus placebo) of -0.4 mm (95% CI -7.6 to 6.7; p = 0.90). The efficacy on primary and secondary outcomes is summarized in the Table 1. In the colchicine group, there were 76 adverse events in 36 (72%) participants and one serious adverse advent. In the placebo group, there were 42 adverse events in 22 (44%) participants and two serious adverse events. Serious adverse events were unrelated to treatment.

Table 1. Changes from baseline in primary and secondary outcomes at week 12 in the ITT population

	Colchicine (n = 50)	Placebo (n=50)	Difference between groups (95% CI)	*P* value
Primary outcome				
VAS pain fingers target hand (0-100), mm	-13·9 (2·8)	-13·5 (2·8)	-0·4 (-7.6 to 6.7)	0.90
Secondary outcomes				
VAS patient global assessment (0-100), mm	-12.4 (2.8)	-11.2 (2.8)	-1.2 (-8.3 to 5.9)	*
AUSCAN function (0-90)	-10.5 (2.1)	-8.3 (2.1)	-2.2 (-7.6 to 3.2)	*
AUSCAN pain (0-50)	-7.8 (1.2)	-5.3 (1.2)	-2.4 (-5.4 to 0.5)	*
Grip strength target hand, N	9.4 (4.0)	14.1 (4.0)	-4.7 (-14.8 to 5.4)	*
EQ-5D quality of life (-0.624 to 1.000)	0.032 (0.011)	0.000 (0.011)	0.032 (0.004 to 0.060)	*
Tender joint count target hand (0-15)	-1.0 (0.2)	-0.8 (0.2)	-0.2 (-0.7 to 0.4)	*
VAS pain thumb base target hand (0-100), mm	-11.9 (2.8)	-10.0 (2.8)	-1.9 (-9.0 to 5.1)	*
OMERACT-OARSI responders†, n (%)	23 (46%)	22 (44%)	OR: 1.1 (0.5 to 2.5)	*

Group values are least squares means (standard error), and contrasts are differences in least square means (95% confidence intervals), unless otherwise stated. AUSCAN: Australian/Canadian hand index score. CI: Confidence interval. EQ-5D: European Quality of Life 5 Dimensions. ITT: Intention-to-treat. OMERACT-OARSI: Outcome Measures in Rheumatology - Osteoarthritis Research Society International. VAS: Visual analogue scale. *As no significant effect was found for the primary outcome, *P* values are not reported for subsequent analysis according to gatekeeping. †OMERACT-OARSI responders are the proportion of responders and the difference is reported as odds ratio (95% CI). The AUSCAN function subscale scores were rescaled from 0-90 to 0-100 for the calculation of OMERACT-OARSI responders.

Conclusion: In people with painful hand osteoarthritis, treatment with 0·5 mg of colchicine twice daily for 12 weeks did not effectively relieve pain and treatment with colchicine was associated with more adverse events.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Anna Døssing: None declared, Marius Henriksen Employee of: MH in on the European Advisory Board for Thuasne Group, Karen Ellegaard: None declared, Sabrina Mai Nielsen: None declared, Lisa Stamp Consultant of: LKS has received consulting fees from Pharmac, Felix C Müller Speakers bureau: FCM has received payment or honoraria from Varian and Siemens Healthineers., Margreet Kloppenburg Speakers bureau: MGK has received payment or honoraria from Galapagos and Jansen, Consultant of: MGK has received consulting fees for Abbvie, Pfizer, Kiniksa, Flexion, Galapagos, CHDR, Novartis, and UCB, Grant/research support from: MGK has received royalties or licenses from Wolters Kluwer and Springer Verlag, Ida Haugen Speakers bureau: IKH has received payment or honoraria from Novartis and GSK, Grant/research support from: IKH has received grants from Pfizer/Lily (ADVANCE), Geraldine McCarthy Grant/research support from: GMcC has received support for attending meeting from Janssen, Philip G Conaghan Speakers bureau: PGC has received payment or honoraria from AbbVie, Consultant of: PGC has received consulting fees from AbbVie, AstraZeneca, Eli Lilly, Galapagos, GlaxoSmithKline, Grunenthal, Janssen, Levicept, Merck, Novartis, Pfizer, Regeneron, Stryker, and UCB, Grant/research support from: PGC has received support from AbbVie for congress attendance., Louise Dahl: None declared, Lene Terslev Speakers bureau: LT has received payment or honoraria from Eli Lilly, Novartis, and Janssen, Employee of: LT is on the advisory board for BMS and Janssen., Roy Altman: None declared, Fabio Becce Consultant of: FB has received consulting fees from Horizon Therapeutics., Elisabeth Ginnerup-Nielsen: None declared, Lene Jensen: None declared, Mikael Boesen: None declared, Robin Christensen: None declared, Ulla Dal: None declared, Henning Bliddal: None declared.
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OP0074

RADIOGRAPHIC AND PAIN OUTCOMES FROM A PHASE 3 EXTENSION STUDY EVALUATING THE SAFETY AND EFFICACY OF LORECIVIVINT IN SUBJECTS WITH SEVERE OSTEOARTHRITIS OF THE KNEE (OA-07): SINGLE BLIND AND CROSSOVER RESULTS

Keywords: Clinical Trials, Osteoarthritis

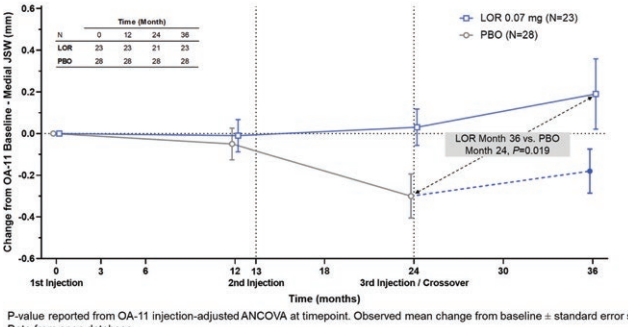
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Background: Knee osteoarthritis (OA) is a common joint disorder associated with pain, disability, and joint damage. An unmet need remains for safe, efficacious treatments for symptoms and disease modification. Lorecivivint (LOR), a novel intra-articular (IA) CLK/DYRK inhibitor thought to modulate Wnt and inflammatory pathways, has previously appeared safe, demonstrated patient-reported outcome (PRO) improvements compared with placebo (PBO), and maintenance of radiographic medial joint space width (JSW).
Objectives: An ongoing extension study, OA-07 (NCT04520607), continues to evaluate LOR safety and efficacy with primary and secondary efficacy outcomes of medial JSW (mm) and Pain Numerical Rating Scale (NRS [0-10]), WOMAC Pain [0-100], and WOMAC Function [0-100], respectively. Preliminary data up to 36 months are reported.
Methods: Participants with structurally advanced (medial JSW 1.5-4 mm) knee OA who completed the parent Phase 3 LOR trial were enrolled into OA-07. At the beginning of the single-blind (participants and investigators blinded) extension Year 1, participants received a repeat injection according to the initial randomized treatment (LOR or PBO). In Year 2 and annually thereafter, all participants (LOR and PBO) received an open-label 0.07 mg, IA LOR injection. The extension trial commenced in July 2020 with clinic visits every six months. Baseline-adjusted ANCOVA was used to

estimate difference between LOR and PBO on outcomes using the OA-07 baseline. Treatment effect at Month 36 was estimated using marginal comparison from baseline-adjusted ANCOVA to a last PBO observation prior to crossover for LOR only. Concordance between OA-07 baseline-adjusted medial JSW change and pain response was conducted for 36 month completers using logistic regression.

Results: 277 subjects (mean age 61.0 ± 8.2 years, BMI 31.8 ± 4.9 kg/m^2, female 62.8%, KL3 45.5%, 67.1% bilaterally symptomatic, mean baseline medial JSW 2.63 ± 0.69 mm, 68.6% medial JSW < 3 mm) were enrolled. LOR appeared safe and well-tolerated, consistent with its previously observed safety profile. At 24 months, the LOR treatment arm showed reduced medial JSW loss compared to placebo: LOR -0.11 (± 0.05) mm (n=111) vs. PBO -0.20 (± 0.05) mm (n=119) (Δ=0.09 mm, 95% CI [-0.06, 0.23], *P*=0.246). The 36-month LOR completers demonstrated continued improvement with LOR (n=21) medial JSW change of 0.03 (± 0.11) mm vs. PBO (n=28) -0.30 (± 0.09) mm (Δ=0.33 mm, 95% CI [0.05, 0.62], P=0.023) at 24 months. At 36 months, LOR medial JSW change was +0.19 (± 0.14) mm (n=23), a difference of -0.49 mm (*P*=0.019) in medial JSW with LOR in comparison to the last PBO measure before crossover at 24 months (Figure 1). Average change from extension baseline to 24 months in Pain NRS was -0.25 (± 0.19) for LOR (n=121) compared to 0.09 (± 0.19) for placebo (n=130) (Δ=-0.34, 95% CI [-0.87, 0.19], *P*=0.207). Similar trends were seen for LOR treatment effect over PBO at 24 months for WOMAC Function Δ=-4.90 (95% CI [-9.92, 0.13], *P*=0.056) and WOMAC Pain Δ=-5.18 (95% CI [-10.28, -0.08], *P*=0.047). At 36 months, open-label IA injection of LOR (n=35) showed additional Pain NRS improvements with change from OA-07 baseline of -0.91 (±0.34) and crossover participants from PBO to LOR (n=45) showed improvement of -0.43 (±0.30). Good concordance was shown between change in medial JSW and at least a 20% improvement in Pain NRS at 36 months (n=20, AUC=0.719).

Figure 1: Change in Medial Joint Space Width in OA-07 from OA-11 Baseline
FAS 36-month completer analysis



P-value reported from OA-11 injection-adjusted ANCOVA at timepoint. Observed mean change from baseline ± standard error shown. Data from open database.

Conclusion: LOR continues to appear safe and well tolerated. A potential benefit of LOR 0.07 mg compared with PBO in medial JSW is observed 12 months after the extension baseline (second overall) injection, which persisted and improved in those who have completed an additional 12 months (total 36 months, after three injections) and in PBO participants who crossed over to active treatment with LOR. Potential LOR benefit compared to PBO is also seen across PROs along with preliminary good concordance data between medial JSW and pain improvement. This study is ongoing.

REFERENCES: NIL.

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Disclosure of Interests: Yusuf Yazici Shareholder of: Biosplice Therapeutics, Employee of: Biosplice Therapeutics, Christopher Swearingen Shareholder of: Biosplice Therapeutics, Employee of: Biosplice Therapeutics, Victor Lopez Shareholder of: Biosplice Therapeutics, Employee of: Biosplice Therapeutics, Jon Britt Shareholder of: Biosplice Therapeutics, Employee of: Biosplice Therapeutics, Sarah Kennedy Shareholder of: Biosplice Therapeutics, Employee of: Biosplice Therapeutics, Jeymi Tambiah Shareholder of: Biosplice Therapeutics, Employee of: Biosplice Therapeutics, Timothy McAlindon Consultant of: Biosplice Therapeutics, Grant/research support from: Biosplice Therapeutics.

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OP0075

EFFICACY, SAFETY, PHARMACOKINETICS AND IMMUNOGENICITY OF REPEATED DOSING OF GSK3858279 IN PATIENTS WITH KNEE OSTEOARTHRITIS: A PHASE I, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

Keywords: Osteoarthritis, Pain

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Background: Chronic pain is an unmet need in osteoarthritis (OA) as current therapies have limited analgesia and side effects. The chemokine CCL17 mediates inflammatory pain and blocking CCL17 (via anti-CCL17 monoclonal antibodies [mAb] or CCL17 knock-out) reduces pain and joint disease in murine arthritis. GSK3858279 is a novel, high affinity, human mAb that functionally inhibits CCL17.

Objectives: To present efficacy, safety, pharmacokinetic (PK) and immunogenicity data from Part B of a first-in-human, 2 part, phase I, randomized, double-blind, placebo (PBO)-controlled study evaluating GSK3858279 for OA pain (NCT03485365).

Methods: Participants with knee OA per ACR criteria, Kellgren and Lawrence (KL) score ≥2 and average daily pain score 4–9 by 11-point numerical rating scale (NRS) were randomised (1:1) to weekly subcutaneous (SC) GSK3858279 or PBO for 8 weeks. Co-primary endpoints were change from baseline (CFB) to Week 8 in average and worst knee pain intensity. Participants completed a daily pain NRS. Pain medication was prohibited, except paracetamol (≤3g/day) as rescue medication (not 24 h before a study visit). Exploratory endpoints included CFB in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function scores. Samples for analysis of GSK3858279 serum concentration and immunogenicity were collected to Week 20. A Bayesian repeated measures model using non-informative priors was fitted to CFB data; 95% credible intervals (CrI) for treatment differences were calculated.

Results: All 48 participants in Part B completed the study (2 participants in the PBO arm discontinued treatment). Participant characteristics were comparable, however more participants in the GSK3858279 arm were male and KL grade 4 (**Table 1**). GSK3858279 was rapidly absorbed after SC administration (median T_{max} ~2 days), with steady concentrations predicted by Week 8. Anti-GSK3858279 Abs were detected in 5/24 (21%) and 1/24 (4%) participants who received GSK3858279 and PBO, respectively; PK profiles for these participants were consistent with profiles in those without anti-drug Abs. For the co-primary endpoints of average and worst knee pain intensity, GSK3858279 showed greater improvement vs PBO at all timepoints (**Figure 1**). At Week 8, the difference (95% CrI) in CFB for GSK3858279 vs PBO was –1.18 (–2.15, –0.20) and –1.09 (–2.29, 0.12) for average and worst knee pain intensity, respectively (probability of true difference <0: >99% and 96%). GSK3858279 showed greater improvement in WOMAC pain and function scores vs PBO (**Figure 1**). At Day 57, the difference (95% CrI) in CFB for GSK3858279 vs PBO was –1.41 (–2.35, –0.46) for pain and –1.29 (–2.28, –0.29) for function (probability of true difference <0: >99% for both). Adverse events (AE) occurred in 21/24 (88%) and 15/24 (63%) participants, GSK3858279 and PBO, respectively. There were no serious AEs or deaths.

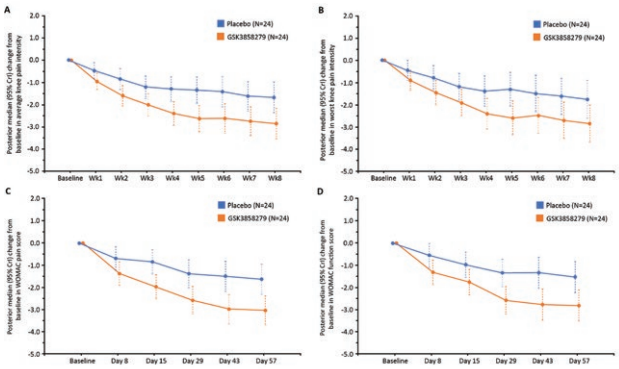
Conclusion: Weekly dosing for 8 weeks with GSK3858279 has clinical activity (improved pain scores) and a favourable safety profile in patients with OA knee pain. These compelling data warrant further study of the effectiveness and safety of GSK3858279 in people with OA pain.

Table 1. Baseline characteristics

	Placebo (N=24)	GSK3858279 (N=24)	All (N=48)
Male	11 (46)	16 (67)	27 (56)
Age, years	59.0 [51–75]	58.5 [46–74]	59.0 [46–75]
Race			
White	24 (100)	23 (96)	47 (98)
Asian	0 (0)	1 (4)	1 (2)
Body mass index, kg/m^2	28.3 [24–35]	29.7 [23–34]	29.2 [23–35]
Kellgren and Lawrence score			
Grade 2	12 (50)	8 (33)	20 (42)
Grade 3	8 (33)	8 (33)	16 (33)
Grade 4	4 (17)	8 (33)	12 (25)
Average knee pain intensity[a]	5.5 [4.0–7.8]	5.3 [4.0–7.4]	5.3 [4.0–7.8]
Worst knee pain intensity[a]	6.0 [4.0–8.0]	6.2 [4.2–8.6]	6.1 [4.0–8.6]
WOMAC Pain score[a]	5.3 [2.6–9.0]	5.5 [2.8–7.0]	5.4 [2.6–9.0]
WOMAC Function score[a]	5.2 [1.6–9.4]	5.5 [1.7–7.5]	5.4 [1.6–9.4]

Data are n (%) or median [range]. [a]11-point numerical rating scale: 0 (no pain/difficulty) to 10 (worst imaginable pain/difficulty). WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Figure. Posterior median change from baseline in average (A) and worst (B) knee pain intensity score, and WOMAC pain (C) and function (D) score



Average and worst knee pain intensity and WOMAC pain and function were assessed by participants using an 11-point numerical rating scale, where scores range from 0 (no pain/difficulty) to 10 (worst imaginable pain/difficulty). All analyses were performed in the intent-to-treat population using a Bayesian repeated measures model adjusting for treatment, week, baseline and the treatment by week and baseline by week interactions using non-informative priors. (A, B) For each assessment visit, the mean average and mean worst pain scores for the 7 days preceding the visit were calculated for each participant. Data available for n=24 for all visits for GSK3858279, and for n=24 (Baseline, Wks 1 and 2), n=23 (Wks 3, 4 and 6), and n=22 (Wk 5, 7, and 8) for placebo. (C, D) Across the assessed timepoints, data were available for n=22–24 for both GSK3858279 and placebo. CrI, credible interval; Wk, Week; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

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OP0076

UPDATE OF THE EULAR RECOMMENDATIONS FOR THE NON-PHARMACOLOGICAL CORE MANAGEMENT OF HIP AND KNEE OSTEOARTHRITIS

Keywords: Non-pharmacological interventions, Osteoarthritis, Quality of care

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Background: The existing EULAR Recommendations for the non-pharmacological core management of hip and knee osteoarthritis (OA) were published in 2013. A considerable number of new studies on various non-pharmacological treatment modalities have been published since then. Hence, it is time to update the Recommendations for the non-pharmacological core management of hip and knee OA.

Objectives: The objective of this project was to perform an updated systematic literature review and to update the 2013 EULAR Recommendations for the non-pharmacological core management of hip and knee osteoarthritis, accordingly.

Methods: The standardised operating procedures for EULAR-endorsed Recommendations [1] were used as a framework for this project. A multi-disciplinary Task Force (TF) including 9 physiotherapists, 6 rheumatologists, 2 orthopaedic surgeons, 2 psychologists, 2 patient research partners, 1 occupational therapist, 1 nurse, 1 general practitioner and 1 nutrition expert from 13 European countries was established. Based on the original search strategy underpinning the original 11 recommendations, 11 updated PICOs (Population, Intervention, Control, Outcome) were agreed upon by the TF members in the first digital meeting in January 2022. Systematic literature searches were conducted from 1st January, 2012 until 27th May, 2022 aiming to identify new evidence related to non-pharmacological core treatment interventions for hip and knee OA. Evidence was primarily collected from published systematic reviews (SRs) and secondarily, from randomised controlled trials (RCTs) if no relevant, updated SR was available. The retrieved evidence was discussed in 5 digital subgroup meetings and subsequently presented to all TF members in the second plenary digital meeting in November 2022. Here, the recommendations were revised based on the new evidence and discussions and TF members voted on each newly proposed recommendation to reach consensus (more than 75 % in favour). After the meeting TF members completed a web-based survey to ascertain the Level of Agreement (LoA) (0-10, 10=totally agree) with each recommendation and prioritize the order of the recommendations for implementation activities.

Results: Based on evidence from 67 SRs and 31 RCTs, the TF agreed to rephrase and change two of the 11 existing recommendations into two overarching principles; one concerning the initial assessment with a biopsychosocial approach and one on the use of shared decision-making in treatment. The remaining 9 original recommendations were revised into 8 updated recommendations, as the recommendations on footwear and on walking aids and other assistive devices were combined. The 8 updated recommendations concern the application of: 1) an individualised, multicomponent management plan; 2) delivery of information, education and self-management strategies; 3) delivery of exercise with adequate dosage and progression; 4) the mode of delivery of exercise; 5) education on maintaining a healthy weight and support with weight loss when indicated; 6) advice on walking aids and assistive devices; 7) work-related advice; and 8) application of behaviour-change techniques to improve lifestyle. The lowest mean LOA for the 8 revised recommendations was 9.2 and the highest 9.8. Recommendation 2) was ranked by the TF as having the highest priority for implementation.

Conclusion: The updated overarching principles and recommendations for the non-pharmacological core management of hip and knee OA are based on previous evidence and on new evidence from relevant SRs and RCTs published during the last 10 years and on discussions by a multi-disciplinary TF. A plan for dissemination and implementation will be developed, with emphasis on the recommendation on patient education, with the ultimate aim to improve the quality of care for people with hip and knee OA.

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OP0077

JOINT DISTRACTION USING AN INTENDED DEVICE FOR KNEE OSTEOARTHRITIS: A PROSPECTIVE TWO-YEAR FOLLOW-UP

Keywords: Osteoarthritis, Non-pharmacological interventions

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Background: Knee distraction (KD) treatment for young (<65 years) patients with end-stage knee osteoarthritis (OA) has previously been shown to successfully postpone a knee arthroplasty for years by reducing pain, improving function, and inducing joint tissue repair.[1] During KD treatment, the tibia and femur are separated ~5 mm for ~6 weeks using an external fixation device. The studies performed thus far have used proof-of-concept medical devices intended for other applications than KD. Recently, the first device specifically designed and intended for KD treatment has been developed.
Objectives: The purpose of the current study was to evaluate the clinical efficacy of this intended device.
Methods: In 5 hospitals, 65 patients with end-stage knee OA, in general practice considered for arthroplasty or high tibial osteotomy, were offered KD treatment. Inclusion criteria included age ≤65 years, BMI <35 kg/m^2 with weight ≤110 kg, sufficient knee stability and physical condition, KL grade ≥2, malalignment ≤10 degrees, no history of inflammatory or septic arthritis. KD was performed according to a standardized protocol. Before and 1 and 2 years after treatment, standardized knee radiographs were performed and patients filled out WOMAC (for pain and function, 0-100, primary clinical outcome) and SF-36 (quality of life, 0-100, secondary outcome) questionnaires. From the radiographs, minimum joint space width (JSW, mm, primary structural outcome) was measured by 1 experienced observer and baseline KL grade was determined. Use of self-reported pain medication (paracetamol, opioids, NSAIDs) and intra-articular injections were registered, as were adverse events. Changes over 2 years were evaluated for statistical significance with paired t-tests for continuous variables and McNemar's tests for categorical variables. For the WOMAC, clinical significance was evaluated as well, on group level defined as an increase of ≥15 points and on individual level using OARSI-OMERACT response criteria. The influence of adverse effects on 2-year changes in primary outcomes was analyzed with independent t-tests.
Results: Of the 65 patients (age: 53.3±6.7; BMI: 28.0±3.2; sex: 38 (55%) male; KL grade 0/1/2/3/4: 0 (0%)/ 7 (11%)/ 26 (40%)/ 23 (36%)/ 9 (14%)), 49 patients completed 2 years follow-up. 1 Patient did not complete treatment, 7 patients received arthroplasty (3 in the 1st year) and 8 patients were lost to follow-up in the 2nd year. The total WOMAC score showed a statistically and clinically significant improvement at 1 and 2 years (+26 and +24 points; Figure 1), as did all subscales (all p<0.001). After 1 year 72% of patients were clinical responders, at 2 years this was reduced to 55%. The minimum radiographic joint space width improved over 1 (+0.5 mm; p<0.001) and 2 (+0.4 mm; p=0.015) years (Figure 1), as did the physical SF-36 (+10 points; p<0.001). The most common adverse event was pin tract infection, experienced by 43 (66%) of patients, in the majority successfully treated with oral antibiotics. In 2 cases hospitalization and/or intravenous antibiotics were needed. 8 Patients experienced device-related complications. None of the complications influenced the 2-year outcomes. Before treatment, 42% of patients used pain medication, which had nearly been halved 1 (23%; p=0.02) and 2 years (29%; p=0.27) post-treatment. In total 12 (18%) patients had received an intra-articular injection before KD treatment, of whom 5 (8%) steroids and 3 (5%) hyaluronic acid. Both in the 1st and 2nd year after treatment, 1 patient (2%) received an injection.
Conclusion: Patients treated with the first device intended for KD treatment showed significant clinical and structural improvement after 1 and 2 years. Importantly, the effect was clinically relevant, as a majority of patients were clinical responders and pain medication use decreased. Long-term evaluation will show whether arthroplasty can be postponed successfully as well.
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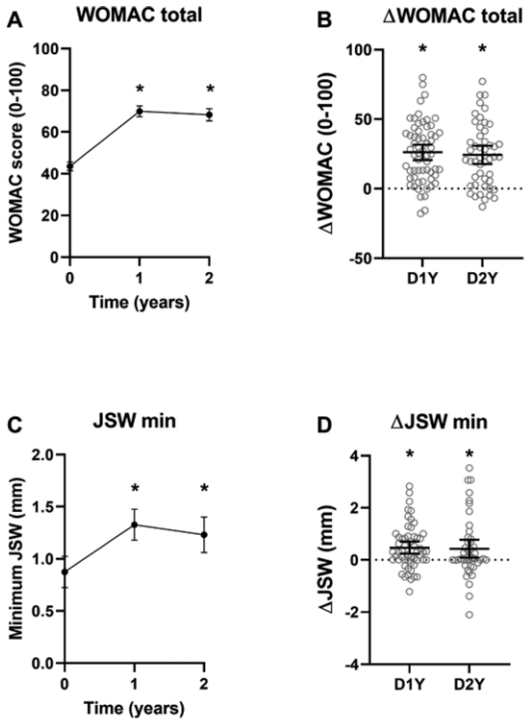


Figure 1: Total WOMAC at baseline (BL) and 1 and 2 years after treatment (A), 1- and 2-year changes in total WOMAC compared to BL (B), minimum joint space width (JSW) at BL and 1 and 2 years after treatment (C), and 1- and 2-year changes in minimum JSW compared to BL (D). (A) and (C) show mean and standard error of the mean, (B) and (D) show mean change and 95% confidence interval. Asterisks indicate statistically significant differences compared to BL (p<0.05).

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COVID 19: A pandemic with a long tail

OP0078

PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES ARE NOT AT INCREASED RISK OF LONG-COVID: DATA FROM A LARGE PROSPECTIVE CONTROLLED COHORT STUDY

Keywords: Epidemiology, COVID, Inflammatory arthritides

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Background: Studies on long-term consequences of COVID-19, commonly referred to as long-COVID, in patients with inflammatory rheumatic diseases (iRD) are still scarce, and available data are heterogeneous and largely inconclusive. In addition, it is unknown whether correctly classifying patients with iRD as long-COVID cases is complicated by increased background noise due to the occurrence of persistent symptoms that could be attributed to both long-COVID and iRD.

Objectives: The primary objective was to compare the risk of developing long-COVID after a SARS-CoV-2 infection with the Omicron variant between patients with iRD and age and sex matched healthy controls. A secondary objective was to compare the prevalence of the different persistent symptoms observed in long-COVID between patients with iRD and healthy controls with and without a history of COVID-19.
Methods: We collected data from participants enrolled in a Dutch prospective cohort study that was designed to compare the disease severity of COVID-19 between iRD patients and healthy controls from the start of the pandemic. Demographic and clinical data, including data on the occurrence of SARS-CoV-2 infections, were collected via online questionnaires. On March 10, 2022, all study participants were asked about the occurrence, onset, severity and duration of persistent symptoms during the first two years of the COVID-19 pandemic, independent of their history with COVID-19. Subsequently, we prospectively monitored a subset of the cohort, participants with a PCR or antigen confirmed SARS-CoV-2 Omicron infection, for COVID-19 sequelae. In line with WHO guidelines, long-COVID cases were defined as participants who reported persistent symptoms that lasted at least 8 weeks, started after the onset and within 3 months of a confirmed SARS-CoV-2 infection, and could not be explained by an alternative diagnosis. Descriptive statistics, logistic regression analyses and Kaplan Meier survival analyses were used for statistical analyses.
Results: A total of 1974 iRD patients and 733 healthy controls participated, of whom 468 (24%) patients and 218 (30%) controls had a SARS-CoV-2 Omicron infection. Of those, 361 (77%) patients and 172 (79%) controls completed COVID-19 sequelae questionnaires. More patients compared to controls fulfilled long-COVID criteria; 77 (21%) vs. 23 (13%) respectively (OR: 1.73, 95% CI: 1.04 – 2.87, *P* 0.03; Table 1). However, the effect attenuated after adjusting for potential confounders (aOR: 1.49, 95% CI: 0.88 – 2.52, *P* 0.14; Table 1). Post-hoc evaluation of covariables in the regression model showed that higher BMI and worse disease severity of the acute infection phase of SARS-CoV-2 were significantly associated with higher odds of developing long-COVID (Table 1). Fatigue and loss of fitness were the most frequently reported symptoms in both iRD patients and healthy controls with long-COVID, and recovery time from long-COVID was similar for patients and controls (*P* 0.47). Lastly, persistent symptoms were reported more frequently by participants with a history of COVID-19 compared to those without a history of COVID-19; 43% of iRD patients vs. 33% of controls with a history of COVID-19, and 21% of iRD patients vs. 11% of controls without a history of COVID-19.
Conclusion: We found that 21% of iRD patients and 13% of healthy controls met WHO-criteria for long-COVID after a SARS-CoV-2 Omicron infection. However, confounding by BMI and severity of the acute infection phase of SARS-CoV-2 attenuated this difference, and the duration of long-COVID was similar between patients and controls. In addition, since more iRD patients than healthy controls without a history of COVID-19 reported symptoms that are also observed in long-COVID, we believe that the observed difference in long-COVID between patients and controls could in part also be explained by clinical manifestations of underlying rheumatic diseases. We therefore conclude that iRD patients are not more susceptible for long-COVID than people from the general population.

Table 1. Regression analyses in participants with a SARS-CoV-2 Omicron infection.

Risk of developing long-COVID				
Univariable model		OR	95% CI	P-value
	Healthy controls*	1.00	-	
	Patients with rheumatic diseases	1.73	(1.04 – 2.87)	**0.03**
Multivariable model				
	Healthy controls*	1.00	-	
	Patients with rheumatic diseases	1.49	(0.88 – 2.52)	0.14
	Age	1.02	(1.00 – 1.12)	0.14
	Sex			
	male sex*	1.00	-	
	female sex	1.09	(0.66 – 1.81)	0.88
	BMI	1.06	(1.01 – 1.12)	**0.02**
	Cardiovascular disease	0.88	(0.66 – 1.81)	0.73
	Pulmonary disease	1.15	(0.56 – 2.37)	0.71
	Severity of acute infection phase of SARS-CoV-2 #			
	WHO severity score < 3*	1.00	-	
	WHO severity score ≥ 3	3.05	(1.80 – 5.19)	**<0.001**

*Table showing results of logistic regression analyses. Data are odds ratios (OR) with corresponding 95% confidence intervals (CI's) and P values. *Reference group. #A WHO score of 1 indicates asymptomatic infection, a score of 2 indicates mild disease without need for assistance, a score of 3 indicates mild disease with need for assistance (ie, could not care for themselves in daily life due to the severity of their symptoms) but no hospitalisation, a score of 4 or higher indicates admission to hospital, intenstive care unit or death. P value < 0.05 was considered statistically significant.*

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OP0079

OMICRON VARIANT INFECTION IN INFLAMMATORY RHEUMATOLOGICAL CONDITIONS - OUTCOMES FROM A COVID-19 NAIVE POPULATION IN AOTEAROA NEW ZEALAND

Keywords: Descriptive Studies, COVID, Registries

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Background: Due to geographic isolation and border controls, Aotearoa New Zealand attained high levels of population coronavirus disease-19 (COVID-19) vaccination before widespread community transmission of Omicron variant COVID-19 in early 2022. This provides a unique opportunity to examine outcomes in people with rheumatic diseases immunologically naive to COVID-19.
Objectives: This study aims to describe the outcomes of Omicron variant COVID-19 infection in people with rheumatic diseases in Aotearoa New Zealand.
Methods: We conducted an observational study of people with inflammatory rheumatic disease and COVID-19 infection from centers in Aotearoa New Zealand between 1 February to 30 April 2022. Data were collected via the Global Rheumatology Alliance Registry, including demographic and rheumatic disease characteristics and COVID-19 vaccination and outcomes. Multivariable logistic regression was used to explore associations of demographic and clinical factors with COVID-19 hospitalisation and death.
Results: A total of 1599 cases were included, with 98% from three hospitals that systematically identified all patients from rheumatology clinics who had COVID-19 infection. At the time of COVID-19 infection, 1513 cases (94.6%) had received at least two COVID-19 vaccinations. Hospitalisation occurred for 104 (6.5%) cases, and 10 (0.6%) patients died. A lower frequency of hospitalisation was seen in cases who had received at least two vaccinations (5.9%), compared to cases who were unvaccinated (20.6%) or who received a single vaccine dose (10.7%). In multivariable adjusted models, people with gout (OR 2.2 95% CI 1.02, 4.77) or connective tissue diseases (CTD) (OR 2.78 CI 1.61, 4.80) had increased risk of the combined outcome of hospitalisation and death, compared to people with inflammatory arthritis. Glucocorticoid and rituximab use were associated with 3 to 6 times higher odds of hospitalization and/or death. All cases who died had three or more co-morbidities associated with a known higher risk of poor outcomes or were over 60 years old.
Conclusion: In this cohort of people with inflammatory rheumatic diseases with high vaccination rates, severe outcomes from Omicron variant COVID-19 were infrequent. The hospitalisation rate during COVID-19 infection was higher in people who had not completed the primary vaccination course, had gout or CTD, and used glucocorticoids. These findings suggest that outcomes of Omicron variant COVID-19 infection among people with rheumatic disease who are vaccinated but immunologically naive to prior COVID-19 variant infections were favorable.
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OP0080

INCIDENCE AND CLINICAL OUTCOME OF COVID-19 RELATED TO POST-VACCINATION ANTIBODY LEVELS IN PATIENTS ON IMMUNOSUPPRESSIVE THERAPY: A PROSPECTIVE STUDY IN THE OMICRON ERA

Keywords: COVID, Vaccination/Immunization, Adaptive immunity

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Background: Patients with immune mediated inflammatory diseases (IMIDs) on immunosuppressive therapies are known to be at greater risk of severe COVID-19 disease, hospitalisation and death. Protective levels of anti-Spike antibodies following vaccination are yet to be determined.
Objectives: To examine whether post-vaccination anti-Spike antibody levels were predictive of breakthrough infection and the clinical outcome of COVID-19.
Methods: The Nor-vaC study is a prospective cohort study that includes IMID patients on immunosuppressive therapies[1]. In the present analyses we included patients who provided post-vaccination samples and responded to follow-up questionnaires after three vaccine doses. Hospital records and the Norwegian Death Cause Registry provided information on hospital admissions and cause of death. Anti-Spike antibody levels were measured 2 – 4 weeks after vaccination. Analyses were performed using a cox-regression with time running from two weeks post 3rd vaccine dose until COVID-19 or a 4th vaccine dose, adjusting for age, sex, diagnosis, medication and comorbidity, with calendar month as a time varying covariate.
Results: A total of 1051 IMID patients (375 rheumatoid arthritis (RA), 148 psoriatic arthritis (PsA), 155 spondyloarthritis (SpA), 215 Crohn's disease (CD), 158 ulcerative colitis (UC)) on immunosuppressive therapies were included in these analyses, median age 56 (IQR 43 – 65), and 586 (56%) female, with an observation period spanning from July 7th 2021 to December 14th 2022. Patients had received either BNT162b2 (61%) or mRNA-1273 (39%) as a 3rd dose. Immunosuppressive medication included TNF inhibitors (TNFi) mono[a]- (41%) or combination therapy[b] (23%), methotrexate (16%), interleukin (IL) inhibitors[c] (5%), janus kinase (JAK) inhibitors[d] (3%), vedolizumab (5%) and other medication[e](2%).
During the observation period 265 patients (25%) were registered with COVID-19 after the 3rd vaccine dose. In total, 24 patients had COVID-19 before the Omicron variant became predominant in Norway (1st January 2022). Symptoms of COVID-19 for more than two weeks were reported by 53 patients (20 %). One patient was hospitalised, and no patients died due to COVID-19 during the observation period. A post-vaccination antibody level above 12.000 BAU/ml gave a reduced risk of clinical COVID-19 infection (hazard ratio (HR) 0.56, p=0.007, 95% CI (0.36, 0.85) (Figure 1). Antibody levels above this cut-off were found in 10 % of patients. The presence of comorbidities (HR 1.85, p = 0.001, 95% CI (1.27,2.70)) or UC (HR 1.6, p= 0.001, 95 %CI (1.11, 2.35) increased the risk of breakthrough infections.
Post-vaccination anti-Spike antibody levels were not associated with duration of COVID-19 over two weeks.
Conclusion: Patients with the highest post-vaccination anti-Spike levels had a lower risk of COVID-19 infection, supporting the role of repeated vaccination in IMID patients on immunosuppressive therapies. These results also underline the good prognosis of Omicron infections in vaccinated IMID patients. Though patients knowing they had low anti-Spike levels may have shielded during periods of high transmission, the absence of severe infections and deaths in this large cohort indicates that low antibody levels did not greatly increase risk of severe COVID-19.
[a]TNF inhibitors: infliximab, etanercept, adalimumab, golimumab, certolizumab pegol.
[b]Combination therapy: methotrexate, sulfasalazine, leflunomide, azathioprine.
[c]IL-inhibitors: tocilizumab, secukinumab.
[d]JAK-inhibitors: filgotinib, baricitinib, upadacitinib, tofacitinib.
[e]Other: abatacept, sulfasalazine, leflunomide, azathioprine.

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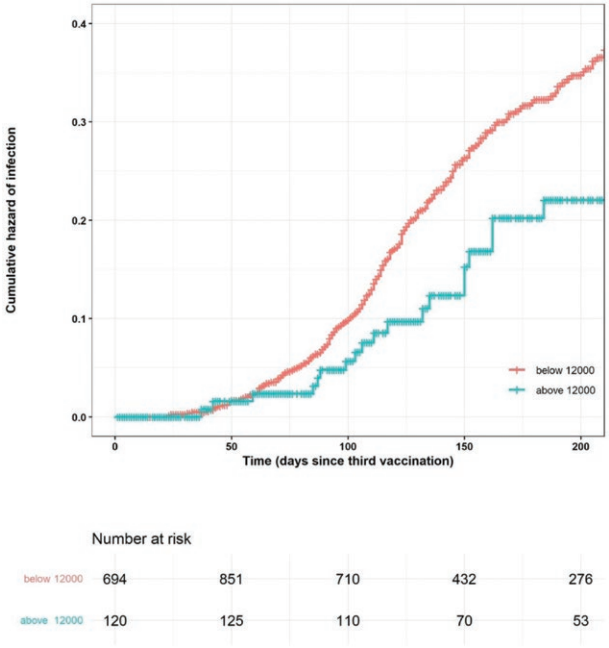


Figure 1. Cumulative hazard of infection for patients with antibodies above 12.000 BAU/ml (green) and those with antibodies below 12.000 BAU/ml (red). Patients with post-vaccination antibody levels above 12.000 BAU were less likely to develop COVID-19 during follow-up.

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OP0081

PREVALENCE, CHARACTERISTICS, AND PREDICTORS OF BREAKTHROUGH COVID-19 INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE COVID-19 VACCINATION IN AUTOIMMUNE DISEASE (COVAD) STUDY

Keywords: Rheumatoid arthritis, COVID, Vaccination/Immunization

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Background: Global data on COVID-19 breakthrough infections (BI) following COVID-19 vaccination among autoimmune rheumatic diseases (AIRDs) and especially rheumatoid arthritis (RA) is scarce.

Objectives: This study aimed to examine the characteristics of COVID-19 BI among patients with RA and compare them with AIRDs and healthy controls (HCs).

Methods: A global e-survey, January-May 2022, collected data on COVID-19 vaccination, and BI in patients with RA, AIRDs, non-rheumatic autoimmune disease (nrAIDs), and HCs. BI was defined as infection after both primary or booster vaccine doses. Severe BI was defined as the need for hospitalization, including intensive unit care, oxygen therapy, or advanced treatment in the form of monoclonal antibodies.

Results: Of the 9595 vaccinated respondents of the e-survey, 3224 (33.6%) reported COVID-19. One BI was reported in 323/1802 (17.9%) patients with RA, 584/3869 (15.0%) patients with other AIRDs, and 467/3435 (13.5%) HCs. Similarly, second BI was reported by 280 (8.6%); 42 (2.3%) among RA, 90 (2.3%) among other AIRDs, and 124 (3.6%) among HCs.

The prevalence of first BI in patients with RA was higher than that in those with AIRDs (OR=1.2; 95%CI=1.1-1.4; p=0.001) and HCs (OR=1.4; 95%CI=1.2-1.6; p<0.001), but similar to nrAIDs (p=0.783). The prevalence of second BI was lower in patients with RA than in HCs (OR=0.6; 95%CI=0.4-0.9; p=0.012) and nrAIDs (OR=0.4; 95%CI=0.2-0.7; p=0.004), but similar to AIRDs (p=0.991). When compared with HCs, patients with RA reported significantly higher joint pain, hospitalizations, and need for advanced treatment at first BI. Patients with RA from very high HDI countries had lower hazard of first BI than those from high HDI countries (HR=0.026; 95%CI=0.001-0.6; p=0.027). Rituximab use predicted more frequent hospitalization (OR=3.4; 95%CI=1.3-11.4; p=0.045) and severe BI (OR=3.0; 95%CI=1.2-7.3; p=0.014).

Conclusion: Nearly one in five patients with RA reported BI. BI prevalence was higher in patients with RA and of higher severity than in HCs. Country HDI was an important determinant of outcomes, suggesting potential impact of environmental dynamics, local vaccination policy, and syndemic constructs that merit further exploration. Rituximab use predicted more frequent hospitalizations and more severe BI.

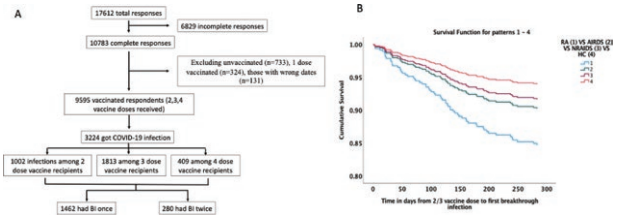


Figure 1. A. Flow chart of respondents, 1B. Survival analysis between RA, AIRDs, nrAIDs, and HC

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OP0082

COVID-19 VACCINE SAFETY DURING PREGNANCY AND BREASTFEEDING IN WOMEN WITH AUTOIMMUNE DISEASES: RESULTS FROM THE COVAD STUDY

Keywords: Pregnancy and reproduction, COVID, Vaccination/Immunization

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Table 1. Characteristics of female subjects according to groups. Percentages in parenthesis. *Pregnancy/breastfeeding status at the time of the survey and/or at the time of at least one dose of COVID-19 vaccine. Chi squared test: ~ p=0.01; ° p=0.03; § p<0.01.

	Total Women (n=6787)	Group A Non-pregnant, non-breastfeeding with AID (n=4862)	Group B Pregnant with AID* (n=40)	Group C Breastfeeding with AID* (n=52)	Group D Non-pregnant, non-breastfeeding HC (n=1749)	Group E Pregnant HC* (n=31)	Group F Breastfeeding HC* (n=53)
Age (median, IQR)	47, 35-58	50, 38-61	34, 31-35.25	33, 30-35	39, 29-49	34, 30-36.5	33, 30-36
Caucasian	3225 (47.5)	2634 (54.1)	12 (30)	22 (42.3)	538 (30.8)	7 (22.6)	12 (22.6)
No comorbidities	3027 (44.6)	1815 (37.3)	19 (47.5)	36 (69.2)	1102 (63)	17 (54.8)	38 (71.7)
Number of vaccinated women, n (%)	6632 (97.7)	4753 (97.8)	40 (100)	50 (96.2)	1710 (97.8)	30 (96.8)	49 (92.5)
≥3 doses	4850 (71.5%)	3583 (73.7%)	26 (65%)	33 (63.5%)	1155 (66%)	23 (74.2%)	30 (56.6%)
No AE	4950 (74.6)	3517 (74)~	22 (55)~	36 (72)	1312 (76.7)	22 (73.3)	36 (73.5)
Injection site (arm) pain and soreness	630 (9.5)	471 (9.9)	7 (17.5)	7 (14)	138 (8.1)	2 (6.7)	5 (10.2)
Minor AE	1614 (24.3)	1232 (25.9)°	16 (40)°	12 (24)	338 (19.8)	7 (23.3)	10 (20.4)
Major AE	285 (4.3)	196 (4.6)§	7 (17.5)§	1 (2)	77 (4.5)	1 (3.3)	3 (6.1)
Hospitalization	74 (1.1)	51 (1.1)	2 (5)	0 (0)	20 (1.2)	0 (0)	1 (2)

of Southern Denmark, Department of Regional Health Research (IRS), Odense, Denmark; [4]*Guys and St Thomas' NHS Foundation Trust, Thrombosis and Hemostasis, London, United Kingdom*; [5]*Maulana Azad Medical College, 2-Bahadurshah Zafar Marg, New Delhi, India*; [6]*Sanjay Gandhi Postgraduate Institute of Medical Sciences, Department of Clinical Immunology and Rheumatology, Lucknow, India*; [7]*Karolinska Institutet and Karolinska University Hospital, Stockholm, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden*; [8]*Faculty of Medicine and Health, Örebro University, Department of Rheumatology, Örebro, Sweden*; [9]*Pontifica Universidad Javeriana, Reference Center for Osteoporosis, Rheumatology and Dermatology, Cali, Colombia*; [10]*Mahidol University, Division of Rheumatology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand*; [11]*Queen Savang Vadhana Memorial Hospital, Department of Medicine, Chonburi, Thailand*; [12]*University Hospital "St. Ivan Rilski", Department of Rheumatology, Sofia, Bulgaria*; [13]*University of Nigeria Teaching Hospital, Ituku-Ozalla/University of Nigeria, Enugu Campus, Department of Medicine, Enugu, Nigeria*; [14]*Sofia University St. Kliment Ohridski, Medical Faculty, Sofia, Bulgaria*; [15]*Institute of Medical Research, Walter and Eliza Hall, Parkville, Australia*; [16]*University of Melbourne, Department of Medical Biology, Parkville, Australia*; [17]*Royal Melbourne Hospital, Department of Rheumatology, Parkville, Australia*; [18]*Byramjee Jeejeebhoy Government Medical College, Sassoon General Hospitals, Pune, India*; [19]*Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Division of Rheumatology, São Paulo, Brazil*; [20]*National Medical Center "La Raza", Instituto Mexicano del Seguro Social, Department of Internal Medicine, General Hospital, Mexico City, Mexico*; [21]*University of Pavia, Rheumatology Unit, Dipartimento di Medicine Interna e Terapia Medica, Pavia, Italy*; [22]*Nippon Medical School Graduate School of Medicine, Department of Allergy and Rheumatology, Tokyo, Japan*; [23]*Friedrich-Alexander-Universität Erlangen-Nürnberg, Medizinische Klinik 3 - Rheumatologie und Immunologie, Universitätsklinikum Erlangen, Erlangen, Germany*; [24]*Mayo Clinic, Division of Rheumatology, Rochester, United States of America*; [25]*Taichung Veterans General Hospital, Division of Allergy, Immunology and Rheumatology, Department of Medical Research, Taichung, Taiwan, Republic of China*; [26].,.,., *United Kingdom*; [27]*School of Biological Sciences, The University of Manchester, Division of Musculoskeletal and Dermatological Sciences, Centre for Musculoskeletal Research, Manchester, United Kingdom*; [28]*Manchester University NHS Foundation Trust, National Institute for Health Research Manchester Biomedical Research Centre, Manchester, United Kingdom*; [29]*Manchester Academic Health Science Centre, Department of Rheumatology, Salford Royal NHS Foundation Trust, Salford, United Kingdom*; [30]*University of Pittsburgh School of Medicine, Division of Rheumatology and Clinical Immunology, Pittsburgh, United States of America*; [31]*New Cross Hospital, Royal Wolverhampton Trust, Department of Rheumatology, Wolverhampton, United Kingdom*

Background: COVID-19 vaccine hesitancy among pregnant and breastfeeding women with autoimmune diseases (AID) is often attributed to the fear of adverse events (AE) and disease flares (DF). No data are available regarding COVID-19 vaccine safety in this population.

Objectives: We aimed at describing delayed-onset (>7 days) vaccine-related AE (minor and major), DF, and related AID treatment modifications from the COVID-19 Vaccination in Autoimmune Diseases (COVAD) study.

Methods: Among complete responses from 9201 participants as of June 21, 2022, 6787 (73.8%) were women. Six subgroups were identified upon diagnosis of AID vs healthy controls (HC) and their pregnancy/breastfeeding status at the time of any dose of vaccine (Figure 1).

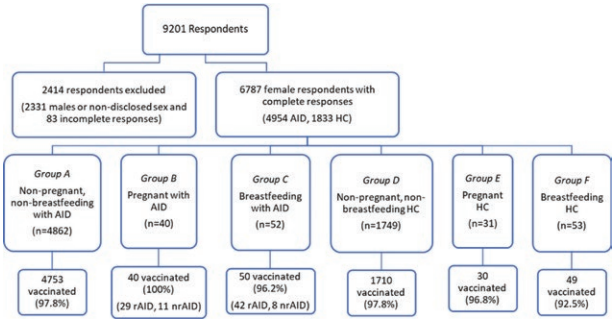


Figure 1. Flowchart of the study. AID: autoimmune diseases; HC: healthy controls; rAID: rheumatic AID; nrAID: non-rheumatic AID.

Results: Forty pregnant and 52 breastfeeding AID patients were identified and their vaccination rates (at least one dose) was 100% and 96.2%, respectively (Table 1). Overall AE, minor AE, and major AE were reported significantly more frequently by pregnant than non-pregnant patients (45% vs. 26%, p=0.01; 40% vs. 25.9%, p=0.03; 17.5% vs. 4.6%, p<0.01), but no difference was found in comparison with pregnant HC. No difference was observed between breastfeeding patients and HC. Post-vaccination DF were reported by 17.5% of pregnant and 20% of breastfeeding patients, and by 18% of age- and disease-matched control patients (n=2315). All DF in pregnant/breastfeeding patients were managed with glucocorticoids and a fifth of them required initiation or change in immunosuppressive treatment.

Conclusion: This study provides the first insights into the safety of COVID-19 vaccination during the antenatal period in women with AID. While AEs were more commonly reported by pregnant patients with AID, these were no higher than among pregnant healthy controls without AID. These observations are reassuring, likely to strengthen physician-patient communication and overcome hesitancy as the benefits for the mother and fetus by passive immunization are likely to overweigh the potential risks of AE and DF.

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OP0083

ANAKINRA PLUS STANDARD OF CARE FOR THE REDUCTION OF HYPERINFLAMMATION AND RESPIRATORY DISTRESS IN PATIENTS WITH SARS-COV-2 INFECTION: A MULTICENTRE, RANDOMISED, OPEN-LABEL PHASE 2/3 TRIAL (ANA-COVID-GEAS STUDY)

Keywords: COVID, bDMARD, Randomized control trial

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Background: COVID-19 pneumonia is often associated with hyperinflammation. The efficacy and security of anakinra in patients with severe COVID-19 pneumonia and hyperinflammation are still unclear.
Objectives: The primary endpoint was the proportion of patients not requiring mechanical ventilation up to 15 days after treatment initiation, assessed on an intention-to-treat-basis.
Methods: A multicentre, randomised, open-label, two-arm phase 2/3 trial was conducted at 12 hospitals in Spain. Adult patients with severe pneumonia were randomly assigned (1:1) to receive either usual standard of care plus anakinra (anakinra group) or usual standard of care alone (SoC group). Anakinra was given at a dose of 100 mg four times a day intravenously. The trial is registered with ClinicalTrials.gov; NCT04443881.
Results: Between 8 May 2020 and 1 March 2021, a total of 179 patients were randomly assigned to the anakinra group (n=92) or to the SoC group (n=87). The proportion of patients not requiring mechanical ventilation up to day 15 was not significantly different between groups (77.1% for Anakinra group vs 85.9% for SoC group, risk ratio 0·90 [95% CI 0·77–1·04]; p=0·16). Anakinra did not result in any difference in time to mechanical ventilation (HR 1·72 [95% CI 0·82-3·62], p=0·14). There was no significant difference between groups in the proportion of patients not requiring invasive mechanical ventilation up to day 15 (RR 0·99 [95% CI 0·88–1·11]; p=1·00).
Conclusion: Anakinra did not prevent the need for mechanical ventilation or reduce mortality risk compared with standard of care alone in hospitalised patients with severe COVID-19

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OP0084 POSSIBLE ROLE OF PEPTIDE EPITOPES OF COVID-19 BNT-162B2 MRNA VACCINE IN FOMENTING AUTOIMMUNITY: AN IN SILICO ANALYSIS

Keywords: Adaptive immunity, Vaccination/Immunization, COVID

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Background: Following the launch of the global COVID-19 vaccination campaign, there have been increased reports of autoimmune diseases developing de novo following vaccination. These cases include rheumatoid arthritis, autoimmune hepatitis, immune thrombotic thrombocytopenia, and connective tissue diseases. Nevertheless, COVID-19 vaccines are considered safe for patients with autoimmune diseases and are strongly recommended.
Objectives: The aim of this in silico analysis is to investigate the presence of protein epitopes encoded by the BNT-162b2 mRNA vaccine, one of the most commonly administered COVID-19 vaccines, that could elicit an aberrant adaptive immune response in predisposed individuals.
Methods: The FASTA sequence of the protein encoded by the BNT-162b2 vaccine was retrieved from http://genome.ucsc.edu and used as a key input to the Immune Epitope Database and Analysis Resource (www.iedb.org). Linear peptides with 90% BLAST homology were selected, and T-cell, B-cell, and MHC ligand assays without MHC restriction were searched and evaluated. HLA-disease associations were screened on the HLA-SPREAD platform (https://hla-spread.igib.res.in) by selecting only positive markers.
Results: A total of 183 epitopes were found, corresponding to 178 SARS-CoV-2 and 5 SARS-CoV spike epitopes, respectively. Results were obtained from 22 T-cell assays, 398 B-cell assays, and 2 MHC ligand assays. Complementary receptors included 1080 T-cell receptors and 0 B-cell receptors.
Specifically, the IEDB_epitope:1329790 (NATNVVIKVCEFQFCNDPFLGVYY) was shown to bind to HLA-DRB1*15:02 and HLA-DRB1*15:03 alleles, whereas the IEDB_epitope:1392457 (TKCTLKSFTVEKGIYQTSNFRVQPT) was reported to bind to HLA-DRB1*07:01, HLA-DRB1*03:01, HLA-DRB3*01:01, and HLA-DRB4*01:01 alleles. The HLA alleles detected were found to be positively associated with various immunological disorders (Table 1).

Table 1. MHC-restricted epitopes of the BNT-162b2 vaccine and potentially associated immunological conditions

Epitope	Assay	MHC molecule	Associated disease (population)
NATNVVIKVCEFQFCNDPFLGVYY + OX(C10)	cellular MHC/ mass spectrometry ligand presentation	HLA-DRB1*15:02	Takayasu arteritis (Japanese) Arthritis (Taiwanese) Scleroderma (Japanese) Colitis (Japanese)
		HLA-DRB1*15:03	Systemic lupus erythematosus (Mexican American)
TKCTLKSFTVEKGIYQTSNFRVQPT + SCM(K2)	as above	HLA-DRB1*07:01	Allergy, hypersensitivity (Caucasian)
		HLA-DRB1*03:01	Type 1 diabetes (African) Sarcoidosis, good prognosis (Finnish)
		HLA-DRB3*01:01	Graves' disease (Caucasian) Thymoma (Caucasian) Sarcoidosis (Scandinavian) Autoimmune hepatitis (Caucasian)
		HLA-DRB4*01:01	Vitiligo (Saudi Arabian)

Conclusion: Similar to the SARS-CoV-2 spike protein, the protein product of the BNT-162b2 mRNA vaccine contains immunogenic epitopes that may trigger autoimmune phenomena in predisposed individuals. Genotyping for HLA alleles may help identify at-risk individuals. However, further research is needed to elucidate the underlying mechanisms and potential clinical implications.

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OP0085 LONGITUDINAL T CELL RESPONSES TO A SERIES OF FOUR SARS-COV-2 VACCINE DOSES OR COVID-19 IN PATIENTS ON TNF INHIBITORS

Keywords: COVID, Vaccination/Immunization, Adaptive immunity

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Background: T cells are critical for control of viral infection with SARS-CoV-2, but knowledge is lacking on cellular immune responses following repeated vaccination and breakthrough infection in immunosuppressed patients.
Objectives: To examine longitudinal T cell responses across diagnoses, following vaccine series and COVID-19 in patients on tumor necrosis factor inhibitors (TNFi).
Methods: The prospective, observational Nor-vaC study included patients with arthritis (spondyloarthritis, rheumatoid arthritis, psoriatic arthritis) or inflammatory bowel disease (IBD) (ulcerative colitis, Crohns disease) on immunosuppressive therapies [1]. Here, we included patients on TNFi mono- or combination therapy immunised with up to four SARS-CoV-2 vaccine doses with or without

breakthrough infection, collecting peripheral blood mononuclear cells (PBMCs) 2-4 weeks after each immunisation. Samples were incubated with SARS-CoV-2 spike, nucleocapside or membrane peptides. The percentage of responding T cells was measured by flow cytometry (2) (≥0.01% increase in responding CD4 cells, ≥0.001% increase in responding CD8 cells, compared to baseline).

Results: Between February 2021 and December 2022, 144 patients on TNFi (monotherapy n=86 (60%), combination with methotrexate or azathioprine n=58 (40%)) were included (median age 48 years [IQR 33-57]; 51% women) (Table 1). The proportions of arthritis vs IBD patients with CD4 responses after 2 vaccine doses were 75% (12/16 patients) vs 86% (25/29), and after 3 doses 83% (10/12) vs 93% (28/30). In total, 80% (4/5) of arthritis patients showed further increases in CD4 responses after a 4th vaccine dose. Conversely, 81% (13/16) of arthritis patients vs. 55% (16/29) of IBD patients had CD8 T cell responses after two doses, and 67% (8/12) vs. 62% (18/29) after three doses. A 3rd and 4th dose induced higher CD8 responses compared to the previous dose in 55% (6/11) and 100% (5/5) of arthritis patients. Arthritis patients had lower T cell responses than IBD patients after the 3rd dose; median CD4 response 0.024% [IQR 0.009-0.036] vs 0.098% [IQR 0.040-0.182], p=0.0004; median CD8 response 0.003% [IQR 0.001-0.016] vs 0.044% [IQR 0.009-0.140], p=0.0032 (Figure 1). This difference remained robust after adjusting for age and sex, p<0.001, but was no longer detected after the 4th vaccine dose. Breakthrough infection elicited increased T cell responses across all diagnoses to spike (p<0.0001), and to nucleocapsid (p=0.002) and membrane proteins (p=0.001) compared to unstimulated T cells. Also, Spike-specific T cell responses increased compared to the 3rd dose (median CD4 T cell response 0.18% vs. 0.06%, p=0.003; CD8 T cell response 0.08% vs. 0.01%, p<0.0001), but to a lesser extent compared to the 4th dose (median CD4 response 0.18% vs. 0.12%, p=0.05; CD8 response 0.08% vs. 0.05%, p=0.26). There were no differences in cellular response between patients on TNFi mono- or combination therapy (p=0.93).

Conclusion: Patients on TNFi show improved cellular responses following each immunisation, with infection generating a strong and broad T cell response. Arthritis patients had significantly lower CD4+ responses compared to IBD patients after three vaccine doses, but with no difference after the 4th dose. These results support giving a 4th vaccine dose to TNFi-treated patients, with particular benefit for arthritis patients.

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Table 1. Number of patients providing T cells after vaccine doses and after COVID-19.

Disease, n (%)	Patients total[a] (n=144)	2 vaccines (n=49)	3 vaccines (n=86)	4 vaccines (n=44)	Hybrid immunity[b] (n=62)
Arthritis	25 (17)	17 (35)	19 (22)	5 (11)	5 (8)
IBD	119 (83)	32 (65)	67 (78)	39 (89)	57 (92)

[a]Sampled at minimum one timepoint[b]3 or 4 vaccine doses, followed by COVID-19

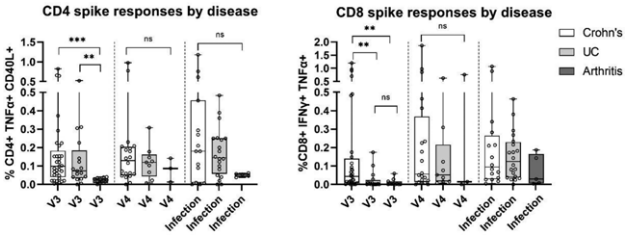


Figure 1. CD4 and CD8 T-cell responses to the 3rd (V3) and 4th (V4) vaccine doses/ three vaccine doses and COVID-19 infection in arthritis and IBD patients measured by TNFα+ CD40L+ (% of CD4+) and IFNγ+ TNFα+ (% of CD8+).

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Moving into better health

OP0086-HPR THE SWEDISH OSTEOARTHRITIS REGISTRY. TRENDS IN SWEDISH OSTEOARTHRITIS HEALTH CARE BETWEEN 2008- 2021

Keywords: Patient information and education, Descriptive Studies, Osteoarthritis

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Background: In 2012 the Swedish national guidelines for osteoarthritis (OA) were published. The guidelines implicit that all patients with OA should obtain information and supervised exercise as first-line intervention and that OA is a clinical, not radiological diagnosis. The Swedish OA registry contains data which measure compliance to the guidelines since 2008 [2].

Objectives: To describe the trends over time from 2008 to 2021 for patients who have received first-line interventions for hip and knee OA in Sweden and adherence of the healthcare staff to the national guidelines.

Methods: Descriptive registry-based study including patients with hip or knee OA who participated in first-line interventions including education and exercise. Data were extracted from the Swedish OA registry between January 1st, 2008, and December 31, 2021. The registry contains patient-reported outcomes and physiotherapist-reported outcomes. In this study the following physiotherapist-reported outcomes were described over time: radiological examination before first-line intervention, if the first-line intervention was given the first time the patient seek health care caused of OA, which explanation patients had been given about their disease, intake of painkillers before the start of first-line intervention and the percent who got supervised exercise >10 times according to the guidelines of OA in Sweden. The following patient-reported outcomes were described over time: mean BMI at the first visit, and mean age at the first visit. To be included in the study, participants had to meet the following criteria: i) clinical diagnosis of OA, with hip or knee OA as the most symptomatic joint, ii) provided 3-month follow-up.

Results: A total of 175 764 participants with hip or knee OA were included in the study. The trends from 2008-2021 showed that the proportion of patients who had a radiological examination before entering the first-line intervention decreased from 97 % to 65 % in men and from 95% to 62 % in women. The proportion of patients who get assess to first-line intervention the first time they seek for their symptoms increased from 4 % to 10 % both in men and women. People that get the correct information about OA increased from 15% to 40 %, and patients that get the explanation that OA was a tear and wear disease decreased from 30 % to 5%. The mean BMI (28) is unchanged over time. The mean age increased from 64 years to 67 years between 2008-2020 but decreased during the covid-19 pandemic to 64 years. The percentage that was given supervised exercise more than 10 times was constant between 2012-2020 at 30 % but decreased during the covid-19 pandemic to 20%.

Conclusion: The results implicit that the implementation of a supported OA self-management program in Sweden has been successful and changed the care given to patients with OA in Sweden. However, the national guidelines for OA, have still not been fully implemented. We need to keep implementing the guidelines so all patients with OA get the first-line intervention at the right time.

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OP0087-HPR HIGH INTENSITY EXERCISE IMPROVES GENERAL AND PHYSICAL FATIGUE IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS

Keywords: Physical therapy/Physiotherapy, Randomized control trial, Rheumatoid arthritis

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Background: Despite more effective control of inflammation by improved pharmacological therapies, persistent pain and fatigue are still a major problem among patients with rheumatoid arthritis (RA), which often leads to slow deterioration of function and general health.
Objectives: To evaluate the effect of high-intensity exercise on fatigue, pain, and general health in patients with established RA.
Methods: Patients with RA (ACR/EULAR 1987/2010 criteria), disease duration > 12 months, were recruited and randomised to either an exercise group or a control group. The exercise program of 12 weeks comprised supervised cardiorespiratory high-intensity interval exercise and strength exercise twice per week plus an additional non-supervised session of the patient´s own choice. The controls received individual information for physical activity according to the general health recommendations and were encouraged to be active on moderate intensive level ≥150 minutes/week. Outcomes. Self-reported ratings on symptoms were evaluated at baseline (BL) and 3 months (M3): Fatigue, using the Multidimensional Fatigue Inventory (MFI 20) scale, including five subscales; general fatigue, physical fatigue, mental fatigue, reduced activity and reduced motivation (range = 4 to 20 for each subscale, higher score = higher degree of fatigue); visual analogue scale (VAS) was used for the assessment of average pain intensity, fatigue and general health during the last week due to the rheumatic disease (0 = no symptom, 100 = worst possible).
Results: A total of 73 patients median age 49 (86.3% women), median disease activity 2.0 (1,34 to 2.56 IQR) (DAS28-ESR) were included in the study. At 3 months, there was a significant improvement on MFI-20 subscales general fatigue (p=0.002) and physical fatigue (p<0.001) in the intervention group when compared with the control group. No significant differences of change were found for the other subscales, general fatigue, reduced activity and reduced motivation or for VAS fatigue. A significant difference of change was found between the groups for VAS Global (p=0.026) while no significant differences of change was found for VAS pain between the groups. Table 1.
Conclusion: A 12-week exercise program of high intensity had beneficial effects on general fatigue and physical fatigue, in patients with established RA whereas the intervention did not influence pain intensity or general health. A multidimensional scale on fatigue appears to better distinguish changes in fatigue than a one-dimensional scale in patients with established RA.

Table 1. Differences between groups in assessment measures at 3 months compared to baseline

	Intervention group (n=37)		Control group (n=36)		Between group
	Baseline	Δ M3-BL (n=35)	Baseline	Δ M3-BL (n=29)	Analysis of change Δ *p*-value
MFI-20					
General fatigue	13,0 (11,0 to 17,5)	-3,0 (-5.0 to 1.0)**	14,0 (12,0 to 17,0)	1.0 (-2.0 to 3.0)	**0,002**
Physical fatigue	13,0 (9,0 to17,05)	-4.0 (-8.0 to -1.0)***	13,0 (10,0 to 16,0)	0.0 (-2.75 to 1.75)	**<0.001**
Mental fatigue	11,0 (7,0 to 12,5)	0.0 (-3.0 to 1.0)	11,0 (9,0 to 13,0)	0.0 (-3.0 to 1.0)	0,784
Reduced motivation	8,0 (5,0 to10,0)	0.0 (-3.0 to 1.0)	9,0 (6,0 to 12,0)	1.0 (-1.0 to 2.0)	0,110
Reduced activity	11,0 (8,0 to13,0)	-1.0 (-5.0 to 1.0)*	11,0 (8,00 to 13,0)	0.0 (-3.0 to 2.75)	0,159
VAS, 0-100 mm					
Fatigue	33.0 (15,9 to 49,2)	-2.0 (-12.0 to 11.8)	27,3 (6,0 to 46.3)	6.4 (-2.6 to 17.8)*	0.079
Pain	14,7 (7.6 to 17.9)	1,0 (-10.5 to 8.7)	12,6 (4.0 to 31.5)	1,4 (-13.4 to 8.1)	0.939
G-health	15.7 (7,0 to 26,8)	0,0 (-10.5 to 5.5)	14.0 (4.0 to 25.2)	2.5 (-0.2 to 29.4)*	**0.026**

Variables are presented as median and IQR. *MFI* Multidimensional Fatigue Inventory, *VAS* Visual Analog Scale Fatigue, Pain, Global. Delta values were compared using the Mann–Whitney *U* test. Within-group comparisons were made with Wilcoxon signed rank test. *Significant difference, p < 0.05. **Significant difference, p < 0.01. ***Significant difference, p < 0.001

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OP0088-HPR FACTORS ASSOCIATED WITH MEETING RECOMMENDED PHYSICAL ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO HAVE POOR PHYSICAL FUNCTION

Keywords: Patient reported outcomes, Lifestyles, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic disease that often leads to a major impact on physical function and quality of life. It is well known that physical activity is an important part of treatment and improve clinical outcome.
Objectives: The aim was to study factors associated with meeting recommended level of physical activity in people with RA with poorer physical function.
Methods: In 2017, a survey was sent to patients included in the BARFOT (Better Anti-Rheumatic pharmacotherapy) cohort [1]. The questionnaire included questions on age, sex, disease duration, smoking, body mass index (BMI), physical function assessed by health assessment questionnaire (HAQ; 0-3, best to worst), numeric rating scale (NRS) pain (0-10, best to worst), NRS fatigue (0-10, best to worst), disease activity assessed by self-reported 28-tender (TJC, 0-28) and swollen joint count (SJC, 0-28), health-related quality of life assessed by Europol 5-dimension 3-level (EQ5D; 0- 1, worst to best), empowerment assessed by the Swedish Rheumatic Disease Empowerment Scale (SWE-RES-23; 1-5, worst to best), cardiovascular diseases (CVD), and antirheumatic treatment, corticosteroids (CS), conventional disease-modifying antirheumatic drug (cDMARD), biologic DMARD (bDMARD). 1065 patients (69%) answered the questionnaire and were dichotomized based on the median of HAQ, which was 0.5. The group with the worst physical function, HAQ >0.5, was further dichotomized based on whether they met the World Health Organisation (WHO) recommended level of physical activity (pulse-increasing physical activity with moderate intensity at least 150 minutes/week or at least 75 minutes/week with high intensity) or not. Median and interquartile range (IQR) and Mann-Whitney U test or chi-2 were used to analyse differences between groups, when appropriate. A logistic regression model adjusting for age and sex was used to study factors associated with fulfilling the recommendations on physical activity.
Results: The patients with the worst physical function, meeting the criteria for recommended physical activity (RPA), had less pain, and fatigue, fewer swollen and tender joints, less CVD 48% vs. 64% (p<0.001), and fewer were obese than those who did not meet the recommendations (Not RPA), Table 1. They also had a better quality of life and a higher degree of empowerment, Table 1. Factors associated with fulfilling the recommended level of physical activity in the group with the worst physical function were obesity, BMI ≥30 kg/m^{2,} (OR 0.51, 95% CI 0.32-0.83), HAQ (OR 0.32, 95% CI 0.21-0.48), NRS pain (OR 0.84, 95% CI 0.77-0.91), NRS fatigue (OR 0.88, 95% CI 0.82-0.95), TJC (OR 0.97, 95% CI 0.95-1.00) and SJC (OR 0.96, 95% CI 0.93-0.99), EQ5D (OR 8.36, 95% CI 3.74-18.64), SWE-RE-S23 (OR 1.40, 95% CI 1.02-1.93). and cardiovascular diseases

(OR 0.65, 95% CI 0.45-0.95). Medical treatment was not associated with meeting the criteria for physical activity.

Conclusion: The results indicate a complex relationship between various factors that can affect the possibility to be physically active when having RA. Disease-related factors such as pain, fatigue, and tender and swollen joints are important to address, but also the health-related quality of life and empowerment, to be able to improve physical activity in individuals with RA that have poor physical function.

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Table 1. Characteristics of those not fulfilling recommended physical activity (Not RPA) vs. those fulfilling recommended physical activity (RPA) at questionnaire

	Not RPA Median (IQR)	RPA Median (IQR)	P-value
n	302	234	
Age, years	73 (14)	68 (15)	**<0.001**
Sex, female, %	77	79	0.62
Disease duration. year	15 (6)	15 (7)	0.47
Ever smoker, %	66	60	0.20
Obese (≥30 kg/m^2), %	23	15	**0.014**
HAQ, 0-3	1.1 (0.9)	0.9 (0.5)	**<0.001**
NRS pain, 0-10	5 (4)	4 (4)	**0.036**
NRS Fatigue, 0-10	6 (3)	5 (4)	0.06
TJC, 0-28	5 (11)	5 (8)	0.26
SJC, 0-28	2 (7)	2 (5)	0.19
EQ5D, 0-1	0.66 (0.23)	0.73 (0.18)	**<0.001**
SWE-RES 23, 1-5	3.6 (0.8)	3.7 (0.8)	**0.02**
No DMARD/CS	24	18	**0.01**
cDMARD	41	38	**0.01**
bDMARD	41	38	**0.01**
Only CS	24	37	**0.01**

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Disclosure of Interests: None Declared.
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OP0089-HPR PILATES IS BETTER THAN WALKING FOR PATIENTS WITH FIBROMYALGIA: A RANDOMIZED CONTROLLED TRIAL

Keywords: Pain, Fibromyalgia, Non-pharmacological interventions

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Background: Fibromyalgia (FM) is defined as a chronic syndrome characterized by diffuse musculoskeletal pain and several symptoms that reflect on the functional capacity and quality of life of the affected patients. Different types of exercises are recommended in the treatment of FM. Pilates is a method of physical conditioning that has been frequently used in rehabilitation programs, due to the benefits perceived in musculoskeletal disorders, as well as in other conditions.

Objectives: To evaluate the efficacy of Pilates method compared to aerobic exercise in pain, quality of life related to the disease, depression, quality of life in general, functional capacity, kinesiophobia, catastrophizing, treatment satisfaction and reduction in the use of medication by women presenting FM.

Methods: Sixty-six female patients diagnosed with FM were included, aging 18 to 65, presenting pain between 3 to 8 in numerical pain scale (NPS). Patients with inflammatory rheumatic diseases, neurological diseases, under psychiatric treatment, who have started or changed physical activities or medication in the last three months, patients with uncontrolled cardiorespiratory and cardiovascular diseases or any condition that may limit the practice of exercises, with non-diabetes mellitus controlled and other musculoskeletal diseases that could prevent the use of this method were excluded. The selected patients were randomized into two groups: Pilates and Control. The Pilates group (PG) had Pilates sessions three times a week for 12 weeks. The Control patients (CG) used a treadmill three times a week for 12 weeks. The treatment sessions in both groups lasted 50 minutes and the groups were instructed to use acetaminophen750 mg each 8 hours in case of pain, but the use was controlled. The evaluations were done by blind assessor at baseline (T0), 45 days (T45), 90 days (90) and 180 (T180) days after initiation of the study using the following instruments: for pain: NPS; Fibromyalgia Impact Questionnaire (FIQ), to evaluate the quality of life related to disease; Beck Depression Inventory (BDI) for depression; The short form 36 (SF-36) to evaluate the quality of life in general; the 6-minutes walking test (6MWT) to evaluate the functional capacity; kinesiophobia scale (Tampa) to evaluate the fear of movement; Fear Avoidance Beliefs Questionnaire (FABQ), to evaluate catastrophizing and the Likert scale to evaluate the patient satisfaction towards the treatment.

Results: Thirty four patients were randomized for the GP and 32 for the CG. The groups were homogeneous at baseline. In the comparison between groups over time, we found better results for PG with statistical differences when compared to CG for: pain (p<0,001), disease-related quality of life (p<0,001), psychological status (p=0,026), some domains of SF-36 – pain (p=0,014) and general health status (p<0,044), kinesiophobia scale (p<0,001), reduction in analgesic consumption (p=0,042) and on the Likert scale (p=0,003).

Conclusion: Pilates method is effective in the treatment of women with FM, presenting pain improvement, quality of life related to the disease, psychological status, the SF-36 (pain, general health) domains, the kinesiophobia scale, the analgesic consumption reduction and satisfaction with treatment with better results when compared to walking.

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Disclosure of Interests: None Declared.
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OP0090-HPR ASSOCIATION BETWEEN GRIP AND CORE MUSCLE STRENGTH IN PEOPLE WITH AXIAL SPONDYLOARTHRITIS (AXSPA) AND HEALTHY CONTROLS

Keywords: Spondyloarthritis, Physical therapy/Physiotherapy

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Background: Regular fitness assessments are part of the group exercise therapy concept for people with axSpA living in Switzerland. Participants ask if their performance is comparable with healthy people, which we cannot answer as no norm data are available. Among others, a test battery measuring the isometric strength endurance of the ventral, lateral, and dorsal core muscle chains (in seconds) is used (Rausch 2020). The core strength endurance test battery (CST) is time-consuming. In contrast, hand grip strength (in kg, Jamar dynamometer) can be tested within a short time and is already used as a substitute for multiple fitness-related tests (Kim 2022).

Objectives: 1) to compare core strength endurance of people with axSpA and healthy controls, and 2) to evaluate if grip strength can be used as a proxy for core strength to reduce the assessment time in people with axSpA.

Methods: Data was collected between April 2021 and December 2022. Data of people with axSpA were taken from the SVMB database of routinely gathered assessment data, and grip strength measurement was added. Further, data of CST and grip strength were collected in healthy controls, recruited from ZHAW staff and local sport clubs. All participants gave written informed consent. To investigate differences between both groups, relevant demographics, core and grip strength measures were compared using Welch Two-sample t-tests and Pearson's Chi[2] test, if appropriate. The associations between grip and core strength were explored through pairwise Spearman rank correlations (R_S) in both groups and sex-specific subgroups. In addition, we fitted linear regression models to the log-transformed data of people with axSpA.

Results: Data from 160 healthy people (50% male, mean age 59.3 (SD 11.47) years) and 122 people with axSpA (58% male, mean age 57.7 (SD 12.1) years) were included. In people with axSpA, mean years since symptoms were 37.3 (SD 24.9), and since diagnosis 29.4 (SD 27.1)). The median BASDAI score was 2.5 (IQR 1.7 – 4.2), and the median ADAS Health index was 3 (IQR 0 – 7). Demographic characteristics (i.e., age, sex, weight, height, BMI, and smoking status) did not differ between groups. However, people with axSpA showed less core strength endurance, measured in seconds: ventral mean difference -28, $p < 0.001$; lateral mean difference -17.1, $p < 0.001$; dorsal mean difference -38.5, $p < 0.001$.

Pairwise correlations in the two groups and sex-specific subgroups are summarized in Table 1.

Table 1. Correlations between grip and core muscle strength endurance in axSpA, healthy controls and sex-specific subgroups

Correlations grip and core strength endurance	People with axSpA (n=112)			Healthy people (n = 160)		
		Females (n=47)	Males (n=65)		Females (n=80)	Males (n=80)
Ventral	R_S = 0.34, 95%CI 0.16 - 0.49	R_S = 0.15, 95%CI -0.15 - 0.43	R_S = 0.29, 95%CI 0.05 - 0.50	R_S = 0.39, 95%CI 0.25 – 0.51	R_S = 0.32, 95%CI 0.12 – 0.51	R_S = 0.15, 95%CI -0.07 – 0.36
Lateral	R_S = 0.33, 95%CI 0.15 - 0.49	R_S = 0.14, 95%CI -0.16 - 0.42	R_S = 0.25, 95%CI -0.001 - 0.47	R_S = 0.51, 95%CI 0.38 – 0.61	RS = 0.46, 95%CI 0.27 – 0.62	R_S = 0.19, 95%CI -0.02 – 0.40
Dorsal	R_S = 0.07, 95%CI -0.13 - 0.27	R_S = 0.16, 95%CI -0.14 - 0.44	R_S = 0.27, 95%CI 0.01 - 0.50	R_S = 0.11, 95% CI -0.04 – 0.26	RS = 0.44, 95%CI 0.24 – 0.60	R_S = 0.05, 95%CI -0.17 – 0.27

The final linear regression model with grip strength as response and core strength, age, and sex as predictors explained 45% of the variability. Significant predictors in the model were ventral core strength endurance, age, and sex, while sex was the predictor with the most considerable effect.

Conclusion: People with axSpA showed lower core muscle strength endurance than healthy individuals. All correlations were small to moderate. The results from the multivariate analysis indicate that core strength endurance measures have only marginal effects on grip strength in people with axSpA. Therefore, grip strength is not appropriate to be used a s a proxy for core strength endurance in people with axSpA and healthy people.

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OP0091-HPR VISCERAL ADIPOSE TISSUE IS ASSOCIATED WITH CARDIORESPIRATORY FITNESS, BUT NOT WITH PHYSICAL ACTIVITY AND DISEASE VARIABLES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Physical therapy/Physiotherapy, Inflammatory arthritides

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Background: Increased body fat is reported in juvenile idiopathic arthritis (JIA) and may, together with disease activity, represent risk factors for the development of cardiovascular disease (CVD). Visceral adipose tissue (VAT) is particularly associated with risk of CVD, but VAT has been scarcely examined in JIA. Physical activity (PA) and cardiorespiratory fitness (CRF) may counteract unfavorable body composition.
Objectives: To examine associations between VAT and PA, CRF and disease variables in patients with JIA diagnosed in the era of biologics.
Methods: 60 patients, aged between 10-16 years, with persistent oligo- or poly-articular disease (extended oligoarthritis and polyarticular RF +/-), were recruited consecutively at Oslo University Hospital in 2015. VAT (g) was estimated by dual-energy X-ray absorptiometry (DXA). PA was measured with accelerometers during seven consecutive days. CRF was directly measured as peak oxygen uptake (VO_{2peak}) during a continuous graded exercise test on a treadmill until exhaustion. We assessed disease activity with the Juvenile Arthritis Disease Activity Scale 71 (JADAS 71) and functional disability with the Childhood Health Assessment Questionnaire (CHAQ). Cross-sectional associations were analyzed with univariate and multiple linear regression analyses.
Results: Complete data was available in 55 (47 girls) patients. Mean (SD) age was 13.4 (2.2) years. Median (25^{th}-75^{th} percentile) VAT (g), JADAS 71 and CHAQ were 61 (21-131), 3.2 (1.1-4.8) and 0.0 (0.0-0.3), respectively. Biologics was used as treatment by 23 (42 %) of patients. There was a significant inverse association between CRF and VAT (p=0.002) using univariate linear regression analysis (Table 1). Measures of PA and disease variables (JADAS 71 and CHAQ) were not statistically significantly associated with VAT. CRF was the only identified correlate for VAT in the best model fit, also after adjustments for age and sex.
Conclusion: In this well-treated patient cohort, CRF was inversely associated with VAT. Measures of PA and traditional disease variables were not associated with VAT. Our study supports that higher CRF is important for a healthy body composition, including VAT in patients with JIA.

Table 1. Associations between visceral adipose tissue mass and cardiorespiratory fitness, physical activity and disease variables

	Univariate regression analyses		Multiple regression analyses	
	Unstandardized B (95 % CI)	P- value	Unstandardized B (95 % CI)	P- value
Visceral adipose tissue (g)				
CRF (VO_{2peak} mL/kg/min)	-6.5 (-10.4, -2.6)	0.002	-6.5 (-10.4, -2.6)	0.002
Vigorous PA (min)	-2.7 (-5.7-0.3)	0.08		
Moderate PA (min)	0.1 (-0.3, 3.2)	0.94		
Sedentary behavior (min)	-0.1 (-0.6, 0.4)	0.64		
JADAS 71 (0-101)	0.2 (-10.8, 11.2)	0.97		
CHAQ (0-3)	-41.6 (-144.1, 60.8)	0.42		
			R^2 adjusted	0.18

In multiple regression analyses, variables with a p value < 0.20 were included. Nonsignificant variables (p ≥ 0.05) were removed until only significant variables (p < 0.05) remained.CRF *Cardiorespiratory fitness*; VO_{2peak} *Peak oxygen uptake*; PA *Physical activity*; JADAS *Juvenile Arthritis Disease Activity Scale;* CHAQ *Childhood Health Assessment Questionnaire*

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0092-HPR THE EFFECTIVENESS OF DIGITAL APPLICATIONS PROVIDING PERSONALIZED EXERCISE VIDEOS IN INDIVIDUALS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES: A SYSTEMATIC REVIEW WITH META-ANALYSIS

Keywords: Education

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Background: Among available digital applications (Apps), those providing personalized video exercises (PEV) may be helpful for individuals with rheumatic and musculoskeletal diseases (RMDs) undergoing functional rehabilitation [1,2,3].
Objectives: We aimed to assess the effectiveness of Apps providing PEV to support rehabilitation for people with disability, on functional capacity, confidence in exercise performance, use of care, health-related quality of life, adherence, and adverse events.
Methods: In this systematic review, we searched MEDLINE, CENTRAL and EMBASE databases up to March 2022. All randomized controlled trials evaluating the effect of Apps providing PEV to support rehabilitation for any condition with RMDs requiring physical rehabilitation were included. Selection, extraction and risk of bias assessment (RoB2) were performed by two independent reviewers. Primary outcome was functional capacity at the end of the intervention. Secondary outcomes included confidence in exercise performance, care consumption, health-related quality of life, adherence, and adverse events. A meta-analysis was performed where possible; the magnitude of the effect was assessed with the standardized mean difference (SMD). REGISTRATION: PROSPERO: CRD42022323670
Results: From 1641 identified references, 7 articles (906 participants, 93% adults) were included. The Apps were mostly commercial (7/10); the videos were mostly elaborated by a physiotherapist (8/10). Duration of App use was 3-48 weeks. All included studies had a high overall risk of bias. Low-quality evidence suggested the use of Apps providing PEV led to a significant, small to moderate improvement in physical function (SMD 0.33 [95% CI 0.16 to 0.50], Phet=0.93;

I^2=0%, 6 studies), confidence in exercise performance (SMD 3.69 [3.41 to 4.17], 1 study), quality of life (SMD 0.70 [95% CI 0.46 to 1.09], 1 study) and adherence (SMD 3.38 [95% CI 0.65 to 6.11], Phet=0.93; I^2=0%, 6 studies). Apps did not influence rate of adverse events.

Conclusion: Apps providing PEV to support exercise performance significantly improved physical function, confidence in exercise performance, quality of life and adherence. However, the level of evidence was low: more robust studies are needed to confirm these results.

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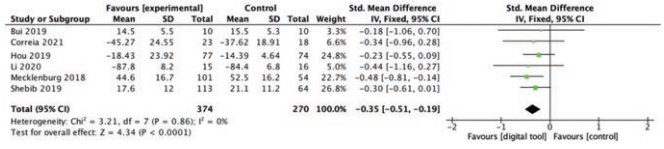


Figure 1. Forest diagram of the effect of digital applications on functional capacity.

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Let's talk about biomarkers – ask the experts

OP0093-PARE

DISCOVERING THE POTENTIAL VALUES OF DIGITAL BIOMARKERS FOR INFLAMMATORY ARTHRITIS PATIENTS, A DESIGN THINKING APPROACH PRELIMINARY RESULTS OF THE PATIENTS' PERSPECTIVE

Keywords: Biomarkers, Self-management, Telemedicine

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Background: The Inflammatory Arthritis (IA) patient population is growing, whilst there already is a shortage of health care professionals (HCPs). It is impossible to meet the future demand for care with the current healthcare system. *Digital biomarkers* are objective, quantifiable, physiological and behavioural data that are collected and measured by means of digital devices [1]. They can support continuous measurements outside the physical confines of the clinical environment and so could help close the gap in healthcare demands.

Objectives: To obtain the patients' insights on disease activity, disease management and care needs; and to empathise with their attitude towards digital biomarkers in order to obtain future directions for digital biomarker development.

Methods: A Design Thinking approach is followed for the development of digital biomarkers in rheumatology. It is a human-centered problem-solving approach that leverages empathy and collective idea generation to tackle complex challenges [2]. Semi-structured focus group discussions, based on the Common Sense Model of Self-Regulation [3], were conducted through 60-minute video conferences. All interviews were audio-recorded, transcribed to verbatim and coded. Results were discussed with our patient partners.

Results: In total 6 focus groups were organised, with a total of 30 IA patients (22 PsA; 8 RA, age 51± 11 years, 48% male, time since diagnosis 7 (3:12,5) years). The main findings were: *Trial and error;* life after diagnosis is marked by trial and error. They need(ed) to learn how and when to listen to their bodies, uncover potential triggers of inflammation and develop appropriate disease management. They felt an urgency to get advice on lifestyle adjustments, career choices and life adaptations, and discuss these with their HCPs and fellow patients. *Role of the HCPs in care needs;* patients visited their HCP for affirmation, reflection and future directions. They often doubted whether their symptoms were rheumatic. Secondly, they wanted to be ensured adverse drug reactions are absent, blood tests brought them peace of mind. Furthermore, consultations were indicated as an obligatory moment of self-reflection. Conversing with their HCP was seen as a reality check and a conversation about (new) options. *Digital Biomarkers;* attitudes towards digital biomarkers varied. Some patients thought it could provide them with deeper insights and reminders before crossing a line. Some patients thought it relevant only for their HCP. They did not want a constant reminder of their disease. Others did not see any additional value as they knew themselves well enough that no device should tell them whether their feelings are true or not.

Conclusion: The following problem statement from the patients' perspective can be formulated; "we suffer from a disease that has turned our lives upside down, we have to cope with it every day. Our learning mechanism is by trial and error. We have to know which activities should be avoided and how to predict the seriousness of a flare. It is difficult to discriminate pain as just pain, from pain as a preceding symptom of flare. The affirmation from our HCPs and our blood results bring us peace of mind. Perhaps, by applying technology, we can speed up our learning process and triggers of flare could be identified. However, one should be mindful of the purpose, the amount of reminders it gives us and the visualisation of our measurements." In general there is no strong resistance to digital biomarkers. However, for future uptake the recorded data should be of clear benefit for the patient.

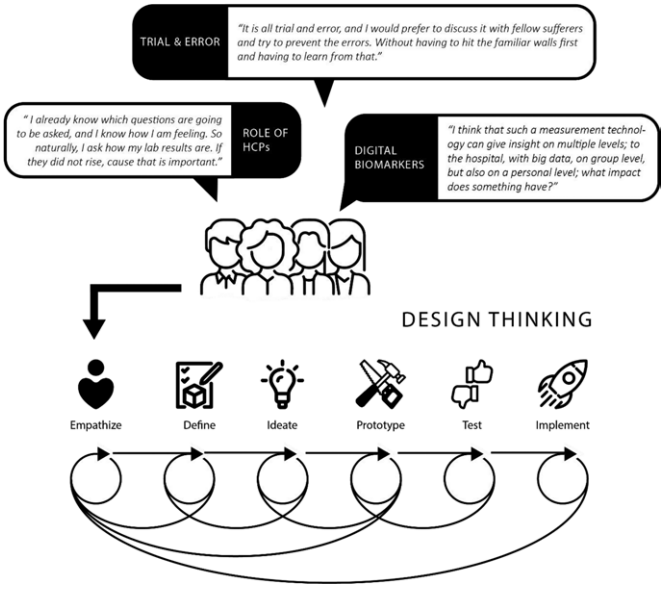


Figure 1. Quotes form patient focus groups and the design thinking process.

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[2] ISBN: 9780262539135
[3] PMID: 27515801

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Fibroblast activation in rheumatic diseases

OP0094

SPATIAL POSITIONING AND MATRIX PROGRAMS OF SYNOVIAL FIBROBLASTS UNDERPIN IMMUNE CELL ORGANISATION AND SYNOVIAL TISSUE PATHOTYPE

Keywords: Synovium, -omics, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is highly heterogenous with distinct cellular and molecular tissue pathotypes that associate with disease outcome[1]. The synovial membrane is the primary target tissue and undergoes significant architectural re-modelling in response to inflammation. While fibroblasts are known to shape immune cell compartmentalisation in secondary lymphoid organs, by producing distinct sets of chemokines and remodelling extracellular matrix (ECM)[2], the mechanisms underlying immune cell localisation in the synovium are poorly understood.

Objectives: To define the functional zonation of the inflamed synovium at the single cell and regional tissue level using spatial transcriptomics and multiplex imaging.

Methods: We performed oligonucleotide probe-based spatially resolved transcriptomics on synovial tissue samples obtained by minimally invasive, ultrasound guided synovial tissue biopsies performed in patients with both rheumatoid arthritis (RA) and osteoarthritis (OA) using the 10x Visium platform. A total of 27 tissue biopsies processed sequencing 34170 spot transcriptomes. Each tissue section was composed on 1-8 fragments of synovial tissue from the same donor biopsy sample within each capture area, to maximise tissue representation and account for sampling variability. Cellular deconvolution of spot transcriptomes was performed using single cell reference datasets. Multiplex imaging was obtained to confirm gene profiles and cell types associated with the specific zonation patterns.

Results: We identified six spatially resolved tissue niches (or zones) within synovial membrane defined by gene expression and comprised of distinct populations of stromal and immune cells. Specific patterns of gene expression were observed in each of these sub-synovial tissue zones that link to functions of immune infiltrate recruitment and organisation. This zonation pattern is maintained across pathotypes (Fibroid, Lymphocytic) and spatial gene expression analysis revealed that RA is associated with specific synovial re-modelling and the formation of lymphocytic niches when compared to OA synovial tissue. We next defined zonation areas by manually annotating immune infiltrates (as aggregates) and vasculature, based on histology. From these, we selected fibroblasts specific to immune aggregate zones and peri-vascular zones (Figure 1). We have identified differences in gene expression between these fibroblasts based on their anatomical location. Peri-vascular fibroblasts have gene expression profiles related to myofibroblast differentiation, ECM deposition and modulation (COMP), but also immune cell recruitment (PLA2G2A), cell activation (FOS & FOSB), and lipid metabolism (APOD), also associated with OA synovium. These fibroblasts display either a TGF-β response or NOTCH3 activated[3] gene expression program and are expanded in the fibroid pauci-Immune) tissue pathotype. Immune interacting (peri-aggregate) fibroblasts in contrast, show specific gene expression profiles linked to ECM regulation (POSTN), degradation (MMP3) and co-ordination of ECM remodelling to recruit immune cells (SPARC), and permit aggregate formation. These fibroblasts display a T-cell interacting[4] and IFN-γ gene expression program and along with IL-1β and TNF-α activated lining layer fibroblasts dominate the stromal cell landscape of the lymphoid tissue pathotype.

Conclusion: We demonstrate that cytokine directed fibroblast-immune cell crosstalk, positional identity, and matrix specific, fibroblast gene expression programs are responsible for localising infiltrating immune cells to specific niches within the tissue and defining functional tissue zonation. These data identify novel therapeutically tractable disease pathways that underpin the pathogenicity of synovial tissue fibroblasts in RA.

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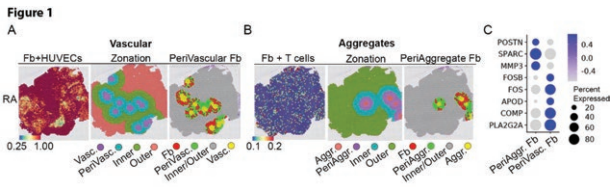


Figure Legend:
(A) Fibroblast (Fb) gene signature upon co-culture with HUVECs mediated by NOTCH3 (Wei et al, 2020) projected as spatially resolved gene expression on RA synovial tissue. Definition of zonation areas around vascular cells and selection of peri-vascular fibroblasts.
(B) Fb gene signature upon co-culture with T cells (Korsunksy et al, 2022) projected as spatially resolved gene expression on RA synovial tissue, definition of zonation areas around aggregates and selection of peri-aggregate fibroblasts.
(C) Expression of key markers genes in peri-aggregate fibroblasts compared to peri-vascular fibroblasts.

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Autoinflammation – the next chapter

OP0095

MONOSODIUM URATE AND CALCIUM PYROPHOSPHATE CRYSTAL-INDUCED INFLAMMATION RELIES ON CELL VOLUME REGULATION AND LRRRC8/VRAC CHANNEL ACTIVATION

Keywords: Inflammatory arthritides, Gout, Crystal Arthritis

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Background: Monosodium urate (MSU) and calcium pyrophosphate (CPP) crystals are responsible for interleukin (IL)-1β dependent acute arthritis. The release of mature IL-1β is dependent on the NLRP3 inflammasome, which can be activated by other sterile stimuli such as hypo-osmolarity and ATP. During extracellular hypotonic stress, there is cellular swelling secondary to water influx. The cell sets up a defence mechanism, called regulatory volume decrease (RVD), allowing it to return to its initial volume. RVD depends on the anion channel VRAC, a hetero-hexamer composed of members of the LRRC8 family. LRRC8A is the obligatory key protein required to form active VRAC channel. Activation of LRRC8/VRAC channel results in an efflux of anions (mainly chloride) and osmolytes leading to water efflux and cell volume reduction.

Objectives: To evaluate the role of the LRRC8/VRAC channel in cell volume regulation and IL-1β release induced by MSU and CPP crystals.

Methods: In-vitro, primed THP-1 monocytes were stimulated by synthetic sterile MSU and CPP and cytokine production was quantified by ELISA. Cell volume variations were visualized by live video recording and cell surface was measured using ImageJ software. The role of the LRRC8/VRAC channel was evaluated using a pharmacological inhibitor DCPIB or by silencing the LRRC8A subunit (shLRRC8A RNA) in these cells. In vivo, MSU and CPP crystals were injected into air pouches created subcutaneously (mimicking synovial cavity) in wild-type mice and conditional LRRC8A Knock-out mice in the macrophagic lineage (Cxcr-3Cre_Lrrc8aflox/flox). Supernatants and pouch lavages were used to measure cytokine production by ELISA.

Results: MSU-and CPP-induced NF-κB activation was reduced in WT THP-1 cells treated with DCPIB and in THP-1 cells where LRRC8A expression was silenced. Similarly, IL-1β production induced by MSU and CPP crystals was substantially decreased in WT THP-1 treated with DCPIB (MSU 5200 vs 1080 pg/ml; CPP 11500 vs 4980, p<0.0001) and in shLRRC8A THP-1 cells compared to crystal-treated WT cells. MSU and CPP crystals exposure induced a biphasic cell volume change characterised by a significant increase followed by a RVD-like phenomenon. These cell volume changes were abolished in the presence of DCPIB and not observed in shLRRC8A THP-1 cells. In vivo, inflammation induced by MSU and CPP crystals assessed in lavage fluid and conventional histology was lower in Cxcr3Cre_Lrrc8aflox/flox mice as compared with wild-type mice in terms of IL-1β production and cell infiltrate.

Conclusion: These results suggested that MSU and CPP crystal-induced inflammation involved and cell volume variation regulated by VRAC/LRRC8 channel.

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Genetics and EpiGenetics of RMDs

OP0096 IMMUNOPHENOTYPING-BASED TRANSCRIPTOME ANALYSIS ON SYSTEMIC IMMUNE-MEDIATED DISEASES

Keywords: Artificial Intelligence, Genetics/Epigenetics, -omics

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Background: Systemic immune-mediated diseases vary in manifestations and pathogenesis. Currently, disease diagnoses and treatments are generally based on clinical symptoms and some specific serological features. Because the diseases share some clinical and pathological features, it is difficult to comprehend the pathogenesis and manage them appropriately. To date, a limited number of studies tried to stratify such patients into some subgroups using the transcriptomic data and molecular patterns [1]; however, the number of included diseases, patients, and transcriptome data were restricted.
Objectives: To identify the significant immune cells forming the diseases and then stratify all patients accordingly, using immunophenotyping and transcriptomic data.
Methods: We performed an integrative analysis of immunophenotyping and bulk RNA-sequence (RNA-seq) on peripheral mononuclear blood cells (PBMC) from patients diagnosed with systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), idiopathic inflammatory myopathy (IIM), systemic sclerosis (SSc), rheumatoid arthritis (RA), and large vessel vasculitis (LVV) in the Immune Cell Gene Expression Atlas from the University of Tokyo (ImmuNexUT) [2]. Immunophenotyping data (29 immune cell subsets) were applied to machine learning approaches, a random forest method, and all patients were stratified by k-means clustering. Then, we conducted a transcriptome analysis, including a differentially expressed gene (DEG) analysis and enrichment analysis (5,484 RNA-sequencing data). Finally, we compared clinical features among the clusters (**Figure 1A**).
Results: A total of 254 patients with systemic immune-mediated diseases -78 SLE, 22 MCTD, 63 IIM, 52 SSc, 20 RA, and 19 LVV- were included. To identify important cells to distinguish the diseases, a random forest algorithm was conducted by applying the immunophenotyping data. Using the top 15 important cells, k-means clustering was performed, and all patients were stratified into three clusters (**Figure 1B**). Naïve $CD8^+$ T cells, memory $CD4^+$ T cells, and non-classical monocytes were predominantly in clusters 1, 2, and 3, respectively (**Figure 1C**). Each disease showed skewed distribution in each cluster, such that SLE patients were predominantly in cluster 2 and most of the SSc patients were included in cluster 3 (**Figure 1B**). Next, we conducted DEG and enrichment analysis on 5,484 RNA-sequencing data of each immune cell and found that the number of DEGs in memory $CD4^+$ T cells in cluster 2, and non-classical monocytes in cluster 3 were increased when compared with other clusters, which were consistent with the cell proportions (**Figure 1D**). The gene ontology analysis showed enrichment of genes associated with adaptive immune response in naïve $CD8^+$ T cells in cluster 1, T cell activation response and an innate immune response in memory $CD4^+$ T cells in cluster 2, and vascular process in the circulatory system in non-classical monocytes in cluster 3, suggesting that even the same diseases can be stratified into each cluster based on specific pathogenesis. Uniquely, patients with common clinical features such as arthritis, the positivity of anti-SS-A antibody, and disease spectrums of MCTD were each accumulated in the different, specific cluster.
Conclusion: This large-scale integration of immunophenotyping and transcriptome analysis on the six systemic immune-mediated diseases revealed all patients were classified into three clusters and each one has specific clinical and transcriptomic features. It may enhance the understanding of the pathogenesis of heterogeneous diseases.

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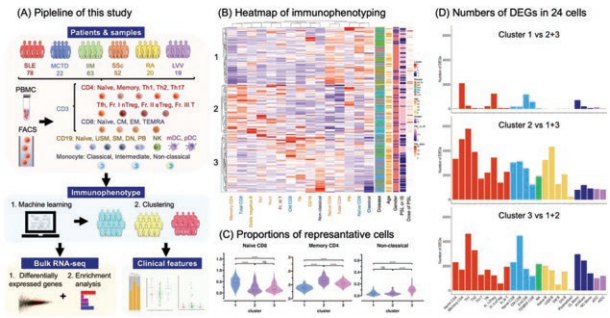


Figure 1.

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OP0097 K4ME3-DOMINANT BIVALENT CHROMATIN REGIONS ASSEMBLE SURVIVIN WITH CHROMATIN REMODELLING COMPLEXES IN CD4 CELLS

Keywords: Rheumatoid arthritis, Genetics/Epigenetics, -omics

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Background: Rheumatoid arthritis (RA) is associated with aberrant epigenomic control which obstructs the proper function of CD4 T cells. Bivalent chromatin regions (BvCR), containing histone H3 tail trimethylation at lysine 4 (H3K4me3) and lysine 27 (H3K27me3), act as a major organizer of the 3D nuclear environment required for efficient T cell development. Survivin has gained importance in RA pathogenesis. Survivin is shown to interact with chromatin genome-wide and regulate gene transcription in the IFNg producing CD4 T cells [1].
Objectives: This study investigates survivin cooperation with nucleosome in BvCR and functional effect of this cooperation on CD4 cell phenotype.
Methods: BvCR were identified in CD4 cells by annotation of H3K4me3, H3K27me3 and H3K27ac binding through chromatin immunoprecipitation and sequencing (ChIPseq). Protein binding was quantified through peak score. An overlap of the H3 peaks and Survivin ChIPseq (12 individual CD4 cultures) by at least one bp was identified through R package ChIPPeakAnno. Changes in H3 peaks in CD4 cells treated with a survivin inhibitor YM155 were assessed. Tag normalization was applied to enable comparison between different ChIPseq. Tag prevalence within the BvCR defined the dominant H3 group. Changeable BvCR were defined by alteration in the dominant-H3 group after YM155 treatment. TF ChIPseq colocalization analysis was performed through ReMap2022 database. To analyse effect of BvCR changeability on transcriptome, we performed RNAseq of YM155-treated CD4 cells (n=4). Overlap of BvCR with regulatory elements (RE) was done through GeneHancer database. TF enrichment analysis was performed through GSEA (Broad Institute).

Results: Integration of H3K4me3, H3K27me3 and H3K27ac ChIP-seq identified 6199 BvCR, 66% of those contained survivin peaks. Fluorescence imaging of effector T cells validated nuclear colocalization of survivin with histone proteins. Of those 6199 BvCR, 43.8% were dominated by H3K4me3, which had also the highest survivin peak scores. Complexes of histone modifiers COMPASS, responsible for H3K4 methylation, and SWI/SNF, responsible for counteracting PRC2-guided H3K27me3, colocalized with BvCR. YM155-treatment significantly increased deposition of both H3K4me3 and H3K27me3. Changeable BvCR frequently acquired a K4me3-dominant status after YM155 treatment. This indicates that survivin contributes to regulation of methylation of lysines in H3 tail within BvCR. TF enrichment analysis of genes connected to the BvCR revealed the role of histone demethylases KDM7A (FDR=1.03e-32), PHF2 (FDR=3.47e-19), KDM5D (FDR=1.51e-15) in their transcription. Strongest overall enrichment was identified in H3K4me3-dominant BvCR colocalized with survivin. Integration of BvCR with CD4 RNA-seq revealed 2469 protein-coding genes connected through RE to H3K4me3-dominant BvCR, which sustained transcriptional activity and 346 of those were differentially expressed (DEG, nom p<0.05) in YM155-treated cells. DEG transcriptionally dependent on the TF families of histone modifiers built a strong SWI/SNF-dependent interaction network acting in biological processes of immune system regulation (FDR=1.07e-6. FOXP1, KLF3, FYB1, BCL2), DNA repair (FDR=5.57e-6. MSH6, MGMT, MCM8, UPF1), and RNA polymerase transcription (FDR=1.22e-8. TCF3, ARID5A, RARA). CD4 cell transcriptomics of randomly selected RA patients demonstrated that a) DEG controlled by the H3K4me3-dominant BvCR were upregulated in survivin-high CD4 cells with proinflammatory Th1 phenotype b) DEG had altered expression in CD4 cells of patients treated with JAK-inhibitors.

Conclusion: This study demonstrates that survivin contributes to regulation of lysine methylation in H3 tail within BvCR, which coordinates activity of the SWI/SNF complex in chromatin remodelling and transcription. We demonstrate that survivin inhibition affects this coordinated activity, and thereby impinge on CD4 activation in RA.

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OP0098 INFLAMMATORY GENE ENHANCERS ARE SHARED IN SYNOVIAL FIBROBLASTS AND MINOR SALIVARY GLAND FIBROBLASTS

Keywords: Cytokines and chemokines, Sjögren syndrome, Rheumatoid arthritis

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Background: Cell type- and stimulus-specific enhancers are key regulatory elements in chronic inflammatory rheumatic diseases, such as rheumatoid arthritis (RA) and Sjögren`s syndrome (SjS). Recent transcriptome profiling of synovial fibroblasts (SF) from patients with RA and minor salivary gland-derived fibroblast (SGF) from patients with SjS point to similarities of fibroblast populations derived from these two chronic inflammatory diseases. Enhancer RNAs (eRNAs) are short-lived non-coding RNAs transcribed from cell type-specific enhancers that facilitate the transcription of their linked coding genes. The activation and interference with transcribed enhancers in SF and SGF has not been studied yet.

Objectives: To characterise the activation and regulation of transcribed inflammatory gene enhancers in RA SF and SGF.

Methods: SF were isolated from synovial tissues of patients with RA undergoing joint replacement surgery. SGF were isolated from minor salivary gland biopsies of patients with a suspected SjS, including samples of patients with SjS (n=3) and controls (n=3) that do not fulfil the classification criteria. The expression of eRNAs in SF (n=9) stimulated with TNF (24h; 10 ng/µl) or left untreated, was detected by cap analysis of gene expression followed by sequencing (CAGEseq). RA SF (n=7) and SGF (n=6) were stimulated with TNF (1, 3, 6, 24h; 10 ng/µl), IL1 (1, 24h; 1 ng/ml), or the Toll-like receptor agonists pIC (1, 24h; 10 µg/ml) and LPS (1, 24h; 100 ng/µl). The expression of selected eRNAs and their corresponding coding genes was analysed by real-time PCR. Samples containing the untranscribed RNA were measured in parallel. To study eRNA regulation, SF were treated with the bromodomain inhibitor I-BET (1 µM; 24h), prior to stimulation with TNF.

Results: We have identified and selected a set of TNF-induced eRNAs for the pro-inflammatory genes *CCL2, IL8*, *IL6, CXCL1* and *CCL20* for a more detailed analysis. These eRNAs were located upstream (eCCL2#1, eCCL2#2, eCXCL1#2, eIL6#1, eIL8#1-3), downstream (eCCL2#3, eCCL2#4, eCXCL1#1) and intronic (eCCL20) at distances between 300 bp to 35.6 kb relative to the transcription start sites of the corresponding coding genes. CAGEseq revealed a patient-dependent variability in eRNA expression, with none of the selected eRNAs being present in SF of all nine patients, and the existence of several TNF-induced eRNAs for individual coding genes. By performing TNF time course experiments in SF, we have detected different patterns of eRNAs: (a) eRNAs, that peaked at 1h (eCCL20, eIL8#2, eCCL2#1), (b) at 6h (eCXCL1#1), (c) or at 24h (eIL8#1, eIL8#3, eIL8#4, eCXCL1#2) after stimulation, and (d) eRNAs that were stably expressed over the time points (eCCL2#2, 3, 4). The same set of eRNAs and corresponding coding genes was induced in SGF, indicating that inflammatory gene enhancers are shared in fibroblasts from different localisation and diseases. All inflammatory stimuli induced the expression of eRNAs in SF and SGF. However, we detected some differences regarding the peak of eRNA expression (eCCL2#2, eCCL2#3, eCXCL1#2) and the potency of different stimuli to induce individual eRNAs. Treatment of SF with I-BET suppressed the expression of all eRNAs tested.

Conclusion: SGF, similar to SF, respond to different pro-inflammatory stimuli by inducing the expression of transcribed eRNAs and their corresponding coding genes. The expression of some eRNAs is maintained for up to 24h, contradicting previous reports that eRNAs are short-lived. Bromodomain inhibitors are sufficient to prevent the activation of eRNAs.

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OP0099 UNVEILING THE COMPLEX GENE REGULATORY MECHANISMS OF PSORIATIC ARTHRITIS THROUGH CHROMATIN CONFORMATION, GENE EXPRESSION AND CHROMATIN ACCESSIBILITY ANALYSIS IN PRIMARY CELLS

Keywords: Psoriatic arthritis, Genetics/Epigenetics, -omics

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Background: GWAS have identified genetic variants associated with many complex diseases. These primarily affect regulatory elements that can affect expression of distal genes through chromatin interaction mechanisms. Previous studies have used functional genomics and chromatin conformation capture techniques to study the functional impact of these genetic variants [1]. However, such studies have predominantly used data generated from cell lines, which behave differently from primary cells. Additionally, there is a lack of research in Psoriatic Arthritis (PsA), which is a highly heterogenous disease that has been understudied and for which there are few effective treatments.

Objectives: We aimed to study how chromatin conformation and gene expression is altered in primary T cells derived from patients with PsA, and to identify how genetic variants alter gene regulatory mechanisms in a population of individuals.

Methods: Genotype data, together with matching high resolution Hi-C, RNA-seq and ATAC-seq was generated from primary $CD4^+$ and $CD8^+$ T cell samples isolated from the blood (n=55) and synovial fluid (n=9) of patients with PsA and blood of healthy controls (n=19).

Results: We found that chromatin conformation is highly cell-type and context specific. Out of 105,956 total loops, 29,454 were differentially interacting

(FDR<0.1) between CD8$^+$ and CD4$^+$ T cells, and 15,597 (FDR<0.1) between CD8$^+$ T cells isolated from synovial fluid compared to those from blood. These differential loops overlap many disease associated GWAS loci such as the *TNIP1* and *STAT2* PsA loci. We identified 312 genotype associated loops, one of which is associated with a risk locus (*GSDMB*) known to be associated with several autoimmune diseases. Moreover, we found that chromatin conformation correlates strongly with differences in gene expression and chromatin accessibility, particularly with genes related to T cell activation and inflammatory pathways. Next, we compared T cells isolated from blood of PsA patients to controls, but few significant differences were identified (Table 1). Segregating the PsA cohort by disease activity and treatment led to the identification of significantly larger differences. We found numerous differentially expressed genes (DEGs) and differential ATAC-seq peaks in patients with or without active disease, and in those receiving or not receiving biological disease-modifying antirheumatic drugs (bDMARD) (Table 1). Furthermore, there were numerous DEGs and differential ATAC-seq peaks in bDMARD responders (n=8) vs non-responders (n=6) (Figure 1, Table 1). DEGs were enriched for pathways involving immune function such as IL-2 and IL-15 signalling. Differential ATAC-seq peaks were enriched for binding sites for transcription factors such as *RUNX1*, *JUN*, *IRF4* and *STAT2*. Furthermore, one of the differential ATAC-seq peaks we identified overlapped SNPs in the psoriasis *RUNX3* locus.

Table 1. Number of DEGs and differential ATAC-seq peaks in the various comparisons for CD4$^+$ and CD8$^+$ T cells (all FDR<0.1).

Comparison	RNA-seq CD4+	RNA-seq CD8+	ATAC-seq CD4+	ATAC-seq CD8+
Patients vs healthy controls	46	200	0	4
Patients with active disease vs remission	169	36	1675	3
bDMARD treatment effect in non-active disease	90	13	75	14
bDMARD treatment effect active disease	967	295	13176	5069
Remission vs active disease without bDMARD	17	21	0	0
Remission vs active disease treated with bDMARD	1034	374	2559	41

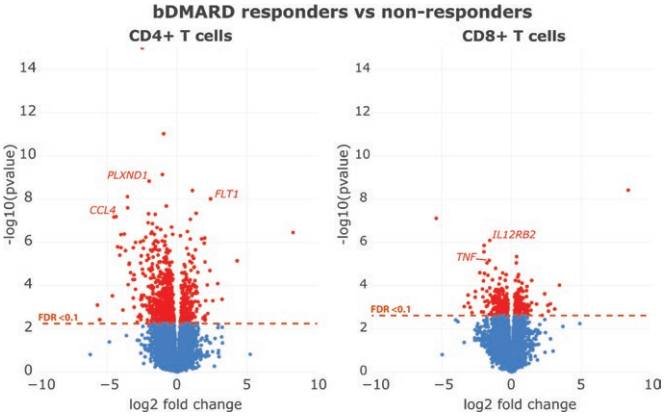


Figure 1. Volcano plot of DEGs between bDMARD responders vs non-responders in CD4$^+$ and CD8$^+$ T cells respectively.

Conclusion: This study provides novel insight into gene regulatory mechanisms, particularly regarding PsA GWAS signals and disease pathogenesis. We identified, for the first time, epigenetic differences correlated with disease severity and treatment response in PsA using primary T cells.

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OP0100

DNA METHYLATION PATTERNS IN CD4+ T CELLS DISCERN SKIN PSORIASIS FROM PSORIATIC ARTHRITIS

Keywords: Adaptive immunity, Psoriatic arthritis, Genetics/Epigenetics

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Background: Psoriasis is a systemic inflammatory disease that primarily affects the skin. Approximately one third of psoriasis patients develop joint involvement and are therefore diagnosed with psoriatic arthritis (PsA). While, in adults, the development of arthritis usually follows skin psoriasis, approximately 15% of patients experience arthritis simultaneously or prior to skin disease. Thus, PsA can be missed, leading to disease progression, damage, and reduced quality of life. Individualized care is complicated by the absence of disease- or outcome-specific biomarkers. While the pathophysiology of psoriasis is incompletely understood, a key role of effector T-cells has been established. Recent studies linked altered DNA methylation with T-cell dysregulation and phenotypical variation between patients.

Objectives: This project aimed to identify disease-associated DNA methylation signatures in CD4$^+$ T-cells from psoriasis and PsA patients as compared to healthy controls that may be used as diagnostic and/or prognostic biomarkers and inform future treatment.

Methods: Peripheral blood samples were collected from 9 healthy controls, 11 skin psoriasis and 8 PsA patients. PBMCs were isolated *ex vivo*, CD4$^+$ T-cells were FACS separated, and genomic DNA was isolated. DNA methylation profiling was performed using the Illumina Human Methylation EPIC 850K platform. Bioinformatic analyses, including gene ontology (GO) and KEGG pathway analysis, were performed using R software (*minfi*, *limma*, *ChAMP*, *DMRcate*, *clusterProfiler*). Flow cytometry datasets were analyzed using *FlowJo*. To identify genes under the control of interferon (IFN), the *Interferome* database was consulted. DNA Methylation Scores were calculated for type I and type II interferons following the method suggested by Björk *et al.* (2020).

Results: Numbers and proportions of CD4$^+$ T-cells did not vary between controls and patients with skin psoriasis or PsA. Furthermore, no differences between controls and patient groups were observed in the proportion of CD4$^+$ T-cell subsets (naïve, central memory, effector memory, CD45RA re-expressing effector memory cells). We detected 820 differentially methylated positions (DMPs) affecting 433 genes in CD4$^+$ T-cells from healthy controls when compared to psoriasis and PsA patients. Based on DMP analyses, groups segregated in principal component (PCA) or partial least-squares discriminant analyses (PLS-DA) (Figure 1). Separation in PLS-DA was centrally influenced by two CGs (cg07021052, cg10687131) localized in *GDF7* (Growth and Differentiation factor 7), which affects T-cell regulatory factors FOXP3 and CTLA4. GO analysis of genes with at least one DMP in their promoter region delivered hypomethylation of genes involved in "negative regulation of focal adhesion assembly", "cell-substrate junction organization" and "regulation of the triglyceride biosynthetic". DNA methylation profiles (855 DMPs affecting 551 genes) distinguished between skin psoriasis and PsA patients; a high proportion of DMPs associated with interferon-regulated genes (68% total: 8.8% type I, 33.5% type II, 23.8% type I and II IFN). GO analysis delivered an enrichment of hypomethylated genes affecting "carboxylic ester hydrolase", "alkyl or aryl group transferase" and "glutathione transferase activity". Notably, we observed a majority DMPs in IFN-related genes when comparing healthy controls with PsA patients (61.9% total: 9.1% type I, 29% type II, 23.8% type I and II IFN) and controls with skin psoriasis patients (62.7% total, 7.7% type I, 31% type II, 24% type I and II IFN). Moreover, DNA methylation calculated for type I and type II IFN-associated genes significantly differed between healthy controls, skin psoriasis and PsA patients.

Conclusion: DNA methylation profiles in CD4+ T-cells discriminate between controls, skin psoriasis and PsA. As DNA methylation signatures may predict disease progression from psoriasis to PsA, they may be applied for molecular patient stratification towards future individualized treatment and care.

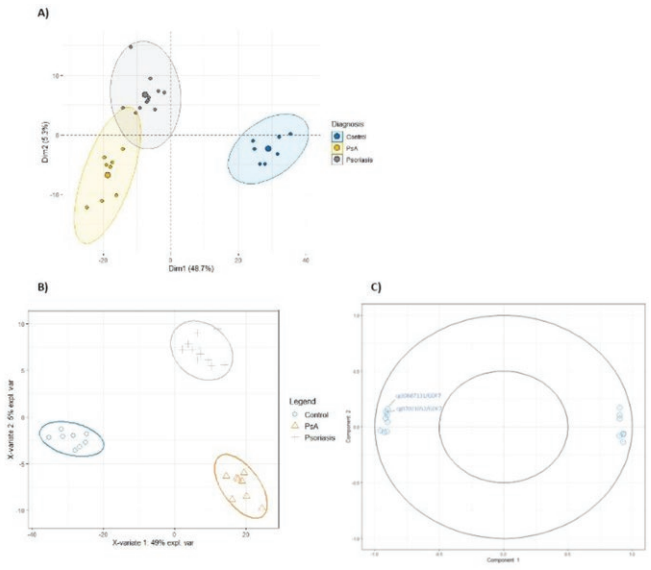


Figure 1: DNA methylation signatures differentiate healthy controls from skin psoriasis and PsA. A) Unsupervised Principal Component Analysis (PCA) of 820 Differentially Methylated Positions (DMP) (FDR p-value: <0.05, $|\Delta\beta|$>0.1) discriminates between healthy controls, skin psoriasis, and PsA patients. B) Supervised Partial Least-Squares Discriminant Analysis (PLS-DA) of the same 820 DMPs (FDR p-value <0.05, $|\Delta\beta|$>0.1) even more clearly separates healthy controls from skin psoriasis and PsA patients. C) Correlation circle plot displaying the 15 DMPs (correlation cutoff 0.9) that primarily contribute to the definition of each component of the PLS-DA. DMPs at cg07021052 and cg10687131 are localized in *GDF7* which affects T-cell regulatory factors FOXP3 and CTLA4.

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4069

OP0101 B CELL POLYGENIC RISK SCORES ASSOCIATED WITH ANTI-DSDNA ANTIBODIES AND NEPHRITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Autoantibodies, Genetics/Epigenetics, Systemic lupus erythematosus

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Background: Lupus nephritis (LN) is one of the main clinical challenges in systemic lupus erythematosus (SLE) and a cause of significant morbidity and mortality. Genetic contribution to SLE pathogenesis is important, and genetic profiling through polygenic risk scores has been shown useful to stratify SLE patients according to dominating molecular disease mechanism.[1] This has not, however, been investigated for specific disease manifestations.
Objectives: In this work, we aimed to investigate associations between B cell polygenic risk scores (PRSs) and disease manifestations in SLE.
Methods: Female patients with SLE (n = 1248) and healthy control individuals (n = 519) were genotyped using Illumina's Global Screening Array. Two PRSs were calculated[2], one including 20 GWS risk loci for SLE in genes assigned to B-cell related pathways according to the KEGG, GO and Reactome databases, and one including a subset of 12 of these genes limited to B-cell activation pathways. PRSs were defined as high in the highest quartile and low in quartile 1-3, and groups were compared by logistic regression (SPSS, version 28.0.1.0). HLA variants HLA-DRB1*03:01 and HLA-DRB1*15:01 were assessed in patients using tag SNPs. A p-value < 0.05 was considered significant.
Results: SLE was more prevalent in individuals with high compared with a low SLE B cell PRS (OR 1.84 (1.42-2.38), p=4.0×10^{-6}) and mean PRS was higher in cases than controls, 2.92 (2.88-2.96) for cases and 2.68 (2.63-2.74) for controls, p = 4.1 × 10^{-11}). Immunologic disorder (ACR -82) and dsDNA antibodies were more prevalent among patients with a high compared with a low SLE B cell PRS (OR 1.44 (1.08-1.93), p=1.4×10^{-2}, and OR 1.47 (1.07-2.01), p=1.8×10^{-2}, for immunologic disorder and dsDNA antibodies, respectively). Also, effect sizes were augmented in patients with HLA risk serotypes HLA-DRB1*03:01 and HLA-DRB1*15:01, with the highest prevalence of dsDNA antibodies (87 %) demonstrated in patients with HLA-DRB1*03/15 +/+ combined with a high SLE B cell PRS (OR 1.64 (1.06-2.54), p = 0.028, for high vs low PRS), Figure 1. Anti-dsDNA antibodies were associated with a higher prevalence of class III or IV nephritis (OR 4.66 (2.78-7.80), p=5.2×10^{-9}) and the prevalence of nephritis according to the ACR-82 criteria was higher in patients with a high compared to patients with a low B cell activation PRS (OR 1.32 (1.00-1.74), p = 0.048). Numerically, a higher prevalence of nephritis (ACR -82) was observed for patients with a high compared with a low SLE B cell PRS, but the difference was not statistically significant (OR 1.20 (0.91-1.59), p = 0.19).
Conclusion: High genetic burden related to B cell function is associated with dsDNA antibody development and LN. Assessing B cell PRSs may be important in order to determine immunologic pathways influencing SLE and to predict clinical phenotype.

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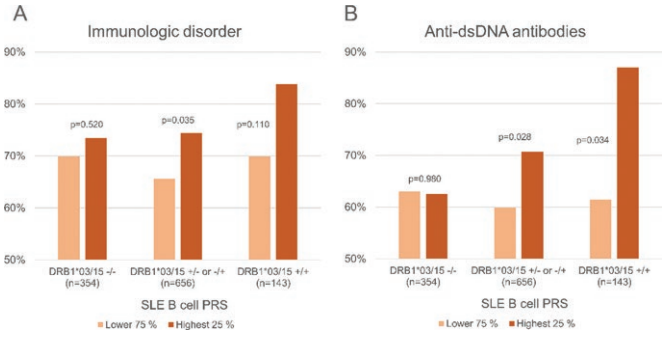


Figure 1. Associations with SLE B cell PRS, immunologic disorder (ACR-82) and anti-dsDNA antibodies in HLA subgroups. Female patients with SLE were stratified into three groups according to HLA-type (positive for HLA-DRB1*03:01 or HLA-DRB1*15:01 (DRB1*03/15 +/- or -/+), positive for both (DRB1*03/15 +/+) or negative for both (DRB1*03/15 -/-) risk variants). Each group was then divided into two groups based on the patients' SLE B cell PRSs (highest quartile or quartile 1-3). Prevalence of immunologic disorder according to the ACR -82 criteria (A) and prevalence of dsDNA antibodies (B) was then calculated for all 6 groups.

ACR, American College of Rheumatology; dsDNA, double-stranded DNA; HLA, human leukocyte antigen; SLE, systemic lupus erythematosus; SNP, single nucleotide polymorphism; PRS, polygenic risk score.

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Disclosure of Interests: None Declared.
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OP0102 IDENTIFICATION OF NEW RISK LOCI AND PATHWAYS INVOLVED IN GCA PATHOGENESIS BY A GENOME-WIDE STUDY

Keywords: Genetics/Epigenetics, -omics, Vasculitis

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Background: Giant cell arteritis (GCA) is a chronic large-vessel vasculitis that affects mainly the aorta and its primary branches, and in Western countries is the most common form of vasculitis in people older than 50 years. The most severe manifestations of GCA include blindness and ischemic stroke caused by occlusion of affected arteries. GCA presents a complex aetiology whose genetic component remains largely unknown. Currently, options for both diagnosis and treatment for this pathology are limited, highlighting the need to better understand the genetic factors involved in susceptibility to GCA.
Objectives: The main goal of this study was to characterise the genetic basis of GCA by performing the largest genome-wide association study (GWAS) in this vasculitis to date.
Methods: A total of 3,498 GCA patients with GCA and 15,550 healthy individuals from ten populations of European ancestry were included in this study. After strict quality controls and imputation, 6,691,294 genetic variants were analysed by logistic regression using the first 10 principal components and sex as covariates. Loci showing a significant (p<5E-8) or suggestive (p<5E-5) association with the disease were selected for functional *in silico* analyses, including causal gene prioritisation with FUMA, enrichment of functional annotations of cell-specific histone marks using GoShifter. Finally, we performed a drug repurposing analysis, by evaluating the proposed mapped genes of the significant loci as targets for approved drug using the DrugBank database, and developed a polygenic risk score (PRS) for GCA susceptibility prediction.
Results: Three risk loci for GCA not previously reported were identified, two of them located in genes related to the vascular endothelial growth factor (VEGF) pathway: *MFGE8* (rs8029053, p=4.96E-8, OR=1.19), encoding lactadherin, and *VTN* (rs704, p=2.75E-9, OR=0.84)], encoding vitronectin; and the third one located in the gene *CCDC25* (rs11782624, p=1.28E-8, OR=1,18), that codifies a receptor of neutrophil extracellular traps (NETs). Additionally, we replicated the associations previously described within the HLA region and the *PLG* gene, which is also involved in angiogenesis. The results of the functional annotation showed that the GCA-associated loci act as regulatory variants influencing gene expression in vascular tissue and immune cell types. Furthermore, we also found a significant enrichment in histone marks in several immune cell types, especially in natural killer cells. The results of the drug repurposing analysis suggest abciximab, an antagonist of the vitronectin protein and approved for the treatment of acute coronary syndrome, as a potential candidate to treat GCA. Finally, the PRS model was best defined by including 28 genetic variants, being capable of identifying a fraction of individuals with more than three times the risk of developing GCA (OR=3.1 [2.1-4.7], p=1.71E-8).
Conclusion: Through the largest genomic study performed in GCA to date, we identified three genetic regions associated with this vasculitis that were not previously reported. These results also identified new physiological pathways and cell types potentially relevant to the development of the disease. These results allowed us to establish a prediction tool for identifying individuals at high-risk for developing GCA and also to propose further investigation of abciximab, a drug that could be potentially repurposed for treatment of GCA.

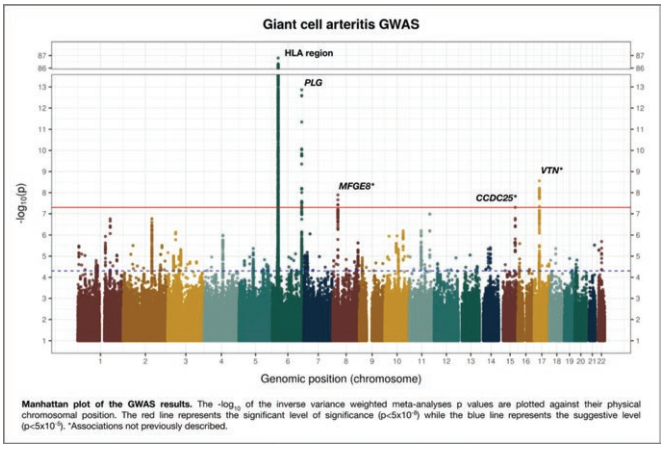


Figure 1.

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OP0103

ANALYSIS OF PROTEIN QUANTITATIVE TRAIL LOCI TO IDENTIFY GENETIC BIOMARKERS OF TREATMENT RESPONSE TO ETANERCEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Genetics/Epigenetics, -omics, Rheumatoid arthritis

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Background: Treatment response to etanercept in patients with rheumatoid arthritis (RA) is heterogeneous, with up to 40% switching due to failure/ineffectiveness[1]. There are no validated pre-treatment biomarkers of response. Due to

their diverse biological roles, proteins can reflect ongoing RA disease processes and may provide biomarkers of response; however, studying proteins in isolation can lead to challenges in separating the cause from the consequence of inflammation. If protein levels are under genetic control, then potentially, stable pre-treatment genetic biomarkers of etanercept response may be identified.
Objectives: To determine whether there is a genetic basis underlying protein expression in patients with RA treated with etanercept.
Methods: Participants were recruited from a UK-based prospective multi-centre study of patients fulfilling either the 1987 ACR or 2010 ACR/EULAR classification criteria for RA, starting etanercept as a first biologic. Quantitative proteomics were performed using Sequential Window Acquisition of all THeoretical fragment ion spectra mass spectrometry (SWATH-MS). Genotyping was carried out using the Illumina Infinium HumanCoreExome 12 BeadChip kit and genotype calling was carried out using GenomeStudio software (both Illumina, San Diego, CA, USA). Following standard genetic QC and imputation, a protein quantitative trait loci (pQTL) analysis was performed using a linear model adjusted for potential confounding covariates (age, biological sex, disease duration, concurrent DMARD use, seropositive status). A suggestive significance level of p<1E-05 was set for *cis* pQTLs; *trans* pQTLs were not considered due to modest sample size. Significance thresholds were adjusted for false discovery rate and subsequently, any adjusted result with $p < 0.05$ was considered to be significant. pQTLs were sought at baseline and after 3 months of treatment.
Results: 147 participants were recruited, with a median age of 56.39 years [IQR 49.34-64.73], median disease duration of 6 years [IQR 2-13] and of whom 108 (75.52%) were female. 482 unique proteins were available for analysis following proteomics and genetics data QC. At baseline (pre-treatment), 2,184 *cis* pQTLs were identified for 60 proteins (this may reflect many pQTLs in strong linkage disequilibrium with one another). After 3 months of treatment, 1,432 *cis* pQTLs were identified for 68 proteins. 2 proteins measured at pre-treatment had pQTLs (*rs150571376*, p_{adj}=3E-03 and *rs188695391*, p_{adj}=1.07E-02) where the protein expression was also associated with DAS28 at 3 months (TCPH, p_{adj}=1.40E-02 and EHD1, p_{adj}=6.54E-03, respectively).
Conclusion: pQTL analysis carried out in RA patients starting etanercept identified numerous loci that are significantly associated with paired protein expression data. 2 baseline proteins, TCPH and EHD1, were found to be associated with post-treatment DAS28 and also had a genetic basis underlying their expression, and these could prove to be valuable candidates for future study, as both proteins are involved in processes during ATP hydrolysis.
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Innate Immunity in Pathogenesis of RMDs

OP0104 NON-CANONICAL NF-κB SIGNALLING IS REQUIRED FOR EXTRATHYMIC AIRE EXPRESSION AND IMMUNOREGULATORY MOLECULES IN CELLS OF THE DENDRITIC LINEAGE

Keywords: Cell biology, Innate immunity

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Background: The transcription factor Autoimmune Regulator (AIRE) is crucial for the establishment of central tolerance in the thymus. Although thymic expression is mainly restricted to medullary epithelial cells, recent studies have identified peripheral $CD45^+$ extrathymic AIRE-expressing cells (eTACs), which share features with antigen presenting cells, such as dendritic cells (DCs). Although, nuclear factor (NF)-κB signaling has been implicated in thymic AIRE expression, stimuli and pathways that induce extrathymic AIRE expression are hitherto unknown.
Objectives: In this study we aimed to unravel the molecular mechanisms underlying the regulation of extrathymic AIRE expression in eTACs and DCs with a focus on NF-κB signaling.
Methods: Confocal and Vectra Polaris multispectral imaging was performed on secondary lymphoid tissues, including tonsils and lymph nodes to identify and characterize eTACs. Second, we employed a novel sorting strategy to isolate DCs and eTACs from tonsil tissue for RNA-sequencing (seq) to generate transcription profiles. To study the regulation of AIRE, monocyte-derived DCs (moDCs), DCs and eTACs were stimulated by anti-CD40 to induce NF-κB activation. Gene transcription and protein expression levels of AIRE, indoleamine 2,3-dioxygenase (IDO), programmed death ligand-1 (PD-L1) and non-canonical NF-κB signalling components were detected by real time-PCR, flow cytometry, Western blot and/or confocal microscopy. Activation of NF-κB signalling was modulated by siRNA-mediated silencing or using a small molecule inhibitor (SMI) of activating kinases.
Results: In human tonsil and lymph node tissue AIRE+ cells were identified, which displayed DC characteristics, including MHCII and CD40, but were relatively low for the pan DC marker CD11c. Bioinformatic analysis on RNA-seq derived gene expression profiles of sorted eTACs and DCs from tonsil tissue revealed an increased expression of AIRE and immunoregulatory genes, including IDO and PD-L1 in eTACs compared to DCs. In addition, the expression of genes implicated in non-canonical NF-κB signaling, including NIK and CD40, were significantly higher in eTACs compared to DCs. CD40 stimulation has been shown to be critical for IDO production by moDCs. CD40-stimulation of moDCs resulted in the activation of non-canonical NF-κB signaling, which was accompanied by upregulation of AIRE, IDO and PD-L1 expression. Interestingly, the induction of AIRE expression was abrogated by siRNA-mediated silencing of NF-κB-inducing kinase (NIK). Likewise, CD40 stimulation of sorted eTACs and DCs resulted elevated AIRE, IDO and PD-L1 expression levels, albeit 5 fold higher AIRE transcription levels were detected in eTAC. Subsequently, modulation of NIK via an SMI resulted in the abrogation of AIRE, IDO and PD-L1 expression in eTACs and DCs. In contrast, specific modulation of canonical NF-κB signaling had no significant effects on AIRE, IDO and PD-L1 expression in CD40-stimulated eTACs and DCs.
Conclusion: Collectively, our data demonstrate that AIRE expression, as well as the expression of the immunoregulatory molecules IDO and PD-L1 in eTACs and DCs can be induced through CD40 stimulation in a non-canonical NF-κB signaling dependent manner. These findings concerning the regulation of AIRE and immunoregulatory molecule expression may point towards a novel role of eTACs in peripheral tolerance.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0105 SINGLE CELL RNASEQ AND FUNCTIONAL STUDIES SUGGEST A ROLE FOR ENTHESIS MESENCHYMAL STEM CELLS RATHER THAN TREGS IN ENTHESIS SOFT TISSUE AND BONE ANCHORAGE SITE IMMUNOMODULATION

Keywords: Enthesitis, Inflammatory arthritides, Innate immunity

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Background: The enthesis is a the key target tissue in spondyloarthritis (SpA) with inflammation evident in both the enthesis soft tissue (EST) and the adjacent anchoring peri-entheseal bone (PEB)[1]. The healthy human spinal enthesis harbour, resident mesenchymal stem cells (MSCs), myeloid cells, innate immune cell populations including γδ T cells, innate lymphoid cells (ILCs), conventional T-cells but a lack of FOXP3+ regulatory T cells (Treg) [2, 3]. Given the predominance of stroma in EST and the known immunomodulatory effects of MSCs it is credible that such cells could assume important enthesis location immunomodulatory function.
Objectives: To investigate the single cell RNAseq (scRNAseq) landscape of EST and PEB tissues. Reflecting RNAseq findings we examined immunomodulatory capacity of MSCs derived from EST and PEB in co-cultures with allogeneic CD3/CD28-stimulated $CD4^+$ T cells.
Methods: For scRNAseq, interspinous ligament and spinous process samples from patients undergoing spinal surgery (n=4). Samples were divided into EST and PEB and enzymatically digested. Following viability enrichment, we performed single cell partitioning with 10x Chromium, followed by oligo-barcoded RNA library generation and Illumina sequencing. For the co-culture, EST and PEB were expanded until passage 2 (n=5) using bone marrow MSCs (BM-MSCs) as control standard (n=2). $CD4^+$ $CD25^-$ T-cells from blood were induced to proliferate using CD3/CD28 stimulation with MSCs/$CD4^+$/$CD25^-$ cell co-cultured at

1:1, 2:1, 4:1, and 8:1 ratios for 5 days. T cells proliferation index was calculated and Treg related markers expressed on MSCs including CD73 and CD39 were measured in PEB and EST.

Results: Following quality control, the transcriptome of 25,635 single cells was analysed. The compositional analysis revealed different abundance, such as stromal cells being more abundant in the EST, and haematopoietic precursors almost exclusively in the PEB. Analysis of the main cell populations revealed: the presence of innate and innate-like lymphocyte subpopulations such as MAIT and γδT cells, and a transcriptional gradient in neutrophils, reflecting various stages of maturation. In the T cell compartment, a putative regulatory (Tr1-like) population characterised by *TGFB1* expression, was more abundant than conventional Foxp3+ Tregs. A number of stromal cells expressed the regulatory marker *NT5E* (CD73).). Consistently with scRNAseq, EST-MSCs expressed CD73 significantly more than PEB-MSCs prior to co-culture ($p<0.001$). with significant upregulation with T- cells coculture ($p<0.05$). EST and PEB derived MSCs showed trilineage differentiation to bone, cartilage and fat[3] and significantly supressed $CD4^+$ $CD25^-$ proliferation in dose dependent manner compared to control co-culture ($p<0.001$). Interestingly, PEB-MSCs showed an increase in the CD39 expression after co-culture with T cells compare to PEB-MSCs with no T cells at ratio 1:4 and 1:8 ($P<0.001$). No EST-MSCs CD39 expresion increase after T cells co-culture was noted but PEB-MSCs CD39 expression increased at 1:4 and 1:8 ratio ($P<0.01$, $P<0.01$ respectively.

Conclusion: Our single-cell transcriptomic analysis suggests that EST and PEB have few Tregs and that other T cells and MSCs possess immunomodulatory functions in these tissues. This immunomodulatory activity may be important at these sites of high mechanical stress to maintain homeostasis.

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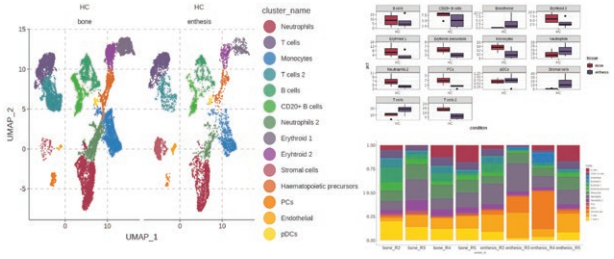


Figure 1. Healthy spinal enthesis dataset paired PEB and EST.A: cluster composition and anatomical distribution. B: Cluster abundance by tissue. C: Per sample cluster abundance

Acknowledgements: NIL.
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OP0106 SYNOVIAL IMPRINTING OF SKIN-DERIVED IMMUNE CELLS INITIATES SPREADING OF INFLAMMATION FROM SKIN TO JOINT IN PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Animal Models, -omics

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Background: Spreading of inflammation from skin to joint is still an unsolved key aspect of psoriatic arthritis (PsA) pathogenesis. Psoriasis (PsO) usually anticipates the joint manifestations, suggesting the existence of a disease mediated skin-joint crosstalk. However, only 30% of the patients with psoriasis develop PsA overtime.[1] To date, it is still obscure why the inflammatory process in some patients with PsO is restrained to the skin, whereas in other patients it spreads to the joints.

Objectives: Using a pre-clinical model of PsA and PsO, we aimed to investigate the skin-joint axis, i.e. the spreading of psoriatic inflammation from the skin to the joints, and to address its role in PsA pathogenesis.

Methods: The IL-23 overexpression (IL-23OE) mouse model of psoriasis was performed in different genetic backgrounds of KAEDE-transgenic mice expressing a photo-convertible fluorescent reporter to assess cell trafficking from inflamed skin to other organs. Psoriatic skin lesions were irradiated with UV light to trigger the photoswitch from $KAEDE^{GREEN}$ to $KAEDE^{RED}$. Migration of immune cells to joints was determined by light sheet fluorescence microscopy (LSFM) and flow cytometry. Imaging flow cytometry was used to determine the phenotype of cells migrating from the skin to other organs. The interactome of skin-derived migrating cells in joints was characterized by single-cell RNA-sequencing (scRNAseq) and functional analyses. Data were validated in synovial biopsies from PsO and PsA patients by imaging mass cytometry.

Results: IL-23 induced initiation of inflammation at the joints was dependent on the genetic background of the mice as assessed by MRI scan and histological analysis. However, migration of immune cells from psoriatic skin to the joints was observed in both strains, protected and non-protected mice from arthritis, although other organs such as spleen and lymph nodes showed no model dependent skin-derived migration. ScRNAseq and computational fate mapping with RNA velocity analysis revealed CD2+ MCHII+ monocytes as predominant cell type escaping the inflamed skin and entering the synovial tissue. In the pre-differentiated stage, those monocytes showed similar phenotypes in both, arthritis protected and non-protected animals. However, after entering the synovial tissue further differentiation into macrophages resulted into two different phenotypes, with pro-inflammatory characteristics in mice developing arthritis. Interactome analyses between local differentiated skin-derived macrophages and tissue resident synovial cells revealed major implication of synovial fibroblasts shaping the fate of skin-derived monocytes into a protective or pro-inflammatory phenotype with capacity to initiate the cascade of inflammation. Imaging mass cytometry of synovial biopsies from patients with PsO and PsA identified niches of the synovial membrane that were protected from inflammation by a similar fibroblastic fate as observed in the murine setting. Protection from arthritis was associated with significantly increased interactions of those protective fibroblasts with innate lymphoid cells (ILC) type 2, inducing pro-survival signals and resulting into activation of pro-resolving ILC2s.[2]

Conclusion: Spreading of inflammation from the skin to the joint can be initiated by skin-derived monocytes. However, the interaction between migrating monocytes and stromal-resident cells is essential to define the fate towards joint inflammation or joint protection in PsA. The data might provide completely new diagnostic opportunities to estimate the risk of PsO patients to develop PsA in the future.

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OP0107 NEUTROPHILS DISPLAY SHARED AND TISSUE-SPECIFIC PHENOTYPES IN INFLAMMATORY ARTHRITIS AND COLITIS

Keywords: Inflammatory arthritides, Innate immunity, Gastrointestinal tract

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Background: Neutrophils are essential in physiological and pathological immune processes through cytokine release, formation of neutrophil extracellular traps and crosstalk with the adaptive immune system. While neutrophils display varying phenotypes as a function of maturation stage, organ and inflammatory trigger, it is poorly understood which neutrophil phenotypes are organ-specific and which are shared. Spondyloarthropathies are a family of diseases with highly variable organ involvement, including colitis and arthritis.

Objectives: Our goal was to understand how neutrophils in the inflamed joint and intestine differ from those in blood and which neutrophil states observed in organs are overlapping and distinct.
Methods: We prospectively collected healthy donor blood, paired blood and synovial fluid from patients with active inflammatory arthritis in which a joint aspiration was diagnostically or therapeutically required, and colon biopsies from patients with inflammatory bowel disease (IBD) in which endoscopy was diagnostically required. Neutrophils were enriched from blood using ACK lysis and from colon biopsies by collagenase digestion. Synovial fluid was diluted, filtered and lysis was performed on samples with visible blood contamination. Technical validation of lysis and digestion of blood cells were performed to control for the influence of these procedures on marker expression. Flow cytometry was applied on the day of sample acquisition to fresh, surface-stained neutrophils to measure protein expression. A multiplex sandwich assay utilizing fluorescent antibody-conjugated beads was used to quantify inflammatory cytokine abundance in concomitant patient sera.
Results: In blood, neutrophils from patients with arthritis or inactive IBD did not show prominent surface protein differences compared to healthy donors. In patients with active colitis, expression of HLA-DR and CCR5 was elevated, while CXCR2 expression was reduced. Compared to blood, neutrophils from colon tissue showed downregulation of CD16, CD62L, ICAM-1, IL-17RA and CXCR2 and upregulation of the aging marker CXCR4. These changes were observed irrespective of disease activity. In addition, neutrophils from colon of patients with active inflammation, but not patients in endoscopic remission, showed a marked increase in expression of CD64 and HLA-DR, and the downregulation of CD62L and CXCR2 was more pronounced. We also identified an expanded population of CCR5+ neutrophils in colon tissue, which was more prominent in inflamed samples. While observable in both tissues, neutrophils in synovial fluid showed a stronger upregulation of HLA-DR and CXCR4 compared to colon. Upregulation of CCR5 and CD64, as well as the downregulation of CD16 were less pronounced. In contrast, synovial fluid neutrophils showed an upregulation of ICAM-1, while this marker was downregulated in the colon. Additionally, synovial fluid neutrophils showed an upregulation of TNF-RII, which was absent in blood and colon tissue. In serum, we observed greater abundance of IL-1β, IFN-α2, IL-33, sTNF-RI and sTNF-RII in endoscopically active IBD patients compared to inactive patients. In contrast, measured IL-10 levels were lower in these patients, underscoring the shift to a pro-inflammatory cytokine environment. Independent of disease activity, measured TNF-α levels were higher in patients with Crohn's disease compared to ulcerative colitis.
Conclusion: Tissue infiltrating neutrophils display a range of phenotypes in both inflammatory arthritis and inflammatory bowel disease. These range from mature cells lacking activation markers and resembling circulating neutrophils, to CD64+ HLA-DR+ CXCR4+ CXCR2- CD16low aged and activated cells, as well as CCR5+ pro-NETotic cells, in varying proportion. Elevated serum levels of innate- associated cytokines and an increased activation phenotype during active colitis suggest a strong neutrophil involvement in active IBD. Organ-specific differences in neutrophil effector states may require special approaches for therapeutic intervention.
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OP0108 MESENCHYMAL STEM CELLS ACCELERATE INFLAMMATION RESOLUTION THROUGH THE RELEASE OF PGE2 AND SPECIALIZED PRO-RESOLVING MEDIATORS IN EXPERIMENTAL GOUT

Keywords: Innate immunity, -omics, Gout

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Background: Mesenchymal stem cells (MSC) have been widely recognised as immunoregulatory agents in multiple inflammatory processes, although its specific effect on the modulation of innate immunity remains elusive. In an experimental well-dissected innate immune disease model such as gouty arthritis, MSC administration reduced the intensity and duration of the inflammatory flare. Specialized pro-resolving mediators (SPM) are derived from arachidonic acid (AA) and omega-3 fatty acids and are processed by the cyclooxygenase or lipoxygenase pathways. They dampen inflammation and promote resolution, decreasing neutrophil infiltrate, enhancing apoptosis, inducing efferocytosis by macrophages and promoting their switch from M1 to M2.
Objectives: To study whether MSC administration can directly trigger the resolution pathways modulating the synthesis of SPM and classical prostanoid mediators in the synovial membrane (SM) of rabbits in an experimental model of gout. The mechanisms by which MSC could modulate SPM synthesis were explored in a co-culture system with macrophages stimulated with MSU (monosodium urate crystals).
Methods: Gouty arthritis was induced in male New Zealand rabbits by intra-articular injection of MSU 50mg/kg (MSU group, n=16). Some of these animals systemically received $5x10^6$ human adipose tissue derived MSC (MSU-MSC group, n=8). All animals were euthanized 24 hours after challenge, when SM were collected. We determined the presence of lipoxin A4 (LXA4), maresin (Mar)-1, Mar-2, protectin D (PD)-1, PD-X, prostaglandin E2 (PGE2) and different SPM precursors in the SM employing mass spectrometry and ELISA. The expression of interleukin (IL)-10, indoleamine 2,3-dioxygenase (IDO) and the SPM receptor FPR2 genes were analysed by qPCR. *In vitro*, PMA-differentiated THP-1 macrophages were stimulated with 150 µg/mL MSU and MSCs were added in transwell in the presence or absence of the COX-2 inhibitor NS-398. SPM and IL-10 were analysed in the conditioned media, while cyclooxygenase and lipoxygenase pathways were studied in both cell types by qPCR.
Results: The decrease in the histological damage and in the presence of inflammatory mediators in the SM of gouty rabbits induced by MSC treatment were preceded by a significant increase in the levels of LXA4, Mar-1, Mar-2, PD-1, PDX, and its lipid precursors 14-HDHA and DHA; and by a marked increase in PGE2, in comparison to those observed in the MSU group. MSU-MSC rabbits showed a significant increase in the gene expression of the anti-inflammatory mediators IL-10, IDO-1, and the SPM receptor FPR2 in the SM, in comparison to MSU group. In vitro, we observed that MSC induced a higher release of LXA4, resolvin-D1, PGE2 and PGF2α to the co-culture media of MSU-stimulated THP-1 and increased the presence of IL-10. The pre-treatment of the MSC with the COX-2 inhibitor before the co-culture with MSU-stimulated THP-1, abolished the release of all SPM and IL-10 to the culture media. In addition, MSC induced a pro-resolutive phenotype in MSU-stimulated THP-1, evidenced by the upregulation in the gene expression of IL-10, IDO-1, PGE2 receptors EP2 and EP-3, COX-2, PGE2 synthase, FPR2 and GPR32, and the downregulation of EP-4, and lipoxygenases-12 and -15. Most of these effects were abrogated by COX-2 inhibition.
Conclusion: Our results show that MSC administration modulate the pro-resolving response in the SM of arthritic rabbits through the synthesis of multiple SPM and their precursors, together with an upregulation of FPR2, a receptor involved in pro-resolving signalling. *In vitro*, MSC were able to modulate THP-1 inflammatory phenotype induced by MSU, promoting the anti-inflammatory and pro-resolving response through the release of SPM, prostanoids and the modulation of FPR2, GPR32 and EP receptor presence. PGE2 depletion in MSC evoked a blockade of the pro-resolving program activation, highlighting its relevance in the modulation of the MSC-mediated anti-inflammatory and pro-resolutive response.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0109 SINGLE-CELL RNA-SEQ REVEALS DIFFERENCES IN METABOLIC PATHWAYS OF MYELOID CELLS IN THE PROGRESSION OF SLE

Keywords: Systemic lupus erythematosus, Innate immunity, -omics

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Background: Systemic Lupus Erythematosus (SLE) is an interferon-related autoimmune disease characterized by immune cell dysfunction and is common among women and minorities. A loss of tolerance to self-antigens leads to increased levels of autoantibodies against nuclear components (ANAs) prior to clinical disease onset. However, only about 4-8% develop an autoimmune disease. Patients with incomplete lupus erythematosus (ILE) exhibit some SLE clinical symptoms with most never progressing to SLE. Exact mechanisms involved in myeloid cell dysregulation and the progression of autoimmune disease remains unclear.
Objectives: Determine whether alterations in myeloid cell population frequencies or activation of particular cellular processes is dysregulated in subjects with pre-clinical disease.

Methods: PBMCs from 32 subjects (ANA-, ANA+, ILE and SLE) were sorted with Nanocellect Wolf microfluidic flow cytometer to remove dead and dying cells. Viable isolated single cells were used to do a multiomics single-cell analysis using 10x Genomics 5' scRNA-Seq/137-plex Total-Seq multiomics kit, that also enable BCR and TCR repertoire analysis. Single-cell transcript and proteogenomics library preparation was done on a 10x Chromium X targeting 20,000 cells per channel, each sample encapsulated in a single channel. Normalized, pooled UDI labeled libraries were sequenced on Illumina Nova-Seq S4 flowcell (PE100, depth of 50,000 reads/cell). Data were analyzed for cluster identification, differential gene signatures in Python. Pathway analysis was performed in Ingenuity Pathway Analysis (IPA).
Results: Across all subjects, 9 distinct myeloid clusters (Classical, Non-classical, Intermediate, CCR4+ monocytes) were identified with a community detection algorithm and visualized with Uniform Manifold Approximation Projection (UMAP). The proportion of cells in those clusters varied by disease group. Fractions of non-classical monocytes appear to be higher in ILE, SLE patients than in ANA- and ANA+ subjects. Classical monocytes have increasing cell fractions with disease progression, except ILE subjects that appear to have lower fractions than the other groups. Intermediate monocytes fractions are higher in ANA- controls and lower in the other groups. Pathway analysis revealed further differences within ethnicities (African, European Americans). Upregulation of autophagy related pathways was observed in AA ANA+ compared to ANA- and ILE, however it is downregulated in EA. Oxidative phosphorylation is upregulated in AA SLE compared to ILE and upregulated in AA ANA+ compared to ANA-. On the contrary, that pathway is upregulated in EA ANA+ compared to ANA- and ILE, as well as SLE compared to ILE. Further differences between subpopulations of major monocyte clusters were also observed.
Conclusion: Dysregulation of signaling in monocyte activation appears to be manifesting in either increased oxidative phosphorylation or alteration in cellular apoptotic or autophagy pathway regulation. Alterations in these processes may vary by ancestral background reflected in the heterogeneity one sees in the presentation of lupus or trajectory of disease.
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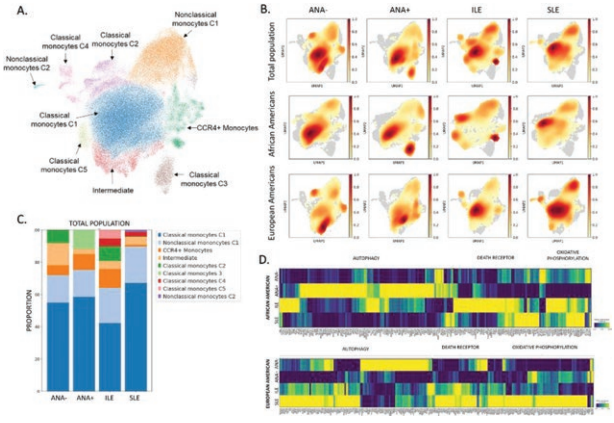


Figure 1. A. UMAP projection of 9 distinct myeloid clusters. B. Myeloid cell density for total population, African Americans and European Americans across 4 disease groups. C. Cell fractions for total population and each distinct cluster by disease group. D. Expression of genes involved in autophagy, death receptor signaling and oxidative phosphorylation pathways by race and disease group.

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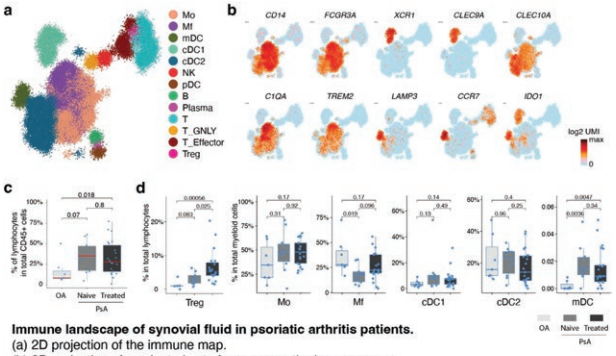
OP0110

SINGLE CELL RNA-SEQ DISSECTION OF THE SYNOVIAL FLUID IN PSORIATIC ARTHRITIS PATIENTS IDENTIFIES MYELOID CELL SUBSETS RELATED TO TREATMENT RESPONSE WITH BDMARDS

Keywords: bDMARD, -omics, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a complex chronic inflammatory disease involving aberrant activation of the innate and the adaptive immune systems[1]. While the adaptive system in the synovial fluid of PsA patients has been recently described at a single cell level [2], a comprehensive map of the myeloid compartment is still lacking. Anti TNF agents are commonly used as the first biologic DMARDs (bDMARDs) after failure of conventional DMARDs (cDMARDs), though up to 30-40% of PsA patients are anti TNF non-responders[3]. The inflammatory pathways leading to anti TNF or other bDMARDs resistance are unknown and biomarkers to predict treatment response are scarce.
Objectives: 1. To construct a comprehensive immune map of the myeloid compartment in the synovial fluid of naïve and treated PsA patients. 2. To identify gene signatures and immune pathways characteristic of anti TNF or other bDMARDs non-responders.
Methods: This pilot study included PsA patients with active knee arthritis enrolled according to CASPAR criteria, including naïve and treated patients.
We obtained synovial fluid by intra-articular aspiration of the involved knee. For each patient we performed single-cell sorting for CD45+ and MHCII+/CD11c+ to enrich for the myeloid compartment (particularly, dendritic cells and monocytes). We used single cell RNA-seq to dissect the immune landscape of the synovial fluid in PsA patients. Osteoarthritis patients with knee involvement were enrolled as a control. PsA Patients were followed for a minimum of 7 months from sampling day (range 7-30 months) and categorized as responders or non-responders according to the DAPSA score.
Results: We analyzed a total of 91,837 cells from 33 PsA Patients (11 naive, 22 under cDMARDs and bDMARDs: 9 anti-TNF and other 9 bDMARDs) and 7 controls (OA). The synovial fluid myeloid compartment of PsA patients was composed of intermediate monocytes (CD14+ CD16+); TREM2 macrophages; conventional dendritic cells: cDC1 (XCR1, CLEC9A), cDC2 (CD1c, CLEC10A) and migratory DCs (mDC: CCR7, LAMP3, IDO1). Intermediate monocytes were the most abundant cell type in the myeloid compartment. Compared to OA controls, PsA patients' synovial fluid was enriched with T regulatory cells (Treg: CD4+ FOXP3+) and migratory DCs (mDC: CCR7, LAMP3, IDO1). Tregs and TREM2 macrophages were more prevalent among treated than naïve PsA patients. We identified a unique cluster of cDC2 and monocytes with shared molecular signature, characteristic of anti TNF or other bDMARDs non-responders. These clusters demonstrated a high expression of interferon signature genes (ISG15, ISG20, IFI27, IFI6, IFIT3, STAT1) and genes related to the immunoproteasome (PSMB9, PSMB8, PSME2, PSME1, POMP). Two patients with severe deformative PsA highly refractory to treatment demonstrated a distinct cDC1 cluster with a high expression of inhibitory genes, such as IDO1, IL4I1, CMTM6 and NFKB1A.



Immune landscape of synovial fluid in psoriatic arthritis patients.
(a) 2D projection of the immune map.
(b) 2D projection of a selected set of genes over the immune map.
(c) Dot plot showing percentages of lymphocytes in total CD45+ immune cells.
(d) Dot plots showing percentages of selected immune cell subsets in total lymphocytes or myeloid cells.

Figure 1.

Conclusion: Our study provides the first unbiased map of the myeloid compartment of the synovial fluid of PsA patients. We identified clinically significant cell-subsets within the cDC2 and monocytes populations associated with anti -TNF or other bDMARDs non-response, illuminating potential biomarkers and future therapeutic targets.
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OP0111 **STROMAL AND ENDOTHELIAL-DERIVED SOLUBLE FACTORS DRIVE A PRO-FIBROTIC MACROPHAGE PHENOTYPE IN MYELOID CELL-RICH RHEUMATOID ARTHRITIS SYNOVIUM**

Keywords: Rheumatoid arthritis, Innate immunity, Synovium

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Background: Prototypically, the synovial tissue in rheumatoid arthritis (RA) is defined by an infiltration of lymphocytes of the adaptive immune system, which contribute to inflammation and joint destruction through the in-situ production of cytokines and autoantibodies. However, synovial histology images across patients have revealed considerable heterogeneity in the types of infiltrating immune cells; some exhibiting dense lymphocyte aggregates, while others are largely devoid of lymphocytes with extensive myeloid cells throughout. These differences may implicate divergent pathologic mechanisms. This diversity of cellular composition across RA synovium was reflected in the recently generated single-cell transcriptomic dataset from the Accelerating Medicines Partnership (AMP) RA/SLE Network, which consisted of >314,000 synovial cells from >70 patients with RA. The macrophage phenotypes differed across tissues with high versus low lymphocyte counts. Specifically, macrophages from tissues with high T cell proportions expressed more *IL1B* and *HBEGF*, while low lymphocyte yet high myeloid proportions in a tissue associated with macrophage expression of *SPP1* and *FN1*. Endothelial-associated TGFβ was upregulated in the lymphocyte-low/myeloid-rich tissues. We thus hypothesized that infiltrating monocytes exposed to the low-lymphocyte/myeloid-rich RA synovium become $SPP1^{hi}$ macrophages after interacting with a combination endothelial-derived TGFβ and stromal derived factors.
Objectives: To identify whether TGFβ and stromal-derived soluble factors are sufficient to polarize immature, blood-derived monocytes into the macrophages found in low-lymphocyte/high myeloid RA synovial tissue.
Methods: $CD14^+$ cells were magnetically isolated from the blood of healthy patients and incubated in media with M-CSF for 24 hours. After incubation with M-CSF, $CD14^+$ cells were co-cultured in a trans-well system with various combinations of RA synovial fibroblasts and recombinant TGFβ for 72 hours. After 72 hours, the cells were prepared for single-cell RNA sequencing. This dataset of cells from this reductionist system was overlayed onto the cell-cluster map algorithm generated by the patient synovial-tissue derived macrophages for direct comparisons.
Results: In the presence of synovial fibroblasts and TGFβ, macrophages had a gene expression program that increased the proportion of macrophages aligning with those found in lymphocyte-low/myeloid-rich synovial tissue. Specifically, the transition of blood monocyte-derived macrophages from a $MERTK^+$ homeostatic, tissue macrophage phenotype into the $SPP1^{hi}$ phenotype. This analysis also showed that macrophages incubated with TGFβ and fibroblasts had higher expression of $SPP1^{hi}$ macrophage cluster marker genes, namely *SPP1, CLEC5A,* and *FN1,* as well as genes that contribute to RA pathogenesis, including *CCL2 and S100A8.*
Conclusion: In conclusion, we have shown that TGFβ and factors derived from synovial stromal cells are sufficient to drive monocytes toward the $SPP1^{hi}$ macrophage phenotype found in myeloid-rich RA synovial tissue. In future experiments, we hope to understand the role these macrophages play in shaping the phenotype of the stromal and endothelial cells they interact with, and whether targeting the generation of these cells represents an effective treatment option for this subset of RA patients.
Acknowledgements: Accelerating Medicines Partnership (AMP) Program: Rheumatoid Arthritis and Systemic Lupus Erythematosu.s.
Disclosure of Interests: None Declared.
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Pathogenic clues to systemic sclerosis and myositis

OP0112 **EXPANSION OF ACTIVATED CD7+ CYTOTOXIC T CELLS AND NK CELLS IN SSC AND PREVENTION OF FIBROBLAST CONTRACTION THROUGH SELECTIVE IMMUNOTOXIN-MEDIATED DEPLETION OF THESE CELLS**

Keywords: Systemic sclerosis, Adaptive immunity, Treat to target

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Background: Systemic sclerosis is characterized by vasculopathy, fibrosis and autoimmune inflammation. Adaptive immune and NK cells express co-stimulatory molecules to regulate effector responses in inflammatory conditions. CD7 is a co-stimulatory molecule induced by IFN-γ signaling on T and NK cells that is downregulated upon residency in tissues such as skin [1].
Objectives: Hypothetically, CD7 is upregulated in IFN-γ driven conditions, allowing targeted depletion of pathogenic cells. In this study, we analyzed expression, regulation and targeting of CD7 in SSc tissues and in a patient treated with anti-CD7 immunotoxin (CD7-IT).
Methods: To identify disease-specific activation markers we compared status of T cell activation in SSc skin compared to blood. To do so, single-cell RNA sequencing datasets containing 60,000 skin and blood immune cells from 109 SSc patients versus 65 healthy donors were analyzed. Twentyone-color flow cytometry (n=50) and 8-color multiplex skin immunofluorescence staining (mIF) (n=30) were used for validation and spatial localization. CD7-IT was used to induce subset-specific depletion in vitro, and ex vivo skin explants. Fibroblasts and immune cells were co-cultured in 3D collagen hydrogel to test effect of targeted immune cell depletion on fibroblast contractility. A single patient was treated with immunotoxin on compassionate use basis.
Results: Sc-RNAseq analysis showed that SSc skin is characterized by increased infiltration of CD7+ cells corresponding to $CD8^+GZMB^+$ and $CD56^+GZMB^+$ cytotoxic T and NK cells. Immunohistochemistry also showed that SSc lesional skin exhibits significantly higher infiltration of these $CD7^+$ (T and NK) cells than non-affected skin (Figure 1). Expansion of $CD7^+$ cytotoxic T cells was also observed in SSc blood. A CD7-targeting IT effectively depleted 85% of $CD7^+$ cytotoxic T and NK cells in vitro, and in ex vivo skin. Strikingly, depletion of $CD7^+$ cells prevented fibroblast activation and contraction in a 3D fibroblast-immune cells co-culture assay. Notably, also in vivo administration of CD7-IT significantly eliminated $CD7^+$ cell subsets in patient's blood and skin.
Conclusion: Together, we show strong presence of CD7 on SSc immune cells and that targetting this molecule depletes T and NK cell populations with potential disease modifying results. Our results pave the way for a novel approach in halting SSc related fibrosis.

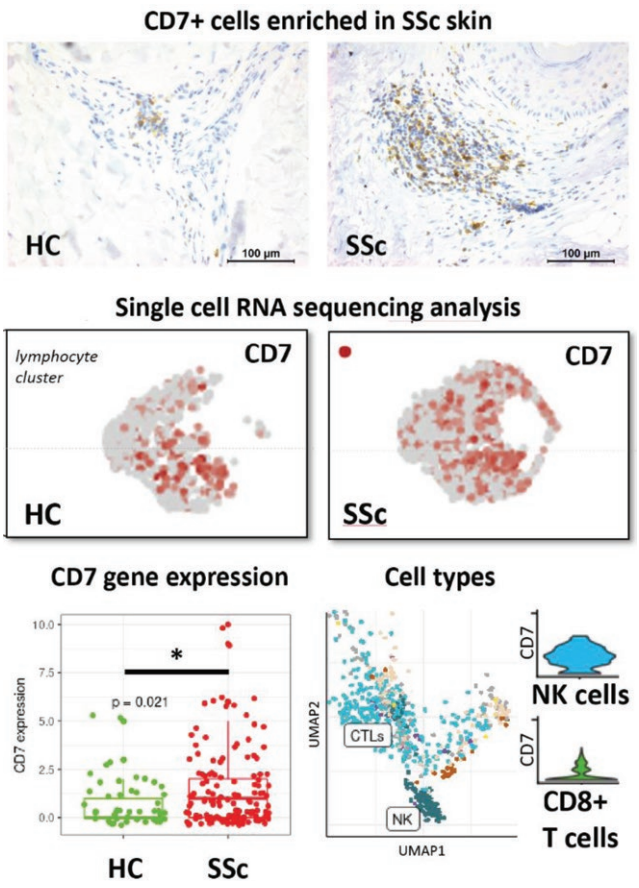


Figure 1. Strong presence of CD7$^+$ cytotoxic T and NK cells in systemic sclerosis skin

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OP0113

THE BETA SECRETASE BACE1 DRIVES SYSTEMIC SCLEROSIS FIBROBLASTS ACTIVATION THROUGH Β-CATENIN AND NOTCH SIGNALLING

Keywords: Skin, Systemic sclerosis, Cell biology

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Background: The beta-amyloid precursor protein cleaving enzyme 1 (BACE1) is well known for its role in the development of Alzheimer's disease via the generation of β-amyloid. Recent publications, including our own, have demonstrated a role for this enzyme in other chronic inflammatory diseases, including type 2 diabetes and cardiovascular disease. However, to date there has been no studies looking into the role of BACE1 in the autoimmune condition Systemic Sclerosis (SSc).
Objectives: The aim of this study was to assess the expression profile of BACE1 in SSc patient samples and investigate the effects of BACE1 inhibitors and siRNA on SSc fibroblast activation.
Methods: Patient fibroblasts were obtained from full thickness forearm skin biopsies from healthy and early diffuse SSc patients. BACE1 was inhibited with 2 specific small molecule inhibitors and siRNA specific to BACE1. Morphogen signalling was activated with recombinant TGF-β, Wnt-3a or the smoothened agonist SAG. A xenotransplant bleomycin mouse model using patient pDC was used to interrogate *in vivo* expression of BACE1 in fibrosis.
Results: Here we show that BACE1 protein levels are elevated in SSc patient skin biopsies. In particular BACE1 was increased in the fibroblasts and endothelial cells of the SSc skin. BACE1 was elevated in isolated dermal fibroblasts grown in culture (2.3 fold increase, N=4). BACE1 protein levels were elevated in the bleomycin skin fibrosis model. Interestingly BACE1 mRNA levels were unaffected in cultured SSc fibroblasts, suggesting a post-translational modification led to the elevated protein levels. Inhibition of BACE1 with small molecule inhibitors (that have been proven safe in phase 1 clinical trials for Alzheimer's) or siRNA blocked pro-fibrotic gene (alpha SMA, Collagen Type 1 and CTGF) expression in SSc fibroblasts. In addition overexpression of BACE1 in healthy fibroblasts resulted in myofibroblast activation (2-fold increase in alpha SMA protein expression). Interestingly overexpression of a BACE1 mutant construct which disrupts the secretase activity of the protein, was unable to induce fibroblast activation. Disruption of BACE1 (with both the inhibitors and siRNA) blocked morphogen mediated fibroblasts activation. The BACE1 inhibitors and siRNA blocked TGF-β, Wnt-3a and Hedgehog mediated alpha-SMA expression in healthy fibroblasts. Furthermore, we show that BACE1 regulation of dermal fibroblast activation was dependent on the β-catenin and Notch signalling pathways. BACE1 ability to regulate non-canonical Wnt receptors led to elevated β-catenin expression which in turn activated the Notch signalling pathway.
Conclusion: This is the first evidence that BACE1 and in particular its secretase activity, plays a role in SSc and fibrosis in general. The ability of BACE1 to regulate SSc fibroblast activation reveals an exciting new therapeutic target in SSc. Several BACE1 inhibitors have been shown to be safe in phase 1 clinical trials for Alzheimer's disease. Future work includes investigating the role of BACE1 in vascular/endothelial cell dysfunction in SSc.

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OP0114

ENDOTHELIAL RESPONSE TO TYPE I INTERFERON CONTRIBUTES TO VASCULOPATHY AND FIBROSIS AND PREDICTS DISEASE PROGRESSION OF SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Skin, Cytokines and chemokines

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Background: Type I interferon (IFN-1) signature is a hallmark of patients with systemic sclerosis (SSc)[1-2]. However, the meaning of the IFN-1 signature for the pathophysiology and clinical manifestations is less clear, and reported associations are rather weak.
Objectives: This study aims to better understand the significance of IFN-1 in SSc clinical stratification and its contribution to disease deterioration.
Methods: For hypothesis generation, we performed single-cell RNA sequencing (scRNAseq) on skin biopsies (SSc=4, control =2) using the BD Rhapsody platform. A publicly available dataset (GSE138669) of skin scRNAseq (dcSSc=12, control =10) was used for validation. IFN-1 signature was mapped, functionally investigated in a bleomycin plus IFNα2-adeno-associated virus (IFNA2-AAV) induced model, and verified in an SSc cohort (n=61).
Results: In discovery data, endothelial cells (EC) had the most prominent IFN-1 response among dermal non-immune cells. EC from postcapillary venules, arterioles and capillaries were the major responders of IFN-1. Ascending IFN-1 signature presented in total EC from control, lcSSc, to dcSSc and was still true in the EC subclusters above. Endothelial-to-mesenchymal transition (EndoMT) scores increased in parallel. The validation data confirmed IFN-1 signature and EndoMT elevation in total and subgroups of EC. IFNA2-AAV deteriorated bleomycin-induced dermal fibrosis, EndoMT, and perivascular fibrosis and caused blood vessel loss via endothelial apoptosis. In SSc skin biopsies, vascular MX1, an IFN-1 response protein, was increased in total SSc and significantly higher in dcSSc than in lcSSc. To predict disease progression in 6-34 months, the baseline vascular MX1 performed similarly to skin score in total SSc and was superior in the dcSSc subpopulation (Figure 1).
Conclusion: The EC IFN-1 signature distinguished SSc skin subtypes and disease progression efficiently and may contribute to vasculopathy and fibrosis.

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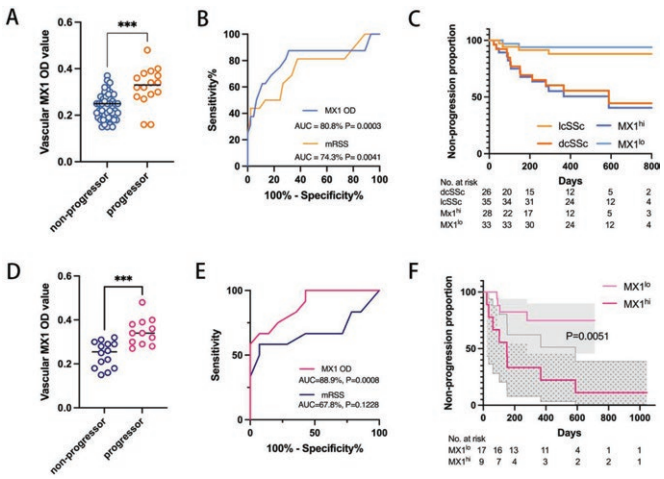


Figure 1. Vascular MX1 is predictive of disease progression in SSc.(A)Vascular MX1 OD value in progressor and non-progressor among all SSc patients.(B)ROC curves of the predictive values for vascular MX1 OD value (blue) and mRSS (yellow) in all SScpatients.(C) Kaplan–Meier analysis of non-progression in patients with low and high vascular MX1 expression as well as patients with lcSSc and dcSSc.(D)Vascular MX1 OD value in progressor and non-progressor among dcSSc patients.(E)ROC curves of the predictive values for vascular MX1 OD value (red) and mRSS (purple) in dcSSc group.(F) Vascular MX1 distinguished disease worsening eddectively in Cox regression for dcSSc.

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Disclosure of Interests: None Declared.
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OP0115 DISTURBED SPATIAL WNT ACTIVATION - A POTENTIAL MEDIATOR OF DISTURBED SKIN POLARIZATION IN SYSTEMIC SCLEROSIS (SSC)

Keywords: Skin, Systemic sclerosis

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Background: Disruption of the skin structure is a central hallmark of Systemic Sclerosis (SSc). Healthy adult human dermis is characterized by a papillary dermis (conic upward papillae with nerve endings, mechanoreceptors, vessels and loose collagen bundles) and a reticular dermis (coarse collagen bundles). In SSc, the dermal structure is disrupted and shifted towards a "reticularized" phenotype with loss of dermal papillae and exaggerated deposition of collagen. Little is known on mechanisms necessary to maintain physiological adult human skin morphology. Evidence from murine experiments suggests that short distance morphogen gradients are necessary for three-dimensional pattern formation in embryonic skin morphogenesis in rodents [1].

OBJECTIVES:

1) to analyze if spatial WNT/β-catenin activation is observed in adult healthy human skin and whether it is altered in fibrosing skin disorders such as SSc
2) to assess whether perturbation of spatial WNT/ β-catenin activation correlates with disruption of physiological skin structure in SSc
3) to analyze whether spatial activation is mimicked in a Wnt-driven murine fibrosis model and can be reverted by overexpression of the endogenous Wnt-antagonist Dkk1

Methods: Dermal skin morphology was quantitatively assessed using HE and trichrome staining of skin sections of 40 SSc patients and 18 healthy controls. Enrichment of papillary and reticular marker genes and WNT target genes in healthy and SSc skin transcriptome were assessed by gene set enrichment analyses using prepublished datasets [2]. Spatial WNT/β-catenin activation was analyzed by RNAscope-in situ hybridization detection of *AXIN2*. Immunofluorescence (IF) staining was performed to detect β-catenin distribution. In addition, skin sections of Wnt10btg- and Dkk/Wnt10btg mice were analyzed.

Results: Here we quantitatively describe a marked decrease of number, area and height of papillary structures in SSc compared to healthy controls. Consistently, papillary/reticular marker gene expression is shifted towards a reticular profile in SSc skin compared to controls. Next, we analyzed whether the expression of WNT3A-regulated target genes is enriched in papillary or reticular gene sets of healthy skin. We observed an enrichment of WNT3A-regulated target genes in papillary gene sets of healthy skin. Consistently, we observed a distinct pattern of spatial distribution of β-catenin-expressing fibroblasts in healthy skin that is disturbed in SSc: In healthy skin, β-catenin-positive fibroblasts were predominantly located in the papillary dermis and the relative amount of β-catenin-expressing fibroblasts was reduced in the reticular part. In contrast, in SSc skin, we observed a 2-fold increase of β-catenin-positive fibroblasts throughout the dermis. A gradient with enrichment of β-catenin-expressing fibroblasts in the papillary layer as observed in healthy skin was no longer detectable in SSc. Confocal imaging suggested increased nuclear accumulation of β-catenin in the reticular dermis compared to the papillary dermis in SSc skin. The loss of spatial WNT activation in SSc was confirmed on a transcriptional level. Interestingly, spatial redistribution of WNT activation is mimicked in Wnt10btg mice compared to wild-type mice and partially reverted by overexpression of the endogenous Wnt antagonist Dkk1. These results suggest that distinct site-specific activation of WNT/β-catenin signaling with a delicate balance of WNT agonists and antagonists might be necessary to maintain and eventually restore physiologic skin integrity in adult human skin.

Conclusion: Our study presents first evidence for a loss of the physiological β-catenin gradient in SSc, associated with a loss of papillary dermal structure. Further analyses of WNT agonists and antagonists spatial distribution and advanced in vitro models mimicking a papillary skin structure will be necessary to better understand mechanisms of skin structure maintenance in healthy adult human skin.

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Disclosure of Interests: Sara Chenguiti Fakhouri: None declared, Laura Konstantinidis: None declared, ZHU Honglin: None declared, Markus Eckstein: None declared, Clara Dees: None declared, Alexander Kreuter: None declared, Michael Sticherling: None declared, Georg Schett: None declared, Distler Jörg Shareholder of: JHWD is stock owner of 4D Science and scientific lead of FibroCure., Consultant of: JHWD has consultancy relationships with Actelion, Active Biotech, Anamar, ARXX, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, Medac, Novartis, Pfizer, RuiYi and UCB., Grant/research support from: JHWD has received research funding from Anamar, Active Biotech, Array Biopharma, ARXX, aTyr, AstraZeneca, BMS, Bayer Pharma, Boehringer Ingelheim, Cantargia, Celgene, CSL Behring, Galapagos, GSK, Inventiva, Kiniksa, Sanofi-Aventis, RedX, UCB., Christina Bergmann Consultant of: CB has received consultancy fees from Pfizer and Boehringer-Ingelheim.
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OP0116 THE AP-1 TRANSCRIPTION FACTOR FOSL-2 DRIVES CARDIAC FIBROSIS AND ARRHYTHMIAS UNDER IMMUNOFIBROTIC CONDITIONS IN SYSTEMIC SCLEROSIS

Keywords: Cardiovascular disease, Heart, Animal Models

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Background: Fibrotic changes in the myocardium and cardiac arrhythmias represent fatal complications in systemic sclerosis (SSc). So far, the underlying mechanisms remain elusive. Mice overexpressing AP-1 family transcription factor Fosl-2 (Fosl-2^{tg}) represent animal model of SSc.
Objectives: We aimed to identify the mechanisms controlling myocardial fibrosis and arrhythmias in SSc.
Methods: Mice overexpressing activator protein-1 transcription factor component Fos-related antigen-2 (Fosl-2^{tg}) and Rag2$^{-/-}$Fosl-2^{tg} mice lacking T and B cells were subjected to study myocardial fibrosis, arrhythmias and response to stress using radiotelemetry, echocardiography and ex-vivo Langendorff-system. Immunohistochemistry/immunofluorescence analyses were used to characterized endomyocardial biopsies (EMBs) of SSc patients with heart failure with or without arrhythmia, and mouse hearts. Cardiac human and mouse fibroblasts were used to evaluate molecular mechanisms using bulk RNA sequencing, qPCR, IF, ELISA, Western blot, Bromodeoxyuridine proliferation assay, senescence associated-β-Galactosidase assay for cell senescence, Caspase Glo 3/7 assay for cell apoptosis and contraction assay.
Results: Fosl-2^{tg} mice showed interstitial cardiac fibrosis with increased numbers of CD45^{-}CD31^{-}Ter119^{-}gp38^{+} cardiac fibroblasts, disorganized connexin 43 and 40 in intercalated discs and deregulated expression of genes controlling conduction system (*Meis1, Nfia*, *Tbx3*, *Sox5*, *Scn10a*, *Kcnq1*, *Scn10a, Nos1ap*). Fosl-2^{tg} mice developed higher heart rate (HR), prolonged QT intervals, arrhythmias with prevalence of premature ventricular contractions, ventricular tachycardias and atrio-ventricular blocks second-degree. QT intervals positively correlated with AV blocks, while QT intervals and AV blocks positively correlated with the disease phenotype and collagen deposition. Fosl-2^{tg} mice showed significantly reduced HR variability in long-term ECG recordings (reduced NN intervals, SDNN, RMSSD, NN6, pNN6), indicating autonomic disbalance with a shift towards increased sympathetic activity. Following stimulation with isoproterenol (ISO) Fosl-2^{tg} mice revealed impaired HR response. Similarly, ex vivo Langendorff-system measurement of HR in the isolated mouse hearts confirmed the abrogated response to ISO stimulation of Fosl-2^{tg} hearts. Immunodeficient Rag2$^{-/-}$Fosl-2^{tg} mice showed no myocardial fibrosis and ECG abnormalities. Transcriptomics analysis of cardiac Rag-2$^{-/-}$Fosl-2^{wt}/Rag2$^{-/-}$Fosl-2^{tg}/Fosl-2^{tg} fibroblasts revealed that systemic inflammation triggered fibrotic and arrhythmogenic alterations while Fosl-2-overexpression mediated profibrotic signature. In human cardiac fibroblasts FOSL-2-overexpression enhanced myofibroblast signature under proinflammatory or profibrotic stimuli. Furthermore, increased numbers of GP38^{+} fibroblasts were detected in FOSL-2-expressing and collagen-rich areas of SSc EMBs.
Conclusion: These results demonstrate that under inflammatory and fibrotic conditions Fosl-2 drives myocardial fibrosis, arrhythmias and causes aberrant response to stress. This mechanism might represent a promising target against increased cardiac disease burden in the immunofibrotic cardiac disorders.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Mara Stellato: None declared, Matthias Dewenter: None declared, Michal Rudnik: None declared, Amela Hukara: None declared, Ozsoy Cagla: None declared, Florian Renoux: None declared, Elena Pachera: None declared, Felix Gantenbein: None declared, Petra Seebeck: None declared, Siim Uhtjaerv: None declared, Elena Osto: None declared, Daniel Razansky: None declared, Karin Klingel: None declared, Jörg Henes: None declared, Oliver Distler Consultant of: OD has/had consultancy relationship with and/or has received research funding from or has served as a speaker for the following companies in the area of potential treatments for systemic sclerosis and its complications in the last three years: Abbvie, Acceleron, Alcimed, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos, Glenmark, Horizon, Inventiva, Kymera, Lupin, Medscape, Miltenyi Biotec, Mitsubishi Tanabe, MSD, Novartis, Prometheus, Roivant, Sanofi and Topadur. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143), Przemysław Błyszczuk: None declared, Gabriela Kania: None declared.
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OP0117 PROTEASOME INHIBITION AS A NEW TREATMENT FOR DERMATOMYOSITIS: RESULTS OF A DRUG REPURPOSING ANALYSIS BASED ON THE TRANSCRIPTOMIC SIGNATURE OF PATIENTS' PERIFASCICULAR FIBERS VALIDATED IN PRE-CLINICAL MODELS

Keywords: Myositis, Rare/orphan diseases

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Background: Dermatomyositis (DM) is an autoimmune myopathy responsible for muscle weakness associated with decreased quality of life and increased mortality. Current treatments are empirical, partially effective, expose to a risk of side effects and a high rate of relapse upon discontinuation. DM muscular histology is characterized by lesions of perifascicular fibers consisting of atrophy, overexpression of type I interferon-dependent genes and mitochondrial dysfunctions of unknown origin [1].
Objectives: The objective of the study was to identify innovative therapeutic strategies for DM, based on the identification of the molecular pathways that underlie perifascicular fibers lesions and the repositioning of drugs already approved in humans.
Methods: To reveal the molecular pathways underlying DM perifascicular fibers lesions, perifascicular and endofascicular fibers from 19 patients with recent and untreated myositis (DM, other myositis) or without myopathy were microdissected by laser, their transcriptome was established by RNA sequencing and analyzed by bioinformatic methods. To identify innovative therapeutic strategies based both on DM pathophysiological mechanisms and on existing drugs, the transcriptomic signature specific to DM perifascicular fibers obtained by microdissection experiments was used for a drug repositioning analysis as described by Karatzas et al. [2]. To validate the predications obtained, the effect of drug candidates already used in humans was tested in *in vitro* and *in vivo* preclinical models: in 1) cultured human muscle cells treated with IFN-I and in 2) a mouse model of myositis experimentally induced by immunization against skeletal muscle fast-type C protein.
Results: Transcriptomic analysis of patient's muscle fibers combined with topographic information (perifascicular VS endofascicular localization) revealed that a proteasome deregulation predominant in the perifascicular fibers is a hallmark of DM. The integration of 3 computer databases of drug repositioning allowed the identification of 9 molecules predicted by at least 2 bases to reverse the pathological signature of the perifascicular fibers of patients with DM. The drug with the highest therapeutic potential was a proteasome inhibitor (Ixazomib). A second proteasome inhibitor (MG-132) was also identified. 2 drugs already used for DM (prednisolone and a JAK inhibitor) was identified with a lower therapeutic score. In the cellular model (human myotubes treated with IFN-I) ixazomib and bortezomib reversed the atrophy and the pathological signature of DM perifascicular fibers identified in the microdissection experiments. In the mouse model of myositis, ixazomib and bortezomib restored muscle strength, decreased blood creatine kinase, and reversed the atrophy of muscle fibers.
Conclusion: Proteasome inhibition could be a new effective therapeutic strategy for DM.
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OP0118 INTEGRATED ANALYSIS OF SINGLE-CELL AND BULK RNA SEQUENCING DATA REVEALS CELLULAR HETEROGENEITY IN THE SKELETAL MUSCLE OF IDIOPATHIC INFLAMMATORY MYOPATHY

Keywords: Cell biology, Myositis

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Background: IIMs-affected muscles showed diverse cellular microenvironments, and specific immune activation is involved in the different types of IIMs. Skeletal muscle cells exhibit immunobiological properties and act as nonprofessional antigen-presenting cells in IIMs.
Objectives: We sought to identify the skeletal muscle cells (SMCs) and immune cell populations in IIMs muscles and understand how alterations in these cell subpopulations lead to muscle damage.
Methods: We performed single-cell RNA-sequencing (scRNA-seq) on muscle tissues from 6 IIMs and 3 normal control (NC), and spatial transcriptomics from 2 IIMs and 1 NC. 76 IIMs and 10 NC were analysed by bulk RNA sequencing.
Results: From the scRNA-seq analysis, remarkable heterogeneity of SMCs and immune cells phenotypes were found and spatially organized in IIMs subgroups. They displayed diverse functions and cell-surface proteins. From the

bulk RNA-seq deconvolution analysis, cell clusters with high expression of type 1 interferon-related genes, such as ISG15+ SMCs, CD4+ISG15+ T cells, FCN1+ISG15+ macrophages and KLRC1+XCL1+ NK cells, were specifically cloned in DM; Cell subpopulations involved in mitochondrial changes, such as Mito_high_CD8+ TEFFs, were expanded in anti-Jo1 ASS group, TPM1+ SMCs and Mito_high_NKs has the highest proportion in anti-SRP IMNM. Mito_high_NKs were positively correlated with serum creatine kinase (CK) in IIM patients. scRNA-seq and spatial transcriptomics combined analysis indicated ligand-receptor pairs MIF→(CD74+CD44)/(CD74+CXCR4) play key roles in the interactions of ANKRD2+ SMCs and inflammatory cells. The levels of CD44 and CXCR4 in muscle tissues were positively correlation with CK, lactate dehydrogenase, aspartate aminotransferase and alanine aminotransferase.

Conclusion: Our results demonstrate previously unrecognized SMCs and immune cells phenotypes in IIMs subgroups, and indicate the interactions of SMCs and immune cells are key pathological mechanisms driving muscle damage.

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OP0119

MUSCLE FIBRE PLAYS A CRUCIAL ROLE IN THE THERAPEUTIC RESPONSE OF MYOSITIS TO GLUCOCORTICOIDS THROUGH THE PARACRINE EFFECT OF EPINEPHRINE ON THE IMMUNE SYSTEM

Keywords: Animal Models, Myositis

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Background: Glucocorticoids (GC) are the first line treatment in myositis.
GC treatment is empirical. Both GC therapeutic and iatrogenic effects are mediated by the glucocorticoid receptor (GR), which is ubiquitously expressed. Our team has recently shown that muscle fibres immuno-metabolic modifications participate to muscle weakness and perpetuation of the disease[1]. Thus, myofibers could be a therapeutic target of GC.

Objectives: To unravel the mechanism of GC therapeutic effect in order to optimize myositis care.

Methods: Experimental myositis (EM) was induced in 8 to 10 week-old C57BL/6J mice through the immunisation against a polypeptide from skeletal muscle fast-type C protein. In order to investigate whether GC target skeletal muscle fibres to elicit their therapeutic response in EM, we generated mice in which GR can be selectively ablated in skeletal muscle fibres in a temporal manner. To this end, EM was induced at day (D) 0 in HSA-Cre-ERT2(tg/0)/GRL2/L2 mice (pre-mutant mice), which express the tamoxifen-dependent CreERT2 recombinase selectively in skelelal muscle fibres and bear two LoxP-flanked GR alleles, as well as in HSA-Cre-ERT2(0/0)/GRL2/L2 littermates, which do not express the recombinase (GRL2/L2 mice). Thus, tamoxifen treatment from D9 to D13 induced GR inactivation in the former mice only, termed hereafter GR(i)skm-/- mice. Mice of both lines were treated by prednisone (PDN) from D14 to D20 at the dose of 1 mg/kg/day by gavage. Grip test was performed at D0, before the 1st PDN administration (D14) and the day before sacrifice (D20). Creatine-kinase (CK) activity assay in serum, muscle histology, immune-cell phenotyping using flow cytometry and gastrocnemius transcriptomic analysis were run. Transcriptomic data were validated in independent mice cohorts, *in vitro* and on human muscle biopsies.

Results: In pre-mutant EM mice at D0 as well as in EM GR(i)skm-/- at D14, muscle strength was similar to that of EM GRL2/L2 mice. At D20, muscle strength was still comparable between V-treated EM GRL2/L2 and GR(i)skm-/- mice. Conversely, PDN treatment did not induce a regain of muscle strength in EM GR(i)skm-/- mice (143.9 vs 175.7 ± 7.5 g in PDN-treated GRL2/L2, p=0.0007). V-treated EM GRL2/L2 and GR(i)skm-/- mice showed a similar increase in serum CK levels at sacrifice. CK decreased only in GRL2/L2 and not in GR(i)skm-/- mice after PDN treatment (146.6 ± 10.9 vs 234.5 ± 10.0 U/l, p=0.002). Although no major differences in the histological inflammatory infiltrate score among the four experimental groups, at muscle flow cytometry, the percentage of proinflammatory macrophages, F4/80-Ly6c-positive, was greater (76% vs 67%, p=0.5) and that of anti-inflammatory macrophages, F4/80-CD206-positive, was lower (12% vs 17%, p=0.7) in PDN-treated GR(i)skm-/- than GRL2/L2 mice suggesting myofiber GR knockout promotes a proinflammatory phenotype in immune cells infiltrate. Strikingly, PDN induced a 3-fold decrease in the percentage of CD8-positive T cells in EM GRL2/L2 mice compared to V-treated EM GRL2/L2 mice (11% vs 29%, p=0.003). This anti-inflammatory effect of PDN was suppressed in PDN-treated EM GR(i)skm-/- mice. Moreover, CD4-CD8 double negative T cells, that inhibit the immune response by killing effector T cells, slightly increased in PDN-treated EM GRL2/L2 compared to V-treated GR L2/L2 mice (35% vs 24%, p=0.2). This effect of PDN was suppressed in PDN-treated EM GR(i)skm-/- mice. Transcriptomic and functional analyses of muscle *in vitro* and *in vivo* demonstrated the importance of epinephrine secreted by the myofibre relaying the effects of GC. The expression of epinephrine by the myofibre in response to GC has been validated in patients with myositis.

Conclusion: Skeletal muscle fibres play a critical role in the GC therapeutic response in myositis through an epinephrine-mediated polarization of inflammatory infiltrate toward an anti-inflammatory phenotype.

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Predictors of outcome in early rheumatoid arthritis_

OP0120

IDENTIFICATION OF EARLY RISK FACTORS IN A NOVEL PREDICTION MODEL FOR ACPA POSITIVE RA

Keywords: Diagnostic Tests, Rheumatoid arthritis, Autoantibodies

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Background: Individuals testing positive for anti-cyclic-citrullinated-peptide-antibodies (Anti-CCP) and musculoskeletal (MSK) complaints are at risk for developing rheumatoid arthritis (RA).

Objectives: We aim to identify factors involved in arthritis progression in a population considered at risk for RA.

Methods: Anti-CCP-positive individuals with MSK complaints referred to rheumatologist in the Region Stockholm were recruited. Individuals lacked arthritis at clinical and ultrasound examination and were followed for ≥3 years or until arthritis diagnosis was made. Blood samples from inclusion were analyzed for 9 selected anti-citrullinated-protein-antibody (ACPA) reactivities (citrullinated α-1-enolase, fibrinogen, filaggrin, histone, vimentin and tenascin peptides); as well as a panel of 92 inflammation-associated proteins and HLA-SE alleles. Cox regression was applied to the data and a predictive multivariate model was identified. Results are shown with a confidence interval (CI) of 95 percent.

Results: 267 individuals were recruited. 101 (38%) developed arthritis in median after 14 months (IQR: 6-27). In the multivariate analysis: ACPA reactivity (HR 8.0, CI 2.9-22, p<0.0001), IL15R-α levels (HR 0.6, CI 0.4-0.9, p 0.006), IL6 levels (HR 1.5, CI 1.2-1.8, p<0.0001) and the presence of tenosynovitis as detected by ultrasound (HR 3.4, CI 2.0-6.0, p<0.0001) were significantly associated with arthritis. Diagnostic accuracy for ACPA reactivity test had a sensitivity of 96% (CI 92-99.8), a specificity of 30% (CI 30-46), a positive predictive value of 51% (CI 43-58) and a negative predictive value of 94% (CI 87-99.7). Diagnostic accuracy for ultrasound assessed tenosynovitis had a sensitivity of 17% (CI 9-24), a specificity of 99% (CI 97-100), a positive predictive value of 89% (CI 74-100) and a negative predictive value of 64% (CI 57-70).

Conclusion: We propose a high-risk RA phase characterized by the presence of certain ACPA reactivities, IL15-Rα, IL6, and tenosynovitis, parameters that could be used to identify individuals at particular low risk and high risk for arthritis progression.

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OP0121 SYNOVIAL CELLULAR NICHES ARE DETERMINANTS OF ARTHRITIS PERSISTENCE VERSUS RESOLUTION IN EARLY UNTREATED ARTHRITIS

Keywords: -omics, Inflammatory arthritides, Rheumatoid arthritis

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Background: Published synovial research largely focuses on persistent clinical syndromes such as RA and PsA. However spontaneously resolving synovitis is a common manifestation of viral infection (parvovirus, influenza), post-bacterial reactive states and metabolic disease such as gout. The study of synovial tissue taken from such patients using advanced single cell methodologies may provide biomarkers of outcome in early disease but is also a valuable resource to understand mechanisms underlying the subversion of healthy mechanisms of resolution resulting in persistent disease.

Objectives: To use single cell RNA sequencing to understand the cellular interactions governing resolution versus persistence of disease in untreated patients with active arthritis.

Methods: Synovial tissue biopsies were obtained using ultrasound guidance from treatment naïve patients in the Birmingham BEACON early arthritis cohort presenting with at least one clinically swollen joint and a joint amenable to ultrasound guided biopsy. Tissue samples from patients who went on to develop RA (n=15) or PsA (n=7) according to ACR criteria or CASPAR criteria at 24month follow-up, and patients whose arthritis spontaneously resolved (n=5) underwent enzymatic disaggregation and were processed through a multimodal single-cell sequencing approach including the characterisation of the transcriptome and 58 surface-protein-panel profile. Sequenced gene libraries were integrated according to batch and sample using the Harmony integrative algorithm before clustering and annotating cell states using canonical marker genes. Seurat-based automated pipelines were used for variable gene identification and clustering. We used DESeq2 to identify per cell type genes, and weighted gene co-expression network analysis (WGCNA) to identify gene programmes associated with persistence (RA and PSA) versus resolving groups. NAMTI was used to identify unique cellular niches associated with persistence or resolution.

Results: ~90,000 viable cells were sequenced and data normalised, clustered and annotated describing over 80 cellular states across eight main synovial cell types (T, B, Plasma, Plasmacytoid DC, myeloid, fibroblast, mural and vascular). A total of 1945 genes varied significantly with prognosis, distributed unequally across cell types (Table 1).

Table 1.

Cell type	T	B	Plasma	DC	Myeloid	Fibroblast	Mural	Vascular
Upregulated resolving	43	300	0	4	378	270	11	153
Upregulated persisting	37	82	3	1	205	223	7	228

Persistence of arthritis was associated with (i) the presence of plasma cells *per se* and (ii) a phenotypic shift in fibroblast, vascular, myeloid, Th, and B-cell populations with enrichment of SPP1+ Myeloid cell populations. Patients with active arthritis destined to resolve exhibited enrichment of Treg cells. Persistent and resolving states were characterised by significant compositional differences in key lining and sublining fibroblast subpopulations including sublining MMP3 positive cells, and by gene expression programmes related to matrix remodeling and fibroblast:macrophage interactions.

Conclusion: Persistence and spontaneous resolution of synovial inflammation are accompanied by characteristic compositional and mechanistic signatures that can be observed in key cellular niches during active early inflammation. There is potential to exploit such signatures with the aim of disrupting persistent inflammation.

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OP0122 MACHINE-LEARNING-ASSISTED ANALYSIS IDENTIFIES DISCRETE PHOSPHORYLATION SIGNATURES IN T AND B LYMPHOCYTES ASSOCIATED WITH EARLY RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Biomarkers, Disease-modifying drugs (DMARDs)

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Background: Delineating systemic immune cell signatures in rheumatoid arthritis (RA) has the potential for understanding pathogenesis and stratifying therapeutics accordingly.

Objectives: To evaluate the phosphoprotein signatures in circulating lymphocytes of early RA patients compared with healthy controls across disease trajectory over one year.

Methods: We used phospho-flow cytometry to measure the phosphorylation state of phosphoproteins in basal (unstimulated), and ex vivo stimulated circulating lymphocytes from 55 early RA patients before and after 6- and 12-month treatment with methotrexate (MTX) and compared these to 37 age- and gender-matched healthy controls. Flow cytometry datasets were analysed using FlowSOM, an unbiased clustering algorithm that partitions cell populations based on marker expression patterns.

Results: Multiple differential phosphorylation signatures are expressed across $CD4^+$ and $CD8^+$ T-cells and $CD19^+$ B-cells that differentiate baseline RA from healthy controls; the signatures normalised towards a healthy state following treatment with MTX. Stimulation of cells from RA patients at baseline is refractory to further stimulus-induced phosphorylation, which was recovered following MTX treatment ($p<0.01$).

Conclusion: This comprehensive and unbiased analysis identified discrete clusters of cells exhibiting unique phosphoprotein signatures associated with early RA that differentiates the systemic immune response from healthy controls. Methotrexate treatment recovers this phosphoprotein signature towards a healthy state.

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OP0123

AUTOANTIBODIES TO JOINT-RELATED PROTEINS PREDICT REMISSION IN NEW ONSET RA WITH HIGH SPECIFICITY

Keywords: Remission, Rheumatoid arthritis, Autoantibodies

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Background: One of the major challenges in the management of rheumatoid arthritis (RA) is to determine individual treatment and predict the prognosis. On a group level, high disease activity and antibodies specific for citrulline (ACPA) and immunoglobulins (RF) are factors associated with poor prognosis. New alternative biomarkers, which could provide more specific information, are antibodies to disease-related targets in the joints [1]

Objectives: To identify circulating autoantibodies to joint-related proteins (hereafter named JointIDs) that predict disease outcome in patients with new onset RA.

Methods: Sera at diagnosis from BARFOT and TIRA-2 cohorts (n=1986) with new onset RA patients were screened with a bead-based multiplex flow immunoassay to detect IgG autoantibodies against 47 peptides derived from joint proteins (JointIDs) (Lönnblom, under review 2023). Disease outcomes included Boolean remission at 6 and 12 months, swollen joint count (SJC) and radiological progression at 12 months (>8% affected feet joints and >3% affected hand joints) in patients who were without joint damage at inclusion. Multivariate logistic regression and zero-inflated negative binomial models adjusted for clinical factors (age, gender, ACPA, RF, changes in medication at 3 and 6 months) were used to identify JointIDs with the strongest potential to predict prognosis.

Results: Six JointIDs were identified as predictors for these disease outcomes in multivariate analyses. Presence of JointID178 predicted an average decrease in SJC at 6 months with 41% and with 33% at 12 months. Presence of at least 2 of the following factors: JointID178 positive and JointID199 negative at inclusion in combination with male sex identified approx. 40% of the patients in Boolean remission at 6 months with approx. 75% specificity (Table 1). A similar test performance was obtained even for Disease Activity Score 28 remission. The sensitivity and specificity for being in Boolean remission at 12 months if the patients were male, negative for JointID199 and in Boolean remission at 6 months was 13% (CI 9%;16%) and 99% (CI 99%;100%), respectively. RF and ACPA did not predict remission but were the strongest predictors of joint destruction at 12 months although with low specificity (58%). Addition of JointID166 significantly increased the specificity at the expense of sensitivity.

Conclusion: Autoantibodies to joint-related proteins at RA diagnosis can predict remission with a high specificity at 6 and 12 months. This knowledge is of clinical importance as patients positive or negative for these JointIDs in combination with clinical factors may potentially guide future treatment choices.

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Table 1. Sensitivity, specificity and AUC for the multivariate models for predicting the different binary outcomes.

Outcome	Predicting factors	AUC (ROC)	Sensitivity (95% CI)	Specificity (95% CI)
Boolean remission at 6 months	If ≥2 of these: JointID178+, JointID199-, sex=male	63%	42% (35%; 49%)	74% (72%; 77%)
	If JointID178+, JointID199-, sex=male	63%	8% (4%; 12%)	98% (97%; 99%)
Boolean remission at 12 months	If ≥2 of these: JointID178+, JointID199-, sex=male	61%	42% (36%; 48%)	76% (73%; 79%)
	If JointID178+, JointID199-, sex=male	61%	8% (5%; 11%)	97% (96%; 98%)
	If JointID199-, sex=male, Booleans remission at 6 months	81%	13% (9%; 16%)	99% (99%; 100%)
Radiological progression	If antiCCP+	70%	82% (74%; 90%)	58% (54%; 62%)
	If antiCCP+, JointID166+	73%	49% (39%; 59%)	82% (79%; 85%)
	If JointID166+, JointID198+	70%	39% (29%; 49%)	86% (83%; 88%)

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OP0124

A REDUCED ULTRASOUND SCANNING PROTOCOL OF 3 JOINTS BILATERALLY IMPROVES PREDICTION OF INFLAMMATORY ARTHRITIS PROGRESSION IN ANTI-CCP ANTIBODIES POSITIVE INDIVIDUALS WITH MUSCULOSKELETAL SYMPTOMS

Keywords: Prognostic factors, Ultrasound, Autoantibodies

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Background: In anti-CCP positive individuals at-risk of developing rheumatoid arthritis (CCP+ at-risk), ultrasound (US) sub-clinical inflammation and bone erosions (BE) are associated with progression to clinical arthritis[1]. However, the additional value of US in predicting progression to inflammatory arthritis (IA) when compared with routinely available clinical/serological variables has not been well defined. Moreover, which and how many joints need to be scanned for optimum predictive accuracy remains unanswered, with most studies adopting extensive US protocols which are not feasible in clinical practice[1].

OBJECTIVES:

1. In CCP+ at-risk with musculoskeletal (MSK) symptoms but no clinical synovitis, to investigate the additional value of US over and above clinical/serological variables in the prediction of IA.
2. To define an attenuated US scanning protocol, suitable for routine clinical use, for predicting IA development in CCP+ at-risk.

Methods: The proportion of 'progressors' to IA at 24 months was evaluated in 417 CCP+ 'at-risk' with MSK symptoms from the Leeds CCP cohort, who were selected for having an US scan at baseline. The US scanning protocol included 18 joints bilaterally [elbow, wrist, MCP joints 1-5, PIP joints 1-5, knee, ankle, MTP joints 2-5]. US synovitis (grey scale ≥1 and power Doppler signal ≥1) and BE were defined according to the EULAR/OMERACT definitions. Routine demographic/clinical data were collected: age, gender, early morning stiffness (EMS) duration, hands and/or feet tenderness on physical examination, anti-CCP antibodies level and rheumatoid factor (RF) status. Two initial multivariable binary regression models with 10-fold cross-validation for IA development at 24 months included all the clinical/serological variables associated with the outcome ("clinical" model) isolated and in combination with US synovitis and/or BE in any of the 36 joints ("clinical-US full" model). Further models explored the prediction accuracy of the clinical variables and US findings (i.e., synovitis and/or BE) in each single joint to identify the most informative scanning sites according to Akaike Information Criterion (AIC). A final model which included clinical/serological predictors and US assessment of 3 joints bilaterally ("clinical-US short" model) was compared to the "clinical-US full" model. The most predictive joints were included in this "short" model only if determining an improvement in the prediction performance (reduction in AIC≥2).

Results: Of the 417 CCP+ at-risk, 92 (22.1%) progressed to IA within 24 months. The following clinical/serological variables were associated with IA development at univariate analysis: age, smoking exposure, EMS duration ≥60 minutes, hands tenderness, RF positivity and high-level anti-CCP antibodies (all $p<0.05$). Moreover, US synovitis and BE in ≥1 of 36 joints were also associated with IA progression ($p<0.01$). The "clinical-US full" model (AUC 0.785, AIC 380.15) performed better than the "clinical" model (AUC 0.713, AIC 409.51) ($p<0.001$) showing an adjusted odds ratio (OR) for IA onset of 3.16 (95% IC 1.79-5.58) for US synovitis and 2.83 (95% IC 1.35-5.93) for BE. The developed "clinical-US short" model - that included US assessment of wrists, knees and MTP5 joints – performed better than the "clinical" model ($p<0.001$) and similarly (AUC 0.781, AIC 381.41) to the "clinical-US full" model ($\Delta AIC<2$) (Figure 1).

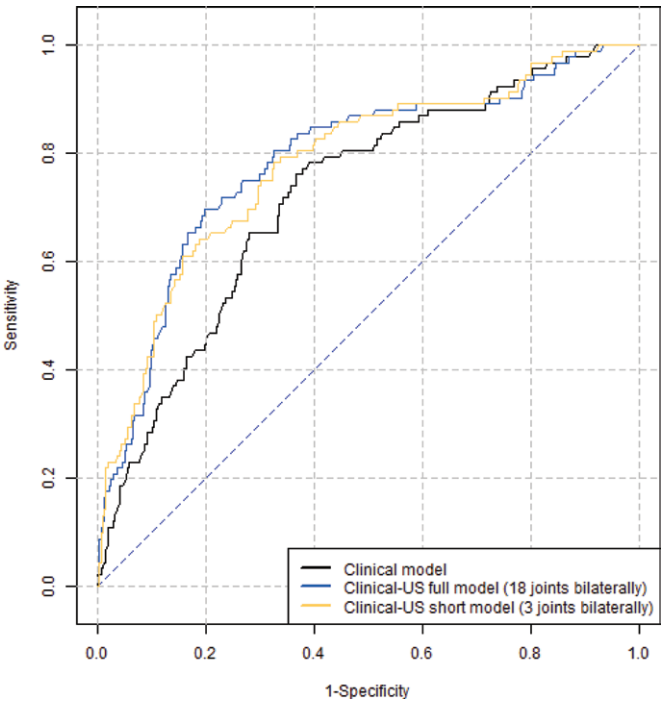


Figure 1.

Conclusion: In CCP+ at-risk with MSK symptoms, US of only 3 joints bilaterally (wrist, knee and MTP5 joint) improved prediction of IA over and above clinical and serological risk factors, performing similarly to an extended research US protocol. This shortened 6 joint US protocol may offer clinically feasible risk prediction, which could be easily incorporated into routine clinical practice.

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OP0125

LIPID MEDIATOR PROFILES ASSOCIATE WITH PROGRESSION TO RA IN ANTI-CITRULLINATED PROTEIN ANTIBODY POSITIVE POPULATIONS

Keywords: Epidemiology, Autoantibodies, -omics

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Background: Lipid mediators are endogenously derived from the metabolism of omega-3 and omega-6 polyunsaturated fatty acids (PUFAs) and have important roles in promoting and resolving inflammation. PUFAs have been implicated in the pathogenesis of systemic inflammatory and autoimmune diseases, including rheumatoid arthritis (RA). Sharing many common pathways and key enzymes, individual lipid mediators may be correlated with one another and can be analyzed in combination as a profile. This study's goal was to determine the association of PUFA-derived lipid mediator profiles with progression from RA-related autoimmunity, a state that can be identified in screened and studied individuals by the presence of peripheral blood anti-citrullinated peptide antibodies (ACPA) autoantibodies in the absence of arthritis, to clinically apparent RA.

Objectives: To identify lipid mediator profiles in the preclinical period that are associated with progression to classifiable RA.

Methods: Using two unique prospective cohorts, the Targeting Immune Responses for Prevention of Rheumatoid Arthritis (TIP-RA) cohort and the Studies of the Etiologies of Rheumatoid Arthritis (SERA) cohort, we followed ACPA positive individuals in the absence of RA at baseline. We followed 81 and 79 participants in TIP-RA and SERA, of which 22 and 18 participants, respectively, developed RA during follow-up based on ACR/EULAR 2010 criteria (**Table 1**). Exposures included concentrations (pg/ml) of lipid mediators quantified from plasma samples via liquid chromatography tandem mass spectrometry, with profiles identified via principal component meta-analysis (metaPCA), which identifies common eigenspace between multiple datasets. Profiles were identified at two time periods: baseline (e.g. study enrollment) and pre-incident RA (just prior to RA in progressors or similar period in non-progressors). For each cohort, a Cox proportional hazard model was developed for each lipid mediator profile, adjusted for shared epitope status, age and smoking status. Meta-analysis was performed for each lipid mediator profile using Fisher's method.

Results: At each cross-section, the top 5 principal components (PC), selected based on scree-plots, were analyzed further. Analysis of the baseline cross-section identified a significant risk profile (baseline PC5, meta HR = 1.28, meta p-value = 0.033) and a suggestive protective profile (baseline PC1, meta HR 0.96, meta p-value = 0.055) associated with RA. The pre-incident RA period identified a significant risk profile (pre-incident RA PC4, meta HR = 1.37, meta p-value = 0.028). **Figure 1** depicts the loading factors for the associated profiles. Both risk profiles (pre-incident RA PC4 and baseline PC5) had a mix of positive and negative loadings corresponding to important lipid mediators that are products of arachidonic acid (ARA) and eicosapentaenoic acid (EPA). These weights suggest higher levels of lipid mediators from EPA (an omega-3 FA) combined with lower levels of lipid mediators from ARA (an omega-6 FA) would be a risk factor for RA. The suggestive protective profile at baseline (baseline PC1) showed important lipid mediators with negative weights only, all high impact lipid mediators being descendants from linoleic acid (an omega-6 fatty acid), with lower levels being protective.

Conclusion: Combinations of lipid mediators show association with progression to RA, identifying multiple targets that could be potentially modulated to prevent the progression of disease.

Table 1. Baseline Demographics of the ACPA+ Populations.

	TIP-RA Unaffected (n = 59)	TIP-RA Progressed to RA (n = 22)	SERA Unaffected (n=61)	SERA Progressed to RA (n = 18)
Female	39 (61%)	16 (73%)	42 (69%)	12 (67%)
Non-Hispanic White	49 (83%)	15 (68%)	53 (87%)	15 (83%)
Shared Epitope	29 (49%)	15 (68%)	27 (44%)	12 (67%)
Age at baseline-year (SD)	58.2 (12.6)	55.8 (12.0)	51.9 (13.8)	50.6 (11.5)
Ever smoked*	18 (31%)	8 (36%)	27 (44%)	8 (47%)
First-degree relative with RA	11 (19%)	4 (18%)	41 (67.2%)	6 (33.3%)
# of Study Visits				
2	6	5	18	9
3	53	7	11	2
≥4	0	10	32	7

*1 SERA subject missing

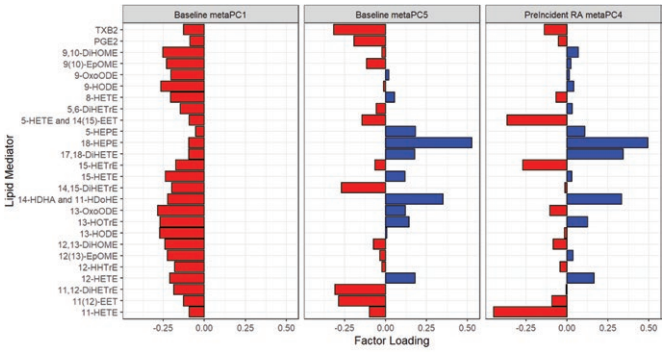


Figure 1. Associated Profile Factor Loadings. The factor loadings for each individual lipid mediator is shown for the profiles with progression to RA (two from the metaPCA at the baseline cross-section and one from the metaPCA from the pre-incident RA cross-section). Red indicates a negative loading, while blue a positive loading.

REFERENCES: NIL.
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OP0126

LONG-TERM FOLLOW UP OF ABATACEPT IN USUAL INTERSTITIAL PNEUMONIA ASSOCIATED TO RHEUMATOID ARTHRITIS. NATIONAL MULTICENTER STUDY OF 172 PATIENTS

Keywords: Lungs, bDMARD, Rheumatoid arthritis

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Background: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). Usual interstitial pneumonia (UIP) is the most frequent, and severe ILD pattern in RA. Abatacept (ABA) has demonstrated effectiveness in RA-ILD during a 12-month period of treatment [1-2].
Objectives: To assess the effectiveness and safety of ABA in RA-ILD patients with radiological pattern of UIP during a long-term follow-up.
Methods: From a large observational multicenter study of 392 RA-ILD patients treated with ABA, we selected those with UIP. We analyzed from baseline the following outcomes: **a)** forced vital capacity (FVC), **b)** diffusing capacity of the lungs for carbon monoxide (DLCO), **c)** chest high resolution computed tomography (HRCT), **d)** dyspnea (modified Medical Research Council scale) and **e)** arthritis activity (DAS28-ESR).
Results: We included a total of 172 patients with UIP (91 women/81 men; mean age 66.9±10.1 years). Baseline demographic and clinical characteristics are shown in **Table 1**. The median ILD duration up to ABA initiation was relatively short, with a median of 11 [3-39] months. Mean baseline values of FVC and DLCO were >80% and >60%, respectively. During the follow-up, median of 24 [10-44] months, 70.2% and 66.9% of patients showed an improvement/ stabilization of FVC and DLCO, respectively. Evolution of these parameters along 48 months is displayed in **Figure 1**. Available chest HRCT images improved/ stabilized in 64.5% of patients. Stabilization or improvement of dyspnea was found in 78.6% of patients. The majority of patients showed articular remission or low activity (mean DAS28-ESR of 4.3±1.5 at baseline and 2.5±1.5 at 48 months). ABA was withdrawn in 39 (22.6%) patients due to ILD worsening (17), articular inefficacy (9), serious infections (7) and other causes (n=6, development of malignancy in 3, diagnosis of giant cell arteritis and change to tocilizumab in 1, and 2 deceases).
Conclusion: ABA shows a lasting effectiveness and safety in RA-ILD patients with UIP, the most aggressive pattern.
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[2] *Rheumatology (Oxford).* 2021 Dec 24;61(1):299-308. doi: 10.1093/rheumatology/keab317

Table 1. Main general features at baseline.

	RA-ILD patients with UIP (n=172)
Age, years mean±SD	67±10
Women, n (%)	91 (53)
Smoker ever, n (%)	87 (51)
ILD duration up to ABA, months, median [IQR]	11 [3-39]
RF// ACPA, n (%)	160 (93)// 153 (89)
DAS28-ESR, mean±SD	4.3±1.5
FVC (% of the predicted), mean±SD	85±22
DLCO (% of the predicted), mean±SD	65±19
ABA monotherapy, n (%)	78 (45)
ABA combined + MTX/other cDMARD, n (%)	94 (55)
Prednisone at baseline, mg/day, median [IQR]	5 [5-10]
Previous immunosuppressive therapy, n (%)	
MTX	122 (71)
Leflunomide	76 (44)
Sulfasalazine	24 (14)
Hydroxychloroquine	49 (29)
Anti-TNF	71 (41)
Rituximab	20 (12)
Tocilizumab	19 (11)

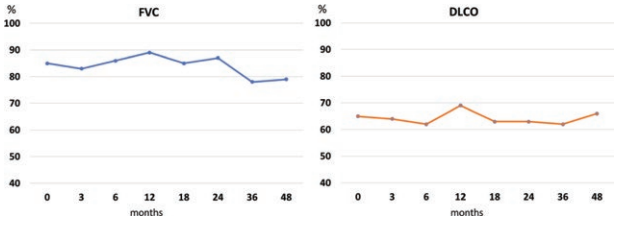


Figure 1. Evolution of pulmonary function tests (mean % of the predicted FVC and DLCO) in RA-ILD patients with UIP pattern at baseline and 48 months.

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OP0127

HARNESSING THE POWER OF RADIOMICS TO PREDICT SURVIVAL IN PATIENTS WITH RA-ILD

Keywords: Artificial Intelligence, Lungs, Rheumatoid arthritis

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Background: Patients with rheumatoid arthritis (RA) and interstitial lung disease (ILD) have increased mortality compared to the general population and factors capable of predicting RA-ILD long-term clinical outcomes are lacking. In oncology, radiomics allows the quantification of tumour phenotype by analysing the characteristics of medical images [2]. The hypothesis of radiomics is that the distinctive imaging features between disease forms may help make a prognosis and predict the therapeutic response for various conditions, thus providing valuable information for personalised therapy and patient management. Using specific software, it is possible to segment organs on high-resolution computed tomography (HRCT) images and extract many features that may uncover disease characteristics that are not detected by the naked eye.
Objectives: We aimed to investigate whether features from whole lung radiomic analysis of HRCT may. alone predict mortality in RA-ILD patients.
Methods: HRCTs of RA patients from January 2012 to March 2022 were analyzed. The time between the first available HRCT and the last follow-up visit or ILD-related death was recorded. We performed a volumetric analysis in 3D Slicer, automatically segmenting the whole lungs and trachea via the Lung CT Analyzer. The PyRadiomics platform (version 3.01) can extract radiomic data from medical imaging, calculate features and return results as continuous variables. In a Python 3.9 environment, we extracted 120 features for segmented regions. A LASSO-Cox model was carried out by considering ILD-related death as the outcome variable and extracting radiomic features as exposure variables.
Results: We retrieved the HRCTs of 30 RA-ILD patients. The median survival time (interquartile range) was 48 months (36–120 months). Thirteen out of 30 (43.33%) patients died during the observation period. Demographics and clinical features have been reported in Table 1. Whole line segmentation was fast and reliable. The model included either the median grey level intensity within the whole lung segmentation (HR 9.35, 95% CI 1.56–v55.86) as a positive predictor of death and the 10th percentile of the number of included voxels (HR 0.20, 95% CI 0.05–0.84), the voxel-based pre-processing information (HR 0.23, 95% CI 0.06–0.82) and the flatness (HR 0.42, 95% CI 0.18–0.98), negatively correlating to mortality. The correlation of grey level values to their respective voxels (HR 1.52 95% CI 0.82–2.83) was also retained as a confounder. We observed that the hazard function followed the 45-degree line very closely except for huge values of time, demonstrating goodness-of-fit (Figure 2, Panel. B).
Conclusion: Radiomics may predict RA-ILD patients' mortality and may promote HRCT as a digital biomarker regardless of the clinical characteristics of the disease.

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Table 1. Patient Characteristics.

	Available Observations	
Male, n (%)	**30**	**11 (36.67)**
Age at HRCT, years, median (IQR)	**30**	**72 (65-78)**
RA disease duration, month, median (IQR)	**30**	**132 (65-278)**
RF positivity, n (%)	**29**	**18 (62.07)**
ACPA positivity n (%)	**30**	**25 (83.33)**
ILD pattern at HRCT, (n%)	**30**	
UIP		**18 (60)**
NSIP		**2 (2.67)**
LIP		**1 (3.33)**
OP		**1 (3.33)**
Unclassifiable		**8 (26.67)**

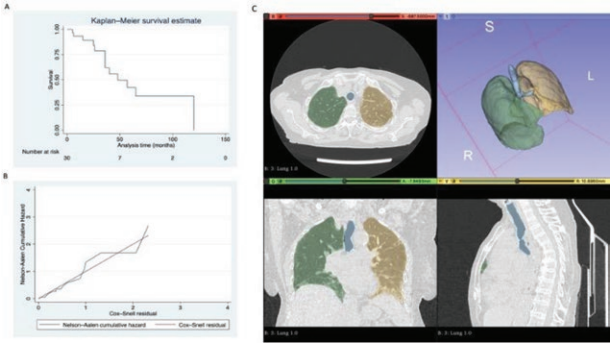


Figure 1. Panel A. Survival function displayed using Kaplan-Meier Estimate, with at-risk table. Deaths have been reported in parentheses. Panel B. Cox-Snell residuals plotted against the Nelson-Aalen cumulative hazard rate function to test the reliability of the model. Hazard function followed the 45-degree line very closely except for huge values of time. Panel C. Automated whole lungs and trachea segmentation using 3D Slicer.

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There is still a lot to SAY about biologicals for RA!

OP0128

PHARMACOKINETICS AND PHARMACODYNAMICS OF METHOTREXATE POLYGLUTAMATE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH LOW OR HIGH DOSE-METHOTREXATE IN COMBINATION WITH ADALIMUMAB: RESULTS FROM THE MIRACLE TRIAL

Keywords: Rheumatoid arthritis, bDMARD

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Background: Concentrations of methotrexate polyglutamates (MTX-PGs) in erythrocytes have been reported to be associated with efficacy and safety in patients with rheumatoid arthritis (RA) treated with MTX. However, little is known about the pharmacokinetics and pharmacodynamics of MTX-PG concentrations and their relationship with disease control and adverse effects in patients treated with MTX and a tumor necrosis factor inhibitor (TNFi), especially in patients whose MTX dose is reduced at TNFi initiation.

Objectives: To clarify the association between the concentrations of MTX-PGs with efficacy and safety of treatment in patients with RA treated with low dose MTX and high dose MTX in combination with adalimumab, a TNFi.

Methods: The MIRACLE study (NCT03505008) was a multinational, randomized study in patients with RA with inadequate response to MTX. Three hundred MTX-naive patients were enrolled in the study and started and increased MTX to the maximum tolerable dose. Patients who did not achieve remission according to simplified disease activity index (SDAI) at week 24 were randomised to the maximum tolerable dose group or the reduced dose group and started subcutaneous adalimumab 40 mg every other week. We measured the concentrations of MTX-PGs in erythrocytes with liquid chromatograph mass spectrometry at weeks 0, 4, 8, 12, 24, 36, and 48 and analysed the association between the concentration of MTX-PGs with the efficacy and safety of adalimumab.

Results: The previously reported results of the MIRACLE trial showed that the efficacy of adalimumab with reduced dose of concomitant MTX was not inferior to that with maximum tolerable dose of MTX (remission rates at week 48: 44.8 % vs 38.4 %, respectively) with better safety profile (adverse events: 19.7% vs 35.3%, respectively). In the maximum tolerable dose group, MTX dose was 13.5± 3.2 mg/week (0.24± 0.1 mg/kg/week) at week 24 and maintained the dose through 48 weeks. In the reduced dose group, MTX dose was reduced from 12.6± 3.1 mg/week (0.23± 0.1 mg/kg/week) to 7.6± 0.5 mg/week (0.14± 0.0 mg/kg/week) at week 24. The concentration of total MTX-PGs in the maximum tolerable dose group was 109.5± 36.7 nmol/L, 99.9± 40.1 nmol/L, and 96.4± 38.3 nmol/L at weeks 24, 36, and 48, respectively. In the reduced dose group, total MTX-PGs concentration was decreased from 113.5± 55.3 nmol/L at week 24 to 80.7± 53.1 nmol/L at week 36 and 68.9± 54.4 nmol/L at week 48 (Figure 1). The decrease in individual MTX-PG levels were more prominent in long and very long chain MTX-PGs compared with short chains; MTX-PG 1-2, 59.0± 44.7 nmol/L at week 24 to 48.9± 43.8 nmol/L at week 36; MTX PG 3-5, 54.5± 28.8 nmol/L at week 24 to 31.8± 18.7 nmol/L at week 36. In both groups, MTX-PG concentrations at week 48 were not different between patients who achieved SDAI remission and those who did not (95.1 nmol/L vs 98.6 nmol/L in the maximum tolerable dose group, p=0.743; 64.3 nmol/L vs 72.9 nmol/L in the reduced dose group, p=0.556, respectively). On the other hand, patients n the reduced dose group who experienced adverse events after week 24 tended to have higher concentartion of total MTX-PGs than those who did not (140.3 nmol/L vs 106.9 nmol/L at week 24, p=0.050; 97.3 nmol/L vs 63.0 nmol/L at week 48, p=0.069, respectively).

Conclusion: The MIRACLE randomised study demonstrated that total MTX-PG concentrations were not relevant for SDAI remission achievement by combined treatment with methotrexate and adalimumab while patients who experienced adverse events were exposed to higher MTX-PG concentrations.

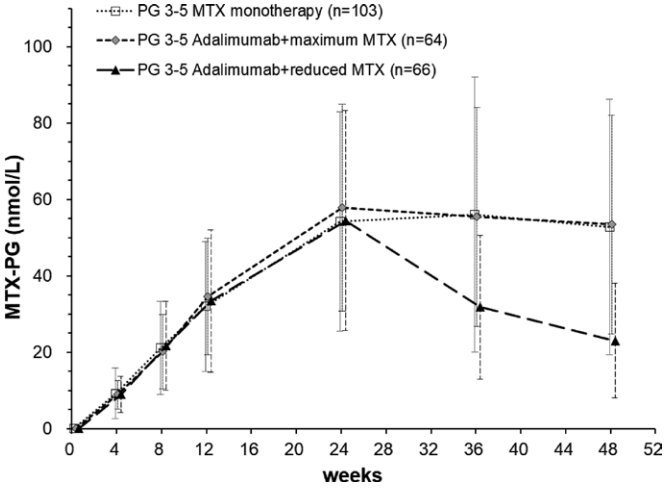


Figure 1.

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Pfizer, Sanofi, Shionogi, UCB, yutaka okano: None declared, Shinji Sato Grant/research support from: AbbVie, Asahi Kasei, Ayumi, Chugai, Diichi Sankyo, Eisai, Eli Lilly, Teijin, Pfizer, Hidekata Yasuoka Speakers bureau: AbbVie, Boehringer-Ingelheim, Gilead, Janssen, Nippon shinyaku, Grant/research support from: Asahi Kasei, Chugai, Eisai, Mitsubishi-Tanabe, Taisho, In Ah Choi Speakers bureau: AbbVie, Eisai, Sung-Hwan Park: None declared, Meng-Yu Weng Paid instructor for: Novartis, Eli Lilly, Chugai, AbbVie, Consultant of: AbbVie, Masataka Kuwana Speakers bureau: AbbVie, Asahi Kasei, Astellas, Boehringer Ingelheim, Chugai, Nippon Shinyaku, Mitsubishi-Tanabe, Consultant of: Boehringer Ingelheim, Kissei, Mochida, Grant/research support from: Boehringer Ingelheim, Ono, MBL, Yun Jong Lee Grant/research support from: Yuhan, Tomonori Ishii Speakers bureau: AbbVie, Asahi Kasei, Astellas, Boehringer Ingelheim, Bristol-Myers Suibb, Chugai, Eisai, Eli Lilly, Gilead, Glaxo Smith Kline, Janssen, Novartis, Pfizer, Jinhyun Kim: None declared, Hideto Kameda Speakers bureau: AbbVie, Asahi Kasei, Astellas, Boehringer, Bristol-Myers, Chugai, Eisai, Eli Lilly, Gilead, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Asahi Kasei, Boehringer, Chugai, Eisai, Mitsubishi-Tanabe, Taisho, Toshihisa Kojima Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly, Pfizer, Taisho, UCB, Han Joo Baek: None declared, Ping-Ning Hsu: None declared, Chun-Ming Huang Paid instructor for: AbbVie, Pfizer, Tien-Tsai Cheng Paid instructor for: AbbVie, Grant/research support from: AbbVie, Wan-Yu Sung: None declared, Wen-Chan Tsai: None declared, Takehiro Taninaga Shareholder of: Eisai, Employee of: Eisai, Masahiko Mori Shareholder of: Eisai, Employee of: Eisai, Hideaki Miyagishi Shareholder of: Eisai, Employee of: Eisai, Yasunori Sato Speakers bureau: Eisai, Kowa, Consultant of: Mochida, Tsutomu Takeuchi Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Mitsubishi-Tanabe, Pfizer, Consultant of: AbbVie, Chugai, Eli Lilly, Gilead, Mitsubishi-Tanabe, Grant/research support from: AbbVie, Asahi Kasei, Ayumi, Chugai, Eisai, Eli Lilly, Mitsubishi-Tanabe, Ono, Yuko Kaneko Speakers bureau: AbbVie, Asahi Kasei, Astellas, Boehringer Ingelheim, Bristol Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer, Grant/research support from: AbbVie,Asahi Kasei, Ayumi, Boehringer Ingelheim, Chugai, Eisai, Mitsubishi-Tanabe.

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OP0129

EFFECTIVENESS OF COBRA-SLIM WITH OR WITHOUT EARLY ACCESS TO A TEMPORARY 6-MONTH COURSE OF ETANERCEPT IN EARLY RA: PRIMARY OUTCOME OF THE 2-YEAR, PRAGMATIC, RANDOMISED CARERA2020 TRIAL

Keywords: Randomized control trial, Rheumatoid arthritis, Treat to target

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Background: EULAR recommends methotrexate (MTX), combined with short-term glucocorticoids as first-line treatment for early Rheumatoid Arthritis (RA). In the CareRA trial, the COBRA-Slim regimen (MTX 15 mg/w + step-down prednisone 30, 20, 12.5, 10, 7.5, 5 mg/d), including a treat to target (T2T) approach starting with addition of leflunomide and only at a later stage bDMARDs, provided the best balance between efficacy, safety and cost-effectiveness. The potential advantage of temporary bDMARD use earlier in the T2T setting needs further investigation.

Objectives: To determine the long-term effectiveness of accelerated access to a temporary course of etanercept compared to addition of leflunomide in patients with early RA who insufficiently respond to initial COBRA-Slim induction therapy.

Methods: DMARD-naïve patients with a recent diagnosis of RA (≤1 year ago) were included in the 2-year, open-label, multicentre, pragmatic randomised controlled superiority trial Care in Early RA 2020 (CareRA2020). All patients started the COBRA-Slim induction regimen. Patients were classified as insufficient responders if, even despite MTX dose increase, they did not achieve DAS28-CRP ≤3.2 between week 8 and week 32 or if DAS28-CRP was ≥2.6 at week 32 regardless of MTX dose. Insufficient responders were randomised to either Standard COBRA-Slim (addition of leflunomide 10 mg/d) or COBRA-Slim Bio-induction (addition of etanercept 50 mg/w for 24 weeks). Additional treatment adaptations followed the T2T principle. Primary outcome was the difference in DAS28-CRP over time, determined via a linear mixed model including random intercepts and a random slope for time, adjusting for baseline DAS28-CRP and seropositivity. Missing data were imputed with the Expectation-Maximisation algorithm.

Results: In total, 276 patients were included, of which 155 (56%) were classified as sufficient and 121 (44%) as insufficient responders. Of the insufficient responders, 9 patients were not randomised by investigator decision, 2 were randomisation errors, 55 were randomised to Standard COBRA-Slim, and 55 to COBRA-Slim Bio-Induction. The mean ± SD area under the DAS28-CRP curve over 104 weeks was 232 ± 66 for the initial sufficient responders, 310 ± 82 for the Standard COBRA-Slim group, and 316 ± 73 for the COBRA-Slim Bio-induction group. Both randomisation groups had comparable DAS28-CRP scores over time (ß = -0.095, 95% CI (-0.299 to 0.108), p=0.351). At the end of the trial, 82% (127/155), 9% (5/55), and 36% (20/55) of patients were on csDMARD monotherapy in the initial sufficient responders, Standard COBRA-Slim, and COBRA-slim Bio-induction group, respectively. Moreover, 6% (9/155) sufficient responders, 58% (32/55) in the Standard COBRA-Slim, and 45% (25/55) in the COBRA-Slim Bio-induction group were treated with a b- or tsDMARD.

Conclusion: More than half of the CareRA2020 participants achieved remission with COBRA-Slim induction therapy. DAS28-CRP over 104 weeks was not superior with COBRA-Slim Bio-induction versus the Standard COBRA-Slim T2T regimen in initial insufficient responders. However, compared to the Standard COBRA-Slim group, more patients in the Bio-induction group were treated with csDMARD monotherapy and less with advanced therapies at the end of the study.

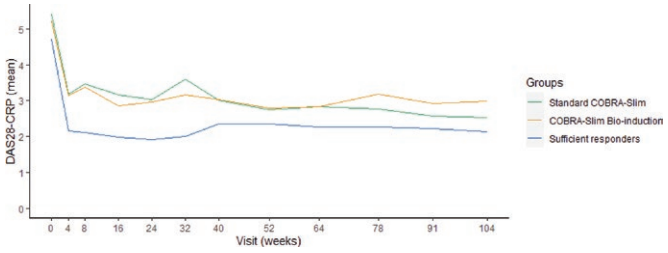


Figure 1. Disease activity evolution during the CareRA2020 trial

Table 1. Baseline characteristics of patients included in the CareRA2020 trial

	Sufficient responders (n=155)	Standard COBRA-Slim (n=55)	COBRA-Slim Bio-induction (n=55)
Sex (female)	66% (103)	75% (41)	69% (38)
Age (years)	54.5 ± 14.0	53.4 ± 13.1	52.5 ± 12.9
Symptom duration (months)	5.0 (3.0 - 9.0)	3.0 (2.0 – 6.0)	4.0 (2.0 – 6.0)
Disease duration (days)	6.0 (1.0 – 20.0)	6.0 (2.0 – 15.0)	7.0 (0.5 – 19.0)
RF and/or ACPA positivity	77% (119)	76% (42)	75% (41)
Erosions present	27% (42)	15% (8)	18% (10)
HAQ (0-3)	1.1 ± 0.7	1.6 ± 0.6	1.5 ± 0.8
PhGA	51.7 ± 19.5	59.5 ± 20.9	55.4 ± 21.0
DAS28-CRP	4.7 ± 1.3	5.4 ± 1.1	5.2 ± 1.3

Expressed in proportions %(n), mean ± SD, or median (IQR).

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Disclosure of Interests: None Declared.

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OP0130

ABATACEPT IN INDIVIDUALS AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS: RESULTS FROM THE ARTHRITIS PREVENTION IN THE PRE-CLINICAL PHASE OF RA WITH ABATACEPT (APIPPRA) TRIAL

Keywords: Randomized control trial

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Background: While genetic and epidemiological factors have been used traditionally to evaluate the risk of developing rheumatoid arthritis (RA), the definition of higher risk states has been refined in more recent years through inclusion of serum autoantibodies and symptom complexes, such as inflammatory joint pain. Data from at risk cohorts have reported rates of progression to RA in excess of 50% over 24 months. These combined features have provided a framework for the design of interception studies, aimed at delaying or preventing RA.

Objectives: We evaluated the feasibility, efficacy and acceptability of T-cell co-stimulation modulation with abatacept in individuals at risk of developing RA in the Arthritis Prevention In the Pre-clinical Phase of RA with Abatacept (APIPPRA) study.

Methods: APIPPRA is a Phase IIB randomised, double blind, placebo-controlled trial recruiting $ACPA^{+}RF^{+}$ or $ACPA^{hi}$ (≥3 x ULN) RF^{-} individuals with arthralgia. Consenting participants were randomised, stratified by gender, smoking status and country, to receive 52 weekly subcutaneous injections of placebo or 125mg abatacept, and followed up for a further 52 weeks after stopping treatment. Exclusion criteria included previous episodes of clinical synovitis, prior corticosteroids or DMARDs. The primary endpoint was the time to development of either clinical synovitis in ≥3 joints, or RA according to ACR/EULAR 2010 criteria, whichever was met first, where joint involvement required swelling. Joint synovitis was confirmed by ultrasonography. The study was powered to detect a 50% reduction in progression in those receiving abatacept. Secondary endpoints included multiple disease activity assessments, the time to commencing DMARDs and/or corticosteroids, X-ray and ultrasound scores, as well as safety data. The main ITT analysis was repeated in a per-protocol population of participants who did not take forbidden medication, and who, in the first year or up to a primary event, had 90% adherence to treatment.

Results: Between December 2014 and January 2019, 280 individuals were evaluated for eligibility across 31 study sites, 28 in the UK and 3 in the Netherlands. Two hundred and thirteen were randomised, 103 to placebo and 110 to abatacept. Mean age was 49 and 77% were female. Ninety-three percent of individuals were $ACPA^{hi}$. Ultrasonography at baseline suggested modest levels of active sub-clinical synovitis (73% of participants with power Doppler score of 0). In total, there were 65 primary outcome events. After stopping treatment at 52 weeks there were 30 events (29%) in the placebo arm and 7 (6%) in the abatacept arm. By the end of the study there were 38 (37%) and 27 (25%) events, respectively, resulting in differences in mean arthritis-free survival time between arms of 99.2 days (95% CI 37.5 – 160.9; *p*-value=0.002), in favour of abatacept. The respective log-rank test for difference in the survival distribution was p=0.044, reflecting a large effect in the first year and convergence over the second year (see Figure 1). The per protocol analysis showed similar results. The cumulative proportion of arthritis-free participants at 52 weeks was 0.692 (SE 0.047) in the placebo arm and 0.928 (SE 0.026) for the abatacept arm, and 0.585 (SE 0.054) for placebo and 0.704 (SE 0.048) for abatacept at 104 weeks. *Post hoc* analysis revealed that individuals with an extended autoantibody profile at baseline were more likely to remain arthritis-free following abatacept therapy. Those treated with abatacept had lower tender joint counts and pain scores during the treatment period, when compared to placebo. There were 4 serious adverse events in the abatacept group and 10 in the placebo group, including two deaths, one in each arm, none deemed attributable to study drug.

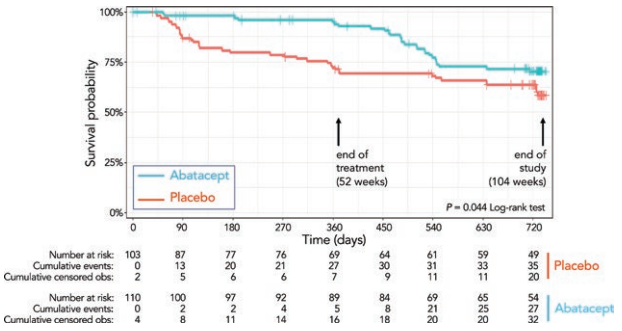


Figure 1.

Conclusion: Therapeutic intervention during the RA at risk phase is feasible, with acceptable safety profiles. T cell co-stimulation modulation with abatacept for 52 weeks showed a reduction in the development of RA over two years. There were no new safety signals.

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OP0131

DISEASE ACTIVITY-GUIDED DOSE OPTIMIZATION INCLUDING DISCONTINUATION OF TNF-INHIBITORS IN RHEUMATOID ARTHRITIS IS EFFECTIVE FOR UP TO 10 YEARS: RESULTS OF THE DRESS STUDY

Keywords: bDMARD, Rheumatoid arthritis, Tapering

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Background: Tumor necrosis factor inhibitors (TNFi) are effective in rheumatoid arthritis (RA) but have their drawbacks such as the need for self-injection, infections and costs. To reduce these disadvantages, disease activity-guided dose optimization (DAGDO) has shown to be an effective and safe strategy.[1] During DAGDO, a stepwise dose reduction of the TNFi is performed if allowed by the disease activity. In the Dose Reduction Strategy of Subcutaneous TNFi (DRESS) study, effectiveness and safety of DAGDO has been shown in RA patients for up to three years.[2, 3] However, long term outcomes of DAGDO are scarce, and it is debated whether a discontinuation attempt should be included.

Objectives: To assess 10-year effectiveness of DAGDO of TNFi in the DRESS cohort, specifically 1) disease activity over time, 2) biological and targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) dose over time, 3)

proportion of patients with a DAGDO attempt, and 4) proportion of patients with a discontinuation attempt and duration of b/tsDMARD discontinuation.
Methods: Observational follow-up (starting from DRESS baseline) of patients who completed the 3-year DRESS extension. During the DRESS intervention phase (month 0-18), RA patients were randomized to DAGDO or continuation of TNFi (adalimumab or etanercept), but thereafter, DAGDO was allowed for all patients. The DAGDO protocol contained the following steps, displayed as a percentage of the current daily dose to the defined daily dose (DDD): 100%-66%-50%-(33%)-0% (full discontinuation). The disease activity was operationalized as the mean time-weighted (MTW) DAS28-CRP. The specific DRESS TNFi and all b/tsDMARD dose over time were displayed as the MTW dose per year in %DDD. The duration of b/tsDMARD discontinuation was analyzed using the time between discontinuation and restart of the same or another b/tsDMARD, or censoring.
Results: 170 patients (of the original 180) could be included in the study (Table 1). The median follow-up time was 10.0 years (IQR 9.3-10.3) and the MTW DAS28-CRP during the whole period 2.13 (95% CI 2.10-2.16) (Figure 1). The DRESS TNFi dose decreased from 97% at baseline (95% CI 96%-99%) to 49% at year 5 (95% CI 42%-56%) and remained stable thereafter (Figure 1). The dose of any b/tsDMARD was comparable although slightly higher. Of the 161 patients with ≥1 DAGDO attempt of their DRESS TNFi during the study, 119 (74%, 95% CI 66%-80%) tapered until full discontinuation. The median time from discontinuation to restart of the first discontinuation attempt was 8 months (IQR 3 – 45 months), and 25 patients (21%, 95% CI 14%-29%) never had to restart their TNFi or another b/tsDMARD throughout the study.
Conclusion: In this 10-year TNFi dose optimization study, we found a stable low disease activity and halved TNFi dose. The inclusion of discontinuation in DAGDO does not seem to cause disease deterioration and b/tsDMARD free remission for a relevant period of time is possible in a non-negligible number of patients. Overall, this study shows effectiveness of DAGDO of TNFi in RA up to 10 years.
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Table 1. Characteristics at DRESS baseline

	Total (n=170)
Female sex	109 (64)
Age (years)	59 ± 10
Disease duration (years)	10 (6-16)
RF positive	136 (80)
ACPA positive	124 (73)
Erosive disease	96 (61)
DAS28-CRP	2.18 ± 0.69
DRESS randomization (DAGDO/usual care)	113/57
DRESS TNFi (etanercept/adalimumab)	112/58
Duration of DRESS TNFi (years)	3.4 ± 2.4
Concomitant csDMARD	113 (66)
≥ 1 previous TNFi used	62 (37, n=166)

Displayed as mean ± standard deviation, median (interquartile range) or number (percentage). RF: rheumatoid factor; ACPA: anti-citrullinated protein antibodies; DAS28-CRP: disease activity score of 28 joints -CRP; csDMARD: conventional synthetic DMARD.

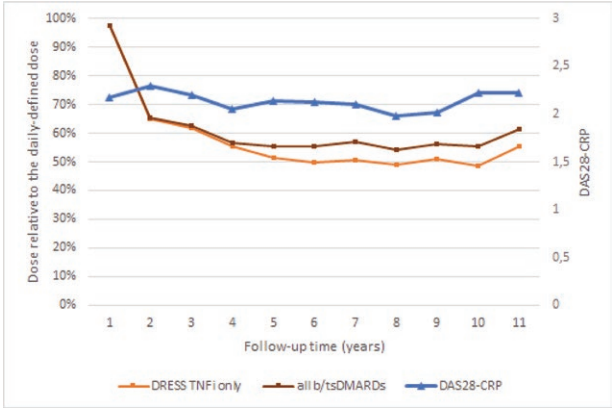


Figure 1. Mean time-weighted medication use and disease activity per subsequent year

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OP0132

CANCERS AND CARDIOVASCULAR DISEASES IN PATIENTS WITH SEROPOSITIVE RHEUMATOID ARTHRITIS TREATED WITH JAK INHIBITORS AND BIOLOGICS

Keywords: Rheumatoid arthritis, Disease-modifying drugs (DMARDs), Targeted synthetic drugs

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Background: Janus kinase inhibitors and biologics (JAKi/biologics) are cornerstone treatments for rheumatoid arthritis (RA).
Objectives: We evaluated the risks of cancers and cardiovascular diseases (CVDs) in patients with seropositive RA (SPRA) treated with JAKi/biologics.
Methods: Patients with new-onset SPRA during 2010–2020 in the national healthcare database were identified. Events of overall and site-specific cancers, as well as CVD outcomes, including deep vein thrombosis, pulmonary embolism, and composite cardiovascular events, were investigated. The relative risk of cancers and CVDs according to treatment was compared by evaluating the incidence rate ratios (IRRs). Time-dependent Cox analyses were performed to evaluate the relationship between JAKi/biologics usage and patient outcomes.
Results: A total of 101,816 and 96,220 patients with SPRA were analyzed for cancers and CVD outcomes, respectively. Compared with patients treated only with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), the IRRs of overall cancers and CVDs in patients administered JAKi/biologics were 0.88 (95% confidence interval [CI] 0.86–0.89) and 0.91 (95% CI 0.90–0.92), respectively. Site-specific lung, liver, prostate, and skin cancers were more frequent in JAKi/biologics users; JAKi did not confer a greater risk of overall CVDs and cancers compared with other biologics and csDMARDs. JAKi/biologics usage was not accounted for overall cancers and CVDs in adjusted Cox analyses.
Conclusion: The incidence of overall cancer and CVD were not increased in patients with SPRA treated with JAKi/biologics and was relatively lower than csDMARDs only users, underscoring optimal disease control for risk mitigation. The higher incidence of several sitespecific cancers requires further investigation.
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Table 1. Number, incidence rate, and incidence rate ratios of 10 most common cancers according to treatment

	Number of events		Age- and sex- adjusted incidence rate/100,000 person-year		
	Patients treated with JAKi/ biologics	Patients treated with only csDMARDs	Patients treated with JAKi/ biologics	Patients treated with only csDMARDs	Incidence rate ratio (95% CI)
Lung (C34)	54	634	218.87	202.93	1.08 (1.04-1.12)
Thyroid (C73)	49	504	43.47	77.58	0.56 (0.52-0.60)
Stomach (C16)	47	454	96.09	115.07	0.84 (0.79-0.88)
Breast (C50)	38	428	25.47	42.50	0.60 (0.55-0.66)
Colon (C18)	19	248	47.57	66.43	0.72 (0.67-0.77)
Liver (C22)	17	160	48.40	37.55	1.29 (1.19-1.39)
Prostate (C61)	9	167	114.61	85.50	1.34 (1.27-1.41)
Skin (C44)	16	142	53.92	32.98	1.63 (1.51-1.77)
Pancreas (C25)	16	103	26.27	28.31	0.93 (0.84-1.02)
Rectum (C20)	2	96	1.00	34.74	0.03 (0.02-0.04)
Others	111	1081	194.38	270.63	0.72 (0.69-0.74)
Total	378	4017	870.04	994.21	0.88 (0.86-0.89)

JAKi: Janus kinase inhibitor, csDMARD: conventional synthetic disease-modifying anti-rheumatic drug.

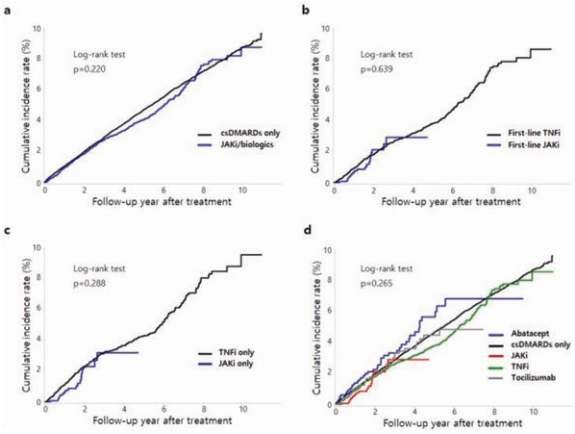


Figure 1. Comparison of cumulative incidence of cancers according to patient treatment

The risk of overall cancers was similar in patients that were (a) prescribed with JAKi/biologics and csDMARDs, as well as in (b) those who used JAKi and TNFi as the first-line treatment. In addition, there was no difference in the incidence of cancers among (c) those who were treated with only JAKi and TNFi during the follow-up and between (d) JAKi, biologics, and csDMARDs users.JAKi: Janus kinase inhibitors, csDMARD: conventional synthetic disease-modifying anti-rheumatic drug, TNFi: tumour necrosis factor-α inhibitor.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0133

DO JAKIS WORK THE BEST AMONG THOSE RA PATIENTS WHERE THEIR SAFETY CONCERNS ARE THE HIGHEST?

Keywords: Rheumatoid arthritis, Targeted synthetic drugs, bDMARD

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Background: Safety is a driving factor when selecting treatment, but the risks should be balanced against the treatment benefits, relative to alternative treatment options. In JAKis, recent evidence of increased safety risks in older patients with cardiovascular (CV) risk factors, have led to concerns. However, an increased risk among certain patients might still be offset by an increasing benefit in the same patient segment, and vice versa. A full understanding of the JAKi benefit-risk profile thus requires a better understanding of the relative (JAKi vs other treatments) benefits in those patients where their relative safety profile may be worse.
Objectives: To assess the observed and adjusted relative effectiveness (remission and response) of JAKis (and non-TNFi bDMARDs) when compared to TNFi, as used in clinical practice, and to assess whether the predicted effectiveness of either drug class is modified by age and the presence of CV risk factors.
Methods: RA patients initiating treatment with a JAKi, non-TNFi, or TNFi 2016-2021 were followed using the Swedish Rheumatology Quality Register. Good EULAR response and remission (CDAI<=2.8) at 6 months were assessed at return visits (within 90 to 270 days after treatment initiation). Non-responder imputation was implemented where treatment ended prior to 210 days after initiation. Crude probabilities of outcomes were presented by age and having ≥1 CV risk factor (Y/N). Linear regression estimated the risk difference (versus TNFi) in age and CV risk groups, adjusted for sex, baseline DAS28 (response) and CDAI (remission), and line of therapy. Probability of outcome was predicted from logistic regression models, fitted to allow effect modification of treatment cohort by age and CV risk score (ERS-RA score), adjusted for sex, baseline DAS28 (response) and CDAI (remission), and line of therapy.
Results: 10,309 treatment episodes contributed data on response at 6 months, and 12,016 episodes with data on remission. Overall, 21% achieved good EULAR response and 11% reached CDAI remission (Table 1). Crude observed risks overall indicated superior response and remission with TNFi versus JAKi (Table 1). Adjusted risk differences suggested superior outcomes in JAKi versus TNFi, overall, and in those with no CV risk for CDAI remission. Patterns of predicted response and remission varied across age and CV ERS-RA score (Figure 1), with JAKis having superior effectiveness overall once adjusting for line of therapy.
Conclusion: Age and CV risk may modify the absolute and relative effectiveness of JAKis vs. TNFi. Further analyses are planned with the aim of presenting these results at EULAR.

Table 1. Observed crude proportions of patients who achieved response and remission, and adjusted* risk differences between JAKi, non-TNFi and TNFi using the latter as reference

	Proportion (N) achieving outcome			Adjusted* risk difference, versus TNFi (95%CI)	
	JAKi	Non-TNFi	TNFi	JAKi	Non-TNFi
Good EULAR response					
N Treatments	1012	2022	4032		
Overall	20% (339)	19% (595)	24% (1490)	4.0% (1.1, 7.0)	2.2% (-0.1, 4.5)
<65 years, no CV	21% (142)	23% (277)	27% (803)	3.5% (-0.3, 7.3)	2.4% (-0.6, 5.5)
<65 years, ≥1 CV	32% (24)	29% (35)	26% (60)	14.6% (1.3, 28.0)	10.7% (-0.1, 21.5)
≥65 years, no CV	25% (83)	24% (168)	30% (352)	4.3% (-1.4, 10.1)	-0.0% (-4.3, 4.3)
≥65 years, ≥1 CV	23% (29)	29% (64)	29% (89)	1.4% (-8.4, 11.1)	3.3% (-4.9, 11.5)
CDAI remission					
N Treatments	1399	2756	5533		
Overall	11% (73)	9% (114)	15% (425)	4.0% (2.3, 6.8)	2.2% (0.1, 3.6)
<65 years, no CV	6% (4)	5% (6)	12% (26)	5.0% (2.0, 8.1)	2.7% (0.3, 5.0)
<65 years, ≥1 CV	13% (40)	10% (64)	14% (159)	-1.8% (-9.3, 5.8)	-2.9% (-8.7, 3.0)
≥65 years, no CV	10% (12)	12% (26)	8% (23)	5.7% (1.0, 10.5)	0.4% (-3.0, 3.9)
≥65 years, ≥1 CV	11% (73)	9% (114)	15% (425)	6.9% (-0.2, 14.0)	6.9% (0.9, 13.0)

*adjusted for sex, baseline DAS28 (response) and CDAI (remission), line of therapy≥1 CV= more than one CV risk factor

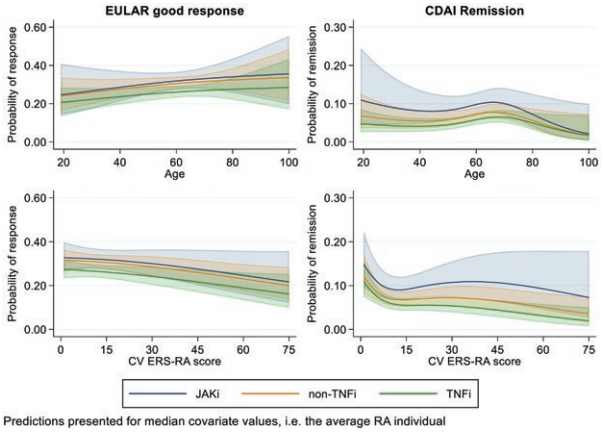


Figure 1. Predicted probability of response and remission at 6 months by age and CV risk of patients with RA treated with JAKi, non-TNFi and TNFi in Sweden, adjusted for sex, baseline DAS28 (response) and CDAI (remission), and line of therapy

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0134

REAL WORLD "POLY-REFRACTORY RA": A RARE BUT UNMET CLINICAL CHALLENGE

Keywords: Rheumatoid arthritis, bDMARD, Ultrasound

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Background: In an age of dose optimization and drug tapering due to excellent conventional (c), biological (b) or targeted synthetic (ts) disease-modifying anti-rheumatic drugs (DMARDs), the fact remains that many patients still have active disease, being therapy refractory, sometimes to multiple DMARDs. In 2021, EULAR defined the term "Difficult-to-treat (D2T) Rheumatoid Arthritis" as failure of two or more different classes of b/tsDMARDs post csDMARDs (1) but the rate of failure to all available DMARD classes in the real-world setting (poly-refractory RA) is not established. Moreover, the DAS-28-CRP score can be elevated in patients with either persistent inflammatory RA (PIRRA) or non-inflammatory RA (NIRRA), where the latter do not benefit from medication change

[2]. PIRRA patients have at least one clinically swollen joint, with objective evidence of active inflammation in power Doppler ultrasound (PDUS), often with elevated CRP levels, whilst NIRRA patients have apparent clinical swelling but absence of PDUS and often normal CRP levels.

Objectives: This study determined the prevalence of EULAR-defined refractory RA (D2T RA) in Leeds. Secondly, we established the prevalence of poly-refractory RA, i.e., patients that failed all available b/tsDMARD classes. Finally, we determined NIRRA/PIRRA phenotypes in refractory disease.

Methods: 1591 RA patients receiving b/ts DMARDs therapy between 2018-2022 were identified as part of a service evaluation, excluding those where DAS-28-CRP was unavailable. Patients fulfilling EULAR-ACR criteria for D2T RA, with DAS-28-CRP≥ 3.2 and US imaging where available were evaluated. Patients were further divided into NIRRA and PIRRA, according to the presence/absence of signs of active synovitis as indicated by PDUS (Figure 1).

Results: 242/1591 (15.2%) met the EULAR D2T criteria of failing at least 2 b/tsDMARDs. 89/1591 (5.6%) failed 2 classes only, with a mean disease duration (mDD) of 11 years. 60/1591 (3.8%) failed 3 classes (mDD= 18) and 52/1591 (3.3%), 4 classes (mDD= 10.5). However, just 41/1591 (2.5%) had poly-refractory RA having failed all 5 classes (mDD= 21). Of them, 37/41 (90%) failed multiple drugs within each class. 4/41 (10%) poly-refractory and 45/242 (18.5%) of all EULAR D2T cases were seronegative. Regarding joint involvement patterns, most had typical small joint RA disease pattern but 26/242 (11%) had a predominant large joint pattern. 18/41 (43%) of the poly-refractory RA group had CRP levels within the normal ranges despite a DAS-28-CRP score above 3.2 (mean DAS-28-CRP of 5.3). 71 D2T RA patients had recent US of clinically involved joints, including 28 poly-refractory RA cases. 18/28 (64%) poly-refractory were considered PIRRA as evidenced by synovial hypertrophy and PDUS positivity in at least one evaluated clinically swollen joint. 32/71 (45%) D2T RA had no signs of active synovitis in PDUS being considered NIRRA. Of them, 17/32 (53%) had no synovial thickening in US in suspected clinically involved joints. Specifically in the poly-refractory group, the CRP levels were within normal ranges in 6/10 (60%) NIRRA patients, while just 7/18 (39%) PIRRA cases had normal CRP levels.

Conclusion: Although 15.2% of Leeds RA patients met the EULAR criteria for D2T RA, real world poly-refractory RA was present in only 2.5%. Almost half of these patients had no PDUS changes on US and/or had normal CRP levels. These findings highlight a twofold clinical challenge in refractory RA with half of this group (both D2T and poly-refractory RA) having true inflammation that may need new mechanisms of action, but the other half would not be likely to benefit from new DMARD treatment strategies.

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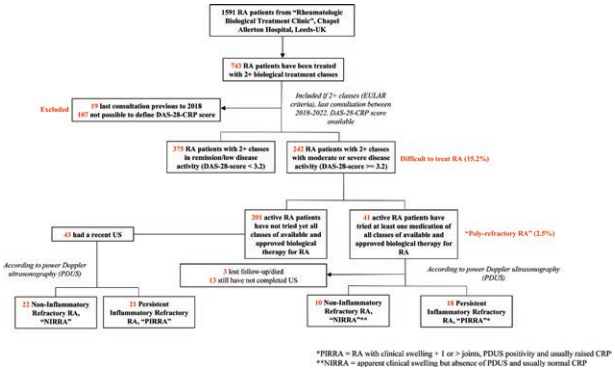


Figure 1. Flow-chart showing the prevalence of poly-refractory, PIRRA and NIRRA patients among Leeds RA patients.

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Disclosure of Interests: None Declared.
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OP0135

RISK OF DEMYELINATING EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TUMOUR NECROSIS FACTOR INHIBITORS: A SYSTEMATIC LITERATURE REVIEW

Keywords: bDMARD, Rheumatoid arthritis, Systematic review

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Background: Several case reports published in the 2000's indicated that demyelinating diseases could be a serious adverse event following TNF inhibitors (TNFi) treatment. However, initial data from biological therapy registries did not bring enough clarification.

Objectives: To investigate whether treatment with biologics or targeted synthetic DMARDs is associated with an increased risk of demyelinating events among patients with rheumatoid arthritis (RA)

Methods: A systematic search was performed in MEDLINE, EMBASE (up to Oct 2022), and by manual references. Selection criteria: (population) patients with RA; (intervention) treatment with any biologic including TNFi and synthetic DMARDs, (outcome) demyelinating event; (study design) observational studies and randomised clinical trials. Titles and abstracts were screened and data were extracted from the selected studies including quality evaluation, and outcomes of interest.

Results: From 368 identified studies, 4 cohorts and 3 nested case-control studies reported risk of demyelinating events following treatment with biologics, mainly TNFi and anakinra, in one study. Most studies included mixed populations of inflammatory arthritis and patients with RA were analysed as a separate subgroup. Two nested case-control reported an increased risk, but in a mixed population, with no analysis of a subgroup of RA. In general, demyelinating events were very uncommon in patients receiving TNFi, with a marginal increased risk in males with RA in 2 studies (Table 1).

Table 1. Characteristics and incidence rates of demyelinating events in the included studies

Study	Design	Population	Outcome
Lingyi 2022 (1)	Nested case-control Canadian healthcare databases	N= 462/296,918 Rheumatic diseases, mixed population	Case = multiple sclerosis Pooled IRR (95% CI): 2.05 (1.13-3.72)
Taylor 2021 (2)	Prospective Cohort British Society for Rheumatology Biologics Register	N= 35/13,489 Mixed population of inflammatory arthritis	Incidence (95% CI): 19.7/100,000 pts-years (13.7-27.3) SIR (95% CI): 1.38 (0.96-1.92) Definite cases: 0.83 (0.51-1.26) Males: 2.75 (1.31-5.06)
Kunchok 2020 (3)	Nested case-control Medical records at Mayo Clinic (USA)	N=106 cases/106 controls Autoimmune diseases	Case = Any inflammatory CNS event OR 4.82 (95%CI 1.62-14.36)
Koop 2020 (4)	Combined biologic registers in Sweden and Denmark	N=271 and 51/111,455 RA pts	Incidence Rate: 0.37-0.39/1000 pt-yrs HR (95% CI) TNFi exposed vs non: Sweden: 0.97 (0.72 to 1.33) Denmark: 1.45 (0.74 to 2.81)
Dreyer 2016 (5)	Register-based cohort study DANBIO	N= 27,880 patients with arthritis and TNFi therapy	SIR 1.11 (95% CI 0.63-1.93) RA: 0.65 (95% CI 0.24–1.72) Males: 3.48 (95% CI 1.45–8.37)
Fernandez-Espartero 2011 (6)	BIOBADASER-Spain	N= 9/13,075 RA pts-years	Incident rate in RA: 0.69 (95% CI: 0.36-1.32) MS 0.05 (95% CI: 0.01-0.33), vs Spanish population 0.02-0.04*1000
Bernatsky 2010 (7)	Nested case-control Administrative data in Canada	N= 104,958 RA pts 81 cases and 810 controls	Adjusted rate ratios (95% CI): TNFi 1.31 (0.68 - 2.50) Anakinra 0.80 (0.29 - 2.24) MTX 1.09 (0.63 - 1.89)

Abbreviations: RA, rheumatoid arthritis; SIR, standardized incidence rate; CI, confidence interval; CNS, central nervous system; HR, hazard ratio; OR, odds ratio; MTX, methotrexate; MS, multiple sclerosis; TNFi, tumour necrosis factor inhibitor.

Conclusion: No consistent and significant risk of demyelinating disease following TNFi treatment was found in RA patients. A marginal and slight increase of risk was found in male RA patients. The small number of events is reassuring when considering the use of TNFi. A careful consideration is recommended in individuals at highest risk of demyelinating diseases.

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The future perspectives in the treatment of SLE & Sjören's

OP0136 **METABOLOMIC SERUM PROFILING IDENTIFIES METABOLITES LINKED TO KIDNEY DAMAGE WHICH ARE MODULATED BY ANIFROLUMAB IN A PHASE 2 TRIAL IN LUPUS NEPHRITIS**

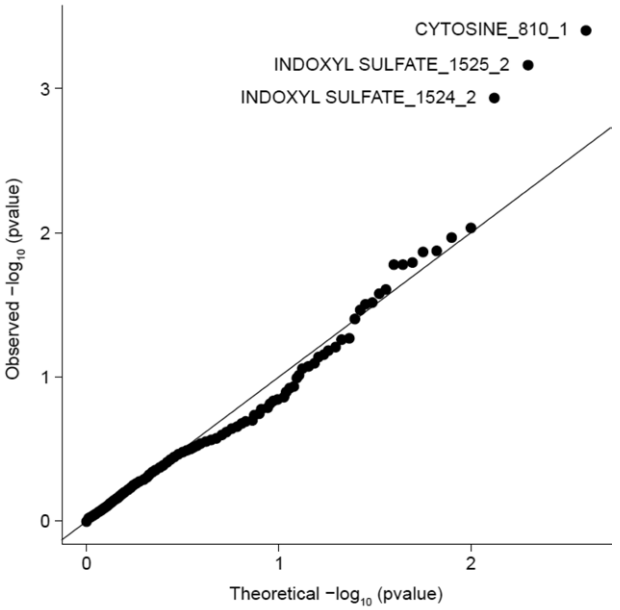
Keywords: -omics, Kidneys, Biomarkers

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Background: Lupus nephritis (LN) is one of the most common severe clinical manifestations of systemic lupus erythematosus (SLE), occurring in 21%–48% of SLE patients.[1] The kidney is the major organ affected in SLE, with persistent inflammation leading to progressive loss of renal function and chronic kidney disease (CKD). The decline in kidney function leads to an accumulation of metabolic waste products normally cleared by the kidneys, known as uremic toxins. Uremic toxins negatively affect multiple organ systems, causing increased cardiovascular and kidney damage, among other effects.[2] Given the clear link to kidney function, uremic toxins may serve as biomarkers of kidney damage and of treatment response. Anifrolumab, a monoclonal antibody that targets the type I interferon (IFN) receptor subunit 1, is approved for moderate to severe SLE treatment[3] and intensified dosing is being evaluated in a phase 3 study for LN treatment.
Objectives: In this study, we conducted unbiased metabolomic serum profiling to identify novel biomarkers of treatment response and provide insights into the mechanism of action of anifrolumab in LN.
Methods: In the 52-week phase 2 clinical trial TULIP-LN (NCT02547922), 147 patients with active LN were randomized 1:1:1 to receive intravenous anifrolumab every 4 weeks at standard SLE dosing (basic regimen [BR], 300 mg), intensified dosing (intensified regimen [IR], 900 mg for the first 3 doses, 300 mg thereafter), or placebo in addition to standard therapy.[4] Serum samples were obtained from 140 of these patients at baseline (BL) and Weeks 12, 24, and 52. Serum metabolites were analyzed using an unbiased liquid chromatography–mass spectrometry-based approach. Metabolites that were differentially modulated in the anifrolumab IR vs placebo group were identified using a mixed effects model evaluating the interaction of metabolite levels and treatment, adjusted for patients' IFN gene signature (IFNGS) status (high/low) and 24-hour urine protein–creatinine ratio (UPCR >3 or ≤3). Relationships between BL metabolite level and clinical characteristics of kidney damage were assessed by Spearman's correlation. Association of BL metabolite levels with complete renal response were evaluated by logistic regression, adjusted for IFNGS and UPCR status.
Results: Our unbiased metabolomic approach identified 2 metabolites significantly impacted by anifrolumab treatment compared with placebo (Figure 1). Cytosine (Cyt) and indoxyl sulfate (IS) levels were significantly reduced following anifrolumab IR treatment compared with placebo, while an intermediate, non-significant reduction was observed longitudinally with anifrolumab BR. At baseline, Cyt and IS serum levels were positively correlated with serum creatinine and negatively correlated with estimated glomerular filtration rate. Baseline IS levels were also associated with complete renal response at Week 52. Compared to the trend observed in nonresponders, IS levels in responders were reduced from BL to Week 52. A trend in reduction of multiple uremic toxins not limited to IS was detected in the anifrolumab-treated group.
Conclusion: In patients with LN, anifrolumab treatment reduced levels of multiple circulating uremic toxins including IS, a known inducer of cardiovascular damage in CKD.[5] Together, correlations with kidney damage measures at baseline and reductions in IS levels in responders vs nonresponders at Week 52 suggest improvements in kidney function following anifrolumab treatment. Overall, our results contribute to a deeper understanding of how inhibition of type I IFN affects renal disease in LN.

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Figure: Identification of metabolites differentially modulated by anifrolumab vs placebo



Metabolite nomenclature includes the Metabolite Name_MS-DIAL Identifier_MSI Level
MSI, Metabolomics Standards Initiative; MS-DIAL, Mass Spectrometry-Data Independent AnaLysis

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Disclosure of Interests: David Jayne Shareholder of: Aurinia, Speakers bureau: GSK, CSL Vifor, Consultant of: AstraZeneca, Chemocentryx, CSL Vifor, GSK, Novartis, Roche, Takeda, Grant/research support from: GSK, Roche, Patrick Gavin Employee of: AstraZeneca, Erik Allman Shareholder of: Primarily AstraZeneca but others through various Exchange Traded Funds (ETFs), Employee of: Previously, Janssen/Johnson & Johnson. Currently, AstraZeneca, Cristina Di Poto Shareholder of: AstraZeneca, Employee of: AstraZeneca, Xiang Tian Shareholder of: AstraZeneca, Employee of: AstraZeneca, Sonja Hess Shareholder of: AstraZeneca, Employee of: AstraZeneca, Madhu Ramaswamy Shareholder of: GSK, Employee of: AstraZeneca (until Jan 2023), GSK (from Jan 2023), Mark Lazarus Consultant of: Paid consulting for Novartis and Sandoz over 2 years ago, Employee of: AstraZeneca, Philip Z Brohawn Shareholder of: AstraZeneca, Employee of: AstraZeneca, Daniel Muthas Shareholder of: AstraZeneca, Employee of: AstraZeneca, Adam Platt Shareholder of: AstraZeneca, Employee of: AstraZeneca, Hussein Al-Mossawi Shareholder of: AstraZeneca, UCB, GSK, Speakers bureau: Novartis, Pfizer, UCB, Consultant of: Novartis, UCB, AbbVie, Grant/research support from: UCB, Employee of: UCB (Previous), AstraZeneca (Current), Catharina Lindholm Shareholder of: AstraZeneca, Employee of: AstraZeneca, Nicola Ferrari Shareholder of: AstraZeneca, Employee of: AstraZeneca.
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OP0137 **EFFICACY AND SAFETY OF TELITACICEPT, A NOVEL BLYS/APRIL DUAL INHIBITOR, IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED 52-WEEK STUDY**

Keywords: Randomized control trial, Systemic lupus erythematosus, Clinical Trials

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Background: Telitacicept (TACI-Fc fusion protein) is a novel BLyS (B-lymphocyte stimulator)/APRIL (a proliferation-inducing ligand) dual inhibitor, which has been approved in 2021 in China for the treatment of patients with active systemic lupus erythematosus (SLE)[1].
Objectives: Assess the efficacy and safety of telitacicept in SLE patients in a double-blind, randomized, placebo-controlled, phase 3 trial.
Methods: In this study, 335 active SLE patients who were receiving stable standard therapy with positive ANA/anti-dsDNA and a SELENA-SLEDAI score ≥8 were randomized 1:1 to receive telitacicept 160 mg (N=167) or placebo (N=168) subcutaneously weekly for 52 weeks. The primary endpoint was the response rate of SLE responder index 4 (SRI4) at Week 52. Key secondary endpoints included: SELENA-SLEDAI, PGA, immunological biomarkers including C3, C4, IgM, IgG, IgA and $CD19^+$ B cells. Safety was assessed during the study.
Results: Baseline demographics and disease characteristics were comparable between the two groups. The primary endpoint at Week 52 was met, with significantly greater proportion of patients in telitacicept 160 mg group vs placebo group achieving SRI4 response (Table 1). SRI4 response was sustained in telitacicept 160 mg group up to Week 52 (Figure 1A). Significantly greater proportions of subjects in telitacicept 160 mg group had improvement in SELENA-SLEDAI and PGA (Table 1 & Figure 1B, 1C). Rapid and sustained increase of C3 and C4 (Figure 1G, 1H), and reduction of IgM, IgG, IgA and $CD19^+$ B cells (Figure 1D, 1E, 1F, 1I) were observed following telitacicept treatment. Incidences of TEAEs and infections were comparable between the two groups. Most of TEAEs were mild to moderate in severity. A greater proportion of patients receiving placebo had SAEs and serious infections compared with telitacicept 160 mg. (Table 1).

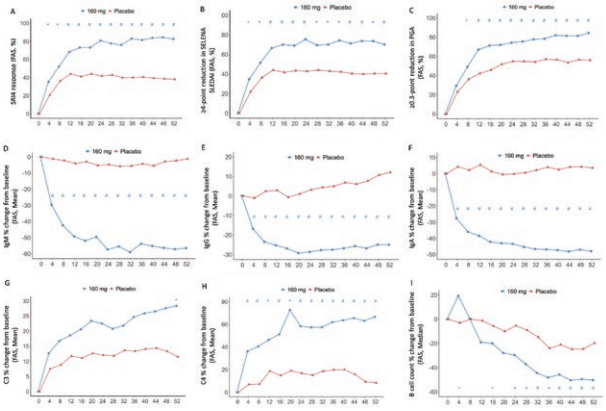


Figure 1. SRI4 Response Rate (A), rate of subjects with improvement in SELENA-SLEDAI (B) and PGA (C) at each visit. Percent (%) change from baseline in IgM (D), IgG (E), IgA (F), C3 (G), C4 (H) and $CD19^+$ B cells (I).$^{\#}$P<0.001 vs. Placebo; †P<0.01 vs. Placebo; $^{+}$P<0.05 vs. Placebo.

Table 1. Key efficacy and safety data.

Efficacy, FAS	**Placebo (N=168)**	**Telitacicept 160 mg (N=167)**
Primary endpoint		
SRI-4 Response at Week 52 (MI), n(%)	64(38.1%)	138(82.6%)$^{\#}$
SRI-4 Response at Week 52 (NRI), n(%)	55(32.7%)	112(67.1%)$^{\#}$
SRI-4 Response at Week 52 (LOCF), n(%)	63(37.5%)	138(82.6%)$^{\#}$
Secondary endpoints$^{\$}$		
≥4-point reduction in SELENA SLEDAI at Week 52, n(%)	68(40.5%)	117(70.1%)$^{\#}$
≥0.3-point reduction in PGA at Week 52, n(%)	94(56%)	141(84.4%)$^{\#}$
Severe SFI flare, Mean±SD	0.6±0.89	0.1±0.44$^{\#}$
Safety, SS	**Placebo (N=168)**	**Telitacicept 160 mg (N=167)**
TEAE, n(%)	142(84.5%)	153(91.6%)
SAE, n(%)	24(14.3%)	12(7.2%)
Infections and infestations^{+} (SOC), n(%)	101(60.1%)	109(65.3%)
Upper respiratory tract infections, n(%)	55(32.7%)	71(42.5%)
Urinary tract infection, n(%)	26(15.5%)	19(11.4%)
Nasopharyngitis, n(%)	11(6.5%)	4(2.4%)
Herpes zoster, n(%)	6(3.6%)	8(4.8%)
Gastroenteritis, n(%)	5(3.0%)	9(5.4%)
Serious Infections	9(5.4%)	2(1.2%)

$^{\#}$p<0.001 vs. Placebo. $^{\$}$Missing data were imputed by multiple imputation. $^{+}$AEs with an incidence of ≥3% in any group were listed. FAS, full analysis set. SRI, SLE responder index. MI, missing data were imputed by multiple imputation. NRI, missing data were imputed as non-response. LOCF, missing data were imputed by last observation carry forward method. PGA, physician's global assessment. SFI, SLE flare index. SS, safety set. TEAE, treatment-emergent adverse event. SAE, serious adverse event. SOC, system organ class.

Conclusion: This phase 3 trial met the primary endpoint. Telitacicept 160 mg showed good clinical benefits and a favorable safety profile in SLE patients.
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Acknowledgements: The patients and their families who participated in this clinical trial.
Disclosure of Interests: Li Wang: None declared, JING LI: None declared, Dong Xu: None declared, Jianmin Fang Shareholder of: RemeGen Co., Ltd, Employee of: RemeGen Co., Ltd, Ronald van Vollenhoven: None declared, Fengchun Zhang: None declared.
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OP0139

EFFICACY AND SAFETY OF ABBV-599 HIGH DOSE (ELSUBRUTINIB 60 MG AND UPADACITINIB 30 MG) AND UPADACITINIB MONOTHERAPY FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS: A PHASE 2, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Keywords: Systemic lupus erythematosus

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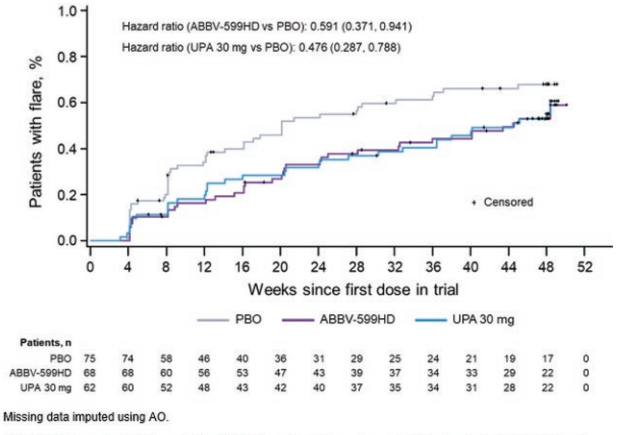
Background: ABBV-599 is a novel combination of elsubrutinib (ELS; a selective BTK inhibitor) and upadacitinib (UPA; a JAK inhibitor) that targets non-overlapping signaling pathways associated with systemic lupus erythematosus (SLE).
Objectives: To report results from SLEek, a phase 2, randomized, placebo (PBO)-controlled, parallel-group, multicenter study evaluating efficacy and safety of ABBV-599 and UPA monotherapy in adults with moderately to severely active SLE (NCT03978520).
Methods: Patients (pts) were randomized 1:1:1:1:1 to once daily (QD) ABBV-599 high dose (HD; ELS 60 mg + UPA 30 mg), ABBV-599 low dose (LD; ELS 60 mg + UPA 15 mg), ELS 60 mg, UPA 30 mg, or PBO. The primary endpoint was the proportion of patients at W24 achieving SLE Responder Index-4 (SRI-4) and steroid dose ≤ 10 mg QD; additional efficacy and safety endpoints through W48 are also reported. The pre-specified 2-sided alpha level was 0.1.
Results: 341 patients were enrolled. After a planned interim analysis when 50% of pts reached W24, the ABBV-599LD and ELS 60 mg arms were discontinued for lack of efficacy (no safety concerns). Of 205 continuing pts (ABBV-599HD n = 68, UPA 30 mg n = 62, PBO n = 75), baseline characteristics were well balanced. The primary endpoint (proportion achieving SRI-4 and steroid dose ≤ 10 mg QD at W24 vs PBO) was met by ABBV-599HD and UPA 30 mg. Key secondary endpoints were also achieved at W48 in both groups (**Table 1**). Overall flares and time to first flare were substantially reduced in the ABBV-599HD and UPA 30 mg groups through W48 (**Figure 1**). Anti-double stranded DNA antibodies were significantly decreased with both treatments. TEAEs considered related to study drug were 42.6% ABBV-599HD, 32.3% UPA 30 mg, and 33.3% PBO. There were no malignancies or VTE. There were 3 non-fatal CV events (1 MI on PBO and 2 ruptured cerebral aneurysms [1 each on ABBV-599HD and UPA 30 mg]); all were assessed as unrelated to study drug by investigators. No new safety signals were observed beyond previously known data for UPA or ELS.
Conclusion: ABBV-599HD (ELS 60 mg + UPA 30 mg) and UPA 30 mg demonstrated significant improvements in SLE disease activity and flares with acceptable safety through 48 weeks.

Table 1. Key Endpoints at Week 48

	PBO (n = 75)	ABBV-599HD (n = 68)	UPA 30 mg (n = 62)
SRI-4 and steroid dose ≤ 10 mg QD, n (%) [95% CI][a]	24 (32.0) [21.4, 42.6]	33 (48.5) [36.7, 60.4]*	27 (43.5) [31.2, 55.9]
SRI-4, n (%) [95% CI][a]	24 (32.0) [21.4, 42.6]	35 (51.5) [39.6, 63.3]*	28 (45.2) [32.8, 57.5]+
BICLA, n (%) [95% CI][a]	19 (25.3) [15.5, 35.2]	33 (48.5) [36.7, 60.4]***	33 (53.2) [40.8, 65.6]***
LLDAS, n (%) [95% CI][a]	18 (24.0) [14.3, 33.7]	27 (39.7) [28.1, 51.3]*	31 (50.0) [37.6, 62.4]***
Joint-Count 50 in patients with ≥ 6 affected joints at baseline, n/n (%) [95% CI][a]	26/59 (44.1) [31.4, 56.7]	37/58 (63.8) [51.4, 76.2]*	34/59 (57.6) [45.0, 70.2] +
CLASI-50 in patients with baseline CLASI ≥ 10, n/n (%) [95% CI][a]	5/14 (35.7) [10.6, 60.8]	6/12 (50.0) [21.7, 78.3]	5/8 (62.5) [29.0, 96.0]*
Change from baseline in steroid dose, mg, LS mean (SE)[b]	−1.5 (0.5)	−1.5 (0.5)	−1.2 (0.5)
SFI, events/patient-years (95% CI)[c]			
Overall flares	2.8 (2.4, 3.3)	1.5 (1.2, 1.9)***	2.0 (1.6, 2.4)**
Mild/moderate flares	2.5 (2.1, 2.9)	1.3 (1.0, 1.6)***	1.9 (1.5, 2.3)*
Severe flares	0.3 (0.2, 0.5)	0.2 (0.1, 0.3)	0.2 (0.1, 0.3) +
Time to first flare by SFI, days, median (Q1, Q3)[c]	141 (57, NE)	312 (114, NE)*	311 (99, NE)**
BILAG-based flare rate, estimated incidence rate[c]	0.57	0.19*	0.26

Data are presented for the full analysis set.[a]Missing data imputed using NRI incorporating multiple imputation to handle missing data due to COVID 19.[b]Missing data imputed using MMRM.[c]Observed data w/o imputation.+*P* <.1; **P* <.05; ***P* <.01, ****P* <.001 vs PBO.ABBV-599HD, elsubrutinib 60 mg QD and UPA 30 mg QD; CLASI-50, ≥ 50% reduction in CLASI activity score; Joint-Count 50, ≥ 50% improvement in tender or swollen lupus joints; LLDAS, Lupus Low Disease Activity State; NE, not estimated; PBO, placebo; SFI, SELENA SLEDAI Flare Index; UPA, upadacitinib.

Figure. Time to First Flare by SELENA SLEDAI Flare Index.



Missing data imputed using AO.

ABBV-599HD, elsubrutinib 60 mg QD and UPA 30 mg QD; AO, as observed; PBO, placebo; SELENA, Safety of Estrogens in Lupus Erythematosus National Assessment; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; UPA, upadacitinib.

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OP0140

REGULATORY T CELL DEFECTS IN SLE AND THERAPY WITH A NOVEL IL-2 MUTEIN: PHASE 1 CLINICAL RESULTS WITH EFAVALEUKIN ALFA

Keywords: Cytokines and chemokines, Systemic lupus erythematosus, Clinical Trials

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Background: Regulatory T cells (Treg) are critical for maintaining self-tolerance and preventing autoimmunity, and IL-2 is essential for their development, survival and suppressive function. Defects in Treg function and the IL-2 receptor are associated with SLE and have been correlated with disease activity.[1,2] Efavaleukin alfa is an IL-2 mutein Fc fusion protein that preferentially binds the high-affinity IL-2 receptor alpha chain (CD25) to selectively promote Treg expansion.
Objectives: To compare Treg functional phenotypes in healthy controls (phase 1a baseline) with SLE patients (at baseline and post-treatment) enrolled in a phase 1b study of efavaleukin alfa in order to characterize Treg defects in SLE and the effects of IL-2-targeted therapy with efavaleukin alfa on Treg expansion.
Methods: Baseline Treg functional phenotyping data from 64 healthy volunteers (ph1a baseline) were compared with Treg data from phase 1b SLE study subjects. The phase 1b, multiple ascending dose study (NCT03451422) included 5 dose cohorts; a total of 35 patients with SLE (with either elevated anti-dsDNA or ANA) were randomized to receive efavaleukin alfa or placebo SC every 2 weeks (Q2W; cohorts 1, 2, 4, and 5) or every week (QW; cohort 3) for a total of 12 weeks. Pharmacodynamic profiles of lymphocyte subsets were evaluated in peripheral blood. Cell subsets were defined as follows: Treg, CD3+CD4+Foxp3+CD127–; $CD25^{bright}$ Treg, Treg with the highest CD25 expression; CD25– Treg, CD3+CD4+Foxp3+CD127–CD25–; and CD4+ Tcon, CD3+CD4+(-Treg).
Results: At baseline, Treg CD25 expression levels were significantly lower in SLE patients compared with healthy subjects (Figure 1a), and CD25 expression on Foxp3+ Treg negatively correlated with anti-dsDNA autoantibodies (Figure 1b). The percentage of CD25– Tregs was significantly higher in SLE patients than healthy subjects and also correlated with anti-dsDNA at baseline. At day 22 in the phase 1b study, after SLE patients randomized to efavaleukin alfa had received 2 doses, Treg CD25 expression was significantly increased above baseline and comparable to the levels in healthy controls (Figure 1a). The number of $CD25^{bright}$ Tregs in SLE patients was inversely correlated with anti-dsDNA at baseline, with a mean peak increase of 53.8-fold above baseline with efavaleukin alfa treatment. The intensity of CD25 on CD4+ Tcon was not significantly different between healthy subjects and SLE patients and was not increased with efavaleukin alfa treatment.
Conclusion: Treg from SLE patients showed defects in IL-2 signaling evidenced by lower CD25 expression that correlated with anti-dsDNA, suggesting a role for reduced IL-2 signaling in SLE autoimmunity. Efavaleukin alfa treatment selectively restored Treg CD25 expression to levels observed in healthy controls without increasing CD25 expression on Tcon. $CD25^{bright}$ Treg, considered a more suppressive Treg population, were expanded with multiple doses of efavaleukin alfa. Although low baseline SLE disease activity and short treatment duration precluded efficacy analysis, clinical correlations with treatment response will be investigated in the ongoing phase 2b adaptive trial of efavaleukin alfa in SLE.

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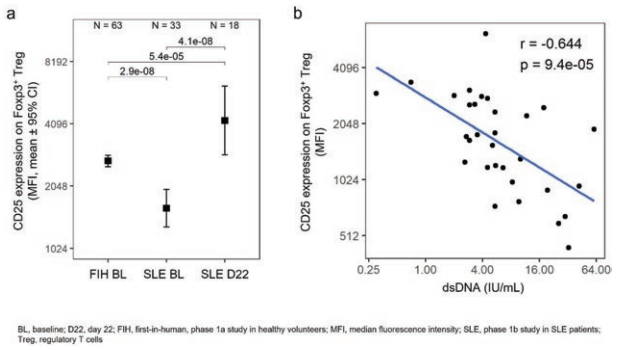


Figure 1. CD25 expression levels on Treg at baseline and with efavaleukin alfa treatment (a) and the baseline correlation to anti-dsDNA antibodies (b)

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Disclosure of Interests: Nandita Sarkar Shareholder of: Amgen Inc., Employee of: Amgen Inc., Xuguang Hu Shareholder of: Amgen Inc., Employee of: Amgen Inc., Nadia Tchao Shareholder of: Amgen Inc., Employee of: Amgen Inc., Richard Furie Consultant of: Amgen Inc., Alan Kivitz Shareholder of: Pfizer, GSK, Gilead, Novartis, and Amgen Inc., Speakers bureau: Merck & Co, Eli Lilly, Novartis, Pfizer, Flexion, AbbVie, Amgen, Genentech, Regeneron, UCB, Horizon, and GSK., Paid instructor for: Merck & Co, Eli Lilly, Novartis, Pfizer, Flexion, AbbVie, Amgen, Genentech, Regeneron, UCB, Horizon, and GSK., Consultant of: AXDEV Group, Pfizer, Janssen, Boehringer Ingelheim, AbbVie, Flexion, Gilead, Grunenthal, Orion, Regeneron, Sun Pharma Advance Research, and ECOR1, Grant/research support from: Amgen Inc., Stanley Cohen Consultant of: Amgen Inc., Kevin Gorski Shareholder of: Amgen Inc., Employee of: Amgen Inc.
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OP0141 LONG TERM SAFETY AND EFFICACY OF CAR-T CELL TREATMENT IN REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS - DATA FROM THE FIRST SEVEN PATIENTS

Keywords: Systemic lupus erythematosus, Remission, Treat to target

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Background: Despite better treatment modalities some patients with systemic lupus erythematosus (SLE) suffer from severe and treatment-resistant disease. This situation puts patients at high risk for organ failure or even death. Furthermore, many patients with SLE have to take long-term, sometimes even life-long immune suppressive medication to control the disease without being able to enjoy drug-free remission. Recently, we reported that deep B cell depletion using a single infusion with autologous CD19 chimeric antigen receptor (CAR) T cells induced drug-free clinical remission in severe SLE patients with refractory disease [1,2]. This abstract presents the long-term clinical efficacy and safety data of the first seven SLE patients receiving autologous CD19-directed CAR-T cell therapy.
Objectives: To test whether administration of autologous CD19 chimeric antigen receptor (CAR) T cells is tolerable and effective in patients with severe refractory SLE.
Methods: Compassionate use program for patients with severe active SLE showing organ involvement and resistance to multiple immune suppressive treatments. Patients received autologous $1x10^6$ CD19-CAR-T cells/kg body weight by single infusion after standard conditioning therapy (cyclophosphamide/fludarabine). The investigational medicinal product MB-CART19.1 was produced as described before [1,2]. All SLE treatments were stopped before CAR-T cell administration. Patients were followed up as in-patients for the first 10 days after CAR T cell administration, then weekly until the end of the first month, then monthly for three months and every three months thereafter. Tolerability was assessed by monitoring for Cytokine-release syndrome (CRS) and Immune-related effector Cell Neurotoxicity Syndrome (ICANS). Preliminary efficacy was assessed by reaching a Lupus Low Disease Activity State (LLDAS) and DORIS remission.
Results: As per January 2023, seven SLE patients (6 female, 1 male, aged range 19-39) had been treated with CD19 CAR-T cells with a median follow up of 13 months (4 months-22months). Patients had active disease with a median SLEDAI of 10 (range: 8-16), with a median of 4 organs involved (range: 8-16) and a median number of 7 failed treatments (range: 4-15). All patients had active kidney disease. In addition, involvement of the heart, lungs, pleura, joints, skin, muscles and bone marrow were documented. Conditioning was done at the described [1,2] dose with the exception of patients 7, who received only 50% of the dose. All patients received a single infusion of $1x10^6$ autologous CD19-CAR-T cells/kg body weight. No ICANS was observed and CRS if observed were mild (grade I). In vivo, CAR-T cells rapidly expanded peaking at day 9 with a median of 26% of circulating T cells being CAR T cells (range: 11-59%). Expansion of CAR-T cells coincidence with the complete depletion of circulating B cells. B cell aplasia lasted for a median of 120 days (range 58-205). All patients experienced drug-free remission as assessed by DORIS remission criteria and met lupus low activity state (LLDAS) usually within the first three months after CAR T cell therapy. Furthermore, seroconversion with loss of dsDNA antibodies and other autoantibodies was observed. To date, no SLE flare occurred despite complete cessation of treatment.
Conclusion: Taken together, these data suggest that CD19 CAR T-cell therapy can abrogate disease and delete autoimmunity in patients with severe SLE. After CD19 CAR T-cell therapy SLE patients remain in drug free-remission of SLE even if B cells recur. This remission can be long-lasting as the longest disease -free observation period is now 22 months.
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	Pat #1	Pat #2	Pat #3	Pat #4	Pat #5	Pat#6	Pat#7
Age (ys)	22	23	22	24	18	33	33
Sex (F/M)	F	M	F	F	F	F	F
Disease Duration (ys)	4	1	6	9	3	18	1
N organs involved	4	3	5	6	4	6	3
N failed treatments	7	5	4	7	5	15	7
Baseline SLEDAI (score)	16	16	10	8	9	16	10
Baseline C3 (mg/dl)	49	43	56	88	68	33	49
Baseline anti-dsDNA (IE/ml)	5600	2060	479	4	52	1335	680
Baseline Proteinuria (mg/g crea)	2015	3080	6539	8096	88	2025	5044
Conditioning Dose (%)	100	100	100	100	100	100	50
Peak CAR T (cells/µl)	167	461	33	697	146	24	117
Peak CAR T (% of T cells)	27	41	11	59	26	13	12
Duration of B cell Aplasia (days)	148	196	120	93	63	205	58
Follow-up (months)	22	16	14	13	11	8	4
Seroconversion	+	+	+	+	+	+	+
SLEDAI (lastfollow-up)	0	0	0	0	0	0	0
LLDAS (lastfollow-up)	+	+	+	+	+	+	+
DORIS Remission (lastfollow-up)	+	+	+	+	+	+	+
CRS (grade 0-4)	0	1	0	1	0	1	1
ICANS (grade 0-4)	0	0	0	0	0	0	0

Table 1 contains baseline demographic data from seven SLE patients treated with CD19 CAR T-cell therapy. Patient number one to seven, age in years (ys), sex in female (F) and male (M). Disease duration in years (ys). Number (N) of organs involved and number (N) of failed treatments, disease activity at baseline presented with SLE disease activity index (SLEDAI). Conditioning dose referred to 1x cyclophosphamide 1g/m2 and 3x fludarabine 25mg/m2. Maximum of CAR-T cell expansion after administration of 1 million CAR-T cells /kg body weight given as peak of CAR-T cells absolute and percent CAR+ of CD3+ T-cells. Efficacy criteria listed as seroconversion, disappearance of SLE specific antibodies (antidsDNA), Lupus Low Disease Activity State (LLDAS), definitions of remission in systemic lupus erythematosus (DORIS) remission. Adverse events listed at Cytokine-release syndrome (CRS) and Immune-related effector Cell Neurotoxicity Syndrome (ICANS) in grade 0-4.

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OP0142

EFFICACY AND SAFETY OF TELITACICEPT, A NOVEL BLYS/APRIL DUAL INHIBITOR, IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: A PHASE 2, RANDOMIZED, PLACEBO-CONTROLLED 24-WEEK STUDY

Keywords: Clinical Trials, Randomized control trial, Sjögren syndrome

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Background: Primary Sjögren's syndrome (pSS) is a chronic systemic autoimmune disease characterized by B-cell hyperactivity. There are still currently no systemic treatments approved for pSS. Telitacicept (TACI-Fc fusion protein) is a novel BLyS (B-lymphocyte stimulator)/APRIL (a proliferation-inducing ligand) dual inhibitor, which has been approved in 2021 in China for the treatment of patients with active systemic lupus erythematosus (SLE)[1].
Objectives: To evaluate the efficacy and safety of telitacicept in patients with pSS.
Methods: In this phase 2, placebo-controlled study, 42 patients with active pSS (ESSDAI score ≥5) were randomized to 3 treatment arms: placebo (N=14), telitacicept 160 mg (N=14) and telitacicept 240 mg (N=14). Study drugs were administered subcutaneously weekly for 24 weeks. The primary endpoint was the change from baseline in the ESSDAI score at week 24. Key secondary endpoints included: ESSPRI, MFI-20, immunological biomarkers including IgG, IgA, IgM and CD19$^+$ B cells. Safety was assessed during the study.
Results: Baseline demographics and disease characteristics were similar among treatment arms. The ESSDAI score and MFI-20 score decreased from baseline through week 24 in telitacicept 160 mg and 240 mg groups (Figure 1A, 1B). Statistically significant improvements were observed for the ESSDAI score and MFI-20 score both at week 12 and week 24 in the telitacicept 160 mg group; statistically significant improvements were observed for the ESSDAI score at week 12 and MFI-20 score at both week 12 and week 24 in the telitacicept 240 mg group (Table 1). Telitacicept treatment produced rapid and sustained reductions in IgG, IgA, IgM and CD19$^+$ B cells (Figure 1C-F). Incidences of treatment-emergent adverse events (TEAEs) were comparable across treatment arms. Most of TEAEs were mild to moderate in severity. Serious adverse events (SAEs) were infrequent and occurred only in the placebo group. Upper respiratory tract infections were the most common infections. (Table 1)

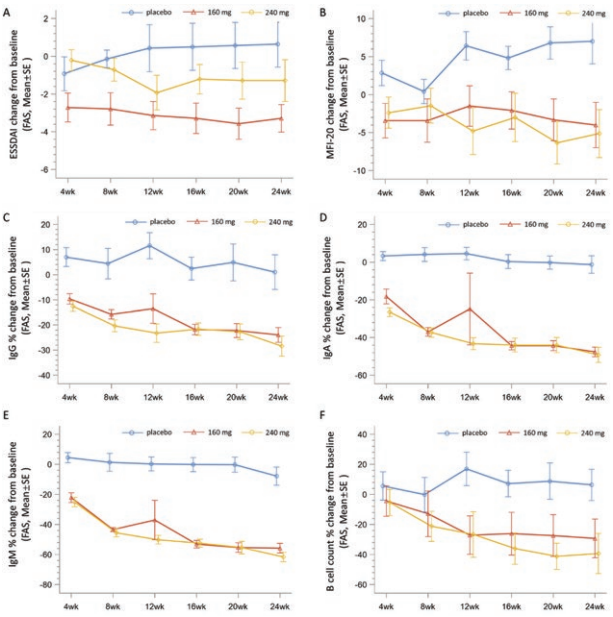


Figure 1. Change from baseline in ESSDAI (A) and MFI-20 (B). Percent (%) change from baseline in IgG (C), IgA (D), IgM (E) and CD19$^+$ B cells (F).

Table 1. Key efficacy and safety data.

Efficacy, FAS	Placebo (N=14)	Telitacicept 160 mg (N=14)	Telitacicept 240 mg (N=14)
ESSDAI change from baseline, LS mean (95%CI)			
Week 12	0.8(-1.0 ~ 2.6)	-3.6(-5.4 ~ -1.8)*	-2.5(-4.4 ~ -0.5)*
Week 24	0.5(-1.5 ~ 2.4)	-3.8(-5.7 ~ -2.0)*	-2.3(-4.4 ~ -0.2)
ESSPRI change from baseline, Mean ±SD			
Week 12	-0.10±1.859	-0.78±1.449	-0.55±1.182
Week 24	-0.76±1.678	-1.09±1.597	-0.61±1.876
MFI-20 change from baseline, Mean ±SD			
Week 12	6.4±6.44	-1.5±9.21*	-4.8±9.72*
Week 24	7.0±9.35	-4.0±10.30*	-5.1±8.94*
Safety, SS	**Placebo (N=14)**	**Telitacicept 160 mg (N=14)**	**Telitacicept 240 mg (N=14)**
TEAE, n(%)	13(92.9%)	12(85.7%)	14(100.0%)
SAE, n(%)	1(7.1%)	0(0)	0(0)
Infections and infestations# (SOC), n(%)	8(57.1%)	9(64.3%)	5(35.7%)
Upper respiratory tract infections, n(%)	7(50.0%)	6(42.9%)	4(28.6%)
Herpes zoster, n(%)	1(7.1%)	2(14.3%)	0(0)
Infectious pneumonia, n(%)	2(14.3%)	0(0)	0(0)

*p<0.05 vs. Placebo. #AEs occoured in ≥ 2 subjects in any group were listed. FAS, full analysis set; SS, safety set; LS, least square; SD, standard deviation; TEAE, treatment-emergent adverse event; SAE, serious adverse event; SOC, system organ class.

Conclusion: Telitacicept showed clinical benefits and a favorable safety profile in patients with pSS.

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OP0143

EFFICACY AND SAFETY OF DAZODALIBEP (VIB4920/HZN4920) IN SUBJECTS WITH SJÖGREN'S SYNDROME: A PHASE 2, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PROOF OF CONCEPT STUDY

Keywords: Safety, Randomized control trial, Sjögren syndrome

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Background: Sjögren's syndrome (SS) is a chronic, systemic autoimmune disease affecting exocrine glands, primarily the salivary and tear glands, with potentially severe manifestations in multiple organs. No approved disease-modifying therapies exist. Dazodalibep (DAZ) is a biologic antagonist of CD40L.
Objectives: The objective of this study was to evaluate the efficacy and safety of DAZ therapy in adult SS subjects with moderate-to-high systemic disease activity (NCT04129164).
Methods: We conducted a randomized, double-blind, placebo-controlled, cross-over study to evaluate DAZ therapy in adult SS subjects with moderate-to-high systemic disease activity, as defined by a EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) score ≥ 5. Eligible subjects were randomized 1:1 to receive intravenous DAZ 1500 mg or placebo (PBO) Q2W x 3 doses, then Q4W x 4 additional doses. Starting on Day 169, subjects initially randomized to DAZ received PBO Q4W x 5 doses and subjects randomized to PBO received DAZ Q4W x 5 doses and were then followed for 12 weeks. The primary endpoint was the change from Baseline in ESSDAI at Day 169. Safety assessments included the incidence of adverse (AEs), serious AEs (SAEs), and AEs of special interest (AESIs).
Results: The 74 randomized subjects all received ≥1 dose of study medication (DAZ, N=36; PBO, N=38). The baseline demographics and disease characteristics were balanced between the two groups. The change from Baseline to Day 169 in ESSDAI score (LS mean ± SE), was -6.3 ± 0.6 in DAZ-treated subjects compared to -4.1 ± 0.6 in the PBO group, a difference of -2.2 (p = 0.0167). Compared to the PBO group, the DAZ group showed positive trends in the EULAR Sjögren's Syndrome Patient Reported Index score, and Functional Assessment of Chronic Illness Therapy-Fatigue score at Day 169. A post-hoc responder analysis of subjects achieving high levels (5 and 6 points) of improvement on ESSDAI favored DAZ (61.1% and 60.0%) over PBO (35.1% and 34.3%). The reported AEs were generally mild through Day 169 and similar in frequency between treatment groups. The most frequently reported AEs occurring in ≥5% of DAZ-treated subjects and >PBO were COVID-19, diarrhea, dizziness, ligament sprain, upper respiratory tract infection, contusion, device allergy, fatigue, hypertension, and oropharyngeal pain. Two SAEs were reported in a single DAZ-treated subject: this subject was a 59-year-old female who experienced a grade 3 SAE of COVID-19 infection and later died of unknown cause 46 days after last administration of DAZ (12 days after COVID-19 diagnosis). There was a single AESI of herpes zoster in a DAZ-treated subject.
Conclusion: DAZ is a potential new therapy for the treatment of systemic disease activity in patients with SS. SS subjects with moderate-to-high systemic disease receiving DAZ experienced a statistically significant reduction in disease activity relative to PBO as measured by the improvement in ESSDAI score. Except for a case of severe COVID-19 infection, DAZ therapy in SS subjects appeared to be well tolerated. Larger controlled trials of DAZ therapy for SS are warranted to further explore its safety profile and confirm its clinical efficacy.

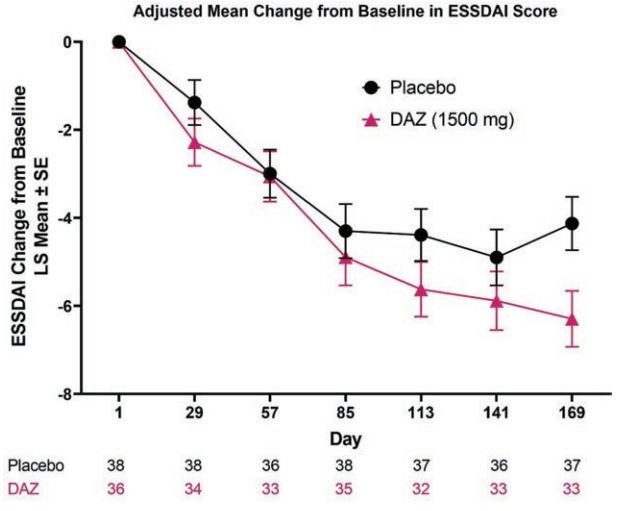


Figure 1.

Table 1. Efficacy and Safety Data

	PBO N=38	DAZ 1500 mg N=36
Efficacy		
ΔESSDAI, LS mean (SE) †	-4.1 (0.6)	-6.3 (0.6)*
ΔESSPRI, LS mean (SE) †	-1.12 (0.29)	-1.80 (0.31)
ΔFACIT-Fatigue, LS mean (SE) †	5.8 (1.6)	8.1 (1.6)
AE Summary, n (%)		
≥1 AE	23 (60.5)	28 (77.8)
≥1 related AE	8 (21)	10 (27.8)
≥1 SAE	0	1 (2.8)
≥1 related SAE	0	0
≥1 AE leading to discontinuation	0	0
≥1 AESI	0	1 (2.8)
≥1 Death	0	1 (2.8)

Efficacy endpoints as of Day 169; † Analyzed using MMRM; Comparisons vs PBO; *p<0.05; AE summaries based on AEs that occurred through Day 169; AE, adverse event; AESI, adverse event of special interest; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI, EULAR Sjögren's Syndrome Patient Reported Index; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; PBO, placebo; SAE, serious adverse event

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Risk factors and their treatment in the progression of osteoarthritis

OP0144

ASSOCIATION OF HEALTHY LIFESTYLES WITH ALL-CAUSE AND CAUSE-SPECIFIC MORTALITY AMONG INDIVIDUALS WITH OSTEOARTHRITIS: A PROSPECTIVE COHORT STUDY OF THE UK BIOBANK

Keywords: Epidemiology, Osteoarthritis, Lifestyles

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Background: Healthy lifestyles are thought to reduce the risk of multiple causes of mortality in general population. However, whether and to what kind of healthy lifestyles could offset the risk of multiple causes of mortality in patients with osteoarthritis (OA) are unknown.

Objectives: This study aimed to investigate the association of both individual and combined healthy lifestyle factors with the risk of all-cause and cause-specific mortality among participants with OA.

Methods: 104,142 OA participants were included from the UK Biobank (mean age 60±7.0). A summed healthy lifestyle score was constructed using body mass index (BMI) and self-reported diet, sleep duration, physical activity, sedentary time, social connection, smoking and alcohol drinking. Restricted cubic spline (RCS) and Cox proportional hazards models were used to examine the associations of individual factors and a combined healthy lifestyle score with the risk of all-cause and cause-specific mortality.

Results: During a median follow-up of 12.7 years, 9915 deaths after the first two years follow-up were recorded. Using RCS models, sleep duration had a U-shaped (with a nadir at 7 h/day), moderate physical activity (MPA) had an L-shaped (with a turning point at 550 min/week), while BMI and vigorous physical activity (VPA) had J-shaped (with turning points at 28 kg/m^2 and 240 min/week respectively) associations with all-cause mortality. In multivariable Cox models, each lifestyle factor was significantly associated with all-cause mortality, and hazard ratios (95%CI) associated with newly constructed healthy lifestyle score (scoring 7-8 vs. 0-2) were 0.29 (0.25-0.35) for all-cause mortality, 0.40 (0.32-0.50) for cancer-cause mortality, 0.22 (0.17-0.30) for cardiovascular disease mortality, 0.27 (0.16-0.48) for digestive-cause mortality and 0.18 (0.12-0.25) for respiratory mortality.

Conclusion: This study introduced a healthy lifestyle pattern that could significantly reduce the risk of all-cause and cause-specific mortalities in OA patients.

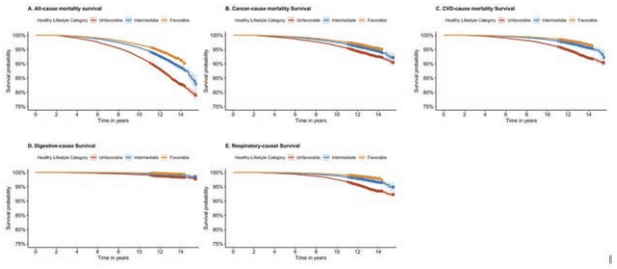


Figure 1. Kaplan-Meier survival curve of healthy lifestyle categories and mortality

Table 1. Multivariable cox regression analysis of lifestyle factors in relation to mortality

	All cause mortality			Cancer cause mortality			CVD cause mortality		
	HR	*95% CI*	*P*	*HR*	*95% CI*	*P*	*HR*	*95% CI*	*P*
Healthy lifestyle score									
0-2	1			1			1		
3	0.65	(0.61,0.7)	**1.35×10^{-30}**	0.71	(0.64,0.79)	**6.63×10^{-10}**	0.63	(0.57,0.7)	**3.63×10^{-17}**
4	0.5	(0.46,0.53)	**1.17×10^{-87}**	0.58	(0.53,0.65)	**1.08×10^{-24}**	0.44	(0.4,0.49)	**1.49×10^{-52}**
5	0.4	(0.37,0.43)	**1.56×10^{-136}**	0.49	(0.45,0.55)	**1.27×10^{-38}**	0.34	(0.3,0.38)	**3.42×10^{-81}**
6	0.36	(0.33,0.39)	**2.01×10^{-118}**	0.46	(0.4,0.52)	**1.88×10^{-35}**	0.31	(0.27,0.36)	**1.55×10^{-62}**
7-8	0.29	(0.25,0.35)	**2.13×10^{-45}**	0.4	(0.32,0.5)	**1.11×10^{-15}**	0.22	(0.17,0.3)	**4.36×10^{-23}**
Healthy BMI	0.84	(0.81,0.88)	**1.54×10^{-14}**	0.9	(0.84,0.95)	**< 0.01**	0.77	(0.72,0.83)	**6.40×10^{-13}**
Healthy diet score									
0	1			1			1		
1	0.82	(0.75,0.9)	**1.24×10^{-05}**	0.78	(0.69,0.89)	**< 0.01**	0.85	(0.74,0.97)	0.02
2	0.76	(0.7,0.83)	**3.52×10^{-10}**	0.75	(0.66,0.84)	**1.84×10^{-06}**	0.78	(0.69,0.89)	**< 0.01**
3	0.71	(0.65,0.77)	**4.26×10^{-15}**	0.7	(0.62,0.79)	**1.29×10^{-08}**	0.68	(0.6,0.78)	**2.15×10^{-08}**
4-5	0.66	(0.6,0.73)	**1.11×10^{-18}**	0.67	(0.59,0.76)	**6.77×10^{-10}**	0.65	(0.57,0.75)	**3.60×10^{-09}**
Healthy sleep	0.81	(0.78,0.85)	**7.67×10^{-24}**	0.9	(0.85,0.95)	**< 0.01**	0.76	(0.71,0.81)	**1.72×10^{-17}**
Healthy physical activity score									
0	1			1			1		
1	0.93	(0.87,1)	0.06	0.92	(0.84,1.01)	0.09	0.95	(0.84,1.06)	0.35
2	0.79	(0.7,0.89)	< 0.001	0.76	(0.65,0.9)	**< 0.01**	0.83	(0.68,1)	0.06
Unhealthy sedentary	1.41	(1.33,1.51)	**3.11×10^{-27}**	1.36	(1.24,1.49)	**1.33×10^{-11}**	1.48	(1.34, 1.64)	**8.52×10^{-15}**
Healthy social connection	0.66	(0.62,0.7)	**7.81×10^{-44}**	0.75	(0.68,0.81)	**4.05×10^{-11}**	0.63	(0.58, 0.69)	**2.18×10^{-23}**
No current smoking	0.5	(0.47,0.52)	**2.19×10^{-142}**	0.49	(0.46,0.53)	**1.35×10^{-73}**	0.51	(0.47, 0.56)	**9.73×10^{-54}**
No current drinking	0.67	(0.63,0.71)	**4.20×10^{-41}**	0.83	(0.76,0.91)	**6.32×10^{-05}**	0.60	(0.55, 0.65)	**2.72×10^{-30}**

Adjustment for age, sex, Townsend deprivation index, race, education, employment;

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Disclosure of Interests: None Declared.
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OP0145

ASSOCIATION OF HEALTHY LIFESTYLE, GENETIC SUSCEPTIBILITY AND INCIDENCE OF OSTEOARTHRITIS: A NATIONAL PROSPECTIVE COHORT STUDY

Keywords: Lifestyles, Osteoarthritis, Genetics/Epigenetics

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Background: Osteoarthritis (OA) is the commonest arthritis worldwide and affects approximately 7% of the global population[1]. Previous studies reported that stick to a healthy lifestyle could reduce the risk of OA[2]. However, whether and to what extent people with different genetic susceptibility of OA could benefit from a healthy lifestyle is still unknown.

Objectives: We aimed to detect the association between healthy lifestyle, genetic susceptibility and incident OA in the UK biobank study.

Methods: After excluding participants with missing data and performing multiple imputation, we included 317884 participants from UK biobank. Lifestyle factors included body mass index (BMI), diet, physical activity, sleep behavior and sedentary behavior. BMI lower than 30 kg/m2 was defined as healthy status. At least

4 of 7 healthy dietary components was defined as healthy diet. Medium level of physical activity (270-660 min/week) was classified as a healthy physical activity for OA. Healthy sleep behaviors were defined as sleep 7–8 h/day. Sedentary time less than 4 hours was regarded as low risk status. The healthy lifestyle score was constructed as the sum of five lifestyle factors, ranging from 0 to 5 and was subsequently categorized into three groups including unfavorable, intermediate and favorable (0–1, 2-3 and 4–5). Genetic susceptibility was calculated by using polygenic risk score (PRS) of OA. Specifically, individual single nucleotide polymorphism (SNP) was coded as 0, 1, and 2 according to the number of risk alleles. The coefficient of significant SNPs of OA reported in previous Genome Wide Association Studies (GWAS) were regarded as weight of genotype of each SNPs. Participants with OA were identified as having a diagnosis using ICD-9 and ICD-10 codes for total/ knee/ hip OA, or were identified as self-reported total/ knee/ hip OA at baseline. Covariates included age, sex, household income, education, deprivation index, glucosamine use and comorbidities. Cox regression analyses were performed to examine the association of healthy lifestyle, genetic susceptibility and incident OA.

Results: Comparing to unfavorable lifestyle, favorable lifestyle was significantly associated with a lower risk of total OA across low, intermediate and high genetic risk groups (HR, 0.64; 95%CI, 0.58-0.70; HR, 0.59; 95%CI, 0.56-0.63 and HR, 0.58; 95%CI, 0.53-0.64, respectively). Favorable lifestyle was also significantly associated with lower risk of knee OA across low, intermediate and high genetic risk groups (HR, 0.40; 95%CI, 0.33-0.48, HR, 0.47, 95%CI, 0.42-0.51 and HR, 0.45; 95%CI, 0.39-0.53, respectively). For hip OA, adherence to favorable lifestyle was also significantly associated with lower risk of OA incidence across low, intermediate and high genetic risk groups (HR, 0.75; 95%CI, 0.62-0.92, HR, 0.65, 95%CI, 0.58-0.72 and HR, 0.75; 95%CI, 0.65-0.88, respectively), compared to unfavorable lifestyle. No significant interaction was detected between lifestyle and PRS for total/ knee/ hip OA.

Conclusion: These data suggest that healthier lifestyle is consistently associated with lower risk of OA, regardless of genetic risks. Our findings highlight the importance of adherence to an overall healthy lifestyle in attenuating the risk of OA.

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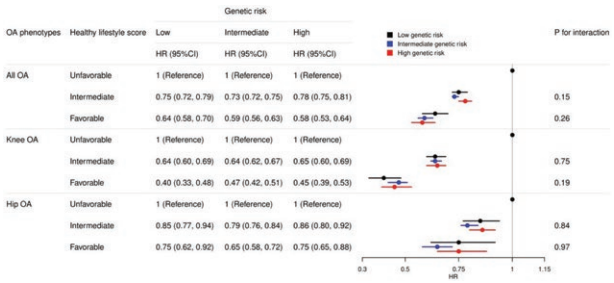


Figure 1. Association between healthy lifestyle score and total/ knee/ hip osteoarthritis stratified by different levels of genetic risk. Abbreviation: OA, osteoarthritis; HR, hazard ratio. P for interaction: interactions between low genetic risk and high genetic risk group.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0146

GENETIC EVIDENCE REVEALS A CAUSAL RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND OSTEOARTHRITIS

Keywords: Genetics/Epigenetics, Osteoarthritis

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Background: Osteoarthritis (OA) is a common musculoskeletal disease [1]. Research evidence indicates that exercise can reduce OA patients' joint pain to an extent [2]. However, the genetic causal relationship between physical activity (PA) and OA remains vague.

Objectives: In our study, Mendelian randomization (MR) was conducted to explore the causal assosiation of PA and OA.

Methods: PA was divided into two different phenotypes, including sedentary behavior and physically active behavior. Genome-wide association study (GWAS) data for PA [3] was obtained from the UK Biobank. We selected single nucleotide polymorphisms (SNPs) that were strongly associated ($p < 5 \times 10-8$) with two PA phenotypes and checked them on PhenoScanner removing SNPs associated with confounders. The OA data was derived from a GWAS among 455,221 individuals (77052 samples and 378169 controls) of European descent [4]. To assess the causality of PA on OA, inverse variance weighting (IVW), MR-Egger, and weighted median (WM), were employed. IVW was applied for the principal analysis. To ensure the robustness of our result, Cochran's Q test, MR-Egger intercept test, and leave-one-out analysis were used to assess the sensitivity of the study.

Results: Among the tested sedentary behavior, the length of mobile phone use increases the risk of knee OA (odds ratio (OR):1.560, 95% confidence interval (CI):1.167-2.086, p=2.683×10-3) and hip or knee OA (OR:1.334, 95%CI:1.026-1.734, p=3.141×10-2). After removing SNPs associated with smoking, alcohol consumption, lymphocyte count, and heart disease, we also found evidence of a potential adverse effect of genetically predicted time spent watching television (TV) on knee OA (OR:1.913, CI:1.450-2.523, p=4.388×10-6) and hip or knee OA (OR:1.611, 95%CI:1.288-2.014, p=2.860×10-5). No potential causal link was observed between physically active behavior and OA through the IVW analysis(p>0.05). MR-Egger and WM yielded identical effects to IVW. Any potential heterogeneity or pleiotropy was not found.

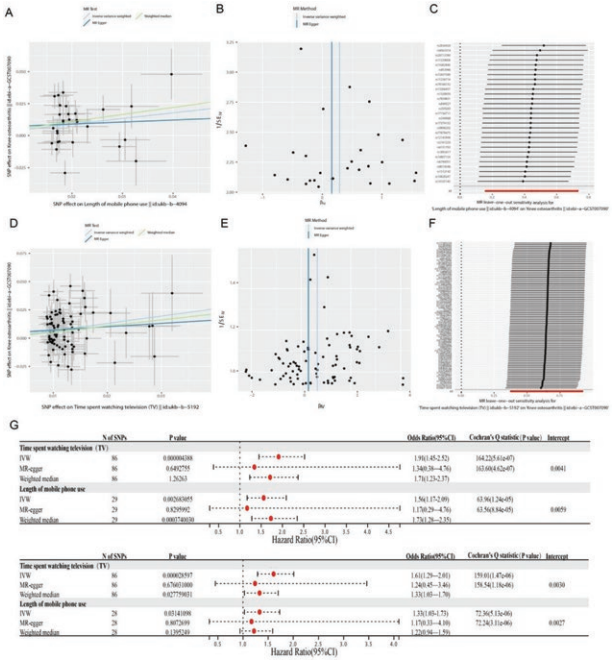


Figure 1. The causal associations between physical activity (PA) and osteoarthritis (OA) were evaluated by the odds ratio (OR) values of IVW, MR-Egger, and WM. Scatter plots (A), funnel plots (B), and leave-one-out plots (C) assessed the length of mobile phone use on the risk of OA. Scatter plots (D), funnel plots (E), and leave-one-out plots (F) assessed the time spent watching television (TV) on the risk of OA. Forest plot (G) of association between PA and OA

Conclusion: Sedentary behavior can increase the risk of OA, but no direct causal relationship is observed between physically active behavior and OA. It indicates that OA patients should avoid a sedentary lifestyle.

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Disclosure of Interests: None Declared.

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OP0147

COMPARED TO PEOPLE WHO NEVER SMOKED, CURRENT SMOKERS BUT NOT FORMER SMOKERS HAVE WORSE KNEE OSTEOARTHRITIS SYMPTOMS AND STRUCTURAL DEFECTS: INDIVIDUAL PARTICIPANT DATA META-ANALYSES OF MULTI-COHORT DATA

Keywords: Osteoarthritis

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Background: As smoking causes inflammation, and inflammation is implicated in the development of osteoarthritis, it is conceivable that smoking would have negative effects on knee osteoarthritis (KOA). However, results from prior studies are controversial and unclear, with some studies even finding that smoking protects against KOA.

Objectives: To describe the association between smoking and KOA (symptoms and structural defects) in people with or at risk of KOA in a multi-cohort study using individual participant data (IPD) meta-analyses, which are considered the 'gold standard' for the synthesis of quantitative evidence.

Methods: We performed IPD meta-analyses using data from three independent cohorts: the Osteoarthritis Initiative (OAI) and the Multicenter Osteoarthritis Study (MOST) from the USA; and the Cohort for Hip and Cohort for Knee (CHECK) from the Netherlands. We assessed the association between smoking status at baseline (never smokers; current smokers; and former smokers) and the outcomes of symptoms and structural defects in KOA, either cross-sectionally at baseline or longitudinally over 4 to 5 years of follow-up. For symptoms, we assessed pain, disability, and stiffness using the Western Ontario and McMaster Universities Arthritis Index (WOMAC). For structural defects, we assessed overall structural defects and three individual structural features (i.e., joint space narrowing; osteophytes on the femoral surface; and osteophytes on the tibial surface), on both the lateral and medial sides of the knee, from radiographs. Overall structural defects were assessed using Kellgren-Lawrence (KL) grades. A knee with a KL grade ≥ 2 is considered to have 'radiographic KOA'. The three individual structural features were assessed using Osteoarthritis Research Society International (OARSI) grades.

Results: We investigated 14,470 knees from 7,304 participants for the outcomes of symptoms, and 12,337 knees from 6,455 participants for the outcomes of structural defects. In our cross-sectional analyses, compared to never smokers, current smokers had baseline scores for pain, disability, and stiffness that were greater by 1.01 (95% confidence interval [CI] 0.60 to 1.41) units, 3.62 (95% CI 2.04 to 5.20) units, and 0.42 (95% CI: 0.29 to 0.54) units, respectively. In contrast, former smokers had baseline scores for pain, disability, and stiffness that were no different from those of never smokers (with differences in scores being 0.11 95% CI: -0.08 to 0.29 units; -0.09 95% CI: -1.14 to 0.97 units; and 0.06 95% CI: -0.08 to 0.20 units, respectively). In terms of structural defects, our cross-sectional analyses showed that neither current smokers nor former smokers were any worse than never smokers with respect to grades for overall structural defects or individual structural features. However, compared to never smokers, current smokers had greater odds of having radiographic KOA (odds ratio [OR] 1.25 95% CI: 1.02 to 1.52), while former smokers were no different from never smokers for this outcome (OR 0.91 95% CI: 0.83 to 1.01). In our longitudinal analyses, compared to never smokers, only one outcome showed a difference between groups. Specifically, current smokers had greater odds of degeneration of the individual structural feature of joint space narrowing on the medial side of the knee over 4 to 5 years of follow-up (OR 1.27 95% CI: 1.01 to 1.60), while former smokers were no different from never smokers for this outcome (OR 1.02 95% CI: 0.84 to 1.24).

Conclusion: Current smoking may have negative effects on, and quitting smoking could be important in preventing or slowing, both the symptoms and structural defects of KOA in people with or at risk of KOA.

Acknowledgements: We acknowledge the contributions of the study participants, investigators, research staff involved, and the provision of data sets and/or research tools from 3 cohort studies: the OAI, the MOST study, and the CHECK study.

Disclosure of Interests: Zubeyir Salis: None declared, Amanda Sainsbury-Salis Speakers bureau: presentation fees and travel reimbursements from Eli Lilly and Co, the Pharmacy Guild of Australia, Novo Nordisk, the Dietitians Association of Australia, Shoalhaven Family Medical Centres, the Pharmaceutical Society of Australia, and Metagenics., Consultant of: Served on the Nestlé Health Science Optifast VLCD advisory board from 2016 to 2018.

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OP0148

ASSOCIATIONS OF CHANGES IN BODY COMPOSITION MEASUREMENTS WITH RADIOGRAPHIC PROGRESSION OF HAND OSTEOARTHRITIS: DATA FROM THE DONG-GU STUDY

Keywords: Osteoarthritis

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Background: Previous studies have found that obesity is a risk factor for hand osteoarthritis (OA), but most have been cross-sectional studies and thus causality is uncertain. Longitudinal studies are instead needed to explore the association between obesity-related characteristics, including fat deposition/distribution and hand OA.

Objectives: The present study examined the association between changes in body composition measurements and the radiographic progression of hand OA in a longitudinal cohort.

Methods: In the Dong-gu Study population, 1,277 patients had hand radiographs at baseline and at the 6-year follow-up. X-rays of the hand joints were scored using a semi-quantitative grading method. Body composition was simultaneously measured in a bioelectrical impedance analysis using an InBody 520 analyzer. The relationship between changes in body composition measurements and the radiographic progression of hand OA was assessed in a multiple linear regression analysis.

Results: Total hand joint scores increased from 16.3 ± 5.74 at baseline to 18.8 ± 8.11 at year 6 ($P < 0.001$). Changes of body mass index, hip circumference (HC), waist-to-hip circumference (WHC), and fat mass were significantly associated with changes in the total hand joint scores ($P = 0.012$, $P < 0.001$, $P = 0.017$, $P = 0.008$, respectively). HC and WHC were significantly associated with radiographic progression of the hand joints, after adjusting for age, sex, physical activity, education status, smoking, alcohol consumption, hypertension, diabetes mellitus, dyslipidemia, chronic pulmonary disease, chronic liver disease, cardiovascular disease, cerebrovascular disease, and malignancy ($P < 0.001$, $P = 0.001$, respectively).

Conclusion: Changes in fat distribution were significantly associated with the radiographic progression of hand OA over 6 years, suggesting a role for the systemic effect of adipose tissue.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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OP0149

BIOMARKERS PROFILING IN OSTEOARTHRITIS PATIENTS WITH AND WITHOUT CHRONIC POSTOPERATIVE PAIN 5 YEARS AFTER TOTAL KNEE REPLACEMENT

Keywords: Pain, Diagnostic Tests, Biomarkers

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Background: Knee osteoarthritis (KOA) is a pathological condition prevalent in the general population. Exercise and pharmaceutical approaches are first-line treatments and the end-stage treatment is total knee replacement (TKR). Interestingly, around 20% of patients experience chronic postoperative pain and the reason for this is not fully understood. Pain in OA is multifactorial and low-grade chronic inflammation has been indicated as a potential cause. Pre-clinical evidence suggests that pro-inflammatory mediators, such as interleukin 6, can sensitize the peripheral and central nerves and these molecules might be associated to clinical pain. Clinical evidence has demonstrated differences in pro-inflammatory mediators when comparing patients with OA and healthy

individuals. A recent study has linked these profiles to chronic postoperative pain after TKR but an in-depth analysis, as seen for neuropathic and widespread pain is needed to advance the field. Currently, no specific biomarkers have been identified, despite initiatives on focused molecular inflammatory mediators. In an attempt to advance the field, a comprehensive analysis of an extensive network of cytokines, chemokines, and growth factors could identify the role of low-grade inflammation in patients with OA and potentially stratify patients more prone to experiencing pain.

Objectives: This study aimed 1) to evaluate preoperative serum levels of 92 inflammatory biomarkers in KOA patients compared to healthy controls, 2) to investigate preoperative differences of inflammatory biomarkers within different subgroups of patients with KOA and link these subgroups to clinical pain before and after TKR surgery.

Methods: Blood samples from preoperative patients with KOA scheduled for TKR (n=200) and healthy participants (n=39) were collected. After centrifugation of the serum was frozen at -80C until analysis. Serum samples were analyzed for inflammatory markers using the OLINK inflammation panel, which included 92 protein markers. Clinical pain was assessed using a Visual Analog Scale (VAS). Moreover, patients completed the Knee injury and Osteoarthritis Outcome Score (KOOS) questionnaire before and 12 months after TKR. Multivariate data analysis was performed to identify differences between patients and controls. Hierarchical cluster analysis (HCA) and Orthogonal Partial least squares discriminant analysis (OPLS-DA) was used for comparing groups (patients vs controls) and to identify subgroups within patients. T-tests were used to evaluate difference within the KOA cohort in terms of VAS and KOOS scores before and 12 months after TKR.

Results: Multivariate analysis showed that 12 proteins were differentially expressed between patients and controls (P<0.05). Hierarchical cluster and OPLS-DA analysis identified two patient subgroups (pat-1, n = 46; pat-2, n= 72) and 23 proteins were dysregulated comparing these two groups (p<0.01). Postoperative VAS and KOOS assessments were significantly different between the two subgroups (p-<0.05).

Conclusion: The present study suggest a low-grade inflammation in patients with KOA when compared to healthy pain free subjects. Additionally, this study suggests that a high inflammatory subgroup for patients with KOA exist and this group is likely to have more clinical and worst function 12-months after TKR.

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Disclosure of Interests: None Declared.

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OP0150 LONG-TERM EFFECTIVENESS OF A LIFESTYLE PROGRAM FOR OSTEOARTHRITIS: ONE-YEAR FOLLOW-UP OF THE "PLANTS FOR JOINTS" RANDOMIZED CLINICAL TRIAL

Keywords: Osteoarthritis, Non-pharmacological interventions, Diet and Nutrition

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Background: The 16-week Plants for Joints (PFJ) multidisciplinary lifestyle program, based on a whole-food plant-based diet, physical activity, and stress management, significantly reduced The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score compared to usual care in patients with knee and/or hip osteoarthritis (OA) and metabolic syndrome.[1,2]

Objectives: To determine the long-term effectiveness of the PFJ program on pain, stiffness, and function in patients with OA.

Methods: In the PFJ randomized clinical trial, patients with knee and/or hip OA and metabolic syndrome were randomized to receive the PFJ program in addition to usual care, or the control group which received usual care. After this 16-week period the control group also received the PFJ program. After completion of the PFJ program all participants were followed-up for one year with biannual visits and 6 adherence-promoting webinars. Medication changes were assessed at one year as an "increase," "stable," or "decrease" compared to baseline. The primary outcome was pain, stiffness, and function assessed by the WOMAC. Secondary outcomes included anthropometric and metabolic markers. A paired sample T-Test was used to determine the significance of the difference in outcomes at the start of the intervention versus at 1-year follow-up.

Results: Of the 64 participants who completed the initial 16-week clinical trial 84% were female with a mean (SD) age of 63 (6) and body mass index of 33 (5) kg/m² at baseline. The 47 (73%) participants who completed the one-year follow-up had a slightly greater average change in WOMAC score (–11.4 vs. –11.0), weight (–5.3 vs. –3.7 kg), and CRP (–1.2 vs. –0.2 mg/l) compared to non-completers, but showed less improvement in HbA1c (–2.1 vs. –2.9 mmol/mol). After a decrease during the PFJ program, the WOMAC score increased slightly again in the year after the program, whereby a mean 8.8-point difference was still observed after one year for completed cases compared to baseline values (95% CI 13.6 to 4.0; $p < 0.01$) (Figure 1). All components of the WOMAC remained significantly improved compared to before the program except for stiffness (Table 1). Of the 24 (38%) participants using pain medication at baseline, 11 (46%) were able to decrease the dosage or stop one or more medications. Pain medication was stable for 3 participants, and increased for 3, of which 1 newly started using medication. Furthermore, 3 (23%) and 8 (33%) participants decreased diabetes and cholesterol medication respectively while only 1 participant increased cholesterol medication. After the 1-year follow-up period weight and HbA1c remained significantly lower compared to baseline, although there was no longer a significant difference in CRP and LDL cholesterol.

Conclusion: The PFJ lifestyle program significantly decreased pain and improved function in patients with OA and metabolic syndrome and its effects were sustained until one year after program completion, with slightly less pain medication. Metabolic benefits found after the lifestyle intervention were partially sustained possibly indicating attenuated adherence to the lifestyle program in the 1-year follow-up.

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Table 1. Plants for Joints cohort at start and end of the 4-month intervention period and during the 1-year follow-up (6 and 12 months after completing the intervention) for completed cases (*n* = 47). Mean difference between start of intervention and end of follow-up.

	Intervention		Follow-up study			
	Start	End	6 months	12 months	Mean difference (95% CI)	*p*-value
WOMAC total	38.4	27	24.1	29.1	–8.8 (–13.7 to –4.0)	<0.001
WOMAC pain	7.3	5.1	4.5	5.6	–1.6 (–2.8 to –0.5)	<0.01
WOMAC stiffness	4	3	2.8	3.3	–0.6 (–1.1 to 0.0)	0.06
WOMAC function	27.1	18.9	16.9	20.2	–6.6 (–10.2 to –3.1)	<0.001
Weight (kg)	96.5	91.2	90.5	93.6	–3.8 (–6.0 to –1.7)	<0.001
LDL cholesterol (mmol/l)	3.6	3.3	3.4	3.5	–0.03 (–0.3 to 0.2)	0.8
HbA1c (mmol/mol)	42.3	40.2	39.9	40.1	–1.0 (–1.9 to –0.02)	<0.05
C-reactive protein (mg/l)	3.6	2.4	2.5	2.9	–1.0 (–2.0 to 0.1)	0.06

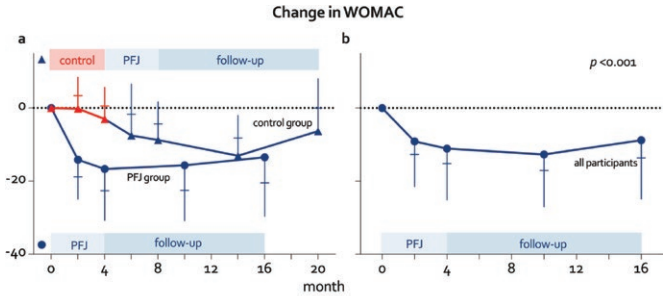


Figure 1: Mean change in WOMAC (a) during the randomized controlled trial phase and one-year follow-up period per trial arm and (b) for both trial arms before and after completing the lifestyle intervention and one year follow-up.

Figure 1.

Acknowledgements: NIL.

Disclosure of Interests: Carlijn Wagenaar: None declared, Wendy Walrabenstein: None declared, Marike van der Leeden: None declared, Martijn Gerritsen Grant/research support from: Received funding for research from Horizon Therapeutics., Jos Twisk: None declared, Martin van der Esch: None declared, Henriët van Middendorp: None declared, Peter Weijs: None declared, Dirkjan van Schaardenburg: None declared.

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OP0151

DULOXETINE PLUS EXERCISE FOR KNEE OSTEOARTHRITIS AND DEPRESSION (DEKODE)

Keywords: Non-pharmacological interventions, Mental health, Comorbidities

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Background: Depression is common in patients with knee OA, and clinical guidelines do not advise treating both conditions simultaneously. However, recent research recommends combining interventions that address symptoms of both conditions to maximize efficacy. Exercise improves pain, disability, and mood, but chronic pain and depression are barriers to physical activity in this population. Duloxetine is indicated to treat neuropathic pain and depression among knee OA patients and could serve as a therapeutic complement to exercise.

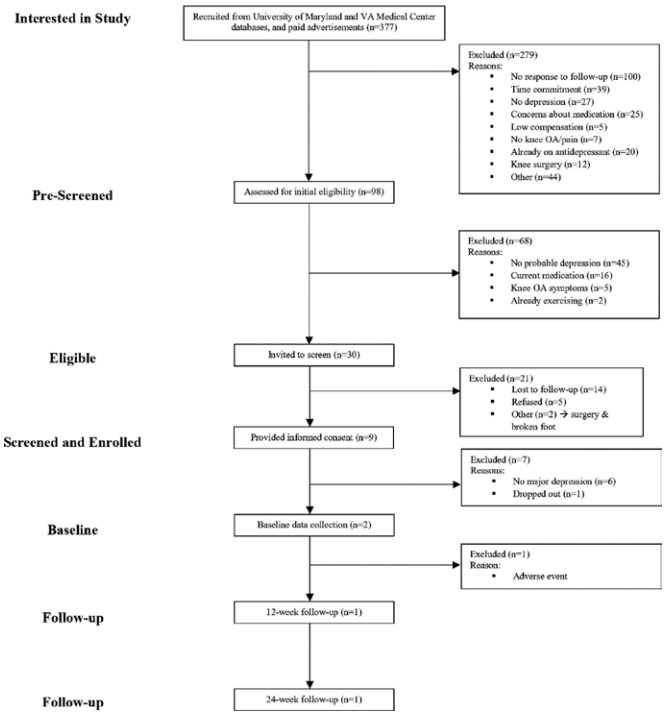
Objectives: To assess the feasibility of a 24-week, center-based, aerobic exercise program, plus duloxetine to treat knee OA and depression.

Methods: Participants were recruited between August 2021 and November 2022 from the University of Maryland and VA Maryland Health Care Systems and study advertisements. Inclusion criteria were: English speaking; age 40 years or older; symptomatic knee OA satisfying ACR criteria; major depression according to the SCID-5 (Structured Clinical Interview for DSM-V, ruling out history of bipolar disorder or psychotic symptoms; substance abuse disorder or suicidal ideation in the last year); no plans for knee surgery; and ability to walk on a treadmill. Exclusions included: exercising at least twice per week; taking duloxetine, antipsychotics, benzodiazepines, or opioid analgesics; cognitive impairment; comorbidity precluding exercise; and pregnant or lactating women. Participants began duloxetine (30 mg/day) as they started exercising, titrating up to a daily optimal dose of 60 mg/day. They were expected to complete 3 supervised treadmill walking sessions per week based on an individualized training plan defined by peak heart rate achieved during a graded exercise test. Data were collected at baseline and 12- and 24-weeks. Feasibility was evaluated via recruitment rates, reasons for drop out, and treatment adherence. Depression and pain severity were measured using the Hamilton Depression Rating Scale (HAM-D) and Knee Injury and Osteoarthritis Outcome Score (KOOS) pain subscale, respectively.

Results: Among 377 interested adults, 98 completed telephone pre-screening (Figure 1). Common reasons for not pre-screening included time commitment (n=39), no depression (n=27), concerns about medication (n=25), already on antidepressants (n=20), and knee surgery (n=12). There were 68 ineligible prescreened individuals who did not satisfy criteria for probable depression (n=45), medications (n=16), knee OA symptoms (n=5), or exercise (n=2). The 30 eligible candidates were invited to in-person screening visits, but 21 did not attend, and only 9 were enrolled. These 9 participants were older women (mean age=64.7 years), 8 identified as Black/African American, 7 attended and/or graduated from college, 3 were married, and 4 were retired. During the in-person screening process, 6 participants did not satisfy DSM-V criteria for major depression, 1 voluntarily withdrew from the study, and only 2 satisfied all eligibility criteria. One participant withdrew at baseline due to a non-study related adverse event and another completed the treatment protocol. The participant who completed the study was almost 100% adherent to duloxetine and experienced a reduction in depression severity from baseline to 24 weeks (HAM-D=25 to 1). By contrast, exercise compliance was low, with only 26% of planned sessions completed, and knee pain severity changed little from baseline (KOOS=41.7 to 44.4).

Conclusion: Treating knee OA and depression with a center-based exercise program and duloxetine had low feasibility. Critical design challenges amenable to change included the time commitment of 3 weekly supervised exercise sessions among interested individuals and depressive symptoms not satisfying diagnostic criteria for major depression for persons who wanted treatment. A hybrid or home-based exercise program plus duloxetine may be more feasible, and knee OA patients with depressive symptoms who are at risk for major depression could benefit from preventive intervention.

Figure 1. Study Sample Flow Diagram



REFERENCES: NIL.

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Crystal arthritis: what is new?

OP0152

DIAGNOSTIC PERFORMANCE OF HIP ULTRASOUND IN CALCIUM PYROPHOSPHATE DEPOSITION DISEASE

Keywords: Ultrasound, Validation, Crystal Arthritis

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Background: Calcium Pyrophosphate Deposition Disease (CPPD) is a chronic and potentially incapacitating disease. The reference standard for its diagnosis is the identification of calcium pyrophosphate (CPP) crystals in synovial fluid. Ultrasound (US) has been proven to be a high-sensibility and specificity tool for diagnosing CPPD. Still, its diagnostic performance for hip joint involvement has yet to be determined.

Objectives: To evaluate the diagnostic performance of US compared with synovial fluid analysis and histopathology (hyaline cartilage, fibrocartilage, synovial membrane) for the identification of hip CPP deposits.

Methods: We included patients older than 50 years with osteoarthritis programmed for hip replacement surgery in a tertiary referral hospital. Patients with an inflammatory or autoimmune rheumatologic disease were excluded. A pre-surgical US of the affected hip was performed with a LOGIQ™e device and a convex transducer (2-5 MHz); the anatomical structures evaluated were the acetabular fibrocartilage (FC) and the hyaline cartilage of the femoral head (HC), video tracking was recorded and a dichotomic score was assigned to determine the presence or absence of CPP deposits (in line with OMERACT definitions). During surgery, a sample of hip synovial fluid was obtained and examined using polarized light microscopy. After surgery, an experimented pathologist examined the FC and HC for CPP crystals.
Results: One hundred patients were included. 54% women with a mean age of 64.8±8.5 years. All patients had advanced osteoarthritis (Kellgren-Lawrence 3 = 33 and Kellgren-Lawrence 4=67; Tönnis 2= 34 and Tönnis 6= 66). A frequency of 62% CPP deposits was found through US examination, of which 19.4% were found on FC, 46.8% on HC, and 33.8% in both. Regarding pathology evaluation, a prevalence of 61% of CPP crystals was found; 13.1% were found on FC, 9.8% were found on HC, and 77.1% were found in both. 33% of patients had synovial effusion and 9% had synovial hypertrophy. Synovial fluid was obtained in 62% of patients, with a median volume of 0.8mL (IQR 0.5-1.5mL), and CPP crystals were found in 19.4% (12/62) of samples. Chondrocalcinosis in XR was found in 10%. A sensitivity of 90% and a specificity of 82% were obtained, the positive predictive value was 89%, and the negative predictive value was 84%. The area under the curve for the US compared with histopathology for the diagnosis of hip CPPD was 0.86 (CI 95% 0.78-0.94) (Figure 1).
Conclusion: US is a valid imaging method with good diagnostic performance for diagnosing CPPD in the hip joint.
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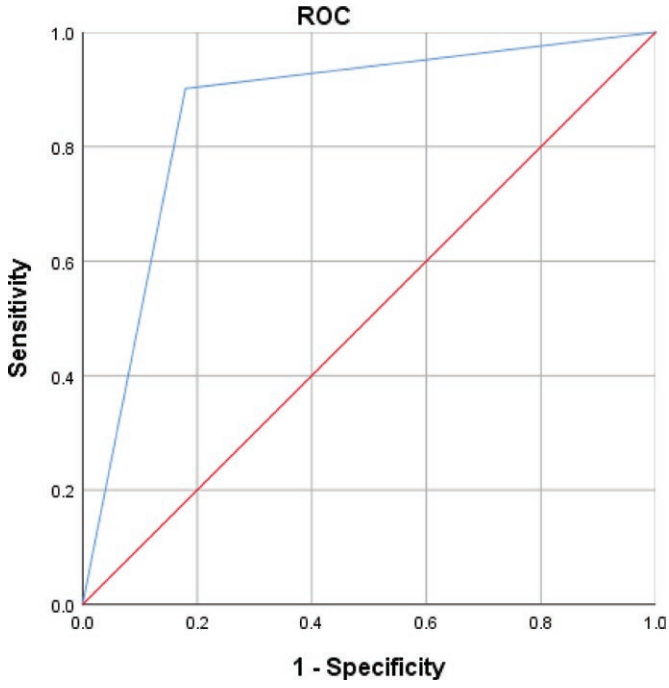


Figure 1. ROC curve of US

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0153

DEVELOPMENT OF A PROVISIONAL SELF-REPORTED DEFINITION FOR ACUTE CALCIUM PYROPHOSPHATE CRYSTAL ARTHRITIS: PRELIMINARY RESULTS OF A MULTICENTRE STUDY

Keywords: Crystal arthritis, Outcome measures, Patient reported outcomes

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Background: Acute calcium pyrophosphate (CPP) crystal arthritis is a common clinical presentation of CPP deposition (CPPD) disease, and recurrent episodes occur in 25% of patients with CPPD disease [1]. Although recent studies have evaluated the short-term efficacy of different drugs in acute CPP crystal arthritis [2-4], future studies would focus on reducing the frequency of these episodes in the long-term.
Objectives: To develop a patient-reported definition for acute CPP crystal arthritis in patients with CPPD disease.
Methods: Consecutive patients with a crystal-proven diagnosis of CPPD disease were enrolled in a cross-sectional study during routine inpatient and outpatient clinical care at five centres from France, Italy, and Spain. Patient-reported questions on the features of acute CPP crystal arthritis as per the OMERACT CPPD Working Group were evaluated by a rheumatologist [5]. The opinion of a second expert rheumatologist was the gold standard. Synovial fluid (SF) leukocyte count >2,000 cells/mcl was the reference standard in a sensitivity analysis. Definitions based on the number of criteria independently associated with acute CPP crystal arthritis and classification and regression tree approaches were developed.
Results: Data for 164 patients with CPPD disease were included. Their mean age was 71.8 years (SD 10.7 years), 104 (63.4%) were female. At the time of the assessment, 60/164 (36.6%) participants had acute CPP crystal arthritis, 25 (15.2%) had chronic inflammatory CPP crystal arthritis and 79 (48.2%) OA+CPPD according to the experts. SF was available in 44/164 (26.8%) participants, and 24/44 (54.6%) had a leukocyte count >2,000 cells/mcl in the SF. Patient-reported warm joint, patient-reported swollen joint, time from the pain-onset to-peak-pain (<48 hours), and patient-reported acute CPP crystal inflammatory arthritis were independently associated with the reference standard in multivariate analysis (Table 1). The greatest discriminating power was noted for the presence of 3 or more of the above 4 criteria [sensitivity 86.7% (95%CI: 75.4%-94.1%) and specificity 88.5% (95%CI: 80.7%-93.9%)] in the main analysis. The sensitivity and specificity of this definition using the SF as the gold standard were 83.3% (62.6%-95.3%) and 85.0% (62.1%-96.8%) (Figure 1). A classification tree identified patient-reported warm joint, followed by patient-reported inflammatory arthritis as the most informative variables for identifying acute CPP crystal arthritis [sensitivity 80.0% (95%CI:67.7%-89.2%) and specificity 90.4% (95%CI:83.0%-95.3%)].
Conclusion: Provisional self-reported definitions for acute CPP crystal arthritis in patients with CPPD were developed. The next step in the development of these criteria will be external validation.
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Table 1. Diagnostic performance of variables considered for the definition of self-reported acute CPP crystal arthritis

	Univariable ROC analysis		Multivariable logistic regression analysis
Self-reported domains	Sensitivity (%) (95%CI)	Specificity (%) (95%CI)	Adjusted OR (95%CI)
Warm joint	81.7 (69.6-90.5)	76.9 (67.6-84.6)	11.2 (3.5-36.2)
Tender joint	78.3 (65.8-87.9)	38.5 (29.1-48.5)	1.0 (0.3-3.6)
Swollen joint	86.7 (75.4-94.1)	70.2 (60.4-78.8)	6.6 (2.1-20.9)
Inflammatory arthritis	83.3 (71.5-91.7)	73.1 (63.5- 81.3)	12.7 (3.8.42.6)
Health assessment questionnaire >0.4/3	83.3 (71.5-91.7)	20.2 (13.0-29.2)	1.4 (0.4-5.3)
Time from the pain-onset to-peak-pain (<48 hours)	78.3 (65.8-87.9)	66.4 (56.4-75.3)	6.8 (2.3-20.5)
Visual Analogue Scale for pain at rest >6/10	43.3 (30.6-56.88	74.0 (64.5-82.1)	0.5 (0.2-1.5)

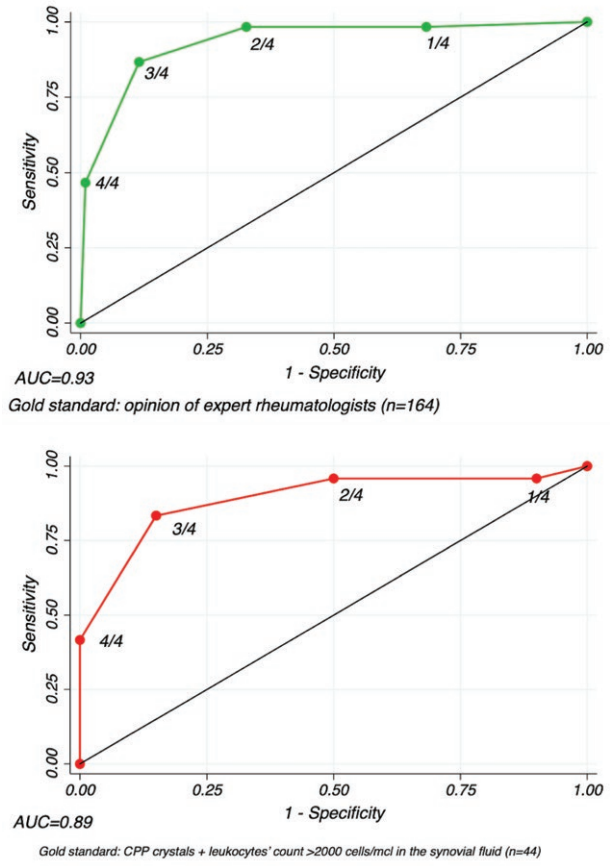


Figure 1. Internal validation of the self-reported definition for acute CPP crystal arthritis (≥3/4 criteria) using different reference standards.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0154

TOPHI AND CAROTID PLAQUE WERE RISK FACTORS OF MACE IN GOUTY ARTHRITIS PATIENTS: A LONGITUDINAL COHORT STUDY

Keywords: Ultrasound, Real-world evidence, Gout

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Background: Patients with gout carry an excess risk for cardiovascular disease (CVD). However, the prevalence of subclinical arthrosclerosis and its relationship with CVD risks and events in gout have not been reported.
Objectives: The objective of this study is to explore whether tophi and subclinical atherosclerosis could predict incident MACE (major adverse cardiac events) in gouty arthritis patients by ultrasonography. Determine whether incorporation of imaging data could improve CV(cardiovascular) risk prediction.
Methods: A single-center, cohort analysis was performed to assess subclinical artheroscelrosis at baseline since 2008. Patients were excluded if they had previous diagnosed CVD or cerabral vascular disease. The outcome of study was first MACE. The presence of subclinical atherosclerosis was assessed by cartoid intima-media thickness (CMIT) and total plaque area (TPA) was determined in a subgroup of patients by ultrasound. Scan of feet and ankles was performed bilaterally by ultrasonography at baseline. The association between tophi, measurements of carotid artherosclerosis and risk of developing and incident MACE was evaluated using Cox proprotional hazards models, with adjustment for the CVD risk scores.
Results: A total of 262 consecutive patients with primary gout were recruited, the mean age was 44.0 years; male 260 (99.2%). After a median follow-up of 10.3 years, 32 (12.2%) had incident MACE ascertained. Cox analysis showed that more than 2 tophi was significantly associated with an increased risk of develping MACE (HR: 9.96, 95%CI 8.89-43.6, *P*=0.001). The association remained significant after adjusting for CV risk scores in the multivariable models. In subgroup analysis, 240 patients had carotid ultrasound assessment, 28 (11.7%) patients experienced a first MACE event. In cox hazards model, which controlled for the CV risk scores, more than 2 tophi (HR 2.12-5.25, *P*<0.05) and and carotid plaque (HR 3.72-4.01, *P*<0.05), were both independent predictor of incident MACE in patients with gout seperately.
Conclusion: The presence of more than 2 tophi and carotid plaque by ultrasound could independently predict MACE in addition to conventional cardiovascular risk factors in gout patients.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0155

CLINICAL IMPACT OF CARDIOVASCULAR MONOSODIUM URATE DEPOSITS MEASURED BY DUAL ENERGY COMPUTED TOMOGRAPHY: A RETROSPECTIVE EVALUATION

Keywords: Gout, Cardiovascular disease, Imaging

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Background: Gout is the most common inflammatory arthritis and doubles the risk of cardiovascular (CV) events.[1] Classical risk calculators like the Framingham risk score fail to sufficiently explain this higher hazard. [2] Recently, MSU deposits were demonstrated in coronary arteries of 86.4% of investigated gout patients and were positively associated with coronary calcium score. [3] So far, however, the significance of these findings on CV events and consequent impact for gout patients is unknown.

Objectives: The aim of this retrospective analysis was to evaluate 1) possible correlations of CV MSU deposits with clinical gout diagnosis 2) the impact of CV MSU deposits on major CV events (MACE) in gout patients.
Methods: All patients, recruited at the radiology department of medical university Innsbruck with clinically suspicion of gout, performed dual energy computed tomography (DECT) of the affected limb and thorax between 01.05.2012 and 01.09.2019. Clinical and laboratory parameters were retrieved from patients´ charts. Classical CV risk factors (diabetes mellitus, smoking status, hypercholesterolemia, arterial hypertension) were evaluated. Medical history review identified the presence of MACE, defined as myocardial infarction and/or stroke. Patients were stratified in gout, hyperuricemia and controls. Gout was defined according to the ACR/EULAR classification criteria [4], uric acid levels over 6 mg/dl or ongoing uric acid lowering treatment without clinical signs of gout specified hyperuricemia patients and control group definition was achieved when uric acid levels were normal without concomitant uric acid lowering therapy and absence of gout symptoms. We performed the $\chi 2$- and Mann-Whitney tests for statistical appraisal of our dataset, using IBM SPSS (version 27). $P < .05$ was used as the cut-off for statistical significance.
Results: Overall, full data sets were available for 189 patients. Out of those, 131 (69.3%) revealed a clinical diagnosis of gout, 50 (38.2%) of these were tophaceous. 35 patients (17.5%) had hyperuricemia and 23 (12,2%) had neither gout nor elevated uric acid levels. Patients with CV MSU deposits (n=85/189, 45%, 62 gout patients, 19 hyperuricemia patients, 4 control patients) revealed higher acute phase reactants [C-reactive protein (p=0,001), erythrocyte sedimentation rate (p=0,007)], uric acid levels (p=0,007) and calcium scores (p<0,001) in comparison to patients without CV MSU deposits. MACE were observed in 35 patients (18.5%) with a higher prevalence in those patients revealing CV MSU deposits (n=22/85, 25,9%) compared to those without CV MSU (n=13/104, 12,5%) (p=0,022). All 22 patients with MACE and CV MSU were gout or hyperuricemia patients (Figure 1).
Conclusion: To our knowledge, this is the first evaluation of clinical features of patients revealing CV MSU deposits detected by DECT. The higher prevalence of MACE in patients with CV MSU deposits may help for risk stratification of gout patients, as classical CV risk scores or laboratory markers fail to identify patients at risk.
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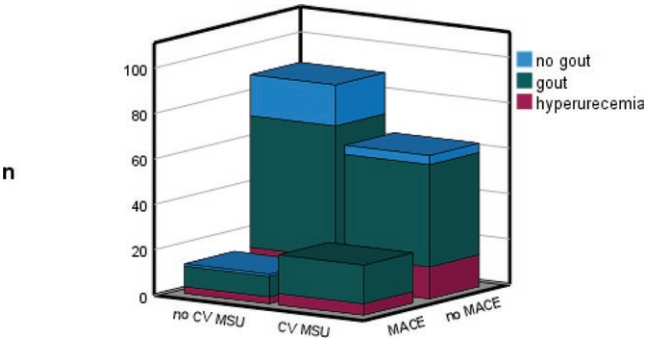


Figure 1. CV MSU deposits and MACE according to gout diagnosis. All patients with MACE and CV MSU were gout or hyperuricemia patients

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0156

INITIATION OF SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITORS AND RECURRENT GOUT FLARES IN GOUT PATIENTS WITH TYPE 2 DIABETES: A GENERAL POPULATION-BASED COHORT STUDY

Keywords: Epidemiology, Cardiovascular disease, Gout

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Background: Gout flares may increase risk of cardiovascular events.[1] Sodium-glucose cotransporter-2 inhibitors (SGLT2i) are associated with lower risk of incident gout (primary prevention); however, their role in recurrent flares among gout patients (secondary prevention), and their cardiovascular risk remains unknown.
Objectives: To assess rate of recurrent gout flares in prevalent gout patients with type 2 diabetes initiating SGLT2i versus dipeptidyl peptidase-4 inhibitors (DPP4i), two second-line glucose-lowering agents for type 2 diabetes.
Methods: This new-user, active comparator cohort study used administrative health data covering nearly all residents of British Columbia, Canada from Jan 2014 to June 2022, including all dispensed prescriptions, regardless of funder. Primary outcome was recurrent gout flare counts, ascertained by emergency department (ED), hospitalization, outpatient, and medication dispensing records.[1] We also restricted to flares requiring hospitalization or ED visit, and stratified by sex, age, gout intensity (presence of ≥1 gout-coded encounter or colchicine dispensing over past year) and diuretic and urate-lowering therapy (ULT) use. Myocardial infarction and stroke were secondary outcomes. We also assessed genital infection as positive control and osteoarthritis as negative control. Poisson and Cox proportional hazards models were used with 1:1 propensity matching.
Results: We included 8150 gout patients with type 2 diabetes (mean age 66, 71% male, 59% with cardiovascular disease). Flare rate was lower among SGLT2i initiators (52.4 events per 1000 person-years) than DPP4i initiators (79.7 events per 1000 person-years): rate ratio (RR) 0.66 (95% CI: 0.57, 0.75) and rate difference (RD) -27.4 (-36.0, -18.7). RR and RD for flares requiring hospitalization or ED visit were 0.52 (0.32, 0.84) and -3.4 (-5.8, -0.9), respectively. Results were consistent regardless of sex or age (**Table 1**). RR was also consistent regardless of baseline gout intensity or diuretic or ULT use, though absolute RD was higher in patients with greater gout intensity: -71.6 [-111.1, -32.1] vs. 20.8 [-28.8, -12.7] per 1000 person-years, respectively. Hazard ratio (HR) and RD were 0.69 (0.54, 0.88) and -7.6 (-12.4, -2.8) per 1000 person-years for myocardial infarction; HR, 0.81 (0.62, 1.05) for stroke. For control outcomes, SGLT2i initiators had higher risk of genital infection, while there was no difference in risk of osteoarthritis (**Table 1**).
Conclusion: For gout patients, SGLT2i may offer pleiotropic cardiovascular and recurrent flare frequency benefits.
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Table 1. Recurrent gout flare count and cardiovascular and control outcomes among gout patients with type 2 diabetes, after propensity-score matching

	SGLT2i compared with DPP4i [Reference]	
Gout Flare Count	**Rate Ratio (95% CI)**	**Rate Difference (95% CI)**
Overall (Primary outcome)	0.66 (0.57, 0.75)	-27.4 (-36.0, -18.7)
Flares requiring hospitalization or emergency visits	0.52 (0.32, 0.84)	-3.4 (-5.8, -0.9)
Subgroups		
Sex		
Men	0.63 (0.54, 0.73)	-33.6 (-44.3, -22.8)
Women	0.43 (0.29, 0.62)	-35.0 (-48.9, -21.0)
Age		
≤ 65 years	0.69 (0.56, 0.85)	-22.9 (-35.8. -10.0)
> 65 years	0.51 (0.42, 0.62)	-45.3 (-58.0, -32.6)
Baseline diuretic use		
Yes	0.75 (0.62, 0.92)	-24.8 (-42.1, -7.5)
No	0.63 (0.52, 0.77)	-24.1 (-34.2, -14.1)
Baseline urate-lowering therapy use		
Yes	0.66 (0.50, 0.87)	-25.2 (-41.8, -8.6)
No	0.56 (0.48, 0.66)	-39.5 (-50.4, -28.7)
Baseline gout intensity		
Higher	0.65 (0.51, 0.82)	-71.6 (-111.1, -32.1)
Lower	0.64 (0.53, 0.76)	-20.8 (-28.8, -12.7)
Cardiovascular Outcomes	**Hazard Ratio (95% CI)**	**Risk Difference (95% CI)**
Myocardial infarction	0.69 (0.54, 0.88)	-7.6 (-12.4, -2.8)
Stroke	0.81 (0.62, 1.05)	-3.9 (-8.3, 0.4)
Control Outcomes	**Hazard Ratio (95% CI)**	**Risk Difference (95% CI)**
Genital infection (POSITIVE)	2.15 (1.39, 3.30)	5.0 (2.2, 7.9)
Osteoarthritis (NEGATIVE)	1.07 (0.95, 1.20)	4.4 (-6.8, 15.7)

SGLT2i, sodium glucose cotransporter-2 inhibitors; DPP4i, dipeptidyl peptidase 4 inhibitors

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Disclosure of Interests: Natalie McCormick: None declared, Chio Yokose: None declared, Jie Wei: None declared, Leo Lu: None declared, Deborah Wexler Consultant of: Served on Data Monitoring Committees for Novo Nordisk, J. Antonio Aviña-Zubieta: None declared, Mary De Vera: None declared, Yuqing Zhang: None declared, Hyon Choi Consultant of: Ironwood, Selecta, Horizon, Takeda, Kowa, and Vaxart., Grant/research support from: Ironwood and Horizon.
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OP0157 GOUT AND RISK OF PARKINSON'S DISEASE, A POPULATION BASED STUDY FROM WESTERN SWEDEN

Keywords: Epidemiology, Crystal Arthritis, Gout

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Background: Gout affects 1-4% of the population in the industrialized world. Increased levels of serum urate is the strongest risk factor and "path variable" for gout development. Parkinson's disease (PD) is the second most common neurodegenerative disease in the world affecting 1% of the population over the age 60 in North America and Western Europe. A reduced risk of PD has been reported in association with smoking, caffeine consumption and higher serum urate levels.
Objectives: To determine the incidence of PD in all patients with gout compared to matched controls in the region of western Sweden (VGR).
Methods: All incident and prevalent gout cases from 2001 through 2019 were identified in the health care consumption database VEGA covering all health care in VGR. A case of gout was defined as having received a diagnosis of gout (M10) from a physician. Up to 5 controls from the census register were included matched by age, gender and municipality at year of first gout diagnosis (index-year). A case of PD was defined as having been given a diagnosis of PD (G20.9) at a visit to a physician. A PD diagnosis in the index-year and the 1 to 19 years before was considered prevalent in cases and controls and they were censored from the study. Cases and controls were followed until first of; end of study (2019-12-31), incident PD diagnosis, migration or death. Data on comorbidities at baseline/indexyear were retrieved from VEGA and information on education, death and migration were retrieved from registers at the National Board of Health and Welfare. Effect of gout on risk of PD was calculated using time dependent COX regression on whole population and stratified by sex, adjusted for age, sex, educational level, risk factors for gout (diabetes, obesity, chronic kidney disease (CKD)) and PD (cerebrovascular disease (CeVD), chronic obstructive pulmonary disease (COPD) as a proxy for smoking and malignant melanoma (MM)).
Results: We identified 48907 cases of gout (67% male) and 198717 (65% male) matched controls with a mean (SD) age of 68 (15) and 67 (15) respectively. In the case population we found 205 prevalent cases of PD compared to 2205 in the controls (prevalence ratio = 0.91 (95% CI:0.87-0.94)). They were all removed from further analysis. All comorbidities, (hypertension, ischemic heart disease, heart failure, CeVD, diabetes, dyslipidemia, obesity, CKD, COPD, and MM were significantly more common in the gout cases vs controls. During a median follow-up time of 5.8 years we identified 364 (0.7%) incident cases of PD in the gout population compared to 1965 (1.0%) in the controls. Adjusting for only age and sex in time dependent COX regression, (Model 1, Table 1) the relative risk reduction in gout patients for incident PD overall was 25% (HR 0.75; 95% CI:0.70-0.84). In age-adjusted models stratified by sex results were similar, HR 0.77 (95% CI:0.68-0.87) for men and HR = 0.69 (95% CI:0.54-0.87) for women. Adjusting also for known risk factors for gout and PD gave similar point estimates (model 2, Table 1).

Table 1. Time dependent COX regression on risk of incident gout in the total population and stratified by age and sex. Model 1 adjusted for age and sex, model 2 adjusted for age, sex, educational level, diabetes, obesity, CKD, CeVD, COPD, MM. HR = hazard ratio, CI confidence interval

	Model 1		**Model 2**	
	HR 95% CI	p-value	HR 95% CI	p-value
Total population	0.75 (0.70-0.84)	<.0001	0.75 (0.67-0.84)	<.0001
Men	0.77 (0.68-0.87)	<.0001	0.77 (0.68-0.88)	<.0001
Women	0.68 (0.53-0.86)	0.0014	0.68 (0.53-0.86)	0.0016
Age group 18-69				
Total population	0.78 (0.65-0.95)	0.0113	0.78 (0.65-0.95)	0.0137
Men	0.80 (0.65-0.99)	0.0415	0.82 (0.66-1.01)	0.0631
Women	0.67 (0.41-1.08)	0.0967	0.61 (0.37-1.00)	0.0505
Age group 70+				
Total population	0.71 (0.62-0.82)	<.0001	0.72 (0.63-0.84)	<.0001
Men	0.73 (0.62-0.85)	<.0001	0.73 (0.62-0.86)	0.0002
Women	0.68 (0.51-0.89)	0.0049	0.70 (0.53-0.93)	0.0130

Conclusion: Gout is associated with a significant risk reduction for incident PD. This may have implications for management of urate lowering therapy in persons with increased risk for PD and for the understanding of PD pathogenesis.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0158 PRODUCTION OF REACTIVE OXYGEN SPECIES IS PRIMED IN BLOOD NEUTROPHILS FROM GOUT PATIENTS

Keywords: Gout, Innate immunity, Cell biology

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Background: Gout is the most common inflammatory arthritis worldwide (1) and disease flares are triggered by the deposition of monosodium urate (MSU) crystals in and around the joints as a result of oversaturation of uric acid (urate) in the bloodstream. Macrophages phagocytose the crystals, leading to inflammasome activation and production of proinflammatory cytokines, mainly IL-1β. Neutrophils are recruited to the gouty inflamed site where they phagocytose the crystals, produce reactive oxygen species (ROS) and cast out neutrophil extracellular traps (NETs), the latter proposed to possess both pro- and anti-inflammatory properties in gout (2, 3). Gout patients have an increased risk for cardiovascular disease (4), and it is a paradox that uric acid, the major risk factor for gout and known to possess antioxidative properties, correlates with conditions associated with oxidative stress, such as cardiovascular disease. How urate levels in circulation affects neutrophil ROS production is unclear.

Objectives: To investigate whether peripheral neutrophils from gout patients respond to MSU crystals similarly as neutrophils form healthy controls.

Methods: Patients with polyarticular gout, diagnosed by a rheumatologist and identified at the Rheumatology Unit at Sahlgrenska University hospital and matched controls were included in the study. Peripheral blood from patients and controls were collected. Circulating blood neutrophils were isolated and intracellular ROS production was detected with luminol-amplified chemiluminescence. Quantification of NET Formation was performed by a fluorescence assay. Expression of surface markers was assessed by flow cytometry [5].

Results: MSU crystals stimulated neutrophils from gout patients to produce intracellular ROS and the response in neutrophils from gout patients was significantly higher as compared to the ROS response in control neutrophils. Neutrophils derived from gout patients were not primed with regard to cell surface markers and NET formation.

Conclusion: Blood neutrophils from gout patients display increased ROS responses both at baseline and upon MSU crystal stimulation. It is possible that small circulating MSU crystals in peripheral blood of gout patients increase neutrophil responsiveness and give rise to the enhanced background activity seen in our ROS experiments. Another explanation could be that pro-inflammatory cytokines in the bloodstream of patients with gout rime neutrophils to produce increased amounts of ROS.

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OP0159 **WITHDRAWN**

New Insights in the care and management of JIA___

OP0160 SUPPORTING CHILDREN AND YOUNG PEOPLE WITH JUVENILE IDIOPATHIC ARTHRITIS IN SCHOOLS, COLLEGES AND OTHER EDUCATIONAL SETTINGS THROUGH SCHOOL TOOLKITS

Keywords: Patient-led research, Education, Patient information and education

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Background: Juvenile Idiopathic Arthritis (JIA) is a heterogenous group of autoimmune disorders characterised by chronic joint inflammation, affecting children and young people (CYP) under the age of 16. CYP with JIA experience considerable physical and psychological impacts due to their condition. CYP spend a considerable amount of time at school, college or other educational settings. Whilst most CYP with JIA are able to access education, many require adaptations, awareness of their needs, or specific support to enable them to fully engage in learning. Families of CYP with JIA have reported a lack of awareness and understanding, and requested resources to enable schools to support their children in school.
Objectives: The aim of this work was to develop a School Toolkit to allow teachers and other school staff to confidently support CYP with JIA, and to assess its initial rollout.
Methods: Using a network of parents of CYP with JIA, including those with experience in working in educational settings, UK-based charity Juvenile Arthritis Research developed a resource aimed at schools, colleges, pre-schools and other educational settings: a Toolkit of information and resources. Given awareness of childhood arthritis is low, the Toolkit includes awareness-raising resources, aimed both at staff and all families connected to the school. Increased awareness can help improve diagnosis times and timely access to treatment in those not yet diagnosed. In addition, the Toolkit contains information about what JIA is, resources for schools to provide targeted interventions, and information on how schools can successfully support CYP with JIA. Finally, each Toolkit contains both a presentation for explaining arthritis to children in a classroom or group assembly setting, and a training presentation for delivery to staff, as well as digital copies of key materials and awareness-raising resources for distribution to parents and families. Recipients were invited to complete a short web-based survey to review the Toolkit.
Results: In the first six months after launching the new School Toolkit, around 100 Toolkits have been sent to schools in the UK, potentially providing information that arthritis affects children to over 100,000 families. Schools have advised they are using the resources in their settings, including giving lessons to children to explain what arthritis is, putting up posters highlighting the key signs and symptoms of JIA, and utilising the staff training resources. Feedback from schools was entirely positive, with one teacher reporting "Wow- it's fantastic. The student presentation is particularly impressive with how it translates all the key information in a child-friendly manner."
Conclusion: The development and supply of a Toolkit specifically for use in schools and colleges has helped raise awareness that children get arthritis, and provided resources to train and support school staff enabling them to confidently support CYP with JIA. Utilising the experience and skills of parents and teachers in the development of the Toolkit has ensured all resources are relevant and address the needs of both families and schools. Toolkits can be requested free of charge by schools in the UK from www.jarproject.org/toolkit.
Acknowledgements: Thanks to the children, young people, families and schools involved in the development of this vital resource.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.607

OP0161 24 MONTH RESULTS ON EFFECTIVENESS AND SAFETY OF A COMPARATIVE STUDY OF TOCILIZUMAB VERSUS TUMOUR NECROSIS FACTOR INHIBITION IN POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

Keywords: bDMARD, Real-world evidence, Registries

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Objectives: To evaluate 24-month effectiveness and tolerability/safety of tocilizumab (TCZ) versus tumour necrosis factor inhibitor (TNFi), analysing predictors of JADAS remission and minimal disease activity (MDA), comparing 1st and 2nd line TCZ.
Methods: BIKER WA 29358 is a 5-year multi-centre prospective, observational cohort study including polyarticular juvenile idiopathic arthritis (JIA) patients in Germany starting treatment between 2015 and 2020 with TCZ and matched patients starting an approved TNFi such as etanercept, adalimumab or golimumab. Clinical disease activity (JADAS), JADAS MDA/remission at 24 months, safety and drug adherence were assessed and compared between cohorts.
Results: The analysis set consisted of 342 participants with 24-month treatment data (TCZ, n=171; TNFi, n=171) (Table 1). Therefore, patients starting on TCZ were older and had a longer disease duration compared to TNFi patients. Efficacy was demonstrated by a marked and comparable decrease of the JADAS10 in upon both TCZ and TNFi from 14.6+/-6.6 and 14.6+/-6.2 at baseline to 2.5+/-3.4 and 2.7+/-3.6 at month 24. TCZ was used as 2nd line biologic in the majority of patients (84%) while TNFi were mostly 1st line biologics (86%). In the last observation carried forward analysis, at 24 month JADAS remission upon TCZ/TNFi treatment was achieved by 84.6%/76.9% in 1st line biologic users and 62.3/66.7% in 2nd line users. JADAS MDA was achieved in 100%/87.9% in 1st line and 84.4%/91.7% in 2nd line users of TCZ/TNFi. After 24 months of treatment residual disease activity as measured by the JADAS10 (mean +/SD) was lower in the 1st line TCZ cohort compared to the 2nd line (1.0+/-1.2 vs. 2.7+/-3.6), while in the TNFi cohort residual JADAS10 was comparable in 1st or 2nd line (2.7+/-3.8 vs. 2.5+/-2.6). Safety was assessed based on adverse events reporting. 113 (66%) patients in the TCZ cohort and 105 (61%) patients in the TNFi cohort reported adverse events with a higher rate in the TCZ cohort (89 vs. 73/100 patient years (PY), RR 1.2 (95%CI 1.0-1.5), p=0.029, Wald-test) as well as the rate of serious adverse events (10 vs. 3/100 PY; p=0.045). Cytopenias were more common in the TCZ cohort (13 vs. 1; p=0.010) and injection site reactions were more common in the TNFi cohort (13 vs. 6/100 PY, p=0.089). There was no case of death and no opportunistic infection. In the TCZ/TNFi cohorts, 71 (42%)/72 (42%) patients discontinued treatment, 43/30 due to lack of efficacy, 14/22 due to remission and 7/6 due to intolerance, respectively.
Conclusion: In this interim analysis, treatment targets were reached with similar frequency after 24 months of treatment with TCZ or TNFi. TCZ was used predominantly as 2nd line biologic. Higher rates of remission and minimal disease activity were observed in 1st line compared to 2nd line TCZ users. More adverse events were reported in the TCZ cohort but no new safety signals were noted. Observation is ongoing.

Table 1. Baseline patients' characteristics

Baseline patients' characteristics	Tocilizumab, N=171	Matched TNFi controls, N=171	P-value
Age at therapy start, mean (SD)	12.1 (3.5)	10.0 (4.4)	<0.001
Disease Duration, years, mean (SD)	5.4 (4.0)	3.2 (3.1)	<0.001
Rheumatoid-factor negative poly JIA, n (%)	115 (67%)	97 (57%)	n.s.
Rheumatoid-factor positive poly JIA, n (%)	17 (10%)	22 (13%)	n.s.
Extended oligoarthritis, n (%)	39 (23%)	52 (30%)	n.s.
Prior bDMARD, n (%)	143 (84%)	24(14%)	<0.001
Concomitant systemic steroids, n (%)	43 (25%)	42 (25%)	n.s.
Concomitant treatment with MTX, n (%)	93 (54%)	133 (78%)	<0.001
Number of active joints, mean (SD)	6.3 (6.9)	5.6 (4.8)	n.s.
CHAQ-DI, mean (SD)	0.61 (0.62)	0.63 (0.62)	n.s.
JADAS-10, mean (SD)	14.6 (6.6)	14,6 (6.2)	n.s.
Month 12 data			
JADAS-10, mean (SD)	3.5 (4.6)	3.8 (5.4)	n.s.
JADAS-MDA (≤6) -LOCF population	72.7%	77.4%	n.s.
JADAS-remission (≤2.7) -LOCF population	60.9%	57.9%	n.s.
Month 24 data			
JADAS-10, mean (SD)	2.7 (3.6)	2.5 (2.6)	n.s.
JADAS-MDA (≤6) -LOCF population	87.0%	85.2%	n.s.
JADAS-remission (≤2.7) -LOCF population	64.9%	69.1%	n.s.

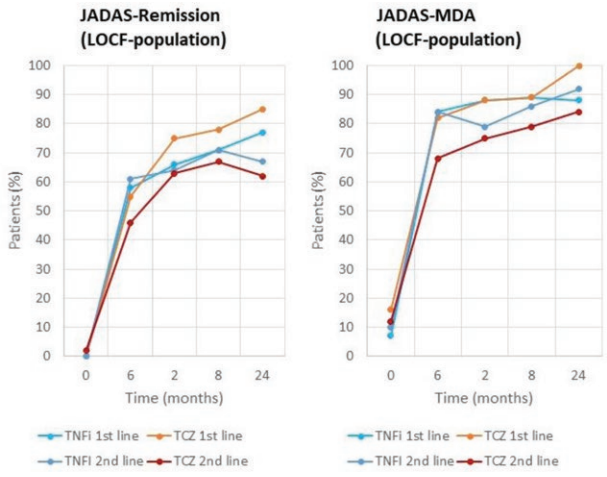


Figure 1.

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OP0162

PATTERNS OF CLINICAL JOINT INFLAMMATION IN JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Inflammatory arthritides, Treat to target

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Background: Juvenile idiopathic arthritis (JIA) often has a relapsing/remitting disease course, but it is not known whether recurrence of inflammation tends to be local.
Objectives: To assess whether JIA joint inflammation recurs locally in the same joints.
Methods: Joints of 91 patients of the BeSt for Kids study, a treat-to-target trial for children with recent-onset oligoarticular (n=11), rheumatoid factor negative polyarticular (n=72) and juvenile psoriatic JIA (n=8), were clinically assessed during two years (10 study visits). The association between joint inflammation at baseline and later inflammation in the same joint was assessed using a multilevel mixed-effects logistic regression model at joint level, adjusted for joint location and time point. With a Poisson model, the association between baseline joint inflammation and the number of study visits at which the same joint was recurrently inflamed (after inactivity of the joint) was tested. To assess whether an association between baseline and later clinical joint inflammation was a specific within-joint association, a permutation test was performed. A statistically significant result ($p<0.05$) indicates that the association between baseline and later joint inflammation is stronger in the observed data than in permutations with comparisons across random joints, suggesting an effect at joint level. To assess whether joint inflammation (ever during follow-up) was associated with radiographic damage (Poznanski Z-score) in the same (wrist) joint, a generalized linear mixed model was used.
Results: Of the 6,097 joints studied, 15% (897) was clinically inflamed at baseline. In 42% (377/897) of those joints, inflammation recurred during follow-up. Joint inflammation at baseline and recurrence of inflammation during follow-up within the three included JIA categories is depicted in Figure 1. Of the joints that became inflamed after the patient had a period of inactive disease, 93% (1,195/1,280) had been previously inflamed. Joint inflammation at baseline was statistically significantly associated with joint inflammation in the same joint during follow-up (OR 3.9, 95% CI 3.5 to 4.4). The association was found in all included JIA categories, although to a different extent (Table 1). Baseline inflammation of a joint was also positively associated with the number of episodes of recurrent joint inflammation in that same joint (IRR 1.6, 95% CI 1.2 to 2.1). The permutation test showed that inflammation during follow-up in a certain joint was better predicted by baseline inflammation of the same joint, than by baseline inflammation of randomly selected other joints ($p<0.001$), confirming a local effect. No statistically significant association was found between joint inflammation in the wrist and local radiographic damage (β 0.17, 95% CI -0.06 to 0.41).

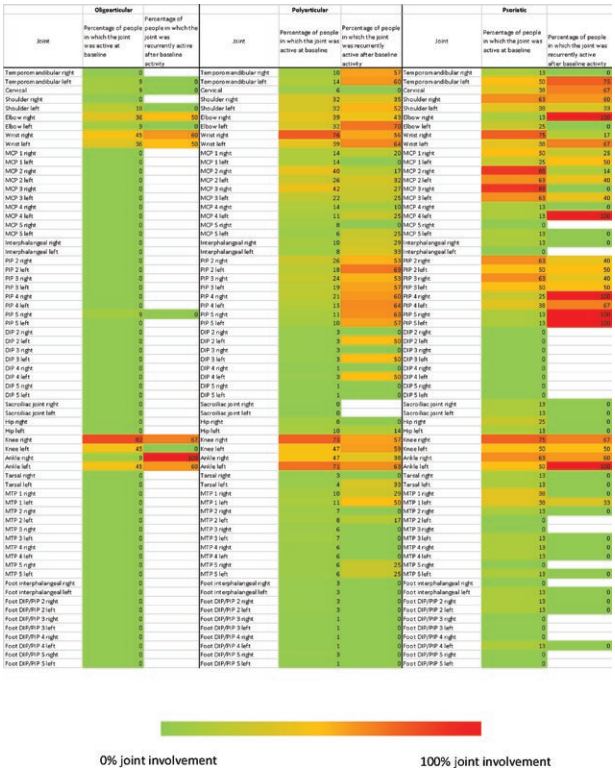


Figure 1. Joint inflammation patterns (joint activity at baseline and local recurrence of joint activity following baseline joint activity) in the three JIA types (oligoarticular, n=11; RF negative polyarticular, n=65, psoriatic, n=25) included in the BeSt for Kids study.

MCP: metacarpophalangeal, PIP: proximal interphalangeal, DIP: distal interphalangeal, MTP: metatarsophalangeal

Conclusion: In JIA, joint inflammation has the tendency to recur multiple times in joints that are clinically inflamed at disease onset. This indicates that local factors might play a role in the processes contributing to JIA flares. These local factors might be a target for new therapies.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Sascha L Heckert: None declared, Petra C E Hissink Muller Grant/research support from: The original BeSt for Kids study received financial support from Pfizer. The authors, not the sponsors, were responsible for the study design, the collection, analyses and interpretation of all data, the writing of this article and the decision to publish., J M van den Berg: None declared, Dieneke Schonenberg-Meinema: None declared, Lisette W A van Suijlekom-Smit: None declared, Marion van Rossum: None declared, Yvonne Koopman-Keemink: None declared, R ten Cate Grant/research support from: The original BeSt for Kids study received financial support from Pfizer. The authors, not the sponsors, were responsible for the study design, the collection, analyses and interpretation of all data, the writing of this article and the decision to publish., Daniëlle M C Brinkman: None declared, Thomas Huizinga: None declared, Cornelia Allaart: None declared, Sytske Anne Bergstra: None declared.
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OP0163

GOLIMUMAB FOR THE TREATMENT OF POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS – AN UPDATE ON SAFETY AND EFFECTIVENESS FROM THE BIKER REGISTRY

Keywords: Safety, bDMARD

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Background: Golimumab (GOL) is approved for treatment of polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years and older. Data on long-term safety of GOL in this indication are limited.
Objectives: To assess long-term safety and effectiveness of GOL in pJIA patients.
Methods: In this ongoing non-interventional observational study, clinical characteristics, disease activity and safety parameters were analysed using the German Biologics in Paediatric Rheumatology (BiKeR) registry. A total of 141 pJIA-patients treated with GOL were frequency matched by body weight with 282 patients receiving alternative tumor necrosis factor inhibitors (aTNFi) and 135 biologic–naïve patients receiving methotrexate (MTX).
Results: Baseline disease activity (measured by number of active joints and JADAS10) of the GOL and other anti-TNF cohort was similar. The GOL cohort tended to have a longer disease duration and more patients were previously exposed to other biologic agents than the other anti-TNF cohort. Compared to MTX cohort, the GOL cohort had a lower baseline disease activity and less concomitant systemic steroids use (Table 1). The clinical effectiveness of GOL in pJIA is highlighted by a decrease of the mean JADAS 10 from 10.7 (±6.5) (baseline) to 4.4 (±5.0) at 24 months. By 24 months, a JADAS 10 minimal disease activity (JADAS 10 ≤3.8) was reached by 50.0% of patients, whereas 34.2 % of patients were in remission (JADAS 10 ≤1) and the PedACR 30/50/70/90 response rates were 73.7/65.8/60.5/47.4% respectively. In the GOL cohort, 12 SAEs were reported, while in the aTNFi cohort 25 SAEs and in the MTX cohort 5 SAEs were observed (Table 1). One serious infectious event (SI) in the GOL cohort, 6 SIs in the aTNFi and one SI in the MTX cohort were observed. A few incident autoimmune events were reported: 4 in the GOL cohort (1 uveitis, 2 psoriasis, 1 inflammatory bowel disease (IBD)), 10 in the aTNFi cohort (6 uveitis, 2 psoriasis, 2 IBD) and 7 in the MTX cohort (6 uveitis, 1 celiac disease) (Table 1). Among the patients with preexisting uveitis at baseline, 10 out of 39 in the GOL cohort and 5 out of 32 in the aTNFi cohort had uveitis flares, whereas there were no patients with preexisting uveitis in the MTX-cohort. No malignancies were reported in any cohort.
Conclusion: Our interim results show an acceptable safety profile of GOL therapy, comparable to treatment with aTNFi or MTX. AE and serious infection rates between the three cohorts were comparable. No new safety signals were identified. Available data supports the effectiveness of GOL in the treatment of pJIA.

Table 1. Patient demographic and clinical parameters and adverse events

	GOL N=141	aTNFi N=282	MTX N=135
Gender female °	116 (82.3)	215 (76.2)	104 (77.0)
Age (yrs)#	12.6±3.5	12.1±4.0	11.3±4.3
Disease duration (yrs)#	7.1±4.4	4.2±3.8	1.0±2.3
RF neg. Polyarthritis °	76 (53.9)	142 (50.4)	85 (63.0)
RF pos. Polyarthritis °	8 (5.7)	40 (14.2)	22 (16.3)
Extended Oligoarthritis °	53 (37.6)	88 (31.2)	23 (17.0)
Psoriatic arthritis °	4 (2.8)	12 (4.3)	5 (3.7)
Pretreatment bDMARD °	113 (80.1)	61 (21.6)	0
Concomitant systemic steroids°	22 (15.6)	69 (24.5)	60 (44.4)
Active joint count #	4.1±4.9	5.1±6.4	9.7±7.1
CHAQ DI #	0.4±0.5	0.5±0.6	0.6±0.6
JADAS10 #	10.7±6.5	12.2±6.2	16.8±6.1
JADAS 10 at month 24 ##	4.4 ±5.0	-	-
AE *	172 95.8 (82.5-111.2)	503 85.1 (78.0-92.9)	200 93.7 (81.6-107.7)
SAE *	12 6.7 (3.8-11.8)	25 4.2 (2.9-6.3)	5 2.3 (1.0-5.6)
Serious infections *	1 0.6 (0.1-4.0)	6 1.0 (0.5-2.3)	1 0.5 (0.1-3.3)
Autoimmune process *	4 2.2 (0.8-5.9)	10 1.7 (0.9-3.1)	7 3.3 (1.6-6.9)
Patients with uveitis flare events with preexisting uveitis at baseline+	10 (of 39)	5 (of 32)	0 (of 0)

Rheumatoid factor (RF), biologic disease modifying antirheumatic drug (bDMARD), childhood health assessment questionnaire disability index (CHAQ Di), juvenile arthritis disease activity index (JADAS), adverse event (AE), patient year (PY), ° n (%) at baseline, # mean±SD at baseline, ## mean±SD, * n, AE rate/100PY (95% CI), + n (of n patients).

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OP0164

SAFETY AND EFFICACY OF UPADACITINIB FOR PEDIATRIC PATIENTS WITH POLYARTICULAR COURSE JUVENILE IDIOPATHIC ARTHRITIS: AN INTERIM ANALYSIS OF AN OPEN-LABEL, PHASE 1 TRIAL

Keywords: Clinical Trials, Safety, Outcome measures

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Background: Novel treatment options are needed for pediatric patients with polyarticular-course juvenile idiopathic arthritis (pcJIA). Upadacitinib (UPA) is an oral, selective Janus kinase (JAK) inhibitor with a positive benefit-risk profile in adult patients with moderate-to-severe active rheumatoid arthritis.[1,2]
Objectives: To evaluate the safety and efficacy of UPA in pediatric patients with pcJIA.
Methods: This open-label, 3-part, phase 1 trial (NCT03725007) enrolled pediatric patients aged 2 to < 18 years with pcJIA and ≥ 5 active joints at 31 sites across North America, Europe, and Asia. UPA was dosed as a twice-daily oral solution or once-daily tablet based on body weight. Part 1 evaluated multiple ascending doses of UPA for 7 days. Parts 2 and 3 evaluated long-term safety and efficacy of UPA for up to 156 weeks. This interim analysis (cutoff date of 22 September 2022) evaluated all available safety data in parts 1, 2, and 3; efficacy was evaluated in parts 1 and 2 through week 12. Efficacy endpoints included the JIA American College of Rheumatology (JIA ACR) 30, 50, and 70 response; the Childhood Health Assessment Questionnaire (C-HAQ); and the 27-point Juvenile Arthritis Disease Activity Score based on C-reactive Protein (JADAS-27 [CRP]).
Results: A total of 57 pediatric patients (78.9% female) with mean (SD) age of 9.5 (4.4) years and mean (SD) weight of 38.1 (20.4) kg received UPA; of these, 51 patients were treated in parts 1 and 2. In part 1, 8 (15.7%) of 51

patients reported adverse events (AEs) through 7 days; no patients reported serious AEs or AEs leading to treatment discontinuation. At a mean (median) duration of exposure of 514.9 (412.0) days, 52 (91.2%) of 57 patients reported AEs that were predominately mild to moderate in severity (**Table 1**). The most common treatment-emergent AEs were COVID-19 infection (n = 23/57, 40.4%), upper respiratory tract infection (n = 23/57, 40.4%), nasopharyngitis (n = 13/57, 22.8%), gastroenteritis (n = 10/57, 17.5%), pyrexia (n = 10/57, 17.5%), abdominal pain (n = 9/57, 15.8%), and nausea (n = 8/57, 14.0%). The most common AEs of special interest included elevated creatine phosphokinase levels (n = 6/57, 10.5%), hepatic disorder (n = 3/57, 5.3%), and neutropenia (n = 2/57, 3.5%); all were nonserious events. Six (31.6%) of 19 patients in the group aged 12 to <18 years reported serious AEs and 2 (10.5%) reported AEs leading to treatment discontinuation. A high proportion of patients across all age groups achieved JIA ACR30, 50, and 70 response at week 12 (**Figure 1**). Improvement from baseline to week 12 in C-HAQ and JADAS-27 [CRP] scores was observed across all age groups.

Conclusion: In pediatric patients with pcJIA, UPA was well tolerated and associated with improvements in disease activity and physical function at week 12.

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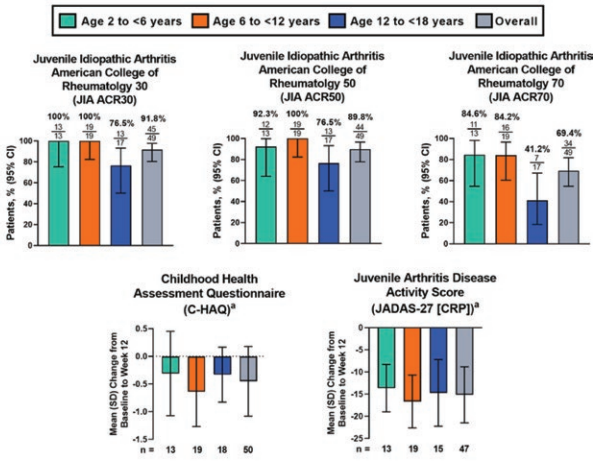
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Table 1. Interim Analysis of Safety of Upadacitinib up to 156 Weeks(All Patients Treated in Parts 1, 2, and 3)

TEAE	Age 2 to <6 years n = 14	Age 6 to <12 years n = 24	Age 12 to <18 years n = 19	Total N = 57
	Patients with TEAE (%)			
Any AE	11 (78.6)	22 (91.7)	19 (100)	52 (91.2)
Any serious AE	0	0	6 (31.6)	6 (10.5)
AE leading to discontinuation of study drug	0	0	2 (10.5)	2 (3.5)
Deaths	0	0	0	0
AEs of special interest				
Serious infections	0	0	1 (5.3)[a]	1 (1.8)[a]
Opportunistic infection	0	0	1 (5.3)[b]	1 (1.8)[b]
Hepatic disorder	0	2 (8.3)[c]	1 (5.3)[c]	3 (5.3)[c]
Anemia	1 (7.1)	0	0	1 (1.8)
Neutropenia	0	2 (8.3)	0	2 (3.5)
Lymphopenia	0	0	1 (5.3)	1 (1.8)
Elevated creatine phosphokinase	0	3 (12.5)	3 (15.8)	6 (10.5)

TEAE, treatment-emergent adverse event.[a]Upper respiratory tract infection.[b]Candida oesophagitis infection.[c]1 hepatosplenomegaly event, 2 high AST events, and 2 high ALT events.

Figure. Interim Analysis of Efficacy of Upadacitinib at Week 12 (Parts 1 and 2)



Numbers above bars are the proportion of patients with response and (n / N).
[a]Negative change from baseline indicates improvement in health or disease activity.

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OP0165

LONG-TERM SAFETY OF BIOLOGICS VS CONVENTIONAL SYNTHETIC TREATMENTS IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

Keywords: Registries, bDMARD

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Background: The better understanding of systemic Juvenile Idiopathic Arthritis (sJIA) pathogenesis and availability of new drugs, such as biologic disease-modifying anti-rheumatic drugs (bDMARDs) specifically dedicated to sJIA, have led to treatment advances that have ameliorated the disease outcome and reduced the use of glucocorticoids. However, published evidence on long term safety data regarding biologic therapies in sJIA is still limited.

Objectives: The objective of the study was to compare the adverse events (AEs) of at least moderate intensity and serious AEs in sJIA patients treated with biologics compared with a cohort treated with csDMARDs (conventional synthetic disease-modifying anti-rheumatic drugs)

Methods: Patients with sJIA, classified according to the International League of Associations for Rheumatology (ILAR), enrolled in the Pharmachild Registry since 2011 and followed up until 31 December 2022 were included. All patients had received at least one bDMARDs or csDMARDs. Those who switched to more than one treatment during the period of observation were assigned only to one group according to the longest time of drug exposure. AEs are reported according to the latest release of the Medical Dictionary for Regulatory Activities (MedDRA, Version 23.1) and were grouped into highest term "System Organ Classes" (SOCs). Frequency of SOCs were analysed. Events repeated for the same SOC in the same patient were counted once in the analysis.

Results: A total of 980 sJIA patients were enrolled, 353 treated with bDMARDs and 627 treated with csDMARDs. The distribution of demographic data was similar in both cohorts, with the exception that the prescription of csDMARDs compared to bDMARDs was more frequent in other continents compared to Europe. As shown in the Table 1, patients in the bDMARDs group developed more frequently infections and infestations (41.4%), skin and subcutaneous tissue disorders (11.3%) and

general disorders and administration site conditions (8.2%) than patients treated with csDMARDs (all p<0.0001). On the other hand, endocrine disorders were more frequent in the csDMARDs group (7.3%, p=0.03). The distribution between other SOCs was similar in children treated with bDMARDs compared with csDMARDsA.
Conclusion: Patients in the bDMARD group had a higher prevalence of infections and skin manifestations when compared with the csDMARDs cohort.

Table 1. Demographics characteristics, number of AEs and frequencies in the complete set. Data presented as n (%). Events with a frequency of > 30 by overall SOC are presented. AEs: adverse events; SOC: system organ class; bDMARDs: biologic disease-modifying anti-rheumatic drugs; csDMARDs conventional synthetic disease-modifying anti-rheumatic drugs.

	bDMARDs N=353	csDMARDs N=627	Overall N=980	p-value
Male	175 (49.6%)	279 (44.5%)	454 (46.3%)	-
Mean (SD) age at onset (years)	6.21 (4.24)	5.77 (4.04)	5.92 (4.12)	-
Age groups (years)				
<2	65 (18.4%)	115 (18.3%)	180 (18.4%)	-
≥2 to 12	242 (68.6%)	444 (70.8%)	686 (70.0%)	-
≥12 to 18	46 (13.0%)	68 (10.9%)	114 (11.6%)	-
≥ 18	0 (0%)	0 (0%)	0 (0%)	-
Age at diagnosis	6.56 (4.3)	6.17 (4.13)	6.31 (4.2)	-
Age at final visit	12.05 (5.4)	12.41 (5.13)	12.28 (5.2)	-
Disease duration	5.84 (4.61)	6.65 (4.63)	6.36 (4.64)	-
Origin-				
Europe	320 (90.7%)	466 (74.3%)	786 (80.2%)	-
Other	33 (9.3%)	161 (25.7%)	194 (19.8%)	-
Concomitant steroid therapy (≥6 months)	165 (46.7%)	414 (66.0%)	579 (59.1%)	<0.0001
SOCs				
Infections and infestations	146 (41.4%)	176 (28.1%)	332	<0.0001
Gastrointestinal disorders	33 (9.3%)	51 (8.1%)	84	0.6
Injury, poisoning and procedural complications	28 (7.9%)	50 (8.0%)	78	0.99
Skin and subcutaneous tissue disorders	40 (11.3%)	27 (4.3%)	67	<0.0001
Blood and lymphatic system disorders	25 (7.1%)	42 (6.7%)	67	0.9
Endocrine disorders	13 (3.7%)	46 (7.3%)	59	0.03
Immune system disorders	14 (4%)	36 (5.7%)	50	0.3
Musculoskeletal and connective tissue disorders	13 (3.7%)	37 (5.9%)	50	0.2
General disorders and administration site conditions	29 (8.2%)	17 (2.7%)	46	<0.0001
Investigations	16 (4.5%)	29 (4.6%)	45	0.99
Nervous system disorders	15 (4.2%)	16 (2.6%)	31	0.2

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OP0166

LONG-TERM FOLLOW-UP OF PATIENTS ADMINISTERED EMAPALUMAB, AN ANTI–INTERFERON-Γ MONOCLONAL ANTIBODY, TO TREAT MACROPHAGE ACTIVATION SYNDROME (MAS) SECONDARY TO SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA)

Keywords: Inflammatory arthritides, Clinical Trials, Safety

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Background: MAS, a form of secondary hemophagocytic lymphohistiocytosis (sHLH), is a severe, life-threatening complication of rheumatic diseases that occurs most frequently in patients (pts) with sJIA and adult-onset Still's disease (AOSD). MAS is characterized by hyperinflammation and overproduction of interferon γ (IFNγ). Treatment with emapalumab, an anti-IFNγ monoclonal antibody, rapidly neutralized IFNγ and controlled MAS secondary to sJIA in pts with an inadequate response to high-dose glucocorticoids (GCs) in a phase 2 study (parent study).[1]
Objectives: To report outcomes and safety among pts with MAS treated with emapalumab after 12 months of follow-up.
Methods: The parent study enrolled pts with sJIA or AOSD who failed high-dose GCs (≥2 mg/kg/day). Pts who received emapalumab in the parent study (6 mg/kg on day [D] 0, followed by 3 mg/kg every 3 days until D15 and twice weekly until D28) and completed short-term follow-up (≥4 weeks) after last drug administration were invited to participate in this long-term follow-up study. Pts were assessed at follow-up Week (W) 2, W3, D30, D100, Month (M) 6 and M12. Emapalumab was not administered during follow-up. Overall MAS activity was monitored using a visual analog scale, comprehensive clinical evaluation and observation of pts' overall status. Serum samples for pharmacokinetic and pharmacodynamic analysis were collected at each study visit while serum emapalumab remained detectable. Safety was monitored throughout.
Results: All 14 pts (sJIA onset at <16 yrs, n=13; 1 had onset at age 16 yrs, 7 months) in the parent study participated in this long-term follow-up study. 6 pts had a history of 19 MAS episodes prior to the parent study. All prior episodes were treated with high-dose GCs; pts were also treated with anakinra (n=7) and/or cyclosporine A (n=8). 13/14 patients achieved MAS remission by W8, with rapid IFNγ neutralization during the parent study, as shown by decreased CXCL9 levels versus baseline. GCs were rapidly tapered in all pts. 13/14 pts did not present with another MAS episode; 1 MAS episode was reported 11 months after the pt stopped emapalumab (serum emapalumab was undetectable). The terminal elimination phase for emapalumab was slow and linear during follow-up (median $t_{½}$, 24 days). CXCL9 and soluble interleukin-2 receptor levels remained close to, or within, the normal range. GC tapering continued during follow-up: at M12, 5 pts were off GCs and 6 pts were receiving <0.3 mg/kg/day of prednisone. 4 sJIA flares (without MAS) occurred during follow-up. In total, 37 adverse events (AEs) were reported by 12 patients, including 3 serious AEs (SAEs), all unrelated to emapalumab: 1 MAS reactivation, 1 sJIA flare and 1 ankle edema. All SAEs resolved spontaneously or with standard treatment. 10 infectious AEs (9 of viral origin) were reported during follow-up; 4 occurred when serum emapalumab levels were measurable and 6 after emapalumab became undetectable (Table 1). No new safety signals were observed. All pts were alive at M12.

Table 1.

N=14	Emapalumab levels ≥lower limit of quantification (LLOQ)	Emapalumab levels <LLOQ
Infection AEs, n	4	6
Pts with ≥1 infection AE, n (%)	2 (14)	5 (35)
Cytomegalovirus (CMV) infection reactivation	0	0
CMV infection	0	0
Epstein Barr infection	0	1
Rhinovirus infection	1	0
Enterovirus infection	0	1
Viral infection	0	1
Viral upper respiratory tract infection	3	2
Nasopharyngitis	0	0
Viral test positive (CMV, adenovirus, BK polyoma virus, respirovirus)	0	0
Cestode infection	0	1

Conclusion: Most pts with MAS who had failed high-dose GCs and responded to emapalumab remained in remission and continued GC tapering during 12 months of follow-up. Any viral infections during follow-up resolved spontaneously

or with standard treatment, confirming the favorable safety profile of emapalumab. A pivotal clinical trial of emapalumab in patients with sHLH and underlying rheumatic disease is ongoing (EMERALD; NCT05001737).

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OP0167

EULAR POINTS TO CONSIDER FOR PATIENT EDUCATION, PAIN MANAGEMENT AND PHYSICAL ACTIVITY ADAPTED TO THE SELF-MANAGEMENT OF JUVENILE-ONSET RHEUMATIC AND MUSCULOSKELETAL DISEASES DURING TRANSITIONAL CARE. THE EULAR MOVE-UP PROJECT

Keywords: Education, Self-management, Telemedicine

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Background: The EULAR task force "Implementation of a mobile health app for the self-management of juvenile-onset rheumatic and musculoskeletal diseases (jRMDs) during transitional care" aims at designing, developing and implementing a self-management program through a smartphone app (i.e., the EULAR Move-Up app). The first step of this task force was to adapt the current EULAR recommendations/points originally developed for adults, to young people (YP) with jRMDs.

Objectives: Adapting EULAR recommendations/points for patient education, pain management and physical activity for self-management of jRMDs during transitional care.

Methods: A multidisciplinary taskforce of 25 members from 11 European countries was convened. Using a Delphi technique, the level of agreement was established by anonymous online voting in three rounds.

Results: Four overarching principles and 8 points to consider were formulated (Table 1). The agreement was high, ranging from 8.7 to 9.9.

Conclusion: This work will feed into an evidence-based framework to inform the development of the EULAR Move-Up app aiming at improving the quality of transitional care of jRMDs.

Table 1. Overarching principles and points to consider for the self-management of juvenile-onset rheumatic and musculoskeletal diseases during transitional care

	Overarching principles	Agreement (0 to 10)
1	YP with jRMDs should be offered education, physical activity advice and pain management recommendations and provided with access to relevant resources during transitional care, as soon as possible following the diagnosis	9.6
2	Health professionals in rheumatology should consider the use of digital health interventions in transitional care to support self-management	9.5
3	The content and delivery of transitional care should be individually tailored and needs-based according to the patients' priorities, preferences, capabilities and resources	9.6
4	Transitional care interventions should have clear personalised aims, which should be evaluated over time, preferably by a combination of objective and subjective (patient-reported outcome measures) assessments	9.9
	Adapted points to consider in education	
1	Education is a planned interactive learning process designed to support and enable YP with jRMDs to manage their health and chronic condition, and optimise their health and well-being during transitional care	9.5
2	Education should consist of a variety of learning formats and the programme should be designed through a shared decision-making process	9.4
3	Education should include the evaluation of outcomes reflecting both the knowledge acquired and, most importantly, translation to behaviour change	8.7
	Adapted points to consider in pain management	
4	All patients and their carers should be offered education on the importance of maintaining healthy body composition and explained that unhealthy body composition could contribute to pain and disability	9.8
5	Non-pharmacological approaches (e.g., physical activity, lifestyle change, psychological interventions) should be prioritised in newly-diagnosed patients and those in transitional care. If indicated, the patient should receive pharmacological treatment according to the most recent recommendations	9.6
	Adapted points to consider on physical activity	
6	Physical activity is part of a healthy lifestyle and should be optimised during the lifespan of individuals of all ages	9.8
7	Physical activity has health benefits for YP with jRMDs during transitional care and helps establishing healthy behaviours and lifestyles during adulthood	9.8
8	Healthcare providers should consider different formats of delivery of physical activity, in line with YP's preferences and disease requirements	9.6

YP = Young people; jRMDs = juvenile-onset rheumatic and musculoskeletal diseases;

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Advances in imaging in rheumatic musculoskeletal disorders

OP0168 **WITHDRAWN**

OP0169 **VESSEL WALL INFLAMMATION DETECTED WITH SUPERB MICROVASCULAR IMAGING IN BEHÇET SYNDROME**

Keywords: Vasculitis, Ultrasound, Behcet's disease

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Background: Superb microvascular imaging (SMI) is a novel technique that provides a more sensitive assessment of small vessels compared to color Doppler US (CDUS), by distinction of low-speed flow signals from motion artifacts. Superficial thrombophlebitis (STM) is a common manifestation in patients with Behçet syndrome (BS) and is thought to be associated with inflammation of the vessel wall rather than a procoagulant state.
Objectives: We aimed to assess STM lesions of patients with BS, together with controls, using SMI.
Methods: We studied 51 BS (16F/35M, mean age:40.6±12.8) patients and 26 non-BS (19F/7M mean age:44.9±11.7) patients with nodular lesions on physical examination. B-mode US, CDUS, PDUS and SMI were performed and recorded by the same radiologist and images were then evaluated by 2 radiologists. Both radiologists were blinded to the diagnoses and to each other's assessments. First, presence/absence of vessel was assessed with CDUS to differentiate STM from erythema nodosum (EN). Then STM lesions were evaluated for the presence/absence of thrombus, vessel wall color-coded signal intensity, and thickness using the imaging modalities defined above. Vessel wall signal intensity was graded into 4 groups according to the percentages of the effected vessel wall area (Grade 0= no signal, Grade 1= < 25%, Grade 2= 25-50%, Grade 3= 50-75%, Grade 4= >75%). CDUS was the gold standard in the final diagnosis of STM. Interobserver reliability was assessed by kappa statistic.
Results: The nodular lesions of 26 BS and 15 non-BS patients were diagnosed as STM (Table 1). The diagnosis was EN in the remaining 25 BS and 11 non-BS patients. SMI showed increased color-coded signal intensity in the vessel wall in patients with STM. We did not observe increased signal intensity in any of the patients with EN. According to the grading system, at least grade 1 or higher vessel-wall signals were detected in 20 BS (77%) patients with STM, in contrast to only 4 (27%) non-BS patients with STM (Table 1). Fifteen of 26 BS patients (58%) had at least grade 2 signal, and 4 of them had halo shaped signals all around the vessel-wall (Figure 1). On the other hand, 3 of 4 non-BS patients (75%) had only grade 1 signal and none of them had grade 4 signal. The interobserver reliability was good (κ=0.87, $p<0.001$).
Conclusion: A high-grade color-coded signal suggesting inflammation of the vessel wall was detected with SMI, in the majority of BS patients with STM. This finding needs to be studied in different vascular lesions of a large number of BS patients together with controls, in order to understand its specificity for BS and its significance.

Table. Comparisons of vessel wall signal intensity in BS vs. non-BS patients with SMI		
	Behçet syndrome (n=51, 35M/16F)	**Non-Behçet syndrome (n=26, 7M/19F)**
Superficial thrombophlebitis n (%)	26 (51)	15 (58)
Vessel wall signal intensity with SMI n (%)		
Grade 0	6 (23)	11 (73)
Grade 1	5 (19)	3 (20)
Grade 2	9 (35)	0
Grade 3	2 (8)	1 (7)
Grade 4	4 (15)	0

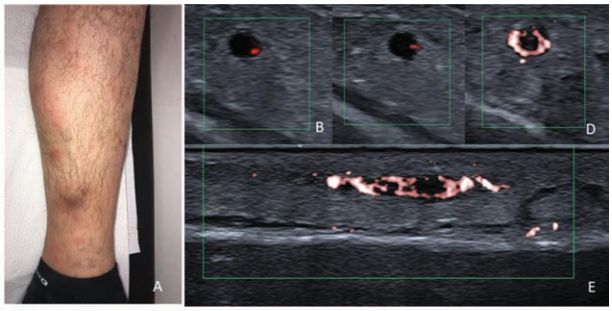


Figure. A-Nodul-like lesion on the posterior side of the cruris, **B**-Color Doppler US, **C**-Power Doppler US, **D**-*Venous halo sign* in axial plane SMI, **E**-Venous wall inflammation in longitudinal plane SMI

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OP0170

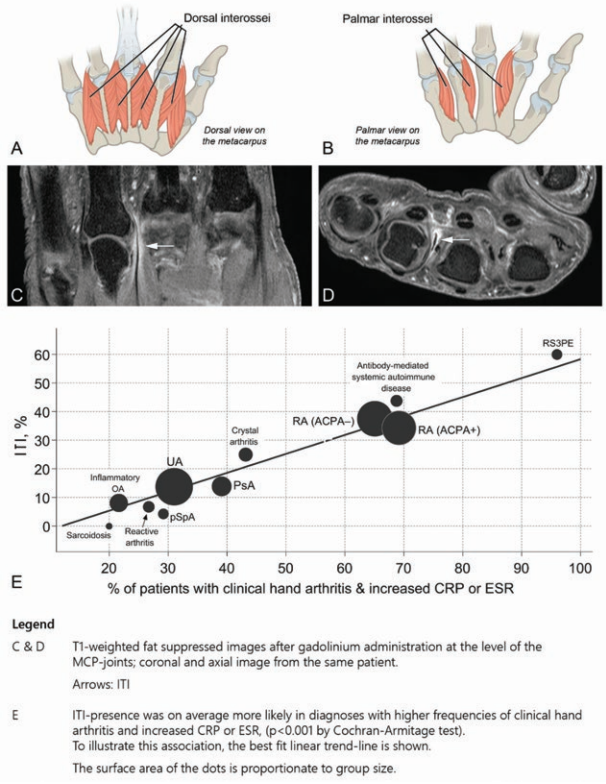
INTEROSSEOUS TENDON INFLAMMATION ACROSS THE EARLY ARTHRITIS SPECTRUM: A 10-YEAR MRI-STUDY INVESTIGATING ITS PREVALENCE AT DIAGNOSIS AND RELATION WITH CLINICAL SIGNS

Keywords: Imaging, Rheumatoid arthritis, Inflammatory arthritides

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Background: Inflammation around the tendons of the hand interosseous muscles (interosseous tendon inflammation; ITI) was recently identified on MRI in a set of RA and arthralgia patients.
Objectives: However, the prevalence of ITI at diagnosis of RA is unknown, as is its prevalence in other arthritides and its relationship with clinical signs. These questions prompted us to perform this large MRI study.
Methods: 1,205 consecutive patients presenting with early arthritis between 2010-2020 underwent contrast-enhanced hand MRI. MRIs were evaluated, blind to clinical data, for ITI lateral of MCP2-5 and for other local inflammation (synovitis/tenosynovitis/osteitis, in line with the RA-MRI-scoring-system (RAMRIS)). ITI-presence at baseline was studied in relation to the diagnosis and clinical characteristics (i.e. joint swelling, and tenderness) using logistic regression and generalised estimating equations.
Results: 36% of early RA patients (n=532) had ITI; this was similar in ACPA-negative(37%) and ACPA-positive RA patients (34%; p=0.53). ITI occurred regularly in RS3PE (60%) and connective tissue diseases (44%), and less frequently in undifferentiated arthritis (UA;14%), psoriatic arthritis (14%), inflammatory osteoarthritis (8%), reactive arthritis (7%), crystal arthritis (7%) and peripheral spondyloarthritis (4%). ITI occurred more often in diagnoses with frequent arthritis of the hands (p<0.001) and increased acute-phase-reactants (p<0.001). Within RA, ITI occurred together with local MCP synovitis (OR 2.4 (95%CI; 1.7-3.4)), tenosynovitis (2.4 (1.8-3.3)) and osteitis (2.2 (1.6-3.1)) on MRI. Moreover, ITI-presence associated with local MCP tenderness (1.6 (1.2-2.1)) and swelling (1.8 (1.3-2.6)), independent of age and MRI-detected synovitis/tenosynovitis/osteitis.
Conclusion: ITI occurs regularly in RA and other arthritides with preferential involvement of hand-joints and increased acute-phase-reactants. At MCP-level, the presence of ITI associates independently with joint-tenderness and -swelling. Hence, ITI is a newly identified inflamed tissue mainly found in arthritides with particularly extensive and symptomatic inflammation.

Figure. Schematic anatomical illustrations of the (**A**) dorsal and (**B**) palmar interossei; (**C&D**) example MR-images of RA-patients with ITI at MCP4 and (**E**) the frequency of ITI per diagnosis according to the frequency of combined clinical hand arthritis and increased CRP or ESR within diagnoses



Legend

C & D T1-weighted fat suppressed images after gadolinium administration at the level of the MCP-joints; coronal and axial image from the same patient.
Arrows: ITI

E ITI-presence was on average more likely in diagnoses with higher frequencies of clinical hand arthritis and increased CRP or ESR, (p<0.001 by Cochran-Armitage test).
To illustrate this association, the best fit linear trend-line is shown.
The surface area of the dots is proportionate to group size.

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OP0171

ADDED VALUE OF FDG-PET/CT TO DETECT AORTIC INVOLVEMENT IN PATIENTS WITH ULTRASOUND PROVEN GIANT CELL ARTERITIS

Keywords: Vasculitis, Imaging, Ultrasound

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Background: Ultrasound (US) can detect signs of large vessel (LV) involvement at axillary, subclavian and carotid arteries of giant cell arteritis (GCA) patients, but has limited access to the thoracic aorta. Although aortic involvement is not routinely evaluated in all patients with GCA, it may cause a life-threatening situation as result of serious complications such as aneurysms or dissection.
Objectives: Our aim is to determine the added value of performing FDG-PET/CT to detect aortitis in patients with US proven GCA and to identify factors associated with aortic involvement.
Methods: Retrospective observational study of patients referred to the US fast track clinics of two academic centres over a 4-years period. Only patients with US proven GCA were included for analysis. Baseline US of cranial and extracranial arteries (carotid, subclavian and axillary) was performed in all patients at diagnosis within 24-48 hours. FDG-PET/CT was performed according to clinician criteria and images were assessed by nuclear medicine physicians. An FDG artery uptake at the thoracic or abdominal aorta higher than liver uptake was defined as aortitis. Between groups comparisons were made in patients with and without aortitis.

Results: Seventy two patients over 186 patients with confirmed GCA by US underwent an FDG-PET/CT (mean age 77 years, 52.8% females). A total of 48 (66.7%) had LV-GCA based on imaging findings, with 29 (40.3%) presenting positive FDG-PET/CT for LV-GCA and 24 (33.3%) presenting artery uptake throughout the aorta suggestive of aortic involvement (Table 1). Only 6 (20.7%) patients had negative US findings of LV-GCA but positive FDG-PET/CT. Among patients with aortitis according to FDG-PET/CT, only 2 (8.3%) had negative US findings of LV-GCA. In contrast, 19 (45.2%) patients with US findings of LV-GCA had negative FDG-PET/CT. Patients with aortitis were younger (68.9 vs 81, p<0.001), more frequently females (79.2% vs 39.6%, p=0.002) and had higher level of platelets (413.4 vs 311.1, p=0014). None of the patients with aortitis referred visual symptoms (0% vs 31.2%, p=0.001) and they presented US signs of LV-GCA more frequently (91.7% vs 41.7%, p<0.001) versus patients without aortic involvement.

Conclusion: FDG-PET/CT can detect aortic involvement in 1 out of every 3 patients with US proven GCA. However, most of these patients show US findings of LV-GCA. In contrast, half of patients with US proven LV-GCA may have negative FDG-PET/CT. Younger and female GCA patients, with thrombocytosis, absence of visual manifestations and US pattern of LV-GCA may present more frequently aortitis by FDG-PET/CT.

Table 1. Clinical and imaging findings of patients included with and without aortic involvement.

	Total n=72	Patients with aortic involvement in FDG-PET/CT n=24 (33.3%)	Patients without aortic involvement in FDG-PET/CT n=48 (66.7%)	p
Demographics				
Age, mean (SD)	77 (9.1)	68.9 (8.1)	81 (6.5)	**<0.001**
Female, n (%)	38 (52.8%)	19 (79.2%)	19 (39.6%)	**0.002**
Clinical variables				
Headache, n (%)	49 (68.1%)	14 (58.3%)	35 (72.9%)	0.211
Jaw claudication, n (%)	16 (22.2%)	4 (16.7%)	12 (25%)	0.423
Visual symptoms, n (%)	15 (20.8%)	0 (0%)	15 (31.2%)	**0.001**
Ocular ischaemia, n (%)	6 (8.3%)	0 (0%)	6 (12.5%)	0.07
Constitutional symptoms, n (%)	42 (58.3%)	17 (70.8%)	25 (52.1%)	0.128
Fever, n (%)	19 (26.4%)	9 (37.5%)	10 (20.8%)	0.130
Morning stiffness in shoulders/neck, n (%)	38 (52.8%)	10 (41.7%)	28 (58.3%)	0.182
Laboratory findings				
CRP (mg/L), mean (SD)	85.8 (79.6)	101.8 (77.8)	77.8 (80.4)	0.230
ESR (mm/h), mean (SD)	68.6 (33.6)	69.7 (31.8)	68 (34.7)	0.839
Haemoglobin (g/dL), mean (SD)	11.9 (1.6)	11.5 (1.5)	12.1 (1.7)	0.139
Platelets 10^9/L, mean (SD)	345.7 (152.1)	413.4 (169.7)	311.11 (131.1)	**0.014**
Histology				
Temporal artery biopsy positive n=22, n (%)	9 (40.9%)	2 (28.6%)	7 (46.7%)	0.421
Imaging				
Positive cranial ACG US, n (%)	50 (69.4%)	10 (41.7%)	40 (83.3%)	**<0.001**
Positive large vessel-GCA US, n (%)	42 (58.3%)	22 (91.7%)	20 (41.7%)	**<0.001**
Negative large vessel-GCA US, n (%)	30 (41.7%)	2 (8.3%)	28 (58.3%)	**<0.001**
Isolated positive large vessel-ACG US, n (%)	22 (30.6%)	14 (58.3%)	8 (16.7%)	**<0.001**

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OP0172

LIMITED DIAGNOSTIC AND PROGNOSTIC VALUE OF RADIOGRAPHS OF HANDS AND FEET IN PATIENTS WITH UNDIFFERENTIATED ARTHRITIS SUSPECTED FOR RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT STUDY

Keywords: Imaging, Rheumatoid arthritis, Diagnostic Tests

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Background: Current recommendations suggest that the diagnostic workup of Undifferentiated Arthritis (UA) should include radiographs of hands and feet (x-HF) as presence of Rheumatoid Arthritis (RA) associated erosions might be of diagnostic and prognostic value. The diagnostic role of x-HF in RA is reflected in ACR/EULAR 2010 criteria, with erosions typical for RA allowing classification of RA even without fulfillment of the scoring system [1]. Additionally, early erosivity is one of the indicators of a poor RA prognosis [2]. RA seems to evolve into a milder disease at presentation, caused by a secular trend towards milder disease, or lead time effects (presenting earlier in disease course) [3]. Both trends would further decrease the prevalence of RA-associated erosions and thus utility of x-HF might have decreased both for diagnosis and identifying poor prognosis patients.

Objectives: To investigate the prevalence and diagnostic and prognostic value of RA-associated erosions on x-HF in a recent cohort of UA patients.

Methods: A retrospective cohort study in consenting UA patients visiting the rheumatology department at the Sint Maartenskliniek between 2012-2018 was done. UA suspected for RA was defined as 1/ current arthritis, 2/ Rheumatoid Factor (RF)/anti-Cyclic Citrullinated Peptide (anti-CCP) were tested, 3/ x-HF was made, 4/ RA was mentioned in the differential diagnosis. Radiological reports of x-HF were judged by experienced musculoskeletal radiologists, and all x-HF with an erosion mentioned in the report were reassessed by two experienced rheumatologists for typical RA-associated erosions. The prevalence of erosions was estimated, as well as whether RA classification (yes/no) or prognostic group (good/poor) were changed by erosivity. Subgroup-analyses were done for seronegative patients (non-elevated RF/anti-CCP) and patients without elevated Acute Phase Reactants (APR; i.e. ESR and CRP) as they might be expected to gain the most diagnostic and prognostic value from conducting x-HF.

Results: 724 patients were included in the analysis, of which 293 (40.5%) patients were eventually clinically diagnosed with RA during the time they were treated. There was a high agreement between 2010 ACR/EULAR classification criteria for RA and the clinical diagnosis reported by the treating rheumatologist (sensitivity of 79% and specificity of 89.6%). RA-associated erosions were found in 30 out of 724 included patients (4.1%, 2.9-5.9). Of the 437 seronegative patients, five (1.1%, 0.5-2.7) radiographs showed erosive disease. Eight out of 385 patients with non-elevated APR (2.1%, 1-4.1) had erosive disease. The x-HF resulted in a change to a positive RA classification in four out of 724 patients (0.5%, 0.2-1.2). X-HF erosivity changed the classification to prognostically unfavorable in five patients (0.6, 0.2-1.4), *Table 1*. In other words: these patients did not have RF or anti-CCP positivity, high disease activity (DAS28 >5.1), but did have the prognostic factor 'early erosive disease'.

Table 1. prevalence of typical RA erosive disease, and diagnostic/prognostic relevance of x-HF.

	All patients (N=724)	Seronegative (N=437)	Non-elevated APR (N=385)
Erosive disease (n (%, CI))	30 (4.1, 2.9-5.9)	5 (1.1, 0.5-2.7)	8 (2.1, 1-4.1)
Erosions relevant for RA classification with 2010 ACR/EULAR criteria (n (%, CI))	4 (0.5, 0.2-1.2)	2 (0.5, 0.1-1.8)	2 (0.5, 0.1-2.1)
Cases classified as prognostically unfavorable due to the X-HF (n (%, CI))	5 (0.6, 0.2-1.4)	3 (0.7, 0.2-2.1)	2 (0.5, 0.1-2.1)

Conclusion: RA-associated erosions at presentation with UA are rare, and their presence rarely leads to a change in diagnosis or prognosis. Routine x-HF should therefore not be recommended in this context. X-HF made for any specific indication might of course be of value, and our results do not generalize to these cases.

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OP0173

CHARACTERIZATION OF AXIAL INVOLVEMENT USING 18F-FLUORIDE PET-CT IN SPONDYLOARTHRITIS PATIENTS

Keywords: Imaging, Spondyloarthritis, Pain

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Background: Nuclear medicine positron emission tomography (PET) has limited evidence in the clinical management of axial Spondylarthritis (AxSpA). The 18F-fluoride isotope is a bone-specific tracer that is incorporated in the skeleton during bone remodelling. Osteoblastic bone remodeling, that culminates in new bone formation in SpA can be molecularly imaged with 18F PET. Although not widely employed, several studies have shown that 18F is an excellent isotope for evaluating sites of active osteoblastic activity[1], and may be used in the assessment of axial involvement in spondyloarthritis[2].
Objectives: Aim of this study is to identify the pattern of distribution of 18F uptake at baseline using the PET-Computerized Tomography (PET-CT) in the early AxSpA identification in patients with inflammatory back pain (IBP) according to ASAS criteria[3].
Methods: We analyzed data of 18F PET-CT in patients presenting IBP suspicious for SpA. Patients were assessed clinically at baseline and according to clinical practice with assignment of a the final diagnosis of axial SpA after at least two years of follow up, according to the ASAS criteria[4]. We evaluated the baseline 18F PET-CT abnormalities and correlated with the final diagnosis.
Results: 125 patients underwent 18F PET-CT. 83 were female (66,4%), and the mean age at evaluation time was 49.58 years (SD 11.03). Patients were classified into 5 groups according to the rheumatological diagnosis made after at least 2 years of follow-up. Ten patients fulfilled New York criteria for Ankylosing Spondylitis (AS), 28 patients fulfilled CASPAR criteria for Psoriatic Arthritis (PsA), 35 patients fulfilled ASAS criteria for undifferentiated SpA, and 12 patients presented axial-SpA related IBD. 40 patients were not classifiable as AxSpA (not-class AxSpA). The prevalence of 18F PET-CT abnormalities highlight differences in SpA phenotypes, shown in colour coding (Figure 1A). Similar results were reported in the chest, in particular among the sterno-clavicular and acromio-clavicular joints (Figure 1B).
Conclusion: Our study showed a clear pattern of abnormalities detected by 18F PET-CT in the spine and chest of AxSpA patients. 18F PET-CT might help clinicians to characterize the axial involvement in SpA patients.
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Fig 1A

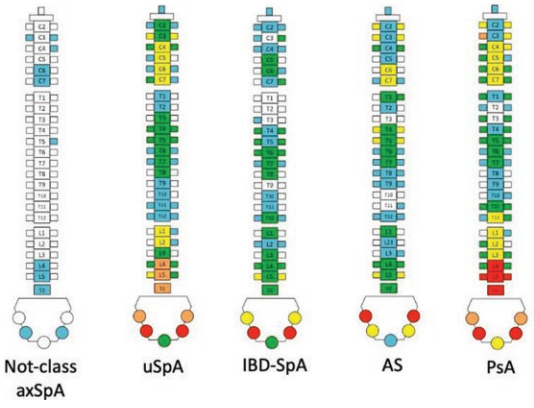


Figure 1A. Distribution of abnormalities detected by F18-PET-CT. In spine lumbar and cervical vertebral and facets uptake were more common in uSpA and PsA.

Fig 1B

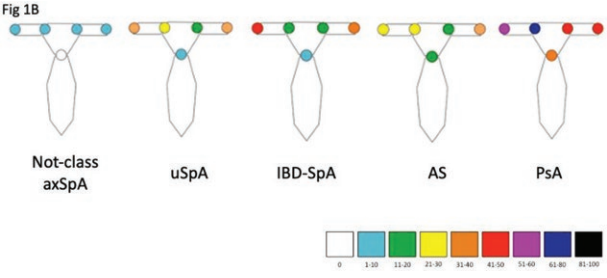


Figure 1B. Distribution of abnormalities detected by F18-PET-CT. In chest joint such as sternoclavicular joint and acromioclavicular joint, the uptake was more common in SpA and PsA.

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OP0174 CHEST RADIOGRAPHS PRE-IMMMUNOSUPPRESSION HELP TO IDENTIFY NON TUBERCULOUS INFECTIONS AND INTERSTITIAL LUNG DISEASES, BUT ADD LITTLE TO LATENT TUBERCULOSIS SCREENING

Keywords: Imaging, Real-world evidence, Diagnostic Tests

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Background: Screening for latent tuberculosis (LTB) using chest x-ray (CXR) and interferon-gamma release assay (IGRA) is standard in patients starting on biologic and immunosuppressive therapies. Our hypothesis is that the CXR does not change management, and we sought to evaluate the additive value of plain radiographs for this purpose in our patients.
Objectives: To retrospectively review all CXRs performed at baseline pre treatment to determine if they provide any additive benefit value to the IGRA LTB screening approach.
Methods: This is a retrospective review of screening practices for LTB in a tertiary referral centre in Ireland, a low prevalence country. We included, 814 patients screened, using CXR and interferon gold release assay (IGRA) over a 5-year period.
Results: The IGRA was positive in 5% (38/814) and indeterminate in 2.5% (20/814), the remainder testing negative. In the IGRA positive group, 15.8% (6/38) had an abnormal CXR. None of these showed changes reflecting prior or active tuberculosis. These showed fibrotic lung disease, consolidations and basal atelectasis. Of those who had an indeterminate IGRA, 45% (9/20) of cases had an abnormal CXR, with one individual report of radiographic evidence of possible prior TB. In those with an abnormal IGRA (positive or indeterminate), the addition of CXR in the screening process changed management in one patient. They were treated for LTBI on the basis of indeterminate IGRA, prior TB contacts, country of origin and other risk factors. The sensitivity of the IGRA alone screening approach was 97.62% when high risk indeterminate results were assumed to have LTB and were treated. The resulting specificity of the IGRA alone approach was 97.80%. The sensitivity of the combined IGRA & subsequent CXR approach was 100% as it was deemed to have captured all actual cases of LTB disease. We acknowledge that this not recognise that IGRA is an imperfect test and assumes that there were no cases of LTB in 756 IGRA negative patients. The specificity of the combined IGRA and subsequent CXR approach remains practically the same at 97.93%.
Conclusion: In conclusion, the clinical utility of the CXR in screening for TB is unclear in this population. The addition of CXR in the screening process only changed management in 1 patient over a 5 year period in this cohort. The incidental identification of interstitial lung diseases and chest infections is of value to patients considering immunosuppression, but is a separate issue to screening for LTB.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0175 RELEVANT FEATURES IN FLUORESCENCE OPTICAL IMAGING FOR DIFFERENTIAL DIAGNOSIS OF RHEUMATIC DISEASES AFFECTING THE HANDS

Keywords: Psoriatic arthritis, Imaging, Rheumatoid arthritis

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Background: Accurate and fast diagnosis of rheumatic diseases affecting the hands is essential for further treatment decision. Different rheumatic diseases affecting the hands present characteristic patterns and features in fluorescence optical imaging (FOI) as outlined in previous studies [1, 2].
Objectives: We tested an atlas of image features in FOI for their ability to differentiate various rheumatic joint diseases such as rheumatoid arthritis (RA), osteoarthritis (OA), psoriatic arthritis (PsA) and connective tissue diseases (CTD) like systemic sclerosis (SSc) and systemic lupus erythematodes (SLE) with the aim to identify specific features for differential diagnosis.

Methods: FOI images from patients with RA, OA, PsA and CTD were analysed by two readers blinded for diagnosis and calibrated against each other, using the prima vista mode (PVM) and the 5-phase model. For the latter, the overall time course of FOI in each hand was divided into 5 phases with a computational algorithm. Phases 1 and 2 describe the inflow (start to 15% and 15%-90% on rising edge), phase 3 is the peak phase and phases 4 and 5 comprise the outflow (90%-36.8% and 36.8% to end on falling edge). Twenty-six different features were defined, for example, the signal enhanced forearm (Y), broad signal enhancement along the finger (B), cloudy signal in the hand (W), secondary Raynaud syndrome (R), and underperfused nail bed region (U) (illustrated in the **Figure 1**). The feature frequency in each patient and phase (PVM, 5-phase) was counted and statistically analysed.
Results: In total, 374 patients (115 RA patients; mean age 54.4; SD 12.6; median 54.5), OA (89; 62.1; 7.4; 63.2), PsA (59; 50.0; 11.4; 49.2) and CTD (111; 52.2; 14.9; 54.5) were included in the feature reading. Statistical results (χ^2, diagnostic odds ratio DOR, sensitivity TPR, specificity TNR, positive predictive value PPV, negative predictive value NPV) are given in the **Table 1**. CTD can best be differentiated from RA, OA and PsA on the basis of the feature Y, in which sensitivity is high in all phases. CTD compared to RA in feature Y gives a similar result as in PsA. The other features B, W, R and U show Phase-dependent high specificity for CTD. Other significant image features from the atlas yield high specificity (70%-98%) while having low sensitivity (12%-52%) (data not presented).
Conclusion: This work supports that FOI feature analysis has the potential for differential diagnosis in rheumatic diseases affecting the hands. Feature Y has the ability to differentiate CTD (here mainly SLE/SSc) from RA, OA, and PsA while the features B, W, R and U can exclude CTD from RA, OA and PsA. In the future, FOI could therefore play an important role in the early arthritis clinic.
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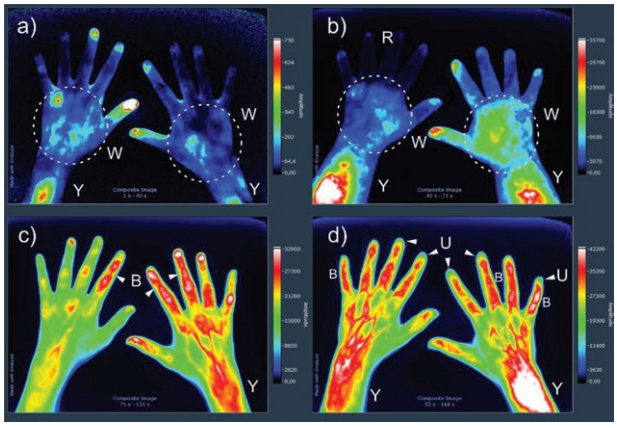


Figure 1. Examples for FOI patterns and features: a) Cloudy pattern in the hand (W) in phase 1; b) secondary Raynaud syndrome (R) in phase 2; c) broad signal enhancement along the finger (B) in phase 3; d) underperfused nailbed (U) in phase 4 and enhanced forearm (Y) in all subfigures.

Table 1. Statistical data for features Y, B, W, R and U comparing connective tissue diseases (CTD) to rheumatoid arthritis (RA), osteoarthritis (OA) and psoriatic arthritis (PsA); Diagnostic odds ratio, DOR; sensitivity TPR; specificity TNR; positive predictive value PPV; negative predictive value NPV.

CTD vs.	Feature	Phase	χ^2	DOR	TPR	TNR	PPV	NPV
OA	**Y**	1	45	4.1	65%	69%	72%	61%
		2	51	4.6	60%	75%	75%	61%
		3	70	6.5	61%	81%	80%	62%
		PVM	72	6.4	79%	63%	73%	70%
	R	2	16	4.5	18%	95%	83%	48%
	U	4	15	3.6	19%	94%	80%	48%
	W	1	19	3.0	35%	85%	74%	51%
PsA	**Y**	1	14	2.4	65%	57%	74%	46%
		2	11	2.1	60%	58%	73%	44%
		3	16	2.5	61%	62%	75%	45%
		PVM	5.9	1.9	79%	33%	69%	45%
	B	3	28	10	27%	97%	94%	41%
	W	1	17	3.4	35%	86%	83%	41%
RA	**W**	1	32	3.8	35%	88%	73%	59%
	B	3	29	4.4	27%	92%	77%	57%

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Non-pharmalogical interventions and outcomes

OP0176-HPR

SELF-MANAGEMENT BEHAVIOUR, ANXIETY AND DEPRESSION IN PATIENTS WITH INFLAMMATORY ARTHRITIS - A CROSS SECTIONAL NATIONWIDE STUDY AMONG >12,000 DANISH PATIENTS

Keywords: Inflammatory arthritides, Health Services Research, Self-management

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Background: Anxiety and depression are the mental health issues most commonly associated with inflammatory arthritis (IA) and the link between mental health issues and poor health outcomes is well-established [1]. European recommendations on self-management in rheumatic and musculoskeletal diseases emphasizes the need to assess mental health regularly [2]. However, little is known about the association between self-management and mental health in IA.
Objectives: To investigate the prevalence of anxiety and depression in patients with IA and evaluate the association of these mental health issues and self-management behavior.
Methods: We conducted a nationwide cross-sectional study among adult Danish patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or spondylarthritis (axSpA). Eligible patients were identified through the Danish Rheumatology database DANBIO and received an electronic questionnaire. The questionnaire covered socio-demographics, self-management behavior and mental health status indicated by the Hospital Anxiety and Depression Scale, a 14-item tool with 2 sub-scales assessing symptoms of anxiety and depression. Self-management behavior was indicated by: *Adherence to treatment* using Compliance Questionnaire Rheumatology-5 item, *Patient activation in healthcare* using two items from the Patient Activation Measure-13 questionnaire and *level of physical activity* covering weekly recommendation from WHO and American College of Sports Medicine. Self-management measures were dichotomized into high or low. Questionnaire data were linked to clinical data from DANBIO. The association between low self-management behaviour and mental health status were estimated using multivariable logistic regression with odds ratios (OR).
Results: A total of 42,407 patients with IA were identified; 30% (N=12,715) completed the questionnaire. Non-responders were younger than responders (60 (±16) vs. 62 (±13) years) with a similar gender distribution (p=0.187). The prevalence of anxiety (HADS-A ≥8) was highest for patients with axSpA (34.5% (95% CI; 32.4; 36.6)) and lowest for patients with RA (22.1% (95% CI: 21.2; 23.0)). Prevalence of depression (HADS-D ≥8) was highest for patients with PsA (27.2% (95%CI: 25.4;29.0)) and lowest for patients with RA 18.6% (95%CI: 17.7;19.4). For both anxiety and depression, the prevalence was higher for women, younger (<55 years), newly diagnosed (<3 years) and patients with basic education. Patients having a clinical level (HADS ≥8) of anxiety and depression were more likely to have low self-management behavior for all included self-management measures (Table 1).

Table 1. Association between mental health issues and self-management behavior

		Adherence to treatment	Patient activation in healthcare		Physical activity
			Can tell when outpatient care is needed	Can handle new situations with health condition	
		OR (95% CI)*	OR (95% CI)*	OR (95% CI)*	OR (95% CI)*
Anxiety	HADS-A ≤7	Ref	Ref	Ref	Ref
	HADS-A 8-10	1.22 (1.09;1.36)	2.33 (2.03;2.68)	2.91 (2.60;3.25)	1.32 (1.18; 1.47)
	HADS-A ≥11	1.41 (1.24;1.60)	4.33 (3.76;4.99)	5.72 (5.03;6.50)	1.62 (1.42;1.85)
Depression	HADS-D ≤7	Ref	Ref	Ref	Ref
	HADS-D 8-10	1.35 (1.20;1.52)	2.97 (2.60;3.39)	3.91 (3.50;4.38)	1.96 (1.74;2.22)
	HADS-D ≥11	1.30 (1.12;1.51)	4.96 (4.24;5.80)	7.09 (6.11;8.22)	2.43 (2.06;2.88)

*Adjusted for age, sex, education. Ref: reference group, low self-management behavior

Conclusion: In this nationwide study, high levels of anxiety and depression were seen among patients with IA. A strong association between anxiety and depression and low self-management behavior was identified. These findings call for a systematic approach in identifying mental health issues in patients with IA.

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OP0177-HPR HEALTH-RELATED QUALITY OF LIFE PROFILES OF ADULTS WITH ARTHRITIS

Keywords: Mental health, Quality of life

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Background: Adults with arthritis display poorer health-related quality of life (HRQOL) than the general population, including greater anxiety, depression, pain, and fatigue, and poorer physical function. Still, arthritis is a variable disease and the impact on HRQOL is heterogeneous in terms of severity and domains of impact. Some factors are associated with HRQOL outcomes in adults with arthritis, though research often focuses on a single outcome (like pain) rather than multiple HRQOL domains simultaneously. Examining protective and risk factors against a constellation of HRQOL outcomes would be beneficial for treatment of arthritis as a disease that impacts multiple areas of patients' lives.

Objectives: We aimed to identify profiles of HRQOL impact using the NIH's Patient-Reported Outcomes Measurement Information System (PROMIS) measures in a sample of adults with arthritis (osteoarthritis, inflammatory arthritis, fibromyalgia; with other arthritis types). We also aimed to identify demographic and clinical factors associated with HRQOL profile membership that serve as protective or risk factors against poor HRQOL outcomes.

Methods: Data including PROMIS measures of physical and social function, sleep disturbance, anxiety, depression, fatigue, and pain interference (PROMIS-29) and emotional support were collected through a national foundation's online survey of adults with arthritis in the U.S. PROMIS T-scores are calibrated with the U.S. general population mean of 50 (SD = 10). Higher function T-scores reflect better functioning and higher symptom T-scores reflect worse symptom burden. We used latent profile analysis (LPA), a patient-centered modeling approach, to characterize the heterogeneity in arthritis patients by clustering them into HRQOL profiles, determined based on statistical model fit and clinical interpretability. Participants were assigned to a HRQOL profile, and we fit a multinomial logistic regression model with HRQOL profile assignment as the outcome (best HRQOL profile as reference group) to determine associations with emotional support and demographic and clinical factors.

Results: We included 25,305 adults with arthritis. The LPA results favored a five-HRQOL profile solution (entropy = 0.83). See Figure 1 for profile details and participant counts. Profile 1 (8% of sample), the best HRQOL group, displayed higher physical and social functioning and lower physical and mental symptoms. Profiles 3 (37% of sample) and 4 (10% of sample) were similar, except those in Profile 4 had reduced anxiety and depression similar to Profile 1. Profile 5 (20% of sample), the worst HRQOL group, displayed mean T-scores close to 2 SDs below the US general population mean. All of the demographic and clinical factors were significant, including arthritis type. Compared to being classified into the best HRQOL group, participants who were unable to work were 39 times (95% CI = 20.35-73.85) more likely to be in the worst HRQOL group as participants who were working. Notably, higher emotional support (95% CI= 0.88-0.89) and starting to exercise (95% CI=0.45-0.70) were associated with a lower likelihood of membership in the worst HRQOL group (Profile 5).

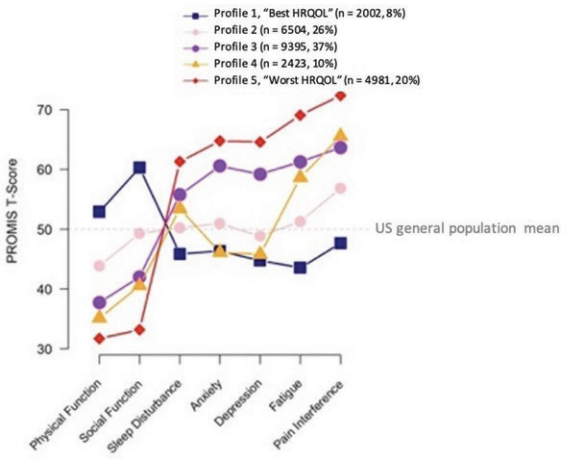
Conclusion: With the exception of the best HRQOL group, all the other HRQOL profiles (92% of sample) had poorer physical function and worse pain interference than the US general population, and elevated depression and anxiety, with some exceptions. Malleable factors such as emotional support and exercise served a protective function. These results highlight the value of considering multiple components of the patient's HRQOL experience alongside treatment options, and the potentially positive impact of interventions beyond medication.

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Figure 1. Five HRQOL Profiles Emerging from the LPA (including "Best" and "Worst" HRQOL)



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OP0178-HPR YOU FIRST: A COST-EFFECTIVE NURSE-LED PATIENT SUPPORT PROGRAMME – RETROSPECTIVE ANALYSIS FROM A LARGE MULTI-ETHNIC SETTING

Keywords: Real-world evidence, Spondyloarthritis, Psoriatic arthritis

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Background: The global impact of COVID-19 on elective rheumatology services is unprecedented, [1,2] and the number of people on waiting lists for consultant-led elective care in the UK has almost doubled. [3] Implementation of patient support programmes that provide an individualised nurse-led service, such as You First, may help to reduce the strain on healthcare resources. You First is aimed at people who have been prescribed secukinumab, an injectable anti-interleukin 17A monoclonal antibody, for approved indications including psoriatic arthritis (PsA), ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis.
Objectives: This retrospective analysis aimed to evaluate the benefits of the You First patient support programme on the Rheumatology service at a large university teaching hospital with a catchment population of 350,000, of whom 40% are from ethnic minorities.
Methods: The analysis included adult participants who were eligible for treatment with secukinumab according to National Institute for Health and Care Excellence criteria and were enrolled in the You First programme. All You First nurses were registered with the Nursing, and Midwifery Council and underwent specific training, competency assessment and validation to ensure they met all regulatory clinical standards of National Health service (NHS) practice. Each participant was assigned to a dedicated nurse who visited the participant's home to provide routine clinical assessments, routine follow-up visits, phlebotomy service, psychological support visits, injection training and routine secukinumab administration, as required. Participants could also schedule regular nurse telephone calls to discuss any disease or drug related concerns such as secukinumab dosing/adherence check and side effect management. All data gathered during the home visits and telephone calls were reported to the treating physicians. Calculation of cost savings was based on the number of visits carried out as part of You First and the cost that the NHS would have incurred if the visit occurred at the hospital (£2.02 for phlebotomy service, £24 for telephone contact, and £99 for each assessment, routine follow-up visits and psychological support visit). Here we present annualised data from 28 February 2019 to 14 July 2022.
Results: In total, 126 participants with PsA (n=81) and AS (n=45) were observed for 17.2 months on average. At baseline, the mean age was 52.7 years and 39.2% of participants were male. During the timeframe of this analysis, You First nurses had 1160 contact points with the clinical team (793 visits; 367 telephone calls). The median (interquartile range) number of visits and telephone calls carried out as part of the programme per participant per year was 6.4 (4.6–11.3): phlebotomy service 0.4 (0.0–1.6), clinical assessments 1.4 (0.0–2.0), routine follow-up visit 1.6 (0.7–3.1), psychological support visit 0.0 (0.0–0.0) and telephone contact 2.0 (1.0–4.7). This translated to an annual cost saving of £64,156.49 (phlebotomy service £335.90, clinical assessments £15,159.13, routine follow-up visits £36,434.58, psychological support visit £368.90, telephone contact £11,857.99).
Conclusion: Implementation of You First at this large university teaching hospital yielded substantial cost savings for the NHS, with outsourced visits providing the most cost savings. You First allowed people with PsA or AS to be managed at home, freeing NHS capacity for appointments with new and complex patients in the clinic.
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OP0179-HPR CHANGES IN WORK ABILITY FOLLOWING REHABILITATION

Keywords: Rehabilitation, Work-related issues, Patient reported outcomes

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Background: Improved work participation is an important goal in rehabilitation, and has important socio-economic benefits. Despite this, there is limited knowledge about how rehabilitation impacts work ability across different diagnostic groups.
Objectives: To examine whether personal and disease-related factors predict changes in self-perceived work ability one year after rehabilitation.
Methods: In a longitudinal multicenter rehabilitation cohort (RehabNytte) 17 rehabilitation centers across Norway recruited more than 3700 patients with rheumatic and musculoskeletal diseases (RMD) as the largest diagnostic group [1]. Participants completed questionnaires at admission and discharge, and after 3, 6 and 12 months. Work ability was self-reported with a single item from the Work Ability Index (WAI) (2), referred to as the Work Ability Scale (WAS), where patients compared their current work ability to their lifetime best on a 0-10 scale (10= best work ability). For the logistic regression analysis WAS was categorized as either low/moderate (≤7) or good/excellent (≥8) [3]. Variables of interest were age, gender, diagnosis (cancer, rheumatic and musculoskeletal diseases, other), comorbidities, health region, education level (low, medium, high), body mass index (BMI), smoking, pain intensity (NRS-scale 0-10) and self-reported health (EuroQol VAS, scale 0-100). Retired patients were removed from analysis. A logistic regression model was fitted with variables individually predicting WAS at 12 months follow up, adjusted for sociodemographic and lifestyle variables and baseline WAS.
Results: Mean age at baseline was 53.3 (13.6) years. Seventy percent were female, 42 % had RMD, 24 % cancers and 33 % other diseases. Mean WAS at baseline (n= 3096) was 3.3 (SD 3.0), which significantly increased to 4.4 (3.2) at 12-months follow-up (n= 2397) ($p<0.001$, Figure 1). Good WAS-score ≥ 8 at 12 months (adjusted for baseline work ability score and BMI) was predicted by high education level, higher age and high self-reported health at baseline, whereas low WAS-score ≤7 was predicted by RMD or cancer diseases, number of comorbidities and higher pain intensity (Table 1, OR in bold indicates $p<0.05$).
Conclusion: In addition to disease- and demographic factors like high age, high education, comorbidities and presence of RMD, changes in work ability scores were related to pain and self-reported health, factors that are modifiable trough rehabilitation.

Table 1. Logistic regression model of work ability 12 months after rehabilitation.

	Work ability	
	Univariable	Multivariable*
Independent variable	OR (95 % CI)	OR (95 % CI)
Age	1.0 (0.99, 1.00)	**1.01** (1.00, 1.02)
Education level		
10 years or less	1 (Ref)	1 (Ref)
High school	**1.56** (1.08, 2.26)	1.25 (0.78, 2.01)
University	**1.96** (1.37, 2.80)	**1.70** (1.07, 2.69)
Diagnosis		
Other disease	1 (Ref)	1 (Ref)
RMDs	0.80 (0.64, 0.99)	**0.60** (1.11, 3.31)
Cancer	**0.64** (0.49, 0.83)	**0.42** (0.26, 0.68)
Comorbidities	**0.84** (0.79, 0.90)	**0.79** (0.71, 0.87)
Pain intensity	**0.86** (0.80, 0.92)	**0.90** (0.83, 0.98)
EuroQol VAS	**1.04** (1.03, 1.04)	**1.02** (1.02, 1.03)

*Final model also adjusted for gender, BMI, health region, and work ability at baseline.

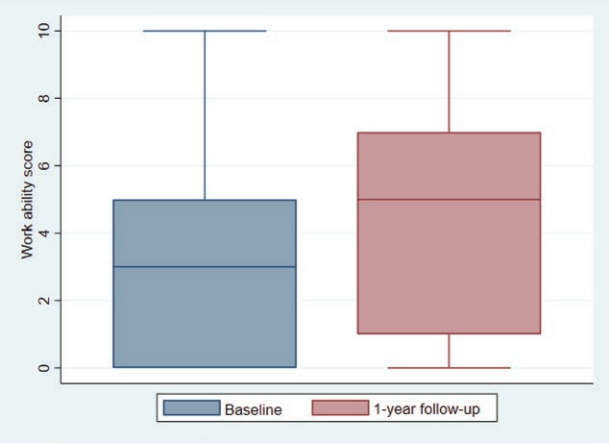


Figure 1. Work ability score (WAS) at baseline n = 3096, and at 1-year follow up n= 2397.

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OP0180-HPR DOES FOLLOW-UP REALLY MATTER? A MIXED METHODS STUDY EXPLORING PATIENTS' PERSPECTIVES ON FOLLOW-UP SUPPORT IN REHABILITATION ACROSS LEVELS OF CARE

Keywords: Quality of care, Rehabilitation, Patient reported outcomes

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Background: Lack of continuity in rehabilitation across levels of care is a known weakness of existing services. The BRIDGE-intervention was developed to improve the quality and continuity of rehabilitation for patients with rheumatic and musculoskeletal diseases (RMDs) by means of goal directed, coordinated, individually tailored follow-up after rehabilitation discharge. The intervention was evaluated in a multi-center randomised controlled trial (the BRIDGE trial) in Norway.
Objectives: The objective of this study was to explore what patients with RDMs need and receive of follow-up support in their municipality of residence after rehabilitation in secondary healthcare, and whether such follow-up impacts on clinical outcomes 1 year after rehabilitation. Further, to compare these findings with patients' experiences with follow-up support to develop a better understanding of how such follow-up works across levels of care.
Methods: The study had a concurrent mixed methods design in which quantitative and qualitative data were collected in parallel, analyzed separately, before integrated into an overall result. All participants in the intervention group (n=168) of the BRIDGE-trial were included. Quantitative data were patient-reported in an electronic portal. Demographic and disease-specific data were collected on admission to rehabilitation. Data on goal attainment (Patient Specific Functional Scale), physical function (30 seconds Sit-To-Stand test), health related quality of life (EQ5D-5L-index), and health status (EQ-VAS) were reported at discharge, 2, 7 and 12 months after rehabilitation. Needs for follow-up were reported at rehabilitation discharge by ticking off a list of 12 predefined options. The patients were categorized into 4 groups based on their needs for follow-up on discharge (yes/no) and the degree of follow-up received according to stated needs the first year after rehabilitation (none/partial/complete). Quantitative data were analyzed using descriptive statistics, ANCOVAs, and linear regression. Qualitative data about patients' experiences with follow-up were collected in semi-structured interviews with 21 patients and analyzed using reflexive thematic analysis. The results were integrated in the overall interpretation and discussion.
Results: The patients most often reported needs for follow-up from General Practitioner, physiotherapist, and social security services, and did mostly receive (> 85%) these services within 1 year after rehabilitation. There were no significant differences between the 4 groups with regard to characteristics at discharge, or clinical outcomes 1 year after rehabilitation. Received individually tailored follow-up was not shown to significantly influence clinical outcomes, and was, surprisingly, associated with reduced patient reported health 1 year after rehabilitation: EQ-VAS β 0.28 [95% CI -0.48, -0.09], p=0.004. The qualitative analysis resulted in three themes: "Contact between service levels" (established through various actors, processes, documents), "Follow-up keeps the rehabilitation process going" (by increasing motivation and focus on goals and self-effort after discharge), and " Loss of momentum' (linked to personal and structural factors).
Conclusion: Patients with RMDs report needs for follow-up from one or more healthcare services after rehabilitation in secondary care. Clinical outcomes 1 year after rehabilitation appeared to be influenced by several other factors than the actual received follow-up support. Health personnel's competence and structural factors across health service levels, such as waiting lists and limited access to care, seemed to be decisive for the progress of the rehabilitation process over time, together with factors related to the individual patient and his/her life situation. The findings can contribute to increased insight into what promotes continuity in rehabilitation processes, effective follow-up, and better health for this patient group.
REFERENCES: NIL.
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OP0181-HPR SOCIO-ECONOMIC, DISEASE-RELATED, AND PERSONAL FACTORS ASSOCIATED WITH PARTICIPATION IN REMOTE FOLLOW-UP IN RHEUMATOID ARTHRITIS – A CROSS-SECTIONAL STUDY

Keywords: Patient reported outcomes, Telemedicine, Rheumatoid arthritis

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Background: Remote follow-up by collecting patient-reported outcome (PRO) measures allows for new opportunities such as real-time monitoring of symptoms and flexible scheduling of hospital visits based on patient needs[1]. In Denmark, a remote PRO-based follow-up intervention has been implemented among outpatients with rheuamtoid arthritis (RA), and today, 35% of the outpatient population attends remote care. However, no study has explored factors associated with participation in remote care.
Objectives: To identify socio-economic, disease-related, and personal factors associated with participation in remote follow-up in RA patients.
Methods: We conducted a cross-sectional study among 775 prevalent RA patients from Aarhus University Hospital. In January 2019, eligible RA patients received an electronic questionnaire, covering health literacy and patient experience regarding involvement and confidence with remote care. In addition, we collected data from nationwide registers regarding socio-economic status, labor market affiliation, and co-morbidity. Associations between register and questionnaire-based factors and remote follow-up were analyzed using multiple logistic regression.
Results: A total of 775 patients were included in the register-based analyses. Since 129 patients did not have a digital mailbox, 646 patients received the electronic questionnaire which was completed by 394 (61%) patients. No labor market attachment and low household income was associated with lower odds for remote follow-up participation (OR 0.53 (95% CI 0.34 – 0.83)) and (OR 0.69

(95% CI 0.48 – 1.00)). Further, a high level of co-morbidity was associated with lower odds for remote follow-up participation compared to a low/medium level of co-morbidity (OR 0.53 (95% CI 0.34 – 0.81)). No association was found between health literacy and remote follow-up. Remote follow-up attendees reported more confidence in remote care (OR 1.33 (95% CI 1.20 – 1.47)).

Conclusion: Patients participating in remote follow-up were more likely attached to the labor market, had higher income levels, had a lower level of comorbidity, and expressed higher confidence in remote care. Future research should focus on how to support RA patients in conventional follow-up to achieve confidence in remote follow-up, as well as increased focus on vulnerable patient groups and the need for differential use of healthcare services.

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OP0182-HPR EFFICACY OF NON-PHARMACOLOGICAL INTERVENTIONS: A SYSTEMATIC REVIEW INFORMING THE 2023 EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF FATIGUE IN PEOPLE WITH INFLAMMATORY RHEUMATIC AND MUSCULOSKELETAL DISEASES

Keywords: Non-pharmacological interventions, Patient reported outcomes, Systematic review

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Background: Several EULAR recommendations for the management of people with specific inflammatory rheumatic and musculoskeletal diseases (I-RMDs) have highlighted the importance of some non-pharmacological interventions in the management of fatigue [1-3]. However, these recommendations are either disease-specific or focusing on a single intervention, and lack an integrated view of the overall evidence for fatigue management with non-pharmacological therapies in the wider context of all I-RMD.

Objectives: To identify the best evidence on the efficacy of non-pharmacological interventions in reducing fatigue in people with I-RMDs and to summarise their safety in the identified studies to inform EULAR recommendations for the management of fatigue in people with I-RMD.

Methods: Systematic review of adults with I-RMD conducted according to the Cochrane Handbook. Search strategy ran in Medline, Embase, Cochrane Library, CINAHL Complete, PEDro, OTseeker and PsycINFO. Assessment of risk of bias, data extraction, and synthesis performed by two reviewers independently. Data pooled in statistical meta-analyses.

Results: From a total of 4,150 records, 454 were selected for full-text review, 82 fulfilled the inclusion criteria, and 55 RCTs were included in meta-analyses. Physical activity or exercise were efficacious in reducing fatigue in rheumatoid arthritis (RA) (SMD=-0.23, p<0.001), systemic lupus erythematosus (SLE) (SMD=-0.54, p=0.04) and spondyloarthritis (SpA) (SMD=-0.94, p<0.001). A reduction in fatigue was also observed in Sjögren's syndrome and systemic sclerosis, although not statistically significant (SMD=-0.83, p=0.21; SMD=-0.66, p=0.06, respectively). Psychoeducational interventions were efficacious in reducing fatigue in RA (SMD=-0.32, p<0.001), but not in SLE (SMD=-0.19, p=0.18). Follow-up models in consultations and multicomponent interventions reduced fatigue in RA, although the effect was not statistically significant (SMD=-0.05, p=0.71; SMD=-0.20, p=0.24, respectively) (**Figure 1**). The narrative results of the RCTs not included in the meta-analysis indicated that several other non-pharmacological interventions were efficacious in reducing fatigue, with reassuring safety results.

Conclusion: Non-pharmacological interventions are efficacious and safe for the management of fatigue in people with I-RMD.

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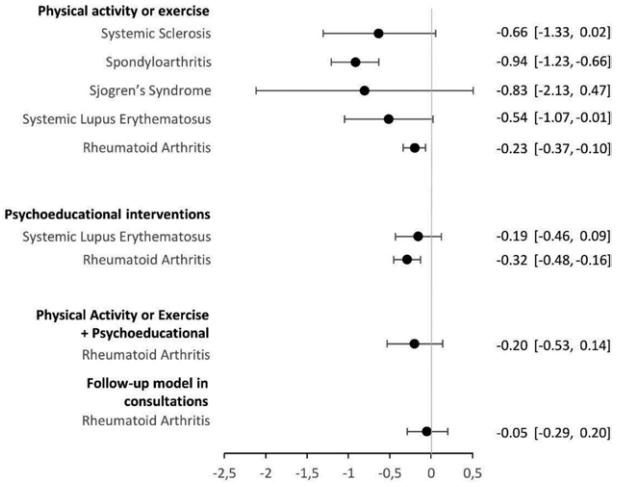


Figure 1. The summary of the meta-analyses

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0 – 100 in 75 minutes; RMDs have no age

OP0183-PARE CO-DESIGNING JIA TOOLBOX: A PROOF-OF-CONCEPT STUDY ASSESSING PROTOTYPE INNOVATIONS TO HELP SELF-MANAGEMENT IN CHILDREN AND YOUNG PEOPLE WITH RHEUMATIC DISEASE

Keywords: Self-management, Inflammatory arthritides, Non-pharmacological interventions

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Background: Juvenile idiopathic arthritis (JIA) is the most frequently occurring rheumatic disease of childhood. It causes ongoing joint inflammation, pain and stiffness making everyday activities difficult. Studies have emphasised the negative impacts JIA has across physical, social, psychological, and educational development. Devices exist to assist with daily activities such as washing, eating, or writing. However, a survey we conducted in 2018 highlighted that the majority of these are designed for adults. Those designed for Children and Young People (CYP) are often either difficult to use, stigmatising, patronising, or fail to address their unique needs and contexts. This has resulted in numerous unmet needs and a lack of effective innovations for this population. The innovation, JIA Toolbox, was co-designed, meaning CYP with JIA, their parents, healthcare professionals, teachers and design researchers collectively collaborated throughout its development. Here, we present the intervention stage of the project, where JIA Toolbox was tested and evaluated by CYP with JIA.

Objectives: To evaluate the potential impacts of JIA Toolbox in improving independence and functional ability of CYP with JIA. To obtain real-world feedback on

JIA Toolbox to inform future device refinement. To provide contemporary data on CYP's experiences of living with JIA to inform future innovation.
Methods: JIA Toolbox was tested over a 9-week period. This suite of innovations consisted of:

- Prototype 1: A wearable pain management device
- Prototype 2: A motivational physiotherapy tool
- Prototype 3: A communication aid for use in school



Fig 1. JIA Toolbox

A sample size of 10 CYP (7-16yrs), their parents and teachers were involved. Whilst small, this number was felt adequate due to the individual and qualitative nature of JIA condition experience.
Their involvement included:

- Training sessions for data collection and prototype use. CYP and their parents recorded their daily experience using a digital booklet with specific questions about their condition and prototype use.
- 3-week baseline data collection without JIA Toolbox.
- 5-week intervention data collection with JIA Toolbox.
- 1-week post intervention data collection without JIA Toolbox.
- End of intervention interview.

Results: Analysis of the findings is currently being undertaken. Preliminary results indicate that 70-90% of the sample group found one or more of the innovations highly beneficial, helping with their overall condition management. Prototype 1 was highlighted as an effective therapeutic aid "it helped soothe my knee, I liked how you can position it exactly where it hurts". One patient found it reduced pain when used with joint injections. Prototype 2 was helpful for physiotherapy exercises "to keep count" and "know how long to hold it for" with preliminary data indicating at least 50% of users increased the regularity of their physio stretches over the intervention period. The innovation acted as an ongoing reminder, "it encouraged him to do his physio stretches as he hadn't been doing any before". Prototype 3 "helped communicate when I was in pain and needed help". The use of this intervention depended on the child's individual confidence, with those feeling less confident, relying more on the technology. These users found it beneficial, "the teacher knew I needed a rest break without me having to say anything in front of the rest of the class". Participants also highlighted areas that could be improved to increase ease of use and engagement.
Conclusion: Based on initial results, the proof-of-concept was successful with these innovations proving to be beneficial to CYP with JIA. The patient data will allow refinement of these devices and provide insights into the lived experiences of CYP with JIA. These devices may have applicability to both adult populations with rheumatic disease and CYP with other conditions. Further research will explore these avenues in the future. Next steps include applying for further funding to undertake a feasibility study with a larger sample population.
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E-health - possibilities and pitfalls

OP0184-PARE HOW REPRESENTATIVE ARE PATIENT REPRESENTATIVES? HEALTH LITERACY SCORES AND PROFILES OF REPRESENTATIVES OF PATIENT ORGANISATIONS AS COMPARED TO AN EXISTING SAMPLE OF PEOPLE WITH RMDS

Keywords: Patient information and education, Self-management, Outcome measures

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Background: Patient organisations are a key resource of information and support for people with rheumatic and musculoskeletal diseases (RMDs). Patient representatives advocate for the development of appropriate resources and provide organisations with a rich range of perspectives, including health literacy strengths, needs and preferences. Health literacy is defined as *"the personal knowledge and competencies that accumulate through daily activities, social interactions and across generations. Personal knowledge and competencies are mediated by the organisational structures and availability of resources that enable people to access, understand, appraise and use information and services in ways that promote and maintain good health and well-being for themselves and those around them"* [1].
Objectives: To identify health literacy strengths and weaknesses among patient representatives of RMD patient organisations, and compare with an existing dataset of people with RMDs attending outpatient rheumatology clinics [2].
Methods: All patient representatives attending the EULAR PARE Conference 2022 were invited to participate in an online survey before the conference. Health literacy was assessed using the Health Literacy Questionnaire (HLQ), which provides scores for nine distinct domains (higher scores being better; scores range 1-4 for domains 1-5, and 1-5 for domains 6-9). The survey also included socio-demographics and health-related characteristics. Hierarchical cluster analysis of patient representatives' HLQ domain scores identified distinct health literacy profiles, based on minimal variance within and maximum variance between profiles. Results were compared with an existing cross-sectional sample of 895 patients with RMDs from different regions in the Netherlands. HLQ domain scores and patient characteristics were compared using chi-square and independent t-tests. Identified health literacy profiles were compared visually using heat maps.
Results: 56 patient representatives completed the survey (76% response rate). Compared to previously surveyed patients, patient representatives were younger (mean ±SD age 49.3±13.0 vs. 61.1±13.9), more often female (79% vs. 49%, p<0.001), more highly educated (79% vs. 24.5% high education, 0% vs. 51% low education, p<0.001), more often employed (64% vs. 33%, p<0.001), and less often of migrant background (7% vs. 18%, p=0.044). Both groups were similar in terms of comorbidities (RDCI = 1.3 vs. 1.2), self-reported health (6.5 vs. 6.4), household (16% vs. 25% living alone) and mastery (20.3 vs. 20.0). Patient representatives scored higher on "3. Actively managing health" (3.1 vs. 2.9, p=0.001 & "5. Critical appraisal of information (3.2 vs. 2.7, p<0.001), but lower on "6. Actively engaging with providers" (3.6 vs. 4.0, p=0.001) & "7. Navigating the health system" (3.5 vs. 3.8, p=0.002). While similar patterns were seen in health literacy profiles, the profiles that represent most complex challenges in the patient survey (representing 16% of patients) were not found among patient representatives (see Figure 1).

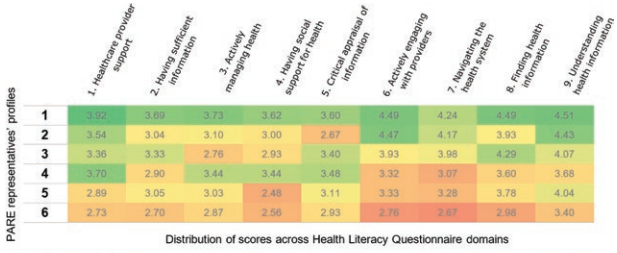


Figure. Heat map of six identified health literacy profiles of patient representatives, showing mean Health Literacy Questionnaire scores per domain for each profile. Colours follow a traffic light sequence: scores marked in red indicate lowest scores (orange = low, yellow = moderate, green = high).

Conclusion: Patient representatives of RMD patient organisations represent diverse profiles of health literacy strengths and weaknesses, but the most complex challenges in the original patient survey were not found. Differences may relate to how patients are selected and supported to become a representative, and how being a representative improves some aspects of health literacy. Patient organisations should take into account that their target population generally has more difficulty actively managing health and critically appraising information, and includes more people with diverse health literacy needs than their patient representatives may report.

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[2] Bakker et al. Arthritis Care Res. 2021;73(1):100-9

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Single-cell omics in Rheumatic diseases

OP0185 IMMUNOPHENOTYPIC ABNORMALITIES REMINISCENT OF ESTABLISHED RHEUMATOID ARTHRITIS ARE PRESENT IN ACPA(+) AT-RISK INDIVIDUALS

Keywords: Rheumatoid arthritis, Biomarkers, -omics

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Background: RA-associated autoantibodies (RF, ACPA) are detectable before the onset of clinically-apparent inflammatory arthritis (IA) and classifiable RA (i.e. "Clinical RA"), defining a state known as 'At-Risk' for future RA. However, RA prevention trials in individuals in this At-Risk state have shown limited success in prevention. A challenge to developing more effective preventive interventions is that the immune phenotype of the At-Risk state remains incompletely understood.
Objectives: The purpose of this study was to (1) evaluate the hypothesis that ACPA(+) At-Risk individuals have immunopathologic features of Clinical RA, and (2) determine additional molecular features that define the At-Risk state. We propose that such features may help to identify biomarkers and causal pathophysiologic mechanisms that could be treatment or prevention targets. Furthermore, At-Risk immune features could improve prediction of future Clinical RA, as well as be used to monitor responses to therapeutic interventions.
Methods: Using a cross-sectional methodology, we analyzed ACPA(+) individuals without baseline IA (i.e. At-Risk) and age, sex and BMI matched ACPA(-) controls without IA (Table 1). We tested plasma proteomics, peripheral blood mononuclear cell (PBMC) composition by flow cytometry, and PBMC transcriptomes by single-cell RNA-sequencing (scRNA-seq). We further compared these findings to immunophenotypes reported in patients with Clinical RA. All studies were performed as part of a collaborative effort between the Allen Institute for Immunology, University of California San Diego, University of Colorado and Benaroya Research Institute.
Results: We observed significant differences in plasma levels of 138 proteins between ACPA(+) individuals vs. controls, including IL-6 (log2 fold change (FC) = 0.59-0.62, adjusted p value (padj) < 0.05), IL1B (log2 FC = 0.44, padj = 0.006), and CCL3 (log2 FC = 0.60, padj = 0.002). These changes also included additional elevated inflammatory chemokines and cytokines that have been reported in Clinical RA. B cell receptor signaling was one of the most significantly enriched protein pathways in ACPA(+) individuals. These proteomic alterations in ACPA(+) individuals were accompanied by numerous PBMC phenotypic changes, notably an increase in IgD- CD27- B cells (log2 FC = 0.814, padj = 0.002). Furthermore, compared to controls, scRNA-seq of IgD- CD27- B cells from ACPA(+) individuals expressed lower levels of genes previously shown to be increased in IgD- CD27- B cells or autoimmune processes, including SAMHD1 (log2 FC = -0.34, padj < 0.05), ARID3A (log2 FC = -0.32, padj < 0.05), and ZC3H12D (log2 FC = -0.30, padj < 0.05), suggesting dysregulation of this compartment at the preclinical stage.
Conclusion: ACPA(+) At-Risk individuals demonstrate numerous immune-related changes that are similar to changes in established Clinical RA, suggesting the ACPA(+) At-Risk state is on a continuum with Clinical RA. Highlighted are plasma proteomics demonstrating cytokine/chemokine elevations and B cell signaling pathways, and PBMC studies demonstrating specific B cell phenotypes and gene expression. These findings provide insights to potential immunopathologic mechanisms that may impact how we define the 'At-Risk' state, may improve prediction of future RA, and suggest targets for interventions or intermediate endpoints in trials for RA prevention.

Table 1. Cohort Information

Variable	ACPA(+) At-Risk	Control	p-value
Clinical Features			
Number	46	52	-
Age at sample draw, median	62	57	0.01
Sex at birth, %			
Female	78.26	78.85	1
Male	21.74	21.15	-
Race, %			
Caucasian	82.61	88.46	0.57
Black	8.70	0.00	0.05
Asian	2.17	7.69	0.37
Other	6.52	3.85	0.66
Ethnicity, %			
Non-hispanic	95.65	96.15	1
Hispanic/Latino	4.35	3.85	-
BMI	26.29	25.59	0.62
Serum Biomarkers			
Serum CCP3, median (IQR)	60 (42.5, 183)	0 (0,2)	< 1e-6
Serum RF IgA, median (IQR)	0.25 (0.25, 4.63)	0 (0,0)	< 1e-6
Serum RF IgM, median (IQR)	0.57 (0.25, 22.23)	0 (0,4.3)	2.5e-4

REFERENCES: NIL.
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OP0186 DISTINCT PERIPHERAL IMMUNOPHENOTYPING UNDERLINES HISTOPATHOLOGICAL FEATURES IN PATIENTS WITH LUPUS NEPHRITIS IN A LARGE MULTI-CENTER COHORT

Keywords: Kidneys, -Omics, Systemic lupus erythematosus

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Background: Lupus nephritis (LN) is a common and severe complication of systemic lupus erythematosus (SLE) requiring renal biopsy to guide treatment decisions. Despite standard-of-care therapy, a third of patients with LN class III, IV, or V show a progressive decline in kidney function, including those with improved proteinuria. Defining LN heterogeneity using a non-invasive approach is a pressing need to improve treatment.

Objectives: To determine circulating immune cell phenotypes characteristic of LN histology.

Methods: Mass cytometry using four 48-marker panels were applied to characterize peripheral blood mononuclear cells (PBMC) from 140 patients with biopsy-proven class III, IV, or V LN and 40 healthy controls included in the Accelerated Medicine Partnership RA/SLE Network Phase II study. After filtering for quality control and correcting for batch effects, we projected cells in a reduced dimensional space and identified cell neighborhoods and clusters using an unsupervised approach. We implemented covarying neighborhood analysis (CNA) to identify cell populations associated with clinical features.

Results: Compared to controls, LN patients displayed marked enrichment of cell neighborhoods that expressed interferon (IFN)-induced proteins including MX1 (p.adj < 0.001) and Siglec1 (p.adj < 0.001), reflecting a simple, cytometric detection of an IFN signature. Detailed immune cell subsetting using the B cell- (Figure 1A), T cell-, myeloid cell-, and NK cell-focused panels identified several alterations in LN patients compared to controls, including increased $CD27^{-}IgD^{-}$(DN) $CD11c^{+}Tbet^{+}$ B cells (OR 1.6, 95%CI 1.3-2.2, p.adj < 0.001) and T peripheral helper cells (OR 1.8, 95%CI 1.3-2.8, p.adj = 0.002), and decreased plasmacytoid dendritic cells (OR 0.6, 95%CI 0.4-0.8, p.adj < 0.001), adjusting for age, sex, ethnicity and race. LN patients with minimal immunosuppression (IS, n=14) displayed similar results. Comparing patients with proliferative LN (class III or IV +/- V, n=94) versus membranous LN (class V, n=46), we observed the most significant alterations within B cells, with enrichment of a naive B cell population characterized as $CD23^{-}$ and $CD21^{dim}$ (Figure 1B,C). The phenotype of this enriched naive B cell population was distinct from transitional and $CD11c^{+}$ 'activated naive' cells (Figure 1D). This B cell population was also associated with increased histologic NIH activity score (Figure 1B,C) even after adjusting for IS, and with positive anti-dsDNA antibody (p = 0.02). To further understand the LN heterogeneity, we clustered LN patients and controls based on proportions of all PBMC subsets using k-means clustering and projected subjects in a UMAP space. We identified two prominent clusters: cluster 1 included only LN patients, and cluster 2 included all controls and 26 LN patients. LN patients in cluster 2 (Control-like) had significantly lower clinical extrarenal activity (coef -1.1, 95%CI -2.1--0.1, p.adj = 0.03) and IFN-induced protein expression (coef -28.0, 95%CI -36.6—19.4, p.adj < 0.001), adjusting for IS. In addition, these patients had significantly higher histologic chronicity (coef 2.39, 95%CI 1.24-3.53, p.adj < 0.001). In line with these findings, we confirmed by CNA the association of increased histologic chronicity with fewer $MX1^{+}$ or $Siglec1^{+}$ IFN-responsive cells, adjusting for IS (p.adj = 0.002, FDR < 10%).

Conclusion: In addition to profoundly impaired circulating immunophenotype observed in LN patients, we identified a difference in naive B cell states in patients with proliferative LN compared to membranous LN. Based on circulating immunophenotype, we identified a subset of SLE patients with low extrarenal activity and increased histologic evidence of chronic kidney damage. These results nominate potential non-invasive biomarkers associated with LN heterogeneity and highlight altered naive B cell activation in proliferative LN.

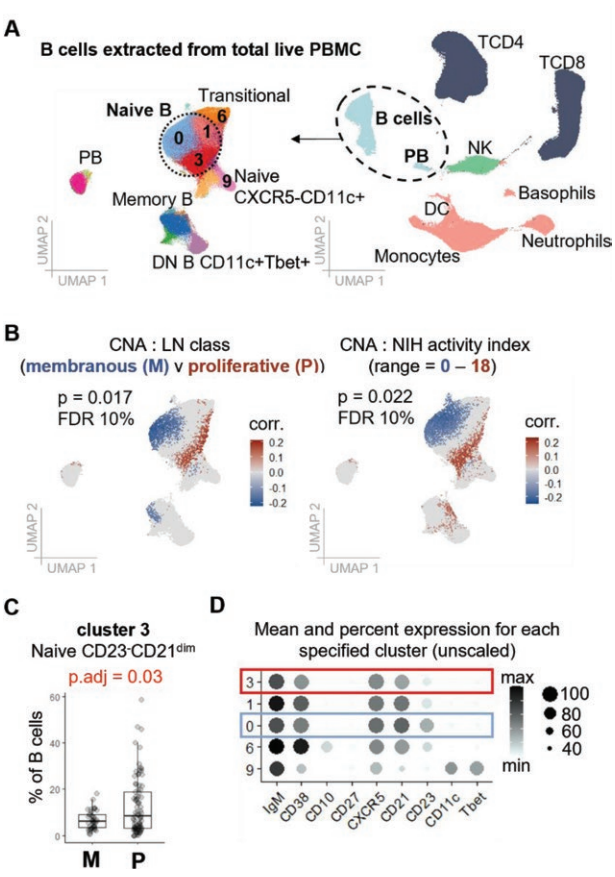


Figure 1.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Spondyloarthritis across the ages

OP0187

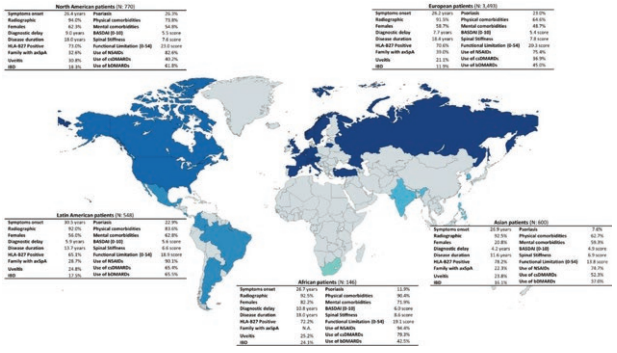
REGIONAL DIFFERENCES IN CLINICAL PHENOTYPE OF AXIAL SPONDYLOARTHRITIS. RESULTS FROM THE INTERNATIONAL MAP OF AXIAL SPONDYLOARTHRITIS (IMAS)

Keywords: Spondyloarthritis, bDMARD, Geographical differences

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Background: Previous studies have suggested there could be regional differences in clinical phenotype of axial spondyloarthritis (axSpA).

Objectives: This analysis aims to explore differences in axSpA clinical phenotype around the world in a large sample of patients included in the International Map of Axial Spondyloarthritis (IMAS).
Methods: IMAS was a cross-sectional online survey (2017-2022) of 5,557 unselected axSpA patients from 27 countries. We analysed across 5 geographic regions the age at onset of symptoms, classification as radiographic or non-radiographic, gender, HLA-B27, axSpA family history, extra-musculoskeletal manifestations (uveitis, inflammatory bowel disease and psoriasis), presence of comorbidities, disease activity (BASDAI), level of spinal stiffness, and treatment (NSAIDs, csDMARDs and bDMARDs). Kruskal-Wallis and chi-square test were used to compare axSpA characteristics across the regions.
Results: 5,557 patients participated in IMAS survey of which 3,493 were from Europe, 770 from North America, 600 from Asia, 548 from Latin America, and 146 from Africa. Results showed statistically significant differences between regions, except for the classification status (radiographic or non-radiographic). Age at onset of symptoms ranged between 25-30 years, and was higher in Latin America as compared to other regions. Diagnostic delay was longest in South Africa and lowest in Asia. The lowest frequency of HLA-B27 positivity was observed in Latin America and the highest in Asia. Family history of SpA was most often recorded in Europe and less often in Asia. All extra-musculoskeletal manifestations included were lowest in Europe compared with other regions. Physical and mental comorbidities were frequent in African patients and less common in Europe and Asia. Mean disease activity (BASDAI) was 5.4, with highest values in South Africa and lowest in Asia. Spinal stiffness was highest in South Africa and lowest in Latin America. Functional limitation was higher in North America and Europe and lower in Asia. Most of the patients had used NSAIDs for their condition and less than half had ever taken csDMARDS; both were more frequent in Latin America and South Africa. Almost half of the patients had ever taken bDMARDs, more frequent being in the Americas (**Map 1**).
Conclusion: There is great heterogeneity of axSpA clinical phenotype presentation around the world. Further understanding of these differences is needed to achieve early diagnosis and initiation of disease treatment in axSpA.



Map 1. The clinical phenotype of axial spondyloarthritis stratified by region (N= 5,557)

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Why is performing a good systematic literature review (SLR) so difficult?

OP0188

IMAGING IN DIAGNOSIS, MONITORING AND OUTCOME PREDICTION OF LARGE VESSEL VASCULITIS: A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2023 UPDATE OF THE EULAR RECOMMENDATIONS

Keywords: Systematic review, Vasculitis, Imaging

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Background: Since the development of the EULAR recommendations for the use of imaging in large vessel vasculitis (LVV) in 2017, new data has emerged in the field of imaging techniques and their application in the diagnosis and follow-up of patients with giant cell arteritis (GCA) and Takayasu arteritis (TAK).
Objectives: To summarize the evidence on different imaging techniques for diagnosis, monitoring, and outcome prediction in LVV in order to inform a EULAR task force updating the recommendations for imaging in LVV.
Methods: Systematic literature review (SLR) on studies published between 2017-2022 on ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET)-CT/MRI and fluorescein angiography in patients with LVV (PROSPERO registration CRD42022360545). Eligible study designs included randomized controlled trials and observational studies but excluded case-controlled studies. Two reviewers independently performed data extraction, synthesis, and risk of bias assessment. For studies on diagnosis, meta-analyses were performed using data from both the original and updated SLR whenever possible. Pooled sensitivities and specificities were obtained by fitting random effects models for all studies and for studies with low risk of bias separately. Meta-analyses were performed in R version 4.2.1. using the "lme4" package. The description of observations without inferences and the heterogeneity of reported data precluded any meta-analysis for outcome prediction or monitoring.
Results: A total of 4696 references were identified. Thirty-eight studies on GCA (n=32), TAK (n=2), and GCA and TAK (n=4) were included through the update, adding up to eighty-one studies from both SLRs. Pooled sensitivities and specificities for US, MRI and PET-CT using a clinical diagnosis of GCA as the reference standard are depicted in Table 1. No studies on the diagnostic value of imaging techniques were found for TAK. The US evaluation of patients with suspected GCA, including the assessment of both cranial and extracranial vessels, showed a higher pooled sensitivity (95%CI) (89% [73%-96%] vs 70% [59%-79%]) and similar specificity (95%CI) (91% [83%-95%] vs 91% [84%-94%]) compared to only including cranial vessels. Studies on outcome prediction (n=5) and monitoring (n=10) reported change of signs of vasculitis along with disease activity and proposed composite scores comprising several vessel territories for US, MRI and PET-CT.
Conclusion: US, MRI and PET-CT revealed a good performance for the diagnosis of GCA. Assessing both cranial and extracranial vessels with US leads to a higher pooled sensitivity with a similar pooled specificity compared to an assessment limited to cranial vessels.

Table 1. Pooled sensitivities and specificities of diagnostic studies on GCA with clinical diagnosis as reference standard

	Index test	Number of studies	Pooled sensitivity (95%CI)	Pooled specificity (95%CI)
All studies	US	23	0.76 (0.66,0.83)	0.91 (0.86,0.94)
	MRI	8	0.82 (0.76,0.86)	0.92 (0.84,0.97)
	PET-CT	5	0.80 (0.70,0.87)	0.91 (0.67,0.98)
Low risk of bias studies	US	8	0.88 (0.83,0.92)	0.96 (0.86,0.99)
	MRI	3	0.81 (0.71,0.89)	0.98 (0.89,1.00)
	PET-CT	4	0.76 (0.67,0.83)	0.95 (0.71,0.99)

GCA, giant cell arteritis; MRI, magnetic resonance imaging; PET-CT, positron emission tomography – computed tomography; US, ultrasound

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Talking about Remission

OP0189

REMISSION CRITERIA GUIDING IMMUNOSUPPRESSIVE THERAPY IN RA: WHICH IS BEST FITTED FOR THIS PURPOSE?

Keywords: Remission, Treat to target, Rheumatoid arthritis

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Background: Remission is the target for the management of rheumatoid arthritis (RA). However, the best definition of remission is still under debate, particularly regarding the inclusion of patient global assessment (PGA).[1] An increased cut-off for PGA (from ≤1 to ≤2cm) was recently proposed by ACR/EULAR for its Boolean-based criteria,[2] but others have suggested to replace PGA by the Physician's Global Assessment (PhGA)[3], or to simply drop PGA (ie, 3-Variable Boolean remission) when the objective is to guide immunosuppressive therapy.[2] Radiographic progression is a relevant reference standard to investigate as outcome of persistent/residual disease activity.

Objectives: To assess which definition of remission best predicts good radiographic outcome (GRO) in RA.

Methods: Meta-analyses using individual patient data (IPD) from 8 randomized controlled trials assessing the efficacy of bDMARDs on radiographic outcomes in RA. Six different definitions of remission were considered: i) The ACR/EULAR Boolean with 4 variables (Boolean 4v) with PGA≤1 (4vPGA); ii) SDAI≤3.3; iii) CDAI≤2.8; iv) Boolean 4v with PGA≤2 (4vPGA2); v) Boolean 4v replacing PGA by PhGA (4vPhGA), and vi) Boolean excluding PGA (3v). Good radiographic outcome (GRO) was defined as an increase of ≤0.5 modified Total Sharp score (mTSS) units. The relationship between achieving each remission definition at 6 and/or 12 months and GRO during the second year was analysed. The pooled probabilities of GRO for the different definitions of remission were estimated and compared, as well as their predictive accuracy (True Positive + True Negative). Meta-analyses were performed using the DerSimonian-Laird random-effects method.

Results: IPD from 4423 patients of 8 RCTs were analysed. 4vPGA remission was achieved by 24.3% of patients and 3V remission by 43.4%. The adoption of the recently proposed PGA≤2 cut-off results in an "in-between" rate of 32.4% (Table 1). GRO was observed in 77.6% of all patients, ranging from 65 to 91% in different trials. GRO among patients achieving remission ranged from 82.4% (3v) to 83.9% (SDAI), without any statistically significant difference between the 6 definitions considered. Boolean 3v remission showed a higher predictive accuracy (51.1%, 95%CI: 46.9-55.6%) than 4vPGA (38.8%, 95%CI: 34.1-43.5%). The 4vPhGA and the 4vPGA2 remission definitions performed in between, providing a correct prediction in 43.8 and 44.8% of the cases, respectively. The performance of SDAI- and CDAI-based definitions were, overall, very similar to that of 4vPGA. (Figure 1)

Table 1. Rates of remission and good radiographic outcomes in the included studies

		Remission at 6 and/or 12-months n (%)			Good Radiographic Outcome n (%)
Trial (year)	N	4vPGA	4vPGA2	3v	ΔmTSS≤0.5
DE019 (2004)	425	68 (16)	94 (22)	113 (27)	297 (70)
TEMPO (2004)	442	113 (26)	156 (35)	204 (46)	330 (75)
COMET (2008)	344	102 (30)	143 (42)	209 (61)	289 (84)
RAPID 1 (2008)	650	177 (27)	243 (37)	320 (49)	508 (78)
RAPID 2 (2009)	417	51 (12)	77 (19)	132 (32)	324 (78)
LITHE (2011)	761	141 (18)	209 (28)	307 (40)	610 (80)
DE013 (2013)	540	156 (29)	175 (32)	206 (38)	351 (65)
FUNCTION (2016)	844	308 (37)	381 (45)	459 (54)	766 (91)
Polled %		24	32*	43*	78
(95% CI)		(18 - 30)	(26 - 39)	(36 - 51)	(71 - 84)

ΔmTSS change in the modified total Sharp score during the second year of follow-up. *p<0.001 when compared with the 4vPGA definition.

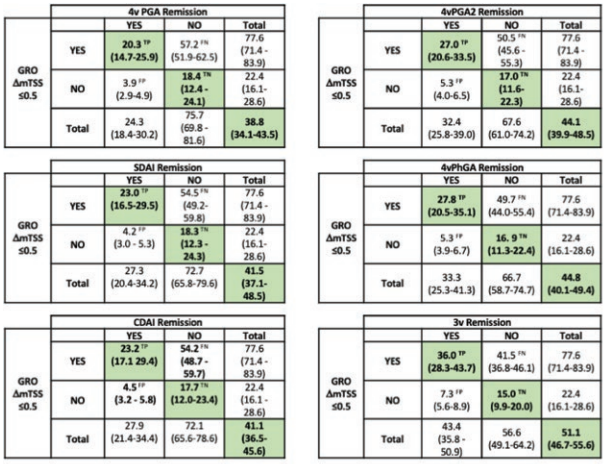


Figure 1: Accuracy of prediction of good radiographic outcome by remission criterion

All meta-analyses used the double arcsine transformation as the preferred method.; 4423 patients were included in GRO analysis; Legend: GRO: Good Radiographic Outcome; TP: True positive, TN: True negative, FP: False positive (risk of undertreatment); FN: False negative (risk of overtreatment). Accurately predicted= TP + TN. Between brackets is the pooled 95% CI.

Conclusion: The Boolean 3v remission provided the most accurate prediction of GRO, even better than 4vPGA2 and 4vPhGA remission. The use of the 3v definition in treatment recommendations would avoid the risk of overtreatment in a significant proportion of patients, with a minor increment in radiographic damage progression, validating 3v-remission as a preferable guide for immunosuppressive treatment. The patient's perspective, which must remain central, is best served by a dedicated autonomous target, rather than PGA: a dual-target approach.

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Artificial Intelligence in Medicine: Chances & Challenges

OP0190

A MACHINE LEARNING MODEL THAT PREDICTS RA PROGRESSION FROM UNDIFFERENTIATED ARTHRITIS -KURAMA AND ANSWER COHORT STUDY-

Keywords: Rheumatoid arthritis, Undifferentiated connective tissue disease, Real-world evidence

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Background: Early diagnosis and treatment of rheumatoid arthritis (RA) improve clinical outcomes. Undifferentiated arthritis (UA) is arthritis that does not fit a specific diagnosis. Half of the UA undergo spontaneous remission, while 30% of cases develop RA. Therefore, in UA, identifying patients at high risk for developing RA and providing close monitoring for those patients is required for early diagnosis and treatment [1]. However, predicting the evolution of UA to RA is still difficult.
Objectives: Machine learning, including deep learning, which is comparable to and in some cases surpasses the performance of human experts, is broadening its application in medicine. This study aims to build a machine-learning model that predicts the development of UA to RA.
Methods: For model training, a total of 322 UA patients in KURAMA cohort were analyzed (Table 1). For variables to train models, we chose 24 clinical features, which are easy to obtain in daily clinical practice. The target variable was the final diagnosis. We built models using Random forest (RF), XGBoost (XGB), Logistic regression (LR), and Deep neural network (DNN) and compared their performances. For model validation, we used data of 88 UA cases in ANSWER cohort (Table 1).
Results: We trained models using 24 clinical parameters at the first clinical visit, performed 10-fold cross-validation, and evaluated model performance by averaging accuracy and AUC. The performance of the models was 73.5%, 74.2%, 74.5%, and 85.1% in precision and 0.760, 0.734, 0.748, and 0.895 in AUC for RF, XGB, LR, and DNN, respectively. DNN showed the highest performance. We then applied the DNN model to external validation data from ANSWER cohort and found that the prediction accuracy was 80.0%.
Conclusion: Using parameters available in clinical practice, we developed a DNN model that effectively predicted RA development in internal and external UA datasets. Applying a machine learning approach might enable identifying patients at high risk of RA progression and improve the clinical management of UA patients.

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Table 1. Baseline patients' characteristics

	KURAMA		ANSWER	
Variables	RA (n=94)	Non-RA (n=228)	RA (n=14)	Non-RA (n=74)
age (median, yr)	60 [46.5-69]	53.5 [44-64]	44 [37.75-53.5]	63 [53.3-69.8]
sex (female%)	72.34%	78.07%	71.43%	64.86%
BMI (median, kg/m^2)	22.03 [20.09-24.29]	21.23 [19.22-23.90]	22.60 [20.85-28.37]	21.55 [19.68-23.44]
Family history of RA (positive %)	31.91%	27.19%	14.29%	17.57%
Smoking (current or past %)	35.11%	30.70%	57.14%	63.51%
CRP (median, mg/dL)	0.3 [0.1-1.1]	0.1 [0-0.1]	0.23 [0.078-0.63]	0.12 [0.04-1.09]
ESR_1h (median, mm)	19 [9-41]	12 [6-19.25]	11 [8-36.75]	13 [7.5-37.5]
RF (median, IU/mL)	8 [8-22.7]	8 [8-18.53]	6 [5-36.75]	7 [5-19]
ACPA (median, U/mL)	0.6 [0.6-0.7]	0.6 [0.6-0.6]	5.6 [0.675-263]	0.7 [0.5-3.05]
MMP-3 (median, ng/mL)	65.85 [43.15-137.58]	46.7 [31.9-62.13]	81.4 [49.03-98.78]	55.35 [39.16-128.15]
Dr_VAS (median, mm)	20 [9.25-33]	7 [2-17.25]	20 [10.5-32.25]	18 [10-33]
Pt_VAS (median, mm)	49.5 [22.25-67.75]	44 [15-55.25]	48.5 [31.5-64.5]	47 [21-68]
DAS28_CRP (median,)	3.22 [2.36-4.08]	2.38 [1.78-2.94]	3.27 [2.38-4.02]	3.09 [2.27-4.20]
HAQ (median)	0.5 [0.125-1]	0.25 [0-0.5]	0.313 [0-0.594]	0.375 [0.125-0.969]
ACR2010_points (median)	4 [3-5]	3 [2-4]	1 [0.25-2.75]	1 [0-2] [Q1-Q3]

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Exploring and managing inequalities in RMD healthcare

OP0191-HPR

SOMEONE LIKE ME: THE EFFICACY OF A PEER MENTORING INTERVENTION ON DISEASE SELF-MANAGEMENT AND HEALTH-RELATED QUALITY OF LIFE AMONG AFRICAN AMERICAN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Keywords: Quality of life, Systemic lupus erythematosus, Self-management

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Background: Disease self-management indicates practical ways to deal with pain, fatigue, and stress and can include better nutrition, exercise, understanding treatment options, and better communication. Evidence-based self-management interventions designed to enhance social support and provide health education, among lupus patients, have demonstrated significant improvements in health distress, self-reported global health, and activity limitation, but African Americans and women are still disproportionately impacted by systemic lupus erythematosus (SLE).
Objectives: The purpose of this study was to determine whether participation in a new, culturally tailored peer mentoring intervention was associated with improvements in disease self-management and health related quality of life (HRQOL) among African American women with systemic lupus erythematosus (SLE).
Methods: The Peer Approaches to Lupus Self-Management (PALS) study was a randomized controlled trial wherein modeling and reinforcement of disease self-management skills by peers (mentors) to other African American women with SLE (mentees) was achieved through a combination of educational and informal phone or video interactions with each other. The control condition included small support groups that met on the same schedule as peer mentoring sessions. The Lupus Quality of Life questionnaire (LUP-QOL), which incorporates the Medical Outcomes Study (MOS) Short Form 36 Health Survey (SF-36) and the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), was used to determine HRQOL, and the Patient Activation Measure (PAM) assessed disease self-management or an individual's knowledge, skill, and confidence for managing their health and healthcare. Generalized Linear Mixed Models were used to determine whether the intervention produced a greater change in these main outcomes from baseline, controlling for education, income, and age, reported.
Results: Of the 314 enrolled PALS participants, 138 were mentored (experimental), 132 participated in small support groups (controls), and 44 served as mentors. Although not statistically significant, there were incrementally improving trends in patient activation as the intervention progressed, among mentors and experimental participants and decreasing trends in depression and anxiety among experimental participants. Measures of social functioning (from the LUP-QOL) and coping (or lupus self-efficacy) significantly improved from baseline, among experimental participants (both $p < 0.05$).
Conclusion: Our findings suggest that participation in a peer mentoring intervention led to improvements in disease self-management and HRQOL, in areas of social functioning, coping, depression, and anxiety, among African American women with SLE. Since these factors are related to disease activity and morbidity/damage, future investigations should consider ways in which this approach can augment clinical care on a larger scale.

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Mind the gap: improving communication and outcomes

OP0192-PARE

GENERE DONNA – THE COMMUNICATION PROJECT ON GENDER MEDICINE AND AUTOIMMUNE DISEASES, SUPPORTING WOMEN WITH RHEUMATIC AND DERMATOLOGIC AUTOIMMUNE DISEASES

Keywords: Patient information and education, Gender/diversity issues, Pregnancy and reproduction

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Background: The World Health Organization (WHO) defines Gender-specific Medicine as the study of how biological and socioeconomic and cultural differences influence people's health. (1) In autoimmune diseases (AD), particularly rheumatic and dermatologic ones, Gender makes the difference. Among millions of people affected worldwide, 80% are Women. (2) AD can arise more frequently in childbearing age, can impact female fertility and pregnancy outcomes, with consequences on the overall quality of life, both for the people affected and their families and caregivers.
Objectives: Genere Donna is a project aimed at setting up an awareness campaign on Gender Medicine focused on rheumatic and dermatologic autoimmune diseases. It spreads and updates a clear information, validated by experts, about Gender Medicine and rheumatic and dermatologic ADs, to improve knowledge, promoting patients' empowerment and the importance of a gender approach in Public Health.
Methods: Genere Donna has been launched in July 2021. The website www.generedonna.it and the social media profiles are the heart of the project, raising awareness also through adv campaigns (SEM and social media) and ad-hoc content marketing. The close teamwork of the main Italian patients' associations ANMAR (Associazione Nazionale Malati Reumatici Onlus), APMARR (Associazione Nazionale Persone con Malattie Reumatologiche e Rare aps) and APIAFCO (Associazione Psoriasici Italiani Amici della Fondazione Corazza) and some authoritative experts KOLs in AD (5 physicians and a welfare expert) is the key for success. Genere Donna is supported by a digital communication agency.
Results: Over 16 months of activity, there were about 160K website users (70% female, 56% of them are 18-44 years old), over 6.6Mln reach and over 220K interactions on social media, and a strong social community of around 27K people was developed. Over 210 questions received through the "Ask the Expert" service. Genere Donna recently received the patronage from SIR-Società Italiana di Reumatologia (Italian Society of Rheumatology) and SIDeMaST, Società Italiana di Dermatologia e Malattie Sessualmente Trasmesse (Italian Society of Dermatology).
Conclusion: The strong need of clear and verified information around Gender Medicine is testified by the wide number of social media interactions and website visits. The good results reached by Genere Donna up to now and many positive comments coming from the community push the project ahead in the future, to be more and more near to the patients affected by rheumatic and dermatologic ADs.
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Figure 1.

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Clinical and molecular differences across sexes in Rheumatic Disease

OP0193

SEX DIMORPHISM ANALYSIS IN A COHORT OF JIA PATIENTS REVEALS DIFFERING GENETIC RISK FACTORS FOR FEMALES AND MALES

Keywords: Inflammatory arthritides, Genetics/Epigenetics, Gender/diversity issues

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Background: Juvenile idiopathic arthritis (JIA) encompasses a group of childhood onset rheumatic diseases that primarily affect females. JIA has been reported to occur in females and males with a 2:1 ratio, however, systemic JIA is reported to occur equally in sexes and enthesitis-related arthritis (ERA) is reported more frequently in male patients. Genetic risk factors may contribute to the sex dimorphism in JIA incidence, however this contribution has yet to be defined.
Objectives: To investigate, using sex dimorphism analysis, whether genetic risk factors for JIA differ in males and females.
Methods: High quality genotype data was available on 3356 JIA cases (females = 2209, males =1147) and 9196 controls (female =4059, males =5137). Our primary analysis combined sex-specific GWAS summary statistics using the GWAMA software package. Summary statistics were calculated using logistic regression with three principal components as covariates using PLINK. The sex-differentiated p-value (p_{diff}) provided overall evidence for association to JIA allowing for differences between males and females,and the heterogeneity p-value (p_{het}) provided evidence to support a difference in effect estimates between sexes. As a secondary analysis we performed a logistic regression, as above, on all samples and included sex as an interaction term (p_{int}). Amino acid residues in HLA genes and alleles were imputed using SNP2HLA and an association test with sex as an interaction term was implemented on markers of interest.
Results: A total of 6571296 SNPs were analysed after quality control. The strongest signal detected using a logistic regression in females was rs9469137 ($p = 1.7x10^{-80}$) and in males it was rs116666910 ($p = 9.7x10^{-59}$). GWAMA supported evidence of sex heterogeneity for these SNPs, rs9469137 $p_{het} = 2.2x10^{-6}$, $OR_{males} = 2.6$, $OR_{females} = 5.3$, rs116666910 $p_{het} = 1.8x10^{-14}$ $OR_{male} = 4.0$, $OR_{female} = 1.6$. The strongest signal from the sex-specific GWAS was rs9266716, $p_{het} = 1.9x10^{-17}$, $p_{int} = 7.7x10^{-18}$, $OR_{male} = 1.2$, $OR_{female} = 0.6$. These SNPs all map to the HLA region, providing strong evidence for sex dimorphism in this region, therefore sex-specific HLA fine mapping was conducted. This analysis revealed that residues at position 13 of *HLA-DRB1* were strongly associated with JIA in females ($p_{female} = 1.8x10^{-124}$). Glycine at position 13 of *HLA-DRB1* was most strongly associated with JIA in females ($OR_{female} = 3.6$, $p_{female} = 4.1x10^{-65}$, $OR_{male} = 1.9$, $p_{male} = 9.6x10^{-13}$). An association test with sex as an interaction term revealed glycine at position 13 as sex dimorphic, $p = 4.3x10^{-7}$. Associations of residues at position 13 of *HLA-DRB1* have previously been reported in JIA, where the cohort consisted of oligoarthritis and rheumatoid factor negative polyarthritis individuals. These ILAR subtypes have a greater frequency in females. *HLA-B27* was detected as strongly associated with JIA in male patients ($p_{male} = 5.4 x10^{-64}$, $OR_{male} = 3.8$, $p_{female} = 2.5x10^{-9}$, $OR_{female} = 1.6$). An association test with sex as an interaction term revealed *HLA-B27* to be strongly sex dimorphic, $p = 7.5x10^{-15}$. *HLA-B27* is a well-established risk factor for ERA, where males are predominately affected. Outside of the HLA region, the strongest associated SNP was rs58020114, $p_{het} = 6.3x10^{-7}$, $p_{int} = 5.7x10^{-7}$ $OR_{male} = 1.3$, $OR_{female} = 0.7$. This SNP is located near the *BPNT2* gene and had a greater effect size in males.
Conclusion: This analysis reveals that there are several sexually dimorphic genetic risk factors that may affect JIA development in males and females. For the first time markers within the *HLA* region have been detected as sex dimorphic. Understanding the genetic risk factors to JIA development will help to further define the disease, which may aid in disease classification and diagnosis in the future. In particular, the substantial differences in effect estimates observed between males and females suggests that sex-specific polygenic risk scores should be considered when HLA signals are incorporated into these efforts.
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Pain in RMDs

OP0194 INFLAMMATION-INDUCED PAIN AND FATIGUE IN FIBROMYALGIA AND ME/CFS AND ROLE OF VARIANT CONNECTIVE TISSUE

Keywords: Fibromyalgia, Cytokines and chemokines, Patient reported outcomes

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Background: Fibromyalgia and ME/CFS are multifaceted conditions with overlapping symptoms(1); the pathophysiological mechanisms are under debate. It remains unclear whether dysregulated inflammation, induced either by an exogenous stimulus (*eg* a virus or other stressor), or autoimmunity, is of prime importance [2].
Objectives: 1. To determine in a novel human model the effects of an *in* vivo inflammatory challenge in the induction of pain and fatigue in fibromyalgia and ME/CFS compared to controls.
2. Explore potential mediators and moderators involved.
Methods: Data were available for 48 patients with confirmed diagnoses of Fibromyalgia and/ or ME/CFS and 22 matched controls, who had undergone a placebo controlled inflammatory challenge (typhoid vaccination) as part of ISRCTN78820481. Participants underwent full research diagnostic evaluation including a hypermobility assessment. Subjective pain and fatigue were assessed after saline injection and typhoid vaccination (VAS). Linear regression models were used to explore predictors, with adjustment for potential confounders (age/gender) and baseline levels as appropriate. Mediation analyses (looking for mechanistic effects) were conducted according to the method of Hayes (3) and mediation considered significant if bootstrapped confidence intervals of the estimated indirect effect did not cross zero. In these mediation analyses predictor variable was group membership (patient or control), outcome variable was change in 1) pain and 2) fatigue induced by challenge and mediators/moderators included change in IL-6 induced by inflammatory challenge and hypermobility features.
Results: Being a patient rather than control significantly predicted inflammation-induced fatigue (B=14.89 (95%CI 3.29-26.50), t=2.56, p=0.013) and pain (B=12.88 (95%CI 0.65-25.10), t=2.11, p=0.039) after adjusting for levels induced by placebo. Induced pain was independently predicted by level of IL-6 induced by inflammatory challenge (B=23.44 (95%CI 5.15-41.72),t=2.57, p=0.013) as was induced fatigue (B=10.63 (95%CI 2.84-18.41), t=2.73, p=0.008) Mediated moderation analyses suggested the link to induced pain and fatigue through induced inflammation was associated with hypermobility features (Index of mediated moderation 11.02 (95%CI 1.45-22.73) and 6.20 (95%CI 0.07-13.64) respectively))
Conclusion: To our knowledge this is the first human study to evaluate directly the effect of an exogenous inflammatory challenge (typhoid vaccination) in a combined group of Fibromyalgia and ME/CFS patients. Il-6 was shown to be a critical mediator. This work strongly supports the hypothesis that inflammation is key to the pathophysiology of ME/CFS. We are evaluating associated CNS inflammation in the model, as well as other associations, such as autonomic dysfunction and hypermobility. Further understanding the mediators involved in the condition should in future open the way to testing targeted anti-inflammatory therapy.
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OP0195 TARGETED ABLATION OF KNEE-INNERVATING NOCICEPTORS HAS PROFOUND EFFECTS ON JOINT DAMAGE IN EXPERIMENTAL OSTEOARTHRITIS

Keywords: Osteoarthritis, Animal models

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Background: Sensory afferents abundantly innervate the knee joint. The vast majority of these are pain-sensing nociceptors, which express the voltage-gated sodium channel, $Na_V1.8$. Using $Na_V1.8$Cre-tdTomato reporter mice, we have documented innervation changes that occur with experimental murine osteoarthritis (OA), including sprouting of nociceptors in the medial synovium and in subchondral bone [1]. Upon intra-articular (IA) injection into the mouse knee, adeno-associated virus serotype AAV.PHP.S is retrogradely transported to the lumbar dorsal root ganglia (DRG), where the cell bodies of sensory neurons reside [2].
Objectives: We leveraged this technique to selectively ablate knee-innervating nociceptors by IA injection of AAV.PHP.S carrying diphtheria toxin A (dtA), and determine the effect on joint damage after destabilization of the medial meniscus (DMM).
Methods: Expt. 1: AAV.PHP.S containing pAAV-EF1a-mCherry-flex-dtA (AAV-dtA) was injected into the right knee of 7-week old male C57BL/6 $Na_V1.8$Cre mice (3 µL, 10^{12} vp/mL). Three weeks later, the TLR2 ligand, Pam3CSK4 (3 µg), was injected into these same knees, followed by knee hyperalgesia measurement (using PAM) over 24-hours [3]. $Na_V1.8$Cre mice injected with AAV.PHP.S-EF1a-flex-GFP (AAV-Control) as well as wild type mice injected with AAV-dtA were included as controls (n=6 mice/group). Expt. 2: AAV-dtA or AAV-Control was injected IA into the right knees of 7-week old male $Na_V1.8$Cre mice and 3 weeks later, DMM surgery was performed (n=19 mice/group). Mice were sacrificed 10 or 17 weeks after DMM, and knees collected for histologu using a modified OARSI scoring system (toluidine blue, frontal plane). Expt. 3: Ten-week old male $Na_V1.8$Cre mice underwent DMM surgery, and 4 weeks later, AAV-dtA or AAV-Control was injected IA into the operated knees (n=12 mice/group). Knees were collected 17 weeks after surgery for histology.
Results: Expt. 1: $Na_V1.8$Cre mice injected with AAV-Control and WT mice injected with AAV-dtA responded to TLR2 stimulation, showing markedly decreased knee pain thresholds between 1 and 6 hours after IA injection of Pam3CSK4, as described [3]. In contrast, $Na_V1.8$Cre mice injected with AAV-dtA did not respond to Pam3CSK4, indicating functional effects of ablating knee-innervating nociceptors with AAV-dtA. Expt. 2: Ten weeks after DMM, all mice showed mild OA joint damage, with no difference between groups (Figure 1A). However, while AAV-Control injected joints showed markedly increased cartilage damage by week 17, AAV-dtA injected joints showed no progression of cartilage degeneration compared to week 10. Osteophytes were comparable between the groups. Expt. 3: Seventeen weeks after DMM, mice that had been injected with AAV-dtA 4 weeks *post* DMM showed markedly increased cartilage degeneration, total joint scores, and osteophyte sizes compared to AAV-controls (Figure 1B).

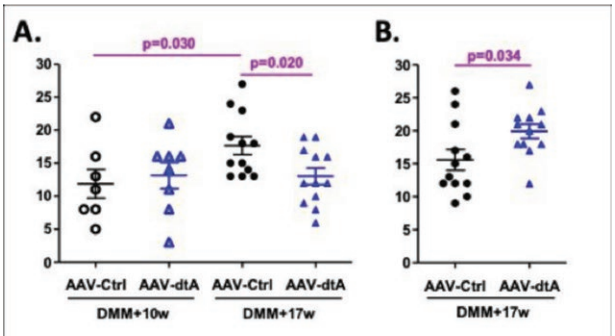


Fig. 1. Cartilage degeneration scores of knee joints 10 or 17 weeks after DMM. (A) AAV-dtA was injected 3 weeks before DMM. (B) AAV-dtA was injected 4 weeks after DMM.

Conclusion: IA delivery of AAV-dtA into enables selective ablation of $Na_V1.8$+ neurons in the knee, as is evident from ablated pain responses to TLR2 stimulation. Experiments in the DMM model revealed a striking effect of ablation of joint nociceptors on joint damage: Nociceptor ablation *before* DMM significantly *attenuated* cartilage degeneration in late stage OA, while ablation of knee nociceptors

after DMM markedly *worsened* joint damage and osteophyte formation. These findings suggest an important role for nociceptors in joint homeostasis, with differential effects if nociceptors are ablated before or after joint damage occurs. Our findings suggest a neurogenic contribution to joint homeostasis. Current work focuses on documenting the joint nociceptive innervation in the different experimental groups, and the relationship with pain.

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OP0196 ANTI-TNF TREATMENT MODIFIES PAIN MODULATION DESCENDING PATHWAYS. A PROSPECTIVE, 6 MONTHS STUDY IN ACTIVE CHRONIC INFLAMMATORY RHEUMATISM PATIENTS' NAÏVE OF BDMARD

Keywords: bDMARD, Rheumatoid arthritis, Pain

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Background: In rheumatoid arthritis (RA) and spondyloarthritis (Spa), persistent pain remains challenging. In active disease, diffuse noxious inhibitory controls (assessed through conditioned pain modulation (CPM)) are impaired [1]. Little is known regarding impairment of pain pathways in patients under bMDARD.
Objectives: The main objective of the RAPID (Rheumatism Pain Inhibitory Descending pathways) study, was to assess descending pain modulation (through CPM paradigm) in patients with active RA or Spa, after introduction of first bDMARD with anti-TNF.
Methods: We included 50 RA and 50 Spa patients with active disease, naïve of bDMARD. We assessed clinical disease variables for patients, together with responses to various psychological questionnaires. All participants underwent QST with the determination of heat and cold pain thresholds (HPT-CPT) on dominant forearm and CPM. CPM paradigm require a conditioning stimulus, here applied to the non-dominant foot (cold circulating bath at 8°C during 1min). Descending pain control was assessed as the change in HPT (in °C) following the conditioning stimulus: the higher the CPM effect, the more efficient the inhibitory control. Patients were followed at 3 and 6 months after TNF inhibitor initiation. At both follow-up visits, clinical monitoring of the rheumatism and repeated thermal QST and CPM.
Results: One hundred patients were included, 59 women, mean age 45.8 (± 14.6) and mean disease duration 7.93 (± 7.96) years. Due to COVID surge 87 patients initiated an anti-TNF, 74 patients completed the follow-up. At 6 months, 40 patients achieved a good therapeutic response (good EULAR response or ASDAS major improvement), 19 patients had a moderate therapeutic response (moderate EULAR response or clinically important improvement) and 15 patients had no therapeutic response. At the end of follow-up, 51 patients were in remission or low disease activity and 47 patients had a pain intensity <4/10. Thermal pain thresholds did not significantly change during follow-up. Mean HPT was at beaseline 42.35°C (+/- 3.68) and at 6 months 42.17°C (+/- 3.67). Mean CPT was at baseline 13.11°C (+/- 10.04) and at 6 months 12.86°C (+/- 9.45). Conditioned pain modulation was significantly changed during follow-up. Mean CPM effect was at baseline 0.25°C (±2.57), 2.64°C (±2.12) at 3 months and 2.96°C (±2.50) at 6 months. At the end of the 6 months follow-up, mean CPM effect was significantly higher in patients with residual mean pain intensity <4/10 compared to patients with persisting pain ≥ 4/10: 3,25°C (± 2,68) vs 2,47 (± 2,11) (p=0.04).
Conclusion: After TNF inhibitor initiation in active RA or SpA, impaired diffuse noxious inhibitory controls are significantly improved. Apart from their articular efficacy, TNF inhibitor have an action on the central nervous system and pain modulation pathways. In patients with persisting pain under bDMARD, diffuse noxious inhibitory controls are not as efficient as patient without residual pain.

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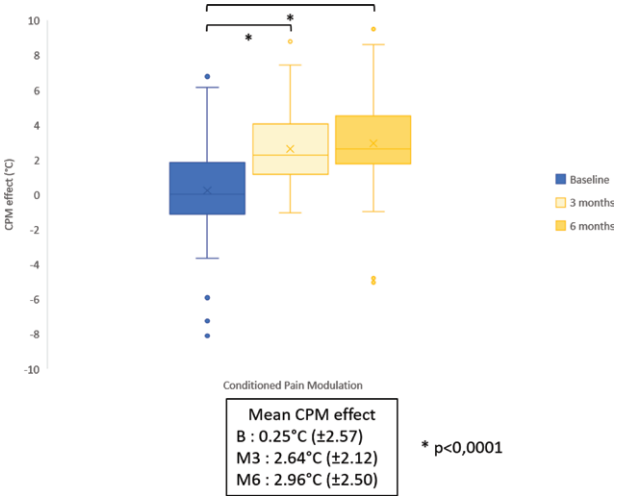


Figure 1.

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Disclosure of Interests: None Declared.

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OP0197 FACTORS ASSOCIATED WITH LONG-TERM OPIOID USE IN FIBROMYALGIA PATIENTS NEWLY STARTED ON AN OPIOID: RESULTS USING UK PRIMARY CARE ELECTRONIC PATIENT RECORDS

Keywords: Artificial intelligence, Fibromyalgia, Prognostic factors

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Background: The impact of the opioid epidemic in North America has caused concern in the United Kingdom and across Europe. Long-term opioid use is associated with several opioid-related harms and adverse outcomes. Fibromyalgia is frequently treated with opioids due to limited therapeutic options. Understanding what factors are associated with long-term opioid use in such patients is the first step in helping to develop targeted interventions for deprescribing.
Objectives: The objective of this study was to (i) quantify the proportion of new opioid users with fibromyalgia who become long-term opioid users (ii) identify risk factors associated with long-term opioid use in fibromyalgia.
Methods: A retrospective cohort study was conducted using data from the Clinical Practice Research Datalink (CPRD). CPRD is a national database of electronic health records within primary care, representation of the UK general population. Fibromyalgia patients without prior cancer who were new opioid users between 01/Jan/2006 and 31/Aug/2021 were included. Long-term opioid use was defined as at least 3 opioid prescriptions issued within a 90-day period, or ≥1 opioid prescription lasting at least 90 days, in the first year of follow-up. Logistic regression analysis and a random forest model were used to identify risk factors related to long-term opioid use. Compared to logistic regression, random forest variable importance measures covered both the effects of individual predictor variables as well as multivariate interactions with other predictor variables. In the random forest model, the mean decrease accuracy (MDA) index to measure the variables' importance was used; the larger the value of the mean decrease accuracy, the more important the variable is.
Results: Of the 28,552 fibromyalgia patients who were new opioids users, 7,375 (26%) became long-term opioid users in the first year. In the fully adjusted logistic regression model, suicide and self-harm (adjusted odds ratio [aOR]: 1.98, 95% confidence interval (CI): 1.72-2.27, p<0.001), substance use disorder (aOR: 2.07, 95%CI: 1.62-2.66, p<0.001), most deprived (Index of Multiple Deprivation (IMD) quintile 5/most deprived, aOR: 1.98, 95%CI: 1.69-2.33, p<0.001, compared with quintile 1/least deprived), obesity (aOR: very severely obese, OR: 2.35, 95%CI: 1.76-3.18, p<0.001) and mean daily morphine milligram equivalents (MME) at

the initiation (High (120-199 MME/day): aOR: 34.81, 95%CI: 18- 78.05, p<0.001 compared to mean daily MME: Low (<50 MME/day)) were associated with higher risk of long-term opioid use. The three most important variables using the random forest model were mean MME/day at initiation (MDA 140), history of suicide and self-harm (MDA 40) and IMD (MDA 30).

Conclusion: Almost 1 in 4 patients with fibromyalgia starting opioids became a long-term opioid user in this nationally representative dataset across the UK within the first year. The dose of initial opioid prescription, high deprivation score, history of suicide and self-harm, substance use disorder and obesity were associated with long-term opioid use.

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Disclosure of Interests: None Declared.

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OP0198 UNSUPERVISED MACHINE LEARNING FOR PATIENT CLUSTERING IN CHRONIC REFRACTORY PAIN SYNDROMES AND FIBROMYALGIA: RESULTS FROM A MULTIMODAL TREATMENT PROGRAM

Keywords: Artificial intelligence, Fibromyalgia

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Background: Chronic Pain Syndromes (CPS), including fibromyalgia (FM), place a significant health and socioeconomic burden. Despite sharing a similar clinical presentation, they are a heterogeneous entity, often with different causes and in association with other conditions. Multimodal treatment programs allow a comprehensive clinical and physical assessment of those patients.

Objectives: The objective of this study is to identify subtypes in CPS patients including primary and secondary FM who were assessed during a two-week multimodal pain management program via an unsupervised machine learning model.

Methods: We collected data from 202 patients as part of a 2-week multimodal pain management program. Clinical features, comorbidities, medications and demographics were collected and patients were assessed by physical and mental questionnaires (e.g. BPI, FABQ, FABQ-W, POAM, HAS, HDS, PCS, TAMPA, OD) before and after the program. There was a weekly interdisciplinary case discussion between rheumatologists, pain specialists, psychiatrists, physiotherapists and occupational therapists. For data analysis, hierarchical agglomerative clusters were generated using the Ward variance minimization algorithm with Euclidean pairwise distances (Python 3.10). The number of clusters was selected by inspecting visualizations (including dendograms and radar plots), in combination with clinical interpretability and utility.

Results: Five patient subtypes with the following characteristics were identified: Cluster 1: Obese men with persisting peripheral and axial musculoskeletal pain, sometimes with an underlying immune-mediated disorder (IMD), poorly responding to disease modifying therapy. Bland psychological evaluation. *Clinical interpretation:* predominantly men in the late 50s. Possibly secondary FM, and/or underlying microcrystalline disorder or inflammatory osteoarthritis. Very closed to psychiatric evaluation or therapy. Cluster 2: Female patients with peripheral and axial pain since childhood or adolescence, sometimes with a post-traumatic stress disorder. Severe sleep problems. *Clinical interpretation*: primary FM, sometimes with an additional traumatic psychological background. Cluster 3: Women with chronic back pain, often with previous (failed) spine surgery. Normal weight. Often polymedication with opioids, antidepressantsants. *Clinical interpretation*: women with lumbar disc degeneration. Sometimes questionable spondylarthritis with refractory lumbar pain despite treatment with biologics. Cluster 4: Patients (men>woman) of younger age with low BMI and hyperlaxity. Peripheral pain of nociplastic character predominates, often since childhood or adolescence. High incidence of depression, anxiety or other psychological conditions. Virtual reality treatment is efficient. *Interpretation:* somatoform pain in younger patients spilled over from adolescence, often with substantial psychiatric comorbidity. Cluster 5: Overweight women in peri-menopause with metabolic syndrome. Axial and peripheral pain. Often use of antidepressants, notably Trazodone. Blood sedimentation rate can be elevated. *Interpretation:* peri-menopausal syndrome in obese patients with pain and low grade inflammation such as bursitis or tenosynovitis.

Conclusion: All five chronic pain phenotypes identified by unsupervised machine learning are consistent with clinical observations. Psychiatric comorbidities are prevalent in all clusters except one, where they may be suppressed. Work disability plays an important role in all patients. In at least two clusters, the pain seems to have its origin in childhood or adolescence. One cluster seems to be particularly influenced by hormonal and metabolic factors.

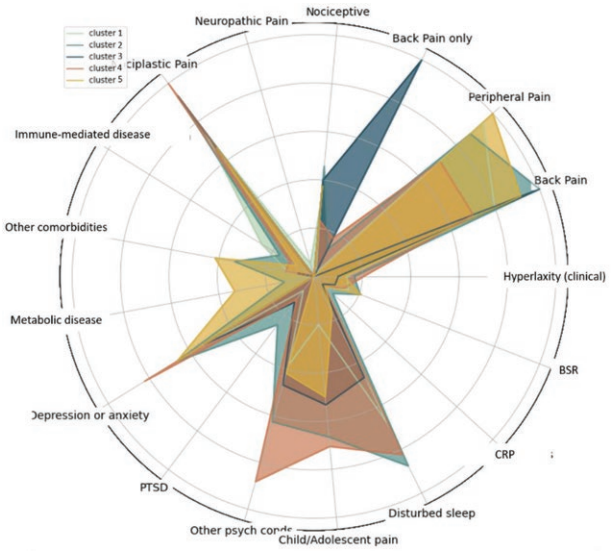


Figure 1. Radar plot of patient clusters. PTSD: Post-traumatic stress disorder. CRP: C-reactive protein, BSR: Blood sedimentation rate.

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Disclosure of Interests: None Declared.

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OP0199 HAND OSTEOARTHRITIS PHENOTYPES AND THEIR ASSOCIATIONS WITH PAIN AND CHANGE IN PAIN

Keywords: Pain, Osteoarthritis

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Background: Hand osteoarthritis (OA) pain is characterized as heterogeneous and multifactorial. Different pain patterns may be explained by underlying phenotypes, which previously have not been explored.

Objectives: Using the biopsychosocial framework, we aimed to identify possible hand OA phenotypes and explore the associations with pain intensity and change in pain during a four-year follow-up.

Methods: Latent class analysis was used to determine classes of people with hand OA, based on baseline examination (2016-17), followed by posterior fit statistics. Biological, psychological, and social domains were examined by self-reported questionnaires, clinical assessment and imaging. Central pain sensitization was tested by pressure pain thresholds (PPT; kg/cm^2) and temporal summation (TS). Pain intensity at baseline and follow-up (2019-21) was self-reported on a Numeric Rating Scale (0-10) for hand and overall bodily pain the last 24 hours. Change in pain was calculated for both pain measures. Differences of the biopsychosocial variables and pain measures were assessed by one-way ANOVAs and chi-squared tests. The relations of the classes to the pain outcomes were analysed by linear regression.

Results: We identified five classes (Table 1). The highest pain intensity was reported by the class with low OA severity but higher burden of the other factors (Class 5), whilst the class with the most OA severity of the hands and lower extremities (Class 4) reported approximately one point less for pain intensity (Figure 1). Classes showed little change in pain and there was no significant difference (data not shown). Significant differences were found across all classes in association to baseline and follow-up pain. However, not for change in pain (data not shown), except Class 5 and change in hand pain (beta (95% CI); 1.13 (0.02, 2.25)). Class 5 indicated the most hand and overall bodily pain in comparison to the reference group (Class 1) with a beta (95% CI) of 3.27 (2.32, 4.22) and 3.08 (2.10, 4.07) at baseline and 2.04 (1.02, 3.06) and 2.74 (1.73, 3.76) at follow-up, respectively. The difference was smaller when comparing for Class 4 to

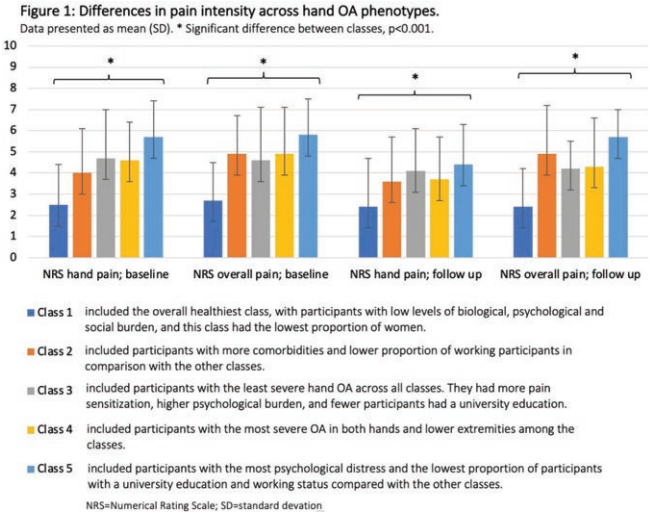
the reference group with a beta (95% CI) of 2.15 (1.27, 3.02) and 2.20 (1.27, 3.13) for hand pain and overall bodily pain at baseline, and a beta (95% CI) of 1.38 (0.46, 2.31) and 1.66 (0.74, 2.58) at follow-up. Class 3 indicated similar baseline values as Class 4 (Hand and overall bodily pain: beta (95%) of 2.24 (1.51, 2.97) and 1.89 (1.12, 2.65)).

Conclusion: We identified five potential hand OA phenotypes which associated with pain intensity at baseline and four years later. The phenotype with low OA severity, but more pain sensitization, comorbidities, higher psychological and social burden reported more pain than the phenotype with the most severe OA in the hands and lower extremities, reflecting the discordance between OA severity and pain experience.

Table 1. Characteristics of the biopsychosocial variables across the hand OA phenotypes. Data presented as mean (SD) unless otherwise indicated.

	Class 1	Class 2	Class 3	Class 4	Class 5	P-value
	N=93, 44%	N=40, 19%	N=38, 18%	N=23, 11%	N=19, 9%	
Biological:						
Age	61 (6)	63 (6)	58 (5)	63 (4)	58 (7)	<0.001
Sex (women), n (%)	75 (80)	38 (95)	33 (87)	22 (96)	17 (90)	0.13
Radiographic hand OA severity	29.8 (16.2)	33.4 (16.9)	21.3 (15.2)	57.7 (12.6)	22.3 (18.7)	<0.001
Hips, knees and feet OA severity	4.4 (3.1)	6.4 (3.3)	3.3 (2.1)	7.7 (4.1)	3.6 (3.6)	<0.001
PPT tibialis anterior	6.6 (2.7)	4.4 (2.4)	4.7 (2.1)	5.5 (2.4)	4.6 (2.7)	<0.001
TS change	1.1 (1.2)	1.9 (1.7)	1.6 (1.5)	1.4 (1.7)	2.8 (1.8)	<0.001
BMI	24.8 (3.7)	30.2 (5.5)	26.0 (4.2)	26.9 (3.6)	28.7 (5.5)	<0.001
Comorbidity burden	4.8 (2.6)	12.2 (2.7)	7.3 (2.7)	7.4 (3.2)	10.9 (4.5)	<0.001
Poor sleep, n (%)	47 (51)	34 (85)	37 (97)	22 (96)	19 (100)	<0.001
Psychological:						
HADS	4.1 (3.4)	7.1 (3.6)	8.3 (4.5)	6.2 (4.7)	19.4 (3.6)	<0.001
ASES	75.9 (11.2)	68.3 (10.7)	61.6 (10.7)	71.3 (13.9)	47.2 (15.5)	<0.001
PCS	7.4 (6.2)	12.5 (8.2)	12.4 (6.0)	10.5 (6.1)	21.1 (7.2)	<0.001
Social:						
University education, n (%)	69 (74)	24 (60)	16 (42)	15 (65)	6 (32)	<0.001
Working, n (%)	72 (77)	8 (20)	24 (63)	12 (55)	8 (42)	<0.001

SD=standard deviation



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OP0200

ORAL DELIVERY OF DELTA-9-TETRAHYDROCANNABINOL PROVIDES SYMPTOM AND DISEASE MODIFICATION USING TWO MODELS OF KNEE OSTEOARTHRITIS

Keywords: Osteoarthritis

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Background: Osteoarthritis (OA) is a whole joint disease that results in joint pain, cartilage degeneration, and synovitis, ultimately reducing the quality of life of those affected. Current therapies only modify pain and there are no approved OA disease-modifying drugs. Recent studies suggest that individuals with OA are self-medicating with cannabis, with some anecdotally reporting reduced joint pain. One of the most prominent cannabinoids in cannabis is delta-9-tetrahydrocannabinolic acid, which produces the psychoactive compound delta-9-tetrahydrocannabinol (THC) upon decarboxylation. THC can signal via CB1 and CB2 cannabinoid receptors to alter intracellular cAMP levels. CB1 and CB2 are found on joint cells, including chondrocytes and fibroblast-like synoviocytes (FLS). Currently, there are no studies linking THC to disease modification in OA.

Objectives: In this study, we investigated the effects and mechanisms of action of THC on pain and disease modification in pre-clinical models of knee OA.

Methods: 14-16 week (wk)-old male C57BL/6 mice underwent sham or destabilization of the medial meniscus (DMM) surgery to induce knee OA. At 1 wk post-surgery, THC (1, 5 or 10 mg/kg) or vehicle was administered 1 day/wk by intra-articular (IA) injection, or 5 days/wk by oral gavage for 9 wks. Von Frey and Open Field testing were performed to evaluate mechanical allodynia and locomotion/anxiety. 10 wks post-surgery joints were subjected to histopathology. For the monosodium iodoacetate (MIA) model of OA pain, knees of 14-wk-old C57BL/6 mice were injected with saline (control) or MIA (0.5 mg) and mice were administered THC (5 or 10mg/kg) 5 days/wk by oral gavage for 3 wks and Von Frey analyses was performed to evaluate mechanical allodynia. For in vitro studies, human FLS and chondrocytes obtained from OA patients undergoing total knee arthroplasty were subjected to flow cytometry and RNA sequencing with/without THC treatment.

Results: IA administration of THC to DMM mice accelerated cartilage degeneration, increased synovitis, and failed to attenuate mechanical allodynia at all doses (n=5/group). Oral administration of THC at all doses reduced cartilage degeneration, with only 10 mg/kg THC also reducing synovitis (n=10-15/group; Figure 1A&B). IHC of DMM joints (n=6/group) suggested significantly decreased αSMA but not nuclear Ki67 expression in the synovial subintima with THC oral gavage administration. Von Frey tests showed that administration of THC by oral gavage reduced mechanical allodynia in DMM mice at 9 wks post-surgery (n=15/group; Figure 1C). Open field tests indicated that THC had no overt effect on the locomotion or anxiety of sham or DMM mice (n=10/group). Studies using

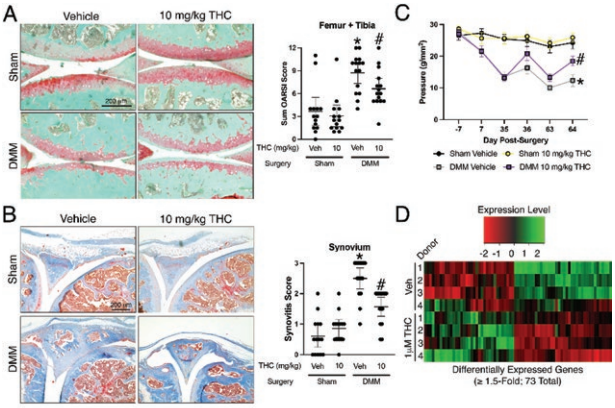


Figure 1. THC administration by oral gavage reduces cartilage degeneration, synovitis and mechanical allodynia in DMM-induced OA mice while in vitro THC treatment of human fibroblast-like synoviocytes modifies select gene expression profiles. Mice received sham or DMM surgery. At one week post-surgery, mice were treated 5 days/week with vehicle (veh; medium chain triglycericde) or 10 mg/kg THC for 9 weeks. Mice were sacrificed at 10 weeks post-surgery. Knee joint sections were stained with Safranin O (A) or Masson's Trichrome (B) for evaluation of cartilage degeneration or synovitis, respectively, by OARSI scoring. Mice were also evaluated for mechanical allodynia (pain) by von Frey analyses (C). (A&B) Data was analyzed by Kruskal-Wallis tests followed by Mann-Whitney post-hoc tests corrected for multiple comparisons using the method of Benjamini, Kreiger and Yekutieli using R v 3.5.03 with coin package v 1.3-24 to account for ties. * or #, $q < 0.05$ compared to all other groups. n = 14 or 15/group. (C) Data was log-transformed prior to analysis by two-way ANOVA followed by multiple comparison's tests using the method of Benjamini, Kreiger and Yekutieli to correct for false-discovery rate. At day 64 post-surgery: *, $q < 0.05$ compared to all other groups; # $q < 0.01$ compared to DMM vehicle and Sham + 10 mg/kg THC groups. n = 15/group. (D) Heat map of genes modified ≥ 1.5-fold in human fibroblast-like synoviocytes treated with vehicle (veh; 0.5% DMSO) or 1uM THC, as determined by RNA sequencing. A total of 35 genes were upregulated and 38 genes were downregulated.

MIA-induced OA mice showed that administration of 10 mg/kg THC by oral gavage also reduced mechanical allodynia (n=10/group) without modifying animal locomotion or anxiety. In vitro, THC treatment of human OA FLS and chondrocytes (n=5 each) increased Annexin V positivity starting at 2.5μM, but not with 1μM THC, as determined by flow cytometry. In cultured OA FLS (n=4), 73 genes were differentially expressed (35 upregulated, 38 downregulated) after treatment with THC compared to vehicle treatment (≥1.5-fold), as determined by RNA sequencing (Figure 1D). Similarly, in OA chondrocytes RNA sequencing (n=4/group), 21 genes (9 upregulated, 12 downregulated) were differentially expressed (≥1.5-fold) after THC treatment. Computational analyses indicated that ECM-related pathways were enriched in the upregulated genes in both fibroblasts and chondrocytes, while lipid/steroid/cholesterol-related pathways were enriched by the downregulated genes in both cell types. 22 common putative transcription factors were also identified as potential regulators of the fibroblast and chondrocyte genes reduced through THC treatment.

Conclusion: Oral administration of 10 mg/kg THC reduced cartilage degeneration and synovitis in DMM mouse knee joints and modified pain responses in DMM and MIA models. JR, AM, HFF share equal first author contribution.

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Disclosure of Interests: None Declared.

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OP0201 INTRA-ARTICULAR INJECTIONS OF TWO LIPOSOMAL ADENOSINE FORMULATIONS PROVIDE SIGNIFICANT PAIN RELIEF AND GAIN IN FUNCTION, IMPROVE COMFORTABLE RANGE OF MOTION AND SLOWED RADIOLOGIC PROGRESSION IN A PRECLINICAL CANINE MODEL OF OSTEOARTHRITIS

Keywords: Osteoarthritis, Cartilage, Pain

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Background: Osteoarthritis (OA) affects 10% of global population and its effective non-surgical treatments represent significant unmet need. There has been a rapid escalation in the annual number of arthroplasties, placing a significant burden on patients and healthcare systems. We previously demonstrated that adenosine and its A2A receptor play critical roles in maintaining joint homeostasis. Adenosine treatment prevents structural progression and preserves articular cartilage in rodent models of OA.

Objectives: To test the new, more stable and long-lasting formulations of liposomal adenosine in the treatment of post-traumatic OA in a preclinical canine model.

Methods: OA was induced by arthroscopic medial meniscus release (MR) in 21 purpose-bred hounds ([10M, 11F]). Evidence of OA was documented at two months after MR (pre-Tx). Knees were injected with 3mL of RgnA09M, RgnA09N (3 mg/ml Adenosine; N=7 each) or saline (9 mg/ml NaCl; N=7) for a total of 3 intra-articular (IA) injections each carried out one month apart. RgnA09M and RgnA09N comprised identical lipid composition but varied in particle size and liposome lamellarity. Blinded assessments for knee pain, function and effusion were performed using validated visual analogue scale (VAS) scoring by a board-certified veterinary surgeon. Comfortable range of motion (CROM) was measured using a standard goniometer and radiographic assessments of knee joints were also performed. Results presented are before surgical induction of OA (pre-MR), at pre-Tx, at 4 months (post-Tx) and the time of humane euthanasia (6 months post-Tx) for histology and histopathology. Blood for biomarkers and synovial fluid were collected at same time points. MRIs were used to evaluate cartilage structure and integrity at pre-Tx and 6 months post-Tx. Wilcoxon matched pair signed rank test was used for statistical analyses.

Results: There was demonstrable symptomatic knee OA at pre-Tx with a 26.3% loss in function, increased joint pain score (2.0±0.9 vs 0 at pre-MR), 10% loss of CROM, development of radiographic OA (1.2±0.5 vs. 0 at pre-MR), observable OA on MRI (3.9±0.9 vs. 0 at pre-MR) and joint effusion (2.3±0.9 vs. 0 at pre-MR). Saline treatment provided no benefits. The IA administration of RgnA09M, led to a steady decrease in pain by 65.0% and 74.3%, at 4mo and 6mo post-Tx respectively, with a corresponding 30.9% and 61.8% gain in function. In comparison, the injection of RgnA09N led to decrease in pain by 80.9% at 4mo but a loss of effect to 74.7 % at 6mo post-Tx. A corresponding trend was observed in the gain of function, with an overall gain of 39.7% at 6mo post-Tx (**Figures 1A** and **1B**). Moreover, injections with RgnA09M, improved CROM to near-normal values at 6mo, while RgnA09N significantly improved it at 4mo **(Figure 1C)**. Compared to saline, both RgnA09M and RgnA09N improved radiographic markers by up to 42.6% at 6mo post-Tx **(Figure 1D)**. In saline-treated dogs there was an improvement in the size of effusions initially, but a loss in benefit as time progressed. In contrary, the magnitude of the change was much greater in those treated with both formulations, and it continued to improve over time **(Figure 1E)**. Finally, at 6mo post-Tx, MRIs showed significant slowing in the progression of OA with RgnA09M by 55.3% and with RgnA09N by 42.8% (**Figure 1F**). Histology and biomarker results are pending.

Conclusion: Three IA injections of RgnA09M and RgnA09N were associated with improved symptomatic knee OA including gain in function and decrease in pain and OA progression compared with saline. The persistent improvement lasted 6 months, indicating symptomatic and mechanistic benefits of the treatment. Moreover, liposomal adenosine injections slowed the progression of OA as observed on radiographs and MRIs. These findings provide the first evidence that IA injection of liposomal adenosine improves pain relief, gain in function, CROM, and prevents radiologic progression in a large animal model of post-traumatic OA.

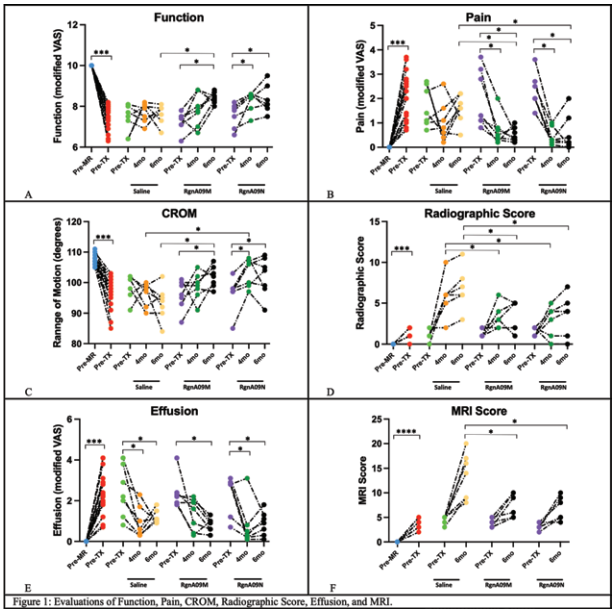


Figure 1: Evaluations of Function, Pain, CROM, Radiographic Score, Effusion, and MRI.

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Disclosure of Interests: Ding Li Shareholder of: Regenosine, Inc., Employee of: Regenosine, Inc., Bruce N. Cronstein Shareholder of: Regenosine, Inc., Grant/research support from: Regenosine, Inc, James Cook Paid instructor for: Journal of Knee Surgery. Midwest Transplant Network. Musculoskeletal Transplant Foundation., Consultant of: Arthrex, Inc. Trupanion., Grant/research support from: AO Trauma. Arthrex, Inc. Collagen Matrix Inc. DePuy. Musculoskeletal Transplant Foundation. Purina. Regenosine, Inc. SITES Medical. Thieme., Chantelle Bozynski: None declared, Siddhesh Angle Shareholder of: Regenosine, Inc., Grant/research support from: Vetosine, Employee of: Regenosine, Inc. Bone Biologics.

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Understanding Treatment response and novel treatment approaches in RA

OP0202 IMMUNOMICS ANALYSIS OF RHEUMATOID ARTHRITIS IDENTIFIED PRECURSOR DENDRITIC CELLS AS A KEY CELL SUBSET OF TREATMENT RESISTANCE

Keywords: Rheumatoid arthritis, -Omics

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Background: To date, there have been no comprehensive studies of the immune cells that play a pivotal role in treatment-resistant rheumatoid arthritis (RA).
Objectives: We performed large scale transcriptome analyses of immune cells in peripheral blood prior to treatment in a total of 55 patients with RA to identify the gene expressions and subsets that predict treatment resistance.
Methods: We isolated 18 peripheral blood immune cell subsets of 55 pre-treatment RA patients and 39 healthy controls, and performed RNA sequencing (Figure 1A). Transcriptome changes in RA and treatment effects were systematically characterized. Association between immune cell gene modules and treatment resistance was evaluated. We validated predictive value of identified parameters for treatment resistance using quantitative polymerase chain reaction (qPCR) and mass cytometric analysis cohorts. We also characterized the identified population by synovial single cell RNA-seq analysis.
Results: Immune cells of RA patients were characterized by enhanced interferon and IL6-JAK-STAT3 signaling that demonstrate partial normalization after treatment. A gene expression module of plasmacytoid dendritic cell (pDC) reflecting the expansion of pre-dendritic cell (pre-DC), which is recently identified subpopulation of DCs (1), exhibited strongest association with treatment resistance (Figure 1B-D). Type I interferon signaling was negatively correlated to pre-DC gene expression. qPCR and mass cytometric analysis validated that the pre-DC associated gene expression and the proportion of pre-DC were significantly higher before treatment in treatment-resistant patients (Figure 1E, F). A cluster of synovial DCs showed both features of pre-DC and proinflammatory conventional DC2s (Figure 1G).
Conclusion: Treatment resistance can be predicted by an increase in pre-DC in the peripheral blood of RA patients prior to starting therapy. This result shows the potential for realizing a stratified therapy of RA based on analysis of pre-DC in peripheral blood.
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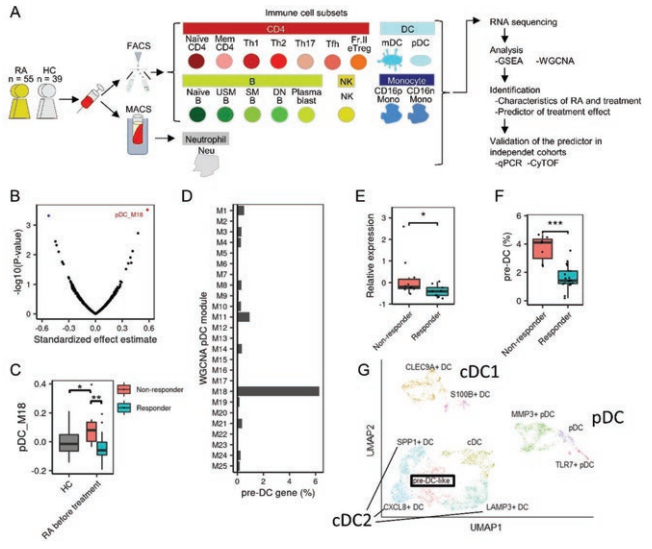


Figure 1. (A) Overview of the study. (B) The assessment was performed using a generalized linear model with failure to achieve CDAI50 at 6 months as the target variable and the eigengene of the module of each immune cell subset as the explanatory variable. Color-coding was performed with Benjamini-Hochberg FDR < 0.10 as the significance level. (C) Comparison of ME expression in the pDC_M18 module in the pre-treatment RA populations and the HC population. (D) Match rate with pDC_M18 genes in each pDC WGCNA module. (E) qPCR was performed on the pDC in peripheral blood before treatment in a separate confirmatory cohort (n = 19) of RA patients before starting a new therapy, and the pDC_M18 expression signatures of the non-responder and responder groups were compared. (F) Immune cells associated with prognosis were searched by mass cytometry of RA patients before ABT treatment initiation. Comparison of proportions of pre-DC relative to DC with treatment prognosis. (G) UMAP plot of synovial DCs from untreated rheumatoid arthritis patient (n=16). *p < 0.05, **p < 0.01. FACS: fluorescence-activated cell sorting, MACS: magnetic-activated cell sorting, GSEA: gene set enrichment analysis, WGCNA: weighted gene co-expression network analysis, ME: module eigengene, UMAP: uniform manifold approximation and projection.

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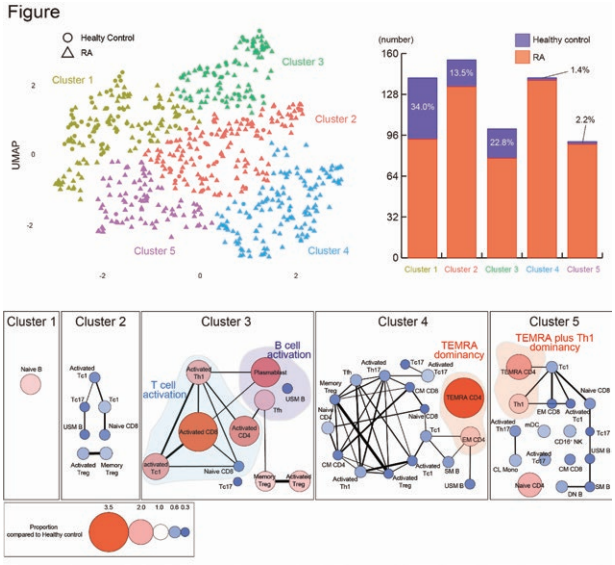
OP0203 IMMUNOPHENOTYPING OF RHEUMATOID ARTHRITIS STRATIFIES FIVE GROUPS THAT HAVE DIFFERENT RESPONSES TO MOLECULAR TARGETED THERAPIES

Keywords: Adaptive immunity, Rheumatoid arthritis, Disease-modifying drugs (DMARDs)

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Background: Different molecular targeted therapies affect immune cell phenotypes and signals differently due to their modes of action[1]. Theoretically, it is possible to use these drugs based on a stratification of rheumatoid arthritis (RA) patients. However, despite innovations in the treatment of RA, precision medicine with the development and application of personalized treatments by molecular targeted therapy is still far from its achievement. At least, precision medicine by a single biomarker is not known to be possible[2].
Objectives: To investigate the possibility of precision medicine based on the immune phenotype of peripheral blood, we stratified RA patients by comprehensive flow cytometric immunophenotyping and evaluated the response to targeted therapy.
Methods: This study enrolled 96 healthy controls (HC) and 533 bio-naive RA patients with moderate to severe disease activity acording to CDAI. The Human Immunology Project, a NIH/FOCIS-developed flow cytometric immune cell profiling method on T cells, B cells, NK cells, dendritic cells, and monocytes, was used to stratify the patients using cluster analysis (Ward and UMAP methods). Inverse probability weighting with propensity scores was used to control for patient characteristics and CDAI was used to measure remission achievement after 6 months of targeted molecular therapy for each stratified subgroup.
Results: The mean age was 63.5 years old, and the disease activity was CDAI 27.1. In comparison to HC, CD4 T cell differentiation was noticeably affected in RA patients, with elevated effector T cells and effector memory T cells re-expressing CD45RA (TEMRA). Meanwhile, there was no meaningful change in the

proportion of Th1, Th17, Treg, and Tfh cells as well as B cells, NK cells, monocytes, and dendritic cells subpopulations. Cluster analysis of the immunophenotypes revealed five main groups of RA patients, with roughly equal numbers of patients in each group. When dimension reduction of their immunophenotypes was performed by UMAP, these groups were clearly separated (Figure 1). One of the five groups had an immunophenotype almost identical to that of healthy controls (cluster 1), two groups were moderately different (clusters 2 and 3), and the last two groups had phenotypes characteristic of RA with little overlap with healthy controls (clusters 4 and 5). These 2 groups were accompanied by a marked increase in TEMRA with increased effector memory T cells (cluster 4) and with increased Th1 (cluster 5). There were few differences in baseline clinical findings such as disease activity and ACPA/RF among the groups. Of note, the clinical efficacy of each targeted therapy was statistically different in each group. In the group with immunophenotypes similar to those of healthy subjects (cluster 1) and the moderately different group (cluster 2), JAK inhibitors and IL-6R antibody treatment were effective, while TNF inhibitors were effective in another moderately different group (cluster 3). CTLA4-Ig and TNF inhibitors were effective in the two groups with phenotypes characteristic of RA (clusters 4 and 5). Immunophenotyping after treatment revealed that the first three groups became comparable to the HC phenotype. However, TEMRA dominancy groups (clusters 4 and 5) remained elevated in TEMRA. Interestingly, CTLA4-Ig decreased the proportion of TEMRA.



Conclusion: RA patients can be stratified into five groups, each of which benefited from different molecular targeted therapies. The increase in CD4 TEMRA in peripheral blood was significant in RA patients, and the proportion was virtually unchanged with treatment. Thus, CD4 TEMRA could be the pathogenic memory cells in RA. Our results may be a milestone in achieving precision medicine.

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OP0204

CIRCULATING CD4+CXCR5+PD-1HI FOLLICULAR HELPER T CELLS ARE ELEVATED IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PREDICT TREATMENT RESPONSE TO ABATACEPT OR TNF BLOCKERS

Keywords: bDMARD, Adaptive immunity, Biomarkers

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Background: CD4+CXCR5+PD-1^{hi} follicular helper (Tfh) T cells typically dwell in the germinal centers (GCs) of lymphoid organs, provide help to autoantibody secreting B cells and play an important role in the pathogenesis of Rheumatoid Arthritis (RA). Circulating counterparts of Tfh (cTfh) cells have been described in human peripheral blood, their frequencies seem to correlate with the pool of prototypical GC Tfh cells, and are expanded in patients with autoimmune conditions including RA. Abatacept (ABT), by interfering with costimulation, can restrain the generation of Tfh cells. The pathogenic implication of Tfh cells may be more prominent in RA patients with higher cTfh cell frequencies and these subjects could be more likely to respond to therapeutic costimulation blockade with ABT.
Objectives: To examine a). The effect of treatment escalation using TNF blockers (TNFb) or ABT, on the frequency of cTfh cells in RA, and b). The relation of the baseline cTfh cell frequency with the clinical response.
Methods: Peripheral blood was drawn from seropositive RA patients with an incomplete response to csDMARDS (n=41) who initiated biological therapy, according to routine clinical practice, with TNFb (n= 19) (10 Etanercept, 3 Adalimumab, 3 Certolizumab, 2 Golimumab, 1 Infliximab) or ABT (n= 22). cTfh cell frequencies were determined by flow cytometry of freshly isolated PBMCs at the basal visit and 12 months (12M) after starting treatment escalation. For each patient, an age and gender-matched healthy control (HC) was also studied at both time points (n=41).
Results: a). Effect of treatment escalation on the cTfh cell frequency. As compared with HC, RA patients receiving csDMARDs demonstrated an increased frequency of cTfh and also of activated ICOS+ cTfh cells (a-cTfh), and this was observed in both treatment escalation groups. A significant improvement of disease activity (ΔDAS28 >2.0) was apparent in all of the patients at 12M. Nevertheless, the cTfh cell frequency did not vary in patients receiving TNFb; conversely, in subjects receiving ABT it significanly decreased to HC levels. At the same time, the frequency of a-cTfh cells was significantly reduced in both groups; however, in the TNFb group it remained above HC whereas in the ABT group it reached magnitudes comparable to HC. b). Relation of the baseline cTfh cell frequency with the clinical response. In the ABT group, the baseline frequencies of cTfh and a-cTfh had been higher for patients who went on to achieve remission at 12M (12Mr), as compared with those who remained active (12Ma) [Tfh logistic regression OR for remission 25.3, 95% CI (12.2-39.8); ROC AUC 0.94(0.83-1), p<0.0005]; as stated above, the 12M frequencies were no longer elevated; in addition there were no differences between the 12Ma and 12Mr subjects. Conversely, in the TNFb group, the baseline frequencies of cTfh and a-cTfh had been lower for 12Mr as compared with 12Ma patients [Tfh OR for not achieving remission 8.5 (4.3-15.5); ROC AUC 0.77(0.54-0.99), p<0.05]; furthermore, the 12M frequencies showed the same pattern: they had not significantly changed, persisted elevated above HC and remained lower in 12Mr as compared with 12Ma patients. The baseline cTfh cutoff frequency for achieving remission in the ABT group was >0.35% (sensitivity 92.7%, specificity 90%). The baseline cTfh cutoff frequency for not achieving remission in the TNFb group was >0.44% (sensitivity 67.7%, specificity 90%).
Conclusion: ABT but not TNFb, is able to curtail cTfh cell numbers in RA, suggesting that costimulation blockade can restrain germinal center overactivity. Higher baseline cTfh cell frequencies predict a good response to ABT and at the same time, a poor response to TNFb. Therefore, immunophenotyping of patients with an incomplete response to csDMARDs can facilitate a personalized therapeutic strategy for treatment escalation.

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OP0205 NANOCATALYTIC TREATMENT USING RU@TIO2 FOR RHEUMATOID ARTHRITIS VIA MACROPHAGE RE-POLARIZATION

Keywords: Animal models, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is an autoimmune disorder that results in synovitis and joint destruction[1]. Macrophages, one of the various inflammatory cells, particularly infiltrate the RA synovial tissue and cause sustained inflammation that promote RA. And the balance of pro-inflammatory M1 macrophages and anti-inflammatory M2 macrophages in RA joints is affected by overexpressed reactive oxygen species (ROS) and hypoxia synovium, which provides potential targets for the RA treatment.
Objectives: With the aim of alleviating the synovial inflammation in RA and restoring the balance of macrophage subtypes, we develop a catalytic nanoparticle named Ru@TiO_2, which can produce O2 and scavenge ROS to reduce M1 macrophages, switch M1 phenotype to M2 phenotype.
Methods: Ru@TiO_2 was synthesized using the hydrothermal method. The morphology and nanoparticle size were observed using the transmission electron microscopy (TEM). The catalytic ROS-scavenging activities and O_2 generation ability were examined through $\bullet O_2^-$ scavenging, H_2O_2 catalytic elimination and O_2 generation assays. For in vitro experiment, the cytotoxicity of Ru@TiO_2 conducted on RAW 264.7 cells was assessed by flow cytometry. To verify M1 to M2 macrophage phenotype transition and hypoxia alleviation, M1 and M2 markers and HIF-1α expression levels were evaluated by using qRT-PCR and Western Blot, respectively. In vivo, anti-inflammatory efficiency was observed after intra-joint injection of Ru@TiO_2 into collagen-induced arthritis mouse. The clinical scores and paw thickness for the inflamed joints with different treatments at various time points were recorded. Ultrasound (US) was used to assess the inflamed joints after treatment and RNA expression levels of M1 and M2 macrophage markers in synovial tissue were evaluated through qRT-PCR. The statistical significance among multiple groups was examined by using one-way ANOVA.
Results: The Ru@TiO_2 were fusiform in shape with an average size of 67 nm. The evaluation of catalytic ROS scavenging activities and O_2 generation performance of Ru@TiO_2 showed that Ru@TiO_2 can achieve about 60% scavenging ratio to $\bullet O_2^-$ and about 80% producing ratio to O_2 at 30 min. Ru@TiO_2 also showed significantly increased H_2O_2 eliminating activity compared to the TiO_2. In vitro, low cytotoxicity of Ru@TiO_2 was displayed and the decrease of intracellular ROS level was most significant with Ru@TiO_2. In addition, M1 macrophage markers (TNF-α and IL-1β) and HIF-1α expression levels were most prominently declined with Ru@TiO_2. And the increase of M2 macrophage markers (Arg-1 and CD206) was most obvious when using Ru@TiO_2. In vivo, the arthritis scores, paw thickness and thickness of articular cavity assessed by US in Ru@TiO_2 group were the lowest when compared with other treated groups. Moreover, RNA expression levels of M1 and M2 macrophage markers in synovial tissue showed the similar tendency as in vitro.
Conclusion: In this study, the Ru@TiO_2 was successfully synthesized with efficient catalytic ROS scavenging activities and O_2 generation ability for the treatment of RA. In vitro, Ru@TiO_2 shows good cell biocompatibility and effective intracellular ROS scavenging ability. Moreover, Ru@TiO_2 alleviate the hypoxia condition in cells by producing O_2. Furthermore, the significant and efficient polarization of M1 to M2 macrophages and suppression of inflammation were achieved both in vitro and in vivo through the treatment of Ru@TiO_2, which indicated the therapeutic potential of Ru@TiO_2 for RA therapy.

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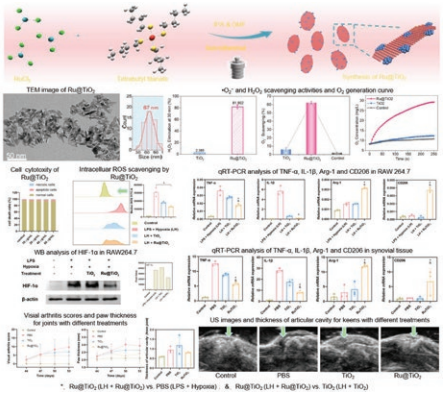


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0206 PEPTONIPHILUS GORBACHII ALLEVIATES COLLAGEN-INDUCED ARTHRITIS IN MICE BY IMPROVING INTESTINAL HOMEOSTASIS AND IMMUNE REGULATION

Keywords: Rheumatoid arthritis, Animal Models

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Background: Although the link between gut microbiota and rheumatoid arthritis (RA) pathogenesis is well established, there is still a lack of information regarding the species-level analysis of microbiota. Recently, studies analyzed blood samples, rather than stool samples, to identify disease-related microbiota at the species level.
Objectives: This study aimed to identify RA-related microbiomes at the species level using serum samples from patients with RA and explore the efficacy as well as mechanisms of candidate microbial species for RA treatment using collegen induced arthritis (CIA) mouse model.
Methods: Serum antibody microarray for 384 microbial species was performed from RA patients (n=81) and healthy control (n=50). We verified the therapeutic effect and mechanism of the candidate microbial species by evaluating arthritis severity, immune response, intestinal barrier integrity, and fecal microbiota using CIA mice.
Results: We discovered 36 altered microbial species in patients with RA compared to healthy controls. In particular, *Peptoniphilus gorbachii* (PG) was increased in RA patients, inversely correlated with RA disease activity, and competed with *Porphyromonas gingivalis* which developed and exacerbated RA. Administration of PG suppressed joint inflammation and bone destruction in CIA mice. PG decreases inflammatory T cells and monocytes in the mesenteric and inguinal lymph nodes. Moreover, PG supplementation restored intestinal barrier integrity, with a decreased level of serum zonulin and increased expression of intestinal tight junction proteins. The abundance of fecal microbiota in PG-treated mice correlated with improved intestinal barrier integrity and decreased inflammatory reactions.
Conclusion: Serum microbial antibody microarray could help with the effective discovery of therapeutic microbial RA targets at the species level. Our results suggest that PG exerts a therapeutic effect by restoring intestinal barrier integrity and suppressing the RA-characteristic immunologic response.

REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1913

OP0207 LIPOSOMAL ANTAGOMIR-155-5P RESTORES ANTI-INFLAMMATORY MACROPHAGES AND IMPROVES ARTHRITIS IN PRE-CLINICAL MODELS OF RHEUMATOID ARTHRITIS

Keywords: Cell biology, Innate immunity, Animal Models

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Background: RA is the most frequent systemic autoimmune disease that primarily affects multiple joints and causes irreversible bone and cartilage destruction in the absence of treatment [1]. Monocytes-macrophages are key players in the pathogenesis of RA and accumulate in the synovial tissue. Besides resident macrophages, blood monocytes can differentiate into monocyte-derived-macrophages that may join the synovium and have different phenotypes and

functions. The "classically activated macrophage phenotype" is considered to be pro-inflammatory and contribute to RA pathogenesis by secreting pro-inflammatory cytokines. The "alternatively activated macrophage phenotype" is considered to be regulatory and anti-inflammatory in tissues. Actually, there is a continuum from pro-inflammatory to anti-inflammatory macrophages, with high plasticity between the different states. We have previously shown that RA patients, and not patients with other inflammatory rheumatic diseases, have an impaired maturation of monocytes in anti-inflammatory-macrophages with increased differentiation in a pro-inflammatory-phenotype. We have found that an increased expression of miR-155 in monocytes/macrophages could be responsible for this defect and thus, could represent a new therapeutic target in RA ([2]).

Objectives: Our aim is to assess if the defect of monocytes polarization in anti-inflammatory-macrophages and the impact of miR-155 in this defect are present in 2 pre-clinical models of RA: the CIA (collagen-induce-arthritis) and STA mice (Serum transfert arhritis), both in which macrophages infiltration of synovium play a key role in pathophysiology. Then, we have test a new therapeutic strategies to correct this defect using PEG-liposomes containing antagomiR-155-5p.

Methods: AntagomiR-155-5p or antagomiR-control were encapsulated in PEG-liposomes of 100 nm in size and -10mV in zeta potential with high antagomiR loading efficiency (above 80%). Mice were injected intravenously with 1,5nmol/100µL PEG-liposomes containing antagomiR-155-5p or control after induction of arthritis.

Results: As in humans, we found that monocytes defect in anti-inflammatory-macrophages was associated with an increase of miR-155-5p in both mouse models. Moreover, we demonstrated the biodistribution of tagged-PEG-liposomes to inflamed joints 1 hour after injection and as well as their subsequent liver's accumulation after 48 hours, indicative of hepatic clearance, in arthritic mice. Subsequently, we demonstrated that treatment with an antagomiR-155-5p encapsulated in PEG-liposomes was able to decrease joint inflammation, to restore bone-marrow monocytes polarization in anti-inflammatory-macrophages, to reduce immune cells infiltration in synovial tissues, to increase the $CD206^+$ and $CD163^+$ tissue infiltrating macrophages and to decrease expression of mRNAs target of miR-155-5p, without any significant functional change in other immune cells including splenic B and T cells.

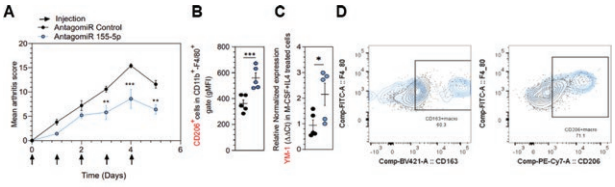


Figure 1: Treatment of STA mice with PEG-liposomes containing antagomiR-control or antagomiR-155-5p. For STA mice, antagomiR-control or 155 entrapped in PEG-liposomes are intravenously injected on days 0, 1, 2, 3, and 4. Mice were evaluated every 2-day, based on a visual scoring scale of the paws with evaluation of the erythema, swelling and ankylosis of each paw (score 1 to 4) **(A)**. The differentiation of sorted bone-marrow monocytes to BMDM-M2 was assessed by flow cytometry with pan-macrophages markers and specific markers of M2 macrophage (CD206) **(B)** and YM-1 relative expression **(C)**. Synovial tissue cells were assessed by flow cytometry analysis using anti-CD45, DUMP channel: CD19-CD3-NK1.1-LY6G, anti-CD11b, anti-F4/80, anti-MHCII, anti-CD64, anti-LY6C, anti-MerTK, anti-CD163, anti-CD206 and anti-CX3CR1. Determination of tissue infiltrating $CD206^+$ or $CD163^+$ macrophages in synovial tissue **(D)**.

Conclusion: The injection of antagomiR-155-5p encapsulated in PEG-liposomes allows delivering small RNA to monocytes/macrophages, lead to reduce joint inflammation in murine models of RA, providing a promising strategy in human disease.

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Disclosure of Interests: None Declared.

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OP0208 MECHANICAL UNLOADING PREVENTED ARTHRITIS IN THE RAT ADJUVANT-INDUCED ARTHRITIS MODEL

Keywords: Rheumatoid arthritis, Animal Models

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Background: Rheumatoid arthritis (RA) is the most common chronic inflammatory rheumatic disease, characterized by synovitis associated with progressive bone loss and joint swelling. The adjuvant-induced arthritis (AIA) model mimics the pathophysiological features of RA, with a very high prevalence and reproducibility. YAP plays a key role in synovial hyperplasia. It is a transcription factor which can be activated in response to inflammation but also by a mechanical stimulus as tissue stiffening. We already showed a decrease arthritis severity by inhibiting YAP in the AIA model [1]. Then, different mechanical challenges could potentially impact arthritis development by regulating YAP.

Objectives: The objective of this study was to investigate the impact of mechanical loading and unloading on the development of arthritis in the AIA model.

Methods: Arthritis was induced in female Lewis rats by injection of the adjuvant *Mycobacterium butyricum*, defining day (D)0. The AIA model normally develops arthritis at D10, with a peak of inflammation at D17 [2]. Rats were randomized into three groups: an AIA+mechanical loading group (n=11) with free access to an activity wheel from D0 to D17, an AIA+mechanical unloading group (n=11) by tail suspension from D0 to D17, and an AIA-only group (n=11) as positive control. Daily clinical monitoring (arthritic index and ankle circumference) was used to follow the progression and severity of arthritis. At D17, the ankles of the rats were collected to perform RT-qPCR.

Results: Arthritis onset was observed at the same time (D10) in the AIA control and AIA+mechanical loading groups with the same kinetic of arthritis index and ankle circumferences. However, the majority of rats in the AIA+mechanical unloading group did not develop any signs of arthritis. At D17, gene expression of YAP and CYR61 (YAP target gene), IL1B, IL6, RANKL, ACP5 (encoding TRAPc), CTSK (encoding cathepsin K), MMP9, and MMP13 was decreased in the ankle of AIA+mechanical unloading rats compared to other groups. In the AIA+ mechanical loading group, rat stopped their physical activity at D10 which may explain the lack of clinical and molecular differences between the AIA and AIA+mechanical loading groups at D17.

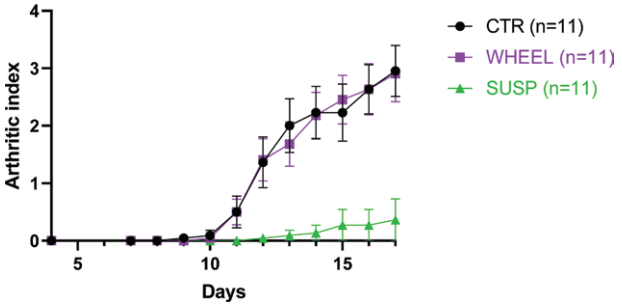


Figure 1. Arthritic index from day(D) 0 to D17 in the AIA control (CTR) group (n=11), the AIA+mechanical loading (WHEEL) group (n=11) and the AIA+mechanical unloading (SUSP) group (n=11).

Conclusion: Mechanical unloading of the hindpaws by the suspension system strongly prevented arthritis by a reduced expression of pro-inflammatory genes, bone resorption, and bone degradation genes. The decrease in inflammation may be partly explained by the decrease in YAP transcriptional activity. Mechanical stress is therefore a key factor in inflammation during AIA. The precise mechanisms linking these two mechanisms are still under investigation.

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Disclosure of Interests: None Declared.

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OP0209 IMPACT OF CHRONIC INFLAMMATION AND COLLAGEN IV FRAGMENT CANSTATIN ON RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS AND ENDOTHELIAL CELL INTERACTIONS IN VITRO AND IN VIVO

Keywords: Cell biology, Synovium, Rheumatoid arthritis

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Background: Increased neovascularization in the inflamed synovium of patients with rheumatoid arthritis (RA) is a pathological feature in the pathogenesis of RA. Key players in RA progression are chronically activated RA synovial fibroblasts (RASF), which secrete proinflammatory factors (e.g. IL-6), proangiogenic

VEGF, IL-11 and matrix metalloproteases (MMP) promoting inflammation, synovial angiogenesis, and invasion of cartilage and bone by degrading the consecutive matrix, resulting in the release of the anti-angiogenic collagen IV fragment canstatin. Canstatin may further activate RASF leading to altered expression of vascular markers such as angiopoietin-2 (ANGPT2) and neovascularization.
Objectives: Analysis of repetitively stimulated RASF- and canstatin-mediated effects on vessel formation in the tube formation assay, in the SCID-mouse model for RA and in synovial tissue of RA patients with respect to ANGPT2 expression and RASF-endothelial cell (EC) interactions.
Methods: 2D tube formation assay was performed using HUVEC seeded on Matrigel. 15% Calcein AM-stained RASF were added. RASF/HUVEC were treated with 0.5µg/ml canstatin. HUVEC were pre-treated with 0.2µg/ml canstatin. RASF were repetitively stimulated three times with 0.05ng/µl IL-1ß every 24h starting at day 2. Tube thickness and the area covered by the formed cellular network were measured. RNA was extracted from tubes and ANGPT2 expression was analysed by qPCR. IL-6 and IL-11 in supernatants were measured by ELISA. Healthy cartilage was subcutaneously co-implanted with RASF into SCID mice. Contralaterally, healthy cartilage without RASF was implanted. Vessel formation was evaluated after 3-45 days. RA and osteoarthritis (OA) synovial tissue was stained for ANGPT2 and CD31.
Results: RASF or HUVEC stimulated once showed a significant IL-6 increase compared to unstimulated controls. After subsequent repetitive stimulation of RASF or HUVEC, a significant decrease in IL-6 (1st stimulation: 5076±1730pg/ml vs. 3rd: 1890±758pg/ml, p<0.0001/ 1st: 488±186pg/ml vs. 3rd: 382±109pg/ml, p=0.041) and IL-11 in RASF (1st: 451±205pg/ml vs. 3rd: 69±51pg/ml, p<0.0001) compared to the first stimulation was observed. Repetitive stimulation of HUVEC+RASF resulted in a significant IL-6 increase for each subsequent stimulation (1st vs. 3rd: p=0.02). RASF significantly reduced tube thickness (22.9µm (SD=6.3) vs. 16.6µm (SD=2.2), p=0.014) and the network area (p<0.0001) and significantly increased ANGPT2 2-fold compared to HUVEC alone. RASF stimulated only once further reduced the network area (p=0.038), while repetitive stimulation significantly attenuated the proinflammatory effect (IL-6, p=0.029). Stimulation of pre-treated HUVEC and unstimulated RASF with canstatin led to disturbed tube formation with reduced tube thickness from 22.9 to 16.9µm (SD=4.4, p=0.011). Co-culture of RASF with pre-treated HUVEC with canstatin further increased the RASF-mediated effect by reducing tube thickness (22.9 to 14.6µm (SD=1.4), p<0.001), with a significant 1.6-fold decrease of ANGPT2. In human RA synovium, ANGPT2 was also found to be significantly upregulated in vessels compared to OA tissue. In SCID mice, RASF-mediated altered vessel formation started at day 3. Helix-like vessels were detectable at early time points of vessel formation in implants with RASF (d3-9), e.g. at day 3, 60% of vessels were helix-like.
Conclusion: RASF induced helix-like vessels in the SCID mouse model suggest an influence on vessel formation. This could be confirmed in vitro as well as on molecular level inducing the vascular marker ANGPT2 in newly formed tubes. ANGPT2-upregulation in vessels was also observed in human RA synovium. Repetitive stimulation of RASF resulted in an inflammatory adjustment to IL-1ß, leading to a significant reduction of IL-6 and improved neovascularization in vitro. The anti-angiogenic canstatin could in part enhance the RASF-mediated effect and was not able to restore RASF-altered tube formation in vitro.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Novel insights into disease taxonomy and immunophenotyping

OP0210 BRUTON'S TYROSINE KINASE (BTK) IS A NOVEL INDEPENDENT BIOMARKER OF LYMPHOMA IN PRIMARY SJÖGREN'S SYNDROME: DATA FROM 346 PATIENTS OF THE ASSESS COHORT

Keywords: Sjögren syndrome, Malignancy, Biomarkers

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Background: Primary Sjögren's syndrome (pSS) is a B-cell driven systemic auto-immune disease associated with the highest risk of lymphoma among systemic auto-immune diseases. In the prospective ASSESS cohort (395 patients enrolled, with a 10-year follow-up), transcriptomic analysis recently showed the association between baseline peripheral blood overexpression of Bruton's tyrosine kinase (BTK) and lymphoma.
Objectives: This study aimed to confirm the transcriptomic findings at the mRNA and protein level and to evaluate the relevance of BTK as a lymphoma predictor with regards to other predictors.
Methods: BTK mRNA expression was assessed using qRTPCR in whole blood samples from 63 patients (12 patients with a history of lymphoma, 9 patients with incident lymphoma occurring during the 10-year follow-up, 21 patients without lymphoma and no risk factors for lymphoma and 21 patients without lymphoma and ESSDAI ≥ 5). BTK protein expression in peripheral blood was analyzed by flow cytometry in 7 healthy controls, 5 pSS patients without risk factors for lymphoma, 8 pSS patients with ESSDAI ≥5, and 6 pSS patients with lymphoma. In 346 patients of the ASSESS cohort for whom all data were available, the association between pSS-related lymphoma and BTK expression at enrolment, with 9 validated lymphoma predictors (parotid enlargement, purpura, ESSDAI ≥ 5, lymphocytopenia, CD4/CD8 ratio ≤ 0.8, RF positivity, cryoglobulinemia, monoclonal component, and low C4) and other potential biomarkers (serum FLT3L, BAFF, digital interferon alpha, gammaglobulins, IgG, beta2microglobulin, kappa and lambda free light chains, quantitative levels of anti-SSA/SSB) was analyzed. Multivariate analyses took into account in a first model, BTK and the 9 validated predictors of pSS-related lymphoma, and in a second model variables associated with lymphoma in univariate analysis selected by a stepwise procedure.
Results: In qRTPCR, BTK was significantly upregulated between pSS patients with and without lymphoma. In flow cytometry, BTK protein expression in $CD19^+$ B cells (p=0.03), and in most B-cell subpopulations, was significantly increased in patients with lymphoma compared to healthy controls. A gradual increase was observed in BTK expression of $CD19^+$ B cells, between patients without risk factors for lymphoma, those with ESSDAI ≥5, and those with lymphoma. In multivariate analysis, taking into account 9 validated predictors of lymphoma in pSS, BTK expression at enrolment was significantly associated with lymphoma (adjusted OR [aOR] 1.45; 95% CI [1.19-1.82]; p<0.001), along with CD4/CD8 ratio ≤ 0.8 (aOR 6.03; 95% CI [1.23-26.13]; p=0.02). In a second model including 4 biomarkers selected by a stepwise procedure, BTK expression remained significantly associated with lymphoma (aOR 1.36; 95% CI [1.14-1.64]; p<0. 001), as well as serum BAFF levels (mean [SD]:1028.5 pg/ml [710.3]; per 1000 BAFF units, aOR 2.04; 95% CI [1.3-3.19]; p=0.001), low C4 (aOR 4.16; 95% CI [1.43-13.88]; p=0.01) and CD4/CD8 ratio ≤0.8 (aOR 10.62; 95% CI [2.49-44.15]; p=0.001).
Conclusion: These results confirm that increased expression of BTK in peripheral blood is associated with pSS-related lymphoma. These results also show the potential interest of combining B-cell (BTK and BAFF) and T-cell (CD4/CD8 ratio)-related biomarkers to evaluate the risk of lymphoma in pSS.
Acknowledgements: To the patients for their participation to the ASSESS cohort; To the investigators of the ASSESS cohort; plateforme de transcriptomique de l'Institut Cochin; centre de ressources biologiques de l'Hôpital Bichat; The French Society of Rheumatology.
Disclosure of Interests: Pierre-Marie DURET: None declared, Cédric Schleiss: None declared, Nathanaël Sedmak: None declared, Nicolas Meyer: None declared, Tao Ye: None declared, Lou Kawka: None declared, Alain Saraux: None declared, Valerie Devauchelle-Pensec: None declared, Divi Cornec: None declared, Claire Larroche: None declared, Aleth Perdriger: None declared, Raphaèle Seror: None declared, Renaud FELTEN: None declared, Jean Sibilia: None declared, Gaetane Nocturne: None declared, Xavier Mariette Consultant of: Astra Zeneca, BMS, Galapagos, GSK, Novartis, Pfizer, Jacques-Eric Gottenberg Consultant of: Astra Zeneca, BMS, Galapagos, GSK, Novartis, Pfizer.
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OP0211 CHANGE IN URINARY BIOMARKERS AT THREE MONTHS PREDICTS 1-YEAR TREATMENT RESPONSE OF LUPUS NEPHRITIS BETTER THAN PROTEINURIA

Keywords: Biomarkers, Systemic lupus erythematosus, -Omics

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Background: A decline of urine protein-to-creatinine ratio (UPCR) to < 0.5 is associated with better long-term preservation of kidney function in lupus nephritis (LN). UPCR < 0.5 defines complete response in guidelines and clinical trials when achieved after 1 or 2 years. Biomarkers of early response are needed to guide early treatment changes. We studied longitudinal urine proteomic profiles in LN to identify early predictors of proteinuric response.
Objectives: Identify early predictors of proteinuric response in LN using longitudinal urine proteomic profiles.
Methods: We quantified 1200 biomarkers (Kiloplex, RayBiotech) in urine samples collected on the day of (73%) or within 3 weeks (27%) of kidney biopsy and week 12, 24, or 52 in LN patients (ISN class III, IV, V, or mixed) with proteinuria > 1 g/d. Response was defined at one year from renal biopsy: Complete = UPCR < 0.5, serum creatinine (sCr) < 125% of baseline, prednisone ≤ 10mg/d; Partial = UPCR < 50% from baseline but >0.5, sCr < 125% of baseline, but prednisone allowed to 15 mg/d; Non responder = not meeting previous definitions.
Results: A total of 127 patients were included: 48 (38%) with pure proliferative LN (class III or IV), 41 (32%) with mixed LN (III or IV +/- V), and 38% (30%) with pure membranous LN. Response was complete in 34 (27%), partial in 29 (23%), and none in 64 (50%). There were no urinary biomarkers at baseline that predicted response. We then analyzed the changes in urinary proteins at 3 months compared to baseline. Patients who responded at 1 year showed an early decline in 51 urinary proteins led by CD163, IL-16, and CD206 (macrophage mannose receptor) (**Figure 1A**) which matched the proteomic signature associated with histological activity (**Figure 1B**). No changes were observed in nonresponders. The decline of several urinary biomarkers at 3 months outperformed a decline in UPCR (clinical standard) in predicting the 1 year response. In particular, a decline of CD163 predicted 1 year response in ROC analysis with an area under the curve (AUC) of 83% compared to an AUC of 75% for UPCR decline. In proliferative LN, urinary biomarkers displayed superior performance with an AUC of 91%, 86%, and 78% for the decline of CD206, CD163, and UPCR, respectively (**Figure 1C-D)**. Pathway enrichment analysis identified leukocyte activation, neutrophil degranulation, and matrix degradation as the main pathways reduced at 3 months in responders.

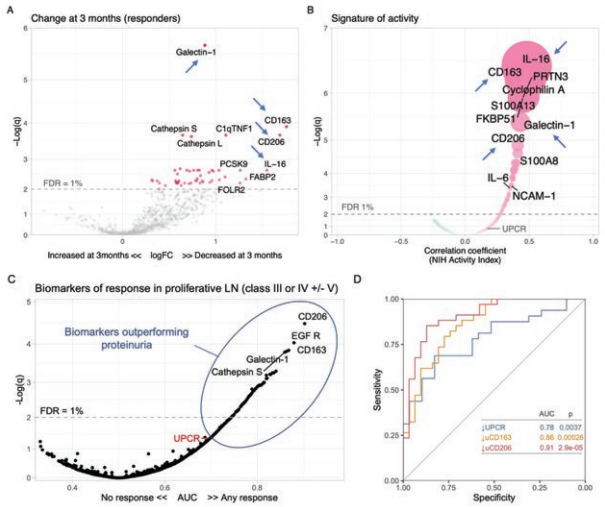


Figure 1.

Conclusion: An early decline in urinary biomarkers of histological activity is associated with proteinuric response at 1 year. These findings indicate that effective immunosuppression induces by three months an immunological response in the kidney that can be noninvasively monitored in the urine. Biomarkers of immunological response outperformed early decline of UPCR, the standard of care, in predicting 1-year proteinuric response, especially in proliferative LN. Because biomarkers of immunological response parallel intrarenal activity, they could detect early treatment response/failure and allow early treatment changes. They could serve as surrogate endpoints in clinical trials. Longitudinal studies are needed to confirm that this immunological response is a better predictor of long-term kidney function preservation than proteinuric responses.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0212 **EXAMINING CLINICAL HETEROGENEITY IN PRIMARY SJOGREN'S SYNDROME: PROTEOMIC AND NETWORK ANALYSIS**

Keywords: -omics, Cytokines and chemokines, Sjögren syndrome

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Background: A symptom-based stratification tool using data from three European cohorts identified four clinical subtypes of pSS: Low symptom burden (LSB), high symptom burden (HSB), dryness dominant with fatigue (DDF), and pain dominant with fatigue (PDF).[1] These subtypes have distinct molecular profiles, clinical manifestations, and responses to immunomodulatory therapies. Detailed knowledge of the biological pathways underlying the clinical subtypes is vital to understanding the clinical heterogeneity of pSS and has relevance for trial design and therapeutic development.
Objectives: Clinical manifestations of an immune-mediated inflammatory disease are likely underpinned by networks of dysregulated biological pathways. Proteomic and network analysis was performed to identify biological pathways that are differentially expressed between the pSS subtypes.
Methods: We profiled serum proteins using O-link technology of 180 pSS subjects (45 subjects of each subtype). We used 5 O-link proteomics panels which included 454 proteins. As we anticipate that these serum proteins may act directly or indirectly through interactions with other proteins, we used a network analysis approach. Using the LSB group as a reference we identified differentially expressed proteins. Network reconstruction was performed using the ARACNE algorithm which calculates mutual information between the variables of a multidimensional dataset to construct a protein network.[2] Differential expression estimates were overlaid on these networks to reveal key regions that are differentially expressed between the phenotypes. Statistical analysis was performed in R v4.1.3 and JMP Pro v15 and network visualisation in cytoscape v3.8.2.
Results: The DDF group is characterised clinically by glandular dysfunction. The DDF proteome demonstrated higher expression of chemokines that orchestrate lymphocyte migration and ectopic lymphoid structure formation in the salivary glands and of cytokines promoting B-cell hyperactivity and autoantibody production. In contrast to DDF, the HSB and PDF groups report extra-glandular manifestations such as pain, fatigue, and mood disturbances. HSB and PDF proteomes show increased expression of proteins linked to the inflammatory response, oxidative stress response and cellular metabolism (IL-1α, IL-6, APE/Ref-1, FOXO1, TIGAR and BACH1). Network analysis revealed distinct clusters of proteins that were upregulated or downregulated between different pSS subtypes, providing added support to the concept that distinct molecular pathways contribute to the clinical manifestations of these subtypes.

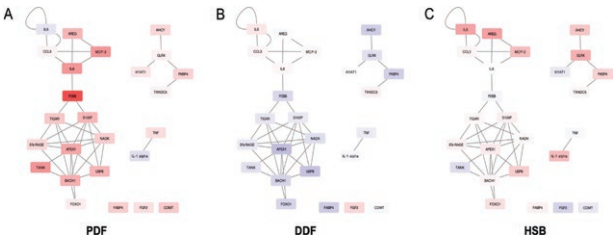


Figure 1. Selected proteins showing differences associated with PDF A), DDF B) and HSB C) subgroups. Derived from ARACNE analysis of protein expression data, nodes represent individual proteins and edges represent the mutual information between nodes. Colour scaling shows estimated difference using LSB as a comparator group, with red indicating higher expression and blue indicating lower expression. Estimates are derived from a generalised linear model post adjustment for baseline age, sex and batch

Conclusion: Protein expression between the clinically distinct pSS subgroups revealed differences in cytokines, chemokines and master transcription factors associated with redox imbalance and altered energy metabolism. Furthermore, the differentially expressed proteins seem to be interrelated in our network

analysis. Our data provide clues to the molecular pathways contributing to the glandular and systemic manifestations of pSS and to potential therapeutic targets for different pSS subgroups.

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Disclosure of Interests: None Declared.

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OP0213 CHARACTERISTIC ENRICHMENT OF ANTIPHOSPHOLIPID-REACTIVE B CELLS AMONG ATYPICAL MEMORY SUBSETS OF PRIMARY APS SUGGEST ONGOING INDUCTION IN EXTRAFOLLICULAR SITES

Keywords: Adaptive immunity, Autoantibodies, Anti-phospholipid syndrome

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Background: Antiphospholipid syndrome (APS) is an autoimmune disease defined by arterial or venous events or pregnancy complications in association with autoantibodies against phospholipids. Despite these autoreactive antibodies, B lineage cells remain poorly studied in APS.[1] Besides triple-positivity of autoantibodies and the occurrence of lupus anticoagulant, there are no biomarkers for risk assessment in APS.[2] Characterization of autoantigen-specific B cells hold promise for better understanding APS pathogenesis which may guide targeted immune therapies including identification of biomarkers.

Objectives: The study characterized B cell subsets among patients with primary (pAPS) and secondary APS (sAPS) compared to healthy controls. In particular, we analyzed phosphatidylcholine (PtC)-specific B cells for their frequency of occurrence and immunophenotype related to disease characteristics.

Methods: We analyzed PBMCs from 20 HCs, 25 pAPS and 16 sAPS patients. Using multi-dimensional flow cytometry, we analyzed the expression of 15 surface markers on B cells including the frequency of PtC-specific B lineage cells. We established a novel assay to detect antigen-specific B cells against PtC as a potential correlate of antiphospholipid antibodies as previously reported for autoreactive B1 cells in mice.[3] The obtained cellular subsets and autoreactive cells were subjected to the FlowSOM algorithm in R to identify B cell clusters through an unbiased strategy.

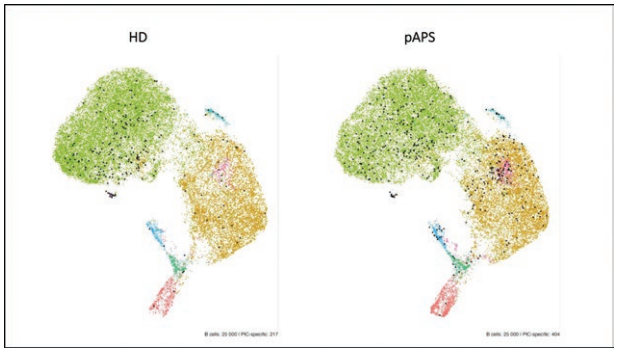


Figure 1. Two-dimensional UMAP for a random subset of 50000 B cells divided by group. Different colors label FlowSOM metaclusters. Clustering was performed on $1.5x10^6$ B cells and 7 surface markers. Black dots represent PtC-specific cells. A significant increase for both total and PtC-specific B cells was observed in the pink cluster for pAPS patients compared to HCs ($p<0.01$). Main clusters: green – naïve, brown – switch memory, red: plasmablasts, pink – pre-switch memory (IgD+/CD24+/CD27+/CD11c+).

Results: pAPS and sAPS patients showed increased frequencies of atypical CD21low as well as CD21low/CD11c+ B cells, most prominent within the IgD+/CD27+ memory compartment (CD21low: $p<0.01$, CD21low/CD11c+: $p<0.001$). We found higher frequencies of total PtC-specific B cells compared to HCs among pAPS in contrast to sAPS patients. In HCs, PtC-specific B cells were found mainly among naïve B cells, while they were significantly enriched within IgD+/CD27+ pre-switch memory B cells in pAPS patients ($p<0.01$). Most notably, high frequencies of PtC-specific IgD+/CD27+ pre-switch memory B cells were associated with a high-risk APS profile according to the EULAR classification criteria ($p<0.05$). Unsupervised FlowSOM clustering identified eight distinct B cell clusters. Remarkably, PtC-reactive memory B cells mainly resided in a unique cluster of IgD+/CD27+/CD21low/CD11c+ memory B cells (**Figure 1**).

Conclusion: Although APS patients carry an overall comparable B cell subset distribution as HCs, increased frequencies of atypical B cells are characteristic of pAPS and sAPS patients. PtC-specific B cells are substantially enriched among memory- and atypical CD21low/ CD11c+ memory B cells in pAPS. The data indicate that there is ongoing induction of autoantigen-specific atypical memory B cells apparently induced outside the germinal centers escaping negative selection.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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OP0214 A MULTI-DIMENSIONAL APPROACH REVEALS A DYSREGULATED SYSTEMIC LUPUS ERYTHEMATOSUS IMMUNE RHEOSTAT WITH AN ABNORMAL IMMUNOREGULATORY RESPONSE AND REDUCED CTLA4 EXPRESSION IN EFFECTOR T CELLS

Keywords: Adaptive immunity, Systemic lupus erythematosus, Biomarkers

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Background: Systemic Lupus Erythematosus (SLE) immunopathogenesis involves a complex network of regulatory and effector cells with its balance constituting an immune rheostat that maintains immune homeostasis. Thus, the disease must be interrogated holistically to identify mechanistically and clinically relevant immune cell subsets for its pathogenesis. There is a crucial unmet need to examine the mechanism of tolerance loss in lupus and identify novel targets for potential therapeutic intervention to improve outcomes.

Objectives: To characterise the SLE immunome holistically and address our hypothesis that SLE is driven dually by an impaired immunoregulatory axis and perturbed immune effector system.

Methods: Forty-one peripheral blood mononuclear cell (PBMC) samples from 26 adult SLE patients and 27 age-matched healthy controls were studied with a 43 markers mass cytometry panel. The SLE patients (23 females) had a median age of 40 (interquartile range [IQR]: 28 to 54) years with a median SLEDAI 2K score of 4 (IQR: 0 to 6). Quality check, batch-effect correction, cell clustering, annotation and visualisation after t-distributed stochastic neighbour embedding (tSNE) dimensional reduction was done using our extended polydimensional immunome characterisation (EPIC) pipeline [1]. Frequencies are expressed as a percentage of total $CD45^+$ PBMC or ratio and described with median and IQR. Statistical significance is defined as $p<0.05$ (Mann-Whitney U test with Bonferroni correction).

Results: Our multi-parametric approach reveals multiple derangements in all the major immune lineages but predominantly in the $CD4^+$ T cell population (Figure 1). Interestingly, there were no significant differences in the memory ($CD45RO^+$) and naïve ($CD45RA^+$) Treg ($CD3^+CD4^+CD25^+Foxp3^+CTLA^+$) subsets between SLE and controls. Instead, an enrichment of an activated memory Treg-like T subset ($CD3^+CD4^+CD45RO^+CD25^-Foxp3^+CTLA^+ICOS^+$) was found in SLE (SLE

versus healthy: 0.86 [0.43 to 1.38]% versus 0.31 [0.24 to 0.42]%, p<0.01). These Treg-like cells do not express CD25, a phenotypic marker for natural Treg cells. Concurrently, there was a significant reduction in CTLA4 expressing naïve non-Treg $CD4^+$ T (effector) cells in lupus (SLE versus healthy: 0.59 [0.40 to 1.11]% versus 2.0 [0.9 to 2.9]%, p<0.01). This was accompanied by a significant reduction in the ratio of $CTLA4^+$ to $CTLA4^-$ naïve non-Treg $TNF\alpha^+$ effector T cells (SLE versus healthy, ratio of $CTLA4^+$ to total naïve non-Treg $TNF\alpha^+$ T cells: 0.14 [0.11 to 0.23] versus 0.33 [0.17 to 0.55], p<0.0001). Additionally, other significant changes such as activated $IL4^+$ T cell subset ($CD3^+CD4^+CD45RA^+HLA\text{-}DR^+IL4^+$) was increased in lupus (SLE versus healthy: 0.30 [0.19 to 0.52]% versus 0.07 [0.05 to 0.12]%, p<0.0001).

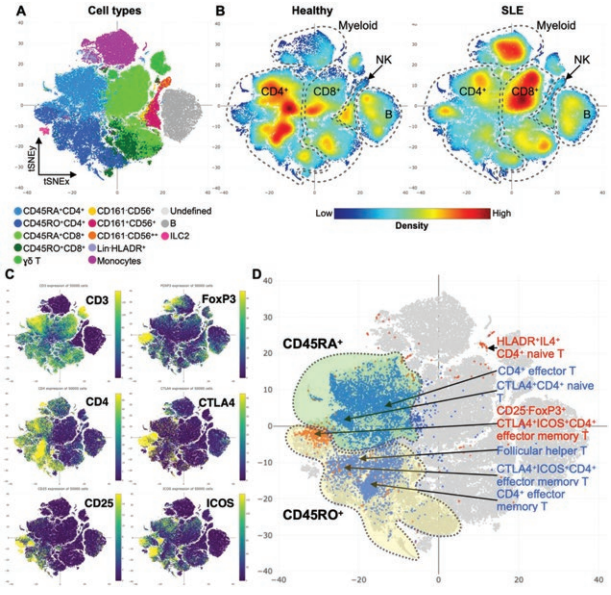


Figure 1. (A) Cell types embedded tSNE plot. **(B)** Healthy and SLE immunomes (Density plots). **(C)** Expression embedded tSNE plots. **(D)** Differentially enriched $CD4^+$ T cell clusters in either healthy or SLE. Blue: significantly increased cell subsets in healthy. Red: significantly increased cell sub-sets in SLE. All plots are derived from a random sampling of 50,000 single-cell events, dimensionally reduced with 43 markers (n=23 healthy and 41 SLE).

Conclusion: There are multiple derangements in the immunoregulatory and effector axes in lupus consistent with its complex immunopathogenesis. The activated CD25 negative Treg-like subset indicates an impaired regulatory response in SLE. The reduced CTLA4 expression in the naïve non-Treg T cells in lupus suggests a perturbed negative feedback mechanism in the effector system. The validation of these results and delineation of the underlying disease mechanisms have translational therapeutic potential.

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Disclosure of Interests: None Declared.

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OP0215 IMMUNOME ANALYSIS INDICATES ROBUST INHIBITION OF PROINFLAMMATORY MEDIATORS UPON LEFLUNOMIDE-HYDROXYCHLOROQUINE COMBINATION THERAPY IN SJÖGREN'S SYNDROME: CXCR3 LIGANDS AS POTENTIAL INFLAMMATORY ENDOTYPE BIOMARKERS.

Keywords: Biomarkers, Sjögren syndrome, Randomized control trial

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Background: Primary Sjögren's syndrome (pSS) is a chronic autoimmune disorder characterized by lymphocytic infiltration and functional impairment of exocrine glands, resulting in dryness of the eyes, mouth and extra-glandular manifestations in numerous organs. Immunopathology in pSS is associated with prominent B cell hyperactivity reflected by elevated serum IgG levels, autoantibody production, immune complex formation, and complement activation [1]. In a recent double blinded placebo controlled randomized trial, we demonstrated unprecedented robust inhibition of B cell hyperactivity and different disease activity parameters (including primary endpoint ESSDAI) by leflunomide-hydroxychloroquine (LEF-HCQ) combination therapy in the treatment of patients with pSS [2].

Objectives: To assess the potential of LEF-HCQ combination therapy to normalize dysregulated inflammatory cytokine levels in pSS patients, and to identify biomarkers that reflect inflammation, monitor changes in disease activity and predict the treatment response.

Methods: We employed a high-throughput protein Olink proteomic assay (Immuno-Oncology panel) in order to determine the blood serum concentrations of 92 immune biomarkers, assessed at baseline and at the clinical endpoint in placebo (n=8) and verum treated patients (n=21). Welch 2-sample t-test and paired t-test were used to calculate differences for unpaired and paired data, respectively and FDR corrected p values were assessed using the Olink Analyze package available on CRAN.

Results: Of the 92 immune biomarkers, 34 were significantly upregulated in pSS patients compared to healthy controls at the onset of the trial (all at least p<0.05). Moreover, the majority of these inflammatory mediators (24/34) were downregulated after 24 weeks of LEF-HCQ treatment (LGALS9, CCL19, IL10, CXCL10, CXCL11, CXCL13, GZMH, CXCL9, and soluble CD28, CD83, CD27, PDCD1, ADGRG1, PD-L1, CRTAM) with 9 returning to healthy control levels (TNF, IL12, GZMA, and soluble LAG3, IL12RB1, TNFRS9/4-1BB, CD4, KLRD1, CD70). Conversely, no significant alterations were observed in the placebo group. Interestingly, changes in ESSDAI scores were significantly (all at least p<0.05) associated with changes in IL13, TNF, PTN, CXCL9, CXCL11 and soluble LAG3 concentrations. In addition, changes in serum IgG and Rheumatoid Factor levels were both significantly associated with changes in soluble CXCL13, GZMA, CXCL9, soluble CD4 and CD28 concentrations. Based on a machine learning approach (sPLS-DA) we identified baseline levels of CXCL9/10/11 as key markers of the treatment response.

Conclusion: LEF-HCQ treatment robustly inhibits inflammatory activity in pSS patients. The correlation of several mediators with clinical activity parameters indicates that these may have value in monitoring the disease activity. Furthermore, the clinical outcome upon LEF/HCQ treatment seems predetermined by an inflammatory endotype, with circulating biomarkers such as CXCR3 ligands as key determinants. These findings represent an important advance in our understanding of the underlying immunopathology of pSS and could help in the development of more personalized and effective treatment approaches for pSS and potentially other rheumatic diseases.

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Disclosure of Interests: None Declared.

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OP0216 THE CLINICAL AND PATHOLOGICAL ROLES OF AUTOANTIBODIES TARGETING BMP SIGNALING IN SYSTEMIC LUPUS ERYTHEMATOSUS-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION

Keywords: Systemic lupus erythematosus, Autoantibodies, Lungs

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Background: Pulmonary arterial hypertension (PAH) is one of the most severe complications and the leading cause of death in patients with systemic lupus erythematosus (SLE). Pathogenic mechanisms leading to SLE-PAH are still not fully understood. In idiopathic PAH, the dysfunction of the bone morphogenetic protein (BMP) pathway was found to be involved in pulmonary artery remodeling [1]. In SLE-PAH, our previous study identified serum autoantibodies targeting BMP receptors (BMPR) as the potential biomarker, including anti-BMPR2, BMPR1A, and Activin Receptor-Like Kinase type 1 (ALK1) antibodies [2]. However, the clinical and pathological roles of the above autoantibodies targeting BMP signaling in SLE-PAH remain uncertain.

Objectives: To investigate the clinical and pathological roles of autoantibodies targeting BMPR2, BMPR1A, and ALK1 in SLE-PAH.

Methods: Patients of SLE-PAH confirmed by right heart catheterization were enrolled and serum levels of autoantibodies targeting BMPR2, BMPR1A, and ALK1 were measured by ELISA. Patients with SLE-PAH were subtyped by

cluster analysis. Survival and treatment goal achievement were further compared between different clusters. The Id1 and phospho-SMAD1/5 (p-SMAD1/5) levels were examined in human pulmonary artery endothelial cells (hPAEC) under the induction of BMP9 combined with anti-BMPR2, anti-ALK1, and anti-BMPR1A neutralizing antibodies (5 μg/mL). The effect of anti-ALK1 antibodies on the extent of monolayer permeability and apoptosis of hPAEC was further examined.
Results: 60 SLE-PAH patients were enrolled and cluster analysis revealed two distinct clusters according to the positivity of autoantibodies targeting BMP signaling and clinical manifestations. Cluster 1 was a "low-antibody and high-disease activity" cluster while cluster 2 was a "high-antibody and low-disease activity" cluster. Patients in cluster 1 showed a higher proportion of nephropathy (76.9%) and SLE activity, however a low positivity rate of autoantibodies targeting BMP signaling. Patients in cluster 2 were characterized by a higher rate of anti-BMPR2 antibodies (82.4%), anti-ALK antibodies (70.6%), and lower SLE activity. Prognostic analysis showed that the proportion of patients who reached the treatment target was relatively higher in cluster 2. Mechanism study showed that the p-SMAD1/5 level and the Id1expression were decreased, indicating the suppression of BMP signaling in the presence of anti-ALK1 antibodies. Functional studies showed that anti-ALK1 antibodies increased the monolayer permeability of hPAEC. The late-stage apoptosis of hPAECs was also induced by anti-ALK1 antibodies.

Table 1. The clinical features of the patients in cluster 1 and cluster 2.

	Cluster 1 (N=26)	Cluster 2 (N=34)	P
Anti-BMPR2 antibodies	5(19.2)	28(82.4)	**<0.001**
Anti-BMPR1A antibodies	8(30.2)	4(1.8)	0.068
Anti-ALK antibodies	5(19.2)	24(70.6)	**<0.001**
Arthritis	12(46.2)	25(73.5)	**0.031**
Nephropathy	20(76.9)	1(2.9)	**<0.001**
SLEDAI	5.46±4.28	2.62±2.10	**0.001**
WHO III/IV	17(65.4)	14(41.2)	0.063

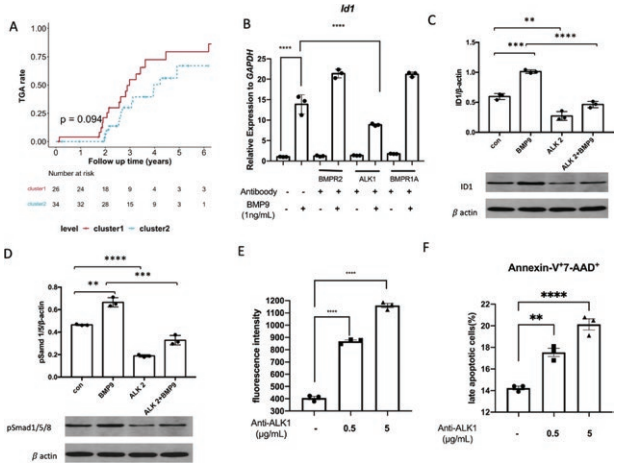


Figure 1. (A). Kaplan-Meier analysis of the prognosis of cluster1 and cluster2. (B) The level of Id1 expression under the induction of anti-BMPR2, anti-ALK1, and anti-BMPR1A antibodies in the presence or absence of BMP9. The ID1 (C) and p-Smad 1/5/8 (D) measured by western blotting under the induction of anti-ALK antibodies, BMP9, or anti-ALK antibodies+ BMP9. The fluorescence of the receiver plate well solution (E) and the percentage of late-stage apoptotic cells (E) under the induction of anti-ALK neutralizing antibodies.

Conclusion: The serum positivity of autoantibodies targeting BMP signaling has clinical potential in dividing SLE-PAH patients into two distinct clusters. The anti-ALK1 antibodies can downregulate BMP signaling and mediate great permeability and apoptosis in hPAECs, which may be involved in the pathogenesis of SLE-PAH.

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OP0217

ANTI-RO52 ANTIBODIES ARE ASSOCIATED WITH HIGHER DISEASE SEVERITY IN PATIENTS WITH SJÖGREN DISEASE THROUGH ACTIVATION OF THE INTERFERON PATHWAY

Keywords: Autoantibodies, Sjögren syndrome, Prognostic factors

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Background: The diagnosis of primary Sjögren Disease (SjD) is currently based on a combination of clinical, histological and biological findings [1]. Current thinking supports anti-Ro60 antibodies as the most specific serum marker, while the impact of anti-Ro52 remains unclear [2].
Objectives: The aim of this study was to characterize the clinical, serological, biological, transcriptomic and interferon profiles of SjD patients according to their anti-Ro52 status and discuss the role of anti-Ro52 in the prognosis of SjD.
Methods: SjD patients were recruited from the European PRECISESADS (378 patients) [3] and the independant Brittany DIApSS cohorts (160 patients) [4]. Four groups were defined: double negative ($Ro52^-/Ro60^-$), isolated anti-Ro52 positive ($Ro52^+$), isolated anti-Ro60 positive ($Ro60^+$), and double positive ($Ro52^+/Ro60^+$) patients. Clinical information, disease activity, and biological markers linked to disease severity were evaluated. Transcriptome data on whole blood by RNAseq and Type I and type II interferon signatures [5,6] were analyzed for PRECISESADS SjD patients.
Results: In both cohorts, arthritis, parotidomegaly, and biological markers (hypergammaglobulinemia, rheumatoid factor and inflammation) [7] were significantly more frequent in the double positive group as compared to other groups. ESSDAI, a score representing systemic activity [8], was also significantly higher in double positive patients compared to the others. Transcriptome analysis demonstrated that anti-Ro52 positivity was associated with a strong interferon pathway activation as the lead cause to explain the clinical associations.
Conclusion: Taken together, these results suggest that SjD patients with anti-Ro52 positivity adopt a more severe phenotype as compared to their negative counterparts, independently of anti-Ro60 positivity.

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Rheumatoid arthritis: new small molecules and old DMARDs

OP0218

INCIDENT MALIGNANCIES IN PATIENTS WITH RHEUMATOID ARTHRITIS IN DAILY RHEUMATOLOGICAL CARE

Keywords: Disease-modifying drugs (DMARDs), Rheumatoid arthritis, Malignancy

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Background: Based on results of the post-authorisation safety trial Oral Surveillance (OS, see [1]), the European and US-American regulatory agencies in 2021 issued warnings about malignancy risk associated with the Janus kinase inhibitor (JAKi) tofacitinib and required changes in labelling.
Objectives: To analyse incident malignancies under treatment with JAKi, tumor necrosis factor inhibitors (TNFi), abatacept (ABA), rituximab (RTX), interleukin 6 inhibitors (IL6i) or conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs - bionaive) in patients with rheumatoid arthritis (RA) observed in daily rheumatological care.
Methods: Data from patients without cancer history from the biologics register RABBIT were included with treatment episodes started 01/2017 - 04/2022. Incidence rates (IR) of malignancies (without non melanoma skin cancer, NMSC) per 1000 patient-years (PY) with 95% confidence intervals (CI) and adjusted hazard ratios (HR) were calculated for all and selected patients according to OS inclusion criteria (age ≥ 50 years and ≥ 1 cardiovascular (CV) risk factor) to compare treatment groups to TNFi. Andersen-Gill regression analysis was used with a 6-month risk window, adjusted via stabilized and winsorized inverse probability of treatment weights taking into account age, sex, smoking, disease activity, prior therapies, comorbidities, and type of enrolling institution (clinic vs. private practice) as covariates. Multiple imputation of missing data was applied.
Results: 2763 JAKi, 3403 TNFi, 744 ABA, 834 RTX, 1125 IL6i and 1130 csDMARD initiations were documented. Patients with a JAKi start were less often men and (except RTX patients) slightly older and had a longer RA disease duration (Table 1). The seropositive proportion and the number of prior treatments with biological (b) or targeted (ts) synthetic DMARDs was higher than in TNFi and csDMARD groups, but lower than in ABA and RTX groups.

Table 1. Patient characteristics at the start of a DMARD episode.

ALL PATIENTS	**JAKi** n=2763	**TNFi** n=3403	**ABA** n=744	**RTX** n=834	**IL6i** n=1125	**csDMARD** n=1130
Age	59.9	57.3	59.6	61.5	58.6	59.6
Men	24%	26%	25.	30%	25%	27%
Disease duration	12.5	9.4	12.0	15.6	11.1	5.9
Seropositivity	79%	74%	81%	92%	79%	67%
DAS28-ESR	2.7	1.0	2.7	5.1	2.5	0
# previous b/tsDMARDs	4.2	4.3	4.4	3.7	4.3	4.2
% of full physical function	65.2	69.3	63.0	64.4	65.5	72.8
# comorbidities	2.2	1.8	2.4	2.5	2.0	1.5
Current smokers	26%	26%	27%	22%	26%	30%
SELECTED PATIENTS*	**JAKi** n=1665	**TNFi** n=1810	**ABA** n=444	**RTX** n=490	**IL6i** n=623	**csDMARD** n=645
Age	64.5	63.7	64.9	66.0	63.5	64.7
Men	27%	30%	29%	36%	28%	30%
Disease duration	13.5	10.2	13.1	16.0	11.9	6.4
Seropositivity	79%	73%	81%	90%	78%	67%
# previous b/tsDMARDs	2.8	1.0	2.7	5.2	2.5	0
DAS28-ESR	4.3	4.5	4.5	3.8	4.4	4.3
% of full physical function	61.5	64.7	59.5	61.7	61.2	70.3
# comorbidities	3.0	2.6	3.2	3.4	2.9	2.2
Current smokers	34%	37%	35%	28%	35%	38%

*Values are given as mean or percentage. *Age ≥50 years and ≥ 1 CV risk factor (hypertension, coronary heart disease, diabetes, hyperlipoproteinaemia, current smoking)*

151 incident malignancies were reported. Across treatments, patients showed comparable IRs between 7 and 11 events per 1000 PY. Among selected patients IRs were higher (13.2 events per 1000 PY in JAKi patients, 95% CI: 9.5 – 17.9). In adjusted analyses, neither JAKi (HR 1.06, 95% CI: 0.70 - 1.61), ABA (HR 0.73, 0.38 - 1.40), RTX (HR 0.86, 0.42 - 1.75), IL6i (HR 0.79, 0.45 - 1.40) nor csDMARDs (HR 2.07, 0.87 - 4.94) showed a significantly altered risk for malignancies compared with TNFi in unselected patients, with similar results in selected patients.

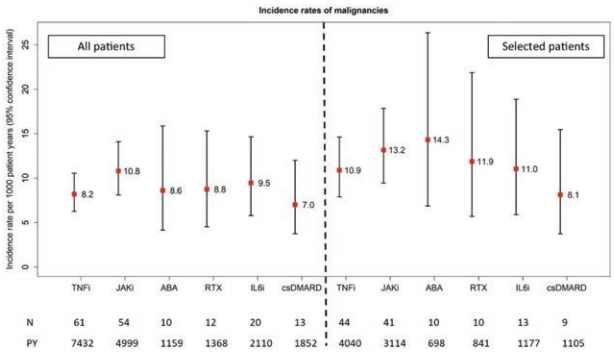


Figure 1. IRs of malignancies (without NMSC) per 1000 PY by treatment group

Conclusion: IR of malignancies in selected patients receiving JAKi in a real-world setting was numerically higher than reported for tofacitinib in OS. However, we found no statistical evidence of an increased malignancy risk with JAKi compared to TNFi, although patients on JAKi were older and had longer disease duration and more previous b/tsDMARDs treatments. Further analyses assessing exposure in terms of treatment duration are needed.

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OP0219

INCIDENCE OF MAJOR ADVERSE CARDIOVASCULAR EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH JAK-INHIBITORS COMPARED TO BDMARDS: DATA FROM AN INTERNATIONAL COLLABORATION OF REGISTRIES (THE "JAK-POT" STUDY)

Keywords: Disease-modifying drugs (DMARDs), Safety, Real-world evidence

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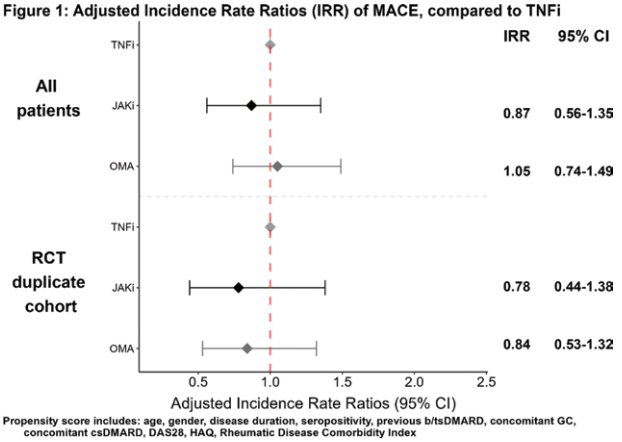
Background: Results of the "ORAL Surveillance" trial showed higher risk of major adverse cardiovascular (CV) events (MACE) for Janus kinase inhibitors (JAKi) than for TNF-inhibitors (TNFi). Currently, there is limited evidence of the real-world cardiovascular safety of JAKi.

Objectives: To assess the incidence of MACE in rheumatoid arthritis (RA) patients treated with JAKi, compared to other biologic agents in a large multi-country real-world population.

Methods: Patients from 14 RA registers from across Europe, Turkey and Québec (Canada), starting JAKi, TNF-inhibitors or bDMARDs with other modes of action (OMA), were included. MACE comprised strokes, myocardial infarctions and transient ischemic attacks and were attributed to a treatment up to 3 months after treatment cessation (except for rituximab for which it was 1 year), loss of follow-up, death or end of study. Incidence rates (IR) of MACE per 1000 patient-years (PY) with 95% confidence intervals (CI) were computed. Poisson regression, with propensity score weighting (including country, disease-, and patient-characteristics, and comorbidities, see Figure 1), was used to obtain adjusted incidence rate ratios (IRR), with 95% CI. A sub-analysis was performed on patients aged ≥ 50 years and ≥ 1 CV risk factor, mimicking the "ORAL Surveillance" trial inclusion criteria (RCT-duplicate cohort).

Results: Over the 50'325 treatment initiations considered (Table 1) in 34'932 patients with a mean follow-up of 2.8 years, 182 incident MACE were reported. Crude incidence was higher for OMA (2.63/1000 PY) than for JAKi (1.76/1000 PY) and TNFi (1.86/1000 PY). The adjusted Poisson regression demonstrated no significant difference in the incidence of MACE between JAKi vs TNFi (IRR = 0.87 (95% CI 0.56; 1.35)), and OMA vs TNFi (IRR = 1.05 (95% CI 0.74; 1.49)) (Figure 1). The RCT-duplicate cohort accounted for 38.4% of treatment courses and had a higher incidence of MACE in each treatment group (OMA: 3.75/1000 PY, JAKi: 2.65/1000 PY, TNFi: 3.48/1000 PY). Similarly to the overall population, no significant difference in the incidence of MACE was observed between JAKi vs TNFi (IRR = 0.78 (95% CI 0.44; 1.38)), and OMA vs TNFi (IRR = 0.84 (95% CI 0.53; 1.32)).

Figure 1: Adjusted Incidence Rate Ratios (IRR) of MACE, compared to TNFi



Propensity score includes: age, gender, disease duration, seropositivity, previous b/tsDMARD, concomitant GC, concomitant csDMARD, DAS28, HAQ, Rheumatic Disease Comorbidity Index

Table 1. Baseline characteristics

	JAKi (TOFA, BARI, UPA, FILGO) n = 12'715	OMA (RITU, TOCI, ABA, SARI) n = 16'048	TNFi (ETN, ADA, GOL, CTZ, IFX) n = 22'102
Treatment duration (median [IQR])	1.4 [0.5, 2.7]	1.3 [0.4, 2.7]	1.5 [0.6, 2.9]
Age (mean (SD))	58.0 (12.4)	59.5 (12.7)	56.5 (13.7)
Female (%)	81.4	79.2	78.4
Disease duration (median [IQR])	11.4 [5.7, 19.0]	12.4 [6.3, 20.7]	9.2 [4.1, 17.0]
Seropositivity (%)	80.5	81.0	75.1
Previous b/ts DMARD (%)			
0	23.3	19.5	44.1
1	22.3	24.8	26.5
2	17.9	21.7	15.5
≥ 3	36.6	33.9	13.9
Concomitant csDMARD (%)			
MTX	22.4	22.4	23.9
MTX + other	9.3	9.9	14.0
other	15.3	18.0	17.7
none	53.0	52.0	44.5
Concomitant GC (%)	44.7	39.8	32.4
CRP (mg/L) (mean (SD))	12.4 (23.2)	13.9 (29.0)	12.5 (23.3)
CDAI (mean (SD))	25.4 (13.9)	22.8 (13.9)	24.7 (13.9)
DAS 28 (mean (SD))	4.7 (1.6)	4.2 (1.7)	4.5 (1.7)
HAQ (mean (SD))	1.2 (0.7)	1.2 (0.8)	1.1 (0.7)
BMI (mean (SD))	27.2 (5.9)	27.3 (5.9)	27.4 (6.3)
Patients with at least one CV risk factor* (%)	54.9	56.6	54.1

csDMARDs = conventional synthetic DMARDs, MTX = methotrexate, GC = glucocorticoids, CRP = C-reactive protein, CDAI = Clinical Disease Activity Index, DAS 28 = Disease Activity Score 28, HAQ = Health Assessment Questionnaire, BMI = Body Mass Index. *Hypertension, hyperlipidaemia, diabetes, smoking, past history of strokes or myocardial infarctions

Conclusion: In this real-world study, including 14 RA registers and all currently available JAKi in the respective countries, we did not find a significantly higher risk of MACE in RA patients treated with JAKi compared to TNFi. Inclusion of other registers to increase the statistical power and the evaluation of other adverse events such as thromboembolic events, cancers and serious infections are planned.

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OP0220 INITIAL GLUCOCORTICOID BRIDGING IN RHEUMATOID ARTHRITIS: DOES IT AFFECT GLUCOCORTICOID USE OVER TIME?

Keywords: Clinical Trials, Rheumatoid arthritis, Tapering

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Background: Glucocorticoid (GC) 'bridging' therapy as temporary part of the initial treatment in rheumatoid arthritis (RA) helps to rapidly suppress disease activity. It has been proposed that patients treated with GC bridging (bridgers) may continue to use more GC later in the disease course than patients who did not receive GC bridging (non-bridgers).
Objectives: To compare GC use over time between RA patients in clinical trials randomized to treatment with or without initial GC bridging.
Methods: Data were available from the BeSt, CareRA and COBRA trials, which included study arms with and without initial GC bridging in addition to csDMARD treatment. GC bridging schedules were planned for a minimal duration of 34 (CareRA), 35 (COBRA) and 36 (BeSt) weeks (Table 1). In an individual patient data (IPD) meta-analysis we compared GC use between bridgers and non-bridgers at 12, 18 and 24 months from baseline as primary outcome. Secondary outcomes were the mean cumulative GC dose until 24 months after baseline with and without the bridging period, number of (study defined) flares (DAS28 increase >1.2 or ΔDAS28 >0.6 and ≥3.2 at previous visit), number of DMARD changes (adding a DMARD or switching between DMARDs) and DAS28 over time. We used mixed effects regression analyses including study arm as random effect. To investigate DAS28 over time, an interaction term between treatment group (whether or not started with GC bridging) and time (as categorical variable) was included.
Results: 252/625 patients (40%) were randomized to GC bridging. Baseline characteristics were comparable between bridgers and non-bridgers. Mean DAS28 improved more rapidly in bridgers in the first 6 months (p<0.01, Figure 1A), but the decrease was similar in both groups thereafter. After the planned end of bridging, GC use was low in both groups (Figure 1B). Only at t=12 months, significantly more bridgers than non-bridgers still or again used GC (OR 3.27 (95% CI 1.06; 10.08)). Disregarding the initial bridging schedules there was no difference between the two groups in cumulative dose, 365 mg (95%CI -62; 793), but the cumulative GC dose including the planned bridging schedules was significantly higher for the bridgers (2889 mg (95% CI 1812; 3967), this can be translated to a difference of 4mg a day for 2 years). The incidence rate ratio (IRR) for (study defined) flares was similar between the groups (IRR 1.14 (95%CI 0.86; 1.50), but the IRR for number of DMARD changes was significantly lower in the bridgers (IRR 0.59 (95%CI 0.38; 0.94)).
Conclusion: After GC bridging therapy (on average 35 weeks), bridgers had an increased risk of using GC at 12 months from baseline compared to non-bridgers, but not thereafter. The bridging schedule determined the cumulative GC dose over time, which after the bridging period was similar in bridgers and non-bridgers. After the end of bridging schedules there were no differences in mean DAS28, number of flares (by study definition) or post-bridging cumulative GC dose, but bridgers had a more rapid decrease of DAS28 in the first 6 months (during bridging schedule) and fewer DMARD changes over time.

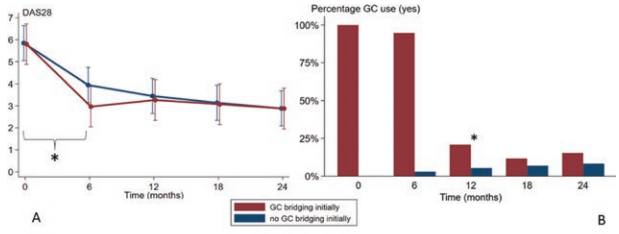


Figure 1. A) Mean DAS28 over time, estimated over 24 months with linear mixed models. Predictive margins are depicted with 95% confidence intervals (CI) as error bars. B) GC use over time for the group that started with GC bridging initially (red) and the group that did not (blue). An asterisk (*) indicates a significant result from the mixed effects regression analyses performed for 12, 18 and 24 months.

Table 1. Overview of the included study arms

	BeSt	COBRA	CareRA
Study arms with GC bridging	*Arm 3 Initial combination therapy*	*Combined treatment arm*	*Low risk group COBRA slim arm*
Initial GC dose	*60mg/day (prednisone) In 7 weeks to 7.5mg/day*	*60mg/day (prednisone)*	*30mg/day (prednisone)*
Tapering to maintenance	*From week 28-36 tapered to zero if DAS≤2.4 for at least 6 months*	*In 6 weeks to 7.5mg/day. From week 29-35 tapered to zero; resume on flare*	*In 5 weeks to 5mg/day From week 28-34 tapered to zero if DAS28(CRP)≤3.2*
Planned end			
DMARD	*MTX 7.5mg/week, increased to 25mg/week if DAS>2.4 after 3 months SSZ 2000mg/day*	*MTX 7.5 mg/week and MTX 15mg/week SSZ 2000mg/day; From week 40-43 MTX tapered to zero; resume on flare*	
Study arms without GC bridging	*Arm 1: Sequential monotherapy; Arm 2: Step up combination therapy: MTX 15mg/week (increased to 25 mg/week if DAS>2.4 after 3 months)*	*Monotherapy arm SSZ 2000 mg/day*	*Low risk group, MTX tight step up arm MTX 15 mg/week*

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OP0221 THERAPY WITH JAK INHIBITORS AND THE RISK OF CARDIOVASCULAR EVENTS IN A DUTCH RHEUMATOID ARTHRITIS POPULATION

Keywords: Rheumatoid arthritis, Cardiovascular disease, Targeted synthetic drugs

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Background: Most of the disease modifying anti-rheumatic drugs (DMARDs) have cardioprotective potential and using them to achieve remission and/or low disease activity in rheumatoid arthritis (RA) importantly diminishes the cardiovascular risk in these patients. Yet for some of these drugs, including JAK-inhibitors, the modulatory effect on cardiovascular risk seems less straightforward [1]. Caution has been advocated recently when using Janus kinase inhibitors (JAKi) in patients with an unfavorable cardiovascular risk profile [2]. For patients who are about to switch medication the decision of giving JAKi can easily be postponed, however for patients in remission while using JAKi the decision to continue or not is much complex and difficult. Therefore, more research into this issue is warranted in order to better guide clinicians in their daily practice.

Objectives: The aim of this study was to investigate the occurrence of cardiovascular events in a large population of RA patients treated with either JAK-inhibitors or other (b)DMARDs, using real-world data.
Methods: Adult RA patients (extrapolated from drug based algorithms), starting a new bDMARD or JAK-inhibitor between August 1st 2017 and January 31st 2022, have been selected from IQVIA's Dutch Real-World Data Longitudinal Prescription database, covering about 63% of outpatient prescriptions in the Netherlands. Study outcome is cardiovascular (CV) event defined as the start of platelet aggregation inhibitors (clopidogrel, prasugrel, ticagrelor, dipyridamol) during study period. The risk of cardiovascular events was estimated using multilevel Poisson regression, adjusted for exposition time and confounders.
Results: In total, 15.191 unique patients were included, with 20.912 treatment episodes with either JAKi (2.090, almost exclusively tofacitinib and baricitinib) or bDMARDs (18.822). Most patients were female (72%) and median age was 62 years. We found a total of 681 CV events occurring during the study period: 48 (2.0 events/100 patient years) during therapy with JAKi and 633 (2.42 events/100 patient years) during therapy with bDMARDs, respectively, resulting in an adjusted incidence risk ratio (IRR) of 0.78 for JAKi compared to bDMARDs (95% confidence interval (CI), 0.56 – 1.10) (Table 1). Subanalysis in patients using either tofacitinib or baricitinib yielded similar results (Table 1). Likewise, RA patients older than 65 years did not have a higher risk for CVD during the therapy with JAKi as compared to those treated with bDMARDs: adjusted IRR 0.78 (95% CI, 0.51 – 1.19).
Conclusion: In the Dutch RA population, the incidence of cardiovascular events in JAKi starters was not higher than in bDMARDs starters, and similar for tofacitinib and baricitinib. These data will further contribute to estimation of the cardiovascular safety of JAKi.
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Table 1. Number of cardiovascular events and IRR for bDMARD and JAK-inhibitor users

	bDMARDs	JAK-inhibitors	Tofacitinib	Baricitinib
N (treatment episodes)	18,822	2,090	1,004	991
CVD events (n)	633	48	25	25
Patient years	26,108	2,373	993	1298
Events/100 patient years	2.42	2.0	2.12	1.93
Crude IRR (95% CI)	Ref 1.0	0.80 (0.57-1.11)	0.81 (0.49-1.31)	0.80 (0.51-1.24)
Adjusted IRR* (95% CI)	Ref 1.0	0.78 (0.56-1.10)	0.88 (0.54-1.44)	0.83 (0.53-1.29)

** adjusted for age, sex, number of used DMARD in the 2 years prior to the index date, diabetes mellitus, use of antihypertensives/statins in 12 months prior to the index date*

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OP0222

TRAJECTORIES OF ANTIMALARIAL ADHERENCE AMONG NEWLY DIAGNOSED RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A POPULATION-BASED COHORT STUDY

Keywords: Systemic lupus erythematosus, Rheumatoid arthritis, Disease-modifying drugs (DMARDs)

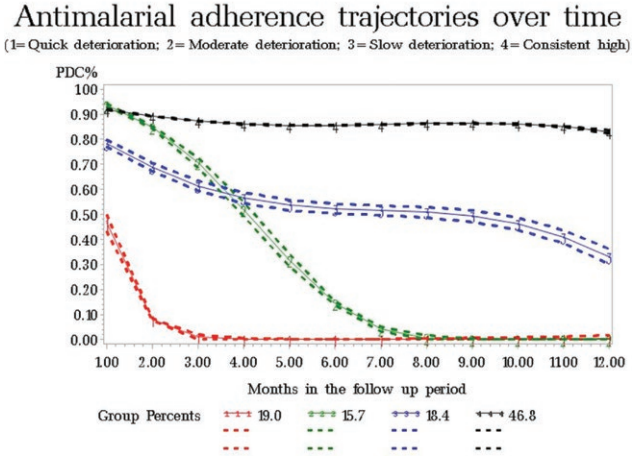
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Background: Adherence to antimalarial regimens are suboptimal in rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients. Also, adherence is dynamic in nature, and varies over the time. Computing a single adherence level over a period may not explain the adherence trajectories of antimalarial in RA and SLE patients over time.
Objectives: To identify the groups of patients with similar patterns or trajectories of antimalarial adherence over time and evaluate the baseline determinants of the group membership of adherence trajectories.
Methods: All patients with incident RA/SLE and incident antimalarial use in British Columbia, Canada, between January 1997 and March 2021, were identified using previously published definitions and administrative health data. Patients were followed up for 12 months from the index date, the time when subjects met RA/SLE criteria and were on antimalarials. We calculated a measure of adherence, the proportion of days covered (PDC) for all patients each month. Then, we used group-based trajectory model (GBTM) analysis on monthly PDC values to identify the latent groups of antimalarial adherence trajectories. The number of groups was selected using the AIC and minimum percentage criterion. Finally, we used an ordered logistic regression to evaluate the baseline determinants of the group membership of adherence trajectories. Baseline determinants of adherence for assessment included sociodemographic factors (neighborhood income quartile, region, age, sex), disease-related factors (disease type (RA vs. SLE), disease duration at index date, hypertension, angina, COPD, modified Charlson comorbidity index), healthcare system factors (hospital visits, physician and specialist visits), and medication use factors (glucocorticoids, immunosuppressives, biologics, Cox-2 selective NSAIDs).
Results: We identified 27,510 patients with incident antimalarial use (23,997 RA and 3,513 SLE patients, mean ± SD age 56.8 ± 15.5 years, 74.8% female). Using GBTM analysis, we identified four groups for antimalarial medication adherence trajectories, representing an ordered pattern of antimalarial adherence from worse to better. Those trajectory groups were - Group 1: quick deterioration (19%), Group 2: moderate deterioration (15.7%), Group 3: slow deterioration (18.4%), and Group 4: consistent high adherence (46.8%) (Figure 1). Significant determinants of the group membership of adherence trajectories from the ordinal logistic regression model are shown in Table 1. The odds of better adherence were higher for those who, at baseline, were older, had higher income, had SLE compared with RA, had hypertension, had rheumatologist visits, and used glucocorticoids, immunosuppressives or Cox-2 selective NSAIDs.

Table 1. Determinants of belonging into better adherence trajectory groups: results from an ordinal logistic regression model including only significant factors.

Factors	Adjusted odds ratio (95% CI)
Age	1.009 (1.008-1.011)
Neighborhood income quartile (Ref: 3)	
1	0.914 (0.854-0.978)
2	0.963 (0.899-1.032)
4	1.075 (1.002-1.153)
5	1.041 (0.969-1.117)
SLE vs RA	1.551 (1.444-1.665)
Have hypertension	1.068 (1.002-1.138)
Have angina	0.878 (0.776-0.995)
Have COPD	0.861 (0.761-0.975)
Rheumatologist visits	1.035 (1.022-1.048)
Glucocorticoids use	1.082 (1.033-1.134)
Immunosuppressives use	1.177 (1.117-1.239)
Cox-2 selective NSAIDs use	1.080 (1.017-1.147)
Biologics use	0.559 (0.426-0.734)

Figure 1: Antimalarial adherence trajectory groups from group-based trajectory model analysis



Conclusion: Among incident RA/SLE incident antimalarial users from a population-based cohort, 53.2% did not continuously adhere to the antimalarial regimen in the first year of treatment. We identified four distinct antimalarial adherence trajectory groups in this study. Sociodemographic, disease-related, healthcare system, and medication use factors associated with better adherence trajectories could help inform strategies to improve antimalarial adherence among RA and SLE patients.
REFERENCES: NIL.
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Disclosure of Interests: None Declared.
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OP0223 THE EFFECT OF ANTIMALARIALS ON THE RISK AND SEVERITY OF BACTERIAL, VIRAL, FUNGAL AND SYSTEMIC-SPECIFIC INFECTIONS IN RHEUMATOID ARTHRITIS

Keywords: Registries, Safety

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Background: Antimalarials (AM) have been related to a lower risk and severity of infections in systemic lupus erythematosus [1], but in rheumatoid arthritis (RA) the results are not unanimously favorable to a possible protective effect exerted by AM [2,3]. In our recent study of RA patients treated with biologic disease modifying anti-rheumatic drugs (bDMARDs) or JAK inhibitors (JAKi), a secondary analysis suggested lower risk of total (25% reduction) and serious infections (47% reduction) with concomitant use of AM [4].
Objectives: To evaluate the association of the use of AM with the risk of total and serious bacterial, viral, fungal and system-specific infections in RA patients treated with conventional synthetic DMARDs (csDMARDs) and/or bDMARDs/JAKi.
Methods: BiobadaBrasil is a multicentric registry-based cohort study of Brazilian patients with rheumatic diseases starting a new csDMARD or their first bDMARD or JAKi [5]. The present analysis includes RA patients recruited from Jan 2009 to Oct 2019, followed-up over one or multiple (up to six) courses of treatment (latest date, Nov 19, 2019) with csDMARDs and/or bDMARDs/JAKi. A treatment course is defined as a period during which the medication scheme of does not change, except for dose adjustments. The primary outcome was the incidence of total infections (SIs) caused by bacteria, viruses and fungi (analyzed separately). The microbiologic etiologic agent was defined by cultural exam or, alternatively, high clinical suspicion, but not all infection had a clearly defined etiology (these ones were excluded from the analysis by etiologic agent). Serious infections according to type of microorganism and system-specific infections served as secondary outcomes. Negative binomial regression with generalized estimating equations (to calculate the incidence rate ratios [ÌRRs]) and extended (frailty) multivariate Cox proportional hazards models were used for statistical analyses (both types of analyses including time- fixed and time-varying covariates over multiple courses of treatment to adjust for confounding).
Results: In total, 1671 patients (2891 treatment courses, 8944.1 patient-years [PY]; most treatment courses [in total, 2335] including bDMARDs or JAKi) were enrolled. AM were used over 512 courses (2036.8 PY) of therapy. The overall incidence of infections caused by bacteria, fungi and viruses were 10.2, 1.9, 1.0/100 PY, respectively. The mIRRs for the primary and secondary outcomes are presented in the Figure 1. There were statistically significant reductions in the risk of serious and non-serious bacterial infections, as wells as serious lower respiratory tract infections, digestive tract infections and those affecting skin or mucosae. These effects were observed regardless of concomitant use or not of bDMARDs/JAKi or methotrexate by the patients.

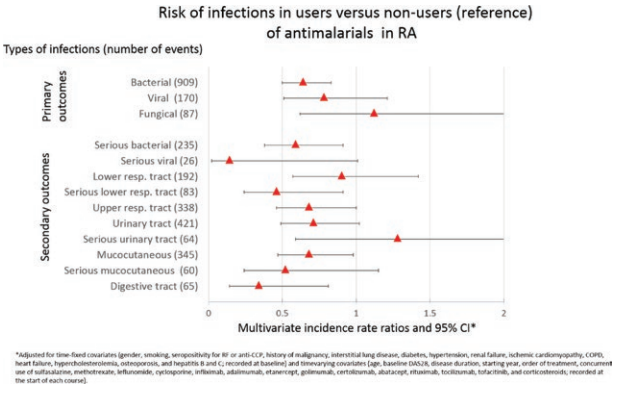


Figure 1.

Conclusion: Among RA patients followed-up in our cohort study, the use of antimalarials was associated with reduction in the risk of bacterial infections, especially serious ones, and there was protection against infections affecting the respiratory and digestive systems and skin/mucosae.

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OP0224 LACK OF FOLYLPOLYGLUTAMATE SYNTHETASE ACTIVITY AND METHOTREXATE POLYGLUTAMYLATION AS UNDERLYING MECHANISMS EXPLAINING WHY METHOTREXATE DOES NOT IMPAIR SPERM QUALITY

Keywords: Disease-modifying drugs (DMARDs), Gender/diversity issues, Pregnancy and reproduction

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Background: We have previously showed that exposure to methotrexate (MTX) was not associated with sperm quality abnormalities or with sperm DNA damage [1]. Nonetheless, a question that remains unanswered is whether MTX and its bioactive forms, the MTX-polyglutamates (MTX-PGs) can be found in spermatozoa. The intracellular conversion of MTX to MTX-PGs is dependent on a process that is catalyzed by the enzyme folylpolyglutamate synthetase (FPGS). Lower FPGS activity and subsequent inefficient polyglutamylation is well-known phenomenon associated with a rapid efflux of MTX from cells [2]. In this regard, recent studies have showed that a significant reduction of FPGS activity is associated with aberrant pre-mRNA splicing of this enzyme, including partial retention of intron 8 (8PR) and a higher ratio of FPGS 8PR over FPGS wild type (WT) [3]. Whether intracellular MTX and the bioactive MTX-PGs can be detected in the spermatozoa and whether spermatozoa have the enzymatic capabilities (FGPS-activity) for the formation of the MTX-PGs has never been studied before.
Objectives: To evaluate if MTX-PGs can be detected in spermatozoa of men exposed to MTX and to evaluate the FPGS enzymatic activity in spermatozoa. Furthermore, MTX-PGs concentration and FPGS activity in spermatozoa will be compared with those present in red blood cells (RBCs) and peripheral blood mononuclear cells (PBMCs).
Methods: This proof of concept translational study was part of the iFAME-MTX study [1]. Blood and semen samples were obtained from 10 adult men diagnosed with an immune-mediated disease (RA, SpA, psoriasis) after 13 weeks of exposure to MTX (cases) and from 4 adult healthy men (controls). Measurement of MTX-PGs in spermatozoa and RBCs was determined by LC-MS/MS methods [4] using stable isotope labelled MTX-PGs_{1-6} as internal standards. FPGS catalytic activity in spermatozoa, RBCs and PBMCs was analyzed in 10 µg protein extracts [3]. Lastly, RNA was isolated from spermatozoa and PBMCs quantitative real-time PCR were performed to quantify the mRNA expression profiles of folate genes in spermatozoa, in particular FPGS 8PR/WT [3]. Continuous variables were compared using a Mann-Whitney test.
Results: MTX-PG_1 was the predominant form of MTX-PGs detected in spermatozoa. Other MTX-PGs forms (MTX-PG_{2-5}) were not or hardly detectable in spermatozoa after MTX exposure (Figure 1A). Furthermore, comparisons with other cell types revealed that MTX-PGs accumulation in spermatozoa is markedly lower than in RBCs and PBMCs (Figure 1B). Consistent with the lack of MTX-PGs formation, FPGS catalytic activity (reported as pmol 15N-MTX-PG2 formed/h/mg protein) in spermatozoa was statistically significant lower (5.1) compared to PBMCs (183, p=<0.005)). Regarding, mRNA expression profiles of folate genes in spermatozoa, a high FPGS 8PR/WT ratio was observed compared to PBMCs.
Conclusion: This is the first study ever conducted to measure the concentration of MTX-PGs and concomitant FPGS activity in spermatozoa. Hardly any bioactive forms of MTX (MTX-PG) could be detected in spermatozoa. This is related to the fact that spermatozoa have very low FPGS activity and hence

lack the capacity to form MTX-PGs. Mechanistically, the low FPGS activity in spermatozoa is likely associated with a higher ratio of mRNA expression of an alternatively spliced form of the FPGS gene (8PR) over the WT transcript. These results support and clarify our previous findings that treatment with MTX does not affect sperm quality parameters and provides further evidence that MTX can be safely used in men with a wish to become a father.

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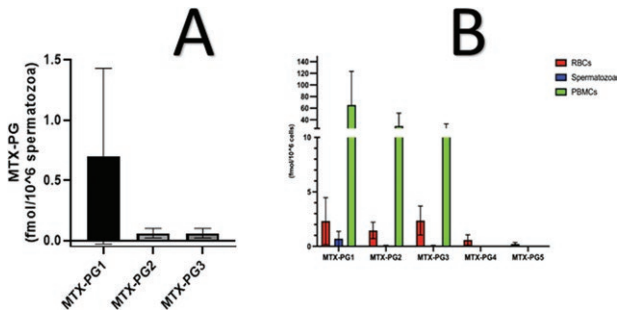


Figure 1. MTX-PG accumulation in spermatozoa (A) compared to RBCs and PBMCs (B).

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OP0225

EVALUATION OF RESPONSE TO ADJUVANTED RECOMBINANT ZOSTER VACCINATION IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING UPADACITINIB: RESULTS FROM A RANDOMIZED TRIAL SUB-STUDY

Keywords: Vaccination/immunization, Rheumatoid arthritis, Targeted synthetic drugs

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Background: Upadacitinib (UPA) is an oral JAK inhibitor (JAKi) approved for the treatment of RA. JAKi have been associated with an elevated risk of herpes zoster (HZ) in patients (pts) with RA. The adjuvanted recombinant zoster vaccine (RZV, Shingrix) was shown to be well-tolerated and effective in preventing HZ in adults aged ≥ 50 years.[1] The efficacy and safety of RZV have not been studied in pts with RA while on UPA in combination with MTX.

Objectives: To assess the immunogenicity of RZV in pts with RA receiving UPA 15 mg once daily (QD) with background MTX.

Methods: Eligible adults aged ≥ 50 years with RA enrolled in the ongoing SELECT-COMPARE phase 3 trial (NCT02629159) received two RZV doses, administered at the baseline and week (wk) 12 visits. Pts should have been on stable doses of UPA 15 mg QD and background MTX for ≥ 8 wks before the first vaccination and ≥ 4 wks after the second vaccination. Antibody titers were collected pre-vaccination (baseline), 4 wks post-dose 1 vaccination (wk 4), and 4 wks post-dose 2 vaccination (wk 16). The primary endpoint was the proportion of pts with a humoral response to RZV defined as ≥ 4-fold increase in pre-vaccination concentration of anti-glycoprotein E [gE] titer levels at wk 16. Secondary endpoints included humoral response to RZV at wk 4 and the geometric mean fold rise (GMFR) in anti-gE antibody levels at wks 4 and 16. Cell-mediated immunogenicity to RZV was an exploratory endpoint evaluated by the frequencies of gE-specific CD4+ [2+] T cells (CD4+ T cells expressing ≥ 2 of 4 activation markers: IFN-γ, IL-2, TNF-α, and CD40 ligand) measured by flow cytometry at wks 4 and 16 in a sub-cohort of pts.

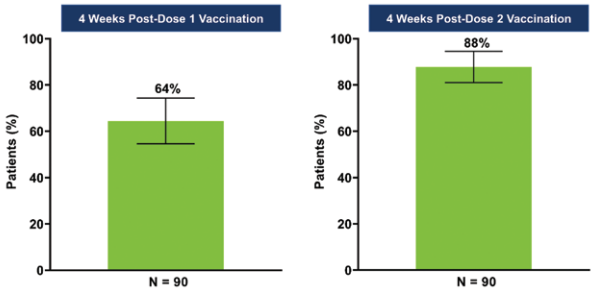
Results: Of the 95 pts who received ≥ 1 RZV dose, 93 (98%) received both RZV doses. Pts had a mean (standard deviation) age of 62.4 (7.5) years. The median (range) disease duration was 11.7 (4.9–41.6) years and duration of UPA exposure was 3.9 (2.9–5.8) years. At baseline, all but 2 pts were receiving concomitant MTX and half (50%) were taking an oral corticosteroid (CS) at a median daily dose of 5.0 mg. One pt discontinued UPA by wk 16. Blood samples were available from 90/93 pts. Satisfactory humoral responses to RZV occurred in 64% (95% confidence interval [CI]: 55–74) of pts at wk 4 and 88% (81–95) at wk 16 (**Figure 1**). Age (50–< 65 years: 85% [95% CI: 75–94]; ≥ 65 years: 94% [85–100]) and concomitant CS (yes: 87% [77–97]; no: 89% [80–98]) use at baseline did not affect humoral responses at wk 16. GMFR in anti-gE antibody levels compared with baseline values were observed at wks 4 (10.2 [95% CI: 7.3–14.3]) and 16 (22.6 [15.9–32.2]). Among the sub-cohort of pts, nearly two-thirds achieved a cell-mediated immune response to RZV (wk 4: n = 21/34, 62% [95% CI: 45–78]; wk 16: n = 25/38; 66% [51–81]). Within 30 days post-vaccination of either RZV dose, no serious adverse events (AEs) (**Table 1**) or HZ were reported. AEs that were possibly related to RZV were reported in 17% of pts. One death occurred more than 30 days after wk 16 due to COVID-19 pneumonia.

Conclusion: More than three-quarters (88%) of pts with RA receiving UPA 15 mg QD on background MTX achieved a satisfactory humoral response to RZV at wk 16. In a subgroup of pts, two-thirds (66%) achieved a cell-mediated immune response to RZV at wk 16. Age and concomitant CS use did not negatively affect RZV response.

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Figure. Proportion of Patients Treated With UPA 15 mg QD and Background MTX Achieving a Humoral Response to RZV 4 Weeks Post-Dose 1 and Post-Dose 2 Vaccination



CI, confidence interval; QD, once daily; RZV, adjuvanted recombinant zoster vaccine; UPA, upadacitinib.
Error bars indicate 95% CI. Number of patients (N = 90) was based on the availability of blood samples collected at the baseline and study visits.
Humoral response to RZV was defined as a ≥ 4-fold increase in pre-vaccination concentration of anti-glycoprotein E titer levels at week 16.

Table 1 . Safety Results Through 30-Days Post-RZV Vaccination in UPA-Treated Patients

Event, n (%)	UPA 15 mg QD (N = 95)
Any AE	38 (40%)
AE with reasonable possibility of being related to UPA[a]	13 (14%)
AE with reasonable possibility of being related to RZV[a]	16 (17%)
Severe AE[b]	1 (1%)
Serious AE	0
AE leading to discontinuation of UPA	0
Death	0

AE, adverse event; QD, once daily; RZV, adjuvanted recombinant zoster vaccine; UPA, upadacitinib. [a]As assessed by the investigator. [b]Hypersensitivity.

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Updates on management and outcomes in SLE and Sjogren syndrome

OP0226

ATTAINMENT OF LUPUS LOW DISEASE ACTIVITY STATE EXCLUSIVE OF REMISSION IS PROTECTIVE AGAINST ADVERSE OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Real-world evidence, Treat to target

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Background: The lupus low disease activity state (LLDAS) treat-to-target definition sets a ceiling for acceptable disease and treatment burden in SLE. Definition of Remission in SLE (DORIS) is a more stringent state, but as it is concentric with LLDAS many patients in LLDAS also meet the DORIS remission definition. Studies in cohorts with a majority of patients in remission poorly separate LLDAS and remission, leading to debate about the independent effects of LLDAS on SLE outcomes.

Objectives: We examined whether being in LLDAS but not remission provided protection against adverse outcomes of flare, irreversible organ damage accrual and mortality in patients with SLE.

Methods: Data from a 13-country longitudinal SLE cohort (ACR/SLICC criteria), collected prospectively between 2013 and 2020, were analysed. Organ damage and flare were captured using SLICC Damage Index and SELENA-SLEDAI Flare Index, respectively. LLDAS was defined as Golder *et al.*, 2019 [1] (SLEDAI<4, no new activity, PGA <1, prednisolone (PNL) <7.5 mg/d, antimalarials (AM) and immunosuppressants (IS) allowed). Remission was defined as Vollenhoven *et al*, 2021 [2] (clinical SLEDAI=0, PGA <0.5, PNL<5 mg/d, AM/IS allowed).

Results: 3,811 patients with ≥ 2 visits followed over a median of 2.8 years [IQR: 1.0 to 5.3] were studied. 80 (2.1%) patients died; 717 (21%) accrued organ damage, and 2,142 (56%) experienced mild-moderate or severe flare during the study period. 55% (n=2,099) attained LLDAS but not remission (LLDAS+REM-) at least once, with a median (IQR) cumulative percent-time spent in LLDAS+REM- of 21.5% [9.8, 42.9]. Overall, 63% attained both LLDAS and remission (LLDAS+REM+) with median (IQR) cumulative time 45% [22, 71]; 18% attained LLDAS+REM-., and 19% of patients never attained LLDAS or REM. Compared to patients who never attained LLDAS or remission (LLDAS-REM-), LLDAS+REM- attainment at any time during the study observation period provided significant protection against subsequent flare and damage accrual, and protection against mortality with borderline statistical significance, after adjusting for potential confounding factors (Table 1). Similarly, ≥50% of cumulative observed time in LLDAS+REM- provided significant protection against flare and damage accrual but not mortality, possibly due to lack of power (Table 1). Protective effects of LLDAS+REM+ were also confirmed.

Table 1. Longitudinal associations of LLDAS+REM- attainment with flare, organ damage accrual and mortality

	Flare$_t$	Damage accrual$_t$	Mortality$_t$
	HR1 (95%CI) p-value	*HR2 (95%CI) p-value*	*HR3 (95%CI) p-value*
Not in LLDAS or REM$_{t-1}$	1.00	1.00	1.00
LLDAS+REM-$_{t-1}$	0.66 (0.60, 073) p<0.0001	0.63 (0.52, 0.77) p<0.0001	0.14 (0.02, 1.07) p=0.059
LLDAS+REM+$_{t-1}$	0.57 (0.52, 0.61) p<0.0001	0.46 (0.39, 0.54) p<0.0001	0.22 (0.08, 0.65) P=0.006
<50%T in LLDAS+REM-$_{t-1}$	1.00	1.00	1.00
≥50%T in LLDAS+REM-$_{t-1}$	0.71 (0.62, 0.81) p<0.0001	0.72 (0.56, 0.92) p=0.010	0.39 (0.14, 1.10) p=0.08
<50%T in LLDAS+REM+$_{t-1}$	1.00	1.00	1.00
≥50%T in LLDAS+REM+$_{t-1}$	0.62 (0.56, 0.67) P<0.0001	0.64 (0.53, 0.76) P<0.0001	0.53 (0.19, 1.43) p=0.21

Hazard ratios adjusted for [1]age and national gross domestic product (GDP); [2]age, GDP and baseline organ damage, and [3]GDP and SDI score. T=time.

Conclusion: Attainment of LLDAS provides significant protection against flare and organ damage accrual even when excluding patients who are also meet the definition of remission. LLDAS is an independent predictor of improved outcomes in SLE.

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OP0227 IMPROVEMENTS AND CHALLENGES OF SYSTEMIC LUPUS ERYTHEMATOSUS ASSOCIATED PULMONARY ARTERIAL HYPERTENSION: A 10-YEAR MULTICENTER COHORT STUDY

Keywords: Systemic lupus erythematosus, Cardiovascular disease, Treat to target

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Background: Previous studies have described improved survival in systemic sclerosis (SSc) associated pulmonary arterial hypertension (PAH)[1-2], yet it is unclear whether survival of systemic lupus erythematosus (SLE) associated PAH has also improved.
Objectives: To describe the CSTAR prospective cohort of SLE-PAH patients, explore changes in characteristics, treatment and 5-year survival in the last decade, and possible reasons for survival change.
Methods: A multicenter prospective cohort of SLE-PAH was established, and divided into cohort A (2011.6-2016.5) and cohort B (2016.6-2021.5) according to the date of their baseline right heart catheterization (RHC). Another singlecenter cohort of idiopathic pulmonary arterial hypertension (IPAH) was consecutively recruited as control to describe the baseline characteristic and survival of SLE-PAH patients simultaneously. Disease characteristics, treatment regimen, and all-cause mortality were compared between cohort A and cohort B. Multi-variable cox regression was used to analyze association between treatment goal achievement and survival.
Results: A total of 610 SLE-PAH and 104 IPAH patients were enrolled. Overall, SLE-PAH patients were younger, predominantly female, had lower NT-proBNP level, better function status, better hemodynamic, and higher 5-year survival than IPAH (81.2% vs 56.0%, p<0.001). Compared with cohort A, patients in cohort B showed lower mPAP and PVR, higher CI, and were more likely to receive intensive immunosuppressants and PAH-targeted medication. 5-year survival rate was also higher in cohort B (88.1% vs 72.9%, p=0.01). In multivariable Cox regression, treatment goal achievement of PAH (HR 0.31, 95%CI 0.12-0.81, p=0.017) and reaching lupus low disease activity state (LLDAS) (HR 0.23, 95%CI 0.08-0.67, p=0.007) were both independently associated with a lower mortality.
Conclusion: This is the largest muticenter prospective SLE-PAH cohort to describe disease characteristics and prognosis. This study showed that survival has improved significantly for SLE-PAH. Early detection of PAH in SLE patients, achieving PAH treatment goal as well as LLDAS for SLE contributed to survival improvement.

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Table 1. Baseline characteristics of SLE-PAH and IPAH patients

	SLE-PAH vs IPAH			Cohort A vs Cohort B		
	SLE-PAH n=610	IPAH n=104	p-value	cohort A n=314	cohort B n=296	p-value
Age at enrollment, years	35.2±9.9	41.8±16.2	**<0.01**	34.8±9.9	35.4±9.9	0.43
Female, No.(%)	601 (98.5%)	71 (68.3)	**<0.01**	312 (99.4)	289 (97.6)	0.10
WHO function class III-IV, No.(%)	254 (47.1)	37 (35.9)	**0.04**	133 (48.7)	121 (45.5)	0.49
6-minute walk distance, m	400±134	347±131	**<0.01**	388±134	418±132	**0.04**
NT-proBNP, ng/L	1923±3059	2715±2839	**0.03**	1861±2640	1974±3378	0.71
Hemodynamics						
mPAP, mmHg	45.4±11.6	56.3±16.8	**<0.01**	46.6±11.8	44.3±11.4	**0.02**
PAWP, mmHg	8.4±3.5	9.2±3.3	**0.04**	7.7±3.5	9.0±3.3	**<0.01**
PVR, WU	9.7±5.1	14.9±9.2	**<0.01**	10.7±5.3	8.8±5.3	**<0.01**
RAP, mmHg	6.5±4.1	8.2±6.4	0.06	6.3±4.2	6.6±3.9	0.31
CI, L/min.m2	2.9±0.9	2.2±0.8	**<0.01**	2.7±0.91	3.0±0.8	**<0.01**
Echocardiography						
Right ventricle diameter, mm	29.1±7.3	33.2±6.5	0.08	29.9±7.4	27.1±7.1	**0.01**
TAPSE, mm	16.4±3.9	13.7±3.5	**<0.01**	/	16.4±3.9	/
Pericardial effusion, No.(%)	229 (43.1)	29 (36.3)	0.28	139 (49.6)	90 (45.9)	**<0.01**
Pulmonary function test						
FVC, (% predicted)	83.2±14.5	95.1±15.9	**<0.01**	80.6±13.3	90.9±15.4	**<0.01**
TLC, (% predicted)	89.0±11.8	96.1±12.3	**<0.001**	88.5±10.9	90.6±14.2	0.29
DLCO, (% predicted)	60.4±15.4	63.2±24.2	0.30	60.9±15.7	59.0±14.5	0.45

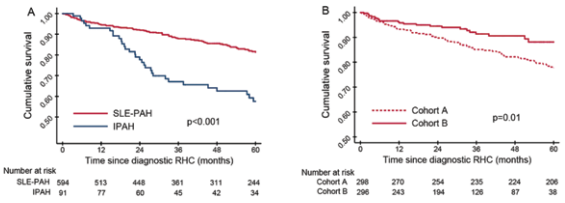


Figure. Kaplan-Meier survival analysis. (A) comparison of 5-year survival between SLE-PAH and IPAH patients. (B) comparison of 5-year survival between cohort A and cohort B. SLE, systemic lupus erythematosus; PAH, pulmonary hypertension; IPAH, idiopathic

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OP0228 COEXISTING TUBULOINTERSTITIAL INFLAMMATION AND DAMAGE IS A RISK FACTOR FOR CHRONIC KIDNEY DISEASE IN PATIENTS WITH LUPUS NEPHRITIS: RESULTS FROM THE KORNET REGISTRY

Keywords: Systemic lupus erythematosus

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Background: An increasing body of evidence suggests a prognostic role of tubulointerstitial lesions in patients with lupus nephritis (LN). Although persistent tubulointerstitial inflammation (TII) usually precedes tubulointerstitial damage (TID) in LN, the two conditions can be simultaneously present to varying degrees.
Objectives: We examined whether coexisting TII/TID predicts progression to chronic kidney disease (CKD) in LN patients.
Methods: The 175 LN patients enrolled in the study had clinical data obtained at the time of renal biopsy and stored in the KORNET registry. These patients were divided into two groups: those with and without coexisting TII/TID. The two groups were compared with respect to their demographic, clinical, histological, laboratory findings, and long-term prognosis. Uni- and multivariable Cox proportional hazard regression models were used to identify independent risk factors for CKD in LN patients.
Results: Of the 175 LN patients, 110 (62.9%) had coexisting TII/TID and 65 (37.1%) did not. Patients with coexisting TII/TID were older, had higher ESR and 24 h proteinuria, and lower eGFR and hemoglobin levels than those without coexisting TII/TID. Anti-Ro and ribosomal-P antibodies were detected less frequently in patients with coexisting TII/TID. In a histological analysis, patients with coexisting TII/TID more often had LN of the proliferative type and a larger proportion had a chronicity score > 4. During a mean follow-up of 89.9 months, CKD and ESRD developed more frequently in patients with than without coexisting TII/TID. Finally, the coexisting TII/TID was associated with a higher risk for CKD progression: adjusted hazard ratio (HR) = 2.677, 95% confidence interval (CI) (1.333, 5.335), p = 0.006 for all LN patients; HR = 3.265, 95% CI (1.451,7.345) for those with class III, IV and V LN; HR = 3.045, 95% CI (1.289, 7.195) for those with class III, IV, V LN, and eGFR ≥ 30 mL/min/1.73 m^2.
Conclusion: LN patients with coexisting TII/TID are at greater risk for deterioration of kidney function at LN onset and for developing CKD over the long-term.

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Disclosure of Interests: None Declared.
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OP0229 CHANGES IN THE CAUSES AND PREDICTORS OF LUPUS MORTALITY IN SPAIN THROUGH THE LAST DECADES: DATA FROM THE RELESSER REGISTRY

Keywords: Prognostic factors, Registries, Systemic lupus erythematosus

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Background: The mortality in Systemic Lupus Erythematosus (SLE) varies largely across different countries most probably due to social, healthcare and ethnic differences. The contemporary cohorts continue to show higher mortality rates in SLE patients as compared with the general population [1,2]. We need to identify demographic, clinical and serological predictors of mortality in SLE in our country, to improve the prognosis of SLE patients.
Objectives: To analyze the causes and identify predictive factors of mortality of SLE, and to assess the time evolution and chronological changes in Spain.
Methods: We performed a cross-sectional and retrospective study analyzing data from the RELESSER cohort (Spanish Registry of SLE of the Spanish Society of Rheumatology). Sociodemographic, clinical and serological variables, comorbidities and treatments, as well as indicators of disease activity, damage and severity were recorded. We excluded patients with lost information about the death variable and analyzed the differential features of deceased patients in comparisons with survivors through different time stages according to the date of diagnosis: until the 1980's; the 1990's and the first decade of the 21st century. Variables associated with mortality in univariate analysis were entered into different multivariate models to determine which ones were independently associated with the outcome of the disease in each decade.
Results: A total of 3665 patients were included, mostly caucasian female with similar general features regardless of the different time stages analyzed. The 18.4% until the 1980´s, the 5.97% in the 1990´s and up to 2.84% of the individuals in the first decade of the 21st century, had died. The main age of death was similar in the different groups, around 55-58 years old (Table 1). The vascular events were the leading cause of death until the 1980´s, while in the last two decades, were infections.
The older age at diagnosis was predictor of mortality in our cohort. Neither gender nor delay in diagnosis was independently associated with mortality, with the exception of the female sex, which behaved as a protective factor until the 1980's. The mortality predictors in our cohort were the presence of hypocomplementemia and organ damage until the 1980´s; thrombocytopenia, antiphospholipid syndrome and valve disease in the 1990´s; serositis, organ damage and depression in the first decade of the 21st century. Conversely, skin involvement was related to greater survival over the last two decades and comorbidities were associated with mortality in all periods of the study.
The use of high doses of corticosteroids (>30mg/day) was predictor of mortality in each time stage, as well as the use of cyclophosphamide and rituximab from the year 2000. Antimalarial treatment was linked to improved survival in all the decades analyzed.
Conclusion: In the RELESSER cohort, the main cause of death in the last decades were infections. However, until the 1980´s, vascular events were predominant. Older age at diagnosis, the use of corticosteroids and comorbidities were associated with a significant increase in mortality in SLE, while antimalarial treatment was linked to improved survival. Data indicate that organ damage is a risk factor and skin involvement is a protective factor against mortality. Differentially, female sex until the 1980´s was independently associated with improved survival, and depression at the beginning of the 21st century was linked to mortality. Our results must be confirmed in prospective studies that minimize methodological limitations.

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Table. General Features

	Until 1980´s	1990´s	21st Century
N (3665)	539	1122	2004
Age at diagnosis, years, mean±SD	28.7 ± 12.6	33.4 ± 14.2	38.3 ± 15.3
Sex, female n (%)	491 (91.1%)	1025 (91.5%)	1770 (88.6%)
Caucasian race (%)	98.5%	96%	90.4%
Delay in diagnosis, months, mean±SD	20.8 ± 52.7	26.2 ± 53.6	28.9 ± 52.6
ACR criteria (≥ 4) (%)	98%	93.9%	88.1%
DECEASED n (%)	99 (18.4%)	67 (5.97%)	57 (2.84%)
Age of death, years, mean±SD	55.21 ± 15.59	57.74 ± 18.61	58.32 ± 19.73
Main cause of death	Vascular events	Infections	Infections

Acknowledgements: Thank you to RELESSER researchers and collaborators, especially to profesor Jaime Calvo-Alén for having helped to develop this study.
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OP0230

USING AN INNOVATIVE DIGITAL TOOL FOR THE ASSESSMENT AND PERSONALIZED RECOMMENDATIONS TO COPE WITH FATIGUE IN SYSTEMIC LUPUS ERYTHEMATOSUS: THE LEAF STUDY

Keywords: Systemic lupus erythematosus, Patient reported outcomes, Patient information and education

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Background: Fatigue is reported as the most prevalent and bothersome symptom by Systemic Lupus Erythematosus (SLE) patients as it may impair key aspects of the quality of life. Assessing and treating fatigue is therefore an important aspect of SLE care. However, fatigue management is complex due to its multifactorial nature, as well as the need for personalized care which may take time that clinicians might lack during routine consultations.
Digital tools are increasingly used for clinical practice, and may offer promising opportunities to assess and manage fatigue in chronic diseases.
Objectives: The aim of the LEAF study was to study the usefulness of an innovative digital tool to manage fatigue in SLE, first by collecting the main characteristics and factors associated with fatigue in SLE at the individual patient-level using self-report questionnaires and then by providing automatically personalized feedback to these SLE patients as how to cope with fatigue.
Methods: We developed an online digital tool, the «Lupus Expert System for Assessment of Fatigue» (LEAF), which was validated with the patient association Lupus Europe. LEAF contains a multilingual questionnaire that measures the intensity and characteristics of fatigue, using the «Fonctional Assessment of Chronic Illness Therapy – Fatigue Scale» (FACIT-Fatigue), the «Multidimensional Fatigue Inventory» (MFI) and a Numerical Rating Scale (NRS), and assesses potential predictors of fatigue, including disease activity, pain, insomnia, anxiety, depression, stress, fibromyalgia (optional) and physical activity using validated self-reported instruments. Once the assessment is completed, LEAF provides automatically personalized feedback and recommendations to cope with fatigue. Participants to the LEAF study had a diagnosis of SLE confirmed by a medical doctor. Patients evaluated how helpful LEAF was and how much they would recommend it to another patient on a 0-5 scale. Fatigue characteristics were described. Associations between significant fatigue (FACIT-Fatigue<34) and its determinants were evaluated in univariate and multivariate analyses.
Results: Between May and November 2022, 1250 participants were included in the LEAF study. Participants were mostly female (95.2%), with a median age of 43 years old (IQR: 34-51). Significant fatigue (FACIT-Fatigue<34) was reported by 78.9% of patients. NRS median score for fatigue intensity was 7 (IQR: 6-8), on a 0-10 scale. MFI median scores were 15 (IQR: 12-17) for physical fatigue, 13 (IQR: 10-16) for mental fatigue, 14 (IQR: 11-16) for reduced activity and 14 (IQR: 11-17) for reduced motivation, on a 4-20 scale.

In univariate analysis, SLE participants with fatigue (FACIT-Fatigue<34) were more likely to be women (p=0.01), perceived their disease as more active (p<0.0001), had higher levels of pain (p<0.0001), anxiety (p<0.0001), depression (p<0.0001), insomnia (p<0.0001), stress (p<0.0001), and were more likely to have fibromyalgia (p<0.0001), compared to patients without significant fatigue. In multivariable analysis, the parameters independently associated with fatigue were insomnia (p=0.0003), significant pain (p=0.002), fibromyalgia (p=0.008), self-reported active SLE (p=0.02), and high level of stress (p=0.045).
Following LEAF feedback, 93.2% of the participants found LEAF helpful (NRS ≥ 3/5) and 92.3% would recommend it to another SLE patient (NRS ≥ 3/5).
Conclusion: In SLE patients, fatigue was frequent, commonly severe, and associated with a significant reduction of activities and motivation. This further confirms the urgent need to develop new tools to assess and treat fatigue in SLE. Our study demonstrates the usefulness of an innovative digital tool to manage fatigue in SLE.
Acknowledgements: We would like to thank all patients who have participated to the LEAF study, and in particular the patient association Lupus Europe.
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OP0231 EVALUATION OF NON-CRITERIA MANIFESTATIONS OF ANTIPHOSPHOLIPID SYNDROME IN PATIENTS WITH SYSTEMIC LUPUSERYTHEMATOSUS ACCORDING TO ANTI-PHOSPHOLIPID ANTIBODY PROFILE

Keywords: Organ damage, Anti-phospholipid syndrome, Registries

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Background: 30% of patients with SLE have APS, so clinical thromboembolic, obstetric and laboratory manifestations have been extensively studied in this population. The association between antiphospholipid antibodies (aPL) and non-thrombotic manifestations that are not part of the Sydney classification criteria for APS are particularly important in patients with SLE.
Objectives: To compare the presence of non-criteria non-thrombotic manifestations of APS in patients with SLE and APS, SLE with positive aPL, SLE with negative antibodies and different outcomes such as mortality, hospitalizations and damage score.
Methods: Observational, analytical and cross-sectional multicenter study. Data were obtained from the review of the RELESSAR database. We included patients ≥ 18 years with diagnosis of SLE according to modified ACR 1984 criteria. The diagnosis of APS was made according to the Sidney Criteria 2006. The sample was classified into three groups based on the presence of established APS (Group 1), aPL carrier (Group 2) and aPL negative (Group 3). Non-criteria manifestations were described and compared in the three groups. Continuous variables were compared by Student's or Mann Whitney's T test, and categorical variables by Chi[2] test or Fisher's exact test. In cases where a significant difference was found between the groups, multiple post hoc comparisons were made.
Results: One thousand two hundred and two patients were included, 1,110 (92.3%) were women. One hundred and sixty patients (13.3%) had APS (group 1), 241 (20.04%) were aPL carrier (group 2) and 801 (66.6%) were negative for aPL (group 3). Patients with APS were older than patients in group 2 [42.6 (SD 13.5) vs 38 (SD 14.2), p 0.001] and 3 [42.6 (SD 13.5) vs 39.5 (SD 14.1) p 0.004]. The disease duration was longer in patients with APS compared to patients with SLE and negative aPL (138 months (SD 113) vs 101 (SD 113) (p <0.001). Table 1 shows non-thrombotic manifestations in the three groups. A higher percentage of patients with hemolytic anemia was observed in the APS group (p=0.001) and in the aPL carrier group (p=0.018) compared to negative aPL group. Patients with APS showed a higher proportion of thrombocytopenia when compared to patients with negative aPL (p=0.039). Acute cranial/peripheral neuropathy was more frequently observed in APS group compared to aPL-negative group (p=0.006). APS group was significantly associated with hospitalizations due SLE flares, morbidity and damage index (Table 2). A higher proportion of patients in the APS group had thrombotic events compared to aPL carrier and aPL negative groups (p<0.05).

Table 1. Non-criteria non-thrombotic manifestations

	APS (group 1)	aPL + (group 2)	aPL – (group 3)	*p*
Hemolytic anemia	31 (19.9%)	37 (15.4%)	75 (9.47%)	<0.001
Thrombocytopenia	41 (26.6%)	56 (23.4%)	138 (17.6%)	0.011
Depression	23 (14.8%)	17 (7.05%)	92 (11.6%)	0.041
Acute Neuropathy	10 (6.62%)	9 (3.73%)	14 (1.77%)	0.002

Table 2. Patient prognostic measures

	APS (group 1)	aPL + (group 2)	aPL – (group 3)	*p*
Hospitalizations	96 (62.3%)	119 (49.8%)	401 (50.4%)	0.02
Charlson Score	2.43 (1.92)	2.01 (1.51)	1.95 (1.46)	0.009
SLICC	1.53 (1.66)	1.04 (1.32)	0.960 (1.34)	<0.001

Conclusion: In this nation-wide SLE cohort, neurological and hematological manifestations were frequently observed in patients with secondary APS. Moreover, these patients had higher rate of hospitalization, damage score and comorbidities.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0232 DEEP LEARNING ACCURATELY PREDICTS FOCUS SCORE AND DIAGNOSIS OF PRIMARY SJÖGREN SYNDROME USING LABIAL SALIVARY GLAND BIOPSIES

Keywords: Artificial intelligence, Sjögren syndrome

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Background: The Focus Score (FS) ≥ 1 in minor labial salivary gland (LSG) biopsies is one of the 2 main items (with anti-SSA positivity) to establish the diagnosis of Primary Sjögren Syndrome's (pSS). As such, correctly assessing the FS is crucial for the diagnosis of pSS. However, the histological interpretation of LSG tissue requires specific expertise and poses a challenge to non-specialized centers. Vivino et al. [1] show up to 53% of reclassification after expert center rescoring. Deep learning algorithms using artificial neural networks are increasingly used to assist pathologists and can be designed to provide explainable predictions using heatmaps. Heatmaps show which part of the sample section is used to perform the prediction, thus reducing the black box effect. This is important to allow adoption of accurate FS scoring using machine learning in clinical practice.
Objectives: Based on minor LSG specimen, we developed two deep learning models, the first one to predict the FS (≥ 1 or < 1) and the other to predict pSS diagnosis.
Methods: LSG slides used for the diagnosis of patients suspected of pSS were included in the study from 3 European centers which are part of the NECESSITY consortium, a European H2020 IMI2 project. Three groups were included: patients with sicca symptoms but without pSS (Sicca group), pSS patients with ≥ 1 FS, and pSS patients with <1 FS. All pSS diagnoses were confirmed by rheumatologists from expert centers. Clinical data regarding demographics, disease duration, FS, autoantibodies, and dryness were also collected. All LSG sections used for the pathologic diagnosis were scanned. Two deep learning models were used: one for FS prediction and the other for diagnosis prediction from the biopsies. The models provided a prediction and scored each sub-region of the tissue slides with a risk score. The risk score was used to interpret the algorithm's result and find which areas of the tissue were most significant for the classification (whether FS or diagnosis). For each model, 70% of patients were used for training and 30% for validation. For the FS task, both the validation and test sets include 54% of ≥ 1 FS patients. Similarly, for the pSS task, both the validation and test sets include 67% of pSS+ patients. The algorithm's performance was measured using the area under the ROC curve (AUROC).
Results: The dataset included 327 patients: 145 from Paris-Saclay university (Bicêtre Hospital), 73 from Queen Mary University London and 109 from the University of Birmingham. For binary FS prediction the AUROC was 0.87, and for the pSS diagnosis prediction, the AUROC was 0.84. When areas used to make the prediction were analyzed, the model unsurprisingly identified lymphocyte foci for the FS prediction task (Figure 1). This provides explainability and allows the pathologist to visually confirm the results of the prediction. Results on the validation sets for the two tasks are available in Table 1.

Table 1. Results on the Validation Sets.

Task	AUROC	Positive Predicted Value (PPV)	Negative Predictive Value (NPV)	Specificity	Sensitivity
FS ≥ 1/ FS < 1 Prediction	0.87	0.76	0.83	0.78	0.81
pSS+/- Prediction	0.84	0.83	0.67	0.64	0.84

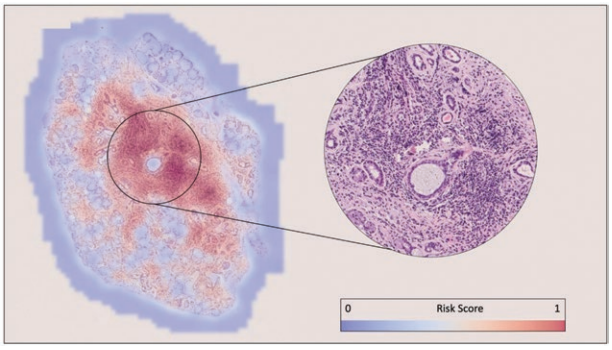


Figure 1. Heatmap Computed from FS Prediction Highlights Lymphocytes.

Conclusion: Deep learning can predict the diagnosis of FS>1 and the diagnosis of pSS with good accuracy. The FS model could represent a valuable help for assisting pathologists who are not experts in oral medicine pathology and reduce their reliance on reference centers. Comprehensive analysis of the tissue areas highlighted by the pSS model paves the way for a better understanding of the disease's physiopathology.

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OP0233 IMPACT OF LYMPHOMA TREATMENT STRATEGY ON HEMATOLOGIC RESPONSE AND AUTOIMMUNE DISEASE ACTIVITY IN SJOGREN PATIENTS DEVELOPING LYMPHOMA

Keywords: Sjögren syndrome, Outcome measures

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Background: Primary Sjögren Syndrome (pSS) patients have an increased risk of Non-Hodgkin lymphoma (NHL). There is no consensus on the therapeutic management of low-grade NHL. Two strategies can be proposed; either a "wait and see" strategy or an active therapeutic strategy.
Objectives: To describe characteristics of NHL in pSS, therapeutic strategies and impact of these strategies on prognosis of lymphoma and of pSS.
Methods: This multicentric retrospective study included all lymphoma patients of the ASSESS cohort, enriched with patients recruited in Rheumatology and Internal Medicine departments. For each patient, we collected biological and clinical manifestations of pSS, lymphoma's characteristics, and treatment strategy. Progression free survival (PFS) (lymphoma-PFS and pSS relapse free survival) and overall survival (OS) were analyzed.
Results: A total of 106 pSS patients who presented a B cell lymphoma between 1985 and 2019 were included. Among them 14 (13%) had diffuse large B cell lymphoma (DLBCL) and 82 pSS patients presented a low-grade B cell-NHL, mucosa-associated lymphoid tissue (MALT) lymphomas being the most frequent histologic subtype occurring in 68/82 (83%) patients.
Among these 82 patients, a "wait and watch strategy" was chosen in 19 (23%) patients; 63 patients received a specific treatment for lymphoma at lymphoma diagnosis including systemic treatment (chemotherapy and/or immunotherapy) in 49 (60%) patients and local therapy (surgery or radiotherapy) in 14 (17%) patients; 10 patients further received rituximab (RTX) maintenance therapy.
Comparison of treated versus not treated patients is presented in the Table 1. Untreated patients were older and had less pulmonary lymphoma location.
We then analyzed the prognosis after a mean follow up of 6.5 years. Nine patients (11%) died during the follow-up. In multivariate analysis, age (HR= 1.16 [1.06-1.27], p = 0.001) and pulmonary location (HR= 8.15 [1.57-42.3], p = 0.013) were associated with death.
Last, we compared OS, lymphoma PFS and pSS relapse PFS in treated versus not treated patients after propensity score weighting We observed that starting an active treatment for NHL at lymphoma diagnosis did not impact OS and lymphoma PFS (HR= 4.81 [0.48-47.9], p=0.2 and HR=1.12 l0.50- 2.48], p=0.8, respectively). Conversely, treating lymphoma had a protective effect on the risk of pSS relapse (HR 0.4 [0.17-0.95], p = 0.038). Last, among patients treated for lymphoma, we observed that no lymphoma relapse occurred in patients who received maintenance therapy with RTX (0/10 events vs 18/53, p = 0.04).
Conclusion: This study based on a large number of pSS patients with lymphoma shows that age and pulmonary location are independently associated with the risk of death. The choice of treating lymphoma at its diagnosis or not does not affect OS and PFS for lymphoma. However treatment of lymphoma reduced the risk of pSS relapse. This should be taken into account when deciding therapeutic strategy in our pSS patients with lymphoma.

Table 1.

Variable	Wait and watch N=19	Active treatment N=63	p-val.
F	18/ 19 (95%)	54/ 63 (86%)	
Age	64.0 (54.0, 75.5)	56.0 (47.0, 65.5)	**0.041**
Time between pSS and lymphoma diagnosis	1.0 (0.0, 8.5)	3.2 (0.1, 9.0)	0.6
ESSDAI	6.0 (4.0, 8.0)	8.0 (5.0, 14.0)	0.2
clinESSDAI	4.0 (3.0, 7.0)	6.5 (4.0, 12.8)	0.091
Biology			
SSA antibodies	14/ 19 (74%)	44/ 61 (72%)	0.9
SSB antibodies	8/ 19 (42%)	23/ 58 (40%)	0.9
Positive rheumatoid factor	14/ 18 (78%)	39/ 54 (78%)	0.8
Low C4	2/ 11 (18%)	15/ 35 (43%)	0.2
Hypergammaglobulinemia	9/ 16 (56%)	30/ 45 (67%)	0.5
Lymphoma type			0.7
MALT lymphoma	15/ 19 (79%)	53/ 63 (84%)	
Nodal marginal zone lymphoma	4/ 19 (21%)	10/ 63 (16%)	
Lymphoma dissemination			
Salivary and/or ganglionar limited	7/ 19 (37%)	35/ 63 (56%)	0.2
Lymphoma spread ≥ 2 locations	9/ 19 (47%)	28/ 63 (44%)	0.8
Lymphoma localization			
Salivary gland limited lymphoma	4/ 19 (21%)	20/ 63 (56%)	0.4
Pulmonary lymphoma involvement	0/ 19 (0%)	13/ 63 (21%)	**0.032**
Salivary gland lymphoma involvement	11/ 19 (58%)	36/ 63 (57%)	>0.9
Outcome			
Median follow-up	7.0 (4.5, 8.5)	6.0 (4.0, 13.5)	0.7
Death	1/ 19 (5.3%)	8/ 63 (13%)	-

REFERENCES: NIL.
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Update on the treatment of scleroderma lung disease

OP0234 **2023 UPDATE OF EULAR RECOMMENDATIONS FOR THE TREATMENT OF SYSTEMIC SCLEROSIS**

Keywords: Systematic review, Clinical trials, Disease-modifying drugs (DMARDs)

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Background: EULAR recommendations for treatment for Systemic Sclerosis (SSc) were last updated in 2017, based on literature up to the end of 2014. The treatment recommendations are among the most cited publication in the field, reflecting their utility both in clinical practice and academic research. In the past 8 years, several important advances have been achieved by the scientific community, with new treatments becoming available and accepted by regulatory authorities.
Objectives: To update the 2017 EULAR recommendations for treatment of SSc, including answers to the 2017 research agenda, new therapeutic questions, and the wealth of newly available evidence.
Methods: Update of previous recommendations was endorsed by EULAR and performed according to the validated methodology. The task force was composed according to recent EULAR guidelines for inclusivity of underrepresented areas of Europe and it consisted of 27 members, including a EULAR endorsed methodologist, 4 fellows, a librarian, one Allied Health Professional and two patient representatives, identified by the Federation of European Scleroderma Associations (FESCA). All centres from the EULAR Scleroderma Trials and Research group (EUSTAR) were invited to review previous questions for Systematic Literature Review (SLR) and propose new ones according to a standardised Delphi approach. A Nominal Group Technique (NGT) exercise was implemented in two rounds for the definition of questions with an 80% agreement threshold. The SLR was conducted with an end date of June 2022, and manually updated to December 2022. Particular attention was dedicated to the 2017 research agenda and new available evidence with matters for detailed discussion and new research agenda also agreed during the NGT.
Results: Sixty-seven clinical questions addressing 24 different interventions were prioritised by the task force for the SLR. The results of the SLR were categorised by level of evidence and grade of recommendations and discussed during the NGT meeting. The procedure resulted in 21 recommendations (instead of 16 in 2017) in 8 clinical domains related to SSc symptoms and organ involvements, including Raynaud's phenomenon, digital ulcers, pulmonary arterial hypertension, scleroderma renal crisis, skin fibrosis, interstitial lung disease, gastrointestinal manifestations and arthritis. Most of the new recommendations were in the field of skin fibrosis and interstitial lung disease, consistent with the research agenda set in 2017. These included recommendations for the use of mycophenolate mofetil, nintedanib, rituximab and tocilizumab for the treatment of these crucial disease manifestations. None of these therapies were present in the 2017 recommendations. Important additions to the future research agenda included targeted therapies for the management of musculoskeletal and gastrointestinal manifestations, calcinosis and the local management of digital ulcers.
Conclusion: The 2023 updates of EULAR recommendations include the first set of synthetic and biological targeted therapies recommended as disease modifying agents for key fibrotic manifestations of systemic sclerosis. While a disease modifying agent or strategy for a comprehensive approach appropriate for all SSc patients is still missing, numerous advances have been achieved since 2017. New, strong evidence is now available to clinicians to better manage patients with this life-threatening condition.
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Disclosure of Interests: Francesco Del Galdo Speakers bureau: Astra-Zeneca, Janssen, Consultant of: Astra Zeneca, Boehringer-Ingelheim, Capella, Chemomab, Janssen, Mitsubishi-Tanabe, Grant/research support from: Abbvie, AstraZeneca, Boheringer-Ingelheim, Capella, Chemomab, Kymab, Janssen, Mitsubishi-Tanabe, Alain LESCOAT: None declared, Philip G Conaghan: None declared, Lidia P. Ananyeva Consultant of: Boehringer Ingelheim and Biocad, Alexandra Balbir-Gurman: None declared, Eugenia Bertoldo: None declared, Vladimira Boyadzhieva: None declared, Ivan Castellví Speakers bureau: Boehringer Ingelheim, Kern, Galápagos, Topandur, & Janssen- Cilag, Consultant of: Boehringer Ingelheim, Kern, Galápagos, Topandur, & Janssen- Cilag, Jelena Colic: None declared, Christopher P Denton Speakers bureau: GlaxoSmithKline, Galapagos, Boehringer. Ingelheim, Roche, CSL Behring, Corbus, Horizon, Capella Bioscience and Arxx Therapeuti, Consultant of: GlaxoSmithKline, Galapagos, Boehringer. Ingelheim, Roche, CSL Behring, Corbus, Horizon, Capella Bioscience and Arxx Therapeuti, Grant/research support from: GlaxoSmithKline, Galapagos, Boehringer. Ingelheim, Roche, CSL Behring, Corbus, Horizon, Capella Bioscience and Arxx Therapeuti, Oliver Distler Speakers bureau: 4P-Pharma, Abbvie, Acceleron, Alcimed, Altavant, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galderma, Galapagos, Glenmark, Gossamer, iQvia, Horizon, Inventiva, Janssen, Kymera, Lupin, Medscape, Merck, Miltenyi

Biotec, Mitsubishi Tanabe, Novartis, Prometheus, Redxpharma, Roivant, Sanofi and Topadur, Consultant of: 4P-Pharma, Abbvie, Acceleron, Alcimed, Altavant, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galderma, Galapagos, Glenmark, Gossamer, iQvia, Horizon, Inventiva, Janssen, Kymera, Lupin, Medscape, Merck, Miltenyi Biotec, Mitsubishi Tanabe, Novartis, Prometheus, Redxpharma, Roivant, Sanofi and Topadur, Khadija El Aoufy: None declared, Jenny Emmel: None declared, Sue Farrington: None declared, Armando Gabrielli: None declared, Ilaria Galetti: None declared, Anna-Maria Hoffmann-Vold Speakers bureau: Boehringer Ingelheim, Jannsen, Medscape, Merck Sharp & Dohme and Roche, Consultant of: ARXX, Boehringer Ingelheim, Genentech, Jannsen, Medscape, Merck Sharp & Dohme and Roche, Grant/research support from: Boehringer Ingelheim, Jannsen, Otylia Kowal-Bielecka Speakers bureau: Abbvie, Boehringer Ingelheim, CSL Behring, Janssen-Cilag, Medac, MSD, Novartis, Pfizer, Sandoz, Consultant of: Abbvie, Boehringer Ingelheim, CSL Behring, Janssen-Cilag, Medac, MSD, Novartis, Pfizer, Sandoz, Grant/research support from: Abbvie, Boehringer Ingelheim, CSL Behring, Janssen-Cilag, Medac, MSD, Novartis, Pfizer, Sandoz, Marco Matucci Cerinic Speakers bureau: Bayer,Biogen, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos, Inventiva,Lilly, MSD, Sandoz, Consultant of: Bayer,Biogen, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos, Inventiva,Lilly, MSD, Sandoz, Grant/research support from: Bayer,Biogen, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos, Inventiva,Lilly, MSD, Sandoz, Ulf Müller-Ladner Speakers bureau: BMS, Galapagos, Medac, Novartis, Janssen, Lilly, Boehringer, Consultant of: BMS, Galapagos, Medac, Novartis, Janssen, Lilly, Boehringer, Predrag Ostojic Speakers bureau: Abbvie, Eli Lilly, Boehringer Ingelheim, Novartis, MSD, Pfizer, Sandoz, Berlin Chemie Menarini, Amicus, EL Pharma, Consultant of: Abbvie, Eli Lilly, Boehringer Ingelheim, Novartis, MSD, Pfizer, Sandoz, Berlin Chemie Menarini, Amicus, EL Pharma, Simona Rednic Speakers bureau: Abbvie, Amgen, AstraZeneca, Boehringer Ingelheim, Ewopharma, Janssen, Novartis, Pfizer, Sanofi, Sandoz, Consultant of: Abbvie, Amgen, AstraZeneca, Boehringer Ingelheim, Ewopharma, Janssen, Novartis, Pfizer, Sanofi, Sandoz, Grant/research support from: Abbvie, Amgen, AstraZeneca, Boehringer Ingelheim, Ewopharma, Janssen, Novartis, Pfizer, Sanofi, Sandoz, Tânia Santiago: None declared, Yossra A. Suliman: None declared, Anna Tarasova: None declared, Madelon Vonk Speakers bureau: Boehringer Ingelheim, Ferrer, Galapagos, GSK, Janssen, MSD and Novartis, Consultant of: Boehringer Ingelheim, Ferrer, Galapagos, GSK, Janssen, MSD and Novartis, Yannick Allanore Consultant of: AbbVie, AstraZeneca, Bayer, Boehringer-Ingelheim, Mylan, Janssen, Medsenic, Prometheus, Sanofi, Roche, Grant/research support from: Alpine Immunosciences, Medsenic, OSE Immunotherapeutics.

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OP0235

DEVELOPMENT AND PRELIMINARY VALIDATION OF THE NOVEL SCLERODERMA CLINICAL TRIALS CONSORTIUM ACTIVITY INDEX

Keywords: Outcome measures, Systemic sclerosis

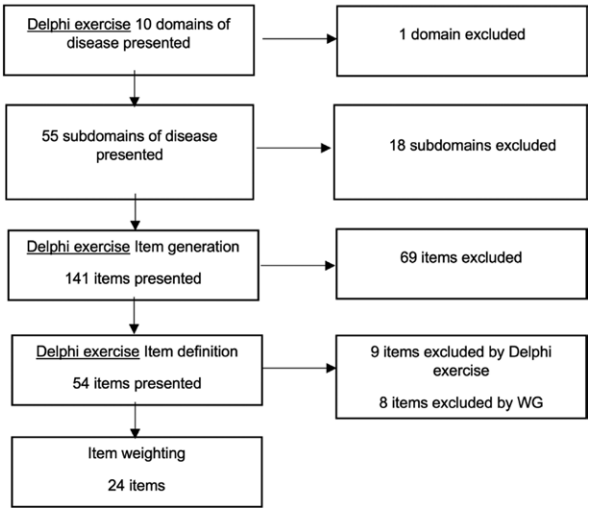
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Background: Accurate measurement of disease activity in systemic sclerosis (SSc) remains a significant challenge. Previous activity indices have been criticised for limitations of face and content validity.

Objectives: The Scleroderma Clinical Trials Consortium (SCTC) convened an Activity Index Working Group to develop a disease activity index (SCTC AI) that has face, content and construct validity.

Methods: Consensus was reached regarding the conceptual definition of disease activity in SSc. All SCTC AI items were required to be measures of the agreed upon construct. See Figure 1 for process of item generation. In all Delphi exercises an *a priori* threshold of 70% agreement was applied for items to be included or excluded from subsequent rounds. Items that did not meet the threshold for inclusion across 2 survey rounds were omitted.

Figure 1 Item generation & reduction



Data from the Australian Scleroderma Cohort Study were used to reduce and weight items. Items were weighted using time dependent Cox proportional hazards regression analysis relative to a combined endpoint of mortality and morbidity (SF 36 physical component score (PCS) below cohort median value). Seven provisional items were not collected in the ASCS. A discrete choice experiment was performed to generate relative weightings for these items. Group based trajectory modelling (GBTM) was used to identify trajectory groups to compare the survival of low vs high disease activity groups using Kaplan Meier survival analyses. Cox proportional hazard modelling was used to evaluate the association between activity scores and mortality, morbidity and SCTC Damage Index (SCTC DI) scores.

Results: The definition of disease activity as agreed by the SCTC AI WG is: *Activity in SSc refers to aspects of disease, attributable to SSc, that are potentially reversible, or can be arrested, with time and/or effective therapy. Disease activity may be associated with morbidity and uncontrolled activity may lead to organ dysfunction and mortality.* A 24 item index, spanning nine domains of disease was generated with a maximum score of 140 (Table 1). GBTM identified 3 trajectory groups: low activity (n=856 (49%) median baseline SCTC AI score 4 (IQR 0-6)); medium activity (n=745 (42%) median baseline SCTC AI score 10 (IQR 6-14)); high activity (n=164 (9%) median baseline SCTC AI score 16 (IQR 10-22)). There was a graded risk of death associated with increasing activity levels. 4 year survival was poorer in the high disease activity group compared to the low disease activity group (75% vs 95%, p<0.01). Patients with a SCTC AI ≥15.5 had a HR 3.5 (2.26-5.42 p<0.01) for death and greater morbidity was observed in individuals with a SCTC AI ≥9.5 (HR 1.90 (1.61-2.24 p<0.01). There was a significant relationship between SCTC AI scores and worsening damage; HR 4.43 (3.51-5.60, p<0.01) for 1 unit increase of SCTC DI for each unit increase in SCTC AI.

Conclusion: We present a novel outcome measure to quantify the burden of disease activity in SSc. We have employed a rigorous consensus based methodology in combination with data driven methods, to develop an outcome measure that has face, content and criterion validity. Further work is required to externally validate and confirm the construct and discriminative validity of the SCTC AI.

Table 1. SCTC Activity Index

Item	Score	Item	Score
Change mRSS ≥ +5 points*	7	New ILD on HRCT	4
New areas of skin thickening*	7	Worsening breathlessness**	4
Worsening skin symptoms**	1	New pulmonary arterial hypertension on RHC	3
Current digital tip ulcer, extra score for >1 digital ulcer	3 (+1)	Active scleroderma renal crisis	10
Current critical digital ischaemia	9	Acute or subacute systolic dysfunction	5
Worsening Raynaud's phenomenon*	1	Active myocarditis	9
Current synovitis	6	Acute pericarditis	6
Current tendon friction rub	7	Elevated troponin	8
Active skeletal myositis	6	Elevated BNP	8
Change FVC ≥ -5%***	8	Worsening gastrointestinal symptoms**	1
Change DLCO ≥ -10%***	7	Elevated CRP	6
Increase ≥10% ILD extent***	7	≥10% unintentional weight loss***	6

*within 3 months**patient-reported in past month***within 6 months

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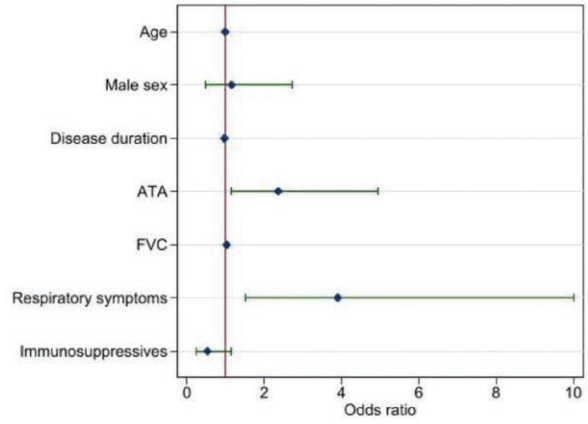
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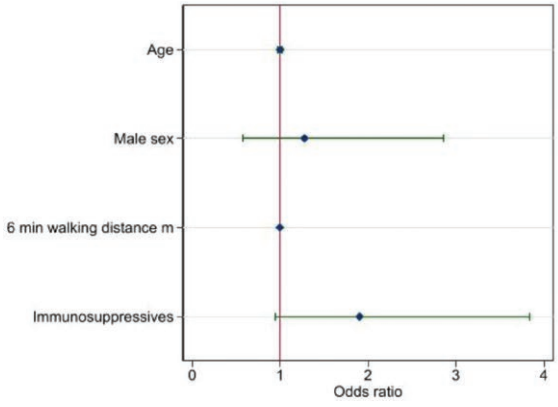
RISK FACTORS FOR SSC-ILD PROGRESSION USING THE NEW PPF GUIDELINE AND INBUILD PF-ILD CRITERIA

Keywords: Lungs, Prognostic factors, Systemic sclerosis

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Background: Interstitial lung disease (ILD) progression can be assessed using different definitions. Declining forced vital capacity (FVC) is the simplest and most accepted. Both progressive pulmonary fibrosis (PPF) as defined by the 2022 ATS/ERS/JRS/ALAT guideline, and progressive fibrosing ILD (PF-ILD) as used in INBUILD, define progressive disease by a composite worsening of lung function, respiratory symptoms and changes on high resolution chest tomography (HRCT), but with differences in the specific criteria. These new definitions have not been applied and compared in SSc-ILD yet.
Objectives: To identify variables predicting SSc-ILD progression using three different definitions of progressive disease.
Methods: We included all SSc patients from the Oslo and Zurich cohorts who had ILD on HRCT. ILD progression was defined as (A) PPF guideline criteria with worsening in 2/3 domains over 12 months including (1) respiratory symptoms; (2) absolute decline in FVC >5% or in DLCO >10% and (3) radiological disease progression. (B) PF-ILD INBUILD criteria with (1) FVC decline ≥10%, (2) FVC decline 5-9% and worsening of respiratory symptoms or increased lung fibrosis on HRCT, or (3) worsening of respiratory symptoms and increased lung fibrosis within 24 months. We compared these to ILD progression defined as FVC decline >5%. Variables for ILD progression chosen by expert opinion were tested in multivariable logistic models adjusted for age, sex and treatment and each model was tested using area under curve (AUC) with an AUC of 0.7 defined as acceptable.
Results: Of 231 included SSc-ILD patients from Oslo and Zurich 43 (19%) fulfilled the PPF, 89 (39%) the PF-ILD INBUILD definitions and 71 (31%) showed FVC decline >5%. The final multivariable logistic model predictive for ILD progression defined as FVC>5% decline included baseline FVC, respiratory symptoms (defined as functional class 3 and 4) and the presence of anti-topoisomerase I antibody (ATA). The model was considered as acceptable (AUC=0.70). The model for PF-ILD included diffuse cutaneous SSc (dcSSc), baseline FVC, respiratory symptoms and six-minute walking distance and had an acceptable AUC of 0.73. PPF was only predicted by reduced six minute walking distance, and the model was not acceptable (AUC=0.64).
Conclusion: Progression is common in SSc-ILD, regardless of definition, but the PPF guideline criteria identified fewer progressors than FVC decline >5% and PF-ILD. We identified different variables predicting progression of FVC decline >5% and PF-ILD but could not identify a model with acceptable performance for PPF. This raises concerns about which definition to use in clinical practice and future studies.





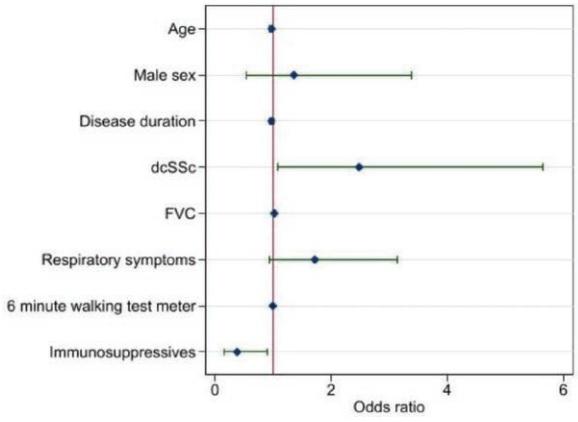


Figure 1. A. Prediction of ILD progression defined by FVC decline >5% (AUC=0.70)
B. Prediction of ILD progression defined as PPF (AUC=0.63)
C. Prediction of ILD progression defined as PF-ILD (AUC=0.73)

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OP0237 USE OF NEUTROPHIL/LYMPHOCYTE AND PLATELET/LYMPHOCYTE RATIOS TO DETECT SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

Keywords: Systemic sclerosis, Diagnostic tests, Biomarkers

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Background: Interstitial lung disease (ILD) remains as a mainly cause of morbidity and mortality in patients with systemic sclerosis (SSc). New markers to early detection of SSc-ILD are an unmet need [1]. Neutrophil/lymphocyte (NLR) and platelet/lymphocyte (PLR) ratios have emerged as potential biomarkers of systemic inflammation in cancer, cardiovascular disorders, infections and rheumatic diseases [2]. Recently, some studies in South Korea and Turkey have showed correlation of NLR and PLR with erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), disease activity, pulmonary and cutaneous involvement in SSc [3,4]. However, manifestations of SSc present variability in different populations. Could NLR and PLR be used as new biomarkers to detect SSc-ILD in Mexican-Mestizo population?
Objectives: To investigate the usefulness of NLR and PLR to detect SSc-ILD.
Methods: A cross-sectional study, where patients > 18 years of age with a diagnosis of SSc according to EULAR/ACR 2013 criteria and diagnosis of ILD by forced vital capacity (FVC) < 70% and > 5% of affected lung area by diffuse ground-glass opacity or pulmonary fibrosis on high-resolution computed tomography (HRCT) were included. Patients with corticosteroid use, malignancy, iron deficiency anemia and active infections were excluded. *European Scleroderma Trials and Research Group* (EUSTAR) disease activity index was used to determine activity. NLR, PLR, ESR, CRP, EUSTAR disease activity score, modified Rodnan skin score (mRSS) were compared between patients with and without SSc-ILD using U Mann-Whitney test. Spearman´s correlations between NLR or PLR and EUSTAR activity index, mRSS, ESR, CRP, FVC and affected lung area HRCT were analyzed. Receiver operating characteristic (ROC) analysis was performed to assess the best cutoff value for detecting SSc-ILD. Test characteristics, including sensitivity, specificity and diagnostic accuracy (DA) were calculated. Multivariate logistic regression analysis (MLRA) for ILD with their odds ratio (OR) and 95% confidence intervals (95% CI) was conducted establishing NLR, PLR as predicting factors adjusted by age, duration and activity of SSc.
Results: Of 74 patients with SSc 94.6% were women. The mean age [standard deviation (SD)] was 49.8 (14.1) years. The median of disease duration [interquartile range 25-75 (IQR)] was 7 (4.7-12) years and subtype of limited cutaneous SSc was presented in 85.1% of patients. A total of 36 (48.6%) patients had ILD; of them 59% had non-specific interstitial pneumonia and 51.3% showed extensive disease on HRCT. Medians of NLR, PLR, ESR, CRP, mRSS and EUSTAR activity index were higher in SSc-ILD patients (p=< 0.001). For NLR, the cut-off value (COV) was 2.05 and the area under the curve (AUC) was 0.887, with sensitivity, specificity and DA of 91.7%, 71.1% and 81.1% respectively. For PLR, the COV was 184.54 and the AUC was 0.743, with sensitivity, specificity and DA of 58.3%, 89.5% and 74.3%, respectively (**Figure 1**). NLR had a strong correlation with PLR (r=0.696) and affected lung area on HRCT (r=0.654) and moderate correlation with FVC (r=0.527) and EUSTAR activity index (r=0.513) (p=< 0.001). In contrast. PLR only had a weak correlation with EUSTAR activity index (r=0.371; p=<0.001). MLRA showed that NLR > 2.05 (OR 5.42, 95% CI 1.47-20.07, p=0.011) and EUSTAR activity index > 2.5 (OR 2.62, 95% CI 1.38-4.96, p=0.003) remained associated with an increased risk of SSc-ILD.
Conclusion: This study suggests that NLR show better DA than PLR, as well it can be a useful screening tool and a low-cost biomarker to detect SSc-ILD in Mexican-Mestizo patients. Also, NLR is associated with an increased risk of SSc-ILD and present a good correlation with affected lung area on HRCT, FVC and disease activity. However, these observations must be confirmed in larger and prospective studies.

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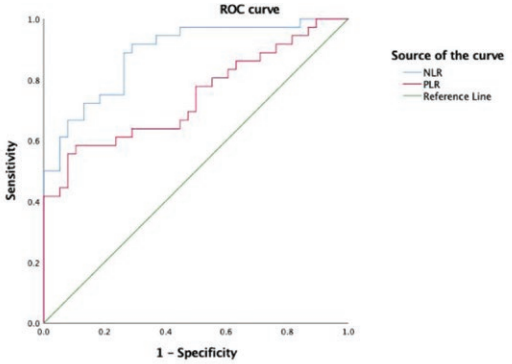


Figure 1. Receiver operating characteristic (ROC) curve analysis of neutrophil/lymhocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) for detecting systemic sclerosis-associated interstitial lung disease. For NLR, the cut-off value was 2.05 and the area under the curve (AUC) was 0.887, with sensitivity, specificity and accuracy of 91.7%, 71.1%, and 81.8% respectively. For PLR, the cut-off value was 184.54 and the AUC was 0.743, with sensitivity, specificity and accuracy of 58.3%, 89.5% and 74.3%, respectively.

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OP0238 IMMUNOSUPPRESSION WITH TARGETED DMARDS REDUCES MORBIDITY AND MORTALITY IN PRE-CAPILLARY PULMONARY HYPERTENSION ASSOCIATED WITH SYSTEMIC SCLEROSIS: A EUSTAR ANALYSIS

Keywords: bDMARD, Systemic sclerosis, Lungs

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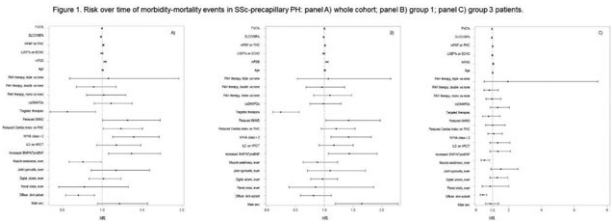
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Background: Pre-capillary pulmonary hypertension (precapPH) affects 9-15% of patients with systemic sclerosis (SSc) and may be associated with interstitial lung disease (ILD) of variable extent. Immunosuppressants (IMS) are standard of care for treating ILD, skin or musculoskeletal manifestations in SSc. However, their beneficial effect on precapPH remains unclear.

Objectives: To determine whether exposure to IMS in SSc-precapPH affects morbidity and mortality in the EUSTAR cohort.

Methods: In the approved EUSTAR project CP111, we included SSc patients with precapPH (mPAP ≥21 mmHg, PWP ≤15 mmHg, PVR ≥2 WU) with data on IMS (csDMARDs - prednisone ≥10 mg/day, cyclophosphamide, mycophenolate mofetil, azathioprine, methotrexate; targeted therapies: abatacept, rituximab, tocilizumab, TNFi, JAKi), pulmonary arterial hypertension (PAH) medications (bosentan, macitentan, ambrisentan, sildenafil, tadalafil, riociguat, selexipag, prostanoids) and at least 3 months follow-up after precapPH diagnosis by right heart catheterization. We considered exposure to a drug if it was ongoing at or prescribed after precapPH diagnosis and administered for at least 30 days. Patients were clustered into group 1 or group 3 precapPH based on ILD presence on HRCT and FVC <70%, as proposed in the INCREASE trial. The morbidity-mortality outcome was defined by the first event between death or precapPH worsening (following the SERAPHIN trial: one of ≥15% 6MWD decrease, worsening of NYHA class, onset of right heart failure, additional PAH medication, starting iv/sc prostanoids, lung transplantation, atrial septostomy). We evaluated the association between IMS and time to first event with a multiple Cox regression model for time dependent covariates, with robust Sandwich variance estimate and backward selection. The baseline confounders were chosen on experts' opinion and included SSc-related risk factors for mortality or IMS prescription (sex, age, diffuse skin subset, renal crisis, digital ulcers, muscle weakness, joint synovitis, ILD on HRCT, LVEF%, FVC%, DLCO%) and PAH risk stratification parameters (mPAP, increased BNP/NTproBNP, NYHA class >II, reduced cardiac index, reduced 6MWD). PAH medications (none, mono, double or triple therapy) were also included as time-dependent confounder.

Results: 755 SSc-precapPH patients from 54 EUSTAR centers were included (18% males, age 63±11 years, disease duration 11±9 years, 29% diffuse skin subset, 60% ILD on HRCT): 377 (50%) received IMS [365 (47%) csDMARDs, 68 (9%) targeted therapies] and 642 (85%) PAH medications. Patients treated with IMS had more frequently ILD (78 vs 43%), diffuse skin (41 vs 18%), joint (16 vs 7%) and muscle (22 vs 10%) involvement. In 2.9 (1.2-5.4) years median follow-up, 546 (70%) patients developed a morbidity-mortality event. While overall IMS exposure did not associate with the outcome, targeted therapies were associated with reduced risk of morbidity-mortality [HR 0.59 (95% CI 0.36-0.96), p=0.04; Figure 1a].


Figure 1. Risk over time of morbidity-mortality events in SSc-precapillary PH: panel A) whole cohort; panel B) group 1; panel C) group 3 patients.

When clustering into group 1 [n=561, 40% IMS, n=32 (6%) targeted therapies] or group 3 [n=194, 80% IMS, n=36 (19%) targeted therapies], less morbidity-mortality events were recorded for group 1 (69% vs 81%). Despite the rarer use, the protective effect of targeted therapies for morbidity-mortality was confirmed in group 1 (HR 0.24, 95% CI 0.02-0.64, p=0.01, Figure 1b) but not in group 3 (Figure 1c). When looking at specific target therapies, a risk reduction for the morbidity-mortality outcome was noted for tocilizumab [in the whole cohort (n treated=21; HR 0.37, 95%CI 0.18-0.77, p=0.03) and in group 1 (n treated=10; HR 0.09, 95% CI 0.01-0.69, p=0.02)] and rituximab (in group 1, n treated= 24, HR 0.29, 95% CI 0.10-0.84, p=0.01).

Conclusion: In this large EUSTAR SSc-precapPH cohort, targeted therapies are associated with a significantly reduced risk of mortality and precapPH worsening over time. This is the first large study adjusted for confounders supporting a potential effect of targeted therapies on SSc-precapPH.

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OP0239

DOES EARLY IMMUNOSUPPRESSIVE THERAPY PREVENT SYSTEMIC SCLEROSIS ASSOCIATED INTERSTITIAL LUNG DISEASE?

Keywords: Systemic sclerosis, Lungs, Epidemiology

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Background: Systemic sclerosis (SSc) is an auto-immune disease characterized by a triad of inflammation, vascular damage and fibrosis. Interstitial lung disease(ILD) is a major contributor to impaired quality of life and a leading cause of death in these patients. While recent studies reported a favorable effect on disease course when starting immunosuppressive(IMS) therapy in mild and moderate ILD, no definite evidence of a preventive mechanism of IMS therapy for ILD onset is established(1, 2).

Objectives: The objective of our study was to explore the association between timing of start IMS therapy and the development of ILD.

Methods: A combined cohort was created from the EUSTAR database and Nijmegen Systemic Sclerosis cohort, including patients: 1) aged 18 years or older 2) treated with IMS (i.e. mycophenolate mofetil, methotrexate, cyclophosphamide and rituximab) after SSc diagnosis 3) negative for signs of ILD on high-resolution CT(HRCT) at or within 2 months after start treatment and 4) no prior treatment with biological or antifibrotic in the preceding years. Data between start of first IMS treatment and five years follow-up were analysed. Disease duration (time between first non-Raynaud phenomenon and start IMS) was dichotomized into early and late treatment using a cut-off point of 3 years. ILD-free survival (absence of HRCT confirmed ILD diagnosis) was assessed with unadjusted Kaplan Meier analysis on complete cases and a cox proportional hazard analysis on imputed data adjusting for confounders.

Results: We identified 1037 patients meeting the eligibility criteria. The early treatment group (n= 539, 52 %) showed a higher prevalence of male sex, diffuse cutaneous SSc (dcSSc, 52.9% vs 36.4%, p= 0.001), anti-topoisomerase I antibody positivity (ATA, 51.0% vs. 42.5%, p= 0.01), anti-RNA polymerase III antibody positivity (ARA, 11.7% vs. 5.4%, p=0.009) and elevated C-reactive protein levels (30.6% vs. 22.6%, p=0.03). Further, patients in the early group had a higher modified Rodnan skin score (mRSS, mean(SD) 13.3(9.7) vs. 9.7(8.9), p= 0.001). The incidence of ILD was 46.1% after mean(SD) 3.6(1.4) years of treatment and not significantly different between the groups (mean(95% CI); early: 47% (43-51) vs. late: 45%(40-50), p= 0.64). The unadjusted Kaplan-Meier survival curve on complete cases (Figure 1) shows no differences in ILD-free survival rates between the early and late treatment group. The hazard ratio for ILD in the early treatment group was 1.11 (95% CI: 0.91-1.36) adjusting for gender, dcSSc, Caucasian ethnicity, ATA, ARA, age, forced vital capacity and diffusing capacity for carbon monoxide at baseline.

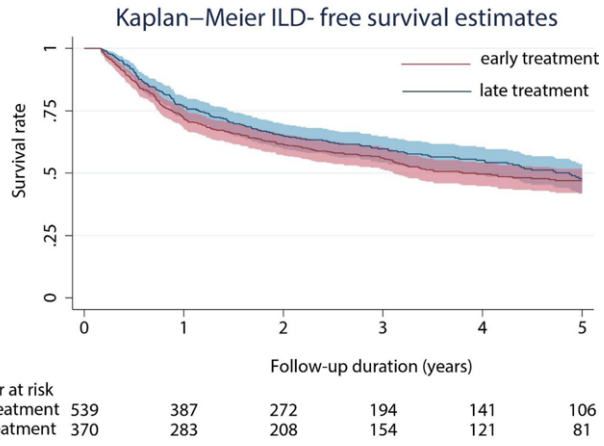


Figure 1. Kaplan Meier curve of ILD- free survival estimates. Survival rate with 95% confidence interval is shown for the early and late treatment group.

Conclusion: Our finding did not confirm a preventive role of early vs. late timing of IMS therapy on ILD development. However, our findings should be interpreted with caution, considering the high inflammatory, ATA-positive enriched nature of the cohort selected, as well as confounding by indication, which cannot be ruled out also after adjusting for other confounding factors.

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[1] Hoa S et al., Rheumatology (Oxford). 2020;59(5):1108-17.

[2] Hoa S et al., Chest. 2021;160(6):2158-62.

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OP0240

A RANDOMIZED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF TACROLIMUS WITH MYCOPHENOLATE MOFETIL IN PATIENTS WITH SYSTEMIC SCLEROSIS - INTERSTITIAL LUNG DISEASE (INSIST TRIAL)

Keywords: Clinical Trials, Systemic sclerosis, Lungs

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Background: Interstitial lung disease in systemic sclerosis(SSc-ILD) is heterogeneous with limited therapeutic options. Mycophenolate mofetil (MMF) is the most commonly used first line agent for SSc-ILD. Tacrolimus has shown promising efficacy in few small case series, and large cohorts of patients with non-SSC-ILD[1], but has never been evaluated in the setting of a clinical trial.
Objectives: To compare the safety and efficacy of Tacrolimus with MMF in patients with progressive SSc-ILD.
Methods: In this single center open labelled, prospective, two-arm parallel group, randomized controlled pilot study (INSIST) conducted between November 2021 to December 2022, patients with progressive ILD (FVC decline >10%) due to SSc, aged between 18-65 years, disease duration <10 years, without concomitant inflammatory myositis, with an FVC of 40-85%, and not having received active immunosuppression other than prednisolone <10mg/day in the last 6 months were randomized to receive either MMF (target dose 2gm/day) or tacrolimus (Max dose-0.075 mg/kg/day; target trough levels- 4-10ng/ml) for 24 weeks. The primary endpoint was the difference in change in FVC% at 24 weeks; secondary outcomes included absolute change in FVC, skin scores, 6-minute walk distance, Mahler's transitional dyspnea index, ACR-CRISS and revised CRISS responses and adverse outcomes. (Trial Reg: CTRI/2021/11/037864)
Results: 25 out of 26 patients (13 in each group) completed 24 weeks follow up. Majority had Anti-Scl 70 positivity (73%) and limited skin disease. At 24 weeks, the mean change in FVC was 4.4% (10.6) and 6.92%(8.4) in the MMF and tacrolimus groups respectively (difference 2.52%, 95% CI (-10.3 to 5.18); p-0.500). All patients on tacrolimus and 85% of patients on MMF had stabilization (ΔFVC% -5% TO 5%) or improvement (ΔFVC%>10%) in lung function. Secondary outcomes were similar between two groups. Subgroup analyses stratified by ILD type, skin involvement at baseline, and early vs late SSc yielded similar results. The mean tacrolimus levels were 4.9 ng/ml(1.47) and the median dose needed to achieve these levels was 4mg/d. No serious adverse events were noted in either group; use of tacrolimus did not result in renal dysfunction or renal crises.
Conclusion: Tacrolimus resulted in comparable improvement to MMF across primary and secondary outcome measures at 24 weeks with a favorable safety profile in patients with SSc ILD. Larger studies with longer follow up are needed to investigate the role of calcineurin inhibitors in SSc.

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Table 1. Primary and Secondary outcomes at 24 weeks

	MMF (n=13)	Tacrolimus (n=13)	P value
Change in FVC (% predicted), mean (SD)	+ 4.4 (10.6)	+ 6.92 (8.4)	Difference 2.52%, 95% CI (-10.3 to 5.18); p-0.500
Absolute change in FVC (ml), mean (SD)	+ 176.8 (305.5)	+130.7 (164.6)	0.636
Change in mRSS, median (IQR)	-1 (-3 to -0.5)	-1 (-1 to -0.5)	0.209
Change in 6MWD (metres), mean (SD)	63.15 (56.72)	32.67 (27.53)	0.094
Change in SGRQ score, mean (SD)	-14.83 (12.40)	-12.97 (11.78)	0.698
Focal Score TDI, median (IQR)	3 (2-4)	3 (2-4)	0.979
Change in SF-36 PCS, mean (SD)	5.59 (4.89)	4.72 (12.91)	0.823
Change in SF-36 MCS, mean (SD)	3.46 (7.86)	5.58 (5.54)	0.446
Change in PGA, median (IQR)	-2.0 (-2.5 to -1.5)	-2.0 (-2 to -1)	0.364
Change in HAQ-DI, median (IQR)	-0.23 (-0.25 to -0.19)	-0.125 (-0.25 to -0.125)	0.393
ACR-CRISS Improvement, n (%)	5 (38.5)	3 (23.1)	0.395
Revised ACR-CRISS responders; n (%)	10 (76.9)	7 (53.9)	0.416

FVC: Forced Vital Capacity; 6MWD- 6 minute walk distance; mRSS- Modified Rodnan Skin Score; SGRQ- St. George Respiratory Questionnaire; HAQ-DI- Health Assessment Questionnaire-Disability Index; TDI- Transitional Dyspnea Index; SF-36- Short Form 36; PCS-Physical component summary; MCS- Mental Component Summary; CRISS - Composite Response Index in Systemic Sclerosis

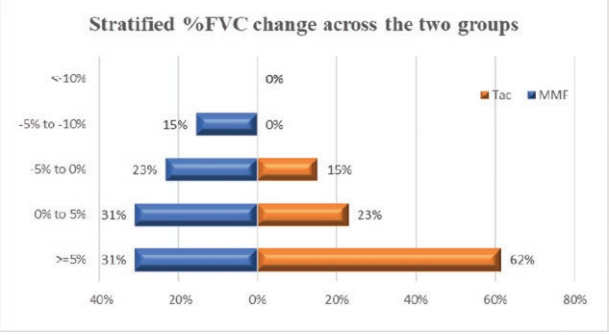


Figure 1. Changes in FVC% stratified by magnitude of change

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OP0241

PROGNOSIS OF PATIENTS WITH SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE AFTER THE LUNG TRANSPLANTATION: A RETROSPECTIVE STUDY

Keywords: Non-pharmacological interventions, Systemic sclerosis, Lungs

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Background: Interstitial lung disease (ILD) is a major complication of systemic sclerosis (SSc) and is associated with mortality [1]. Lung transplantation (LT) is a therapeutic option for advanced SSc-associated ILD (SSc-ILD). However, there is a lack of LT data for SSc-ILD in non-Western populations.
Objectives: We aimed to assess the survival data of patients with SSc-ILD on the LT waiting list and evaluate post-transplant outcomes for SSc-ILD and idiopathic pulmonary fibrosis (IPF) in an Asian LT centre.
Methods: A single-centre retrospective study. Using the LT candidate database at Kyoto University Hospital, patients with SSc-ILD who were registered for deceased LT were identified. To investigate post-transplant outcomes, recipients who underwent LT for SSc-ILD and IPF between February 2002 and April 2022 were also identified from the LT recipient database. Clinical data and outcomes were analyzed.

Results: This study included 29 patients registered for deceased LT between 2010 and 2022 (Table 1). Ten patients received deceased-donor LT (34%), two received living-donor LT (7%), seven died while waiting for LT (24%), and ten survived on the waiting list (34%). The median waiting time from registration to deceased-donor LT was 28.9 months (range 22.3-30.3). The median duration from registration to living-donor LT or death (events) was 6.5 months (range 4.1-14.7). Pulmonary hypertension was associated with mortality or switching to living-donor LT while waiting for deceased LT. In post-transplant analysis, 15 and 20 patients received LT for SSc-ILD and IPF between February 2002 and April 2022, respectively. Lung transplantation recipients showed an improved forced vital capacity with a median of 55.1% at baseline, 65.8% at 6 months and 80.3% at 12 months post-transplant. The estimated 5-year survival rates for post-transplant patients with SSc-ILD or IPF were 86.2% and 55.3%, respectively (log-rank, P = 0.33) (Figure 1).
Conclusion: Lung transplantation is an acceptable treatment for Asian patients with severe SSc-ILD. Further research is needed to determine the optimal time for referral to LT centres for patients with SSc-ILD.
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[1] Tyndall AJ et al. Ann Rheum Dis 2010;69:1809–15.

Table 1. Demographic characteristics of systemic sclerosis-associated interstitial lung disease patients registered on lung transplantation waiting list.

	Patients (N=29)
Age, mean (S.D.)	47.2 (9.5)
Female, n (%)	18 (62)
Disease duration (Y), median (IQR)	7.0 [5.1, 12.3]
SSc subtypes (lcSSc/dcSSc)	14/15
Raynaud phenomenon, n (%)	27 (93)
Digital ulcer, n (%)	2 (7)
PH, n (%)	14 (48)
GI involvement, n (%)	20 (69)
SRC history. n (%)	1 (3)
PSL, n (%)	25 (86)
Calcineurin inhibitors, n (%)	10 (34)
IVCY (previous use), n (%)	11 (38)
ACA, n (%)	3 (12)
ATA, n (%)	15 (56)
RNA polymerase-III, n (%)	0 (0)
U1-RNP, n (%)	4 (15)
%FVC, median (IQR)	51.1 [44.7, 57.4]
%DLCO, median (IQR)	28.6 [21.8, 35.1]
LTOT, n (%)	23 (79)

ACA, anti-centromere antibody; ATA, anti-topoisomerase-1 antibody; dcSSc, diffuse cutaneous systemic sclerosis; DLCO, diffusing capacity of the lungs for carbon monoxide; FVC, forced vital capacity; GI, gastrointestinal; ILD, interstitial lung disease; IQR, interquartile range; IVCY, intravenous cyclophosphamide; lcSSc, limited cutaneous systemic sclerosis; LTOT, long-term oxygen therapy; PH, pulmonary hypertension; PSL, prednisolone; RNA, ribonucleic acid; RNP, ribonucleoprotein; S.D., standard deviation; SRC, scleroderma renal crisis; SSc, systemic sclerosis; Y, year/s.

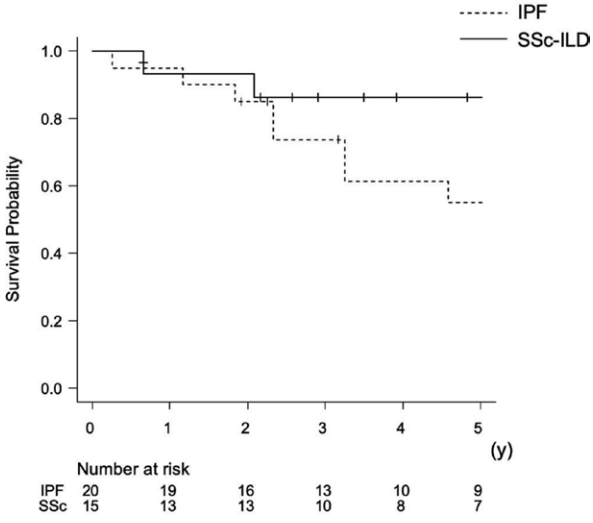


Figure 1. The estimated 5-year post-transplant survival curves (re-transplantation-censored) post-transplant in patients with systemic sclerosis-related interstitial lung disease and idiopathic pulmonary fibrosis.

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Disclosure of Interests: None Declared.
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Osteoporosis

OP0242

PROPORTION OF PATIENTS REACHING THE BONE MINERAL DENSITY (BMD) SURROGATE THRESHOLD EFFECT (STE) WITH BISPHOSPHONATES, DENOSUMAB AND TERIPARATIDE

Keywords: Bone diseases, Osteoporosis, Real-world evidence

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Background: The bone mineral density (BMD) surrogate threshold effect (STE) is the change in BMD that can predict a fracture risk reduction with 95% certainty. The STE estimates for changes in total hip BMD have been recently validated by the FNIH-ASBMR SABRE Project.
Objectives: We evaluated the proportion of patients reaching the STEs with anti-osteoporotic medications in real-life.
Methods: We retrieved longitudinal data on women at high risk of fracture initiating an anti-osteoporotic treatment. Kaplan-Meier curves with log-rank tests were employed to analyze the proportion of patients reaching STEs over the time with various anti-osteoporotic treatments. Herein we present the proportion of patients achieving STEs for the lowest (1.8% increase in total hip BMD for all fractures, 1.4% for vertebral fractures and 3.2% for hip fractures) and highest risk reduction (5.1% increase in total hip BMD for >30% risk reduction for all fractures, 4.6% for >50% risk reduction for vertebral fractures and 5.8% for >30% risk reduction for hip fractures).
Results: Baseline and follow-up data from 1,272 women initiating an anti-osteoporotic treatment were available. 807 started bisphosphonates, 386 started denosumab and 79 started teriparatide. Median follow-up time was 2.18 years (IQR 1.47-3.87 years). In Table 1 are presented the proportion of patients reaching various STEs stratified for treatment. The Kaplan-Meier estimate curve for bisphosphonates vs denosumab vs teriparatide showing the proportion of patients reaching various STEs over the time are presented in **figure 1** (log-rank p <0.001 for teriparatide vs bisphosphonates at 2 years and denosumab vs bisphosphonates at 2, 4 and 6 years; log-rank p NS for teriparatide vs denosumab at 2 years).

Table 1. Proportion of patients increasing BMD at 24 months above STEs

Fracture risk reduction	STE (%)	Bisphosphonates	Denosumab	Teriparatide
All fractures				
Any	1.8	24.2	48.5	62.9
>30%	5.1	18.6	39.9	64.5
Vertebral Fractures				
Any	1.4	24.4	49.1	62.9
>50%	4.6	19.1	41.3	60.5
Hip Fractures				
Any	3.2	21.4	46.9	61.4
>30%	5.8	17.7	38.0	59.8

Conclusion: In the present real-life study, a smaller proportion of patients treated with bisphosphonates reached the BMD STEs at 2 years of treatment as compared to denosumab and teriparatide. Nearly all subjects reached STEs at 6 years of follow-up.

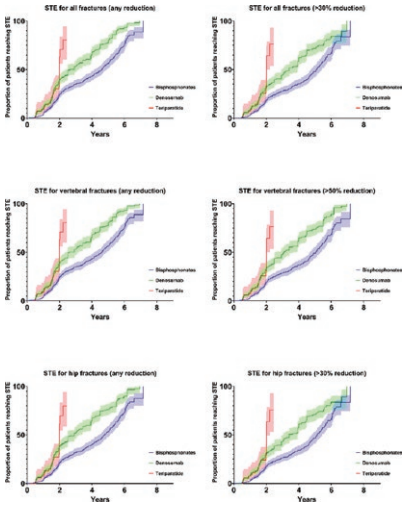


Figure 1. Kaplan-Meier estimate curve for bisphosphonates vs denosumab vs teriparatide showing the proportion of patients reaching various STEs over the time

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OP0243 PROTON PUMP INHIBITOR USE IS ASSOCIATED WITH IMPAIRED BONE MINERAL DENSITY BUT NOT BONE MICROARCHITECTURE IN PATIENTS WITH INFLAMMATORY RHEUMATIC AND MUSCULOSKELETAL DISEASES TAKING GLUCOCORTICOIDS

Keywords: Real-world evidence, Osteoporosis, Epidemiology

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Background: Patients with inflammatory rheumatic and musculoskeletal diseases (iRMDs) are at increased risk of osteoporosis and fragility fractures. For this population, the question of whether proton pump inhibitor (PPI) intake contributes to that risk has not yet been definitively answered. Prior studies have yielded conflicting results, did not account for over-the-counter use of PPI, and major confounders were unmeasured. In addition, bone microarchitecture as a potential mediator of fracture risk has not been studied.
Objectives: To assess the effect of regular PPI intake on bone mineral density (BMD) and microarchitecture in patients with iRMDs.
Methods: Cross-sectional baseline data from the single center Rh-GIOP cohort ("Glucocorticoid-induced Osteoporosis in Patients with Chronic Inflammatory Rheumatic Diseases or Psoriasis") were used. Briefly, patients with iRMDs were prospectively enrolled and assessed with DXA scans, laboratory testing, and bone-health-related questionnaires since 2015. Regular PPI and glucocorticoid (GC) use were ascertained by both chart review and patient self-report. Three co-primary outcomes (all reported as T-scores) were defined: BMD of the left femoral neck and the lumbar spine, and the trabecular bone score (TBS). The latter is a measure correlating with lumbar vertebrae's microarchitecture and is measured in a subset. Inverse probability of treatment weighting adjusted for the following confounders: age, sex, body mass index, iRMD type, C-reactive protein, current and cumulative GC dose, NSAID use, smoking, alcohol consumption, functional status (Health Assessment Questionnaire), disease duration, bisphosphonate use, chronic kidney disease stage, presence of diabetes mellitus, and frequency of exercise. We investigated whether dose-response relationships were present ("high dose" of >20mg/d vs. "low dose" of ≤20mg/d pantoprazole equivalent) and conducted an additional analysis with an interaction term for GC use. All analyses were based on linear regression models. Multiple imputation with 100 imputations was used to account for missing data (~4%). A detailed prespecified statistical analysis plan with a gatekeeping procedure for statistical testing was followed.
Results: 1,495 patients (75.3% women; mean age 62.6 ± 13.1 years; 49.2% with regular PPI use [of those: 63.1% high dose]) were included. Most patients had a diagnosis of rheumatoid arthritis (37.5%), followed by 25.3% connective tissue diseases, 16% vasculitides, 14.2% spondyloarthropathies, and 7% others. 63.8% used GCs (median dose 5mg/d). In both adjusted and unadjusted analyses, PPI users had lower BMD at both the left femoral neck and the lumbar spine (**Table 1**). Interestingly, differences between PPI users and non-users were only present in the subset of patients concurrently using GCs (data not shown). There was no statistically significant difference in BMD when comparing high and low dose PPI users (all P ≥ 0.52). TBS (n = 389) was similar in PPI users and non-users (**Table 1**).
Conclusion: Loss of BMD (seen at both lumbar spine and left femoral neck) rather than impairment of bone microarchitecture seems to be driving the increased fracture risk seen with PPI use in patients with iRMDs. The negative association between PPI use and BMD appears to be dependent on concurrent GC use.

Table 1.

	PPI use	No PPI use	Contrast	P-value
Crude (unadjusted)				
Left femoral neck	-1.24 (-1.36 to -1.13)	-1.01 (-1.12 to -0.89)	-0.24 (-0.11 to -0.37)	<0.001
Lumbar spine	-0.87 (-1.06 to -0.69)	-0.64 (-0.79 to -0.48)	-0.23 (-0.05 to 0.42)	0.01
Trabecular bone score	1.28 (1.24 to 1.31)	1.30 (1.26 to 1.33)	-0.02 (-0.06 to 0.02)	0.35
Adjusted				
Left femoral neck	-1.24 (-1.36 to -1.13)	-1.08 (-1.27 to -0.88)	-0.17 (-0.35 to 0.01)	0.07
Lumbar spine	-0.87 (-1.06 to -0.69)	-0.62 (-0.83 to -0.41)	-0.25 (-0.47 to -0.04)	0.02
Trabecular bone score	1.28 (1.24 to 1.31)	1.27 (1.24 to 1.31)	0.00 (-0.04 to 0.04)	0.97

Numbers are estimated marginal means and 95% confidence intervals.

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OP0244 DISEASE SEVERITY IS ASSOCIATED WITH OSTEOPOROSIS AND FRAGILITY FRACTURES IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Bone diseases, Osteoporosis, Systemic sclerosis

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Background: Patients with systemic sclerosis (SSc) are at an increased risk for osteoporosis (OP) and associated fragility fractures [1]. The prevalence of osteodensitometric OP has been estimated to range from 16% to 60% [2]. However, the risks factors and the mechanisms driving bone loss in patients with SSc remain elusive. The role of "general" determinants such as higher age and low body mass index (BMI) is well established (3) but their interaction with disease-specific factors is unclear. An association between OP and the cutaneous subset (diffuse or limited skin extent) (3, 4) or disease-specific antibodies (anti-centromere or anti-topoisomerase I antibodies) (5, 6) is controversial.
Objectives: Our objectives in the present study were. (i)to evaluate the prevalence of clinical OP and fragility fractures in a large population of SSc patients; (ii) and to identify potential disease-specific factors for OP in this population.
Methods: This cross-sectional study was based on two large European prospective cohorts of SSc patients with retrospective collection of bone health data. OP was defined as the presence of a T-score below -2.5 at femoral neck or lumbar spine and/or a previous major osteoporotic fracture and/or the prescription of anti-osteoporotic therapy. Long-term therapy with glucocorticoids (GCs) was

defined by a daily prednisone equivalent dose above 2.5 mg for more than 3 months. Age, female sex, BMI and treatment with proton pump inhibitors (PPIs) as predefined risk factors according to published evidence, as well as clinically relevant factors associated with a p-value <0.05 in univariable analyses, after correction for multiple comparison, were implemented into a multivariable logistic regression model.

Results: A total of 932 patients fulfilling the ACR/EULAR 2013 classification criteria were included in the study, followed prospectively in two university hospitals: Lille (n=485) and Berlin (n=447; of which 72 were patients of the Rh-GIOP prospective cohort). The two cohorts were studied separately. The prevalence of OP was 32% in Berlin and 23% in Lille (p=0.003), fragility fractures occurred in 22% and 18% respectively. Multivariable analysis in the Berlin cohort (Figure 1A) indicated that higher age (OR 1.05 [95%CI 1.03 to 1.07], p<0.001), female sex (OR 2.70 [95%CI 1.29 to 5.65], p=0.009), diffuse skin extent (OR 5.03 [95%CI 2.50 to 10.10], p<0.001), low BMI (OR 0.94 [95%CI 0.88 to 0.99], p=0.009), WHO-FC III-IV dyspnea (OR 2.06 [95%CI 1.16-3.67], p=0.014), receiving GCs (OR 1.78 [95%CI 1.10 to 3.17], p=0.026) or PPIs (OR 1.87 [95%CI 1.10 to 3.17], p=0.020) were associated with OP. In the Lille cohort, multivariable analysis (Figure 1B) confirmed the association of OP with higher age (OR 1.06 [95%CI 1.04 to 1.08], p<0.001), GCs use (OR 4.48 [95%CI 2.42 to 8.26], p<0.001), and with anti-topoisomerase I antibody positivity (OR 2.22 [95%CI 1.18 to 4.16], p=0.013).

Conclusion: Our data support a multifactorial etiopathogenesis of OP in SSc: besides common risk-factors for OP such as higher age, female sex, and BMI, several disease specific characteristics were associated with OP, such as SSc severity as reflected by diffuse skin extent and presence of antitopoisomerase I antibodies as well as severe dyspnea and SSc treatment (PPIs and GCs). These findings help to identify patients with SSc at particular risk for OP in clinical practice.

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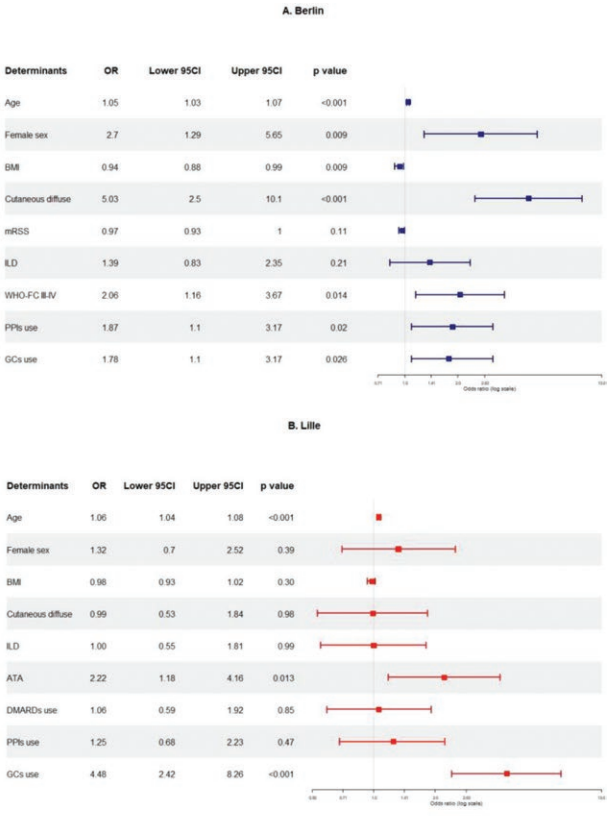


Figure 1. Determinants of OP in two cohorts of SSc patients. (A) Berlin (n=447), (B) Lille (n=485). Forest plots indicate Odds ratio (OR) with lower and upper 95%CI (confidence interval). ATA: Anti-topoisomerase I antibodies; BMI: body mass index; DLCO: diffusing capacity for carbon monoxide; GCs: Glucocorticoids; ILD: interstitial lung disease; mRSS: modified Rodnan Skin Score; PPIs: Proton pump inhibitors; WHO-FC: WHO functional class.

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OP0245 THE EFFECTIVENESS OF AN OSTEOPOROSIS REFRACTURE PREVENTION PROGRAMME – A COMPARISON OF TWO AUSTRALIAN RURAL CENTRES USING POPULATION DATABASE LINKAGE

Keywords: Osteoporosis

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Background: Despite widespread availability of effective bone protective medications and knowledge that minimal trauma fractures (MTFs) identify those at high risk of re-fracture, treatment of osteoporosis following MTF is poor. An effective way to address this gap is establishment of a fracture liaison service (FLS) where a fracture liaison coordinator coordinates case-finding and bone health management, usually in collaboration with a local medical "champion".

Objectives: To determine the effect of a Fracture Liaison Service (FLS)/Osteoporosis Refracture Prevention (ORP) programme on refracture rates.

Methods: Coffs Harbour (population 80 000) on the mid-north coast of New South Wales (NSW, Australia's most populous state), had a FLS established in July 2012. The comparator was the similar-sized city of Port Macquarie, located 160 km south which did not have an FLS established until 2019. The study population was residents aged ≥ 50 years with a fracture diagnosis recorded on admission to hospital, or on discharge without an admission record by the Emergency Department (ED) between the financial years of 2007/08 and 2017/18. Refracture rates were calculated for those with a recorded index fracture using NSW Health hospital admission and ED presentation data. Cumulative refracture rates were calculated using Kaplan–Meier methods accounting for follow-up time and deaths and adjusted for age, sex and fracture type. Trends in one- to five-year cumulative refracture rates from year of index fracture were also calculated. Annual health service utilisation associated with refracture was calculated using the total number of public hospital admissions, ED presentations and outpatient service events. Any admission or ED presentation with a fracture diagnosis occurring within 28 days of index fracture or refracture was considered part of the same episode of care.

Results: In those aged ≥50 yo, compared to "business and usual" (BAU), there was a 7% reduction in total fractures (n=6190 observed, versus n=6628 projected BAU, 95% confidence interval [95CI] 6270 - 6985; p=0.02) and a 9% reduction in total refractures (n=1709 observed, versus 1869 projected BAU, 95%CI 1768 - 1970; p=0.002) over the 7-year study period for Coffs Harbour. This reduction was

not observed in Port Macquarie or in the rest of the state of NSW. Cumulative adjusted refractures rates for Coffs Harbour were as follows: 1-year 7%, 2-years 13%, 3-years 19%, 4-years 24%, 5 years 29%. Females had higher refractures rates compared to males and having a diagnosis of osteoporosis at time of index fracture was associated with higher refractures rates.
Conclusion: An FLS/ORP programme is associated with a reduction in total fractures and refractures rates. However, refracture rates were higher in Coffs Harbour, a rural centre, compared to pooled statewide data.
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Disclosure of Interests: None Declared.
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OP0246 **ROMOSOZUMAB VERSUS DENOSUMAB IN HIGH-RISK PATIENTS WITH GLUCOCORTICOID-INDUCED OSTEOPOROSIS: A PILOT RANDOMIZED CONTROLLED TRIAL**

Keywords: Clinical trials, Osteoporosis, Randomized control trial

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Objectives: To compare the efficacy and safety of romozosumab (ROMO) and denosumab (DEN) in high-risk patients with glucocorticoid (GC)-induced osteoporosis (GIOP).
Methods: Design: A pilot open randomized controlled trial.
Method: Adult patients (≥18 years) who were receiving daily prednisolone dose of ≥5mg/day for ≥12 months and had moderate/high risk of osteoporotic fracture (a history of fragility fracture, DEXA T score ≤-2.5 [age ≥40 years] or Z scores ≤-3.0 [age <40 years] or high risk of 10-year major fracture estimated by FRAX) were included. Participants were given daily calcium and vitamin D and existing bisphosphonates were discontinued. Subjects were randomized by blocks to receive either ROMO (210mg SC monthly) or DEN (60mg SC every 6 months) for 12 months, followed by DEN (60mg every 6 months) for 12 more months in both arms. The primary efficacy end point was the change in bone mineral density (BMD) at the lumbar spine from baseline to month 12. Secondary end points included BMD change at the non-dominant hip and femoral neck at month 12, change in bone turnover markers, new vertebral fractures, change in BMD at the hip and spine at month 24 and adverse events.
Results: Of 70 patients recruited, 63(90%) completed the study (age 62.6±9.1 years; 96% women; 35 each assigned to ROMO or DEN). Underlying medical diseases were systemic lupus erythematosus (51%), rheumatoid arthritis (29%), inflammatory myopathies (9%) and others. The mean prednisolone dose at entry was 6.6±3.5mg/day. Osteoporosis at spine/hip/femoral neck and a history of fragility fracture was present in 34(48.6%) and 35(50%) patients, respectively. Oral bisphosphonates were being used in 33(47%) patients prior to first dose of the study drugs. While the baseline demographics and osteoporosis risk factors were not significantly different between the two groups, ROMO-treated patients had lower hip/femoral neck BMD and serum vitamin D3 levels than those treated with DEN. At month 12, a significant increase in spine BMD was observed in both the ROMO (+7.3±4.5%; p<0.001) and DEN (+2.3±3.1%; p<0.001) groups of patients. The inter-group difference in spine BMD at month 12 was statistically significant after adjustment for baseline BMD values, age, sex, osteoporosis risk factors and the cumulative prednisolone doses in 12 months (p<0.001). The corresponding increase in hip BMD were +1.6%±3.3% (p=0.01) in the ROMO group and +1.6%±2.6% (p=0.003) in the DEN group. No significant inter-group difference in hip BMD was observed after adjustment for the same confounding factors. The increase in femoral neck BMD from baseline to month 12 was not significant in both groups. In DEN-treated patients, both serum CTX (-34.7±54.8%; p=0.002) and P1NP (-35.1±43.3%; p<0.001) dropped significantly from baseline to month 12. However, in the ROMO group, a non-significant drop in CTX (-18.1±76.9%; p=0.18) but increase in P1NP (+1.7±70.3%; p=0.89) was observed. Only one new vertebral fracture developed in the ROMO group at 12m. The commonest adverse event (AE) was self-limiting injection site pain/redness, which was significantly more common in ROMO-treated patients. Post-injection musculoskeletal pain was reported in 2 and 3 patients in the ROMO and DEN group of patients, respectively. Mild hypocalcemia and hypercalcemia were observed in 2 DEN-treated patients. No serious AEs were reported. The 24m data of this study are pending.
Conclusion: Romosozumab was superior to denosumab in raising the spine BMD at month 12 in chronic GC users with high fracture risk. Both drugs were well-tolerated. Romosozumab may offer a new treatment option for GIOP in high-risk patients.
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OP0248 **WITHDRAWN**

OP0249

IS PREVENTION BETTER THAN CURE? DATA FROM A MONOCENTRIC RANDOMIZED CLINICAL TRIAL TO PREVENT ACUTE PHASE REACTION RELATED TO INTRAVENOUS BISPHOSPHONATES

Keywords: Osteoporosis, Randomized control trial, Bone diseases

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Background: Acute phase reaction (APR) is a transient flu-like syndrome with fever, chills, fatigue, malaise, and musculoskeletal symptoms, often occurring 24-36 hours after intravenous bisphosphonates (IV-BPs) administration and usually resolving within 2-3 days[1]. Avoiding APR could increase patients' compliance to treatment and reduce patients' discomfort.
Objectives: In this monocentric, randomized, open-label, parallel-group study, we examined the efficacy of low dose of 6metilprednisone (6MP), paracetamol (PAR) or placebo (PBO) in reducing the incidence of APR.
Methods: We prospectively enrolled patients from March 2022 to December 2022. Patients were randomly allocated to PAR 1000 mg BID for 3 days, 6MP 4 mg BID for 3 days or PBO after IV-BPs (zoledronate (ZOL) 5 mg or neridronate (NER) 100 mg). A scale ranging from 0=absence, 1=mild, 2=moderate, and 3=severe was used to rate symptoms. Arthromyalgia (AM) included arthralgia, myalgia, arthritis, and chest pain; systemic symptoms (SS) included headache, nausea, fatigue, fever, and Health Assessment Questionnaire (HAQ). AM, CS, fever and HAQ were assessed at baseline and at day 4. APR was defined as the worsening of >2 points in AM, CS score, fever (>37.5°), and/or the worsening of 22% or increase of 0.25 in HAQ score[2]. Comparisons were performed by T test and chi-square test. Logistic regression was used to analyze protective and predictive factors for APR occurrence. All patients have signed informed consent.
Results: Ninety-five patients were enrolled: mean age±standard deviation (SD) was 57.0±14.6 yrs, mean BMI±SD was 24.51±4.1, 69.5% females, 70.5% menopausal women, 10.5% had previous exposure to oral BPs. Fourteen patients were under chronic treatment with statins. Patients were treated with BPs for osteoporosis (n=16; 17%), Paget's disease of bone (n=5; 5%) and complex regional pain syndrome type 1 (n=74; 78%). 29 patients were allocated in 6MP arm, 29 in the PAR arm and 37 in the PBO arm. The incidence rates of AM and SS in ZOL were 46.7% and 60%, respectively. The incidence rate of AM and SS in NER were 38.8% and 21.4%, respectively. 6MP prophylaxis significantly reduced the incidence of AM (p=0.03) and HAQ worsening of 22% or increase of 0.25 (p=0.01 and p=0.05, respectively), but did not prevent the incidence of SS (p=0.23). PAR and PBO did not modify the incidence of AM, SS, and worsening of HAQ. Chronic use of statins prevented incidence of AM and worsening of HAQ (p=0.029 and p=0.015, respectively) but did not impact SS score. Previous therapy with oral BPs did not prevent APR. Among protective variables for the incidence of AM were recognized older age (OR 0,95, CI 1.01-1.11, p=0.02) and 6MP prophylaxis (OR 5.0, CI 1.79-22.97, p=0.03). Concomitant statins, previous exposure to oral BPs, 25OH vitamin D3 (25OHD3) serum levels or 25OHD3 ongoing supplementation did not prevent APR. Higher BMI (OR 1.32, CI 1.07-1.65, p=0.01) and treatment with ZOL (OR 31.6, CI 2.3-431.96, p=0.01) were predictive factors for the occurrence of fever.
Conclusion: Our data demonstrated that low dose 6MP prophylaxis is effective in preventing the most common features of APR, compared to PAR or PBO. In contrast to literature, previous exposition to oral BPs, normal 25OHD3 serum levels or 25OHD3 supplementation did not have impact on the occurrence of APR.

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New evidence on IgG4-related and rare autoinflammatory diseases

OP0250

A PHASE II PROSPECTIVE TRIAL OF AZACITIDINE IN STEROID-DEPENDENT OR REFRACTORY SYSTEMIC AUTOIMMUNE/INFLAMMATORY DISORDERS AND VEXAS SYNDROME ASSOCIATED WITH MDS AND CMML

Keywords: Vasculitis, Treat to target, Randomized control trial

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Background: Systemic autoimmune and inflammatory disorders (SAID) are underestimated, and potentially life-threatening complications observed in 15-25% of myelodysplastic neoplasms (MDS) and chronic myelomonocytic leukemia (CMML), although pathophysiological links between both types of disorders remain uncertain. In 2020, Beck *et al.* described VEXAS (Vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome (OMIM #301054, defined by the presence of *UBA1* mutations, in patients with severe systemic inflammation, chronic fever, 30% of whom had concurrent MDS. VEXAS is typically associated with refractoriness to conventional immunosuppressive therapies (IST) and dismal prognosis, and prospectively evaluated effective treatment strategies remain to be established. In MDS/CMML patients with concomitant SAID, but no *UBA1* mutation, we and others observed a high incidence of mutations of the epigenetic regulators *TET2* and *IDH1/2*, whose presence correlated with defects in adaptive T lymphocyte homeostasis.
Objectives: This led us to launch a prospective phase II trial of AZA in patients with MDS/CMML and steroid dependent/refractory SAID.
Methods: This prospective open-label, single-arm multicenter, phase II study trial (ClinicalTrials.gov identifier: NCT02985190) was sponsored by the Groupe Francophone des Myélodysplasies (GFM, French MDS group). Celgene Corporation supplied the study drug but did not contribute to data collection or analysis. Eligible criteria were: (1) age ≥18 years (2) revised IPSS (IPSS-R) intermediate

2 or high, or IPSS-R low or intermediate-1 with significant cytopenia (i.e., transfusion dependent anemia resistant to erythropoietin-stimulating agents and/or platelets below 30 G/L or below 50 G/L with bleeding, and/or ANC < 0.5 G/l with infectious complications), (3) SAID defined according to usual international criteria for each SAID (all cases were centrally reviewed by expert internists AM and VJ) (4) steroid resistance or dependence of SAID, defined as the inability to decrease the dose of steroids below 15 mg/day during at least 2 months.

Results: Thirty patients were included between July 2017 and June 2020 in 18 centers, 29 of whom received at least one cycle of AZA and were considered evaluable. Twelve of the 29 patients (41%) were retrospectively found positive for *UBA1* mutation (VEXAS syndrome), while in the remaining cases SAID included inflammatory arthritis (n=6) (rheumatoid arthritis (n=3), undifferentiated (n=2) and psoriasis arthritis (n=1)), unclassified vasculitis (n=3), neutrophilic dermatosis (n=3), unclassified SAID (n=2), systemic lupus erythematosus (SLE), relapsing scleritis and immune thrombocytopenia in one case each. After 6 cycles, 19 patients (66%) had obtained SAID response (including 8 CR and 11 PR), while 10 SAID remained stable and none had progressed. The daily dose of steroids decreased from a median of 50 mg/day (95% CI [40-71]) at AZA onset to 15 mg/day (95% CI [13-31]) (p<0.0001) and 10 mg/day (95% CI [5-10]) (p<0.0001) of prednisone equivalent after 3 and 6 cycles respectively. Median steroid daily dose was lower in SAID responders compared to non-responders after 3 (15 mg/day [12-25] versus 50 mg/day [46-60], p=0.04) and 6 (8 [4-10] versus 33 [21-35], p=0.05) cycles of AZA. Median steroid daily dose did not decrease after 6 cycles of AZA.

Conclusion: Thus, in this prospective trial, 66% of MDS/CMML patients with SAID obtained SAID complete or partial response after 6 cycles of AZA. We observed an important and sustained steroid-sparing effect of AZA, with reduction to a median dose below 10 mg/day of prednisone equivalent after 6 cycles. AZA also yielded hematological response in 59% of the patients, and 88% of hematological responders had concomitant SAID response.

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OP0251 CLINICAL FEATURES AND TREATMENT-RELATED OUTCOMES OF IGG4-RELATED DISEASE FROM A LARGE EUROPEAN STUDY COHORT

Keywords: Gastrointestinal tract, Rare/orphan diseases, Geographical differences

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Background: IgG4-related disease is an increasingly recognized systemic fibro-inflammatory disorder involving almost any organ system. Most available data on treatment strategies and natural history of IgG4-RD are currently derived from large cohorts from the United States and Asian Countries. Real-life studies addressing the epidemiology, clinical manifestations, and treatment strategies of IgG4-RD in Europe are limited to smaller cohorts from single center experiences.

Objectives: To characterize the epidemiology, clinical manifestations, and response to treatment of IgG4-RD patients in Europe.

Methods: A pan-European registry (PrescrAIP) was set in place to retrospectively analyse adults diagnosed with IgG4-RD from 2005 and 2020 in 42 European university hospitals. Comprehensive diagnostic criteria and organ-specific criteria were used to diagnose IgG4-RD and central validation was applied. Data on disease epidemiology, clinical characteristics, treatment, and outcomes were retrospectively collected from the hospitals' medical records using a REDCap-based electronic case record form. The IgG4-RD responder index was used to assess response to therapy. Predictors of relapse were identified using multivariable logistic regression analysis after correcting for confounders.

Results: 1079 individuals with suspected IgG4-RD were screened but only 735 were diagnosed with IgG4-RD and considered for analysis (69% male; median age 57years; 85% Caucasian). 45% of patients had multiorgan (>=2) involvement (Table 1). Pancreas, salivary glands, and biliary tree were the most frequently involved organs. Steroid-treatment was started in 634 patients; 9 (1%) were lost to follow-up; 79% (496/625) had a complete response, 18% (111/625) had a partial response, and 3% (18/625) did not respond. 95 patients were not treated; 61% (58/95) had spontaneous complete response, 19% (18/95) had partial response, and 10% (9/95) did not respond. Higher daily steroid dose (>0.4mg/kg prednisone equivalent) was as effective as lower dose (<0.4mg/kg) (OR 0.428; 95%CI 0.054-3.387) for inducing disease response. Similarly, longer induction of remission treatment (> 2 weeks) was as effective as shorter therapy (<2 weeks) (OR 0.908; 95%CI 0.818-1.009). Elevated IgG4 levels were independently associated with a decreased chance of complete response (OR 0.639; 95%CI 0.427-0.955). Relapse occurred in 30% of patients. Relapse within 6 months of remission induction were independent of the steroid tapering duration, induction treatment duration, and total cumulative dose. Parenchymal enlargement (OR 0.390, 95%CI 0.167-0.910) and addition of maintenance therapy with immunosuppressive agents were independently associated with fewer relapses at 6 months (OR 0.299, 95%CI 0.120-0.740). No difference between maintenance therapy with glucocorticoids and rituximab was observed in maintaining disease response.

Conclusion: This is the first pan-European study addressing the epidemiological and clinical features of IgG4-RD in Europe. Our study indicates that patients with elevated IgG4 level may need closer monitoring during remission induction and that 0.4mg/kg/day of prednisone equivalent for at least 2 weeks represents the most effective strategy to induce IgG4-RD remission.

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Table 1. Characteristics of IgG4-RD patients at diagnosis. *ULN, upper limit of normal.*

Patient characteristics	Total (N=735)
Male sex	509 (69)
Age, median (IQR), y	57 (27)
Diabetes mellitus	213 (29)
Pancreatic exocrine insufficiency	190 (26)
Symptoms	
Incidental finding	32 (4)
Obstructive jaundice	381 (52)
Abdominal pain	471 (64)
Weight loss	270 (37)
Acute pancreatitis	76 (10)
Other organ involvement	329 (45)
Orbit	12 (2)
Bilateral salivary glands	54 (7)
Thyroid	13 (2)
Pulmonary	38 (5)
(Peri)aorta	17 (2)
Retroperitoneal fibrosis	24 (3)
Sclerosing cholangitis/ biliary tree	262 (36)
Renal	49 (7)
IgG4 > 1x ULN	440 (60)

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OP0252

LONG-TERM SAFETY AND EFFECTIVENESS OF CANAKINUMAB IN CRYOPYRIN-ASSOCIATED PERIODIC SYNDROMES (CAPS) – 4-YEARS DATA FROM THE RELIANCE REGISTRY

Keywords: Real-world evidence, Rare/orphan diseases, Innate immunity

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Background: CAPS (Cryopyrin-associated periodic fever syndromes) are monogenic autoinflammatory diseases causing great burden to patients due to severe systemic and organ inflammation caused by increased production of interleukin-1β (IL-1β). In clinical trials as well as in real-life, the monoclonal antibody canakinumab (CAN) effectively inhibits IL-1β and results in rapid suppression of CAPS symptoms.

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

Methods: This prospective, non-interventional, observational study enrolls patients with clinically confirmed diagnoses of CAPS routinely receiving CAN. Clinical data, physician assessments and patient-reported outcomes are evaluated in 6-monthly intervals.

Results: 107 CAPS patients (53% female; 16% NOMID/CINCA subtypes) were enrolled by December 2022. At baseline, median age was 23 years and median duration of prior CAN treatment was 6 years. 92% of patients received greater than standard dose CAN. 75% of the patients were in disease remission at month 48 by physician assessment. Patients report stable low level disease activity (median 2.0 at baseline and 1.5 at month 48) and fatigue (median 3.0 at baseline and 1.0 at month 48). No relevant differences regarding subtype severity were observed (**Table 1**). At baseline vs. month 48, 46% vs. 50% of patients experienced impairment of social life and 32% vs. 25% reported days off from school or work due to the disease. Severe adverse events (SAE) suspected to be drug-related were reported for N=9 (8.4%) CAPS patients. The incidence rate (IR) per 100 patient-years kept stable over time.

Conclusion: The 48-month interim analysis of the RELIANCE registry demonstrates that long-term CAN treatment is safe and effective in patients with CAPS, independent of subtype severity.

Table 1. Assessment of clinical CAPS disease activity and laboratory markers over time.

	Baseline		24 months		48 months	
	NOMID/ CINCA	MWS, FCAS	NOMID/ CINCA	MWS, FCAS	NOMID/ CINCA	MWS, FCAS
Number* of patients, N	17	80	10	54	3	13
Number (%**) of patients with days absent from work/school during last 6 months	6 (35)	25 (32)	2 (20)	20 (37)	0 (0)	4 (31)
Number (%**) of patients in disease remission (physician assessment)	13 (77)	53 (68)	8 (80)	33 (61)	2 (67)	10 (77)
Patient's assessment of current disease activity; 0–10, median (min; max)	1.0 (0; 7)	2.0 (0; 7)	2.0 (0; 4)	1.0 (0; 8)	0.0 (0; 0)	2.0 (0; 5)
Patient's assessment of current fatigue; 0–10, median (min; max)	3.0 (0; 9)	3.0 (0; 9)	2.0 (0; 7)	2.0 (0; 9)	0.0 (0; 0)	1.0 (0; 7)
Number (%**) of patients without impairment of social life by the disease	5 (56)	29 (57)	3 (50)	25 (63)	0 (0)	2 (67)
Current influence of the disease on mood; % of patients** with negative | positive | no influence	30 | 10 | 60	23 | 19 | 59	17 | 33 | 50	24 | 37 | 40	0 | 0 | 0	25 | 25 | 50
CRP, median (mg/dl)	0.2	0.1	0.3	0.2	0.9	0.1
SAA, median (mg/dl)	0.4	0.4	0.9	0.4	0.6	0.2
ESR, median (mm/h)	6.0	5.0	8.0	5.0	5.0	2.5
SAE	**Number of events**			**IR‡ per 100 patient-years**		
All types of SAE	65			22.85		
SADR	28#			9.84		
NOMID/CINCA	0			0		
MWS/FACS	26			11.55		

Abdominal pain, Alport's syndrome, appendicitis, arthralgia, blister, cardiovascular disorder, chest pain, circulatory collapse, dehydration, diplopia, dyspnoea, erythema, febrile convulsion, gastroenteritis, glomerulonephritis, haemophilus test positive, myalgia, oedema, pneumonia, premature delivery, skin discolouration, tonsillectomy, tonsillitis bacterial, tonsillitis streptococcal, vision blurred (all N=1 event), pyrexia (N=3 events)

*subtype not reported for all patients. **not reported for all patients. ‡IR = number of events * 36525/ sum of observation days (=103905)CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; SAA, serum amyloid A; SADR, serious adverse drug reaction

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OP0253

REAL-WORLD DEMOGRAPHICS, CLINICAL CHARACTERISTICS, AND TREATMENT PATTERNS OF PATIENTS TREATED WITH EMAPALUMAB FOR SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN THE UNITED STATES: THE REAL-HLH STUDY

Keywords: Real-world evidence, Outcome measures, Cytokines and chemokines

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Background: Hemophagocytic lymphohistiocytosis (HLH) is a rare, life-threatening, hyperinflammatory syndrome caused by overproduction of proinflammatory cytokines, e.g., interferon gamma (IFNγ).[1,2] Secondary HLH (sHLH) occurs in the context of an underlying disease (e.g., rheumatologic, malignancy, or iatrogenic) and/or an infectious trigger.[1,2] Emapalumab is a fully human anti-IFNγ monoclonal antibody that binds to and neutralizes the biological activity of IFNγ. It was approved by the FDA in 2018 for adults and children with primary HLH with refractory, recurrent, or progressive disease, or intolerance to conventional HLH therapy. Since its approval, real-world evidence on the use of emapalumab in routine clinical setting is limited.[3-5] The REAL-HLH study assessed real-world treatment patterns among patients treated with emapalumab.
Objectives: To describe the demographics, clinical characteristics, and treatment patterns among the subset of patients with physician-reported diagnosis of sHLH treated with emapalumab.
Methods: A retrospective medical chart review conducted across 33 US hospitals identified patients treated with ≥1 dose of emapalumab between November 20, 2018, and October 31, 2021. Data on the subset of patients with sHLH extracted from time of emapalumab initiation to end of data availability, death, or study end (December 31, 2021) are presented.
Results: Overall, 57/105 (54.3%) enrolled patients had a physician-reported diagnosis of sHLH (mean age [± SD] 10.4 [7.6] years). Majority of patients were non-White (63.2%) and male (52.6%). At diagnosis, mean age (±SD) was 9.3 (7.5) years and 15/17 (88.2%) patients with available data met ≥5 of 8 HLH-2004 diagnostic criteria. Underlying disease and/or triggers were identified in 53/57 (92.9%) patients; 22/53 (41.5%) had a single trigger and 31/53 (58.5%) had multiple triggers. Infections (32/53; 60.4%), malignancy (18/53; 34%), rheumatologic disease (11/53; 20.8%), and iatrogenic (6/53; 11.3%) were the most common triggers. Epstein-Barr virus (11/25; 44%) was the most common viral (25/32; 78.1%) infection. At time of emapalumab initiation, 73.7% of patients had received prior treatments with other HLH-related therapies, including corticosteroids, and 62.5% of patients were in the intensive care unit. Emapalumab was mainly initiated for treatment of refractory (42.1%), progressive (29.8%), and recurrent (14%) disease. The median (range) time to emapalumab initiation from diagnosis was 16.5 (1-2278) days. Median (range) treatment duration with emapalumab was 38.0 (1-397) days. Median (range) emapalumab starting dose was 1.1 (0.7-5.9) mg/kg and cumulative treatment dose was 21.3 (1-336.5) mg/kg. Median (range) maximum administered emapalumab dose was 2.3 (0.7-12.5) mg/kg.
Conclusion: This is the first study to report real-world treatment patterns with emapalumab across a diverse patient population with sHLH. A pivotal clinical trial of emapalumab in patients with sHLH and underlying rheumatologic disease is ongoing (NCT05001737).

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OP0254

INSIGHTS FROM A NOVEL MONOGENIC AUTOIMMUNE DISEASE: OVERVIEW OF A MULTICENTRIC EUROPEAN COHORT OF 27 PATIENTS WITH COPA SYNDROME

Keywords: Genetics/epigenetics, Innate immunity, Rare/orphan diseases

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Background: COPA syndrome is a recently described monogenic autoimmune disease due to heterozygous mutations in *COPA*. COPA syndrome demonstrates considerable phenotypic overlap with SAVI (STING-associated vasculopathy with onset in infancy) due to gain-of-function mutations in STING. Interestingly, while both disorders are characterised by enhanced type I interferon signalling, neither disease is associated with systemic lupus erythematosus (SLE) – challenging classical dogma linking interferon upregulation and lupus.
Objectives: Our aim was to gather a European cohort of COPA patients to better delineate the clinical phenotype of this rare monogenic disorder.
Methods: Assessment of clinical, radiological, immunological and therapeutic data from 27 patients (13 families) with molecularly confirmed COPA syndrome.
Results: Twenty-seven individuals with pathogenic COPA mutations were included. Among them, 20 patients presented with at least one clinical manifestation evocative of COPA syndrome (clinical penetrance of 74.1%). Symptomatic patients were female in 13 (65%) cases with a median age at disease onset of 4 years (0-50). All COPA mutations were inherited in an autosomal dominant pattern except for one that occurred *de novo*. Pulmonary involvement was observed in 16 (80%) patients, with interstitial lung disease (ILD) in most cases (n=13, 65%), diffuse alveolar haemorrhage (DAH) in 5 (25%) individuals and the association of ILD and DAH in 3 (15%) patients. Twelve (60%) patients demonstrated joint involvement of variable severity: 4 (20%) individuals experiencing deforming arthritis including one requiring bilateral knee arthroplasty, 6 (30%) patients had polyarticular arthritis and two (10%) patients presented with isolated arthralgias. Renal disease was observed in three (15%) individuals, manifest as either proliferative glomerulonephritis (n=2) or membranous glomerulonephritis (n=1). Previously undescribed features were noted i.e. cutaneous involvement - acral ulcers, vitiligo and nasal perforation (n=3, 15%), cardiac disease (n=2, 10%), gastrointestinal dysfunction (n=2, 10%), and cytolytic hepatitis (n=1). When tested, 14 (93.9%) patients had positive autoantibodies. When assessed, immunophenotyping showed a mild T-cell lymphopenia, with an excess of naive T CD8+ cells and a defect of memory T CD8+ cells recorded in one patient. All patients explored exhibited elevated IFN alpha protein levels and high IFN signature scores. The IFN signature was mildly positive in half of the clinically asymptomatic individuals assessed. The majority (60%) of patients were treated with corticosteroids and immunosuppressants, ten (50%) received biotherapies and eight (40%) patients are currently under JAK1/2 inhibition.
Conclusion: We report the first European cohort of COPA patients. While confirming the core organ features (lung, joint and kidney) of COPA syndrome, our data expand the phenotype to include cardiac, skin and digestive features, further

demonstrating the clinical overlap with SAVI and other type I interferonopathies, while also highlighting the possibility of isolated organ involvement. We confirm a high level of clinical non-penetrance, which can present a diagnostic challenge and indicates the need to better understand the underlying pathophysiology. In view of current (JAK inhibitors) and potential future targeted therapies, we suggest a requirement to assess IFN pathway status and/or perform sequencing in the case of suggestive features, even in the absence of a familial history.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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OP0255 IGG4-RELATED DISEASE ACTIVITY ASSESSMENT INFLUENCED BY USE OF 18F-FDG PET/CT: DATA FROM A NORWEGIAN COHORT

Keywords: Rare/orphan diseases, Imaging, Outcome measures

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Background: The IgG4-related disease (IgG4-RD) responder index (RI) is a validated tool to assess disease activity in IgG4-RD [1]. The RI reflects symptoms attributable to active IgG4-RD as well as relevant findings from the physical examination, imaging and laboratory evaluations, with higher scores reflecting more active disease. Multiorgan involvement and higher RI scores were identified as risk factors for relapse [2], indicating a need for more aggressive treatment. Whole-body ^{18}F-FDG PET/CT is a sensitive technique for detecting foci of active inflammation, but its use is limited by cost and availability. Furthermore, whether ^{18}F-FDG PET/CT detects additional organ manifestations which influence RI and treatment decisions, is largely unknown.

Objectives: To compare performance of a pure clinical RI model (c-RI) and a c-RI with addition of ^{18}F-FDG PET/CT (c-PET-RI) in a well-characterized Norwegian IgG4-RD cohort.

Methods: Adult patients with IgG4-RD seen at the Oslo University Hospital were included if they had performed both ^{18}F-FDG PET/CT and a comprehensive assessment by a rheumatologist within a four-week interval. In each patient, we calculated c-RI from symptoms, clinical examination, and laboratory studies, and c-PET-RI from the c-RI plus the score from pathological ^{18}F-FDG organ uptake on the whole-body PET. Both indices were calculated using data from NOSVAR research registry and electronic medical records. We defined IgG4-RD disease activity as low if RI was ≤ 3 and high if RI was > 3 points. We assessed associations of elevated CRP and serum IgG4 (s-IgG4) with reclassification (discrepancy change in disease activity scores (c-PET-RI – c-RI)) by applying logistic regression with odds ratio (OR) and 95% CI to identify patients in which performing ^{18}F-FDG PET/CT is likely to change treatment decisions.

Results: The study cohort included 53 IgG4-RD patients, of whom 30 had c-RI ≤ 3 points, consistent with low disease activity. In 15/30 patients (50%) with c-RI ≤ 3, the corresponding c-PET-RI was > 3 points, consistent with high disease activity. In these 15 patients, the mean increase in RI points from the ^{18}F-FDG PET/CT was 6.4 (range 2-12). We found that 14 of these 15 patients (93%) had elevated s-IgG4 and 6 (40%) had elevated CRP. In logistic regression analysis, elevated s-IgG4, but not CRP, was strongly associated with reclassification to high disease activity after^{18}F-FDG PET/CT (OR 16.0, 95% CI 1.7-154.6, p = 0.017). Of the 9 patients with c-RI ≤ 3 and normal s-IgG4, only one (11%) was reclassified to high disease activity after ^{18}F-FDG PET/CT.

Conclusion: In IgG4-RD patients with low disease activity by clinical and laboratory assessment (c-RI), elevated s-IgG4 is associated with detection of asymptomatic organ involvement by ^{18}F-FDG PET/CT (c-PET-RI). Hence, evaluation with ^{18}F-FDG PET/CT should be considered in patients with c-RI ≤ 3 points and elevated s-IgG4 to tailor management. In contrast, in patients with c-RI ≤ 3 points and normal s-IgG4, the added yield of ^{18}F-FDG PET/CT appears to be low.

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Table 1.

Total cohort (n = 53)			
Treatment naïve at time of ^{18}F-FDG PET/CT, n (%)	35 (66)		
c-RI high disease activity (RI > 3), n (%)	23 (43)		
c-PET-RI high disease activity (RI > 3), n (%)	38 (72)		
Factors associated with reclassification to high disease activity after ^{18}F-FDG PET/CT			
	OR	95% CI	p-value
Elevated s-IgG4 (> 2.01 g/L)	16.0	1.7-154.6	0.017
s-IgG4 (per g/L unit increase)	1.5	1.1-2.2	0.020
CRP (per mg/L unit increase)	1.1	0.9-1.3	0.317

Acknowledgements: NIL.

Disclosure of Interests: Jens Vikse Speakers bureau: Boehringer-Ingelheim, Novartis, Consultant of: Jupiter Life Science, Novartis, Øyvind Midtvedt: None declared, Øyvind Molberg: None declared, Bjørg Tilde Svanes Fevang Speakers bureau: UCB, Consultant of: Lilly, Øyvind Palm: None declared, Torhild Garen: None declared, Katrine Brække Norheim: None declared, Mona Revheim: None declared, Kjersti Johnsrud: None declared, Håvard Fretheim Speakers bureau: Boehringer Ingelheim, Consultant of: Bayer, Grant/research support from: GSK/Actelion, Marianne Wallenius: None declared, Gunnstein Bakland Consultant of: UCB, Anna-Maria Hoffmann-Vold Speakers bureau: Boehringer Ingelheim, Jannsen, Medscape, Merck Sharp & Dohme and Roche, Consultant of: ARXX, Boehringer Ingelheim, Genentech, Jannsen, Medscape, Merck Sharp & Dohme and Roche, Grant/research support from: Boehringer Ingelheim, Jannsen.

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OP0256 VALIDATION OF THE 2019 ACR/EULAR CLASSIFICATION CRITERIA FOR IGG4-RELATED DISEASE AND THE JAPANESE ORGAN-SPECIFIC DIAGNOSTIC CRITERIA IN A JAPANESE IGG4-RELATED PERIAORTITIS/RETROPERITONEAL FIBROSIS COHORT: A NATIONWIDE MULTICENTER STUDY

Keywords: Diagnostic tests

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Background: Diagnosing IgG4-related periaortitis/retroperitoneal fibrosis (IgG4-PA/RPF) is often challenging, especially in PA/RPF-limited cases, due to the difficulty in obtaining periaortic/retroperitoneal specimens. In addition to the Japanese diagnostic criteria for IgG4-PA/RPF [1], the 2019 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for IgG4-related disease (IgG4-RD) [2] have not been validated for IgG4-PA/RPF diagnosis in daily clinical practice.

Objectives: This study aimed to validate the ACR/EULAR classification criteria and the Japanese organ-specific diagnostic criteria in a Japanese cohort of patients with IgG4-related PA/RPF.

Methods: In this nationwide multicenter study, we retrospectively reviewed the medical records of 110 patients with IgG4-PA/RPF and 79 non-IgG4-RD patients (mimickers) diagnosed by experts. Using the collected data, we calculated sensitivity and specificity in both the ACR/EULAR classification criteria and the Japanese diagnostic criteria. To clarify the characteristics of false-negative cases of IgG4-PA/RPF, we compared the clinical features between the false-negative and true-positive cases.

Results: Patients with IgG4-PA/RPF and mimickers had a median age of 70 and 71 years, and were 90% and 68% male, respectively. The final diagnoses of mimickers mainly consisted of non-IgG4-related idiopathic PA/RPF, lymphoma, Takayasu arteritis, giant cell arteritis, and atherosclerotic or infectious aortic aneurysm. The ACR/EULAR classification criteria had a sensitivity of 52% and a specificity of 95%. Of the 53 false-negative cases, 13 did not fulfill the entry criteria, 13 fulfilled one exclusion criterion, and 36 did not achieve sufficient inclusion criteria scores. Compared with the true-positive cases, the false-negative cases had significantly lower serum IgG4, IgG, and IgE levels, higher serum C3 and C4 levels, and lower prevalence of extra-vascular/retroperitoneal lesions; frequency of periaortic/retroperitoneal biopsies (36% vs 37%), frequency of storiform fibrosis and obliterative phlebitis in the obtained specimens, and numbers of infiltrating IgG4-positive cells were similar between the false-negative and true-positive cases. The Japanese diagnostic criteria for IgG4-PA/RPF had a sensitivity of 63% and a specificity of 99% when definite and probable diagnoses in the diagnostic criteria were regarded as a diagnosis of IgG4-PA/RPF (a strict version). When definite, probable, and possible diagnoses were regarded as a diagnosis of IgG4-PA/RPF (a lenient version), the diagnostic criteria had a sensitivity of 95% and a specificity of 90%.

Conclusion: The present study suggests that the 2019 ACR/EULAR classification criteria for IgG4-RD and a strict version of the Japanese diagnostic criteria for IgG4-PA/RPF have an excellent diagnostic specificity in daily clinical practice. A lenient version of the Japanese diagnostic criteria serves as more sensitive criteria, although care should be taken to avoid misdiagnoses for mimickers due to the relatively low specificity.

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Disclosure of Interests: None Declared.

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OP0257 CANAKINUMAB IN THE TREATMENT OF ADULT-ONSET STILL'S DISEASE: LONG TERM DATA FROM A MONOCENTRIC COHORT

Keywords: Innate immunity, bDMARD

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Background: Adult-onset Still's disease (AOSD) is a rare autoinflammatory disease whose clinical spectrum encompasses protean and potentially life-threatening manifestations. While glucocorticoids represent the mainstay of the treatment of patients with AOSD, no guidelines are available to guide the approach to refractory patients. Canakinumab – a monoclonal antibody targeting interleukin 1β – has been increasingly used in this scenario with promising results, though long-term efficacy data are scant.

Objectives: To evaluate the efficacy and long-term persistency of canakinumab in patients with AOSD.

Methods: We retrospectively identified patients with AOSD followed-up at our Center who were treated with canakinumab for at least 12 months. Data about demographics, disease features, and treatment history were then collected. The therapeutic efficacy of canakinumab was evaluated on the basis of the modifications of glucocorticoid doses, *Pouchot scores,* C-reactive protein, and ferritin levels during the treatment course. Finally, the drug retention rate of canakinumab at 24 months was obtained.

Results: In our cohort, we identified 25 patients with AOSD treated with canakinumab for at least 12 months. Median age at disease onset was 35 (IQR 25-56) years and median follow-up duration was 24 (IQR 12-41) months. Clinical features of the study population are shown in **Table 1**. The most frequent reason (21 [84%] patients) for the start of IL-1β inhibition was a persistent disease activity. Canakinumab led to remission in all but two patients and, overall, was associated with a significant reduction in glucocorticoid doses, *Pouchot scores*, C-reactive protein and ferritin levels (**Figure 1**). The overall retention rate at 24 months was 93% and no adverse reactions to canakinumab were reported.

Conclusion: Our study confirms – in one of the largest monocentric cohorts described to date – that canakinumab is highly effective in patients with AOSD. Canakinumab was associated with a significant clinical and biochemical improvement in most patients from our cohort and was characterized by a very high long-term retention rate.

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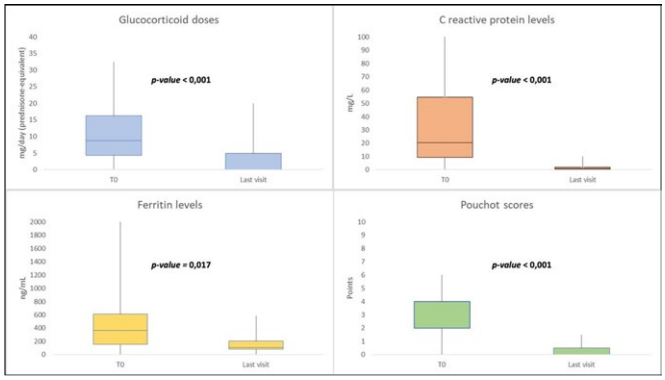


Figure 1. Boxplots reporting the modifications in glucocorticoid doses, C-reactive protein and ferritin levels, and Pouchot scores following the start of canakinumab (T0). Reported *p-values* were calculated with Mann-Whitney test.

Table 1. Demographic and disease features of patients with adult-onset Still's disease from our cohort. Continuous and categorical variables are reported as median (interquartile range) and absolute frequency (percentage), respectively. Glucocorticoid dose and age are expressed in mg (prednisone-equivalent) and years, respectively.

Variable	Study population (n=25)
Age	35 (25-56)
Male sex	13 (52%)
Fever	25 (100%)
Rash	19 (76%)
Arthritis	15 (60%)
Serositis	3 (12%)
Lymphadenopathy	11 (44%)
Pharyngitis	10 (40%)
GC dose at CNK start	50 (30-75)
Previous DMARDs	18 (72%)
MTX	12 (48%)
ANK	9 (36%)
Concomitant DMARDs	17 (68%)
MTX	11 (44%)

ANK, anakinra; CNK, canakinumab; DMARD, disease modifying anti-rheumatic drug; GC, glucocorticoids, MTX, methotrexate.

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New insights form epidemiology and public health

OP0258 RISK OF INCIDENT GOUT ASSOCIATED WITH INITIATION OF SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITORS VERSUS OTHER SECOND-LINE AGENTS AMONG METFORMIN USERS WITH TYPE 2 DIABETES

Keywords: Gout, Epidemiology

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Background: Sodium-Glucose Cotransporter Type 2 Inhibitors (SGLT2i) are a revolutionary second-line treatment for type 2 diabetes associated with lower risk of cardiovascular and all-cause mortality, heart failure, and chronic kidney disease progression. Many trials have also found SGLT2i lower serum urate levels. However, data on gout risk are limited and the few available prior studies were not specific to those using metformin, the primary target populations of recent landmark trials like GRADE.

Objectives: To emulate recent clinical trials and compare incident gout risk among metformin-treated patients with type 2 diabetes initiating SGLT2i versus second-line type 2 diabetes treatments (glucagon-like peptide-1 receptor agonist [GLP1RA], dipeptidyl peptidase 4 inhibitors [DPP4i] or sulfonylureas).

Methods: We performed a new user, active comparator, population-based cohort study using administrative health data for nearly all residents of British Columbia, Canada from Jan 2014 to June 2022, including all dispensed prescriptions, regardless of funder. A cohort of adults with type 2 diabetes using metformin (first-line therapy) was identified from ICD codes and dispensing data. Primary outcome was incident gout, defined as inpatient or outpatient diagnosis of gout plus dispensing of a gout medication within 14 days, and no prior recorded gout diagnosis. We also stratified by sex, age, and baseline diuretic use. Cox proportional hazards models were used with propensity score overlap weighting. To evaluate reproducibility and for spurious associations, we also assessed for risk of genital infection (for which we expected SGLT2i would have a positive association), and for the risk of any osteoarthritis encounter, a negative control outcome for which we expected a null association.

Results: Hazard ratio (HR) for incident gout associated with SGLT2i initiation was 0.54 (95% CI: 0.39, 0.74) vs. DPP-4i (among n=27,791 type 2 diabetes patients), 0.39 (0.24, 0.62) for SGLT2i vs. GLP1RA initiation (n=19,875 patients), and 0.61 (0.46, 0.80) for SGLT2i vs. sulfonylurea initiation (n=71,625 patients) (**Table 1**). Results were consistent regardless of sex or age or baseline diuretic use. For control outcomes, SGLT2i initiators had higher risk of genital infection, as expected, while there was no difference in risk of osteoarthritis (**Table 1**).

Conclusion: SGLT2i initiation among metformin-treated patients with type 2 diabetes was associated with substantially lower risk of incident gout (i.e., primary prevention), compared with initiation of any other second-line options. Along with its known urate-lowering, as well as cardiovascular and survival benefits, SGLT2i could reduce risk of incident gout substantially for diabetes patients who need second-line agent after metformin.

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Table 1. Risk of incident gout and control outcomes among patients with type 2 diabetes treated with metformin, after propensity-score overlap weighting

	SGLT2i compared with DPP4i [Reference]	SGLT2i compared with GLP1RA [Reference]	SGLT2i compared with Sulfonylureas [Reference]
Incident Gout	**Hazard Ratio (95% CI)**		
Overall (Primary Outcome)	0.54 (0.39, 0.74)	0.39 (0.24, 0.62)	0.61 (0.46, 0.80)
Subgroups			
Sex			
Men	0.57 (0.37, 0.86)	0.29 (0.16, 0.49)	0.58 (0.41, 0.81)
Women	0.49 (0.29, 0.82)	0.59 (0.28, 1.27)	0.66 (0.42, 1.05)
Age			
≤ 65 years	0.61 (0.39, 0.95)	0.39 (0.21, 0.70)	0.63 (0.43, 0.91)
> 65 years	0.49 (0.30, 0.82)	0.39 (0.19, 0.83)	0.63 (0.41, 0.95)
Baseline diuretic use			
Yes	0.54 (0.35, 0.84)	0.40 (0.21, 0.75)	0.73 (0.51, 1.06)
No	0.55 (0.34, 0.90)	0.37 (0.18, 0.75)	0.51 (0.34, 0.78)
Control Outcomes	**Hazard Ratio (95% CI)**		
Genital infection (POSITIVE CONTROL)	2.35 (1.85, 2.99)	3.50 (2.43, 5.04)	1.69 (1.46, 1.95)
Osteoarthritis (NEGATIVE CONTROL)	1.06 (0.86, 1.30)	0.91 (0.65, 1.27)	1.12 (0.95, 1.30)

SGLT2i, sodium glucose cotransporter-2 inhibitor; DPP4i, dipeptidyl peptidase 4 inhibitor; GLP1RA, glucagon-like peptide-1 receptor agonist

Acknowledgements: NIL.

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OP0259 WHITE MATTER HYPERINTENSITY VOLUME IN UK BIOBANK PATIENTS WITH RHEUMATOID ARTHRITIS AND ULCERATIVE COLITIS

Keywords: Imaging, Rheumatoid arthritis, Epidemiology

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Background: Rheumatoid arthritis (RA) and ulcerative colitis (UC) both result in higher levels of systemic inflammation and represent a significantly higher risk of cerebrovascular disease. The presence of this systemic inflammation has been linked to central nervous system effects and both diseases have increased rates of fatigue, brain fog and depression. Additionally, systemic inflammation has been implicated in decreasing the integrity of the blood brain barrier and potentially resulting in further involvement of the central nervous system in autoimmune diseases.

Objectives: The increased presence of white matter hyperintensities (WMH) has been proposed as a potential link to the central symptoms reported and the increased prevalence of cerebrovascular accidents in these diseases [1]. The present study aimed to analyse total volume of WMH in patients with RA and UC as compared to matched controls.

Methods: Data from 1,968 individuals in the UK Biobank Imaging sub-study were included in the present study [2]. This was divided into two separate patient populations with separate control groups matched to each in a 1:3 patient:control ratio. Data from 252 individuals (mean age ± SD =65.52 ± 7.03, 71.4% females) were included in the RA patient group with 756 age and sex matched controls (mean age ± SD = 65.52 ± 7.02, 71.4% females). Data from 240 individuals (mean age ± SD = 63.98 ± 7.06, 50.8% females) were included in the UC patient group with 720 age and sex matched controls (mean age ± SD = 63.98 ± 7.05, 50.8% females). This study utilised the total volume of WMH acquired using an automated segmentation approach called BIANCA and provided directly by the UKBiobank. Volumes were taken as a ratio of total brain volume and log transformed prior to a linear model regression being performed. Two separate models were run. One with age, sex, and ICV as covariates and a second model additionally including hypertension.

Results: We observed significantly larger total WMH volume in RA patients when compared to controls in model 1 (difference in WMH volume: 2286.0 mm^3, SD ±84.5, p = 2.0e-08). The Cohen's effect size was *d* = 0.36 [95% CI 0.21, 0.5]. This effect was still substantial even with hypertension added as a covariate in model 2 (p = 3.7e-06). There was also a smaller, but still significant difference seen in UC patients compared to controls (difference in WMH volume: 237.1 mm^3, SD ±82.1, p = 0.003). The Cohen's effect size was *d* = 0.19 [95% CI 0.04, 0.33]. As with the RA population hypertension is a strong contributing factor, however, the p value was still significant in model 2 (p = 0.03).

Conclusion: This is evidence that there is a cerebrovascular component to these diseases and that people with higher WMH burden may be at a higher risk of developing neurocognitive sequalae as part the disease. Further analysis of spatial mapping of WMH could provide further context for whether there are different patterns or distributions between RA and UC which could contribute to different central nervous system symptoms or cerebrovascular health risk factors.

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Acknowledgements: NIL.

Disclosure of Interests: Jennifer Cox Grant/research support from: I am a GSK funded PhD student at King's College London, Employee of: I previously worked for GlaxoSmithKline, Marius de Groot Shareholder of: Dr. de Groot is a GSK employee with company shares, Employee of: Dr. de Groot is a current employee of GSK, James Cole: None declared, Steven Williams Consultant of: Dr. Williams has previously consulted for a number of pharmaceutical companies including GlaxoSmithKline, Johnson & Johnson and Pfizer., Grant/research support from: Dr. Williams has received research funding from Bionomics, Eli Lilly, the Engineering and Physical Sciences Research Council, GlaxoSmithKline, Johnson & Johnson, Lundbeck, the National Institute of Health Research, Pfizer, Takeda, and Wellcome Trust., Employee of: Dr. Williams previously worked for Pfizer.

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OP0260 GLOBAL TREND OF THE SURVIVAL OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS BETWEEN THE 1950S TO 2020

Keywords: Organ damage, Epidemiology, Systemic lupus erythematosus

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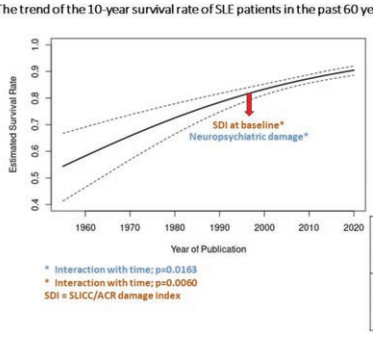
Background: The trend of, and the impact of major organ damage on the short- and longer-term survival of patients with systemic lupus erythematosus (SLE) globally over the past 60 years have not been systematically studied by meta-analyses, particularly regarding the impact of the interaction between time and major organ damage on the trend of the survival of patients with SLE.

Objectives: To study the trend of, and the impact of major organ damage and demographically relevant factors on the short (5-year) and longer-term (10-, 15- and 20-year) survival rates of patients with SLE in the past 60 years by random-effects meta-analyses and meta-regression. The meta-analytical method that examines the impact of the interaction between time in terms of year of publication and major organ damage on the trend of the overall survival rates of SLE patients was employed.

Methods: Observational studies that were written in English and reported the survival rates of patients with SLE published between the 1950 and 2021 were searched, identified and extracted from PubMed and EmBase. Studies which only reported survival rates shorter than 5 years were excluded. The effect sizes of the overall 5-, 10-, 15- and 20-year survival rates and their respective trends over time of patients with SLE were determined by random-effects meta-analyses. Meta-regression analyses were conducted to investigate the impact of covariates, including the interaction between the year of publication (time) and factors including major organ damage that comprised cardiovascular, renal, neuropsychiatric and musculoskeletal damage, proportion of female SLE patients in respective studies and regions (including Asia, Europe, Middle East, North America, South America, Oceania and others) where the studies were conducted.

Results: In total, 281 observational studies that were published between 1955 and 2020 were identified and eligible for analyses. The overall 5- and 10-year survival rates of SLE patients increased from 71.82% to 94.27%, and from 58.23% to 90.44%, respectively, from 1960 to 2020. The overall 15-year survival rate of SLE patients increased from 64.36% in the 1980s to 85.00% in 2020, while that of 20-year survival rate increased from 58.82% to 84.02% from 1990 to 2020. The impact of the following interactions with the year of publication (time) on survival increased yearly with statistical significance in the meta-regression analyses. These covariates included the effect of cardiovascular damage on the 5-year survival rate (β=0.0092, SE=0.0045, p=0.0406), SLICC/ACR damage index score at baseline on the 10-year survival rate (β=0.6116, SE=0.2227, p=0.0060), neuropsychiatric damage on both the 5-year (β=0.0048, SE=0.0020, p=0.0163) and 10-year (β=0.0041, SE=0.0019, p=0.0279) survival rates (Figure 1). In addition, the interaction between the proportion of female SLE patients and the year of publication had significant impact on both the 5-year (β=0.0014, SE=0.0006, p=0.0216) and 10-year survival rates (β=0.0014, SE=0.06 p=0.0255). Analyses of the interactions between the time of publication and regions where studies were conducted did not reveal significant impact of their interactions on the short- and longer-term survival in patients with SLE.

Conclusion: Both the short- and longer-term survival of patients with SLE have been increasing steadily from the 1950s to 2020. While cardiovascular damage impacted significantly the 5-year survival rate, neuropsychiatric and overall SLE disease damage at baseline with their interactions with time, exerted a significant impact on the 10-year survival rate of patients with SLE since the 1950s. Although the 15- and 20-year survival rates of SLE patients have been promisingly increasing, more studies are required to further address the determinants of these longer-term survival rates. The impact of sex difference with its interaction with time on the survival of SLE patients require more focused and mechanistic studies.



Year	Predicted 10-year survival	95% CI	
1960	0.58	0.47	0.69
1970	0.66	0.57	0.74
1980	0.73	0.66	0.78
1990	0.78	0.75	0.81
2000	0.83	0.81	0.85
2010	0.87	0.86	0.89
2020	0.90	0.87	0.92
Predicted 15-year survival (an overall aggregate from 1980-2020)	0.80	0.76	0.83
Predicted 20-year survival (an overall aggregate from 1990-2020)	0.79	0.74	0.83

Figure 1.

REFERENCES: NIL.

Acknowledgements: NIL.

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OP0261 THE NATURAL SEQUENCE IN WHICH SUBCLINICALLY INFLAMED JOINT TISSUES PROGRESS TO CLINICAL ARTHRITIS OR SUBSIDE; A STUDY ON SERIAL MRIS IN THE PLACEBO-ARM OF THE TREAT EARLIER TRIAL

Keywords: Synovium, Imaging, Rheumatoid arthritis

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Background: Clinical arthritis is the hallmark of rheumatoid arthritis (RA), yet the trajectory in which arthritis develops at tissue-level remains elusive.

Objectives: We hypothesized that subclinical inflammation in different joint tissues (synovitis, tenosynovitis and osteitis) increases in a distinct temporal order in clinically suspect arthralgia (CSA) patients who develop RA, and subsides in a different sequence when CSA spontaneously resolves.

Methods: 185 serial MRIs from CSA-patients with subclinical joint inflammation from the placebo-arm of the TREAT EARLIER trial were studied: 52 MRIs from 21 RA-progressors (performed 1-year and 4-months before and upon RA-development) and 133 MRIs from 35 patients with spontaneous resolution of pain (MRIs at baseline, 4, 12 and 24 months). MRIs were scored for osteitis, synovitis and tenosynovitis. Cross-lagged models evaluated two types of time-patterns between pairs of inflamed tissues: a simultaneous pattern (coinciding change) and a subsequent pattern (inflammatory change in one tissue preceding change in another tissue).

Results: During RA-development, synovitis, tenosynovitis and osteitis increased simultaneously. Furthermore, increasing osteitis in the final 4-months before RA-diagnosis followed incrementing tenosynovitis and synovitis during 1-year to 4-months before RA-diagnosis ($p<0.01$). Expanding osteitis occurred just before RA-development in both ACPA-positive and ACPA-negative RA. During resolution, besides simultaneous decreases, declining tenosynovitis in the first 4-months after CSA-onset preceded decreases in synovitis and osteitis during 4-12 months ($p=0.02$; $p<0.01$).

Conclusion: Natural sequences in subclinical inflammation of different joint tissues were identified, deepening our understanding of arthritis and RA-development. During progression to RA, increasing osteitis followed previous increases in tenosynovitis/synovitis. During resolution, tenosynovitis decreased first, followed by decreasing synovitis and osteitis.

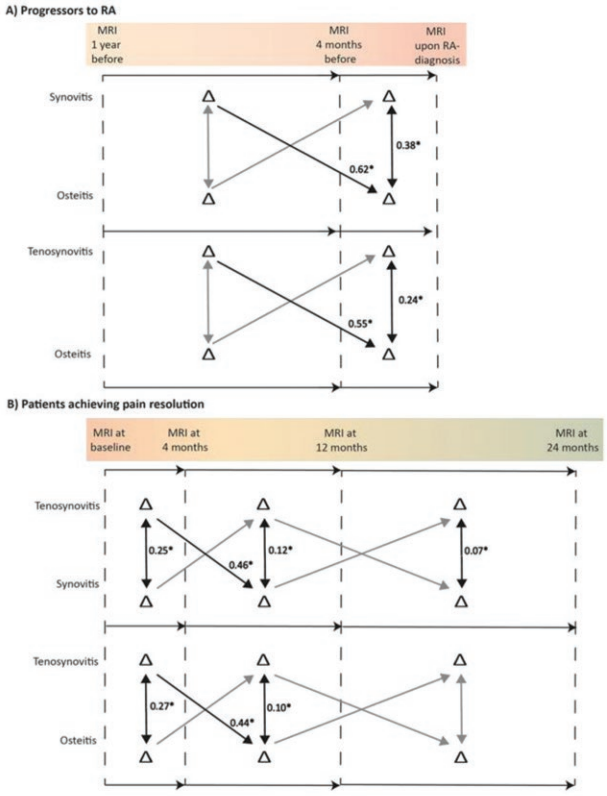


Figure 1. Graphic depiction of simultaneous and subsequent increase (Δ) of inflammation in pairs of different joint tissues during the two intervals in the year before arthritis development (A) and simultaneous and subsequent decrease (Δ) of inflammation in pairs of different joint tissues in patients achieving pain resolution (B)

Legend figure 1. Vertical arrows depict simultaneous inflammatory change in two joint tissues. Diagonal, crossing arrows depict time orders. Estimates represent the proportion of change in inflammation in two tissues that is not explained by other patterns, and are independent of scale. Higher values indicate higher explanation, and a value of 0 indicates no explanation. Statistical significant estimates are given in black with *, non-significant effects are given in grey.

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Disclosure of Interests: None Declared.
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OP0262

INCREASED FERTILITY AMONG 10865 MEN WITH CHRONIC INFLAMMATORY JOINT DISEASES IN NORWAY

Keywords: Epidemiology, Pregnancy and reproduction, Inflammatory arthritides

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Background: In the field of rheumatology, fertility has been reported impaired in Norwegian women with inflammatory joint diseases (IJDs) [1]. There is, however, limited data regarding fertility in male patients. The iFAME-fertility study found an association between inflammatory arthritis and reduced male fertility [2], underlining the need for a large-scale study. In the current project, we address this knowledge gap.

Objectives: To examine whether inflammatory joint diseases (IJDs) have an impact on men's fertility, measured as number of children per man and proportion of childless men.

Methods: We performed a nation-wide, population-based cohort study. Male patients with IJDs (n = 10,865) collected from the Norwegian Arthritis Registry in 2021 were individually matched 1:5 on birth year, sex, and county of residence, with individuals without IJDs obtained from the National Population Register (n = 54,325). Data regarding births was obtained from the Medical Birth Registry of Norway. We compared the mean number of children per man in the patient group and in the comparison group using paired t-tests, and the proportion of childless men using Cochran–Mantel–Haenszel chi-squared tests.

Results: The mean number of children per man in the patient group was 1.80 versus 1.69 in the comparison group ($p < 0.001$). Altogether, 21% of our patients were childless vs 27% in the comparison group ($p < 0.001$, Figure 1). The difference in number of children between patients and comparison group was highest for those diagnosed after year 2000 and these patients had the comparatively lowest risk of being childless. The differences were less evident for those diagnosed before 2000 (Table 1). Age at diagnosis did not influence fertility (Table 1).

Conclusion: In this large nationwide study, fertility in male patients with IJDs was not reduced compared to controls, neither when examining the number of children per man, nor when looking at the proportion of childless men. Interestingly, we observed a higher fertility rate in male IJD patients than in the comparison group for patients diagnosed after year 2000. The reason for this observation is unknown. Factors associated with getting or having an IJD may influence fertility. An interesting hypothesis is a possible positive impact of new immune modulating drugs introduced after year 2000.

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Table 1. Mean number of children and proportion of childless men according to time and age at diagnosis.

Time at diagnosis	Age (years) at diagnosis	No. of Patients	Mean no. of children			Childless men (%)		
			Patients	Comparisons	*P*-value	Patients	Comparisons	*P*-value
1967 -1985*		575	1.92	1.87		16.9	21.0	
	0- 20	161	1.73	1.81	0.43	21.7	22.9	0.84
	21 - 30	275	2.04	1.93	0.14	12.7	19.2	0.01
	31 - 40	104	2.09	1.94	0.28	16.3	19.0	0.61
	41 - 50	34	1.44	1.45	0.98	26.4	32.3	0.60
1986 - 1999		1360	1.83	1.83		19.0	21.9	
	0- 20	118	1.58	1.52	0.65	28.0	31.2	0.56
	21 - 30	415	1.72	1.72	0.91	22.2	26.3	0.09
	31 - 40	382	1.96	1.98	0.78	16.5	18.5	0.40
	41 - 50	323	1.98	1.96	0.79	13.9	16.8	0.22
2000 - 2021		8930	1.79	1.65		21.4	27.8	
	0- 20	173	0.46	0.46	1.00	73.4	74.1	0.91
	21 - 30	1069	1.05	0.91	<0.001	46.7	52.5	<0.001
	31 - 40	1705	1.67	1.48	<0.001	22.8	32.1	<0.001
	41 - 50	1999	1.92	1.77	<0.001	17.4	24.1	<0.001

* The Medical Birth Registry contains information about all births in Norway since 1967, and children born before this are not registered. This gives a lower mean no. of children per man, mainly affecting men 41 – 50 years of age in the 1967 - 1985 era.

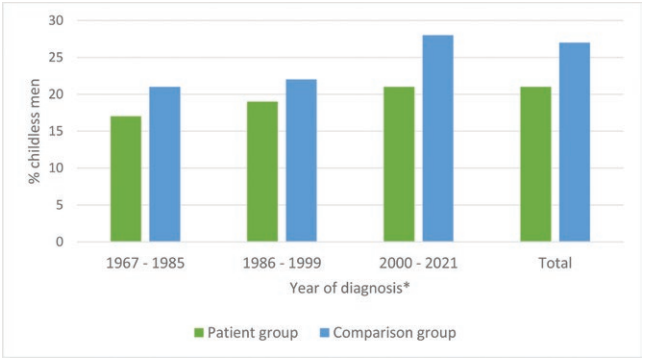


Figure 1. Proportion of childless men.*Treatment eras reflect major changes in treatment strategy for the IJDs – methotrexate from the late 1980s and biological treatment from the early 2000s.

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Disclosure of Interests: None Declared.
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OP0263

INFLAMMATORY RHEUMATIC DISEASES HAVE BROAD IMPACT ON REPRODUCTIVE HEALTH – A NATIONWIDE EVALUATION AND SYSTEMATIC COMPARISON ACROSS RHEUMATIC DISEASES

Keywords: Pregnancy and reproduction

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Background: Inflammatory rheumatic diseases (IRDs) affect men and women of reproductive age. The lack of reproductive health studies on IRDs hinders making evidence-based recommendations on fertility preservation, prevention of pregnancy complications, and management of the IRDs during reproductive years.
Objectives: To systematically estimate the impact of IRDs on diverse reproductive outcomes and compare the effects to those observed for other immune-mediated inflammatory diseases.
Methods: The total Finnish population (FinRegistry; N=5,339,804) was linked to nationwide registries (inpatient and outpatient care, and Medical Birth Register covering all live births since 1987, N=1,920,411 births). We focused on seropositive and seronegative rheumatoid arthritis (RA), ankylosing spondylitis (AS), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), systemic lupus erythematosus (SLE), and Sjögren syndrome (SS), selecting individuals born 1964–1984 diagnosed with the IRD before age 30, and 20 sex, birth-year, and education level-matched controls. The patterns were compared to a range of other immune-mediated inflammatory diseases, such as type 1 diabetes, inflammatory bowel disease, and hypothyroidism.
Results: The case count of women with an IRD ranged from 412 for PsA to 1,487 for seropositive RA (mean age range at diagnosis 11.0 in JIA to 25.7 in AS). Women with IRD experienced a higher prevalence of childlessness than controls (mean difference 4.2%, largest in JIA at 9.3%), had fewer children (mean 0.2 fewer, highest in JIA at 0.3 fewer), and the start and end of reproduction were slightly shifted towards an earlier age. Also men with an IRD experienced a higher prevalence of childlessness than controls (mean difference 4.1%, largest in SLE at 11.0%). Overall, the impact was similar in other immune-mediated inflammatory diseases in both women and men, with high variability between diseases. For maternal health conditions, five IRDs showed an elevated risk for pre-eclampsia, with the largest effect size observed for SLE (OR 2.65, 95%CI 1.94–3.62). No elevated risk was observed for gestational diabetes in any of the IRDs. Many of the IRDs were associated with at least one of the ten evaluated adverse perinatal outcomes, such risk of nonelective Caesarean section, and admission to neonatal ICU (**Figure 1**), with the largest effect sizes observed for SLE and SS.

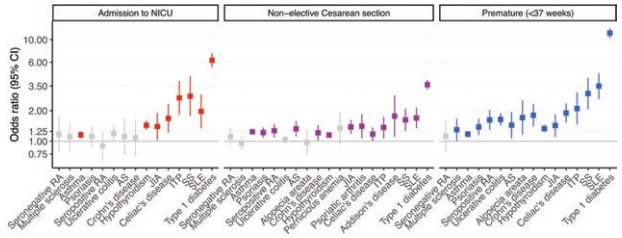


Figure 1. Systematical analysis of perinatal outcomes, with results shown for three of the ten evaluated perinatal outcomes. Results are shown for diseases with over 20 cases for the outcome and associations with p-value >0.05 are shown in gray. NICU = neonatal ICU, ITP = immune thrombocytopenic purpura.

Conclusion: In this comprehensive, nationwide evaluation of reproductive health metrics, we observed widespread impact of IRDs on reproductive health. The effects were comparable to many other immune-mediated inflammatory diseases, but we also observed high variability between diseases. Overall, these findings emphasize the need for further research, and the importance of counseling on reproductive health in both men and women with IRDs.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Nina Mars: None declared, Anne Kerola Speakers bureau: Boehringer-Ingelheim, Sanofi, Consultant of: Advisory boards of Pfizer, Gilead and Boehringer-Ingelheim, Grant/research support from: Congress travel sponsorship from Pfizer and Mylan., Kari Eklund: None declared, Hannele Laivuori: None declared, Samuli Ripatti: None declared, Antti Palomäki Speakers bureau: Boehringer-Ingelheim, Pfizer, Sanofi, Consultant of: Pfizer, AbbVie and Amgen, Fin Registry: None declared.
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OP0264

COST-UTILITY OF A PROGRESSIVE SPACING OF TOCILIZUMAB OR ABATACEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SUSTAINED REMISSION: A MEDICO-ECONOMIC ANALYSIS OF THE TOLEDO TRIAL

Keywords: Clinical trials, bDMARD, Rheumatoid arthritis

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Background: Biologic Disease Modifying Anti-Rheumatic Drugs (bDMARDs) progressive tapering is a real opportunity in people living with rheumatoid arthritis (RA) having achieved remission both from the patient and the Society perspectives. The ToLEDo (Towards the Lowest Efficacious Dose) trial aimed to assess a disease activity-driven progressive tapering strategy of tocilizumab (TCZ) or abatacept (ABA) compared to their maintenance at full dose in RA patients in sustained remission. Non-inferiority (NI) was not demonstrated in terms of disease activity (primary endpoint) nor relapses, major relapses, radiographic progression (secondary endpoints) [1].
Objectives: The aim of this secondary analysis was to assess the cost-utility of the spacing strategy (S-arm) in the ToLEDo trial compared to full dose maintenance (M-arm).
Methods: The ToLEDo trial is a multicenter 2-year NI randomized open-label controlled trial, which enrolled 228 patients (113 in the S-arm and 115 in the M-arm). A cost-utility analysis was conducted on the per protocol population. In each arm, health benefits were estimated every 6 months by Short Form Health Survey (SF-6D) and EuroQoL (EQ-5D)-derived utility measurements. Cost elicitation integrated health resource use including bDMARD costs (direct cost) as well as productivity loss (indirect cost) using the friction cost method. The incremental cost-utility ratios (ICUR) were calculated by dividing the difference of costs between S-arm and M-arm by the difference of utilities between the 2 arms. 95% confidence interval (95%CI) were calculated by bootstrap (20,000 iterations). The incremental net benefit (INB) was calculated for willingness to pay (WTP) values ranging from 0 to 150,000€. The analyses were replicated using SF-6D (primary analysis) or EQ-5D, and in ABA and TCZ subgroups. Acceptability analyses as well as stochastic sensitivity analyses (simulating costs and utilities using MCMC algorithms) were also performed.
Results: Overall, 178 patients were included (82 in S-arm, 96 in M-arm) in the per protocol analysis. At the end of the follow-up in the S-arm, 15.0% of patients discontinued their biologic, 48.7% spaced the injections, and 36.3% remained at the standard dose. The difference in terms of two-years utility gains between S-arm and M-arm was 0.004 (95%CI -0.012, 0.021) with SF-6D. The difference of total costs between S-arm and M-arm was -4,275 € (95%CI -5,955 to -2,542). The estimated ICUR of the spacing strategy over the maintenance at full dose was €932,003 saved per QALY (95% CI -7,534,788 to 6,720,372) with SF-6D. The INB was 4,734.6€ for a WTP of 100,000€. With a willingness to accept of 0 €/QALY lost, the probability to be cost-effective for the spacing strategy was 70.6% (***Figure 1***). The results were consistent when using EQ-5D-derived utilities, in ABA and TCZ subgroups, as well as in the stochastic sensitivity analyses (***Table 1***).
Conclusion: Although the ToLEDo trial did not demonstrate non-inferiority, the tested disease activity-driven tapering strategy was not associated with health loss in terms of utilities and incurred for substantial cost savings, making this strategy potentially dominant.
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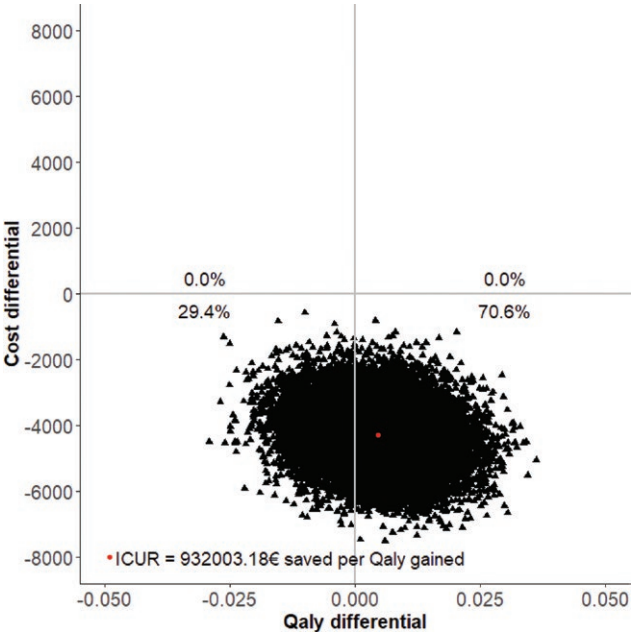


Figure 1. cost-utility plane (spacing versus maintenance), with utilities derived from PP SF-6D

Table 1. ICUR in ABA subgroup, TCZ subgroup, using EQ-5D-derived utilities, and stochastic sensitivity analysis

	ABA subgroup (PP SF-6D)	TCZ subgroup (PP SF-6D)	PP EQ-5D	Stochastic sensitivity analysis (PP SF-6D)
ICUR, €/QALY gained	-420,076.22 (95%CI -1,044,462 ; 1,461,037)	-1,008,225 (95%CI -2,436,237; 1,898,967)	-52,005 (95%CI -458,934; 369,967)	-481,029.28 (95%CI -1,300,747; 1,867,263)

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OP0265

WORK PARTICIPATION AND THE COVID19 PANDEMIC: A DUTCH PROSPECTIVE COHORT STUDY IN PEOPLE WITH INFLAMMATORY RHEUMATIC DISEASES AND HEALTHY CONTROLS

Keywords: COVID, Work-related issues

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Background: People with inflammatory rheumatic diseases (iRD), such as rheumatoid arthritis (RA) and spondyloarthritis (SpA), experience restrictions in work participation. In times of crisis, such as the coronavirus disease 2019 (COVID19) pandemic, people with iRD might be more vulnerable for adverse work outcomes (i.e. (partial) job loss and sick leave) and restrictions in work ability while at work.

Objectives: To (a) compare occurrence of adverse work outcome (AWO) and change in work ability during the first two years of the pandemic (2020-2022), as well as current (2022) work ability, between people with iRD and healthy controls in the Netherlands; (b) understand which subgroups of patients are most vulnerable to incur work participation outcomes; and (c) explore the role of remote work characteristics on work performance.

Methods: Data from a Dutch longitudinal study on COVID19 at Reade and Amsterdam UMC were used. Information about work was collected at one fixed timepoint. Patients (18-67 years) with iRD and controls were asked in March 2022 to answer questions on work participation and their work situation in March 2020 (pre-pandemic; retrospectively) and March 2022 (current). AWO was defined as any of: (1) shift between 2020-2022 from employment to unemployment; or from full to part-time employment; (2) reduction in working hours; (3) ongoing long-term sick leave. Work ability (change and current) was assessed with the Work Ability Index (range 0 [worst] to 10 [best]). Outcomes were compared between groups (iRD vs control) with statistical tests. Multivariable logistic or linear regression analyses were used to explore the associations between iRD and AWO or (change in) work ability. Interactions (effect modification) were tested and, if present, analyses were stratified. The role of remote work factors on remote work performance was described.

Results: In total, 1,438 iRD patients and 526 controls of working age (18-67) participated. The majority was female (67%) and was employed pre-pandemic (69% patients, 84% controls). Patients mainly had RA or SpA (85%). In pre-pandemic employed subjects, 227 patients (23%) and 79 controls (18%) experienced AWO (p=0.04). Only 35 patients (4%) and 12 controls (2%) of these, attributed this to COVID (impact by personal health or national pandemic measures; p=0.36). Logistic regressions of AWO were stratified because of interactions between group and sex, comorbidities or a physically demanding job. In all models, patients were more likely than controls to experience AWO (range OR 1.63 to 3.34 across models, Figure 1), and especially patients with comorbidities or a physically demanding job. Of note, COVID-related AWO was not significantly more likely in patients (OR=1.62, 95%CI 0.80-3.27). Change in work ability during the pandemic did not differ between groups (-0.3 (SD 1.8) patients vs -0.2 (SD 1.6) controls, p=0.38), and regression analyses also did not reveal significant differences. Linear regression of current work ability (stratified by sex due to interaction) showed female patients compared to female controls experienced lower work ability (B=-0.66; 95%CI -0.92 to -0.40), while this was not observed in males. Past SARS-CoV-2 infection was not associated with AWO/work ability. When working remotely, care for children and absence of colleagues had both positive (19% and 24%, resp.) and negative (34% and 57%, resp.) influence on work performance, while employer support and reduced commuting time had positive influence (83% and 86%, resp.).

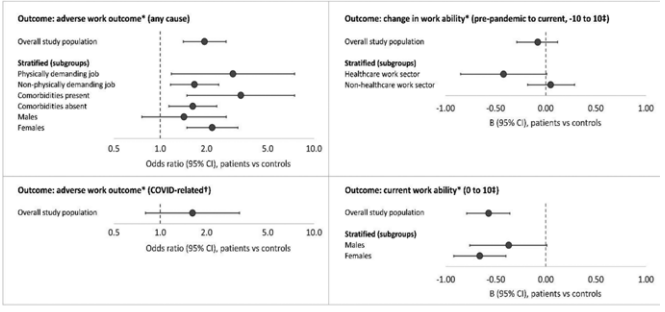


Figure. Association between group (patients vs controls) and adverse work outcome or (change in) work ability. An odds ratio >1 or a B <0 indicate a worse outcome in patients compared to controls (occurrence of adverse work outcome, a greater decrease in work ability or lower current work ability). *Covariables explored in models (forward method, retained if confounder for group and outcome, or if significantly associated with outcome): age, gender, education, comorbidities, past COVID infection, COVID vaccination, work sector, job demands, employment contract, working hours per week, work location. †COVID-related adverse work outcome defined as adverse work outcome attributed by the patient to either impact of COVID on personal health or impact of national pandemic measures.

Conclusion: During the COVID pandemic, patients experienced more AWO than healthy controls, and especially patients with physically demanding jobs and comorbidities were at higher risk. However, the frequency of COVID-related AWO was low and did not differ substantially between patients and controls. A likely explanation is that the governmental support for employers protected those in vulnerable positions, such as patients with iRD.

REFERENCES: NIL.

Acknowledgements: NIL.

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Epidemiology, risk and prediction of risk

OP0266 HIGHER RISK OF LUPUS MORTALITY IN URBANIZED THAN IN LESS-URBANIZED NEIGHBORHOODS

Keywords: Geographical differences, Systemic lupus erythematosus, Prognostic factors

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Background: Lupus mortality differs by sex, race/ethnicity, and geographical region in the United States, with females, blacks, and residents of the South census region experiencing higher age-standardized mortality rates relative to their respective reference groups, as revealed by the analysis of aggregated mortality data using the CDC-WONDER database (Yen E, et al, Ann Intern Med 2017; Singh RR and Yen E, Lupus 2018). These aggregate data are limited by observation at the population level. We seek to examine mortality data at the individual level to characterize how where you live can impact your risk of death from lupus. Specifically, how living in a specific neighborhood as defined by the rural-urban continuum codes (RUCC) can influence your overall lupus mortality.
Objectives: Analyze the risk of lupus death relative to all-cause deaths (other than lupus) by RUCC adjusted for sex, race/ethnicity, and age groups.
Methods: We used the individual mortality dataset provided by the Centers for Disease Control and Prevention. The study population comprises all (>99%) deaths in the United States from 2006 to 2011. The primary outcome is lupus listed as the cause of death identified from ICD 10 codes (M321, M328, M329). The primary exposure is the RUCC listed on the death certificate at the time of death. We constructed a multivariate logistic regression model adjusting for known covariates that could influence the outcome including sex, ethnicity/race, and age. We also analyzed for any potential effect modifiers between RUCC and other demographic variables.
Results: From 2006 to 2011, there were 5,430 lupus deaths and 6,286,020 all-cause deaths in the United States. The adjusted odds of lupus vs. all-cause deaths was higher in metro-urbanized area than in less urbanized (odds ratio 0.729 [95% CI 0.651 to 0.816], p<0.0001), thinly populated (0.831 [0.660-1.046], p = NS), and non-metro urbanized (0.951 [0.845-1.070], p=NS). The odds of lupus/all-cause deaths was higher in non-Hispanic black (2.758 [2.573-2.957], p<0.0001), Hispanic (2.350 [2.150-2.568], p<0.0001), and non-Hispanic other (2.242 [1.975-2.546], p<0.0001) than in non-Hispanic white persons; lower in males (0.121 [0.112-0.131], p<0.0001) than females, and in age group 45-64 years (0.586 [0.548-0.627], p<0.0001) and ≥65 years (0.124 [0.115-0.133], p<0.0001) than in <45 year group. There was an interaction between age and RUCC in influencing lupus death risk, with higher lupus/all-cause death risk in non-metro urbanized (p<0.001) and less urbanized areas (p=0.034) than in metro-urbanized areas in decedents ≥65 years.
Conclusion: This study reveals an association between rural-urban residence and odds of dying from lupus after adjusting for sex, ethnicity/race, and age. Comprehensive studies to identify determinants of higher lupus deaths in metro-urbanized areas are needed to address the poor lupus outcome in the high-risk populations.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2818

OP0267 THE PREDICTIVE ACCURACY OF CARDIOVASCULAR RISK PREDICTION TOOLS IN INFLAMMATORY ARTHRITIS

Keywords: Diagnostic tests, Cardiovascular disease, Prognostic factors

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Background: Cardiovascular risk prediction tools designed for the general population often underestimate and occasionally overestimate cardiovascular risk in individuals with rheumatoid arthritis. Incidence of cardiovascular disease is also recognised to be increased in individuals with other inflammatory arthritides.
Objectives: To investigate performance of three common cardiovascular risk prediction tools (QRISK-3, Framingham Risk Score and Reynolds Risk Score) in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS). We also compare performance in patients with psoriasis, since it is closely related to PsA, and a non-inflammatory disease, osteoarthritis (OA).
Methods: We utilise primary care records from the Clinical Practice Research Datalink (CPRD) Aurum database and identify individuals with diagnostic codes for each condition. We calculated their 10-year cardiovascular risk using each risk tool, and compared this to their observed outcomes. Discrimination (how well the tool separates CVD cases and non-cases) was assessed using time-dependent (to account for censoring in follow up) Area-under-ROC-curve (AUC), sensitivity, specificity, positive and negative predictive values (using 10% and 20% predicted risk to determine high risk of CVD). Calibration (how well predicted risks match observed risks) of each risk prediction tool was assessed by comparing the observed and predicted risks in deciles of predicted risk for each disease group.
Results: Time-dependent AUC for QRISK3 ranged between 0.697 for patients with osteoarthritis to 0.815 for patients with psoriasis, indicating reasonably good predictive performance (Figure 1). AUC for the Framingham Risk score were similar, whilst the Reynold's Risk Score achieved slightly lower AUCs in this cohort, ranging between 0.640 for patients with osteoarthritis and 0.752 for patients with psoriasis. In general, the Framingham Risk Score was reasonably well calibrated for each condition but underpredicted risk for patients with RA or OA. The Reynold's Risk Score tended to underpredict CVD risk, whilst the QRISK3 score overpredicted CVD risk, especially for the most high-risk individuals.
Conclusion: In general, CVD risk for individuals with RA, AS, PsA, psoriasis, or OA were less accurately predicted using each of the 3 CVD risk prediction tools than the reported accuracies in the original publications. There is a need for specific risk prediction tools for rheumatic conditions.

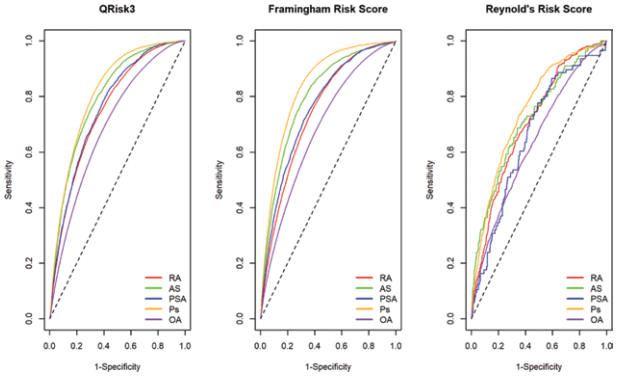


Figure 1. ROC curves for cardiovascular risk prediction in each rheumatic disease using the QRISK-3, Framingham and Reynolds Risk Scores.

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Disclosure of Interests: David Hughes Grant/research support from: This study was supported by a grant from a charitable organisation, the Psoriasis and Psoriatic Arthritis alliance (PAPAA)., Sizheng Steven Zhao Grant/research support from: This study was supported by a grant from a charitable organisation, the Psoriasis and Psoriatic Arthritis alliance (PAPAA).
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OP0268 IMPACT OF MENOPAUSAL TREATMENTS IN FUNCTIONAL DECLINE ON WOMEN WITH RHEUMATOID ARTHRITIS

Keywords: Pregnancy and reproduction, Rheumatoid arthritis, Real-world evidence

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Background: Women with Rheumatoid Arthritis (RA) experience changes in disease development and progression surrounding reproductive and hormonal events, including menopause. In our prior work, women with RA had better functional status prior to menopause and experienced worsening functional decline after menopause [1].
Objectives: The purpose of this study is to investigate how menopausal treatments affect functional decline in women with RA.
Methods: Women with RA participating in the Forward Databank from 2000 through 2022 with a reported menopausal status or not having a menstrual period for 1 year were eligible. Women who were on hormonal contraceptive were excluded. Hormonal replacement therapy (HRT) users were matched 1:1

to non-users by year of HRT initiation (index date). The primary outcome was function measured by Heath Assessment Questionnaire (HAQ) and HRT as primary exposure. Descriptive statistics were used to characterize patients at baseline by HRT exposure. Gaussian GEE models were used (robust SE) to assess the association between HAQ and HRT adjusting for the following confounders: demographics, reproductive history, clinical measures, and treatments. Best model was searched using QIC in a backward selection manner.

Results: 4123 women who have initiated HRT were matched by year of initiation to 4123 non-HRT users after menopause (mean year was 2004). At baseline, HRT users tended to be younger, have higher income, shorter reproductive length, and more comorbidities. No differences were found in pain and patient global as well as DMARD treatment, although HRT-users had higher use of non-hormonal treatments (Table 1). Overall, patients had a median follow-up of 6 years (IQR 3- 10) years with 2 years (IQR 1- 4) years of HRT exposure. HRT users had consistently better HAQ (although with a small effect) when compared to non-users (coef. -0.02 (95% CI, -0.03; -0.01) P<0.001). HAQ was also inversely associated with the age when women started menopause (-0.008 (95%CI (-0.009; -0.006), P<0.001); each year after menopause the HAQ increased by 0.008, which was slight better for HRT users (Figure 1).

Conclusion: HRT use was associated with better functional status, although of modest magnitude. Longer reproductive duration seemed protective for function, but worsening slightly after menopause. Future work is needed to assess the safety profile of HRT regarding incidence of malignancies, cardiovascular events, and osteoporosis.

REFERENCE:

[1] Mollard E, Pedro S, Chakravarty E, Clowse M, Schumacher R, Michaud K. The impact of menopause on functional status in women with rheumatoid arthritis. Rheumatology (Oxford). 2018 May 1;57(5):798-802.

Table 1. Baseline comparison of HRT users vs non-users in matched sample

Variable, mean (SD) or %	Non HRT users n=4123	HRT users n=4123	p
Age, yr	62.8 (10.7)	60.3 (9.3)	0.000
White race, %	92.3	94.3	0.000
Education, yr	13.49 (2.26)	13.80 (2.29)	0.000
Annual income, 10^3 US$	44.8 (31.29)	54.0 (31.98)	0.000
Married, %	61.1	71.2	0.000
RA duration, yr	15.1 (12.21)	15.7 (12.27)	0.013
Menopause age, yr (n=8215)	45.8 (8.00)	43.1 (8.77)	0.000
Reproductive life, yr (n=7383)	33.1 (8.10)	30.4 (8.81)	0.000
Ever pregnant, % (n=4270)	87.9	88.2	0.748
Current smoker, %	7.0	5.7	0.011
BMI, kg/m^2	28.9 (7.24)	27.6 (6.38)	0.000
RD Comorbidity Index (0-9)	1.7 (1.53)	1.8 (1.51)	0.027
HAQ-DI (0-3)	1.2 (0.70)	1.1 (0.70)	0.000
Patient global (0-10)	3.6 (2.48)	3.5 (2.49)	0.706
Pain VAS (0-10)	4.0 (2.78)	3.9 (2.80)	0.667
csDMARD use, %	78.1	78.7	0.454
TNF use, %	38.2	38.1	0.946
NTNF use, %	7.4	7.4	0.933
Non hormonal meds (gabapentin, SSRI, SNRI), %	20.3	26.1	0.000

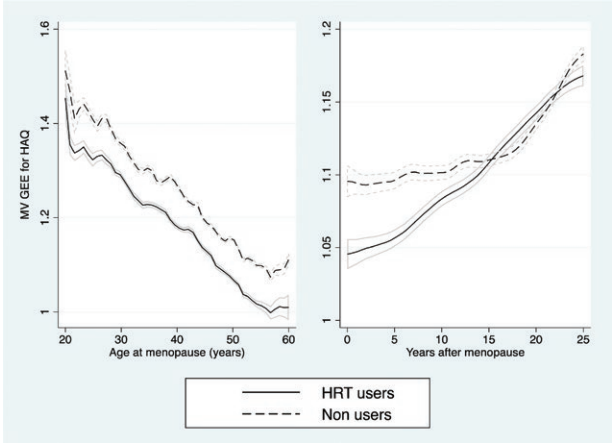


Figure 1. Projections from the multivariate GEE model for HAQ against (left) age at menopause (years); (right) years after menopause. Model adjusted for cubic spline with 4 knots (48, 61, 70 & 83 years), White race, education (yrs), total income, employment, marital status, RA duration, smoking, alcohol use, BMI, RD comorbidity index, NTNF use, and non-hormonal treatments, and age at menopause/years after menopause

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4660

OP0269

DEVELOPMENT AND EVALUATION OF MACHINE LEARNING ALGORITHMS FOR THE PREDICTION OF OPIOID-RELATED DEATHS AMONG UK PATIENTS WITH NON-CANCER PAIN

Keywords: Outcome measures, Artificial intelligence, Pain

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Background: There has been a sharp rise in opioid use for non-cancer pain globally, including for rheumatic and musculoskeletal conditions. Despite increased awareness of adverse effects, they remain commonly prescribed in most countries. Clinical prediction models (CPMs) offer the possibility of assessing individual risk allowing better allocation of resources towards those at risk. Machine learning (ML) approaches can address nonlinear relationships and complex interactions between variables and are increasingly used to develop CPMs.

Objectives: To develop, validate, and compare the performance of three CPMs based on regression and ML, which leverage primary care data to estimate the risk of opioid-related death in patients prescribed opioids for non-cancer pain.

Methods: Patients ≥18 years old without prior cancer who were prescribed any opioid between 01/01/2006 and 31/12/2017 were identified in the Clinical Practice Research Datalink (CPRD), representative of national patient data from UK primary care. Only new opioid users were included. Index date was date of first prescription, with censoring at withdrawal from the CPRD or after not having an opioid prescription for two years. Baseline data were extracted from each patient's records, including demographic information, comorbidities, concomitant medications, and the opioid type being prescribed. 49 candidate predictors were used to train three competing risk models: a Fine&Gray regression model with LASSO regularisation, a survival random forest (RF), and a neural network (DeepHit). The outcome was opioid-related mortality and other cause mortality the competing event, defined using a curated ICD-10 codelist. Predictive performance of the models, like area under the receiver characteristic operator curve (AUCROC) were calculated using 5-fold cross validation.

Results: We included a total of 1,029,681 patients, of which 1,240 experienced an opioid-related death, and 52,833 experienced a competing death. The Fine&Gray, RF and DeepHit models achieved average AUCROC values of 0.83(95% CI: 0.81-0.85), 0.78(0.77-0.79) and 0.81(0.80-0.82) respectively (Figure 1). At optimum risk cut point, as per Youden's index, the models achieved sensitivities of 0.82(0.78-0.85), 0.75(0.67-0.82) and 0.80(0.78-0.83), and specificities of 0.78(0.73-0.82), 0.75(0.68-0.83) and 0.78(0.75-0.8) when predicting 12-month risk, respectively. In the Fine&Gray model, factors associated with increased risk were history of substance use disorder (hazards ratio [HR]: 3.40, 95% CI:3.12-3.69) and alcohol abuse (HR:3.07, 95% CI:2.93-3.22). COPD (HR:1.53, 95% CI:1.48-1.58) and moderate liver disease (HR:1.31, 95% CI:0.99-1.63) were the comorbidities associated with highest risk. Morphine (HR:2.39, 95% CI:2.08-2.69) and oxycodone (HR:1.10, 95% CI:1.00-1.20) at initiation and concomitant gabapentinoids (HR:1.99, 95% CI:1.80-2.18) and benzodiazepines (HR:1.30, 95% CI:1.24-1.36) were associated with an increased risk. HR for rheumatologic diseases was 1.08 (95% CI:1.01-1.14).

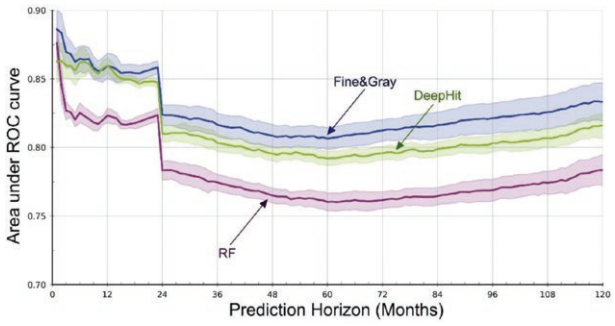


Figure 1. AUCROC of the three models vs. prediction horizon of the model. 95% CI of mean performance shaded.

Conclusion: The Fine&Gray and DeepHit models showed comparable discriminative performance. Substance abuse, lung and liver comorbidities, morphine or oxycodone at initiation and co-prescription of gabapentinoids and benzodiazepine, were some of the factors associated with a higher risk of opioid-related mortality.
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Disclosure of Interests: None Declared.
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OP0270 TARGETED THERAPIES FOR SEVERE IMMUNE-RELATED ADVERSE EVENTS OF IMMUNE CHECKPOINT INHIBITORS ARE NOT ASSOCIATED WITH A WORSE PROGNOSIS

Keywords: Targeted synthetic drugs, bDMARD, Malignancy

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Background: In about 10% of patients, the immune response to immune checkpoint inhibitors (ICI) exceeds the anti-tumor response and leads to autoimmune complications (immune-related Adverse Events, irAEs), which can sometimes be severe and require the use of targeted therapies. Two studies recently reported a deleterious impact of targeted therapies on the survival of patients with irAEs.
Objectives: To compare overall survival in patients treated or not with a biological or targeted synthetic DMARD (b/tsDMARD) for an hospitalized irAE.
Methods: All adults included in the French national health database who initiated an ICI between 2014 and 2019, for any type of cancer, were retrospectively analyzed. Follow-up was analyzed between 2013 to 2020, to have a one-year look-back and one year look-ahead period. The occurrence of an irAE during ICI treatment or in the 12 months after its last administration was defined by the combination of (1) hospitalization for a cause evoking an irAE of any nature, except endocrinopathy, and (2) either the discontinuation of the ICI, or the initiation of corticosteroids, or of a conventional DMARD or a b/tsDMARD, or a new recognition as a long-term disabling condition (LTD) for an autoimmune or inflammatory disease. Patients with irAE treated with b/tsDMARD were matched (1:3) at the time they initiated b/tsDMARD to those who did not initiate b/tsDMARD, using a dynamic propensity score calculated every 30 days. The propensity score included gender, age, type of cancer, type of ICI, time from cancer to initiation of ICI and from initiation of ICI to irAE, use of corticosteroids, hospitalization in intensive care unit, type of irAE, number of LTDs, Charlson's index and FDep social deprivation index. Overall survival was compared between the two groups using a Cox model. A sensibility analysis restricted to gastrointestinal and rheumatic irAEs was performed.
Results: 71,723 patients (men: 66.0%, median age: 66 years) initiating an ICI were analyzed. An hospitalized irAE occurred in 7883 patients (11.0%). irAE occurred at a median time of 72 days after ICI initiation, and the 4 more frequent were gastrointestinal (inflammatory colitis, 4.7%), cardiologic (2.0%), rheumatic (1.8%), and pulmonary (1.7%). Median patient follow-up after irAE was 356 days. Mortality after irAE was 4.8% at 1 month and 11.3% at 3 months. After matching, 325 patients were treated for an irAE with a b/tsMDARD (Infliximab (57.7%), Rituximab (25.5%), Tocilizumab (4.2%), Vedolizumab (3.3%), others (9.3%)), including 257 and 40 for a gastrointestinal or rheumatic irAE, respectively. They were compared to 975 patients who were not treated with a b/tsDMARD. The median time from ICI initiation to irAE was well balanced by matching (93 versus 92 days, respectively). ICI was discontinued in 25.4% of b/tsDMARD treated patients patients within 3 months after the irAE, compared to 20.9% in the group not treated with a b/tsDMARD. Mortality after irAEs was 6.8% and 7.6% at 3 months, respectively, and 16.0% and 17.9% at 6 months, respectively. Overall survival whatever the type of irAE did not significantly differ in patients treated with or without a b/tsDMARD (HR=0.87, CI=[0.74, 1.03]), or in patients treated for a rheumatic irAE (HR=0.80, CI=[0.51, 1.25]). Overall survival was significantly improved in gastrointestinal irAE in patients treated with a b/tsDMARD compared to patients not treated with a b/tsDMARD (HR=0.80, CI=[0.66, 0.97]).
Conclusion: In one of the largest study to date in terms of number of hospitalized irAEs and number of b/tsDMARD-treated patients, targeted therapies were not associated with a worse prognosis and significantly improved overall survival in patients with induced colitis, the most frequent and one of the most severe irAEs.

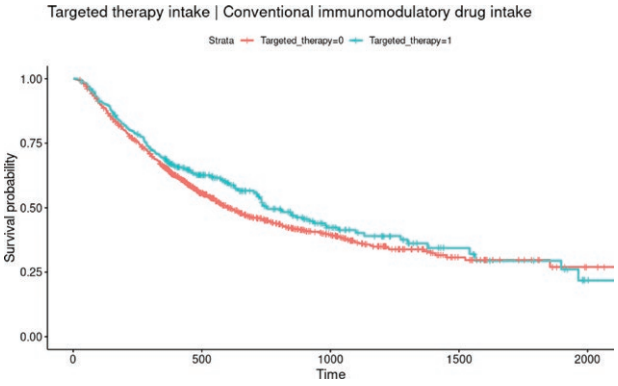


Figure 1. Overall survival in days in patients treated with a b/tsDMARD (blue) or not (red)

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OP0271 INCIDENCE OF PSORIATIC ARTHRITIS AND PREVALENCE OF UNDIAGNOSED CASES IN A UK PRIMARY CARE POPULATION FOLLOWED PROSPECTIVELY FOR 2 YEARS - RESULTS FROM THE TUDOR RANDOMIZED CLINICAL TRIAL

Keywords: Psoriatic arthritis, Skin, Epidemiology

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Background: The incidence of psoriatic arthritis (PsA) in a psoriasis population has been reported to be somewhere between 20 to 300 per 10,000 person years (p-yrs) (1,2), the wide range reflecting differences in the population setting and the methods of ascertaining a diagnosis. A higher incidence is generally found in studies combining active screening and physical examination. However, accurate estimates of incidence and prevalence of undiagnosed disease are needed to inform the timing and cost-effectiveness of community screening in a general population with psoriasis.
Objectives: To determine the annual incidence of PsA in a UK primary care population with pre-existing psoriasis over two years after excluding baseline prevalence of existing and undiagnosed disease.
Methods: TUDOR (Total bUrDen of psORiasis) was a multi-centre, prospective, two-arm parallel-group cluster randomised controlled trial of the early identification of PsA by annual rheumatological assessment (termed Early Surveillance (ES) arm) versus standard care (SC) arm in people with psoriasis identified in primary care. Participants in the ES arm were recruited from primary care records held in 72 participating practices, invited to attend for a health check that included a screening examination for psoriatic arthritis and if the screen was positive their general practitioner was requested to refer them to the local rheumatology service to confirm a final diagnosis of PsA. The incidence reported here is from the ES arm, excludes prevalent cases of PsA identified at baseline and reports incidence at follow-up visits at 12 and 24 months.
Results: In the ES arm, 64 of 826 participants (7.7% (95% CI: 5.9, 9.6)) had a diagnosis of PsA, of whom 43 of 793 were diagnosed from the initial screening

visit, corresponding to a prevalence of undiagnosed PsA at baseline of 5.4% (95% CI: 3.8, 7.0). Fourteen of 511 participants attending a 12-month screen developed PsA over that interval giving an incidence of 274 per 10,000 p-yrs (95% CI: 132 to 416 per 10,000 p-yrs) and another 7 of 444 participants attending the 24-month visit developed PsA giving an incidence of 158 per 10,000 p-yrs (95% CI: 42 to 274 per 10,000 p-yrs). The combined incidence over 2 years was 220 per 10,000 p-yrs (95% CI: 127 to 313 per 10,000 p-yrs).

Conclusion: In the ES arm of TUDOR where participants with psoriasis were screened and examined for the presence of PsA at baseline, 12 months and 24 months, the estimated cumulative incidence of PsA over a 2 year period was 220 per 10,000 p-yrs, that is in keeping with a higher incidence of PsA than that found when relying on health records alone. The long term clinical and cost-effectiveness of screening from the TUDOR trial remains under investigation.

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OP0272 EARLY RESPONSE IN RHEUMATOID FACTOR LEVELS PREDICTS SUBSEQUENT CLINICAL RESPONSE TO DISEASE MODIFYING TREATMENT OF RHEUMATOID ARTHRITIS

Keywords: Prognostic factors, Rheumatoid arthritis, Treat to target

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Background: Rheumatoid factors (RF) are well established prognostic biomarkers in rheumatoid arthritis (RA), but the clinical relevance of their dynamics is not yet well understood. Here, we evaluate the implications of changes in RF levels in RA patients with newly initiated disease modifying (DMARD) treatment.
Objectives: To analyze how early responses of RF levels relate to subsequent disease activity outcomes in RF positive RA patients initiating DMARD treatment.
Methods: We analyzed data from 1999 RA outpatients, starting either a conventional (csDMARD) or biologic/targeted synthetic DMARD (btsDMARD). RF response to treatment was defined as a ≥50% reduction in RF levels or complete seroconversion to RF negativity. We investigated the prognostic implication of early RF response on the timing of achieving disease control as defined by Simplified Disease Activity Index (SDAI) low disease activity (LDA) or remission (REM) in patients with SDAI moderate or high disease activity (MDA/HDA) at baseline. We analyzed the first two years of each treatment segment; patients, who did not reach LDA/REM within two years, or patients who switched therapy within this time frame were censored in this Kaplan Meier analysis. In a Cox proportional hazard model we adjusted the observed effects for gender, age and disease duration, as well as for SDAI at month 3.
Results: RF response (as defined above) to treatment was observed in 11%, 25.5% and 41% of RF positive RA patients at 3, 6 and 12 months after treatment initiation, respectively; RF response was seen in comparable frequency in csDMARD and btsDMARD treated patients (Table 1). LDA or REM by SDAI in patients with MDA or HDA was achieved significantly earlier in RF responders as compared to non-responders (Wilcoxon p=0.042 for csDMARDs, p=0.005 for btsDMARDs). Crude effects of RF response on achieving LDA/REM were highly significant in the Kaplan Meier analysis (p<0.0001; Figure 1) and remained so after adjusting for multiple variables including disease activity levels at 3 months (p<0.0001); in a pooled analysis of all DMARD starts (N = 736), the adjusted Hazard Ratio (HR) for LDA or REM in the RF response group was 1.73 (95% confidence interval: 1.23 to 2.42), compared to the RF non-responders.

Table 1. Baseline data and RF response rates at month 3 after start of csDMARD or btsDMARD therapy; RF response is defined as ≥50% reduction in baseline RF levels or complete seroconversion to RF negativity.

	csDMARD	btsDMARD
N total	1394	566
% female	76.2	81.8
Disease duration years (median [IQR])	0.32 [0.00, 4.8]	5.92 [2.17, 13.32]
SDAI baseline (mean (SD))	18.78 (12.91)	19.11 (13.00)
% RF elevated at baseline	58.82	62.19
RF in U/ml (mean (SD))	187.29 (411.79)	201.58 (430.04)
N RF positive with follow-up data available	801	332
% seroconversion 3 months	3.6	2.7
% 50% reduction 3 months	10.5	8.4
% 50% reduction or seroconversion 3 months	**11.9**	**10.2**

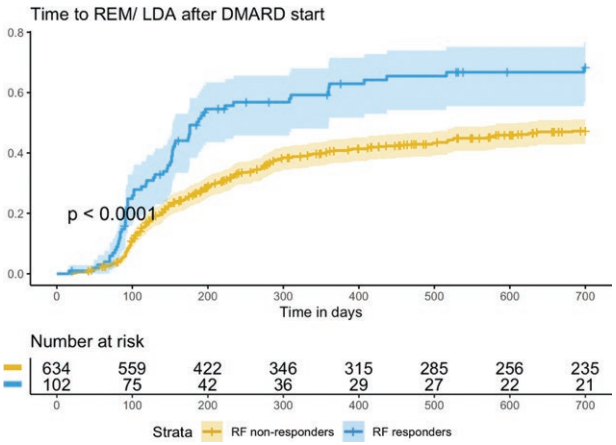


Figure 1. Time to event analysis (inverted Kaplan Meier curve) showing time to first SDAI LDA or REM (SDAI≤11) in RF positive RA patients who started DMARD treatment in MDA/HDA; analysis is stratified by RF response (50% reduction in RF levels or seroconversion at 3 months) or non-response (neither 50% response nor seroconversion); observations were censored at 2 years or switch of treatment (whichever was first). Panel displays pooled analysis of csDMARD starts (n=502) and btsDMARD starts (n=234).

Conclusion: Change in RF levels or complete seroconversion at the 3-month timepoint predict the achievement and timing of treatment goals within a 6 to 24-month period after treatment initiation. This finding was independent of disease activity improvement at 3 months, and may therefore serve as an additional early biomarker in assessing a patient's future chance of achieving treatment targets in RA.

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OP0273 LONGITUDINAL TRAJECTORIES OF RENAL FUNCTION IN ANCA-ASSOCIATED VASCULITIS: FINDINGS FROM THE EXPANDED MASS GENERAL BRIGHAM COHORT

Keywords: Kidneys, Organ damage, Vasculitis

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Background: Renal vasculitis, leading to a spectrum of chronic kidney disease (CKD) and end-stage renal disease (ESRD), is common in ANCA-associated vasculitis (AAV). The longitudinal course of renal dysfunction in AAV has only recently been described quantitatively.(1, 2)
Objectives: To confirm and further describe the longitudinal trajectory of renal function in an expanded AAV cohort.
Methods: We included patients from the Mass General Brigham AAV cohort, a consecutive inception cohort (2002-2022). We required at least 2 measurements of renal function including one "baseline" measurement (+/- 30 d from treatment initiation date, the index date). Renal function was assessed up to monthly between -12 m and +24 m relative to the index date. We used group-based trajectory modeling to identify renal function trajectories. Between-group differences (between all 4 groups) were assessed using the chi-square test and Kruskall-Wallis tests; time to ESRD was compared using the log-rank test.
Results: Among 375 patients, we identified 4 renal trajectory groups: rapid decline (N=23 [6%]), impaired (N=109 [29%]), preserved (N=216 [58%]), and recovery (N=27 [7%]) (**Figure 1**). Median posterior probability of group membership was >0.99, indicating excellent model fit. Age, sex, race and ANCA type were not statistically different between groups. Baseline comorbidity (by Charlson Comorbidity Index) was highest in the rapid decline group, and higher in the impaired compared to the preserved and recovery groups (p<0.001; **Table 1**). There was a strong trend toward hypertension being more common in the rapid decline and recovery groups vs the impaired and preserved groups (p=0.06). The baseline Birmingham Vasculitis Activity Score was higher in the rapid decline (6 [4, 7]) and recovery (6 [4, 9]) groups, compared to the impaired (5 [4, 6.5]) and preserved (4 [3, 6]) groups (p<0.001). ESRD occurred in 49 patients, including

22 (96%) in the rapid decline group, compared to 11 (10%) in impaired, 15 (7%) in preserved and 1 (4%) in the recovery group. Median time to ESRD was <1 m in the rapid decline group vs 3.5 y (IQR 0, 6.8) in impaired and 2.5 y (IQR 0, 5.6) in the preserved group (log-rank p<0.001). ESRD was attributed to active AAV in 91% of cases in the rapid decline group, compared to 45% of impaired and 33% of the preserved group (p=0.01). Clinically significant CKD (eGFR<30 ml/min/1.73m2) was present in a majority of the impaired group at 1, 2 and 5 y, but was less common in the preserved group (p<0.001 at all 3 timepoints).

Conclusion: We confirmed 4 distinct renal trajectory groups in an expanded AAV cohort. Trajectory groups were distinguished by differences in baseline comorbidity, rates of ESRD and CKD, and etiology and timing of ESRD. These findings emphasize the need for additional studies investigating temporal factors mediating these associations.

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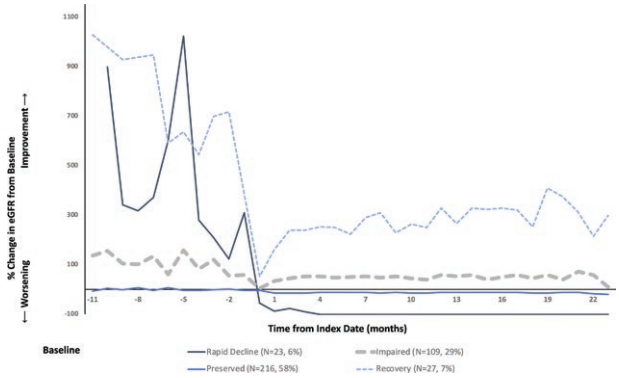


Figure 1.

Table 1.

	Overall (N=375)	Rapid decline (N=23)	Impaired (N=109)	Preserved (N=216)	Recovery (N=27)	p-value
Baseline characteristics						
Age at diagnosis (mean, SD)	62 (17)	65 (17)	64 (16)	61 (17)	64 (18)	0.22
Female (N, %)	226 (60)	13 (57)	63 (58)	136 (63)	14 (52)	0.60
BVAS/GPA (median, IQR)	5 (4-6)	6 (4-7)	5 (4-6.5)	4 (3-6)	6 (4-9)	<0.001
Charlson Comorbidity Index	3 (1-5)	5 (3-7)	4 (2-6)	2 (1-5)	3 (2-5)	<0.001
Diabetes mellitus (N, %)	50 (13)	3 (13)	16 (15)	29 (14)	2 (7)	0.80
Hypertension	135 (36)	13 (57)	40 (37)	69 (32)	13 (48)	0.06
eGFR (±30d, median, IQR)	51 (21-88)	7 (6-10)	27 (18-39)	82 (56-97)	10 (8-16)	<0.001
Outcomes						
Permanent ESRD*	49 (13)	22 (96)	11 (10)	15 (7)	1 (4)	<0.0001
Due to active AAV	30 (61)	20 (91)	5 (45)	5 (33)	0 (0)	0.01
Time to ESRD (y)*	0.1 (0.0-3.5)	0.01 (0-0.1)	3.5 (0-6.8)	2.5 (0-5.6)	10 (10-10)	<0.001
CKD ≥III at 1 y	210 (56)	23 (100)	93 (85)	67 (31)	27 (100)	<0.001
CKD ≥III at 2 y	144 (49)	13 (100)	62 (70)	58 (33)	11 (69)	<0.001
CKD ≥III at 5 y	88 (48)	10 (100)	37 (69)	36 (34)	5 (38)	<0.001

*Among patients who experienced ESRD.

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Disclosure of Interests: None Declared.
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Self-management and education

OP0274-HPR

PATIENTS' AND CLINICIANS' PERSPECTIVES AND EXPERIENCES ON EDUCATION AND SUPPORT ABOUT METHOTREXATE: FINDINGS FROM A SURVEY TO 24 EUROPEAN COUNTRIES

Keywords: Patient information and education, Nursing, Disease-modifying drugs (DMARDs)

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Background: Methotrexate (MTX) is the first-line drug in the treatment of rheumatoid arthritis (RA) and many other rheumatic and musculoskeletal diseases (RMDs). It is widely recognized that patients prescribed with this, or other similar drugs, should be properly educated, namely by rheumatology nurses,[1] to better understand why and how to take it, the possible side effects and how to prevent and manage them. However, high disparities may exist across European countries regarding patient education (PE) and support about MTX.

Objectives: To assess patients' and clinicians' perspectives and experiences on education and support received about MTX treatment in Europe.

Methods: A survey was developed by a team of international researchers and clinicians, including rheumatology nurses (from adult and paediatric care), a pharmacist, a rheumatologist, and patient representatives. Common and sample-specific questions were conceived for adult patients or carers (≥18 years) of children/young with RMDs, nurses, and physicians working in rheumatology in Europe. The survey was available in English and, for patients, in 12 additional languages, disseminated between May and December 2022. Ethics committee approval was obtained (116_CEIPC/2022_IPC).

Results: Complete responses were obtained from 1536 patients (52% with RA), 154 careers, 335 nurses, and 299 physicians (96% rheumatologists), from 24 European Countries, mainly from Northern (nurses) and Southern Europe (patients and physicians) (Table 1). Only 28% of patients had a specific nurse consultation when they started oral MTX, slightly increasing when the subcutaneous form was prescribed (42%), with variations across Europe, being higher in the Western (43%) and Northern (39%) and lower in Eastern (29%) and Southern (11%). These patients' perspectives are somewhat in line with physicians' perspectives, although according to nurses the access to them is higher, independent of the form of prescription (Table 1). Clinicians perceive higher opportunities to discuss patients' MTX concerns than the patients themselves (Table 1). Patients had more opportunities to voice their concerns (≥7 on a scale from 0 to 10) about MTX before starting it, in Western (57%) and Northern (42%) than in Southern (36%) and Eastern (31%) Europe. According to 47% of nurses, PE occurs on the same day of prescription, with the consultation lasting between 10-30 minutes in 50% of cases or even less than 10' (15%). 37% of nurses do not perform MTX-related follow-up appointments. Only half of the nurses (49%) received specific training to advise patients about MTX (data not shown).

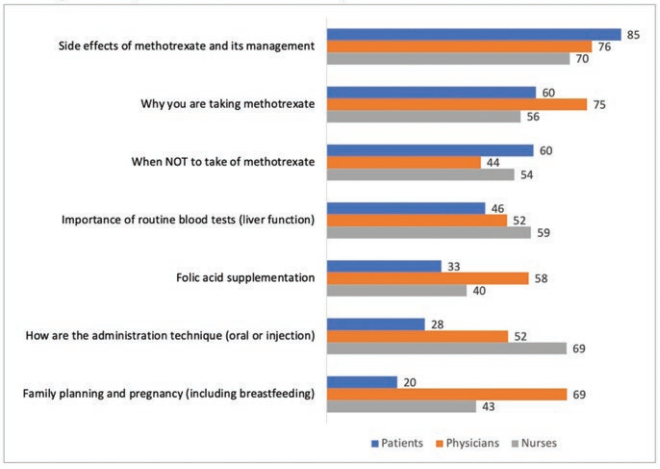
Table 1. Distribution of survey responses across Europe and education opportunities about MTX

		Patients and carers (n=1690)	Nurses (n=335)	Physicians (n=297)
European Region[a]	% North	22	52	21
	% South	37	10	46
	% East	21	17	22
	% West	20	21	11
Based on your experience, does every patient that initiates MTX have at least one educational session with a nurse?	% Yes, both oral and SC	--	61	30
	% yes, only if SC	--	25	31
Have you had an educational session with a nurse at start of…				
oral MTX?	% yes	28	--	--
SC MTX?	% yes	42	--	--
Opportunity to discuss concerns about MTX before starting it (from 0 to 10)	mean (SD)	4.9 (3.9)	7.6 (3.3)	8.6 (1.8)

a. According to United Nations geoscheme.

The priority ranking of topics to be addressed was also assessed, with agreement on the top one (side effects and their management) (Figure 1).

Figure 1 – Top-ranked* areas to address in patient education about Methotrexate



* Ordered by patients' ranking. All participants were given a list of 16 side-effects and asked to select top 5.

Around 77% of patients had/have concerns about potential unpleasant side effects, which were discussed with health professionals (mainly with rheumatologists) in 68% of the cases, despite not being clarified 46% of the times.

Conclusion: PE and support about MTX are unequal across Europe and can be improved by providing opportunities to clarify concerns, namely by providing patients with more access to nursing consultations. There is an overall agreement between patients and clinicians regarding key information areas of education, although a tailored approach is required.

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OP0275-HPR 'IT'S A LOT TO TAKE IN': A SYSTEMATIC REVIEW OF THE INFORMATION NEEDS OF PEOPLE WITH INFLAMMATORY ARTHRITIS STARTING METHOTREXATE

Keywords: Patient information and education, Disease-modifying drugs (DMARDs), Systematic review

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Background: Guidelines recommend that people with Inflammatory Arthritis have access to tailored information when starting treatment with Methotrexate (MTX) [1]. It is not known what information people with Inflammatory Arthritis (IA) need to take MTX. Many people have concerns about the risk-benefit profile of MTX and so do not start or continue MTX.

Objectives: To identify and synthesize knowledge of the characteristics, content and preferred format of information that people with IA need to take MTX.

Methods: A PROSPERO registered systematic literature search (CRD42022325249) was conducted using Medline, Embase, Cinahl, PsychInfo, GreyEU, Web of Science and Open Dissertation databases. All full-length articles and conference abstracts identifying information and support needs of people with Inflammatory Arthritis, and oral or sub-cutaneous MTX as the main conventional DMARD considered in the study were assessed for inclusion. The systematic review was conducted and reported in accordance with the Joanna Briggs Institute methodological guidance for Mixed Methods Systematic Reviews [2] using a convergent integrated approach and the standards of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) Statement.

Results: 8468 studies were identified. 169 studies were reviewed by full text of which 13 studies met the inclusion criteria. Seven quantitative studies used cross-sectional internet (n=2), postal (n=2), and rheumatology clinic (n=3) surveys, two mixed methods studies, one cross-sectional survey with clinic observations and one cross-sectional survey and focus group, and four qualitative (one interview and three focus group) studies. The combined studies included 3425 adults over the age of 18 years (20-84 yrs), most were female (71%, n=2434). More people were enrolled into studies (n6) involving people with a diagnosis of Rheumatoid Arthritis (n=2278) than studies (n=7) involving people with IA (n=840). Studies were conducted in the UK (n=4), Netherlands (n=3), Spain (n=2), Australia (n=2), Canada (n=1) and Japan (n=1) and reported in English. Quantitative results were qualitized. Three main themes were identified, with an overarching theme of a need for person-centred information about Methotrexate. 1: Information to support understanding and acceptance of the need for treatment with MTX: Learning about IA diagnosis, rationale for MTX in context of IA, benefits of MTX) 2: Concerns about MTX: including risk, likelihood and management of side effects, drug interactions, impacts upon lifestyle, developing medication self-management skills 3: Content and methods of information delivery: information sources, importance of support from healthcare professionals (hcp), family and friends, value of a therapeutic relationship with hcp.

Conclusion: People with IA have individual, multi-faceted information and support needs about both their condition and MTX, to enable them to take MTX. Further research is recommended to explore a) the expectations of information and support before receiving information about MTX, b) experiences of people receiving information at the time of starting MTX and c) strategies to improve information and support during the course of taking MTX.

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Disclosure of Interests: None Declared.

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OP0276-HPR DAY-TO-DAY FLUCTUATIONS OF FATIGUE IN SYSTEMIC SCLEROSIS

Keywords: Patient reported outcomes, Quality of life, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is a rare auto-immune disease with a huge impact on physical health as well as social well-being, with fatigue being the major problem experienced by patients with respect to their well-being [1].

While fatigue is being reported to be fluctuating and unpredictable, the dynamic nature of fatigue is not well understood [1, 2].

Objectives: To examine the within-person fluctuations and clinically meaningful changes in fatigue, as well as the within-person association of fatigue and time-varying determinants in SSc.

Methods: We performed a daily-diary study in adult patients with a clinical diagnosis of SSc. Patients with pulmonary hypertension or severe pulmonary function disturbances (i.e. vital capacity and diffusing capacity for carbon monoxide < 50%) were excluded. During 14 days patients completed daily assessments at four fixed time points (i.e. 9 a.m., 1 p.m., 5 p.m., 9 p.m.) of fatigue severity and time-varying determinants (i.e. negative affect, positive affect, pain, quality of sleep and perceived exertion of physical activity. As proxy for clinical meaningful change in fatigue the probability of acute change(PAC) was assessed, i.e. the chance that change in day-to-day fatigue levels exceeded the minimally clinical important difference for fatigue[3]. Using multilevel models the within-person fluctuations in fatigue and its association with time-varying determinants were examined. Based on the extent of clustering, the time-varying determinants were disentangled into their corresponding levels (within persons (within day as well as across days) and between persons) and added to the multilevel model. Models were adjusted for confounding (i.e. BMI, sex, age, and history of covid-infection) where appropriate.

Results: Fifty-seven patients with SSc, 35% male with mean(SD) age 54.3(14.6) years, participated. The disease duration was mean(SD) 6.9(4.8) years and 29.8 % was diagnosed with diffuse cutaneous SSc. Eighty percent of all observations were completed. During the study period, change in day-to-day level fatigue exceeded the MCID mean(SD) 5.7(1.9) times. The PAC was mean(SD) 0.44(0.14), ranging from 0.08-0.77. For fatigue a between-person variation of 49% and a within-person variation of 51% was observed. With respect to confounders, only BMI was significant in the models for time-varying negative and positive affect. The final models showed significant within-person association with fatigue fluctuations and changes in time-varying determinants within a day, between days and between patients (Table 1).

Conclusion: This is the first quantitative study showing that fatigue in SSc is characterized by a dynamic course and that approximately half of the day-to-day fluctuations are clinically meaningful, confirming the results of qualitative studies[2]. Moreover, when patients reported more fatigue than usual, they also reported more pain, more negative affect, less positive affect, more perceived exertion of physical activity, and worse quality of sleep than usual.

Table 1. Association of within-person fluctuations of fatigue and time-varying determinants at each level. All β are significant (p-value< 0.05). * corrected for BMI, β: regression coefficient, N/A: not applicable.

Within-person fatigue fluctuation	β (95% ci) level 1 within- day	β level(95% ci) 2 between days	β level (95% ci) 3 between patients
Negative affect *	0.44(0.37, 0.51)	0.41(0.31, 0.50)	0.72(0.46, 0.98)
Positive affect *	-0.60(-0.66, -0.53)	-0.61(-0.69, -0.53)	-0.74(-1.05, -0.42)
Pain	0.46(0.39, 0.52)	0.49(0.37, 0.62)	0.48(0.33, 0.62)
Perceived exertion of physical activity	0.19(0.15, 0.24)	0.25(0.16, 0.35)	0.76(0.48, 1.04)
Quality of sleep	N/A	-0.20(-0.27, -0.14)	-0.48(-0.80, -0.16)

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OP0277-HPR **WITHDRAWN**

OP0278-HPR

THE RELATIONSHIP BETWEEN HEALTH LITERACY AND TREATMENT STATUS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS WHO ACHIEVED LUPUS LOW DISEASE ACTIVITY STATE: THE TRUMP2-SLE PROJECT

Keywords: Patient reported outcomes, Systemic lupus erythematosus, Treat to target

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Background: Although the relationship between health literacy and treatment outcome has been reported in certain illnesses[1,2], it remains unclear how health literacy affects treatment selection.
Objectives: This study aims to determine the relationship between health literacy and treatment status in patients with systemic lupus erythematosus (SLE) who have achieved a low disease activity state (LLDAS).
Methods: A cross-sectional study was conducted on 266 SLE patients who had achieved LLDAS, registered in the TRUMP[2]-SLE study[3], an ongoing multicenter cohort study conducted at five academic centers in Japan. The main exposure was the health literacy (scores 0-56) of the enrolled patients, as measured by the 14-item Communicative Critical Health Literacy Scale (FCCHL). The primary outcomes were daily glucocorticoid dose, hydroxychloroquine (HCQ) use, and immunosuppressant use. A secondary outcome was chronic damage measured by Systemic Lupus International Collaborating Clinics-Damage Index (SLICC-DI). Odds ratios (ORs) to assess the relationship between health literacy and treatment status were estimated with adjustment for confounders (age, sex, income, education, disease duration, and SLICC-DI).
Results: The median age of the patients was 47 years (interquartile range [IQR], 36-58), 88% were female, and the median disease duration was 13 years (IQR, 7-20). The median FCCHL score were 3.1 (IQR, 3.0-3.5). The median daily glucocorticoid dose (prednisolone equivalent) was 4 mg (IQR 2-5). HCQ was used in 122 (45.9%) and immunosuppressant was used in 174 (65.4%) of enrolled patients, respectively. FCCHL score were not associated with glucocorticoid dose (r^2 = 0.015). FCCHL score was not statistically different between patients with and without immunosuppressants (median 3.07 [IQR, 2.79-3.36] and 3.04 [IQR, 2.71-3.29], p = 0.81) but statistically different between patients with and without HCQ (median 3.14 [IQR, 2.36-3.93] and 3.00 [IQR, 2.71-3.25], p = 0.0028). After adjustment for confounders, HCQ use was significantly associated with FCCHL score (OR: 2.27, 95% confidence interval: 1.19-4.36). FCCHL score was not statistically associated with SLICC-DI (r^2 = 0.0091).
Conclusion: Even among the SLE patients who have achieved LLDAS, the preference of HCQ usage may vary depending on health literacy.
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OP0279-HPR

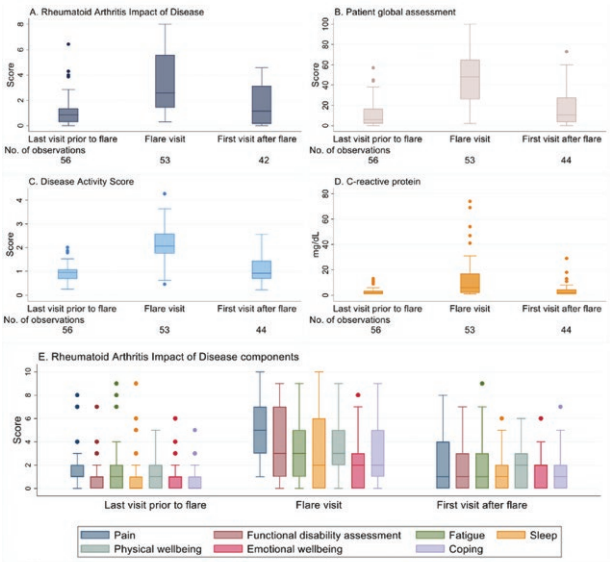
RESPONSIVENESS AND DISCRIMINATIVE ABILITY OF THE RHEUMATOID ARTHRITIS IMPACT OF DISEASE (RAID) SCORE TO CLINICAL DISEASE FLARE: DATA FROM THE DMARD TAPERING ARCTIC REWIND TRIALS

Keywords: Rheumatoid arthritis, Patient reported outcomes, Self-management

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Background: The Rheumatoid Arthritis Impact of Disease (RAID) is a patient-reported outcome measure (PROM) originating from a EULAR initiative. It supports patient-centered care and shared decision-making between patient and rheumatologist regarding treatment and adjustment of medication. RAID could be a useful tool in remote monitoring, and its association with disease activity is thus of interest.[1] It is not known if RAID is responsive and discriminative to disease activity flares.
Objectives: To explore the responsiveness of the RAID (sum score and single domain scores) to clinical disease flare and to assess its discriminative ability with regard to flare.
Methods: We used data from the two Norwegian multicenter ARCTIC REWIND trials assessing tapering of TNFi and csDMARDs (ClinicalTrials.gov: NCT01881308).[2] Eligible participants had RA (ACR/EULAR 2010 criteria), were in sustained remission for ≥12 months on stable DMARDs with Disease Activity Score (DAS) remission combined with no swollen joints at inclusion. In the TNFi trial, patients were randomized to stable TNFi or tapering to discontinuation of TNFi (stable csDMARD comedication). Patients in the csDMARD trial were randomized to stable or half dose treatment for the first year. Study visits with assessment of disease activity were conducted every four months, if a flare was suspected between visits the patient was seen within a week. Flare was defined as a combination of DAS>1.6, an increase in DAS ≥0.6 units from the previous visit and minimum two swollen joints. If a patient did not fulfill these criteria, a disease flare could be recorded if both the patient and investigator agreed that a clinically significant flare had occurred. If a flare was confirmed, the full dose of the study medication was reinstated or (in the stable-dose group) treatment adjusted according to current recommendations. We evaluated the median RAID score and single domains at the last visit before flare, flare visit and first visit after flare in relation to the suggested ≤2 RAID threshold for patient acceptable symptom state (PASS), and assessed the changes between those visits using Wilcoxon rank-sum test.[3] The ability of RAID to detect disease flare was assessed using the area under the ROC curve (AUC) based on logistic regression models. For comparison, similar analyses were performed for patient global assessment (PGA), DAS and C-reactive protein (CRP).
Results: Of the 248 patients included, 159 (64%) were female. Mean (SD) age and disease duration were 56 (11.8) and 6.3 (5.7) years. For patients who experienced a flare the median (IQR) RAID score was 0.9 (0.3, 1.4) at last visit prior to flare with 86% of scores within the PASS range. At the flare visit median RAID was 2.6 (1.4, 5.6) with only 30% of scores within the PASS range (**Figure 1**). Similar changes were observed in DAS, PGA and CRP. All seven RAID domains increased significantly at the flare visit (p-values < 0.01), with the largest increase in pain (**Figure 1**). According to the AUC analyses the estimated accuracy in detecting flare was high for RAID, but higher for DAS and PGA. CRP was less accurate in detecting flare (**Table 1**).
Conclusion: There was a clinically and statistically significant increase in median RAID score and all single domains of RAID at flare visit, supporting its responsiveness to clinical disease flares. Both RAID and PGA discriminated well between flare and non-flare, hence both PROMs might contribute in early identification of flare and patients who might need an adjustment of medication, in a regular clinical setting as well as in remote monitoring of disease activity.
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Figure 1. Outcome measures at last visit before flare, at flare visit and first visit after flare. A: Rheumatoid Arthritis Impact of Disease[1] B: Patient global assessment VAS[2] C: Disease Activity Score[3] D: C-reactive Protein[4] E: Rheumatoid Arthritis Impact of Disease components



[1]RAID (NRS 0-10). [2]Patient global assessment (PGA) of the disease activity from 0-100 mm on a visual analogue scale. [3]Disease Activity Score (0-10) includes a swollen joint count of 44 joints, assessment of tender joints by Ritchie Articular Index, erythrocyte sedimentation rate (ESR) and PGA. [4]C-reactive protein (mg/dL)

Table 1. AUCs (95% CI) for performance of outcomes in discriminating between flare and non-flare.

Outcomes	AUC (95% CI)
RAID score	0.88 (0.82, 0.93)
PGA	0.92 (0.88, 0.96)
DAS	0.94 (0.90, 0.99)
CRP	0.77 (0.68, 0.84)

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OP0280-HPR VALIDATION OF A NEW GLUCOCORTICOID-SPECIFIC PATIENT REPORTED OUTCOME QUESTIONNAIRE (THE STEROID PRO)

Keywords: Outcome measures, Quality of life, Patient reported outcomes

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Background: Glucocorticoids are used in the treatment of a broad range of rheumatic conditions but can have a significant impact on health-related quality of life[1]. In-depth qualitative interviews with patients who have experience of glucocorticoid treatment for their rheumatic disease, from the UK, USA and Australia, were used to develop candidate items for a treatment-specific Patient Reported Outcome Measure (PROM): the Steroid PRO.

Objectives: We aimed to complete the development and validation of the Steroid PRO through use of a cross-cultural validation study.
Methods: This was a cross-sectional online study of adults taking glucocorticoids for a rheumatic disease, from the UK, USA, Australia and New Zealand. A steering committee comprising methodologists, clinicians and patient research partners (PRPs) oversaw the study. The survey was distributed via social media with support from patient groups. Baseline data included: (i) demographics - age, gender, country, ethnicity, educational level; (ii) clinical information - diagnosis, glucocorticoid dose; (iii) 40 candidate items for the Steroid-PRO, developed in a previous qualitative study; (iv) EQ5D-5L. Optional follow-up data collected 3-5 days later: (i) the Steroid PRO candidate items; (ii) a condition change question. After descriptive analysis, iterative testing with Rasch measurement model and exploratory factor analysis (EFA) informed item reduction and established structural validity, reliability and unidimensionality of the final Steroid PRO. Item reduction was based on clinical importance, lack of fit to the Rasch model, and redundancy. Evidence of discriminative validity of the Steroid PRO was established by comparing its scores for participants receiving lower dose glucocorticoid (up to 10 mg) versus higher dose (>10 mg). Intraclass correlation (ICC) between baseline and follow-up was calculated for patients who reported 'no change' compared with 3-5 days ago.
Results: A total of 946 patients returned complete responses at baseline (follow-up: 447 responses). They were from UK, n=743 (78.5%); USA, n=139 (14.7%); Australia, n=59 (6.2%). Their mean age was 57.6 (SD=13.6); 833 (88%) were women. They were treated for inflammatory arthritis (n=194), connective tissue disease and/or vasculitis (n=398), and giant cell arteritis and/or polymyalgia rheumatica (n=341). A total of 25 items were removed due to floor effects and lack of fit to the Rasch model. Iterative discussions between statisticians, clinicians and PRPs ensured that items of high clinical importance were retained. The remaining 15 items showed a satisfactory fit to the model. EFA suggested a scale structure with four domains: Participation (4 items), Appearance (3 items), Psychological (5 items), and Treatment concerns (3 items). PRPs were involved in naming the domains. The 4-domain structure was supported by the Rasch model, confirming construct validity; $\chi 2$=47.82 (DF=36), p=0.899; and reliability (Person Separation Index, PSI=0.757). Total scores also fitted the Rasch model, therefore both domain and total scores will be psychometrically appropriate for use as a repeated measure. A good fit to the Rasch model was also seen across the disease groups with items distributed equally across the three groups. Patients on a lower glucocorticoid dose had lower Steroid PRO domain scores than those receiving higher dose (discriminant validity). ICC between baseline and follow-up ranged from 0.892 to 0.942 (95%CI 0.868 to 0.953) suggesting excellent (test-retest) reliability.
Conclusion: The final Steroid PRO is a 15-item, valid and reliable 4-domain scale measuring the impact of glucocorticoid therapy on HRQoL of people with rheumatic diseases.
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PARE Abstract Session

OP0281-PARE LUPUS EUROPE'S PATIENT ADVISORY NETWORK – A HUGE DOUBLE SUCCESS

Keywords: Patient-led research, Best practices

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Background: Financial and Human Resources are 2 key issues faced by European federations of Patient organisations and limiting their impact. This reality is

also a vicious circle as volunteers are needed to deliver the projects, themselves forming the basis to fund the organisation. When preparing its 2018-2023 strategic plan, Lupus Europe was confronted with this frustrating reality with incomes stagnating around 40,000€/year, just enough to cover its basic operations, convention and few limited size projects.
Objectives: To step change Lupus Europe's development and unlock both the funding and volunteering recruitment bottlenecks by creating an energising Patient Advisory Network.
Methods: As part of its 2018-22 strategic plan discussions, the Lupus Europe designed the structure of a Patient Advisory Network (PAN) as a key way to reach its objectives, in a way that combined both volunteers and sponsors motivation factors. For volunteers, the PAN offered an opportunity to move from a victim of the disease position to that of an actor of the change, working together with other fellows, equally motivated. Initial patients were selected based on their positive energy and desire to change things and grow skills. We identified (web based) opportunities to grow the needed skills, and encouraged participation. Finalising the team charter, drafted by the board, became the first exercise of the team, which then dedicated itself to support projects from academics, clinicians or industry, and work on own lupus Europe projects. The visibility of the PAN quickly became an additional motivator, and many applications to join were received. PAN members agreed that potential remuneration for their work would accrue to Lupus Europe and be used to motivate and reward the group. For sponsors, we redesigned our partnership proposal, using the PAN to step change engagement levels. We asked our sponsors for a leap of faith that we could drive this to success, and that they would benefit from it as much as we would by making our community more vibrant. We also offered to all a sample of what the team could do to support key projects. We engaged with academics to identify valuable projects and asked them to give training to the team. In parallel, we invested some of our savings to fund initial costs, and provided soft skills training for the group. Two years later, we applied and obtained EMA recognition as EMA eligible entity. Early successes boosted the team's morale and helped reach out to more partners. This in turn allowed us to "put the program on steroids", multiplying our support to the group and the number of projects generated by Lupus Europe. Things we had never imagined being able to do by ourselves, like the Living with Lupus survey (5000+ answers) or lupus100.org (info on lupus in 18 languages) were "suddenly" all feasible. In 2022 we recognised most experienced members as Fellows offering an aspirational "path for growth" to all, from trainee to ambassador to expert and Fellow.
Results: 5 years after its start, the PAN is now rich of 23 highly motivated members working on 25 projects (50/50 industry/non-industry) including some of our own design. It is recognised as a best in class organisation, and keeps growing, enabling us to achieve results we could not have dreamed of 5 years ago. Lupus Europe's funding jumped from 40k in 2017 to more than 300k in 2021, allowing to do more projects, invite PAN members to SL Euro or EULAR and professionalise some of our support. It also increased our independence from pharma, as we feel free to say no to any funder we don't fully feel happy with (and we did it already twice!)
Conclusion: The PAN project as transformed lupus Europe from a minimalist federation to the key voice and support of people living with lupus in Europe.
Acknowledgements: Many thanks to LUPUS EUROPE's Patient Advisory Network members whose enthusiasm and commitment has been critical for the success of this project.
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OP0282-PARE WORLD ARTHRITIS DAY, A UNIQUE CAMPAIGN

Keywords: Best practices

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Background: Since its establishment in 1996, World Arthritis Day is celebrated every year on the 12th of October, across the world and in my country as well. Several events-campaigns, take place aiming to raise awareness among the general public, stakeholders, politicians and people with Rheumatic and Musculoskeletal diseases, health care professionals, elected officials and the relevant governmental authorities. Giving the message to the public about the early symptoms, the importance of early diagnosis, the importance of proper therapy and the importance of managing the disease is the aim of the existence of the day. Our organisation traditionally for this day, organizes big Campaigns among all the above in addition to achieve recognition of the Organization in the General Public. In 2021 for the first year, we established very successfully a new campaign called, <Wear me>. In this campaign, the idea was to engage People and Companies to wear a T-shirt for us. In 2022 the target was bigger than the previous year. The idea was to create text through a photo. As we all know, picture talk more to people than words. These days, with the internet overuse and Social Media's role in our lives, words and pictures pass in front of us, in hundreds every day. We wanted a strong IMAGE to make people curious about RMDs and about our organisation.
Objectives: The major objectives were:

- To raise awareness of WAD.
- To increase the Prevention of RMDs.
- To make our league more popular.
- To become more familiar and recognizable with our new name and logo.
-T o get involved in the campaign more people than in 2021.

Methods: Six months before the WAD, a Task Force for the campaign was established, to build the Action Plan. Without h a very good plan, we can't have a successful campaign. After several meetings and discussions, the action plan was ready four months before the WAD.Main target: to involve 2000 People (we had 1.400 people in 2021), to wear a t-shirt with our logo on the 12th of October 2022. In addition, our prompt was to take a photo, post it on their social media, use the hashtag (#) and the name of our organisation. The Action plan had four Phases: First, contact the people and the companies, by writing two letters, one for those that they participated in the previous year to ask them to stand with us, again and the second one for new companies or people that we wanted to approach for participating in this year campaign.Second, to find funds for the campaign and for purchase the T-Shirts.Third, to deliver all the T-shirts on time and fourth, to be able to Post or Re- Post all the photos on organization's FB page.
Results: Our results were over and above our expectations! Achieving goals: We contact many small and medium local companies, coffee chains, hairdressing salons, gyms, physiotherapists,health insurance companies, pharmacies etc... Schools and municipality employees. We involved doctors, nurses, famous people, athletes, actors, singers, journalists, football players, athletes' teams, politicians and the president of Cyprus Parliament.A lot of TVs and Radio Channels cover the campaign, even some of them wore our T-shirts during the shows all day. We reached over and above our target of the use of T-Shirt.2700 people wore the t-shirt with the logo of our organisation, on the 12th of October 2022. The FB results were extremely positive! The organization's FB page reached 30000 views, the whole week. The FB page had an average of 213% increase in visiting compared to the previous week.
Conclusion: Compare to the previous year, almost twice the number of participants wore our t-shirt. Engagement on Facebook was satisfactory. The hashtag was applied as a caption to the pictures taken. There was a big discussion on social media and TV shows about the campaign. A lot of people were asking to buy the t-shirt to support our league. A lot of people were calling our offices to get information about our services and our programs. The general conclusion is that the need of raising awareness for RMDs is still high.
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[2] Assessment of action plan of WAD, 2022
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OP0283-PARE HELLENIC LEAGUE'S AGAINST RHEUMATISM'S SCHOOL OF HEALTH EDUCATION

Keywords: Quality of care, Patient information and education, Best practices

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Background: The more time healthcare professionals spend with patients the better the health outcomes become. Therefore, education seems to play a crucial role for the quality of life not only for the patients but also for the health care costs and the future cost projections that depend on the health outcomes of everyone.
Objectives: Aim of the School of Health Education is to give the opportunity to participants to familiarize themselves with frequently used terminology in everyday clinical practice, to become accustomed in using the common medical language when describing their symptoms to their doctors so that they will have a common ground. Basic goal of this education is for every patient to understand a bit more about concepts such as medications, adverse events, pharmacovigilance etc.

Methods: Interactive live events, of approximately 2hour duration, have already take place in 15 cities of Greece. In the year 2020 COVID restrictions did not allow for such events to be organized. The project will start again during 2023. Speakers in the events were: rheumatologists, general physicians, anesthesiologists, psychiatrists, psychologists, gynecologists, clinical pharmacologists and others.
Results: Over 1800 patients, caregivers, members of the public, stakeholders, members of the local authorities, healthcare professional and others participated in the live events. Handouts and printed material from HELAR/ELEANA were given to participants as well an evaluation form to complete. The events generated a lot of press locally and nationally, with 4 press conferences, 25 press releases, 18 TV interviews and 10 radio interviews.
Conclusion: Publicity and participation in the events showed that patient education is quite important for the patients and the local communities. Since 2020 and the COVID pandemic there has been a shift towards public health issues and health education creating a unique opportunity for HELAR/ELEANA's School of Health Education to be adapted and become once more available for the patients living with an RMD. This time the new version could be either a virtual version or a live version for many more patients, caregivers and the public to be able to attend.
Acknowledgements: Hellenic League Against Rheumatism is grateful to Dimitrios Kouvelas, MD, BPharm, PhD, Professor of Pharmacology and Clinical Pharmacology, Head of the Dept of Clinical Pharmacology, School of Medicine, Aristotle University of Thessaloniki for his precious scientific contribution, implementation and for being the main speaker voluntarily. The School of Health Education was awarded the bronze prize by the Health Care Business Awards in 2019.
Disclosure of Interests: KATY ANTONOPOULOU: None declared, ATHANASIA PAPPA: None declared, DIMITRIOS KOUVELAS Consultant of: DEMO, STILVI, Nadia Malliou: None declared, Katerina Tsekoura: None declared, MACHI SALAMALIKI: None declared, EVANGELIA OIKONOMOULA: None declared, KATERINA ROUSTA: None declared.
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OP0284-PARE IPARE – GLOBAL COLLABORATION OF PATIENT ORGANISATIONS FOR THE BENEFIT OF RMD PATIENTS

Keywords: Patient information and education, Best practices, Geographical differences

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Background: Rheumatic and musculoskeletal diseases (RMDs) are a burden for individuals and a challenge to healthcare systems. Comparing the current and the future number of rheumatologists and the frequency of RMDs, studies state a huge gap. Another key issue is the uneven distribution of rheumatologists in most countries. These deficits are glaring in low and middle income countries in particular. In sub-Saharan Africa e.g. just in the past 20 years more attention has been drawn to non-communicable diseases. Great challenges exist in Latin America. Patient organisations (POs) offer information and assistance, are competence networks, represent and advocate for patients' interests and needs and play a pivotal role in healthcare systems.
Objectives: Overarching: With its activities IPARE aims at contributing to a world, where RMDs are recognized, prevented and cured, and patient-centredness is an integral part of health care delivery.
The **specific** aims are.

- To connect and exchange with national patient organisations and continental networks/organisations of patient organisations from other continents than Europe.
- To develop, step by step, a network of globally active national POs, national umbrella POs and continental POs.
- To initiate collaborative projects in the field of education, research, quality of care, congress and advocacy.
- To share best practices aiming at developing and supporting POs and pan-continental POs.
- To promote the access to and the exchange at conferences and congresses for RMDs.

Methods: IPARE is a PARE project group embedded in the PARE Sub-Committee „Community Relations", meaning all EULAR regulations will apply. A small project group consisting of representatives from South and Central America, North America, Africa and Europe has been established. We are aiming at enlarging the group (e.g. by having a representative from Asia), but the total number should not exceed 10 in order to work efficiently. After an introductory in-person meeting at the PARE Conference in October the members decided to meet virtually every 6-8 weeks. Webinars are offered every 2-3 months. Aspects of membership, objectives, mode of working were defined.
Results: The project group members identified - in spite of different health care systems, economic statuses and the extent of the deficits - certain commonalities like lack of rheumatologists (in particular lack of paediatric rheumatologists), shortage of health professionals (e.g. nurses, physiotherapists trained for the treatment of RMDs), delayed diagnosis, access to medical treatment according to internationally accepted treatment recommendations, insufficient non-pharmacological treatment, needs to educate the public and create awareness for RMDs and the situation of people with an RMD, research and patient involvement in research. The group developed a first list of items how these deficits could be tackled, how we can collaborate being aware of the fact that national peculiarities and features and language items have to be taken into account if any material will be produced. To avoid duplication and to check what already exists, an inventory list of informative and educational material is being established. A first webinar open to all representatives of international patient organisations is determined for February.
Conclusion: The project group members work with great enthusiasm, are eager to share knowledge and want to learn what can be implemented in their organisations and countries. In addition the group members focus on supranational issues. The project group members share, learn and convey to support implementation.
REFERENCE:
[1] Objectives have to be approved by the PARE Council.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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OP0285-PARE THE USE OF OBJECTS TO EXPERIENCE INFLAMMATORY RHEUMATIC DISEASES IN ORDER TO INCREASE KNOWLEDGE AND UNDERSTANDING THROUGH PERSPECTIVE- TAKING, WITH A FOCUS ON ENHANCING EMPATHY

Keywords: Patient information and education, Mental health, Education

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Background: People with chronic diseases often experience little sympathy towards their situation and are in many cases stigmatized. The deficiency of knowledge is one main problem that leads to said lack of understanding. For people with RMDs this leads to the exclusion from social life and has a negative impact on their mental health. To reverse this trend, more innovative methods are needed to promote understanding in society as well as in the personal environment of people with debilitating diseases. This abstract presents a Master-Thesis in the field of Intermedia, created by a Student with an RMD. The paper examines existing methods for communicating understanding of chronic illnesses through media using scenography. It assesses which methods of communication can be used to increase empathy towards physically disabled people and thereby improve their inclusion in society. Using the findings of this research, the student created a concept for a public exhibition.
Objectives: Promote empathy towards disabled and chronically ill people. Educate adults in their function as role models for children, to improve early inclusion. Achieve a long-term change in society, to foster inclusion of persons affected by an RMD in society.
Methods: Examples of different performances of illness and their impact on those affected are gathered and discussed. The analysis contains aspects of the communicative methods that have not yet been researched or sufficiently explored. In the field of rheumatic diseases there are not many innovative methods to educate society about the psychosocial impact that an RMD has on the person affected. Existing materials are mainly targeting patients or their close ones. Public campaigning primarily focuses on medical facts. Research shows that immersive experience is more effective in educating than reading, hearing, or viewing information. The combination of facts and an immersive experience strengthens the learning effect and can have a sustainable impact on people's behaviour. Through immersive experience, there is a possibility to build and strengthen empathy. These factors are significant for the structure of the exhibition.
Results: The concept of the exhibition is based on existing best practice examples and researched methods. The Visitors are confronted with the topic of chronic diseases in an immersive way. The exhibition is sequenced to first get the visitor's attention by vision, followed by the possibility to physically get in touch with the exhibition's artefacts that imitate various symptoms. For instance, they can try on splints or sit on a manipulated chair. The elaborated concept is enclosed within the original thesis, to present the path of experience with the contents. The developed artefacts were tested and are based on several interviews for their suitability and their effectiveness. Their relevance was confirmed.



Graphic 1. Mockup of the exhibition

Conclusion: Research underpins the need for innovative methods to promote understanding of people with RMDs. Considering research, the developed concept with a combination of facts and immersive experience is likely to be successful in strengthening empathy towards chronically ill people. The design of the mobile exhibition is scalable. The concept is gladly shared with other patient organisations and is ready to be put into reality.

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OP0286-PARE UNMET NEEDS IN RESEARCH, HOW PATIENTS CAN COLLABORATE:THE EXAMPLE OF NECESSITY

Keywords: Patient information and education, Sjögren syndrome, Patient reported outcomes

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Background: NeceSSity stands for "New Clinical Endpoints in primary Sjögren's Syndrome: an Interventional Trial based on stratifYing patients". International consortium involving 25 partners (20 academics, 4 pharma and 1 patient association) funded by the Innovative Medicines Initiative (IMI2), this public-private partnership between EU and EFPIA specifically requested the involvement of Sjögren's patients.

Objectives: Determine realistically the role patients should play and elucidate their added value in such a project.

Methods: A patient association has been included from the beginning of the project (even before submission) as partner and is involved in 6 out of 10 Working Packages (WPs).

Results: Patients were involved in the conception and design of the study. In particular, they established a Patient Advisory Group (PAG). The PAG participated in the creation of the website and the design of lay versions in several languages, reviewed and adapted protocol and consent forms, largely contributed to the creation of STAR, the new primary endpoint assessment score, and participated in dissemination and communication. Patients have an active advocacy role in this project. As the voice of a large Sjögren's community with sometimes major disparities in care, the PAG has been active in participating in the different meetings and supporting and promoting the project to the general public and Health Authorities. As a culmination of the first phase, 20 patients provided valuable input, particularly during the development of STAR, to ensure that the validated clinical endpoints are relevant for patients, raising issues that had not been considered fully, if at all. The opinions expressed by patients during the Delphi Survey contributed substantially to this evaluation tool, taking into account the patient's feelings, which are often poorly evaluated or ignored. This future "gold standard", which will be presented to the EMA and FDA, could not have been developed without the participation of patients. In addition, patients were invited to test a webapp that will serve as an evaluation tool throughout the clinical trial. The feedback from the PAG will contribute to the success of this patient-reported outcome tool and has helped to correct issues to ensure its success during the clinical trial.

Conclusion: Patient involvement in research is now widely accepted and the benefits are clear. The authorities now frequently require validation by patients. It is quite possible to work in harmony, bearing in mind the constraints and specificities of each stakeholder, in particular that patient participation is voluntary and that their health might not allow them to react immediately. Clinicians, researchers and patients have complementary skills and perspectives which, when shared, will strengthen the project.

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Disclosure of Interests: None Declared.

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OP0287-PARE PATIENT AND PUBLIC INVOLVEMENT IN THE IMPLEMENTATION OF RESEARCH

Keywords: Real-world evidence, Best practices, Patient information and education

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Background: Patient and Public Involvement and Engagement (PPIE) is now common practice in the design and delivery of arthritis research studies in the UK. Yet PPIE in the implementation of this research into practice is a novel and developing area. Coordinated, planned collaboration and relationship building with patients and the public in communities and health settings into which research will be implemented can facilitate greater impact of research findings. It can provide patients with accessible evidence based knowledge to enable more control in decision making about their own condition.

Objectives: To describe the work of an established group of patients and the public working collaboratively alongside healthcare professionals, researchers and knowledge brokers to actively implement arthritis research evidence into practice.

Methods: The Link Group (n=10 members) meets six times a year to provide meaningful patient and public input and oversight to all implementation projects delivered by the Impact Accelerator Unit, Keele University (UK). Members have links to community, charity, public and patient networks, helping to facilitate the movement of knowledge and evidence based innovations into wider use, nationally and internationally. Link Group task and finish meetings take place according to project demand to co-create strategies to implement research evidence. Roles and responsibilities are identified early on, members attend project operational core groups and ongoing feedback on implementation progress is provided. Link Group members work with researchers (to ensure evidence based messages are included in innovations), healthcare professionals (to discuss how innovations can be best used in clinical practice) and knowledge brokers (to design the finished output and collate all information). Patients, carers and the public contribute valuable knowledge to the process of implementation, including their own experiences of living with arthritis, attitudes and beliefs regarding the healthcare system and knowledge of networks to open up new ways to share innovations.

Results: Link Group members have:

- Co-developed funding applications and research designs to ensure early preparation for implementation, providing advice and support for methods of impact and implementation to be considered by researchers.
- Co-created patient facing resources in a range of formats and for different demographics. For example, evidence based guidebooks, posters, leaflets, animations and infographics for people with arthritis and people with long term pain and mental health (www.jigsaw-e.com / www.beefree.org.uk). The Link Group make sure the language in patient facing resources is easily understood, visuals are engaging and diversity is represented.
- Co-developed a simple, trusted guide summarising current physiotherapy arthritis research, making complex information more accessible and

consequently supporting high-quality care by facilitating discussions between patients and physiotherapists (https://evidence.nihr.ac.uk/wp-content/uploads/2020/09/Moving-Forward-FINAL-August-2020_Pages.pdf).
- Taken patient facing innovations and resources into local community and volunteer groups, given talks at peer-to-peer information events and shared resources digitally via social media to networks.

Conclusion: PPIE in implementation can facilitate the successful implementation of research evidence into practice, for the benefit of people with arthritis. An established patient and public group can provide community insight and 'real world' perspective which can strengthen diversity and reach, and make evidence based research innovations more accessible, relatable and useful in clinical practice. Link Group members have developed a sense of ownership of the innovations that are being implemented and as such are passionate about their work: *"Straightforward information and practical advice, choosing words and pictures to reflect a healthy life, working closely as a team, a cog within a wheel, creating something special, a resource with appeal"* - Link Group member.

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KD is part funded by the National Institute for Health and Care Research (NIHR) Applied Health Research Collaboration (ARC) West Midlands (NIHR 200165) and is an NIHR Senior Investigator (ID NIHR 200259).
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OP0288-PARE PATIENT PERCEPTIONS OF RHEUMATOID ARTHRITIS BLOOD WORK AND UTILITY OF A TEST PREDICTING RESPONSE TO NEW MEDICATION: A CROSS-SECTIONAL SURVEY IN THE ARTHRITISPOWER

Keywords: Biomarkers, Rheumatoid arthritis, Disease-modifying drugs (DMARDs)

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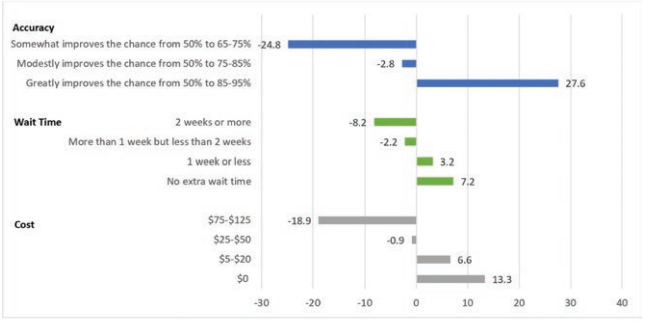
Background: No published studies have assessed the perspectives of people with RA (pts) on disease-related lab testing and its role in treatment decision-making.
Objectives: Our objective was to examine how pts perceive RA-related lab testing and pts' perceived utility of a blood test to predict treatment response to a new RA medication.
Methods: A cross-sectional survey was developed with input from pts, rheumatologists, researchers, and pt advocates. Members of ArthritisPower with a self-reported physician diagnosis of RA were invited to participate in the online survey which included questions related to reasons for lab testing, plus a choice-based conjoint analysis (CA) exercise to determine how pts value different attributes of a blood test to predict treatment response. For the CA, 48 different hypothetical test characteristics (bundles) were created based on different combinations of 3 test attributes (Accuracy, Wait Time, Cost), each with 3-4 levels. Each pt responded to 5 questions asking them to choose between two of these hypothetical tests, randomized by the Qualtrics survey platform.
Results: During May-June 2022, 405 RA pts completed the survey, of whom 86.7% were female, 89.9% white, mean age of 57.9 (SD 11.6) years. Pts were on the following medications: 75.1% csDMARD, 53.6% bDMARD, 17.8% tsDMARD (not mutually exclusive). Most pts perceived their doctor orders laboratory work to check for active inflammation (85.9%) or assess side effects of medications (81.2%). Pts reported that their rheumatologists most often ordered complete blood counts, liver function tests, CRP and ESR to monitor RA, and felt CRP was most helpful to themselves in understanding their disease activity (Table 1). Most pts worried their current RA medication would stop working (91.4%) and they would waste time trying an RA medication that may not work for them (81.7%). If pts were required to change RA treatments in the future, a majority (89.2%) would be very/extremely interested in a blood test that could help predict whether such new medication would be effective. Highly accurate test results (improving chance RA medication will work from 50% to 85-95%) were more important to pts than low cost (<$20) or minimal wait time (<7 days) (Figure 1).
Conclusion: Most pts consider RA-related blood work to be important for monitoring active inflammation and medication side effects, and felt CRP was most helpful in understanding disease activity. For a test predicting treatment response, patients valued accuracy over cost or wait time.

Table 1. Patient Perceptions of Utility of RA-Related Blood Work, n=405

	Used by Physicians To Monitor RA[a] n (%)	Used by Physicians When Considering Changing Medications[b] n (%)	Useful for Patients to Understand Disease Activity[c] n (%)
Complete blood count (CBC)	322 **(79.5)**	170 (42.0)	128 (31.6)
Liver function tests, kidney tests and/or complete metabolic panel	312 (77.0)	174 (43.0)	140 (34.6)
C-reactive protein (CRP)	269 (66.4)	162 (40.0)	197 **(48.6)**
Erythrocyte sedimentation rate (ESR)	238 (58.8)	181 (37.3)	174 (43.0)
Vitamin levels (e.g. vitamin D, iron, calcium)	118 (29.1)	66 (16.3)	63 (15.6)
None/I don't know	42 (10.3)	197 **(48.7)**	123 (30.4)
Vectra DA (multi-biomarker disease activity)	25 (6.2)	35 (8.6)	57 (14.1)

[a] Patients were asked to select which test(s) their rheumatologist orders for routine RA monitoring[b] Patients were asked to select which test(s) their rheumatologist orders when considering changing RA medications[c] Patients were asked to select which test(s) they consider most useful to understand their RA disease activityBolded values are top selections for each column

Figure 1. Relative Utility Value[1] for Each Attribute of a Patient Blood Test to Predict Whether an RA Medication Will Work Well for Them, n=405



[1]The measure of preference for each level of an attribute. The greater a level's relative utility value is, the more it enhances a bundle by being present.

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The promise of health literacy in clinical care

OP0289 INEQUITIES IN ARTHRITIS CARE IN CANADA: AN INTERSECTIONAL ANALYSIS OF BIPOC WOMEN

Keywords: Gender/diversity issues, Patient-led research, Health services research

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Background: Individuals that belong to ethnic minority groups are at greater risk of developing different forms of arthritis and often experience poorer health outcomes when compared to white patients[1]. BIPOC women are especially susceptible to inequities due to the social determinants of health such as education, income and housing[2]; yet interventions are rarely targeted to meet their specific needs, preferences and values.
Objectives: The aim of this community-led Survey was to identify observable disparities in access to and benefits from health care (HC) services between white and Black, Indigenous and Person of Colour (BIPOC) respondents who identified as Women.
Methods: ACE conducted a 33-question online Survey (Aug 2-19, 2022) in English and French. The Survey was conducted in partnership with Research Co., a public opinion firm. Respondents answered questions regarding sociodemographic information, HC access, HC providers, unfavourable experiences, and information seeking habits. Data were analysed in subgroups and aggregate (including incomplete survey responses). Chi-square tests (exact tests where possible) were used to test for associations.
Results: A total of 1,249 responses were received. 732 (59%) respondents identified as women, 484 (39%) men, 16 (1%) non-binary. Of the women who responded, 163 (22%) identified as BIPOC (including 39 Black, 58 Indigenous, 86 POC), and 569 (78%) as white. Women reported greater barriers to accessing HC compared to men, namely travel (29% vs. 19%) and previous unpleasant experiences (18% vs. 10%). More BIPOC women (68%) experienced barriers compared to white women (56%), the most prominent being time (40% vs. 30%) and language (21% vs. 5%). Overall, interactions with HC providers and rheumatologists were rated similarly between BIPOC women and white women. However, significantly less BIPOC women reported being comfortable asking about medications (27% vs 39%), discomfort (30% vs 43%), and pain (39% vs 50%). When asked what characteristics they looked for in HC providers, significant differences were revealed between BIPOC and white women **[Figure 1].** Overall BIPOC women (14%) reported experiencing discrimination based on gender twice as often as white women (7%), and seven times as often as white men (2%). Further, BIPOC women were seven times as likely to report experiencing ethnicity-based discrimination "often" (8.7%), when compared to white women (1.2%). Results were even more profound for Indigenous women who were 16 times as likely to report experiencing ethnicity-based discrimination "often" (19.6%), when compared to white women (1.2%). Both BIPOC men and women more often turn to family, friends, coworkers, traditional healers, and elders for health information when compared to white respondents. BIPOC women reported being less trusting of certain information sources when compared to white women, specifically patient organizations (11% vs 21%) and official public health websites (55% vs 70%).
Conclusion: Our findings suggest that BIPOC women face unique and disproportionate barriers as well as complex experiences of discrimination when accessing arthritis care. Importantly, BIPOC respondents, in particular BIPOC women, seem to benefit less from their HC interactions. The data further reinforce current literature that calls for the creation of culturally safe spaces and culturally sensitive resources. It is critical for all levels of the health care system to adopt an intersectional lens to better understand and address systemic inequities.

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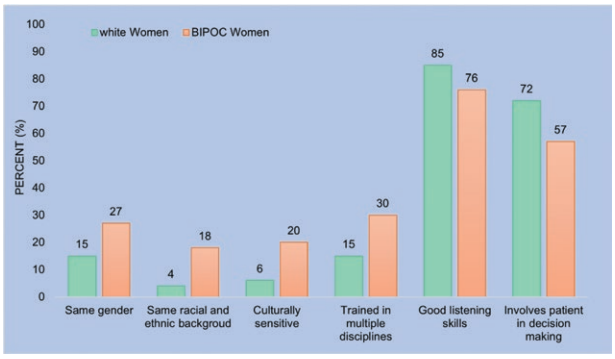


Figure 1. Preferred characteristics of HC providers (white vs BIPOC women)

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Disclosure of Interests: None Declared.
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OP0290 WORSE OUTCOMES LINKED TO ETHNICITY FOR THE EARLY TREATMENT OF REFRACTORY SLE: RESULTS FROM THE BILAG-BR

Keywords: Registries, Real-world evidence, Systemic lupus erythematosus

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Background: SLE more commonly affects non-White populations who suffer higher disease activity and greater damage accrual.
Objectives: To describe differential response of patients with moderate-severe SLE in the UK by ethnic background.
Methods: Patients commencing rituximab (RTX), belimumab or a standard of care medication (SoC) for SLE in the BILAG-BR were analysed over 12 months. Major clinical response (MCR) was defined as a SLEDAI-2K ≤4 at 12 months. Deprivation was measured using English indices of deprivation 2019 decile (EID, 1= most deprived, 10=least). MCR was compared using multivariate logistic regression (reference group: White background; adjusted for age, gender and EID). Missing data were imputed using random forest in R V4.2.1 (package: missForest V.1.5).
Results: 1601 SLE patients (Female=1447 [90.4%], median age [IQR]: 39.9 [31.0-50.6] years) commenced therapy from September 2010-September 2022 (RTX: N=1177, belimumab: N=193, SOC: N=231). 905 (56.5%) were White, 233 (14.6%) were Black, 197 were Indo-Asian, 81 (5.1%) were Chinese/ East Asian, and 60 were of Multiple-Mixed background and 125 (7.8%) preferred not to say. 1,364 (85.2%) patients were taking glucocorticoids (GC) at baseline (median dose [IQR]: 7 [4.5-11.1] mg daily). MCR was achieved in 901 (56.3%) patients at 12 months. Black patients had a higher SLEDAI-2K score at baseline compared with white individuals (Figure 1). Black, East-Asian/ Chinese patients, and Multiple-Mixed ethnic background patients received a higher GC dose at baseline (Table 1). Black, Indo-Asian and Multiple-Mixed background patients were more likely to be in a lower EID. In patients receiving RTX, Black (adjusted OR 0.36 [95%CI 0.25-0.52]) and Indo-Asian (0.42 0.18-0.96)) patients were less likely to achieve MCR. In patients receiving belimumab, Black (0.65 [0.44-0.96]) and Indo-Asian patients (0.29 [0.09-0.93]) were also less likely to have an MCR. Absolute reduction in SLEDAI-2K was similar for each ethnic group.

Table 1. Demographic and clinical data by ethnic background. Data presented as median (IQR) or N (%), with respective *p values* computed with chi² or Kruskall–Wallis test

	White	Black	Indo-Asian	Chinese/ East Asian	Multiple/ Mixed	*p-value*
	(N=905)	(N=233)	(N=197)	(N=81)	(N=60)	
Age (years)	43.9 (33.5-54.4)	39.2 (30.1-47.6)	36.2 (27.2-43.2)	32.3 (25.0-39.2)	35.0 (27.5-45.6)	<0.001
Female	816 (90.2)	220 (94.4)	168 (85.3)	74 (91.4)	57 (95.0)	0.035
Disease duration (years)	5.92 (2.90-11.8)	6.68 (3.31-11.3)	5.54 (2.73-9.93)	4.95 (2.74-8.20)	7.23 (4.11-10.2)	0.0854
Deprivation Decile (EID)	5.00 (4.00-7.00)	4.00 (2.00-5.00)	4.00 (2.00-6.00)	5.00 (3.00-7.00)	4.00 (2.75-6.25)	<0.001
Renal involvement (ever)	301 (33.3)	119 (51.1)	123 (62.4)	60 (74.1)	39 (65.0)	<0.001
Therapy						0.0808
SoC	125 (13.8)	28 (12.0)	41 (20.8)	9 (11.1)	5 (8.3)	
Rituximab	677 (74.8)	165 (70.8)	134 (68.0)	63 (77.8)	50 (83.3)	
Belimumab	103 (11.4)	40 (17.2)	22 (11.2)	9 (11.1)	5 (8.3)	
Current pulse steroids	291 (32.2)	68 (29.2)	77 (39.1)	20 (24.7)	10 (16.7)	<0.001
Current steroid dose (mg)	5.00 (2.00-8.50)	7.50 (4.00-12.0)	6.00 (3.50-10.0)	10.0 (5.50-18.0)	8.50 (5.00-15.3)	<0.001

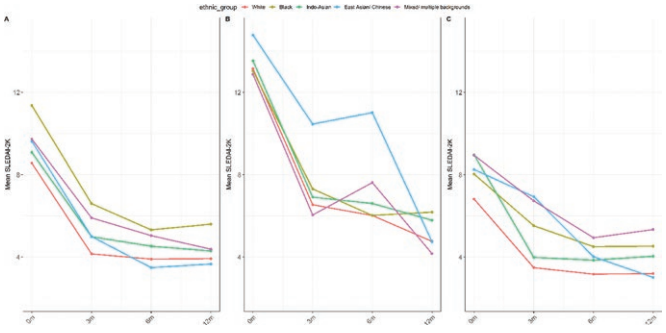


Figure 1. Mean SLEDAI-2K at baseline, 3, 6 and 12 months, in A) Rituximab (n=1089), B) Belimumab (n=179) and C) SoC (n=208) treated patients

Conclusion: Although absolute reduction in disease activity was similar across ethnic backgrounds, obtaining a MCR following treatment was lower in Black and Indo-Asian patients, in part reflecting higher baseline disease activity, but not explained by level of social deprivation; an observation not confined to a single treatment. There is a need for investigation into the drivers of these inequitable outcomes and reappraisal of treat-to-target strategies in these populations.

REFERENCES: NIL.

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Disclosure of Interests: Sarah Dyball: None declared, Mia Rodziewicz: None declared, Emily Sutton: None declared, Ben Parker: None declared, Ian N. Bruce Speakers bureau: GSK, Astra Zeneca, Janssen, Consultant of: GSK, Astra Zeneca, Aurinia, Lilly, Grant/research support from: GSK, Astra Zeneca, Janssen.

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Cell activation pathways in RMDs

OP0291 **ACUTE PHASE REACTANT OROSOMUCOID-2 DIRECTLY PROMOTES RHEUMATOID INFLAMMATION**

Keywords: Rheumatoid arthritis, Cytokines and chemokines, Synovium

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Background: Acute phase response is a systematic reaction of organisms. It occurs when the homeostasis of our body is broken by infection, tissue injury, and inflammation. Since most of these acute phase reactants can be rapidly secreted to the blood in response to infection or inflammation, they have been utilized as serum diagnostic markers to predict the activity and outcomes of chronic inflammatory diseases. In recent years, evidence has emerged that some of these acute phase reactants can go beyond simply being useful as diagnostic markers. Studies have shown that they can directly function as immune modulators.

Objectives: To determine whether orsomucoid-2 (ORM2), an acute phase reactant mainly synthesized in the liver, directly contributes to chronic inflammation.

Methods: ORM2 expression was determined by ELISA and immunostaining. Fibroblast-like synoviocytes (FLSs) and macrophages were cultured in the presence of recombinant ORM2. NF-κB and p38 MAP kinase expression levels were assessed by Western blot analysis. Knockdown experiments were carried out using siRNAs for NF-κB p65, p38, and glycophorin C (GYPC). Proximity ligation assay was performed to test the molecular interaction between ORM2 and GYPC. Recombinant ORM2 was injected into the affected joints of mice with IL-1β-induced arthritis.

Results: ORM2 expression was elevated in the sera, synovial fluids, and synovia of patients with rheumatoid arthritis (RA). Major cell types producing ORM2 were synovial macrophages and FLSs. Recombinant ORM2 robustly upregulated IL-6, TNF-α, IL-8, and CCL2 produced by macrophages and/or FLSs of RA patients via NF-κB and p38 MAPK pathways. GYPC was the receptor of ORM2 on synovial macrophages and FLSs. Such an increase by ORM2 was reproduced in mouse macrophages and FLSs. Intra-articular injection of ORM2 promoted the severity of arthritis in mice and accelerated the infiltration of macrophages in affected joints. Moreover, in RA patients, circulating ORM2 levels correlated with disease activity assessed by DAS28 and well represented radiographic progression in 2 years.

Conclusion: Acute phase protein ORM2 can directly increase the production of pro-inflammatory cytokines/chemokines by macrophages and FLSs and promote chronic arthritis in mice, suggesting that it could be a new therapeutic target for RA.

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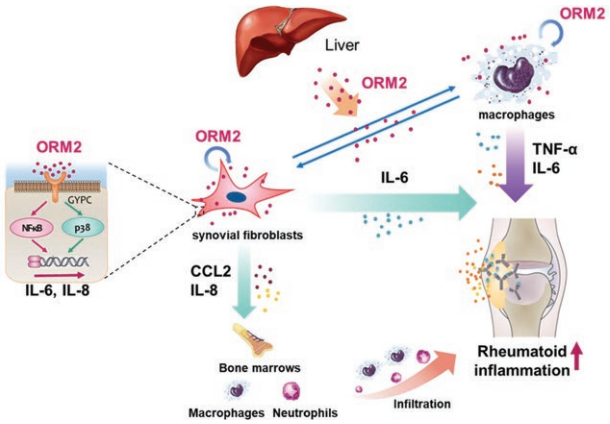


Figure 1. Hypothetical model for ORM2-dictated reciprocal activation of macrophages and FLSs in RA. Under high inflammatory conditions, ORM2 is actively produced from arthritic joints, particularly by stimulation of synovial macrophages and fibroblasts with TNF-α, IL-1, and Toll-like receptor-4 agonists, as well as from the liver. The secreted ORM2 in turn binds to a functional receptor GYPC on RA-FLSs, activates NF-κB and p38 MAP kinase pathways, and then directly induces production of pro-inflammatory cytokines (e.g., IL-6, TNF- α) and chemokines (e.g., IL-8, CCL2) via the two signaling pathways. Resultant cytokines and chemokine can amplify chronic inflammation by further activating macrophages and FLSs and by facilitating recruitment of monocytes and neutrophils to inflamed joints. As a result, more activated macrophages and FLSs can secrete greater amounts of ORM2 and thereby lead to ORM2-centered mutual activation of macrophages and FLSs, constructing a feed-forward cycle of rheumatoid inflammation.

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Disclosure of Interests: None Declared.

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Inborn errors of Immunity and autoimmune / inflammatory rheumatic disorders: What can we learn?

OP0292

MUTATIONS IN DNASE1L3 CAUSING FAMILIAL HYPOCOMPLEMENTEMIC URTICARIAL VASCULITIS AND EARLY ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Genetics/Epigenetics

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Background: Systemic lupus erythematosus (SLE) is a multisystemic autoimmune disease with several aberrancies in the immune system[1]. Genetics factors are central to understanding the pathophysiology especially in patients with monogenic lupus (single-gene mutation)[2]. Anecdotally, we observe a relatively high prevalence of familial SLE in our region (UAE/Arab regions). Studying the genetics of such cases have yielded gene mutations known to cause SLE. Here we report 3 siblings with mutations in *DNAES1L3* causing SLE and hypocomplementenemic urticarial vasculitis (HUVS)[3].
Objectives: To report the clinical and genetic presentation of 3 siblings with monogenic SLE and HUVS and discuss clinicopathologic correlations.
Methods: The patients were identified through our SLE clinical cohort. Informed consent was obtained from the patients/guardians to participate in our institution's "Mendelian Project" research study. The study is approved by the local IRB committee. Whole exome sequencing (WES) was performed. The results of the initial sequencing were analyzed in the context of the clinical presentation of SLE and HUVS.
Results: Genetic analysis via WES revealed a homozygous *DNASE1L3* variant at c.572A>G; p. Asn191Ser for the 3 affected siblings classified as variant of unknow significance (VUS). The mother and healthy sibling were heterozygous (carrier) for the variant. This indicate that the variant is segregating with the family for SLE. *DNASE1L3* variant c.572A>G, p.Asn191Ser is a novel variant that was not reported previously in the literature or human genetic mutation database (HGMD). Computational (in-silico) pathogenicity prediction tools predicted damaging effect of the variant (PolyPhen: damaging, SIFT: Deleterious, Conservation: high). Clinical and laboratory features are presented in Table 1. All three siblings developed HUVS as the initial manifestation which was confirmed by skin biopsy. In the older siblings who eventually met the criteria for SLE, the HUVS resolved as other SLE symptoms emerged. The youngest sibling has not met criteria for SLE and only has skin involvement with debilitating HUVS (tender lesions and swollen hands/feet). This patient was found to have very low levels of C1q without anti-C1q antibodies. Screening for mutations in C1q was negative. Of note, the HUVS has been the most severe in this patient.

Table 1. Clinical and lab features of the 3 patients.

	Patient 1	Patient 2	Patient 3
Age at onset	13 months	2 years	3 years
Age at SLE diagnosis	N/A	6 years	3 years
Current age	2 years	7 years	17 years
Clinical findings			
HUVS	+[#]	+	+[#]
Fever	+	+	+
Lymphadenopathy	+	+	-
Arthritis	-	-	-
Mucocutaneous ulcers	-	-	-
Glomerulonephritis	-	Class II/V	Class IV
Lab findings			
Positive ANA	-	+	+
Positive anti-dsDNA	-	+	+
Low C3/low C4	+/-	+/-	+/+
Low C1q/anti-C1q antibodies	+/-[$]	NA/NA	NA/NA
↓Hgb/↓WBC/↓plt	+/-/-	-/+/-	+/-/-
↓ IgG	-	-	+
Positive aPLs	-	-	-

[#] HUVS confirmed by skin biopsy. [$] Mutation in C1q gene not detected.

Conclusion: *DNASE1L3* genetic variants contribute to monogenic SLE. This report supports prior literature linking *DNAES1L3* deficiency to HUVS in addition to SLE. Further analysis of the effect of this variant on the immune system and link to C1q deficiency or consumption may shed light on relevant immune mechanisms related to SLE.

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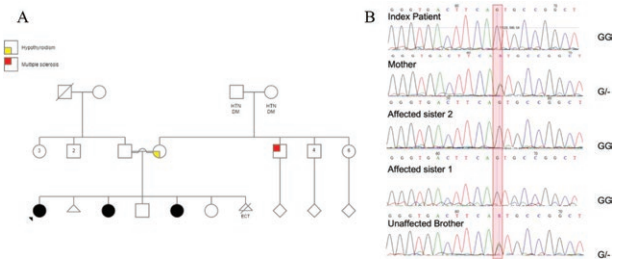


Figure 1. A. Family pedigree of index case (youngest sibling) with DNASE1L3 (c.572A>G, p.Asn191Ser). B. A segregation analysis of DNASE1L3 gene variant c.572A>G, p.Asn191Ser for the family members. The red bar highlighting the genotype of the patients and family members.

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Disclosure of Interests: None Declared.
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Neutrophil dysregulation in systemic lupus erythematosus

OP0293

ANTI-CITRULLINATED HISTONE MONOCLONAL ANTIBODY CIT-013, A DUAL ACTION THERAPEUTIC FOR NEUTROPHIL EXTRACELLULAR TRAP ASSOCIATED AUTOIMMUNE DISEASES

Keywords: Cell biology, Innate immunity, Rheumatoid arthritis

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Background: Neutrophil extracellular traps (NETs) contribute to the pathophysiology of multiple inflammatory and autoimmune diseases. Targeting the NETosis pathway has demonstrated significant therapeutic potency in various disease models (Chirivi *et al*., 2021). Here we describe a first in class monoclonal antibody (CIT-013) with high affinity for citrullinated histones H2A and H4 which inhibits NETosis and reduces tissue NET burden *in vivo* with significant anti-inflammatory consequences. CIT-013 is currently in phase 1 clinical trials with phase 2a studies in RA due to commence in 2024.
Objectives: The objective of the current study was to further unravel CIT-013's mode of action. Questions which we wanted to answer are: 1) How and when does CIT-013 interfere with the NETosis pathway?, and 2) what is the faith of CIT-013 opsonized NETs and netting neutrophils? Furthermore, we investigated whether CIT-013's epitope is expressed in rheumatoid arthritis (RA) synovial tissue.
Methods: *In vitro* life imaging studies using neutrophils and macrophages in combination with monovalent as well as bivalent CIT-013 have been performed to investigate CIT-013's mode of action. An *in vivo* lung inflammation mouse model was used to investigate CIT-013's effect on NET burden as well as phagocytic macrophages. Finally, the presence of CIT-013's epitope in human RA synovial tissues was investigated using immunohistochemistry techniques.
Results: Detection of CIT-013 epitopes in RA synovium provides evidence that RA is an autoimmune disease with excessive citrullinated-NETs that can be targeted by CIT-013. We show that CIT-013 acts upon the final stage of NETosis, binding to its chromatin epitopes when plasma membrane integrity is compromised to prevent NET release. Bivalency of CIT-013 is necessary for NETosis inhibition. In addition, we show that CIT-013 binding to NETs and netting neutrophils enhances their phagocytosis by macrophages. Furthermore, we demonstrate that a mouse variant of CIT-013 reduces tissue NET burden *in vivo* at least in part through enhanced macrophage phagocytosis.

Conclusion: Since NETs contribute to the pathophysiology of many immune mediated inflammatory diseases, including autoimmune diseases such as RA, CIT-013's unique ability to both inhibit NET release and enhance NET clearance indicates the importance of this first in class therapeutic antibody as a new emerging therapy.

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Disclosure of Interests: Maarten van der Linden Shareholder of: Stock options, Employee of: Employee of Citryll, Sangeeta Kumari Shareholder of: Stock options, Employee of: Employee of Citryll, Daphne Montizaan Shareholder of: Stock options, Employee of: Employee of Citryll, Stephanie van Dalen Shareholder of: Stock options, Employee of: Employee of Citryll, Annemarie Kip Shareholder of: Stock options, Employee of: Employee of Citryll, Martyn Foster: None declared, Inge Reinieren Employee of: Past employee of Citryll, Elsa Neubert: None declared, Luise Erpenbeck: None declared, Tirza Bruurmijn Shareholder of: Stock options, Employee of: Employee of Citryll, Peter van Zandvoort Shareholder of: Stock options, Employee of: Employee of Citryll, Paul Vink Employee of: Former employee of Citryll, Eric Meldrum Shareholder of: Stock options, Employee of: Employee of Citryll, Helmuth van Es Shareholder of: Stock options and shares, Employee of: Employee of Citryll, Renato Chirivi Shareholder of: Stock options and shares, Employee of: Employee of Citryll.

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Insights into gout management

OP0295

A 12-WEEK, RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED, PHASE 2B STUDY OF SAFETY, TOLERABILITY AND EFFICACY OF AR882 IN GOUT PATIENTS

Keywords: Gout, Randomized control trial

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Background: Despite gout being the most common inflammatory arthritis, there remains an unmet need for more effective treatment. AR882 is a novel, potent, and selective uric acid transporter 1 (URAT1) inhibitor in development for the treatment of gout and tophaceous gout. AR882 was well tolerated, including patients with various degrees of renal insufficiency, and has consistently demonstrated robust sUA lowering in multiple clinical trials.

Objectives: This global phase 2b trial is a randomized, double-blinded, placebo-controlled, 12-week study to evaluate the safety, tolerability, and efficacy of AR882 versus placebo in patients with gout.

Methods: The trial recruited patients 18 to 75 years of age with eGFR >30 mL/min across 20 sites in the US, Australia, and Taiwan, who met the ACR/EULAR Gout Classification Criteria. Following gout flare prophylaxis for 10 days, patients received either once-daily AR882 50 mg, AR882 75 mg, or matching placebo for 12 weeks. Blood samples were collected every two weeks through Week 12 for laboratory tests, sUA and pharmacokinetic measurements. Efficacy endpoint was the percent of patients who reached sUA below 6, 5, 4, and 3 mg/dL. Safety including vital signs and electrocardiograms were collected throughout the study.

Results: A total of 140 patients were enrolled in this study. The majority of patients were male (93.6%) and white (58%), followed by Asian (28%) and Black or African (15%). The baseline sUA level was 8.6 (±1.3) mg/dL; mean age 54.3 (24-73) years; mean body weight 96.4 (±17.8) kg. Major comorbidities seen in patients included hypertension (47%), hyperlipidemia (35%), renal insufficiency (34%), arthritis (23%), diabetes (19%), cardiovascular disease (15%), lung disease (11%), and liver disease (5%). Following 12 weeks of treatment, median sUA levels were reduced from baseline 8.6 mg/dL to 3.5 mg/dL with 75 mg and 5.0 mg/dL with 50 mg. No change was observed in the placebo group. At Week 12, 89%, 82%, 63% and 29% of patients achieved < 6, <5, <4 and <3 mg/dL, respectively, in the 75 mg group. In the 50 mg group, 78%, 50%, 8% of patients achieved < 6, <5 and <4 mg/dL, respectively. The sUA lowering effect was similar for three consecutive measurements between Week 8 and 12. There were no serious adverse events in AR882 treated patients. Mild or moderate adverse events including diarrhea, headache, and upper respiratory infection were observed in this study. A total of 65 gout flare incidents were observed and evenly distributed across groups during the 12-week treatment.

Conclusion: The majority of patients receiving AR882 had achieved sUA levels below 5 or 4 mg/dL, which are two key thresholds for more efficient flare and tophi reductions[1][2]. AR882 was well tolerated over the 12-week treatment period and patients with comorbidities did not require any adjustments in management of the diseases while treated with AR882. This study suggests AR882 may offer improved efficacy with acceptable safety compared to existing therapies for gout and may have utility in the treatment of patients across the spectrum of gout including those with severe or refractory disease.

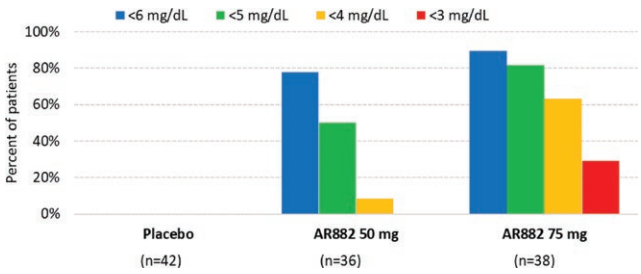


Figure 1. Percent of Patients with sUA at Targets following 12-week Treatment of AR882 or Placebo.

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Disclosure of Interests: James Cheng-Chung Wei: None declared, Roy M. Fleischmann Speakers bureau: AbbVie, Pfizer Inc, Consultant of: AbbVie, Amgen Inc., Biogen, Bristol Myers Squibb, Eli Lilly and Company, Galapagos, Galvani, Gilead, GSK plc, Janssen Pharmaceuticals, Novartis AG, Union Chimique Belge (UCB), Grant/research support from: AbbVie, Amgen Inc., Biogen, Bristol Myers Squibb, Eli Lilly and Company, Flexion, Galapagos, Galvani, Genentech, Gilead, GSK plc, Horizon, Janssen Pharmaceuticals, Novartis AG, UCB, Viela, Sarah Morris Shareholder of: Arthrosi therapeutics, Employee of: Arthrosi therapeutics, Elizabeth Polvent Shareholder of: Arthrosi therapeutics, Employee of: Arthrosi therapeutics, Zancong Shen Shareholder of: Arthrosi therapeutics, Employee of: Arthrosi therapeutics, Andrea Clouser Roche Shareholder of: Arthrosi therapeutics, Employee of: Arthrosi therapeutics, Vijay Hingorani Consultant of: Arthrosi therapeutics, Shunqi Yan Shareholder of: Arthrosi therapeutics, Employee of: Arthrosi therapeutics, Li-Tain Yeh Shareholder of: Arthrosi therapeutics, Employee of: Arthrosi therapeutics, Robert Keenan Shareholder of: Arthrosi therapeutics, Employee of: Arthrosi therapeutics.

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OP0296

CRYSTAL DEPOSITIONS ASSESSED BY ULTRASOUND AND DECT DECREASE DURING TREATMENT AND PREDICTS REDUCED NUMBERS OF FLARES; TWO-YEARS RESULTS FROM THE NOR-GOUT TREAT-TO-TARGET STUDY

Keywords: Imaging, Gout, Ultrasound

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Background: Gout is caused by depositions of monosodium uric acid crystals in joints and tissues which triggers highly painful flares. Serum urate lowering treatment (ULT) reduces the number of flares.

Objectives: To explore the change of crystal depositions assessed by ultrasound and dual energy computer tomography (DECT) for two years, and the associations between depositions and occurrence of flare during the first year of ULT.

Methods: Patients with crystal-proven gout who presented themselves after a recent gout flare and with serum uric acid (sUA) level (>360 µmol/L) were consecutively included (the NOR-Gout study (1,2)). They were followed monthly if needed with increase of ULT to achieve sUA <360 µmol/L (or <300 µmol/L if clinical tophus) as well as flare prophylaxis for 3-6 months. The patients were assessed clinically and by laboratory tests. Information about flares before the visit was collected (numbers year 1, only occurrence year 2). A comprehensive ultrasound assessment (General Electric E9) at baseline, 12 and 24 months was performed using semi-quantitative scoring of MSU depositions (using definitions and scoring system defined by OMERACT of double contour (DC), tophi and aggregates), and examination of bilateral radiocarpal, MCP 2 and MTP 1 joints, triceps, and quadriceps insertions, patellar (proximal and distal) and Achilles tendons as well as distal femur

(maximal flexed knee) and talar cartilage). In addition, DECT (General Electric Discovery CT750 HD) of both feet were performed. Total sum scores of US depositions (DC, tophi and aggregates) or DECT depositions were calculated, as well as US sum scores only of the feet for comparison with DECT. Comparisons were performed by Wilcoxon or Mann-Whitney. Logistic regression explored if flare occurring during 0-3 or 0-12 months was predicted by US or DECT (controlling for age, sex, disease duration and presence of clinical tophus).

Results: 209 patients were included (mean (SD) age 56.4 (13.8) years, time since first flare (disease duration) 7.9 (7.7) years, 95.5% men). During year 1 and 2 patients with flares compared with no flares had higher baseline US and DECT scores ($p<0.05$). The total sum scores of US (DC, tophi and aggregates) and DECT decreased during the study ($p<0.001$ for all, table 1). Figure 1 shows the parallel decrease of depositions in feet by US and DECT (all changes $p<0.001$). During the first year there were median (range) 2 (0-14) flares. At least one flare was seen in 81% the first year, but only in 26% the second year. Baseline total US sum scores predicted flare the first 3 months (DC; $p=0.031$, $\beta=0.113$, total sum score; $p=0.047$, $\beta=1.026$) and baseline DECT predicted flare both at 3 and 12 months ($p=0.014$, $\beta=1.086$ and $p=0.010$, $\beta=1.193$, respectively).

Conclusion: Baseline levels of US and DECT depositions were higher in patients having flare during the study. The amount of crystal depositions in both imaging modalities decreased substantially during ULT as did occurrence of flare. Baseline US and DECT depositions predicted flare during follow-up. Thus, patients should be encouraged to follow a treat-to-target procedure of sUA reduction to reduce both depositions and flares.

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Table 1. Mean (SD) of ultrasound and DECT scores.

Sum scores	Baseline	12 months	24 months
Ultrasound - Double contour	4.3 (3.5)	1.3 (2.2)	0.7 (1.4)
Ultrasound – Tophi	6.5 (6.5)	3.8 (5.2)	2.4 (3.7)
Ultrasound - Aggregates	9.3 (5.6)	6.7 (5.1)	5.5 (4.7)
Ultrasound –Double contour, Tophi, Agregates	20.0 (13.9)	11.7 (11.3)	8.6 (8.8)
Dual energy computer tomography (DECT)	4.7 (6.4)	2.8 (4.8)	1.5 (3.2)

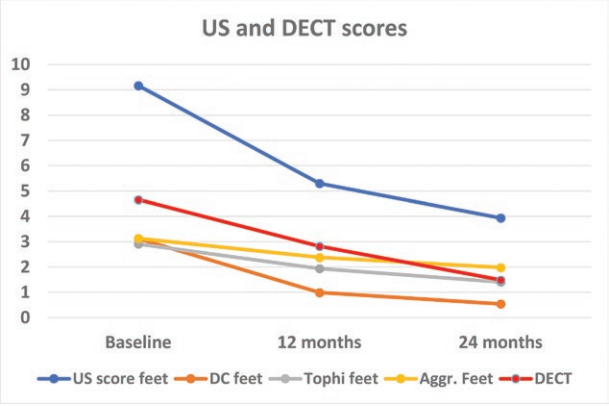


Figure 1. Ultrasound scores and DECT only from the feet

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Exploring the spectrum of bone inflammatory disorders across the life course

OP0298 **CHRONIC NON-BACTERIAL OSTEOMYELITIS (CNO) AND BONE MINERAL DENSITY**

Keywords: Vitamin D, Bone diseases, Osteoporosis

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Background: Chronic nonbacterial osteomyelitis (CNO) is an inflammatory bone disorder that generally affects children.[1] In the absence of accepted diagnostic criteria or clinical/radiological biomarkers, CNO remains a diagnosis of exclusion.[2] Chronic pain and/or bone fractures (vertebral compression fractures) are observed in patients with CNO, just as in severe vitamin D deficiency and osteoporosis.

Objectives: We aim to show the relationship between CNO and bone mineral density and investigate whether osteoporosis with/without vitamin D deficiency can cause challenges in the treatment of CNO.

Methods: We reviewed the charts of all CNO patients followed up between January 2015 and April 2022 in the Department of Pediatric Rheumatology in Hacettepe University, Ankara, Turkey. The diagnosis was confirmed by expert consultant pediatric rheumatologists and radiologists. Demographic and clinical characteristics of patients, 25 OH vitamin D (25[OH]D) level status (N:>20 ng/ml [50 nmol/L]), radiological findings as well as medical treatments were evaluated. A score between -1.1 and -2.4 is classified as osteopenia. A score of -2.5 and below is defined as osteoporosis. In the pediatric population, osteoporosis is a clinical diagnosis and is reserved for those patients with a BMD Z- score less than or equal to -2.0 in combination with a significant fracture. In addition, patients were divided into two groups: receiving nonsteroidal anti-inflammatory drugs (NSAIDs) and/or cDMARDs (Group 1) and receiving TNF inhibitors (TNFi) and/or bisphosphonate (Group 2).

Results: A total of 80 patients (females 53%) were included in this study. The median age at diagnosis of CNO was 7 (1-17) years. Overall, vitamin D level was available before diagnosis in 52/80 (65%) patients, 17 of which were normal, while 35 patients had deficiency (25[OH]D <20 ng/ml [50 nmol/L]). Bone mineral density was studied in 39 patients, normal in 18, osteoporotic in 13, and osteopenic in 8 patients. 23 patients were treated with IV bisphosphonate (pamidronate [PAM]). Among the patients receiving PAM, 10 had a severe deficiency of 25[OH]D (<10 ng/ml), and 1 had osteopenia, 10 had osteoporosis in DEXA. Forty-one patients were treated with TNFi (34 used ETA, 5 ADA, 2 INF). There was no patient with osteoporosis in Group 1 (n=26), it was statistically significant. ($p=0.031$). In Group 2 (n=54), 12 patients (38.7%) were normal, 13 patients (41.9%) had osteoporosis, and six patients (19.3%) had osteopenia. The overall history of bone fractures (long bone, vertebral body) was present on admission in eleven patients (7 osteoporosis, 2 normal BMD, 2 NA). All patients with fractures were treated with PAM as the first-line treatment, and they benefited from this drug ($p=0.013$). In Group 2, 25[OH]D vitamin level was lower than Group 1, although it was not statistically significant. ($p=0.183$) (Table 1)

Conclusion: Patients with normal bone mineral density responded well to DMARD/NSAID, better than the remaining patients, and they did not need alternative treatment. Vitamin D deficiency and/or osteopenia may lead to a more refractory course; thus, it should be monitored effectively in patients with CNO.

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Table 1. Association between the drugs and BMD

	Group 1 (DMARD/NSAID) (n=26)	Group 2 (PAM/TNFi) (n=54)	P<0.05
BMD Z score	0.6 (min-1.8, max1.02)	-1.2 (min-3.8, max 3.2)	0.280
Osteoporosis	0	13	0.043*
Osteopenia	2	6	
Normal	6	12	
Fracture	0	11	0.012*
(25[OH]D vitamin level <20 ng/ml	9	26	0.186
>20 ng/ml	7	10	

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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Pain relief - what can be done?

OP0299-PARE **MEASURING THE IMPACT OF DIGITAL THERAPEUTICS ON QUALITY OF LIFE AND SYMPTOM BURDEN IN PATIENTS WITH RHEUMATOID ARTHRITIS USING RAID SCALE**

Keywords: Patient reported outcomes, Quality of life, Rheumatoid arthritis

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Background: Rheumatoid arthritis(RA) is a systemic chronic autoimmune disease that involves inflammatory arthritis with varying severity showing various symptoms like pain, fatigue, and sleep disturbances impacting and reducing the quality of life(QoL).[1] Patients with RA experience reduced QoL, physical and emotional health as well as level of independence etc and they are more likely to suffer from anxiety, depression and low self-esteem, with high levels of associated mortality and suicide.[3] Addressing the need to improve the quality of life and symptom burden for these patients are vital where Digital solutions play an incredibly significant role. These solutions are also helpful in self-management of disease and symptoms.
Objectives: To assess the impact of a digital health program on the quality of life and symptom burden of patients suffering from Rheumatoid Arthritis.
Methods: An interventional trial including an RA patient support program was delivered by Wellthy Care digital platform over a period of 16 weeks. Recruitment of 30 patients was done using a convenient sampling method. Patients who were diagnosed with RA were included in the trial. Patients who were under 18, pregnant/lactating, and with hearing disability were excluded. The program included interventions such as physiotherapy sessions, CBT (cognitive behavioural therapy) counselling, tracking of symptoms, lifestyle counselling, disease awareness and self-management training of symptoms at home. The rheumatoid arthritis impact of disease (RAID) [2] questionnaire, a validated questionnaire was administered to assess seven important patient domains of disease impact (pain, function, fatigue, sleep disturbance, emotional well-being, physical well-being, coping) at baseline and at the end of the program.
Results: The Mean RAID score of the patients at baseline was 4.99 and at endline was 0.737. The impact percentage of program in improvement of symptoms like Pain, Difficulty in doing daily physical activities, Fatigue, Sleep difficulty, level of physical well-being, level of emotional well being were 85.66%, 86.40%, 88.81%, 96.47%, 85.66%, 93.89% respectively. The Paired T-test witnessed significant improvement in symptoms like pain, sleep disturbances, fatigue, difficulty in performing physical activities ($p<0.001$).
Conclusion: Digital therapeutics play a highly significant role in improving the quality of life and reducing the symptom burden of RA patients. The digital patient support program led to meaningful changes in a patient's quality of life as well as symptoms within a few weeks, even when the patient previously failed to experience a good prognosis during the treatment. Patients reported a highly significant improvement in Pain, Fatigue and Sleep disturbances, which improved the quality of life and patient's outlook of the overall treatment and adherence. These digital solutions can be considered as holistic care and integrated with routine supportive care in practice to provide improved patient-centred care. RAID score functions well as a good patient reported outcome measure in routine health care for patients with RA.
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Disclosure of Interests: None Declared.
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Treating to Target: Challenges across the life course

OP0300 **INCREASING THE ETANERCEPT DOSE IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS: DOES IT HELP REACHING THE TREATMENT TARGET? A POST-HOC ANALYSIS OF THE BEST4KIDS RANDOMISED CLINICAL TRIAL**

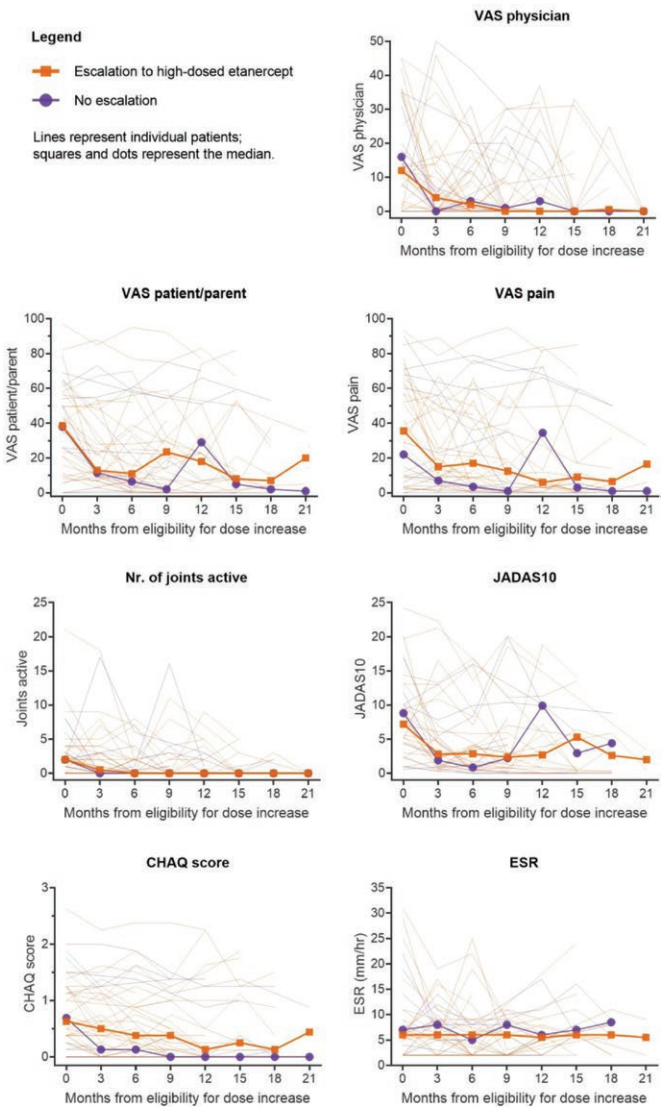
Keywords: Clinical trials, bDMARD

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Background: Etanercept is a frequently used second-line therapy for juvenile idiopathic arthritis (JIA). It is unknown whether higher doses of etanercept result in better clinical outcomes, but most studies only evaluated doses up to the most commonly used 0.8 mg/kg/week (max 50mg/week).[1] Although higher doses are used off-label in clinical practice, the literature lacks an in-depth description of patients receiving such treatment.
Objectives: To describe the clinical course of JIA-patients that received high-dose etanercept (1.6 mg/kg/week; max 50mg/week) as part of the Best4Kids trial.
Methods: In a single-blinded treatment-strategy trial, patients with oligoarticular JIA, RF-negative polyarticular JIA or juvenile psoriatic arthritis were randomised across three treatment-strategy arms: (1) sequential DMARD-monotherapy (sulfasalazine or methotrexate (MTX)), (2) combination-therapy MTX+6 weeks prednisolone and (3) combination therapy MTX+etanercept.[2] A protocolised treat-to-target approach aiming for inactive disease was used during 24 months follow-up. Treatment was escalated in case of persistent disease-activity or tapered in case of inactive disease. In any treatment-arm patients could eventually escalate from regular to high-dose etanercept alongside MTX 10mg/m2/week. For comparison we studied patients who did not receive high-dose etanercept due to decisions overriding the trial-protocol by the treating paediatrician and/or the patient/parents.
Results: Of the 94 randomised patients, 32 received high-dose etanercept (69% female, median age 6 years (IQR 4-10), median time from baseline 10 months (7-16), median dose 1.3 mg/kg/week (1.1-1.5)). Follow-up was up to 2 years from baseline (median follow-up 24.6 months). Clinical measures of disease-activity decreased largely within 3 months (Figure 1): median VAS-physician from 12 to 4 ($p=0.022$), VAS-patient/parent from 38.5 to 13 ($p=0.003$), VAS pain from 35.5 to 15 ($p=0.030$), number of active joints from 2 to 0.5 ($p=0.12$) and JADAS10 from 7.2 to 2.8 ($p=0.008$). Functional status (CHAQ-score) improved more gradually and ESR remained stable. A comparable pattern of clinical parameters over time was observed in 11 patients (73% girls, median age 8 (IQR 6-9)) who were not escalated to high-dose etanercept despite eligibility according to trial-protocol. In both the high-dose and the comparison group the percentage of patients with inactive disease 6 months after eligibility for dose-increase was 56%. In the high-dose group, 18 out of 32 patients (56%) experienced 26 infectious adverse events (AEs, on average 0.20 events per visit following dose-increase). No serious AEs (SAEs) were recorded after dose-increase. Among the 11 patients who did not receive high-dose etanercept, 4 patients (36%) subsequently experienced 5 infectious AEs (on average 0.11 events per visit); this included one SAE requiring hospitalisation. Findings were similar when one patient who switched to infliximab, instead of maintaining the regular etanercept dose, was excluded from the comparison group.
Conclusion: Escalation to high-dose etanercept was generally followed by meaningful clinical improvement within 3 months. However, non-escalators experienced comparable improvement. These data do not suggest superior clinical outcomes after etanercept dose increase, while there was a potential trend for more (non-severe) infectious AEs. Larger studies are needed to more closely examine outcomes, adverse events and cost-effectiveness of high dose etanercept.

Figure. Clinical parameters over time after etanercept dose increase (orange) and after not escalating to high-dose etanercept despite eligiblity (purple)

Time-point zero = visit of eligibility for etanercept dose increase



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Disclosure of Interests: None Declared.

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Predicting remission and flare

OP0301

THE OPTIMAL THRESHOLDS FOR PATIENT GLOBAL ASSESSMENT IN DEFINING REMISSION DIFFER ACCORDING TO THE AUTOANTIBODY STATUS IN EARLY RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Autoantibodies, Patient reported outcomes

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Background: In rheumatoid arthritis (RA), the patient global assessment (PGA) is influenced by a multitude of factors that may vary over time and in relation to certain disease characteristics [1]. The inclusion of the PGA in the definition of remission and the cut-offs that better guarantee good functional and structural outcomes remain therefore uncertain [2,3].

Objectives: Aim of our study was to investigate the thresholds of the PGA capable of identifying sustained suppression of inflammation and functional integrity in patients with early RA in relation to the autoantibody status.

Methods: Data were retrieved from a prospective monocentric cohort of 810 patients with early RA (<12 months of symptoms at inclusion) with an observation period of 24 months after treatment institution with methotrexate aimed at the achievement of low disease activity. Patients were evaluated for the achievement of Boolean 3-variable (3-v) remission (swollen joint count, tender joint count, and C-reactive protein all ≤1) at any time-point in the first 12 months. The thresholds of the PGA at the time of 3-v remission that best predicted persistence of 3-v remission after 6 months, and normal function (health Assessment Questionnaire, HAQ, ≤0.5) after 12 months were investigated through receiver operating curve (ROC) analyses in autoantibody-positive and –negative patients separately.

Results: A total of 749/810 (92.5%) patients had follow-up data available until month 24. Of them, 390 (52.1%) achieved 3-v remission in the first year of observation after a median (IQR) of 6 (2-9) months. Autoantibody-positive patients showed a trend for earlier 3-v remission (adjusted HR [95% CI] 1.21 [0.99-1.48]). Among patients achieving 3-v remission, 193 (49.5%) maintained 3-v remission after 6 months, without significant differences in relation to the autoantibody status. Normal function after 12 months characterized slightly more autoantibody-positive than –negative patients (91.2% vs 83.3%, p=0.15). The best cut-off values of the PGA capable of predicting persistence of 3-v remission and normal function in autoantibody-positive patients were ≤9 (AUC 0.76) and ≤13 (AUC 0.73), respectively (**Table 1**). The corresponding thresholds in autoantibody-negative patients were ≤20 (AUC 0.75) and ≤21 (AUC 0.69).

Table 1. Performance of PGA thresholds for predicting persistence of remission and normal function

Ab-pos							Ab-neg						
Persistence of 3-v remission													
Criterion	**Sens**	**95% CI**		**Spec**	**95% CI**	**+LR**	**-LR**	**Criterion**	**Sens**	**95% CI**	**Spec**	**95% CI**	**+LR**	**-LR**
≤9	76.1	66.1-84.4		75.8	65.9-84	3.14	0.32	≤20	84.2	75.6-90.7	62.8	52.6-72.1	2.26	0.25
Normal function														
≤13	81.7	74-87	9	68.8	41.3-89	2.61	0.27	≤21	66.7	57.4-75.1	74.2	55.4-88.1	2.58	0.45

Conclusion: Increasing the threshold of the PGA to ≤20 in patients with early RA is associated with sustained suppression of inflammation and good functional outcomes in autoantibody-negative patients. In contrast, in autoantibody-positive patients, a stringent threshold of ≤10 remains optimal.

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Acknowledgements: NIL.

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DATA MATTERS: keeping track of your health information

OP0302-PARE THE INTERNATIONAL MAP OF AXIAL SPONDYLOARTHRITIS GLOBAL REPORT: SUPPORTING THE INCLUSION OF THE PATIENT PERSPECTIVE IN POLICY AND CLINICAL PRACTICE

Keywords: Lifestyles, Real-world evidence, Quality of life

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic musculoskeletal disease that can lead to chronic pain, structural damage, and disability. It often has a significant physical impact, causes psychological distress and can disrupt every aspect of a patient's life. While scientific research in axSpA has grown significantly, the patient perspective remains insufficiently explored and the disease burden continues to be underestimated. The International Map of Axial Spondyloarthritis (IMAS) is a research initiative of the impact and burden of axSpA from the patient perspective, identifying the unmet needs of axSpA patients and exploring impact beyond solely the physical symptoms.
Objectives: By producing an accessible global report on the results of IMAS, ASIF aim to provide its member organisations with much needed, robust evidence of the impact of the disease. The report will be used to raise awareness of the reality of axSpA, particularly amongst healthcare providers and policy makers; with the intention of incorporating the patient perspective much more into clinical practice and policy. The report also provides patients and their carers with a better insight into axSpA experiences around the world.
Methods: This research is a collaboration between the Axial Spondyloarthritis International Federation (ASIF), the University of Seville and Novartis Pharma AG. ASIF and its members have supported recruitment of survey participants from 27 countries across Europe, Asia, North, Central and South America, and Africa. In total 5,557 people completed the survey, providing a unique insight into how axSpA effects daily life. IMAS collected information through a comprehensive questionnaire of over 120 items on socio-demographics; behaviour; disease diagnosis and characteristics; comorbidities; psychological distress; healthcare utilization; treatments; disease activity; physical activity and limitations; working life; relationships; and the hopes and fears of patients. The ASIF IMAS sub-committee reviewed the global dataset results and agreed the scope of the global report. The IMAS scientific committee also reviewed the result, identifying key findings. ASIF held webinars with its members to seek their feedback on the results; asking them how they would use such a report how it can support their work.
Results: 5,557 axSpA patients participated in IMAS. The mean age was 43.9 years, 55.4% were women, 46.2% had university education, and 48.5% were employed. 20.6% were on sick leave (temporary or permanent), 71.4% had difficulty finding a job due to axSpA, and 71.0% reported work-related issues. Patients' mean diagnostic delay was 7.4 years, disease activity measured by the BASDAI was 5.4 (out of 10), and risk of poor mental health measured by the GHQ-12 was identified in 59.4% of respondents. In addition, patients had a mean of 2 physical comorbidities. The report, which will be translated into a number of languages, includes data on all topics that were collected by IMAS. But at the request of our members, it focusses on the journey to diagnosis; physical and mental health; daily life impact; accessing treatment and care; and hopes and fears. Gender and regional differences are reported on in each of the chapters.
Conclusion: IMAS has shown the global profile of axSpA patients, quantifying and highlighting unmet needs, including unacceptable delay in diagnosis, high disease activity, work-related problems, and poor mental health in axSpA patients worldwide. The global report on IMAS will provide ASIF's members with empirical evidence of the impact of axSpA on a person's life in order to support their awareness and advocacy work. IMAS was recognised when it won the EFPIA Connecting Healthcare 2021 Awards for its ability to bring patients and medical professionals together in an initiative aimed at improving the quality of life of people living with axSpA from around the world.
REFERENCES: NIL.
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OP0303-PARE MULTI-STAKEHOLDER CO-CREATION TO FACILITATE CLINICAL TRIAL RECRUITMENT - A FEASIBILITY STUDY

Keywords: Clinical trials, Patient information and education

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Background: Recruitment for clinical trials remains a hurdle, causing potential delays in bringing innovative treatments to patients. Furthermore, there is not much communication about clinical trials towards the patient population and the general population has a lot of misconceptions around clinical trials. Communication about clinical trials is also subjected to a strict regulatory framework, especially in Europe. The information that can be found online is often in English and difficult to understand for the lay public.
Objectives: For this reason, a feasibility study has been performed to develop a clinical trial portal for Belgium that allows users to search for trials in a local and lay language, while offering the portal to patient organisations and hospitals to receive updates on newly initiated trials.
Methods: During the feasibility study the following aspects have been analysed by organising multi-stakeholder workshops, involving patient representatives and patient organisations (20), hospitals (8), HCPs (14), industry and representatives (10) of the Belgian medicines agency:user expectations, technical considerations, legal restrictions, regulatory and compliance aspects. Based on the multi-stakeholder workshops, a prototype has been developed that has been tested via user validation workshops. For the field of rheumatology, ReumaNet has represented the RMD community.
Results: The result of the feasibility study revealed that only 15% of patient organisations (out of 190) mention clinical trials on their website, out of 140 websites of hospitals, only 16% mention clinical trials, while 2% have a search engine to search for ongoing studies. All academic hospitals (7) had a section dedicated to trials on their website. There was a great interest from the patient community (over 20 PAG participants) and the HCP representatives. A legal analysis has also set a framework for compliant communication about clinical trials to the lay public as well as a GDPR framework to define privacy related aspects of the portal.The portal has been launched in September 2022 as a first version, an improved version with a PAG dashboard is launched in February 2023.
Conclusion: Based on the feasibility study, a clear need was identified to further develop the clinical trial portal in co-creation with the various stakeholders.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Mitchell Silva Speakers bureau: Paid as a speaker in various pharmaceutical companies to give presentations about patient engagement. These include: AstraZeneca, Boehringer Ingelheim, Roche and MSD., Consultant of: Paid as a consultant to provide input on patient engagement strategy for various companies, including Roche, AstraZeneca, MSD, Janssen, GSK, Takeda, Boehringer Ingelheim, Merck, Nele Caeyers: None declared.
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ANCA-associated vasculitis

OP0304 BENRALIZUMAB FOR EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA): RESULTS FROM A EUROPEAN MULTICENTER STUDY ON 121 PATIENTS

Keywords: Real-world evidence, bDMARD, Vasculitis

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is an ANCA-associated vasculitis characterized by asthma, ear-nose-throat (ENT) manifestations, peripheral hypereosinophilia and systemic vasculitic involvement [1]. Increased serum levels of interleukin 5 (IL-5) have been observed in eosinophilic disorders, including EGPA, and a genome-wide association study identified the IL-5 region as a major EGPA-associated loci [2]. On these bases, an increasing interest is focusing on benralizumab (an IL-5 receptor antagonist approved for severe eosinophilic asthma at the dosage of 30mg every 4 weeks for 3 administrations, then every 8 weeks) as a new potential therapy for EGPA. Following the promising results of a pilot study on 10 patients [3], a randomized double-blind trial is ongoing to assess the efficacy and safety of benralizumab at a higher dosage (30mg/4 weeks), as compared to mepolizumab (another IL-5 inhibitor approved for EGPA) in patients with EGPA (NCT04157348). In the meanwhile, isolated cases of patients with refractory EGPA, successfully treated with benralizumab, have been described in the literature [4,5].
Objectives: This study aimed to assess the efficacy and safety of benralizumab in a multicenter European cohort of patients with EGPA.
Methods: The study included patients with EGPA treated with benralizumab at 28 centers belonging to the European EGPA Study Group. Efficacy and safety outcomes were assessed after 3, 6 and 12 months of treatment. Complete response (CR) was defined as no disease activity (Birmingham Vasculitis Activity Score [BVAS] = 0) and a daily prednisone equivalent dose ≤4 mg. Respiratory outcomes included asthma, ENT manifestations and lung function.
Results: A cohort of 121 patients with EGPA was included. All were treated with benralizumab at the dosage approved for eosinophilic asthma (30mg every 4 weeks for 3 administrations, then every 8 weeks). The proportion of patients meeting the criteria for CR was 16% at 3 months, 26% at 6 months and 46% at 12 months of follow-up (**Table 1**). During follow-up, a drop in BVAS was recorded, from a median score of 3 (IQR 2-8) at baseline to 0 (0-2) at month 3 and 6 and to 0 (0-1) at month 12 (p<0.001 at all timepoints). Regarding respiratory outcomes, the proportion of patients reporting active asthmatic decreased from 94% at baseline to 39% at 3 months (p<0.001), and that of patients with active ENT manifestations decreased from 70% at baseline to 49% at 3 months (p<0.001), with concomitant improvements in lung function. 19 patients experienced adverse events, three requiring hospitalization.
Conclusion: The results from this large European real-world study suggest that benralizumab, at the dosage approved for severe eosinophilic asthma, could be effective and safe to control respiratory EGPA manifestations and overall disease activity.
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Table 1. Efficacy outcomes

	Benralizumab 3 months beginning (t0)		p-value (t3 vs t0)	6 months	p-value (t6 vs t0)	12 months	p-value (t12 vs t0)
N patients	*121*	*121*		*101*		*85*	
Complete response	-	15/96 (15.6%)		23/87 (26.4%)		32/69 (46.4%)	
BVAS, median (IQR)	3 (2-8)	0 (0-2) [n=96]	<0.001*	0 (0-2) [n=87]	<0.001*	0 (0-1) [n=69]	<0.001*
Respiratory involvement							
Pulmonary	114 (94.2)	43/111 (38.7)	<0.001*	36 (35.6)	<0.001*	33 (38.8)	<0.001*
ENT	85 (70.3)	54/111 (48.6)	<0.001*	46 (45.5)	<0.001*	40 (47.1)	<0.001*

BVAS= Birmingham Vasculitis Activity Score; ENT= ear-nose-throat; IQR= interquartile range.

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OP0305 THE BURDEN OF MULTIMORBIDITY IN ANCA-ASSOCIATED VASCULITIS: A COHORT STUDY

Keywords: Comorbidities, Vasculitis, Epidemiology

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Background: With improvements in the risks of relapse and mortality in ANCA-associated vasculitis (AAV), a better understanding of disease- and treatment-related complications in people with AAV is necessary to optimize outcomes and personalize care. Multimorbidity (MM) is a patient-centered approach to measuring complications and is defined as the presence of multiple chronic conditions[1]. MM is associated with risk of death and quality of life in other conditions. MM remains poorly understood in AAV[2].
Objectives: To determine the burden of multimorbidity in AAV.
Methods: We used the 2002-2019 Mass General Brigham (MGB) AAV cohort: an inception cohort of consecutive MPO- or PR3-ANCA+ incident AAV cases at a multi-center healthcare system in New England, USA. Comparators without systemic rheumatic disease were identified from MGB and matched to cases (10:1 ratio) by encounter date, age, sex, and race. We adapted a definition of MM as the presence of ≥ 2 of 37 chronic conditions, identified by use of ICD-9/10 codes ≥ twice over ≥ 30 days[1]. Manifestations of AAV (e.g., kidney disease) were excluded from the MM definition. Conditions present ≥ 6 months prior to the index date (date of treatment initiation) were excluded. First, we determined the proportion of cases and comparators with MM using the Aalen-Johansen method, accounting for the competing risks of death and loss to follow up. Second, we used Cox proportional hazard models to estimate the hazard ratio (HR) of MM in cases vs comparators and restricted mean survival time to estimate days free of MM in cases vs comparators. Third, we used latent class analysis to characterize clusters of morbidity among people with MM.
Results: There were 547 cases matched to 5,259 comparators (Table 1); mean age was 59 years and the majority were female (61%) and white (88%). Median follow-up in cases and comparators was 102 months and 66 months, respectively. MM was substantially more common in cases vs comparators and AAV cases had nearly an 8-fold higher risk of MM vs comparators (Figure 1, HR 7.6, 95% CI 6.6-8.7). Over 5 years, each case had an average of 707 fewer days with MM than comparators (963.4 vs 1670.5 days, p<0.001). At 1 year, two clusters of MM in AAV were identified with 76% and 24% captured in Clusters 1A and 1B, respectively. Hypertension and hyperlipidemia were common in Cluster 1A whereas Cluster 1B was characterized by painful conditions (e.g., headache, back pain, GERD). At 2 years, two clusters were identified with 82% and 18% captured in Clusters 2A and 2B. Cluster 2B was distinguished from 2A by a high burden of cardiovascular (CV) and pulmonary disease along with typical CV risk factors. At 5 years, three clusters were identified with 81%, 11%, and 8% captured in Cluster 5A, 5B, and 5C. Morbidities most common in Cluster 5A were hypertension and hyperlipidemia. Cluster 5B was distinguished by a higher burden of CV and pulmonary disease whereas Cluster 5C had the highest burden of certain glucocorticoid toxicities (e.g., osteoporosis, obesity, hypertension).
Conclusion: AAV is associated with a high burden of MM and carries a greater risk of MM than the general population. MM in AAV is characterized by clusters defined by morbidity burdens that vary over disease course and reflect a high impact of disease and its treatment. The development of interventions to prevent MM and minimize its impacts are needed. These findings identify an important

direction for future investigations to improve the care and outcomes of patients with AAV.

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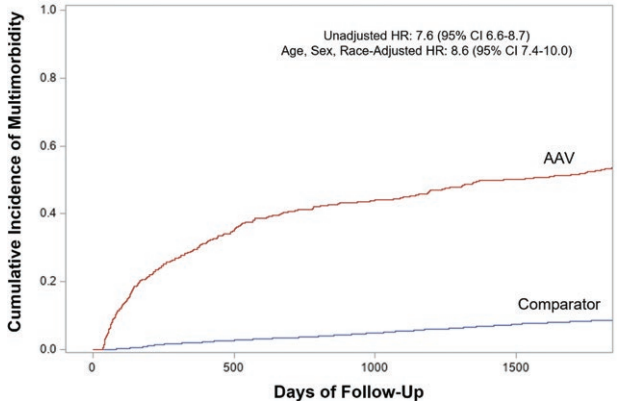
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Table 1. The Burden of Multimorbidity in AAV

	AAV Cases	Comparators
N	547	5259
Age (mean, SD)	59 (17)	59 (17)
Female (%)	39%	39%
Race		
White	88%	92%
Black/African American	2%	2%
Asian	1%	1%
Other	2%	2%
Unknown	3%	1%
BMI (mean, SD)	28.3 (6.9)	28.5 (7.3)
Proportion with Multimorbidity		
Year 1	37.8%	5.7%
Year 2	50.7%	8.7%
Year 3	54.4%	11.8%
Year 4	61.4%	14.9%
Year 5	66.2%	19.1%
Days Free from Multimorbidity*		
Year 1	282	353
Year 2	489	696
Year 3	666	1028
Year 4	823	1353
Year 5	963	1671

*Adjusted for age, sex, race

Figure: The Risk of Multimorbidity in AAV vs Comparators



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Disclosure of Interests: None Declared.
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Supporting patients in taking active part in their care

OP0306-HPR **POINTS TO CONSIDER FOR PATIENT EDUCATION PROVIDED BY NURSES ON METHOTREXATE USE. A EUROPEAN CONSENSUS INITIATIVE**

Keywords: Self-management, Nursing, Patient information and education

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Background: Methotrexate (MTX) is the anchor and most prescribed disease-modifying anti-rheumatic drug (DMARD) for inflammatory rheumatic diseases (IRDs). This treatment can be very efficacious but can also have serious, life-threatening side effects. Adequate education and follow-up of patients/carers are therefore essential and dedicated rheumatology nurse consultations are an important part of this. However, many patients across European countries do not have access to these nurse consultations and there are no agreed and clearly defined standards of care on this topic[1].

Objectives: To develop points-to-consider (PtC), based on the best available evidence and experts' opinion, on the nursing education of patients (or carers) with IRDs taking MTX.

Methods: A nominal group of adult and pediatric nurses (n=19) from 16 European countries, one rheumatologist, one pharmacist, and two patients, was established by the Portuguese Association of Health Professionals in Rheumatology (APPSReuma). The group convened virtually to agree on the protocol for developing the PtC, including the research questions for a scoping review and for a European survey to collect patients', nurses' and rheumatologists' experiences and perceptions about MTX education. The results from the scoping review and the surveys (presented elsewhere) were then used to devise and refine overarching principles and specific PtC statements through two virtual meetings and one online Delphi questionnaire. European Standard Operating Procedures for the development of recommendations/PtC were used.[2]

Results: The group reached consensus on three overarching statements and five PtC (Table 1). Almost all PtC were based on available scientific evidence, and all obtained high levels of agreement (>8/10).

Table 1. Points-to-consider for the nursing education of patients/carers taking methotrexate.

#	Overarching Principles	Level of Evidence	Strength of recomendation	Agreement Mean (SD)	Agreement % ≥8
1	All patients prescribed MTX and their carers should receive treatment-specific education.	--	--	9.4 (1.5)	94
2	Education for patients prescribed MTX needs to be ongoing and requires continuous review by the rheumatology team.	--	--	9.5 (1.1.)	94
3	Nurses should have access to training regarding methotrexate treatment and stay up to date through continuous education	--	--	9.5 (0.9)	94
	PtC				
1	Patients prescribed MTX and their carers should be offered education by a nurse when starting treatment, changing the route and when required by the patient.	3	C-D	9.7 (0.6)	100
2	Patients prescribed MTX should have access to a nurse for needs-based education to improve treatment knowledge#, enhance satisfaction with care and quality of life*	#3 *4	#C *D	9.8 (0.5)	100
3	Nurses should support patients and carers with relevant self-management skills related to MTX treatment, to ensure safety and improve self-efficacy.	3	C	9.8 (0.4)	100
4	Education about MTX should be tailored to the individual patient/carer needs.	3	C	9.7 (0.7)	100
5	Education on MTX for patients and carers can be delivered through face-to-face or online interactions, supplemented where necessary by telephone consultations, written or online resources.	3	C	9.4 (1.7)	94
6	Nurses should promote and support adherence to MTX by identifying and discussing potential barriers and facilitators.	3	C	9.7 (0.6)	100

Conclusion: A set of PtC to improve the quality of care provided to patients with IRDs and their carers regarding the education and support that should be provided by nurses specifically on MTX use, has been developed. The ultimate goal is to optimize MTX intake, improve efficacy, reduce side effects and ensure adherence to treatment. A plan is currently underway for the uptake and implementation of these PtC, recognizing the crucial role that the multi-professional rheumatology team plays in this.

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"So what now?" - living and planning life while co-existing with an RMD

OP0307-PARE WHAT ARE THE UNMET NEEDS OF PREGNANT PATIENTS DIAGNOSED WITH INFLAMMATORY RHEUMATIC DISEASES RECEIVING CARE IN A HIGHLY SPECIALIZED REPRODUCTIVE RHEUMATOLOGY CENTER? THE RESULTS OF THE CAPRI STUDY

Keywords: Pregnancy and reproduction, Patient information and education

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Background: Inflammatory rheumatic diseases (RD) often affects women in their childbearing years. Despite extensive counselling, we noticed that in RD patients there is an increasing need of more information concerning pregnancy and parenting. This suggests that there are still unexplored information needs regarding pregnancy and parenting in women with RD. To our knowledge, there are no studies exploring these unidentified information needs.

Objectives: The aim of this study was to evaluate the unmet needs of women diagnosed with RD that received highly specialized care in a tertiary Reproductive Rheumatology center.

Methods: Women (≥18 years) diagnosed with RD (such as rheumatoid arthritis, spondyloarthritis, psoriatic arthritis or juvenile idiopathic arthritis), who were followed-up by the Reproductive Rheumatology team from the Department of Rheumatology of the Erasmus University Medical Center were invited to complete an online questionnaire. The questionnaire was divided into different sections: pre-conception, pregnancy, post-partum, parenthood and support received/needed by informal caregivers such as family, friends, neighbors etc. The questions were related to the support and information provided by the team, problems experienced, unmet needs and the patient's general characteristics. The patients were offered the possibility to give additional remarks (free text). Descriptive statistics were used to represent the outcomes.

Results: From a total of 181 women who were invited to fill out the online questionnaire, 95 women (52%) completed the questionnaire. It concerns women in the age between 22 and 45 (mean of 33yrs), with a RD, who received their first (n=56), second, or third baby between 2019 and 2021. Overall, the care of the rheumatology team was highly rated by the women (satisfaction score of 88 (scale 0-100) for the rheumatologist and 92 (scale 0-100) for the rheumatology nurses) (Table 1). 18 Women (19%) experienced any problem during the period around their delivery and/or post-partum. Six women indicated that their problems persisted. A lack of mental health support regarding disease coping (4 out 6) was the most frequently mentioned persisting problem. In addition 2 out of 6 women indicated a need for additional communication with the rheumatology team regarding information, indication and adjustment of their medication between the regular outpatient clinic visits.

Conclusion: The care provided by the Reproductive Rheumatology team was highly rated by the majority of the women. Nevertheless, the following unmet needs were identified: a) mental health support regarding disease coping and, b) the opportunity to communicate about medication beyond the regular outpatient visits. Despite a very high satisfaction rate of patients treated by the Reproductive Rheumatology team some of them experience health problems that remain unsolved. This will help us to improve our patient-centered care as we aim at matching our care as appropriately as possible to patient needs. In the future, we want to identify the characteristics of the women who need more information, more mental support and, more contact between the regular consults, so we can help them solve their problems and fill their needs.

Table 1

	N=103
Age years mean, (range)	32.5 (22-45)
Diagnosis, n (%)	
• Rheumatoid arthritis	43 (41.7%)
• Psoriatic arthritis	17 (16.5%)
• Spondyloarthritis	16 (15.5%)
• Juvenile Idiopathic arthritis	15 (14.56)
• Other immunological disease	3 (2.9%)
• Other forms of arthritis	1 (0.9%)
Number of children, mean (%)	1.4 (1-3)
Age of youngest months, mean	13.9 (1-30)
Age at diagnosis mean, (range)	
• Rheumatoid arthritis	25 (0-39)
• Psoriatic arthritis	26.5 (18-33)
• Spondyloarthritis	28.8 (19-39)
• Juvenile Idiopathic arthritis	7.9 (2-16)
Counselling received n (%)	96 (96.97)
Higher professional education and university educated, n (%)	57 (64.77)
Working hours weekly, n (range)	27.5 (8-40)
Support, n (%)	
• Partner	96 (93.20)
• Family	41 (39.81)
• Others	7 (6.8)
Information received in the Department of Rheumatology, n (%)	
• Rheumatology nurse	13 (13.54)
• Rheumatologists	3 (3.13)
• Both	80 (83.33)
Problems experienced during pre-conception, pregnancy, after birth n, (%)	
• Yes	18 (19.15)
• No	76 (80.85)
Did you solve the problems? n (%)	
• Yes	6 (33.3)
• Partially	6 (33.3)
• No	6 (33.3)
Are you satisfied with the counseling received from the rheumatology nurse? (0-100) mean, range	92.74 (45-100)
Are you satisfied with the counseling received from the rheumatologist? (0-100) mean, range	88.47 (36-100)

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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Late-Breaking Oral Abstracts

LB0001 HEAD-TO-HEAD COMPARISON OF TLL-018 AND TOFACITINIB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: INTERIM RESULTS FROM A PHASE IIA STUDY

Topic: 16. Rheumatoid arthritis - non biologic treatment and small molecules

Keywords: Rheumatoid arthritis, Clinical Trials, Targeted synthetic drugs

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Background: None of the currently approved treatments for rheumatoid arthritis (RA) can achieve ACR50 in >50% of the patients, and ~20% of the RA patients are considered "difficult to treat", failing ≥2 targeted therapies. TLL-018 is a highly selective dual JAK1/TYK2 inhibitor. Its TYK2 activity might contribute to efficacy in RA patients.
Objectives: Compare efficacy of TLL-018 with tofacitinib in RA patients.
Methods: 101 patients with moderate-to-severe active RA who had inadequate response or were intolerant to methotrexate were randomized (1:1:1:1 ratio) to receive twice-daily oral TLL-018 10mg, 20mg, 30mg or tofacitinib 5mg. After 12-weeks of treatment, patients who achieved ACR50 continue the same treatment, and those who didn't change treatment as follows: patients on tofacitinib and TLL-018 10mg change to TLL-018 20mg; patients on 20mg and 30mg change to or continue 30mg TLL-018. The Primary endpoint is the proportion of patients achieving ACR50 at Week 12. Secondary endpoints include the proportion of patients achieving DAS28-CRP <2.6, ACR20, ACR70 at all scheduled time points, ACR50 at scheduled time points exclude week 12, CDAI and other parameters at 12 week. Safety was assessed via adverse event (AE) and laboratory examinations.
Results: 101 patients were randomized, ~50% of them also had prior bDMARDs and ~30% had prior JAK inhibitors. Demographics and baseline disease characteristics were balanced across treatment arms. At week 12, ACR50 response rates in TLL-018 treated groups [10mg, 20mg and 30mg, 48.0% (95% CI, 28.42 - 67.58), 65.4% (95% CI, 47.10 - 83.67), 72.0% (95% CI, 54.40 - 89.60), respectively] were higher than that for tofacitinib [41.7% (21.94 - 61.39)]. TLL-018 20 and 30mg were statistically superior to tofacitinib (p<0.05). Proportions of patients achieving clinical remission (DAS28-CRP<2.6) at week 12 were 39.1%, 34.8%, 54.5% and 17.4% at week 12 for the 10, 20, 30mg TLL-018 and tofacitinib, respectively. TLL-018 20 and 30mg demonstrated high efficacy in patients who had prior bDMARDs, achieving ACR50 rates of >66%. TLL-018 20mg dramatically improved responses in patients who didn't achieve ACR50 on tofacitinib at week 12. The most frequently reported treatment-emergent AEs were hyperlipidemia and respiratory infection in TLL-018 or tofacitinib-treated patients. There was one case of malignancy in tofacitinib treatment group. No death, venous thromboembolism or major adverse cardiovascular event was observed in the study. (The data cut-off time was December 19th).
Conclusion: TLL-018 20 and 30mg demonstrated superior efficacy over tofacitinib in RA patients, suggesting that inhibition of TYK2, in addition to JAK1, enhances efficacy. TLL-018 was well tolerated with most AEs being Grade 1 or 2 as expected from this class of compounds. No unexpected safety concerns were observed in the study. TLL-018 20 and/or 30mg BID warrants further studies in "difficult to treat" RA patients.
REFERENCES: NIL.
Acknowledgements: NIL.
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LB0002 SAFETY & EFFICACY OF SEL-212 IN PATIENTS WITH GOUT REFRACTORY TO COVENTIONAL TREATMENT: OUTCOMES FROM TWO RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED, MULTICENTER PHASE III STUDIES

Topic: 28. Crystal diseases, metabolic bone diseases other than osteoporosis

Keywords: Crystal Arthritis, Gout, Randomized control trial

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Background: Despite availability of effective therapies for gout, a small proportion of patients suffer from refractory gout and/or are intolerant to standard therapies [1]. In these patients, the inability to maintain serum uric acid (sUA) levels < 6 mg/dL may lead to severe clinical manifestations for which uricase-based therapies can be highly effective, though also immunogenic. SEL-212 is a once-monthly, novel 2-component, sequential uricase-based infusion therapy being investigated in patients with refractory gout. SEL-212 consists of an infusion of tolerogenic nanoparticles containing rapamycin (SEL-110) followed by pegadricase (SEL-037). The intent of this drug combination is to inhibit the formation of anti-uricase antibodies without the need for separate immunosuppressant therapies [2].
Objectives: DISSOLVE I and II (D1 and D2, respectively) evaluated the safety and efficacy of SEL-212 in adults with refractory gout.
Methods: D1 (US Study, 12 months) and D2 (Global Study, 6 months), were placebo-controlled, double-blind, randomized clinical trials that evaluated two dose levels of SEL-110 (0.15 mg/kg [high-dose] or 0.1 mg/kg [low-dose]) prior to SEL-037 (0.2 mg/kg) infusion in adults (19-80 years). Participants with a history of symptomatic gout were enrolled if they had ≥ 3 gout flares within 18 months prior to screening or ≥ 1 tophus or a current diagnosis of gouty arthritis, failed to normalize sUA and control symptoms with any xanthine oxidase inhibitor, and were not previously exposed to a uricase-based therapy. Participants were randomized 1:1:1 between the two doses of SEL-212 and placebo administered intravenously every 28 days for 6 treatments. D1 participants were continued in a 6-month blinded extension phase under the initial treatment conditions (Fig. 1). The primary endpoint was defined as the percentage of participants who achieved and maintained sUA < 6 mg/dL for ≥ 80% of the sixth 28-day treatment period (TP6) in the active treatment groups versus placebo (response rate). Safety and tolerability were assessed through monitoring of adverse events (AEs) and laboratory testing.
Results: A total of 265 participants (D1, n=112 (96% male, 66% ≥ 50 years); D2, n=153 (97% male, 72% ≥ 50 years) were randomized into the three treatment arms. Response rates in all treatment groups were significantly different from placebo (p ≤ 0.0015), with 56% and 47% of participants responding in the high-dose group and 48% and 41% in the low-dose group for D1 and D2, respectively (Table 1). The response rates in participants aged ≥ 50 years were 65% and 48% in the high-dose groups and 47% and 45% in the low-dose groups for D1 and D2, respectively (p ≤ 0.0044 vs placebo). Across all participants in the treatment groups, median sUA levels were reduced by ~96% and ~75% from baseline at TP6 for D1 and D2, respectively (p<0.001 vs placebo). The safety profile of SEL-212 was favorable, with 3.4% and 4.5% of participants experiencing infusion reactions in the high and low-dose groups, respectively. Reports of gout flares were comparable between treatment groups and placebo. Six participants (3.4%) in the pooled active treatment groups experienced treatment-related serious AEs (n=4 anaphylaxis, n=2 gout flares).
Conclusion: In the DISSOLVE trials, once-monthly treatment with SEL-212 demonstrated statistically significant response rates and reductions in sUA versus placebo. The safety profile of SEL-212 was consistent with that of uricase therapies. Targeted immunomodulation with SEL-212 has the potential to provide a new uricase-based treatment option for patients with gout refractory to conventional therapies without the need for traditional immunosuppressants.
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[1] Edwards NL. *Arthritis Rheum* 2008;58(9):2587-90.
[2] Sands E, *et al. Nat Commun* 2022;13:272.

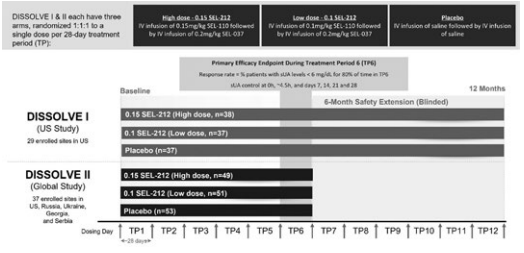


Figure 1. DISSOLVE I & II Study Design.

Table 1. Primary Efficacy Endpoint.

	DISSOLVE I			DISSOLVE II		
N	High dose (38)	Low dose (37)	Placebo (37)	High dose (49)	Low dose (51)	Placebo (53)
Response rate %	**56**	**48**	**4**	**47**	**41**	**12**
Risk Difference [97.5% CI]	53 [32, 73]	44 [23, 64]	-	35 [14, 56]	28 [8, 48]	-
p-value [1]	<0.0001	<0.0001	-	0.0002	0.0015	-

[1] p-value vs placebo (Mantel-Haenszel test)

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LB0003 DAZODALIBEP (VIB4920/HZN4920) IN SJÖGREN'S SUBJECTS WITH AN UNACCEPTABLE SYMPTOM BURDEN: SAFETY AND EFFICACY FROM A PHASE 2, RANDOMIZED, DOUBLE-BLIND STUDY

Topic: 17. SLE, Sjögren's and APS – treatment

Keywords: Safety, Randomized control trial, Sjögren syndrome

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Background: Sjögren's is a systemic autoimmune disease associated with marked morbidity and poor health-related quality of life, generally driven by the cardinal symptoms of the disease: dryness, pain, and fatigue (assessed via EULAR Sjögren's Syndrome Patient Reported Index [ESSPRI]). The population of Sjögren's patients with unacceptable symptomatic burden independent of systemic involvement represents a substantial proportion of Sjögren's patients who have largely been excluded from recent trials despite significant disease burden and overall unacceptable health status.
Objectives: The objective of this study (NCT04129164) was to evaluate the efficacy and safety of dazodalibep (DAZ), a non-antibody biologic antagonist of CD40L, in adult Sjögren's subjects with an unacceptable symptom burden but limited systemic organ involvement.
Methods: This was a randomized, double-blind, placebo-controlled, crossover study of DAZ in adult Sjögren's subjects with an unacceptable symptom burden but limited systemic organ involvement, as defined by having an ESSPRI score ≥ 5 and EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) score <5. Eligible subjects were randomized 1:1 to receive intravenous DAZ 1500mg or placebo (PBO) Q2W x 3 doses, then Q4W x 4 additional doses. Starting on Day 169, subjects initially randomized to DAZ received PBO Q4W x 5 doses and subjects randomized to PBO received DAZ Q4W x 5 doses and were then followed for 12 weeks. The primary endpoint was the change from baseline in ESSPRI at Day 169. Safety was also evaluated.
Results: A total of 109 subjects were randomized and received ≥1 dose of study medication (DAZ, N=54; PBO, N=55). The mean (standard deviation) age of subjects was 49.9 (12.1) years and most were female (94.5%). The change from baseline to Day 169 in ESSPRI (LS mean ± SE) was –1.80 ± 0.23 in the DAZ group compared to –0.53 ± 0.23 in the PBO group, a difference of –1.27 ± 0.33 (p = 0.0002). The change from baseline to Day 169 in each of the three domains of ESSPRI was significantly greater in the DAZ group compared to PBO (dryness: p = 0.0066; fatigue: p = 0.0022; pain: p = 0.0010). At Day 169, a significantly larger proportion of DAZ-treated subjects achieved a ≥1 point or ≥15% reduction in ESSPRI relative to PBO (66.7% vs 32.7%; p =0.008). The improvement from baseline to day 169 in the Functional Assessment of Chronic Illness Therapy-Fatigue score (LS mean ± SE) was significantly greater in the DAZ group (8.1 ± 1.4) relative to PBO (2.8 ± 1.4; p = 0.0095). Greater numerical improvement in DAZ-treated subjects was observed for the Ocular Surface Disease Index (–14.0 ± 3.0 vs –8.5 ± 2.9; p = 0.1936) and Patient's Global Impression of Severity (–0.6 ± 0.1 vs –0.4 ± 0.1; p = 0.1781) at Day 169 relative to PBO. Through Day 169, a total of 75 subjects reported an adverse event (AE; DAZ: 37 [68.5%]; PBO: 38 [69.1%]) and the majority were mild/moderate in severity. The most frequently reported AEs occurring in ≥5% of DAZ-treated subjects were COVID-19, nasopharyngitis, anemia, and diarrhea. There were three serious AEs in the DAZ group (pneumonia influenza, post-acute COVID-19 syndrome, and gammopathy) and one in the PBO group (neutropenia). All serious AEs were deemed by investigators to be unrelated to study medication. One subject in the DAZ group discontinued the study due to an AE compared to two subjects in the PBO group.
Conclusion: In this study of Sjögren's subjects with an unacceptable symptom burden but limited systemic organ involvement, the primary endpoint was achieved. DAZ-treated subjects experienced a statistically significant and clinically meaningful improvement in the key subjective symptoms of Sjögren's relative to PBO as measured by the improvement in ESSPRI and associated responder analysis. DAZ therapy was generally safe and well tolerated. Larger trials of DAZ therapy for Sjögren's are warranted to further explore its safety profile and confirm its clinical efficacy.

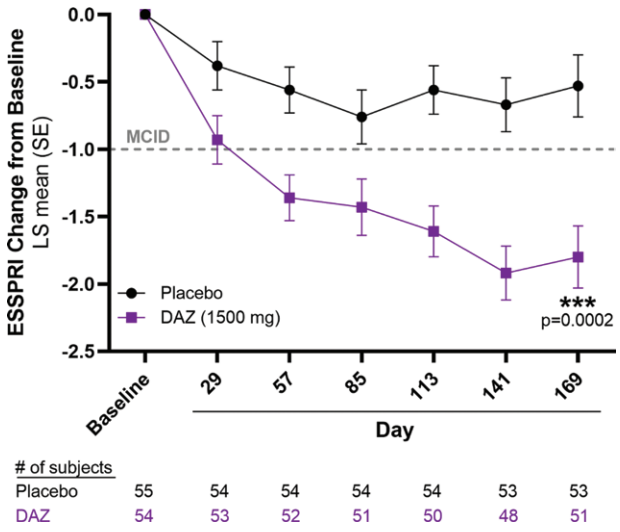


Figure 1. Adjusted Mean Change from Baseline in ESSPRI Score. Dashed line represents the MCID. Data analyzed using MMRM. ESSPRI, EULAR Sjögren's Syndrome Patient Reported Index; LS, least squares; MCID, minimal clinically important difference; SE, standard error.

REFERENCES: NIL.
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LB0004 PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS (PSLE) PATIENT STRATIFICATION AND HIGH-PERFORMANCE SERUM BIOMARKERS IDENTIFIED RESPONDERS TO STATIN AND PATIENTS WITH HIGH CARDIOVASCULAR RISK IN THE APPLE TRIAL (ATORVASTATIN FOR ATHEROSCLEROSIS PROGRESSION IN PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS)

Topic: 11. Basic and translational science in paediatric rheumatology

Keywords: Biomarkers, Randomized control trial, Rare/orphan diseases

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Background: Paediatric Systemic Lupus Erythematosus (pSLE) is associated with increased risk of atherosclerosis compared to adult-onset SLE. The APPLE trial is the largest investigator-led randomised control trial in pSLE, which tested the effect of atorvastatin vs. placebo for prevention of atherosclerosis progression over 36 months, using carotid intima-media thickness (CIMT) as primary outcome.
Objectives: We aimed to investigate:
1. patient stratification strategies to identify responders to statin in a trial which did not meet the primary outcome as well as.
2. novel high-performance biomarkers of atherosclerosis progression in the APPLE trial to establish which pSLE patients were at risk for atherosclerosis progression even if they did not respond to statin.
Methods: Unsupervised clustering analysis was used to stratify pSLE patients by their baseline CIMT and identify patterns of CIMT progression over 36 months. In-depth metabolomic analysis was performed to identify lipidomic signatures predictive of CIMT progression in both placebo and statin arm. Correlation and univariate regression analyses explored associations between patient, disease characteristics and serum biomarkers (Nightingale platform). Machine learning techniques and ROC analyses were used to identify and validate a serum metabolomic signature of high CIMT progression.
Results: Baseline CIMT stratified pSLE patients (N=151) into three groups with distinct CIMT progression trajectories irrespective of the treatment allocation. Two distinct CIMT progression rates (high vs. low), over 36 months were identified in the placebo group (N=60), while patients treated with atorvastatin (N=61) had three distinct CIMT trajectories (high, intermediate and low progression), not predicted by any of the numerous patient and disease determinants, including serum biomarkers, lipid profile and homocysteine levels, collected as part of the APPLE trial protocol. A robust and novel metabolomic signature predictive of high CIMT progression was identified (AUC = 80.7%) in the placebo arm, which could be used to identify patients at risk of atherosclerosis progression in pSLE. pSLE patients with low rate CIMT progression identified by the CIMT stratification benefitted from treatment with atorvastatin (P= 0.035), providing evidence that the lack of patient stratification led to the negative results of the APPLE trial.
Conclusion: This analysis of the APPLE trial provides novel evidence for the significant heterogeneity of subclinical atherosclerosis in pSLE and its distinct progression trajectories irrespective of treatment allocation, and identified pSLE patients who responded to statin, with implications for future patient stratification for clinical trials. We also showed that in- depth metabolomic signature can identify with better performance that any other biomarkers available, patients at risk for atherosclerosis progression with potential role for long-term cardiovascular risk management in pSLE.
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Disclosure of Interests: None Declared.
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LB0005 RITUXIMAB OBJECTIVE OUTCOME MEASURES TRIAL IN SLE (ROOTS): A DOUBLE-BLIND RANDOMISED PLACEBO-CONTROLLED FEASIBILITY TRIAL

Topic: 17. SLE, Sjögren's and APS – treatment

Keywords: Randomized control trial, Systemic lupus erythematosus, bDMARD

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Background: Many new medicines in SLE have not met endpoints in placebo-controlled RCTs even when other evidence indicates that they are effective. Reasons suggested are inclusion of patients with inactive disease, inaccurate or subjective outcome measures that seek to address diverse manifestations, and comparator arms that include excessive glucocorticoid dose.
Objectives: (i) To evaluate the feasibility of a novel trial design focusing on musculoskeletal SLE with objective eligibility criteria and endpoints and a low-dose glucocorticoid standard of care. (ii) To provide preliminary evidence for efficacy of rituximab. (iii) To provide additional validation of outcome measures.
Methods: Adults with SLE were enrolled if they had clinical synovitis and/or ultrasound (US) tenosynovitis and/or positive power Doppler (PD) in ≥1 joint despite stable background therapies including a maximum 10mg prednisolone. Patients were randomized to 1000mg rituximab (Rixathon, RTX) or placebo, on days 1 and 15. Blinded infusions were preceded by 100mg methylprednisolone. Outcome measures, including BILAG-2004, SLEDAI-2K, The Lupus Arthritis and Musculoskeletal Disease Activity Score (LAMDA), tender and swollen joint counts, physician global, patient MSK pain and global VAS, patient reported outcome measures, BICLA, SRI-4 were evaluated monthly. US of both hands and wrists was performed at 0 and 16 weeks. The primary endpoint was overall feasibility. The key efficacy timepoint was 16 weeks. After 16 weeks placebo patients with active disease were eligible for rescue rituximab with repeat follow up timepoints. US and LAMDA were validated against BILAG-MSK improvement at 16 weeks using regression models adjusted for baseline.
Results: Of 35 patients invited, 35 attended screened and consented, 6 were ineligible and 2 withdrew prior to baseline. Of 27 patients randomised, 12 were randomised to placebo, of whom 9 received rescue therapy. All completed ≥16 weeks follow up and 25/27 completed all follow up visits. 24/27 (89%) patients were female, 17/27 (63%) were white, 7/27 (26%) were South Asian. Mean (SD) age was 49.7 (12.7) and disease duration 6.7 (9.0). BILAG MSK domain at baseline was scored A in 7/27 (26%), B in 16/27 (59%) and C in 2/27 (7.4%). B scores were also present in mucocutaneous in 2/27 patients and constitutional in 1/27. At 16 weeks, BILAG-MSK response was significantly associated with improvement in LAMDA (OR 0.48, 95% CI 0.18, 0.84); US joints grey-scale (OR 0.56, 95% CI 0.28, 0.85) and US tendons PD (OR 0.33, 95% CI 0.04, 1.01). No substantive difference between arms in efficacy variables was found at week 16. Unexpectedly, results suggested greater improvement in some outcomes in patients who received methylprednisolone and placebo compared to methylprednisolone and rituximab. These measures then converged by 16 weeks (Figure 1). Pooling all rituximab cycles administered (as initial therapy or as rescue) showed improvement in PGA, Physician MSK VAS, joints GS and joints PD scores and LAMDA, but not Global BILAG, SLEDAI-2K, tender or swollen joint counts or and LupusQoL domain or patient VAS at week 16.
Conclusion: design dedicated to MSK SLE was feasible. The new outcome measures of LAMDA and MSK US were validated against BILAG-MSK; these outcomes should be included in a definitive trial. While not powered to measure efficacy, exploratory analysis suggests unexpectedly greater improvement in patients who received methylprednisolone with placebo compared to methylprednisolone with rituximab at early time points after infusion, later converging by week 16. Meanwhile there was an overall improvement in LAMDA and US at 16 weeks across all RTX cycles administered. In a definitive trial, early assessment of efficacy should be retrained, but longer observation without retreatment may be required to assess the efficacy of RTX in this population.

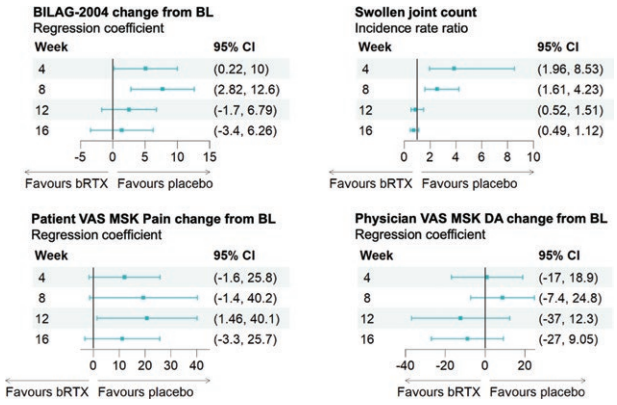


Figure 1.

REFERENCES: NIL.
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LB0006 COVID-19 SEVERITY, BREAKTHROUGH INFECTIONS AND ANTI-SARS-COV-2 VACCINE SAFETY IN YOUNG PEOPLE WITH RHEUMATIC AND NON-RHEUMATIC AUTOIMMUNE DISEASES: RESULTS FROM THE COVAD1 AND COVAD2 PROJECTS

Topic: 30. COVID-19

Keywords: Vaccination/Immunization, Safety, COVID

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Background: Notwithstanding the wealth of literature on COVID-19, studies focusing on young people with autoimmune diseases (ADs) are lacking. Despite their younger age, they may have been exposed to immunosuppressants (IS) for longer than older adults, particularly if diagnosed at pediatric age.
Objectives: To determine early (within 7 days) and late (after 7 days) anti-SARS-CoV-2 vaccine-related adverse events (AEs), post-vaccine disease flares, COVID-19 severity and breakthrough infections (B-INFs) in young people with rheumatic diseases (RMDs) and non-rheumatic (nr)-ADs compared to healthy controls (HC).
Methods: The EULAR Young PARE definition was used to classify young patients (18-35 years old). Data were captured through the international COVID-19 Vaccination in AD (COVAD) 1 and 2 questionnaires (covering the years 2021 and 2022) and variables differing across groups in univariable analysis were included in multivariable analysis adjusting for baseline factors defined a priori.
Results: Of 20,685 complete responses, 6010 were from young people (1692 RMD, 400 nrADs, 3918 HC). RMDs and nr-ADs comprised mainly females of Caucasian, Asian and Hispanic ethnicities. Before vaccination, <5% and 7% of nrAD were taking glucocorticoids (GC) or immunosuppressants (IS) other than GC vs 30% GC and >80% IS in RMDs. Over 80% of total responders had received ≥2 vaccine doses.

1) AEs after 1 or 2 doses. Early mild AEs were more frequent in RMDs and nr-ADs compared to HC [RMD vs HC odds ratio (OR) (95% confidence interval (CI)) 2.4 (2.0-3.1); nr-AD vs HC 2.0 (1.4-2.9)]. Injection site pain, headache and fatigue were the most frequent mild AE in all 3 groups, but they were more frequent in nr-AD than in HC and RMD. Fever and chills were also more frequent in nr-AD compared to HC and to RMD. The frequency of late mild AEs after either of the 2 doses was < 10% in all 3 groups with no differences between groups. Severe AEs were < 2% in all groups, with no differences between the first and second dose.
2) AEs after 3 or 4 doses. The frequency of late mild AEs after any dose (1, 2 3 or 4) was < 20% in all 3 groups with no differences between groups. Severe AEs after the third dose were <3%. In the 1417 responders that received a fourth dose, only two (1 RMD and 1 HC) reported AEs (0.1%).
3) Pre-vaccine vs breakthrough infections (B-INFs). The frequency of reported SARS-CoV-2 infections was similar in all groups (RMD=28%, nr-ADs=25%, HC=28%). However, RMD patients reported only one infection more frequently than nrADs and HC, while nrADs reported ≥ 2 infections more frequently than RMD. Pre-vaccine infections were less frequent in RMD vs HC (OR=0.6, 95% CI= 0.4-0.9), but similar in nr-AD vs HC. In contrast, the frequency of B-INFs was higher in RMD vs HC (OR=2.7 95% CI 2.1-3.5), while it was similar in nr-AD vs HC. Regarding the clinical profiles of pre-vaccine infections versus B-INFs, no differences were observed among nrADs whereas in RMD a significantly lower frequency of loss of smell and loss of taste was reported for B-INFs. Less than 5% of total respondents received advanced therapies for SARS-CoV-2 infection.
4) Post-vaccination disease flares: Self-reported disease flares after the second vaccine dose were reported by 10% or RMD and 7% of nrAD patients. Of these, approximately half reported requiring a change in their medications (increased dose/addition of a new IS and/or GC).

Conclusion: This study provides the first detailed exploration of the SARS-CoV2 spectrum in young people with RMDs and nrADs compared to HC and highlights important similarities and differences between disease groups. In fact, despite being less exposed to GC and IS, nr-AD reported a higher number of SARS-CoV-2 infections, no difference in the clinical picture of pre-vaccine infections vs B-INFs and a more pronounced burden of post-vaccine mild AEs after earlier doses compared to RMD. These findings may highlight that in young people the type of disease rather than IS therapy may be more important to influence the vaccine safety and the features of B-INFs.
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Prehabilitation to increase treatment success in rheumatology

LB0007

SHORT- AND LONG-TERM EFFECTS OF HIGH-INTENSITY INTERVAL TRAINING IN PATIENTS WITH INFLAMMATORY JOINT DISEASE: THE EXEHEART RANDOMIZED CONTROLLED TRIAL

Topic: 39. Rehabilitation

Keywords: Cardiovascular disease, Non-pharmacological interventions, Randomized control trial

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Table 1. Effects of HIIT at 3 and 6 months. Data presented as mean (SD).

	HIIT group Baseline	Follow-up	Control group Baseline	Follow-up	*n*	Mean group difference (95%CI)[a]	*p*
VO_{2peak}, mL/kg/min Baseline to 3 months	30.4 (5.9)	32.9 (6.4)	30.1 (7.9)	30.3 (7.5)	60§	2.5 (0.9-4.0)	<0.01
Baseline to 6 months	30.4 (5.9)	33.2 (7.4)	30.4 (8.0)	30.7 (7.8)	60§	2.6 (0.8-4.3)	<0.01
Fatigue, NRS 0-10, 0= no fatigue Baseline to 3 months	3.1 (2.1)	3.0 (1.9)	3.6 (2.5)	3.5 (2.7)	59 58	-0.1 (-0.9-0.8)	0.87 0.41
Baseline to 6 months	3.1 (2.1)	3.1 (2.2)	3.6 (2.5)	3.8 (2.4)		-0.4 (-1.2-0.5)[b]	
Pain, NRS 0-10, 0= no pain Baseline to 3 months	2.9 (2.1)	2.8 (1.8)	2.9 (2.5)	3.1 (2.7)	59 58	-0.3 (-1.3-0.7)[b] -0.4 (-1.2-0.5)	0.57 0.38
Baseline to 6 months	2.9 (2.2)	2.9 (2.0)	2.9 (2.5)	3.2 (2.4)			

§ Primary analysis with multiple imputation of estimate, *n*=60. [a]ANCOVA; gender, group, age and baseline value as covariates. [b]Bootstrap CI with 10000 replications. HIIT: High-intensity Interval Training, NRS: Numeric rating scale, VO_{2peak}: Peak oxygen uptake

Background: Cardiorespiratory fitness (CRF) is recognized as an independent risk factor for cardiovascular disease (CVD) and improved CRF associates with lower risk of CVD [1]. High-intensity interval training (HIIT) is an effective mode of exercise to increase CRF. However, HIIT is seldom utilized in physiotherapy primary care in the context of inflammatory joint disease (IJD), and the sustainable effects of HIIT have been questioned [2].
Objectives: To investigate short- and long-term effects of twelve weeks of supervised HIIT in physiotherapy primary care on CRF, pain and fatigue in patients with IJD.
Methods: In this assessor-blinded randomized controlled trial (NCT04922840), 60 patients were allocated to a control group (n=30) or a HIIT group (n=30) that received a 12-week intervention in physiotherapy primary care including two weekly supervised 4x4 minute HIIT sessions at 90-95% peak heart rate and one non-supervised exercise session at moderate intensity. Patients were assessed at baseline, 3 and 6 months. Primary outcome was change in CRF from baseline to 3 months, measured as peak oxygen uptake (VO_{2peak}) by a cardiopulmonary exercise test. Secondary outcomes were pain and fatigue (Numeric Rating Scale 0-10, 0= no pain/fatigue). Group differences were assessed by pre-specified intention-to-treat analysis of covariance with multiple imputation of missing data for the primary outcome. Per-protocol analysis was applied for the primary outcome.
Results: Median age was 59 years (IQR 52-63) and 34 participants (57%) were female. A total of 55 patients completed assessment at 3 and 6 months for the primary outcome; 27 in the HIIT group and 28 in the control group. Following HIIT, there was a significant between-group difference in VO_{2peak} (2.5 mL/kg/min, p<0.01) in favor of the exercise group at 3 months with no corresponding differences in pain and fatigue (Table 1). At 6 months, the between-group difference in VO_{2peak} was maintained (2.6 ml/kg/min, p<0.01) and there were no significant differences in pain and fatigue (Table 1). Per-protocol analysis at 3 months showed a between-group difference in VO_{2peak} (3.2 mL/kg/min, p<0.001, 95% CI 1.7-4.8) in the 19 (70%) patients that adhered to ≥17/24 HIIT sessions compared to the 20 (71%) control group patients that refrained from aerobic exercise.
Conclusion: CRF increased in patients with IJD following 12 weeks of supervised HIIT and the effect was maintained at 6 months. The beneficial response on CRF was not accompanied by changes in pain or fatigue and the intervention can be regarded as feasible in physiotherapy primary care. HIIT is a viable physiotherapy intervention with sustainable effects in patients with IJD.
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Neutrophil dysregulation in systemic lupus erythematosus

LB0008

NOVEL PATHOGENETIC MECHANISMS MEDIATED BY DYSREGULATION OF TRIM21-STING-TYPE I INTERFERON AXIS IN LUPUS

Topic: 08. SLE, Sjögren's and APS - aetiology, pathogenesis and animal models

Keywords: Autoantibodies, Systemic lupus erythematosus, Biomarkers

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Background: Tripartite motif-containing protein (TRIM) 21 is an E3 uniquitin-protein ligase, involved in the ubiquitin-dependent proteolysis pathway of various proteins including factors related to type I interferon pathways. Although the presence of autoantibodies against TRIM21 in various autoimmune diseases suggests potential pathogenetic roles, no studies have clarified its exact implications especially in lupus.
Objectives: We aimed to elucidate the functions of TRIM21 in dysregulation of type I interferon signals in lupus.
Methods: To investigate effects of TRIM21 dysfunction in lupus pathogenesis, two independent lupus animal models, the R848-induced model and the B6/*lpr* mice model were performed using TRIM21 knockout mice and their phenotypes and immunological profiles were determined. In addition, we investigated the degree of TRIM21 dysfunction and therapeutic effects of *in vivo* delivery of TRIM21 in MRL/*lpr* mice. To evaluate the E3 ubiquitin ligase activity of TRIM21 for targeted proteins in type I interferon pathways, we performed specialized immunoblot assay.
Results: The R848-induced model and the B6/*lpr* model both presented with more severe lupus-like phenotypes such as nephritis, lymphadenopathies, and inflammatory immune cell profiles in TRIM21 knockout mice than in control mice. TRIM21 deficiency resulted in activation of intracellular factors related to type I interferon pathways such as STING, TBK1, and IRF3 in both models. MRL/*lpr* mice presented with activation of type I interferon pathways including STING, TBK1, and IRF3, and decreased expressions of TRIM21. Overexpression of TRIM21 attenuated the disease phenotypes in MRL/*lpr* mice. Using immunoblot assay, we observed E3 ubiquitin ligase activity of TRIM21 directly targeting STING via the proteasome pathway.

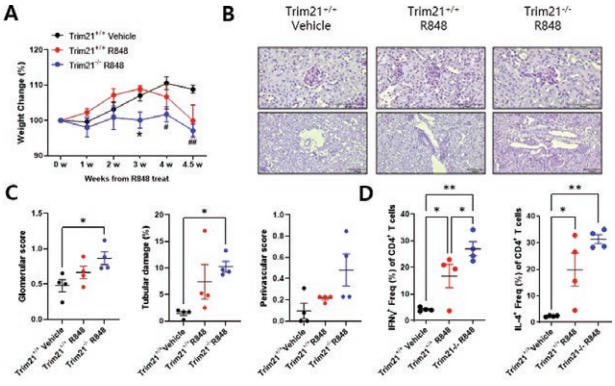


Figure 1.
(A) Bodyweight changes of R848- or vehicle-treated mice. (B) Representative images of H&E-stained kidney tissues from R848- or vehicle-treated mice. (C) Glomerular score, tubular damage score, and perivascular pathology score of kidney tissues from R848- or vehicle-treated mice. (D) Percentages of interferon-gamma-positive or IL-4-positive CD4+ T cells from R848- or vehicle-treated mice.

Conclusion: TRIM21 dysfunction induced dysregulation of STING-type I interferon pathways and exacerbates the disease in lupus animal models. Targeting TRIM21-STING-type I interferon axis can be a novel therapeutic strategy in lupus treatment.
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EULAR Recommendations

LB0009

EULAR RECOMMENDATIONS FOR THE USE OF IMAGING IN LARGE VESSEL VASCULITIS IN CLINICAL PRACTICE: 2023 UPDATE

Topic: 19. Vasculitis – large vessel vasculitis

Keywords: Vasculitis, Imaging, Quality of care

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Background: Imaging recommendations for primary large vessel vasculitis (LVV) were developed in 2018. Several new studies have emerged since then, and an update of the original statements was required.

Objectives: To update the recommendations for the use of imaging in LVV.

Methods: A systematic literature review update was performed to retrieve new evidence on ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT) and [18F]-fluorodeoxyglucose positron emission tomography (FDG-PET) for diagnosis, monitoring and outcome prediction in LVV. The task force consisted of 24 physicians, health professionals and patients from 14 countries.

Results: Three overarching principles and eight recommendations were agreed (Table 1). Compared to the 2018 version, US is now recommended as first line imaging test in all patients with suspected GCA, and axillary arteries should be included in the standard examination. As an alternative to US, cranial and extracranial arteries can be examined by FDG-PET or MRI. For Takayasu arteritis, MRI is the preferred imaging modality; CT or FDG-PET are alternatives. Although imaging is not routinely recommended for follow-up, US, FDG-PET or MRI may be used for assessing vessel abnormalities in LVV patients with suspected relapse, particularly when laboratory markers of inflammation are unreliable. MRA, CTA or US may be used for long-term monitoring of structural damage, particularly at sites of preceding vascular inflammation.

Conclusion: The 2023 recommendations provide up-to-date guidance for the role of imaging in the diagnosis and assessment of patients with (suspected) LVV.

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Table 1. Recommendations for the use of imaging in large vessel vasculitis in clinical practice

Overarching principles
A. In patients with suspected GCA, an early imaging test is recommended to support the clinical diagnosis of GCA, assuming high expertise and prompt availability of the imaging technique. Imaging should not delay initiation of treatment.
B. Imaging examination should be done by a trained specialist using appropriate equipment, standardized operational procedures and settings.
C. In patients in whom there is a high clinical suspicion of GCA and a positive imaging result, the diagnosis of GCA may be made without an additional test (biopsy or further imaging). In patients with a low clinical probability and a negative imaging result, the diagnosis of GCA can be considered unlikely. In all other situations (including the case of an inconclusive imaging result), additional efforts towards a diagnosis are necessary.
Recommendations
1. Ultrasound of temporal and axillary arteries should be considered as the first imaging modality to investigate mural inflammatory changes in patients with suspected GCA.
2. High resolution MRI or FDG-PET can be used as alternatives to ultrasound for the assessment of cranial arteries in patients with suspected GCA.
3. FDG-PET, alternatively MRI or CT, can be used for the detection of mural inflammation or luminal changes of extracranial arteries in patients with suspected GCA.
4. In patients with suspected TAK, MRI to investigate mural inflammation or luminal changes should be used as the first imaging test to make a diagnosis of TAK.
5. FDG-PET, CT or ultrasound may be used as alternative imaging modalities in patients with suspected TAK. Ultrasound is of limited value for assessment of the thoracic aorta.
6. Conventional angiography is not recommended for the diagnosis of GCA or TAK as it has been superseded by the previously mentioned imaging modalities.
7. In case of a suspected relapse of GCA or TAK, particularly when laboratory markers of disease activity are unreliable, ultrasound, FDG-PET or alternatively MRI may be considered for the assessment of vessel abnormalities. Imaging is not routinely recommended for patients in clinical and biochemical remission.
8. In patients with GCA or TAK, MRA, CTA or ultrasound of extracranial vessels may be used for long-term monitoring of structural damage, particularly at sites of preceding vascular inflammation. The frequency of screening as well as the imaging method applied should be decided on an individual basis.

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Poster Tours

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

POS0001 A NOVEL METHOTREXATE TARGET TP63 SUPPRESSES FOXP3 EXPRESSION AND EXACERBATES AUTOIMMUNE ARTHRITIS

Keywords: Rheumatoid arthritis, Animal Models, Disease-modifying Drugs (DMARDs)

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease characterized by autoreactive T cell activity and the presence of autoantibodies [1]. Although methotrexate (MTX) is well-recognized as the "anchor drug" for the treatment of RA [2], its precise mechanism, except antifolate activity, is largely unknown.
Objectives: The aim of this study was to elucidate a molecular target of MTX and to determine the role of the target molecule in $CD4^+$ T cells.
Methods: We examined comprehensive gene expression profiles of $CD4^+$ T cells by DNA microarray before and after MTX treatment in RA patients. We also examined the role of Tp63, a possible target of MTX, in human/mouse $CD4^+$ T cells.
Results: TP63 was the most significantly downregulated gene in $CD4^+$ T cells of RA patients after MTX treatment. TAp63, an isoform of Tp63, was highly expressed in human/mouse Th17 cells but rarely expressed in Treg cells, and MTX suppressed its expression in vitro. By comparing the comprehensive gene expression profiles between human Th17 cells overexpressing TAp63α and those with TAp63 knockdown, Foxp3 was identified as one of the downregulated genes by TAp63. Reporter assays revealed that TAp63α suppressed the activation of the Foxp3 CNS2 enhancer. TAp63 knockdown in induced-Tregs promoted Foxp3 CNS2 hypomethylation and enhanced suppressive activity of induced-Tregs. Moreover, the severity of arthritis was ameliorated in SCID mice transferred with SKG $CD4^+$ T cells with TAp63 knockdown compared to those with non-silencing.
Conclusion: TAp63 suppresses Foxp3 expression and exacerbates autoimmune arthritis.
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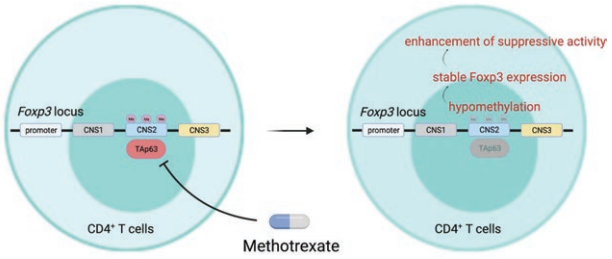


Figure 1.

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POS0002 MICROBIOTA-DERIVED HISTAMINE INDUCES RESOLUTION OF SYNOVIAL INFLAMMATION VIA CELLS OF THE NERVOUS SYSTEM

Keywords: Diet and Nutrition, Rheumatoid arthritis, Gastrointestinal tract

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Background: Intestinal dysbiosis has been associated with the development and progression of rheumatoid arthritis (RA) [*1].* Microbiota-derived metabolites such as short-chain fatty acids (SCFA) gained attention in research of inflammatory diseases as promising targets for new therapeutics. Previous work in our lab showed the potent preventive effect of SCFA on the onset of inflammatory arthritis (*2, 3*). Although effective potential therapeutic approaches are arising, their underlying mechanisms remain elusive [*4-6].* Cellular derived histamine is considered as pro-inflammatory mediator to induce acute allergic symptoms and to maintain chronicity. Interestingly, we identified an unexpected pro-resolving pathway of SCFA-induced histamine secretion by the gut microbiota. In contrast to the effective, direct Treg inducing 2-week delayed resolving effects of the SCFA propionate, we report on an indirect but ten times faster histamine-mediated pro-resolving mechanism via cells of the nervous system.
Objectives: To understand the rapid pro-resolving effects of microbiota-derived histamine on synovial inflammation.
Methods: We used 16s rRNA sequencing, HPLC size chromatography exclusion, FMT and meta-transcriptomics to assess propionate-induced changes in microbiota composition and the secreted metabolite profile. Mice with collagen- or serum-induced arthritis (CIA/SIA) were treated orally, i.p. or intrathecally with histamine or specific receptor agonists. Cellular changes in spleen, lymph nodes and joints were assessed by Cytek spectral flow cytometry, inflammatory infiltration and bone erosion were analyzed by histology and µCT. We analyzed differences in CNS and PNS via RNAseq of the spinal cord and peripheral nerves. Effects on vessel leakiness and cell infiltration in the inflamed joints were assessed via lightsheet microscopy and in vivo PET-CT.
Results: Here, we show that therapeutic treatment of CIA mice with the SCFA propionate starting from peak of disease (30 dpi) strongly induced resolution of synovial inflammation after 14 days of treatment. We demonstrate that oral propionate-treatment causes beneficial changes in the microbiota composition and thereby alters the secreted metabolite profile. These metabolites are able to induce rapid resolution of inflammation already after 2 days. By untargeted metabolomics we were able to identify histamine as highly potent metabolite that is increased upon propionate treatment. Oral treatment of CIA mice with histamine or a histamine 3 receptor (H3R) agonist significantly improved clinical symptoms. H3R is mainly expressed on cells of the nervous system. Upon oral H3R treatment we found alterations in activation marker expression in the spinal cord. We further were able to identify changes in the composition and activation of spinal cord (CNS) and the N. plantaris (PNS) of arthritic mice induced by H3R agonist treatment through RNAseq. Moreover, lightsheet microscopy and in vivo PET-CT scans revealed alterations in vessel leakiness and cell infiltration in the inflamed joints.
Conclusion: In summary, these data show that the SCFA propionate effectively regulates ongoing inflammation by promoting histamine secretion of the gut microbiota and subsequent H3R-mediated neuronal effector functions that drive the fast resolution of synovial inflammation.
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POS0003 HUMAN LYMPH NODE STROMAL CELLS MAINTAIN FOXP3+ REGULATORY T CELLS IN A HLA-DR DEPENDENT MANNER

Keywords: Adaptive immunity, Cell biology, Rheumatoid arthritis

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Background: Animal studies have shown that lymph node stromal cells (LNSCs) are key players in peripheral tolerance through their capacity to present self-antigens in MHC class II to CD4+ T cells thereby controlling auto-reactivity and humoral response. Thus, it has been suggested that dysfunctional LNSCs may play a role in the breaking of tolerance observed in autoimmune diseases like rheumatoid arthritis (RA), where there is a genetic association with the HLA-DR locus.
Objectives: We hypothesise that human LNSCs from healthy individuals without autoimmunity can express HLA-DR and maintain FOXP3+ regulatory T cells, a process which may be disturbed in LNSCs from RA patients.
Methods: Lymph node needle biopsies were collected from healthy volunteers, autoantibody positive RA-risk individuals and RA patients. In addition, lymph node stromal cells (fibroblasts) and paired peripheral blood mononuclear cells were obtained from non-RA controls. A combination of imaging techniques including spectral analyser, ImageStream, confocal and electron microscopy was used to determine the expression of HLA-DR directly *ex vivo* and on *in vitro* cultured LNSCs. To investigate the ability of these LNSCs to maintain regulatory T cells we employed an *in vitro* system where LNSCs were co-cultured with autologous CD4+ T cells for 72 hours. Subsequently flow cytometry analysis was used to determine the presence of FOXP3+ regulatory T cells.
Results: The presence of lymphocytes induced HLA-DR expression on cultured LNSCs from non-RA controls. The presence of LNSCs within this autologous co-culture model is crucial for maintaining CD25+ CD127- FOXP3+ regulatory T cells. To investigate possible mechanisms for this maintenance we used blocking antibodies for both HLA-DR and interleukin 2 (IL-2) in our system and showed that the maintenance of FOXP3+ regulatory T cells required both HLA-DR and IL-2. In the context of autoimmunity we were able to show that lymph node biopsies from RA patients directly analysed *ex vivo* have a significant reduction in the frequency of HLA-DR+ LNSCs compared to control individuals and those at risk of developing the disease.
Conclusion: Overall, these results indicate an important role for HLA-DR expressing LNSCs in maintaining tolerance within the lymph node, a process that may be dysfunctional in the context of autoimmunity where tolerance is broken.
Acknowledgements: We thank our study subjects for participating in the study, the AMC radiology department for lymph node tissue sampling and the rheumatology lab for sample processing. The research leading to these results was funded by an AMC fellowship (to L.G.M.v.B.), the Dutch Arthritis Foundation LLP-30, a ZonMw TOP project 91217014 and the Dutch Organization for Health Research and Development (ZonMw) VIDI n° 91718371 (to L.G.M.v.B).
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POS0004 PRO-INFLAMMATORY ANTI-MODIFIED PROTEIN AUTOANTIBODIES DERIVED FROM BONE MARROW, SYNOVIAL, AND LUNG B CELLS PREFERENTIALLY TARGET MALONDIALDEHYDE-ACETALDEHYDE CROSS-LINKED MOLECULAR STRUCTURES

Keywords: Autoantibodies, Rheumatoid arthritis, Adaptive immunity

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Background: Autoantibodies to malondialdehyde (MDA) proteins constitute a subset of anti-modified protein autoantibodies (AMPA) in rheumatoid arthritis (RA), which is not directly overlapping with citrulline reactivity. We have previously shown that IgM anti-MDA is prominent in the natural antibody repertoire at birth and may have homeostatic roles. Yet, IgG anti-MDA is elevated in RA and correlates with DAS28, CRP, IL6 and TNF-α [1]. Moreover, RA-derived anti-MDA monoclonal antibodies induce bone erosion and osteoclastogenesis by modulating cell metabolism [2]. MDA is an oxidation-associated reactive aldehyde that together with acetaldehyde (AA) mediates formation of a range of amino acid adducts including linear MDA-lysine, fluorescent MAA-lysine, and intramolecular cross-linking. MDA/MAA proteins carry multiple adduct-variants, and we here propose that distinct subsets of anti-MDA/MAA antibodies, defined based on the MDA-induced molecular structures recognized, have different pathogenic properties. Moreover, we have investigated the presence of class-switched MDA+ B cells in RA synovium, bone marrow, and bronchoalveolar lavage (BAL).
Objectives: Identification of RA MDA+ B cells from different compartments and distinct MDA/MAA reactivity patterns.
Methods: Human recombinant mAbs were generated from single-cell sorted B cells from BAL and bone marrow (n=148) and screened for reactivity to MDA and MAA modified antigens. MDA-cyanoborohydride and MDA/MAA-hapten proteins without cross-linking were used for characterization. Serology screening of IgG reactivity to MAA-BSA was performed as previously described [3].
Results: IgG MAA-reactivity is elevated in 49% of ACPA+ RA patients (n=278) compared to 14% of population controls (n=437). We did not detect any significant increase in IgG anti-MAA in ACPA+ RA-risk individuals at baseline,14% had high anti-MAA (n=263), compared to controls. But for risk-individuals that developed arthritis, anti-MAA levels increased at onset of arthritis with 26% displaying elevated levels (n=53). We identified IgG+ MDA+ cells among RA bone marrow plasma cells and BAL B cells from both early RA and ACPA+ RA-risk, which could be compared to three previously identified RA synovial clones. Seven out of eight investigated clones carried somatic hypermutations (SHM). Interestingly, all clones with SHM were found to specifically target MAA cross-linked structures rather than MDA- or MAA-hapten, while the germline-encoded synovial clone F04 bound strongly to linear MDA-lysine in proteins and peptides. Germline converting resulted in reduced MDA/MAA binding, suggesting different origin of the clones compared to F04. All binding was independent of protein backbone. Yet, only a subset of MAA-selective clones with SHM induced robust TNF-α expression in monocyte-derived macrophages and enhanced osteoclastogenesis.
Conclusion: MDA/MAA positive B cells can be identified in bone marrow and synovium in established RA and in the lungs of early and RA-risk individuals, but serum levels are only increased in conjunction with onset of arthritis and with inflammation. SHM and class-switching suggest affinity maturation and T-cell dependence of these responses. Distinct targeting of different MDA/MAA molecular structures was observed. Future studies will elucidate how MDA recognition patters are related to the anti-MDA inflammatory and bone-modulating properties and disease stages.
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POS0005 IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOSITIS, MUSCLE-RESTRICTED TCR CLONES SHARE STRUCTURAL FEATURES, WHILE THEIR EXPANSION CORRELATES WITH DISEASE ACTIVITY

Keywords: Myositis, Cell biology, Adaptive immunity

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Background: T cells of different lineages including cytotoxic T cells have been implicated in the pathogenesis of idiopathic inflammatory myopathies [1]. However, the question of whether the T cell response in muscle is reflective of the peripheral blood response remains to be fully answered.
Objectives: To characterize the T cell receptor (TCRβ) repertoire in peripheral blood and muscle tissues of treatment naïve patients with newly diagnosed idiopathic inflammatory myopathies (IIMs).
Methods: High throughput RNA sequencing of the TCRβ chain was performed in peripheral blood and muscle tissue in twenty newly-diagnosed treatment-naïve IIM patients and healthy controls. Results thereof were correlated with markers of disease activity.
Results: Muscle tissue of IIM patients show more expansion of TCRβ clones and decreased diversity when compared to peripheral of IIM as well as healthy controls (both p=0.0001). Several expanded TCRβ clones in muscle tissue are tissue restricted and cannot be retrieved in peripheral blood. These clones have significantly longer CDR3 regions when compared to clones (also) found in circulation (p=0.0002), while their CDR3 region is more hydrophobic (p<0.01). Network analysis shows that clonal TCR signatures are shared between patients. Increased

clonal expansion in muscle tissue is significantly correlated with increased CK levels (p=0.03), and tends to correlate with decreased muscle strength (p=0.08).
Conclusion: Network analysis of clones in muscle of IIM patients shows shared clusters of sequences across patients. Muscle-restricted TCRβ clones show specific structural features in their T cell receptor, and clonal TCR expansion in muscle tissue is associated with disease activity. These findings indicate that specific clonal T cell responses in muscle tissue act as key players in the pathogenesis of IIM.
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POS0006 AUTOREACTIVE B CELLS IN RHEUMATOID ARTHRITIS ARE RECENTLY ACTIVATED AND SHOW LARGE EXPANSIONS OF CXCR3+ ANTIBODY-SECRETING CELLS

Keywords: Adaptive immunity, Cell biology, Rheumatoid arthritis

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Background: Many autoimmune diseases (AIDs) are characterized by aberrant, autoreactive B cell responses and autoantibody production. Rheumatoid arthritis (RA) is a common AID in which autoantibodies recognizing post-translational modifications (PTMs), collectively called anti-modified protein antibodies (AMPA), are intimately associated with disease pathogenesis. Previously, we observed that memory B cells (mBC) against one of these PTM-antigens, citrulline, are highly activated. This phenotype persists for years in patients with established disease [1]. The evolution, dynamics and more detailed phenotypic characteristics of the PTM-directed B cell compartment are still ill defined, however, partly owing to challenges linked to the visualization of such cells in human samples and the limitations of conventional flow cytometry. Here, we visualized the autoreactive B cell response against three different PTM antigens (citrulline, homocitrulline, acetyllysine) by spectral flow cytometry, allowing us to address cross-reactivity on the B cell level and to perform deep phenotypic profiling of individual B cell compartments.
Objectives: To develop a detailed understanding of the autoreactive B cell response against PTM-antigens in RA with the aim to elucidate features associated with its cross-reactivity, state of activation in the disease context, and its remarkable persistence for years without signs of exhaustion or decay.
Methods: We developed a spectral flow cytometry staining approach using differentially labelled streptavidin molecules coupled to individual PTM-antigens. B cells reactive to each antigen were identified together in individual samples by double staining for each antigen, while at the same time excluding cells reactive to either arginine or lysine control peptides. This combinatorial staining was further extended by the concomitant visualization of tetanus-toxoid specific B cells and expression levels of various activation and homing markers, and applied to peripheral blood samples of patients with established RA. Importantly, we performed intracellular stainings, allowing us to additionally enumerate and characterize circulating plasmablasts and plasmacells.
Results: We successfully visualized autoreactive B cells directed against different PTM-antigens and their subset distribution in individual patient samples. We observed extensive cross-reactivity against all three PTM antigens with citrulline as dominant antigen. Unsupervised clustering revealed several memory B cell populations, with most autoreactive B cells populating the most recently activated, mostly class-switched, $CD80^{high}CD24^{low}CD21^{low}$ mBC compartment. We also noted large expansions of $CXCR3^+$ IgG or IgA-expressing antibody secreting cells (ASC), comprising up to 50% of the autoreactive B cell compartment. Anti-tetanus toxoid B cells clustered with a different, more resting mBC subset.
Conclusion: Our results identify citrulline as the most prominent antigen recognized by AMPA-expressing B cells. The study highlights the recent and persistent activation state of PTM-reactive mBC and their continuous differentiation towards ASC. Such ASC may home towards CXCR3 ligands known to be abundant in the synovial compartment. This degree of mBC activation was also found in patients with low clinical disease activity scores, indicating that conventional therapeutic interventions may suppress inflammation but fail to silence the most disease-specific autoreactive B cell response in RA. Targeting this compartment may therefore be relevant for future therapeutic interventions aiming at the induction of tolerance and/or permanent cure. Finally, the combinatorial staining approach presented will be a valuable tool to delineate the development of PTM-directed autoimmunity in the pre-disease phase as well as its state of activation in phases of sustained drug-free remission and/or during tolerogenic interventions.
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POS0007 KYV-101, A FULLY HUMAN CD19 CAR T CELL GENERATED FROM AUTOIMMUNE PATIENT LYMPHOCYTES, DEMONSTRATES CAR-MEDIATED AND CD19-DEPENDENT ACTIVITY AGAINST AUTOLOGOUS B CELLS

Keywords: Adaptive immunity, Systemic lupus erythematosus, Autoantibodies

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Background: A significant unmet medical need remains in the treatment of relapsed and/or refractory B cell-driven autoimmune diseases, including lupus nephritis (LN). The presence of autoantibodies is a hallmark of such diseases and implicates dysregulated B cell function in their pathogenesis. The central role of B cells in these diseases is also supported by the presence of B cells in diseased tissues and the efficacious responses reported with biologic therapies that target B cells. KYV-101 is an autologous CD19 CAR-T cell therapy that depletes pathogenic B cells. Importantly, the CD19 CAR utilized in KYV-101 was previously tested in B-cell lymphoma patients and demonstrated efficacy with an improved safety profile [1]. Since CD19 CAR-T cells target and lyse B cells in both circulation and tissues, a more complete depletion of autoreactive B cells is expected with KYV-101, resulting in better disease control and clinical remission than the current immunotherapies.
Objectives: To demonstrate the CAR-mediated and CD19-dependent activity of KYV-101 against autologous, patient-derived primary B cells.
Methods: Autologous $CD4^+$ and $CD8^+$ T cells were enriched from healthy donors (HD), systemic lupus erythematosus (SLE), LN or other autoimmune patients. KYV-101 CAR T cells were transduced with a lentiviral vector encoding a fully human single-chain variable fragment (scFV) CD19-targeting domain, a CD8α hinge and transmembrane domain, a CD28 cytoplasmic costimulatory domain, and a CD3ζ cytoplasmic domain. The CAR-mediated and CD19-dependent activity of KYV-101 was monitored *in vitro* in a set of cytotoxicity, cytokine release and proliferation studies, in response to either $CD19^+$ target cell lines or autologous, patient-derived primary $CD19^+$ B cells.
Results: Following a 24-hour incubation, KYV-101 generated from HDs or autoimmune patients induced greater and dose-dependent cytotoxicity of both the human $CD19^+$ NALM6 cell line and autologous, patient-derived primary B cells than their respective untransduced control T cells. Moreover, an effector cell dose-dependent increase in the production of cytokines such as IFNγ was also observed following co-culture. In contrast, no differences in cytotoxicity nor cytokine production were observed when $CD19^-$ target cells (K562 or U937 cells) were co-cultured with KYV-101 or untransduced control T cells. In addition, following a 96-hour incubation, KYV-101 generated from HDs or autoimmune patients proliferated when co-cultured with the NALM6 cells and autologous, patient derived primary B cells, whereas substantially lower levels of proliferation were observed in the untransduced control T cells co-cultured with NALM6 or autologous, patient-derived primary B cells or in KYV-101 and untransduced control T cells co-cultured with the $CD19^-$ cell lines K562 and U937.
Conclusion: KYV-101 generated from autoimmune disease patient lymphocytes demonstrates CAR-mediated and CD19-dependent activity against autologous, patient-derived primary B cells and thus represents a novel therapeutic option for the depletion of pathogenic B cells in autoimmune patients.
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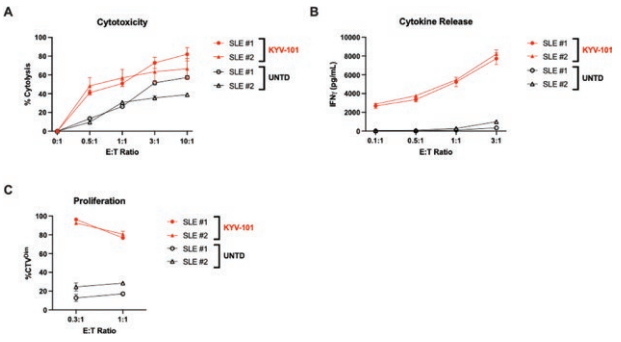


Figure 1. KYV-101-mediated A) cytotoxicity, B) cytokine release and C) proliferation when co-cultured with autologous, patient-derived $CD19^+$ human B cells.

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Disclosure of Interests: Soo Park Employee of: Kyverna Therapeutics, Ames Register Employee of: Kyverna Therapeutics, Ho-Young Lee Employee of: Kyverna Therapeutics, Gloria Lutzny-Geier Grant/research support from: Kyverna Therapeutics, Michael Aigner Grant/research support from: Kyverna Therapeutics, Mackensen Andreas Grant/research support from: Kyverna Therapeutics, Georg Schett Grant/research support from: Kyverna Therapeutics, Dominique Borie Employee of: Kyverna Therapeutics, James Chung Employee of: Kyverna Therapeutics, Charles Kaplan Employee of: Kyverna Therapeutics.

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POS0008 STRATIFICATION OF NEGATIVE, SEROCONVERTED AND PERSISTENTLY POSITIVE THROMBOTIC PRIMARY ANTIPHOSPHOLIPID SYNDROME PATIENTS WITH DISTINCT FOLLICULAR HELPER T CELLS SUBSETS

Keywords: Anti-phospholipid syndrome, Autoantibodies, Adaptive immunity

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Background: Primary antiphospholipid syndrome (PAPS) is caused by autoantibodies targeting protein-binding phospholipids (aPL)[1]. Follicular helper T (Tfh) and follicular regulatory T cells (Tfr) are critical for antibody production in germinal centres[2], but their role in PAPS is scarcely studied. Some patients remain persistently positive for aPL, while others become seronegative during disease progression[3]. Whether aPL status mirror immunological changes over time is not known.
Objectives: To phenotypically characterize Tfh/Tfr subsets in PAPS and explore the association with previous/current aPL status.
Methods: We prospectively recruited 73 adult thrombotic PAPS patients (Sidney criteria; ≥1 year disease duration) and 24 age- and sex-matched healthy donors (HD). Regardless of lupus anticoagulant (LA) status, patients were categorized in three groups according to aPL (anticardiolipin [ACL] IgM and/or IgG; ß2-glycoprotein [ß2GPI] IgM and/or IgG) profile: NN – previous and current aPL negative, ie, only positive for LA (n=40); PP – previous and current aPL positive (n=20); and PN – previous aPL positive, currently aPL negative (n=13). We considered aPL <30 UQ as negative (ELISA immunoassays). Tfh ($CD4^+FoxP_3^-CD25^-CD45RO^+CXCR5^+$), activated Tfh ($PD1^+ICOS^+$ Tfh), Tfh1-like ($CXCR3^+CCR6^-$ Tfh), Tfh2-like ($CXCR3^-CCR6^-$ Tfh), Tfh17-like ($CXCR3^+CCR6^+$ Tfh), Treg ($CD4^+CD25^+FoxP_3^+$), and Tfr ($CD4^+CD25^+FoxP_3^+CXCR5^+$) cells were analysed by flow cytometry using cryopreserved peripheral blood mononuclear cells. GraphPad Prism version 8 software was used for statistical analysis and p values <0,05 were considered significant.
Results: Most patients were women (n=43, 59%), with a mean age at disease onset of 42±13 years, and a mean disease duration of 8±7 years. Venous thrombosis was the most common first manifestation (53%), and pregnancy comorbidity were present 10% of women. At presentation, aPL positivity were as follows: LA, 70%; ACL IgG and/or IgM, 44%; ß2GPI IgG and/or IgM, 33%; triple positive, 16%. Circulating Tfh and Treg cells were comparable between HD and all APS patients (**Figure 1A and 1B**). Among APS, PP patients had higher frequency of Tfh compared to NN (p=0.047) but not with PN patients. Within the Tfh subset, activated Tfh cells were significantly increased in PP compared to NN (p=0.005) and PN patients (p=0.049), whereas no difference was seen between the latter group and NN patients, and between HD and all APS patients (**Figure 1C**). The frequencies of Tfh1-like and Tfh17-like cells were comparable between all groups, but Tfh2-like cells were decreased in PP compared to NN patients (p=0.008), and similarly distributed among all other groups (**Figure 1D to F**). In the regulatory compartment, circulating Tfr and Tfr/Tfh ratio were significantly increased in PP patients compared to NN (p<0.001; p=0.001) and PN patients (p=0.004; p=0.042) (**Figure 1G and 1H**). No difference was observed between NN and PN patients nor between HD and all APS patients.
Conclusion: Our preliminary results show that in thrombotic PAPS, imbalance of circulating Tfh and Tfr subsets change according to aPL profile. Increased $PD1^+ICOS^+$ Tfh and Tfr cells, and Tfr/Tfh ratio indicates ongoing humoral response in persistently positive patients. These changes are lost after seroconversion with T follicular cells subsets being similar to persistently negative PAPS patients.
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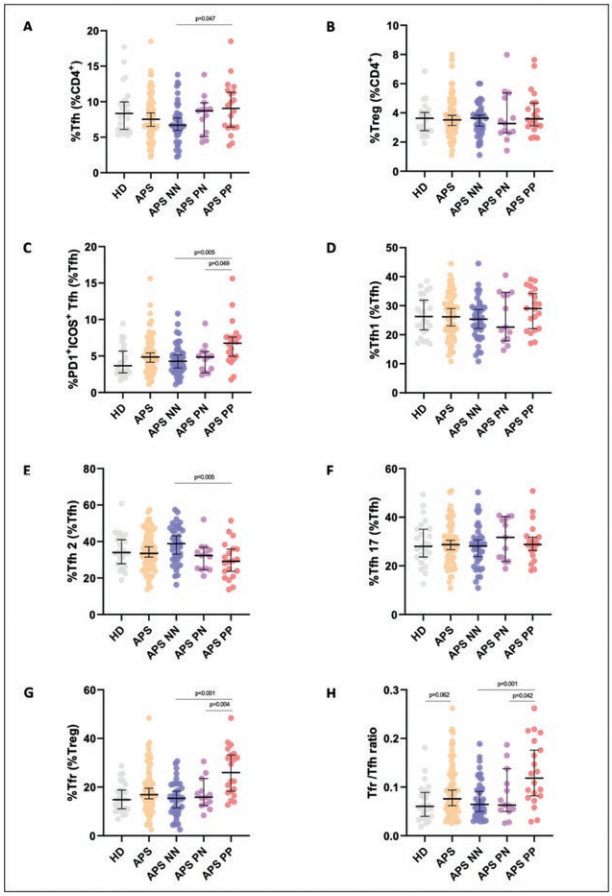


Figure 1. T follicular cells subsets distribution.

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POS0009 LYMPH NODES AND PERIPHERAL BLOOD HARBOR EXPANDED T CELL RECEPTOR CLONES DURING THE PRECLINICAL PHASE OF RHEUMATOID ARTHRITIS WHICH PERSIST ON ARTHRITIS ONSET

Keywords: Adaptive immunity, Rheumatoid arthritis

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Background: Immunological and genetic studies implicate T cells in the initiation and progression of rheumatoid arthritis (RA) [1]. Additionally, the diversity of the T cell repertoire is known to be reduced in RA, suggesting an enrichment of disease related clonal signatures [2].
Objectives: To study whether changes in the T-cell receptor repertoire (TCR) in lymph node (LN) and peripheral blood (PB) precede the onset of arthritis in seropositive at-risk individuals.
Methods: Unique molecular identifier (UMI)-based RNA sequencing of the TCRβ repertoire in LN biopsies and PB was performed in 9 healthy controls and 26 IgM-RF and/or ACPA positive at-risk individuals. Six of these individuals developed arthritis (RA) during at least 3 years of follow-up. PB and LN biopsies were analyzed during the at-risk phase and at RA onset.
Results: The TCRβ repertoire in LNs of autoantibody positive at-risk individuals harbors expanded TCRβ clones which can hardly be found in LNs of healthy controls. Regardless of whether the at-risk individuals developed arthritis or not, expanded TCRβ clones in LNs could be retrieved in peripheral blood. On RA onset, the LNs showed a marked decrease in the diversity of their TCRβ repertoire and, expanded TCRβ clones present during the at-risk phase could still be found in lymph nodes on arthritis onset.
Conclusion: Expanded TCRβ clones are present in lymph nodes and peripheral blood of individuals at risk of developing RA which can be retrieved in peripheral blood. Expanded TCRβ clones present in LNs during the at-risk phase persist on arthritis onset. Our analyses show a clear decrease in the diversity of the TCRβ repertoire towards onset of RA, implicating a key role for T-cell adaptive responses in steering onset of seropositive RA.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Rheumatoid arthritis-aetiology, pathogenesis and animal models

POS0010 **PROTEOMIC LANDSCAPE OF SYNOVIAL TISSUE IN RHEUMATOID ARTHRITIS AND DETERMINANTS OF SYNOVIAL HISTOLOGICAL PATHOTYPES**

Keywords: -omics, Synovium, Rheumatoid arthritis

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Background: Pathological mechanisms in the affected synovial joints in rheumatoid arthritis (RA) and factors contributing to synovial histological heterogeneity, which may impact treatment outcomes, remain largely unexplored at the protein level. Mapping the proteomic landscape of RA-affected synovial tissue (ST) and identifying determinants of synovial pathotypes could provide insights into RA's pathological mechanisms, identify new therapeutic targets, and pave the way for personalized medicine options.
Objectives: To map the proteomic landscape and dysregulated biological pathways in ST and plasma at multiple stages of RA. Through this investigation, the study also aims to identify the molecular and cellular determinants of synovial histological pathotypes in early untreated RA patients.
Methods: ST and matched plasma samples from patients with early untreated RA (ERA) (n = 20) and longstanding RA (LRA) (n = 20), as well as healthy controls (HC) (n = 16) were collected at baseline and at six months follow-up (RA patients only). ST biopsies were collected from the wrist via an ultrasound-guided synovial biopsy procedure (RA patients), or via arthroscopic guidance (HC). Samples were then characterized using discovery proteomics profiling. Comparisons were made between HC versus ERA or LRA at both timepoints, and proteins were regarded as differentially abundant at 5% FDR and a log2-fold change ±2.0 (ST proteins) or ±1.5 (plasma proteins). Next, the molecular and cellular determinants of synovial histological pathotypes were identified in untreated ERA patients by integrating the ST proteome, plasma proteome, Krenn synovitis score, number of circulating immune cells and scores of CD3 (T cells), CD20 (B cells), CD68 (Macrophages) and CD138 (Plasma cells) synovial immune infiltration.
Results: 335 plasma proteins and 3416 ST proteins were identified and quantified. *Plasma proteins*: CRP and SAA1 were overabundant in ERA compared to HC at baseline, but no proteins were differentially abundant in ERA compared to HC at follow-up (Figure 1 A-B). CRP was overabundant in LRA compared to HC at both timepoints (Figure 1 C-D). *Synovial tissue proteins*: In ERA patients 243 proteins were differentially abundant at baseline, but only 114 were differentially abundant at follow-up (Figure 1 E-F). In LRA patients, 216 and 284 proteins were differentially abundant at baseline and follow-up, respectively (Figure 1 G-H). Largely the same biological processes were dysregulated in ERA at baseline and in LRA at both timepoints. However, biological processes related to complement cascade, acute inflammatory response, scavenging of heme from plasma among others, tended to be less dysregulated in ERA patients at follow-up. Finally, data integration identified proteomic and cellular signatures underlying synovial pathotypes, that suggests the difference between lymphoid, myeloid, and fibroid pathotypes is a continuous spectrum that is linearly modellable. Proteins involved in negative regulation of: peptidase/protease activity, hemostasis and wound healing were underabundant in the lymphoid pathotype compared to the fibroid pathotype and to a lesser degree, the myeloid pathotype. Proteins that were involved in various aspects of antibody production were overabundant in the lymphoid pathotype compared to the fibroid pathotype and to a lesser degree, the myeloid pathotype.

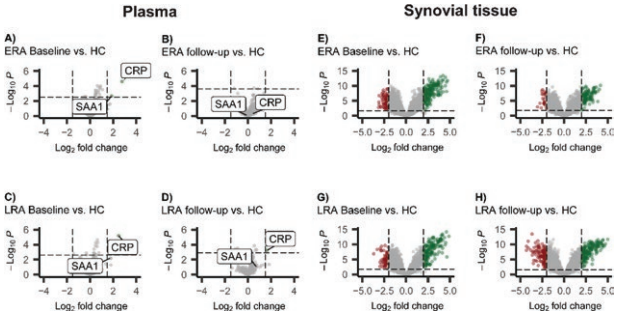


Figure 1. Comparison between plasma and synovial tissue proteomes of early untreated rheumatoid arthritis patients (ERA) or longstanding rheumatoid arthritis (LRA) at baseline or follow-up versus healthy controls.

Conclusion: The study revealed new insights into the proteomic landscape of the synovium in RA, elucidating the pathological mechanisms occurring in the synovium at different stages of disease. Additionally, the study identified a linear proteomic and cellular difference between the lymphoid, myeloid, and fibroid synovial pathotypes in untreated ERA patients, rather than distinct signatures for each pathotype.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0011 **LKB1 ALLEVIATES MIGRATION OF FIBROBLAST-LIKE SYNOVIOCYTES FROM RHEUMATOID ARTHRITIS PATIENTS VIA REGULATION OF SLC7A11-MEDIATED ROS SIGNALING**

Keywords: Rheumatoid arthritis

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Background: Liver kinase B1 (LKB1) is known as a tumor suppressor gene and an antioxidant regulator in cancer. We previously reported that LKB1 knock-down increased the expression of reactive oxygen species (ROS) and migration of fibroblast-like synoviocytes (FLS) from rheumatoid arthritis (RA) patients. However, the relative signaling remains unclear in RA.
Objectives: This study aimed to examine the signaling pathway of LKB1 in correlation with migration of FLS from RA.
Methods: Synovial tissues were obtained from RA patients (n=10) who were undergoing synovectomy or joint replacement. Isolated FLS were transfected with siRNA duplex targeting constructs for LKB1 or SLC7A11(solute carrier family 7 member 11, also known as xCT) using lipofectamine reagent. After incubation, expressions of target molecules were evaluated by real-time PCR and

western blot analysis. ROS levels were analyzed with MitoSOX red mitochondrial superoxide indicator using flow cytometry analysis. Cell migratory ability was examined using transwell migration assay and invaded cells were stained with crystal violet. For quantification, the crystal violet dye was eluted with 0.1% sodium dodecyl sulfate (SDS). A769662 was treated as a specific activator of AMPK (AMP-activated protein kinase)-mediated signaling.

Results: When RA FLS were stimulated with recombinant interleukin 17 (IL-17; 10ng/ml) and tumor necrosis factor alpha (TNF-α; 10ng/ml), SLC7A11 expression was markedly decreased. Following LKB1 knock-down for 24h, the protein level of SLC7A11 was also decreased in RA FLS. To determine whether SLC7A11 directly regulates FLS migration, SLC7A11 siRNA was transfected and then analyzed intracellular ROS level and performed transwell assay. SLC7A11 inhibition induced ROS expression (1.74-fold) and migration ability (1.74-fold) compared to control in RA FLS. Next, cells were treated with A769662 for AMPK activation, which is directly phosphorylated by LKB1 stimulation. LKB1 knockdown reduced SLA7A11 level and that decrease was certainly recovered by A769662 treatment. On the other hand, NOX4 expression was increased by LKB1 siRNA, and that increase was suppressed by AMPK activation. LKB1 siRNA induced ROS levels also down regulated by A769662 treatment. When LKB1 inhibition enhanced cell migration about 1.81-fold, and those increases were also reduced in 0.92-fold by AMPK activation compared to control.

Conclusion: These findings suggests that LKB1 regulate ROS production and SLC7A11 expression and, eventually lead to decrease migration, thereby further contributing to alleviate inflammation of RA FLS.

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POS0012 THE EXPANSION OF CD4CD8 DOUBLE-POSITIVE T CELLS OF CD4 ORIGIN IS SPECIFIC FOR RHEUMATOID ARTHRITIS AND LINKED TO DISEASE ACTIVITY

Keywords: Adaptive immunity, Inflammatory arthritides, Rheumatoid arthritis

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Background: CD4CD8 double-positive (DP) T cells are expanded in rheumatoid arthritis (RA) and associated with erosive disease [1]. The majority of DP T cells in the periphery have an effector phenotype and were reported to originate from either CD4 or CD8 single-positive (SP) T cells [2]. DP T cells of CD4 origin express a CD8αα homodimer, corresponding to a CD4+CD8^{low} fluorescence pattern in flow cytometry, while DP T cells of CD8 origin express a CD8αβ heterodimer, which results in a CD4+CD8^{high} pattern. Reports on the presence of polyfunctional CD4+CD8^{low} T cells in RA patients and individuals at risk of RA (3) suggest DP T cells of CD4 origin to be relevant for RA pathogenesis.

Objectives: This study aims to confirm and characterize the role of DP T cells of CD4 origin, or CD4+CD8^{low} T cells, in the context of RA.

Methods: DP T cells and their subpopulations were measured by flow cytometry in the peripheral blood of 53 newly diagnosed RA patients and compared to a cohort of patients with psoriatic arthritis (PsA) (n=52), as well as age-matched healthy donors (n=50). The CMV infection status of all subjects was assessed by a CMV IgG and IgM ELISA. In an independent cohort of 70 RA patients, the surface markers LIR1 and PD1 were measured on all T cells using flow cytometry. Lastly, a prospective study followed the changes in CD4+CD8^{low} T cell frequency in patients with early RA treated with MTX or Abatacept.

Results: Only DP T cells of CD4 origin (CD4+CD8^{low}) are significantly expanded in RA (figure 1A), while the frequency of DP T cells of CD8 origin (CD4+CD8^{high}) is similar to patients with PsA and healthy controls. The expansion of CD4+CD8^{low} T cells is associated with latent CMV infection in all three cohorts. However, CMV+ RA patients have significantly more DP T cells of CD4 origin than CMV+ healthy controls (figure 1B), indicating that CMV positivity is not the only driver of DP T cell expansion. DP T cells of CD4 origin express the senescence marker LIR1 and the exhaustion marker PD1 more often than their CD4 SP counterparts (figure 1C). In RA, CD4+CD8^{low} T cells correlate with DAS28-CRP (r=0.35, p=0.01), indicating a link with disease activity. The frequency of CD4+CD8^{low} T cells were measured in early RA patients before treatment (visit 1, V1), after one month (visit 2, V2) and three months (visit 3, V3) of treatment. Clinically efficacious treatment with abatacept was found to significantly reduce the frequency of CD4+CD8^{low} T cells after three months (mean change -0.09%, p=0.02), while methotrexate treatment did not (mean change -0.03%, p=0.83, figure 1D).

Conclusion: DP T cells of CD4 origin (CD4+CD8^{low} T cells) are frequently expanded in the peripheral blood of RA patients, but not in PsA patients or age-matched healthy individuals. DP T cells of CD8 origin are not expanded in RA or PsA compared to healthy controls. The association of CD4+CD8^{low} DP T cells with CMV seropositivity, as well as the increased LIR1 and PD1 expression, suggest they belong to a chronically stimulated, antigen-experienced cell population. Importantly, these cells are associated with disease activity in RA and show a significant reduction in the peripheral blood after treatment with a T cell-targeting agent. This confirms their role in RA pathogenesis and suggests their potential as a therapeutic target or biomarker for response.

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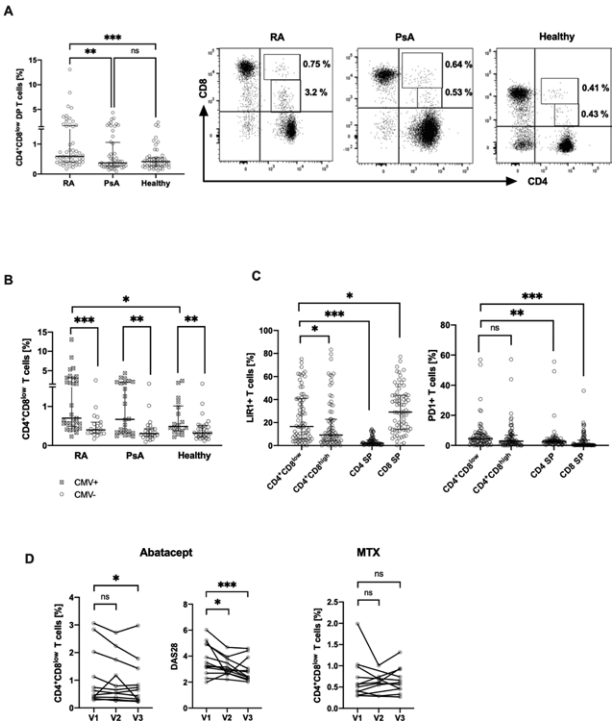


Figure 1. CD4+CD8^{low} double-positive T cells in rheumatoid arthritis.

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Disclosure of Interests: None Declared.
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POS0013 25-HYDROXYCHOLESTEROL IN THE PATHOGENESIS OF RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Adaptive immunity

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Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by synovial inflammation, in which the imbalance of CD4$^+$ T cells plays an important role. 25-hydroxycholesterol (25-HC) is an important regulator of the mevalonate pathway in cholesterol metabolism. Previous studies have suggested that 25-HC may inhibit the transformation of CD4$^+$ T cells from interferon-γ (IFN-γ) $^+$CD4$^+$ T cells to IL-10$^+$CD4$^+$ T cells through the interaction with liver X receptor (LXR), therefore decreasing the expression of IL-10.

Objectives: This study aims to explore the mechanism by which 25-HC promotes the inflammatory process of RA by regulating the phenotypic transformation of

$CD4^+$ T cells through histological and cellular and molecular biology techniques, and propose possible molecular regulatory pathways.
Methods: Patients with RA from December 2019 to January 2022, and gender and age-matched osteoarthritis (OA) and healthy controls (HC) were enrolled. Peripheral blood mononuclear cells (PBMC) and synovial fluid mononuclear cells (SFMC) were collected and $CD4^+$ T cells were sorted by magnetic beads. The expression levels of different phenotypes of $CD4^+$ T cells and important cytokines were analyzed by flow cytometry; the secretion levels of IL-10 and IFN-γ were detected by ELISA technology. In the intervention experiment, the $CD4^+$ T cells were treated with different concentrations of atorvastatin to inhibit the cholesterol metabolism mevalonate pathway and supplement mevalonate acid, and then $CD4^+$ T cell phenotype and cytokine expression were detected. The synovial tissues were obtained from RA and OA patients receiving joint replacement surgery, and the expressions of 25-hydroxycholesterol hydroxylase (CH25H) and LXR were detected by immunohistochemistry and multiplex immunofluorescence. Real-time PCR and Western Blot were used to detect the expression of inflammasome signaling pathway of $CD4^+$ T cells. CH25H was knocked down suing small interfering RNA (siRNA), and the effects of knockdown of CH25H on inflammasome and the effect on the transformation of $CD4^+$ T cells were detected by the above methods.
Results: (1) $IL\text{-}10^+CD4^+$ T cells in PBMC/SFMC of RA patients were significantly lower than HC/OA, as well as the expression of IL-10. After interfering the mevalonate pathway by atorvastatin, the ratio of $IL\text{-}10^+IFN\text{-}\gamma^+CD4^+$ T cells and $IL\text{-}10^+IFN\text{-}\gamma^-CD4^+$ T cells as well as the expression of IL-10 decreased in a concentration-dependent manner. The down-regulation effect induced by atorvastatin was compensated after the supplementation of mevalonate acid. (2) The expressions of CH25H and LXR in $CD4^+$ T cells of RA synovial tissue increased detected by immunohistochemistry and multiplex immunofluorescence, and the expressions of CH25H, LXR and caspase-1 in $CD4^+$ T cells in synovial fluid were found increased by Western Blot, as compared with that of OA. (3) After the successful knockdown of CH25H confirmed by Real-time PCR and Western Blot, a significant decrease in the proportion of $IL\text{-}10^-IFN\text{-}\gamma^+CD4^+$ T cells, and increase in proportion of $IL\text{-}10^+IFN\text{-}\gamma^-CD4^+$ T cells were found in RA patients, accompanied with increase in $IL\text{-}10^+CD4^+$ T cells, while the proportion of $IFN\text{-}\gamma^+CD4^+$ T cells and expression of IL-10 decreased significantly. After supplementation with 25-HC, the siRNA-CH25H-mediated decrease in $IL\text{-}10^+CD4^+$ T cells was reversed and $IFN\text{-}\gamma^+CD4^+$ T cell formation was reduced. Meanwhile, the expression of NLRP3 and activated caspase-1 (capsase-1 p20) in peripheral blood $CD4^+$ T cells was reduced, and could eliminate after supplementation with 25-HC.
Conclusion: In peripheral $CD4^+$ T cells in RA patients, 25-HC may activate the NLRP3 inflammasome through CH25H-LXR pathway, thereby inhibiting the phenotypic transformation of $IFN\text{-}\gamma^+CD4^+$ T cells to $IL\text{-}10^+CD4^+$ T cells, and eventually promoting the inflammatory process in RA. These findings provide new clue for the mechanism of $CD4^+$ T cells in the pathogenesis of RA and suggest that the cholesterol metabolism pathway may become a new target of RA treatment.
REFERENCES: NIL.
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Disclosure of Interests: None Declared.
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POS0014 **SINGLE-CELL PERIPHERAL BLOOD ANALYSIS IDENTIFIES KEY IMMUNE SIGNATURES ASSOCIATED WITH REFRACTORY RHEUMATOID ARTHRITIS**

Keywords: Rheumatoid arthritis, Biomarkers, -omics

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Background: Refractory rheumatoid arthritis (refRA) persists in the targeted therapy era with up to 20% of patients failing multiple classes of biologic (b) and/or targeted synthetic (ts) DMARDs.[1,2] Currently, there is limited understanding of the immune composition of refRA.
Objectives: To characterise the peripheral immune landscape of patients with refRA as compared to early RA.
Methods: In the Leeds observational cohort study, peripheral blood mononuclear cells were collected from 30 treatment naïve early rheumatoid arthritis (ERA) and 23 refractory rheumatoid arthritis (refRA) patients. ERA patients have <12 months symptoms duration and refRA patients had active (at least moderate disease) RA despite ≥2 classes of b and/or ts DMARDs. Using a panel of 36 antibodies, we conducted mass cytometry by time of flight (CyTOF) analysis to identify alterations in peripheral immune cell subsets and functional markers between ERA and refRA, using unsupervised clustering and linear mixed-effects models, which adjusted for age, sex, seropositivity and batch. A false discovery rate of 0.05 was applied. All analyses were performed using R v4.0.2.
Results: The cohort had a higher proportion of females (73.3% ERA and 87% refRA) and a median age of 61 years. The majority were seropositive (86.7% ERA, 91.3% reRA). Among the refRA patients, median number of failed b/tsDMARDs was 3 (range 2-7). Overall, we identified 17 phenotypically distinct subsets from the immune cell population. ERA and refRA had similar abundance of immune cell sub-populations. However, functional marker differences in these cell subpopulations were observed between refRA and ERA: higher TNFR expression (monocytes, dendritic and FCÎµRI+ cells), CD80 (FCÎµRI+ cells), CD28 (neutrophils), granzyme B (CD4+ naïve T cells), and lower CTLA4 (monocytes), CD127 (NK cells), CD38 (basophils), NKP46 (CD8+ naïve T cells) and PD1 (CD4+ naïve T cells).
Conclusion: We report alteration in the functional profile across multiple immune cell types between refRA and ERA. These findings provide new insights into immunological traits of refRA and potential targets for therapy.
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Table 1.

Cell type	Marker	Adjusted p-value	Coefficient
Increased expression			
Dendritic	TNFR2	0.02	0.28
Monocytes	TNFR2	0.01	0.22
CD4+ Naïve T	Granzyme B	0.04	0.32
FCÎµRI+	CD80	0.01	0.06
FCÎµRI+	TNFR2	0.01	0.18
Neutrophils	CD28	0.01	0.05
Reduced expression			
Monocytes	CTLA4	0.04	-0.03
CD4+ Naïve T	PD1	0.02	-0.04
CD8+ Naïve T	NKP46	0.04	-0.04
Natural killer	CD127	0.04	-0.04
Basophils	CD38	0.04	-0.08

Functional makers differences (refRA vs ERA): Table 1 shows functional markers expression across immune cell clusters in refRA compared to ERA, using linear mixed modelling (FDR <0.05).
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Disclosure of Interests: None Declared.
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POS0015 **WITHDRAWN**

POS0016 **SERUM AMYLOID A CONNECTS LIVER AND JOINT TO PROMOTE MACROPHAGE ACTIVATION AND CHRONIC ARTHRITIS VIA NFAT5**

Keywords: Innate immunity, Rheumatoid arthritis, Biomarkers

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Background: The nuclear factor of activated T-cells 5 (NFAT5) is a member of the Rel family of transcription factors that can be activated by hypertonic stimuli [1]. It remains unclear, however, whether NFAT5 is required for damage-associated molecular patterns (DAMPs)-triggered inflammation and immunity. Serum amyloid a(SAA) is an endogenous toll-like receptor (TLR) ligand functioning as a DAMP responds to bacterial endotoxins [2]. In response to infection and inflammation, innate immune cells secrete pro-inflammatory cytokines, in particular IL-1β and TNF-α, to which the liver responds by producing acute-phase reactants [3]. Further identification of such pathologic process by acute-phase reactants will allow for better selection of therapeutic targets as well as a greater understanding of the mechanisms underlying chronic inflammation.

Objectives: To investigate SAA, an acute phase reactant as well as a TLR ligand, activates NFAT5 in macrophages of arthritic joints after being secreted from the liver and thereby promotes chronic inflammation.

Methods: SAA-induced upregulation of NFAT5 expression and activity in RAW264.7 cells, mice bone marrow derived macrophages and human peripheral CD14+ monocytes were assessed by western blot and/or luciferase reporter assays. SAA-accelerated arthritis in mice was generated by injecting SAA (5 μg ×1) in the affected joint of mice with a suboptimal form of IL-1β-induced arthritis, which was induced by injection of methylated bovine serum albumin (mBSA, 200 μg ×1) and/or IL-1β (250 ng ×2). Decrease in arthritis severity and inflammatory cell infiltration by *Nfat5*- and *Tlr2*/4-deficient mice, specific knockout of myeloid *Nfat5*. We used adenoviral vector system and overexpressed SAA gene in the liver exacerbates chronic arthritis in mice.

Results: Like hypertonic stimuli, several damage-associated molecular patterns (DAMPs), including SAA, MRP8, and HMGB1, can induce expression of NFAT5, an osmo-sensitive transcription factor. In particular, acute phase reactant SAA substantially increased NFAT5 expression and activity in RAW 264.7 and primary macrophages. SAA-mediated NFAT5 upregulation was operative via TLR2/4-JNK signaling pathway in macrophages. In addition, triggering of the 'SAA-TLR2/4-NFAT5' axis provoked migration and chemotaxis of macrophages and aggravated chronic arthritis in a CCL2-dependent manner. Intra-articular injection of SAA markedly accelerated macrophage infiltration and arthritis progression in mice. By contrast, genetic ablation of NFAT5 or TLR2/4 rescued the pathology induced by SAA, confirming the SAA-TLR2/4-NFAT5 axis in *vivo*. Myeloid-specific depletion of NFAT5 also attenuated SAA-accelerated arthritis. Notably, chronic arthritis in mice strikingly induced SAA overexpression in the liver. Conversely, forced overexpression of the SAA gene in the liver accelerated joint damage, indicating that the liver contributes to bolstering chronic inflammation at remote sites by secreting SAA.

Conclusion: In summary, this study underscores the importance of the SAA-TLR2/4-NFAT5 axis in innate immunity, suggesting that acute phase reactant SAA mediates mutual interactions between the liver and joints and ultimately aggravates chronic arthritis by enhancing macrophage activation.

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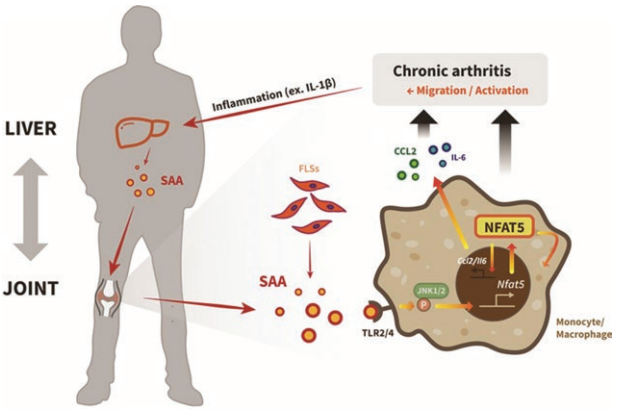


Figure 1.

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Disclosure of Interests: None Declared.

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POS0017 **WITHDRAWN**

POS0018

HUMAN MONOCLONAL ANTIBODIES DERIVED FROM GINGIVAL TISSUE B CELLS BIND MALONDIALDEHYDE (MDA)-MODIFIED SELF-PROTEINS AND EXACERBATES ARTHRITIS – A NOVEL AUTOIMMUNE LINK BETWEEN INFLAMED GUMS AND JOINTS

Keywords: Autoantibodies, Rheumatoid arthritis

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Background: Based on an epidemiological association between periodontitis (PD) and rheumatoid (RA) arthritis[1], with oral dysbiosis[2] and jawbone destruction[3] preceding the onset of RA, a causative link between periodontal infection and RA has been proposed. However, the mechanisms remain to be explained. Both gingival and synovial inflammation associate with malondialdehyde (MDA) protein modifications[4], a posttranslational modification linked to oxidative stress. While MDA IgM are part of the natural antibody response, MDA IgG levels are elevated in RA and correlate with disease activity[5]. Moreover, RA joint B-cell derived MDA-reactive monoclonal antibodies (mAb) promote bone erosion and osteoclastogenesis[6], suggesting pathogenic properties. Here we explore MDA-autoimmunity as an etiological link between inflamed gums and joints.
Objectives: To investigate if mAbs derived from gingival tissue (GT) B cells of PD patients bind MDA-modified self-proteins and whether they are pro-arthritogenic.
Methods: Recombinant mAbs (n=38) were generated as human IgG1 from single-cell sorted gingival tissue (GT) B cells of one PD patient with RA (PD/RA) and one PD patient without RA (PD only), and screened by ELISA for binding to MDA-modified and native albumin, fibrinogen and low-density lipoprotein. Three GT mAbs *versus* one isotype control mAb were assayed *in vitro* for TNF production by monocyte-derived macrophages stimulated by LPS (n=7 healthy donors), and two GT mAbs *versus* one isotype control mAb were examined *in vivo* in the collagen type II (CII) antibody-induced arthritis (CAIA) model (n=5 mice/group). Briefly, arthritis was induced in BALB/c mice by *i.v.* injection of 1.5mg anti-CII antibody cocktail together with 1mg GT or control mAb, followed by 25ug LPS on day 3. Arthritis scores and prevalence were recorded daily for two weeks; statistical analysis was performed using repetitive-measure one-way ANOVA with Geisser-Greenhouse correction and Holm-Šidák's multiple comparisons test.
Results: Three GT mAbs from the RA/PD patient and one from the PD-only patient bound MDA-modified self-proteins but not the native counterparts; all other GT mAbs were negative. The MDA-reactive GT B cell clones were class-switched (n=3 IgG+; n=1 IgA+) with 21-50 somatic hypermutations. The GT mAb with the strongest MDA-reactivity – derived from an IgA+ GT B cell isolated from the PD/RA patient – enhanced TNF production in LPS-stimulated macrophages, and exacerbated arthritis with prolonged arthritis, higher arthritis scores ($p<0.05$) and higher disease prevalence ($p<0.001$), see figure 1 below.

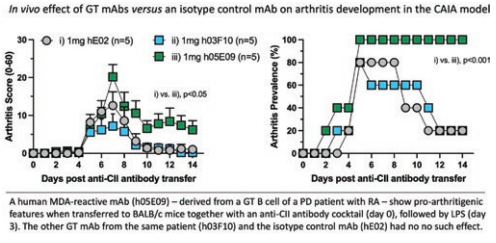


Figure 1.

Conclusion: Here we show that MDA-autoreactive B cells with features of T-cell driven affinity maturation are present in the gum mucosa of PD patients with or without RA. Moreover, that antibodies from one such clone can exacerbate arthritis. Further studies are needed in order to elucidate the mechanisms involved, and to determine if possibly enhanced TNF production via antibody-mediated modulation of macrophage responses could play a role. Taken together, this pilot study supports further research into MDA-autoimmunity as an etiological link between periodontal infection and RA.

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Contemporary clinical topics in psoriatic arthritis

POS0019

PREDICTION OF PSORIATIC ARTHRITIS TOOL (PRESTO): DEVELOPMENT AND PERFORMANCE OF A NEW SCORING SYSTEM FOR PSORIATIC ARTHRITIS RISK

Keywords: Epidemiology, Spondyloarthritis, Psoriatic arthritis

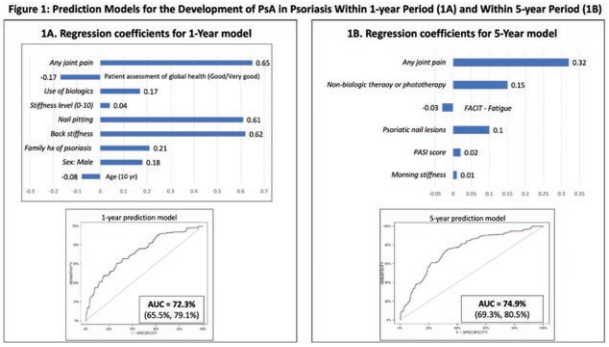
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Background: A simple, scalable tool that identifies psoriasis patients at high risk for developing psoriatic arthritis (PsA) could improve early detection and facilitate early intervention for this conditon. However, no such prediction tool currently exists.
Objectives: Our overall objective is to develop an accurate risk prediction model for the development of PsA and to assess its performance among patients with psoriasis.
Methods: In this longitudinal cohort study we analyzed data from the International Psoriasis and Arthritis Team (IPART) study, a prospective cohort of psoriasis patients without PsA at the time of enrollment. The participants were followed prospectively from 2006 to 2019, and their PsA status was assessed annually by a rheumatologist. Information about their demographics, psoriasis characteristics, co-morbidities, medications and musculoskeletal symptoms was used to develop prediction models for PsA. Penalized binary regression models were used for variable selection while adjusting for psoriasis duration; the stacked LASSO with equal weights was adopted to deal with multiple imputed datasets for incomplete data. Risks of developing PsA over 1- and 5-year time horizons were estimated. Internal validity was assessed using 5-fold cross-validation. Model performance was assessed by the area under the curve (AUC), and calibration plots.
Results: A total of 635 psoriasis patients were analyzed (mean duration of follow up 7.7 years). 51 and 71 patients developed PsA during the 1-year and 5-year periods, respectively. The risk of developing PsA within 1 year was associated with younger age, male sex, family history of psoriasis, back stiffness, nail pitting, level of stiffness, use of biologic medications, patient global assessment of health and pain severity (AUC 72.3, 95% confidence interval (CI) 65.5, 79.1, Figure 1A). The risk of developing PsA within 5 years was associated with morning stiffness, psoriatic nail lesion, psoriasis severity (by PASI), fatigue severity (by FACIT-fatigue), pain severity and use of systemic non-biologic medication or phototherapy (AUC 74.9, 95% CI 69.3, 80.5, Figure 1B). Calibration plots showed reasonable agreement between predicted and observed probabilities. The sensitivity and specificity for a 2.5% probability of PsA onset within 1 year were 54.5% and 75%, respectively. The sensitivity and specificity for a 5% probability of PsA onset within 5 years period were 61.1% and 77%, respectively.
Conclusion: The development of PsA within clinically meaningful time frames can be predicted with reasonable accuracy for psoriasis patients. Additional work is underway to validate these models in external cohorts of psoriasis patients.

REFERENCE:

[1] The calculator can be found in the URL: http://142.1.174.73:9080/Web_KC

Figure 1: Prediction Models for the Development of PsA in Psoriasis Within 1-year Period (1A) and Within 5-year Period (1B)



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POS0020

DOES SUBJECTIVELY PERCEIVED LOSS OF HAND FUNCTION SUFFICIENTLY REPRESENT ULTRASONOGRAPHY-DETECTED SYNOVITIS AND TENOSYNOVITIS IN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS?

Keywords: Patient reported outcomes, Ultrasound, Psoriatic arthritis

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Background: In the clinical routine patient reported outcome measures (PROMs) such as the 'Disability of the Arm, Shoulder and Hand Questionnaire' (Quick-DASH) [1], 'Score for the Assessment and quantification of Chronic Rheumatic Affections of the Hands' (SF-SACRAH) [2] and the ´Health Assessment Questionnaire´ (HAQ) [3] are common for assessing functional status and hand involvement in rheumatic diseases [4] while ultrasonography (US) is a cost-effective, reliable imaging technology for grading and monitoring synovitis and tenosynovitis [5]. However, it is unclear, if subjective perceived impairment can be associated with US-detected synovitis or tenosynovitis in patients with psoriatic arthritis (PsA) and psoriasis (Pso).
Objectives: To correlate subjective hand function with the grade of synovitis and tenosynovitis by US (greyscale (GS), power Doppler (PD) activity) in patients with PsA and Pso.
Methods: PsA and Pso patients recruited from the Rheumatology Department at the University Hospital Erlangen were enrolled in this cross-sectional study after giving written informed consent. Patients completed the HAQ-DI, SF-SACRAH and Quick-DASH questionnaires and subject characteristics (age, sex, disease) were recorded. The examining physician performed a bilateral US (Samsung HS40, South Korea; Esaote Mylab Twice, Italy) of the flexor tendons of all fingers and metacarpophalangeal (MCP) joints 2-5 and both wrists. Each joint was examined by GS (score 0-3) and PD (score 0-3) and flexor tendons were scanned in GS (0/1) and with PD (0-3) following the EULAR-OMERACT scoring system [5]. For statistical analysis patients with either a positive synovitis or tenosynovitis score ≥1 were included. A repeated measure correlation analysis was performed, at the intra-individual level, to measures the overall

strength and direction of the linear relationship between the PROMs with US scores.

Results: A total of 106 patients (40 PsA/66 Pso: age 47.5(12.3)/43.6(14.1) years, 63%/61% male) participated in this study. US-activity is listed in Table 1. Moderate positive correlations were detected for GS tenosynovitis score in digit 1 with both, Quick-DASH (r=0.352, p=0.038) and HAQ-DI (r=0.399, p=0.036) and also for GS tenosynovitis score in digit 4 with Quick-DASH (r=0.354, p=0.037). Overall GS synovitis score (MCP 2-5 + wrist) shows a moderate negative correlation with Quick-DASH (r=-0.323, p=0.031) and HAQ-DI (r=-0.477, p=0.002), as does PD tenosynovitis score in digit 1 (r=-0.386, p=0.022) and 3 (r=-0.386, p=0.022) with SF-SACRAH. HAQ-DI, SF-SACRAH and Quick-DASH correlated strongly with each other (r>0.7, p<0.001).

Table 1. Ultrasound activity versus non-activity by group.

Ultrasound Scores, active (score≥1)/non-active	Psoriatic Arthritis	Psoriasis
Greyscale Synovitis	20/20	13/53
Doppler Synovits	7/33	1/65
Greyscale Tenosynovitis	14/26	7/59
Doppler Tenosynovitis	11/29	1/65

Conclusion: Only the grade of chronic tenosynovitis is partially represented in Quick-DASH and HAQ-DI, while synovitis scores are negatively related to them. Surprisingly, worse hand function detected by the most hand-specific questionnaire, SF-SACRAH, was associated with less acute tenosynovitis. While Quick-DASH and HAQ-DI focus on tasks which require sufficient hand strength, the SF-SACRAH focuses on activities demanding fine motor skills, which seems to be less affected by tenosynovitis. Varying correlations of the different PROMs with the US scores have already been described for patients with rheumatoid arthritis [6]. Subjectively perceived hand function does not sufficiently reflect grade of synovitis and tenosynovitis and therefore more sensible functional outcome parameters are required.

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POS0021

COMPARATIVE PROFILING OF SERUM PROTEIN BIOMARKERS AND DISEASE ACTIVITY ACROSS VARIOUS DISEASE DOMAINS IN PATIENTS WITH PSORIATIC ARTHRITIS (PSA)

Keywords: Biomarkers, Psoriatic arthritis

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Background: Psoriatic Arthritis (PsA) is a complex, heterogeneous disease with chronic inflammation. Disease manifestations include the peripheral joint inflammation, dactylitis, enthesitis and skin psoriasis. Chronic inflammation is associated with structural damage, which jeopardize long-term functional ability. Sensitive biomarkers reflecting disease activity in various disease domains are lacking.

Objectives: To define the molecular basis of inflammation in different disease domains through comparative profiling of serum proteins.

Methods: This is a cross-sectional study in patients with PsA. Clinical assessment of inflammation in the peripheral joint (clinical Disease Activity in Psoriatic Arthritis [cDAPSA] and swollen joint count), dactylitis digit count, skin (Psoriasis Activity and Severity Index [PASI]) and enthesis (Leeds enthesitis index) were performed. Blood samples were collected for biomarker assay including 48 cytokines, chemokines, growth and angiogenic factors using the Bio-Rad Bioplex assay1 (Table 1). Levels of selected serum proteins were compared between different disease activity scores across various domains using adjusted linear regression with least absolute shrinkage and selection operator (LASSO) modeling.

Results: 100 PsA patients were recruited (age: 51±11 years, male: 52 (52%), disease duration: 9.0±3 years). The cohort had moderate disease activity (DAPSA: 24.4±14.6; PASI: 6.0±7.2). 53 (53%) and 11 (11%) patients were using conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) and biologic DMARDs (bDMARDs) respectively. Using LASSO regression analysis, biomarkers correlating with peripheral joint inflammation were IFN-γ, IL6, SCF and MCP1, while MIP-1α and β-NGF were related to dactylitis. Biomarkers correlating with skin severity were IP10, M-CSF and eotaxin, while IL8, M-CSF and CTACK were related to enthesitis. Details of biomarkers independent predicting various disease severity are listed in table 2-3.

Conclusion: Comparative serum protein biomarker profiling represents a viable method for distinguishing active inflammation in the various disease domains which may be a step forward towards personalized medicine.

Table 1 – 48 biomarker panel

Cellular cytokine

IFN-α	Interferon-α
IFN-γ	Interferon-γ
IL 9	Interleukin 9
IL12 p40	Interleukin 12 p40 subunit
IL12 p70	Interleukin 12 p70 subunit
IL15	Interleukin 15
IL16	Interleukin 16
IL17	Interleukin 17
IL18	Interleukin 18
IL1ra	Interleukin 1 receptor antagonist
IL1β	Interleukin 1β
IL2	Interleukin 2
IL2ra	Interleukin 2 receptor antagonist
IL3	Interleukin 3
IL7	Interleukin 7
MIF	Migration inhibitory factor
TNFα	tumour necrosis factor α
TNFβ	tumour necrosis factor β
TRAIL	tumour necrosis factor - related apoptosis-inducing ligand

Humoral cytokine

IL10	Interleukin 10
IL13	Interleukin 13
IL1α	Interleukin 1α
IL4	Interleukin 4
IL5	Interleukin 5
IL6	Interleukin 6

Chemokine

CTACK	Cutaneous T cell- attracting chemokine
Eotaxin	Eotaxin
IL8	Interleukin 8
IP10	Interferon gamma-induced protein 10
MCP1	Monocyte chemoattractant protein 1
MCP3	Monocyte Chemotactic Protein 3
MIG	Monokine induced by interferon (IFN)-γ
MIP-1α	Macrophage inflammatory protein 1α
MIP-1β	Macrophage inflammatory protein 1β
RANTES	RANTES
SDF-1α	Stromal cell-derived factor 1α

Growth and angiogenic factors

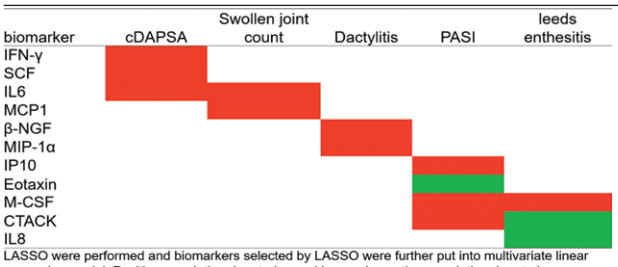
Basic_FGF	Basic Fibroblast growth factor
G_CSF	Granulocyte colony-stimulating factor
GM_CSF	Granulocyte-macrophage colony-stimulating factor
GRO	Growth-regulated oncogene
HGF	Hepatocyte growth factor
LIF	Leukemia inhibitory factor
M-CSF	Macrophage colony-stimulating factor
PDGF	Platelet-derived growth factor
SCF	Stem Cell Factor
SCGF-β	Stem cell growth factor
VEGF	Vascular endothelial growth factor
β-NGF	Nerve growth factor

Table 2. LASSO regression on various disease activity scores across various disease domains

Predictor	β	95% CI	*p*
cDAPSA			
IFN-γ	0.436	0.014 to 0.858	0.043
IL6	0.104	0.009 to 0.199	0.032
SCF	0.09	0.048 to 0.132	<0.001
Swollen joint count			
IL6	0.037	0.015 to 0.060	0.001
MCP1	0.028	0.010 to 0.046	0.003
Dactylitis			
MIP-1α	0.109	0.026 to 0.191	0.010
β-NGF	0.36	0.110 to 0.610	0.005
PASI			
IP10	0.001	0 to 0.001	0.027
M-CSF	0.022	0.003 to 0.040	0.024
CTACK	0.001	0 to 0.001	0.034
Eotaxin	-0.013	-0.02 to -0.005	0.001
Enthesitis			
IL8	-0.032	-0.062 to -0.001	0.042
M-CSF	0.026	0 to 0.052	0.050
CTACK	-0.001	-0.002 to 0	0.010

cDAPSA - clinical Disease Activity in Psoriatic Arthritis; IFN-γ - Interferon-γ; IL – interleukin; SCF - Stem Cell Factor; MCP1 - Monocyte chemoattractant protein 1; MIP-1- Macrophage inflammatory protein 1α; β-NGF - Nerve growth factor; IP10 - Interferon gamma-induced protein 10; M-CSF - Macrophage colony-stimulating factor; CTACK - Cutaneous T cell- attracting chemokine.

Table 3. Biomarker independently correlating with various disease severity scores across various disease domains



LASSO were performed and biomarkers selected by LASSO were further put into multivariate linear regression model. Positive correlation denoted as red box and negative correlation denoted as green box as above.

cDAPSA - clinical Disease Activity in Psoriatic Arthritis; IFN-γ - Interferon-γ; IL – interleukin; SCF - Stem Cell Factor; MCP1 - Monocyte chemoattractant protein 1; MIP-1 - Macrophage inflammatory protein 1α; β-NGF - Nerve growth factor; IP10 - Interferon gamma-induced protein 10; M-CSF - Macrophage colony-stimulating factor; CTACK - Cutaneous T cell- attracting chemokine.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0022 NAFLD IN PSORIATIC DISEASE: IDENTIFYING PATIENTS AT HIGH RISK OF SERIOUS LIVER DISEASE

Keywords: Comorbidities, Real-world evidence, Psoriatic arthritis

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Background: Patients with psoriatic disease(PsD) [psoriasis(PsO) and psoriatic arthritis(PsA)] are at greater risk of non-alcoholic fatty liver disease(NAFLD) and NAFLD-associated fibrosis/cirrhosis compared with the general population and other inflammatory arthritis(1) independent of disease-modifying medications [biological(b)DMARDs or methotrexate(MTX)][2]. Conversely, using these medications in patients with significant NAFLD might accelerate progression to fibrosis/cirrhosis[1]. The Leeds Teaching Hospitals NHS Trust(LTHT) NAFLD screening pathway is not validated in PsD and may underestimate prevalence of NAFLD in PsD[3].

OBJECTIVES:

1. To assess the prevalence of NAFLD in our PsD population
2. To determine the effectiveness of the LTHT NAFLD pathway for identifying PsD patients at risk of fibrosis/cirrhosis

Methods: This audit included consecutive patients from the Leeds Specialist Spondyloarthritis and Dermatology departments who underwent screening for NAFLD fibrosis/cirrhosis using the LTHT pathway. Briefly, patients are first screened using ELF and FIB4 scores. ELF>9.5 and FIB4 >1.45 triggers referral for fibroscan and hepatology opinion. A fibroscan >10 was considered indicative of clinically significant NAFLD. We compared baseline demographics (age, sex, BMI, diabetic status), biochemistry (ALT, AST, platelet count, albumin, hepatitis B and C), and NAFLD screening tests (ELF, FIB4 and fibroscan +/- liver ultrasound and biopsy) with the final hepatology diagnosis (NAFLD/ fibrosis/ cirrhosis/ other). We compared results from our PsD patients and patients with other inflammatory arthritis (Other IA).

Results: Overall 110 patients were included; 86.4% (95/110) PsD, and 14.6% (15/110) Other IA. Regarding demographic and clinical variables, age, sex, BMI, AST, ALT, platelets and albumin were similar between all groups. Other IA patients were more likely to be male and taking bDMARD monotherapy. No PsO patients were taking bDMARDs and over half were on no DMARD(Table 1). ELF scores were higher in the PsO group, possibly because the P3NP peptide (part of the ELF score) may be elevated in active skin PsO. Contrastingly, FIB-4 scores were higher in PsA compared with all other groups. Higher FIB4 scores, but not ELF scores, were associated with a fibroscan score >10 and a diagnosis of NAFLD fibrosis/cirrhosis in PsA (p=0.05 and p=0.09 respectively).

Conclusion: PsA patients had higher rates of significant fibrosis/cirrhosis compared with patients with Other IA. FIB-4 was better than ELF at identifying PsA patients requiring a fibroscan to exclude significant fibrosis/ cirrhosis. Findings will now be validated in a larger prospective cohort study.

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Table 1. Summary of demographic and clinical data for the cohort

	PsA(n=59)	PsO(n=36)	Other IA(n=15)
Age(years)	52(±15)	48(±13)	49(±15)
Sex(% male)	58(34/59)	47(17/36)	80(12/15)
BMI(kg/m²)	33(±5)	31(±7)	33(±7)
Diabetes(%)			
Yes	21(12/58)	11(4/36)	20(3/15)
No	67(39/58)	81(29/36)	73(11/15)
Impaired Glucose Tolerance	13(7/58)	9(3/36)	7(1/15)
DMARDs			
MTX	32(19/59)	39(14/36)	20(3/15)
bDMARD	9(5/59)	0	67(10/15)
MTX + bDMARD	36(21/59)	0	7(1/15)
Other	2(1/59)	3(1/36)	0
None	22(13/59)	58(21/36)	7(1/15)
ALT	57(±32)	37(±26)	89(±45)
AST	42(±22)	31(±16)	63(±41)
Hepatitis B or C	1(1/59)	0	0
ELF >9.5(%)	46(22/48)	70(23/33)	36(4/11)
FIB-4 >1.3(%)	38(19/50)	20(7/35)	27(3/11)
Fibroscan median liver stiffness >10(%)	31(15/48)	83(5/6)	25(3/12)
Liver US			
Cirrhosis/fibrosis	10(4/41)	15(2/13)	8(1/13)
NAFLD	73(30/41)	77(10/13)	77(10/13)
Other	17(7/41)	0	0
Normal liver	0	8(1/13)	15(2/13)
Biopsy			
Cirrhosis/fibrosis	46(5/11)	0	0
NAFLD	46(5/11)	0	0
Other	0	0	0
Normal	9(1/11)	0	0
Diagnosis (%)			
Cirrhosis/fibrosis	12(7/59)	6(2/36)	7(1/15)
NAFLD	66(39/59)	19(7/36)	80(11/15)
Other	5(3/59)	75(27/36)	0
Normal	15(9/59)	0	13(2/15)
Awaiting diagnosis	1(1/59)	0	0

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Disclosure of Interests: None Declared.
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POS0023 PERFORMANCE OF BASDAI VS. ASDAS IN EVALUATING AXIAL INVOLVEMENT IN PATIENTS WITH PSA TREATED WITH GUSELKUMAB: POOLED ANALYSIS OF TWO PHASE 3 STUDIES

Keywords: Psoriatic arthritis

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Background: Although the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is used to assess the activity of axial disease in patients (pts) with psoriatic arthritis (PsA), only one of its questions is specific to axial symptoms. Alternatively, the Ankylosing Spondylitis Disease Activity Score (ASDAS) excludes assessment of enthesitis, gives less weight to peripheral activity and is considered more objective than the BASDAI.

Objectives: The current post hoc analysis aimed to compare the performance of BASDAI and ASDAS in evaluating symptoms of axial involvement in pts with axial PsA (axPsA).

Methods: Pts enrolled in the DISCOVER-1 (D1) and DISCOVER-2 (D2) studies were adults with active PsA despite standard therapies. D1 pts had ≥3 swollen and ≥3 tender joints (SJC; TJC) and C-reactive protein (CRP) ≥0.3 mg/dL; D2 pts had SJC ≥5, TJC ≥5 and CRP ≥0.6 mg/dL. 31% of D1 pts received 1-2 prior tumor necrosis factor inhibitors; D2 pts were biologic-naïve. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo with crossover to GUS Q4W at W24. axPsA was defined by presence of sacroiliitis based on previous radiograph or magnetic resonance (MR) imaging confirmation. Data were pooled across all treatment groups. In addition to BASDAI and ASDAS, modified versions excluding the peripheral arthritis and enthesitis questions (mBASDAI) and the peripheral arthritis question (mASDAS) were calculated. Normalized (scale of 0-10) versions of ASDAS and mASDAS were calculated based on maximum scores of ≈7 and ≈6.3, respectively. The correlation of BASDAI/mBASDAI and ASDAS/mASDAS with SJC, TJC, enthesitis, Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue, pt pain, pt global, and physician global was assessed with Pearson's correlation coefficient. The cross-sectional and longitudinal (W52) effects of Leeds enthesitis index (LEI), SJC, and axPsA on BASDAI/mBASDAI and ASDAS/mASDAS were assessed with mixed models.

Results: 436 pts with available baseline (BL) BASDAI information were included in the analysis. In pts with axPsA, BASDAI showed weak correlation with SJC, TJC, LEI, and physician global; moderate correlation with fatigue; and strong correlation with pt global and pt pain. Similar results were observed for ASDAS and modified versions. Among pts without axPsA, correlations of BASDAI and ASDAS with SJC, TJC, and LEI remained weak; correlations with pt global and pt pain remained strong. Longitudinally, among pts with and without BL enthesitis, respectively, LEI and SJC showed significant but not clinically important associations with either outcome. Presence of axial disease was associated with significantly greater BASDAI and ASDAS scores, at BL and longitudinally, without differences in the incremental effect on BASDAI, normalized ASDAS, or their modified versions.

Conclusion: In pts with axPsA, the BASDAI and ASDAS performed similarly, with both demonstrating weak correlations with peripheral arthritis and moderate/strong correlations with pt fatigue and pain. The BASDAI and ASDAS also showed similar ability to discern changes in axial disease activity. These results suggest that both BASDAI and ASDAS are valid, and perform comparably, in assessing activity of axial disease in PsA pts.

REFERENCES: NIL.

Acknowledgements: NIL.

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POS0024 RETENTION RATE OF TNF INHIBITORS (TNFI), ANTI-IL17, AND ANTI-IL12/23 DRUGS IN A SINGLE-CENTER COHORT OF PSORIATIC ARTHRITIS PATIENTS

Keywords: Inflammatory arthritides, bDMARD, Psoriatic arthritis

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Background: During the last decades, it has been proposed to widen the horizons of psoriatic patients under a broader clinical concept of psoriatic disease (PD) encompassing both articular and extra-articular features. The most recent international recommendations on psoriatic arthritis (PsA) management highlight the need to personalize therapeutic strategies based on articular and extra-articular manifestations, such as axial or peripheral involvement and severity of skin psoriasis. Lacking specific recommendations for PsA comorbidities treatment, management decisions are often driven by drugs safety profiles and experience gathered from other rheumatologic diseases, such as rheumatoid arthritis. In the last years, new drugs have been approved for PsA management, expanding the possibility to personalize treatment choice in patients with PsA.

Objectives: Our study aims at evaluating the retention rate of bDMARDs with different mechanism of action (MoA) (TNFi vs non-TNFi) and factors associated with drug suspension in a single-center cohort of PsA patients. Furthermore, we aim to investigate whether demographic and clinical factors (among which comorbidities) could drive the choice of bDMARDs between TNFi and non-TNFi.

Methods: A retrospective cohort from a single-center real-word clinical setting has been collected. A total of 241 bDMARDs therapy courses (155 TNFi drugs, 65 anti-IL-17 drugs, and 21 anti-IL12/IL-23) were analyzed. Bivariate analyses were performed to assess the presence of demographic and clinical features, as well as comorbidities, associated with bDMARDs discontinuation in the TNFi and non-TNFi groups. Further, we conducted survival analysis and Cox regression, in order to individuate the possible predictors of failure among patients receiving TNFi and non-TNFi.

Results: In the bivariate analyses of TNFi and non-TNFi groups we found a lower age at TNFi start (46 years, IQR 45-54 vs 50.5 years, IQR 42-61; p=0.004) as well as a lower proportion of patients with skin psoriasis (65.8% vs 88.4%, p<0.001). Survival analysis showed no significant differences between TNFi and non-TNFi groups. Cox regression individuated fibromyalgia as a predictor of drug failure (HR 3.40, 1.92-6.03; p<0.001) and first line bDMARDs as protective factor (HR 0.46, 0.25-0.88; p=0.019). Lastly, among TNFi courses, fibromyalgia was associated with drug suspension (HR 6.52, 3.16-13.46; p<0.001), while only a trend of significance for skin psoriasis as risk factor for drug failure was shown (HR 2.38, CI 1.00 - 5.66, p=0.05).

Conclusion: This study provides information about clinical and demographic factors associated with retention rates of bDMARDs from a real-life, single-center cohort of PsA patients. In our study, TNFi and non-TNFi drugs had similar retention. Fibromyalgia and skin psoriasis seem to be the major predicted of drug discontinuation; in contrast, a lower failure risk has been observed in first-line treatment course.

Table 1. Cox-regression analysis of predictors of drug discontinuation for the overall PsA population

	Haz. Ratio	Std. Err.	p-value	95% conf. interval
Age	0.992	0.011	0.456	0.970 - 1.014
Male sex	0.649	0.202	0.165	0.353 - 1.195
Psoriasis	1.299	0.483	0.483	0.626 - 2.696
Fybromialgia	2.931	0.877	**< 0.001**	1.630 - 5.27
Disease duration	1.003	0.003	0.302	0.997 - 1.010
Axial subset	0.618	0.179	0.096	0.350 - 1.090
First line	0.465	0.151	**0.019**	0.246 - 0.881

REFERENCES: NIL.

Acknowledgements: NIL.

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POS0025 COMBINED NAILFOLD CAPILLAROSCOPY AND ULTRASONOGRAPHY OF THE NAIL-ENTHESIS COMPLEX TO DISCRIMINATE PSORIATIC DISEASE FROM RHEUMATOID ARTHRITIS PATIENTS AND HEALTHY SUBJECTS

Keywords: Ultrasound, Artificial Intelligence, Psoriatic arthritis

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Background: The distal interphalangeal joint (DIP), the extensor tendon enthesis and fingernail, in psoriatic arthritis (PsA) represent a very interesting site where the dermatologic, synovial, and entheseal features of the disease merge. The nail-enthesis complex (NEC) can be well analysed with ultrasound (US),

and the nailfold is the ideal site to assess angiogenesis, another typical feature of psoriatic synovitis, with both power Doppler (PD) and nailfold videocapillaroscopy (NVC). Studies have shown that PsA patients may have differences in the structure of the nail complex and capillaries compared with healthy individuals. No study has combined the two techniques.

Objectives: To evaluate the ability of combined US examination of the NEC and NVC to differentiate PsA from psoriasis (PSO), rheumatoid arthritis (RA), and healthy subjects (HC).

Methods: Twenty age- and sex-matched subjects per group were consecutively enrolled. Each subject was blindly assessed and underwent US of the NEC, NVC, and clinical examination. For the US examination, the nail plate, matrix, and bed were assessed in grayscale (GS) and with PD according to the Brown University Nail Enthesis Scale (BUNES)[1]. For the nail plate, the Wortsman[2] classification was also evaluated. The thickness of the nail plate, matrix, and nail bed were measured. Mean values of 10 digits were used for the analysis. Capillary density, number of microhaemorrhages, tortuous capillaries, ectasia, and ramified capillaries were assessed at NVC. Mean values were calculated for II-V digits in both hands. After excluding subjects with missing values, differences among groups were analysed with Kruskal-Wallis test. US and NVC variables were then included in a K-Means clustering model. The number of clusters was determined using the elbow method. Factor analysis was performed to explain the clustering results. The number of factors was selected using the Scree plot method.

Results: The BUNES GS total score, the BUNES GS score for the plate, and the Wortsman score were significantly lower in HC compared to all other groups. BUNES GS for the plate was higher in PSO than in HC. The number of tortuous capillaries was higher in PsA than in PSO and HC, but not in RA. The clustering model identified five clusters (Figure 1A), showing good separation of PsA and HC. PSO were distributed from cluster 2 to cluster 5 and RA among all clusters. At factor analysis (Figure 1B), all US GS variables loaded on factor 1, US PD variables loaded on factor 2, matrix and bed thickness loaded on factor 3, and number of tortuous capillaries and ectasias loaded on factor 4. Loadings of Factor 5 and 6 were below 0.5.

Conclusion: The results of this pilot study confirm that PsA patients have significant changes in the structure of the NEC compared with healthy subjects. However, most of these changes do not appear to be specific to PsA, as they are also found in PSO and, most surprisingly, in RA where DIP joint involvement is not present. Interestingly, PsA patients appear to have higher numbers of tortuous capillaries compared with PSO and HC, consistent with increased angiogenesis in the synovium. The combined evaluation seems to provide a good distinction between PsA and HC. Not surprisingly, PSO patients clustered closer to PsA (although with significant overlap with HC), which may be due to subclinical involvement. RA patients are distributed among all clusters and have alterations similar to those of PsA. This study does not provide a clear explanation for this phenomenon, and further studies are needed. This pilot study allowed us to identify US and NVC features that can be selected and applied in a prospective study that includes early undifferentiated arthritides and new-onset PSO, to understand whether the observed differences occur early in the disease and whether changes occur during the course of the disease. A larger sample size could also improve the accuracy of the clustering model.

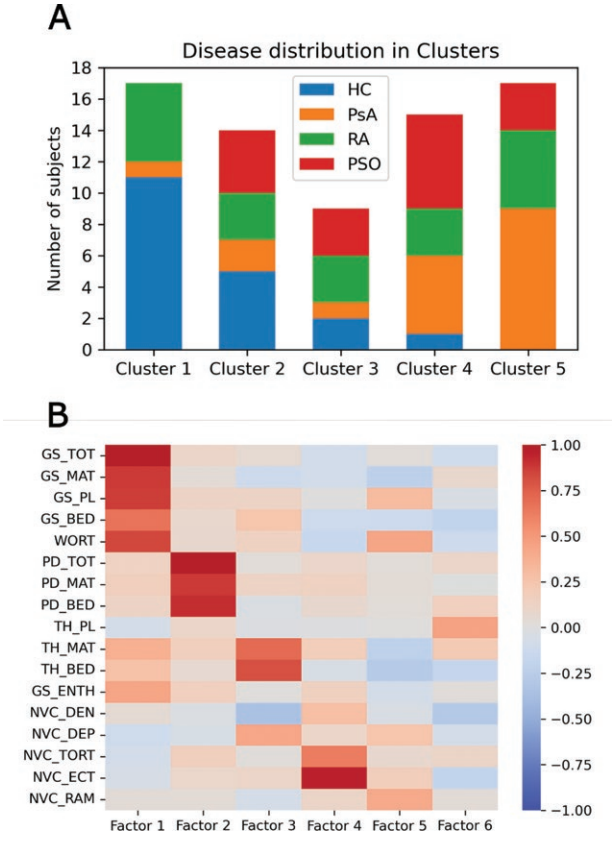


Figure 1.

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POS0026

THE INDEPENDENT INFLUENCE OF SEX ON THE DISEASE IMPACT DOMAINS IN PSORIATIC ARTHRITIS IS MODEST, ONCE CONFOUNDERS ARE TAKEN INTO ACCOUNT

Keywords: Psoriatic arthritis, Gender/diversity issues

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Background: Female sex has been associated to higher disease impact in psoriatic arthritis (PsA), as measured by the PsA Impact of Disease (PSAID) questionnaire. However, it is unclear whether sex can influence all different PSAID domains (physical and psychological), or some of them, and whether confounders might be responsible for this association.

Objectives: 1) to assess the impact of sex on each of the 12 PSAID domains, and 2) to correct this association for known confounders, including fibromyalgia, to evaluate the independent effect of sex on each of them.

Methods: Consecutive PsA patients, classified according to CASPAR criteria, attending our tertiary center between January and December 2022 were included. Demographic data, patient history, disease activity indices [Visual Analogue Scale (VAS) of pain and disease activity, Disease Activity in PsA (DAPSA) score) and functional indices (Health Assessment Questionnaire, HAQ) were collected. Impact of the disease was assessed by PSAID 12. Patients' characteristics were compared between men and women with descriptive statistics. Multiple linear regression models were built, having the 12 PSAID domains and total PSAID as outcomes (=13 outcomes), and sex as main independent variable. The crude and adjusted association between sex and each of the outcomes were studied. Namely, models were adjusted for: 1) age and DAPSA; 2) age, DAPSA and fibromyalgia. R[2] was used to measure the proportion of PSAID variance explained by sex. F-change test was used to evaluate if the addition of fibromyalgia as a confounder significantly contributed to improve the model fit.

Results: A total of 190 PsA patients were enrolled, 42% males, disease duration was 7.5±7.6 years. VAS pain, VAS disease activity, HAQ, all the 12 PSAID domains, and DAPSA were significantly higher in females ($p<0.05$). The univariate models having the PSAID domains as outcomes, and sex as independent variable, showed significant negative associations between the two (**Table 1**). R^2 values highlighted that a small proportion of the PSAID variance was explained by sex only ($R^2$0.04-0.15). In the models corrected for age and DAPSA (model group 1, **Table 1**), male sex was a negative independent predictor of some of the PSAID domains (fatigue, work and leisure, functional capacity, discomfort, sleep disturbance, coping and depression). The addition of fibromyalgia as a confounder (model group 2, **Table 1**) significantly improved the model fit for many of the PSAID outcomes, and male sex remained independently associated only to functional capacity and coping.

Conclusion: Sex alone is not able to explain PSAID variability, although it could have a higher impact on functional capacity and coping. More research is needed in order to understand the contextual factors that could explain the differences in PsA impact between men and women.

Table 1. Association between male sex (independent variable) and the PSAID domains (outcomes)

	B-coefficient (95%CI) for male sex		
Outcomes-PSAID domains	**Unadjusted**	**Adjusted models 1**	**Adjusted models 2**
1. pain	**-1.9 (-3.2 -0.5)**	-1.0 (-2.0 0.0)	NA
2. fatigue	**-2.0 (-3.4 -0.7)**	**-1.4 (-2.7 -0.1)**	-0.9 (-2.2 0.3)
3. skin problems	**-1.1 (-2.2 -0.1)**	-0.6 (-1.8 0.6)	-0.2 (-1.5 1.0)
4. work & leisure	**-2.1 (-3.5 -0.7)**	**-1.2 (-2.5 -0.5)**	-0.8 (-2.0 0.3)
5. functional capacity	**-2.2 (-3.5 -0.9)**	**-1.4 (-2.4 -0.4)**	**-1.0 (-2.0 -0.0)**
6. discomfort	**-1.9 (-3,2 -0.6)**	**-1.2 (-2.3 -0.1)**	-0.9 (-2.1 0.2)
7. sleep disturbance	**-2.8 (-4.2 -1.5)**	**-2.8 (-4.2 -1.4)**	-2.2 (-3.6 0.8)
8. coping	**-2.1 (-3.4 -0.9)**	**-2.1 (-3.4 -0.8)**	**-1.8 (-3.1 -0.5)**
9. anxiety	**-1.0 (-2.4 0.3)**	-0.3 (-1.8 1.1)	NA
10. embarassment/shame	**-1.1 (-2.2 0.0)**	-0.5 (-1.8 0.7)	NA
11.social participation	**-1.2 (-2.4 -0.0)**	-0.4 (-1.6 0.8)	NA
12. depression	**-1.8 (-3.1 -0.55)**	**-1.5 (-2.8 -0.1)**	NA
PSAIDtot	**-1.9 (-2.9 -0.8)**	**-1.0 (-2.0 -0.0)**	**-0.6 (1.6 0.3)**

Legend. Models 1: corrected for age and DAPSA; Models 2: corrected for age, DAPSA, fibromyalgia. Significant results in bold. NA=Not Applicable (model not presented because the variable "fibromyalgia" did not significantly improve the model's fit)

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Disclosure of Interests: None Declared.
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POS0027

INDIVIDUAL ENTHESEAL POINTS HAVE DIFFERENTIAL FREQUENCY OF INVOLVEMENT AND IMPACT ON PATIENT REPORTED OUTCOMES IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: POOLED ANALYSIS OF TWO PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDIES

Keywords: Enthesitis, Psoriatic arthritis, Patient reported outcomes

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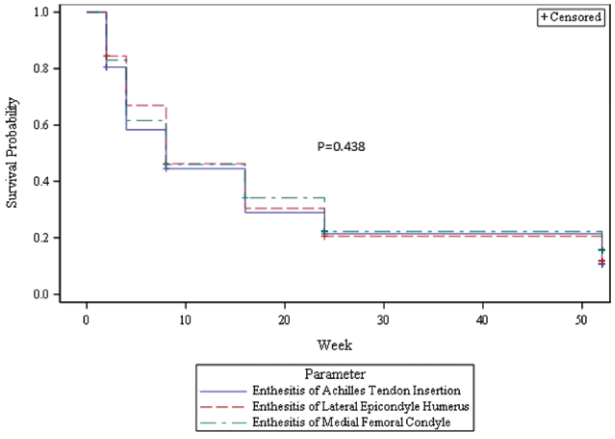
Background: In patients (pts) with mono/oligoarticular psoriatic arthritis (PsA), swelling or tenderness of specific joints can be associated with poorer pt-reported outcomes (PROs) and physician global assessment[1]. We hypothesize that location of affected entheseal points may also have differential impact on PROs or time to enthesitis resolution with guselkumab (GUS).
Objectives: (1) Describe the distribution of affected entheseal points in pts with active polyarticular PsA; (2) evaluate the impact of anatomical location of enthesitis and Leeds enthesitis index (LEI) score on pt-reported pain (PtP), pt global assessment (PtGA), and functional status; and (3) compare the time to resolution of each entheseal point following treatment with GUS.
Methods: This post-hoc analysis used pooled data from adults with active PsA, despite standard therapies, from the DISCOVER-1 and -2 studies who were randomized to GUS 100 mg every 4 weeks (Q4W) or at W0, W4, then Q8W. Only pts with baseline (BL) enthesitis were included (N=473). Proportions of pts with enthesitis were determined for each entheseal point assessed by LEI score. Longitudinal impact of LEI score and location of individual entheseal points on PtP, PtGA, and health assessment questionnaire disability index (HAQ-DI), upon adjusting for potential confounders (age, sex, body mass index, prior TNFi use, BL PsA duration, SJC, TJC), was assessed with mixed models for repeated measures through W52. Time to resolution of enthesitis at each anatomical location was assessed with Kaplan-Meier survival analysis.
Results: Approximately half (49.5%) of GUS-randomized pts with BL enthesitis had an LEI score of 1 or 2. The most commonly affected entheseal point was Achilles tendon insertion among both pts with BL enthesitis and pts with an LEI score of 1 or 2. Through W52, higher BL LEI score was associated with increased PtP, PtGA, and HAQ-DI scores (**Table 1**). Of the individual entheseal points assessed, enthesitis of Achilles tendon insertion had the greatest impact on all PROs and enthesitis of medial femoral condyle the least. Following GUS treatment, median time to enthesitis resolution was W8 for each of the three anatomical locations assessed by the LEI (**Figure 1**).
Conclusion: In this population of pts with active polyarticular PsA, Achilles tendon insertion was the most commonly affected entheseal point and more highly associated with worse PtP, PtGA, and functional status. GUS treatment was associated with rapid enthesitis resolution, including resolution of Achilles enthesitis.
REFERENCE:
[1] Ayan G. Int J Rheum Dis. 2020;23(8):1094-9.

Table 1. Parameter Estimates[§] (95% Confidence Limits) of Association of LEI Score or Individual Entheseal Points with PROs (Higher Parameter Estimates Indicate Greater Association)

Determinant	Presence/ # of points	PtP (0-100)	PtGA (0-100)	HAQ-DI (0-3)
LEI Score		**0.8 (0.3, 1.2)†**	**1.7 (1.1, 2.3)‡**	**0.01 (0.004, 0.02)†**
Enthesitis of Achilles Tendon Insertion	Yes vs. No¥	**3.7 (1.8, 5.6)†**	2.0 (-0.5, 4.6)	0.04 (-0.001, 0.08)
	2 vs. 0¥	**2.3 (0.7, 4.0)†**	**4.6 (2.4, 6.8)‡**	**0.04 (0.01, 0.08)***
	1 vs. 0¥	**3.5 (1.9, 5.1)‡**	**3.2 (1.1, 5.4)†**	**0.05 (0.02, 0.08)†**
Enthesitis of Lateral Epicondyle Humerus	Yes vs. No¥	**3.0 (1.0, 4.9)†**	0.9 (-1.6, 3.4)	0.02 (-0.02, 0.06)
	2 vs. 0¥	**1.8 (0.1, 3.6)***	**3.8 (1.6, 6.1)†**	0.02 (-0.02, 0.05)
	1 vs. 0¥	**2.5 (0.9, 4.0)†**	1.8 (-0.2, 3.8)	**0.03 (0.001, 0.07)***
Enthesitis of Medial Femoral Condyle	Yes vs. No¥	1.0 (-1.0, 3.0)	-0.04 (-2.7, 2.6)	-0.01 (-0.05, 0.03)
	2 vs. 0¥	0.3 (-1.4, 1.9)	2.0 (-0.2, 4.1)	0.02 (-0.01, 0.06)
	1 vs. 0¥	0.1 (-1.5, 1.8)	1.6 (-0.5, 3.7)	-0.02 (-0.05, 0.01)

[§]Parameter estimates correspond to the incremental increase in each PRO for 'Yes vs No', '2 vs 0', and '1 vs 0' or for every increase in LEI score by one unit.¥Categories 'No' and '0' correspond to pts with BL enthesitis who do not have enthesitis of the individual entheseal point. *p <0.05; †p <0.01; ‡p ≤0.0001. Bold text=statistical significance.

Figure. Time to Resolution of Enthesitis by Anatomical Location



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Disclosure of Interests: Laura Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Medac, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Galapagos, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Iain McInnes Shareholder of: Causeway Therapeutics, Evelo Compugen, Consultant of: AbbVie, Amgen, Astra Zeneca, Bristol Myers Squibb, Eli Lilly, Cabaletta, Compugen, GSK, Gilead, Janssen, Novartis, Pfizer, Sanofi, Roche, and UCB, Grant/research support from: Amgen, Astra Zeneca, Bristol Myers Squibb, Eli Lilly, GSK, Janssen, Novartis, Roche, and UCB, Sibel Aydin Consultant of: AbbVie, Celgene, Eli Lilly, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Celgene, Eli Lilly, Novartis, Pfizer, and UCB, Mitsumasa Kishimoto Speakers bureau: AbbVie, Amgen, Asahi-Kasei Pharma, Astellas, Ayumi Pharma, Bristol Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Kyowa Kirin, Novartis, Ono, Pfizer, Tanabe-Mitsubishi, and UCB, Consultant of: AbbVie, Amgen, Asahi-Kasei Pharma, Astellas, Ayumi Pharma, Bristol Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Kyowa Kirin, Novartis, Ono, Pfizer, Tanabe-Mitsubishi, and UCB., Philip J Mease Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma, and UCB, Consultant of: AbbVie, Aclaris, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GSK, Inmagene, Janssen,

Novartis, Pfizer, Sun Pharma, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Sun Pharma, and UCB, May Shawi Shareholder of: Johnson & Johnson, Employee of: Immunology Global Medical Affairs, Janssen Pharmaceutical Companies of Johnson & Johnson, Miriam Zimmermann Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Emmanouil Rampakakis Consultant of: Janssen, Employee of: JSS Medical Research, Inc., Frederic Lavie Shareholder of: Johnson & Johnson, Employee of: Immunology Global Medical Affairs, Janssen Pharmaceutical Companies of Johnson & Johnson, Dennis McGonagle Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB.

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POS0028 COMPARATIVE STUDY BETWEEN THE VITACORA AND PSAID QUESTIONNAIRES IN ESTIMATING QUALITY OF LIFE IN PATIENTS WITH PSORIATIC ARTHRITIS

Keywords: Quality of life

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Background: Health-related quality of life (HRQoL) is a frequently underestimated aspect in psoriatic arthritis (PsA). There are different instruments to estimate HRQoL in PsA, but they are rarely used.
Objectives: Our objective was to compare the clinimetric capabilities of the VITACORA[1] and PsAID[2] (Psoriatic Arthritis Impact of Disease) questionnaires to assess HRQoL in PsA routine management.
Methods: Forty-five consecutive patients with PsA were recruited, mean age 55 ± 13 years, mean disease duration 8.2 ± 6.1 years, 24 men and 21 women. Disease activity was estimated using DAPSA (Disease Activity index for PsA), and HRQoL using VITACORA and PsAID. The construct and discriminant validity of the VITACORA (Pearson correlation and ROC curves) was analyzed. It must be taken into account that in the VITACORA questionnaire, the higher the value, the better the HRQoL, while in the PsAID the exact opposite occurs. Statistical significance was established at a p value < 0.05. The statistical software R was used.
Results: Fifty-eight percent and 42% of the subjects were under biological and conventional systemic therapy, respectively. Most patients showed good control of their disease, median DAPSA 11.3 (IQR: 8.02-19.3), median PsAID 2.71 (IQR: 1.06-5). The correlation between VITACORA and PsAID was high, r: -0.7 (95% CI: -0.84 to -0.46), p<0.0001, Figure 1. The VITACORA values ranged from 6 to 94. The discriminant validity determined that a VITACORA in the range 6-29 corresponded to a DAPSA high disease activity, a range 30-44 corresponded to a DAPSA moderate activity, and a range 45-95 corresponded with low DAPSA activity. The cut-off to determine an acceptable symptomatic state (PsAID ≤4) corresponded to a VITACORA value ≥ 66 with an area under ROC curve of 0.85 (95%CI: 0.71-0.98).
Conclusion: The VITACORA questionnaire has good discriminant and construct validity, and its clinimetric performance is similar to the PsAID in estimating HRQoL in clinical routine. Either of the two questionnaires could be used to assess this aspect of health in PsA. A VITACORA value ≥ 66 could be a good treatment target.
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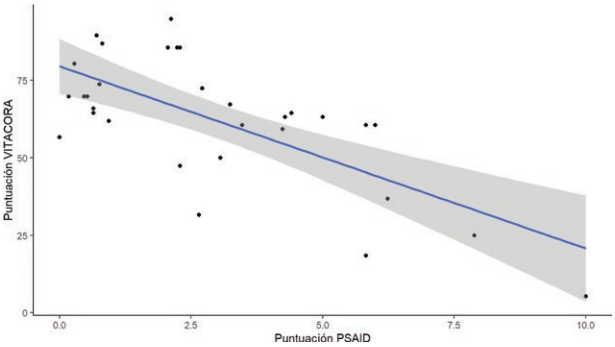


Figure 1. Correlation between VITACORA and PsAID

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0029 WHOLE SPINE MRI IN AXIAL PSORIATIC ARTHRITIS

Keywords: Spondyloarthritis, Imaging, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is known to have symptoms clinically in multiple domains, one of which is the axial lesion. The ASAS classification criteria for axial spondyloarthritis include confirmation of sacroiliitis on x-ray or MRI, but there is no definition or specific imaging studies that have been determined for axial psoriatic arthritis (axPsA).
Objectives: This study aimed to investigate the usefulness of whole spine MRI including all spines and sacroiliac joints in patients with axPsA.
Methods: We retrospectively analyzed the medical records of PsA patients who were underwent whole spine MRI and diagnosed that had axial lesions. PsA was classified according to Classification Criteria for Psoriatic Arthritis (CASPAR) criteria and axPsA was diagnosed by a radiologist specializing in musculoskeletal lesions, especially spondyloarthritis. We analyzed patients' characteristics and MRI findings.
Results: The mean age of the 43 patients was 47.47 (±12.7) years, and 26 (60.5%) were male. The time from onset of PsA to MRI imaging was 7.98 [3.34, 18.65] years. 24 (55.8%) patients had sacroiliac joint involvement and 39 (90.7%) patients had spinal involvement. 15 (34.9%), 25 (58.1%), and 28 (65.1%) had cervical, thoracic, and lumbar spine, respectively.
Conclusion: In this study, about half of the patients had no MRI findings of the sacroiliac joint. On the other hand, spinal lesions were more common. Although sacroiliac joint MRI is usually performed for diagnosis in axial spondyloarthritis, imaging of the sacroiliac joints alone may be insufficient in cases of axPsA, because it is known that there are patients who do not have lesions in the sacroiliac joints but in the spine alone.(1) This study showed that whole spine MRI imaging was considered useful to avoid overlooking spinal lesions which is important for axPsA.
REFERENCE:
[1] Rheumatology (Oxford). 2020 Jun 1;59(6):1193-1195

Table 1. Baseline characteristics

Age (years)	47.5 (12.7)
Male sex, n (%)	26 (60.5)
BMI (kg/m^2)	23.57 (3.5)
Duration between inflammatory musculoskeletal symptom onset to diagnosis [IQR, days]	1415.0 [371.5, 6177.0]
Duration of disease [IQR, days]	2914.0 [1219.5, 6808.0]
Definite inflammatory back pain, n (%)	31 (72.1)
C-reactive protein (mg/dl)	0.12 [0.04, 0.57]
Peripheral involvement, n (%)	42 (97.7)
Psoriasis, n (%)	40 (93.0)
IBD, n (%)	1 (2.3)

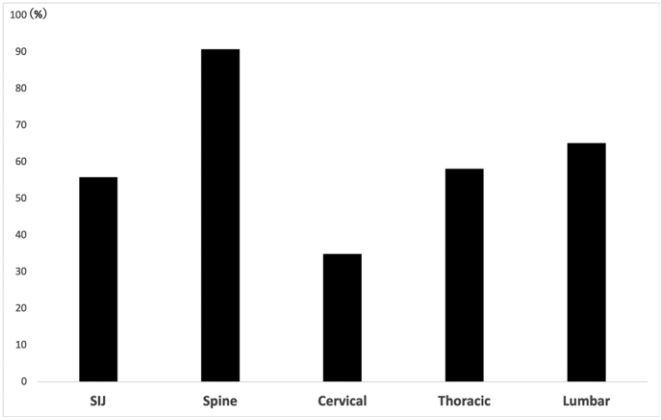


Figure 1. Radiographic patterns of patients with axial psoriatic arthritis

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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RA is more than just joints

POS0030

METHOTREXATE USE ASSOCIATES WITH ISCHEMIC CARDIOVASCULAR RISK REDUCTION IN MALES BUT NOT FEMALES WITH RHEUMATOID ARTHRITIS

Keywords: Cardiovascular disease, Rheumatoid arthritis

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Background: Patients with rheumatoid arthritis (RA) experience higher cardiovascular risk compared to individuals without inflammatory rheumatic disease. Observational studies indicate that methotrexate (MTX) may decrease cardiovascular risk in patients with RA. It is, however, unclear whether sex differentially impacts cardiovascular risk in MTX users and non-users and whether men and women derive equal benefit from methotrexate use.
Objectives: We here explored the influence of sex on cardiovascular risk in MTX nonusers and users. We further evaluated the effect of MTX treatment on cardiovascular risk in males and females with RA.
Methods: We evaluated 4362 patients with RA and no atherosclerotic cardiovascular disease, prospectively included in an international observational cohort [*An Int*ernationa*l C*ardiovascular *C*onsortium for people with *RA* (ATACC-RA)]. Outcomes of interest were (a) major adverse cardiovascular events (MACE) defined as cardiovascular death, non-fatal myocardial infarction or stroke and (b) any ischemic cardiovascular events (CVE) including MACE, stable angina, coronary revascularization, transient ischemic attack and peripheral arterial disease with or without revascularization. Missing covariate data were imputed using multiple imputation with 10 repetitions. Multivariable Cox models stratified by center evaluated the impact of sex, baseline MTX use and their interaction on CVE risk after adjusting for age, hypertension, diabetes, family history of coronary artery disease, smoking, total cholesterol to high-density lipoprotein cholesterol ratio, disease duration, and disease activity score (DAS28 ESR). Two corroborating sensitivity analyses were conducted; The first used inverse probability of treatment weights to balance differences in MTX treated and untreated patients. The second included patients enrolled in the cohort on or after January 1, 2000, when MTX use became more prevalent among enrollees.
Results: There were 237 first MACE and 358 total ischemic CVE recorded during the entire follow-up period. Male sex associated with an 81% and 58% greater risk of MACE and any ischemic CVE, respectively (Figure 1). Among MTX nonusers, incidence of MACE and any ischemic CVE was higher in males [17.6 (95% CI 14.4-21.3) and 24.5 (20.7-28.9) events/1000PY, respectively] compared to females [6.9 (5.7-8.4) and 11.4 (9.8-13.3) events/1000PY respectively, all p for difference<0.001]. In adjusted Cox models, male nonusers had a 2.09-fold higher risk of MACE and 74% higher risk of any ischemic CVE compared to female nonusers (both p<0.001, Figure 1). In contrast, among MTX users, incidence of MACE and any ischemic CVE was not significantly different in males [4.2 (1.7-10.0) and 7.6 (4.0-14.6) events/1000PY, respectively] than females [6.4 (4.4-9.2) and 9.4 (6.9-12.8) events/1000PY, respectively] and sex was not associated with event risk in MTX users in adjusted models. Moreover, among males, MTX use associated with a 66% reduced risk of MACE and 55% reduction in any ischemic CVE (p=0.026 and 0.024, respectively). In contrast, MTX use was not associated with MACE or any ischemic CVE in females [adjusted hazard ratio 1.33 (0.83-2.14) and 1.21 (0.81-1.79) respectively]. Both sensitivity analyses yielded similar results.
Conclusion: RA males not using MTX exhibit higher risk of MACE and any ischemic CVE compared to female nonusers, while no differences are observed between male and female MTX users. Baseline MTX use associated with reduction in the risk of MACE and all ischemic cardiovascular events in males but not females with RA.

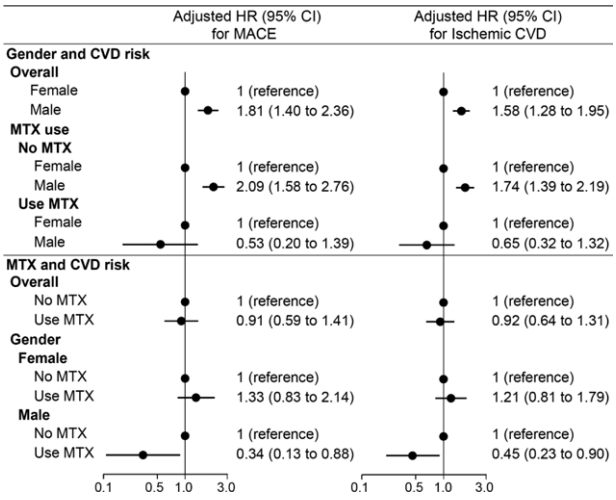


Figure 1. Impact of sex in methotrexate nonusers and users and effect of methotrexate treatment for females and males

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: George Karpouzas Speakers bureau: Sanofi/Genzyme/Regeneron, BMS, Consultant of: Sanofi/Genzyme/Regeneron, Janssen, Grant/research support from: Pfizer, Sarah Ormseth: None declared, Piet van Riel: None declared, Cynthia S. Crowson: None declared, Elena Myasoedova: None declared, Sherine Gabriel: None declared, Miguel A González-Gay: None declared, Alfonso Corrales: None declared, Solbritt Rantapää Dahlqvist: None declared, Petros Sfikakis: None declared, Patrick Dessein: None declared, Linda Tsang: None declared, Carol Hitchon: None declared, Hani El-Gabalawy: None declared, Virginia Pascual: None declared, Iris Jazmin Colunga-Pedraza: None declared, Dionicio Ángel Galarza-Delgado: None declared, José Ramón Azpiri-López: None declared, Silvia Rollefstad: None declared, Anne Grete Semb: None declared, Durga Prasanna Misra: None declared, George Kitas: None declared, Ellen-Margrethe Hauge: None declared.
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POS0031

DO COMORBIDITIES INCREASE THE RISK OF FAILURE TO REACH REMISSION IN EARLY RHEUMATOID ARTHRITIS PATIENTS RECEIVING METHOTREXATE AS FIRST-LINE THERAPY?

Keywords: Comorbidities, Rheumatoid arthritis, Remission

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Background: Previous studies have reported that some comorbidities associate with a lower probability of remission in patients with established rheumatoid arthritis (RA).[1, 2] Evidence on whether comorbidities affect remission in DMARD-naïve patients with early RA is, however, lacking. We have recently shown that most patients with early RA, irrespective of comorbidities, receive methotrexate (MTX) in DMARD monotherapy as first-line therapy.[3]
Objectives: The aim of this study is to examine whether specific comorbidities or overall comorbidity burden affect the likelihood of remission on MTX in DMARD monotherapy as first treatment in patients with early RA.
Methods: We included patients with a new RA diagnosis in the Swedish Rheumatology Quality register (SRQ) during 2007 to 2020, in total 11,001 incident RA cases, of whom 67% were female and 69% seropositive. Of these, 8,273 had a follow-up visit at 3 months. Information on comorbidities five years before RA diagnosis was retrieved from the Swedish National Patient Register and information on prescribed drugs 1.5 year before RA diagnosis from the Prescribed Drug Register. Comorbidity diagnoses were grouped into 10 categories (table 1). Disease activity measures were captured through SRQ. The primary outcome measure was failure to reach DAS28 remission, with Boolean, SDAI, CDAI remission, EULAR response and no swollen joints as secondary outcomes. Modified Poisson regression was used to calculate the relative risks of failure to reach remission, in relation to the comorbidities, adjusted for sex and age.
Results: In total, 53% of the RA patients had failed to reach DAS28 remission after 3 months of MTX monotherapy, ranging from 68% among the patients with

psychiatric diagnoses to 48% of the patients with a history of cancer (figure 1). The relative risk of not reaching DAS28 remission after 3 months (table 1) was increased for patients with endocrine (RR:1.08, 95% CI 1.01 to 1.15) or gastrointestinal (RR 1.16, 95% CI 1.03 to 1.30) diseases, previous hospitalisation due to infectious diseases (RR= 1.21, 95% CI 1.06 to 1.38), psychiatric comorbidity (RR: 1.24, 95% CI 1.15 to 1.35) and respiratory diseases (RR=1.16, 95% CI 1.01 to 1.32). The comorbidity burden also associated with lower remission rates, with a 27% higher risk of not reaching DAS28 remission for the patients with ≥3 comorbidity categories compared to patients without comorbidities. A similar pattern was observed for the secondary outcome measures.

Conclusion: Specific comorbidities and the overall comorbidity burden associate with failure to reach remission to MTX as DMARD monotherapy in early RA patients. Comorbidities may be an important factor when assessing treatment outcomes in early RA.

Table 1. Relative risk of failure to reach DAS28 remission at 3 months after initiating methotrexate monotherapy in early RA, by comorbidity categories.

	Relative risk (95% CI)*
Cardiovascular	1.02 (0.93 to 1.12)
Non-cardiac vascular	1.01 (0.95 to 1.07)
Malignant	0.90 (0.81 to 1.00)
Endocrine	**1.08 (1.01 to 1.15)**
Gastrointestinal	**1.16 (1.03 to 1.30)**
Infectious	**1.21 (1.06 to 1.38)**
Chronic kidney	1.38 (0.89 to 2.16)
Neurological	1.11 (1.00 to 1.23)
Psychiatric	**1.24 (1.15 to 1.35)**
Respiratory	**1.16 (1.01 to 1.32)**

*Adjusted for sex and age. Number of patients with DAS28 at 3 months: 7643.Significant findings in bold.

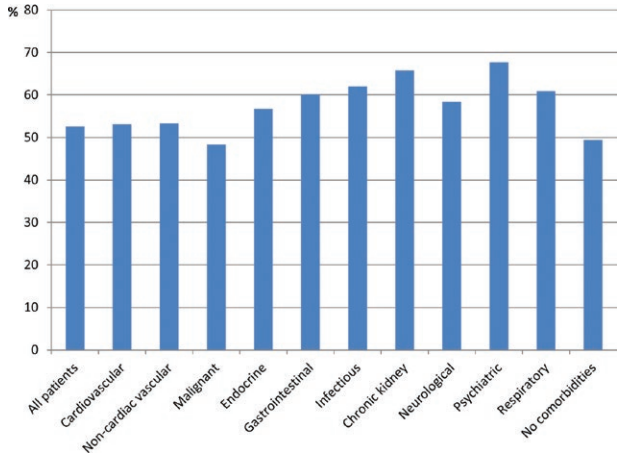


Figure 1. Proportion with failure to reach DAS28 remission at 3 months after initiating methotrexate monotherapy in early RA, by comorbidity categories.

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POS0032

TARGETS THAT WORK: IDENTIFYING MODIFIABLE PREDICTORS OF PRESENTEEISM OVER ONE YEAR IN WORKERS WITH INFLAMMATORY ARTHRITIS

Keywords: Patient reported outcomes, Work-related issues, Inflammatory arthritides

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Background: Inflammatory arthritis (IA) impacts work outcomes and workers' lives. Advancements in treatment have improved work disability (WD) but presenteeism remains a major problem, lacking clear targets for intervention.

Objectives: Identify predictors of presenteeism over 1-year follow-up in workers with IA.

Methods: We designed a prospective observational study analyzing data from the RCT evaluating the Making it Work™ program, an online employment intervention. Participants were recruited in 3 Canadian provinces from rheumatologist practices, consumer organizations and arthritis programs. Eligibility: diagnosis of IA, employed, age 18-59, and concerned about ability to work. Presenteeism was assessed at 0-6-12 mos., using the RA Work Instability Scale (RAWIS, range 0-23). Candidate predictors measured at baseline (bsl.) included sociodemographic characteristics (age, sex, ethnicity, education, marital status, dependents < age 19); disease variables, (arthritis type, physical function [Health Assessment Quest., HAQ II], disease activity [RA Disease Activity Index, RADAI], fatigue [Multidimensional Assessment of Fatigue, MAF], depression [Patient Health Quest. 9, PHQ 9], sleep [Insomnia Severity Index, ISI], number of limiting comorbidities); work-related variables (occupation, self-employment, job strain, arthritis-work spillover, self-efficacy at work, job satisfaction, importance of working, family support for work, no. hours worked per week, job autonomy, physical demand, psychological demands, and decision latitude from the Job Content Quest. [JCQ]). Important bsl. predictors of presenteeism were identified using multivariable linear regression, and linear mixed effect models, with stepwise model selection procedure optimizing Akaike Information criterion (AIC), a commonly used statistical measure and asymptotically equivalent to using cross-validation to compare models. Finally, interaction terms were tested in the model.

Results: A total of 564 participants (mean (SD) age: 45.7(9.9) yrs, 77.8% female, 81.5 % Caucasian, 49.7% RA, 19.7% SpA, 17.0% PsA and 13.7% SLE or another CTD) were recruited. Bsl. median RAWIS (q25,q75) was 11 (7, 15). More job strain, arthritis-work spillover, job physical demand, fatigue, disease activity, and insomnia were associated with worse presenteeism, and better self-efficacy and functional status were associated with better presenteeism (Table 1). Self-efficacy modified the effect of disease activity, physical function and fatigue on presenteeism, and disclosure was associated with greater worsening of presenteeism in women than men (Figure 1).

Conclusion: This study identified key modifiable predictors of presenteeism over one year in workers with IA. These results provide useful information to healthcare professionals, researchers and patients.

Table 1. Baseline predictors of presenteeism at baseline and follow up visits over 1 year

Baseline predictors	Model1. RAWIS Baseline δ			Model2. RAWIS Over 1 yr. f.u. §		
	β	95%CI	p-value	β	95%CI	p-value
Job Strain (1-5)	1.61	1.2, 2.0	<.001	1.61	1.2, 2.0	<.0001
Arthritis-Work Spillover (1-5)	1.41	1.0, 1.8	<.001	1.22	.9, 1.7	<.0001
Fatigue (1-50)	.06	.0,.1	.002	.06	.0,.1	.001
Self Efficacy at Work (1-10)	-.36	-.6, -.1	.001	-.32	-.5, -.1	.003
Functional Status (0-3)	2.28	1.6, 3.0	<.001	2.05	1.4, 2.7	<.0001
Disease Activity (0-10)	.31	.1,.5	.002	.30	.1,.5	.001
Insomnia (0-28)				.05	.0,.1	.050
Physical demand (1-4)	.62	.4,.9	<.001	.57	.3,.8	<.0001
Female	1.04	.4, 1.7	.001	.85	.2, 1.5	.007
Disclosure, yes	.93	.3, 1.5	.003	.67	.1, 1.2	.021
Completed Post Second. educ., yes				-.48	-1.0,.1	.105
AIC	2853.83			7590.918		
R^2	adj. R^2:.70, predicted R^2:.69			model:.94/ fixed:.56/ random:.39		

δ Linear regression model § Linear mixed effects model Both models adjusted for calendar time, program allocation, age, ethnicity and occupation

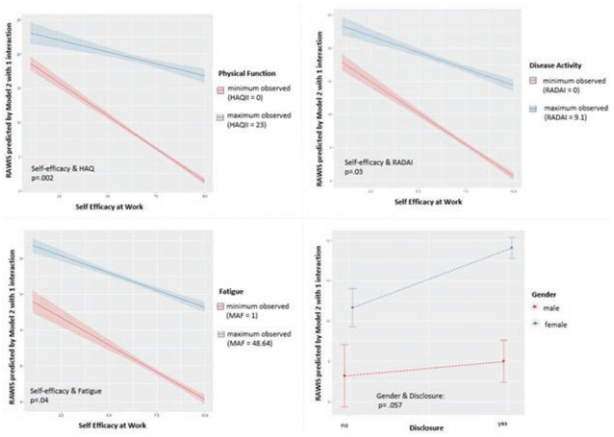


Figure 1. Interaction plots. **Model 2**: linear mixed-effects model using predictors at baseline and RAWIS over 1 year (Table 1)

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POS0033

RISK OF OSTEOARTICULAR INFECTION AND DEATH FOLLOWING STAPHYLOCOCCUS AUREUS BACTEREMIA IN PATIENTS WITH AND WITHOUT RHEUMATOID ARTHRITIS – A DANISH NATIONWIDE REGISTRY-BASED COHORT STUDY

Keywords: Rheumatoid arthritis, Comorbidities, bDMARD

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Background: Patients with rheumatoid arthritis (RA) are at increased risk of *S. aureus* bacteremia (SAB) compared with the general population.[1] SAB has high mortality and osteoarticular infection (OAI) is a feared complication associated with persistent pain and disability. It remains unclear if RA is associated with increased risk of OAI or death following SAB. [2, 3]

Objectives: To compare risk of OAI and death in SAB patients with and without RA and to assess risk factors for OAI in RA patients including risk associated with antirheumatic treatment.

Methods: Nationwide cohort study of Danish patients with microbiologically verified first-time SAB from 1 January 2006 to 31 December 2018. We identified RA, OAI, vital status, comorbidities, and RA-related clinical characteristics in the rheumatology registry, DANBIO and other national registries. We estimated 90-day cumulative incidence of OAI (in patients without OAI before SAB) and all-cause mortality (all patients). We computed hazard ratios (HR) by multivariate Cox regression adjusted for a priori known risk factors for each outcome.

Results: We identified 18,274 patients with SAB (n=367 with RA). In RA versus (vs.) non-RA, women comprised 62% vs. 37% and median age was 73 years (interquartile range 65; 80) vs. 70 years (59; 82). Prior OAI (0-3 months before SAB) was diagnosed in 4% vs. 2%. The 90-day cumulative incidence of OAI was 23.1% (95% CI 18.8; 27.6) in RA patients vs. 12.5% (12.1; 13.0) in non-RA (**Figure 1**) (HR 1.93 (1.54; 2.41) adjusted for age, sex, calendar year, and diabetes mellitus). In RA, use of tumor necrosis factor inhibitors (TNFi) and orthopedic implants were associated with OAI risk (**Table 1**). Mortality was similar in SAB patients with (35.4% (30.6; 40.3)) and without RA (33.9% (33.2; 34.5) (Figure), (HR 1.04 (0.87; 1.24) adjusted for age, sex, calendar year, chronic liver disease, chronic obstructive pulmonary disease, cancer, congestive heart failure, renal failure).

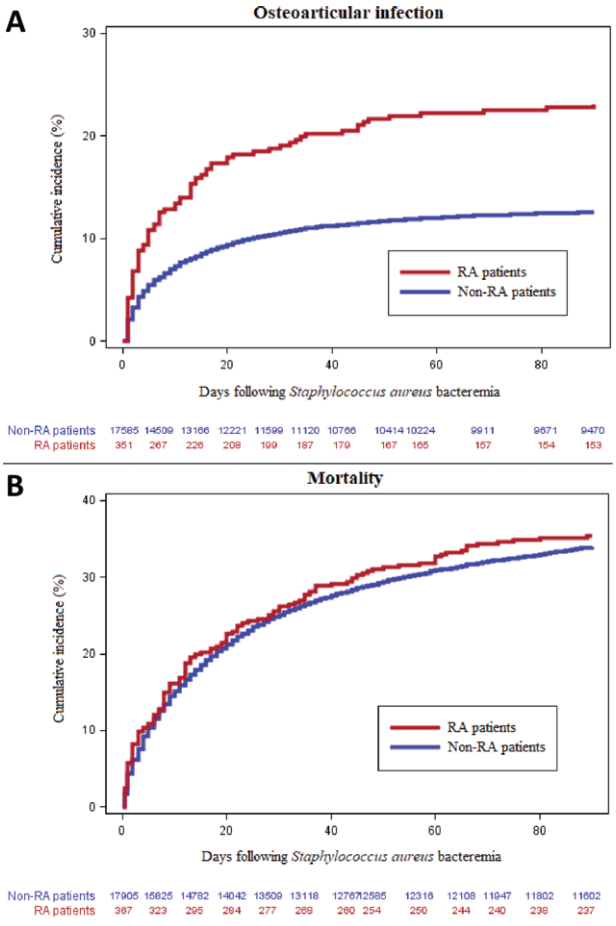


Figure Cumulative incidence of osteoarticular infection (panel A) and death (panel B) 90 days following *S. aureus* bacteremia among patients with and without rheumatoid arthritis (RA) in Denmark from 2006 to 2018.

Table 1. Characteristics of patients with rheumatoid arthritis (RA) and *S. aureus* bacteremia in Denmark from 2006-2018 and associated risk of osteoarticular infection (OAI).

		Total, n (%)[a]	OAI, n	90-day cumulative incidence % (95% CI)	Adjusted* HR (95% CI)
bDMARDs	Non-user	281 (77)	53	19.4 (15.0; 24.3)	Ref.
	User	86 (23)	28	35.9 (25.4; 46.5)	**1.74 (1.07; 2.81)**
	Former user	18 (5)	5	27.8 (9.6; 49.6)	NA
	Current user	68 (19)	23	38.3 (26.1; 50.4)	**1.92 (1.15; 3.20)**
	Mode of action				
	TNFi	50 (14)	18	41.9 (27.0; 56.1)	**2.27 (1.29; 3.98)**
	Non-TNFi	18 (5)	5	29.4 (9.9; 52.41)	NA
Oral glucocorticoids	Non-user	141 (38)	31	23.1 (16.4; 30.6)	Ref.
	User	226 (62)	50	23.0 (17.7; 28.8)	0.92 (0.57; 1.49)
	Former user	64 (17)	13	21.0 (11.8; 31.9)	0.78 (0.40; 1.53)
	Current user	162 (44)	37	23.9 (17.5; 30.8)	0.99 (0.59; 1.67)
	Daily dose (mg)				
	≤5.0	128 (35)	31	25.4 (18.1; 33.4)	1.04 (0.60; 1.78)
	>5.0	34 (9)	6	18.2 (7.2; 33.1)	NA
Orthopedic implants	No	177 (48)	29	16.7 (11.6; 22.6)	Ref.
	Yes	190 (52)	52	29.4 (22.9; 36.2)	**1.75 (1.08; 2.85)**

*age, sex, calendar year, diabetes mellitus, csDMARD use, serostatus, RA disease duration and remaining variables in table.[a] n (%) of all patients with RA (n=367). Analyses were restricted to patients without recent OAI (n=351).bDMARD, biological disease-modifying antirheumatic drugs; csDMARD, conventional synthetic DMARD; HR, hazard ratio; CI, confidence interval; Ref., reference; NA, not applicable (few events)

Conclusion: Nearly one in four patients with RA experienced an osteoarticular infection following *S. aureus* bacteremia compared with one in eight patients without RA. In patients with RA, current TNFi use and orthopedic implants were associated with increased osteoarticular infection risk. One in three patients died, with no difference between patients with and without RA. These findings highlight the need for vigilance when RA patients present with SAB to ensure timely identification of OAI.

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POS0034 BIOLOGIC USE REGULATES THE IMPACT OF INFLAMMATION ON ISCHEMIC CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS

Keywords: Cardiovascular disease, Rheumatoid arthritis

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Background: Chronic inflammation contributes to enhanced cardiovascular risk in patients with rheumatoid arthritis (RA). Biologic disease modifying antirheumatic drugs (bDMARDs) have been shown to effectively control inflammation in many conventional synthetic DMARD non-responders and improve cardiovascular outcomes.

Objectives: We here explored whether baseline bDMARD use may influence the impact of disease activity and systemic inflammation on long-term cardiovascular risk in patients with RA.

Methods: We studied 4370 patients with RA who were free of cardiovascular disease upon registration to *A*n *In*ternational *C*ardiovascular *C*onsortium for people with *RA* (ATACC-RA) and followed prospectively. Prespecified outcomes included (a) major adverse cardiovascular events (MACE) defined as non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death and (b) any ischemic cardiovascular events (CVE) comprising MACE, coronary revascularization, stable angina pectoris, transient ischemic attack and peripheral arterial disease with or without revascularization. Missing covariate data were imputed using multiple imputation with 10 repetitions. Multivariable Cox models stratified by center evaluated the impact of disease activity [based on 28 joint counts and C-reactive protein (DAS28-CRP)], systemic inflammation (CRP), bDMARD use and their respective interactions on CVE risk after adjusting for age, gender, hypertension, diabetes, family history of CAD, smoking and total cholesterol to high-density lipoprotein ratio. Two corroborating sensitivity analyses were performed; the first included patients enrolled in the cohort on or after January 1, 2000, when bDMARD use became more prevalent among enrollees. The second used inverse probability of treatment weights (IPTW) to balance differences in bDMARD treated and untreated patients.

Results: Throughout 26534 patient years of follow-up, 239 first MACE and 362 total ischemic CVE were recorded. Among bDMARD nonusers, incidence of MACE and any ischemic CVE was [9.3 (95% CI 8.2-10.6) and 14.2 (12.8-15.8) events/1000PY respectively. Corresponding rates for bDMARD users were [5.4 (95% CI 2.9-10.1) and 8.2 (5.0-13.6) events/1000PY respectively. In the entire cohort, DAS-28 CRP and CRP(ln) associated with greater risk of MACE [(adjusted hazards ratio [HR] 1.19 (95%CI 1.06-1.34), p=0.004 and HR 1.15 (1.02-1.28), p=0.017 respectively], while for all ischemic CVE the association was significant for DAS-28 CRP [adjusted HR 1.1 (95%CI 1.07 to 1.30)], but not CRP(ln) [HR 1.06 (0.97 to 1.16)]. In bDMARD nonusers at baseline, higher DAS28-CRP and CRP(ln) associated with greater risk of MACE [adjusted HR 1.21 (95%CI 1.07-1.37), p=0.002 and HR 1.16 (1.04-1.30), p=0.009 respectively]. However, this was not the case in bDMARD users [p-for-interaction= 0.017 and 0.011 correspondingly, Figure 1]. In contrast, no significant interaction between DAS28-CRP or CRP and bDMARD use on any ischemic CVE risk was observed (p-for-interaction= 0.167 and 0.237 respectively). Both sensitivity analyses yielded similar results.

Conclusion: Higher disease activity and systemic inflammation at baseline associated with greater risk of MACE in bDMARD nonusers but not in patients receiving bDMARDs. This may suggest the presence of additional bDMARD-specific benefits directly on atherosclerotic plaque —such as plaque stabilization[1]— above and beyond their effects on systemic inflammation.

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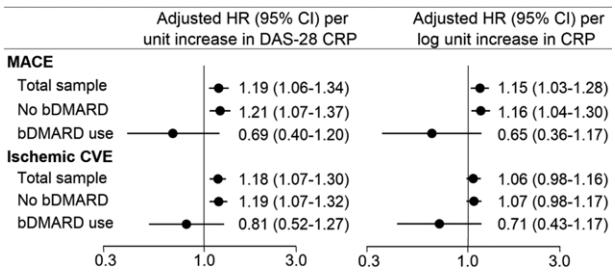


Figure 1. bDMARD use regulates the effect of inflammation on ischemic cardiovascular risk in patients with RA.

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POS0035 INFLUENCE OF INTERSTITIAL LUNG DISEASE DURATION ON THE TREATMENT OF RHEUMATOID ARTHRITIS-INTERSTITIAL LUNG DISEASE. NATIONAL MULTICENTER STUDY OF 392 PATIENTS WITH ABATACEPT

Keywords: Lungs, Rheumatoid arthritis, Disease-modifying Drugs (DMARDs)

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Background: Interstitial lung disease (ILD) is a severe complication of rheumatoid arthritis (RA). Abatacept (ABA) has demonstrated efficacy in the treatment of RA-ILD, especially if it is initiated early during the ILD **[1-2].**

Objectives: To compare the efficacy of ABA in RA-ILD patients according to ILD duration.

Methods: National multicenter study of 392 RA-ILD patients treated with ABA. Patients with ABA initiation early in the disease (during the first 6 months since ILD diagnosis) were compared to those in whom ABA was started after 2 years of ILD diagnosis ("early" vs "late" group, respectively). We analyzed in the 2 groups the following outcomes: a) forced vital capacity (FVC), b) diffusing capacity of the lungs for carbon monoxide (DLCO), c) chest high resolution computed tomography (HRCT), d) dyspnea and e) arthritis activity.

Results: A total of 157 patients were included in the "early" group and 135 patients in the "late" group. Baseline demographic and clinical characteristics are shown in Table 1. Mean baseline values of FVC were significantly higher in the "early" group. The evolution of FVC and DLCO for 48 months is shown in Figure 1. Both parameters remained stable during 12 months of ABA therapy, with no statistically significant differences found (although lower stable values of FVC in the "late" group). Available chest HRCT images improved/stabilized in 75% and 51% of patients in the "early" and "late" group, respectively. Stabilization or improvement of dyspnea was found in most patients of both groups.

Conclusion: Our results suggest that an early administration of ABA in RA-ILD may be preferable to preserve lung function. However, treatment with ABA at any time of the course in the ILD seems to prevent interstitial lung progression.

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Table 1. Main general features at baseline of RA-ILD patients with EARLY vs LATE initiation of ABA in ILD course.

	All RA-ILD (n=392)	EARLY RA-ILD (n=157)	LATE RA-ILD (n=135)	EARLY vs LATE p
Age years mean±SD	65 ± 10	66 ± 10	66 ± 10	0.97
Women n (%)	226 (58)	88 (56)	80 (59)	0.58
Smoker ever n (%)	210 (54)	86 (55)	68 (50)	0.45
ILD duration up to ABA months median [IQR]	11 [3-38]	2 [1-4]	51 [36-89]	**<0.001**
RF n (%); ACPA n (%)	347 (89); 344 (89)	138 (88); 136 (87)	123 (91); 118 (89)	0.37; 0.56
DAS28-ESR	4.35 ± 1.58	4.16 ± 1.61	4.40 ± 1.59	0.26
ILD pattern n (%)				
NIU	172 (44)	68 (44)	56 (42)	0.95
NINE	117 (30)	48 (31)	43 (33)	
FVC (% pred) mean±SD	87 ± 21	89 ± 28	82 ± 19	0.015
DLCO (% pred) mean±SD	67 ± 20	66 ± 20	65 ± 21	0.76
ABA monotherapy n (%)	179 (46)	72 (46)	62 (46)	0.99
ABA combined n (%)	211 (54)	85 (54)	72 (53)	
Prednisone at baseline, mg/day median [IQR]	5 (5-10)	7.5 (5-10)	5 (5-10)	0.57
Previous IS therapy n (%)				
MTX	293 (75)	126 (81)	97 (72)	0.073
LFN	175 (45)	68 (43)	61 (45)	0.75
SSZ	57 (15)	24 (15)	18 (13)	0.64
HCQ	107 (27)	54 (34)	42 (31)	0.55
Anti-TNF; RTX; TCZ	107 (15); 51 (13); 43 (11)	51 (34); 17 (11); 20 (13)	34 (25); 19 (14); 15 (11)	0.17; 0.40; 0.67

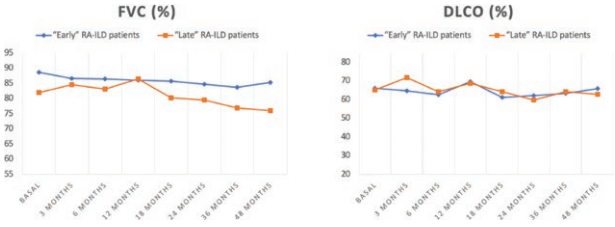


Figure 1. Evolution of pulmonary function in RA-ILD patients with EARLY and LATE initiation of ABA in ILD course.

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Carreira: None declared, J M Blanco: None declared, Carlos Fernández-Díaz: None declared, J. Loricera: None declared, Iván Ferraz-Amaro: None declared, Diego Ferrer: None declared, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, lilly, Bristol-Myers, Janssen, Galapagos and MSD, Consultant of: Abbvie, Pfizer, Roche, lilly, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD, novartis and Roche.

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POS0036 SUBSEQUENT HOSPITALIZATIONS FOR OR WITH PSYCHIATRIC DISORDERS IN INDIVIDUALS WITH PRE-EXISTING RHEUMATOID ARTHRITIS AND SPONDYLARTHRITIS: A NATIONAL REGISTRY-BASED RETROSPECTIVE COHORT STUDY

Keywords: Mental health, Real-world evidence, Comorbidities

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Background: The crosslink between rheumatic diseases (RD) and psychiatric disorders (PD) has been suggested, particularly due to systemic inflammation and the psycho-social impact of chronic painful experience in patients with RD.
Objectives: In the present study, we investigated the risk of subsequent hospitalization (1) for PD and (2) either for or with PD in cohorts of patients with specific pre-existing RD.
Methods: In this retrospective cohort study, we utilized data from the Czech nation-wide registers of all-cause hospitalizations and deaths. The study consisted of individuals first hospitalized with (1) rheumatoid arthritis (RA; International Classification of Diseases 10th Revision (ICD-10) codes M05 and M06) and (2) spondylarthritis (SpA; ICD-10 codes M07, M45 and M46[1, 8, 9]) in the time-period from 1999 to 2011 (index hospitalization) and counterparts without the respective diseases, exactly matched on age, sex, month and year at the index hospitalization (1:5). The risk of subsequent hospitalization (1) for and (2) either for or with each diagnostic group of PD (ICD-10 codes F0x + G20 and G30, F1x, F2x, F3x, F4x and F5x) arising in the period of five or more years (up to 2017) from the index hospitalization was assessed using stratified Cox proportional hazards models, controlling for deaths occurring in this time-period and adjusting for age, sex and month and year at the index hospitalization. We assessed the risk (1) of being hospitalized for PD (ie, primary diagnosis) and (2) of being hospitalized for or with PD (ie, either primary or secondary diagnosis) separately. For the respective analyses, we excluded individuals who were (1) hospitalized for PD and (2) hospitalized either for or with PD five or more years (up to 1994) prior to the index hospitalization, separately for each diagnostic group of PD. Thus, we effectively created 24 matched cohorts overall. The results are expressed as hazard ratios (HR) with 95% confidence intervals (95% CI).
Results: When considering hospitalizations specifically for PD, the total number of individuals in the RA cohorts ranged from 92,694 to 93,768 and from 31,488 to 32,088 individuals in the SpA cohorts, whereas when considering hospitalizations either for or with PD, the number of individuals in the RA cohorts ranged from 91,290 to 93,726 and from 30,852 to 32,070 individuals in the SpA cohorts. We found that individuals with SpA had an elevated risk of hospitalization for anxiety disorders (1.36; 1.08 to 1.70), when compared with matched counterparts. Conversely, we found that individuals with RA had a decreased risk of hospitalization for substance use disorders (0.58; 0.46 to 0.72). Next, we found that individuals with RA and SpA had an elevated risk of being hospitalized either for or with mood disorders (1.18; 1.06 to 1.31 and 1.26; 1.02 to 1.54) and anxiety disorders (1.24; 1.12 to 1.36 and 1.32; 1.11 to 1.56). In addition to this, people with RA had a higher risk of being hospitalized either for or with organic PD (1.25; 1.16 to 1.35) and people with SpA demonstrated an increased risk for hospitalization listing behavioral syndromes associated with physiological disturbances and physical factors as one of the diagnosis (2.73; 1.59 to 4.71). Conversely, people with RA had a lower risk of being hospitalized either for or with substance use disorders (0.77; 0.68 to 0.87). For the other PD outcomes in people with RA and SpA, the 95% CIs covered a range from decreased to increased risk.
Conclusion: Individuals with RA and SpA seem to have a higher risk of developing a range of PD, when compared with matched counterparts. The detected differences suggest that clinical vigilance and provision of mental health services to affected individuals require further attention.
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POS0037 VALIDATION OF DIAGNOSTIC CODES FOR DEMENTIA IN A RHEUMATOID ARTHRITIS POPULATION-BASED COHORT

Keywords: Cognitive Function, Rheumatoid arthritis, Validation

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Background: Dementia is a major global mental health problem. The prevalence of dementia is increasing dramatically with increasing life longevity and population aging. Several studies found increased risk of dementia in patients with rheumatoid arthritis (RA) and reported a possibility of mitigating this risk with antirheumatic treatments. The underlying mechanisms for these associations are not fully understood and require further study. As clinical verification of the diagnosis may not be readily available, especially in retrospective observational studies, diagnostic codes can be used. However, performance of diagnostic codes for dementia case identification has not been validated in RA cohorts.
Objectives: To validate the use of ICD-9/10-CM diagnostic codes for dementia identification against diagnostic criteria for dementia in individuals with and without RA using retrospective manual verification of cases.
Methods: This retrospective population-based study included residents of a geographically well-defined area with incident RA based on the 1987 American College of Rheumatology (ACR) classification criteria in 1980-2018. All adult (≥18 years) cases of RA were included and matched (1:1) by age, sex, calendar year, and county to non-RA controls. Dementia case identification using ICD-9/10-CM diagnostic codes from the Charlson comorbidity index was validated against dementia diagnosis based on Diagnostic criteria in Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV). DSM-IV criteria were verified by manual records review.
Results: A total of 3,116 individuals (1558 RA cases and 1558 non-RA controls) were included. Mean age 56.2 years; 68% females in both groups; mean (SD) age at the last follow-up was 68.7 (14.7) years for RA cases and 69.6 (15.4) years for non-RA controls. At the time of the last follow-up, there were 202 (13%) patients with one diagnostic code for dementia, 136 (9%) with two diagnostic codes for dementia, and 137 (9%) with a confirmed diagnosis of dementia per DSM-IV. The respective numbers in non-RA controls are 216 (14%); 147 (9%) and 149 (10%). Mean (SD) duration between accumulating two ICD codes and diagnosis verification by DSM-IV was an absolute difference of 1.0 (1.8) years in RA and 1.2 (1.7) years in non-RA. Table 1 summarizes the results of validation analyses. Positive predictive value (PPV) and specificity were higher with the use of 2 ICD codes in the combined cohort (PPV 81.3), in RA cases (PPV 81.6) and in non-RA controls (PPV 80.9). PPV for two diagnostic codes was highest also in patients born in 1892-1934 (PPV 85.7) than in the more recent birth cohorts: 1935-1949 (PPV 77.6).
Conclusion: The ICD-9/10-CM codes for dementia performed equally well against DSM-IV criteria in the retrospective population-based cohort of individuals with RA and in matched non-RA controls, identifying true dementia cases with approximately 80% probability. The PPV was higher in older birth cohorts than in younger birth cohorts, reflecting the higher prevalence of dementia in older adults. The use of ICD-9/10-CM codes from Charlson comorbidity index is acceptable for dementia case identification in patients with RA, especially in older adults, although additional parameters (e.g., number of diagnostic codes) need to be considered.

Table 1. Performance of ICD-9/10-CM code-based definitions of dementia against DSM-IV criteria

Definition	Sensitivity, rate (CI)	Specificity, rate (CI)	PPV, rate (CI)	NPV, rate (CI)	Accuracy, rate (CI)
Overall					
1 code	90.9 (87.6-94.2)	94.4 (93.6-95.3)	62.2 (57.6-66.8)	99.04 (98.7-99.4)	94.1 (93.3-94.9)
2 codes	80.4 (75.8-85.02)	98.1 (97.6-98.6)	81.3 (76.7-85.8)	98.02 (97.5-98.5)	96.5 (95.9-97.1)
RA					
1 code	89.8 (84.7-94.8)	94.4 (93.2-95.6)	60.9 (54.2-67.6)	98.9 (98.4-99.5)	94.03 (92.9-95.2)
2 codes	81.02 (74.5-87.6)	98.2 (97.6-98.9)	81.6 (75.1-88.1)	98.2 (97.5-98.9)	96.7 (95.8-97.6)
Non-RA					
1 code	91.9 (87.6-96.3)	94.4 (93.2-95.6)	63.4 (57.0-69.8)	99.1 (98.6-99.6)	94.2 (92.9-95.3)
2 codes	79.9 (73.4-86.3)	98.01 (97.3-98.7)	80.9 (74.6-87.3)	97.9 (97.1-98.6)	96.3 (95.3-97.2)

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POS0038

UTILIZATION OF CARDIOVASCULAR PREVENTIVE SERVICES IN A RHEUMATOID ARTHRITIS POPULATION BASED COHORT

Keywords: Rheumatoid arthritis, Comorbidities, Cardiovascular disease

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Background: Rheumatoid arthritis (RA) increases the burden of cardiovascular disease (CVD). Fasting blood glucose, fasting lipoprotein profiles, and blood pressure measurements are recommended at regular intervals to screen for classical CVD risk factors of diabetes mellitus (DM), hyperlipidemia (HLD), and hypertension (HTN), respectively.
Objectives: Our objectives were 1) to perform a contemporary assessment of the trends of CVD preventive service utilization in patients with RA compared to matched non-RA comparators, 2) identify RA patient characteristics that may influence trends in preventive services utilization, and 3) assess how a diagnosis of RA alone influences approaches to CVD prevention compared to the other classical CVD risk factors.
Methods: Inpatient and outpatient medical records for each potential case were manually reviewed. All incident patients fulfilled the 1987 American College of Rheumatology (ACR) classification criteria for RA or the 2010 European League Against Rheumatism (EULAR)/ American College of Rheumatology (ACR) criteria. All ≥19-year-old patients with an RA diagnosis living in an 8-county region on January 1, 2015 (index date), were included and matched (1:1) by sex, age, and county to non-RA comparators. Rates of screening for the classical CVD risk factors were compared between groups using Cox models with adjustment for age, sex, and race.
Results: DM screening was more common among patients with RA ([HR] 1.10, 95% CI 1.01–1.19), as was HTN screening ([HR] 1.37, 95% CI 1.24–1.52). However, HLD screening in RA was similar to comparators ([HR] 0.99, 95%CI 0.89–1.10). RA patient characteristics that influenced classical CVD risk factor screening included: smoking history, obesity, RA duration of < 5 years, older age at the time of RA diagnosis, a higher Charlson comorbidity index, the use of >90 days of glucocorticoid therapy before the index date, the use of disease modifying anti-rheumatic drugs before the index date, and living in the lowest quartile of the Area Deprivation Index within our cohort. Lastly, patients with RA and no classical CVD risk factors had a lower probability of undergoing DM ([HR] 0.67, 95% CI 0.57–0.78) and HLD screening ([HR] 0.65, 95% CI 0.54–0.79) than non-RA patients with one classical CVD risk factor diagnosis. HTN screening was similar between both groups ([HR] 1.01, 95% CI 0.83–1.23).
Conclusion: RA patients undergo CVD preventive screening at rates at least comparable to the general population. However, despite the equivalent-to-higher CVD risk, RA does not appear to be approached as aggressively as traditional CVD risk factors. (1,2) These findings demonstrate an opportunity to improve RA patient care. While EULAR provides guidance for stratifying CVD risk in patients with inflammatory joint disease, there is no equivalent guidance from American medical bodies. (3) Given our findings, clinical practice in the United States could benefit from establishing such recommendations. These recommendations should be forceful in framing RA as conferring an equivalent-to-higher CVD risk as the classical CVD risk factors.

Table 1. Cumulative Incidence of Screenings

	5-year Cumulative Incidence, (95% CI)		
	All RA Patients	**All Non-RA Patients**	**HR**
DM Screening	94.0% (92.6 – 95.3)	93.8% (92.4 – 95.2)	1.10 (1.01 – 1.19)
HTN Screening	99.1% (98.5 – 99.8)	96.3% (95.0 – 97.6)	1.37 (1.24 – 1.52)
HLD Screening	74.3% (71.5 – 77.1)	75.2% (72.5 – 78.1)	0.99 (0.89 – 1.10)

	RA w/o CVD Risk Factors	**Non-RA w/ only 1 CVD Risk Factor**	**HR**
DM Screening RA w/o CVD Risk Factors = 477 Non-RA, Only 1 CVD Risk Factor (HTN or HLD) = 382	91.9% (88.8 – 95.1)	98.9% (98.0 – 99.9)	0.67 (0.57–0.78)
HTN Screening RA w/o CVD Risk Factors = 579 Non-RA, Only 1 CVD Risk Factor (HLD or DM) = 160	99.6% (99.2 – 100)	99.0% (97.0 – 100)	1.01 (0.83–1.23)
HLD Screening RA w/o CVD Risk Factors = 579 Non-RA, Only 1 CVD Risk Factor (HTN or DM) = 248	71.3% (67.1 – 75.8)	84.9% (78.7 – 91.6)	0.65 (0.54–0.79)

CI: confidence interval; HR: hazard ratio

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Disease mechanisms in spondylarthritis

POS0039

A MULTIOMICS PLASMA ANALYSIS REVEALS NEW PATHWAYS CENTRAL IN DRIVING INFLAMMATION IN SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Biomarkers

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Background: Biochemical and clinical disease activity markers in spondyloarthritis (SpA) remain scarce. In addition, understanding the pathways driving disease progression with a combination of bone formation and bone erosions still remain to be fully elucidated. Anti-TNF-α and anti-IL-17A treatment decrease clinical symptoms and partly limit structural changes, but still disease progression and treatment failure occur.
Objectives: We used an unbiased multiomics plasma analysis to identify inflammatory proteins associated with disease activity and structural changes. Subsequently, some of the identified proteins were investigated in biopsies from the spine and in cells, and synovial fluid from the peripheral joint.
Methods: Blood was obtained from patients with early (eSpA) before and 1 year after start of anti-TNF treatment (n=30). Markers of disease activity included; BASDAI, ASDAS, CRP. Osteitis, bone marrow edema and new bone formation were evaluated by MRI scan of the total spine and the SI-joint at baseline and after 1 year of treatment. Healthy controls (HCs) were age and gender matched (n=15). From patients with long-standing SpA (lsSpA, symptom duration >8 years) with a joint effusion, both blood (n= 8) and synovial fluid (SF) (n=6) was obtained. An O-link based multipanel analysis covering 92 proteins was performed on plasma and synovial fluid. Cells were stained for flow. Facet joint biopsies originated from lsSpA patients undergoing surgery for polysegmental correction of rigid hyperkyphosis. These were stained by immune fluorescence. $P < 0.05$ was accepted as significant.
Results: The multiomics analysis revealed 18 proteins significantly increased at baseline compared to after one year of anti-TNF treatment, among these were CCL3, CCL4, CXCL10, CXCL13, IL-6 and PD-L1 (all adjusted $p<0.05$). All targets correlated with baseline CRP, and except for PD-L1, also with ASDAS, BASDAI and BASMI (all rho >0.4). Baseline CXCL13, IL-6 and PD-L1 also correlated to baseline spinal MRI inflammation (rho>0.4). Furthermore, baseline CXCL13 and IL-6 were associated with spinal MRI inflammation after one year of treatment (rho>0.4). CXCL13 was also increased in synovial fluid from lsSpA patients. CXCL13 was not increased in eSpA compared to HCs, but the receptor for CXCL13, CXCR5 was increased on CD4+ PBMCs from eSpA patients compared to HCs (17.3% vs 12.3%, $p<0.01$). eSpA CD4+ PBMCs did not differ from HC CD4+ PBMCs when investigating general activity markers, including CD69,

CD25 and PD-1. Evaluating the central site of pathology, CXCL13 was highly expressed in the inflamed facet joints (Figure 1).
Conclusion: The multiomics analysis revealed multiple cytokines to be activated in eSpA patients. The early disease is characterized by T cell activity in combination with macrophage and monocyte attractive chemokines. CXCL13 stands out as a chemokine of particular interest, being increased both in eSpA, at the central- and peripheral site of pathology, and associated with structural changes in time. The CXCR5-CXCL13 axis could be an important new axis in understanding SpA disease pathology, serving both as a biomarker for disease severity and progression, but also lead to new targets of treatment.

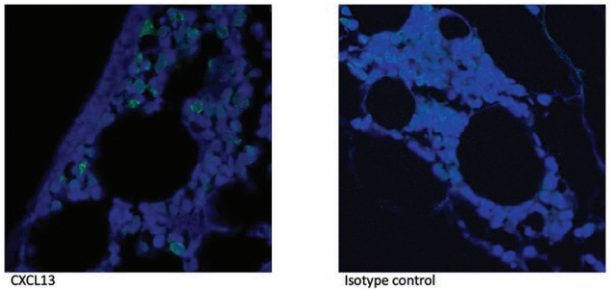


Figure 1.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0040 SILENCING OF JOINT FIBROBLAST TO PROTECT FROM JOINT DAMAGE

Keywords: Spondyloarthritis, Disease-modifying Drugs (DMARDs), Inflammatory arthritides

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Background: Despite significant progress in the development of targeted biologic therapies for the treatment of chronic inflammatory joint diseases such as rheumatoid arthritis or psoriatic arthritis, more than 40% of patients still record gradual loss of joint function, mostly because of failure to archive complete remission. Herein, persistent joint fibroblast activity leads to continuous destruction of the joint, whereas its inhibition/silencing prevents joint damage despite presence of a residual inflammation[1]. Persistent activation of the joint fibroblasts leads to destruction of the joint[1], and silencing both, inflammation and mesenchymal activation is required to protect joints from damage.
Objectives: Protection from joint damage-especially when complete remission cannot be achieved-is a need that might be met by pharmacological targeting of fibroblasts. We aimed to reprogram fibroblasts, from pro-inflammatory and tissue damaging phenotype to a tissue preserving and anti-inflammatory phenotype as a new promising treatment strategy.
Methods: Single-cell RNA sequencing of sorted synovial fibroblasts and imaging mass cytometry from different mouse models of arthritis (TNFtg, *Il23* overexpression, KBxN serum transfer) were used to map fibroblast heterogeneity. Co-culture experiments were performed with sorted fibroblasts and innate lymphoid cells (ILCs) *in vitro*. For functional proof of concept, animals were treated with blocking and activating antibodies in the aforementioned arthritis models. Validation in human synovial biopsies by imaging mass cytometry and spatial transcriptomics was performed.
Results: Through data analysis of joint fibroblast scRNAseq, spatial transcriptomics, and imaging mass cytometry during joint inflammation and its resolution, we observed high plasticity of joint fibroblast populations. By analyzing single-cell dynamics, we identified transdifferentiation of fibroblasts from a MMP3+/IL-6+ destructive state to a DKK3+ protective phenotype upon DMARD-induced resolution and revealed the underlying molecular processes. We identified a novel DKK3+ fibroblast subtype in joints of patients with rheumatoid arthritis and spondyloarthritis (axial spondyloarthritis, peripheral spondyloarthritis, psoriatic arthritis) that protects against joint damage and actively induces resolution of inflammation, by stimulating type 2 ILCs, which are known cellular components for activation of regulatory T cells and pro-resolving eosinophil granulocytes in the joint[2]. We identified the functionally relevant pathway of type 2 IIC activation by fibroblasts. Drug-induced activation of this pathway resulted in activation of pro-resolving ILC2s/Tregs/eosinophil granulocytes in association with a sharp decrease in inflammation and cartilage and bone destruction.
Conclusion: This new treatment approach might have several advantages over anti-inflammatory drugs. (i) no interference with important defence mechanisms against pathogens and no increased risk of opportunistic infections, (ii) activation of a mechanism that retains tissue integrity, (iii) option to combine with anti-inflammatory drugs, making silencing of fibroblasts to a new tool of disease control.
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Disclosure of Interests: None Declared.
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POS0041 UPREGULATION OF SSP1 (OSTEOPONTIN) BY ADIPOSE TISSUE-DERIVED MESENCHYMAL STEM CELLS OCCURS WITH THE CONTINUOUS MECHANICAL LOAD BUT IS STRONGLY RESTRICTED IN INF-G/TNF-A/IL-22 MICROENVIRONMENT

Keywords: Spondyloarthritis

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Background: The interplay between the inflammatory part of the disease and osteogenesis in axial spondyloarthritis (AxSpA) is incompletely understood. It is believed that inflammation triggers the process of new bone formation on the one hand, but the regulation of these phenomena is distinct on the other. An assumption that disease-related osteoproliferation in AxSpA is governed by the complex interplay of inflammation, hormonal or growth factors, and mechanical load has been made. A recent study demonstrated that a pro-inflammatory environment, consisting of interferon-γ (INF-γ) and tumor necrosis factor-α (TNF-α), allowed IL-22-induced proliferation and migration of mesenchymal stem cells (MSc) [1].
Objectives: To examine the influence of continuous mechanical load (CML) on the osteogenic behavior of MSc with or without INF-γ/TNF-α/IL-22 or testosterone exposure.
Methods: Adipose tissue-derived MCs, characterized by $CD90^+$, $CD73^+$, $CD13^+$, $CD45^-$, $CD31^-$, isolated from the adipose tissue of a healthy donor and kindly donated by Bonus BioGroup, Haifa, Israel, were cultured for two weeks without or under CML of 2 gr/cm^2, applied by transparent glass cubes placed on the plates covering the well, in the following conditions: a. osteogenic differentiation medium (ODM) with no additions of cytokines or testosterone; b. ODM with the addition of testosterone, 0.01 μM; c. ODM with the addition of INF-γ (2.5ng/ml), TNF-α (1ng/ml), and IL-22 (0.5ng/ml); d.ODM with the addition of both three cytokines above and testosterone. Real-time PCR for *ALPL, RUNX2, SPP1, BMP2,* and *Col1A1* was performed and analyzed by the ThermoFisher cloud data analysis program (https://thermofisher.com/il/en/home/digital-science/thermo-fisher-connect/all-analysis-modules.html). ΔΔCt and RQ ($2^{-\Delta\Delta CT}$) were calculated, with the results presented in a histogram graph as fold-change (Figure 1).
Results: CML induced significant upregulation of *SSP1*, or osteopontin (OPN), by MSc. However, this effect was almost completely abolished in the presence of INF-γ/TNF-α/IL-22.

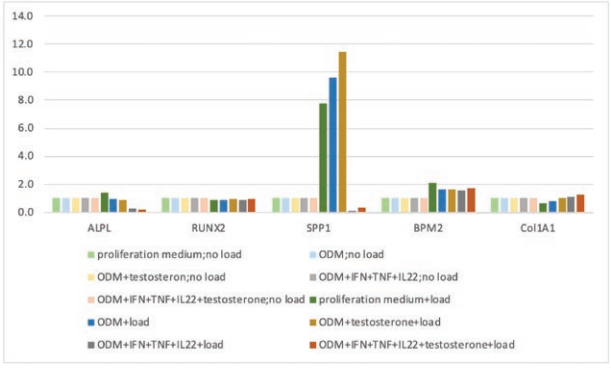


Figure 1. RQ ($2^{-\Delta\Delta CT}$) for mechanical load effect. Samples without mechanical load were used as a reference. ODM – osteogenic differentiation medium; IFN – interferon-γ; TNF – tumor necrosis factor-α; IL-22 – interleukin-22

Conclusion: Increased OPN production by MSc can link mechanical load and new bone formation after the resolution of the inflammatory phase in AxSpA.

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Acknowledgements: Genomics Center of Technion, Haifa, Israel, for performing real-time PCR tests for the study.

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POS0042 HIGH-THROUGHPUT TRANSCRIPTOMIC PROFILING OF PERIPHERAL BLOOD MONONUCLEAR CELLS IN AXIAL SPONDYLOARTHRITIS PATIENTS REVEALS CO-EXPRESSED GENE MODULES ASSOCIATED WITH RADIOGRAPHIC DAMAGE

Keywords: Genetics/Epigenetics, Biomarkers, Spondyloarthritis

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Background: The use of high throughput techniques such as transcriptomic sequencing has recently made considerable progress in the identification of molecular profiles involved in the pathogenesis of chronic autoinflammatory diseases. To date, only a few studies have been carried out in axial spondyloarthritis (axSpA), which would allow the identification of new therapeutic targets and disease biomarkers.

Objectives: 1) To identify clusters of highly correlated genes enriched in biological functions and specific molecular pathways involved in the pathogenesis of axSpA. 2) To study the association between the molecular signatures identified and the clinical-analytical profile of the disease.

Methods: Cross-sectional study including 75 axSpA patients from the CASTRO cohort who underwent an exhaustive clinical evaluation including disease activity and functional limitation, structural damage, and spinal mobility. Additionally, analytical parameters were measured and the carotid intima-media thickness was evaluated by carotid eco-doppler. Mononuclear cells were purified from peripheral blood, and RNA was isolated. RNA from 25 axSpA patients was sequenced using the Illumina platform. For the identification of patient subgroups and the generation of co-expressed gene modules, the "hierarchical clustering" and WGCNA ("Weight gene correlation network analysis") methodologies were used, respectively. Functional analysis of the genes conforming each module was carried out to identify enriched pathways and functions using the EnrichR platform. Hub genes were measured through high throughput PCR (Fluidigm Biomark HD) in a validation cohort of 50 axSpA patients. Association and correlation studies between the molecular and clinical profiles were performed. *In vitro* studies in peripheral blood mononuclear cells (PBMCs) from patients belonging to different molecular clusters were performed.

Results: Unsupervised analysis of the transcriptome revealed the presence of two "clusters" of axSpA patients, clearly differentiated by their molecular and clinical profiles. Specifically, the molecular analysis distinguished patients with longer disease duration, greater disease activity, radiographic damage, and cardiovascular risk. WGCNA identified 11 highly co-expressed modules. Among them, six were differentially expressed between the two clusters, being responsible for the molecular and clinical distinction of those groups. The functional analysis of these 6 gene modules revealed the enrichment of these genes in pathways related to inflammation, oxidative metabolism, proliferation of B and T lymphocytes, immune response, and the increase of cell survival. Finally, key genes were identified within each module ("hub genes"), whose expression was associated with a more active phenotype of the disease such as ALOX5, GAB2, PSMD13, CASP8, NOTCH e ITGA4. Hub genes were validated in an additional cohort of 50 axSpA patients and correlated with mSASSS. Treatment of PBMCs from patients belonging to the two different clusters with autologous serum induced a different expression of genes involved in cell activation and inflammation.

Conclusion: 1) The whole transcriptomic analysis by RNAseq in peripheral mononuclear cells from axSpA patients distinguished, in an unsupervised manner, subgroups of patients with distinctive clinical profiles. 2)The analysis of gene modules identified new pathways and molecular functions potentially involved in the pathophysiology of the disease. Funded by ISCIII (PMP21/00119) co-financed by ERDF, Andalusian Foundation of Rheumatology (FAR).

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0043 COMPLEMENT IN RADIOGRAPHIC AXSPA – BIOMARKERS OF RADIOGRAPHIC PROGRESSION? POST HOC ANALYSIS FROM CONSUL, A LONGITUDINAL MULTI-CENTER RANDOMIZED CONTROLLED TRIAL COHORT OF AXSPA-PATIENTS WITH A HIGH RISK OF STRUCTURAL PROGRESSION INITIATING TREATMENT WITH TNF-I

Keywords: Innate immunity, bDMARD, Spondyloarthritis

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Background: The biological processes involved in the development of structural changes associated with radiographic axial spondyloarthritis (r-axSpA) remain largely unraveled. Still, high disease activity, elevated C-reactive protein (CRP), and existing syndesmophytes are associated with radiographic progression. The complement system is an inflammation-generating part of the innate immune system. Animal models have shown inhibition of complement activation to diminish structural changes associated with axSpA [1].

Objectives: This project aimed to investigate complement activation and serum levels of complement proteins and their correlations with radiographic spinal progression over a two years follow-up period in a longitudinal cohort of axSpA patients with active r-axSpA, and high risk of radiographic progression, recruited from the randomized controlled trial CONSUL.

Methods: All patients had active r-axSpA and risk factors for radiographic spinal progression (BASDAI ≥4, and elevated CRP and/ or ≥1 syndesmophyte(s)). Serum samples were collected at baseline (n = 96) and after 108 weeks (n = 89) of TNF-I therapy and analyzed by immunoassays for complement lectin pathway proteins (L-ficolin, M-ficolin, H-ficolin, CL-L1, MBL, MASP-1, MASP-2, MASP-3, and MAp44) and the complement activation product C3dg. X-rays were performed at baseline and after 108 weeks and read blinded for clinical data and chronology by three independent expert readers. New bone formation was defined as the growth of syndesmophyte(s) and/or new syndesmophyte(s) determined by 3-reader-agreement.

Results: Patient characteristics are shown in Table 1. In total, 19 patients developed new bone formation at week 108. Baseline serum levels of MASP-1, MASP-2, and C3dg were elevated in patients with new bone formation, whereas baseline serum levels of MASP-3 were decreased (all p<0.05). Baseline MASP-1, MASP-3, and C3dg predicted the development of new bone formation in a univariate logistic regression analysis, whereas CRP did not. Baseline MASP-1, MASP-3, and C3dg remained significant in a multivariate logistic regression analysis. L-ficolin and C3dg levels at week 108 were elevated in patients with new bone formation, and the serum levels at week 108 predicted development of new bone formation in a univariate logistic regression analysis. In a multivariate regression analysis, C3dg remained significant (p<0.05).

Conclusion: In this study, complement activation measured by C3dg and serum levels of MASP-1 and MASP-3, prior to TNF-I therapy, predicted development of new bone formation at week 108. Furthermore, elevated levels of C3dg and L-ficolin at week 108 were associated with new bone formation. These findings support the involvement of complement activation in new bone formation in r-axSpA.

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Table 1. Baseline demographics of the investigated patient population from the CONSUL RCT (*n* = 96)

Age, median (IQR)	37 (31-45)
Male, n (%)	70 (73)
HLA-B27 positive, n (%)	80 (83)
Previous bDMARD treatment, n (%)	21 (22)
Symptom duration in years, median (IQR)	12 (6.0-20)
Smoking, n (%)	36 (38)
mSASSS, median (IQR)	5.0 (0.3-18)
Syndesmophytes, median (IQR)	1.8 (0-6.3)
Presence of ≥1 syndesmophyte(s)δ, n (%)	47 (49)
CRP, median (IQR)	9.2 (3.2-19)
Elevated CRP (>5 mg/L), n (%)	64 (67)
ASDAS-CRP, median (IQR)	3.6 (3.1-4.1)
BASDAI, median (IQR)	6.2 (5.2-6.8)

δDetermined by 3 expert readers blinded for clinical data.

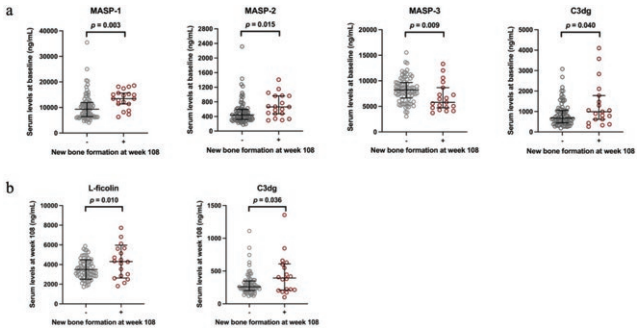


Figure 1. a) Baseline MASP-1, MASP-2, MASP-3, and C3dg levels according to development of new bone formation at week 108. **b)** L-ficolin and C3dg levels at week 108 according to development of new bone formation at week 108. New bone formation: growth of syndesmophytes and/or new syndesmophytes determined by 3-reader-agreement. *p*-values indicate comparisons between groups by t-test. Bars indicate median and IQR (MASP-1, MASP-2, MASP-3, C3dg), and mean and sd (L-ficolin).

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POS0044 EVIDENCE OF A CAUSAL RELATIONSHIP BETWEEN HYPERLIPIDEMIA AND PSORIASIS AND PSORIATIC ARTHRITIS: A MENDELIAN RANDOMIZATION STUDY

Keywords: Genetics/Epigenetics, Spondyloarthritis

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Background: Psoriatic disease (psoriasis and psoriatic arthritis) is a common inflammatory disease associated with obesity. However, recent studies suggest that lipid changes, rather than obesity, may independently drive psoriatic disease [1]. Mendelian randomization (MR) can assess the causal effect of modifiable exposure by measuring the variation of genes of known function.
Objectives: In this study, we perform a two-sample mendelian randomization to investigate the possible causal relationship between polygenic hyperlipidemia and psoriatic disease (psoriasis and psoriatic arthritis).
Methods: The study cohorts (psoriasis, psoriatic arthritis, hyperlipidemia, and controls of European ancestry) were identified from the FinnGen biobank, an academia/industry collaboration aiming to identify genotype-phenotype correlations in the Finnish founder population. Hyperlipidemia was identified by code E4_HYPERLIPNAS, which represents disorders of lipoprotein metabolism and other lipidaemias [2]. The L12_psoriasis code and psoriatic arthritis by M13_PSORIARTH code identified psoriatic arthritis. The control population was selected after excluding E4_MEABOLIA, psoriasis, and psoriatic arthritis when appropriate. Genome-wide association studies (GWAS) and summarized data were extracted from public IEU datasets. The single-nucleotide polymorphisms (SNPs) were used as instrumental variables (IV) to identify the potential causal effect. The SNP selection was performed by considering the genome-wide significance, clumping, linkage disequilibrium, and minor allele frequency. The effect alleles were harmonized for exposures and outcomes. An inverse variance weighted (IVW) model was used to estimate causality for each IV in this two-sample MR study. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for causal estimations. The MR was performed in both directions to explore the possibility of reverse causality.
Results: 4535 patients with hyperlipidemia, 4510 with psoriasis, and 1553 patients with psoriatic arthritis (PsA) were identified from the FinnGenn biobank based on their id as noted above. The control patients ranged from 147,221 to 212,242, depending on the cohort being compared. Genetic instruments comprising 5 SNPs for hyperlipidemia, 16 SNPs for psoriasis and 4 SNPs for PsA were used for this two-sample MR. A significant causal effect was noted in hyperlipidemia and psoriasis (OR 1.26 (95% CI 1.097-1.439; p < 0.00009) and hyperlipidemia and PsA (OR 1.35 (95% CI 1.08-1.68; p=0.007) but no causal effect was noted in the reverse direction with psoriasis leading to hyperlipidemia OR 1.02 (95% CI 0.977-1.07; p=0.31) and PsA leading to hyperlipidemia OR 1.03 (95% CI 0,987 to 1.08; p=0.15).
Conclusion: Our two-sample MR study genetically predicted that hyperlipidemia has a potential causal association with psoriatic disease, which leads to a higher risk of psoriasis and PsA. Further validation and molecular studies are required to understand this relationship. If these results were to be validated, targeted reduction of hyperlipidemia may help modify the expression of psoriatic disease.
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Acknowledgements: NIL.

Disclosure of Interests: Quan Li: None declared, Amanda Dohey: None declared, Dianne Codner: None declared, Proton Rahman Speakers bureau: Abbott, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, and Pfizer, Consultant of: Abbott, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, and Pfizer, Grant/research support from: Janssen and Novartis.

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POS0045 CHILDHOOD INFECTIONS AND PERINATAL FACTORS AS RISK FACTORS FOR ANKYLOSING SPONDYLITIS – RESULTS FROM A NATIONWIDE CASE-CONTROL STUDY

Keywords: Spondyloarthritis, Epidemiology, Registries

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Background: A growing body of evidence suggests that there are associations between perinatal factors or early life exposures and later development of chronic inflammatory diseases. For ankylosing spondylitis (AS), previous studies have found increased risks associated with birth order and childhood respiratory tract infections, while breast-feeding and childhood appendicitis have been found protective.
Objectives: To identify early life risk factors for AS, with focus on perinatal characteristics and childhood infections.
Methods: People with AS from the Swedish National Patient Register, born 1973-2004, were matched 1:5 on age, sex, and place of residence to general population controls. Conditional logistic regression was used to compare odds ratios for AS in relation to potential risk factors identified in the Medical Birth Register and the National Patient Register.
Results: People with AS (n=5427) had significantly more hospitalizations for infections before age 16 compared to controls (n=21523), and had more often gone through a tonsillectomy (table 1). People with AS were also more likely to be born in the winter months, and to have an older sibling, while having a sibling overall (older or younger) resulted in an odds ratio for AS of 1.01 (0.93-1.11). No association was seen with factors such as maternal age, Caesarean delivery, or a 1 SD change in weight for gestational age (table 1). Odds ratios for AS associated with being born small or large for gestational age (>2 SD below or above sex-specific mean weight) was 1.10 (0.93-1.30) and 0.89 (0.74-1.08), respectively. In line with previous data, childhood appendectomy was associated with an odds ratio <1, but the estimate did not reach statistical significance.

Table 1. Perinatal factors and childhood infections in people with AS and general population controls, with odds ratios from conditional logistic regression

	AS cases* (n=5472)	Controls* (n=21523)	OR (95% CI)	Adj. OR† (95% CI)
Maternal age, years	27.4 (5.0)	27.4 (5.1)	1.00 (0.99-1.00)	1.00 (0.99-1.00)
Smoking, early pregnancy	669 (12.2)	2683 (12.5)	1.00 (0.90-1.11)	1.01 (0.90-1.13)
Maternal BMI	22.6 (3.3)	22.8 (3.6)	1.00 (0.98-1.01)	1.00 (0.98-1.01)
Weight for gestational age, SDs	-0.10 (1.12)	-0.10 (1.10)	1.01 (0.98-1.03)	1.01 (0.98-1.04)
Caesarean delivery	604 (11.0)	2253 (10.5)	1.07 (0.97-1.18)	1.07 (0.97-1.18)
No. of older siblings				
0	2110 (38.6)	8897 (41.3)	Ref	Ref
1	2121 (38.8)	7872 (36.6)	1.14 (1.06-1.22)	1.17 (1.09-1.26)
≥2	1241 (22.7)	4754 (22.1)	1.11 (1.03-1.20)	1.19 (1.09-1.31)
Season of birth				
Dec-Feb	1361 (24.9)	5039 (23.4)	Ref	Ref
March-May	1573 (28.7)	5985 (27.8)	0.97 (0.89-1.05)	0.97 (0.89-1.05)
June-Aug	1349 (24.7)	5461 (25.4)	0.91 (0.84-0.99)	0.91 (0.84-0.99)
Sep-Nov	1189 (21.7)	5038 (23.4)	0.87 (0.79-0.95)	0.87 (0.80-0.95)
Serious infection‡	1362 (25.0)	4898 (22.8)	1.12 (1.05-1.21)	1.12 (1.05-1.21)
Tonsillectomy‡	272 (5.0)	840 (3.9)	1.28 (1.11-1.48)	1.28 (1.11-1.48)
Appendectomy‡	123 (2.3)	566 (2.6)	0.86 (0.70-1.05)	0.86 (0.70-1.05)

* Numbers are n (%) or mean (SD). † Adjusted for maternal age, maternal BMI, maternal smoking, parents born in Nordic country, maternal disposable income, maternal educational level, maternal inflammatory disease (hospitalization for spondyloarthritis, inflammatory bowel disease, or psoriasis), sex of child, and multiple birth. ‡ Before age 16, with people diagnosed with AS before age 16 excluded.

Conclusion: Childhood exposures related to infections seem to play a role in later development of AS, while factors generally associated with foetal growth do not.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0046 AUTOINFLAMMATORY GENETIC VARIANTS ARE OVER-REPRESENTED IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS COMPARED TO RHEUMATOID ARTHRITIS AND PSORIASIS

Keywords: Spondyloarthritis, Innate immunity, Genetics/Epigenetics

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Background: Ankylosing Spondylitis (AS) and psoriatic arthritis (PsA) are chronic inflammatory diseases of undetermined etiology. Both entities exhibit features of autoimmunity (exhibited by clonal expansion of T cell populations) and autoinflammation, as noted by the aberrant activity of innate and innate-like cells [1].

Objectives: In this study, we screen for genetic variants associated with known autoinflammatory disease in patients with AS, PsA, and compare it to rheumatoid arthritis (RA) and psoriasis (Ps).

Methods: The UK genome biobank identified exomes of AS, PsA, RA, and Ps patients. Autoinflammatory genes were selected from the blueprint autoinflammatory syndrome panel [2]. Twenty thousand nine hundred five missense mutations were identified from the 47 autoinflammatory genes in the blueprint panel and screened in these four cohorts. Mutational burden, mutation number, and mutation rate in these 47 genes were calculated.

Results: Exonic mutations of 1264 in AS, 886 in PsA, 5361 in RA and 5567 in Ps patients from the UK biobank were enrolled and analyzed in this study. The number of autoinflammatory variants identified was 937 in AS, 780 in PsA, 2081 in RA and 2015 in Ps. The average mutation rate in 47 genes is around 0.26 for these four diseases. The autoinflammatory panel's average mutation burden was not significantly different between these diseases (116 in AS and PsA, 118 in RA and Ps). However, when we accounted for the number of individuals screened, AS and PsA had a higher mean number of autoinflammatory variants than RA and Ps. Specifically, AS and PsA patients had a mean number of 0.741 and 0.880 variants per individual, respectively, compared to 0.388 and 0.362 for RA and Ps, respectively.

Conclusion: This study strengths the role of autoinflammation in AS and PsA as we report an overabundance of autoinflammatory variants in AS and PsA compared to RA and psoriasis. Consideration of autoinflammatory etiology may impact current diagnostic and therapeutic approaches.

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Table 1. Autoinflammatory variants in AS, PsA, RA and Ps

Disease	No. of Patients	No. of Autoinflammatory Variants	Average No. of Autoinflammatory Variants per patient
AS	1264	937	0.741
PsA	886	780	0.880
RA	5361	2081	0.388
Ps	5567	2015	0.362

Acknowledgements: NIL.

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POS0047 THE COMPLEMENT FACTOR H-RELATED PROTEIN-5 EXACERBATES PATHOLOGICAL BONE FORMATION OF ANKYLOSING SPONDYLITIS

Keywords: Spondyloarthritis, Animal Models

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Background: The complement factor H-related protein-5 (FHR-5), a member of the human factor H protein family, enhances complement activation. The influence of complement activation on bone and joint was recognized in bone fracture healing, arthritis, and osteomyelitis. Recently, FHR-5 has been linked to eye, kidney, infection, cancer and autoimmune diseases. FHR-5 was also significantly up-regulated in proteomic analysis of serum and synovial fluid for ankylosing spondylitis (AS).

Objectives: We aimed to evaluate whether FHR-5 exacerbates bone inflammation and ectopic formation of AS.

Methods: The study included 65 patients with AS and 25 healthy controls (HC). Collected sera were divided into three groups according to HC, two AS groups (low CRP and high CRP) based on the CRP 0.8. Human TNF, IL6, IL-17, IL-23, and FHR-5 in three groups were measured with ELISA and human FHR-5 levels were compared to TNF, IL-6, IL-17, and IL-23 levels. In addition, soluble FHR-5 proteins were administered with Curdlan-injected SKG mice 2 time for a week and monitored for 5 weeks *In vivo* model. Foot and ankle were evaluated by micro-CT, Hematoxylin and Eosin for histological observation, and Safranin O for cartilages. Moreover, these finding were further assessed in the AS-osteoprogenitor *In vitro* model.

Results: In consistent with human data, proinflammatory cytokines (TNF, IL-6, IL-17A, and IL-23) and CFHR5 were elevated in AS group compared to HC group. FHR5 levels were not significantly correlated with proinflammatory cytokines, whereas FHR5 levels in AS were only positively correlated with the high CRP group. Notably, treatment with soluble FHR5 has no effect on clinical arthritis scores and thickness at hindpaw in Curdlan-injected SKG, but significantly increased the ectopic bone formation at the calcaneus and tibia bones of ankle as revealed by micro-CT image and quantification. Basal FHR5 expression was upregulated in AS-osteoprogenitors compared to control cells. Also, treatment with FHR5 remarkedly induced bone mineralization status of AS-osteoprogenitors during osteogenic differentiation accompanied by MMP13 expression.

Conclusion: We provide the first evidence demonstrating that FHR-5 can exacerbate pathological bone formation of AS. Therapeutic modulation of FHR-5 could be promising for future treatment of AS.

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Disclosure of Interests: None Declared.

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POS0048 LIPOPOLYSACCHARIDE ACTIVATED ENTHESEAL MYELOID CELL INHIBITION WITH UPADACITINIB PARADOXICALLY INCREASES MYELOID PRO-INFLAMMATORY CYTOKINES INCLUDING TNF AND IL-23 BY RESTRAINING AN IL-10 NEGATIVE FEEDBACK-BUT T-CELL TNFA AND IL-17 IS STRONGLY BLOCKED

Keywords: Enthesitis, Cytokines and chemokines, Targeted synthetic drugs

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Background: Upadacitinib is effective in spondyloarthritis (SpA) associated arthropathy and is licensed for ankylosing spondylitis and psoriatic arthritis. Collectively SpA is linked to enthesitis with both myeloid lineage and T-lineage cells contributing to the IL-23/IL-17 and TNF axes that underscore disease.
Objectives: To investigate the effect of upadacitinib on an in vitro human enthesis model by focusing separately on the IL-23/IL-17 axis component myeloid and T-cells to better elucidate mechanisms of action in vivo.
Methods: Normal spinous process enthesis (n=26) was obtained from patients undergoing spinal decompression or surgery for scoliosis correction as previously described [1]. Enthesis cells were subsequently isolated by mechanical digestion. Entheseal myeloid cells were stimulated with LPS with and without upadacitinib. IL-23, TNFα and other proinflammatory cytokines in the supernatants were quantified using ELISA. IL-23 levels were measured after myeloid cell stimulation with LPS in the presence of upadacitinib and IL-10. IL-23 levels were also measured after stimulation with LPS in the presence of an IL-10Rα blocking antibody. Entheseal cells were stimulated with anti-CD3 with or without LPS, Th17-driving cytokines (IL-23 and IL-1β) and upadacitinib. Supernatants were measured by ELISA and cytokine-positive cell populations assessed by intracellular flow cytometry.
Results: Unexpectedly, upadacitinib significantly increased myeloid cell secretion of IL-23, TNFα and other proinflammatory cytokines after stimulation with LPS (Figure 1) (LPS = 51.2 pg/ml vs LPS + 1 μM Upa = 1048 pg/ml IL-23, n= 11). Addition of recombinant IL-10 attenuated such IL-23. Blockade of the IL-10 receptor with a blocking antibody increased IL-23 secretion from myeloid cells after stimulation with LPS (100 ng/ml IL-10 = 2.79 mean fold increase in IL-23, n=5). Despite this effect, upadacitinib strongly blocked TNFα and IL-17 from Th17 and Tc17 entheseal derived cells stimulated with exogenous IL-23 (138.19 pg/ml vs 14.2 pg/ml IL-17A after addition of 1 μM Upa to Th17 driving conditions, n = 5). Furthermore, addition of upadacitinib to LPS + anti-CD3 activated entheseal cells strongly downregulated T-cell derived IL-17 and TNFα despite a simultaneous increase in myeloid IL-23.
Conclusion: LPS activated myeloid cells, predominantly monocyte lineage further increase key cytokines IL-23 and TNFα post upadacitinib. This involves IL-10 pathway inhibition. However, in this system T-cell derived cytokine production is completely blocked despite elevation of myeloid IL-23 and TNFα. These unexpected findings highlight the pivotal role of T-cell derived cytokines in SpA given the known efficacy of JAK inhibition and these findings merit consideration in other domains such as intestinal inflammation that may have a greater innate immune driven component.
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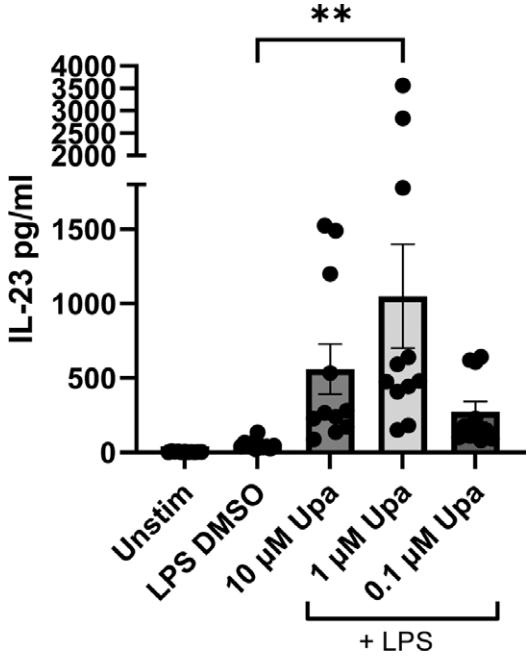


Figure 1. Upadacitinib exacerbates LPS-induced IL-23

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Tapering, drug retention and predictors of response

POS0049

CLINICAL AND RADIOGRAPHIC RESULTS OF TAPERING AND WITHDRAWING CSDMARDS VERSUS STABLE TREATMENT IN RHEUMATOID ARTHRITIS REMISSION: 3-YEAR RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

Keywords: Tapering, Remission, Randomized control trial

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Background: Tapering of disease modifying antirheumatic drugs (DMARDs) to achieve drug-free remission is a goal for the growing group of rheumatoid arthritis (RA) patients in remission. However, the long-term effects of tapering or withdrawal of DMARDs remain unclear.
Objectives: To compare the 3-year clinical and radiographic outcomes of three conventional synthetic DMARD (csDMARD) treatment strategies (continued stable treatment, half-dose treatment and tapering to withdrawal) among patients in sustained RA remission.
Methods: ARCTIC REWIND was a randomized, multicenter, open-label, clinical trial enrolling 160 RA patients in sustained remission for ≥1 year on stable csDMARD therapy from 10 different Norwegian rheumatology departments.(1) At baseline, patients were randomized 2:1:1 to stable csDMARDs, half-dose csDMARDs, or half-dose csDMARDs for one year, followed by withdrawal of all csDMARDs ("tapering to withdrawal"). The primary endpoint was absence of disease activity flare over the 3-year study period. A flare was defined as a combination of disease activity score (DAS)>1.6, an increase in DAS ≥0.6 units since the previous visit and ≥2 swollen joints, or if the physician and patient agreed that a clinically significant flare had occurred. Full-dose csDMARD treatment was reinstated upon flare. Secondary endpoints included remission (DAS, ACR/EULAR Boolean) at 1, 2 and 3 years, and 3-year change in radiographic joint damage evaluated by van der Heijde-Sharp score (vdHSS). Data were analyzed using Kaplan-Meier, Mann-Whitney test, Cox and mixed effect logistic regression, with stratification or adjustment for study center.
Results: Of 156 patients who received the allocated treatment strategy, 139 patients completed 3-years follow-up without major protocol violation. Mean baseline methotrexate dose/week was 19.0 mg in the stable group, 19.4 mg in half-dose, and 19.5 mg in the withdrawal group, and mean DAS at baseline was 0.8 in all groups. During the 3-year study period, 80.1% remained flare-free in the stable csDMARD group, 59.5% in the half-dose and 40.8% in the withdrawal group (**Figure 1**), with corresponding adjusted hazard ratio (aHR) for flare of 2.7 (95% CI: 1.3 to 5.5) in the half-dose group and 4.1 (2.1 to 8.0) in the withdrawal group, compared to stable csDMARD. The aHR was 1.5 (0.8 to 3.0) in the withdrawal group compared to the half-dose group. For all groups, a majority were in remission at 1, 2 and 3 years **(Table 1)**, with the only significant group difference for ACR/EULAR Boolean remission at 3 years, with risk difference for withdrawal vs stable dose -25% (-45 to -6). Mean/median change in vdHSS after 3 years were 0.3/0.0 in the

stable group, 1.0/0.5 in the half-dose group, and 0.7/0.0 in the tapering to withdrawal group, with significant difference between the stable and half-dose group, p<0.01. Sensitivity analyses in the full analysis population gave similar results.
Conclusion: These 3-year data show that 41% of patients in the tapering to withdrawal arm achieved long-term drug-free remission, indicating that this is a realistic option for some RA patients in sustained remission. The two tapering strategies were associated with an increased risk of flares compared to full-dose csDMARD, and the half-dose group had more radiographic change. However, there were no differences in DAS-remission at the end of the study period. Further research identifying prognostic factors for successful tapering is needed.
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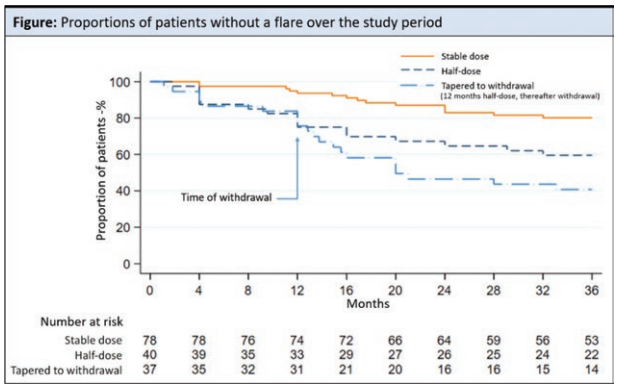


Table 1. Remission at 12, 24 and 36 months

	Stable dose	Half-dose	Tapered to withdrawal*
DAS remission			
12 months	71/77 (92%)	34/39 (87%)	29/36 (81%)
24 months	64/73 (88%)	33/37 (89%)	33/35 (94%)
36 months	64/67 (96%)	34/36 (94%)	31/34 (91%)
ACR/EULAR 2011 Boolean remission			
12 months	56/77 (73%)	25/39 (64%)	22/36 (61%)
24 months	47/73 (64%)	21/37 (57%)	20/35 (57%)
36 months	55/67 (82%)	25/36 (69%)	19/34 (56%)

*12 months half-dose, thereafter withdrawal

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POS0050 TAPERING GLUCOCORTICOIDS AND RISK OF FLARE IN RHEUMATOID ARTHRITIS ON BIOLOGICAL DISEASE MODIFYING ANTIRHEUMATIC DRUGS (bDMARDS)

Keywords: Real-world evidence, Tapering, Rheumatoid arthritis

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Background: Glucocorticoids are still a mainstream of rheumatoid arthritis (RA) treatment. Reducing glucocorticoids should be attempted in all patients. However, choosing the right tapering strategy is challenging.
Objectives: The primary aim of our study is to determine the dose-response association between glucocorticoid tapering and risk of flare in RA.
Methods: We conducted a case-crossover study to determine the factors associated to higher risk of flare in patients with RA. In case-crossover studies time-varying factors are assessed before events (hazard periods) and before control periods. We defined hazard periods as the 6 months immediately preceding flares of RA. Control periods were the 6 months prior to visits without flare. Exposure of interest was the tapering of glucocorticoids to various doses. The time-variant independent variable of interest (exposure) was the tapering of glucocorticoids during the hazard periods vs control periods. Tapering of glucocorticoids was defined as the reduction of glucocorticoids dose from prior visit. Conditional logistic regression analysis was employed to determine the association between tapering of glucocorticoids with flare risk. We adjusted, as per case-crossover design, for relevant time-varying confounders (i.e., bDMARD use, csDMARD use, NSAID use and disease activity).
Results: 508 RA patients were included in the study and 267 (52.5%) had at least a flare and served as the case-crossover study population. 1,545 visits were available for analysis and 345 (22.3%) flares were recorded. Tapering of glucocorticoids was done in 176 (81.5% of 216) patients and discontinuation was attained, at least once, in 125 (57.8% of 216) patients. Definitive discontinuation was achieved in 101 patients (46.7%) at a median follow-up of 884 days (IQR 700-976 days). Discontinuation of glucocorticoids (i.e., tapering to doses of 0 mg/day) and tapering to 0-2.5 mg/day was associated with higher risk of flare (aOR of 1.45 [95% CI 1.13-2.24] and aOR of 1.37 [95% CI 1.06-2.01] respectively). Tapering to doses >2.5 mg/day was not associated with significantly higher risk of flare. In **figure 1** is depicted the smoothed line for dose-response association between glucocorticoid tapering and risk of flare. Apparently, tapering the doses to >2.5 mg/day did not result in an increased risk of flare.
Conclusion: We found that tapering to doses of >2.5 mg/day was generally effective in terms of risk of flare. Flare risk was higher when glucocorticoids were tapered to doses ≤2.5 mg/day. Our study might help design new tapering strategies in patients with RA on bDMARDs.

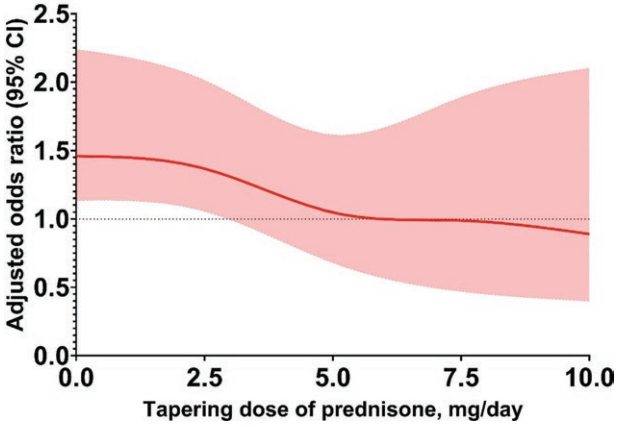


Figure 1. Dose-response association between tapering of glucocorticoids and risk of flare *The curve was interpolated using the conditional logistic regression model. The curve was smoothed with restricted cubic splines with knots at 0-2.5 mg/day, 2.5-5 mg/day, 5-7.5 mg/day and ≥7.5 mg/day. The reference was not tapering.*

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Giovanni Adami Speakers bureau: Theramex, Eli-Lilly, BMS, Amgen, UCB, Fresenius Kabi, Galapagos, Angelo Fassio: None declared, Davide Gatti: None declared, Camilla Benini: None declared, Ombretta Viapiana: None declared, Davide Bertelle: None declared, Maurizio Rossini: None declared.
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POS0051 DRUG RETENTION AND REASONS FOR DISCONTINUATION OF BIOLOGICS AND JAK INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS – THE ANSWER COHORT STUDY

Keywords: Disease-modifying Drugs (DMARDs), Rheumatoid arthritis, Real-world evidence

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Background: 2022 EULAR recommendation announced that both biological disease-modifying antirheumatic drugs (bDMARDs) and janus kinase inhibitors (JAKi) are considered in the phase II treatment of rheumatoid arthritis (RA). However, we still lack reliable evidence of direct comparison between these agents' retention, which may reflect effectiveness and safety.

Objectives: The aim of this multi-center (7 university-related hospitals)[1]-[3], retrospective study is to clarify the factors affecting treatment retention of bDMARDs and JAKi in a real-world setting.

Methods: This study assessed 6,666 treatment courses of bDMARDs and JAKi introduced from 2001 to 2022 (TNF inhibitors [TNFi]=3,577, anti-IL-6 receptor antibody [aIL-6R]=1,497, cytotoxic T lymphocyte-associated antigen-4-Ig [CTLA4-Ig]=1,139, JAKi=453; Bio/JAK naive cases 55.4%, baseline age 58.8 years, female 82.6%, disease duration 9.7 years, DAS28-ESR 4.3, concomitant methotrexate [MTX] [52.8%], other csDMARDs [26.0%], and oral glucocorticoid [GC] [36.4%]). Reasons for discontinuation were classified into four categories by each attending physician: 1) lack of effectiveness (primary and secondary), 2) toxic adverse events (infection, malignancies, and cardiovascular events, et al.), 3) non-toxic reasons (patient preference, change in hospital, and pregnancy, et al.), and 4) remission. Retention rates of each discontinuation reason were estimated at 36 months using the Kaplan-Meier method and adjusted for potential clinical confounders (age, sex, concomitant GC, MTX, and other csDMARDs, switched number of bDMARDs or JAKi, and prior use of TNFi, aIL-6R, CTLA4-Ig, or JAKi) using Cox proportional hazards modeling.

Results: Adjusted retention rates for each discontinuation reason were as follows: due to lack of effectiveness was aIL-6R=80.9%, JAKi=75.2%, CTLA4-Ig=73.6%, and TNFi=66.1% (Cox P<0.001 between 4 groups) (figure 1a), due to toxic adverse events was CTLA4-Ig=88.0%, JAKi=86.4%, aIL-6R=84.1%, and TNFi=83.6% (Cox P=0.052) (figure 1b), due to non-toxic reasons was aIL-6R=86.9%, TNFi=85.9%, JAKi=85.9%, and CTLA4-Ig=82.6% (Cox P=0.064), and due to remission was JAKi=97.1%, CTLA4-Ig=96.7%, aIL-6R=96.0%, and TNFi=94.9% (Cox P=0.18). Compared to TNFi, aIL-6R (hazard ratio [HR]=0.54, 95%CI=0.47–0.61, P<0.001), JAKi (HR=0.69, 95%CI=0.56–0.85, P<0.001), and CTLA4-Ig (HR=0.75, 95%CI=0.66–0.86, P<0.001) showed lower discontinuation rate due to lack of effectiveness. Compared to TNFi, CTLA4-Ig showed lower discontinuation rate due to toxic adverse events (HR=0.77, 95%CI=0.63–0.93, P=0.008) and remission (HR=0.67, 95%CI=0.46–0.98, P=0.041). Other factors increasing drug discontinuation due to lack of effectiveness was switched number of bDMARDs or JAKi (HR=1.42, 95%CI=1.24–1.63, P<0.001), concomitant GC (HR=1.17, 95%CI=1.06–1.29, P=0.0018), and prior aIL-6R use (HR=1.24, 95%CI=1.05–1.45, P=0.011). On the other hand, higher age (HR=1.01, 95%CI=1.00–1.02, P<0.001) and concomitant GC (HR=1.29, 95%CI=0.47–0.61, P<0.001) increased drug discontinuation due to toxic adverse events.

Conclusion: Adjusted by potential confounders, aIL-6R showed lowest discontinuation due to lack of effectiveness, and CTLA4-Ig showed lowest discontinuation due to toxic adverse events. Besides the difference of bDMARDs and JAKi, concomitant GC increased drug discontinuation due to lack of effectiveness and toxic adverse events.

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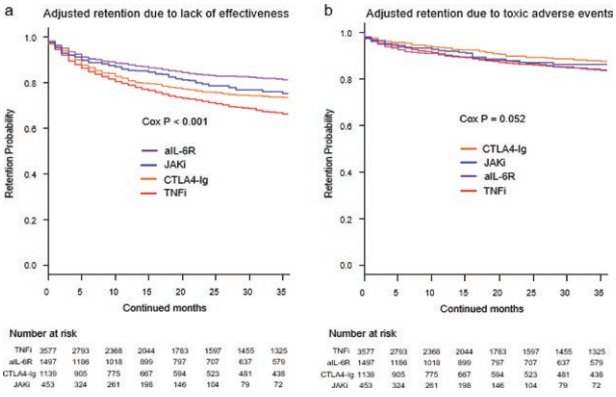


Figure 1.

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POS0052

FIVE-YEAR FOLLOW-UP OF A 2-YEAR MRI TREAT-TO-TARGET STRATEGY ON RADIOGRAPHIC DAMAGE PROGRESSION IN RHEUMATOID ARTHRITIS PATIENTS IN CLINICAL REMISSION - THE IMAGINE-MORE STUDY

Keywords: Imaging, Rheumatoid arthritis, Treat to target

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Background: Radiographic joint damage progresses in 20-30% of rheumatoid arthritis (RA) patients despite fulfilling clinical remission criteria [1]. Osteitis assessed on MRI predicts subsequent bone damage progression [2]. Therefore, targeting absence of osteitis combined with clinical remission may improve long-term radiographic outcomes.

Objectives: To investigate whether a 2-year MRI treat-to-target (MRI T2T) strategy targeting absence of osteitis combined with clinical remission, compared to a conventional T2T strategy targeting clinical remission only, could reduce radiographic joint damage progression over 5 years in RA patients.

Methods: IMAGINE-more was designed as a three-year observational extension study of the 2-year IMAGINE-RA randomized clinical trial [3]. IMAGINE-RA included 200 RA patients in clinical remission (DAS28-CRP<3.2 and no swollen joints), with erosive disease (bone erosion on conventional radiography), and treated with csDMARDs. The objective was to investigate whether an MRI T2T strategy targeting absence of osteitis combined with clinical remission (DAS28-CRP≤3.2 and no swollen joints) as compared to a conventional T2T strategy, targeting clinical remission only, could improve remission rates and prevent radiographic joint damage progression. If treatment target was not met, treatment was intensified stepwise starting with increment in csDMARDs and subsequently adding biologics. Participants in the IMAGINE-more study were managed in routine clinical practice in outpatient clinics. Clinical examinations and radiographs of hands and feet (also obtained at baseline, year 1 and 2 in IMAGINE-RA) were done year 3, 4 and 5. The primary endpoint was the proportion of patients with no radiographic progression (increase in total van der Heijde-modified Sharp score (vdHSS) ≤0) from baseline to year 5. Secondary endpoints were 0-5 years changes in total vdHSS, vdHSS erosion and joint space narrowing (JSN) scores. Dichotomous endpoints were estimated by logistic regression, while median differences were calculated for the continuous outcome measures.

Results: Informed consent to participation in IMAGINE-more was obtained from 131 patients (59 from the original MRI T2T group). Of these, 14 patients (24%) in the MRI T2T group and 19 patients (26%) in the conventional T2T group had no radiographic progression from baseline to year 5 (OR 0.70 [0.28 to 1.71]). As illustrated in the Table 1 and Figure 1, the median progression in total vdHSS from baseline to 5 years was low, with no differences between treatment groups.

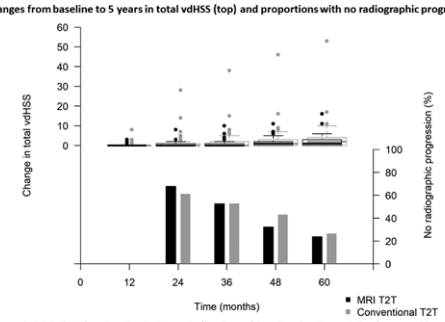
Table 1. Radiographic endpoints at 5 years (change from baseline - year 0)*

	n	MRI T2T	n	Conventional T2T	Difference between groups	P value
Primary endpoint						
No radiographic progression, No. (%)	59	14 (24%)	72	19 (26%)	OR=0.70 (0.28 to 1.71)	0.431
Key secondary endpoint						
Change in total vdHSS (0-448)	47	1.0 [0.0-3.0]	56	2.0 [0.0-4.0]	0.0 (-1.0 to 0.0)	0.515
Other secondary endpoints						
Change in erosion (0-280)	47	1.0 [0.0-2.0]	56	1.0 [0.0-3.0]	0.0 (0.0 to 0.0)	0.967
Change in JSN (0-168)	47	0.0 [0.0-0.5]	56	0.0 [0.0-1.3]	0.0 (0.0 to 0.0)	0.565

Group contrasts are presented as No. (%) for dichotomous data and medians [IQR] for continuous data. OR (95%CI) were estimated from logistic regression adjusted for a propensity score and with non-responder imputation. For endpoints with continuous data median differences (95%CI) were calculated based on the ITT population (no manual imputation)

*In addition to the radiographic endpoints, the full IMAGINE-more study includes a clinical co-primary endpoint, and several secondary endpoints.

Figure: Changes from baseline to 5 years in total vdHSS (top) and proportions with no radiographic progression (bottom)



Illustrates the change in total vdHSS from baseline to 60 months (i.e., 5 years) based on the ITT population (no manual imputation done), as well as the proportions with no radiographic progression (delta total vdHSS<0) in each group from baseline to 60 months, with non-responder imputation.

Conclusion: A 2-year combined MRI T2T and clinical T2T strategy, compared with a conventional clinical T2T strategy alone, did not result in reduced radiographic progression in the long term over 5 years in RA patients with erosive disease in clinical remission.

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Disclosure of Interests: Signe Møller-Bisgaard Grant/research support from: Study support from AbbVie, Kim Hørslev-Petersen: None declared, Lykke Midtbøll Ørnbjerg: None declared, Bo Ejbjerg: None declared, Merete Lund Hetland: None declared, Jakob Møllenbach Møller: None declared, Robin Christensen: None declared, Sabrina Mai Nielsen: None declared, Daniel Glinatsi: None declared, Mikael Boesen Shareholder of: Minority shareholder in Image Analysis Group LTD, London UK, Speakers bureau: AbbVie, Celgene, Eli Lilly, Image Analysis Group, Novartis, Pfizer, UCB and Esaote, Paid instructor for: Novartis and Eli Lilly, Consultant of: Novartis, Grant/research support from: AbbVie, Celgene, Novo Nordisk and Novartis, Kristian Stengaard-Pedersen Consultant of: Pfizer, AbbVie, Grant/research support from: Roche, Pfizer, AbbVie and Medoc., Ole Madsen: None declared, Bente Jensen: None declared, Jan Alexander Villadsen: None declared, Ellen Margrethe Hauge Shareholder of: Novartis, AbbVie, Sanofi, Sobi, Grant/research support from: esearch funding to Aarhus University Hospital from Novo Nordic Foundation, Danish Rheumatism Association, Danish Regions Medicine Grants, Roche, Novartis, AbbVie, Oliver Hendricks Speakers bureau: Pfizer, Lilly, Novartis, Hanne Merete Lindegaard: None declared, Niels Steen Krogh: None declared, Anne Grethe Jurik: None declared, Henrik Thomsen: None declared, Mikkel Østergaard Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Galapagos, Gilead, Hospira, Janssen, MEDAC, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Grant/research support from: Abbvie, BMS, Merck, Novartis and UCB.

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POS0053

EARLY DIAGNOSIS, PROMPT INITIATION OF METHOTREXATE AND TREATMENT STEERED-TO-TARGET DO NOT ABROGATE THE RISK OF BEING MULTIDRUG REFRACTORY FOR PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Disease-modifying Drugs (DMARDs), Rheumatoid arthritis, Prognostic factors

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Background: The management of rheumatoid arthritis (RA) has substantially improved during the last few decades; despite that, a significant proportion of patients remain refractory to conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), as well as to one or more biologic/target-synthetic (b/ts) DMARDs. It is estimated the overall proportion of refractory RA is around 3-17%. Refractory disease has been defined among patients with established, long-standing, RA. However, at present time, it is not known whether early diagnosis, prompt institution of DMARD within the window of opportunity and treatment steered-to-target are efficacious to prevent multidrug failure in patients with new-diagnosed RA.

Objectives: First, to assess if an Early Arthritis Clinic (EAC) background – early diagnosis and treatment within the "window of opportunity", disease management according to treat-to-target (T2) strategy – reduces the risk of being DMARDs refractory; secondly, to detect possible predictors of refractoriness in patients escalated to b/tsDMARDs.

Methods: Data were retrieved from a prospective monocentric cohort of 810 patients with early RA (symptoms duration <12 months at inclusion) diagnosed between 2005-2017 and treated with csDMARDs (methotrexate in 90.4% of the cases) according to a T2T strategy in the setting of an EAC. The population of interest included all patients escalated to b/tsDMARDs because of inefficacy/intolerance to csDMARDs. The frequency and factors associated with failure to first and second b/tsDMARDs were analysed by logistic regression.

Results: A total of 135/816 (16.5%) early RA patients required treatment escalation to a b/tsDMARDs after a median (IQR) of 18.5 (11-39) months from diagnosis; of them, 117 had follow-up visits available for a median (IQR) of 96 (37-122.5) months after treatment initiation. Fifty-six patients (50.4%) failed the first b/tsDMARD after a median (IQR) of 14 (7.3-44.3) months due to inefficacy/side effects. The rates of failure of the second and third b/tsDMARD were 20.5% and 19.7%. Thirteen patients (11.1%) could be defined D2T, having failed a median (IQR) number of 2 (2-3) b/tsDMARDs with different mechanisms of action, and 3 (2.8-4) different b/tsDMARDs in general. By logistic regression, significant predictors of first b/tsDMARD failure were disease duration ≤24 months

and autoantibody-negativity (respectively HR 1.89, 1.01-4.12, p=0.03; HR 1.66, 1.00-3.15, p=0.04). The latter confirms to be a significant predictor of second b/tsDMARD failure as well (HR 2.13, 1.08-4.17, p=0.03). At univariable analysis, significant predictors of D2T were concomitant diagnosis of fibromyalgia, autoantibody-negative status and lower doses of methotrexate. At bivariate logistic regression, fibromyalgia and autoantibody-negative RA maintained independent association with adjusted ORs (95% CI) of 3.6 (1.02-16.4) and 4.3 (1.01-24.1), respectively.

Conclusion: Early diagnosis, prompt initiation of methotrexate and management according to T2T strategy have substantially improved RA outcomes, and only about 16% of patients require escalation to second-line therapies. However, in those refractory to csDMARD, EAC setting seems not to ameliorate treatment persistence, as retention rates of b/tsDMARDs are similar to those observed in established disease. Early methotrexate inefficacy and autoantibody-negative disease appear to be predictive of first b/tsDMARD failure; moreover, patients with autoantibody-negative disease maintain a higher risk of failure of subsequent lines of therapies. Collectively, our findings suggest the need for a more tailored approach to refractory RA patients, especially to autoantibody-negative ones.

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Disclosure of Interests: None Declared.

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POS0054 SOCIOECONOMIC DEPRIVATION IS ASSOCIATED WITH REDUCED RESPONSE AND LOWER TREATMENT PERSISTENCE WITH ANTI-TNF THERAPIES IN PEOPLE WITH RHEUMATOID ARTHRITIS

Keywords: Epidemiology, bDMARD, Rheumatoid arthritis

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Background: Recent global health crises have highlighted the importance of socioeconomic (SE) inequalities and its influence on health provision and outcomes. The impact of SE deprivation on treatment of rheumatoid arthritis (RA) is understudied in contemporary biologic-treated populations.

Objectives: To investigate the association between SE deprivation and outcomes of TNF inhibitor (TNFi) treatment.

Methods: Individuals commencing their first TNFi in the BSR Biologics Register for RA from 2001 to 2020 were included. SE deprivation was proxied using the Index of Multiple Deprivation (IMD), which measures relative deprivation of geographic areas. Using the participants' residential postcode, each individual was assigned a relative rank score and categorised into the 20% most deprived, middle 40%, and 40% least deprived; thresholds were chosen because IMD gives greater distinction within the most deprived areas. DAS28, low disease activity (LDA) and EULAR response at 6 months were compared using linear, logistic and ordinal logistic regression models with the 40% least deprived as referent. Risk of drug discontinuation was compared using Cox models. Models were first unadjusted, then adjusted for potential confounders and/or mediators, namely age, gender, baseline DAS28, BMI, HAQ, number of comorbidities, age at diagnosis, ever smoking status and rheumatoid factor status. Multiple imputation was used for missing data.

Results: 17,117 individuals were included (mean age 56 (SD12) years, 76% female), of whom 3002 (18%) were in the 20% most, 6999 (41%) in the middle 40%, and 7116 (41%) in the 40% least deprived groups (Table 1). The 20% most deprived group had higher DAS28 at 6 months (beta=0.30, 95%CI 0.22-0.37) and were less likely to achieve LDA (OR 0.76; 0.68-0.84) and EULAR response (OR 0.73; 0.67-0.80) in unadjusted models. They were also more likely to discontinue treatment (HR 1.19; 1.13-1.25). Adjusted estimates were broadly similar (Table 1).

Conclusion: SE deprivation is associated with reduced response to TNFi and increased risk of treatment discontinuation. Estimates were largely unchanged despite adjusting for potential mediators. SE inequality embodies a multitude of factors that can be intervened upon, including behaviours and biases of clinicians or institutes, which should be a focus of future research.

Table 1. Baseline characteristics and treatment outcome across groups of socioeconomic deprivation.

Baseline characteristics	40% least deprived (n=7116)	Middle 40% (n=6999)	20% most deprived (n=3002)	p
Age, years	57.4 (12.3)	56.1 (12.4)	54.7 (12.2)	<0.001
Female	5465 (77%)	5268 (75%)	2271 (76%)	0.094
RF positive	4275 (63%)	4308 (65%)	1868 (66%)	0.014
Age at diagnosis, years	45.5 (14.1)	44.4 (13.8)	44.0 (13.3)	<0.001
BMI	27.0 (7.4)	27.6 (7.9)	28.2 (8.1)	<0.001
Ever smoked	3762 (55%)	4123 (61%)	1949 (68%)	<0.001
DAS28	6.3 (1.1)	6.3 (1.1)	6.3 (1.1)	0.054
ESR (mm/hr)	35.0 (19.0, 57.0)	36.0 (20.0, 60.0)	36.0 (20.0, 58.0)	0.010
CRP (mg/l)	21.0 (8.0, 48.0)	21.0 (8.5, 47.0)	21.0 (8.9, 47.0)	0.86
HAQ	1.8 (0.7)	1.9 (0.7)	2.0 (0.6)	<0.001
≥1 comorbidities	4079 (57%)	4174 (60%)	1965 (65%)	<0.001
Treatment outcomes*				
DAS28 at 6 months	referent	b=0.14 (0.08, 0.20)	b=0.21 (0.13, 0.29)	
Low disease activity at 6 months	referent	OR 0.85 (0.77, 0.93)	OR 0.84 (0.73, 0.96)	
EULAR response at 6 months	referent	OR 0.87 (0.80, 0.94)	OR 0.79 (0.71, 0.87)	
Drug discontinuation	referent	HR 1.05 (1.01, 1.10)	HR 1.13 (1.07, 1.20)	

Data shown as mean (SD), median (IQR) or n (%) RF, rheumatoid factor; HAQ, health assessment questionnaire.*Models adjusted for age, gender, baseline DAS28 (or DAS28 components in respective models), BMI, HAQ, number of comorbidities, age at diagnosis, ever smoking status and rheumatoid factor status

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POS0055 BEYOND THE WINDOW: EFFECTS OF LONG-TERM TIGHT CONTROL IN EARLY-TREATED RHEUMATOID ARTHRITIS UNDER REAL-LIFE CONDITIONS

Keywords: Treat to target, Rheumatoid arthritis, Real-world evidence

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Background: Early treatment, within the window of opportunity, treat-to-target-(T2T) and tight control (TC) are fundamental principles of management in rheumatoid arthritis (RA). The Brasília Cohort of Early Rheumatoid Arthritis (BSB Cohort) is a real-life cohort designed and conducted under these principles.[1] The REAL study (Rheumatoid Arthritis in Real Life in Brazil) is a prospective multicentric cohort of patients with RA encompassing 11 public healthcare centers in Brazil, designed to reflect real-life, conventional managements conditions.[2]

Objectives: To compare early-treated patients with RA managed under the principles of T2T and TC vs. those exposed to conventional management in the long term, as for relevant clinical and radiographic outcomes, in real-life settings.

Methods: Participants from the BSB Cohort (under T2T and TC management) were compared to three randomly selected subsamples from the REAL study (REAL1, REAL2 and REAL3, exposed to conventional management). All patients initiated treatment with disease-modifying drugs (DMARD) within one

year of symptom onset. The groups were compared regarding the occurrence of erosive disease, use of corticosteroids (CE) and immunobiologicals (bDMARD), remission rates according to DAS 28-ESR and physical function (Health Assessment Questionnaire - HAQ).

Results: A total of 256 patients were included (64 from the BSB Cohort and 64 patients from each of the REAL1, 2 and 3 subsamples), predominantly female (88.3%), white (52%), with a mean age of 53.7 years, positive rheumatoid factor (73.4%), mean total disease duration of 94.1 months and delay time between first symptoms and use of first DMARD of 6.94 months. The groups compared did not differ significantly in terms of gender (χ^2 =6.19, p=0.103), race (χ^2 =7.68, p=0.053), age (F=1.28, p=0.279), presence of positive rheumatoid factor (χ^2 =1.89, p=0.594), mean disease duration (F=1.96, p=0.120) and time delay of symptoms until use of the first DMARD (F=0.34, p =0.793). The BSB Cohort showed significantly less frequency of erosive disease, use of CE and bDMARD, and higher DAS 28-ESR remission rate (Figure 1). Mean HAQ score was lower in the BSB Cohort (0.546) than in the REAL1 (1.033), REAL2 (0.821) and REAL3 (0.748), F=5,23, p=0,02. Mean DAS 28-ESR was lower in the BSB Cohort (2,90) than in the REAL1 (3,68), REAL2 (3,44) and REAL3 (3,21), F=3,43, p=0,018.

Conclusion: Under real-life conditions, in the long-term, adherence to T2T and TC principles was found essential to preserve the expected benefits of the early RA treatment within the window of opportunity, in terms of less occurrence of erosive disease, less use of CE and bDMARD, higher DAS 28-ESR remission rate and better physical function (lower HAQ score).

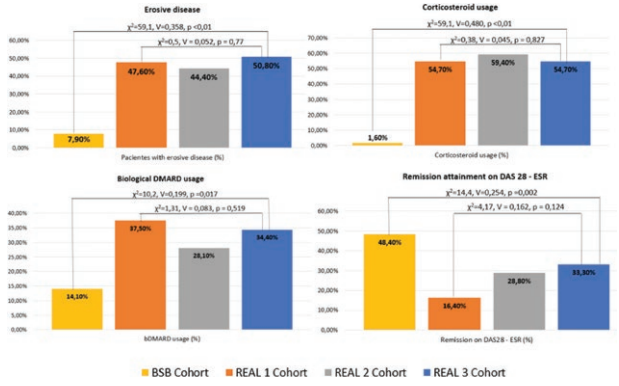


Figure 1. Comparison of the occurrence of erosive disease, CE and bDMARD use and the DAS 28-ESR remission rate in the BSB Cohort (strict control) and REAL cohorts 1, 2 and 3 (conventional control).Note: χ^2=chi squared; V=Crammer's V, p=p value (significant at <0.05).

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Disclosure of Interests: None Declared.

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POS0056

LYME ARTHRITIS. A RARE BUT IMPORTANT CAUSE OF MONO – OR OLIGO ARTHRITIS IN DENMARK: A CASE SERIES OF LYME ARTHRITIS IN FOUR DANISH MALE PATIENTS

Keywords: Inflammatory arthritides, Infection-related RMDs

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Background: Lyme arthritis (LA) is a rare manifestation of Lyme borreliosis in Denmark with an unknown incidence [1-2]. Typically, LA present with persistent or intermittent mono-arthritis in large joints especially the knees [3-4]. Clinically, LA does not differ significantly from other rheumatological oligoarthritic disorders, and due to a supposed low incidence, it poses a differential diagnostic challenge with risk of misdiagnosis.

Objectives: To describe a case series of four Danish patients diagnosed with LA from 2021-2022.

Methods: A case series.

Results: We describe a case series consisting of four Danish patients diagnosed with LA at the Department of Rheumatology, Esbjerg Hospital within a year (2021-2022). All patients presented with recurrent knee joint swelling, yet one patient also had arthritis in the upper extremities. All four patients reported previous tick bite, but none had a history of erythema migrans. The diagnosis was delayed up to one year due to lack of attention to LA as a potential differential diagnosis. The diagnosis was established based on the Borrelia burgdorferi sensu lato complex (B.b.s.l.) anti-IgG antibodies in patient serum and detection of B.b.s.l. DNA by real-time PCR of synovial fluid. All patients received antibiotics in a four-weeks period. However, one patient was re-treated because of recurrence of joint swelling in the upper extremities and detection of B.b.s.l. DNA by PCR in synovial fluid from the wrist joint, after completing the first line-antibiotic regimen. Three patients have fully recovered and have shown no sign of arthritis in a period ranging from 4 to 15 months. One patient is currently treated with Methotrexate.

Conclusion: This case series demonstrates that LA is an important differential diagnosis in persistent or intermittent mono – or oligo arthritis, especially in the knee joint. Lack of routine assessment of tick risk behavior, antibody status and/or assessment of the presence of B.b.s.l. DNA in synovial fluid by PCR methods, can lead to underdiagnosed cases. Obviously, insufficient examination can lead to a falsely assumed low incidence. It could be considered that the low incidence of LA in Denmark partly is caused by lack of attention to B.b.s.l. as a possible explanation for mono- or oligo arthritis. Clearly, this can lead to mistreatment.

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Table 1. Characteristics of four Danish patients diagnosed with Lyme arthritis

Gender	Age at diagnosis (years)	Joint affected	History of tick bite	History of EM	IgG seropositive	IgM seropositive	PCR positive for B.b.s.l in synovial fluid	CRP (mg/l)	Duration of arthritis prior to antibiotic treatment (months)	Intraarticular steroid injections before antibiotic treatment	Treatment after LA diagnosis
Male	78	Right knee Right wrist	+	-	+	+	+	36	38	Frequent[#]	Ceftriaxone (two course) [*]
Male	41	Bilateral knee Right wrist	+	-	+	+	+	105	14	Frequent[#]	Ceftriaxone[*] MTX[+]
Male	69	Right knee	+	-	+	+	+	13	10	Frequent[#]	Ceftriaxone[*]
Male	78	Right Knee	+	-	+	-	+	2	3	2 times	Doxycyclin

EM: Erythema migrans. IgG: immunoglobulin type G. IgM: immunoglobin type M. PCR: Polymerase chain reaction. *B.b.*s.l: Borrelia burgdorferi sensu lato. CRP: C-reactive protein. LA: Lyme arthritis. [#] Frequent steroid injections is defined as ≥three injections; [*] Ceftriaxone: Intravenous ceftriaxone 2grams daily for 28 days; [+] MTX: Methotrexate

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0057

WHICH ADVANCED TREATMENT SHOULD BE USED FOLLOWING THE FAILURE OF A FIRST-LINE ANTI-TNF IN PATIENTS WITH RHEUMATOID ARTHRITIS? 15 YEARS OF EVIDENCE FROM THE QUEBEC REGISTRY RHUMADATA™

Keywords: Rheumatoid arthritis, Registries, Real-world evidence

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Background: Since 2000, advanced therapies (AT) have revolutionized rheumatoid arthritis (RA) treatment. Initially, TNF-targeted therapies were the only options. Then, therapies with different modes of action (OMA) appeared. Habits and medication availability often determine second-line AT choices. Research suggests that specific sequences provide better long-term effectiveness [1,2].
Objectives: Evaluate which alternative medication provides the best sustainability following first-line TNF failure.
Methods: Data from AT prescribed since January 2007 was extracted from RHUMADATA™. Patients were followed until treatment discontinuation, loss to follow-up, or November 25, 2022. A descriptive statistic was used to compare patient characteristics. Kaplan-Meier was used to compare treatment discontinuation rates.
Results: A total of 611 patients (320 TNFi and 291 1237 OMA were included. The mean age at diagnosis was 44.5 (14.4) and 43.9 (14.8) in the TNFi and OMA groups, and disease duration at treatment initiation (TI) was 14.1 (11.1) and 12.9 (12.9). Women made up 72.8% and 81.1% of these groups. The age-adjusted Charlson Comorbidity index (ACCI) was 2.15 (1.7) and 2.1 (1.7). Patients reported more comorbidities, pain and fatigue, longer duration of morning stiffness, and higher HAQ score and disease activity in the OMA group (Table 1). The physician's global assessment of disease activity and the number of swollen and tender joints were also higher in the OMA group. OMAs retention was higher (Figure 1, logrank=0.0134) than TNFi retention following initial TNFi-IR. In a stratified analysis, rituximab (adjusted (Sidak) logrank=0.0048) had higher retention.
Conclusion: When a first TNFi fails, switching to an OMA, especially rituximab, appears to be the best strategy. Adequate assessment of more recent agents require longer observation periods.

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Table 1. Characteristics of selected patients at TI

Variable	OMA (N=291)	TNFi (N=320)	P-Value
Age at diagnosis, years	43.9 ± 14.8 (N=291)	44.5 ± 14.4 (N=320)	0.6324[1]
Disease duration at TI, years	12.9 ± 10.4 (N=291)	14.1 ± 11.1 (N=320)	0.1741[1]
Women, n (%)	236 (81.1%)	233 (72.8%)	0.0166[2]
ACCI	2.1 ± 1.7 (N=291)	2.1 ± 1.7 (N=320)	0.9498[1]
Hyperlipidemia[3]	118 (40.6%)	126 (39.4%)	0.8042[2]
Diabetes[3]	55 (18.9%)	48 (15.0%)	0.2340[2]
Hypertension[3]	160 (55.0%)	171 (53.4%)	0.7452[2]
COPD[3]	113 (38.8%)	102 (31.9%)	0.0755[2]
CVD[3]	53 (18.2%)	48 (15.0%)	0.3265[2]
Patient global, 1 to 10 visual analog scale [VAS]	5.3 ± 2.6 (N=200)	4.0 ± 2.8 (N=176)	<.0001[1]
Patient pain, VAS	5.8 ± 2.8 (N=200)	4.3 ± 3.0 (N=176)	<.0001[1]
Patient fatigue, VAS	5.5 ± 2.9 (N=200)	4.1 ± 3.2 (N=176)	<.0001[1]
Duration of morning stiffness, minutes	124.6 ± 284.1 (N=201)	71.7 ± 215.7 (N=175)	0.0451[1]
HAQ score	1.4 ± 0.6 (N=202)	1.1 ± 0.7 (N=176)	<.0001[1]
Physician global assessment, VAS	4.6 ± 2.7 (N=138)	2.9 ± 2.5 (N=121)	<.0001[1]
Swollen joint count,/28 joints	8.0 ± 5.2 (N=165)	4.9 ± 6.0 (N=142)	<.0001[1]
Tender joint count,/28 joints	7.2 ± 6.0 (N=165)	4.3 ± 5.6 (N=142)	<.0001[1]
RF, ever positive	194 (69.8%)	200 (65.4%)	0.2887[2]
ACPA, ever positive	168 (62.9%)	168 (61.1%)	0.7234[2]
ESR at TI, mm/hr	26.9 ± 23.5 (N=211)	21.6 ± 18.2 (N=183)	0.0136[1]
CRP at TI, mg/L	15.4 ± 23.0 (N=224)	8.9 ± 14.4 (N=211)	0.0005[1]

Continuous data are presented as mean ± standard deviation (N=X), where X represents the number of non-missing data points, and categorical data are expressed as n (%). P-values are based on [1]pooled variance t-test or [2] Fisher's exact tests. [3] The presence of comorbidity is based on an established diagnosis and/or comorbidity-specific drug use.

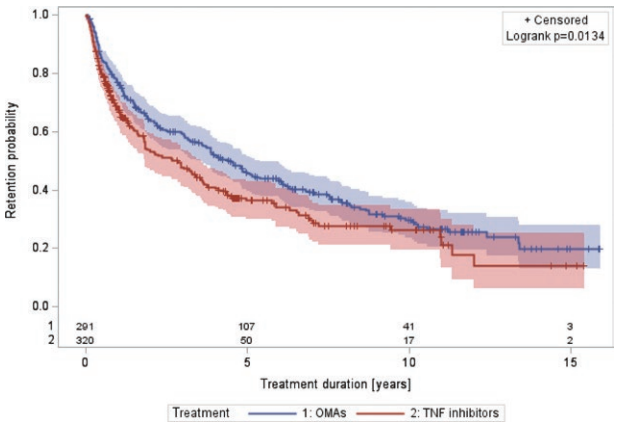


Figure 1.

Acknowledgements: NIL.

Disclosure of Interests: Denis Choquette Speakers bureau: Abbvie, Amgen, Eli Lilly, Fresenius Kabi, Novartis, Pfizer, Sandoz, Tevepharm, Consultant of: Abbvie, Amgen, Eli Lilly, Fresenius Kabi, Novartis, Pfizer, Sandoz, Tevepharm, Grant/research support from: Abbvie, Amgen, Eli Lilly, Fresenius Kabi, Novartis, Pfizer, Sandoz, Tevepharm, Louis Bessette Speakers bureau: Abbvie, Amgen, BMS, Eli Lilly, Fresenius Kabi, Janssen, Novartis, Pfizer, Sandoz, Tevepharm, UCB, Consultant of: Abbvie, Amgen, BMS, Celgene, Eli Lilly, Fresenius Kabi, Janssen, Novartis, Pfizer, Sandoz, Sanofi-Genzyme, Tevepharm, UCB, Grant/research support from: Abbvie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, Sandoz, Sanofi-Genzyme, UCB, Loïc Choquette Sauvageau: None declared, Jacques Brown Speakers bureau: Amgen, Janssen, Consultant of: Amgen, Gilead, Paladin, Pfizer, Ultragenyx, Isabelle Ferdinand Speakers bureau: Pfizer, Consultant of: Abbvie, Eli Lilly, Fresenius Kabi, Janssen, Novartis, Pfizer, UCB, Paul Haraoui Speakers bureau: Pfizer, Consultant of: Abbvie, Amgen, Lilly, Pfizer, Sandoz, UCB, Grant/research support from: Abbvie, Amgen, Pfizer, UCB, Maxine Joly-Chevrier: None declared, Ariel Masetto Speakers bureau: Abbvie, Janssen, Novartis, Pfizer, Consultant of: Abbvie, Janssen, Novartis, Pfizer, Sanofi-Genzyme, UCB, Grant/research support from: Novartis, Frédéric Massicotte Speakers bureau: Jansen, Consultant of: Abbvie, Eli Lilly, Janssen, Pfizer, Valerie Nadon Consultant of: Abbvie, Eli Lilly, Janssen, Pfizer, Roche, Sanofi-Genzyme, Jean-Pierre Pelletier Shareholder of: ArthroLab Inc., Consultant of: TRB Chemedica SA, Grant/research support from: TRB Chemedica SA, Jean-Pierre Raynauld Speakers bureau: Abbvie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Pfizer, Sandoz, Sanofi-Genzyme, Consultant of: Abbvie, ArthroLab Inc., Janssen, Pfizer, Sanofi-Genzyme, Diane Sauvageau: None declared, Angèle Turcotte: None declared, Édith Villeneuve Speakers bureau: Abbvie, BMS, Novartis, Pfizer, Consultant of: Abbvie, Amgen, Novartis, Pfizer, Louis Coupal: None declared.
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POS0058

OBESITY ASSOCIATES WITH HIGHER LEVELS OF INFLAMMATION DURING THE DISEASE COURSE, BUT ONLY IN ACPA-POSITIVE RA

Keywords: Rheumatoid arthritis, Comorbidities, Outcome measures

N. Den Hollander[1], A. M. P. Boeren[2], A. Van der Helm – van Mil[1,2], H. W. Van Steenbergen[1]. *[1]Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands; [2]Erasmus MC, Rheumatology, Rotterdam, Netherlands*

Background: Obese rheumatoid arthritis(RA) patients have higher disease activity scores(DAS) and lower odds of achieving remission. Although it has been convincingly shown that obese RA-patients experience more pain and have lower wellbeing scores, results are conflicting whether obesity has "pro-inflammatory effects" measured by higher swollen joint count(SJC) and CRP-levels. Additionally, associations of obesity with the DAS-components have not been studied longitudinally and it is unknown whether "pro-inflammatory effects" are similarly present in ACPA-positive and -negative RA. As in vitro data suggested that ACPA can enhance inflammatory-responses, we hypothesized that the association of obesity with SJC and CRP is strongest in ACPA-positive RA.
Objectives: To increase the understanding regarding the effect of obesity on the course of disease activity by studying associations of obesity with DAS-components in ACPA-positive and ACPA-negative RA.
Methods: We studied 649 RA-patients (358 ACPA-positive, 291 ACPA-negative), consecutively included in Leiden Early Arthritis Clinic from May 2011 onwards, and with a total of 2871 DAS-measurements over 5 years. Courses of DAS44 and

DAS-components (SJC-44, TJC-53, CRP and VAS(0-100)) were compared between RA-patients with normal weight (BMI 18.5-24.9; reference category), overweight (25.0-29.9) and obese patients(≥30.0), stratified for ACPA-positivity. Linear mixed models and Poisson mixed models with a knot at 4 months were used.

Results: Obese patients had a 0.32 units higher DAS compared to normal weight at diagnosis, this persisted during follow-up. Stratification for ACPA revealed that obese ACPA-positive patients had a 0.43 units(95%CI 0.22,0.64) higher DAS over time, whereas this difference was smaller and not statistically significant in ACPA-negative RA (0.19 units; 95%CI -0.01, 0.38). In ACPA-positive RA, all DAS-components were significantly higher during all 5 years of follow-up in obese patients compared to normal weight: SJC +60% (IRR1.60; 95%CI 1.18, 2.16), CRP +3.7mg/L (95%CI 0.95, 6.53), TJC +55% (IRR1.55; 95%CI 1.15, 2.10) and VAS +9 units (95%CI 4.09, 14.16; Figure 1). However, in ACPA-negative RA, obese patients only had a statistically non-significant trend towards (22%) higher TJC (IRR1.22; 95%CI 0.96, 1.55) and (4 units) higher VAS (95%CI -0.41, 9.00). Moreover, in ACPA-negative RA obesity was not associated with higher SJC and CRP.

Conclusion: Although obesity confers risk for higher DAS-scores over time, the effects of obesity on higher SJC and CRP-levels are restricted to ACPA-positive RA. This is the first demonstration that the influence of obesity on the course of RA is different for the two RA-subtypes.

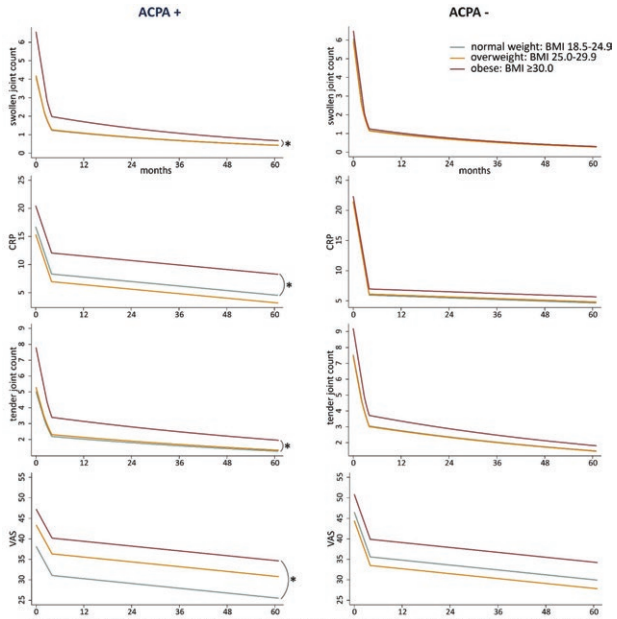


Figure 1. Obesity is associated with more swollen joints and higher CRP-levels over time in ACPA positive but not in ACPA negative RA patients

REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1965

POS0059 **WITHDRAWN**

PARE Poster Tour 1

POS0060-PARE **UNDERSTANDING THE PATIENT PERSPECTIVE IN LIVING WITH AND TREATING SPONDYLOARTHRITIS**

Keywords: Quality of life, Spondyloarthritis, Patient information and education

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Background: Spondyloarthritis (SpA), the group of conditions that includes ankylosing spondylitis, psoriatic arthritis, and non-radiographic axial spondyloarthritis, among others, can lead to symptoms of pain, stiffness, and swelling. The burden of disease can affect patients' quality of life.
Objectives: Patient research was undertaken to explore the impact of spondyloarthritis on quality of life, patients' ability to manage the disease, as well as experiences with healthcare providers. Better understanding is crucial to improving HCP-patient interactions, helping patients get on the right treatment path, and improving health outcomes.
Methods: In July 2022 an email invitation to an online survey was sent to members of MySpondylitisTeam, a social network of over 88,000 people. In total, 361 members completed the 25-question survey.
Results: 92% of members report that spondyloarthritis interrupts their quality of life (62% strongly agree and 30% somewhat agree) (Figure 1). SpA takes both a physical and emotional toll. 88% report it makes it hard to do everyday activities (54% strongly agree and 34% somewhat agree). Symptoms extend well beyond lower back, joint and hip pain (92%, 84%, and 81% experienced in the past year respectively). Virtually all experience fatigue (91%). Additionally, 61% have experienced symptoms of depression (63%) or anxiety (61%) in the past year. At the same time, just 52% believe they can ask doctors and have meaningful discussions about SpA and how best to manage it (27% strongly agree and 25% somewhat agree) (Figure 2). Only 35% are satisfied with the care they receive from the doctor who primarily treats their SpA. 38% indicate that the doctor recommends treatment based on their personal needs, and 36% indicate that the doctor addresses their SpA symptoms.

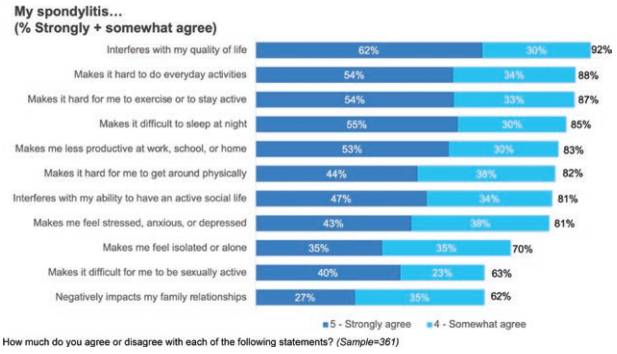


Figure 1. Impact on Quality of Life

How much do you agree or disagree with each of the following statements? *(Sample=361)*

Discussions with the doctor who primarily treats spondylitis *Among all who see a doctor*	
Listens to me and understands my specific needs	35%
Recommends treatment based on my personal needs	38%
Recommends regular check-ups to assess how I am doing	46%
Has developed a long-term treatment plan	20%
Provides information on potential side effects of different treatments	25%
Provides information on potential effectiveness of different treatments	29%
Addresses symptoms of spondylitis such as pain or fatigue	36%
None of the above	30%

Figure 2. Patient Discussions With Doctors

Which of the following reflect the discussions you have with the doctor who primarily treats your spondylitis? Please select all that apply. *(Sample=304)*

Conclusion: Understanding the needs of SpA patients provides significant opportunities for rheumatologists and primary care physicians to better support and educate their patients. This includes discussing potential treatment options, listening to patient concerns, and acknowledging the mental health challenges.
References: None to report.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0061-PARE **DEVELOPMENT OF AN EDUCATIONAL MATERIAL TO PROMOTE HEALTH IN FIBROMYALGIA FOR THE SUBWAY IN THE CITY OF SÃO PAULO, BRAZIL**

Keywords: Fibromyalgia, Non-pharmacological interventions, Patient information and education

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Background: The recommendations reviewed by the European League Against Rheumatism (EULAR) for the management of fibromyalgia indicate the importance of combining pharmacological and non-pharmacological interventions. In addition, these guidelines highlight that the initial non-pharmacological strategy should be patient education centered on the process of adapting and coping with fibromyalgia in quality of life.
Objectives: Develop and validate an educational material to promote health in fibromyalgia and disseminate it to the community in the subway of São Paulo - SP, Brazil.
Methods: For the construction of educational material for dissemination, the following steps were followed: Step 1: Identification of the needs of individuals with fibromyalgia and health professionals in which a qualitative research was carried out, through a focus group (a group of patients with fibromyalgia and another of health professionals). Twelve individuals with fibromyalgia and 10 health



Figure 1. Educational material to promote health in fibromyalgia in Brazil.Source: the authors.

professionals in Brazil were invited to participate. The group meeting sought to identify, through the participants' speech, what are the needs and problems reported by individuals with fibromyalgia and the possibilities of guidance by an interdisciplinary team of professionals to meet the needs and solve the problems. Qualitative data were analyzed using the content analysis method proposed by Bardin. The construction of the educational material used the Paulo Freire method, which began with an important survey to identify the primary needs of the participants so that they could be worked on so that, subsequently, the awareness process would take place. The researchers developed educational material containing information that was listed by individuals with fibromyalgia and health professionals. The educational material was made in online format.

Results: The educational material was developed based on the contents proposed in the previous phases and is shown in Figure 1.

Conclusion: The present study can contribute to the dissemination of educational strategies that promote health in fibromyalgia, for patients and for community, in order to disseminate scientific knowledge about the syndrome.

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POS0062-PARE GREAT SUCCESS FOR THE GERMAN PATIENT RESEARCH PARTNERS (PRPS): FROM THE CALL TO TENDER TO WINNING THE AWARD

Keywords: Patient-led research, Best practices, Patient information and education

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Background: The Deutsche Rheuma-Liga is a patient organisation with about 270 000 members. We have a long history of an established PRP network. We enjoy an excellent cooperation with our professional PRP-facilitator from the steering committee of our organisation. Our patient organisation provides tools, the PRP reference-cards and a helpful brochure, and takes care of the continuing education of the PRPs.

Objectives: In 2022, the Deutsche Rheumastiftung (DRS; German Rheumatism Foundation) for the first time launched the call for the „Projektpreis". Four prizes were awarded with 10.000 € per prize; and at least one of them had to be a participatory research project. This was the starting point for the German PRP network. The immediate aim was to win at least one of the awards. The overarching aim was to realise, for the first time in the field of German rheumatology, a research project initiated by PRPs.

Methods: In order to forward the call and set out the details of the applications, the first meeting was organised by our research facilitator. We discussed various ideas and evaluated whether the objectives can be achieved or not. The subsequent meetings were organised by the PRPs themselves. We improved the initial ideas and searched for supporting researchers, in order to substantiate the planned research projects and write the applications.

Results: Not all ideas from our PRPs were submitted, because of time limitations and difficulties in finding an adequate researcher. In the end, three participatory research projects from German PRPs applied for the "Projektpreis". The topics of the applications were a) money for disseminating the outcomes of a participatory research project addressing fatigue in Lupus patients, b) initiation of a participatory research project investigating how patients search, find and use web-based disease information in everyday life and c) initiation of a participatory research project investigating biomarkers for fibromyalgia. The total number of applications submitted to the DRS was 14. Finally, two participatory research projects from German PRPs won two of the four prizes. The award ceremony took place during the scientific congress of the German Society for Rheumatology in Berlin.

Conclusion: It was a great honour for the German PRPs receiving the awards for applications based on their own initial ideas. For the Deutsche Rheuma-Liga this was a great success in terms of supporting participatory research. This example shall encourage other patient organisation to be confident in finding and creating their own participation-research project.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0063-PARE PIONEERING HEALTH CENTER FOR RMD PATIENTS BY HELLENIC LEAGUE AGAINST RHEUMATISM (KAVALA BRUNCH)

Keywords: Best practices, Quality of care, Quality of life

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Background: It is common ground, especially in rural and semi-rural areas, that Rheumatic Diseases (RD) patients are, usually, treated by the health and social care system as "consumers" rather than "partners". Moreover, the same system restricts specialized professionals (occupational-therapists, physiotherapists, etc.), of the proper exercise of their duties, that is providing psychological and social support to the patients.

Objectives: The creation of a pioneering health center for RMD patients, with patient – centered structure, free of charge, with access to a variety of services and supported by a multidisciplinary team of volunteers.

Methods: The health center is staffed by 18 persons. They are 14 health professionals in general medicine, rheumatology, physiotherapy, psychiatry, nutrition, occupational therapy, nursing, gymnastics, social working, pedo-physiotherapy and 4 for secretariat. They are all working voluntarily.

The services provided by HELAR/ELEANA's branch in Kavala in the pioneering Health Center are:

A. Assistance to RMD patients by
   - informing and guiding
   - providing psychological support
   - consulting about professional re-orientation
   - providing healthcare with medication

B. Raising awareness about the importance of RD's to the general public and all competent agencies and stakeholders

C. Promoting research for better understanding and treatment of RMDs.

The team adopts an integrated, comprehensive approach with patients' autonomy, values and expectations at its core.

Results: During the period 13/11/22 - 23/12/22, 68 patients were examined by the team, 61 females (average age 63.29 (sd=4.9) and 7 males average age 66.7 (sd=6.4). 42 out of the total were from Chrisoupolis, with basic education level, and low economic status. According Arithmetical Pain Scale (NRS) males scored average 6.71 (sd1.1) and females 6.33 (sd=1.4). Analysis showed a strong correlation between pain and rigidity (p=0.001). More than 3 specialists were used for every patient. All patients had a follow-up visit and are still being followed up by our team.

Conclusion: The pioneering Health Center of HELAR/ELEANA offers its services to patients whose medical needs can be met within the capability of its staff and facilities. The population served at Health Center includes all ages regardless of national or ethnic origin, economic status, lifestyle, creed, or philosophical beliefs. Patients can expect appropriate procedures, treatments, interventions and care will be provided according to established policies, procedures, protocols and order sets that have been developed to ensure patient safety and positive outcomes. Appropriateness of procedures, treatments, interventions, and care are based upon patient assessments, re-assessments, and desired outcomes. Respect for patient individual needs, rights and confidentiality are maintained. The scientific evaluation of the effects of RMDs will help us to improve their clinical picture as a whole. Future use of specific tools and scales is expected to be implemented to measure broader and more specific indicators to evaluate the effectiveness of Health Center's services.

Acknowledgements: In this effort, we were granted institutional support from Nestos' Municipality, providing us with the building and covering all the fixed costs.
Disclosure of Interests: None Declared.
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POS0064-PARE PATIENT REPORTED BENEFITS OF PARTICIPATING IN AN ONLINE HEALTH COMMUNITY IN MANAGING RHEUMATOID ARTHRITIS

Keywords: Quality of life, Rheumatoid arthritis, Self-management

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Background: Previous research has shown that participation in online health communities can increase patient engagement, improve patient education, and help empower patients to achieve better health outcomes. This study was designed to measure the impact of one such community on patient outcomes.
Objectives: Patient research was undertaken to better understand the impact of rheumatoid arthritis (RA) on quality of life (QoL) and the perceived benefit that participating in a patient social community in RA has on improving health outcomes. This includes better QoL, better understanding of and adherence to treatments and improved relationships with one's doctor.
Methods: In August 2022, an email invitation to an online survey was sent to US members of myRAteam, a social network of over 197,000 people. In total, 745 members completed the survey. All respondents were 21 or older and self-reported as diagnosed with RA.
Results: The far-reaching impact of RA on QoL was evident in that most respondents reported that they find it hard to exercise (90%) and do everyday chores (90%). Respondents also reported that RA interferes with sleep (83%) and having an active social life (80%). The emotional toll of RA manifested with respondents feeling isolated/alone (71%), anxious (75%), and depressed (77%). While RA patients had a good understanding of the role medications play in slowing RA progression (91%) and potential symptoms they might experience (90%), only half (53%) felt they could avoid triggers that worsen RA. Top reasons for joining myRAteam included seeking information/ways to manage RA and being able to connect with others living with RA. Specifically, respondents were looking to gain insights from others' experiences (65%), gather information about RA (60%), better understand treatment options (59%) and have a way to connect with others (45%) for support and tips for living with RA. Newly diagnosed patients were much more likely to join myRAteam to understand what to expect after their diagnosis (68% versus 38% for those living with RA for more than a year), to get information about RA (70% versus 59%) and to better manage their symptoms (67% versus 52%). Almost all (90%) reported benefiting from joining myRAteam, including gaining knowledge about RA (77%), having better knowledge of/ability to stay on medication (56%) and having an improved relationship with their doctor (68%). Additionally, 66% benefited from receiving some form of social/emotional support from others. Specifically, they felt less isolated or alone (41%), better able to cope with the emotional toll of RA overall (37%) and less anxious or depressed (20%). Benefits were particularly evident for frequent visitors. For example, 85% of daily visitors to myRAteam are able to find information/resources to manage RA and 75% have experienced an improved relationship with their doctor. And 53% of frequent visitors feel less isolated/alone versus 29% of less active users.

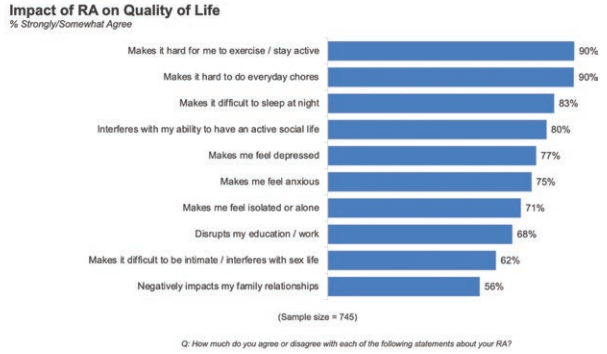


Figure 1.

Table 1.

Benefits of Joining myRAteam	Total Sample (N = 745)
Net Improved Knowledge About RA	**77%**
Understand symptoms of RA	55%
Find useful ideas to improve QoL	48%
Net Social Impact	**66%**
Feel less isolated/alone	41%
Better able to cope with emotional burden	37%
Net Medication Awareness/Adherence	**56%**
Discover different treatment options	44%
Better manage medication side effects	21%
Stay on prescribed treatment longer	16%
Net Improved HCP Relationship	**68%**
Ask better informed questions	47%
Raise concerns about RA symptoms	37%
Have quality conversations	30%

Conclusion: People with RA, particularly those recently diagnosed, are turning to online communities to find disease-specific medical information and support that they are not getting elsewhere. The majority of those surveyed report several benefits from participating in this community that are linked to improved health. Educating patients on the benefits of participating in a health-related social community can lead to less isolation and other mental health challenges, better informed patients, better treatment adherence and more empowered and productive conversations with the treating doctor. Reaching newly diagnosed patients can help lessen the burden of disease and set patients on the right treatment course to slow progression from the onset.
References: None to report.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0065-PARE EDUCATION FOR PATIENTS, DESIGNED BY PATIENTS: THE EXPERIENCE IN THE DESIGN OF A RHEUMATOID ARTHRITIS PRIMER

Keywords: Patient information and education, Rheumatoid arthritis, Education

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Background: In 2018, thanks to the support of a government entity, the UniversitAR multi-component educational program was launched; which trained more than 300 patients and certified 50 expert patients in Rheumatoid Arthritis in 2021. In this educational process, patients received training in various knowledge topics for disease care: definitions, signs and symptoms, treatment, medical team, therapeutic adherence, quality of life and transformation of personal behavior to manage relationships and situations. As a result, the educational program proposed the design of educational material that would be useful for the patient population.
Objectives: The objective of this project was to design a primer for patients with rheumatoid arthritis, which helps them understand the disease and the importance of long-term treatment, understand and apply therapeutic adherence, and change the way in which patients assume their role in treatment.
Methods: An editorial committee was created to write the primer. This committee was made up of 8 patient experts in rheumatoid arthritis, 1 rheumatologist, a coordinator of education programs for chronic patients, and a team of content reviewers. The writing of the primer began with a selection of the thematic contents with the greatest impact in their educational process and the writing of the initial manuscript began (by patients for patients). Afterwards, a first revision of the manuscript was made and some contents were adjusted according to the clinimetric standards for international rheumatology. Finally, the manuscript was submitted for review by the team of rheumatologists and the interdisciplinary team, thus creating the final version of the primer.
Results: In December 2022, an event for patients with Rheumatoid Arthritis was held. In this event the primer was presented and its purposes were explained. The primer gathers topics such as: disease definitions, signs and symptoms, diagnosis and treatment, disease impact, therapeutic adherence, myths and beliefs, the medical team, health literacy, and expert patients (See figure 1). In 2023, this primer will be delivered to all patients so that they can have a source of consultation and information.

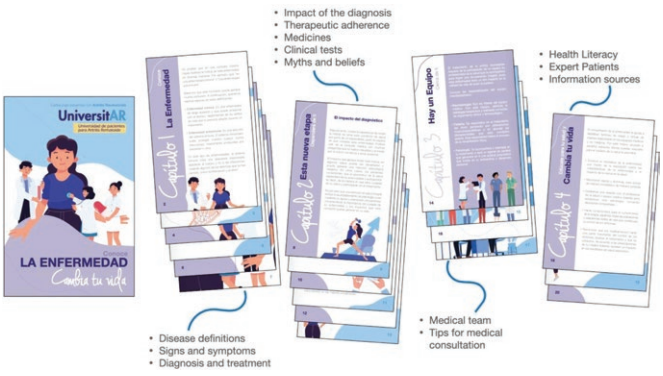


Figure 1.

Conclusion: It is important to support the dissemination of educational content so that patients have reliable, accurate and oriented information to improve their participation with medical teams in shared decision-making to achieve therapeutic objectives together.

Acknowledgements: We thank the Ministry of Science, Technology and Innovation MINCIENCIAS for allowing us to design this primer and for being able to train our patients. Also, we thank the patients who are part of the editorial committee that designed this primer.

Disclosure of Interests: Fernando Rodriguez: None declared, Liliana Realpe: None declared, Zohelia Castaño: None declared, Gabriel-Santiago Rodríguez-Vargas: None declared, Adriana Rojas-Villarraga: None declared, Pedro Santos-Moreno Speakers bureau: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi, Grant/research support from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi.

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POS0066-PARE LIFE WITH A CHRONIC ILLNESS - WHAT NOW? HOW TO LIVE WITH AXIAL SPONDYLOARTHRITIS, A LIFELONG ILLNESS

Keywords: Spondyloarthritis

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Background: Axial spondyloarthritis is a chronic inflammatory joint disease, which mainly attacks the pelvis, back, neck and thorax, but peripheral joints can also be affected. This patient group is affected to a very varying degree and the disease varies throughout the course of the disease. Some have mild symptoms and may be without ailments for long periods of time. Others have major ailments and may experience increasing stiffness in the back. The average age at the onset of symptoms of AS is 26 years.

Objectives: The aim of this campaign is to focus on life with a chronic illness. How to mentally master your illness and accept it, but also how to be active with the disease. The campaign aims to break down prejudices and discrimination that chronic sufferers are faced with in society, for example that they are weaker or lazier than others. These prejudices help to make the disease a strain mentally as well. Many patients struggle to accept that they have contracted a chronic illness, a disease that stays with you for life.

Methods: Giving this campaign a face, we used a world-renowned photographer and social debates Morten Krogvold to take pictures of Felix Baldauf, world champion in wrestling, living with axial spondyloarthritis. Films were made of Felix's story, about the road to a diagnosis and about the afterlife diagnosis. In the films, Felix honestly tell how tough and difficult this road has been for him, but at the same time he talks about how life has changed now that he has been diagnosed and properly treated. His goal is now a gold medal in wrestling at the 2024 Olympics, even though he's living with axial spondyloarthritis, which shows that it is possible to live a good life with the disease and have an active physical life. In order to get as much attention as possible about the campaign, it was launched at political week in Arendal. The films and photos are being shared in social media, and we have published digital booklet with artistic photos. The main film has so far reached 3200 people. We had an event at Litteraturhuset in Oslo together with a rheumatologist and a physiotherapist where we talked about being able to live a good life with the disease. We also recorded a podcast about the campaign.

Results: By using famous people the campaign has gained a familiar face and at the same time received a lot of attention. Felix tells about a great mental strain not knowing what was wrong with him, but it is fantastic to see that it is possible to live well with the disease when getting treatment.

Conclusion: The campaign gives hope and inspiration to patients that it is possible to live well with the disease. It shows that you can be very physically active, but at the same time show that there are both ups and downs with the disease. Felix's openness about the disease leaves hope for other patients, that one can live a good and active life with the disease.

Acknowledgements: The patient campaign is supported by the Norwegian Directorate of Health, Novartis, AbbVie.

Disclosure of Interests: Lillann Wermskog Grant/research support from:: I have not personally received a grant, but Spafo has received funding from Novartis, Abbvie, UCB Pharma, Takeda, Pfizer, Lilly, Employee of: Yes, Novartis, Lise Mette Eidet Grant/research support from: I have not personally received a grant, but Spafo has received funding from Novartis, Abbvie, UCB Pharma, Takeda Pfizer, Lilly, Kari Lilleby Employee of: I am employed by Novartis Pharma.

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POS0067-PARE USING AI BASED TECHNOLOGY TO GAIN INSIGHTS FROM OSTEOARTHRITIS PATIENTS IN THE UK VIA SOCIAL LISTENING

Keywords: Osteoarthritis, Real-world evidence, Artificial Intelligence

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Background: Osteoarthritis (OA) is a chronic degenerative joint condition associated with joint pain, stiffness, and mobility problems. More than half of OA patients live with moderate or severe pain[1], impacting all aspects of their lives and decreasing their overall Quality of Life (QoL). Social listening enables insight generation beyond the healthcare setting, demonstrating a more comprehensive view on disease burden and patient experiences. This study utilizes a unique approach based on Artificial Intelligence that analyses high volumes of data both quantitatively and qualitatively of patient-authored content.

Objectives: The study aims at exploring patient-generated online data as a source for capturing the real-world experience of OA patients, as reported by a large online population in the UK. A particular focus is on understanding the individually perceived disease burden in terms of symptoms, patient-reported QoL[2] and surgical treatment options.

Methods: A sample of real-world data from online health communities in the UK was collected between Oct 2019 until Jan 2022, resulting in a data set comprising n=6,354 algorithmically identified OA patients and n=42,353 posts (documents). OA-specific concepts to identify patient experiences were algorithmically coded using supervised machine learning, natural language processing (NLP) and knowledge graph tagging. An algorithmic stack of 40+ dedicated NLP analyzers was applied to detect key concepts and their relations of the patient experience in the posts (symptoms, their severity, impacts on QoL facets, perception of treatment options). Data were collected and processed in an anonymized, secure, and reliable way to ensure privacy and ethical aspects.

Results: Age could be algorithmically determined for N=1,012 patients (16 % of total patients), 56% of whom are older than 50 years. Pain was the most discussed symptom (58% of patients; N=3,703). N=1,508 patients underwent surgeries, with hip (N=762) and knee replacements (N=674) as most reported procedures. Recreation & Leisure and Mobility were the most prominent QoL aspects (31% and 28% of patients). Healthcare availability (e.g. access to treatments) was raised by N=668 patients (11%); a proportion of these (N=150) also underwent hip or knee replacement, with more than half reporting having been on a "waiting list" for their surgical procedure.

Figure 1 shows five QoL aspects most relevant for patients with knee or hip replacement, together with improvement or worsening of the respective QoL aspect. Notably, a majority of patients in both groups report mobility and healthcare availability to deteriorate rather than improve.

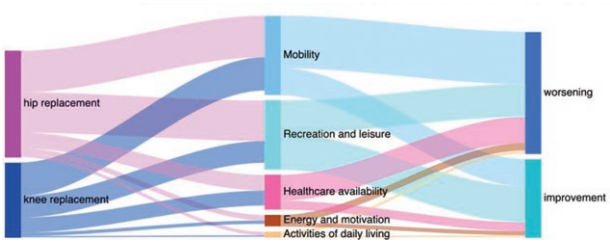


Figure 1. Sankey chart illustrating improvement or worsening (right) of the five most mentioned QoL aspects (middle) of patients with a knee or hip replacement procedure (n=266 documents)

Conclusion: This social listening study indicates pain as the most burdensome OA symptom and sheds light on the QoL impact of surgical procedures. Given limitations of social listening studies (e.g. number of identifiable age groups or gender)[3], the results need to undergo further validation by patient representatives and clinical experts. Yet, this novel method complements common approaches by providing an understanding of patients' perspectives outside the clinic, representing the voices of vulnerable populations who may not otherwise participate in clinical or epidemiological studies.

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POS0068-PARE VITORIA, A VIRTUAL ASSISTANT TO PROMOTE EDUCATION AND AWARENESS ON JUVENILE RHEUMATIC MUSCULOSKELETAL DISEASES

Keywords: Patient information and education, Non-pharmacological interventions, Self-management

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Background: The range of musculoskeletal and connective tissue conditions that manifest in children is referred to as paediatric rheumatic diseases[1]. Juvenile idiopathic arthritis (JIA) is the most common childhood chronic rheumatic disease[2]. This disease is the most frequent cause of chronic pain in young people, which negatively affects their quality of life. To mitigate the burden of chronic condition, self-management (e.g., lifestyle) should be combined with medical management. More effective information strategies are required to respond to the needs of those living with rheumatic diseases and their caregivers. Virtual Humans (VH) have been utilized in interactive computational simulations to boost users' acceptability and knowledge of health conditions while also promoting lifestyle changes in healthy individuals or in the management of chronic illnesses, such as juvenile rheumatic musculoskeletal diseases (RMDs)[3,4].

Objectives: This project aimed to develop a web application to support education for disease management and health promotion, in children and young people with RMDs, their caregivers and peers[5].

Methods: The use of gamification as well as a virtual character incorporated in a narrative, with the dual goal of maintaining user engagement and improving the play experience, was the core idea underpinning the development of our application. Group discussions with youngsters (members of the patient organisation ANDAI) were used to obtain feedback and experiences from application users during the requirement phase, intermediate feedback and testing the developed application. The application was also assessed by an evaluation survey following the testing phase.

Results: A virtual assistant was developed to communicate with users through speech (voice and subtitles) as well as face and body motions[6]. This 2D animated young female model, portrays a character with juvenile RMDs and shares information about her lived experiences with the illness. An assessment of user knowledge follows each interaction. Users are encouraged to play and learn more by awarding points and digital badges for right answers or by displaying the solutions when incorrect answers are chosen. In short, on a scale of 1 to 5, 83% of the participants in application testing rated the application with maximal punctuation, indicating that users, which were children with RMDs, their young relatives and/or friends, found this tool useful.

Conclusion: A virtual assistant web application that uses a narrative approach and gamification concepts to encourage education on juvenile RMDs was successfully developed. This web application is intended to be lodged on the ANDAI website to convey easy access. In addition, this tool will be also made available in tablets at the waiting room of paediatric rheumatology services, facilitating education when children are diagnosed.

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Disclosure of Interests: None Declared.

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POS0069-PARE HOW TO REACH MORE PEOPLE WITH RMD THROUGH DIGITAL COUNSELLING

Keywords: Self-management, Mental health, Patient information and education

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Background: The Danish Rheumatism Association has a professional counselling service, where our 82.000 members can call or write to get help and answers to their questions. The association had planned to make our counselling offers more digital over time but due to corona in 2020 we decided to advance the launch of these digital offers since all our usual meetings and activities got cancelled overnight.

Objectives: The association wants to be as relevant as possible to all people with RMD and therefore we wish to be present, not only at our usual platforms, but also through digital solutions. Since 2020 the professional counselling has, in collaboration with the communication department, made short videos on SoMe and broadcasted live events on relevant topics with experts, where the viewers have the possibility to interact with questions and emoji's during the live events. It is also possible to watch the live events afterwards. Since 2022 the association has increased the digital offers within counselling to also include explainer videos and livestreaming from public meetings at hospitals. Our aim is to give relevant information that help people with RMD to improve their capability of self-management and get them to connect and interact even more with us.

Methods: The first digital events were made with a handheld mobile camera and the sound was not very good. The events were transmitted live on the association's Facebook page. This new way of approaching people with RMD with professional counselling through live events was successful and had more viewers than we had expected even though the quality in the beginning was poor. This shows that even with scarce resources you can still reach many people with RMD through digital solutions. After a while we hired a professional company to make our live events more professional with correct light and sound, and today we are on a much higher level than at the beginning of our digital transmissions. We have also expanded our ways of making live events from 1-2 experts talking on a specific topic to also include panel discussions, live broadcasting from large public events, explainer videos, live interviews with medical doctors at hospitals etc.

Results: In 2022 the professional counselling service have produced 2 explainers, 8 live events and 12 videos. The topics of the broadcasts were for example pain, sexuality, exercise, mental health, social issues, newly diagnosed etc. The number of people we have reached with the digital counselling will be elaborated on the EULAR congress. We have indications showing that more young people are aware of the association and our professional counselling after having provided more digital services with the possibility to interact or to watch it whenever it suits the person. Furthermore it is a cost effective way to reach a lot of people at one time compared to our 1-on-1 phone consultations in our professional counselling. The downside of doing digital events is that you do not get the personal and direct connection between the professional and the person with RMD and the advice that is given will be more general compared to a telephone conversation. Furthermore, it requires access to the Internet and a Facebook account or similar. Some elderly people can therefore not participate

in these events. However, in 2022 we offered physical events as well. We are trying to reach out as broadly as we can in order to meet the different needs from people with RMD.
Conclusion: The use of live events and videos is a way to unfold the professional counselling service in order to give help and advice to a broader audience. It has been a huge success with many viewers who interact with us. These digital offers are contributing to make the Danish Rheumatism Association appear as a modern and progressive association. An important notice when wanting to become more digitalized as a patient organization is, that even on a low budget you can reach many people with RMD as long as the content is relevant. We will for sure develop even more digital offers in the future regarding patient information and education in order to improve the quality of life for more people with RMD.
References: None.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.856

POS0070-PARE **CAREGIVER BURDEN AMONG IDIOPATHIC INFLAMMATORY MYOPATHY (IIM) CAREGIVERS**

Keywords: Myositis, Patient-led research, Quality of life

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Background: Idiopathic inflammatory myopathies (IIMs) often lead to severe impairments in quality-of-life related to physical and emotional burdens. While the healthcare delivery burden in patients with specific types of IIMs has been explored[1], little is known about caregivers' burden, especially in rare diseses.[2]
Objectives: Myositis Support and Understanding (MSU), a non-profit patient-led advocacy organization for IIMs, distributed a survey to its members to better understand caregiver burden. The aim of this study was to evaluate the association between caregiver burden by IIM subtype and factors that impact caregiver wellbeing.
Methods: *Data Source:* An anonymous survey was distributed via RedCAP to MSU members worldwide. A total of 120 caregivers (age range: 30-89) responded to the survey over the course of 4 weeks. *Survey*: Demographic, diagnostic information, and disease duration data was collected from participants and their caregivers. The Zarit Burden Interview (ZBI), a validated instrument for a diverse range of patients and caregivers, was used to determine caregiver burden, testing domains including health, mental well-being, personal relationships, physical overload, social support, and home environment[3]. *Statistical analysis*: Pearson chi-square test was performed to assess the association between duration of caregiving, myositis type, and caregiver age on the social well-being of caregivers. Regression analysis was also conducted to identify risk factors for increased caregiver burden. Significance was set at $p<0.05$.
Results: Most of the caregivers in this study were responsible for the care of participants with inclusion body myositis (IBM, 64%) followed by dermatomyositis (DM, 22%). Caregivers reported that 74% of IIM patients under their care had moderate to severe difficulties with mobility and required help some or most of the time. A total of 102 caregivers completed the ZBI: reported burden was mild to moderate in 44%, moderate to severe in 25%, and severe in 4% of caregivers. There was a high degree of at least moderate severity burden in IBM (33%), DM (25%), and polymyositis (25%).
Conclusion: Caregivers face a high degree of burden, most evident in IBM. Burden positively correlated with disease duration with an inflection time of 6 years, thereafter caregivers reported increased burden. The domains that were most impacted include personal strain, social and family life, role strain, and loss of control over one's life. Insights from this study can help create specific emotional coping strategies for myositis patients and their caregivers.
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HPR Poster Tour: Diverse interventions and patient perspectives

POS0071-HPR **PHYSICAL THERAPY, PHYSICAL ACTIVITY AND PHYSICAL FITNESS IN PSORIATIC ARTHRITIS: A SYSTEMATIC REVIEW**

Keywords: Physical therapy/Physiotherapy, Psoriatic arthritis, Systematic review

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Background: Patients with psoriatic arthritis (PsA) have a remarkable increased risk for cardiometabolic comorbidities impacting their disease management and functioning. Studies in the general population have demonstrated that higher levels of physical activity, better cardiorespiratory fitness and muscle strength improve cardiovascular and all-cause mortality risk.[1] Physical therapy is highly recommended as part of the non-pharmacological management of PsA patients.[2-4] Physical activity recommendations were composed but specific guidance on the type, duration or intensity was not provided.[5] Therefore, a summary of the available evidence on physical therapy, physical activity and physical fitness in PsA patients is needed to strengthen the non-pharmacological management.
Objectives: This study aimed to systematically review and appraise the quality of research on physical therapy, physical activity and physical fitness in PsA patients.
Methods: The protocol was prospectively registered at the PROSPERO database (ID 255501). A systematic literature search was performed in May 2022, using four different databases (Medline, Embase, Web of Science and Cochrane library). We included papers examining physical therapy, physical activity and physical fitness (cardiorespiratory and muscular fitness) in PsA patients, with a minimum age of 18 years and diagnosed by a physician, classification criteria or self-reported. A mixed population of patients with rheumatic and musculoskeletal diseases was allowed if the proportion of PsA patients was at least 10%. All eligible interventional or observational (quantitative or qualitative) studies with a full-text paper written in English or Dutch were included without restrictions regarding the publication year. The quality was assessed through the Newcastle-Ottawa Scale and the Revised Cochrane risk-of-bias tool for randomized trials. A meta-analysis was not possible due to the wide variety of interventions and outcomes. Therefore, a narrative synthesis was used.
Results: After deduplication, a total of 6026 abstracts were retrieved, of which 380 abstracts were selected for full-text analysis. Ultimately, 85 papers published between 1994 and 2022 were included, of which 6 papers were added from screening references. Most studies were cross-sectional (n=31) or randomized controlled trials (RCT; n=18). Forty-seven % of the studies consisted of PsA patients only. Low risk of bias was scored in 2 RCTs, 1 cohort study (n=3), 4 case-control (n=9) and 7 cross-sectional studies. The risk of bias was mainly increased due to selection bias, the use of non-validated and/or patient-reported outcomes and the lack of blinding possibilities in case of physical therapy intervention. In 23 papers physical activity was measured, of which 8 studies used a validated questionnaire and only 1 study used an objective method. Cardiorespiratory and muscular fitness were assessed in 5 and 9 studies respectively. A variety of physical therapy interventions were studied: resistance training (n=1), cardiorespiratory training (n=2), mind-body exercises (n=3), behavioural change programs (n=2), therapeutic modalities (n=4) and mixed rehabilitation programs (n=5). One RCT with low risk of bias evaluated an increase in cardiorespiratory fitness and a reduction in truncal fat percentage in PsA patients after 11 weeks of high intensity interval training. Qualitative research (n=11) emphasized the need of patients for education.
Conclusion: Scientific evidence on physical therapy, physical activity and physical fitness in PsA is limited. Further research is needed on non-pharmacological interventions and aspects in general, especially on physical fitness.

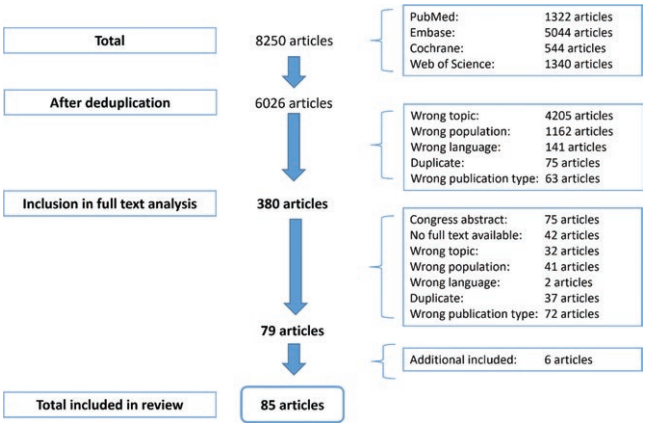


Figure 1. PRISMA flow diagram of the study selection process

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5778

POS0072-HPR EXERCISES TRAINING AS A TREATMENT FOR RHEUMATOID CACHEXIA IN RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Non-pharmacological interventions, Rheumatoid arthritis, Physical therapy/Physiotherapy

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Background: Rheumatoid arthritis (RA) is a systemic inflammatory autoimmune disease that characterized by chronic, symmetric and erosive synovitis that may lead to severe disability and impairments. RA patients frequently have adverse changes in their body composition, with a decrease in muscle mass and an increase in fat mass, a syndrome that is termed rheumatoid cachexia (RC). RC is associated with chronic inflammation, impaired muscle mass and strength and body mass loss, all of which are classical targets of exercise training.
Objectives: This systematic review and meta-analysis aimed to determine the effects of exercise training on body composition included fat mass, lean body mass and muscle strength in patients with rheumatoid arthritis.
Methods: We searched PubMed/Medline, Web of Science, EMBASE, CINHAL, Scopus, Cochrane Library, Google Scholar and Science Direct for relevant articles until November 2022. Systematic review included randomised controlled trials and controlled trials. Pre- and post- exercises intervention data on our primary outcomes included body composition [e.g., using BMI, bioelectrical impedance analysis, fat-free mass index (FFMI)] and isometric knee muscle strength. Two authors independently screened records and data were extracted using Microsoft Excel and exported to STATA version 15.0 software for analysis. Risk of bias was assessed and a random-effects model was used to pool effect sizes by standardized mean differences (SMD).
Results: Six studies with a total of 119 patients with RA in the meta-analysis. Exercises interventions had a median (range) duration of 14 (12-24) weeks and including progressive resistance training, high-intensity resistance training, proprioceptive exercises and water-based exercises programs. Exercises interventions a superior effect compare to control on both fat mass [SDM -0.20 (%95 CI – 1.20, 0.79), p<0.001, I^2; %91], lean body mass [SDM 0.66 (%95 CI -0.77, 2.09), p< 0.001, I^2; %95] and isometric knee extensor muscle strength [SDM 3.01 (0.59, 5.43), p<0.001, I^2; %97] (Figure 1).
Conclusion: Our meta-analysis indicates different exercises trainings effectively decreased fat mass and increased isometric extensor muscle strength and lean mass in patients with RA thereby slowing or reversing RC.
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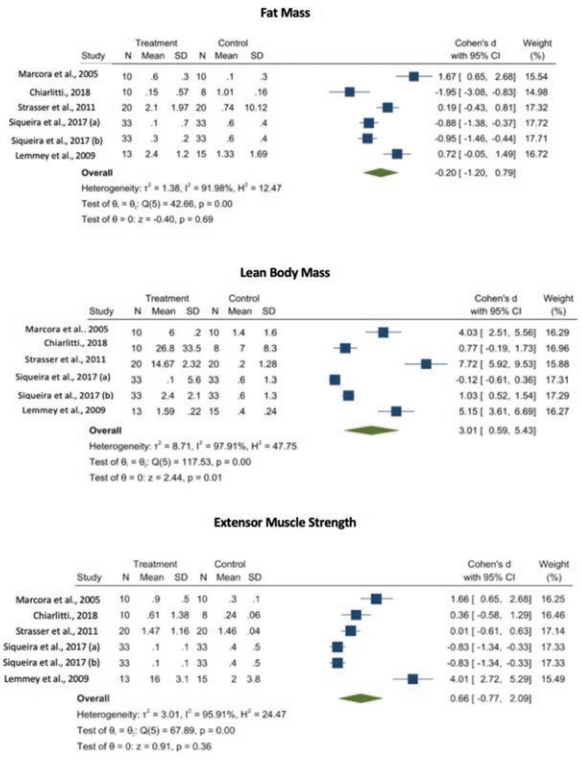


Figure 1. Forest plot of RC parameters (fat mass, lean body mass and muscle strength) for exercise training versus control groups at weeks 12 and 24

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0073-HPR APPLICABILITY OF THE DIGITAL PHYSIOTHERAPY INTERVENTIONS FOR RHEUMATIC AND MUSCULOSKELETAL CONDITIONS IN TURKEY: A MIX METHOD STUDY

Keywords: Physical therapy/Physiotherapy, Qualitative research methods, Telemedicine

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Background: Physiotherapy and rehabilitation have been impacted by digitalization in the healthcare system [1]. For the transfer and dissemination of the developed digital health interventions (DHI) to the clinic, the perspectives of physiotherapists—one of the stakeholders in the rehabilitation process—on digital health practices are essential [2].
Objectives: The aim is to determine the usability of digital health technologies in rheumatic and musculoskeletal physiotherapy and rehabilitation and determine the perspective of physiotherapists, perceived facilitating factors and barriers.
Methods: Both quantitative and qualitative data were collected for this study. In the qualitative part of the study, 21 physiotherapists who are working with rheumatic and musculoskeletal conditions were included in the study. Three focus group interviews were conducted with 7 physiotherapists in each group. In the quantitative part of the study, 393 physical therapists were reached through the snowball sampling method. A questionnaire created by the research team was conducted. The SPSS22 program was used for quantitative data statistics, while the NVivo12 program was used to analyze the qualitative data.
Results: Following the focus group interviews, five themes emerged. The themes are as follows: Digital health applications used by physiotherapists for self-educational purposes, DHI used in physiotherapy, barriers to the use of DHI in physiotherapy, benefits of using DHI in physiotherapy, and popularizing the use of DHI in physiotherapy. The themes are summarized in Table 1. The participants reported utilizing DHI in assessment (29.3%), treatment (34.4%), and follow-up (44,8%). The main perceived benefits to use of DHI in physical therapy settings were facilitating patients' follow up (90.8%), and participation (81.7%).

The main perceived barriers to use of DHI in physical therapy settings were high cost (77.8%), and lack of appropriate DHI to Turkish population (71.5%).
Conclusion: This study is the first to present the views of physiotherapists in Turkey on the use of DHI in physiotherapy. Participants are willing to use digital health interventions, but due to obstacles that prevent their use in physiotherapy, there are still some limitations on their use. They contend that for DHI to be widely used, physiotherapists and patients must be educated about them, and the state must support their use and multidisciplinary development.
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Table 1. Key themes, categories and nodes

Key themes	Categories	Nodes
DHI Used in Physiotherapy	Purposes of Using Digital Health Interventions in Physiotherapy	consultancy evaluation feedback tracking progress treatment follow-up patient and family education out-of-session arrangements professional development
Barriers to Use of DHI in Physiotherapy	Technological barriers	accessibility to technology lack of technology infrastructure digital health literacy technology acceptance data security
	Clinical barriers	inappropriate clinical conditions lack of physical contact fear of losing the physical therapist's control and trivializing the physical therapist's presence
Benefits of using DHI in physiotherapy		accessibility (to patient and physiotherapist) motivation follow-up objective, standard data
Expanding the Use of DHI in Physiotherapy		education creating a need public promotion multidisciplinary development of interventions professionalization positive user experience

Abbreviations: DHI: Digital Health Interventions

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0074-HPR EFFICACY OF E-CONSULTS COMPARED TO IN-PERSON REFERRALS OF ANA POSITIVE PATIENTS TO RHEUMATOLOGY CLINIC

Keywords: Descriptive Studies, Health Services Research, Telemedicine

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Background: Antinuclear antibodies (ANA) are autoantibodies associated with several autoimmune diseases but are also present in healthy individuals due to their role in the body's biological immune response. Thus, testing for ANA in an ambulatory setting could be inappropriately ordered and misinterpreted. Yet, delay in proper management of patients with rheumatologic presentations could result in increased morbidity and health care expenditure. Electronic consultation, or eConsults, could be utilized by primary care providers (PCPs) as a convenient tool to expedite access to rheumatology specialists and optimize care.
Objectives: To assess the efficacy of eConsults in terms of resource utilization and time to referral when compared to in-person referrals of ANA+ patients.
Methods: In this retrospective cohort study, we reviewed the charts of 131 ANA+ patients within the Yale New Haven Health System seen from August 2019 to September 2022. The charts were divided into cases referred by eConsult and by in-person referrals. Time from chart order to eConsult or in-person consultation, diagnosis after consult completion, and laboratory workup results were evaluated. Relative risks (RR) were calculated to compare the efficacy of eConsults vs. in-person referrals in diagnosing connective tissue diseases (CTD) and initiating appropriate referrals. A chi-square test of independence was conducted to determine if there was an association between ESR/CRP levels and conversion to in-person follow-up appointments in eConsult patients.
Results: Among the 131 ANA+ patients seen by their PCPs, 91 (69.5%) were referred through eConsult and 40 (30.5%) were in-person referrals to a rheumatologist. The average time from the initial eConsult request to completion of the consult was 1.46 ± 2.54 days while in-person consults required longer wait times of 76.63 ± 48.61 days.

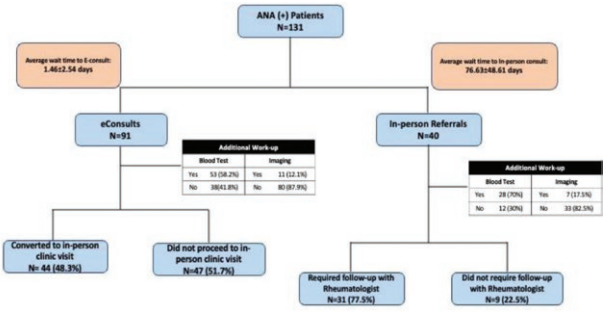


Figure 1. Flow Diagram of ANA+ patients referred for eConsult and In-person Rheumatology specialty clinic

Of the 91 eConsult patients, 44 (48.4%) were converted to face-to-face (FTF) consultation with a rheumatologist. Patients evaluated through eConsults were less likely to be referred to a rheumatologist (RR = 0.61, 95% CI 0.46 – 0.80) when compared to in-person referrals. Patients referred through eConsults were twice as likely to be diagnosed with CTD relative to those that were not scheduled for an FTF visit after an eConsult was completed (RR = 2.49, 95% CI 1.28 – 4.84). For the converted patients, 21 (47.7%) were diagnosed with CTD. For those that did not convert to a FTF referral, only 9 (19.1%) were eventually diagnosed with a CTD. Of the 40 in-person patient referrals, 31 (77.5%) were scheduled to follow-up with a rheumatologist; the majority of which (N = 30, 96.8%) were ultimately diagnosed with CTD. Elevated ESR/CRP levels were found in 19 (43.2%) eConsult patients that had converted and 16 (34%) patients that did not convert to FTF. For eConsult patients, there was no significant relationship found between ESR/CRP levels and conversion to a FTF appointment ($\chi^2(1, N = 74) = 3.299$, $p = 0.07$).

Conclusion: Electronic consultation is an easy and timely method for referral to the rheumatology clinic. In this study, ANA+ patients requiring an urgent consultation were identified earlier through an eConsult compared to an in-person referral. eConsults were also capable of identifying cases that required specialist treatment; 80.9% of patients that weren't referred would not receive a CTD diagnosis in the future. Thus, eConsults should be considered an effective and efficient tool in properly referring patients with rheumatologic presentations and parsing out cases that would not require specialist care.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0075-HPR OPPORTUNITIES AND CHALLENGES IN WEB-BASED PATIENT EDUCATION FROM THE PERSPECTIVE OF PATIENTS WITH RHEUMATOID ARTHRITIS – A QUALITATIVE STUDY

Keywords: Self-management, Patient information and education, Rheumatoid arthritis

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Background: Self-management skills are important for people with inflammatory rheumatic diseases, and can be supported through patient education (PE) (1, 2). Following an increasing use of telehealth (3), digital PE is gaining ground to support patients' self-management skills, but the evidence is still limited. Currently, we are testing the effectiveness of a digital PE e-learning program designed for people with rheumatoid arthritis (RA), the WebRA trial [4]. In the present qualitative study, we aimed to provide in-depth insight into patient perspectives of the e-learning program.
Objectives: To explore patients' perceptions of taking part in web-based PE, and how this contributes to self-management of RA.
Methods: We conducted 20 individual qualitative interviews based on the 'Interpretive Description' methodology, an inductive research strategy implying an iterative process of data collection and analysis. Newly diagnosed RA-patients were recruited from the intervention group of the WebRA trial after having finalized their one-year follow-up period [4]. A purposive sampling strategy was used to achieve information power by inclusion of participants with different sex, age, and sociodemographic background. The analysis contained a descriptive part followed by interpretation and extraction of main messages.
Results: Overall, participants had positive perceptions of the e-learning program, and only minor technical difficulties were identified. Advantages of e-learning were flexibility, the possibility for repetition, varied and entertaining presentation forms, availability, and learning in familiar and calm surroundings. Disadvantages were described as missing the dialogue with health care providers (HCPs), and therefore unmet relational support needs. The degree to which e-learning perceived to play a role for acquiring knowledge about RA differed. For the majority, a need for insight and clarity into the condition led to an active approach in using e-learning, whereas a minor group had a more hesitant approach, and postponed the use of the program, e.g. because of mental distress following the diagnosis or by oversight. The program was mostly used immediately after having received the diagnosis and only to a limited extent in the time hereafter. This was explained by fulfilled informational needs, a need for normality and a desire for focusing on everyday life. Participants found that the e-learning program facilitated learning and contributed to self-management of their disease. Patients, however, relied on more than knowledge in their self-management including the interaction between information and knowledge, relational support from HCPs, own experiences, and an underlying positive attitude towards living with the disease.
Conclusion: Most patients consider web-based PE to be a well-suited solution for self-management support. The opportunities of e-learning are related to information and knowledge support whereas challenges cover relational and emotional support needs. Thus, it is suggested that future organization of PE offer different forms and combinations of PE to accommodate different needs and preferences of patients throughout the disease course.

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Figure 1. The role of e-Learning and components of self-management in patients newly diagnosed with RA.

Acknowledgements: NIL.
Disclosure of Interests: Line Raunsbæk Knudsen Speakers bureau: Novartis, Eli Lily, Phizer, Kirsten Lomborg Speakers bureau: Novo Nordisk, AstraZeneca, Boehringer-Ingelheim, Ellen-Margrethe Hauge Speakers bureau: Fees for speaking and/or consulting from Novartis, AbbVie, Sanofi, Sobi, Paid instructor for: Has been principal investigator in trials by SynACT Pharma, and involved as site principal investigator in trials by AbbVie, Novartis, Novo, Sanofi., Grant/research support from: Research funding to Aarhus University Hospital from Novo Nordic Foundation, Danish Rheumatism Association, Danish Regions Medicine Grants, Roche, Novartis, AbbVie. , Heidi A. Zangi: None declared, Annette de Thurah: None declared.
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POS0076-HPR EXERCISE COMBINED WITH ACCEPTANCE AND COMMITMENT THERAPY FOR ADULTS WITH CHRONIC PAIN: A RANDOMIZED CONTROLLED TRIAL ONE YEAR FOLLOW-UP

Keywords: Physical therapy/Physiotherapy, Randomized control trial, Pain

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Background: Acceptance and Commitment Therapy (ACT) is a type of Cognitive Behavioral Therapy (CBT) that has demonstrated positive outcomes in individuals with chronic pain. There has been limited research to date investigating the efficacy of ACT when combined with physical exercise.
Objectives: The purpose of this randomized controlled trial (RCT) was to compare the effect of an 8-week combined Acceptance and Commitment Therapy (ACT) and supervised exercise program (ExACT) with a supervised exercise program for people with chronic pain at one-year follow-up. The results for 12-week follow up for this RCT have previously been published[1].
Methods: 175 people with chronic pain were randomly assigned to the ExACT or supervised exercise only group. The ExACT group completed an 8-week ACT programme with a clinical psychologist in addition to supervised exercise classes with a physiotherapist. The control group attended an 8-week supervised exercise class only. Adults (aged ≥ 18 years) with any type of chronic pain (other than cancer pain) diagnosed by a medical doctor, and who reported a score of ≥2 on the Brief Pain Inventory Interference Scale (BPI-IS) were eligible for inclusion in the study. Outcome measures including the primary outcome BPI-IS, Pain Catastrophizing Scale (PCS), Patient Health Questionnaire (PHQ 9), General Anxiety Disorder (GAD 7), Chronic Pain Acceptance Questionnaire (CPAQ) and Pain Self Efficacy Questionnaire (PSEQ) were administered at baseline, post intervention, at 12-month follow-up and 1 year following completion of the intervention. Data were analyzed using a linear mixed-effects model.
Results: No significant differences were observed between groups for the primary outcome BPI-IS at 1-year follow up. There were clinically and statistically significant improvements between groups for the PCS total scale and 3 PCS subscales ($P<0.005$) in favour of the ExACT group. Significant differences were observed within both groups at 1-year follow-up for the PHQ-9, GAD-7, and CAPQ, and in the ExACT group only for the PSEQ.
Conclusion: Long-term improvements in pain catastrophizing, and within-group improvements in pain interference and severity, suggest that exercise combined with ACT may be an effective intervention for the long-term management of chronic pain. Future studies could investigate factors that predict a response to these types of interventions with a view to enhancing treatment outcomes for people with chronic pain.

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POS0077-HPR

ENHANCING CURRENT GUIDANCE FOR PSORIATIC ARTHRITIS AND ITS COMORBIDITIES: RECOMMENDATIONS FROM AN EXPERT CONSENSUS PANEL OF HEALTHCARE PROFESSIONALS IN THE UK

Keywords: Quality of care, Best practices, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis occurring in 20–30% of patients with psoriasis.[1] Timely diagnosis is important because untreated PsA can lead to irreversible joint damage[1] and functional disability.[2] While existing national and international guidelines, such as those provided by EULAR, BSR, ACR/National Psoriasis Foundation and GRAPPA, cover a wide range of aspects of diagnosis and pharmacological management of PsA, gaps have been identified relating to the application of guidance in clinical practice, ongoing non-pharmacological management, and quality of care benchmarking, often related to a lack of evidence. In response, an expert UK consensus group aimed to enhance current guidance.

Objectives: To develop an evidence- and consensus-based set of recommendations for the management of PsA in routine clinical practice that adds value to existing guidelines, suggests minimum and best quality standards for day-to-day PsA management and provides a set of practical strategies to achieve these quality standards, with the aim of supporting clinicians.

Methods: A steering committee (SC) was formed of 12 experts in the fields of rheumatology, dermatology and primary care. At an initial meeting, consensus themes were discussed and agreed (PsA diagnosis, disease assessment, comorbidities, and management) and consensus questions were drafted. A targeted literature review of PubMed and Embase following a PICO framework was conducted to gather scientific evidence supporting a selection of the questions, while others were agreed to be more appropriate to answer using expert clinical experience. At a second meeting, recommendations were drafted in response to the identified questions, covering gaps in current guidelines. For the next stage, an extended faculty was recruited including rheumatologists (32), dermatologists (6), primary care representatives (3), specialist nurses (5), academics (12) and members of the Brit-PACT patient group [6]. In an online voting platform, the SC and extended faculty entered an agreement score for each recommendation. Consensus was achieved when 75% of respondents agreed in the range of 7–9 on a 9-point scale.

Results: The SC and extended faculty agreed on 34 statements covering 15 questions on PsA diagnosis, disease assessment, comorbidities, and management. The diagnosis theme focussed on strategies to identify PsA early and refer appropriately, the assessment of diagnostic indicators, and guidance on the use of screening tools. The use of imaging to support diagnosis, and appropriate referral time frames were also covered in detail. Recommendations on disease assessment centred on holistic consideration of disease activity, functional impairment and impact from a patient perspective, as well as how to implement shared decision-making. Specific guidance for measurements to be performed at clinic visits was included. For comorbidities, recommendations were made for assessment and management, with specific guidance for high-impact conditions, such as depression and obesity, and those with implications for PsA pharmacological therapy. Management statements (which excluded guidance on pharmacological therapies in extant guidelines) covered multidisciplinary team working, implementation of lifestyle modifications, and treat-to-target strategies built upon the parameters of greatest importance to individual patients. The use of corticosteroids was recommended to be minimised where feasible.

Conclusion: This expert consensus programme identified critical areas beyond pharmacological therapy where existing guidance on PsA management could be enhanced and be of greater practical relevance to clinicians. This work will also be developed into a clinical resource to support healthcare professionals in the care of patients with PsA.

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POS0078-HPR

INVESTIGATING THE ROLE OF BIOPSYCHOSOCIAL FEATURES IN DISEASE MANAGEMENT OF INDIVIDUALS DIAGNOSED WITH SYSTEMIC SCLEROSIS

Keywords: Mental health, Pain, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is a rare chronic rheumatic disease that causes heterogeneous clinical symptoms with involvement of the skin and internal organs. SSc causes chronic pain and fatigue in the musculoskeletal system as well as many emotional and psychological disorders that affect their functionality. Therefore, it has been reported that evaluation of biopsychosocial characteristics may be important in the disease management of these individuals (1, 2).

Objectives: The aim of this study was to investigate the role of biopsychosocial characteristics in disease management of individuals with SSc.

Methods: The study included 71 individuals who are diagnosed with SSc, and their demographic information was recorded. The Cognitive Exercise Therapy Approach-Biopsychosocial Questionnaire (BETY-BQ) is used in individuals with rheumatism as a scale developed on individuals with rheumatologic diseases and can evaluate the individual holistically. The BETY-BQ has a content that provides biopsychosocial measurement with the subheadings of pain, functionality, emotional status, sociability, sexuality, and sleep quality. Biopsychosocial characteristics of individuals were evaluated with the BETY-BQ [3]. Correlation coefficients and statistical significance were analyzed using "Spearman" correlation test.

Results: The mean age of the individuals included in the study was 50.38 ± 12.39 years. The median value of the BETY-BQ was 52 (min: 0 max: 112) and the median values of the sub-headings were as follows; pain 10 (min: 0 max: 20), functionality 12 (min: 0 max: 35), emotional status 16 (min: 0 max: 40), sociability 4 (min: 0 max: 12), sexuality 3 (min: 0 max: 8), sleep quality 3 (min: 0 max: 4). High and very high positive correlations were found between the BETY-BQ total score and all parameters, and significant positive correlations were found between the parameters themselves (p<0.005) (Table 1).

Table 1. BETY-BQ correlation coefficients of individuals with SSc

BETY-BQ (rho)	Total Score	Pain	Functionality	Emotional Status	Sociability	Sexuality	Sleep quality
Total Score	1						
Pain	0,809**	1					
Functionality	0,849**	0,581**	1				
Emotional Status	0,930**	0,795**	0,664**	1			
Sociability	0,799**	0,597**	0,556**	0,791**	1		
Sexuality	0,625**	0,360*	0,557**	0,496**	0,468**	1	
Sleep quality	0,707**	0,610**	0,573**	0,612**	0,527**	0,436**	1

*p<0,05, **p<0,001

Conclusion: According to the results of this study, it was observed that the biopsychosocial characteristics of individuals with SSc were affected by each other. Biopsychosocial status was most affected by emotional status and least affected by sexuality. It was found that pain, functionality, and sleep quality were mostly related to emotional status; sociality was most related to pain and sexuality was most related to functionality. The effect of good emotional status of individuals with SSc on other parameters was remarkable. The results were interpreted as demonstrating the need for biopsychosocial approaches focusing on biopsychosocial effects, especially emotional status, in the disease management of individuals with SSc.

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POS0079-HPR PATIENT-REPORTED OUTCOMES MEASURES FOR SYSTEMIC LUPUS ERYTHEMATOSUS: AN EXPERT DELPHI CONSENSUS TO GUIDE IMPLEMENTATION IN ROUTINE CARE

Keywords: Systemic lupus erythematosus, Patient reported outcomes

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Background: Patient-reported outcome measures (PROMs) are useful to incorporate the patient's perspective in the disease decision-making process, which has been identified as one of the main challenges in the management of Systemic Lupus Erythematosus (SLE) patients [1,2].

Objectives: To establish expert recommendations to incorporate PROMs on the current management and empowerment of patients with SLE.

Methods: After a scoping review of the literature and structured interviews with SLE patients (n=9) a survey-based questionnaires were developed by a scientific committee (5 rheumatologists, 1 H. pharmacist and 1 nurse). Using a Delphi approach, consensus was reached regarding the role of PROMs in SLE patients, strategies and more feasible measures to be incorporated in routine care.

Results: A total of 59 experts participated: 51% rheumatologist, 17% internists, 8% nephrologist, 3% dermatologist, and 20% other health professionals in rheumatology (nurses, pharmacists, and psychologists). Around 50% of participants were women, with a mean of 18 years of experience managing SLE patients. Panelists agreed on the following recommendations: incorporating the patient's perspective through the use PROMs (83%), utility of a digital tool to collect PROMs connected to the electronic medical record (85%), incorporating other health professionals to support patients to complete PROMs (77%), a multidisciplinary approach to improve specialists' interaction/coordination (79%), and incorporating H. pharmacists to improve medication management (70%). Panelists agreed that PROMs can facilitate patient participation in decision-making with an adherence to treatment improvement (72%). Consensus was reached on the appropriateness of the following PROMs in routine care: a Visual Analog Scale (VAS) 0-100 for pain (83%), fatigue (73%), and patient global assessment (76%), the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT) for fatigue (75%), and the Lupus Impact Tracker (LIT) (75%) to evaluate health-related quality of life.

Conclusion: Strategies to promote a holistic and integrated approach including the creation of multidisciplinary teams and the incorporation of patient's perspective using PROMs, such as VAS-pain, VAS-fatigue, FACIT-Fatigue, VAS-PGA and LIT, are recommended to improve SLE management in routine care.

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POS0080-HPR LONG-TERM EFFECTIVENESS OF A LIFESTYLE PROGRAM FOR RHEUMATOID ARTHRITIS: ONE-YEAR FOLLOW-UP OF THE "PLANTS FOR JOINTS" RANDOMIZED CLINICAL TRIAL

Keywords: Diet and Nutrition, Non-pharmacological interventions, Rheumatoid arthritis

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Background: The 16-week Plants for Joints (PFJ) multidisciplinary lifestyle program, based on a whole-food plant-based diet, physical activity, and stress management, significantly reduced 28-joint Disease Activity Score (DAS28) score compared to usual care in patients with rheumatoid arthritis (RA).[1,2]

Objectives: To determine the long-term effectiveness of the PFJ lifestyle program on disease activity in patients with RA.

Methods: In the PFJ assessor-blind randomized clinical trial, patients with RA and a DAS28 score ≥ 2.6 and ≤ 5.1 were randomized to receive the PFJ program in addition to usual care, or the control group which received usual care. After this 16-week period the control group also received the PFJ program. After completion of the PFJ program all participants were followed-up for one year with biannual visits and 6 adherence-promoting webinars. If participants had a DAS28 score <2.6 they were instructed to taper anti-rheumatic medication following a pre-specified protocol. Medication changes were assessed at one year as an "increase," "stable," or "decrease" compared to baseline by an independent committee. Secondary outcomes included anthropometric and metabolic markers. A paired sample T-Test between 1-year follow-up and start of intervention was performed.

Results: Of 77 participants who completed the initial 16-week clinical trial 92% were female with a mean (SD) age of 55 (12) and body mass index of 26 (4) kg/m² at baseline. The 65 (84%) participants who completed the one-year follow-up had a greater average change in DAS28 score (–0.9 vs. –0.05) compared to non-completers. In the year after completing the PFJ program the DAS28 score continued to improve slightly whereby a mean 1.01-point difference was observed after one year for the completed cases compared to baseline values (95% CI 0.76 to 1.26; $p < 0.001$) (Figure 1). All components of the DAS28 improved significantly compared to before the program (Table 1). Significant improvements were found in both the seropositive and seronegative subgroups. Of the 61 participants using anti-rheumatic medication at baseline, 27 (44%) were able to decrease the dosage or stop one or more medications. Antirheumatic medication was stable for 16 participants, and increased for 13, of which 5 newly started using medication. 45 participants (58%) had improved DAS28 scores (of which 20 had a DAS28 <2.6) with stable or less medication compared to baseline. After the 1-year follow-up period there was no longer a significant difference in weight or HbA1c although LDL cholesterol remained significantly lower compared to baseline.

Conclusion: The PFJ lifestyle program significantly decreased disease activity in patients with RA and its effects were sustained until one year after program completion, with slightly less anti-rheumatic medication. Metabolic benefits found after the lifestyle intervention were only partially sustained possibly indicating attenuated adherence to the lifestyle program in the 1-year follow-up.

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Table 1. Plants for Joints cohort at start and end of the 4-month intervention period and during the 1-year follow-up (6 and 12 months after completing the intervention) for completed cases (n = 65). Variables reported as mean or number [% of all participants (*n* = 77)]. Mean difference between start of intervention and end of follow-up. ESR = erythrocyte sedimentation rate.

	Intervention	Follow-up study				
	Start	End	6 months	12 months	Mean difference (95% CI)	*p*-value
DAS28	3.86	2.94	2.66	2.84	–1.01 (–1.26 to –0.76)	<0.001
Swollen joint count	2.1	1.4	1.2	1.1	–1.1 (–1.8 to –0.4)	0.003
Tender joint count	3.9	1.8	1.3	2.2	–1.9 (–2.7 to –1.0)	<0.001
General health (VAS)	47.9	27.5	26	24.9	–23.6 (–29.8 to –17.3)	<0.001
ESR (mm/hour)	20.5	18.5	16.5	16.5	–3.9 (–7.4 to –0.4)	0.03
DAS28 <2.6		27 [35]	28 [36]	25 [33]		
Weight (kg)	75.2	71.8	73.2	74.2	–0.5 (–1.6 to 0.6)	0.3
LDL cholesterol (mmol/l)	3.1	2.7	2.8	2.9	–0.2 (–0.35 to –0.01)	0.04
HbA1c (mmol/mol)	36.9	35.9	36.9	36.5	–0.3 (–1.1 to 0.4)	0.3

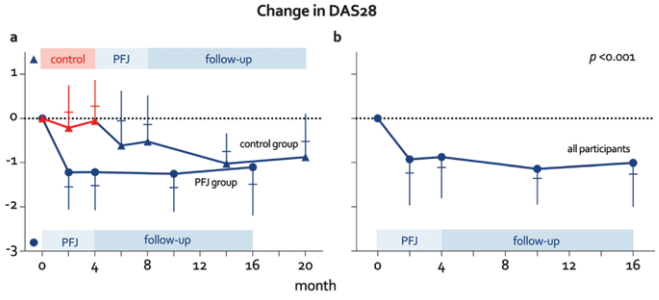


Figure 1: Mean change in DAS28 (a) during the randomized controlled trial phase and one-year follow-up period per trial arm and (b) for both trial arms before and after completing the lifestyle intervention and one year follow-up.

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POS0081-HPR

PATIENTS' PERCEPTIONS OF LIFESTYLE INTERVENTIONS IN EARLY RHEUMATOID ARTHRITIS – A QUALITATIVE STUDY

Keywords: Rheumatoid arthritis, Lifestyles, Qualitative research methods

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Background: Patients with early rheumatoid arthritis (RA) benefit from combining pharmacological and non-pharmacological interventions to prevent damage to cartilage and bone, relieve symptoms, and improve or normalize physical function, quality of life, and social and work capacity. Healthy lifestyle habits, including regular physical activity, a healthy diet, and smoking cessation can lower the increased risk of cardiovascular diseases and improve symptoms and quality of life in patients with RA. In addition, smoking and alcohol may interfere with anti-inflammatory medication, which is why lifestyle interventions are essential in managing patients with early RA. According to international and national recommendations, healthcare professionals are expected to discuss healthy lifestyle habits with all patients with inflammatory arthritis [1]. Despite this, the effect of lifestyle discussions and how patients perceive lifestyle interventions in rheumatology care are scarcely studied.

Objectives: To explore how patients with early RA perceive lifestyle interventions in rheumatology care.

Methods: In this explorative qualitative study, 18 patients with RA followed at an early RA clinic with tight control by a rheumatologist and a rheumatology nurse during the first 2 years, were included. This also included a multidisciplinary team contact with a physiotherapist and an occupational therapist 8-12 weeks after treatment initiation and, if needed, a social worker and additional contacts with the team. Individual interviews were conducted with 12 women and 6 men, aged 23 to 74, with a disease duration of 2-3 years at the time of the interview. The main question was: "Can you tell me about your perceptions of lifestyle interventions in rheumatology care?" The interviews were analyzed with latent qualitative content analysis (2), and three categories and an overarching theme emerged (Table 1).

Results: Patients perceived that lifestyle interventions in rheumatology care enable self-management in early RA. The usefulness of lifestyle interventions was perceived to depend on personal preferences of lifestyle support and prioritization of lifestyle interventions. The design of lifestyle interventions should be based on a person-centred approach, patient education, and recurrent lifestyle support. To promote healthy lifestyle habits, the outcome of lifestyle interventions should contribute to the knowledge of healthy lifestyle habits, motivation for lifestyle changes, and empowerment in patients with early RA.

Conclusion: Patients perceived that the usefulness, design, and outcome of lifestyle interventions in rheumatology care are essential when enabling self-management in patients with early RA.

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Table 1. Overview of the overarching theme, categories, and sub-categories describing patients' perceptions of lifestyle interventions in rheumatology care

Overarching theme	**Lifestyle interventions in rheumatology care enable self-management in early RA**		
Categories	**The usefulness of lifestyle interventions**	**The design of lifestyle interventions**	**The outcomes of lifestyle interventions**
Sub-categories	Personal preferences for lifestyle support	Person-centred approach	Knowledge of healthy lifestyle habits
	Prioritization of lifestyle interventions	Patient education	Motivation for lifestyle changes
		Recurrent lifestyle support	Patient empowerment

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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All about Crystal arthritis I

POS0082

APPLICATION OF THE NEW 2022 ACR/EULAR CLASSIFICATION CRITERIA FOR CALCIUM PYROPHOSPHATE DEPOSITION DISEASE (CPPD) IN A COHORT OF PATIENTS DIAGNOSED WITH SERONEGATIVE RHEUMATOID ARTHRITIS

Keywords: Crystal Arthritis, Descriptive Studies, Rheumatoid arthritis

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Background: The ACR/EULAR group released the first-ever provisional classification criteria for calcium pyrophosphate deposition disease (CPPD) at the ACR congress in November 2022. These criteria are based on an adjusted domain scoring system including demographic, clinical and radiological characteristics, and synovial fluid crystal analysis. The differential diagnosis in CPPD must be made with rheumatoid arthritis (RA) and monosodium urate crystal deposition disease.
Objectives: To study the percentage of patients diagnosed with seronegative RA who meet the new 2022 ACR/EULAR classification criteria for CPPD (final score ≥57). To determine the clinical and demographic differences between patients with a diagnosis of seronegative RA who meet or not the classification criteria for CPPD.
Methods: An observational retrospective cross-sectional study was performed including all the patients from a monographic RA clinic between September and December 2022. Demographic, clinical, analytical and imaging variables (simple radiology and ultrasound) were collected. The 2022 ACR/EULAR provisional classification criteria for CPPD were applied.
Results: Overall, 364 patients with RA were identified and those with seropositivity for RF and/or ACPAs were excluded. A total of 96 (24.4%) patients were included, 74.7% females, with a mean age at onset of symptoms of 59.3 (±16.4) years and 8.35 years of disease duration. A total of 18 patients (18.9%) met the classification criteria for CPPD. The characteristics and differences between the patients who met or not the criteria are shown in Table 1. The patients who met the CPPD criteria were older (p=0.048) and had a different clinical presentation (p=0.010) relating to the time-course of inflammatory arthritis (persistent, 1 typical episode, >1 typical episode, others). No significant differences were observed between groups in the location of joint clinical involvement. There was a statistically significant association (p=0.000) between the presence of radiological chondrocalcinosis (CC) and the fulfillment of criteria for CPPD, being detected in 66.6% of patients with CPPD versus none with seronegative RA without CPPD. Similarly, there was a significant association (p=0.000) between osteoarthritis in typical locations for CPPD (bilateral radiocarpal, scaphoid/trapezium/trapezoid without rhizarthrosis, 2nd and 3rd MCF) and compliance with criteria for CPPD, being detected in 55.5% of patients with CPPD. A higher prevalence of erosions was detected in patients with CPPD (44.4%) versus seronegative RA without CPPD (27.3%), without statistical significance. No significant treatment differences were observed in both subgroups. Of the patients with criteria for CPPD, 74% were being treated with synthetic of biological disease modifying antirheumatic drugs (DMARDs).

Table 1. Characteristics of the sample according to the fullfilment or not of the new 2022 ACR/EULAR classification criteria for CPPD.

	Total (n=95)	Seronegative RA with CPPD* (n=18)	Seronegative RA without CPPD (n=77)	p
Female gender, n (%)	71 (74.7%)	16 (88.8%)	55 (71.4%)	0.142
Age at onset (years), p50	63	69.5	61	**0.048**
Disease duration (years), p50	7	6	7	0.952
Time-course, n (%)				**0.010**
- Persistent arthritis	38 (40%)	4 (21.1%)	34 (44.5%)	
- 1 typical episode	0 (0%)	0 (0%)	0 (0%)	
- >1 typical episode	39 (41.1%)	13 (72.2%)	26 (33.8%)	
- Others	18 (18.8%	1 (5.3%)	17 (22.1%)	
Erosions, n (%)	29 (30.5%)	8 (44.4%)	21 (27.3%)	0.091
Treatment, n (%)				0.854
Prednisone	21 (21.9%)	4 (21.1%)	17 (22.1%)	
sDMARD	45 (46.9%)	10 (52.6%)	35 (45.5%)	
bDMARD	19 (20%	3 (16.6%)	4 (20.8%)	
Combination therapy	10 (10.4%)	1 (5.3%)	9 (11.7%)	

Conclusion: A total of 18 (18.9%) patients with seronegative RA from a monographic RA unit met the new 2022 ACR/EULAR provisional classification criteria for CPPD. Age at diagnosis and clinical presentation were different between patients with RA who met criteria for CPPD and those who did not.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0083

A SYSTEMATIC LITERATURE REVIEW INFORMING THE EULAR RECOMMENDATIONS FOR THE USE OF IMAGING IN CRYSTAL-INDUCED ARTHRITIS IN CLINICAL PRACTICE

Keywords: Gout, Crystal Arthritis, Imaging

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Background: The increased availability of imaging techniques has led to their more extensive use in rheumatological practice. In the context of crystal-induced arthritis (CiA), evidence-based recommendations for their use are lacking.
Objectives: To systematically assess current literature regarding the use of imaging in CiA.
Methods: After the identification of the areas of interest and 14 research questions for the application of imaging in CiA, we performed 4 separate systematic literature searches (per disease and per indication) in Embase, Medline, and Central regarding the use of imaging for the diagnosis, monitoring and prediction of outcome and treatment effects of gout, calcium pyrophosphate dihydrate crystal deposition disease (CPPD) and basic calcium phosphate/hydroxyapatite crystal deposition disease (BCPD), as well as for guiding intra-articular procedures and patient education. Titles and abstracts were screened, the full-text of the eligible articles were reviewed and data of the included studies were extracted. Risk of bias was assessed validated instruments based on study type.
Results: The overview of the included studies for each research question and imaging modality is shown in Table 1. For gout, out of 2915 studies, 88 studies were finally included (table 1, figure 1). The majority of diagnostic studies reported good to excellent (≥80%) sensitivity and specificity of DECT and US for diagnosis. Conventional radiographs (CR) and computed tomography (CT) showed high specificity but lower sensitivity in most studies. The majority of the follow-up studies showed a significant change of crystal deposition by US and DECT and inflammatory signs by US. An increase of structural damage was shown in some studies by CR and CT, mainly after a follow-up of at least 2 years. For CPPD, out of 687 studies, 50 studies were included (table 1, figure 1). Diagnostic studies on CR and US generally showed high specificity in all joints, in particular wrists and knees, while sensitivity was more variable, but generally high. There was a single study on monitoring, while 9 studies assessed the prognostic role of CPPD on CR and MRI in patients with OA, with contradicting results. Evidence on the application of DECT was scarce. For BCPD/HADD, out of 1389 abstracts, 55 studies were included (table 1, figure 1). There were 2 diagnostic studies, one on CR, reporting good performance, and one on MRI, with suboptimal performance. The utility of imaging in monitoring was assessed in 43 studies, mostly on CR and US of the shoulder, the majority reporting a reduction in the size of deposits, while 12 studies with contrasting results assessed the role of CR, US and MRI for prediction of treatment response. The search on patient education retrieved 254 studies, of which 2 could be included, which suggest a potential role of DECT in patient education. No studies on the role of imaging to guide procedures in CiA could be included in the final review (table 1, figure 1).
Conclusion: The present SLR has provided background evidence for the development of EULAR recommendations on the use of imaging in CiA in clinical practice.

Table 1. Overview of the included studies for each research question and imaging modality.

	Number of included studies						
	CR	US	MRI	DECT	CT	Other*	Total**
Gout							
RQ1- diagnosis	7	23	0	28	3	1	45
RQ2- monitoring	7	12	1	11	3	0	30
RQ3- prediction of outcome	2	0	0	0	0	0	2
RQ4- prediction of treatment effect	0	3	0	1	0	0	3
CPPD							
RQ5- diagnosis	23	26	2	3	6	0	44
RQ6- monitoring	1	0	0	0	0	0	1
RQ7- prediction of outcome	9	0	0	0	0	0	9
RQ8- prediction of treatment effect	0	0	0	0	0	0	0
BCPD							
RQ9- diagnosis	1	1	1	0	0	0	3
RQ10- monitoring	38	7	0	0	0	0	45
RQ11- prediction of outcome	0	0	0	0	0	0	0
RQ12- prediction of treatment effect	9	5	1	0	0	0	15
IMAGING-GUIDED PROCEDURES							
RQ13- guiding aspiration	0	0	0	0	0	0	0
PATIENT EDUCATION							
RQ14- patient education	0	0	0	2	0	0	2

* Sheer wave elastography**Some studies assessed multiple imaging modalities

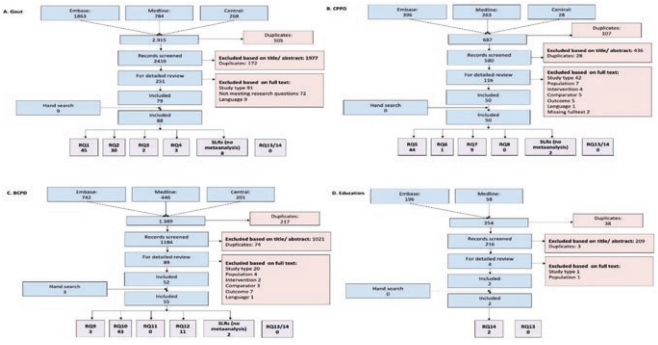


Figure 1. Flow chart

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POS0084

THE NOMENCLATURE OF CALCIUM PYROPHOSPHATE DEPOSITION (CPPD) DISEASE – RESULTS OF A SYSTEMATIC LITERATURE REVIEW FOR THE GOUT, HYPERURICEMIA AND CRYSTAL-ASSOCIATED DISEASE NETWORK (G-CAN) CPPD NOMENCLATURE PROJECT

Keywords: Crystal Arthritis, Descriptive Studies, Systematic review

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Background: Despite prior attempts at standardising terminology of calcium pyrophosphate deposition (CPPD) disease (including the 2011 EULAR recommendations for CPPD terminology), many different terms are still used interchangeably to describe the disease, its elements, and its states (Tedeschi SK, Curr Rheumatol Rep 2019). This confusing nomenclature has important implications for research and for patient care. The G-CAN has developed a CPPD Nomenclature Project which aims to achieve international consensus about the nomenclature of CPPD.

Objectives: In this first step of the project, the aim was to identify the definitions, the disease elements and the clinical states of CPPD and their corresponding labels in the scientific literature.

Methods: A systematic literature search was performed in the PubMed database starting from 01/01/2000 to 31/01/2022. The search was restricted to studies on humans and in English language. Eight reviewers independently extracted terms related to disease definition, aetiology, pathogenesis, clinical presentation, imaging features and clinical states of CPPD. An *a priori* list of disease elements and clinical states was generated by the authors and further elements were added during data collection as appropriate. Labels for each identified disease element and clinical state were extracted and analysed to determine their frequency. An additional analysis was performed to evaluate the uptake of the 2011 EULAR recommendations on CPPD terminology after 2011.

Results: A total of 2392 articles were identified using the search criteria. We preliminarily evaluated 623 articles of which 246 were included. The list of evaluated elements is showed in **Figure 1**. There was great inconsistency in the terminology used for the disease, its elements and its states. The 3 most common labels used to identify the disease were "pseudogout", "calcium pyrophosphate deposition disease" and "chondrocalcinosis". The most common acronym used was "CPPD", mostly with the meaning of "calcium pyrophosphate deposition disease" or "calcium pyrophosphate deposition" (**Table 1**). The 2 most commonly used labels describing "an episode of acute CPPD arthritis" were "pseudogout" (31%), and "acute calcium pyrophosphate crystal arthritis" (10%). For "more than one episode of acute CPPD arthritis", "recurrent pseudogout" (17%) or "recurrent arthritis" (10%) were the most used labels. "Chronic calcium pyrophosphate crystal arthritis" (13%) and "pseudo-rheumatoid arthritis" (11%) were the most commonly used labels to describe "persistent inflammatory arthritis due to CPPD". The most used labels used to identify "osteoarthritis with evidence of CPPD" were "pseudo-osteoarthritis" (11%) and "calcium pyrophosphate crystal deposition with osteoarthritis" (9%). The use of "pseudo-form" labels mostly occurred before the 2011 EULAR recommendations.

Conclusion: These preliminary results demonstrate the variability and lack of precision in the labels used to describe CPPD disease. The next steps of the project will be to achieve agreement about CPPD disease nomenclature through a Delphi exercise and consensus meeting, and to develop an easily understandable common language definition to facilitate communication with patients.

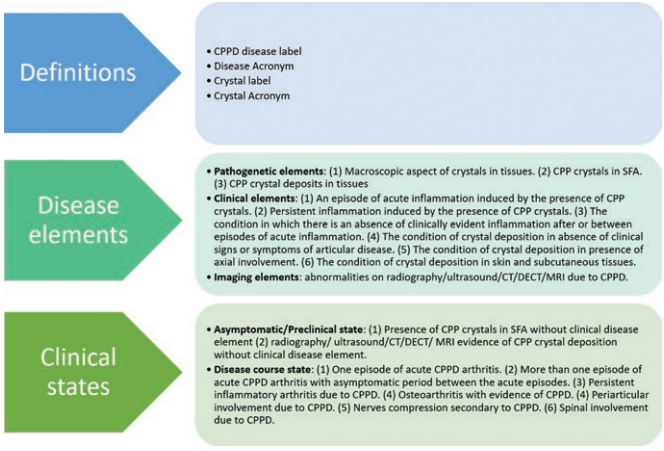


Figure 1. List of definitions, disease elements and clinical states

Table 1. Example of labels extracted for calcium pyrophosphate deposition disease

Element	Label	Frequency
CPPD disease label	Pseudogout	28%
	Calcium pyrophosphate deposition disease	14%
	Chondrocalcinosis	14%
	Calcium pyrophosphate dihydrate deposition disease	9%
	Calcium pyrophosphate dihydrate crystal deposition disease	7%
	Other	28%
Acronym	CPPD	68%
	CPDD	11%
	CC	9.4%
	CPPD-CDD	2.4%
	CPPDD	1.6%
	Other	7.6%
Acronym meaning	Calcium pyrophosphate deposition disease	26%
	Calcium pyrophosphate deposition	19.7%
	Calcium pyrophosphate dihydrate deposition disease	9.4%
	Calcium pyrophosphate crystal deposition	9.4%
	Chondrocalcinosis	9.4%
	Other	26%

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Acknowledgements: NIL.
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POS0085

MICROSCOPIC AND ULTRASONOGRAPHIC EXAMINATION OF CRYSTAL RELATED ARTHRITIS IN PATIENTS WITH KNEE EFFUSION

Keywords: Ultrasound, Crystal Arthritis

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Background: Routine search for crystals is recommended in all synovial fluid (SF) aspirates from undiagnosed arthritis. Definitive diagnosis of crystal related arthritis (CRA) is based on identification of crystals in SF. However, SF analysis is sometimes difficult to perform. Therefore, assessment of imaging techniques can be useful. In the latest recommendations for the diagnosis and management of CRA, the diagnostic potential of ultrasound (US) has been recognized[1,2].
Objectives: The aim of this study was to evaluate the contribution of ultrasonography to the SF analysis, which should be performed routinely in patients with knee effusion to exclude infection and to detect CRA.
Methods: Patients, in outpatient clinic, above 18 years of age with unilateral knee effusion were included. Ultrasonography of the involved knees were performed in all patients after the evaluation and physical examination. In ultrasonographic examination; hyperechoic bands within the femoral hyaline cartilage (sandwich appearance) and/or hyperechoic sparkling spots in meniscal fibrocartilage (meniscus calcification) were considered indicative of Calcium pyrophosphate deposition disease (CPPD); in addition, hyperechoic spots in the effusion and tendon calcifications were recorded. Ultrasonography guided synovial fluid aspiration was performed. The sample was examined macroscopically and microscopically. Then, radiographic evaluations were done for searching chondrocalcinosis.
Results: Eighty-five patients (56 F,29 M) with unilateral knee effusion were evaluated. Mean age was 60.98 ±11,95 years. CPPD was diagnosed with detecting calcium pyrophosphate (CPP) crystals in synovial fluid analysis in 15 of 85 patients. Two of these patients had previous diagnosis of rheumatoid arthritis (RA), 1 spondyloarthritis, 1 gout and 11 osteoarthritis. Of the remaining 70 patients, 1 was considered as spondyloarthritis, 4 as RA and 65 as exacerbation of osteoarthritis. The detection of CPP crystal in the microscopic examination was accepted as the gold standard for the diagnosis of CPPD, sensitivity and specificity values were 93.33% and 80% for ultrasonography, 46.67% and 98.57% for radiography, respectively (Table 1). Inter-rater agreement for US was found to be 93.3% (kappa value: 0.81; very good agreement) with the evaluation of 40 patients separately by two physicians. Intra-rater agreement for US was found to be 96.67% (kappa value: 0.83; very good agreement) when the recorded images were re-evaluated.
Conclusion: When crystal related arthritis is suspected especially in elderly patient with knee effusion, ultrasonography found as a useful diagnostic method in clinical practice because it is highly sensitive and specific in determining crystal accumulations.
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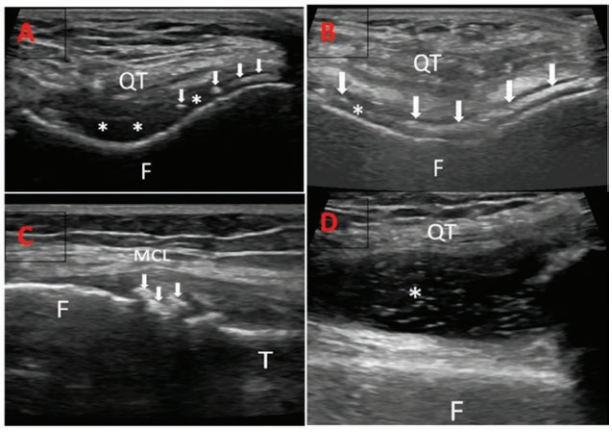


Figure 1. Ultrasound images. Knee. A and B. Sandwich appereance (arrows). C. Meniscus calcification (arrows). D. Hyperechoic spots in the effusion (asterix). F femur, T tibia, QT quadriceps tendon, MCL medial collateral ligament

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Disclosure of Interests: None Declared.
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POS0086

A TRANSVERSAL STUDY OF 826 UNTREATED GOUT PATIENTS SHOWS THAT ECHOGENICITY OF THE RENAL MEDULLA INCREASES WITH GOUT DURATION/SEVERITY AND STEROID USE

Keywords: Kidneys, Gout, Ultrasound

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Background: Diffuse hyperechogenicity of the kidney pyramids, detected by kidney ultrasound (US) scan, has been reported as a frequent finding in severe, untreated, tophaceous gout. It seemed related to crystal deposition in the renal medulla and correlated with kidney function decrease, reviving the concept of gouty microcrystalline nephropathy [1].
Objectives: To confirm this finding and to detect its progression with gout duration.
Methods: Patients fulfilled the ACR/EULAR criteria, were not treated by urate-lowering drugs (ULD) at the time of examination; 44 % had received short courses of ULD in the past. They underwent kidney US scans by an experienced radiologist, who classified each kidney into 3 grades according to the presence and degree of hyperechogenicity of the renal pyramids, as compared to the renal cortex. Grade 0 was defined as no medulla hyperechogenicity; grade 1 by the observation of hyperechogenic spots in 1 or 2 renal pyramids; grade 3 as a diffuse hyperechogenicity of at least 3 pyramids (out of 5 scanned). Demographic variables, comorbidities, gout and biochemical features were retrieved from electronic files. US scans of the

Table 1. Ultrasound and conventional radiology diagnostic test properties for the detection of CPP crystals using synovial fluid analysis as the reference method

		Synovial fluid analysis: CPP crystals		P	Sensitivity,%	Specificity, %	PPV,%	NPV, %	Accuracy, %
		Negative	Positive						
		n	n						
US: sandwich appearance	**Negative**	60	4	<0.001	73.33	85.71	52.38	93.75	83.52
	Positive	10	11						
US: meniscus calcification	**Negative**	64	5	<0.001	66.67	91.43	62.50	92.75	87.05
	Positive	6	10						
US: sandwich appearance or meniscus calcification	**Negative**	56	1	<0.001	93.33	80	50	98.25	82.35
	Positive	14	14						
Conventional radiology: chondrocalcinosis	**Neagative**	69	8	<0.001	46.67	98.57	87.50	89.61	89.41
	Positive	1	7						

PPV: Positive predictive value, NPV:: Negative predictive value, CPP: Calcium pyrophosphate, US: Ultrasound

MTP joints allowed gradation of double contours from 0 to 3. Links between patients 'features and renal medulla staging were assessed by Fisher exact or Kruskall and Wallis tests according to the type of variables. Multivariable analysis included all statistically significant features, with model selection on p.value using a proportional odds logistic regression model. All test were two-sided.

Results: 826 consecutive new patients were included from August 1 to December 24, 2022. 88 % were males, median age was 49 years, median BMI 24.22kg/m^2, median gout duration 5 years, 70 % of patients had clinical tophi, median uricemia was 488,6 µmol/l, median creatininemia 83.5 mmol/l, median eGFR 93ml/min. Both kidneys were classified at the same grade in every all patients. 65.5% of patients were at grade 0, 17.8 % at grade 1 and 16.7 % at grade 3. Table 1 shows links of the extent of medulla hyperechogenicity with patients 'features. By multivariable analysis, positive correlation was found with male sex, hypertension, gout duration, tophi, double contours and uricemia; BMI, eGFR and cortilsolemia negatively correlated.

Conclusion: Hyperechogenicity of the renal medullas progressively increased with gout duration, MSU deposition and steroid treatment, and associated with decrease of renal function and hypertension. These observations reinforce the early indication of ULDs in gouty patients.

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Table 1. Main features of gouty patients by grades of medulla hyperechogenicity

	Grade 0 n = 541	Grade 1 n = 147	Grade 2 n = 138	p value	p.value Multi
Age (y) median [IQR]	47 [38, 56]	51 [44, 59]	54 [45, 62]	<0.001	
Males n (%)	441 (81.7)	147 (100.0)	138 (100)	<0.001	<0.001
BMI (kg/m^2) median [IQR]	24.4 [22.5, 26.7]	24.1 [22.5, 26.1]	23.3 [21.2, 25.8]	0.003	<0.001
Hypertension n (%)	145 (26.8)	54 (36.7)	88 (63.8)	<0.001	0.006
CHD n (%)	6 (1.1)	7 (4.8)	7 (5.1)	0.003	
Type 2 diabetes n (%)	62 (11.5)	17 (11.6)	27 (19.6)	0.04	
Gout duration (y) median [IQR]	4 [2, 7]	7 [4, 11]	11 [8, 17]	<0.001	<0.001
Tophi n (%)	298 (55.1)	14 (95.9)	137 (99.3)	<0.001	<0.001
Urinary stone n (%)	23 (4.3)	18 (12.2)	13 (9.4)	0.001	
SUA (umol/l) median [IQR]	437 [322, 548]	533 [432, 602]	558 [493, 618]	<0.001	<0.001
Creatininemia (mmol/l) median [IQR]	81 [67, 92]	87 [76, 106]	93 [79, 107]	<0.001	
eGFR > 60 ml/min n (%)	506 (93.5)	128 (87.1)	112 (81.2)	<0.001	
Maximum double contours				<0.001	<0.001
0 n (%)	17 (34.1)	0 (0.0)	0 (0.0)		
Thin n (%)	86 (20.7)	8 (5.4)	1 (0.7)		
Medium n (%)	306 (73.6)	114 (77.6)	66 (47.8)		
Thick n (%)	7 (1.7)	25 (17.0)	71 (51.4)		
8 am cortisol median [IQR]	7.55 [3.58,10.33]	6.60 [1.95,10.72]	1.91 [0,59,8.06]	<0.001	0.005

y: years; IQR: interquartile range; BMI: body mass index; CHD: coronary heart disease; eGFR estimated glomerular filtration rate (MDRD)

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0087

ADHERENCE TO EULAR SERUM URATE MONITORING GUIDELINES AMONGST OLDER ADULTS WITH GOUT IN ONTARIO, CANADA: A POPULATION-BASED STUDY

Keywords: Quality of care, Gout, Crystal Arthritis

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Background: Serum urate (SUA) monitoring plays an important role in the treat-to-target recommendations of gout. Adherence to SUA monitoring recommendations after initiation of urate lowering therapy (ULT) is unknown.

Objectives: We assessed the proportion of older adults with gout undergoing SUA testing 6-months after ULT initiation and associated patient and physician-level factors.

Methods: This population-based retrospective cohort study identified patients aged ≥ 66 with gout and newly dispensed ULT between January 1, 2010 and March 31, 2019 from physician billing and pharmacy claims data in Ontario, Canada. We characterized the proportion of patients that received SUA testing within 6-months after ULT dispensation. Multi-level logistic regression clustered by ULT prescriber evaluated factors associated with SUA monitoring by 6-months including patient, prescriber characteristics, prescription information and health-care usage factors.

Results: 44,438 patients with mean (SD) age of 76.0 (7.3) years and 64.4% males were included. Family physicians prescribed 79.1% of all ULTs. SUA testing was lowest in 2010 at 56.4% and rose over time to 71.3% in 2019 (p <0.0001). By 2019, SUA monitoring was highest amongst rheumatologists (93.9%) and lowest amongst family physicians (67.4%) (Figure 1). Compared with rheumatologists, family physicians (OR 0.26, 95% CI: 0.23–0.29), internists (OR 0.34, 95% CI: 0.29–0.39), nephrologists (OR 0.37, 95% CI: 0.30–0.45) and other specialties (OR 0.25, 95% CI: 0.21–0.29) were less likely to test SUA, as were male physicians (OR 0.87, 95% CI: 0.83–0.91). Patient factors associated with lower odds of SUA monitoring included: rural residence (OR 0.81, 95% CI: 0.77–0.86), lower socioeconomic status (OR 0.91, 95% CI: 0.85–0.97) and patient comorbidities. Correlates of SUA monitoring included: chronic kidney disease (OR 1.40, 95% CI: 1.32–1.49) hypertension (OR 1.11, 95% CI: 1.04–1.18), diabetes (OR 1.17, 95% CI: 1.12–1.22) and co-prescription of colchicine/oral corticosteroids (OR 1.31, 95% CI: 1.23–1.40) (Table 1).

Conclusion: While most gout patients under rheumatology care were adherent to EULAR monitoring recommendations, at the population-level, SUA monitoring is suboptimal amongst older adults with gout initiating ULT but improving over time. ULT prescriber, patient and prescription characteristics affected SUA monitoring. These findings suggest care variations and the need to mobilize quality improvement activities in chronic gout management.

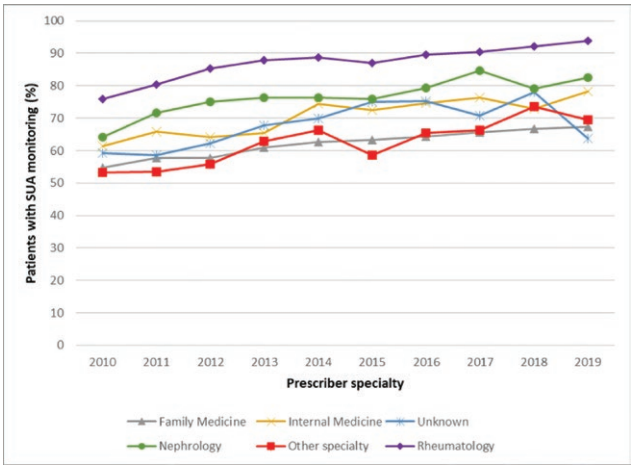


Figure 1. The proportion of patients with SUA testing within 6-months after index ULT dispensation stratified by prescriber primary specialty

Table 1. Logistic regression analysis for factors and their association with SUA testing within 6 months after starting ULT

Characteristics	Odds Ratio (95% CI)
Prescriber	
Age < 45 years (referenced to age ≥65)	1.02 (0.96, 1.09)
Age 45 to 64 years (referenced to age ≥65)	1.02 (0.97, 1.08)
Male	0.87 (0.83, 0.91)
Gout practice volume (referenced to top quartile)	
1	1.05 (0.98, 1.12)
2	1.06 (0.99, 1.13)
3	1.06 (0.99, 1.12)
Specialty (referenced to rheumatologist)	
Family physician	0.26 (0.23, 0.29)
Internist	0.34 (0.29, 0.39)
Nephrologist	0.37 (0.30, 0.45)
Other	0.25 (0.21, 0.29)
Patient	
Age (by 1 year)	0.99 (0.99, 1.00)
Male	0.99 (0.95, 1.04)
Income quintile (referenced to highest)	
1 (lowest)	0.91 (0.85, 0.97)
2	0.93 (0.88, 1.00)
3	0.88 (0.82, 0.94)
4	0.99 (0.93, 1.06)
Rural residence (referenced to urban)	0.81 (0.77, 0.86)
Chronic kidney disease	1.40 (1.32, 1.49)
Hypertension	1.11 (1.04, 1.18)
Diabetes	1.17 (1.12, 1.22)
COPD	0.94 (0.90, 0.99)
Prior cardiovascular event	0.85 (0.79, 0.91)
Nephrolithiasis	1.06 (0.92, 1.22)
Cancer	0.94 (0.83, 1.05)
Calendar year of ULT prescription (referenced to 2010-2014)	

2015-2019	1.26 (1.21, 1.31)
Co-prescription of colchicine/oral corticosteroid	1.31 (1.23, 1.40)
ULT dose (referenced to allopurinol ≤ 50 mg daily)	
Allopurinol 51-100 mg	0.72 (0.61, 0.84)
Allopurinol >100 mg	0.55 (0.47, 0.65)
Febuxostat	0.57 (0.34, 0.97)
Probenecid	0.43 (0.27, 0.70)
ED visits for gout (referenced to 0)	
1	1.00 (0.94, 1.07)
≥2	0.91 (0.81, 1.04)
Presence of primary care physician	1.18 (0.93, 1.49)

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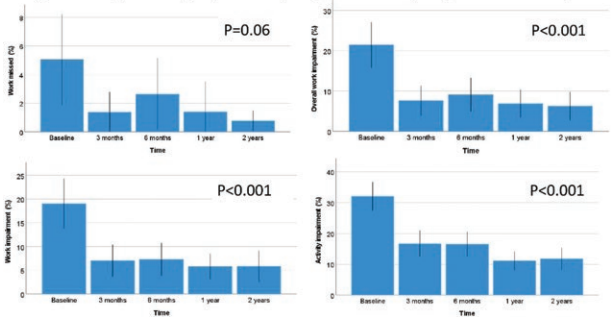
POS0088 WORK PRODUCTIVITY IN GOUT – RESULTS FROM THE NOR-GOUT LONGITUDINAL 2-YEAR TREAT-TO-TARGET STUDY

Keywords: Work-related issues, Crystal Arthritis, Epidemiology

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Background: Gout causes pain and reduced health related quality of life. There are no longitudinal studies on work productivity in patients who are being treated-to target for their serum urate in clinical practice.
Objectives: We examined whether work productivity in gout patients changed over 2 years after intensive treatment with ULT, and if disease related factors could predict changes in work productivity.
Methods: Patients with crystal-proven gout and a recent gout flare and increased serum urate (sUA) level (>360 µmol/L) were consecutively included in the NOR-Gout observational study [1]. They were treated to target with an educational intervention by a study nurse and escalating urate lowering medication (allopurinol or febuxostat) with frequent control visits to achieve low serum urate at target. Work productivity and activity impairment were assessed using the Work Productivity Activity Index (WPAI) questionnaire at baseline, after 3 months, 6 months, 1 and 2 years. The WPAI consists of six questions to determine employment status during the last 7 days: hours missed from work due to the disease; hours missed from work for other reasons; hours worked, the degree to which the disease affected work productivity while at work; and the degree to which the disease affected activities outside of work. Four scores were derived: percentage of missed work (absenteeism), percentage of impaired productivity while at work (presenteeism), overall work impairment that combines absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. Greater scores indicate greater impairment. Questions related to absenteeism and presenteeism were applicable only for patients who were working. Other assessments included clinical, demographic and lifestyle variables, and questionnaires, comorbidities from the Self-Administered Comorbidity Questionnaire, pain, physical function from the Health Assessment Questionnaire (HAQ), SF-36 physical and mental components, self-efficacy, and the Beliefs about Medicines Questionnaire (BMQ) with subscales of beliefs in harm, overuse, necessity, and concerns about medication. Descriptive statistics used ANOVA, and linear regression model after logarithmic transformation of the 4 WPAI outcomes. Final regression models were also adjusted for baseline, age, gender, disease duration and comorbidities.
Results: Patients were predominantly male (95%) with mean age 56.4 years (SD 13.7 years) and disease duration almost 8 years, 17% had subcutaneous tophi. At baseline 64.4 % were working, 64.0% at year one and 61.3% after 2 years. sUA was at target <360µmol/L in 85% after one and 79% after 2 years, while a flare was experienced by 81% and 26% during year 1 and year 2, respectively. WPAI scores were at baseline: 5.0% work missed, 19.1% work impairment, 21.4% overall work impairment and 32.1% activity impairment (Figure 1). Scores were at 3 months, after the recent flare leading to inclusion into the study, improved and remained then stable over 2 years. Baseline assessments of work productivity, comorbidities as well as concerns about medication independently predicted changes in work productivity outcomes at 1 year.
Conclusion: In patients with gout who were intensively treated to the sUA target, work productivity and activity impairment were largely unchanged over 2 years and at 1 year and were predicted by comorbidities and patient concerns about medication.
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Figure 1 Work productivity impact index (WPAI) scores over 2 years (means and 95% CI)



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Disclosure of Interests: Till Uhlig Consultant of: Grünenthal, Novartis, Lars Fridtjof Karoliussen: None declared, Joe Sexton: None declared, Sella Aarrestad Provan Consultant of: Böhringer Ingelheim, Tore K. Kvien Consultant of: AbbVie, MSD, UCB, Hospira/Pfizer, BMS, Sanofi, Celltrion, Sandoz, Amgen, and Galapagos, Espen A Haavardsholm Consultant of: Pfizer, UCB, Eli Lilly, Celgene, Janssen-Cilag, AbbVie and Gilead, Hilde Berner Hammer Consultant of: AbbVie, Lilly, UCB and Novartis.
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POS0089 A DIAGNOSTIC PERFORMANCE STUDY ON RAMAN SPECTROSCOPY INTEGRATED WITH POLARIZED LIGHT MICROSCOPY FOR THE IDENTIFICATION OF MONOSODIUM URATE IN GOUT

Keywords: Gout, Crystal Arthritis, Diagnostic Tests

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Background: The diagnosis in gout and other crystallopathies is commonly based on polarized light microscopy (PLM) of synovial fluid aspirates. This technique is flawed, however, due to subjectivity, limited reproducibility, and oversensitivity due to artifacts [1]. There is a need for innovative methods to perform synovial fluid analysis with more objectivity/reproducibility. Raman spectroscopy has been applied for identification of MSU in gout, with different technical approaches [2]. Although results are promising, there are no real diagnostic accuracy measures available for any application of Raman spectroscopy in rheumatology.
Objectives: To enhance the chemical analytical performance of PLM, we have integrated a Raman spectroscope within a standard polarized light microscope (iRPolM). In this study, we investigated the performance of iRPolM as a next-generation method for synovial fluid analysis in gout.
Methods: This is a prospective study, including 200 samples from a peripheral swollen joint subject for diagnostic analysis. The participants formed a consecutive series. Diagnostic performance was measured against the 2015 ACR/EULAR gout classification criteria set, which includes PLM analysis. Furthermore, we compared the analytical performance of iRPolM to identify MSU crystals with ordinary PLM analysis by an experienced rheumatologist.
RESULTS:

Table 1. Diagnostic and analytical performance of iRPolM. Values given with 95% confidence intervals.

	Diagnostic performance of iRPolM against 2015 ACR/EULAR classification criteria	Analytical performance of iRPolM against PLM by rheumatologist
Sensitivity	77.6% (95% CI 65.8-86.9%)	91.2% (95% CI 80.7-97.1%)
Specificity	97.7% (95% CI 93.5-99.5%),	97.6% (95% CI 93.0-99.5%)
Positive predictive value	94.5% (95% CI 84.9-98.2%)	94.6% (95% CI 85.0-98.2%),
Negative predictive value	89.7% (95% CI 84.7-93.1%),	96.0% (95% CI 91.2-98.2%)
Accuracy	91.0% (95% CI 86.2-94.6%)	95.6% (95% CI 91.4-98.2%)
Positive likelihood ratio	34.4 (95% CI 11.2-106.1)	37.4 (95% CI 12.2-114.7)
Negative likelihood ratio	0.23 (95% CI 0.15-0.36)	0.09 (95% CI 0.04 to 0.21)

67 patients were classified as gout according to 2015 ACR/EULAR classification criteria. 55 samples were positive for MSU according to PLM analysis. iRPolM identified MSU in 55 patients, 52 of which positive for gout. The inter-rater agreement between PLM and iRPolM was very high ($\kappa = 0.90$).

Conclusion: We demonstrate that Raman spectroscopy integrated with polarized light microscopy has a high diagnostic performance as it comes to identification of MSU in synovial fluid samples. Furthermore, Raman Spectroscopy could provide definitive outcomes in cases where analysists with polarized light

microscopy faced uncertainties or lookalikes, for example by identifying birefringent objects as glass slivers, microplastics or other non-MSU crystal types. These results show that Raman spectroscopy is a powerful analytical tool for clinicians, and a potential candidate for replacement or enhancement of PLM in clinical care where higher specificity is needed. Raman spectroscopy gives an excellent specificity on the nature of a birefringent object even with lookalikes, improving the specificity of a difficult microscopical diagnosis.

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POS0090

DYSBIOSIS OF GUT MICROBIOME, BILE ACID COMPOSITIONS, AND PREVALENCE OF HYPERURICEMIA: DATA FROM THE XIANGYA HYPERURICEMIA STUDY

Keywords: -omics, Gout

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Background: Hyperuricemia is a pre-requisite for gout, and often co-occurs with other metabolic diseases[1]. Emerging evidence suggests that gut microbiota is an important factor in the development of metabolic diseases[2]. Moreover, altered gut microbiota, ascertained using 16S rRNA-based sequencing method, has been linked to hyperuricemia[3]. However, the 16S rRNA technique has limited resolution to differentiate closely related species. Therefore, the hyperuricemia associated specific species and underlying mechanism remain unclear. Additionally, cross-talk between bile acid metabolites and the gut microbiome has been implicated in metabolic diseases, implying potential effect of bile acid metabolism in the pathogenesis of hyperuricemia.

Objectives: The aim of this study was to examine the relation of gut microbiome based on shotgun metagenomic sequencing to prevalent hyperuricemia and potential mediators of bile acids.

Methods: Participants were derived from a community-based observational study, the Xiangya Hyperuricemia Study. Hyperuricemia was defined as serum urate level > 404 μmol/L. Gut microbial composition was determined using shotgun metagenomic sequencing and plasma bile acids were measured by high-performance liquid chromatography mass spectrometry. The Chao1 index (i.e., richness) and Shannon index (i.e., diversity) of microbial genes and taxa and the difference of microbial composition, indicated by Bray-Curtis distance between participants with and without hyperuricemia were assessed. The association between gut microbiome and prevalence of hyperuricemia and the extent to which the association was mediated by plasma bile acids were also evaluated.

Results: Among 1,379 participants, the prevalence of hyperuricemia was 13.4% (n = 185) (Figure 1 A). Decreased microbial richness and diversity, altered composition of gut microbiome and lower relative abundance of seventeen key species *Coprococcus comes*, *Dorea longicatena*, *Desulfovibrio piger*, *Ruminococcus sp003526955*, *Holdemanella sp002299315*, *Ruminococcus sp000437175*, *Ruminococcus sp000437095*, *Coprococcus eutactus*, *Blautia sp900066335*, *Blautia sp900066205*, *Blautia sp900066505*, *Ruminococcus sp003011855*, *Blautia sp900120195*, *Blautia sp000285855*, *Dorea formicigenerans*, *Acetatifactor sp900066365* and *Blautia wexlerae* were significantly associated with prevalent hyperuricemia (Figure 1 B and C). High levels of taurochenodeoxycholic acid (TCDCA) and low levels of deoxycholic acid (DCA) were associated with high prevalence of hyperuricemia (Figure 1 D and E). Inversely associations between these key species and hyperuricemia were partially mediated through their effect on the levels of TCDCA and DCA. For instance, the indirect effects (OR) of relative abundance of *Coprococcus comes* on hyperuricemia through DCA and TCDCA were 0.97 (95% CI: 0.94 to 1.00) and 0.98 (95% CI: 0.97 to 1.00), respectively, and the corresponding percentage of mediation were 12.0% and 7.4% respectively. The indirect effects of *Dorea longicatena* on hyperuricemia via DCA and TCDCA were 0.97 (95% CI: 0.95 to 1.00) and 0.98 (95% CI: 0.97, 1.00), and the percentage of their mediation effect were 10.1% and 6.0%, respectively (Figure 1 F).

Conclusion: We identified several key species of gut microbiome for hyperuricemia and demonstrated that the association between gut microbiome dysbiosis and prevalent hyperuricemia is partially mediated via bile acids. These findings provide new sights into the role of microbiome and bile acids in the development of hyperuricemia and may contribute to translational opportunities.

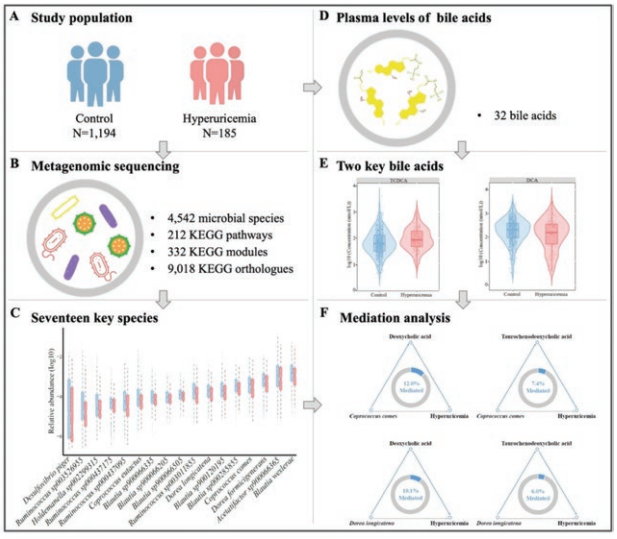


Figure 1 (A) 1194 healthy control and 185 participants with hyperuricemia were included in this study. **(B, C)** Gut microbial composition was determined using shotgun metagenomic sequencing and seventeen key microbiome species were significantly associated with prevalent hyperuricemia. **(D, E)** Plasma bile acids were measured by high-performance liquid chromatography mass spectrometry and two key bile acids, taurochenodeoxycholic acid (TCDCA) and deoxycholic acid (DCA), were associated with prevalence of hyperuricemia. **(F)** Examples of mediating effects of bile acids on the relationship between key species and prevalence of hyperuricemia.

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Vessels in flames

POS0091 **USE OF HIGH-PLEX DATA REVEALS NOVEL INSIGHTS INTO THE TEMPORAL ARTERY OF GIANT CELL ARTERITIS**

Keywords: Biomarkers, Vasculitis, Treat to target

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Background: Giant cell arteritis (GCA) is the most common systemic vasculitis that triggers acute arterial occlusion and can even lead to death over the age of 50 [1]. While mechanism underlying GCA are predominantly derived from inflammatory response, none of the anti-inflammatory drugs currently used limit efficiently patient's disease course. It was previously shown that histopathological lesions involve the three layers of the artery wall called adventitia, media, and intima. Activation of adventitial dendritic cells is the initial trigger of the vascular remodeling in GCA leading to intimal hyperplasia but the early molecular mechanism that activates those cells remains unknown. Our hypothesis is that each layer of the artery, perivascular tissue included, shows a unique transcriptomic signature which could define and explain the different molecular events in the inflammatory and vascular remodeling processes in GCA. For that, whole tissue spatial transcriptomics analysis offers advanced opportunities in elucidating functional mechanisms of pathologic tissues with complex organization such as GCA especially in human temporal artery, the most frequently affected artery in GCA.
Objectives: Uncover the key coding genes to define new biomarkers or pathways associated with GCA by performing the first *in situ* spatial profiling characterization of molecular actors involved in temporal arteries from GCA patients in comparison to normal arteries.
Methods: From human formalin-fixed paraffin-embedded temporal artery biopsy samples (GCA n=9; controls n=7), we performed a whole transcriptome analysis by using NanoString GeoMx Digital Spatial Profiler (DSP) [2]. A total of 59 individual regions of interest (ROIs) were created within each of the 4 layers for each individual artery. After ROIs collection and library construction, samples were sequenced on the Illumina NovaSeq 6000 platform and reads were digitally quantified and normalized using GeoMx DSP Data Analysis software. Differential expressed genes (DEGs) (fold change >2 or <-2, p-adjusted <0.05) were compared for each layer, to build a spatial and pharmacogenomic network in disease course.
Results: Overall, we found that most of the transcriptome studied (12076 genes) was upregulated in GCA arteries. Precisely, 350, 340, 142 and 5 DEGs were found in intima, media, adventitia, and perivascular tissue respectively. Enrichment analysis highlighted that inflammation/immune-related functions and vascular remodeling were significantly limited to intima and media layers. Upregulated immune-related functions concerned macrophage differentiation & T cell, B cell, complement activations. Regarding vascular remodeling pathways, we found an upregulation of: (i) collagen metabolic process and fibroblast proliferation concerning the 3 artery layers, (ii) angiogenesis & epithelial cell migration in intima and media layers, (iii) smooth muscle cell proliferation & ossification in intima layer. Our pharmacogenomic network analysis identified genes that could potentially be targeted by immunosuppressive drugs currently approved or new immunotherapies.
Conclusion: Our findings provide the first *in situ* spatial profiling characterization of molecular actors involved in GCA which is essential for the discovery of potential new therapeutic targets to cure this disease. The differential spatial upregulation of genes involved in inflammatory process and vascular remodeling suggests a differential chronological involvement of each layer of the artery.
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Disclosure of Interests: None Declared.
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POS0092 **SPATIAL DISTRIBUTION OF DISTINCT FIBROBLAST SUBTYPES IN GIANT CELL ARTERITIS**

Keywords: Descriptive Studies, Vasculitis

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Background: Giant cell arteritis (GCA) is a systemic vasculitis of large- and medium-sized arteries which is characterized by granulomatous inflammation and vascular remodeling. The pathogenesis of GCA starts in the adventitia where fibroblasts are the major cell population. Fibroblasts are recognized for synthesizing and remodeling the extracellular matrix (ECM), but their phenotype and role in GCA-affected blood vessels is largely unknown.
Objectives: To explore the distribution of fibroblast phenotypes and their link to vascular remodeling in GCA.
Methods: Temporal artery biopsies (TABs) from patients with GCA (n=9) and controls (n=9), and aorta tissues from GCA (n=9) and atherosclerosis (AS, n=11)-related aneurysm were examined. Immunohistochemical staining for CD90 (pan-fibroblast), fibroblast activation protein alpha (FAP, activated fibroblast marker), podoplanin (immunofibroblast marker), CD248 (fibrosis-related marker), alpha-smooth muscle actin (αSMA, myofibroblast marker) was performed to evaluate the distribution of fibroblast subtypes. The expression of transforming growth factor beta (TGFβ), fibroblast growth factor 21 (FGF21), platelet derived growth factor AA (PDGFAA) and PDGFB as markers of active remodeling pathways was also determined. For each marker the percentage of positive cells was determined by Qupath 0.3.0.
Results: TABs from GCA patients showed increased expression of CD90, FAP, podoplanin, CD248, FGF21, PDGFAA and PDGFB in the adventitia and intima compared with the controls. Isolated higher expression of TGFβ in the adventitia and αSMA in the intima was also documented. $CD90^+FAP^+$ activated fibroblasts and $CD90^+$podoplanin$^+$ immunofibroblasts were predominantly located in the adventitia, whereas αSMA^+ myofibroblasts were observed mainly in the intima, and $CD248^+$ fibroblasts in the adventitia-media border and intima. High expression of FAP, CD248, FGF21 and PDGFB in the media-intima was associated with intimal hyperplasia in GCA-positive TABs. GCA-affected aortas showed different patterns: $CD90^+FAP^+$ activated fibroblasts, $CD90^+$podoplanin$^+$ immunofibroblasts and $CD248^+$ fibroblasts accumulated especially in the structurally disrupted media, which was associated with abundant expression of PDGFB and FGF21. These three fibroblast phenotypes were hardly observed in AS-affected aortas. We also observed expression of CD90, FAP, podoplanin and CD248 in the artery tertiary lymphoid organs (ATLOs) of the adventitia in GCA-affected aortas. αSMA^+ myofibroblasts were expressed at similar levels in GCA and AS-affected aorta tissues, being mainly located in the intima.
Conclusion: This study documents a distinct spatial distribution pattern of fibroblast subtypes in GCA-affected temporal arteries and aorta tissues and their association with markers of active remodeling pathways. Further research is needed to dissect the precise role of these fibroblast subtypes in the pathobiology of GCA.
REFERENCES: NIL.

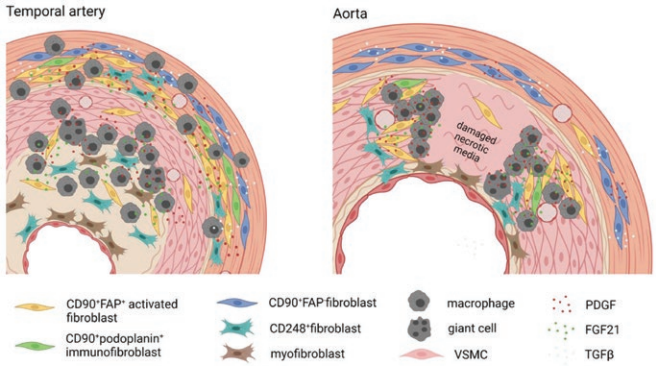


Figure 1. Fibroblast heterogeneity in giant cell arteritis. (made with Biorender)

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POS0093

TRANSCRIPTOMIC AND METHYLOMIC PROFILING OF CD4+ T-CELLS IN GIANT CELL ARTERITIS WITH DIFFERENT DISEASE ACTIVITY

Keywords: -omics, Genetics/Epigenetics, Vasculitis

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Background: Giant cell arteritis (GCA) is an inflammatory large-vessels vasculitis representing an important clinical challenge. First, an early diagnosis of GCA is difficult due to the clinical heterogeneity and the lack of specific biomarkers. In addition, although the therapy generally used are glucocorticoids (GC), relapses are common when GC are tapered [1]. The etiology of this disorder is complex in which multiple genetic and epigenetic factors contribute to its development [1]. Although the pathogenic mechanisms remain insufficiently understood, a central role for CD4+ T-cells has been demonstrated [2]. In this context, understanding how the transcriptome and methylome of this cell type are altered in GCA patients and how they are influenced by GC will yield new insights into the pathogenesis of this vasculitis.
Objectives: To shed light into GCA pathogenesis and to identify molecular mechanisms that might serve as novel biomarkers or potential drug targets, we characterized the transcriptome and methylome signatures of GCA CD4+ T-cells and the way these cells are affected by remission and by the effect of GC.
Methods: Both DNA and RNA were isolated from CD4+ lymphocytes positively sorted by flow cytometry from whole blood. Subsequently, DNA methylation profiling with the Illumina Infinium Methylation EPIC array and RNA-sequencing were carried out. After quality controls, epigenome- and transcriptome-wide association were performed for 81 samples: 23 healthy controls and 58 GCA patients grouped in three different clinical status (active before starting GC [n= 13], in remission with GC [n= 22], and in remission without GC [n= 23]).
Results: The results of this work revealed a profound dysregulation in both the gene expression and DNA methylation patterns of CD4+ T-cells of GCA patients. Particularly, CD4+ T-cells from GCA patients with an active state of the disease before starting GC treatment showed substantial changes in inflammatory processes, such as NOTCH1, interleukin-6 (IL-6), IL-1 and vitamin D receptor signalling pathways, among others. In addition, we also observed alterations in molecular pathways related with angiogenesis, the vascular endothelial growth factor (VEGF) receptor, and with the differentiation of T helper 2 (Th2), including the IL-2/STAT5 and IL-4 pathways. Interestingly, our findings also indicated that the pro-inflammatory expression profiles observed in the active disease are lost when the disease subsides, and that GC therapy significantly remodels both the transcriptome and the methylome of CD4+ T-cells. Particularly, changes in molecular mechanisms related to drug metabolism, such as GC receptor genes and glucuronosyltransferase family genes were also found.
Conclusion: The results of the transcriptome and methylome characterization of GCA CD4+ T-cells have provided new evidences of genes and pathways contributing to the pathogenic role of this cell type in GCA, providing a clearer picture of the molecular processes driving disease activity and how they vary in response to GC treatment.
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Disclosure of Interests: None Declared.
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POS0094

INSIGHT INTO GIANT CELL ARTERITIS PATHOGENESIS BY NANOSTRING NCOUNTER GENE EXPRESSION PROFILING IN TEMPORAL ARTERY BIOPSIES

Keywords: -omics, Vasculitis

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Background: Giant Cell Arteritis (GCA) is a systemic inflammatory disease that affects large and medium-sized arteries. It is the most common vasculitis in people older than 50 years of age [1]. Temporal artery biopsies (TABs) are routinely performed for diagnosis, giving the invaluable opportunity to analyze inflamed tissues. Different histological patterns of inflammation can be found in TABs: transmural inflammation (TMI) is the most frequent pattern (78% of the positive TABs), while inflammation limited to adventitia (ILA) can be found in 7% of the positive TABs [2]. It is not known if ILA precedes TMI or if they are distinct GCA subsets. Knowledge on disease pathogenesis is growing [3], but high-throughput assays in TABs are still scarce [4-7]. GCA patients are actually treated with glucocorticoids, irrespective of clinical presentations and inflammation patterns. It is necessary to increase the knowledge on the molecular features of GCA to implement precision medicine.
Objectives: To identify differentially expressed genes (DEGs) in TAB from patients with GCA versus controls. To increase the knowledge on TMI and ILA histological patterns in GCA.
Methods: A retrospective cohort of patients subjected to TABs at AUSL-IRCCS at Reggio Emilia (Italy) was included: 42 patients had GCA with TMI; 7 patients had GCA with ILA; 7 patients had normal TABs and received a different diagnosis. All the patients with TMI and normal TABs were naïve from therapy while 4/7 patients with ILA were receiving glucocorticoids at the time of TABs. RNA was extracted from formalin-fixed paraffin-embedded TABs. The expression of 770 genes was profiled with the NanoString nCounter PanCancer Immune Profiling Panel. Data were analyzed with nSolver software 4.0. Background thresholding using the negative control probes was applied, then data were normalized over the positive control probes and 18 housekeeper genes. DEGs with fold changes >2.0 and Benjamini-Yekutieli adjusted p-values <0.05 were considered significant. Unsupervised clustering was performed with nSolver. Pathway analysis was performed with DAVID.
Results: Unsupervised clustering based on the expression of the 770 genes revealed two groups of samples: the first group contained all the normal TABs plus TABs with ILA, while the second group contained 41/42 TABs with TMI. In particular, TNF superfamily genes or genes related to senescence allowed to cluster TABs with TMI from ILA and normal TABs. TABs with TMI showed 31 down- and 268 up-regulated genes compared to normal TABs; 20 down- and 135 up-regulated genes compared to TABs with ILA. TABs with ILA revealed a gene expression profile similar to normal TABs: 47 genes reached fold changes >2.0, but p-values did not maintain statistical significance after correction for multiple testing. These genes were also modulated in TABs with TMI. The chemokine CCL18 was the top up-regulated gene, while the cell adhesion molecule MCAM was the top down-regulated gene in TMI. CD86 costimulatory molecule, a marker of antigen-presenting cells, was detected only in TMI. JAK3 resulted increased in TMI, while JAK1 and JAK2 were not modulated. CD27 activating immune checkpoint was detected in all the TABs with TMI and 6/7 TABs with ILA, while it was not detected in normal TABs. The following pathways were enriched with DEGs: chemokine and TLR signaling, antigen processing and presentation via MHC class II, positive regulation of T cell activation, cellular responses to IL-1, TNF, IFNγ.
Conclusion: TABs with TMI had a distinct transcriptome compared to TABs with ILA. A set of genes were deregulated in TABs both with TMI and ILA versus normal TABs, indicating that ILA might represent the early stages of the disease. Gene profiling allowed to deepen the knowledge on GCA pathogenesis.
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Acknowledgements: Azienda Unità Sanitaria Locale (AUSL)-IRCCS, Reggio Emilia, Italy: “Bando per la valorizzazione della Ricerca Istituzionale 2019” and Foundation for Research in Rheumatology (FOREUM).
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POS0095

SINGLE-CELL LANDSCAPE OF CD4+ T LYMPHOCYTES REVEALS A POTENTIAL ROLE OF CYTOTOXIC CELLS IN GIANT CELL ARTERITIS

Keywords: Vasculitis, Adaptive immunity, -omics

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Background: Giant cell arteritis (GCA) is a systemic vasculitis mediated by an aberrant immunological response against the endothelium of medium- and large-sized blood vessels [1]. Even though the pathogenic mechanisms that drive GCA are yet to be settled, there is strong evidence that CD4$^+$ T lymphocytes play a crucial role in the development of this vasculitis [2]. Recently, single-cell RNA sequencing has resulted in a scientific and technological revolution, enabling the characterization of the gene expression profile of thousands of individual cells in different tissues [3]. This approach has allowed the identification of new cell subtypes, some of them being exclusively represented in pathogenesis, and has also proved useful as a tool for reporting new disease-specific biomarkers.
Objectives: In this study, we aimed to define new pathological mechanisms driving GCA through the comprehensive characterization of the gene expression profile of CD4$^+$ T cells by performing single-cell RNA sequencing in GCA patients and healthy controls.
Methods: CD4$^+$ T cells from whole blood of 16 individuals (eight GCA patients and eight sex- and age-matched healthy controls) were obtained. Based on clinical parameters, five patients were classified as active GCA and 3 of them as patients in remission. Single-cell libraries were prepared from isolated CD4$^+$ T cells using the '*Chromium Single Cell Gene Expression*' (10X Genomics). Sequencing data were pre-processed with the CellRangerV3.0 software. Then, quality control analysis, dimensionality reduction, clustering and differential gene expression profiling were conducted with the R package Seurat V4[4].
Results: A total of 114.799 cells were analyzed and classified into 13 clusters according to their transcriptomic profile. Manual annotation of the different clusters based on canonical markers permitted the identification of 6 distinct CD4$^+$ T cell types including naïve (Tnaïve), central memory (T_{CM}), effector memory (T_{EM}), effector memory expressing granzyme K (T_{EM} *GZMK*$^+$), regulatory (Tregs) and cytotoxic T lymphocytes (CTL). The comparative analysis of cell type composition between the different subgroups showed a significant reduction of the cytotoxic cell compartment in GCA patients in remission compared with active patients (p=0.011) and controls (p=0.045) as well as a decreased frequency of Tregs in active patients compared with healthy individuals (p=0.029). In addition, differential expression analysis evidenced a significant overexpression of granzyme B (*GZMB*) and the zinc finger protein 683 (*HOBIT),* both involved in cytotoxic processes, in CTLs of active patients compared with patients in remission (p=0.017) and controls (p=1.14x10-49), respectively. Moreover, in both active and in remission patients, the Treg compartment showed a reduced expression of genes related to regulatory functions, like *HLA-DRA* (p=3.34x10-7) and *LGALS1* (p=1.14x10-8), compared with healthy controls.
Conclusion: The first single-cell atlas of CD4$^+$ T cells in GCA provided evidence for the first time of a potential pathogenic role of CD4$^+$ T cells with cytotoxic functions in this vasculitis and supported the crucial role of Tregs in the pathogenesis of GCA.

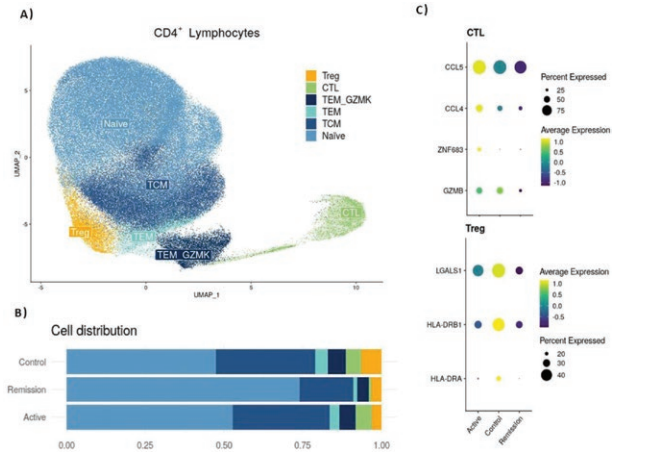


Figure 1. T CD4$^+$ cell overview in GCA. (A) UMAP of CD4$^+$ T cells distributed by expression. (B) Barplot of each T cell sub-type contribution. (C) Dotplot of CTL and Treg clusters for specific genetic markers classified per group. Dot size indicates proportion of cells expressing the gene, color indicates average of expression.

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Disclosure of Interests: None Declared.
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POS0096

HYPOXIA AND MPO-ANCA IgG INDUCED BIOPHYSICAL CHANGES IN NEUTROPHILS MAY PROMOTE ENDOTHELIAL INJURY IN ANCA ASSOCIATED VASCULITIS

Keywords: Vasculitis

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Background: ANCA associated vasculitis (AAV) is characterised by neutrophil-mediated endothelial damage. Neutrophil deformability impacts their ability to traffic through microvasculature. Distinct biophysical properties of neutrophils in patients with active AAV, e.g. in response to ANCA or hypoxia in inflamed tissues, may contribute to endothelial injury.
Objectives: Investigate how MPO-ANCA IgG (ANCA) treatment and/or hypoxia affect the actin cytoskeleton or biophysical properties of neutrophils, and whether this phenotype is replicated in patients with active AAV.
Methods: Whole blood and isolated neutrophils from patients with active AAV (AAV), patients with AAV in remission (rAAV) or healthy controls (HC) was analysed using real time deformability cytometry (RT-DC), a novel microfluidic technique able to identify individual cell biophysical profiles. Deformation was calculated using ShapeOut. Neutrophils were isolated using immunomagnetic separation. Cells were primed with TNF (2 ng/mL, 15 min) and stimulated with healthy donor IgG (CIgG), or ANCA IgG (100 ug/mL, 1 h) under normoxia (21% O_2) or hypoxia (5% O_2). Cells were stained for F actin (AF488 Phalloidin) and imaged using confocal microscopy. Cell area and total percentage phalloidin staining was analysed (ImageJ).
Results: AAV neutrophils (n=27) were significantly stiffer than rAAV (n=25) or HC (n=15), displaying decreased deformation (median 0.085, 0.086, and 0.076 au for HC, rAAV, and AAV respectively, p=0.0001). There was an inverse correlation between AAV neutrophil deformation and disease activity as measured by BVAS score (r=-0.573, p=0.032). This phenotype of decreased deformation was replicated by ANCA stimulation of HC neutrophils (median 0.086, 0.085 and 0.082 for untreated, CIgG, and ANCA respectively, p=0.05). Hypoxia prevented the effect of ANCA stimulation on HC neutrophils (median 0.078, 0.077, and 0.079 au for untreated, CIgG, and ANCA respectively, ns). ANCA stimulation of HC neutrophils increased cell area (mean 51.56/63.07/88.61 um^2, p=0.0008) and total actin signal (mean 27.61/25.86/44.30%, p=<0.0001) (untreated, CIgG, ANCA respectively, Fig 1A-C). At baseline, hypoxic neutrophils were larger with increased actin staining. Under hypoxia the effect of ANCA stimulation was diminished, with a smaller increase in area (mean 60.34/67.48/71.15 um^2, p=0.0011) and total actin signal (mean 38.15/46.01/45.49%, p=0.0255) compared to normoxia (Fig 1D-F). AAV neutrophils (n=8) were significantly larger, with more F-actin at baseline and showed a larger increase in actin following ANCA stimulation compared to HC cells: area (mean 75.73/98.68/121.25 um^2, p=0.0088) and total actin signal (mean 51.74/74.85/83.44%, p=0.0032) (Fig 1G-I).
Conclusion: Neutrophils from patients with active AAV display distinct physical properties, which correlate with disease activity. Similar results are seen when neutrophils are stimulated *in vitro* with ANCA. In keeping with this, increased neutrophil actin polymerisation and marked lamellopodia formation is seen following ANCA stimulation *in vitro*, with the greatest effect seen when cells from patients with active AAV were used. Of interest, incubation under hypoxic conditions diminished the effect of ANCA stimulation suggesting that hypoxia can modulate actin polymerisation. This phenotype of increased cell stiffness in AAV may be due to reorganisation of the actin cytoskeleton and lead to increased neutrophil retention in pulmonary and renal microvasculature, thus increasing the potential for

neutrophil-endothelial cell interactions and microvascular damage. Therefore, targeting cytoskeletal changes in AAV may offer a route to improve clinical outcomes.

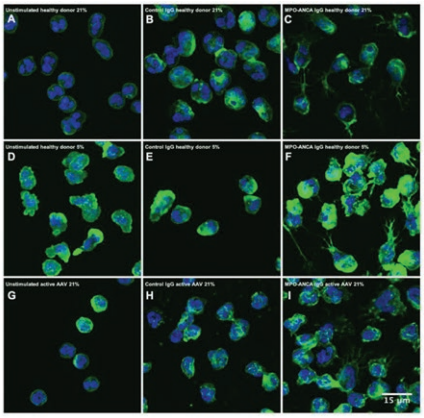


Figure 1: Effect of hypoxia and MPO-ANCA IgG stimulation on neutrophil size and F-actin polymerisation in healthy control and active AAV neutrophils.

Neutrophils ($2x10^5$) were primed with 2 ng/mL TNF for 15 min and stimulated with 100 ug/mL of control or MPO-ANCA IgG for 1 hour. Neutrophils were stained for Phalloidin (AF488, green) and mounted with VectaShield[R] Antifade Mounting Medium with DAPI (blue) and imaged at 63x using confocal microscopy (representative images shown). A-C: HC 21% (n=14); D-F: HC 5% O2 (n=14); G-I: AAV 21% O2 (n=8). A, D, G: Unstimulated; B, E, H: Control IgG; C F, I: MPO-ANCA IgG.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0097 ASSOCIATION BETWEEN LOSS OF IMMUNE CHECKPOINT PROGRAMMED CELL DEATH PROTEIN 1 AND ACTIVE ANCA-ASSOCIATED RENAL VASCULITIS

Keywords: Vasculitis, Kidneys

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Background: Immune checkpoint inhibitors (ICIs) have made an important contribution on the survival of patients with certain cancers. ICIs interrupt co-inhibitory signalling pathways mediated by programmed cell death protein 1 (PD-1), programmed cell death protein-ligand 1 (PD-L1), and cytotoxic T lymphocyte-associated antigen (CTLA-4) that result in the elimination of cancer cells by stimulating the immune system.
Objectives: Immune-related adverse events have also been described and attributed to an enhanced immune system activation. Recent observations have suggested dysregulation of immune checkpoints in active antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Therefore, we here aimed to analyze abundance of immune checkpoint molecules PD-1/PD-L1 and its implications in ANCA-associated renal vasculitis.
Methods: We here analyzed intrarenal PD-1 and PD-L1 by immunostaining in a total number of 15 kidney biopsies with ANCA-associated renal vasculitis in correlation with glomerular and tubulointer-stitial lesions. For independent validation, publicly available datasets were analyzed for PD-1 expression (encoded by PDCD1).
Results: We here observed a predominant tubulointerstitial expression of PD-1 that is decreased in ANCA-associated renal vasculitis. Moreover, loss of tubulointerstitial PD-1 correlated with active ANCA-associated renal vasculitis. Consistent to the observed association with active glomerular and tubulointerstitial lesions, we identified that interstitial PD-1 correlated with tubular and/or glomerular PD-L1 positivity. Finally, PD-1 was associated with decreased local synthesis of complement factor B. Interestingly, we did not observe a correlation between PD-1 and complement C5 or its C5a receptor. Combined with our observations, this may implicate a link between im-paired PD-1/PD-L1 signalling, complement factor B, and active ANCA-associated renal vasculitis.
Conclusion: These findings could be of relevance because experimental data have already been described that PD-1 agonism can be used therapeutically to attenuate autoimmunity in multiple disease models. Furthermore, targeted therapy against complement C5/C5a receptor and factor B are both available and currently evolving in the treatment of AAV. Therefore, this pilot study expands our current knowledge and describes a potential interplay between immune checkpoints and the alternative complement pathway in active ANCA-associated renal vasculitis.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Björn Tampe Grant/research support from: Support from Evotec and Vifor.
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POS0098 IDENTIFICATION OF THE CENTRAL TOLERANCE CHECKPOINT FOR AUTOREACTIVE PROTEINASE 3+ B CELLS IN HUMAN BONE MARROW

Keywords: Adaptive immunity, Vasculitis, Biomarkers

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Background: Autoreactive proteinase 3 (PR3+) B cells have recently been phenotypically and functionally characterized, and the presence of defective central antigen-independent and peripheral antigen-dependent checkpoints in patients with ANCA-associated vasculitis (AAV) has been shown. This work aimed to investigate the central tolerance-checkpoint controlling immature PR3+ B cells in the bone marrow (BM), before their migration into the periphery as transitional B cells.
Objectives: We investigated the presence and the specific phenotypic features of PR3+ B cells in BM mononuclear cells (BMMC) of non-vasculitis controls (No-AAV), comparing them to paired peripheral blood mononuclear cells (PBMC) of No-AAV and PBMC of PR3-AAV patients, and the central tolerance-checkpoint for PR3+ B cells.
Methods: We used a customized flow-cytometry assay, using PR3 as ligand to target autoreactive PR3+ B cells (PR3+B cells). Adult PR3-ANCA positive AAV (PR3-AAV) patients with a clinical diagnosis of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) were selected among consecutive subjects with AAV seen in our Rheumatology Unit. Subjects without vasculitis (No AAV) were selected among consecutive subjects undergoing bone marrow aspirate to exclude hematologic conditions of myeloid origin and eventually resulted healthy or in long-term complete remission during follow-up of myeloid neoplasms. PMBC from AAV patients and paired samples of BMMC and PBMC from No AAV were collected and analyzed.
Results: The proportion of PR3+ B cells within BMMC (median [IQR25-75%]; 1.98%[1.77-2.75]) was higher than within PBMC of No-AAV (0.9%[0.63-1.44], $p<0.01$ by paired comparison) and similar to their proportion within PBMC of PR3-AAV patients (1.82%[1.66-3.21]; $p>0.05$). When focusing on immature/transitional CD24++CD38++B cells only in No-AAV, we observed distinct phenotypes within BMMC versus PBMC (i.e. higher proportion of CD27-CD10+ and lower expression of CD21, IgD, IgM within BMMC versus PBMC), representing two separate developmental steps of B cell maturation. Within CD24++CD38++ B cells, BMMC contained the greatest proportion of PR3+ B cells as compared to PBMC (3.35%[1.99-4.92] versus 1.23%[0.62-1.55], $p<0.01$). We observed a significant decline of the PR3+ fraction from T1-like/immature subset (IgD-IgM+; 2.80%[1.23-4.02]) to T2-like/early transitional subset (IgD+IgM+; 1.76%[0.96-2.68], $p<0.01$) in BMMC, while no significant reduction was observed between the latter subset and the transitional compartment of PBMC (1.26%[0.62-1.56], $p>0.05$).
Conclusion: To prevent PR3-related autoimmunity, autoreactive PR3+ B cells pass a stringent selection in the BM, and their removal by central tolerance-checkpoint activity occurs mainly between T1-like/immature to T2-like/early transitional B cells of BMMC.
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POS0099 THE DIVERSITY AND DISTRIBUTION OF HLA-DRB1 ALLELES IN THE POPULATION OF CROATIAN PATIENTS WITH IGA VASCULITIS (IgAV)

Keywords: Vasculitis, Genetics/Epigenetics

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Background: IgA vasculitis (IgAV) is a small vessel vasculitis occurring predominantly in childhood. Studies concerning the genetic background of IgAV have confirmed that susceptibility to the disease may be influenced by Human Leukocyte Antigens (HLA), with HLA-DRB1 gene showing a strong association with the disease.
Objectives: We aimed to investigate HLA-DRB1 polymorphism among Croatian patients with IgAV and to determine if there are associations with disease susceptibility and clinical heterogeneity.
Methods: 123 IgAV patients, fulfilling the diagnostic EULAR/PRINTO/PRES criteria from three pediatric rheumatology centers and 202 unrelated healthy individuals were enrolled. Genomic DNA was extracted from whole peripheral blood. The HLA-DRB1 alleles were analysed using the Next Generation Sequencing (NGS) method.
Results: Among 123 patients with IgAV, 68 were girls and 55 were boys with median age 6.3 (4.5-8.2) years at the time of diagnosis. All patients had purpuric rash, 75.7% had arthralgia or arthritis, 32.5% had affected gastrointestinal (GI) system, while 25.2% patients developed IgA vasculitis nephritis (IgAVN). The HLA-DRB1*12:01 allele was associated with an increased risk for IgAV (OR 4.45, 95% CI=1.17-16.95, P=0.03), while HLA-DRB1*11:01 allele was associated with an increased risk for GI involvement in patients who developed IgAV (OR 3.29, 95% CI=1.2-8.98, P=0.031). A marginally significant (P=0.068) higher frequency of the HLA DRB1*10:01 allele in patients with GI symptoms was observed. No significant differences were found in the distribution of HLA DRB1 alleles between patients with IgAVN and those who did not develop nephritis.
Conclusion: Our results demonstrated that HLA-DRB1*12:01 allele was associated with susceptibility to IgAV in the Croatian children, while HLA-DRB1*11:01 allele showed association with GI manifestations of the disease.
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Disclosure of Interests: None Declared.
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POS0100

TARGETING NF-κB SIGNALLING IN B LINEAGE CELLS AS A POTENTIAL NOVEL TREATMENT STRATEGY FOR ANCA-ASSOCIATED VASCULITIS

Keywords: Autoantibodies, Adaptive immunity, Vasculitis

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Background: B cells are crucially important in the pathogenesis of many autoimmune diseases, including ANCA-associated vasculitis (AAV), which is further demonstrated by the beneficial clinical effects of rituximab (anti-CD20) B cell targeted therapy. Despite its advantages, this treatment strategy results in long-term B cell depletion and fails to target long-lived plasma cells, rendering an unmet need for more reversible and combined B and plasma cell targeting approaches to achieve long-term disease remission. This aim may be reached by targeting signalling pathways essential for different B cell functions. The canonical and non-canonical NF-κB signalling pathways regulate fundamental B and/or plasma cell responses downstream of various B cell surface receptors, including the B cell receptor, CD40, and TLRs.
Objectives: To study potential alterations in NF-κB signalling in B lineage cells and to evaluate the effects of targeting NF-κB on B cell responses in general, and more specifically on proliferation, plasmablast differentiation and (auto)antibody production in B cells from AAV patients.
Methods: Memory B cells were obtained from AAV patients and healthy donors (HD), and gene expression profiles were generated by RNA-sequencing. Functional assays were performed by culturing PMBCs from AAV patients and HD with stimuli mimicking T cell-dependent (anti-CD40/IL-21) and T cell-independent (CpG/IL-2) conditions. Pharmacological inhibitors of Inhibitor-of-κB-kinase-β (IKKβ, canonical pathway) or NF-κB inducing kinase (NIK, non-canonical pathway) were added to the cultures. Downstream NF-κB signalling was determined by Western blot. After 6-day cultures, B cell proliferation and differentiation were determined by flow cytometry, and ELISA was performed for the detection of (auto)antibody production.
Results: Memory B cells from AAV patients with active disease exhibited an increased expression of NF-κB-associated genes compared to patients in remission and HD. Targeting IKKβ or NIK in AAV and HD B cells effectively blocked downstream canonical or non-canonical NF-κB signalling, respectively. IKKβ and NIK inhibition significantly reduced B cell proliferation in both stimulatory conditions of the functional assay. In addition, IKKβ and NIK inhibitors attenuated B cell differentiation into plasmablasts and antibody production, including anti-proteinase-3 (PR3) autoantibodies. Interestingly, the effects of NIK inhibition appeared to be B cell-specific, as T cell proliferation was largely unaffected.
Conclusion: These data reveal that NF-κB-associated genes are upregulated in memory B cells from AAV patients with active disease and that targeting of NF-κB signalling inhibits B cell responses that are important contributors to the autoimmune process, including autoantibody production. These findings suggest that targeting NF-κB, and particularly NIK, may be developed into a novel more reversible and B cell directed treatment modality for AAV.
REFERENCES: NIL.
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Remarkable Findings in OA Clinical Research

POS0101

FRAILTY CHANGES FOLLOWING TOTAL KNEE ARTHROPLASTY ARE ASSOCIATED WITH FUNCTIONAL IMPROVEMENT RATHER THAN PAIN RELIEF IN THE PATIENTS WITH END-STAGE KNEE ARTHROSIS

Keywords: Osteoarthritis, Motor function, Sarcopenia

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Background: Knee joint disorders in the elderly result in physical frailty and limiting healthy living. Although total knee arthroplasty (TKA) achieves significant pain relief and functional improvement, the effect of TKA on Frailty is not clear.
Objectives: This study aimed to investigate the change in frailty at 1 year postoperatively in patients undergoing primary TKA and to examine the correlated factors with this frailty change.

Methods: Patients with end-stage knee arthrosis who underwent primary TKA at our hospital between July 2020 and May 2021 were included with written consent. Basic attributes such as age, gender and BMI, with appendicular skeletal muscle mass (ASMI) by whole-body mode DXA, presence of sarcopenia by Asian Working Group for Sarcopenia 2019 criteria were measured preoperatively, and VAS for pain during walking, clinical assessment of knee joint function (Knee Society Score: KSS), quadriceps muscle strength by dynamometer, range of motion (ROM), and walking speed were measured before and one year after surgery. The relationship between the changes in the degree of frailty (Japanese Cardiovascular Health Study criteria for frailty) before and 1 year postoperatively.
Results: Seventy-five patients (59 women, mean age 75 years) were included in the study. In univariate analysis, KSS, ROM, muscle strength, and VAS for pain were significantly improved at 1 year after TKA compared to preoperative values ($p<0.0001$, 0.0001, 0.0001, 0.0001: pared *t*-test). The number of frail patients was decreased from 24 to 18 following TKA ($p=0.002$: Fisher's exact test). Multivariate analysis of the association of changes in frailty using ordinal logistic regression showed a positive correlation between improvement in walking speed and improvement in muscle strength ($p=0.01$, $p=0.02$), but not with sex, age, preoperative ASMI or presence of sarcopenia, improvement in pain while walking or ROM (Table 1).
Conclusion: The number of patients with frailty significantly decreased 1 year after TKA; the factors associated with changes in frailty were improvements in gait speed and muscle strength, suggesting that functional improvement rather than the pain-relieving effects of TKA contributed to the improvement in frail.

Table 1.

Factor	Odds Ratio	95% Confidence interval	p value
sex (male)	1.35	[0.22, 9.01]	0.75
age (year)	1.00	[0.93, 1.08]	0.99
appendicular skeletal muscle mass index (kg/m^2)	1.77	[0.79, 4.11]	0.17
presence of sarcopenia	1.84	[0.11, 35.30]	0.68
difference in range of motion (degree)	1.01	[0.95, 1.06]	0.85
difference in quadriceps power (N)	0.99	[0.98, 1.00]	0.02*
difference in waling speed (m/sec)	0.08	[0.01, 0.51]	0.01*
difference in VAS for gait pain	0.98	[0.96, 1.00]	0.09

Acknowledgements: We are grateful to Toshiko Yokoi, Mayu Hashizume, Madoka Sakai, Mayu Ikemizu for the data collection. We also wish to thank all the PT staffs in our hospital who participated in this study.
Disclosure of Interests: None Declared.
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POS0102 CALCIUM CONTAINING CRYSTALS ARE HIGHLY PREVALENT IN JOINT FLUID OF ADVANCED OSTEOARTHRITIS OF THE KNEE

Keywords: Diagnostic Tests, Osteoarthritis, Crystal Arthritis

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Background: Calcium containing crystals in osteoarthritis (OA) are of interest in the field of rheumatology, as they potentially stimulate the NRLP-3 inflammasome and may become treatable with novel therapeutics. Previous studies using scanning electron microscopy and polarization microscopy (PLM) demonstrated a presence of calcium pyrophosphate (CPP) and basic calcium phosphate (BCP) crystals in early and advanced OA [1]. Calcium carbonate crystals have been found in cartilage specimens of advanced OA and have recently been shown to potentially occur early in development of cartilage calcification [2]
Objectives: In this study we attempt to identify calcium containing crystals in joint fluid of patients with late-stage OA using Raman spectroscopy.
Methods: Synovial fluid samples from advanced knee OA cases were collected from the Maastricht University Medical Center (MUMC+) experimental orthopaedics biobank. This biobank contains synovial fluid samples from patients undergoing total knee replacement surgery for advanced osteoarthritis. The population includes both males and females and all patients were above 18 years of age. Samples were frozen at -80°C. No preservatives were used. Maastricht University Medical Hospital (METC azM/UM) approved sample collection. Patients gave written informed consent before collection of their synovial fluid. Samples were analyzed with an integrated Raman polarized light microscope (H-iRPolM, Hybriscan Technologies B.V., Nijkerk, the Netherlands). For each sample, 20 µl of synovial fluid was pipetted on a microscope slide. Birefringent crystals were localized with PLM and then scanned with the integrated Raman spectrometer. For each particle, the Raman spectrum from 0-3600 cm^{-1} was measured for 1 s/pixel with a laser power of 10 mW and a 532 nm laser. Analysis time per particle was 1-2 minutes depending on particle size. Spectra were analysed by a trained analyst (TN, CO). Samples were considered positive for a certain type of crystal if at least one crystal with a distinctive spectrum could be identified.
Results: Calcium containing crystals were present in all (100%) of the 36 samples. 34 (94.4%) of the samples contained calcite (calcium carbonate) crystals. Dolomite (calcium magnesium carbonate) crystals were present in 10 (27.8%) samples, 9 (25.0%) samples contained both types of calcium carbonate crystals. CPP crystals were present in 33.3% of samples. All the CPP crystals were identified as triclinic CPP, amorphic or monoclinic CPP were not identified. Basic calcium phosphate crystals were present in 9 (25.0%) samples, all of which were hydroxyapatite. Calcium oxalate crystals were present in 7 (19.4%) samples, 3 of which were identified as calcium oxalate dihydrate (COD) and 4 of which were identified as calcium oxalate monohydrate. Most of the samples (80.6%) contained more than one type of calcium crystal, but CPP and BCP were never identified simultaneously in one sample. One patient had some MSU crystals. Raman spectra of identified particles are shown in figure 1.

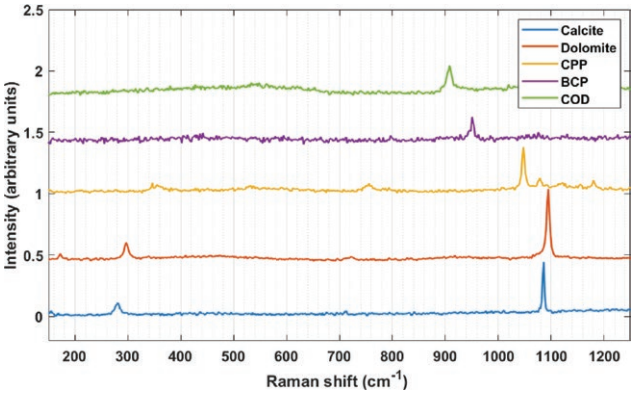


Figure 1. Raman spectra of identified calcium containing crystals.

Conclusion: Calcium containing crystals are common in synovial fluid samples from knee joints in patients with end-stage osteoarthritis. Raman spectroscopy is a novel technique for rheumatology which enables reliable detection and objective identification of crystals such as calcium carbonate. The observation of calcium carbonate (calcite) crystals in synovial fluids of OA patients is novel and a promising subject of further study. Pathways to presentation in synovial fluid and inflammatory properties should be investigated.
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POS0103 PAIN AND FUNCTIONAL IMPAIRMENT ARE MORE PROMINENT IN EROSIVE HAND OSTEOARTHRITIS THAN IN TREATED RHEUMATOID ARTHRITIS: A COMPARATIVE STUDY BETWEEN DIGICOD AND ESPOIR COHORTS

Keywords: Osteoarthritis, Rheumatoid arthritis, Quality of life

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Background: The common belief is to consider hand osteoarthritis (HOA) as a less severe disease with a better functional prognosis and a lower global burden than rheumatoid arthritis (RA). However, this paradigm may no longer be true considering the striking efficacy of targeted therapies in RA compared to the weak efficacy of therapies in the most severe form of HOA, namely erosive HOA (EHOA), which impacts 10-20% of symptomatic HOA [1]. Few studies addressed this issue [2].
Objectives: We aimed to compare the burdens of established EHOA and RA. The objectives were to compare pain, functional impairment, quality of life and the prevalence of comorbidities and of cardiovascular diseases (CVD) between established EHOA and RA.
Methods: DIGital Cohort Osteoarthritis Design (DIGICOD) is a French cohort of symptomatic HOA (at least 2 painful joints) with at baseline a mean ± SD disease duration of 12.9 ± 9.6 years [3]. This study involved the EHOA patients, from inclusion visit of DIGICOD, defined by at least 1 erosive joint according to the Verbruggen score. RA patients fulfilling ACR/EULAR 2010 criteria at the 10th year visit were selected from the ESPOIR cohort (Étude et Suivi des Polyarthrites Indifférenciées Récentes), a French cohort of early RA [4]. Pain intensity at rest or mobilization (0-100mm visual analogical scale (VAS)≥40/100), fatigue (VAS fatigue≥25/100), function (normalized (0-100) scores of Health assessment questionnaire for RA, and AUStralian CANadian Osteoarthritis Hand Index for EHOA > 16.7) were analyzed and compared between EHOA and RA using logistic regression models adjusted on age, gender, BMI, comorbidities and socio-educational level. The risk to have ≥2 comorbidities (among CVD, cancer, hemopathy, fracture) or at least 1 CVD (among high blood pressure, diabetes, dyslipidemia, myocardial infarction, stroke) were compared between EHOA and RA adjusted on age, gender, BMI and socio-educational level. Odds ratios (OR) and their 95% confidence intervals (CIs) were reported (EOHA versus RA).
Results: We analyzed 138 patients with EHOA and 379 with RA. The median [interquartile] age of EHOA patients was higher than RA patients (67.3 [64.3; 72.2] vs 48.6 [39.9; 55.6] years, p<0.001). The disease duration, at the evaluation time, was 13.5 [7.0; 20.0] for EHOA and 10.5 years [10.3; 10.7] for RA patients. RA was anti-CCP antibodies positive for 56% of patients and in remission for 61% (DAS28 < 2.6). RA patients were treated by methotrexate (82%), biologics (37%) and 25% by corticosteroids while 20% of EHOA patients received oral non-steroidal anti-inflammatory drugs. EHOA patients had more painful joints in the hands than RA patients (4.0 [2.0;8.8] vs 0.0 [0.0;3.0], p< 0.001). In the adjusted analysis, EHOA was associated with more pain at mobilization (OR = 3.13 95% CI [1.74 to 5.68] p< 0.001) and more functional impairment (OR = 2.27 CI 95% [1.26 to4.17], p = 0.007) (Figure 1). There was no difference for pain at rest and for fatigue VAS. For comorbidities, the proportions of EHOA patients with ≥2 comorbidities were higher than RA patients (37.7% vs 27.5%). However, when we stratified by age, the proportions of patients with ≥2 comorbidities were higher in RA patients between 50 and 70 years old (30.2% vs 47.1%) compared to EHOA patients. In adjusted analysis, the risk to have ≥2 comorbidities was lower in EHOA than in RA patients (OR = 0.25 CI 95% [0.13 to0.48]; p< 0.001) while there was no difference for CVD risk.
Conclusion: After more than 10 years of disease duration, EHOA is associated with more pain and more functional impairment but less comorbidities than RA. This study highlights the significant unmet need for effective therapies for patients with EHOA.

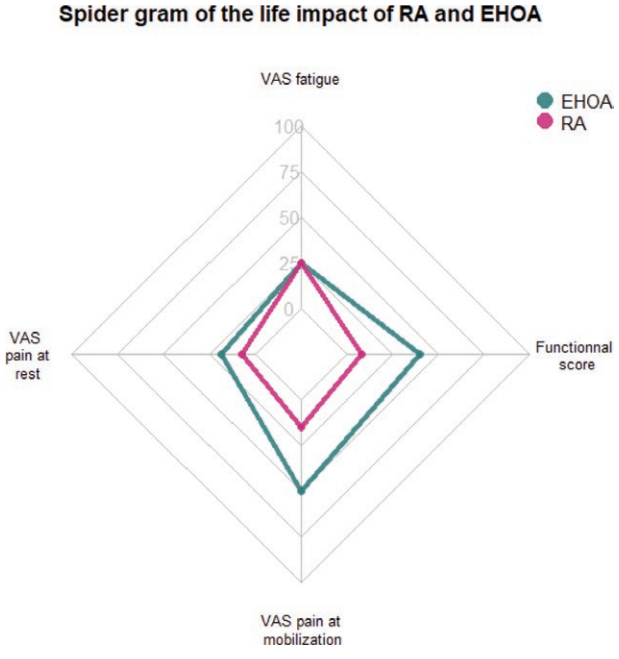


Figure 1. Spider gram of the life impact of RA and EHOA

VAS = visual analogical scale, EHOA = erosive hand osteoarthritis; RA: rheumatoid arthritis.

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POS0104

A PHASE 2B DOUBLE-BLIND PLACEBO-CONTROLLED RANDOMIZED CLINICAL TRIAL OF SB-061, AN AGGRECAN MIMETIC, IN SUBJECTS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS

Keywords: Osteoarthritis, Randomized control trial, Clinical Trials

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Background: Osteoarthritis (OA) is a chronic disease characterized by degradation of joint structures including the subchondral bone, the synovium, and cartilage. Aggrecan constitutes a major component of hyaline cartilage and plays an important role for its normal function. In OA, aggrecan is gradually lost, which together with cytokines, proteases, and circulating pro-inflammatory fragments of hyaluronic acid (HA) further accelerates tissue destruction. SB-061 is an aggrecan mimetic, composed of a backbone of chondroitin sulfate conjugated to a HA peptide coating protein. SB-061 is believed to bind HA fragments in the synovium. Hence, SB-061 acts upstream in the inflammatory cascade, thereby potentially reducing both pain as well as structural deterioration [1].
Objectives: To evaluate the efficacy and safety of intra-articular injections of SB-061 in subjects with knee OA.
Methods: This was a randomized, placebo-controlled, double-blind phase II study comparing quarterly intra-articular injections of SB-061 with placebo (isotonic saline) for 52 weeks (EudraCT No. 2019-004515-31). Eligible subjects had a Kellgren-Lawrence (KL) grade of 2 or 3 on X-ray of the target knee and a Western Ontario and McMasters Osteoarthritis Index (WOMAC) pain score ≥20 out of 50 at screening and baseline visits. Subjects having used any medication known to affect the joints up to 3 months prior to the study or having any other knee condition were excluded. Any use of analgesic medication was prohibited during the study, except for rescue medication (paracetamol/acetaminophen). The primary endpoint was the change from baseline (CFB) in WOMAC pain at Week 8 after first injection. Secondary endpoints were CFB in WOMAC function and total, ICOAP and the Patient Global Assessment (PGA), and 20-meter walk test. Exploratory structural endpoints included CFB in knee cartilage thickness and volume, and bone shape as measured by magnetic resonance imaging (MRI), and CFB in the radiographic minimum joint-space width (JSW).
Results: A total of 288 subjects were randomized to SB-061 (n= 145) or placebo (n=143), and of these 252 (87.5%) completed injections. The two groups were well-balanced in terms of the main clinical and radiographic parameters, and reflective of a typical OA clinical trial population. The primary endpoint was not met, as there was no significant difference in the CFB of the WOMAC pain score (0-50) at Week 8 between the groups (LSmean difference: 0.00, 95% CI -4.33; 4.34, p=0.999, nor at any other time point during the trial (Figure 1). Similarly, neither of the secondary endpoints of changes from baseline in WOMAC function, WOMAC total, ICOAP, PGA, and 20-meter walk test indicated any significant difference between SB-061 and placebo. There was no significant difference between groups in CFB in JSW or any of the MRI parameters. The frequency and type of adverse events was similar between groups receiving SB-061 and placebo. SB-061 was well-tolerated.

Conclusion: Intra-articular injections of SB-061 administered quarterly for one year in patients with knee OA was safe but did not show any statistically significant effect on knee pain nor on other symptomatic or structural entities compared to placebo.

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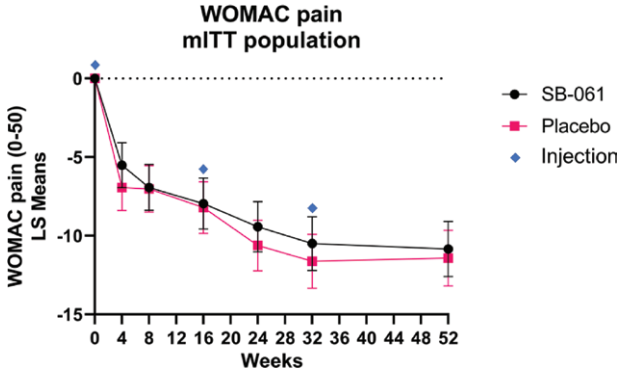


Figure 1.

Acknowledgements: NIL.

Disclosure of Interests: Asger Reinstrup Bihlet Employee of: Employee and shareholder in Nordic Bioscience., Inger Byrjalsen Employee of: Previous employee in Nordic Bioscience., Kamilla Mundbjerg Employee of: Employee in Nordic Bioscience Clinical Development., Peter Alexandersen Employee of: Part-time employee Nordic Bioscience Clinical Development., Helene Rovsing: None declared, Tobias Axelsen: None declared, Jeppe Ragnar Andersen Employee of: Employee and shareholder in Nordic Bioscience., Anna Metnik Employee of: Employee in Nordic Bioscience Clinical Development., Nathan Bachtell: None declared, Alan Brett Employee of: Employee and shareholder in Stryker., Claus Christiansen Employee of: Shareholder in Nordic Bioscience.

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POS0105 CHANGES IN RADIOGRAPHIC SIGNS IN PATIENTS WITH HAND OSTEOARTHRITIS DURING 2 YEARS

Keywords: Osteoarthritis, Epidemiology

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Background: Hand osteoarthritis is a disorder that often evolves slowly. Some patients may have structural progression over a short term.

Objectives: We aimed to investigate which patients show radiographic progression over 2 years and what their determinants are.

Methods: Data from the ongoing HOSTAS (Hand OSTeoArthritis in Secondary care) cohort were used, consisting of 538 consecutive patients with primary hand OA diagnosed by their rheumatologist, followed for two years. Hand radiographs were obtained at baseline and year two. Questionnaires regarding demographics, disease and patient characteristics and the Australian Canadian Hand osteoarthritis index (AUSCAN) were collected. Hand radiographs were scored blinded, paired and in chronological order, using the Osteoarthritis Research Society International (OARSI) system (osteophytes (OP) and joint space narrowing (JSN), scored 0-3) per joint (summed for total 0-96). Intra-observer reliability was high, (intra-class correlation (ICC) 0.99 and 1.00 at baseline for OP and JSN sumscores, respectively). Reliability for change scores was high (ICC 0.77 and 0.86, for OP and JSN, respectively). The smallest detectable changes were 0.92 for OP (cut-off 1) and 1.32 for JSN (cut-off 2). Cut-offs were used to classify progressors (increase) or non-progressors (stable or decrease). Additionally, baseline radiographs were scored using the Kellgren-Lawrence system (0-4 per joint, total 0-120). Erosive disease was defined as at least 1 joint in the Verbruggen-Veys erosive or remodeling phase. Progressor and non-progressor groups were analysed for determinants using logistic regression.

Results: 442 patients had radiographs assessed at baseline and year 2, with mean (SD) age 61 (8.4) years and 85% female. Median (IQR) baseline OP/JSN sumscores were 9 (5-18) and 9 (4-19), respectively. Based on the SDC, 272/417 (65%) participants progressed on OP scores (median [IQR] change 1 [0-2]) and 135/419 (32%) on JSN scores (median [IQR] change 1 [0-2]). Four and 18 had a decrease in OP and JSN, respectively. Progression of OP was positively associated with erosive disease, measures of radiographic damage at baseline and female sex. Progression of JSN was positively associated with age, erosive disease and radiographic damage at baseline. Progression of JSN showed a positive association with changes in AUSCAN scores over 2 years.

Conclusion: Over 2 years, considerable radiographic progression was seen. Especially patients with erosive disease and the most severe radiographic damage at baseline were at risk for progression. Progression of JSN was associated with changes in pain and function. Progression in JSN was associated with age, whereas OP was with female sex. These findings may potentially represent different underlying pathogenetic mechanisms.

Table 1. Associations with change in osteophytes

	Odds ratio (95% confidence interval)	
	Increase in osteophytes (n=272)	**Increase in joint space narrowing (n=135)**
Patient characteristics at baseline		
Female sex[1]	1.71 (0.95-3.05)	1.03 (0.56-1.94)
Age; mean (SD)[2]	1.00 (0.98-1.03)	1.04 (1.01-1.06)
BMI; mean (SD)[3]	0.97 (0.93-1.02)	0.97 (0.93-1.02)
Radiographic outcomes at baseline		
KL sum score (0-120); median (IQR)	1.03 (1.02-1.05)	1.03 (1.02-1.05)
Osteophyte sum score (0-96); median (IQR)	1.04 (1.01-1.07)	1.05 (1.03-1.07)
Joint space narrowing sum score (0-96); median (IQR)	1.06 (1.04-1.09)	1.04 (1.02-1.06)
Erosive disease	3.15 (1.86-5.53)	2.01 (1.25-3.24)
Patient reported outcome measures		
Change in AUSCAN baseline – year 2	0.98 (0.92-1.03)	1.06 (1.00-1.13)
Pain (0-20)	1.00 (0.97-1.03)	1.06 (1.03-1.11)
Function (0-36)		

Non-progression group as index group for both osteophytes and joint space narrowing. Groups defined according to smallest detectable change in osteophyte/joint space narrowing sum score for both hands. Analyses are adjusted for age, sex and BMI, unless stated otherwise. [1]Adjusted for age and BMI. [2]Adjusted for sex and BMI. [3]Adjusted for age and sex. BMI = body mass index. KL = Kellgren-lawrence. AUSCAN = Australian Canadian hand osteoarthritis index.

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POS0106 INTRA-ARTICULAR MM-II, A NOVEL SUSPENSION OF LARGE EMPTY MULTILAMELLAR LIPOSOMES, IN PAINFUL KNEE OSTEOARTHRITIS: A 26 WEEK PHASE 2B RANDOMIZED TRIAL

Keywords: Osteoarthritis, Clinical Trials

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Background: MM-II, a novel suspension of empty large multilamellar liposomes composed of dimyristoylphosphatidylcholine (DMPC) and dipalmitoylphosphatidylcholine (DPPC), has demonstrated beneficial effects in OA animal models. In a prior first-in-man study, MM-II demonstrated the ability to lower pain in knee OA patients for up to 3 months.

Objectives: The aims of this phase 2b study were to determine an effective dose, the durability of response, and the safety of MM-II in patients with symptomatic knee OA.

Methods: Consented participants were enrolled in a 6-arm randomized, double-blind, placebo-controlled 26-week trial evaluating a single IA injection of

MM-II at doses of 1ml, 3ml and 6ml (150mM concentration of lipids) and placebo of matching volumes. Key inclusion criteria: age ≥ 40 years, KL grades 2 or 3, ACR OA criteria, WOMAC A pain ≥2 (0-4 Likert scale), VAS ≥50 and ≤90 (100mm scale), and intolerance/inadequate response to NSAIDs or acetaminophen. Primary endpoint was change in WOMAC A pain score at week (Wk) 12; secondary endpoints included weekly average daily pain score (ADP, e-diary) at Wks 12 & 26, WOMAC A pain at 26 wks, Patient Global Assessment (PGA) and WOMAC B and C at Wks 12 & 26, and use of rescue medication. Randomization was stratified by BMI (< 30, 30 ≤BMI<35, and BMI ≥ 35) and baseline knee pain (VAS≤74, VAS≥ 75). Statistical analysis for the primary endpoint was analyzed based on FAS using a mixed model repeated measures (MMRM) with fixed effects for treatment group, visit (Wk 1-12), and treatment-by-visit interaction and covariates of site, baseline WOMAC pain, BMI and VAS groups. Subjects were included as random effects. Treatment differences were estimated using least square means (LSM) with 95% CIs. Step-down Dunnett's hierarchical testing procedure compared the active doses to 3 mL placebo to adjust for multiplicity. Confidence intervals were unadjusted.

Results: 397 participants were randomized with no significant differences in baseline demographics or clinical characteristics across all treatment groups. Mean age was 62.7 (SD 8.1) years; participants were predominantly female (65.0%) and white (67.0%) with mean BMI 30.8 (SD 6.1) kg/m2. Overall, 6.8% of participants discontinued the study. The primary endpoint of WOMAC A change from baseline to Wk 12 showed LSM difference of -0.24, 95% confidence interval (CI) -0.476, -0.004, p = 0.085 for the 3ml group and -0.02, 95% CI -0.269, 0.222, p = 0.85 for the 6ml group, both vs 3ml placebo, adjusted for multiplicity. The results of the 3ml group were sustained to Wk 26. Nominal significance was seen at some time points. When comparing 3ml MM-II to the pooled placebo groups, the LSM difference in change from baseline of the WOMAC A at Wk 12 was -0.28, 95% confidence interval (CI) -0.484, -0.068, p = 0.018 adjusted for multiplicity. The LSM differences in weekly ADP scores were nominally significant at Wks 12 and 26 for the MM-II 3ml group vs 3 ml placebo: -10.9, 95% CI (-18.88, -2.83), p = 0.008 and -11.8, 95% CI (-20.19, -3.34), p =0.006, though the 6ml group was not significant (Figure 1). The changes in use of rescue medication corresponded to changes in symptoms during the trial. Treatment was well tolerated with TEAEs reported in 2.6% of MM-II and 2.9% of control participants. Injection site reactions were similar in the treatment and control groups, 1.9% and 2.9%, respectively.

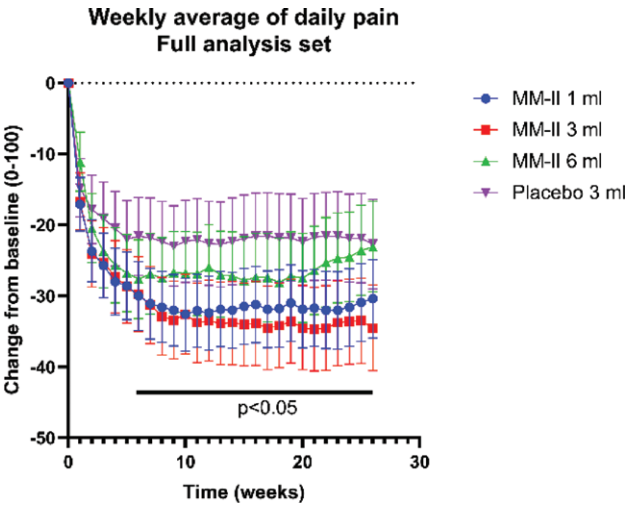


Figure 1.

Conclusion: Differences between MM-II and placebo in WOMAC A were not statistically significant at Wk 12, though WOMAC reductions were nominally significant at some time points, and when comparing 3ml MM-II to the pooled placebo groups, results were nominally significant at Wk 12. MM-II at 3ml dose demonstrated consistent and durable reduction in weekly knee ADP scores, nominally significant compared to placebo, as early as Wk 6, with efficacy maintained through Wk 26. Treatment with MM-II was well tolerated with low levels of adverse events. MMI-II may have the ability to provide durable and relevant pain relief, warranting confirmation in further clinical studies.

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POS0107 ULTRASONOGRAPHY MAY IMPROVE OSTEOARTHRITIS PAIN PREDICTION: AN ARTIFICIAL INTELLIGENCE APPROACH

Keywords: Pain, Ultrasound, Artificial Intelligence

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Background: Knee osteoarthritis (OA) pain scores only moderately correlate with conventional radiographic findings—likely because pain has a multifactorial etiology. Ultrasound (US) can capture soft tissue structures which are known to be involved in pain pathophysiology but may not be visible in knee radiographs. Importantly, US is a cost-effective and portable imaging technology that can be performed at the point of care by non-radiologists. Therefore, US may have utility in understanding variance in pain attributed to knee OA.

Objectives: Our objective was to demonstrate if adding US features to computer vision analysis of radiographic images improves machine learning-based prediction of Knee injury and Osteoarthritis Outcome Score (KOOS) Pain scores in knee OA.

Methods: 116 subjects with end-stage knee OA were included in the study and were grouped into training and testing sets with an 80:20 split. Posterior anterior flexion view x-rays and standardized knee US images were collected. A fellowship-trained musculoskeletal radiologist read 26 ultrasound continuous and ordinal features. All x-rays were pre-processed by cropping and applying Contrast Limited Adaptive Histogram Equalization. The processed images were resized to 224 x 224 pixels, stacked to form three-channel images, and mean-subtracted with respect to ImageNet (**Figure 1**). We generated the radiograph input feature vectors by using a pretrained ResNet50 model with a global average pooling layer replacing the classification head. We trained models to predict KOOS Pain with only radiograph image embeddings, solely US features, or multimodal inputs by concatenating the two feature vectors. For radiograph image embeddings and ultrasound feature vectors, we applied min-max normalization with the respective extrema of the training dataset for each feature. As a secondary analysis, we trained additional models to predict KOOS Symptoms and KOOS Function in Daily Living (ADL) sub-scores. Across all inputs and target variables, we used five-fold cross-validation for model selection across random forest regressors and histogram-based gradient boosting regression trees from the scikit-learn package, CatBoost regressors, and XGBoost regressors. All models were trained using default hyperparameters defined by the respective model packages during model selection and final training. We report and compare model performance using Pearson r correlation coefficient, mean absolute error, and root mean squared error. All performance metrics were calculated using the scikit-learn and SciPy packages.

Results: When predicting KOOS Pain scores, radiographic image data alone (r = 0.26) or ultrasound scores alone (r = -0.17) did not perform as well as the multimodal model (r = 0.34) where both radiographic and ultrasound measurements were included (**Table 1**). For prediction of KOOS Symptoms scores, an input of radiographic image data alone (r = 0.45) correlated better than when either ultrasound features alone (r = -0.16) or the multimodal model (r = 0.28) were used as inputs. Similarly, when predicting KOOS ADL scores, radiographic image data alone (r = 0.14) correlated better than ultrasound features alone (r = -0.20) or the multimodal model (r = -0.03).

Conclusion: Combining US features with knee radiographs may improve performance for predicting KOOS Pain scores in patients with end-stage knee OA, but did not improve the prediction of KOOS Symptoms or ADL scores. Our results suggest that soft tissue features captured by US can help us understand differences and underlying mechanisms in pain attributed to OA.



Figure 1. Preprocessing pipeline. a) The original image input. b) We manually mask all artifacts using the lowest pixel intensity value of the image, apply contrast limited adaptive histogram equalization (CLAHE), and crop a 140 x 140mm region of interest (ROI) centered on a manually annotated point. c) The cropped ROI is resized to 224 x 224 pixels. d) The grayscale ROI is stacked three times to form a three-channel image. e) Apply ImageNet normalization to the image.

Table 1. Model performance by input

Target	Inputs	Model	MAE	RMSE	Pearson r
KOOS Pain	X-ray	CatBoost	13.32	15.77	0.26
	US	Histogram-based Gradient Boosting Regression	16.58	19.96	-0.17
	X-ray + US	CatBoost	13.11	15.48	0.34
KOOS Symptoms	X-ray	Random Forest	13.97	17.42	0.45
	US	Random Forest	17.40	21.25	-0.16
	X-ray + US	CatBoost	13.91	18.19	0.28
KOOS ADL	X-ray	CatBoost	16.16	19.39	0.14
	US	CatBoost	18.23	21.68	-0.20
	X-ray + US	Random Forest	16.83	20.01	-0.03

US = Ultrasound

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POS0108 WOMAC KNEE PAIN: DOES IT WALK THE WALK?

Keywords: Imaging, Pain, Osteoarthritis

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Background: Due to its major public health impact, knee osteoarthritis (KOA) has been designated as a serious disease by the US Food and Drug Administration (FDA). Approval of a disease modifying osteoarthritis drug (DMOAD) to slow or prevent disease progression hinges on demonstrating both symptomatic (i.e., how a patient feels or functions) and structural improvement. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the questionnaire most commonly used to assess symptomatic improvement, may not adequately reflect pain reporting due to KOA. The lack of DMOAD approval to date has largely been attributed to the lack of clinical translation of structural benefits that also yield symptomatic improvements. Drugs targeting inflammation are an example of a therapeutic approach that has yielded evidence of structural benefit but not symptomatic improvement as assessed by the WOMAC.

Objectives: Evaluate potential heterogeneity of the effects of structural damage on knee pain reporting across activities assessed in the WOMAC pain subscale following recent development of radiographic knee osteoarthritis.

Methods: The Osteoarthritis Initiative is a longitudinal observational study of participants with or at risk of symptomatic knee OA. We identified incident cases of radiographic KOA, defined as Kellgren-Lawrence [KL] grade 2 or 3 based on centrally graded x-rays. Participants underwent bilateral posteroanterior fixed-flexion weight-bearing knee radiography at clinic visits annually or biannually through year 10. Non-contrast 3T MRI was also acquired at clinic visits up to year 8. Musculoskeletal radiologists graded structural damage, including effusion-synovitis (ES), Hoffa-synovitis (HS), bone marrow lesions (BMLs), cartilage and meniscal damage using the MRI Osteoarthritis Knee Score (MOAKS). The WOMAC knee pain subscale is calculated by adding reported pain scores from various activities, including walking on a flat surface, going up or down stairs, at night while in bed, sitting or lying down, and standing, during the last seven days, rated on a 5-point scale from none (0), mild (1), moderate (2), severe (3), or extreme [4]. Pain in each knee was reported separately. We fit a proportional odds logistic regression to model the ordinal pain scores reported for each activity on the WOMAC pain scale using penalized maximum likelihood estimation; predictors included each of the MRI structural damage scores, KL grade, age, and BMI at the same clinic visit, as well as sex and race. We estimated the predicted probability of pain rated moderate or worse ($Pr[Y \geq 2 \mid X]$), and reported nonparametric bootstrap 95% confidence intervals (CI) with cluster sampling at the participant-level.

Results: We identified 690 knees contributed by 623 participants that developed radiographic KOA. The mean participant age was 65 years (SD 9), mean BMI was 29.3 (SD 4.8), 66% reported female sex and 83% self-identified as white. The predicted probability of knee pain rated moderate or worse (≥2) increased with greater ES during walking and stair climbing, but there was no evidence that ES affected knee pain while in bed, sitting or lying down, or standing (Figure 1). We did not find evidence that HS, BMLs, cartilage or meniscal damage affected the WOMAC knee pain items cross-sectionally in our fully adjusted models.

Conclusion: Our study suggests that ES seen on MRI produces heterogeneous effects on pain reporting, depending on the type of activity. Treatments that are developed to target inflammation may reduce pain during some activities, such as walking and stair climbing, but may have little benefit during other activities, such as sitting or lying down. If a treatment effectively reduces or limits structural damage that differentially impacts pain across the activities included in the WOMAC pain subscale, analysis that focuses only on the WOMAC pain subscale score may mask the clinical benefit of the treatment.

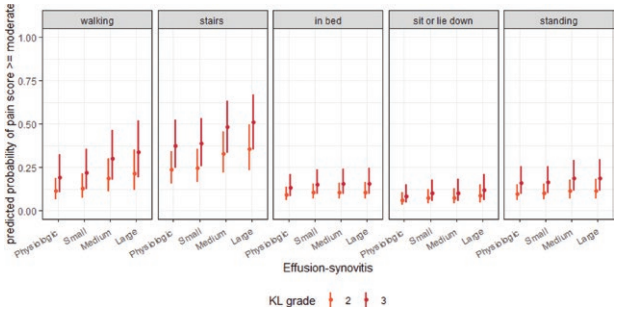


Figure 1.

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POS0109 CAN GAIT PATTERNS IN KNEE OSTEOARTHRITIS PATIENTS BE EXPLAINED OR PREDICTED BY JOINT STRUCTURE?

Keywords: Imaging, Osteoarthritis

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Background: This study uses gait measurements and imaging techniques in knee osteoarthritis (OA) patients to investigate the association between gait patterns and joint structure.

Objectives: To analyze whether 1) gait patterns can be explained by joint structure and 2) longitudinal gait alterations can be predicted by joint structure in people with knee OA.

Methods: In the IMI-APPROACH cohort, 297 people with knee OA were included at 5 sites in Europe. At baseline and two years, full gait kinematic data was collected from all participants using the GaitSmart system (Dynamic Metrics Limited, Codicote, UK). Radiographs and MRI scans of their index knee were performed for evaluation of joint structure. The GaitSmart measures included for the current study were range of motion (ROM) of the hip, thigh, knee in swing and stance phase, and calves in the sagittal plane, and medial-lateral movement of the thigh and calf, all for the index leg. Stride duration and speed were included as well. From the radiographs, the minimum joint space width (JSW), femorotibial angle, mean whole-joint subchondral bone density (SBD), and total whole-joint osteophyte area were determined. From the MRI scans, mean whole-joint femorotibial cartilage thickness (FTC) was determined and MOAKS scoring for synovitis, effusion, meniscus signal and meniscal extrusion were performed. For the meniscal parameters, the maximum score across all regions was used. All GaitSmart parameters were compared between baseline and two years with paired t-tests to quantify gait alterations over two years. For the comparisons with joint structure, principal component analyses (PCA) was performed on the gait parameters first, to discover underlying domains. Univariate backwards linear regression models with each of the GaitSmart domains as dependent variable were used to analyze how joint structure influences gait or predicts gait change over two years. Three models were run: one with participant demographics (age, sex, BMI) only, one with structural imaging parameters only, and one combining the first two models.

Results: 284 Participants (age 66.5±7.1, BMI 28.0±5.4, 65 (23%) male, 154 (54%) radiographic OA) had baseline GaitSmart data (211 had two-year data). PCA identified three gait domains: upper leg (speed, duration, thigh ROM and hip ROM), lower leg (knee ROM in stance and swing, calf ROM), and medial-lateral movement (thigh and calf medial-lateral movement). Over two years the lower leg parameters showed a slight deterioration, though only knee ROM in swing phase changed significantly (-1.5±6.9 degree, p=0.002). The upper leg parameters showed minor non-significant improvement over two years; the medial-lateral parameters showed opposing non-significant changes. Results of all models are summarized in Table 1. Cross-sectionally, male sex, higher BMI, higher SBD and synovitis absence were associated with worse upper leg function. Change in upper leg gait was predicted by sex only, with male sex resulting in less function improvement. For lower leg gait, female sex, higher BMI, bigger osteophytes, higher FTC, absence of effusion and presence of synovitis lead to worse function (i.e. larger ROM) cross-sectionally. Worsening lower leg gait could be predicted by higher age and BMI, presence of synovitis and smaller osteophytes. Neither demographics nor joint structure was significantly associated with or predictive for changes in medial-lateral gait.

Conclusion: Joint structure could partially explain gait and even predict gait changes in people with knee OA especially for the lower leg, providing a significant association between OA symptoms and joint structure, although only for a limited part (low R^2 values; Table 1) and not for medial-lateral movement. Surprisingly, synovitis and osteophyte size showed contrasting associations with lower leg gait that may be explained by half of the patients not having radiographic OA and should be investigated further. Parameters indicating more severe OA (e.g. lower JSW and FTC, higher age and SBD) were generally associated with more impaired gait.

Table 1: Baseline associations and two-year prediction of changes in the different gait domains, for participant demographics (model 1), joint structure (model 2), and a combination (model 3).

GaitSmart domain	Model 1: demographics		Model 2: joint structure		Model 3: model 1 + model 2	
	Variables	R^2	Variables	R^2	Variables	R^2
Baseline associations						
Upper leg	• Sex (β=-0.11; p=0.062) • BMI (β=-0.21; p<0.001)	0.058	• SBD (β=-0.14; p=0.027) • Synovitis (β=0.11; p=0.090)	0.026	• Sex (β=-0.14; p=0.018) • BMI (β=-0.23; p<0.001) • Synovitis (β=0.12; p=0.051)	0.080
Lower leg	• Sex (β=0.27; p<0.001) • BMI (β=-0.28; p<0.001)	0.142	• FTC (β=0.11; p=0.059) • Osteophytes (β=-0.26; p<0.001) • Synovitis (β=0.15; p=0.023) • Effusion (β=-0.16; p=0.022)	0.136	• Sex (β=0.30 p<0.001) • BMI (β=-0.23; p<0.001) • Osteophytes (β=-0.33; p<0.001)	0.241
Medial-lateral	None	-	None	-	None	-
Two-year change prediction						
Upper leg	• Sex (β=-0.15; p=0.026)	0.024	None	-	• Sex (β=-0.15; p=0.026)	0.024
Lower leg	• Age (β=-0.17; p=0.016) • BMI (β=-0.18; p=0.010)	0.048	• Osteophytes (β=0.175; p=0.017) • Synovitis (β=-0.21; p=0.004)	0.053	• Age (β=-0.14; p=0.046) • BMI (β=-0.17; p=0.014) • Osteophytes (β=0.20; p=0.006) • Synovitis (β=-0.18; p=0.013)	0.094
Medial-lateral	None	-	None	-	None	-

FTC: femorotibial cartilage thickness; SBD: subchondral bone density. Sex was coded 1 for female and 2 for male.

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POS0110 ARTHROSCOPY IS NECESSARY TO DETECT CARTILAGE DAMAGE IN NON-ADVANCED KNEE OA

Keywords: Osteoarthritis

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Background: Knee osteoarthritis (OA) is characterized by the slow deterioration of articular cartilage that takes years to destroy the tissue. Magnetic resonance imaging (MRI) is commonly used for quantitative assessment of articular cartilage, and thus proposed by many authors as a substitute for X-ray, which requires longer periods of time --at least 3 years between images-- to detect changes. Drug agencies continue to consider X-ray outcomes preferable for clinical trials, as the

superiority of MRI over X-ray is not clear. More importantly, these measurements have not been compared with direct visualization of the cartilage.
Objectives: To evaluate cartilage width as well as early cartilage lesions by X-ray and MRI techniques, comparing these observations with those obtained by direct visualization of cartilage during arthroscopy (ARTH) in a population with non-advanced knee OA.
Methods: We prospectively recruited 105 patients (>18 y.o) with knee pain of more than 3 months´ duration who underwent diagnostic knee ARTH due to uncertain origin knee pain or meniscal tear. WOMAC score was used to assess joint pain and function. Standardized weight-bearing extended anteroposterior digital X-ray were performed aligning the center of the beam with de femorotibial joint space. Images without correct alignment of the tibial plateau were discarded. By X-ray, OA grade was assessed by the Kellgren and Lawrence score (KLS). Medial and lateral joint space width (JSW) was measured on X-ray at the mid-surface of the affected knees in a blind manner. By MRI, cartilage lesions were classified into 3 categories (MRI score, MRI-S): normal (no damage), low grade (fibrillation or thickening <50%) or high grade (thickening >50% or loss). Knee ARTH was performed through two portals according to standard practice and cartilage lesions assessed by Outerbridge score (OBS). Bonferroni-corrected ANOVA test for continuous variables, Chi-square or Fisher's test for discrete variables, normality with Shapiro-Wilk and Kolmogorv-Smirnov tests, concordance between groups with weighted Kappa index, correlation between OBS and cartilage measurement with Spearman's correlation were performed employing Python 3.7 and SPSS25 for Windows 10.
Results: The correlation between X-ray JSW measurement and the OBS was null (r=-0.052). No good agreement was found between the OA grade assessed by KLS and OBS, nor between MRI-S and OBS. Cartilage deterioration evaluated by X-ray and MRI showed a lower degree of tissue damage than that observed by ARTH visualization (Table 1).

Table 1. (a) Agreement between OBS and KLS (64 patients) and between OBS and MRI-S (96 patients) in the medial (b), lateral (c) and femoropatellar (d) compartments of the damaged knee.

		OBS 0	OBS 1	OBS 2	OBS 3	OBS 4	Kappa
KLS	Grade 0	16	3	3	8	3	0,16
(a)	Grade 1	7	1	2	5	3	
	Grade 2	2	1	3	3	3	
	Grade 3	0	0	0	1	0	
	Grade 4	0	0	0	0	0	
MRI-S	Normal	39	7	8	9	6	0,48
medial	Low	5	0	3	0	1	
(b)	High	0	1	1	11	5	
MRI-S	Normal	62	10	5	4	0	0,37
lateral	Low	3	0	0	0	1	
(c)	High	4	2	0	1	4	
MRI-S	Normal	39	6	7	7	0	0,20
femoropatellar	Low	6	0	2	3	0	
(d)	High	12	1	6	6	1	

The WOMAC score was significantly different between patients with different OBS. Then, there was a significant increase in the WOMAC score in patients with OBS 2, 3 and 4 with respect to patients with score 0, p=0.009. In patients with OBS 0, 1, 2, 3, and 4, the WOMAC scores were (mean±SD): 41±22; 47±14; 50±23*; 56±19*; and 60±20*, respectively; *p<0.05 vs. OBS grade 0. However, no significant differences in the WOMAC score between patients with different grades of cartilage deterioration were observed when it was assessed by MRI or X-ray.

Conclusion: ARTH enabled to detect cartilage damage with higher precision than X-ray or MRI. In addition, the ARTH assessment was able to explain the different pain and function levels, since patients with different OBS showed different WOMAC scores. MRI can detect joint lesions in the extra-articular space or related to bone damage, which are not observable with ARTH. Therefore, for clinical trials assessing structure progression, ARTH evaluation combined with MRI would be the most appropriate techniques to accurately measure cartilage deterioration.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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A novel journey into SLE, Sjogren and APS

POS0111 **PILOT STUDY ON EVOKED COMPOUND ACTION POTENTIAL CONTROLLED CLOSED-LOOP SPINAL CORD STIMULATION IN TREATMENT OF RAYNAUD'S PHENOMENON**

Keywords: Investor initiated trial, Pain, Imaging

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Background: Raynaud's Phenomenon (RP) is an episodically occurring vasospasm of the peripheral arteries that leads to paleness, cyanosis and/or erythema, causing severe pain, sometimes paresthesia and rarely leading to ulceration of the digits and toes. In severe cases, RP patients have physical and functional impairments that substantially affect their ability to work. There are few reports, mostly case series, on the utility of spinal cord stimulation (SCS) to treat RP. However, there is a lack of objective evidence on the physiological effects (e.g., vasodilation) of SCS in this condition. Here, we present clinical outcomes of severe RP patients treated with evoked compound action potential (ECAP)-controlled closed-loop SCS.
Objectives: Severe primary and secondary RP patients can be treated with evoked compound action potential (ECAP)-controlled closed-loop SCS. High-resolution Doppler ultrasound can be used as objective evidence on the physiological effects (e.g., vasodilation) of SCS in RP patients.
Methods: This is a prospective, single-center pilot study to evaluate the effectiveness of ECAP-controlled closed-loop SCS in treating RP. Subjects who meet the inclusion/exclusion criteria, complete all baseline assessments, and sign an informed consent will be considered enrolled (10 in total). Patient outcomes such as Raynaud Condition Score, Raynaud Severity Score, Raynaud Frequency Score, Cochin Hand Function Scale, SHAQ RP VAS, EQ-5D-5L, PGIC and objective peripheral circulation assessments using high-resolution Doppler ultrasound of digital arteries will be reported.
Results: The mean age ± standard deviation (± SD) of the ten patients is 45.5 ± 15.5 years. The mean baseline (± standard error mean (SEM); n = 9) weekly attack frequency was 21.8 ± 5.9 and decreased to 7.7 ± 2.1 after the test phase (n = 9), 4.8 ± 1.7 1-month after implantation (n = 8), 12.4 ± 6.2 3-months after implantation (n = 8) and to 12.6 ± 4.6 6-months after implantation (n = 8). The mean baseline (± SEM; n = 9) severity of attacks was 6.7 ± 0.4 which decreased to 4.9 ± 0.6 after the test phase (n = 9), 4.6 ± 0.9 1-month after implantation (n = 9), 3.8 ± 0.9 3-months after implantation (n = 8) and to 3.3 ± 0.6 6-months after implantation (n = 8). The mean baseline (± SEM; n = 9) Raynaud's condition score was 6.6 ± 0.7 and decreased to 4.4 ± 0.7 after the test phase (n = 9), 4.3 ± 1.0 1-month after implantation (n = 9), 3.4 ± 1.0 3-months after implantation (n = 8) and to 2.6 ± 0.7 6-months after implantation (n = 8). The mean baseline (± SEM; n = 9) for pathological arterial occlusion was 8.6 ± 1.5, with hands warmed in a finger bath. After the trial period (trial-end; n = 9), the mean total score (± SEM) for pathological artery occlusions decreased to 1.9 ± 1.0, and to 2.0 ± 1.1 1-month after implantation (1-month; n = 9), and to 2.1 ± 2.0 3-months after implantation (3-months; n = 8), and to 4.9 ± 2.6 6-months after implantation (6-months; n = 8). The mean baseline (± SEM; n = 9) cochin hand function scale score was 31.6 ± 8.2 and decreased to 24.7 ± 8.0 after the test phase (n = 9), 18.9 ± 7.8 1-month after implantation (n = 9), 19.5 ± 7.5 3-months after implantation (n = 8) and to 17.4 ± 7.7 6-months after implantation (n = 8). The mean patient global impression scale score at 1-month was (± SEM; n = 9) 2.4 ± 0.3, 2.8 ± 0.4 3-months after implantation (n = 8) and decreased to 2.3 ± 0.4 6-months after implantation (n = 8).

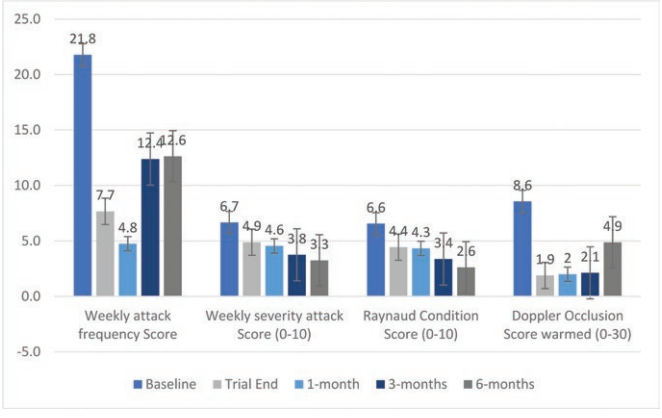


Figure 1.

Conclusion: This study demonstrates for the first time that RP-related pathological arterial occlusions can be treated effectively with a novel ECAP-controlled closed-loop-SCS system. In conclusion, ECAP-controlled closed-loop-SCS alleviates RP symptoms and improves peripheral blood flow. Longer-term follow up and larger controlled studies are needed to confirm these preliminary results.
REFERENCES: NIL.
Acknowledgements: NIL.
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POS0112

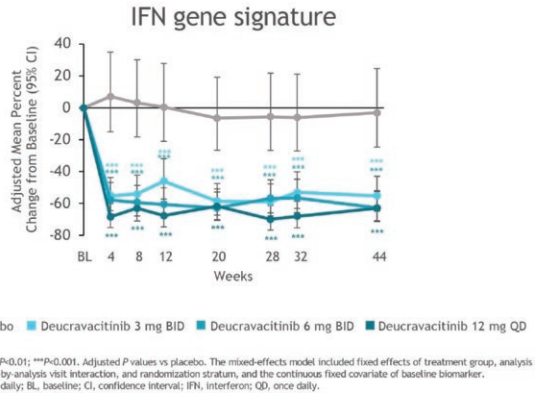
DEUCRAVACITINIB REDUCES INTERFERONS, B-CELL PATHWAYS, AND SEROLOGICAL BIOMARKERS OF SYSTEMIC LUPUS DISEASE ACTIVITY: PHARMACODYNAMIC ANALYSIS FROM THE PHASE 2 PAISLEY STUDY

Keywords: Systemic lupus erythematosus, Targeted synthetic drugs, Biomarkers

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Background: Tyrosine kinase 2 (TYK2) mediates signaling of key cytokines (eg, type 1 IFNs, IL-23, and IL-12) involved in systemic lupus erythematosus (SLE) pathogenesis. Deucravacitinib is a first-in-class, oral, selective, allosteric TYK2 inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis.[1,2] Deucravacitinib demonstrated a favorable safety and efficacy profile in a phase 2 trial in patients with psoriatic arthritis[3] and a phase 2 trial in patients with active SLE (PAISLEY; NCT03252587).[4]
Objectives: This analysis evaluated the effect of deucravacitinib on biomarkers of TYK2-mediated pathways, B-cell pathways, and serological biomarkers in patients in the phase 2 PAISLEY SLE trial.
Methods: The 48-week PAISLEY trial randomized 363 patients with SLE 1:1:1:1 to placebo or deucravacitinib 3 mg twice daily (BID), 6 mg BID, or 12 mg once daily (QD). Whole blood transcripts, serum proteins, blood cell subsets, and antibody profiles at screening and baseline through week 48 were measured by immunoassays and flow cytometry. In a substudy, samples were collected from 83 subjects 22 to 114 hours after the initial dose. Samples from demographically matched healthy subjects were collected and measured for comparison.
Results: At screening, 42 genes/modules and 75 proteins were differentially expressed compared with healthy subjects, with fold change >1.5 and adjusted *P* value <0.05. With deucravacitinib treatment, significant reductions were observed in IFNα (at week 48) and IFNλ (week 2 through week 48), and IFNγ was numerically lower after week 12. Deucravacitinib significantly inhibited IFN-regulated gene (IRG) expression from week 4 through week 44 (**Figure 1**). Deucravacitinib, but not placebo, reduced expression of cytokines and chemokines downstream of IFN activity, including BAFF, CXCL10, and MCP2. Adjusted mean percent changes from baseline at week 48 after treatment with deucravacitinib 3 mg BID, 6 mg BID, or 12 mg QD were –26%, –31%, and –30% for MCP2 and –42%, –43%, and –48% for CXCL10, respectively. Selected cytokines and chemokines including IFNλ, CXCL10, CCL19, and MCP2 were significantly reduced in the BID-dosed arms as early as 2 to 3 days after dose initiation. With deucravacitinib treatment, lymphocyte and neutrophil counts and complement levels increased, while markers associated with B-cell activation and differentiation including BLC (CXCL13), CD38 (gene expression), and autoantibodies were reduced.
Conclusion: Deucravacitinib suppressed IFN production, IRG expression, IFN-inducible proteins, B-cell pathway markers, and serological biomarkers, consistent with clinical symptom improvements in SLE patients treated with deucravacitinib.

Figure. Deucravacitinib, but not placebo, reduced biomarkers of IFN-regulated gene expression



*P<0.05; **P<0.01; ***P<0.001. Adjusted *P* values vs placebo. The mixed-effects model included fixed effects of treatment group, analysis visit, treatment-by-analysis visit interaction, and randomization stratum, and the continuous fixed covariate of baseline biomarker.
BID, twice daily; BL, baseline; CI, confidence interval; IFN, interferon; QD, once daily.

Suppression of both IFN and B-cell pathways suggests a broad reduction in lupus pathophysiology. These results provide a molecular framework for understanding how deucravacitinib modifies molecular networks in SLE and support the continued investigation of deucravacitinib as a treatment for SLE in phase 3 trials.

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POS0113

LONG-TERM REMISSIONS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR AUTOIMMUNE DISEASES – A 25 YEARS SINGLE CENTER EXPERIENCE

Keywords: Systemic sclerosis, Systemic lupus erythematosus, Adaptive immunity

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Background: The introduction of novel targeted biologic therapies has dramatically improved the treatment landscape for autoimmune diseases (AD). However, although providing more specificity, such therapies routinely depend on continuous or repeated administration, with a cumulative risk of long-term side effects, and are not curative. In contrast, immunoablation followed by hematopoietic stem cell transplantation (HSCT) has emerged as a promising on-off therapy over the past decades, to provide long-term remissions even in patients with severe courses of their disease, through the restoration of immunologic self-tolerance [1].
Objectives: Here, we summarize the outcomes of AD patients receiving HSCT at the Charité – University Medicine between February 1998 and October 2015.
Methods: In this retrospective study, the clinical outcome of 22 patients was analyzed, who received a $CD34^+$-selected autologous HSCT after immunoablation with 200mg/kg cyclophosphamide and 90mg/kg rabbit antithymocyte globulin (ATG) for autoimmune diseases. Indication for transplant were systemic lupus erythematosus (SLE, n=10), systemic sclerosis (SSc, n=4), vasculitis (n=3), multiple sclerosis (MS, n=2), polychondritis (n=1), chronic inflammatory demyelinating polyneuropathy (CIDP, n=1) and autoimmune hemolytic anaemia (AIHA, n=1). The median age at transplant was 29 years (range 16-48), and 82% of patients were female. Multiparamter flow cytometry was applied to characterize peripheral blood lymphocytes subsets, assessment of SIGLEC-1 expression on monocytes as surrogate for type-I interferon (IFN-I) activity in SLE.
Results: With a median follow-up of 78 months (range 0.1-300), the overall survival was 76.4% and progression-free survival 58.2%, respectively. 3 deaths were regarded treatment related (2 infections in SLE and 1 cardiac failure in SSc). One patient had persisting disease (AIHA) and 4 relapses occurred in SLE patients at 18, 36, 81 and 83 months, respectively. Remaining patients are in stable clinical remission for up to 25 years post-transplant, despite discontinuation of immunosuppressive therapy in most cases. HSCT was associated with significant reduction or normalization of autoantibody levels and a profound reconfiguration of the adaptive immune system, the latter characterised by a re-emergence of naïve T cells with markers of recent thymic emigrants, including $Foxp3^+$ Tregs and regeneration of naïve B cells. In SLE patients, SIGLEC-1 expression on monocytes

completely normalized suggesting an abrogation of type I interferon signalling in responding patients.

Conclusion: Our data provide the `proof-of-concept` that a chronic autoimmune system can be reset into a naïve and self-tolerant state by immunoablation and HSCT, providing a potential curative treatment option. Although initially applied as salvage therapy in severely affected patients with poor outcomes, transplantation related mortality has gradually improved over the past years, due to accumulating centre experience, better patient selection and improved supportive care. Therefore, HSCT still resembles a promising treatment option, especially in those patients with insufficient response to standard-of-care, with poor prognosis and live-threatening disease, in which the risk:benefit ratio of HSCT seems acceptable.

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POS0114 A PLACEBO-CONTROLLED PHASE 1 STUDY IN HEALTHY ADULT VOLUNTEERS OF THE SAFETY, TOLERABILITY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF ALPN-303, A POTENT DUAL BAFF/APRIL ANTAGONIST, FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Randomized control trial, Clinical Trials

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Background: Povetacicept (ALPN-303) is an Fc fusion protein of a variant, engineered transmembrane activator and calcium-modulating cyclophilin ligand interactor (TACI) domain which mediates significantly more potent inhibitory activity than wild type (WT) TACI-Fc or B cell activating factor (BAFF)- or a proliferation inducing ligand (APRIL)-specific monoclonal antibodies, with enhanced pharmacokinetic (PK) and immunomodulatory properties versus WT TACI-Fc in preclinical studies. Povetacicept may therefore significantly improve clinical outcomes in systemic lupus erythematosus (SLE) and other B cell-related diseases.

Objectives: This study was designed to evaluate the safety, tolerability, PK, and pharmacodynamics (PD) of povetacicept in adult healthy volunteers (HV).

Methods: In this first-in-human study (NCT05034484), 66 HV were randomized 4:2 into single ascending dose cohorts of intravenous (IV) or subcutaneous (SC) povetacicept or placebo. Participants were followed to assess safety and PK, circulating immunoglobulins (Ig), and circulating leukocyte populations.

Results: Povetacicept has been well tolerated in all cohorts evaluated as single IV or SC doses of up to 960 mg. Overall, it exhibits dose-related PK and expected PD effects, including dose-related reductions in serum IgA, IgM, IgG (Figure 1), and in circulating antibody-secreting cells (ASC; plasmablasts and plasma cells). These PD effects appear greater than those reported for WT TACI-Fc molecules in HV and appear to be saturated at doses ≥80 mg. Coverage of free APRIL was maintained for 2-3 weeks with 80 mg and ≥4 weeks with 240 mg, respectively. The most frequent adverse event (AE) has been mild headache. To date, there have been no imbalances of infections between the placebo and dosed groups, no treatment-related serious AEs, no administration-related reactions other than mild injection site pain (reported in one each of placebo- and povetacicept-treated participants), and no adverse trends in safety laboratories (Table 1).

Conclusion: To date, povetacicept has demonstrated acceptable safety and tolerability and exhibits expected PD effects on circulating Ig and ASC. These findings support future clinical development of povetacicept in patients with SLE and/or other B-cell- and/or autoantibody-related diseases.

REFERENCES: NIL.

Table 1. Treatment-Emergent Adverse Events

Treatment-Emergent Adverse Event (TEAE)	All Placebo (N=22)	All Povetacicept (N=44)
Any TEAE	12 (55%)	27 (61%)
Grade 1	7 (32%)	20 (45%)
Grade 2	4 (18%)	6 (14%)
Grade 3	1 (5%)	1 (2%)
Any Adverse Event of Interest	1 (5%)	1 (2%)
Administration-Related Reaction	1 (5%)	1 (2%)
Injection Site Pain (Grade 1)		
Most Common TEAEs		
Preferred Term (Any Grade)	**All Placebo (N=22)**	**All Povetacicept (N=44)**
Headache or Migraine	4 (18%)	11 (25%)
Grade 1	4 (18%)	9 (20%)
Grade 2	0	2 (5%)
Infections	4 (18%)	6 (14%)
Grade 1	3 (14%)	5 (11%)
Grade 2	1 (5%)	1 (2%)
Dizziness	1 (5%)	5 (11%)
Grade 1	1 (5%)	4 (9%)
Grade 2	0	1 (2%)
Hypogammaglobulinemia	0	4 (9%)
Grade 1	0	4 (9%)

Data Extract: July 29, 2022

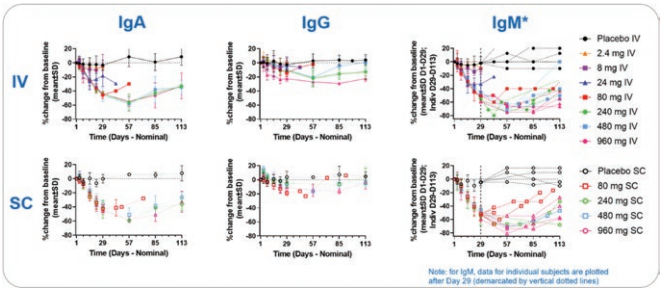


Figure 1. Povetacicept Dose-Dependently Reduces Circulating ImmunoglobulinsEffects generally appear saturated ≥ 80 mg for ≥ 4 weeks.

Acknowledgements: NIL.

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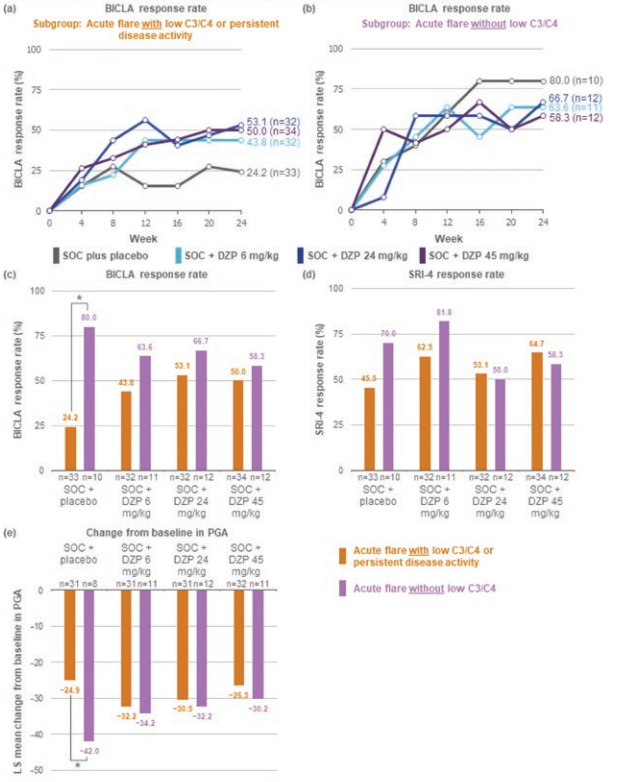
POS0115 DAPIROLIZUMAB PEGOL EFFICACY BY SUBGROUPS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A POST HOC ANALYSIS OF PHASE 2 CLINICAL TRIAL DATA

Keywords: Clinical Trials, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) clinical trials are challenged by high placebo response rates. Subgroup analyses of historic SLE clinical trial data have identified acute flares with normal complement levels as potential predictors of high placebo response.
Objectives: To assess the treatment effect of dapirolizumab pegol (DZP; a polyethylene glycol conjugated antigen-binding fragment lacking a functional Fc domain, which inhibits the CD40–CD40 ligand interaction) in patients from the phase 2b trial in SLE,[1] who fulfilled one or both of the characteristics identified as potential predictors of placebo response.
Methods: Post hoc analyses were performed on data from a phase 2b trial (NCT02804763), in which patients received placebo or DZP (6/24/45 mg/kg), alongside standard of care (SOC) for 24 weeks.[1] Efficacy was compared between two subgroups: (**1**) acute flare with low C3/C4 or persistent disease activity, vs (**2**) acute flare without low C3/C4. In the subgroup analyses, disease activity at screening was defined using British Isles Lupus Assessment Group (BILAG) 2004 item level scores either as acute flare (worsening/new symptoms) or persistent (symptoms rated as the same) based on the past 4 weeks compared with the 4 weeks prior to those, and low C3/C4 was defined as below the lower limit of normal at screening. Outcomes assessed were BILAG-based Composite Lupus Assessment (BICLA) response, SLE Responder Index-4 (SRI-4) response, and change from baseline in Physician's Global Assessment (PGA) at Week 24. Binary outcomes were analysed using logistic regression (p-values reported for odds ratio vs acute flare without low C3/C4), and continuous outcomes were analysed using mixed models with repeat measures (p-values reported for difference vs acute flare without low C3/C4).
Results: Figure 1a and **1b** show BICLA responses in the subgroups over time; similar patterns were seen for the other outcomes. At Week 24, higher BICLA response rates were achieved across all treatment arms in the acute flare without low C3/C4 subgroup compared with the other subgroup (**Figure 1c**). This pattern was particularly evident in patients receiving SOC plus placebo, where there was a significant 3-fold difference in BICLA response rates between the subgroups (80.0% vs 24.2%; p=0.005). Patients who received SOC plus placebo in the acute flare without low C3/C4 subgroup also achieved numerically higher SRI-4 response rates than the acute flare with low C3/C4 or persistent disease activity subgroup. A similar pattern was observed for patients who received SOC plus 6 mg/kg DZP; however, comparable SRI-4 response rates were observed between subgroups in patients who received SOC plus 24/45 mg/kg DZP (**Figure 1d**). At Week 24, greater changes from baseline in PGA were achieved in patients receiving SOC plus placebo in the acute flare without low C3/C4 subgroup than in the acute flare with low C3/C4 or persistent disease activity subgroup (least squares mean: –42.0 vs –24.9; p=0.0268). Comparable changes in PGA were seen between subgroups for patients receiving SOC plus DZP (**Figure 1e**).
Conclusion: Despite the limited sample size, patients with acute flare with normal complement levels were more likely to achieve responses to SOC plus placebo, diminishing the DZP treatment effect. These data suggest that SLE trial design may need to consider baseline clinical and serologic activity patterns to adequately assess treatment efficacy.

Figure. Efficacy outcomes by subgroups: (a, b) BICLA response rate over time to Week 24, (c) BICLA response rate at Week 24, (d) SRI-4 response rate at Week 24, (e) change from baseline in PGA at Week 24



*p<0.05; (b) odds ratio vs acute flare without low C3/C4; (e) difference vs acute flare without low C3/C4. Missing data for (a–d) were imputed using mNRI; (e) observed case data with no imputation.

Abbreviations: BICLA: British Isles Lupus Assessment Group-based Composite Lupus Assessment; DZP: dapirolizumab pegol; LS: least square; mNRI: modified non-responder imputation; PGA: Physician's Global Assessment; SOC: standard of care; SRI-4: Systemic Lupus Erythematosus Responder Index-4.

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POS0116

EFFICACY AND SAFETY OF VOCLOSPORIN ACROSS PATIENT SUBGROUPS WITH PROTEINURIA ≥2 MG/MG: AN INTEGRATED ANALYSIS OF THE AURA-LV AND AURORA 1 STUDIES

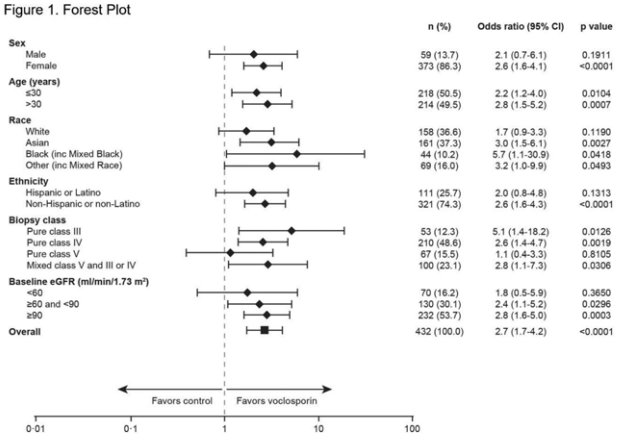
Keywords: Systemic lupus erythematosus, Clinical Trials

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Background: Proteinuria is the most common manifestation of lupus nephritis (LN) and is a mediator of progressive kidney damage. Early reductions in urine protein creatinine ratio (UPCR) have shown to be predictive of improved long-term outcomes in LN. However, recent studies with monoclonal antibody therapies have demonstrated a lack of efficacy in patients with high proteinuria (UPCR ≥2 to ≥3 mg/mg), potentially due to an increase in renal excretion of drug.[1][4] In a pooled analysis of the Phase 2 AURA-LV and Phase 3 AURORA 1 studies, the addition of voclosporin to mycophenolate mofetil (MMF) and low-dose steroids resulted in earlier and greater reductions in proteinuria across biopsy classes, races, and ethnicities.[5]
Objectives: To further characterize the efficacy and safety of voclosporin in patients with high proteinuria, we have analyzed outcomes in various subpopulations of patients with UPCR ≥2 mg/mg using the pooled dataset.
Methods: Both studies enrolled patients with biopsy-proven LN (Class III, IV, or V ± III/IV) with 6 months (or up to 2 years in AURORA 1) and proteinuria ≥1.5 mg/mg (≥2 mg/mg for Class V). Patients were randomized to voclosporin (23.7 mg BID) or placebo and treated for up to one year (48 weeks [AURA-LV], 52 weeks [AURORA 1]); all patients received MMF and low-dose steroids. For this post-hoc analysis, complete renal response (CRR) rates were evaluated in patients with baseline UPCR ≥2 mg/mg. Complete renal response was defined as UPCR ≤0.5 mg/mg with stable renal function, low-dose steroids, and no rescue medication. Subgroup analyses were based on the following: sex, age, race, ethnicity, biopsy class, and estimated glomerular filtration rate [eGFR] at baseline. Adverse events (AEs) and mean eGFR levels over time were also assessed.
Results: Of the 268 and 266 patients included in the voclosporin and control arms of the pooled analysis, respectively, 217 and 215 patients had a baseline UPCR ≥2 mg/mg (mean [SD], 5.2 [3.4] vs. 4.6 [2.9] mg/mg, respectively). At one year, the change from baseline in least squares (LS) mean (SE) UPCR was -3.8 (0.1) mg/mg in the voclosporin arm compared to -3.1 (0.2) mg/mg in the control arm (difference vs. control, -0.7; p=0.0003). A significantly greater percentage of voclosporin-treated patients achieved CRR at one year compared to the control arm (41.0% vs. 21.9%; odds ratio [OR] 2.48, p<0.0001). CRR rates were numerically greater in voclosporin-treated patients in both sexes and across all ages, races, ethnicities, biopsy classes, and baseline eGFR levels assessed, with OR >1 (Figure 1). Across biopsy classes, the highest rates of CRR were observed in Class III patients treated with voclosporin (50% vs 16.1% in control, p=0.0126), followed by Class IV (44% vs. 23.8%, p=0.0019), Class V with III or IV lesions (37.7% vs. 17% p=0.0306), and Class V (31.3% vs. 28.6%, p=0.81). Similar rates of AEs were reported in both arms, and mean eGFR levels were similar and stable over one year of treatment (Figure 2).
Conclusion: Consistent with results from the overall pooled study population, patients with UPCR ≥2 mg/mg at baseline treated with voclosporin achieved significantly higher renal response rates than patients treated with MMF and low-dose steroids alone regardless of baseline demographics or clinical

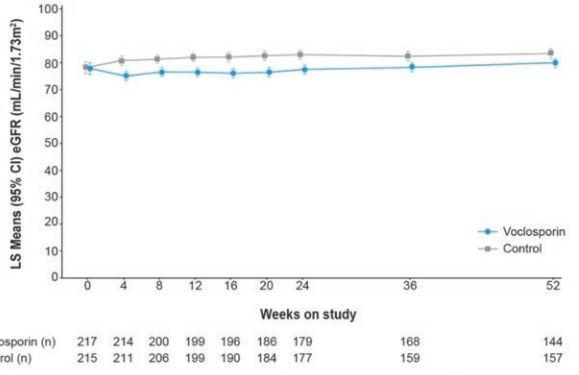
characteristics. This is clinically relevant given the lack of safe and effective therapies for patients with high proteinuria.

Figure 1. Forest Plot



Post hoc analysis of patients with baseline UPCR ≥2 mg/mg includes pooled data from the 23.7 mg BID voclosporin arms and control arms in AURA-LV and AURORA 1. Data include up to 48 weeks from AURA-LV and 52 weeks from AURORA 1. Odds ratio (OR) >1 demonstrates treatment benefit of voclosporin. CI, confidence interval; eGFR, estimated glomerular filtration rate; UPCR, urine protein creatinine ratio.

Figure 2. LS Mean eGFR over Time



Voclosporin (n)	217	214	200	199	196	186	179	168	144
Control (n)	215	211	206	199	190	184	177	159	157

Post hoc analysis of patients with baseline UPCR ≥2 mg/mg includes pooled data from the 23.7 mg BID voclosporin arms and control arms of AURA-LV and AURORA 1. Data include up to 48 weeks from AURA-LV and up to 52 weeks from AURORA 1. Renal function was assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a prespecified ceiling of 90 mL/min/1.73 m². CI, confidence interval; eGFR, estimated glomerular filtration rate; LSMean, least squares mean.

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Disclosure of Interests: Emily Littlejohn Speakers bureau: Aurinia Pharmaceuticals Inc., Consultant of: GSK, Salem Almaani Consultant of: Chemocentryx, Aurinia Pharmaceuticals Inc., Kezar, Vanessa Birardi Shareholder of: Aurinia Pharmaceuticals Inc., Employee of: Aurinia Pharmaceuticals Inc., Ernie Yap Shareholder of: Aurinia Pharmaceuticals Inc., Employee of: Aurinia Pharmaceuticals Inc., Chris Collins Shareholder of: Aurinia Pharmaceuticals Inc., Employee of: Aurinia Pharmaceuticals Inc.

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POS0117 REMIBRUTINIB SPECIFICALLY DOWNREGULATES MARKERS OF MEMORY B CELL SUBSETS IN SJÖGREN'S PATIENTS (SJS) IN THE LOUISSE PHASE 2 CLINICAL TRIAL

Keywords: Biomarkers, Sjögren syndrome, Clinical Trials

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Background: Remibrutinib is a selective, covalent and potent inhibitor of Bruton's tyrosine kinase (BTK) in development for several autoimmune and auto-allergic indications showing promising clinical safety and efficacy (Kaul et al 2021, Maurer et al 2022). Sjögren's (SjS) is a chronic autoimmune disorder characterized by dryness in the eyes and mouth, fatigue, joint pain, and reduced quality of life (Mariette et al 2018). Remibrutinib may be particularly promising for the treatment of SjS due to its ability to target underlying B cell abnormalities and showed promising efficacy in a Ph2 SjS trial (Dörner et al 2022).

Objectives: The aim of this exploratory biomarker study within the LOUiSSe trial was to identify protein and transcript signatures in the blood of patients with active SjS that are associated with remibrutinib treatment.

Methods: We conducted the LOUiSSe Ph2 clinical trial (NCT04035668) to evaluate the safety and efficacy of remibrutinib in patients with moderate to severe SjS. The study design was a randomized, double-blind, placebo-controlled, multi-center trial. Blood samples were collected at baseline and 24 weeks after treatment began. Protein profiles were generated using a Multiplex 7K aptamer profiling, and transcriptomics analysis was performed on RNA extracted from whole blood. By comparing the treatment and the placebo groups over time using multivariate linear regression models, we identified proteins and genes that were differentially modulated by remibrutinib. The gene signature identified by Yao et al (2009) was used as a reference for the interferon signature.

Results: We observed a consistent downregulation of 35 proteins associated with B cell activity, including CD23, FCRL1, FAIM3, and FCRL4, in all treatment groups receiving remibrutinib compared to the placebo group after 24 weeks of treatment. These modulated proteins are involved in multiple pathways related to B-cell activation and function, including B-cell receptor signaling, Fc receptor signaling, and platelet activation. Whole blood bulk mRNA sequencing revealed that the remibrutinib group showed a significant downregulation of a 34-gene signature, most of which are known to be important for B-cell activation and immunoglobulin production. The top two most significantly downregulated genes, FCRL5 and SOX5, were previously identified as being highly enriched in a circulating tissue-like memory B-cell subset. This observation is also corroborated by the proteomics profiling analysis, where FCRL4 known to co-localize in the same memory B-cell subset (Verstappen et al 2020, Götz et al 2008), was heavily decreased by the treatment. Despite the specific and strong effects on B-cells, estimation of cell type proportions using RNA-seq revealed no significant changes, suggesting that remibrutinib does not affect the overall B-cell numbers and the relative proportions of its major subsets, like plasma cells, naïve and memory B-cells. Results from both proteomics and transcriptomics profiling suggest that remibrutinib treatment does not modulate the interferon signature.

Conclusion: Our analysis of serum proteins and whole blood transcripts showed that remibrutinib treatment was associated with a significant downregulation of proteins and genes enriched in FcRL4+ B cells, a subset of tissue-resident memory B cells that are expanded in inflamed tissues and found in the salivary glands of SjS patients. These findings suggest that remibrutinib may have a particularly strong inhibitory effect on this subset. Additionally, many genes and proteins involved in B-cell activation, differentiation, and maturation were also downregulated, indicating that remibrutinib has a potent effect on multiple B-cell pathways.

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Acknowledgements: NIL.

Disclosure of Interests: Andrea Grioni Shareholder of: Novartis, Employee of: Novartis, Aida Santos da Costa Shareholder of: Novartis, Employee of: Novartis, Enrico Ferrero Shareholder of: Novartis, Employee of: Novartis, Valeria De Luca Shareholder of: Novartis, Employee of: Novartis, Rainer Hillenbrand Shareholder of: Novartis, Employee of: Novartis, Andre da Costa Shareholder of: Novartis, Employee of: Novartis, Bruno Cenni Shareholder of: Novartis, Employee of: Novartis, Martin Kaul Shareholder of: Novartis, Employee of: Novartis, Thomas Dörner Consultant of: study support and honoraria for scientific advice: Novartis, Eli Lilly, EMD, BMS; Janssen; AbbVie, Roche/GNE, Richard Siegel Shareholder of: Novartis, Employee of: Novartis.

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POS0118 ADDING HYDROXYCHLOROQUINE IN REFRACTORY OBSTETRIC APS: OBSTETRIC OUTCOMES IN 182 PREGNANCIES

Keywords: Anti-phospholipid syndrome, Pregnancy and reproduction

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Background: Pregnancy complications in obstetric APS (OAPS) include recurrent early pregnancy loss, fetal death, or premature birth due to preeclampsia,

intrauterine growth restriction or placental insufficiency. The standard of care (SC) with low dose aspirin (LDA) and heparin has dramatically improved obstetric results, however 20-30% still have adverse outcomes despite treatment. Retrospective studies have shown good results with the addition of Hydroxychloroquine (HCQ). HCQ may have a beneficial effect in APS due to its anti-inflammatory, immunomodulatory and antithrombotic properties. Recently, EULAR recommended its use in refractory cases. Previously, in a retrospective study we reported that the addition of HCQ in women with primary OAPS and a pregnancy failure with SC was associated with a higher rate of live births (97 vs 62%) and a lower frequency of pregnancy complications (8 vs 37%) compared with conventional treatment. In this new study we show obstetric results from a larger cohort of refractory OAPS patients treated with HCQ.

Objectives: To assess pregnancy outcomes in a large cohort of women with refractory OAPS treated with Hydroxychloroquine in addition to conventional treatment.

Methods: This was an observational, retrospective, single-center cohort study. We analyzed pregnancy outcomes in women with refractory primary OAPS (2004-2022) who received HCQ 400 mg + enoxaparin 60 mg + LDA in their subsequent pregnancies.

Results: We evaluated 182 pregnancies in one hundred and seventy- three women (21-51y) treated with the addition of HCQ and a previous failure with conventional treatment; 18,9% of them had triple antibodies positivity. Live birth rate was 94% (CI 95%: 89,5-96,5). Term deliveries occurred in 95% of the pregnancies, mean gestational age at birth was 38 weeks (28-39) and mean weight 3021g (915g-4300g). Sixty percent were cesarean sections and 40 % vaginal deliveries. Pregnancy complications occurred in 12 % of the pregnancies (CI 95%: 7,3-19,5). Early pregnancy losses before 10 weeks occurred in 6% of the pregnancies. There were no late fetal deaths. Six patients who presented mild cutaneous allergy had to interrupt HCQ and were excluded from the analysis.

Conclusion: These results add observational evidence in favor of using Hydroxychloroquine in refractory Obstetric APS patients until results from ongoing RCT are published.

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Disclosure of Interests: None Declared.

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POS0119 XmAb564, A NOVEL POTENCY-REDUCED IL-2 FC FUSION PROTEIN SELECTIVELY EXPANDS REGULATORY T CELLS: RESULTS FROM A SINGLE ASCENDING DOSE STUDY IN HEALTHY ADULT VOLUNTEERS

Keywords: Systemic lupus erythematosus, Randomized control trial, Biomarkers

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Background: Interleukin 2 (IL-2) signaling is essential for the development, survival, and suppressive function of T regulatory cells (Tregs). Diminished IL-2 signaling and Treg functional impairment are associated with autoimmune diseases, including systemic lupus erythematosus (SLE)[1]-[3]. XmAb564 is a potency reduced, monomeric human IL-2 heterodimeric Fc-fusion protein with extended half-life and increased binding affinity for IL-2 receptor alpha (CD25) to selectively expand Tregs, being developed for the treatment of autoimmune diseases.

Objectives: In this first-in-human, placebo-controlled, double-blind, single ascending-dose study, healthy adult volunteers received XmAb564 and were evaluated for safety, tolerability, pharmacokinetics (PK), and pharmacodynamic (PD) for 30-45 days.

Methods: Subjects received SC doses of XmAb564 at 0.003, 0.007, 0.015, 0.025, 0.040, and 0.065 mg/kg in 6 cohorts (6 active:2 placebo per cohort). Levels of immune cell populations in whole blood were assessed by flow cytometry for total Tregs (CD4+CD25+FoxP3+) and CD25^{bright} Tregs (CD4+CD25brightFoxP3+), as well as NK (CD56+) cells, CD4+ and CD8+ T conventional cells (Tcon).

Results: A single dose of XmAb564 was well tolerated, with no dose-limiting toxicities, no Grade 3 or greater adverse events (AEs), no serious AEs, no deaths, nor clinically significant laboratory safety abnormalities. AEs attributed to XmAb564 were mainly mild to moderate self-limited injection site reactions. Asymptomatic transient elevations of peripheral eosinophils were observed in a dose-dependent manner, similar to those reported with other biologics in the class. After a single dose of subcutaneous administration, XmAb564 exposure increased in a dose-dependent manner with dose-proportional C_{max} and non-linear clearance owing to the expected increase in target receptor expression (CD25) in response to XmAb564 and dynamic target-mediated drug disposition across the range of doses studied from 0.003 to 0.065 mg/kg.

The primary effect of XmAb564 was seen on total Tregs and particularly the CD25^{bright} Treg subset (Figure 1A, B). The elevations peaked at approximately Day 12 and remained elevated for at least 21 days following drug administration. At the highest dose of 0.065 mg/kg, the mean peak increase in numbers of Tregs and CD25^{bright} Tregs were 8-fold and 117-fold above baseline, respectively. At that same 0.065 mg/kg dose level, there was a trend of mean increase of 2.6-fold, 2.3-fold, and 2.2-fold in numbers of NK, CD4$^+$ and CD8$^+$ Tcon cells, respectively.

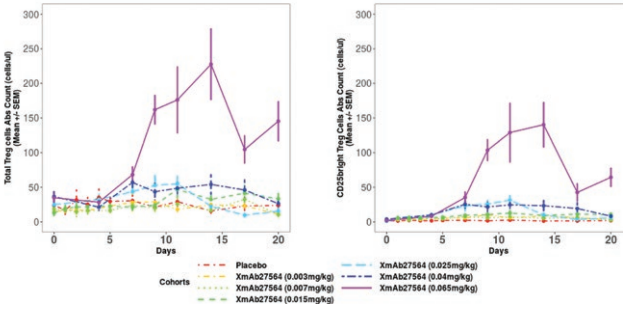


Figure 1.

Conclusion: XmAb564 selectively induced Tregs and was well tolerated. XmAb564 PK and PD potentially supports extended multi-week dosing intervals and has a Treg induction magnitude and durability that may be competitive or superior to other candidates in clinic, providing the rationale for clinical evaluation across a broad range of inflammatory diseases.

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POS0120 SAFETY AND EFFICACY OF SUBCUTANEOUS (S.C.) DOSE IANALUMAB (VAY736; ANTI-BAFFR mAb) ADMINISTERED MONTHLY OVER 28 WEEKS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Keywords: Randomized control trial, Systemic lupus erythematosus, Clinical Trials

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Background: Ianalumab (VAY736) is a novel defucosylated, human IgG1 mAb targeting the receptor for B cell Activating Factor of TNF Family (BAFF-R), providing both enhanced antibody-dependent cellular cytotoxicity-mediated depletion of B cells and blockade of BAFF:BAFF-R signaling that drives B cell differentiation, proliferation and survival.

Objectives: Evaluate safety and efficacy of ianalumab in patients with active SLE.

Methods: Multi-center, randomised, parallel group, double-blind trial consisting of 2 separate, placebo-controlled treatment cohorts for ianalumab and for iscalimab (CFZ533; anti-CD40 mAb) randomised 1:1 between active:placebo. Patients (ianalumab cohort n= 67, iscalimab cohort n= 40) with ANA ≥1:80 and meeting ≥4/11 ACR 1997 SLE classification criteria, with SLEDAI-2K score ≥6 and BILAG-2004 ≥1 'A' or two 'B' scores that included activity in either mucocutaneous and/or musculoskeletal domains were enrolled from 19 Dec 2018 through 31 Jan 2022. Here we report interim analysis results for ianalumab treatment cohort (active n=34, placebo n=33) completing the 28-week blinded treatment period, which comprised of monthly s.c. injection of ianalumab 300 mg or placebo. Outcomes were measured at baseline (BL) and weeks (w) 4, 8, 12, 16, 24 and 28. The primary w28 outcome was proportion of patients meeting composite endpoint requirements consisting of patients who both achieved SRI-4 and also tapered predniso(lo)ne ≤5 mg/d or ≤ BL dose, whichever was lower, by w16 and kept within that range to w28. Other outcomes included safety and tolerability, incidence of BILAG-2004 moderate or severe flares, proportion of patients achieving Lupus Low Disease Activity State (LLDAS), change from BL in SLEDAI-2K and BILAG-2004, physician/patient global visual analog scale (VAS) assessments and laboratory markers of inflammation and immune activation. Post-w28 patients received open-label ianalumab for 20w, then safety follow up off treatment up to 2 years (y).

Results: Median age was 42y and 39y for ianalumab and placebo arms, respectively, with 8 males (ianalumab: 2, placebo: 6). BL median (*range*) values for ianalumab and placebo arms, respectively, were: SLEDAI-2K scores 10 (*6-32*) and 10 (*4-18*), and predniso(lo)ne 10.0 mg (*0-30.0*) and 10.0 mg (*2.5-27.5*). Proportion of patients treated with ianalumab or placebo, respectively, achieving SRI-4 at w28 (Figure 1) was 70.6% (n=24) vs. 24.2% (n=8), and also meeting composite endpoint (Figure 1 insert): 44.1% (n=15) vs. 9.1% (n=3). Ianalumab showed benefit vs placebo in other outcomes (Table 1) for incidence moderate or severe flare, time to moderate or severe flare, achieving w28 LLDAS, and serum levels of complement and autoantibodies. No drug-related SAEs were reported with ianalumab during blinded or subsequent 20w open-label treatment. There were 2 AE-related dropouts occurring during open-label treatment, one in ianalumab arm (morphoea) and one with placebo (worsening of SLE). Pandemic-related discontinuations included one from each arm during the blinded treatment period, and 2 occurring post-w28 in the ianalumab arm: one each in open label and during safety follow up.

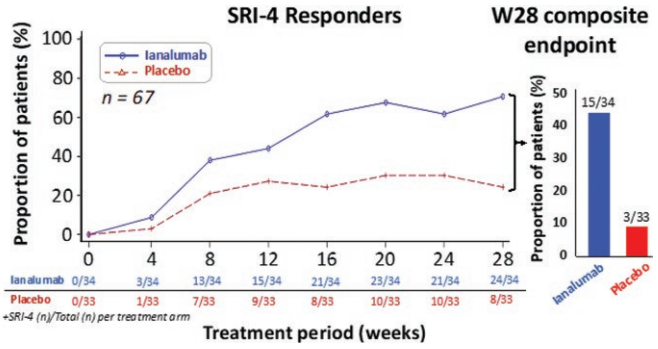
Conclusion: Treatment of SLE with ianalumab was well tolerated and met the composite primary endpoint of SRI-4 response with sustained steroid reduction, with additional benefits seen across other study endpoints. These positive results support further evaluation of ianalumab in SLE.

Table 1. Selected secondary and exploratory outcomes

Outcomes		Ianalumab (n=34)	Placebo (n=33)
Incidence of flare*	n (%)	15 (44)	21 (64)
Time to first flare* (Days)	Mean (SD)	108 (73)	87 (39)
	Median (range)	87 (29-276)	84 (30-170)
Week 28 LLDAS	n (%)	9 (27)	3 (9)
Ratio BL at Week 28			
Serum C3	Geo-mean	1.13 (1.05, 1.22)	0.95 (0.88, 1.03)
Serum C4	(95% CI)	1.44 (1.24, 1.67)	1.01 (0.90, 1.13)
Anti-dsDNA		0.52 (0.39, 0.70)	0.88 (0.73, 1.06)
Anti-CXCL13		0.50 (0.37, 0.67)	0.83 (0.68, 1.02)
Anti-C1q		0.70 (0.56, 0.87)	0.85 (0.71, 1.02)

*Moderate or severe: post-BL BILAG 2004 domain activity ≥1 'A' or ≥2 'B'

Figure: Proportion of patients with SRI-4 and achieving Week 28 composite endpoint



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Outcome of scleroderma and related syndromes

POS0121

COMPARISON OF FOUR RISK STRATIFICATION MODELS FOR PREDICTION OF MORTALITY IN SSc-PAH IN THE EUSTAR COHORT

Keywords: Systemic sclerosis, Heart, Prognostic factors

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Background: Pulmonary arterial hypertension (PAH) is a major cause of mortality in systemic sclerosis (SSc). The 2022 ESC/ERS Guidelines recommend a comprehensive risk stratification at PAH diagnosis to guide optimized management. Several risk stratification tools have been developed in PAH. These strategies have not previously been compared, and have not been applied in SSc-PAH using the new haemodynamic definition.

Objectives: To assess the performance of current risk stratification tools to predict mortality in SSc-PAH.

Methods: We included patients from the EUSTAR registry who were diagnosed with SSc-PAH between 2001-2022 (Project Number: CP122). PAH was defined according to the new definition (mean pulmonary arterial pressure >20 mmHg, pulmonary artery wedge pressure ≤15 mmHg and pulmonary vascular resistance >2 WU). Patients with significant interstitial lung disease (ILD), defined as extent of ILD >20% on HRCT or FVC <70% in patients with missing quantification, were excluded. We applied four different approaches:

(I) The 2022 ESC/ERS 3-strata approach includes up to 17 parameters according to the risk table.[1] Each parameter was graded from 1 to 3 representing low to high risk, with the mean defining the risk category.

(II) The 2022 ESC/ERS 4-strata approach equals (I), but divides the intermediate-risk group into two groups based on the mean score.

(III) COMPERA 2.0 stratifies patients into four risk groups based on WHO-functional class (FC), six-minute walk distance (6MWD), and NT-proBNP.[2] Each parameter was graded from 1 to 4 representing low to high risk, with the mean defining the risk category.

(IV) REVEAL Lite 2 stratifies patients into three risk groups based on six weighted variables (WHO-FC, systolic blood pressure, heart rate, 6MWD, NT-pro-BNP, eGFR)[3]

We analysed transplant-free survival and performed Cox regression adjusted for general and SSc-specific factors associated with worse outcome (age, male sex, DLCO, FVC, disease subtype and PAH treatment). Harrell's C-index and ROC analysis with area under the curve (AUC) were applied to compare the performance and discriminating ability of the models with >0.7 considered as acceptable.

Results: Of 955 patients who had right heart catheterization, 430 (45%) were diagnosed with SSc-PAH. Among these, 86% were females, mean age was 65 years, and 82% had limited cutaneous SSc. Over median 40 (Q1-Q3: 17-68) months follow-up, 172 died and 14 had lung transplants. The overall 1-, 3- and 5-year transplant-free survival was 91%, 77% and 60%, respectively. In univariable Cox regression only COMPERA 2.0 had acceptable predictive value with a C-index >0.7 (Table 1). In adjusted multivariable Cox regression, all the risk stratification approaches predicted mortality with increased HR at higher risk scores (Figure 1 A-D). All adjusted models were acceptable, but COMPERA 2.0 was the most accurate to predict mortality (C-index=0.78, AUC=0.74) (Table 1, Figure 1C). However, this model did not discriminate intermediate-low risk from low risk (HR 1.39, 95% CI (0.59, 3.25), p=0.45). The models discriminating abilities were not significantly different (p=0.27).

Table 1. Harrell's C-index and AUC in the four approaches

	Univariable analysis		Adjusted multivariable analysis	
	C-index	AUC (p=0.08)	C-index	AUC (p=0.27)
ESC/ERS 3-strata	0.622	0.641	0.703	0.688
ESC/ERS 4-strata	0.653	0.669	0.710	0.693
COMPERA 2.0	0.728	0.712	0.779	0.737
REVEAL Lite 2	0.697	0.698	0.753	0.718

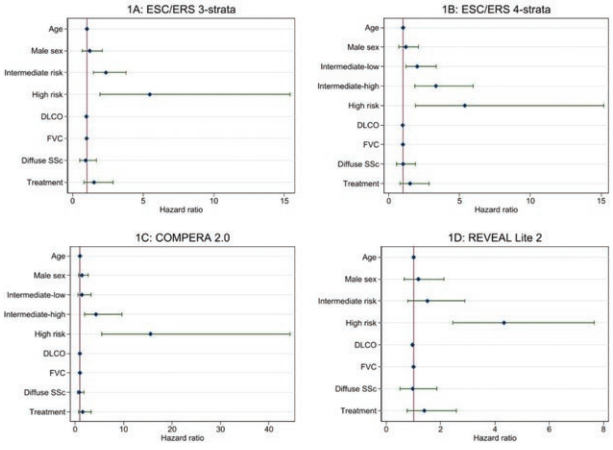


Figure 1. Forest plots of the multivariable cox regression models

Conclusion: In SSc-PAH, we suggest that the application of risk stratification at time of PAH diagnosis should take SSc-specific variables into account. In particular, the COMPERA 2.0 risk stratification model performs best, does not require invasive measurements and uses parameters easily collected at each clinical visit, making it readily applicable in clinical practice. Importantly, this approach identifies patients at intermediate-high and high risk who need more aggressive management.

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POS0122

INVESTIGATION OF SERUM MARKER LEVELS IN CONNECTIVE TISSUE DISEASES DEVELOPING ILD

Keywords: Biomarkers, Systemic sclerosis, Lungs

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Background: Connective tissue disease (CTD) is an umbrella term for a heterogeneous group of autoimmune diseases affecting the connective tissue in various organs. One of the most serious complications associated with CTDs is interstitial lung disease (ILD), which results in significant morbidity and mortality. A subset of CTD-ILD patients shows progressive disease, which is associated with an even worse prognosis. Previous studies have identified dysregulations of biomarkers including CX3CL1, CCL2, CCL17 and CCL18 in systemic sclerosis (SSc) showing an association with ILD [1-4]. For other CTD-ILD it is less clear, which biomarkers are associated with ILD and ILD progression and few studies have assessed circulating biomarkers across CTD-ILDs.

Objectives: To investigate circulating biomarkers in CTD-ILD and in progressive CTD-ILD patients.

Methods: Serum samples from SSc (n=292), primary sjogrens syndrome (pSS) (n=132), mixed connective tissue disease (MCTD) (n=162), anti-syntetase syndrome (ASS) (n=72) patients and healthy controls (HC) (n=100) collected at Oslo University Hospital (OUH) were analyzed by ELISA for selected biomarkers (CX3CL1, CCL2, CCL17, CCL18). SSc samples were used as the reference disease to compare with mean levels of serum markers in pSS, ASS and MCTD. ILD was diagnosed on high resolution computed tomography (HRCT). Forced vital capacity (FVC) was available at baseline and 12 +/- 3 months. ILD progression defined as an absolute FVC% predicted decline of ≥10% was assessed. Descriptive statistics and logistic regression with odds ratio (OR) and 95%CI were performed.

Results: Serum levels of CX3CL1 and CCL18 were significantly higher in all the CTDs (p<0.001) compared to HC. CCL2 and CCL17 levels were significantly higher in SSc (p=0.001 and p<0.001), ASS (p<0.001 and p=0.004) and MCTD (p<0.001 and p<0.001) compared to HC, but not in pSS (p=0.230 and p=0.087). Of all CTD patients, 267/658 (41%) were diagnosed with ILD (table 1). Of these patients 80 (30%) showed ILD progression, where data were obtained for SSc, pSS and ASS (Tabel 1). All the markers were significantly higher in patients with ILD compared to no ILD in SSc and pSS, while only CCL17 was significantly higher inn ASS-ILD and none in MCTD-ILD. When using SSc-ILD as reference disease, serum levels of CX3CL1 were significantly higher in pSS-ILD (p<0.001) and MCTD-ILD (p<0.001), and CCL18 was significantly lower in MCTD-ILD (p<0.001). Serum levels of CCL2 and CCL17 did not significantly differ between SSc-ILD and the other CTD-ILDs (Figure 1A). From logistic regression analysis of the patient with ILD progression, CCL18 (OR: 1.19, 95%CI, p=0.001) were the only marker significantly associated with ILD progression. When adjusting for CTD with SSc as reference disease, the only marker significantly associated with ILD progression was also here CCL18 (OR: 1.06, 95%CI: 1.03-1.09, p<0.001) (Figure 1B).

Conclusion: In this large CTD cohort, we show that CCL2 and CCL17 are increased across all CTD patients with ILD compared to no ILD, which could help us to identify patients with ILD. ILD progression was only associated with CCL18, which was driven by the SSc-ILD subpopulation.

Table 1. Clinical and demographic data

	SSc (n=292)	pSS (n=132)	ASS (n=72)	MCTD (n=162)
Females, no (%)	239 (61)	123 (93)	48 (67)	128 (79)
Age at disease onset, yrs (SD)	48 (15.4)	52 (14.1)	49 (12.8)	35 (15.7)
FVC baseline, % (SD)	95 (20.3)	99 (12.7)	85 (21.8)	92 (18.5)
ILD, no (%)	140 (47.9)	16 (12.1)	60 (83.3)	51 (31.5)
ILD progression, n (%)	74 (26)	3 (19)	3 (6)	-
Mean CCL18, ng/ml	49.3 (10.8)	47.4 (12.5)	50.5 (11.2)	43.8 (9.8)
Mean CCL2, ng/ml	0.6 (0.7)	0.5 (0.2)	0.9 (0.5)	0.7 (0.8)
Mean CCL17, ng/ml	0.6 (0.5)	0.5 (0.5)	0.6 (0.5)	0.6 (0.6)
Mean CX3CL1, ng/ml	1.9 (2.5)	3.2 (6.3)	2.0 (2.9)	3.4 (5.6)

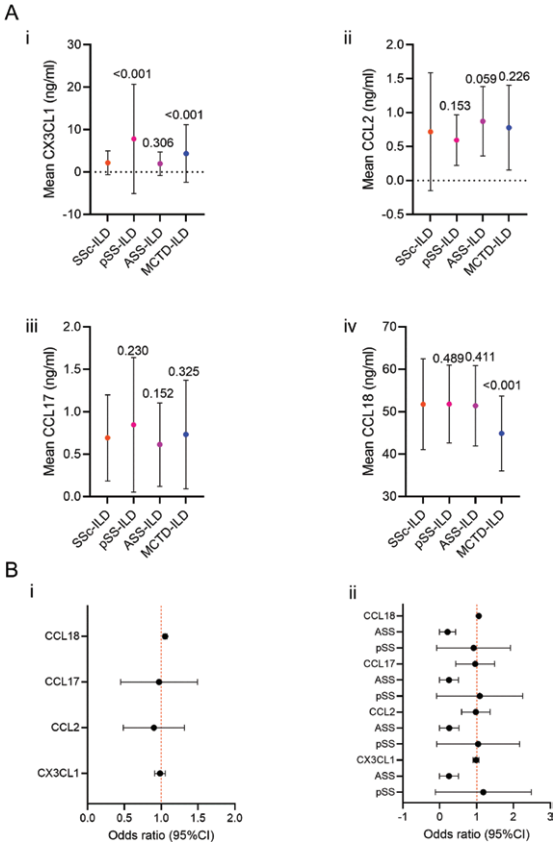


Figure 1. (A) Mean levels of markers in SSc-ILD, pSS-ILD, ASS-ILD and MCTD-ILD, and (B) association of circulating markers with ILD progression using SSc-ILD as the reference.

REFERENCES: NIL.

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POS0123 ASSOCIATION OF LUNG IMAGING PATTERN WITH PROGNOSIS AND IMMUNOSUPPRESSION RESPONSE IN CONNECTIVE TISSUE DISEASE ASSOCIATED INTERSTITIAL LUNG DISEASE

Keywords: Prognostic factors, Imaging, Lungs

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Background: Prognosis in connective tissue disease associated interstitial lung disease (CTD-ILD) is influenced by the underlying diagnosis and chest imaging pattern. Usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP), and fibrotic hypersensitivity pneumonitis (fHP) patterns can be found across all CTD-ILD subtypes although their impact on disease evolution and treatment response is unclear.

Objectives: Our goal was to examine the association of lung imaging pattern with CTD-ILD progression, mortality, and immunosuppression response.

Methods: 615 patients with CTD-ILD enrolled in the Canadian Registry for Pulmonary Fibrosis had high-resolution chest computed tomography (HRCT) from their first ILD clinic visit reviewed in standardized multidisciplinary discussion. All CTD diagnoses were rheumatologist-confirmed. Experienced chest radiologists blinded to clinical data categorized each case into five groups: UIP, NSIP, organizing pneumonia (OP), fHP, and other patterns. Longitudinal percent-predicted forced vital capacity (FVC) and transplant-free survival were compared between imaging groups using linear mixed effects and Cox proportional hazards models adjusted for age, sex, smoking pack-years, and baseline FVC. Linear mixed effects models were used to compare pre- and post-treatment rate of FVC decline in patients with ≥6 months follow-up before and after treatment with mycophenolate, azathioprine, rituximab, cyclophosphamide, and/or tocilizumab. UIP was the reference group for all comparisons.

Results: The most frequent CTD subtypes were systemic sclerosis (SSc) (33%), rheumatoid arthritis (RA) (20%), and idiopathic inflammatory myopathy (IIM) (16%) with NSIP pattern present in 54% of all CTD-ILD (Table 1). On multivariable analyses among all CTD-ILD patients, NSIP was associated with a slower rate of FVC decline by 1.1%/year (0.2, 1.9) and a lower mortality HR (95%CI) of 0.65 (0.45, 0.93) compared to UIP. OP was also associated with a slower rate of FVC decline by 3.5%/year (2.0, 4.9) and a lower mortality HR (95%CI) of 0.18 (0.05, 0.57) compared to UIP. In contrast, fHP had a higher mortality HR (95%CI) of 1.58 (1.01, 2.40). The rate of FVC decline after treatment was not significantly different compared to pre-treatment in the UIP group but was slower in the NSIP group by 2.1%/year (1.4, 2.8). Subgroup analyses in RA-ILD and SSc-ILD showed the persistence of fHP having a higher mortality compared to UIP in RA-ILD.

Conclusion: The presence of an NSIP pattern was associated with improved outcomes and immunosuppression response compared to UIP in the overall CTD-ILD group. The findings of fHP associated with worse survival compared to UIP in CTD-ILD and in the RA-ILD are novel. These findings need to be further confirmed in disease specific cohorts and randomized trials of immunosuppression in patients with CTD-ILD.

Table 1. Association between imaging patterns with FVC decline, mortality, and immunosupression response in CTD-ILD

Imaging pattern	Difference in the annualized rate of FVC change between imaging patterns (95%CI)	Mortality Hazard ratio (95%CI)	Difference in the annualized rate of FVC change Pre- vs Post-Treatment (95%CI)
UIP	Reference group	Reference group	0.1 (-1.4,1.7)
NSIP	1.1 (0.2, 1.9)	0.65 (0.45, 0.93)	2.1 (1.4, 2.8)
OP	3.5 (2.0, 4.9)	0.18 (0.05, 0.57	NA
fHP	-0.7 (-2.0, 0.6)	1.58 (1.01, 2.48)	NA
Other	0.2 (-1.0, 1.4)	0.63 (0.36, 1.08)	NA

All models were adjusted for age, sex, smoking pack years, and baseline FVC95%CI = 95% confidence interval, UIP = Usual interstitial pneumonia, NSIP = Nonspecific interstitial pneumonia, OP = organizing pneumonia, fHP = fibrotic hypersensitivity pneumonitis, Other = other imaging patterns including lymphocytic interstitial pneumonia, desquamative interstitial pneumonia, pleuralparenchymal fibroelastosis, unclassifiable

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POS0124 SURVIVAL ANALYSIS IN CONNECTIVE TISSUE DISEASES WITH INTERSTITIAL LUNG DISEASE COMPARED TO IDIOPATHIC PULMONARY FIBROSIS: MULTICENTRE ITALIAN STUDY

Keywords: Systemic sclerosis, Lungs, Myositis

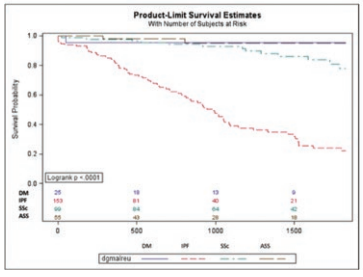
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Background: Interstitial lung disease (ILD) is a major cause of mortality in patients with connective tissue diseases (CTDs). Previous studies have shown a worse survival in patients with idiopathic pulmonary fibrosis (IPF) (1-2), however, these studies were mainly focused on patients with rheumatoid arthritis, whereas few data are available for patients with other CTDs.

Objectives: The aim of this study was to assess the 5-year survival in an Italian multicenter cohort of ILD patients suffering from systemic sclerosis (SSc), dermatomyositis (DM), and anti-synthetase syndrome (ASS) compared to IPF patients.

Methods: Demographic and clinical data of patients with SSc, DM and ASS were retrospectively recorded from January 2015 for the purpose of this study. The baseline time was a diagnosis of ILD confirmed by computed tomography (CT) scan of the chest. The IPF cohort was used as control group. Progressive lung disease was defined when the patient presented within 24 months after the diagnosis of ILD with at least one of these characteristics: a) a relative decline in FVC of at least 10% of expected value; b) a relative decline in FVC from 5% to less than 10% of the expected value and a worsening of respiratory symptoms or an increase in the extent of lung fibrosis on high-resolution CT scan; c) a worsening of respiratory symptoms and an increase in the extent of lung fibrosis on high resolution CT scan. All data were reported and analyzed with standard descriptive statistics, as appropriate. The 5-year survival was assessed with the Kaplan-Meyer method; univariate and multivariate Cox-regression models were built to look for possible risk factors. Data were analyzed with SAS/STAT Statistics version 9.4 (SAS Institute, Cary, NC, USA).
Results: The overall cohort included 177 CTD-ILD patients (99 SSc, 25 DM, 53 ASS) and 153 IPF patients. At ILD diagnosis, as expected, CTD patients were younger [median age (IQR); IPF: 68 (63-73) years, SSc 58 (46-66) years, DM 54 (51-65) years and ASS: 59 (60-67) years; p <0.001 vs IPF] and predominantly female (IPF: 23%, SSc 83.5%, DM 81% and ASS 65%; p <0.001 vs IPF). Usual interstitial pneumonia was observed in a low number of CTD patients, evidenced in 11 (11.5%) SSc, 7 (12.9%) ASS and 4 (16.6%) DM patients. At ILD diagnosis, the median (IQR) value of forced vital capacity (FVC%) was similar between IPF [75%(64-91)], DM [79%(60-90)] and ASS [77.5%(64-93)], while was significantly higher in SSc patients [94%(79-106), p<0.001 vs IPF]. At baseline, all CTDs showed a higher mean (SD) value of diffusing capacity for carbon monoxide (DLCO%) [SSc: 63%(18), DM: 62%(23), ASS: 63%(22)] than IPF [50%(15); p<0.001]. During follow-up, 10 (9.7%) patients with SSc, 4 (16%) with DM and 3 (8%) with ASS showed a progressive subset of ILD. CTDs showed better 5-year survival compared to IPF (log rank: p<0.0001) (Figure 1). Multivariate Cox analysis highlighted that male gender (HR: 2.29, 95% CI 1.25-4.18), age at diagnosis (HR: 1.07, 95% CI 1.04-1.10) and DLCO at baseline (HR: 0.95, 95% CI 0.94-0.97) were independent prognostic factors in CTD-ILD.

Figure 1. 5-year survival in patients with systemic sclerosis (SSc), dermatomyositis (DM), Anti-synthetase syndrome (ASS) and idiopathic pulmonary fibrosis (IPF)



Conclusion: The prognosis of CTD patients with lung fibrosis appears to be significantly better than those with IPF. The early detection of lung involvement in at-risk patients like SSc, DM and ASS, and the availability of effective immunosuppressive treatment may explain this discrepancy. Of note male patients, older age and compromised DLCO at baseline represent poor prognostic factors.

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Disclosure of Interests: None Declared.
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POS0125 SUSTAINED COMPLETE B CELL DEPLETION IS ASSOCIATED WITH RITUXIMAB EFFICACY IN CONNECTIVE TISSUE DISORDERS - ASSOCIATED INTERSTITIAL LUNG DISEASE

Keywords: Lungs, Systemic sclerosis

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Background: The benefit of RTX has been suggested for interstitial lung disease (ILD) associated with connective tissue disorders (CTD). Preliminary data have suggested that B cell depletion measured 2 weeks after the first RTX infusion was predictive of short-term treatment response at 6 months in systemic sclerosis (SSc)-ILD.
Objectives: To determine whether the quality of B cell depletion was associated with therapeutic response to RTX in CTD-ILD.
Methods: Retrospective monocentric study including all patients treated at least 1 year with RTX for SSc- or MCTD-ILD. The observation period was defined by to the time from the first to the last RTX infusion. ILD was identified based on high-resolution CT. The results of forced vital capacity (FVC) and carbon monoxide diffusion capacity (DLCO) were collected at the time of the first RTX infusion, at month 12 and at the time of the last RTX infusion. B cell immunophenotyping was performed the day of each RTX infusion (Aquios, Beckman Coulter). B cell depletion was defined by CD19 <18/µL. The primary outcome was the absolute change from baseline of FVC (L) at 12 months and at the last RTX infusion according to complete or incomplete B cell depletion within the observation period. Secondary outcomes were the course of DLCO at the same time points according to B cell depletion and the analysis of the % of good RTX responders at 12 months and at the last RTX infusion, defined by at least 5% improvement in %FVC compared to baseline.
Results: 17 patients (12 SSc and 5 MCTD) were included, with a median age of 59 years (95% confidence interval, CI, 48-63 years) and a median disease duration of 8 years (95% CI 5-11 years). The median duration of RTX exposition was 45 months (95% CI 19-90 months), the median number of infusions was 8/patient (95% CI 5-14) and the cumulative RTX dose was 7g (95% CI 5-14g). These parameters were similar in the 9 patients with complete B cell depletion (CD19: 15/µL, 95% CI 14-18/µL, **Figure 1A-B**) and the 8 patients with incomplete B cell depletion (CD19: 70/µL, 95% CI 18-126/µL, **Figure 1A-B**) during RTX exposition. The absolute change from baseline of the FVC was different according to B cell depletion during the observation period. In the subset of patients who maintained complete B cell depletion (**Figure 1C**), median FVC increased from 2.58 L (95% CI 1.13-4.08 L) to 3.08 L (95% CI 1.34-4.64 L) at month 12 (p=0.004) and 3.22 L (95% CI 1.57-4.19 L) at the last RTX infusion (p=0.019) (**Figure 1D**). Conversely, in the subset of patients with constant incomplete B cell depletion (**Figure 1C)**, FVC initially increased from 2.04 L (95% CI 0.99-3.24 L) to 2.23 L (95% CI 0.83-3.35 L) at month 12 (p=0.039) before decreasing to 1.89 L (95% CI 1.00-3.24 L) (p=0.37) (**Figure 1D**). The absolute change from baseline of DLCO did not significantly differ according to B cell depletion. In addition, The percentage of patients with any FVC improvement was higher in the subset of patients who maintained complete BC depletion at 1 year (6/9, 67% vs. 4/8, 50%) and at the last RTX infusion (8/9, 89% vs. 4/8, 50). Conversely, median DLCO did not significantly differ according to BC depletion.
Conclusion: These results highlight the importance of obtaining and maintaining B cell depletion to gain clinically relevant efficacy of RTX in CTD-ILD. CD19 measurement at each infusion is a relevant tool to monitor RTX efficacy in daily practice.

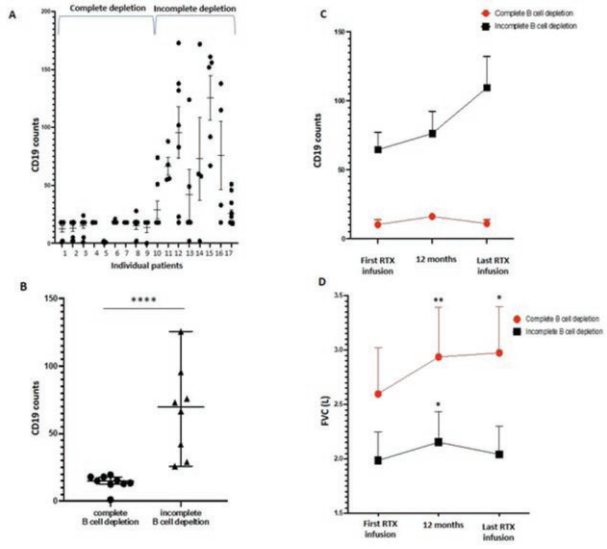


Figure 1. A, Individual CD19 counts measured prior to each RTX infusion. **B,** Comparison of CD19 counts between patients with or without complete B cell depletion. Each point represents the median CD19 value measured at each infusion per patient during the observation period (at least 3 measures per patient). Data are shown as median and 95% confidence interval. **** p<0.0001 by Mann Whitney test. **C,** Course of CD19 during the observation period according to B cell depletion. **D,** Course of FVC during the observation period according to B cell depletion; *p<0.05 and **p<0.01 vs baseline value by the Wilcoxon matched pairs signed rank test.

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POS0126

CONTINUED TREATMENT WITH NINTEDANIB IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD): THREE-YEAR DATA FROM SENSCIS-ON

Keywords: Systemic sclerosis, Clinical Trials, Lungs

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Background: In the randomised placebo-controlled SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 44%, with adverse events that were manageable for most patients. SENSCIS-ON is an open-label extension study investigating adverse events and decline in FVC in patients with SSc-ILD treated with nintedanib over the longer term.

Objectives: To assess adverse events and decline in FVC in patients treated with open-label nintedanib over 148 weeks of SENSCIS-ON.

Methods: In the SENSCIS trial, patients received nintedanib or placebo until the last patient reached week 52 but for ≤100 weeks. Patients with SSc-ILD who completed SENSCIS or a drug–drug interaction (DDI) study of nintedanib and oral contraceptive in which female patients with SSc-ILD received nintedanib for ≥14 days to approximately 28 days were eligible to enter SENSCIS-ON. We analysed adverse events and changes from baseline in FVC (mL) over 148 weeks in patients who received nintedanib in SENSCIS and continued nintedanib in SENSCIS-ON ("continued nintedanib" group) and in patients who received placebo in SENSCIS or who received nintedanib for ≤28 days in the DDI study ("initiated nintedanib" group). Analyses were descriptive. Analyses of FVC were based on observed data available at the respective time-point.

Results: The continued nintedanib group comprised 197 patients and the initiated nintedanib group comprised 247 patients (231 from SENSCIS, 16 from the DDI study). In these groups, respectively, mean (SD) FVC at the start of SENSCIS-ON was 2379 (754) mL and 70.4 (18.1) % predicted and 2443 (814) mL and 70.8 (17.9) % predicted. In total, 126 (64.0%) and 125 (50.6%) patients in the continued nintedanib and initiated nintedanib groups, respectively, were still receiving nintedanib at week 148 of SENSCIS-ON. Diarrhoea was the most frequent adverse event (Table 1). Serious adverse events were reported in 76 (38.6%) patients in the continued nintedanib group and 95 (38.5%) patients in the initiated nintedanib group. Among patients who continued nintedanib and initiated nintedanib, respectively, 53 (26.9%) and 148 (59.9%) had ≥1 dose reduction and 72 (36.5%) and 131 (53.0%) had ≥1 treatment interruption. Adverse events led to discontinuation of nintedanib in 29 (14.7%) patients in the continued nintedanib group and 72 (29.1%) patients in the initiated nintedanib group. Mean (SE) changes in FVC from baseline to week 148 of SENSCIS-ON were −189.1 (29.5) mL in the continued nintedanib group and −126.4 (26.4) mL in the initiated nintedanib group (Figure 1).

Conclusion: The safety profile of nintedanib over 148 weeks of SENSCIS-ON was consistent with that reported in SENSCIS, characterized mainly by gastrointestinal events that were manageable for most patients. These results support the potential use of nintedanib in the long-term treatment of patients with SSc-ILD.

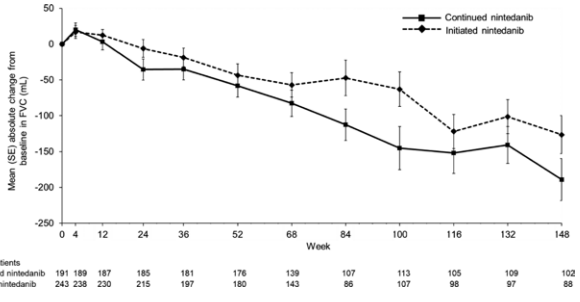


Figure 1. Change in FVC (mL) over 148 weeks in SENSCIS-ON

Table 1. Most frequent adverse events over 148 weeks in SENSCIS-ON

	Continued nintedanib (n=197)	Initiated nintedanib (n=247)
Diarrhoea	152 (77.2)	183 (74.1)
Nausea	43 (21.8)	73 (29.6)
Skin ulcer	48 (24.4)	54 (21.9)
Vomiting	38 (19.3)	59 (23.9)
Liver test abnormalities	31 (15.7)	63 (25.5)
Upper respiratory tract infection	39 (19.8)	33 (13.4)
Nasopharyngitis	31 (15.7)	40 (16.2)
Cough	36 (18.3)	33 (13.4)
Arthralgia	34 (17.3)	32 (13.0)
Weight decreased	23 (11.7)	33 (13.4)
Abdominal pain	10 (5.1)	36 (14.6)
Gastrointestinal oesophageal reflux disease	24 (12.2)	15 (6.1)

Data are n (%) of patients with ≥1 such event reported over 148 weeks (or until 7 days after last trial drug intake for patients who discontinued trial drug before week 148). Adverse events were coded according to preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA) except for liver test abnormalities, which were based on the standardised MedDRA query "liver related investigations, signs and symptoms" (broad definition). Events reported in >12% of patients in either group are shown.

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POS0127

RISK OF NEW-ONSET DEPRESSION IN PATIENTS WITH SYSTEMIC SCLEROSIS: A NATIONWIDE POPULATION-BASED STUDY

Keywords: Systemic sclerosis

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Background: Systemic sclerosis (SSc) is a rare chronic inflammatory disease characterized by vasculopathy, autoimmunity and progressive fibrosis in various organs including skin, lung, and gastrointestinal tract. The patients with SSc are suffered from various symptoms such as dyspnea, cough, and gradual skin and joint contracture, resulting in significant physical and psychological burden. Psychological symptoms in SSc patients include pain, depression, and concerns about appearance disfigurement. Previous studies have reported that depression

is common in SSc patients, ranging from 36% to 65%. However, no study has unveiled the risk of new-onset depression in SSc patients.

Objectives: The present study was conducted to determine whether SSc is an indeed risk factor for the development of new-onset depression. To determine whether the incidence rate (IR) of new-onset depression in SSc patients is higher than in normal subjects, we used data from a nationwide health care database.

Methods: We selected subjects from National Health Insurance System database who were diagnosed with SSc between 2010 and 2016. Subjects who did not get a general health checkup in the previous 2 years, who were diagnosed with depression before their SSc diagnosis, who were less than 20 years old, or who had missing data were excluded. To minimize the possibility of reverse causality, an analysis with a 1-year lag was performed. Kaplan-Meier analysis was conducted to assess the incidence of new-onset depression, and Cox proportional hazards regression was used to calculate adjusted and unadjusted hazard ratio (HR) and 95% CIs. HR for new-onset depression was adjusted for age, sex, smoking, drinking, physical activity, body mass index (BMI), income, diabetes, hypertension, and dyslipidemia.

Results: A total of 1,063 SSc patients (female 82.4 %) and 3,189 age-, sex-matched non-SSc controls with mean (SD) age of 53.1 (10.6) years were included in the analysis. During follow-up periods after 1 year of lag time, the cumulative incidence of new-onset depression was significantly higher in patients with SSc vs controls (38.7 vs. 27.7 IR per 1000 person-years). After adjusting for covariates (age, sex, smoking, drinking, physical activity, BMI, income, diabetes, hypertension, and dyslipidemia), the presence of SSc was associated with 38.1 % increased risk of new-onset depression (HR 1.381; 95% CI, 1.128-1.691), compared with controls. SSc disease itself was determined as an independent risk factor for new-onset depression in subjects with younger age (age < 65 years; HR 1.41; 95% CI 1.122-1.773), female gender (HR 1.415; 95% CI 1.139-1.759), and absence of regular exercise (HR 1.433; 95% CI 1.143-1.795), after adjusting for covariates. Interestingly, the risk of new-onset depression after SSc diagnosis was found to be relatively higher in the low-income group (HR 1.667; 95% CI 1.121-2.479 vs HR 1.303; 95% CI 1.028-1.650).

Conclusion: The present study suggests that the SSc diagnosis is associated with a significantly increased cumulative incidence and risk of new-onset depression. This association is more pronounced in female gender, younger age group, and those who do not exercise regularly. Regular assessment of the occurrence of depressive symptoms should be more emphasized in the patients with SSc after diagnosis.

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POS0128 **WITHDRAWN**

POS0129 **DIFFERENTIALLY EXPRESSED GENES (DEGS) IN PATIENTS WITH DERMATOMYOSITIS AND JUVENILE DERMATOMYOSITIS**

Keywords: Biomarkers, -omics, Myositis

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Background: Dermatomyositis (DM) and Juvenile Dermatomyositis (JDM) are englobed in the spectrum of inflammatory myopathies. These are autoimmune

diseases that cause heliotropic rash in most patients, which then develop proximal muscles weakness and skin lesions [1]. Key findings in patients with these pathologies include anti-Mi2, anti-Jo1, and anti-P155/P140 antibodies in plasma, as well as B-cells and plasma cells infiltrates with an upregulated Type I Interferon (IFN) signature in muscle biopsies [2]. However, the pathophysiology underlying this condition has not been fully comprehended; even less, diagnostic biomarkers that could identify early stages of the disease.

Objectives: We aimed to identify overlapped genes across datasets of gene expression from patients with DM and JDM doing an integrative bioinformatics analysis.

Methods: A search strategy was designed in the Gene Expression Omnibus platform to identify datasets of gene expression profiling by array experiments in patients with DM and JDM. The inclusion criteria were: 1) Assays performed in humans, 2) Inclusion of healthy controls in the datasets, and 3) Data analysis with GEO2R. The exclusion criteria were 1) Incomplete information of the genes, and 2) Gene expression by RNAseq. DEGs were selected when $p < 0.05$ and log fold change > 2 or < -2. Functional enrichment analysis was realized with free access platforms GeneMania and DAVID with the significant overlapped genes. A protein-protein interaction (PPI) analysis was constructed with STRING and a topological interaction network using CytoHubba to identify genes with the strongest interactions. A prediction of transcription factors that can serve as possible therapeutic targets was realized with iRegulon.

Results: 102 overlapped DEGs from DM and 13 overlapped DEGs from JDM were found within their datasets. Out of those DEGs, 5 were shared between DM and JDM. Prediction analysis yielded 20 co-expressed genes. DAVID analysis showed the top 3 biological processes in which the 25 genes are involved, most of them belonging to the Type I IFN signature (Table 1). Topological analysis yielded 10 genes with the strongest interactions between them, and the transcription factor listed as possible therapeutic target was STAT1.

Table 1. DAVID analysis shows the processes involving those genes, most of them belonging to the Interferon Signature.

Functional Enrichment Analysis		
Term	**Gene Count**	**P-value**
Defense response to virus	19	1,9E-30
Response to virus	13	1,8E-21
Negative regulation of the viral genome	8	9,1E-14

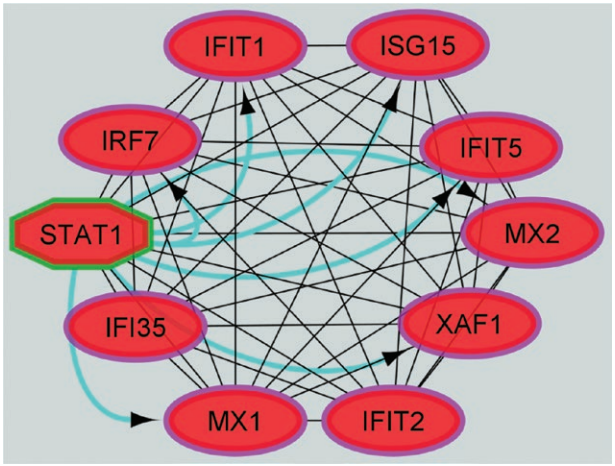


Figure 1. Topologic analysis displays the 10 genes with the strongest interactions. All the genes belong to the Interferon Signature and STAT1 regulates 7 out of 10.

Conclusion: We aimed to identify DEGs that participate in the pathophysiology of DM and JDM. Those genes mostly participate in responses to viral infections, in which the type I IFN signature is present. These genes may serve in the future as possible biomarkers for early diagnosis. An *in vivo* analysis in patients with these diseases is needed to validate these findings. Janus Kinase Inhibitors (Jakinibs) have been used to treat JDM patients, showing positive results [3]. We suggest more clinical trials to test the effectiveness and tolerability of Jakinibs to treat these conditions.

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POS0130

INFLAMMATORY ACTIVITY IS ASSOCIATED WITH COGNITIVE IMPAIRMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Cognitive Function, Rheumatoid arthritis, Comorbidities

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Background: Patients with rheumatoid arthritis (RA) present cognitive impairment at a frequency of 38% to 71%.

Objectives: To study whether there is an association between high sustained inflammatory activity and cognitive impairment in RA patients.

Methods: Design and protocol: controlled cross-sectional observational study of a prospective cohort of patients with RA. Cases: patients with RA from a prospective cohort with onset >16 years and who were selected to start first biologic treatment for moderate-high inflammatory activity. Controls: subjects without inflammatory disease, matched for sex and age with cases. All participants performed the same neuropsychological battery. Variables: the main variable was cognitive impairment defined by a score of < 26 points in the Montreal Cognitive Assessment questionnaire (MoCA test). As secondary variables we included the score in each of the items of the MoCA test separately; the direct and inverse digits span; the STROOP test for the assessment of processing speed (STROOP-P), selective attention (STROOP-C) and inhibition (STROOP-PC); and the Hospital Anxiety and Depression Scale (HADS). Other variables included average inflammatory activity by DAS28-ESR since diagnosis, epidemiological characteristics, comorbidities and treatments.

Results: Sixty-two subjects were included. The baseline characteristics are shown in Table 1. RA patients presented a higher frequency of cognitive impairment than controls (64.5% vs. 38.7%; p=0.042), as well as lower mean (SD) values on the MoCA test (23.1 [3.8] vs. 25.1 [3.8]; p=0.046). Fewer RA patients compared to controls achieved the memory item (22 [81.5] vs 30 [100.0]; p = 0.014), naming (24 [88.0] vs 30 [100.0]; p = 0.031), and presented lower mean (SD) values in attention (3.5 [1.5] vs 4.4 [1.4]; p = 0.039). Scores for all subtests are shown in Figure 1. Factors that were associated in multivariate analysis with cognitive impairment in the total sample were age (OR [95% CI], 1.171 [1.068-1.284]; p=0.001), RA diagnosis (OR [95% CI], 4.712 [1.069-12.772]; p=0.041) and university studies (OR [95% CI], 0.089 [0.010-0.829]; p=0.034) (R2 = 0.405). The model in RA patients found association of cognitive impairment with age (OR [95% CI], 1.230 [1.020-1.485]; p=0.030), and mean DAS28-ESR (OR [95% CI], 1.704 [1.072-4.003]; p=0.048) (R2 = 0.380). Statistical analysis: descriptive analysis, bivariate analysis between patients and controls, as well as between patients with and without cognitive impairment; and two multivariate logistic regression analyses were performed to analyze the factors associated.

Conclusion: Patients with RA and high inflammatory activity more frequently presented cognitive impairment compared to the controls. The most affected domains were memory, naming and attention. Factors associated with cognitive impairment were age, educational level and mean DAS28-ESR.

Table 1. Baseline characteristics of 31 RA patients and 31 controls

VARIABLE	RA N= 31	CONTROL N = 31	P-VALUE
Sex, female, n (%)	27 (87.1)	27 (87.1)	1.000
Age years, mean (SD)	57.3 (10,6)	56.3 (10.9)	0.670
Academic level			0.454
Basic schooling, n (%)	14 (45.2)	15 (48.4)	
Non-university higher education, n (%)	13 (41.9)	9 (29.0)	
University studies, n (%)	4 (12.9)	7 (22.6)	
Time since diagnosis of RA, months, median (IQR)	79.4 (31.2-191.0)		

Diagnostic delay, median (RIC), months	8.0 (4.0-12.2)		
Rheumatoid factor >10 U/ml, n (%)	27 (87.0)	0 (0.0)	<0.001
ACPA > 20 U//ml, n (%)	26 (83.0)	0 (0.0)	<0.001
DAS28-ESR, mean (SD)	3,9 (0.8)		
HAQ, mean (SD)	1,1 (0.6)		
Methotrexate, n (%)	22 (71.0)		
Hydroxychloroquine, n (%)	5 (16.1)		
Leflunomide, n (%)	2 (6.5)		
Sulfasalazine, n (%)	2 (6.5)		
Cognitive impairment (<26 MoCA), n (%)	20 (64.5)	12 (38.7)	0.042
Depression (HADS>11), n (%)	5 (16.1)	1 (3.2)	0.086
Anxiety (HADS>11), n (%)	9 (29.0)	5 (16.1)	0.224

Abbreviation: ACPA: anti-citrullinated C-peptide antibodies; DAS28-ESR: 28-joint Disease Activity Score; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire

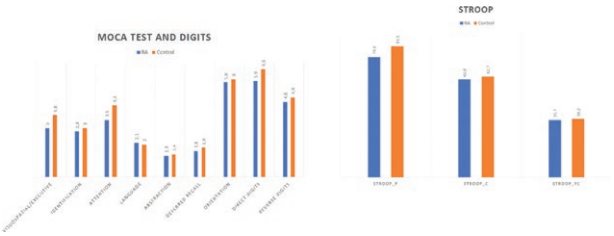


Figure 1. Comparison of mean values of cognitive subtests between patients and controls

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POS0131

RELATION BETWEEN COVID-19 AND ANCA VASCULITIS. STUDY IN A SINGLE UNIVERSITY HOSPITAL

Keywords: Vasculitis, Autoantibodies, COVID

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Background: Anti-neutrophil cytoplasmic antibodies (ANCA) associated vasculitis (AAV) is a small vessel vasculitis. Hallmarked by the presence of antibodies against antigens in cytoplasmic granules of neutrophils. Different microbiological agents and vaccines can trigger an AAV, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infection and Coronavirus disease 2019 (COVID-19) vaccine.
Objectives: To compare: a) proportion of positive ANCA (+ANCA) test in 2019 (COVID-19 pre-pandemic) vs 2021 (COVID-19 pandemic), b) clinical features and **c)** vasculitis activity between vasculitis related to COVID 19 vaccination vs non-related.
Methods: All ANCA tests performed in 2019 and 2021 in a referral hospital were reviewed. Additionally, we studied 18 +ANCA patients diagnosed in 2021 and accepted to participate in present study. The patients were divided in two groups: a) +ANCA after SARS-CoV-2 mRNA vaccine (COVID-related) and +ANCA before COVID-19 vaccine (COVID-nonrelated). Diagnosis of underlying AAV was based on ACR/EULAR 2022 criteria. Disease activity was assessed with Birmingham Vasculitis Activity Score (BVAS). ANCA testing was done by chemiluminescence assay using IO-FLASH (Inova, San Diego, CA) according to the instructions of the manufacturer.
Results: ANCA tests were positive in 14 of 1287 cases (1.1%) and in 32 of 1434 (2.2%) cases in 2019 and 2021, respectively (figure 1, the differences were statistically significant (p=0.020). The main features of 18 ANCA+ patients diagnosed in 2021 are summarized in table 1. COVID-19 related patients showed a median of 7 points on BVAS score compared of the median of 5 points on BVAS score on not related patients.
Conclusion: There seems to be an increase of +ANCA at the expense of anti-PR3 antibodies following the COVID-19 vaccine. In patients with +ANCA following vaccination there seems to be an increased disease activity according to BVAS score without reaching statistical significance.

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Table 1. Main general features of 18 patients with ANCA+ test diagnosed in 2021.

FEATURES	All cases n= 18	Related n= 13	Non-related n= 5	p*
Age (years), mean±SD	62±17	67±15.3	52±16.5	0.167
Male/ Female n, (% male)	10/8 (55.6)	9/4 (69.2%)	1/4(20)	0.067
ANCA-test specificity, n (%)				
MPO-ANCA	9 (50)	7 (53.8)	2(40)	0.609
PR3-ANCA	8 (44.4)	5 (38.5)	3(60)	0.423
Both	1 (5.6)	1 (7.7)	0	-
CRP (mg/dL), median [IQR]	2,4 [0.4-10.7]	3.8 [0.4-10.1]	1 [0.4-10.9]	0.802
ESR, mm/1st hours, median [IQR]	50 [25-104]	47 [25.3-71.8]	50 [25-120]	0.634
BVAS, median [IQR]	6.5 [4.2-8]	7 [4-8]	5 [5-8]	0.842
FFS, n (%)				
0	3 (16.7)	2 (15.4)	1 (20)	0.819
≥1	15 (83.3)	11 (84.6)	4 (80)	0.819
ENT involvement, n (%)	12(66.7)	10 (76.9)	2 (40)	0.148
MSK involvement, n (%)	11(61.1)	7(53.8)	4 (80)	0.322
CNS/PNS involvement, n (%)	10 (55.6)	7 (53.8)	3 (60)	0.819
Lung involvement, n (%)	9 (50)	6 (46.2)	3 (60)	0.609
Kidney involvement, n (%)	8 (44.4)	7 (53.8)	1 (40)	0.208
Ocular involvement, n (%)	2 (11.1)	2 (15.4)	0	0.366
Cutaneous involvement, n (%)	2 (11.1)	0	2 (40)	0.019

*p values according to Man Whitney test.
Abbreviations (in alphabetical order):AAV: anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis; ACR: American college of Rheumatology; ANCA: Antineutrophil cytoplasmic antibody; BVAS: Birmingham Vasculitis Activity Score; CNS: central nervous system; CRP: C-Reactive protein; dL: deciliter; ENT: ear, nose, throat; ESR: erythrocyte sedimentation rate; FFS: Five-Factors Score; g; IQR: Interquartile range; mg: milligram; MSK: musculoskeletal; MPO-ANCA= ANCA specific for myeloperoxidase; n=Number; PNS: peripheral nervous system; PR3-ANCA= ANCA specific for proteinase 3; SD: Standard Deviation

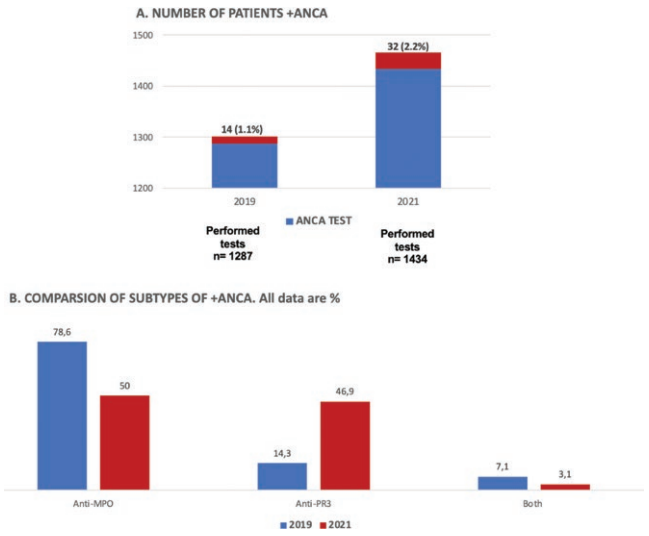


Figure 1. Comparison of ANCA test in 2019 and 2021.

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What's new in Paediatric RMDs?

POS0132 OUTCOMES FOLLOWING SWITCHING FROM ORIGINATOR TO BIOSIMILAR IN CHILDREN AND YOUNG PEOPLE WITH JIA

Keywords: bDMARD, Epidemiology

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Background: There are many biosimilar products available to use in children and young people with JIA. Due to competitive pricing, patients are being switched from biologic originator to biosimilar (non-medical switch).
Objectives: This analysis aims to describe characteristics of, and outcomes, following TNF-inhibitor originator to biosimilar switch in JIA.
Methods: All patients in the UK JIA Biologics Register switching from an originator to a biosimilar of the same product were identified. Patient characteristics are presented, including time on originator prior to switch. Patients were followed until their final follow-up form was returned. For those with >1 year of follow-up post-switch, treatment persistence and reasons for stopping are described.
Results: As of 24-Nov-2022, 211 children and young people had switched from originator to biosimilar; 132 adalimumab, 55 etanercept, and 24 infliximab (table 1). Switching was seen in all ILAR categories. Patients were predominantly female (64%), median age at JIA diagnosis six years, 11 years at originator start, 14 years at biosimilar start, median time on originator 2.2 years. Most patients had started originator as their first biologic (73%) and most started biosimilar with no significant treatment gaps. Six patients reported >1 year gap between originator stop and biosimilar start, suggesting a planned period off biologic therapy (two stopped for adverse event, four unknown). Of the 143 patients with >1 year of follow-up available after switching (median 1.9 years per patient), 82 remained on biosimilar at their final follow-up, whilst 61 had stopped therapy. Of those who stopped, 11 had stopped for remission, 13 stopped for ineffectiveness, 20 for adverse event, and 17 other/missing reason. Forty-one patients then re-started biologic therapy (including four of the remission patients); 17 switched back to the originator mostly due to an adverse event on the biosimilar, and 24 started a different biologic therapy mostly due to inefficacy of the biosimilar.

Table 1.

	All patients N=211
Female	134 (64%)
ILAR	
Oligoarticular Persistent	28 (13%)
Oligoarticular Extended	50 (24%)
RF- Polyarticular	75 (36%)
RF+ Polyarticular	10 (5%)
Systemic	1 (<1%)
Psoriatic	9 (4%)
Enthesitis-Related	25 (12%)
Undifferentiated	13 (6%)
Age, years	
At diagnosis	6 (3, 11); N=208
At originator	11 (8, 13)
At switch to biosimilar	14 (11, 16)
Biologic therapy	
Adalimumab	132 (63%)
Etanercept	55 (26%)
Infliximab	24 (11%)
Line of biologic therapy (originator)	N=207
First-line	152 (73%)
Second-line	39 (19%)
Third-(or more)-line	18 (8%)
Time on originator, years	2.2 (1.3, 3.4)
Available follow-up time after switching to biosimilar, years	
Number of patients with available follow-up	N=198
Min-Max	0.03 to 4.66 years
Median (IQR)	1.6 (0.9, 2.2)
Those with one year follow-up: what happened?	
Number of patients with one year of follow-up available	N=143
Min-Max	1.02 to 4.66 years
Median (IQR)	1.9 (1.4, 2.5)
Still on biosimilar	82 (57%)
Stopped biosimilar	
Stop Reason:	61 (43%)
Ineffectiveness	*13/61 (21%)*
Adverse Event	*20/61 (33%)*
Other/Missing	*17/61 (28%)*
Remission	*11/61 (18%)*
Those who stopped: what happened?	
Number of patients who stopped biosimilar therapy	N=61
Switched Biologic	**41 (67%)**
Back to Originator	17/41 (41%)
Reason stopped biosimilar and switched back to originator:	*12 Adverse event* *3 Other/Missing* *2 Remission*
Different Biologic	24/41 (59%)
Reason stopped biosimilar and started a different biologic:	*11 Inefficacy* *2 Adverse event* *9 Other/Missing* *2 Remission*

Conclusion: Many children with JIA have now been switched from TNF-inhibitor originator to biosimilar product, with the majority still receiving their biosimilar after one year. Switching back to originator was uncommon, 12% overall after one year, suggesting good tolerance of non-medical switching in this patient population.
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Disclosure of Interests: Lianne Kearsley-Fleet: None declared, Eileen Baildam: None declared, Michael Beresford: None declared, Sharon Douglas: None declared, Helen Foster: None declared, Taunton Southwood: None declared, Kimme Hyrich Speakers bureau: Non-personal speaker's fees from Abbvie, all unrelated to this abstract., Grant/research support from: Grant income from BMS, UCB, and Pfizer, all unrelated to this abstract, and is supported by the NIHR Manchester Biomedical Research Centre.
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POS0133 TRADITIONAL LABORATORY PARAMETERS AND NEW BIOMARKERS IN MACROPHAGE ACTIVATION SYNDROME (MAS) AND SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (sHLH)

Keywords: Biomarkers, Cytokines and chemokines, Innate immunity

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Background: Macrophage Activation Syndrome (MAS) and Secondary Hemophagocytic Lymphohistiocytosis (sHLH) are hyperinflammatory conditions, in which IFNγ plays a pivotal role. Prompt recognition and early treatment are essential to improve the outcome and the mortality rate.
Objectives: This is a retrospective multicenter study. We correlated traditional laboratory parameters of hyperinflammation with IL-18 and IFNγ related biomarkers. We have also evaluated the diagnostic and prognostic role of IL-18, CXCL9, CXCL10 and neopterin in patients with MAS and sHLH.
Methods: One hundred-six patients from 6 Italian centers were enrolled: 41 with sHLH, 41 with MAS in the context of sJIA, and 24 with sJIA without MAS. The samples were collected at three different time points: active disease (T0), 7-10 days from starting therapy (T1) and in clinical inactive disease on medication (from 1 to 3 months from onset) (T2). Serum levels of IL-18 and of the IFN-γ related biomarkers (CXCL9, CXCL10, Neopterin) were measured by ELISA.
Results: A total of 378 samples were collected. Laboratory features at T0 are detailed in table 1. Using the 2016 classification criteria for MAS, we can confirm that platelet count is a specific parameter, only 2 patients with sJIA had a value $<181x10^9$/liter. Instead ferritin is a sensitive parameter, 94.4% of patients with

MAS had ferritin >684 mg/ml. Lactate dehydrogenase (LDH) values were statistically higher in MAS and sHLH compared to sJIA. ROC curve of LDH values in MAS showed a statistically significant area under the curve (AUC= 78.2%, p-value <0.0001). A cut-off of 683 U/L had a sensitivity of 73.6% and a specificity of 70.3%. IL-18, CXCL9, CXCL10 and neopterin levels in T0 were significantly higher in MAS and sHLH compared to sJIA. In MAS, IL-18 levels were significantly higher compared to sHLH (p<0.0001). The ROC curves performed for each biomarker showed a statistically significant AUCs (p<0.01), except for IL-18 in sHLH. We have identified a cut off value for each biomarker in MAS (CXCL9 900 pg/ml, CXCL10 260 pg/ml, neopterin 5.0 ng/ml, IL-18 82996 pg/ml) and sHLH (CXCL9 2145 pg/ml, CXCL10 270 pg/ml, neopterin 7.1 ng/ml). In T0 neopterin correlates significantly with IL-18, CXCL9 and CXCL10 in MAS group but not in sHLH. We found also strong correlation between CXCL9 and CXCL10 only in MAS group.

Table 1. Laboratory parameters in T0. Values are shown as median (IQR); p-value: Mann-Whitney U test.

	MAS (N=54)	sHLH (N=48)	sJIA (N=4)	MAS vs sHLH	MAS vs sJIA	sHLH vs sJIA
Ferritin (ng/ml)	4755 (1816-10988)	4098 (2075-16867)	717 (335-2313)	0.77	**<0.0001**	**<0.0001**
Platelet count (x10^9/l)	199 (107-314)	97 (47-184)	450 (343-570)	**0.0003**	**<0.0001**	**<0.0001**
AST (U/L)	85 (51-146)	150 (51-340)	30 (22-44)	0.06	**<0.0001**	**<0.0001**
Triglycerides (mg/dl)	188 (148-263)	226 (166-381)	105 (75-139)	0.11	**<0.0001**	**<0.0001**
Fibrinogen (mg/dl)	337 (222-433)	228 (137-331)	572 (482-692)	**0.003**	**<0.0001**	**<0.0001**
LDH (U/L)	965 (679-1369)	1255 (701-2748)	587 (365-724)	0.10	**<0.0001**	**<0.0001**
CXCL9 (pg/ml)	2236 (675-9670)	4159 (1880-10016)	300 (300-1979)	0.14	**<0.0001**	**<0.0001**
Neopterin (ng/ml)	9.4 (5.0-16.2)	20.3 (9.6-35.0)	4.2 (3.0-7.2)	**0.0018**	**<0.0001**	**<0.0001**
IL-18 (pg/ml)	170338 (83277-287152)	11787 (21881120)	36764 (8958-82714)	**<0.0001**	**<0.0001**	0.19

Conclusion: Platelet count and ferritin have high specificity and sensitivity, respectively, to diagnose MAS in the context of sJIA. Even if LDH is not included in 2016 classification criteria for MAS in sJIA, we have found that this parameter could help to discriminate MAS in sJIA, in addition to the others. Our results confirm that IL-18 and the IFN-γ related biomarkers are significantly higher in patients with MAS and sHLH and might be useful to diagnose MAS/sHLH. IL-18 could help to distinguish sHLH from MAS and MAS from active sJIA.

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POS0134

LEARNING FROM LONGITUDINAL DATA IN CHILDHOOD ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: WHICH BIOMARKERS HAVE PREDICTIVE VALUE FOR ENDOTHELIAL INVOLVEMENT?

Keywords: Biomarkers, Cytokines and chemokines, Systemic lupus erythematosus

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Background: In (childhood-onset) systemic lupus erythematosus ((c)SLE), patients have an increased risk of developing premature atherosclerosis [1]. The pathophysiological mechanisms for this atherosclerosis are not completely understood. Besides traditional risk factors, the endothelium plays a major role [2]. Dysregulated endothelial cell markers and proteins involved in endothelial function in SLE are not always correlated to disease activity, which could mean that the endothelium stays in a dysregulated state in SLE, even with low disease activity (Bergkamp et al*., submitted*). However, previous studies were mostly cross-sectional and only performed in adult SLE, while childhood-onset SLE (cSLE) has a longer and more severe course [3,4].

Objectives: To measure the serum levels of a panel of SLE-associated markers involved in endothelial cell (EC) function, in longitudinal samples of cSLE patients (active vs. low SLE disease activity index (SLEDAI)) and to compare them with healthy controls and assess their correlation with disease activity.

Methods: Blood samples and patient characteristics were collected from a multicentre longitudinal cSLE study and compared with age- and sex-matched healthy controls (HC). Disease activity was evaluated by SLEDAI-2K, with cut-offs for active (>4) versus low (≤4) activity. Serum levels of CXCL12 (SDF-1), TWEAK, VEGF, CXCL10 (IP-10), ADAMTS13, Angiopoietin-2, Pentraxin-3, E-Selectin, Thrombomodulin, P-selectin, CCL2 (MCP-1), VCAM-1, ICAM-1, vWF-A2 and Gas6 were measured in two cSLE samples (t=1 and t=2) and in HC (1 sample). Patient groups and healthy controls were compared by t-tests and ANOVA, with significance for $p < 0.05$. Correlations between marker serum levels and SLEDAI were calculated with Pearson correlation.

Results: This study included 47 cSLE patients (30 treatment-naïve) and 42 healthy controls. Mean age at diagnosis in cSLE was 14 (± 2.33) years. Median SLEDAI at t=1 was 12 (IQR 6-18). Median SLEDAI t=2 was 2.5 (IQR 2-6). Time between two blood samples was 14.5 months (IQR 9-24 months). Median disease duration at t=1 was 0 months (IQR 0-18 months) and at t=2 16.5 months (IQR 10-53 months). Ethnic background in patients was 42.6% Caucasian, 36.2% African/Afro-Caribbean, 8.5% North-African/Middle East, 4.3% Asian and 8.5% mixed/other ethnic background. At t=1, serum levels of CXCL10 (p=0.01), Thrombomodulin (p=0.03) and VCAM-1 (p=0.01) were higher in the group with active cSLE compared to those with low disease activity. Serum levels for CXCL10, Pentraxin-3, Thrombomodulin, P-selectin, vWF-A2 and Gas6 correlated with SLEDAI score. Angiopoietin-2 and VCAM-1 were upregulated in cSLE patients versus healthy controls (both p<0.001),but not related to disease activity (figure 1A). Levels of CXCL10, Angiopoietin-2, Pentraxin-3, E-Selectin, CCL2, VCAM-1 and vWF-A2 decreased over time, while serum levels of TWEAK increased over time (all p<0.05) (figure 1B).

Conclusion: At different time points, serum levels of Angiopoietin-2 (t=1), VCAM-1 (t=1) and TWEAK (t=2) were increased in cSLE patients, irrespective of disease activity. These markers represent activation of ECs with vascular inflammation, EC activation and a pro-angiogenic state. The endothelium in cSLE seems to stay in an active state, even in low disease activity (SLEDAI≤4). Our findings suggest that some EC markers might be useful as biomarkers for predicting the ongoing risk for endothelial dysfunction in cSLE.

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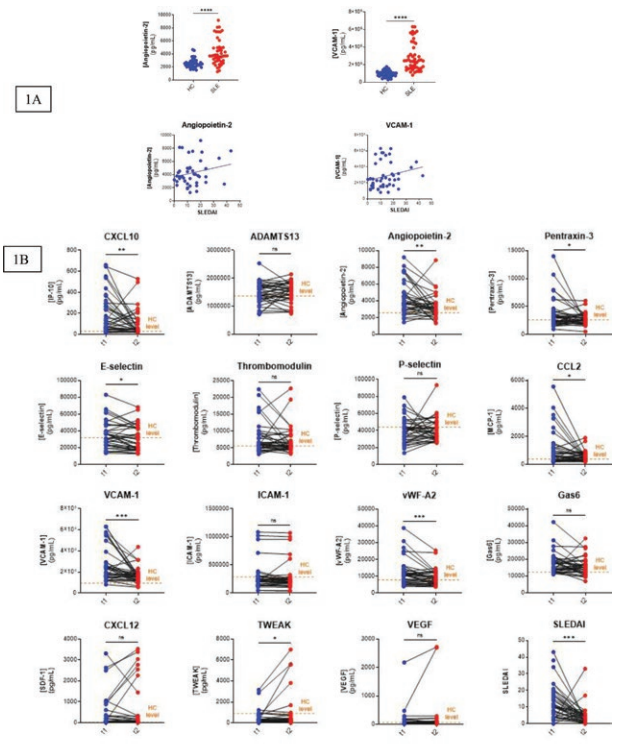


Figure 1A: Angiopoietin-2 and VCAM-1 at t=1 in cSLE patients versus healthy controls and with Pearson correlation in relation to disease activity (not significant, p>0.05)
Figure 1B: Serum levels of markers in cSLE over time and SLEDAI over time (t=1: mean SLEDAI 13.0, t=2: mean SLEDAI 4.5).

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POS0135 GENETICAL AND PHENOTYPICAL FINDINGS OF CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Genetics/Epigenetics

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease which leads to inflammation and organ damage caused by immune complex deposition. Classically, childhood SLE has been considered as a polygenic autoimmune disease; however, a pediatric monogenic lupus-like phenotype (LL) is emerging due to the recent recognition of several related novel high-penetrance gene variants. This fact associated to the high degree of concordance among monozygotic twins, supports the importance of genetic background in cSLE pathogenesis.
Objectives: To identify the presence of variants in gene related to monogenic lupus and their relationship with clinical manifestations in cSLE or LL.
Methods: A descriptive, observational, cross-sectional study was carried out in children with cSLE or LL. The genetic analysis (Sanger/Clinical Exome Sequencing) was performed from isolated DNA obtained from blood sample.
Results: Forty-five children were included in the study. The genetic analysis detected at least one variant in 14 (31.1%) children, 5 (35.7%) with cSLE and 9 (64.3%) with LL. Of those who carry a genetic variant, the median age at disease onset was 11 years (range: 2-16) and 85.7% were female; most of them Caucasians (85.7%). Seven (50%) and 3 (21.4%) out of 14 patients had a positive family and/or a personal history for autoimmune diseases, respectively. Regarding clinical manifestations at onset, musculoskeletal were the most frequent (10 patients, 71.4%), followed by hematological (9 patients, 64.3%), cutaneous (9 patients, 64.3%), constitutional with fever (8 patients, 57.1%), neurological (7 patients, 50%), renal (5 patients, 35.7%), cardiac (3 patients, 21.4%) and pulmonary (2 patients, 14.3%) manifestations. Related to immunological parameters, 13 (92.8%) were ANA positive, 7 (50%) anti-dsDNA, 4 (28.6%) ENA and 3 (21.4%) aPL positive. Both C3 and C4 were low in 8 (57.1.4%) children and isolated C3 levels were low in 4 (28.6%) patients. Among the variants, we found that only two patients who carry a *TREX* variant showed normal C3 and C4 levels; one of them presented with lupus pernio as reported in literature. Also, we identified the same *RNASEH2B (c.868G>A)* variant in two siblings with similar phenotypes and *TLR7 (c.1520T>C)* variant in two siblings of other family. The patient who carried the *SHOC2* variant presented polyarthritis and serositis, while the patient with the *TNFRSF13B* variant onset with a glomerulonephritis. Those manifestations have already been described related to these genes. Variants and phenotypes are detailed in Table 1.
Conclusion: Around 30% pediatric patients with cSLE or LL showed at least one variant in gene related to monogenic-lupus and some of them with similar phenotypes to those already described. This fact may suggest the genetics potential contribution to the cSLE pathogenesis. Further studies are necessary to confirm these data.

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Disclosure of Interests: None Declared.
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POS0136 PERFORMANCE OF THE AMERICAN COLLEGE OF RHEUMATOLOGY-1997, THE SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS-2012, AND THE EUROPEAN LEAGUE AGAINST RHEUMATISM-2019 CRITERIA FOR CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: A SOUTHEAST ASIA VALIDATION STUDY

Keywords: Validation, Systemic lupus erythematosus

Table 1.

Gene	Diagn	Skin N=6	MSK N=8	Hematological N=6	Fever N=7	Lung N=2	Cardiac N=3	NRL N=7	Renal N=5	C3/C4 N=12	ANA N= 13 DNA N=7
ADAR c.16-8 T>C	SLE	x	Arthralgia	↓ Hb, L, N	+	x	x	x	x	↓/↓	+/+
TNFAIP3 c.2170A>C	SLE	Rash	x	↓ Hb, L, N	+	x	Conduction disorder	x	LN	↓/↓	+/+
RNASEH2B c.105 107delAAT	SLE	x	Arthralgia	↓ PLT, L	+	x	Serositis	x	x	↓/N	+/-
SHOC2	SLE	Rash	Arthritis	↓ Hb, PLT, L	+	Serositis	Serositis	x	LN type III	↓/↓	+/+
IFIH1 c.2807+1G>A	SLE	Oral ulcers	Arthralgia	↓ PLT	-	x	x	x	x	↓/↓	+/+
TREX c.797A>G; TNFAIP3 c.1405C>G	LL	Rash, oral ulcers, lupus pernio	Arthralgia	x	-	x	x	Headache	x	N/N	+/-
DNASE1 c.105G>C	LL	Rash	Arthritis	↓ Hb, L, N, PLT	-	x	x	x	x	↓/N	+/-
RNASEH2B c.868G>A; C1S c.619C>T	LL	x	Arthralgia	x	-	x	x	Headache	x	↓/N	-/-
RNASEH2B c.868G>A; TLR7 c.3094G>A; STAT5A c.1248C>G	LL	x	Arthralgia	x	+	x	x	Headache	x	↓/N	+/-
TREX1c.341G>A	LL	x	x	x	-	ILD	x	WMI	x	N/N	+/-
TNFRSF13B c.41G>A	LL	Rash	x	x	+	x	x	x	MP GMN	↓/↓	+/+
TLR7 c.1520T>C	LL	Rash	Arthritis	↓ PLT	+	x	x	TE	MP GMN	↓/↓	+ +
TLR7 c.1520T>C	LL	Rash	x	↓ N	+	x	x	SNC calcifications	x	↓/↓	+/-
C2 c.719G>T PEPD c.703G>A CYBB c.593G>A	LL	Rash	Arthritis	↓ Hb, L	+	x	x	SNC calcifications	MP GMN	↓/↓	+/+

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Background: Classification criteria for systemic lupus erythematosus (SLE) include the American College of Rheumatology (ACR) 1997, the Systemic Lupus International Collaborating Clinics (SLICC) and the European League Against Rheumatism (EULAR)/ACR criteria[1]. Their performance in a primarily Asian childhood-onset SLE (cSLE) population remains unclear as the clinical manifestation frequencies are different[2].
Objectives: To evaluate the diagnostic performance of ACR-1997, SLICC-2012, and EULAR/ACR-2019 criteria in a cSLE cohort in Singapore.
Methods: Cases were physician-diagnosed cSLE, while controls were children with mixed and undifferentiated connective tissue disease that posed an initial diagnostic challenge. Retrospective data were reviewed to establish the three criteria fulfilled at diagnosis and over time.
Results: The study population included 120 cSLE cases and 36 controls, Table 1. Among cSLE patients, low C3/4 (94.2%), immunologic (93.3%), hematologic manifestations (90.0%) and arthritis (60.8%) were the most common over time. At diagnosis, 102 (85%) patients fulfilled all criteria, Figure 1. SLICC-2012 had the highest sensitivity (97.5%) and negative predictive value (NPV, 89.3%), while ACR-1997 had the highest specificity (91.7%) and positive predictive value (PPV, 97.2%). All criteria had diagnostic accuracies of ≥ 85%. Over time, 113 (94.2%) fulfilled all criteria. SLICC-2012 remained the criteria with highest sensitivity (99.2%) and NPV (94.7%), while ACR-1997 remained the criteria with highest specificity (75.0%) and PPV (92.7%). Only SLICC-2012 and ACR-1997 had ≥ 85% diagnostic accuracy over time.
Conclusion: This is the first study evaluating the SLE classification criteria performance in Southeast Asian cSLE cohort. SLICC-2012 criterion has the highest sensitivity and diagnostic accuracy, with acceptable specificity in our cohort, especially early in the disease course. The EULAR/ACR-2019 criteria does not confer additional benefits compared to the earlier two criteria.
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Table 1. Clinical characteristics of cohort at diagnosis

Clinical characteristics	At diagnosis		Over time	
	Cases, n = 120	Controls, n = 36	Cases, n=120	Controls, n = 36
Female	99 (82.5)	32 (88.9)		
Age at diagnosis (years)	12.9 (10.6 – 14.4)	14.4 (11.9 – 16.0)		
Fever	**72 (60.0)**	9 (25.0)	**74 (61.7)**	9 (25.0)
Malar rash	53 (44.2)	1 (2.8)	58 (48.3)	1 (2.8)
Discoid rash	14 (11.7)	0 (0)	22 (18.3)	0 (0)
Photosensitivity	17 (14.2)	2 (5.6)	19 (15.8)	2 (5.6)
Oral ulcer	39 (32.5)	1 (2.8)	43 (35.8)	1 (2.8)
Alopecia	37 (30.8)	3 (8.3)	54 (45.0)	3 (8.3)
Hematologic	**100 (83.3)**	**19 (52.8)**	**108 (90.0)**	**21 (58.3)**
Renal	44 (36.7)	1 (2.8)	56 (46.7)	1 (2.8)
Neurological	6 (5.0)	0 (0)	9 (7.5)	0 (0)
Arthritis	**61 (50.8)**	16 (44.4)	**73 (60.8)**	17 (47.2)
Serositis	11 (9.2)	1 (2.8)	16 (13.3)	1 (2.8)
Low C3/4	**97 (80.8)**	13 (36.1)	**113 (94.2)**	**18 (50.0)**
ANA	**118 (98.3)**	**34 (94.4)**	**118 (98.3)**	**35 (97.2)**
Anti-dsDNA	**105 (87.5)**	12 (33.3)	**106 (88.3)**	13 (36.1)
Anti-Smith	46 (38.3)	5 (13.9)	48 (40.0)	7 (19.4)
Antiphospholipid antibodies	31 (25.8)	3 (8.3)	36 (30.0)	3 (8.3)

*data in median (interquartile range) and number (%). Features with ≥ 50% are highlighted in bold. ANA: antinuclear antibody; dsDNA: double-stranded DNA

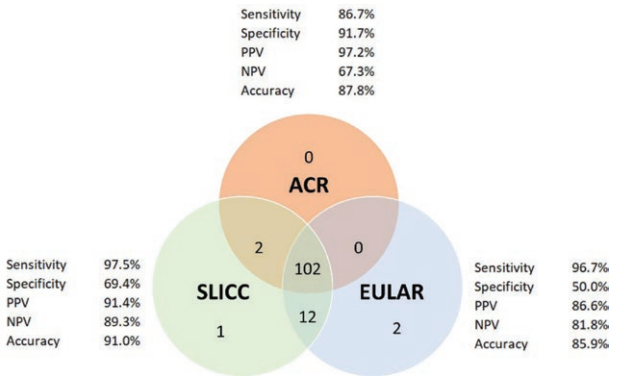


Figure 1. Diagnostic performance of all three classification criteria and the number of cSLE patients fulfilling each criterion at diagnosis

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POS0137

SERIOUS INFECTIONS IN JUVENILE SLE: INCIDENCE, PREDICTORS AND IMPACT ON LONG TERM OUTCOMES IN A SOUTH ASIAN COHORT

Keywords: Prognostic factors, Systemic lupus erythematosus

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Background: Infections are a major cause of morbidity and mortality in juvenile systemic lupus erythematosus (SLE).
Objectives: We assessed the incidence and risk factors for major infections in juvenile SLE.
Methods: A retrospective review of 225 patients of juvenile SLE (ACR 1997 criteria) with age <18 years visiting the rheumatology clinic at a single centre between 2000 to 2020 was done from clinical case records and data from the hospital electronic health records. Serious infection was defined as the need for hospitalization, or infection resulting in disability or death. Cox regression was used to determine factors associated with a serious infection and the effect of serious infection on overall survival.
Results: Among the 225 children (197 girls) with a mean age of 13.89 ±3.42 years and a cumulative follow up of 1153.45 person-years. A total of 80 serious infections occurred in 63 (28% of the cohort) individuals at a rate of 69.35 serious infections per 1000 person-years of follow-up. A second serious infection occurred in 12 children and 5 of them developed a third serious infection. Among the microbiologically confirmed cases (78.75% of cases) Bacterial infections were most common (N=33) and included S. Aureus (11), *E. Coli* (7), *K. Pneumoniae* (3), *E. Fecalis* (3), *S. Pneumoniae* (2), *Acinetobacter spp.* (2), Citrobacter (2), Salmonella (2) and *P. Aeruginosa* [1]. Twenty six (32.5%) opportunistic infections occurred: Mycobacterium tuberculosis (18), Cytomegalovirus (3), disseminated Herpes zoster (4) and invasive candidiasis (1) with 15 (83.3%) of the tuberculosis cases being extrapulmonary. On multivariate analysis fever at baseline(HR 8.51, 1.17-61.44), gastrointestinal involvement (HR 4.73, 1.13-19.94), current steroid dose (HR 1.36,1.14-1.62), average cumulative steroid dose per year (HR 1.004, 1.002-1.005) and cyclophosphamide use (HR 2.22, 1.11-4.46) were associated with serious infection (Table 1). Hospitalization rates were significantly higher in those with any serious infection (Rate ratio 2.79, 1.81-3.77). Serious infection led to more damage accrual (SLICC damage index 1.04 vs 0.22). Serious infection-free survival at 1 year, 5 years and 10 years was 84% (79.1-89.2) and 72% (65.4-79.2). There were 19 deaths with infection attributable mortality in 10 (52.6%). Serious infection predisposed to higher overall mortality (Figure 1).

Conclusion: Serious infections are a major cause of mortality and damage accrual in SLE. Constitutional symptoms, gastrointestinal involvement, current and cumulative steroid dose and cyclophosphamide use predict serious infections. TB prophylaxis in patients with SLE should be considered in endemic areas, especially when using high-dose steroid therapy.

Table 1. Cox proportional hazard models for predictors of infection

Covariates	Hazard ratio	95% CI
Fever*	**8.51**	**1.17-61.45**
Serositis	0.81	0.41-1.59
Gastrointestinal involvement*	**4.76**	**1.94-19.94**
Major organ manifestation	1.07	0.49-2.31
SLEDAI-2K	0.99	0.95-1.05
Daily steroid dose (/10mg)*	**1.36**	**1.14-1.62**
Mean cumulative steroid dose*	**1.004**	**1.002-1.005**
Albumin	1.01	0.66-1.55
Absolute lymphocyte count	0.99	0.99-1
Cyclophosphamide use*	**2.22**	**1.11-4.46**

*-significant baseline predictors of serious infection on follow up. Major organ manifestation referes to presence of nephritis or neuropsychiatric lupus.

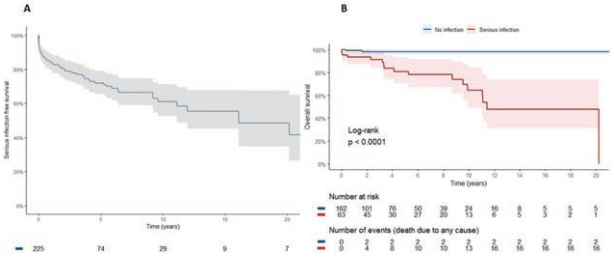


Figure 1. A. The Kaplan meier survival curve depicts time to first serious infection. B. The Kaplan meier survival curve shows the overall survival difference between those with any serious infection ever compared to those with no serious infection in the disease course.

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POS0138 EFFICACY AND SAFETY OF BELIMUMAB IN ADULTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: PRELIMINARY RESULTS FROM A PROSPECTIVE OBSERVATIONAL STUDY

Keywords: Outcome measures, bDMARD, Systemic lupus erythematosus

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Background: Childhood-onset Systemic Lupus Erythematosus (cSLE) is a rare autoimmune disease with multi-system manifestations, more severe disease course and higher frequency of morbidity than adult-onset SLE. Belimumab is the first treatment for cSLE approved for children ≥5 years of age.
Objectives: To investigate the efficacy and safety of Belimumab in adult patients with cSLE.
Methods: A prospective observational (non-interventional) study, involving adult patients with cSLE was conducted. During the 9-yearstudy period (01/2015 to 12/2022), adults with **a** cSLE diagnosis and Belimumab receivers (by intravenous or subcutaneous administration) for >12 consecutive months were enrolled. All patients met the revised 1997 American College of Rheumatology (ACR) or 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria and were followed at regular intervals (up to 6 months) in the **T**ransition **R**heumatology **O**utpatient **C**linic. SLE activity was defined according to SLEDAI-2K and the SELENA-SLEDAI Physician Global Assessment (PGA), scale 0–3 [1]. At the last follow-up visit, response to therapy was assessed by Lupus Low Disease Activity State (LLDAS), remission state and SLE Responder Index (SRI4). LLDAS was defined as: i) SLEDAI-2K ≤4, with no activity in major systems ii) no new lupus disease activity compared to previous evaluation iii) a SELENA-SLEDAI PGA ≤1 iv) current prednisolone (or equivalent) dose ≤7.5 mg daily and v) standard maintenance doses of immunosuppressive drugs. [2]. Remission was defined as i) clinical SLEDAI-2K=0 ii) dose of prednisone ≤5 mg/day according to the DORIS definition [3]. SRI4 was defined as i) ≥4-point reduction from baseline in SELENA-SLEDAI score, ii) no worsening in PGA and iii) no new BILAG A organ domain score or 2 new BILAG B organ domain scores compared with baseline [4].
Results: A total of 15 patients (14 females) were enrolled in the study. At baseline, the patients' current mean (SD) age was 25.4 (7) years and the interval from disease onset to first Belimumab administration 12.4 (7.3) years. Half of the patients had a history of lupus nephritis and 42.8% were aPL positive. All patients were under hydroxychloroquine treatment and 80% of them were additionally receiving a second immunosuppressive agent (Methotrexate, MMF, Azathioprine). Glucocorticoids (GCs) were concomitantly administered in 13 (86.6%) patients in a dose of ≥7.5mg in 57.1% of them. The patients' SLEDAI-2K mean (SD) score before Belimumab initiation was 12.1 (2.3), indicating high disease activity. The mean (SD) duration of Belimumab administration was 36.2 (1.9) months. At the last follow up visit, ongoing therapy with Belimumab was recorded in 66.7% of the cohort. SLEDAI-2K mean (SD) score was reduced to 3.5 (2.3), 1 patient (6.6 %) was in remission, 9 (60%) patients had mild and none high disease activity. The majority (78.5%) met the LLDAS definition and 78.5% were SRI4 Responders. Half of the patients (53.8%) achieved lower doses or discontinuation of GCs and 26.7% accomplished a reduction of the immunosuppressant's dose. Reasons for Belimumab discontinuation included pregnancy issues, infection and low adherence (3, 1, 1 patient respectively). None of the patients experienced a serious adverse event.
Conclusion: In this cohort of adult patients with cSLE, Belimumab was well-tolerated and effectively reduced disease activity allowing the downstream of GCs's dose.

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POS0139 DIFFUSE JUVENILE SYSTEMIC SCLEROSIS PATIENTS SHOW DISTINCT ORGAN INVOLVEMENT, ANTIBODY PATTERN AND HAVE SIGNIFICANTLY MORE SEVERE DISEASE IN THE LARGEST JSSC COHORT OF THE WORLD. RESULTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT

Keywords: Systemic sclerosis

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Background: Juvenile systemic sclerosis (jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children. In adult patients there are significant differences between the clinical presentation of diffuse and limited subtypes. We reviewed clinical differences in presentation of subtypes in patients in the juvenile systemic scleroderma inception cohort (jSScC).
Objectives: To study the clinical presentation of jSSc patients with diffuse (djSSc) and limited (ljSSc) subtypes.
Methods: We reviewed the baseline clinical characteristics of the patients, who were recruited to the jSScC till December 2022. jSScC is a prospective cohort of jSSc patients, who developed the first non-Raynaud´s symptom before the age of 16 years and are under the age of 18 years at the time of inclusion.
Results: The JSScC included 232 patients, 68% (n=159) had diffuse subtype. The median age at onset of Raynaud phenomenon was 10.4 years (7.3-12.9), at the first non-Raynaud symptom 10.9 years (7.3-13.0) and median disease duration 2.5 years (1.0-4.6). The female/male ratio was significantly lower in the djSSc subtype

(3:1 versus 5:1, p<0.001). Antibody profile was similar, with the exception of a significantly higher number of anticentromere positive patients in the ljSSc. Decreased FVC<80% was found in approximately 30% and decreased DLCO<80% was found in around 40% in both subtypes. Abnormal HRCT findings were found in 44% of patients. Pulmonary hypertension assessed by ultrasound occurred in approximately 5% in both groups and gastrointestinal involvement in 43% of djSSc and 36% in ljSSc (p=0.303). Patients with djSSc had significantly higher modified Rodnan Skin Score, more frequently sclerodactyly, a history of digital ulceration active ulceration, telangiectasia, a decreased Body Mass Index z score ≤ -2 and decreased joint range of motion. Patients with ljSSc had significantly higher rate of cardiac involvement. Regarding patient related outcomes assessed by VAS 0-100 djSSc patients had more severe disease also physician related outcome assessed by VAS 0-100 were significantly higher in djSSc (see Table 1).

Table 1. Comparison of subtypes at time of inclusion in the cohort

	Whole Group N=232	Diffuse Subtype N=159	Limited Subtype N=73	P value
Anticentromere	5% (7/156)	2% (2/106)	10% (5/50)	0.022
MRSS, median (IQR)	10 (4 – 20)	16 (8 - 27)	4 (0 – 8)	0.001
Gottron Papules	26% (59/228)	31% (48/155)	15% (11/73)	0.011
Sclerodactyly	75% (165/219)	85% (127/150)	55% (38/69)	<0.001
Telangiectasia	37% (77/209)	44%(62/141)	22% (15/68)	0.002
History of ulceration	52% (119/229)	62% (98/158)	30% (21/71)	<0.001
Active ulceration	17% (39/229)	21% (33/158)	8% (6/71)	0.021
Only Cardiac involvement	5% (12/232)	3% (4/159)	11% (8/73)	0.007
BMI < - 2 z score	15% (33/217)	20% (29/148)	6% (4/69)	0.008
Joints with decreased range	59% (136/231)	64% (101/158)	48% (35/73)	0.022
Physician Reported (Median, IQR)				
Physician global disease activity	30 (20 – 45) n=197	35 (20– 50) n=138	20 (10 – 30) n=59	0.001
Physician global disease damage	30 (15 – 40) n=195	30 (20 – 45) n=138	20 (5 – 30) n=57	0.004
Physician ulceration activity	0 (0 – 16) n=216	5 (0 – 20) n=154	0 (0 – 0) n=62	0.018
Patient Reported (Median, IQR)				
Patient global disease activity	40 (20 – 50) n=178	40 (20 – 50) n=129	30 (15 – 55) n=49	0.024
Patient global disease damage	30 (15 – 60) n=177	40 (20 – 60) n=128	25 (5 – 55) n=49	0.001
Patient Raynaud activity	30 (10 – 60) n=202	30 (10 – 60) n=145	15 (0 – 55) n=57	0.001
Patient ulceration activity	0 (0 – 30) n=203	10 (0 – 30) n=145	0 (0 – 20) n=58	0.001

Conclusion: In the largest jSSc cohort in the world, djSSc patients have a significantly more severe disease. Patients and physician related outcomes were significantly more severe in djSSc group. Interestingly, we found no differences regarding interstitial lung disease, pulmonary hypertension or gastrointestinal involvement, although the number of patients with decreased BMI ≤ -2 z score was significantly higher in the djSSc patients.

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POS0140 PATIENT AND PHYSICIAN REPORTED OUTCOMES OF JUVENILE SYSTEMIC SCLEROSIS PATIENTS SIGNIFICANTLY IMPROVE OVER 24 MONTHS OBSERVATION PERIOD IN THE JUVENILE SYSTEMIC SCLERODERMA INCEPTION COHORT

Keywords: Systemic sclerosis

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Background: Juvenile systemic sclerosis (jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children. The Juvenile Systemic Scleroderma Inception cohort (jSScC) is the largest cohort of jSSc patients in the world. The jSScC collects data prospectively in jSSc, allowing the evaluation of the development of organ involvement and patient and physician reported outcomes in jSSc over time.

Objectives: To review the changes in the clinical characteristics, and patient and physician reported outcomes, over a 24 month observation period from the time of inclusion into the cohort.

Methods: The jSScC cohort enrolls jSSc patients who developed the first non-Raynaud´s symptom before the age of 16 years and are under the age of 18 years at the time of inclusion. We reviewed jSScC patient clinical data and patient and physician reported outcomes, who had 24 months follow up from the time of inclusion until 1st of December 2022.

Results: We extracted data from 90 patients, 77% of them had the diffuse subtype. The female/male ratio was 3.5:1. Median age of onset of Raynaud´s was 9.4 years and the median age of onset of non-Raynaud´s was 10.0 years. Eighty-nine percent of the patients were treated with disease modifying anti-rheumatic drugs (DMARDs) at time of inclusion in the cohort (T0) and 96% after 24 months (T24). Median disease duration was 2.4 years at T0. No patient died during the follow up. Antibody profile stayed unchanged. Only 3 clinical parameters changed and all improved significantly, the median modified Rodnan skin score improved from 11 to 8 (p=0.021), number of patients with joints with pain on motion decreased from 21% to 10% (p=0.04) and the number of patients with muscle weakness decreased from 13% to 4% (p=0.03). All other organ involvement did not show any statistically significant change from T0 to T24. All collected patient reported outcomes improved significantly from T0 to T24: the patient reported disease activity by VAS 0-100 from 40 to 20 (p=0.001), the patient reported disease damage by VAS 0-100 from 35 to 20 (p=0.027), patient reported ulceration activity by VAS 0-100) from 8 to 0 (p=0.001) and the patient reported Raynaud activity by VAS 0-100 from 20 to 10 (p=0.002). Two of the three physician reported outcomes improved significantly, the physician global disease activity by VAS 0-100 from 30 to 20 (p=0.001) and physician reported ulceration activity by VAS 0-100 from 5 to 0 (p=0.017). (Table 1.)

Table 1. Items with significant improvement over 24 months observation period in the cohort

	0 month N=90	24-month follow-up N=90	P Value
MRSS, median (IQR)	11 (5 – 20)	8 (2 – 20)	0.021
Presence of joints with pain on motion	21% (19/89)	10% (9/89)	0.040
Muscle Weakness	13% (10/75)	4% (3/81)	0.030
Physician global disease activity	30 (20 – 45) n=71	20 (10 – 33) n=83	0.001
Physician ulceration activity	5 (0 – 19) n=86	0 (0 – 10) n=89	0.017
Patient global disease activity	40 (20 – 54) n=66	20 (10 – 30) n=76	0.001
Patient global disease damage	35 (20 – 60) n=66	20 (10 – 35) n=76	0.027
Patient Raynaud activity	20 (0 – 50) n=83	10 (0 – 26) n=84	0.002
Patient ulceration activity	8 (0 – 28) n=84	0 (0 – 10) n=84	0.001

Conclusion: Skin and musculoskeletal clinical features improved over 24 months, with almost all patients on DMARDs, supporting the response of these features to therapy. It was promising that internal organ involvement, like cardiac, lung and gastrointestinal, did not significantly worsen or increase. The most striking observation is the positive direction and improvement all patients and two of the three physician reported outcome measures over 24 months in this large international cohort.

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POS0141 APPLICATION OF CRISS SCORE, REVISED CRISS SCORE AND RCID SCORE IN PATIENTS WITH JUVENILE SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis

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Background: Juvenile systemic sclerosis (jSSc) is a rare disease in childhood. To date, no composite response index exists to assess treatment effect in jSSc patients. ACR CRISS score (probability of improvement ranging from 0 to 1 based on mRSS, FVC%, PtGA, MDGA and HAQ-DI) and revised ACR CRISS (rCRISS, proportion of patients who improve in ≥ 3/5 ACR CRISS core items by a certain percentage, e.g. 30%, except 5% for FVC) were developed by experts in the field as outcome measures in adult patients with SSc. In addition, the Ranked Composite Important Difference (RCID) score was recently introduced as anchor to the ACR CRISS.

Objectives: We aimed to study the applicability and performance of the ACR CRISS, rCRISS and RCID in a prospectively followed cohort of patients with diffuse cutaneous jSSc.

Methods: Data from the international jSSc inceptions cohort were used for this analysis. The ACR CRISS, rCRISS and RCID were calculated between baseline and 12-months follow-up according to the scoring algorithms. Missing values in the core items were estimated by multiple imputation by chained equations. Here we aimed to determine the value of the response measures to detect clinically change defined by the anchor questions about change (much better or little better versus almost the same, little worse or much worse) in patients overall health due to scleroderma since the last visit provided by the treating physicians and parents or patients (aged > 12 years).

Results: We included 95 jSSc patients with diffuse cutaneous subtype with available baseline and 12-months visit. Seventy-nine percent were female, the mean age at enrollment was 13.0 (3.8) and the mean disease duration was 3.1 (2.8) years. Among 95 patients, 57% were treated with steroids, 47% with methotrexate, 27% with MMF and 3% with a biological at baseline. ACR CRISS showed a ceiling effect (>.998) in 51% and a floor effect (<0.005) in 26% of patients. Patients who reported at least moderate improvement had a median ACR CRISS of 0.99 and in mean 2.6 (1.3) core items that improved by ≥20% from baseline to 12-months follow-up. The rCRISS 20/30/50 responses were 59%/49%/33% in patients who reported improvement (table 1) and 25%/25%/8% in patients with worsening. The RCID was approximately normal distributed (mean 20.7, SD 43.4). Mean (SD) RCID for patients who reported worsening was -10.5 (38.6) vs RCID of 20.7 (45.2) for patients who reported improvement. RCID scores for physician reported anchors of worsening or improvement were 6.5 (44.2) and 18 (45.4), respectively. The concordance between a positive RCID score and rCRISS 20/30 was moderate (rCRISS 20 and RCID, 43%, kappa=0.43; rCRISS 30 and RCID, 38%, kappa=0.36).

Table 1. ACR CRISS, rCRISS and RCID score by patients and physicians ratings about scleroderma disease course

	Worsening/ no improvement reported by patients (n=12)	Improvement reported by patients (n=49)	P value	Worsening/ no improvement reported by physicians (n=14)	Improvement reported by physicians (n=50)	P value
Median ACR CRISS score (IQR)	0.0 (0 to 0.75)	0.99 (0 to 1.0)	0.007	0.35 (0 to 0.99)	0.99 (0 to 1.0)	0.037
rCRISS response 20%	3(25%)	29 (59%)	0.034	5 (36%)	29 (58%)	0.140
rCRISS response 30%	3 (25%)	24 (49%)	0.134	2 (14%)	27 (54%)	0.008
rCRISS response 50%	1 (8%)	16 (33%)	0.092	0 (0%)	18 (36%)	0.008
Mean RCID score (SD)	-10.5 (38.6)	20.7 (45.2)	0.031	6.5 (44.2)	18 (45.4)	0.411

CRISS = Composite Response Index in Systemic Sclerosis; RCID=Ranked Compsoite Important Difference; rCRISS = revised Composite Response Index in Systemic Sclerosis; SD = standard deviation

Conclusion: Our data confirmed the presence of a ceiling and floor effect of ACR CRISS as shown in studies of adult SSc patients. The CRISS, rCRISS and RCID response distinguished between patients who rated their disease course since last visit as worsened or improved. Future studies should focus on the determination of specific pediatric weights for the CRISS and RCID components rather than extrapolation from adult SSc. In general, the RCID offers a meaningful tool in order to determine response to therapy in future clinical trials in jSSc patients.

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POS0142 THE ASSOCIATION OF AUTOANTIBODIES WITH CLINICAL MANIFESTATIONS AND LONG-TERM REMISSIONS IN COMPARISON WITH JUVENILE- AND ADULT-ONSET IDIOPATHIC INFLAMMATORY MYOPATHIES

Keywords: Autoantibodies, Remission, Myositis

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Background: The associations of myositis-specific autoantibodies (MSAs) and myositis-associated autoantibodies (MAAs) with clinical features and remission in idiopathic inflammatory myopathy (IIM) are different between those of juvenile-onset (JIIM) and adult-onset.

Objectives: Since the associations in JIIM had not been fully elucidated, we analyzed them comparing that in adults using clinical information and autoantibodies.

Methods: A total of 320 cases of IIMs (juvenile-onset, 2004-2021, n=34; adult-onset, 2018-2021, n=286) with a history of attendance at our hospital were retrospectively analyzed using medical records. Remission without glucocorticoids and immunosuppressive drugs for 30 years was also examined. MSAs were identified by assays of RNA immunoprecipitation (IP), protein IP, protein IP-blot, and ELISA. Logistic regression analysis, Mann-Whitney U test, Fisher's exact test, and log-rank test were performed.

Results: In JIIM, anti-MDA5 (15%) and anti-TIF1-γ (15%) were the most frequent MSAs, followed by anti-ARS (9%) and anti-NXP2 (6%) (Table 1). In particular, the frequency of anti-ARS was significantly lower in juveniles whereas it was the highest in adults (9% vs. 32%, respectively, p=0.01). Anti-SRP and anti-Mi-2 were not identified in juveniles, although they were identified with low frequencies in adults. In MAAs (juvenile-onset vs. adult-onset), anti-Ku (9% vs. 2%, p=0.03) and anti-U1-RNP (18% vs. 4%, p=0.02) were more common in juveniles while anti-SS-A (15% vs. 16%, p=1) was not significantly different between juveniles and adults. Dermatomyositis tended to be more dominant than polymyositis in juveniles than in adults (76% vs. 59%, p=0.06) (Table 1). Fever was more frequently observed in juveniles (74% vs. 12%, p<0.0001) and interstitial lung disease (ILD) was less frequently observed in juveniles than adults (29% vs. 66%, p<0.0001). Malignancy was observed in 2 juvenile-onset patients (6%) during 14.7±12.3 years while in 32 adult-onset patients (12%) during 6.8±7.5 years (p=0.56). Anti-NXP2 (n=1) and anti-PL12 (n=1) were observed in juveniles. In contrast, anti-TIF1-γ (n=11/32, 34%) was mainly observed in adults. Anti-MDA5 (OR [95%CI]: 14.0 [1.31, 150]) in juveniles and anti-ARS (23.2 [7.07, 76.1]) and anti-MDA5 (13.3 [4.03, 43.8]) in adults were associated with ILD. Anti-MDA5 was poorly associated with muscle symptoms in both juveniles (0.06 [0.004, 0.88]) and adults (0.43 [0.22, 0.85]). The rate of drug-free remission for 30 years in juveniles is higher than that in adults (32% vs 7%, respectively, p<0.0001, Figure 1). The drug-free remission in juveniles was observed in the order of anti-TIF1-γ, anti-NXP2, anti-MDA5, and anti-ARS, reaching a plateau at 5.7 years. In contrast, the remission in adults was observed in the order of anti-MDA5, anti-TIF1-γ, anti-SRP, and anti-ARS. The use of glucocorticoid (88% vs. 91%, p=0.76) was similar in juveniles and adults, while methotrexate (32% vs. 8%, p=0.0002) was used more frequently in juveniles.

Conclusion: There were differences in the clinical characteristics of IIM and autoantibodies between juvenile-onset and adult-onset. Further analysis is needed in a larger sample size.

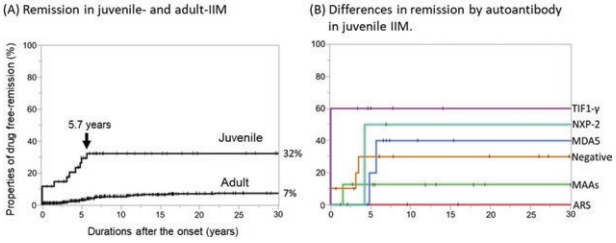
REFERENCES: NIL.

Table 1. The differences of clinical manifestations in juvenile- and adult-IIM

	Juvenile (n=34)	Adult (n=286)	P value
Sex	F:26 (74%), M:8 (26%)	F:217 (75%), M:72 (25%)	1
Age at onset (y.o.)	10.3±5.8	53.5±14.1	<.0001*
Diagnosis (DM, PM)	DM:26 (76%), PM:8 (24%)	DM:168 (59%), PM:115 (41%)	0.06
Skin rash	27 (79%)	170 (59%)	0.025*
Muscle symptom	29 (85%)	243 (87%)	0.79
Interstitial lung disease	10 (29%)	187 (66%)	<.0001*
Fever	20 (74%)	35 (12%)	<.0001*
Elevation of CRP	14 (44%)	184 (64%)	0.03*
Malignancy	2 (6%)	32 (12%)	0.56
Overlap	10 (29%)	38 (24%)	0.51
Anti-ARS	3 (9%)	86 (32%)	0.01*
Anti-MDA5	5 (15%)	62 (23%)	0.50
Anti-TIF1-γ	5 (15%)	21 (8%)	0.16
Anti-Mi-2	0 (0%)	6 (2%)	1
Anti-SRP	0 (0%)	21 (8%)	0.15
Anti-NXP2	2 (6%)	3 (1%)	0.09
Anti-Ku	3 (9%)	4 (2%)	0.03*
Anti-U1-RNP	6 (18%)	11 (4%)	0.02*
Anti-SS-A/Ro	5 (15%)	42 (16%)	1

*p<0.05

Figure 1. Remission without Glucocorticoid and Immunosuppression in juvenile- and adult-IIM



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Pathogenic pathways in Systemic Sclerosis and Myositis

POS0143

TISSUE RESIDENT MEMORY AND CYTOTOXIC T CELLS ARE CLONALLY EXPANDED IN THE MUSCLE OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Keywords: Adaptive immunity, Myositis, Biomarkers

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Background: Idiopathic inflammatory myopathies (IIM) are rare autoimmune systemic diseases characterized by muscle weakness and presence of muscle-infiltrating T cells. IIM represent a clinical challenge due to heterogeneity of symptoms and variability of response to immunosuppressive treatment.
Objectives: We aimed to explore the mechanisms involved in T cell migration and persistence in the muscle tissues of patients with IIM.
Methods: We performed single-cell RNA sequencing on muscle-infiltrating and peripheral blood (PB) memory T cells from patients with recently diagnosed IIM (n=7) from the Rheumatology Clinic, Karolinska University Hospital. Briefly, after enzymatic digestion of fresh muscle tissue, we single-cell sorted T cells from seven patients who also presented muscle infiltrates by histopathological analysis: immune-mediated necrotizing myopathy (IMNM) n=2; inclusion body myositis (IBM) n=2; dermatomyositis (DM) n=1; and antisynthetase syndrome (ASyS) n=1 and a non-inflammatory myopathy. Muscle T cells were sorted based on the co-expression of CD45 and CD3, whereas PB memory T cells were sorted based on the exclusion of naïve $CD45RA^+CCR7^+$ $CD3^+$ T cells. We also aligned the TCR sequences. We had access to additional muscle and PB samples from two patients after immunosuppressive treatment. Description of the methodology is presented in Figure 1.
Results: After quality control, filtering, and normalization processes of the gene expression matrix, the total number of T cells recovered from the analysis was 2,844, out of which 1,427 were isolated from the muscle and 1,417 cells from PB. Muscle and PB T cells grouped separately indicating different gene signature. Three different clusters containing muscle T cells (cluster 1), PB CD8+ T cells (cluster 2) and PB CD4+ T cells (cluster 3) were identified, showing different transcriptomic signature between muscle and PB T cells. After unsupervised clustering of gene expression, we identified 15 distinct T-cell clusters annotated based on differentially expressed genes and visualized by UMAP. We found enrichment in the muscle compartment compared to blood for the following clusters: tissue-resident memory (T_{RM}) T cells, muscle central memory (CM) CD4+ T cells, muscle effector memory (EM)T cells, EGR1hi and T_{RM} genes, and Tregs. All clusters were present in all patients except for the Tregs cluster, which was not detected in the patient with ASyS. A distinct signature between muscle T cells and blood memory T cells was revealed by the differential expression of genes involved in transcription, migration, dephosphorylation, cell cycle, metabolism, cytoskeleton and signalling. Additionally, expanded T-cell clones were observed in all patients' muscle tissue, ranging between 20-50% of all TCR sequences. We could identify expanded T-cell clones persisting at follow-up in the muscle of one patient with IMNM and another with ASyS after immunosuppressive treatment.
Conclusion: Our study reveals a muscle T-cell signature in patients with IIM and a transcriptomic map to identify possible novel therapeutic targets in IIM, where muscle-infiltrating T cells are predominantly composed of cytotoxic, effector memory, tissue-resident, proliferating and regulatory T cells. The expression of tissue-resident memory (T_{RM}) receptors and the presence of clonally expanded T-cell clones in the muscle of all patients with IIM imply the role of these cells in disease pathogenesis.

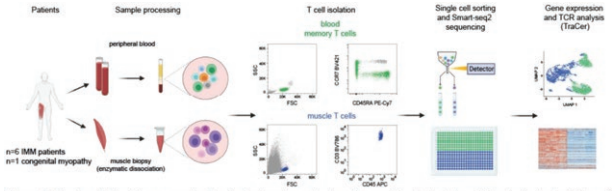


Figure 1. Single cell identifies a muscle T-cell signature in patients with myositis. Technical workflow including isolation of memory T cells from peripheral blood (PB, in green) and muscle T cells (in blue) from muscle biopsies, followed by Smart-seq2 single cell sequencing in six patients with IIM and one with an undefined myopathy.

REFERENCES: NIL.
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Disclosure of Interests: Angeles Shunashy Galindo-Feria: None declared, Alexandra Argyriou: None declared, Begum Horuluoglu: None declared, Juan Sebastian Díaz-Boada: None declared, Antonella Notarnicola: None declared, Lara Dani: None declared, Annika van Vollenhoven: None declared, Daniel Ramsköld: None declared, Inger Nennesmo: None declared, Maryam Dastmalchi: None declared, Ingrid E. Lundberg Shareholder of: Stock shares in Roche and Novartis., Paid instructor for: Has been serving on the advisory board for Corbus Pharmaceutical, EMD Serono. Research & Development Institute, Argenx, Octapharma, Pfizer, Kezaar, Orphazyme and Janssen, Consultant of: Corbus Pharmaceuticals, Inc, Grant/research support from: Astra Zeneca, Lina M. Diaz-Gallo: None declared, Karine Chemin: None declared.
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POS0144

miRNA CARGO CHARACTERIZATION FROM CIRCULATING EXTRACELLULAR VESICLES IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES (IIM) HIGHLIGHTS PECULIAR EPIGENETIC PROFILES ACROSS DEFINITE IIM SUBSETS AND DIFFERENT CLINICAL MANIFESTATIONS

Keywords: Myositis, Biomarkers, -omics

M. Gatto[1], C. Franco[1], A. Giannella[2], L. Bertazza[3], M. Gasparotto[1], A. Ghirardello[1], G. Ceolotto[2], A. Doria[1]. [1]*University of Padova, Unit of Rheumatology, Department of Medicine, Padua, Italy*; [2]*University of Padova, Metabolic Disease Unit, Deparment of Medicine, Padua, Italy*; [3]*University of Padova, Unit of Endocrinology, Department of Medicine, Padua, Italy*

Background: Idiopathic Inflammatory myopathies (IIM) are heterogeneous systemic autoimmune diseases for which biomarkers are needed. Extracellular vesicles (EVs) are cell-derived nanoparticles regulating several biological functions[1]. Growing evidence supports the role of EVs in the pathogenesis of systemic autoimmune diseases[2].
Objectives: To evaluate the EVs-microRNA (miRNA) profile among distinct clinical manifestations and subsets of IIM, and healthy donors (HD).

Methods: We enrolled adult (≥18 years) consecutive IIM patients (EULAR 2017 criteria) and sex- and age-matched HD. Circulating EVs were isolated from plasma through size exclusion chromatography and ultra-filtration. miRNA isolation was performed using Qiagen miRNeasy Serum/Plasma Advanced kit and miRNA quantification and analysis through next generation sequencing (NGS). Comparisons were carried out using Student's t-test or one-way ANOVA with multiple comparisons.
Results: We included 60 IIM patients (females 61.7%; mean age 56.3±13.1 years; seropositive 78.3%; clinically active 56.7%; on immunosuppressants (any): 63.3%) and 60 HD. miRNA analysis was performed on 21 IIM patients and 21 HD considering a comprehensive pool of 100 miRNAs. Ten miRNAs resulted significantly dysregulated between patients and HD (**Table 1**). Among miRNAs upregulated in patients, some exhibit immunoregulatory functions (hsa-miR-222-3p, hsa-miR185-5p) while others are involved in oncogenesis (hsa-miR-486-5p, has-miR-451a, hsa-miR-15a-5p)[3]. Conversely, downregulated miRNAs in patients usually display anti-inflammatory and anti-neoplastic properties (hsa-let-7 group)[1,3]. More specific EVs-miRNA profiles were identified considering IIM subsets and organ involvement (lung, skin and muscles). Patients with Cancer-associated myositis displayed down-regulated hsa-miR-23b-3p (p=0.03), hsa-miR-374a-5p (p=0.01), hsa-miR-361-5p (p=0.046), hsa-miR-143-3p (p=0.03) and up-regulated hsa-miR-26b-5p (p=0.046). Anti-synthetase syndrome patients showed up-regulated hsa-miR-30c-5p (p=0.033) and hsa-miR-186-5p (p=0.024). Dermatomyositis patients displayed up-regulated hsa-miR-125b-5p (p=0.02), hsa-miR-29c-3p (p=0.027), hsa-miR-361-5p (p=0.039). According to different clinical manifestations, hsa-miR-451a, hsa-miR-29a-3p, hsa-miR-342-2p and hsa-miR-146b-5p were up-regulated in active myositis, and hsa-miR-222-3p, hsa-miR-144-5p, hsa-miR-101-3p, hsa-miR-19b-3p, hsa-miR-25-3p in active skin and Gottron's lesions.
Conclusion: Differential expression of EVs-miRNAs across IIM subsets suggests peculiar epigenetic footprints to distinguish specific IIM phenotypes and clinical manifestations, which may shed light on disease mechanisms and possibly generate tailored treatment targets (**Figure 1**). Circulating EVs might serve as IIM biomarkers and for early stratification of disease manifestations.

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Table 1. EV-miRNAs with significantly different expressions in IIM (n=21) vs. HDs (n=21) [indicated Fold Change and p values]

EV-miRNAs	Fold Change	p-value	IIM vs. HDs
hsa-miR-451°	1.919321	0.0000759	Up-regulated
hsa-miR-15a-5p	1.275568	0.022154	Up-regulated
hsa-miR-486-5p	1.446866	0.00114	Up-regulated
hsa-miR-222-3p	1.845142	0.001526	Up-regulated
hsa-miR-32-5p	1.778544	0.018901	Up-regulated
hsa-miR-185-5p	1.454742	0.00529	Up-regulated
hsa-let-7e-5p	-1.56348	0.00157	Down-regulated
hsa-let-7a-5p	-1.55167	0.001512	Down-regulated
hsa-let-7f-5p	-1.29617	0.018207	Down-regulated
hsa-let-7b-5p	-1.50724	0.000313	Down-regulated

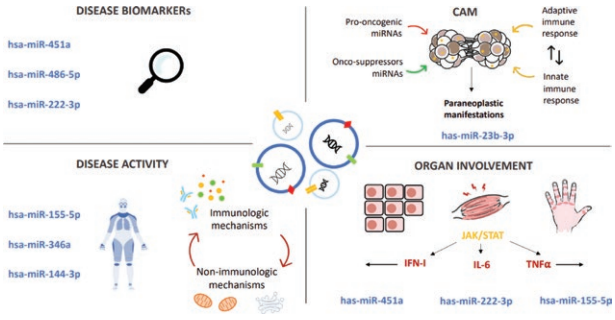


Figure 1. Summary of EVs-miRNA putative roles in a IIM cohort

Acknowledgements: NIL.
Disclosure of Interests: Mariele Gatto Speakers bureau: GSK, Chiara Franco: None declared, Alessandra Giannella: None declared, Loris Bertazza: None declared, Michela Gasparotto: None declared, Anna Ghirardello: None declared, Giulio Ceolotto: None declared, Andrea Doria Speakers bureau: GSK, Pfizer, AZ, Celgene, EliLilly, BMS, Roche.

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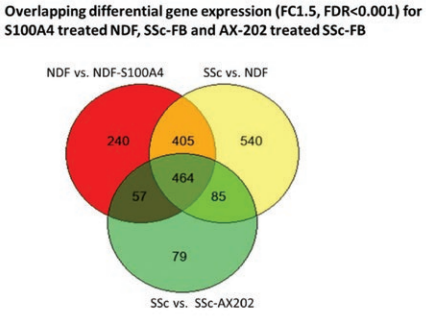
POS0145 **CLINICAL AND PATHOGENIC SIGNIFICANCE OF S100A4 OVEREXPRESSION IN SYSTEMIC SCLEROSIS**

Keywords: Innate immunity, Cell biology, Systemic sclerosis

V. Ong[1], X. Shiwen[1], F. Zhang[1], R. Maclean[1], K. Clark[1], S. Borchert[2], R. I. Hussain[2], J. Klingelhöfer[2], J. Hallén[2], C. P. Denton3. *[1]Centre for Rheumatology, University College London Royal Free Campus, London, United Kingdom*; *[2]Arxx Therapeutics, 0349, Oslo, Norway*; *[1]Centre for Rheumatology, University College London Royal Free Campus, London, United Kingdom*

Background: S100A4 belongs to a family of proteins originally defined by solubility of the prototypic members in 100% saturated ammonium sulphate. Preclinical studies suggest that extracellular S100A4 as a Damage Associated Molecular Pattern (DAMP) protein is upregulated upon stress or injury and may be a target for antifibrotic therapy.
Objectives: We explored expression and function of S100A4 as a driver of fibroblast activation in systemic sclerosis (SSc).
Methods: S100A4 protein concentration was measured by ELISA in serum of SSc (n=94) and healthy controls (n=15). Association of serum level with major organ complications and skin score (mRSS) was determined. S100A4 protein expression in supernatant and cell layer of skin fibroblast cultures from diffuse cutaneous SSc (SScF, n=6) and healthy controls (NF, n=6) was assessed. Recombinant S100A4 and a high affinity anti-S100A4 neutralising monoclonal antibody (AX-202) were used to investigate the profibrotic molecular, functional and genomic phenotype in SSc and control fibroblasts.
Results: Median [range] S100A4 (ng/ml) was higher in serum of SSc (89.9 [15.0-240.0]) than healthy controls (71.4 [7.9-131.8]; p=0.027). There was significant association with SSc-ILD (p=0.025, n=55), scleroderma renal crisis (p=0.026, n=4) and trend of increase in pulmonary hypertension (p=0.075, n=7) and a trend for S100A4 to fall in longer disease duration (r=-0.18, p=0.09) and a weak correlation (r=0.28, p=0.07) with current mRSS but not peak mRSS in dcSSc. Median [range] S100A4 (ng/ml) was higher in culture supernatants of SScF (4.19 [0.52-8.42]) than NF (0.28 [0.02-3.29]; p<0.0001) and SSc cell layer had increased levels by Western blot analysis (mean [sd] RDU NF 0.50 [0.91]; SScF 8.16 [2.49]; p<0.0001). S100A4 induced a fibrotic phenotype in NF with concentration-dependent increase in Col1, SMA and CTGF expression, and promotion of migration (scratch wound assay) and 3D type I collagen gel contraction that was attenuated by AX-202. AX-202 also reduced the constitutive profibrotic gene and protein expression phenotype of SScF. The effect of S100A4 was significantly attenuated by SB431524, a specific inhibitor of ALK5 (p<0.0001 ANOVA)

A.



B.

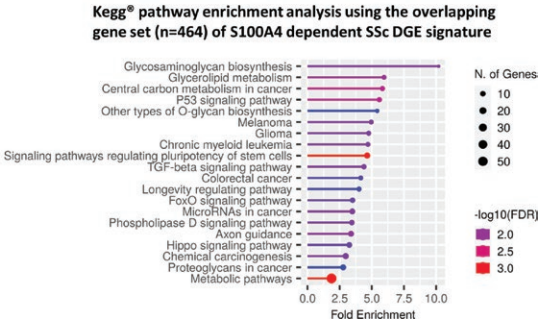


Figure 1.

using qPCR assays across treatment groups for Col1, SMA and CTGF. Gene expression data (qPCR) confirmed protein expression. Genome-wide RNAseq analysis identified an S100A4 activated signature in NF overlapping the hallmark gene expression signature of SScF. Thus, 464 differentially expressed genes (FDR<0.001 and FC>1.5) induced in NF by S100A4, were also constitutively overexpressed, and downregulated by AX-202, in SScF (**Figure 1A**). Pathway mapping of these S100A4 dependent genes in SSc showed the most significant enriched Kegg pathways (FDR<0.001) were regulation of stem cell pluripotency (4.6-fold) and metabolic pathways (1.9-fold) (**Figure 1B**).

Conclusion: Our findings provide compelling evidence supporting a profibrotic role for S100A4 in fibroblast activation in SSc and suggest that serum level may be a biomarker of major organ manifestations and disease severity. This study supports examining the therapeutic potential of targeting S100A4 in SSc are warranted.

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Disclosure of Interests: Voon Ong Speakers bureau: Boehringer Ingelheim, Xu Shiwen: None declared, Fenge Zhang: None declared, Rory Maclean: None declared, Kristina Clark: None declared, Signe Borchert Employee of: Arxx Therapeutics, Rizwan I Hussain Employee of: Arxx Therapeutics, Jörg Klingelhöfer Employee of: Arxx Therapeutics, Jonas Hallén Employee of: Arxx Therapeutics, Christopher P Denton Speakers bureau: Janssen; Boehringer Ingelheim, Consultant of: GSK; CSL Behring; Boehringer Ingelheim; Merck; Roche; Sanofi, Grant/research support from: GSK; CSL Behring; Inventiva; Horizon; Arxx Therapeutics.

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POS0146 BIOSAMPLES FROM VEDOSS PATIENTS SHOW CLASSIC PATHOLOGICAL SIGNS OF SCLERODERMA:OPPORTUNITY FOR A BIOLOGICAL DIAGNOSIS OF DISEASE

Keywords: Systemic sclerosis, Autoantibodies, Cytokines and chemokines

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Background: The five-year analysis of the EUSTAR multicentre prospective study for Very Early Diagnosis Of Systemic Sclerosis (VEDOSS) has recently indicated that RP patients with one more VEDOSS criteria have an increased risk of SSc progression, indicating a window of opportunity for early detection of SSc and clinical and therapeutic intervention. Furthermore, it warrants further evaluation of VEDOSS biosamples to enhance our understanding of SSc pathogenesis.

Objectives: Here we aimed to determine whether sera, skin or dermal fibroblasts cultured from VEDOSS patients showed any biological hallmark of SSc.

Methods: Sixty-four VEDOSS sera samples were tested for expression of IFN inducible chemokines (CXCL-9,10 and 11 and CCL2, 8 and 19) and biomarker of extracellular matrix turnover (ELF test). 3mm skin biopsies were taken from the forearms from 11 skin biopsies from the forearm of VEDOSS patients and 5 healthy controls and 6 SSc patients. Biopsies was subjected to histology analysis, including haematoxylin and eosin (H&E) and masson trichrome (MT) staining and immunohistological staining (IHC) for CD45, pSTAT1 and MX1. In addition, 7 VEDOSS skin biopsies, along with 2 healthy control and 3 SSc, were used to explant fibroblasts cell lines. mRNA and protein were isolated from primary fibroblasts and processed for RT-qPCR and western blotting analyses and collagen gel contractability assessed.

Results: Sera from VEDOSS patients showed significantly higher IFN-inducible chemokines compared to HC and an intermediate levels compared to SSc [Mean (STDV) HC= 4.69(0.29) vs. VEDOSS= 4.93 (0.39); SSc= 5.30 (0.54)]. ELF score was within normal range for most patients with VEDOSS and showed no statistical difference to HC. Skin biopsies from VEDOSS patients showed evidence of fibrosis and increased collagen bundles within the dermis evidenced in H&E and MT staining, as usually seen in SSc, compared to HC. IHC showed increased number of CD45+ cells in VEDOSS. Semiquantitative analysis of histopathological samples indicated a significant correlation between MT and CD45 staining for VEDOSS (R=0.8828 P=0.0016). In vitro, fibroblasts from VEDOSS patients showed an average 5-fold higher collagen mRNA levels compared to HC fibroblasts, at a similar range to that seen in SSc fibroblasts, confirmed at protein level via western blotting. Furthermore, VEDOSS fibroblasts induced greater gel contraction compared to HC.

Conclusion: Although pilot in nature, this study suggests that patients with no clinical signs of skin fibrosis in their forearms already show biomarker signs of SSc both in their sera, skin biopsies and fibroblast level. Our data indicate that skin thickening is a late manifestation of SSc pathogenesis and early window of opportunity of patients with VEDOSS could be targeted for immune intervention and antifibrotic intervention.

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Acknowledgements: NIL.

Disclosure of Interests: Rebecca Ross: None declared, Emily Clarke: None declared, Will Merchant: None declared, Begoña Caballero-Ruiz: None declared, Ioanna Georgiou: None declared, Antonio Carriero: None declared, Giuseppina Abignano: None declared, Ariane Herrick Consultant of: ALH has undertaken consultancy work for Boehringer-Ingelheim, Gesynta, Camurus and CSL Behring, has received research funding from Actelion and Gesynta, and has received speaker's fees from Actelion., Grant/research support from: ALH has undertaken consultancy work for Boehringer-Ingelheim, Gesynta, Camurus and CSL Behring, has received research funding from Actelion and Gesynta, and has received speaker's fees from Actelion., Christopher P Denton Consultant of: Chris Denton, PhD, FRCP has served as an advisor or consultant for: Actelion Pharmaceuticals, Biogen Idec, CSL Behring, GSK, Inventiva, MedImmune Inc., Merck, Roche, and Takeda and has served as a speaker or a member of a speakers bureau for Actelion Pharmaceuticals, CSL Behring, GSK, and Novartis Pharmaceuticals., Natalia Riobo-Del Galdo: None declared, Francesco Del Galdo Consultant of: F.D.G. has received research funding and/or consulting fees or other remuneration from GlaxoSmithKline, AstraZeneca, Boehringer Ingelheim, Actelion, Capella Bioscience, Chemomab, Kymab, Actelion, iqvia, and Mitsubishi Tanabe, Grant/research support from: F.D.G. has received research funding and/or consulting fees or other remuneration from GlaxoSmithKline, AstraZeneca, Boehringer Ingelheim, Actelion, Capella Bioscience, Chemomab, Kymab, Actelion, iqvia, and Mitsubishi Tanabe.

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POS0147 αVβ3 INTEGRIN AS A LINKER BETWEEN FIBROSIS AND THYROID HORMONES CROSSTALK

Keywords: Cell biology

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by tissue fibrosis of the skin and internal organs. Key players in SSc are myofibroblast cells (MF) that produce large amounts of extracellular matrix (ECM), which facilitates fibrosis. TGFβ is a key factor involved in MF differentiation and collagen-rich ECM (fibrotic-ECM) secretion. Most of the TGFβ is bound to the ECM through latency-associated peptide (LAP) that contains the amino acid sequence arginine-glycine-asparagine (RGD motif). In order to be active, TGFβ must be released from the ECM by proteases like MMP9 or αv integrins that bind LAP through their RGD recognition site. MF express high levels of the integrin αvβ3. Interestingly, αvβ3 is a special integrin since it also serves as a membrane thyroid hormone (TH) receptor that binds T3 and especially T4. The TH binding sites are located proximal to the RGD binding site. MF also express high levels of the pro-fibrotic miRNA-21, which regulates the TGFβ pathway and the level of DIO3 enzyme, which degrades T3. T3 attenuates fibrotic processes. Since high levels of αvβ3 integrin are expressed by MF in the fibrotic sites and the TH binding site of αvβ3 is close to the RGD recognition site, we hypothesized that the TH binding site of αvβ3 is involved in mediating the fibrotic process.

Objectives: 1. To examine the effect of fibrotic-ECM produced by dermal fibroblasts (DF) triggered by TGFβ, on naive DF phenotype and their αvβ3 expression; 2. To examine the connection between the thyroid hormone binding site of αvβ3 integrin to fibrosis-related processes.

Methods: DF were isolated from healthy skin, cultured without/with TGFβ, and removed by NH_4OH, leaving the normal/ fibrotic ECMs in the wells. ECMs were evaluated for collagen-I and TGFβ levels (Immunohistochemistry, western blot). The effect of the normal/fibrotic ECMs on the following parameters of naïve DF was evaluated: phenotype; expression of MF biomarkers (collagen, elastin and αSMA), expression of αvβ3 integrin, miRNA-21, and DIO3 enzyme; activation of the TGFβ pathway (Smad3 phosphorylation); and MMP9 activity (automatic cell counter, western-blot, RT-qPCR, gelatin zymography). Moreover, the effect of tetraiodothyroacetic acid (tetrac, T4 derivative, and αvβ3 ligand) on the fibrotic-ECM ability to induce DF differentiation into MF and to express αvβ3, miRNA-21 and DIO3 was studied. Last, free T3 levels were measured in 18 SSc patients

of whom 7 had pulmonary arterial hypertension (PAH). The patients were divided according to high (n=6)/low (n=12) T3 levels into 2 groups and the difference in circulating miRNA-21 levels between the groups was evaluated.
Results: Fibrotic-ECMs generated by TGFβ-triggered DF had higher levels of collagen-I and TGFβ in comparison to normal ECM. In comparison to the normal ECM, the fibrotic-ECM increased the followings in the DF: 1) ability to liberate TGFβ from the ECM by increasing MMP-9 activity and αv expression. 2) TGFβ activation and differentiation to MF evidenced by increased expression of phosphorylated Smad3, αSMA, collagen, and elastin, and increased proliferation. 3) Expression of αvβ3, miRNA-21 and DIO3 (all changes in 1-3: 24-123%↑, p≤0.05). The addition of tetrac to DF cultured on fibrotic-ECM downregulated cell proliferation, collagen, elastin and aSMA expression to the levels found in DF cultured on normal ECM. Furthermore, it reduced αvβ3, miRNA-21, and DIO3 levels. Accordingly, decreased miRNA-21 levels were found in the high T3 SSc group, compared to the low T3 group that contained all the PAH patients (p≤0.05).
Conclusion: Our results demonstrated the existence of a vicious cycle: TGF-triggered DF produced a fibrotic-ECM that promoted bystanders' DF differentiation to MF. Using this model, we demonstrated that tetrac binding to αvβ3 integrin inhibited the differentiation of DF to MF, and their ability to activate the αvβ3/miRNA-21/DIO3/T3 pathway. These results suggest that the thyroid hormone binding site of αvβ3 may be a potential target for the treatment of fibrosis.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0148 STIFFNESS INDUCED PROGRESSION OF FIBROSIS BY SORBIN AND SH3 DOMAIN-CONTAINING PROTEIN2 IN SYSTEMIC SCLEROSIS

Keywords: -omics, Systemic sclerosis, Skin

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Background: Persistently activated fibroblasts status leads to progressive extracellular matrix (ECM) deposition and tissue remodeling. The hallmark of systemic sclerosis (SSc) is collagen accumulation in organs, mainly in skin and lung. Despite intensive progress in understanding disease occurence, SSc remains an intriguing disease with unknown pathology and high mortality. Sorbin and SH3 domain-containing protein2, encoded by SORBS2 is a key member of the sorbin homology family of adapter and scaffold proteins. Recent studies suggest that SORBS2 plays a role in cardiac disease, however there is no available data about its role in fibrotic conditions.
Objectives: We aimed to investigate the role of SORBS2 in the pathogenesis of SSc.
Methods: To identify molecules specifically upregulated in persistently activated fibroblasts, human fibroblasts were chronically stimulated with TGF-β and analyzed by RNA-sequencing. To evaluate the functional implication of tissue elasticity on the transcriptome of fibroblasts, multiwell stiffness assays were performed. SORBS2 expression was further analyzed in skin samples of patients with SSc and murine models of fibrosis. Fibroblast specific SORBS2 knockout mice were challenged with bleomycin to induce skin and lung fibrosis. Further specific readouts like collagen content, skin thickness, myofibroblast count, CT scans were performed.
Results: Upon chronic TGF-β stimulation of human normal skin fibroblasts we identified SORBS2, as significantly upregulated molecule. SORBS2 is implicated in cytoskeletal organization, cell adhesion and different signaling pathways. Moreover, extracellular stiffness induced upregulation of SORBS2 mRNA level in fibroblasts. Deletion of SORBS2 in fibroblasts led to a change of the diameter of collagen fibers and modified the elastic index of the tissue. SORBS2 expression is not only elevated in different animal models of fibrosis, but also in fibrotic skin samples of SSc patients. SORBS2 knockout mice (KO) developed significantly less skin fibrosis upon bleomycin challenge in comparison to wild type mice (WT), as assessed by measurement of dermal thickness, myofibroblast counts and hydroxyproline content. *Col1a1*, *Col1a2* and expression of *αSMA* were significantly lower in SORBS2 KO mice in comparison to SORBS2 WT mice. Similarly, fibroblast specific knockout of SORBS2 showed protective effects in bleomycin induced lung fibrosis. CT scans of the lungs showed statistically significant less fibrotic changes in SORBS2 KO mice in comparison to wild type mice.
Conclusion: SORBS2 is engaged in a vicious circle of fibrosis. Triggered by chronic TGF-β stimulation, SORBS2 is further upregulated by the increasing stiffness of the extracellular matrix. This leads to persistently high levels of SORBS2 resulting into further production of ECM products. Deleting SORBS2 has potent antifibrotic effects in animal models of skin and lung fibrosis. As most of the currently used therapeutic approaches are focussed on early stages of the disease, SORBS2 might be an interesting new therapeutic target in established stages of SSc.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0149 WITHDRAWN

POS0150 AUTOANTIBODIES AGAINST FIBROBLAST GROWTH FACTOR (FGF-2), PLACENTAL GROWTH FACTOR (PLGF) AND BETA-ADRENERGIC RECEPTOR 1 (ADRB1) IN AN ALTERED NETWORK OF AUTOANTIBODIES IN SYSTEMIC SCLEROSIS

Keywords: Biomarkers, Systemic sclerosis, Autoantibodies

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Background: Autoantibodies (ab) against G protein-coupled receptors (GPCR), such as ab against angiotensin II receptor type 1 (AT1R), endothelin receptor type A (ETAR) or CXC chemokine receptor 3 and 4 (CXCR3/4) may contribute to the pathogenesis of systemic sclerosis (SSc) [1]. AT1R- and ETAR-ab are associated with SSc-related mortality and CXCR3/4- ab predict a deteriorating pulmonary fibrosis [2,3].
Objectives: We aim to identify new ab targets and ab discriminating healthy controls (HC) from SSc patients or SSc clinical phenotypes, organ involvements and therapy.
Methods: Serum ab levels against a panel of GPCR, GF and GFR were measured by ELISA in SSc (n=177) and compared to HC (n=88). Gender matched and age adjusted data were screened for univariate differences of ab levels in clinical phenotypes, explored for multivariate predictive performance of ab levels by a random-forest classifier and tested for differences of ab correlations.
Results: In SSc ab levels against 19 targets were higher compared to HC. Abs against fibroblast growth factor-2 (FGF-2), beta-adrenergic receptor 1 (ADRB1), and placental growth factor (PIGF) discriminated best SSc patients from HC. Multivariate predictions supported the ranking value of FGF-2 and ADRB1-abs for SSc and abs against ADRB1/2, muscarinic receptor 1 (M1R) and alpha-adrenergic receptor 2 ADRA2 for diffuse cutaneous SSc (dSSc) versus limited cutaneous SSc (lSSc). Ab levels were denser and stronger correlated in SSc than in HC (figure 1), suggesting a disturbed regulation of ab with a prominent role of FGF-2-abs in SSc. Comparing dSSc to lSSc, dSSc showed higher ab levels and correlated with several disease characteristics, but the multivariate classification showed poor accuracy.

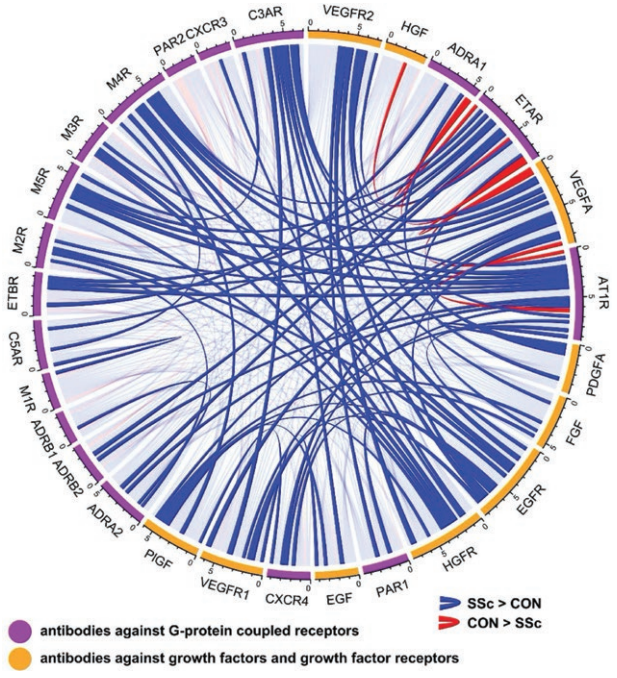


Figure 1. Different univariate correlations between abs in HC and SSc. The correlations of the ab concentrations are generally increased in SSc compared to HC. Largest accumulated differences are found for ETAR, VEGFA, AT1R and EGFR as indicated by the covered degrees in the circle. Dark bands depict significant differences after FDR-correction (p <.05)

Conclusion: SSc is characterized by both quantitative and qualitative alterations in ab levels and ab correlations. This study reveals ab against FGF-2, ADRB1 and PIGF to be new biomarkers of SSc. Alterations within these ab correlation networks could help to identify pathways promoting SSc and its clinical manifestations.

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POS0151

SINGLE-CELL RNA SEQUENCING OF BRONCHOALVEOLAR LAVAGE FLUID AND BLOOD REVEALS DISEASE-SPECIFIC CHARACTERISTICS OF IMMUNE CELLS IN CONNECTIVE TISSUE DISEASE-ASSOCIATED INTERSTITIAL LUNG DISEASE PATIENTS

Keywords: Lungs, Genetics/Epigenetics

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Background: Connective tissue disease-associated interstitial lung disease (CTD-ILD) is a serious complication and an important prognostic factor of various autoimmune diseases. Many cell types and both innate and adaptive immune systems are implicated in the pathogenesis of fibrotic lung injury. The presentation and clinical course of CTD-ILD are diverse, and the heterogeneity reflects differences in underlying pathogenic mechanisms.
Objectives: The objective of this study is to reveal the different characteristics of immune cells among diseases.
Methods: We collected bronchoalveolar lavage fluid (BALF) and peripheral blood from patients who newly complicated interstitial lung disease and agreed to participate in this study; 5 patients with Sjögren syndrome (SS), 8 patients with dermatomyositis (DM), 6 patients with rheumatoid arthritis (RA), 7 patients with systemic sclerosis (SSc), 4 patients with ANCA-associated vasculitis (AAV), and 12 patients with idiopathic interstitial pneumonia (IIP) included. We applied Seq-Well, a portable platform of single-cell RNA sequencing[1], to analyze gene expressions in immune cells in BALF and blood. We compared the distribution of immune cells and differential gene expressions in BALF and blood among diseases.
Results: We compared immune cell numbers in BALF among diseases. We found more T cells in patients with DM and SS, more B cells in patients with SS, more neutrophils in patients with RA, and more alveolar macrophages (AMs) in patients with AAV or SSc. We further performed gene ontology enrichment analysis of each immune cells in BALF. In patients with DM, the gene expression pathways related to the response to virus was increased in T cells. On the other hand, in patients with SS, the gene expression pathways involved in innate immunity and antigen presentation were enhanced in B cells. In addition, the gene expression associated with T cell activation was enhanced in T cells. In neutrophils from patients with RA, the gene expression involved in inflammation was increased. We next performed gene ontology enrichment analysis of blood. In monocytes and neutrophils, patients with DM had increased gene expression pathways associated with viruses, while patients with SS had increased gene expression of both innate immune pathways and acquired immunity. These results suggested that the common pathways were enhanced in BALF lymphocytes and in blood monocytes and neutrophils in patients with DM and SS.
Conclusion: Our comprehensive single-cell analysis of BALF and blood from CTD-ILD patients has revealed that the phenotypes and states of immune cells differ among diseases (Figure 1). We found that the common pathways were enhanced in BALF and blood, i.e., pathways associated with response to virus were enhanced in DM while innate immunity and antigen presentation pathways were enhanced in SS, suggesting the relationship between systemic immune abnormality and ILD. These results may lead to the optimal diagnosis and the precision medicine for patients with CTD-ILDs.

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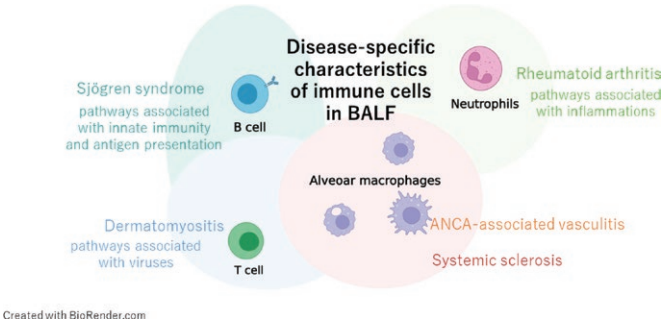


Figure 1.

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POS0152

PLATELET EXTRACELLULAR VESICLES MODULATE NEUTROPHIL STATE IN SYSTEMIC SCLEROSIS VIA HMGB1

Keywords: Lungs, Innate immunity, Systemic sclerosis

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Background: Platelet extracellular vesicles (Plt-EVs) expressing the damage-associated molecular pattern prototypic signal, high mobility group box 1 (HMGB1), accumulate in the blood of patients with systemic sclerosis (SSc) and per se promote autoimmunity, fibrosis and vascular inflammation [1, 2]. A poorly understood defect in critical players in sprouting angiogenesis, angiopoietins and the angiopoietin receptor, TIE2 is also an hallmark of SSc. Normal neutrophils respond to angiopoietin 1 and other stimuli by undergoing activation and upregulating the Tie2 expression [3].

Objectives: We reasoned that HMGB1 could be a putative candidate signal supporting neutrophils Tie2 overexpression, as it plays a critical role in neutrophil activation and is present as an EV-associated bioactive molecule in the blood of SSc patients[1, 2].

Methods: Neutrophil Tie2 expression was assessed in the blood of 39 patients with SSc and 43 healthy donors (HD) sex- aged matched, by flow cytometry and confirmed by immunogold at electron microscopy. Tie2 expression was determined in freshly purified normal neutrophils stimulated with Plt-EVs from SSc patients or from HD or stimulated with rHMGB1 in vitro. Moreover Plt-EVs purified from the plasma of SSc patients or from HD were injected in the tail vein of NSG mice (that are receptive to human tissues). 18 hours after injection the expression of Tie2 of neutrophils in blood and lung histology were analyzed. Box A and low molecular weight heparin (LMWH) have been used as HMGB1 antagonists in vitro and in vivo.

Results: Most SSc neutrophils express Tie2 (84.7±2.4% vs 8.3±1.1% in HD; p <0.0001) regardless of the extent of systemic inflammation. HMGB1 and Plt-EV expressing HMGB1 purified from the plasma of patients with SSc induced up-regulation of TIE2 *in vitro*. Tie2 induction was abrogated by Box A and LMWH. Plt-EVs from SSc patients (but not from the plasma of HD) injected in immune-deficient NSG mice dramatically upregulated Tie2 neutrophil expression. Neutrophil Tie2 upregulation abated in the presence of HMGB1 inhibitors, BoxA and LMWH. Immunohistochemitry revealed lung fibrosis associated with massive infiltration by Tie2+ neutrophils. Neutrophil ablation by liposome-encapsulated clodronate prevented SSc Plt-EV-induced lung fibrosis, thus causally linking neutrophil activation, Tie2 neutrophil-expressing pulmonary infiltration and tissue remodelling.

Conclusion: Our data highlight the role of the platelet HMGB1/neutrophil axis in SSc vascular inflammation and fibrosis.

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Disclosure of Interests: None Declared.

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New developments in imaging in rheumatology

POS0153 MACROPHAGE [11C]-DPA-713 PET-CT IMAGING TO PREDICT EARLY ANTI-TNF TREATMENT OUTCOME IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Imaging, Qualitative research methods

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Background: Treatment of rheumatoid arthritis (RA) using anti-tumor necrosis factor (TNF) biologics has greatly benefited patients since their introduction, with an expected treatment response rate of up to 50-70% [1]. This however, leaves 30-50% of patients taking ineffective medication whilst being exposed to the potential side-effects of anti-TNF. Current patient care requires clinical evaluation of 3 to 6 months before effectiveness can reliably be assessed. Quantitative macrophage positron emission tomography (PET) has shown potential to predict clinical response at an early stage of treatment [2]. The new generation translocator protein (TSPO) tracer [11C]-DPA-713 has demonstrated excellent properties for imaging of arthritis by targeting synovial macrophages [2, 3].
Objectives: To determine whether quantitative whole body [11C]-DPA-713 PET/CT imaging at 0-4 weeks of anti-TNF treatment in clinically active RA patients is associated with clinical response at 26 weeks.
Methods: Whole body [11C]-DPA-713 PET/CT scans were performed at baseline and after 4 weeks of treatment with anti-TNF in n=20 clinically active RA patients. All patients were either anti-TNF naïve or switched to an anti-TNF agent without previous primary failure to anti-TNF. Co-treatment with DMARD and/or low dose (≤ 10 mg dd) was allowed and was stable for at least 4 weeks. Clinical follow-up was conducted with the Disease Activity Score 44 (DAS44) after 26 weeks of treatment. PET/CT scans were quantitatively analyzed using in-house software. Regions of interest (ROIs) were delineated on PET/CT per individual joint in all joints evaluated using the DAS44 and CT as anatomical reference. Standardized uptake values (SUVs) normalized for body weight were calculated in these ROIs to determine quantitative tracer uptake per joint. PET outcome at baseline and 4 weeks of anti-TNF treatment was compared with the DAS44 scores at 26 weeks of treatment.
Results: Included patients were mostly female (70%) and aged 61.5 ± 12.8. Baseline DAS44 was 2,5 ± 1 and all demonstrated visually enhanced tracer uptake in one or more joints on PET/CT. After 26 weeks 30% showed no response, 20% moderate response and 50% good response to treatment according to EULAR response criteria. Baseline mean PET/CT scores of all joints per patient already correlated significantly with DAS44 at 26 weeks (T=0, R^2 = 0.547, p = <0,001). In smaller joint clusters the highest correlation was found for the metacarpal-phalangeal joints (T=0, R^2 = 0.650, p = <0.001). Furthermore, PET/CT outcomes at 4 weeks of anti-TNF treatment also had significant correlation with DAS44 at 26 weeks for those same measurements: mean score of all joints: T=4, R^2 = 0,530, p = <0,001, mean score MCPs: T=4, R^2 = 0.728, p = <0,001.

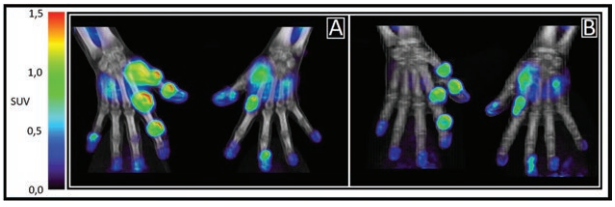


Figure 1. Changes in [11C]-DPA713 uptake in MCP joints of an RA patient responding to anti-TNF treatment, before (A) and after 4 weeks after initiation of anti-TNF treatment (B).

Conclusion: Quantitative whole body macrophage C-11-DPA713 PET/CT joint assessment correlated already at baseline, and also at 4 weeks of anti-TNF treatment with clinical response at 6 months of treatment. Therefore, quantitative non-invasive macrophage PET/CT shows promise for very early prediction and treatment stratification of anti-TNF in RA patients. Further studies will be focused on development of standardized and (semi-)automated PET quantification protocols to facilitate implementation in clinical trials and practice.
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POS0154 A DEEP LEARNING MODEL TO LOCATE INFLAMMATORY CHANGES IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Artificial Intelligence, Imaging

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Background: Magnetic Resonance Imaging (MRI) is one of the most sensitive imaging modalities to monitor affected joints and detect inflammatory signs related to Rheumatoid Arthritis (RA). Finding and tracking inflamed areas can help to evaluate patients status, and start treatment in a very early stage. The RAMRIS [1] scoring system is being used to assess the extent of inflammation by scoring specific areas to quantify synovitis, tenosynovitis and bone marrow edema. Deep Learning (DL) may, however, provide more accurate and specific quantifications.
Objectives: We aimed to develop a change map that locates RA progression over time, using MRI scans of the wrist. Our purpose was to develop an automatic, hypothesis-free DL model that considers the entire MRI for detecting all possible longitudinal changes related to RA between baseline and follow-up wrist MRIs.
Methods: Wrist contrast-enhanced T1-weighted fat-suppressed MRI scans of 236 patients from four time points (baseline, with 4, 12, and 24 months follow-up) were collected [1]. An unsupervised DL model was developed together with image processing techniques to detect a pixel-level progression within wrist MRI scans between baseline and the last follow-up MRIs. This model predicts the MRI appearance of the follow-up scan, based on the baseline scan, by learning from MRI time sequences of all patients in the training set. Similarly, the baseline scan was predicted backwards in time, based on the follow-up scan (see Figure 1). Subsequently, by comparing the predicted and true MRI image, pixel-level changes can be determined between the two MRI scans. For prediction, we used a U-Net [2] to reconstruct follow-up images from baseline and vice versa. After pre-training, two copies of the trained model and a joint loss function were used for final training (a dual branch U-Net); the first branch is trained to generate a follow-up image and the second branch to create a baseline image. After final training, two difference maps were obtained by subtracting the baseline image from the predicted follow-up image and by subtracting the follow-up image from the predicted baseline image. Since real changes appear in pixels with positive values, Otsu thresholding was applied only on the positive differences to generate two change maps, where the first change map shows intensity reduction (areas of remission) and the second indicates increased intensity (areas of progression). With fusion of the obtained change maps we obtained the final change map that can highlight the changes in both directions.
Results: As can be seen from Figure 1, the proposed model could find local pixel-level changes, highlighting RA remission/progression over time. The red overlay shows a reduction in intensity, the blue overlay indicate an increase in intensity. To show the performance of the proposed model, the results were compared with a baseline model, that simply subtracts the original follow-up from the baseline image. As can be seen from the provided examples, the proposed model is less sensitive to imaging artifacts.
Conclusion: A comparative DL-model is proposed to find inflammatory changes in wrist MRI scans. Despite being an unsupervised model (sometimes detecting changes, in e.g. vessels, that are presumed to be unrelated to RA), the results are promising, since the change maps contain less artifacts as compared to simple image subtraction.
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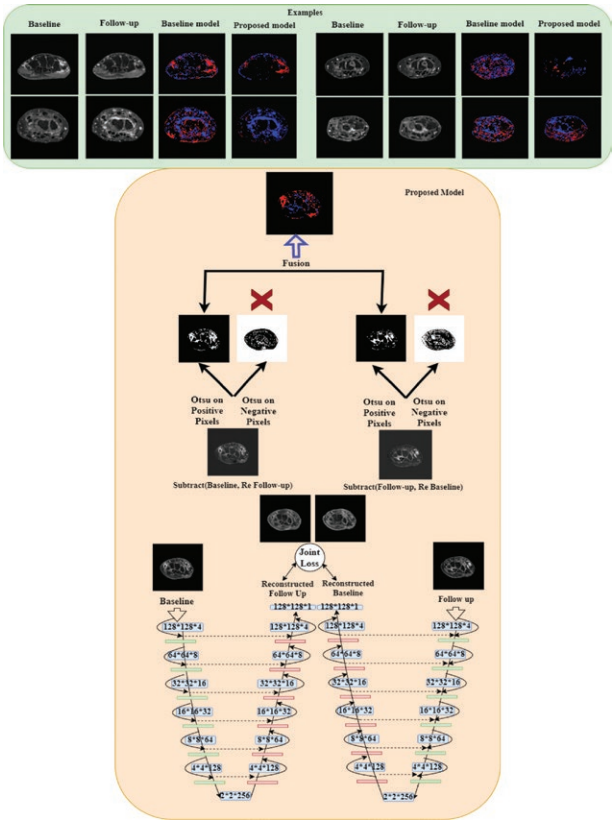


Figure 1. Overview of the proposed model and examples of obtained change maps.

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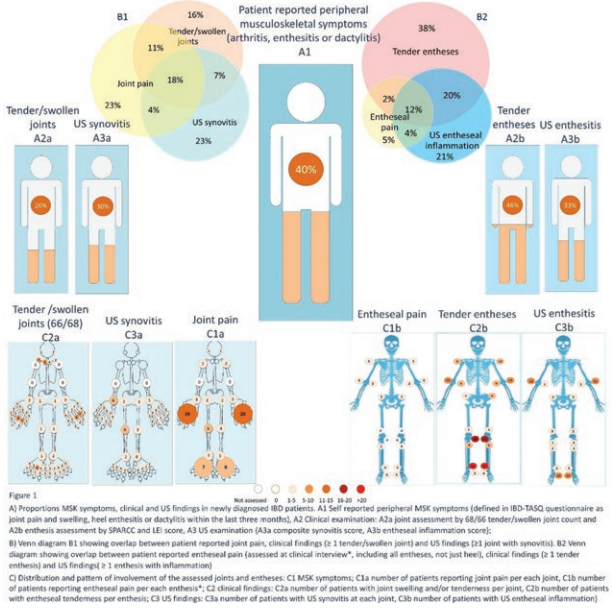
POS0155

PERIPHERAL JOINT AND ENTHESIS INVOLVEMENT IN NEWLY DIAGNOSED PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD): SYMPTOMS, CLINICAL AND ULTRASONOGRAPHIC FINDINGS

Keywords: Gastrointestinal tract, Spondyloarthritis, Imaging

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Background: Peripheral musculoskeletal (MSK) symptoms are the most common extra intestinal manifestations (EIMs) in IBD patients, with substantial impact on quality of life. IBD related spondyloarthritis (IBD-SpA) often requires a multidisciplinary evaluation to enable optimal choice of treatment and patient care, but systematic rheumatological characterisation of this population is scarce [1]. Characterisation of IBD-SpA is challenged by the variety of MSK involvement (from arthralgia to ankylosing spondylitis), the co-existence of osteoarthritis, overuse enthesopathies or fibromyalgia, and by the heterogeneity in methodologies used to describe the SpA features. Recently developed recommendations for endpoints for EIMs in IBD trials [2] were applied in the present study.
Objectives: To determine the prevalence and distribution of inflammatory lesions in peripheral joints and entheses in newly diagnosed IBD patients, assessed for presence of MSK symptoms, and by rheumatological and ultrasound (US) evaluation.
Methods: Patients from the IBD prognosis inception cohort (IBD-Pro) were consecutively included [2]. They reported MSK symptoms using a validated questionnaire (IBD-TASQ). A clinical examination was performed by rheumatologist, as was US examination (grey scale (GS) and colour Doppler (CD)) of 38 peripheral joints and 14 entheses, applying OMERACT-EULAR definitions and scoring systems for synovitis and enthesitis [3]. Synovitis was defined as GS score ≥2 and/or CD≥1 and entheseal inflammation was defined as presence of hypoechogenicity/thickening and/or CD score ≥1. Further, OMERACT-EULAR sum score (GLOESS) was calculated (0-114).
Results: 110 newly diagnosed IBD patients (mean age 42, 39% male) were included (34% Crohn's disease, 59% ulcerative colitis (UC), 5% unclassified IBD). The IBD disease activity scores indicated mild activity in UC patients (Simple Clinical Colitis Activity Index mean (SD) 6.7 (3.6) - max score 19, and low in Crohn (Harvey-Bradshaw Index for Chron's disease 4.5 (2.9)- max score 18). Four patients received systemic glucocorticoids (2%) or biologics (2%) at the time of rheumatological evaluation. History of psoriasis was reported in 2% and uveitis in 5% of the patients. 40% of the patients reported positive history for ≥1 MSK symptom (Figure 1, A1); joint pain and swelling were the most common complaints (30%), followed by heel enthesitis (17%) and dactylitis in 20%. Patient pain VAS was low, mean (SD) 13(25). Clinical examination revealed 53% of all patients having arthritis and/or enthesitis and fulfilled ASAS classification criteria for peripheral SpA (25% ≥1 tender joint, 12% ≥1 swollen joint, 46% ≥1 tender enthesis, 38% both ≥1 tender/swollen joint and ≥1 tender enthesis). Figure 1 (part A2a, A2b) shows joint and enthesis involvement. US found inflammation in ≥1 joint or enthesis in 47% of the IBD patients - synovitis in 30%, mean GLOESS sum score 5.2 SD (4.6) and entheseal inflammation in 33% (US enthesitis sum, mean (SD) 2.6(2). (Figure 1, part A3a, A3b). Among those patients reporting entheseal pain, 71% had ≥1 tender enthesis at clinical evaluation and 64% had entheseal inflammation by US. Among those reporting joint pain, 55% had ≥1 tender or swollen joint, and



41% US synovitis. Figure 1 (part B1, B2) displays the overlap between patient-reported symptoms, clinical and US findings. In the asymptomatic patients (60 %) 59% of the patients with clinical signs of arthritis and 79% of those with enthesitis were asymptomatic. US enthesitis and synovitis were also observed in 69% and 58%, respectively, of the asymptomatic patients.

Conclusion: At the time of IBD diagnosis 53% fulfilled ASAS classification criteria for peripheral SpA and 47% had objectively verified synovitis and/or enthesitis by US indicating that SpA may be underdiagnosed among IBD patients.

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POS0156

BONE DENSITY, MICROSTRUCTURE AND BIOMECHANICS OVER A 7-YEAR OBSERVATION PERIOD IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS - INFLUENCE OF AUTOIMMUNITY, DISEASE ACTIVITY AND BIOLOGICAL DMARD TREATMENT

Keywords: Inflammatory arthritides, Disease-modifying Drugs (DMARDs), Imaging

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Background: Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) are characterized by a deterioration of bone mass, bone microstructure and biomechanics [1, 2]. However, little evidence is available on the long-term evolution of these bone properties and the impact of autoimmunity, disease activity and targeted anti-inflammatory therapy.

Objectives: To evaluate the longitudinal course of peripheral volumetric bone mineral density (vBMD), microstructure and biomechanics in patients with seropositive RA (RA+), seronegative RA (RA-) and PsA (i) by diagnosis (ii) disease activity and (iii) ever use of biologic/targeted synthetic (b/ts) DMARDs.

Methods: RA+, RA-, PsA patients who had at least one high-resolution CT scan were included. Prospectively collected longitudinal data from the distal radius. vBMD, microstructure and biomechanical properties were assessed and data on treatments and disease activity (DAS-28) were collected. We described and summarized the time course of these measurements, using linear regression models as age and sex adjusted time-conditional means and mean differences by disease category, time-varying weighted average disease activity and intervening b/tsDMARD treatments.

Results: We analyzed 946 scans from 412 patients (193 RA+, 68 RA-, 151 PsA) with a median CT follow-up duration of 24 months (IQR 0 to 47). (Table 1). Overall, bone quality showed a downward course over time. RA+ patients showed lower total and trabecular bone densities compared to patients with psoriatic arthritis throughout the time course. (Figure 1a). RA+ patients also showed decreasing trabecular number with increasing trabecular thickness, trabecular irregularity and trabecular separation over time in comparison to PsA (Figure 1 b) suggesting a gradual disappearance of the thinner trabeculae. We detected significant time/DAS-28 interactions in PSA patients indicating faster cortical bone loss over time with increasing DAS-28 (p interaction =0.049), in RA- patients showing faster trabecular bone loss over time with higher disease activity (p.interaction 0.044) and in RA+ patients for trabecular density (p interaction 0.038), bone stiffness (p interaction 0.022) and failure load (p interaction 0.034) indicating a faster deterioration of bone quality over time with increasing disease activity. Interestingly, RA+ patients exposed to b/tsDMARDs had numerically lower bone density compared to unexposed patients, whereas the temporal pattern suggested a more stable vBMD over time as opposed to a deteriorating pattern in the unexposed. However, the uncertainty in these analyses was large and none of the time-exposure interactions or pairwise differences over time between ever vs. never exposed categories were significant.

Conclusion: Autoimmunity impairs bone health over time and is particularly associated with impaired trabecular bone quality. Good control of disease activity in RA+, RA-, and PsA patients may be helpful in preventing bone loss and deterioration of bone microstructure, and biomechanics. Specific contribution of b/tsDMARDs to the time course of bone quality at the radius needs further clarification.

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Table 1. Patient characteristics

	Diagnosis		
	PsA	RA seronegative	RA seropositive
N	151	68	193
Age, years, mean (SD)	51.7 (12.2)	58.8 (12.2)	53.9 (12.5)
Females, n(%)	72 (47.7)	49 (72.1)	131 (67.9)
Disease duration, years median (IQR)	3.0 (1.0-10.0)	3.0 (1.0-8.0)	5.0 (0.0-13.0)
Follow-up duration, months, median (IQR)	24.7 (0.0-48.0)	16.4 (0.0-42.7)	25.2 (0.0-47.9)
No of scans, n (%)			
1	48 (31.8)	21 (30.9)	50 (25.9)
2	56 (37.1)	29 (42.6)	56 (29.0)
3	31 (20.5)	12 (17.6)	49 (25.4)
>4	16 (10.6)	6 (8.8)	38 (19.7)
Glucocorticoid use, n (%)	57 (37.7)	52 (76.5)	149 (77.2)
csDMARDs use, n (%)	24 (15.9)	25 (36.8)	59 (30.6)
b/tsDMARDs use, n (%)	127 (84.1)	43 (63.2)	134 (69.4)

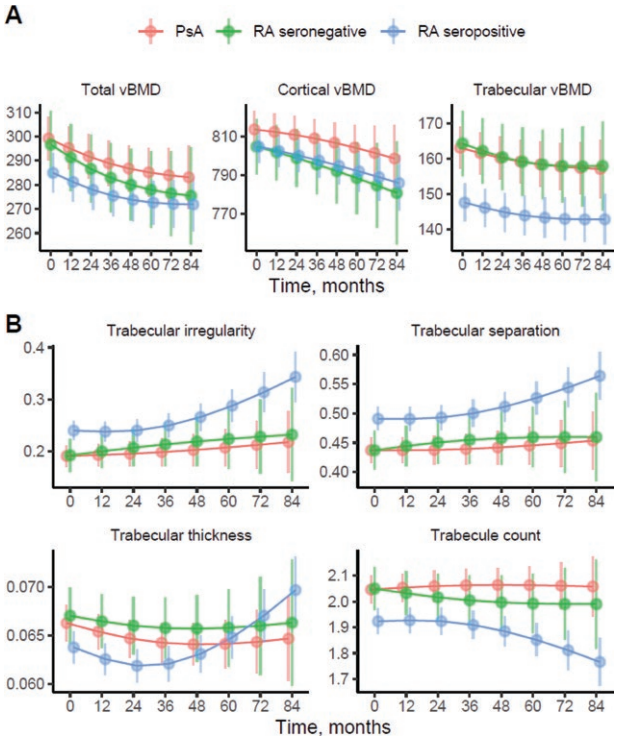


Figure 1. Time course of bone density (A) and microstructure (B) in patients with PsA and RA.

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Disclosure of Interests: None Declared.
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POS0157 POST-STRESS ELASTOGRAPHIC DIFFERENCES AT ACHILLES ENTHESIS AS AN OUTCOME MEASURE IN THE ASSESMENT OF PATIENTS WITH PSORIATIC ARTHRITIS IN REMISSION

Keywords: Psoriatic arthritis, Physical therapy/Physiotherapy, Ultrasound

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Background: Tendon elastography has demonstrated the ability to discriminate between healthy subjects and patients with spondyloarthritis. Its greatest strength is its ability to reliably quantify the stiffness of a soft structure. However, its use in anatomical load-bearing entheses has not been sufficiently explored. The use of quantifiable enthesis assessment methods would open up multiple possibilities in both the diagnosis and follow-up of inflammatory enthesis diseases.
Objectives: To evaluate the response to mechanical stress through elastography in the enthesis of the Achilles tendon among patients with psoriatic arthritis (PsA) in remission treated with anti-IL17 therapies, with other non-anti-IL17 therapies, and healthy controls.
Methods: Observational, multicenter, non-blind study. The elastography results before and after physical exercise of patients with PsA in remission treated with therapies aIL17, therapies other than aIL17 (non-aIL17) were compared with those of healthy subjects matched by age (+/- 4 years), sex, and body fat percentage (BFP) (+/- 4%). Elastography was performed with a GE Logic S8 sonograph with a linear 6MHz probe. The region of interest (ROI) was the Achilles' enthesis identified distal to the vertex of the pre-Achilles bursa choosing the greatest thickness in the longitudinal plane. Each assessment was the result of the average of five consecutive determinations. Body composition was determined using an OMROM Healthcare model BF511 impedance meter. Physical exercise performed on a SALTER activeHealth PT-0083 magnetic bike, at an intensity of +80% and up to 300Kcal. A before and after analysis was performed using the T-Student's test for interdependent samples. The main outcome variable was the variability of the Achilles enthesis stiffness after physical exertion.
Results: The elastographic results of 14 patients on aIL17 therapies, 15 on non-aIL17 therapies, and 28 healthy controls were compared. The demographic and constitutional distribution was homogeneous in the three groups (p=0.221 for age, p=0.983 for BFP). The Achilles enthesis height ± standard deviation (mm) in controls was 4.27 ± 0.45 in controls, 4.78 ± 0.56 in non-aIL17 patients, and 4.66 ± 0.47 in aIL17 patients (p=.005 in controls vs. non-aIL17). Baseline, enthesis rigidity in the controls, aIL17 and non-aIL17 group was 210.2±21.9, 183.7±7 and 201.17±6.1 Kpa, respectively (p<.001 in controls vs. non-aIL17, p=.016 in non-aIL17). aIL17 vs. aIL17). After exercising, the same measurements were 227.5±21.2, 195.3±8.3, and 219.1±9.1 Kpa (p<.001 in control vs. non-aIL17, p<.001 in non-aIL17 and aIL17). The change experienced in the stiffness after the effort given between the three groups determined a mean change of 17.3±29.5 Kpa (t=3.113, p=.004) in the controls, of 5.1±3 Kpa (t=6.52, p<.001) in the non-aIL17 group and 17.9±6.5 Kpa (t=10.303, p<.001) in the aIL-17 group. The increases in stiffness with exercise were comparable between controls and the aIL-17 group (p=.919), and both were significantly higher than the non-aIL-17 group (p<.001).
Conclusion: In patients in remission, the known immediate adaptability of the entheses to physical exercise through increased rigidity can be verified by elastography in patients with PsA and controls. Patients treated with aIL17 therapies exhibited adaptive elastographic responses to enthesis exercises that were indistinguishable from healthy controls and significantly higher than those not treated with aIL17. These findings lay the groundwork for using elastography as an outcome variable in the evolutionary study of entheses in patients with other forms of spondyloarthritis.

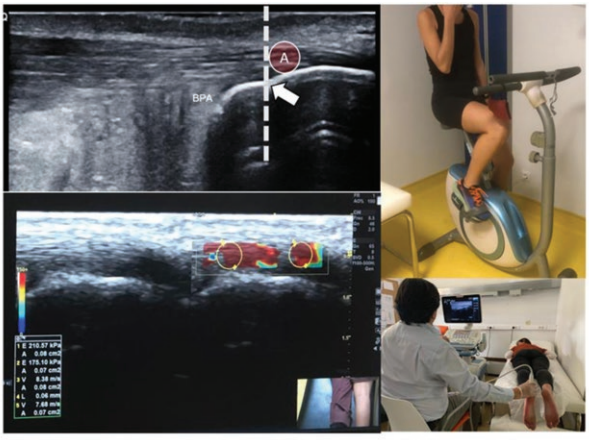


Fig1: A. Ilustration of the location of the Achilles' enthesis proximal to the vertex of the preachilles bursa (BPA). Elastrographic measurements were performed in a 10 mm diameter area at the location shown (A). B. controlled exercise with homogeneous caloric target to participants using an adjustable magnetic resistance bike. C. Determination of the rectangle of interest (ROI) to select the circumferences in the enthesic territory. The color gradient that references the detected stiffness is shown. D. Procedure for measuring the height of the patellar tendon in the longitudinal and posterior plane of the pre-exercise elastography.

References: NIL.
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Disclosure of Interests: Carlos Guillén-Astete Speakers bureau: Janssen, Novartis, Galapagos, Paid instructor for: Novartis, Janssen, Galapagos, Consultant of: Novartis, Galapagos, Janssen, Grant/research support from: Grunenthal, Novartis, Aliuska Palomeque: None declared, Marta Serrano Warleta: None declared, Rosa Manzo: None declared.
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POS0158 WITHDRAWN

POS0159 **THE OMERACT GIANT CELL ARTERITIS ULTRASONOGRAPHY SCORE: A POTENTIAL USEFUL OUTCOME TO ASSESS THE RISK OF RELAPSE DURING FOLLOW-UP**

Keywords: Vasculitis, Imaging, Ultrasound

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Background: The OMERACT ultrasonography large vessel vasculitis working group has recently developed an ultrasound (US) composite score, the OMERACT giant cell arteritis (GCA) Ultrasonography Score (OGUS), to assess the extent of vascular inflammation by US and to monitor disease activity in patients with GCA[1].
Objectives: Our objective was to assess the sensitivity to change of this score and to determine whether OGUS variations after treatment are associated with the risk of relapse during follow-up.
Methods: Retrospective observational study of patients referred to a US GCA fast track clinic of an academic center over a 2-year period with GCA clinical confirmation. All patients underwent baseline US evaluation at the time of diagnosis and at 3- and 6-month visits per protocol. OGUS was calculated as the sum of intima media thickness (IMT) in every segment divided by the rounded cut-off values of IMTs in each segment (0.4 mm for the common trunk of superficial temporal arteries, 0.3 mm for the parietal and frontal branches and 1 mm for the axillary arteries). The total sum was divided by the number of segments available. OGUS score >1 indicates abnormal exam. EULAR definitions for remission and major and minor relapse were checked for every patient at 3 and 6 months. Patients were treated according to clinical response with standard therapy. Sensitivity to change of OGUS was calculated as negative values of standardized mean difference (SMD) for each visit separately. The t-student test for paired samples was used for comparing baseline and follow-up OGUS assessments. 0-3 and 0-6-months OGUS variations were compared between patients with and without relapse during follow-up and with and without achievement of remission at 6 months.
Results: A total of 35 GCA patients were included for analysis (mean age 77.4 years, 62.9 % females). Ten (28.6%) patients relapsed at 3 or 6 months during follow-up, of whom 8 (22.9%) showed a minor relapse. EULAR definition of remission at 6 months was achieved by 18 (51.4%) patients. Mean (SD) baseline OGUS was 1.34 (0.34). OGUS improved significantly at 3 (1.34 vs 1.14, p=0.013) and 6 months (1.34 vs 1.1, p<0.01). The SMD of OGUS between baseline and 3 and 6 months was -0.49 and -0.61, respectively. 0-3- and 0-6-month OGUS variations in patients with and without relapse during follow-up and patients with and without achievement of remission at 6 months are shown in detail in Table 1. Mean 0-6-month OGUS improvement was significantly lower in patients with relapse during follow-up (-0.08 vs 0.35, p=0.049). On the other hand, mean 0-6-month OGUS improvement was greater in patients achieving remission at 6 months (0.35 vs 0.04, p=0.042).
Conclusion: OGUS shows moderate sensitivity to change in patients with GCA after standard therapy at 3 and 6 months. The absence of OGUS improvement during follow-up is associated with the risk of relapse and the probability of not achieving remission. These findings highlight the usefulness of this tool in clinical practice and may support personalized medicine decisions during treatment tapering.
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Table 1. 0-3- and 0-6-months OGUS variations in patients with and without relapse during follow-up and with and without achievement of remission at 6-months.

Parameter	All patients n = 35	Relapse during follow-up n = 10	No relapse during follow-up n = 25	p	Remission at 6-months n=18*	No remission at 6-months n=13*	p
0-3-months OGUS variations, mean (SD)	0.2 (0.39)	0.04 (0.57)	0.26 (0.29)	0.311	0.23 (0.25)	0.18 (0.57)	0.821
0-6-months OGUS variations, mean (SD)	0.24 (0.36)	-0.08 (0.45)	0.35 (0.24)	**0.049**	0.35 (0.26)	0.04 (0.45)	**0.042**
3-6-months OGUS variations, mean (SD)	0.04 (0.37)	-0.04 (0.62)	0.11 (0.19)	0.391	0.13 (0.19)	-0.03 (0.57)	0.345

Abbreviations: SD: standard deviation; OGUS: OMERACT Giant cell arteritis Ultrasonography Score. *31 patients completed an US exam at 6 months.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6368

POS0160 **WITHDRAWN**

POS0161

AN ULTRASOUND SCORING SYSTEM BASED ON THE SIZE AND NUMBER OF EROSIONS IS RELIABLE IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Cartilage, Ultrasound

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Background: Ultrasound has been shown to be a valid tool for the evaluation of bone erosions in rheumatoid arthritis (RA), yet a consensual scoring system is lacking.
Objectives: To assess the reliability of a semiquantitative scoring system for assessing structural bone erosion by ultrasound in a web-based reliability exercise.
Methods: A task force of the OMERACT Ultrasound Working Group developed definitions and a scoring system for grading bone erosions which takes both the size and number of erosions into consideration. Pairs of static images (longitudinal and transverse) in DICOM format of metacarpophalangeal and proximal interphalangeal joints 2-5 were acquired prospectively in healthy controls and in RA patients with varying degrees of pathology by the task force members. A dataset of anonymized images, representing various grades was created and utilized in a web-based exercise using the cmrad.com cloud platform which allowed the participants to measure the size of the erosions and use the discrete measures and the number of erosions to grade each joint according to the scoring system. Both the longitudinal and transverse scans were considered and the largest diameter chosen for each erosion. Intra- and inter-reader reliability of the scoring system was assessed using kappa statistics.

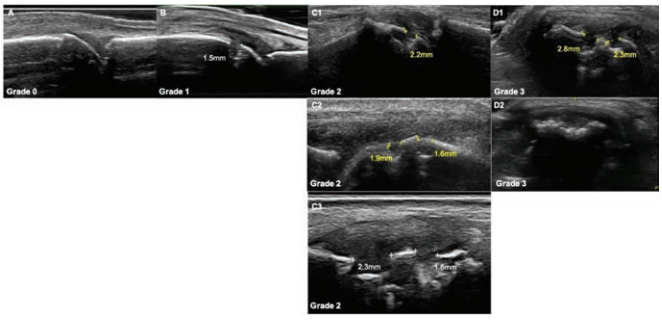


Figure 1. Representative images of the different grades of the scoring system for bone erosion in rheumatoid arthritis. A) grade 0: intact cortical bone; **B)** grade 1: single small erosion (diameter: ≤2mm); **C1)** grade 2: single large erosion (diameter: >2mm); **C2)** grade 2: 2 small erosions; **C3)** grade 2: 1 large and 1 small erosion; **D1)** grade 3: 2 large erosions; **D2)** grade 3: ≥3 erosions, regardless of size

Results: A 4-grade semiquantitative scoring system was developed: grade 0) intact cortical bone; grade 1) single small erosion (diameter: ≤2mm); grade 2) single large erosion (diameter: >2mm) or 2 small erosions or 1 large and 1 small erosion; grade 3) 2 large erosions or ≥3 erosions, regardless of size (Figure 1). A dataset composed of 45 anonymised image pairs (90 single images) was graded by 20 task force members in two rounds separated by 10 days. The intra-reader (mean: 0.79; 95% confidence interval: 0.75-0.84) reliability was excellent and the inter-reader (mean: 0.75; 95% confidence interval: 0.74-0.76) reliability was substantial.
Conclusion: This preliminary OMERACT scoring system for bone erosions of the finger joints in RA has demonstrated excellent reliability on static images. Further studies are required to evaluate the reliability of the combined acquisition and reading of images in patients.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0162

VALIDITY OF SIMPLIFIED ULTRASONOGRAPHIC ASSESSMENTS OF JOINT INFLAMMATION IN RHEUMATOID ARTHRITIS

Keywords: Ultrasound, Rheumatoid arthritis

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Background: Musculoskeletal ultrasound (MSK US) is a valuable tool to aid management of inflammatory arthritis. It's use in clinical practice is limited by the feasibility and time constraints of performing a full 44 or 78 joint ultrasound.
Objectives: Our objective was to determine the validity of four previously published simplified approaches (6 joint[1], 12 joint[2], hands only[3] and data driven[4] US models) in a new patient cohort, in order to guide future choice of targeted MSK US protocol in research and clinical practice.
Methods: Sequential patients with rheumatoid arthritis, diagnosed according the 1987 ACR criteria, with a DAS28ESR score ≥ 3.2 underwent clinical assessment and 44 joint US at Guy's Hospital. Grey scale (GS) and power doppler (PD) were graded semi quantitatively, according to the EULAR-OMERACT criteria. All the joints scored in the simplified 6 joint, 12 joint, hands only and "data driven" models were included in the current 44 joint US. However, the number of synovial recesses examined differed from those in the simplified models. Sensitivity of the simplified models to detect GS and PD signal, compared to the extended 44 joint US was calculated. Content validity was evaluated by correlating the 44-joint US count with the simplified models using Spearman's correlation coefficient. The proportion of information retained by the simplified models compared with the 44 joint US was assessed using linear regression analysis.
Results: 158 patients were enrolled in the study, with a mean age of 58.9 years (SD 12.95), 78.5% Female, 67.7% RhF positive and a median disease duration of 10 years (IQR 5-19.2). Median DAS 28 was 4.8 (IQR 3.9-5.6) and pain VAS 55 (IQR 40-70). GS and PD positivity was most common at the wrist and the MTP joints (Figure 1). All simplified assessment models were sensitive and able to detect >85% of patients with GS≥ 2 PD≥1 evaluated using the 44 joint (6 joint GS≥ 2 135 (88.2%), PD≥1 75 (86.2%), 12 joint GS≥ 2 137 (89.5%), PD≥1 76 (87.4%), Hands only GS≥ 2 138 (90.2%), PD≥1 80 (92%), Data Driven GS≥ 2 149 (97.2%), PD≥1 82 (94.3%). GS, PD and total scores for all the simplified models significantly correlated with the scores from the 44 joint US (Table 1). The "data driven" model had the highest correlation and retained the greatest proportion of information compared with the total 44 joint US scores.
Conclusion: This study validates the use of the 6 joint, 12 joint, hands only and data driven approaches in a new patient cohort. The data driven approach was the most sensitive and retained the greatest proportion of information. Simplified US models enable the routine use of musculoskeletal US in clinical practice.
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[4] Aga, A.-B. *et al.* First step in the development of an ultrasound joint inflammation score for rheumatoid arthritis using a data-driven approach. *Ann Rheum Dis* **75**, 1444–1451 (2016).

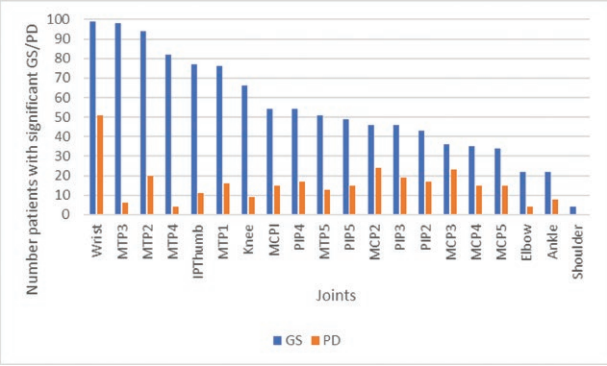


Figure 1. Joints are shown in order of prevalence of GS =≥ 2 and PD≥1 findings. Highest synovial recess and side (Right or Left) was taken as the measure of frequency.

Table 1. Correlation coefficients between simplified model scores and 44 joint US scores. GS, PD and total (sum of GS and PD) are presented in Column 1,2, and 3. Proportion of information in the total score retained(R2) by simplified models are presented in column 4.

	GS	PD	Total score	Total score R2
6 joint US[5]	0.791*	0.913*	0.826*	0.713*
12 joint US[8]	0.826*	0.928*	0.858*	0.800*
Hands only US[7]	0.887*	0.963*	0.913*	0.900*
Data driven US[6]	0.912*	0.963*	0.932*	0.927*

*Significant at the 0.01 level (2 tailed)

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Systemic lupus erythematosus, Sjogren's syndrome and anti-phospholipid syndrome: clinical aspects

POS0163 PERFORMANCE OF THE SALIVARY GLAND ULTRASONOGRAPHY OMERACT SCORE IN THE ACR-EULAR CLASSIFICATION CRITERIA FOR SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Ultrasound, Diagnostic Tests

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Background: Ultrasonography is a tool to assess the involvement of major salivary glands in patients with Sjögren's syndrome (SS). Recently, the Outcome Measures in Rheumatology (OMERACT) scoring system has been developed for salivary gland ultrasonography (SGUS) in SS.[1] Incorporation of this scoring system in the 2016 American College of Rheumatology (ACR)-European League Against Rheumatism (EULAR) classification criteria might be of aid in the classification of SS.

Objectives: To investigate if addition of the OMERACT SGUS score influences the performance of the 2016 ACR-EULAR classification criteria for SS in daily clinical practice.

Methods: This retrospective, cross-sectional study included consecutive patients of ≥18 years who visited the University Medical Centre Groningen (UMCG) between January 2017 and December 2021 for a diagnostic trajectory to determine whether they had SS. All items of the 2016 ACR-EULAR criteria were collected. Ultrasonographic images were assessed by using the Hocevar score. A transformation table was made by two experienced ultrasonographers (AS and KD) to transform the Hocevar score to the OMERACT SGUS score (range 0-12). Clinical diagnosis by the treating physician was used as gold standard. Receiver operating characteristic (ROC) analysis with area under the curve (AUC) was used to analyse the accuracy of the SGUS OMERACT score, the current ACR-EULAR classification criteria and the ACR-EULAR criteria with addition of the SGUS OMERACT score as well as to explore the optimal cut-off point to predict clinical diagnosis.

Results: Of the 419 included patients, mean age was 53±14 years, 366 (87%) were female and 164 (39%) were diagnosed with SS. Median (IQR) of the SGUS OMERACT score was 7 (4-10) in the SS group versus 1 (0-2) in the non-SS group (Table 1). The SGUS OMERACT score predicted the clinical diagnosis of SS with good accuracy, with an AUC of 0.868 (95% CI 0.830-0.906). The optimal cut-off point of the total OMERACT score to predict clinical diagnosis was ≥5, with a sensitivity of 68.9% and a specificity of 91.4%. An OMERACT score of ≥2 in at least 1 gland showed a sensitivity of 75.6% and a specificity of 85.5%. The current ACR-EULAR classification criteria showed excellent accuracy to predict clinical diagnosis, with an AUC of 0.956 (0.937-0.975). When incorporating the SGUS OMERACT score (defined as total score ≥5) as additional item in the ACR/EULAR criteria, the AUC was 0.968 (0.953-0.983). When incorporating the SGUS OMERACT score (defined as ≥2 points in 1 gland) as an additional item, the AUC was 0.967 (0.951-0.982). With the original ACR/EULAR cut-off score of ≥4 for classification as SS, the sensitivity was 92.7% and the specificity 87.5% for the current ACR-EULAR classification criteria, 93.3% and 87.1% for the ACR-EULAR criteria with addition of SGUS OMERACT positivity based on total score ≥5, and 93.9% and 85.5% for the ACR-EULAR criteria with addition of SGUS OMERACT positivity based on ≥2 points in 1 gland.

Conclusion: Incorporating SGUS in the criteria extends the diagnostics options in patients suspected with SS. The accuracy of the ACR-EULAR classification criteria in predicting the clinical diagnosis of SS remained high after incorporating the SGUS OMERACT score.

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Table 1. Characteristics of study population

Characteristics	SS (n = 164)	No SS (n = 255)	P-value
Age (years)	53 ± 14	53 ± 14	0.777
Sex (female)	143/164 (87.2)	223/255 (87.5)	0.939
FS ≥1 in salivary gland biopsy	107/133 (80.5)	22/158 (13.9)	<0.001
Anti-SSA positive	131/164 (79.9)	32/253 (12.6)	<0.001
Ocular staining score ≥5*	34/164 (20.7)	15/255 (5.88)	<0.001
Schirmer ≤5 mm*	109/158 (69.0)	128/242 (52.9)	0.001
Unstimulated whole saliva ≤0.1 ml/min	91/162 (56.2)	90/253 (35.6)	<0.001
Total OMERACT score (0-12)	7 [4-10]	1 [0-2]	<0.001
Total OMERACT score ≥5 in 4 glands	113/164 (68.9)	22/255 (8.63)	<0.001
OMERACT score ≥2 in at least 1 gland	124/164 (75.6)	37/255 (14.5)	<0.001

2.Data presented as mean ± SD, median [IQR] or n (%)3.* Scored in at least 1 eye

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POS0164 CHARACTERIZATION OF PULMONARY MANIFESTATIONS OF SJÖGREN SYNDROME: A MULTICENTER RETROSPECTIVE STUDY

Keywords: Descriptive Studies, Sjögren syndrome, Lungs

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Background: Primary Sjögren syndrome (pSS) is a systemic autoimmune disease that may complicate with pulmonary manifestations in up to 16% of patients [1], including interstitial lung disease (SS-ILD) and airway disease (SS-AD).
Objectives: To assess the associated factors with SS-ILD and SS-AD.
Secondary objectives: to describe these manifestations and to investigate their prognosis.
Methods: We performed a retrospective multicentric study involving 9 French centers. We included pSS patients fulfilling the ACR/EULAR 2016 criteria and having a pulmonary disease associated with pSS evidenced by at least one clinician and one computed tomography (CT) report. We collected clinical and biological data at the visit giving access to the most exhaustive collection, pulmonary function test (PFT) and CT scans of the patients. CT scans were reviewed by a radiologist specialist in thoracic diseases. SS-ILD were considered progressive if there were at least a 10% decrease of the forced vital capacity (FVC) between 2 consecutive measurements. SS-ILD and SS-AD were compared to pSS controls with no history of pulmonary involvement, matched on age and disease duration with a 2/1 ratio.
Results: We included 56 SS-ILD, 31 SS-AD and 174 pSS controls. Comparison of SS-ILD, SS-AD and pSS controls is shown in **Table 1**. We found that SS-ILD and SS-AD had higher disease activity (ESSDAI) and B cell biological markers at visit time. Incident lymphomas were more prevalent in SS-ILD. SS-ILD were mostly nonspecific interstitial pneumonia (NSIP, n=16, 36%), usual or probable usual interstitial pneumonia (UIP, n=8, 18%), indeterminate for UIP (n=8, 18%) and lymphoid interstitial pneumonia (LIP, n=4, 9%). Fibrosis features were observed in 43% of cases. 44% of SS-ILD were progressive, independently of pSS characteristics and CT pattern, despite any significant evolution of PFT parameters of overall SS-ILD within 7 years follow-up (**Figure 1A**). We indirectly assessed the impact of the first line of systemic treatments in SS-ILD comparing PFT evolution of treated (43%) and untreated patients. We found that treated SS-ILD tended to have reduce PFT deterioration than non-treated patients with a 6 years follow-up [especially FVC and total lung capacity (TLC)], with a trend to improved FVC and forced expiratory volume (FEV1) with cyclophosphamide and rituximab (**Figure 1C-D**). SS-AD were mostly diffuse, associating bronchiolitis and bronchiectasis in 60% of cases. Here again, we did not find a significant worsening of PFT parameters with 9 years follow-up in SS-AD (**Figure 1B**), despite CT abnormalities worsening in 41% of cases at 6 years.

Table 1. Comparison between SS-ILD, SS-AD and pSS control

	SS-ILD, n=56	pSS control, n=112	SS-AD, n=31	pSS control, n=62
Clinical feature:				
Age, mean	56	56	56	56
Women	49 (87)	103 (92)	30 (97)	58 (93)
Death	7 (13)	7 (6)	2 (7)	3 (5)
Muscular	7 (13)*	3 (3)	3(10)	3 (5)
Splenomegaly	5 (9)*	1 (1)	2 (6)	2 (3)
ESSDAI, mean	16*	4	10*	4
ESSDAI (pulmonary excluded), mean	9*	4	7*	4
Incident lymphoma	5 (9)*	0	1(3)	0
Biology:				
Anti-SSA	41 (76)*	66 (59)	21 (70)	38 (65)
Anti-RNP	11 (22)*	2 (2)	0	1 (2)
Gammaglobulinemia, mean	23*	18	19	18
Beta2-microglobulinemia, mean	3*	2	3*	2

Data are n (%) unless otherwise indicated. Stars indicate significant comparisons to pSS control. Mann-Whitney and Fisher's exact test were used. *: p<0.05.

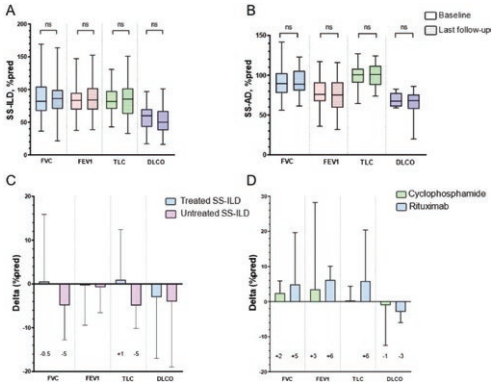


Figure 1. PFT evolution of SS-ILD and SS-AD Comparison of baseline and last follow-up PFT of SS-ILD (A) and SS-AD (B). Delta between last follow-up and baseline PFT of treated compared to untreated SS-ILD (C). Delta between post-therapeutical and pre-therapeutical PFT for cyclophosphamide and rituximab (D). Wilcoxon test was used. *: p<0.05.

Conclusion: SS-ILD are usually fibrosing and progressive manifestations of pSS, associated with disease activity, incident lymphoma and B cell biological markers. Despite the absence of randomized trials in SS-ILD, our results suggest an effect of the therapeutics. SS-AD are also associated with the disease activity and seems to progress slowly.
REFERENCE:
[1] Ramos-Casals et al., Rheumatology. 2015;54(12):2230-8.
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Disclosure of Interests: None Declared.
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POS0165

DETERMINATION OF DISTINCT PHENOTYPES OF PRIMARY SJÖGREN'S DISEASE USING CLUSTER ANALYSIS BASED ON CLINICAL AND BIOLOGICAL MANIFESTATIONS: DATA FROM 458 PATIENTS FROM THE PARIS SACLAY SJÖGREN'S SYNDROME COHORT

Keywords: Sjögren syndrome

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Background: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease, with heterogenous manifestations. Main symptoms included dryness features due to the exocrinopathy, fatigue, and joint pain. In addition, systemic manifestations occur in approximately 30 to 40% of the patients with pSS. Previous attempts made to determine distinct pSS phenotypes used only symptom-based classifications, neglecting the B-cell biological activity and the systemic manifestations, which are clearly linked with disease prognosis.
Objectives: We aimed to identify distinct phenotypes among pSS patients, based on all disease features, including symptoms, systemic manifestations, and biological features, using a non-supervised hierarchical cluster analysis.
Methods: We included pSS patients enrolled in the prospective French Paris-Saclay cohort, if satisfying the ACR/EULAR criteria. We performed an unsupervised multiple correspondence analysis using 26 selected variables to widely cover pSS manifestations: VAS for pain, fatigue, ocular and oral dryness; systemic manifestations as defined by ESSDAI domains; biological parameters such as rheumatoid factor (RF), anti-SSA, -SSB, -RNP, -centromere, -DNA antibodies, high IgG levels, monoclonal component, cryoglobulinemia, low C4 levels; and abnormal Schirmer's test and presence of focal sialadenitis. The first axes were then considered to perform hierarchical clustering based on the Ward method. The number of clusters was determined visually on the plotted dendrogram and with the gain in inertia.
Results: We included 458 pSS patients in the analyses (95% women, median age 49 yrs). Cluster hierarchical classification yield in three homogenous groups of patients.

1. Cluster 1 (n=121) included patients with high symptom burden (median [IQR] ESSPRI 6.6 [5.6–7.7]), but low systemic activity (ESSDAI 1; [0-2])
2. Cluster 2 (n=110) included a higher proportion of men (15%) and of patients from African ancestry (19%), with high level of dryness (overall dryness VAS 66 [46–81]) and fatigue (VAS 70 [45–84] but low level of pain (pain VAS 53 [20–77]; high systemic activity (ESSDAI 5 [2–8]): lymphadenopathy (11%), cutaneous (7%), pulmonary (12%), PNS (11%), and articular (40%) involvements; frequent other auto-antibodies: anti-RNP (9.2%), anti-centromere (12%), anti-DNA (16%) and cryoglobulinemia (3.5%).
3. Cluster 3 (n=195) included younger patients (median age 44 yrs), with low symptom burden (ESSPRI 4.9 [3.3–6.2]), low systemic activity (ESSDAI 2 [1–4]), but with frequent B-cell activation signs: biological ESSDAI domain (58%), high IgG levels (52%), rheumatoid factors (58%), low C4 levels (22%); and higher rates of anti-SSA (86%) and -SSB (46%) antibodies.

Patients with history of lymphoma were identified in cluster 2 (n=8, 5.6%) and 3 (n=7, 3.6%).
Conclusion: Using an unsupervised clustering method, and including parameter that encompass all disease features, we identified three distinct subgroups of pSS patients that were 1/ high symptom burden without systemic features; 2/ Systemic features 3/ B-cell biologically active with low-symptom burden. Our study highlights the underlying idea of heterogeneous pathophysiological mechanisms and could help further stratifications among pSS patients. Further studies are needed to assess whether disease evolution is different across these subgroups.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.

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POS0166 OUTCOME OF PREGNANCY IN WOMEN WITH PRIMARY SJÖGREN'S SYNDROME COMPARED TO THE GENERAL POPULATION: THE FRENCH MULTICENTER PROSPECTIVE GR2 STUDY

Keywords: Prognostic factors, Pregnancy and reproduction, Sjögren syndrome

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Background: In the context of primary Sjögren's syndrome (pSS), only retrospective studies have investigated pregnancy outcomes with heterogeneous methods and contradictory results. An increased adverse pregnancy outcome (APO) frequency was found in most case-control studies, including more miscarriage and intrauterine fetal death (IUFD), preterm delivery, small for gestational age and intra-uterine growth retardation, as well as an elevated number of cesarean sections. Moreover, these studies rarely analyzed the impact of pregnancy on the course of pSS.
Objectives: To describe outcome of pregnancies, identify predictive factors for disease flares and APO in pSS patients and compare their risk of adverse pregnancy, delivery and birth outcomes to those of the general population.
Methods: The GR2 study is a French multicentric prospective cohort of pregnancies in women affected with auto-immune diseases. The ENP 2016 is a French national perinatal survey on a sample of around 14.000 births. We included GR2 pSS women fulfilling ACR/EULAR 2016 criteria with an ongoing pregnancy at 12 weeks' gestation. EULAR Sjögren's Syndrome Disease Activity Index and Patient Reported Index (ESSDAI and ESSPRI) were recorded at the first trimester of each pregnancy (baseline or bESSDAI), each trimester and at delivery, and a cumulative ESSDAI (cESSDAI) was calculated, defined as the sum of each domain maximum score during follow-up before pregnancy. A pSS flare was defined as an increase ≥3 points of the ESSDAI. APO were defined as the occurrence of any of the following events: unexplained IUFD ≥12 weeks, neonatal death, placental insufficiency (intrauterine growth restriction, preeclampsia/eclampsia, HELLP syndrome, and/or placental abruption) leading to a premature delivery <37 weeks or small for gestational age birth weight. To determine predictive factors for pSS flares we excluded pregnancies included after 18 weeks and for APO also excluded twin pregnancies and aborted pregnancies. We compared the risk of adverse pregnancy, delivery and birth outcomes occurring ≥ 20 weeks in pSS pregnancies (including those with congenital atrioventricular block) to general population pregnancies from the ENP 2016, after matching (ratio 1:4) on age, parity, residential area and on the type of pregnancy (singleton vs multiple pregnancy).
Results: 106 pregnancies occurred in 96 pSS women. A history of pSS systemic activity was found in 92/102 (90.2%) patients and a systemic activity at inclusion in 48/106 (45.3%). pSS flares occurred in 12/93 (12.9%) pregnancies. Analyses did not identify any baseline parameter associated with the risk of pSS flare, in particular no association with ethnicity, cESSDAI, bESSDAI, or bESSPRI, biological markers of activity or type of autoantibodies. APO occurred in 6/88 (6.8%) [APO-BLOCK in 13/106 (12.3%)] pregnancies including only one with a pSS flare (Table 1). Women with and without APO had comparable age, weight, smoking status, cESSDAI, bESSDAI or bESSPRI at inclusion. However, women with APO had more often antiphospholipid (aPL) antibodies (n available=55, 50% vs 3.9%, p=0.02) and a trend for more frequent RNP antibodies was found (33.3% vs 5.7%, p=0.07). Treatment exposure did not differ between groups. APO frequency in pSS did not differ from that of the ENP population (8.6% vs. 6.7%, OR= 1.31, 95% IC [0.53-2.98], p=0.52). No difference was found in cesarian section rates (21.9% vs 22.9%, p=0.94) and birth outcomes (including APGAR5 and newborns ICU hospitalizations) between both groups.
Conclusion: pSS flares and APO were observed respectively in 12.9% and 6.8% of pregnancies but rarely occurred together. aPL antibodies were associated with a higher risk of APO and a trend for anti-RNP antibodies was found. Adverse pregnancy, delivery and birth outcomes in pSS women were comparable to those of the general population.
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POS0167 THE ANTIMALARIAL PROTECTIVE EFFECT AND A CLEAR CUT-OFF POINT FOR STEROID CUMULATIVE DOSE ASSOCIATED WITH DAMAGE ACCRUAL ON A 10-YEAR FOLLOW-UP SYSTEMIC LUPUS ERYTHEMATOSUS COHORT

Keywords: Organ damage, Systemic lupus erythematosus

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Background: Assessing damage accrual (DA) in patients with systemic lupus erythematosus (SLE) is complex but mandatory. Damage might be caused by the disease itself, comorbidities, and/or its pharmacological treatment or both. Among the pharmacological agents used to treat SLE, glucocorticoids (GC) are arguably the main cause of damage followed by lupus flares [1,2].
Objectives: This study aims to identify precise values of damage accrual related to damage in the long-term, the predictive positive and negative values for damage accrual of different steroid burden cut-offs points and the influence of other drugs, socioeconomic, ethnical and clinical aspects with damage in lupus patients.
Methods: A 10-years follow-up cohort of initially 190 patients, 147 alive at the end, with data regarding SLICC/ACR damage index (SDI) [3], clinical, social, economic and ethnical characteristics were recorded. SDI and medications accrual including GC were analyzed yearly both by patients interviews and chart reviews. A receiver operator characteristic (ROC) curve was developed to better comprehend relations among GC and damage, non-parametric data was analyzed by Mann-Whitney test and regression analyses was performed with Pearson test to evaluate factors related to DA over 10 years.
Results: Patients already with damage at baseline (SDI > 0) needed lesser GC accrual to develop new damage (4.2 g x 7.0 g, $p = 0.022$). Mean annual accrual of GC over a cut-off determined by the ROC curve analyses of 3.0 g (mean 8.22 mg per day) was independently associated with damage enhancement by SDI during the 10 years follow-up period compared to less than 3.0 g per year (OR=

5.32 p = 0.001) on multivariate logistic analyses (MLA) using stepwise forward, patients with mean GC annual accrual above this point present a positive predictor value (PPV) for DA of 88.7 %. Other cut-off points were evaluated and even for mean annual GC accrual of 0.5 g (approximately 1.37 mg per day) patients above this lower cut-off point had a PPV for DA greater than 75 % and the negative predictive value for the ones under this point was only 45.8 %. Patients using antimalarials (AMA) showed a protective effect for developing new damage (OR= 0.12, p = 0.009) on MLA and presented a higher proportion of patients under the 3.0 g/year of mean annual GC accrual (p = 0.005). Patients with lupus nephritis (OR= 2.50, p = 0.030), pleuritis (OR= 4.00, p = 0.003), age older than 44 years (OR= 5.14, p = 0.003) at recruitment and the use of azathioprine during the follow-up period (OR = 2.32, p = 0.044) were also independently associated with damage on MLA with stepwise forward.

Conclusion: The present cohort study findings highlight the protective effect of AMA regarding damage and its possible relation with a lower GC burden in the long-term. The harmful effects of GC on DA measured by SDI in patients with lupus is ratified. In contrast with other studies, it is shown that even low doses of GC might be associated with DA when chronically used in the long-term and no safe GC burden was found. There might be no safe GC dose for patients with more than a decade of SLE and physicians might need to pursuit SLE treatment with zero GC dose for the long-term when disease remission is established as soon as possible.

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POS0168 IMPACT OF THE HYDROXYCHLOROQUINE LEVEL ON THE ECG QT INTERVAL IN PATIENTS WITH SYSTEMIC RHEUMATIC AUTOIMMUNE DISEASES: A REAL-LIFE STUDY

Keywords: Safety, Systemic lupus erythematosus, Cardiovascular disease

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Background: NIL.

Objectives: To analyze the impact of the serum level of HCQ on the QTc interval, in patients with rheumatic systemic autoimmune diseases (RSAD), treated with this drug a long time.

Methods: Retrospective study, among patients with RSAD, treated with HCQ > 1 year, dose 200-400 mg/day (cases). Serum HCQ level was measured and the QTc interval of the ECG. Patients with EASR not treated with HCQ were included as a control group for QTc: weight, current treatment, and ECG was performed to obtain QTc. In patients with RSAD, the following was collected: 1) Epidemiological data of the patient 2) RSAD: diagnosis, year of diagnosis, time of evolution of the disease, own clinical and autoimmunity data, treatment and dose 3) HCQ: time in treatment, toxicity, symptoms and serum level. 4) ECG; QTc and heart rate (HR).

Results: 142 patients treated with HCQ for a mean of 8.3 (SD: 6.4) years, at a mean dose of 245 mcg/L (83.8), and 3.7 (1.3) mg/kg/day, are included. 129 (91%) are women, mean age: 57 (14.5) years, weight: 66 (15) kg. Diagnosis distribution: SLE: 72 (50%) patients, RA: 37 (26%), Sjögren syndrome: 18 (13%), palindromic rheumatism: 4 (3%), psoriatic arthritis: 3 (2%), antiphospholipid syndrome: 2 (1%) and other collagen diseases: 2 (1%) patients. Mean HCQ serum level: 185.6 mcg/L (124): 25 (28%) with a level <100 mcg/L (mean: 58 [28.5] mcg/L) and 117 (72%) >100 mcg/L (mean: 224 mcg/L [116]). On ECG, the mean HR: 72 bpm (11) and the mean QTc interval: 419 (33) ms, being prolonged (>440 ms) in 39 (27%) patients (range: 441-510 ms). Ten (7%) patients reported symptoms: palpitations: 7 (70%), dizziness in 2 (20%) and 1 (10%) patient an isolated pseudosyncopal picture (QTc: 441 ms); 58 (41%) patients were receiving treatment with a drug related to the risk of QTc prolongation: Possible (P: authorized doses, no risk of TdP): 8 (14%) patient, Conditional (C: risk in certain circumstances: excessive dose, interactions): 44 (76%), Defined (D: risk of TdP when used in licensed indications): 1 (2%). When comparing the mean QTc result of the EASR group treated with HCQ and the control group without HCQ (n: 32), no differences were detected (419.4 [33] vs 436 [51], p=0.072).

Among patients with HCQ level >100 mcg/L (n: 117/82%) vs <100 mcg/L (n: 25/18%), the mean daily dose of HCQ received (250 mg [87.7] vs 220 mg [57.7], p=0.33) and the one adjusted to the weight of the patient in both is higher (3.76 [1.4] mg/kg vs 3.18 [1] mg/kg, p=0.016). No relationship was observed between the HCQ level and the QTc result. The 39 (27%) patients with QTc >440 ms vs the 103 (73%) with QTc ≤ 440 ms were significantly older (61 [14] years vs 55 [14] years, p=0.007) and higher heart rate (75 [12] bpm vs 71 [10.6] bpm, p=0.016). No differences were detected between QTc result and HCQ dose or level.

Conclusion: In patients with EASR treated with maintenance doses of HCQ: 1) The serum level of HCQ is not related to prolongation of the QTc interval of the ECG. 2) QTc is significantly related to age and heart rate. 3) 40% of patients with prolonged HCQ treatment also receive other common drugs that can influence the QTc, however, it does not seem to cause symptoms of interest. 4) The EASR per se does not affect the QTc result.

Table 1. Characteristics of the patients with according to the result of the QTc and the level of HCQ

	QTc >440 ms N: 39 (27%)	**QTc <440 ms N: 103 (73%)**	p
Age, mean (SD)	61 (14.4)	55 (14)	**0.007**
Female, n (%)	36 (92)	93 (90)	0.85
QTc, mean (SD)	455.7 (14.8)	405 (28)	**0.0001**
Heart rate, mean (SD)	75 (12)	71 (10.6)	**0.016**
Weight, mean (SD)	70.4 (15.4)	68.5 (15.2)	0.61
HCQ;			
Dose mcg/L, mean (SD)	246.5 (88.4)	244.6 (82.5)	0.15
Mg/kg HCQ, mean (SD)	3.61 (1.44)	3.68 (1.3)	0.79
Years in HCQ, mean (SD)	8.7 (6.3)	8.2 (6.5)	0.48
HCQ serum level mcg/L, mean (SD)	192.5 (131.5)	182.3 (121.5)	0.67
Range	10-603	10-658	-
	HCQ >100 mcg/L N: 117 (82%)	**HCQ <100 mcg/L N: 25 (18%)**	**p**
HCQ serum level, mean (SD)	224.1 (116)	58 (28.4)	**0.0001**
QTc, mean (SD)	417 (34)	427.5 (28)	0.10
Dose mcg/L, mean (SD)	250.4 (87.7)	220 (57.7)	**0.033**
Mg/kg HCQ, mean (SD)	3.76 (1.4)	3.18 (1.0)	**0.016**
Years in HCQ, mean (SD)	8.03 (6.4)	9.81 (6.4)	0.20
Weight, mean (SD)	68.4 (15)	72 (16)	0.30

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POS0169 PREDICTORS OF FIRST HOSPITALIZATIONS DUE TO DISEASE ACTIVITY AND INFECTIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

Keywords: Registries, Systemic lupus erythematosus, Real-world evidence

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Background: Systemic Lupus Erythematosus (SLE) patients experience frequent hospitalizations; lupus flares and infections have been shown to be the two most common causes.
Objectives: The aim of this study is to describe the main causes and predictors of first hospitalizations due to disease activity and infections in SLE patients.
Methods: SLE patients from GLADEL, a multi-ethnic, multi-national Latin-American (LA) cohort were studied. The first hospitalization during these patients' follow-up due to either infection and/or SLE disease activity was examined. Baseline sociodemographic, clinical, damage (SDI) and treatments were evaluated as possible predictors. First, descriptive analyses were performed. Predictors of infection or SLE disease activity associated hospitalization were identified using univariate and multivariate logistic.
Results: A total of 1341 patients were included; 1201 (89.6%) were female. Their median interquartile range (IQR) age at diagnosis was 27 (20-37) years and their median IQR follow up time 27.5 (4.7-62.2) months. 456 (34.9%) patients were hospitalized; 344 (75.4%), 85 (18.6%) and 27 (5.9%) were hospitalized for disease activity, infections, or both, respectively, as depicted in Graph 1. In the multivariable analysis, arthritis was associated with hospitalizations due to infection. Serositis, disease activity and damage were associated with hospitalizations due to disease activity. Older age, higher socioeconomic status and antimalarial use were found to be protective, as depicted in table 1.
Conclusion: In this large LA lupus cohort, one third of the patients had at least one hospitalization; of them, were due to SLE disease activity. Our findings call attention for controlling disease activity and preventing damage using antimalarials early in the disease course disease to prevent the first hospitalization.
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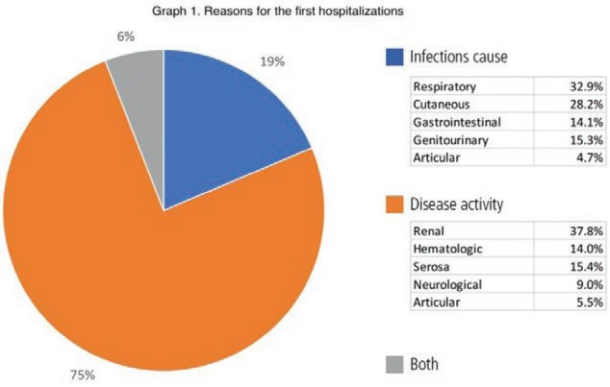


Figure 1.

POS0170

ALL-CAUSE MORTALITY AND THE INCIDENCE OF CANCER IN PATIENTS WITH MODERATE-TO-SEVERE SLE: RESULTS FROM THE BRITISH ISLES LUPUS ASSESSMENT GROUP BIOLOGICS REGISTRY (BILAG-BR)

Keywords: Real-world evidence, Registries, Systemic lupus erythematosus

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Background: Patients with systemic lupus erythematosus (SLE) are known to have an increased mortality and risk of certain cancers compared to the general population.

Table 1. Univariable and multivariable logistic regression analysis of predictors of hospitalization due to disease activity and infections in patients with SLE

INFECTIONS	Univariable OR (95% CI)	p value	Multivariable OR (95% CI)	p value	ACTIVITY	Univariable OR (95% CI)	p value	Multivariable OR (95% CI)	p value
Gender, Female	1.14 (0.54-2.41)	0.73			**Gender**, Female	0.89 (0.60-1.32)	0.56		
Age at diagnosis	1.00 (0.98-1.02)	0.78			**Age at diagnosis**	0.98 (0.97-0.99)	<0.001	0.98 (0.97-0.99)	0.02
Ethnicity	Ref.	0.16			**Ethnicity**	Ref.	0.16		
Caucasians	1.47 (0.90-2.38)				Caucasians	1.26 (0.96-1.65)			
Mestizo	0.84 (0.36-1.95)				Mestizo	1.51 (1.02-2.23)			
ALA	2.34 (0.86-6.39)				ALA	1.13 (0.55-2.31)			
Others					Others				
Socioeconomic status	0.60 (0.25-1.42)	0.16			**Socioeconomic status**	0.24 (0.13-0.44)	<.0001	0.32 (0.17-0.61)	0.002
High	0.63 (0.37-1.07)				High	0.75 (0.57-0.98)		0.89 (0.65-1.22)	
Medium	Ref.				Medium	Ref.		Ref.	
Low					Low				
SDI[*b]	1.11 (0.93-1.33)	0.25			**SDI** [ab]	1.52 (1.37-1.70)	<.0001	1.33 (1.18-1.50)	<.0001
SLEDAI*	1.02 (0.99-1.04)	0.20			**SLEDAI** [a]	1.07 (1.05-1.09)	<.0001	1.05 (1.03-1.07)	<.0001
Arthritis	1.90 (0.99-3.64)	0.05	1.93 (1.01-3.72)	0.05	**Arthritis**	0.83 (0.62-1.11)	0.21		
Serositis	1.27 (0.78-2.07)	0.34			**Serositis**	1.62 (1.23-2.14)	<0.001	1.40 (1.02-1.92)	0.04
Renal	1.38 (0.89-2.15)	0.15			**Renal**	2.31 (1.79-2.96)	<.0001		
Anti-dsDNA	1.38 (0.76-2.52)	0.29			**Anti-dsDNA**	1.40 (1.01-1.94)	0.04		
Antimalarial use	1.35 (0.86-2.12)	0.19			**Antimalarial use**	0.52 (0.39-0.70)	<.0001	0.71 (0.51-0.98)	0.04
Prednisone[c]	Ref.	0.08			**Prednisone**[c]	Ref.	0.79		
None	1.56 (0.36-6.86)				None	0.76 (0.30-1.90)			
<7.5mg/d	1.44 (0.62-3.32)				<7.5mg/d	0.86 (0.53-1.38)			
7.5-15mg/d	2.07 (1.22-3.52)				7.5-15mg/d	0.84 (0.61-1.16)			
15-60mg/d	1.84 (0.97-3.49)				15-60mg/d	0.89 (0.60-1.31)			
≥60mg/d					≥60mg/d				

ALA: African Latin American; LDAS: Low disease activity; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Disease Index, * At cohort entry, [a]At diagnosis, [b]Increase on per 1 unit, [c] highest dose

Objectives: We aimed to characterise the all-cause mortality rate (MR) and the incidence of cancer in SLE patients receiving biologic and standard of care (SoC) therapies.
Methods: Patients recruited to the BILAG-BR 2010-2021 were included. Demographic and clinical data were recorded at recruitment. Mortality and malignancy data were collected from study centres, the UK Office of National Statistics and the National Cancer Register. Cox regression models were used to estimate the hazard ratios (HRs) of mortality and cancer in biologic-treated patients compared to SoC. Mortality models were adjusted for age, gender, co-morbidity, SLICC damage index (SDI) and hydroxychloroquine (HCQ) use. The standardised mortality ratio (SMR) and standardised incidence ratio (SIR) were calculated using death and cancer rates for the general UK population.
Results: During follow-up, (1463 patients with 5,962 person years [pys]), 32 incident cancers occurred in 31 individuals, a median (IQR) of 1.31 (0.63-3.36) years after registration. The overall incidence was 6.0 (3.8-7.6) per 1000 pys. Compared to the UK general population, the SIR (95% CI) was 1.21 (0.85-1.72). Using SoC as the comparator, the age and gender adjusted HR was 1.49 (0.57-3.92) for rituximab and 2.47 (0.57-10.58) for belimumab. Across the whole cohort, associated risk factors (table 1), included age at recruitment (HR 1.05 [1.02-1.08]) and male sex (HR 2.68 [1.13-6.41]). Following registration, 54 deaths occurred after a median of 1.8 (0.8-3.3) years. Crude MR was 9.15 (7.0-11.9) per 1000 pys. The SMR was 4.74 (3.63-6.19). The most common causes of death were infection (22, 40.7%), SLE (11, 20.3%) and cancer (6, 11.1%). MR was 3.3 (1.3-8.9) per 1000 py in the SoC, 11.3 (8.5-15.0) in the rituximab and 2.5 (0.4-17.9) in the belimumab group. Risk factors included age at recruitment (HR 1.07 [1.05-1.09]) and SDI (HR 1.34 [1.08-1.67]. HCQ use was protective (HR 0.30 [0.14-0.65]). In multivariate analysis, compared to SoC, risk was similar in rituximab (HR 2.36 [0.69-8.10) and belimumab groups (HR 1.41 [0.14-14.14]).
Conclusion: Although overall numbers are low, mortality rate and incidence of cancer appears to be broadly similar in SoC, rituximab and belimumab treated patients.

Table 1. Risk factors associated with risk of cancer and death in a cohort of patients with moderate-severe SLE

	Cancer		Death	
	Hazard ratio (HR) (95% CI)	Adjusted HR* (95% CI)	HR (95% CI)	Adjusted HR** (95% CI)
Age at recruitment (per year)	**1.07 (1.04-1.09)**	**1.05 (1.02-1.08)**	**1.07 (1.05-1.09)**	**1.04 (1.02 -1.07)**
Male sex	**3.51 (1.57-7.86)**	**2.68 (1.13-6.41)**	**2.06 (1.01-4.22)**	1.48 (0.54 -4.05)
Disease duration	1.02 (0.99-1.05)	-	1.01 (0.98-1.03)	-
SLICC damage index score at baseline (per unit increase)	1.20 (0.96-1.49)	-	**1.58 (1.39-1.81)**	**1.37 (1.11-1.68)**
SLEDAI at baseline (per unit increase)	0.99 (0.93-1.05)	-	1.01 (0.97-1.06)	-
Smoking ever	1.46 (0.69-3.06)	-	1.49 (0.79-2.81)	-
Previous cancer	**2.81 (1.15-6.85)**	2.05 (0.81-5.22)	**3.29 (1.58-6.82)**	2.03 (0.83-5.02)
Myocardial infarction	2.57 (0.61-10.80)	-	**5.33 (2.26-12.55)**	0.93 (0.22-4.00)
Diabetes mellitus	0.59 (0.08-4.34)	-	**3.85 (1.79-8.25)**	1.63 (0.53-4.98)
Hypertension	**2.21 (1.05-4.67)**	1.45 (0.67-3.13)	**1.81 (1.00-3.26)**	0.73 (0.32-1.67)
Ethnicity	**2.68 (1.20-5.99)**	1.77 (0.68-4.58)	**1.85 (1.05-3.26)**	0.96 (0.41-2.23)
Prednisolone dose at baseline (per mg)	0.99 (0.94-1.03)	-	0.98 (0.94-1.02)	-
Previous:				
Hydroxychloroquine	0.84 (0.32-2.18)	-	**0.33 (0.18-0.60)**	**0.31 (0.15-0.69)**
Mycophenolate mofetil	0.82 (0.39-1.69)	-	1.16 (0.66-2.07)	-
Cyclophosphamide	1.30 (060-2.83)	-	1.1 (0.65-2.14)	-

*Adjusted for age, sex, previous cancer, hypertension and ethnicity**Age, sex, previous cancer, myocardial infarction, diabetes mellitus, hypertension, white ethnicity and HCQ use

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POS0171

PATIENT-DOCTOR COMMUNICATION GAP - RESULTS OF A SPEED-SHOP ON "LUPUS FLARE" AT LUPUS2022 MEETINGS

Keywords: Patient reported outcomes, Quality of care, Systemic lupus erythematosus

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Background: The Patient – Doctor communication gap is often discussed, and is one of the obstacles pointed by patients and doctors alike in the fruitful co-working of optimal treatments. Recognizing the difference between doctors and patients approach when confronted to a lupus flare is critical to bridge this gap and increase the effectiveness of jointly agreed treatment plans.
Objectives: Identify potential discrepancies between patient and doctors discussion starting points when facing a lupus flare. Are they "talking the same thing?", "do they have similar concerns in their minds?"
Methods: As part of the SL Euro lupus 2022 congress 57 participants, doctors and patients, took part in a speed-workshop to identify first "what makes them identify an event as a lupus flare" and then their "key concerns when facing a lupus flare". Answers were provided on post-its of different colours per type of participants, forcing short answers focusing on key aspects. The commonalities and discrepancies where then identified for further handling.
Results: A total of 57 statements identifying a lupus flare were collected and classified assessable (visible/ measurable) items, or specific symptoms. The results highlighted that the communication difficulty between patients and doctors starts from the very feeling of what a flare is. 91% of patients include in their recognition of a flare a factor that cannot be "easily" objectivated by a doctor such as fatigue (59.1%), or pain (50%). Only 36% of patients include an externally visible factors, most often fever. In contrast, 88% of doctors require an externally visible/measurable factor to "identify" a flare. These 2 different starting points can create a first communication gap, as well as a difference in the qualification of an event as a flare or not. A total of 93 concerns, sorted in "huge", "big", or "mid" were collected from participants. These items could be classified in 4 key groups: concerns around daily life & logistics; overall anxiety; symptoms and medication. When confronted to an event considered as a flare, patients have a perspective focusing on the impact of flares on their daily life and logistics (35% of huge concerns, 30% of all concerns), and face anxiety over disease/life in the future (30% of all concerns 19% of huge concerns); on the contrary the doctor's focus is on symptoms (67% of huge concerns, 46% of all concerns) and medications (29% of all concerns), with only 7% of the doctors focusing on the patients "immediate" daily life/logistics issues, and 18% on anxiety. This discrepancy of concern also hinders the patient-doctor communication.
Conclusion: Doctors and Patients starting points and concerns with regards to a lupus flare appear perfectly logical and fitting each individual's role in the relationship, with the doctor's primarily focused on the disease, and the patient on "how to live with it". However this different view may create an initial gap which needs to be bridged to enhance the therapeutic relationship. Acknowledging the existence of this gap is likely a first step towards an improved patient-doctor communication.
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POS0172

ARTERIAL STIFFNESS IN ANTIPHOSPHOLIPID SYNDROME: COMPARISON WITH DIABETES MELLITUS AND HEALTHY CONTROLS

Keywords: Anti-phospholipid syndrome, Cardiovascular disease

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Background: Patients with Antiphospholipid Syndrome (APS) carry an increased burden of cardiovascular morbidity and mortality and have higher prevalence of traditional cardiovascular risk factors (CVRFs) and subclinical atherosclerosis [1]. Arterial stiffness (ArS) has emerged as an independent predictor of future cardiovascular events and death in the general population, beyond the effect of traditional CVRFs [2].

Objectives: We aimed to compare ArS measures in thrombotic APS patients and age- and sex-matched patients with diabetes mellitus (DM) and healthy controls (HC), and identify potential predictors of increased ArS in patients with APS.
Methods: ArS was evaluated by carotid-femoral Pulse Wave Velocity (cfPWV) and Augmentation Index normalized to 75 beats per minute (AIx@75) using the SphygmoCor device. All participants also underwent ultrasound examination of the carotid and femoral arteries for the detection of atherosclerotic plaques. Multivariate analysis was applied for comparing ArS measures between groups and for the assessment of ArS predictors in the APS group.
Results: One-hundred and ten APS patients (70.9% female, mean age: 45.4 years), and equal numbers of DM patients and HC were included. After adjustment for age, sex, traditional CVRFs and atherosclerotic plaque presence, APS exhibited similar cfPWV (p=0.456) but increased AIx@75 (beta=4.640, 1.668-7.611, p=0.002) versus HC. APS patients had lower cfPWV (p<0.001) but similar AIx@75, (p=0.150) compared to DM patients. Using multiple linear regression analysis, cfPWV in APS group was independently associated with age (beta=0.056, 0.034-0.078, p<0.001), mean arterial pressure (MAP) (beta=0.070, 0.043-0.097, p<0.001), atherosclerotic plaques in femoral arteries (beta=0.732, 0.053-1.411, p=0.035) and anti-β2GPI IgM positivity (beta=0.696, 0.201-1.191, p=0.006). AIx@75 was associated with age (beta=0.334, 0.117-0.551, p=0.003), female sex (beta=7.447, 2.312-12.581, p=0.005) and MAP (beta=0.425, 0.187-0.663, p=0.001).
Conclusion: Patients with APS exhibit comparable cfPWV to healthy individuals but elevated AIx@75, similar to DM, implying impaired vascular health in APS. Age, female sex, MAP, atherosclerotic plaques and anti-β2GPI IgM are linked with enhanced arterial stiffening in APS. Given its prognostic value, ArS evaluation may help to improve cardiovascular risk stratification in APS patients.

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bDMARDS in RA 2.0: about the good and the bad___

POS0173 **GENDER DIFFERENCES IN TREATMENT RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TUMOR NECROSIS FACTOR INHIBITOR: A COHORT STUDY FROM THE DANBIO REGISTRY**

Keywords: Gender/diversity issues, bDMARD

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Background: TNF-inhibitors (TNFI) have improved the treatment of rheumatoid arthritis (RA) over the last two decades, but it is uncertain how much gender affects treatment response and drug adherence.
Objectives: The aim of this population-based study is to investigate effect of gender overall and across different age groups on treatment response and drug adherence in patients with RA treated with their first TNFI.
Methods: The study is an observational, nationwide cohort study using the DANBIO register linked by patients' unique civil registration number to The Danish Civil Registration System and The Danish National Prescription Registry. RA patients starting their first TNFI between 1st of January 2006 and 31st of December 2020 were included. Modified Poisson regression with robust variance estimator was used to calculate the relative risk (RR) with 95% confidence interval (95% CI) of having a good EULAR response at 4 and 12 months, respectively, comparing men to women. Linear regression was used to estimate mean difference in DAS28-CRP. The data was also analyzed in age groups to display a possible age-dependent gender effect. To quantify drug adherence for men compared to women, a crude and adjusted cause-specific Cox regression for treatment termination was performed. Hazard ratios (HR) are presented with 95% CI for 0-1, >1-3 and >3-5 years after TNFi treatment start. The Aalen-Johansen estimator was presented to illustrate cause-specific treatment termination.
Results: From DANBIO, 7386 RA patients starting their first TNFI were identified; and of these 5523 (75%) were women. Women had higher DAS28-CRP at baseline, 4 and 12 months, than men. At 4 months no significant difference in treatment responses was observed, but a tendency of better response in men compared to women was seen among patients ≤50 years (Table 1). At 12 months visit the EULAR over all good response rate was significantly higher among men, RR adjusted was 1.13 (1.05;1.21). The same trend was seen in all age groups at 12 months though not statistically significant. The hazard for termination of first TNFI treatment due to no effect, adverse events, infections, cancer or reason not stated was lower in men compared to women. HR within the first year was 0.90 (0.83;0.96), 1-3 years 0.91 (0.83;0.99), and from 3-5 years 0.93 (0.81;1.06), and did not change when adjusting for age, baseline DAS28-CRP, disease duration, co-treatment with scDMARD, and seropositivity. 10 years drug adherence is shown in figure 1.
Conclusion: After 4 and 12 months of treatment with first TNFI women have slightly higher DAS28-CRP and overall lower chance of achieving EULAR good response. In addition, women have an increased risk of discontinuation which deserves further attention.

Table 1. Mean difference in DAS28-CRP and relative risk of EULAR good response in men compared to women 4 and 12 months after initiation of first tumor necrosis factor inhibitor.

	4 months		12 months	
Age at TNFI start (Years)	**DAS28-CRP** MD (95%CI)	**Good response** RR (95%CI)	**DAS28-CRP** MD (95%CI)	**Good response** RR (95%CI)
18-40	0.39 (0.18 to 0.61)	1.18 (0.95 to 1.46)	0.31 (0.05 to 0.57)	1.12 (0.91 to 1.39)
>40-50	0.18 (-0.03 to 0.38)	1.20 (1.00 to 1.43)	0.13 (-0.09 to 0.35)	1.02 (0.85 to 1.23)
>50-60	0.18 (0.03 to 0.33)	0.95 (0.82 to 1.11)	0.22 (0.05 to 0.40)	1.10 (0.95 to 1.27)
>60-70	0.16 (0.02 to0.31)	0.95 (0.82 to 1.10)	0.25, (0.11 to 0.39)	1.11 (0.97 to 1.28)
>70	0.17 (-0.05 to 0.39)	0.93 (0.72 to 1.2)	0.20 (-0.06 to 0.45)	1.12 (0.90 to 1.40)
All	0.19 (0.11 to 0.27)	1.02 (0.94 to 1.10)	0.22 (0.13 to 0.30)	1.10 (1.02 to 1.18)
All - adjusted		1.07 (0.99 to 1.16)		1.13 (1.05 to 1.21)

DAS28-CRP: Disease Activity Score28-C-Reactive Protein, MD: mean difference, RR: relative risk, 95%CI: 95% confidence interval. Relative risk for achieving good response is adjusted for cotreatment with csDMARD, seropositivity, calendar time of initiation of TNFI, disease duration, age, and baseline DAS28-CRP.

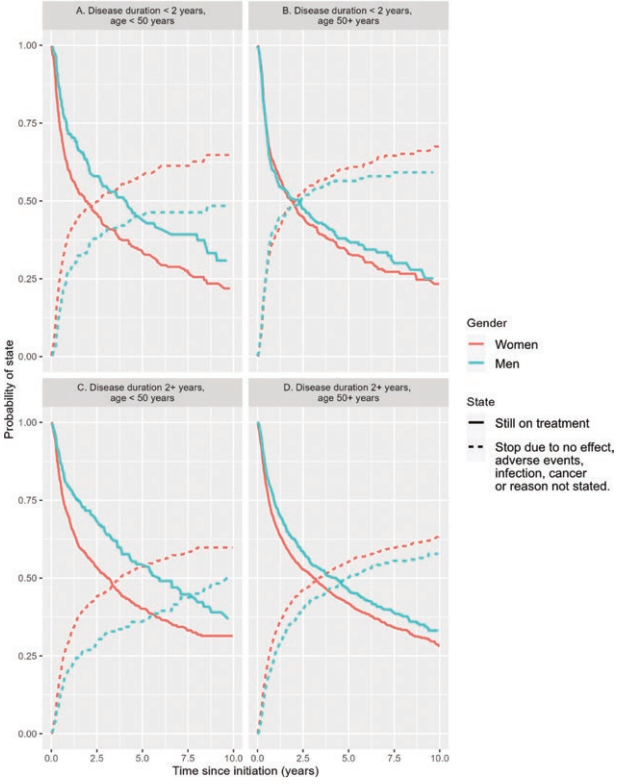


Figure 1: Competing risk curve for treatment stop. Decreasing line indicate drug adherence, increasing lines indicate cumulative incidence of cause-specific treatment stop. Patients with less than 2 years of disease duration younger than 50 years (A) and 50 years or older (B), and patients with more than 2 years of disease duration younger than 50 years (C) and 50 years or older (D).

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POS0174 THE IMPACT OF DIFFERENT DMARDS ON MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PREVALENT INTERSTITIAL LUNG DISEASE

Keywords: Disease-modifying Drugs (DMARDs), Lungs, Rheumatoid arthritis

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Background: Interstitial lung disease (ILD) is one of the most common extra-articular manifestations of rheumatoid arthritis (RA) with a high mortality risk. Only few studies examined the association between RA treatment and mortality in patients with RA-ILD, and these studies do not include all available DMARDs and tend to be of poor quality [1].
Objectives: To investigate the impact of treatment on all-cause mortality in patients with RA-ILD taking inflammation, traditional risk factors and comorbidities into account.
Methods: RA patients enrolled and observed in the biologics register RABBIT between 01/2007 and 10/2021 with an ILD, reported either at enrolment or during follow-up, were selected for the analysis. Observation started at the time of ILD reporting (= baseline) death, dropout or end of follow-up, whichever came first. Time-varying cox regression (= main model) was applied, taking into account all treatment exposures and covariates on a monthly basis (Figure 1). Sensitivity analyses comprised two alternative treatment exposures: a cumulative model (calculated as cumulative exposure in months for every treatment divided by total months of observation time), and an intention-to-treat model (treatment at baseline as exposure). Missing data was imputed 10 times. All models were adjusted by inverse probability weighting and number of comorbidities as covariate.
Results: Out of 15,566 cohort participants, 381 patients were identified as prevalent ILD cases. The total observed time was 1,258 person years, and 97 patients (25 %) died. Patients exposed to T cell co-stimulation modulator (T cell), B cell targeted therapy (B cell), and Janus kinase inhibitors (JAKi) had higher RA disease scores and multiple comorbidities (Table 1). In contrast, patients with csDMARD therapy or tumour necrosis factor inhibitor (TNFi) were less affected overall. Those receiving interleukin-6 inhibitors (IL6i) were the youngest and had a comparable number of comorbidities as patients with csDMARDs or TNFi. Patients not exposed to any DMARD differed from the other treatment groups in having lower disease activity, but a higher number of comorbidities and prior treatments. The main Cox regression model showed a 2.8-fold higher mortality risk for patients receiving no DMARD treatment compared to TNFi (Figure 1). Numerically, hazard ratios < 1 were observed for IL6i, T cell, B cell, JAKi and csDMARD in reference to TNFi but without statistical significance. The results of the sensitivity analyses pointed in the same direction.
Conclusion: To our knowledge, this is the first study to investigate the risk of all-cause mortality in RA-ILD for all available DMARD treatments jointly, using month-level data. In accordance with the few existing recommendations and studies, all non-TNFi-biologics as well as JAKi showed a protective signal compared to TNFi in all three regression models. Furthermore, patients who did not receive any DMARD had an increased risk of mortality. However, the study sample size was small, the results should thus be interpreted with caution.
REFERENCE:
[1] PMID: 36064885

Table 1. Characteristics by treatment group at time of ILD reporting

	TNFi	*csDMARD*	*IL6i*	*T cell*	*B cell*	*JAKi*	*No DMARD therapy*
N	114	61	33	60	64	19	30
Follow-up (py)	345	147	140	179	308	78	109
Age, years	66.4	64.6	63.7	67.1	64.6	65.3	66.6
Female, %	50	52.5	48.5	58.3	57.8	36.8	63.3
Disease duration, years	11.6	11.0	9.5	11.8	12.9	14.2	11.1
Rheumatoid factor +, %	85.1	75.4	81.8	83.3	92.2	84.2	76.7
DAS28-ESR	4.6	4.6	4.9	5.1	5.0	5.2	4.0
% of physical function (FFbH)	64.0	70.0	60.4	54.4	54.4	59.4	63.3
CRP, mg/l	12.8	10.6	12.9	17	18.6	8	12.3
No. of comorbidities	3.6	4	3.9	5.2	4.6	5.4	5.0
Glucocorticoid dose ≥10 mg/d, %	19.3	9.8	21.2	18.3	15.6	10.5	13.3
No. of prior biologics or JAKi	0.7	1.0.	1.8	1.4	2.0	1.5	2.2

Values are means unless otherwise specified

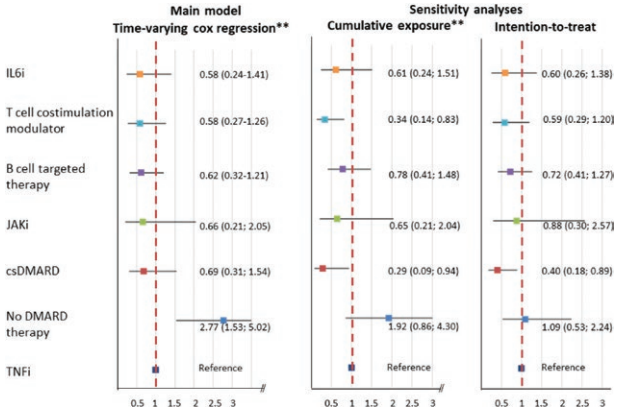


Figure 1. Hazard ratios of inverse probability weighted. * Cox regression models *Includes: age, disease duration, gender, FFbH, categorized glucocorticoids (dose) and CRP at baseline, rheumatoid factor, year of inclusion. ** An additional 6 months were added as risk window

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POS0175 "DO DISEASE MODIFYING ANTIRHEUMATIC DRUGS INFLUENCE THE FRACTURE RISK IN RHEUMATOID ARTHRITIS?" THE HUNT STUDY, NORWAY

Keywords: Epidemiology, bDMARD, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is associated with reduced bone mineral density and increased fracture risk. Bone sparing properties are reported for biological (b) disease-modifying antirheumatic drugs (DMARDs) (1), but previous studies have not found bDMARDs to reduce fracture risk [2]. Knowledge is sparce regarding fracture risk in individuals with RA using different types of DMARDs compared to the general population.
Objectives: To investigate the effect of RA on fracture risk, and examine if bDMARD treatment influences this association.
Methods: The Trøndelag Health Study (HUNT) is a population-based longitudinal study in central Norway. We included all participants who had attended at least one of the latest three HUNT surveys, using the first participation as baseline. RA status was obtained by linkage to the patient records at the regional hospital using International Classification of Disease codes (ICD9 and 10) for Major Osteoporotic Fractures (MOF), as well as further validation of medical records regarding date of RA diagnosis and use of DMARDs (divided into the following groups: never DMARDs, conventional synthetic(cs) DMARDs only, or ever bDMARDs). All RA diagnoses were validated according to American College of Rheumatology/ European League Against Rheumatism criteria[3]. RA status was registered at baseline and updated if RA was diagnosed later. Participants were followed until the first MOF, death, emigration, or end of follow-up on 21.10.2021. Cox regression was used to estimate hazard ratios (HR) for MOF in RA participants in general and by treatment group, compared to the people without RA. Confounders were identified using directed acyclic graphs (DAGs) and included sex, age at inclusion and smoking status at baseline.
Results: In total, 96,354 participants were included, 1,033 with RA (mean age 55.5 years, 65.8% women) and 95,321without RA (mean age 46.3 years, 53.0% women). Overall, 401 participants were diagnosed with RA before inclusion in HUNT and 632 during follow-up.

Table 1. RA independent of treatment was associated with almost 50% increased risk of MOF compared to non-RA (HR 1.44). By treatment group, never DMARDs had highest risk of MOF, followed by csDMARDs. Treatment with bDMARDs was not associated with MOF. Incidence rates (IR) per 1000 person-years were higher in RA overall and in all DMARD treatment groups compared to non-RA.

	Participants	MOF			Unadjusted	Adjusted	
	n	n	IR	95% CI	HR	HR	95 % CI
Non-RA	95,321	10,503	7.0	6.9-7.2			
RA independent of treatment	1,033	221	18.0	15.8-20.5	2.35	1.44	1.25-1.65
RA treatment group							
Never DMARDs	57	17	33.4	20.7-53.7	4.42	2.05	1.28-3.31
csDMARDs only	727	175	20.5	17.7-23.8	2.68	1.50	1.29-1.75
Ever bDMARDs	230	27	8.8	6.0-12.8	1.13	1.03	0.70-1.50

Adjusted for age at inclusion, sex, and smoking status at baseline. CI: confidence interval. DMARDs group missing for 19 RA participants including 2 individuals with a MOF.

Conclusion: RA was associated with MOF. However, in RA individuals treated with bDMARDs, an association with MOF was not seen. This is an encouraging result and might be of importance when evaluation future treatment regiments in this patient group.
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Disclosure of Interests: Ingebjørg Tronstad: None declared, Mari Hoff: None declared, Julie Horn: None declared, Sigrid Anna Vikjord: None declared, Vibeke Videm: None declared, Tom Nilsen: None declared, Arnulf Langhammer Speakers bureau: Paid as speaker by AstraZeneca, Boehringer Ingelheim, Glaxo-Smith-Klein, Consultant of: Paid consultant for Boehringer Ingelheim and AstraZeneca.
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POS0176 DRUG RETENTION OF BIOLOGICS OR JAKI IN RHEUMATOID ARTHRITIS PATIENTS WHO FAILED TREATMENT WITH JAKI: RESULTS FROM THE ANSWER COHORT

Keywords: bDMARD, Real-world evidence, Rheumatoid arthritis

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Background: Few studies have addressed what is the optimal therapeutic option in patients with rheumatoid arthritis (RA) who failed treatment with JAK inhibitors (JAKi).
Objectives: The aim of this study was to evaluate the drug retention, efficacy, and safety of biologics or JAKi in patients who showed an inadequate response to JAKi in a multicenter longitudinal cohort.
Methods: Patients who showed an inadequate response to JAKi and then switched to TNF inhibitors [TNFi], IL-6 inhibitors [IL-6i], or other JAKi were enrolled in this study. The drug retention rates of the three treatment groups were estimated at 12 months using the Kaplan-Meier method and compared after adjusting for potential confounders using Cox proportional hazards models. Disease activities evaluated with Clinical Disease Activity Index (CDAI) were also compared at 1, 3, 6, and 12 months between the three groups using the Mann-Whitney U test or the Wilcoxon signed-rank test. The reasons for drug discontinuation were analyzed using Fisher's exact test.
Results: A total of 140 treatment courses (TCs) from 106 patients were included (TNFi: 36 TCs, IL-6i: 34 TCs, and JAKi: 70 TCs). Baseline characteristics showed no difference in sex, disease duration, number of previous biologics/JAKi use, and ACPA positivity between the three groups, but the concomitant PSL dose was significantly lower in the JAKi group than in other groups (P=0.049). After adjusting potential confounders, drug retention rates of the three treatment groups did not differ; however, when limited to patients who initiated subsequent biologics/JAKi within 100 days after the termination of prior treatment with JAKi, the TNFi group exhibited a superior drug retention rate compared to the JAKi group (P=0.048, Figure 1A-1C). Regarding disease activity, the baseline CDAI of the TNFi group was significantly higher than the other groups (P=0.01, Figure 1D, 1E); however, the TNFi group tended to show better improvement in disease activity than the other groups. The reasons for drug discontinuation were not different between the three groups.
Conclusion: TNFi may have a therapeutic advantage compared to other therapeutic options in patients who failed treatment with JAKi.

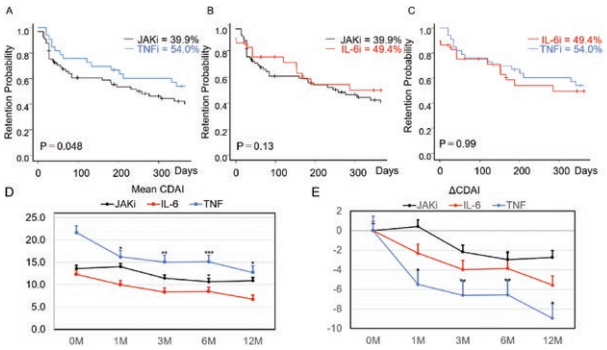


Figure 1. (A) Comparison of drug retention between JAKi and TNFi. (B) Comparison of drug retention between JAKi and IL-6i. (C) Comparison of drug retention between TNFi and IL-6i. (D) Time course of mean CDAI in the three treatment groups. (E) Time course of CDAI improvement compared in the three treatment groups. TNFi, TNF inhibitors; IL-6i, IL-6 inhibitors; JAKi, JAK inhibitors; CDAI, Clinical Disease Activity Index.

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POS0177

INFECTION INCIDENCE, TIMING, AND DOSE DEPENDENCY IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH RITUXIMAB: A RETROSPECTIVE COHORT STUDY

Keywords: Disease-modifying Drugs (DMARDs), Rheumatoid arthritis, bDMARD

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Background: Rituximab (RTX) is a safe and effective treatment for rheumatoid arthritis (RA). In The Netherlands, RTX is usually administered intravenously every six months in standard low dose (2x500 mg or 1x1000 mg). Ultra-low doses (1x500 or 1x200 mg every six months) have shown to be effective as well for continued treatment for RA patients who are in remission.[1] Despite its efficacy and safety, there are some concerns about infection risk for RTX. Preliminary data suggest a dose and time dependent infection risk with a higher risk in higher doses and shortly after infusion.[1,2]
Objectives: The aim of this study was to compare infection incidence rates (IRs) in a real-life population of RA patients between standard low or ultra-low dosed RTX, with an additional focus on time since last infusion.
Methods: RA patients treated with standard low or ultra-low dosed RTX in the Sint Maartenskliniek (The Netherlands) between 2012 and 2021 were included in this retrospective cohort study. Patient-, disease-, treatment- and infection characteristics were retrieved from electronic health records. Infusions given within 30 days were considered as one RTX treatment. As RTX is usually given every six months, only infections occurring within 6 months after administration were included. In absence of the exact date of an infection, the start date was imputed using single imputation based on the known start week, month or period of infection. Infection IRs, dose-dependency and time relations with RTX infusion were analyzed using mixed-effects Poisson regression with correction for confounders. After Bonferroni correction, results were considered statistically significant if p<0.025.
Results: Among 490 patients followed for 1254 patient years, 819 infections were identified (65/100 patient years). Most infections were mild (89%) and respiratory tract infections were most prevalent (49%). Infection IRs were 41, 54 and 71 per 100 patient years for doses of 200 mg, 500 mg and 1000 mg, respectively. Incidence rate ratio (IRR) was significantly lower only for 200 mg in comparison to 1000 mg (adjusted IRR 0.64 (95% CI 0.45-0.93, p=0.019)). Infections seemed to occur more frequently – although not statistically significant - within the first two months after infusion in comparison to later on in the treatment cycle (table 1).
Conclusion: Ultra-low dosing, and especially 200 mg, of RTX is associated with a lower infection risk in RA. Additionally, a trend of higher IR of infections shortly after infusion was found. Therefore, future optimization focusing on ultra-low dosing and slow release of RTX (e.g. by subcutaneous administration) may further lower infection risk in addition to reducing costs and administration time. In clinical practice, physicians should consider offering 500 mg and especially 200 mg RTX dosage to RA patients in sustained remission, instead of continuing the 1000mg dosage.
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Table 1. Infection rates and last received RTX dose/ time since last RTX infusion

Last received dose			
	1000 mg	**500 mg**	**200 mg**
Infections (n)	654	129	36
Patient years	926	241	87
Incidence rate (n/100 patient years)	71	54	41
Crude IRR (95% CI)	1.00 (ref.)	0.77 (0.62-0.95, p=0.014)	0.59 (0.41-0.85, p=0.004)
Adjusted IRR (95% CI)	1.00 (ref.)	0.82 (0.66-1.02, p=0.071)	0.64 (0.45-0.93, p=0.019)
Time since last infusion			
	0-2 months	**2-4 months**	**4-6 months**
Infections (n)	317	259	243
Patient years	443	425	386
Incidence rate (n/100 patient years)	72	61	63
Crude IRR (95% CI)	1.00 (ref.)	0.85 (0.72-1.01, p=0.060)	0.89 (0.75-1.05, p=0.160)
Adjusted IRR (95% CI)	1.00 (ref.)	0.86 (0.73-1.01, p=0.070)	0.90 (0.76-1.07, p=0.244)

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POS0178

DISEASE ACTIVITY GUIDED TAPERING OF RITUXIMAB IN CLINICAL PRACTICE: A RETROSPECTIVE COHORT STUDY OF RHEUMATOID ARTHRITIS PATIENTS

Keywords: Rheumatoid arthritis, Tapering, bDMARD

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Background: The REDO trial (REtreatment with Rituximab in RhEumatoid arthritis: Disease Outcome after Dose Optimisation) showed that ultra-low-dose (500mg or 200mg) rituximab (RTX) was similarly effective to 1000mg in the majority of rheumatoid arthritis (RA) patients. [1] These results led to the implementation of a disease activity guided dose optimization (DAGDO) protocol for RTX at the Sint Maartenskliniek since January 2019. This protocol includes stepwise tapering of RTX (after the initial dose of 1000mg) towards 500mg, 200mg and full withdrawal if DAS28-CRP < 2.4 (or 2.9 in patients with disease duration >3 years).
Objectives: We aimed to validate the findings from the REDO study in clinical practice, by determining the effect of RTX tapering on disease activity and RTX dosage compared to standard low dose RTX treatment (≥1000mg every six months).
Methods: A retrospective cohort was conducted of patients who 1) used RTX between April 2012 and February 2022, 2) had a clinical diagnosis of rheumatoid arthritis (according to either 1987 or 2010 ACR criteria, and/or by clinical diagnosis from the treating rheumatologist, 3) were eligible for dose reduction (i.e. reached a DAS28-CRP score of 3.5 or lower for at least 6 consecutive months during RTX use), and 4) had at least two DAS28-CRP measurements during follow-up. We identified three treatment periods for which we compared the mean disease activity scores: (i) full dose RTX continuation period, (ii) RTX DAGDO period, and (iii) stable RTX dose (and interval) after DAGDO (at least 12 months after the last tapering attempt). Primary outcome was the difference in mean DAS28-CRP between the three treatment periods. This was analysed using a linear mixed-model with a random intercept, including age, disease duration, concomitant csDMARD use (all

at moment of DAS28 measurement), seropositivity for ACPA and/or rheumatoid factor and sex as potential confounders. The mean percentage of the rituximab Daily Defined Dose (%DDD) per treatment period was calculated as secondary outcome, with 1000mg/6months as 100% reference.

Results: A total of 387 patients were included in the cohort, with a mean of 9.2 DAS28-CRP measurements (SD: 6.0) available per patient. Median follow-up time was 46 months (IQR: 25-78). 299 patients attempted tapering during follow-up and entered period 2 at least once, of whom 226 also entered period 3. The mean DAS28-CRP was 2.37 (95% CI: 2.29, 2.44) for period 1, 2.32 (95% CI: 2.24, 2.40) for period 2, and 2.27 (95% CI: 2.18, 2.36) for period 3, the latter significantly lower compared to period 1 (p=0.022). The mean percentage of the DDD for the three time periods was 111% for the continuation period; 64% in the DAGDO period and 71% in the stable RTX dosage period.

Conclusion: This relatively large retrospective cohort study shows that DAGDO of RTX is effective for rheumatoid arthritis patients doing well on full dose rituximab, and leads to relevant dose reduction. The lower mean disease activity scores in period 3 may be affected by survival bias, as solely patients using RTX successfully for a longer time reach period 3. However most patients that entered period 2 also entered period 3, and mean disease activity in period 2 was not increased compared to period 1. Wide implementation of tapering protocols for RTX in RA patients should be contemplated.

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[1] LM Verhoef et al. Ultralow dose of rituximab for continued treatment of rheumatoid arthritis (REDO study): a randomized controlled non-inferiority trial. Lancet Rheumatol 2019;1: 145–53.

AQ1 **Table 1. Baseline characteristics of the cohort**

	N=387
Age	63 (12)
Female sex	282 (73%)
Time since diagnosis (years)	12 (5-19)
Seropositivity (RA/ACPA)	333 (86%)
Number of previous bDMARDs	0: 30 (8%)
	1: 57 (15%)
	2: 205 (53%)
	≥3: 95 (29%)
Concomitant use of ≥1 csDMARD during follow-up	289 (75%)
Follow up time (months)	46 (25-78)

Data are n (%), mean (SD) or median (IQR). RF: rheumatoid factor; ACPA: Anti-cyclic citrullinated peptides; bDMARDs: biological DMARDs; csDMARDs: conventional DMARDs.

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POS0179 PAIN CHARACTERISTICS IN PEOPLE WITH ACTIVE RHEUMATOID ARTHRITIS RECEIVING ADALIMUMAB AND ABATACEPT: A FEASIBILITY TRIAL OF NOCICEPTIVE, NEUROPATHIC AND PAIN SENSITISATION COMPONENTS

Keywords: Pain, Clinical Trials, bDMARD

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Background: There has been recent advancement of our understanding of pain in rheumatoid arthritis (RA). With the advent of biologic disease-modifying anti-rheumatic drugs (DMARDs), clinicians managing RA have a wide range of treatments to manage active disease. Many DMARDs are effective at achieving suppression of inflammation, but pain remains a key issue in RA. Despite nociceptive pain being a major feature of RA, other aspects of RA pain are associated with neuropathic and nociplastic components. Nociplastic pain is described as widespread, without evidence of proportionate tissue or nerve damage. Pain processing by the central nervous system can maintain and increase RA pain.

Objectives: This study aimed to evaluate the causes and underlying mechanisms of pain in RA by conducting a randomised feasibility trial. Our study evaluated the pain characteristics in subjects with RA randomised to different classes of biologic therapy including TNF inhibitors (adalimumab) and T cell modulators (abatacept). In this study, we evaluated distinct aspects of pain including nociception by Visual Analog Scale (VAS), neuropathic (PainDETECT questionnaire) and nociplastic pain components using pain pressure thresholds (PPT) by quantitative sensory testing (QST).

Methods: A total of 25 participants were recruited between August 2020 and October 2022; 13 subjects were randomised to adalimumab and 12 to abatacept. All participants continued with methotrexate therapy during the study ranging between 10-25 mg weekly. The primary outcome measures included change in VAS for pain, painDETECT and PPT after 12 months' treatment in each arm. PPT were measured using a hand-held algometer (Somedic) in the wrist and finger joints, large joints, sternum and malleolus, with 3 readings taken per region and a mean value recorded (kPa) as we have previously described [1]. Subjects were also stratified by CCP antibody status.

Results: The mean age was similar in the two groups (abatacept: mean (SD) 56.5 (13.5) years versus adalimumab: 53.9 (12.4) years). There were 12 (92%) female participants in the abatacept group and 10 (83%) in the adalimumab group. All subjects recruited to the study had a Disease Activity Score (DAS28) greater than 5.1 at baseline. There was an improvement from baseline over 12 months of follow-up in VAS pain, with a mean (SEM) of 3.7 (0.82) in the abatacept group and 2.3 (1.10) in the adalimumab group. For painDETECT measures, there was an improvement in painDETECT scores from baseline over 12 months of treatment (mean (SEM)) by 5.8 (1.93) in the abatacept group and 4.6 (2.54) in the adalimumab group. The change in PPT measures over 12 months is shown in Figure 1. Higher (positive) values for PPT indicate a higher pain threshold, Figure 1 shows a mean improvement with all subjects being able to tolerate more pain on pressure algometry.

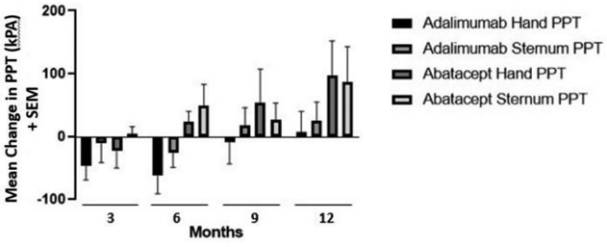


Figure 1. Changes in PPT in the study population over time

Conclusion: This study demonstrates that subjects with active RA demonstrate specific modalities of pain, including nociceptive, neuropathic and nociplastic elements. Furthermore, biologic therapies with different mechanisms of action may improve RA pain through distinct mechanisms. A greater improvement was observed in central (sternum) and peripheral (hand) pain sensitisation with abatacept compared with adalimumab after 12 months' treatment. It is suggested that abatacept, a T-cell modulator, resulted in a greater improvement in pain sensitisation compared with adalimumab. Since T cells are involved in pain mediation, including by infiltrating nerves and impacting memory T cell function, further work is required to investigate the impact of T cell modulation on pain in RA. Larger future studies are required for validation of our findings.

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POS0180 ACR20 RESPONSE AS SURROGATE OF ACR70 RESPONSE IN RHEUMATOID ARTHRITIS: A TRIAL-LEVEL ANALYSIS FROM A SYSTEMATIC REVIEW OF RANDOMIZED TRIALS

Keywords: bDMARD, Clinical Trials

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Background: The approval by medicines regulatory agencies of new therapeutic agents in rheumatoid arthritis (RA) is based on results of phase III randomized controlled trials. The RA trials have been mainly used ACR20 response as primary endpoint. Conversely, this outcome is not clinically relevant for significant improvement of patient's quality of lile.
Objectives: We aimed to explore the surrogacy between ACR20 and ACR70 in rheumatoid arthritis.
Methods: We performed a systematic review search by screening randomized clinical trials registered in MEDLINE, EMBASE and the Cochrane Library between January 1990 and June 2021. We included all randomized trials (phase II and III trials, including multiarm design) that compared biotherapies or JAK inhibitors with csDMARDs or placebo with available ACR20 and ACR70 response. The coefficient of determination R2trial between these two outcomes were estimated using weighted metaregression. To validate the surrogacy, the coefficient of determination (R^2trial) should be superior than 0.65 and close to 1. The lower limit of 95% prediction interval needed to be upper than 0.5 to predict a weak surrogacy and upper than 0.72 to predict a strong surrogacy. The 95% prediction interval for R2trial was calculated with the percentile bootstrapping method.
Results: We included 189 randomized trials totalizing 81,734 patients. Using 322 comparisons, the coefficient of determination R^2trial for estimating the relation between ACR20 on ACR70 responses is 0.55 (95% prediction interval 0.47-0.63). In subgroup analyses, the R^2trial for the anti-TNF therapeutic class was 0.69 (95% prediction interval 0.56-0.78). The R^2trial in other subgroup analyses (double-blind design, superiority studies, multicentric studies, year of publication, corticosteroid use, small-study effect, and other therapeutic classes) were not relevant for surrogacy.
Conclusion: There is no surrogacy between ACR20 and ACR70 in RA. The use of ACR20 as primary outcomes should be limited to phase II trials and is not suitable for health technology assessment of benefit-risk ratio.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0181

THE IMPACT OF AUTOANTIBODIES (RF AND ACPA) ON THE EFFICACY OF BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS: META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Keywords: Outcome measures, bDMARD, Rheumatoid arthritis

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Background: The impact of autoantibodies on the efficacy of biological disease-modifying antirheumatic drugs (bDMARDs) in patients with rheumatoid arthritis (RA) is not yet clear. Despite the fact that this information has been collected by several randomized controlled trials (RCTs), efficacy data for seropositive and seronegative patients separately have generally not been published.
Objectives: To comprehensively investigate the efficacy of bDMARDs in patients with RA with RF/ACPA compared to patients without these autoantibodies.
Methods: Previous systematic literature reviews performed by EULAR RA management task forces were searched for relevant RCTs published before February 2016[1–3]. RCTs including both autoantibody-positive (≤80% of total population) and -negative RA patients were eligible. We contacted authors and/or sponsors of RCTs to report aggregate results from analyses of individual patient data on clinical efficacy outcomes stratified for the presence of autoantibodies (RF+ vs RF-, ACPA+ vs ACPA-). Per trial, relative risks (RR) or mean differences comparing two groups (RF+ vs RF-, ACPA+ vs ACPA-) were calculated for various outcomes (ACR 20/50/70, DAS28 remission, delta DAS28, delta HAQ and radiographic progression) at the timing of the primary endpoint for the bDMARD-arm and the non-bDMARD-arm separately. Subsequently, relative risk ratios (RRRs) were computed, as the ratio of RR of the bDMARD-arm and the RR from the non-bDMARD-treated arm, reflecting whether seropositivity preferentially affected treatment response to bDMARD therapy. A meta-analysis was conducted using a mixed-effect meta-regression in subgroups of patients according to baseline autoantibody status.
Results: Data from 28 eligible RCTs were analyzed and from 23 pooled: 6 including csDMARD-naïve patients, 14 including csDMARD-inadequate responders (csDMARD-IR) and 3 including tumor necrosis factor inhibitor (TNFi)-IR patients. In csDMARD-naïve and csDMARD-IR, seropositivity was not associated with a better response to bDMARDs: Pooled 6-month ACR20 RRRs were 1.02 (0.88-1.18) and 1.09 (0.90-1.32), respectively (Figure 1A and B). Other outcomes followed the same pattern, with no difference between the groups. In TNFi-IR patients, based on 3 trials, the 6-month ACR20 RRR was 2.28 (1.31-3.95) (Figure 1C), favouring efficacy in seropositive patients. Other outcomes showed a similar effect, although with large confidence intervals and several reflecting a non-significant difference between the groups (Table 1).
Conclusion: In csDMARD-naïve and csDMARD-IR patients, autoantibodies did not have an impact on the efficacy of bDMARDs in RA. In TNFi-IR patients, there is a possible higher efficacy of bDMARDs in the seropositive group, but the low number of trials, large confidence intervals and inconsistent results across outcomes ask for caution in the interpretation. Seronegative TNF-IR patients may have very heterogenous underlying pathophysiological mechanisms, with a lower probability of good treatment response. Overall, in less treatment-resistant patients, the presence of autoantibodies was not associated with the treatment effect of bDMARDs.
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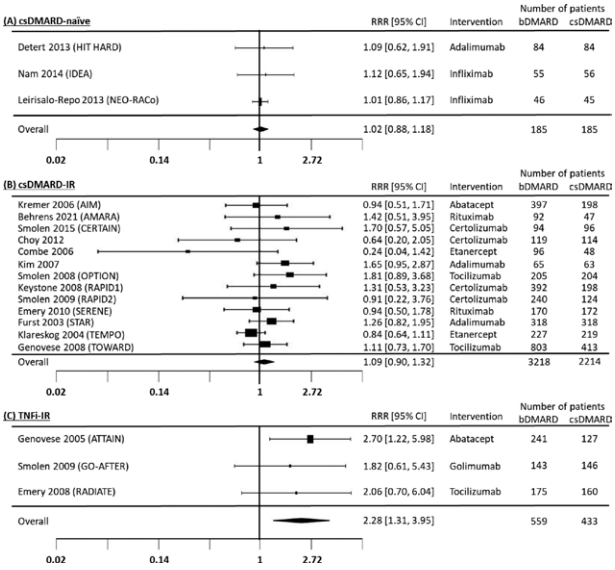


Figure 1. Forest plot for the Relative Risk Ratio for ACR20 at 6 months comparing RF(+)/RF(-) in bDMARD+csDMARD vs RF(+)/ RF(-) in csDMARD.

Table 1. Pooled outcomes in seropositive (RF+) vs seronegative (RF-) TNFi-IR patients at 6 months.

Outcomes	Relative risk ratios/Differences of differences (95% CI)	I^2
	Relative Risk Ratios (95%CI)	
ACR20	**2.28 (1.31, 3.95)**	0%
ACR50	**4.50 (1.35, 15.02)**	0%
ACR70	3.69 (0.42, 32.62)	0%
DAS28-ESR remission	6.56 (0.69, 62.00)	0%
DAS28-CRP remission	4.08 (0.38, 44.14)	0%
	Difference of differences (95% CI)	
Delta DAS28-ESR	**-0.57 (-1.04, -0.10)**	1.06%
Delta DAS28-CRP	-0.45 (-0.95, 0.05)	28.93%
Delta HAQ	-0.04 (-0.21, 0.12)	0%

Statistically significant values ($p < 0.05$) in bold.

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POS0182

RISK-BENEFIT ASSESSMENT OF THE USE OF RITUXIMAB FOR RHEUMATOID ARTHRITIS IN REAL LIFE: FINDINGS FROM 1984 PATIENTS FROM THE FRENCH AUTOIMMUNITY AND RITUXIMAB REGISTRY

Keywords: Rheumatoid arthritis, bDMARD, Safety

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Background: Most randomized clinical trials (RCTs) are explanatory studies examining whether a therapy can work under ideal circumstances. Rituximab (RTX) has been approved for treatment of rheumatoid arthritis (RA) following the results of three RCTs [1–3], including about 1000 patients. However, less than 10% of real-life patients was found to be eligible to these registration trials, because of restrictive inclusion criteria or exclusion criteria such as co-morbidities or undesired co-medication, which questions external validity of these RCTs. Whether the efficacy, tolerance or safety data obtained in highly selected RCTs patients can be extrapolated to a more heterogeneous sample of patients receiving RTX in daily practice, remains to be elucidated.

Objectives: We aimed to identify the main reasons limiting the eligibility of routine care patients in RTX-registration RCTs, and to investigate the relationships between the number of eligibility (both inclusion and exclusion) criteria and RTX efficacy and safety in a real-life scenario.

Methods: The AIR registry is a French nationwide, multicentre, prospective cohort study aiming at investigating efficacy and safety of RTX in a real-life setting. We retrieved eligibility criteria of the drug-registration trials evaluating rituximab for RA and applied them to our population. We compared the EULAR response (moderate-to-good) at 12 months and the incidence of serious adverse events (AEs, including severe infections, malignancies, major adverse cardiovascular events, and death) at 12 months between eligible and non-eligible patients. We modelized the risk-benefit ratios according to the number of fulfilled critical eligibility, defined by those associated with response and severe AEs, respectively, after backward stepwise variable elimination.

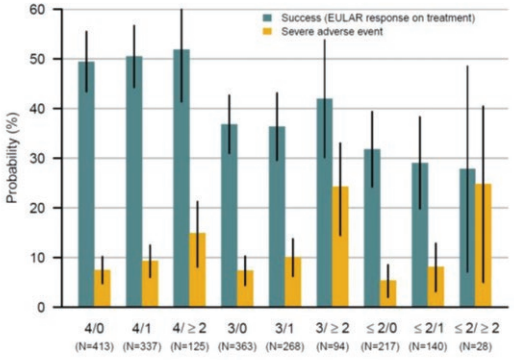
Results: Among 1989 RA patients included in the AIR registry, only 9 to 12% fulfilled all main eligibility criteria for the 3 drug-registration trials. The main unfulfilled inclusion criteria were an elevated CRP or ESR level (67.5%), erosive changes on bone X-ray (68.1%), and a swollen joints count ≥4/28 (74.6%). The main exclusion reasons were a history of severe or recurrent infection (35%), another severe uncontrolled disease (16%), neoplasia (14%), a high prednisone dose (≥ 10 mg/day for 26%), the use of another DMARD than methotrexate (16%) and ACR functional class IV disease (15%). Compared with RCT-eligible patients, non-eligible patients had less frequently moderate-to-good EULAR response (40.3% versus 46.9%, P=0.044), and had a smaller change in DAS-28 (-1.2 vs -1.4; 95% CI 0.1 to 0.5; P=0.005) at 12 months. Compared to patients with no exclusion criterion, patients with at least one critical exclusion criterion had a higher risk of severe AEs (HR 3.03, 95% CI 2.25–4.06 for ≥ 3 exclusion criteria compared to none). While the probability of EULAR response decreased with the number of unmet critical inclusion criteria, the probability of severe AEs increased with the number of exclusion criteria (Figure 1), highly decreasing the incremental risk-benefit ratio.

Conclusion: Few RA patients treated with rituximab fulfilled the eligibility criteria of the main drug-registration trials. Non-eligible patients had less chance of treatment response, and a higher risk of severe adverse events. This suggests that the efficacy and safety data from those trials cannot be extrapolated to RA patients in daily practice.

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Figure. Probabilities of treatment response and of severe adverse events according to the number of fulfilled critical inclusion and exclusion criteria.



X-axis: Number of met critical inclusion criteria / number of met critical exclusion criteria (number of patients). Critical inclusion criteria included a swollen joints count ≥4/28, a tender joints count ≥4/28, CRP ≥15 mg/L or ESR ≥28 mm, and presence of rheumatoid factor. Critical exclusion criteria included age >80, systemic disease associated with RA, ACR functional class IV, concurrent use of any other DMARD (except methotrexate) and a prednisone dose > 10 mg/day.

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Disclosure of Interests: None Declared.

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All about Crystal arthritis II

POS0183 THE UPDATED CARDIOVASCULAR RISK ESTIMATION SCALE SCORE2 DOES NOT IMPROVE THE PRECISION IN PREDICTING CARDIOVASCULAR EVENTS IN PATIENTS WITH GOUT

Keywords: Gout, Crystal Arthritis

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Background: Cardiovascular (CV) risk in gout is increased due to the accumulation of CV risk factors and persistent inflammation. Therefore, it is necessary to have precise evaluation strategies to categorize the risk of patients with gout in order to optimize their treatment. In previous studies, we have seen that the usual prediction scales SCORE and Framingham Heart Study are not accurate in detecting patients with gout and carotid atheroma plaques (PMID 28093417). The SCORE2 version, an update of the SCORE tool, performed similarly in predicting the presence of those plaques [1], although it remains unknown its predictive capacity of CV events in patients with gout.
Objectives: To evaluate the precision of SCORE2 in predicting CV events in patients with gout, with a comparison with prior SCORE and Framingham Heart Study tools.
Methods: We conducted a retrospective post-hoc study on new patients with crystal-proven gouts, from our inception cohort focused on evaluating their CV risk. The recruitment period was 2014-2018. For the present analysis, we selected patients eligible for SCORE2 calculation (without established CV disease, diabetes with vascular involvement or severe renal disease), and we collected the occurrence of a first major CV event (stroke, acute myocardial infarction (AMI), congestive heart failure (CHF), peripheral artery disease (PAD), and CV death) from their electronic records, occurring from study inclusion up to the event, end of follow-up or 03/31/2022. We calculated their incidence rate (IR) and evaluated the predictive capacity for CV events of SCORE 2, SCORE and REGICOR (Framingham equation calibrated for the Spanish population) (PMID: 2622955) tools using a Cox regression model that allows to estimate their hazard ratio with 95% confidence intervals (CI).
Results: Of the initial sample of 356 patients, 193 (54.2%) were selected for this analysis. They were mainly men (94.8%) of middle age (average 56.8 years), with an average of 8.2 years since the first gout flare. Almost all patients originate from low CV risk geographical regions, but only 32 patients (16.6%) classified at high risk by SCORE2. The median follow-up time was 6.4 years (p25-75 5.1-7.1). During the follow-up, 10 patients had a first CV event (3 cases of stroke, 2 of AMI, 2 of CHF, 2 of PA, and one patient died from a CV cause). The IR of CV events in this subset was 0.83 cases per 100 patient-years. In terms of predicting CV events in patients with gout, the SCORE2 tool did not show a better performance than the SCORE and REGICOR (Framingham) tools **(Table 1)**.

Table 1.

	HAZARD RATIO (IC95%)	*P*
SCORE2 (continuous)	1.10 (0.99-1.21)	0.068
SCORE2 categories		
SCORE2_low risk	1.00 (ref)	-
SCORE2_moderate risk	0.97 (0.19-5.01)	0.973
SCORE2_high risk	2.34 (0.39-14.05)	0.351
SCORE2_high risk (yes/no)	2.39 (0.62-9.27)	0.207
SCORE (continuous)	1.09 (0.91-1.29)	0.349
SCORE categories		
SCORE_low risk	1.00 (ref)	-
SCORE_moderado	0.70 (0.07-6.72)	0.757
SCORE_high risk	1.74 (0.20-14.87)	0.615
SCORE_very high risk	15.20 (0.94-244.85)	0.055
SCORE_very high risk (yes/no)	13.70 (1.72-109.02)	0.013
REGICOR (continuous)	1.10 (1.00-1.22)	0.059
REGICOR categories		
REGICOR_low risk	1.00 (ref)	-
REGICOR_moderate risk	2.58 (0.67-9.98)	0.171
REGICOR_high risk	0.00	0.988
REGICOR moderate-high (yes/no)	2.47 (0.64-9.57)	0.190

Conclusion: The SCORE2 tool significate no improvement on accurately predicting CV events in patients with gout compared to previous SCORE and Framingham Heart Study scales. Our data should be replicated in regions with higher CV risk estimates.

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Disclosure of Interests: None Declared.
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POS0184 U-SHAPED ASSOCIATION OF SERUM URATE WITH ALL-CAUSE MORTALITY IN GOUT PATIENTS: NHANES 2007-2018

Keywords: Gout

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Background: The EULAR guideline for the management of gout recommended a target serum urate (sUA) level of less than 6 mg/dl in gout patients and less than 5 mg/dl in tophaceous gout patients [1]. This recommendation is based on the evidence that achieving these targets will reduce gout attacks and tophi size. However, less is known about the impact of sUA on mortality in gout patients.
Objectives: To explore the relationship between sUA level and all-cause mortality in gout patients.
Methods: The present prospective cohort study included participants 20 years or older with gout enrolled from the 2007-2008 through 2017-2018 annual NHANES cycles. The data of mortality and its underlying causes to 31 December 2019 were obtained from the National Death Index records. The relationship of gout patients between sUA level and mortality were analyzed by Cox proportional hazards analysis, the restricted cubic spline regression analysis and two piece-wise regression model.
Results: A total of 1442 gout patients were included with median follow-up period 63 (interquartile range, 33-102) months. Compared with gout patients with sUA less than 6mg/dl, gout patients with sUA>6mg/dl were characterized by greater age, more often men, higher BMI and higher prevalence of hyperlipidemia (P <0.05). Cox proportional hazards analysis showed that sUA was a risk factor of mortality (HR 1.09, 95% CI 1.02 to 1.16) after adjusted by age, sex, race, education, BMI, smoking, cardiovascular disease, hyperlipidemia, hypertension and diabetes mellitus. However, restricted cubic spline regression analysis showed a U-shaped relationship between sUA and all-cause mortality (Pnon-linear <0.001, Figure 1). Two piece-wise regression model revealed sUA level of 6.2 mg/dl corresponded to the lowest mortality risk. For those patients with sUA less than 6mg/dl, the risk of all-cause death was borderline reduced 12% (HR 0.88, 95% CI 0.72 to 1.07) with each sUA unit increase. After 6 mg/dl, the risk of all-cause death increased 26% (HR 1.26, 95% CI 1.14 to 1.40) for each sUA unit increase.
Conclusion: There is a U-Shaped association of sUA with all-cause mortality in gout patients. Target sUA of less than 6 mg/dl is rational as it corresponds to the interval of lowest mortality. Randomized trials with mortality as an endpoint are warranted to determine target sUA for gout patients.

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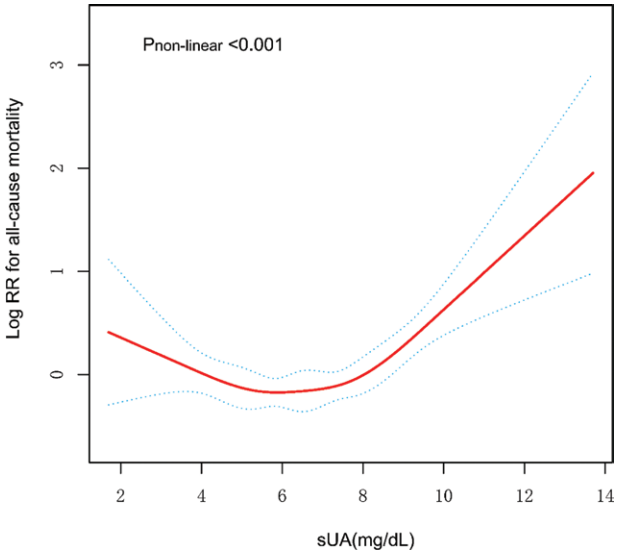


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0185 SYSTEMIC IMMUNE-INFLAMMATION INDEX TO ALL-CAUSE MORTALITY IN GOUT PATIENTS: NHANES 2007-2018

Keywords: Crystal Arthritis

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Background: Systemic immune inflammatory index (SII) is a new marker of inflammation. SII is associated with increased cancer risk and mortality in cardiovascular and cancer patients. However, the effect of SII on mortality in gout patients is rarely reported in the literature.
Objectives: To study the relationship between SII level and all-cause mortality in gout patients.
Methods: This prospective cohort study included participants 20 years or older with gout enrolled from the 2007-2008 through 2017-2018 annual NHANES cycles. The data of mortality and its underlying causes to 31 December 2019 were obtained from the National Death Index records. The SII level was calculated as the platelet counts × neutrophil counts/lymphocyte counts. Gout patients were grouped according to low, middle and high tertile of SII. Generalize linear regression was used to study variables influencing SII. The relationship between SII level and mortality were analyzed by Cox proportional hazards analysis.
Results: A total of 1334 gout patients were included with median follow-up time 68 months (34 months, 106 months). As shown in the Table 1, gout patients with high SII level were characterized by more having chronic kidney diseases, diabetes mellitus and less fiber intake (P <0.05). The generalized linear model found that SII level was positively correlated with diabetes mellitus (P<0.05), and negatively correlated with men, eGFR, fiber intake (P<0.05). Kaplan Meier survival curve showed that mortality was highest in the high SII group (Figure 1). Cox proportional hazards analysis after multivariable adjustment showed that taking low SII group as the reference group, mortality was elevated in the high SII groups (Table 1).
Conclusion: High SII is a predictor of all-cause death in gout patients.

Table 1. Characteristics of gout patients according to low, middle and high tertile of SII.

SII tertile	Low (N=445)	Middle (N=444)	High (N=445)	P-value
Age, years	60.0(53.0,69.0)	62.0(52.0,70.0)	63.0(54.0,71.0)	0.398
Sex, %				0.407
Male	69.3 (60.1,77.1)	73.1 (67.1,78.3)	66.5(59.8,72.5)	
Education				0.199
<high school , %	5.0 (3.3,7.5)	5.8 (3.7,8.8)	5.6 (3.9,7.8)	
High school , %	11.0 (8.0,15.0)	9.1 (6.6,12.4)	10.7 (7.6,14.8)	
High School Graduate or Equivalent , %	21.3 (16.4,27.2)	23.9 (18.2,30.8)	30.4(24.5,37.0)	
College and above , %	62.7 (55.7,69.2)	61.2 (54.1,68.0)	53.4(46.5,60.2)	
Body mass index, kg/m²	30.6(27.0,34.7)	31.2(28.0,35.2)	31.0(27.0,36.4)	0.465
Serum urate (sUA), mg/dL	6.4(5.2,7.4)	6.4(5.5,7.7)	6.6(5.3,7.7)	0.781
Estimated glomerular filtration rate (eGFR), ml/(min·1.73m2)	79.7(63.3,94.0)	78.8(61.5.3,92.8)	73.5(56.6,91.3)	0.060
Chronic kidney disease, %	27.2 (22.0,33.0)	38.9 (32.4,45.9)	40.4(34.4,46.6)	0.004
Cardiovascular disease, %	25.2 (19.8,31.4)	27.5 (22.8,32.8)	30.4(25.4,35.8)	0.387
Diabetes mellitus, %	26.2 (21.9,31.1)	36.7 (29.3,44.7)	38.6(31.8,45.8)	0.018
Hyperlipidemia, %	81.3 (73.6,87.2)	89.2 (85.2,92.1)	83.9(77.6,88.7)	0.075
Hypertension, %	73.7 (67.7,79.0)	75.1 (68.3,80.8)	78.5(72.3,83.6)	0.509
Fiber, g	16.4(10.0,23.3)	14.2(9.5,21.0)	13.2(8.1,19.9)	0.005
Number of death, %	12.1 (9.4,15.4)	15.0 (11.8,19.0)	22.3(18.0,27.3)	<0.001
Hazard ratio (95% CI)*	1.0	1.07(0.73,1.58)	1.56(1.01-2.41)	-

*Hazard ratio analysis were adjusted by age, sex, race, education, BMI, smoking, cardiovascular disease, hyperlipidemia, hypertension and diabetes mellitus, eGFR and dietary covariates.

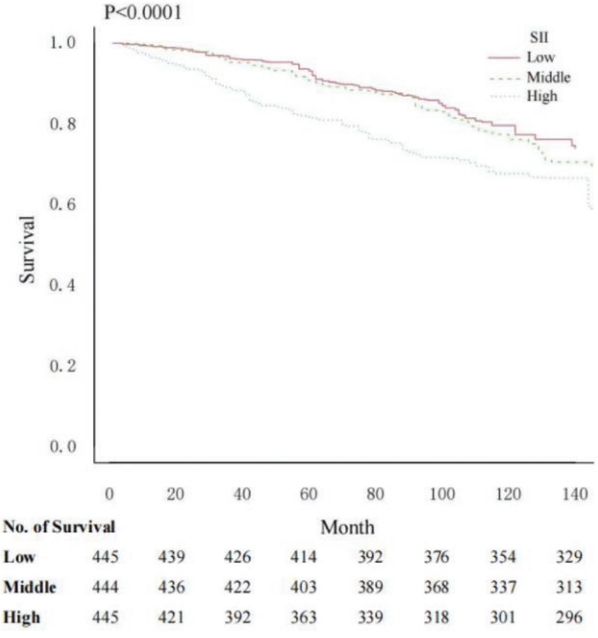


Figure 1. The Kaplan–Meier curves for all-cause mortality by subgroups of SII.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3874

POS0186 OBSTRUCTIVE SLEEP APNEA: A CONTRIBUTING FACTOR IN GOUT?

Keywords: Epidemiology, Comorbidities, Gout

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Background: As per World Health Organization, 7.44 million cases of gout were estimated globally in 2017 (incidence, 0.097%), with a prevalence of 41.22 million cases (0.54%).[1] Obstructive sleep apnea (OSA) is a co-morbidity that has shared risk factors with gout as well as causes pathophysiological mechanisms causing hyperuricemia. The relationship remains contentious. There have been studies, mainly in the UK, which have shown 1.5 times increased risk of gout in patients with OSA [2,3]. While the study by Durme et al shows that the association disappears after statistical adjustment for BMI, renal function, heart failure, and use of diuretics.[4] Thus, it becomes vital to contribute to the existing literature to investigate this relationship further.
Objectives: The aim of the study is to understand the relationship between OSA and Gout.
Methods: TrinetX, a global federated research network that provides a dataset of electronic medical records from different healthcare organizations (HCOs), was utilized. Initial query was made to isolate patients who had a BMI greater than 30 and then 2 groups were made on the presence or absence of OSA. Further, propensity score matching (PSM) was carried out to match age, sex, race, chronic kidney disease, heart failure, and use of diuretics. Compare outcome analytic function was utilized to map the co-relation with Gout.
Results: A total of 3,541,566 patients who had a BMI>30 were identified, out of which 817,638 (23.09%) patients had OSA. Patients in OSA group were older as compared to patients in non-OSA group (59.8 ± 14.3 years vs 54 ± 17.2 years). Females made up 50% of the OSA group while they were predominant (65%) in the non-OSA group. Caucasians were the predominant race, followed by African

Americans. 7.19% of patients with OSA had Gout, while 2.84% without OSA had gout (p<0.0001). The odds of having gout is 2.65 times higher in patients with OSA than patients without OSA (hazard ratio is 2.393, 95% confidence interval (CI) 2.367-2.419, p<0.0001). After PSM, both groups had 801,526 patients. 6.93% patients with OSA had gout while 4.63% of patients without OSA had gout (p<0.0001). Odds ratio =1.533, (95% CI 1.512 - 1.554, p<0.0001) and hazard ratio was 1.404 (95% CI 1.386-1.423).

Conclusion: Our study demonstrated that there is a strong correlation between Gout and OSA. Hypoxia-induced hyperuricemia is the most widespread explanation.[5] However, there are many confounding factors that prompted us to carry out matching for demographics and, more importantly for chronic kidney disease, heart failure as well as the use of diuretics. Statistically significant odds ratio after matching attests to the fact that there is a robust correlation between gout and OSA. Limitation of this study was the lack of testing of this hypothesis on patients with BMI<30. Prospective cohort studies are required to further test the strength of the relationship between OSA and Gout.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0187 HEPATIC STEATOSIS AND FIBROSIS IN PATIENTS WITH GOUT DETECTED BY ELASTOGRAPHY

Keywords: Imaging, Comorbidities, Gout

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Background: Gout is associated with non-alcoholic fatty liver disease (NAFLD), but neither the frequency nor severity of NAFLD in gout is well described. Elastography is a well-established ultrasonic method to evaluate both steatosis and fibrosis in the liver but has not been applied to evaluate gout patients.

Objectives: To determine how common hepatic steatosis and fibrosis are in patients with gout using FibroScan technology?

Methods: We employed FibroScan technology, a validated transient elastography method, to evaluate patients with gout. Consecutive gout patients with insurance coverage were evaluated at one center from 11/1/2016 - 11/12021. We assessed the Fibrosis score (kPA) that measures liver stiffness (E score) and the controlled attenuation parameter dB/m (CAP) score that assesses steatosis. In addition, we assessed the four-factor fibrosis (FIB-4) Index formula that combines the patient's age with aspartate aminotransferase (AST), alanine aminotransferase (ALT), and platelet count.

Results: 47 gout patients (7 females, 14.9%; 40 males, 85.1%) were evaluated. The mean age was 59.8 years, and the mean BMI was 30.95 kg/m2. Tophi were present in 11 (26.2% of those with recorded information). The disease's duration ranged from 0-49 years. Comorbidities included: dyslipidemia (86.7%), diabetes (31.1%), hypertension (63.6%), CHF (12.8%), CAD (12.8%), chronic kidney disease (19.15%), known liver disease (33.3%) and current alcohol consumption (46.8%). 53.7% (n=29) had hyperuricemia (serum urate (SU) >6.8 mg/dL) and 54.4% had elevations of either ALT or AST. Hepatic steatosis (CAP >238 dB/m) was found in 40 (85.1%) and was not significantly different in males or females (p=0.37) or those with CHF (p=0.87), CAD (p=0.94), hypertension (p=0.17), diabetes (p=0.68), dyslipidemia (p=0.59) or the presence of known liver diseases (p=0.37). CAP correlated with BMI (r=0.53, p=0.0001) but not age, SU, glucose, triglycerides, ALT, AST, FIB-4, or Fibrosis scores. By FibroScan, 9 (19.1%) had evidence of fibrosis (E score >7), including one with moderate and 8 with severe fibrosis (cirrhosis). Moderate or severe fibrosis was significantly associated with age (p=0.03) and known liver disease (p=0.003), but not ancestry, gender, BMI, triglycerides, HDL, glucose, gout duration, CHF, CAD, hypertension, dyslipidemia, or diabetes. SU was comparable in those with or without moderate or severe fibrosis (p=0.24). The Fib-4 score was significantly greater in those with severe or moderate fibrosis (3.77) versus those with no or mild fibrosis (1.59, p=0.0045). There was a significant correlation between the Fibrosis score and FIB-4 score (r2=0.24, p=0.0009) but not between the Fibrosis score and ALT (p=0.44) or AST(p=0.41).

Conclusion: Hepatic steatosis and fibrosis are common in patients with gout but not associated with typical gout comorbidities. Screening for NAFLD with elastography should confirm the actual frequency of NAFLD in gout and provide a means to manage this comorbidity more effectively.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Naomi Schlesinger Consultant of: has been on advisory boards and consulting for Novartis, Horizon Pharma, SOBI, Protalix, and ANI., Ankoor Patel: None declared, Vinod Rustgi: None declared, Anthony Yeo: None declared, Peter Lipsky: None declared.

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POS0188 HYPERURICEMIA IS ASSOCIATED WITH CORONARY ARTERY ATHEROSCLEROSIS IN MEN: RESULTS FROM THE SCAPIS STUDY

Keywords: Cardiovascular disease, Crystal Arthritis

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Background: There is considerable controversy on whether elevated urate levels are independently associated with the development of cardiovascular disease (CVD). Segment involvement score (SIS), as a marker of subclinical atherosclerosis, represents the total number of coronary segments with atherosclerotic plaque, calcified and/or non-calcified, and thus reflects the overall burden of coronary atherosclerosis. Extent of coronary artery disease as quantified by SIS is a strong, independent predictor of cardiovascular events [1]. Whether urate levels are associated with SIS has not been previously studied.

Objectives: To study the association between hyperuricemia and SIS in the participants of the Swedish Cardiopulmonary Bioimage Study (SCAPIS).

Methods: SCAPIS is a nationwide, population-based study aiming to improve CVD risk prediction. The study included randomly selected individuals aged 50-64 years recruited at six university hospitals in Sweden during the period 2013-2018 (N= 30,000 participants). We used data from SCAPIS Gothenburg (N= 4,949 participants), including urate levels and SIS, measured by computed tomography angiography (CTA). Individuals with known coronary heart disease and/or gout were excluded. Hyperuricemia was defined as urate levels ≥ 405 µmol/L. The association between hyperuricemia and SIS was assessed by multivariate logistic regression analysis. We calculated Odds ratios (OR) and 95% confidence intervals (CI), crude and with adjustments for age, smoking, body mass index (BMI), diabetes, dyslipidemia, and hypertension. A SIS score >0 was considered to indicate the presence of coronary atherosclerosis and was used as the cutoff value.

Results: In total, 2,438 men (mean age, 57.3 years) and 2,511 women (mean age, 57.4 years) were included. Urate levels were higher in men than in women (mean levels, 348 *vs* 270 µmol/L respectively). Hyperuricemia was more common in men than in women (18% *vs* 2%). Age, BMI, and hypertension showed no differences between men and women, while diabetes and dyslipidemia were more common in men than in women (4% *vs* 2% and 13% *vs* 9%, respectively). Any CTA-detected atherosclerosis (SIS>0) was found in 1,404 (57.6%) men and 752 (30%) women. Hyperuricemia was significantly associated with SIS>0 in men (OR, 1.3; 95%CI, 1.04-1.6), but not in women (OR, 1.3; 95%CI, 0.7-2.3) in the multivariate logistic regression analysis (Table 1).

Conclusion: Hyperuricemia was independently associated with the presence of coronary artery atherosclerosis, as reflected by SIS, in men but not in women. Findings are compatible with a pathophysiological role of urate in atherosclerosis. Whether the observed difference between sexes reflects biological differences in effect of urate or is explained by other factors, such as later onset of atherosclerosis or less statistical power in women will be examined in follow-up studies.

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Table 1. Association between hyperuricemia and coronary artery atherosclerosis, defined as SIS>0.

Urate levels, µmol/L	Men N=2,438				Women N=2,511			
	Unadjusted OR (95%CI)	p-value	Adjusted OR* (95%CI)	p-value	Unadjusted OR (95%CI)	p-value	Adjusted OR* (95%CI)	p-value
<404, ref	1		1		1		1	
≥405	1.5 (1.2-1.9)	0.0002	1.3 (1.04-1.6)	0.02	2.2 (1.3-3.8)	0.003	1.3 (0.7-2.3)	0.4

*Adjusted for age, smoking, body mass index, diabetes, dyslipidemia, and hypertension.SIS, segment involvement score; OR, odds ratio; CI, confidence interval

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Disclosure of Interests: Panagiota Drivelegka: None declared, Helena Forsblad-d'Elia: None declared, Göran Bergström: None declared, Erika Fagman: None declared, Lennart T.H. Jacobsson Speakers bureau: Lennart Jacobsson has received fees for lecturing and Advisory Board meetings from Eli-Lily, Galapagos, Jansen and Novartis, Mats Dehlin: None declared.
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POS0189 COMPARATIVE RISK OF RETINAL VASCULAR COMPLICATIONS IN PATIENTS WITH GOUT INITIATING FEBUXOSTAT VERSUS ALLOPURINOL: A POPULATION-BASED COHORT STUDY

Keywords: Gout, Real-world evidence

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Background: Comparative cardiovascular (CV) safety studies on patients with gout have showed in general a similar risk between allopurinol and febuxostat. However, the data have been derived from macrovascular rather than microvascular CV outcomes.
Objectives: In this study, we aimed to compare the risk of retinal vascular complications among patients with gout initiating febuxostat versus allopurinol.
Methods: Using the 2012-2020 Korean National Health Insurance service database, we conducted a population-based cohort study on patients with gout aged ≥40 years initiating febuxostat or allopurinol. After 1:1 propensity score (PS) matching in non-diabetes (non-DM) and DM subgroups, respectively, on >60 covariates, subgroups were merged for a main cohort. The primary outcome was a composite of retinal vascular complications (retinal vascular occlusions, retinal disorders of retinopathy and vascular changes, degeneration, and hemorrhage, and other retinal disorders). DM retinopathy was investigated as a secondary outcome in DM subgroup. We used Cox proportional hazard models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) comparing allopurinol and febuxostat users. Subgroup-specific HRs were pooled by a fixed effect model.
Results: We included 89,642 PS-matched pairs of febuxostat and allopurinol users in non-DM subgroup and 28,734 PS-matched pairs in DM subgroup, with 118,876 pairs in total (mean 57.3 years, 83.7% male). During a mean 223 days of follow-up, 1,318 composite outcomes occurred. The pooled HR [95% CI] for retinal microvascular complications was 0.98 [0.83-1.15] with 0.94 [0.76-1.15] in non-DM and 1.05 [0.80-1.39] in DM subgroup. The HR [95% CI] for DM retinopathy of 0.86 [0.67-1.11].
Conclusion: In this large cohort study on patients with gout, we found a similar risk of retinal microvascular complications.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1377

POS0190 INFLUENCE OF AGE, PERIOD, AND BIRTH COHORT EFFECTS ON SECULAR TREND IN GOUT INCIDENCE IN THE UNITED KINGDOM

Keywords: Gout, Descriptive Studies, Epidemiology

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Background: The risk of incident gout in the United Kingdom (UK) appears to have declined since 2013.[1] However, whether this is temporary or likely to continue is unclear.
Objectives: To examine the influence of age, calendar year, and year of birth on recent gout incidence in the UK.
Methods: Using data from IQVIA Medical Research Database in the UK, we identified incident gout by READ codes from 1999 to 2019. We grouped age, calendar year, and year of birth into 3-year categories. We assessed the effect of age, calendar year, and birth cohort categories on the incidence rate of gout using the age-period-cohort model among all participants and in men and women separately.
Results: Over the 21 years, there were 164,588 incident gout cases. The incidence rate of gout increased with age until age 80, then leveled off (P for trend <0.001) (Figure 1A). The gout incidence increased from 1999 to 2013, then declined (Figure 1B). The incidence rate of gout was higher in the late birth cohorts than in the early birth cohorts from the Year 1999 to the Year 2013 (Figure 1C); however, such a trend was reversed after the Year 2013, with the incidence rate of gout being higher in the early birth cohorts than that in the late birth cohorts (Figure 1D). Similar patterns were observed in men and women.
Conclusion: Using the age-period-cohort model, we found that the risk of gout in the UK increased from 1999 to 2013 and then declined afterward. These

Table 1. Comparative risk for retinal microvascular complications between febuxostat versus allopurinol initiators

AQ1

	Allopurinol initiators (n=118,376)			Febuxostat initiators (Ref) (n=118,376)				
Outcomes	Events	PY	IR[1] (95% CI)	Events	PY	IR[1] (95% CI)	HR (95% CI)	Pooled HR (95% CI)
Composite of retinal microvascular complications (ICD10: H34.x, H35.x, H36.x excluding diabetic retinopathy)								0.98 (0.83-1.15)
DM[2]	202	17559	1.15 (0.99-1.31)	285	22586	1.26 (1.12-1.41)	1.05 (0.80-1.39)	
Non-DM[3]	341	44331	0.77 (0.69-0.85)	490	60610	0.81 (0.74-0.88)	0.94 (0.76-1.15)	
Retinal vascular occlusions (ICD10: H34.x)								0.89 (0.52-1.53)
DM[2]	15	17787	0.08 (0.04-0.13)	33	22877	0.14 (0.10-0.19)	0.80 (0.32-2.03)	
Non-DM[3]	35	44645	0.08 (0.05-0.10)	47	61065	0.08 (0.06-0.10)	0.94 (0.49-1.83)	
Retinopathy or macular/retinal degeneration (ICD10: H35.x)								1.00 (0.84-1.20)
DM[2]	183	17578	1.04 (0.89-1.19)	248	22618	1.10 (0.96-1.23)	1.05 (0.78-1.42)	
Non-DM[3]	304	44365	0.69 (0.61-0.76)	436	60666	0.72 (0.65-0.79)	0.98 (0.78-1.22)	
Retinopathy with underlying disease excluding diabetic retinopathy (ICD10: H36.x)								0.75 (0.28-1.98)
DM[2]	7	17792	0.04 (0.01-0.07)	12	22900	0.05 (0.02-0.08)	1.67 (0.40-6.97)	
Non-DM[3]	10	44673	0.02 (0.01-0.04)	17	61095	0.03 (0.02-0.04)	0.38 (0.10-1.41)	
Diabetic retinopathy								
DM[2]	198	17574	1.13 (0.97-1.28)	286	22566	1.27 (1.21-1.41)	0.86 (0.67-1.11)	

[1]IR is per 100 person-years, [2]28734 pairs in DM groups, [3]89642 pairs in non-DM groupsCI, confidence interval; DM, diabetes mellitus; HR, hazard ratio; IR, incidence rate; PY, person-years.

findings suggest that some environmental factors occurring after 2013 may play role. Such a downward trend of the risk of gout may continue if these environmental factors are still present.

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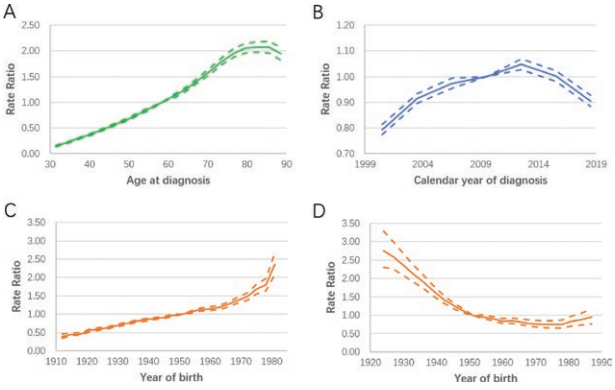


Figure 1. (A) Age rate ratios and the corresponding 95% confidence intervals of gout incidence. The relative risk of each age category compared with the reference age category (57-59) was adjusted for the calendar year and birth cohort. **(B)** Calendar year rate ratios and 95% confidence intervals of gout incidence. The relative risk of each calendar year compared with the reference calendar year (2008-2010) was adjusted for age and birth cohort. **(C)** Cohort rate ratios and the corresponding 95% confidence intervals of gout incidence. The relative risk of each birth cohort (1911-1982) compared with the reference birth cohort (1950-1952) was adjusted for age and calendar year. **(D)** Cohort rate ratios and the corresponding 95% confidence intervals of gout incidence. The relative risk of each birth cohort (1923-1988) compared with the reference birth cohort (1950-1952) was adjusted for age and calendar year.

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POS0191 GENETIC EVIDENCE REVEALS A CAUSAL RELATIONSHIP BETWEEN TRIGLYCERIDE AND GOUT

Keywords: Gout, Genetics/Epigenetics, Lifestyles

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Background: Gout is caused by hyperuricemia that leads to the formation and deposition of monosodium urate (MSU) crystals, which is characterized by acute episodes of joint inflammation [1]. Epidemiological studies observed increased levels of triglycerides in gout [2,3]. Triglyceride is a kind of adipokine primarily transported by very low-density lipoprotein. Enriched in very low-density lipoprotein triglycerides was significantly associated with gout in hyperuricemia [2]. However, the causal association between triglycerides and gout remains unclear.

Objectives: This study aims to use a two-sample Mendelian randomization (MR) to examine associations of triglycerides with gout.

Methods: Summary data for triglycerides used in this study were obtained from a genome-wide association study (GWAS), which included 441,016 European participants within the UK Biobank [4]. The gout GWAS datasets were from a large-scale meta-analysis, which included 69,374 individuals (2,115 cases and 67,259 controls) from European [5]. We selected genetic variation highly related to triglyceride ($P < 5.00E-8$, r2=0.001) as the potential instrumental variables. Three MR methods, namely inverse-variance weighted (IVW), weighted median, and MR-Egger, were applied for MR analysis. For sensitivity analysis, we used common statistical methods, namely Cochran's Q test, MR-Egger intercept analysis, the funnel plot, and the leave-one-out analysis.

Results: After accounting for LD and the harmonization process, the total number of variants included in the MR investigating the effect of triglycerides on gout was 166. Triglycerides were a risk factor for gout (odds ratio (OR)=1.49, 95% confidence interval (CI):1.22-1.82, P=8.16E-05), which was consistent with the MR-Egger (OR=1.40, 95%CI:1.11-1.89, p= 2.93E-02). Cochran's Q test and MR-Egger intercept showed no evidence of heterogeneity and horizontal pleiotropy (MR-Egger-intercept: 0.0025, P=0.583). The leave-one-out analysis also failed to detect any SNPs that may have a disproportional effect (Figure 1).

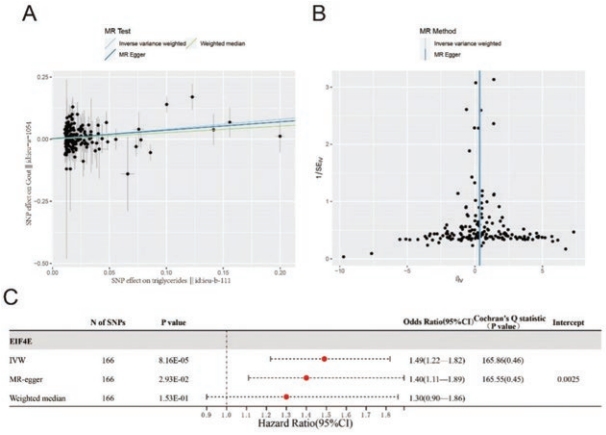


Figure 1. MR analysis results for triglycerides and gout. (A) Scatter plot of single nucleotide polymorphism (SNP) potential effects on triglycerides and gout. The slope of fitted lines represents the estimated MR effect per method. (B) Funnel plot for triglycerides shows the estimation using the inverse of the standard error of the causal estimate with each individual SNP as a tool. (C) Forest plot showing MR analysis results to evaluate the causal association between triglycerides and gout using three methods.

Conclusion: Triglyceride was a hazard factor for gout, even in the absence of hyperuricemia, suggesting that controlling the level of triglyceride and paying attention to diet may be beneficial to prevent the occurrence of gout.

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Disclosure of Interests: None Declared.

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PARE Poster Tour 2

POS0192-PARE TOWARDS A NEW APPROACH ON RESEARCH DESIGNS: PATIENTS AND HEALTHCARE PROFESSIONALS CO-CREATING AND CO-DEVELOPING A MOBILE APPLICATION FOR THE SELF-MANAGEMENT OF CHRONIC PAIN IN OSTEOARTHRITIS. THE TOUS INCLUDE PROJECT

Keywords: Self-management, Patient-led research, Osteoarthritis

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Background: Treatment options for pain in osteoarthritis (OA) aim to reduce or help patients manage their pain efficiently. According to guidelines non-pharmacological therapies are the first treatment option and pharmacological therapies follow. But in many cases pharmacological options are the first choice and researchers are trying to find better ways for OA pain management for both patients and HCPs.

Objectives: Aim of this presentation is to showcase an innovative research design where patients are involved in a project from the planning phase to the implementation and development phase step by step working together with healthcare professionals. The project itself, TOUS Include, aims to integrate a digital intervention and educational activities into a patient centered mobile health application for both the patients and the healthcare professionals to use to help them better manage chronic pain of osteoarthritis.

Methods: The project is co-designed and co-developed from one phase to another. Phase I used a mixed methods gap analysis leading to the basic unmet needs that both groups, patients and HCPs, had regarding management and treatment of chronic pain of OA. Moving on to phase II, co-creation sessions in groups of patients and HCPs led to the basic scenarios, common mistakes and incorrect pathways that both groups take when dealing with everyday pain in OA. Meanwhile educational videos and webinars have taken place with participation from both groups for patients and HCPs.

Results: For phase III, developing of the virtual patient scenarios for the mobile health application, which will be one of the main features of the digital intervention, using data from phase I and II, results have already shown that there is a gap in patient and HCPs communication. The qualitative analysis of data showed that patients' health literacy could be a reason for that as well as lack of enough time for consultations. Another main point is that both groups use more frequently (32,7%) medication to manage chronic pain of OA rather than a non-pharmacological option such as physiotherapy (21,8%). Finally, analysis showed that both patients (medium=4.92) and HCPs (medium=4.7) thought that participating in co-creative sessions is very important (1=lowest, 5=highest).

Conclusion: This innovative research design has involved patients from day one. Its planning, conceptualization and implementation has been involving patients not only at the receiving end of an intervention but as an integral part of the research team, the design and implementation. The TOUS Include project is a collaboration of patients, patient organizations, a university department, a professional health care professionals' society and healthcare professionals. It's quite inclusive, thus an example that could easily showcase how research designs for patients could involve them from beginning to end for the benefit of everyone involved.

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Disclosure of Interests: None Declared.

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POS0193-PARE TIME TO RESEARCH - STRENGTHENING PATIENT RESEARCH PARTNER 2022

Keywords: Education, Rheumatoid arthritis, Clinical Trials

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Background: In Europe the role of patients is growing significantly. In Serbia it is not a case. Our aim is to create a PRP network to bring research closer to patients. Through this network, trust between rheumatologists/researchers and patients, should be increased. Looking in the countries around, Serbia has the longest waiting period for permits to introduce studies. Involving patients in research activities and their active role will provide better chances for patients to be introduced and treated with innovative drugs. Patient's perspective is important part of research, their needs, experiences and even doubts will contribute a lot to research. There are more than 70,000 people who suffer from some kind of inflammatory rheumatic diseases (IRD) in Serbia. These diseases are significant burden for our society. There are quite a few innovative drugs in Serbia, but however, innovative drugs are still unavailable for some diagnosis such as Systemic Lupus Erythematosus, Systemic Sclerosis, Vasculitis, Sjogren.

Objectives: The aims of this EULAR campaign were for us to:

- improve patients education about importance of research in order to increase the availability of innovative drugs with colaboration with Rheumatology Association of Serbia (RAS) and Serbian Association of Health Professionals in Rheumatology (SAHPR)
- found national PRP network
- motivate researchers to accept and involve patients in research as equal team member
- encourage patients to participate/take an active role in research to increase patients' trust in studies
- increase the mutual trust between patients and rheumatologists and health professionals.

Methods: Association of Rheumatic Diseases Patients of the Republic of Serbia now have 15 PRPs. They are members of national PRP network in Serbia. ORS improved cooperation with The Association of the manufacturers of innovative drugs INOVIA, with Medicines and Medical Devices Agency of Serbia – ALIMS, with CRA Academy. Director of the Association of Manufacturers of Innovative Medicines INOVIA, and director of CRA Academy invited us from ORS to promote the campaign "Time2Research" on their events in September and December months, ALIMS (Drug and Medical Device Agency) offered its assistance in improving the legislation for PRPs.

Results: Association of Rheumatic Diseases Patients of the Republic of Serbia now have 15 PRPs. They are members of national PRP network in Serbia. ORS improved cooperation with The Association of the manufacturers of innovative drugs INOVIA, with Medicines and Medical Devices Agency of Serbia – ALIMS, with CRA Academy. Director of the Association of Manufacturers of Innovative Medicines INOVIA, and director of CRA Academy invited us from ORS to promote the campaign "Time2Research" on their events in September and December months, ALIMS (Drug and Medical Device Agency) offered its assistance in improving the legislation for PRPs.

Conclusion: As the PRP network is a completely new institution in Serbia we have to explore all the opportunities for its implementation. We are proud that we establish a PRP network of 15 PRPs and we are making a plan how to engageas many of them as we can. We want to include our PRPs who know English well in the EULAR PRP network.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0194-PARE PEOPLE WITH AN RMD: MAKING A MEDICATION CHOICE TOGETHER WITH THE HEALTHCARE PROFESSIONALS

Keywords: Outcome measures, Patient reported outcomes, Self-management

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Background: Research shows that people with Rheumatic and Musculoskeletal Diseases (RMDs), who decide together with their healthcare professionals make better informed treatment choices. They are also more likely to adhere to their treatment or medication use. A conversation aid can help people with an RMD to become aware of their most important preferences and questions about medication. These preferences and questions can set the agenda for a good conversation in the consultation room between the patient and the healthcare professional. Together with the healthcare professional the conversation can focus on the most important benefits, risks and preferences of someone with an RMD, when a medication choice has to be made.

OBJECTIVES:

- To develop conversation aids, that:
- oallow people with an RMD to become aware of the most important preferences in making a medication choice
- oguide people with an RMD in how to discuss these most important aspects with a healthcare professional
- To develop conversation aids that guide healthcare professionals in giving complete information about:
- oall important aspects of the medication
- ohaving a rheumatic and musculoskeletal disease (RMD)

This in order to make the best fitting medication choice together.

Methods: In the first step of the process 2 focus groups were organized. The first focus group consisted of patients of the Erasmus Medical Centre (5 participants) and patient research partners (PRPs) of the National Association ReumaZorg Nederland (RZN) (4 participants). The second focus group consisted of RMD health care professionals (5 rheumatologists, 1 pharmacist, 7 RMD nurses). The aim of the focus groups was to get an overview of important information that has to be shared, when a choice in RMD medication is to be made. In the second step, the output of both focus groups formed the starting point for the content of the conversation aids about medication choices. In the conversation aids all important information, that should be shared when a medication choice has to be made, was formulated in simple short sentences. After that, the content of the conversation aids was assessed by participants of both focus groups. In the third step, a draft version of the conversation aids about medication choices was designed. The conversation aids were designed using the same layout as our earlier developed conversation aids 'What is important to you and how can you talk about this?'. This draft version was again evaluated by participants of both focus groups, until we reached a final version.

Results: A total of 4 conversation aids (https://reumazorgnederland.nl/samen-beslissen-medicijnkaarten/) were developed.

- Who are you?: To allow people with an RMD to share their preferences with regards to shared decision making (SDM), about the way they like to receive information and about the way they prefer to take their medication.
- About medication: To allow healthcare professionals to give a complete overview of the most important aspects of RMD medication and to allow people with an RMD to share their most important questions about RMD medication.
- Groups of medication: To give an overview of the different groups of RMD medications.
- About arthritis: To give an overview of the most important aspects of having an RMD.

The 5th developed conversation aid (https://reumazorgnederland.nl/samen-beslissen-medicijnkaarten/) focused on reliable sources for information.

- More information: A conversation aid with reliable sources to obtain more information about shared decision making, about having a rheumatic and musculoskeletal disease (RMD) and about RMD medication.

EXAMPLE OF THE FIRST PART OF CONVERSATION AID 'WHO ARE YOU?'



Figure 1.

Conclusion: These conversation aids can encourage and advance a good conversation about RMD medication, that best fits the patient's need and preferences, when having an RMD. They stimulate both the patient as well as the healthcare professional to share much-needed information, when making a choice in medication. A patient organisation can play an important role in developing a conversation aid to support patients.

Acknowledgements: A special word of gratitude goes out to the patient research partners who contributed to the patient perspective in this project by either being part of the working group or by sharing their perspectives in the focus group. Our gratitude also goes out to all the RMD professionals who shared their opinion in the focusgroup.

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POS0195-PARE PATIENT'S AWARENESS TOWARDS PHYSICAL ACTIVITY IN THE TREATMENT OF AXIAL SPONDYLOARTHRITIS

Keywords: Physical therapy/Physiotherapy, Patient information and education

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Background: The course of axSpA is often characterized by impairments in physical function and mobility. Regular physical activity (PA) is a cornerstone of axSpA management. Recent EULAR recommendations for PA have stressed the importance of their implementation [1].

Objectives: To investigate the awareness on and individual implementation of PA in axSpA patients.

Methods: Patients with axSpA and impaired physical function (BASFI score ≥2.0) were recruited consecutively. All patients underwent a clinical examination including assessments of disease activity, physical function, mobility and global function and also filled out structured questionnaires on knowledge, awareness and individual attitudes to PA.

Results: Out of a total of 100 patients enrolled, 96 were included in the final analysis. Most respondents (n=82, 85.4%) were aware that PA has significant health benefits for patients with axSpA. Even though less than half of the patients (n=44, 45.8%) were aware that recommendations about PA do exist, 45 patients (46.9%) did already fulfil these in terms of frequency/week. 75 (78.1%) of patients knew that every adult should perform activities that maintain or increase muscular strength and endurance for a minimum of 2 days/week, while a majority 90 (93.8%) agree with this statement only 46 (47.9%) did fulfil these recommendations. The majority of patients (n=61, 67.7%) had been informed about the benefits of PA by their physician, and physiotherapy had often been prescribed (n=61, 63.3%). Many patients (n=51, 53.1%) reported to perform individual exercise programs, and some (n=22, 22.9%) supervised PA (Table 1).

Conclusion: Even though the majority of axSpA patients are not aware of the recent EULAR recommendations for PA, many understand and agree that PA is beneficial for their health status, while about half of them already fulfill them in their daily life. Measurements for dissemination and implementations on PA recommendations as a treatment target in a broad patient population need to be developed in order to serve the EULAR recommendations for PA. Part of this work was supported by an unrestricted grant by Novartis Pharma GmbH.

Table 1. Knowledge of WHO and EULAR PA recommendations and personal experience of axSpA patient´s, behavior and strategies with PA (n=96)

Statement,	Knowledge of Statement, yes, n (%)	Agreement with statement, yes, n (%)
The WHO general recommendations propose that all healthy adults aged 18–65 years should participate in moderate intensity aerobic PA for a minimum of 30 minutes on 5 days/week or vigorous intensity aerobic activity for a minimum of 20 min on 3 days/week.	44 (45.8)	73 (76.0)
Physical activity has health benefits for patients with axSpA.	82 (85.4)	86 (89.6)
The general PA recommendations are applicable to patients with axSpA (EULAR recommendations for PA)	41 (42.7)	83 (86.5)
Statement/Question,	**Statement applicable for me, yes, n (%)**	
All healthy adults aged 18–65 years should participate in moderate intensity aerobic PA for a minimum of 30min on 5 days/week or vigorous intensity aerobic activity for a minimum of 20min on 3 days/week.	45 (46.9)	
Every adult should perform activities that maintain or increase muscular strength and endurance for a minimum of 2 days/week.	46 (47.9)	
Did your physician ever promoted PA to you?	65 (67.7)	
Did your physician prescribe physiotherapy for you within the last 6 months?	61 (63.5)	
Do you use electronic applications (apps) for physical activity (e.g. fitness programs, pedometer)?	51 (53.1)	
Do you think that such electronic programs (including apps for the mobile phone) are useful?	72 (75.0)	
Do you perform individual exercise (at least 1x/week)?	51 (53.1)	
Do you perform group training (at least 1x/week)?	20 (20.8)	
Do you perform supervised PA (at least 1x/week)?	22 (22.9)	

PA: Physical Activity, WHO: World Health organization; apps: electronic applications

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Disclosure of Interests: None Declared.

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POS0196-PARE SELF-MANAGEMENT STRATEGIES AND SELF-EFFICACY IN PEOPLE LIVING WITH INFLAMMATORY ARTHRITIS: INSIGHTS FROM A QUALITY IMPROVEMENT PROJECT AT A TERTIARY RHEUMATOLOGY CENTRE

Keywords: Inflammatory arthritides, Self-management, Quality of care

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Background: The 2021 EULAR guidelines on self-management have made recommendations (rec) to aid with the implementation of self-management strategies in inflammatory arthritis (IA) [1]. Their aim is to support patients and encourage a patient-centred care approach which can improve both patient experience and outcomes in IA. Self-management can increase self-efficacy which can in turn improve adherence and outcomes for several self-management strategies [2].

Objectives: To assess the implementation of self-management recommendations into routine clinical care of IA patients at a large tertiary rheumatology centre in London. To explore how implementation (or not) of these recommendations may affect self-efficacy.

Methods: A retrospective analysis of the records of patients attending IA clinics at a large tertiary centre in London was undertaken from January 2022 to November 2022. Inclusion criteria included a diagnosis of either RA, PsA or AS. Specific questions addressing the uptake of the 2021 EULAR recommendations were developed (Table 1). The electronic notes were reviewed by two fellows who additionally interviewed patients via telephone, to explore whether the recommendations were addressed at their clinical encounter with the health care professional. Questions to the patients included specific ones addressing self-efficacy using the validated general self-efficacy (GSE) scale. Comparisons between groups were done with χ^2 tests, paired T-tests and Wilcoxon's Rank sum where appropriate.

Results: Fifty patients were included: 50% with RA, 24% with PsA and 26% with SpA. The mean (SD) age of participants was 48 (13) years. The median DAS was 4 (3-5) in RA, SJC and TJC was 2.0 (0.0-10.0) and 2.0 (0.0-8.0) respectively in PsA patients with the median BASDAI of 4 (2-6) in SpA (Table 1). The median GSE was 14 (12-25), where a higher score indicates more self-efficacy. 78% of patients reported feeling involved in the planning of their care and were made aware of the multidisciplinary team (rec 1). 30% felt they were given enough information on disease management (rec 2). Goals and practical points on physical and psychological interventions (rec 3) were mentioned to 50%. For patients where >50% of the self-management recommendations were addressed the mean GSE was 12.64 compared to a mean of 10.52 when <50% of self-management recommendations were addressed.

Conclusion: This study demonstrates that self-management recommendations are not fully and consistently addressed in routine clinics. Furthermore, patient self-efficacy was low/moderate suggesting that clinicians need to do better at discussing and supporting self-management strategies to improve self-efficacy which may also improve disease outcomes.

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POS0197-PARE ANDAI EDUCATIONAL SUMMER CAMP: IMPACT IN CHILDREN AND TEENAGERS WITH JUVENILE RHEUMATIC MUSCULOSKELETAL DISEASES

Keywords: Patient information and education, Non-pharmacological interventions, Best practices

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Background: Paediatric rheumatic diseases include the spectrum of musculoskeletal and connective tissue disorders occurring during childhood[1]. In addition to the physical effects, rheumatic diseases, as chronic conditions, pose a considerable risk for developing psychological distress[2]. Offering an educational camp to children and teenagers with disabilities or chronic diseases is one strategy to enhance adjustment and reduce the psychosocial risk factors related to chronic illness[3]. Thus, a summer camp for children and teenagers with juvenile rheumatic musculoskeletal diseases (RMDs) was created in Portugal in 2018 by the National Association of Patients with Juvenil Arthritis (ANDAI) – the ANDAI Educational Summer Camp (ESC). This annual event (online during the pandemic) provides recreational and supporting facilities for children and teenagers with juvenile RMDs during the summer holiday period. The main goal of ANDAI ESC is to promote the sharing of experiences as well as to support and work on confidence in coping with challenges of a RMD in childhood/youth.

Objectives: This study aims to assess the impact of ANDAI ESC on the lives of children and young people with RMDs. In addition, it also aims to make this project known to the rheumatology community, as well as to inspire other groups and patient associations.

Methods: Participant's data such as age, gender, diagnostic and treatment was collected. The clinical, social and psychological impact of ESC was assessed by a questionnaire applied to the participants after the ANDAI ESC. The perceived impact of the ANDAI ESC by health professionals' volunteers was also evaluated by a different questionnaire.
Results: Forty-five children or young people with RMDs participated in one or more editions of the ANDAI ESC. The median number of participants in ANDAI ESC was 17(9) participants per edition, with a majority of female participants (62%). The median age of participants in the different editions was 12(4) years old. Of those invited to participate in this study, 22 children (48% response rate) and 11 health professionals (53% response rate) completed the survey. The great majority of the participants (95,5%) recognized the positive impact of the ESC on understanding and acceptance of the disease. In fact, after participating in ANDAI ESC, 90.5% of these children claim to have a more optimistic perspective on the evolution of their disease. In addition, when asked on a scale from 0 (no impact) to 10 (significant impact) about the perceived outcome of ESC on their RMD patients, 88.8% of the participating health professionals marked the three higher scaled levels, agreeing that it had a positive effect on these children.
Conclusion: In conclusion this study demonstrates that ANDAI ESC improved patient's confidence in coping with the challenges of a RMD in childhood/youth, reaching the objectives initially defined. Thus, ANDAI ESC proved to be an important resource to the juvenile RMD community in Portugal.
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POS0198-PARE CREATING A CAPABILITY BUILDING PROGRAM BASED ON PATIENT COMMUNITY'S ACTUAL NEEDS AND PRIORITIES: THE SJÖGREN EUROPE EXPERIENCE

Keywords: Best practices, Patient information and education, Sjögren syndrome

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Background: Patients & their representatives are an important stakeholder in healthcare discussions. However, these individuals sometimes lack the appropriate knowledge & training to fully contribute to healthcare decision-making. The Sjogren's community in Europe is represented by groups of various capacities & expertise at the country level but with large national disparities. Sjögren Europe, the European Federation of national associations representing Sjögren's patients, seeks to support as widely as possible its members in leveraging their voice systematically & consistently in multi-stakeholder healthcare discussions, including participating in scientific research & collaborating with medical, social & political institutions.
Objectives: The SE Member Capability Building Program was co-created by Sjögren Europe & the Novartis Immunology Global Patient Engagement team to respond to the needs of the European Sjögren's community, as reported by Sjögren Europe member organizations. Specifically, the program supports Sjögren's patient organizations in building capability and capacity in areas that most matter to them, sharing local experiences & best practices & increasing advocates' knowledge, skills & confidence as leaders of their organizations.
Methods: The content of the Capability Building Program was shaped through a self-assessment in which participating organization self-identified strategic priorities, desired areas for expansion, and current barriers to growth. Questions in the self-assessment were taken from validated, third-party resources, including the PatientView methodology for assessing capacity and impact of patient organizations across eight key indicators[1]. These indicators are business stability, e-communication, services to patients, networking with stakeholders, networking with peer patient organizations, reputation, impact on health policy, and resilience. The results of this assessment were discussed individually with patient organization leaders to outline personalized opportunities for growth. The results were also used to inform a broader webinar training series based on commonly shared challenges & prioritized needs.
Results: 7 SE member organizations, representing 7 countries, participated in the self-assessment highlighting various shared gaps & learning opportunities across the community. Organizational strategy, staff recruitment & retention, external communication strategy & financial strategy were identified as current gaps. Patient organization involvement in drug development, approval & reimbursement processes was identified as an area where all groups would like to learn more. The resulting webinar training series addresses each of these areas of interest to the community. The first webinar "External Communication Strategy: Actionable recommendations for creating awareness campaigns and partnering with the media" was offered November 2022 with an overwhelmingly positive response from the community. Additional webinars are planned for 2023 and will be focused on the above topics.
Conclusion: The self-assessment was crucial in detailing where Sjögren Europe member organizations stand today & where they wish to be in the future. This allowed for the creation of a responsive and actionable webinar training program that meets the actual needs and priorities of the Sjögren's community in Europe. The Member organizations have reported feeling heard and valued as a result of this initiative. The very good feedback encourages us to continue these concrete actions for patient organizations. Program is also a great example of a genuine partnership, following the EFPIA code of conduct[2], between a patient organization and the pharmaceutical industry.
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[2] European Federation of Pharmaceutical Industries and Associations (EFPIA). Working with Patient Organisations. https://efpia.eu/relationships-code/patient-organisations/
Acknowledgements: NIL.
Disclosure of Interests: Katy Antonopoulou: None declared, Ana Vieira: None declared, CORALIE BOUILLOT: None declared, Joyce Koelewijn-Tukker: None declared, Mascha Oosterbaan: None declared, Monia Steenackers Employee of: NOVARTIS PHARMA, Veronica Lopez Gousset Employee of: I am an employee of VLG Consulting which is cooperating with NOVARTIS PHARMA thus I am cooperating with NOVARTIS PHARMA.
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POS0199-PARE RHEUMATOLOGICAL PATIENTS' KNOWLEDGE OF, BELIEFS ABOUT, AND PRACTICES IN USING PHYTOTHERAPY: AN EXPLORATORY STUDY

Keywords: Patient information and education, Descriptive Studies

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Background: Phytotherapy has emerged as a new concept and has quickly and widely spread in recent years. Studies on phytopharmaceuticals in rheumatology practice are very limited.
Objectives: In this study, we aimed to examine the knowledge of, beliefs about, and practices in using phytotherapy in patients who use biological agents, which we can classify as the last and most potent step in treating rheumatological diseases.
Methods: In the first part of the questionnaire, there are 11 questions including the demographic data of the person, and in the second part, there are 17 questions that aim to learn the level of knowledge about phytotherapy and the use of phytopharmaceuticals. The questionnaire was administered face-to-face to patients with rheumatology using biological therapy who gave consent to participate.
Results: The questionnaire was completed by 100 patients, 51 of them women. The mean age was 39±9 years. 39% of the patients were postgraduate and 23% were at the high school. Of the participants, 45 were diagnosed with ankylosing spondylitis(AS) and 29 with rheumatoid arthritis(RA). The duration of rheumatologic disease was 12.2 years All patients were followed up with biological therapy, 35% were using infliximab and 15% were using adalimumab. The mean duration of biological treatment was 6 years. Of the 100 participants, 60% had information about phytotherapy, and 35 of them had obtained it from social media and television. In general, participants had a positive opinion about phytotherapy, and most didn't obtain approval from their physicians for the use of phytotherapy. Among phytopharmaceutical, participants mostly used green tea(30%), linden(27%), centaury(26%), curcumin(20%). There were 5 participants who experienced side effects related to the use of phytopharmaceuticals. 68% of the patients thought that phytopharmaceuticals had fewer side effects than biological therapy. 55 patients said that they would not use biological therapy if cured with phytopharmaceutical use.

Conclusion: It is inevitable that patients with chronic diseases want to use phytopharmaceuticals, as determined in our questionnaire results. Healthcare professionals should be careful about establishing a proper and reassuring relationship with patients and avoid criticizing them for preferring these methods. Patients should be informed about the use of phytotherapy, and be warned about its potential risks and side effects.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0200-PARE HOW USER INVOLVEMENT INCREASED THE QUALITY OF PROS

Keywords: Quality of care, Patient information and education, Patient reported outcomes

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Background: In the DANBIO Registry patients with inflammatory arthritis have entered PROs for more than 20 years. In 2016 a group of patients suggested that their experiences and opinions about entering PROs should be taken into account, as the they found room for improvement. In 2018 a qualitative research study confirmed knowledge gaps in the use and purpose of DANBIO – gaps among patients, front personal and health care providers. In 2022 new results could be implemented.

Objectives: After the research study three different goals were set up:

[1] To increase knowledge of the DANBIO Registry being used for three different purposes.

[2] To make patients aware that they can enter PROs in different ways.

[3] To assure better quality of PROs by enhancing patient's adherence.

Methods: An interdisciplinary user group was established. The group consisted of patients with different types of inflammatory arhtritis, rheumatologists, nurses etc. The group decided to produce different materials for different platforms. The group produced the materials themselves in a cooperation with room for everyone's professional qualifications. The patients could offer patient's experiences as well as being persons with competences from education and worklife.

Results: Three user guides about the use of DANBIO were produced for three target groups. A group of patients scripted, filmed and produced a 5 minutes video providing the patients with relevant knowledge of PROs in DANBIO. The video was filmed at four different rheumatological departments and in patient's private homes. The video wil be shown in the waiting rooms of the hospitals and it can be seen on the Internet.

Conclusion: The work of the user group created a joint understanding and a multi pronged perspective on what "good quality" means in rheumatological care. By clarifying how the same data was presented and used differently various solutions were created to meet the need for more knowledge from staff, increase patient's confidence in entering PROs and increase knowledge of the DANBIO registry in general. The video is provided with English subtitles and can be shown if this abstract is chosen for presentation.

REFERENCE:

[1] www.danbio.dk - www.gigtforeningen.dk

Acknowledgements: DANBIO.

Disclosure of Interests: None Declared.

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POS0201-PARE "MOOD IS HAPPY AND DOWNRIGHT WILD" - HEALTH PROMOTION AND WELL-BEING THROUGH PEER-LED GROUP ACTIVITY

Keywords: Patient information and education, Non-pharmacological interventions, Self-management

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Background: Self-management refers to an individual's abilities and behavior to maintain and improve their own well-being and monitor and control the physical and psychosocial reactions related to their condition to maintain a satisfactory quality of life [1,2]. Self-management is an essential part of treatment alongside medical care. Peer support is based on sharing of information and experiential knowledge among persons living with the same condition. Peer support is seen more and more important in healthcare, and it has been used to improve overall health and promote health behavior and self-management. [3].

Objectives: To promote the health and well-being of those living with rheumatic and/or musculoskeletal diseases, and to support their ability to cope with illness through peer-led "Reumatroppi" group activity. The aim of the group activity is to help participants notice things that increase well-being and health in their everyday lives and turn their thoughts to positive things.

Methods: The Finnish Rheumatism Association trains volunteers to become "Reumatroppi" group instructors. Trained volunteers set up a group and receive a written material consisting of thirty nonmedical health-related topics that are scientifically studied and relevant in management of rheumatic and/or musculoskeletal diseases. Topics include, for instance, resistance exercise, cardiovascular health, nutrition, recovery and rest. In addition, topics such as literature, music, nature, and creativity are included to broaden the view of self-management. The group meets regularly to discuss varying topics and share their experiences and thoughts. In addition, the group does joyous tasks together both indoors and outdoors. A task related to the topic is also given at home before next meeting. Self-report questionnaires with quantitative and qualitative questions are administered to the participants at the end of the group.

Results: In 2021-2022, 86% of participants (n=80) reported paying more attention to their health behaviors (incl. physical activity, nutrition, rest). Additionally, 91% of the participants stated that they had tried to improve their own well-being and health in their everyday lives. 76% of participants had reduced sitting and sedentary time. It is also noteworthy that 80% of the participants reported better mood, and 81% had experienced more enthusiasm in their everyday lives. In addition, 71% of the participants reported that they had been (physically) more active and found more arts in their lives during the group. 81% of the participants had also found new friends in the group.

Conclusion: Peer-led "Reumatroppi" group activity has been able to raise the awareness for self-management among those living with rheumatic and/or musculoskeletal disease. The participants have paid more attention to their health behavior and found new resources that promote their overall well-being.

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[2] Luo, W. et al. 2020. In Mohammed Reem (eds.) Self-Management in Patients with Rheumatoid Arthritis. Rheumatoid Arthritis - Other Perspectives towards a Better Practice. doi: 10.5772/intechopen.91047

[3] Doull, M. et al. 2017. Peer support strategies for improving the health and well-being of individuals with chronic diseases. Cochrane Database Systematic Review 27 (6), CD005352. doi: 10.1002/14651858.CD005352.pub

Acknowledgements: The Reumatroppi project is funded by the Funding Centre for Social Welfare and Health Organisations (STEA).

Disclosure of Interests: None Declared.

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POS0202-PARE CHRONICALLY ACTIVE - A PATIENT EMPOWERMENT PROGRAM WITH PEER SUPPORT

Keywords: Work-related issues, Self-management, Best practices

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Background: Work life disability as a result from musculoskeletal conditions is a tremendous burden both on society and the individual. In Norway 1/3 of all disability pensions are granted on the background of rheumatic disease and musculoskeletal condition. The actual process of getting access to welfare support or a disability pension is built in such a way that it shames and diminishes the individual's sense of value. The process of getting help is in essence DIS-empowering, and trains the patients to hopelessness. The health care system and state pension system have no effective means of helping people overcome the mental and psychological stigmas and traumas associated with their disability. As Norway's largest patient organization in the musculo-skeletal field, we have a strong core of trained and experienced peer supporters. In 2012 we decided to leverage this base of peer supporters to make a positive, solution oriented, patient led self management course that can help patients break the negative cycle of passivity.

Objectives: To create and test a 5-day intensive intervention leading the patients through a guided empowerment process to learn symptom management and health mastery in a safe setting supported by their peers.

Methods: We combined methods from creative process management with existing science based methods on symptom management, motivation, empowerment and lifestyle change, to build a program for the patients consisting of 5 modules. The modules were designed to lead the participants through a group process that activated each individuals inner motivation for making effective lifestyle changes and healthy choices. As part of the process they received a solid framework for continued social support through their local chapter of the patient organization and in an online community. Each module combines 90 minutes of teaching with 30 minutes of physical activity: One module includes mindfulness practice for stress relief and relaxation. The course was called "Sykt Aktiv" which

roughly translates to "Chronically Active", and was marketed in social media to the age group 25-55. 20 participants were included in the first cohort back in 2014, since then the program has been reiterated, improved and repeated on a yearly basis.

Results: After the course, the participants reported that they had learnt a lot and it felt inspiring. But the interesting results came after 1-2 years, when several of the participants were able to go back to work, and they reported that what they learnt in the #SyktAKTIV/ #ChronicallyActive course had been what helped them find the way back.

Conclusion: A peer supported intervention organized by a patient organization has potential to help people with chronic pain and rheumatic conditions return to work life and lead healthy and active lives despite chronic illness.

Additional information: The creators behind this project have had the intention of sending an abstract about it to EULAR at least for the last 6 years. Unfortunately my organization has not seen itself able to prioritize spending money on sending staff to the EULAR congress for many years. Also, my own rheumatic conditions (I have had Scleroderma and Rheumatoid Arthritis since the age 11 & 19) always flare up during winter, and I am usually unable to work during this time of year. I am aware that this abstract doesn't hold the correct scientific standard, but I don't have the spoons (ref. Spoon Theory) to check all the references and have a scientist help me with getting things right. Luckily - the actual conference is in June, and at that time I am usually in a very much stronger physical condition, so I can guarantee that I will be able to participate and present this project orally.

REFERENCES: As stated above, I don't have the spoons to find all the references for this now, but you can contact my colleagues at REMEDY to vouch for my method and my ability to deliver good oral presentations:

Prof. Dr. Espen Haavardsholm.

PhD. Rikke Helene Moen.

Also: Read the original Spoon Theory, by Lupus patient Christine Miserandino here: https://butyoudontlooksick.com/articles/written-by-christine/the-spoon-theory/

Acknowledgements: Kristin Kaldestad Urrang.

Disclosure of Interests: Anna Fryxelius Consultant of: Pfizer - I held a creative project management workshop for a small team at the Oslo Office in 2012

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HPR Poster Tour: Challenges in daily life for people with RMDs

POS0203-HPR THE RELATIONSHIP BETWEEN PATIENT-REPORTED QUALITY OF LIFE AND PHYSICIAN-DERIVED CLINICAL OUTCOMES IN RHEUMATOID ARTHRITIS: AN ANALYSIS FROM THE AUSTRALIAN OPAL DATASET

Keywords: Rheumatoid arthritis, Patient reported outcomes, Real-world evidence

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Background: Remission or low disease activity (LDA) are the common therapeutic targets in the treat-to-target strategy for patients with rheumatoid arthritis (RA). Despite achieving these targets however, some patients continue to experience residual symptoms including pain, fatigue and functional loss. Patient reported outcomes (PROs) are an important tool to better understand the lived experience of the patient which is often not adequately captured by traditional disease activity measurements.

Objectives: To describe the levels of pain, fatigue, mood disturbance and physical function in a large cohort of Australian patients with RA and how they correlate with traditional clinical disease activity measures.

Methods: Clinical data were sourced from the OPAL dataset which is an aggregated collection of data extracted from the electronic medical record (EMR, Audit4, Software4Specialists Pty Ltd) of patients receiving routine care from 112 rheumatologists across Australia. Validated PRO questionnaires were electronically delivered to patients through their EMR via email or completed using a smart device in the waiting room prior to the consultation. Completed questionnaires were securely integrated into the patients EMR for review at the next consultation[1]. Patients with a physician diagnosis of RA and ≥6 months of disease activity recorded who had responded to at least one PRO (Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F), Patient Health Questionnaire-2 (PHQ-2), pain visual analogue scale (VAS) or the Multi-Dimensional Health Assessment Questionnaire (MD-HAQ)), between April 2020 and April 2022 were included. Disease activity was assessed using DAS28(3)-CRP which includes swollen and tender joint counts and CRP, but excludes the patient global assessment.

Results: 1,397 patients completed a pain VAS, 2,180 a FACIT-F, 2,101 a PHQ-2 and 2,243 a MD-HAQ during the study window. The median age of patients with a completed questionnaire was 62 years and 77.1% were female. Levels of pain, fatigue, mood disturbance and physical function for patients with RA are shown in Table 1. Overall, a substantial percentage of patients, (n=519, 37.2%), reported experiencing unacceptable pain (>40mm VAS) and clinically relevant fatigue (FACIT-F ≤ 34) (n=867, 39.8%). Higher levels of pain, fatigue and mood disturbance was associated with higher DAS28(3)-CRP disease activity. Of patients in DAS28(3)-CRP remission or LDA, 32.7% reported unacceptable levels of pain, 36.1% reported clinically relevant fatigue and 11.2% reported possible depression.

Conclusion: In general, we found that higher disease activity scores were associated with high levels of pain, fatigue, anhedonia and depressed moods. In addition, there exists a substantial cohort of patients in routine clinical care with swollen and tender joints counts and CRP levels indicative of remission or LDA that continued to experience unacceptable levels of pain and clinically relevant fatigue.

REFERENCE:

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Table 1. Levels of pain, fatigue, mood disturbance and physical function for patients with rheumatoid arthritis.

Feature	Category	(n, %)
Pain VAS	Unacceptable pain (>40mm)	519 (37.2%)
(n = 1397)	**No pain or acceptable (≤ 40mm)**	**878 (62.8%)**
FACIT-F	Clinically-relevant fatigue (≤ 34)	867 (39.8%)
(n = 2180)	**No fatigue or not clinically-relevant (> 34)**	**1313 (60.2%)**
PHQ-2 Category	Possible depression (≥3)	250 (11.9%)
(n = 2101)	**No depression (< 3)**	**1857 (88.1%)**
MD-HAQ Category	Severe	14 (0.6%)
(n = 2243)	Moderate	438 (19.5%)
	Mild	**913 (40.7%)**
	Minimal	**878 (39.1%)**

Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F); Patient Health Questionnaire-2 (PHQ-2); pain visual analogue scale (VAS); Multi-Dimensional Health Assessment Questionnaire (MD-HAQ).

Acknowledgements: The authors acknowledge the members of OPAL Rheumatology Ltd and their patients for providing clinical data for this study, and Software4Specialists Pty Ltd for providing the Audit4 platform. This study was conducted with the support of an investigator-initiated study grant provided by AbbVie Australia.

Disclosure of Interests: None Declared.

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POS0204-HPR THE ROLE OF ARTIFICIAL INTELLIGENCE IN DETECTING DISTINCTIVE FACIAL FEATURES IN PATIENTS WITH SYSTEMIC SCLEROSIS, A PILOT STUDY

Keywords: Systemic sclerosis, Artificial Intelligence, Diagnostic Tests

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Background: Scleroderma (SSc) is a rare autoimmune fibrosing multisystem disease with high rates of morbidity and mortality. Scleroderma is usually diagnosed by rheumatologists and/or dermatologists. However, a delay in disease recognition may occur due to a delay in referral, as internists and family physicians are not familiar with the disease and its features. Even though, the facial features of the disease are characteristic for scleroderma, diagnosis is usually based on other signs and symptoms (e.g., skin thickening on extremities), and confirmed with investigations such as autoantibody tests, HRCT, and endoscopies. Late presentation of SSc pts. to rheumatologists is commonly reported[1]; patients with dcSSc generally presented to their primary health care Practitioner (HCP) after symptoms had persisted for up to 1 year. **We hypothesize that** facial features of SSc patients are distinctive and can be detected by a trained AI system after processing a mobile phone picture of SSc patient's face through Convolutional Neural Networks (CNN). This system could be used by family practioner and internists, aiding them to increase suspicion of SSc and refer patients in a timely manner.
Objectives: In a pilot study, we aim to examine the ability of an AI facial recognition system to identify SSc related facial features.
Methods: Images of SSc pts were compared to a group of age and sex matched normal faces. Deep Learning (DL) - Artificial Intelligence (AI) algorithms evaluated all the pixels in the facial map and identified their utility in the facial recognition prediction models. Using a transfer learning implementation developed by the Danish Viceron ApS AI company. This core model is well-established and experienced algorithm for AI facial feature recognition, based on > 1 million general public faces for facial feature recognition. AI evaluated multiple layers of mathematical models, either isolated or pooled to generate a predictive model and eliminate unnecessary data. Smoothing and uniformity protocols were established for the obtained through preprocessing for the Convolutional Neural Networks (CNN) (Figure 1).
Results: Images of 60 SSc pts from the internet were compared to a group of age and sex matched normal faces. We developed models among the 60 SSc facial images and matched controls that were able to identify SSc distinctive facial features with variable specificity and sensitivity. Multiple AI models were used on the training set which includes the first 40 patients and as a partial validation step on the other 20 patients with an equal baseline group built from normal faces. The best pre-trained model, fine-tuned on the training set, achieved 80-90% accuracy on the respective datasets. A larger data set, may provide better accuracy, allowing for more generalized facial recognition. The latter is planned, given the initial reasonable success from the pilot study.
Conclusion: Automated pre-processing and the application of AI algorithms in SSc face identification, gave encouraging pilot results (80-90% accuracy). Further testing to develop a larger protocol to establish the effects of race/ethnicity, sex, age, disease duration, disease activity is warranted.
REFERENCE:
[1] Oliver Distler et al Factors influencing early referral, early diagnosis and management in patients with diffuse cutaneous systemic sclerosis, *Rheumatology*, Issue 5, May 2018,

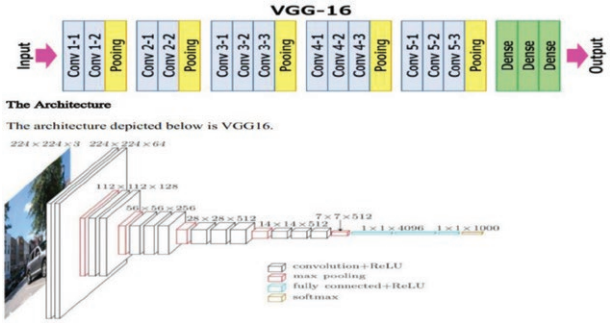


Figure 1. The Visual Geometry Group (VGG)-16 CNN architecture and Inception-V3 architecture represent baseline Deep Learning solutions. Based on the robustness the (VGG)-16 CNN architecture was chosen as a starting point.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0205-HPR

CHARACTERISATION OF RESEARCH PARTICIPANTS: A PRELIMINARY EXPLORATION USING ELECTRONIC PATIENT CASE RECORDS (EPCR)

Keywords: Gender/diversity issues, Descriptive Studies, Health Services Research

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Background: A priority of the National Institute of Health Research is to ensure that research is inclusive at all levels. Underrepresentation of specific demographics affects the generalisability and external validity of trial findings. Clinical research participants should be a proportional and accurate representation of the patient population using the healthcare services. To ensure meaningful outcomes of clinical research, studies require engagement of participants from varied demographics. In April 2019 a new EPCR system (EPIC) was introduced at University College London Hospital (UCLH) that allows data searches of up to 10,000 records. As a first step towards incorporating these priorities in our research work, we explored the EPCR system to establish the characteristics of our research active population.
Objectives: 1. Compare the demographic identifiers of rheumatology patients at UCLH against the patients that have participated in rheumatology research at UCLH. 2. Establish underrepresented groups within the research cohort.
Methods: We extracted a random dataset of 10,000 patients who were associated with the rheumatology department using the electronic patient record database and identified the subgroup of research participants. The demographic identifiers: ethnicity, age, gender, and postcode were extracted for the entire dataset. The deprivation indices were determined using postcodes (1 most deprived, 10 least deprived)[1]. Ethnicity, age, gender, and indices of deprivation were compared between the groups. For descriptive analysis of this work we used the percentage of the population for each identifier of the rheumatology cohort and compared this to the research subgroup.
Results: There were 990 (9.9%) patients who were recorded as a participant of a research project. The ethnicities that had a higher percentage representation in the research subgroup were Black Caribbean (2.96% v 4.65% difference of 1.68) Other Black Background (1.14% v 2.53% difference of 1.38) and Other Mixed Background (1.29% v 2.32% difference of 1.04). Other White Background (9.49% v 7.27% difference of 2.22), Not Stated/ Unknown (2.99% v 1.11% difference of 1.88%) and White British (56.24% v 54.95% difference of 1.29) ethnic profiles had a lower percentage representation in the research subgroup when compared to the rheumatology cohort.

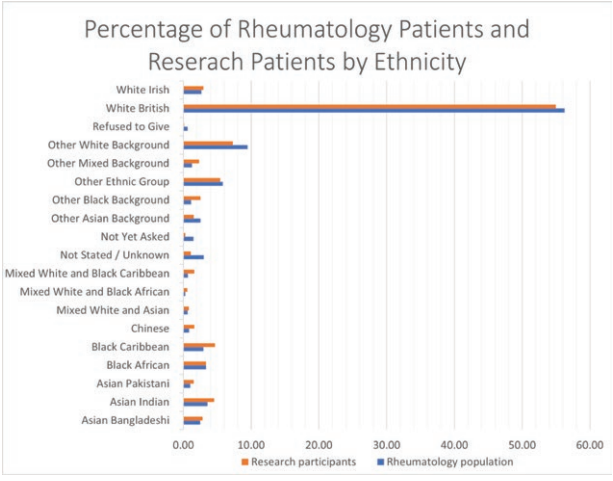


Figure 1.

All patients had a recorded gender of male or female. The rheumatology population was 60.97% female compared to 76.26% in the research subgroup. The deprivation index was 5.39 for the rheumatology cohort compared to the research

population of 5.24. A difference of 12.5 years was seen between the median age of rheumatology patients (61 years) compared to research participants (48.5 years).

Conclusion: From this random dataset analysis approximately 10% of the rheumatology population participated in research. The demographic profile of ethnicity and indices of deprivation were similar across both groups, however proportionately the research subgroup is younger and has higher representation of women compared to the rheumatology population. Limitations of this work include exclusion of research participants prior to the installation of the EPCR, incomplete documentation of research participation within EPCR and sample size limited to 10,000 of the rheumatology population. However, selection bias is reduced due to the large random sample size and generalisability and representativeness is an advantage of this. In view of the low uptake of research participation, it is very important to identify barriers to increasing engagement and involvement in research. Further research is warranted to explore if there are particular age groups that are underrepresented and establish reasons for lack of engagement of men in rheumatology clinical research.

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POS0206-HPR POSTPARTUM DEPRESSION AMONG REPRODUCTIVE-AGE WOMEN WITH AND WITHOUT RHEUMATIC DISEASE: A POPULATION-BASED MATCHED COHORT STUDY

Keywords: Pregnancy and reproduction, Epidemiology, Spondyloarthritis

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Background: Postpartum depression is a psychiatric illness that occurs after the birth of a child and affects 12.5% of women in the United States (1) and 17.2% of women globally [2]. Women of reproductive age with rheumatic diseases (RD) are at increased risk of clinical depression [3]. However, research examining postpartum depression in women with RD is scarce.

Objectives: We examined postpartum depression among women with axial spondyloarthritis (axSpA), rheumatoid arthritis (RA), or psoriatic arthritis (PsA) compared to a matched population without RD in the United States.

Methods: A retrospective analysis using data from the 2013-2018 IBM MarketScan Commercial Claims and Encounters Database was conducted. Pregnant women with axSpA, RA, or PsA were identified, and the date of delivery was used as the index date. We restricted the sample to women ≤ 55 years with continuous enrollment ≥ 6 months before date of last menstrual period and throughout pregnancy (baseline period). Each patient was matched with four individuals without RD on: 1) maternal age at delivery; 2) prior history of depression; and 2) duration of depression before delivery. The outcome of interest was a diagnosis of depression within one year of the index date. Cox frailty proportional hazards models adjusting for sociodemographic and clinical characteristics in the baseline period were used to estimate the crude and adjusted hazard ratios and 95% confidence interval (CI) of incident postpartum depression among women with axSpA, RA, or PsA (axSpA/RA/PsA group) compared to the matched non-RD comparison group.

Results: Overall, 2,667 women with axSpA, RA, or PsA and 10,668 patients without any RD were included. The average age at baseline was 33 years (SD: 5.0), and nearly two in five women were older than 35 years. The median follow-up time in days was 256 (Interquartile range (IQR): 553) and 265 (IQR: 564) for the axSpA/RA/PsA and matched non-RD comparison groups. Development of postpartum depression was more common in the axSpA/RA/PsA group relative to the matched non-RD comparison group (axSpA/RA/PsA group: 17.2%; matched non-RD comparison group: 12.8%; adjusted hazard ratio: 1.22 [95% CI, 1.09 – 1.36). Factors such as pre-existing comorbidities, maternal complications during pregnancy, and antidepressants use at baseline were associated with development of postpartum depression.

Conclusion: The rate of postpartum depression is significantly higher in women of reproductive age with axSpA, RA, or PsA compared to those without RD. Results from this study demonstrate that strategies to monitor postpartum depression after delivery in patients with RD must be developed and implemented to assure prompt referral of affected mothers for appropriate evaluation and treatment.

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Disclosure of Interests: None Declared.

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POS0207-HPR FEAR OF MOVEMENT MEDIATES THE RELATIONSHIP BETWEEN PAIN CATASTROPHISING AND PHYSICAL FUNCTION IN PEOPLE LIVING WITH AXIAL SPONDYLOARTHRITIS: A CROSS-SECTIONAL MEDIATION ANALYSIS

Keywords: Pain, Spondyloarthritis, Patient reported outcomes

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Background: Axial spondyloarthritis (axSpA) typically affects the axial skeleton and sacroiliac joints causing patients to experience pain, reduced movement, and impaired physical function. A range of treatment options are available to help axSpA patients reduce pain and maintain physical function and thereby enhance health-related quality of life. The European Alliance of Associations for Rheumatology (EULAR) identified activity as integral to the management of inflammatory arthritides, however, the majority of people living with axSpA are not sufficiently active to maintain physical function [1]. According to the Fear-Avoidance Model of Pain, fear of movement and pain catastrophizing contribute to poorer physical function via reduced activity and disuse [2]. Yet to date, no research has tested the theorized mediating role of fear of movement in the relationship between pain catastrophizing and physical function in people living with axSpA.

Objectives: To examine the mediating role of fear of movement in the relationship between pain catastrophizing and physical function in people living with axSpA.

Methods: Participants (*N* = 98, 70% female, *M* Age = 45.62 SD 12.16) completed an online survey (December 2020 – May 2021) distributed in the United Kingdom via the National Axial Spondyloarthritis Society (n ≈ 3,500; NASS, 2019). The Tampa Scale for Kinesiophobia (TSK-11) was used to measure fear of movement with participants rating 11-items from 1 (strongly disagree) to 4 (strongly agree). The Pain Catastrophising Scale (PCS) contains 13-items, each rated on a scale from 0 (not at all) to 4 (all the time). Both instruments have shown strong internal consistency in people living with axSpA [3,4]. The Bath Ankylosing Spondylitis Functional Index (BASFI) was used to assess physical function with higher scores indicating poorer function. Data were analysed using IBM SPSS (Version 28). The PROCESS SPSS macro was used, and interpretation made using the percentile bootstrap 95% confidence intervals from 5000 bootstrap samples. Standardised effects with values.01,.09, and.25 represent small, medium, and large effects [5].

RESULTS:

Table 1. Descriptive statistics and Bivariate correlations for the variables.

		M	*SD*	2	3
1	Pain Catastrophizing	18.34	13.65	.647**	.419**
2	Fear of Movement	24.99	7.22		.414**
3	Physical Function	3.73	2.59		

Bivariate correlations showed pain catastrophizing to have a significant medium and positive relationship with physical function and a large positive relationship with fear of movement. Mediation analysis (F = 12.67, p <.05, R^2 =.21) revealed that pain catastrophizing had a large positive direct effect on physical function (β=.259) and fear of movement (β=.647). Fear of movement had a large positive direct effect on physical function (β=.246). A significant medium and positive indirect effect of pain catastrophising on physical function via fear of movement was observed (β=.160, CI =.002 -.320).

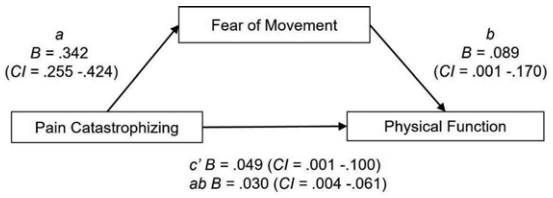


Figure 1. Path model with unstandardised regression coefficients *(B)* and percentile bootstrap confidence intervals (*CI*) identifying the mediating effect of fear of movement in the relationship between pain catastrophising and physical function. *c'* = direct effect, *ab* = indirect effect

Conclusion: Pain catastrophizing is experienced by people living with axSpA and can lead to the avoidance of movement, and as a result, compromised physical function. Our test of the Fear-Avoidance Model showed that pain catastrophizing significantly predicted the physical function of people living with axSpA and that this relationship was mediated by fear of movement. Fear of movement is a modifiable construct that can be a treatment target for health professionals to improve the physical function of people living with axSpA. Identifying modifiable factors that contribute to disease outcomes is critical to improve the care and quality of life for people living with a disease currently without a cure.

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POS0208-HPR PATIENT CHARACTERISTICS AND DIAGNOSIS SETTING OF PATIENTS WITH PAIN ASSOCIATED WITH OSTEOARTHRITIS OF THE KNEE IN GERMANY: A RETROSPECTIVE HEALTH CLAIMS DATA ANALYSIS

Keywords: Osteoarthritis, Pain

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Background: Osteoarthritis of the knee (knee OA) is the most prevalent form of OA in Germany as well as globally[1], frequently leading to pain and functional limitations. Several risk factors have been identified for osteoarthritis, which can be divided into those at the person level (age, sex, obesity, genetic predisposition, physical activity and diet) and those at the joint level (injuries, malposition and overstress)[2]. Patients with OA-like symptoms may present to a number of different medical specialties and therefore arrive at a diagnosis of Knee OA via different routes. The Knee OA population is a highly co-morbid one. In addition to obesity, Knee OA patients often present with hypertension and diabetes[3].

Objectives: The study focuses on knee OA in Germany, aiming to determine the prevalence of OA in the years 2015-2020, diagnosis setting and comorbidities of patients between 2015 and 2020.

Methods: A non-interventional, retrospective health claims data analysis, performed with anonymized, age- and sex-representative sample of the Institute for Applied Health Research Berlin GmbH (InGef) database. The database used for this study includes approximately 4.8 million persons from approx. 60 statutory health insurances (SHI) and is representative for the German population [6]. Patients ≥18 years of age were analyzed cross-sectionally for each year 2015-2020. Using ICD-10-GM and ATC codes.

Results: The prevalence of knee OA ranged from 7.1% in 2015 to 7.6% in 2019, dropping to 7.4% in 2020. The incidence showed a less linear pattern ranging from 1.71% of patients in 2015 and 2016, 1.67% in 2017, 1.61% in 2018, 1.67 in 2019 to 1.46% of patients in 2020. Females and patients aged ≥66 years had both a higher prevalence and incidence proportion compared to males and younger persons. First diagnosis for most patients was made in an outpatient setting (93.4%) by orthopedics (49.88%), general practitioners (28.17%) and specialists (Internist; 9.34%). Most prevalent co-morbidities for patients with Knee OA in all years observed was primary hypertension with >70%. Other metabolic disorders like disorders of lipoprotein metabolism (around 50%), overweight and obesity (28-30%), type 2 diabetes mellitus (around 27%) are among the 10 most common ones. Other musculoskeletal disorders are frequent (dorsalgia 54%; spondylosis 33-34%). The percentage of patients with major depressive disorders is high in all years (23%).

Conclusion: The number of patients with knee OA is slowly increasing from 2015-2019 possibly due to the growing German population, however slightly decreasing in 2020. Diagnosis is mainly done by an orthopedist or general practitioner. The increasing number of certain co-morbidities, mainly of the cardiovascular system (hypertension with the highest percentage), but also due to metabolic condition (Disorders of lipoprotein metabolism and other lipidemias, overweight and obesity, type 2 diabetes) demonstrates that the percentage of patients with known risk factors for knee OA is increasing. Treating pain in patients with co-morbidities can be challenging due to managing drug-drug interactions given the considerable number of treatments patients could be receiving. This can be a high risk for these patients as physicians do not always know about non-prescription co-medications. Models of care for patients with knee OA which include tolerable, non-systemic pain treatments, enabling patient physiotherapy and management of other aspects of their health actively may be a key advancement.

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POS0209-HPR WITHDRAWN

POS0210-HPR

PATIENTS WITH ANKYLOSING SPONDYLITIS HAVE AN IMPAIRED DIETARY INTAKE – PRELIMINARY RESULTS FROM PATIENTS IN SWEDEN

Keywords: Diet and Nutrition

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Background: Ankylosing Spondylitis (AS) is one of most common chronic inflammatory rheumatic diseases, affecting about 0.2 % of the population. As of today, there is no specific dietary guideline for managing AS patients, and no RCT-studies on diet intervention have been published. Furthermore, there is a lack of data on the relevance of dietary quality on disease outcomes in AS patients.

Objectives: The aim of this study was to assess dietary nutrient intake in AS patients and examine whether it differs compared to persons without AS.

Methods: AS patients (modified NY criteria) at the rheumatology clinic in Region Västerbotten, northern Sweden, were invited to take part in the Backbone study which investigates disease severity and comorbidities [1]. In total, 155 patients were included. Nutritional intake was assessed by the semi-quantitative food frequency questionnaire MiniMealQ [2]. Controls were collected from the Swedish CArdioPulmonary BioImage Study (n = 30154) (3), a study that invited randomly selected participants from the Swedish population register, 50-64 years of age. Out of the 155 patients with AS, 81 (52.3%) were in the same age-span. Four controls were collected for each AS patient, matched on age (± 1 year), sex and geographic location. Data on dietary intake was available for 318 controls. Statistical comparisons between patients with AS and controls were done by T-test, Fisher's exact test and by exact conditional logistic regression analysis, adjusted for country of birth, educational level, single household, weight, smoking status and energy intake. Variables already adjusted for energy intake (energy percentages, fiber density and energy intake itself), were analyzed without additional adjustment for energy intake.

Results: Characteristics of the AS patients and controls are shown in the Table 1. AS patients had a higher proportional intake of carbohydrate coupled with a lower fiber density, a lower intake of marine omega-3 fatty acids (Figure 1). Further, a lower intake of vitamin-D, E and K was seen as well as a lower intake of selenium, folate, magnesium, phosphorus, potassium, vitamin-A and β-carotene (a marker of vegetable and fruit intake).

Conclusion: Our results suggest that AS patients have an impaired dietary intake. Notably, intake was lower in several nutrients theorized to have anti-inflammatory properties (fiber density, marine-omega-3 fatty acids, vitamin-D and selenium). Further, we propose that nutrition screening might be incorporated in the management of AS patients since they appear to have an increased risk of nutritional deficiencies.

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Table 1. Characteristics of patients with ankylosing spondylitis and age- and sex-matched controls

	Patients with AS, n = 81	Controls, n = 318	
	Mean ± SD or N (%)	Mean ± SD or N (%)	P-value
Age (year)	57.9 ± 4.8	58 ± 4.6	0.9
Male	54 (66.6)	210 (66.0)	1.0
Height (cm)	171.5 ± 9.6	174.7 ± 8.5	**0.003**
Weight (kg)	84.9 ± 21.8	82.9 ± 15.8	0.4
Symptom duration (year)	34.6 ± 8.4	-	
HLA-B27 positive	80 (98.8)	-	
ASDAS-CRP	1.9 ± 0.76	-	
BASFI	3.3 ± 2.2	-	
mSASSS [1]	22.3 ± 22.1	-	
Median (25p, 75p)	16.0 (3.8, 34.8)	-	
Energy intake (kcal)	1810 ± 727	1740 ± 653	0.4
Born in Sweden	79 (97.5)	296 (93.1)	0.1
Single household	18 (22.2)	51 (16.0)	0.2
Ever been a smoker	42 (51.8)	142 (44.7)	0.3
Educational level			0.2
Junior high school or lower	6 (7.4)	35 (11.0)	
Senior high school	51 (62.9)	166 (52.2)	
College or university	24 (39.6)	117 (36.7)	

[1] Due to non-normal distribution, median and 25th and 75th percentiles are shown.

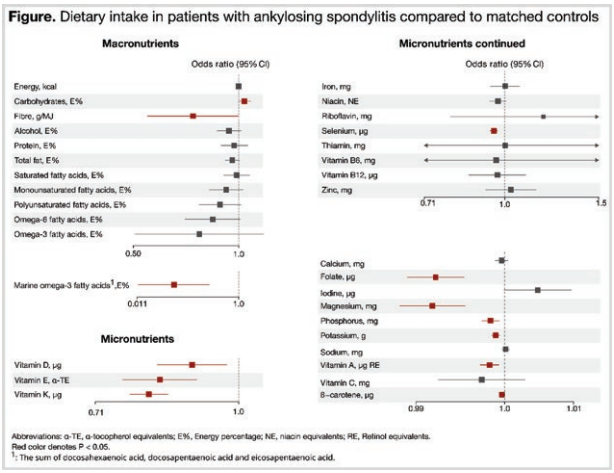


Figure. Dietary intake in patients with ankylosing spondylitis compared to matched controls

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Disclosure of Interests: None Declared.
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POS0211-HPR REDUCED SLEEP QUALITY IS HIGHLY PREVALENT AND ASSOCIATED WITH PHYSICAL FUNCTION AND CARDIORESPIRATORY FITNESS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Physical therapy/Physiotherapy, Rehabilitation, Spondyloarthritis

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Background: Sleep is an important aspect of health for patients with axial spondyloarthritis (axSpA)[1], and it is therefore essential to identify modifiable factors related to reduced sleep quality.
Objectives: To assess sleep quality and the associations between sleep quality and physical function, cardiorespiratory fitness and spinal mobility in patients with axSpA.
Methods: In this cross-sectional study, baseline data from the ESpA trial[2] was used. The assessments included sleep quality (Pittsburg Sleep Quality Index, PSQI) assessing 7 aspects of sleep quality (each scored 0-3, ≥2 reduced sleep quality), summed into a global score (0-21, 21=worst), performance-based physical function (Ankylosing Spondylitis (AS) Performance Index, ASPI; time), patient-reported physical function (Bath AS Functional Index, BASFI; 0-10, 10=worst), cardiorespiratory fitness (VO_2peak, ml/kg/min) and spinal mobility (Bath AS Metrology Index, BASMI; 0-10, 10=worst). Associations between PSQI (global score) and ASPI, BASFI, $V0_2$peak and BASMI were examined in separate models using linear regression analyses, controlling for age and sex.
Results: A total of 99 patients with axSpA were included, 55% male, mean age 46 years and 72% with high disease activity (ASDAS >2.1). Reduced sleep quality (PSQI global score >5) was found in 85% of the patients. The most frequently affected aspect was sleep disturbances (65%) followed by poor subjective sleep quality (53%), daytime dysfunction (41%) and increased sleep latency (41%) (figure 1). Adjusted for age and sex, statistically significant associations were observed between PSQI and ASPI (β=0.10, 95% CI=0.01, 0.19) and BASFI (β=0.85, 95% CI=0.51,1.20) and an inverse association between PSQI and VO_2peak (β= -0.14, 95% CI=-0.27, -0.01) (table 1), indicating that better sleep quality is associated with better performance-based and patient-reported physical function and higher cardiorespiratory fitness. There was no association between PSQI and BASMI.
Conclusion: Reduced sleep quality is highly prevalent in patients with axSpA, with disrupted sleep most frequently reported. Better sleep quality was associated with better physical function and higher cardiorespiratory fitness, but there was no association with spinal mobility. The results signify physical function and cardiorespiratory fitness as modifiable factors that are independently associated with sleep quality in patients with axSpA.

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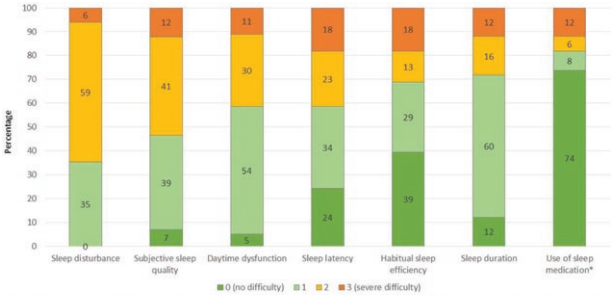


Figure. Bar graphs illustrating the proportion of patients with axial spondyloarthritis (n=99) scores in the different aspects of sleep quality included in Pittsburgh sleep quality index. In each aspect, the score ranges from zero to three, and a score ≥2 indicates reduced sleep quality.
*Score: 0 = not during the past month, 1 = less than once a week, 2 = once or twice a week, 3 = three or more times a week

Table 1. Associations between sleep quality and performance-based physical function, patient-reported physical function, cardiorespiratory fitness and spinal mobility in patients with axial spondyloarthritis

		Sleep quality (PSQI global score 0-21, 21 = worst)	
	n	Crude estimates β (95% CI)	Adjusted estimates β (95% CI)
Performance-based physical function (ASPI, time in sec)	66	**0.10 (0.02, 0.18)**	**0.10 (0.01, 0.19)**
Patient-reported physical function (BASFI, 0-10, 10=worst)	99	**0.84 (0.50, 1.18)**	**0.85 (0.51, 1.20)**
Cardiorespiratory fitness (VO_2peak, ml/kg/min)	99	**-0.12 (-0.23, -0.01)**	**-0.14 (-0.27, -0.01)**
Spinal mobility (BASMI, 0-10, 10=worst)	98	0.12 (-0.46, 0.70)	0.19 (-0.43, 0.82)

Univariate and multivariate linear regression analyses of association between sleep quality and performance-based physical function, patient-reported physical function, cardiorespiratory fitness and spinal mobility, respectively. Age and sex were entered as covariates in the adjusted estimates. ASPI: Ankylosing Spondylitis (AS) Performance Index, BASFI: Bath AS Functional Index, BASMI: Bath AS Metrology Index, PSQI: Pittsburgh Sleep Quality Index, VO_2peak: peak oxygen uptake

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POS0212-HPR VOCATIONAL REHABILITATION FOR PEOPLE WITH INFLAMMATORY ARTHRITIS – AN EMPLOYER PERSPECTIVE

Keywords: Work-related issues, Inflammatory arthritides, Non-pharmacological interventions

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Background: After diagnosis, people with inflammatory arthritis (IA), i.e., rheumatoid arthritis, psoriatic arthritis and axial spondyloarthritis, often experience reduced work ability and increased sick leave. As a result, they have an increased risk of job loss and permanent exclusion from the labour market.

Vocational rehabilitation (VR) is complex. VR includes a variety of components that aim to increase work ability and prevent sick leave and job loss. Effects of VR for people with IA are sparse [1]. To develop relevant VR in Denmark for people with IA, a good understanding of the employer perspective is important, as their involvement is crucial to effective VR.

Objectives: To explore how employers support their employees with IA to maintain their jobs and prevent sickness absenteeism and job loss.

Methods: A qualitative, explorative design was applied, based on a phenomenological and hermeneutic approach. We invited employer representatives (n=13) from workplaces where people with IA were employed (public and private companies with 11- 380 employees). An interview guide was developed based on qualitative research and the theory of occupational justice [2]. Individual semi-structured interviews were performed from November 2020 to February 2021. Data were analysed using Kirsti Malterud's systematic text condensation.

Results: Three themes were derived from the analysis:

1) *Participation in work*. All employer representatives were aware of and wanted to help solve their employees' challenges at work, but it was complicated and time consuming for them. They supported their employees through adaptation and prioritising of work tasks, arranged flexible working hours and were aware of the employee's need to balance work and family in everyday life. The employer representatives considered that the employees needed to be motivated, if job loss was to be prevented.
2) *Relationship between employer and employee.* In general, the employer representatives found it important for the employee to have trust in the employer and ask for help, in order to receive support. To prevent job loss, the relationship was essential. Furthermore, they made a big effort in supporting the employee. They stretched to meet the needs of their employees and they found that empathy was an important quality.
3) *Multidisciplinary collaboration.* The employer representatives involved the municipal job centres regarding legislative offers when necessary, and they requested the employee for collaboration with the healthcare professionals involved in treating the employees' IA. Furthermore, they asked for guidance from relevant trade unions, to find out about legislation in relation to sick leave.

Conclusion: Overall, the employer representatives wanted to support their employees with IA and to be involved in VR, even though preventing sick leave and job loss was experienced as complicated, time consuming and costly for the companies.

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POS0213-HPR ESTIMATING REPLACEMENT OF SEDENTARY TIME WITH LIGHT AND MODERATE INTENSITY PHYSICAL ACTIVITY TO REDUCE CHRONIC MUSCULOSKELETAL PAIN AND FUNCTIONAL LIMITATION IN THE GENERAL POPULATION: THE JOHNSTON COUNTY HEALTH STUDY

Keywords: Osteoarthritis, Physical therapy/Physiotherapy, Rehabilitation

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Background: Chronic musculoskeletal pain (CMP) is a major public health issue given its high prevalence and negative consequences on pain and physical function. One potential approach to mitigate the symptoms of CMP is to replace sedentary time (*i.e*, sitting and resting during waking hours) with light intensity (*e.g.*, playing cards or light cooking) or moderate intensity *(e.g.*, brisk walking) activity. Little is known, however, about what intensity of physical activity (light or moderate) may be needed to replace sedentary behaviors in order to reduce CMP and functional limitation.

Objectives: The purpose of this study was to model replacement of sedentary time with light- and moderate-intensity physical activity and explore its association with reducing risk of CMP and functional limitation in adults from a large general population cohort.

Methods: We used cross-sectional data from the Johnston County Health Study (JoCoHS), which is actively enrolling adults 35-70 years of age from the general population of Johnston County, North Carolina, USA. Physical activity data measured with a hip-worn ActiGraph GT3X monitor were collected over 7 days. We applied standard methods for processing and classifying time spent in sedentary, light, and moderate physical activity. Our study outcomes included CMP, defined as having at least moderate pain on most days of any one month in the last 12 months in any joint, and functional limitation defined as having a walking speed in the slowest sex-specific tertile, which was < 0.6 m/s. We calculated Odds Ratios (OR) with 95% confidence intervals (CI) using logistic regression with Isotemporal Substitution of exposure terms for each intensity of physical activity (light or moderate) and sedentary time. ORs were adjusted for age, sex, and BMI.

Results: As of 12/15/2022, 414 adults had complete clinical and physical activity data (age [mean] (sd) 55.5 years (9.5), BMI 32.9 (8.1), 68% women, 23% Black), 74% had CMP and 33% had functional limitation. Average sedentary time was 9.1 hours/day. Modeling replacement of 10 min/day of sedentary time with 10 min/day of light intensity activity was not associated with CMP (adjusted OR 0.99, 95% CI [0.99, 1.02]), but did reduce the odds of functional limitation by 3% which met statistical significance (adjusted OR 0.97, 95% CI [0.94, 1.00]). Modeling replacement of 10 min/day of sedentary time with 10 min/day of moderate intensity activity reduced the odds of CMP by 11% (adjusted OR 0.89, 95% CI [0.80, 1.00]), and reduced the odds of functional limitation by 12%, though narrowly missing statistical significance (adjusted OR 0.88, 95% CI [0.76. 1.01]).

Conclusion: Substituting light intensity activity for sedentary time was associated with a lower occurrence of functional limitation, but not CMP. Substituting moderate intensity for sedentary time was associated with less CMP with a trend for less functional limitation. These preliminary findings suggest that participation in moderate intensity physical activity may have stronger protective effects for CMP and functional limitation than light intensity physical activity.

Table 1. Preliminary cross-sectional data at baseline showing the relation of removing sedentary time and adding light and moderate physical activity with odds of prevalent chronic musculoskeletal pain and functional limitation from n=414 JoCoHS participants. Bold indicates p<0.05.

Remove	Add	Prevalent Chronic Musculoskeletal Pain (95% CI)*	Prevalent Functional Limitation (95% CI)*
10 min/day sedentary time	10 min/day light intensity activity	0.99 (0.99, 1.02)	**0.97 (0.94, 1.00)**
10 min/day sedentary time	10 min/day moderate intensity activity	**0.89 (0.80, 1.00)**	0.88 (0.76, 1.01)

* Odds Ratios and 95% CI are adjusted for age, sex, and BMI.

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People with burning vessels

POS0214

IN-DEPTH ANALYSIS OF DISEASE MANIFESTATIONS IN ANCA-ASSOCIATED VASCULITIDES IDENTIFIES DISTINCT CLINICAL PHENOTYPES, EMPHASIZING THE IMPACT OF SEX AND AGE AT DIAGNOSIS

Keywords: Autoantibodies, Vasculitis

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Background: Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), two different ANCA-associated vasculitides (AAV), are clinically heterogeneous. Little is known about potential differences in clinical presentation of disease between females and males and between patients diagnosed at a young versus at an older age. Likewise, associations between different clinical manifestations have not been thoroughly investigated.
Objectives: To improve care and prediction of outcome in patients with AAV, the aims of this study were to identify and thoroughly characterize subgroups of AAV patients, stratified for sex, age at diagnosis and clinical manifestations.
Methods: In a systematic multicenter study, adult patients diagnosed with GPA or MPA were included between 2008-2018. Clinical data including sex, age at diagnosis, ANCA-specificity, relapse and cumulative disease involvement of ear-nose-throat (ENT), lungs, eyes, kidneys, muscles/joints, skin, central nervous system (CNS), peripheral nervous system (PNS), gastrointestinal tract (GI) and heart were collected from medical records. Organ involvements were analyzed for associations with sex, age at diagnosis and relapse, in GPA and MPA, separately, using logistic regression. Agglomerative hierarchical cluster analysis was performed using the Ward method, based on the n number of axes explaining ≥90% of total variability in multiple correspondence analysis of the collected clinical data in GPA and MPA. The optimal number of clusters was estimated by determining the gain in within-cluster inertia achieved at each clustering step[1].
Results: In total, 1156 patients (578 females, 578 males) were included in the study; 922 were classified as GPA, 234 as MPA. In GPA, pulmonary and renal involvement, as well as PR3-ANCA, were significantly associated with male sex, whereas MPO-ANCA was associated with female sex. In MPA, the only difference between the sexes was an older age at diagnosis in males than females. In GPA, the age at diagnosis showed a bimodal pattern with two peaks of incidence with mean (range) at 22.4 (9-31) and 57.1 (32-91) years of age, respectively. Comparing GPA patients younger than 32 years old at diagnosis with those older than 32 identified a significantly higher prevalence of females, ENT- and GI involvement and relapse rate in the younger group and PNS involvement in the older group. In all GPA patients, relapse was associated with pulmonary involvement, whereas in MPA relapse was associated with musculoskeletal involvement. Hierarchical cluster analysis of GPA and MPA identified five and seven distinct clusters, respectively. For both diseases, three of the clusters were defined by heart-, CNS- and GI involvement, respectively. In GPA, the largest cluster was defined by PR3-ANCA and ENT involvement and the fifth cluster by MPO-ANCA, female dominance and a low rate of ENT involvement. The additional four clusters in MPA were defined by i) eye involvement, ii) absence of renal involvement, iii) PR3-ANCA and iv) MPO-ANCA with renal involvement (largest), respectively. In addition, in several of the clusters in both GPA and MPA, there was a significant enrichment or depletion of additional clinical manifestations, in comparison with the largest cluster.

Conclusion: The results of this study indicate distinct disease courses of GPA in females and males, and strongly suggest that sex and age at diagnosis should be considered in the clinical assessment of disease outcome in GPA patients. The identification of associations between different clinical manifestations in the cluster analysis may facilitate the prediction of organ involvements in patients with AAV, and, subsequently, clinical decision-making.

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POS0215

CLASSIC VERSUS ATYPICAL POLYMYALGIA RHEUMATICA: TWO SIDES OF THE SAME COIN OR MISCLASSIFICATION?

Keywords: Imaging, Myositis, Pain

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Background: PMR is usually diagnosed based on the patient's clinical history and confirmed by the presence of an elevated inflammatory markers ESR and CRP. Once the diagnosis is confirmed, steroid therapy is commenced, and their response is usually rapid and dramatic. However, sometimes patients may present with symptoms similar to PMR but do not meet the 2012 EULAR/ACR criteria. It is not well known if these atypical patients represent a subtype of PMR or another musculoskeletal inflammatory condition.
Objectives: 1. to compare the clinical, laboratory and sonographic patterns in patients presenting with classic PMR versus those with atypical PMR symptoms. 2. To assess whether ultrasonography of the shoulders and hips has added value for PMR subclassification.
Methods: Longitudinal multi-center prospective study of patients presenting with PMR symptoms and their respective US scans of the shoulders and hips. The patients were stratified into a cohort of classic PMR who meet the 2012 EULAR/ACR criteria; and a group of atypical PMR presenting with symptoms similar to classic PMR but did not fulfil the 2012 EULAR/ACR criteria. Every patient was assessed clinically, had blood tests for ESR, CRP, basic rheumatology blood profile, urine analysis (to rule out microscopic hematuria), CK, bone profile, rheumatoid factor, anti-CCP, ANA, TSH and HbA1c. US scan was carried out for both shoulders and hips. The patients were treated according to agreed protocol and monitored for 12-months.
Results: 104 patients (68 women and 36 men) with a mean age±SD of 63.2±9.7 years. Eighty-one (84/104) patients had classic PMR and 20 (19.3%) atypical PMR. Patients with atypical PMR had shorter duration of symptoms (8.1 + 1.3 Vs 14.6 + 1.5 weeks). In the atypical PMR patients, pain in the hip/pelvic girdle was more frequent (100% vs 60.1%), whereas shoulder girdle pain was less (50% vs 98), in comparison to the classic PMR patients. Arthritis was less common in the atypical PMR cohort (15% Vs 42%), similarly GCA was less prevalent in the atypical PMR (5% Vs 20.2%). Patients with classic PMR were more likely to have bilateral abnormal ultrasound findings in the shoulder (particularly subdeltoid bursitis [92%] and biceps tenosynovitis [83.3%]), as well as in the hips [78.6%] than the atypical PMR subjects where US findings tend to be unilateral (shoulder 50% and the hip 75%). Systematic symptoms: fatigue, weight loss, fever were more common in the classic PMR than atypical PMR (%). No significant difference on comparing morning stiffness in both groups. Both patients' groups responded very well to steroid therapy with significant improvement in the symptoms in 2-4 weeks' time.

Conclusion: Patients with atypical PMR could represent an early form of the classic PMR. Atypical PMR used to have a shorter evolution of symptoms, have predominantly hip/pelvic girdle affection. US of the shoulders and hips may have an added value for stratifying PMR patients and differentiating atypical PMR from other musculoskeletal conditions.

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POS0216 A PROSPECTIVE COMPARATIVE STUDY OF TEMPORAL ARTERY ULTRASOUND, TEMPORAL ARTERY BIOPSY, TEMPORAL ARTERY MAGNETIC RESONANCE ANGIOGRAPHY AND ACR GCA CLASSIFICATION CRITERIA IN AN INCEPTION GCA COHORT

Keywords: Vasculitis, Diagnostic Tests, Ultrasound

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Background: Temporal Artery Biopsy (TAB) is costly, invasive and has a false negative rate as high as 60% [1]. Temporal Artery Ultrasound (TAUS) and Superficial Temporal Artery (STA) MR-Angiography (MRA) have shown widely disparate results in studies to date [1-3]. ACR GCA Classification Criteria are often mis-used in clinical practice as diagnostic criteria.

Objectives: In this prospective study, we compare TAUS, TAB and STA MRA to physician diagnosis of GCA at 6 months.

Methods: We performed a prospective study of all new referrals (n=124) to our Rapid Access GCA clinic over 18 months. US of all 6 branches of the STA and both axillary arteries was performed using a GE P9 device. Abnormalities considered indicative of vasculitis in the STA included the halo sign (Figure 1) and non-compressible arteries with a thickened intima-media complex [4]. In the axillary arteries, a halo sign and an intima-media thickness of >1.0mm was considered positive. A subset of our patients were referred for TAB and/or MRA. MRAs were scored 0-4 based on mural wall thickness and signal intensity of mural peri-adventitial contrast enhancement [5]. We compared results to a clinical diagnosis of GCA at 6 months, verified by 2 rheumatologists. We performed Chi-Square tests with ROC analyses to determine the performance of each diagnostic modality.

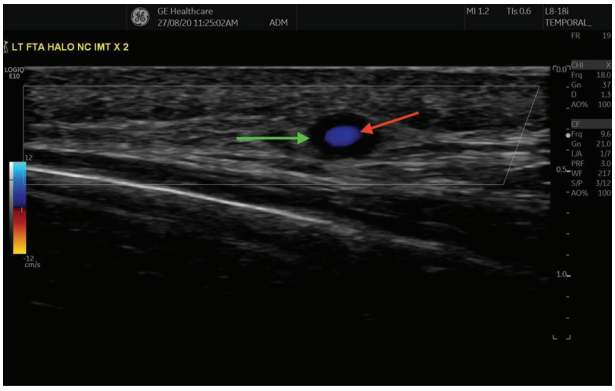


Figure 1. Transverse view of STA, demonstrating a halo sign, as indicated by the anechoic region (green arrow) surrounding the inner Doppler (red arrow) signal.

Results: Sixty-six patients had a clinical diagnosis of GCA of which 58% were males (n=38) with a mean age of 73.3 years. The performance of the various diagnostic tools is outlined in table 1.

Table 1. Sensitivities, Specificities and Area Under the Curve (AUC) values for Temporal and Axillary Artery Ultrasound, ACR GCA Classification Criteria, Temporal Artery Biopsy and Superficial Temporal Artery Magnetic Resonance Angiography for physician-verified diagnosis of GCA at 6 months. CI = Confidence Intervals.

Tool	n=	Sensitivity (%)	Specificity (%)	p-value	AUC	CI	p-value
US	124	86.4	82.8	<0.005	0.846	0.772-0.920	< 0.005
ACR CC	124	72.7	70.7	<0.005	0.717	0.625-0.809	<0.005
TAB	64	40.4	100	<0.05	0.702	0.568-0.836	<0.05
STA MRA	22	47.1%	20%	0.193	0.335	0.072-0.598	0.273

Conclusion: TAUS is a reliable tool for diagnosing GCA with a high degree of sensitivity and specificity. TAUS outperforms TAB, MRA and ACR GCA Classification Criteria when compared to a clinical diagnosis of GCA at 6 months. We propose that TAUS should replace TAB as the gold standard diagnostic test and that all rheumatologists should acquire the necessary skills to accurately perform this investigation as part of routine clinical care.

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POS0217 ASSOCIATION BETWEEN VASCULAR FDG UPTAKE AND AORTIC DIMENSIONS IN GIANT CELL ARTERITIS: A PROSPECTIVE STUDY

Keywords: Vasculitis, Imaging

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Background: Patients with giant cell arteritis (GCA) have an increased risk of developing aortic aneurysms. Retrospective studies have shown that ^{18}F-fluorodeoxyglucose (FDG) uptake in large vessels at diagnosis increases the risk of developing aortic complications during follow-up.

Objectives: To prospectively evaluate the association between vascular FDG uptake at diagnosis and the evolution of aortic diameter and volume in patients with GCA.

Methods: GCA patients who had FDG positron emission tomography (PET) imaging at diagnosis within 3 days of initiation of glucocorticoids and who were prospectively followed for at least 2 years were included. PET scans were visually scored (0-3) at 7 vascular areas and a total vascular score (TVS) was calculated, ranging from 0 to 21. Patients underwent a computed tomography (CT) scan at diagnosis and yearly thereafter for a maximum of 10 years. The association between vascular FDG uptake and aortic diameter and volume was estimated by linear mixed effect models with random intercept and slope adjusted for age, sex, cardiovascular risk factors, CT or PET/CT scan and intravenous contrast. The ascending aorta, aortic arch, and descending aorta were considered aneurysmatic when the diameter was ≥45, ≥40, and ≥35 mm, respectively.

Results: Hundred patients (mean age 70 years, 68% females) were included, of which 74 patients had FDG uptake ≥2 in any large vessel, 60 in the thoracic aorta and 49 in the abdominal aorta. Median follow-up was 80 months (IQR 47-110). The increase in ascending and descending aortic diameter and in thoracic aortic volume was higher in patients with vascular FDG uptake ≥2 compared to those without (**Table 1**). This increase was also significantly associated with TVS (**Figure 1**). FDG uptake was not associated with an increase in abdominal aortic diameter nor volume. Thoracic aortic aneurysms were more frequently observed in patients with thoracic aortic FDG uptake (27% versus 10%, aOR 6.6, 95%-CI 1.8-31.0, p=0.009) with a median time since diagnosis of 40 months (IQR 18-61). Two patients with high TVS (15 and 16) needed surgery for thoracic aortic aneurysm.

Conclusion: Thoracic aortic FDG uptake at diagnosis is an independent risk factor for developing thoracic aortic aneurysm in GCA patients. Higher TVS was associated with greater yearly increase in thoracic aortic volume and diameter. Follow-up of aortic dimensions may be necessary in these patients.

Table 1. Evolution of the aortic diameter (in mm) and volume (in cm³) per year in patients with (PET positive) and without (PET negative) vascular FDG uptake ≥2

FDG uptake ≥2 in any large vessel			
	Regression coefficient (95% CI)		**p-value**
	PET negative	**PET positive**	
Volume of thoracic aorta	2.40 (-0.40 – 5.21)	6.80 (5.09 – 8.53)	0.008
Volume of abdominal aorta	0.28 (-0.48 – 1.04)	0.12 (-0.33 – 0.57)	0.72
Diameter of thoracic aorta			
◦ Ascending aorta	0.10 (-0.10 – 0.30)	0.41 (0.29 – 0.53)	0.009
◦ Aortic arch	0.21 (0.05 – 0.37)	0.35 (0.25 – 0.45)	0.14
◦ Descending aorta	0.11 (-0.06 – 0.27)	0.34 (0.24 – 0.44)	0.01
Diameter of abdominal aorta			
◦ Suprarenal aorta	0.07 (-0.04 – 0.17)	0.11 (0.04 – 0.17)	0.51
◦ Juxtarenal aorta	0.14 (0.03 – 0.25)	0.14 (0.07 – 0.21)	0.98
◦ Infrarenal aorta	0.15 (0.07 – 0.23)	0.08 (0.03 – 0.12)	0.11
FDG uptake ≥2 in thoracic aorta			
	Regression coefficient (95% CI)		**p-value**
	PET negative	**PET positive**	
Volume of thoracic aorta	3.13 (0.86 – 5.43)	7.32 (5.44 – 9.22)	0.005
Diameter of thoracic aorta			
◦ Ascending aorta	0.15 (-0.02 – 0.31)	0.45 (0.31 – 0.58)	0.005
◦ Aortic arch	0.22 (0.09 – 0.35)	0.37 (0.27 – 0.48)	0.07
◦ Descending aorta	0.18 (0.05 – 0.32)	0.35 (0.23 – 0.46)	0.06
FDG uptake ≥2 in abdominal aorta			
	Regression coefficient (95% CI)		**p-value**
	PET negative	**PET positive**	
Volume of abdominal aorta	0.08 (-0.45 – 0.61)	0.23 (-0.33 – 0.78)	0.69
Diameter of abdominal aorta			
◦ Suprarenal aorta	0.07 (-0.00 – 0.14)	0.12 (0.05 – 0.20)	0.32
◦ Juxtarenal aorta	0.13 (0.05 – 0.20)	0.15 (0.07 – 0.23)	0.70
◦ Infrarenal aorta	0.12 (0.07 – 0.18)	0.06 (0.00 – 0.12)	0.12

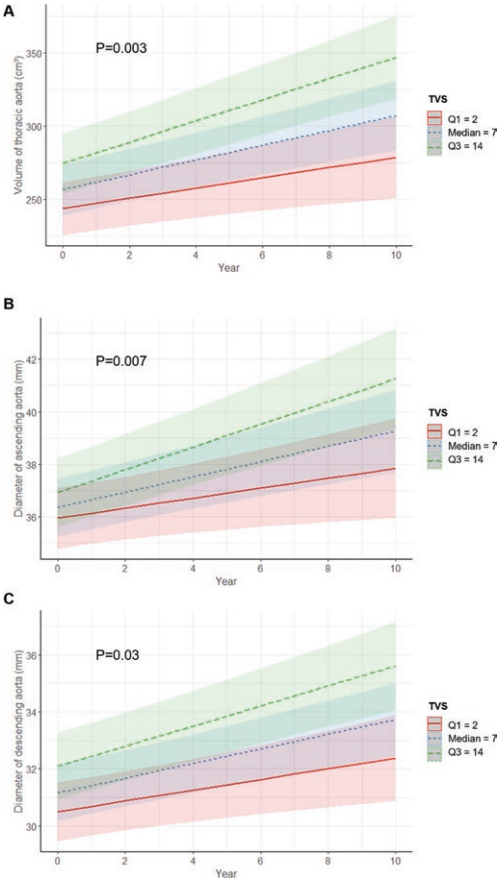


Figure 1. Association between TVS and (A) volume of thoracic aorta, (B) diameter of ascending aorta and (C) diameter of descending aorta

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0219 **WITHDRAWN**

POS0220 **WITHDRAWN**

POS0221 **CLINICAL, LABORATORY AND ULTRASONOGRAPHIC FINDINGS AT BASELINE CAN PREDICT THE LONG-TERM OUTCOME OF POLYMYALGIA RHEUMATICA**

Keywords: Inflammatory arthritides, Ultrasound, Vasculitis

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Background: No definite clinical, laboratory or imaging finding has been identified to predict prognosis and different clinical course of PMR, nor the risk of further relapses.

Objectives: Primary endpoint was to assess the rate of PMR patients who, during the follow-up, undergo a diagnosis of GCA and arthritis, as well as to assess which clinical, laboratory and US findings are associated to a diagnostic shift and predict the long-term evolution of PMR. Secondary endpoint was to assess the optimal use of US in PMR.

Methods: All patients who were diagnosed with PMR in our Rheumatology Unit from January 2017 to January 2022 and followed-up for at least 12 months were retrospectively included. If performed at the time of diagnosis, musculoskeletal and temporal (TA) and axillary arteries (AxA) US findings were recorded, too.
Results: A total of 201 patients (mean age 73.4 ± 7.63, M/F 89/112) were included. According to the US performed at baseline, patients were subdivided in 4 subgroups: in 32 of them, the diagnosis was only clinical (A); 35 underwent shoulders, hips, wrists and knees US (B); 48 underwent shoulders, hips, TA and AxA US (C), while 86 shoulders, hips, wrists, knees, TA and AxA US (D). At baseline, 14/132 (10.6%) of patients from groups C and D displayed findings consistent with GCA. During the follow-up, 47%, 52.8% and 60% of PMR patients who were re-evaluated at 12, 24 and 36 months, respectively, had a change in diagnosis (**figure 1**). The multivariate logistic regression showed that bilateral LHBT tenosynovitis at onset was the variable that better defined the persistence in PMR diagnosis (p=0.05, OR 8.425), whereas GH synovitis (p=0.022, OR 0.074) and RF positivity (p=0.028, OR 0.993) were the variables associated to a diagnostic shift on the follow-up. The model that better described (AUROC 0.854) a patient with a PMR-onset with subsequent diagnostic shift comprised higher frequency of bilateral GH synovitis, bilateral shoulder PD, higher values of CRP, WBC, PLT and Hb and longer time to obtain remission. On the other hand, the ones maintaining diagnosis of PMR had bilateral exudative LHBT tenosynovitis (OR 8.425) and SA-SD bursitis (OR 2.619), higher values of ESR (OR 1.015), lower values of Hb (OR 0.428) and shorter time to remission (OR 1.076). Continuous variables were included in a hierarchical clustering analysis identifying two groups. Cluster 2 identified older patients, with lower systemic inflammation, lower levels of WBC, PLT and Hb, who had a higher persistence in PMR diagnosis at 12 (42.7% vs 29.3%), 24 (37.2% vs 25.6%) and 36 months (36.4% vs 21.2%). Cluster 2 had lower frequency of PD positivity (PD 0 in 39.1% on shoulders and 47.1% on wrists) or peripheral synovitis (absence of synovitis on knee and MCF in 43.9% and 50% respectively), more frequent flares, and were taking PDN at 12 (until 45.8%) and 24 months (until 30.8%). An environmental trigger before onset were more commonly reported (in 5,8% vaccinations before onset, vs 1.4% in cluster 1) The comparisons among the B, C and D and A showed significant differences in diagnosis at 12 (p=0.0145) and 24 months (p=0.0432) and dosage of GC at 12 months (p=0.0009). At 12 months the complete withdrawal of PDN was achieved in a significant (p=0.002) lower number of patients belonging to group A (6.4%) when compared to group B (28.1%), C (37,5%) and D (12.9%). A direct correlation was obtained between GC dosage at 12 and 24 months (Spearman rho 0.284, p=0.002). Finally, a longer time to remission correlated positively with CRP and negatively with Hb, while fever at disease onset positively with ESR.
Conclusion: More than half patients fulfilling criteria for PMR have their diagnosis changed during follow-up. The early use of US is associated with a more accurate diagnosis at baseline, as well as to a lower cumulative dosage of PDN. The early diagnosis of GCA is possible only in case of AxA and TA US at diagnosis. On the other hand, the lack of US is associated to a prolonged PDN treatment. Patient with a definite subset of clinical (fever, short time to remission), laboratory (lower Hb and CRP, higher ESR) and US findings (lower PD signal, LHBT tenosynovitis) are more prone to maintain the diagnosis of PMR during the follow-up.

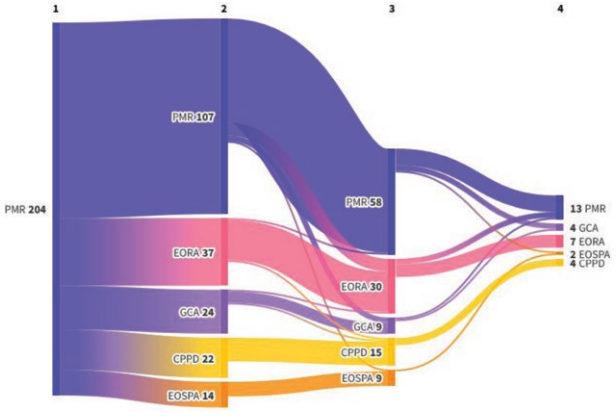


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0222

EFFICACY AND SAFETY OF AVACOPAN IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS RECEIVING RITUXIMAB IN THE ADVOCATE TRIAL

Keywords: Randomized control trial, Clinical Trials, Vasculitis

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Background: The randomized, double-blind, double-dummy, controlled Phase 3 ADVOCATE trial tested whether avacopan, an oral selective C5a receptor inhibitor approved for the treatment of ANCA-associated vasculitis (AAV), could replace a glucocorticoid (GC)-tapering regimen. Randomization was stratified according to vasculitis disease status (newly diagnosed or relapsing), ANCA status (anti-proteinase 3 (PR3) positive or anti-myeloperoxidase positive), and immunosuppressive treatment (cyclophosphamide (CYC) or rituximab (RTX)).[1] American College of Rheumatology/Vasculitis Foundation guidelines recommend induction treatment with RTX over CYC.[2] For relapsing disease, EULAR guidelines recommend RTX.[3]
Objectives: To evaluate the efficacy and safety of avacopan in patients in the RTX stratum of the ADVOCATE trial.
Methods: Primary efficacy endpoints were the proportion of patients achieving disease remission at week 26 and sustained remission at week 52 (Birmingham Vasculitis Activity Score (BVAS) of 0 and no GC use for AAV 4 weeks before measurement). RTX was administered intravenously 375 mg/m^2 once weekly for 4 weeks beginning on Day 1. The protocol did not include repeat dosing of RTX, according to its approved labeled regimen at the time.
Results: A total 214 of 330 patients (64.8%) comprised the RTX stratum. At baseline, patients were 60 years old (mean), ~76% had renal vasculitis (based on BVAS), ~46% were PR3-ANCA positive, and ~58% were newly diagnosed. Men constituted 57.0% of the avacopan group and 48.6% of the prednisone group. Baseline estimated glomerular filtration rate (eGFR) was 57.1±32.2 and 56.0±33.4 mL/min/1.73 m^2 (mean±SD), for the avacopan and prednisone groups, respectively. Remission at week 26 was 77.6% in the avacopan group and 75.7% in the prednisone group (**Table 1**). Sustained remission at week 52 was 71.0% in the avacopan group and 56.1% in the prednisone group (**Table 1**), estimated common difference, 16.5 percentage points; 95% confidence interval, 4.3 to 28.6; P=0.004 for superiority. Additionally, there were numerical improvements in relapse rate, albuminuria, and lower GC-associated toxicity in the avacopan group versus the prednisone group. The proportion of patients experiencing a serious treatment emergent adverse event (TEAE) was 34.6% (n = 37) with 62 events in the avacopan group compared to 39.3% (n = 42) with 91 events in the prednisone group (**Table 1**).
Conclusion: This analysis from the ADVOCATE trial of patients with AAV receiving RTX showed a significantly increased sustained remission rate at week 52 in the avacopan group compared to the prednisone group. Compared to the prednisone group, patients in the avacopan group had numerical improvements in remission at week 26, relapse rate, eGFR, albuminuria, and less GC toxicity. There was no increase in serious TEAEs in patients treated with avacopan. These results demonstrate the efficacy of avacopan for achieving and sustaining remission in patients with AAV treated with RTX.
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Table 1. Efficacy and Safety for Patients with ANCA-Associated Vasculitis in the Rituximab Stratum in the ADVOCATE Trial

	Avacopan Group (N=107)	Prednisone Group (N=107)
Remission at Week 26, n (%)	83 (77.6%)	81 (75.7%)
Sustained remission at Week 52, n (%)	76 (71.0%)	60 (56.1%)
Relapse rate, n (%)	9 (8.7%)	21 (20.2%)
eGFR change at Week 52, mL/min/1.73 m^2, mean + SEM	5.9 + 1.56	3.2 + 1.56
UACR percent change at Week 4, geometric mean	-43.4%	8.3%
GTI-CWS at Week 26, mean ± SEM	36.8 ± 3.62	52.9 ± 4.92
GTI-AIS at Week 26, mean ± SEM	11.7 ± 3.42	19.8 ± 4.31
Any Serious Treatment Emergent Adverse Event; patient experiencing events, n (%), number of events (n)	37 (34.6%), 62 events	42 (39.3%), 91 events

eGFR=estimated glomerular filtration rate; UACR=urinary albumin:creatinine ratio; GTI-CWS=Glucocorticoid Toxicity Index Cumulative Worsening Score; GTI-AIS=Glucocorticoid Toxicity Index Aggregate Improvement Score

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Disclosure of Interests: Duvuru Geetha Consultant of: ChemoCentryx (a wholly owned subsidiary of Amgen), Aurinia, Otsuka, GSK, Anisha Dua Consultant of: ChemoCentryx (a wholly owned subsidiary of Amgen), Novartis, Sanofi, Abbvie, Huibin Yue Employee of: ChemoCentryx, Amgen, Carlo Salvarani: None declared, David Jayne Consultant of: AstraZeneca, Boehringer Ingelheim, ChemoCentryx (a wholly owned subsidiary of Amgen), GSK, Novartis, Roche, CSL Vifor, Grant/ research support from: GSK, Roche, Peter A Merkel Shareholder of: Royalties from UpToDate, Consultant of: AstraZeneca, Boehringher-Ingelheim, Bristol-Myers Squibb, ChemoCentryx (a wholly owned subsidiary of Amgen), CSL Behring, Dynacure, EMDSerono, Forbius, GlaxoSmithKline, Immagene, InflaRx, Jannsen, Jubilant, Kyverna, Magenta, MiroBio, Mitsubishi, Neutrolis, Novartis, NS Pharma, Otsuka, Q32, Regeneron, Sparrow, Takeda, Grant/research support from: AstraZeneca, Boehringher-Ingelheim, Bristol-Myers Squibb, ChemoCentryx (a wholly owned subsidiary of Amgen), CSL Behring, Dynacure, EMDSerono, Forbius, GlaxoSmithKline, Immagene, InflaRx, Jannsen, Jubilant, Kyverna, Magenta, MiroBio, Mitsubishi, Neutrolis, Novartis, NS Pharma, Otsuka, Q32, Regeneron, Sparrow, Takeda.
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POS0223

LONG-TERM SURVEILLANCE STUDY OF RITUXIMAB (MABTHERA)-TREATED PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS (GPA) OR MICROSCOPIC POLYANGIITIS (MPA): RITUXIMAB SURVEILLANCE STUDY IN VASCULITIS (RIVAS)

Keywords: Real-world evidence, Vasculitis

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Background: Rituximab is used for remission induction, and for the prevention of relapse in ANCA-associated vasculitis (AAV). However, the long-term safety of rituximab in the real-world setting remains unclear.
Objectives: To evaluate the incidence of safety events (serious adverse events and adverse events of special interest) and risk profile of rituximab and to compare the time to first safety event between a rituximab cohort and a cohort treated with other therapies over 6 months to 15 years from first exposure.
Methods: RIVAS was a retrospective, observational study including patients with GPA/MPA who had received rituximab (MabThera) or other treatments between 2003 and 2018 at Addenbrooke's hospital, Cambridge, UK. Clinical and laboratory variables were collected at baseline and every 12-18 months until 30 September 2018. To calculate the time to event, Time 0 was defined as either initiation of MabThera treatment for the rituximab cohort or the time of first disease flare/diagnosis for the control cohort. The primary endpoint was the time to first safety event. Key secondary endpoints were time to first pre-categorized safety event such as serious infection and cardiovascular disorders. The time to second safety event was an exploratory endpoint.
Results: 392 GPA/MPA patients were enrolled: 247 in the rituximab and 145 in the control cohort with a total of 2,217 person-years (mean study duration 5.7 years). Mean age was 61 years, 52% were female, 77% had GPA and 23% MPA. The mean disease duration at baseline was 55.3 months (SD 70.2) in the rituximab, while 33.3 months (SD 63.8) in the control arm. Baseline characteristics were not matched between groups reflecting the predominant use of rituximab for relapsing or refractory disease. Five hundred and thirty-three safety events occurred in 164 patients (66%) in the rituximab and 170 in 78 patients (54%) in the control group. Sixty-seven patients (27%) in the rituximab group and 19 patients (13%) in the control group experienced serious infection (Table 1). Thirty patients (12%) in the rituximab group developed severe hypogammaglobulinemia (IgG <3 g/l) requiring treatment/change of treatment or hypogammaglobulinemia requiring IVIg and 19 (8%) received IVIg compared to 3 (2%) and 1 (0.7%) patient in the control group. There were no differences in incidence rates for malignancy, cardiovascular events or renal insufficiency between groups. There was no difference in the time to first safety event between groups (HR 1.32, 95%CI 0.952-1.83, p=0.096), nor in the time to first pre-categorized safety event. However, a shorter time to second safety event was observed in the rituximab group (HR 1.98, 95%CI 1.25-3.13, p=0.004) (Figure 1). Predictors of safety events were older age, higher vasculitis damage scores and chronic pulmonary and renal disease. The relative risk of serious infection was higher in the rituximab group (unadjusted relative risk (RR) 2.07; 95%CI 1.30-3.30).
Conclusion: Over 60% of patients with GPA/MPA experienced a safety event in their disease course. Rituximab did not increase the risk of experiencing a first safety event but the time to second safety event was shorter in the rituximab group. Limitations of the trial design do not permit firm conclusions concerning differences between treatment groups.

Table 1. Safety events by event category for rituximab and control groups

Event type	Events(n)/ Patients (n(%)) Rituximab	Events(n)/ Patients (n(%)) Control
All safety events	533/ 164 (66%)	170/ 78 (54%)
Serious infection	124/ 67 (27%)	29/ 19 (13%)
Cardiovascular disorder	42/ 36 (15%)	22/ 18 (12%)
Haematological events	35/ 31 (13%)	9/ 9 (6%)
Malignant events	28/ 21 (9%)	21/ 16 (11%)
Renal Insufficiency	21/ 15 (6%)	20/ 15 (10%)
PML	1/ 1 (0.4%)	0/ 0 (0%)
Additional safety events	282/ 122 (49%)	69/ 48 (33%)

n, number; PML, progressive multifocal leukoencephalopathy.

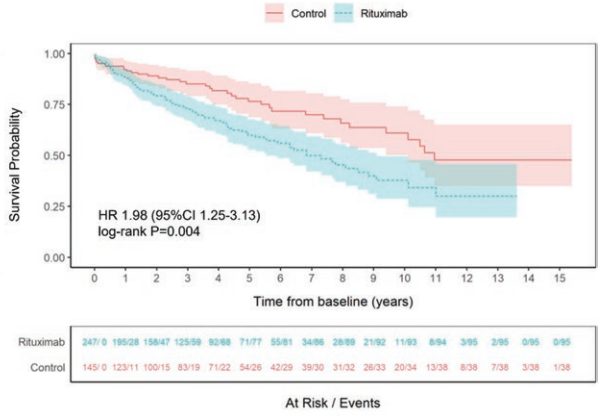


Figure 1. Time to second safety event for the rituximab and the control group

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Lisa Uchida: None declared, Claudia Loechel: None declared, Marianna Nodale: None declared, Simon Bond: None declared, David Jayne Shareholder of: Aurinia, Speakers bureau: GSK, CSL Vifor, Consultant of: Astra-Zeneca, Chemocentryx, GSK, Novartis, Roche, Takeda, CSL Vifor, Grant/ research support from: GSK, Roche.
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Treatment in psoriatic arthritis on the move

POS0224

ENHANCED SURVEILLANCE FOR THE DETECTION OF PSORIATIC ARTHRITIS IN A UK PRIMARY CARE PSORIASIS POPULATION VERSUS USUAL CARE: RESULTS AT 24 MONTHS FROM THE THE TOTAL BURDEN OF PSORIASIS (TUDOR) RANDOMISED CONTROL TRIAL

Keywords: Clinical Trials, Psoriatic arthritis, Randomized control trial

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Background: Delay in the diagnosis of psoriatic arthritis may be associated with poorer outcome. However, the effectiveness of strategies to enable early detection of psoriatic arthritis in a primary care population with psoriasis have not been investigated in a prospective randomised control trial.
Objectives: The primary objective was to determine whether early detection of undiagnosed PsA in people with psoriasis by an enhanced surveillance (ES) intervention compared to standard care (SC) improves outcome in physical function at 24 months post-registration. Secondary objectives were to compare disease activity and impact of disease between groups in those participants diagnosed with PsA.

Methods: A multi-centre, prospective, parallel group cluster randomised controlled trial in patients with psoriasis with no prior diagnosis of PsA was conducted. GP practices were randomised in a 1:1 allocation ratio with stratification for GP practice list size and Central Commissioning Group (CCG). A total of 133 GP practices and 2226 participants were required to achieve a target sample size for the primary analysis population of 148 participants (74 per group) with a positive diagnosis of PsA; the latter corresponding to 80% power for detecting the MCID in the primary outcome measure of 0.35 units. Participants recruited were managed according to either SC, or ES by annual rheumatological assessment. Participants with suspected inflammatory arthritis were referred, via their GP, to the local rheumatology outpatient clinic at participating hospitals for an assessment of PsA by the 'treating rheumatologist' (ES arm: at baseline, 12 and 24 months; SC arm: at 24 months). Participants diagnosed with PsA then entered the PsA-care pathway element of the trial. The primary outcome measure was the HAQ_DI at 24 months post registration in participants diagnosed with PsA. Secondary outcome measures, PASDAS and PsAID-12, were assessed over time in participants with a positive diagnosis of PsA.

Results: A total of 2225 participants across 135 GP practices were registered, corresponding to 1123 allocated to ES and 1102 to SC; primary analysis population consisted of 87 participants with a positive diagnosis of PsA: 64 in ES, 23 in SC (Figure one). Baseline characteristics were similar across both treatment groups. The adjusted odds ratio (OR) for achieving a HAQ-DI score of 0 at 24 months post registration in ES compared to SC was 0.64 (95% CI (0.17, 2.38)), indicating no evidence of a difference between treatment groups (p=0.5075). Moreover, the adjusted OR of achieving a higher (non-zero) HAQ-DI score at 24 months post registration in ES relative to SC arm was 1.12 (95% CI: 0.67, 1.86), again indicating no evidence of a difference between the two treatment groups (p=0.6612). There was high variability on the impact of the disease between participants over time, although the impact is generally low in this group of participants with an 'early' diagnosis of PsA. Moreover, the overall PASDAS score and component scores over time post PsA diagnosis show high variability in PsA disease activity. No adverse events were reported.

Conclusion: There was insufficient evidence that early diagnosis by ES and subsequent treatment improves physical function compared to SC in patients with psoriasis. Limitations included the trial being underpowered for demonstrating the pre-specified treatment effect; only 6.2% of participants recruited had a positive diagnosis of PsA, much lower than assumed (18%). The imbalance observed between treatment groups (~ 3:1 ratio (ES:SC)), is largely explained by the lower proportion of participants especially in the SC arm attending the screening visit at 24 months, and delays between referral and attending appointment with the treating clinician, all further exacerbated by the Covid-19 pandemic. Furthermore, a longer duration of follow-up may be necessary to detect differences in outcome and is planned.

References: Nil.

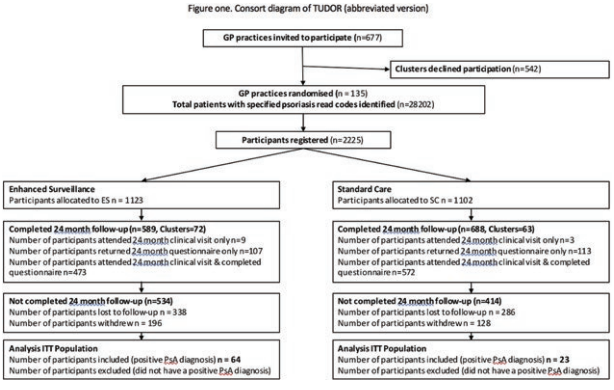


Figure 1.

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Disclosure of Interests: None Declared.

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POS0225

HOW WELL DOES ULTRASOUND-ASSESSED SYNOVITIS IN REDUCED JOINT SETS PREDICT THE RESPONSE TO SECUKINUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO CONVENTIONAL DMARDS? - EXPLORATORY RESULTS FROM A PHASE 3B STUDY

Keywords: Psoriatic arthritis, bDMARD

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Background: Power Doppler ultrasound (PDUS) is a powerful diagnostic tool with high accessibility and reproducibility, allowing the visualisation of morphological and inflammatory changes of the synovium. The ULTIMATE study (NCT02662985) was the first large, randomised, double-blind, placebo-controlled, multicentre PDUS phase 3b study in psoriatic arthritis (PsA) that utilised the Global EULAR-OMERACT- Synovitis Score (GLOESS), to demonstrate the responsiveness of PDUS to detect early and continuous decrease in the synovitis score.[1] However, the ultrasound assessment for GLOESS is time-consuming due to the number of joints assessed.

Objectives: The aim of this study was to investigate the performance of different reduced joint sets to predict response to secukinumab, compared with the 24 paired joints included in the validated GLOESS.

Methods: ULTIMATE was a 52-week study, with a 12-week double-blind, placebo-controlled period followed by a 12-week open-label treatment period and a 6-month extension period.[1,2] The GLOESS comprises the sum of PDUS scores of 24 paired joints (potential score range: 0–144). A cluster image map was constructed to identify highly correlated joint clusters, based on the change from baseline of the composite PDUS scores at joint level. A reduced set of joints was selected based on either a mathematical approach that used the correlation clusters along with the joint level variations and joint location (Model 1 and Model 2) or a pragmatic approach that selected joints most frequently found to be active by ultrasound, in PsA in clinical practice (Model 3). Linear models with reduced joint sets predicted the actual GLOESS at each time point utilising 60% of data randomly selected from the study. The remaining 40% were used for model validation and diagnostics.

Results: Three models were established with reduced joint sets (12–18 pairs). The joints included in each linear model are summarised in **Table 1**. **Figure 1** depicts the trajectory of the two mathematical models and the pragmatic model versus the actual GLOESS in the secukinumab and placebo-secukinumab groups assessed by change from baseline to Week 24. Compared to GLOESS, all reduced PDUS joint sets demonstrated similar responsiveness to secukinumab from baseline to Week 24.

Conclusion: These results demonstrated similar responsiveness to secukinumab with reduced joint sets as the validated GLOESS, supporting the development of a scoring system with reduced number of joint evaluations that would increase feasibility by reducing the assessment time. Further studies are needed to confirm the validity and utility of the reduced joint set ultrasound scores in other PsA cohorts.

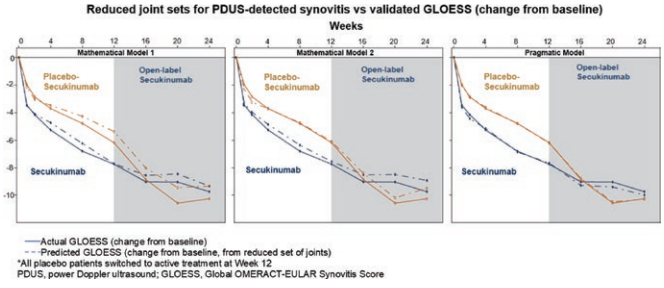
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Table 1. Joints included[1] across 3 ultrasound-detected synovitis models, indicated by green shading

Joint Pairs	Mathematical Model 1 (N=12)	Mathematical Model 2 (N=12)	Pragmatic Model (N=18)
DIP2	■	■	
Elbow	■	■	■
Knee	■	■	
MCP1		■	■
MCP2	■		■
MCP3		■	■
MCP4			■
MCP5	■		■
MTP1	■	■	■
MTP2	■	■	■
MTP3			■
MTP4	■	■	■
MTP5			■
PIP1	■	■	■
PIP2			■
PIP3	■	■	■
PIP4			■
PIP5			■
Tibiotalar/Wrist	■	■	■

DIP, distal interphalangeal; MCP, metacarpophalangeal; MTP, metatarsophalangeal; N, number of joint pairs used in the model; PIP, proximal interphalangeal



Acknowledgements: NIL.

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POS0226

APREMILAST REDUCES INFLAMMATION AS MEASURED BY MRI OF THE HAND IN PATIENTS WITH PSORIATIC ARTHRITIS: PRIMARY RESULTS FROM THE PHASE 4 MOSAIC STUDY

Keywords: Outcome measures, Imaging, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is characterized by inflammatory arthritis, enthesitis, dactylitis, and spondylitis. Apremilast is an oral immunomodulating phosphodiesterase-4 inhibitor approved for the treatment of PsA. The impact of apremilast on objective measures of inflammation and structural progression of PsA has not yet been characterized. Here, we evaluate the efficacy of apremilast 30 mg BID (APR) on inflammation measured by dedicated MRI of the hand.

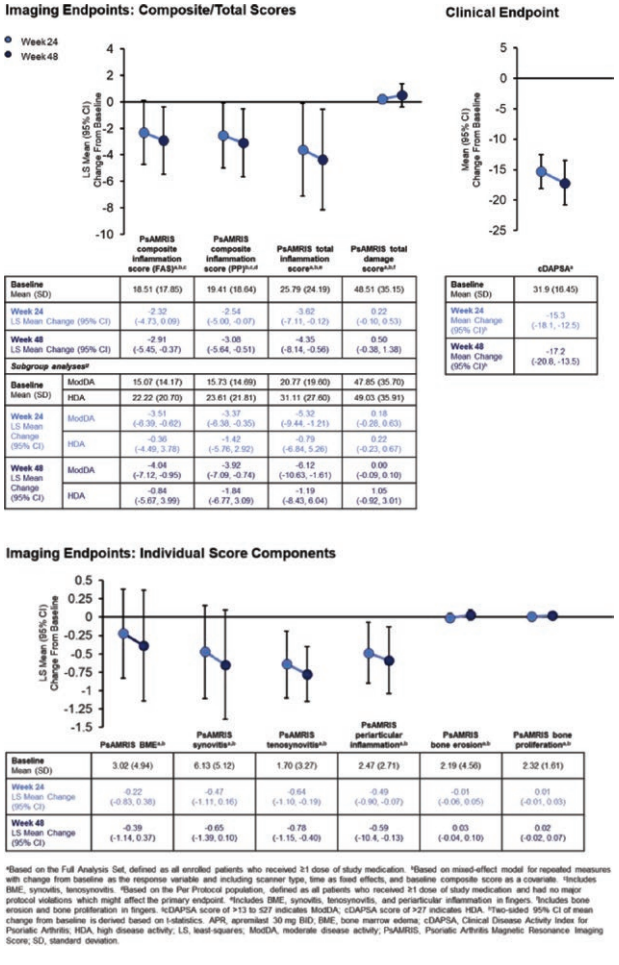
Objectives: To evaluate the efficacy of APR on inflammation and imaging outcomes and the safety profile of APR in this setting.

Methods: MOSAIC (NCT03783026) was a phase 4, multicenter, single-arm, open-label study in patients (pts) with active PsA (≥3 months but ≤5 years since diagnosis, meeting CASPAR criteria for PsA) evaluating APR as monotherapy or in combination with stable methotrexate. Pts were treated with APR for 48 weeks and had MRI of the hand (contrast-enhanced) performed at baseline (BL), Week 24, and Week 48. All images were read and adjudicated by 2 experienced readers blinded to clinical information and time of acquisition. The primary endpoint was change from BL in the composite score of hand bone marrow edema (BME), synovitis, and tenosynovitis in fingers 2–5, as assessed by the PsA MRI Score (PsAMRIS) at Week 24. Total inflammation score, comprised of BME, synovitis, tenosynovitis, and periarticular inflammation in fingers, was also assessed. Structural progression was assessed by the total hand damage score (determined by bone erosion and bone proliferation in fingers 2–5). Subgroup analyses based on BL disease activity as measured by Clinical Disease Activity Index for Psoriatic Arthritis (cDAPSA) were performed for key endpoints.

Results: A total of 122 pts enrolled and received APR. Mean age was 47 years, 55% were women, and mean duration of PsA was 1.9 years. The Full Analysis Set (FAS) included 98 pts evaluable for the primary endpoint (having BL and Week 24 data); 4 had major protocol deviations and 94 were evaluable as part of the per protocol (PP) population. The least-squares (LS) mean (95% CI) change from BL in the composite inflammation score of BME, synovitis, and tenosynovitis as assessed by PsAMRIS (FAS) was -2.32 (-4.73, 0.09) at Week 24 and -2.91 (-5.45, -0.37) at Week 48 (**Figure 1**). In the PP population, the LS mean (95% CI) change from BL in the composite score at Weeks 24 and 48 indicated a significant reduction of disease activity (**Figure 1**). Significant improvements from BL were seen in total inflammation scores (BME + synovitis + tenosynovitis + periarticular inflammation) in the FAS (**Figure 1**). The structural outcome indicated by the total hand damage score, including bone erosion, showed no significant change from BL to Week 48 (**Figure 1**). Pts also experienced significant improvements from BL in cDAPSA at Weeks 24 and 48 (**Figure 1**). Subgroup analyses based on disease activity at BL showed significant improvements from BL in inflammation in pts with moderate disease activity (ModDA; cDAPSA score >13 to ≤27) and no significant change from BL in total damage (**Figure 1**). Though it was insignificant, pts with high disease activity (HDA; cDAPSA score >27) did have improvement from BL in inflammation indices (**Figure 1**). Common treatment-emergent adverse events were diarrhea (33.6%), nausea (12.3%), headache (10.7%), nasopharyngitis (7.4%), and dyspepsia (6.6%). No new safety signals were identified.

Conclusion: Pts with PsA treated with APR had improvements in both clinical indices and objective MRI indices of inflammation assessed by PsAMRIS in the target hand at Week 24 and Week 48, confirming an effect of APR on clinical and inflammatory manifestations of PsA. Pts with ModDA seemed to have

greater improvement from BL in MRI inflammation scores than pts with HDA. No significant structural progression was observed. These results offer important insights on the effect of apremilast in PsA and highlight the value of using MRI and PsAMRIS as measures of inflammatory disease activity and change following treatment.



[a]Based on the Full Analysis Set, defined as all enrolled patients who received ≥1 dose of study medication. [b]Based on mixed-effect model for repeated measures with change from baseline as the response variable and including scanner type, time as fixed effects, and baseline composite score as a covariate. [c]Includes BME, synovitis, tenosynovitis. [d]Based on the Per Protocol population, defined as all patients who received ≥1 dose of study medication and had no major protocol violations which might affect the primary endpoint. [e]Includes BME, synovitis, tenosynovitis, and periarticular inflammation in fingers. [f]Includes bone erosion and bone proliferation in fingers. [g]cDAPSA score of >13 to ≤27 indicates ModDA; cDAPSA score of >27 indicates HDA. [h]Two-sided 95% CI of mean change from baseline is derived based on t-statistics. APR, apremilast 30 mg BID; BME, bone marrow edema; cDAPSA, Clinical Disease Activity Index for Psoriatic Arthritis; HDA, high disease activity; LS, least-squares; ModDA, moderate disease activity; PsAMRIS, Psoriatic Arthritis Magnetic Resonance Imaging Score; SD, standard deviation.

Figure 1.

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POS0227

SERUM EXTRACELLULAR MATRIX BIOMARKERS IDENTIFY RESPONSE TO GUSELKUMAB IN PSORIATIC ARTHRITIS: POST-HOC ANALYSIS FROM A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY THROUGH 2 YEARS

Keywords: Psoriatic arthritis, Biomarkers

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Background: Psoriatic arthritis (PsA) is a progressive, joint-degenerative inflammatory disease with cartilage destruction, bone erosion and growth, and synovitis. Extracellular matrix (ECM) remodeling is also observed in skin lesions in patients with PsA. Guselkumab (GUS), an interleukin-23p19-subunit monoclonal antibody, demonstrated robust efficacy compared with placebo in patients with active PsA in two Phase 3 studies, DISCOVER-1 and DISCOVER-2.[1,2] GUS also reduced serum ECM biomarkers shown to be elevated in patients with PsA.[3]

Objectives: To identify treatment responders among PsA patients receiving GUS, using serum biomarkers of collagen formation, degradation, and vimentin degradation.

Methods: Available baseline serum ECM biomarker data from patients who consented to participate in the 2-year DISCOVER-2 trial (NCT0315828) were included in the post hoc analysis. Biomarkers of collagen formation (PRO-C2, PRO-C3, PRO-C4, and PRO-C6), degradation (C1M, C2M, and C6M), and citrullinated and degraded vimentin were measured by immunoassays. Baseline ECM biomarker levels from all available patients were log-transformed and standardized by mean centering and scaling by the standard deviation prior to K-means clustering. In GUS-treated patients, between-cluster comparisons for major demographic and clinical parameters were performed using Mann-Whitney or chi-squared tests. Relationships between observed clinical response (ACR20, ACR50, PASI100) at Week (W)24, W52, and W100 and baseline levels of biomarkers were investigated. Analysis of PASI response was performed in patients with baseline body surface area (BSA) ≥3% and Investigator's Global Assessment (IGA) of psoriasis score ≥2.

Results: Two distinct clusters were identified using baseline serum ECM biomarkers from all patients (Figure 1). Patients in Cluster 1 generally had lower levels of ECM biomarkers than patients in Cluster 2. In GUS-treated patients, those in Cluster 2 had a higher (all $p<0.05$) baseline PASI score (median 7.3 vs 5.1), swollen joint count (12.0 vs 10.0), C-reactive protein (2.0 vs 1.0 mg/dL), and PsA-modified vdH-S score (26.5 vs 13.0). Relative to patients in Cluster 1, GUS-treated patients in Cluster 2 showed a greater ACR20 response rate at W24

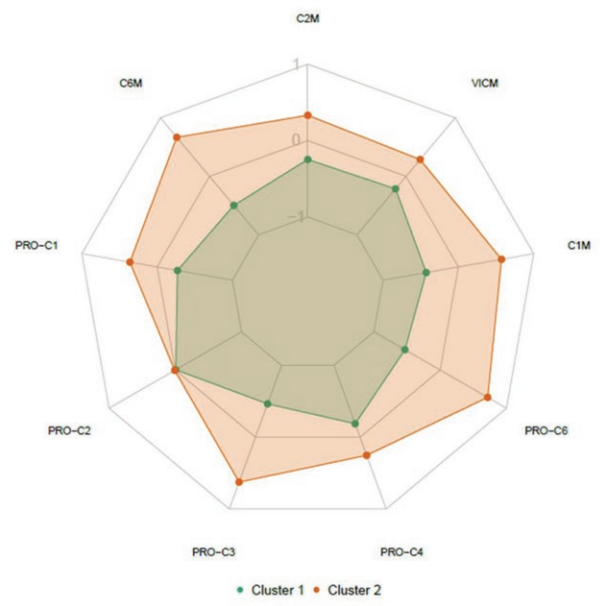
(72% vs 57%, p=0.039) and W52 (80% vs 66%, p=0.037) and a greater ACR50 response rate at W100 (64% vs 47%, p=0.031), indicating patients with high levels of these biomarkers were more likely to achieve an ACR response. For patients with at least mild skin disease at baseline (BSA≥3% and IGA≥2), those in Cluster 1 demonstrated a higher PASI100 response rate at W100 than patients in Cluster 2 (71% vs 54%, p=0.046).

Conclusion: Patients with higher levels of baseline ECM biomarkers (Cluster 2) that correspond with greater peripheral joint inflammation demonstrated higher ACR20 and ACR50 response rates when treated with GUS, while patients with lower levels of these ECM biomarkers (Cluster 1) demonstrated higher rates of complete skin clearance (PASI100). These findings may provide a step towards patient stratification and precision medicine for guiding the use of biologic immunomodulatory treatments in patients with PsA.

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Figure 1: Radar Plot showing means of standardized biomarker levels by cluster.



Cluster 1: Low ECM turnover – Most biomarker levels are below the mean (0) of the population

Cluster 2: High ECM turnover – All biomarker levels are above the mean (0) of the population

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POS0228

MINIMAL IMPORTANT DIFFERENCE (MID), MINIMAL DETECTABLE CHANGE (MDC), AND DISEASE ACTIVITY THRESHOLDS FOR TWO NOVEL COMPOSITE INSTRUMENTS (3VAS, 4VAS) IN PATIENTS WITH PSORIATIC ARTHRITIS: POOLED ANALYSIS OF THREE PHASE 3 STUDIES

Keywords: Psoriatic arthritis

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Background: Though continuous composite measures of disease activity for psoriatic arthritis (PsA) assessment exist, abbreviated measures that are more feasible for screening in routine clinical practice are needed. The 3 Visual Analogue Scale (VAS) and 4VAS scores were developed by abridging the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) Composite Exercise (GRACE) measure to be the first short multidimensional composite measures specifically for use in PsA routine clinical care. The measures were shown to have superior performance than several established composite measures using small datasets.

Objectives: To further test 3VAS/4VAS in observational and trial datasets, as GRAPPA members recommended.

Methods: This post-hoc analysis of the DISCOVER 1/2 and COSMOS studies used pooled data through week (W) 24 from all treatment groups across studies. The correlation of 3VAS/4VAS with Disease Activity Index for PsA (DAPSA), PsA Disease Activity Score (PASDAS), physician global assessment (PhGA), and patient GA (PtGA) was assessed with Pearson's correlation coefficient. Minimal Important Difference (MID) was assessed with 4 distribution-based methods (based on standard error of the measurement, effect size, reliable change index [RCI], and RCI_{diff}). Minimal detectable change (MDC) was assessed with the standard formula: MDC = 1.96*sqrt(2)*sd*sqrt(1-ICC). Clinically relevant thresholds for low, moderate and high disease activity were estimated with receiver operating characteristic analysis and DAPSA (≤4, >4 – ≤14, >14 – ≤28, >28), PASDAS (≤1.9, >1.9 – ≤3.2, >3.2 – <5.4, ≥5.4), and PhGA/PtGA (≤1, >1 – ≤3, >3 – ≤6, >6 cm) as anchors.

Results: 1405 patients were included, of whom 51.3% were male, with a mean (SD) age of 47.1 (11.8) and PsA duration of 6.4 (6.5) years. At baseline, the mean (SD) 3VAS, 4VAS, DAPSA, PASDAS, PhGA, and PtGA scores of 6.4 (1.6), 6.3 (1.6), 45.8 (20.2), 6.5 (1.1), 6.5 (1.6), and 6.7 (2.0), respectively, reflected high levels of disease activity. Through W24, both 3VAS and 4VAS showed very strong correlation with PtGA (r_{3VAS}=0.92, r_{4VAS}=0.94) and PASDAS (r_{3VAS}=0.81, r_{4VAS}=0.82), strong with PhGA (r_{3VAS}=0.77, r_{4VAS}=0.74), and moderate to strong with DAPSA (r_{3VAS}=0.59, r_{4VAS}=0.61). Calculated MIDs were 0.9 (range: 0.7-1.3 across methodologies) for 3VAS and 0.9 (range: 0.6-1.3) for 4VAS (**Table 1**). MDC estimates were 3.3 (range 2.1-4.2 across follow-up intervals) for 3VAS and 3.2 (range: 2.0-4.0) for 4VAS. Cut-off values for low, moderate, and high disease activity were 2.0, 3.4, and 4.9 for 3VAS and 2.1, 3.5 and 5.1 for 4VAS, respectively (**Figure 1**).

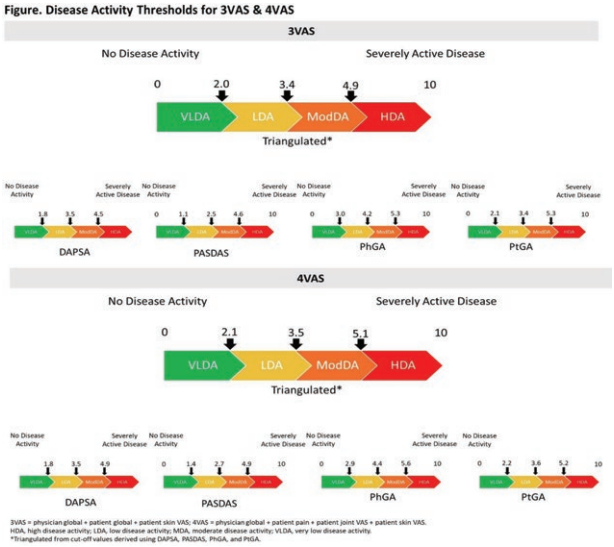
Conclusion: Using a large pooled clinical trial dataset of patients with active PsA, we have calculated clinically relevant thresholds for improvement and disease activity for 3VAS and 4VAS. These estimates are generally comparable to those previously reported and can be used to set treatment targets and screen disease activity in routine care when resources are limited or during remote patient monitoring.

Table 1. MID for 3VAS, 4VAS, DAPSA, PASDAS, PhGA, and PtGA

Parameter	Distribution #1	Distribution #2	Distribution #3†	Distribution #4†	Mean‡
3VAS	0.7	0.8	1.3	0.9	**0.9**
4VAS	0.6	0.8	1.3	0.9	**0.9**
PhGA, VAS cm	0.7	0.8	1.6	1.1	**1.1**
PtGA, VAS cm	0.9	1.0	0.9	0.7	**0.9**
DAPSA	6.2	10.1	1.1	0.8	**4.6**
PASDAS	0.4	0.5	1.8	1.3	**1.0**

†Triangulated from MIC values derived from each visit pair (BL to W8, BL to W16, BL to W24, W8 to W16, W16 to W24) ‡Triangulated from MDC values derived from Distribution #1, #2, #3, and #4 **Distribution #1**=Baseline sd * sqrt(1 – Cronbach's Alpha) **Distribution #2**=0.5 * baseline sd **Distribution #3**=(first visit score – last visit score)/((baseline sd*sqrt(1 – Cronbach's Alpha)) **Distribution #4**=(first visit score – last visit score)/(sqrt(2)*(baseline sd*sqrt(1 – Cronbach's Alpha))

Figure. Disease Activity Thresholds for 3VAS & 4VAS



3VAS = physician global + patient global + patient skin VAS; 4VAS = physician global + patient pain + patient joint VAS + patient skin VAS. HDA, high disease activity; LDA, low disease activity; MDA, moderate disease activity; VLDA, very low disease activity. *Triangulated from cut-off values derived using DAPSA, PASDAS, PhGA, and PtGA.

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POS0229

COMBINING MTX DOES NOT RESULT IN AN ADDITIONAL EFFICACY OF UST TREATMENT IN POLYARTHRITIC PSA: SUBGROUP ANALYSIS FROM A RANDOMIZED PLACEBO-CONTROLLED INVESTIGATOR INITIATED CLINICAL TRIAL

Keywords: Outcome measures, Psoriatic arthritis, Randomized control trial

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Background: BDMARD treatment in PsA patients usually requires treatment failure/intolerance to csDMARDs. The value of MTX in combination with bDMARDs is still unclear; an increase of efficacy is expected in polyarthritis. We designed an investigator-initiated, randomized, placebo-controlled trial (IIT) in active PsA to examine if outcomes of UST in combination with MTX (either newly initiated or ongoing) are different from UST only (+PBO), especially with focus on peripheral arthritic dominant PsA.

Objectives: To compare ACR20/50/70 and MDA response rates at week 24 in treatment groups stratified by number of affected joints (oligo- vs polyarthritis).

Methods: 186 patients with active PsA (defined as TJC≥4, SJC≥4 [68/66 joint count] and DAS28≥3.2) were screened for eligibility, 173 patients were randomized to UST+MTX (new or ongoing) or UST+PBO. 166 patients were included into the analysis. The cohort was stratified by number of affected joints: oligoarthritis (< 5 joints) and polyarthritis (≥ 5 joints.); for polyarthritis with additional subgroups (5-7, 8-10 and with >10 joints affected). Response rates (ACR20, 50, 70 response, MDA and 50% reduction in SJC/TJC) were calculated.

Results: BL data were well-balanced between treatment groups/subgroups (table 1) with exception to TJC/SJC. Independent from the number of affected joints, at week 24 no differences between the response behaviour were seen between UST (UST+PBO) or UST+MTX. By trend, UST+PBO showed better response in oligoarthritis and polyarthritis with >10 joints affected, whereas polyarthritis with affected joints >5 and <10 joints showed similar results for UST+PBO and UST+MTX (figure 1).

Conclusion: IL12/23 inhibition with UST is an effective treatment for active PsA independent of MTX use. Data from this subgroup analysis of the IIT indicate that additional MTX has no positive impact on UST efficacy, especially in focus on the arthritic PsA phenotype independent from the number of affected joints.

Table 1. Baseline Characteristics: Subgroup analysis with stratification by number of affected joints at Baseline

Parameters	UST + PBO, Oligoarthritis (< 5 joints)	UST + MTX, Oligoarthritis (< 5 joints)	UST + PBO, Polyarthritis (5-7 joints)	UST + MTX, Polyarthritis (5-7 joints)	UST + PBO, Polyarthritis (8-10 joints)	UST + MTX, Polyarthritis (8-10 joints)	UST + PBO, Polyarthritis (>10 joints)	UST + MTX, Polyarthritis (>10 joints)
	N=10 (6%)	N=10 (6 %)	N=29 (17,5%)	N=31 (18,7%)	N=22 (13,3%)	N=24 (14,5%)	N=18 (10,8%)	N=22 (13,3%)
Sex [Female]	2 (20.0%)	5 (50.0%)	14 (48.3%)	10 (32.3%)	8 (36.4%)	14 (58.3%)	8 (44.4%)	8 (36.4%)
Age [years]	50.4 (SD 14.7)	45.6 (SD 16.5)	46.9 (SD 16.2)	49.1 (SD 13.4)	44.3 (SD 11.6)	51.3 (SD 11.4)	49.6 (SD 14.4)	48.6 (SD 13.2)
Age at PsA diagnosis [years]	48.5 (SD 15.3)	39.6 (SD 15.5)	41.9 (SD 16.4)	43.2 (SD 12.8)	41.5 (SD 12.2)	49.3 (SD 11.5)	45.1 (SD 14.5)	44.0 (SD 13.3)
DAPSA [LOCF]	25.1 (SD 6.3)	23.7 (SD 5.5)	28.7 (SD 5.5)	29.7 (SD 9.0)	33.9 (SD 6.7)	36.0 (SD 12.2)	51.7 (SD 15.6)	53.5 (SD 17.6)
TJC68 [LOCF]	6.0 (6.0 to 14.0)	7.5 (5.0 to 13.0)	10.0 (7.0 to 12.0)	9.0 (6.0 to 14.0)	12.0 (9.0 to 16.0)	11.0 (9.0 to 19.0)	18.5 (15.0 to 24.0)	17.0 (14.0 to 30.0)
SJC66 [LOCF]	4.0 (3.0 to 4.0)	4.0 (4.0 to 4.0)	6.0 (5.0 to 6.0)	6.0 (5.0 to 7.0)	8.0 (8.0 to 10.0)	8.0 (8.0 to 9.5)	14.0 (12.0 to 17.0)	16.0 (14.0 to 22.0)
BSA [%]	1.0 (0.3 to 3.4)	1.2 (0.5 to 3.0)	1.8 (0.9 to 8.3)	2.8 (1.0 to 12.0)	2.0 (1.0 to 4.0)	3.7 (1.0 to 6.5)	1.0 (0.6 to 2.0)	4.5 (0.9 to 18.0)
PASI	2.7 (0.3 to 7.7)	1.2 (0.6 to 2.3)	2.4 (0.6 to 5.0)	2.8 (0.4 to 6.4)	3.0 (0.6 to 6.5)	3.7 (1.7 to 7.1)	1.7 (0.3 to 6.0)	4.5 (1.2 to 8.4)
HAQ-DI [LOCF]	0.7 (0.4 to 1.3)	0.7 (0.3 to 1.3)	0.9 (0.4 to 1.5)	0.9 (0.5 to 1.5)	0.6 (0.4 to 1.0)	0.8 (0.3 to 1.3)	1.3 (0.9 to 1.5)	0.8 (0.3 to 1.6)
DLQI [LOCF]	5.5 (1.0 to 7.0)	4.5 (1.0 to 9.0)	4.0 (1.0 to 9.0)	7.0 (3.0 to 14.0)	6.5 (2.0 to 12.0)	7.0 (2.5 to 13.0)	6.5 (1.0 to 12.0)	11.5 (3.0 to 17.0)

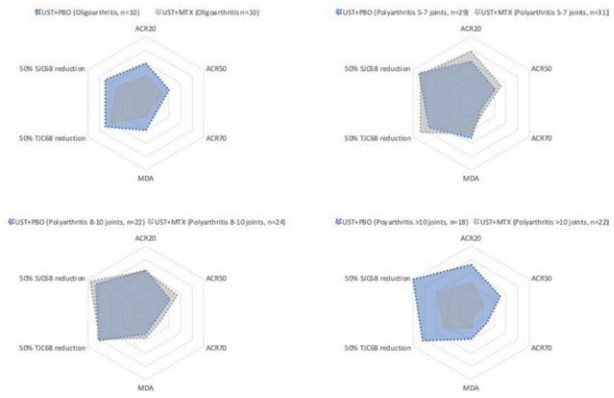


Figure 1. Response to the different treatment regimes, stratified by number of affected joints at Baseline (mITT population)

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POS0230

DISAGREEMENT BETWEEN PATIENT AND PHYSICIAN GLOBAL ASSESSMENT OVER TIME IN PSORIATIC ARTHRITIS: INSIGHT INTO TREATMENT PRIORITIES

Keywords: Patient reported outcomes, Psoriatic arthritis

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Background: The PsA core domain set developed by the Outcome Measures in Rheumatology working group includes musculoskeletal disease, fatigue, physical function, and structural damage, of which arthritis activity, pain, and fatigue were identified as essential by both patients (Pts) and physicians (Phs).[1-2] Assessing agreement between Pt and Ph global assessments (GA) may provide valuable insight into differential importance of specific PsA manifestations to Pts vs Phs. Although previous studies have assessed Pt/Ph disagreement, they have not evaluated potential variation over time.[3]

Objectives: To assess agreement of PtGA and PhGA through week (W) 24 and identify factors driving disagreement between PtGA and PhGA using pooled data (N=1120) from the phase 3 DISCOVER (D)-1 & -2 studies of the fully human IL-23p19 subunit inhibitor (i), guselkumab (GUS).

Methods: Pts with active PsA despite standard therapies (D1: ≥3 swollen/tender joint counts [SJC/TJC], CRP ≥0.3 mg/dL, ~30% with prior TNFi; D2: ≥5 SJC/TJC, CRP ≥0.6 mg/dL, biologic-naïve) were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, Q8W; or placebo. Pt/Ph agreement was defined as a difference of -15<PhGA-PtGA<15. Determinants of PhGA exceeding PtGA by ≥15 (PhGA>PtGA) and PtGA exceeding PhGA by ≥15 (PtGA>PhGA) among pts with PtGA/PhGA disagreement were assessed with the same logistic regression model considering pt demographics, disease characteristics, and pt-reported outcomes (PROs). The effect of GUS on disease parameters identified as determinants of PtGA vs. PhGA disagreement was assessed with repeated measures mixed models adjusting for treatment group, baseline (BL) levels, prior TNFi use, and BL DMARD use.

Results: At BL, mean (SD) SJC=11.5 (7.4), TJC=20.6 (13.3), FACIT-Fatigue score=29.9 (10.0), PtGA=66.9 (19.9), and PhGA=64.8 (15.9) were consistent with moderate to high disease activity. Agreement between PtGA and PhGA was seen in most instances (61.2%); 23.2% of cases were characterized by PtGA>PhGA and 15.7% by PhGA>PtGA. The proportion of pts with PtGA>PhGA increased to 39.1% at W24, while that with PhGA>PtGA decreased to 11.2%. The main determinant of PtGA>PhGA was higher Pt Pain (all time points); additional factors included worse physical health-related quality of life at BL and worse fatigue at W24 **(Table 1)**. Conversely, Phs emphasized objective disease measures, namely higher SJC (all time points) and TJC (W8 to W24), and elevated CRP (BL to W16). GUS treatment was associated with prompt and sustained significant improvements in all identified determinants, including those driving PtGA>PhGA **(Figure 1)**.

Conclusion: PtGA and PhGA were aligned in most encounters. PtGA>PhGA disagreement was driven by pain, fatigue, and physical health being weighed more by Pts than Phs. These findings have important implications in shared decision making and highlight the need to prioritize treatments addressing the full spectrum of PsA symptoms, including PROs.

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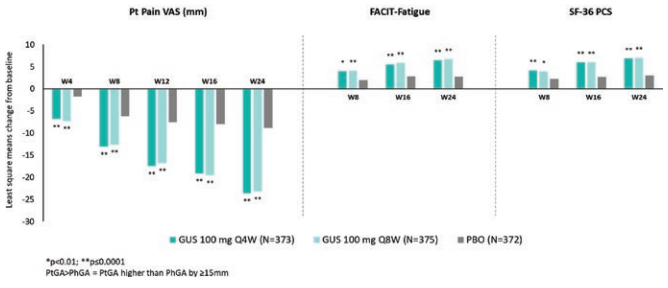
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Table 1. Factors Associated with PhGA>PtGA and PtGA>PhGA Through W24

Visit	Predictors of Interest[¥]	Odds Ratio (95% CI)	
		PhGA>PtGA	PtGA>PhGA
BL (N=434)	CRP (mg/dL)	1.13 (1.00-1.27)*	
	Pt Pain (VAS mm)		0.94 (0.92-0.95)‡
	SF-36 PCS		1.04 (1.00-1.08)*
	SJC66	1.04 (1.00-1.07)*	
W8 (N=524)	CRP (mg/dL)	1.24 (1.04-1.47)*	
	Pt Pain (VAS mm)		0.92 (0.90-0.93)‡
	SJC66	1.14 (1.08-1.20)‡	
	TJC68	1.06 (1.03-1.09)‡	
W16 (N=528)	CRP (mg/dL)	1.40 (1.14-1.71)†	
	Pt Pain (VAS mm)		0.91 (0.89-0.93)‡
	SJC66	1.14 (1.07-1.21)‡	
	TJC68	1.08 (1.04-1.11)‡	
W24 (N=548)	Pt Pain (VAS mm)		0.92 (0.91-0.94)‡
	SJC66	1.14 (1.08-1.21)‡	
	TJC68	1.07 (1.04-1.10)‡	
	FACIT-Fatigue		1.05 (1.02-1.09)†

*p <0.05, †p <0.01, ‡p ≤0.0001 ¥Variables retained after backward selection; prior TNFi use was significant for W8/W24 but not shown. Other variables considered were age, sex, obesity, BL PsA duration, axial involvement, enthesitis, dactylitis, psoriasis, physical function, SF-36 MCS.

Figure. Effect of GUS on Disease Parameters Associated with PtGA>PhGA



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POS0231

SUSTAINED EFFICACY AND SAFETY OF BIMEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND PRIOR INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITORS: RESULTS FROM THE PHASE 3 BE COMPLETE STUDY AND ITS OPEN-LABEL EXTENSION UP TO 1 YEAR

Keywords: Clinical Trials, Psoriatic arthritis

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Background: Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has shown superior efficacy to 16 weeks (wks) vs placebo (PBO) and tolerability in patients (pts) with active psoriatic arthritis (PsA) in the phase 3 BE OPTIMAL and BE COMPLETE studies.[1,2] Efficacy of BKZ to 52 wks has also been demonstrated in the BE OPTIMAL study of biologic-naïve pts with PsA.[3]

Objectives: To assess long-term efficacy and safety of BKZ treatment up to 52 wks in pts with active PsA and prior inadequate response or intolerance to tumour necrosis factor inhibitors (TNFi-IR).

Methods: BE COMPLETE (NCT03896581) included a 16-wk double-blind, PBO-controlled period. Wk 16 completers were eligible for entry into BE VITAL (NCT04009499; open-label extension). BE VITAL included pts from BE OPTIMAL and BE COMPLETE; data here are for pts randomised at baseline (BL [Wk 0]) of BE COMPLETE only, up to 1 yr. Pts were randomised 2:1 to subcutaneous BKZ 160 mg every 4 wks or PBO. At Wk 16, PBO pts switched to BKZ (PBO/BKZ; received 36 wks of BKZ treatment up to Wk 52). Efficacy data reported are observed case or using non-responder imputation (binary) or multiple imputation (continuous). The number of treatment-emergent adverse events (TEAEs) to Wk 52 are reported for pts who received ≥1 dose of BKZ, including pts who switched from PBO to BKZ at Wk 16.

Results: 388/400 (97.0%) pts completed Wk 16; 377 (94.3%) entered BE VITAL and 347 (86.8%) completed Wk 52. Improved efficacy responses with BKZ treatment were sustained from Wk 16 to Wk 52 (**Table 1**). At Wk 52, 51.7% BKZ and 40.6% PBO/BKZ pts achieved American College of Rheumatology (ACR)50. In pts with BL psoriasis (≥3% body surface area), 65.9% BKZ and 60.2% PBO/BKZ pts achieved Psoriasis Area Severity Index (PASI)100 (complete skin clearance) at Wk 52 (**Figure 1**). At Wk 52, 47.2% BKZ and 33.1% PBO/BKZ pts achieved minimal disease activity (MDA). To Wk 52, 243/388 (62.6%) pts had ≥1 TEAE whilst receiving BKZ (exposure-adjusted incidence rate per 100 pt-years [EAIR/100 PY]: 126.0); 23 (5.9%) pts reported a serious TEAE (7.0/100 PY). Malignancies (excluding non melanomic skin cancers) were reported by 2 (0.7%) pts receiving BKZ (0.77/100PY). *Candida* infections were reported by 25 (6.4%) pts receiving BKZ (7.7/100 PY); all were reported as mild or moderate by investigators; none were systemic. Two cases of oral candidiasis led to study discontinuation. There was one death (sudden death; pt with history of cardiac events), two adjudicated major adverse cardiac events and no definite or probable adjudicated inflammatory bowel disease.

Conclusion: In pts with PsA and TNFi-IR, BKZ demonstrated sustained clinical efficacy from Wk 16 up to Wk 52. The safety profile was consistent with previous reports.[1–3]

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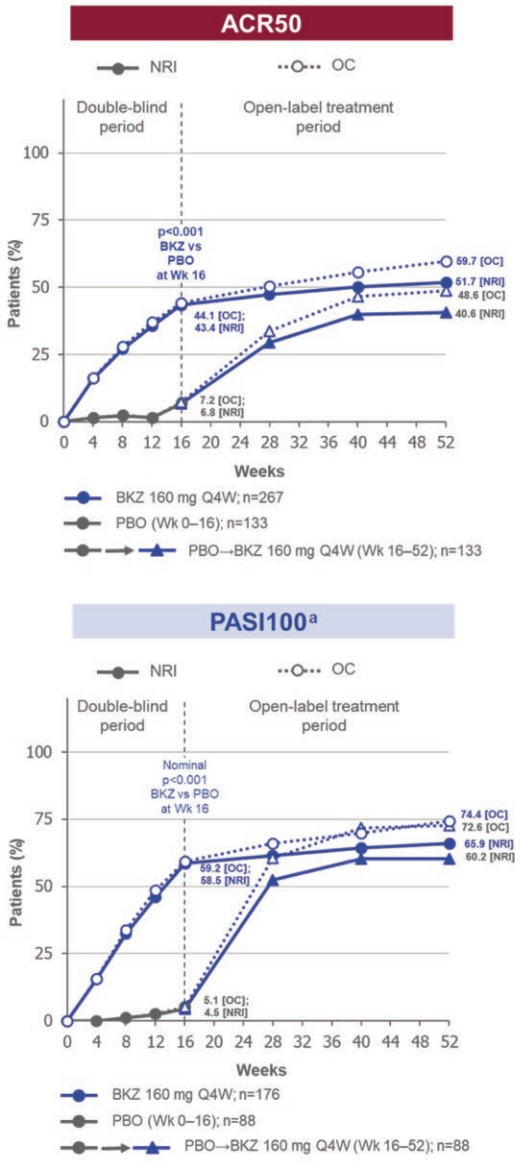
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Table 1. Efficacy at Wk 16 and Wk 52

	Wk 16		Wk 52	
	PBO N=133	BKZ 160 mg Q4W N=267	PBO/BKZ 160 mg Q4W N=133	BKZ 160 mg Q4W N=267
ACR20 [NRI]	21 (15.8)	179 (67.0)	80 (60.2)	182 (68.2)
ACR70 [NRI]	1 (0.8)	71 (26.6)	34 (25.6)	95 (35.6)
PASI75 [NRI][a]	9 (10.2)	145 (82.4)	71 (80.7)	148 (84.1)
PASI90 [NRI][a]	6 (6.8)	121 (68.8)	65 (73.9)	131 (74.4)
MDA responder rate [NRI]	8 (6.0)	118 (44.2)	44 (33.1)	126 (47.2)
HAQ-DI CfB [MI], mean (SE)	–0.07 (0.04)	–0.38 (0.03)	–0.35 (0.05)	–0.39 (0.03)
mNAPSI resolution [NRI][b]	12 (14.5)	73 (45.9)	51 (61.4)	107 (67.3)
Enthesitis resolution [NRI][c]	8 (22.2)	52 (49.1)	21 (58.3)	60 (56.6)
Dactylitis resolution [NRI][d]	6 (42.9)	24 (70.6)	12 (85.7)	29 (85.3)
	Wk 16		Wk 40[e]	
SF-36 PCS CfB [MI], mean (SE)	1.4 (0.7)	7.3 (0.5)	7.3 (0.9)	8.4 (0.6)

Randomised set. n (%) unless otherwise specified. [a]In pts with psoriasis affecting ≥3% body surface area at BL. [b]In pts with mNAPSI >0 at BL, PBO n=83, BKZ n=159; [c]In pts with LEI >0 at BL, PBO n=36, BKZ n=106; [d]In pts with LDI >0 at BL, PBO n=14, BKZ n=34; [e]Data not collected at Wk 52.

Figure. ACR50 and PASI100 responses over time to Wk 52 [NRI and OC]



Randomised set. [a]In pts with psoriasis affecting ≥3% body surface area at BL. For binary variables, p values were obtained from logistic regression with treatment, prior TNFi exposure and region as factors. Nominal p values are not powered or adjusted for multiplicity and should not be used to assess statistical significance. ACR50 responders using OC (n/Nsub) at Wk 16: BKZ 116/263, PBO 9/125; at Wk 52: BKZ 138/231, PBO→BKZ 54/111. PASI100 responders (OC: n/Nsub) at Wk 16: BKZ 103/174, PBO 4/79; at Wk 52: BKZ 116/156, Wk 52 PBO→BKZ 53/73.

Abbreviations: ACR: American College of Rheumatology; ACR20/50/70: ≥20/50/70% improvement in ACR criteria; BKZ: bimekizumab; BL: baseline; CfB: change from baseline; HAQ-DI: Health Assessment Questionnaire – Disability Index; LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; MDA: minimal disease activity; MI: multiple imputation; mNAPSI: modified Nail Psoriasis Severity Index; NRI: non-responder imputation; OC: observed case; PASI: Psoriasis Area and Severity Index; PASI75/90/100: 75/90/100% improvement in PASI; PBO: placebo; PCS: Physical Component Summary; Pt: patient; Q4W: every four weeks; SE: standard error; SF-36: Short-Form 36-item Health Survey; TNFi: tumour necrosis factor inhibitor; Wk: Week.

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POS0232

POST-MARKETING SAFETY SURVEILLANCE OF TOFACITINIB OVER 9 YEARS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

Keywords: Safety, Targeted synthetic drugs, Real-world evidence

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Background: The safety of tofacitinib in patients (pts) with rheumatoid arthritis (RA) and psoriatic arthritis (PsA) has been demonstrated in clinical studies with up to 9.5 and 4 years (yrs) of observation, respectively. Real-world

post-marketing surveillance (PMS) safety data comprised of spontaneous and voluntary adverse event (AE) reports for tofacitinib have been published for RA and ulcerative colitis, but not PsA.

Objectives: To further characterise the real-world safety profile of tofacitinib in RA and PsA.

Methods: AE reports were collected from 6 Nov 2012–6 Nov 2021 (RA) and 14 Dec 2017–6 Nov 2021 (PsA) from the Pfizer safety database. Tofacitinib was approved in the US for RA on 6 Nov 2012 (immediate release [IR]) and 24 Feb 2016 (extended release [XR]), and for PsA on 14 Dec 2017 (IR and XR). Safety endpoints included AEs, serious AEs (SAEs), AEs of special interest (AESI) and fatal cases. Pt years (PY) of exposure were estimated from IQVIA commercial sales data from 61 countries and 1 region. Number (N), frequency and reporting rates (RR; number of events/100 PY of estimated exposure) for each endpoint were summarised by indication (RA/PsA) and formulation (IR [5 or 10 mg twice daily], XR [11 mg once daily] or all tofacitinib [IR+XR]). A sensitivity analysis truncated the analysis period to the first 4 yrs post approval for RA (2012–16), to align with the duration of PsA data.

Results: Of the 73 525 case reports (68 131 RA/5394 PsA), 4239/368 (6.2%/6.8%) did not report a formulation and were excluded. Most AE reports were for females (RA: 81.8%/PsA: 71.3%); around half were submitted by healthcare professionals (49.8%/63.1%) and the majority were from North America (80.1%/82.3%). Almost all XR reports (RA/PsA: 93.0%/97.0%) originated from North America (IR reports: 72.3%/68.6%). For both indications, the RR for AEs was higher with XR vs IR; RR and frequency of SAEs, AESIs and fatal cases were mostly similar between XR and IR (Table 1). The most frequently reported AEs in RA and PsA by Preferred Term included drug ineffective, pain, condition aggravated, headache and arthralgia (Figure 1). Off label use was more frequently reported in PsA than RA (Figure 1). In the first 4 yrs post approval of the IR formulation for RA (IR/XR: 49 439/2000 PY), AEs, SAEs and fatal cases RRs were 95.9/147.0, 19.1/24.5 and 0.4/0.4, respectively.

Table 1. Safety summary

RA	Tofacitinib IR 312 632 PY			Tofacitinib XR 126 738 PY			All tofacitinib 439 370 PY		
	N	%	RR	N	%	RR	N	%	RR
AEs	137 476		44.0	82 153		64.8	219 629		50.0
SAEs	24 966	18.2	8.0	11 978	14.6	9.5	36 944	16.8	8.4
Serious infections	4944	3.6	1.6	2467	3.0	2.0	7411	3.4	1.7
HZ	1194	0.9	0.4	529	0.6	0.4	1723	0.8	0.4
CV events[a]	773	0.6	0.3	413	0.5	0.3	1186	0.5	0.3
Malignancy[b]	941	0.7	0.3	429	0.5	0.3	1370	0.6	0.3
VTE	318	0.2	0.1	150	0.2	0.1	468	0.2	0.1
Fatal cases	839	2.1[c]	0.3	279	1.2[c]	0.2	1118	1.8[c]	0.3
PsA	**Tofacitinib IR 14 000 PY**			**Tofacitinib XR 6706 PY**			**All tofacitinib 20 706 PY**		
	N	%	RR	N	%	RR	N	%	RR
AEs	8349		59.6	7602		113.4	15 951		77.0
SAEs	1136	13.6	8.1	912	12.0	13.6	2048	12.8	9.9
Serious infections	239	2.9	1.7	200	2.6	3.0	439	2.8	2.1
HZ	49	0.6	0.4	35	0.5	0.5	84	0.5	0.4
CV events[a]	44	0.5	0.3	25	0.3	0.4	69	0.4	0.3
Malignancy[b]	30	0.4	0.2	27	0.4	0.4	57	0.4	0.3
VTE	27	0.3	0.2	12	0.2	0.2	39	0.2	0.2
Fatal cases	22	0.9[c]	0.2	19	0.8[c]	0.3	41	0.8[c]	0.2

All cases reported ≥1 AE and ≥0 SAE [a]Includes Standardised MedDRA Queries: central nervous system vascular disorders, myocardial infarction and associated terms, ischaemic heart disease and associated terms; and Preferred Terms: cardiac death, cardiac failure congestive, sudden cardiac death and pulmonary embolism [b]Excluding non-melanoma skin cancer [c]Based on total case reports by formulation: RA, 39 744 IR/24 148 XR; PsA: 2601 IR/2425 XRCV, cardiovascular; HZ, herpes zoster; MedDRA, Medical Dictionary for Regulatory Activities; VTE, venous thromboembolism

Conclusion: Tofacitinib PMS safety data from submitted AE reports were consistent for RA and PsA and aligned with the established safety profile. Reporting bias, reporter identity, regional differences in formulation use and exposure data (lower XR vs IR; estimation from commercial sales data) limit interpretation.

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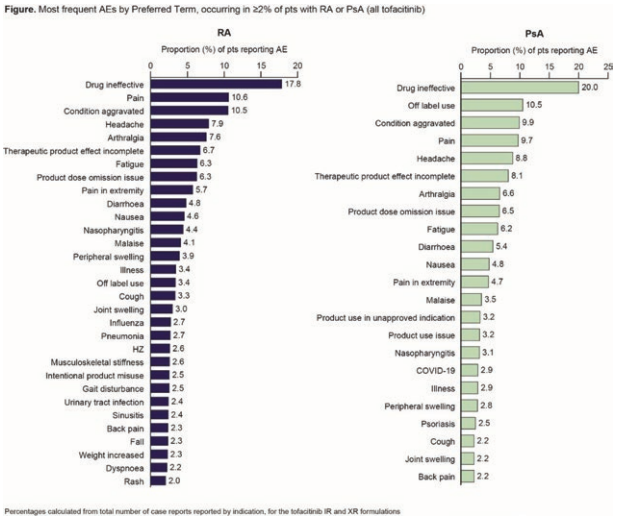


Figure. Most frequent AEs by Preferred Term, occurring in ≥2% of pts with RA or PsA (all tofacitinib)

Percentages calculated from total number of case reports reported by indication, for the tofacitinib IR and XR formulations

MoonLake, Novartis, Pfizer Inc and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc and UCB, Stanley B. Cohen Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Gilead Sciences, Merck and Pfizer Inc, Yoshiya Tanaka Speakers bureau: AbbVie, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly, Gilead Sciences, GSK, Mitsubishi-Tanabe and Pfizer Inc, Grant/research support from: AbbVie, Asahi-Kasei, Boehringer Ingelheim, Chugai, Daiichi Sankyo, Eisai and Takeda, Ivana Vranic Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Edward Nagy Shareholder of: Pfizer Ltd, Employee of: Pfizer Ltd, Allshine Chen Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Irina Lazariciu Employee of: IQVIA, who were paid contractors to Pfizer Inc in the development of this abstract and in providing statistical support, Kenneth Kwok Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Lara Fallon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Cassandra Kinch Shareholder of: Pfizer Inc, Employee of: Pfizer Inc.

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POS0233

DISEASE COURSE AND PREDICTORS FOR ACHIEVING 6-MONTH MINIMAL DISEASE ACTIVITY IN PATIENTS WITH EARLY PSORIATIC ARTHRITIS FROM THE ITALIAN PROSPECTIVE SIRENA STUDY

Keywords: Disease-modifying Drugs (DMARDs), Psoriatic arthritis, Real-world evidence

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Background: Data on Psoriatic Arthritis (PsA) patients naive to any Disease Modifying Anti-Rheumatic Drugs (DMARDs) are limited.

Objectives: To describe the clinical course and predictors for achieving Minimal Disease Activity (MDA) in PsA patients starting DMARDs in a real-world setting.

Methods: PsA patients were enrolled in SIRENA (Clinicaltrials.gov identifier NCT03131661), an Italian Registry of Spondyloarthritis (SpA) patients classified according to ASAS criteria and naive to any DMARDs for SpA [1]. Clinical data were collected at baseline and every 6 months up to the 24-month observation period. Predictors of 6-month MDA were identified through univariate and multivariate analyses.

Results: Out of 350 SpA cases, 203 patients received a diagnosis of PsA (at baseline: mean age 51.2 years; men 51.7%; newly diagnosis 77.3%; time to diagnosis <24 months 68%; mainly axial 4.4%; monoarticular/oligoarticular/polyarticular 9.9/31.5/48.8%; active skin psoriasis 84.3%; enthesitis 38.5%; dactylitis 24%; nail psoriasis 39.7%). At baseline, 100/203 patients (49.3%)

were prescribed conventional DMARDs, 50 (24.6%) biological DMARDs and 27 (13.3%) other systemic treatments, mostly non-steroidal anti-inflammatory drugs. During the 2-year observation period, 79 patients (38.9%) started the first biologic after a conventional DMARD with a median time of 6.8 months and a second biologic after 10.0 months. Clinical and Patient Reported Outcomes markedly improved overtime (Table 1). MDA was achieved by 102/158 patients (64.6%) at least once in the observation period (median time to first MDA according to Kaplan-Meier: 10 months) and by 65/150 patients (43.3%) at 6 months. In univariate analysis, female gender, Body Surface Area (BSA) <3% and higher scores in Health Assessment Questionnaire-Disability Index (HAQ-DI) were associated with a decreased odds ratio of reaching MDA at 6 months while mono-oligoarticular involvement, newly PsA diagnosis and lower Disease Activity in PSoriatic Arthritis (DAPSA) score were associated with an increased odds ratio (Figure 1). Smoking, alcohol, presence of enthesitis/dactylitis/nail psoriasis, Disease Activity Score-28 (DAS-28), number of comorbidities, body mass index and patient VAS global assessment (PtGA) were not significantly associated with 6-month MDA achievement. In multivariate analyses no factor was identified as significant predictor of MDA at 6 months.

Conclusion: In an early PsA population, treatments with predominantly conventional DMARDs and biologics markedly improved disease outcomes, with 43% of patients achieving MDA at 6 months. Female gender, BSA <3% and higher HAQ-DI scores were associated with a decreased odds ratio while new PsA diagnosis, mono-oligoarticular involvement and lower DAPSA score were associated with an increased odds ratio for 6-month MDA.

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[1] Zabotti A, et al. Front Med 2021;8: 711875.

Table 1. Disease outcomes

	Baseline [n=203]	6 months [n=171]	12 months [n=130]	18 months [n=109]	24 months [n=120]
SJC66	3.0 (4.0)	1.1 (3.0)	0.7 (1.4)	0.6 (1.9)	0.6 (2)
TJC68	7.2 (8.8)	2.8 (5.3)	1.8 (2.4)	1.8 (4.9)	1.8 (5.0)
PhGA VAS	46.6 (25.5)	25.1 (22.1)	23.4 (21.6)	18.7 (19.3)	18.2 (19.4)
MASES	3.2 (2.6)	2.6 (2.6)	2.4 82.5)	2.9 (3.0)	1.8 (0.9)
BSA <3%, n (%)	124 (72.5)	127 (92.0)	100 (91.7)	87 (95.6)	96 (98.0)
Nail psoriasis	7.5 (6.6)	5.3 (6.3)	4.2 (5.9)	3.6 (5.3)	4.2 (5.6)
Dactylitis	1.6 (1.3)	0.7 (0.8)	0.4 (0.7)	0.4 (1.1)	0 (0)
Fibromyalgia, n (%)	5 (2.5)	7 (4.1)	2 (1.6)	2 (1.8)	3 (2.5)
DAS28	3.6 (1.2)	2.3 (1.1)	2.2 (0.9)	2.1 (0.8)	2.0 (0.9)
DAS28 ≤3.2, n (%)	62 (37.8)	95 (79.8)	80 (87.0)	72 (88.9)	64 (87.7)
DAPSA	21.8 (13.6)	10.6 (12.8)	8.9 (7.0)	7.6 (6.7)	6.6 (7.2)
DAPSA ≤14, n (%)	51 (30.0)	90 (72.6)	76 (78.4)	70 (82.4)	72 (87.8)
BASDAI	5.1 (2.5)	3.0 (2.4) - 2.7	2.8 (2.3)	2.9 (2.4)	2.2 (2.1)
HAQ-DI	0.71 (0.63)	0.43 (0.48)	0.39 (0.49)	0.42 (0.46)	0.37 (0.48)
PtGA VAS	51.2 (26.0)	30.3 (26.1)	30.0 (25.7)	29.2 (24.5)	21.5 (23.0)

Data are reported as mean (SD), unless otherwise specified.

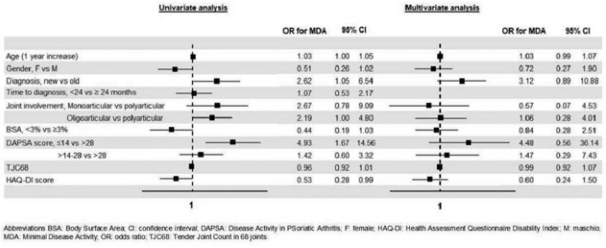


Figure 1. Results on predictors of achieving MDA at 6 months

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Innate Immunity and Autoinflammation

POS0234 **P.E148Q POTENTIATES PYRIN INFLAMMASOME ACTIVATION**

Keywords: Innate immunity, Registries, Genetics/Epigenetics

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Background: The p.E148Q variant in pyrin is present in different populations at a frequency up to 29%[1], and has been associated with inflammatory diseases including vasculitis and familial Mediterranean fever (FMF)[2,3]. The pathogenicity of p.E148Q in FMF is unclear, highly debated in the literature especially when observed *in cis or in trans* to a single, typically recessive, mutation. If it could modify the expressivity of a pathogenic allele and acts as a risk factor for diseases is not known.

Objectives: We Interrogated the Australian Autoinflammatory Disease RegistrY (AADRY) to find candidate inheritance patterns for the p.E148Q variant in pyrin. We then performed functional validation to determine whether p.E148Q increases the ability of pyrin to form an active inflammasome complex in cell lines. Finaly, the ability of p.E148Q to increase the effect of a known pathogenic mutation in *cis* or *trans* was assessed.

Methods: The allele p.E148Q in patients with auto-inflammatory diseases and their families in AADRY was assessed. Different pyrin variant combinations were

Figure

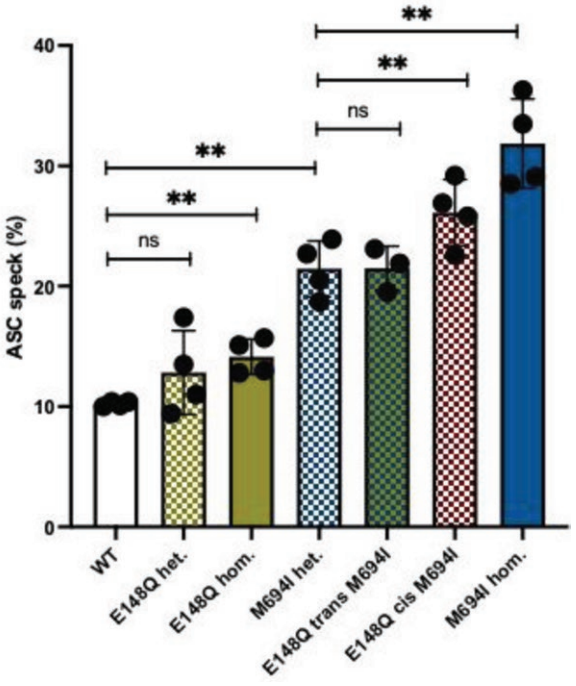


Figure 1. Heterozygous p.E148Q in cis with p. M694I potentiates the effect of p.M694I in response to TcdB

HEK293T cells stably expressing ASC EGFP and transiently co-transfected with mCherry tagged WT pyrin, p.M694I and p.E148Q-M694I then stimulated with TcdB. FACS analysis revealed a statistically increased ASC speck formation for cells expressing the p.E148Q variant compared to the WT allele and for cells co-expressing p.E148Q *in cis* of p.M694I and the WT allele (E148Q cis M694I) compared to the cells expressing p.M694I pyrin (M694I heterozygous). Data are pooled from 4 independent experiments. Error bars represent mean +/- SEM. Statistics used is the paired Student t-test. **P<0.01, ns; non-significant. Het .=heterozygous, Hom.=homozygous.

tested in HEK293T cells stably expressing the adaptor protein apoptosis-associated speck-like (ASC) which were analysed by flow cytometry to visualise inflammasome formation, with and without stimulation by *Clostridium difficile* toxin B (TcdB). Inflammasome dependent cytokine secretion was also quantified by ELISA of supernatants from THP-1 cells transduced with lentiviral expression vectors.

Results: In AADRY, we observed the p.E148Q allele in individuals with autoinflammatory diseases alone or in conjunction with other pyrin variants. Two FMF families harbored the allele p.M694I-E148Q *in cis* with dominant heritability. In vitro, p.E148Q pyrin could spontaneously potentiate inflammasome formation, with increased IL-1β and IL-18 secretion. p.E148Q *in cis* to classical FMF mutations provided significant potentiation of inflammasome formation.

Conclusion: The p.E148Q variant in pyrin potentiates inflammasome activation in vitro. *In cis*, this effect is additive to known pathogenic FMF mutations. These observations may help to explain the association of p.E148Q with FMF and other inflammatory diseases.

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POS0235 ANTI-INFLAMMATORY EFFECTS OF TIP-1 AND MIP-2 TREATMENT THROUGH TLRS BLOCKADE IN AOSD ANIMAL MODEL

Keywords: Treat to target, Animal Models

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Background: Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disease manifesting with a typical skin rash, hepatosplenomegaly, persistent high fever, and leukocytosis. There is no suitable animal model to research for AOSD. The signaling of Toll-like receptors (TLR) as pattern-recognizing receptors is necessary for pathogen recognition by the innate immunity. Recent studies have shown the TLR-mediated inflammation could be an important role in pathogenesis of AOSD. TLR inhibitor peptide 1 (TIP-1) and MAL/MyD88 inhibitory peptide 2 (MIP-2) have been evaluated with blocking peptide activity to bind TIR domain, which is recognition of the danger- or pathogen-associated molecular patterns (DAMP or PAMP).

Objectives: This study tried to evaluated that these inhibitory peptides could suppress their inflammation and improve clinical manifestations in animal models of AOSD.

Methods: *Mycobacterium* mixed Freund's complete adjuvant (CFA, 1.5 mg/ml) was subcutaneously injected into IFNγ knock-out (IFNγ KO) mice to inducing AOSD. TIP-1 or MIP-2 (10 nmol/g) was intraperitoneally administered every day for 4 weeks. Fever and body weight were checked every week. The size of lymph node (LN) and spleen was measured when the animals were sacrificed. The level of IL-1β and IL-18 in serum were measured by ELISA. Downstream of TLRs signal pathway, MyD88 and NFκB, were confirmed by WB.

Results: *Mycobacterium* mixed CFA injected IFNγ KO mice showed a significantly higher fever than normal mice (p= 0.0009). These fever were significantly reduced after TLR inhibitory peptide treatment (TIP-1; p=0.008, MIP-2; p=0.029). In addition, hypertrophy of the spleen and LN was found in IFNγ KO mice, which were statistically significantly improved through TLR inhibitor injection (TIP-1 and MIP-2, p<0.05). The level of IL-1β and IL-18 in serum were significantly increased in the CFA injected IFNγ KO mice and increased inflammatory cytokines was decreased by TLR inhibition (TIP-1 and MIP-2, p<0.05). MyD88 and phosphorylated NFκB were increased in LN of CFA injected IFNγ KO mice and the proteins was down-regulated with treatment of TIP-1 or MIP-2. The IL-1β expression in LN and spleen was increased in CFA injected IFNγ KO mice and it decreased in TIP1 or MIP-2 treated mice.

Conclusion: Abnormal fever, lymph node and spleen tissue enlargement, and increase in serum inflammatory cytokines (IL-1β, IL-18), etc., have been confirmed that the symptoms accompanying adult-type Still's disease appear in animals. In addition, it was confirmed that these immune responses were reduced in the TLR inhibitor treatment group. Collectively, these in vivo findings mean that *Mycobacterium* mixed CFA injected IFNγ KO mice was showed pathological features of AOSD and TIP-1and MIP-2 has broad specificity for TLRs and should be effective plausible candidate for the treatment of AOSD.

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POS0236 ROLE OF NLRP3 INFLAMMASOME-DERIVED ASC SPECKS IN ADULT-ONSET STILL'S DISEASE

Keywords: Biomarkers, Innate immunity, Rare/orphan diseases

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Background: The NLRP3 inflammasome is a critical multi-molecular platform involved in mediating innate immune responses, and could play a role in Adult onset Still's disease (AOSD). Upon NLRP3 inflammasome activation, a large protein complex assembles, resulting in the re-localisation of apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC), secretion of IL-1β and IL-18, and ASC aggregation into a single inflammasome speck. ASC specks are considered as potential biomarkers for inflammatory disorders, with subsequent release into the bloodstream during pyroptosis. Somatic variants in NLRP3 have also been observed in phenocopies of autoinflammatory disorders and their role in AOSD has been postulated.

Objectives: To investigate the role of NLRP3-derived ASC protein specks as a potential disease activity biomarker and *NLRP3* genetic variants in the pathogenesis of AOSD.

Methods: Sera from 103 AOSD patients [treatment naïve, on treatment, and patients who previously failed several bDMARDs and were involved in CONSIDER clinical trial (n=30)] were analysed. These were compared to Systemic Juvenile Idiopathic Arthritis (sJIA, n=14), Cryopyrin Associated Periodic Syndrome (CAPS, n=9), Schnitzler's syndrome (n=10) and Familial Mediterranean Fever (FMF, n=27) patients. Extracellular NLRP3-derived ASC specks were identified using flow cytometry (double positivity for ASC-PE and NLRP3-APC), gating for events around 1µm in size, in sera. To determine if ASC/NLRP3 speck levels provide additional biological information, the correlation between the specks and known biomarkers (such as IL-18 and C-reactive protein (CRP)) were analysed in sera. This involved cytokine profiling, using 13-plex Inflammatory LEGENDplex assay and high-sensitivity CRP ELISAs. Deep whole exome sequencing (WES x100) (analysis restricted to autoinflammatory panel) was carried out on DNA from the 30 CONSIDER trial patients.

Results: In serological analyses, extracellular ASC/NLRP3 speck levels were increased in AOSD patients compared to 32 healthy control (HC) sera ($p<0.01$, Figure 1A). ASC/NLRP3 levels defined three subgroups of AOSD patients (low, moderate and high). High ASC/NLRP3 levels were present in all pre-treatment sera from CONSIDER trial patients ($p< 0.001$), compared to HC, suggesting their role may be dependent on the stage of the disease process. Interestingly, these patients were still responsive to canakinumab, showing significant reduction in extracellular ASC/NLRP3 levels in CONSIDER clinical trial cohort (baseline to week 12), compared to placebo ($p<0.01$) (Figure 1B) [1]. There was no correlation between ASC/NLRP3 specks and CRP levels (Figure 1C) or ASC/NLRP3 and total IL-18. No germline or somatic variants in *NLRP3* were identified from patients in the CONSIDER cohort despite very high levels of ASC/NLRP3 specks being detected in their serum.

Conclusion: This study involved development of an assay that quantifies extracellular ASC specks as a biomarker of NLRP3 activation, to improve diagnoses and classification of SAIDs, particularly those with sporadic or unknown causes, such as AOSD. Increased levels of extracellular NLRP3-derived ASC specks were found in sera of AOSD compared to HC and autoinflammatory disease controls. Our findings also demonstrate heterogeneity within AOSD cohorts, with high-ASC speck levels in therapy-resistant CONSIDER trial patients suggesting the role of ASC specks may be dependent on the particular stage of the disease. Further analysis of rare somatic variants in genes associated with myelodysplastic syndrome, another condition associated with elevated ASC/NLRP3 specks and systemic inflammation, is currently underway, since this may provide an alternative explanation for our findings.

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POS0237

ADULT-ONSET STILL'S DISEASE AND COVID 19 SHARE GENETIC EXPRESSION RELATED TO HYPERINFLAMMATION: DEFINING THE POSSIBLE ROLE OF THE SPECIALIZED PRO-RESOLVING LIPID MEDIATOR PROTECTIN D1 IN MODULATING MACROPHAGES POLARIZATION AND FUNCTION

Keywords: -omics, COVID, Innate immunity

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Background: COVID-19 and autoinflammatory diseases, such as Adult-onset Still's Disease (AOSD), are characterized by a massive production and uncontrolled secretion of pro-inflammatory cytokines. The specialized pro-resolving lipid mediators (SPMs) family is one the most important processes counteracting hyperinflammation inducing tissue repair and homeostasis restoration. Among SPMs, Protectin D1 is able to exert antiviral features in animal models.

Objectives: The aim of this study was to compare the transcriptome of peripheral blood mononuclear cells (PBMCs) from patients with AOSD and COVID-19 and to evaluate the role of PD1 on those diseases, especially in modulating macrophages polarization.

Methods: This study enrolled patients with AOSD, COVID-19, and healthy donors (HD). Next-generation deep sequencing was performed on to identify the differences in PBMCs transcripts profiles. Plasma levels of PD1 were assessed by commercial ELISA kits. Monocytes-derived macrophages were polarized into M1 and M2 phenotype. We analyzed the effect of PD1 on macrophages differentiation. At 10 days, macrophages were analyzed for surface. expression of subtypes markers by flow cytometry. Cytokines production was measured in supernatants using Bio-Plex Pro Human Cytokine 17-plex Assay kit (Bio-Rad).

Results: All COVID-19 participants (n=21) were hospitalized. We found statistically significant higher ferritin levels between intensive care unit (ICU) and non-ICU patients ($p=0.006$), and higher procalcitonin ($p=0.03$). Five patients with AOSD, out of 13, had a systemic score (SS) ≥1. The most frequent manifestations were arthralgia (8/13), arthritis (5/13) and fever (3/13). Moreover, we found higher levels of ferritin and CRP in the AOSD SS ≥1 group as compared to AOSD SS=0 group. We also enrolled thirteen HD age- and sex-matched to AOSD patients. Transcriptome analysis of PBMCs from HD, AOSD, and COVID-19 patients is reported in Figure 1, showing the PCA plot (A), the pathway analysis by Pantherdb.org (B), the volcano plots representing differential expression analysis of genes in COVID-19 vs HD, AOSD vs HD, and COVID-19 vs AOSD (C), and the transcriptome heatmaps (D), showing that inflammation- and lipid catabolism-related genes are specifically dysregulated and those associated with monocytes phenotype and function were upregulated in COVID-19 and AOSD patients compared to HDs.

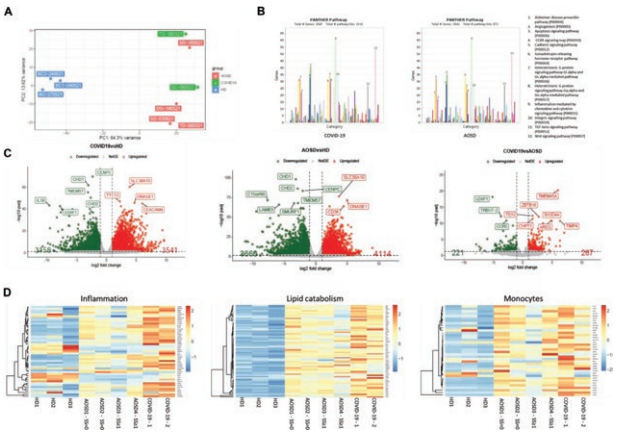


Figure 1.

Patients affected by COVID-19, hospitalized in intensive care unit (ICU), showed higher levels of PD1 compared to not-ICU hospitalized patients and HDs (ICU COVID-19 vs not-ICU COVID-19, p= 0.02; HDs vs ICU COVID-19, p= 0.0006). PD1 levels were increased in AOSD patients with SS ≥1 compared to patients with SS=0 (p=0.028) and HD (p=0.048). PD1 stimulation increased the expression of CD206 in M2 monocytes-derived macrophages from both COVID-19 and AOSD patients (COVID-19: untreated vs PD1, p=0.0098; AOSD: untreated vs PD1 p= 0.0234), whilst PD1 did not affect CD80 expression in both M1 and M2 macrophages and CD206 expression in M1 macrophages. A significant increase of both IL-10 and macrophage inflammatory protein (MIP-1β) was observed in M2 macrophages from COVID-19 patients after PD1 stimulation (IL-10, p= 0.03; MIP-1β, p= 0.003); the same results were found in AOSD patients (IL-10, p= 0.03; MIP-1β, p= 0.03).

Conclusion: PD1 can induce pro-resolutory programs in both AOSD and COVID-19 increasing M2 polarization and inducing their activity. PD1-treated M2 macrophages from AOSD and COVID-19 patients increased the production of IL-10, thus promoting anti-inflammation, and enhanced homeostatic restoration through MIP-1β production.

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POS0238 IMPLICATION OF THE CSF1-CSF1R PATHWAY IN THE CROSSTALK BETWEEN SYNOVIAL FIBROBLASTS AND MACROPHAGES IN PIGMENTED VILLONODULAR SYNOVITIS

Keywords: Synovium, Innate immunity, Rare/orphan diseases

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Background: Pigmented villonodular synovitis (PVNS) is a rare joint disease with an estimated incidence of 14 per million per year, arising from synovia that results in a secondary inflammatory joint response, pain and destruction. PVNS is associated with abnormal fibroblastic cells, often involving a specific chromosomal translocation, t(1;2) (CSF-1;COL6A3), resulting in the overexpression of colony-stimulating factor 1 (CSF1 or M-CSF), recruitment of CSF1 receptor (CSF1R) macrophages and fusion in giant cells. Despite therapeutic option such as surgery, the risk of recurrence of the synovitis remains high (50%). This has led to the development of systemic therapies targeting the CSF1 pathway (kinase inhibitors such as Imatinib, monoclonal antibodies) that have shown their efficacy is about 30% of patients but with significant and sometimes serious adverse effects. Therefore, there is currently a clear medical need to improve the management of patients with PVNS.

Objectives: To better decipher the mechanisms leading to the development of PVNS and study the crosstalk between synovial fibroblasts and macrophages in this disease.

Methods: Synovial tissue from newly diagnosed PVNS (diffuse or localized forms) patients was used for this analysis. Histology H&E staining and immunohistochemistry was performed. Single cell analysis was performed on 5 patients. We implemented a primary culture of synovial fibroblasts from PVNS biopsies stimulated with pro-inflammatory cytokines. We studied the effect of culture supernatant on blood derived monocytes/macrophages.

Results: Immunohistochemistry revealed the presence of synovial PDPN+ fibroblasts, CD31+ endothelial cells, Ki67+ proliferating cells, MERTK+ and CCR2+ infiltrating the tissues. We performed single-cell RNA sequencing (n=5 patients). Combined with public scRNAseq datasets, we observed that PVNS (n=8) lining PDPN+PRG4+ fibroblasts are the main sources and express higher levels of CSF1 than in osteoarthritis (OA, n=3) or rheumatoid arthritis (RA, n=4). All macrophage subsets (tissue resident TIMD4+ or LYVE1+ or infiltrating inflammatory macrophages) highly express CSF1R that could explain their enrichment (2 folds, p<0.05), especially in the localized forms of PVNS. Ratio between fibroblasts and macrophages was increase in the diffuse forms of the disease. We next study the in vitro crosstalk between fibroblasts and macrophages. For this purpose, we analysed conditioned media (CM) from PVNS synovial fibroblasts (n=3). After treatment with TNFa or IL1b, enhanced secretion of CSF1 was observed and the CM had an enhanced capacity to sustain viability of blood derived monocytes/macrophages (2-3 folds, p<0.05). In this setting, the potent CSF1R inhibitor Imatinib totally reversed macrophage viability to baseline (p<0.05).

Conclusion: This study highlights the key role played by synovial fibroblasts and macrophages in PVNS pathogenesis. An inflammatory vicious cycle takes place between these two cell types, implicating CSF1-CSF1R. Efficient targeting of this pathway is the subject of current research and we already validated a PVNS mouse model using xenografted PVNS human biopsies that will be useful to study for example the local delivery of CSF1R kinase inhibitors or neutralizing antibodies.

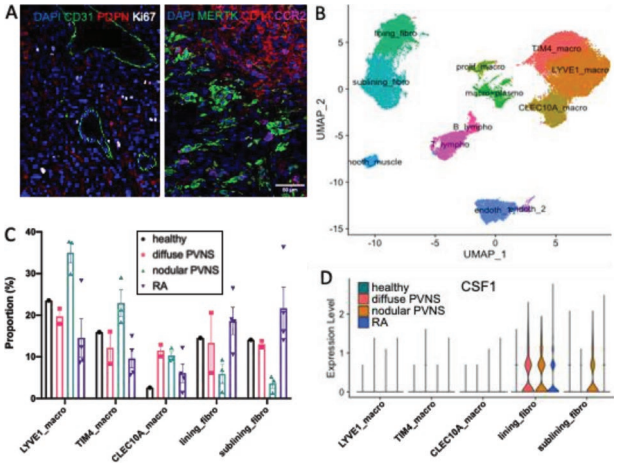


Figure 1. Histology and scRNAseq of PVNS. A. Characterisation of synovial PDPN+ fibroblasts, CD31+ endothelial cells, Ki67+ proliferating cells, MERTK+ and CCR2+ macrophages in a localized PVNS by immunofluorescence. B. scRNAseq analysis (10X genomics) of synovial cells in healthy, diffuse/localized PVNS and RA (n=10 patients). C. Higher proportion of anti-inflammatory TIM4+ and LYVE+ macrophages in localized PVNS. D. High expression of CSF1 in lining fibroblasts of PVNS patients

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POS0239 JAK-INHIBITORS SUPPRESS IFN-DEPENDENT ANTIGEN PRESENTATION IN CDC42HICD14+ CELLS

Keywords: Rheumatoid arthritis, Innate immunity, Disease-modifying Drugs (DMARDs)

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Background: We have recently shown that Rho GTPase activation in macrophages results in arthritis development in mice. These macrophages show a tight interaction with T cells leading to suppression of cell homing and regulate migration of thymic T regulatory cells to periphery contributing arthritis development[1].
Objectives: To translate findings in experimental arthritis to human RA, we explore the phenotype of *CDC42*^{hi}CD14$^+$ cells in blood and synovial tissue of RA patients and investigate how anti-rheumatic treatment intervene with the Rho GTPase-dependent molecular mechanisms of arthritis.
Methods: We used transcriptome (RNAseq) of CD14$^+$ and CD4$^+$ cells of 77 active RA patients naïve to TNF-inhibitors (TNFi) and of 59 inactive RA patients treated with methotrexate (MTX, n=18), TNFi (n=10) and JAK-inhibitors (JAKi, n=24), or having no DMARD treatment (n=7). In both cohorts, patients were stratified by mean expression of *CDC42* in CD14$^+$ cells to mimic activation of Rho GTPases. Differentially expressed genes (DEG) were identified by DESeq2 (nominal p<0.05). Transcriptomics of CD14$^+$ and CD4$^+$ cells were analyzed and translated into clinical correlates of inflammation and disease activity by DAS28. Additionally, we investigated a cluster of *CDC42*^{hi} macrophages in synovial tissue (STM) using single cell RNAseq in 25 patients[2].
Results: In two independent sets, *CDC42*^{hi}CD14$^+$ cells were characterized by enrichment of DEG operating in the oxidative phosphorylation, proteasome activity and RNA transcription. Many DEG were under transcriptional control of NFE2L1, known to supervise those processes. DEG with strong correlation to *CDC42* defined the metabolic signature (MetSig) of *CDC42*^{hi}CD14$^+$ cells, which summarized the expression of *ATP5BP*, *COX7A2*, *PSMB6*, *PSME3, GTF3C6,* and *GTF2E2*. High MetSig recognized CD14$^+$ cells enriched with MHC transcripts, components in peptide loading and expression of proteasome subunits. MetSig^{hi}CD14$^+$ cells had high chemokine and cytokine production and migratory phenotype. Analyzing STM, we identified *CDC42*^{hi}STM with high MetSig expressing complete set of immunoproteasome genes, high levels of MHC receptors and peptide loading proteins. Additionally, this STM cluster was affected by IFN-γ. We experimentally confirmed that immunoproteasome expression in CD14$^+$ cells was dependent on IFN-γ and not hypoxia, common at inflammation. Examining effect of antirheumatic treatment, we found *CDC42*^{hi}CD14$^+$ cells were infrequent (*OR*= 11.9, [3.4, 49.7], p<0.0001) and the MetSig reduced (p=0.0004) in patients treated with JAKi compared to other DMARDs. Concurrently, CD14$^+$ cells of those patients had low production of TNF-α, IL-6, IL-1β, CXCL8 and IL-10 (all, p<0.05). mRNA of immunoproteasome subunits, peptide loading proteins and MHC-II (including *HLA-DRB1*) were downregulated. Analysis of CD4$^+$ cells of JAKi treated patients showed upregulation of TCR components and high expression of Rho GTPases. This indicated a disruption of CD14$^+$/CD4$^+$ interaction in the immunological synapse. To investigate a direct effect of JAKi on the MetSig genes and immunoproteasome, we treated CD14$^+$ cell cultures with tofacitinib. JAKi upregulated *NFE2L1* and decreased expression of the immunoproteasome subunits, but expression of MetSig remained unchanged. Lastly, we investigated connection between the MetSig and RA disease activity (by DAS28) in a regression model. The model identified patients, which had a strong dependence between these parameters. At bottom of the model were patients with low DAS28 and MetSig, mostly treated with JAKi. Consequently, patients at the upper part may represent suitable candidates for JAKi-treatment.
Conclusion: This study demonstrates that CDC42-related metabolic signature identifies antigen-presenting CD14$^+$ cells that migrate to joints to coordinate autoimmunity. JAKi suppress the antigen presenting capacity of CD14$^+$ cells. The MetSig in CD14$^+$ cells may identify candidate patients for JAKi treatment.
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Acknowledgements: We thank the research nurses Anneli Lund and Marie-Louise Andersson at Rheumatology Clinic, Sahlgrenska University Hospital, Gothenburg, for blood sampling. We thank all RA patients who participated. We appreciate support of Aridaman Pandit and Weiyang Tao at Center for Translational Immunology, University Medical Center Utrecht, NL, sharing data of the BiOCURA cohort. We are thankful to Prof. Marcela Pekna at Clinical Neuroscience, University of Gothenburg, assisting with hypoxia experiments.
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POS0240 EFFECT OF METHOTREXATE UPON OXIDATIVE STRESS MEDIATED TRANS-DIFFERENTIATION OF NEUTROPHILS IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Innate immunity, Disease-modifying Drugs (DMARDs)

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Background: Rheumatoid arthritis (RA), a chronic systemic autoimmune disorder, is associated with inflammation coupled with oxidative stress, and translates into infiltration of immune cells in inflamed joints i.e. predominantly neutrophils (~90%). In previous studies, a subpopulation of accumulated neutrophils trans-differentiated into neutrophil-dendritic cell hybrids or N-DCs (CD66b$^+$/CD83$^+$). This N-DCs acquired antigen presenting properties (HLA-DR$^+$/CD80$^+$/CD86$^+$) and generated enhanced reactive oxygen species (ROS), collectively causing oxidative damage in the synovial fluid (SF) [**1**,**2**]. The impact of Methotrexate (MTX) upon redox status along with trans-differentiation and degree of apoptosis in neutrophils remains unclear and was the focus of this study.
Objectives: As oxidative stress is known to facilitate trans-differentiation of neutrophils, a critical factor for disease progression, the impact of MTX was studied on the status of trans-differentiation i.e. CD83$^+$/HLA-DR$^+$ in neutrophils sourced from healthy controls along with their status of activation, generation of ROS and degree of apoptosis.
Methods: In the SF of RA cases (n=25), frequency of trans-differentiation was examined by immunophenotyping (CD66b, CD83, HLA-DR). The *ex-vivo* effect of MTX on neutrophils (+/- Phorbol Myristate Acetate or PMA; to mimic the redox microenvironment in SF of RA) sourced from healthy controls was studied in terms of their status of trans-differentiation (CD66b$^+$/CD83$^+$/HLA-DR$^+$), activation (Myeloperoxidase or MPO$^+$), generation of ROS using CMH_2DCFDA and proportion of apoptosis (Annexin V$^+$, pro-apoptotic Caspase 3$^+$, anti-apoptotic Bcl-2$^+$) in flow cytometer.
Results: In the SF of RA cases, frequency of trans-differentiation (CD66b$^+$/CD83$^+$/HLA-DR$^+$) correlated positively with DAS28-CRP (r= 0.70, p<0.001), culminating in their disease promoting role. MTX (at non-toxic concentrations, 0-100 µM) did not impact on generation of ROS in neutrophils sourced from healthy controls. However, when oxidative stress was induced by PMA, MTX in a dose dependent fashion synergistically facilitated a redox imbalance (enhanced frequency of ROS^{high} neutrophils) coupled with enhanced trans-differentiation (CD83^{high}), antigen presentation (HLA-DR^{high}), activation (%MPO$^+$) and apoptosis i.e increased Annexin V$^+$, Caspase 3$^+$ along with compromised Bcl-2.
Conclusion: Oxidative stress can trigger trans-differentiation of neutrophils, which is a crucial for disease progression, and preventing trans-differentiation can be a potential therapeutic target in RA. Although MTX, an immunomdulator is the drug of choice for treatment of RA, our studies exert a certain degree of caution, as MTX in an enhanced pro-oxidant milieu facilitated generation of oxidative stress, and could impact on disease progression.
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POS0241 MONOCYTE-DERIVED TRANSCRIPTOMES EXPLAIN THE INEFFECTIVENESS OF ABATACEPT IN RHEUMATOID ARTHRITIS

Keywords: -omics, bDMARD, Rheumatoid arthritis

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Background: The factors contributing to the efficacy of abatacept in patients with rheumatoid arthritis (RA) remain unknown.
Objectives: We aimed to identify cellular, transcriptomic, and proteomic features that predict responses or resistance to abatacept.
Methods: Blood samples were collected from 22 RA patients treated with abatacept at the initiation and after three months of treatment. Response to treatment was defined based on the EULAR response criteria, and seven patients were classified as responders and the others as non-responders. We quantified gene expression levels in peripheral blood mononuclear cells (PBMCs) by RNA-Seq, 67 plasma protein levels by multiplexed immunoassay, and the expression of surface molecules (CD3, 19, and 56) by flow cytometry, in addition to collecting clinical characteristics. Additionally, three gene expression data sets concerning the efficacy of abatacept[1–3], comprising 37 responders and 50 non-responders in total, were used to replicate the current study. We compared the gene expression of responders versus non-responders in each set and meta-analyzed the results.
Results: Among the clinical characteristics, the number of monocytes was significantly higher in the non-responders before treatment (p = 0.01). Regarding the transcriptome data, we found 952 differentially expressed genes (DEGs) between the responders and the non-responders before treatment initiation. A cell-type enrichment analysis showed that the DEGs were enriched in monocytes ($p = 8.7 \times 10^{-212}$, Figure 1A). Additionally, gene set enrichment analysis showed enrichment in the gene module, including *MYD88* and *TIRAP*, with the strongest significance among all of the pathways tested. When we estimated the expression of *MYD88* and *TIRAP* in monocytes by deconvolution analysis, the non-responders had higher expression before treatment initiation (p = 0.04 and 0.03, respectively). Among the 67 protein levels, two exhibited a correlation with the expression of the module ($p < 0.05$). Of these, hepatocyte growth factor (HGF), which is produced by monocytes, was present at significantly higher concentrations in non-responders before treatment (p = 0.02). The analysis of the replication sets identified 1,695 DEGs. These were also enriched for the genes expressed in monocytes ($p = 2.9 \times 10^{-90}$, Figure 1B) but not for the module detected in the current study. Among the DEGs, those expressed in monocytes were enriched for the genes involved in the aerobic electron transport system in mitochondria based on gene set enrichment analysis.

Conclusion: Monocyte-derived transcriptomic features before treatment underlay the differences in abatacept efficacy. The pathway activated in monocytes was the *MYD88*/*TIRAP*-HGF axis in the current study, but that pathway in the replication set was the aerobic electron transport system. Overall, our results highlight the contribution of monocytes as the cells responsible for abatacept-treatment resistance and the heterogeneity of activated pathways within them.

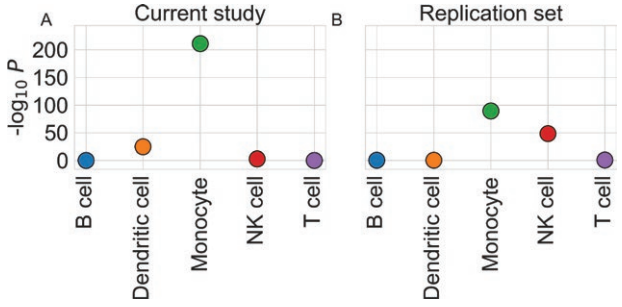


Figure 1. Results of cell type enrichment analysis of differentially expressed genes (DEGs) concerning response to abatacept.

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POS0242 RESPONSE TO ABATACEPT IN RHEUMATOID ARTHRITIS PATIENTS REQUIRES A SPECIFIC MACROPHAGE POLARISATION

Keywords: Innate immunity, Rheumatoid arthritis

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Background: Abatacept (ABA), a biologic treatment for rheumatoid arthritis (RA), is a recombinant fusion protein composed of the extracellular domain of human CTLA-4 combined with the Fc portion of human IgG1. Lack of response to treatment occurs in 30 % of RA patients, highlighting the need to better understanding its mechanism of action and to identify predictive factors of response. Although ABA is considered to interrupt the costimulatory signal, the importance of this mechanism on the drug effect lacks evidence. Moreover, therapies targeting T cells were disappointing in RA [1]. In contrast, ABA has been shown to induce reverse signaling in antigen-presenting cells, by activating the indolamine 2,3-dioxygenase (IDO) pathway (a strong tolerogenic enzyme) in macrophages and dendritic cells [2]. ABA also acts on nitric oxide (NO) production, a proinflammatory molecule capable of inhibiting IDO action, although conflicting data have been reported.

Objectives: The objective of this study was to evaluate the importance of direct mechanisms on antigen-presenting cells and identify biomarkers of the response to ABA.
Methods: Sera (n = 71) and RNA from whole blood (n = 57) were collected from RA patients before treatment by ABA. Abundance of GM-CSF, gamma interferon (IFNg), IL-10, IDO, iNOS were quantified using ELISA and addressable laser bead assay (ALBIA). RT-qPCR was performed on *IDO1* transcript. Response to ABA was assessed 6 months after its introduction, using EULAR response criteria. A costimulation *in vitro* model was developed: monocytes-derived macrophages (using GM-CSF or M-CSF) from healthy donors were polarized 8 days with LP, with or without IFNg. T cells were cocultured with anti-CD3, with or without ABA, anti-CD28 antibodies or IDO inhibitor (1-MTDT). Proliferation was assessed using CFSE.
Results: Before ABA therapy, GM-CSF, IFNg and IL-10 in sera were increased in serum of good responders compared to non-responders. Our costimulation model showed that in macrophages exposed to GM-CSF, IFNg, LPS, ABA inhibited lymphocyte proliferation by 53%. Inhibition by ABA was only 10% when macrophages has not been exposed to IFNg, suggesting a central role of this cytokines. Furthermore, inhibition was only achieved when both GM-CSF + IFNγ were used, highlighting the need for a combination of these two factors. In presence of GM-CSF with IFNg + LPS + ABA, IDO was increased in macrophages. ABA increased iNOS production in macrophages when either IFNg or GM-CSF were not involved in their polarisation, neutralising IDO and leading to T cell proliferation. These results show a balance between iNOS and IDO in macrophages, modulated by IFNγ and GM-CSF. In RA patients, ABA could release the tolerogenic potential of polarized macrophages, decreasing T cell proliferation. Accordingly, iNOS increased in non-responders' sera after 6 months of ABA treatment while *IDO1* expression increased in good responders whole blood RNA. In fact, in ABA responders, IDO increase in macrophages enabling a tolerogenic effect since iNOS is not induced.
CONCLUSION:

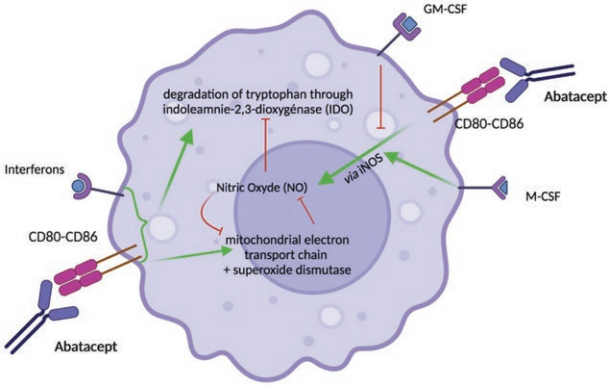


Figure 1. Abatacept direct signaling on antigen presenting cells.

Specific macrophage polarisation with IFNg and GM-CSF, leading to an increase in IDO production without increasing iNOS after treatment, could be the key to achieving a good response to ABA. This finding supports the macrophage-mediated action of ABA and may contribute to the development of a prediction system for abatacept response based on macrophage polarisation.
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POS0243 KYNURENINE METABOLITES LIMIT INFLAMMATION THROUGH TRICARBOXYLIC ACID CYCLE (TCA) REMODELING

Keywords: Innate immunity, Cell biology, Rheumatoid arthritis

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Background: Following LPS stimulation, extensive transcriptional and metabolic reprogramming leads to metabolic remodeling that allows macrophages to dynamically adopt to environmental cues.[1] A failure to accurately orchestrate macrophage responses can skew immune responses towards inflammation and various disease states.[2]
Objectives: Macrophages have a central role in Rheumatoid arthritis (RA) by promoting chronic inflammation and joint destruction. Although targeted biologicals have transformed treatment options for RA patients, almost half of them fail to achieve clinical remission[2]. Better understanding of the regulation of key immuno-metabolic pathways in macrophages of RA patients will inform on how cellular metabolism and inflammation interlink to identify novel metabolism-related therapeutic targets.
Methods: To delineate disease-specific effects in monocytes and macrophages derived from RA patients compared to healthy individuals we performed whole transcriptome analysis (RNA-Sequencing) and untargeted metabolomics. By integrating these datasets with metabolite assessment in the serum of RA patients, we found upregulation of Indoleamine 2, 3-dioxygenase 1 (IDO1) and cumulation of L-kynurenine (KYN) to be hindered in peripheral blood monocytes and macrophages derived from rheumatoid arthritis (RA) patients compared to healthy individuals in response to LPS.
Results: In macrophages, we identified cumulation of KYN in response to LPS, to limit pro-inflammatory macrophage functions through tricarboxylic acid (TCA) cycle remodeling, characterized by decreased succinate-dehydrogenase (SDH) activity and increased Gluthathione synthesis. Aligning with these findings, kynurenine exerted anti-inflammatory effects when administrated to LPS-activated macrophages in vitro by limiting the production of Interferon gamma (IFNγ) and Tumor Necrosis Factor (TNF). Using the small molecule IDO1 inhibitor Linrodostat and exogenously added KYN we showed that KYN accumulation in response to LPS regulates the glycolytic switch and cumulation of metabolites associated with inflammation such as glycolytic intermediates and the TCA cycle intermediates Succinate and Itaconate.
Conclusion: Collectively, our data highlight KYN as a key immunometabolite that directly interferes with macrophage activation and suggest that dysregulation of the kynurenine pathway in RA patients mediates inflammation and disease progression.
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Everything you need to know about managing in axSpA

POS0244 PROTOCOL VIOLATION IN A TREAT-TO-TARGET STRATEGY IN AXIAL SPONDYLOARTHRITIS: DATA FROM THE OPEN-LABEL, PRAGMATIC, CLUSTER-RANDOMISED TICOSPA TRIAL

Keywords: Randomized control trial, Treat to target, Spondyloarthritis

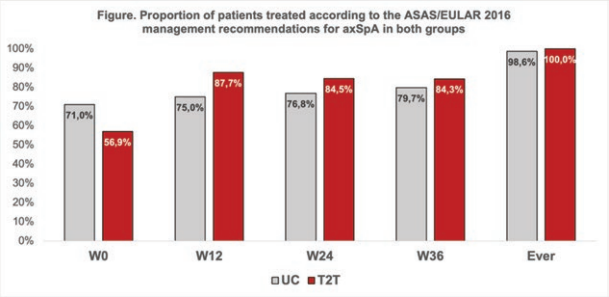
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Background: Despite the ASAS-HI (primary outcome) did not reach statistical significance in the TICOSPA trial, other clinically relevant secondary outcomes were numerically higher in the treat-to-target (T2T) strategy in comparison to Usual Care (UC), including the ASAS-HI. Three hypotheses have been considered to explain this observation: a lack of power, the risk of protocol violations in the T2T arm and the potential optimal care in the UC arm.
Objectives: a) To evaluate the proportion of patients (pts) with protocol violations in the T2T group during the 48 weeks (48W) of follow up as well as the impact and predictive factors of such violation; b) to compare the proportion of pts treated according to the ASAS/EULAR 2016 management recommendations for axSpA over the follow-up period in both arms.
Methods: *Study design:* pragmatic, prospective, cluster-randomized controlled, 48W trial (NCT03043846) with 18 participating centers. *Inclusion criteria*: Pts with a diagnosis of axSpA and fulfilling ASAS criteria, non-optimally treated with NSAIDs, bDMARD-naïve and ASDAS >2.1. *Study treatment regimens:* SpA expert centers were selected to participate in the study: then, they were randomly allocated (1:1) to the treatment arm: a) T2T: the management strategy was pre-specified based on strict application of 2016 ASAS/EULAR axSpA recommendations (Q4W), with a target of ASDAS <2.1; b) UC: treatment decisions at the rheumatologist's discretion (Q12W). *Statistical analysis*: *a) Protocol violations:* in the T2T arm were evaluated at every visit by the question "Was the recommendation for treatment from last visit followed by physician and patient?". Factors associated with at least one protocol violation over the study were evaluated using multivariate logistic regression. Outcomes at 48W were compared between T2T violators (T2T-V) vs. T2T non-violators (T2T-NV) vs. UC using ANOVA test; b) *optimal care in UC:* proportion of pts treated according to the 2016 ASAS/EULAR recommendations over the follow-up period in both arms were compared.
Results: 160 pts initiated the trial (T2T:80 and UC:80). *a) Protocol violations:* In the T2T arm, 41/80 (51.2%) pts violated the protocol during at least one visit. A total of 27.7% violations were represented by a lack of switching to a second NSAID and 41.2% by a lack of initiation of a first bDMARD. Baseline predictive factors independently associated with the protocol violation were the country (France vs. others; OR 3.8 (95%CI 1.1-15.0)), female sex (OR 4.4 (1.5-15.1)), diagnosis delay ≤7 years (OR 3.4 (1.1-11.9)), HLA-B27 negative (OR 6.4 (1.6-32.2)) and CRP≥6mg/L (OR 4.2 (1.3-15.9)). After 48W of follow-up, T2T-NV vs. T2T-V showed similar ratios of ASAS-HI improvement. ASDAS-LDA, ASDAS-ID and ASDAS-CII outcomes were more prevalent in T2T-NV vs. T2T-V, although these differences did not reach statistical significance (Table 1). b) *Optimal care in UC*: the proportion of pts managed according to the 2016 ASAS/EULAR recommendations was very high in both arms, i.e. always above 75% also in the UC arm, although no statistical differences were found (p=0.490) (Figure 1).

Table 1. Impact of protocol violation across groups

	Groups			p-value			
	T2T-NV N = 39	T2T-V N = 41	UC N = 80	ANOVA	T2T-NV vs. T2T-V	T2T-NV vs. UC	T2T-V vs. UC
ASAS40 W48	14 (35.9%)	16 (39.0%)	19 (24.1%)	0.177	0.773	0.177	0.087
ASDAS-LDA W48	24 (61.5%)	19 (46.3%)	32 (40.5%)	0.087	0.173	**0.027**	0.504
ASDAS-ID W48	11 (28.2%)	8 (19.5%)	10 (12.7%)	0.117	0.361	**0.038**	0.319
ASDAS-CII W48	22 (56.4%)	16 (39.0%)	26 (32.9%)	**0.049**	0.120	**0.015**	0.506
ASDAS-MI W48	6 (15.4%)	8 (19.5%)	9 (11.4%)	0.479	0.627	0.565	0.226
ASAS-HI improvement W48	14 (35.9%)	16 (39.0%)	21 (26.6%)	0.322	0.773	0.297	0.162

Conclusion: The prevalence of pts violating the protocol in the T2T arm was high, although it did not explain the non-significance of the primary outcome in the TICOSPA trial (ASAS-HI improvement). In contrast, the proportion of pts managed according to the ASAS/EULAR recommendations in the UC arm was very high, suggesting that the UC group was optimally treated.



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POS0245 BLOOD-BASED EXTRACELLULAR MATRIX BIOMARKERS CAN IDENTIFY ENDOTYPES OF PATIENTS WITH AXSPA AND RESPONDERS TO ADALIMUMAB TREATMENT

Keywords: Spondyloarthritis, Biomarkers

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease associated with extracellular matrix (ECM) remodelling of the cartilage, bone, and connective tissues. Adalimumab (ADA) is an effective treatment, but not all patients respond, and this may relate to subtypes of the disease (endotypes). Serological quantification of ECM-mediated biomarkers may be useful to identify axSpA endotypes and monitor treatment response to ADA.
Objectives: 1) To identify endotypes of patients with axSpA using blood-based ECM biomarkers at baseline and 2) To investigate differences in response to ADA by BASDAI and ASDAS criteria within the endotypes.
Methods: ECM biomarkers were measured in serum from patients with axSpA in the three studies (MASH (n=41), DANISH (n=49) and ASIM (n= 45)) at baseline [1–3]. MASH was a cross-sectional study while in DANISH and ASIM patients were randomised to receive treatment with ADA 40 mg or placebo every other week (e.o.w.) for 6 or 12 weeks (ASIM and DANISH, respectively) followed by ADA 40 mg e.o.w. for an additional 18 or 12 weeks (ASIM and DANISH, respectively). Biomarkers of type II collagen formation (PRO-C2), type I collagen degradation (C1M), inflammation (CRP, CRPM) citrullinated and degraded vimentin (VICM) and neutrophil activity (CPa9-HNE) were measured by immunoassays. Biomarker data was log-transformed, standardized by mean centering and scaled by the standard deviation prior to principal component analysis (PCA) and K-means clustering. Response to ADA based on BASDAI50 response, ASDAS clinical important improvement (CII) and major improvement (MI) at study week 24 was compared in the PCA components and between clusters using Mann-Whitney tests. Key demographic parameters were also compared between clusters using Mann-Whitney and chi-squared tests.
Results: The variability of baseline ECM biomarker data among patients with axSpA was mainly explained by two dimensions (PC1 and PC2). Type I collagen degradation and inflammation biomarkers (C1M and CRP), reflecting tissue inflammation, were the primary contributors to PC1, whereas type II collagen formation (PRO-C2), reflecting cartilage turnover, contributed the most to PC2 (Figure 1A). In ADA-treated patients, BASDAI50 responders, patients with

ASDAS CII, and ASDAS MI had a higher score in PC1 compared to BASDAI50 non-responders, patients with no ASDAS CII and no ASDAS MI, respectively (p=.05, p<.001, p<.001). No differences were observed in PC2. Two distinct clusters were identified from the PC1 and PC2 (Figure 1). Patients in Cluster 1 had higher levels of ECM biomarkers, a greater BASDAI50 response compared to those in Cluster 2 (89.5% vs. 73.2%) and a higher % of patients with ASDAS CII and ASDAS MI (73.7% vs. 32.1% and 92 % vs. 73%, all p<.05). No significant differences were observed in the demographic parameters between Clusters.

Conclusion: The PCA analysis identified two orthogonal dimensions related to: inflammation (driven by C1M and CRP) and cartilage turnover (driven by PRO-C2). Two clusters were determined. Patients from Cluster 1, associated with high inflammation, demonstrated a greater BASDAI50 response and ASDAS improvement when treated with ADA than those from Cluster 2. These findings may help profiling treatment response within patients with axSpA.

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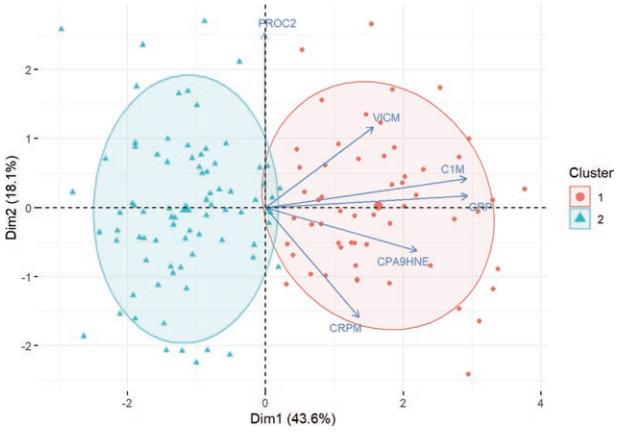


Figure 1. PCA Biplot of individuals and principal component dimensions. Cluster differentiation is shown by colour.

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POS0246 BIMEKIZUMAB REDUCED MRI INFLAMMATORY LESIONS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: WEEK 52 RESULTS FROM THE BE MOBILE 1 AND BE MOBILE 2 PHASE 3 STUDIES

Keywords: Spondyloarthritis, Clinical Trials, bDMARD

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Background: Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated consistent and sustained efficacy up to Week (Wk) 52 across the full spectrum of axial spondyloarthritis (axSpA), in patients (pts) with non-radiographic axSpA (nr-axSpA) and radiographic axSpA (r-axSpA; i.e. ankylosing spondylitis).[1,2]

Objectives: To evaluate the impact of BKZ on MRI inflammatory lesions of the sacroiliac joints (SIJ) and spine to Wk 52 in the phase 3 studies BE MOBILE 1 (nr-axSpA) and BE MOBILE 2 (r-axSpA).

Methods: BE MOBILE 1 (NCT03928704) and BE MOBILE 2 (NCT03928743) study designs have been reported previously.[1] From Wk 16, all pts received subcutaneous BKZ 160 mg every 4 wks (Q4W). MRI endpoints (Spondyloarthritis Research Consortium of Canada [SPARCC] SIJ and ASspiMRI-a Berlin modification [hereafter termed 'Berlin spine'] inflammation scores) were assessed at baseline (BL), Wk 16 and Wk 52 via central reading by two independent expert readers with an adjudicator, and were measured in the subset of pts in the MRI sub-studies. SPARCC SIJ and Berlin spine scores range from 0–72 and 0–69, respectively, with lower scores indicating less inflammation. We report observed case mean absolute SPARCC SIJ and Berlin spine scores and the proportion of pts with inflammation of the SIJ/spine at BL achieving MRI remission (SPARCC SIJ <2; Berlin spine ≤2)[3] to Wk 52.

Results: At BL, 60% of pts with nr-axSpA (152/254) and 42% of pts with r-axSpA (138/332) had SPARCC SIJ assessments as part of the MRI sub-studies; 57% (146/254) and 41% of pts (137/332) had Berlin spine assessments, respectively. Of these, 63% of nr-axSpA (BKZ: 50, placebo [PBO]: 46) and 46% of r-axSpA (BKZ: 42, PBO: 21) pts had SIJ inflammation (SPARCC SIJ ≥2)[3] at BL; 21% (BKZ: 17, PBO: 13) and 41% (BKZ: 36, PBO: 20) had spine inflammation (Berlin spine >2)[3] at BL, respectively. At BL, mean SPARCC SIJ and Berlin spine scores were comparable between BKZ- and PBO-randomised pts (**Figure 1**). Reductions in mean absolute SPARCC SIJ and Berlin spine scores observed at Wk 16 were maintained to Wk 52 for continuous BKZ pts; pts who switched from PBO to BKZ at Wk 16 (PBO-switcher) reached similar levels of improvement to continuous BKZ pts at Wk 52 (**Figure 1**). Among pts with SIJ inflammation at BL, a greater proportion of BKZ- vs PBO-randomised pts achieved SPARCC SIJ remission at Wk 16; a similar pattern was observed for pts with inflammation of the spine at BL, with a greater proportion of BKZ- vs PBO-randomised pts achieving Berlin spine remission at Wk 16 (**Table 1**). The proportion of continuous BKZ and PBO-switcher pts achieving MRI remission largely improved to Wk 52 (**Table 1**).

Conclusion: Across the axSpA spectrum, dual inhibition of IL-17A and IL-17F with BKZ resulted in a reduction in MRI inflammatory lesions of the SIJ and spine and an increased proportion of pts achieving MRI remission at Wk 52.

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Disclosure of Interests: Xenofon Baraliakos Speakers bureau: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer and UCB Pharma, Paid instructor for: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer and UCB Pharma, Consultant of: AbbVie, BMS, Chugai, Eli Lilly, Galapagos, Gilead, MSD, Novartis, Pfizer and UCB Pharma, Victoria Navarro-Compán Speakers bureau: AbbVie, Eli Lilly, Janssen, MSD, Novartis, Pfizer and UCB Pharma, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer and UCB Pharma, Grant/research support from: AbbVie and Novartis, Denis Poddubnyy Speakers bureau: AbbVie, BMS, Eli Lilly, MSD, Novartis, Pfizer and UCB Pharma, Consultant of: AbbVie, Biocad, Eli Lilly, Gilead, GSK, MSD, Moonlake, Novartis, Pfizer, Samsung Bioepis and UCB Pharma, Grant/research support from: AbbVie, Eli Lilly, MSD, Novartis and Pfizer, Maureen Dubreuil Consultant of: Amgen and UCB Pharma, Grant/research support from: Pfizer paid to institution, Alexander Bennett Speakers bureau: AbbVie, Eli Lilly, MSD, Novartis, Pfizer and UCB Pharma, Paid instructor for: AbbVie, Biogen, Novartis, Pfizer and UCB Pharma, Grant/research support from: Pfizer, Lennart Jans Speakers bureau: AbbVie, Novartis, Eli Lilly and UCB Pharma, Ute Massow Employee of: UCB Pharma, Carmen Fleurinck Employee of: UCB Pharma, Thomas Vaux Employee of: UCB Pharma, Alicia Ellis Employee of: UCB Pharma, Natasha de Peyrecave Employee of: UCB Pharma, Walter P Maksymowych Speakers bureau: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer and UCB Pharma, Consultant of: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer and UCB Pharma, Grant/research support from: AbbVie, Janssen, Novartis, Pfizer and UCB Pharma, Employee of: Chief Medical Officer for CARE ARTHRITIS.

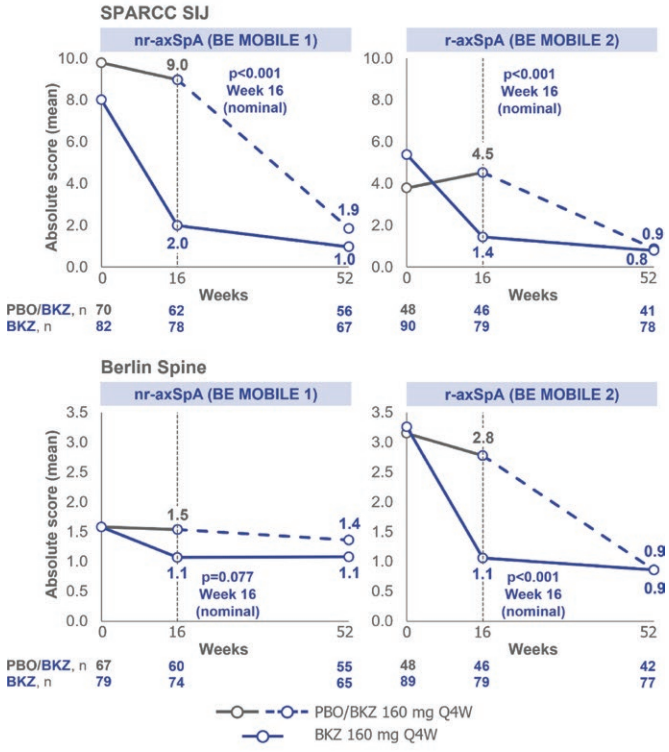
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Table 1. Proportion of pts with inflammation of the SIJ/spine at BL achieving MRI remission [OC]

		Wk 16		Wk 52	
n/N (%)		PBO	BKZ 160 mg Q4W	PBO→ BKZ 160 mg Q4W	BKZ 160 mg Q4W
SPARCC SIJ remission[a]	BE MOBILE 1 (nr-axSpA)	9/42 (21.4)	30/48 (62.5)	20/35 (57.1)	32/40 (80.0)
	BE MOBILE 2 (r-axSpA)	4/21 (19.0)	23/41 (56.1)	12/18 (66.7)	28/37 (75.7)
Berlin spine remission[b]	BE MOBILE 1 (nr-axSpA)	1/12 (8.3)	8/15 (53.3)	3/11 (27.3)	6/15 (40.0)
	BE MOBILE 2 (r-axSpA)	2/18 (11.1)	23/31 (74.2)	10/16 (62.5)	23/30 (76.7)

Randomised set (includes only pts in MRI sub-studies). [a]SPARCC SIJ <2, assessed in the subgroup of pts with SPARCC SIJ ≥2 at BL; [b]Berlin spine ≤2, assessed in the subgroup of pts with Berlin spine >2 at BL.

Figure. Mean MRI inflammation scores up to Wk 52 in pts with nr-axSpA and r-axSpA [OC]



Randomised set (includes only pts in MRI sub-studies).

Abbreviations: BKZ: bimekizumab; BL: baseline; IL: interleukin; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; OC: observed case; PBO: placebo; pts: patients; Q4W: every four weeks; r-axSpA: radiographic axial spondyloarthritis; SIJ: sacroiliac joint; SPARCC: Spondyloarthritis Research Consortium of Canada; Wk: Week.

POS0247

RESOLUTION OF ENTHESITIS AND PERIPHERAL ARTHRITIS WITH BIMEKIZUMAB IN PATIENTS WITH AXIAL SPODYLOARTHRITIS: WEEK 52 RESULTS FROM THE BE MOBILE 1 AND BE MOBILE 2 PHASE 3 STUDIES

Keywords: Enthesitis, bDMARD, Spondyloarthritis

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Background: A history of enthesitis or peripheral arthritis has been reported in >30% of patients (pts) with axial spondyloarthritis (axSpA),[1] both of which contribute to disease burden. Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated efficacy in phase 3 parallel studies in pts with non-radiographic (nr-)axSpA (BE MOBILE 1) and radiographic axSpA (r-axSpA i.e. ankylosing spondylitis; BE MOBILE 2).[2,3]

Objectives: To evaluate the impact of BKZ on the main peripheral manifestations of axSpA, to Week (Wk) 52.

Methods: Pts in BE MOBILE 1 (NCT03928704; nr-axSpA) met Assessment of SpondyloArthritis International Society (ASAS) classification criteria, pts in BE MOBILE 2 (NCT03928743; r-axSpA) met both modified New York and ASAS criteria. Pts were randomised to receive subcutaneous BKZ 160 mg every 4 wks (Q4W) or placebo (PBO) to Wk 16. From Wk 16 all pts received BKZ 160 mg Q4W.[2] Among pts with enthesitis (Maastricht Ankylosing Spondylitis Enthesitis [MASES]>0), at least one swollen joint (SJC>0), or at least one tender joint (TJC>0) at baseline (BL), we report mean change from baseline (CfB) using multiple imputation (MI). Pts (%) achieving complete resolution of enthesitis (MASES=0 in pts with MASES >0 at BL) and peripheral arthritis (SJC=0 in pts with SJC >0 at BL, assessed in 44 joints) using non-responder imputation, is also reported.

Results: At BL, 73.2% nr-axSpA pts (BKZ: 94/128, PBO: 92/126) and 59.9% r-axSpA pts (BKZ: 132/221, PBO: 67/111) had enthesitis; peripheral arthritis (SJC >0) was present in 34.6% (BKZ: 45/128, PBO: 43/126) and 19.9% (BKZ: 44/221, PBO: 22/111) of nr-axSpA and r-axSpA pts, respectively. BL MASES, SJC and TJC were largely similar between treatment arms (**Table 1**). Across the axSpA spectrum, greater mean CfB in MASES was achieved with BKZ vs PBO at Wk 16; improvements continued to Wk 52 with continuous BKZ and in pts switching from PBO to BKZ at Wk 16 (**Table 1**). Similarly, >50% BKZ pts achieved complete resolution of enthesitis at Wk 16 vs <33% of PBO pts; by Wk 52, responses of PBO/BKZ-switchers approached those of BKZ pts (**Figure 1**). At Wk 16, greater mean CfB in SJC and TJC was achieved with BKZ vs PBO-randomised pts with nr-axSpA. Improvements largely continued to Wk 52 with BKZ for both continuous BKZ and PBO/BKZ-switcher pts (**Table 1**). Resolution of peripheral arthritis was achieved by >57% of BKZ vs >41% of PBO-randomised pts at Wk 16; by Wk 52, proportions were similar among continuous BKZ and PBO/BKZ-switcher pts (**Figure 1**).

Table 1. Mean BL and CfB in enthesitis and peripheral arthritis [MI]

		BL		Wk 16 CfB			Wk 52 CfB	
Mean (SE)		PBO	BKZ 160 mg Q4W	PBO	BKZ 160 mg Q4W	Nominal p value	PBO/BKZ 160 mg Q4W	BKZ 160 mg Q4W
MASES[a]	nr-axSpA[b]	4.9 (0.4)	4.8 (0.3)	−1.3 (0.3)	−2.4 (0.3)	0.013	−2.9 (0.4)	−3.6 (0.3)
	r-axSpA[c]	4.4 (0.3)	4.2 (0.3)	−1.5 (0.3)	−2.4 (0.3)	0.003	−3.2 (0.3)	−2.9 (0.3)
SJC[d]	nr-axSpA[e]	3.8 (0.5)	4.2 (0.8)	−1.3 (0.6)	−3.1 (0.7)	0.007	−2.9 (0.4)	−2.5 (0.8)
	r-axSpA[f]	3.9 (0.7)	4.7 (0.6)	−2.1 (0.5)	−3.6 (0.5)	0.074	−3.6 (0.8)	−4.2 (0.6)
TJC[g]	nr-axSpA[h]	6.3 (0.6)	6.0 (0.8)	−1.1 (0.5)	−3.0 (0.7)	0.008	−3.5 (0.6)	−4.0 (0.8)
	r-axSpA[i]	5.4 (0.6)	5.3 (0.6)	−2.9 (0.5)	−2.5 (0.4)	0.401	−4.5 (0.6)	−4.0 (0.5)

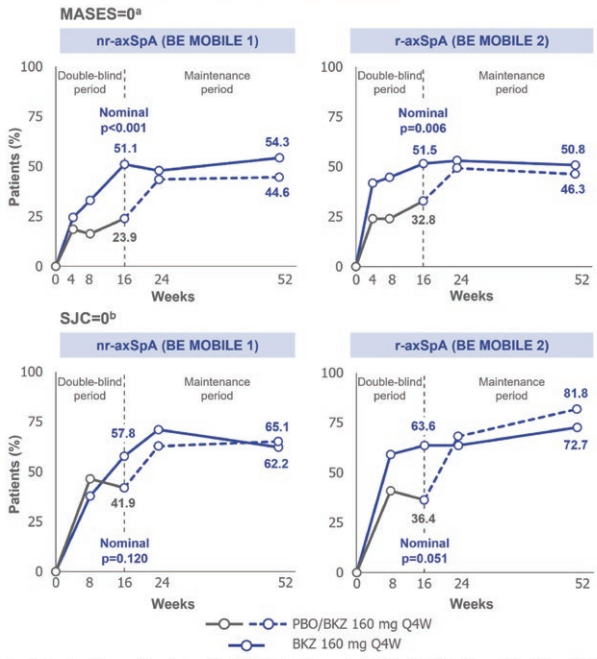
Randomised set. [a]Assessed in pts with: [a]MASES >0 at BL: [b]PBO n=92; BKZ n=94; [c]PBO n=67; BKZ n=132; [d]SJC >0 at BL: [e]PBO n=43; BKZ n=45; [f]PBO n=22; BKZ n=44; [g]TJC >0 at BL: [h]PBO n=85; BKZ n=78; [i]PBO n=61; BKZ n=116. P values without any multiplicity adjustment are indicated as nominal p values and should not be used as an indicator of statistical significance.

Conclusion: BKZ treatment resulted in sustained improvements in peripheral manifestations across the axSpA spectrum. Resolution of enthesitis was achieved in ~half of BKZ-treated pts by Wk 52; a similar pattern was observed for peripheral arthritis, with more than half of pts achieving resolution to Wk 52.

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Figure. Resolution of enthesitis and peripheral arthritis to Wk 52 [NRI]



Randomised set. Assessed in patients with: [a]MASES >0 at BL: nr-axSpA: PBO n=92, BKZ n=94; r-axSpA: PBO n=67, BKZ n=132, or [b]SJC >0 at BL: nr-axSpA: PBO n=43, BKZ n=45; r-axSpA: PBO n=22, BKZ n=44. P values represent odd ratios for BKZ vs PBO comparison, calculated using logistic regression with factors for treatment, region, MRI/CRP classification (BE MOBILE 1 only) and prior TNFi exposure (BE MOBILE 2 only). P values without any multiplicity adjustment are indicated as nominal p values and should not be used as an indicator of statistical significance.

Abbreviations: BKZ: bimekizumab; BL: baseline; CfB: change from baseline; MASES: Maastricht ankylosing spondylitis enthesitis score; MI: multiple imputation; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; PBO: placebo; Q4W: every four weeks; r-axSpA: radiographic axial spondyloarthritis; SE: standard error; SJC: swollen joint count; TJC: tender joint count; Wk: week.

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POS0248

EXPLORING TUMOUR NECROSIS FACTOR INHIBITOR DRUG LEVELS DURING DISEASE ACTIVITY-GUIDED TAPERING IN PATIENTS WITH INFLAMMATORY ARTHRITIS: SECONDARY ANALYSES FROM THE BIODOPT TRIAL

Keywords: bDMARD, Inflammatory arthritides, Tapering

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Background: Fluctuations in tumour necrosis factor inhibitor (TNFi) drug levels in patients with inflammatory arthritis (IA) during disease activity-guided tapering is not well described.

Objectives: To compare TNFi drug-levels in the tapering group, relative to the control group, from baseline to month 18 based on data from the BIODOPT trial.

Methods: BIODOPT was designed as a pragmatic, multicentre, randomised controlled, open-label trial (EudraCT 2017-001970-41) of 18 months duration [1]. Patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) in sustained (≥12 month) low disease activity (LDA) and treated with TNFi at baseline were enrolled and randomised into a disease activity-guided tapering or control in a 2:1 ratio. Blood samples at baseline and month 18 were analysed for TNFi drug levels. Based on previous research, the TNFi drug level category was considered intermediate if values were between: adalimumab 5.0-8.0 mg/L, certolizumab pegol 14.7-40.0 mg/L, etanercept 1.8-4.6 mg/L, golimumab 1.0-3.0 mg/L, or infliximab 1.6-5.0 mg/L. Values greater or lesser were considered as high or low TNFi category, respectively. A mixed Poisson regression with robust variance estimator was used for the analyses on TNFi categories; missing data were imputed as low TNFi category.

Results: Of 129 TNFi-treated patients, 88 were randomised to tapering and 41 to a control arm with standard care. Blood samples at baseline and month 18 were available for: tapering group 89% (78/88) and control group 90% (37/41). As expected, baseline TNFi categories were comparable between groups as presented in ***Figure 1***. At 18 months, fewer patients in the tapering group were in the high TNFi category, relative risk: RR: 0.53 (95%CI 0.31 to 0.90, *P*=0.02), ***Table 1***. Even though more patients in the tapering group were in the low TNFi category at 18 months, the difference was non-significant, RR: 1.47 (95%CI: 0.94 to 2.32, P=0.09). The observed changes in TNFi categories between groups from baseline to 18 months indicates acceptable compliance to the trial interventions. At 18 months, 32% (28/88) in the tapering group and 0% (0/41) in the control group had achieved ≥50% dose reduction of their TNFi and were in LDA. The majority of patients in the tapering group were in the high (39% [11/28]) or intermediate (39% [11/28]) TNFi category at baseline; only 22% (6/28) were in the low TNFi category. Thus, indicating a greater chance of successful tapering for patients with high or intermediate TNFi drug levels at baseline.

Conclusion: Successful TNFi tapering was associated with high or intermediate TNFi levels at baseline. Fewer patients in the tapering group were in the high TNFi category at 18 months; thus, indicating acceptable compliance to the trial interventions. Further research is needed for the implications of therapeutic drug monitoring in the management of rheumatic diseases.

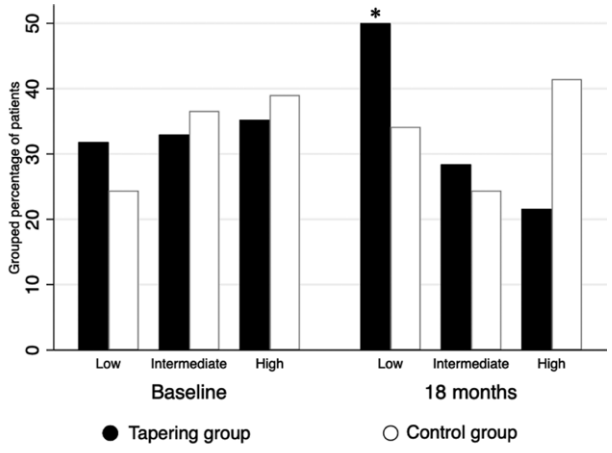
Table 1. TNFi drug level categories at 18 months.

Variable	18 months		
	Tapering group *N=88*	**Control group** *N=41*	**Between group difference RR (95%CI)**
TNFi drug level category:			
High, n (%)	19 (22%)	17 (42%)	0.53 (0.31 to 0.90)
Intermediate, n (%)	25 (28%)	10 (24%)	1.12 (0.60 to 2.09)
Low, n (%)	44 (50%)	14 (34%)	1.47 (0.94 to 2.32)

N: number, RR: relative risk, 95%CI: 95% confidence interval, TNFI: tumour-necrosis factor inhibitor.

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Adalimumab: Low <5.0 mg/L, Intermediate 5.0–8.0 mg/L, High >8 mg/L.
Certolizumab pegol: Low <14.7 mg/L, Intermediate 14.7– 40.0 mg/L, High, >40.0 mg/L.
Etanercept: Low <1.8 mg/L, Intermediate 1.8– 4.6 mg/L, High >4.6 mg/L.
Golimumab: Low <1.0 mg/L, Intermediate 1.0– 3.0 mg/L, High >3.0 mg/L.
Infliximab: Low < 1.66 mg/L, Intermediate 1.66– 5.0 mg/L, High >5.0 mg/L.

Figure 1: TNFi drug level categories in the tapering and control group during the study period. Statistically significant between group difference is marked with *.

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POS0249

SEX DIFFERENCES IN PATIENT-REPORTED OUTCOMES IN AXIAL SPONDYLOARTHRITIS PATIENTS TREATED WITH TUMOR NECROSIS FACTOR INHIBITORS: RESULTS FROM A MULTINATIONAL OBSERVATIONAL COHORT STUDY

Keywords: Patient reported outcomes, bDMARD, Gender/diversity issues

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Background: Women with axial spondyloarthritis (axSpA) tend to have higher scores on patient-reported outcome measures (PROMs), such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Bath Ankylosing Spondylitis Functional Index (BASFI), compared to men with the same condition. However, it is not well known whether these sex differences are maintained over time during treatment with tumor necrosis factor inhibitors (TNFi), or which factors can potentially explain these sex-based differences.

Objectives: To examine sex differences in BASDAI and BASFI over time in axSpA patients treated with their first TNFi, and to identify potential factors contributing to observed sex differences.

Methods: Pooled data were collected from biologic-naive axSpA patients initiating their first TNFi in the EuroSpA registries. A three-level linear mixed model structure was employed to analyze sex differences in PROMs (BASDAI and BASFI, scale 0-100) over time (sex*time), accounting for correlations between repeated measurements within subjects and between subjects within countries. Baseline characteristics were explored as potential explanatory variables for observed sex differences over time, and interactions between sex, time, and explanatory variables were analyzed. Univariable analysis was performed by incorporating one explanatory variable at a time, while multivariable analysis was used to investigate the effect of multiple explanatory variables on the regression coefficient of sex*time. Only explanatory variables that affected this regression coefficient by more than 10% in univariable analysis were considered for multivariable analysis. A complete case analysis was performed when data were missing for explanatory variables.

Results: This study analyzed data from 11,753 axSpA patients (37% female) with at least two BASDAI measurements over two years, and from 9,780 patients (38% female) with at least two BASFI measurements over the same period. At baseline, women were older and had higher BASDAI/BASFI scores, while men had higher CRP levels, longer disease duration, and higher HLA-B27 positivity. During the follow-up period, women had significantly higher mean BASDAI scores than men (mean difference 6.05; 95% CI 5.27 to 6.83). Additionally, the differences in BASDAI scores between women and men increased by an average of 0.67 (95% CI 0.04 to 1.29) per year. These findings indicate that the sex differences in BASDAI scores persisted and increased over time. In the univariable analysis of explanatory variables, increased age (-8.9%) and longer disease duration (-4.7%) notably explained the sex differences in the BASDAI scores (Figure 1). However, no explanatory variables were eligible for inclusion in the multivariable analysis. We also observed that the sex differences in BASDAI scores were reduced over time in HLA-B27-positive patients, but increased in those with psoriasis (Figure 1). Although women had slightly higher overall BASFI scores than men (mean difference 3.25; 95% CI 2.32 to 4.19), this difference did not vary by time (β = 0.25; 95% CI -0.36 to 0.86).

Conclusion: Women with axSpA treated with their first TNFi had significantly higher mean BASDAI and BASFI scores compared to men over a two-year follow-up period. The mean difference in BASDAI scores increased slightly over time, and the magnitude of this difference was affected by HLA-B27 positivity (reduced) and psoriasis (increased). Further research is needed to understand the mechanisms behind these sex differences and their clinical implications.

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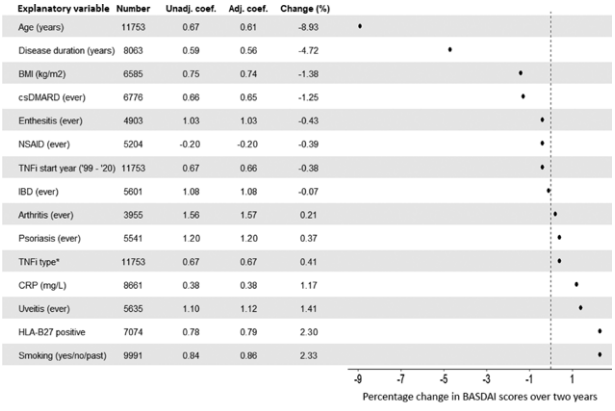


Figure. Explanatory variables and their effect on sex differences in BASDAI scores (scale 0 - 100) over two years of follow-up, where one unit of time is equivalent to one year. The figure presents the unadjusted coefficients (sex*time) and adjusted coefficients for the explanatory variables and the corresponding (percentage) change. There was a relevant interaction between sex, time, and (1) ever having psoriasis (β=5.07) and (2) HLA-B27 positivity (β=-2.46).
*The different TNFi types were: infliximab, etanercept, adalimumab, certolizumab and golimumab.

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POS0250

PLACEBO-CONTROLLED EFFICACY AND SAFETY OF UPADACITINIB THROUGH ONE YEAR IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis

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Background: Upadacitinib (UPA), a Janus kinase inhibitor, was effective and well tolerated in patients (pts) with non-radiographic axial spondyloarthritis (nr-axSpA) through 14 weeks (wks) of treatment.[1]

Objectives: This analysis assessed the efficacy and safety of UPA vs placebo (PBO) through 1 year.

Methods: The SELECT-AXIS 2 nr-axSpA study included a 52-wk randomized, double-blind, PBO-controlled period. Enrolled adults had a clinical diagnosis of active nr-axSpA fulfilling the 2009 ASAS classification criteria, objective signs of inflammation based on MRI sacroiliitis and/or elevated C-reactive protein, and an inadequate response to NSAIDs. One-third of pts had an inadequate response to biologic DMARDs. Pts were randomized 1:1 to UPA 15 mg once daily or PBO. Concomitant medications, including NSAIDs, had to be kept stable through wk 52. The study protocol outlined that pts who did not achieve ASAS20 at any two consecutive study visits between wks 24 to 52 should receive rescue therapy with NSAIDs, corticosteroids, conventional synthetic/biologic DMARDs, or analgesics. Cochran-Mantel-Haenszel (CMH) test with non-responder imputation incorporating multiple imputation (NRI-MI) was used to handle missing data and intercurrent events for binary efficacy endpoints. Mixed-effect model repeated measures (MMRM) was used to assess continuous efficacy endpoints. NRI was used for binary endpoints after rescue and as observed analysis excluding data after rescue for continuous endpoints. Treatment-emergent adverse events (TEAEs) are reported through wk 52.

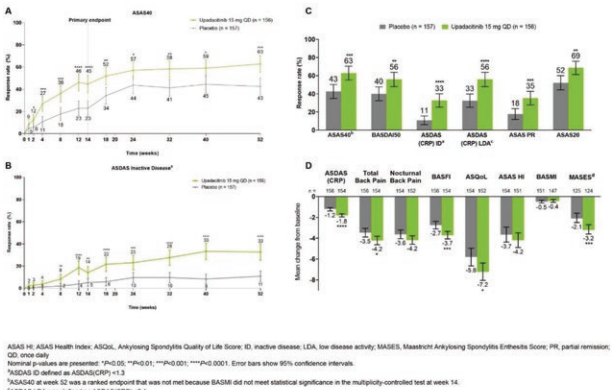
Results: Of the 314 pts randomized, 259 (82%; UPA, n=130; PBO, n=129) completed wk 52 on study drug. More pts achieved an ASAS40 response with UPA vs PBO from wks 14 to 52 with a 20% treatment difference at wk 52 (63% vs 43%; nominal *P* <.001; **Figure 1**). The proportion of pts achieving ASDAS inactive disease with UPA remained higher than PBO at wk 52 (33% vs 11%; nominal *P* <.0001; **Figure 1**). Consistent improvements and maintenance of efficacy were also seen across other disease activity measures. Between wks 24 and 52, fewer pts on UPA (9%) than PBO (17%) received rescue therapy. A similar proportion of pts in each treatment group had a TEAE (**Table 1**). Infections were the most common TEAE; the rates of serious infections and herpes zoster were higher with UPA vs PBO, although no new serious infections were reported from wks 14 to 52. COVID-19 events were balanced between treatment groups. No opportunistic infections, malignancy excluding non-melanoma skin cancer, adjudicated major adverse cardiovascular events, inflammatory bowel disease, or deaths were reported. Two pts (1.3%) on PBO had adjudicated venous thromboembolic events.

Conclusion: UPA showed consistent improvement and maintenance of efficacy vs PBO through 1 year across multiple disease activity measures. No new safety risks were identified with longer-term UPA exposure. These results continue to support the benefit of UPA in pts with active nr-axSpA.

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Figure. ASAS40 (A) and ASDAS Inactive Disease (B) Responses Through Week 52 With Additional Efficacy Endpoints at Week 52 (C, D)



ASAS HI: ASAS Health Index; ASQoL, Ankylosing Spondylitis Quality of Life Score; ID, inactive disease; LDA, low disease activity; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; PR, partial remission; QD, once daily
Nominal p-values are presented: *P<0.05; **P<0.01; ***P<0.001; ****P<0.0001. Error bars show 95% confidence intervals.
‡ASDAS ID defined as ASDAS(CRP) <1.3
†ASAS40 at week 52 was a ranked endpoint that was not met because BASMI did not meet statistical significance in the multiplicity-controlled test at week 14.
‡ASDAS LDA was defined as ASDAS(CRP) <2.1
§MASES was assessed in patient with baseline enthesitis (n=125 in the placebo group; n=124 in the upadacitinib group)

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Table 1. Safety through week 52

Event, n (%)	PBO (n = 157)	UPA 15 mg QD (n = 156)
Any AE	103 (66%)	107 (69%)
Serious AE	6 (3.8%)	6 (3.8%)
AE leading to D/C	4 (2.5%)	6 (3.8%)
COVID-19-related AE	22 (14%)	24 (15%)
Deaths	0	0
Infection	60 (38%)	68 (44%)
Serious infection	1 (0.6%)	2 (1.3%)
Herpes zoster	1 (0.6%)	5 (3.2%)
Malignancy other than NMSC	0	0
NMSC	1 (0.6%)	0
Hepatic disorder	7 (4.5%)	6 (3.8%)
Neutropenia	1 (0.6%)	8 (5.1%)
MACE (adjudicated)	0	0
VTE (adjudicated)	2 (1.3%)[a]	0
Uveitis[b]	3 (1.9%)	2 (1.3%)
Inflammatory bowel disease	0	0

[a]Both patients had non-serious events of deep vein thrombosis in the lower limb with risk factors including obesity and prior deep vein thrombosis in one patient and concomitant COVID-19 infection in the other patient.[b]Three events of uveitis occurred in each treatment group (among n = 3 patients in the PBO group and n = 2 patients in the UPA group); two events in the PBO group and one in the UPA group occurred in patients with a history of uveitis.

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POS0251 RISK OF CARDIOVASCULAR DISEASE ASSOCIATED WITH LONG-TERM USE OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN ANKYLOSING SPONDYLITIS

Keywords: Cardiovascular disease, Epidemiology, Spondyloarthritis

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Background: Ankylosing spondylitis (AS) is associated with increased cardiovascular disease, but there are limited data as to whether prolonged treatment with non-steroidal anti-inflammatory drugs (NSAIDs) increases the cardiovascular risk in AS patients. We aimed to examine the risk of cardiovascular disease associated with long-term use of NSAIDs in a large real-world AS cohort.

Objectives: We aimed to examine the risk of cardiovascular disease associated with long-term use of NSAIDs in a large real-world AS cohort.

Methods: A nationwide population-based cohort of patients with AS and matched controls without AS were analysed. The primary outcome was cardiovascular disease, a composite outcome of ischemic heart disease, stroke, or congestive heart failure. Long-term use of NSAIDs was defined as use of NSAIDs for more than 365 cumulative defined daily doses. The association between long-term use of NSAIDs and incident cardiovascular disease was examined using a multivariable Cox proportional hazards regression model in both AS and non-AS populations.

Results: Among 19,775 patients with AS and 59,325 matched controls without AS, there were 1,663 and 4,308 incident cases of cardiovascular disease, showing an incidence of 16.9 and 13.8 per 1,000 person-years, respectively. Long-term use of NSAIDs increased the risk of cardiovascular disease in non-AS controls (adjusted hazard ratio [aHR], 1.29; 95% confidence interval [CI], 1.17–1.43). In contrast, long-term use of NSAIDs did not increase the risk of cardiovascular disease in AS patients (aHR, 0.97; 95% CI, 0.86–1.09; adjusted for age, sex, socioeconomic status, body mass index, smoking status, hypertension, diabetes, hyperlipidemia, and tumor necrosis factor inhibitor use).

Conclusion: Prolonged NSAID treatment in AS patients may not be as harmful as in the general population regarding cardiovascular risk.

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POS0252 DIFFERENCES IN SERUM DRUG LEVELS AND ANTI-DRUG ANTIBODIES IN PATIENTS WITH INFLAMMATORY ARTHRITIS TREATED WITH ORIGINATOR VS BIOSIMILAR ADALIMUMAB

Keywords: bDMARD, Inflammatory arthritides

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Background: Serum drug levels and anti-drug antibodies (ADAb) impact the therapeutic effectiveness of most TNF-inhibitors. Possible differences in immunogenicity profile and pharmacokinetics across biosimilar and originator TNFi are still to be elucidated.

Objectives: To compare serum drug levels, ADAb and treatment effect in patients treated with originator (Humira) vs biosimilar (Hyrimoz) adalimumab.

Methods: Patients with a clinical diagnosis of spondyloarthritis (SpA), rheumatoid arthritis (RA), psoriatic arthritis (PsA) or other inflammatory arthritis (adult JIA or unspecified polyarthritis) enrolled in the observational NOR-DMARD study and starting treatment with adalimumab were included in the present analyses. Patients were started on originator adalimumab (Humira) up to January 2020 and biosimilar adalimumab (Hyrimoz) from January 2020, based on a national annual tender system for biological drugs in Norway. Serum drug levels and neutralising ADAb were measured using an in-house fluorescence method and compared between groups by Mann-Whitney U test and $\chi 2$-test respectively, in addition to multivariable regression analyses adjusted for age, sex, previous use of bDMARDs, smoking and co-medication with methotrexate. Treatment response at 3 months was defined by Major or Clinically Important improvement in SpA and EULAR good or moderate response in RA, PsA and other inflammatory arthritis, and, and compared by $\chi 2$-test. Drug survival the first two years of adalimumab treatment was explored by Kaplan-Meier curves and Cox proportional hazard regression analysis.

Results: A total of 378 patients (177 SpA, 98 RA, 70 PsA, 33 other) (median age 45.7 years [SD 14.2], 174 [46%]) female) were included. 240 (63%) patients started originator and 138 (37%) started biosimilar adalimumab. 139/378 (37%) patients used methotrexate as co-medication, the proportions and dosage were comparable for originator and biosimilar adalimumab. Patients on originator adalimumab had lower serum drug levels (6.5 mg/L [IQR 3.0-9.8] vs 8.3 mg/L [IQR 5.4-11.1], p=0.0003) (Figure 1A), and a higher rate of ADAb formation (33 [14%] vs 6 [4%], p= 0.004) compared to patients treated with biosimilar adalimumab. The differences in serum drug levels and ADAb were consistent in multivariable

regression analyses (p= 0.032 and p= 0.020 respectively) and across diagnostic groups. There was no difference in treatment response or drug survival between originator and biosimilar adalimumab. (Table 1 and Figure 1B)

Conclusion: This observational study showed higher occurrence of ADAb formation and lower adalimumab serum levels in patients on adalimumab originator vs biosimilar, indicating differences in the immunogenicity profile. There was, however, no significant difference in clinical outcomes.

Table 1.

	Originator (Humira) (240)	Biosimilar (Hyrimoz) (138)	P-value
Diagnosis			
SpA	113 (47%)	64 (46%)	
RA	59 (23%)	39 (29%)	
PsA	41 (17%)	29 (21%)	
Other	27 (13%)	6 (4%)	
Co-medication methotrexate	86 (36%)	53 (38%)	0.53 #
Previous use of bDMARDs	90 (38%)	39 (29%)	0.048 #
Disease duration, median years (IQR)	4.5 (IQR 1.2-13)	4.8 (0.9-11.6)	0.79 *
Responders at 3 months, no (%)			
SpA	53/111 (48%)	29/59 (49%)	0.86 #
RA	35/57 (61%)	28/39 (72%)	0.29 #
PsA	25/41 (61%)	22/28 (79%)	0.12 #
Other	17/27 (63%)	4/5 (80%)	0.46 #

*ranksum test #chi square test

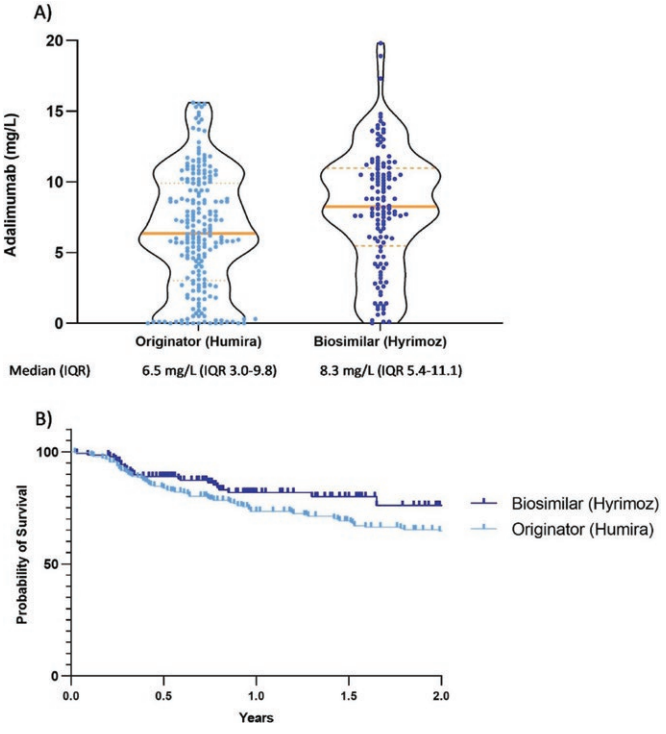


Figure 1. Serum adalimumab levels and drug survival, all diagnoses. A) Violin plot showing the probability density of the data at different values. Each data point is a participant, and the solid orange line show the group median. **B)** Drug survival the first two years of adalimumab treatment, stratified by originator (Humira) and biosimilar (Hyrimoz). P=0.14 (logrank test, not significant)

REFERENCES: NIL.

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POS0253

FACTORS ASSOCIATED WITH TREATMENT PATHWAYS IN EARLY AXIAL SPONDYLOARTHRITIS: A MULTISTATE ANALYSIS OF THE 10-YEAR FOLLOW-UP OF THE DESIR COHORT

Keywords: Descriptive Studies, Spondyloarthritis

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Background: Current recommendations for the management of patients with axial spondyloarthritis (axSpA) emphasize the need of individualized strategy in the therapeutic decision [1,2]. Thus, many factors seem to impact this strategy.

Objectives: The objectives of the study were to describe the therapeutic strategies observed in axSpA, and to assess the factors associated with treatment changes over time.

Methods: This study included patients with axSpA from the French prospective cohort DESIR, with a follow-up of 10 years. A multi-state model was built, including 4 treatment states with an increasing gradation ("none", "non-steroidal anti-inflammatory drugs (NSAID)", "conventional synthetic DMARD (csDMARD)", "TNF inhibitors (TNFi)"), and 6 possible transitions from one state to another. Estimation of the restricted mean sojourn times spent in each state from the state occupation probabilities was performed. Then, Cox regression models were used to study the potential impact of factors on transitions.

Results: 686 of the 708 patients which had more than one visit were analyzed. At cohort entry, 199 (29.0%) were untreated, 427 (62.2%) received NSAID, and 60 (8.7%) received csDMARD. Over the 10 years of follow-up, patients mostly received NSAID (46.4% of the time) followed by TNFi (24.4% of the time). In multivariable analysis (**figure 1**), presence of sacroiliitis on radiography, internal bowel disease and articular index were associated with transition to NSAID. Duration in the previous state was often a significant protective factor associated with transition to csDMARD or TNFi. Finally, the several disease activity outcomes were associated with most transitions.

Conclusion: This was the first study using a multistate model to easily represent the different states, transitions and their associated factors. There appeared to be subcategories of axSpA patients with different management (including some without any treatment), and a significant proportion of patients treated with csDMARD.

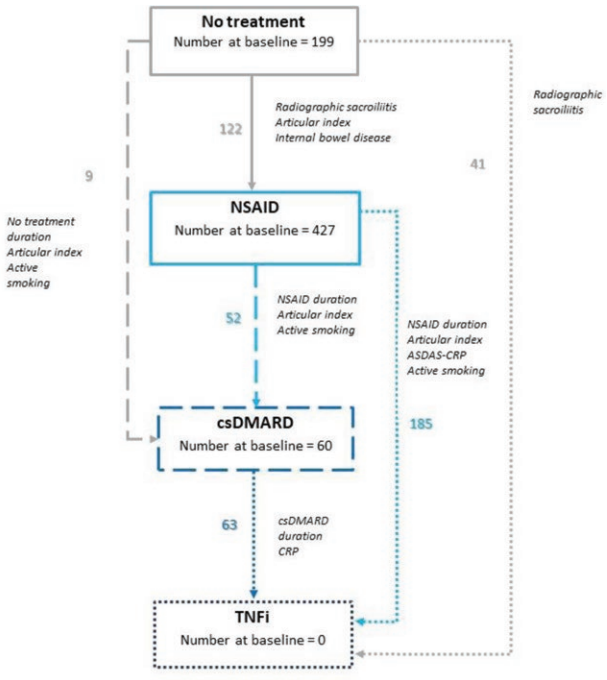


Figure 1. Multistate model representation. Each arrow corresponds to a possible transition (n=6). Number at baseline denotes the number of patients who started from the state at baseline. The number of events and factors significantly associated with each transition in the multivariable analysis are written near to the corresponding arrow.NSAID refers to non-steroids anti-inflammatory drugs, csDMARD stands for conventional synthetic Disease Modifying Anti-Rheumatic Drug, and TNFi for tumor necrosis factor inhibitors.

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POS0254 PREDICTING SUCCESSFUL TAPERING OF BIOLOGICS IN PATIENTS WITH INFLAMMATORY ARTHRITIS: SECONDARY ANALYSES FROM THE BIODOPT TRIAL

Keywords: Tapering, Inflammatory arthritides, bDMARD

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Background: Identification of predictors for successful tapering of biologics in patients with inflammatory arthritis (IA) can help to guide physicians and patients; but, evidence is lacking.

Objectives: To identify possible predictors for successful tapering of biological disease modifying anti-rheumatic drugs (bDMARDs) from baseline characteristics.

Methods: BIODOPT was a randomised, open-label, equivalence trial (EudraCT 2017-001970-41) where adults with rheumatoid arthritis (RA; n=61), psoriatic arthritis (PsA; n=26), or axial spondyloarthritis (axSpA; n=55) in ≥12 months low disease activity (LDA) were randomised 2:1 to disease activity-guided tapering or to continuation of biologics as usual care. Successful tapering at 18 months was pre-defined as patients who could reduce their biologic dose ≥50% while still being in LDA. Modified poisson regression with robust variance estimator was used for the analyses. Univariable analyses were: tapering group, sex, age, education, tobacco use, body mass index, comorbidity, arthritis characteristics i.e., diagnosis, duration, duration from diagnosis to treatment start, on ≥2 conventional synthetic DMARDs, on methotrexate, on tumour necrosis factor inhibitor (TNFi), on first bDMARD, on bDMARD number ≥3, duration of bDMARD, duration of remission on bDMARD, duration of LDA on bDMARD, previous bDMARD tapering, C-reactive protein (CRP) before first bDMARD, Health Assessment Questionnaire Disability Index (HAQ-DI), Pain Visual Analog Scale (VAS), Fatigue VAS, Patient Global Health VAS, Short Form Health Survey 36 (SF-36) physical and mental component summary (PCS and MCS), tender joints, Physician Global Health VAS, CRP, and in remission. Potentially important variables (univariate p<0.10) were included in the multivariable model. C-statistics was used to assess model prediction.

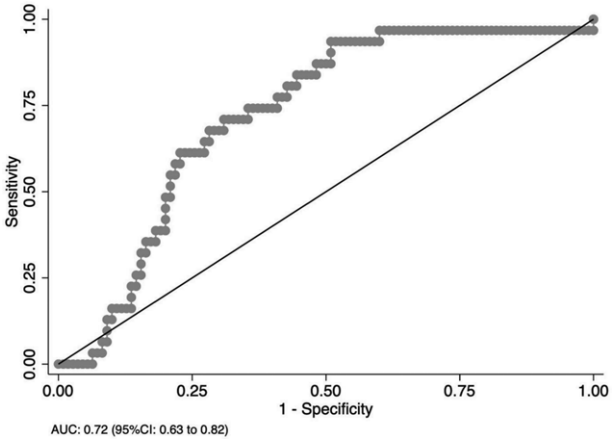
Results: One-hundred-and-forty-two patients were randomised to tapering (n=95) or control (n=47) of which 32% (30/95) and 2% (1/47) achieved successful bDMARD tapering at 18 months. A statistically significant associations (univariate p<0.10) was identified between successful tapering and tapering group, HAQ-DI, Pain VAS, Fatigue VAS, Patient Global Health VAS, SF-36 PCS, and SF-36 MCS, ***Table 1***. However, the only independent predictor for achieving successful tapering in the multivariable model was allocation to the tapering group, risk ratio (RR): 14.0 (95%CI: 1.9-101.3). Interestingly, individuals with a better mental health state (higher SF-36 MCS) were potentially more likely to achieve successful tapering; RR: 1.06 (95%CI: 0.99-1.13). A sensitivity analysis only including tapering group and SF-36 MCS found both variables to be independent predictors, tapering group: RR 14.3 (95%CI: 2.0-101.9) and SF-36 MCS: RR: 1.06 (95%CI: 1.01-1.11). The multivariable model gave reasonable prediction, ***Figure 1***.

Conclusion: One-third of patients with IA achieved successful tapering when the bDMARD dosing interval was spaced after a disease activity-guided tapering algorithm. The choice of initiating tapering (allocation to tapering) was the only independent predictor; therefore, physicians should keep the option in mind when patients are in sustained LDA. Moreover, better baseline mental health seemed to have potential importance which points to the value of patient comprehension and willingness to engage in the tapering approach.

Table 1. Regression analyses on variables included in the multivariable model for prediction of successful tapering at 18 months.

Baseline variables	Univariable analysis RR (95%CI)	P-value	Multivariable analysis RR (95%CI)	P-value
Tapering group	14.8 (2.1-106.3)	0.007	14.0 (1.9-101.3)	0.009
HAQ-DI	0.44 (0.20-1.00)	0.049	0.60 (0.26-1.37)	0.221
Pain VAS	0.96 (0.93-1.00)	0.024	0.99 (0.94-1.04)	0.720
Fatigue VAS	0.99 (0.97-1.00)	0.072	1.01 (0.99-1.02)	0.495
Patient global health VAS	0.97 (0.95-0.99)	0.011	1.00 (0.97-1.03)	0.955
SF-36 PCS	1.06 (1.00-1.11)	0.045	1.00 (0.93-1.07)	0.915
SF-36 MCS	1.06 (1.01-1.12)	0.011	1.06 (0.99-1.13)	0.097

Figure 1: Area under the receiver operator curve for the multivariable model



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Disclosure of Interests: Line Uhrenholt Speakers bureau: AbbVie, Eli-Lilly, Janssen, and Novartis, Kirsten Duch: None declared, Robin Christensen: None declared, Lene Dreyer Speakers bureau: Eli Lilly, Galderma, and Janssen, Grant/research support from: BMS, Ellen-Margrethe Hauge Speakers bureau: AbbVie, Sanofi, Sobi, MSD, and UCB, Grant/research support from: Research grants to Aarhus University Hospital from Danish Regions Medicine Grants, Danish Rheumatism Association, Roche, Novartis, and Novo Nordic Foundation, Annette Schlemmer Speakers bureau: Eli-Lilly, Merck, and Novartis, Peter C. Taylor Speakers bureau: AbbVie, Consultant of: AbbVie, Biogen, Bristol Myers Squibb, Eli-Lilly, Fresenius, Galapagos, Gilead Sciences, Glax-oSmithKline, Janssen, Nordic Pharma, Pfizer Inc, Roche, and UCB, Grant/research support from: Galapagos, Salome Kristensen: None declared.

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Pain in RMDs

POS0255 A PRO-NOCICEPTIVE POPULATION OF NEUTROPHILS INFILTRATE SENSORY GANGLIA AND MEDIATE CHRONIC WIDESPREAD PAIN IN FIBROMYALGIA SYNDROME

Keywords: Pain, Fibromyalgia, Innate immunity

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Background: Although the aetiology of chronic widespread pain in fibromyalgia syndrome is unknown and generally recognised as a central pain syndrome, several recent studies point towards a peripheral aetiology. Aberrant activity of immune cells and associated cytokine signalling has also been linked to

fibromyalgia syndrome. Neutrophils are polymorphonuclear granulocytes that normally exist in circulation to function as primary mediators of rapid innate host defence, releasing extracellular vesicles as functional mobile units. Surprisingly, neutrophils are found in increased circulatory levels and with enhanced chemotactic and microbicidal properties in fibromyalgia patients. Furthermore, we have recently shown a key role for neutrophils in mediating the spatiotemporal spread of hypersensitivity in a hyperalgesic priming model of chronic widespread pain. Our data also shows a fundamental pro-nociceptive action of neutrophils derived from patients or mice with chronic widespread pain when administered to naïve recipient mice.

Objectives: The mechanisms by which neutrophils can sensitise sensory neurons to cause pain signalling is still unclear but is likely linked to a distinct subpopulation of neutrophils characterised by altered surface protein expression. We aim to identify a specific neutrophil subpopulation that sensitises nociceptive neurons either through cell-cell interactions or mediated via neutrophil-derived extracellular vesicles (NDEVs) to produce chronic widespread pain in fibromyalgia syndrome.

Methods: To identify a pro-nociceptive neutrophil population, we used neutrophils from fibromyalgia patients and pain free controls, characterising proteomic differences between the cohorts by FACS. Furthermore, we have employed functional assays of neutrophil reactivity, including quantification of reaction oxygen species (ROS) production and neutrophil extracellular trap generation (NETosis) to characterise specific functional differences which may responsible their pro-nociceptive capacity. To assess the role of NDEVs in neutrophils pro-nociceptive actions we have isolated and performed phenotypic characterisation of NDEVs from patient and pain-free controls. Finally, we used primary sensory neuron cultures to assess the effect of neutrophils and NDEVs on neuronal excitability using functional assays (calcium imaging and *in vitro* electrophysiology) to demonstrate the capacity of neutrophils to sensitise peripheral sensory neurons.

Results: Proteomic characterisation of neutrophils derived from patients with fibromyalgia pain vs pain free subjects reveals a distinct population of cells, including altered expression of cell surface markers CD62L and CXCR2. Quantification of ROS generation also reveals changes in cells derived from patients when compared to pain free counterparts, alongside increased NETosis which may reflect specific mechanisms employed by cells to sensitise peripheral neurons following trafficking to DRG. We observe increased NDEV release from patient cells alongside specific phenotypic differences, including an upregulation of surface markers, mirroring what we observe within the parent cells.

Moreover, *in vitro* systems, including electrophysiology recording and calcium imaging reveal increased neuronal responses to both patient cells and patient cell-derived NDEVs.

Conclusion: We show a surprising role of neutrophils, a short-lived immune cell, in the aetiology of chronic widespread pain in fibromyalgia syndrome. Our data demonstrates altered proteomic profiles and distinct phenotypic differences in both circulating neutrophils and NDEVs from patients, supporting an immunological basis for chronic widespread pain in fibromyalgia and a novel mechanism of nociplastic pain.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0256 IDENTIFICATION OF TWO BIOLOGICAL SUBTYPES OF CRPS

Keywords: Pain, Skin

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Background: Patients with Complex Regional Pain Syndrome (CRPS) present prolonged and debilitating pain and tissue damage. To date, treatment remains a challenge. Biological phenotyping has not been performed yet, and thus, molecular therapies are missing.

Objectives: To determine whether different biological CRPS subtypes exist and to provide a molecular profile of these subtypes.

Methods: CRPS patients fulfilling the *Budapest criteria* were included. Body Perception Disturbance (BPD) and pain scores (0-100) questionnaires were recorded. Skin punch biopsies (3 millimetres) from the affected and non-affected sides (n=6+6) and matching blood samples were taken. Biopsies were split in two for transcriptomic and histological analyses. Blood was processed to collect plasma after centrifugation and peripheral blood mononuclear cells (PBMCs) with a Ficoll gradient. Total RNA was isolated from skin biopsies and from PBMCs for bulk sequencing. Differentially expressed genes (DEGs) were determined using DESeq2 generalised linear model (p≤0.01, log2 ratio≥0.5). Hierarchical clustering and principal component analysis (PCA) were performed on raw transcriptomic data to identify patient sub-populations. Cell types were approximated in skin and PBMCs with deconvolution analysis using RNA sequencing databases with known cell frequencies (PRESS cohort and immunedeconv, respectively).

Twenty pro- and anti-inflammatory plasma cytokines were measured using chemiluminescence-based assays (MSD U-PLEX Viral Combo 1). Histological slides were scored (0-3) blinded by a dermato-pathologist based on a panel of 10 morphological and cellular characteristics. Protein levels, histological evaluations and demographic data were compared between CRPS clusters using unpaired t-tests.

Results: Six women with CRPS 1 of the hand (n=5) and foot (n=1) participated in the study. Mean age was 47.3 ± 14.2 yrs and mean symptom duration was 57.8 ± 44.2 weeks. Skin transcriptomics showed 427 DEGs when comparing affected vs. non-affected samples (**Figure 1a**). Samples clustered by patient rather than affected/non-affected side (**Figure 1b**). PCA of only the affected samples displayed two clusters (PC1=56%, PC2=17%) (**Figure 1c**). Further evaluation of all affected samples by deconvolution analysis suggested two distinct cellular signatures, clustering patients in the same way as the PCA. Keratinocyte-related genes were upregulated in cluster 1 (n=3) and strong fibroblast, microvascular endothelial cell, monocyte and M1 macrophage signatures were found in cluster 2 (n=3) (**Figure 1d**). Consequently, gene ontology (GO) of each cluster showed enrichment of epidermis development and downregulation of peptidase terms in cluster 1 and extracellular matrix and collagen fibril organisation in cluster 2. Histopathological examinations did not show any difference between subtypes.

PCA of PBMCs transcriptome validated the same distribution of patients into two clusters (PC1=62%, PC2=16%) (**Figure 1e**). A total of 2'328 DEGs were found between both clusters, with an overrepresentation of immune and inflammatory response, and neutrophil degranulation and chemotaxis-related terms in cluster 1 (n=2) according to GO. Deconvolution analysis confirmed the presence of a stronger signature of neutrophils and M2 macrophages in cluster 1 than cluster 2. Blood cytokine quantification showed that interleukin-1 receptor antagonist (IL-1RA) levels were 1.9 times higher in cluster 1 than in cluster 2 (n=3+3, p=0.02) (**Figure 1f**). Consistently, transcriptomic data indicated that cluster 1 had higher expression of IL-1RA encoding gene (IL-1RN) in matching skin (log2 ratio=0.88, FDR=0.06) and PBMCs (log2 ratio=1.1, FDR≤0.01,) than cluster 2.

There was no significant difference in age or symptoms duration between clusters, but pain and BPD questionnaires revealed differences between groups, suggesting that the clusters might be clinically distinguishable (**Figure 1g**).

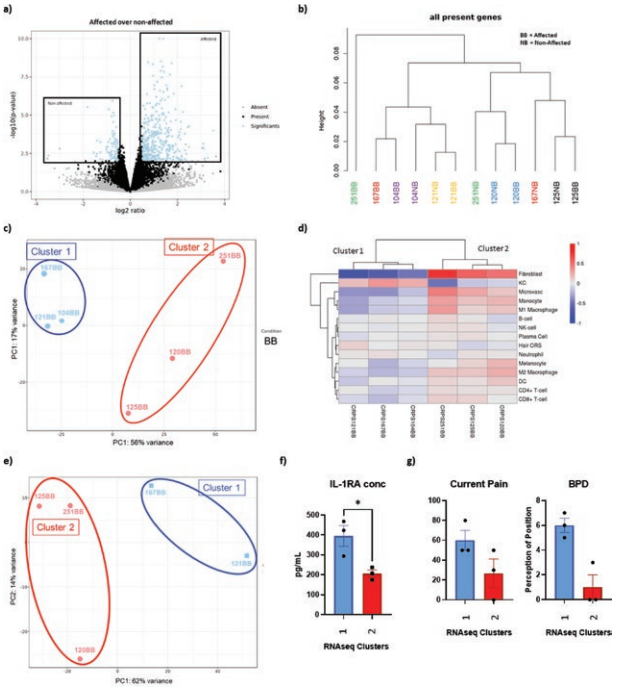


Figure 1.

Conclusion: Our findings suggest the existence of two biological CRPS subtypes. Molecular patterns could facilitate the development of targeted therapies.

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Acknowledgements: NIL.

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POS0257 PAINWAVES: THE POTENTIAL OF MACHINE LEARNING TO DIFFERENTIATE CHRONIC PAIN COHORTS USING ELECTROENCEPHALOGRAPHY

Keywords: Pain, Imaging, Artificial Intelligence

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Background: Chronic pain is highly prevalent, debilitating and lacks effective treatments. Experimental and neuroimaging research demonstrates abnormal central pain processing[1]. However, robust brain-based biomarkers that could inform targeted treatments are lacking. Electroencephalography (EEG) is the optimal tool to investigate dynamic abnormalities in pain processing to reveal underlying mechanisms. Early evidence from EEG studies in Fibromyalgia (FM) indicate potential mechanisms such as thalamocortical dysrhythmia[2], demonstrated by alterations in the Alpha and Theta frequency bands. However, existing studies employ rudimentary analyses failing to account for the multivariate and temporal nature of EEG data. State-of-the-art machine learning (ML) approaches provide unique opportunities to generate a deeper understanding of EEG signatures in chronic pain and identify specific biomarkers that could be used to differentiate mechanistic subtypes.
Objectives: This preliminary work aims to establish whether a state-of-the-art ML classifier can differentiate patients with FM from healthy controls based on their EEG characteristics.
Methods: The dataset used was collected through The VIPA Study (ISRCTN46681140). Patients with FM satisfied the 2016 FM classification criteria. High-density 64-channel EEG data using an electrolyte gel-based active electrode system was collected at rest with participants' eyes closed over 2 minutes. Individual Fast Fourier Transforms were applied to overlapping time windows to extract EEG frequency band power whilst retaining temporal information. Frequency bands were used as features to train a classification model (definitions of frequency ranges in Table 1). One of the fastest, most accurate state-of-the-art time-series classification ML algorithms (mini-ROCKET) was used via the sktime python toolkit. To obtain unbiased accuracy estimates across all participants, a 'leave-one-out' strategy was used. Accuracy of the algorithm was reported; defined by the number of correct predictions divided by the total number of predictions for each frequency band (2-class problem, chance estimates 0.5-0.6 based on $p<0.05$).
Results: Data from 23 patients with FM (mean age 46 ±14yrs, 87% female) and 14 healthy controls (mean age 71 ±7yrs, 50% female) were analysed. Patients with FM had moderate self-reported pain (5.5 ±2.3 VAS) and disease severity (mean FIQR 65.4 ±16.6) at baseline. Theta and Alpha were the most discriminatory frequency bands, with mini-ROCKET able to classify participants with 70.7% accuracy. The Beta frequency band was less discriminatory (63.4%) but still above predicted chance estimates. Delta frequency band was least discriminatory (51.2%).
Conclusion: Preliminary results indicate that machine learning can be successfully used to differentiate patients with Fibromyalgia from healthy controls based on EEG measures of the Alpha and Theta frequency bands. Alterations in Alpha and Theta have been demonstrated in previous non-ML research, indicating potential underlying abnormalities in the interaction between the thalamus and cortex which may be related to central mechanisms underlying chronic pain. Further work is required in larger, matched cohorts to validate these findings, but this early work highlights the future potential of EEG and ML in both understanding brain-based pain mechanisms and using EEG features to differentiate chronic pain subgroups.
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Table 1. Classifier accuracy across the EEG frequency bands (FM vs Control)

Frequency Band	Accuracy of mini-ROCKET classifier
Delta (2-4hz)	0.512 (51.2%)
Theta (4-8hz)	0.707 (70.7%)
Alpha (8-12hz)	0.707 (70.7%)
Beta (12-30hz)	0.634 (63.4%)
Gamma (30-40hz)	0.610 (61.0%)

Acknowledgements: Professor Alexander Macgregor for his mentorship and support to the lead author during this work.
Disclosure of Interests: None Declared.
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POS0258 USING REAL-TIME PATIENT-GENERATED DATA FROM MOBILE HEALTH DEVICES TO CHARACTERISE PAIN FLARES IN RHEUMATOID ARTHRITIS

Keywords: Pain, Rheumatoid arthritis

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Background: Pain flares in rheumatoid arthritis (RA) often refer to episodes of increased pain severity accompanied by pain impact. Describing the prevalence and predictors of pain flare occurrence is difficult since there are no agreed classification criteria[1]. Patient-generated data collected in real-time with mobile health (mHealth) devices provide an opportunity to identify individual patterns and triggers in pain dynamics over time[2].
Objectives: We aim to characterise pain flares and pre-flare exposures using real-time mHealth data from patients with RA.
Methods: In a 30-day mHealth study[3] we collected daily reports of pain severity on a five-point scale (ranging from none to very severe pain) via a smartphone app to define the onset and ending criteria for three types of pain flares, including 1) above average: pain severity greater than the personal median score, 2) significant change: two-point increase in pain severity from yesterday, and 3) absolute impact: two-point increase in pain severity from yesterday and pain severity greater than three. All pain flare types end when pain severity returns to the personal median score or lower. Exposures of the preceding periods were self-rated sleep quality, mood, anxiety and fatigue (all scales range 1-5, higher scores are worse) using the same study app, and passively recorded total time asleep (hr), sleep efficiency (%), sleep latency (min) and physical activity (min) via a wrist-worn accelerometer. We report the 30-day monthly pain flare rate, the average duration of pain flares and summarise average exposures one-day and three-day before pain flare onset.
Results: We analysed 253 participants who provided at least seven days of data (81.8% females; mean age = 59.9, average years with RA = 12.1). A total of 6,244 daily reports were included in the analysis. Pain flare occurrence decreased when applying more complex definitions. 31% of participants had pain flares under the most stringent definition of absolute impact, with two episodes per month (Table 1). Across all types, 75% of pain flares lasted two days before returning (Median = 1, IQR = 1-2) but could persist up to 11 days (Figure 1). Pre-flare exposures did not differ between pain flare types nor between the preceding periods. Participants reported fair sleep quality (Median = 3), feeling quite happy (Median = 2), not anxious (Median = 1) and mild fatigue (Median = 2) prior to pain flare onset. Objective exposures showed a daily average of 7-hour sleep with 83% efficiency, under 20 minutes to fall asleep, and approximately 50 minutes being active.

Table 1. Pain flare characteristics

Type	Number of participants with ≥1 pain flare(s) (%)	Total number of pain flares	Monthly pain flare rate (SD)
Above average	224 (88.5)	788	4.3 (2.2)
Significant change	108 (42.7)	171	2.0 (1.1)
Absolute impact	78 (30.8)	116	2.0 (1.1)

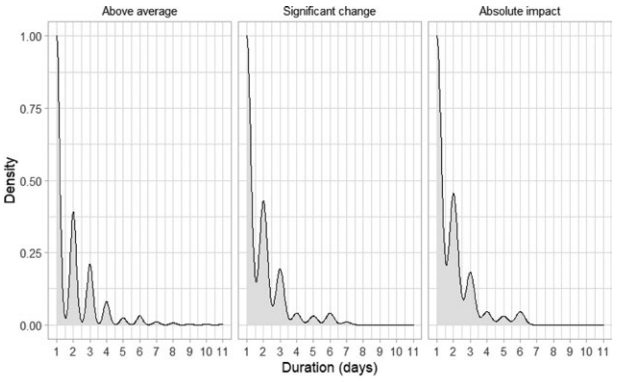


Figure. Pain flare duration

Conclusion: Using three increasingly complex definitions, we found pain flares were common and lasted up to 11 days based on self-reported pain severity. Future analysis should examine the role of pain impact and compare within-person exposures during pre-flare periods with non-flare periods.

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Disclosure of Interests: None Declared.

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POS0259 DO CHRONIC PAIN IN MULTIPLE SITES AND WIDESPREAD PAIN INCREASE RISK OF INCIDENT DEMENTIA?

Keywords: Pain

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Background: Chronic musculoskeletal pain has been linked to dementia; however, chronic pain typically occurs in multiple sites, and no study has investigated the associations between number of chronic pain sites and risk of all-cause dementia and its subtypes.

Objectives: To investigate whether greater number of chronic pain sites is associated with a higher risk of dementia and its subtypes.

Methods: Participants (N=356,383) in the UK Biobank who were dementia-free at baseline were included. Pain in the hip, knee, back and neck/shoulder, or 'all over the body' and its duration were assessed. Participants were categorized into six groups: no chronic pain, and chronic pain in 1, 2, 3 and 4-sites and 'all over the body' (widespread pain). All-cause dementia and its subtypes were ascertained using hospital inpatient and death registry records. Cox regression was used to investigate the associations between number of chronic pain sites and incidence of all-cause dementia and its subtypes.

Results: Over a median follow-up of 13 years (interquartile range: 12.6–14.0), 4,959 participants developed dementia. After adjustment for sociodemographic, body mass index, lifestyle, comorbidities, pain medications, psychological problems and sleep factors, greater number of chronic pain sites was associated with an increased risk of incident all-cause dementia (Hazard ratio [HR]=1.08 per 1-site increase, 95%CI 1.06–1.11) and Alzheimer's disease (HR=1.09 per 1-site increase, 95%CI 1.04–1.13) in a dose-response manner, but not vascular and frontotemporal dementia. Relative to participants without chronic pain, participants having chronic pain in 2-, 3-, 4-sites and widespread pain had a higher risk of incident all-cause dementia after adjusting for confounding factors (2-sites: HR=1.18, 95%CI 1.08–1.29; 3-sites: HR=1.22, 95%CI 1.08–1.38; 4-sites: HR=1.42, 95%CI 1.19–1.70; widespread pain: HR=1.52, 95%CI 1.26–1.82). Similar results were observed for Alzheimer's disease.

Conclusion: Greater number of chronic pain sites was associated with an increased risk of incident all-cause dementia and Alzheimer's disease, suggesting that chronic pain in multiple sites may contribute to individuals' dementia risk and is an underestimated risk factor for dementia.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0260 CHILDHOOD BULLYING AND MUSCULOSKELETAL PAIN IN ADOLESCENCE: A PROSPECTIVE STUDY OF REPORTED PAIN HISTORY AND QUANTITATIVE SENSORY TESTING

Keywords: Pain, Epidemiology, Patient reported outcomes

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Background: Psychosocial circumstances are strongly associated with the onset and prognosis of chronic musculoskeletal (MSK) pain. However, it is unknown they precede, coexist with or follow MSK pain conditions. Bullying during youth is a particularly damaging but modifiable social experience that is known to interfere with health status, potentially including pain memories and responses to noxious stimuli.

Objectives: We aimed to quantify the longitudinal associations between bullying profiles and musculoskeletal pain (reported history and pressure pain sensitivity) in a large population-based cohort of adolescents followed since birth.

Methods: We used data from the 10 and 13 years waves of the Generation XXI birth cohort study based in Porto, Portugal. Data on youth pain history were collected during face to face interviews from parents (age 10) and adolescents (age 13) using the Luebeck pain screening questionnaire. MSK pain was considered present when the participant had recurrent pain in one of the following sites: back, neck, shoulders, upper/lower limbs, hips, or generalized MSK pain. A subsample of the cohort underwent quantitative sensory testing using computerized deep tissue cuff pressure algometry in the legs, which allowed estimating pain detection/tolerance thresholds, and measuring pain intensity ratings. Bullying profiles were computed for the 10 and 13 years waves based on responses to the Bully Scale Survey and participants were classified as "victim only", "both victim and aggressor", "aggressor only", or "not involved". Cross-sectional and longitudinal associations between bullying profiles and reported pain were quantified using relative risks (RR) and 95% confidence intervals (95% CI) obtained using Poisson regression. Associations between bullying and pain sensitivity were estimated using linear regression coefficients and 95% CI. Estimates were adjusted for sex and number of Adverse Childhood Experiences adapted from the questionnaire by Felitti et al.

Results: Among the 4049 adolescents examined, bullying profiles at age 10 were associated with MSK pain at age 13, whereas there were no associations between MSK pain at age 10 and bullying profiles at 13. Cross-sectional associations between bullying and MSK pain history were present at 10 and 13 years. When compared to adolescents "not involved" in bullying, those who reported being victims at age 10 had higher risk of reporting MSK pain at age 13: RR (95% CI) 1.28 (1.06, 1.55) for "victims only" and 1.30 (1.06, 1.58) among "both victims and aggressors" (Figure below). "Aggressors only" did not show clear differences in terms of pain history. Among the 1727 adolescents who underwent cuff pressure algometry, those who were "victims only" at age 10 had lower average pain detection and tolerance thresholds at 13 years [linear regression coefficients (95% CI): -1.81 (-3.29, -0.33) for detection and -2.73 (-5.17, -0.29) for tolerance], as well as higher pain intensity ratings [0.37 (0.07, 0.68) and 0.39 (0.06, 0.72)], when compared with adolescents not involved in bullying. No differences were seen for the remaining bullying profiles.

Conclusion: Our study provides prospective evidence that bullying victimization is more likely to lead to negative reported MSK pain experiences than the reverse. Bullying may have long-term influence on the risk of chronic musculoskeletal pain and may interfere with somatosensory responses to painful stimuli.

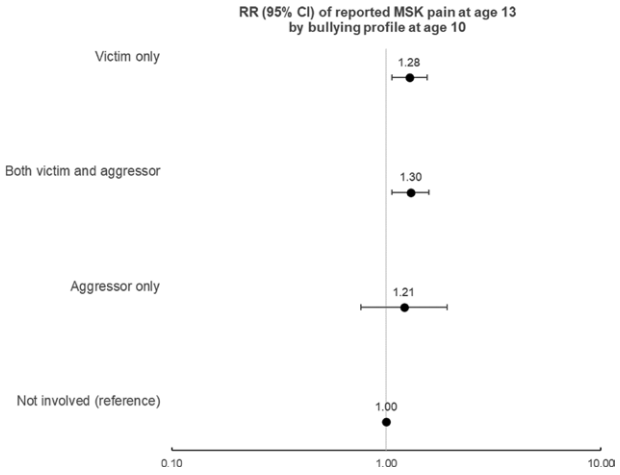


Figure 1.

Acknowledgements: This work was supported by FOREUM - Foundation for Research in Rheumatology (Career Research Grant). Cohort funded by EPIUnit at ISPUP, Universidade do Porto (UID/DTP/04750/2019), Regional Department of the Portuguese Ministry of Health and Calouste Gulbenkian Foundation. MT was funded by the ERDF, through the North Regional Operational Program in the framework of the project HEALTH-UNORTE (NORTE-01-0145-FEDER-000039). Graven-Nielsen et al (CNAP, Aalborg University) provided algometry protocols.
Disclosure of Interests: None Declared.
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POS0261 ASSOCIATIONS BETWEEN PAIN SENSITIZATION AND PHYSICAL FUNCTION IN PEOPLE WITH HAND OSTEOARTHRITIS: RESULTS FROM THE NOR-HAND STUDY

Keywords: Osteoarthritis, Pain

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Background: Pain sensitization is an important component of the pain experience in many persons with osteoarthritis (OA). Knee OA studies have suggested that pain sensitization is associated with functional limitations, but the evidence in hand OA is sparse.
Objectives: To assess whether pain sensitization is associated with physical function in people with hand OA.
Methods: We included 206 participants in cross-sectional analyses from the follow-up visit of the Nor-Hand study. Measures of pain sensitization included pressure pain thresholds (PPTs) by a handheld algometer, and temporal summation (TS) defined as increased pain during repeated stimuli. Pain and function in hands and knees/hips were self-reported on the AUSCAN and WOMAC indices, respectively. Performance-based measures of physical function included hand grip strength, the 30-second chair stand test and the 40-meter walk test (reported as walking speed). Associations between sex-standardized PPT and TS values and physical function were assessed using linear regression adjusted for potential confounders (see Table 1). The possible mediating effect of self-reported pain severity was examined with causal inference-based mediation analyses.
Results: The median (IQR) age was 65 (60-69) years and 86% were female. People with higher PPTs at or near the hand or knee, which may represent less peripheral and/or central sensitization, reported better function in hands and knees/hips and performed better on the performance tests than people with lower PPTs (Table 1), although not statistically significant for all outcomes. Also, a higher PPT at the trapezius muscle, representing less central sensitization, was associated with better function in the lower extremities (Table 1). No associations were found between pain sensitization and the chair stand test (data not shown), or between TS (measure of central sensitization) and hand or lower extremity function. The effects of PPTs on self-reported AUSCAN hand function appeared to be largely mediated through self-reported hand pain (e.g., indirect effect of PPT at the wrist mediated through hand pain: -1.19, 95% CI -1.95, -0.43, and direct effect: -0.20, 95% CI -0.90, 0.51). Effects of PPTs on grip strength were mediated through pain to a lesser extent (e.g., indirect effect of PPT at the wrist mediated through hand pain: 0.12, 95% CI -0.10, 0.34, and direct effect: 1.21, 95% CI 0.29, 2.13). Similarly, the mediating effects of knee/hip pain were larger in analyses of self-reported function than for performance-based measures of lower extremity function (data not shown).
Conclusion: Our results suggest that peripheral sensitization and possibly also central sensitization, are associated with impaired function in hands and lower extremities. For both the hand and lower extremities, measures of sensitization may have direct effects on performance-based measures of function, whereas the effect of sensitization on self-reported function appears to be mediated through self-reported pain severity.

Table 1. Associations between measures of sensitization and function

	AUSCAN hand function (range 0-36)	Grip strength (kg)	WOMAC knee/hip function (range 0-68)	40-meter walk test (m/s)
PPT finger joint	**-1.42 (-2.42, -0.43)**	**1.25 (0.35, 2.14)**	**-1.73 (-3.40, -0.05)**	0.03 (-0.01, 0.06)
PPT wrist	**-1.39 (-2.38, -0.39)**	**1.33 (0.41, 2.24)**	-1.66 (-3.37, 0.04)	0.03 (-0.01, 0.06)
PPT trapezius muscle	-0.80 (-1.81, 0.22)	0.66 (-0.25, 1.57)	**-1.76 (-3.47, -0.05)**	**0.04 (0.00, 0.07)**
PPT tibialis anterior muscle	-0.76 (-1.77, 0.26)	0.74 (-0.17, 1.65)	-1.57 (-3.29, 0.14)	**0.05 (0.01, 0.08)**
Temporal summation	-0.08 (-1.07, 0.91)	-0.28 (-1.17, 0.61)	0.96 (-0.75, 2.67)	-0.01 (-0.05, 0.02)

Adjusted for age, sex, body mass index, education, physical activity, and Kellgren-Lawrence sum score of the hands in the analyses of hand function or ultrasound-detected osteophytes in the knees, hips and feet in the analyses of lower extremity function. Presented as beta (95% CI) per standard deviation of sex-standardized PPT and TS.

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Disclosure of Interests: Marthe Gløersen: None declared, Pernille Steen Pettersen: None declared, Tuhina Neogi Consultant of: Novartis, Pfizer-Lilly, Regeneron, Grant/research support from: Pfizer, Joe Sexton: None declared, Tore K. Kvien Speakers bureau: Grünenthal, Sandoz, UCB, Consultant of: AbbVie, Amgen, Celltrion, Gilead, Novartis, Pfizer, Sandoz, UCB, Grant/research support from: AbbVie, Amgen, BMS, Galapagos, Novartis, Pfizer, UCB, Hilde Berner Hammer Speakers bureau: AbbVie, UCB, Lilly, Novartis, Grant/research support from: AbbVie, Pfizer, Roche, Ida K. Haugen Consultant of: Novartis, GSK, Grant/research support from: Pfizer/Lily.
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POS0262 VALUE OF SMALL FIBER NEUROPATHY IN FIBROMYALGIA PATIENTS IN A RHEUMATOLOGICAL SETTING

Keywords: Patient reported outcomes, Fibromyalgia, Pain

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Background: Small fiber neuropathy (SFN), a polyneuropathy (PNP) affecting A-delta and C-fibers has been described in patients with fibromyalgia (FM). Different patterns of small fiber damage may characterize distinct subtypes of FM.
Objectives: To investigate the value of detecting different degrees of SFN in patients diagnosed with FM.
Methods: Consecutive patients who were treated for pain exacerbation of FM at a university specialized tertiary center were included in the study after informed consent. Patients had to fulfil the 2016 ACR diagnostic criteria for FM and other inflammatory rheumatic musculoskeletal diseases (RMD) were excluded. The rheumatological therapy included pain pharmacotherapy, balneo-physical treatment, physiotherapy and occupational therapy. All patients underwent a careful rheumatologic and neurologic physical clinical examination including a Schirmer-Test for dry eyes and were asked to fill out questionnaires, in which data on pain, depression, neuropathic symptoms, sleep quality, daytime sleepiness, fatigue, and quality of life were assessed. Thereafter small fiber tests were performed in the neurologic department including a skin punch biopsy on the upper and lower leg and a corneal confocal microscopy (CCM).
Results: Overall, 93 patients (86 females, 92.5%, mean age 54±10.1, mean disease duration 4.9±5.3 years) were included, 25 received anticonvulsants (26.9%) and 15 opioids (16.1%) for pain treatment. Intraepidermal nerve fiber density (IENFD) as

Table 1. Scores of the questionnaires of all subgroups

	normal IENFD	reduced IENFD at different biopsy sites	p-value	distally reduced IENFD	p-value	proximally reduced IENFD	p-value	generalized reduced IENFD	p-value
numerical pain scale	7.6±1.5	7.6±1.3	0.912	7.8±0.9	0.714	8.4±1.2	0.198	7.4±1.3	0.507
Fibromyalgia Impact Questionnaire (FIQ)	73.4±13.1	70.1±11.1	0.192	69.1±15.5	0.578	74.2±10.5	0.925	70.5±10.6	0.129
Widespread pain Index (WPI)*	94.3%	100%	0.067	100%	0.522	100%	0.494	100%	0.115
Neuropathic Pain Symptom Inventory	0.2±0.1	0.2±0.1	0.079	0.2±0.1	0.478	0.2±0.1	0.435	0.2±0.1	0.078
Ocular Surface Disease Index**	37.1%	27.6%	0.440	28.6%	0.548	32.5%	0.682	27.9%	0.504
Pittsburgh Sleep Quality Index	13.7±3.3	13.5±3.4	0.914	15.3±2.7	0.275	13.5±3.2	0.937	13.3±3.6	0.628

*criteria fulfilled, **normal

detected by skin biopsy was reduced in 58 patients (62.4%), 43 of whom (74.1%) had reduced IENFD at both proximal and distal sites. CCM showed pathologic findings in 18 patients with reduced IENFD at any site (31%) and in 8 with normal IENFD (22.9%), with dry eyes being present in 13 (22.4%) and 6 (17.1%) of those patients, respectively. There was no difference in pain, depression, neuropathic symptoms, sleep quality, daytime sleepiness, fatigue, or quality of life scores between groups (Table 1).

Conclusion: In this FM population with high disease burden and indication for inpatient therapy, small fiber pathology as found by skin biopsies and CCM was present in more than two third of the FM patients suggesting that there are subgroups. However, there were no significant clinical differences between patients with and without SFN. Further analysis should explore, whether both subgroups differ in their long-term outcome after the inpatient treatment.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0263 PREVALENCE OF OCCIPITAL PROTUBERANCE ENTHESOPHYTE IN NON-INFLAMMATORY AND INFLAMMATORY RHEUMATIC DISEASES: SANZ SIGN

Keywords: Spondyloarthritis, Enthesitis, Rheumatoid arthritis

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Background: The exostosis of occipital protuberance was described recently in non-inflammatory processes[1]. Despite of enthesophytes are usually seen in radiographs of older asymptomatic population, in the last few years the presence of occipital protuberance enthesophyte (OPE) has been observed frequently in young patients, with a prevalence of 41% in adults younger than 30-year-old[2]. To our knowledge OPE has not been described in inflammatory rheumatic diseases.

Objectives: To determine the prevalence of OPE in non-inflammatory processes (NIP), psoriatic arthritis (PsA), spondyloarthritis (SpA) and rheumatoid arthritis (RA).

Methods: Retrospective descriptive and comparative study of cervical radiographs randomly collected from patients older than 18 years old attended in a rheumatology consult of a tertiary hospital from July 2022 to January 2023 until 30 patients per group were completed (total of 120 patients). We classified patients in four groups by diagnosis: NIP (traffic accident and spine surgery excluded), PsA, SpA and RA. The following variables were collected: sex, age at the time of radiograph was performed, OPE (yes/no) evaluated by a senior rheumatology resident (4 years of experience) and by a senior rheumatologist (25 years of experience). Descriptive statistics were used for the presentation of the results and Cohen's Kappa coefficient was calculated to quantify the degree of agreement in the diagnosis of enthesophyte presence between both rheumatologists. Chi square test with Yates correction was performed to compare sex and prevalence between groups and ANOVA to compare mean age.

Results: A total of 120 patients were collected, 30 patients per group. Seventy point eight per cent were women; mean age was 58.5 years with a standard deviation of 15. The groups were homogeneous (sex was performed by Chi Square test, $p < 0.0001$; mean age was performed by ANOVA, $p = 0.006$). Sixty-one of 120 patients (51 %) had OPE (23 % in non-inflammatory group, 60 % in inflammatory group); OPE prevalence was statistically significant in inflammatory diseases ($p < 0.001$). Stratified analysis by sex ($p = 0.2$) and age ($p = 0.06$) between inflammatory and non-inflammatory pathology showed no differences, although incidence of OPE in non-inflammatory processes tends to increase with older age. Results by group are shown in *Table 1*. *Figure 1* shows different types of enthesophyte morphology. The global degree of agreement according to Cohen's Kappa index was 0.8, representing 89 % agreement (substantial degree); the best degree of agreement was obtained in SpA (Cohen's Kappa index 0.9, representing 97 % agreement, almost perfect degree).

Conclusion: To our knowledge this is the first study about the prevalence of OPE in inflammatory and non-inflammatory rheumatic diseases, being more prevalent in inflammatory diseases 60 % ($p < 0.001$), especially in spondyloarthritis and psoriatic arthritis. The global degree of agreement between a senior rheumatology resident and a senior rheumatologist was substantial, being almost perfect in spondylarthritis. We will conduct a new study to find out whether different morphology of occipital enthesophytes is associated to any inflammatory rheumatic disease.

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Table 1. Description of groups

Groups	NON-inflammatory	Psoriatic arthritis	Spondyloarthrtitis	Rheumatoid arthritis	Total
n	30	30	30	30	120
Sex women (%)	27 (90)	16 (53)	13 (43)	30 (100)	85 (71)
Age (mean ± SD)	66.3 ± 13.5	56.8 ± 12.8	54.5 ± 16.8	57.1 ± 14.12	58.5 ± 15
prevalence (%)	7 (6)	21 (17.5)	21 (17.5)	12 (10)	61 (51)
Cohen's Kappa index	0.7	0.8	0.9	0.4	0.8
p value	p < 0.001	p = 0.0007	p = 0.0007	p = 0.27	

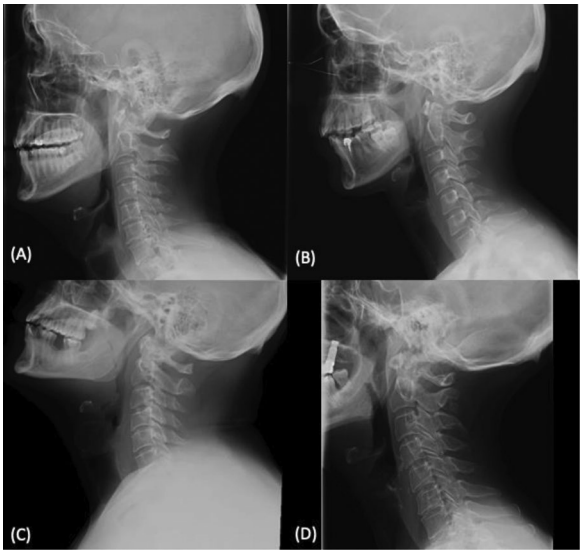


Figure 1. Types of morphology of OPE. (A) Non-inflammatory. (B) Psoriatic arthritis. (C) Spondyloarthritis. (D) Rheumatoid arthritis.

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Disclosure of Interests: None Declared.

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POS0264 PALMITOYLETHANOLAMIDE (PEA) AND ACETYL-L-CARNITINE (ALC) ACT SYNERGISTICALLY WITH DULOXETINE AND PREGABALIN IN FIBROMYALGIA: PROSPECTIVE AND RETROSPECTIVE ANALYSES

Keywords: Clinical Trials, Fibromyalgia, Diet and Nutrition

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Background: Fibromyalgia (FM) is characterized by debilitating pain that is unresponsive to standard analgesics and the multi-modal approach, including drugs' combination, represents the standard of care. Combination therapeutic strategies also include the integration of drugs and nutraceuticals. Both palmitoylethanolamide (PEA) and acetyl-L-carnitine (ALC) have demonstrated an effect on chronic widespread pain (CWP).
Objectives: The aim of this study was to evaluate the efficacy of pregabalin (PGB) and duloxetine (DLX) supplemented with palmitoylethanolamide (PEA) and acetyl-L-carnitine (ALC) in FM patients over a 24-week period.
Methods: After 6 months of stable treatment with DLX+PGB, FM patients were randomized to continue the treatment (Group 1) or to add PEA (600 mg BID)+ALC (500 mg BID) at the ongoing treatment (Group 2). Patients were then followed for 24 weeks. Cumulative disease severity, estimated using the Widespread Pain Index (WPI) (primary outcome), the revised Fibromyalgia Impact Questionnaire (FIQR), and the modified Fibromyalgia Assessment Status (FASmod) (secondary outcomes), was calculated every two weeks during the 24-week follow-up and expressed as time-integrated values (AUC).
Results: One hundred and forty-two FM patients started the study (91.5%), 130 completed both steps, respectively 68 patients in Group 1 and 62 in Group 2. After 24 weeks of follow-up after randomization, Group 2 experienced an adjunctive significant improvement in WPI, FIQR (Figure 1), and FASmod, compared to Group 1. Although there was some fluctuation in both Groups throughout the study period, the AUC values of the WPI scores steadily decreased in Group 2 (p=0.048). Group 2 showed better outcomes also in terms of FIQR and FASmod scores' AUC values (p=0.033 and p=0.017, respectively).

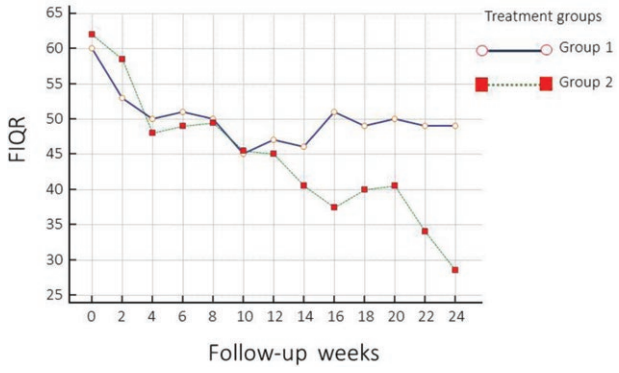


Figure 1. Comparison of the trend of the mean values of the FIQR in the two groups.

Conclusion: This study supports the supplementary value of PEA+ALC in FM patients care and, to best of our knowledge, it is the first study investigating this association treatment.
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Disclosure of Interests: None Declared.
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POS0265 ASSOCIATION OF PREGABALIN VS GABAPENTIN WITH INCIDENT CONGESTIVE HEART FAILURE IN PATIENTS WITH NON-CANCER PAIN

Keywords: Pain, Cardiovascular disease, Heart

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Background: Chronic pain affects 30% of all patients in developed countries, accounting for up to 35% of prescriptions in acute care settings. Non-opioid pain medications are widely utilized for treatment of non-cancer chronic pain. Among these, pregabalin is a commonly prescribed anticonvulsant, which works by antagonizing L-type calcium channels, decreasing the release of neurotransmitters[1]. Pregabalin use has been associated with reports of congestive heart failure (CHF), including peripheral and pulmonary edema[2-4]. However, the relationship between CHF incidence and pregabalin use among patients at the highest risk of adverse reactions (i.e., senior patients with various co-morbidities) remains unclear.
Objectives: To compare incident CHF among new users of pregabalin versus gabapentin (the active comparator) in Medicare beneficiaries treated for non-cancer chronic pain.
Methods: This was a retrospective cohort study among Medicare beneficiaries aged 65-89 years old with chronic non-cancer pain, without prior history of CHF. We included patients who were newly prescribed users of pregabalin or gabapentin were followed up between 2015-2018. The outcome was incident CHF, ascertained by hospital admissions or emergency room visits with ICD 9 and or 10 codes in the first position codes. Inverse probability of treatment weighting was used to account for differences between pregabalin and gabapentin users in time-dependent analysis (i.e., Cox proportional-hazards regressions). Covariates used in the propensity scoring were selected based on prior knowledge and literature review, and included categories such as concurrent baseline cardiovascular, neurologic, pain, and psychiatric diagnoses and corresponding medications including opioids and antipsychotics. Non-diagnostic covariates were included, as well as demographics, socioeconomic status, and indicators/metrics of health care utilization.
Results: This study included 17,756 new users of pregabalin and 221,053 new users of gabapentin. The cohort was predominantly female gender (66.7%), and non-Hispanic White (79.9%), with a median age of 73 (IQR: 69-78) years. The most common diagnostic indications for pregabalin and gabapentin were musculoskeletal and back pain. Prior to inverse probability weighting, pregabalin vs gabapentin users had higher daily short-acting opioid morphine equivalent doses (median; 18.0 vs 8.9 mg/d), higher use of coxibs (8.6% vs 4.9%), and higher prevalence of diabetic neuropathy (15.9% vs 11.3%) and fibromyalgia (19.9% vs 13.2%). After propensity score weighting, none of the covariates had a standardized difference>0.10. During 110,439 person-years of follow-up, 1,428 patients developed new CHF. The outcome rate for CHF incidence was 18.67 per 1000 person-years for pregabalin vs 12.57 per 1000-person years for gabapentin (adjusted HR 1.48 [95% CI, 1.20-1.81]).
Conclusion: In this retrospective study of Medicare beneficiaries aged 65-89 years with chronic non-cancer pain, new users of pregabalin had higher rates of incident CHF hospitalizations or emergency room visits compared to new users of gabapentin.
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Disclosure of Interests: None Declared.
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All about COVID-19 in Rheumatology

POS0266 CELLULAR IMMUNE RESPONSE PERSISTENCE AFTER COVID-19 MRNA VACCINES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS UNDER RITUXIMAB

Keywords: Rheumatoid arthritis, Vaccination/Immunization, COVID

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Background: Humoral response induced by anti-SARS-CoV-2 mRNA vaccine is significantly lower or even absent in patients with inflammatory rheumatic diseases treated with anti-CD20 therapies such as Rituximab (RTX) than in those treated with cytokine therapies (e.g., anti-TNF or anti-IL6) [1]. However, a specific cellular immune response exists 1 or 2 months after vaccination (2, 3). As

cytotoxic T cells are considered as essential components of the antiviral defense arsenal, and since it is not clear when to do booster shots, analysis of thespecific T response over the long term could be a useful decision-making tool.

Objectives: This study aims to compare the spike-specific T lymphocytes response in a cohort of Rheumatoid Arthritis (RA) patients under RTX or other therapies (csDMARDs, anti-TNF). Our secondary goal was to assess the retention of this response up to 18 months after the last COVID boost (vaccine or infection).

Methods: Patients. Our study cohort included 75 consecutive adult patients with ACPA positive RA, followed at the rheumatology department of Sainte Marguerite Hospital (Marseille, France), prospectively enrolled from April 2022 to October 2022. RA patients fulfilled the 2010 ACR/EULAR criteria for RA and had received at least two doses of SARS-COV-2 mRNA vaccine, whether they had or not a history of COVID.

Samples. Heparin-anticoagulated single blood sample was collected for each patient to assess CD19+ cell count, IgG level, and SARS-CoV-2 serology. Cellular immune response was assessed by flow cytometry with a previously described procedure [4]. Briefly, 250 µL of whole blood were incubated per condition, including a negative control, Spike peptides from JPT* collection and CEFX peptides (mix of viral peptides) as a positive control. Marker expression was measured with a three-laser 13-color CytoFLEX flow cytometer. T lymphocytes were divided into T4 lymphocytes (LT4) or T8 lymphocytes (LT8) depending on CD8 expression. Finally, CD69, CD154, CD137 and CD107a expressions were monitored to characterize LT4 or LT8 activation.

Ethics. All patients gave informed written consent for this study in accordance with Helsinki declaration. Patient data were pseudo-anonymized. Sample collection was approved by the national ethics committee under the number DC-2008-327.

Results: Patient characteristics: 51 RA patients were treated with RTX, 24 were treated with csDMARDs or other bDMARDs.

Humoral response against SARS CoV 2: 30/51 (59%) RA RTX patients versus 13/14 (93%) non RTX patients had a humoral immune response (p = 0.024) with a median titer of 130 BAU/mL versus 688 BAU/mL.

T cell specific response: LT4 and LT8 Spike-specific responses were defined by the difference of response between Spike peptides from SARS CoV 2 stimulation and no peptides stimulation. The response was divided into quartiles, patients in the upper 3 quartiles were considered to have a specific response. In RA RTX patients, specific LT8 response was shown in 90% of patients versus 42% in non RTX patients (p < 0.0001), and specific LT4 response was shown in 76 % of patients versus 75% in non RTX patients (p = 0.42).

Long term T cell specific response (Figure 1). RA patients treated with RTX maintained a specific LT4 and LT8 response against Spike peptides with no decrease up to 18 months after the last SARS-COV-2 boost (vaccine dose or COVID 19 infection).

Conclusion: Specific LT4 response against Spike peptides was similar in the RTX treated and non-treated RA patients. This was even stronger for the specific LT8 response. The Spike specific T-cell response was maintained in both groups up to 18 months after the last vaccine dose or COVID infection independently to the specific humoral response. This method of analyzing the specific T response against the Spike protein could be used in personalized medicine to decide when revaccination is necessary in a given patient.

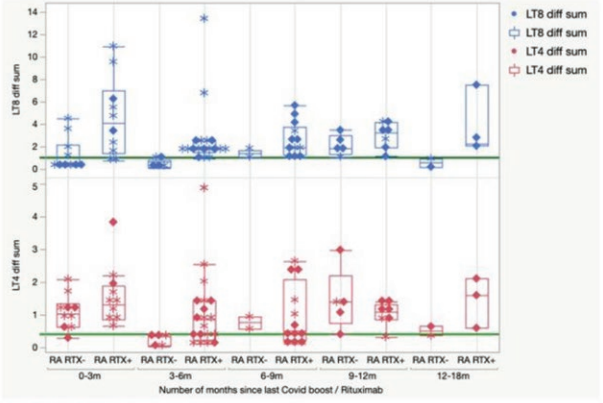


FIGURE 1: Specific T-cell response against Spike peptides among time
RA RTX+: patients with rheumatoid arthritis under RITUXIMAB (RTX).
RA RTX-: patients with rheumatoid arthritis treated with other bDMARD or only csDMARD.
LT diff sum: The LT Spike-specific response is defined by the difference of response between Spike peptides stimulation and no peptides stimulation. Sum is the sum of specific T lymphocytes subtypes response (CD154, CD107a, CD137, CD154/ CD107a, CD137/ CD107a, CD154/ CD137). In RTX treated patients, there is no difference for specific LT4 or LT8 response during time (non-parametric Wilcoxon test for each pair of interval, P>0,05). In non RTX patients, patients had a lower response in the 3-6 months response interval comparing to others (non-parametric Wilcoxon test for each pair of intervals, P< 0,01)
•Patients with a history of COVID-19 infection
Green line: first quartile of response threshold.

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Disclosure of Interests: Juliette MARIN: None declared, Pénélope BOURGOIN: None declared, Noémie SAVERNA: None declared, Celia Cartagena García: None declared, Pierre Lafforgue: None declared, Jean Roudier Grant/research support from: Our research lab received financial support from Bristol Myers Squibb, Celltrion HealthCare, Galapagos, Lilly France, Novartis, Nordic Pharma, Pfizer, and Sanofi Aventis; Amgen in the last 3 years, Jean-Marc BUSNEL: None declared, Nathalie Balandraud Speakers bureau: speaker for BMS, Novartis, MSD in the last 3 years, Consultant of: consultant for Roche Chugai and Lilly in the last 3 years, Grant/research support from: Our lab received financial support from Bristol Myers Squibb, Celltrion HealthCare, Galapagos, Lilly France, Novartis, Nordic Pharma, Pfizer, and Sanofi Aventis; Amgen in the last 3 years.
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POS0267

MORTALITY OUTCOME OF ACUTE MYOCARDIAL INFRACTION AND ACUTE HEART FAILURE HOSPITALIZATION IN RHEUMATIC DISEASES PATIENTS PRE-COVID-19 VS. COVID-19 PANDEMIC FROM 2016-2020 NATIONAL INPATIENT SAMPLE (NIS) DATABASE

Keywords: Cardiovascular disease, COVID, Outcome measures

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Background: Rheumatic diseases such as rheumatoid arthritis (RA) and Systemic lupus erythematosus (SLE) were known for increased prevalence and risk of death from cardiovascular disease (CVD) due to systemic inflammation in conjunction with other environmental risk factors and genetic predispositions.[1] The COVID-19 pandemic is of the leading causes for the increased age-adjusted mortality rate in 2020 due to various unforeseeable conditions including unequitable healthcare resource distribution, decrease access to medical treatment other than for COVID-19 infection.

Objectives: To investigate if the presence of the COVID-19 had an impact on the mortality outcome of acute myocardial infraction (AMI) and acute heart failure (AHF) in rheumatic diseases (RDs) including patients with RA, SLE, psoriasis/ psoriatic arthritis, gout, myositis and vasculitis, and sarcoidosis in the United States using the NIS inpatient database from 2016-2020.

Methods: Using NIS database from 2016-2020, we identified patients with a primary admission diagnosis of AMI or AHF using ICD-10 codes. For each admission, we calculated ascertained mortality risk. The association of RDs with inpatient mortality was calculated using multivariable logistic regression. Mortality outcomes from 2016-2019 was compared to 2020, which was the year COVID-19 pandemic initiated.

Results: We identified a total of 691,834 AMI/AHF hospitalizations from 2016-2019, of which 39,047 patients had RDs. During the pre-COVID-19 time, the inpatient mortality was significantly higher in the non-RDs group (4.1% vs 3.3%, *p*=<0.001). In multivariable logistic regression model, after adjusting for age, race, gender, region, income and confounding comorbidities, patients in the RDs group had a lower odd ratio of inpatient mortality in AMI/AHF compared to non-RDs group (OR=0.71, *p*=<0.001). During the pandemic year, total AMI/ AHF hospitalizations were 121,285, and 5,813 of them were patients had RDs. Again the hospitalization mortality was higher in the non-RDs group with clinical significance of *p*= <0.001 (4.8% vs. 3.4%). Interestingly, in terms of the COVID-19 infection rate, patients the non-RDs group had a higher infection rate when comparing to RDs (25% vs 23%, *p*=0.047). The odd ratio for AMI/AHF hospitalization mortality was again significantly lower in RDs groups compared to non-RD's group (OR=0.65, *p*=<0.001).

Conclusion: Based on our analysis, the presence of co-morbid RDs was not associated with an increased mortality in patients hospitalized with AMI/AHF. These results may be attributed to the use of biologic agents in RDs patients in reducing systemic inflammation. The lower COVID-19 infection rate in RDs patients could be related to the early and aggressive implementation of social distancing and telehealth appointments in the US during the COVID-19 pandemic.

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Table 1. Demographic, Outcomes and Adjusted Odd Ratio of Hospital Mortality of Acute Myocardial Infraction and Acute Heart Failure Exacerbation in Patient Without and With Rheumatic Diseases 2016-2020

Characteristics/outcome 2016-2019	Without RDs 691,834	With RDs* 39,047	p-value	Characteristics/outcome 2020	Without RDs 121,285	With RDs* 5,813	p-value
Mortality (%)	**4.1**	3.3	<0.001	**Mortality**	**4.8**	3.4	<0.001
Age (Year, mean)	68	**71**	<0.001	**Age (Year, mean)**	67	**70**	<0.001
Female (%)	**41**	35	<0.001	**Female (%)**	**37**	31	<0.001
Length of Stay (day)	3	**4**	<0.001	**Length of Stay (day)**	**3**	**3**	<0.001
				COVID-19 Infection Rate (%) ¥	**25**	23	0.047
Characteristics/outcome 2016-2019	**Odd Ratio**	**95% CI**	***p*-value**	**Characteristics/outcome 2020**	**Odd Ratio**	**95% CI**	***p*-value**
Mortality	0.71	(0.60, 0.83)	<0.001	**Mortality**	0.65	(0.56, 0.76)	<0.001
Length of Stay	1.01	(1.01, 1.02)	<0.001	**Length of Stay**	1.01	(1.00, 1.01)	<0.001

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Disclosure of Interests: None Declared.
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POS0268

PRE-EXPOSURE PROPHYLAXIS WITH TIXAGEVIMAB/CILGAVIMAB IS EFFECTIVE IN LIMITING THE RISK AND THE SEVERITY OF COVID-19 IN PATIENTS WITH AUTOIMMUNE OR INFLAMMATORY DISEASES AT INCREASED RISK OF SEVERE COVID-19 WHO ARE POOR RESPONDERS TO VACCINATION

Keywords: Disease-modifying Drugs (DMARDs), COVID, Vaccination/ Immunization

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Background: Patients with autoimmune or inflammatory diseases treated with immunosuppressants such as anti-CD20 are at increased risk for severe COVID-19 and have a high probability of insufficient response to vaccination. The monoclonal antibody combination tixagevimab/cilgavimab has received early access approval to reduce the frequency of symptomatic COVID-19 in immunocompromised patients at risk for severe COVID-19 and unresponsive to vaccination.
Objectives: We aim to evaluate the clinical efficacy of tixagevimab/cilgavimab in pre-exposure prophylaxis in patients with increased risk of severe COVID-19 in rheumatology.
Methods: In this multicenter observational study conducted between December 2021 and August 2022, we included patients with autoimmune or inflammatory diseases who received at least one intramuscular injection of tixagevimab/cilgavimab as pre-exposure prophylaxis in 3 French rheumatology units. Occurrence of COVID-19 was assessed during usual follow-up or by phone call. The endpoint was the incidence of COVID-19 and its severity.
Results: tixagevimab/cilgavimab was administered to 115 patients, median age 62 years (52-71), with chronic arthritis (n=53), connective tissue disease (n=38) or vasculitis (n=11). The main background immunosuppressants were rituximab (n=98), methotrexate (n=48), mycophenolate mofetil (n=19), cyclophosphamide (n=15), azathioprine (n=12), and corticosteroids (n=62, median dose 5 mg, CI95% 5-8). During a median follow-up of 128 days (93-173), COVID-19 occurred in 23/115 patients (20%) with Omicron identified for the 8 genotyped patients. During the study period, the average weekly incidence was 1071 per 100.000 inhabitants in Ile-de-France vs. 588 per 100.000 in our patients. Patients who received a 2-injections regimen had a lower risk of infection than patients with a single injection (16/49, 33%, vs. 5/64, 8%, p=0.0012). The COVID-19+ patients did not differ from uninfected patients in terms of age, comorbidities, type and duration of underlying disease, extra-articular organ involvement or background immunosuppressants. All COVID-19 cases were non-severe, there were no deaths. The tolerance of injections was excellent, with no side effects observed.
Conclusion: In a population with autoimmune or inflammatory diseases at increased risk of severe COVID-19 with a poor response to vaccination, pre-exposure prophylaxis by tixagevimab/cilgavimab limited the risk of infection and the severity of COVID-19. This study supports the use of COVID-19 serological tests in this patient population in order to detect those who do not respond adequately to vaccination since pre-exposure treatments and/or early treatments are available.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0269

COVID-19 SEVERITY AND VACCINE BREAKTHROUGH INFECTIONS IN SJÖGREN'S SYNDROME: RESULTS FROM THE COVAD STUDY

Keywords: Vaccination/Immunization, COVID, Sjögren syndrome

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Background: Despite the increasing number of studies on COVID-19 infection in people with rheumatic and musculoskeletal diseases (RMDs), data on Sjögren's syndrome (SS) is limited.
Objectives: To determine the spectrum and severity of pre-vaccine and post-vaccine breakthrough COVID-19 infections (B-INFs) among patients with SS compared to other connective tissue diseases (CTDs), non-rheumatic autoimmune diseases (nrADs), and healthy controls (HC).
Methods: Data were collected using the COVID-19 Vaccination in Autoimmune Diseases (COVAD) questionnaire (March–December 2021) and analysed to compare frequencies and identify associations with demographic, disease-specific and vaccine-specific variables (for B-INFs).
Results: Among 9462 complete respondents, 356 were patients with SS, of which 129 had primary (p) SS and 227 had SS associated (a) with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc) or inflammatory myopathies (IM). Patients with SS were compared to 1586 patients with other CTDs (RA, SLE, SSc or IIM)] but without SS, 825 patients with nrADs and 4712 healthy controls (HC). SS patients had mean age of 52.3 years, mean disease duration was 12 years; 94.5% were females, 68% were Caucasian. Overall COVID-19 infection was reported by 14% of patients with SS and 19.2% of HC (odds ratio (OR)=0.7; 95% confidence interval (CI)=0.5-0.9). The majority of cases occurred prior to the first vaccine dose with no differences across groups in the proportion of B-INFs (SS: 21.6%; other CTD: 20%; nrAD: 19.8%; HC: 19.4%). In the SS group, age and disease duration were similar in patients with either pre-vaccine infections or B-INFs. When comparing pSS and aSS, the overall number of COVID-19 infections was comparable, regardless of the timing (before or after vaccination). Over 80% of SS patients were symptomatic and the symptom duration was similar regardless of the timing of infection, however the symptom burden was different, with certain manifestations absent in B-INFs (oral ulcers, nausea/vomiting, skin rashes, loss of smell/taste) (Figure 1). When focusing on pSS and aSS separately, fever was never reported in aSS B-INFs, whereas other symptoms were equally distributed in pre-vaccine infections and B-INFs. When comparing SS to other CTDs and HC, it emerged that during B-INFs, patients with SS had more frequently chest pain (OR=6.5; 95% CI=

1.8-23 vs NC; OR=11.2; 95% CI=1.7-72 vs other CTDs) and headache (OR= 4.6; 95% CI= 1.1-20 vs other CTDs). Hospitalization for B-INF was required by only one patient with SS patient (pSS) who also required oxygen therapy. Conversely 17% of patients with SS (with an equal distribution between pSS and aSS) required hospitalization for pre-vaccine infections. Although the overall hospitalization rate did not differ across groups, patients with SS needed oxygen therapy more frequently than HCs (OR=9; 95% CI=1.04-78) and other CTDs (OR=19.5; 95% CI= 1.8-213). When comparing pSS and aSS, the need for hospitalization and, if hospitalised, the need of oxygen therapy were comparable for infections before vaccination and B-INFs. In pSS, B-INFs mainly occured after BNT162b2 vaccine (37%) and ChAdOx1 nCoV-19 (37%) with few cases after the other vaccines, whereas in aSS B-INFs occurred after either BNT162b2 vaccine (67%) or BBIBP-CorV (33%).

Conclusion: Our data demonstrated that B-INfs in patients with SS are less severe than those observed pre-vaccination. This strengthens the rationale for COVID-19 vaccination in patients with SS.

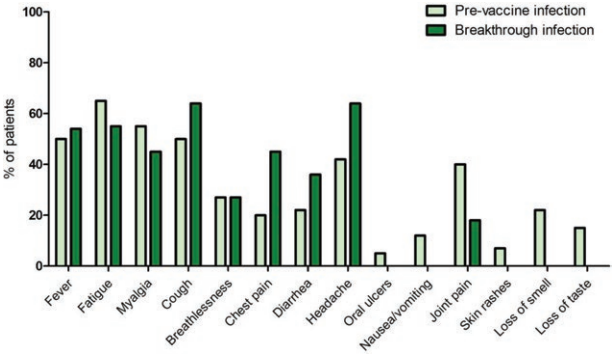


Figure 1. The clinical picture of anti-SARS-CoV-2 infection in patients with Sjögren's syndrome

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POS0270

BURDEN OF COVID-19 IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES: INSIGHTS FROM A SWISS APP-BASED SURVEY

Keywords: COVID, Quality of life, Registries

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Background: COVID-19 comes with a significant medical risk for patients with inflammatory rheumatic diseases, with an increased risk of infection and severe outcomes[1]. The vulnerability of rheumatologic patients might also affect their quality of life[2], for example by keeping up protective measures (masking, restriction of social contacts, etc.) while the general Swiss public no longer does so.

Objectives: The aim of this study was to better understand the health-related burden of COVID-19 among patients with inflammatory rheumatic diseases and to investigate factors contributing to a different perception of the burden of COVID-19.

Methods: We included all patients registered in the Swiss Clinical Quality Management (SCQM) registry with rheumatoid arthritis (RA), axial spondylarthritis (axSpA), psoriatic arthritis (PsA), undifferentiated arthritis, polymyalgia rheumatica or giant cell arteritis who answered the questionnaire in the mobile My-SCQM app between the 4.11 and 11.12.2022. The questionnaire contained questions about the extent to which the pandemic is affecting patients' personal and social lives. We performed descriptive analysis on the whole population and also in subgroups according to 5 treatment groups, assigned in the following order: rituximab > JAK-inhibitors > other b/tsDMARDs > csDMARDs > none of these treatments. This means that someone taking e.g., both a JAKi and a csDMARD will be assigned to the JAKi category.

Results: The questionnaire was answered by 1357 individuals with a median age of 57 years. 63% of participants were female. 33% are living in a household with children. 36% were diagnosed with RA, 34% with axSpA, 22% with PsA and 8% with another inflammatory rheumatic disease. A total of 100 patients were prescribed csDMARDs, 94 JAKi, 18 rituximab, 695 other b/tsDMARDs, and 450 patients received none of these treatments (Table 1). 10% of patients feel their general lives are affected by COVID-19 at a level of more than 7 out of a 10 scale. 3% of the participants report that COVID-19 impacts their social environment (family and friends) as a potentially dangerous disease at a level of more than 7 out of 10 scale. After being vaccinated against COVID-19, 33% of patients report no fear of the disease, however, 27% of participants still state that their anxiety against the virus remained unchanged. There is a trend towards persistence of fear in those taking rituximab (35%) compared to the participants in other groups (26% and 20% respectively in csDMARDs and JAKi takers). More than half of the population still wear masks, and rituximab users are the most likely to wear them (72% of these individuals still do), followed by individuals on JAKi (65%) (Figure 1).

Conclusion: Our study revealed that after around two years of the COVID-19 pandemic, the burden of COVID-19 in patients with inflammatory rheumatic diseases in Switzerland is generally low, although it appears higher in patients with JAKi and rituximab, and that for a minority the quality-of-life still remains impacted.

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Table 1. Basic characteristics of study population.

Variable	Level	Overall	Rituximab	JAKi	Other b/tsDMARDs	csDMARDs	None of the above	Unclear
n		*1357*	*18*	*94*	*695*	*100*	*161*	*289*
Gender (%)	Men	*508 (374)*	*3 (16.7)*	*19 (20.2)*	*291 (41.9)*	*39 (39)*	*63 (39)*	*93 (32)*
Age (median)		*57*	*59*	*59*	*56*	*59*	*55*	*58*
Diagnosis Group (%)	RA	*498 (36.7)*	*18 (100)*	*67 (71.3)*	*188 (27)*	*69 (69)*	*33 (20.5)*	*123 (42.6)*
	axSpA	*462 (34)*	*0*	*11 (11.7)*	*270 (38.8)*	*10 (10)*	*87 (54)*	*84 (29)*
	PsA	*296 (21.8)*	*0*	*11 (11.7)*	*187 (26.9)*	*15 (15)*	*19 (11.8)*	*64 (22)*
	RZA/ PMR	*13 (1)*	*0*	*0*	*3 (0.4)*	*0*	*7 (4.3)*	*3 (1)*
	UA	*88 (6.5)*	*0*	*5 (5.3)*	*47 (6.8)*	*6 (6)*	*15 (9.3)*	*15 (5.2)*

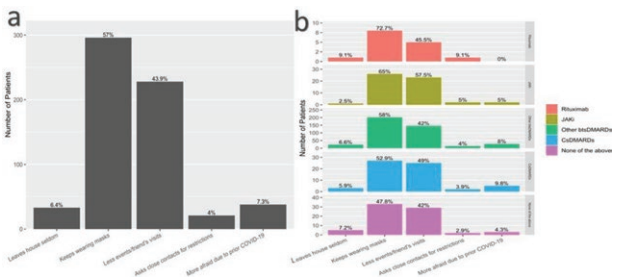


Figure 1. Participants' description of their current situation concerning COVID-19 (YES/NO option per criteria): a. overall b. by treatment group.

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Disclosure of Interests: Christoph Blapp: None declared, Shekoofeh Yaghmaei Employee of: AstraZeneca, Adrian Ciurea: None declared, Almut Scherer: None declared, Marco Kuster Employee of: AstraZeneca, Kim Lauper Speakers bureau: Pfizer, Viatris and Galapagos, Consultant of: Pfizer, Grant/research support from: Eli-Lilly.
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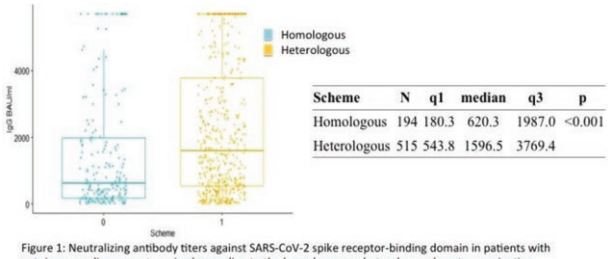
POS0271

HETEROLOGOUS COVID-19 BOOSTER VACCINATION PRODUCED GREATER ANTIBODY TITERS IN AUTOIMMUNE DISEASE PATIENTS: DATA FROM MULTICENTRIC PROSPECTIVE PHASE IV SAFER STUDY

Keywords: Registries, COVID, Vaccination/Immunization

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Background: The ChAdOx1, Coronavac, BNT162B2 and Janssen vaccines are available for the primary and booster immunization of immunosuppressed patients. However, there are few studies in the literature that assess the immunogenicity and safety of the different platforms COVID-19 vaccines in patients with autoimmune diseases (AID).
Objectives: The present study aims to evaluate the immunogenicity through anti-spike IgG antibodies 28 days after the booster dose in the heterologous boost groups compared with homologous regimen of the vaccine against COVID-19 in patients with AID.
Methods: These data are from SAFER study: "Safety and efficacy on Covid-19 Vaccine in Rheumatic Disease", a multicentric prospective phase IV study, in real life, in Brazil, started on May 2021. Data from this analysis were from 8 centers, from all Brazilian areas, after 2 or 3 doses of vaccine against COVID-19 in patients with AID age ≥ 18 years. Exclusion criteria were pregnancy, previous severe adverse events (AE) to any vaccine or other imunosuppression causes. Demographics, diagnoses and therapeutic regimens were collected via participant report through the Research Electronic Data Capture tool. Available vaccines were adenoviral vectored vaccine (ChAdOx1, Astrazeneca and Ad26.COV2-S, Janssen), mRNA vaccine (BNT162b2, Pfizer–BioNTech) or inactivated SARS-COV-2 vaccine (Coronavac). Participants were followed up by means of blood collection for measurement of IgG antibody against SARS-CoV-2 spike receptor-binding domain by chemiluminescence (SARS-CoV-2-IgG-II Quant assay, Abbott-Laboratories) at baseline and 28 days after the first, 2nd and 3rd doses. The seropositivity was defined for titers IgG-Spike ≥7.1 BAU/mL. The ANOVA, the post-hoc Tukey and pairwise comparisons tests were used to compare the IgG-S titles between the groups. An alpha level of 5% significance was used in all analyses.
Results: A total of 1096 participants were included and followed from the first dose. 709 patients AID received the complete 3-dose regimen: systemic lupus erythematosus (N=238, 33.6%), rheumatoid arthritis (N=143, 20.2%), spondyloarthritis (N=96, 13.5%), primary Sjögren's syndrome (N=56, 7.9),), inflammatory bowel disease (N=50, 7,1%), vasculitis (N=31, 4.4%), systemic sclerosis (N=25, 3.5%), Behçet syndrome (N= 19, 2.7%) myositis (N= 12, 1.7%), other systemic AID (N= 39, 5.5%). Mean age was 41.59 (12.2), female N=556, (78.4%) and admixed race (N=370, 52.2%). Primary immunization was performed with Coronavac in 265 (37.4%), ChAdOx1 in 403 (56.8%) and Pfizer in 41 (5.8%) AID patients. After the 2nd dose (28 days), the booster was performed with Coronavac (N=10, 1.4%), ChAdOx1 (N=226, 31.9%), Pfizer (N=464, 65.4%) and Janssen (N=9, 1.3%). Anti-spike IgG antibodies were analyzed in the 657 patients who received the three doses. All patients had a substantial increase in IgG antibody concentrations 28dy after the booster vaccine with median 275.9 BAU/ml (88.8 - 1000.9) vs. 1217.2 (402.3 - 3213.7) booster vaccine. All heterologous regimens (N=515) had anti-spike IgG responses at day 28 that were superior to homologous booster (N=194) with median titers 1596.5 (543.9-3769.4) vs. 620.3 BAU/mL (180.3-1987.0), p<0.001 (figure 1). The seropositivity rates were higher and similar in both groups (Heterologous 98.4% vs. Homologous 95.9%, p=0.07).



Scheme	N	q1	median	q3	p
Homologous	194	180.3	620.3	1987.0	<0.001
Heterologous	515	543.8	1596.5	3769.4	

Figure 1: Neutralizing antibody titers against SARS-CoV-2 spike receptor-binding domain in patients with autoimmune diseases categorized according to the homologous or heterelogous booster vaccination.

Conclusion: All vaccines administered as third dose induced an increase in IgG-S titers antibodies, which could improve protection against COVID-19 in AID patients. Heterologous booster vaccination produced greater humoral immune responses than homologous booster, which is relevant in this immunosuppressed population.
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POS0272

IMPACT OF THE COVID-19 PANDEMIC ON ADHERENCE TO DISEASE MODIFYING DRUGS AMONG PATIENTS WITH RHEUMATIC DISEASES: A POPULATION-BASED, INTERRUPTED TIME SERIES ANALYSIS

Keywords: COVID, Disease-modifying Drugs (DMARDs)

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Background: Although studies have quantified adherence to medications among patients with rheumatic diseases (RD) during the COVID-19, lack of direct pre-pandemic comparison precludes understanding of impact of the pandemic.

Objectives: Our objective was to evaluate the effect of the COVID-19 pandemic on adherence to disease modifying drugs (DMARDs) including conventional synthetic (csDMARDs) and targeted synthetic (tsDMARDs).
Methods: We linked population-based health data on all physician visits, hospital admissions, and all dispensed medications, regardless of payer in British Columbia from 01/01/1996 to 3/31/2021. We identified prescriptions for csDMARDs (including methotrexate, hydroxychloroquine) and tsDMARDs, namely anti-TNFs (including infliximab, etanercept, adalimumab) and rituximab using drug identification numbers among indicated individuals with RD. We defined March 11, 2020, as the 'index date' which corresponded to the date that mitigation measures for the COVID-19 pandemic were first introduced. We assessed adherence as proportion days covered (PDC), calculated monthly in the 12 months before and 12 months after the index date. We used interrupted time-series models, namely segmented regression to estimate changes and trends in adherence before and after the index date.
Results: Our analysis showed that the mean PDCs for all included DMARDs stayed relatively steady in the 12 months before and after mitigation measures were introduced (see **Table 1**). Adherence was highest among anti-TNFs, methotrexate, and azathioprine. Anti-TNFs were on a downward trajectory 12 months prior to the index date. Interrupted time-series modeling demonstrated statistically significant differences in the trends in PDCs post- vs. pre-mitigation measures for all anti-TNFS (slope [∂]: 1.38, standard error [SE]: 0.23), infliximab (∂: 1.35, SE: 0.23), adalimumab (∂: 0.82, SE: 0.25), and etanercept (∂: 1.07, SE: 0.25) (see **Figure 1a**). Conversely, the csDMARDs were on a flatter trajectory, and methotrexate (∂: -0.53, SE: 0.16), leflunomide (∂: 0.43, SE: 0.08), mycophenolate (∂: -1.26, SE: 0.48), cyclophosphamide (∂: 0.29, SE: 0.05), minocycline (∂: 0.04, SE: 0.02), chloroquine (∂: 0.02, SE: 0.00) showed statistically significant changes in estimated PDC trajectory after mitigation measures were introduced (see **Figure 1b**).
Conclusion: This population-based study demonstrates that messaging and pandemic mitigation measures did not affect adherence to DMARDs.

Table 1. Mean PDC 1 year before and after mitigation measures for the COVID-19 pandemic were introduced.

Medication		Mean PDC (%) 12 months before index date	Mean PDC (%) 12 months after index date
csDMARDs	methotrexate	28.9	26.8
	azathioprine	21.8	19.5
	sulfasalazine	16.2	14.9
	leflunomide	14.3	13.0
	cyclosporine	13.7	11.5
	hydroxychloroquine	10.5	9.6
	mycophenolate	4.5	2.9
	antimalarials	4.4	3.9
	penicillamine	3.5	3.4
	cyclophosphamide	1.5	0.7
	chlorambucil	1.2	0.4
	minocycline	1.1	0.9
	gold	0.5	0.2
	chloroquine	0.1	0.0
tsDMARDs	anti-TNFs	52.1	49.2
	infliximab	41.8	38.3
	adalimumab	40.3	36.8
	etanercept	31.8	28.9
	rituximab	3.4	2.9

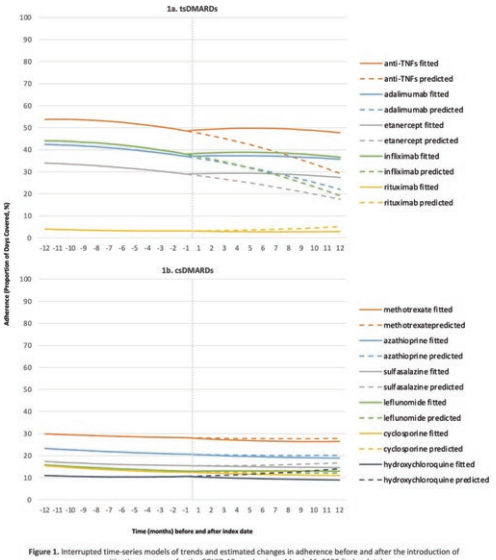


Figure 1. Interrupted time-series models of trends and estimated changes in adherence before and after the introduction of mitigation measures for the COVID-10 pandemic on March 11, 2020 (index date).

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POS0273

POST COVID-19 SYNDROME IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES: RESULTS FROM THE COVAD STUDY

Keywords: Vaccination/Immunization, COVID, Patient reported outcomes

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Background: Post COVID-19 syndrome (PCS) is an emerging cause of morbidity and poor quality of life in COVID-19 survivors [1, 2].

Objectives: We aimed to assess the prevalence, risk factors, outcomes, and association with disease flares of PCS in patients with autoimmune rheumatic diseases (AIRDs) and non-rheumatic autoimmune diseases (nrAIDs), both vulnerable groups understudied in the current literature using data from the 2nd COVID-19 Vaccination in Autoimmune Diseases (COVAD) global multicentre patient self-reported e-survey.

Methods: The survey was circulated from February to July 2022 by the international COVAD Study Group (157 collaborators from 106 countries), and demographics, comorbidities, AIRD/nrAID status, COVID-19 history, vaccination details, and PROMIS physical and mental function were recorded. PCS was defined as symptom resolution time >90 days following acute COVID-19. Predictors of PCS were analysed using regression models for the different groups.

Results: 7666 total respondents completed the survey. Of these, 2650 respondents with complete responses had positive COVID-19 infection, and 1677 (45.0% AIRDs, 12.5% nrAIDs, 42.5% HCs) completed the survey >90 days post acute COVID-19. Of these, 136 (8.1%) had PCS. Prevalence of PCS was higher in AIRDs (10.8%) than healthy controls HCs (5.3%) (OR: 2.1; 95%CI: 1.4-3.1, p=0.002). Across the entire cohort, a higher risk of PCS was seen in women (OR: 2.9; 95%CI: 1.1-7.7, p=0.037), patients with long duration of AIRDs/nrAIDs (OR 1.01; 95%CI: 1.0-1.02, p=0.016), those with comorbidities (OR: 2.8; 95%CI: 1.4-5.7, p=0.005), and patients requiring oxygen supplementation for severe acute COVID-19 (OR: 3.8; 95%CI: 1.1-13.6, p=0.039). Among patients with AIRDs, comorbidities (OR 2.0; 95%CI: 1.08-3.6, p=0.026), and advanced treatment (OR: 1.9; 95%CI: 1.08-3.3, p=0.024), or intensive care (OR: 3.8; 95%CI: 1.01-14.4, p=0.047) for severe COVID-19 were risk factors for PCS. Notably, patients who developed PCS had poorer PROMIS global physical [15 (12-17) vs 12 (9-15)] and mental health [14 (11-16) vs 11 (8-14)] scores than those without PCS.

Conclusion: Individuals with AIRDs have a greater risk of PCS than HCs. Associated comorbid conditions, and advanced treatment or intensive care unit admission for severe COVID-19 confer a higher risk of PCS. It is imperative to identify risk factors for PCS for immediate multidisciplinary management in anticipation of poor physical and mental health.

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POS0274

PROSPECTIVE EVALUATION OF THE EFFECT OF THE VACCINE AGAINST SARS-COV-2 IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM SAFER STUDY

Keywords: COVID, Vaccination/Immunization, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease, which presents an immune disorder that leads to the production of autoantibodies with potential involvement of multiple organs. Infections are one of the most frequent causes of hospitalization and death in lupus patients, and SARS-CoV-2 infection has been a global threat since March 2020. Immunization of these patients has been strongly recommended, although vaccine evaluation studies have not included this profile of patients.

Objectives: To evaluate the immunogenicity and safety after 2 doses of the vaccine against SARS-CoV2 in patients with SLE.

Methods: Subgroup of SLE patients from the prospective multicenter cohort of patients with immune-mediated diseases "SAFER" – Safety and Efficacy on COVID-19 Vaccine in Rheumatic Disease, a phase IV study. Vaccination against SARS-CoV-2 took place with vaccines approved by Brazilian regulatory bodies CoronaVac (Inactivated SARS-CoV-2 Vaccine), ChadOx-1 (AstraZeneca) and BNT162b2 (Pfizer-BioNTech) and this project followed in line with the guidelines of the National Immunization Plan in Brazil. Patients aged 18 years or older with a previous diagnosis of SLE (according to the 2019 ACR/EULAR criteria) were included. Patients were evaluated by telephone contact and in a face-to-face visit on the 28th day after each dose. Patients were followed up by means of blood collection for measurement of IgG antibody against SARS-COV-2 by chemiluminescence and disease activity assessed using SLEDAI-2K score.

Results: A total of 367 individuals with SLE were included, of whom 207 received 2 doses of CoronaVac, 128 received 2 doses of ChadOx-1 and 32 received 2 doses of BNT162b2. 90% of the subjects were female with a mean age of 37 years. About 42% (154) of the individuals included did not have any other associated comorbidity. 50% (182) of patients were using oral glucocorticoids and azathioprine was the most frequent immunosuppressive therapy. Regarding disease activity parameters, 38% (140) of patients had zero SLEDAI-2K at baseline and 41% (147) had zero SLEDAI-2K 28 days after the 2nd dose. Anti-DNA positivity was 30.7% (16/52) at inclusion and 32.6% (17/52) 28 days after the 2nd dose. Complement consumption was present in 18% (10/55) at inclusion and in 14.5% (8/55) 28 days after the 2nd vaccine dose. The geometric mean titers of IgG antibodies against SARS-COV-2 increased in the different vaccine groups, log 2.27 BAU/mL at inclusion and log 5.58 BAU/mL 28 days after the 2nd dose. Antibody titers after second dose varied between different vaccines, 4.96 BAU/mL CoronaVac, 6.00 BAU/mL ChadOx-1 and 7.31 BAU/mL BNT162b2 vaccine, $p < 0.001$. Only 3.54% (13/367) patients had covid-19 infection after the 15th day of the second dose of immunization, 9 of them having received 2 doses of CoronaVac, 4 of them of ChadOx-1 and none of them receiving BNT162b2, with p-value of 0.63.

Conclusion: This study suggests that vaccines against SARS-COV-2 are safe in SLE patients. Induction of immunogenicity occurred in different vaccine regimens. Only 3.5% of individuals had COVID-19 infection with no difference between the types of vaccines evaluated. Future analyzes to explore the association of the effect of immunosuppressive medication, as well as the impact of booster doses and longer follow-up on clinical outcome will be performed.

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POS0275

COVID-19 INFECTION IN PATIENTS WITH RHEUMATIC DISEASE DURING OMICRON OUTBREAK IN SOUTH KOREA: A SINGLE-CENTER PROSPECTIVE STUDY

Keywords: Epidemiology, COVID

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Background: High transmissibility and immune evasion of SARS-CoV-2 Omicron variant made it dominant variant worldwide since January 2022. Before Omicron era, several studies demonstrated that autoimmune inflammatory rheumatic disease (AIIRD) patients were vulnerable to COVID-19 infection compared to general population. However, there is a lack of epidemiologic data regarding COVID-19 outbreak in patients with AIIRD in Omicron era.

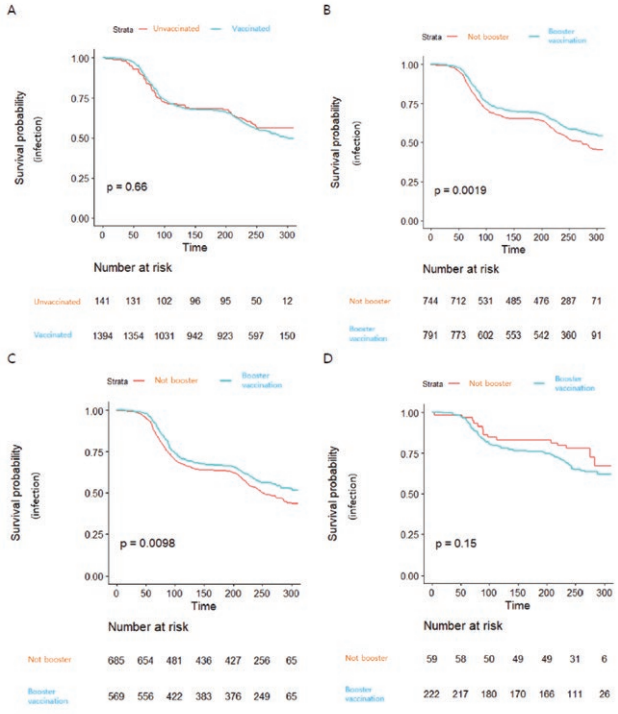
Objectives: To identify incidence rate, hospitalization rate and potential risk factors for COVID-19 outcomes in AIIRD patients during Omicron outbreak.

Methods: This study was a prospective longitudinal study from January 1 to October 31, 2022. We included patients who visited rheumatology outpatient clinic in a nationwide, tertiary referral center in South Korea. Included patients were classified into two groups (AIIRD and non-AIIRD groups) based on underlying disease. Vaccination and infection history of COVID-19 were obtained through self-report via questionnaire and data from Korea Disease Control and Prevention Agency (KDCA). Main outcome of this study was an incidence of COVID-19 infection during the observation period. Clinical factors associated with the incidence of COVID-19 infection were investigated using Cox proportional hazard model. In the final multivariable model, clinical factors that showed a relevant association ($P < 0.1$) with the outcome in the univariable analysis were included as covariates.

Results: A total of 1,814 patients were analyzed (AIIRD group: 1,535, non-AIIRD group: 279). The COVID-19 incidence in AIIRD group (47.6%) was higher than that reported in general population of South Korea (43.9%) and this trend was prominent in those aged < 70 years. Longitudinal change in COVID-19 incidence during the observation period showed two peaks in March and August in both groups, which was the same trend with general population. There were 30 cases of hospitalization due to COVID-19 infection, with the rate was comparable between AIIRD and non-AIIRD groups (1.7% vs. 1.5%, $P = 0.970$). The incidence rate of COVID-19 in the AIIRD group was comparable to that in the non-AIIRD group (47.6% vs. 44.8%, $P = 0.386$). In the AIIRD group, COVID-19 infection occurred less frequently in patients with old age (≥70 years) and those receiving glucocorticoid treatment. Other clinical factors such as use of DMARDs and biologics, and underlying diseases were not associated with COVID-19 incidence in the multivariable analysis. Of note, at least one COVID-19 vaccination did not lower its incidence (unadjusted HR 1.06 [95% CI 0.82-1.38]). Although patients who received booster vaccination were less likely to be infected with COVID-19 (unadjusted HR 0.79 [0.68-0.92]), this protective effect was significant only in patient younger than 70 years (Figure 1).

Conclusion: During the Omicron outbreak in South Korea, incidence of COVID-19 infection in patients with AIIRD and non-AIIRD was comparable. Immunomodulatory agents and specific rheumatic diseases did not increase the COVID-19 incidence, and booster vaccination against COVID-19 decreased the infection only in patients younger than 70 years.

(Figure) Association between baseline vaccination status and COVID-19 infection in AIIRD group



Baseline vaccination status: (A) at least one vaccination (B) booster vaccination (all age) (C) booster vaccination (age<70) (D) booster vaccination (age≥70)

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0276

SARS-COV-2 INFECTION OUTCOMES IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES -A DANISH NATIONWIDE COHORT STUDY

Keywords: COVID, Prognostic factors, Vaccination/Immunization

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Background: The SARS-CoV-2 pandemic initially raised concerns about the risk of severe infection in patients with inflammatory rheumatic diseases (IRD).
Objectives: In a setting with an excessive SARS-CoV-2 test strategy and availability of effective vaccines we aimed to investigate if patients with (IRD) face greater risk of contracting SARS-CoV-2 infection and have an increased risk of hospitalization, assisted ventilation and death compared to the general population.
Methods: This large nationwide, population-based register study compared the outcomes of SARS-CoV-2 infection in Danish patients with IRD (n=65.603) to matched population controls (n=656.030), from the first registration of SARS-CoV-2 (March 2020 to October 2022). The IRD population included 1,903 ANCA associated and necrotizing vasculitis; 30,391 rheumatoid arthritis; 2,444 Systemic lupus erythematosus; 1,538 systemic scleroderma; 2,521 sjogren's syndrome; 5,875 giant cell arteritis and 20,931 spondylarthritis and psoriasis arthritis patients. Cox regression analyses were used to calculate incidence rate ratios (IRRs) for SARS-CoV-2 infection outcomes.
Results: We observed a discrete difference in time to first and second positive SARS-COV-2 test in IRD patients compared to the general population (IRR=1.05 95% CI (1.03-1.06) and (IRR=1.17 95% 1.11-1.24). The risk of hospital contact with COVID-19 and severe COVID-19 was increased in IRD patients compared to population controls (IRR=1.92, 95% CI 1.79-2.06) and (IRR= 2.16, 95% CI 1.91-2.45). Also, the risk if hospitalization requiring assisted ventilation (IRR=2.40, 95% CI 1.93-2.99) and for hospitalization with COVID-19 leading to death were increased in the IRD population (IRR=2.02 95% CI 1.66-2.45). The risk of hospitalization with severe COVID-19 was remarkably reduced after third SARS-CoV-2 vaccination.
Conclusion: IRD patients have a risk of SARS-Cov-2 which nearly corresponds to the general population but have a substantial increased risk of hospitalization with COVID-19, severe COVID-19, requiring assisted ventilation and COVID-19 leading to death compared to the general population. A third SARS-CoV-2 vaccination was associated with reduced need for hospitalization with COVID-19 and reduced the risk of death.
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Table 1. Relative risk (95%CI) of first positive SARS CoV-2-test, vaccination, hospitalization and death in patients with inflammatory rheumatic diseases vs. general population controls in Denmark, March 1. 2020 to October 1. 2022.

	Total	ANCA associated vasculitis	Rheumatoid arthritis	Systemic lupus erythomatosus	Systemic Scleroderma	Sjogren syndrome	Giant cell arteritis	Spondyl artritis and Psoriatic arthritis
Total number (n)	65.603	1.903	30.391	2.444	1.538	2.521	5.875	20.931
Outcome	IRR (95%CI)							
Time to first positive SARS-CoV-2 test	1.05 (1.03-1.06)	1.10 (1.02-1.19)	1.04 (1.02-1.06)	0.90 (0.85-0.96)	0.96 (0.88-1.05)	0.96 (0.89-1.02)	1.12 (1.06-1.18)	1.12 (1.06-1.18)
Time to second positive SARS-CoV-2 test	1.17 (1.11-1.24)	1.92 (1.40-2.64)	1.21 (1.10-1.33)	0.89 (0.68-1.17)	0.87 (0.57-1.33)	0.94 (0.69-1.29)	1.36 (1.00-1.84)	1.14 (1.04-1.24)
Time to first positive hospital contact with covid-19	1.92 (1.79-2.06)	6.19 (4.41-8.69)	1.91 (1.71-2.13)	3.01 (2.04-4.43)	3.04 (1.90-4.86)	2.51 (1.63-3.86)	3.01 (2.04-4.43)	3.01 (2.04-4.43)
Time to hospitalization with severe covid-19	2.16 (1.91-2.45)	8.22 (4.77-14.16)	2.00 (1.66-2.42)	3.62 (1.61-8.16)	3.66 (1.62-8.23)	2.10 (0.92-4.80)	1.60 (1.04-2.48)	1.55 (1.16-2.07)
Time to hospitalization with assisted ventilation	2.40 (1.93-2.99)	8.98 (3.97-20.33)	1.99 (1.42-2.79)	5.05 (1.02-25.04)	6.13 (1.87-20.07)	0.83 (0.10-6.91)	2.14 (0.98-4.67)	2.14 (0.98-4.67)
Time to hospitalization with covid-19 followed by death	2.02 (1.66-2.45)	6.31 (2.49-15.99)	2.47 (1.89-3.23)	3.78 (0.85-16.90)	1.90 (0.50-7.17)	2.49 (0.46-13.61)	1.13 (0.63-2.01)	1.00 (0.54-1.85)
Time to Severe covid-19 after 3. vaccination	0.42 (0.25-0.72)	1.02 (0.25-4.18)	0.38 (0.17-0.86)	0.08 (0.01-0.50)	NA	NA	0.19 (0.03-1.10)	0.35 (0.07-1.09)

Advances in our care of children and young people with JIA

POS0277 SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED LUNG DISEASE IN EUROPE

Keywords: Lungs

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Background: Chronic parenchymal lung disease (LD) is a new emerging severe life-threatening complication of sJIA. The number of sJIA patients with LD is apparently increasing and interestingly they are reported more frequently in North America. Data regarding frequency and features of sJIA-LD in Europe are not available.
Objectives: To evaluate the burden of sJIA-LD in Europe.
Methods: Patients with diagnosis of sJIA with LD, including pulmonary alveolar proteinosis (PAP), interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH), followed in European paediatric rheumatology centres were identified through a survey sent to the members of the MAS/SJIA Working Party.
Results: Data from 34 sJIA-LD patients, diagnosed in 15 European paediatric rheumatology centres between 2007 and 2022, were collected. 33 patients were Caucasian and 1 was African-American; 21 were female. The median age at sJIA onset was 6 years and LD occurred after a median time of 2 years. 19 patients had a chronic persistent sJIA course, 14 had a polycyclic course and only 1 patient had a monocyclic course; 29 (85%) had active sJIA at time of LD diagnosis. During the disease course, 28 (82%) patients developed MAS, 12 (35%) of whom had MAS at sJIA onset and 19 (56%) had full-blown MAS at time of LD diagnosis; 23 (68%) patients had >1 MAS episode. 28 (82 %) patients were treated with at least one IL-1 or IL-6 inhibitor before LD diagnosis: 15 with canakinumab, 24 with anakinra and 13 with tocilizumab; 13 (38%) patients experienced drug adverse reaction to a cytokine inhibitor: 9 to tocilizumab and 4 to anakinra. 24 (70%) patients developed ILD, 6 (18%) PAP and 4 (12%) PAH. 15 (44%) patients presented acute digital clubbing; 16 (47%) patients developed hypoxia and 9 (26%) developed pulmonary hypertension. A chest CT scan was performed in all patients with evidence of septal thickening, peri-bronchovascular thickening and ground glass opacities in the majority of patients (26, 18 and 18 respectively). In 17 patients a bronchoalveolar lavage was performed and 12 underwent a lung biopsy. The histopathological pattern was alveolar proteinosis in 5 patients, endogenous lipoid pneumonia in 3, vasculitis in 1 and fibrosis in 1. Half of the patients (17) required ICU admission and 6 (18%) died. All the patients were treated with glucocorticoids (GCs) at time of diagnosis, and 26 received IL-1 or IL-6 inhibitor after the diagnosis (13 canakinumab, 20 anakinra, 14 tocilizumab).
Conclusion: Lung involvement is an emerging life-threatening complication of sJIA and patients are also diagnosed in Europe. Prompt recognition is crucial and new therapeutic strategies are needed to reduce the risk and improve the outcome of this complication.

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POS0278 EFFICACY AND SAFETY OF SECUKINUMAB IN JUVENILE IDIOPATHIC ARTHRITIS: INTERIM RESULTS FROM THE EXTENSION OF THE JUNIPERA TRIAL

Keywords: bDMARD, Clinical Trials

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Background: Secukinumab has demonstrated efficacy and safety in patients with enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) categories of juvenile idiopathic arthritis (JIA) for up to 2 years.[1] After completion of a 2-year core study (JUNIPERA), a long-term extension (LTE) study was conducted to evaluate the continued efficacy and safety of secukinumab.
Objectives: To report interim efficacy and safety results of the LTE study of secukinumab in patients with ERA and JPsA.
Methods: In the core study, a total of 86 patients (2 to <18 years of age) received secukinumab up to week 12 in the open-label (OL) period.[1] JIA ACR30 responders at week 12 (n=75) were subsequently randomised to secukinumab (n=37) or placebo (n=38) up to week 100 in study period 2. Those who flared after randomisation (secukinumab, n=10; placebo, n=21) received OL secukinumab up to week 100.[1] A total of 54 out of 61 patients who had completed the core study consented to enter the LTE study and received secukinumab (s.c.) (75/150 mg in patients <50/ ≥50 kg) every 4 weeks up to 4 years. Patients whose signs and symptoms were not fully controlled, as judged by the investigator in

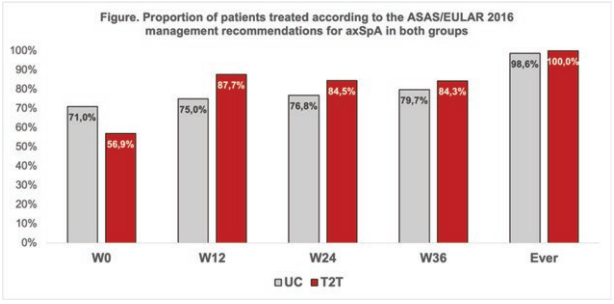
the LTE, could have dose escalation of their secukinumab dose from 75 mg to 150 mg or 150 mg to 300 mg. Median Juvenile Arthritis Disease Activity Scores (JADAS)-27 were presented up to week 156 for efficacy, and adverse events (AEs) and serious AEs were presented for the entire treatment period up to the cut-off date (maximum up to week 232).

Results: JADAS-27 in the core study and in the LTE are presented in the **Figure 1**. A total of 19 patients had dose escalation in the LTE: 8 patients from 75 mg to 150 mg and 11 patients from 150 mg to 300 mg. The overall exposure-adjusted incidence rate per 100 patient-years (PY) of treatment-emergent AEs was 98.4 PY in the entire JIA population. The most commonly reported AEs (preferred term, safety set 5% cut off) were nasopharyngitis (n=9, 16.7%) and arthralgia (n=8, 14.8%). One major adverse cardiovascular event, not related to the study drug, and 2 cases of uveitis were reported. No cases of Crohn's disease or deaths were reported, and no patient discontinued treatment due to an AE.

Conclusion: With secukinumab treatment, the JADAS-27 inactive disease status was sustained from week 104 to week 156 in patients with JIA who had completed the 2-year core study and enrolled in the LTE study. Safety data were consistent with adult and paediatric indications, with no new or unexpected safety signals.

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Disclosure of Interests: Nicolino Ruperto Speakers bureau: Ablynx, AstraZeneca-Medimmune, Bayer, Biogen, Boehringer, Bristol Myers and Squibb, Celgene, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sinergie, Sobi and UCB, Consultant of: Ablynx, AstraZeneca-Medimmune, Bayer, Biogen, Boehringer, Bristol Myers and Squibb, Celgene, Eli-Lilly, EMD Serono, Glaxo Smith and Kline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sinergie, Sobi and UCB, Grant/research support from: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi, Ivan Foeldvari Consultant of: Novartis, BMF, Bayer, Genentech, Sanofi, Abbvie, Chugai, Medac, BMS, Pfizer, Ekaterina Alexeeva Speakers bureau: Novartis, Pfizer, Sanofi, MSD, Amgen, Eli Lilly, Roche, Grant/research support from: Novartis, Pfizer, Sanofi, MSD, Amgen, Eli Lilly, Roche, NURAY AKTAY AYAZ: None declared, Grant Schulert Consultant of: Novartis, Grant/research support from: Novartis, Seza Özen: None declared, Artem Popov: None declared, Athimalaipet Ramanan Speakers bureau: Roche, Sobi, Eli Lilly, UCB, Novartis, Christiaan Scott: None declared, Betul Sozeri: None declared, Elena Zholobova Speakers bureau: Abbvie, Pfizer, Roche, Novartis, Grant/research support from: Pfizer, Novartis, Sudhanshu Chakraborty Shareholder of: IQVIA, Employee of: IQVIA, Xuan Zhu Shareholder of: Novartis, Employee of: Novartis, Ruvie Martin Shareholder of: Novartis, Employee of: Novartis, sarah whelan Shareholder of: Novartis, Employee of: Novartis, Sharonjeet Kaur Shareholder of: Novartis, Employee of: Novartis, Luminita Pricop Shareholder of: Novartis, Employee of: Novartis, Daniel J Lovell Speakers bureau: Abbott, Novartis, Consultant of: AstraZeneca, Wyeth, Amgen, Abbott, Pfizer, Hoffmann-La Roche, Novartis, UBC, Janssen, GlaxoSmithKline, Boehringer Ingelheim, Celgene, Bristol Myers Squibb, AbbVie, Alberto Martini Speakers bureau: Eli Lilly, EMD Serono, Janssen, Novartis, Pfizer, Abbvie, Consultant of: Eli Lilly, EMD Serono, Janssen, Novartis, Pfizer, Abbvie, Hermine Brunner Speakers bureau: Pfizer, Roche and GlaxoSmithKline, Consultant of: Aurinia, Abbvie, AstraZeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Celgene, Eli Lilly, EMD Serono, GlaxoSmithKline, F. Hoffmann-La Roche, Merck, Novartis, R-Pharm, Sanofi, Pfizer, Grant/research support from: Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, F. Hoffmann-La Roche, Janssen, Novartis, and Pfizer.

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POS0279 IDENTIFICATION OF PREDICTIVE FACTORS OF FLARE AFTER ANAKINRA WITHDRAWAL IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FROM A SINGLE CENTRE

Keywords: Outcome measures, Tapering, Inflammatory arthritides

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Background: Systemic juvenile idiopathic arthritis (sJIA) is a rare autoinflammatory disease of unknown etiology. Several uncontrolled studies showed that early treatment with anakinra is associated with a better outcome, according to the "window of opportunity" hypothesis. However, very limited scientific evidence is available on withdrawal strategy. So far, anakinra withdrawal modalities are heterogeneous among the different rheumatology centres.

Objectives: The aim of this study was to identify predictive factors of disease flare, as elements suggestive of persistent course of the disease, in patients with sJIA after anakinra withdrawal. We also described our withdrawal strategy in sJIA patients who reached clinical inactive disease (CID) off glucocorticoids (GCs).

Methods: We retrospectively analysed data of 39 sJIA patients followed in our centre who stopped anakinra after reaching CID off GCs for at least 6 months before the withdrawal. Eight patients withdrew anakinra abruptly while 31 patients did it after tapering throughout one or two steps (alternate-day and/or once every three days regimens) of anakinra administration. All patients underwent a follow up of 24 months after withdrawal. They were subsequently divided into two groups according to the presence or the absence of disease flare during the follow up. Demographic, clinical and laboratory data of the patients were evaluated in univariate and multivariate analysis as predictors of flare.

Results: During the follow up, 10/39 patients (25.6%) flared after a median time from anakinra withdrawal of 7.9 months. In univariate analysis the variable most strongly related with the absence of flare was the disease duration from the onset to starting of anakinra ($p = 0.0046$), with an optimal cut-off of 3 months. Patients who started anakinra ≥ 3 months after disease onset had an 8-fold higher risk of flare after anakinra discontinuation (CI 95 2.0-32.4; $p = 0.0003$) (Figure 1). Furthermore, we observed that a higher dose of anakinra (≥2 mg/kg/day) was associated with a lower risk of flare ($p = 0.065$). We also demonstrated that patients who tapered therapy before withdrawal were significantly associated with a lower percentage of flare compared to the ones who withdrew anakinra abruptly, with a 4-fold lower risk of flare (CI 95 1.47-10.1; $p = 0.0164$). Lastly, we constructed a model analysing at the same time disease duration, anakinra dose at baseline and anakinra tapering. In this model, disease duration ≥ 3 months at baseline resulted to be the only variable significantly associated with flare after anakinra withdrawal with an Odds Ratio of 15.16 (CI 95 1.7-131.9; $p = 0.014$).

Conclusion: Our results strengthen the evidence on IL-1 inhibition in sJIA treatment and provide new ones supporting the "window of opportunity" hypothesis. Early anakinra treatment may predict a good short-term outcome and also potentially prevent the development of a persistent disease course. These observations have a strong clinical relevance, an early diagnosis and a targeted treatment could control the disease and could also modify its natural history.

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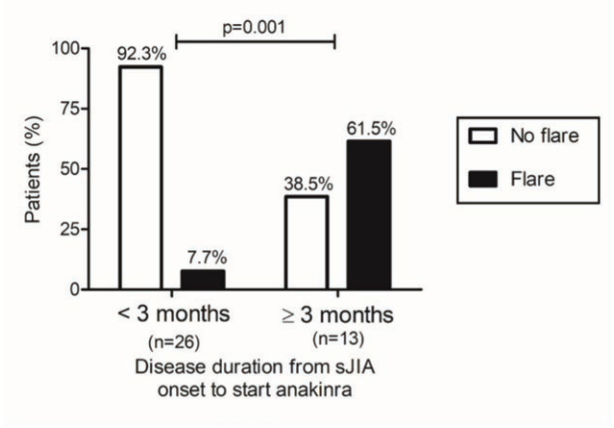


Figure 1. Relationship between disease duration from disease onset to starting of anakinra and rate of flare within the 24 months follow up after anakinra withdrawal.

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POS0280 EARLY EXPERIENCE WITH JAK INHIBITORS IN JIA IN ROUTINE CLINICAL PRACTICE

Keywords: Epidemiology, bDMARD

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Background: For the past 20 years, biologic (b)DMARDs have been the main treatment option for children and young people with JIA where an initial conventional-synthetic DMARD has not been effective. Since 2021, tofacitinib, a Janus Kinase (JAK) inhibitor has become available for the treatment of JIA. In the phase 3 randomised controlled withdrawal design trial, tofacitinib demonstrated superior efficacy over placebo, although only 38% of patients had prior bDMARD exposure. There is little information on the use of JAK inhibitor in the real-world.

Objectives: This analysis aims to describe the early experience of children and young people with JIA in a real-world cohort receiving JAK inhibitor in the United Kingdom (UK).

Methods: All patients in the UK JIA Biologics Register starting a JAK inhibitor were identified. Patient characteristics are presented at the time of treatment start, including age, disease duration and prior bDMARDs. Patients were followed until their latest follow-up form was returned. Active joint count (AJC) was reported at start of therapy and after 6 months. Status at their last follow-up was reported including treatment persistence.

Results: As of 21-Nov-2022, 14 children and young people across most ILAR categories had been treated with a JAK inhibitor; 12 baricitinib, 2 tofacitinib (table 1). Median age at JAK inhibitor start was 16 years (interquartile range [IQR] 13-17) and median disease duration was 6 years (IQR 4-7). All patients had prior bDMARD exposure, with 12 out of the 14 having more than 2 prior bDMARDs (range 2-6). Ten patients had follow-up available after the start of JAK inhibitor (median 1.4 years of follow-up available; median 0.8 years on treatment available). At the latest follow-up, 6 patients remained on JAK inhibitor, whilst 4 patients had discontinued (3 for ineffectiveness). No venothromboembolism (VTE) have been reported. In eight patients who had disease activity data available at the start of treatment, median active AJC was 9 (IQR 5-25). In the six patients who had disease activity data available after 6 months of JAK inhibitor treatment, median AJC was 2 (IQR 0-4).

Table 1.

	All patients N=14
Female, n (%)	11 (79%)
ILAR, n (%)	
Oligoarticular (persistent or extended)	3 (21%)
Polyarticular RF-negative	6 (43%)
Polyarticular RF-positive	3 (21%)
Psoriatic arthritis	2 (14%)
Median (IQR) age at JAK inhibitor start (years)	16 (13, 17)
Median (IQR) disease duration at JAK inhibitor start (years)	6 (4, 7)
	N=13
JAK inhibitor, n (%)	
Baricitinib	12 (86%)
Tofacitinib	2 (14%)
Line of b/tsDMARD therapy, n (%)	
First/second-line	2 (14%)
Third-line	4 (29%)
Fourth-line	2 (14%)
Fifth-line	2 (14%)
Sixth-line	2 (14%)
Seventh-line	2 (14%)
Prior Biologics, n	N=13
Prior TNF *(etanercept, infliximab, adalimumab)*	13/13
Prior B-cell depleting agent *(rituximab)*	2/13
Prior T-cell depleting agent *(abatacept)*	3/13
Prior interleukin inhibitor *(tocilizumab, secukinumab)*	8/13
Patients with follow-up available, n	N=10
Median (IQR) time until end of follow-up, years	1.4 (0.5, 1.8)
Median (IQR) time on treatment, years	0.8 (0.3, 1.4)
At last follow-up:	
Still on JAK treatment	*6/10*
Median (IQR) time on treatment, years	*0.9 (0.3, 1.4)*
Stopped treatment	*4/10*
Median (IQR) time on treatment, years	*0.8 (0.3, 1.5)*
Stopped for ineffectiveness	*3/4*

Conclusion: In this cohort, the initial patients with JIA prescribed JAK inhibitor have largely received these drugs prior to marketing authorisation in JIA, with most receiving it as a later stage biologic/targeted-synthetic DMARD. Most patients were still receiving treatment almost 11 months after starting a JAK inhibitor. These data suggest that JAK inhibitors could be a very effective treatment for children and young people with JIA, even after a high number of prior bDMARDs.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Lianne Kearsley-Fleet: None declared, Eileen Baildam: None declared, Michael Beresford: None declared, Sharon Douglas: None declared, Helen Foster: None declared, Taunton Southwood: None declared, Kimme Hyrich Speakers bureau: Non-personal speaker's fees from Abbvie, all unrelated to this abstract., Grant/research support from: Grant income from BMS, UCB, and Pfizer, all unrelated to this abstract, and is supported by the NIHR Manchester Biomedical Research Centre.

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POS0281 SAFETY OF BIOSIMILARS THERAPIES FOR THE TREATMENT OF JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FROM THE SPANISH REGISTRY OF ADVERSE EVENTS WITH BIOLOGIC THERAPIES (BIOBADASER)

Keywords: bDMARD

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood. The treatment of JIA has been revolutionized by the use of biologic agents. The use of biosimilar disease modifying antirheumatic drugs (bsDMARD) therapy in young adults is not well studied, therefore more evidence regarding drug safety is needed.

Objectives: Our aim is to assess the safety of bsDMARD therapy in JIA.
Methods: Data was obtained from BIOBADASER, a multicenter prospective registry based on routine clinical practice. All patients diagnosed before age 16 in our database between 2000 and 2022 were included in the analysis. JIA is classified into 7 subgroups: systemic, persistent or extended oligoarthritis, RF positive polyarthritis, RF negative polyarthritis, enthesitis-related arthritis, psoriatic arthritis, and undifferentiated arthritis. Due to the registry design, it was not possible to identify each of the JIA subgroups; thus, we classified them into oligo/polyarticular JIA, JIA related to enthesitis, and psoriatic JIA. Adverse events were coded using version 13.0 MedDRA (Medical Dictionary for Regulatory Activities). Proportions, means and standard deviations (SD) were used to describe our population. Incidence rates (IR) of adverse events and 95% confidence intervals were calculated, and Poisson regression was used to estimate incidence rate ratios (IRR), adjusting by sex, diagnosis type, age at start of therapy (≤16 years vs >16 years) and line of treatment as confounding variables.
Results: From a total of 313 patients, 130 (41.5%) use biosimilars therapies, 60.8% of which were women (n= 79). Mean age at diagnosis was 11.2 years (SD= 6.1) and mean age at the start of treatment was 25.1 (SD= 13.4). Patients were classified as oligo/polyarticular JIA (79.2%), JIA related to enthesitis (16.2%) and psoriatic JIA (4.6%). Methotrexate was used in combination in 39.1% of the bsDMARD treatments. The most commonly used drug was Adalimumab (56.8%), followed by Etanercept (28.7%). Table 1 shows incidence rates for adverse events according to severity. For all adverse events, IR is greater in biosimilars compared to original biologic disease modifying antirheumatic drugs (bDMARDs), although the latter have a higher IR of serious adverse events. The IRR was 1.33 (95% CI 1.1-1.6), thus, the risk of adverse events was greater among bsDMARD compared to the original bDMARDs.
Conclusion: The risk of adverse events occurrence is a higher among patients treated with bsDMARD drugs. Although this project allowed us to examine long-term biosimilars safety in JIA, large registries that focus on such patients are needed to better understand rare adverse events.
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Table 1. Incidence rates bsDMARD vs original bDMRADs

Incidence Rate (95% CI) per 1000 Patient-Years

Type of therapy	Original	Biosimilar
Total adverse events	400.4 (367.50 - 436.40)	529.6 (444.10 - 631.60)
Serious	62.4 (50.2-77.6)	51.3 (29.1-90.3)
Fatal	0 (0-0)	0 (0-0)

Table 2. Incidence rate ratios calculated using Poisson regression model

	IRR (95% confidence interval)	p-value
Biosimilars (ref originals)	1,33 (1.10 - 1.62)	0,004
Female (ref males)	1,57 (1.29 - 1.92)	<0.001
Treatment initiation after 16 years old	1,34 (1.10 - 1.63)	0,004
Diagnosis (ref JIA)		
JIA related to enthesitis	1,41 (1.12 - 1.79)	0,003
Psoriatic JIA	1,20 (0.80 - 1.80)	0,37
2nd or later line of treatment (ref 1st line)	1,16 (0.99 - 1.37)	0,062

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Disclosure of Interests: : None declared.
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POS0282 PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) ON INTENSIVE TREATMENT FREQUENTLY PRESENT ALEXITHYMIA OVER FATIGUE, ANXIETY, AND DEPRESSION, DESPITE LOW DISEASE ASSESSMENT PARAMETERS

Keywords: Inflammatory arthritides, Patient reported outcomes, Quality of life

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Background: Psychological factors influence quality of life, disease perception, engagement and adherence to treatment in patients with Juvenile Idiopathic Arthritis (JIA). While anxiety and/or depression have been often documented in JIA, alexithymia has been seldom investigated.

Objectives: 1.To investigate the frequency of psychic symptoms in JIA patients at a single tertiary care center, including depressive, anxiety and alexithymic symptoms. 2.To investigate correlation between psychic symptoms and demographic and clinical parameters.
Methods: JIA patients aged 8-17 years and consecutively seen from March to November 2022 were invited to undergo psychological standardized tests: the Patient Health Questionnaire-9 items (PHQ9), self-administered measure of depressive symptoms; the Generalised Anxiety Disorder (GAD7) test; the Self-administered Psychiatric Scales for Children and Adolescents anxiety-related areas (SAFA-A), depression-related areas (SAFA-D) and somatic areas (SAFA-S); the PedsQL™ Multidimensional Fatigue Scale; PedsQL™ Rheumatology Module Pain and Hurt; the Toronto Alexithymia Scale (TAS-20); the Visual Analogue Scale (VAS) for pain intensity. Demographic data, clinical and laboratory parameters for disease assessment on the same visit were also recorded. Data were analyzed with descriptive statistics. Categorical data were represented as counts and percentages, while continuous data were represented as means and standard deviations or medians and ranges. Data were checked for normality. For normally distributed data, appropriate parametric statistical testes were employed, for non normally distributed data, non-parametric statistical tests were employed. Comparison in the frequency of the psychological symptoms in presence/absence of pain, active, painful/tender or limited joints was assessed. Significant level was set at $p<0.05$. All statistical analyses were performed using R (version R 4.0.3).
Results: Thirty-seven JIA patients were enrolled in the study: 64.9% were females, 38% with persistent oligoarthritis, 22% extended oligoarthritis and 40% polyarthritis, and 32% with chronic uveitis ever. Median age was of 12.6 years (IQR 9.3-15.3), with a median disease duration of 5.5 years (IQR 3.6-7.6). Respectiveley, 96% and 95% of patients were receiving csDMARDS and bDMARDS. All disease parameters showed very low level of disease activity and disability. PHQ9 and GAD7 were pathologic in 41% and 44%, respectively; borderline or clinically pathologic scores were found in 27%, 29%, and 13% for SAFA-D, SAFA-A, SAFA-S, respectively. Of note, TAS-20 was borderline or pathologic in 32% of patients. No psychic symptoms, demographic variables or clinical features showed an association with disease parameters. No significant differences were found between patients with and without pain on VAS, active joints, painful/tender or limited joints.
Conclusion: In a selected cohort of JIA patients on intensive treatment, low disease activity and few limited joints psychological parameters for depression and anxiety were detectable in a sizable proportion; a higher percentage of patients reported fatigue; alexithymia was even more frequent, regardless disease assessment variables. Our findings support the rationale for adopting routine psychological assessment and intervention in JIA patients, and for extending psychological investigations to their parents/guardians.
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Disclosure of Interests: None declared.
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POS0283 EFFECT OF CUSTOMISED FOOT ORTHOSES ON PEAK PRESSURE AND PRESSURE TIME INTEGRALS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A RANDOMISED CLINICAL TRIAL

Keywords: Randomized control trial

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Background: Children with juvenile idiopathic arthritis (JIA) often exhibit joint symptoms in the lower limb. Prolonged joint disease may cause further physical and functional impairment, which can lead to significant disturbances in gait such as abnormal pressure distributions and sub-optimal peak plantar pressures [1-3]. Recent studies have shown that children with JIA compared to an age and sex matched cohort displayed significantly higher peak pressures (PP) in most areas of the plantar foot [2]. Research also showed that children with JIA are displaying elevated pressure time integrals (PTI), meaning they are spending higher amounts

of time in the stance phase of gait and less in the swing phase and thus a less propulsive gait [2]. To our knowledge only one previous clinical trial has explored the effect of a mechanical intervention such as foot orthoses (FOs) to improve the distribution of peak plantar pressures in children with JIA [4].

Objectives: The aim of our randomised clinical trial is to further evaluate the effect of customised prefabricated FOs in improving PTI and PP in children with JIA.

Methods: A multicentre, parallel design, single-blinded randomised clinical trial was used to assess the impact of customised preformed FOs on plantar pressures in children with JIA. Children with a diagnosis of JIA, exhibiting lower limb symptoms and aged 5-18 were eligible. The trial group received a low-density full length, Slimflex Simple device which was customised chair side and the control group received a sham device. PP and PTI were used as the main gait outcomes and were measured using portable Tekscan gait analysis technology at baseline, 3 and 6 months. PP were measured using kilo pascals (kPa) and PTI measured kPa per seconds (kPa/s). Differences at each follow-up were assessed using the Wilcoxon rank sum test.

Results: A total of 66 participants were recruited. Customised prefabricated FOs were effective in altering plantar pressures in children with JIA versus a control device. Reductions of PP in the heel (baseline p=<0.001 (-104.33 kPa), 3-month p=0.004 (-126.16 kPa)), forefoot (baseline p=0.027 (-131.5 kPa)), 5th metatarsophalangeal joint (baseline p=0.007 (-37.17 kPa), 3-month p=0.001 (-69.5 kPa), 6-month p=0.016 (-50.91 kPa)) were statistically significant in favour of the trial group. These results were also positively correlated with PTI with the trial group spending less time and pressure on the heel, forefoot and rearfoot than the control. Finally, PP and PTI reductions were also associated with statistically significant increased midfoot contact with the trial device at baseline (29.84 kPa), 3 (24 kPa) and 6-month (43.75 kPa) data collections, showing that the trial intervention was successful in capturing the arch profile of participants and redistributing pressure. The trial intervention was safe and well accepted by participants, which is reflected in the high retention rate (92%).

Conclusion: Clinicians may prescribe customised prefabricated FOs in children with JIA to deflect pressure from painful joints and redistribute from high pressure areas such as the rearfoot and forefoot.

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POS0284 COVID-19 SYMPTOMS AND DISEASE COURSE IN GERMAN PEDIATRIC RHEUMATOLOGY PATIENTS REPORTED TO BIKER

Keywords: COVID, Disease-modifying Drugs (DMARDs), bDMARD

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Background: COVID-19 has shaped the world over the last 3 years. Although the risk for severe COVID-19 progression in children is low it might be aggravated by chronic rheumatic disease or treatment with immunosuppressive drugs.

Objectives: We analyzed clinical data of COVID-19 cases among paediatric patients with rheumatic diseases reported to BIKER between March 2020 and December 2022.

Methods: The main task of the German BIKER (Biologics in Pediatric Rheumatology) registry is safety monitoring of biologic therapies in JIA. After the onset of the COVID-19 pandemic, the survey was expanded with a standardized form to proactively interview all participating centers about occurrence, presentation and outcome of SARS-CoV-2 infections in children with rheumatic diseases.

Results: A total of 68 centres participated in the survey. Clinical data from 928 COVID infections in 885 patients with rheumatic diseases could be analyzed. JIA was the most common diagnosis with (717 infections), followed by genetic autoinflammation (103 infections), systemic autoimmune diseases (78 infections), idiopathic uveitis (n=25), vasculitis (n=5). In 374 reported COVID infections (40%), patients were receiving conventional DMARDs, in 331 (36%) biologics, mainly TNF inhibitors (TNFi, n=241 (26%)). In 567 reports (61%) patients used either a biologic or a DMARD, in 339 reports patients (37%) did not use any antirheumatic medication including steroid. Over the last 3 years, COVID-19 occurred in Germany in 5 distinguishable waves, calendar weeks (CW) 10-30 in 2020, CW 21/2020 – 8/2021(both predominantly wild-type variant), CW 9-27 in 2021 (Alpha variant in the majority of infections), CW 28-51 in 2021 (Delta variant), since CW 52/2021 (several Omikron variants; Robert-Koch Institute: VOC_VOI_Tabelle.xlsx; live.com)) In our cohort, patients with SARS-CoV-2 infection were slightly older during the 1st and 2nd wave (mean age 12.7+/-3.5 and 12.8+/-4.3 years) compared to the 4th and 5th wave with 11.4+/-3.9 and 11.4+/-4.2 years; p=0.01. 160 asymptomatic SARS-CoV-2 infections were reported, frequencies of symptoms associated with COVID-19 are shown in table 1. Five patients were hospitalized for 4-7 days. A 3½-year-old female patient succumbed during the first wave with encephalopathy and respiratory failure. The patient had been treated with MTX and steroids for systemic JIA. Genetic testing revealed a congenital immunodeficiency. No other patient needed ventilation or intensive care. One case of uncomplicated PIMS in an MTX treated JIA patient was reported. The duration of SARS-CoV-2 infection-associated symptoms was markably shorter during the 5th wave with 6.7+/-5.1 days, compared with reports from the other 4 waves (Table1). The duration of symptoms was higher in MTX treated patients (10.2+/-8.4 days) compared to patients without treatment (7.7+/-10.8; p=0.004) or patients treated with TNFi (8.2+/-4.8, p=0.002). Although patients treated with steroids also had a longer duration of symptoms (9.7+/-7.0), this was not significant.

Conclusion: Except for one patient with congenital immunodeficiency who died, no case of severe COVID-19 was reported in our cohort. At the time of infection, over 60% of patients had been treated with conventional DMARDs and/or biologics. Although MTX treated patients had a slightly longer duration of symptoms, antirheumatic treatment did not appear to have a negative impact on severity or outcome of SARS-CoV-2 infection.

Table 1. Characteristics and frequency of symptoms in SARS-CoV-2 infections

N or mean (SD)	1st wave N=20	2nd wave N=84	3rd wave N=38	4th wave N=124	5th wave N=662
female	14	53	27	75	432
age at COVID-19, years	12.7 (3.5)	12.8 (4.3)	11.8 (3.5)	11.4 (3.9)	11.4 (4.2)
asymptomatic	1	26	13	26	94
duration of symptoms; days,	11.9 (14.7)	9.2 (7.0)	14.1 (11.6)	10.3 (7.6)	6.7 (5.1)
fever	12	18	5	41	306
cough	10	15	6	52	245
rhinitis	5	26	13	44	289
headache	4	16	12	27	171
sore throat	6	11	3	9	132
musculosceletal pain	2	7	5	13	48
loss of smell/taste	7	11	6	21	13
fatigue	4	8	8	26	80
dizziness	1	2	2	1	16
gastrointestinal symptoms	1	5	1	8	64
dyspnea		1	1	1	7
pneumonia				1	1
bronchitis				1	

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POS0285 TEMPOROMANDIBULAR JOINT INVOLVEMENT IN JUVENILE IDIOPATHIC ARTHRITIS: THE ROLE OF MAGNETIC RESONANCE IMAGING IN THE EVALUATION OF THE SILENT JOINT

Keywords: Imaging

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Background: Temporomandibular joint (TMJ) involvement is frequent in patients with Juvenile Idiopathic Arthritis (JIA) and may cause severe craniofacial growth disturbances. Contrast-enhanced MRI is considered the best available tool for TMJ assessment[1].

Objectives: To investigate the agreement between MRI and physical examination in the detection of TMJ involvement; to describe the evolution of TMJ activity and osteochondral damage by means of MRI during disease course; to evaluate the relationship between socio-demographic, clinical variables and radiologic outcomes in terms of resolution of inflammation and structural damage progression.

Methods: 121 JIA patients with TMJ involvement who underwent at least 2 MRI examinations in our Centre between 2012 and 2022 were included in this retrospective study. TMJ inflammation and damage were evaluated according to the MRI scoring system proposed by the OMERACT (*Outcome Measures in Rheumatology and Clinical Trials*)[2]. The agreement between physical examination and MRI was analysed by means of Cohen's kappa coefficient. The relationship between socio-demographic and clinical variables and radiologic outcomes was estimated by bivariate analyses. Comparison between survival curves for damage progression was done by the Log-Rank test.

Results: 339 TMJ MRIs obtained from 121 JIA patients were reviewed. First MRI was performed at a median time of 0.6 years (0.2-1.5) after TMJ symptoms onset. Baseline MRI showed active synovitis in 85 out of 121 patients (70.2%) and condylar damage in 112 (92.6%) patients. A poor agreement was found between physical examination and MRI (right TMJ Cohen's kappa = 0.15; left TMJ Cohen's kappa = 0.26). MRI showed active TMJ synovitis in 63% of the exams performed in patients who were in clinical remission according to Wallace criteria. During follow-up, synovitis improved in 56.2% of patients and structural damage progression was observed in 21.0% of patients. Younger age (< 9.4 years) at onset of TMJ involvement was associated with the resolution of the inflammatory process (p=0.023) and with a lower rate of structural damage progression (p=0.027). Significant association was observed between persistence of TMJ synovial inflammation and damage progression (p=0.0013). Higher baseline MRI synovitis (p=0.018) and bone erosion scores (p<0.0001) were associated with the development of a severe osteochondral damage at last follow-up MRI.

Conclusion: Our study confirms that TMJ involvement is clinically silent in most of JIA patients and supports the role of MRI in the diagnosis and monitoring of TMJ arthritis. Active TMJ synovitis was found in a substantial proportion of patients in clinical remission with relevant implications for the therapeutic strategy. Old age at TMJ onset, a high degree of synovial inflammation and its persistence over time were negative prognostic factors for the development of severe TMJ damage.

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POS0286 TREATMENT OF A LARGE COHORT OF CHILDHOOD CHRONIC IDIOPATHIC UVEITIS: A MULTICENTRIC LARGE COHORT

Keywords: Uveitis, Descriptive Studies, bDMARD

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Background: Childhood Chronic Idiopathic Uveitis (cCIU) is a severe ocular condition that account for the 40% of uveitis in children. Its timely and proper treatment is critical to prevent severe complications.

Objectives: The purpose of this study was to describe the treatments of a large cohort of cCIU.

Methods: This is a retrospective medical chart review study of cCIU followed at Meyer children's hospital IRCCS and Bristol Royal hospital for children (1st Jan2019 - 31st Jan 2020). Children were included if they have a diagnosis of CIU prior to 16 years old according to SUN. We collected demographic, clinical and laboratory data. Achievement of remission on treatment was evaluated as persistent inactivity for at least 3 months without drops and systemic corticosteroids.

Results: Data about 126 cCIU (61 female, median age at onset 9.3 years (3-16), ANA positive in 33 (77.6%)) were collected. 68 have anterior uveitis, 29 intermediate, 15 anterior + intermediate, 1 posterior and 13 panuveitis. Excluding the patient with posterior involvement, 97 children (77.6%) underwent to at least one systemic treatment, 65 (52%) to two, 18 (14.4%) to three and 2 (1.6%) to four (Infliximab and tacrolimus), with a median follow-up of 46 months (IQR 22-67). The first drug was administered after a median time of 5 months (IQR 2-10). Treatments performed were summarized in table 1. Among the first line treatment, children treated with adalimumab are more likely to achieve remission and maintain remission for a longer time after drug withdrawal compared to the other drugs (χ^2 7.59 p 0.006 and p 0.036 respectively). No significant differences have been evaluated stratifying analysis for anatomical subtype, ANA status, ethnicity,

Table 1. Treatment performed in cohort of Childhood CNIU

Treatment	First Course of Systemic treatment					Second course of systemic treatment					Third course of Systemic treatment				
	Overall (97)	Mtx (89)	MM (1)	ADA (7)*	P value	Overall (65)	Mtx (6)	ADA (45)	MM (14)	P value	Overall (18)	ADA (16)	MM (1)	IFN (1)	P value
Concomitant therapy		**2 MTX*					*41 MTX and 2 MM (Group ADA)*					*11 MTX, 5 MMF, 1 AZA*			
Time of administration median (IQR)	5 (2-10)	5 (2-9)	4	10 (3-24)	NS	15 (8.25-27)	44.5 (35.2-53.5)	12 (7-19.5)	16 (7.7-32)	**<0.001**	43.5 (327-55)	47 (12-90)	48	27	Ns
Duration of therapy	23 (10-36)	24 (11-38)	5	22 (7-24)	NS	24 (11.25-34.75)	21.5 (9.7-26)	23 (11.2-32.7)	33.5 (6.5-52.5)	NS	19 (7-33)	21.6 (2-55)	2	55	Ns
Achievement of remission on therapy N (%)	45/90 (50%)	38/83	-	**7/7**	**χ^2 7.59 p 0.006**	52/56 (91.2%)	5/6	**38/39**	9/12	**χ^2 6.29 p 0.04**	14/15 (93.3%)	13/14	-	1/1	ns
Time for achievement remission	6 (5-7)	6 (5-7.5)		5 (4-6.75)	NS	6 (5-9)	5 (4.5-7.5)	6 (5-9)	9 (4-11.5)	Ns	6 (4-9.25)	6.6 (4-12)	-	9	Ns
N of pts who stop drug for persistent remission	23 (25%)	21/38	-	2/7	NS	26 (41.5%)	3	19	4	NS	3 (18.7%)	3/15	0	0	ns
Relapse out of therapy N (%)	13 (56.5%)	12/21	-	1/2	NS	17 (63%)	0	**15**	2	**χ^2 6.6 p 0.03**	1/3 (33.3%)	1/3	-	-	ns
Time free from relapse out of therapy	3 (2-21)	**3 (2-20)**	**-**	**40 (2-40)**	**0.036**	6 (3.75-9)	4 (2-4)	6 (4-9)	6.5 (3.5-33.5)	ns	8 (8-12)	8 (8-12)	-	-	Ns

List of abbreviations: ADA: adalimumab, MM: mycophenolate mofetil, MTX methotrexate, IFN: infliximab, N number, IQR interquartile range, NS non significant.

sex, ESR and CRP at onset for achievement remission with the first line treatment. However, patients treated with methotrexate who did not achieve remission have lower visual acuity in LogMar (0.53 vs 0.36, Mann-Whitney U test p 0.02). The superiority of Adalimumab in terms of remission achievement was confirmed when it was used as second line treatment too (χ^2 6.29 p 0.04), however they relapsed more frequently out of therapy (χ^2 6.6 p 0.03). Moreover, with the II line treatment, panuveitis showed higher proportion of remission achievement with adalimumab and worse response to MMF (χ^2 2 p 0.03).

Conclusion: Treatment of cCIU is extremely challenging, achieving remission with the first line treatment in only the 50% of patients. However, patients treated with adalimumab have better chance to achieve remission and patients who showed worse visual acuity at onset would benefit of a more aggressive treatment with biologics since onset.

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POS0287 TOFACITINIB IN JUVENILE IDIOPATHIC ARTHRITIS: FIRST YEAR EXPERIENCE

Keywords: Targeted synthetic drugs, Registries

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Background: Tofacitinib is an oral Janus kinase inhibitor recently approved for the treatment of polyarticular juvenile idiopathic arthritis (pJIA) and juvenile psoriatic arthritis (jPsA) aged 2 to <18 years. Data out of clinical practice so far are rare.

Objectives: To characterize JIA cohorts treated with tofacitinib and to evaluate efficacy and tolerance in clinical practice.

Methods: The German BIKER data base was screened for JIA patients aged 2 to <18 years who were started on tofacitinib until December. 31st, 2022

Results: Patient demographic and disease characteristics are presented in Table 1. Primary diagnoses were either polyarticular JIA rheumatoid factor positive (n=4) or negative (n=18), extended oligoarthritis (n=7), jPsA (n=2), ERA-JIA (n=2), persistent oligoarthritis (n=1) and systemic onset JIA (n=1). The patient's age varied from 6.9 to 18.0 years at start of treatment and the disease duration range was 2.3 – 16.6 years. In most cases, patients were extensively pretreated with biologics (mean 2.7). One patient had received 7 biologics, four each received 5 or 4 biologics, six received 3, ten received 2 and 8 received 1 biologic before. In a single case, tofacitinib was used directly after failure of methotrexate. Tofacitinib was administered orally BID in 35 JIA patients at a daily total dosage of 0.18 +/-0.06 mg/kg. Tablets with dosages of 5 mg BID were used in 31 patients. Oral solution was used in 4 patients (up to 4 mg BID). Efficacy data and safety data were available from 17 patients. A decrease of the JADAS10 (Median; IQR) from 10.1 (5.5;13.2) to 3.0 (1.3;6.3), of the number of active joints (from 4 (1;6) to 0 (0;1), of the patient's/parent's global VAS (from 30 (6;50) to 11 (2.5;22), the physician's global (from, 28 (18;41) to 7 (0.8;10) was noted. PedACR 30/50/70/90 criteria were fulfilled by 53%/47%/41%/24% at last observation. There were 11 adverse events (AE) in 10/35 patients (29%), including lack of efficacy (n=7), and each one upper respiratory tract infection, COVID19, headache, bone pain. There was no serious AE or severe AE reported. 8 patients (22.9%) discontinued tofacitinib after 0.6-6.7 months. Tofacitinib was stopped in 6 due to inefficacy, in 1 due to bone pain and in 1 because of patient's decision.

Conclusion: In this preliminary analysis of pediatric patients with JIA, tofacitinib use was safe and well tolerated. Treatment was associated with an improvement in signs and symptoms of arthritis and global disease activity at last observation although the cohort of patients has been heavily pretreated with DMARDs and biologics. The BIKER registry is planning to further follow JIA patients.

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Table 1. Patient baseline demographic characteristics

	Total Cohort (N=35)
Age, years Mean (SD)	14.2+/-3.0
Range	7.0-18.0
Disease duration, years Mean (SD)	8.6+/-3.9
Range	2.3-16.6
Weight, kg Mean (SD)	52.9+/-17.9
Range	21-108.5
Tofacitinib Dosage, mg/kg Mean (SD)	0.18+/-0.06
Concommitant Tx	
methotrexate	9 (25.7%)
sulfasalazine	1; 2.9%
hydroxychloroquine	1; 2.9%
leflunomide	1; 2.9%
JIA category, n;%	
RF+ polyarthritis	16.4; 11.4%
RF- polyarthritis	18; 51.4%
Extended oligoarth.	7; 20%
Persist. oligoarth.	1; 2.9%
ERA-JIA	2; 5.7%
Juv. Psoriatic arhr.	2; 5.7%
Systemic onset JIA	1; 2.9%
Pretreatment, n;%	
Methotrexate	35; 100%
Abatacept	8; 22.9%
Adalimumab	24; 68.6%
Anakinra	2; 5.7%
Canakinumab	1; 2.9%
Etanercept	32; 91.4%
Golimumab	16; 45.7%
Secukinumab	3; 8.6%
Tocilizumab	28; 77%
Active joints	
mean+/-SD	4.3+/-5.22
median (IQR)	2(1;6)
Physician global	
mean+/-SD	35+/-22
median (IQR)	33.5(22; 49)
Pat/Parent global	
mean+/-SD	33+/26
median (IQR)	30 (6.5;55.5)
JADAS10	
mean+/-SD	10.1+/-6.1
median (IQR)	8.8 (5.4; 14.0)
CHAQ-DI	
mean+/-SD	0.56+/-6.5
median (IQR)	0.375 (0; 0.875)

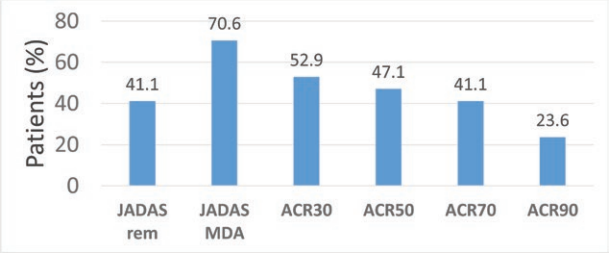


Figure 1. Efficacy targets at last observation in 17 patients (Ref.)

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Molecular and metabolic biomarkers of activity, severity and response to treatment

POS0288 DEGRANULATING PR3+ MYELOID CELLS CHARACTERIZE PROLIFERATIVE LUPUS NEPHRITIS

Keywords: Kidneys, Systemic lupus erythematosus, Cell biology

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Background: Despite optimal treatment, lupus nephritis (LN) remains associated with irreversible kidney damage[1]. A better understanding of the mechanisms underlying LN pathogenesis is needed to develop better treatment targets. As part of the Accelerating Medicines Partnership (AMP), we discovered that urinary PR3, a myeloid degranulation product, correlated with histological activity implicating neutrophil/monocyte degranulation in proliferative LN, the most aggressive type[2]. PR3 is a serine protease that can mediate kidney damage. Mature neutrophils with classical polylobate nuclei are rare in LN kidney biopsies. However, recent evidence displayed how immature, degranulating myeloid cells have been implicated in the pathogenesis of LN[3], but their role in mediating kidney damage is not completely understood.
Objectives: To investigate PR3+ cells in LN kidney, their association with histopathological features, and define their immunophenotype.
Methods: We performed multiplexed histology using serial immunohistochemistry (sIHC)[4] on archival LN kidney biopsies to quantify the expression of PR3 and multiple cell lineage markers (20-plex). Image analysis including deconvolution, cell segmentation, glomerular annotation, and quantitative histology was performed using Indica HALO. The analysis was limited to renal cortex.
Results: A total of 11 patients with LN who underwent a clinically indicated kidney biopsy were enrolled: 6 (55%) with pure proliferative LN (ISN/RPS class III or IV) and 5 (45%) with pure membranous LN. PR3+ cells were identified in all LN biopsies (range 343-7625 per sample). Most PR3+ cells did not show a polylobate nucleus. The majority of PR3+ cells were in the tubulointersitium (Figure 1A). However, accounting for the smaller glomerular area, there was a higher density of PR3+ cells in the glomeruli (Figure 1A-C). PR3+ cell abundance was higher in proliferative LN, especially in the glomeruli (Figure 1A-C). Glomerular PR3+ cell density very strongly correlated with histological activity measured by the NIH Activity Index (Pearson's r=0.97, p=5*10^{-5}; Figure 1D). Preliminary serial IHC analysis showed that PR3+ cells coexpressed MPO and variably coexpressed CD66b and CD14, but not neutrophil elastase, CD3, or CD20.

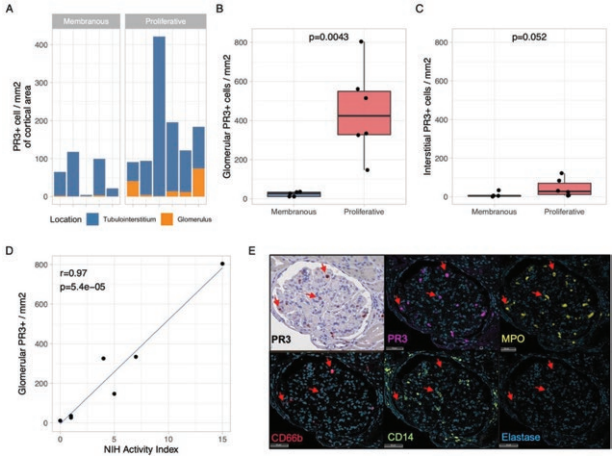


Figure 1.

Conclusion: PR3+ cells are abundant in LN. PR3+ cells are increased in proliferative LN and are strongly associated with histological activity thereby characterizing a more aggressive phenotype. This population densely infiltrated the glomeruli emphasizing a potential role in the endothelial pathogenic process. In preliminary analysis, kidney infiltrating PR3+ cells were not polymorphonucleated, did not express neutrophil elastase, and variably expressed CD14 suggesting a phenotype consistent with degranulating monocyte or an immature myeloid population. We previously showed the association between urinary PR3 and histological activity suggesting that intrarenal PR3+ cells are actively degranulating and therefore likely inducing kidney damage. These findings nominate PR3+ cells as a potential therapeutic target. Spatial transcriptomics and proteomic studies are ongoing to define the lineage and function of these cells.

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Disclosure of Interests: None declared.
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POS0289 SERUM SOLUBLE MEDIATOR SIGNATURES OF LUPUS NEPHRITIS HISTOLOGICAL FEATURES AND RESPONSE TO TREATMENT

Keywords: Cytokines and chemokines, Systemic lupus erythematosus, Biomarkers

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Background: There is a pressing need to identify novel therapeutic approaches and noninvasive biomarkers in lupus nephritis (LN).
Objectives: In this study, we quantified serum soluble mediators in the large Accelerating Medicines Partnership (AMP) LN longitudinal cohort to identify novel biomarkers of histological features and treatment response and provide insights into the pathogenesis of LN.
Methods: SLE patients meeting ACR or SLICC criteria (n=268) undergoing a clinically indicated kidney biopsy with a urine protein/creatinine (UPCR) ≥0.5 were recruited for this study as part of the AMP. Serum samples were collected from patients at the time of diagnostic kidney biopsy and 3-, 6-, and 12-months post-biopsy and from 22 healthy donors (HD). Concentrations of 51 analytes, including cytokines, chemokines, and TNFR superfamily members, were analyzed by xMAP multiplex assays on the Bio-Rad BioPlex200 array system. TACE levels were determined by ELISA. Clinical response was determined at 12-months post-biopsy using the Abatacept and Cyclophosphamide Combination Efficacy and Safety Study definitions in patients with a baseline UPCR >1.0 and International Society of Nephrology/Renal Pathology Society class III, IV, V, or combination thereof.
Results: LN patients demonstrated heterogeneity in serum soluble mediator concentrations (Figure 1A). Most soluble mediators were elevated in LN patients compared to HD. Within LN, patients with proliferative LN (class III +/- V or class IV +/-V) displayed a distinct signature. In particular, patients with pure proliferative LN (class III or IV) had higher serum levels of immune mediators, such as IFNβ and IL-1β, compared to nonproliferative LN, including pure membranous (class V) LN. In addition, several serum immune mediators correlated with intrarenal LN activity (NIH Activity Index), with syndecan-1 (CD138) and TNF-RII exhibiting the highest correlation (Figure 1B). In contrast, stem cell factor (SCF) and TNF-RI had the highest correlation with the chronicity index. In proliferative LN, the concentrations of many immune mediators declined in treatment responders. For example, syndecan-1 and TNF-RII decreased in complete and partial responders but not in nonresponders (Figure 1C). In contrast, SCF levels remained relatively stable regardless of response status.

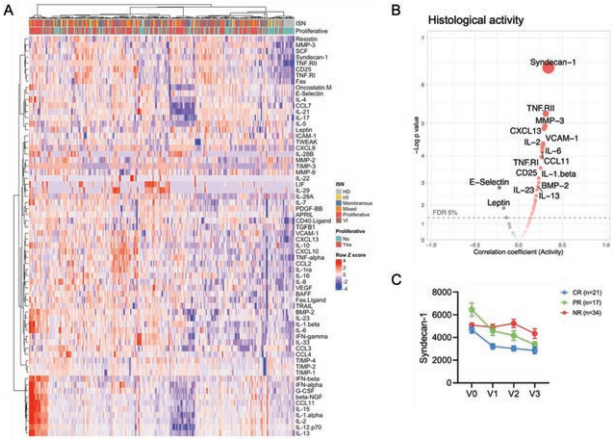


Figure 1.

Conclusion: Distinct histological features of LN are paralleled by specific signatures of circulating soluble mediators. Within LN, proliferative LN is associated with higher circulating levels of inflammatory cytokines, notably, type 1 IFNs. Furthermore, a decline in the titers of several immune mediators correlated with LN activity was associated with treatment response, suggesting a possible role in LN pathogenesis. These signatures and trajectories provide insight into LN pathogenesis, heterogeneity, and biomarker development.

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Acknowledgements: NIL.

Disclosure of Interests: None declared.

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POS0290 NOVEL ANTI-MITOCHONDRIAL ANTIBODIES IDENTIFY PATIENTS WITH PROPENSITY TO THROMBOGENESIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Autoantibodies, Biomarkers

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Background: Venous and arterial thrombotic events are leading causes of mortality in systemic lupus erythematosus (SLE), amounting to up to a quarter of deaths[1]. Other than traditional risk factors, SLE-specific factors, including chronic inflammation, have also been shown to contribute to thrombosis development. Nonetheless, the four times higher relative risk of thrombosis compared to healthy individuals is not fully accounted to the presence of conventional cardiovascular risk factors and anti-phospholipid antibodies[1]. As such, novel biomarkers of thrombosis are needed in early identification and preventative management of SLE patients.

Objectives: To characterize novel antibodies directed against mitochondrial constituents, and investigate their capacity to stratify patients based on thrombotic events.

Methods: Highly purified mitochondria were isolated from HepG2 cells (ATCC HB-8065TM) as previously described[2]. Briefly, cells were harvested and homogenized by a glass Douncer, followed by sequential centrifugation. Upon DNase-mediated removal of extracellular DNA, ultra-pure mitochondria (confirmed by flow cytometry, qPCR, and Western blot), labeled with MitoTracker, were incubated with sera (diluted 1:100) from SLE patients or healthy individuals. Binding of IgG to the mitochondrial outer membrane was detected using a secondary FITC-conjugated anti-human-IgG antibody, and analyzed by FACS. In some experiments, mitochondria were treated with trypsin (0.05%) prior to incubation with sera. Finally, reactivity towards mitochondrial protein lysate was confirmed using WB. Samples and clinical data from SLE patients (n=92) and healthy individuals (n=80) were provided from Division of Rheumatology, Lund University, Sweden. Statistical analyses were performed on SPSS 22.0. Mann-Whitney test was performed, with a p-value of 0.05 or below deemed as significant. Data protection and patient anonymization were ensured in accordance with regulation by Research Advisory Boards.

Results: Based on our novel flow cytometry assay, quantifying anti-mitochondrial antibodies (AMA) targeting the outer mitochondrial membrane, a large proportion (40.8%) of SLE patients were deemed positive for AMA using the 95th percentile of healthy controls as a cut-off. Presence of AMA was associated with severe SLE manifestations, including history of nephritis (OR = 3.3, p=0.02), anti-phospholipid syndrome (APS; OR = 5.7, p=0.02), and venous thromboembolism (OR = 6.7, p=0.008), the latter which was not seen in our cohort for isolated presence of anti-cardiolipin (aCL) antibodies (OR = 2.2, p=0.17), neither for lupus anticoagulant (OR 5.0, p=0.08) or anti-beta-2 glycoprotein 1 (OR 1.1, p=0.93). Pre-treatment of mitochondria with trypsin induced loss of binding of sera-derived antibodies (p<0.01), suggesting that AMA were targeting protein components of mitochondria, and not phospholipids, as is the case of aCL. WB confirmed presence of reactivity towards mitochondrial protein antigens, in particular of 35 and 60 kDa, though reactivity towards other protein antigens, including 17 kDa ones, were also seen in some patients, with the latter being associated with APS (p=0.008).

Conclusion: SLE patients positive for novel AMAs targeting mitochondrial outer membrane proteins develop severe lupus manifestations, including venous thromboembolism. Future studies are warranted to further characterize the novel antibodies, as well as determine their prognostic value.

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Disclosure of Interests: None declared.

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POS0291 IDENTIFICATION OF SUBSETS OF SLE PATIENTS RESPONSIVE TO IBERDOMIDE BY TRANSCRIPTOMIC ANALYSIS OF BASELINE SAMPLES

Keywords: Artificial Intelligence, Systemic lupus erythematosus, Clinical Trials

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Background: Iberdomide is a high affinity cereblon ligand that promotes ubiquitylation and proteasomal degradation of Ikaros (IKZF1) and Aiolos (IKZF3) transcription factors and, thereby altering specific aspects of immune responsiveness. Iberdomide has been shown to be efficacious in a randomized controlled trial in patients with generalized SLE (NCT03161483) and to be specifically effective in patients with high baseline expression of the interferon gene signature (IGS)[1,2].

Objectives: The goal of this study was to identify subsets of SLE patients responsive to iberdomide more effectively by analyzing baseline gene expression profiles.

Methods: Baseline whole blood samples from 276 female SLE patients from the phase 2b iberdomide trial were utilized for this analysis. These patients had a >/= 6 month history of SLE and disease activity determined by SLEDAI-2K >/=6. Patients were randomized to placebo, or one of three doses of iberdomide (0.15, 0.3 or 0.45 mg per day). Clinical response was determined by the SLE Responder Index 4 (SRI-4) at 24 weeks. RNAseq was performed and analyzed by Gene Set Variation Analysis (GSVA) using 32 informative gene modules and K-means clustering.

Results: Whole blood K-means clustering of the GSVA scores yielded 5 clusters or endotypes (Figure 1). Cluster 0 had the fewest molecular abnormalities, whereas Cluster 1 had the most disturbances in immune function, including enrichments in the interferon gene signature (IGS), immunoproteasome, IL-1/inflammasome pathway, and neutrophil/granulocyte genes. Clusters 2-3 had intermediate degrees of abnormal enrichment in specific gene modules. Cluster 4 had high IGS, immunoproteasome, plasma cells/Ig chains, and IL-23 complex genes. No differences were noted between the subsets with regard to steroid or hydroxychloroquine use and differed only slightly in disease activity as measured by SLEDAI-2K. In general, cluster 1 had the most severe clinical laboratory measures with the highest anti-dsDNA antibodies and lowest C3 and C4. Clinical responses to iberdomide were confined to clusters 1 and 4. Effect sizes of responses in these groups approximated 30%. Other clusters had higher placebo responses and no additional response to iberdomide.

Conclusion: K-means clustering of GSVA scores from baseline samples of the iberdomide trial successfully clustered patients into endotypes that exhibited differences in response to iberdomide treatment, with the greatest responses observed in patients with the highest IGS, immunoproteasome, plasma cell, inflammasome, and IL-23 pathways. Gene expression based subsetting (endotyping) may be useful to enrich trials for responsive patients.

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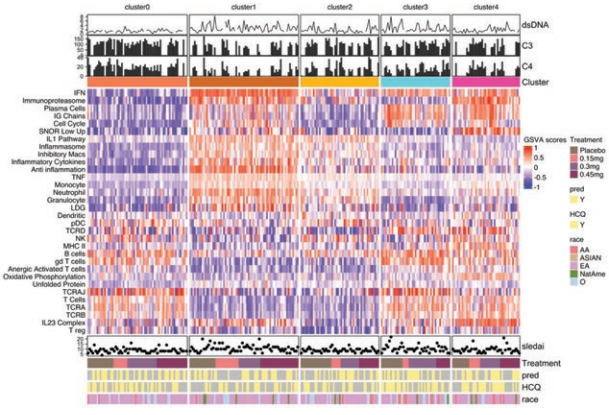


Figure 1. K-means clustering of GSVA scores from baseline gene expression profiles effectively identifies 5 subsets of SLE patients.

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Disclosure of Interests: Prathyusha Bachali: None declared, Yanhua Hu Shareholder of: BMS, Employee of: BMS, Nikolay Delev Shareholder of: BMS,

Employee of: BMS, Peter Schafer Shareholder of: BMS, Employee of: BMS, Peter Lipsky: None declared.
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POS0292 TRANSCRIPTOMIC PROFILING OF SJOGREN'S SALIVARY GLANDS IDENTIFIES FOLLICULAR AND EXTRA-FOLLICULAR GENE SIGNATURES ASSOCIATED WITH RHEUMATOID FACTOR SEROPOSITIVITY

Keywords: Autoantibodies, Sjögren syndrome

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Background: The presence of circulating rheumatoid factor (RF) and the formation of ectopic lymphoid structures (ELS) in labial salivary glands (SG) of patients with Sjögren's Syndrome (SS) have been reported as independent risk factors associated with the development of SG B-cell MALT lymphoma (MALT-L). Neoplastic MALT-L B-cells express highly hypermutated B-cell receptors bearing RF immunoreactivity in up to 50% of the cases, but whether their maturation and proliferation is dependent on ELS or is also induced by extrafollicular responses in the SG is currently unclear. The definition of ELS and their association with circulating autoantibodies has so far relied on SG histopathology which bears significant limitations. Conversely, molecular pathology analysis through whole-tissue RNA Sequencing (RNASeq) has allowed a better definition of disease heterogeneity and disease taxonomy.
Objectives: To perform transcriptomic profiling of SS minor SG tissue characterised by different degrees of inflammatory aggregate organization and to identify transcriptomic clusters and gene signatures associated with peripheral and histological biomarkers of disease.
Methods: Labial SG were obtained from 99 patients including SS with and without ELS (respectively ELS+ and ELS-, as assessed by immunohistochemistry) and non-specific chronic sialadenitis (Sicca). Total RNA was extracted, complementary DNA libraries were prepared and sequenced. Differentially expressed genes (DEG), deconvolution and pathway analysis were performed.
Results: Unsupervised gene clustering by differential expression between sicca and SS confirmed a clear transcriptome segregation between the two diagnoses. As expected, in SS SG expression of genes associated with inflammation and adaptive immune responses was upregulated (e.g. CCR7, CD19, CR2, CXCL13, CXCL9, CXCR5, FCRL3, FCRL4, IL21R, MS4A1, PAX5, SLAMF6, TLR10) (Figure A). Bulk RNAseq cell deconvolution confirmed immune cell enrichment (Th, B and plasma cells) in SS SG, especially those ELS+. A three-way comparison among sicca, ELS+ and ELS- SG, showed only a few genes specifically associated to ELS- and sicca, whereas most of the DEGs were either ELS+ specific or common to all SS (Figure B). Results of pathway analysis on ELS+ and SS-associated DEGs showed very similar profiles characterised by adaptive and interferon-associated pathway activation. Weighted Gene Co-Expression Network analysis showed higher activation of anti-viral pathways in ELS-SG, where ELS+ SG were enriched in adaptive immune pathways. Principal component analysis on SS SG mRNA showed that a significant proportion of variability was associated with the presence of RF in the serum of patients independently of the presence of ELS. Surprisingly, transcriptome clustering was closer between ELS+/RF+ and ELS-/RF+ SG than the clustering of ELS+/RF- with ELS-/RF- SG. Accordingly, SG of RF+ patients showed significant upregulation of B cell-associated genes (e.g. CXCL13, MS4A1). However, while SG transcriptomes of ELS+/RF+ were characterised by genes associated with germinal centre formation (e.g IL21, AICDA, LTB), transcriptomes from ELS-/RF+ SG displayed a unique set of DEGs such as BCL2, TRIM22, XAF1, DDX58, DDX60 and IFIT1. Conversely, a similar analysis performed based on anti-Ro/SSA and/or anti-La/SSB did not yield any significant differences in gene expression.
Conclusion: A comprehensive bulk RNA sequencing analysis of SS and sicca patients SG showed that higher tissue inflammation with features of functional germinal centres is associated to the presence of both RF and ELS, rather than ELS alone. Furthermore, the existence of a RF-driven SG transcriptome independent of the presence of ELS suggest that both follicular and extra-follicular responses support the selection of B-cells with RF immunoreactivity within the SG of SS patients and could be involved in B-cell lymphomagenesis.

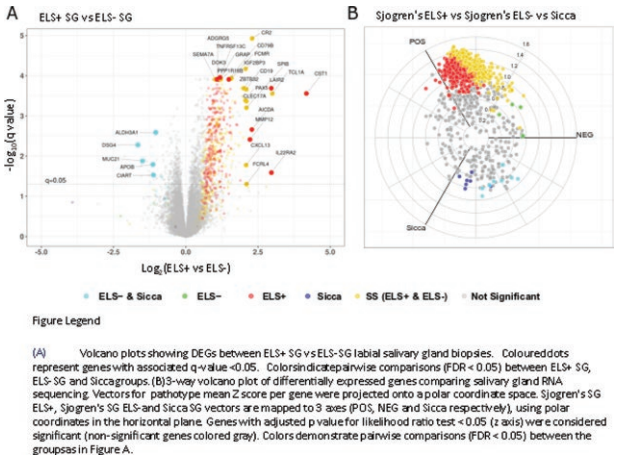


Figure Legend

(A) Volcano plots showing DEGs between ELS+ SG vs ELS- SG labial salivary gland biopsies. Coloured dots represent genes with associated q-value <0.05. Colors indicate pairwise comparisons (FDR < 0.05) between ELS+ SG, ELS- SG and Sicca groups. (B) 3-way volcano plot of differentially expressed genes comparing salivary gland RNA sequencing. Vectors for pathotype mean Z score per gene were projected onto a polar coordinate space. Sjogren's SG ELS+, Sjogren's SG ELS- and Sicca SG vectors are mapped to 3 axes (POS, NEG and Sicca respectively), using polar coordinates in the horizontal plane. Genes with adjusted p value for likelihood ratio test < 0.05 (z axis) were considered significant (non-significant genes colored gray). Colors demonstrate pairwise comparisons (FDR < 0.05) between the groups as in Figure A.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Elena Pontarini: None declared, Davide Lucchesi: None declared, Katriona Goldmann: None declared, Myles Lewis: None declared, Qingxuan Song Employee of: Janssen Pharmaceuticals, Inc., Spring House, PA, USA, Elizabeth Thomas Employee of: Janssen Pharmaceuticals, Inc., Spring House, PA, USA, Ling-Yang Hao Employee of: Janssen Pharmaceuticals, Inc., Spring House, PA, USA, Kathy Sivils Employee of: Janssen Pharmaceuticals, Inc., Spring House, PA, USA, Costantino Pitzalis: None declared, Michele Bombardieri Speakers bureau: UCB, Janssen, Consultant of: GSK, Janssen, MedImmune, Grant/research support from: Janssen, MedImmune.
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POS0293 METABOLOMIC IN ANTIPHOSPHOLIPID SYNDROME STRATIFIED PATIENTS ACCORDING TO THEIR THROMBOTIC RISK

Keywords: Artificial Intelligence, Cardiovascular disease, Anti-phospholipid syndrome

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Background: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder inducing hypercoagulable state that causes arterial, venous, or microvascular thrombosis, atherosclerosis, and pregnancy morbidity. Timely diagnosis and truthful monitoring of disease are decisive to improve the accuracy of therapy.
Objectives: 1. To map metabolic signatures in sera of APS patients and investigate its association with clinical features of the disease. 2. To investigate the short-term effects of *in vivo* ubiquinol (reduced coenzyme Q10 [Qred]) supplementation.
Methods: Serum nuclear magnetic resonance (NMR) metabolomics (>250 metabolites, Nightingale) covering glycolysis metabolites, amino acids and 130 lipid measures was performed on a cohort of primary APS patients (n=150) and 43 healthy donors (HD). Extensive clinical and analytical profile of recruited subjects was performed. NMR data were analyzed in MetaboAnalyst 5.0 software platform. To evaluate the contribution of metabolomic profiles to disease features, unsupervised machine learning clustering analyses were developed. Separately, 33 APS patients treated with Ubiquinol (Qred, reduced CoQ10, 200 mg/day) as an adjuvant treatment to standard therapy for one month, were also studied.
Results: Fifty-three metabolites were significantly altered in APS patients compared to HCs, involving decreased atheroprotective HDL subsets, sphingomyelins, phospholipids, and histidine, and increased proatherogenic VLDL subsets and fatty acids (MUFA, omega-3). Unbiased hierarchical clustering of metabolomic data identified two patient groups, presenting different metabolomic profiles. Clinically, although no differences were found in terms of age, gender, disease duration, or treatments, patients belonging to cluster 1 (C1) were characterized by higher thrombotic risk status (aGAPSS over 12), and prevalence of triple positivity for antiphospholipid antibody profile than C2 patients. Besides, C1 patients showed preponderance of arterial thrombosis, and comprised APS patients with

higher CV risk (elevated incidence of atheroma plaques, dyslipidemia, obesity, and hypertension). One hundred and forty-three metabolites were found deregulated between clusters. Thus, compared to C2, C1 had decreased atheroprotective HDL and increased atherogenic VLDL and LDL lipoproteins, increased triglycerides, fatty acids, apolipoproteins (ApoB), glycolysis related metabolites (glucose and pyruvate), amino acids (Leu, Tyr, Val, Phe, Ile), inflammation related metabolites (GlycA), and other lipids involved in immune cells activity, such as phosphatidylcholines, sphingomyelins, phosphoglycerides, and cholines. Of note, 28 metabolites were found altered in patients with thrombosis. Logistic regression analyses identified several metabolites which levels distinguished thrombotic APS patients with high accuracy, including VLDL and HDL subsets, fatty acids, amino acids, glucose and creatinine, all reportedly associated to enhanced CV risk. *In vivo*, Qred supplementation of APS patients partially reversed the altered serum metabolic profile linked to the development of atherosclerosis and thrombosis.

Conclusion: 1. APS patients have a distinctive metabolomic profile, with abnormalities associated with the pathogenesis of the disease, which are partially modified in vivo by Qred supplementation. 2. We have identified for the first time a metabolomic fingerprint able to stratify APS disease according to their thrombotic risk, which might pave the way for the development of new tools to improve their clinical management. Supported by ISCIII: (PI21/0591), and RICORS (RD21/0002/0033) co-financed by FEDER.

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Acknowledgements: NIL.

Disclosure of Interests: None declared.

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POS0294 MITOCHONDRIAL DYSFUNCTION AND SENESCENCE OF NAÏVE T CELLS IN SJÖGREN´S SYNDROME

Keywords: Animal Models, Sjögren syndrome, Cell biology

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Background: Primary Sjögren's Syndrome (pSS) is a systemic autoimmune disorder characterized by lymphocytic infiltrations in exocrine glands. T-cells are considered major players in the pathogenesis of pSS. Previously, we reported premature aging and impaired homeostatic proliferation of pSS naïve CD4+ T-cells leading to peripheral lymphopenia [1]. Id3-deficient mice (Id3KO) develop a Sjögren's-like syndrome and are used as an animal model for pSS [2].

Objectives: As mitochondrial function has been linked to premature aging and homeostasis of T cells, we assessed the mitochondrial status of T cells in pSS patients and the Id3KO mouse model of pSS.

Methods: Total immune cells were isolated from venous blood, lymph nodes and the spleens of Id3KO and wild type (WT) mice. Flow cytometric analysis was performed to characterize markers of cellular senescence p53, senescence-associated β-galactosidase (SA-β-GAL), and apoptotic rate in T-cell subsets. Staining with mitochondrion-selective fluorescent dyes MitoTracker Green, MitoTracker Deep Red, MitoSox Red was performed to assess mitochondrial mass, membrane potential (MtMP) and superoxide production, respectively. Similar analyses were performed on human T-cells from peripheral blood mononuclear cells of pSS patients and matched healthy individuals (HC).

Results: Similar to pSS patients, ID3KO mice show signs of pre-mature aging. The naïve cell compartment in CD4+ and CD8+ T-cells was significantly decreased in all studied tissues when compared to WT mice. Markers of cellular senescence, p53 and SA-β-GAL activity were increased in naïve CD4+ and CD8+ T cells. Apoptotic rate was also higher in Id3 KO T-cells. ID3 KO T-cells also exhibited a remarkable decrease of mitochondrial mass and MtMP. Despite having reduced mitochondrial mass and MtMP, we observed that Id3-deficient T-cells produced a higher amount of mitochondrial superoxide compared to WT mice. Again, naïve CD4+ T-cells were most affected by this increase. In line with our findings in ID3 KO mice, naïve CD4+ and CD8+ T-cells isolated from pSS patients produced significantly higher amounts of mitochondrial superoxide than those of HC.

Conclusion: In human pSS and mice with a pSS phenotype, naïve T cells are diminished and exhibit signs of pre-mature aging associated with significant accumulation of mitochondrial superoxide. ID3 KO mice may serve as a tool to test whether these changes are cause or consequence of pSS pathophysiology.

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Disclosure of Interests: None declared.

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POS0295 CD4+ T CELLS DEMONSTRATE METABOLIC REPROGRAMMING CHARACTERISED BY INCREASED REACTIVE OXYGEN SPECIES FORMATION AND ENHANCED ATP GENERATION IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Adaptive immunity

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Background: Systemic lupus erythematosus (SLE) is characterised by chronic stimulation of the innate and adaptive immune response. Oxidative stress resulting from Reactive Oxygen Species (ROS) generation is another hallmark of the disease. Mitochondria are a primary source of ROS and play a key role in energy metabolism via Oxidative Phosphorylation (OXPHOS), a vital pathway in maintaining the aberrant immunological response seen in the disease. Currently a number of novel therapeutics focusing on abnormal mitochondrial energy metabolism are under investigation in a variety of autoimmune diseases. Understanding abnormal immune cell mitochondrial function therefore represents an important area for identifying potential future targets in the treatment of SLE.

Objectives: To assess for evidence of abnormal mitochondrial function and associated ROS generation in the adaptive immune response in SLE.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood collected from patients with SLE recruited from the UCLH Lupus Clinic, England (n=37) and age/sex matched healthy controls (HC, n=20). Flow cytometry was used to quantify median fluorescence intensity (MFI) of cellular mitochondrial mass (MitoTracker) and mitochondria derived ROS generation (MitoSOX) in CD4+ and CD8+ T cells plus CD19+ B cells. Real-time CD4+ T cell mitochondrial metabolic function was assessed using SeaHorse Respirometry MitoStress Test. To assess for the role of cellular activation in CD4+ T cells, 24-hour anti-CD3/CD28 stimulation culture was conducted.

Results: Results are outlined in Figure 1. Briefly, mitochondrial mass was significantly higher in SLE CD4+ and CD19+ cells when compared with HC (A). CD8+ cells derived from patients with SLE showed higher amounts of mitochondrial ROS generation (B). When correcting for mitochondrial mass, individual mitochondria-derived ROS generation was significantly higher in CD4, CD8 and CD19+ cells in SLE when compared with HC (C). SeaHorse Respirometry revealed basal CD4+ respiration was higher in SLE when compared with HC (D), although there was no significant difference in maximal mitochondrial respiratory capacity (E). Proton leak, a marker of mitochondrial damage, was significantly higher in SLE than HC (F). CD4+ T cells from patients with SLE also showed enhanced mitochondrial ATP production when compared with HC (G), although spare respiratory capacity was significantly reduced in SLE (H) suggesting that mitochondria function in the disease is close to maximum with little scope for further upregulation. Mitochondrial uncoupling efficacy is an important mechanism through which higher rates of OXPHOS can be achieved and this appears to be downregulated in SLE (I). Activation of SLE CD4+ T cells appeared to drive higher rates of ROS production in both CD4+ and CD8+ cells (J). Interestingly, CD19+ ROS production was also increased, suggesting that T cell secreted cytokines following activation may also induce B cell ROS generation. Stimulation of SLE CD4+ T cells additionally increased basal mitochondrial respiration when compared with unstimulated SLE CD4+ T cells (K).

Conclusion: Increased mitochondrial mass seen in CD4+ and CD19+ SLE cells could be a result of enhanced immune cell senescence, commonly observed in the state of chronic immune activation. At baseline, SLE derived CD4+ T cells were noted to generate ATP through OXPHOS at a higher rate than HC thus suggesting chronic cellulation activation (and is further enhanced following T cell stimulation). CD4+ T cells also demonstrate a number of important pathological abnormalities in SLE, including high levels of proton leak, reduced spare respiratory capacity and lower ability for mitochondrial uncoupling. This may suggest that chronic activation is in turn resulting in mitochondrial damage and less efficient energy metabolism, resulting in ROS generation. Targeting this abnormal immune cell metabolic pathway therefore represents a novel therapeutic strategy.

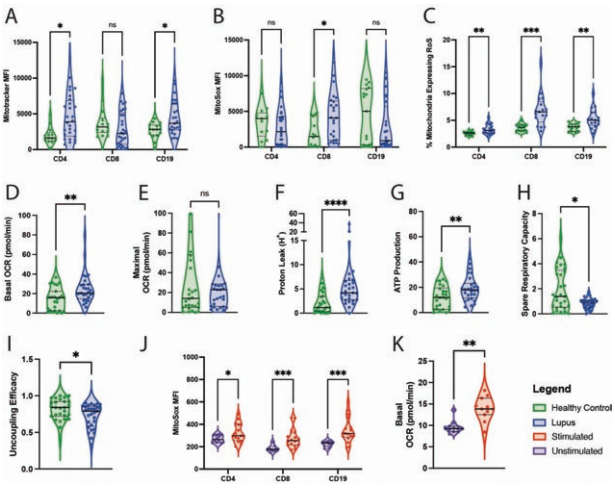


Figure 1.

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POS0296

GENE EXPRESSION IN SLE PATIENTS, DOMINATED BY UNIQUE B CELL PROFILES, DISTINGUISHES THOSE WITH CLINICAL IMPROVEMENT FROM ABATACEPT

Keywords: Clinical Trials, Systemic lupus erythematosus, Biomarkers

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Background: Abatacept (ABA or CTLA4Ig) is a fusion protein that interferes with co-stimulation of T cells and antigen-presenting cells by inhibiting interactions between CD28 and CD80/86. ABA is effective in rheumatoid arthritis, but clinical trials of patients with Systemic Lupus Erythematosus (SLE) have produced disappointing results. Exploratory analyses of clinical subsets has led to the hypothesis that ABA might benefit some SLE patients depending on disease severity or outcome defnitions[1,2], but identification of reproducible predictors of response remains elusive.
Objectives: We used data and samples collected from previous clinical trials to identify pathways of SLE pathogenesis and potential biomarkers which predict clinical response to ABA.
Methods: Samples were obtained from 20 patients from the ABC study which evaluated ABA in SLE patients without organ-threatening disease on limited background medications and 46 patients from the ACCESS trial of ABA in active nephritis patients on a background of low dose cyclophosphamide followed by azathioprine. Neither trial met their key endpoints vs placebo. Pre-treatment gene expression profiles were compared in those who did or did not achieve clinical response to ABA. HSIC-Lasso[3] was employed to select the top 20 independent features from whole blood transcriptomic profiles which best distinguished responders and non-responders across both trials. B cells, monocytes, and T cells were isolated from ABC patient PBMCs for further cell type-specific transcriptomic profiling. Differentially expressed genes (DEGs) were identified in each cell type by DESeq2 at false discovery rate < 0.1.
Results: Pre-treatment DEGs associated with abatacept responders were cell type-specific, with the most distinctions observed in B cells (Figure 1). These DEGs included FCRLA, CXCR3, and TNFRSF17, indicating baseline differences in B cell activation and differentiation in responding patients. Baseline whole blood expression patterns could distinguish later response vs non-response to ABA in both clinical trials (Figure 1). Transcripts identified by HSIC-Lasso included multiple unannotated lncRNAs and pseudogenes, as well as transcription factors, transporters, and enzymatic components of cell structure and metabolism. Random forest modeling and receiver operating characteristics (ROC) were employed to test the ability of differentiating transcripts to predict response (Figure 1). 5-fold cross validation of the predictor on a training set of 52 samples had 85.8 (± 2.2) % accuracy with ROC AUC: 0.939 (± 0.0166). 14 confirmation samples were similarly modeled and achieved an accuracy of 83.3% with ROC AUC: 0.944.
Conclusion: The pathophysiology of SLE is heterogeneous and complex, but approaches to predict treatment response by patterns of gene expression may help identify patients most likely to benefit from a given treatment.

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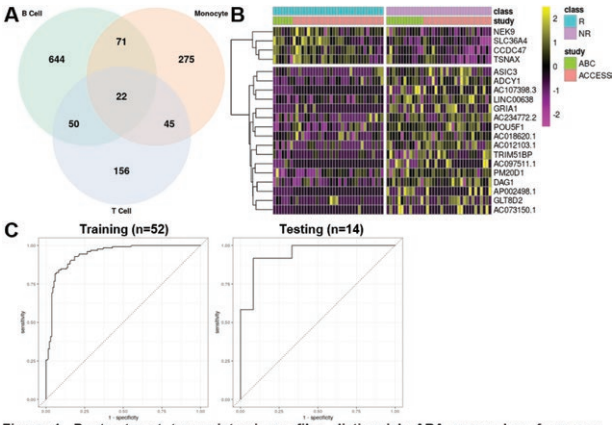


Figure 1. Pre-treatment transcriptomic profiles distinguish ABA responders from non-responders. (A) Venn diagram indicating DEGs shared between cell types in ABA responders and non-responders from ABC. Significance was determined at false discovery rate < 0.1. **(B)** Heatmap of whole blood transcripts selected by HSIC-Lasso across both trials. Batch-corrected, variance stabilized transformed counts were normalized to z-scores for visualization. Transcripts were clustered hierarchically. **(C)** ROC curves of a random forest predictor modeled on the selected trasncripts in (B) for a training set of 52 patients and a testing set of 14 patients.

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POS0297

PROTEOMIC ANALYSIS OF HISTOLOGICAL LESIONS LUPUS NEPHRITIS IDENTIFIES AN INFLAMMATORY SIGNATURE OF FIBROUS CRESCENTS

Keywords: -omics, Systemic lupus erythematosus, Kidneys

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Background: We employed urine proteomics to define the molecular signatures associated with the histological features quantified by the NIH activity and chronicity indices.
Objectives: We employed urine proteomics to define the molecular signatures associated with the histological features quantified by the NIH activity and chronicity indices.

Methods: Glomerular and interstitial lesions in lupus nephritis were quantified (scored 0-3) based on the revised 2018 International Society of Nephrology/ Renal Pathology Society (ISN/RPS) classification for lupus nephritis and the modified NIH scoring system by a central renal pathologist (JH). Urinary proteins (1200 biomarkers, RayBiotech Kiloplex) were quantified in urine samples collected on the day of (73%) or within 3 weeks of (27%) the diagnostic kidney biopsy. Proteomic signatures of each lesion were defined based on Spearman correlations of each urine protein with each pathologic lesion.
Results: Ninety-one biopsies were included: 32 (35%) with pure proliferative LN, 33 (36%) with pure membranous LN, and 26 (29%) with mixed LN. The 5 most correlated urinary proteins and each pathologic feature are summarized in Figure 1A-B. Most lesions in the activity or chronicity indices shared a similar signature within their respective index. In contrast, fibrous crescents displayed an inflammatory signature (CD73, MMP9, MIP1b, and IL-8) despite being part of the NIH chronicity index. Hierarchical clustering based on proteomic signatures revealed that fibrous crescents were more similar to activity-related lesions (Figure 1C). Interstitial inflammation (activity) was correlated with biomarkers associated with both active and chronic lesions.

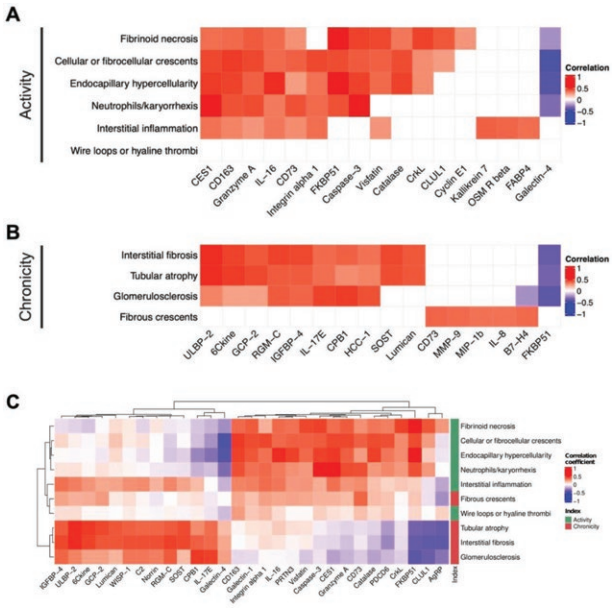


Figure 1.

Conclusion: Although fibrous crescents are considered inactive lesions that follow crescentic glomerulonephritis, urine proteomics revealed inflammatory activity associated with fibrous crescents. Several cell types such macrophages, fibroblasts, neutrophils, lymphocytes, and epithelial cells are critical in the formation of crescents. Higher levels of CD73, IL-8 and MMP9 indicate the presence of an inflammatory response involved in glomerular remodeling after extra-capillary proliferation that have an important role in kidney damage. The presence of fibrous crescents in kidney biopsies may indicate ongoing potentially treatable inflammation. Interstitial inflammation, which is linked to worse clinical outcomes, showed a distinct proteomic signature combining both activity and chronicity. A better understanding of the pathophysiology of processes including fibrous crescents and interstitial inflammation is needed to tailor treatment of these pathways leading to chronic damage.
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Acknowledgements: NIL.
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Clinical aspects of spondyloarthritis

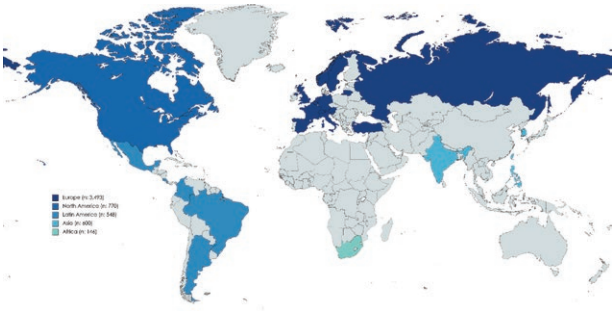
POS0298

THE INTERNATIONAL MAP OF AXIAL SPONDYLOARTHRITIS (IMAS). RESULTS FROM THE PERSPECTIVE OF 5,557 PATIENTS FROM 27 COUNTRIES AROUND THE WORLD

Keywords: Patient reported outcomes, Spondyloarthritis

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Background: The International Map of Axial Spondyloarthritis (IMAS) is a global assessment of the impact and burden of axial spondyloarthritis (axSpA) from the patient perspective, and identifying the unmet needs of axSpA patients through a survey. This research started in 2016 with the Atlas of Axial Spondyloarthritis in Spain, expanded in 2017-2018 to 13 European countries giving rise to the European Map of Axial Spondyloarthritis (EMAS) and further expanding worldwide across 27 countries to become the International Map of Axial Spondyloarthritis (IMAS).
Objectives: Here we present the scope of the study, distribution and main characteristics of patients included and instruments to collect data, as well as highlighting the impact of the disease.
Methods: This research is a collaboration between the Axial Spondyloarthritis International Federation (ASIF), the University of Seville and Novartis Pharma AG together with a scientific committee composed of axSpA patient representatives, rheumatologists, psychologists, and researchers. IMAS collected information through an online cross-sectional survey (2017-2022) from unselected axSpA patients from Europe, Asia, North America, Latin America and Africa. The inclusion criteria were: age ≥ 18 years, residents in the specified country, a diagnosis of axSpA (self-reported AS/nr-axSpA) and under the care of an health care professional. Patients completed a comprehensive questionnaire containing over 120 items on socio-demographics, health behaviours, diagnosis and disease characteristics, comorbidities, mental health (General Health Questionnaire- GHQ-12), healthcare resource utilization, pharmacological treatments, disease activity (BASDAI), physical activity and functioning, employment, and disease related fears and hopes.
Results: 5,557 axSpA patients participated in IMAS. The mean age was 43.9±12.8 years, 55.4% were women, 46.2% had university education and 48.5% were employed. 20.6% were on sick leave (temporary or permanent), 71.4% had difficulty finding job due to axSpA and 71.0% reported work-related issues. Patients' diagnostic delay was a mean of 7.4±9.0 years (median: 4.0), and the mean disease duration was 17.1±13.3 years. 75.0% of patients had active disease and 59.4% were at risk of poor mental health. In addition, patients had a mean of 2 physical comorbidities. On average, patients had visited primary care physicians 4.6 times and the rheumatologist 3.6 times in the year prior to the survey. 78.6% had ever taken NSAIDs, 43.6% csDMARDs and 48.8% bDMARDs. The greatest fear of these patients was disease progression (55.9%), while the greatest hope was to be able to relief pain (54.2%).
Conclusion: IMAS is the largest survey in geographical reach and this is the first-time global results are presented. IMAS has shown the global profile of axSpA patients, highlighting unmet needs, including unacceptable delays in diagnosis, and high burden of the disease in axSpA patients worldwide. This global dataset will enable more detailed investigations to obtain evidence on the critical issues that matter to patients around the world in order to improve their care and quality of life.



Map 1. Distribution of IMAS patients by region (N= 5,557)

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POS0299 NEUROPATHIC AND NEUROPLASTIC PAIN COMPONENTS DETERMINE THE PRESENCE OF RESIDUAL SYMPTOMS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS RECEIVING BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

Keywords: Spondyloarthritis, Pain, bDMARD

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Background: Several studies have investigated neuropathic pain (NP) as a component of chronic pain in patients with axial spondyloarthritis (axSpA)/ ankylosing spondylitis (AS) and showed a wide frequency range from 22 – 56.9% [1, 2]. Neuroplastic processes leading to central sensitization have been described as another component of pain chronification in rheumatic diseases [3]. Widespread pain is considered a characteristic of central sensitization [4]. It is, however, unclear, what is the relevance of neuropathic and neuroplastic components of pain for the treatment response and the presence of residual symptoms in patients with radiographic axSpA (r-axSpA) treated with biological disease-modifying anti-rheumatic drugs (bDMARDs)

Objectives: To investigate the impact of neuropathic pain and neuroplastic/ widespread pain on residual disease activity in patients with r-axSpA receiving (bDMARDs).

Methods: Patients with r-axSpA (AS fulfilling the modified New York criteria) and starting a bDMARD therapy were recruited between 2015 and 2019 and followed up in an extension of the prospective German Spondyloarthritis Inception Cohort (GESPIC). Neuropathic pain was quantified using the pain detect questionnaire (PD), whereas neuroplastic pain was quantified using the Widespread Pain Index (WPI). Disease activity was measured using the Ankylosing Spondylitis Disease Activity Score – C-reactive protein (ASDAS-CRP) score. Simple and multiple linear and logistic regression analyses were performed to determine the effects of NP and WPI on the ASDAS status score under bDMARD treatment.

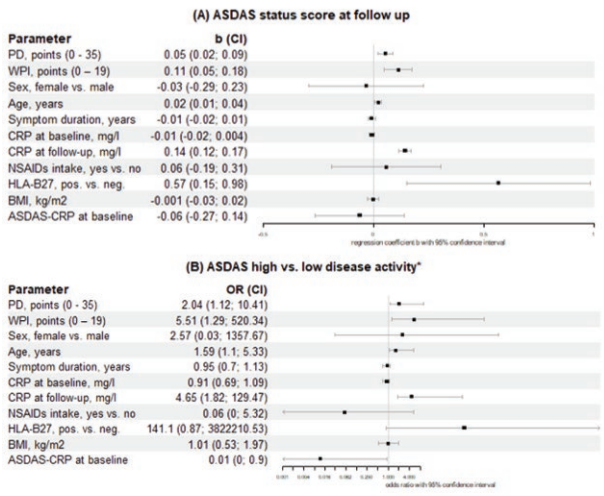
Results: A total of 130 patients with r-axSpA were included in this cohort. PD and WPI scores were available at at least one follow-up time-point in 99 patients. Of these 70 were receiving bDMARD treatment (n=68 under TNFi and n=2 under IL17 inhibitors) with no missing data and could be included in this analysis. The first follow-up point with available PD and WPI scores while under bDMARD treatment was used for the analysis.

Table 1. Baseline characteristics.

Characteristic	n = 70
Female sex	49(70)
Age, years	37.27±10.77
HLA-B27 positive	64(91.4)
BMI, kg/m²	25.57±4.49
Current smokers	28(40)
Symptom duration, years	12.53±10.83
Elevated CRP, >5 mg/l	43(61.4)
ASDAS-CRP	3.41±0.82
current NSAIDs intake	56(80)

Data are expressed as n(%) or mean ± standard deviation, BMI: Body mass index, CRP: C-reactive protein, ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score – C-reactive protein, NSAIDs: Nonsteroidal anti-inflammatory drugs The mean (±SD) bDMARD treatment duration was 2.79 ± 1.40 (range: 0.27 – 5.01) years at the time point of PD and WPI measurement. Higher PD and WPI scores at follow up showed a significant association with higher ASDAS-CRP scores in a multiple linear regression model. This was also true for age, HLA-B27 and the CRP level at follow-up. Logistic regression analysis showed that a high PD score and a high WPI score were also associated with higher odds of having high/ very high disease activity (ASDAS >2.1) independently of other factors including elevated CRP.

Figure1: Association between the ASDAS-CRP score at follow-up (A) and ASDAS high/very high disease activity at follow-up (B) with the presence of neuropathic (PD) and neuroplastic (WPI) symptoms in multiple regression analyses.



*defined as ASDAS-CRP score higher than 2.1 or lower respectively, PD: Pain detect, WPI: Widespread Pain Index, CRP: C- reactive protein, NSAIDs: Nonsteroidal anti-inflammatory drugs, BMI: Body mass index, ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score – C-reactive protein

Conclusion: Both PD and WPI reflecting neuropathic and neuroplastic components of pain showed association with residual symptoms (as reflected by higher ASDAS) independently of systemic inflammation (as reflected by elevated CRP) in patients with r-axSpA receiving bDMARD treatment.

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POS0300 PATIENT ACCEPTABLE SYMPTOM STATE IN RELATION TO DISEASE ACTIVITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS FROM A LARGE STANDARD-OF-CARE COHORT

Keywords: Patient reported outcomes, Outcome measures, Spondyloarthritis

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Background: The patient acceptable symptom state (PASS) is the level beyond which patients consider themselves well. This concept can help to interpret results of clinical trials and enhance physician-patient communication in daily clinical practice.(1)

Objectives: To explore the association of PASS with disease activity according to ASDAS and other patient- and disease characteristics in a large standard-of-care cohort of patients with in axial spondyloarthritis (axSpA).
Methods: Patients from the Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort visiting the outpatient clinic between May 2016 and October 2019 were included in this cross-sectional analysis. Patient characteristics and clinical assessments were measured according to the standardized GLAS protocol. Additionally, patients were asked to fill out the PASS question: "Considering all the different ways axSpA is affecting you and if you stay in this state for the next months, do you consider your current state satisfactory? ("yes": PASS/"no": non-PASS). Logistic regression analysis was used to explore patient and disease characteristics associated with PASS. ROC analysis with area under the curve (AUC) was used to analyze the accuracy of the ASDAS and the optimal cut-off point to predict PASS according to the highest Youden's index.
Results: Of the 673 included axSpA patients, 63% were male, mean was age 48±14 years, median symptom duration 19 (11-31) years and mean ASDAS 2.3 (±0.9). In total, the vast majority (76%) reported an acceptable symptom state according to the PASS question. Patients in the PASS group had significantly lower ASDAS compared to the non-PASS group (mean 2.0 ±0.8 vs. 3.2 ±0.8). Patients with an acceptable symptom state also had significantly lower BASDAI scores, were more often male, had longer symptom duration, had less tender entheses, used less often NSAIDs, experienced better physical function (BASFI) and quality of life (ASQoL), and had less radiographic damage (mSASSS) (Table 1). In multivariable regression analysis, lower ASDAS (OR: 4.45 (3.26-6.09)), longer symptom duration (OR 0.97 (0.95-0.99)) and absence of tender enthesis (OR 1.74 (1.85-2.79)) were independently associated with presence of PASS (Nagelkerke R^2: 0.38). The ASDAS showed good accuracy to predict PASS, with an AUC of 0.84 (95% CI 0.80-0.85). The optimal cut-off point of ASDAS for presence of PASS was 2.7 (sensitivity 77%, specificity 78%). A total of 214 patients had had an acceptable symptom state but active disease according to the ASDAS cut-off value for active disease of 2.1, this is 44% of patients being in PASS.
Conclusion: In axSpA patients from a standard of care cohort, 76% had an acceptable symptom state. Lower ASDAS, longer symptom duration, and absence of tender enthesis were independently associated with an acceptable symptom state. AxSpA patients experiencing an acceptable symptom state can still have active disease according to the ASDAS.

Table 1. Patient characteristics

	Total n= 673	PASS n=514 (76%)	Non-PASS n= 159 (24%)	p-value
Age (years)	48 (14)	49 (±13)	45 (±14)	<0.01*
Male gender	425 (63%)	336 (65%)	89 (56%)	0.04*
Symptom duration (years)	19 (11-31)	20 (12-31)	15 (7-29)	<0.01*
HLA B27+	539 (78%)	405 (79%)	125 (79%)	0.47
Diagnosis: - nr-axSpA	166 (27%)	113 (22%)	53 (36%)	<0.01*
-AS	462 (73%)	359 (70%)	93 (64%)	
BMI	26.6 (23.7-29.9)	26.6 (23.7-29.7)	27.1 (23.8-30.7)	0.33
ASDAS	2.3 (±0.9)	2.0 (±0.8)	3.2 (±0.8)	<0.01*
ASDAS >2.1	350 (55%)	214 (44%)	136 (91%)	<0.01
CRP	2 (2-6)	2 (2-6)	3 (2-8)	0.02*
BASDAI (0-10)	3.7 (2.0-5.6)	2.9 (1.6-4.8)	6.1(4.6-7.3)	0.02*
Presence of tender enthesis	245 (38%)	152 (31%)	93 (61%)	<0.01*
mSASSS (0-72)	6.3 (1.5-18.2)	6.8 (1.8-20.5)	4.7 (1.0-8.6)	0.03*
NSAID use	411 (61%)	301 (59%)	110 (70%)	<0.02*
cDMARD use	51 (8%)	36 (7%)	15 (10%)	0.31
bDMARDs use	309 (46%)	231 (45%)	78 (49%)	0.41
ASQoL (0-18)	5.0 (2.0-9.0)	4.0 (1.0-7.0)	10.0 (7.0-13.6)	<0.01*

Data presented as number of patients (%), mean ± SD or median (IQR).. *p-value ≤ 0.05.

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POS0301 IMPACT OF NSAIDS ON 8-YEAR INCIDENCE OF MAJOR CARDIOVASCULAR EVENTS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

Keywords: Cardiovascular disease, Spondyloarthritis

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease associated with the occurrence of major cardiovascular events (MACEs). The effect of AS treatments on the occurrence of MACEs is poorly studied, especially for non-steroidal anti-inflammatory drugs (NSAIDs), whose cardiovascular risk remains debated in this disease.
Objectives: To determine the incidence of MACEs in patients newly benefiting from long-term illness (LTI) for AS and to study the relationship between AS treatments and MACEs.
Methods: This national cohort study was based on the national health data system Système National des Données de Santé (SNDS), a French national medico-administrative database containing data containing administrative data, data on LTIs, outpatient care and medication consumption, and hospitalizations of all beneficiaries of the French health insurance system. All patients newly benefiting from the LTI #27 "severe spondyloarthritis", with associated diagnostic code M45 (AS), between 2010 and 2013, were included. The use of LTI allowed us to build a cohort of patients with a supposedly active disease, the SNDS, being a medico-administrative database, having no data on the activity of the disease. All patients with active SpA despite NSAID treatment, and therefore requiring disease-modifying anti-rheumatic drugs (DMARDs), were theoretically newly enrolled in the LTI scheme. The end date of follow-up was 31 December 2018. The occurrence of MACEs (stroke and myocardial infarction [MI]) and comorbidities (diabetes, hypertension, dyslipidemia, smoking, obesity, chronic kidney disease, atherosclerosis, and depression) were identified using algorithms previously described in the literature. An analysis taking into account the competitive risk of death and an inverse propensity score weighting (determining the likelihood of NSAID treatment) was performed to compute cumulative incidence functions and determine the subhazard ratios (SHRs) for the occurrence of MACEs for the different treatments of interest.
Results: Between 2010 and 2013, 22929 patients were included (mean age 43.0 (SD 13.9) years, 44.9% male). During follow-up, 344 MACEs (195 strokes, 152 MI) and 415 deaths were identified. The cumulative 8-year incidences of MACE, stroke and MI were 1.81% [1.61-2.05], 0.97% [0.83-1.14] and 0.85% [0.71-1.04] respectively. The occurrence of MACE was associated in univariate analysis with age (SHR: 1.07 [1.06-1.07]), male sex (SHR: 1.61 [1.31-2.00]), diabetes (SHR: 2.21 [1.63-3.00]), dyslipidaemia (SHR: 3.67 [2.96-4.57]), and hypertension (SHR: 3.74 [2.87-7.49]) (p<0.001 in all cases). After inverse propensity score weighting, NSAIDs (SHR: 0.40 [0.32-0.49], p<0.001) and anti-TNFs (SHR: 0.61 [0.47-0.81], p<0.001) were associated with a lower risk of MACE occurrence, which was not the case for conventional synthetic DMARDs (SHR: 0.89 [0.63-1.24]) and anti-IL17 (SHR: 2.06 [0.78-5.44]). Similar results for DMARDs were found when stratifying the analysis on the presence or absence of NSAID treatment (Table 1).
Conclusion: The incidence of MACEs at eight years is low in patients newly benefiting from LTI for AS. Our results support the hypothesis of a protective role of NSAIDs and anti-TNF drugs on cardiovascular risk in these patients.

Table 1. Inverse Probability Treatment Analysis with stabilized weighted subhazard ratio (wSHR) and its 95% confidence interval [95% CI] stratified by non-steroidal anti-inflammatory drugs (NSAIDs) treatment.

	wSHR [95% CI] global	wSHR [95% CI] in patients treated with NSAIDs	wSHR [95% CI] in patients NOT treated with NSAIDs
NSAIDs	0.39*** [0.32-0.50]	N/A	N/A
csDMARDs	0.89 [0.63-1.24]	0.91 [0.58-1.43]	1.02 [0.61-1.71]
Anti-TNF	0.61*** [0.46-0.80]	0.68* [0.47-0.99]	0.57** [0.38-0.85]
Anti-IL17	2.10 [0.79-5.57]	2.88 [0.73-11.3]	1.90 [0.47-7.72]

* p<0.05, ** p<0.01, *** p<0.001, otherwise non-significant

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POS0302 TREAT-TO-TARGET IN SPONDYLOARTHRITIS (SPA): ARE THERE SEX-RELATED DIFFERENTIAL RESPONSES?

Keywords: Spondyloarthritis

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Background: Studies have reported that female patients with spondyloarthritis (SpA) have different disease courses and treatment responses compared to male patients. Whether patients' sex, the biological attributes associated with being male or female, is associated with a different outcome after receiving one-year of tight control, treat-to-target (T2T) strategy remain uncertain.
Objectives: This study aimed to evaluate the differences in the clinical response between male and female patients from the Asia Pacific League of Associations for Rheumatology (APLAR) SpA Registry.
Methods: Patients who fulfilled the CASPAR 2006 classification criteria for psoriatic arthritis (PsA) and 2009 ASAS classification for axial spondylitis (AxSpA) were recruited. They received 1 year of protocolized treatment aiming at 1) minimal disease activity (MDA) *or Disease Activity in Psoriatic Arthritis* (DAPSA) low disease activity (LDA) for PsA patients, and 2) *Ankylosing Spondylitis Disease Activity Score* (*ASDAS*) LDA for AxSpA patients. Patients were assessed every 3 monthly and treatment was escalated if target was not reached.
Results: 63 male (age: 45±15 years, 27 PsA, 36 AxSpA) and 36 female (age: 46±12 years, 22 PsA, 14 AxSpA) subjects from 6 Asia-Pacific regions were included. At baseline, male had more tender joints but less severe enthesitis than female. Male AxSpA patients had a lower Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) but male PsA patients had a higher DAPSA. Other baseline characteristics were shown in Table 1. During the study period, the use of conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) decreased slightly, while the use of biologics (bDMARDs) significantly increased across both sexes (Figure 1). After 1-year treatment, there were significant improvements in disease activity in the entire cohort (DAPSA: 15.3±11.6 at baseline vs 10.1±11.2 at 1-year, p=0.002; ASDAS: 2.4±1.0 at baseline vs 1.9±0.9 at 1-year, p=0.003). Despite having lower CRP levels (2.3 ± 2.5mg/L in female vs 8.7±17.7mg/L in male, p=0.008) and higher bDMARDs use in female patients (54% in female vs 45% in male) at 1-year, their clinical responses were less optimal compared to male patients. Female patients had a higher patients' global assessment score (3.9±2.4 in female vs 2.9±2.2 in male, p=0.035). Disease activity in female PsA patients and the number of tender joint count in both PsA and AxSpA increased while that in male patients improved (% change in DAPSA: -47% in male vs +19% in female, p=0.003); % change in tender joint count: -70% in male vs +19% in female, p=0.014). Both patients' and physicians' global assessment scores increased in female SpA patients whilst that in male SpA patients decreased. There was also a trend showing less improvement in other parameters in female patients (Figure 1).

Table 1. Demographics, clinical features and disease activity in patients with Spondyloarthritis in APLAR region at baseline, stratified by gender

	Male (n=63)	Female (n=36)	*p*
Age, years	45 ± 15	46 ± 12	
Presence of sacroiliitis in Xray[1]	35 97%	8 57%	*
NRS Patients' pain assessment, 0-10	3.9 ± 2.2	4.3 ± 2.2	
NRS Patients' global assessment, 0-10	3.9 ± 2.3	4.3 ± 2.0	
NRS Physicians' global assessment, 0-10	3.5 ± 2.3	3.4 ± 2.0	
TJ count, 0-68	2.8 ± 5.3	1.0 ± 1.3	*
SJ count, 0-66	1.5 ± 3.4	0.7 ± 1.3	
Dactylitis digits	0.3 ± 1.4	0.1 ± 0.4	
PASI[2]	3.56 ± 5.84	1.68 ± 2.58	
SPRACC, 0-15	0 ± 1	1 ± 1	*
ESR, mm/h	20 ± 18	27 ± 22	
CRP, mg/L	18.0 ± 55.6	7.5 ± 10.2	
MDA achieved[2]	8 29.6%	9 49.9%	
DAPSA[2]	17.57 ± 13.57	10.40 ± 5.76	*
ASDAS CRP[1]	2.29 ± 1.00	2.90 ± 0.93	
BASDAI[1]	3.0 ± 1.8	5.1 ± 2.4	*
BASFI[1]	2.2 ± 1.9	4.5 ± 2.5	*
BASMI[1]	3 ± 2	2 ± 1	*
HAQ-DI	0.395 ± 0.493	0.622 ± 0.574	*

[1]For Axial SpA only, [2]for PsA only.

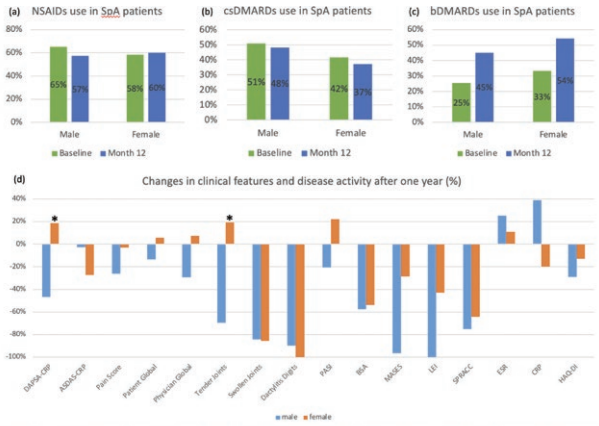


Figure 1 - NSAIDs (a) / csDMARDs (b) / bDMARDs (c) use at baseline and 1-year and changes in clinical features and disease activity after 1-year treatment (d) in male and female SpA patients.

Conclusion: There may be differential treat-to-target responses between male and female SpA patients. The causes of such differential characteristics should be further explored to potentially implement a sex-specific treat-to-target strategy for spondyloarthritis.
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POS0303 IMPACT OF PREGNANCY ON SACROILIAC IMAGING IN WOMEN WITH AXIAL SPONDYLOARTHRITIS: RESULTS OF THE ANALYSIS OF THE DESIR COHORT

Keywords: Spondyloarthritis, Descriptive Studies, Imaging

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Background: Axial spondyloarthritis (axSpA) is typically characterized by imaging (radiographs or MRI) abnormalities of the sacroiliac joints (SIJ). Also, inflammatory lesions of the SIJ have been observed in healthy women post-partum [1,2]. However, the impact of pregnancy on imaging abnormalities in women with axSpA is unknown.
Objectives: The objective of this study was to evaluate impact of pregnancy on SIJ imaging in patients with early axSpA.
Methods: Data of all women with early axSpA from the DESIR prospective cohort were included, with a follow-up of 5 years. Description of demographic disease characteristics, obstetric history, and SIJ imaging abnormalities (i.e. sacroiliitis on radiographs and on MRI, based on local and central reading) was performed in all women. SIJ abnormalities were compared depending on the history of past pregnancy (t-test and chi-square as appropriate). Furthermore, in nulligravidae females at baseline who presented an incident pregnancy during follow-up, SIJ abnormalities were compared before/after pregnancy, using paired-test.
Results: 381 patients were included in the analysis. 142 (37%) were nulligravidae at baseline, and were younger (28 vs 39 years old) and had higher educational level (74 vs 52% university level). Sacroiliitis on MRI and X-ray were more frequent in nulligravidae women (16.9% vs 9.9%, p = 0.05 and 33.8% vs 19.4%, p < 0.01, respectively). Among them, 38 (10% of all patients) presented an incident pregnancy during follow-up and had an available imaging before and after pregnancy: overall no significant changes were observed with regard to both radiographic and MRI imaging abnormalities of the SIJ, except for an increase on the New York score of the left SIJ, and surprisingly, a trend towards a reduction on the proportion of MRI sacroiliitis and SPARCC score after pregnancy (**table 1**).

Table 1. Imaging characteristics in women with axSpA who had first pregnancy during follow up, with description before/after delivery and paired-test with Mc Nemar of Student test (for binary and continuous variables, respectively).

Imaging criteria *(mean (sd) or number (%))*	**Before pregnancy (N = 38)**	**After delivery (N = 38)**	**Paired test (Mc Nemar or Student)**
Radiographic criteria			
X-ray sacroiliitis	8 (21.1%)	9 (23.7 %)	p = 0.37
New York score on right sacroiliac joint	0.66 (1.06)	0.67 (0.86)	p = 1
New York score on left sacroiliac joint	0.67 (1.07)	0.95 (0.95)	**p = 0.037**
Any erosion in the sacroiliac joints	9 (23.7%)	9 (23.7%)	p = 0.48
Any joint widening in the sacroiliac joints	0	3 (7.9%)	NA
Any sclerosis in the sacroiliac joints	6 (15.8%)	9 (23.7%)	p = 0.13
Any partial or total ankylosis in the sacroiliac joints	1 (2.6%)	2 (5.3%)	p = 0.48
MRI criteria			
Sacroiliitis on MRI	18 (47.3%)	2 (5.2%)	p = 0.074
SPARCC score	3.94 (7.63)	0.39 (0.74)	p = 0.15
≥ 3 fatty lesions on MRI	4 (10.5%)	1 (2.6%)	p = 1
≥ 3 erosions on MRI	1 (2.6%)	0	NA
≥ 5 fatty lesions and/or erosions on MRI	1 (2.6%)	1 (2.6%)	p = 1
Number of any lesions on sacroiliac joint (0 to 144)	1.81 (3.36)	1.8 (2.92)	p = 0.1
Number of enthesitis (0 to 12)	0 (0)	0 (0)	NA
Number of erosions (0 to 40)	0.84 (2.36)	0.42 (0.7)	p = 1
Number of fatty lesions (0 to 40)	0.97 (2.01)	1 (2.02)	p = 0.15
Number of sclerosis (0 to 40)	0 (0)	0.26 (0.86)	p = 0.29
Number of partial or total ankylosis (0 to 24)	0 (0)	0 (0)	NA

Conclusion: In an early SpA cohort, the occurrence of a first pregnancy did not seem to increase the number of imaging abnormalities of the SIJ.

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POS0304 IN-SILICO MODELLING OF THE SACROILIAC JOINTS DEMONSTRATES INFLUENCE OF JOINT FORM VARIATION ON MECHANICAL STRESS

Keywords: Spondyloarthritis, Imaging, Gender/diversity issues

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Background: Recent studies have uncovered an association between atypical joint form morphology and mechanical disease of the sacroiliac joints [1] and sclerosis in healthy controls [2]. A possible explanation for the effect is a change in load distribution in atypical joint forms and thus increased mechanical stress in affected patients.

Objectives: To investigate the effect of joint morphology on joint stress, using finite element models (FEM).

Methods: FE models were computed using dedicated software (Amira Software, Zuse Institute Berlin and Thermo Fisher Scientific, 2021), from CT scans of five patients without disease of the sacroiliac joints from a retrospective patient cohort[2]. Selected were patients with known anatomical variants (accessory joint, crescent-shaped ilium and intra-articular joint form variant; all female individuals) as well as a typical male and a typical female joint, based on radiological assessment. The models included both information on bone elasticity, derived from bone density on CT and stiffness of ligaments and muscles from the literature (visualization in Figure 1). Lastly, loading conditions during bipedal walking were simulated in all models, drawing from in-vivo data. Mean von Mises stress as well as percentage of joint surface above critical stress value (defined as 7 MPa) during y-axis loading (e.g. standing upright) and bipedal walking were compared between different joint morphologies.

Results: Table 1 provides a summary of the results. In axial loading (=y-axis stress) highest median stress and 99th percentile stress was observed in the crescent-shaped ilium with 12.5 Mpa and 28.8 Mpa respectively, while the iliosacral complex exhibited the lowest median stress (7.0 MPa) and the second highest 99th percentile value (25.1 MPa), indicating a less even distribution of stress. For bipedal walking the highest stress was also observed in the crescent shaped ilium with 64.2% of joint surface showing more than 7 Mpa during ipsilateral toe off vs. only 22.7% in the iliosacral complex. In all load scenarios, stresses were higher in the typical female joint than in the typical male joint.

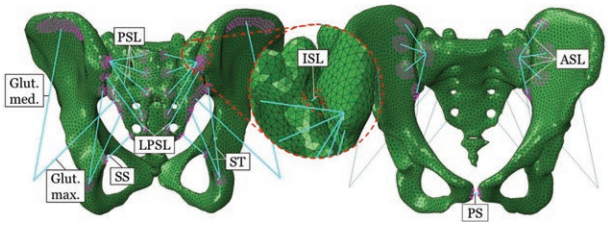


Figure 1. Example of FE-model with ligaments and muscles. Left=posterior view; right=frontal view. Glut. Med.=gluteus medius muscle; Glut. Max.=gluteus maximus mscle; SS=sacrospinous ligament; PSL=posterior sacroiliac ligament; LPSL=long posterior sacroiliac ligament. ST=sacrotuberous ligament; ISL=interosseous sacroiliac ligament; ASL=anterior sacroiliac ligament; PS=pubic symphysis;.

Table 1 . Summary of results. 99th percentile=value, below which 99% of measured values within the joint lie. Static y-axis=axial or downward stress, e.g. during standing upright; IHS=ipsilateral heel strike; CTO=contralateral toe off; CHS=contralateral heel strike; ITO=ipsilateral heel strike.

Joint form	**Von Mises stress [Mpa]**		**%joint surface above 7Mpa**					
	Median	**99th percentile**	**Static y-axis**	**Gait cycle phase**				
				IHS	**CTO**	**Swing**	**CHS**	**ITO**
Typical female	8.1	18.9	61	49	56	34	39	51
Typical male	8.5	18.2	66	38	26	20	39	16
Crescent-shaped	12.5	28.8	92	43	54	27	43	64
Iliosacral complex	7.0	25.1	50	26	21	13	20	23
Accessory joint	9.9	20.0	72	43	38	28	31	46

Conclusion: Finite element modelling revealed differences in load extent and distribution across different sacroiliac joint morphologies, strengthening the evidence, that morphology may play a role in mechanical joint stress. Further studies with larger numbers of computed models per joint form are needed to validate these first exploratory results.

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POS0305 CONTINUING TNFI AFTER PREGNANCY DIAGNOSIS IN WOMEN WITH CHRONIC RHEUMATIC INFLAMMATORY DISEASES IS NOT ASSOCIATED WITH WORSE OBSTETRICAL OR INFECTIOUS OUTCOMES: THE RESULTS OF AN EMULATED TARGET TRIAL

Keywords: Spondyloarthritis, Pregnancy and reproduction, Disease-modifying Drugs (DMARDs)

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Background: Continuation of biologics during pregnancy in patients with chronic inflammatory diseases during pregnancy is still a difficult medical decision. Many women with chronic rheumatic inflammatory diseases (CRID) decide to stop tumor necrosis factor inhibitors (TNFi) treatment once pregnancy is confirmed to avoid potential adverse fetal events but taking the risk of inflammatory flare.

Objectives: To compare in real life settings the pregnancy outcomes of two treatment strategies among women with CRID: to continue TNFi vs. stop TNFi upon pregnancy diagnosis.
Methods: the French nationwide health insurance database (*Système National des Données de Santé*) was used to emulate a target trial in adult women, with CRID (i.e., rheumatoid arthritis, psoriatic arthritis or spondyloarthritis), having started a singleton pregnancy between 2008 and 2017, and and being treated with TNFi upon pregnancy diagnosis. We compared the frequency of unfavorable pregnancy outcomes (malformations, obstetrical complications, and infections) between the treatment strategies at pregnancy diagnosis, using inverse probability weighted marginal models.
Results: A total of 1466 pregnancies were included, and among them, TNFi treatment was discontinued after pregnancy diagnosis in 74%. Mean (SD) age of women at the start of pregnancy was 31 (5) years and mean (SD) disease duration was 4 (5) years. Continuation of TNFi was not associated with increased frequencies of unfavorable pregnancy outcomes: interestingly, the proportion of pregnancies with at least one unfavorable obstetrical outcome tended to be lower in the group of patients continuing the TNFi after pregnancy diagnosis but without reaching statistical significance: 66 (17.3%) vs. 201 (18.5%) in the group continuing vs. discontinuing, respectively (adjusted RR= 0.79 [95% CI, 0.57; 1.10]). Also, there was a trend for a lower frequency of severe maternal infections in the group continuing the TNFi (7 (1.8%) vs. 36 (3.3%), (aRR=0.43 [0.16; 1.14]). Table.
Limitation: Algorithms rather than clinical data were used to identify patients with CRID, pregnancies, obstetrical outcomes, malformation and serious infections.

Table 1.

	Outcomes	TNFi continuation after pregnancy diagnosis		*p*
		Yes (N, %)	No (N, %)	
Obstetrical	Spontaneous abortion	2 (0.5%)	22 (2.0%)	0.06
	Stillbirth	0 (0.0%)	3 (0.3%)	-
	Medical termination of pregnancy	2 (0.5%)	4 (0.4%)	-
	Preterm birth (GA between 22 and 37 weeks among live birth)	35 (9.2%)	109 (10.1%)	-
	Small for GA (<10th percentile)	29 (7.6%)	75 (6.9%)	-
	Cesarean delivery	99 (25.9%)	273 (25.2%)	0.06
	Eclampsia/Pre-eclampsia	6 (1.6%)	17 (1.6%)	-
	Extra-uterine pregnancy	0 (0.0%)	2 (0.2%)	-
Maternal hospitalization for infection (during pregnancy and 6 weeks post-delivery)		7 (1.8%)	36 (3.3%)	0.09
Major congenital malformation		9 (2.4%)	31 (2.9%)	-

Footnotes: -: *the model did not converge due to the low number of events; GA= gestational age*

Conclusion: In pregnant women with CRID treated with TNFi until pregnancy diagnosis, neither unfavorable obstetrical outcomes nor severe infections were significantly increased in patients continuing TNFi during pregnancy, compared with a strategy of stopping TNFi.
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POS0306

INVOLVEMENT OF CENTRAL SENSITIZATION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS; A BIOPSYCHOSOCIAL APPROACH

Keywords: Spondyloarthritis, Pain

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Background: Chronic (inflammatory) back pain is a key symptom of axial spondylarthritis (axSpA) and still present in a large proportion of patients on long-term biological treatment. This pain may not only be of inflammatory origin, but also due to altered pain processing of the central nervous system such as central sensitization (CS). Biological, psychological and social factors contribute to the development and maintenance of CS. A high score on the Central Sensitization Inventory (CSI), is associated with disease activity in axSpA.[1] In absence of a gold standard, Quantitative Sensory Testing (QST) is currently understood as an optimal indirect assessment of altered somatosensory function. However, QST is not always feasible in clinical practice, and CSI could serve as an alternative.
Objectives: To explore: 1) to what extent altered somatosensory function related to CS is present in patients with axSpA; 2) associations with QST and psychosocial factors related to CS.
Methods: Consecutive outpatients from the Groningen Leeuwarden axSpA cohort, fulfilling the ASAS classification criteria, were included. Participants underwent QST according to a standardized protocol, including assessment of Pain Pressure Threshold (PPT) at 11 sites, Temporal Summation (TS) at 3 sites and Conditioned Pain Modulation (CPM). Widespread low PPTs, high TS (both pain facilitation) and positive CPM (impaired pain inhibition) are indicators of CS. Participants also filled out the CSI, illness perception (IPQ-R), pain catastrophizing (PCS), fatigue (MFIS), anxiety and depression (HADS), coping (CORS) and physical activity (mSQUASH). Analyses were stratified for CSI cut-off value ≥40 indicating probable CS. Univariable and multivariable linear regression analyses were used to investigate the association of CSI, the questionnaires, QST, and patient and disease related assessments.
Results: 201 patients were included, median age was 50 years [IQR 38-58], 63% were male, 64% were classified as radiographic axSpA, 79% were HLA-B27+, median symptom duration was 12 years [IQR 5-24], mean $ASDAS_{CRP}$ was 2.1 ± 1.0. In total, 40% patients scored ≥40 on the CSI. In these patients PPTs at all sites except the m. trapezius left were significantly lower and TS significantly higher at the non-painful and painful area compared to patients with CSI scores < 40 (Table 1). No significant differences in TS at the non-dominant forearm and CPM were found. In univariable linear regression, sex, ASDAS, BASFI, PPT scores, PCS, IPQ-R identity, IPQ-R emotional representations, IPQ-R consequences, MFIS, HADS anxiety, CORS pain decreasing activities and mSQUASH were all significantly associated with the CSI. In the multivariable regression model, 5 variables (MFIS, IPQ-R Identity, sex, HADS anxiety, and PCS) were independently associated with the CSI. Explained variance of this model was 78%. Excluding the CSI questions with potential overlap with symptoms related to axSpA resulted in a comparable model.
Conclusion: This large study including QST confirms that altered somatosensory function related to CS is present in a subgroup of patients with axSpA. In addition, the CSI strongly reflect psychosocial factors related to CS. These results addresses the importance of the multifactorial biopsychosocial perspective of pain within the management of axSpA.
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Table 1. QST distributions stratified for CSI (n=201)

		CSI <40	CSI ≥40
PPT			
thenar	left	37.2 ± 18.2	27.7 ± 12.3*
	right	40.7 ± 19.1	30.3 ± 15.4*
m. trapezius	left	38.6 ± 20.0	30.4 ± 21.4
	right	38.2 ± 20.0	30.1 ± 18.7*
m. rectus femoris	left	54.6 ± 26.1	42.3 ± 21.8*
	right	53.2 ± 26.6	38.6 ± 23.1*
m. abductor hallucis	left	36.4 ± 18.6	29.3 ± 14.1*
	right	38.3 ± 19.7	30.0 ± 16.2*
reference area[a]		37.7 ± 21.7	27.8 ± 17.4*
painful area		31.4 [22.2-48.6]	21.0 [14.4-34.8]*
TS			
non-dominant forearm		0.5 [0.1-1.3]	0.8 [0.2-2.1]
reference area[a]		0.6 [0.1-1.3]	1.3 [0.4-2.3]*
painful area		0.7[(0.1-1.6]	1.4 [0.3-3.0]*
CPM			
non-dominant m. rectus femoris		2.7 ± 13.1	0.4 ± 9.7

*Statistically significant at p<0.004 (Bonferroni).

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Original perspectives on old DMARDs and new small molecules in rheumatoid arthritis

POS0307

A PHASE 2 TRIAL OF PERESOLIMAB FOR ADULTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Clinical Trials, Autoantibodies

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Background: Peresolimab is a humanized immunoglobulin G1 monoclonal antibody that stimulates human programmed cell death protein 1 (PD-1). We hypothesized that peresolimab binding to PD-1, a checkpoint inhibitory receptor, could stimulate physiological immune inhibitory pathways to restore immune homeostasis; this represents a novel approach to treating patients with autoimmune or autoinflammatory diseases.

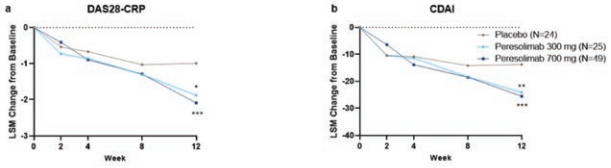
Objectives: The objective of this study was to evaluate efficacy and safety of peresolimab in adult participants with moderate-to-severe rheumatoid arthritis (RA).

Methods: A Phase 2a, placebo-controlled, double-blind, randomized clinical trial (NCT04634253) evaluated the efficacy and safety of peresolimab in adult participants with moderately to severely active RA, who had an inadequate response to prior disease modifying drugs, either conventional (csDMARDs), biologic (bDMARDs) or synthetic (tsDMARDS). Treatment comparisons versus placebo were made using mixed effects model for repeated measures (MMRM) and using logistic regression model for continuous and binary endpoints, respectively. Nominal p-values are reported. Missing data for binary endpoints were imputed as non-response.

Results: One hundred and one patients were randomly assigned 2:1:1 to receive intravenous peresolimab 700 mg (n = 49), 300 mg (n = 25), or placebo (n = 24) Q4W; 98 participants received at least one dose of study treatment and were included in the analysis. Baseline demographics and disease activity were similar among groups. The majority (83.7%) of participants were female. At baseline, the mean (SD) duration of RA was 10.0 (8.0) years, and the mean (SD) DAS28-CRP score was 5.9 (0.85). This trial met its primary endpoint of a significantly greater improvement from baseline at Week 12 in DAS28-CRP score in participants treated with peresolimab vs participants treated with placebo at both tested doses (700 mg [p < 0.001] and 300 mg [p = 0.017], figure 1a). Significant improvements were seen in CDAI between participants treated with either peresolimab dose (figure 1b) relative to placebo, and for ACR20 (p < 0.05) for participants treated with peresolimab 700 mg relative to placebo by Week 12 (table 1). Peresolimab exhibited a safety and tolerability profile that supports further clinical evaluation in immunologic disease.

Conclusion: Peresolimab, a PD-1 receptor agonist, was superior to placebo at Week 12 for several key endpoints in RA. Safety events were similar between treatment groups.

Figure 1. Change in baseline of DAS28-CRP and CDAI LSM up to Week 12



DAS28-CRP = disease activity score-28 for RA with C-reactive protein. LSM = least squares mean. CDAI = clinical disease activity index. *p value < 0.05, **p value < 0.01, ***p value < 0.001.

Table 1. Primary and Secondary Efficacy Outcomes at Week 12†

	Placebo (N=24)	Peresolimab 300mg (N=25)	Peresolimab 700mg (N=49)
Primary endpoint			
DAS28-CRP CFB LSM (SE)	-0.99 (0.261)	-1.88 (0.249)*	-2.09 (0.184)***
Secondary endpoints			
ACR20 – n (%)	10 (41.7)	11 (44.0)	35 (71.4)*
ACR50 – n (%)	5 (20.8)	5 (20.0)	19 (38.8)
ACR70 – n (%)	4 (16.7)	1 (4.0)	10 (20.4)
TJC68 CFB LSM (SE)	-6.89 (1.846)	-12.08 (1.814)*	-12.33 (1.288)*
SJC66 CFB LSM (SE)	-6.18 (1.091)	-10.22 (1.082)*	-10.49 (0.759)**
PGA (VAS) CFB LSM (SE)	-25.35 (5.162)	-39.07 (5.130)	-38.55 (3.576)*
PatGA (VAS) CFB LSM (SE)	-21.66 (5.390)	-24.27 (5.285)	-29.67 (3.741)
Arthritis Pain (VAS) CFB LSM (SE)	-17.94 (5.101)	-23.50 (5.000)	-31.55 (3.535)*
HAQ-DI CFB LSM (SE)	-0.41 (0.109)	-0.35 (0.107)	-0.42 (0.076)
hsCRP CFB LSM (SE)	1.34 (3.717)	-5.26 (3.626)	-0.66 (2.574)
CDAI CFB LSM (SE)	-13.75 (2.709)	-24.06 (2.628)**	-25.51 (1.854)***
SDAI CFB LSM (SE)	-13.80 (2.664)	-25.06 (2.571)**	-26.90 (1.880)***

DAS28-CRP = disease activity score-28 for RA with C-reactive protein. ACR = American college of rheumatology. CFB = change from baseline. TJC68 = tender joint count of 68 joints. SJC66 = swollen joint count of 66 joints. VAS = visual analogue scale. PGA = physician's global assessment of disease activity. PatGA = patient's global assessment of disease activity. HAQ-DI = health assessment questionnaire – disability index. hsCRP = high sensitivity C-reactive protein. CDAI = clinical disease activity index. SDAI = simplified disease activity index. †Least squares mean (SE) are reported, unless otherwise stated. *p value < 0.05. **p value < 0.01. ***p value < 0.001.

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POS0308

LONG-TERM CLINICAL PROFILE OF FILGOTINIB (FIL) IN PATIENTS (PTS) WITH RHEUMATOID ARTHRITIS (RA) BY CARDIOVASCULAR (CV) RISK FACTORS: A POST HOC SUBGROUP ANALYSIS

Keywords: Rheumatoid arthritis, Cardiovascular disease, Targeted synthetic drugs

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Background: FIL is an oral Janus kinase 1 preferential inhibitor for the treatment of moderate to severe active RA. A previous pooled analysis reported long-term safety and efficacy for FIL 200 mg (FIL200) vs FIL 100 mg (FIL100) in pts aged ≥65 and <65 y.[1]

Objectives: To report updated long-term safety and efficacy in 4 subgroups of pts with RA (aged <65 y, ≥65 y, <65 y without CV risk, and ≥65 y or with CV risk), treated with FIL200 vs FIL100.

Methods: This *post hoc* analysis pooled data from phase 2 (DARWIN 1–3; NCT01888874, NCT01894516, NCT02065700) and phase 3 (FINCH 1–4; NCT02889796, NCT02873936, NCT02886728, NCT03025308) trials. Data for long-term extensions (LTEs) were as of May 2, 2022 (DARWIN 3), and May 6, 2022 (FINCH 4). Analyses were by age (<65 vs ≥65 y) and subgroup (<65 y without CV risk factor vs ≥65 y or ≥1 CV risk factor). CV risk factors were: family history of CV disease; history of dyslipidemia, diabetes mellitus or CV disease; hypertension, ischemic vascular conditions, peripheral vascular disease, extra-articular manifestations of RA; or ever smoked. The as-treated analysis set included data for pts receiving ≥1 FIL dose. Exposure-adjusted incidence rates (EAIRs)/100 patient-years of exposure (PYE) of selected adverse events (AEs), and % of pts achieving Disease Activity Score for 28 joints with C-reactive protein (DAS28-CRP) of <2.6 or ≤3.2 through Week 156 in FINCH 4, are reported.

Results: Baseline characteristics by age have been reported.[1] Baseline disease characteristics by age or CV risk factor were similar for disease severity and concurrent treatment. EAIRs for any treatment-emergent AEs (TEAEs) were generally higher in pts aged ≥65 (120.40) vs <65 y (97.86), and higher in pts aged ≥65 y or with CV risk (120.45) vs pts aged <65 y without CV risk (81.83). Pts aged ≥65 y, followed by the broader subgroup with CV risk factors (i.e. ≥65 y or ≥1 CV risk) had higher EAIRs of serious TEAEs and TEAEs leading to discontinuation vs other subgroups, indicating age is a key risk factor alongside other CV risk factors for developing AEs (data not shown). In pts aged ≥65 y, lower incidences of malignancies (excluding non-melanoma skin cancer [NMSC]), NMSC, herpes zoster (HZ) and TEAEs leading to death were observed with FIL100 than FIL200 (**Figure 1**). In the broader subgroup with risk factors (i.e. aged ≥65 y or ≥1 CV risk factor), EAIRs of AEs were generally lower vs pts aged ≥65 y, indicating greater influence of age. EAIRs of AEs for subgroups (aged <65 y without CV risk; ≥65 y or ≥1 CV risk) for FIL200 and FIL100 are shown (**Figure 1**). Rates of DAS28-CRP <2.6 or ≤3.2 in all subgroups (FINCH 4) were maintained with FIL100 and FIL200 to Week 156 (**Table 1**).

Conclusion: This *post hoc* analysis (in pts ≥65 y or with ≥1 CV risk factor) suggests that age is an important risk factor in the evaluation of the FIL200 safety profile. Future studies are needed to address the relative contribution of age to traditional CV risk factors. In FINCH 4, efficacy was maintained in all subgroups.

REFERENCE:

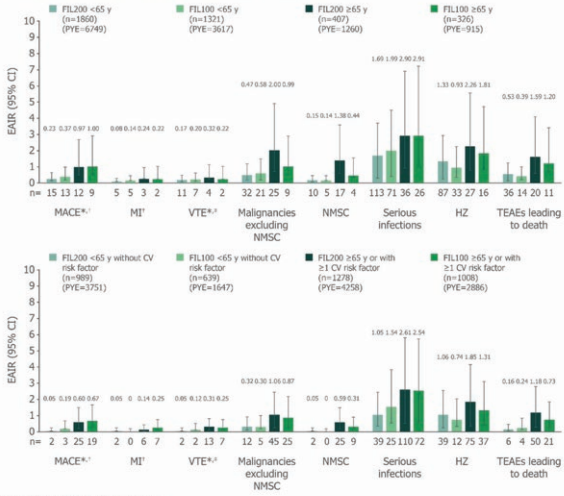
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Table 1. DAS28-CRP <2.6 and ≤3.2 from LTE baseline to Week 156, by age, CV risk and FIL dose (safety analysis set, observed values)

LTE Week	<65 y		≥65 y		<65 y without CV risk factor		≥65 y or with ≥1 CV risk factor	
	FIL100 n=944	FIL200 n=1256	FIL100 n=255	FIL200 n=274	FIL100 n=419	FIL200 n=640	FIL100 n=780	FIL200 n=890
	Patients achieving DAS28-CRP <2.6 (%)							
Baseline	46.8	54.5	50.8	59.5	48.2	57.4	47.3	54.0
12	49.0	61.3	55.8	62.0	48.8	65.0	51.3	58.9
24	50.5	62.7	55.2	66.3	48.7	64.7	52.9	62.3
48	51.1	64.2	57.8	65.7	51.6	67.2	53.0	62.4
108	54.2	65.0	58.8	70.2	52.3	67.8	56.7	64.3
156	52.9	64.2	58.9	63.5	51.6	62.9	55.4	64.9
	Patients achieving DAS28-CRP ≤3.2 (%)							
Baseline	66.9	73.7	69.8	74.8	68.8	76.3	66.8	72.2
12	66.8	75.7	71.9	74.4	67.3	80.2	68.2	72.1
24	70.4	78.0	70.4	79.2	70.2	80.4	70.5	76.7
48	71.2	79.1	73.3	78.2	71.4	82.3	71.8	76.4
108	70.4	79.8	75.8	82.0	71.2	82.5	71.6	78.3
156	72.0	81.7	77.8	82.6	70.9	81.6	72.6	82.4

No missing data imputation was performed.

Figure. EAIR of AEs by age and CV risk (safety analysis set, as treated)



EAIRs/100 PYE, censored at time of first event.
*MACE and VTE only included positively adjudicated events with a cutoff of April 3, 2022. †MACE comprised CV events leading to death, MI and stroke; for subcategories of stroke and MI, both fatal and non-fatal events were considered. For VTE subcategories, PE, DVT and 'other' were considered.
DVT, deep vein thrombosis; MACE, major adverse cardiovascular event; MI, myocardial infarction; PE, pulmonary embolism; VTE, venous thromboembolism.

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POS0309 TIME TRENDS IN GLUCOCORTICOID USE IN RHEUMATOID ARTHRITIS DURING THE BIOLOGICS ERA: 1999-2018

Keywords: Epidemiology, Treat to target, Rheumatoid arthritis

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Background: Clinical guidelines recommend minimizing glucocorticoid use among patients with rheumatoid arthritis (RA) and many new therapeutic options

in recent decades offer alternatives to glucocorticoids, but it is unknown whether glucocorticoid use has declined in patients with RA.

Objectives: To examine time trends in glucocorticoid use among patients diagnosed with rheumatoid arthritis (RA) during the biologic era.

Methods: A population-based inception cohort of RA patients diagnosed during 1999 - 2018 was followed longitudinally through their medical records until death, migration or 12/31/2020. All patients fulfilled 1987 and/or 2010 American College of Rheumatology classification criteria for RA. Glucocorticoid start and stop dates were collected along with dosages in prednisone equivalents. The cumulative incidence of glucocorticoid initiation and discontinuation adjusted for the competing risk of death was estimated. Cox models adjusted for age and sex were used to compare trends between time periods.

Results: The study population was comprised of 399 patients (71% females) diagnosed in 1999 – 2008 and 430 patients (67% females) diagnosed in 2009 – 2018. Glucocorticoid use was initiated within 6 months of meeting RA criteria in 66.7% of patients in 1999-2008 and 70.9% of patients in 2009-2018, corresponding to a 29% increase in hazard for initiation of glucocorticoids in 2009-2018 (adjusted hazard ratio [HR]: 1.29; 95% confidence interval[CI]: 1.09-1.53). Among glucocorticoid users, similar rates of glucocorticoid discontinuation within 6 months after glucocorticoid initiation were observed in patients with RA incidence in 1999 – 2008 and 2009 – 2018 (39.1% versus 42.9%, respectively), with no significant association in adjusted Cox models (HR: 1.11; 95% CI: 0.93-1.31). Even in the 2009-2018 cohort, a large proportion of patients with RA (52%) remained on glucocorticoids beyond 3 months, and 30% were still on glucocorticoids after 2 years. Older patients with RA were more likely to initiate glucocorticoids (HR 1.06 per 10 year increase in age, 95% CI 1.00-1.13) and less likely to discontinue glucocorticoids (HR 0.91 per 10 year increase in age, 95% CI 0.86-0.96). There was no difference in the initiation of glucocorticoids by sex. Although females had a higher discontinuation rate within the first 12 months, afterwards discontinuation rates of glucocorticoids were similar in females and males. Smokers were less likely to discontinue glucocorticoids compared to non-smokers (HR 0.65; 95% CI: 0.51-0.82).

Conclusion: More patients are initiating glucocorticoids early in their disease course now compared to previously despite the availability of biologics and other disease modifying antirheumatic drugs. The rates of glucocorticoid discontinuation are similar. A substantial proportion of patients remain on glucocorticoids for more than 3 months with a large proportion continuing use of glucocorticoidss even beyond 2 years. Real world use of glucocorticoids in patients with RA is not optimal or improving despite advances in RA therapy.

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Disclosure of Interests: Lisa Crowson: None declared, John M Davis III Grant/research support from: Pfizer, Andrew Hanson: None declared, Elena Myasoedova: None declared, Vanessa Kronzer: None declared, Ashima Makol Consultant of: Boehringer Ingelheim, Lynne Peterson: None declared, Delamo Bekele: None declared, Cynthia S. Crowson: None declared.

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POS0310

IDENTIFICATION OF NOVEL SMALL MOLECULES THROUGH UNBIASED HIGH-THROUGHPUT SCREENING FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

Keywords: Disease-modifying Drugs (DMARDs), Cytokines and chemokines, Rheumatoid arthritis

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Background: Rheumatoid Arthritis (RA) is an autoimmune chronic disease characterized by the inflammation of multiple joints, ultimately leading to deformity, pain and swelling [1]. Currently, no preventing therapy exists for RA, and 20%-30% of RA patients do not respond to available treatments [2]. These therapies target late phases of the inflammation process (e.g. cytokine signalling) [1], when the microenvironment is highly inflammatory and therefore challenging to control. Developing therapies targeting inflammation upstream (i.e. cytokine secretion) could have a positive impact on refractive RA. In this regard, we have previously identified through an unbiased high-throughput screening a total of 27 small molecules (23 novel and 4 repurposing drugs) with previously unknown anti-inflammatory capabilities.

Objectives: To validate the effects of these small molecules in peripheral blood mononuclear cells (PBMCs) under different types of activation stimuli, and to identify molecules capable of reducing the secretion of proinflammatory cytokines relevant in rheumatic diseases (namely TNF-α and/or IL-1β), employing a high-throughput approach.

Methods: First, different treatment methods were tested on PBMCs to identify those providing the best measuring window for the cytokines of interest. For that purpose, thawed PBMCs were exposed to PAMP (LPS) and/or DAMP (ATP) at different times, and cytokine secretion quantified. Subsequently, the potential cytotoxic effects of the small molecules were analysed at five different concentrations with several viability kits (fixable live/dead stains, AlamarBlue and ATPLite). Finally, for evaluating the anti-inflammatory potential of the small molecules the compounds were added to PAMP-only- and PAMP+DAMP-treated PBMCs at five concentrations, and viability and TNF-α and IL-1β secretion measured at four different time points.

Results: We found that, at different pharmacological concentrations (nM-μM), treatment conditions and time points, the compounds have no cytotoxic effects in PBMCs, with the only exception of one compound being toxic at the highest concentration tested. We then compared the levels of cytokine secretion with vehicle alone *versus* each of the small molecules and considered that a small molecule was of interest if induced at least a 20% reduction on the secretion levels of the cytokine of interest. We observed several combinations of effects (molecules acting on IL-1B, TNF-α or both, or only showing effect with PAMP-only or PAMP+DAMP treatment), suggesting that our molecules target different components of the intracellular machinery. For example, several molecules diminished TNF-α secretion after PAMP treatment, but not when the DAMP was added to the culture, and viceversa. The Figure shows representative results of compounds #7, #28 and #29, which reduce the secretion of TNF-α in PAMP-only treated PBMCs. We then tested the small molecules with the stronger effect at the lowest concentration in PBMCs from treatment-naïve RA patients, analysing both the intracellular and extracellular cytokine levels by flow cytometry and ELISA, respectively.

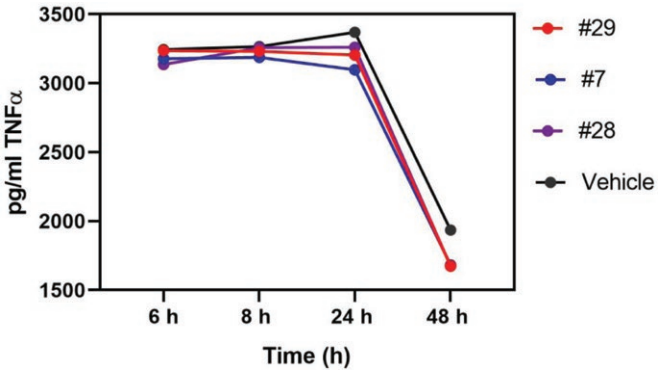


Figure 1. representative example of three novel small molecules (named #7, #28 and #29) capable of reducing the secretion of TNF-α in PAMP-only treated PBMCs at different time points.

Conclusion: We found that our novel and repurposing small molecules showed no cytotoxicity effects in primary PBMCs, and that they induced a reduction on proinflammatory cytokine secretion from PAMP-only and PMAP+DAMP-treated PBMCs. Further characterization of these small molecules, through the identification of their mechanism of action and molecular target, will open new avenues in the treatment of rheumatic diseases, by providing novel drugs targeting novel pathways and that could be administered orally, improving quality of life and adherence to treatment.

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POS0311 IL-6 INHIBITORS AND JAK INHIBITORS: WHICH OF THESE DRUGS, INHIBITING A COMMON PATHWAY, HAS AN ADVANTAGE IN PREVENTING BONE DESTRUCTION IN RA?

Keywords: bDMARD, Targeted synthetic drugs, Rheumatoid arthritis

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Background: To date, there are no head-to-head clinical trials directly comparing the effects between IL-6i and JAKi on bone destruction in RA. In recent years, a series of JAK inhibitors (JAKi) have been introduced, all of which have JAK1 inhibitory activity, and inhibition of IL-6 signaling plays an important role in their pharmacological actions. IL-6 inhibitors (IL-6i) have been also commonly used for rheumatoid arthritis (RA), and several anti-receptor antibodies are in clinical application. Recent studies have revealed the molecular basis of the immune cell-fibroblast-bone triad interactions in RA bone destruction[1-3].
Objectives: To examine changes in peripheral blood gene expression after IL-6i or JAKi treatment, which inhibit common pathways, and to estimate their respective effects on the bone immune system.
Methods: Peripheral blood gene expression changes in 38 RA patients (Tocilizumab (TCZ)=13, Tofacitinib (TOF)=15, Baricitinib (BAR)=10) were analyzed before and 3 months after the initiation of treatment using next generation sequencing. Changes in gene expression of molecules involved in bone immunity were analyzed before and after each treatment.
Results: Comparison of L-6i and JAKi showed that JAKi treatment significantly suppressed RANKL expression in peripheral blood. At the same time, significant suppression of RANK, ETS1, and IL-34 gene expression was also observed with JAKi treatment. Comparison of TOF and BAR treatment showed significant suppression of IL-4 expression in TOF and significant suppression of MMP-2 and IL-12 expression in BAR.
Conclusion: JAKi suppressed RANKL expression significantly compared to IL-6i, suggesting that JAKi is more potent than IL-6i in suppressing bone destruction. Furthermore, assuming that the promoter regions of RANK in synovial osteoclasts and ETS1 in fibroblasts are similar to those in peripheral blood, the following prediction emerges. Namely, JAKi suppresses RANK and ETS1 expression more than IL-6i, suggesting that JAKi may be favorable for preventing bone destruction in terms of (1) suppressing osteoclast differentiation and (2) suppressing tissue-destructive fibroblast generation.

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POS0312 WITHDRAWN

POS0313 INVESTIGATING THE RELATIONSHIP BETWEEN METHOTREXATE ADHERENCE AND BIOLOGIC RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: bDMARD, Rheumatoid arthritis, Disease-modifying Drugs (DMARDs)

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Background: In rheumatoid arthritis (RA), methotrexate (MTX) adherence is highly variable and typically suboptimal, with reports of adherence 59% (underuse) to 107% (overuse) [1]. Non-adherence to MTX may explain non-response and the need to start or switch to biologic therapies. Concomitant use of MTX is associated with reduced anti-drug antibodies in patients prescribed biologics such as adalimumab, therefore promoting MTX adherence should be a priority [2]. MTX biochemical adherence can be objectively measured using HPLC-SRM-MS [3]
Objectives: To investigate the biochemical MTX adherence in RA patients commencing a biologic and its association with EULAR response.

Methods: This analysis used data from the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS), a one-year UK prospective cohort study of patients with RA commencing a biological drug. Prior to biologics commencement, demographic and clinical data were collected. Serum samples were sampled for MTX biochemical adherence at baseline (pre-treatment of biologics), then 3 and 6 months post-first dose. MTX concentration was measured by HPLC-SRM-MS. Time to processing variable was also noted by calculating the difference between the time the sample was processed and the time the blood was sampled. Adherence was calculated based on a cut-off limit taken from a validated MTX adherence assay. A chi-square test was used to investigate the association between adherence and biologic response. Linear regression investigated the relationship between MTX level and time to processing.

Results: 582 patients were included; 75% female, mean (S.D.) age 58 (12) years. Table 1 summarises the baseline characteristics for all patients. There was no significant relationship between adherence at pre-treatment with EULAR response at 6 month (p=0.17). However, those who were biochemically adherent to MTX at 6 months had a statistically significantly better response to biologic therapy (p=0.04). It is also found that despite being a responder to the biologic, 37% were non-adherent to MTX. However, there was no significant relationship between MTX level and time to processing thus it is unlikely to be due to the stability of MTX in blood over time.

Conclusion: Patients who were adherent to MTX, assessed biochemically, at 6 months after starting biologic therapy had better response to treatment, which may further strengthens the evidence to support the importance of concomitant use of MTX with biologics.

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Table 1. Baseline characteristics of 582 patients.

	Adherent (63%)			Non-Adherent (37%)		
Female gender (%)	71%			76%		
Age (years)	58 (20-83)			57 (18-84)		
Biologics (%)	**Drug name:**	**n**	**%**	**Drug name:**	**n**	**%**
	Etanercept (and biosimilars)	72	19.55	Etanercept (and biosimilars)	35	16.35
	Adalimumab (and biosimilars)	163	44.36	Infliximab (and biosimilars)	1	0.47
	Rituximab (and biosimilars)	21	5.73	Adalimumab (and biosimilars)	65	30.37
	Abatacept	77	20.98	Rituximab	24	11.21
	Golimumab	4	1.09	Other biologic	2	0.94
	Tocilizumab	7	1.91	Abatacept	54	25.23
	Certolizumab	7	1.91	Golimumab	1	0.47
	Tofacit(Xeljanz)	3	0.82	Tocilizumab	15	7.01
	Baricitinib (Olumiant)	13	3.54	Certolizumab	4	1.87
				Tofacit(Xeljanz)	1	0.47
				Baricitinib (Olumiant)	13	6.07
	TOTAL	**367**	**100**	**Total**	**215**	**100**

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POS0314

CAN METHOTREXATE INFLUENCE SEXUAL DYSFUNCTION IN MALE PATIENTS: ANALYSIS OF THE IIEF5 QUESTIONNAIRE AND HORMONAL STATUS

Keywords: Safety, Rheumatoid arthritis, Disease-modifying Drugs (DMARDs)

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Background: Methotrexate (MTX) is the anchor drug of Rheumatoid Arthritis (RA) treatment. It is a safe and handy drug, but it has several well-known side effects mainly not severe such as nausea, fatigue, alopecia, or an increase in transaminases. In the last years, sexual dysfunction has been reported as a rare adverse effect of MTX therapy.

Objectives: To explore this, the aim of this study is to evaluate the impact of MTX on erectile function in male patients through the IIEF5 questionnaire and hormonal dosage.

Methods: Male patients affected by inflammatory arthritis (Rheumatoid Arthritis or Psoriatic Arthritis [PsA]) according to the 2010 EULAR/ACR diagnostic criteria for RA and the 2006 CASPAR criteria for PsA and treated with chronic MTX were enrolled. Age-matched patients affected by chronic arthritis not treated with MTX were enrolled as control. Each patient underwent blood collection for a complete serum sexual hormone evaluation. IIEF5 questionnaire which consists of 5 items with a maximum score of 25 was administered to the patients.

Results: 109 patients were included, 77 in the MTX group (Group A) and 32 in the control group (Group B). The clinical and demographic features of both groups are reported in Table 1. Among the MTX group, 61 have a RA diagnosis, while the remaining 18 were affected by PsA. The median disease duration of RA and PsA patients was respectively 108 months (IQR 138) and 66 months (IQR 114). The median MTX dose was 10 mg (IQR 7.5) with a median MTX duration therapy of 8 years (IQR 17). The total IIEF5 score was lower in patients treated with MTX compared to the control group without reaching a statistically significant result (19 [IQR 11] *versus* 20 [IQR 7.7]; p=0.15, Graph 1A). However, when comparing the IIEF5 score between MTX exposed versus non-exposed patients stratifying by years of treatment, the total IIEF5 score of patients treated with MTX ≥ 5 years was statistically significantly lower when compared to those non MTX- exposed patients (17 [IQR 15] *versus* 20 [IQR 7.7]; p=0.04) and compared to those treated for < 5 years (17 [IQR 15] *versus* 20 [IQR 7]; p=0.01) (Graph 1B).

Table 1.

		Group A	Group B	p
Age	**Median (IQR)**	54 (28)	53.5 (20.5)	0.50
BMI		25.4 (3.85)	25.6 (5.8)	0.78
Arterial Hypertension	**(N%)**	23 (29.1)	23 (71.8)	**<0.0001**
Hypercholesterolemia		18 (33)	11(34.3)	0.20
Type 2 diabetes		3 (3.8)	6 (18.7)	**0.008**
Hyperplasia Prostatic		2 (2.5)	0 (0.0)	0.99
Depression/Psychotropic Therapy		8 (10.1)	5 (15.6)	0.51
Marriage		53 (67)	23 (71.8)	0.65
Alcohol (N° units/ day)		1 (2.5)	1 (2.0)	0.71
Children (N°)		1 (2)	2 (2)	0.73
Total Testosterone Median	**Median (IQR)**	16,3 (8.2)	14,8	**0.04**
SHBG		53,9 (29,15)	47.6	0.07
LH		5,6 (4,15)	5.35	0.59
FSH		5,2 (5,30)	6.65	0.98
E2		24 (13,25)	20	**0.01**
PRL		7 (3,55)	8.05	0.52
DHEA		4,7 (4,1)	3.85	0.64
GH		94 (19)	98	0.34

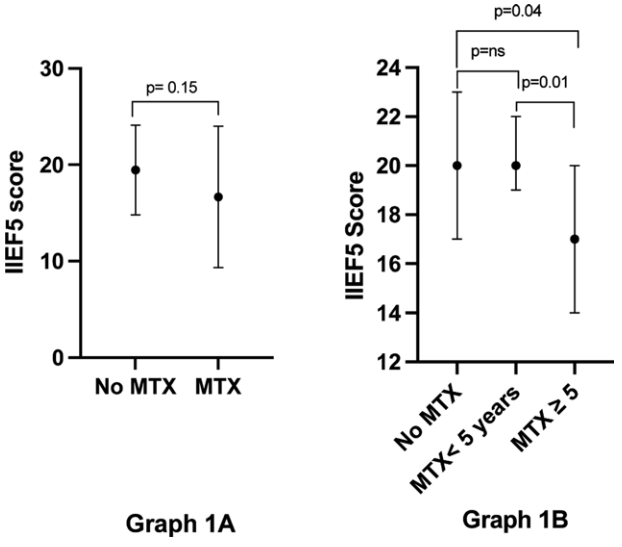


Figure 1. A) Comparison of IIEF5 score in MTX exposed versus non-exposed patients. B) patients stratified by age (< 5 years and ≥ years).

In the univariate analysis, a negative correlation between the total IIEF5 score and MTX exposure (years) has been identified (r= - 0.20 CI [-0.38 - -0.04]; p= 0.039). Age was the variable whit the strongest negative association with the IIEF5 score (r= - 0,42 CI [-0.57 to - 0.25]; p< 0.0001). MTX exposure was still associated with a lower IIEF5 score when adjusted for age (β Estimate= -2,63; CI [-5,13 to -0,13]; p=0,0391). Among the other variables, LH (r=-0,24; CI [-0,42 to -0,04]; p=0,01), FSH (r=-0,21; CI [-0,39 to -0,006]; p=0,04) and E2 (r=-0,21; CI [-0,40 to -0,009]; p=0,03) negatively correlated whit IIEF5 score while DHEA, was the only with a weak positive association (r=0,22; CI [0,02 to 0,40]; p=0,03). Patients affected by arterial hypertension and hypercholesterolemia showed lower scores compared to non-affected patients (p=0.04; p=0.03; p=0.045). In the multivariate analysis, age was the only factor associated with a decrement of IIEF5-score (β -0,21 [-0,32 to -0,094]; p=0,0005).

Conclusion: Long-term MTX exposure was associated with sexual dysfunction reported by a lower IIEF5 score in male patients adjusted for age. The preliminary results need to be confirmed in larger prospective studies.

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Disclosure of Interests: None Declared.

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POS0315 ACUTE CARDIOVASCULAR EVENTS RISK IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB OR TNF INHIBITORS, A NATIONWIDE COHORT STUDY: RELATION STUDY

Keywords: Rheumatoid arthritis, Targeted synthetic drugs, Real-world evidence

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Background: Patients with IMID, and notably patients with rheumatoid arthritis (RA), are at increased risk of major adverse cardiovascular event (MACE) compared with the general population [1,2]. It is hence paramount to assess the impact of biological or targeted DMARD (e.g., tofacitinib and TNFi) on the risk of MACE in patients already at-risk, particularly in the context of ORAL Surveillance which showed a higher risk MACE with tofacitinib, in comparison with TNFI, in RA patients [3].

Objectives: To assess the impact of tofacitinib and TNFi on the risk of MACE in patients with RA treated in real-world clinical practice.

Methods: The RELATION study is a retrospective observational cohort study using the French nationwide healthcare database (SNDS). Patients aged 18 years or older, affiliated to the national health insurance with a diagnosis of RA and initiating tofacitinib after November 1, 2017 or TNFi after January 1, 2010 (including adalimumab, etanercept, or other TNFi, without previous exposure to tofacitinib) were followed from treatment initiation to December 31, 2020. Patients with a previous history of MACE in the 4 years preceding cohort entry were excluded. All MACE excluding cardiovascular (CV) death were defined by the first hospitalization for MACE during follow-up. Comorbidities and traditional CV risk factors were identified using hospitalizations, procedures, or medication dispensing in the 4 years prior cohort entry. The unadjusted incidence rate (IR) of MACE excluding CV death was assessed in patients initiating either tofacitinib or a TNFi (with associated 95% confidence intervals (95% CI)). A 1:3 PS matching was conducted to balance the baseline characteristics of patients initiating tofacitinib and TNFi. Cox proportional hazards regression models were used to compare the risk of MACE with tofacitinib vs TNFi during the follow-up period.

Results: Between 2010 and 2020, a total of 39,578 patients with RA were included in the study. Among these, 2,811 initiated tofacitinib and 36,767 initiated a TNFi (adalimumab: 10,621, etanercept: 16,512, other TNFi: 9,634). Patients had a mean age of 53 years at cohort entry, and 72% to 81% were women. Around 61% of the cohort had at least one CV risk factor (66.3%for tofacitinib compared to 60.9% for TNFi). The two major co-medications at treatment initiation in the two groups were methotrexate (60.9%) and corticosteroids (50.8%).

After PS matching, the tofacitinib cohort included 2,628 patients, and the TNFi cohort included 7,884 patients. Over a median follow-up period of 11.21 months (tofacitinib: 8.54 months, TNFi: 12.43 months), 25 incident MACE occurred in the tofacitinib group (IR: 9.86 (6.66–14.60) per 1,000 patient-year (PY)) and 159 occurred in the TNFi group (9.59 (8.21–11.20)). The risk of MACE (overall) was similar with tofacitinib vs TNFi (adjusted HR 1.06 [95% CI 0.68, 1.64]; p=0.8127). Similar results were found for ischemic heart disease (HR 0.71 [95% CI 0.35, 1.44]; p=0.3433) and cerebrovascular disease (HR 1.41 [95% CI 0.73, 2.73]; p=0.3116). For peripheral artery disease, the number of events was too low to perform these analyses.

Conclusion: In this large population-based study, tofacitinib was not associated with an increased risk of MACE in comparison with TNFi in patients with RA treated in real-world settings. Studies with longer follow-up durations may be necessary to understand the long-term implications of tofacitinib vs TNFi on the risk of MACE.

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POS0316 SURVIVIN REGULATES T CELL RESPONSES THROUGH DEPOSITION OF HISTONE H3 MARKS AND MODULATES RESPONSE TO TREATMENT WITH JAK-INHIBITORS

Keywords: Targeted synthetic drugs, Adaptive immunity, Rheumatoid arthritis

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Background: Multiple genetic polymorphisms are associated with high risk for rheumatoid arthritis (RA) [1]. The importance of epigenetic processes has been postulated, but precise molecular mechanisms behind these associations remain largely unexplored. Survivin is an important player in RA, which has been recently shown essential for IFNg signaling in CD4 T lymphocytes acting in partnership with IRF1 [2].

Objectives: We study how survivin-dependent epigenetic deposition of histone H3 tails in RA risk loci affects function of $CD4^+$ T cells and response to JAK inhibition.

Methods: Chromatin of $CD4^+$ cells (n=12) was immunoprecipitated with antibodies to histone H3K27ac, H3K4me3, and survivin, and sequenced (ChIP-seq, Illumina). Parallel ChIP-seq and RNA-seq was done in $CD4^+$ cells treated with survivin inhibitor YM155. Peaks with change >30% in deposition of H3K27ac and/or H3K4me3 upon YM155-treatment were annotated to the genomic regulatory elements (RE) via GeneHancer database. Single nucleotide polymorphism (SNP) related to RA risk were identified within those RE. $CD4^+$ T cell transcriptomics by RNA-seq was done in 24 random RA patients and in 59 RA patients treated with MTX (n=18), TNFi (n=10), JAKi (n=24) and having no DMARDs (n=7). The genes differentially expressed (DEG, nominal p<0.05) in $BIRC5^{hi}$ and JAKi-treated $CD4^+$ cells were identified by DESeq2 (R-studio, Bioconductor).

Results: Deposition of 15% (1705/11152) of H3K4me3 and 17% (1943/11530) of H3K27ac peaks changed >30% upon survivin-inhibition. Approximately 50% of these peaks overlapped with survivin peaks. The change in H3K4me3 peaks was significantly larger if the peak colocalized with survivin peak. These peaks were located within 228 RE, 28 of these RE contained 52 RA risk SNPs. Among others, changeable peaks were accumulated within ICOS/CTLA4/CD28 locus and contained 7 SNPs. Majority of genes connected to the SNP-containing RE (110/153 genes) were transcriptionally different in $BIRC5^{hi}CD4^+$T cells and participated in the regulation of immune system (GO:0002682, FDR=4.3e-4), regulation of IL2 production (GO:0032663, FDR=0.019), TNF mediated signaling (GO:0033209, FDR=5.4e-3). These SNP-RE connected genes formed three independent clusters 1) TCR receptor co-stimulators (CD40, ICOS, CTLA4, CD28, CD244, TRAF6 and TBX21, SLAMF1, TNFRSF9), 2) connected to the LCK interacting transmembrane adaptor 1 (LIME1, SLC2A4RG, ZGPAT, GMEB2, TNFRSF6B, RTEL1) and 3) heat-shock proteins (HSPD1, HSP90AB1, HDAC7, KPNB1). The clusters were functionally connected to survivin partners IRF1 and SMAD3. Notably, transcription of CD28, ICOS, and SLAMF1 functionally connected to IRF1, and CHERP, HDAC7, PRPF6 and SRSF10 functionally connected to SMAD3 were significantly changed (all, nominal p<0.05) in CD4+ cells upon survivin inhibition by YM155. Since survivin mediates IFNg-dependent processes [2], we analyzed transcription of 110 SNP-RE connected DEG in $CD4^+$ cells of JAKi-treated RA patients. We found that DEG in the IRF1 and SMAD3 clusters were inversely affected by JAKi, e.g., IRF1-related CD28, ICOS, and SLAMF1 upregulated after survivin inhibition were suppressed

by JAKi, while SMAD3 related CHERP, PRPF6 down-regulated by survivin inhibition were upregulated in CD4+ cells of JAKi-treated patients. Effect of JAKi in the IRF1-related genes was executed only in BIRC5^{lo}CD4^{+} cells and remained unchanged in BIRC5^{hi}CD4^{+} cells.

Conclusion: This study shows that survivin contributes to deposition of histone H3K27ac and H3K4me4 marks in proximity of RA-risk genes and control immune system regulators in CD4 T cells. JAK-inhibitors operate downstream of survivin and high levels of survivin may impede JAKi-treatment.

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Disclosure of Interests: None Declared.

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Early RA and comorbidities

POS0317 IT'S TIME TO END THE STIGMA SURROUNDING INFECTIOUS MUSCULOSKELETAL DISEASES: A Q-METHODOLOGY STUDY

Keywords: Patient reported outcomes, Infection-related RMDs

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Background: Although it still remains a rare disease, spondylodiscitis has been on the rise in the past decades. Early diagnosis can be difficult, but Improved diagnostic techniques and modern treatments have reduced patient mortality. However, the management of these patients comes up against a certain number of issues, including stigma. This stigmatization of the spondylodiscitis patient represents a real problem on the daily life. This considerably hinders his reintegration.

Objectives: The aim of this study is to explore prevailing prespectives concerning stigma among patients treated for spondyloscitis and so to identify potential determinants of these beliefs.

Methods: A Q- methodology study was carried out on patients treated for spondylodiscitis over a two-year period at a single spine center. The socio-demographic data, clinical, radiological, biological and therapeutic parameters were collected. Participants ranked 20 opinion statements about the impact of their disease on their daily life (social life, mental health, professional life, sex life) on an agreement scale. A by-person factor analysis identified common patterns in the rankings. These patterns represent the different viewpoints among the patients. Data from interviews, in which they explained their ranking, was used to further interpret the viewpoints. All data was collected after patient consent and was analyzed using the SPSS statistical package.

Results: Thirty patients were selected for the study, with a sex ratio (M/ F) of 1.57. Their average age was 56 [18_73].

The analysis revealed four viewpoints. At least 2 participants were significantly associated with each factor ($p<0.05$).

1)« The subject of stigma must be seriously addressed by health professionals and authorities »

2)« lack of self-esteem has limited my social life »

3)« challenged doubly, both by the disease and by the stigma associated with it »

4)« physical changes make me feel less confident about sex ».

In our series, there were positive correlations between gender, VAS (visual analog scale) spinal pain, presence of spinal syndrome and viewpoint 2: p=0.035, p=0.04 and p=0.008, respectively. In the same way, there were positive correlations between high pain catastrophizing scores and viewpoint 3: p=0.02. Viewpoint 4 was associated to depression thoughts, according to the hospital anxiety and depression scale: HAD: p=0.03.

Conclusion: We identified 4 viewpoints on the impact of spondylodiscitis on daily life. In fact, we have noticed that this disease affects relationships and self-confidence. It can lead also to the exclusion of the individual. Therefore, Various strategies are needed to combat the stigma related to infectious musculoskeletal diseases such as spondylodiscitis, which remains a frequent problem with multiple consequences.

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Disclosure of Interests: None Declared.

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POS0318 DISTINCTION AND PROGNOSIS OF EARLY ARTHRITIS PHENOTYPES: AN ANALYSIS IN THREE EUROPEAN COHORTS

Keywords: Real-world evidence, Prognostic factors, Rheumatoid arthritis

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Background: Patients (pts) with early arthritis (EA) may present with more or less classical inflammatory disease phenotypes. It is difficult to discern at presentation those who will evolve to a well-defined phenotype (e.g., rheumatoid arthritis; RA) from those who will remain undifferentiated or even will have non-inflammatory disease. The 2010 RA classification criteria were developed to promote early identification of RA and were validated against the external standard of 'expert diagnosis', a well-known approach that -however- may lead to circularity.

Objectives: Obtain a more unbiased insight into the 'Gestalt' of EA, by circumventing expert opinion, and investigating the latent phenotypes underlying EA and whether there are differences in prognosis across these phenotypes over time.

Methods: Three cohorts of pts with EA (Reade, ESPOIR and EAC) were analyzed separately. Clinical data were collected up to 12 (ESPOIR), 13 (Reade) or 24 (EAC) years. Hands and feet radiographs were scored, according to the Sharp van der Heijde method (SvdH) up to 10 (ESPOIR), 13 (Reade) and 14 (EAC) years. Latent class analysis was used to estimate the latent (i.e., unobserved) classes of EA. Each class was labelled by us, according to its most prominent features. Outcomes were functional disability, quantified by the health assessment questionnaire (HAQ), quality of life (QoL) quantified by the short form 36 physical (SF36 PC) and mental (SF36 MC) components (in ESPOIR) and radiographic damage (SvdH score). The association between class-membership and each outcome over time was tested in multivariable GEE models.

Results: In total, 390 (Reade), 798 (ESPOIR) and 1878 (EAC) pts were included. In ESPOIR, 4 latent classes could be distinguished (Figure 1); Two classes had a high likelihood of symmetrical polyarthritis. One of these, labelled as autoimmune inflammatory polyarthritis (AIPA), had a high likelihood of acute phase reactants (APR)-elevation and autoantibody (AB)-positivity, while the other (mild inflammatory polyarthritis; MIPA) had not. The third class had fewer joints involved (oligoarthritis of upper limbs; OAUL) and the fourth included pts with oligoarthritis of the lower limbs (OALL). All classes, except the latter, were also identified in Reade. In the EAC, OAUL could further be divided into autoimmune OAUL (AIOAUL) and mild-inflammatory OAUL (MIOAUL). In all cohorts, SvdH-scores were consistently worse in classes with AB and APR present (AIPA) than in those without. An example from the EAC cohort shows pts in the MIPA-class had on average 18.5 SvdH-units less than patients in the AIPA-class (Table 1). However, the mean HAQ- and SF36-scores were remarkably similar over time across all classes. The few statistically significant effect-sizes were small and of no clinical relevance.

Conclusion: EA pts presenting with elevated (APR and autoantibodies) markers, the phenotype most consistent with the 'classic RA-construct', develop more radiographic damage than those without these markers. However, pts with more damage do not necessarily have worse physical function or QoL (measured up to 24 years). These results may justify immediate DMARD-treatment for preventing damage for the proportion of EA-patients that present with an AIPA-phenotype, but not necessarily for all others.

Table 1. Prognosis of EA phenotypes

	HAQ (0-3) β (95% CI)	SF36 PC (0-100) β (95% CI)	SF36 MC (0-100) β (95% CI)	SvdH (0-448) β (95% CI)
		Reade		
MIPA vs AIPA	**0.2 (0.1; 0.3)**	*	*	**-7.0 (-9.4; -4.5)**
OAUL vs AIPA	0.0 (-0.2; 0.1)	*	*	-2.7 (-5.9; 0.5)
		ESPOIR		
MIPA vs AIPA	0.0 (-0.1; 0.1)	-0.2 (-1.5; 1.1)	-0.2 (-1.8; 1.3)	**-4.3 (-6.5; -2.2)**
OAUL vs AIPA	**-0.1 (-0.1; 0.0)**	0.5 (-0.5; 1.4)	-0.7 (-2.0; 0.5)	-0.8 (-3.1; 1.5)
OALL vs AIPA	0.0 (-0.2; 0.1)	-1.0 (-3.4; 1.4)	-1.7 (-5.1; 1.7)	**-4.5 (-6.8; -2.2)**
		EAC		
MIPA vs AIPA	**-0.1 (-0.2; 0.0)**	*	*	**-18.5 (-25.2; -11.9)**
AIOAUL vs AIPA	-0.1 (-0.2; 0.0)	*	*	-6.3 (-15.1; 2.6)
MIOAUL vs AIPA	0.0 (-0.1; 0.1)	*	*	0.7 (-5.3; 6.7)
OALL vs AIPA	-0.1 (-0.2; 0.1)	*	*	-6.8 (-19.2; 5.5)

ESPOIR: models adjusted for age, gender, DAS28, NSAIDs, GCs, csDMARDs, bDMARDs. Reade and EAC: age, gender and DAS28. * Not available.

Figure. Latent class analysis models in Reade, ESPOIR and EAC

	Reade (N=390)				ESPOIR (N=798)				EAC (N=1878)				
	AIPA (P*=0.71)	MIPA (P*=0.15)	OAUL (P*=0.13)	OALL (P=0.00)	AIPA (P*=0.50)	MIPA (P*=0.15)	OAUL (P*=0.33)	OALL (P*=0.02)	AIPA (P*=0.26)	MIPA (P*=0.23)	AIOAUL (P*=0.08)	MIOAUL (P*=0.21)	OAUL (P=0.29) OALL (P*=0.22)
Arthritis of small joints	1.00	1.00	0.98		1.00	1.00	0.99	0.00	1.00	0.98	0.73	1.00	0.00
(Sub)acute onset	NA	NA	NA		0.60	0.56	0.57	0.54	0.57	0.59	0.37	0.66	0.71
Symmetric arthritis	0.98	1.00	0.41		0.99	0.99	0.42	0.50	0.96	1.00	0.45	0.05	0.29
Morning stiffness ≥ 60 min.	0.56	0.89	0.39		0.62	0.48	0.39	0.46	0.66	0.48	0.45	0.21	0.20
Arthritis in upper limbs	1.00	0.98	0.87		1.00	1.00	1.00	0.22	0.99	0.91	0.88	0.82	0.09
Polyarthritis	0.98	1.00	0.00		0.89	1.00	0.02	0.00	0.96	0.78	0.00	0.13	0.00
ESR and/or CRP elevated	0.75	0.48	0.41		1.00	0.00	0.65	0.81	0.86	0.63	0.65	0.55	0.65
Positive RF and/or ACPA	0.74	0.00	0.59		0.61	0.35	0.48	0.08	0.63	0.17	0.71	0.17	0.12
Family history of RA	0.39	0.19	0.42		0.13	0.21	0.13	0.15	0.28	0.19	0.25	0.19	0.14
≥3 joints erosion score ≥1†	0.08	0.00	0.03		0.02	0.00	0.02	0.00	0.55	0.00	0.58	0.02	0.03
≥ 1 comorbidity	0.01	0.00	0.00		0.44	0.49	0.38	0.25	0.41	0.28	0.42	0.34	0.31
Current smoker	0.28	0.28	0.29		0.46	0.47	0.48	0.49	0.25	0.24	0.23	0.27	0.25
Overweight	0.56	0.65	0.40		0.47	0.37	0.41	0.28	0.39	0.29	0.33	0.33	0.24

The figure displays the main results of the LCA separately in each cohort. * Probability of the latent class. Values in cells are the conditional probability for each feature within each latent class (range: 0–1). Red: highlights dominant features (probability >50%) within each class. † Sharp van der Heijde erosion score ≥1 in ≥ 3 joints according to ≥2 out of 3 central readers in ESPOIR and according to one central reader in Reade and EAC. **AIPA, autoimmune inflammatory polyarthritis; MIPA, mild inflammatory polyarthritis; OAUL, oligoarthritis of upper limbs; OALL, oligoarthritis of lower limbs; AIOAUL, autoimmune inflammatory oligoarthritis of upper limbs; MIOAUL, mild inflammatory oligoarthritis of upper limbs.**

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POS0319 THE COURSE OF SYMPTOMS IN CLINICALLY SUSPECT ARTHRALGIA AND ITS RELATION WITH SUBCLINICAL JOINT-INFLAMMATION DURING PROGRESSION TO RA: IS IT SIMILAR IN ACPA-POSITIVE AND ACPA-NEGATIVE DISEASE?

Keywords: Patient reported outcomes, Imaging, Rheumatoid arthritis

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Background: ACPA-positive and ACPA-negative RA have differences in genetic and environmental risk factors and in the severity of the disease course after diagnosis. However, the clinical presentation at RA-diagnosis is similar, as is the clinical presentation in the at-risk stage of clinically suspect arthralgia (CSA). We hypothesized that these clinical similarities at the end of the trajectory of RA-development imply a shared path in symptom development and progression before diagnosis. So far the course of symptoms during progression from CSA to RA and the association with the course of subclinical joint-inflammation is unknown.
Objectives: We studied the course of cardinal symptoms and subclinical joint-inflammation and the longitudinal relation in ACPA-positive and ACPA-negative disease. Relations were also studied in CSA-patients who did not develop RA.
Methods: CSA-patients from the Leiden CSA-cohort (n=664) and the placebo-arm of the TREAT EARLIER trial (n=117) were followed on development of inflammatory arthritis (IA) at physical examination, during which 136 patients developed IA and 645 did not. Symptoms of morning stiffness, pain and fatigue (with a numerical rating scale: 0-100) and presenteeism (productivity loss at work with the WPAI-questionnaire: 0-100%) were assessed at baseline and 4/12/24 months thereafter. Subclinical joint-inflammation (sum of synovitis/tenosynovitis/osteitis) was assessed at baseline and upon IA-development with contrast-enhanced 1.5T MRI of hand/foot. Linear and Poisson mixed models were used.
Results: Of the patients with IA-development, 66 (49%) were ACPA-positive. Both in ACPA-positive and ACPA-negative patients, symptoms (morning stiffness, presenteeism, fatigue) and subclinical joint-inflammation increased towards IA-development, and decreased or stabilized in patients without IA-development (Figure 1A). The course of pain, morning stiffness and presenteeism were significantly associated with the course of subclinical joint-inflammation in ACPA-positive CSA-patients during progression to RA. In ACPA-negative CSA-patients developing ACPA-negative RA, these effect sizes were smaller and not statistically significant (Figure 1B). Although the group-size of ACPA-positive CSA-patients not developing RA was smaller (n=47) than that of ACPA-negative non-progressing CSA (n=555), also here the decrease in symptoms seemed to have a stronger relationship with decreasing joint-inflammation in ACPA-positive than in ACPA-negative patients.
Conclusion: The severity of symptom development before diagnosis in ACPA-positive RA relates more strongly to increasing subclinical joint-inflammation than in ACPA-negative RA. This points towards differences in processes underlying the disease burden in ACPA-positive and ACPA-negative RA.

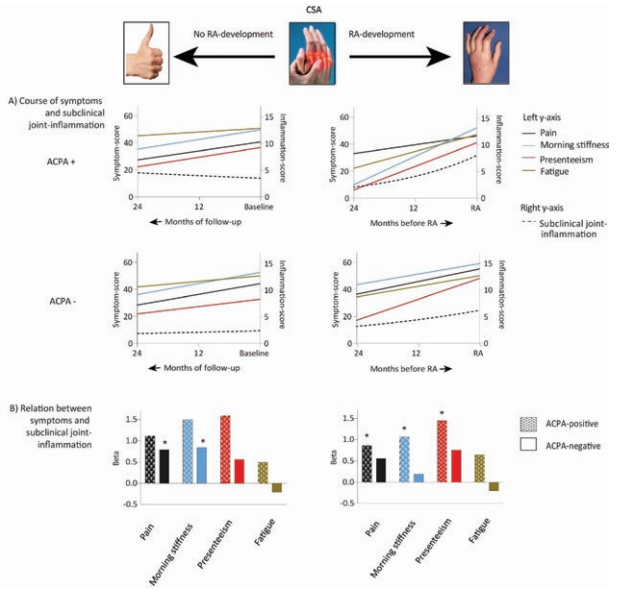


Figure 1. A) The course of symptoms and subclinical joint-inflammation in CSA-patients without and with RA-development and B) their longitudinal relation for ACPA-positive and ACPA-negative patients

Legend: A) Lines depict the course of symptoms (left y-axis) and subclinical joint-inflammation (right y-axis). This is shown separately for CSA-patients who did not develop RA; Figure A left, and those who did develop RA; Figure A right. B) Demonstrated are the effect sizes of 1 point increase in subclinical joint-inflammation over time on increase in symptoms over time. E.g. a beta of 0.8 for pain in ACPA-positive patients developing RA, implies that 1 point increase in inflammation over time gives 0.8 point more pain during the course towards RA-development.
Abbreviations: ACPA= anti-citrullinated protein antibodies; CSA= clinically suspect arthralgia; RA=rheumatoid arthritis.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0320 ARTIFICIAL INTELLIGENCE BASED APPROACH TO PREDICT THE DISEASE COURSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Prognostic factors, Artificial Intelligence, Rheumatoid arthritis

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Background: Rheumatoid Arthritis (RA) is an autoimmune disease which affects approximately 0.8% of the Finnish population. Increasing number of conventional and biological antirheumatic drugs is currently available for the treatment of RA. However, for the optimal use of these drugs and for example for the decision when to start biological medication, it would be of utmost importance to be able to predict the disease course of the patient during the patient's visit at the clinic.
Objectives: The disease course of the patients differs widely and predicting the disease course is challenging. Therefore, our objective was to use patient-specific disease characteristics and to develop an artificial intelligence (AI) method for predicting the future disease course. Our patient material includes 1881 patients, with both sero positive and negative diseases (ICD-10-codes M05 and M06).
Methods: We used a machine learning method which takes as input patient information such as demographic information and clinical variables. The target value that the method tries to predict is the DAS28-CRP disease marker a year from the present time. The train and test sets were balanced so that each DAS28-CRP value is expressed equally. The machine learning model was a voting ensemble with Random

Forest and Extreme Random Trees classifiers and with different scalers (Geurts et al. 2006). The number of training instances was 1504 and test set consisted of 377 patients. The number of features was 30. The patients were classified to 4 classes: inactive, low, high and very high according to the activity marker DAS28-CRP.

Results: The AUC value of the classifier was 0.71. This provides adequate extra information for the clinicians when they consider the patient's treatment. If the method shows that the patient is likely to get worse, treatment can be intensified and extra visits to the policlinic can be scheduled. If the model predicts that disease is getting better, visits can be more infrequent. Figure 1 shows the most important variables used by the classification algorithm. The AI algorithm gives good predictions (Table 1), even though errors between two adjacent activity classes are common. For example, when the true class is very high, the algorithm gives 88 high or very high predictions (94%), and only 6 clearly wrong answers (6%). When the true class is high, the results are more spread, with 42 cases (45%) being in the low or inactive class and 51 (55%) cases in the more active class. The low and inactive classes are predicted quite well.

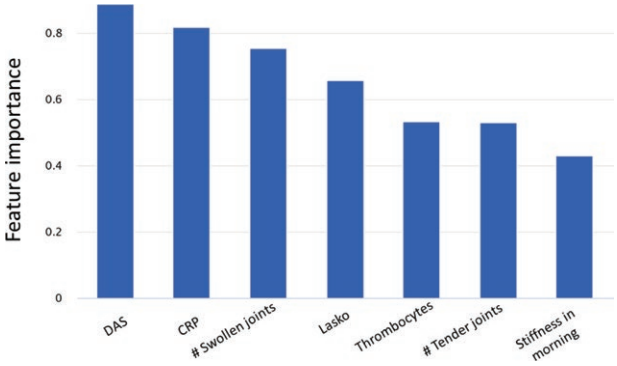
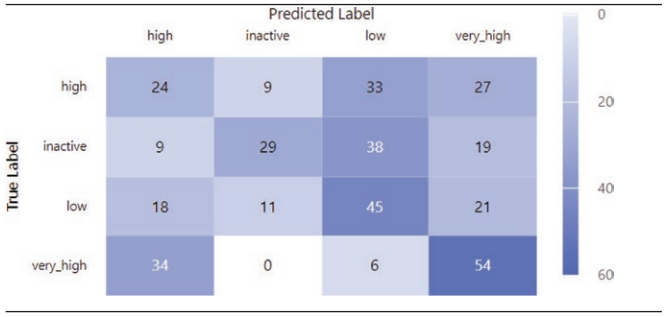


Figure 1. Overall feature importance for all classes. The higher the bar, the more useful the feature is in classifying the patients.

Table 1. A confusion matrix of classifying the test material. In the left are the true labels and on top the predicted labels. The classes low and very high have been most successfully predicted.



Conclusion: The algorithm shows promising results especially in predicting very high disease activity. An algorithm with AUC 0.71 cannot reliably classify patients independently, but it can aid the clinician in giving insights into the patients' current status and how likely the worsening of the disease is. The AI method chosen for this purpose is a white-box approach, meaning that the clinician can immediately see which factors were deemed important by the algorithm to produce this prediction.

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POS0321

LYMPHOCYTE SUBSETS- AND ACPA-BASED PREDICTIVE MODEL FOR PROGRESSION TO CLINICAL ARTHRITIS IN AT-RISK INDIVIDUALS WITH ARTHRALGIA

Keywords: Biomarkers, Autoantibodies, Rheumatoid arthritis

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Background: The presence of antibodies against citrullinated proteins (ACPA) significantly increases the risk of developing rheumatoid arthritis (RA). The clinical definition of individuals with arthralgia at risk of progression to RA (clinically suspect arthralgia, CSA) was established by EULAR irrespective of the ACPA status. Dysregulation of lymphocyte subpopulations (including NK and B cells) was previously described in early and established RA.

Objectives: To propose the predictive model for progression to arthritis based on peripheral lymphocyte subsets and ACPA in at-risk individuals with arthralgia.

Methods: Individuals from the At Risk of RA (ARRA) prospective observational cohort were defined as having arthralgia without arthritis on the examination of 66 joints at baseline and being either ACPA+ and/or meeting the EULAR definition of CSA (further CSA+, fulfilling at least 3 out of 7 parameters). All individuals signed informed consent prior to study enrolment. Peripheral blood samples were analysed at baseline by flow cytometry. The percentage of CD19+ B cells, CD3+ T cells, CD3+CD4+ Th cells, CD3+CD8+ Tc cells, CD3-CD16/56+ NK cells, CD3+CD16/56+ NK-T cells, and CD3bright γδ-T cells were detected within the CD45+CD14- lymphocyte population. Robust ANOVA was used to evaluate the effect of ACPA positivity or the CSA definition. A logistic regression model with a baseline percentage of lymphocyte subpopulations as predictors was constructed to discriminate between progressors to arthritis and non-progressors. The preselection of the best subset of predictors was performed using a stepwise selection based on the Akaike Information Criterion. The models considered were evaluated using ROC curves.

Results: Out of 191 at-risk individuals, 36 developed clinical arthritis (progressors) within a median of 9 months of follow-up and with a median symptom duration of 31,65 months [IQR=44,25], CRP 5,30 mg/l [IQR=12,21] and DAS28(CRP) 4,62 [IQR=2,18] at the time of manifestation. Progressors included 39% ACPA+, 25% CSA+, and 36% both ACPA+ and CSA+ individuals. For the construction of predictive models, 81 individuals (median age 51 years [IQR=17], 89% females) who have not yet progressed to arthritis (non-progressors) with symptom duration longer than 12 months were included to avoid disqualification of non-progressors limited by CSA definition (symptom duration <12 months). Forty-seven % of them were ACPA+, 36% were CSA+, and 17% were ACPA+ and CSA+, with median symptom duration at baseline being 36 months [IQR=36] and median CRP 1,64 mg/l [IQR=3,28]. No statistically significant differences in lymphocyte subpopulations between ACPA+ and ACPA- or CSA+ and CSA- individuals were found. The resulting predictive model for arthritis development performed in all ARRA individuals based on CD19%, NK%, and anti-CCP IgG U/ml showed AUC=0.732 ($p<0.001$). According to this model, a high percentage of CD19+ B lymphocytes and high anti-CCP IgG levels, and a low percentage of NK cells increase the probability of developing clinical arthritis. When the model with the same set of predictors was applied to ACPA+ individuals, AUC was even higher (AUC=0.804; $p<0.0001$). However, we were not able to construct a well-performing classification model in ACPA- individuals. The CSA definition appears of no predictive value in our at-risk cohort.

Conclusion: We propose a predictive model based on baseline levels of lymphocyte subpopulations and ACPA levels to distinguish individuals with arthralgia who progress to clinical arthritis from non-progressors, especially applicable in ACPA+ individuals. The final model includes B cells and NK cells, which are involved in the pathogenesis of RA. This preliminary model built in the ARRA cohort requires further validation in larger at-risk of RA cohorts.

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Disclosure of Interests: None Declared.

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POS0322

CLINICAL DISEASE ACTIVITY INDEX REMISSION IN RHEUMATOID ARTHRITIS AT 6 MONTHS IS ASSOCIATED WITH HIGHER FREQUENCY OF TRANSITIONAL B CELLS AT DIAGNOSIS

Keywords: Remission, Adaptive immunity, Rheumatoid arthritis

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Background: Early intervention and implementation of effective treatment is a significant predictor of positive long-term prognosis for rheumatoid arthritis (RA). However, despite major advances in treatment options there are currently no biomarkers to clinically guide treatment selection or to identify individuals who do not respond fully to first line therapy. B cells are known to contribute to RA pathogenesis as exemplified by the success of B cell depleting treatments. It is well known that there are changes in the circulating B cell compartment in both new onset and established RA that include reduced memory B cells and increased naïve and transitional B cells. Among transitional B cells there is a subpopulation described as regulatory B cells (Bregs) that is characterised by markers such as high levels of CD24/CD38, and CD1d as well as PDL1 and production of IL-10. To investigate the predictive potential of the B cell compartment for disease outcome, the different B cell populations must be further divided into specific subset and studied in well characterised cohort followed over time.
Objectives: To identify a B cell subset(s) at clinical onset that predict clinical disease activity index (CDAI) remission 6 months after start of treatment.
Methods: Flow cytometry analysis of peripheral blood B cell subsets was conducted on untreated, early RA patients (ueRA; according to ACR/EULAR 1987/2010 criteria; n=71) and sex matched healthy controls (n=24). PBMCs were stained for the following markers: CD19, CD21, CD27, IgD, CD24, CD38, PD1, PDL1. Patients were then treated with methotrexate and randomised to combination with a) prednisolone; b) certolizumab; c) tocilizumab; or d) abatacept. Patients were grouped based on disease remission status at 6 months (remission n=29; no remission n=42) as defined by a clinical disease activity index (CDAI) <2.8. The predictive value of these population frequencies for remission detection was modelled with receiver operating characteristic (ROC) analysis. Peripheral blood from a second ueRA cohort (n=32) and additional healthy donors (n=11) were analysed by flow cytometry including CD1d, PD1 and PDL1.
Results: Relative to patients who reached CDAI remission, individuals who did not respond to this extent to first line therapy at 6 months had significantly reduced frequencies of transitional ($CD19^+$ $CD24^{++}$ $CD38^{++}$), and $PD1^+$ B cells ($CD19^+$ $PD1^+$ $CD21^-$) at diagnosis (Figure 1), which inversely correlated with CDAI at 6 months (r=–0.355, p=0.002; and r=–0.245, p=0.039 respectively). The predictive value of these subset frequencies for remission was modelled with ROC analysis. Both transitional and $PD1^+$ B cell frequencies had significant predictive capabilities and an AUC of 0.67 and 0.7 respectively (Figure 1). Follow-up analysis in the second RA cohort showed that $CD1d^+$ transitional B cells in ueRA patients (median 14.75%; range 9.4-23.4%; n=32) were significantly increased (p<0.0001, Mann-Whitney) relative to healthy donors (median 8.9%; range 4.4-12.9%; n=11).
Conclusion: A reduced frequency of transitional and $PD1^+$ B cells at diagnosis in ueRA patients was associated with failure to reach CDAI remission within 6 months of treatment. As transitional B cells in ueRA patients express markers closely linked to Bregs, we speculate that the lower transitional B cell frequencies we observed at diagnosis may indicate fewer circulating Bregs and thereby worse conditions for endogenous disease control. Thus, monitoring of transitional B cell frequencies at the point of RA diagnosis may aid in the identification of patients who are less likely to reach remission at 6 months and therefore subjected to additional clinical surveillance.

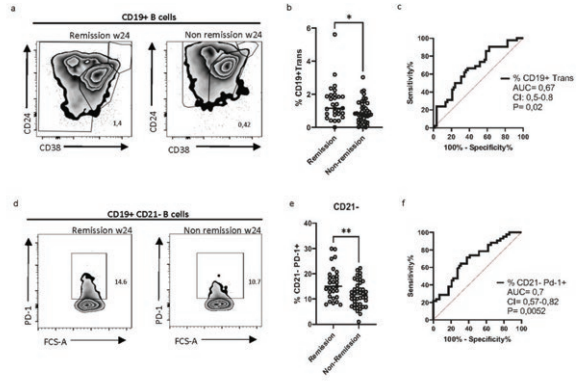


Figure 1. Transitional and PD1+ B cells reduced in treatment refractive RA patients.
a) Patients are subdivided based on 6 month remission status and baseline (samples at diagnosis) peripheral blood B cells analysed by flow cytometry. Transitional cells gated as $CD24^{++}$ $CD38^{++}$ within CD19+ B cells. Representative plots shown for both groups. b) Frequencies of baseline transitional B cells (as a proportion of total B cells) in patients who reach remission and patients who do not reach remission. Mann-whitney U test, * <0.05. c) ROC curve of the frequency of transitional B cells at baseline for prediction of remission by 6 months. d) PD1 gated on CD19+ CD21– B cells. Representative plots shown for both groups. e) Frequencies of baseline PD1+ B cells (as a proportion of total B cells) in patients who reach remission and patients who do not reach remission. Mann-Whitney U test, ** <0.01. f) ROC curve of the frequency of PD1+ B cells at baseline for prediction of remission by 6 months.

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POS0323

INDIVIDUALS AT RISK FOR RHEUMATOID ARTHRITIS – SELF MONITORING OF SYMPTOMS USING A DIGITAL APPLICATION ENABLES IDENTIFICATION OF HIGH RISK PATIENTS - RESULTS FROM THE PROSPECTIVE REMTORA TRIAL

Keywords: Rheumatoid arthritis, Education, Self-management

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Background: Individuals at risk for rheumatoid Arthritis (RA) typically describe diffuse, fluctuating and flare-like symptoms followed by symptom-free periods. In this pre-disease continuum preplanned physical visits reveal only a fraction of symptoms and rudimentarily capture the burden of disease. Implementation of a smartphone-based patient self-monitoring approach could help to characterize the burden of pre-stage disease and enable a timely start of therapy. (1,2)
Objectives: The aim of this study is to evaluate the implementation of a smartphone-based remote patient self-monitoring application in patients in the prodromal phase of RA and to create a predictive tool for the distinction of high-risk and low-risk patients.
Methods: Individuals at risk for RA fulfilling the following inclusion criteria were recruited in a prospective 6-month trial: Proof of anti-citrullinated peptide antibodies (ACPA), no clinically detectable synovial swelling at doctors visit, smartphone ownership. Participants were recruited from a prospective at-risk cohort and provided written consent (ethics-approval: 333_16B and 21_21B). All individuals were presented two standardized, self-produced educational videos about joint self-examination and pre-clinical RA and were informed about the remote monitoring option, using the CE-certified ABATON app. A new adaptive questionnaire-based algorithm “REMOTRA; REMote moniToring in pReclinical Arthritis” was developed including typical RA symptoms such as pain, swelling, morning stiffness and intake of pain medication. The criteria are weighted and added to a quantitative score from 0 to 15 pts. A cut-off value from 10 or more was defined as being highly symptomatic. The total number of questions varies depending on the answers given. Questionnaire frequency was based on shared-decision-making (every 7, 14 or 30 days). App usability and acceptance was measured using the System Usability Scale (SUS) and Net Promoter Score (NPS). Routine clinical visits were scheduled on a regular basis every 3 months.
Results: 79 patients were approached and 43 patients consented to participate (13 male; mean age: 49.3; 7-day/14-day/30-day interval: 3/15/25). Three patients (7%) developed RA during the six months of study follow-up. Patient acceptance of the questionnaire decreased during the trial, from an NPS of 21.8 (47.8% promoters) at 3 months down to 8.3 (45.8% promoters) at six months. The education videos were well accepted with an NPS of 31.6 (joint self-examination; 57.9% promoters) and 54.4 (Pre-RA; 63.6% promoters). Questionnaire usability was continuously rated as high with an average SUS of 88.1/100 (SD: 5,5) at three months and 85.4/100 (SD: 16.0) at six months. The most frequently reported symptoms were joint pain (78.0%, n=32), followed by joint swelling (73.2%, n=30) and morning stiffness (43.9%, n=18). 58.5% (n=24) took analgesics and 29.3% (n=12) took prednisolone at least once. Seven patients (16.3%) reported no symptoms during the six months. None of the patients with a REMOTRA -Score <10 developed RA (negative predictive value: 100%). However, patients with a score of 10 or more were diagnosed with a RA in their next consultation with a probability of 12% (positive predictive value). Monitoring adherence was high with a mean of 4.6 (SD: 2.0) months app usage and 57.1% completing all questionnaires.
Conclusion: Our study shows that individuals at-risk for RA appreciate standardized digital disease education and mostly adhere to a telemedicine monitoring program. Remote self-monitoring sheds light on disease progress of at-risk patients. Further development and testing of this method may be worthwhile for a better informed and efficient utilization of limited in-person visit slots.

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POS0324

OBESITY IS A RISK FACTOR FOR POOR RESPONSE TO TREATMENT IN EARLY RHEUMATOID ARTHRITIS - A NORD-STAR SPIN-OFF STUDY

Keywords: Randomized control trial, Prognostic factors, Rheumatoid arthritis

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Background: Several therapeutic options are currently available to treat rheumatoid arthritis (RA); however, the response to treatment is highly variable, and not all patients achieve clinical remission [1]. Obesity is suggested to lower the chances of remission [2], even though a recent observational study has shown that obesity is not associated with reduced response to conventional synthetic anti-rheumatic drugs in patients with early RA [3].

Objectives: The aim of this study is to determine if obesity affects the response to treatment in participants with early RA.

Methods: This report includes 393 Swedish patients from the NORD-STAR study, which is a multicenter, randomized trial on 812 patients with untreated early RA [4]. The 393 participants have been randomized at baseline into 4 arms of treatment: methotrexate combined with (1) prednisolone, (2) certolizumab, (3) abatacept, or (4) tocilizumab. Scores for disease activity and blood samples were measured and collected before randomization and at 24-week follow-up. Multiple linear regression and binary logistic regression analyses were performed after adjustment for sex, baseline age, anti-citrullinated peptide antibody status, current smoking, disease activity score- C-reactive protein (DAS28-CRP), and treatment randomization. The outcomes for this report were: DAS28-CRP ≤3.2 (DAS28-CRP low disease activity), DAS28-CRP ≤2.6 (DAS28-CRP remission) and clinical disease activity index (CDAI) ≤2.8 (CDAI remission).

Results: In total, 75 (19%) participants had obesity at baseline, defined as body mass index (BMI) ≥30 kg/m^2. The percentage of patients with obesity in each treatment group was (1) 25%, (2) 15%, (3) 19% and (4) 19%. At baseline, there were no differences in terms of disease activity indices and inflammation parameters between patients with BMI <30 vs. ≥30 kg/m^2, except for the number of swollen joints (SJC28), which was slightly lower in those with obesity (mean+SD, 8±5 vs. 9±5, p=0.018). At 24-week follow-up, patients with obesity had higher disease activity indices and inflammation parameters compared to patients with lower BMI (Table 1). Moreover, patients with obesity had a lower chance of achieving response to treatment as measured by DAS28-CRP ≤3.2 (OR 0.5, 95% CI 0.2 - 0.9, p=0.025), DAS28-CRP ≤2.6 (OR 0.4, 95% CI 0.2 - 0.6, p <0.001) and CDAI remission (OR 0.4, 95% CI 0.2 - 0.8, p=0.006), compared to patients with lower BMI (Figure 1). BMI-treatment interaction was not significant for any score of disease activity.

Conclusion: In patients with early RA, obesity was not associated with higher disease activity before treatment initiation. However, 24 weeks after treatment, patients with obesity had higher disease activity and lower chances to respond to therapy compared to patients with lower BMI irrespective of treatment.

Table 1. Disease activity scores and inflammatory parameters at 24 weeks follow-up stratified by baseline BMI

	BMI (kg/m^2)		P-values
	< 30	≥ 30	
DAS28-ESR	2.2±1.1	2.8±1.2	<0.001
DAS28-CRP	2.1±0.9	2.6±1.0	<0.001
CDAI	5.0±5.3	7.5±6.4	0.001
SJC28	0.7±1.4	0.9±1.4	0.418
TJC28	1.8±3.1	3.0±4.2	0.256
Global VAS, patient, mm	17±18	25±22	<0.001
Global VAS, investigator, mm	8±9	11±11	0.018
ESR, mm/h	11±10	15±16	0.031
CRP, mg/L	2.2±3.1	4.4±7.1	<0.001

Abbreviations: TJC28, tender joint count; VAS, visual analogue scale of pain; ESR, erythrocyte sedimentation rate.

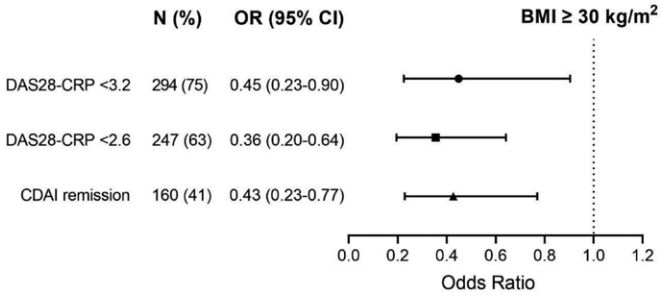


Figure 1. Multivariable binary logistic regression analysis for response to treatment at 24 weeks (reference category: BMI< 30 kg/m^2)

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POS0325 RHEUMATOID ARTHRITIS PATIENTS AND WEATHER PATTERNS: A RHUMADATA™ STUDY OF 14,200 PATIENT-REPORTED OUTCOMES MATCHED WITH METEOROLOGICAL DATA

Keywords: Real-world evidence, Patient reported outcomes, Rheumatoid arthritis

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Background: Anecdotally, patients with rheumatoid arthritis (RA) report seasonal changes in their symptoms. Anatomically, atmospheric pressure variations are captured by baroreceptors, which may generate this perception.
Objectives: To correlate seasonal changes with subjective assessment scores.
Methods: Environment Canada provided meteorological data from 2015 to 2020 for Montreal (Dorval). Hourly measurements of temperature, relative humidity, and pressure were available. We matched daily meteorological data with patient-reported pain (PtP), fatigue (PtF), and disease activity (PtGA) assessments from RHUMADATA™ participants. We calculated daily means, minimums, and maximums, as well as changes from the previous day for the winter and summer months. For the years 2015 to 2020, Pearson Correlation Coefficients (PCCs) were computed between Patient Reported Outcomes (PROs) and weather measurements. Optimal regression models (OM) were derived based on Akaike's Information Criteria (AIC).
Results: RA patients' PROs were matched with meteorological data (7411 winter measurements and 6789 summer measurements). At the time of the first PRO assessment, the mean age and disease duration were 60.1(13.5) and 10.5 (10.4), and 74.6% of patients were women. Patients provided an average of 14 PROs. In winter, PtP, PtF and PtGA were 3.48 (2.79), 3.49 (2.96) and 3.42 (2.66), and 3.45 (2.81), 3.46 (2.96) and 3.33 (2.63) in summer. PtGA was statistically higher in winter (p-value=0.0379). PCC and OMs are shown in Table 1. In winter, all correlations are very weak (less than 0.19). PtGA is not correlated with any weather measures in both winter and summer. PtP and PtF correlate with some weather measures in both seasons.
Conclusion: In this study of 14200 wheather-matched PROs, mean PtP, PtF, and PtGA scores are higher in winter among RA patients, but the differences are small. Few meteorological measures are significantly correlated with PROs, and all correlations are very weak. Meteorological variables explain a quite small percentage of the variation in PRO variation (small R-square). No consistent relationship between PROs and meteorological conditions is reported by other smaller studies.
REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: Maxine Joly-Chevrier: None declared, Louis Coupal: None declared, Loïc Choquette Sauvageau: None declared, Denis Choquette Speakers bureau: Abbvie, Amgen, Eli Lilly, Fresenius Kabi, Novartis, Pfizer, Sandoz, Tevapharm, Consultant of: Abbvie, Amgen, Eli Lilly, Fresenius Kabi, Novartis, Pfizer, Sandoz, Tevapharm, Grant/research support from: Abbvie, Amgen, Eli Lilly, Fresenius Kabi, Novartis, Pfizer, Sandoz, Tevapharm.
DOI: 10.1136/annrheumdis-2023-eular.1455

POS0326 POLYGENIC RISK SCORE OF RHEUMATOID ARTHRITIS PREDICTS BONY EROSION

Keywords: Prognostic factors, Rheumatoid arthritis, Genetics/Epigenetics

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Background: Polygenic risk scores (PRS) are widely used to estimate disease risks and predict clinical outcomes. However, differences exist among PRS derived from genome-wide association study (GWAS) of ethnicities across the globe.
Objectives: We aimed to build up PRS for predicting the development of rheumatoid arthritis (RA) in a Taiwanese population and investigate whether PRS of RA may be associated with bone erosion.
Methods: We constructed PRS using GWAS data from a hospital-based cohort of 2044 RA cases and 7950 non-RA controls participating in the Taiwan Precision Medicine Initiative. LDpred2, PLINK and PRsice2 models were used to evaluate the area under curve (AUC) of RA susceptibility in both training and testing datasets (1022 RA cases and 3975 controls).

Table 1. Pearson correlation coefficients and "best" regression models.

		Winter (Dec 1st to Mar 31st)						Summer (Jun 1st to Sep 30th)					
		PtP		PtF		PtGA		PtP		PtF		PtGA	
		PCC[1,2]	OM[3]	PCC	OM	PCC	OM	PCC[1]	OM	PCC	OM	PCC	OM
R^2			0.0016		0.0023		0.0010		0.0004		0.0016		0.0001
Intercept			7.637		9.934		3.317		3.515		3.521		3.457
Temperature	Min	-0.011	0.043	-0.024 δ		-0.015		0.005		-0.001		0.006	
	Max	-0.018		-0.030 γ		-0.023		0.001		0.002		0.000	
	Mean	-0.016	-0.054	-0.030 γ	-0.015	-0.021		0.004		0.003		0.004	
	Mean-Mean[4]	0.006		0.008		0.000		0.000		-0.018		-0.003	
	Min-Max[4]	0.002	0.013	0.003		0.002		0.003		-0.003		-0.004	
	Max-Min[4]	0.013		0.019	-0.017	0.008		-0.004		-0.030 δ	-0.035	-0.003	
Relative humidity	Min	0.024 δ		0.026 δ		0.012		-0.005		-0.015		-0.010	
	Max	0.012		0.022		0.004	-0.006	0.000		-0.018		-0.013	
	Mean	0.027 δ		0.028 δ		0.015	0.009	-0.007		-0.021		-0.015	
	Mean-Mean	0.014		0.013		0.012		-0.006		-0.008		-0.006	
	Min-Max	-0.009		-0.004		-0.006		0.001		0.005		-0.001	
	Max-Min	-0.020		0.025 δ		0.014		-0.006		-0.011		-0.008	
Atmospheric pressure	Min	-0.015		-0.022	-0.006	-0.012		-0.007		0.011	0.048	0.006	
	Max	-0.013	-0.004	-0.020		-0.015		-0.006		0.002		-0.001	0.003
	Mean	-0.013		-0.020		-0.015		-0.006		0.006	-0.045	0.002	
	Mean-Mean	-0.013		-0.020		-0.012		0.001		0.019		0.014	
	Min-Max	-0.008		-0.019		-0.014		0.000		0.012		0.009	
	Max-Min	-0.013		-0.019		-0.005		0.003	0.011	0.026 δ		0.020	

[1] PCC=Pearson Correlation Coefficients. [2] γ: 0.001<p≤0.01, δ: 0.01<p≤0.05. [3] The best model was selected by computing Akaike's Information Criteria (AIC) for all possible subsets of multiple regression models for main effects. The model with the smallest AIC value is deemed the "best" model. [4] Difference from the previous day.

Demographic data, seropositivity of rheumatoid factor (RF), anti-citrullinated protein antibody (ACPA), treatment with biological and targeted synthetic disease modifying anti-rheumatic drugs (bDMARDs and tsDMARDs) and bone erosions by either plain x ray or ultrasonography were compared among quantiles of PRS.

Results: PRS of 97,396 single nucleotide polymorphisms derived from LDpred2 exhibited the highest AUC for predicting the development of RA in the overall dataset as compared with the remaining algorithms. Participants with the top RA-PRS quantile have the highest proportion of RF and ACPA positivity (74.8% & 65.0%, respectively), bone erosion (86.4%) and higher chance to receive bDMARDs or tsDMARDs (42.3%) as compared to the counterparts. In addition, RA-PRS quantile was a significant risk for bone erosion in the multivariate regression model with the adjustment of RF, ACPA positivity and therapeutic medication, specifically in the group of age < 60 years.

Conclusion: PRS is associated with seropositivity, erosive bone disease, need for advanced therapy in Taiwanese patients with RA.

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Table 1. Basic demographics of 2042 participants with RA by RA-PRS quantiles

	1st quantile (n=511)		2nd quantile (n=510)		3rd quantile (n=510)		4th quantile (n=511)		*p* value
	N	%	N	%	N	%	N	%	
RA diagnosis age < 60 years	362	70.84	389	76.27	386	75.69	400	78.28	0.04
Female gender	404	79.06	414	81.18	402	78.82	391	76.52	0.34
BMI	23.7	4.10	24.3	4.41	23.9	4.14	23.6	4.06	0.04
Smoking	40	7.83	40	7.84	42	8.24	42	8.22	0.99
RF positivity	249	57.37	274	60.62	303	65.16	345	74.84	<0.0001
ACPA positivity	153	38.83	201	48.32	256	60.52	282	64.98	<0.0001
ESR (mm/hr)	31.38	26.18	32.56	29.24	33.61	27.82	35.93	29.05	0.07
CRP (mg/L)	0.77	1.80	0.89	1.90	0.79	2.21	0.97	2.21	0.39
DAS28	4.29	1.44	4.27	1.44	4.12	1.35	4.42	1.47	0.10
Periodontitis	36	7.05	32	6.27	37	7.25	30	5.87	0.79
Boen erosion	158	77.07	193	78.78	227	85.34	255	86.44	0.01
Glucocorticoid	402	78.67	421	82.55	432	84.71	446	87.28	0.002
Methotrexate	280	54.79	320	62.75	353	69.22	390	76.32	<0.0001
Hydroxychloroquine	412	80.63	432	84.71	444	87.06	452	88.45	0.003
Sulfasalazine	151	29.55	195	38.24	188	36.86	223	43.64	<0.0001
Target therapies	135	26.42	162	31.76	194	38.04	216	42.27	<0.0001
TNFi	88	17.22	102	20	130	25.49	153	29.94	<0.0001
Non-TNFi	56	10.96	81	15.88	92	18.04	105	20.55	0.0003
JAKi	31	6.07	41	8.04	48	9.41	41	8.02	0.26

By ANOVA test.RA: rheumatoid arthritis; PRS: polygenic risk score; BMI: body mass index; RF: rheumatoid factor; ACPA: anti-citrullinated protein antibody; ESR: erythrocyte sedimentation rate; CRP: C reactive protein; DAS28: disease activity score by 28 joints; TNFi: tumor necrosis factor inhibitor; JAKi: Janus kinase inhibitor

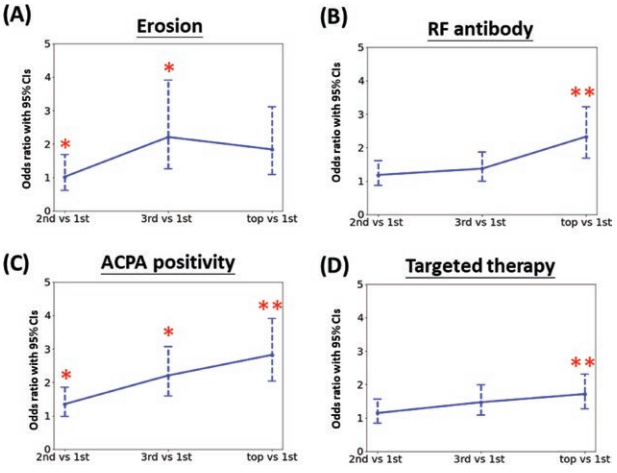


Figure 1. Risk of (A) bone erosion (B) RF positivity (C) ACPA positivity (D) targeted therapy in second, third and top quantiles as compared to the first quantile in participants aged < 60 years. RF: rheumatoid factor; ACPA: anti-citrullinated protein antibody. * $p < 0.05$

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Disclosure of Interests: None Declared.

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POS0327

SPEED OF RESPONSE MATTERS: POST-HOC ANALYSIS OF PATIENTS WITH EARLY SERONEGATIVE RHEUMATOID ARTHRITIS INCLUDED IN THE CARERA TRIAL

Keywords: Randomized control trial, Rheumatoid arthritis, Outcome measures

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Background: Seronegative rheumatoid arthritis (RA) patients have been historically considered to have a milder disease course.

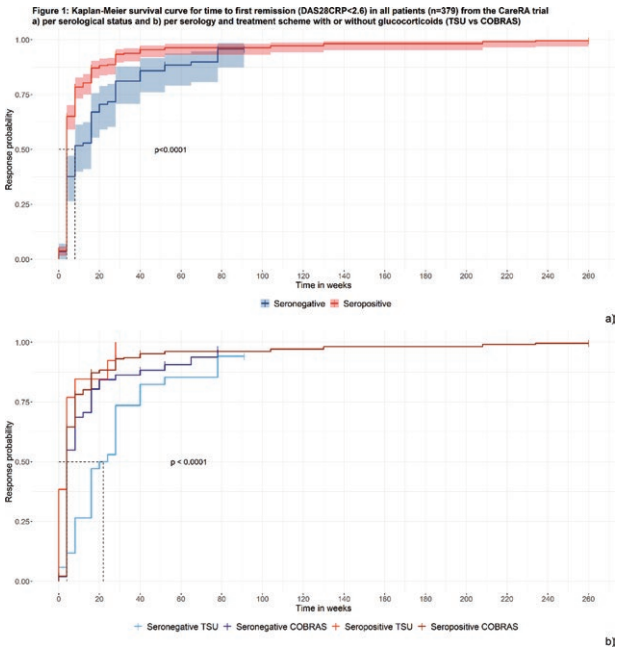
Objectives: We aimed to compare the disease course in seronegative and seropositive patients from the Care in early RA (CareRA) trial.

Methods: We used data from the 2-year RCT CareRA and its 3-year observational follow-up, CareRA plus. Patients completing the year 2 visit of CareRA were eligible for participation in CareRA plus, in which patients were evaluated every 6 months till year 5. The CareRA trial included patients early RA (≤1 year) and naïve to disease-modifying anti-rheumatic drugs. Patients were stratified in a low- and high-risk group according to prognostic markers and randomized to one of four different treatment schemes: a) MTX and a step-down glucocorticoid (GC) scheme (COBRA Slim) b) this combination with either sulphasalazine (COBRA Classic) or c) leflunomide (COBRA Avant-Garde) in high-risk patients, and d) MTX without GCs (Tight-Step-Up: TSU) or e) COBRA Slim in low-risk patients. Treating-to-target, steering at low disease activity (≤3.2) measured in 28 joints with C-reactive protein (DAS28CRP) was applied while aiming for remission (<2.6) as final outcome. Differences in demographic, clinical and laboratory variables were tested with Wilcoxon rank or Chi-square. Multiple testing was corrected with Holms-Bonferroni. Survival analysis using Kaplan-Meier and Cox regression compared (a) time to first remission (DAS28CRP<2.6), (b) time to first loss of disease-control (DAS28CRP>3.2) in those reaching remission, and all subsequent losses of disease-control as recurrent events between seropositive (ACPA or RF positive) and seronegative (ACPA and RF negative) patients. Survival curves were compared with log rank. To model recurrent events, an extended Cox model with random effect, including the presence of erosions at baseline, disease duration, gender, current smoking, treatment scheme with or without GCs and DAS28CRP at baseline and week 16 was used. Multiple imputation (m=100) was used to handle missing data.

Results: Of the 379 included patients, 83 (23%) were seronegative while 292 (77%) were seropositive. Seronegative patients had a similar median age (54 vs 53 years, p=0.58), BMI (26.5 vs 25.7 kg/m^2, p=1.0), presence of erosions (26% vs 25%, p=1.0) and gender distribution (76% vs 68% females, p=1.0), compared to seropositive patients. However, median disease activity was higher in seronegative patients at baseline: DAS28CRP (5.1 vs 4.7, p<0.01), 28 swollen joint count (8 vs 6, p<0.01) and 28 tender joint count (10 vs 7, p<0.001). DAS28CRP remained significantly higher at week 8 (3.0 vs 2.1, p<0.001), but became comparable by year 1 (2.0 for both p=1.0). There was a significant difference in time to first treatment response between seronegative and seropositive patients as depicted in the inverted Kaplan-Meier plot (Figure 1a). Time to first remission was significantly shorter for seropositive (median 4 weeks IQR 4;8) versus seronegative (8 weeks IQR 4:28) patients (p<0.001). When accounting for the treatment, all COBRA schemes with GCs increased the chance of reaching remission by 58% (HR 1.58; 95%CI 1.10-2.27; p<0.05) compared to TSU (Figure 1b). For the time to first and consecutive losses of disease control after remission, one point higher DAS28CRP at week 16 increased the risk of losing disease control by 59% (HR 1.59; 95%CI 1.38-1.82; p<0.0001), serology status was not significantly predictive of loss of response.

Conclusion: In CareRA, seronegative patients, who have been historically considered to have a milder form of the disease, had a higher initial disease activity, longer time to first treatment response and greatly benefited from an initial treatment scheme that included glucocorticoids. Speed of response during the window of opportunity for RA has been highly advocated. Our findings highlight

that seronegative RA requires an equally intensive initial treat-to-target therapy as seropositive RA to reap the benefits of the window of opportunity.



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Osteoarthritis: novel prospects

POS0329

CHONDROCYTE SUBPOPULATIONS AND CANONICAL PATHWAYS ASSOCIATED WITH HAND OSTEOARTHRITIS: DISCOVERY BY SINGLE-CELL TRANSCRIPTOMIC ANALYSIS AND VALIDATION BY TWO INDEPENDENT POPULATION-BASED STUDIES

Keywords: Osteoarthritis, Cartilage

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Background: Hand osteoarthritis is a common heterogeneous joint disorder with differences in aetiology and pathophysiology from the large weight-bearing knee or hip osteoarthritis.[1]-[3] Its pathophysiological mechanism remains largely unexplored, partially because of limited access to clinical sample tissues and lack of animal models.[2] To date, there is no known cure for hand osteoarthritis, indicating an urgent need for better understanding of the underlying mechanisms so that appropriate treatment strategies can be developed to target this disabling disease.

Objectives: We aimed to identify hand joint chondrocyte subpopulations and investigate the molecular mechanism of hand osteoarthritis by performing single-cell RNA sequencing (scRNA-seq) analysis, and verify the findings in two large independent population-based studies.

Methods: We obtained hand interphalangeal joints from five donors who had destructive forearm injury. Using scRNA-seq analysis, we analysed the cellular composition and subpopulation-specific gene expression of hand articular cartilage, and then compared these features between cartilages from joints with macroscopically confirmed osteoarthritis and those without osteoarthritis. To verify the findings, we conducted a Mendelian randomisation study in the UK Biobank and a cross-sectional study using data collected from the Xiangya Osteoarthritis Study. Figure 1 shows the schematic illustration of this study.

Results: Of 105,142 cells we identified 13 subpopulations, including a novel inflammatory chondrocyte subpopulation that specifically expressed genes related to inflammatory and immune response. Fibrocartilage chondrocytes represented a major source of osteoarthritis-related proteases and exhibited an extensive alteration of gene expression patterns in osteoarthritic cartilage compared with non-osteoarthritic cartilage. Both inflammatory chondrocytes and fibrocartilage chondrocytes showed a trend towards increased numbers in osteoarthritic cartilage. In these two subpopulations from osteoarthritic cartilage, the ferroptosis pathway was enriched, in which the expression of iron overload-related genes, eg, *FTH1*, was elevated. These findings are further validated by two independent population-based studies. Among participants (n=332,668) in the UK Biobank, genetic predisposition to higher expression of *FTH1* mRNA significantly increased the risk of hand osteoarthritis (OR=1·07, 95%CI:1·02-1·11). Among participants (n=1,241) from the Xiangya Osteoarthritis Study, high levels of serum ferritin (encoded by *FTH1*), a biomarker of body iron overload, were significantly associated with a high prevalence of hand osteoarthritis (*P*-for-trend=0·037).

Conclusion: Our datasets will be valuable as a rich resource for molecular and cellular exploration and open new possibilities for the research of molecular mechanism, drug development and precise treatment for hand osteoarthritis. Inflammatory and fibrocartilage chondrocytes are key subpopulations and ferroptosis may be a key pathway in hand osteoarthritis. Markers of these chondrocyte subpopulations, as well as ferroptosis inhibitors or iron chelators, could be focus of attention in future studies.

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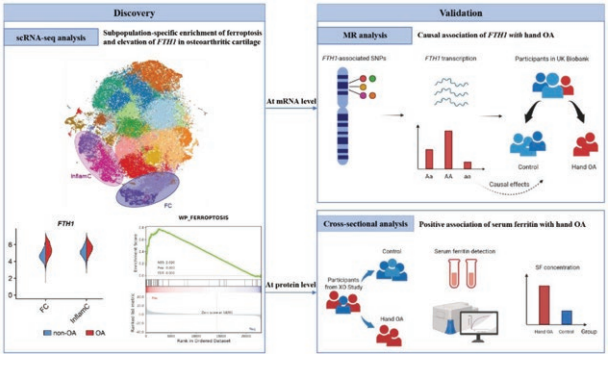


Figure 1. The schematic illustration of this study.

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POS0330 SYNOVIAL M1 MACROPHAGES AND FIBROBLASTS DUAL-TARGETING LIPOSOMES ASSISTED DELIVERY OF TRIAMCINOLONE ACETONIDE IS EFFECTIVE AGAINST JOINT PAIN AND CARTILAGE DEGENERATION IN OSTEOARTHRITIS

Keywords: Treat to target, Pain, Osteoarthritis

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Background: The latest professional guidelines recommend intra-articular (IA) glucocorticoids (GCs) for pain relief in patients with knee osteoarthritis (OA). However, their effect is small-to-moderate and short-term only[1]. There is also concern about the possible risk of cartilage deterioration caused by repeated IA GCs. M1 macrophages and activated synovial fibroblasts (SFs) mutually contribute to the propagation of joint pain and cartilage destruction in OA by constructing a positive feedback loop. To alleviate joint pain more effectively over a longer period without increasing the risk of cartilage deterioration, we developed nano-porous cellular membrane (NM) camouflaged liposome (NM@Lip) for targeted delivery of triamcinolone acetate (TA), one of the IA GCs most commonly used for OA, to both M1 macrophages and activated SFs in the synovium of osteoarthritic joints.

Objectives: To investigate the phenotypic reprogramming effect of TA-loaded NM@Lip (TA-NM@Lip) in M1 macrophages and activated SFs and determine their ability in relieving pain and alleviate OA progression in rodent models.

Methods: TA-NM@Lip was fabricated using the thin-film hydration method. The mRNA and protein levels of pathogenic mediators secreted by M1 macrophages and activated SFs treated with free TA, TA-loaded liposome (TA-Lip) or TA-NM@Lip for 24 h were measured using real-time PCR, RNA sequencing, ELISA and Immunofluorescence staining. To evaluate the joint retention time of NM@Lip, 1,1'-dioctadecyl-3,3,3',3'-tetramethyl indodicarbocyanine, 4-chlorobenzenesulfonate salt (DiD) solution, DiD-loaded Lip or DiD-loaded NM@Lip was injected intra-articularly into the osteoarthritic joints of monosodium iodoacetate (MIA) rats and the fluorescence images were captured by In Vivo Imaging System for 28 days. To study the therapeutic effect of different TA formulations, triamcinolone acetonide injection (TA IR), TA-Lip, TA-NM@Lip, or blank NM@Lip was injected intra-articularly into the osteoarthritic knee of MIA rats at one week after MIA injection or at one week and five weeks after anterior cruciate ligament transection combined with partial medial meniscectomy (ACLT + pMMx) surgery. Mechanical allodynia and hind paw weight distribution were assessed to determine the rats' pain-related behavior. The phenotypic alteration ability and therapeutic efficacy of TA IR, TA-Lip, TA-NM@Lip, and NM@Lip were verified by micro-computed tomography, histological and immunofluorescence staining.

Results: TA-NM@Lip was the most efficient in downregulating the expression of M1-related genes and upregulating M2-related genes compared with other treatment groups. The mRNA and protein levels of pro-inflammatory cytokines, adhesion molecule and proteolytic enzyme secreted by activated SFs were significantly downregulated by TA-NM@Lip. NM@Lip was retained in the joint for up to 28 days and selectively distributed into both M1 macrophages and activated SFs in synovium with low distribution in cartilage. In MIA-induced model, a single IA injection of TA-NM@Lip attenuated synovitis and achieved complete pain relief without inducing adverse effects. In ACLT + pMMx-induced model, repeated TA-NM@Lip did not cause apoptosis of chondrocytes or damage cartilage and attenuated cartilage degeneration.

Conclusion: TA-NM@Lip exhibited extended joint-retention time and selectively remodeled the phenotype of synovial M1 macrophages and activated SFs in OA joints. This dual-targeting scaffold effectively attenuated synovitis, decreased cartilage degeneration, and achieved complete relief of joint pain in two distinct rodent models of OA.

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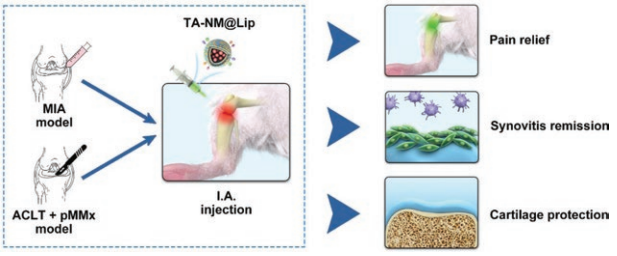


Figure 1. Schematics illustrating intra-articular injection of TA-NM@Lip can effectively relief pain, alleviate synovitis and protect cartilage in MIA rats and ACLT + pMMx rats.

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Disclosure of Interests: None Declared.

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POS0331 MOLECULAR MECHANISMS OF CHONDROPROTECTION INDUCED BY ROR2 BLOCKADE

Keywords: Osteoarthritis, Cell biology

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Background: We previously reported that ROR2 blockade (ROR2i) induces chondrogenesis *in vitro* and *in vivo*, improving pain and cartilage integrity following joint destabilization in mice (Thorup *et al.*, 2020). Downregulation of YAP signalling was required for chondrogenesis induced by ROR2i, but *per se* not sufficient. Overexpression of constitutively active YAP negated ROR2i-induced chondrogenesis, but the YAP inhibitor Verteporfin was unable to induce chondrogenesis. This means that something else must take place in addition to YAP inhibition for ROR2i to induce chondrogenesis.

Objectives: In this study, we used a phosphoproteomic approach to detail downstream ROR2 signalling in chondrogenic cells.

Methods: Cartilage differentiation was assessed in C3H10T1/2 cells cultured in micromass using Alcian Blue staining and the expression of mRNA encoding chondrogenic markers. Osteogenesis was assessed by molecular marker analysis, alkaline phosphatase activity and alizarin red staining. Phosphoproteomics screening was performed by precipitation of phosphoproteins on TiO2 columns followed by mass spectroscopy. Ror2-/- C3H10T1/2 cells using CRISPR/Cas9.

Results: In keeping with the delayed endochondral ossification and chondrocyte hypertrophy observed in Ror2-/- mice (DeChiara *et al.*, 2000), Ror2-/- C3H10T1/2 cells failed to undergo osteogenesis when exposed to osteogenic medium as assessed by alkaline phosphatase activity, extracellular matrix calcification and expression of hypertrophy/osteogenic markers. We established suitable time points for ROR-2 mediated phosphorylation events based on ERK (early) and JNK (late) phosphorylation following stimulation with WNT5A. Phosphoproteomics analysis using a label-free approach, revealed 1109 early (5 min) phosphorylation events that were ROR2 dependent (taking place in the wild type but

not in the Ror2-/- CRISPR cells) and 708 at 15 minutes. In keeping with the requirement of YAP for ROR2i-dependent chondrogenesis (Thorup *et al.*, 2020), several phosphorylation events of molecules within the YAP pathway occurred including YAP and LATS1/2. In keeping with this, YAP dependent transcription was modulated by WNT5A in a ROR2-dependent manner in a reporter assay. Several phosphorylation sites were non-conventional, suggesting a complex, non-canonical, regulation of YAP by ROR2. Other signalling pathways, previously known to be involved in chondrogenesis, were involved including insulin, autophagy and focal adhesion. Many phosphorylation events were previously poorly characterised.

Conclusion: ROR2i induces modulation of several signalling pathway in addition to YAP. The hierarchy of these phosphorylation events needs to be resolved to identify the detailed molecular mechanism underpinning the efficacy of ROR2i in osteoarthritis.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0332 **WITHDRAWN**

POS0333 **NLRP12 EXACERBATES OSTEOARTHRITIS BY PROMOTING DEGRADATION OF NOD2 IN SYNOVIAL MACROPHAGES**

Keywords: Synovium, Innate immunity, Osteoarthritis

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Background: Osteoarthritis is the most common degenerative bone and joint disease. Hypothesis has been widely accepted that osteoarthritis (OA) starts from cartilage injury and loss, while emerging evidences suggest that synovial inflammation precedes cartilage loss during the progression of OA [1]. Activation of macrophages plays a crucial part in synovial inflammation in OA [2]. In our previous researches, we have demonstrated NOD2 as an inhibitor of macrophage activation *in vitro*. Besides, bioinformatic analysis suggested a potential link between NLRP12 and NOD2.

Objectives: To investigate the role of NOD2 in OA *in vivo* and explore the potential interaction between NOD2 and NLRP12.

Methods: We established CIOA (Collagenase-induced OA) model with 8-week-old C57BL/6J mice, and injected NOD2 over-expression (oe-NOD2) lentiviral vectors into the knee joint cavity as experimental group (CIOA + oe-NOD2), with the empty vectors as control (CIOA + Mock). 8 weeks later, the knee joints were harvested and stained with Safranin O/fast green. Besides, three-dimensional reconstruction of Micro-CT images were employed to evaluate the pathological changes of OA. In addition, we applied lentiviral transfection, co-immunoprecipitation (Co-IP), and ubiquitination assays to investigate the interaction between NOD2 and NLRP12, as well as its mechanism of action in the regulation of macrophage activation.

Results: *In vivo* over-expression of NOD2 showed significant inhibition of pathological changes (Figure 1A, 1B). Though NLRP12 had no impact on mRNA level of NOD2 in RAW264.7 macrophages (Figure 1C), NOD2 expression at protein level was negatively correlated with NLRP12 (Figure 1D), suggesting that NLRP12 may influence the degradation of NOD2. Co-IP experiments also confirmed the existence of interaction between NLRP12 and NOD2 at protein level, which was influence by MG132, inhibitor of ubiquitin-proteasome pathway (Figure 1E). Besides, NLRP12 over-expression impaired inhibition of macrophage inflammation by NOD2 (Figure 1F). Since HSP90 binds NOD2 to prevent its

proteasomal degradation via poly-ubiquitination (Poly-Ub) [3], we therefore performed Co-IP and Poly-Ub assays. NLRP12 was associated with reduced binding of HSP90 with NOD2, greater scale of K48 Poly-Ub assembling on NOD2, and thus lower level of NOD2 protein. Furthermore, proteasomal degradation of NOD2 was blocked by MG132, though interrupted binding between NOD2 and HSP90, and accumulation of Poly-Ub chains (Figure 1G). These findings suggested sequestration of HSP90 from binding NOD2 by NOD2-NLRP12 interaction, which leaded to assembly of K48 Poly-Ub chains onto NOD2, and its proteasomal degradation (Figure 1H).

Conclusion: NOD2 was demonstrated as an inhibitor of OA *in vivo*, in consistence with our previous *in vitro* data. Besides, NLRP12 interacted with NOD2, and promoted its Poly-Ub and subsequent proteasomal degradation. Our findings highlighted the impressive potential of NLRP12 to be a preventative and therapeutic target in OA, though more in-depth investigations are indispensable before further conclusion is reached.

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Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.749

POS0334 LYSYL OXIDASES (LOX(L)) PROMOTE PATHOLOGIC CHONDROCYTE CALCIFICATION

Keywords: Cartilage, Animal Models, Crystal Arthritis

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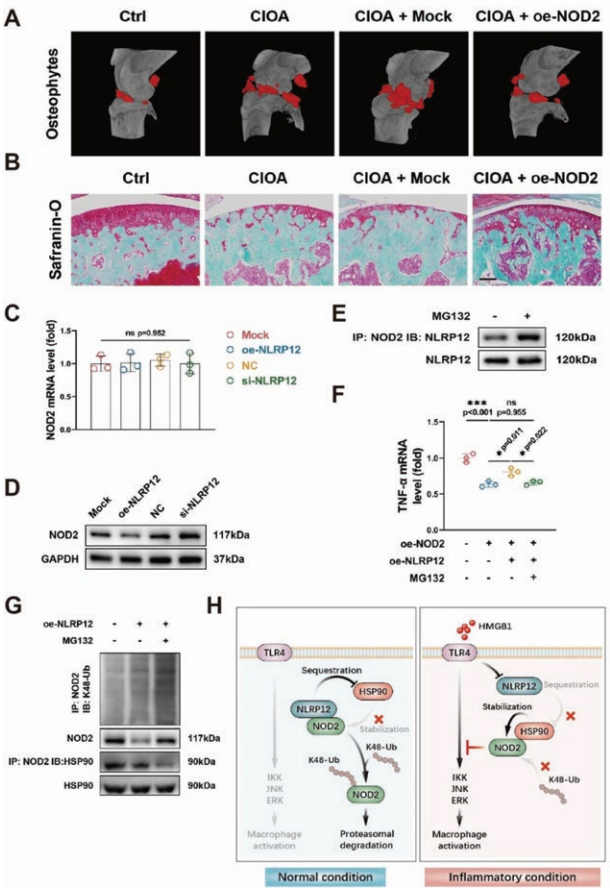


Figure 1. (A-B) Micro-CT and Safranin O/fast green staining of mouse knee joints (n=6 for each group) (Scale bar = 100 μm) (C-D) Influence of NLRP12 on mRNA and protein level of NOD2 in macrophages (E) Interaction between NOD2 and NLRP12 (F) Effect of NLRP12 on the inhibitory effect of macrophage activation by NOD2 (G) Effect of NLRP12 on Poly-Ub and HSP90 binding of NOD2 (H) Schematic diagram

Background: Pathologic calcification (PC) is the deposition of calcium-containing crystals in soft tissues. PC of cartilage is a hallmark of osteoarthritis (OA), a degenerative joint disease characterized by cartilage degradation. The interplay between calcification- and extracellular matrix (ECM) formation, maturation and degradation in cartilage is not fully understood.

Objectives: We aim to reveal the role of lysyl oxidases (LOX(L)), a family of extracellular enzymes that catalyze collagen crosslinking, in OA cartilage calcification.

Methods: We induced *in vitro* chondrocytes calcification with calcifying medium (CM = BGJb +10% FBS+ 20mM β-glycerophosphate + 50μg/ml ascorbic acid) or control (Nt = DMEM high glucose + 10% FBS), and treated or not with 500μM β-aminoproprionitrile (BAPN). Gene expression was analyzed by qRT-PCR, Il-6 in cell supernantants by ELISA, mitochondrial and cytoplasmic reactive oxygen species (ROS) by use of the kits MitoSOX and DHE (Life Technologies). We induced i*n vivo* murine knee calcifications using the menisectomy (MNX) mode, where medial meniscus is removed in the right knee, while the left knee is sham operated. During two months, mice were injected with PBS or BAPN 50mg/Kg twice per week, and given 1mg/ml BAPN in drinking water. New calcific formation in knees were analyzed by microCT. Bioinformatics analysis was performed with an online tool at www.systems-genetics.org/mmad, using the Modules by Module section in GeneBridge. Manhattan plots were generated by correlating collagen fibril organization module (GO:0030199, representing LOX/L family of enzymes, and calcification-, chondrocyte hypertrophy- and catabolic enzymes-associated modules.

Results: Our findings revealed that CM and calcium-containing crystals induced lox(l) activity in murine chondrocytes *in vitro*. Conversely, treatment with the lox(l) pan-inhibitor BAPN, decreased crystal production in vitro, while decreasing calcification gene expression of *Anx5*, *PC1*, *Pit-1/2* and Alp activity. Intriguingly, we identified that the pro-calcifying effects of LOX/L were mediated via their classical cross-linking activity, as diminished cross-links in pre-formed extracellular matrix reduced in parallel chondrocyte calcification, with specific suppression of *Anx5* and *Pit-1/2* genes. Additionally, BAPN reverted the hypertrophic phenotype of calcifying chondrocytes, reducing expression of *Runx2* and *Col10* and increasing that of early differentiation *Sox9* and *Col2*. In the same conditions, LOX/L inhibition downregulated *Col1* and *Col3*, whose uncontrolled production can lead to ECM fibrosis and calcification. BAPN also inhibited the expression and release of pro-calcifying cytokine Il-6, while also reducing mitochondrial and cytoplasmic ROS, known to be associated with PC. Additionally, we revealed in calcifying chondrocytes that BAPN inhibition decreased cartilage catabolic enzymes genes (*Mmp3*, *Mmp13* and *Adamts5*). In line, treatment with BAPN in an *in vivo* murine OA model based on meniscectomy, led to decreased knee joints calcifications, while not affecting the bone mineral density of the knee. We also confirmed the role of lox/l in human OA cartilage calcification. Indeed. LOX(L) inhibition by BAPN led to reduced crystal production in primary human OA chondrocytes. Finally, a bioinformatics transcript analysis of available human and murine databases obtained from tissues potentially undergoing PC, further confirmed a positive association between LOX(L)/collagen fibril organization module and calcification-, chondrocyte hypertrophy- and catabolic enzymes-associated modules.

Conclusion: Collectively, our results revealed for the first time a pro-calcifying effect of LOX(L) in chondrocytes, through classical (cross-linking of extracellular matrix) and non-classical pathways (i.e. chondrocyte hypertrophy, increased matrix synthesis and degradation, and exacerbated IL-6 and ROS production). In conclusion, LOX(L) provide a novel target for future therapies aimed at treating pathologic cartilage calcification.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0335 EXOSOMES TRANSMIT DAMAGE SIGNALS FROM INFRAPATELLAR FAT PAD AND EXACERBATE CHONDROCYTE SENESCENCE IN OSTEOARTHRITIS

Keywords: Osteoarthritis, Treat to target

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Background: Infrapatellar fat pad (IPFP) is closely associated with the development and progression of knee osteoarthritis (OA)[1-5], but the underlying mechanism remains unclear.

Objectives: This study aims to investigate the role and regulatory mechanisms of osteoarthritic infrapatellar fat pad (IPFP) tissue-derived exosomes (IPFP-Exos) in chondrocytes senescence and osteoarthritis (OA) progression.
Methods: The IPFP were collected from late-stage OA patients with knee arthroplasty. The role of endogenous osteoarthritic IPFP-Exos was measured in human IPFP explants coculturing with chondrocytes and mice post-traumatic OA models induced by destabilization of the medial meniscus (DMM) surgery with GW4869 or vehicle treatment. Extraction of IPFP tissue exosomes was performed by ultracentrifugation. Chondrocytes degradation and cellular senescence were assessed by qRT-PCR, western blotting, alcian blue and toluidine blue staining, immunofluorescence and senescence-associated beta-galactosidase staining, respectively. MiRNA sequencing was employed in IPFP-Exos to explore its cargoes. Luciferase reporter assay was used to reveal the interaction between exosomal miRNAs and their downstream mRNA target.
Results: Osteoarthritic IPFP tissue could secret exosomes and delivery them into articular chondrocytes. Inhibition of endogenous osteoarthritic IPFP-Exos significantly alleviated cartilage distruction. Functional assays *in vitro* demonstrated that IPFP-Exos significantly promoted chondrocyte extracellular matrix (ECM) catabolism and cellular senescence. Moreover, further experiments demonstrated that IPFP-Exos induced ECM degradation in human and mice cartilage explants and aggravated the progression of experimental OA mice model. Mechanistically, highly enriched let-7b-5p and let-7c-5p in IPFP tissue-derived exosomes were essential to mediate detrimental effects by directly decreasing senescence negative regulator, lamin B receptor (LBR). Notably, intra-articular injection of antagomirs inhibiting let-7b-5p and let-7c-5p in mice increased LBR expression, suppressed chondrocyte senescence and ameliorated the progression of experimental OA model.
Conclusion: This study highlights the function and mechanism of the IPFP-Exos in the progression of OA. Targeting IPFP-Exos cargoes of let-7b-5p and let-7c-5p provide a potential prevention strategy for OA.
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Disclosure of Interests: : None declared.
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POS0336 **PERIPHERAL IMMUNOME DYSREGULATIONS REFLECT OSTEOARTHRITIS (OA) JOINT DISEASE SEVERITY**

Keywords: -omics, Osteoarthritis

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Background: Osteoarthritis (OA) is a prevalent condition that is especially common among people of advanced ages. It is due to cartilage degeneration which leads to loss of mobility and chronic pain. Currently, there is no disease-modifying drugs to treat OA and the standard of care is pain management, and eventual joint replacement for end-stage disease. It is recognized that OA pathogenesis involves a complex interplay of joint damage, poor cartilage regeneration, and inflammation. However, much is unknown how the peripheral immunome architecture is perturbed by the local joint inflammation.
Objectives: To investigate how the peripheral immunome is dysregulated by local joint inflammation as a result of knee OA, and whether different immune subsets are dysregulated at different stages of OA severity.
Methods: We employed the use of mass cytometry time-of-flight (CyTOF) to investigate peripheral blood mononuclear cells (PBMCs) obtained from patients with OA and healthy controls (HCs). 64 patients with different severity of OA, based on radiographic Kellgren-Lawrence scores, and 37 age, sex, and race-matched HCs were enrolled in this study. To broadly capture the dysregulations in the different immune subsets, we designed two CyTOF marker panels that cover major innate and adaptive immune cell lineages to interrogate these samples. To investigate possible relationships between the peripheral and joint immunome dysregulations, digital deconvolution of RNA-sequencing data obtained from OA synovial samples to estimate immune subset frequency changes in the joint was also conducted.
Results: We observed dysregulations in both the innate and adaptive compartments of the OA peripheral immunome as compared to HCs, and different immune subsets were dysregulated at different OA severity. In early OA, there is an involvement of inflammatory immune subsets, namely natural killer (NK) and gamma-delta T cells, suggesting the possibility of these subsets infiltrating the joint to initiate and perpetuate joint inflammation in OA. As the disease progresses to late OA, we discovered further involvement of CD45RO+ and CTLA-4+/PD-1+ T cell subsets suggesting memory formation and immune exhaustion. Furthermore, we also observed an involvement of regulatory subsets in late OA suggesting the homeostatic attempts to temper the chronic inflammation at the OA joint. Comparing with our analysis of the digital deconvolution of RNA-seq data of OA synovia, NK cells, monocytes, gamma-delta T cells, and resting memory T cell subsets were found to be dysregulated in both the peripheral and joint immunomes, suggesting possible trafficking dynamics and functional relationship between the two immunomes.

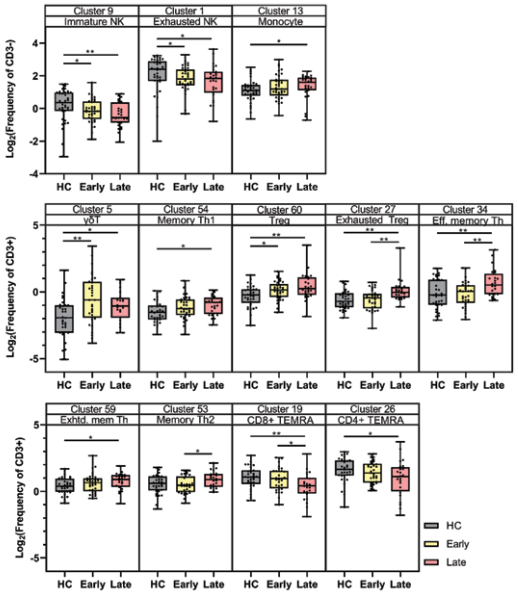


Figure 1.

Conclusion: Our study revealed dynamic peripheral immunome changes that provide insights to the immunopathogenesis of OA. By uncovering these underlying peripheral immunome disruptions in OA, we provide further evidence that the immune system plays an important role in OA disease process.
Acknowledgements: This research was supported by Duke-NUS Medical School under the Duke/Duke-NUS Research Collaboration Award (Duke/Duke-NUS/RECA/2012/2005), National Research Foundation Singapore under its National Medical Research Countil (NMRC)'s Transition Award Grant (CIRB

Ref. No.:2019/2094) and NMRC Clinician-Scientist Award: Investigator Category (NMRC/CSA-INV/0022/2017), and Ministry of Health, Singapore, under its MOH Health Services Research Competitive Research Grant (HSR-CRG) (HSRG14may017).

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POS0337 CHARACTERIZATION OF CIRCULATING CHONDROPROGENITOR CELLS IN PATIENTS AFFECTED BY OSTEOARTHRITIS

Keywords: Osteoarthritis, Non-pharmacological interventions, Cartilage

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Background: Osteoarthritis (OA) is a common chronic degenerative disease caused by progressive cartilage degradation [1]. In OA, regenerative medicine based on mesenchymal stem cells (MSCs) is considered the most promising method for restoring articular cartilage [2]. However, the high heterogeneity of MSCs together with invasive and painful procedures for stem cell isolation represent the main challenges of tissue engineering technology (3)[4]. In this regard, a homogeneous population of MSCs, the chondroprogenitor cells (CPs), have been recently discovered in human bone [5].

Objectives: In the light of these considerations, the purpose of this study was to identify CPs in OA. In addition, we aimed to differentiate circulating MSCs into chondrocytes for their in vitro characterization.

Methods: For this study, 10 patients affected by widespread OA [10F; median age 62 years, IQR 9; median disease duration 19 years, IQR 4] related and 10 healthy donors (HD) matched by sex and age were enrolled. A blood sample was collected from each participant to the study for the characterization of three CP populations [5]. In summary, after the isolation of CD45- cells from 500 µl of whole blood using anti-CD45+ magnetic beads, samples were labeled with anti-CD146-PE, anti-CD73-APC, anti-CD164 – FITC and PDPN PerCP/Cyanine5.5 antibodies. The acquisition was performed on a FACSCalibur cytometer. Data was analyzed using the Cell Quest Pro software. For in vitro culture of circulating MSCs, peripheral blood mononuclear cells (PBMCs) were isolated by Ficoll-gradient protocol and were cultured in DMEM supplemented with 20% FBS and 1% antibiotic–antimycotic. At 60–80% of confluence, the adherent cells were cultured in Complete Chondrogenesis Differentiation Medium for 7 days. At the end of in vitro chondrogenesis, morphological analysis was performed by bright-field microscopy. After in vitro differentiation, samples were labeled with anti-CD44-PerCP, anti-CD151-APC and anti-CD49c-PE antibodies, for the analysis of chondrogenic capacity. In addition, cell apoptosis was analyzed using AV-FITC and PI apoptosis detection kit.

Results: Flow Cytometry analysis identified CPs in peripheral blood. Interestingly, the two populations CD45-, PDPN +, CD146-, CD73 +, CD164+ and CD45-, PDPN +, CD146-, CD73-, CD164 + were significantly decreased in OA patients compared to HD (0.82% ± 0.46 vs 4.13% ± 1.92, 0.65% ± 0.22 vs 3.74% ± 1.10, p = 0.0065 and p = 0.0022, respectively) (Figure 1a). During in vitro expansion, MSCs of OA patients were numerically lower than HD (Figure 1b). Moreover, after in vitro chondrogenesis, OA chondrocytes showed a more rounded shape and a volumetric enlargement, which are features typical of chondrocyte hypertrophy (Figure 1c). Flow cytometry results showed that chondrogenic superficial markers, i.e CD44, CD151, and CD49c, were significantly lower in OA chondrocytes to HD (p=0.0009, p=0.0042 and p=0.0002, respectively) (Figure 1d). Lastly, apoptosis was significantly higher in OA chondrocytes than in HD (p=0.004) (Figure 1e).

Conclusion: The results of this study demonstrated a lower percentage of circulating CPs in patients affected by OA compared to HD. Furthermore, OA circulating MSCs showed a reduced chondrogenic capacity supported by a high number of hypertrophic chondrocytes and an increase in apoptosis levels. Further studies are need to clarify the possible application of circulating CPs in cartilage regenerative therapy.

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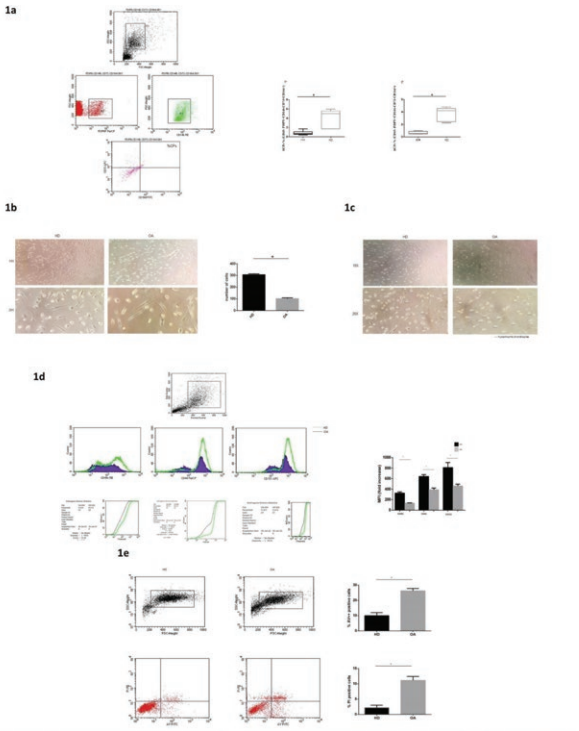


Figure 1a. Flow cytometry strategy for the analysis and characterization of circulating CPs. The upper left panel represented the morphology of CPs cells (CD45-). Within the R1 region, PDPN+ cells (R2) were identified; CD146- (R3) cells were identified within the R2 region; three CPs were identified within the R3 region: CD73+/CD164+, CD73+/CD164-, CD73-/CD164+. Box plots showed the percentage of CPs in OA and HD.
Figure 1b. Circulating MSCs morphology. Panels showed the morphology of circulating MSCs from HD and OA at 20x and 10x magnification. The histogram displayed the number of MSCs in HD and OA.
Figure 1c. Chondrocytes morphology. Panels showed the morphology of chondrocytes from HD and OA at 20x and 10x magnification. Blue bar indicated the chondrocyte size.
Figure 1d. Flow cytometry analysis of chondrogenic capacity. The upper left panel represented the morphology of chondrocytes. The lower panels showed the expression of the surface antigens CD49c, CD44 and CD151 in HD (grey line) and in OA patients (purple). The histogram displayed the expression of surface molecules in HD and OA.
Figure 1e. Flow cytometry analysis of chondrocytes apoptosis. The upper left panel represented the morphology of chondrocytes. The lower panels showed the percentage of annexin V (AV) and PI-positive cells by flow cytometry in chondrocytes from HD and OA. Histograms represented the percentage of apoptotic/necrotic cells in HD and OA.
For each experiment *p < 0.05.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Beyond the crystal ball

POS0338

DEVELOPMENT AND VALIDATION OF RANKED COMPOSITE IMPORTANT DIFFERENCE (RCID) SCORE IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

Keywords: Randomized control trial, Patient-led research, Systemic sclerosis

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Background: The revised Combined Response Index in diffuse cutaneous Systemic Sclerosis (dcSSc) (rCRISS) is a composite outcome measure relying on 6 core set variables including Organ Failure, Forced Vital Capacity (FVC), HAQ-DI and modified Rodnan skin score (mRSS), together with patient and clinician global assessments of disease activity [1]. rCRISS is calculated in patients not experiencing any organ failure and reported as proportion of patients who improve a given % (20,30,40 etc) in at least 3 domains. rCRISS discriminated treatment vs placebo in 3 randomised, placebo-controlled trials on early diffuse SSc [1]. Notwithstanding, it is not clear what is the minimal rCRISS score that captures an overall improvement in disease. Further, being developed as a response index, patients that do not experience a predefined organ failure but do worsen in their disease cannot be scored or discriminated from patients that simply do not improve.

Objectives: To improve the clinical interpretation of the rCRISS by creating a continuous ranked score of clinician and patient meaningful changes in its individual measures.

Methods: Following OmerACT guidelines, 100 physicians with experience in dcSSc and 100 patients with dcSSc who have participated in a dcSSc trial were identified in 5 continents. An adaptive survey was developed, based on 1000Minds conjoint analysis software. Patients and doctors were asked to choose, on successive pairs of two hypothetical patients, who had better or worse outcome according to presence of organ failure and Minimally Clinical Important Differences (MCID) in two domains among FVC, HAQ-DI and mRSS. Pairwise comparisons of choices were analysed utilising PAPRIKA methodology [2] to rank and weight the MCIDs against each other. The resulting score was tested in the same cohort utilised for rCRISS development. Briefly, 354 SSc patients data from three randomized, placebo-controlled trials (Asset, Foccussced and Fasscinate) were randomised in 10 development (2/3 pts) and validation (1/3 pts) sets, stratified by study and treatment group. Mean scores of the replicate datasets were calculated for active and placebo treatments. Bootstrapping was employed to determine 95% Confidence Intervals. Kappa statistics were used to analyse concordance.

Results: 160 of the 200 participants completed the survey. Discrete choices conjoint analysis defined ranks and relative weights of the 4 domains in the improved and worsened outcomes groups. A continuous composite ranked score reflecting the relative weighting of the individual outcome measures (Ranked Composite Important Difference, RCID) was developed. The score ranges from -1 (worst possible outcome) to 1 (best possible outcome), with patients who experience no organ failure and do not meet any MCID in any of the 3 domains scoring 0. Positive RCID scores showed a strong correlation with ACR CRISS >0.6 with kappa statistics in development and validation sets of 0.71 (CI 0.64,0.73) and 0.71 (0.66,0.84), respectively. 73.1% of subjects with positive RCIDs (74% in the validation set) met revised CRISS10, with 63.7 and 51.3 meeting rCRISS 20% and 30%, respectively. rCRISS scores between 20 and 30 were associated with only positive RCIDs. Additionally, 32% (C.I 29.7,34.3) of subjects on active treatment showed a positive RCID (>0) vs 25.8 (CI: 23.3,26.6) in the placebo group. Data were confirmed in the validation set (31.7 vs 27.1). Conversely, 12.3% (10.7,14) of subjects on treatment arms showed negative RCID (Any worsening, <0) vs 21.1 (19.2,23.3) in the placebo groups.

Conclusion: Our process adopted a robust methodology with a large patient representation in outcome measure development, to develop a patient and physician derived anchor (RCID) to other composite scores, such as ACR CRISS and revised CRISS. RCID provides a clinician and patient meaningful score that can be used as a dichotomous variable with a positive (improved) or negative (worsened) outcome.

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POS0339

HIGH-GRADE SYNOVITIS ASSOCIATES WITH CLINICAL MARKERS AND RESPONSE TO DMARDS THERAPY IN CHRONIC INFLAMMATORY ARTHRITIS: POST HOC ANALYSIS OF A PROSPECTIVE STUDY

Keywords: Psoriatic arthritis, Synovium, Rheumatoid arthritis

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Background: Inflammatory arthritis (IA), such as rheumatoid arthritis (RA) and psoriatic arthritis (PsA), are characterized by the presence of chronic synovitis. The Krenn synovitis score (KSS), a semi-quantitative histopathological score, allows the discrimination between high-grade and low-grade synovitis [1]. Although KSS could be potential useful for profiling patients with IA, its associations with clinical and treatment features are not yet thoroughly described.

Objectives: The aim of this post hoc analysis was to identify clinical and instrumental correlates of KSS and to evaluate the association between high-grade synovitis and treatment response in a prospective cohort of IA including both RA and PsA patients.

Methods: Clinical, laboratory and ultrasound (US) data were retrieved from RA and PsA patients recruited in MATRIX cohort. Inclusion criteria were age ≥18 years, RA (ACR/EULAR 2010) or PsA (CASPAR criteria) diagnosis, presence of active disease with eligibility to start/modify new DMARDs therapy. Patients underwent US-guided synovial biopsy of one of the most involved joint (knee or wrist) before starting/modifying DMARDs treatment according to treat-to-target strategy. The samples were analysed by an expert pathologist and KSS was calculated. Univariate and multivariate logistic regression analyses were performed to evaluate the relation between KSS and baseline variables. The association between KSS and treatment response, defined by ACR20, DAS28 remission and the newest ACR/EULAR remission criteria (2) at 6 months of follow-up, was investigated in univariate logistic regression analysis.

Results: 50 patients, 31 RA and 19 PsA, completed 6 months of follow-up after synovial biopsy. Baseline characteristics did not differ between RA e PsA patients except for F/M ratio (77% vs 32%, p=0.001). Four patients (8%) were treatment-naïve and, within the refractory patients (46/50, 92%), 19 (38%) were previously treated with b/tsDMARDs. GCs exposure was reported for 17/31 (55%) RA and 8/19 (42%) PSA patients. KSS was available for 47 patients and the median value was 6.00 (IQR 4.00-7.00) in RA samples and 4.00 (IQR 3.00-5.75) in PsA. Inflammatory infiltrates score was significantly higher in RA than in PsA patients (median 3.00 vs 2.00, p=0.034)(Figure 11A). At univariate analysis, the presence of C reactive protein (CRP)≥0.5 mg/dl, erythrocyte sedimentation rate (ESR)≥30 mm, DAS28-ESR, joint stiffness in the biopsied joint (VAS≥60 mm), moderate to high synovial effusion and moderate to high power Doppler signal detected by US at baseline evaluation in the biopsied joint all associated with increased risk of high-grade synovitis. Fibromyalgia, instead, associated with a reduced risk of high-grade synovitis. At multivariate analysis, US effusion (OR 7.18, 95%CI 1.49, 47.98), CRP (OR 5.66, 95%CI 1.23, 33.22) and joint stiffness (OR 7.67, 95%CI 1.31, 73.51) significantly associated with high-grade KSS (Figure 1B). After 24 weeks (33/50 new b/tsDMARDs, 6/50 new csDMARDs

initiated), 24/48 patients achieved DAS28 remission, 18/48 ACR/EULAR remission and 26/50 ACR20. Univariate analysis revealed increased OR of remission/response for patients with high-grade synovitis (ACR20 OR 4.57, 95%CI 1.36, 17.01, p=0.017; DAS28 remission OR 5.85, 95%CI 1.60, 25.48, p=0.011; ACR/EULAR OR 7.50, 95%CI 1.69, 53.49, p=0.017) (Figure 1C). The interaction between KSS and diagnosis had no significant impact on the outcome.

Conclusion: KSS is a simple and feasible tool for disease stratification of patients with IA, recommended in synovial biopsy research. In our study, high CRP, joint stiffness and US presence of synovial effusion correlated with the presence of high-grade synovitis. High grade synovitis was associated with increased probability of achieving remission 6 months after therapy upgrade in active IA patients independently from diagnosis.

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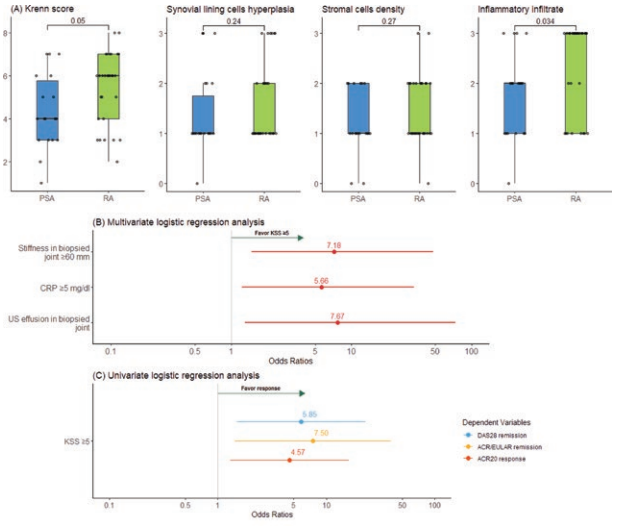


Figure 1 – (A) Differences between RA and PsA patients in KSS and its subcomponents. (B) Multivariate logistic regression model fitted for high grade synovitis with CRP ≥ 0.5 mg/dl, US synovial effusion score ≥2 and joint stiffness ≥60 mm in VAS scale. Variables were selected with backward stepwise method. (C) Univariable logistic regression model fitted with high grade synovitis for ACR/EULAR remission or ACR20 response or DAS28 remission at 24 weeks.

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POS0340 PROGNOSTIC FACTORS OF INTERSTITIAL LUNG DISEASE: A 10-YEAR LONGITUDINAL COHORT ANALYSIS

Keywords: Prognostic factors, Imaging, Lungs

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Background: Interstitial lung disease (ILD), defined as interstitial pneumonia (IP) and pulmonary fibrosis, has a variety of backgrounds. Connective tissue diseases (CTD) is one of the leading causes of ILD, and the concept of "IP with an autoimmune feature (IPAF)" has been established [1]. It has been reported that CTD-related ILD (CTD-ILD) and IPAF have a better prognosis than idiopathic pulmonary fibrosis [2]. However, prognostic differences and factors among CTD-ILD, IPAF, and other ILDs (OILD) remain unknown.

Objectives: This study aimed to analyze the prognosis and its factors in patients with CTD-ILD and IPAF compared to those with OILD.

Methods: We retrospectively collected data from 642 patients diagnosed as "IP" or "pulmonary fibrosis" between 2010 and 2021 at Tomakomai City Hospital. ILD diagnosis was performed by CT scan with 2 rheumatologists. We classified ILD into 3 groups of CTD-ILD, IPAF, and OILD. Mortality and prognostic factors were assessed using Kaplan-Meier methods and Cox proportional hazards models. In addition, we analyzed hospitalization free survival using Kaplan-Meier methods.

Results: Clinical characteristics of the patients are shown in Table 1. The CTD-ILD and IPAF patients were younger, and less frequently complicated by coronary artery disease and chronic heart failure. In addition, more patients in the IPAF and CTD-ILD groups showed a Non-specific interstitial pneumonia (NSIP) pattern on initial CT, while OILD group showed a usual interstitial pneumonia (UIP) and diffuse alveolar damage (DAD) pattern. C-reactive protein (CRP) levels were lower in the IPAF and CTD-ILD group.

The prognosis of CTD-ILD and IPAF group was better than OILD group (Figure1, adjusted p<0.001, <0.01, respectively), but that of CTD-ILD and IPAF was similar (adjusted p=1.0). Multivariate analysis revealed the ILD classification was not independent prognostic factor (p=0.11, Hazard ratio (HR) 0.85, [0.70-1.04]). However, age (p<0.001, HR1.03, [1.02-1.05]), sex (p<0.001, HR 2.08, [1.51-2.87]), initial CT patterns as UIP (p<0.01, HR 2.68, [1.27-5.67]) and DAD (p<0.001, HR 7.99, [3.85-16.60]) were independent prognostic factors. The leading causes of death (CTD-ILD vs. IPAF vs. OILD) were IP (48.2% vs. 55.6% vs. 44.7%, p=0.05), infection (10.8% vs. 22.2% vs. 18.4%, p = 0.07), and malignancy (24.1% vs. 5.6% vs. 7.9%, p = 0.03). In the analysis of event free survival, there was no difference among three groups (p =0.80), and the most common cause was the infection in the CTD-ILD group (36.1%) and primary disease in the OILD and IPAF groups (29.0%, 36.4%, respectively).

Table 1. patient's background

	OILD	IPAF	CTD-ILD	*p* value
N	388	81	173	
Male (%)	271 (69.8)	39 (48.1)	56 (32.4)	<0.001
Age (mean (SD))	74.0 (11.7)	70.2 (12.3)	67.1 (12.9)	<0.001
CT pattern				
NSIP (%)	138 (35.6)	48 (59.3)	114 (65.9)	<0.001
UIP (%)	175 (45.1)	26 (32.1)	45 (26.0)	<0.001
OP (%)	28 (7.2)	3 (3.7)	8 (4.6)	0.3
DAD (%)	47 (12.1)	4 (4.9)	6 (3.5)	0.002
Comorbidity				
DM (%)	132 (34.0)	29 (35.8)	43 (24.9)	0.07
Coronary artery disease (%)	65 (16.8)	8 (9.9)	3 (1.7)	<0.001
COPD (%)	25 (6.4)	7 (8.6)	3 (1.7)	0.03
Thyroid disease (%)	30 (7.7)	8 (9.9)	16 (9.2)	0.7
CKD (%)	18 (4.6)	3 (3.7)	4 (2.3)	0.4
CHF (%)	71 (18.3)	11 (13.6)	8 (4.6)	<0.001
Labo Data				
CRP, mg/dL (mean (SD))	5.6 (7.1)	4.1 (6.1)	3.3 (4.9)	0.001
LDH, U/L (mean (SD))	300.1 (190.0)	258.9 (81.1)	293.3 (176.0)	0.2
KL-6, U/mL (mean (SD))	1056.4 (1064.2)	1108.2 (923.52)	962.0 (867.0)	0.5

DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease, CHF: chronic heart failure

Conclusion: Unexpectedly, complication of autoimmune features was not a prognostic predictor of ILD. Age, sex, initial CRP level and CT patterns such as UIP and DAD, at the initial diagnosis were critical prognostic factors.

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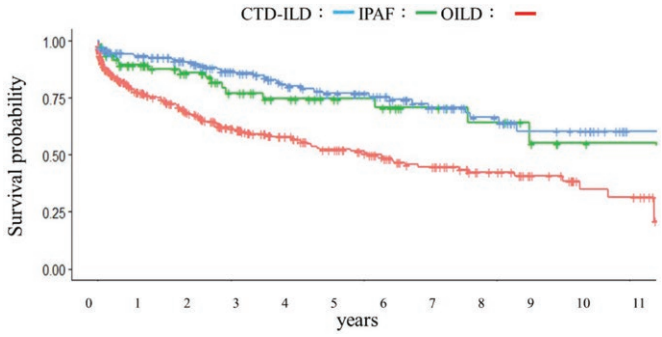


Figure 1. Kaplan-Meier methods of the three groups

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POS0341 PERFORMANCE ANALYSIS OF A DEEP LEARNING ALGORITHM TO DETECT POSITIVE SIJ MRI ACCORDING TO THE ASAS DEFINITION IN AXSPA PATIENTS

Keywords: Spondyloarthritis, Artificial Intelligence, Imaging

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Background: Magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ) is an essential tool in the evaluation of patients with axial spondyloarthritis (axSpA). In-depth knowledge of characteristic MRI lesions and their definitions, as well as reliability of identification and scoring, varies amongst general radiologists and rheumatologists.[1] A deep learning algorithm was developed to detect the presence of inflammation in SIJ MRI (MRI+) scans with promising results.[2]

Objectives: The aim of this diagnostic performance study was to assess the ability of a deep learning algorithm to identify MRI+ scans in a study cohort of axSpA patients.

Methods: 731 baseline SIJ MRI scans were collected from two prospective randomised controlled trial cohorts in patients with non-radiographic (nr-) and radiographic (r-) axSpA (RAPID-axSpA [NCT01087762] and C-OPTIMISE [NCT02505542])[3,4] and were centrally evaluated by two expert readers (and adjudicator in case of disagreement) for the presence of inflammation by the 2009 Assessment in SpondyloArthritis international Society (ASAS) definition.[5] The MRI scans were processed by the previously trained deep learning algorithm,[2] blinded to clinical information and central expert readings.

Performance evaluation included sensitivity, specificity, positive and negative predictive values (PPV and NPV), Cohen's Kappa and the absolute agreement to assess the agreement between the deep learning algorithm and the human readers for the classification of MRI-SIJ scans. Bootstrapping was used to construct the 95% confidence interval (CI).

Results: Pooling the patients from RAPID-axSpA (n=152) and C-OPTIMISE (n=579) yielded a validation set of 731 patients (mean age: 34.2 years, SD: 8.6; 69.1% male) of which 44.6% were patients with nr-axSpA and 59.6% were MRI+ as per central readings.

Comparing the trained algorithm with the human central readings for the classification of MRI+/MRI– on the pooled validation set yielded a sensitivity of 70% (95% CI: 66–73%), specificity of 81% (95% CI: 78–84%), PPV of 84% (95% CI: 82–87%), NPV of 64% (95% CI: 61–68%), Cohen's kappa of 0.49 (95% CI: 0.43–0.55), and absolute agreement of 74% (95% CI: 72–77%; **Table 1**).

Conclusion: A previously trained deep learning algorithm enabled acceptable detection of the presence of inflammation according to the 2009 ASAS MRI definition in axSpA patients from two clinical trials. This suggests that an MRI+ detection algorithm has the potential to support clinicians in identifying axSpA patients.

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Table 1. Performance results comparing the algorithm and the human readers for the classification of MRI-SIJ scans. The metric values are point estimate (95% CI).

Metric	All (N=731)	RAPID-axSpA (N=152)	C-OPTIMISE (N=579)
Central reading, MRI+; n(%)	436 (59.6%)	99 (65.1%)	337 (58.2%)
Sensitivity	0.70 (95% CI: 0.66–0.73)	0.66 (95% CI: 0.58–0.73)	0.71 (95% CI: 0.67–0.75)
Specificity	0.81 (95% CI: 0.78–0.84)	0.89 (95% CI: 0.82–0.95)	0.79 (95% CI: 0.75–0.83)
PPV	0.84 (95% CI: 0.82–0.87)	0.92 (95% CI: 0.87–0.96)	0.83 (95% CI: 0.79–0.86)
NPV	0.64 (95% CI: 0.61–0.68)	0.58 (95% CI: 0.50–0.67)	0.66 (95% CI: 0.62–0.70)
Cohen's kappa	0.49 (95% CI: 0.43–0.55)	0.48 (95% CI: 0.36–0.61)	0.49 (95% CI: 0.42–0.56)
Absolute agreement	0.74 (95% CI: 0.72–0.77)	0.74 (95% CI: 0.68–0.79)	0.74 (95% CI: 0.72–0.77)

CI: confidence interval; MRI: magnetic resonance imaging; NPV: negative predictive value; PPV: positive predictive value; SIJ: sacroiliac joints.

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POS0342

PERFORMANCE OF THE EULAR SYSTEMIC SCLEROSIS IMPACT OF DISEASE (SCLEROID) QUESTIONNAIRE AS A PATIENT REPORTED OUTCOME MEASURE FOR PATIENTS WITH DIFFUSE SYSTEMIC SCLEROSIS

Keywords: Patient-led research, Patient reported outcomes, Systemic sclerosis

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Background: There is a high unmet need for disease-modifying antifibrotic therapies in diffuse cutaneous systemic sclerosis (dcSSc) which could improve the outcome of this severe disease. Patient reported outcome measures (PROMs) are important and mandatory for randomized clinical trials (RCTs). The EULAR-endorsed ScleroID is the first comprehensive PROM specifically developed by SSc patients and experts to reflect the disease impact of SSc and showed a good performance in the clinical validation study [1]. However, most RCTs focus on dcSSc patients, hence a validated PROM to reflect the disease burden experienced by patients with dcSSc is needed and a detailed analysis of ScleroID in this subset of patients is lacking.

Objectives: To investigate the performance of the EULAR ScleroID in patients with dcSSc as a prerequisite for its use as a PROM in RCTs testing potentially disease-modifying drugs.

Methods: This is a subanalysis of all patients with dcSSc from the large, multicentric, ScleroID validation cohort [1]. As comparators, SSc-HAQ, EQ-5D, SF-36 were included. The study had a longitudinal arm with a reliability visit at 7+/- 3 days and a 12-month follow-up visit [1]. The performance of ScleroID in dcSSc was assessed according to the OMERACT filter [1].

Results: 152 dcSSc patients with a baseline visit were analyzed (44, 28.9% male, median age 54 years, median disease duration 7 years). ScleroID performed well as a PROM reflecting the disease impact of dcSSc: it showed a good construct validity with high Spearman's correlation coefficients with comparators (SSc-HAQ, 0.79, 95%CI [0.69, 0.86]; HAQ-DI, 0.72 95%CI [0.60, 0.80]; SF-36 physical score, -0.69 95%CI [-0.77, -0.60]). Furthermore, the internal consistency was strong:

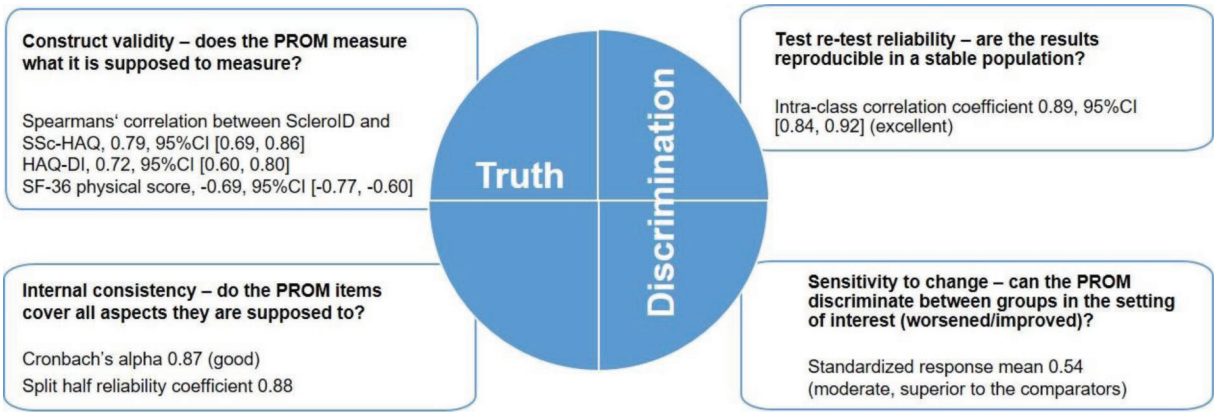


Figure 1. Performance of ScleroID in dcSSc by the OMERACT filter for truth and discrimination.

Cronbach's alpha was 0.87 and the split half reliability coefficient was 0.88. In the longitudinal arm, 44 patients had a test-retest reliability visit and 113 a follow-up visit, of whom 19/113 (16.8%) reported a significant change at 12 months follow-up (11 improved, 8 worsened). ScleroID showed a good consistency and discrimination ability with excellent test-retest reliability (intra-class correlation coefficient 0.89, 95%CI [0.84, 0.92]) and moderate sensitivity to change (standardized response mean 0.54), superior to the comparators (SSc-HAQ, 0.01; HAQ-DI, -0.07; SF-36 physical score, -0.43). The results are summarized in Figure 1.

Conclusion: The EULAR ScleroID, which is a novel, brief, disease specific, patient-derived, disease impact PROM, performs well for patients with dcSSc. This supports the inclusion and further analysis of ScleroID as a PROM to reflect patients' perspective in RCTs.

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POS0343

STATINS INFLUENCE THE RELATIONSHIP BETWEEN ATP-BINDING CASSETTE TRANSPORTER A1 (ABCA1)-MEDIATED CHOLESTEROL EFFLUX AND CORONARY ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS

Keywords: Cardiovascular disease, Biomarkers, Rheumatoid arthritis

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Background: High-density lipoprotein (HDL) mediated cholesterol efflux capacity (CEC) is facilitated by various membrane transporters based on the maturity of the acceptor HDL particles. ATP-binding-cassette membrane transporter A1 (ABCA1) exports cholesterol to immature discoidal HDL particles triggering their maturation to spherical HDL, which in turn serve as cholesterol acceptors for antiatherogenic ABCG1 mediated export. In the context of active RA, increasing ABCA1 CEC may result from reduced HDL particle maturation due to impairment of lecithin-cholesterol acyltransferase, leading to decreased ABCG1 CEC, cholesterol transfer from discoidal HDL to low-density lipoprotein (LDL) and its reloading on macrophages, as well as increased triglycerides favoring a proatherogenic phenotype. Beyond lowering LDL levels, statins have various pleiotropic effects including anti-inflammatory activities, but it is unknown whether they modulate the impact of HDL CEC on atherosclerosis in RA.

Objectives: We here explored associations between ABCA1 CEC, coronary atherosclerosis and cardiovascular risk in RA and the influence of statins on those relationships.

Methods: Coronary atherosclerosis (noncalcified, partially or fully calcified, low attenuation plaques and coronary artery calcium [CAC] score) was evaluated with computed tomography angiography in 140 patients without cardiovascular disease and reassessed in 99 after 6.9±0.4 years. ABCA1 CEC and ABCG1 CEC were measured in J774 macrophages and Chinese hamster ovary cells as previously described. Cox regression evaluated the association between ABCA1 and cardiovascular risk. Multivariable negative binomial and robust logistic regression tested associations of ABCA1 CEC and its interactions with statin therapy on various plaque numbers at baseline, follow-up and CAC progression.

Results: ABCA1 CEC inversely correlated with ABCG1 CEC (Pearson r = -0.167, p=0.049) and directly correlated with triglyceride levels (Pearson r = 0.239, p=0.004), reflecting its association with a proatherogenic phenotype. ABCA1 CEC (per 1 SD increment) associated with long-term cardiovascular risk after adjustments for cardiovascular risk score and baseline plaque burden [HR 2.05 (95% CI 1.20-3.48), Figure 1A]. ABCA1 CEC had no main effect on baseline plaque burden or progression. Instead, its impact on the respective outcomes was influenced by baseline statin use and daily average dose of statin correspondingly. ABCA1 CEC inversely associated with stenotic plaque severity in statin users but not in nonusers (p for interaction = 0.011, Figure 1B). Higher ABCA1 CEC further associated with fewer noncalcified plaques (Figure 1C) and lower noncalcified plaque stenotic severity (Figure 1D) in statin users but not nonusers (p for interaction = 0.024 and 0.023 respectively). Higher ABCA1 CEC associated with fewer low attenuation plaques in statin users but more in nonusers (p for interaction ≤0.001, Figure 1E) and statin users displayed fewer low attenuation plaques compared to nonusers at high (≥+1 SD) but not low (≤-1 SD) ABCA1 CEC. Moreover, ABCA1 CEC inversely associated with CAC progression in patients using high daily atorvastatin equivalent dose (+1 SD) but not nonusers (p for interaction = 0.008, Figure 1F).

Conclusion: In a proatherogenic milieu typical of active RA, including a block in HDL maturation, increased triglycerides and LDL oxidation, increasing ABCA1 activity as the predominant CEC pathway is insufficient to counterbalance and may in fact associate with vascular damage and plaque vulnerability. Statin use, by decreasing triglycerides, LDL levels and oxidation, may reduce cell cholesterol overload, thus unmasking the atheroprotective effects of ABCA1 CEC.

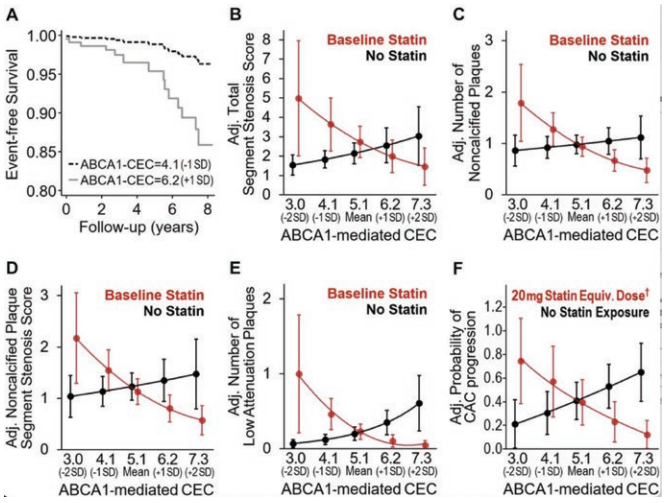


Figure 1. Associations of ABCA1 with cardiovascular risk (A) and influence of statins on the relationships between ABCA1, baseline plaque burden (B-E) and CAC progression (F)

REFERENCES: NIL.

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POS0344

BASDAI CUT-OFFS FOR DISEASE ACTIVITY CORRESPONDING TO ASDAS-ESR CUT-OFFS IN AXIAL SPONDYLARTHRITIS – RESULTS FROM THE EUROSPA COLLABORATION

Keywords: Outcome measures, Patient reported outcomes, Validation

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Background: The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is often used for classifying patients according to disease activity states. BASDAI values of 2, 4 and 6 have been applied as cut-offs for inactive disease (ID), between low disease activity (LDA) and high disease activity (HDA) and for very high disease activity (VHDA), respectively, although these cut-off values have not been validated.

Objectives: We aimed to (i) identify BASDAI cut-offs for disease activity states corresponding to the Ankylosing Spondylitis Disease Activity Score (ASDAS) cut-offs, and (ii) investigate the impact of gender on the BASDAI cut-offs.

Methods: Prospectively collected real-world data from axSpA patients receiving tumour necrosis factor inhibitors (TNFi) from countries participating in the European Spondyloarthritis (EuroSpA) Research Collaboration Network were analysed [1]. We chose the ASDAS version based on erythrocyte sedimentation rate (ASDAS-ESR) for which the cut-offs were first developed [2]. Hence, data from 10 registries in EuroSpA with available BASDAI and ASDAS-ESR were included. Analyses were restricted to patients' first TNFi series with available data. To have the best representation of the disease activity states, follow-up data (6, 12 or 24 months) were used to select the cut-offs for ID and between LDA and HDA, while baseline data were used to select the cut-off for VHDA. We performed receiver operating characteristic (ROC) analyses to determine the optimal BASDAI values corresponding to ASDAS-ESR cut-offs using the Youden index (=sensitivity+specificity-1). Furthermore, we carried out separate ROC analyses to identify gender-specific BASDAI cut-offs. Finally, the level of agreement between the new BASDAI cut-offs and the ASDAS-ESR cut-offs was assessed.

Results: We included 4,672 axSpA patients (2,775 (59%) men) with a registration of both BASDAI and ASDAS-ESR at baseline and at least one follow-up visit. Mean (SD) BASDAI and ASDAS-ESR were 5.7 (2.1) and 3.3 (1.0) at baseline, and 3.0 (2.3) and 1.9 (1.0) at follow-up, respectively. The optimal BASDAI values corresponding to ASDAS-ESR 1.3, 2.1 and 3.5 were 2.1, 3.3 and 6.3, respectively (Figure 1). When comparing the BASDAI and ASDAS-ESR cut-offs, the level of agreement was lower for the VHDA cut-off compared to the other disease activity states (Table 1). The gender-specific BASDAI cut-offs corresponding to ASDAS-ESR cut-offs (i.e., 1.3, 2.1 and 3.5) were 2.1, 3.1 and 6.2 for men and 2.1, 3.3 and 6.4 for women, respectively (Figure 1). We also observed that fewer women met the ID and LDA cut-offs of <1.3 and <2.1 than men (Table 1).

Conclusion: The BASDAI cut-offs corresponding to ASDAS-ESR 1.3, 2.1 and 3.5 were 2.1, 3.3 and 6.3, respectively. There was no evidence of a clinically relevant difference in BASDAI cut-offs between men and women.

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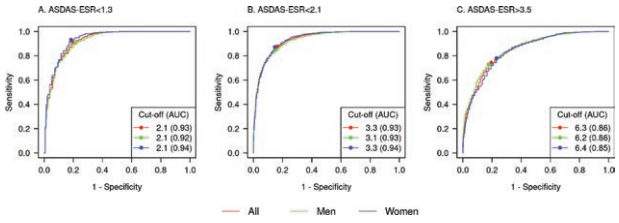


Figure 1. ROC curves and optimal cut-offs for BASDAI corresponding to ASDAS-CRP cut-offs. AUC: area under the curve.

Table 1. Statistical measures of agreement between BASDAI and ASDAS-ESR cut-offs

Cut-offs between ID and LDA (follow-up)						
	BASDAI<C1 (%)	ASDAS-ESR<1.3 (%)	Disc (%)	SE	SP	κ
All	42.4	33.2	15.9	0.90	0.81	0.67
Men	48.1	40.6	16.2	0.89	0.80	0.67
Women	34.0	22.5	15.3	0.92	0.83	0.63
Cut-offs between LDA and HDA (follow-up)						
	BASDAI<C2 (%)	ASDAS-ESR<2.1 (%)	Disc (%)	SE	SP	κ
All	60.5	63.7	14.4	0.86	0.85	0.69
Men	63.9	71.2	15.7	0.84	0.85	0.64
Women	51.6	52.8	14.2	0.85	0.86	0.71
Cut-offs between HDA and VHDA (baseline)						
	BASDAI>C3 (%)	ASDAS-ESR>3.5 (%)	Disc (%)	SE	SP	κ
All	40.8	42.5	21.9	0.72	0.82	0.55
Men	38.7	42.0	21.4	0.71	0.84	0.56
Women	44.0	43.2	23.0	0.74	0.79	0.53

C1: 2.1, 2.1 and 2.1 for all patients, men and women, respectively; C2: 3.3, 3.1 and 3.3 for all patients, men and women, respectively; C3: 6.3, 6.2 and 6.4 for all patients, men and women, respectively.C: cut-off; Disc: proportion of discordance; SE: sensitivity; SP: specificity; κ: kappa coefficient.

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Daniela Di Giuseppe: None declared, Karel Pavelka Speakers bureau: Speaker fees from Pfizer, MSD, BMS, UCB, Amgen, Egis, Roche, AbbVie, Consultant of: Consulting fees from Pfizer, MSD, BMS, UCB, Amgen, Egis, Roche, AbbVie, Jakub Zavada Speakers bureau: Speaker fees from Abbvie, Elli-Lilly, Sandoz, Novartis, Egis, UCB, Consultant of: Consulting fees from Abbvie, Elli-Lilly, Sandoz, Novartis, Egis, UCB, Sella Aarrestad Provan Consultant of: Boehringer Ingelheim, Grant/research support from: Boehringer Ingelheim, Maria Jose Santos Speakers bureau: Speaker fees from Abbvie, AstraZeneca, Lilly, Novartis, Pfizer, Ana Maria Rodrigues Speakers bureau: Speaking fees from Abbvie, Amgen, Consultant of: Consulting fees from Abbvie, Amgen, Grant/research support from: Research grant from Novartis, Pfizer, Amgen, Adrian Ciurea Speakers bureau: Speaking fees from AbbVie, Eli Lilly, Merck Sharp & Dohme, Novartis, Pfizer, Consultant of: Consulting fees from AbbVie, Eli Lilly, Merck Sharp & Dohme, Novartis, Pfizer, Michael J. Nissen Speakers bureau: Speaking fees from AbbVie, Eli Lilly, Merck Sharp & Dohme, Novartis, Pfizer, Consultant of: Consulting fees from AbbVie, Eli Lilly, Merck Sharp & Dohme, Novartis, Pfizer, Catalin Codreanu Speakers bureau: Speaker fees from AbbVie, Amgen, Boehringer Ingelheim, Ewopharma, Lilly, Novartis, Pfizer, Consultant of: Consultancy fees from AbbVie, Amgen, Boehringer Ingelheim, Ewopharma, Lilly, Novartis, Pfizer, Corina Mogosan: None declared, Ziga Rotar Speakers bureau: Abbvie, Novartis, MSD, Medis, Biogen, Eli Lilly, Pfizer, Sanofi, Lek, Janssen, Consultant of: Abbvie, Novartis, MSD, Medis, Biogen, Eli Lilly, Pfizer, Sanofi, Lek, Janssen, Matija Tomsic Speakers bureau: Speaking fees from Abbvie, Amgen, Biogen, Eli Lilly, Janssen, Medis, MSD, Novartis, Pfizer, Sanofi, Sandoz-Lek, Consultant of: Consulting fees from Abbvie, Amgen, Biogen, Eli Lilly, Janssen, Medis, MSD, Novartis, Pfizer, Sanofi, Sandoz-Lek, Gary Macfarlane Grant/research support from: Research grant from GSK, Gareth Jones Speakers bureau: Speaker fee from Janssen, Grant/research support from: Research grants from AbbVie, Pfizer, UCB, Amgen, GSK, Dan Nordström Speakers bureau: Speaking fees from Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche and UCB, Consultant of: Consulting fees from Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche and UCB, Grant/research support from: MSD, Anna-Mari Hokkanen Grant/research support from: Grant/research support from MSD, Irene van der Horst-Bruinsma Consultant of: Consultant for Abbvie, UCB, MSD, Novartis, Lilly, Grant/research support from: Unrestricted Grants received for investigator initiated studies from MSD, Pfizer, AbbVie, UCB. Fees received for Lectures from BMS, AbbVie, Pfizer, MSD, Pasoon Hellamand Grant/research support from: Research grant from Novartis, Mikkel Østergaard Speakers bureau: Speaker fees from Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, UCB, Consultant of: Consultancy fees from Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, UCB, Merete Lund Hetland Speakers bureau: Speaker for Pfizer, Medac, Sandoz, Grant/research support from: Research grants from Abbvie, Biogen, BMS, Celltrion, Eli Lilly, Janssen Biologics B.V, Lundbeck Fonden, MSD, Medac, Pfizer, Roche, Samsung Biopies, Sandoz, Novartis.

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POS0345

ADALIMUMAB SERUM DRUG LEVELS AND ANTI-DRUG ANTIBODIES: ASSOCIATION TO DISEASE ACTIVITY AND DRUG SURVIVAL IN INFLAMMATORY ARTHRITIS PATIENTS

Keywords: Inflammatory arthritides, bDMARD

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Background: Lack of response to TNF-inhibitors (TNFi) can be caused by subtherapeutic drug levels and anti-drug antibodies (ADAb). Therapeutic-drug-monitoring (TDM) can help clinicians tailor treatment and may improve effectiveness, safety and cost-effectiveness of TNFi. For TDM to be validated as a clinical tool, therapeutic ranges must be identified.

Objectives: To explore the association between adalimumab serum drug level, treatment response and drug survival in patients with inflammatory arthritis, with the intention to identify a therapeutic range. In addition, to assess frequency and clinical implications of ADAb formation.

Methods: Patients with a clinical diagnosis of rheumatoid arthritis (RA), spondyloarthritis (SpA) or psoriatic arthritis (PsA) starting treatment with adalimumab and enrolled in the observational NOR-DMARD study were included. Treatment response at 3 months was defined as EULAR good or moderate response in RA/PsA and ASDAS Major or Clinically Important Improvement in SpA. Serum drug levels and ADAb at 3 months were measured using an in-house fluorescence method, with ADAb measured in patients with serum drug levels < 3mg/L. Comparisons of serum drug level and ADAb formation between diagnosis groups was done by Mann-Whitney U and $\chi 2$ test, respectively. Multivariate logistic regression analyses were used to assess serum drug level and treatment response and Cox proportional hazard regression analyses were used to assess drug survival and serum drug level, ADAb formation and methotrexate use, all analyses adjusted for age, sex and previous use of bDMARDs.

Results: A total of 343 patients (98 RA, 70 PsA, 177 SpA) were included (median age 46.0 years [SD 14.1], 182 [53%] female). 123/340 (36%) patients used methotrexate as co-medication. The median serum drug level at 3 months was 7.3 mg/L (IQR 3.7-10.3) and 34 (10 %) patients developed ADAb, these findings were comparable across diagnoses, (Figure 1A). Serum drug levels at 3 months were higher in responders (7.8 mg/L [IQR 5.4-10.5]) than in non-responders (6 mg/L [IQR 2.6-9.6]), p=0.0014. Percent distribution of responders at 3 months stratified by serum adalimumab levels by percentile distribution suggested that the therapeutic ranges were 6 -12 mg/L for RA/PsA and >1.4 mg/L SpA, with no upper cut-off detected in SpA, (Figure 1B and C). RA and PsA patients with serum adalimumab > 6 mg/L had higher odds for response to therapy at 3 months (Odds Ratio [OR] 2.2 [95% CI 1.1 – 4.5], p=0.026), and lower treatment discontinuation rate (Hazard Ratio [HR] 0.43 [95% CI 0.27-0.80], p= 0.006). No additional benefit was found with serum drug levels >12 mg/L. SpA patients with serum adalimumab level >1.4 mg/L had higher odds for response (OR 4.7 [95% CI 1.4-15], p=0.01) Further, in these patients treatment discontinuation was seen at a lower rate (HR 0.35 [95% CI 0.17-0.73], p= 0.005). Patients with ADAb at 3 months discontinued treatment at a higher rate (HR 3.4 [95% CI 2.1-5.3], p=<0.001). In RA/PsA patients, co-medication with methotrexate was associated with higher serum drug levels (8.4 mg/L [IQR 5.3-10.9] vs 5.8 mg/L [IQR 1.2-8.7], p=0.0003), lower rate of ADAb (6% vs 22 %, p<0.0001) and better drug survival (HR for drug discontinuation 0.50 [95% CI 0.29-0.87] p= 0.013).

Conclusion: This study is the first to explore associations between adalimumab serum levels and clinical outcomes across all inflammatory arthritides. Higher adalimumab drug levels were associated with clinical response at 3 months and long-term drug survival. This study suggests 6 - and 1.4 mg/L as lower target adalimumab levels for RA/PsA and SpA respectively and contributes to the development of TDM algorithms for adalimumab in arthritis patients.

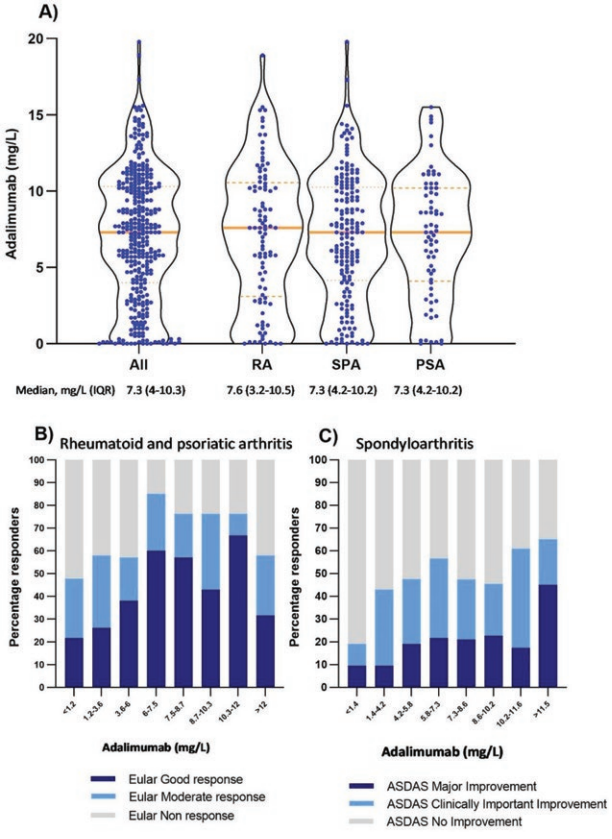


Figure 1. Serum adalimumab levels at 3 months. A) Violin plot. Each data point is a participant, and the solid orange line show the group median. **B) and C)** Percent distri bution of responders at 3 months stratified by serum adalimumab levels. Adalimumab groups are divided by percentile distribution.

REFERENCES: NIL.
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POS0346 DEVELOPMENT AND VALIDATION OF PROGNOSTIC MODELS FOR THE INCIDENCE OF RADIOGRAPHIC KNEE OSTEOARTHRITIS BASED ON NOVEL PROTEIN BIOMARKERS

Keywords: Biomarkers, Prognostic factors, Osteoarthritis

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Background: Knee Osteoarthritis (KOA) is one of the most prevalent and disabling rheumatic diseases. The inability to detect early disease stages and the lack of effective treatments leave KOA patients without non-surgical clinical options. The early diagnosis of KOA at asymptomatic stages is crucial to improve the prompt management of the patients, in order to prevent or slow the course of the disease. Major research interest is focused on discovering prognostic markers useful to identify individuals at high risk of developing KOA before joint damage appears.
Objectives: To develop a prognostic model useful to predict the incidence of radiographic knee osteoarthritis (rKOA).
Methods: This study involved subjects without established KOA according to the Kellgren and Lawrence classification scale (KL=0-1), who were enrolled in the Osteoarthritis Initiative (OAI) cohort and the Prospective Cohort of A Coruña (PROCOAC). We developed two predictive models for rKOA incidence within 96 months of follow-up among participants in the OAI cohort. The protein biomarker candidates APOA1, APOA4, ZA2G and A2AP were quantified in serum using a custom-made multiplex protein microarray. The prospective association of the protein levels with rKOA incidence, defined as progressing to KL≥2 during 96-months follow-up, was evaluated to develop the models based on the protein biomarkers, sociodemographic, anthropometric and non-radiographic clinical measurements. Their predictive capacity was assessed using the area under the curve (AUC). The performance of the models was externally validated in the PROCOAC cohort.
Results: We included 602 participants from the OAI cohort in the development dataset, which had a KL ≤1 at baseline. From these, 390 did not present any radiographic signs of KOA (KL=0) in both knees. The model built exclusively with demographic and clinical data (age, sex, BMI and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain score) from patients with KL ≤1 (early KOA) at baseline showed an AUC=0,719 to predict rKOA incidence during the follow-up. The inclusion of ZA2G, A2AP and APOA1 significantly improved its predictive performance, yielding an AUC= 0,793. When only subjects with KL=0 in both knees at baseline were included, the clinical model predicts the future development of rKOA with an AUC=0,724 and achieved a significantly higher AUC=0,798 with the addition of the 4 biomarkers (Figure 1). No differences were found in the predictive performance for the proposed models between the development and validation cohorts (Table 1).
Conclusion: Two prognostic models have been developed to predict rKOA incidence based on the measurement of four novel protein biomarkers.

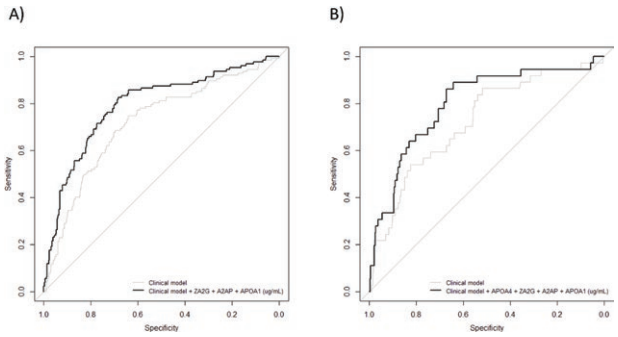


Figure 1. Overlapping of the AUCs obtained from the clinical models (grey line) and the clinical models with the biomarkers (black line) to predict the incidence of radiographic KOA during the follow-up period in the development cohort (OAI). A) Clinical model (AUC= 0,719) and the clinical model with the 4-biomarkers (AUC=0,793) in patients with KL≤1 at baseline; B) Clinical model (AUC= 0,724) and the clinical model with the 4-biomarkers (AUC=0,798) in patients with KL=0 at baseline.

Table 1. Comparison of the performance of the proposed models in the development (OAI) and validation (PROCOAC) cohorts.

Clinical model + biomarkers	AUC (95%CI) Development cohort	AUC (95%CI) Validation cohort	p-value
KL ≤1	0,793 (0,746-0,839)	0,677 (0,564-0,791)	0,224
KL=0	0,798 (0,718-0,879)	0,761 (0,626-0,896)	0,640

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POS0347 DETERMINANTS OF PATIENT AND PHYSICIAN GLOBAL ASSESSMENT OF DISEASE ACTIVITY IN SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Pain, Psoriatic arthritis

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Background: Patient's and Physician's Global Assessment of Disease Activity (PtGA and PhGA) are important measures in Spondyloarthritis (SpA), but often provide discordant results. Some data show that patient-physician discordance can result in patient poor adherence to treatment and healthcare costs in SpA.[1]
Objectives: We intended to assess the principal determinants of both PtGA and PhGA in SpA patients under biologic treatment.
Methods: We performed a cross-sectional study, including patients with SpA under biologic treatment registered in the Rheumatic Diseases Portuguese Register (Reuma.pt), consecutively evaluated in a tertiary hospital center. Sociodemographic and clinical data were collected. PtGA and PhGA were measured on a Visual Analogue Scale of 0-100. To identify determinants of PtGA and PhGA, we performed firstly a univariate analysis with the independent variables and subsequently a multiple linear regression. SPSS v.24 was used for statistical analysis.
Results: We evaluated 186 patients with SpA according to ASAS criteria, under biologic treatment. Most patients were male (53.20%) with a mean age of 52.15 (SD=12.9) years-old at the time of last medical appointment. PtGA and PhGA were significantly different. Clinical and laboratory characteristics of patients are shown in table 1. There was a positive correlation between higher PtGA and older age, unemployment, number of tender joints, HAQ, HADS, BASDAI, number of comorbidities and daily medication. There was also an association with the concomitant presence of osteoarthrosis, fibromyalgia, C reactive protein

(CRP), erythrocyte sedimentation rate (ESR) and daily prednisolone intake. On the other side, we found a negative correlation with SF-36, FACIT and EQ5D. The multiple linear regression shows that the SF-36 (p=0.001), BASDAI (p<0.001) and being unemployed (p=0.042) were the most preponderant determinants in PtGA explaining 85% of the variability noted in PtGA (R^2 = 0.846; R^2_a= 0.828). Regarding PhGA we found a positive correlation between the number of tender and swollen joints, CRP and daily prednisolone intake. In multivariable analyses the main determinants of PhGA were the number of swollen joints and higher CRP (R^2 = 0.867; R^2_a= 0.829).

Table 1. Clinical and laboratory characteristics of patients with spondyloarthritis.

Age (years), mean ± SD	52.2 ± 12.9
Gender – male, %(n/N)	53.2% (99/186)
Patient Global VAS, mean ± SD	34.4 ± 27.2
Patient pain VAS, mean ± SD	31.9 ± 26.3
Patient back pain VAS, mean ± SD	25.0 ± 26.9
Physician Global VAS, mean ± SD	7.4 ± 12.7
Patient-physician discordance mean ± SD	27.8 ± 24.0
HAQ, median (IQR)	0.8 (1.1)
BASDAI, median (IQR)	2.5 (3.7)
BASFI, median (IQR)	2.4 (4.4)
Short Form (36) Health Survey (SF-36), mean ± SD	455.7 ± 167.2
FACIT, mean ± SD	35.6 ± 11.4
HADS, median (IQR)	Anxiety: 6 (8.0) Depression: 5 (8.0)
EQ5D, median (IQR)	0.4824 ± 0.4058
Daily medication, median (IQR	3 (3)

BASDAI: Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; EQ5D: EuroQol-5 dimension; FACIT: Functional Assessment of Chronic Illness Therapy; HADS: Hospital Anxiety and Depression scales; HAQ: Health Assessment Questionnaire; VAS: Visual Analogue Scale

Conclusion: We have demonstrated that comorbidities, employment status, and other factors not directly related to the disease are also determinants in PtGA. On the other hand, more objective data such as swollen joints and increased CRP were predominant in PhGA construct.

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Genetic Determinants of Clinical Phenotypes

POS0348

ACTIVATING STAT3 MUTATIONS IN CD8+ T CELLS CORRELATE TO SEROLOGICAL POSITIVITY IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Genetics/Epigenetics, Rheumatoid arthritis, Autoantibodies

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Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease that leads to inflammation and bone erosion of synovial joints. Serological markers such as rheumatoid factor (RF) and anti-CCP antibodies are commonly elevated, and cytotoxic CD8+ T-cell expansions have been implicated in disease pathogenesis. Large granular lymphocyte (LGL) leukemia is a rare hematologic malignancy characterized by clonal expansion of CD8+ cytotoxic T-cells. A major hallmark of all LGL leukemia is increased *STAT3* activation. About 50% of patients have somatic activating mutations in *STAT3*, the most common being Y640F and D661Y. Additionally, *STAT3* mutations correlate with numerous clinical features in LGL leukemia. LGL leukemia patients with *STAT3* mutations are more likely to respond to methotrexate treatment, tend to have low neutrophil counts, and clinical features can differ between mutation types (e.g. Y640F vs D661Y). Approximately one third of LGL leukemia patients also suffer from RA, and those with *STAT3* mutations are more likely to exhibit concomitant RA. Those patients with both diseases also tend to have increased positivity for serological markers like RF and anti-CCP antibodies than patients with either disease alone[1].

Objectives: Based on disease overlap between LGL leukemia and RA, and a putative role for CD8+ T-cells in RA, we hypothesized that *STAT3* mutations may be detected in the CD8+ T cells of RA patients without LGL leukemia and correlate with RA clinical characteristics.

Methods: Blood samples, clinical parameters, and demographic data were collected from RA patients (n=96), many of whom were on immunosuppressives such as methotrexate, and healthy controls (n=9). CD8+ cell DNA was isolated and analyzed via droplet digital (dd)PCR to detect common *STAT3* mutations in LGL leukemia: Y640F, D661Y, and mutations in the S614 to G618 region. RA samples were divided into wild-type (WT) vs. *STAT3*-mutant groups using a variant allele frequency (VAF) cutoff of 0.05%, and clinical parameters were correlated to mutation status.

Results: Overall, RA patients had statistically different levels of STAT3 mutations compared to controls (D661Y p=0.0005, Y640F p=0.0185). In particular, many more low level (0.005-0.05% VAF) mutations were detected in the RA population (43/96 Y640F, 59/96 D661Y) vs. healthy controls (0/9 Y640F, 0/9 D661Y). Additionally, 3/96 RA samples had a *STAT3* mutation at a VAF (>5%) large enough to be indicative of CD8+ T cell clonality compared to 0/96 controls (Table 1). Multiple serological RA markers were more frequently positive in *STAT3* mutant (80%-91%) relative to WT RA samples (44%-55%) (RF p=0.0005, anti-CCP p=0.018, double positivity p=0.006), with overall RF levels also significantly elevated (p=0.008) in *STAT3* mutant RA samples (Figure 1). Anti-CCP positivity was more common in Y640F patients (9/9) than D661Y (7/12).

Table 1. *STAT3* mutations were detected by ddPCR analysis of CD8+ T-cell DNA

Healthy Control Samples	<0.005%	0.005%-0.05%	0.05%-5%	5%
Y640F	8/9	0/9	1/9	0/9
D661Y	9/9	0/9	0/9	0/9
S614R_G618R	n/a	n/a	n/a	0/9
RA Samples	**<0.005%**	**0.005%-0.05%**	**0.05%-5%**	**5%**
Y640F	42/96	43/96	10/96	1/96
D661Y	23/96	59/96	14/96	0/96
S614-G618 Region	n/a	n/a	n/a	2/96

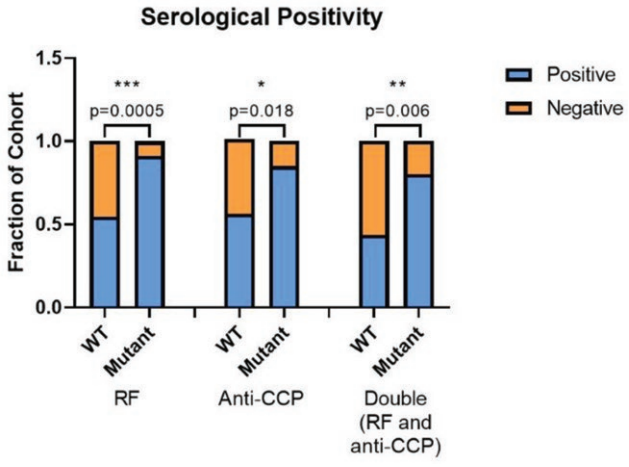


Figure 1. Presence of *STAT3* mutation correlates to increased serological positivity in RA patients

Conclusion: Taken together, the presence of *STAT3* activating mutations in CD8+ T-cells and the association of mutations with sero-positivity suggest that *STAT3* activating mutations may play a role in the pathogenesis and clinical features in a subset of patients with RA. Further study will determine the impacts of *STAT3* mutation presence on disease severity, prognosis, and selection of treatment options/potential treatment responses.

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POS0349 ABSENCE OF ASSOCIATION OF COMPLEMENT C4 GENETIC DIVERSITY WITH SERUM COMPLEMENTS, AUTOANTIBODIES AND DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Innate immunity, Systemic lupus erythematosus, Genetics/ Epigenetics

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Background: Systemic Lupus Erythematosus (SLE) is characterized by low levels of serum C3 and C4. Low complements in SLE may either be due to increased consumption or decreased synthesis, the exact mechanisms of which is unknown. *C4* gene has copy number variations and exists as two functionally distinct but genetically homologous isoforms, *C4A* (0-8 copies) and *C4B* (0-3 copies). The genes are either long (L) or short (S) based on a 6.4kb Human Endogenous Retrovirus K (*HERV-K*) insertion. Low copy numbers of complement C4 genes in systemic autoimmune disorders and its link with autoantibodies, disease subgroups have been reported.

Objectives: To characterize *C4* and *C4-HERV* genetic diversity in SLE and its relationship with serum complement levels, autoantibodies, disease activity, clinical subgroups and HLA.

Methods: Genomic DNA from 70 SLE and 90 controls were used to characterize the copy numbers of *C4A* and *C4B* genes and the frequency of HERV insertion (*C4AL, C4BL*) using droplet digital polymerase chain reaction. High resolution typing of 8 HLA genes was done using next generation sequencing. Chi-square test was used to compare the frequencies of *C4*, *C4-HERV* structural elements and HLA between groups. Correlation with complement levels, number of autoantibodies present, SLEDAI and clinical subgroups was done using Spearman's nonparametric test.

Results: In this cohort, total *C4* gene copies ranged from 2-6 with two copies of *C4A* and *C4B* genes being frequent; there were no C4 null alleles, and a negative correlation was noted between C4A and C4B copy numbers (r=-0.3713; p<0.001; Figure 1). Compared to controls, presence of two or less copies of *C4A* gene was associated with SLE risk while C4B frequency was comparable between the groups. Significantly increased frequency of *HERV* insertion in C4A than in C4B gene was observed. Of the 34 different *C4-HERV* genotypes observed, 7 were at a frequency greater than 5%. Though the frequency of *AL-AL-BL-BS* genotype was overrepresented in SLE, the difference was not statistically significant. The *AL-AL-AL-BS* genotype was significantly higher in controls than SLE (9% vs 1%, p=0.04; Table 1). HLA-DPA1*02 and DPB1*13 were more frequent in subjects with C4B >2 copies than in those with C4B ≤2 copies (33% vs 61%; Pc=0.04 & 5% vs 28%; Pc=0.04). There was no correlation between the *C4* as well as *C4-HERV* gene copy numbers and serum levels of complement, autoantibodies, SLEDAI and SLE clinical subgroups (Figure 1)

Conclusion: Our data show that, although the *C4A* and *C4B* gene diversity is different between cases and controls, it does not correlate with serum complement levels, autoantibodies, disease activity and clinical subgroups in SLE. Low *C4A* copy number and increased insertion of HERV in *C4A* may be a risk for SLE. Our findings in this small cohort need further validation in a larger homogenous SLE cohort.

Table 1. ***C4*** **Genetic diversity in SLE**

C4A copy numbers	SLE; n=70	%	HC; n=90	%	P	OR	95% CI
≤2	56	80%	53	59%	**0.005**	**2.79**	1.29 to 6.22
>2	14	20%	37	41%	0.005	0.36	0.16 to 0.77
C4B **copy numbers**							
≤2	56	80%	81	90%	NS	0.44	0.16 to 1.20
>2	14	20%	9	10%	NS	2.25	0.84 to 6.30
SLE *C4-HERV*	**C4A; n=70**	**%**	**C4B; n=70**	**%**	**P**	**OR**	**95% CI**
0 HERV insertion	2	3	19	27	0.000	0.08	0.01-0.36
1-3 HERV insertion	68	97	51	73	**0.000**	**12.67**	2.81-115.30
C4 genotypes	**SLE; n=70**	**%**	**HC; n=90**	%	**P value**	**OR**	**95% CI**
AL-AL-BL-BS	14	20%	12	13%	NS		
AL-AL-AL-BS	1	1%	8	9%	0.04	0.15	0.00 to 1.16
AL-AL-AS-BL-BS	8	11%	8	9%	NS		
AL-AL-AS-BL-BL	1	1%	7	8%	NS		
AL-AL-BL	4	6%	7	8%	NS		
AL-AL-BL-BL	7	10%	6	7%	NS		
AL-AL-BS-BS	7	10%	6	7%	NS		
AL-AL-BS	5	7%	4	4%	NS		

C4, Complement C4; HERV, Human Endogenous Retro Virus; SLE, Systemic Lupus Erythematosus; HC, Healthy Controls; P<0.05 considered significant

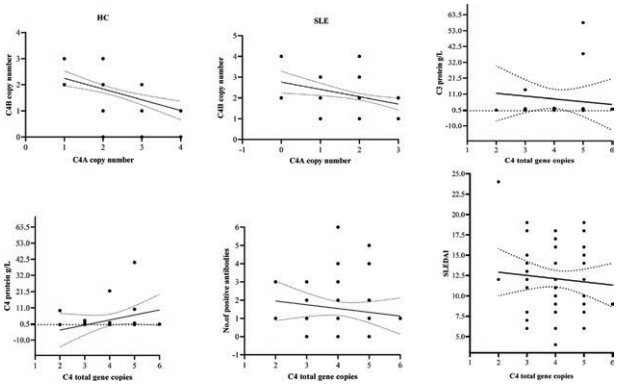


Figure 1. Association of C4 gene copy numbers with serum complements, autoantibodies & SLEDAI

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POS0350 PROXIMITY EXTENSION ASSAY AS A NOVEL TECHNOLOGY FOR BOOSTING MOLECULAR CHARACTERIZATION AND PERSONALIZED CLINICAL MANAGEMENT OF RHEUMATIC DISEASES

Keywords: Biomarkers

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Background: Rheumatic diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), systemic sclerosis (SSc), axial spondyloarthritis (axSpA), and psoriatic arthritis (PsA) are characterized by a complex clinical and molecular heterogeneity. Novel and disruptive technologies might shed light on their pathogenesis and clinical management.

Objectives: To evaluate the potential of the innovative proteomic technology "proximity extension assay" (PEA) to identify useful biomarkers, subgroups of patients, and novel insight into rheumatic diseases.

Methods: 533 consecutive patients with rheumatic diseases (141 SLE, 120 RA, 72 SSc, 100 axSpA and 100 PsA) and 50 healthy donors (HDs) were included in

the study where serum samples and clinical data were obtained. A signature of 368 proteins divided into 4 panels of 92 biomarkers associated with Inflammation (SLE, RA, SpA, and HDs), Organ Damage (SLE, SSc, and HDs), cardiovascular disease (RA, SpA, PsA, and HDs), and cardiometabolism (RA and HDs) was analysed by using PEA technology from Olink through its corelab Cobiomic Bioscience SL. PEA technology, already endorsed by more than 1000 peer-reviewed publications, recognizes proteins using antibody-pairs containing unique DNA sequences which are amplified by real-time PCR. Data analysis included t-test, unsupervised clustering analysis, ROC curves, and PCA among others.

Results: In SLE patients, the unsupervised cluster analysis using the circulating proteome identified 2 clusters with distinctive clinical features mainly differentiating disease activity and the presence of renal damage. Several proteins were also identified as novel non-invasive biomarkers of lupus nephropathy. Similarly, in SSc, a panel of proteins related to organ damage identified a subgroup of patients characterized by multiple organ involvement including lung and skin fibrosis and oesophageal dysmotility, along with a preponderance of anti-scl70 antibodies positivity. In axSpA patients, the levels of several proteins related to inflammation and cardiovascular disease (CVD) were altered compared with HDs and associated with key clinical features.

In RA, a specific signature of chemokines before therapy identified non-responders patients to anti-TNF therapy and Methotrexate after 3 months of treatment, pointing out its role as a predictor of therapy response. Moreover, several proteins associated with CVD and metabolism were modulated by the effect of Methotrexate and Tofacitinib, which also underlined their role as biomarkers for treatment monitoring. In PsA patients, numerous proteins related to CVD were up-regulated in relation to HDs and associated with clinical markers of CVD risk. Various circulating proteins also distinguished the presence of insulin resistance, high activity, and poor therapeutic outcome to Methotrexate and Apremilast. Furthermore, the PEA analysis of the inflammatory proteome in PsA synovial fluid revealed novel biomarkers of disease and potential therapeutic targets.

Conclusion: PEA technology might boost the future of precision medicine in rheumatic diseases through the identification of novel biomarkers of disease and therapy response and the stratification of patients with key clinical and molecular features.

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POS0351 MULTI-OMICS ANALYSIS IDENTIFIES DIFFERENTIAL LIPID REGULATION AS A POTENTIAL MECHANISM UNDERPINNING METHOTREXATE RESPONSE IN RHEUMATOID ARTHRITIS

Keywords: Biomarkers, Rheumatoid arthritis, -omics

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes inflammation and joint damage, leading to disability and reduced quality of life. Methotrexate (MTX) is a widely used disease-modifying anti-rheumatic drug that is initially prescribed to reduce inflammation and slowing disease progression in RA; however, approximately 40% of treated patients do not experience a satisfactory response to this drug. Identifying reliable surrogate biomarkers of MTX response would facilitate precision medicine strategies and improve patient outcomes.

Objectives: To identify blood-based transcriptomic and metabolomic biomarkers of MTX response in patients with RA.

Methods: Whole blood samples were taken from patients taking part in the Rheumatoid Arthritis Medication Study (RAMS), an observational longitudinal cohort of early RA patients starting MTX for the first time in the UK. RNA-seq data was generated using the Illumina NovaSeq 6000 platform of patients before and after 4 weeks MTX treatment. Treatment response was determined after 6 months on drug and patients were classified as good or non-responders using established EULAR response criteria. Differential gene expression analysis was performed using glmmSeq [1], which uses generalized linear mixed model with negative binomial distribution. Models were parameterized with size factor and dispersion estimated using DESeq2 [2]. The regression model included patient ID as a random effect and an interaction term was included between time-point and response category. Two-hundred and fifty targeted metabolites were quantified in serum samples from the same patients as above using nuclear magnetic resonance (NMR) based technology. Metabolomics data were normalised using probabilistic quotient normalization and scaled with pareto-scaling. Partial least-square regression (PLSR) and linear mixed effects models (constructed as above) were used to identify differentially expressed metabolites. All linear mixed models were adjusted for baseline disease activity (DAS28). Enrichment analysis for differentially expressed genes was performed using Metascape [3].

Results: In total, 100 patients were analysed (69 good-responders and 31 non-responders). Following quality control, 17,298 genes were tested for differential expression, 25 were significantly associated with response (fold change ≥ 1.5 at baseline, adjusted p-value < 0.05). Of these, 4 were enriched in monocarboxylic acid (which includes fatty acid) metabolism. Differential regulation of this biological process was also observed in the metabolomics profile where low-density lipoprotein cholesterol and triglycerides were associated with MTX treatment response; this was observed using both PLSR (AUC: 0.75) and linear mixed effects models (p-value < 0.05).

Conclusion: Whole blood multi-omics analysis has the potential to identify biomarkers and biological processes underpinning MTX response in RA. Further research is needed to understand and confirm the relationship between monocarboxylic acid metabolism and MTX response in this disease.

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Disclosure of Interests: Chuan Fu Yap: None declared, Nisha Nair: None declared, Suzanne Verstappen: None declared, Kimme Hyrich Speakers bureau: Abbvie, Grant/research support from: Pfizer, Bristol Myers Squibb, Anne Barton Speakers bureau: Galapagos, Grant/research support from: Pfizer, Bristol Myers Squibb, Scipher Medicine, Galapagos, Darren Plant Grant/research support from: Bristoly Myers Squibb.

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POS0352 GENETIC DETERMINANTS OF RESPONSE TO ABATACEPT IN PATIENTS WITH IGG4-RELATED DISEASE

Keywords: Adaptive immunity, Disease-modifying Drugs (DMARDs), Rare/orphan diseases

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Background: IgG4-related disease (IgG4RD) is a fibro-inflammatory disorder of unknown etiology. Emerging evidence indicates that chronic inflammation in IgG4RD is sustained by persistent mutual activation of antigen-specific B and T lymphocytes. Targeting B-T cell co-stimulation represents, therefore, a rationale therapeutic approach for IgG4RD.

Objectives: Threefold aim of the present work was (i) to assess the efficacy of abatacept (a selective inhibitor of B-T cell co-stimulation based on a replica of CTLA4) for the treatment of IgG4RD; (ii) to study T cell activation in IgG4RD patients; and (iii) to identify functional and genetic predictors of response to abatacept in IgG4RD patients.

Methods: Three patients with active IgG4RD (Pt1-3) were treated with monthly intravenous infusions of abatacept (750mg) for 6 months without concomitant glucocorticoids. All patients underwent 18F-FDG PET scan before treatment and after 6 infusions to assess disease response. To identify functional and genetic predictors of response to abatacept we used multicolour flow-cytometry and Whole Exome Sequencing (WES). Flow-cytometry using CD3, CD19, CD4, CD25, and CTLA4 antibodies was performed to assess CD4+ T cell activation upon exposure to recombinant humanized CD3/CD28 after 120 hours in vitro colture. Results were compared to 10 healthy controls and 10 patients with rheumatoid arthritis (RA). WES was performed to screen for mutations of a panel of 452 genes related to known monogenic immune mediated diseases.

Results: Pt 1 was a 47 years old male with bilateral submandibular gland involvement (Figure - A - *arrow*; B - *arrows*) and subcutaneous lesions (B - *circle*). Pt2 was a 78 years old woman with right orbital pseudotumor (Figure - A – *arrow*; B - arrow), sinonasal involvement (B - *arrowhead*), and skin lesions (B - *asterisk*). Pt3 was a 68 years old woman with left lacrimal and parotid glands involvement (Figure - A - *arrows*; B - *arrows*). Abatacept led to a marked decrease of the dimension and 18-F FDG uptake of IgG4RD lesions in Pt1 and Pt2. Pt3 showed increased pathological 18F-FDG uptake of her orbital pseudotumor with minimal morphologic changes at magnetic resonance, consistent with metabolic

progression. In vitro, there was no difference in CTLA4 expression at baseline between IgG4RD patients and controls (p>0.05). Yet, upon activation, IgG4RD patients displayed a premature decrease of CTLA4 expression on T cells compared to healthy donors (p<0.01), suggesting a defective T cell inhibition. Similar results were observed in patients with RA. Accordingly, IgG4RD patients showed expansion of activated CD25+ T cells compared to healthy controls (p<0.05). WES of the three IgG4RD patients treated with abatacept found eterozigous germline mutations of LRBA gene (p.Arg2646His (c.7937G>A)) (Pt1), CTLA4 gene (p.Gly109Glu (c.326G>A)) (Pt2), and DOCK8 gene (p.Gln1550Leu (c.4649A>T)) (Pt3). None of these mutations has been previously reported in the medical literature and remains of uncertain significance but all had a CADD score > 20, thus predicting deleterious impact on protein structure. Of note, mutations in LRBA, CTLA4, and DOCK8 genes are all associated with systemic autoimmunity, lymphoproliferation, and immune deficiency. In particular, as opposed to DOCK8 gene, LRBA and CTLA4 genes encode for functionally related proteins as LRBA regulates the reclycing of CTLA4 on T cell membrane upon antigen engagement to inhibit T cell activation.

Conclusion: In the present work we demonstrate that CD4+ T cells from IgG4RD patients show aberrant activation associated with a reduced expression of the inhibitory molecule CTLA4. Yet, not all patients respond to abatacept suggesting that IgG4RD is sustained by additional pathological mechanisms in at least a proportion of patients. Patients responding to abatacept display, indeed, germline mutations of uncertain significance in CTLA4 pathway and may represent ideal candidates for treatment with abatacept.

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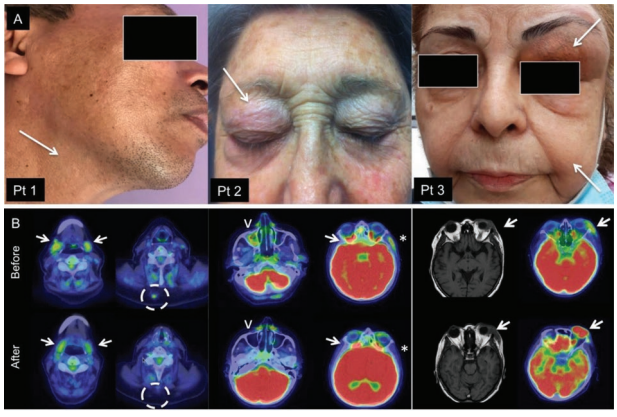


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2566

POS0353

DNA METHYLOME ALTERATIONS AS POTENTIAL DIAGNOSTIC AND PROGNOSTIC BIOMARKERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Genetics/Epigenetics, Rheumatoid arthritis, Biomarkers

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Background: The etiology of rheumatoid arthritis (RA) is not entirely known. Epigenetic modifications could be the link between genetic and environmental factors related to the appearance and evolution of RA.

Objectives: To identify differential DNA methylation patterns throughout the entire genome in patients with RA versus healthy controls, as well as epigenetic changes that may predict greater disease severity.

Methods: Cross-sectional study of a prospective cohort, in which 64 subjects were studied: 16 severe RA, 16 non-severe RA and 32 healthy controls. The severity phenotype was defined according to an average of moderate-high inflammatory activity defined by an accumulated Disease activity score (DAS28-ESR) ≥3.2, positivity for rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA), as well as higher *Collinsela aerofaciens* levels (OTU ≥0.15) [1,2]. DNA methylation was determined using *Infinium Methylation EPIC BeadChip* (Illumina, San Diego, CA, USA). The methylation level of each cytosine was expressed as β-value. ANOVA and bivariate analysis were performed to compare between groups of subjects. Multivariate logistic regression models were performed to identify factors associated with RA and severe RA phenotype.

Results: The majority (75%) were female with a mean age of 57.6 ± 9.4 years. The patients with RA, in comparison with the controls, had higher smoking habits (62.5% *vs.* 40.7%; p=0.015) and obesity (53.1% *vs.* 28.1%; p=0.012). Among patients, subjects with severe RA compared with non-severe had a higher mean DAS28-ESR (3.9 ± 0.6 vs. 3.3 ± 0.2 mg/l, p=0.001), and higher abundance in *Collinsela* (median (IQR), 0.3 (0.1-1.7) vs. 0.1 (0.0-0.4), p=0.003); as well as a higher frequency of erosions (93.8% *vs.* 50.0%; p=0.006), elevated ACPA (68.8% *vs.* 31.1%; p=0.034) and treatment with biological therapy (56.3% *vs.* 12.5%, p=0.009). Regarding the methylation analysis, those CpGs related to genes or pseudogenes, with a minimum β value change of ± 0.10 between groups and p value ≤ 0.01 were selected (Figure 1). The described CpG sites located in differentially methylated regions, together with other CpGs, were proposed as possible biomarkers (Table 1). In addition, cg06166490 was also considered, since it is located in a differentially methylated region with an adjusted p-value <0.00001. Of these CpGs, 5 CpG sites were associated with the presence of RA, and 2 CpG sites were associated with disease severity (Table 1).

Conclusion: DNA methylation level at specific CpG sites is associated with RA patients. The present study identified epigenome marks related to RA and possible disease severity, which warrant further investigation and could be useful in the diagnosis and management of the disease.

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Table 1. CpG sites selected as possible potential biomarkers

ID Probe	Region	Gene symbol	Multivariate Logistic Regression
			Model 1 (R^2=0,618)
cg16474696	Promoter	MRI1	OR: 1.04, 95%IC (1.00-1.07), p=0.034
cg15741931	Promoter	UBAP2L	OR: 1.12, 95%IC (1.04-1.21), p=0.003
cg06508795	Body	DCC	OR: 1.05, 95%IC (1.00-1.07), p=0.012
cg05510714	Body	KYNU	OR: 0.94, 95%IC (0.89-0.98), p=0.026
cg06166490	Promoter	Hoxa2	OR: 1.23, 95%IC (1.07-1.41), p=0.003
			Model 2 (R^2=0,381)
cg08586441	Body	TEC	OR: 1.07, 95%IC (1.00-1.15), p=0.037
cg14435720	Body	*MIR126*	
cg19405177	Body	*PLEC1*	
cg09497409	Promoter	*LASS4*	OR: 1.17, 95%IC (1.02-1.35), p=0.019
cg25251562	Promoter	ALLC	

Model 1: Dependent variable: Patients (1) vs. Controls (0). Model 2: Dependent variable: severe RA (1) vs. Non-severe RA (0). Age and sex were variables included in both models.

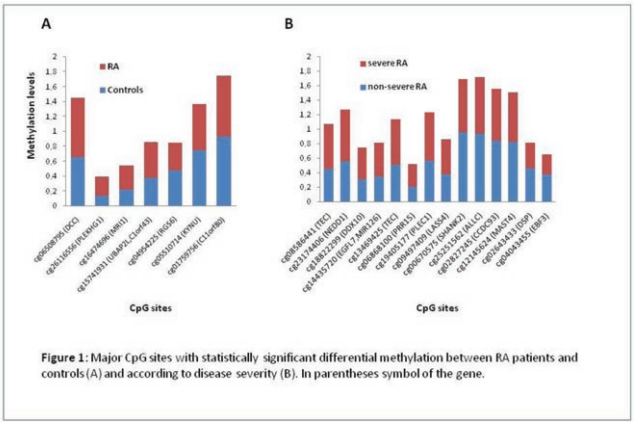


Figure 1: Major CpG sites with statistically significant differential methylation between RA patients and controls (A) and according to disease severity (B). In parentheses symbol of the gene.

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Disclosure of Interests: None Declared.
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POS0354

IDENTIFICATION OF SOMATIC MUTATIONS IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

Keywords: Vasculitis, Genetics/Epigenetics

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Background: Growing evidence reveals a pathological role of somatic mutations in various autoimmune diseases, such as the mutation in *UBA1* in VEXAS syndrome, *CARD11* and *KLHL6* in cryoglobulinemic vasculitis, or *STAT3* in Felty's syndrome[1]. Somatic mutations might also be involved in the pathogenesis of ANCA-associated vasculitis (AAV), which typically manifests in middle-aged and elderly individuals.
Objectives: We aimed to identify somatic mutations in patients with AAV.
Methods: We collected whole blood and obtained peripheral blood mononuclear cells (PBMCs) and neutrophils from patients with AAV in active-disease status (n=16), as well as from patients with other autoimmune diseases (n=8) as disease controls, and healthy subjects (n=10). In addition, we collected these specimens from 12 out of the 16 patients with AAV after remission induction. We performed RNA sequencing (RNA-seq) on the obtained cells and whole genome sequencing (WGS) on DNA extracted from the whole blood. Somatic mutations were detected by comparing the RNA and DNA sequences[2].
Results: After stringent quality control, we identified 108 somatic mutations across 16 patients in active-disease status. The mean coverage of RNA-Seq at the mutation site was 100.9 ± 367.8 ×, and that of WGS was 14.4 ± 4.3 ×, while the mean allele fraction was 22.9 ± 20.5%. One or more mutations were detected in each of the 15 (93.8%) patients. The median mutation count of each patient was 4.0, which was not significantly different from disease controls or samples after remission induction. We mapped one gene to each of the 108 mutations, resulting in 95 genes in total. Mutations for six of the 95 genes were observed in two or more patients, and two of them were related to the ubiquitin system. Of the 108 mutations, 37 were missense, and 20 were predicted to be deleterious (combined annotation-dependent depletion Phred score > 20). Among the 20 mutations, the *HIST2H2AC* mutation (NM_003517: p.L86P) in neutrophils was observed in two patients. To evaluate the functional outcome of the 20 mutations, we analysed the data on knocking out the corresponding genes using CRISPR in K562 cells[3]. The results showed that the expression of genes related to antigen presentation was increased in *HEATR1* and *RPL18* knockouts. When we followed up with 12 of the 16 patients after remission induction, 81.4% of the somatic mutations were no longer detected. Additionally, 91.7% of the deleterious mutations disappeared.
Conclusion: We found somatic mutations with potential pathological effects in some patients with AAV exhibiting active-disease status. Notably, the majority of these mutations were not detected after remission induction.
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Disclosure of Interests: None Declared.
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POS0355

CLINICAL TRAIT-SPECIFIC GENETIC ANALYSIS IN BEHÇET'S DISEASE IDENTIFIES NOVEL LOCI ASSOCIATED WITH OCULAR AND NEUROLOGICAL INVOLVEMENT

Keywords: Behcet's disease, Genetics/Epigenetics

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Background: Behçet's disease is a complex inflammatory vasculitis with a broad spectrum of clinical manifestations.
Objectives: The purpose of this study was to investigate the genetics underlying specific clinical features of Behçet's disease in a group of patients with > 5 years of follow up.
Methods: A total of 436 patients with Behçet's disease from Turkey were studied. Genotyping was performed using the Infinium ImmunoArray-24 BeadChip. After imputation and quality control measures, logistic regressions adjusting for sex and the first five principal components were performed for each clinical trait using a case-case genetic analysis approach. A weighted genetic risk score was calculated for each clinical feature.
Results: Genetic association analyses of previously identified susceptibility loci in Behçet's disease revealed a genetic association between ocular lesions and *HLA-B/MICA* (rs116799036: OR=1.85, 95% CI=1.35-2.52, p-value=$1.1x10^{-4}$). The genetic risk score was significantly higher in Behçet's disease patients with ocular lesions compared with those without ocular involvement, and is explained by the genetic variation in the HLA region. New genetic loci predisposing to specific clinical features in Behçet's disease were suggested when genome-wide variants were evaluated. The most significant associations were observed in ocular involvement with *SLCO4A* (rs6062789: OR=0.41 (95% CI=0.30-0.58), p-value=$1.92x10^{-7}$), and neurological involvement with *DDX60L* (rs62334264: OR= 4.12 (95% CI 2.34 to 7.24), p-value = $8.85x10^{-7}$).
Conclusion: Our results emphasize the role of genetic factors in predisposing to specific clinical manifestations in Behçet's disease, and might shed additional light into disease heterogeneity, pathogenesis, and variability of Behçet's disease presentation across populations.
References: None.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0356

EVALUATION OF FC GAMMA RECEPTOR (FCΓR/ FCGR) & CYP GENETIC POLYMORPHISM AND ITS PHARMACOGENOMIC CORRELATION WITH RITUXIMAB AND CYCLOPHOSPHAMIDE RESPONSE IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY ASSOCIATED VASCULITIS

Keywords: Remission, Vasculitis, Genetics/Epigenetics

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Background: The antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) are three discrete entities – Granulomatosis with polyangiitis (GPA), Microscopic polyangiitis (MPA), and Eosinophilic granulomatosis with polyangiitis (EGPA). They present with a plethora of signs and symptoms resulting in significant burden of mortality and morbidity. There is huge lacuna in the knowledge of relationship between various genes affecting pharmacogenetics of AAV and its implications in context of therapeutic complications. We thus intend to evaluate genotypic polymorphism in FcγR family & CYP genes affecting pharmaco-biological response of Rituximab and Cyclophosphamide respectively in AAV patients undergoing induction treatment.
Objectives: To study the single nucleotide polymorphism (SNP) of the FcγR family (FcγRIIIA, FcγRIIA, FcγRIIB) in patients receiving Rituximab (RTX) and the SNPs of CYP2C19*2 (rs4244285), CYP2B6 (rs321137) polymorphisms in patients receiving Cyclophosphamide (CYC) using polymerase chain reaction. Additionally, to correlate the genetic polymorphism of AAV patients with Rituximab and Cyclophosphamide treatment response.
Methods: This study was a prospective cohort study in which AAV patients undergoing induction treatment were enrolled from Jan 2021 to Dec 2022 in Clinical Rheumatology Department at PGIMER Chandigarh, India. Functional SNPs for FcγR(FcγRIIb 695T>C, FcγRIIIa 559T>G and FcγRIIa 519G>A) and

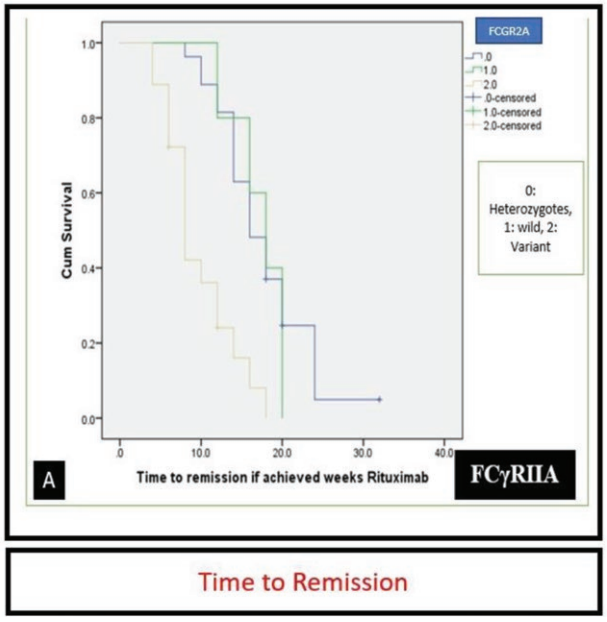
CYP enzymes (CYP2C19 681G>A, CYP2B6 1459C>T) were assesed by Sanger sequencing of PCR amplified genomic DNA. The end points were to detect associations between the tested SNPs and status of remission at six months and complete remission at end of the study.

Results: In this study we recruited ninty seven patients of AAV in Indian population. Table 1 summarises the baseline clinical characterisitics of the study population. FcγRIIA variant (v) allele frequency was more than wild allele (W) frequency in the study population. The time to achieve remission was significantly lower (mean:9.22 weeks) in FcγRIIA variant genotype polymorphism (FcγRIIa 519AA) in comparison to wild and heterozygotes variants (mean: 17.25 weeks) of FcγRIIA at site 131 (519G>A), as shown in Figure1. There were no significant difference observed in CYP polymorphism and cyclophosphamide response.

Table 1. Clinical and demographic characteristics of 97 AAV patients

Characteristic	N (%) or mean
Sex	
Male	38 (39%)
Female	59 (61%)
Male: Female Ratio	1:1.55
Mean age at diagnosis (years) ±SD	42.10 ± 15.57
Patient profile	
Newly diagnosed	31
Follow-up	66
AAV Subtypes	
GPA	82
MPA	8
EGPA	7
Signs and symptoms, n(%)	
Constitutional	76 (78.3%)
Sino-nasal	62 (63.9%)
Auditory	36 (37%)
Pulmonary	71 (73.2%)
Renal	52 (53.6%)
GIT	14 (14.4%)
CVS	12 (12.37%)
Skin	20 (20.6%)
CNS	23 (23.7%)
PNS	24 (24.7%)
Eyes	42 (43.2%)
Outcomes characteristics	
Number of patients achieving Remission (at 6 months of induction)	88
Number of patients achieving Complete Remission (at time of analysis)	40

Figure 1: Effect of SNP of FcγR2A at site 131 (519G>A); 0: heterozygotes(519 GA), 1: wild (519GG), 2: variant(519 AA)



Conclusion: This study is one of the first to evaluate the pharmacogenomic profile of AAV in Indian population. We observed highly significant association of SNPs of FcγRIIa 131 site variant/519AA genotype with early remission and complete remission after induction treatment with rituximab. This data could further help in tailored treatment of AAV patients and may also serve as a prognostic marker.

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Disclosure of Interests: None Declared.

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POS0357

A NOVEL MUTATION IN ALPL GENE CAUSING ADULT AUTOSOMAL DOMINANT HYPOPHOSPHATASIA IN A FAMILY OF SOUTHERN SPAIN: PHENOTYPE CHARACTERIZATION

Keywords: Genetics/Epigenetics, Rare/orphan diseases, Bone diseases

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Background: Tissue non-specific alkaline phosphatase (TNSALP) is essential for bone and tooth extracellular matrix mineralization. The gene encoding TNSALP (ALPL) is located on the long arm of chromosome 2. More than 400 ALPL variants exist. Low enzymatic activity of serum alkaline phosphatase (ALP) due to gene mutations leads to hypophosphatasia (HPP), a heterogeneous clinical condition ranging from asymptomatic or mild adult forms to severe perinatal disease. Adult's HPP most typical features are stress fractures and early loss of dentition.

Objectives: To describe the clinical phenotype and laboratory features in a family suffering from HPP in which a new gene variant was detected.

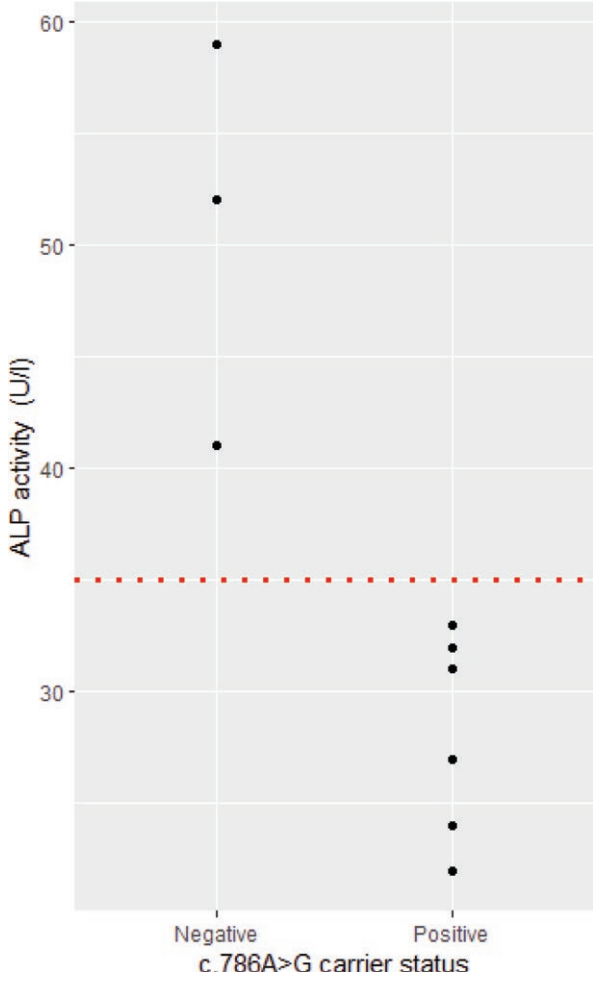
Methods: A descriptive observational study of a family belonging to the Virgen de Valme Hospital area (Seville) was conducted through a primary identification of an index case with low level of ALP in whom a novel ALPL gene mutation was found. Members from three family generations were screened for low level of ALP to select patients meeting laboratory criteria for HPP. To assess family segregation, phenotype and clinical relevance of this mutation, genetic analysis of those with confirmed low ALP and a selection of members with normal ALP levels was done. Epidemiological, clinical, laboratory and genetic study variables were collected. A descriptive quantitative analysis of the data was performed.

Results: We studied 16 members corresponding to three generations of the same family suspected to have familial hypophosphatasia. The index case was a 57-year-old male with chronic pain, problems with dentition and previous history of fractures. ALP screening found 8/16 (50%) patients with low level. Genetic testing was performed for 7/16 patients and 3/16 with low and normal ALP levels, respectively. A familial carrier variant c.786A>G heterozygotic single-nucleotide polymorphism (SNP) in the ALPL gene was found in all patients with low ALP (Graph 1). Clinical and laboratory features for the seven positive carriers are shown in Table 1. Most fractures were due to non-minor trauma. Chronic arthralgia was the main articular complaint. All laboratory values were within normal range, ruling out secondary causes of HPP. Only one patient presented with high pyridoxal-5'-phosphate (PLP).

Conclusion: We present a new autosomal dominant inheritance mutation in the ALPL gene that causes HPP. Variable clinical expressivity is observed. Dentition problems and recurrent fractures predominate, associated with chronic pain. Early diagnosis and genetic counselling may be important, although further studies and a larger population are required to establish the definitive pathologic relevance of this variant.

Table 1. Epidemiological, clinical and laboratory characteristics of positive mutation carriers (n = 7). ALP: alkaline phosphatase; PLP: pyridoxal-5'- phosphate; 25-OH-VitD: 25-hydroxy-vitamin D; PTH: parathyroid hormone; TSH: thyroid stimulating hormone.

Baseline characteristics (n = 7)			
Sex	Male	3 (42.8%)	
	Female	4 (57.2%)	
Age (mean, sd)	55.6 ± 13.2 years		
Early dentition loss	Yes	1 (14.3%)	
	No	6 (85.7%)	
Fracture history	Yes	4 (57.1%)	
	No	3 (42.9%)	
Articular manifestations	Yes	7 (100%)	
	No	0 (0%)	
Laboratory values			
	Mean, sd	Minimum	Maximum
ALP (U/l)	28 ± 4.16	22	33
PLP (nmol/l)	88 ± 49.1	26.5	178
Calcium (mg/dl)	9.83 ± 0.43	9.3	10.4
Phosphorus (mg/dl)	3.72 ± 0.53	2.7	4.2
Magnesium (mg/dl)	1.91 ± 0.15	1.7	2.1
25-OH-Vit-D (ng/ml)	71.2 ± 10.8	57.5	87.2
PTH (pg/ml)	28.6 ± 8.01	15.3	34.5
Vitamin B12 (pg/ml)	489 ± 135	285	645
TSH (µU/ml)	1.73 ± 0.92	0.84	3.64
Cortisol (µg/dl)	13.3 ± 3.48	7.9	18



Graph 1. ALP enzymatic activity according to gene mutation carrier status. Red dotted line represents the lower laboratory limit for ALP.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0358

JAK2 MUTATION, TNF-A AND IL 6 PREDICT RESPONSE TO JAK INHIBITOR IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Rheumatoid arthritis, Prognostic factors

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Background: STAT4 is activated by the JAK family members Tyk2 and JAK2 in response to IL and TNF, with subsequent down-stream signaling to promote Th1 mediated autoimmunity [1]. JAK inhibitors [2] are type of medication that function by inhibiting activity of one or more of the Janus kinase family of enzymes. These inhibitors have therapeutic application in the treatment of cancer and inflammatory diseases such as rheumatoid arthritis [3].
Objectives: Study impact of JAK2 mutation, TNF-α and IL 6 levels on response to JAK inhibitors and ACR response criteria.
Methods: The study included 120 newly diagnosed rheumatoid arthritis patients and 80 matched controls. All patients started therapy with csDMARDs. 70 patients failed to achieve adequate response so, they were shifted to Baricitinib. JAK2 mutation assessed by PCR in blood samples, TNF-α and IL 6 were measured by ELISA in serum of patients at diagnosis, before and after Baricitinib treatment.
Results: 102 females (85%) and 18 males (15%) with age mean ± SD (years); (47.7±7.5). Pretreatment JAK2 mutation, TNF-α and IL 6 were significantly high in patients than control. JAK2 mutation were more presented in young age patients (mean ± SD; 47.1 ±3.2 vs 51.4 ± 7.9 in mutant vs non-mutant JAK2 patients, respectively with *P* 0.03). Mutant JAK2 was significantly linked to severity of disease by DAS28; 70% of patients with DAS28 (≤ 2.6) were non-mutant JAK2 vs 30% patients mutant JAK2 while 73.1% of patients with DAS28 (> 5.1) were mutant JAK2 vs 26.9% patients non-mutant JAK2 (P 0.04). 70 patients were csDMARD incomplete responders. Jak2 mutation was significantly presented in these group comparing to patients achieved response to csDMARDs (P 0.002) associated with significant high serum TNF-α (P 0.03) and IL 6 (P 0.001). These refractory patients allowed to receive Baricitinib (single or with other antirheumatic). ACR20 response criteria was significantly better in patients with JAK2 mutation compared with those non mutant after Baricitinib therapy at week 12 (65 versus 31 percent, P 0.04). Also, Baricitinib responders were significantly have high serum TNF-α (P 0.002) and marginal significance high serum IL 6 (P 0.06).
Conclusion: JAK2 mutation in RA patients associated with high disease activity score and inadequate response to csDMARDs. Pretreatment detection of JAK2 mutation in RA patients with high serum level of TNF-α and IL 6 predict a good response to JAK inhibitors with better ACR response criteria.

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Table 1.

JAK2 mutation and response to **csDMARDs in all studied patients**			
	Non Mutant JAK2	**Mutant JAK2**	**P**
Responders no. (%)	23 (72%)	9 (28%)	0.002
Non responders no. (%)	27 (38.5%)	43 (61.4%)	
JAK2 mutation and DAS28 **in all studied patients**			
DAS28	**Non Mutant JAK2**	**Mutant JAK2**	**P**
Remission (≤ 2.6)	14 (70%)	6 (30%)	0.04
Low disease activity (≤ 3.2)	5 (41.7%)	7 (58.3%)	
Moderate disease activity (3.2 - 5.1)	6 (40%)	9 (60%)	
Sever disease activity (>5.1)	13 (23.6%)	42 (76.4%)	

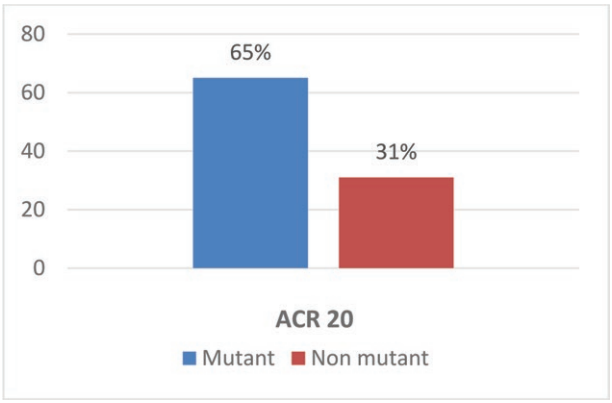


Figure 1.

JAK2 mutation and ACR20 after **Baricitinib treatment.**
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.840

Impact of sex on disease pathogenesis and outcome

POS0359

SEX-RELATED INEQUITY IN RANDOMIZED CONTROLLED TRIALS IN PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

Keywords: Psoriatic arthritis, Spondyloarthritis, Clinical Trials

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Background: Sex is an important determinant of health including response to therapy. Limited information exists on representation and reporting of results by sex in randomized controlled trials (RCTs) in patients with psoriatic arthritis (PsA).
Objectives: Through a systematic literature review and meta-analysis of RCTs in PsA, we aimed to assess potential health inequities in sex-related dimensions by describing the proportion of trials reporting sex-disaggregated data and by comparing the efficacy of advanced therapies between male and female participants.
Methods: We performed a systematic literature search of Medline, Embase and Central databases, and conference abstract archives from January 1, 2000 to June 30, 2022. We included RCTs that reported sex-disaggregated results and assessed the efficacy of an advanced therapy (biologic or targeted synthetic) in adult participants with PsA. Efficacy end points included the proportion of participants achieving minimal disease activity (MDA) or meeting the American College of Rheumatology 20 (ACR20) and ACR50 response criteria at the primary endpoint of the trial. We used random-effect models to calculate pooled effects for responses in males vs. females for the different classes of advanced therapies (Odds Ratio (OR) and 95% Confidence interval (CI)).
Results: We included a total of 52 RCTs, accounting for 21,769 participants, in the review. An equal participation of male and female patients was found (50.1% male participants). Only 9 trials (17.3%, 5,604 participants) reported sex-disaggregated baseline characteristics, 16 trials (30.7%, 9,028 participants) reported sex-disaggregated efficacy endpoints and 2 trials (3.8%, 1,005 participants) reported sex-disaggregated safety endpoints. Female patients had significantly higher baseline tender joint count, Health Assessment Questionnaire Disability Index, physician and patient global assessment of disease activity and pain scores. Male patients had significantly higher baseline psoriasis area and severity index (PASI) and CRP. Differences in pooled estimates of efficacy endpoints were evident for male and female patients across the different classes of advanced therapies. The probability of achieving ACR20 responses was significantly higher in male vs. female patients for IL-17 inhibitors (i) (OR 1.76, 95% CI 1.33, 2.34), IL-23i (OR 1.46, 95% CI 1.20, 1.78), IL-12/23i (OR 2.66, 95% CI 1.39, 5.09) and TNFi (OR 1.67, 95% CI 1.20, 2.34), but not for JAKi (OR 1.10, 95% CI 0.87, 1.38). [**Figure 1A**] Similarly, the probability of achieving ACR50 responses was significantly higher in males vs. females with all advanced therapies, except JAKi (OR 1.09, 95% CI 0.73, 1.62) **[Figure 1B]**. The probability of achieving MDA was higher in males across all classes of advanced therapies, including IL-17i (OR 1.99, 95% CI 1.50, 2.63), IL-23i (OR 1.79, 95% CI 1.29, 2.50), TNFi (OR 2.62, 95% CI 1.54, 4.44) and JAKi (OR 1.77, 95% CI 1.15, 2.73) and IL-12/23i (OR 1.82, 95% CI 0.97, 3.40). Male and female patients had similar probabilities for achieving ACR20 responses when using placebo (OR 1.04, 95% CI 0.86, 1.27).
Conclusion: Based on the reported results, female patients participating in RCTs are less likely to achieve efficacy end points for most classes of advanced therapies. Some differences in responses were found across classes of advanced therapies. RCTs should report sex-disaggregated results to identify sex-related differences in efficacy and safety outcomes which will inform patient-centered therapeutic strategies.

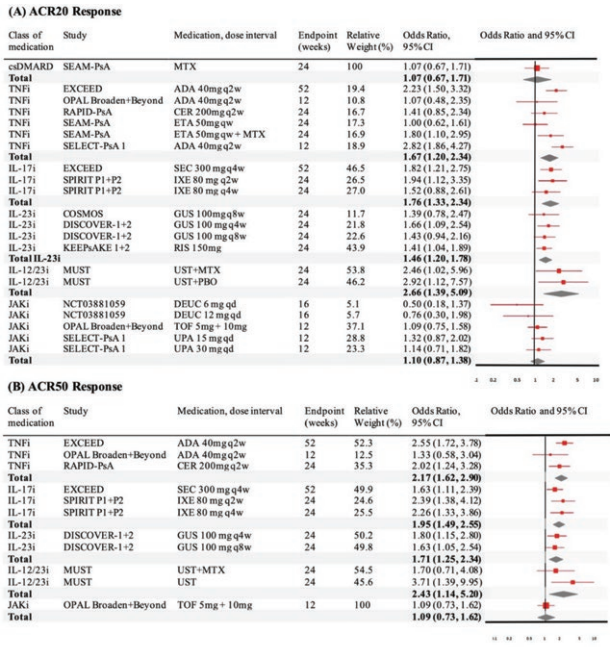


Figure 1. Random-effects meta-analysis of the efficacy of advanced therapies, by (A) ACR20, (B) ACR50 response between male and female patients with psoriatic arthritis. CI, confidence interval; ACR, American College of Rheumatology; ADA, Adalimumab; DEUC, Deucravacitinib; CER, Certolizumab; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; ETA, etacercept; GUS, Guselkumab; IL-17i, interleukin-17 inhibitor; IL-12/23i, interleukin-12/23 inhibitor; IL-23i, interleukin-23 inhibitor; IXE, Ixekizumab; JAKi, janus kinase inhibitor; MTX, methotrexate; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; Q8W, every 8 weeks; RIS, Risankizumab; SEC, secukinumab; TOF, Tofacitinib, TNFi, tumour necrosis factor inhibitor; UPA, Upadacitinib; UST, Ustekinumab.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Lihi Eder Grant/research support from: Received educational and research grants from Abbvie, UCB, Pfizer, Janssen, Novartis, Eli Lilly, Sandoz, Fresenius Kabi, Sivakami Mylvaganam: None declared, Jordi Pardo Pardo: None declared, Jennifer Petkovic: None declared, Vibeke Strand: None declared, Philip J Mease Speakers bureau: Abbvie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Consultant of: Abbvie, Acelyrin, Aclaris, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Immagene, Janssen, Moonlake, Novartis, Pfizer, Sun Pharma, UCB, Grant/research support from: Abbvie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Sun Pharma, UCB, Keith Colaco: None declared.
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POS0360

X-CHROMOSOME DOSAGE, RATHER THAN THE GONADAL SEX ITSELF, MAJORLY CONTRIBUTES TO SEX BIAS IN AUTOIMMUNITY IN HUMANS

Keywords: Autoantibodies, Gender/diversity issues

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Background: Most autoimmune diseases exhibit a profound female sex bias. Mechanisms underlying this sexual dimorphism remain unclear. We previously reported that the XX sex chromosome complement, as compared to XY, imparts greater susceptibility to autoimmune diseases such as lupus in experimental models (Smith-Bouvier D, et al, J Exp Med 2008). Gonadectomized XX female

mice had more anti-DNA antibodies, autoimmune pathology, and mortality than XY female (Sry^{ko}) mice. Similarly, gonadectomized XX male (Sry^{Tg}) mice had more severe autoimmune disease than XY male ($Sry^{ko}Sry^{Tg}$). To begin to translate these murine findings onto humans, we asked if sex chromosome dosage plays a role in predisposition to autoimmunity.

Objectives: To test the hypothesis that X chromosome dosage, rather than the female sex itself, imparts susceptibility to autoimmunity in humans.

Methods: We administered autoimmune disease and connective tissue disease questionnaires and analyzed serum autoantibody levels in males and females with sex chromosome aneuploidy including males with two X chromosomes (XX males, including Klinefelter's syndrome) and females with one X chromosome (X0 females, including Turner's syndrome) and their respective male and female controls with normal sex chromosome numbers.

Results: Levels of IgG anti-chromatin, anti-nucleosome and anti-histone (H2A, H2B and H3) autoantibodies were significantly higher in XX males (47,XXY; 48,XXYY, and mosaics) compared to 46,XY men. XX males, however, did not have non-specific B cell hyper-reactivity, as the levels of anti-thyroid peroxidase antibody that is associated with autoimmune thyroiditis were similar between the two groups and antibodies against intrinsic factor which are present in patients with autoimmune gastritis/pernicious anemia were reduced in XX males than in XY males. In contrast to the increased frequency of autoantibodies against systemic autoantigens in XX males vs. XY males, such autoantibodies were reduced in X0 females as compared to XX females. However, autoantibodies against organ-specific autoantigens such as thyroid and gliadin were higher in X0 females than in XX females. A preliminary analysis of clinical questionnaire revealed an increase in autoimmune conditions in XX males when compared with known population prevalence of these diseases. Preliminary immune phenotyping of peripheral blood cells conducted thus far show altered frequency and/or function of natural killer T-cells, CD8+ T cells or IL-4/IL-17 producing cells in individuals with sex chromosome aneuploidy compared to their respective controls.

Conclusion: These data suggest that humans with two X chromosomes as compared to those with one X chromosome, regardless of their gonadal sex, exhibit increased susceptibility to systemic autoimmunity. Preliminary evidence also suggests a differential regulation of systemic versus organ-specific autoimmunity in persons with sex chromosome aneuploidy.

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Disclosure of Interests: None Declared.

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POS0361

COMPREHENSIVE TRANSCRIPTOMIC CHARACTERIZATION REVEALS CORE GENES AND MODULES ASSOCIATED WITH SEX-DEPENDENT MOLECULAR PAIN MECHANISMS IN OSTEOARTHRITIS

Keywords: Pain, Gender/diversity issues, Osteoarthritis

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Background: Female sex is identified as a key nonmodifiable risk factor in the development of OA, particularly after the age of 55. Additionally, women appear to have a lower threshold for pain and present with more chronic pain conditions than men. Our previous studies demonstrated that female mice develop pain at the same time as male mice despite having reduced levels of joint damage, indicating the existence of sex-dependent mechanisms for the induction of pain. In non-arthritis murine pain models, different immune cells in the dorsal root ganglia (DRG) appear to contribute to sex-dependent differences in sensitization. Furthermore, we have recently uncovered cellular and molecular differences between immune cells and inflammatory profiles in the DRGs and joints of male and female mice with collagen antibody-induced arthritis.

Objectives: Search for putative pain pathways and associated temporal patterns in male and female mice subjected to surgically induced OA.

Methods: C57BL/6 male and female mice (10-week-old, n=5 per group, i.e., surgery, sex, and timepoint) were randomized subjected to either sham surgery or partial meniscectomy (PMX). Static weight bearing measurements were performed using a Linton Incapacitance Tester. Mice underwent a 2-week acclimatization post-surgery, followed by weekly measurement between week 5 to 12. L3-L4 DRGs were harvested for RNA sequencing at week 6, 10 and 12 post-surgery. The Weighted Gene Co-expression Network Analysis (WGCNA) package in R was used to construct a signed co-expression network from the expression data.

Results: Considering all groups, a tendency to pain-related behavior was observed at week 10 post-surgery, and a statistically significant difference in weight bearing found at week 12 when the PMX group was compared with sham group. We performed WGCNA to identify modules that were related to surgery and sex using 6-, 10-, and 12-week samples, respectively. For the 6-week network, 14 modules were identified. Only associations with sex were observed, with 3 modules positively related with male and 1 module positively related with female. For the 10-week network, 14 modules were identified. 6 modules were related by single trait, 3 of which were positively related with male, 2 of which were positively related with PMX, and 1 of which weas negatively related with PMX. In addition, 1 module was related with both surgery and sex, whereby it was negatively related with PMX and positively with being female. For the 12-week network, 19 modules were identified. Most significant associations were observed only with PMX, where 5 modules showed positive associations and 3 modules showed negative associations. Furthermore, greenyellow module was related with both surgery and sex, positively related with PMX and being female. As a result, this module was chosen to investigate further. According to the threshold (MM > 0.8 and GS > 0.2), 102 candidate hub genes were obtained in this module. When PPI analysis was performed, 14 candidate hub genes (top 5%, ranked by the MCC scoring method) were obtained. In total, 9 overlapping genes (Npy, Tac1, Calca, Gap43, Bdnf, Shc1, Ngfr, Casp3 and Jun) were identified as hub genes. The enriched biological process was 'neurotrophin TRK receptor signaling pathway'. And the enriched KEGG pathway were 'neurotrophin signaling pathway' and 'MAPK signaling pathway'.

Conclusion: This study reveals sex, disease and time-dependent changes in the DRG transcriptome during the development of painful OA. Importantly, our findings highlight a distinct TrkA and neurotrophin signaling signature that is evident at 12 weeks post-surgery only in OA-induced pain-related behaviors in female mice.

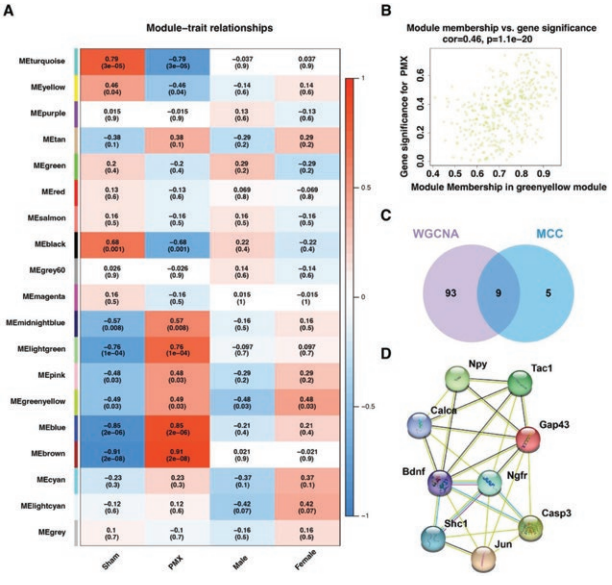


Figure 1. The construction of DRG transcriptomic gene network by WGCNA for week 12 post-surgery. (A) Association between modules and sample trait data. (B) The MM versus GS scatterplot for PMX in greenyellow module. (C)Venn diagram of the identified hub genes. (D) PPI network visualization of hub genes by Maximal Clique Centrality (MCC).

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0362 SEX-RELATED DIFFERENCES IN CHARACTERISTICS AND MORTALITY OF PATIENTS WITH RHEUMATOID ARTHRITIS AND CONCOMITANT HEART FAILURE

Keywords: Outcome measures, Rheumatoid arthritis, Heart

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Background: Heart failure (HF) is a common co-morbidity of rheumatoid arthritis (RA) with a high mortality risk [1]. In the general population, significant sex-related differences in HF including aetiology, pathophysiological mechanisms and age are observed, emphasizing the importance to stratify analyses by sex [2] and there is increasing evidence that mortality rates of females are lower, which cannot be explained by comorbidities, HF characteristics or HF medical treatment [3].
Objectives: To investigate sex specific differences in patient characteristics and their association with mortality in RA patients with concomitant HF.
Methods: RA-patients enrolled and observed in the German biologics register RABBIT between 01/2007 and 04/2022 were selected for the analysis if they presented HF either at enrolment or during follow-up. Observation started at the time of HF reporting (=baseline) and ended at death, dropout or end of follow-up, whichever came first. Baseline patient characteristics were stratified by sex. Cox proportional hazard regression with sex as exposure of interest was applied, adjusted for age (model 1) and further adjusted for comorbidities and RA specific characteristics (model 2). Missing values were imputed once.
Results: Out of 15,917 cohort participants (11,835 females, 74%), 718 patients were identified as prevalent HF cases (473 females, 66%). Females with HF were on average 1.7 years older, had worse physical function and longer RA disease duration compared to males. Females were more likely to have osteoporosis and less likely to have ischemic heart disease (Table 1). 25% of the females and 34% of the males died after a mean follow-up time of 39 and 36 months, respectively. Females had a significant lower risk of death compared to males regardless of adjustment (model 1: HR=0.57 [0.43-0.76]; model 2: HR=0.51 [0.37-0.71], Figure 1).
Conclusion: Our findings demonstrate a longer survival for females compared to males in a cohort of patients with RA and concomitant HF. The difference could not be explained by age, comorbidities and RA-related characteristics at baseline. The observed differences in the clinical profile and mortality highlight the need for research stratifying by sex when investigating cardiac events.
REFERENCES:
[1] PMID: 32378457
[2] PMID: 31544235
[3] PMID: 36386322

Table 1. Baseline characteristics by sex at time of HF reporting

	female	*male*		*female*	*male*
N	473	245	History of comorbidities		
Age, years	70.4 ± 9.5	68.7 ± 10.4	Ischemic heart disease	164 (34.7)	127 (51.8)
RA disease duration, years	15.2 ± 11.6	10.5 ± 9.0	Diabetes	134 (28.3)	79 (32.2)
Rheumatoid factor positive	314 (66.4)	160 (65.3)	Dyslipidemia	130 (27.5)	80 (32.7)
DAS28-ESR	4.5 ± 1.4	4.3 ± 1.6	Chronic lung disease	95 (20.1)	65 (26.5)
% of full physical function	49.1 ± 23.8	59.5 ± 25.6	Chronic kidney disease	150 (31.7)	92 (37.6)
CRP, mg/l	14.5 ± 23.2	15.7 ± 19.1	Chronic liver disease	29 (6.1)	28 (11.4)
Glucocorticoid dose ≥10 mg/d	66 (14.0)	29 (11.8)	Osteoporosis	216 (45.7)	61 (24.9)
TNFi	146 (30.9)	82 (33.5)	No. of comorbidities	5.8 ± 3.0	6.2 ± 3.3
T cell	40 (8.5)	32 (13.1)			
B cell	69 (14.6)	27 (11.0)			
IL6i	44 (9.3)	26 (10.6)			
JAKi	31 (6.6)	13 (5.3)			
csDMARDs	105 (22.2)	48 (19.6)			
No DMARD therapy	38 (8)	17 (6.9)			

Values are numbers (percent) or means ± standard deviation.TNFi: tumour necrosis factor inhibitor, T cell: T cell co-stimulation modulator, B cell: B cell targeted therapy, IL6i: interleukin-6 inhibitors, JAKi: Janus kinase inhibitors, csDMARD: conventional synthetic disease-modifying anti-rheumatic drugs

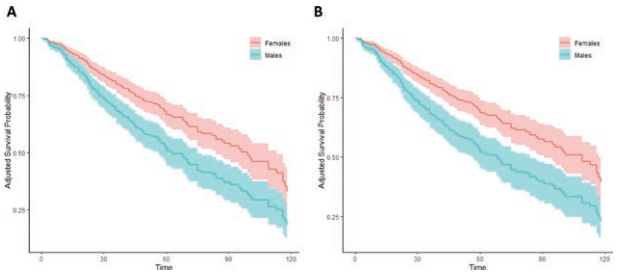


Figure 1. Sex differences in adjusted survival curves. A: adjusted for age; B: adjusted for age, RA disease duration, rheumatoid factor, % of full physical function, high glucocorticoid dose and CRP at baseline, year of HF >2012, DMARD treatment as cumulative exposure in months divided by the total observation months, history of ischemic heart disease, osteoporosis, chronic kidney disease, chronic liver disease and chronic lung disease; Time = Months

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POS0363 SEX DIFFERENCES IN CARDIOVASCULAR AND DISEASE-RELATED FEATURES IN AXIAL SPONDYLOARTHRITIS. A MULTICENTERSTUDYOF 912 PATIENTS

Keywords: Cardiovascular disease, Spondyloarthritis, Gender/diversity issues

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Background: There is increasing evidence revealing sex differences in the manifestations of axial spondyloarthritis (axSpA). However, the results in this regard are heterogeneous and studies that analyze the influence of sex on cardiovascular (CV) risk are lacking.
Objectives: To assess the CV profile of male and female axSpA patients and to determine the potential impact of sex-specific disease-related characteristics on atherosclerosis in these patients.

Methods: This is a cross-sectional study of the AtheSpAin cohort, a Spanish multicenter cohort to study atherosclerosis in axSpA. Data on clinical and subclinical atherosclerosis, as well as CV and disease-related characteristics were collected in 912 patients.

Results: 611 men and 301 women were recruited for this study. Smoking habit (p=0.033), hypertension (p=0.009), and dyslipidemia (p=0.015) were less prevalent in women, who also showed less severe atherosclerosis measured by the presence of carotid plaques (p=0.001), carotid intima-media thickness (IMT) values (p<0.001), and CV events (p=0.008). After adjustment for traditional CV risk factors only the results regarding carotid IMT remained statistically significant. Regarding disease-related features, radiographic axSpA (r-axSpA) was more common in men (p<0.001). Women with axSpA showed a shorter disease duration (p<0.001), a lower prevalence of psoriasis (p=0.008), higher ESR levels at diagnosis (p=0.038) and more active disease measured by ASDAS (p=0.012) and BASDAI (p<0.001). However, they had less structural damage (mSASSS, p<0.001) and mobility limitation (BASMI, p=0.033). These differences that remained statistically significant after adjustment for r-axSpA/nr-axSpA, disease duration or smoking. Remarkably, many of these sex-related differentiating characteristics were associated with subclinical atherosclerosis (table 1). To clarify if this finding could lead to sex differences in the atherosclerotic burden, we compared the prevalence of carotid plaques in men and women with the same level of CV risk stratified according to the SCORE. Within the category of low-moderate SCORE, men showed more severe atherosclerosis than women (p=0.050), which could be related to a longer disease duration (p=0.004), higher mSASSS (p=0.001) and BASMI (p=0.071) values. However, in patients with high-very high SCORE, carotid plaques were more commonly observed in the female group (p=0.025), which was characterized by a higher inflammatory burden (ESR at diagnosis, p=0.007) and worse BASFI (p=0.011) compared with men, with no differences regarding disease duration, mSASSS or BASMI.

Conclusion: Although the burden of traditional CV risk factors leading to more severe atherosclerotic disease is greater in men with axSpA, potential sex-related proatherogenic features of axSpA also appear to have an impact on CV risk. This may be especially applicable to women at high CV risk, who have a greater inflammatory response, worse functional impairment, and more severe subclinical atherosclerosis than males, suggesting a closer interaction between atherosclerosis and disease burden in women with axSpA.

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Table 1. Disease-related factors associated with carotid plaques in male and female patients with axSpA older than 35 years old

	Males		Females	
	OR (95% CI)	**p***	**OR (95% CI)**	**p***
Disease duration	**1.05 (1.04-1.07)**	**<0.001**	**1.05 (1.03-1.08)**	**<0.001**
ESR at diagnosis	1.01 (1.00-1.02)	0.06	**1.02 (1.01-1.04)**	**0.001**
BASFI	**1.18 (1.10-1.26)**	**<0.001**	**1.22 (1.08-1.38)**	**0.001**
BASMI	**1.32 (1.20-1.46)**	**<0.001**	**1.27 (1.07-1.51)**	**0.006**
mSASSS	**1.02 (1.01-1.04)**	**<0.01**	**1.04 (1.00-1.08)**	**0.04**
Psoriasis	1.12 (0.67-1.86)	0.67	**2.65 1.00-6.97)**	**0.05**
BASDAI	**1.11 (1.02-1.20)**	**0.01**	1.12 (0.98-1.28)	0.08
ASDAS	**1.25 (1.04-1.50)**	**0.02**	1.28 (0.95-1.72)	0.10

O OR: odds ratio * *adjusted for age and smoking

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POS0364

SEX DIFFERENTIAL IMPACT OF CO-MORBIDITIES ON DISEASE ACTIVITY IN SPONDYLOARTHRITIS: DATA FROM COMOSPA STUDY

Keywords: Spondyloarthritis, Registries

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Background: Previous studies have examined the distinct phenotypes and the factors linked to disease activity and response to treatment in spondyloarthritis (SpA), some reporting several differences between men and women. However, there is still scarce literature on sex differences in SpA co-morbidities such as cardiovascular (CV) risk factors, osteoporosis, neoplasms or infections, or exploring sex differential impacts of these co-morbidities in the disease activity of SpA patients.

Objectives: To characterize differences in SpA associated co-morbidities between male and female patients and to evaluate the existence of a differential impact of these comorbidities on the disease activity between SpA gender.

Methods: This is a post-hoc analysis of the COMOSPA study which included 3982 patients with SpA, 2588 male patients and 1394 female patients. Differences in co-morbidities regarding sex were assessed using logistic regression models. Co-morbidities were evaluated for their impact on disease activity indexes with linear models, which included sex and the comorbidity as explanatory variables, as well as their interaction. Age and treatment with bDMARDS were included as confounders. We retrieved odds ratios (OR) and group differences from these models to measure the magnitude of the effects and determined statistical significance at a level of p<0.05 using Wald tests.

Results: After statistical control for age and bDMARDS, our analysis found that men had a higher prevalence of several cardiovascular comorbidities such as hypertension (OR, 95%CI) (1.47, 1.23 - 1.77), dyslipidemia (1.29, 1.07 - 1.56), ischemic heart disease (2.77, 1.72 - 4.65) and renal deficiency (2.36, 1.46 - 4.01). Additionally, a greater proportion of men had a history of tuberculosis (1.59, 1.45 - 3.95), and a lower prevalence of fibromyalgia (0.47, 0.39 - 0.57). However, we did not find differences between men and women in terms of prevalence of neoplasms, osteoporosis, gastrointestinal disease, or severe infection (Table 1). Several co-morbidities were associated with disease activity equally in both sex, including CV conditions, severe infection, osteoporosis, chronic obstructive pulmonary disease, gastrointestinal disease and fibromyalgia. When comparing men and women patients, gastrointestinal ulcer and fibromyalgia associates with ASDAS and BASDAI and have a differential impact depending on sex. Specifically, fibromyalgia has a higher impact in men (ASDAS: 1.367 vs 1.612; BASDAI: 4.28 vs 4.70) (Figure 1).

Conclusion: Our data show that co-morbidities occur similarly in men and female SpA patients, except for a higher frequency of CV co-morbidities in men and a higher prevalence of fibromyalgia in women. Moreover, fibromyalgia and gastro-intestinal ulcer evidenced a sex-specific association with disease activity among all the co-morbidities studied.

Figure 1. Co-morbidities affecting ASDAS with differential impact depending on sex

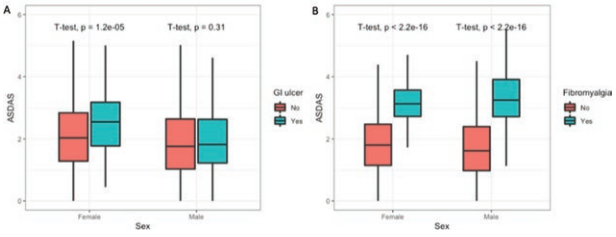


Table 1.

	SpA patients				
	Male, n=2588	**Female, n=1394**	**p-value**	**OR adjusted for age and ever bDMARDs**	**p-value**
Age,years	42.9 (14.1)	45.1 (13.4)	**<0.001**		
Hypertension	590/2570 (23%)	292/1388 (21%)	NS	1.47 (1.23 - 1.77)	**<0.001**
Diabetes	147/2570 (5.7%)	72/1387 (5.2%)	NS	1.27 (0.94 - 1.72)	NS
Dyslipidemia	438/2556 (17.1%)	218/1380 (15.8%)	NS	1.29 (1.07 - 1.56)	**0.009**
Renal deficiency	74/2571 (2.9%)	20/1387 (1.4%)	**0.005**	2.36 (1.46 - 4.01)	**<0.001**
Ischemic heart disease	85/2569 (3.3%)	21/1386 (1.5%)	**0.001**	2.77 (1.72 - 4.65)	**<0.001**
Stroke	37/2570 (1.4%)	13/1381 (0.9%)	NS	1.86 (1.00 - 3.66)	NS
History of tuberculosis	79/2548 (3.1%)	21/1382 (1.5%)	**0.003**	2.34 (1.45 - 3.95)	**<0.001**
Hospitalized for severe infection	76/2556 (3%)	39/1385 (2.8%)	NS	1.08 (0.73 - 1.61)	NS
Any neoplasm*	60/2486 (2.4%)	26/1342 (1.9%)	NS	1.51 (0.94 - 2.48)	NS
Osteoporosis	341/2574 (13.2%)	188/1388 (13.5%)	NS	1.06 (0.87 - 1.29)	NS
Any GI (diverticulitis or GI ulcer)	291/2558 (11.4%)	174/1376 (12.6%)	NS	0.93 (0.76 - 1.14)	NS
FM (extreme PRO definition)	265/2569 (10.3%)	271/1384 (19.6%)	**<0.001**	0.47 (0.39 - 0.57)	**<0.001**

SpA= spondyloarthritis; GI= gastro-intestinal; bDMARDs: biological disease-modifying anti-rheumatic drugs; FM= fibromyalgia

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0365 SEX DIFFERENCES CONCERNING EXPERIENCED PAIN IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Pain, Spondyloarthritis, Gender/diversity issues

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Background: Research shows that there are significant sex differences in experienced pain. Contributing factors are neuroanatomical, hormonal, neuro-immunological, psychological, social, cultural, and comorbidities. Women have more and different expression of nociceptors, and a stronger proinflammatory response to tissue damage than men. Women also use different coping styles regarding to pain and tend to engage more in pain catastrophizing. Therefore, women may experiencing more severe pain than men. Also in axial spondyloarthritis (axSpA), higher pain scores are observed in women compared to men with axSpA.[1] Sex differences in experienced pain within axSpA is not well studied. It is unclear if differences are related to the involvement of altered pain processing of the central nervous system (CNS) including central sensitization (CS) and/or psycho-social aspects.
Objectives: To explore sex differences in pain perception, coping with pain, pain catastrophizing and altered pain processing of the CNS in patients with axSpA.
Methods: A cross-sectional study of consecutive outpatients from the Groningen Leeuwarden axSpA (GLAS) cohort, fulfilling the ASAS classification criteria. Participants filled out the Central Sensitization Inventory (CSI), Pain Catastrophizing Scale (PCS) Coping with Rheumatic Stressors (CORS), and underwent Quantitative Sensory Testing (QST) according to a standardized protocol, including Pain Threshold Testing (PTT) at 11 sites, Temporal Summation (TS) at 3 sites and Conditioned Pain Modulation (CPM). Widespread low PPTs, high TS (both pain facilitation) and positive CPM (impaired pain inhibition) are indicators of CS. Independent Samples T Test and Mann-Whitney U Test were used for normally- and non-normally distributed data resp.. Bonferroni correction was applied for multiple significance testing and P-value was determined at 0.004.
Results: 201 patients were included, 128 men and 73 women with no significant differences in the patient characteristics; median age (50.8 vs 51.6 years), median symptom duration (22.0 vs 21.0 years) and median CRP (1.8 vs 2.5). Significant differences between men and women were observed for the classification radiographic axSpA (71.9% vs 50.7%), HLA-B27 status (84.1% vs 67.1%), mean BMI (27.2 ± 4.9 vs 29.0 ± 6.9), mean $ASDAS_{CRP}$ (2.1 ± 0.8 vs 2.5 ± 0.9) and mean BASDAI (3.4 ± 2.1 vs 4.7 ± 2.1). Women scored significantly higher on the CSI and used the coping styles comforting cognitions, decreased activities and diverted attention more often (CORS). Concerning the involvement of altered pain processing of the CNS, women had significantly lower PPTs. TS and CPM were comparable in men and women (Table 1).
Conclusion: In patients with axSpA, significant sex differences in pain coping styles, CSI score and PPTs were observed. Therefore, sex differences should be taken into account in the management of pain in daily clinical practice and in pain research in these patients.

Table 1. Characteristics and assessments stratified for sex (n=201)

	Men (n=128)	Women (n=73)
CSI-A (0-100)	30.6 ± 13.8	41.5 ± 13.6*
PCS (0-52)	11.0 [5.0-20.0]	14.0 [5.0-19.5]
CORS pain		
Comforting cognitions	27.8 ± 4.9	29.9 ± 4.1*
Decreasing activities	18.8 ± 4.5	21.0 ± 4.3*
Diverting attention	20.1 ± 4.7	22.3 ± 3.9*
PPT (N)		
Thenar, left/right	37.4 ±17.5/40.6 ± 19.1	26.1 ± 12.1/29.0 ±14.2*
M. trapezius, left/right	40.1 ± 22.8/39.4 ± 20.9	26.8 ± 13.5/26.8 ± 14.5*
M. rectus femoris, left/right	58.0 ± 25.1/55.9 ± 26.8	35.2 ± 17.9/32.1 ± 16.3*
M. abductor hallucis, left/right	37.0 ± 18.4/38.6 ± 19.8	27.5 ± 13.2/28.7 ± 15.1*
Non-painful area	38.6 ± 22.1	25.0 ± 13.8*
Painful area	32.2 [22.4-51.6]	19.8 [13.0-28.7]*
TS (VAS)		
Non-dominant forearm	0.6 [0.1-1.2]	0.7 [0.2-2.1]
Non-painful area	0.8 [0.2-1.5]	1.1 [0.2-2.2]
Painful area	0.8 [0.2-1.6]	1.3 [0.3-2.7]
CPM (N)		
Non-dominant m. rectus femoris	2.8 ± 13.5	0.2 ± 8.3

*Statistically significant at p<0.004 (Bonferroni correction).

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POS0366 SEXUAL DYSFUNCTION IN SPONDYLOARTHRITIS PATIENTS: DIFFERENCES BETWEEN MALES AND FEMALES PATIENTS IN A REAL-WORLD SETTING

Keywords: Gender/diversity issues

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Background: In the field of rheumatology in general and in the context of spondylarthritis (SpA) more specifically, gender medicine is gaining more recognition and relevance. Available data suggest female patients feature higher diagnostic deladelayspared to males. Furthermore, female SpA patients experience higher disease activity, lower response rates to treatment and, less probability to achieve remission. Sexual dysfunctions are an aspect little investigated in SpA. Disease features and disease activity are known to influence sexual health. Conversely, little is known about the difference existing in sexual satisfaction in males and females affected by SpA.
Objectives: To investigate the sexual function and satisfaction in female and male patients affected by SpA and identify gender-specific features.
Methods: We conducted a cross-sectional study enrolling consecutive SpA patients satisfying ASAS criteria attending the SpA clinic of a tertiary university rheumatology clinic. Demographic and clinical characteristics were collected alongside with validated gender-specific questionnaire for the evaluation of sexual function. For male assessment, we used the international index of erectile function (IIEF) and the Premature Ejaculation Diagnostic Tool (PEDT); whereas in women we used The Female Sexual Function Index (FSFI) that explores domains such as desire, arousal, lubrification, orgasm, satisfaction, and pain. To evaluate the correlation between the presence of sexual dysfunction and disease characteristics or therapies we used the Spearman test and the univariate and multivariate tests.
Results: 73 males and 64 females were recruited, and the two groups were comparable with similar mean age, BMI, and disease duration (patients' characteristics are shown in table 1). PEDT test showed that 9.5% (5 male patients) had probable premature ejaculation and 15% (8 male patients) had premature ejaculation. According to IIEF sexual dysfunction was present in 19.4% of cases as mild dysfunction in 15.5% as moderate dysfunction and in 5.4% as severe dysfunction. Univariate and multivariate analysis showed a correlation between sexual dysfunction and mood disorders and premature ejaculation in men (p=0.02). The prevalence of premature ejaculation was not influenced by disease characteristics or activity or therapies. Sexual dysfunction in males was associated only with the use of NSAID (p=0.04). Evaluating the female group, FSFI showed that 85% (54 female patients) had sexual dysfunction. In the univariate and multivariate analysis, we found correlations between age (p=0.07), mood disorders (p=0.04), dyslipidemia (p=0.006), and BASDAI (p=0.04). Fibromyalgia was detected only in women.
Conclusion: This data demonstrates that sexual function is impaired in an extremely high percentage of female SpA patients, which contributes to the higher burden of SpA on women. Sexuality is still a little explored topic in SpA, despite is a relevant aspect of quality of life and determinant of psychological health. Therefore, it is necessary to thoroughly investigate the impact that the disease and comorbidities have on the sexual life of these patients with a particular focus on females.

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Table 1. Demographic features of the patients

	MALES (n=73)	FEMALES (n=64)	
AGE (mean)	49.4 (46.5-52.3)	51.1 (48.9-53.2)	P=0.8
BMI (mean)	27.5 (26.5-28.4)	27.5 (25.9-29)	P=1
SMOKE (n)			
Yes	16	3	P=0.002
No	35	42	P=0.4
past	6	5	P=0.7
DISEASE DURATION (years)	14.4 (12.1-16.7)	12.6 (9.9-15.2)	P=0.6
COMORBIDITIES (n)			
Inflammatory Bowel Disease	5	5	P=1
Arterial Hypertension	25	14	P=0.07
Diabetes	7	3	P=0.2
Depression and anxiety	25	37	P=0.12
Dyslipidemia	25	12	P= 0.03
Past CV event	4	2	P=0.4
Fibromyalgia	0	23	P=<0.001
Neurologic diseases	0	2	
Cancers	1	5	P=0.1
DAPSA (mean)	5.3 (3.5-7)	8.2 (6.7-9.7)	P=0.4
BASDAI (mean)	2 (1.4-2.6)	4 (3.5-4.8)	P=0.4
csDMARDs (n)	13	26	P=0.03
Methotrexate	8	15	
Sulfasalazine	5	10	
Leflunomide	0	0	
FANS (n)	6	13	P=0.1
bDMARDs (n)	63	41	P=0.03
ANTI-TNF	41	20	
ANTI-IL17	18	13	
ANTI-IL12/23	2	2	
ANTI-IL23	0	0	

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POS0367

FILLING GAPS IN FEMALE GOUT: A CROSS-SECTIONAL STUDY OF 192,000 PATIENTS HOSPITALIZED WITH GOUT FROM 2005 TO 2015

Keywords: Gender/diversity issues, Comorbidities, Gout

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Background: Patients with gout show several comorbidities, especially cardiovascular, renal and metabolic diseases. The odds of developing new comorbidities increase progressively since the first flare, with a higher risk than general population. Female gout has received little attention in the published literature, although clinical experience and some studies suggest different clinical picture with higher mortality.
Objectives: To compare the distribution of comorbidities by sex in hospitalized patients with gout in Spain.
Methods: Retrospective, nation-based cohort study. The Minimal Basic Data Set from all Spanish hospitalizations including gout as either primary or secondary diagnosis (ICD-9 coding) from 2005 to 2015 was collected. The comorbidities of interest were obesity, dyslipidemia, chronic kidney disease, diabetes mellitus, coronary heart disease, chronic heart failure, peripheral vascular disease, arrhythmia, venous thromboembolism, cerebrovascular disease, dementia, urinary tract infection, pneumonia, sepsis, obstructive pulmonary disease, liver disease and rheumatological disease. Arterial hypertension and urinary lithiasis were not analyzed since they were underrepresented in the dataset. Comparative analyses were performed by sex. Later, stratification by age was performed and the population was divided by sextets (≤70years; 71-80years; 81-85years; 86-90years; 91-95years; >95years). A multiple logistic regression model was built to discern the strength of association of comorbidities with each sex, for the entire population and stratifying by age (≤60years and >60years). Additionally, a decision tree was constructed to have sex predicting algorithms based on the presence of comorbidities.
Results: 192,037 admissions were analyzed, 5.47% (n=10,512) with gout as primary diagnosis. 158,646 cases occurred in men (82.6%), significantly younger than women (64.0±14.4 vs 73.9±13.7 years; p<0.001). Female predominant comorbidities were obesity (16.3% vs 10.8%), dyslipidemia (31.8% vs 30.7%), chronic kidney disease (33.8% vs 25.1%), diabetes (36.2% vs 25.9%), heart failure (31.8% vs 16.6%), dementia (2.1% vs 1.2%), urinary tract infection (12.0% vs 5.4%) and concurrent rheumatic disease (2.6% vs 1.4%). Otherwise, male predominant comorbidities were coronary heart disease (21.8% vs 16.9%), peripheral artery disease (3.8% vs 1.2%), liver disease (2.2% vs 1.3%), pneumonia (4.5% vs 3.8%) and obstructive pulmonary disease (8.9% vs 2.3%). No differences were seen for others. After age stratification, differences in dementia were no longer significant. Multiple logistic regression, with an accuracy score of 68.5%, confirmed a differential comorbidity profile between men and women (**Figure 1**). After age stratification, for <60years renal and rheumatic diseases were closely linked to women with gout, whilst in >60years heart failure was the leading. For men, coronary heart disease and obstructive pulmonary disease were the chief associations. A decision tree algorithm was built [1], with an accuracy of 74.4%.

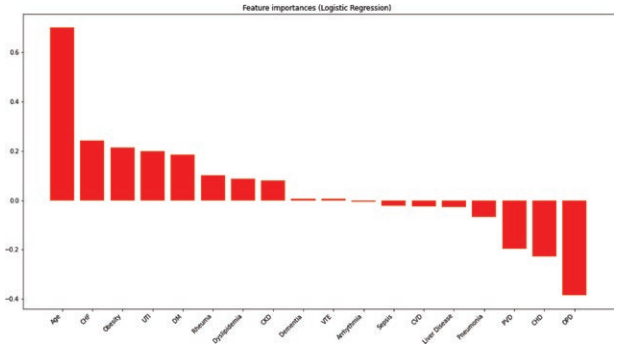


Figure 1. CHF: chronic heart failure; UTI: urinary tract infection; DM: diabetes mellitus; Rheuma: rheumatological disease; CKD: chronic kidney disease; VTE: venous thromboembolism; CVD: cerebrovascular disease; PVD: peripheral vascular disease; CHD: coronary heart disease; OPD: obstructive pulmonary disease. Positive coefficients associate with women with gout, negative ones otherwise.

Conclusion: A nation-wide analysis of 11years of hospitalizations with gout confirm a different comorbidity profile between men and women. Women with gout were significantly older and more likely to suffer from heart failure, obesity, urinary infection and diabetes. Association between sex and certain comorbidities is intense enough for sex prediction by an algorithm with considerable accuracy. A different approach for female gout is thus needed, to reduce gender blindness.
REFERENCE:
[1] "Decision Tree Algorithm - Sex and Comorbidities in gout", Mendeley Data, V1, doi: 10.17632/j4vf42jhkw.1
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Disclosure of Interests: None Declared.
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Health, public health and health services

POS0368 PERSISTENT PREMATURE MORTALITY IN GOUT: NATIONWIDE PROSPECTIVE COHORT STUDY

Keywords: Gender/diversity issues, Epidemiology, Gout

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Background: A recent UK study reported a higher cardiovascular event risk after gout flare episodes,[1] which may translate to premature mortality for gout patients over the long term. Prior studies reported premature mortality in gout, but did not compare demographic subgroups, and it is unknown whether the excess risk has improved over recent years at a national level.
Objectives: We prospectively evaluated the association between gout and the risk of all-cause and cardiovascular mortality in the latest US general population data and compared with the prior data.
Methods: Using nationally representative samples of US adults in the National Health and Nutrition Examination Survey (NHANES), linked prospectively with vital statistics data, we examined the association between gout and mortality and compared Early (NHANES III: 1988-1994) and Late cohorts (2007-2016), as well as key demographic subgroups defined by age, sex, and self-reported race/ethnicity (Black vs. White). Hazard ratios (HRs) were calculated over 10 years adjusting for atherosclerotic cardiovascular disease (ASCVD) risk factors, cardiometabolic comorbidities, kidney function, and relevant medications.
Results: Adjusted HR for all-cause mortality comparing US adults with and without gout in aggregate was 1.19 (95% CI, 1.08–1.32), with the same HR in the Early and Late cohorts (1.19; 1.02–1.38 and 1.19, 1.03–1.37, respectively) (**Figure 1**). HR was larger among those < 60 years (1.62; 95% CI, 1.19–2.19; p-interaction < 0.001 vs. age **>=** 60 years) and among women (1.33; 95% CI, 1.11–1.60, p-interaction=0.03 vs. men) (**Table 1**), and was also prominent among Black individuals (HR, 1.40; 95% CI, 1.12–1.74). Corresponding HR for cardiovascular mortality in the late cohort was 1.39 (95% CI, 1.09–1.78). All associations remained similar when adjusting for serum urate levels.
Conclusion: This representative cohort study illustrates premature mortality in gout at a national level, even after accounting for serum urate levels, which has not improved over past decades. Excess mortality was higher among women and younger adults, and was more prominent among Black individuals; the latter group already experiences an excess *prevalence* of gout at the US national level, compared to White individuals (age- and sex-adjusted odds ratio for gout=1.5 (1.2 to 1.7)).[2] These data are suggestive of continued shortcomings in current gout care practices and a compelling need to understand and mitigate the premature mortality risk in gout, especially for women and Black individuals.
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[2] McCormick N, Lu N, Yokose C, et al. Racial and Sex Disparities in Gout in US Adults. JAMA Network Open. 2022;5(8):e2226804.

Table 1. Association between gout and all-cause mortality according to time period and demographic groups, truncated at 10 years: Hazard ratio (HR) and 95% confidence intervals

Gout Compared with No Gout [Reference]	Early Cohort: NHANES III (1988-1994)	Late Cohort: NHANES 2007–2016	P for interaction
Adjusted HR*	1.20 (1.03 to 1.40)	1.19 (1.04 to 1.37)	> 0.95
+ uric acid adjusted HR	1.19 (1.02 to 1.38)	1.19 (1.03 to 1.37)	> 0.95
	Combined Cohort for Subgroup Effects		**P for interaction**
By Age	**Age < 60**	**Age >= 60**	
Adjusted HR*	1.62 (1.19 to 2.19)	1.15 (1.03 to 1.28)	< 0.001
+ uric acid adjusted HR	1.50 (1.11 to 2.04)	1.15 (1.03 to 1.28)	0.002
By Sex	**Female**	**Male**	
Adjusted HR*	1.33 (1.11 to 1.60)	1.13 (1.00 to 1.28)	0.03
+ uric acid adjusted HR	1.32 (1.10 to 1.58)	1.13 (1.00 to 1.28)	0.04
By Race	**Black**	**White**	
Adjusted HR*	1.40 (1.12 to 1.74)	1.13 (1.00 to 1.28)	0.18
+ uric acid adjusted HR	1.36 (1.09 to 1.70)	1.13 (1.00 to 1.29)	0.22

* Adjusted for age, sex, race, NHANES cycle, body mass index, education, smoking status, alcohol intake, total cholesterol, HDL, systolic and diastolic blood pressure, aspirin, diuretic, statin, and anti-hypertensive medication use, post-menopausal status (women), heart disease, diabetes, and estimated glomerular filtration rate (continuous)

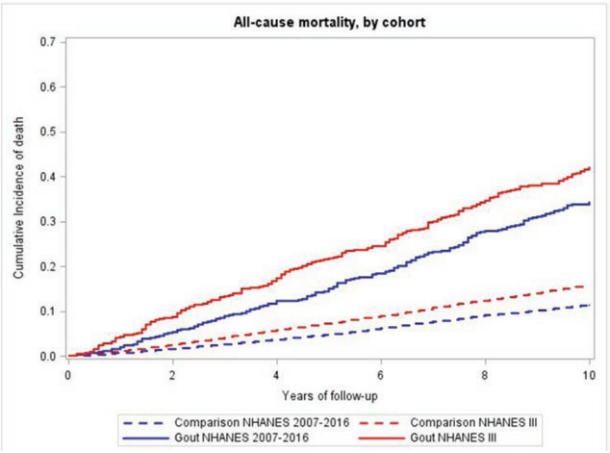


Figure 1. Cumulative incidence of death by cohorts and gout status, follow-up truncated at 10 years

Acknowledgements: NIL.
Disclosure of Interests: Natalie McCormick: None declared, Chio Yokose: None declared, Kehuan Lin: None declared, Leo Lu: None declared, Amit Joshi Employee of: Regeneron, Hyon Choi Consultant of: Ironwood, Selecta, Horizon, Takeda, Kowa, and Vaxart, Grant/research support from: Ironwood and Horizon.
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POS0369 TREATMENT RELATED COST SAVINGS DUE TO EARLY IDENTIFICATION OF RHEUMATOID ARTHRITIS

Keywords: Epidemiology, bDMARD, Rheumatoid arthritis

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Background: EULAR guidelines advocate early detection and treatment of rheumatoid arthritis (RA) to induce a milder disease course. It was shown that early detection and treatment prevents erosive disease and maintains functional capabilities. Despite of that, the effect of early detection of RA on treatment related costs has never been investigated. Due to rising health care costs, it is important for society to keep health care affordable.
Objectives: Our objective was to investigate whether early identification and treatment of RA patients (within 12 weeks after symptom onset) results in a reduction of treatment related costs when compared to a patient group that was seen after 12 weeks after symptom onset, stratified for ACPA status.
Methods: Patients were obtained from the Leiden Early Arthritis Clinic (EAC), an inception cohort consisting of patients presenting with recent onset arthritis with a symptom duration ≤ 2 years. All consecutive RA patients fulfilling the 1987 and/or 2010 criteria, and who started a DMARD, included between May 2011 and December 2017 were evaluated, allowing a follow-up of 5 years. In this inclusion period, referral strategies were optimized for early recognition of RA. Early treatment start was defined as within 12 weeks after symptom onset. Information on medication use was obtained from prescription data from electronic patient records. Prices were used from both 2012 (at time of prescription) and 2022 (current). ACPA-positive and ACPA-negative RA were studied separately. Inverse probability weighting accounted for differences in patient characteristics between the early and late groups. The weighted average difference in medication costs was estimated with a generalized linear model with a log link and gamma distribution.
Results: In total, 196 RA patients were ACPA-positive and 235 patients were ACPA-negative. Median (IQR) symptom duration was 5.5 (3-9) weeks in the early group, and 29.7 (19-53) weeks for the late group for ACPA-positive patients, and 6.4 (4-9) weeks and 26 (17-50) weeks in the ACPA-negative patients. At diagnosis, the early group of both ACPA-negative and ACPA-positive patients had more severe inflammation compared to the late group. After 5 years, 6% of ACPA-negative patients and 20% of ACPA-positive patients had used ≥1 biological. The average number of biologics within these patients was 1 in the early ACPA-negative group, 1.4 in the ACPA-negative late group, and 1.9 and 2 in ACPA-positive early and late groups. When using current price levels (2022), mean (sd) cost of treatment over 5 years was €11250 (25774) for ACPA-positive patients, and €3526 (11556) for ACPA-negative patients, while treatment costs among biological users was €44788 (36360) for ACPA-positive and 40896 (25123) for ACPA-negative RA. After weighting, within ACPA-negative RA costs were lower in the early compared to the late group (€2877 versus €4213, respectively), β=1.46 (95%CI 0.32 – 3.4),

indicating 46% higher costs in the late group. For ACPA-positive patients, costs were more similar (€11631 and €10988 respectively for the early and late group, β=0.96, 95%CI 0.52 – 1.8)(figure 1A). When 2012 prices were used, costs were in general higher: €14482 (29101) and €5158 (17897) for ACPA-positive and ACPA-negative patients, respectively. Comparing late and early groups using 2012 prices provided similar results in ACPA-negative RA (β=1.34 (95%CI 0.54 – 3.3), and a larger difference in costs for ACPA-positive RA (β=0.77 (95%CI 0.44 – 1.35)).

Conclusion: Treatment-related costs of ACPA-positive RA are higher compared to ACPA-negative RA. However, early detection and treatment has the greatest impact on reducing treatment costs in ACPA-negative RA.

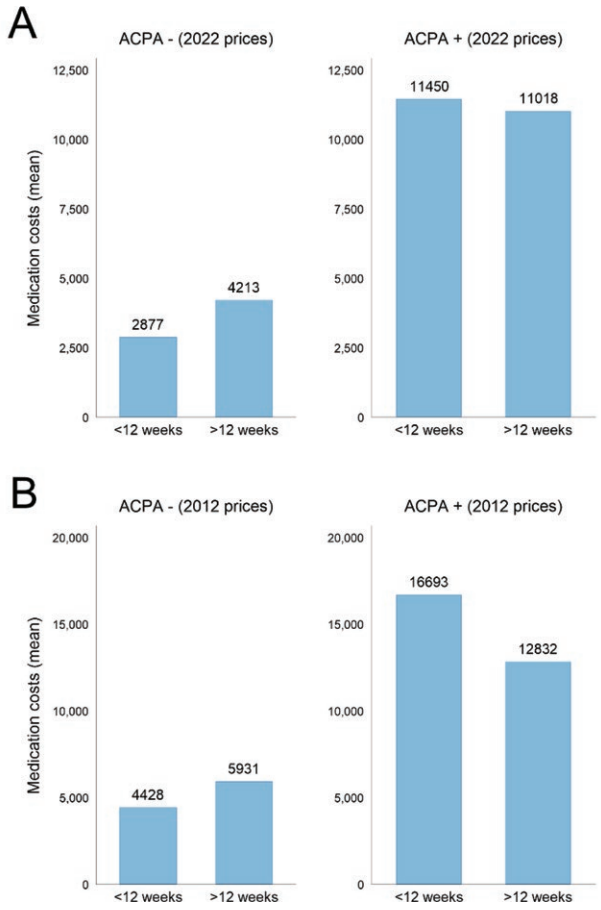


Figure 1. (A) Medication costs over 5 years indicated for ACPA-positive and ACPA-negative RA using current prices (2022), comparing early (<12 weeks after symptom onset) and later referral (>12 weeks after symptom onset). (B) Medication costs in euros over 5 years using prices at time of prescription (2012). ACPA: anti-citrullinated protein antibody

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POS0370

2023 EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF FATIGUE IN PEOPLE WITH INFLAMMATORY RHEUMATIC AND MUSCULOSKELETAL DISEASES

Keywords: Patient reported outcomes, Health Services Research

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Background: Fatigue is prevalent in people with inflammatory rheumatic and musculoskeletal diseases (I-RMDs) and recognised as one of the most challenging symptoms to manage [1]. The existence of multiple factors associated with fatigue, the lack of clarity around underlying pathophysiological mechanisms and the limited evidence about what helps have led to a multifaceted and often fragmented approach to symptom management. However, there are no recommendations for fatigue management in people with I-RMDs, and this lack of guidance has been challenging for those living with fatigue as well as for healthcare professionals delivering clinical care.

Objectives: To develop EULAR recommendations for the management of fatigue in people with I-RMDs.

Methods: A multi-disciplinary taskforce comprising 26 members from 14 European countries was convened and two systematic reviews were conducted. The taskforce developed recommendations based on evidence from the systematic reviews and taskforce members' personal and professional experience of fatigue in I-RMDs.

Table 1. EULAR overarching principles and recommendations for the management of fatigue in people with I-RMDs.

Overarching principles		
1. Health professionals should be aware that fatigue encompasses multiple and mutually interacting biological, psychological and social factors. 2. In people with I-RMDs, fatigue should be monitored, and management options should be offered as part of their clinical care. 3. Management of fatigue should be a shared decision between the person with an I-RMD and healthcare and well-being professionals. 4. Management of fatigue should be based on the needs and preferences of people with I-RMDs, as well as their clinical disease activity, comorbidities and other individual psychosocial and/or contextual factors.		
Recommendations	**LoE**	**GoR**
1. Healthcare professionals should incorporate regular assessment of fatigue severity, impact and coping strategies into clinical consultations.	5	D
2. As part of their clinical care, people with I-RMDs and fatigue should be offered access to tailored physical activity interventions and encouraged to engage in long-term physical activity.	1a	A
3. As part of their clinical care, people with I-RMDs and fatigue should be offered access to structured and tailored psychoeducational interventions.	1a	A
4. The presence or worsening of fatigue should trigger evaluation of inflammatory disease activity status and consideration of immunomodulatory treatment initiation or change, if clinically indicated.	1a	A

I-RMDs, inflammatory rheumatic and musculoskeletal diseases; GoR, Grade of recommendation; LoE, Level of Evidence. GoR and LoE as per 2011 Oxford Centre for Evidence Based Medicine Levels of Evidence.

Results: Four overarching principles and four recommendations were developed (Table 1), including health professionals' awareness that fatigue should be monitored and assessed and that people with I-RMDs should be offered management options. Shared decisions about fatigue management should consider the needs and preferences of individuals, their clinical disease activity, comorbidities and other psychosocial and contextual factors (**Table 1**).

Conclusion: These 2023 EULAR recommendations provide consensus and up-to-date guidance on the management of fatigue in people with I-RMDs.

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[1] Dures E, et al. Fatigue in inflammatory arthritis. Best Pract Res Clin Rheumatol 2020;34.

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POS0371 DEVELOPMENT AND EVALUATION OF A TEXT-ANALYTICS ALGORITHM FOR AUTOMATED APPLICATION OF NATIONAL COVID-19 SHIELDING CRITERIA IN RHEUMATOLOGY PATIENTS

Keywords: Health Services Research, Safety, Disease-modifying Drugs (DMARDs)

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Background: Efficient pandemic planning is a key for providing a timely response to any developing disease outbreak. For example, at the beginning of the current Coronavirus disease 2019 (COVID-19) pandemic, the UK's Scientific Committee issued extreme social distancing measures, termed 'shielding', that were aimed at a subset of the UK population who were deemed especially vulnerable to infection. In April 2020 the British Society for Rheumatology (BSR) issued a risk stratification guide to identify patients at the highest risk of COVID-19 requiring shielding. This guidance was based on patients' age, comorbidities, and immunosuppressive therapies, including biologics that are not captured in primary care records. This meant rheumatologists needed to manually review outpatient letters to score patients' risk. The process required considerable clinician time, with shielding decisions not always transparently communicated.

Objectives: Our aim was to develop an automated shielding algorithm by text-mining outpatient letter diagnoses and medications, reducing the need for future manual review.

Methods: Rheumatology outpatient letters from Salford Royal Hospital, a large UK tertiary hospital, were retrieved between 2013-2020. The two most recent letters for each patient were extracted, created before 01.04.2020 when BSR guidance was published. Free-text diagnoses were processed using Intelligent Medical Objects software1 (Concept Tagger), which utilised interface terminology for each condition mapped to a SNOMED-CT code. We developed the Medication Concept Recognition tool (MedCore Named Entity Recognition) to retrieve medications type, dose, duration and status (active/past) at the time of the letter. The medication status was established based on the heading where they appeared (e.g. past medications, current medications), but incorporated additional information such as medication stop dates. The age, diagnosis and medication variables were then combined to output the BSR shielding score. The algorithm's performance was calculated using clinical review as the gold standard.

Results: To allow for the comparison with manual decisions, we focused on all 895 patients who were reviewed clinically. 64 patients (7.1%) had not consented for their data to be used for research as part of the national opt-out scheme. After removing duplicates, 803 patients were used to run the algorithm. 5,942 free-text diagnoses were extracted and mapped to SNOMED CT, with 13,665 free-text medications. The automated algorithm demonstrated a sensitivity of 80.3% (95% CI: 74.7, 85.2%) and specificity of 92.2% (95% CI: 89.7, 94.2%). Positive likelihood ratio was 10.3 (95% CI: 7.7, 13.7), negative likelihood ratio was 0.21 (95% CI: 0.16, 0.28), F1 score was 0.81. False positive rate was 7.9%, whilst false negative rate was 19.7%. Further evaluation of false positives/negatives revealed clinician interpretation of BSR guidance and misclassification of medications status were important contributing factors.

Conclusion: An automated algorithm for risk stratification has several advantages including reducing clinician time for manual review to allow more time for direct care, improving efficiency and transparently communicating decisions based on individual risk. With further development, it has the potential to be adapted for future public health initiatives that requires prompt automated review of hospital outpatient letters.

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POS0372 GROUP-BASED TRAJECTORIES OF ADHERENCE TO ANTI-TUMOUR NECROSIS FACTOR (TNF) AGENTS: A POPULATION-BASED LONGITUDINAL STUDY

Keywords: Health Services Research, Inflammatory arthritides, bDMARD

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Background: Studies of adherence to biologic disease modifying anti-rheumatic drugs (bDMARDs), namely anti-TNFs, have been largely limited to short durations or used traditional methods that do not capture the dynamic nature of medication taking.

Objectives: Our objective was to characterize long-term trajectories of adherence to anti-TNFs and evaluate associated factors.

Methods: We linked population-based health data on all physician visits, hospital admissions, and all dispensed medications, regardless of payer in British Columbia from 01/01/1996 to 3/31/2021. We identified prescriptions for anti-TNFs (including infliximab, etanercept, adalimumab) using drug identification numbers among indicated individuals (e.g., rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis) with at ≥6 years of continuous data following initiation. We used group-based trajectory models (GBTMs), a semi-parametric application of finite mixture modeling which detects longitudinal patterns in a repeatedly measured outcome, to identify and group individuals with similar patterns of bDMARD use (i.e., 'adherence trajectory group') over 6 years of follow-up. We then evaluated factors associated with each adherence trajectory group using multinomial logistic regression.

Results: We identified 1,593 patients prescribed anti-TNFs, of which 59.7% were female with a mean age of 45.2 ± 13.2 years. Group-based trajectory modeling identified 4 distinct adherence trajectories for anti-TNFs overall (**Figure 1a**): "moderate then high adherence" (Group 1; n = 814, 51.1% of the cohort), "moderate then low adherence" (Group 2; n = 314, 19.7%), "low adherence, declining to discontinuation" (Group 3; n = 291, 18.3%), and "low then high adherence" (Group 4; n = 174, 10.9%). Specific group-based trajectories for adalimumab, etanercept, and infliximab are presented in **Figure 1b-d**. Among anti-TNFs, number of prior hospitalizations was significantly associated with initial low adherence increasing to high adherence (Group 4) compared to initial moderate adherence increasing to high adherence (Group 1)(odds ratio 1.41; 95% confidence interval: 1.19, 1.68).

Conclusion: This population-based study demonstrates the heterogeneity in real-world patterns of anti-TNFs use. Findings also suggest the inadequacy of clinical and demographic characteristics in predicting patients' adherence trajectories.

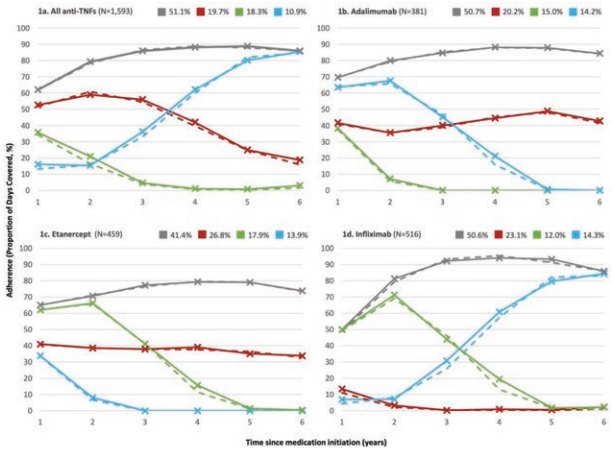


Figure 1. Longitudinal adherence trajectories of anti-TNFs

Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0373

A SYSTEMATIC LITERATURE REVIEW OF RANDOMISED CONTROLLED TRIALS EVALUATING COLCHICINE FOR CARDIOVASCULAR PREVENTION: THERE IS AN ELEPHANT IN THE ROOM

Keywords: Systematic review, Cardiovascular disease

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Background: Colchicine (COL) is widely used in rheumatology for treatment and prophylaxis of acute gout flares, other crystal diseases, and autoinflammatory diseases. In recent years evidence on the efficacy of COL for the prevention and treatment of cardiovascular diseases (CVD) has accrued. Since patients with gout and other inflammatory RMDs have a higher CV risk, COL may be a useful resource for CV prevention in rheumatology.
Objectives: To review the randomised controlled trials (RCT) investigating the use of COL for CV prevention from a rheumatology perspective.
Methods: A systematic literature review (SLR) of 7 databases was conducted following the PICO framework. Three researchers independently screened abstracts and titles and then full texts were reviewed to determine eligibility (RCTs enrolling adult subjects with or w/o history of CVD treated with COL for CV prevention). Data from eligible articles were extracted and risk of bias (RoB) was assessed with validated tools.
Results: A total of 3867 articles were retrieved and screened, 174 articles were read in full and 20 of them were eligible for inclusion. Of 19440 enrolled patients, 9655 were randomised to receive COL at a dose varying between 0.5mg/day and 2mg/day and for a period ranging between 10 days and several months (covering in part or in full the study follow-up period). Main inclusion criteria were recent acute coronary syndrome or planned cardiac surgery. In two studies, patients with stable chronic heart failure or stable coronary disease were recruited. The primary outcome varied across studies, being for example new-onset CV events, need of hospital admission, CV death, a composite index including all of these, or serum concentrations of high-sensitivity C-reactive protein. Median follow up time was largely different across studies allowing to stratify them in short term (<1 month, 2 studies), medium term (1-3 months, 7 studies), long term (4-6 months, 4 studies), very long term (>6 months, 4 studies) studies. The remaining studies assessed in-hospital events. In 7 out of 20 RCTs previous or ongoing COL use for any indication was as exclusion criterion. However, no further details about the reason for taking COL was provided. Male gender was predominant in all studies (between 65 and 96%) whereas mean age ranged between 59 and 69 years. A thorough CV history was collected at recruitment, however there was no mention to uric acid levels or a previous diagnosis of gout. Furthermore, 3 RCTs excluded patients with known autoimmune/inflammatory disease (in 2 of them ongoing immunosuppressive or steroid therapy was an additional exclusion criterion) however the other RCTs did not mention coexisting autoimmune/inflammatory diseases. The primary endpoint was met by 0/2 (0%) short term studies, 4/7 (57%) medium term studies, 2/4 (50%) long term studies and 2/4 (50%) very long-term studies. Neither of the studies assessing in-hospital events met the primary endpoint.
Conclusion: Our SLR of RCTs showed that COL may be useful in preventing new CV events/CV death in the general population when administrated for at least on month. However, the overall lack of information about coexisting gout/other inflammatory RMDs does not allow to derive meaningful data to be applied in rheumatology practice. Future RCTs should consider this aspect when defining the eligibility criteria and describing the patient cohorts since COL may be even more effective in patients that display a higher CV risk due to an underlying inflammatory disease. This may ultimately increase the likelihood to achieve the study primary endpoints.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0374

HOW WELL DO EULAR/ASAS-EULAR AND NATIONAL TREATMENT RECOMMENDATIONS FOR PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS ALIGN? IS IT TIME FOR AN UPDATE OF NATIONAL TREATMENT RECOMMENDATIONS?

Keywords: Psoriatic arthritis, Health Services Research, Spondyloarthritis

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Background: National treatment recommendations are often used to optimize patient care and may differ from international recommendations. Although such potential heterogeneity may affect outcomes, mapping of these differences across European countries was last performed more than a decade ago for axial spondyloarthritis (axSpA) and has never been undertaken in psoriatic arthritis (PsA).[1]
Objectives: To assess differences and similarities between the EULAR and ASAS-EULAR recommendations for the treatment of patients with PsA and axSpA, respectively, versus national PsA and axSpA treatment recommendations across Europe.
Methods: Rheumatologists from 15 European countries (Czech Republic, Denmark, Estonia, Finland, Iceland, Italy, Netherlands, Norway, Portugal, Romania, Slovenia, Spain, Sweden, Switzerland, and the United Kingdom) compared the most recent national treatment recommendations for PsA and axSpA with the "EULAR recommendations for the management of PsA with pharmacological therapies: 2019 update"[2] and the "2016 update of the ASAS-EULAR recommendations for axSpA"[3], in an online survey conducted between October 2021 and April 2022. The study was an initiative of the European Spondyloarthritis Research Collaboration Network (EuroSpA RCN).[4]
Results: Three countries (Czech Republic, Netherlands, and Spain) followed all EULAR recommendations for treating patients with PsA and four countries (Czech Republic, Italy, Spain, and Switzerland) all ASAS-EULAR recommendations for axSpA. A total of 4/15 countries had no national treatment recommendations for PsA or axSpA, but had other rules or regulations to follow, for which the comparisons in this study were then performed. The Netherlands had national treatment recommendations for axSpA, but not yet for PsA, for which EULAR recommendations were followed. In six countries, the national treatment recommendations for PsA predated the 2019 EULAR recommendations and in one country the national treatment recommendations for axSpA predated the 2016 ASAS-EULAR recommendations. More differences were seen between the EULAR and the national treatment recommendations for PsA than between the ASAS-EULAR and the national treatment recommendations for axSpA (Figure 1). Discrepancies between international and national treatment recommendations included: Entry criteria for start of a biologic/targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) varied and were the most stringent in Romania, where DAPSA>28 for PsA and BASDAI>6 and ASDAS≥2.5 for axSpA were required for the start of a bDMARD. Regarding PsA, in two countries (Finland and Switzerland) a conventional synthetic DMARD should be initiated before a b/tsDMARD including in patients with predominantly enthesal or axial disease. In several countries, no preference for IL17 inhibitors was given for PsA patients with significant skin involvement. The positioning of Janus Kinase inhibitors (JAKi) differed across countries, e.g. in Estonia JAKi were indicated after failure of two tumor necrosis factor inhibitors and in Romania JAKi were positioned at the same level as bDMARDs. Phosphodiesterase-4 inhibitors were not in use or not reimbursed

in most countries. Analgesics were not specifically mentioned in several of the national treatment recommendations.

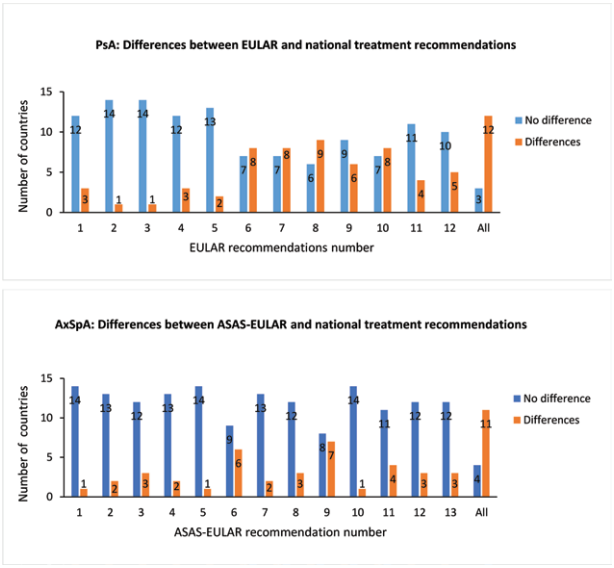


Figure 1.

Conclusion: Only a few European countries incorporated all EULAR and ASAS/EULAR treatment recommendations in their national recommendations. The potential impact of this on access to b/tsDMARD treatments needs to be further explored.

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POS0375 CONVENTIONAL-DOSE VERSUS HALF-DOSE OF SULFAMETHOXAZOLE–TRIMETHOPRIM IN THE PROPHYLAXIS FOR PNEUMOCYSTIS PNEUMONIA: A 52-WEEK, RANDOMIZED, OPEN-LABEL, TWO-ARM, PARALLEL-GROUP, MULTICENTER CONTROLLED TRIAL

Keywords: Comorbidities, Safety

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Background: Pneumocystis pneumonia (PCP) is a potentially life-threatening opportunistic infection. Sulfamethoxazole–trimethoprim (SMX/TMP) is effective in preventing pneumocystis pneumonia in patients with systemic rheumatic disease. However, the frequency of adverse events (AEs) due to SMX/TMP in rheumatic disease patients is higher than in the general population. The EULAR recommendation 2022 was described as "Of note, there is some evidence that reduced doses (eg, half-strength, daily) may also be effective and associated with fewer adverse events" [1].

Objectives: This study aimed to identify the optimal dose of SMX/TMP for the prophylaxis of PCP in patients with systemic rheumatic disease.

Methods: Our protocols of this study were described previously [2]. This study was a 52-week, randomized, open-label, two-arm, parallel-group, multicenter controlled trial. We compared a full-dose group (SMX/TMP at 400/80 mg daily) with a half-dose group (SMX/TMP at 200/40 mg daily). Inclusion criteria were follows: aged over 20 years; admission to our hospitals for diagnosis and/or treatment of new-onset or relapsed systemic rheumatic diseases from April 1, 2018, to March 31, 2021; current treatment with at least 0.6 mg/kg/day of oral prednisolone or equivalent doses of corticosteroids with or without any immunosuppressant; no prior treatment with SMX/TMP, pentamidine isethionate, dapsone, or atovaquone; Serum creatinine levels within the institution's normal range; Able and willing to provide written informed consent. Exclusion criteria were follows: contraindications to SMX/TMP; past history of PCP; prior treatment with biologic agents; currently uncontrollable complications; body weight below 40 kg; currently pregnant or nursing; unable to begin SMX/TMP within 14 days of starting prednisolone; unable to provide informed consent. The Mann–Whitney U test was used for non-normally distributed variables. Categorical variables were compared using Fisher's exact test. The discontinuation rate of SMP/TMP in each group was compared by plotting Kaplan–Meier survival curves and evaluating them with the log-rank test.

Results: Forty-two patients in full-dose group and 43 patients in half-dose group were analyzed. Since all patients were not developed with PCP while taking SMX/TMP, the results of the primary outcome measure of current as the number of patients in each treatment arm who were diagnosed with PCP were both 0. The discontinuation rates were 38% in full-dose group vs 16% in half-dose group (p value = 0.028).

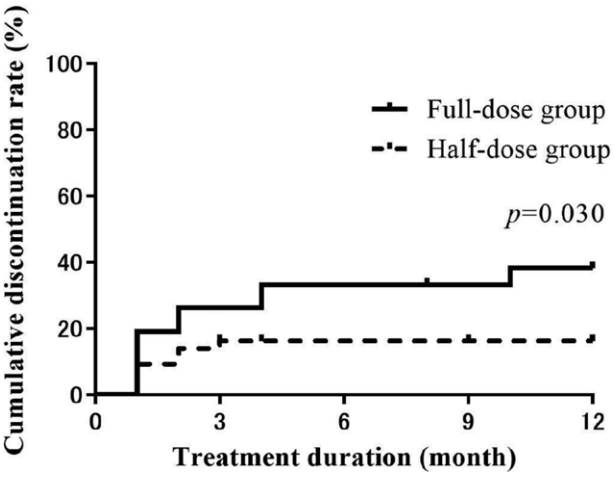


Figure 1.

Conclusion: Half-dose regimen of TMP/SMX may be better to reduce AEs than full-dose regimen in prophylaxis for PCP in patients with systemic rheumatic disease.

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POS0376

DOES A MANDATORY SWITCH FROM ORIGINATOR ADALIMUMAB TO BIOSIMILAR GP2017 OR SB5 LEAD TO INCREASED HOSPITAL COSTS? A DANBIO STUDY OF >1,300 PATIENTS WITH INFLAMMATORY ARTHRITIS

Keywords: Real-world evidence, bDMARD, Health Services Research

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Background: In 2018, Danish national guidelines dictated a mandatory switch from originator to biosimilar adalimumab based on geographical residence, i.e., GP2017 in Eastern regions and SB5 in Western regions of Denmark[1]. The switch was motivated by cost savings (approx. 34-49%). Concerns were raised if hospitals would encounter additional costs as a result of increased numbers of outpatient visits/contacts (due to patient concerns, education, treatment monitoring).

Objectives: To investigate if the switch from originator to either of the adalimumab biosimilars led to increased hospital costs, defined as all in- and outpatient contacts.

Methods: Observational cohort study with surrogate cluster (i.e. geographical) pseudo-randomization. Patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloartritis (AxSpA), who performed an adalimumab biosimilar switch were identified in the rheumatology registry, DANBIO. Hospital contacts were identified through linkage to the National Patient Registry. Hospital costs (based on DRG tariffs) were reported 9 months pre- and post-switch. In addition, the difference between pre- and postswitch costs was estimated by a generalized estimation equations (GEE) model. Medication costs of adalimumab originator and biosimilars were not available, and thus not included in the model.

Results: 1,318 patients were included (51% male, mean disease duration 16 years) and switched to either GP2017 (n=621) or SB5 (n=695). Baseline characteristics for both treatment groups stratified by diagnosis are given in **Table 1.** Monthly hospital costs 9 months pre- and post-switch were largely similar or decreased post-switch (**Figure 1**). No increase was found in the adjusted analyses (GEE); hospital costs decreased post-switch (by approximately 15%) for GP2017 switchers, especially PsA (estimate 0.83; 95% CI 0.75-0.92) and AxSpA patients (estimate 0.85;0.77-0.93), whereas no significant changes were found for SB5 switchers (**Table 1**).

Conclusion: In this study of >1,300 patient with inflammatory arthritis, we found no sign of increased healthcare hospital costs 9 months following a nationwide mandatory adalimumab originator to biosimilar switch. Our findings were strengthened by similar results regardless of whether patients switched to GP2017 or SB5.

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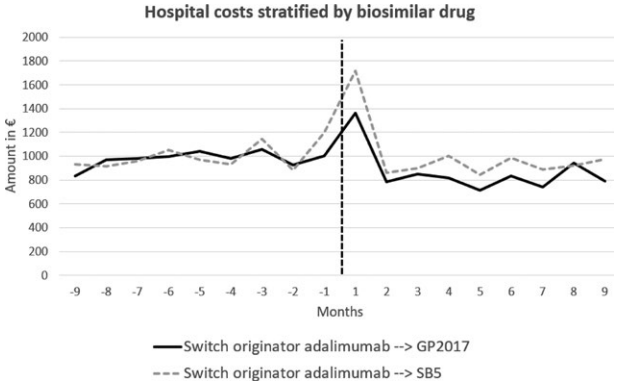


Figure 1. Hospital costs stratified by biosimilar drug. Black dotted line indicates time of switch. y-axis: Mean cost per patient per month

Table 1.

Baseline characteristics of patients who switched from originator adalimumab to biosimilar GP2017 or SB5, stratified by diagnosis

	GP2017 (n=621)			SB5 (n=695)		
	PSA	**RA**	**AxSpA**	**PsA**	**RA**	**AxSpA**
Number of patients (N)	146	213	262	173	253	269
Age, years (mean, SD)	54 (11)	62 (11)	48 (12)	55 (11)	63 (10)	49 (11)
Female, n (%)	80 (55)	158 (74)	82 (31)	58 (34)	181 (72)	89 (3)
Disease duration, years (mean, SD)	14 (7)	18 (9)	14 (10)	15 (8)	19 (10)	14 (8)
Duration of originator adalimumab treatment before switch (n,%)						
<6 years	43 (29)	59 (28)	72 (27)	36 (21)	34 (13)	68 (25)
≥6 years	103 (71)	154 (72)	190 (73)	137 (79)	219 (87)	201 (75)
Stopped biosimilar treatment within 180 days (n, %)	10 (7)	8 (4)	15 (6)	6 (4)	18 (7)	16 (6)

GLM regression estimates for costs after versus before switching, stratified by drug and diagnosis*

	GP2017			SB5		
	PsA	**RA**	**AxSpA**	**PsA**	**RA**	**AxSpA**
Total hospital costs	**0.83 (0.75-0.92)§**	0.99 (0.86-1.14)	**0.85 (0.77-0.93)§**	1.03 (0.95-1.13)	1.00 (0.93-1.08)	1.01 (0.91-1.12)

*Adjusted for gender, age, duration of treatment with originator drug (6+ years=1), stopped the medication within 6 months (yes-no) and comorbidity (number of WHO 21 chapters excluding WHO 13 ICD-10M). After=1 included as a dummy variable, and the estimates for this shows whether there were changes over time. §p-values <0.05.

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POS0377

ACCURACY OF AN AI-BASED SYMPTOM CHECKER AND AN ONLINE SELF-REFERRAL TOOL IN RHEUMATOLOGY: RESULTS FROM A MULTICENTER RANDOMIZED CONTROLLED TRIAL

Keywords: Validation, Real-world evidence, Telemedicine

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Background: Inflammatory rheumatic diseases (IRD) are often diagnosed too late due to non-specific symptoms and the lack of specialists in rheumatology. Digital diagnostic decision support systems (DDSS) promise to accelerate diagnosis and decrease the overall healthcare burden.
Objectives: To assess the ability of an artificial intelligence (AI)-based symptom checker (Ada) and an online self-referral tool (Rheport) to diagnose inflammatory rheumatic diseases (IRD).
Methods: In a prospective, multicenter open-label controlled randomized cross-over trial patients newly presenting to a rheumatology center were randomly assigned in a 1:1 ratio to complete a symptom assessment with Ada or Rheport followed by a crossover to the other respective diagnostic decision support system (DDSS). The primary outcome was correct identification of a patient with IRD by the DDSS, defined as the presence of any IRD in the list of suggested diagnoses with Ada or a pre-specified threshold score with Rheport. Physicians' diagnosis was the gold standard.
Results: In total, 600 patients were included and 214 (36%) patients were eventually diagnosed with an IRD by a physician. Rheport showed a sensitivity of 62% and specificity of 47% for IRDs. Ada's top 1 (D1) and top 5 disease suggestions (D5) showed a sensitivity of 52% and 66% and a specificity of 68% and 54% concerning IRDs, respectively. Ada, in comparison to Rheport, was more likely to correctly identify patients with an IRD when used as the first DDSS (OR: 1.09, 95% CI: 1.01 to 1.18) however this finding was not consistent after cross-over (OR: 0.97, 95% CI: 0.90 to 1.05).
Conclusion: The diagnostic capability of both DDSS for IRDs was not promising in this high-prevalence patient population referred for subspecialty evaluation. Although the overall numbers suggest that AI-based Ada demonstrated a slightly higher specificity and sensitivity compared to the questionnaire-based Rheport, Ada was not consistently better than Rheport in correctly identifying patients with an IRD when the use sequence of the apps was taken into account. Our results indicate that, strict regulation and drastic improvement is necessary to ensure safety and effectiveness of DDSS.
Acknowledgements: This study was partially funded by Novartis Pharma GmbH.
Disclosure of Interests: Johannes Knitza Speakers bureau: Abbvie, Novartis, Lilly, Medac, BMS, Sanofi, Amgen, Gilead, UCB, ABATON, GSK, Werfen, Vila Health, Böhringer Ingelheim, Janssen, Galapagos, Chugai, Celltrion, Grant/research support from: This study has been partially supported by Novartis Pharma GmbH. Others: Abbvie, Novartis, Thermo Fisher, UCB, ABATON, Sanofi, DFG, EIT Health, Koray Tascilar: None declared, Franziska Fuchs: None declared, Jacob Mohn: None declared, David Simon: None declared, Arnd Kleyer: None declared, Christina Bergmann: None declared, Hannah Labinsky: None declared, Harriet Morf: None declared, Elizabeth Araujo: None declared, Daniela Bohr: None declared, Felix Muehlensiepen: None declared, Matthias Englbrecht: None declared, Wolfgang Vorbrüggen: None declared, Cay-Benedict von der Decken: None declared, Stefan Kleinert: None declared, Andreas Ramming: None declared, Joerg Distler: None declared, Peter Bartz-Bazzanella: None declared, Nicolas Vuillerme: None declared, Georg Schett: None declared, Martin Welcker Grant/research support from: Novartis Pharma GmbH, Axel Hueber Grant/research support from: Novartis Pharma GmbH.
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Touring the landscape of epidemiology

POS0378

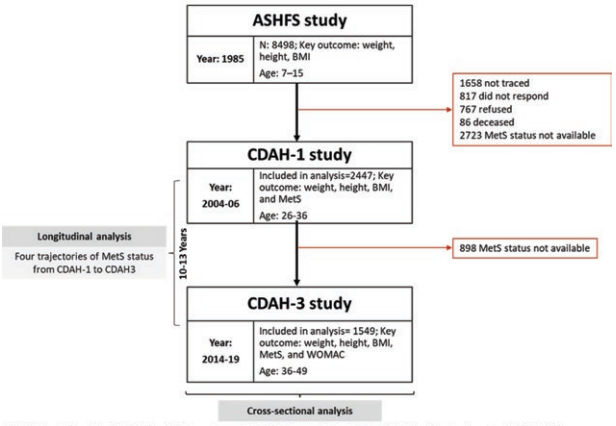
ASSOCIATION BETWEEN METABOLIC SYNDROME AND KNEE PAIN IN MIDDLE-AGED ADULTS OVER 10-13 YEARS

Keywords: Pain, Osteoarthritis, Epidemiology

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Background: Metabolic syndrome (MetS) is characterized by an increased waist circumference, dyslipidaemia (elevated triglycerides and reduced high-density lipoprotein (HDL)), hypertension and hyperglycaemia. MetS has been suggested as having a role in osteoarthritis (OA) pathogenesis. Few studies have described the association of MetS with joint pain in older adults with OA; however, none has described the association between MetS and knee pain in a middle-aged adult population.
Objectives: We aimed to describe the association of MetS and trajectories of MetS over 10-13 years with knee symptoms in general population-based middle-aged adults.
Methods: Fasting blood biochemistry, waist circumference and blood pressure measures collected during the Childhood Determinants of Adult Health (CDAH)-1 study (year:2004-6; n = 2447) and at 10-13 year follow-up at CDAH-3 (n = 1549) were used to define MetS using the International Diabetes Federation (IDF) definition. Knee symptoms were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale at the CDAH-3 follow-up (mid-adulthood). Univariable and multivariable (adjusted for age, sex, and body mass index (BMI)) zero-inflated Poisson (ZIP) regression models were used for analysis.

Figure 1: Participant flowchart



ASHFS: Australian Schools Health and Fitness Survey; BMI: body mass index; CDAH: Childhood Determinants of Adult Health; MetS: Metabolic syndrome; WOMAC: Western Ontario and McMaster University Osteoarthritis Index

Results: Overall, the prevalence of MetS increased from 8% (mean age:31.48±2.60; female:52.06%) to 13% (mean age: 44±2.90; female: 53.78%) over 10-13 years. Four MetS trajectories were identified—'No MetS' (85.01%); 'Improved MetS' (2.14%), 'Incident MetS' (8.81%), and 'Persistent MetS, (4.04%). The presence of MetS at any point, compared to no MetS, was significantly associated with worse knee symptoms at follow-up. Notably, 'Incident MetS' was most strongly associated with knee symptoms [RoM: 1.56;95%CI: 1.48,1.65] and pain [RoM:1.52;95%CI:1.37,1.70] at follow-up (**Table 1**).

Table 1. Association between trajectories of metabolic syndrome and knee symptoms

Variable (*Type*)	Association of MetS with knee symptoms at CDAH-3	
	Unadjusted RoM (95% CI) p-value	Adjusted‡ RoM (95% CI) p-value
Four trajectories of MetS status from CDAH-1 to CDAH3 (*Predictor*)		
WOMAC total (*outcome*)		
No MetS (*Predictor*)	1 (Ref)	1 (Ref)
Improved MetS (*Predictor*)	**1.44 (1.24, 1.66) p<0.001**	**1.22 (1.05, 1.41) P=0.009**
Incident MetS (*Predictor*)	**1.80 (1.71, 1.90) p<0.001**	**1.56 (1.48, 1.65) p<0.001**
Persistent MetS (*Predictor*)	**1.45 (1.35, 1.56) p<0.001**	**1.15 (1.06, 1.25) P=0.001**
P_{trend}	**p<0.001**	**p<0.001**
WOMAC pain (*outcome*)		
No MetS (*Predictor*)	1 (Ref)	1 (Ref)
Improved MetS (*Predictor*)	1.12 (0.83, 1.52) p=0.444	0.96 (0.71, 1.31) P=0.804
Incident MetS (*Predictor*)	**1.69 (1.53, 1.87) p<0.001**	**1.52 (1.37, 1.70) p<0.001**
Persistent MetS (*Predictor*)	**1.23 (1.06, 1.42) P=0.005**	1.02 (0.87 1.20) p<0.804
P_{trend}	**p<0.001**	**p<0.001**
WOMAC Stiffness (*outcome*)		
No MetS (*Predictor*)	1 (Ref)	1 (Ref)
Improved MetS (*Predictor*)	1.38 (0.95, 2.01) p=0.090	1.20 (0.81, 1.77) P=0.363
Incident MetS (*Predictor*)	**1.27 (1.10, 1.46) p=0.001**	1.16 (0.99, 1.35) p=0.066
Persistent MetS (*Predictor*)	**1.26 (1.03, 1.53) P=0.022**	1.06 (0.84, 1.33) P=0.621
P_{trend}	**p<0.001**	P=0.166
WOMAC Function (*outcome*)		
No MetS (*Predictor*)	1 (Ref)	1 (Ref)
Improved MetS (*Predictor*)	1.23 (1.02, 1.47) p=0.028	1.05 (0.88, 1.27) P=0.571
Incident MetS (*Predictor*)	**1.76 (1.65, 1.87) p<0.001**	**1.56 (1.45, 1.67) p<0.001**
Persistent MetS (*Predictor*)	**1.45 (1.32, 1.59) p<0.001**	**1.16 (1.05, 1.29) P=0.005**
P_{trend}	**p<0.001**	**p<0.001**

BMI: body mass index, CDAH: Childhood Determinants of Adult Health, CI: confidence interval, n: number of patients at the respective time point, MetS: metabolic syndrome, RoM: ratio of means; WOMAC: Western Ontario MacMaster osteoarthritis score‡Model adjusted for age, sex, and BMI**Bold** denotes statistical significance, p<0.05

Conclusion: In a middle-aged population-based sample, there was an independent positive association between MetS and knee symptoms. The MetS developed in mid-adulthood was most strongly associated with knee symptoms compared to those who had MetS in young adulthood or at both time points.

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Disclosure of Interests: None Declared.

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POS0379 WHEN SHOULD WE USE MARGINAL STRUCTURAL MODELS FOR DRUG STUDIES IN RHEUMATOLOGY? THE EXAMPLE OF CORTICOSTEROIDS AND INFECTIONS IN RHEUMATOID ARTHRITIS

Keywords: Education, Real-world evidence, Epidemiology

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Background: The use and dosing of pharmacotherapy for chronic inflammatory disease is commonly changed over time, adapting to previous treatment response, current disease activity, tolerability, and onset of adverse events. This makes evaluating the treatments difficult, as the treatment received over time becomes entangled with time-varying confounding factors, even if the initial treatment choice was randomized. To naïvely adjust for these time-varying factors in regression models have long been recognized by epidemiologists to introduce bias in most realistic settings, and marginal structural models (MSM) has been proposed as a less biased alternative. Despite this, MSMs are used very sparingly in drug studies in rheumatology.

Objectives: The objective of this work is to explain the rationale for why MSMs are recommended in the context of time-varying drug use and confounding factors, and what may go wrong if they are not used. The method will be demonstrated by comparing the incidence of serious infections between different oral glucocorticoid (GC) dose patterns over the first three years after first RA diagnosis, adjusting for time-varying confounders in MSM or through conventional regression models.

Methods: For the demonstration study, we followed 9654 recently diagnosed RA patients for three years from their first rheumatology visit in the Swedish rheumatology register (SRQ), 2007 to 2018. Follow-up was divided into 3-month periods. An average oral prednisone daily-dose was calculated for each period and categorized into "no use," "low" (≤10mg/day) and "high" (>10mg/day) doses. The MSM was implemented through sequential inverse probability of treatment weighting across time periods, accounting for demographic factors, current DAS28 and HAQ, co-medication and history of comorbidity. The incidence of serious infections (hospitalization for infection identified through the Swedish National Patient Register) was modelled by pooled logistic regression allowing separate effects for recent and past GC. We compared confounding adjustment via conventional regression versus MSM.

Results: An increased incidence of serious infections was associated with higher compared to lower doses and with more recent compared to past GC. Although in theory less biased by confounding factors, the results from MSMs were similar to those from conventional regression. Compared to no glucocorticoids, exposure to low doses during the first year added 1.9 infection cases per 100 patients (95%CI 0.9-2.9) at three years, while exposure to high doses added 4.1 (2.5-5.9) cases.

Conclusion: Our results broadly agree with previous observational studies showing a dose dependent increased risk of infection associated with (recent) use of oral glucocorticoids. Although theoretically the MSM has the potential to be less biased than ordinary regression models, the results from the two models were almost indistinguishable in this realistic example, and the implementation of the MSM led to limitations in the study design (including the categorization of exposure), and was very time consuming both in programming and computation time compared to the more widely used option. This similarity in results is not guaranteed however, and the biases that MSMs were designed to avoid should be kept in mind in all studies of drugs were the use may change over time in response to possibly confounding factors.

REFERENCES: NIL.

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POS0380 PERFORMANCE OF EYE SIGN IN DIAGNOSING PATIENTS WITH NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Diagnostic Tests, Systemic lupus erythematosus, Prognostic factors

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Background: The featured alterations of eye sign has been reported (1) in patients with neuropsychiatric systemic lupus erythematosus (NPSLE). Whether eye sign can predict NPSLE remains unknown.

Objectives: To investigate the performances of potential predictors and predictive models utilizing eye sign in classifying NPSLE.

Methods: Patients (>18 years) fulfilled the SLE diagnosis (2) were consecutively enrolled from 30 September 2016 to 30 September 2017. The diagnosis of NPSLE was evaluated and based on the consensus from rheumatologist, neurologist, radiologist and psychiatrist. Bulbar conjunctival microvascular changes in eye sign were performed and scored for all SLE patients by rheumatologist using our criteria. NP assessments were evaluating in all SLE patients by psychiatrist, including the mini-mental state examination (MMSE), self-rating anxiety scale (SAS), self-rating depression scale (SDS). Demographic and clinical data were compared between two groups and to identify potential predictors for NPSLE by using multivariable logistic regression analysis. The receiver operating characteristic (ROC) curve was plotted and the area under the curve (AUC) was used to evaluate the performance of the models in the prediction of NPSLE.

Results: 120 SLE patients were recruited (30 [24-41] years) including 30 NPSLE and 90 non-NPSLE. Totally 39 NP events were recorded in these NPSLE patients. NPSLE had higher disease activity (reflected as SLEDAI and ESR), more prevalence of positive antiphospholipid antibody (aPL), poorer NP assessments than non-NPSLE group. Eye sign examination showed NPSLE group had significantly changes of ramified loops, microangloma, wound spot, worse vascular tone and

higher total score than non-NPSLE group. In multivariable logistic analysis, model 1 showed total score of eye sign was the only predictor for NPSLE; while in model 2, except for SLEDAI, specific items of ramified loops, microangloma and wound spot were predictors for NPSLE (Table 1). Predictive model 1 utilizing total score as predictor showed AUC of 0.933 with sensitivity of 83.3%, specificity of 93.3%; model 2 including SLEDAI, ramified loops, microangloma and wound spot demonstrated an AUC of 0.960 with sensitivity of 86.7%, specificity of 95.6% (Figure 1).
Conclusion: In conclusion, ramified loops, microangioma and wound spot in eye sign were independent predictors in addition to SLEDAI for patients with NPSLE.
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[1] Wu R. Role of eye's sign in patients with neuropsychiatric disorders of systemic lupus erythematosus. Rheumatol Int. 2014 Apr;34(4):583-6.
[2] Petri M, Orbai AM, Alarcon GS, Gordon C, Merrill JT, Fortin PR, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum. 2012;64(8):2677-86.

Table 1. Multivariable logistic regression analysis of predictors for developing NPSLE.

	Model 1		Model 2	
	OR 95%CI	P value	OR 95%CI	P value
ACCI	3.94 (0.82-18.89)	0.087	8.43 (0.96-74.22)	0.055
aPL	10.43 (0.65-166.61)	0.097	7.50 (0.18-319.42)	0.292
Rp	3.83 (0.47-31.41)	0.211	40.93 (0.36-4607.34)	0.124
SLEDAI	1.53 (0.98-2.38)	0.061	1.59 (1.01-2.50)	0.044*
ESR	0.97 (0.88-1.08)	0.616	0.99 (0.87-1.08)	0.992
MMSE	1.27 (0.79-2.03)	0.321	1.26 (0.62-2.57)	0.525
SAS	0.95 (0.87-1.04)	0.239	0.97 (0.87-1.08)	0.645
SDS	1.01 (0.92-1.10)	0.902	0.97 (1.03-1.11)	0.547
Ramified loops			39.54 (1.06-1472.48)	0.046*
Vascular tone			0.74 (2.63-157.60)	0.945
Microangloma			5.85 (1.23-27.92)	0.027*
Wound spot			6.95 (1.04-46.25)	0.045*
Total score	3.68 (1.62-8.36)	0.002*		

*Statistically significant at p <0.05.ACCI: age adjusted Charlson Comorbidity Index; aPL: Antiphospholipid antibody; Rp: Raynauds' phenomenon; SLEDAI: Systemic lupus erythematosus disease activity index; ESR: Erythrocyte sedimentation rate; MMSE: The mini-mental state examination; SAS: Self-rating anxiety scale; SDS: Self-rating depression scale.

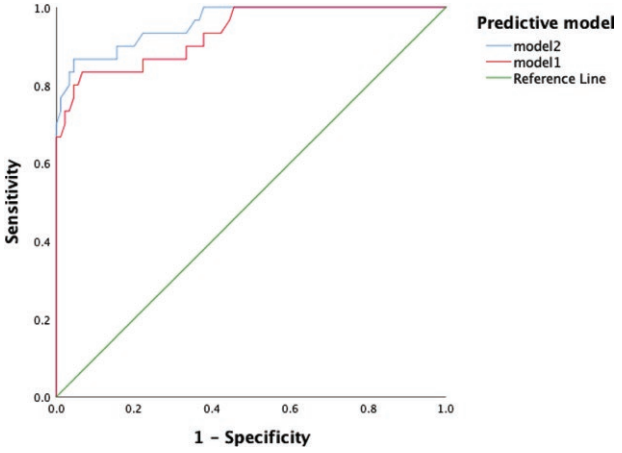


Figure 2. The association between predictive models and NPSLE assessed using receiver operating characteristic (ROC) curves.

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Disclosure of Interests: None Declared.
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POS0381

FACTORS ASSOCIATED WITH PREGNANCY-RELATED CONCERNS IN WOMEN WITH INFLAMMATORY RHEUMATIC DISEASES – AN ANALYSIS OF A NATIONWIDE PREGNANCY COHORT

Keywords: Patient reported outcomes, Registries, Pregnancy and reproduction

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Background: Pregnancies in women with chronic diseases are often accompanied by concerns about possible complications during pregnancy and about the health of the child [1]. In women with inflammatory rheumatic diseases (IRD) this can lead to a reduced number of offspring [2]. To date, surveys and interviews, but no data quantifying these worries and factors influencing them, have been published.
Objectives: To investigate and quantify pregnancy concerns in women with various underlying IRD, and to identify factors that have an impact on these sorrows.
Methods: The German registry Rhekiss is a nationwide, multicentre, web-based longitudinal cohort study, which was initiated in 2015 to investigate pregnancies and related issues in women with various IRD. Women can either be enrolled if they are planning a pregnancy (cohort 1) or if they are already pregnant prior to gestational week 20 (cohort 2). Rheumatologist- and patient-reported data are captured at regular, pre-defined follow-up visits. For this analysis, women who had answered the question regarding their concerns about their pregnancy and child's health due to the IRD were included. Categorical answers as well as patient characteristics were analysed descriptively. The impact of different factors associated with patients' anxieties was estimated by multivariable ordinal logistic regression using the proportional odds model and combining the two cohorts. Missing values were replaced by single imputation.
Results: Between 09/2015 and 10/2022, a total of 2,240 patients were enrolled, including 708 in cohort 1 and 1,532 in cohort 2. Out of those, n=455 and n=784, respectively, were eligible for the analysis. Women of both cohorts were on average 32-34 years old and had a mean disease duration of 8-9 years (table 1). A total of 31% of women in cohort 1 and 22% in cohort 2 stated that they are concerned "a lot" (figure 1). Answers of patients varied between the IRD diagnoses. A significant association with higher levels of worry was found in patients with a greater disease impact, measured by the patient-reported RAID score, an established seven-item composite index for assessing the disease burden in rheumatic diseases [3, 4], (Odds ratio 1.35 [95% confidence interval 1.27; 1.43]). A similar association was found with nulligravidity (1.29 [1.01; 1.65]) and with recent treatment changes (1.26 [1.00; 1.60]). Higher age was related with a lower level of concern (0.96 [0.94; 0.99]). No significant relationship was found for the number of underlying comorbidities (1.13 [0.98; 1.29]). Furthermore, patients who were already pregnant at enrolment were less worried than patients planning a pregnancy (0.74 [0.60; 0.93]).
Conclusion: At least one in five women with IRD is "very concerned" about pregnancy and infant health due to the underlying rheumatic disease. A higher RAID score, nulligravidity, treatment changes and younger age were associated with higher levels of concern. Therefore, patient concerns should be an essential part of individual counselling for women with IRD who want to become pregnant or are already pregnant.
REFERENCES:
[1] PMID: 26039501
[2] PMID: 22344961
[3] PMID: 21540201
[4] PMID: 35793877

Table 1. Characteristics of patients stratified by level of concern.

	Cohort 1				Cohort 2			
	Not at all	Not really	A little	A lot	Not at all	Not really	A little	A lot
Number of patients	36	61	219	140	55	155	398	176
Age in years (mean)	32.0	32.7	32.0	31.5	34.3	32.9	32.6	32.1
Disease duration in years (mean)	7.9	7.7	8.2	8.0	8.6	8.7	7.9	7.7
Moderate-severe disease	50.0%	58.0%	61.3%	61.1%	41.9%	51.2%	52.4%	61.9%
RAID score (mean)	1.4	1.9	2.0	3.2	1.0	1.7	2.3	3.2
Current flare	22.2%	11.1%	10.5%	15.8%	0	4.7%	11.1%	12.3%
Treatment changes*	31.4%	54.1%	53.9%	61.4%	35.3%	40.3%	44.5%	45.8%
Nulligravidity	50.0%	68.5%	69.3%	70.3%	45.2%	54.7%	53.8%	59.9%
Number of comorbidities (mean)	0.4	0.4	0.5	0.6	0.8	0.6	0.5	0.8

*Either due to the plan to become pregnant or the ongoing pregnancy, respectively.

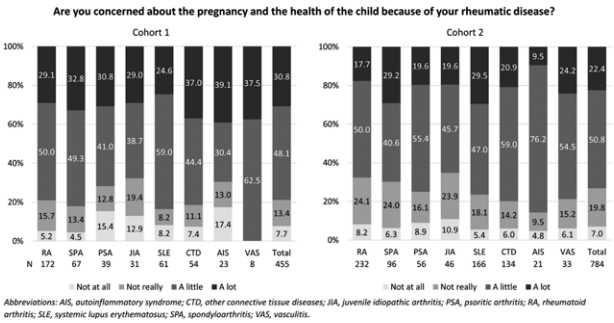


Figure 1. Level of concerns stratified by cohort and by IRD diagnosis.

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POS0382 **WITHDRAWN**

POS0383 **FATIGUE IS FREQUENT IN INFLAMMATORY RHEUMATIC DISEASES: DESCRIPTIVE DATA FROM THE NATIONAL DATABASE OF THE GERMAN COLLABORATIVE ARTHRITIS CENTRES**

Keywords: Health Services Research, Quality of life, Epidemiology

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Background: Fatigue is a major symptom in patients with inflammatory rheumatic diseases (IRD) that often severely affects quality of life and participation. While improved treatment strategies have reduced radiologic progression, fatigue often persists [1].
Objectives: To explore the frequency of fatigue and its relationship to physician- and other patient-reported outcomes in patients with IRD.

Methods: In 2020, 7637 patients with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), psoriatic arthritis (PsA) or systemic lupus erythematosus (SLE) reported fatigue in the National Database of the German Collaborative Arthritis Centres [2]. Fatigue, pain, physician (PhGl) and patient global (PtGl) disease activity, PtGl health status (all on numeric rating scales, 0-10) were categorized into three groups (mild (0-3), moderate (4-6), severe [7-10]. Depressive symptoms assessed by WHO-5 well-being (0-100) were categorized to no (>50), mild (29-50) and moderate to severe (<29). The frequency and severity of fatigue was compared in terms of the rheumatic diseases, age, sex, disease duration and sociodemographics. Violin plots show the relationship between fatigue and the other outcomes.

Results: A total of 4900 patients (84%) reported fatigue. Higher mean values were observed in patients with axSpA (4.3) compared to PsA (3.9), RA (3.8) and SLE (3.7) (table 1). Female and elderly patients, singles, and patients with little education years reported more fatigue. No difference in fatigue severity was found between patients with initial diagnosis and those with long-term disease. More fatigue was related to a poorer global health status, higher PhGl and PtGl disease activity, higher levels of pain, and more severe depressive symptoms (figure 1). Patients with concomitant fibromyalgia or depression reported worse fatigue compared to those with no or other comorbidities.

Table 1. Patient characteristics

	RA	axSpA	PsA	SLE
Number of cases	4863	777	1223	774
Female (%)	75	35	52	88
Age, in years (mean±SD)	63±14	51±14	58±13	47±15
Disease duration, in years (mean±SD)	14±11	20±13	15±11	17±11
% with Fatigue	**84**	**90**	**84**	**78**
Fatigue (mean±SD)	**3.8±2.8**	**4.3±2.8**	**3.9±2.9**	**3.7±3.0**
PtGl health status (mean±SD)	3.8±2.3	4.0±2.3	3.8±2.4	3.5±2.3
PtGl disease activity (mean±SD)	3.5±2.4	3.8±2.4	3.6±2.4	2.7±2.4
PhGl disease activity (mean±SD)	1.5±1.7	1.8±1.9	1.7±1.8	1.5±1.5
WHO-5 (mean±SD)	54±27	50±25	55±27	54±27

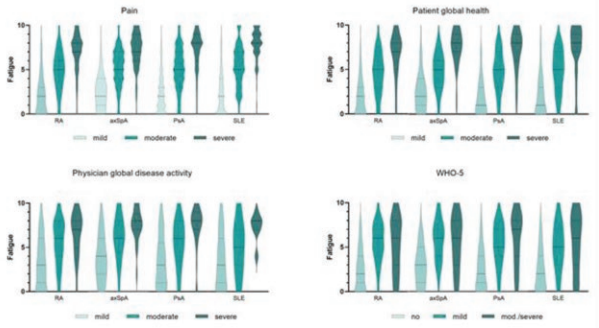


Figure 1. Relationship between fatigue and pain, global health, disease activity and depressive symptoms

Conclusion: Fatigue is a frequent symptom across various inflammatory rheumatic diseases. A strong relationship to global health, disease activity, pain and depressive symptoms needs to be considered in the (individual) therapeutic management of the diseases that relies on a shared decision making.

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[1] PMID 26509063,

[2] PMID: 35793877

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Disclosure of Interests: Christina Duesing Speakers bureau: Novartis, GSK, medac, Consultant of: GSK, Katja Thiele: None declared, Katinka Albrecht: None declared, Siegfried Wassenberg: None declared, Johanna Callhoff Speakers bureau: Janssen Cilag GmbH, Jutta Richter: None declared.

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POS0384

THE PREVALENCE AND INCIDENCE OF PSORIASIS AND PSORIATIC ARTHRITIS IN ENGLAND FROM 2009-2019: AN OBSERVATIONAL STUDY USING PRIMARY CARE DATA

Keywords: Psoriatic arthritis, Epidemiology, Real-world evidence

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Background: Psoriasis (PsO) and psoriatic arthritis (PsA) can greatly impact quality of life and result in substantial personal and societal costs. Complete and up to date data on the prevalence and incidence of these conditions and whether these change over time and vary by age is important for healthcare service planning so that specialist care and funding can be appropriately allocated.

Objectives: To determine the prevalence and incidence of PsO and PsA in males and females from 2009-2019 across all age groups in England.

Methods: We used Clinical Practice Research Datalink AURUM, a primary care electronic health record database, including 20% of the English population. The codes used to identify patients with PsO and PsA were selected by rheumatologists and dermatologists and cross-checked with published code lists from other studies to ensure inclusion of all relevant codes. All included patients must have data for at least 1 year before their diagnosis. The annual incidence and point prevalence were calculated from 2009-2019 and stratified by age/sex. The study period ended in 2019 to avoid COVID-19 pandemic affecting results.

Results: The prevalence of PsO and PsA in males and females increased annually, peaking in 2019 (PsO males 2.41% [95% confidence interval (CI) 2.40, 2.42]; PsO females 2.60% [95% CI 2.59-2.61]; PsA males 0.20% [95% CI 0.20-0.20]; PsA females 0.21% [95% CI 0.21- 0.22]), as illustrated in Table 1. In 2019, the prevalence of PsO and PsA was highest in the over 65 years age group; PsO 4.25% [95% CI 4.22-4.28] and PsA 0.38% [95% CI 0.37-0.38]. The annual incidence (per 100,000 person years) of PsO has gradually decreased in males (from 168 (164-171) in 2009 to 148 (145-151) in 2019) but in females it has been stable with a slight annual decrease (from 180 (177-184) in 2009 to 173 (170-176) in 2019). The annual incidence for PsA has increased in both males and females (13 (12-14) in 2009 and 15 (14-16) in 2019 for males and 12 (11-13) in 2009 and 18 (17-19) in 2019 for females).

Table 1. Prevalence of PsO and PsA from 2009-2019 in England

Year	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Population (n)	10733831	10910802	11031850	11180367	11343299	11224934	11378422	11657996	11933626	12234325	12420998
PsO (n)	216841	229106	239819	250667	259988	268032	276804	286499	295712	304568	311104
PsO prevalence (%, 95%CI)											
-Male	1.98 (1.96-1.99)	2.06 (2.05- 2.07)	2.13 (2.12-2.14)	2.19 (2.18-2.20)	2.24 (2.23- 2.25)	2.33 (2.32- 2.34)	2.37 (2.36- 2.38)	2.39 (2.38- 2.40)	2.40 (2.39- 2.41)	2.40 (2.39- 2.42)	2.41 (2.40- 2.42)
-Female	2.07 (2.05- 2.08)	2.14 (2.13- 2.16)	2.22 (2.21- 2.23)	2.29 (2.28- 2.31)	2.35 (2.33- 2.36)	2.45 (2.43- 2.46)	2.50 (2.49- 2.51)	2.53 (2.52- 2.54)	2.56 (2.54- 2.57)	2.58 (2.56- 2.59)	2.60 (2.59- 2.61)
PsO incidence (100,000 person years)											
-Male	168 (164-171)	158 (155- 162)	161 (158-165)	153 (150-157)	161 (157- 164)	156 (153- 159)	155 (152- 159)	154 (151- 157)	153 (150-156)	150 (147-153)	148 (145-151)
-Female	180 (177-184)	176 (172-179)	181 (177-184)	171 (167-174)	175 (171-178)	176 (172-180)	179 (176-183)	178 (174-181)	177 (174-181)	174 (170-177)	173 (170-176)
PsA (n)	14445	15443	16468	17522	18545	19618	20720	21994	23257	24514	25683
PsA prevalence (%, 95%CI)											
-Male	0.14 (0.14- 0.14)	0.15 (0.14- 0.15)	0.15 (0.15- 0.16)	0.16 (0.16- 0.16)	0.17 (0.16- 0.17)	0.18 (0.17- 0.18)	0.18 (0.18- 0.19)	0.19 (0.18- 0.19)	0.19 (0.19- 0.20)	0.20 (0.19- 0.20)	0.20 (0.20- 0.20)
-Female	0.13 (0.13- 0.13)	0.14 (0.13- 0.14)	0.15 (0.14- 0.15)	0.15 (0.15- 0.16)	0.16 (0.16- 0.16)	0.17 (0.17- 0.18)	0.18 (0.18- 0.18)	0.19 (0.19- 0.19)	0.20 (0.19- 0.20)	0.20 (0.20- 0.21)	0.21 (0.21- 0.22)
PsA incidence (100,000 person years)											
-Male	13 (12- 14)	12 (11- 13)	13 (12- 14)	12 (11- 13)	13 (12-14)	14 (13- 15)	14 (13- 15)	14 (13-15)	1514-16)	14(13- 15)	15 (14-16)
-Female	12 (11- 13)	13 (12- 14)	13 (12- 14)	14 (13-15)	14 (13-15)	15 (14-16)	17 (16- 18)	16 (15- 17)	17 (16- 18)	18 (17-19)	18 (17-19)

Conclusion: The increasing prevalence of PsO and PsA highlights the importance of organising healthcare services to meet this need, particularly in the elderly population.

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POS0385 SQUASH VERSUS ACTIHEART-MEASURED PHYSICAL ACTIVITY IN THE MIDDLE-AGED GENERAL POPULATION: THE NEO STUDY

Keywords: Patient reported outcomes, Lifestyles, Epidemiology

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Background: Adequate physical activity levels have been associated with wide-ranging beneficial health outcomes. It is therefore important to adequately measure physical activity. This is often done by the SQUASH (Short Questionnaire to Assess Health-enhancing physical activity), a patient-assessed instrument. However, this is a subjective method of which data on validity in large, middle-aged population groups are lacking.

Objectives: To assess 1) the construct validity of the SQUASH, and 2) participant characteristics associated with difference between SQUASH and ActiHeart outcome.

Methods: Cross-sectional data from the population-based Netherlands Epidemiology of Obesity (NEO) study were used, of which participants were 45 to 65 years of age. Physical activity (in Metabolic Equivalent of Task (MET) hours) was assessed using the SQUASH on one week and in a random subset using the ActiHeart accelerometer for approximately 96 hours continuously, extrapolated to one week. Convergent validity of the SQUASH was assessed by calculating Spearman's rank correlation between the SQUASH and the ActiHeart. Extreme group validity was assessed based on the difference in SQUASH activity between 1) 25% of participants with highest and lowest activity according to ActiHeart 2) participants with and without any comorbidity, and 3) participants with BMI< 25 kg/m2 versus participants with BMI> 30 kg/m2. Discriminative validity was assessed by a lack of Spearman's rank correlation between SQUASH physical activity and participant height (correlation <0.10). Participant characteristics associated with the difference between SQUASH and ActiHeart outcome were assessed by comparing quintiles of SQUASH minus ActiHeart outcome with a reference quintile (=quintile with lowest difference between SQUASH and ActiHeart).

Results: SQUASH data were available for 6,550 participants (mean age 56 years, 56% women, 24% having any comorbidity) of which 875 had ActiHeart data. Median (interquartile range) physical activity was 118 (76;154) MET hours/week according to the SQUASH and 75 (58;99) according to the ActiHeart (mean difference 47 (standard deviation 63)). The Bland-Altman plot of the difference between SQUASH and ActiHeart measurement per patient is shown in figure 1. Convergent validity was weak (ρ = 0.20, p < 0.01). Participants with the 25% highest ActiHeart scores had 38 MET hours/week more SQUASH activity (95% confidence interval (95%CI) 27;50) than the lowest 25%. Participants with any comorbidity had -13 (95%CI -17;-9) MET hours per week of SQUASH compared with those without any comorbidity, participants with BMI > 30 had -13 (-17;-9) MET hours per week compared with BMI< 25 kg/m2. Discriminative validity was present (ρ = 0.01, p = 0.41). Cut-offs of the quintiles of participants according to SQUASH minus ActiHeart physical activity (range: -61 to 411) were: -6, 27, 61 and 91 MET hours/week (reference quintile: -6;27). Men were overrepresented in the lowest quintile of SQUASH minus ActiHeart activity (-161 to 6 MET hours/week, odds ratio (OR) for being male compared with the reference quintile: 2.35 (95%CI 1.52;3.64)). Men were also overrepresented in the second-highest quintile (61 to 91 MET hours/week, OR 1.89 (95%CI 1.23;2.94)) and highest quintile (91 to 411 MET hours/week, OR 2.47 (95%CI 1.61;3.84)).

Conclusion: In this study to investigate the convergent validity of the SQUASH, there were differences between MET hours assessed by SQUASH and ActiHeart, with weak correlation between these instruments; SQUASH activity was on average higher than ActiHeart. However, discriminative and extreme group validity of the SQUASH was present. Men appeared more prone for a difference between SQUASH and ActiHeart outcome than women. These results indicate that construct validity of the SQUASH is sub ideal, although an alternative explanation could be that SQUASH and ActiHeart measure different domains or have different underlying methods. This underscores the importance of further study on adequate physical activity measurement.

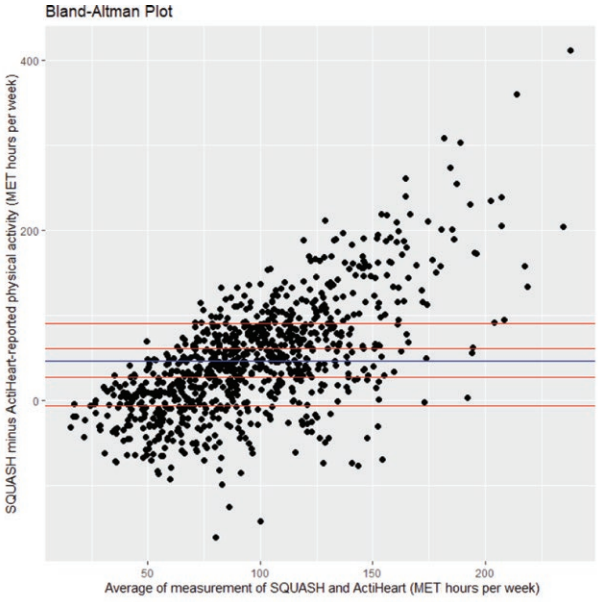


Figure 1. Bland Altman plot of SQUASH and ActiHeart physical activity (n=875). The blue line signifies the mean difference between these two instruments, and the red lines signify quintiles of difference between SQUASH and Actiheart.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0386 IMMUNE CHECKPOINT INHIBITORS: FAIL TO KEEP A CHECK ON AUTOIMMUNE DISEASES

Keywords: Epidemiology, Malignancy, Targeted synthetic drugs

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Background: The introduction of immune checkpoint inhibitors (ICIs) has revolutionized cancer treatment. ICIs augment antitumor activity by blocking the binding of checkpoint proteins with their partner proteins. This inhibition is a negative regulator on T cell cytotoxicity causing the unrestraint killing of tumor cells, a loss of self-tolerance, and increased risk of inducing autoimmunity.[1][1]

Objectives: The study was undertaken to establish correlation between the use of ICIs and autoimmune conditions (ACs), and to study trends in incidence and prevalence of ACs in patients treated with ICIs.

Methods: TrinetX, a global federated research network that provides a dataset of electronic medical records from different healthcare organizations (HCOs) was utilized. Initial query was made to isolate patients who had a diagnosis of "Neoplasm" (International Classification of Diseases, 10th version (ICD-10) Code C00 - D49). Two cohorts were made, on basis of ICIs use. Propensity score matching was carried out to match age, race and gender. Compare outcome analytic function was utilized to map the co-relation with ACs. ACs included were Systemic Connective Tissue Disorders (ICD-10:M30-M36), Rheumatoid Arthritis (ICD-10:M05, M06), Arthropathic Psoriasis (ICD10 L40.5). 9 FDA-approved checkpoint inhibitors were included in our study: Atezolizumab, Avelumab, Cemiplimab, Dostarlimab, Durvalumab, Ipilimumab, Nivolumab, Pembrolizumab, and Relatlimab.[2]

Results: A total of 12,009,334 patients had a diagnosis of neoplasm out of which 72,865 (0.61%) patients were taking ICIs. Patients in ICIs group were older as compared to patients in non-ICIs group (68 ±12.6 years vs 62.7±17.7 years). Males were predominant in ICIs group (58% vs 42%) while they were in minority in the non ICIs group (43% vs 57%). Caucasians were the predominant race followed by unknown race and then African Americans (76% vs 13% vs 9% in

ICI group, and 63% vs 25% vs 10% in non-ICI group). 5.16% of patients in the ICIs group had ACs while only 4.17% of patients in non ICIs group had ACs (p<0.0001). The hazard ratio (HR) of having ACs was higher in ICIs group as compared to non ICIs group (HR = 1.96, 95% confidence interval (CI), 1.898-2.024, p<0.0001). After propensity score matching, both groups had 72,865 patients. 5.16% patients in the ICIs group had ACs, while only 4.46% of patients in the non ICIs group had ACs. HR was 1.925 (95% CI, 1.831-2.025, p<0.0001). As shown in the graph below, the incidence of autoimmune conditions increased from 0.79% in 2015 to 2.16% in 2021 in ICIs group. Similarly, prevalence also increased from 2.97% in 2015 to 8.06% in 2021.

Conclusion: Although ICIs transformed the cancer management landscape, it is important to be aware of its effects on autoimmune disorders. Incidence and prevalence of ACs have increased in patients with neoplasm treated with ICI over the years. It can also be seen that HR of having outcome of ACs is higher in ICI group. There is a need for a prospective study to correlate the causality of development of AC with use of ICI.

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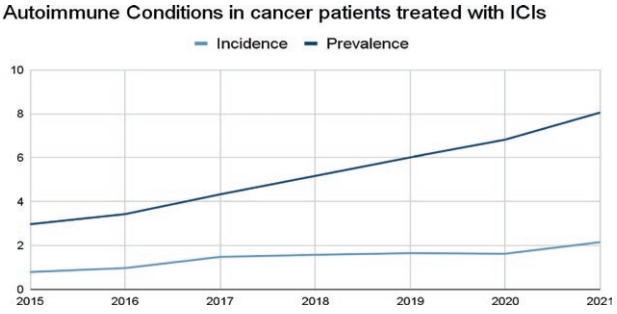


Figure 1.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0387

IMPACT OF RHEUMATIC DISEASE SUB-TYPES ON MATERNAL AND NEONATAL OUTCOMES: A POPULATION LEVEL ANALYSIS

Keywords: Pregnancy and reproduction, Rheumatoid arthritis, Systemic lupus erythematosus

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Background: There are limited data on the differing effect of rheumatic diseases (RD), including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondyloarthritis (SpA) and systemic lupus erythematosus (SLE), on maternal and neonatal outcomes.

Objectives: We evaluated the impact of four rheumatic diseases (RA, SpA, PsA and SLE) on maternal and neonatal outcomes at a population level. We also examined medication use during pregnancy across these four groups.

Methods: A contemporary pregnancy cohort of 452,273 singleton live birth events of 307,590 women was assembled for the province of Alberta, Canada. We identified 5 groups: (1) no rheumatic disease (no RD, n=449,933 pregnancies), (2) RA (n=1214), (3) PsA (n=177), (4) SpA (n=445) and SLE (n=504). We compared maternal and neonatal outcomes, comorbidity burden, and medication use among the 5 groups.

Results: Across all groups, mothers were predominantly ethnically Caucasian (>90%), residing in urban residences (>75%), and multiparous (> 58%). Maternal comorbidities including renal, vascular diseases and hypertension were most prevalent in SLE mothers. Rates of preclampsia, caesarean section and induction were highest in mothers with SLE. Pregnant women with SLE were the most likely to have preterm delivery (18.3%) and NICU admission at birth (21.8%) followed by RA (preterm delivery 11.3%, NICU admission at birth 12.8%) compared to those with PsA, SpA or no RD (Figure 1). Prednisone use for at least 28 days or any duration during pregnancy was highest amongst mothers with SLE (8.9%) followed by RA (7%) (Table 1). Antimalarial use for at least 28 days or any duration during pregnancy was highest in SLE mothers (32.7%) followed by RA mothers (18.5%) while biologic medications were used mostly in mothers with RA (10.5%).

Conclusion: Women with SLE had the worst maternal and neonatal outcomes and highest medication use followed by RA, with varying degrees for those with PsA and SpA compared to controls. The extent to which these outcomes are related to differing medication use, such as higher rates of prednisone and lower rates of antimalarials in mothers with SLE, and lower use of biologics in RA mothers, requires further exploration.

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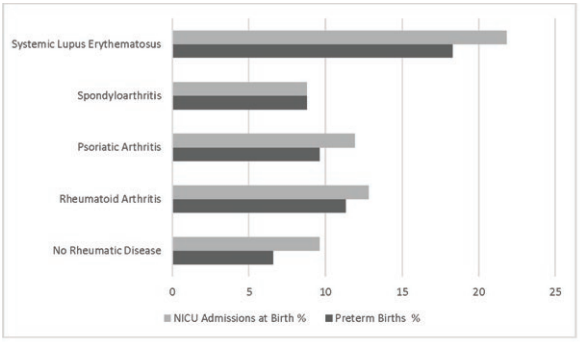


Figure 1. Percentage of Preterm Births and NICU Admissions at Birth for Women With RA, PsA, SpA, and SLE compared to Women with no RD.

Table 1. Rheumatic disease medications dispensed during pregnancy in patients with RA, PsA, SpA and SLE

Medication	RA	PsA	SpA	SLE
Total N	1214	177	445	504
Medications Dispensed for 28 days or more during pregnancy # (%)				
Prednisone	85 (7.0)	2 (1.1)	1 (0.2)	45 (8.9)
NSAIDs	63 (5.2)	4 (2.3)	14 (3.1)	14 (2.8)
Anti-malarials	220 (18.1)	5 (2.8)	2 (0.4)	164 (32.5)
Biologic Medications*	124 (10.2)	10 (5.6)	35 (7.9)	2 (0.4)
DMARDs**	111 (9.1)	3 (1.7)	4 (0.9)	26 (5.2)
Medications Dispensed for any length during pregnancy # (%)				
Prednisone	120 (9.9)	7 (4.0)	4 (0.9)	57 (11.3)
NSAIDs	117 (9.6)	5 (2.8)	30 (6.7)	29 (5.8)
Anti-malarials	224 (18.5)	5 (2.8)	2 (0.4)	165 (32.7)
Biologic Medications*	128 (10.5)	10 (5.6)	36 (8.1)	2 (0.4)
DMARDs**	115 (9.5)	4 (2.3)	4 (0.9)	27 (5.4)

(*Etanercept, infliximab, adalimumab, certolizumab, golimumab, abatacept, rituximab, tocilizumab, belimumab; **Sulfasalazine, cyclosporin, sodium aurothiomalate, mycophenolic acid, azathioprine, cyclophosphamide, methotrexate)

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Osteoporosis

POS0388

IMPACT OF GLUCOCORTICOIDS AND ANTI-OSTEOPOROTIC TREATMENT ON BONE HEALTH IN PATIENTS WITH INFLAMMATORY RHEUMATIC MUSCULOSKELETAL DISEASES (IRMD): A LONGITUDINAL STUDY

Keywords: Real-world evidence, Osteoporosis, Inflammatory arthritides

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Background: The negative effects of glucocorticoids (GCs) on the bone depend on dose and treatment duration. However, it is unclear whether a safe dose exists, especially for patients with inflammatory rheumatic musculoskeletal diseases (iRMDs).

Objectives: The primary objective of the present study was to determine, in a real-life setting, the risk of fragility fracture associated with the dose of glucocorticoids in iRMD.

Methods: We conducted a longitudinal cohort study on women with iRMD. Data were extracted from the DeFRA database (2012-2020). DeFRA is a fracture risk assessment tool similar to FRAX. Bone mineral density and fractures were assessed prospectively and compared to a matched cohort (propensity score matching, PSM with age, T-score and the % 10-year fracture risk estimated with DeFRA fracture risk assessment tool). Kaplan-Meier curves with log-rank test were made for iRMD (stratified for glucocorticoid use and dosage) and matched cohort respectively.
Results: 884 women with iRMD and 1,766 controls (age, T-score, and 10-year fracture risk matched) were included in the study and followed for up to 6 years. BMD levels decreased significantly in all GCs users not receiving anti-osteoporosis treatment (-4.26% p 0.0011, -4.23% p 0.0422, -2.66% p 0.0006 for ≥5mg/day, 2.5mg to 5mg and 0 to 2.5mg/day of prednisolone, respectively). As regards patients receiving anti-osteoporosis medications, BMD levels decreased significantly only in patients receiving ≥5mg/day of pred eq (-3.01%, p 0.0012), whereas in patients receiving 2.5mg to 5mg and 0 to 2.5mg/day, concomitantly treated with anti-osteoporotic drugs, BMD did not decrease significantly (+3.10% p NS, +1.12% p NS, respectively). **figure 1A**. Fracture incidence was greater in patients with iRMD compared to controls but only GC doses above 5mg/day were associated with significantly higher risk of fracture **figure 1B**. 21, 12 and 29 fractures were reported for patients receiving ≥5mg/day, 2.5mg to 5mg and 0 to 2.5mg/day respectively, corresponding to a crude fracture rate of 4.8 fractures per 100 person-year, 2.8 fractures per 100 person-year and 2.5 fractures per 100 person-year respectively. 103 fractures were registered in the PSM cohort (crude fracture rate of 2.2 fractures per 100 person-year). We also explored the effects of GC on serum C-terminal telopeptide of type 1 collagen (CTX) in a subset of patients with available data (n=335). We found that the proportion of patients with low bone turnover (<400ng/L) was numerically greater in patients receiving ≥5mg/day compared to other doses and controls (p NS)
Conclusion: GC doses as low as 2.5mg/day were associated with BMD loss in iRMD but this effect was preventable. BMD loss in patients taking ≥5 mg/day was not totally prevented by anti-osteoporotic medications currently used in clinical practice, resulting in higher risk of fracture.

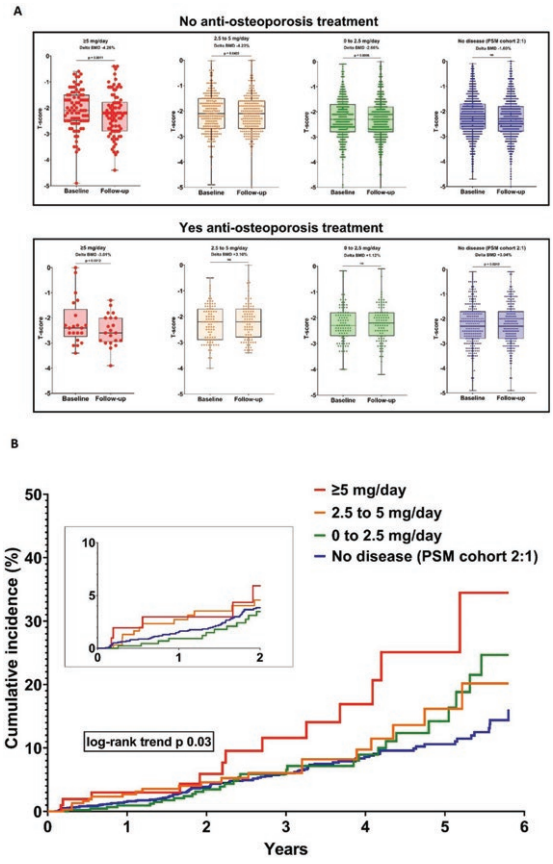


Figure 1.

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Acknowledgements: NIL.
Disclosure of Interests: Giovanni Adami Speakers bureau: Theramex, Eli-Lilly, BMS, Amgen, UCB, Fresenius Kabi, Galapagos, Angelo Fassio: None declared, Camilla Benini: None declared, Ombretta Viapiana: None declared, Davide Gatti: None declared, Davide Bertelle: None declared, Maurizio Rossini: None declared.
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POS0389

THE PREVALENCE OF GLUCOCORTICOID PRESCRIPTIONS IN ICELAND OVER 17 YEARS AND ACTIVE OSTEOPOROSIS PREVENTION FOR LONG-TERM USERS

Keywords: Osteoporosis, Quality of care, Registries

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Background: Glucocorticoid steroids (GCS) are frequently prescribed, and side effects are well-known, such as corticosteroid-induced osteoporosis (CIOP).
Objectives: To estimate the nationwide trend in the prevalence of glucocorticoid prescription over 17 years and to elucidate the proportion of patients on long-term GCS therapy who receive active bone protective therapy.
Methods: This retrospective observational registry study extended over 17 years (2003-2020). Data were retrieved from the Icelandic Prescription Medicine Register (IPMR) on all delivered GCS (ACT: H02AB) for oral use. Long-term users were defined as those who annually received ≥90 defined daily doses of GCS. We defined an individual on active bone protective therapy if, within ±45 days of receiving a prescription for GCS, they also filled a prescription of a bone protective agent.
Results: Annually, 3.8% of the Icelandic population received oral GCS, from 3.3% in 2006 to 4.3% in 2017. There was a significant increase in prescriptions over the study period (p<0.00001). Prednisolone was most frequently prescribed (Figure 1). Females dispatched GCS prescriptions more often than males (55.8%). Males and females reached their peak prevalence between the ages of 60 and 70. Prescription rates of GCS were stable for all age groups except for the 90+ age group, where prescription rates increased significantly (p<0.00001). Family medicine practitioners prescribed the highest amount of GCS, followed by physicians in specialist training, rheumatologists, oncologists, and internists (Table I). Of those who received prescriptions of GCS, 12.2% - 18.1% were classified as long-term users, representing 0.5% - 0.7% of the population. In the first years of the study there was an increase in the percentage of patients on long-term GCS therapy who received active bone protective therapy and the percentage remained stable around 22.5% until 2013. Since then, a declining number of patients have been receiving bone-protective therapy. Only 13.0% of chronic users received bone protective therapy in 2020.
Conclusion: Use of GCS has increased during the last two decades despite improvements in biological therapies for inflammatory disorders. The percentage of long-term users has remained stable. Meanwhile, the use of bone-protective therapy is declining. Thus, improvements in prophylaxis for corticosteroid-induced osteoporosis are urgently needed for patients who require long-term treatment with GCS.

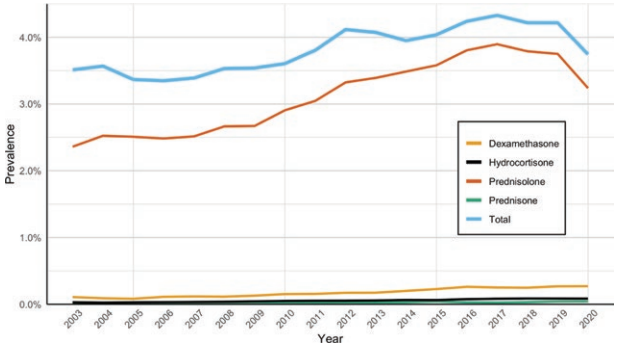


Figure 1. The prevalence of prescriptions of different oral GCS medications per year as well as the total prescription prevalence of all GCS in Iceland from 2003 to 2020 (light blue line).

Table 1. The top ten specialities that most frequently prescribed oral glucocorticoids

Medical specialty	DDD	Number of prescriptions
Family medicine	5430678	158426
Physicians in specialist training	3253469	82057
Rheumatology	2073992	31785
Oncology	1552214	17398
Internal medicine	1218651	22300
Pulmonology	1088164	21109
Medical students	837952	21641
Immunology	794420	18495
Haematology	709694	5788
Endocrinology	671149	11816

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Hulda Hrund Bjornsdottir: None declared, Olafur Einarsson: None declared, Gerdur Gröndal: None declared, Björn Gudbjornsson Speakers bureau: Novartis, Amgen, Nordic Pharma. Unrelated to this work, Consultant of: B. Gudbjornsson has received consulting fees from Novartis unrelated to this study.
DOI: 10.1136/annrheumdis-2023-eular.1842

POS0390 PRIOR ANTIRESORPTIVE TREATMENT REDUCES LUMBAR SPINE BMD RESPONSE TO ROMOSOZUMAB IN CAUCASIAN POSTMENOPAUSAL WOMEN WITH SEVERE OSTEOPOROSIS

Keywords: Osteoporosis, Real-world evidence, Bone diseases

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Background: Romosozumab, a monoclonal antibody against sclerostin, is a newly licensed dual-acting osteoporosis (OP) treatment for patients at very high fracture risk. Most patients included in the pivotal trials (ARCH[1] and FRAME [2]) were treatment naïve. However, many patients in day-to-day clinical practice who are eligible for anabolic therapy have been pre-treated with antiresorptive medications.
Objectives: Our aim was to analyse bone mineral density (BMD) treatment response to Romosozumab in patients with severe osteoporosis who are attending the osteoporosis clinic. A further objective was to analyse whether pre-treatment with antiresorptive osteoporosis medication (OPTx) influences the BMD treatment response at any BMD site.
Methods: Retrospective single-centre analysis of patients who have completed a 12-month course of monthly sc Romosozumab treatment (210mg) between February 2021 and November 2022. Local guidance recommends the use of Romosozumab in patients with severe spinal OP with at least two moderate vertebral fractures and OP at the hip as defined by DXA. BMD assessment was usually performed with DXA at baseline and after treatment completion.
Results: Out of 56 patients offered Romosozumab, 52 agreed to start treatment and 47 patients completed the full course of therapy. All patients were postmenopausal women with an average age of 73.1± 9.7 years and BMI of 24.4 ±7.1 kg/m^2. The baseline 10% major osteoporotic fracture risk as calculated by FRAX was 32.2 ±13.5. Mean baseline BMD lumbar spine (LS) T-score was -3.8 ±1.0 and total hip (TH) T-score was -3.0 ±0.7. The vast majority (95%) of patients had a history of vertebral fractures and half of the patients (50%) had a history of an additional non-vertebral fracture. 31 (66%) patients were treatment naïve or had recent antiresorptive treatment for less than 6 months, the remainder of patients received recently mostly oral or parenteral bisphosphonate treatment. After 12 months the overall mean % change BMD at the LS was 14.1 ±9.4 and 5.7 ± 5.6 at the TH site. Spine BMD increase was significantly higher in treatment naïve patients than in patients who had previous OPTx over 6 months (17.3 ±9.0 vs 7.6 ±6.9; p<0.01). Prior OPTx however did not seem to influence TH BMD response to Romosozumab (5.1 ±6.3 vs 6.1 ±5.1 in OPTxnaive patients) as shown in Figure1. Age (*r =-.37 p <.05; Spearman's rho)* and prior OPTx (r= -.49 *p<0.01)* are inversely related to LS BMD increase. Multivariate regression analysis including age, baseline spine BMD and prior OPTx identified prior OPTx as independent predictor (beta$_{St}$= 0.422; p<0.05) of spine BMD response to Romosozumab treatment.
Conclusion: The overall BMD response at LS and TH site after 12 months Romosozumab treatment in real world is similar to that reported in the ARCH trial. Pre-treatment with antiresorptive treatment seems to significantly dampen the BMD response at the lumbar spine, which highlights the importance of the choice of OPTx sequence.

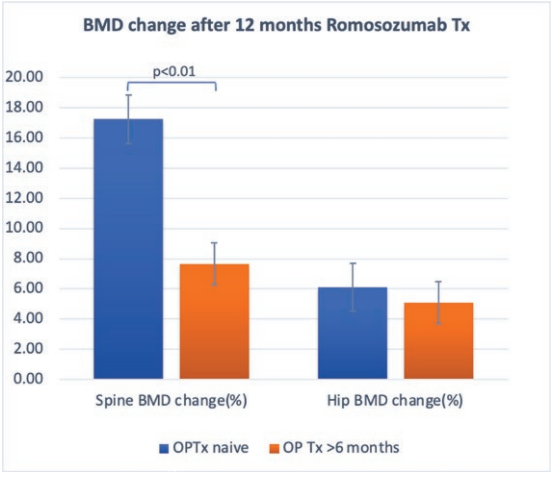


Figure 1. Bone mineral density (BMD) change (%) after 1 year treatment with Romosozumab; OP Tx = treatment with antiresorptive osteoporosis medication; OPTx naïve= no previous osteoporosis treatment or treatment for less than 6 months

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Acknowledgements: NIL.
Disclosure of Interests: Pollie Ravji: None declared, Morven McRorie: None declared, Kathryn Berg: None declared, Stuart Ralston Grant/research support from: UCB, Kyowa Kirin, AstraZeneca, Eli Lilly and Novartis, Barbara Hauser Speakers bureau: UCB, Chugai-Roche, Astellas, Effrx, Consultant of: Fresenius-Kabi, Celltrion Healthcare, Gedeon-Richter, UCB.
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POS0391 INCREASED RISK OF OSTEOPOROSIS AND HEAD OF FEMUR FRACTURES IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER - A LARGE RETROSPECTIVE COHORT STUDY

Keywords: Epidemiology, Osteoporosis

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Background: Chronic inflammatory conditions are characterized by an inflammatory milieu and increased exposure to glucocorticoids both resulting in increased risk of osteoporosis and subsequently bone fractures. Familial-Mediterranean-Fever (FMF) is a prototypical autoinflammatory disorder not treated with steroids. FMF association with osteoporosis and risk for femur fractures is not well evaluated.
Objectives: To evaluate the incidence of osteoporosis and head of femur fractures in FMF patients compared to the general population.
Methods: A retrospective cohort study using the electronic database of Clalit Health Services (CHS), the largest health organization in Israel. All FMF patients diagnosed between 2000-2016 were included with age-, sex- matched controls in 1:1 ratio. Follow-up continued until the first diagnosis of osteoporosis or femur fracture. The incidence of these conditions was compared between the groups using univariate and multivariate models adjusting for cardiovascular risk-factors.
Results: 9,769 FMF patients were followed for a median period of 12.5 years. 304 FMF patients were diagnosed with osteoporosis compared to 191 controls, resulting in an incidence rate (per 10,000 persons-years) of 28.8 (95%CI 15.7-32.5), and 17.8 (95%CI 15.4-20.6) respectively, and a crude HR of 1.62 (95% CI 1.35-1.93;p<0.001). Patients were diagnosed with osteoporosis at a considerably younger age than controls (60.1±12.4 vs 62.5±11.0 years; p=0.028).

Table 1. Incidence of osteoporosis and head of femur fracture in FMF patients compared to controls, time to event analysis.

Group	Variables	FMF	Controls
Osteoporosis	Events, n	304	191
	Age at osteoporosis, mean ±SD	60.1 ± 12.4*	62.5 ±11.0
	Follow-up time, person-years	105,480	107,068
	Follow-up time, median (IQR)	12.5 (6.8-14.6)	12.6 (7.1-14.7)
	Incidence rate per 10,000 person-years, (95%CI)	28.8 (25.7 to 32.5)	17.8 (15.4 to 20.6)
	Unadjusted HR (95%CI)	1.62 (1.35 to 1.93) **	reference
	Age-and-sex adjusted HR (95%CI)	1.80 (1.50 to 2.15) **	reference
	Multivariate¶ HR (95%CI)	1.73 (1.43 to 2.10) **	reference
Head of Femur Fracture	Events, n	56	35
	Age at femur fractures, mean ±SD	69.8 ± 13.1	65.1 ±19.9
	Follow-up time, person-years	105,718	105,813
	Follow-up time, median (IQR)	12.5 (7.2-14.4)	12.5 (7.2-14.4)
	Incidence rate per 10,000 person-years, (95%CI)	5.3 (4.0 to 6.9)	3.3 (2.3 to 4.6)
	Unadjusted HR (95%CI)	1.60 (1.05 to 2.44) *	reference
	Age-and-sex adjusted HR (95%CI)	1.61 (1.06 to 2.46) *	reference
	Multivariate¶ HR (95%CI)	1.58 (1.02 to 2.44) *	reference

¶ Adjusted for age, sex, ethnicity, socioeconomic status, obesity, smoking, diabetes, alcohol abuse, lupus, rheumatoid arthritis, sarcoidosis, thyroid dysfunction, parathyroid dysfunction, chronic renal failure, and amyloidosis.* P-value< 0.05. ** P-value<0.001.Abbreviations: CI, confidence interval, HR, hazard ratio, IQR, interquartile-range; FMF, familial-Mediterranean-fever.

Regarding femur fractures, 56 FMF patients were diagnosed with the condition compared to 35 controls, resulting in an incidence rate (per 10,000 persons-years) of 5.3 (95%CI 4.0-6.9), and 3.3 (95%CI 2.3-4.6) respectively, and a crude HR of 1.60 (95% CI 1.05 to 2.44;p<0.05). Predictors of osteoporosis or femur fractures among FMF patients included older age, Arab ethnicity, as well as North African origin. In contrast, obesity was considered a protective factor, while colchicine treatment did not significantly affect the risk of these outcomes.

Conclusion: FMF patients are at increased risk for osteoporosis and consequently femur fractures.

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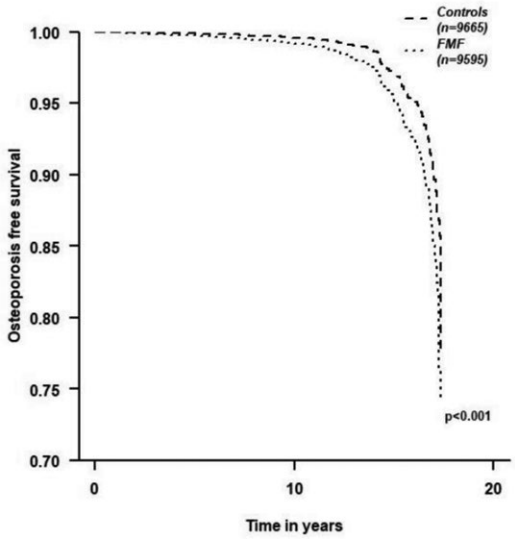


Figure 1. Kaplan-Meyer osteoporosis free survival times for FMF cohort patients vs. controls

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0392

EFFECTIVENESS OF THE ACTIVEHIP+ MHEALTH SYSTEM ON THE FUNCIONAL STATUS, PAIN AND FEAR OF FALLING IN OLDER ADULTS WITH HIP FRACTURE: A RANDOMISED CLINICAL TRIAL

Keywords: Telemedicine, Clinical Trials, Osteoporosis

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Background: Osteoporotic hip fracture causes a high level of dependency in older adults, as their functional status suddenly decreases greatly. In addition, the high level of pain and the fear of falling that they frequently experience maintain this decrease in functional status for a longer period. Digital health, the promotion of health through the use of Information and Communication Technologies, emerges as an option for the rehabilitation of older adults with hip fracture.

Objectives: To test the effectiveness of the co-created ActiveHip+ mHealth system on the recovery of the functional status and the decrease of the pain and fear of falling in older adults with hip fracture.

Methods: A total of 110 older adults with hip fracture and their family caregivers were recruited from hospitals in southern Spain. Participants were randomly assigned to an intervention group (n = 55), in which rehabilitation was performed through ActiveHip+, or to a control group (n = 55), in which they received standard rehabilitation for a hip fracture from the Andalusian Public Health System. Participants were assessed during the hospital stay and 3 months after surgery. Feasibility assessment was done through adoption (participation proportion), usage (access to the app), satisfaction with the app (Net Promoter Score) and user perception of the quality of the app (Mobile App Rating Scale). Clinical assessment was conducted through patient-reported outcomes, such as the Functional Independence Measure and the New Mobility Score Spanish version for functional status, the Numerical Rating Scale for pain and the Short Falls Efficacy Scale-International for fear of falling.

Results: We obtained positive results in terms of feasibility as we observed 88% adoption, 82% usage, 8.35/10 in satisfaction with the app and 4.3/5 in perceived quality of the app.The functional status of patients allocated to the intervention group (those using ActiveHip+) had a statistically significant greater recovery than participants of the control group at 3-months (medium effect size: 0.70 Cohen's d; p = 0.02) and (medium effect size: 0.62 Cohen's d; p = 0.03) respectively. In addition, the level of pain was statistically significant lower in participants of the intervention group than those in the control group (medium effect size: 0.45; Cohen's d p = 0.03). Regarding the fear of falling, there was no statistically significant difference (medium effect size: 0.32 Cohen's d; p = 0.17).

Conclusion: The ActiveHip+ mHealth system is effective in the recovery of the functional status and the decrease of pain in older adults with hip fracture. However, it was not effective on the decrease of the fear of falling.

Table 1. Baseline characteristics and pre-interventions raw of sample divided by groups.

Variable	Intervention group (*n* = 46)	Control group (*n* = 53)	P
Age (years), Mean (SD)	79.70 (7.2)	79.94 (7.8)	0.73
Sex, *n* (%)			0.83
Women	33 (72)	37 (70)	
Men	13 (28)	16 (30)	
Type of injury, *n* (%)			0.58
Fracture Cervical Femoral (Intracapsular)	21 (46)	22 (42)	
Fracture Trochanteric (Extracapsular)	20 (43)	23 (43)	
No fracture, but degeneration	5 (11)	8 (15)	
Type of surgery, *n* (%)			0.94
Prosthesis	14 (65)	13 (25)	
Screw Plate	30 (31)	35 (66)	
PFN-A Nail	1 (2)	5 (9)	
Others	1 (2)	0 (0)	
Hospital stay (days), Mean (SD)	6.83 (4.2)	5.64 (3.3)	0.08
Functional status at hospital discharge	78.13 (19.23)	75,26 (13,39)	0.36
FIM (Total score 18-126) Mean (SD)	5.89 (2.31)	6.58 (1.73)	0.26
NMS-ES (Total score 0-9) Mean (SD)			
Fear of falling at hospital discharge	19.37 (7.2)	20.08 (5.18)	0.58
SFES-I (Total score 7-28) Mean (SD)			
Pain level at hospital discharge	5.89 (2.31)	6.58 (1.73)	0.91
NRS (Total score 0-10) Mean (SD)			

n = sample size; SD = standard deviation; PFN-A = Proximal Femoral Nail; FIM = Functional Independence Measure; NMS-ES = New Mobility Score Spanish version; SFES-I = Short Falls Efficacy Scale; NRS = Numeric rating scale

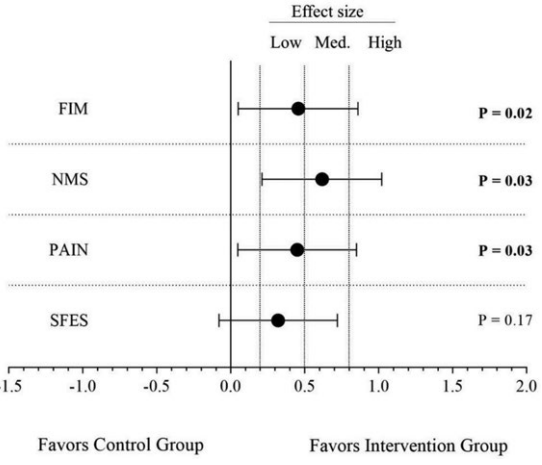


Figure 1. Effect sizes of the ActiveHip+ mHealth system on the functional status, pain and fear of falling (per-protocol analysis).

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0393 DEFINING THE KEY ATTRIBUTES OF A CLINICIAN WITH COMPETENCE IN BONE HEALTH MANAGEMENT

Keywords: Descriptive Studies, Osteoporosis

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Background: Osteoporosis and fragility fractures are managed by clinicians across a variety of specialties and there is no specific certification in osteoporosis diagnosis and management. These clinicians are an integral part of interventions aimed to improve bone health care (e.g., fracture liaison service [FLS]). Yet, the key skills and attributes of a clinician with competence in bone health management have not been established in a systematic fashion.
Objectives: We conducted a Delphi exercise and a discrete choice experiment (DCE) to generate a decision rule aiming to define the minimal attributes of a clinician best poised to assess and treat people with osteoporosis and serve as a referral source for post-fracture management.
Methods: In part 1, we used a modification of the Delphi method with two rounds. Clinicians with experience in treating osteoporosis and representatives of patient advocacy groups were purposively sampled to participate. Participants asynchronously generated a list of desirable characteristics/skills of a "clinician with competence in bone health". Characteristics were coded and organized into non-overlapping themes or "attributes" with sub-themes or "levels" within each attribute. Participants prioritized and ranked levels in order of perceived importance for inclusion in the definition for a bone health clinician. Levels within attributes associated with the highest median scores were included in the final list of criteria. In part 2, participants ranked 20 hypothetical clinicians defined by various levels of attributes from highest to lowest likelihood of being a bone health clinician to identify the minimal threshold for defining competence in managing bone health. Consistency amongst rankings was evaluated using intraclass correlation coefficients (ICC). In part 3, we conducted a DCE to generate a weighted importance score for each independent and mutually exclusive attribute and level such that the sum of weights across the highest level within each attribute would equal 100%. The threshold for competence was the total weighted score at which ≥70% of participants agreed a clinician had bone health competence.
Results: Part 1 included 13 participants, and 11 completed the DCE survey. Those who completed part 1 included 3 endocrinologists, 3 rheumatologists, 1 orthopedist, 3 general internists, and 3 representatives of patient advocacy groups. The Delphi exercise generated a list of N=108 characteristics, which were coded and grouped into common themes/attributes. Through an iterative process with 2 rounds of piloting, the attribute categories were reduced to 8 broad categories with a total of 20 levels. The participants' rankings of the relative probability that each of the 20 hypothetical clinician cases represented a clinician with adequate competence in bone health is plotted in **Figure 1**. The ICC for agreement across participants was 0.90 (95% confidence interval [CI]: 0.83, 0.95). The maximum possible score in the final criteria was 25. A threshold score of ≥12 classified a clinician as having adequate competence in bone health. For example, a clinician that prescribes all osteoporosis drugs, performs osteoporosis workup/ treatment monitoring, and leads or participates in an FLS would receive 5, 3.5, and 3.5 points, respectively, that summed would reach the threshold.
Conclusion: We developed a numeric additive decision rule to classify clinicians across multiple specialties with competence in evaluating and treating patients with osteoporosis. Our data provides the critical definition of a "clinician with competence in bone health" that may be useful for identifying and qualifying the skill of clinicians who may be included in interventional studies or clinical activities that aim improve bone health care.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Lesley Jackson: None declared, Sindhu Johnson: None declared, Ellen McNeeley: None declared, Kenneth Saag Grant/research support from: Amgen, Horizon, LG Chem, Radius, SOBI, Maria Danila Consultant of: UCB, Grant/research support from: Pfizer.
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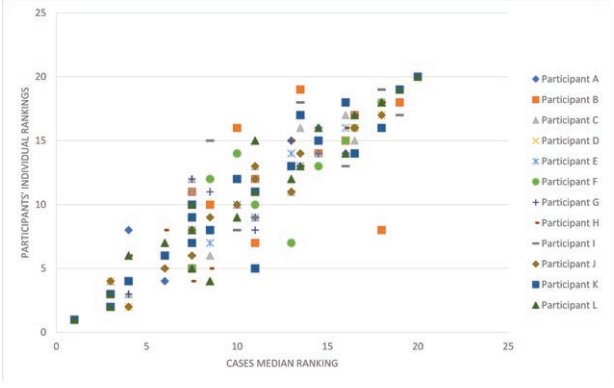


Figure 1. Participants' rankings of the probability that each case represents a clinician with competence in bone health. Cases are presented in the order of the median rank (x-axis). The case rankings (y-axis) are those assigned by each participant (A-L).

POS0394 WITHDRAWN

POS0395

DIFFERENCE IN PREDICTORS OF FRACTURES IN PATIENTS WITH SEVERE VERSUS ESTABLISHED OSTEOPOROSIS

Keywords: Osteoporosis

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Background: The FRAX™ risk assessment tool is utilised to predict fracture risk in patients with poor bone health. It uses the bone mineral density (BMD) at the non-dominant femoral neck. The performance of the tool in predicting fractures with worsening BMD has not been examined.
Objectives: The aim of this study was to investigate whether different factors within the FRAX™ tool are more predictive of severe osteoporosis; defined by a T score of -3.5 and below, compared to patients with a t score of -2.5 to -3.49.
Methods: Two patient cohorts were identified from patients referred for routine DEXA scans between 2004 and 2019, in the Northwest of England. The first cohort (group A) consisted of patients with a T score between -2.5 and -3.5 and the second cohort (group B) consisted of patients with a T score of -3.5 and below. The FRAX risk factors and the BMD data were analysed, using a Student's T test for continuous variables and a Chi Squared test for categorical variables. Univariate and multivariate logistic regression models were also fitted examining the differences in the FRAX™ risk factors and severe osteoporosis prediction. The sites measured included an average of L1-L4, right and left femoral neck in which their BMD mean and both their respective BMD totals were analysed. FRAX™ risk factors included age, weight, height, BMI, sex, previous fracture, parent fractured hip, smoking, steroid use, rheumatoid arthritis, alcohol consumption and coeliac disease/malabsorption.
Results: 31,547 patients were included in the analysis, with a mean age of 64.9 years (SD = 12.9). The number of individuals in group A were 4,714 (81.54%) and 1,067 (18.46%) in group B. Table one depicts the differences in the FRAX™ risk factors between the two groups and the odds ratios. Age, weight, height, BMI and current smoking were statistically significant in predicting severe osteoporosis. Lower weight, height and BMI was associated with group B. In addition, increased age and current smoking was also associated with group B. There was no significant difference between group A and B in regard to sex, previous fracture, parent fractured hip, steroid use, rheumatoid arthritis, alcohol consumption or coeliac disease/malabsorption.
Conclusion: The results of this study indicate that certain risk factors used in the FRAX™ scoring are more predictive of a severe osteoporosis than others. In addition, research providing insight into utilising FRAX™ variables in fracture prediction in patients with severe osteoporosis will provide valuable insight.

Table 1. The differences in the FRAX™ characteristics between group A and B, the corresponding odds ratio and confidence interval

Characteristic	Group A	Group B	Odds ratio and confidence interval
Average age in years (SD)	72.52 (10.80)	75.52 (11.18)	1.10* [1.02,1.04]
Average weight in kilograms (SD)	63.27 (13.27)	55.94 (14.02)	0.95* [0.95,0.96]
Average height in centimetres (SD)	158.96 (8.44)	155.89 (10.48)	0.96* [0.95,0.97]
Average BMI in kg/m^2 (SD)	25.02 (4.82)	24.16 (26.62)	0.91* [0.90,0.92]
Sex	Female - 3,844 (81.54%) Male – 870 (18.46%)	Female – 854 (80.04%) Male – 213 (19.96%)	1.10 [0.93,1.30]
Previous fracture	2 (0.04%)	1 (0.09%)	2.21 [0.20, 24.4]
Parent fractured hip	65 (1.38%)	9 (0.84%)	0.61 [0.30,1.23]
Current smoking	1,792 (38%)	445 (41.71%)	1.17* [1.01,1.34]
Steroids (current)	1,165 (24.71%)	271 (25.4%)	1.04 [0.89,1.21]
Rheumatoid arthritis	362 (7.68%)	88 (8.25%)	1.08 [0.85,1.38]
Alcohol consumption	284 (6.02%)	68 (6.37%)	1.06 [0.81,1.40]
Coeliac disease/ malabsorption	183 (3.88%)	50 (4.69%)	1.22 [0.88,1.67]

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POS0396

DISEASE SEVERITY IS ASSOCIATED WITH LOW BONE MINERAL DENSITY AND OSTEOPOROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Epidemiology, Systemic lupus erythematosus, Osteoporosis

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Background: Patients with systemic lupus erythematosus (SLE) are at an increased risk for osteoporosis and fragility fractures.[1] This risk is mediated by a variety of factors such as chronic inflammation, treatment with glucocorticoids (GC), vitamin D deficiency, and others.[2] The role of disease-specific factors of SLE has not been fully elucidated.
Objectives: We aimed to identify factors associated with bone mineral density and osteoporosis including fragility fractures to better understand the interplay between disease-specific factors and general risk factors that drive bone loss in this patient population.
Methods: Rh-GIOP is a prospective observational cohort study investigating bone health in consecutive patients ≥18 years with inflammatory rheumatic diseases and current or prior GC treatment. This cross-sectional analysis assessed the baseline visits of all patients with SLE fulfilling the EULAR/ACR 2019 SLE classification criteria. Multivariable linear regressions models were fitted to identify factors associated with bone mineral density (BMD). As a second outcome, we investigated factors associated with clinical osteoporosis (defined by either a T-Score of ≤ -2,5, anti-osteoporotic treatment and/or fragility fractures) by multivariable logistic regression analysis.
Results: Baseline data from 110 patients with SLE were analyzed. The mean age was 48.1±14.5 years, mean disease duration 16.3±9.9 years, and 41% of the cohort was identified as having osteoporosis (OP). Lupus nephritis was present in 35% of the SLE patients, of whom 55% had active nephritic disease at baseline osteoporosis screening visit. Class IV and V accounted for most nephritis cases (61%). In multivariable linear regression analysis, lupus nephritis class IV and V (reg. coefficient (95%CI): -0.745 (-1.395;-0.095)), the presence of U1-RNP antibodies (-0.750 (-1.314;-0,187)) as well as C-reactive protein (CRP, -0.015 (-0.026;-0.003)) and longer disease duration (-0.037 (-0.056;-0.018)) were significantly associated with low BMD. Conversely, clinical remission (defined as SLEDAI-2K=0 and GC dosage ≤5 mg prednisone equivalent per day) was positively associated with BMD (0.447 (0.037;0.857)), as were Siglec-1 levels on monocytes as surrogate for Type-I interferon activity (0.558 (0.150;0.967)), BMI (0.045 (0.014;0.076)), and health assessment questionnaire (HAQ, 0.307 (0.078;0.536)). In multivariable logistic regression analysis, active lupus nephritis (OR (95%CI): 7.42 (1.256;43.868)) was strongly associated with OP in patients with SLE. Additionally, age (1.06 (1.020;1.100)), HAQ (0.29 (0.120;0.682)) and complement factor 3 (1.27 (1.002;1.601)) were found to be significantly related to the presence of OP. Neither current GC use, cumulative GC dose nor GC duration were significantly associated with BMD or clinical OP.
Conclusion: In patients with SLE, indicators of disease severity, expressed by (active) lupus nephritis, high CRP, U1-RNP antibodies, and long disease duration, are related to poor bone health in addition to commonly known risk factors

such as low BMI and higher age. The knowledge of these disease-specific factors helps to identify patients with SLE at particular high risk for OP and fragility fractures.

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POS0397 SHORT-TERM (2 YEARS) FRACTURE RISK PREDICTION: A MACHINE LEARNING APPROACH

Keywords: Real-world evidence, Osteoporosis, Bone diseases

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Background: Osteoporotic fractures continue to be a major cause of global health concerns around the world. The most common risk scores (FRAX, DeFRA) are evaluating this risk within a 10-yearstime window, which might not be suitable for evaluating shorter term risk, or quickly progressing patients.

Objectives: The objective of the present analysis is to develop 2-year fracture risk scoring models using Machine Learning (ML) techniques and compare their performance with the DeFRA tool.

Methods: Data were obtained from web-based fracture risk assessment tool (DeFRA) used in Italy. This tool is a derived version of the FRAX and can be accessed through a website (https://defra-osteoporosi.it/). 33 clinical and densitometric variables were used to compute the DeFRA risk score, with variable degree of completeness for each patient. After eliminating the attributes with a large number of missing values, and eliminating the patient with large outlier values for any of the attributes, the dataset was reduced to 2516 patients (with follow-up visits) and 15 attributes (Age, Weight, Height, BMI, Smoking, Alcohol, Familial Fractures/Osteoporosis, Previous femur or vertebra fractures, Previous other fractures, Comorbidities, Prednisone mg equivalent per day, T-score femoral-neck, T-score spine, Serum CTX levels, Anti-osteoporotic therapy prescribed). For the development of the machine-learning prediction, the dataset has been randomly divided into a train-set and a test-set, and the train-set has been synthetically balanced using Synthetic Minority Oversampling Technique (SMOTE). A Logistic Regression (LR) model and a Random Forest (RF) model have been optimized on the train-set for predicting the patients who incurred either a hip fracture, or any major osteoporotic fracture, or both in the 2 years following the baseline visit. DeFRA risk score is used as a benchmark for the prediction of either hip fracture or of any major fracture within 2-years.

Results: The DeFRA score, when used to predict the patients incurring a hip fracture within 2 years, has an Area Under the Receiver-Operating Curve(AUROC) of 0.52, compared to 0.76 for Random Forest and 0.81 for Logistic Regression. When looking at other major osteoporotic fractures, the AUROC is 0.59 for DeFRA, 0.77 for LR and 0.80 for RF, and when looking at any fracture the values are 0.58, 0.78, 0.80 for DeFRA, LR and RF respectively. Performance metrics including accuracy, sensitivity, and specificity are summarized in Table 1.

Table 1.

Table I: Performance of DeFRA and machine learning classifier in predicting patients incurring an osteoporotic fracture within 2 years

	Hip fracture			Major osteoporotic fracture			Any fracture		
	DeFRA	LR	RF	DeFRA	LR	RF	DeFRA	LR	RF
AUROC	0.52	0.81	0.76	0.59	0.77	0.80	0.58	0.78	0.80
Accuracy	0.62	0.63	0.92	0.68	0.69	0.89	0.61	0.71	0.90
Sensitivity	0.40	0.76	0.29	0.49	0.76	0.34	0.54	0.79	0.34
Specificity	0.63	0.62	0.95	0.69	0.69	0.93	0.61	0.70	0.95

Conclusion: Currently usedrisk scores for osteoporotic fractures are developed within a 10-years time window, which might be toolong to stratify the most at risk-patients or those that are showing a fast-progressing disease. This isreflected by the poor predictive performance of DeFRA when looking at a 2-years time window. Machine-learning (either logistic regression or random forest) could greatly improve the predictive performance ofa scoring system to identify the patients most likely to incur an osteoporotic fracture in the short term,thus requiring shorter follow-ups.

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POS0398 DETERMINANTS OF MORTALITY AND IMMINENT RE-FRACTURE IN PATIENTS HOSPITALIZED FOR SEVERE OSTEOPOROTIC FRACTURES

Keywords: Osteoporosis

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Background: Patients hospitalized for severe osteoporotic fractures are at increased risk of morbidity and mortality. It is recommended to improve their medical management by Fracture Liaisons Services (FLS) organization.

Objectives: Our aim was to assess the determinants of mortality and imminent refracture in those patients followed in FLS.

Methods: The CROSS study is a national, prospective, observational, multicenter study conducted in 12 centers with Fracture Liaison Services (FLS). Patients included were men and women above 60 years, hospitalized for a recent (less than 3 months) severe fragility fracture (hip, pelvis, humerus or vertebrae) that occurred after a low-energy trauma. Patients with either a non-severe fracture, a pathological fracture, a high trauma fracture or a per-prosthetic fracture were not included. At baseline and 2 years we have collected sociodemographic data, fracture event, bone risk factors, factors of falling, FRAX items, history of treatments, comorbidities, Charlson score and DXA measurement. To assess the risk factors for new severe fracture or death, a multivariate Cox proportional hazard multivariate analysis was performed.

Results: 895 patients were included in the cohort with the following fracture location distribution: clinical vertebrae 43.3%, hip 37.5%, pelvis 10.3%, and humerus 11.1%. Most patients were women (79%) with a median age of 81 years (71-85). 40% had a previous history of fragility fracture after 40 years. Only 17.7% received an anti-osteoporotic treatment in the 5 years prior baseline whereas 21.4% received a calcium supplementation and 43.6% received a vitamin D supplementation. At baseline 48% of patients had densitometric osteoporosis. Over the 2 years of follow-up (data completed for 95% of population), 116 severe fractures in 110 patients (12.9%) and 80 deaths (8.9%) occurred. 49.1% of patients were prescribed an antiosteoporotic treatment after the fracture (75% of bisphosphonates), that was initiated within the 3 months following fracture event in 63 % of the cases. Multivariate analysis showed that reduced spinal BMD (OR=24.6 CI 95% 2.84-247, p=0.027), recurrent falls (OR= 2.80 (1.11-6.65), p=0.023), antiosteoporotic treatment initiation (OR= 2.17, CI 95% 1.19-4.08, p=0.013) and increased age (OR=1,04 CI 95% 1,01-1.08, p=0.027) were significantly associated with the risk of a new severe fracture. Use of walking aids (RR=2.71 (CI 95% 1.15-6.39), p=0.02), diabetes (RR=3.70 (CI 95% 1.04 to 13.2), p=0.044), metastatic cancer (RR=15,5 (CI 95% 1.08 to 221), p=0.043) were positively associated with risk of death whereas antiosteoporotic initiation was negatively associated with this risk (OR=0.19 (CI 95% 0.07 to 0.49), p<0.001).

Conclusion: In patients hospitalized for severe osteoporotic fractures and managed in a FLS setting, initiation of an anti-osteoporotic treatment is associated with a decreased risk of mortality. In this population, a low BMD was a strong determinant of an imminent fracture risk.

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Poster View

Osteo arthritis, aetiology, pathology and animal models

POS0399 **THE ION CHANNEL TRPV4 PARTICIPATES IN THE CARTILAGE PROTECTION OF IGURATIMOD ON KNEE OSTEOARTHRITIS**

Keywords: Cartilage, Disease-modifying drugs (DMARDs), Osteoarthritis

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Background: Osteoarthritis (OA) is the leading cause of disability for bone and joint diseases. Cartilage injury is its pathological basis. There is a lack of therapeutic drugs with clear cartilage protection in clinic. Iguratimod (IGU) has cartilage protection effect in the treatment of rheumatoid arthritis, but it is not clear whether it also has cartilage protection effect on OA.
Objectives: To investigated the efficacy and mechanism of Iguratimod (IGU) on cartilage protection effect on knee osteoarthritis (OA).
Methods: Type VII collagenase was injected into the knee joint cavity of C57BL6/N rats to establish a model of CIOA (Collagenase-induced Osteoarthritis), to establish the model of osteoarthritis, followed by IGU given by intragastrium at 10mg/kg. μCT and Immunohistochemistry (IHC) were used to evaluate the structural changes of OA knee joint, the degree of destruction of knee cartilage layer and subchondral bone. IHC and qPCR were used to evaluated the expression of TPRV4 in chondrocytes of OA rats. Chondrocytes were processed by IGU at the cellular level, and the concentration of glycosaminoglycan secreted and the expression of chondrogenic differentiation factor in cells were further detected. TRPV4 ion channel inhibitor and interfering RNA technology were used to verify whether TRPV4 was involved in the effect of IGU on cartilage.
Results: It was found that IGU could change the pain sensitivity of OA model rats and effectively reduce the pain of OA rats. μCT showed that IGU could effectively inhibit the subchondral bone injury of knee joint in OA rats; Toluidine blue staining and Safranin O-Fast Green staining of rats knee joint also showed that IGU treatment could delay the degeneration of knee cartilage of rats with OA. At the cellular level, it was found by qPCR that IGU could effectively promote the expression of mRNA levels of Sox9 and Col2a, markers of chondrogenesis, in chondrocytes. Alcian blue staining also showed that IGU promoted chondrocyte secretion of glycosaminoglycan; Moreover, the results of scratch experiment also showed that IGU promoted the migration of chondrocytes. The results addressed above all indicated that IGU could promote the differentiation of chondrocytes. The expression of transient receptor point vanillin 4 (TRPV4) in OA rats chondrocytes in the treatment group of IGU was increased. We used ion channel inhibitors and interfering RNA technology to show that IGU played a role in delaying cartilage damage, promoting cartilage differentiation and migration by regulating the function of TRPV4.
Conclusion: IGU can effectively alleviate the pain of OA model rats, and exert cartilage protection by regulating TRPV4. The results offer new treatment options for osteoarthritis.
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POS0400 **A CAUSATIVE ROLE FOR PERIARTICULAR SKELETAL MUSCLE WEAKNESS IN THE PROGRESSION OF JOINT DAMAGE AND PAIN IN OA**

Keywords: Pain, Cartilage, Osteoarthritis

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Background: Although OA is regarded as a disease of the articular cartilage, recent research has demonstrated whole-joint pathology, including synovial inflammation, subchondral bone sclerosis, osteophyte formation, and changes in periarticular muscles that surround the affected joint. There is also increasing evidence that the consequences of knee OA are associated with decreased lower limb muscle strength and function. It is unclear whether the change in periarticular muscle is the cause or result of disease progression, however.
Objectives: This study investigated changes in periarticular muscle during the progression of osteoarthritis (OA), as well as the cause-and-effect relationship between muscle weakness and OA, in a mouse model of OA achieved by destabilization of the medial meniscus (DMM).
Methods: Knee OA was induced by DMM in 10-week-old male C57BL/6 mice. Pathological muscle phenotypes in the tibialis anterior (TA) and quadriceps muscles were assessed in both the early and late stages of OA with muscle-fiber cross-sectional area analysis, markers of myogenesis, as well as the proliferation of satellite cells. OA pathology and pain behavior were examined with OARSI grade, von Frey filament threshold and pressure algometer. Periarticular muscle weakness was induced by multiple rounds of barium chloride injections after DMM induction. In addition, myostatin knockout.mice with muscle hypertrophy phenotype was used to evaluate the influence of muscle mass on pain and joint destruction after DMM.
Results: Morphological alterations in the TA and quadriceps in DMM mice included variations in muscle-fiber size, aberrant muscle fibrosis, inflammatory cell infiltration, and decreased muscle mass. Periarticular muscle fibers isolated from DMM mice showed reductions in cell number and myogenic capacity, as well as the proliferation of satellite cells. DMM mice exhibited exacerbated articular cartilage destruction, subchondral bone sclerosis, synovitis and pain after muscle injury compared to the DMM + vehicle group. Myostatin knockout mice were characterized by attenuated OA and the complete abrogation of pain behavior after DMM.
Conclusion: DMM-induced knee OA resulted in morphological changes in periarticular muscle, in a manner that coincided with muscle atrophy. Joint destruction and pain after DMM were aggravated by muscle weakness and alleviated by muscle hypertrophy. Our results suggest a causative role for muscle weakness in the progression of joint damage and pain in OA.
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POS0401 OSTEOARTHRITIS SYNOVIAL MACROPHAGES HAVE A TOLERIZED PHENOTYPE AND A VERY WEAK CORTICOSTEROID RESPONSE

Keywords: Osteoarthritis, Innate immunity, Cell biology

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Background: The majority of osteoarthritis (OA) patients show synovial inflammation. Intra-articular corticosteroid injections are often given to decrease this inflammation. Whereas these provide relatively short-term alleviation of clinical symptoms, they do not improve long-term disease prognosis. Monocytes/macrophages are key cells in OA synovial inflammation. Whereas past research mainly focused on pro-inflammatory M1-like and anti-inflammatory M2-like macrophages, a second logic related to long-term macrophage polarization is interesting to study; macrophage training versus tolerization that is the result of prior exposure of monocytes/macrophages to different inflammatory cues. This process is also referred to as innate immune memory.

Objectives: Here, we investigated what could underlie the absence of long-term amelioration of OA by corticosteroids. Hereto, we compared global RNA profiles of OA synovium macrophages with well-defined *in vitro* trained and tolerized monocyte-derived macrophage models, all in the presence or absence of corticosteroids.

Methods: Macrophages were obtained from OA synovium (OA-Mf) using tissue digestion followed by CD14+ MACS isolation or differentiated from blood-derived CD14+ monocytes using medium with human pooled serum. Tolerance and training was induced in monocyte-derived macrophages using 5 ng/mL LPS (LPS-Mf), mimicking macrophage paralysis as observed in sepsis, or 10 µg/ml β-glucan (BG-Mf), which mimics non-specific vaccination against an ulterior lethal pathogen exposure by generating macrophages that present robust M1 responses upon TLR receptor stimulation, during the first 24 hours of differentiation respectively. Samples were treated with 1 µM triamcinolone acetonide (TA) or DMSO for 4 hours. The genome-wide transcriptomic response to corticosteroids was determined using RNA sequencing.

Results: TA exposure of trained BG-Mf and tolerized LPS-Mf significantly altered the expression of 201 and 257 RNA transcripts, respectively. In contrast, in OA-Mf only 12 RNA transcripts were significantly regulated, indicating a globally paralyzed TA response. Interestingly, evaluation of the IL1, and C-C motif chemokine ligand (CCL) and CXCL clusters of chemotactic factors showed close resemblance between OA and tolerized but not trained macrophages in terms of basal expression, although only one gene in these clusters (*IL36RN*) was significantly regulated by TA in the OA-Mf. This indicates that OA-Mf have a state that is related to the memory of inflammation as in the LPS-Mf for key pathways involved in OA and further confirms that the OA-Mf have a weak TA response. However, this did not extend to all genes significantly induced by LPS (n= 895), since OA-Mf clustered apart from the LPS-Mf and BG-Mf, indicating a distinct global pro-inflammatory mRNA expression profile when compared with both tolerized and trained monocyte-derived macrophages. Finally, we observed that OA-Mf have a matrix-metalloproteinase (MMP) expression profile that is consistent with a macrophage phenotype, since they express *MMP9*, *MMP14*, and *MMP19*, but furthermore very strongly express *MMP1*, *MMP2*, *MMP3*, and *MMP10* that are not expressed by our monocyte-derived macrophage models, highlighting their unique phenotype. Again, corticosteroid treatment of OA-Mf could not repress MMP expression.

Conclusion: OA synovial macrophages have an inflammatory polarization state that closely resembles the tolerized macrophage state in terms of relevant secreted cytokines and chemokines transcripts. Furthermore, they show a very weak corticosteroid response, which might explain why corticosteroid treatment fails to ameliorate long-term pathology and symptoms in OA patients.

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POS0402 LYSYL OXIDASE (LOX) AND LYSYL OXIDASE-LIKE 2 (LOXL2) CONTRIBUTE TO CARTILAGE CALCIFICATION DURING OSTEOARTHRITIS

Keywords: Crystal arthritis, Osteoarthritis, Cartilage

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Background: Cartilage pathological calcification is a hallmark of osteoarthritis (OA), a degenerative disease characterized by articular cartilage degradation that leads to joint pain and impaired movement. We previously demonstrated that lysyl oxidase-like enzymes (LOX(L), which include five enzymes, LOX and LOXL1-4), that catalyze the crosslinking of collagen and elastin fibers of the extracellular matrix (ECM), play a crucial role in cartilage calcification (Bernabei et al, in preparation). Indeed, the pan-LOX(L) inhibitor BAPN decreased crystal production in chondrocytes, but the identification of the crucial LOX(L) involved in this process remained to be established.

Objectives: To identify the specific LOX(L) involved in cartilage calcification during OA.

Methods: *In vitro*, murine chondrocytes (primary cells or ATDC5 cells) were cultured in normal medium ((Nt), DMEM high glucose + 10% FBS) or calcifying medium ((CM), BGJb +10% FBS+ 20mM β-glycerophosphate + 50µg/ml ascorbic acid). The expression of Lox was silenced using siRNA at 100nM ((siLox), OriGene). Gene expression was measured by qPCR. Calcium-containing crystals were evidenced by alizarin red staining and quantified by cetylpiridinium dissolution of crystals. *In vivo*, mice were subjected to meniscectomy (MNX) in the right knee or sham operated in the left. *Ex vivo*, cartilage explants from undamaged or damaged cartilage regions were obtained from 7 OA patients undergoing knee replacement surgery. Immunohistochemistry (IHC) was performed on murine knees and human cartilage sections ((anti-LOX or anti-LOXL2 rabbit polyclonal antibodies (Proteintech or Genetex respectively). Calcification was detected by Alizarin red staining on histological sections, and proteoglycan loss by safranin-O staining. Mouse gene expression data from primary articular chondrocytes treated with interleukin-1β (IL-1β) for 24h were obtained from GEO (identifier: GSE104793).

Results: *Lox* expression was increased in murine chondrocytes stimulated with calcification medium (CM), but not *Loxl2*. Similarly, transcriptome data from primary mouse articular chondrocyte treated with IL-1β, revealed that both *Lox* and *Loxl2* were markedly upregulated in treated cells. We then evaluated Lox and Loxl2 modulation by IHC in calcified cartilage in the MNX OA model. Both Lox and Loxl2 were increased in MNX cartilage compared to sham cartilage and at an even higher extent in osteophytes and in newly formed calcified deposits appearing in MNX knees. In human OA cartilage we found massive calcification and proteoglycan loss in damaged areas compared to undamaged. In line with murine data, we revealed increased LOX and LOXL2 expression in damaged human cartilage, both in chondrocytes and in the extracellular matrix in correspondence to calcified regions. Next, we performed *in vitro* Lox RNA silencing using siLox or siControl RNA transfected ATDC5 cells (siLox cells or siCtrl cells). Lox expression was decreased by more than 80% in siLox cells compared to siCtrl cells. Most importantly, in CM, siLox cells calcified less as demonstrated by alizarin red quantification. Furthermore, gene expression data showed inhibition of calcification gene *Annexin 5* by Lox silencing. In agreement, we found an increase of early differentiation genes *Sox9* and *Col2*, along with significant downregulation of hypertrophic marker *Col10*. However, no effect by Lox silencing was found on fibrotic genes (*Col1, Col3*) and on pro-calcifying cytokine interleukin-6 (*Il-6*). Additionally, we revealed a trend towards decreased mitochondrial reactive oxygen species in siLox cells. Finally, Lox silencing decreased gene expression of the ECM catabolic enzyme *Mmp13*.

Conclusion: Our data revealed that LOX and LOXL2 are increased in calcified areas of murine and human cartilage. Additionally, *in vitro* inhibition of Lox prevents at least in part, calcium-crystal deposition, chondrocyte hypertrophy, and *Mmp13* catabolic enzyme expression. Altogether, our results suggest that both LOX and LOXL2 might play a role in cartilage calcification and OA.

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POS0403

SENSITIVITY OF AUTOMATED, U-NET-BASED SEGMENTATION TO LAMINAR CARTILAGE TRANSVERSE RELAXATION TIME (T2) IN KNEES WITH DIFFERENCES IN CONTRALATERAL OSTEOARTHRITIS STATUS – DATA FROM THE THE OA-BIO CONSORTIUM

Keywords: Imaging, Osteoarthritis

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Background: Radiographically normal knees with contralateral (CL) radiographic joint space narrowing (JSN) are at elevated risk of incident radiographic osteoarthritis (ROA). We previously observed increased superficial femorotibial cartilage layer transverse relaxation time (T2) on magnetic resonance images (MRI) of 39 KLG0 knees (0=normal) with advanced ROA in the contralateral knee (CL JSN), compared with 39 (1:1-matched) KLG0 knees without evidence of CL ROA (bilateral KLG0) [1]. These results suggest that cartilage matrix degeneration occurs in radiographically normal knees with CL JSN, and can be detected in vivo using MRI [1]. Application to larger cohorts, however, will benefit from fully automated image segmentation, as manual segmentation is a labor-intensive process.

Objectives: To evaluate the performance of U-Net-based cartilage segmentation, using an artificial intelligence (AI), i.e. convolutional neuronal network (CNN) approach, combined with fully automated detection of bony landmarks and the specific MRI slices requiring cartilage segmentation. The U-Net results were compared with those from manual segmentation, and the fully automated technology was applied to a larger (extended) control group.

Methods: U-Nets were trained from manual, quality-controlled cartilage segmentations in sagittal MESE images of the Osteoarthritis Initiative healthy reference cohort (n=92; HRC), one on the medial (MFTC) and one on the lateral femorotibial compartment (LFTC). All 7 echos (10-70 ms) were used. A 3rd U-Net was trained from manual, quality-controlled bone segmentations in 60 OAI HRC knees. The latter was used for automated detection of the weight-bearing femoral region of interest. The automated bone segmentation was registered to an atlas comprising both bone and cartilage segmentation, for identifying the slices required for cartilage segmentation. Automated post-processing was employed to correct obvious segmentation errors. This pipeline was first applied to n=39 dataset pairs (KLG0 with CL JSN vs. bilateral KLG0 knees) [1]. Then it was applied to n=642 bilateral KLG0 knees, to extend the limited paired case-control design (n=39) to a much larger control cohort. The agreement of the U-Net-based vs. manual segmentation was evaluated using the Dice Similarity Coefficient (DSC). Actual differences in cartilage T2 between a) 39 case vs. 39 control knees were compared between manual [1] vs. fully automated segmentation, and b) 39 case vs. 642 control knees (U-Net). Cohen's D was used as a measure of effect size.

Results: The DSC for the 2x39 knees with manual segmentations available ranged from 0.83±0.05 to 0.87±0.04 across the medial/lateral tibia and femur. When applied to the 39 pairs of case vs. control knees, fully automated segmentation identified differences in superficial layer T2, with the effect size apparently larger (Cohen's D MFTC/LFTC: 0.62/0.50) than that obtained from manual segmentation (0.46/0.48). Further, the U-Net was more sensitive to deep layer T2 differences (MFTC/LFTC: 0.36/0.50) than manual segmentation (0.25/0.35). When comparing the case knees to 642 control knees, the fully automated segmentation showed similar between-group differences (0.57/0.48 for superficial T2).

Conclusion: Fully automated segmentation of the femorotibial cartilage, in combination with automated detection of the relevant slices and femoral region of interest, showed high agreement with manual segmentation. The pipeline was able to reproduce differences in laminar T2 observed by manual segmentations [1], indicating early superficial cartilage matrix degeneration in radiographically normal knees with advanced contralateral radiographic KOA (JSN). The proposed fully automated analysis pipeline was readily expanded to a much larger cohort and thus represents a promising tool for future clinical studies on early cartilage change.

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POS0404

SOLUBLE LOW AFFINITY NERVE GROWTH FACTOR RECEPTOR (LNGFR) MAY REGULATE PAIN IN KNEE OSTEOARTHRITIS

Keywords: Pain, Osteoarthritis, Biomarkers

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Background: Osteoarthritis (OA) is a disease of the entire joint. OA causes significant pain that has been linked to increased neurotrophin concentrations, including mature nerve growth factor β-NGF[2]. β-NGF antagonism was efficacious in reducing OA pain in clinical trials but was associated with rapidly progressive OA[1], hampering mainstream delivery of this treatment. β-NGF binds to tropomyosin receptor kinase A (TrkA) and low-affinity NGF receptor (LNGFR), a tumour necrosis factor receptor (TNFR) superfamily member. Given that TNFR superfamily member shedding regulates inflammation and immunity, soluble LNGFR (sLNGFR) shedding might be important in pain regulation[3] and association between these molecules and OA-related knee pain may point to an alternative, less harmful approach to β-NGF antagonism and pain reduction.

Objectives: Therefore, we investigated the association between (synovial fluid) SF levels of soluble LNGFR, TrkA, proNGF and NGF and other relevant neurotrophins with OA-related knee pain. Key cytokines involved in TNFR family receptor shedding were also investigated.

Methods: SF was procured from 42 subjects with severe OA at the time of arthroplasty. VAS pain scores were recorded pre-operatively. In-house developed ELISAs, commercial ELISAs and LEGENDplex™ were used to measure sLNGFR, TrkA, proNGF, β–NGF, other neurotrophins and cytokines including TNF-α. Statistical analysis was implemented using Graphpad Prism software, version 9.0. Data normality was analysed using Kolmogorov-Smirnov and Shapiro-Wilk testing. The Spearman rank correlation test and multivariate linear regression analyses were performed to assess the correlations. Statistical significance was defined as $p<0.05$.

Results: VAS pain score positively correlated with β–NGF ($r=0.34$, $p<0.05$) and TrkA ($r=0.33$, $p<0.05$, $r=0.32$, $p>0.05$). There was a positive association trend with NT-3 and BDNF with a negative trend for ProNGF. sLNGFR. The β–NGF/TrkA ratio showed a strong positive correlation with VAS ($r=0.80$, $p<0.001$). However, there was no correlation between pain and the β–NGF/sLNGFR ratio ($r=-0.08$, $p>0.05$). TNF-α positively correlated with β–NGF ($r= 0.83$, $p<0.001$), NT-3 ($r= 0.66$, $p<0.01$), and BDNF ($r= 0.50$, $p<0.05$) and negatively with ProNGF ($r= -0.74$, $p<0.01$). Additionally, TNF-α positively correlated with TrkA ($r=0.62$, $p>0.05$) and sLNGFR ($r=0.26$, $p>0.05$).

Conclusion: Our results align well with the previously-proposed β–NGF pain molecular pathway and suggest that inflammation-related endogenous cleavage of sLNGFR, but not TrkA may modulate pain *in vivo* in OA as sLNGFR act as sink of the endogenous NGF. These novel findings may provide new avenues for safe and effective pain reduction strategies in OA.

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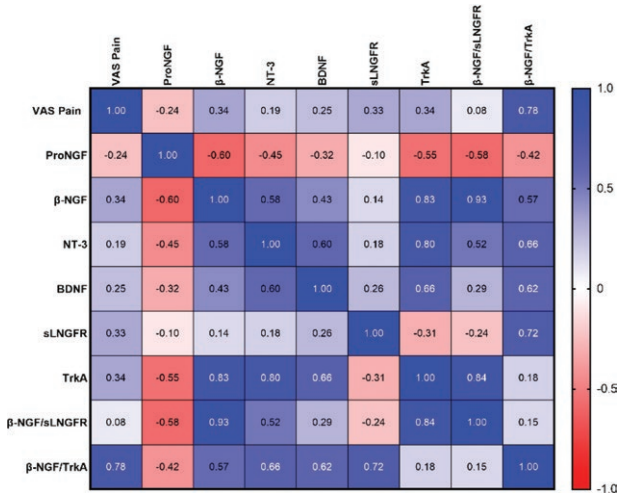


Figure 1. Correlation matrix between pain score and neurotrophins and neurotrophins receptors all depicted as a heat map.

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POS0405 TREATMENT WITH INTEGRIN A10B1-SELECTED MESENCHYMAL STEM CELLS ALLEVIATES POST-TRAUMATIC OSTEOARTHRITIS DEVELOPMENT IN AN EQUINE MODEL

Keywords: Osteoarthritis, Disease-modifying drugs (DMARDs), Animal models

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Background: Mesenchymal stem cells (MSCs) have gained much attention for their potential to treat osteoarthritis (OA) due to their regenerative and immunomodulatory properties. So far, studies have shown varying results, potentially due to variations in the MSC preparations. Previously it was shown that integrin $\alpha 10\beta 1$-selected equine MSCs (integrin α10-MSCs) decrease cartilage degradation and bone sclerosis in an experimental equine post-traumatic OA model[1], and that integrin $\alpha 10\beta 1$-selected human MSCs could to home to experimental cartilage defects in rabbit knees and directly participate in new cartilage formation[2].
Objectives: This study investigated disease modifying effects of integrin $\alpha 10\beta 1$-selected MSCs in terms of joint function, cartilage structure and immunomodulation in an experimental equine post-traumatic OA model.
Methods: This was a non-randomized and partially blinded experimental study including 17 Standardbred trotters. OA was induced using the carpal osteochondral fragment model. On day 18 after surgery, the treatment-group (n = 8, all females) received $20x10^6$ allogeneic adipose tissue-derived integrin α10-MSCs from a male equine donor. The control group was left untreated (n = 9). From day 14 after surgery and until study termination on day 70, the horses underwent weekly joint and lameness examinations (AAEP score and flexion tests) and synovial fluid collection. After euthanasia, the carpi were evaluated by computed tomography (CT), magnetic resonance imaging (MRI), macroscopic pathology and histology evaluation. MSCs were traced through PCR detection of the Y-chromosome in the cell pellet from the synovial fluid samples and in tissue samples from cartilage, synovial membrane, and subchondral bone from the osteochondral fragment site, collected postmortem.
Results: A significant improvement of lameness scores (p=0.02) and response to flexion (p=0.004) over time was observed in the treatment group, while the untreated group had no change in lameness and a smaller decrease in flexion response (p=0.03). No joint flares were seen after MSC treatment. The integrin α10-MSCs treated horses had significantly less macroscopic cartilage pathology (p=0.019), lower cartilage histology score (p=0.037) and showed a better but not statistically significant (p=0.069) healing of the osteochondral fragment on CT. Prostaglandin E2 (PGE2) and interleukin-10 (IL-10) were significantly increased in the synovial fluid of the treated group on day 21 (p=0.018 and p=0.035, resp) and on day 28 (p=0.0606 and p=0.042, resp) compared to day 18. Interleukin-6 (IL-6) showed a non-significant increase in the treated group on day 21 (p=0.085). MSCs were detected in the synovial fluid of the treated horses on day 21 (n=8), day 28 (n=1) and day 35 (n=2) and in the cartilage/subchondral bone (n=7) at study termination (day 70), which was 52 days after integrin α10-MSC treatment.
Conclusion: Intra-articular injection of integrin α10-MSCs is safe, alleviates the development of pathological changes in the joint and improves joint function in an equine post-traumatic OA model. In addition, integrin α10-MSCs were still present in the joint 52 days after treatment. This suggests that that integrin α10-MSCs hold potential to be a disease modifying treatment of OA.
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POS0406 INCREASE OF CARTILAGE REGENERATION BY IFN-Γ IN CARTILAGE INJURY MOUSE MODEL

Keywords: Cartilage

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Background: Until now, there was no effective cure for cartilage injury and degeneration commonly occurring in joint injury and OA. The efficiency of cartilage regeneration in young people is generally considered higher than in the elderly.
Objectives: In this study we investigated candidate genes associated with cartilage regeneration in knee joints of young and adult mice using a full-thickness cartilage injury (FTCI) mouse model.
Methods: Young (3 week-old) and adult mice (9 week-old) were subjected to FTCI and cartilage was harvested at 3, 7, and 14 days after FTCI. Cartilage regeneration was evaluated with safranin O staining and immunohistochemistry. For discovery of novel genes associated with cartilage regeneration, RNA-seq analysis was performed. For differentiation into chondrocytes, ATDC5 cells were monolayer and 3D cultured in DMEM containing insulin-transferrin-selenium (ITS) for 7 and 14 days. Chondrocyte specific IFN- γ receptor 1 knock out mice were created to examine the influence of IFN signaling in cartilage repair.
Results: Cartilage regeneration significantly increased in damaged region of FTCI in young mice compared with that of adult mice at 7 and 14 days. Gene expression profiles of cartilage from young and adult mice of 3 day (damaged stage) and 14 day (repair stage) after FTCI were examined by RNA-seq analysis. A total of 1115 (448 up- and 667 down-regulated) and 2294 (726 up- and 1568 down-regulated) differentially expressed genes (DEGs) were identified in young mice compared with adult mice at 3 and 14 days after FTCI, respectively. Gene ontology (GO) analysis revealed that genes responsible for interferon gamma (IFN-γ) and innate immune response, and cell proliferation, cell-substrate adhesion, and wound response were significantly up-regulated in the young mice at 3 and 14 days after FTCI, respectively. In particular, our data using monolayer and micromass culture of ATDC5 cells showed that blockade of IFN-γ signal by small interference RNA (si-IFN-γ receptor) suppressed synthesis of anabolic factors, including ACAN and Col II, along with decreased chondrogenic differentiation of ATDC5 cells, whereas treatment with IFN-γ (20 ng/ml) up-regulated synthesis of anabolic factors and chondrogenic differentiation. Cartilage repair score after FTCI was significantly worse in chondrocyte specific IFN- γ receptor 1 knock out mice compared to WT.

Conclusion: IFN-γ signaling may play a critical role in the process of cartilage regeneration.

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POS0407 CHEMICALLY AND MECHANICALLY ACTIVATED PIEZO1 LEADS TO CHANGES IN THE EXPRESSION OF ECM-MODULATING FACTORS THAT DIFFER BETWEEN HEALTHY AND HUMAN OA CHONDROCYTES

Keywords: Cell biology, Cartilage, Osteoarthritis

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Background: Osteoarthritis (OA) is the most common degenerative joint disease that causes functional limitations in addition to pain and has become a major global health problem in recent decades. Meta-analysis of studies on patients with knee OA showed that physical exercise can function as a clinically relevant, effective intervention and non-drug treatment for reducing pain and improving physical activity in patients with OA [1]. In chondrocytes, the perception and transduction of mechanical signals leading to changes in $[Ca^{2+}]_i$ is orchestrated by mechanosensitive ion channels [2].

Objectives: Piezo1 represents a mechanosensitive cation channel (MSC) that allows Ca^{2+} influx in chondrocytes and acts as an important mechanotransducer that senses deleterious mechanical stresses (high strains) [3]. Numerous studies have shown that Ca^{2+} regulation in conjunction with mechanical stimulation is crucial for the behaviour and function of chondrocytes and the balanced assembly of the ECM. The underlying mechanism could influence the expression profile as a consequence of mechanical stimulation. Differences in this regard between primary human chondrocytes isolated from knees of OA patients (pCHOA) and healthy chondrocytes could explain the altered sensitivity to mechanical stimuli in OA.

Methods: Mechanical stimulation of chondrocytes was performed by the use of the flexcell system whereas in parallel cells were chemically activated via different concentrations of the Piezo agonist Yoda1. Changes in expression were analysed by qPCR for metalloproteinases (MMP1, 3,13), inflammatory cytokines (IL6, IL8, IL4) and ECM relevant components (Col-I, Col-II, BMP2). The decreased expression of Yoda1 by siRNA knockdown was used to more clearly map the effect of MSC on ECM under mechanical stimulation.

Results: Chondrocytes responded to flexcell tension stimulation with decreased expression of MMP3 and IL6, whereas application of Yoda1 resulted in an opposite effect. In healthy chondrocytes the MMP expression was more enhanced than in OA chondrocytes whereas in both cell types the same reduction for TIMP-2 through the activation of Piezo1 was detected. Yoda1 increased IL6 and IL8 expression while IL4 was reduced. The knock-out of Piezo1 can partially reverse these effects.

Conclusion: Performing expression studies in the context of mechanical stimulation and targeting Piezo1 in OA and healthy chondrocytes may reveal OA-specific changes in mechanisms of mechanical signal transduction. Furthermore, this may provide further insight into the extent to which OA cells exhibit differential sensitization to mechanical signals.

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POS0408 DEFECTIVE AUTOPHAGY IS ASSOCIATED WITH CHONDROCYTE SENESCENCE AND JOINT DAMAGE

Keywords: Cell biology, Osteoarthritis

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Background: Aging is a main risk factor of many major human diseases, including Osteoarthritis (OA). Compromised autophagy, a hallmark of aging, is involved in joint aging and OA and its activation protects against joint damage and disease. However, targets underlying this defective mechanism are still unknown.

Objectives: *Here, we aimed to identify targets regulating autophagy* with potential clinical relevance in joint aging and OA.

Methods: We performed a quantitative proteomic analysis of defective autophagy by Atg5 knockdown in human OA chondrocytes by using iTRAQ (isobaric tags for relative and absolute quantitation) labeling coupled LC/MS/MS. Protein identification and quantification were performed using Protein Pilot Software v 4.0. Each MS/MS spectrum was searched in the Uniprot/Swissprot database for *Homo sapiens*. Human cartilage and chondrocytes from healthy, aging and OA subjects were employed to investigate the role of Lamin A/C in aging and disease by western blot, and inmunohistochemistry. To test the relevance of Lamin A/C accumulation in joint tissues, a mutant mice model of accelerated aging by genetic deletion of Zinc Metalloproteinase STE24 (*Zmpste24*$^{-/-}$) was employed. The functional consequences of Lamin A/C accumulation on macroautophagy, inflammation, and senescence were determined in human chondrocytes. To evaluate the therapeutic effect of regulating Lamin A/C in human chondrocytes, Lonafarnib, an FDA approved drug for Progeria Syndrome, acting as Lamin A/C accumulation inhibitor, was employed.

Results: 24 out of 487 proteins were significantly altered ($p<0.05$) in response to defective autophagy. Cytoskeleton organization, collagen catabolism, oxidative stress, and aging pathways were affected. Interestingly, Lamin A/C, a nuclear envelope protein implicated in cell senescence and aging, was found upregulated under defective autophagy. Increased Lamin A/C expression was found in human chondrocytes with reduced macroautophagy. Furthermore, increased Lamin A/C expression is found in aging and OA human cartilage. Importantly, *Zmpste24* KO mice showed bone damage and intervertebral disc degeneration (IDD), suggesting that Lamin A/C accumulation associated to deficient autophagy is correlated with aging and OA phenotype. Human chondrocyte premature aging by genetic knockdown of *Zmpste24*, lead to Lamin A/C accumulation, accompanied by a reduction of macroautophagy by *MAP1LC3B* downregulation, increased inflammation, cartilage degradation and senescence represented by upregulation of *NFKB/RELA, MMP13, CDKN1A and CDKN1A* respectively. Remarkably, inhibition of Lamin A/C accumulation by Lonafarnib upregulates macroautophagy and protects against inflammation, cartilage degradation and chondrocyte senescence.

Conclusion: The results suggest that increased LMNA due to autophagy defects compromises chondrocyte homeostasis and joint integrity, potentially contributing to systemic maladaptation that occurs in aging. Therefore, targeting Lamin A/C might be a promising strategy to develop novel therapeutics for cartilage aging and OA.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0409 IMPLICATION OF GLYPICANS AND NOTUM IN BONE MARROW MESENCHYMAL STROMAL CELLS DURING OSTEOGENIC DIFFERENTIATION IN OSTEOARTHRITIC DISEASE

Keywords: Bone diseases, Cell biology, Osteoarthritis

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Background: Osteoarthritis (OA) is accompanied by an excessive formation of underlying bone caused by homeostatic alterations. It has been described that in OA joints there is an up-regulation of the WNT/β-catenine pathway driving to the differentiation of Mesenchymal Stromal Cells (MSCs) into osteocytes [1]. Glypicans 1-6 act as co-receptors of WNT pathway, improving interactions between molecules [2]. On the other hand, NOTUM plays a role as a negative regulator of the pathway preventing WNT binding to its receptors and favouring the soluble form of Glypicans [3]. All these evidences lead us to think about the importance of Glypicans 1-6 and NOTUM in the osteogenic differentiation of MSCs in OA disease.
Objectives: To determine the differences at gene and protein levels of Glypicans 1-6 and NOTUM in MSCs between OA patients and controls at baseline and during induced *in vitro* osteogenic differentiation.
Methods: Bone Marrow Mesenchymal Stromal Cells (BM-MSCs) from both, 8 OA patients and 8 healthy donors were isolated from BM samples. BM samples were obtained by joint replacement and traumatic fractures. BM-MSCs were cultured during 21 days with normal culture medium and with osteogenic inducing medium. Cells and supernatant were recovered at 1, 7, 14 and 21 days. Protein levels were determined by ELISA in cells supernatant. Extraction and purification of RNA from cells and cDNA synthesis were performed. Glypicans 1-6 and NOTUM gene-expression was analysed by qPCR and normalized with housekeeping genes β-actin and RNA18S. The data were calculated with the method of fold change ($2^{-\Delta\Delta Ct}$). Statical analysis were performed with GraphPad Prism 8.0. For the detection of outliers, the ROUT method (Q=1%) was used. Data were analyzed using t-test.
Results: The mRNA levels of cells with normal culture medium were up-regulated in GPC6 (t=7d; p=0,016) in OA patients. During osteogenic differentiation, was observed a statistically significant up-regulation in levels of OA patients vs controls of GPC2 (t=14d; p=0,034), GPC4 (t=14d, p=0,025; t=21d, p=0,017), GPC5 (t=14d, p=0,007), GPC6 (t=14d, p=0,013) and *NOTUM* (t=14d, p=0,009) and down-regulation of GPC3 (t=7d, p=0,034). In addition, protein levels of NOTUM were lower compared to the control group in OA BM-MSCs (t=1d, p=0,049) and in the differentiation to osteocytes (t=1d, p=0,049; t=7d, p=0,043; t=14d, p=0,016). GPC3 levels were higher OA patients in all the times and in the two conditions (p < 0,0001). In the differentiation, GPC2 were lower (t=7d, p< 0,0001). GPC1, GPC4 and GPC6 were not present in any case.
Conclusion: Our results evidence a dysregulation in the glypicans in BM-MSCs of OA patients and, specially, during osteogenic differentiation. NOTUM, extracellular negative regulator of the WNT/β-catenine signaling pathway, is decreased at protein level in OA patients, despite the fact that gene expression is elevated. Thus, our data confirm the differences in expression in NOTUM and Glypicans between OA patients and healthy controls. Further studies are needed proposing these molecules, specially NOTUM, as an effective treatment of the disease.
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Disclosure of Interests: None Declared.
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POS0410 **A BIOPSYCHOSOCIAL APPROACH TO PHENOTYPE KNEE OSTEOARTHRITIS PATIENTS AWAITING TOTAL KNEE ARTHROPLASTY: A CROSS-SECTIONAL STUDY**

Keywords: Pain, Osteoarthritis

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Background: Knee osteoarthritis (KOA) is a heterogenous disease, meaning individuals can present with various signs and symptoms related to different biopsychosocial (BPS) factors [1,2]. Several phenotypes can as such be expected. Phenotyping KOA patients, specifically those awaiting total knee arthroplasty (TKA), could be relevant, because a substantial part of patients (20%) reports chronic post-TKA pain [3]. Various preoperative phenotypic factors related to domains of the BPS model have been described, but consensus and a classification of patients based on these factors is still lacking [4–7].
Objectives: The aim of this exploratory study is to identify phenotypes based on BPS related factors in KOA patients awaiting TKA.
Methods: Participants were included if they were diagnosed with KOA and waiting for TKA surgery in one of the four participating hospitals in Belgium and the Netherlands. A cross-sectional latent profile analysis was conducted in MPlus [8] containing the grade of KOA before TKA surgery (structural variable); body mass index and glycated hemoglobin value (metabolic variables); isometric strength of m. Quadriceps and m. Hamstrings of the affected leg, proprioceptive accuracy of the affected leg, and physical function (functional variables); pain intensity scores and symptoms related to altered somatosensory processing (pain-related variables); pain catastrophizing, depression, anxiety symptoms, expectations and satisfaction (psychological variables); and work and education level (social variables). Data were checked for multicollinearity and multivariate outliers. The ideal model was chosen based on qualitative evaluation, goodness of fit and classification uncertainty.
Results: 224 participants were included of which 109 women (65.19 +/- 8.18 years old) and 108 men (66.92 +/- 7.18 years old). A model with 2 phenotypes was found to be most appropriate. Both phenotypes differed in 13 out of 19 continuous variables. Phenotype 1 (72% of all participants) was characterized by scoring better on at least one of all metabolic, functional, psychological and pain-related continuous variables compared to phenotype 2 (28% of all participants), except for glycated hemoglobin value, proprioception, expectations, and widespread temporal summation and conditioned pain modulation (part of somatosensory processing variables). Concerning categorical variables, phenotype 1 (72%) was characterized by having a lower probability to have a Kellgren & Lawrence (K&L) scale 2 compared with patients in phenotype 2 (28%). The probabilities of the other categorical variables did not differ between the two phenotypes.
Conclusion: A model with 2 phenotypes in KOA patients awaiting TKA appeared the most appropriate, which confirmed the existence of a group that experiences disturbed somatosensory processing signs in combination with worse results on psychological (pain catastrophizing, fear and depression), functional (strength and physical function), structural (higher possibility to have a K&L grade 2 compared to the other phenotype) and metabolic factors (body mass index), and a group that does not present this disruption in combination with better results on the aforementioned BPS factors. Further research is necessary and should also investigate if different phenotypes react differently regarding treatment outcome after TKA.
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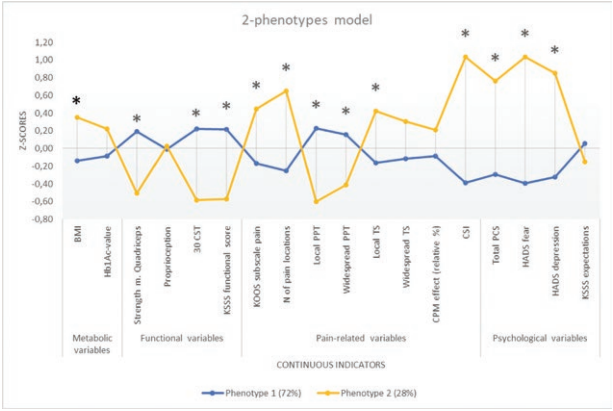


Figure 1.

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POS0411

PROFILING THE HISTONE LANDSCAPE IN OSTEOARTHRITIS: ENRICHMENT OF HISTONE VARIANT H3.3 AND ITS ASSOCIATED POST-TRANSLATIONAL MODIFICATIONS

Keywords: Genetics/Epigenetics, Osteoarthritis, Cartilage

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Background: Nucleosomes, the basic structural unit of chromatin, are composed of DNA wrapped around an octameric core of histone proteins. The latter is usually comprised by canonical histones H2A, H2B, H3 and H4[1]. These can be replaced by histone variants, which provide structural and functional changes to the nucleosome[2]. Histones are prone to undergo post-translational modifications (PTMs) that can modify chromatin conformation to induce changes in gene expression[3]. Recent evidence supports that epigenetic mechanisms, such as DNA methylation and non-coding RNA modifications, are involved in the pathogenesis of osteoarthritis (OA). Nevertheless, histone modifications mainly remain an unexplored epigenetic mechanism in OA.
Objectives: The aim of the present study was to identify, characterize and compare the histone profile in human articular cartilage samples from normal (N) and OA patients to provide novel insights into the role of histones in the development of OA.
Methods: Histones were extracted from 3 N and 3 OA cartilage samples following a protocol based on acid extraction previously described by our group. Prior to mass spectrometry (MS) analysis, samples were reduced with dithiothreitol and alkylated with iodoacetamide. After an overnight digestion with trypsin, peptides were desalted via StageTips. Samples were injected on a nanoElute LC coupled to a high-resolution timsTOF (Bruker). Peptides were analyzed in DDA mode with PASEF enabled. Raw data were processed using PEAKS Studio 10.6. software against the Human UniProtKB/Swiss-Prot database. Search parameters were: trypsin digestion, one missed cleavage allowed, 15.0 ppm parent mass tolerance, 0.05 Da fragment mass tolerance and carbamidomethylation as fixed modification. To identify and quantify the most studied biological modifications, "PTM" and "Label-free" modules from PEAKS were employed.
Results: Our histone extraction protocol successfully enriched the samples for subsequent MS analysis. The most detected PTMs are among the most studied, including methylation, acetylation, ubiquitination, phosphorylation, deamidation, biotinylation, citrullination, and ADP-ribosylation. PTMs were found in core histones H2A, H2B, H3, H4 and linker histone H1. Moreover, PTMs were detected in some of their variants. Strikingly, we found that the histone variant H3.3 is significantly increased in OA cartilage compared to N cartilage (2.67×104 ± 9.56×103 vs. 3.11×103 ± 1.71×103) (Figure 1 A). Further H3.3 analysis showed three differentially abundant PTMs between OA and N (Figure 1 B). Acetylation of lysine 18 (K18ac) was more abundant in N cartilage. Monomethylation of K79 (K79me1) was upregulated in OA samples. Likewise, dimethylation of K36 (K36me2) was also more abundant in OA cartilage.
Conclusion: The histone variant H3.3, which associates with decondensed states of chromatin and transcriptionally active sites, is upregulated in human OA cartilage. Furthermore, we identified three H3.3-associated PTMs that are differentially expressed in OA and N cartilage. These data provide new insights into the epigenetic landscape of OA and could contribute to the search for novel therapeutic targets to treat the disease.

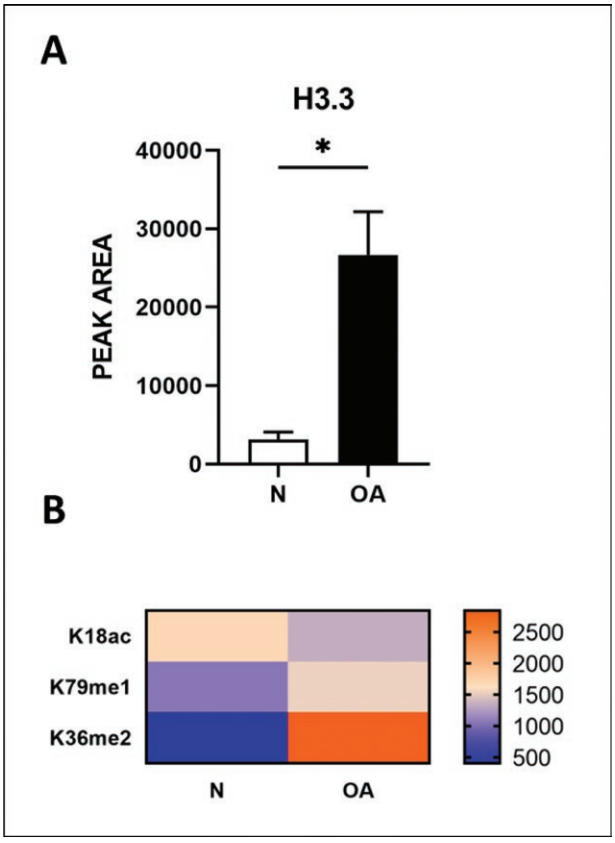


Figure 1. (A) Histone variant H3.3 abundance in N *vs* OA. Data were analyzed using Student's t-test and plotted as mean ± SEM. *p <0.05. Log2 fold change >1 or <-1. (B) Heatmap of histone variant H3.3 PTMs in N *vs* OA.

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POS0412

INTRA-ARTICULAR INJECTION OF STIGMASTEROL LOADED NANOPARTICLES IS EFFECTIVE IN INHIBITING JOINTS DESTRUCTION IN OSTEOARTHRITIS RAT MODEL

Keywords: Animal models, Osteoarthritis, Cartilage

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Background: Stigmasterol is the most abundant plant sterols and its chemical structure is very close to cholesterol. Stigmaterol inhibits pro-inflammatory and matrix degradative mediators typically involved in cartilage degradation through inhibition of the nuclear factor kappa-B (NF-κB) pathway and attenuates chondrocyte injury induced by interleukin-1β (IL-1β). Mesoporous silica nanomaterials (MSNs) have been proven to be promising nanoparticles due to their superior loading capability, multitudinous functionalization, and biocompatibility. Since

osteoarthritis (OA) is mainly developed in weight bearing or overused joints, the locally sustained therapy using nanoparticles is effective for targeting inflammatory component of OA.

Objectives: This study aimed to investigate the effects of intra-articular injection of rebamipide loaded MSNs in OA rat model.

Methods: We modified the surface of MSNs using tannic acid and anchor the stigmasterol that allow the sustained release of stigmasterol from nanoparticles. In vitro, lipopolysaccharide induced RAW cell were used to investigate the cytotoxicity and anti-inflammatory effect of stigmasterol-loaded MSNs. In vivo, monosodium iodoacetate (MIA)-induced OA rats were divided into five groups, consisting of healthy control rats and rats injected with MIA alone or in combination with MSNs, stigmasterol (10 μg)/MSNs, stigmasterol (50 μg)/MSNs. The levels of IL-6, matrix metalloproteinase-3 (MMP-3), and tumor necrosis factor- α (TNF-α) measured periodically and the micro-computed tomography (CT) and histological examination was performed at eight week.

Results: In vitro, stigmasterol/MSNs dose-dependently suppressed the levels of pro-inflammatory mediators, including IL-6, MMP-3 and TNF-α. In vivo, the levels of pro-inflammatory components most markedly decreased in the intra-articularly injected stigmasterol (50 μg)/MSNs group compared to other groups. Micro-CT images and histological evaluations showed that the intra-articular injection of stigmasterol/MSNs also inhibited cartilage degeneration dose-dependently.

Conclusion: Using a chemically induced rat model of OA, intra-articular delivery of stigmasterol was associated with decreased local and systemic inflammatory response decreased joint degradation and arthritic progression.

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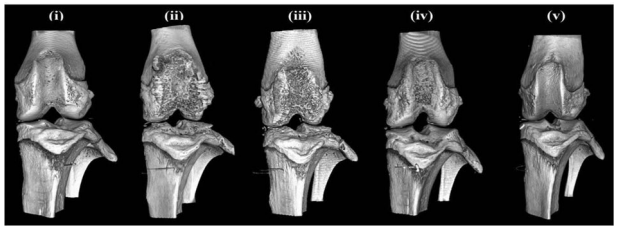


Figure 1. Micro-CT images of the rat knee joint at the 8th weeks after treatments of (i) control, (ii) MIA, (iii) MSNs, (iv) stigmasterol(10 μg)/MSNs, and (v) stigmasterol(50 μg)/MSNs.

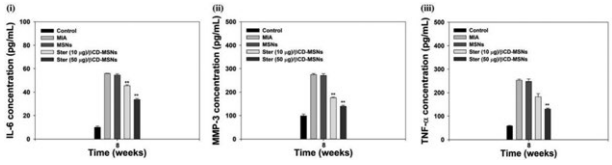


Figure 2. The levels of (i) IL-6, (ii) MMP-3 and (iii) TNF-α at serum from MIA-induced OA rat model at 8th weeks after MSNs, stigmasterol(10 μg)/MSNs and stigmasterol(50 μg)/MSNs treatment.

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Disclosure of Interests: None Declared.
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POS0413 SEX DIFFERENCES IN A MURINE MODEL OF OSTEOARTHRITIS

Keywords: Pain, Osteoarthritis, Animal models

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Background: Pain is the leading cause of disability in osteoarthritis (OA), but the correlations between structural changes of the joint and functional changes in pain-related outcomes remains poorly understood. Animal models of OA have poor translational outputs to improve pain management in OA[1,2]. Moreover, several studies demonstrate a higher prevalence of chronic pain in the female OA population[3,4] and sex differences that can give rise to distinct pain mechanisms in male and female rodents with OA[5].

Objectives: We aim to define the translational value of a murine model of surgically-induced OA with meniscal/ligamentous injury (MLI), in terms of the progressive nature of joint degeneration, temporal delay in development of chronic pain following joint damage and potential sex differences.

Methods: *Model*: OA was induced in 10-week-old C57BL/6J mice under isoflurane anaesthesia with resection of the medial collateral ligament (MCL), meniscotibial ligament and removal of the medial meniscus. *Behaviour*: Sensory thresholds were assessed using the up-down von Frey, hindlimb capacitance, Hargreaves', hotplate and dry ice tests. Affective behaviours were measured using hotplate and open field assay. *In vivo electrophysiology*: Extracellular recordings of L4 dorsal horn neurones was performed in anesthetised mice. Mechanically and thermally evoked action potentials were quantified. *MicroCT*: Bone mineral density was measured along the growth plate and BoneJ was used for microarchitecture analysis to determine 3D geometric parameters. *Histological OA scoring and immunohistochemistry*: Coronal sequential paraffin sections were stained with Safranin-O for OA severity scoring using the Osteoarthritis Research Society International grading system. Additional knee sections were stained for neo-innervation using anti-PGP9.5. *RNASeq:* RNA was extracted from L3-L5 ipsilateral DRGs and differentially expressed transcripts generated by GeneWiz.

Results: We observed progressive development of persistent mechanical and cold hypersensitivity in MLI mice compared to Sham controls. We also observed contralateral hypersensitivity, indicative of nociplastic pain. Female mice expressed an earlier onset and greater extent of hypersensitivity compared to male mice. The temporal delay in the expression of hindlimb hypersensitivity correlates with a loss of cartilage integrity measured by OARSI scoring of the knee joint in both males and females. Affective behaviours are also correlated with changes in sensory thresholds, indicating emotional processing of nociceptive inputs form the injured knee. We observed greater PGP9.5 staining in female MLI mice and key transcriptional changes in DRG neurons.

Conclusion: Our data demonstrates that the MLI model reproduces clinical features of nociplastic pain and cartilage loss in OA. We identify structural changes in the knee joint that correlate with pain behaviour, as well as sex differences in knee innervation, transcriptomic profiles of primary sensory neurons and pain behaviour that is exacerbated in female mice, informing on sex specific pain mechanisms. This establishes the use of MLI surgery as a clinically relevant mouse model for OA pain.

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Disclosure of Interests: None Declared.
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POS0414 ASSOCIATIONS BETWEEN BONE MARROW ADIPOCYTE SIZE, BONE REMODELLING AND BODY MASS INDEX IN PATIENTS WITH BASE OF THE THUMB OSTEOARTHRITIS

Keywords: Bone diseases, Osteoarthritis, Descriptive studies

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Background: Subchondral bone sclerosis, osteophyte formation and bone marrow lesions are radiographic hallmarks of base of the thumb osteoarthritis (CMC-1 OA)[1]. High body mass index (BMI) and obesity are major risk factors for CMC-1 OA [2]. Adipose tissue-derived systemic factors, such as lipids and adipokines, have been proposed as mediators of such increased risk at a non-weight bearing joint. In support of this hypothesis, alterations in systemic lipid levels have been found to partially associate with the severity of hand OA [3]. It

is unknown whether subchondral marrow adipose tissue contributes to development and progression of CMC-1 OA.
Objectives: To determine whether bone marrow adipocyte (BMAd) size, as a surrogate marker of adipocyte lipolysis and (dys)function, differed as a function of the extent of subchondral bone remodelling and BMI in CMC-1 OA.
Methods: Trapezium bone resections were harvested from 14 consecutive CMC-1 OA patients (9 female, 63±11 years, 26±6 kg/m^2) undergoing arthroplasty. BMAd size, osteoblast numbers and OA severity were determined by histomorphometry. Expression of the lipolytic enzyme monoacylglycerol lipase (MGLL) on bone marrow-resident cells was assessed by immunohistochemistry.
Results: Eight out of fourteen specimens displayed regions of increased bone remodelling and osteoblast numbers, which were classified by histology as subchondral sclerosis (n=6) and central osteophyte formation (n=2). BMAd size was significantly reduced (p=0.02) in the remodelling (839±319 µm^2) compared with non-remodelling regions (1438±578 µm^2), independent of OA severity. BMAd size was positively correlated with BMI (r=0.63, p=0.03), but in non-remodelling regions only. MGLL was differentially expressed both in terms of quantity and cell type in non-remodelling and remodelling regions (Figure 1). Surprisingly, MGLL was strongly expressed by osteoblasts and blood vessels rather than mature BMAd in remodelling regions.
Conclusion: Collectively, these data suggest that BMAd properties in the CMC-1 joint may be BMI-dependent. Increased lipolytic activity in subchondral bone marrow adipose tissue may be fueling pathologic bone formation in CMC-1 OA.
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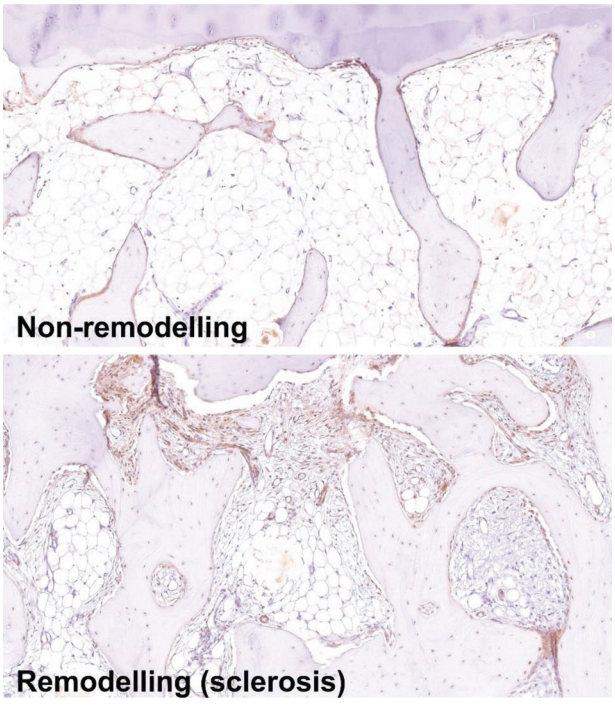


Figure 1.

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Disclosure of Interests: None Declared.
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POS0415 **ADIPOCYTE-OSTEOBLAST CROSSTALK IN SUBCHONDRAL BONE MARROW: NEW THERAPEUTIC TARGET IN OSTEOARTHRITIS**

Keywords: Bone diseases, Biomarkers, Osteoarthritis

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Background: Subchondral sclerosis and bone marrow adipose tissue (BMAT) lesions are radiographic hallmarks of knee osteoarthritis (OA). Energy supply through lipolysis of bone marrow adipocytes (BMAd) has recently been established as a crucial mechanism to fuel bone regeneration and maintain bone mass during energy deficits. It is unknown whether subchondral BMAd may contribute to subchondral sclerosis in OA through a similar mechanism.
Objectives: The goal of this study was to determine whether BMAd-derived factors differed as a function of the extent of subchondral sclerosis and to evaluate effects of lipolysis-modulating treatments in a human knee OA explant model.
Methods: Non-sclerotic (NS) and sclerotic (SC) osteochondral tissue chips (n=48 each) were explanted from tibial plateaus and treated with an activator (forskolin) or inhibitor (pioglitazone, metformin) of lipolysis. Secreted free fatty acids (FFA), triglycerides (TGL), adiponectin, IL-6 and ALP activity were measured in supernatants.
Results: Adiponectin (1.6-fold), TGL (1.7-fold) and ALP activity (6.7-fold) levels were increased in SC compared with donor-matched NS tissues (p<0.05). Interestingly, FFA (r=0.60) and adiponectin (r=0.76) were positively correlated with ALP activity (p<0.01) in SC tissues only (Figure 1). Modulation of lipolysis affected secretion of FFA and TGL (p<0.01), but not adiponectin, in NS tissues only. ALP activity remained unaffected by any treatment in NS or SC tissues. Metformin treatment reduced IL-6 secretion 4-fold (p<0.05) in SC tissues.
Conclusion: Collectively these data support the new paradigm that BMAd-derived factors may play a previously unrecognized role in regulating pathological bone remodelling in human OA.

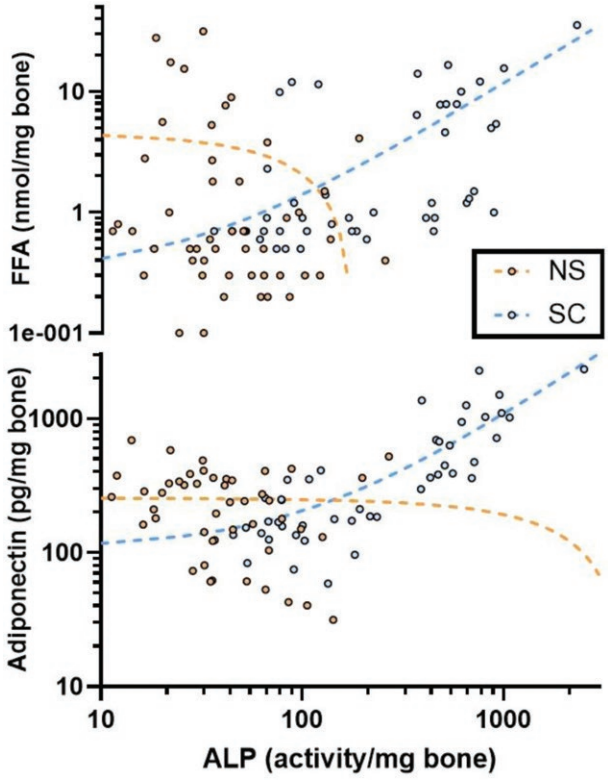


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Spine, mechanical musculoskeletal problems, local soft tissue disorders

POS0416 **DISTINCT DEGENERATION MECHANISMS IN INTERVERTEBRAL DISCS ADJACENT TO MODIC CHANGES**

Keywords: -omics

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Background: Modic changes (MC) are painful vertebral bone marrow lesions and are often found in patients with chronic low back pain. The adjacent intervertebral disc (IVD) seems to play an important role: the rapidly degrading disc stands in an inflammatory cross-talk with the MC bone marrow and MC develop almost always simultaneously cranial and caudal to a degenerated IVDs. Few studies have investigated expression of inflammatory cytokines and proteases expressed by IVD cells adjacent to MC, however, how this affects the ECM degeneration has not been determined.
Objectives: The aim of this study was to identify MC-specific mechanisms in degenerated discs. We hypothesize that the 'Modic discs' have a distinct disc matrix degradome.
Methods: Degenerated lumbar IVDs from MC1 (n=26), MC2 (n=20) and non-MC (n=19) levels from gender and age matched patients undergoing spinal fusion surgery were collected. Degradome was measured with N-terminal amine isotopic labeling of substrates (TAILS) liquid chromatography tandem mass spectrometry (LC-MS/MS). TAILS allows to identify degraded proteins by detecting de novo N-terminal peptides. Sequence motifs were calculated using TwoSample Logo web application to identify significantly enriched amino acids around the cleavage site of the top 50 upregulated peptides. Since proteases have preferences for amino acid sequences, different sequence motifs can indicate activity of different proteases. Proteases were matched to cleavage sites of the top 50 enriched MC1 and MC2 peptides using TopFINDer database.
Results: Mean degree of disc degeneration as measured by Pfirrmann grade was not significantly different between all groups (MC1: 3.8 ± 0.9, MC2: 4.2 ± 0.6, non-MC: 3.6 ± 0.8). A total of 487 (MC1), 419 (MC2), and 404 (non-MC) different protein fragments were detected of which 21.0%, 12.2% and 9.4% were unique to MC1, MC2, and non-MC, respectively (Figure 1a). Comparing MC1 to non-MC discs, the degradome was more complex with a variety of ECM fragments enriched (e.g. type II collagen, fibrinogen), while fragments of type I collagen, clusterin, and fibronectin were depleted (Figure 1b). In MC2 discs, mainly fibronectin and clusterin were enriched, while type I collagen was depleted (Figure 1b). Sequence motifs show unique cleavage preferences for each group (Figure 1c) indicating activity of different proteases in MC1 and MC2 discs. TopFinder identified neutrophil elastase as an important protease in all groups targeting cleavage of different proteins. In MC1 and MC2 IVDs kallikrein 3 as well as MMP9 and MMP2 are associated with found cleavage products. Finally, in MC1 TopFINDer uniquely identifies multiple fragments created by MMP2, MMP7, MMP12, MMP13 or cathepsin B.
Conclusion: MC1, MC2 and non-MC discs have different ECM degradomes that may be caused by the activity of different proteases. Differences in disc degeneration mechanisms and in the type and amount of bioactive ECM fragments explain why not all degenerating discs lead to adjacent MCs.

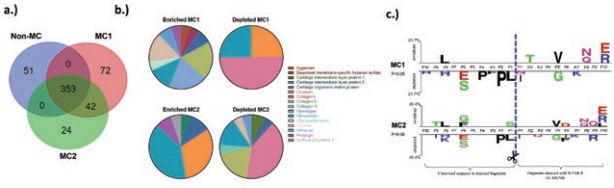


Fig. 1: a.) Number of peptides identified in each group b.) Respective proteins of which the 50 most enriched peptides (left) and 50 most depleted peptides (right) per group derive from. c.) Sequence logos to represent difference in fragmentation pattern of MC1, MC2 and non-MC discs. Unique amino acids significantly ($p<0.05$) enriched around cleavage site P1'/P1 (dotted line) compared to unique non-MC disc peptides.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Tamara Mengis: None declared, Irina Heggli: None declared, Nick Herger: None declared, Borbala Aradi-Vegh: None declared, Bernd Roschitzki: None declared, Jonas Grossmann: None declared, Florian Brunner: None declared, Roy Marcus: None declared, Mazda Farshad: None declared, Oliver Distler Speakers bureau: Bayer, Boehringer Ingelheim, Janssen, Medscape, Consultant of: 4P-Pharma, Abbvie, Acceleron, Alcimed, Altavant Sciences, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos, Glenmark, Horizon, Inventiva, Kymera, Lupin, Miltenyi Biotec, Mitsubishi Tanabe, MSD, Novartis, Pfizer, Prometheus, Redxpharna, Roivant, Sanofi and Topadur, Grant/research support from: BI, Kymera, Mitsubishi Tanabe, Stefan Dudli: None declared.
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POS0417 ACTIVATED NEUTROPHILS DEGRADE CARTILAGE ENDPLATES

Keywords: Cartilage, -omics, Innate immunity

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Background: Modic type 1 changes (MC1) are painful vertebral bone marrow lesions often found in patients with chronic low back pain. Damage of the endplate associates with MC1, is a risk factor for MC1 progression, and associates with pain. Recent evidence suggests a role of MC bone marrow neutrophils in endplate damage.
Objectives: The aim of this study was 1) to show that MC1 bone marrow neutrophils are activated and 2) to show that activated blood neutrophils degrade cartilage endplates (CEPs).
Methods: From MC1 patients undergoing lumbar spinal fusion, MC1 and intra-patient control bone marrow neutrophils ($CD45^+CD66b^+$) were isolated from bone marrow aspirates by cell sorting. Bulk RNA sequencing was performed (n = 5+5), differentially expressed genes (DEGs) were identified, and enrichment analysis was performed. In addition, neutrophil activation was assessed as CD66b expression by flow cytometry (n = 3+3). To assess the effect of activated neutrophils on CEP degradation, a neutrophil-mediated CEP damage model was established. Blood neutrophils were isolated from one donor and exposed to lumbar CEPs. A lumbar CEP was collected from six patients undergoing spinal fusion. From each CEP, three punch biopsies (ø=4-mm) were taken and halved. The six CEP biopsy halves per patient (1A,1B; 2A, 2B; 3A, 3B) were exposed for 18 h at 37 °C to: 1A) 0.75 U/ml collagenase P (positive control) and 1B) Hanks balanced salt solution (negative control); 2A) conditioned medium from 25 mio/ml activated neutrophils (100 nM PMA, 3 h, 37 °C) and 2B) conditioned medium from 25 mio/ml non-activated neutrophils; 3A) conditioned medium from 12.5 mio/ml activated neutrophils (100 nM PMA, 3 h, 37 °C) and 3B) conditioned medium from 12.5 mio/ml non-activated neutrophils. Exposure supernatant and CEP tissues were assayed for sulphated glycosaminoglycans (sGAG) and hydroxyproline (as measure for total collagen). Release of sGAG and hydroxyproline from condition 1A, 2A, and 3A was normalized to condition 1B, 2B and 3B, respectively. Relative release was tested against null hypothesis (μ0 = 100%) using a one sample t-test.
Results: 185 genes were differentially expressed between MC1 and control vertebral bone marrow neutrophils. Enrichment analysis revealed an activated pro-inflammatory transcriptome (**Figure 1a**). Flow cytometric analysis confirmed neutrophil activation on protein level (measured as % of $CD66^{high}$) in MC1 (control: 43.1% ± 15.7%, MC1: 54.1% ± 16.7%, p = 0.018) (**Figure 1b**).
Exposure of CEP tissues to conditioned medium from activated neutrophils significantly increased the release of sGAG from the CEP tissues in a dose-dependent manner (25 mio/ml: 380.1% ± 177%, p = 0.012; 12.5 mio/ml: 123.7% ± 22.3%, p = 0.048, positive control: 545.0 % ± 302.8 %, p = 0.016) (**Figure 1c**) but there was no significant hydroxyproline release (not shown).
Our data shows that neutrophils in MC1 bone marrow are activated and activated blood neutrophils degrade CEPs. Hence, neutrophils in MC1 bone marrow might promote and exacerbate CEP damage. Therefore, MC1 are not just reactive changes but can drive CEP damage that enhances a vicious inflammatory crosstalk with the adjacent disc.

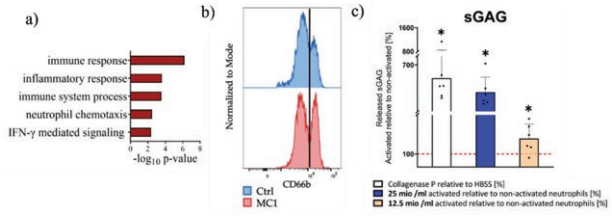


Figure 1. (a) Top 5 upregulated biological processes in MC1 bone marrow neutrophils (b) Representative flow cytometry image c) Relative sGAG released from CEP tissues. * P < 0.05.

Conclusion: We identified neutrophils as a potentially important player in MC1. Therefore, the present findings could have implications for treatment strategies to mitigate CEP damage in MC1.
REFERENCES: NIL.
Acknowledgements: We thank the FOREUM Foundation for supporting this project.

Disclosure of Interests: Irina Heggli: None declared, Mohamed Habib: None declared, Justin Scheer: None declared, Nick Herger: None declared, Tamara Mengis: None declared, Christoph Laux: None declared, Florian Wanivenhaus: None declared, Jose Miguel Spirig: None declared, Michael Betz: None declared, Mazda Farshad: None declared, Oliver Distler Speakers bureau: Bayer, Boehringer Ingelheim, Janssen, Medscape, Consultant of: 4P-Pharma, Abbvie, Acceleron, Alcimed, Altavant Siences, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos, Glenmark, Horizon, Inventiva, Kymera, Lupin, Miltenyi Biotec, Mitsubishi Tanabe, MSD, Novartis, Pfizer, Prometheus, Redxpharna, Roivant, Sanofi and Topadur, Grant/research support from: Kymera, Mitsubishi Tanabe, Boehringer Ingelheim, Aaron Fields: None declared, Stefan Dudli: None declared.
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Bone diseases, aetiology, pathology and animal models

POS0418 SREBP2 REGULATES OSTEOCLAST DIFFERENTIATION AND PROTECTS MICE FROM INFLAMMATORY BONE LOSS

Keywords: Inflammatory arthritides, Bone diseases, Animal models

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Background: Bone erosion is a key clinical feature of inflammatory osteolysis. Emerging evidence shows a link between biological lipids and the pathogenesis of bone loss in inflammatory conditions. Osteoclasts are the sole bone resorbing cells and are responsible for bone erosion. Sterol regulatory element binding protein 2 (SREBP2) is a key transcription factor for cholesterol biosynthesis and a sensor for intracellular lipids.
Objectives: We aim to test the role of SREBP2 in physiological and pathological bone resorption.
Methods: Lysozyme M promoter-driven Cre transgene on the C57/BL6 background mice and $Srebp^{flox/flox}$ mice were crossed to generate $Srebp2^{fl/fl}$LysM-Cre (referred to as $SREBP2^{\Delta M}$ mice). Micro-computed tomography (μCT) analysis was performed to analyze bone volume and architecture. Mouse bone marrow-derived macrophages were cultured with receptor activator of nuclear factor-kappa beta ligand (RANKL) and macrophage colony stimulating factor (M-CSF)-containing conditioned media in α-minimum essential medium supplemented with 10% fetal bovine serum for three days to generate osteoclasts.
For the supracalvarial osteolysis model, recombinant human tumor necrosis factor-α (TNFα, 40μg/kg) was injected daily into calvarial periosteum in 12-week-old female control and $SREBP2^{\Delta M}$ mice for five consecutive days.
Results: μCT analysis of the femurs of 12-week-old female mice revealed a significant decrease in trabecular bone mass of $SREBP2^{\Delta M}$ mice relative to control mice. In contrast, cortical parameters, including cortical bone volume/tissue volume (BV/TV) and porosity, were comparable between the two groups. Bone histomorphometric analysis of the femur indicated that the trabecular osteoclast numbers, surface area, and bone resorption activity were significantly higher in $SREBP2^{\Delta M}$ mice than in control mice. However, there was no difference in mineral apposition rate and bone formation rate between $SREBP2^{\Delta M}$ mice and control mice. Consistent with in vivo findings, RANKL-induced in vitro osteoclast differentiation was accelerated in SREBP2-deficient cells compared to control cells, as measured by the formation of TRAP+ multinucleated cells. Moreover, in TNFα and RANKL co-treatment settings, SREBP2 deficiency enhanced TNFα-mediated enhancement of osteoclastogenesis compared to control cells. In the supracalvarial osteolysis model, TNFα administration over calvaria increased bone resorption pit area in $SREBP2^{\Delta M}$ mice compared to littermate control mice. μCT analysis revealed a significant decrease in calvaria bone volume/tissue volume and apparent density of $SREBP2^{\Delta M}$ mice compared to control mice. The histomorphometric analysis demonstrated significant increases in trabecular osteoclast numbers and surface area in $SREBP2^{\Delta M}$ mice relative to littermate control mice, suggesting that inflammatory osteolysis is enhanced under SREBP2 deficiency.
Conclusion: Using the myeloid-specific SREBP2-deficient model, we demonstrated that SREBP2 negatively regulates in vitro and in vivo osteoclastogenesis. SREBP2-deficient mice exhibit an osteoporotic phenotype. SREBP2 deficiency exacerbates TNFα-induced osteolysis in mice, supporting a protective role of SREBP2 in inflammation-associated pathological bone loss.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0419 THE ROLE OF OROSOMUCOID 2 IN THE REGULATION OF BONE REMODELING BY INHIBITING OSTEOCLASTOGENESIS AND PROMOTING OSTEOGENESIS

Keywords: Osteoporosis, Biomarkers, Animal models

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Background: Orosomucoid (ORM) is one of the acute phase reactant protein family and is expressed in hepatocytes and secreted into plasma under stress conditions such as tissue injury, infection, and inflammation. Three types of ORM are known to date (ORM1, 2 and 3), and ORM2 is mainly expressed in bone marrow cells. ORM2 has only some studies on hepatic metabolism, inflammation and immune regulation, and no studies on bone metabolism have been reported.
Objectives: The aim of this study is to reveal the role of ORM2 in the differentiation and function of osteoclasts and osteoblasts.
Methods: To determine the effect of ORM2 on RANKL-induced osteoclast differentiation and function, we performed TRAP staining, F-actin stating, and bone resorbing assay using ORM2 recombinant protein or ORM2 siRNA. Also, the effect of ORM2 on osteogenesis was confirmed by ALP and ARS assay. The intracellular mechanisms responsible for the dual regulation of osteoclastogenesis and osteogenesis of ORM2 were revealed by western blotting and quantitative real-time RT-PCR.
Results: We found that ORM2 is a potential target for osteoporosis therapeutics, as treatment with this agent enhances osteoblast differentiation and bone growth and suppresses osteoclast differentiation and bone resorption by performing gain- and loss-of-function studies. During ORM2-mediated regulation of osteoclastogenesis, phosphorylation of early signal transducers such as p38, JNK, Akt, IκB, PLCγ2, and Btk was affected, which in turn altered the mRNA and protein levels of c-Fos and NFATc1. ORM2 also increased ALP, Alizarin Red-mineralization activity, and the expression of osteoblastogenic gene markers, such as Runx2, osteocalcin (OCN), and ALP in mouse calvarial primary osteoblasts, and activated the p38-Runx2 pathway, which enhanced osteoblast differentiation.
Conclusion: we suggest that ORM2 may be a promising candidate for gene therapy for bone metabolic diseases, and further serve as a potentially important biomarker in the field of bone disease diagnosis.
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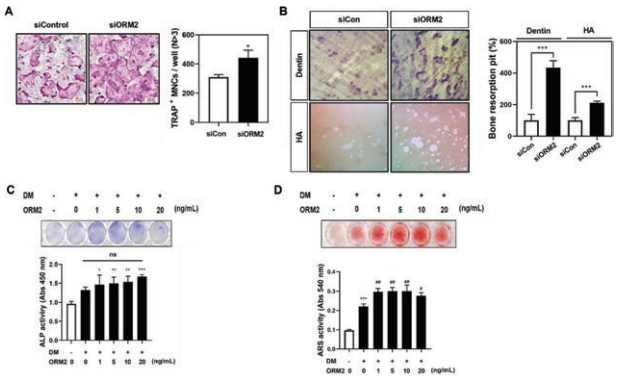


Figure 1. The effect of ORM2 in RANKL-induced osteoclast differentiation and osteoblast differentiation. (A) BMMs transfected with negative control siRNA (siControl) or siRNA against ORM2 (siORM2) were cultured with M-CSF (30 ng/mL) and the indicated concentrations of RANKL for TRAP staining. The TRAP-positive MNCs were counted as mature osteoclasts. $^{*}P < 0.05$ versus siControl group. (B) Mature osteoclasts transfected with siControl and siORM2 were cultured in a hydroxyapatite-coated plate and dentin slice to detect resorption pits. The number of TRAP-positive MNCs and relative resorption areas in the hydroxyapatite-coated plate and dentin slice were quantified. $^{***}P < 0.001$ versus siControl group. (C and D) Osteoblasts treated with the indicated concentration of recombinant protein were cultured for seven days to perform ALP staining and activity assay. The calcium deposits for matrix mineralization were measured by ARS staining after 21 days of culture and the intensity of staining was quantified with CPC.

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Disclosure of Interests: None Declared.
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POS0420 GENERATION OF A HUMAN 3D IN VITRO BONE MODEL THAT MIMICS GLUCOCORTICOID-INDUCED OSTEOPOROSIS

Keywords: Bone diseases, Osteoporosis

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Background: Osteoporosis is a bone disease characterized by low bone mass and changes in bone architecture, leading to pain and reduced mobility in patients. Glucocorticoid-induced osteoporosis (GIOP) is the best known form of secondary osteoporosis. Glucocorticoids (GC) are commonly used to treat inflammation, such as in rheumatic diseases. However, GC use can have a negative effect on the skeletal system and lead to osteoporosis.
Objectives: (i) Establishing and characterizing a human *in vitro* bone model consisting of osteoblasts and osteoclasts embedded in β-TCP ("healthy" bone model), (ii) treatment with dexamethasone to induce GIOP ("osteoporotic" bone model) and (iii) using this model as a testing platform for the treatment of osteoporosis.
Methods: Our model includes osteoblasts and osteoclasts, which are mainly responsible for bone remodeling. We defined an osteoclast differentiation protocol using low-attachment plates and cultured the cells for 21 days in αMEM medium, 5% FCS, 5% human AB serum, 2 mmol L-glutamine, 25 ng/ml M-CSF, and 50 ng/ml RANKL. To provide the basic scaffold for the structure of the "healthy" bone model, mesenchymal stromal cells (MSCs) were seeded on β-tricalcium phosphate (β-TCP). This bone model, consisting of differentiated osteogenic cells, was fully characterized in our previous work [1].
Results: The multinuclearity, typical ß-actin ring formation, cellular activity by TRAP staining and functionality in resorption assays proved functional osteoclasts. Our protocol allowed us to passage these cells without cell loss or loss of function. To establish the previously "healthy" (i.e., untreated) bone model, we seeded osteoclasts onto a pre-seeded β-TCP construct and cultured the co-culture for 7 days. We then analyzed the supernatant and detected marked secretion of RANKL, MMP-9, and free phosphate. This indicates the functionality of both osteoclasts and osteoblasts in our 3D model. Subsequently, the healthy model will be transferred to the osteoporosis-simulating model where treatment with dexamethasone will be applied. Once established, we plan to use the model we have developed for in vitro preclinical trials to test marketed drugs.
Conclusion: Ultimately, we will obtain an *in vitro* 3D co-culture of osteoblasts/osteoclasts simulating human native bone, which will be treated with dexamethasone to mimic key aspects of GIOP *in vitro*.
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POS0421 GLUCOSE TRANSPORTER 1 REGULATES MECHANICAL STRESS-ACTIVATED SUBCHONDRAL BONE FORMATION VIA THE SIGNAL TRANSDUCTION NETWORK OF CELLULAR ENERGY SENSOR, NAD+-DEPENDENT DEACETYLASE (SIRTUIN 1) AND OSTEOGENIC TRANSCRIPTION FACTOR, RUNT-RELATED TRANSCRIPTION FACTOR 2 (RUNX2), IN SUBCHONDRAL BONE TISSUE

Keywords: Cartilage, Cell biology, Osteoarthritis

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Background: Mechanical stress is an important factor affecting bone and cartilage tissue homeostasis in osteoarthritis (OA). We focused on the interaction among mechanical stress, glucose uptake via glucose transporter 1 (Glut1) and the cellular energy sensor sirtuin 1 (SIRT1) in energy metabolism, since it has been recognized that SIRT1, an NAD+-dependent deacetylase, may function as a master regulator of mechanical stress response as well as cellular energy metabolism Also, it has already been demonstrated that SIRT1 regulates the activity of the osteogenic transcription factor, runt-related transcription factor 2 (Runx2).
Objectives: Purpose of this study was to determine whether mechanical force affects the expression of factors regulating energy metabolism and transcription factors controlling subchondral bone formation and ossification in OA.
Methods: Comparative analyses of the expression of Glut1, SIRT1 and Runx2 in osteoblasts and chondrocytes were performed after mechanical loading of a 3D cell–collagen sponge construct.
Results: Mechanical loading increased osteoblast activity. Mechanical loading significantly increased the expression of Glut1, significantly decreased the expression of SIRT1 and increased the expression of Runx2 in osteoblasts in comparison with non-loaded osteoblasts. Incubation with Glut1 inhibitor blocked mechanical stress-induced changes in SIRT1 and Runx2 in osteoblasts. In contrast to osteoblasts, expressions of Glut1, SIRT1 and Runx2 in chondrocytes were decreased by loading. Over loading reduced chondrocyte activity (production of proteoglycan, type II collagen).
Conclusion: Our present study indicated that mechanical stress induced upregulation of Glut1, downregulation of SIRT1, and upregulation of Runx2 in osteoblasts, but not in chondrocytes. Since SIRT1 is known to negatively regulate Runx2 activity, mechanical stress-induced downregulation of SIRT1 may lead to upregulation of Runx2, resulting in osteoblast differentiation and bone formation. Incubation with Glut1 inhibitor blocked mechanical stress-induced changes in SIRT1 and Runx2 suggesting that Glut1 is necessary to mediate the responses of SIRT1 and Runx2 to mechanical loading. These results suggest that Glut1 regulates mechanical stress-activated subchondral bone formation and ossification via the signal transduction network of cellular energy sensors, sirtuin 1 and Runx2, in OA.
REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Spondyloarthritis - aetiology, pathogenesis and animal models

POS0422 METABOLOMIC FINGERPRINT TO DISCRIMINATE REMISSION FROM ACTIVE DISEASE AND HEALTHY CONTROLS IN PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Biomarkers, Remission

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Background: Among the unmet needs in psoriatic arthritis (PsA), the discovery of molecular players and biomarkers of disease activity or clinical remission achievement, remains unsolved. Metabolomics is a valuable technology in identifying biomarkers, by the study of a set of small molecules produced by the catabolism or anabolism of an organism in response to physiological or pathological states, allowing to better understand the disease-related variations downstream of the genome and proteome.

Objectives: In this pilot study, we have compared the serum metabolomics profile of patients with psoriatic arthritis with active or clinically inactive disease state compared with healty controls, using Nuclear Magnetic Resonance Spectroscopy (^{1}H-NMR).

Methods: From a cohort of 300 PsA patients according to CASPAR criteria, we selected 30 PsA with active disease state by DAPSA > 14 score (no bDMARDs ongoing) (A), 38 patients (peripheral arthritis subset) with >1-year remission by antiTNFα assessed by DAPSA ≤ 4 (B) and 32 healthy controls (C) matching for mean age and gender ratio. The sera metabolomics profile of 100 subjects was analyzed with a Varian UNITY INOVA 500 MHz NMR spectrometer, combined with Multivariate statistical Analysis (MVA). Principal Component Analysis (PCA) and Orthogonal Partial Least-Squares Discriminant Analysis (OPLS-DA) were applied. The model's goodness was evaluated using a permutation test (Q2 intercept value <0.005).

Results: The represented OPLS-DA models (Figure 1) exhibited a clear separation between subjects with active disease (red dots) and healthy controls (green dots), and patients with active disease or clinical remission state (blue dots), indicating significant differences in the serum metabolomics profile between all compared conditions. Interestingly, the OPLS-DA model shows how the PsA patients in the remission state have a profile which does not completely overlap with healthy subjects. The validity of the OPLS-DA models was evaluated through a permutation test using 500 times (Table 1) and indicate the great statistical validity of the OPLS-DA reported models.

Conclusion: The metabolomic profile of PsA patients with different disease state and healthy subjects reveal a high grade of dissimilarity between all compared conditions: remarkably, the metabolomic profile of patients with the drug-induced clinical remission appears still different from a healthy condition, perhaps reflecting molecular modifications induced by the great response to TNFalpha inhibition sustaining the clinical remission of PsA disease. Supplementary analysis of single-spectra is ongoing to obtain a list of metabolites differentially expressed in all conditions, and on this field further explorations are needed to validate metabolomics biomarkers that can accurately and reliably measure PsA disease activity or remission achievement, as well as to identify the metabolic fingerprint of antiTNFα-treatment success.

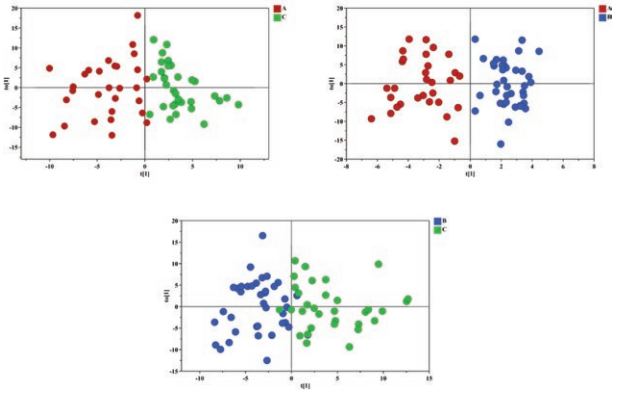


Figure 1. OPLS-DA scores plots of ^{1}H NMR spectra of sera samples. Red dots: (A) active PsA patients; blue dots: (B) remission PsA patients; green dots: (C) healthy controls.

Table 1. Parameters for OPLS-DA models

	OPLS-DA models				Permutation (500 times)*	
active PsA patients *vs* healthy controls	Components[a]	R2Xcum[b]	R2Ycum[c]	Q2cum[d]	R2 intercept	Q2 intercept
	1P+1O	0.406	0.665	0.517	0.330	-0.336
active PsA patients *vs* remission PsA patients	1P+2O	0.481	0.824	0.504	0.461	-0.424
remission PsA patients *vs* healthy controls	1P+1O	0.389	0.611	0.429	0.318	-0.331

[a]The number of Predictive and Orthogonal components used to create the statistical models.[b,c] R2X and R2Y indicated the cumulative explained fraction of the variation of the X block and Y block for the extracted components.[d] Q_2 cum values indicated cumulative predicted fraction of the variation of the Y block for the extracted components.*An Q2 intercept value less than 0.005 are indicative of a valid model.

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Disclosure of Interests: None Declared.

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POS0423 PLASMA METABOLOMIC PROFILES OF PATIENTS WITH ACTIVE PERIPHERAL PSORIATIC ARTHRITIS CAN DIFFERENTIATE TREATMENT RESPONDERS FROM FAILURES: EXPLORATORY FINDINGS FROM THE FLORA TRIAL

Keywords: -omics, Psoriatic arthritis, Gastrointestinal tract

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Background: Metabolite profiling of biofluids has an emergent role in exploring the contribution of host-microbiome interactions to the treatment response of immune-mediated arthritis.[1]

Objectives: As part of the FLORA trial (exploring the impact of gut microbiome manipulation upon response to methotrexate [MTX]),[2] we investigated plasma metabolomic profiles of adults with psoriatic arthritis (PsA) and whether they correlated with the primary trial outcome, which was clinical response to MTX (responder vs failure) following one faecal microbiota transplant (FMT) or sham transplant.

Methods: Thirty-one PsA patients with active peripheral disease, despite at least 3 months of steady-state dose MTX, were included in the 26-week, double-blind, parallel-group, 1:1 randomised, sham-controlled, superiority trial (FLORA trial; NCT03058900).[2] Patients were randomly allocated to receive either one gastroscopic-guided FMT (n = 15) or sham transplant (n = 16). Each FMT product encompassed 50 g of processed faeces obtained from one of four healthy, thoroughly screened donors. Patients continued MTX throughout the trial. The primary trial endpoint was the proportion of treatment failures through 26 weeks, defined as need for treatment escalation (in most cases instigation of TNF inhibitors) due to insufficient improvement of disease activity or disease worsening.[2] Li-Hep plasma samples were collected at baseline, week 4, 12, and 26. The metabolic profiles were measured using ^{1}H Nuclear Magnetic Resonance (NMR). We used a supervised multivariate orthogonal partial least squares-discriminant analysis (OPLS-DA) to model metabolic differences among groups.

Results: Twenty women and eleven men with a mean age of 50.7 years (SD = 13.6) and a mean swollen joint count of 7.1 (SD = 2.8) were included in the trial.[2] We were able to annotate 40 plasma metabolites in the baseline samples. No differences in baseline plasma profiles were observed between patients allocated to FMT and sham (OPLS-DA model; Q2 = -0.452, p = 1). However, the OPLS-DA analysis revealed a significant model for treatment responders (n = 19) vs failures (n = 12) among all patients, Figure 1. Correlations between metabolites and the primary trial outcome with a correlation coefficient (r) ≥0.50 are presented in Table 1. When patients were stratified for intervention type, the models continued to show significant separation (FMT arm: Q2 = 0.383, p < 0.0001; sham arm: Q2 = 0.260, p = 0.002). In both the FMT and the sham models, glucose (r = 0.67 and r = 0.63) correlated positively with treatment failure

while lysine (r = -0.83 and r = -0.65) and phenylacetate (r = -0.66 and r = -0.51) correlated with successful treatment response.

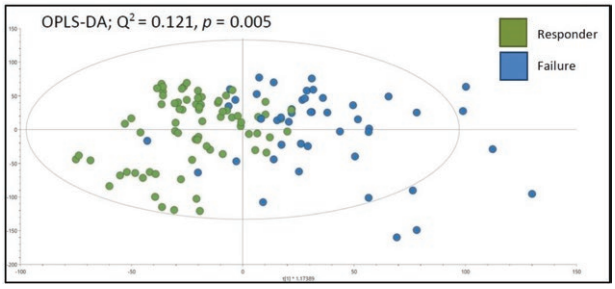


Figure 1. OPLS-DA model that significantly separates treatment responders (n = 19) from failures (n = 12) based on their plasma metabolomic profiles. Plot includes ^{1}H-NMR plasma profile for all patients at all timepoints.

Table 1. Plasma metabolites associated with successful treatment response (green) vs failure (blue) in the Figure 1 model.

Plasma metabolite	Correlation coefficient	Positive correlation with
Lysine	-0.61	Responder
Valine	-0.54	Responder
Serine	-0.50	Responder
Alanine	0.82	Failure
N-acetylglutamine	0.81	Failure
Glucose	0.80	Failure
Lipid CH2CO	0.80	Failure
Citrate	0.78	Failure

Conclusion: In the FLORA trial, plasma metabolomic profiles of patients with active, peripheral PsA significantly discriminated between treatment responders and failures. This discriminatory power was the case for the entire trial population as well as for each of the two treatment arms (FMT vs sham).

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Disclosure of Interests: None Declared.

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POS0424 CHARACTERIZATION OF THE INFLAMMATORY PROTEOME OF SYNOVIAL FLUID FROM PATIENTS WITH PSORIATIC ARTHRITIS: POTENTIAL TREATMENT TARGETS

Keywords: Synovium, Psoriatic arthritis, Biomarkers

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Background: Synovial membrane inflammation, driven by effector T-cell activation and altered inflammatory cytokine expression, is a key feature of this psoriatic arthritis. The proximity extension assay (PEA) technique could contribute to identifying novel protein biomarkers associated with PsA and to improving the biological understanding and the future management of PsA, leading to novel intervention targets.

Objectives: 1) To characterize the inflammatory proteome of synovial fluid (SF) from patients with Psoriatic Arthritis (PsA) using a next generation proteomics technique, and 2) to evaluate its potential to stratify patients according to clinical features.

Methods: Inflammatory proteome profile of SF from thirteen PsA patients with active knee arthritis were analysed using PEA technology (Olink Target 96 Inflammation panel, Cobiomic Biosciences). Four patients with OA were included as control group.

Results: Seventy-nine inflammation-related proteins were detected in SF from PsA patients (SF-PsA). Unsupervised analyses of the molecular proteome profile in SF-PsA identified two specific phenotypes characterized by higher or lower levels of inflammation-related proteins. Clinically, SF-PsA with higher levels of inflammatory proteins also showed increased systemic inflammation and altered glucose and lipid metabolisms. Besides, SF from PsA patients showed 39 out of 79 proteins significantly altered compared to SF-OA specifically related to cell migration and inflammatory response. Among these, molecules such as TNFα, IL-17A, IL-6, IL-10, IL-8, ENRAGE, CCL20, TNFSF-14, OSM, IFNγ, MCP-3, CXCL-11, MCP4, CASP-8, CXCL-6, CD-6, ADA, CXCL-10, TNFβ and IL-7 showed the most significantly alteration.

Conclusion: This is the first study that characterizes the inflammatory landscape of synovial fluid of PsA patients by analyzing a panel of 92 inflammatory proteins using PEA technology. Novel SF proteins have been described as potential pathogenic molecules involved in the pathogenesis of PsA. Despite the flare, inflammatory proteome could distinguish two different phenotypes related to systemic inflammation and lipid and glucose alterations.

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Disclosure of Interests: None Declared.

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POS0425 SINGLE-CELL RNA SEQUENCING OF SYNOVIAL TISSUE-DERIVED MYELOID CELLS IN PSORIATIC ARTHRITIS PATIENTS ACROSS DISEASE PHASES

Keywords: Synovium, Biomarkers, Innate immunity

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Background: Single cell technologies (scRNAseq) are increasingly applied in rheumatology to identify key cellular phenotypes that drive disease pathogenesis, enabling to deconvolute cellular heterogeneity within tissues.

Objectives: To investigate ST heterogeneity in terms of myeloid cells enrichment and distribution across different disease phases on ST samples obtained from US-guided biopsies in a bio-samples dataset of patients with Psoriatic Arthritis (PsA).

Methods: 17 patients fulfilling the CASPAR criteria[1] for PsA underwent US-guided ST biopsy and were included. At baseline, patients were categorized based on their disease phase: n=4 naïve to DMARDs; n=3 resistant to c-DMARDs; n=5 resistant to b-DMARDs; n=2 Difficult to treat and n=3 in sustained clinical and US remission or in low disease activity (LDA) state. All ST specimens were processed for phenotyping and sorting. Alive cells were sorted and loaded onto a Chromium Controller (10x Genomics) for single-cell partitioning, followed by library preparation according to the Chromium Next GEM Single Cell 3′ Reagent Kits v3.1 (Dual Index) protocol. Single-cell libraries were sequenced on the Illumina HiSeq 4000 system to a minimum depth of 20,000 reads per cell.

Results: After standard data processing and quality control procedures, we obtained transcriptomic profiles for 16701 synovial tissue-derived cells. For analysis of ST myeloid compartment only, 10194 cells were computationally isolated with the subset function from other cell types based on expression of CD14,MARCO,LYZ,CD11b and CD64. We identified 10 different myeloid subclusters from the scRNA-seq profiles using SCTransform integration: 2 clusters of lining layer and 8 sublining layer macrophage named after main differentially expressed (DE) genes (adjusted P < 0.05 by Bonferroni correction and multiple test correction, multiplied by number of tests) and according to the nomenclature established in Alivernini et al 20202. Each cell type group is present across all disease conditions but differences in relative proportions were detected.Specifically, ST of patients with active PsA resistant to pharmacological treatment was significantly enriched in sublining MerTKnegSPP1pos macrophages. In addition, we observed pro-inflammatory changes in lining layer TREM2pos STMs as compared to patients who achieved Remission/LDA status(p<0.001 for both).

Conclusion: MerTKnegSPP1pos STM macrophage may contribute to synovial pathology of PsA resistant to pharmacological treatment.

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Disclosure of Interests: None Declared.

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POS0426 PKM2 PROMOTES PRO-INFLAMMATORY MACROPHAGE ACTIVATION IN ANKYLOSING SPONDYLITIS

Keywords: Innate immunity, Spondyloarthritis

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Background: Macrophages are vital effector cells in ankylosing spondylitis (AS), leading to autoimmune tissue inflammation through varied effector functions [1]. The pro-inflammation potential of macrophages depends on their metabolic environment. Macrophages also work as principal regulators in T lymphocyte activation. To meet amplified bioenergetic and biosynthetic demands, metabolic pathways are joined to facilitate the proliferation and effector molecule production. A critical question is whether glycolysis and the rate-limiting enzyme, pyruvate kinase isoenzyme M2 (PKM2) could positively influence AS macrophages' inflammatory function.
Objectives: The objectives of the study was to investigate the effect of glycolysis and PKM2 on AS macrophage functions featured by the secretion of inflammatory cytokines and the presentations of co-stimulatory signals.
Methods: Peripheral blood mononuclear cells (PBMC) were isolated from AS patients and differentiated into macrophages by M-CSF. Macrophages were further differentiated into M1 or M2 macrophages by stimulation with IFN-γ and LPS, or IL-4 and of IL-13. For glycolysis inhibition, cells were treated with 10mM of 2-Deoxy-D-glucose (2-DG). For inhibition of *PKM2*, macrophages were treated with 0.25μM of Shikonin. The RNA expressions of proinflammatory cytokines and glycolysis-related genes were detected by qPCR. Immunoblotting, ELISA and confocal miroscopy was applied to examine the expression of *PKM2*. Extracellular acidification rate (ECAR) analysis was performed to assess glycolysis. The expressions of surface molecule CD80, CD86, and HLA-DR were measured using CytoFLEX flow cytometer.
Results: AS macrophages are prone to produce excessive inflammation, including *TNFα*, *IL1β*, and *IL23,* and are at overactive status by exhibiting stronger co-stimulatory signals, such as CD80, CD86, and HLA-DR. Meanwhile, we found that patient-derived M1 macrophages intensified glycolysis, captured as a higher ECAR. Obviously, upregulation of *PKM2* and *GLUT1* has been observed on AS-derived monocytes and macrophages, especially on M1 macrophages, indicating a glucose metabolic alteration in AS macrophages. To investigate how glycolysis impacts macrophage inflammatory ability, 2-DG and Shikonin were applied to AS M1 macrophages, respectively. Consequently, both inhibitors could lessen pro-inflammatory function and reverse overactive status of AS macrophages, potentially favoring disease treatment.
Conclusion: We emphasized hyper-metabolic M1 macrophages of AS and suggested an essential role for PKM2 in inflammatory effector functions of AS macrophages. Targeting PKM2 to inhibit glycolysis in an overactive macrophage may provide novel therapeutic methods for AS inflammation.

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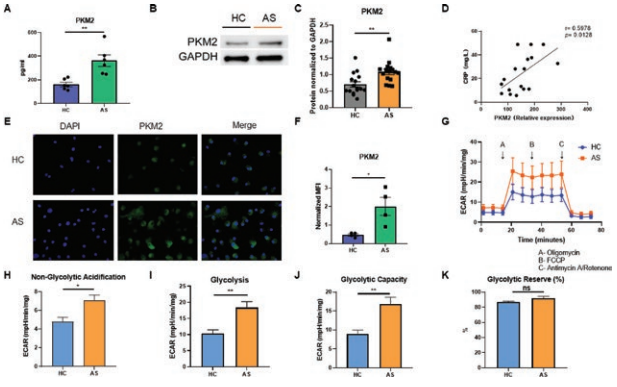


Figure 1. AS-derived M1 macrophage presents with more PKM2 and glycolysis. Circulating monocytes from HC and AS were differentiated into moncyte-derived macrophages. They were then activated into M1 type with LPS/IFN-γ for 24 h. A. Concentrations of PKM2 in HC and AS plasma measured by ELISA. N=6. B-C. Immunoblotting of PKM2 protein among HC and AS patients. N=16. D. Correlation between serum CRP and *PKM2* mRNA expression. N=17. E-F. Confocal images were acquired in ex vivo–generated macrophages stimulated with LPS/IFN-γ for 24 h and stained with anti-PKM2 (green). Nuclei were localized by DAPI (blue). The bar graph represents averaged data from experiments quantifying the fluorescent signal (n = 4 HC and 4 AS patients). G-K. Glycolysis assays in macrophages were evaluated with the Seahorse Bioscience XF96 analyzer by adding test agents in order of 1, oligomycin; 2, FCCP; 3, antimycin A/rotenone. Summarized graphs from 6 HC and 8 AS patients were shown.

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POS0427 PROSTAGLANDIN E2 CONTROLS THE METABOLIC ADAPTATION OF T CELLS TO THE INTESTINAL MICROENVIRONMENT

Keywords: -omics, Adaptive immunity, Gastrointestinal tract

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Background: Immune cells must adapt to different environments during the course of an immune response, such as during their transition from lymph nodes to peripheral tissues.
Objectives: We studied the adaptation of $CD8^+$ T cells to the intestinal microenvironment and how this process shapes their residency in the gut. Investigation of this process will lead to the identification of tissue-specific mechanisms to target $CD8^+$ T cell function in a gut-restricted manner.
Methods: We explored the adaptation of $CD8^+$ T cells to the intestinal microenvironment using single cell RNA and antibody sequencing, mass spectrometry-based metabolomic approaches, CRISPR-Cas9 gene editing, and in vivo mouse models of intestinal infection.
Results: $CD8^+$ T cells progressively remodel their transcriptome and surface phenotype as they acquire gut residency, and downregulate expression of mitochondrial genes. Human and mouse gut-resident $CD8^+$ T cells have reduced mitochondrial mass, but maintain a viable energy balance to sustain their function. We found that the intestinal microenvironment is rich in prostaglandin E_2 (PGE_2), which drives mitochondrial depolarization in $CD8^+$ T cells. Consequently, these cells engage autophagy to clear depolarized mitochondria, and enhance glutathione synthesis to scavenge reactive oxygen species (ROS) that result from mitochondrial depolarization. Impairing PGE_2 sensing promotes $CD8^+$ T cell accumulation in the gut, while tampering with autophagy and glutathione negatively impacts the T cell population.
Conclusion: A PGE_2-autophagy-glutathione axis defines the metabolic adaptation of $CD8^+$ T cells to the intestinal microenvironment, to ultimately influence the T cell pool.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0428 EFFECTOR ACTIVITY OF CXCR3+ CD8 T CELL IS REGULATED BY GLUT1-MEDIATED METABOLIC REPROGRAMMING TOWARD GLYCOLYSIS AND INVOLVED IN SPONDYLOARTHRITIS PATHOGENESIS

Keywords: Adaptive immunity, Spondyloarthritis

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Background: Although T cell metabolism has recently attracted attention as a key regulator of immune responses, the molecular mechanisms underlying the expression of effector functions in human T cells are still poorly understood. T cell metabolism is postulated to be involved in the development of autoimmune diseases by regulating the expression of its effector functions.
Objectives: In this study, we examined the association of metabolic pathways with effector function activity in human T cells. We further investigated the involvement of the identified metabolic pathways in the pathogenesis of autoimmune

diseases using the two representative autoimmune arthritis samples, spondyloarthritis (SpA) and rheumatoid arthritis (RA).
Methods: Metabolism-related cell surface transporters (GLUT1, LAT1, and ASCT2) were examined for their expression levels in CD8 T cells and CD4 T cells from peripheral blood using flow cytometry and Western blotting. Cell survival rate was examined in cultured cells under condition of glucose supply or depletion for 6 days. We comprehensively analyzed the expression of metabolic enzymes in CXCR3+CD8 T cells and CXCR3-CD8 T cells using bulk RNA-seq data. We investigated the effects of metabolic-related transporters on the ability to produce inflammatory cytokines (TNF and IFNγ) using inhibitors. Whole blood samples were freshly obtained from active, treatment-naïve patients with SpA (n=15) and RA (n=25), or healthy controls (HC, n=11) and analyzed by flow cytometry. Phenotype and metabolic enzyme expression of T cells in the synovial fluids of patients were also analyzed employing bulk RNA-seq data.
Results: Among metabolic transporters, GLUT1 was found to be expressed at the protein level specifically on CD8 T cells but not CD4 T cells in human peripheral blood. Functional experiments confirmed that CD8 T cells depended on glucose supply to maintain their cell survival compared to CD4 T cells. Interestingly, exploratory experiments revealed that among CD8 T cells, the viability of CXCR3+CD8 T cells was particularly dependent on glucose supply. In line with that, comprehensive analysis by RNA-seq data revealed that CXCR3+CD8 T cells had enhanced expression of glycolytic enzymes, including *GLUT1*, compared to CXCR3-CD8 T cells. Validation by flow cytometry also confirmed the elevated GLUT1 level at the protein expression in CXCR3+CD8 T cells than in CXCR3-CD8 T cells. Importantly, CXCR3+CD8 T cells had higher effector function activity than CXCR3-CD8 T cells in producing TNF and IFNγ, which was significantly reduced by inhibiting GLUT1 function or depleting glucose. Of note, GLUT1 expression level in CD8 T cells was significantly higher in SpA compared with RA and HC. In addition, proportion of CXCR3+CD8 T cells in peripheral blood was specifically increased in SpA compared with RA and HC (P<0.0001 and P<0.001, respectively). Furthermore, CXCR3+CD8 T cells in peripheral blood from SpA patients had significantly higher expression of GLUT1 compared to CXCR3-CD8 T cells (P<0.0001). Finally, CD8 T cells in the synovial fluids of SpA patients showed dominant *CXCR3* expression and higher expression of *GLUT1* among metabolic enzymes, exhibiting their effector activity.
Conclusion: Our results demonstrate that CXCR3+CD8 T cells exhibit higher effector activity than other CD8 T cell phenotypes, regulated by GLUT1-mediated metabolic reprogramming toward glycolysis. GLUT1-high CXCR3+CD8 T cells may be involved in SpA pathogenesis.
REFERENCE:
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0429

THE COMPLEMENT SYSTEM AND RESPONSE TO TNF INHIBITION IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS. POST HOC ANALYSIS FROM CONSUL, A LONGITUDINAL MULTI-CENTER RCT COHORT OF R-AXSPA-PATIENTS WITH A HIGH RISK OF STRUCTURAL PROGRESSION INITIATING TREATMENT WITH TNF-INHIBITOR

Keywords: Spondyloarthritis, Innate immunity, bDMARD

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Background: The pathogenesis of axial spondyloarthritis (axSpA) remains largely unexplained, but recent evidence supports an involvement of the innate immune system. The lectin pathway (LP) of complement activation plays an essential role in innate immunity. Previous studies have shown that elevated levels of specific complement proteins are associated with disease activity in axSpA. However, little is known about alterations in LP proteins and complement activation in relation to treatment with TNF-inhibitors (TNF-I).
Objectives: To determine changes in LP protein levels and complement activation in a longitudinal multi-center cohort of axSpA-patients with high disease activity from the RCT CONSUL before and after 12 weeks of treatment with a TNF-I. Furthermore, to investigate the correlations between LP protein levels, and disease activity, and treatment response.
Methods: Serum samples at baseline and after 12 weeks of treatment with the TNF-I golimumab were obtained from 108 radiographic axSpA-patients with high disease activity (BASDAI ≥4) and high risk for radiographic progression (elevated CRP or ≥1 syndesmophyte present at inclusion) recruited from the CONSUL cohort. Serum levels of the LP proteins MBL, CL-L1, H-ficolin, L-ficolin, M-ficolin, MASP-1, MASP-2, MASP-3, and MAp44, and complement activation product C3dg were measured by immunoassays.
Results: Serum levels of L-ficolin, M-ficolin, MBL, MAp44, and C3dg decreased significantly after 12 weeks of treatment with TNF-I, whereas serum levels of MASP-3 and CL-L1 increased significantly (Figure 1). After adjustment for CRP, significant changes were observed for L-ficolin, M-ficolin, MASP-1, MASP-2, MASP-3, and MAp44. Baseline serum levels of L-ficolin, M-ficolin, and C3dg correlated positively with baseline ASDAS-CRP (Spearman's rho 0.290, 0.190, and 0.328, respectively, all p<0.05), whereas baseline MASP-1 and MAp44 correlated negatively with baseline ASDAS-CRP (Spearman's rho -0.204, and -0.218, respectively, both p<0.05). In a univariate logistic regression analysis, baseline serum levels of MASP-1 predicted achievement of clinical important improvement (ΔASDAS≥1.1) at week 12, and baseline serum levels of C3dg predicted inactive disease (ASDAS<1.3) at week 12. In corresponding multivariate logistic regression analyses, only C3dg remained significantly associated with inactive disease (ASDAS<1.3) (p = 0.025).
Conclusion: Baseline serum levels of L-ficolin, M-ficolin and C3dg correlated positively with baseline ASDAS-CRP, and the protein serum levels decreased significantly after TNF-I therapy. Baseline levels of complement activation measured by C3dg predicted achievement of inactive disease (ASDAS<1.3) at week 12 in both a univariate and a multivariate logistic regression analysis. Our findings suggest an involvement of the complement system in the underlying inflammatory processes of axSpA and prompt further investigations.

Table 1. Baseline demographics of the investigated patient population from the CONSUL RCT (n = 108)

Age, median (IQR)	38 (31-49)
Male, n (%)	77 (71)
HLA-B27 positive, n (%)	89 (82)
Previous treatment with bDMARD, n (%)	26 (24)
Time since diagnosis in years, median (IQR)	3.0 (0.0-9.0)
Years since onset of symptoms, median (IQR)	12 (6.0-21.0)
CRP, mg/L (IQR)	9.1 (4.1-20)
Elevated CRP (> 5mg/L), n (%)	75 (69)
mSASSS, median (IQR)	4.3 (0.3-18)[#]
Syndemophytes present, median (IQR)	1.6 (0.0-6.3)[#]
Presence of ≥1 syndesmophyte(s) [§], n (%)	43 (48) [#]
ASDAS-CRP, median (IQR)	3.6 (3.1-4.1)
BASDAI, median (IQR)	6.2 (5.2-7.0)
BASFI, median (IQR)	5.2 (4.0-6.4)

[§] Determined by 3 calibrated readers blinded for clinical data. [#] data available on n = 89

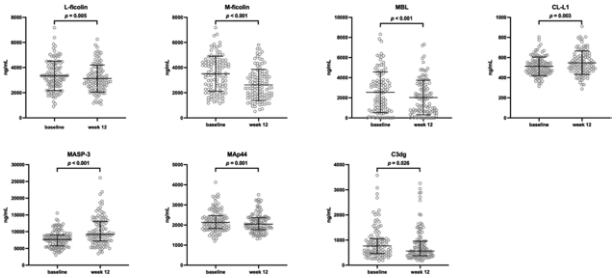


Figure 1. Differences in lectin pathway protein serum levels were compared by paired t-tests. Bars indicate median and IQR (MASP-3, MAp44, and C3dg) or mean and sd (L-ficolin, M-ficolin, MBL, and CL-L1).

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POS0430

THE EXPANDED CD21LOW B CELL SUBPOPULATION IN ANKYLOSING SPONDYLITIS CONSISTS MAINLY OF UNMUTATED ANTIGEN-INEXPERIENCED CELLS THAT ARE CLONALLY RELATED TO MEMORY B CELLS AND PLASMABLASTS

Keywords: Spondyloarthritis, Adaptive immunity, Cell biology

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Background: The role of B cells in the pathogenesis of ankylosing spondylitis (AS) remains relatively understudied. Nevertheless, available evidence shows presence of B cells at sites of inflammation, higher frequencies of circulating plasmablasts, presence of autoantibodies and beneficial results of B cell depleting therapy with rituximab [1]. We observed previously that a subpopulation of $CD27^-$ B cells, characterized by low expression of the complement receptor CD21 ($CD21^{low}$), is increased in patients with AS and patients with primary Sjogren's syndrome (pSS), a typical B cell mediated systemic autoimmune disease [2]. These $CD21^{low}CD38^{low}CD27^-$ B cells display a pro-inflammatory phenotype, suggestive for a pathogenic role.
Objectives: To gain insight into the origin of these $CD21^{low}CD38^{low}CD27^-$ B cells we analysed the mutation status of the immunoglobulin heavy chain variable (IGHV) gene regions in the total B cell compartment, $CD21^{low}$ B cell subpopulations and plasmablasts in AS patients in comparison to pSS patients and healthy donors (HD). In addition, we investigated clonal relations between $CD21^{low}$ B cell subpopulations and plasmablasts in AS.
Methods: RNA was isolated from sorted total B cells ($CD19^+$), two $CD21^{low}$ B cell populations ($CD21^{low}CD38^{low}CD27^-$ and $CD21^{low}CD38^{low}CD27^+$) and plasmablasts ($CD19^+CD38^{++}CD27^+$) from peripheral mononuclear cells of 10 AS patients fulfilling the mNY criteria (mean age 46 ± 9 years, 60% male, mean ASDAS 2.3 ± 0.8, all HLA-B27+), 10 sex- and age-matched HDs (mean age 48 ± 21 years, 60% male) and 10 age-matched pSS patients (mean age 46 ± 9 years, 20% male). Repertoire analysis of the B cell receptor heavy chain was performed using high throughput sequencing on the Illumina MiSeq Platform. Sequences were analyzed for degree of somatic hypermutation, usage of immunoglobulin heavy chain variable (IGHV) and joining (IGHJ) regions and clonal relationships.
Results: IGHV sequences with identical heavy chain CDR3 regions were grouped together and were defined as a clone. Analysis of the IGHV mutation status in $CD21^{low}$ B cells revealed that the majority of clones (71% SD ± 14.1) in the $CD21^{low}CD38^{low}CD27^-$ subset from patients with AS consisted of clones with a low mutation rate (0-2 mutations in the IGHV region) (Figure 1b). On the contrary, most of the clones in the $CD21^{low}CD38^{low}CD27^+$ (49% SD ± 12.5) and plasmablasts (59% SD ± 12.7) subsets were clones with a higher mutation load (>10 mutations in the IGHV region). A similar mutational pattern was seen in pSS patients and HDs. In AS, IGHV3 and IGHJ4 family genes were predominantly used (Figure 1c). However, we observed no differences in family gene usage among B cell subsets nor between groups. To investigate clonal relationships we performed a CDR3 amino acid network analysis on the top 100 most expanded clones per subset in AS patients and found that the $CD21^{low}CD38^{low}CD27^-$ subset shared more clones with the $CD21^{low}CD38^{low}CD27^+$ subset (median 3.0 (0.8-7.0 IQR), p< 0.05) compared to plasmablasts (median 0.0 (0-1.3 IQR).
Conclusion: This study shows that the expanded circulating $CD21^{low}CD38^{low}CD27^-$ B cell population in AS consists mainly of antigen-inexperienced cells. The presence of shared clones with their $CD27^+$ counterpart and plasmablasts suggest that the three subsets are to some extent related. Hence, $CD21^{low}CD38^{low}CD27^-$ B cells may differentiate towards $CD21^{low}CD38^{low}CD27^+$ B cells and plasmablasts. The relative roles of these $CD21^{low}$ B cell subsets and plasmablasts in AS pathogenesis remain to be established.

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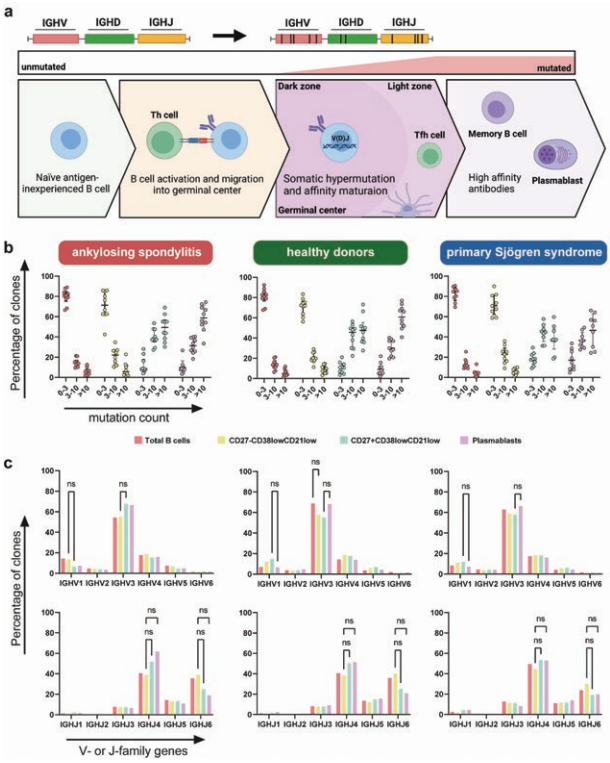


Figure 1.

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POS0431

GOBLET CELL SPECIFIC ANTI-APOPTOTIC ROLE OF INTERLEUKIN-24 IN SPONDYLOARTHRITIS-ASSOCIATED ILEITIS

Keywords: Gastrointestinal tract, Spondyloarthritis, Cell biology

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Background: Spondyloarthritis (SpA) is characterised by chronic debilitating axial and peripheral joint inflammation, often concomitant with inflammatory bowel disease (IBD)-like gut phenotypes. However, the contribution of extra-articular gut pathologies to SpA is not well understood. The $ZAP\text{-}70^{W163C}$ BALB/c (SKG) mouse model of SpA develop chronic arthritis, spondylitis and IBD-like ileitis commencing from 1 week after intraperitoneal curdlan injection with characteristic interleukin-23-dependent gut dysbiosis, endoplasmic reticulum (ER) stress and goblet cell depletion. The cytokine interleukin-24 (IL-24) was first described to promote ER stress-mediated apoptosis in damaged tumour cells without harming normal cells. Conversely, IL-24 attenuated cell death in a liver damage model. IL-24 levels were increased in the synovial fluid in SpA and in the colon in IBD.
Objectives: Since, in both IBD and SpA, gut dysbiosis and mucus depletion promote goblet cell stress and apoptosis, we therefore assessed the role of gut derived IL-24 in ER stress-mediated apoptosis in SpA.
Methods: Ileal histology sections from curdlan-treated SKG mice were stained with Alcian blue staining or immunofluorescence (IF) using an anti-IL-24 Ab. The human $MUC2^{hi}$ colonic epithelial cell line, LS-174T was compared to the $MUC2^{low}$ colonic epithelial line HT-29 after induction of ER stress with SERCA-inhibitor thapsigargin in the presence of IL-24 or control siRNA. Gene expression was analysed by RT-qPCR and protein by Western Blot or flow cytometry.

Results: Naïve SKG ileum displayed dysbiosis with increased expression of ER stress markers *Grp78, sXBP1*, *CHOP* and reduced mucin staining. After curdlan treatment, goblet cell numbers were decreased and *Il24* mRNA was increased compared to BALB/c controls. By IF, IL-24 localized to the goblet cells of the ileum in SKG and BALB/c mice and 2 weeks post curdlan, ileal goblet cell number was correlated with IL-24 staining intensity. In $MUC2^{hi}$ LS-174T but not $MUC2^{low}$ HT-29 cells, thapsigargin induced a rapid and transient increase in *Il24* transcription and subsequent ER stress with *CHOP* induction, suggesting an acute goblet cell-specific response associated with high mucus production. IL-24 knockdown in LS-174T increased ER stress and apoptosis including increased *CHOP*, *DR5* and active caspase 3 expression.
Conclusion: Despite goblet cell IL-24 over-expression in dysbiotic naïve SKG ileum, goblet cell loss due to stress associated with increased mucus production also depletes IL-24. In an in vitro model of goblet cell stress, IL-24 mitigates ER stress-induced apoptosis, suggesting that IL-24 production in SKG ileum is insufficient to prevent the disease cascade that commences with goblet cell apoptosis and epithelial barrier breakdown.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0432 CHARACTERIZATION OF THE CARDIOVASCULAR DISEASE PROTEOMIC PROFILE IN SPONDYLOARTHRITIS PATIENTS: POTENTIAL BIOMARKERS FOR PERSISTENT INFLAMMATION

Keywords: Biomarkers, Cardiovascular disease, Spondyloarthritis

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Background: patients with Spondyloarthritis (SpA) have an increased risk of cardiovascular disease. Taking into account the strong relationship between inflammation and CVD, there is an urgent need to identify different molecular drivers of CVD signs and their association with inflammation.
Objectives: to investigate the alteration of CVD-related proteins in the plasma of SpA patients, their association with clinical features, and to evaluate their potential role as biomarkers for the identification of persistent inflammation.
Methods: a cross-sectional study including 120 patients with SpA and 30 age-sex-matched healthy donors (HDs) was carried out. Clinical and laboratory parameters and CVD risk factors were recorded. To measure the presence of persistent inflammation, levels of c-reactive protein (CRP) were collected retrospectively for 5 years previous to the study, a patient was considered to have persistent inflammation with increased CRP in at least 50% of the measures during the previous 5 years. Levels of 92 proteins with a recognized role in CVD were analyzed in the plasma using proximity extension assay (PEA) technology (Olink Target 96 CVD III panel, Cobiomic Biosciences).
Results: SpA patients showed higher rates of CVD comorbidities compared to HDs. Plasma levels of TNF-R1, RARRES-2, CHI3L1, PGLYRP-1, CTSD, UPAR, IL2RA, TIMP-4, CTSB, GDF-15, MMP-9, and PDGF-A were significantly increased in SpA compared to HDs. Specifically, these proteins are also related to biological processes such as neutrophil degranulation, immune response, cell activation, atherosclerosis, apoptosis, and inflammatory response. Besides, a significant alteration of these CVD-related proteins in SpA was also associated with the presence of arterial hypertension, insulin resistance, obesity, hyperuricemia, and high levels of acute phase reactants. 36% of SpA patients displayed persistence of inflammation. Interestingly, SpA patients with persistent inflammation showed higher levels of ankylosing spondylitis disease activity (ASDAS) score, CRP, glucose, complement component 3, and lower levels of HDL-cholesterol and apolipoprotein A compared to SpA patients with non-persistent inflammation, suggesting the relationship of inflammation with metabolic alterations. In addition, 8 out of 12 CVD-related proteins altered in SpA patients were specifically changed in patients with persistent inflammation: MMP-9, RARRES-2, PGLYRP-1, UPAR, TNF-R1, PDGF-A, IL-2RA and GDF-15, highlighting levels of MMP-9 protein as a potential biomarker for persistent inflammation in SpA (AUC=0.796 p>0.0001).
Conclusion: 1) SpA patients show an altered CVD proteome profile which is strongly associated with CVD risk factors and clinical inflammatory markers, 2) SpA patients with persistent inflammation display a deeper alteration in their plasma CVD protein pattern suggesting the link between subclinical CVD risk and the chronic inflammation, and 3) this study identifies novel potential biomarkers to distinguish SpA patients with persistent inflammation. Funded by ISCIII (PI20/00079, PMP21/00119, and RICOR-RD21/0002/0033) co-financed by ERDF.
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Disclosure of Interests: None Declared.
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POS0433 RELATIONSHIP BETWEEN MIRNA-1-3P, INTERLEUKIN-17 AND TUMOR NECROSIS FACTOR IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Genetics/Epigenetics, Biomarkers

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Background: microRNAs (miRNAs) are small non-coding RNAs that can regulate gene expression and mirror the patient's health condition. miRNAs deregulation is considered a crucial factor in the development and progression of various diseases, including axial spondyloarthritis (axSpA) [1].
Objectives: The aim of the study was to profile the miRNome of peripheral blood mononuclear cells (PBMCs), to identify specific miRNAs and their association with several cytokines, axSpA disease activity and spinal impairment.
Methods: Massive parallel sequencing (MPS, Ilumina) was performed for miRNAs profiling in 96 subjects (38 patients with non-radiographic (nr-) axSpA, 38 patients with radiographic (r-) axSpA and 20 healthy controls (HC)). The expression of candidate miRNAs was validated using the qRT-PCR system (SmartChip) on a new cohort of 47 patients with nr-axSpA, 44 patients with r-axSpA and 50 HC. Disease activity was determined using C-reactive protein (CRP) and Ankylosing Spondylitis Disease Activity Score (ASDAS). Radiographs of the cervical and lumbar spine were assessed by two independent blinded readers using modified Stoke Ankylosing Spondylitis *Spine* Score (mSASSS). We employed DESeq2 and generalized linear modelling with a negative binomial assumption (GLM-NB) to evaluate the association of candidate miRNAs to the radiographic form, ASDAS and CRP. Linear modelling was used to determine the association between miRNAs and laboratory/clinical parameters adjusted for CRP, age and sex.
Results: MPS detected 432 miRNAs; however, only 90 miRNAs passed through the selection criteria ($p<0.05$, BaseMean>10, the difference in log2FC>0.5). We selected 45 miRNAs for validation based on the selection criteria and the literature. We validated miR-1-3p ($p=0.006$, FC=1.757) to be upregulated and miR-1248 ($p=0.002$, FC=-1.125) and miR-1246 ($p=0.002$, FC = -1.125) to be downregulated in patients with axSpA compared to HC. In addition, the expression of miR-1-3p correlated with the plasma levels of IL-17 ($p=0.016$, $\tau=0.25$) and TNF ($p=0.028$, $\tau=0.22$), but not with the gene expression of IL-17 or TNF in PBMCs. miR-1-3p ($p=0.039$, $\beta=0.665$) as well as miR-1248 ($p<0.001$, $\beta=-0.207$) correlated with the IL-6 gene expression in PBMCs. None of the miRNAs distinguished between radiographic and non-radiographic disease or correlated with disease activity or radiographic spinal impairment.
Conclusion: This cross-sectional study failed to demonstrate association between cellular miRNAs, disease activity or spinal impairment, but the association between miR-1-3p, IL-17 and TNF may suggest its role in the pathogenesis of axSpA.
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POS0434 CCL20 INHIBITION AMELIORATES PERIPHERAL ARTHRITIS IN ANKYLOSING SPONDYLITIS

Keywords: Animal models, Adaptive immunity, Spondyloarthritis

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Background: Ankylosing spondylitis (AS) is a rheumatic disease characterized by chronic inflammation. Several lines of evidence implicate interleukin (IL)-17A-secreting T helper (Th)17 cells in AS pathogenesis. One of the receptors of Th17 cell, C-C motif chemokine ligand 20 (CCL20) is known to attract C-C chemokine receptor 6 (CCR6) expressing cells to the site of inflammation. However, the role and mechanisms of CCL20 in AS are not well understood.
Objectives: Therefore, this study aimed to evaluate the function of CCL20 in patients with AS.
Methods: Peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs) were obtained from AS patients. Inflammatory cytokine-producing cells were analyzed using flow cytometry and enzyme-linked immunosorbent assay (ELISA). To determine the direct effect of cell migration in the presence of CCL20, a transwell migration assay was performed. In in vivo experiments, SKG mice were treated with either CCL20 blocking antibody or isotype control antibody. Clinical signs of mice were monitored twice a week and scored by two independent observers. At the experimental endpoint, specimens of the ankle was obtained from mice. Two blinded readers then performed pathological scoring for arthritis using immunohistochemistry.
Results: IL-17A producing cells were significantly higher expressed in SFMCs of AS patients than in PBMCs of AS or healthy controls. CCL20-positive cells showed significantly increased IL-17A production than CCL20-negative cells. To confirm the relationship between CCL20 and IL-17A production, IL-17A expression was observed with either CCL20 agonist or antagonist. Treatment with CCL20 agonist showed an increase in IL-17A in PBMCs from AS patients. Meanwhile decreasing IL-17A level was observed in SFMCs from AS patients when treated with CCL20 inhibitors. In cell migration assay experiments, cell migration increased when CCL20 was added to the CD4-positive cells. In an vivo model, CCL20 inhibitors significantly suppressed arthritis symptoms (Figure 1). In addition, histologic evaluation showed that mice treated with CCL20 inhibitor had lower arthritis scores than isotype-treated control mice.
Conclusion: This study demonstrates CCL20 blockade improved joint inflammation in AS. Therefore, CCL20-target therapy could be a promising treatment for AS.

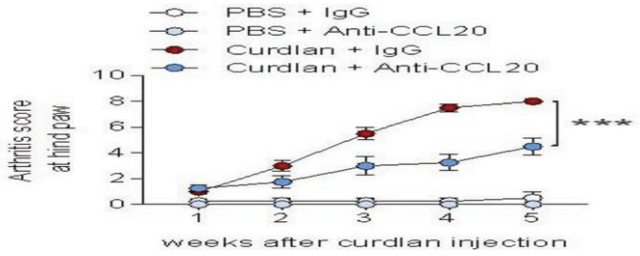


Figure 1. CCL20 Inhibition ameliorates peripheral arthritis in SKG mice

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POS0435 PEPTIDE-BASED VACCINE TARGETING IL17A ATTENUATES EXPERIMENTAL SPONDYLOARTHRITIS INHLA-B27 TRANSGENIC RATS

Keywords: Animal models, Spondyloarthritis

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Background: Ankylosing spondylitis (AS) is one of the major diseases in spondyloarthritis (SpA). HLA-B27 is known as a genetic risk factor for AS. Recent lines of evidence suggests that IL-23/IL-17 axis strongly contributes to AS.
Objectives: This study was to assess the efficacy of IL17A peptide-based vaccine on the SpA manifestations in model rat.
Methods: HLA-B27/human beta 2 -microglobulin transgenic rats were immunized with heat-inactivated Mycobacterium Tuberculosis (MT) to develop spondylitis and arthritis as an experimental spondyloarthritis model after 3 times immunization with KLH-conjugated IL17A peptide-based vaccine with alum adjuvant. IL17A antibody titer was assessed by ELISA, and arthritis score and joint thickness was monitored twice a week. At 9 weeks, joints of ankle and spine were collected to analyzed by histological analysis and realtime PCR for evaluation of inflammation and bone remodeling. Moreover, heart, liver, and lung were also collected for safety assessment by HE staining.
Results: IL17A peptide-based vaccine with alum adjuvant successfully induced antibody production, and suppressed arthritis score and joint thickness. X-ray and histological analysis showed that enthesitis, bone destruction, and new bone formation were inhibited by IL-17A vaccine. Moreover, SpA-induced expression of IL17A-related inflammatory- and bone remodeling molecules were down-regulated in the ankle and spine. Finally, IL-17A vaccine had no tissue damage by histological analysis.
Conclusion: These data showed that peptide-based vaccine targeting IL-17A prevented SpA phenotype in heat-inactivated Mycobacterium Tuberculosis-induced SpA model in HLA-B27/human beta 2 microglobulin transgenic rats. IL17A-peptide based vaccine can be a therapeutic option for SpA treatment.

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POS0436 INCREASED EXPRESSION OF PATHWAYS INVOLVED IN B CELL ACTIVATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

Keywords: Spondyloarthritis, Cell biology, Adaptive immunity

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Background: In spite of advancements in treatment of ankylosing spondylitis (AS), its pathogenesis remains incompletely understood. The current evidence suggests that AS is both an autoinflammatory and autoimmune disease involving innate immune cells along with autoreactive lymphocytes. B cells have received little attention regarding their role in the pathogenesis of ankylosing spondylitis (AS), although the available evidence shows presence of B cells at inflammatory sites, imbalances in B cell subsets, presence of autoantibodies (anti-CD74/CLIP), and beneficial effects of B cell depletion (anti-CD20) with rituximab [1]. In AS, the overarching picture portrays increased B cell activation, although it is unclear whether B cells directly affect pathogenesis, or are merely bystanders in the disease process.
Objectives: Our main objective was to study gene expression and gene signalling pathways involved in B cell activation in AS. To this end, we analysed the transcriptomic profile of isolated peripheral B cells from AS patients, healthy donors (HD) and patients with primary Sjögren syndrome (pSS), a typical B-cell-associated autoimmune disease.
Methods: RNA was isolated from $CD19^+$ B cells sorted from peripheral blood mononuclear cells of 8 AS patients (mean age 48.0 ± 9.7 years, 63% male, mean ASDAS 2.5 ± 0.7), 8 sex and age-matched HDs (42.3 ± 17.8 years, 63% male) and 8 age-matched pSS patients (48.4 ± 17.8 years, 13% male). Next, characterization of differentially expressed genes was performed using transcriptomic analysis by the NanoString nCounter Autoimmune Profiling Panel, which utilizes a direct hybridization technique without PCR amplification. After normalization and z-score scaling of pathway genes, pathway scores were calculated based on the first principle component using nCounter advanced analysis software. P-values <0.05 were considered significant.
Results: All samples passed quality control, except for one pSS patient sample that was being flagged as an outlier by the nCounter advanced analyses software. Analysis of differential gene expression between AS patients and HDs revealed upregulation of 8 genes, including *MAPK14*, *KMT2A* and *PKM*, in B

cells from AS patients, and downregulation of two genes, *DDIT4* and *ATG5*. In AS patients, the relative expression of B cell receptor (BCR) signalling (n=60 genes) and Fc receptors and phagocytosis (n=55 genes) pathway genes were both significantly enriched compared to HDs (*Figure 1*). Although not significant, these pathways also displayed higher pathway scores in pSS patients compared to HDs (P=0.30 and P=0.37, respectively). Other gene pathways involved in B cell activation, such as toll-like receptor signalling were not significantly enriched.
Conclusion: In this study, we observed several differentially expressed genes involved in signal transduction pathways in B cells from AS patients. Furthermore, we showed increased expression of gene pathways involved in B cell activation in patients with AS compared to HDs. The BCR-mediated activation in AS displays similarities to a bona fide autoimmune disease pSS. These results suggest active involvement of B cells in the disease process of AS.

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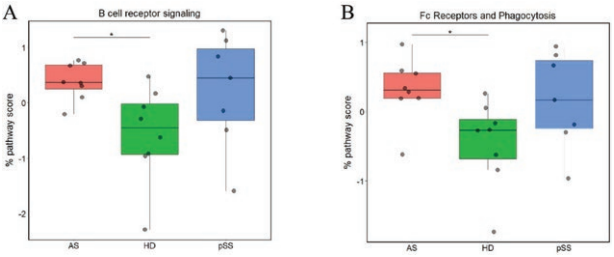


Figure 1. Gene pathway scores of (A) B cell receptor signalling and (B) Fc receptors and phagocytosis between AS, pSS patients and HDs. P-values <0.05 were considered significant.

Acknowledgements: NIL.

Disclosure of Interests: Rick Wilbrink: None declared, Anneke Spoorenberg Consultant of: Abbvie, Pfizer, MSD, UCB, Lilly and Novartis, Grant/research support from: Abbvie, Pfizer, Union Chimique Belge (UCB), Novartis, Frans G.M. Kroese Speakers bureau: BMS Roche and Jannsen-Cilag, Consultant of: BMS, Grant/research support from: unrestricted grants from BMS, Gwenny M. Verstappen: None declared.

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POS0437 **WITHDRAWN**

POS0438 **IDENTIFICATION OF THREE AUTOPHAGY-RELATED HUB BIOMARKERS OF ANKYLOSING SPONDYLITIS VIA BIOINFORMATICS ANALYSIS OF RNA SEQUENCING DATA OF MACROPHAGES**

Keywords: Innate immunity, Spondyloarthritis, Biomarkers

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Background: Autophagy is associated with the occurrence and progression of a variety of diseases, such as cancers, cardiovascular diseases, and autoimmune diseases. Ankylosing spondylitis (AS) is a chronic inflammatory disease. Its pathological feature includes local infiltration of inflammatory cells among which macrophages play a dominant role [1]. Currently, previous studies have confirmed that autophagy may be involved in the occurrence and development of autoimmune diseases, such as AS [2]. However, there are few articles discussing which molecule plays a key role in the progress of autophagy of macrophage in patient with AS.
Objectives: This study aimed to detect gene expression in macrophages that originated from peripheral blood mononuclear cells (PBMC) in patients with AS by RNA sequencing (RNA seq) technology, and to identify underlying autophagy-related genes of AS by bioinformatics analysis.
Methods: Peripheral blood mononuclear cells (PBMC) from 4 cases of AS and 4 cases of healthy control (HC) from were isolated and differentiated into M1 macrophages. These cells were then sent to BGI company for RNA seq. Then, Gene

Set Enrichment Analysis (GSEA) enrichment analysis, screening of differentially expressed genes (DEGs), Gene Ontology (GO) function annotation, Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis of DEGs were conducted. Protein-Protein Interaction (PPI) network of DEGs was constructed, and cluster association analysis was performed by MOCDE plug-in in ctyoscape software. Human autophagy-related genes were downloaded from Human Autophagy Database (HADb). Finally, we took the intersected of human autophagy-related genes and those involved in the top 5 clusters by cluster association analysis.

Results: 1467 DEGs were identified by DESeq2 package in R. Among them, 384 genes were significantly up-regulated while 1083 genes were significantly down-regulated. GO and KEGG enrichment analysis of DEGs revealed several terms related to cell cycle. GSEA analysis of all sequencing data revealed a number of terms related to cell cycle and lysosomes. The PPI network of 1467 DEGs was constructed by using STRING database, and 45 clusters were obtained by using MOCDE plug-in of cytoscape software for cluster association analysis. The intersection of genes involved in the top 5 clusters and 219 autophagy-related genes downloaded from HADb were conducted to obtain 3 autophagy-related genes of AS, which were *BIRC5*, *TP53* and *CTSB*.

Conclusion: Through RNA seq and bioinformatics analysis, we identified 3 potential autophagy-related genes of AS. *BIRC5*, *TP53* and *CTSB* may inhibit the occurrence and development of AS by regulating autophagy.

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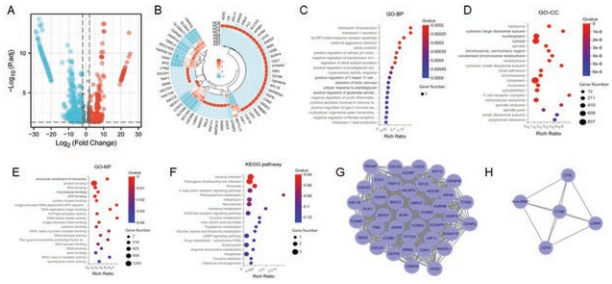


Figure 1A. The volcano plots of differentially expressed genes. The red dots showed high expressed genes and the blue dots displayed low expressed genes.

Figure 1B. The heatmap of top 30 significantly up-regulated and top 30 significantly down-regulated differentially expressed genes. The red dots reflected high expressed genes and the blue dots revealed genes with low expression.

Figure 1C-F. The bubble plots of GO function annotation and KEGG pathway analysis of differentially expressed genes

Figure 1G-H. The top 2 clusters by cluster association analysis

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0439 SCREENING FOR PLASMA BIOMARKERS PREDICTING RADIOGRAPHIC PROGRESSION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A PRELIMINARY STUDY

Keywords: -omics, Spondyloarthritis, Biomarkers

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Background: Axial spondyloarthritis (AxSpA) is an immune-mediated rheumatic disease that has a significant impact on a patient's quality of life. Therefore, early diagnosis and recognition of patients with potentially rapid structural progression of the disease are of great importance.

Objectives: This study aimed to investigate proteomic data in patients' plasma to discover candidate biomarkers differentiating axSpA patients with radiographic progression after two years.

Methods: A cohort of 20 patients with axSpA was selected based on the radiographic progression for the purpose of this preliminary study. Baseline and two-year radiographs of the cervical and lumbar spine were independently assessed by two blinded readers using modified Stoke Ankylosing Spondylitis *Spine* Score (mSASSS). No radiographic progression and significant radiographic progression were characterized as a change in mSASSS ≤0 and >2, respectively, from baseline to year two. Disease activity was determined using C-reactive protein (CRP), Ankylosing Spondylitis Disease Activity Score (ASDAS) and Bath Ankylosing Spondylitis Activity Disease Activity Index (BASDAI). The proteome of the plasma samples was profiled using liquid chromatography with tandem mass spectrometry detection, and the difference in protein concentration was evaluated using linear mixed-effects modelling.

Results: Our cohort included ten patients without radiographic spinal progression (mean±SD age 34.9±9.0 years, 40% female) and ten patients (mean±SD age 40.8±9.0 years, 40% female) who developed the progression after two years (mean±SD change in mSASSS 9.88±5.1). Additionally, of all included patients, 14 were classified as radiographic axSpA (mean±SD age 36.9±8.6 years, 28.6% female) and six as non-radiographic axSpA (mean±SD age 40.2±9.2 years, 66.7% female). The high-throughput profiling of plasma proteome detected 489 quantifiable proteins and our statistical analysis revealed 30 proteins with different concentrations between patients without and with radiographic progression ($p<0.05$ for all). Out of these proteins, haptoglobin (1.76-fold, $p<0.001$) and serum amyloid P-component (SAP) (1.57-fold, $p<0.001$) were upregulated, while gelsolin (1.23-fold, $p = 0.001$) was downregulated in patients with mSASSS progression compared to those without radiographic progression (Figure 1A). In addition, all these proteins significantly correlated with mSASSS, CRP or ASDAS (Figure 1B). However, after adjustment for CRP, only SAP and gelsolin, which were previously associated with axSpA[1,2], were independently associated with structural progression.

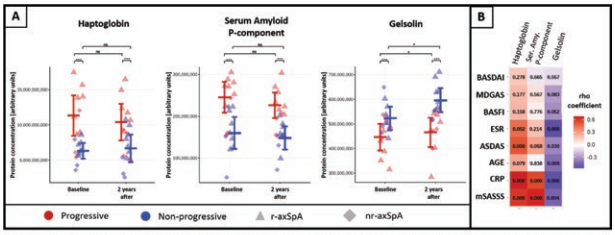


Figure 1 – A) Three candidate proteins with the potential to predict radiographic progression in axSpA. The error bars represent 95% confidence intervals with the mean for patients with or without mSASSS progression. *p-values* show statistical significance between depicted pairwise comparisons computed from linear mixed-effect models. (*** $p < 0.001$; * $p < 0.05$; ns – non-significant). Patients with and without mSASSS progression are coloured in red and blue, respectively, and radiographic (r-) and non-radiographic (nr-) axSpA patients are depicted as triangles and diamonds, respectively. B) Correlation matrix of three candidate proteins and selected clinical parameters. The matrix included *p-values* and the colour indicates the strength and direction of Spearman's coefficient (rho).

Conclusion: We identified two plasma proteins with the potential to independently predict the radiographic progression of axSpA. Further studies in a larger cohort of patients are needed to validate these data.

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POS0440 INCREASED FREQUENCY OF ACTIVATED MAIT CELLS EXPRESSING THE GUT HOMING RECEPTOR CCR9 IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Gastrointestinal tract, Innate immunity

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Background: MAIT (mucosal associated invariant T) cells are involved in mucosa defense against bacteria. This cellular subset is characterized by a semi-invariant αβ TCR and the expression of CD161. In patients with axial spondyloarthritis (ax SpA), previous works reported a decreased frequency of circulating MAIT cells compared to normal subjects. IL-17A is a relevant cytokine involved in SpA pathophysiology. MAIT cells are a cellular source of IL-17 and IL-17$^+$ MAIT cells were found increased in ax SpA. We have previously reported an increased frequency of IFNγ$^+$/IL-17$^+$ MAIT cells as well as IL-22$^+$ MAIT cells in ax SpA[1].
Objectives: In this study, we aimed to complete our previous results by evaluating activation markers and chemokine receptor/integrin expression, especially those for gut homing, in MAIT cells.
Methods: patients exhibited ax SpA (ASAS criteria) with a radiographic (r-ax SpA) or non-radiographic (nr-ax SpA) form. They all were under NSAIDs and biologic naïve. Healthy subjects were recruited as controls (HC). Circulating CD4$^+$ and CD8$^+$ T cells and MAIT cells were determined on blood samples by single platform flow cytometry (Cytoflex, Beckman Coulter). MAIT cells were identified by the co-expression of CD3, CD161 and TCRα7.2. In each subpopulation, we examined the expression of CD26, CD69, CCR9 and CD49d integrin.
Results: 26 patients were included (11 r-ax SpA: 9 males [M]; mean age 54.1 ± 19.6 years; disease duration: 16.2 years; ASDAS score: 4.1; and 15 nr-ax SpA: 7 M; age: 36.4 ± 1.3; ASDAS: 5.6) and 27 HC (16 M; age: 43 ± 12.7). In patients with r-ax SpA, we observed an increased frequency of activated CD3$^+$ CD69$^+$ MAIT cells and CD3$^+$ MAIT cells expressing the gut homing markers CCR9 and CD49d, as compared to HC ($p < 0.05$). These higher frequencies were not observed in patients with nr-ax SpA. In addition, when examining the CD8$^+$ MAIT population, similar higher frequencies of cells positive for CD69, CCR9 and CD49d were observed in patients with r-ax SpA compared to HC and patients with nr-ax SpA ($p<0.01$ and $p<0.05$, respectively).These modifications were specific for MAIT cells and were not observed in conventional CD4$^+$ or CD8$^+$ T lymphocytes.

Table.

	HC	r-ax SpA	nr-ax SpA
% CD69$^+$ MAIT CD3$^+$	18.4 ± 9.9	**28.3** ± 14.7 *	19.7 ± 10.3
% CD69$^+$ MAIT CD8$^+$	19.1 ± 11.4	**29.5** ± 15.6 *	20.8 ± 12.0
% CD49d$^+$CCR9$^+$ MAIT CD3$^+$	1.6 ± 1.7	**2.5** ± 1.6 *	1.9 ± 2.3
% CD49d$^+$CCR9$^+$ MAIT CD8$^+$	1.4 ± 1.7	**2.5** ± 1.8**	1.7 ± 2

Conclusion: Patients with r-ax SpA are characterized by an increased frequency of activated MAIT cells that expressed homing receptors (chemokine and integrin) for the gut. These results confirm that MAIT cells are altered in ax SpA and highlight the relationships between ax SpA and gut inflammation, especially for the radiographic form.

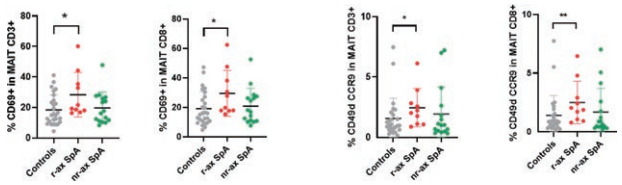


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POS0441

SPONDYLOARTHRITIS IMMUNOLOGICAL AND TISSUES FEATURES DIFFER ACCORDING TO THE COHEXISTING INFLAMMATORY BOWEL DISEASE: A CROSS-SECTIONAL STUDY

Keywords: Cytokines and chemokines, Spondyloarthritis, Gastrointestinal tract

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Background: Spondyloarthritis (SpA) and Inflammatory Bowel Disease (IBD) share some common pathogenetic pathways and a broad spectrum of clinical manifestations, laboratory and imaging features. How intestinal involvement affects SpA clinical and biological aspects remains unexplored and can be help in the SpA and IBD management.
Objectives: To define immunological and synovial and bowel tissues characteristics in SpA associated or not with IBD.
Methods: Forty-one SpA patients (22 SpA+IBD+ and 19 SpA+IBD-) and 50 IBD patients (control group, SpA-IBD+) were enrolled. Both category presented patients at beginning of a new biologic treatment. Upon enrolled, demographic, clinical and ultrasound features were collected for each patient. Peripheral venous blood and faecal samples were collected for each patients to determine IL-17A, TNF-alpha and sTREM1 plasmatic level and intestinal microbiota respectively. Moreover, patients with SpA underwent to the biopsy of the synovial membrane in order to assess the degree of inflammation, according to the Krenn Score (KSS).
Results: Considering intestinal involvement, SpA+IBD- showed a tendency of more severe synovitis grade compared to SpA+IBD+ (KSS: 3.00 (1.25-4.75) vs 1.50 (1.00-3.00) respectively, p: 0.059) and, considering SpA whole cohort, KSS directly correlated with inflammatory status assessed by CRP level (R: 0.540, p: 0.001). Considering the SpA and IBD whole cohort, articular and intestinal involvement affect cytokines levels independently from treatment: sTREM1 level was higher in SpA than in IBD (413 (247-563) vs 290 (220-344) pg/ml respectively, p: 0.003) and IL-17A level in SpA+IBD- vs SpA-IBD+ (0.49 (0.25-0.97) vs 1.00 (0.50-2.05) pg/ml respectively, p: 0.041), with direct correlation between sTREM1 and the clinical and synovial tissue aspects. Finally, regardless of intestinal involvement, SpA presented peculiar species richness and overall faecal microbiome composition compared to SpA-IBD+ with a significant difference between alpha and beta difference between these groups (p: 0.003 and p: 0.001 respectively).
Conclusion: SpA associated with the intestinal involvement present specific cytokines profile, synovial tissue features and faecal microbiome composition compared to SpA without IBD. These peculiar features can help in the management of SpA with or without intestinal involvement.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Simone Perniola Speakers bureau: ABBVIE, ELI LILLY ITALIA, GALAPAGOS BIOPHARMA, PFIZER, NOVARTIS, Consultant of: ABBVIE, ELI LILLY ITALIA, GALAPAGOS BIOPHARMA, PFIZER, Barbara Tolusso: None declared, Clara Di Mario: None declared, Daniela Pugliese: None declared, Dario Bruno: None declared, Marco Gessi: None declared, Laura Parisio: None declared, Giuseppe Privitera: None declared, Luisa Guidi: None declared, Stefano Alivernini Speakers bureau: ABBVIE, ELI LILLY ITALIA, PFIZER, NOVARTIS, Consultant of: ABBVIE, ELI LILLY ITALIA, PFIZER, NOVARTIS, Grant/research support from: PFIZER, Elisa Gremese Speakers bureau: ABBVIE, ELI LILLY ITALIA, PFIZER, NOVARTIS, Consultant of: ABBVIE, ELI LILLY ITALIA, PFIZER, NOVARTIS, Grant/research support from: ABBVIE.
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Rheumatoid arthritis - prognosis, predictors and outcome

POS0442 ENDOCITRULLINATION OF RA AUTOANTIGENS IS MORE ABUNDANT THAN C-TERMINAL CITRULLINATION IN THE GINGIVAL CREVICULAR FLUID OF ANTI-CCP POSITIVE AT-RISK INDIVIDUALS WITH PERIODONTAL DISEASE BUT NO SYNOVITIS

Keywords: Inflammatory arthritides

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Background: RA autoimmunity may be initiated at mucosal sites, including the periodontium. Anti-CCP positive at-risk individuals without synovitis (CCP+ at-risk) have an increased prevalence of periodontal disease (PD) and *Porphyromonas gingivalis* and an oral dysbiosis [1]. *P gingivalis* preferentially citrullinates C-terminal peptides by virtue of its peptidylarginine deiminase (PPAD) enzyme (2), whereas other periodontal bacteria predominantly induce endocitrullination [3]. These factors may trigger anti-citrullinated protein antibodies (ACPA), although the relative contribution of local C-terminal and endocitrullination is unclear.

Objectives: To determine the relative abundance of endo- and C-terminally citrullinated RA autoantigens in the gingival crevicular fluid (GCF) of CCP+ at-risk individuals with PD compared with controls.

Methods: CCP+ at-risk were identified from a UK cohort of anti-CCP+ individuals with musculoskeletal symptoms but no clinical synovitis. CCP+ at-risk underwent comprehensive periodontal assessment by a dentist, including GCF sampling from periodontally diseased sites. Control subjects (i.e. CCP-) with and without periodontal disease were also sampled. GCF was analysed by liquid chromatography mass spectrometry/mass spectrometry (LC-MS/MS) to identify endo- and C-terminally citrullinated peptides. The t-test was used for the statistical analysis.

Results: 25 CCP+ at-risk, 9 and 10 controls with and without PD respectively underwent GCF sampling. Mass spectrometry identified citrullination in 114 proteins in GCF, including 16 RA autoantigens (vimentin, myeloid cell nuclear differentiation antigen, keratin (type I/II cytoskeletal), heterogeneous nuclear ribonucleoprotein (A2/B1, K and U), fibrinogen (alpha and beta chain), histone (H1.4, H1.5, H1x, and H4), actin (cytoplasmic 2), apolipoprotein (A-I and A-IV)). In CCP+ at-risk with PD and controls without PD there was higher total abundance of endocitrullinated RA autoantigens compared with c-terminal citrullinated autoantigens in GCF ($p<0.05$, Figure 1). In CCP+ at-risk with PD 15 endocitrullinated RA autoantigens compared with only 4 C-terminally citrullinated RA autoantigens were identified (Figure 1). Fewer citrullinated RA autoantigens were identified in control subjects compared with CCP+ at-risk. More endocitrullinated compared with C-terminally citrullinated RA autoantigens were identified in controls with and without PD (Figure 1).

Conclusion: Several citrullinated RA autoantigens are present in the GCF of CCP+ at-risk individuals with periodontal disease but no synovitis. We identified endocitrullination as generally more abundant than C-terminal citrullination in both CCP+ at-risk and seronegative controls, suggesting PPAD may not be the primary source of citrullination. These data support the hypothesis that local citrullination of RA autoantigens at the periodontium may be an early driver of the ACPA response in RA.

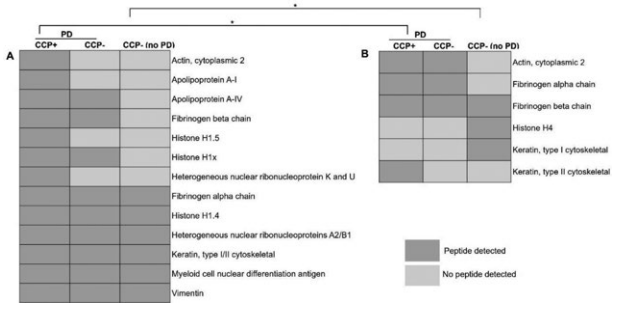


Figure 1. Citrullinated RA autoantigens in gingival crevicular fluid (GCF) samples. **(A)** Endocitrullinated RA autoantigens. **(B)** C-terminal citrullinated RA autoantigens. * indicates *p* value < 0.05, t-test. PD: periodontal disease; CCP+: anti-CCP positive individuals with new musculoskeletal symptoms but no synovitis; CCP-: anti-CCP negative individuals without musculoskeletal symptoms or synovitis.

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POS0443 CLINICAL OUTCOMES OF ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS WHO UNDERWENT PERCUTANEOUS CORONARY INTERVENTION: A NATIONWIDE COHORT STUDY

Keywords: Rheumatoid arthritis, Cardiovascular disease

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Background: Rheumatoid arthritis (RA), a systemic inflammatory arthritis, is associated with an increased risk of cardiovascular disease. Despite an increased proportion of elderly patients with RA and an increased prevalence of patients with RA undergoing percutaneous coronary intervention (PCI), studies on the PCI outcomes in elderly patients with RA are limited and controversial.

Objectives: This study aimed to evaluate the prognosis of elderly patients with and without RA who underwent PCI and the risk factors associated with the prognosis.

Methods: The Korean National Health Insurance Service claims database was used to extract data on 74623 patients (14,074 patients with RA and 60,549 patients without RA) aged 65 years or older who were diagnosed with acute coronary syndrome and underwent PCI between 2008 and 2019. The primary outcome was all-cause mortality between elderly patients with and without RA. The secondary outcome was all-cause mortality in elderly patients with RA who consist of patients with elderly onset RA that manifests after the age of 65 years and elderly patients who presented with young onset RA earlier in life.

Results: During a 10-year follow-up, the survival rate was lower in patients with RA than in those without RA (with RA: 53.7% vs. without RA: 58.3%, log-rank $P<0.001$). Compared to patients without RA, patients with elderly onset RA have poor survival outcomes and patients with young onset RA have good survival outcomes (with elderly onset RA: 48.1% vs. with young onset RA: 73.7% vs. without RA: 58.3%, log-rank $P<0.001$). Multivariable logistic regression analyses showed that diabetes mellitus (hazard ratio (HR) 1.39, 95% confidence intervals (CI) 1.35-1.43, $P<0.001$), chronic kidney disease (HR=3.97, 95% CI 3.63-4.34, $P<0.001$), and PCI due to myocardial infarction (HR=1.35, 95% CI 1.33-1.37, $P<0.001$) were the independent risk factors for all-cause mortality.

Conclusion: Elderly patients with RA who underwent PCI for acute coronary syndrome have an increased rate of all-cause mortality compared to general elderly patients. Among elderly patients with RA, patients with elderly onset RA particularly have poor survival outcomes. Based on the aspects of RA and cardiovascular disease in elderly patients, the clinical practice should focus on more detailed and active secondary prevention methods for a better prognosis.

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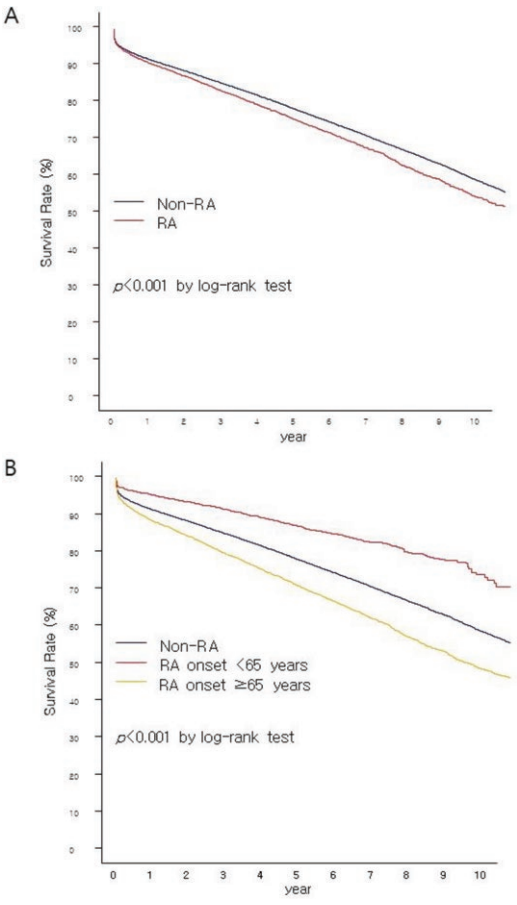


Figure 1. Survival rates from all-cause mortality through a period of 10 years. Kaplan-Meier curves are shown for the long-term survival in elderly patients with and without RA (A), according to age at the time of diagnosis of RA (B).

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POS0445

MORTALITY TRENDS AMONG RHEUMATOID ARTHRITIS PATIENTS IN WESTERN AUSTRALIA

Keywords: Rheumatoid arthritis

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Background: Mortality rates for patients with Rheumatoid Arthritis (RA) have reportedly improved in the past decades due to increasing access to specialised rheumatology care [1], early introduction of DMARDs with combination regimens [2], and subsequent biologics therapies [3]. However, the mortality rate remains higher than the general population, reducing the life expectancy by approximately ten years [4-5]. With scarce comparative data on mortality in Australian RA patients, we investigated temporal changes in standardised mortality rates for RA patients using longitudinal linked population-wide health data in Western Australia (WA) over the period 1980 to 2015.
Objectives: The aim of the study to estimate temporal standardised mortality rates over a 35-year period and identified leading causes of death and measured median Years Lost in a large RA cohort.
Methods: The study included 17,125 patients with a first-time hospital contact for RA (ICD-10-AM M05.00–M06.99 and ICD-9-AM 714) in the study period. Standardised mortality rate ratios (SMRRs) for the RA cohort versus the WA general population was estimated using direct age standardisation. We analysed temporal trends over death dates, causes from the WA death registry, and measured median Years of Life Lost by subtracting an individual's death age from their remaining life expectancy based on the Australian Government Actuary Life Table.
Results: Over the study period, SMRR was 2.5-folds (95%CI: 2.52-2.65) higher for RA patients than for the general population (Table 1), with a sex- and age-specific SMRR of 2.24 (95%CI 2.15–2.34) in males and 3.09 (95%CI 3.00–3.19) in females (Figure 1). The overall leading causes of death were diseases of the circulatory system, except among 30-44-year-olds in the 1991–2000 period, neoplasm was the leading cause of death. The median life years lost for the RA cohort were 5.7 years for females and 5.1 years for males over the study period (Table 1).
Conclusion: The mortality rate in RA patients in WA has decreased but remains higher than in Australian population. Malignant neoplasms were the second leading causes of death, and lung cancer was leading cause of cancer mortality. Together these data demonstrate the importance of screening and management for comorbidities in RA patients, especially cancer.

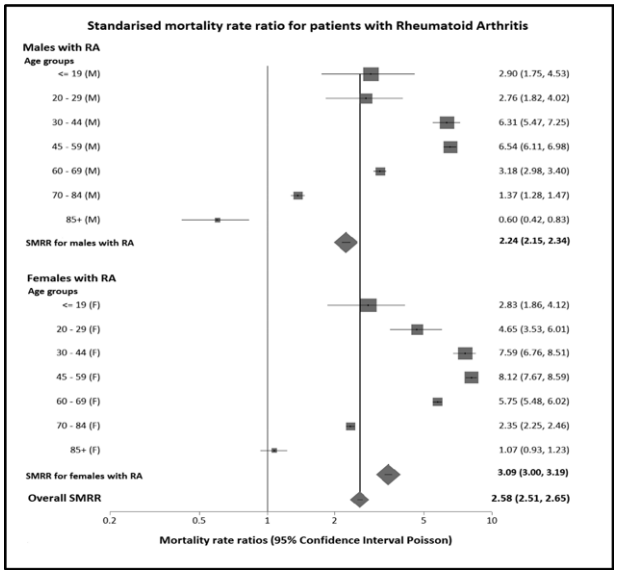


Figure 1. Standardised mortality rate ratios for patients with Rheumatoid Arthritis by sex and age in Western Australia (1980- 2015). RA= Rheumatoid Arthritis, M= Male, F= Female, SMMR= Standardised mortality rate ratio.

Table 1. The median life years lost for the Rheumatoid Arthritis cohort over study time periods.

RA cohort	Females		Male	
Median life years lost	**Median (IQR)**	**Percentage change (%)**	**Median (IQR)**	**Percentage change (%)**
Study periods				
1980- 2015	5.1 (3.4-8)	-	5.7 (3.9- 9.1)	-
1980- 1990	6.1 (4.4- 9.4)	0.0	7.4 (5-10.2)	0.0
1991- 2000	5.4 (3.7-8)	-11.5	5.9 (4.1- 9.3)	-20.3
2001- 2010	4.6 (3.2-7.3)	-14.8	5.0 (3.6- 8.3)	-15.3
2011- 2015	4.3 (3.1- 7.7)	- 6.5	5.2 (3.4- 9.1)	4.0

RA= Rheumatoid Arthritis, IQR= Interquartile Range.

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Registrations and staff at the Western Australian Data Linkage Branch to assist in the provision of data. Special thanks to the University of Western Australia to support KA with an Australian Government Research Training Program PhD Scholarship and the Australian Rheumatology Association WA for Research Fellowship Award.

Disclosure of Interests: Khalid Almutairi: None declared, Charles Inderjeeth Speakers bureau: Eli Lilly, David Preen: None declared, Helen Keen Speakers bureau: Pfizer Australia and Abbvie Australia, Johannes Nossent Speakers bureau: Janssen.

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POS0446 URINARY METHOTREXATE DOSAGE AS AN ADHERENCE MEASUREMENT IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Epidemiology, Disease-modifying drugs (DMARDs), Treat to target

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Background: Non-adherence to rheumatoid arthritis treatments is common and must be identified, especially with the treat-to-target strategy. A methotrexate (MTX) urinary dosage (METU) was developed using high performance liquid chromatography by spectrometry method (HPLC-MS/MS).

Objectives: The aim of our study was to assess medication compliance for MTX in RA using METU under real-life conditions and to compare it with the usual indirect adherence measurement techniques.

Methods: We conducted a prospective study at the CHU de Reims. Patient inclusion comprised of RA patients over 18 years old who have been using MTX for more than 6 months. Patients were invited to fill demographic, clinical and psychological datas and other adherence measurement techniques (the CQR and the MPR). A urinary sample was taken to measure MTX and information about tolerance were collected through the MISS questionnaire.

Results: 84 patients with RA were analyzed, 26 using oral MTX and 58 subcutaneous MTX; 73% female, mean age 61.5 years, mean dose 15mg/week, 62% associated with biotherapy. 77 patients (91.7%) were adherent to treatment according to METU, whereas MPR and CQR reported less adherence (69.5% and 61.9% respectively). MPR and METU were not significantly different in subcutaneous MTX users (p = 0,059). Non-adherent patients had a higher number of tender joints and CRP value.

Table 1. Comparison's results of the different adherence measurement techniques.

Adherence	PO + SC (n=84)	P-value	SC (n = 58)	P-value
METU	**91,7%** (83,6 – 96,6) n = 77	x	91,4 (81,0 - 97,1) n = 53	x
MPR	69,5% (58,4 – 79,2)* n = 57	< 0,05	77,6 (64,7 – 87,5) n = 45	0,059
CQR	61,9% (50,7 – 72,3) n = 52	< 0,05	63,8 (50,1 – 76,0) n = 37	< 0,05

*2 missing data

Conclusion: This is the largest study evaluating MTX adherence treatment in RA patients using a urinary dosage. We identified that indirect adherence measurements did not reflect real life adherence. METU can be used in RA patients with unexplained response to treatment before escalating therapeutic strategy.

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POS0447 DIFFICULTIES TO SLEEP EXPLAIN HIGH PATIENT REPORTED OUTCOMES VALUES IN PATIENTS WITH INFLAMMATORY ARTHRITIS WITH NO SWOLLEN JOINTS

Keywords: Outcome measures

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Background: Patient reported outcomes (PROs) are valuable tools to understand how a patient is doing. Patient self-report of pain, fatigue and global health on a 100 mm Visual Analog Scale are routine measures in rheumatology and may be interpreted as measures of disease activity.

Objectives: To study whether good/poor sleep influences other clinical measures in patients with psoriatic arthritis (PsA) and rheumatoid arthritis (RA).

Methods: A total of 13527 (72 % female) patients with rheumatoid arthritis (RA) and 3644 (52 % female) patients with psoriatic arthritis (PsA) were identified in the Finnish national quality register for inflammatory arthritides. Clinical data from the most recent outpatient clinic visit between January 1st 2021 to July 31st 2022 was used in this study. Patients were divided into groups by self-reported difficulty to sleep on a MDHAQ question "over the last week, were you able to get a good night's sleep" with response options "without any difficulty" and "with some difficulty" as good sleep and "with much difficulty" and "unable to do" as poor sleep. Median values with interquartile ranges of other clinical measures were compared between the groups. Descriptive statistics and regression models were used for comparison with p=0.05 as a threshold for statistical significance.

Results: The mean (SD) age was 62 (14) for patients with RA and 55 (14) for patients with PsA. A total of 16 % of RA patients and 22 % of PsA patients had poor sleep. The values for DAS28, SJC 66, TJC 68, CRP and ESR were low and similar in patients with poor sleep and good sleep. The VAS-values for pain, fatigue and PGA for RA patients with good sleep were 18 (6, 40), 17 (4, 42) and 23 (9, 46) and 54 (29, 74), 64 (43, 80) and 56 (39, 72) (p<0.001 for all comparisons) for patients with poor sleep. In patients with PsA, the corresponding numbers were 20 (6, 41), 17 (4, 40) and 19 (6, 38) and 59 (36, 74), 66 (44, 81) and 56 (38, 73) (p<0.001 for all comparisons). The results were similar for PROs in patients with PsA (n=942) and RA (n=2861) with an SJC66 of 0. (Figure 1.)

Conclusion: The assessment of sleep is crucial for patients presenting severe symptoms without markers of disease activity.

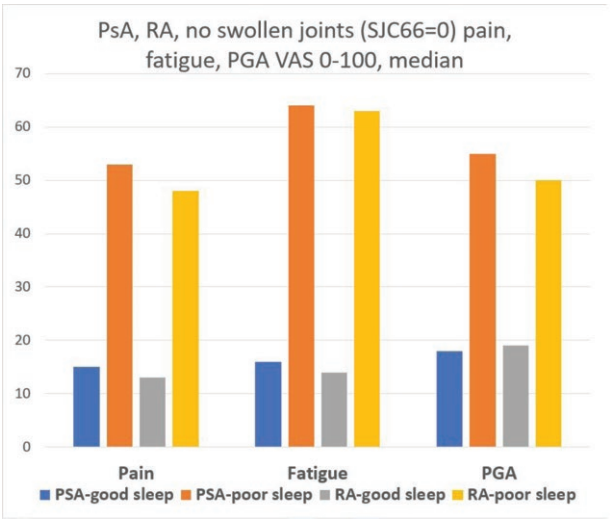


Figure 1. Median VAS-values for pain, fatigue and PGA in patients with PsA and RA with poor sleep and good sleep. All patients had no swollen joints.

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Acknowledgements: NIL.
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POS0448

IDENTIFICATION OF JOINT LOCATIONS IN AN EARLY RHEUMATOID ARTHRITIS COHORT AS A CHARACTERISTIC OF DISEASE SEVERITY AND RESPONSE TO METHOTREXATE, DATA FROM THE ERA-UCLOUVAIN BRUSSELS COHORT

Keywords: Descriptive studies, Rheumatoid arthritis, Prognostic factors

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Background: Early RA patients (ERA pts) often present with different areas of joint involvement, but limited data exist to identify which specific joint locations may be indicative of greater disease severity.
Objectives: This analysis investigated the baseline (BL) prevalence of swelling, tenderness and erosions in individual joint locations and their possible association with disease characteristics, prognostic factors and response to Methotrexate (MTX) in a cohort of ERA pts.
Methods: This analysis was based on data from the ERA UCLouvain Brussels cohort in which patients were included according the ACR/EULAR 2010 criteria and naïve to DMARDs. The physician assessed prevalence of BL individual swollen and tender joint status (present, absent) through a physical examination. The joint count includes 44 joints. Similarly, all patient and RA characteristics were collected. The association between BL swelling, tender, erosions and disease characteristics was investigated for each individual joint. Remission rates (DAS28-CRP < 2.6) in patients treated only with MTX were assessed in order to analyze the correlation with BL joint location.
Results: BL location of each swollen, tender, or erosive joint (44 joints) is summarized in Table 1:

Table 1.

N=452*2	Total Erosives (%)	Total Swollen (%)	Total Tender (%)
Shoulders	2 (0%)	27 (3%)	225 (25%)
Elbows	0 (0%)	74 (8%)	139 (15%)
Wrists	**69 (8%)**	**515 (57%)**	**459 (51%)**
Knees	1 (0%)	186 (21%)	270 (30%)
Ankles	1 (0%)	209 (23%)	266 (29%)
MCP1	29 (3%)	**251 (28%)**	266 (29%)
MCP2	47 (5%)	**311 (34%)**	**303 (34%)**
MCP3	36 (4%)	**235 (26%)**	272 (30%)
MCP4	18 (2%)	75 (8%)	161 (18%)
MCP5	21 (2%)	89 (10%)	174 (19%)
PIP1	8 (1%)	89 (10%)	96 (11%)
PIP2	18 (2%)	**351 (39%)**	**338 (37%)**
PIP3	14 (2%)	**358 (40%)**	**332 (37%)**
PIP4	17 (2%)	178 (20%)	242 (27%)
PIP5	11 (1%)	151 (17%)	221 (24%)
MTP1	**53 (6%)**	67 (7%)	187 (21%)
MTP2	**55 (6%)**	166 (18%)	281 (31%)
MTP3	**80 (9%)**	169 (19%)	295 (33%)
MTP4	45 (5%)	114 (13%)	263 (29%)
MTP5	**128 (14%)**	70 (8%)	192 (21%)

The most frequent swollen joint was the wrist (57%), followed by PIP3 (40%) and PIP2 (39%), MCP2 (34%), MCP1 (28%) and MCP3 (26%). Erosions were most frequent in MTP5 (14%), MTP3 (9%), wrists (8%), MTP1 and MTP2 (6%). Swollen and tender joints were well associated except for shoulder (3% vs 25%), wrist (8% vs 15%) and MTP (see table 1).We found a significant correlation between erosion and swelling for wrists, MCP1-3 joints and MTP1-5 joints. As expected, erosive joint was observed first in MTP5 (14%) followed by the MTP3 (9%) and the wrist (8%). MTP4 and 5 joint locations were more present in younger and MCP 2-4 in older patients. BL swelling in the large size joints (knee, elbow, shoulder and ankle), in the medium size joint (wrist) and the small size joints (only MCP3, IPP 1, 2 and MTP5) was highly associated with higher DAS28-CRP*. BL swelling of the MCP1, 3, 4; MTP 1,2, 5 was associated with erosive disease. In contrast, swelling of the knee was correlated with non erosive and seronegative RA. Swelling of joint location such as knee, shoulder, ankle, MCP 1-5, MTP1, 5 and IPP 1, 2 was significantly correlated with a higher HAQ. Only swelling of MTP1, 2, 5 was associated with the presence of ACPA antibodies. No difference was observed for smoking habits and gender. Comparison between BL joint location in patients achieving remission or not has been evaluated. Patients with BL erosion and swelling in the feet responded less to MTX of non-response (respectively 18,2% vs 35.1% and 25% vs 35.1%). For patients with swollen wrist, we observed the same trend without significance. Smoking habits and rheumatoid factor positivity were more present in the non-responder group (29.6% and 66.1% versus 14% and 46.5%).

Conclusion: In our cohort of ERA naïve to DMARD, swelling was most present in wrist and hand joints (PIP 3 and 2). Erosions were most frequent in MTP joints and wrist. Clinical response to MTX was poorer in patients with swelling of the wrist and feet as well as erosion of the feet. Joint location could be an additional prognostic factor in ERA for severity and response to MTX suggesting more intensive therapy.
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Disclosure of Interests: None Declared.
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POS0449

PRESENCE OF PERIODONTAL DISEASE AND THE INCIDENCE OF INFLAMMATORY ARTHRITIDES IN THE GENERAL POPULATION: DATA FROM THE UK BIOBANK

Keywords: Rheumatoid arthritis, Psoriatic arthritis, Inflammatory arthritides

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Background: Patients with inflammatory arthritides (IA) are now recognized to present with inflammation in the periodontium frequently. However, the association between signs of periodontal inflammation and IA onset has been poorly described in the existing literature.
Objectives: To investigate the association between periodontal disease and the development of inflammatory arthritides (IA) in the general population.
Methods: In total, 489,125 participants from the UK Biobank without a previous history of rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA) were enrolled. The primary outcome was the incidence of IA, which was a composite of RA, AS, and PsA according to the presence of periodontal disease based on self-reported oral health indicators. Multivariate Cox proportional hazard regression analyses using four different models were performed to assess the association between periodontal disease and IA development.
Results: In all, 86,905 and 402,220 individuals were categorized as with and without periodontal disease, respectively. Cox hazard analysis indicated that the presence of periodontal disease was an independent predictor of the occurrence of composite outcomes of IA, which was also consistent for RA and AS. Significant associations were found to be consistent in the four Cox models and were replicated even when different criteria were used to define periodontal disease. Subgroup analyses indicated that periodontal disease was associated with an increased RA risk in those aged <60 years, and this risk was persistent for both male and female patients and for patients with seropositive/seronegative RA.
Conclusion: Self-reported periodontal disease is associated with IA incidence in participants included in the UK Biobank, particularly for RA and AS. Higher clinical attention and optimal dental care in patients with signs of periodontal disease may be recommended for early disease detection and for reducing this risk.

Table 1. Hazard ratios for the risk of incident inflammatory arthritis according to the presence of periodontal disease

	Events, n (%)	Person-years	Incidence rate 10,000 person-years	Model 1	Model 2	Model 3	Model 4
Inflammatory arthritides	8672 (1.8)	5,817,784	14.9				
Without (n=402,220)	6998 (1.7)	4,789,623	14.6	Reference	Reference	Reference	Reference
With (n=86,905)	1674 (1.9)	1,028,161	16.2	1.11 (1.05–1.17) <0.001	1.15 (1.08–1.23) <0.001	1.14 (1.07–1.22) <0.001	1.11 (1.03–1.19) 0.003
Rheumatoid arthritis	7409 (1.5)	5,825,688	12.7				
Without (n=402,220)	5973 (1.5)	4,796,037	12.4	Reference	Reference	Reference	Reference
With (n=86,905)	1436 (1.7)	1,029,651	13.9	1.12(1.06–1.18) <0.001	1.17 (1.09–1.25) <0.001	1.16 (1.08–1.24) <0.001	1.15 (1.07–1.24) <0.001
Ankylosing spondylitis	2661 (0.5)	5,851,479	4.5				
Without (n=402,220)	2137 (0.5)	4,816,805	4.4	Reference	Reference	Reference	Reference
With (n=86,905)	524 (0.6)	1,034,673	5.0	1.14 (1.03–1.25) 0.009	1.18 (1.06–1.31) 0.002	1.16 (1.04–1.30) 0.008	1.15 (1.02–1.30) 0.010
Psoriatic arthritis	877 (0.2)	5,865,731	1.4				
Without (n=402,220)	718 (0.2)	4,828,230	1.4	Reference	Reference	Reference	Reference
With (n=86,905)	159 (0.2)	1,037,501	1.5	1.03 (0.86–1.22) 0.340	1.01 (0.83–1.22) 0.940	0.97 (0.79–1.19) 0.750	0.97 (0.79–1.20) 0.770

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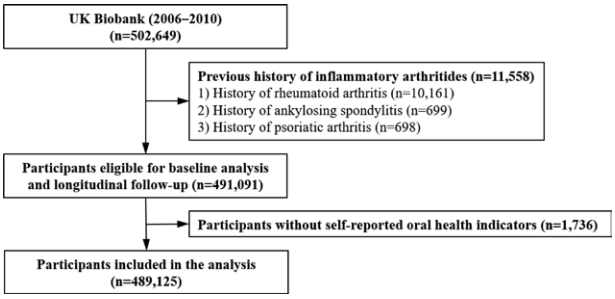


Figure 1.

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POS0450

MORTALITY AND CAUSES OF DEATH IN A LARGE COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS: A POPULATION-BASED STUDY

Keywords: Comorbidities, Outcome measures, Rheumatoid arthritis

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Background: Whether or not in the last years mortality is still increased in RA patients compared to the general population is controversial.

Objectives: To assess mortality rates (MRs), standardized mortality ratios (SMRs), and causes of death in Rheumatoid Arthritis (RA) in a population-based study.

Methods: We analyzed linked administrative health databases of the Veneto Region (Italy, 4,900,000 residents): the population registry, where all residents are recorded, was linked with healthcare co-payments exemptions, hospital discharge records, and mortality records. RA was defined by a healthcare copayment exemption for or any hospital diagnosis of RA. We analyzed all-cause mortality until December 31, 2020. MRs per 1,000 were stratified by year, sex, and age group. SMRs were derived, by comparing MRs of the general regional population. Causes of death were coded using the ICD-10 coding system and were available until 31/12/2020; they were grouped in: RA, infectious diseases, cardiovascular diseases (CVD), cancer, diabetes, or others.

Results: Between 2012 and 2020, 7,435 deaths among 37,996 RA prevalent cases occurred, corresponding to an average annual standardized MR of 32.2 (95% CI 31.5; 33.0) per 1,000 persons. The median (IQR) age at death was 83 years (77-88), lower in males (81, 75-86) compared to females (84, 78-89). Standardized MR was higher in males than in females (41.3, 95% 39.05-43.2 vs. 29.5, 95% CI 28.7-30.3); notably, this was true across all age groups (Table 1). Causes of death were CVD 2,735 (37.1%), cancer 1,519 (20.6%), infections 827 (11.2%), RA 352 (4.8%), diabetes 208 (2.8%), trauma, poisoning, or post-surgical/procedural complications 197 (2.7%), and others 1,532 (20.6%). Out of 12,875 incident RA patients, 1,288 died during the study period, corresponding to a mortality rate of 21.3 (95% CI 20.2-22.5). The distribution of causes of death among incident cases was comparable to that observed among prevalent cases. Overall SMR was 1.28 (95% CI 1.21-1.35) and was higher in younger patients (<45 years old: 2.15, 95% CI 0.93-4.24) (Figure 1). Eight-year survival was significantly affected by age at diagnosis: 98.8% (95% CI 98.1%-99.2%) in patients aged <50 years, 95.8% (94.5%-96.8%) in patients aged 50-59, 94.2% (92.2%-95.7%) in patients aged 60-64, 84.1% (81.7%-86.2%) in those aged 65-75, and 48.4% (45%-51.6%) in those aged >75 years.

Conclusion: Standardized mortality ratio is slightly increased in RA patients compared to the general population, especially in younger patients. Despite that, eight-year survival in subjects <49 is good. CVD and cancer represent the main causes of death in RA, whereas therapy-related complications such as infections account for a low proportion of deceases.

Table 1. Deaths and mortality rates among 37,996 prevalent RA cases (2012 - 2021).

Year	Patients at Jan 1st			Deaths Jan 1st - Dec 31st			Rate x1000 residents with RA			Standardized mortality rates x1000 residents (95% CI)		
	TOT	M	F	TOT	M	F	TOT	M	F	TOT	M	F
2012	23402	5811	17591	705	199	506	30,1	34,2	28,8	34,3 (31,8; 36,9)	46,8 (39,9; 53,8)	30,7 (28,0; 33,4)
2013	24035	5983	18052	721	201	520	30,0	33,6	28,8	32,7 (30,3; 35,1)	43,5 (37,2; 49,9)	29,4 (26,8; 31,9)
2014	24715	6194	18521	713	199	514	28,8	32,1	27,8	30,8 (28,5; 33,1)	39,0 (33,4; 44,6)	27,9 (25,5; 30,3)
2015	25557	6436	19121	814	209	605	31,9	32,5	31,6	33,1 (30,8; 35,3)	39,8 (34,2; 45,4)	31,1 (28,7; 33,6)
2016	26173	6656	19517	797	216	581	30,5	32,5	29,8	30,9 (28,8; 33,1)	37,6 (32,4; 42,7)	28,6 (26,3; 30,9)
2017	26928	6924	20004	883	248	635	32,8	35,8	31,7	32,8 (30,6; 35,0)	41,9 (36,5; 47,2)	30,2 (27,8; 32,5)
2018	27582	7095	20487	887	261	626	32,2	36,8	30,6	31,5 (29,4; 33,6)	41,9 (36,7; 47,1)	28,6 (26,3; 30,8)
2019	28239	7296	20943	888	242	646	31,4	33,2	30,8	30,4 (28,4; 32,4)	37,3 (32,5; 42,1)	28,3 (26,1; 30,5)
2020	28740	7446	21294	1027	304	723	35,7	40,8	34,0	33,7 (31,6; 35,8)	45,0 (39,8; 50,1)	30,5 (28,2; 32,7)
2012-2020	**235371**	**59841**	**175530**	**7435**	**2079**	**5356**	**31,6**	**34,7**	**30,5**	**32,2 (31,5; 33,0)**	**41,3 (39,5; 43,2)**	**29,5 (28,7; 30,3)**

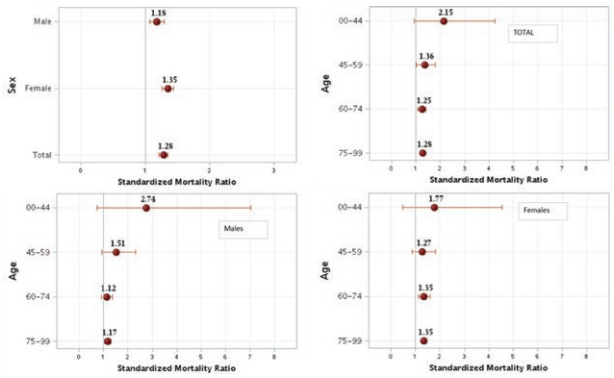


Figure 1. Standardized mortality ratios among 12,875 incident RA cases according to sex and age

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0451 POOR SLEEP QUALITY INCREASES PRESENTEEISM BUT NOT ABSENTEEISM IN RA PATIENTS

Keywords: Patient reported outcomes, Work-related issues, Rheumatoid arthritis

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Background: Patients with inflammatory arthritis frequently suffer from poor sleep affecting their quality of life and work productivity i.e., higher presenteeism reflecting the disability to concentrate on work tasks despite being present at work. Sleep disturbances are reported to be more related to emotional factors than activity of the disease. However, sleep quality is rarely assessed in daily rheumatological practice and only few patients receive treatment for insomnia. Assessing sleep quality in MDHAQ form on a scale from 0 (without any difficulty) to 3 (unable to do) could be a simple tool to identify patients who need more profound evaluation of sleep disorders and intervention aimed at improving their work efficiency.
Objectives: Assessing the relationship between sleep quality and work outcomes in patients with rheumatoid arthritis (RA) by 1) evaluating the frequency of sleep disorders according to 0–3-point scale in MDHAQ form 2) finding a cut-off point for presenteeism and absenteeism discriminating patients with or without sleep disturbances and 3) defining the association between disease activity, sleep quality and work outcomes.
Methods: Cross sectional study of one year data from PolNorRHEUMA registry. Sleep assessment was based on MDHAQ, and patients were categorized into 4 groups according to the severity of sleep disorders. To assess presenteeism and absenteeism we used the Work Productivity and Activity Impairment Questionnaire (WPAI). The results were obtained using STATISTICA Tibco 13.3 software. All continuous variables were non-normally distributed, thus were presented in the manuscript as a median and compared by Mann-Whitney U-test, Kruskal-Wallis or multiple repetition test. To assess the point discriminating between different groups of patients depending on the severity of the sleep disorder, the cut-off point of presenteeism was calculated based on receiver operating characteristic (ROC) curves.
Results: Among 250 adult patients with RA, 63 (25%) didn't have ANY difficulties with sleep, 130 (52%) had SOME, 43 (17%) had MUCH and 14 (6%) were UNABLE to sleep. After analyzing 130 available WPAI questionnaires, we found that the cut-off value for presenteeism of 40% differentiates people with good sleep (MDHAQ sleep= 0 and 1) from those with a poor sleep (MDHAQ sleep = 2 and 3) whereas the cut-off = 10% differentiate group with no sleep disorders from group 1+2+3 combined. Interestingly, no such relation was found for absenteeism. Patients with poor sleep were significantly older, had higher BMI, DAS28, SJC and TJC (but not ESR and CRP), higher pain, joint pain and fatigue. After adjusting for age, sex, BMI, and CRP we found positive association between presenteeism and MDHAQ sleep score, TJC and morning stiffness (beta=11.6, beta=0.9, beta=8.36 respectively) but no association with SJC. Only 16 (6,4%) patients received treatment for insomnia.
Conclusion: Poor sleep quality according to MDHAQ indicates a very high presenteeism and poor work productivity, with no influence on absenteeism. Sleep, TJC and morning stiffness but no other disease activity parameters contribute to presenteeism. Scoring 2 or 3 in a question regarding sleep quality in the MDHAQ form should lead to sleep evaluation and specific intervention, independent of RA activity.
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POS0452 DIAGNOSTIC AND PROGNOSTIC ROLE OF SERUM KL-6 IN RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

Keywords: Lungs, Biomarkers, Rheumatoid arthritis

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Background: Interstitial lung disease (ILD) is one of the leading causes of morbidity and premature mortality in rheumatoid arthritis (RA) patients. Some studies have shown that Krebs von den Lungen-6 (KL-6) may be a valuable biomarker for diagnosis and stratifying prognosis in Rheumatoid Arthritis-Associated Interstitial Lung Disease (RA-ILD).
Objectives: To evaluate the diagnostic and prognostic value of serum KL-6 in RA-ILD patients.
Methods: We conducted a retrospective study that included patients with RA (ACR/EULAR 2010 criteria) with available KL-6 data measured in blood serum at study enrolment. Patients were evaluated between February 2017 and October 2019 at a single center. ILD was diagnosed by high-resolution computed tomography (HRCT) and confirmed by a multidisciplinary committee. Serum KL-6 levels were measured by Lumipulse G KL-6 Kit (Fujirebio, Japan), using Chemiluminescent enzyme immunoassay (CLEIA). The reference value for KL-6 in healthy subjects was 118-627 U/mL. The inter-assay variation coefficient of the reagent was ≤ 4.4%. We performed a bivariate analysis according to the presence of ILD and high levels of KL-6. Mortality was assessed in December 2022 by medical chart review.
Results: A total of 166 patients were included (36 RA-ILD and 130 RA-non-ILD). Patient baseline characteristics were as follows: female gender 76.5%, mean age 62.9 ± 12.3 years, mean disease duration 9.1 ± 8.7 years, RF positive 66.3%, anti-CCP positive 85.5%, erosive disease 56.0%, and mean DAS28 3.0. The median follow-up period was 5 years (IQR 4.0–5.0). At baseline, patients with RA-ILD were older (69.9 ± 16.1 vs. 60.9 ± 12.3 years; p<0.001), were more frequently males (36.1% vs. 20.0%; p=0.044), had a longer disease duration (12.2 ± 1.3 vs. 8.3 ± 8.7 years; p=0.020), had higher RF titers (412.1 ± 120.5 vs. 165.6 ± 221.1; p<0.001), had a higher disease activity (DAS28 3.7 ± 0.2 vs. 2.8 ± 1.1; p<0.001), and higher mortality (33.3% vs. 9.2%; p<0.001). Among RA-ILD patients at baseline, the median FVC and DLco (% predicted value) were 79 (IQR 72.6–87.0) and 60 (IQR 49.0–70.4), respectively. Usual interstitial pneumonia (UIP) was the predominant pattern at HRCT in half of the patients (18/36). The mean serum KL-6 level at baseline was 513.1 ± 480.1 U/mL. KL-6 levels were abnormally elevated in 35 patients (21.0%). Serum levels of KL-6 in the RA-ILD group were significantly higher than those in the RA-non-ILD group

(884.0 ± 134.6 vs. 410.4 ± 262.4 U/mL; p<0.001). Patients with high KL-6 had a higher prevalence of RA-ILD (54.3% vs. 13.0%; p<0.001) and UIP pattern at HRCT (22.9% vs. 7.6%; p<0.001), as well as higher mortality (34.3% vs. 9.2%; p<0.001) (**Table 1**). During follow-up, 24 (14.5%) patients died, mainly due to respiratory infections (62.5%). The median time to death was 20 months (IQR 7.0–29.0).

Conclusion: Our results suggest that high KL-6 levels might be helpful as a biomarker for diagnosis and prognosis stratification in patients with RA-ILD, especially in patients with UIP pattern at HRCT.

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Table 1. Baseline characteristics in patients with RA according to serum KL-6 status.

Variable	All population N=166	High KL-6 n=35	Normal KL-6 n=131	*P*
Age, years	62.9 ± 12.3	**68.0 ± 10.0**	61.5 ± 12.5	**0.005**
Male gender	39 (23.5)	12 (34.3)	27 (20.6)	0.090
Ever smoking	86 (51.8)	18 (51.4)	68 (51.9)	0.871
RA duration, years	9.1 ± 8.7	10.7 ± 7.8	8.7 ± 8.9	0.250
RF, positive	110 (66.3)	25 (71.4)	85 (64.9)	0.467
RF, titer (IU)	219.1 ± 399.5	**395.5 ± 685.0**	172.0 ± 263.2	**0.003**
ACPA, positive	142 (85.5)	28 (80.0)	114 (87.0)	0.294
ACPA, titer (CU)	1201.6 ± 2107.4	1257.6 ± 1096.2	1186.7 ± 2306.8	0.860
DAS28-ESR	3.0 ± 1.2	3.3 ± 1.3	2.9 ± 1.2	0.094
GC, current	99 (59.6)	**27 (77.1)**	72 (55.0)	**0.018**
MTX, current	101 (69.8)	20 (57.1)	81 (61.8)	0.614
bDMARD, current	51 (30.7)	9 (25.7)	**42 (32.1)**	**0.020**
RA-ILD	36 (21.7)	**19 (54.3)**	17 (13)	**<0.001**
UIP pattern (HRCT)	18 (18.8)	**8 (22.9)**	10 (7.6)	**<0.001**
FVC, % predicted	79.7 ± 16.2	77.1 ± 15.7	82.8 ± 16.7	0.289
DLco, % predicted	63.0 ± 16.6	59.2 ± 17.3	67.9 ± 14.8	0.116
Mortality	24 (14.5)	**12 (34.3)**	12 (9.2)	**<0.001**

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POS0453 BASELINE PREVALENCE AND FACTORS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE IN TWO RHEUMATOID ARTHRITIS INCEPTION COHORTS IN THE UK

Keywords: Lungs, Comorbidities, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic, inflammatory disease with interstitial lung disease (ILD) being an important extra-articular manifestation, associated with significant morbidity and mortality.

Objectives: To determine the prevalence of ILD at time of RA diagnosis and identify baseline independent factors associated with ILD.

Methods: Two early inception cohorts (1986-2001) were used: the early RA network (ERAN) and the early RA study (ERAS). Socio-demographic, clinical and laboratory measures were recorded at baseline, 6 months and yearly thereafter. Baseline variables collected and included in analyses were: seropositivity, body mass index (BMI), ethnicity, measures of deprivation, smoking status. Comorbidity burden was evaluated using the rheumatic disease comorbidity index (RDCI). Baseline prevalence (proportion of individuals with ILD at baseline) and 95% confidence interval was estimated. Multivariable regression analyses were performed to identify risk factors at baseline associated with RA-ILD development. Multiple imputation was used for missing data.

Results: Data from a total of 2701 patients were included in the study, from whom 101 patients were diagnosed with ILD. Follow up was up to 25 years (mean 6.8 years); 75% of patients followed for ≥10 years. Of these, 12% had ILD at baseline; 46% were diagnosed with ILD during follow up and 43% were diagnosed with ILD post-mortem. The estimated prevalence of ILD at baseline was 0.44% (95% CI 0.19% to 0.69%). Univariable analyses of baseline factors showed age at onset (p<0.001), ever smoking (p=0.010), seropositivity (p=0.002), RDCI (p<0.001) and lung disease (p<0.001) to be associated with developing RA-ILD. Multivariable logistic regression showed age at onset (OR 1.03, 95% CI 1.01 to 1.05), seropositivity (OR 2.39, 95% CI 1.27 to 4.50) and ever smoking (OR 2.01, 95% CI 1.16 to 3.50) to be associated with ILD development. An increase in RDCI predicted higher ILD (OR 1.46, 95% CI 1.16 to 1.82). More recent recruitment year into the cohort was associated with decreased odds of developing ILD.

Table 1. Univariable and Multivariable Analyses.

Baseline Variables	Univariable analysis		Multivariable analysis	
	Odds Ratio (95% CI)	p-value	All comorbidities (n=2,689) Odds Ratio (95% CI)	Lung Disease (n=2,689) Odds Ratio (95% CI)
Age at onset *(years)*	1.03 (1.02, 1.05)	<0.001	1.03 (1.01, 1.05)**	1.03 (1.02, 1.05)**
Female Gender	0.56 (0.37, 0.86)	0.009	0.74 (0.47, 1.16)	0.74 (0.47, 1.16)
Minority Ethnicity	1.94 (0.76, 4.91)	0.201	-	-
IMD quintile	0.91 (0.77, 1.07)	0.243	-	-
Ever Smoked#	1.91 (1.15, 3.15)	0.010	2.01 (1.16, 3.50)*	2.01 (1.20, 3.38)**
Recruitment year	0.98 (0.95, 1.01)	0.146	0.95 (0.93, 0.98)**	0.97 (0.94, 0.99)*
Body Mass Index *(kg/m^2)*	0.99 (0.95, 1.04)	0.706	-	-
HAQ-DI	1.21 (0.92, 1.58)	0.172	-	-
DAS28	1.09 (0.93, 1.27)	0.279	-	-
Seropositive#	2.40 (1.29, 4.44)	0.002	2.39 (1.27, 4.50)**	2.57 (1.37, 4.85)**
Time to DMARD *(months)*	1.01 (1.00, 1.02)	0.183	-	-
RDCI	1.51 (1.24, 1.83)	<0.001	1.46 (1.16, 1.82)**	-
Lung disease	5.29 (3.12, 8.96)	<0.001	-	4.69 (2.72, 8.08)**

*IMD: Index of Multiple Deprivation, HAQ-DI: Health Assessment Questionnaire Disability Index, DAS28: Disease Activity Score 28 joint count, RDCI: Rheumatic Diseases Comorbidity Index**p<0.01, *p<0.05# Imputed values*

Conclusion: Baseline prevalence of ILD was very low. Seropositivity, smoking, higher comorbidity burden and age at onset increased the odds of subsequent ILD development. Identifying RA-ILD predictors early on is important to ensure appropriate screening, timely diagnosis and treatment.

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POS0454

WHAT ROLE DO SOCIOECONOMIC FACTORS PLAY IN PATIENTS WITH PERSISTENT ACTIVE RHEUMATOID ARTHRITIS? DATA FROM A LARGE UK EARLY INFLAMMATORY ARTHRITIS AUDIT

Keywords: Registries, Rheumatoid arthritis, Prognostic factors

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Background: The basis for progression to a refractory disease state in up to 20% of patients with rheumatoid arthritis (RA) is unclear. Recent evidence suggests that non-biological characteristics, such as psychosocial factors, may interplay with biological (disease-related) factors to drive refractory disease in inflammatory arthritis[1].

Objectives: To explore which biological and non-biological factors associate with persistent active RA (pactiveRA) in the first year, despite use of conventional synthetic DMARDs.

Methods: Observational cohort data from adult early RA patients in the National Early Inflammatory Arthritis Audit (NEIAA) across England and Wales between May 2018 and Oct 2022, were acquired. Patients were defined as having pactiveRA based on three consecutive Disease Activity Scores (DAS28) of >3.2 at baseline, three and 12 months of follow up. Controlled RA (contRA) was defined as patients with a DAS28 ≤ 3.2 at the three and 12 month time-points, (having started off with a baseline DAS28 of >3.2). Univariable, followed by multivariable analyses were applied, the latter using stepwise forward logistic regression to explore associations with pactiveRA. PactiveRA status was used as the outcome variable. Age and gender were included in the models as a priori, with socioeconomic variables handled as the main independent variables (social deprivation, smoking-status and comorbidities) of interest, followed by clinical variables.

Results: A total of 682 patients with pactiveRA and 1,026 contRA patients were included. Compared to contRA, patients with pactiveRA were younger (aged 58, interquartile range (IQR): 49, 67) vs (62, IQR: 52,72), included more females (69% vs 59%), were current or ex-smokers, and more likely to have depression, lung and gastrointestinal disease. Also, patients with pactiveRA had worse scores in patient reported outcomes at baseline and Patient Health Questionnaire Anxiety and Depression Screener. Logistic regression results are summarised in the Table 1. Age, gender, living in a socially deprived area and being an ex or current smoker, were independently associated with pactiveRA in models controlling for markers of disease severity (seropositivity). Baseline corticosteroid use was also associated with pactiveRA (p<0.05 for all) and having a concomitant diagnosis of depression, odds ratio (OR) 2.30 (95%CI: 1.67,3.17), lung disease OR 1.46 (95%CI: 1.14,1.86) and gastric ulcer OR 1.71 (95%CI: 1.17,2.50) were significantly related to pactiveRA.

Conclusion: Sociodemographic factors (age, gender) and living in socially deprived areas were all associated with pactiveRA, independent of clinical and disease characteristics. Identifying 'adverse' socioeconomic factors that could drive persistent active disease early in the disease process, can help tailor interventions according to individual characteristics and need.

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Table 1. PactiveRA: association with socioeconomic clinical and treatment variables

Independent predictors at baseline	Univariable analysis OR (95% CI)	Multivariable analysis OR (95% CI)
Age (years)	0.99 (0.98,0.99)	0.99 (0.98,0.99)
Female gender	1.37 (1.15,1.63)	1.38 (1.16,1.64)
IMD (less social deprivation)	0.91 (0.88,0.94)	0.92 (0.89,0.95)
Ever smoked (referent never-smoked)	1.21 (1.02,1.43)	1.22 (1.02,1.47)
Depression	2.30 (1.67,3.17)	2.15 (1.54,3.01)
Lung disease	1.46 (1.14,1.86)	1.44 (1.12,1.85)
Stomach ulcer	1.71 (1.17,2.50)	1.72 (1.17,2.52)
CCP and RA seropositivity	0.80 (0.67,0.94)	0.69 (0.58,0.83)
Corticosteroids	1.52 (1.18,1.96)	1.50 (1.16,1.94)

Persistent active (pactiveRA) defined as DAS28 >3.2 at baseline, 3 and 12 moths of follow-up.CCP: cyclic citrullinated peptide; IMD: index of multiple deprivation; RF: rheumatoid factor.(p<0.05 for all predictors).

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POS0455 **WITHDRAWN**

POS0456

ASSESSMENT OF CLINICAL FEATURES AS PREDICTORS OF INADEQUATE RESPONSE TO TNFI THERAPIES—FURTHER ANALYSIS OF THE MOLECULAR SIGNATURE RESPONSE CLASSIFIER

Keywords: Biomarkers, Rheumatoid arthritis, Artificial intelligence

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Background: Clinical and molecular features have been used to predict how RA patients will respond to distinct treatments. Clinical datasets are more readily available, more easily analyzed, and less costly to obtain than are molecular datasets [1]. But predictions based on clinical features alone are usually insufficiently reliable for deciding among treatment options [2]. Although molecular features are increasingly valuable for predicting treatment responses [3], physicians are often uncertain whether it is necessary to consider molecular measures [4]. And health care providers must determine whether the benefits of using molecular datasets justify their added costs. The molecular signature response classifier (MSRC) uses clinical features and molecular (genomic and serologic) features to identify RA patients unlikely to adequately respond to TNFi therapies [5]. But the relative contribution of clinical and molecular features to MSRC performance has yet to be fully addressed. This information is invaluable because most RA patients respond inadequately to their initial treatments and response-prediction classifiers offer much promise for improving patient outcomes.

Objectives: Our objective was to evaluate how well clinical features alone predict inadequate TNFi responses in the patient cohort used for developing the MSRC.

Methods: Clinical features (sex, body mass index, and patient global assessment) and molecular features (expression levels of 8 genes, 10 single nucleotide polymorphisms, anti-CCP, and CRP) for RA patients in the CERTAIN study were described [5]. ACR50 at 6 months was the primary outcome defining response. The cohort was divided into a training set (n = 143) and a validation set (n = 175). Predictive models were trained through repeated cross-validation by using a random forest machine learning algorithm on 80% of the training data (n = 114); models were optimized by validation on the remaining 20% (n = 29). The final model was built on the entire training data set. Performance was then evaluated on the validation set (n = 175) and reported as area under the receiver operating characteristic curve (AUC). All statistical analyses were performed by using Python 3.7.6.

Results: Classifier performance when using only molecular features (AUC, 0.65–0.68) was better than its performance when using only clinical ones (AUC, 0.41–0.60) (Table 1). Classifier performance was best when using combined molecular and clinical features (AUC, 0.65–0.68).

Table. Prediction of inadequate ACR50 response to TNFi therapies

Features[a]	AUC (cross validation)	AUC (validation)
Molecular and clinical features	0.65	0.68
Molecular features	0.60	0.63
Clinical features	0.41	0.60
BMI	0.54	0.49
PtGA	0.43	0.51
Sex	0.53	0.59

Abbreviations: anti-CCP, anti-cyclic citrullinated protein; AUC, area under the receiver operating characteristic curve; CRP, C-reactive protein; BMI, body mass index; PtGA, patient global assessment; SNP, single nucleotide polymorphisms

[a] Features are considered in combination as part of a random forest model

Conclusion: These results confirm the importance of including molecular features in TNFi response–prediction models. Identifying new molecular biomarkers of treatment response can help address prediction challenges caused by the heterogeneity of RA. And considering clinical and molecular features together, with other assessments increases the predictive performance of precision medicine tests such as the MSRC.

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POS0457

ASSOCIATION BETWEEN METHOTREXATE USE AND LYMPHOMA IN RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

Keywords: Systematic review, Epidemiology, Rheumatoid arthritis

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Background: Rheumatoid Arthritis (RA) is associated with an increased risk of lymphoma compared to the general population, which has been attributed to increased disease activity (1, 2). By decreasing RA disease activity, methotrexate could potentially help to reduce the risk of lymphoma development; however, there are conflicting data in the literature.

Objectives: To perform systematic literature review to evaluate the association between use of methotrexate in RA and the risk of developing lymphoma.

Methods: A systematic literature search was performed using the PubMed, Embase, and Cochrane Central Register of Controlled Trials from inception through December 9, 2021. The search was limited to observational studies and randomized controlled trials (RCT) published in English that evaluated the association between use of MTX in RA and the development of lymphoma. Case series and reports were excluded. Two authors independently extracted data from final articles using a predefined data abstraction form and conflicts were resolved by a third reviewer. Quality assessments were performed.

Results: The study identification and selection process are summarized in **Figure 1.** Of the initial 839 articles identified, only eight articles met the eligibility criteria. The characteristics of these studies are depicted in **Table 1**. These were mostly observational studies except one RCT. Study sample sizes varied from 160 to 20,000 patients with RA. Five studies reported the odds/hazards ratio of occurrence of lymphoma in patients exposed to methotrexate versus not exposed to methotrexate. Three studies compared risk of lymphoma development in RA patients treated with methotrexate versus other biological DMARD of which one was an RCT. Most of the studies adjusted for variables such as age, sex, RA disease activity measures and inflammatory markers, concomitant RA medications and risk factors for cancer and RA. Of the eight studies, six did not find a significant association between MTX use and lymphoma, while two studies, conducted in Japan, reported a significant association. Included studies were of moderate to high quality. The heterogeneity of the included studies precluded conducting a meta-analysis.

Conclusion: While there are conflicting data regarding the role of MTX in lymphomagenesis in RA, we observed that a majority of high-quality epidemiologic studies did not support an association between MTX use and development of lymphoma. Only two studies from Japan reported an association between MTX use and development of lymphoma.

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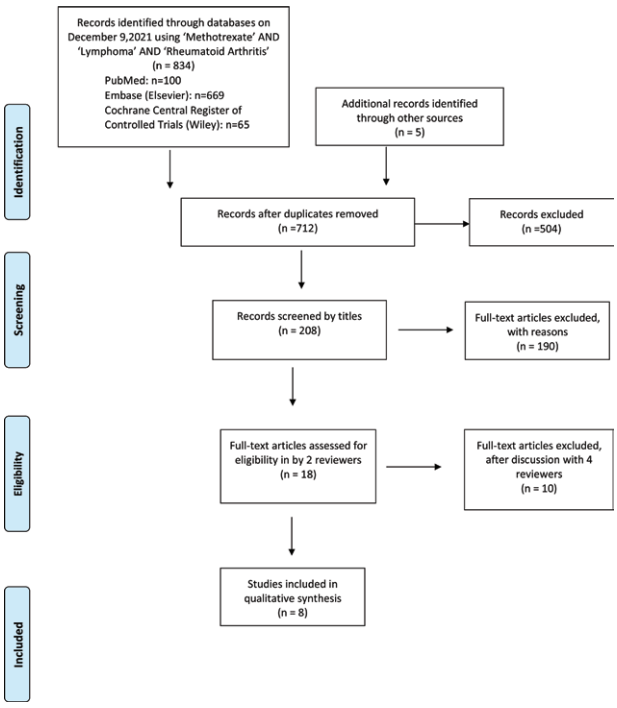


Table 1. Characteristics of the included studies

Author, year	Study location; period	Number of patients with RA	Number of patients with lymphoma	Effect estimates of the association (95% CI)
Bernatsky, 2008	Canada; 1980-2003	23 733	346	OR 1.23 (0.97-1.57)
Hashimoto, 2015	Japan; 2002 - 2012	66,953 patient - years	63	**OR 3.5 (2.0–6.3)**
Hellgren, 2017	Sweden; 1997-2012	12,656	62	RR =0.9 (0.8–1.0)
Kedra, 2021	France; 1971–2016	162	54	-Univariate analysis: OR - 1.0 (0.3 to 3.4); p value 0.97 -Sensitivity analysis: OR - 0.78 (0.10-5.93); p value 1.00
Honda, 2022	Japan; 2011	9815	68	MTX use versus no MTX use based on MTX dose: 0 to 8 mg: **HR: 2.35 (1.25-4.42)**; >8 mg: **HR 4.39 (2.07-9.32)**
Setoguchi, 2006	US and Canada; 1994 -2004	7,830	58	bDMARD versus MTX; HR:1.11 (0.51–2.37)
Lee, 2014	151 centers worldwide; 2010- 2013.	958	3	3 lymphomas in Tofacitinib group; 0 in MTX group
Solomon, 2014	US; 2001 -2010	6806	2865 Person-years	TNFI versus MTX; HR- 0.15 (0.01–2.19)

CI- Confidence Interval; OR- Odds Ratio; RR- Relative Risk; MTX- Methotrexate; HR- Hazard Ratio; DMARD- Disease Modifying Antirheumatic Drug; TNFI- Tumor Necrosis Factor Inhibitor; RA- Rheumatoid arthritis

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POS0458

HAVING MORE TENDER THAN SWOLLEN JOINTS IS ASSOCIATED WITH WORSE FUNCTION, PAIN INTERFERENCE, SOCIAL PARTICIPATION AND OTHER HR-QOL OUTCOMES IN THE FIRST YEAR FOLLOWING RA DIAGNOSIS: RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT STUDY

Keywords: Real-world evidence, Quality of life, Rheumatoid arthritis

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Background: Newly diagnosed RA patients seen in routine care may present with more tender than swollen joints, that can persist throughout their early RA treatment. Little is known, about the impact of these tender-swollen joint count differences (TSJD) on patient-reported outcome measures (PROMs), such as function, pain interference, social participation and other health-related quality of life (HR-QoL) outcomes.

Objectives: Our objective was to estimate the impact of TSJD on PROMs in the first year following RA diagnosis, and whether associations may vary by type of joint involvement (small vs large).

Methods: Data were from patients with active, early RA (symptoms<1 year, CDAI>2.8) enrolled in the Canadian Early Arthritis Cohort (CATCH) who completed detailed clinical assessments and PROMs including the PROMIS-29 (physical function, social participation, pain interference, fatigue, sleep disturbance, anxiety and depression) at baseline, 3-,6- and 12-month between Jan 2016 and Aug 2022. 28-tender and 28-swollen joint counts (including 6 large and 22 small-joints) were performed by rheumatology team members. TSJD were calculated by subtracting SJC from TJC at each visit and categorized as <=0, 1-4, 5-6, 7+. Adjusted associations between repeated measures of TSJD and PROMIS-29 HR-QoL domains were estimated in separate linear-mixed models adjusted for age, sex, education, smoking, comorbidities, osteoarthritis/back pain, and RA treatment. Stratified analyses by large vs small TSJD were also performed to examine potential differential impacts by joint distribution.

Results: 547 eligible early RA patients (70% female, mean (SD) age 56(15) years, mean (SD) disease duration 5.3 (2.9) months) evaluated at baseline. 287 (52%) had TSJD score>0. Of these, scores ranged from 1 to 4 in 200 (37%), 5 to 6 in 41 (8%) and 7+ in 46 (8%). The frequency of TSJD>0 decreased from 52% at BL to 32% at 12-months. Adjusted mean-change scores in all PROMIS-29 measures were worse with higher TSJDs over 1-year follow-up (Figure 1). TSJD 1 to 4 and >7 were associated with worse mean-change T scores for all PROMIS29 outcomes, with TSJD>7 showing more pronounced worsening in physical function -2.6 [-4.0, -1.2] and participation satisfaction -3.5 [-5.3, -1.7] (negative scores indicating more impairment). Worse mean-change T scores in symptoms were also associated with TSJD>7 (positive scores indicating worse symptoms): pain interference 5.2 [3.5,6.9], fatigue 4.0 [2.1, 5.8], sleep problems 3.0 [1.4, 4.5], anxiety 2.1 [0.4, 3.8] and depression 2.0 [0.4, 3.7). There were fewer scores of TSJD 5 to 6, which was associated with worse mean-change scores in function, social participation and pain interference. The most striking mean-change scores were seen for large joint-TSJD scores of 5 to 6 in PROMIS function -6.1 [-10.3, -1.9] and social participation -6.1 [-11.6, -0.6], pain interference 6.6 [1.5, 11.7], compared to those found with small joint-TSJD and 28 joint-TSJD. Large joint -TSJD scores 1 to 4 were also associated with worse mean-change scores for all PROMIS measures.

Conclusion: Over half of patients with eRA have more tender than swollen joints, which persists in a third of patients. An increased TSJD score is associated with worse function, pain interference, social participation, and other HR-QoL outcomes over 1-year of follow-up. TSJD thresholds of 1 to 4 and >7 were associated with worsening of all PROMIS-29 outcomes. Having more tender than swollen large joints, at thresholds of 1 to 4 and 5 to 6, was associated with the most pronounced worsening of PROMs. Elevated TSJD assessment, especially in large-joints may help identify patients likely to experience worse outcomes.

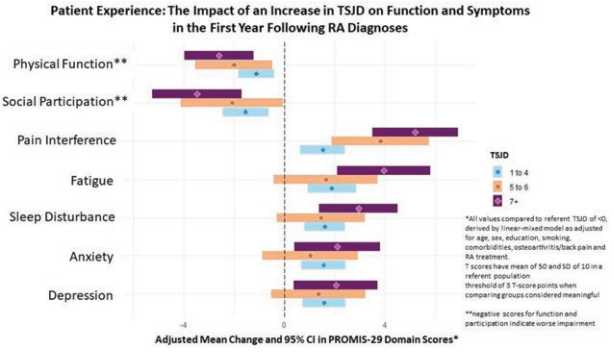


Figure 1.

The impact from and persistence of predominantly tender joints supports a need to identify early interventions.

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POS0459 CALPROTECTIN HAS BETTER PREDICTION OF OBJECTIVE ASSESSMENTS OF INFLAMMATION THAN CRP OR ESR; RESULTS FROM TWO NORWEGIAN COHORTS OF EARLY OR ESTABLISHED RA

Keywords: Biomarkers, Rheumatoid arthritis, Ultrasound

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Background: Inflammatory laboratory markers predicting response to medication would be useful in the clinics. Two Norwegian cohorts of early or established RA patients included in the NORA study (a Nordic multi-centre study exploring personalized medicine in RA) were used to explore the predictive value of calprotectin, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).

Objectives: To explore the associations between calprotectin, CRP, ESR, and clinical disease activity assessments, and to explore the predictive value of these inflammatory markers on clinical and ultrasound (US) examinations.

Methods: Two cohorts were included; 1. Patients with early RA initiating methotrexate (the ARCTIC step-up, treat-to-target randomized study [1] (230 patients, mean (SD) age 51.5 (13.7) years, disease duration 0.6 (0.5) years, 61% women, 81% anti-CCP positive) and 2. Patients with established RA initiating a biologic disease-modifying anti-rheumatic drug (the ULRABIT cohort [2]) (209 patients (mean (SD) age 53.3 (13.2) years, disease duration 10.0 (8.8) years, 81% women, 80% anti-CCP positive). Both cohorts were assessed by clinical (tender/swollen 28 joints (TJC/SJC), physician's global assessment (PhGA), patient's global assessment (PGA) and pain), laboratory and comprehensive US examinations (grey scale and power Doppler of 36 joints) at baseline, 1 and 3 months (half of the early RA cohort US only at baseline). Calprotectin (measured by use of FEIA (Thermo Fisher)), CRP and ESR (inhouse methods) were assessed at treatment start and at one month in both cohorts. Correlations were analysed by Spearman. Baseline and 1-month levels of calprotectin, CRP or ESR were explored by linear regression for prediction of 3 months results of objective (US, SJC, PhGA) and subjective (TJC, PGA, pain) measures of disease activity (adjusted for age, gender, and disease duration) giving R-squared (95% CI obtained by bootstrapping (percentile intervals and 1000 bootstrap replications)).

Results: The correlations between baseline levels of calprotectin and SJC28/PhGA were 0.34-0.56 in the two cohorts, with corresponding correlations for CRP of 0.25-0.46, and ESR 0.23-0.50 (all p<0.001), and lower correlations with TJC28, PGA and pain (median 0.25 (range 0.04-0.35). Calprotectin and CRP were predictive of the objective inflammatory variables in both cohorts (Table 1), with calprotectin having the highest R-squares, and calprotectin had better prediction than CRP and ESR in established RA (p<0.05).

Conclusion: The laboratory markers had highest correlations with the more objective assessments. Calprotectin was superior to CRP and ESR for prediction of the objective disease activity variables. Thus, calprotectin may have added value in clinical evaluation of inflammatory activity in RA patients.

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POS0460 IMPACT OF MAINTENANCE THERAPY WITH LOW-DOSE GLUCOCORTICOIDS IN PATIENTS UNDERGOING BIOLOGICAL AND TARGETED SYNTHETIC DMARDS FOR RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Real-world evidence, bDMARD

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Table 1. Linear regression including baseline and 1-month results of the laboratory variables exploring their predicting value of 3 months ultrasound and clinical assessments (adjusted for age, gender, and disease duration) with R squares, presented as percentages with 95% CI.

	Objective measures at 3 months				Subjective measures at 3 months		
	Sum score power Doppler	Sum score grey scale	Swollen joint count	Examiner's global VAS	Tender joint count	Patient's global VAS	Pain VAS
Early RA patients							
Calprotectin	67 (3,92)**	37 (3,69)**	40 (2,75)**	9 (-2,31)*	1 (-3,26)	4 (0,18)	-4 (-4,15)
CRP	32 (0, 72)**	26 (4,61)**	21 (-1,62)**	10 (-2,36)*	5 (-1,29)	17 (3,39)**	2 (-3,26)
ESR	-1 (-3,22)	2 (-2,24)	-2 (-3,16)	0 (-3,18)	2 (-2,23)	0 (-4,19)	-4 (-5,11)
Established RA patients							
Calprotectin	21 (6,50)**	26 (12,46)**	21 (8,42)**	24 (11,40)**	0 (-2,13)	5 (1,17)*	6 (2,19)*
CRP	9 (2,30)*	11 (8,31)*	10 (3,29)*	20 (8,41)**	2 (-1,19)	4(0,18)*	7 (2,20)*
ESR	7 (1,25)*	8 (2,23)*	7 (1,23)*	17 (6,34)**	2 (-1,18)	4 (0,18)	6 (1,18)*

*p<0.05, **p<0.001

Background: The benefit and harms of low-dose glucocorticoid (GC) therapy for established rheumatoid arthritis (RA) in combination with biological and targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs) are uncertain.
Objectives: We investigated the effect of b/tsDMARDs on concomitant GC therapy among people with RA and the impact of low-dose GC therapy on disease activity and comorbidities.
Methods: This was an observational, monocentric, prospective study. We enrolled all RA patients who started their first b/tsDMARD between 2015 and 2020, excluding those with overlapped connective tissue diseases. The primary outcome was the odds ratio (OR) of persistent GC discontinuation at month 36 (M36), as assessed through multivariable logistic regression. We defined persistent GC discontinuation if GC therapy was not prescribed for ≥2 consecutive visits after 24 months. Secondary outcomes were the marginal means of prednisone daily dose and disease activity score in 28 joints (DAS28) with C-reactive protein (CRP) over three years estimated through repeated-measures analysis of covariance. Analyses were adjusted for age, sex, disease duration, seropositivity, baseline DAS28 or GC dose. The impact of low-dose GC therapy on comorbidities and disease activity was also evaluated.
Results: This inception cohort comprised 371 RA patients initiating their first b/tsDMARD: tumor necrosis factor inhibitors (n=298; 80.3%), abatacept (n=47; 12.7%), tocilizumab (n=11, 3.0%), rituximab (n=9; 2.4%), Janus kinase inhibitors (n=9; 1.6%). b/tsDMARDs were combined with low-dose GC therapy in 65% of patients at baseline, decreasing to 42% at M36. After starting b/tsDMARDs, the median (10th-90th percentile) dose of prednisone decreased from 5 (2-10) at baseline to 2.5 (0-5) mg daily at M36. The most decrease in prednisone dose occurred within the first six months of b/tsDMARD therapy. Persistent GC discontinuation was achieved in 23% of patients during follow-up, with a significantly higher discontinuation rate (34%) and a trend for lower exposure to GC therapy after M24 in patients diagnosed in the last decade compared to older cohorts (**Figure 1A**). Patients who discontinued GC therapy persistently were significantly younger (52 vs 59 years), had shorter disease duration (9 vs 13 years), more swollen joints (6 vs 4) and greater patient global assessment (65 vs 55 mm), and received higher doses of methotrexate (14 vs 12 mg/w). After accounting for confounders, patients who discontinued GC therapy persistently did not show worse disease control over time (**Figure 1B**) whilst developed less cardiovascular disease, especially hypertension (9% vs 19%, p=0.023) and coronary artery disease (0% vs 4.6%, p=0.044). Changing the molecular targets of b/tsDMARDs did not yield higher odds of persistent GC therapy discontinuation than keeping the initial drug class; in contrast, GC persistent discontinuation was less likely in older patients with longer disease duration (Table 1). Patients refractory to more than three b/tsDMARDs classes had numerically higher disease activity and received more prednisone during follow-up (**Figures 1C and D**).

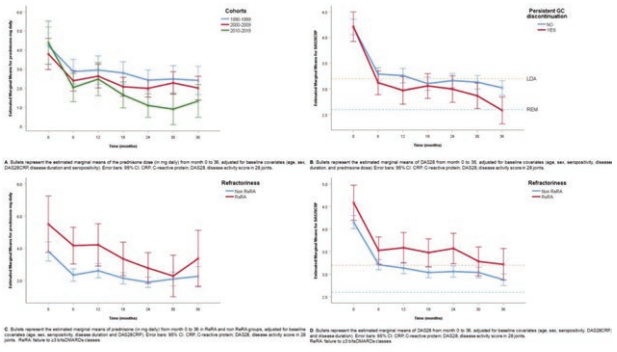


Figure 1.

Table 1. Multivariable logistic regression of persistent GC discontinuation among RA patients on b/tsDMARDs

	P-value	OR	95% CI (inferior)	95% CI (superior)
Disease duration, years	**0.011**	0.96	0.93	0.99
Age, every five years increase	**0.009**	0.88	0.80	0.97
DAS28CRP	0.253	1.14	0.91	1.43
Switch (vs no switch)	0.521			
1 switch	0.309	1.38	0.74	2.59
≥2 switch	0.320	1.40	0.72	2.69

CI, confidence interval; CRP, C-reactive protein; DAS28, disease activity score in 28 joints; OR, odds ratio; PtGA, patient global assessment. Multivariable logistic regression with persistent GC discontinuation as the outcome.

Conclusion: Low-dose GC therapy for RA persists in the majority of patients despite intensive use of b/tsDMARDs, yet is associated with cardiovascular morbidity and negligible effect on disease activity. This study also highlights a trend towards less reliance on GC therapy over the past 30 years.

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POS0461

AN INCREASE IN ULTRASOUND JOINT INFLAMMATION OCCURS WHEN ANTI-CCP POSITIVE AT-RISK INDIVIDUALS WITH SUBCLINICAL SYNOVITIS PROGRESS TO INFLAMMATORY ARTHRITIS

Keywords: Ultrasound, Rheumatoid arthritis, Imaging

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Background: Anti-CCP+ at-risk individuals with musculoskeletal (MSK) symptoms and subclinical synovitis on ultrasound (US) are at high risk of developing inflammatory arthritis (IA). The accepted standard practice is to initiate treatment at progression rather than in the pre-rheumatoid arthritis (RA) phase when they do not have clinical synovitis [1].
Objectives: We aimed to determine whether imaging characteristics change when individuals with pre-RA progress to IA in order to inform the optimal window of opportunity for therapeutic interventions.
Methods: Anti-CCP+ at-risk individuals with MSK symptoms but no clinical synovitis from the Leeds CCP cohort were selected for having US subclinical synovitis [Grey scale (GS) ≥1 and Power Doppler (PD) ≥1] prior to IA development and a further US scan performed at clinical synovitis onset (i.e. progression). The US protocol included the metacarpophalangeal joints (MCPJs), proximal interphalangeal joints, wrists, elbows, knees, ankles, second-fifth metatarsophalangeal joints, extensor carpi ulnaris and finger flexor tendons. US PD and GS synovitis were scored semi-quantitatively (0-3) according to EULAR/OMERACT. At patient level, total GS and PD scores were compared between scans. Change on US in the joints that became clinically swollen was also assessed. Early morning stiffness (EMS) and 44 tender joint count (TJC) were compared between scans. Wilcoxon signed-rank tests were conducted for comparisons.
Results: Forty-six CCP+ at-risk individuals were identified. The mean age was 57.4 (± 13.3), 91.3% had high titre CCP levels (≥ 3x upper limit of normal) and 60.9% were Rheumatoid Factor positive. The median US scan interval was 3.5 months (IQR 1.25-8.75). EMS increased between scans (median of 20 [IQR 0-60] to 75 [IQR 30-173] minutes [p = 0.048]) as did TJC (median 2 [IQR 1-7] to 6 [IQR 2-13] [p=0.001]. On US (Table 1), at patient level the overall burden of PD in the joints increased at IA progression, trending towards significance. The overall burden of GS did not increase. PD in the MCPJs and MCP and wrist joints combined increased significantly. GS at the elbows also significantly increased. There was no significant increase in tendon GS or PD. At joint level PD increased in joints that were swollen at progression and GS increased with a trend towards significance. Non-swollen joints did not change.
Conclusion: A marked increase in US joint inflammation occurs when CCP+ at-risk individuals with subclinical synovitis on US progress from pre-RA to

Table 1. Changes on Ultrasound from first visit with subclinical synovitis to second visit at progression to RA.

	Visit 1: US subclinical synovitis	Visit 2: Progression to IA	P-value
Total PD score*	3 (1.25-5)	4 (2-7.25)	p=0.063
Total GS score*	23 (12-28)	21 (13-33.5)	P=0.170
PD score MCPJs*	0 (0-2)	1.5 (0-3)	**p=0.008**
GS score MCPJs*	5 (3-10)	5 (2.7.75)	p=0.139
PD score Wrists*	1 (0-2)	1 (0-2)	p=0.153
GS score Wrists*	3 (2-4)	3 (2.25-4)	p=0.181
PD score MCPJs + Wrists*	1 (0.25-3)	2 (1.25-4.75)	**p=0.002**
GS score MCPJs + Wrists*	10.5 (6-16.8)	12 (7.25-15.8)	p=0.337
PD score Elbows*	0 (0-0)	0 (0-0)	-
GS score Elbows*	0 (0-0)	0 (0-1)	**p=0.009**
GS score in Joints that became swollen at IA progression*	3 (1-5)	3 (2-6,5)	p=0.061
PD score in Joints that became swollen at IA progression*	1 (0-2)	2 (0-3)	**p=0.036**

*Median (IQR)

clinical arthritis. This is particularly evident in MCPJs, wrist joints and joints that become clinically swollen. This marked increased in ultrasound joint inflammation at progression is accompanied by a significant increase in EMS and tender joints. Intervening when at-risk individuals have subclinical synovitis may represent a window of opportunity to prevent the rapid increase in ultrasound joint inflammation that occurs with the onset of joint swelling.

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POS0462 CLINICAL PARAMETERS AFFECTING QUALITY OF LIFE IN PATIENT WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Outcome measures, Quality of life

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Background: Under the treat-to-target strategies, patient with rheumatoid arthritis (RA) has achieved clinical remission in a major population, however, the impact on the quality of life remains controversial. The relationship between quality of life and disease activity control, pain control, and functional capacity control needs to be clarified.

Objectives: This study aims to clarify the influence of clinical parameters on the quality of life in patients with RA.

Methods: In this study, Patient with RA who was monitored with simplified disease activity index (SDAI) as a disease activity indicator, health assessment questionnaire disability index (HAQ-DI) as a functional capacity indicator, pain score using a visual analog scale (PS-VAS) as a pain grade indicator, EuroQol-5th dimension with 5 lines (EQ5D-5L) as a quality of life indicator, and measured Sharp/van der Heijde score (SHS) as a joint deformity indicator from the start of treatment (baseline) since January 2016, were recruited. Association between EQ5D-5L and other parameters such as gender, age, SDAI, PS-VAS, SHS, and HAQ-DI was statistically evaluated at baseline and at last observation, and change between the two periods using linear regression analysis with multivariate model.

Results: A total of 538 patients were included in the study. The female gender rate was 73.4%, and mean values at the baseline and at the last observation were 67.2 and 73.2 (age), 12.7 and 4.4 (SDAI), 49.3 and 46.4 (SHS), 35.4 and 24.5 (PS-VAS), 0.487 and 0.498 (HAQ-DI), and 0.755 and 0.825 (EQ5D-5L), respectively. All of these parameters were significantly different between the two periods. EQ5D-5L at baseline correlated significantly with HAQ-DI and PS-VAS, and their beta values were -0.604 and -0.444, respectively. EQ5D-5L at the last observation correlated significantly with SDAI, HAQ-DI, and PS-VAS at the last observation, and their beta values were -0.04, -0.623, and -0.099, respectively. When the last values of these parameters were divided by value at the baseline and the change from the baseline to the last observation, EQ5D-5L at the last observation correlated significantly with both of baseline and the change of all of SDAI, HAQ-DI, and PS-VAS, and their beta values were -0.439, -0.493, -0.143, 0.547, 0.605, and 0.139 for SDAI, HAQ-DI, PS-VAS at the baseline, and those change from the baseline to the last observation, respectively.

Conclusion: Quality of life in RA patients depends on disease activity control, pain control, and functional capacity. These variables could be controllable by treatment.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0463 ASSOCIATION OF CIRCULATING LEVELS OF ANTI-CARP ANTIBODIES WITH DISEASE ACTIVITY AND RADIOLOGICAL DAMAGE IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Biomarkers, Rheumatoid arthritis, Autoantibodies

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Background: In rheumatoid arthritis (RA) the identification of specific autoantibodies is crucial for an earlier diagnosis and stratification of patients according to different disease phenotypes. Autoantibodies directed against carbamylated proteins (anti-CarP) have been recently identified [1] as predictors for RA development [2]. Anti-CarP antibodies are associated with more severe RA, in particular in anti-citrullinated peptide antibodies (ACPA) negative RA patients [3].

Objectives: To determine the frequency of positive anti-CarP antibody in a real-life cohort of RA patients on synthetic and biologic disease-modifying antirheumatic drugs (DMARDs) and their association with radiological damage and disease activity.

Methods: The study is an open-label, observational, cross-sectional study, including 69 patients with RA according to ACR/ EULAR 2010 criteria, treated with synthetic and biological DMARDs. The control group consisted of 16 healthy controls (HC). The study was approved by institutional Ethical Committee and patients signed the Informed Consent. Circulating levels of anti-CarP antibodies were determined at baseline visit by commercial ELISA anti-CarP quantitative sandwich immunoassay (cut-off value 6 ng/ml). Articular X-rays were performed within 6 months of the baseline to define the presence of erosions. RA disease activity (DAS28 CRP) was assessed. Pearson χ^2 test, Wilcoxon test or Kruskall- Wallis test was used, as appropriate. Spearman rank-order correlation coefficient was applied for continuous variables. A multivariable logistic regression model was performed to assess prognostic variables on damage.

Results: Anti-CarP antibodies were positive in 35% of RA patients and no antibodies were found in HC. One quarter (4/17) of seronegative RA patients were anti-CarP positive. All anti-CarP positive and RF/ ACPA negative patients had radiological evidence of erosions and a moderate disease activity (DAS28 CRP 3.60± 0.58) and disability (HAQ-DI 0.70± 0.13). In all RA patients, a positive correlation between levels of anti-CarP antibodies and DAS28 CRP (p =0.0003; Spearman r = 0.4829) was found. Furthermore, 87% of anti-CarP positive patients had erosions. The multivariable logistic regression model suggested that disease activity and higher levels of anti-Carp antibodies were significant predictors for the presence of erosions. There was a greater number of erosions in patients with active disease (OR 1.31, 95% CI [1.14, 1.63]) and those with a higher levels of anti-CarP antibodies (OR1.66,95% CI [1.28, 2.37]).

Conclusion: Anti-CarP antibodies were present in a significant number of RA patients and those with higher circulating levels had higher disease activity and a greater occurrence of radiological damage. Further larger studies are warranted to better understand the clinical significance of anti-CarP antibodies in RA.

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Table 1. Demographic, lifestyle and clinical characteristics

Characteristic	RA patients (69)	HC (16)	p
Sex (F/M)	56/13	13/3	NS
Age (yrs)	58 ±11.22	56 ±4.28	NS
Smoking			
- Smokers	36 (52%)	10 (62%)	NS
- Non-smokers	33 (48%)	6 (38%)	
DAS28 CRP	3.7±0.13	NA	
HAQ-DI	0.7±0.04	NA	
RhF	55 (79%)	0	
ACPA	48 (69%)	0	
Anti-CarP	24 (35%)	0	
MTX	27 (39%)	NA	
MTX + biologics	12 (17%)	NA	
Corticosteroids	56 (81%)	NA	

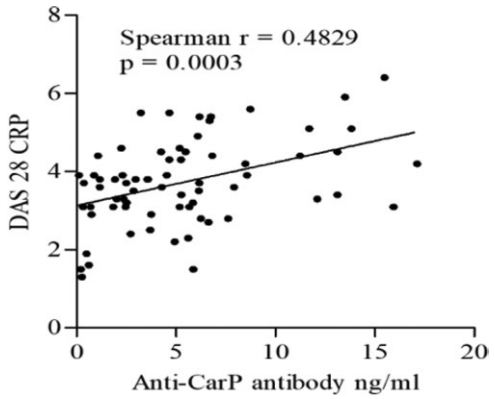


Figure 1. Correlation of anti-CarP circulating levels with DAS28 CRP in all RA patients

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Disclosure of Interests: None Declared.
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POS0464 **DISEASE-AGNOSTIC SELF-MANAGEMENT PROGRAM: IMPACT ON DISEASE ACTIVITY AND HEALTH RELATED QUALITY OF LIFE MEASURES FOR PATIENTS LIVING WITH CHRONIC INFLAMMATORY ARTHRITIS**

Keywords: Inflammatory arthritides, Patient reported outcomes, Self-management

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Background: Agnostic approach refers to strategy that is generalized so that it is interoperable among various disorders or systems. In general, regardless of the underlying specific pathology, patients prioritize which self-management strategy they would like to start with according to their own requirements. They also select the issues they would like to address based on their individual perceptions of ability, need and context. Therefore, implementation of a disease-agnostic self-management program is a key priority to optimize the care of patients with chronic inflammatory arthritis.
Objectives: To determine, based on self-efficacy theory, the effectiveness of a disease-agnostic self-management program which can be undertaken by the individual inflammatory arthritis patient in any sequence to meet his/her specific needs.
Methods: Prospective multi-center assessment of patients with inflammatory arthritis, who were randomly assigned to either a 16-week program in self-management (intervention group, n = 121) or standard care for rheumatology (control group, n = 120). The program is composed of 4-arms: joint learn, joint change, joint-cise and joint act [1]. The patient is free to choose whichever component of the program that meets his/her individual requirement. Outcome variables were assessed at baseline and 6-, and 12-months after commencement of the intervention. This included measures of disease activity, adherence to therapy, motivation, functional disability, and quality of life.
Results: The intervention group included patients living with rheumatoid arthritis (30 patients), psoriatic arthritis (30 patients), lupus (30 patients), and osteoarthritis (31 patients). The mean age of participants (96 females [79.3%], 25 males [20.7%]) was 54.3+3.51 years. There was no significant difference on comparing the baseline characteristics and variables between the two groups. At 6-months following initiation of the self-management program, when compared to the control group, there was significantly better improvement in the intervention group patients' motivation score ($p< 0.05$), functional ability ($p< 0.05$) as well as quality of life ($p< 0.05$). At 12-months follow-up, the self-management intervention demonstrated improvement for disease activity (effect size 1.4). Similarly, there was improvement of the patients' adherence to therapy ($P<0.01$) in the intervention group.
Conclusion: Results suggest that disease-agnostic self-management improves disease activity scores as well as patient-reported outcomes regardless of patient diagnosis. Enhancing patients' capacity to deal with the burden of chronic inflammatory arthritis disease plays a vital role in their long-term management. Longer duration of self-management training and increased follow-up time are required to incorporate lifestyle changes.

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POS0465 **ONLINE SELF-MANAGEMENT PROGRAM: A STEP FORWARD TOWARDS DIGITAL PLATFORM FOR PATIENT-TARGETED E-HEALTH**

Keywords: Patient reported outcomes, Inflammatory arthritides, Self-management

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Background: Self-management is a vital component of successful inflammatory arthritis management. In contrast to the traditional medical model of care, self-management underscores the importance of collaborative, interactive care between the patient and the healthcare professional rather than one-way, passive care from the rheumatologist to the patient. In theory, patient-targeted e-Health tools enable the arthritic patients to implement self-management into their disease management and reach their own health-related goals. Yet the outcomes and early evidence about patient targeted e-Health and its consequence on self-management are mixed.
Objectives: To assess the feasibility of using an e-health intervention to improve the self-management abilities of rheumatoid arthritis patients.
Methods: Prospective multi-center randomized controlled assessment of rheumatoid patients with inflammatory arthritis. Using a 1:1 allocation ratio, patients were randomly assigned to either intervention group (112 patients) or control group (112 patients). The intervention was in the form of online access to educate and facilitate patients' ability to monitor and self-manage their arthritis. The patients had the opportunity to track their symptoms, self-management approaches and goals, medical therapy use, functional ability and quality of life. Specific e-health self-management approaches were made available for the self-management of fatigue, sleep disturbance and pain. Outcome variables were assessed at baseline and 6-, and 12-months after commencement of the intervention. This included measures of disease activity, adherence to therapy, patient motivation, functional disability, and quality of life. The primary outcome measure was self-management ability measured by the Patient Motivation Measure [1]. Secondary outcome measures include disease activity score, levels of fatigue, pain, functional ability, quality of life and adherence to therapy.
Results: The mean age of participants was 53.6+4.62 years. There was no significant difference on comparing the baseline characteristics and variables between the two study groups. At 6-months, when compared to the control group following the initiation of the online self-management program, in the intervention group, there was significantly higher improvement in the patients' motivation score ($p< 0.05$). At 12-months follow-up, the online self-management intervention demonstrated improvement for disease activity (effect size 1.3), functional ability ($p< 0.05$), quality of life ($p< 0.05$) as well as adherence to therapy ($p< 0.01$) in in comparison to the control group.
Conclusion: Results revealed that the online technology-enhanced self-management intervention did improve rheumatoid arthritis patients' self-management ability and health outcomes. Direct access to the health information on the Internet (or diagnostic apps on a smartphone) can help arthritic patients not only to self-manage their health issues, but also leads to lessening uncertainty, stress, and avoidance.

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POS0466

INTERIM UPDATE ON BASELINE CHARACTERISTICS AND EFFECTIVENESS FROM A PROSPECTIVE OBSERVATIONAL STUDY OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) TREATED WITH FILGOTINIB (FILOSOPHY)

Keywords: Rheumatoid arthritis, Real-world evidence, Patient reported outcomes

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Background: Filgotinib (FIL) is a preferential oral Janus kinase (JAK) 1 inhibitor for the treatment of RA. Efficacy of FIL has been demonstrated in clinical trials. To assess effectiveness in a real-world setting, a phase 4 study of FIL (FILOSOPHY; NCT04871919) in patients with RA is ongoing in Europe.

Objectives: To report baseline characteristics and interim efficacy data (up to 6 months) in the first 480 patients treated in FILOSOPHY.

Methods: FILOSOPHY is a prospective, observational study, in which approximately 1500 adults with moderate to severe active RA, who are prescribed FIL for the first time and in accordance with the product label in daily practice, will be enrolled. We report interim baseline demographics, disease characteristics, prior treatments, and reasons for starting FIL. We assessed disease activity at baseline, and Months 1, 3 and 6, via Clinical Disease Activity Index (CDAI) and Disease Activity Score in 28 joints–C-reactive protein (DAS28-CRP) and two electronically collected patient-reported outcome (PRO) measures at baseline, Week 1–4, and Months 3 and 6: pain (using a 10-cm visual analog scale [VAS]) and fatigue (via the Functional Assessment of Chronic Illness Therapy–Fatigue scale [FACIT-F]). The proportion of patients with minimal clinically important difference (MCID) in FACIT-F (≥4.0 change from baseline) and VAS pain (≤–10-mm change from baseline) at Month 6 was assessed. A repeated measurements model was used to estimate the least squares (LS) mean change from baseline in CDAI and FACIT-F.

Results: Of the 480 treated patients by the end of June 2022, 73.1% were female, mean (standard deviation [SD]) age was 57.6 (11.5) years, RA duration was 10.4 (9.4) years, BMI was 27.6 (5.7) kg/m^2, 28 tender joint count was 8.6 (6.9), and 28 swollen joint count was 5.6 (5.2). A total of 45.2% of patients were positive for rheumatoid factor and/or anti-citrullinated peptide antibody. Over half of patients (57.5%) had received prior biologic disease-modifying antirheumatic drugs (DMARDs; **Table 1**) and18.3% prior targeted synthetic DMARDs. FIL was started due to inadequate response (36.3%), loss of response (50.6%) or intolerance (non-allergic) (7.7%) to previous treatment (other reasons/missing data accounted for 5.4% of patients). Most patients (91.9%) received FIL 200 mg; 8.1% received FIL 100 mg (**Table 1**). FIL monotherapy was taken by 52.9% of patients, while 45.6% received FIL in combination with conventional synthetic DMARDs. Improvements from baseline to Month 6 were observed in CDAI (LS mean change [standard error; SE]: –15.8 [1.0]; **Figure 1** shows median CDAI over time) and DAS28-CRP (LS mean change [SE]: –1.8 [0.1]). Improvements from baseline to Month 6 were also observed for PROs; at Month 6, 54.2% and 65.0% of patients had an MCID from baseline in FACIT-F and VAS pain score, respectively.

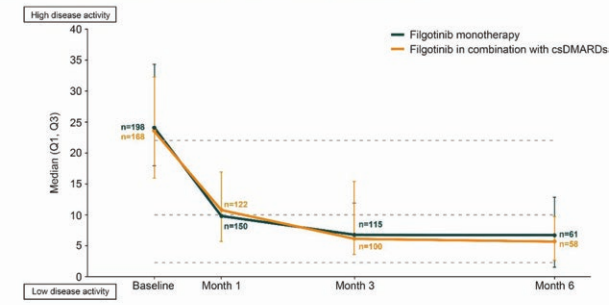
Conclusion: Preliminary 6-month data indicate rapid improvements with FIL treatment, which were seen as early as 4 weeks for disease activity and as early as 1 week for pain and fatigue. Similar effects were seen with FIL monotherapy and combination therapy. Long-term follow-up is needed to further evaluate disease outcomes.

Table 1. Demographics, prior and current treatments

	Total N=480 n (%)
Age ≥65 years	148 (30.8)
Former/current smoker*	167 (34.8)
Prior treatments	
≥1 csDMARD	434 (90.4)
≥1 bDMARD	276 (57.5)
≥1 tsDMARD	88 (18.3)
Glucocorticoids for RA	310 (64.6)
FIL dose at study start	
200 mg	441 (91.9)†
100 mg	39 (8.1)‡
Treatment at study start	
FIL monotherapy	254 (52.9)
With glucocorticoids for RA	104 (21.7)
FIL in combination with csDMARD	219 (45.6)
FIL in combination with methotrexate	182 (37.9)
With glucocorticoids for RA	88 (18.3)
FIL in combination with other csDMARD	37 (7.7)
With glucocorticoids for RA	12 (2.5)

(b/cs/ts)DMARD, (biologic/conventional synthetic/targeted synthetic) disease-modifying antirheumatic drug; SD, standard deviation.*Data missing for 110 patients (22.9%).†Median age 57 years.‡Median age 73 years.

Figure. Progression of disease activity (as measured by CDAI) over time



CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; Q, Quartile. Dashed lines indicate CDAI scores of 2.8, 10 and 22.

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Disclosure of Interests: Roberto Caporali Speakers bureau: AbbVie, Amgen, BMS, Celltrion, Fresenius, Galapagos, Janssen, Lilly, Novartis, Pfizer, UCB, Consultant of: AbbVie, Fresenius, Galapagos, Lilly, Novartis, Pfizer, UCB, Jérôme Avouac Speakers bureau: AbbVie, AstraZeneca, BMS, Eli Lilly, Galapagos, MSD, Novartis, Pfizer, Sandoz, Sanofi, Consultant of: AbbVie, Fresenius Kabi, Galapagos, Sanofi, Grant/research support from: BMS, Fresenius Kabi, Novartis, Pfizer, Karen Bevers Grant/research support from: Galapagos, Gerd Rüdiger Burmester Speakers bureau: AbbVie, Amgen, BMS, Chugai, Galapagos, Lilly, Pfizer, Sanofi, Consultant of: AbbVie, Amgen, BMS, Galapagos, Lilly, Pfizer, Sanofi, Thomas Debray Consultant of: Biogen, Galapagos, Gilead, Francesco De Leonardis Employee of: Galapagos, Kristina Harris Shareholder of: Galapagos, Employee of: Galapagos, Neil Betteridge Consultant of: Amgen, ASIF, Edwards Lifesciences, Eli Lilly, EULAR, Global Alliance for Musculoskeletal Health, Global Alliance for Patient Access, Grunenthal, Heart Valve Voice, Pfizer, Sanofi, Genzyme, Susana Romero-Yuste Speakers bureau: AbbVie, Biogen, BMS, Lilly, Pfizer, Consultant of: Sanofi, Lilly, Grant/research support from: Lilly, MSD, Patrick Verschueren Speakers bureau: AbbVie, Eli Lilly, Galapagos, Roularta, Consultant of: Celltrion, Eli Lilly, Galapagos, Gilead, Nordic Pharma, Sidekick Health, Grant/research support from: Galapagos, Pfizer, Monia Zignani Shareholder of: Galapagos, Employee of: Galapagos, James Galloway Speakers bureau: AbbVie, Biogen, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Roche, UCB, Consultant of: AbbVie, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Grant/research support from: AstraZeneca, Celgene, Gilead, Janssen, Medicago, Novavax, Pfizer.

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POS0467

DISCORDANCE IN PATIENT AND EVALUATOR GLOBAL ASSESSMENT OF DISEASE ACTIVITY OVER TIME AND ACROSS DISEASE ACTIVITY LEVELS IN RECENT-ONSET RHEUMATOID ARTHRITIS

Keywords: Real-world evidence, Rheumatoid arthritis, Patient reported outcomes

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Background: Treatment of rheumatoid arthritis (RA) aims to achieve remission or at least low disease activity. Composite measures (e.g. SDAI) to measure RA disease activity usually incorporate patient (PGA) and evaluator (EGA) global assessments. EGA and PGA are often discordant, reflecting divergences in evaluation of disease impact and potentially towards therapeutic goals.
Objectives: Patient vs Physician (PGA – EGA) discordance was evaluated according to disease duration over 5 years and to concomitant SDAI scores.
Methods: Demographics, clinical and serological variables, radiographic damage (Sharp van der Heijde scores), treatments, comorbidities, and Patient-Reported Outcomes (function, depression and coping with disease) were collected at baseline (median symptom duration 3.7 months) and at 12, 18, 30, 42 and 60 months from symptom onset. EGA and PGA were reported using a 0-10 cm visual analog scale (VAS). PGA-EGA discordance was divided in four subgroups[1]: negative discordance group (<-1 cm), concordance group (≥-1cm and ≤+1 cm), positive discordance group I (>1 cm and ≤3 cm) and group II (>3 cm).
Results: We included 822 patients from the prospective longitudinal Early Undifferentiated PolyArthritis (EUPA) cohort of recent-onset inflammatory arthritis. At baseline, concordance was present in 27.3 %, 24.9% in negative discordance and 47.8% in positive discordance (25.9 % group I and 21.9 % group II). Over 60 months, concordance increased to 45.7%, negative discordance decreased to 7.7%, while positive discordant groups remained stable (46.4 % at 5 years). Although prevalence was stable at a group level, only 40% of patients remained in positive discordance Group II over time. In positive discordant groups, patients were younger (median 58,6 years group I and 59,8 years group II, p <0.003), had higher functional impact (M-HAQ ≥1, 46.3 % to 50.2 % p <0.001), fewer tender and swollen joints (p <0.0001), but rated higher for pain, fatigue, sleep (p <0.0001) and depression (CES-D, median score 18 for both groups, p <0.005). Concordance was most frequent in remission, negative discordance in high disease activity, while group I positive discordance remained stable independent of disease activity. Group II positive discordance was highest (35-38%) with low or moderate disease activity.
Conclusion: In this longitudinal prospective study of patients with early arthritis, almost half evaluated their global disease activity worse than the evaluator (positive discordance) and this proportion remained stable up to 60 months. Patients in positive discordant group were younger and reported higher functional impact, pain, fatigue, poor sleep and more symptoms of depression but had lower tender and swollen joint counts. Concordance was best when in remission. Negative discordance increased with disease activity. Mild positive discordance (Group I) was stable at 25%, independent of disease activity and disease duration. Marked positive discordance (Group II) was stable over time and more prevalent with low/moderate disease activity.

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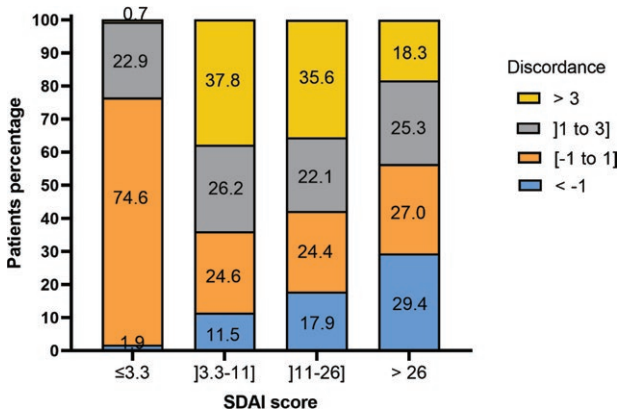


Figure 1.

Table 1.

Visit	Negative discordance <-1		Concordance [-1 to 1]		Positive discordance Group I [1 to 3]		Positive discordance Group II > 3	
	N (%)	SDAI*	N (%)	SDAI*	N (%)	SDAI*	N (%)	SDAI*
Baseline (n =822)	205 (24.9)	33.3 (23-49.3)	224 (27.3)	29.5 (17.1-45.5)	213 (25.9)	29.1 (19.6-43.5)	180 (21.9)	26.2 (19.6-38.6)
12 m (n=440)	67 (15.2)	13.6 (5.6-21.5)	156 (35.3)	3.5 (1.1-13.6)	114 (25.9)	6.9 (3.4-18)	103 (23.5)	10.7 (7-16.5)
18 m (n=699)	72 (10.3)	10.9 (5.5-20.3)	294 (42.1)	2.3 (1-7.7)	162 (23.2)	5.1 (3.1-10.1)	171 (24.5)	9.9 (6.7-14.7)
30 m (n=629)	62 (9.9)	11.9 (5.7-20.5)	268 (42.6)	1.9 (0.7-5.2)	162 (25.8)	3.6 (2.5-7.6)	137 (21.8)	8.7 (6.2-12.1)
42 m (n=578)	49 (8.5)	12.5 (6.4-24.9)	267 (46.2)	1.5 (0.6-3.8)	126 (21.8)	4.5 (2.2-7.9)	136 (23.5)	8.2 (5.9-12.9)
60 m (n=508)	39 (7.7)	8.4 (5.3-17.1)	232 (45.7)	1.3 (0.6-3.6)	113 (22.2)	4.5 (2.7-10.1)	124 (24.4)	7.7 (5.6-10.6)

* Median (Interquartile range (IQR))

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POS0468

A PREDICTION MODEL FOR SWITCHING OF BIOLOGICS AND TSDMARDS IN RHEUMATOID ARTHRITIS

Keywords: Prognostic factors, Registries

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Background: Patients with rheumatoid arthritis (RA) have many options for biologic therapy both within treatment classes and across differing mechanisms of action, but the lack of predictability of treatment response and failure can be frustrating for patients and physicians. Rheumatologists longitudinally collect patient and physician reported measurements as a part of routine clinical care that can be used for prediction of outcomes [1]. Harnessing data regularly collected to monitor RA to inform treatment decision making could improve patient care.
Objectives: To develop a readily usable model with data collected in clinical care at preceding visits to predict the probability of switching biologic at a subsequent clinic visit
Methods: Patients were drawn from the CorEvitas (formerly CORRONA) registry and were adults over the age of 18 with a diagnosis of RA. The study matched patients who switched biologics with control patients who had not switched biologics; the cohort was divided into a training and test set for prediction model development and validation. Switchers: RA patients initiating a biologic/tsdmard and switching to another biologic/tsDMARD with at least two prior visits to the switch while on drug. Visits prior to the switch were between 2 and 12 months before. Control visit: Patient visits while still on initiated drug with at least 2 visits prior while on drug; next visit could not be a discontinuation or switch. A control visit was matched to a switch visit within 2 months of time from initiation by drug class and prior biologic experience. Pairs of control-switch visits were divided into a training (60%) and test set (40%). Using the training set, best subset regression, lasso and elastic net methods were used to determine the best potential models. Area under the ROC curve was used for the final selection of best model and estimated coefficients of this model were applied to the test data set to predict switching. Change in disease activity measures had a non-linear association with switching and were fit using linear splines with a knot at zero.
Results: A total of 5050 patients were included, 3016 in the training and 2034 in the test dataset. The average age was 59.6, the majority were female (3998, 79.2%), and the average duration of RA at the time of switch or control visit was 12.8 years. The final model included prior CDAI by category, prior patient pain measurement, change in CDAI from baseline, age group, and number of prior

biologics which were significantly associated (either positively or negatively) with switching biologics (Table 1). The area under the ROC curve was 0.690 for this model with the training dataset (Figure 1). The model was then applied to the test data with similar performance; the area under the ROC curve was 0.687 (Figure 1).
Conclusion: We developed a simple model to determine the probability of switching biologics for RA at the following clinic visit. This could be incorporated into the electronic medical records or used as an application to give clinicians more information about their patient's trajectory and likelihood of failing a biologic.
REFERENCES:

[1] Novella-Navarro M et al. Predictive model to identify multiple failure to biological therapy in patients with rheumatoid arthritis. Ther Adv Musculoskelet Dis. 2022 Oct 6;14:1759720X221124028.

Table 1. Prediction model in training data set

Predictor	Odds Ratio	95% CI	coefficient
CDAI prior to switch			
Remission (ref)	1		
Low	1.75	(1.390 to 2.203)	0.559
Moderate	2.394	(1.845 to 3.107)	0.873
Severe	2.964	(2.141 to 4.103)	1.086
Pt Pain prior to switch (0-100)	1.01	(1.006 to 1.013)	0.010
Age (yrs)			
≤40 (ref)	1		
41-50	0.958	(0.684 to 1.341)	-0.043
51-60	0.823	(0.603 to 1.123)	-0.195
61-70	0.747	(0.549 to 1.017)	-0.291
>70	0.606	(0.436 to 0.843)	-0.501
Prior no. of biologics/tsDMARDs			
0	1		
1	0.904	(0.749 to 1.090)	-0.101
2	0.788	(0.630 to 0.984)	-0.239
3+	0.706	(0.558 to 0.893)	-0.348
Change in CDAI at prior to switch (spline at zero)			
<0	1.011	(1.004 to 1.018)	0.011
>0	1.044	(1.022 to 1.067)	0.043

CDAI: clinical disease activity index; DMARD: disease modifying anti-rheumatic drugs; ts: targeted synthetic; ref: reference

Figure 1: Predicted probability of switching based on model estimated using training data set, and applied to test data set



Area under ROC curve: 0.690 Area under ROC curve: 0.687

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POS0469

BEHOLD THE WINDOW, MIND THE BUILDING! LONG-TERM BENEFITS FROM EARLY RHEUMATOID ARTHRITIS TREATMENT VANISHED UNDER REAL-LIFE CONDITIONS: RESULTS FROM THE REAL STUDY

Keywords: Rheumatoid arthritis

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Background: In experimental settings, early treatment is associated with better outcomes in rheumatoid arthritis (RA), underpinning the concept of a "window of opportunity". Under real-life conditions, though, the long-term maintenance of such benefits is uncertain.
Objectives: To assess the long-term maintenance of expected clinical benefits associated with early RA treatment under real-life conditions.
Methods: Adults meeting the ACR/EULAR (2010) criteria for RA were included. The participants had long-standing disease, been followed up in 11 healthcare centers in Brazil as part of the REAL study. [1] Individuals whose treatment had been initiated within 6 months of disease onset were compared with those treated for the first time only later on. Disease activity (DAS28-CRP), physical function (HAQ) and the presence of erosive disease were evaluated. Chi-squared and t tests, along with logistic and linear regression were used to verify associations. p-values < 0.05 were deemed significant. The study received ethical approval, and all participants gave informed consent.
Results: 995 participants were included; 89.6% female; 56% white. The mean (SD) age was 56.8 (11.6) years; cumulative schooling years: 8.1 (4.25). The median (IQR) disease duration was 147 (81–236) months. Rheumatoid factor was positive in 77.6%. The mean (SD) DAS28 was 3.28 (1.38); median (IQR) HAQ score: 0.750 (0.250–1.500). Erosive disease occurred in 54.2%. Table 1 compares early- vs. late-treated patients, showing small effect sizes in clinical outcomes. After adjusting for age, schooling years, disease duration and corticosteroid use, early treatment was no longer an independent predictor of DAS28 scores ($\beta = 0.153$; p = 0.160), HAQ scores ($\beta = 0.023$; p = 0.682) or erosive disease [Exp(β) = 0.926; p = 0.626].
Conclusion: In long-standing RA, only small differences in disease activity, physical function and erosive disease were associated with early or late initial treatment. After adjusting for confounders, these differences vanished, indicating that beyond the "window" of opportunity lies a "building" of continued disease management, which might be of even greater relevance for the long-term outcomes in real-life settings.
REFERENCE:

[1] da Rocha Castelar-Pinheiro et al. The REAL study: a nationwide prospective study of rheumatoid arthritis in Brazil. Advances in Rheumatology (2018) 58:9.

Table 1. Comparisons between participants with long-standing rheumatoid arthritis, initially exposed to early (<= 6 months) vs. late (> 6 months) treatment regarding symptoms onset.

Characteristics	Treatment Initiation (6-month cutoff)		Effect sizes[(a)] [95% CI]		p-values
	Early (N = 279)	Late (N = 716)			
Background features					
Female gender	90% (n=251)	89.5% (n=641)	0.95 [0.60, 1.51]*	V = 0.01	0.838
Non-white race	40.1% (n=112)	45.5% (n=326)	1.25 [0.94, 1.65]*	V = 0.05	0.124
Positive rheumatoid factor	77.1% (n=212)	77.9% (n=549)	1.05 [0.75, 1.46]*	V = 0.01	0.792
Corticosteroids use	41.6% (n=116)	49.9% (n=357)	1.40 [1.06, 1.85]*	V = 0.08	0.019**
Biological DMARD use	35.5% (n=99)	32.8% (n=235)	0.89 [0.66, 1.19]*	V = 0.03	0.424
Age, years, mean (SD)	55.5 (12.5)	57.3 (11.2)	1.8 [0.2, 3.4]†	d = 0.15	0.029**
Schooling years, mean (SD)	8.8 (4.4)	7.8 (4.2)	-1.0 [-1.6, -0.5]†	d = 0.25	0.001**
Disease duration[(b)], median (IQR)	113 (65–182)	161 (90–257)	50.5 [36.5, 64.5]†	d = 0.44	<0.001**
Clinical outcomes					
DAS28-CRP score, mean (SD)	3.08 (1.38)	3.35 (1.37)	0.28 [0.07, 0.48]†	d = 0.20	0.009**
HAQ score, median (IQR)	0.625 (0.125–1.375)	0.875 (0.344–1.500)	0.125 [0.018, 0.232]†	d = 0.16	0.022**
Erosive disease	48.9% (n=133)	56.3% (n=398)	1.35 [1.02, 1.78]*	V = 0.07	0.037**

(a) Effect sizes: odds ratios and Cramer's V for proportions; mean differences and Cohen's d for continuous variables. (b) In months, upon study inclusion. **p-values significant at <0.05.

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POS0470 A MACHINE LEARNING MODEL FOR IDENTIFYING IMPORTANT CLINICAL VARIABLES AND PREDICTING ONE-YEAR TREATMENT RETENTION IN PATIENTS WITH RHEUMATOID ARTHRITIS PERFORMING AN INFLIXIMAB BIOSIMILAR-TO-BIOSIMILAR SWITCH

Keywords: Prognostic factors, Artificial intelligence, Rheumatoid arthritis

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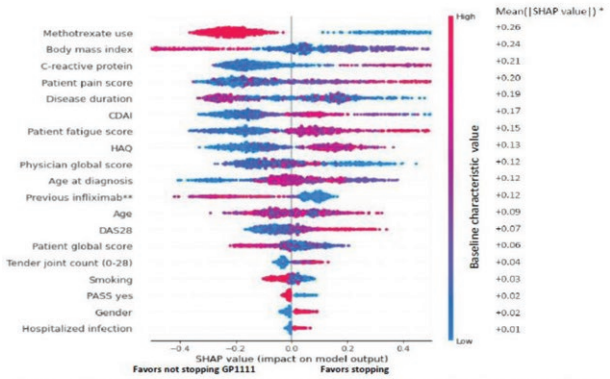
Background: In Denmark, a nationwide mandatory infliximab biosimilar-to-biosimilar switch, from CT-P13 to GP1111, was recently conducted in patients with rheumatoid arthritis (RA) to save costs (ref). It is of interest to identify patients having favorable outcomes based on clinical characteristics at time of switch.
Objectives: We aimed to explore important baseline clinical factors by implementing a robust machine learning (ML) model to predict one-year GP1111 treatment retention.
Methods: Patients with RA who performed a biosimilar-to-biosimilar switch from CT-P13 to GP1111 between April 2019 -Feb 2020 (=switchers) were identified in the nationwide DANBIO registry. Clinical characteristics at GP1111 start (=baseline) were identified in DANBIO and through linkage to national patient registries (comorbidities). Missing baseline data were estimated using Multivariate Imputation by Chained Equations (20 imputations). A tree-based algorithm Extreme Gradient Boosting (XGBoost) was used to predict main outcome, defined as stop of GP1111 during one year of follow-up (stop/no stop). Contributing baseline characteristics were investigated as SHAP values. Due to imbalanced dataset (low stop rate), the ML model excellently predicted the majority outcome (no stop) but poorly the minority (stop). Thus, we incorporated rebalancing strategies (Random Oversampling, ROS, Random Undersampling, RUS, Synthetic Minority Oversampling Technique, SMOTE, Near Miss Algorithm, NearMiss) and the performance was inspected (confusion matrix). Optimal cut-offs (thresholds) were identified by Youden Index, Receiver Operating Characteristic Curve (ROC), Precision-Recall Curve to improve model-performance for the minority outcome. Analyses were performed in R and Python.
Results: We included 685 RA switchers whereof 17% stopped GP1111 during one year of follow-up (**Table 1**). SHAP values for 26 characteristics were investigated (**Figure 1**, see footnote). The ranges for accuracy and Area Under the ROC (AUC) were 79-87% and 0.78-0.85, with specificity and sensitivity ranging 0.79-0.99 and 0.01-0.12 respectively. This indicated a high true negative rate (specificity, predicting no stop of GP1111) and low true positive rate (sensitivity) i.e., poor prediction of GP1111 stop. With oversampling and undersampling methods, ranges for accuracy and AUC were 60-87% and 0.60-0.87 respectively, with specificity ranging 0.61-0.73 and sensitivity 0.50-0.67 corresponding to a higher true positive rate. This could be explained by RUS and NearMiss removing data from majority outcome and by ROS and SMOTE adding data to the minority outcome. Optimal threshold methods resulted in higher true positive rates and with a range for accuracy 70-85% (specificity 0.67-0.74, sensitivity 0.66-0.76).

Table 1. Baseline characteristics in switchers. Stratified by stop/no stop of GP1111 during one year of follow-up

	No stop	Stop
Number of patients, n (%)	571 (83)	114 (17)
Female, %	70	65
Age, years	47 (35, 56)	48 (37, 57)
CDAI	4 (2,8)	8 (4,13)
CRP, mg/L	2 (1, 5)	4 (1, 12)
Concomitant methotrexate, %	78	61
Body mass index, kg/m2	25 (22, 29)	24 (22,27)
HAQ	0.5 (0.1, 1.1)	1.0 (0.5, 1.5)
Disease duration, years	11 (5, 20)	8 (5, 13)
Physician global, VAS, mm	5 (2,10)	8 (2,20)
Patient pain VAS, mm	22 (8, 43)	37 (22, 70)

Numbers are median (IQR) unless otherwise stated

Figure. Machine Learning (ML) model with SHAP values for baseline characteristics



Beeswarm plot. The plot shows how the baseline characteristics of each patient affect the prediction of the ML model towards either stop or no stop of GP1111.
The x-axis stands for SHAP values, and in the y-axis the baseline characteristics. Each point in the plot is one SHAP value for a given patient. Red color means a high baseline value and blue color means a low baseline value. Variables are sorted by their mean absolute SHAP value in descending order with most important variables at the top. The further away from the vertical line at x=0, the larger the impact on the prediction. Negative SHAP values are contributing to increased chance towards not stopping GP1111, while positive SHAP values are pushing the model prediction towards stop of GP1111. As examples, methotrexate use (i.e., red color) has negative SHAP values indicating a change towards not stopping GP1111, high values of fatigue scores (red color) indicate a change towards stop of GP1111, low values of C-reactive protein (blue color) indicate a change towards not stopping GP1111. Variables with little impact are not shown (e.g., comorbidities, swollen joint count)
**Mean absolute SHAP values for prediction model*
***Previous treatment with infliximab oriainator*

Conclusion: We implemented a robust machine learning model for predicting one-year retention in infliximab switchers and identified important baseline clinical characteristics. However, the model was challenged by imbalanced data (low stop rate) which was overcome by oversampling methods and optimal cut-offs. Careful methodological considerations are needed when advanced statistical models are applied to imbalanced datasets.

REFERENCE:

[1] Nabi et al, doi: 10.1136/rmdopen-2022-002560

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POS0471 SPECIFIC SYMPTOM CLUSTERS AT DIAGNOSIS SIGNAL A POORER EARLY RA PROGNOSIS: DATA FROM THE CANADIAN EARLY ARTHRITIS COHORT

Keywords: Rheumatoid arthritis, Patient reported outcomes, Epidemiology

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Background: Early RA is characterized by multiple symptoms that impact daily function and HRQL. Little is known about whether there are symptom clusters evident at diagnosis that could identify patients with a poorer prognosis, or the stability of clusters over time.
Objectives: To identify patient-reported symptom clusters at RA diagnosis, associated sociodemographic and RA characteristics, and the stability of clusters over the first 6 months.
Methods: Using data from the Canadian Early Arthritis Cohort (CATCH), we applied **latent class analysis** with baseline PROMIS-29 pain, fatigue, depression, anxiety, and sleep scores to select relevant symptoms and levels using AIC, BIC, G-square and log-likelihood results. Baseline PRO and clinical differences among clusters were compared. Next, we evaluated the stability of these clusters at 3 and 6 months. **Latent transition analysis** was used to estimate the probability of transitioning among classes.

Results: The sample included 310 adults with a new RA diagnosis, with 6-month PROs available, and who were MTX naïve at baseline. Participants had a mean age 56, CDAI 29.3, and symptoms for 5 months; 67% were women and 78% White. The optimal symptom set included pain, fatigue, depression, and anxiety (levels: none, mild, moderate, severe). We identified 4 clusters: **Minimal** (12%); **Moderate Pain Dominant** (40%); **Multiple Moderate-Severe** (35%); and **Multiple Mild** (11%). Clusters had similar sociodemographics except **Minimal** were slightly older and less female; SJC and TJC were similar among classes **Multiple Mild** or **Moderate-Severe** classes had significantly worse mood and sleep (Table 1). More patients in **Multiple Moderate-Severe** and **Moderate Pain** had parenteral steroids whereas numerically more in **Minimal** or **Multiple Mild** groups were on oral steroids. RA Participant Characteristics around diagnosis by symptom clusters.

Table 1.

Baseline Values (mean SD, N %)	Minimal N=38 (12%)	Moderate Pain N=124 (40%)	Multiple Moderate-Severe N=114 (37%)	Multiple Mild N=34 (11%)	SIG
Patient Global (0-10)	2.6 (2.4)	4.8 (2.3)	6.9 (2.0)	3.9 (2.2)	<0.0001
PROMIS-29					
Anxiety > 55	1 (3%)	15 (12%)	108 (95%)	28 (82%)	<0.0001
Depression > 55	0 (0%)	14 (11%)	100 (88%)	22 (65%)	<0.0001
Fatigue > 55	3 (8%)	49 (40%)	106 (93%)	12 (35%)	<0.0001
Pain Interference > 55	0 (0%)	124 (100%)	113 (99%)	25 (74%)	<0.0001
Physical Function < 45	9 (24%)	107 (86%)	111 (97%)	25 (74%)	<0.0001
Participation < 45	5 (13%)	81 (65%)	108 (95%)	17 (50%)	<0.0001
Sleep > 55	2 (5%)	46 (37%)	88 (77%)	17 (50%)	<0.0001
Physical Function (0-10)	2.9 (2.3)	6.1 (2.4)	7.7 (1.9)	4.2 (2.7)	<0.0001
Stiffness (0-10)	3.2 (2.4)	6.3 (2.4)	7.7 (1.8)	4.3 (2.3)	<0.0001
Oral steroids	16 (42%)	40 (32%)	29 (25%)	14 (41%)	0.1470
Parenteral steroids	**8 (21%)**	**44 (35%)**	**62 (54%)**	**7 (21%)**	**<0.0001**
TJC-28, median (IQR)	8 (6,12)	9 (5,13)	9 (5,13)	7 (5,12)	0.4626
SJC-28, median (IQR)	7 (5,12)	8 (4,12)	7 (4,12)	6 (3,11)	0.4396
CDAI, mean (SD)	**25.5 (11.4)**	**29.2 (12.7)**	**32.0 (14.0)**	**24.8 (12.6)**	**0.0103**

Substantial improvement was evident in 67% at 3 months (42% **Minimal,** 25% **Multiple Mild;** Figure 1). At 6 months, 45% were **Minimal** and 25% **Multiple Mild**. The best prognosis was for **Minimal**; almost all stayed **Minimal** at 3 (95%) and 6 (87%) months. Next best was **Moderate Pain** where 71% improved (**Minimal** 64%; **Multiple Mild** 7%). A poorer prognosis was seen for **Multiple Moderate-Severe**: at 3 months, 61% improved (13% **Minimal**, 33% **Multiple Mild**). **Multiple Mild** also were less likely to improve with 11% **Minimal** and 6% worsening by 3 months.

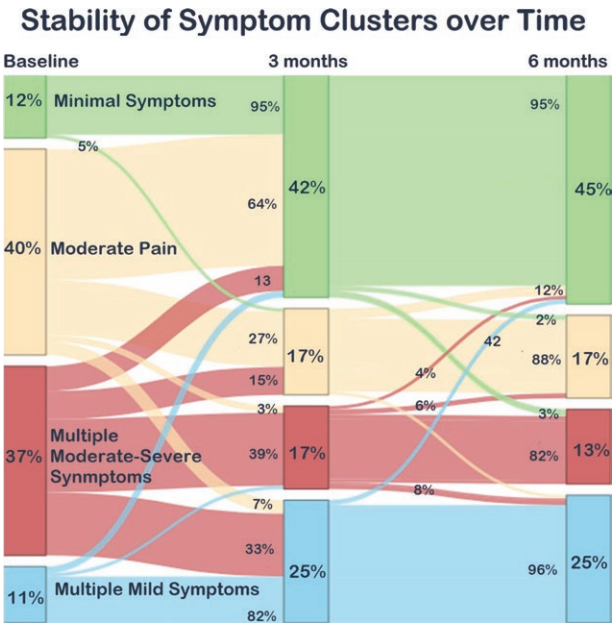


Figure 1.

Conclusion: In this large early RA cohort, we identified 4 distinct symptom clusters around diagnosis that were stable over 6 months and had distinct PRO profiles. At baseline, most (70%) participants were classified as **Moderate Pain Dominant** or **Multiple Moderate Symptoms**; the remainder had **minimal or multiple mild symptoms**. By examining symptom clusters, we found more homogeneous groups of patients. Our results also suggested that having multiple symptoms around diagnosis was associated with less improvement over the first 6 months, and may signal a more guarded prognosis for symptom improvement and HRQL in early RA.

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Disclosure of Interests: Susan J. Bartlett Speakers bureau: Amgen, Janssen, Organon, Merck, Pfizer, Sandoz, Consultant of: Janssen, Merck, Organon, Sandoz, Clifton O Bingham: None declared, Orit Schieir: None declared, Marie-France Valois: None declared, Gilles Boire Speakers bureau: Merck, BMS, Pfizer, Janssen, Consultant of: Amgen, BMS, Celgene, Eli Lilly, Pfizer, Grant/research support from: Amgen, Abbvie, BMS, Eli Lilly, Merck, Novartis, Pfizer, Sandoz, Janet Pope Speakers bureau: UCB, Sandoz, Consultant of: AbbVie, Actelion, Amgen, Bayer, BMS, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead, Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Grant/research support from: Abbvie, BMS, Eli Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Louis Bessette Speakers bureau: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Consultant of: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Carter Thorne Consultant of: Abbvie, Amgen, Celgene, Centocor, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, Grant/research support from: Abbvie, Celgene, CaREBiodam, Novartis, Pfizer, Diane Tin: None declared, Carol Hitchon Grant/research support from: Pfizer and UCB, Glen Hazlewood: None declared, Edward Keystone Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Pfizer Pharmaceuticals, Sanofi Genzyme, UCB, Consultant of: AbbVie, Amgen, AstraZeneca Pharma, Bristol-Myers Squibb Company, Celltrion, Myriad Autoimmune, F. Hoffmann-La Roche Inc, Genentech Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepsis, Grant/research support from: AbbVie, Amgen, Gilead Sciences, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, PuraPharm, Sanofi, Vivian Bykerk Consultant of: Amgen, BMS, Gilead, Regeneron, UCB, Grant/research support from: Amgen, BMS, Genzyme, Pfizer, Regeneron Sanofi Aventis, UCB.

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POS0472

TREATMENT RESPONSE TO INTRAMUSCULAR STEROIDS IN PATIENTS LIVING WITH RHEUMATOID ARTHRITIS: AN EXPLORATORY ANALYSIS USING TRACKED DAILY SYMPTOMS

Keywords: Telemedicine, Patient reported outcomes, Epidemiology

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Background: Current understanding of treatment response is largely based on patient recollection at infrequent clinic appointments, which introduces inaccuracies through recall error. Real-time patient-reported symptom data collected frequently following an intervention could improve our understanding of treatment response, facilitating better clinical decision making.

Objectives: Our exploratory analysis reports a case-series of patients who used the Remote Monitoring of Rheumatoid Arthritis (REMORA) smartphone-app for daily symptom tracking, evaluating their longitudinal pain-scores following intramuscular (IM) steroids to determine the duration and extent of treatment response.

Methods: We identified patients participating in the REMORA study Nov 2021-Sep 2022 who received an IM steroid. Concomitant disease-modifying medications were noted. Daily pain scores (out of 10) from 10 days preceding the injection and 8 weeks following were analysed. Analysis was based on the following definitions: [1] Pre-injection pain score: mean pain-score in the 10 days preceding injection; [2] Response (Y/N): ≥1 day of pain score <[1]; [3] Response start time: the day following injection; [4] End of response: first date following injection with pain score ≥[1]; [5] Response duration: number of days between [3] and [4]; [6] Average pain-score response: mean pain score during [5]; [7] Nadir pain score response: lowest pain score during [5]; [8] Average pain score improvement: difference between [1] and [6]; [9] Maximum pain score improvement: difference between [1] and [7].

Results: Thirty-two patients were identified for inclusion, of whom 6 received ≥1 steroid injections. In total 9 injections were given. Pre-injection pain scores ranged 3.33-9.29. Seven injections demonstrated response, 2 did not. Of the responders, duration ranged 1-54 days (median 9 days); average pain score improvement ranged 0.14-5.33 (median 3.33); maximum pain score improvement ranged 0.14-7.00 (median 4.33). Table 1 summarises our results. Figure 1 demonstrates the patterns of treatment response for each steroid injection.

Table 1. individual treatment response and demographic data

Injection number (patient number)	Age (years)	Sex (M/F)	Concomitant drugs during analysis period	IM steroid dose (mg)	Response (Y/N)	Response duration (days)	Pre-injection pain score	Average pain score response	Nadir pain score response	Average pain score improvement	Maximum pain score improvement
1 (1)	30	M	MTX	120	Y	9	7.33	4.00	3.00	3.33	4.33
2 (1)	30	M	MTX, SSZ	120	Y	10	8.00	2.67	1.00	5.33	7.00
3 (1)	30	M		180	Y	9	5.40	1.80	1.00	3.60	4.40
4 (2)	53	F	MTX, HCQ	120	Y	7	3.33	3.00	3.00	0.14	0.14
5 (3)	52	M	MTX	160	Y	1	5.75	4.00	4.00	1.67	1.67
6 (3)	52	M	SSZ	160	N		9.29				
7 (4)	53	M	MTX	120	Y	41	4.56	2.21	1.00	2.35	3.56
8 (5)	65	M	SSZ, HCQ	120	Y	54	7.00	2.56	1.00	4.44	6.00
9 (6)	40	F	MTX, SSZ	120	N		5.56				
					Range (Median)	1-54 (9)	3.33-9.29 (5.75)	1.80-4.00 (2.67)	1.00-4.00 (1)	0.14-5.33 (3.33)	0.14-7.00 (4.33)

MTX: Methotrexate; SSZ: Sulfasalazine; HCQ: Hydroxychloroquine

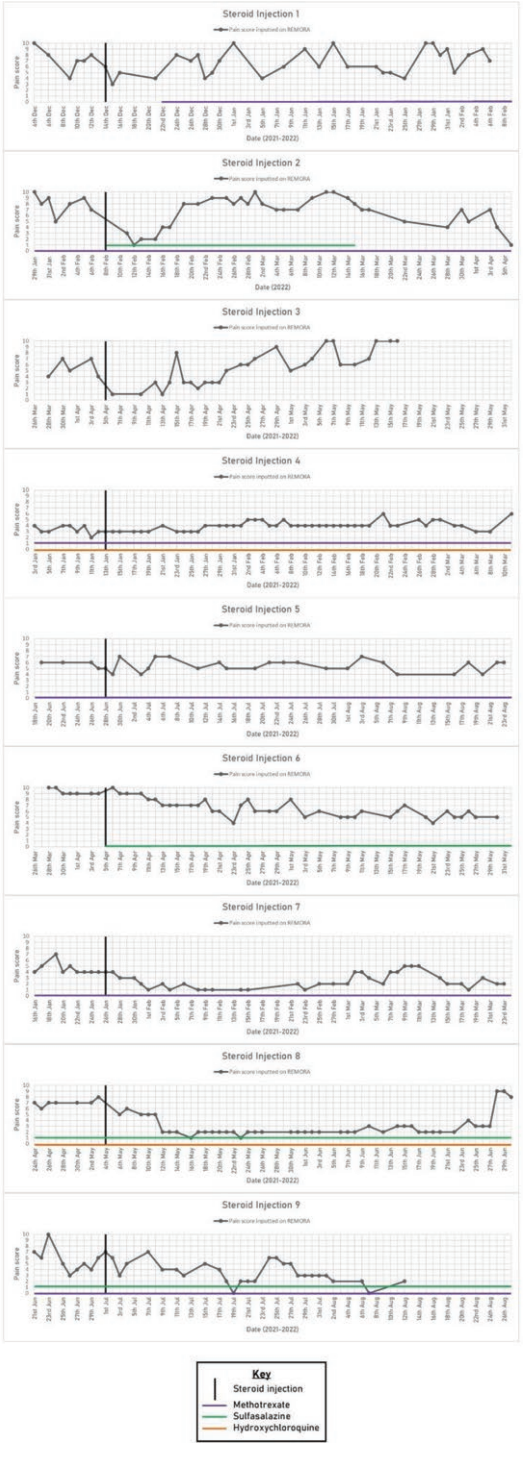


Figure 1. patterns of treatment response to IM steroids and concomitant therapies

Conclusion: Smartphone-based remote monitoring has the potential to improve clinical care for people living with rheumatoid arthritis. In this analysis, we demonstrated a novel means to accurately assess treatment response using tracked symptom data. The duration and extent of response to steroid injections was quantified for all participants, data which is typically imprecise and relies on recall. In these preliminary results, response duration was shorter, and pain score improvement was smaller, than anticipated. Analysis of tracked symptom data across a larger population may help to identify treatment responder characteristics, supporting more targeted therapeutic strategies. This has significant implications for high-cost drugs such as biologics. Further work is required to develop consensus definitions for treatment response and disease activity in time-series data, and a means to account for the effects of concomitant drugs.

REFERENCES: NIL.

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POS0473

ASSESSMENT OF THE LEVELS OF 14-3-3H PROTEIN, A NOVEL BIOMARKER, IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ITS CORRELATION WITH DISEASE ACTIVITY

Keywords: Biomarkers, Diagnostic tests, Rheumatoid arthritis

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Background: Rheumatoid Arthritis (RA) is a common inflammatory arthritis. Current ACR-EULAR classification criteria for RA include joint involvement, immunological markers {Rheumatoid factor (RF) and Anti-citrullinated protein antibody (ACPA)}, inflammatory markers {Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)}, and symptom duration. But these markers are not 100% accurate for RA. A meta-analysis found sensitivity and specificity of RF and ACPA to be 69% & 85% and 67% & 95% respectively [1]. There is a need for new biomarkers that can increase accuracy of RA diagnosis, one such marker is 14-3-3η protein which is a pro-inflammatory mediator and can serve as a diagnostic and prognostic marker and a potential therapeutic target in RA patients [2,3].

OBJECTIVES:

- Assess 14-3-3η protein levels in RA patients.
- Compare positivity rates of 14-3-3η to RF and ACPA.
- See association between 14-3-3η levels and disease activity.

Methods: 78 RA cases and 78 age & sex matched healthy controls were enrolled. Inclusion criteria were RA diagnosis (as per 2010 ACR/EULAR criteria), age above 18 years. Patients with any other disease & pregnant females were excluded. DAS28-ESR scoring was done. Blood was collected and tested for ESR, CRP, RF, ACPA, and 14-3-3η protein using ELISA.

Results: Mean age in years in cases and controls was 41.71 and 41.37 respectively. 88% participants were females. Median disease duration was 32.5 months, median tender joint count was 4.50 and median swollen joint count was 1. Mean ESR in cases & controls was 32.41 ± 18.8 mm and 10.79 ± 3.49 mm respectively ($p=0.001$). CRP was positive in 70.5% cases & 11.5% controls ($p < 0.001$), RF in 88.5% cases & 11.5% controls ($p < 0.001$) and ACPA in 73% cases & none of the controls ($p < 0.001$). Mean 14-3-3η protein levels (ng/ml) were 7.61 ± 2.55 in cases and 0.73 ± 0.43 in controls ($p < 0.001$); 7.64 ± 2.62 in seropositive cases and 7.18 ± 1.62 in seronegative cases ($p =0.673$). There was a significant difference between 14-3-3η protein levels in seronegative patients and controls ($p= 0.001$).14-3-3η protein levels had no correlation with RF/ACPA positivity ($p= 0.965$) (Figure 1). Mean 14-3-3η protein levels (ng/ml) in patients in "remission"

(as per DAS28-ESR) was 5.71± 2.50, while the levels(ng/ml) in patients in low, moderate, and high disease activity were 8.58 ± 4.04, 6.98 ± 1.00 and 8.36 ± 2.62 respectively (p= 0.020). The sensitivity and specificity of RF were 88.5% each, of 14-3-3η was 100% and 90.1% respectively and that of ACPA were 73.1% and 100% respectively. 14-3-3η protein had higher sensitivity than the other 2 biomarkers (p=0.001). ROC curve suggested the ideal cut-off of 14-3-3η protein to be 1.14 ng/ml with a sensitivity of 100% and a specificity of 90.1%. When RF and ACPA were combined, the sensitivity and specificity were 96.9% and 88.5% respectively. When 14-3-3η was combined with RF, sensitivity, and specificity was 100% and 79.7% respectively while it was 100% and 90.1% respectively when 14-3-3η was combined with ACPA. Thus, 14-3-3η protein increased the sensitivity of RF and ACPA.

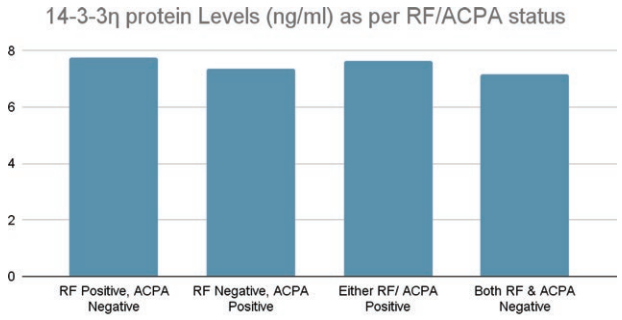


Figure 1

Conclusion: 14-3-3η protein levels are significantly raised in both seropositive and seronegative RA patients and it does not depend on RF or ACPA. 14-3-3η protein increases the sensitivity of RF and ACPA in RA diagnosis and should be included as an additional test in evaluation of RA patients.

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POS0474

FACTORS ASSOCIATED WITH EROSIVE RHEUMATOID ARTHRITIS, A MULTIMARKER PRINCIPAL COMPONENT ANALYSIS (PCA) AND PRINCIPAL COMPONENT REGRESSION (PCR) ANALYSIS

Keywords: Bone diseases, Rheumatoid arthritis, Biomarkers

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Background: Various clinical (disease activity, seropositive RA etc.) and metabolic risk factors (Dkk1 etc.) have been associated with erosive rheumatoid arthritis (RA). However, such risk factors might be intertwined, and multicollinearity might reduce our ability to discern the individual contribution to erosive score. Principal component analysis (PCA) is statistical technique for reducing dataset's dimension and principal component regression (PCR) is a regression analysis based on PCA. PCR overcomes the multicollinearity problem.

Objectives: To investigate the clinical and bone metabolic risk factors associated with erosive RA using PCA and PCR.

Methods: We conducted a cross-sectional analysis on seropositive RA patients not responding to first-level disease-modifying antirheumatic drug, candidate to bDMARD treatment. Clinical, radiographic (both hands and feet x-ray), laboratoristic and densitometric (BMD parameters were collected. Sharp van der Heijde Score (SvdHS) was calculated by two independent readers. Serum samples were collected and assayed for C-terminal telopeptide of type I collagen (CTX), Procollagen I Intact N-Terminal Peptide (P1NP), Dkk1, Sclerostin (SOST), 25-OH-Vitamin D (VitD), and PTH. PCA was applied to reduce dimensionality of the dataset and find clusters of variables recording largely redundant information. PCs were selected based on eigenvalues explaining >75% of total variance. PCR was used to predict the SvdHS. Results were analyzed using PCA package on GraphPad Prism version 9.5.0 for Windows, GraphPad Software, San Diego, California USA.

Results: 62 RA patients aged 57.2 years (SD 12.1) were consecutively enrolled. Mean DAS28-CRP was 4.17 (SD 1.27) and median SvdHS was 24 (IQR 12-53). The loadings plot (**Figure 1**) shows the clusters of correlated variables in the dataset (vectors). In **Table 1** are presented the results of the PCR with SvdHS as outcome. We found that age, GC treatment, ACPA titer, RF titer, CRP levels, ESR, CTX serum levels and Dkk1 serum levels were significantly positively correlated with SvdHS, whereas P1nP serum levels and PGA were negatively correlated with SvdHS.

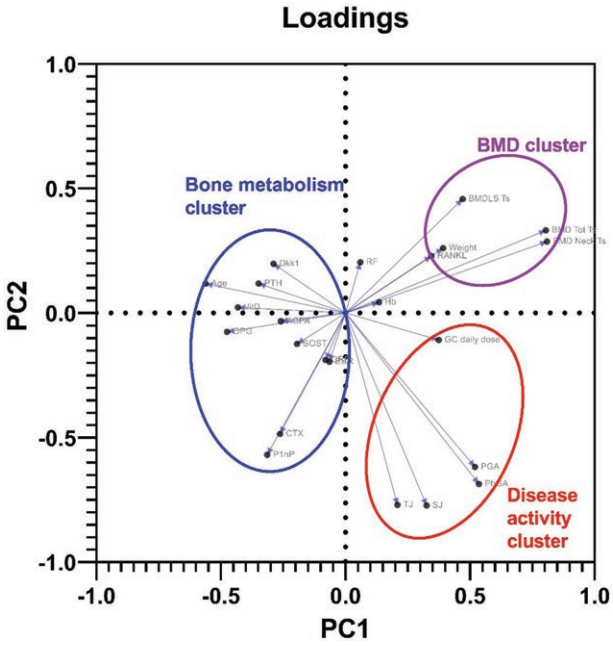


Figure 1. Loadings plot from PCA. When the vectors are close, forming a small angle, the two variables they represent are positively correlated. If they meet each other at 90°, they are not likely to be correlated. When they diverge and form a large angle (close to 180°), they are negative correlated.

Table 1. Results of the principal component regression (PCR) analysis

Variable	Estimate	Standard error	P value
Intercept	-13,85	26,92	0,61
Age	**0,54**	**0,18**	**0,006**
Weight	0,004	0,13	0,97
GC daily dose	**2,05**	**0,68**	**0,007**
TJ	-0,22	0,29	0,45
SJ	-0,06	0,34	0,85
PGA	**-2,08**	**0,84**	**0,02**
PhGA	-0,45	1,04	0,66
ACPA	**0,007**	**0,003**	**0,03**
RF	**0,10**	**0,04**	**0,01**
CRP	**0,39**	**0,15**	**0,01**
ESR	**0,44**	**0,12**	**0,002**
Hb	-0,14	0,16	0,40
CTX	**30,05**	**13,62**	**0,03**
P1nP	**-0,20**	**0,08**	**0,01**
Dkk1	**0,32**	**0,14**	**0,03**
SOST	0,18	0,28	0,52
OPG	-0,39	0,72	0,59
RANKL	-12,86	13,49	0,3514
PTH	-0,2879	0,1694	0,1041
VitD	0,1291	0,1990	0,5235
BMD LS Ts	1,163	1,694	0,4999
BMD Neck Ts	-0,8988	1,585	0,5766
BMD Tot Ts	-0,7266	1,492	0,6314

Conclusion: We found that age, seropositivity, and inflammation were the independent clinical risk factors associated with erosive RA. CTX and Dkk1 serum levels were the metabolic factors independently associated with erosive disease whereas P1nP serum levels were associated with less erosions.

REFERENCES: NIL.

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POS0475 FACTORS INFLUENCING ACCEPTANCE AND PERSISTENCE OF ELECTRONIC PATIENT-REPORTED OUTCOMES COLLECTION IN A REAL-WORLD CLINICAL SETTING

Keywords: Patient reported outcomes, Rheumatoid arthritis, Health Services Research

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Background: Rheumatoid arthritis (RA) has a relapsing-remitting nature, making it difficult to predict when patients should be seen. Collection of patient-reported outcomes (PROs) effectively communicates patients' disease experiences. However, certain factors could impact the utilization and persistence of PROs collection.

Objectives: To explore the impact of demographic, clinical parameters on acceptance and long-term utilization of smartphone application (app) for electronic PROs (ePROs) collection.

Methods: A retrospective analysis of anonymized data collected through app as part of routine care delivered in outpatient clinic at North Bristol NHS Trust. Patients agreed to use a smartphone-based diary (LivingWith) to record disease activity between appointments by reporting weekly RAPID3, HAQ every 28 days. 28 tender/swollen joint count (JC) could also be assessed. Patients with ≥1 record were analyzed, including all reports until last follow-up. Disease activity and disability categories were defined on baseline RAPID3, HAQ scores [1,2]. Mean and SD or median and IQR were reported. T-test, Mann–Whitney U, Kruskal–Wallis tests were used. Kaplan-Meier analysis was produced. Statistical tests were performed using Stata 16.1 (StataCorp, USA) and RStudio V.1.4.1717.

Results: 306 (81.4%) patients had completed both questionnaires, 16.2% just RAPID3, and 2.4% only HAQ. 74% of participants were women with mean age 56±14. 27(6.7%) of patients didn't provide either RAPID or HAQ and assessed only 28 JC. The median number of completed records for RAPID3 and HAQ was 10 [4;31] and 4 [2;10] respectively. The median number of days following registration when the first ePRO was completed was 9 [0;17] for RAPID3 and 4 [0; 32.5] for HAQ. The median time between ePRO completion was 13 days [8;29] for RAPID3 and 29 days [3; 483] for HAQ. The median RAPID3 score was 10.5 [5.6;15.9] and HAQ score 1.02 [0.5;1.625]. The median period [CI] for patients' app engagement for RAPID3 was 67 weeks [55;83], for HAQ 48 weeks [36;60] (Figure 1). Demographic parameters at the registration as well as baseline disease activity and disability categories had no clear relationship with patient engagement in app use (Table 1).

Table 1. The impact of demographic and clinical factors on the persistence of ePROs collection.

Baseline factor	Max elapsed days Median [IQR]		ePROs number Median [IQR]		Average days between ePROs Median [IQR]	
	Rapid3	*HAQ*	*Rapid3*	*HAQ*	*RAPID3*	*HAQ*
Female (n=227)	270[57;560]	167[0;471]	9 [4;29]	4 [1;10]	14 [8;31]	28 [0;47]
Male (n=79)	315[114;595]	259[28;504]	16 [5;44]	5 [2;11]	11 [8;24]	29 [14;53]
p-value	0.41	0.20	0.023	0.18	0.21	0.26
Age, years:						
<50 (n=102)	243[63;511]	158 [22;447]	8[4;20]	4 [2;8]	16 [10;34]	33 [10;50]
50-59 (n=72)	265[53;543]	157[0;476]	8 [4;28]	4 [1;11]	15 [7;34]	46 [28;46]
60-69 (n=75)	281[99;610]	224[13;524]	14[4;43]	5 [2;11]	12 [7;29]	29 [7;48]
>70 (n=57)	379[11;595]	201[2;450]	17[5;59]	4 [2;11]	10 [7;24]	26 [1;43]
p-value	0.58	0.74	0.04	0.34	0.07	0.57
RAPID3:						
<2.0 (n=28)	280[39;616]	210[0;539]	9[3;36]	5 [1;13]	16 [8;30]	27 [0;41]
2.1-4.0 (n=19)	486[141;602]	382[110;602]	19[5;69]	7 [4;16]	9 [8;20]	36 [22;45]
>4.0 (n=259)	262[63;546]	172[4;447]	9[4;30]	4 [2;10]	13 [8;30]	28 [2;49]
p-value	0.44	0.24	0.15	0.16	0.59	0.60
HAQ:						
≤1.0 (n=153)	262[77; 560]	175[0;532]	11[4;31]	4 [1;11]	13 [8;28]	29 [0;47]
>1.0-≤2.0 (n=121)	329[109;607]	212[21;437]	9[5;33]	4 [2;11]	15 [8;33]	30 [11;50]
>2.0-≤3.0 (n=32)	193[35;548]	42 [0; 364]	8[3;23]	2 [1;6]	12 [7;18]	14 [0;32]
p-value	0.38	0.15	0.73	0.12	0.17	0.07

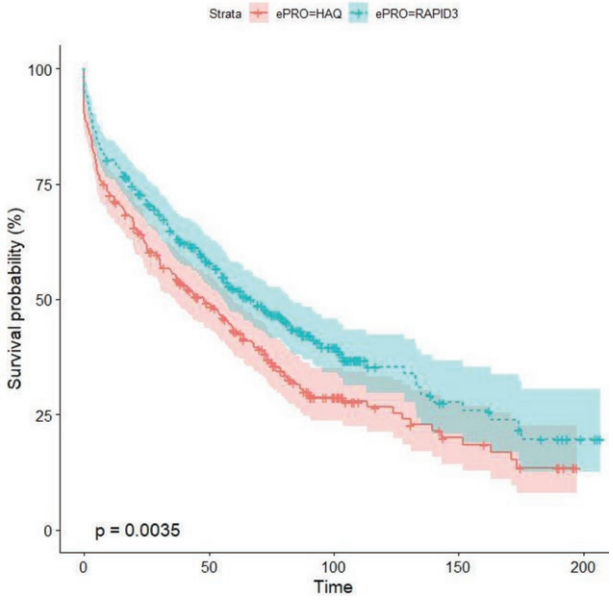


Figure 1. Patient engagement in the app.* Time in weeks

Conclusion: PROs collection provides valuable information on effectiveness and tolerability of health interventions. Patients' engagement in reporting decreases over time, suggesting the importance of reinforcement. Neither age, gender nor baseline clinical status appeared to be related to patient reporting persistence.

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POS0476 QUANTIFICATION OF REFERRAL BIAS IN PATIENT- AND CLINICIAN-REPORTED MEASURES OF RHEUMATOID ARTHRITIS SEVERITY BY GEOGRAPHIC DISTANCE FROM AN ACADEMIC RHEUMATOLOGY CENTER

Keywords: Geographical differences, Patient reported outcomes, Rheumatoid arthritis

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Background: Systematic bias to greater severity of rheumatoid arthritis (RA) is often presumed to exist in patients referred for evaluation at academic centers. However, the magnitude of this potential bias has not been quantified to our knowledge.

Objectives: The objective was to test the hypothesis that patients in a referral population have greater RA severity based on both patient- and clinician-reported measures than local patients.

Methods: This study included eligible patients with RA who attended an in-person or virtual appointment in the outpatient rheumatology clinic at an academic center between 1/1/2020 and 10/28/2021. RA was defined by at least 2 ICD-10 diagnosis codes ≥30 days but <2 years apart plus use of a qualifying RA medication. Referral population was ascertained by geographic distance from patient residence to the clinic building and categorized as local, <50 miles; regional, ≥50 to <150 miles; or national/international, ≥150 miles. Data were collected from the electronic health records for patient-reported and clinician-reported measures of disease severity. Patient-reported measures included global pain, global arthritis, and Patient-Reported Outcomes Information System (PROMIS)

computer adaptive tests for Pain Interference, Fatigue, Physical Function, and Ability to Participate in Social Roles and Activities. Chi-square or Kruskal-Wallis tests were used to analyze differences between groups, adjusting for age at the clinic visit and sex. Linear regression models were used to test for differences between groups in PROMIS measures and Clinical Disease Activity Index (CDAI), adjusting for age, sex, race/ethnicity, and appointment type (new vs. established).

Results: The study population included 3220 patients with RA, including 1631 local, 956 regional, and 633 national/international patients. Overall, mean (SD) age was 62.9 (13.7) yrs., 2312 (72%) were female, and 2947 (91.5%) were in-person visits. Proportions of new patients in the local, regional, and national/international populations were 5%, 9%, and 17%, respectively. All PROMIS measures were available within 7 days of appointment for 2677 (83%) patients, with no differences between groups (p = 0.394). Regional and national/international patients had significantly higher global pain, pain interference, and fatigue and significantly lower physical function and ability to participate than local patients. Regression analysis showed that regional and national/international patients had higher pain interference (on average: 1.3 and 1.6 units; p<0.001 and p<0.001, respectively) and worse physical function (on average: -1.0 and -2.2 units; p=0.008 and p<0.001, respectively) than local referent patients, adjusting for age, sex, race/ethnicity, and appointment type. In contrast, there were no significant differences between groups in CDAI (on average for regional and national/international: 0.3 and 1.1 units; p=0.73 and p=0.29, respectively).

Variable	Local (n = 1631)	Regional (n = 956)	National/ International (n = 633)	Total (n = 3220)	p
Global pain score (0-100)	35.9 (29.2)	39.5 (29.0)	41.8 (30.6)	38.2 (29.5)	0.002
PROMIS T-scores					
Pain Interference	57.0 (8.3)	58.4 (8.3)	58.8 (8.4)	57.8 (8.4)	<0.001
Fatigue	53.5 (9.6)	54.9 (9.8)	56.2 (10.1)	54.4 (9.8)	<0.001
Physical Function	42.4 (8.8)	41.2 (8.2)	40.0 (8.6)	41.6 (8.6)	<0.001
Ability to Participate	50.3 (9.1)	48.5 (9.4)	47.4 (9.2)	49.2 (9.3)	<0.001
Clinical Disease Activity Index	12.2 (11.7)	12.2 (10.7)	13.4 (12.1)	12.4 (11.5)	0.44
C-reactive protein, mg/L	7.8 (11.5)	7.2 (10.9)	7.9 (11.7)	7.6 (11.4)	0.99

Values are mean (SD) or number (%).

Conclusion: Referral bias by geographic distance from the outpatient rheumatology clinic is more evident in patient-reported than clinician-reported measures of RA severity. The findings inform the interpretation of RA disease severity measures in clinical practice and research and highlight the importance of patient-reported outcome measures.

REFERENCES: NIL.

Acknowledgements: NIL.

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POS0477

RELATIONSHIP BETWEEN SHARED EPITOPE STATUS AND REFRACTORY RHEUMATOID ARTHRITIS

Keywords: Registries, Biomarkers, Rheumatoid arthritis

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Background: Despite major advances in rheumatoid arthritis (RA) treatment and the improved outcomes that have been associated with the expanding number of advanced therapies available, a substantial number of patients are refractory to multiple biologics. To understand the mechanisms behind refractory RA (reRA) and ultimately improve therapies tailored to individuals, a better understanding of associated factors is necessary. The shared epitope (SE) is an amino acid sequence motif coded by several HLA-DRB1 alleles that are overrepresented among people with RA and is associated with the production of anti-citrullinated protein antibodies.

Objectives: To characterize the relationship between SE status and risk of developing refractory RA.

Methods: Participants in FORWARD, The National Databank for Rheumatic Diseases, with RA, high-resolution HLA-DRB1 typing, no history of biologic use at study entry, and subsequent exposure to one or more biologics were included. The reRA group included participants with exposure to at least three biologics while under observation. Those who used a single biologic with continued use for at least two years during observation comprised the comparison non-refractory group. Descriptive statistics for each group were calculated at initiation of first biologic. Significance was assessed with Fisher's exact tests and Mann-Whitney U tests (p<0.05), as appropriate. Logistic regression was used to determine the relationship between shared epitope status and baseline odds of becoming refractory.

Results: Characteristics of the 70 participants that met inclusion criteria are presented in Table 1. Several covariates varied significantly by refractory group, but these differences were attenuated in adjusted models. SE positive individuals had significantly lower odds of becoming refractory, a relationship that remained consistent with varying model complexity (Figure 1; OR [95% CI] 0.16 [0.05, 0.49] in univariate model; p=0.001). HLA-DRB1*04:01 was the only SE positive allele independently associated with nonrefractory status (p=0.036; data for other alleles not shown).

Conclusion: In this cohort, individuals with RA who are SE positive were less likely to be refractory to multiple biologics. This relationship appears to be primarily the result of the HLA-DRB1*04:01 allele rather than any other alleles associated with SE positivity. These findings suggest that SE positive individuals with RA are more likely to find success with their first biologic, while SE negative individuals may be more likely to cycle through multiple biologics. Ongoing and future work will investigate this relationship further and assess whether these results remain consistent when using varying definitions of reRA.

Table 1. Baseline (initiation of first biologic) characteristics of study participants. Values are mean (SD) unless otherwise noted.

	Non-Refractory n=48	Refractory n=22	p
SE positive, %	81.3	40.9	0.002
≥1 copy of HLA-DRB1*04:01, %	52.1	22.7	0.036
Age, years	57.2 (12.6)	55.0 (9.7)	0.266
Female sex, %	93.8	86.4	0.370
White race, %	95.7	85.7	0.167
Time since symptom onset, years	11.3 (11.3)	7.3 (7.1)	0.132
Observation time, years	6.9 (4.4)	11.6 (5.5)	<0.001
Hx smoking, %	27.1	36.4	0.575
BMI, kg/m^2	27.0 (5.5)	32.4 (7.8)	0.011
Hx cancer, %	14.6	9.1	0.709
Hx pulmonary disorder, %	18.8	27.3	0.532
Hx GI disorder, %	35.4	59.1	0.074
Concomitant steroid use, %	25.0	50.0	0.055
Concomitant csDMARD use, %	89.6	81.8	0.448
Pain VAS, 0-10	2.5 (2.3)	4.1 (2.8)	0.011
Global severity VAS, 0-10	2.7 (2.4)	4.4 (2.5)	0.013
HAQ-II, 0-3	0.69 (0.56)	1.01 (0.52)	0.023

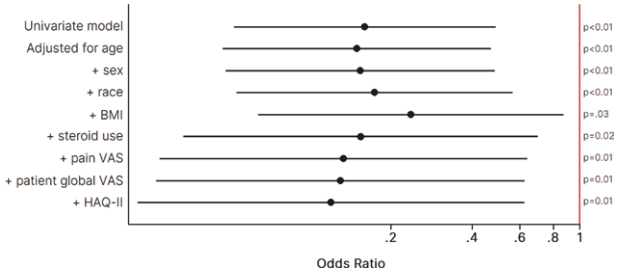


Figure 1. Odds of becoming refractory by SE status. Odds ratios for becoming refractory when SE positive are shown for 9 unique models of increasing complexity. Each model includes a new covariate and all previously listed covariates. P-values for the SE positive covariate are displayed to the right of each associated OR and 95% CI.

REFERENCES: NIL.

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POS0478

FACTORS ASSOCIATED WITH PERSISTENTLY HIGH HAQ-DI SCORE IN RA PATIENTS UNDER B/TSDMARDS: LONGITUDINAL ANALYSIS OF HURBIO SINGLE CENTER REGISTRY

Keywords: Rheumatoid arthritis, bDMARD, Outcome measures

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Background: Health Assessment Questionnaire-Disability Index (HAQ-DI) is a widely-used and accepted instrument for the functional assessment of rheumatoid arthritis (RA) patients.
Objectives: Our aim was to determine the related factors with persistently high HAQ-DI scores in RA patients using b/tsDMARDS.
Methods: RA patients prescribed with b/tsDMARds, registered to Hacettepe University Biologic Registry (HURBIO), had HAQ-DI score ≥1 at baseline assessment and had at least five follow-up visits, were grouped into 3, hypothetically, according to HAQ-DI scores at each of the first five follow-up visit. Group 1 was "persistently-low HAQ-DI score <1" and had HAQ-DI score lower than one at each visit; group 2 was ''floating HAQ around 1" who had at least one visit HAQ-DI score above one and HAQ-DI score below 1; group 3 was "persistently-high HAQ-DI score <1" who had HAQ-DI score higher than one at each visit. Baseline demographic, disease, and treatment characteristics were recorded. Multinomial logistic regression for females and multiple logistic regression for males (as group 3 had no males) was done to reveal associated factors.
Results: A total of 194 patients (89.7% female) were included. Groups 1,2, and 3 consisted of 58 (29.9%), 111 (57.2%), and 25 (12.9%) patients. All patients in group 3 were female. RA disease duration, the time between RA diagnosis and b/tsDMARD initiation, RF negativity, and baseline HAQ-DI score were higher in group 3 compared to other groups (**Table 1**). Multinomial logistic regression revealed several associated factors (OR, 95%CI) for females;

- group 2 over group 1: **being obese (3.0 (1.4-6.4), p=0.004),** negative RF (0.5 (0.2-1.2), p=0.13), using non-anti-TNF (2.1 (0.9-4.8), p=0.07), diagnosis-treatment initiation duration (per 1 year) (1.0 (0.9-1.1), p=0.85)
- group 3 over group 1: being obese (0.9 (0.3-3.0), p=0.88), **negative RF (5.2 (1.4-18.6), p=0.012)**, **using non-anti-TNF (9.5 (1.8-52.6), p=0.009), diagnosis-treatment initiation duration (per 1 year) (1.1 (1.05-1.112), p=0.001)**
- This model classified 61% of the patients correctly.

There was no significant associated factor for males.

Table. Baseline demographic and disease-related characteristics of RA patients (HAQ-DI≥1) prescribed b/tsDMARD (n=194)

	Persistently-low HAQ (<1) (n=58, 29.9%)	Floating HAQ around 1 (n=111,57.2%)	Persistently-high HAQ (≥1) (n=25, 12.9%)	p
Female (n,%)	47 (81)	102 (91.9)	**25 (100)**	0.017
Age at RA diagnosis, mean (SD)	42.5 (11.4)	45.6 (11.4)	46.5 (12.6)	0.20
RA Disease Duration, mean (SD)	13.8 (7.3)	14.3 (7.4)	**21.1 (11.4)**	<0.001
Duration between RA diagnosis and biologic treatment initiation, mean (SD)	6.3 (7.0)	7.4 (6.8)	**13.7 (10.6)**	<0.001
Marrital status (n,%)				0.25
- Single	6 (10.3)	8 (7.2)	0	
- Married	52 (89.7)	103 (92.8)	25 (100)	
Education (n,%)				0.054
- <High school	33 (56.9)	83 (74.8)	20 (83.3)	
- High School	10 (17.2)	13 (11.7)	3 (12.5)	
- >High School	15 (25.9)	15 (13.5)	1 (4.2)	
BMI ≥ 30 kg/m² (n,%)	**24 (41.4)**	71 (64.0)	14 (56.0)	0.019
Primary smoking (n,%)				
- Ever	24 (41.4)	38 (34.2)	6 (24.0)	0.30
- Never	34 (58.6)	73 (65.8)	19 (76.0)	
Serology (n,%)				
- RF +	38 (65.5)	84 (76.4)	**12 (48.0)**	0.016
- CCP +	32 (71.1)	61 (60.4)	12 (54.4)	0.33
- RF or CCP +	40 (76.9)	90 (81.8)	19 (76.0)	0.68
Disease activity assessment (baseline), mean (SD)				
- CRP	3.7 (3.7)	3.6 (4.7)	2.9 (3.9)	0.73
- DAS28	5.2 (1.0)	5.4 (1.1)	5.5 (0.8)	0.34
- HAQ-DI	1.5 (0.4)	1.6 (0.4)	**1.8 (0.5)**	0.002
- TJC	7.0 (4.1)	8.2 (5.0)	9.1 (4.1)	0.20
- SJC	3.4 (2.4)	4.3 (3.6)	3.8 (2.9)	0.13
- Global VAS	70.0 (13.7)	71.8 (16.3)	75.5 (13.4)	0.31
- Pain VAS	73.3 (14.5)	74.2 (18.5)	77.3 (10.8)	0.64
Treatment (n,%)				
csDMARDs				
- Steroids	41 (71.9)	80 (72.7)	18 (72.0)	0.99
- Methotrexate	31 (54.4)	59 (53.6)	11 (44.0)	0.65
- Leflunomide	20 (35.1)	54 (49.1)	15 (60.0)	0.08
- Sulphasalazine	26 (45.6)	42 (38.2)	9 (36.0)	0.59
- HQ	34 (59.6)	72 (65.5)	14 (56.0)	0.59
b/tsDMARDs				
- Anti-TNF	33 (56.9)	64 (57.7)	12 (48.0)	0.67
- Non-Anti-TNF	37 (63.8)	90 (81.1)	22 (88.0)	**0.015**
- Sequential anti-TNF/non-anti-TNF (or vice versa)	12 (20.7)	43 (38.7)	9 (36.0)	0.06

BMI: Body mass index, CCP: Cyclic citrullinated peptide, DAS28: Disease activity score, HAQ-DI: Health assessment questionnaire disability index, RA: Rheumatoid arthritis, RF: Rheumatoid factor, SD: Standard deviation, SCJ: Swollen joint count, TNF: Tissue necrosis factor, TJC: Tender joint count, VAS: Visual analog scale

Conclusion: RA patients are still away from good functional status. According to the results of this study, clinicians should treat RA earlier and increase the sensitivity of management dynamics in RF-negative and obese patients. Whether anti-TNFs or non-anti-TNFs work better on functionality should be interpreted cautiously, even if it remained statistically significant in the multivariable model.
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POS0479

THE PROGNOSTIC INFLAMMATORY AND NUTRITIONAL INDEX (PINI) IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Diet and nutrition, Prognostic factors

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Background: Malnutrition and inflammation are closely related in rheumatoid arthritis (RA). The Prognostic Inflammatory and Nutritional Index (PINI) is a tool assessing the risk of malnutrition-related complications. It combines the determination of two inflammatory and two nutritional proteins.
Objectives: The aim of our study was to calculate the PINI in elderly patients with RA and to determine its relationship with the disease parameters.
Methods: This is a cross-sectional study including patients aged 65 years or older and followed for RA. Disease activity was assessed using the DAS28 score. Functional impact was measured using the HAQ score. Nutritional status was assessed using the Mini-Nutritional Assessment (MNA). The PINI was calculated as follows: Orosomucoid (g/L) × CRP (mg/L)/ albumin (g/L) × prealbumin (mg/L).
Results: Forty patients were enrolled. There were 33 women (82.5%) and 7 men (17.5%). The mean age was 68.37±4.70 years [65-82]. The median duration of disease progression was 11 years with an IQR of [2.45-16.5]. The mean DAS28 was 3.57±1.32 [1.5-6.8]. The mean HAQ score was 1.5±0.53 [0.37-2.6]. The mean MNA score was 20.25±4.5 [8-27.5]. According to the MNA, 22 patients (55%) were at risk of developing undernutrition and 10 patients (25%) were malnourished. The median PINI was 1.77 with an IQR of [0.47-10.21] and extremes ranging from 0.05 to 222.16. Patients were stratified according to PINI score as follows: 13 patients (32.5%) had a normal PINI of less than 1, while 27 patients (67.5%) had a PINI ≥ 1, indicating a risk of undernutrition-related complications. Of these patients with PINI ≥ 1: 18 patients (45%) had a low risk (PINI between 1 and 10), 4 patients (10%) had a moderate risk (PINI between 10 and 20), 2 patients (5%) had a high risk (PINI between 21 and 30) and 3 patients (7.5%) had a life-threatening risk (PINI > 30). Comparison between RA patients with PINI ≥ 1 and PINI < 1 showed a statistically significant difference for acute phase proteins (CRP (p=0.018), haptoglobin (p=0.04)). DAS28 score was significantly higher in the PINI ≥ 1 group (p=0.009), as well as the HAQ score (p=0.004). However, no significant differences were observed concerning the age (p=0.07), gender (p=0.3), duration of the disease (p=0.12), ESR (p=0.7) or MNA (p=0.2).
Conclusion: In our study, 67.5% of the patients were at risk of undernutrition-related complications as assessed by the PINI. This tool seems to be interesting for predicting disease activity, functional impairment and inflammation in RA elderly patients.
REFERENCES: NIL.
Acknowledgements: NIL.
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POS0480

ULTRASOUND SYNOVITIS AND NEUTROPHILIC ACTIVITY MARKERS (PLASMA CALPROTECTIN AND NEUTROPHIL EXTRACELLULAR TRAPS) IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING BIOLOGICAL OR JAK INHIBITORS

Keywords: Rheumatoid arthritis, Biomarkers, Ultrasound

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Background: Studies have shown an association between active synovitis measured by ultrasound (US) with plasma calprotectin in rheumatoid arthritis (RA) patients [1]. Neutrophil extracellular traps (NETs) may play a pathogenetic role in RA [2]. Elevated plasma NETs have been observed in RA patients, although their association with disease activity is unclear. No studies have analyzed the association between NETs remnants and US synovitis in RA

Objectives: To analyse whether plasma calprotectin and NETs remnants are associated with synovial inflammation measured by US in patients with established RA treated with biological therapies or JAK inhibitors (JAKi).

Methods: Observational cross-sectional study. RA patients (ACR/EULAR 2010) receiving treatment with biologic DMARDs (IL6 inhibitors (IL6i), TNF inhibitors (antiTNF), rituximab (RTX)) or JAKi) were consecutively included regardless of disease activity and previous therapy. Clinical disease activity indexes and laboratory parameters of inflammation were evaluated. Plasma calprotectin was analysed. Plasma levels of elastase-DNA (EN-DNA) and histone-DNA complex (H_3-DNA) (NETs remnants) were examined using a home-made ELISA test. Joint US of both hands was evaluated and graded according to Szudlarek's score. The synovial hypertrophy (SH), power Doppler (PD) and the total score (SH+PD) was calculated. US active synovitis as previously defined (3) was calculated (SH ≥ 2 + PD ≥1). A correlation study between neutrophilic markers and US scores was made.

Results: 101 RA patients (91% female, 86% seropositive (RF and/or ACPA) were included. Mean age was 55.4 ±12.1 yrs and the mean RA duration was 15.4 ±9.5 yrs. 78 received treatment with biologics (45 IL6i, 30 antiTNF and 3 RTX) and 23 JAKi. Mean DAS28, CDAI and SDAI were 3.19, 12 and 13 respectively. Low disease activity or remission (CDA<10) were found in 56 patients (54.5%). Mean total US score was 12.7 ±13.7 and US active synovitis was found in 69 patients (69.8%). Means levels of plasma calprotectin were 0.98 µg/ml ±1.4 and plasma NETs remnants were 1.1 ±0.4 (EN-DNA) and 0.9 ±0.08(H3-DNA) [Table 1]. Plasma NETs remnants were not correlated with any US scores. Calprotectin correlated moderately with US scores (ρ between 0.54 and 0.60, p<0.001). There was no correlation between both NETs remnants and calprotectin levels. Mean calprotectin levels were significantly higher in patients with US active synovitis (1.28 vs 0.35 µg/ml, p<0.001) but NETs remnants were not (data not shown). The lack of correlation between NETs and US scores was observed in all therapeutic groups.

Table 1. Clinical and laboratory characteristics

	IL6i n 45	JAKi n 23	AntiTNF n 30	RTX n 3	Total n101
Age	56.4±11.3	53.9±12.5	55.4±13.1	50.9±14.3	55.4±12.1
Female	42(93.3)	20 (87)	27(90)	3(100)	92(91.1)
Seropositive (ACPA/ RF)	39(86.7)	22(95.7)	23(76.7)	3(100)	101(86.1)
Disease duration (years)	16.4±8.1	12.2±9.3	16.5±11.6	14.6±8.5	15.4±9.51
28TJC	4.1±5.8	3.7±5.4	2.3±3.7	14.3±2.1	3.8±5.4
28SJC	1.6±2.3	2.0±2.7	2.2±0.5	9,3±0.5	1.8±2.7
DAS28	2.8±1.2	3.7±1.4	3.1±1.1	6.3±0.6	3.2±1.3
CDAI	12.0±10.6	12.4±9.3	9.9±9.4	40.1±0,8	12.3±10.1
SDAI	12.4±10.7	13.1±9.6	11.03±11.1	42.8±3.08	13.04±11.6
hs PCR (mg/dL)	0.1± 0.2	0.4±0.43	0.7± 2.5	2.3±2.6	0.45±1.4
Plasma calprotectin (µg/ml)	0.73±0.64	0.93±1.02	1.25±2.24	2.47±1.45	0.98±1.45
EN-DNA	1.1±0.4	1.1±0.3	1,1±0.6	0,9±0.1	1.1±0.4
H_3-DNA	1.1±0.3	1.1±0.2	1,1±0.2	0,8±0.5	1.1±0.4
SH score	6.20±5.6	7.6±7.6	6.83±6.6	32.7±8.1	7.5±7.8
PD score	4.9±5.0	5.0±6.1	4.35±6.0	20.0±10.5	5.2±6.2
Total US score	11.1±10.3	12.6±13.4	11.1±12.4	52.7±15.8	12.7±13.6

Results are mean ±standard deviation or number of patients (%)

Conclusion: Plasma calprotectin but not NET remnants were associated with synovial inflammation measured by US in established RA patients receiving biologic or JAKi therapy. The two markers may play a different pathogenetic role in RA.

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POS0481 BONE EDEMA IN MRI IS MORE ASSOCIATED WITH RAPID RADIOGRAPHIC PROGRESSION THAN CLINICALLY RELEVANT RADIOGRAPHIC PROGRESSION.

Keywords: Imaging, Rheumatoid arthritis

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Background: Rapid radiographic progression (RRP) is selected as one of the risk factors for difficult- to- treat RA, which needs to be resolved as soon as possible. Logistic progression models for RRP have been reported for a long time. Vanier et al. recently reported a newly logistic model which is constituted by high CRP levels (>30mg/L), the number of swollen joints, RF positivity, and the existence of bone erosion by pooling individual data from 2 cohorts and 3 clinical trials. On the other hand, EULAR recommendations for imaging were published, in which MRI bone oedema was an independent and strong predictor for joint destruction. We previously reported that extensive bone marrow edema (BE) determined by hand MRI is a prognostic indicator for rapid radiographic progression in MTX inadequate response to early RA treated with MTX+ Adalimumab combination therapy [1].

Objectives: To clarify, association of BE with RRP using the clinical data in RA patients treated with conventional synthetic(cs) DMARDs.

Methods: At first, baseline data of 108 non-RRP patients and 47 clinically relevant radiographic progression (CRRP) +RRP patients were statistically compared. Secondly, background data of 13 CRRP and 34 RRP patients were compared. MRI of affected joints (mostly hands) were taken and patents were divided into two groups by existence or non-existence of BE.

Results: As shown in Table 1A, short duration, high BE rate, high DAS28-ESR (baseline), high CRP levels, high mTSS, high yearly progression of mTSS were observed in RRP +CRRP group compared with non-RRP. Table 1B showed that only the rate of BE is higher in RRP group compared with CRRP group.

Conclusion: BE may be a possible prognostic factor for RRP and more associated with RRP than CRRP.

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Table 1A.

	non RRP group(N=108)	RRP group(N=47)	P value
age	65.4(+-11.8)	63.6(+-13.0)	N.S
duration(month)	108(48-171.0)	47(18-146.5)	<0.01
MTX dose	6(0-8)	8(0-11)	P=0.05
complication(+, -)	22, 86	16, 31	N.S
MRI BE(+, -)	13, 95	39, 8	<0.01
DAS28-ESR 0M	4.57(+-1.14)	4.68(+-1.46)	N.S
DAS28-ESR 0M(high, not high)	29, 78	20, 24	<0.05
SJC	5(3-6)	6(3-8)	N.S
SJC(=>7, 7>)	26, 81	18, 29	N.S
TJC	5(2-8)	4(1-8)	N.S
pVAS	45.3(+-23.8)	45.3(+-24.5)	N.S
RF 0M	51(11.8-166.6)	102(24.6-244.0)	N.S
RF 0M(negative,positive)	33, 75	9, 38	N.S
CRP	0.31(0.10-1.18)	0.94(0.17-2.04)	<0.05
CRP(negative, positive)	52, 56	14, 33	<0.05
ESR	22(11.0-43.3)	36(15.5-47.5)	N.S
mTSS 0M	22(12.0-72.5)	39(21.5-69.0)	P<0.05
Δ mTSS/Y	0(0-0.4)	6.2(4.7-12.0)	P<0.01
MMP-3 0M	112.0(54.3-212.0)	134.0(91.6-245.8)	N.S

Table 1B.

	RRP group(N=34)	CRRP group(N=13)	P value
age	65.9(+-13.6)	57.6(+-9.22)	N.S
duration(month)	41.5(13.8-135)	96.0(60.0-156)	N.S
MTX dose	8(0-11.5)	8(6-10.0)	N.S
complication(+, -)	21,13	10,3	N.S
MRI BE(+, -)	31, 3	8, 5	<0.05
DAS28-ESR 0M	4.63(+-1.50)	4.80(+-1.40)	N.S
DAS28-ESR 0M(high, not high)	14, 17	6, 7	N.S
SJC	5.79(+-3.27)	5.77(+-3.19)	N.S
SJC(=>7, 7>)	13, 21	5, 8	N.S
TJC	5.21(+-5.12)	6.00(+-5.92)	N.S
pVAS	46.8(+-25.4)	41.4(+-22.4)	N.S
RF 0M	168.5(+-178.0)	122.1(+-145.7)	N.S
RF 0M(negative,positive)	6, 28	3, 10	N.S
CRP	0.92(0.16-2.59)	1.00(0.49-1.64)	N.S
CRP(negative, positive)	11, 23	3, 10	N.S
ESR	37,7(+-26.6)	37.0(+-27.9)	N.S
mTSS 0M	39(19.5-63.8)	46(31.0-95.0)	N.S
Δ mTSS/Y	9.55(6.0-15.8)	3.70(3.5-4.00)	P<0.01
MMP-3 0	207.6(+-223.1)	162.1(+-94.4)	N.S

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POS0482

PATIENT CENTERED- TREAT TO TARGET- DISEASE SPECIFIC GUIDELINES: EXPANDING THE PERTINENCE OF CLINICAL PRACTICE GUIDELINES TO PATIENTS

Keywords: Treat to target, Rheumatoid arthritis, Outcome measures

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Background: Although all patients present unique biopsychosocial contexts, the care of inflammatory arthritis patients is particularly complicated by the interaction of multiple factors. Advocates of patient- centered care identify that the best way to manage complex patients is through comprehensive treatment strategies that can adapt to the nuances of individual contexts. Recently published disease specific, patient centered national clinical guidelines for inflammatory arthritis [1] represent a model of care that can be fit for standard, disease-oriented patients' management.
Objectives: To assess for the outcomes of indiscriminately implementing individual, disease-specific treatment strategies in standard clinical practice for the treatment of inflammatory arthritis and its impact on the disease activity measures as well as patient reported outcomes.
Methods: A 12-month multicenter, randomized study compared standard care with patient-centered, Treat to Target (T2T) management of inflammatory arthritis. All patients completed patient reported outcome measures [2]. Regular appointments were delivered by specially trained rheumatologists who kept a record of the clinical assessments, medication titration, patient reported outcomes, self-management, psychosocial support and motivation score. The primary outcome was 12-month remission assessed using the Disease Activity Score for 28 joints using ESR (DAS28-ESR). Secondary outcomes included fatigue, functional disability, quality of life and motivation levels.
Results: 297 rheumatoid arthritis patients were screened and randomized (149 Treat to Target management; 148 standard care); 269 (90.6%) patients had their 12-month outcomes completed. Patient centered treat to target management increased DAS28-ESR 12-month remissions compared to standard care (43% vs 22%, p = 0.004). Patient centered T2T management also significantly increased prevalence of those who achieved DAS28-ESR low disease activity scores. (38% vs 23%, p = 0.005). In addition, it substantially improved patients' functional ability (0.4 + 0.2 Vs 1.1 + 0.3, p< 0.01), quality of life (0.6 + 0.2 Vs 1.2 + 0.5, p< 0.01), reduced fatigue (4.2 + 1.3 Vs 6.8 + 1.6, p< 0.01). Motivation score was higher in the T2T cohort (8.4 + 1.3 Vs 5.7 + 2.1, p< 0.05). There was no evidence that serious adverse events (patient centered T2T management =14 vs standard care =12) or other adverse events (112 vs 106) differed in both groups.
Conclusion: More patients achieve the treatment target of remissions or low disease activity status. There were greater improvements in patient reported outcomes, functional ability, fatigue as well as motivation. In the meantime, there were no more harms. Patient centered T2T clinical guidelines are able to provide condition-specific guidance on how one would optimally manage a disease tailored to the individual patient's requirements.
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POS0483

PATIENT-PHYSICIAN DISCORDANCE IN DISEASE ACTIVITY ASSESSMENT IS ASSOCIATED WITH LESS CONSISTENT TREAT-TO-TARGET IMPLEMENTATION, IMPAIRING REMISSION OUTCOMES IN EARLY RA: A POST-HOC MEDIATION ANALYSIS OF THE CARERA TRIAL

Keywords: Rheumatoid arthritis, Patient reported outcomes, Treat to target

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Background: A treat-to-target (T2T) approach improves outcomes of rheumatoid arthritis (RA). However, T2T is applied in only two-thirds of real-world visits, while patient satisfaction, engagement and treatment success improve when patients and rheumatologists agree over T2T goals [1]. Consequently, discordance between patients' and rheumatologists' views on disease activity might hamper T2T implementation, impairing outcomes.
Objectives: To assess if patient-physician discordance in disease activity assessment affects the likelihood of T2T being applied, and how this influences remission.
Methods: This was a post-hoc analysis of the 2-year pragmatic randomized trial Care in early RA (CareRA), which compared several DMARD regimens with/without bridging glucocorticoids, in treatment-naïve patients with early RA. The trial was guided by T2T: during the first year, the protocol mandated specific DMARD adaptations in case of DAS28-CRP >3.2, with documentation of reasons for non-adherence. From week 52 onwards, treatment was at the rheumatologists' discretion. For each patient, we quantified T2T implementation as the proportion of study visits where DMARD treatment was adapted when DAS28-CRP was >3.2. Patient-physician discordance was defined by the discordance score (DS)[2], a weighted difference between patient-reported and clinical/laboratory outcomes, ranging from -1 to 1 with values >0 implying relatively more patient-perceived disease impact. First, we examined the longitudinal association between the DS and T2T implementation with a generalized linear mixed model (GLMM) adjusted for age, sex, autoantibodies, treatment, Rheumatic Disease Comorbidity Index and number of previous DMARDs. Additionally, we studied the association between time-varying DS, T2T implementation and the odds of remission (SDAI ≤3.3) at year 2, using a multilevel mediation model clustered within individual patients. All study visits until year 2 or drop-out were considered, with no imputation of missing treatment information. Other missingness was handled with multiple imputation.
Results: In all, 379 patients were included in CareRA, 322 of whom completed the trial. Over 2 years, 3129 follow-up visits with available treatment information took place. On 445 (14%) of these visits, DAS28-CRP was >3.2, and DMARD treatment was adapted in 217/445 (49%) of such cases. T2T use declined over time and was consistently lower during the second trial year, where treatment was no longer protocolized, with T2T implementation ranging from 52-66% in year 1 and from 17-38% in year 2. The mean DS was higher on visits where T2T was not applied (0.33 [SD 0.17]) than on T2T visits (0.18 [SD 0.17], p <0.001). In the GLMM, higher DS was associated with a lower probability of T2T being applied (OR 0.62 [95% CI 0.55-0.69] for 0.1 increase on DS, p <0.001). In multilevel mediation analysis, higher DS over time was associated with decreased odds of remission at year 2, and this effect was partly mediated by lower T2T implementation (Figure 1).
Conclusion: Patient-physician discordance in disease activity assessment was associated with a decreased probability of achieving remission. This association was partly explained by rheumatologists appearing less likely to apply a T2T strategy when their assessment of disease activity differed from the patient's. These findings highlight the importance of an open dialogue between physicians and patients about their evaluation of disease activity before applying this as a target for treatment modification.
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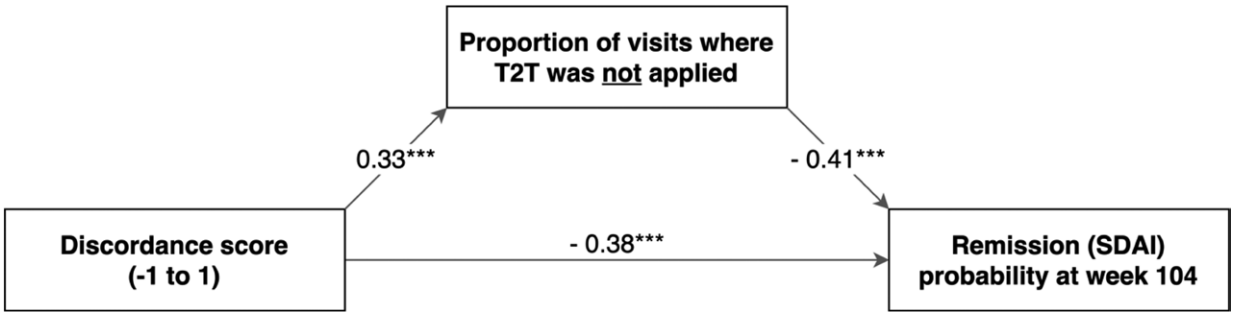


Figure 1. Mediation analysis of the association between discordance score over time, T2T implementation and the probability of remission at year 2. Reported are the standardized regression coefficients with indicators of significance (*** p < 0.001). *T2T = treat-to-target, SDAI = Simple Disease Activity Index*

POS0484

HIGH ANTI-CCP LEVEL AND FEMALE GENDER ARE ASSOCIATED WITH PROGRESSION TO PERSISTENT ARTHRITIS IN PATIENTS WITH PALINDROMIC RHEUMATISM; RESULTS OF A UK PROSPECTIVE COHORT STUDY

Keywords: Rheumatoid arthritis, Autoantibodies

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Background: Palindromic rheumatism (PR) is a recognised precursor of rheumatoid arthritis (RA) and is characterised by episodic flares of pain and swelling in and around joints [1]. Up to 50% of PR patients will progress to persistent arthritis (PA) [1]. However, PR is challenging to identify and study longitudinally and risk factors for progression remain unclear [1]. This is the first large UK prospective PR cohort study describing risk factors in patients with PR, the majority of whom were treatment naïve at baseline.

Objectives: To investigate baseline risk factors associated with progression to PA in PR patients.

Methods: Patients with suspected PR were recruited to the Leeds PR cohort from regional primary care and secondary care referrals. In the absence of an accepted classification criteria, PR was defined as 'a confirmed history or physical examination consistent with episodes of joint pain and swelling that returned to normal between episodes in the absence of an alternative diagnosis' [2]. At baseline, a comprehensive set of clinical, imaging, serological and immunogenetic parameters was assessed. Patients were monitored at 3 monthly intervals for the first year, then 6 monthly or earlier if clinically indicated. Progression to PA was defined by the presence of at least one tender and swollen joint confirmed by a rheumatologist, which persisted for at least 3 weeks. Baseline variables included in the analysis were: age, smoking status, gender, first degree relative with RA, time interval between flares, number of joints typically affected in a flare, wrist joint involvement in flares, hand joint involvement in flares, HLA DR shared epitope (SE), anti-CCP status, rheumatoid factor status and DMARD use during follow up. Cox regression analysis identified factors associated with progression to PA using the R statistical program. Model discrimination, using concordance index, was 0.741.

Results: 161 patients were followed between July 2008 and December 2022. 32% (51/161) of patients developed PA after a median of 12 months. 90% (46/51) of progressors met criteria for RA. 90% (145/161) of patients were DMARD naive at baseline. Cox regression showed female gender (HR 2.7, CI 1.2-6.0, p=0.01) and high anti-CCP level (> 3X upper limit of normal range) (HR 6.1, CI 1.9-19, p=0.004) were associated with progression to PA. Flares in joints of the hands was found to be protective (HR 0.3, CI 0.1-0.9, p= 0.04). Typical involvement of < 3 joints in flares was also protective, with a trend towards significance (HR 0.4, CI 0.1-1.0, p=0.05). The remaining variables including frequency of flares, HLA DR SE and DMARD exposure were not associated with progression status.

Table 1. Variables shown to be significantly protective or predictive of persistent arthritis. Number of joints in a typical flare was borderline significant. ULN: Upper Limit of Normal, Ref: Reference

Baseline Variable		Progressors n= 51		Non Progressors n=110		HR	95% CI		P Value
		n	%	n	%				
Gender	Male	11	22	39	35	Ref			
	Female	40	78	71	65	2.75	1.25	6.05	0.01
Typical No. of joints affected in flares	>4	15	29	25	23	Ref			
	<3	31	61	79	72	0.43	0.18	1.00	0.05
Hand Joint involvement in flares	Absent	7	14	13	12	Ref			
	Present	30	59	80	73	0.38	0.15	0.97	0.04
Anti-CCP Antibody	Negative	7	14	56	51	Ref			
	Positive< 3 x ULN	2	4	9	8	1.71	0.28	10.49	0.55
	Positive >3x ULN	41	80	45	41	6.12	1.90	19.73	0.004

Conclusion: In patients with PR, female gender and high anti-CCP level were associated with progression to PA. Conversely, hand joint involvement and flares typically affecting <3 joints were protective. These data provide novel insights into the natural history of PR and will inform a risk stratification model for monitoring and early therapeutic intervention.

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POS0485

FATIGUE USING PATIENT-REPORTED OUTCOMES MEASUREMENT INFORMATION SYSTEM (PROMIS) AND ITS RELATIONSHIP WITH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS: A PROSPECTIVE STUDY FROM INDIA

Keywords: Treat to target, Rheumatoid arthritis, Patient reported outcomes

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Background: Fatigue in rheumatoid arthritis (RA) is common, overwhelming and plays a key role in patients' perception of the disease and strongly influences global assessment [1]. While fatigue in RA has no internationally accepted definition, it is multidimensional and has an inconsistent association with disease activity in different populations with very few studies from India [2, 3].

Objectives: To determine the relationship between fatigue as measured by Patient-Reported Outcomes Measurement Information System (PROMIS) fatigue raw score with disease activity in patients with RA. To determine the predictors of fatigue in patients with RA.

Methods: A longitudinal study was conducted from January 2021 to December 2022 after Ethics Committee approval in patients with RA enrolled at our rheumatology clinic providing care to >450 patients with RA, in a tertiary care hospital. Fatigue (PROMIS Fatigue-short form 7a), patient assessment of global disease activity (PtGA), Disease Activity Score (DAS28), and Clinical Disease Activity Index (CDAI) were measured. Serum samples for interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α) were collected and stored at -80^0 C. Relationship of fatigue was examined with age, hemoglobin, serum vitamin D3, TNF-α, and IL-6 using Spearman correlation coefficient. A Receiver Operating Characteristic (ROC) curve was constructed to determine the optimal PROMIS cut-off for defining PtGA >2. Binary logistic regression analysis was used to assess predictors fatigue.

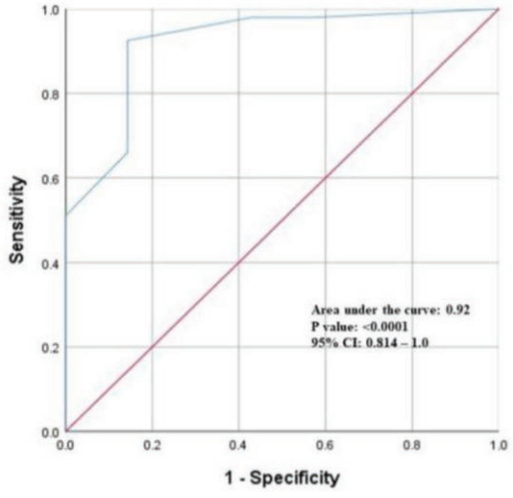
Results: One hundred and fifty-four patients were enrolled, of whom 133 (86.3%) were females, 103 were reassessed at 6 months (85.4% females). All were on conventional disease-modifying antirheumatic drugs. Patients in remission using DAS28 were 9.7% (n = 15) and 52.4% (n = 54) and remission/low disease activity (LDA) based on CDAI <10 were 13.6% (n = 21) and 68.9% (n = 71) at enrolment and 6 months respectively. There was a significant reduction in median PROMIS at 6 months from 19(11) to 16(7) (p<0.0001). PROMIS was significantly lower in those with remission/LDA based on CDAI (p<0.0001) and DAS28 remission at enrolment and 6 months (p = 0.012 and 0.015 respectively). PROMIS >11 had 93.8% sensitivity and 78.6% specificity to predict PtGA >2 (AUC 0.92, 95% CI 0.81 - 1.00, P <0.0001) (Figure 1). PROMIS >11 was present in 89% at enrolment and 82.5% at 6 months. Age, hemoglobin, serum vitamin D3, TNF-α, and IL-6 had no correlation with fatigue. DAS28, CDAI, sleep (Pittsburgh Sleep Quality Index - PSQI), and depression (Patient Health Questionnaire - PHQ-9) were significant predictors of PROMIS >11 (Table 1).

Conclusion: Fatigue is a significant problem in RA. A PROMIS score of 11 may be an acceptable cut-off for our population. Though fatigue improved with the treat-to-target approach, further studies are needed to determine if it is meaningful for patients. Along with disease activity, addressing sleep and depression is important in managing fatigue.

Table 1. Predictors of fatigue (n= 154)

Predictors	Odds ratio (95% CI)	P value
PSQI	2.31(1.45 - 3.69)	<0.0001
PHQ-9	4.38 (2.16 - 8.89)	<0.0001
CDAI	1.26 (1.13 - 1.39)	<0.0001
DAS28	2.87 (1.72 - 4.79)	<0.0001

Fig 1: ROC curve of PROMIS raw score with patient global assessment of disease activity



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Disclosure of Interests: None Declared.

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POS0486

CHARACTERISTICS OF RHEUMATOID ARTHRITIS PATIENTS WHO ACHIEVE REMISSION AFTER 2022 AMERICAN COLLEGE OF RHEUMATOLOGY/ EUROPEAN ALLIANCE OF ASSOCIATION FOR RHEUMATOLOGY REVISED REMISSION CRITERIA APPLICATION

Keywords: Real-world evidence, Remission, Rheumatoid arthritis

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Background: In 2011, the American College of Rheumatology (ACR) and European League Against Rheumatism (formerly European Alliance of Association for Rheumatology [EULAR]) developed two new definitions for remission for rheumatoid arthritis (RA) clinical trials and in clinical practice [1]: Boolean-based definition and index-based definition (simplified disease activity index: SDAI). The 2011 Boolean based definition (Boolean 1.0 [B1R]) required each of the four core set variables (tender joint count, swollen joint count, patient assessment of global disease activity [PtGA, cm], and C-reactive protein [CRP, mg/dl]) to have a value of ≤1. B1R is the most stringent remission criteria and discrepancies between B1R and SDAI were highlighted. In 2022, the ACR and EULAR validated and approved a Boolean remission (Boolean 2.0 [B2R]) revision in which the PtGA threshold was set at ≤2 [2]. Although the RA patient number who achieved remission by B2R definition increased due to the PtGA threshold change, the characteristics of those who were newly included in the remission criteria are unknown.

Objectives: This cross-sectional retrospective study investigated the characteristics of RA patients who were newly included in the remission criteria after B2R application in daily clinical practice.

Methods: Toyohashi RA Database (TRAD) data from 2021 was used, which is a single-center retrospective data collection. Once a year cross-sectional data was included in TRAD such as basic patients' characteristics, RA disease activity, laboratory data, and medication data. A total of 469 RA patients and 611 RA patients were categorized in B1R and in B2R, respectively, among the 1020 RA patients registered in the TRAD 2021 data. New remission criteria entries after B2R application were 142. Cross-sectional data described below were compared between B1R and B2 1R: age, gender, RA disease duration, rheumatoid factor (RF) positivity and anti-cyclic citrullinate protein antibody (ACPA), Steinbrocker stage and class, medication information at the time of survey, CRP value and erythrocyte sedimentation rate, modified health assessment questionnaire (mHAQ), and concomitant osteoporosis (OP). Univariate analysis by Mann Whitney U-test or Chi square test was initially performed between B1R and B2-1R. Subsequently, multivariate analysis was performed using selected variables, which were statistically significant between the two groups by logistic regression analysis. P < 0.05 was considered as statistically significant.

Results: The number of RA patients in remission state increased by 30.3% by B2R application. Statistically significant differences by univariate analysis were found in the following variables (mean values or percentage in B1R/B2-1R): RA disease duration (11.3/15.5 years), RF positive ratio (70.2/79.9%), RF titer (94.4/132.8 IU/ml), ACPA positive rate (71.5/80.9%), ACPA titer (226.9/322.3 U/ml), %stage III+IV (45.6/63.4%), %btDMARDs (40.1/51.4%), mHAQ (0.11/0.28), and %OP concomitant (32.0/46.5%). Multivariate analysis results were shown in the Table 1. mHAQ in B2-1R was significantly worse compared with that in B1R.

Conclusion: New B2R application increased the RA patient number in remission state. RA patient characteristics in B2-1R were with: longer disease duration, more seropositivity, more joint damage, treated with more intensive medications, especially worse physical function, and increased concomitant OP.

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Table 1.

Table. Univariate and multivariate logistic analysis for patients' characteristics of new remission-achieved patients with rheumatoid arthritis

Variables	Unadjusted ORs (95% CI)	*p*	Adjusted ORs (95% CI)	*p*
Female (to male)	1.315 (0.841-2.058)	0.230		
Age (per year)	0.990 (0.976-1.003)	0.125		
RA duration (per year)	1.040 (1.022-1.059)	<0.001	1.014 (0.990-1.038)	0.265
RF titer	1.001 (1.000-1.002)	0.045		
ACPA titer	1.001 (1.000-1.001)	0.027	1.000 (1.000-1.001)	0.089
Stage III+IV (to I+II)	2.064 (1.402-3.039)	<0.001	1.473 (0.914-1.001)	0.112
Class 3+4 (to 1+2)	1.787 (0.840-3.803)	0.132		
Methotrexate use	1.021 (0.974-1.069)	0.391		
Glucocorticoid use	1.078 (0.980-1.184)	0.122		
btDMARD use	1.581 (1.084-2.306)	0.017	1.167 (0.764-1.783)	0.474
C-reactive protein	1.483 (0.592-3.719)	0.401		
ESR	1.002 (0.994-1.010)	0.600		
mHAQ	4.386 (2.536-7.585)	<0.001	2.860 (1.537-5.320)	<0.001
Osteoporosis	1.615 (1.104-2.363)	0.014	1.191 (0.774-1.833)	0.427

RF was excluded in multivariate analysis due to close correlation with ACPA.
RA: rheumatoid arthritis, RF: rheumatoid factor, ACPA: anti-citrullinate protein antibody, btDMARD: biological and targeted disease-modifying anti-rheumatic drugs, ESR: erythrocyte sedimentation rate, mHAQ: modified health assessment questionnaire

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0487 DISENTANGLING HETEROGENEITY IN CONTEMPORARY UNDIFFERENTIATED ARTHRITIS – A LARGE COHORT STUDY USING LATENT CLASS ANALYSIS

Keywords: Remission, Outcome measures, Rheumatoid arthritis

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Background: Undifferentiated arthritis (UA) is considered to be heterogenous and consists of subgroups, this notion is affirmed by differences in disease course, varying from spontaneous resolution of arthritis to RA-development.

Objectives: We aimed to identify homogeneous subgroups within UA based on a combination of clinical features and thereafter to relate these to the outcomes spontaneous resolution and RA-development. These outcomes can only be studied in UA-patients in which DMARD-treatment does not influence the natural disease course; these cohorts are scarce.

Methods: We studied ACPA-negative UA-patients, defined as not-fulfilling 1987-/2010-RA-criteria nor having an alternate diagnosis, consecutively included in the Leiden Early Arthritis Clinic between 1993-2006, when early DMARD-treatment in UA was infrequent. Latent Class Analysis was used to identify subgroups based on a combination of clinical features (e.g. symptom characteristics, physical examination, laboratory tests). Within these subgroups, test-characteristics were assessed for spontaneous-resolution of arthritis (defined as spontaneous resolution of arthritis without DMARD-treatment) and RA-development within 1 year.

Results: 310 consecutive UA-patients were studied. Five classes were identified: location and number of swollen joints were most distinguishing. Classes were characterized by: 1) polyarthritis, often symmetric 2) oligoarthritis, frequently with subacute onset, 3) wrist-monoarthritis, often with subacute onset, increased BMI and without morning stiffness, 4) small-joint monoarthritis, often without increased acute phase reactants, and 5) large-joint monoarthritis, often with subacute onset. Studying the classes in relation to the outcomes revealed that the majority of patients without spontaneous resolution were not included in the classes characterised by monoarthritis (specificity >90%). In addition, patients who developed RA were infrequent in the monoarthritis classes (sensitivity <7%).

Conclusion: Using a data-driven unsupervised approach, five subgroups within contemporary UA were identified. These subgroups have differences in the natural course of disease.

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Disclosure of Interests: None Declared.

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POS0488 THE IMPACT OF ACHIEVING EARLY-SUSTAINED REMISSION USING BOOLEAN 2.0 CRITERIA ON PREVENTING FUNCTIONAL IMPAIRMENT IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Remission

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Background: Rheumatoid Arthritis (RA) is associated with functional impairment and disability. With the 2022 revision of the Boolean remission criteria, more patients can classified as achieving remission and the revised version also increases the agreement with index-based remission criteria without jeopardising predictive value for radiographic or functional outcomes. Whether achieving sustained Boolean 2.0 remission using a treat-to-target strategy aiming can prevent functional impairment in the long-term measured using the Health Assessment Questionnaires Disability Index (HAQ-DI) would need to be addressed.

Objectives: This retrospective study aims to explore the impact of sustained remission classified under the revised Boolean 2.0 criteria on HAQ-DI score.

Methods: The data was retrieved from the Clinical Rheumatology Systematic Treat-to-target (T2T) in Asia Leadership (CRYSTAL) registry. Early RA patients with symptoms onset less than 2 years were recruited between 2012-2018. All patients received a treat-to-target treatment strategy aiming at remission and had been followed for 5 years. Swollen joint count (SJC), tender joint count (TJC), Patient global assessment (PtGA), CRP levels, and HAQ-DI were recorded. Patients were classified into two groups: patients achieved Boolean 2.0 remission in both the first and second year (Early-Sustained Remission (ESR) Group), and patients who did not (Non-ESR group).

Results: The data of 236 patients were retrieved. 57 (24.2%) of them were classified as ESR group and 166 (70.3%) were in Non-ESR group (Table 1). The average HAQ-DI score was lower in the ESR group in the second, third, fourth and fifth year compared to the Non-ESR group with $p \leq 0.001$ [year 1: 0.097 ± 0.218 vs 0.403 ± 0.465; year 2: 0.143 ± 0.267 vs 0.421 ± 0.452; year 3: 0.212 ± 0.339 vs 0.476 ± 0.59; year 4: 0.232 ± 0.358 vs 0.457 ± 0.566] (Figure 1).

Conclusion: T2T aiming at achieving Boolean 2.0 remission in the first two years could be considered in clinical use for maintaining a lower functional impairment in the long term.

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Table 1. Baseline demographics

	ESR group (N=57)	*Non-ESR group (N=166)*	*p*
Age	51 ± 13	54 ± 11	0.125
Sex, male	16 (28.1%)	34 (20.5%)	0.236
Disease activity/ disability index			
VAS pain score, 0-100	42.9 ± 22.7	49.38 ± 23.3	0.072
VAS patients' global score, 0-100	49.5 ± 24.9	55.5 ± 22.9	0.097
VAS physicians' global score	48.8 ± 26.1	55.2 ± 25.5	0.103
Tender joint count, 0-28	6 ± 5	8 ± 6	0.009
Swollen joint count, 0-28	4 ± 3	5 ± 4	0.350
CRP, mg/L	17.1 ± 25.6	24.1 ± 38.1	0.201
HAQ-DI, 0-3	0.75 ± 0.62	0.90 ± 0.65	0.121

[1] Visual analog scale, range 0-100; [2] Health Assessment Questionnaire Disability Index, range 0-3

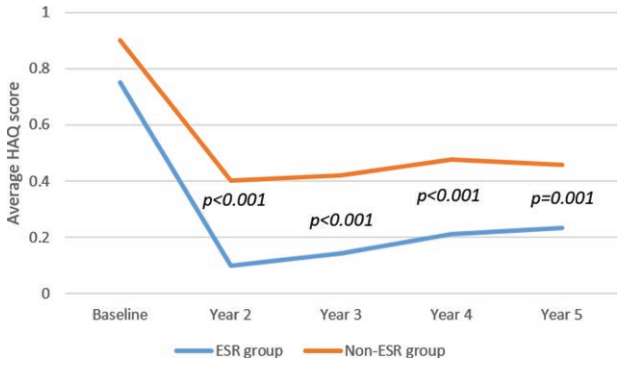


Figure 1. The impact of early-sustained Boolean 2.0 remission on HAQ-DI score

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POS0489

PREDICTIVE FACTORS FOR THE FLARE OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) IN ULTRASOUND REMISSION (US-R)

Keywords: Rheumatoid arthritis, Remission, Ultrasound

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Background: Flares are frequent in patients with rheumatoid arthritis(RA), with 30–50% experiencing a disease flare within the first 2 years of clinical remission(CR). Ultrasound (US) synovitis despite CR have more subsequent flares than those who show both CR and ultrasound remission(USR). Plenty of studies examined clinical course and predictive factors for flare among patients with RA in CR or LDA. But few studies have examined those with USR and using US as daily rheumatologic practice through a follow-up period. Therefore, the clinical course and flare predictor of RA patients in US-R under daily US practice is unclear.
Objectives: The objective of this study among RA patients in CR/LDA with USR under on-demand and yearly US practice was as follows (1) to investigate the clinical course and change of disease activity from baseline, (2) to investigate the predictive factors for the flare over 2 years.
Methods: All patients met the following criteria: (1) RA classified according to the American College of Rheumatology (ACR) 2010 revised criteria; (2) age >18 years; (3) at least 12 months disease duration; (4) maintaining the same RA treatment at least 6 months; (5) being in CR or LDA according to either DAS28 CRP or SADI/CDAI; (6) being in USR. USR was defined as absence of joint synovitis, tenditis, tenosynovitis in the bilateral wrist, 2nd-5th MCP and PIP joints, and any tender or swollen joints. Demographic and treatment characteristics, clinical dates, US assessment were evaluated at the time of baseline, 1-year, and 2-years (yearly-US). US was additionally assessed if the patients showed clinical manifestations of the flare in any period (on-demand US). Questionnaires were also collected at baseline to assess physical function, psychiatric disorders and catastrophizing: HAQ-DI, BS-POP and Pain Catastrophizing Scale (PCS). Rheumatologists could employ DMARD treatment as an individual approach based on the joint decision between the patient and the rheumatologist without any restrictions. The flare was defined when patients received additional DMARD or glucocorticoids or encountered Power Doppler (PD) US flare. Baseline factors for the shorter time to the flare were analyzed by multivariate COX regression analysis, adjusting for age, gender, BMI, and DAS28 CRP. A P value ≤ 0.05 was regarded as being significant. All analyses were performed with EZR statistical software.
Results: In total, 85 patients were enrolled in the study. Baseline characteristics are depicted in Table 1. 62 patients (73%) fulfilled CR criteria. The change of DAS28-CRP from baseline to 1-year and 2-years was -0.1±0.7, -0.08±0.75. The rate of LDA/CR and USR was as follows: 92% and 91% at 1-year, 90% and 89% at 2-years. Over 2 years, 35 patients (42%) had the flare and the mean time to the flare was 11.8±7.0 months. PDUS flares were reported in 4 patients (5%) at 1-year and 2-year US assessment, even though they had no clinical signs of flares. An association of ACPA (HR=2.6, 95%CI:1.0-6.9, p=0.05), Stage III (HR=4.2, 95%CI:1.5-11.6, p=0.005), CRP (HR=21.9, 95% CI:3.5-137, p<0.001), opioids use (HR=5.8, 95% CI:2.0-17, p=0.001) on the shorter time to the flare was revealed. CR, DMARD treatment, HAQ-DI, BS-POP, and Pain Catastrophizing Scale (PCS) were not associated with the flare.
Conclusion: Under on-demand and yearly US assessment over 2 years for RA patients in LDA/CR with USR, the flare occurred frequently but most of the patients showed sustained LDA/CR and USR at 1- year and 2- years. Baseline factors should be considered for predicting the flare.

Table 1.

variable	mean (SD) /n (%)
N=85	
Age, (year) , mean (SD)	68.7 (11.7)
Female, n (%)	61 (71.8)
BMI	22(4.3)
Disease duration (year)	9.2 (8.0)
musculoskeletal co-morbidity, n (%)	33 (38)
psychiatric disorder n, (%)	9 (10.6)
Pain Catastrophizing Scale, 0-52	15(13)
Stage (I/II/III/IV)	31/32/16/6
Tender joints (of 28) , n	1.0 (1.3)
Swollen joints (of 28) , n	0.3 (0.9)
ACPA-positve, n (%)	64 (75)
DAS28 CRP	1.9±0.6
CDAI	4.0 (2.8)
HAQ-DI	0.26 (0.5)
CRP (mg/dl)	0.15(0.1)
bDMARDs use, n (%)	19 (22)
tsDMARDs use, n (%)	12(14)
MTX use, n(%)	28(67)
PSL use, n(%)	15(17)

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Osteoporosis

POS0490

SERUM LEVELS OF BONE TURNOVER MARKERS, ESTABLISHING Z-SCORES FOR USE IN RESEARCH AND DAILY CLINICAL PRACTICE: DATA FROM A DUTCH HEALTHY REFERENCE COHORT

Keywords: Bone diseases, Osteoporosis, Diagnostic tests

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Background: Bone turnover markers (BTM) reflect specific processes or aspects of bone (re)modeling. Their dynamic character provides additional information regarding the current status and balance of bone metabolism. Measurement of BTM is clinically relevant and common in patients with osteoporosis and other bone-related disease such as inflammatory rheumatic diseases as axial spondyloarthritis (axSpA). BTM can attribute to the diagnostic workup as well as treatment monitoring. Interpretation of absolute values is difficult as these are highly influenced by age and gender, which complicates data interpretation and comparison of studies involving BTM. In previous research, we used BTM Z-scores to study the effect of biological therapy on the course of BTM in patients with axSpA [1, 2].
Objectives: To establish BTM reference values based on widely used BTM assays and/or automated immunoassay platforms. that can be used to calculate Z-scores to correct for the normal influence of age and gender.
Methods: Serum markers of collagen resorption, bone regulation, collagen formation and facilitator of bone mineralization (sCTX, OC, PINP and BALP, respectively) were measured in volunteers without bone-related diseases/abnormalities. Assays were conducted in a ISO certified specialized routine diagnostic laboratory. Raw data was plotted, gender-specific age cohorts were established based on the distribution of the data and subsequently their respective means and standard deviations were calculated. Z-scores can be calculated using these reference values to correct for the normal influence of age and gender on BTM.
Results: In total, 856 individuals were included, of which 486 (57%) were female. Individuals were aged between 7 and 70 years. Highest serum levels of BTM were found in childhood and puberty. Peak levels are higher in boys than girls and prevail at later ages. In adults, BTM levels decrease before reaching stable nadir levels. For the calculation of Z-scores below the age of 20 years, intervals of one year were needed due to the change in BTM activity. In adults, 10-year reference cohorts could be established in order to calculate Z-scores (Figure 1). As example, a male of 40 years with a serum PINP level of 70.0 ng/mL has a Z-score of 1.56. At the age of 60, his PINP levels remained 70.0 ng/mL, which corresponds to a Z-score of 2.73. Despite the absence of change in absolute levels of PINP, Z-scores do indicate a large increase not only compared to the previous measurement but also compared to the reference population matched for age and gender.

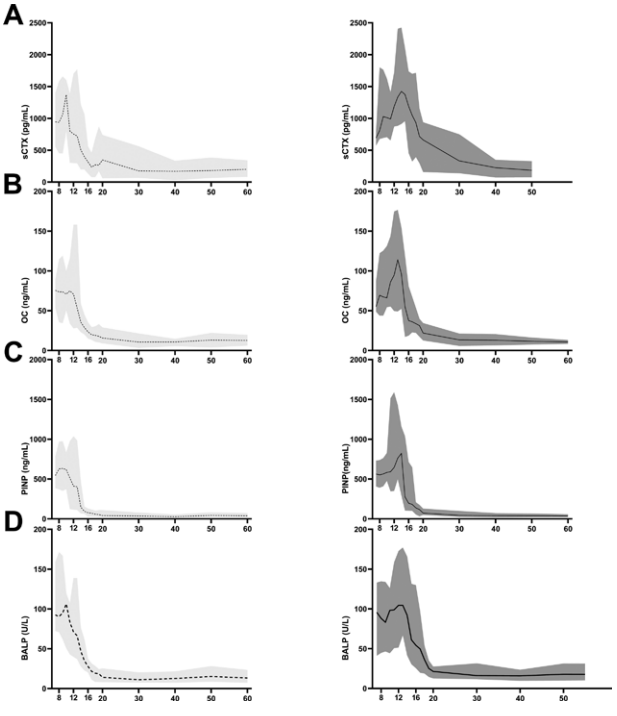


Figure 1. Median and P3-97 serum levels of sCTX(A), OC (B), PINP (C) and BALP (D) in females and males of a healthy reference cohort (---; female, —; male).

Conclusion: With our data, Z-scores of sCTX, OC, PINP and BALP can be calculated using reference categories (for age and gender) of mainly Caucasian volunteers representative for the normal population. BTM Z-scores facilitate harmonization of data interpretation in both daily clinical practice and research. This is especially important in (rheumatic) diseases with known aberrant bone metabolism as axSpA or (secondary) osteoporosis.

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[2] Siderius et al. Annals of the Rheumatic Diseases (2022) 81(Suppl 1) 779-780

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POS0491

EVALUATION OF FRACTURE PREVALENCE AND RISK IN A MONOCENTRIC COHORT OF PATIENTS WITH NON-METASTATIC BREAST CANCER IN ADJUVANT ENDOCRINE THERAPY TREATED WITH ANTIRESORPTIVE DRUGS

Keywords: Bone diseases, Osteoporosis, Malignancy

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Background: Bone loss is one of the major long-term side effects of adjuvant endocrine therapy for breast cancer. There is limited consensus on how to accurately assess fracture risk in this setting. Many trials showed the effectiveness of antiresorptive drugs in preventing the loss of bone mineral density (BMD) and, consequently, reducing fracture risk [1].
Objectives: Our study aims to investigate osteoporotic fractures prevalence and to assess the age adjusted fractures risk in breast cancer patients receiving AET and treated with antiresorptive drugs. Moreover, we analyzed differences in terms of clinical features and outcomes between patients treated with denosumab (DMAB) or bisphosphonates (BPs), and examined variations in biochemical markers of bone turnover and densitometric values to assess the effects of each antiresorptive medication.
Methods: In this monocentric, retrospective, non-randomized cohort study we enrolled patients with non-metastatic breast cancer who received at least 5 years of AET and were treated with DMABs or BPs. We retrieved demographic and clinical data pertaining to the cancer characteristics and the osteoporotic risk at the start of the antiresorptive therapy (baseline), as well as serum levels of C-terminal telopeptide of type I collagen (CTX), vitamin D, parathyroid hormone (PTH), and densitometric data (DXA) at baseline and at 24 months.
Results: We enrolled 120 patients, 38 on DMABs and 82 on BPs. During a median follow-up of 32 months (24-38), 16 (13.3%) fractured at least once. At baseline, the latter had lower BMI [22 kg/m^2 (21-27) vs 24 kg/m^2 (20-26), p=0.043], higher prevalence of osteoporosis (12/16 vs 35/104, p=0.002), higher prevalence of prior fractures (8/16 vs 15/104, p=0.003), and lower AET exposure time [2.7 years (1.2-3.7) vs 3.8 years (2.4-5.8), p=0.008]. In age-adjusted Cox-proportional model, a history of previous fractures and BMD at the femoral neck <-2 at baseline were associated with higher fracture risk [HR 7.8 (2.7-22.9), p<0.001, and HR 3.4 (1.1-10.4), p=0.033, respectively], whereas higher levels of vitamin D resulted protective [HR 0.7 (0.5-0.9), p=0.010]. AET exposure time and the type of antiresorptive drug, instead, had no impact on the fracture risk. Patients who received DMAB had significantly lower levels of vitamin D, age and AET exposure time [33 ng/ml (26-39) vs 36 ng/ml (30-41), p=0.022, 55 years (10.2) vs 60 years (9.1), p=0.008, and 2.9 years (2.0-4.4) vs 3.9 years (2.6-5.9), p=0.014, correspondingly]. At 24 months, both medications were successful in reducing serum levels of bone resorption markers and increasing densitometric values. The DMAB group experienced substantially larger BMD increases in the lumbar spine and femoral neck [respectively, +9.0% (+4.2/+19.8) vs +3.3% (-1.3/+6.6), p<0.001, and +6.1% (+2.2/+15.5) vs +0.7% (-3.5/+4.4), p<0.001].
Conclusion: The frequency of fractures tends to stay high in women receiving AET even if on antiresorptive drugs despite biochemical and instrumental improvements, indicating the existence of other concurrent processes of bone damage. To enable quick management of bone health-related issues, a thorough

risk assessment must be done at the moment AET is started. When given based on risk stratification, DMABs and BPs seem to have comparable antifracture effectiveness profiles. DMAB, however, was more successful in increasing BMD over time. Whatever the case, we found that appropriate vitamin D supplementation is advised throughout AET.

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Disclosure of Interests: None Declared.

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POS0492 ASSESSMENT OF OSTEOPOROSIS AND VERTEBRAL FRACTURE RISK BY OPPORTUNISTIC BONE MINERAL DENSITY (BMD) MEASUREMENT ON CHOLINE PET/CT IN PATIENTS WITH PROSTATE CANCER (HORM-OS PROJECT)

Keywords: Bone diseases, Osteoporosis, Imaging

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Background: Androgen deprivation therapy (ADT) is central in the management of advanced prostate cancer (PCa) but is associated with bone loss and occurrence of osteoporosis and fracture. Dual-energy x-ray absorptiometry (DXA) is recommended when starting ADT but is rarely done. Opportunistic measurement of bone mineral density (BMD) on CT has been proposed to improve osteoporosis screening in the general population, but has not been evaluated in PCa. Choline PET/CT (chPET/CT) is frequently used to identify the recurrence of PCa and/or search for metastasis.

Objectives: The objectives were to demonstrate the feasibility of using chPET/CT in comparison to the CT scan for opportunistic screening of osteoporosis and to describe the pet/ct-derived BMD and the prevalence of osteoporotic vertebral fracture in patients with PCa.

Methods: Between 2020 and 2022, we identified 171 PET/CT from 136 patients in the database of the nuclear medicine department of our tertiary center. We focused on chPET/CT. Among these patients, we identified those with a CT within 6 months before or after the chPET/CT to compare the BMD values between these 2 exams. BMD estimation was performed by 4 blinded readers (2 rheumatologists and 2 radiologists) on a 200-mm² trabecular bone area by a standardized method, on L1 vertebrae in axial section. Assessment of vertebral fractures and metastasis was performed on the entire spine in sagittal section. Demographic, clinical and treatments information have been collected blind from the reading of the images. Spearman coefficient and t-test were used for continuous variables and chi square test was used for dichotomous variables.

Results: We identified 93 PCa patients with chPET-CT including 29 with a CT within 6 months. The mean age was 74 years old (± 8.6), and mean BMI was 26.9 kg/m² (± 5.2). Forty-one patients (44%) smoked or had smoked. ChPET/CT was performed for newly-diagnosed PCa in 36.6%, for suspicion of recurrence in 59.1% or as simple follow-up for 4.3%. Twelve patients (12.9%) had fractures and 20 (21.5%) had metastasis. Also, 39 patients (42%) were already on ADT with a mean duration of 21.4 ± 31.6 months. First, we compared BMD measurement on both chPET/CT and CT in the 29 patients. The mean BMD on L1 vertebrae was similar between the 2 exams (125 ± 51.1 and 128 ± 42.4 HU respectively on chPET-CT and CT) and correlated well ($k = 0.7$; $p < 0.001$). Then, we measured the pet/ct-derived BMD on the whole cohort. The mean BMD was 125 HU (± 50.7). Increasing age was significantly correlated with decreased BMD ($k = -0.315$; $p < 0.001$). There was no correlation between BMI and BMD ($k = 0.02$; $p = 0.87$). The mean BMD was 123 HU (± 51.6) in patients who smoked or had smoked, compared with 138 HU (± 45.8) in non-smokers ($p = 0.11$). The mean BMD in patients already on ADT was 114 HU (± 56.2), compared with 127 HU (± 42.1) in others ($p = 0.17$). Among the 39 patients on ADT, there was a nonsignificant trend toward decreased BMD with increased ADT duration ($k = -0.27$; $p = 0.1$). Interestingly we found a significant decreased BMD for patients with fracture compared to those without fracture (mean BMD = 82.6 ± 42.9 vs 131 ± 49; $p < 0.01$). A cut-off of 100 HU has recently been published on CT to define patients at risk for bone complications. Here, we identified 24.7% patients with a BMD < 100 HU. These patients were more likely to have vertebral fracture compared to those with a BMD > 100 HU (30.4% vs 7.1% of fracture; $p < 0.01$).

Conclusion: This study demonstrates the feasibility of using chPET-CT for opportunistic screening for osteoporosis in PCa. Bone disease was frequent in this population, 13% patients had fractures and almost 25% had a BMD < 100 HU. Pet/ct-BMD seemed to be of interest for screening patients at risk of fracture. A prospective study will validate the interest of this approach and its impact on the management of osteoporosis in these patients.

REFERENCES: NIL.

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Disclosure of Interests: None Declared.

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POS0493 PREVALENCE AND INCIDENCE OF OSTEOPOROTIC VERTEBRAL FRACTURE IN NON SMALL CELL LUNG CANCER: ANALYSIS OF A 289 PATIENTS COHORT

Keywords: Bone diseases, Malignancy, Osteoporosis

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Background: The recent use of targeted therapies and immunotherapy has considerably improved the survival of patients with Non-Small Cell Lung Cancer (NSCLC), in particular metastatic ones. In this new era, it is relevant to look at the comorbidities affecting the quality of life and potentially the prognosis of NSCLC. Due to shared risk factors (tobacco, corticosteroid therapy, radiotherapy); osteoporosis is a comorbidity of interest in the context of NSCLC.

Objectives: The aim of our study was to establish the prevalence and incidence of osteoporotic vertebral fractures (OVF), the risk factors for incident OFV, and impact on survival of incident OFV.

Methods: This retrospective observational single-center study was conducted in the thoracic oncology clinic (Bichat University Hospital, AP-HP Paris, France), between January 2021 and July 2021. Consecutive patients followed for NSCLC were included in this study. The following data were collected (a) demographic characteristics such as gender, age, height and weight, BMI, smoking status, alcool intake (b) NSCLC characteristics such as histology, date of biopsy that resulted in the diagnostic of NSCLC, cancer stage (absence or presence of metastasis, including bone metastasis). Treatments received were collected a) oral corticosteroids (10 mg or more per day of prednisone or equivalent, for at least 2 weeks, in the last 2 years) b) anti-resorptive therapy (bisphosphonate, denosumab) c) local or systemic cancer treatment (surgery, radiotherapy, immunotherapy, chemotherapy and/or target treatment). We defined inclusion by the first thoraco-abominopelvic CT performed for the NSCLC extension assessment at diagnosis. We defined end of follow-up by the last TAP-CT available. We proceed to a double-blind lecture of TAP CT (rheumatologist and radiologist) to evaluate the presence of vertebral fracture: prevalent or incident, its nature (osteoporotic or metastatic), the number and localization. We also measure CT attenuation (Hounsfield unit [HU]) value of L1. Survival was assessed as of August 26, 2022.

Results: We included 289 patients: 162 males (56%), mean age 66.4years old. Eightt-two percent of patients were current or past smokers (42 ± 22 number of year smoking) and 22% consumed alcohol regularly. The mean BMI was 24.7 ± 5.0 kg/m². Seventy-eight percent had an adenocarcinoma and 18% a squamous cell carcinoma. Sixty one percent of patients had a metastatic cancer, including 25% of bone metastatsis. The mean follow-up time was 36.3 ± 29.4 months. At inclusion, 31 of the 289 had an OFV, for 40 OFV (24 thoracic, 16 lumbar, mean 1.3 ± 0.6 OFV per patient). The prevalence at inclusion was therefore 10.7%. At end of follow-up, 23.2% of patients (67/289) had an OVF. During the follow up of 36 ± 29 months: 36 patients had an incident OFV. The incidence of OVF was 12.5%. Ninety-seven OFV occurred (68 thoracic, 29 lumbar). Median time to incident OVF was 13 months [6.7; 21.2]. In univariate analysis (Table 1), the risk factor of OVF were: age ($p=0.036$), BMI <19kg/m² ($p <0.01$), steroid use ($p<0.001$), and radiotherapy ($p = 0.036$), UH in L1 at inclusion (HR 0.986, $p <0.001$) In multivariate analysis, BMI <19kg/m² ($p=0.01$), steroid use ($p<0.001$), HU in L1 at inclusion ((HR adjusted: 0,985, $p = 0.003$) were independent risk factor of incident OVF. Median survival was 80 months in the incident OVF group and was not reached in the patients without incident OVF ($p =0.074$, Image 1).

Conclusion: In our population, prevalence of OVF at inclusion was 10.7%. Incidence was 12.5% during a mean follow up of 36 months. Occurrence of a new OVF may have an impact on survival. Presence of OVF and UH in L1 should be evaluated systematically during NSCLC follow up. We should pay more attention to this population, in order to prescribe preventive anti-resorptive drugs if needed.

Table 1. characteristics of patient with and without osteoporotic vertebral fracture (OVF).

Characteristics	Incident OFV (n=37)	No OVF (n= 222)	P (univariate)
Age (yo)	**71.2 ± 10.4**	65.5 ± 11.1	**0.036**
Gender masculin, n (%)	19 (53%)	127 (57%)	0.738
Current or past smoker, n (%)	32 (89%)	175 (80%)	0.260
Alcool abuse, n (%)	8 (23%)	48 (23%)	1
Mean BMI (kg/cm²)	**23.6 ± 4.8**	**25.0 ± 5.1**	**<0.001**
Pathology -adenocarcinoma -squamous cell carcinoma	24 (67%) 6 (19%)	169 (77%) 32 (15%)	0.417
Metastasis, n (%) (inclusion/end of follow up)	17 (47%) / 25 (69%)	117 (53%) / 149 (68)	0.866
Bone metastasis, n (%) (inclusion/end of follow up)	8 (22%) / 13 (36%)	44 (20%) / 63 (29%)	0.752
CT attenuation in L1, moy (UH)	**123.0 ± 44.4**	**170.5 ± 51.4**	**<0.001**
Steroid use, n (%)	**12 (33%)**	**29 (13%)**	**<0.001**
Radiotherapy, n (%)	**11 (31%)**	**42 (19%)**	**0.036**
Anti-resorptive drugs, n (%)	7 (19%)	31 (11%)	0.417

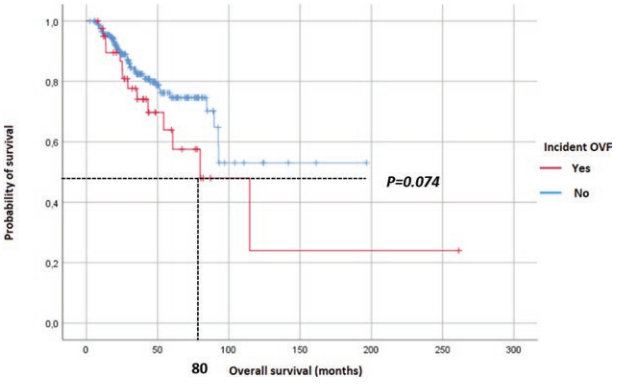


Image 1. The Kaplan-Meier probability of survival for patient with or without incident osteoporotic vertebral fracture (OVF).

REFERENCES: NIL.
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Disclosure of Interests: Esther Ebstein Consultant of: BMS - Abbvie - Galapagos, Pauline Brocard: None declared, Ghassen Soussi: None declared, Ralph Khoury: None declared, Antoine Khalil: None declared, Marine Forien Consultant of: Abbvie - BMS, Sebastien Ottaviani Consultant of: Abbvie - BMS - UCB, Gerard Zalcman: None declared, Philippe Dieudé Consultant of: Pfizer - BMS - Abbvie - UCB, Valerie Gounant: None declared.
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POS0494 DEVELOPMENT AND VALIDATION OF A QUESTIONNAIRE FOR PRE-ROMOSOZUMAB THERAPY SCREENING

Keywords: Patient reported outcomes, Osteoporosis, Quality of care

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Background: Romosozumab has expanded the osteoporosis management options in postmenopausal women who are at very high risk of fracture. Romosozumab has dual mechanism of action as it modulates both bone formation and bone resorption and aims to achieve optimal fracture prevention. While Romosozumab appears to have a generally manageable tolerability profile, extra clinical experience is required to, more definitively, establish its efficacy and safety. Romosozumab is contraindicated in patients with past history of myocardial infarction and stroke. Currently there is no tool to screen osteoporosis patients for Romosozumab contraindications.
Objectives: To develop a questionnaire for pre-Romosozumab therapy screening for use in standard clinical practice.
Methods: The Pre-Romosozumab screening questionnaire was conceptualized based on frameworks used by the WHO Quality of Life tool and the PROMIS. Initially, review of the literature and cognitive interviews held with physicians with special interest in bone health, patients, osteoporosis nurses, and outpatient managers were conducted to identify item pool of questions. Item selection and reduction was achieved based on patients as well as an interdisciplinary group of specialists. Rasch and internal consistency reliability analyses were implemented. The questionnaire included 5 main categories which are patient-centred: 1. Patient's anthropometric measures, 2. items specifically linked to Romosozumab indications and contraindications, 3. Self-completed Fracture risk assessment, 4. Current medication(s), 5. Comorbidities. The answers to the questions were compared to the patients' notes. Comprehensibility was assessed using numerical visual analogue scale [0-10].
Results: The developed questionnaire is composed of 2-pages. Page-1 to be self-completed by the patient to screen for any possible contraindication to Romosozumab therapy, current medications, and comorbidities. Page-2 is to be completed by the treating health care professional and it includes information of how this patient meets the prescribing recommendations for Romosozumab. The primary screening questionnaire contained 15 items; all met the minimum acceptable value of 0.81 for item-level content validity index. Using exploratory factor analysis (EFA), four factors (intrapersonal-psychological, intrapersonal-cognitive, provider-related, and socio-economic reasons) were assessed, and Cronbach's alpha coefficient of 0.79, 0.86, 0.79, and 0.81, respectively, were identified. The reliability of the questionnaire (r = 0.88) was confirmed. The questionnaire showed also a high degree of comprehensibility (9.6).
Conclusion: The questionnaire is a valid and reliable instrument that can be used in standard practice to pre-screen patients identified as candidates for Romosozumab therapy. The questionnaire achieved high degree of comprehensibility.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0495 PREVALENCE AND RISK FACTORS OF OSTEOPOROSIS IN A BELGIAN COHORT OF LUNG TRANSPLANTATION CANDIDATES: THE PROGRES STUDY

Keywords: Bone diseases, Osteoporosis, Lungs

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Background: Few data are available on the incidence of osteoporosis (OP) in end-stage pulmonary diseases, particularly in lung transplant candidates. Yet, organ transplantation can be accompanied by low bone mineral density (BMD) owing to immunosuppressive therapy, particularly with oral glucocorticoids (GCs) use.
Objectives: Our primary aim was to evaluate the prevalence and therapeutic management of OP in lung transplant candidates. Our second objective was to determine the risk factors associated with OP, including the type of respiratory disorder.
Methods: We included 198 patients (103 women) out of 388 screened for lung transplantation at our institution between January 1998 and December 2020. BMD, measured by Dual-energy X-ray absorptiometry (DXA, Hologic (t-m)) at the lumbar spine (LS), total hip (TH), and femoral neck (FN), vertebral fracture assessment (VFA), as well as previous major osteoporotic fracture (MOF), were recorded. We systematically collected well-recognized OP risk factors, along with other factors suspected of affecting BMD such as inhaled (i) GCs use, pulmonary function tests, hypoxemia and type of pulmonary disorder.
Results: OP, as defined by BMD values (T-score ≤ -2.5) and/or fragility fracture (FF), MOF and/or vertebral fractures (VF), was observed in 118 patients (59.6%). Among these patients, 54 (45.8%) had only a T-score ≤ -2.5, while 36 (30.5%) had only an FF, with predominant vertebral fractures (77.8%). The median age (IQR) of the study population was 58 years (53.0-62.0), and 59 years in OP patients (54.2-62.0). Mean T-scores (±SD) were -1.62±1.52 at the LS, -1.43±1.05 at the TH and -1.98±1.14 at the FN. Mean T-scores (±SD) in OP patients were -2.15±1.31, -1.87±0.93 and -2.44±1.03, respectively. The mean (±SD) ten-year probability of major osteoporotic fracture assessed by the FRAX algorithms (FRAX score) was 11.6±11.2 %, and the mean FRAX adjusted to GCs dose (±SD) was 12.0±12.1 %. Nighty-eight patients (49.5%) achieved intervention threshold adjusted for age based on FRAX results

and 110 patients (55.6%) when FRAX was adjusted to GCs dose. Seventy-eight OP patients (66.1%) achieved the FRAX intervention threshold, of whom 53 (67.9%) received calcium and/or vitamin D and 33 (42.3%) had received an add-on therapy, mostly a bisphosphonate (n=23, 69.7%) or denosumab (n=4, 12.1%). Eighty-four OP patients (71.2%) achieved the FRAX intervention threshold adjusted to GCs dose, of whom 59 (70.2%) received calcium and/or vitamin D and 37 (44.5%) had received an add-on therapy, mostly a bisphosphonate (n=25, 67.6%) or denosumab (n=5, 13.5%). Thirty-six OP patients (30.5%), 18 patients (33.3%) with only a T-score ≤ -2.5 and 12 patients with only an FF, did not receive any medication. In total, 153 patients had a chronic obstructive pulmonary disease (COPD, 77.3%), 33 an interstitial lung disease (ILD, 16.3%) and 12 (6.1%) suffered from another pulmonary disease. Among OP patients, 102 had a COPD (86.4%), 12 an ILD (10.2%) and 4 (3.4%) suffered from another pulmonary disease. Lower BMI, iGCs use, COPD, reduced FVC and severely impaired FEV1/FVC ratio were associated with OP. GCs treatment was associated with FF, regardless of the daily dosage.

Conclusion: Most of lung transplant candidates were suffering from OP and one third suffered from FF. Thus, performing DXA and VFA should be recommended in lung transplant candidates in order to start adequate osteoporosis treatment before lung transplantation. This is even more important in COPD patients, as this population displays an increased risk of OP compared to other end-stage diseases. OP diagnosis is important in those patients as their risk of fracture is likely to increase after transplantation. The large proportion of untreated (or insufficiently treated) patients stressed the need to develop specific strategies in this field. Finally, controlling some risk factors is crucial for the management and prevention of OP, for instance by, at least, tapering the dosage of both oral and inhaled GCs.

Table 1.

	All Patients (n=198)	OP patients (n=118)	Non-OP (n=80)
Age, y (median and IQR)	58.0 (53.3-62.0)	59.0 (54.2-62.0)	57.0 (52.0-62.0)
BMI, kg/m² (mean ± SD)	23.1 ± 4.7	22.2±4.6	24.3±4.6
GCs use, n (%)	154 (77.8)	94 (79.7)	60 (75.0)
iGCs use, n (%)	155 (78.3)	99 (83.9)	56 (70.0)
COPD, n (%)	153 (77.3)	102 (86.4)	44 (55.0)
FEV1, % PV (median and IQR)	23.0 (19.0-35.0)	22.0 (19.0-28.0)	28.0 (20.0-52.7)
FVC, % of PV (median and IQR)	60.0 (49.0-75.0)	58.0 (48.0-71.0)	64.0 (50.0-77.2)
FEV1/FVC ratio (median and IQR)	41.0 (35.0-57.0)	40.0 (35.0-48.0)	49.5 (35.7-93.2)
T-score ≤ -2.5, n (%)	54 (27.3)	54 (45.8)	NA
FF, n (%)	36 (18.2)	36 (30.5)	NA
T-score ≤ -2.5 and FF, n (%)	28 (14.1)	28 (23.7)	NA
Risk factors for OP, OR (CI) – p value			
BMI	NA	0.43 (0.20-0.92) – 0.03	NA
GCs use	NA	1.31 (0.66-2.57) – 0.44	NA
iGCs use	NA	2.23 (1.13-4.48) – 0.02	NA
FVC	NA	0.49 (0.25-0.94) – 0.03	NA
FEV1/FVC ratio	NA	0.38 (0.17-0.86) – 0.02	NA
COPD	NA	3.62 (1.83-7.42) – 0.0003	NA

Abbreviations. BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; FF, fragility fracture; FVC, forced vital capacity; iGCs : inhaled glucocorticoids; IQR, interquartile range; GCs, oral glucocorticoids; NA, not applicable; OP, osteoporosis; OR, odds ratio; PV, Pulmonary volume; SD, standard deviation; y, years

REFERENCES: NIL.

Acknowledgements: NIL.

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POS0496

MANAGEMENT OF OSTEOPOROSIS IN PATIENTS WITH SYSTEMIC MASTOCYTOSIS: A MONOCENTRIC EXPERT CENTRE EXPERIENCE

Keywords: Bone diseases, Osteoporosis, Rare/orphan diseases

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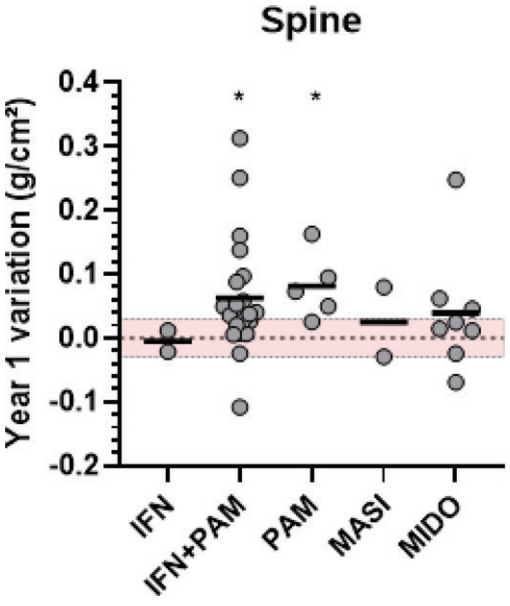
Background: Systemic mastocytosis (SM) is a rare clonal mast cell disease, associated with vertebral osteoporosis (OP) in ~30% of the patients. This OP frequently leads to multiple vertebral fractures, in particular in young or premenopausal patients. To date, experts in the field recommend the use of bisphosphonates as first line therapy [1], or alternatively interferon alfa [2]. However, data regarding treatments efficacy, and regarding the optimal strategy are scarce. Especially, usefulness of mastocytosis-specific treatments is still to be established.

Objectives: To evaluate the clinical and the densitometric efficacy of various treatment regimen for osteoporosis, over 1 year, in patients with systemic mastocytosis.

Methods: We retrospectively analysed demographic, clinical (including new fragility fractures occurrence), biological and densitometric data of patients from our expert centre (CEREMAST), from 2010 to 2022. All patients fulfilled the WHO criteria for systemic mastocytosis and had osteoporosis defined as either a history of fragility fracture or a T-score <-2.5 SD. We evaluated bone mineral density (BMD) by DXA, and the occurrence of fracture, at initiation and after 1 year of exposure to the following treatment for SM-related osteoporosis: interferon alfa 2a (IFN), combination of interferon & monthly pamidronate (IFN+PAM), pamidronate (PAM, monthly in 4 patients, quarterly in 1), masitinib (MASI), and midostaurin (MIDO). IFN+PAM was proposed preferentially to patients with severe osteoporosis and multiple vertebral fractures. PAM was proposed in case of refusal of IFN, or contra-indication to IFN, or additional cause of osteoporosis for which IFN use would not be relevant. Values are reported as mean (+/-SD). Least significant change for BMD was 0.03 g/cm². Baseline and year-1 BMD were compared by a paired t-test. A p-value <0.05 was considered as significant.

Results: We included 37 osteoporotic patients with SM. Thirty-four patients had an indolent SM, 1 had a SM with associated haematological neoplasm, and 2 had an aggressive form. The mean age at diagnosis was 53.5 (+/-12.7) years, with 54.1% of women. Mean lumbar T-score was -2.4 (+/-1.7). Mean hip T-score was -1.8 (+/-0.8). Importantly, 81.1% had history of fragility fractures, and among them 96.6% had vertebral fractures. The mean number of vertebral fractures was 3.6 (+/-3.1) per patient. Two patients were exposed to IFN, 21 to IFN+PAM, 5 to PAM, 2 to MASI, and 9 to MIDO. Among patients treated by MIDO, 2 had prior exposure to IFN+PAM. One patient from the MIDO group and 1 patient from the MASI group were concomitantly exposed to bisphosphonates (respectively alendronate and zoledronate). Regarding treatments efficacy, IFN+PAM and PAM significantly improved BMD (see Figure 1). Two patients treated by IFN+PAM developed an additional vertebral fracture during the first year of follow-up, at 6- and 8-months post-treatment initiation. Importantly, these patients had 4 and 7 vertebral fractures prior treatment.

Conclusion: Our data show that monthly pamidronate, and combination of interferon & pamidronate improve BMD and may reduce fracture risk over 1 year in SM. Conversely, our data do not support the use of interferon monotherapy or midostaurin as preferred strategy in patients with severe osteoporosis. Usefulness of masitinib, and of recent tyrosine kinase inhibitors needs further studies in this population.



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Disclosure of Interests: None Declared.

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POS0497

ROMOSOZUMAB AS A TREATMENT AFTER BISPHOSPHONATE OR FOR OSTEOPOROSIS WITH T-SCORE≦-2.5 IN CLINICAL PRACTICE

Keywords: Real-world evidence, Rheumatoid arthritis, Osteoporosis

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Background: Romosozumab (ROMO) is an antisclerostin antibody that is used in the treatment of severe osteoporosis (OP). In March 2019, ROMO was approved for use in Japan for treating severe OP in clinical practice, causing an increase in its prescription in our institute. Although efficacy data for ROMO have been presented in clinical trials, there is a lack of real-world data. In our experience, ROMO treatment results in significant bone mineral density (BMD) gain in some patients, but not all. Therefore, understanding the efficacy of ROMO treatments in groups of patients frequency treated with ROMO in real-world clinical practice is essential.
Objectives: This study investigated the efficacy of a 12-month ROMO treatment in patients with OP and explored the efficacy as a treatment after bisphosphonate (BP) or for OP with T-score≦-2.5.
Methods: Our study included 64 patients with OP, who were started on ROMO treatment between June 2019and August 2021. The following information was collected: 1) baseline characteristics, 2) time-course of BMD (lumbar spine [LS] and total hip [TH]) and bone turnover markers (BTM; bone-specific alkaline phosphatase [BAP], type I procollagen-N-propeptide [P1NP], type I procollagen-N-propeptide [NTX], and tartrate-resistant acid phosphatase-5b [TRACP-5b]), 3) BMD outcomes as a treatment after BP or for OP patients with T-score≦-2.5.
Results: 1) The mean age of the participants was 72.4 years (59 female and five male). Of the 64 understudied patients, 84.4% had past insufficiency fractures, whereas 29.7% had been treated with concomitant prednisolone. Furthermore, 22 patients had primary OP, 24 had rheumatoid arthritis, 15 had glucocorticoid-induced OP, and three had other conditions. Pretreatments for OP were BP (44 patients), denosumab (6), selective estrogen receptor modulator (5), activated vitamin D (2), none (5), and daily teriparatide (1). 2) Both mean LS- and TH-BMD significantly increased in the patients for whom ROMO administration was continued for 12 months. The average percentage changes of LS- and TH-BMD were +6.6% and +1.6% at six months and +11.0% and +2.7% at 12 months, respectively. However, BAP and P1NP increased steeply at one month, followed by a gradual decrease. As observed, the average percentage changes of BAP and P1NP were +68.7% and +167.8% at one month, +47.6% and +84.3%at six months, and +20.2% and +41.5% at 12 months, respectively. The results also showed that TRACP-5b decreased from one to 12 months, with the average percentage changes being -15.1% at one month, -3.5% at six months, and -6.2% at 12 months. Moreover, NTX, a bone-resorptive marker, was slightly increased during ROMO treatment. 3) In 44 patients treated with ROMO after BP, the average percentage changes of LS- and TH-BMD were +5.7% and +1.7% at six months and +9.2% and +2.4% at 12 months, respectively. The average percentage changes of BAP and P1NP were +74.0% and +189.9% at one month, +39.5% and +65.3% at six months, and +17.7% and +36.6% at 12 months, respectively. TRACP-5b decreased from one to 12 months, with the average percentage changes being -14.7% at one month, -2.8% at six months, and -6.6% at 12 months. In 23 patients with baseline LS T-score≦-2.5, the average percentage changes of LS-BMD were +6.3% at six months and +11.8% at 12 months. 21.7% of patients reached LS T-score>-2.5 at 12 months. In 24 patients with baseline TH T-score≦-2.5, the average percentage changes of LS-BMD were +2.3% at six months and +3.1% at 12 months. 20.8% of patients reached LS T-score>-2.5 at 12 months.
Conclusion: ROMO treatments rapidly increased BMD, especially LS-BMD, and changed BTM after one month in both treatment after BP and OP with T-score≦-2.5.

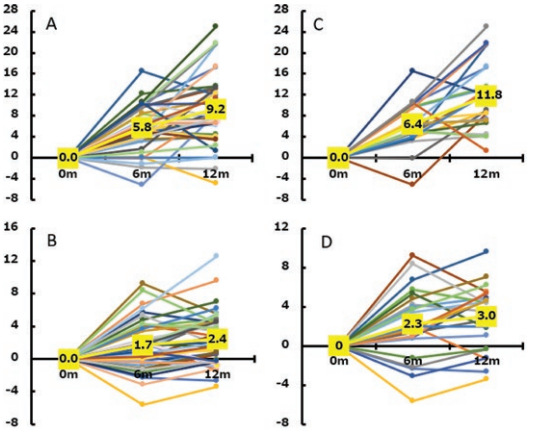


Figure: Time-course of % Change of Bone Mineral Density
A: Lumbar spine bone mineral density in patients after bisphosphonate
B: Total hip bone mineral density in patients after bisphosphonate
C: Lumbar spine bone mineral density in patients with lumbar spine T-score ≦ -2.5
D: Total hip bone mineral density in patients with total hip T-score ≦ -2.5
Bold lines indicated averaged values. Thin lines indicated individual values of each patient.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0498

RISK WEIGHT CALCULATION OF CANDIDATE VARIANTS FOR INCIDENT MAJOR OSTEOPOROTIC FRACTURE IN PATIENTS WITH RHEUMATIC DISEASES

Keywords: Prognostic factors, Validation, Osteoporosis

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Background: Incidental osteoporotic fractures are one of the serious comorbidities in patients with rheumatic disease (RD). However, no comprehensive treatment criteria exist to prevent these fractures.
Objectives: The purpose of this study is to develop criteria and assess the validity of the criteria using retrospective cohort data.
Methods: Patients with RDs who were treated for more than one year were picked up in the study. The patients were followed up with blood tests including cystatin C (CysC) every 3 months. Bone mineral density (BMD) using dual-energy X-ray absorptive densitometry was measured annually. Comorbidities, presence of prevalent osteoporotic fracture, and habitual tastes such as alcohol drinking and current smoking were picked up at the initiation of treatment (baseline). The primary endpoint was incidental osteoporotic fractures (inc-OF). Patients were followed up until December 2022, unless censored by death, loss of follow-up, or dropping out due to admission to a nursing home. Candidate risk factors, with these significant differences between groups with OF and without OF, were demonstrated using Mann-Whitney U-test, for incident OF and were evaluated using a cox regression analysis with the univariate model. Risk weights of each factor were calculated using risk ratio and beta-value. The total risk weight for each patient (TRW) was determined by summarizing the risk weight of each factor. Receiver operating characteristics (ROC) analysis was tested in order to determine the area under the curve (AUC) and the cut-off index (COI). Finally, a chi-square test was also performed in regard to anti-osteoporotic drug administration after baseline (OPD).
Results: A total of 1228 patients in these 345 males and 883 females were included. The mean age at baseline was 77.7 years old, and the mean follow-up period was 40.2 months. Background RDs were 761 with rheumatoid arthritis, 163 with psoriatic arthritis, 99 with Sjogren syndrome, 65 with pustulosis palmaris et plantaris, 48 with systemic lupus erythematosus, 24 with ankylosing spondylitis, 19 with systemic sclerosis, 16 with ulcerative colitis, 12 with Behçet's disease, 4 with polymyositis/dermatomyositis, 3 with mixed connective tissue disease, 3 with familial Mediterranean fever, and 1 with polyarteritis nodosa. Picked-up factors were the presence of pre-OF, estimated glomerular filtration rate using CysC (eGFR), T-score in the lumbar spine (LS) and in the femoral neck (FN), number of comorbidities (nCom), presence of diabetes mellitus (DM), hypertension (HT), hyperlipidemia (HL), chronic obstructive pulmonary diseases (COPD), insomnia, cognitive impairment (CI), musculoskeletal ambulation disability symptom complex (MADS), disuse, neuromuscular diseases (NMD), and polypharmacy (PPs) at baseline. Risk ratios, beta-values, p-values, and calculated risk weights in these factors were shown in Table 1. The mean TRW in patients was 66.7 in the group with inc-OF and 138.4 in the group with no incident OF (p<0.001). The AUC was 0.787 and the COI was 93.6 with 80.4% and 68.8% of sensitivity and specificity, respectively (p<0.001). OPD was administrated in 341 patients of the 471 TRW positive group in whom 299 did not have inc-OF, whereas, in the 164 patients of the 757 TRW negative group, only 10 had inc-OF.
Conclusion: A novel evaluation system for osteoporosis treatment should be a numerical system that summarizes adding risk weight of each candidate factor.

Table 1. Risk ratios, beta-values, p-values, and calculated risk weights in variants

variant	risk ratio	beta	p	risk weight
eGFR≦72.0	2.06	0.719	<0.001	28
T-score_LS	1.46	0.378	<0.05	12
T-score_FN	1.32	0.279	<0.05	4.5
nCom≧11	1.43	0.354	<0.05	10.5
DM	1.46	0.379	<0.05	12
HT	1.44	0.367	<0.05	12
HL	1.01	0.039	<0.05	1
COPD	1.38	0.031	<0.05	1
insomnia	1.19	0.175	<0.05	4
CI	1.47	0.387	<0.05	12
MADS	1.95	0.669	<0.001	28
disuse	1.90	0.644	<0.001	24
NMD	2.36	0.859	<0.01	45
PPs	1.43	0.356	<0.05	4.5
pre-OF	1.63	0.491	<0.001	94

REFERENCES: NIL.
Acknowledgements: NIL.

Disclosure of Interests: None Declared.
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POS0499 DIFFERENCES IN FRACTURE RISK IN PATIENTS WITH DISCORDANT BONE MINERAL DENSITY IN THE HIPS: OBSERVATIONAL STUDY

Keywords: Osteoporosis, Epidemiology, Bone diseases

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Background: Osteoporosis is a condition characterised by low bone mineral density (BMD) and is associated with increased risk of fractures and subsequent increased morbidity and mortality. The usual sites of BMD measurements are either the non-dominant hip or the spine. The hip is used to predict fracture risk using the FRAX™ tool. Some patients have a different BMD as shown by their T scores in the contralateral hip.
Objectives: This study aimed to ascertain whether patients significantly discordant in their BMD on the contralateral hip have a different risk for fractures.
Methods: Data from a dual-energy x-ray absorptiometry (DEXA) scanner in the North West of England were used. Patients who were referred between 2004-2011 were studied. Patients had both hips scanned as well as risk factors and presence of fracture recorded. Data collected included age, sex, height, weight, BMI, history of fractures, rheumatoid arthritis status, smoking status, alcohol use and malabsorption. Those that had a BMD T-score difference of either greater than or equal +1 SD or -1SD were considered to have discordant hips. These two groups were compared using independent sample t-tests for continuous variables and chi-squared tests for categorical variables. Logistic models were then fitted to look at the odds of fracture in each group.
Results: The hip T-scores of 35759 patients were measured. Mean age was 62.17 (±12.78) with 84.16% being female. There were 15287 (42.75%) who had discordant hips. The odds ratio for the measured risk factors and the association with fracture are shown in **Table 1** below.

Table 1. Odds ratio of risk factors for patients with non-discordant and discordant hips

Risk factor	Whole Group	Non-Discordant	Discordant	Odds Ratio (95% CI)
Age (Years) Mean (SD)	62.17 (±12.78)	63.11 (±12.86)	60.92 (±12.55	0.987 (0.985-0.988)
Height (cm) Mean (SD)	161.87 (±8.30)	162.30 (±8.36)	161.31 (±8.17)	0.986 (0.983-0.988)
Weight (Kg) Mean (SD)	70.35 (±15.33)	71.40 (±15.74)	68.96 (±14.64)	0.989 (0.988-0.991)
BMI (Kg/m^2) Mean (SD)	26.80 (±5.25)	27.06 (±5.38)	26.45 (±5.04)	0.978 (0.974-0.982)
Female (%)	84.16	83.09	85.60	1.209 (1.141-1.282)
Alcohol Use (%)	5.02	6.96	2.41	0.331 (0.294-0.371)
Rheumatoid Arthritis Status (%)	4.27	5.34	2.83	0.516 (0.461-0.578)
Smoking Status (%)	26.24	36.13	12.99	0.264 (0.250-0.279)
Fracture (%)	34.08	32.11	36.72	1.227 (1.174-1.282)
Family History of Osteoporosis (%)	11.88	16.29	5.97	0.327 (0.302-0.352)
Steroid Use (%)	21.05	23.52	17.75	0.702 (0.666-0.740)
Malabsorption (%)	10.66	14.14	6.01	0.388 (0.359-0.419)

Conclusion: Hip discordance might be associated with adverse risk factors such as increased frequency of fractures. Measuring BMD of both hips could give a better estimate of future fracture risk. Further analysis of a subset from this group will be explored and presented.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0500 OSTEOPOROSIS IS UNCOMMON IN EARLY CLONAL MAST CELL DISORDERS

Keywords: Osteoporosis, Rare/orphan diseases, Bone diseases

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Background: Indolent systemic mastocytosis (ISM) is a hematological disease frequently associated with vertebral osteoporosis (OP) and subsequent vertebral fractures. The natural history of this OP remains unclear. Importantly, we do not know whether OP represents an early event triggered alongside mast cell abnormalities. Experts in the field recently introduced the debated concept of "pre-ISM" to refer to patients with abnormal clonal mast cells and clinical repercussions who do not fulfill the criteria for ISM [1]. These patients can be considered as having an early clonal mast cell disorder (cMCD).
Objectives: To describe OP in patients with cMCD and to compare osteoporosis characteristics of early cMCD patients to those of ISM patients.
Methods: We retrospectively analyzed clinical, biological and densitometric data of 40 cMCD and 135 ISM patients from the mastocytosis expert center (CEREMAST) in Toulouse. Data normality was tested by a Shapiro-Wilk normality test. Comparisons between subgroups were performed using: Student's t-test for the normally distributed data, a non-parametric Wilcoxon rank-sum test for non-normally distributed data, and Fisher's exact test (or chi-square test if appropriate) for dichotomous variables. A p-value <0.05 was considered statistically significant with a 95% confidence interval (CI).
Results: OP (12.5 vs 34.1%) and vertebral fractures (5.0 vs 18.5%) were significantly less frequent in the early cMCD population. Most patients with OP and vertebral fractures in the cMCD group had the usual risk factors for OP.

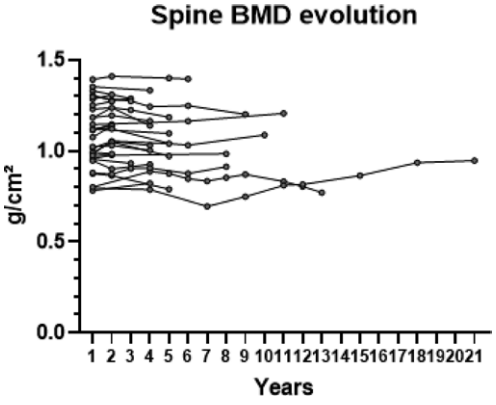


Figure 1.

Crosslaps levels were similar, but bone marrow tryptase was higher in the ISM group (159 ng/mL +/- 310 *vs* 1481 +/- 4910; p<0.0001). Short-term (1 year) and long-term (see Figure 1) analysis of BMD in the cMCD group, showed stable BMD over time. Interestingly, the only cMCD patient with a typical ISM-like OP had high bone marrow tryptase, developed bone marrow KIT mutation during follow-up, and had a family history of ISM. Our data show that OP is not a common clinical finding in early cMCD. When OP and fractures occur in cMCD, they differ from the usual phenotype of ISM bone fragility.
Conclusion: Our findings suggest that in most early cMCD patients, the meaning and management of OP differ from that of OP in ISM. Prospective longitudinal studies and the validation of predictors are needed to identify the minority of cMCD patients developing ISM-related OP.
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POS0501 INVESTIGATING THE PREDICTORS OF ONE VERSUS MANY FRACTURES IN MALES REFERRED FOR BMD ASSESSMENT: AN OBSERVATIONAL COHORT STUDY

Keywords: Bone diseases, Epidemiology, Osteoporosis

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Background: Currently there exists limited data around predictors of osteoporosis as well as fragility fractures in men.[1] It is therefore important to understand the determinants of poor bone health in males and thus predicators of fractures to help deliver optimal care. Males referred for Bone Mineral Density (BMD) estimation are a good source of exploring such predictors of fractures. We sought to investigate the determinants of one versus many fractures in a population of males routinely referred for BMD estimation using Dual X-Ray Absorptiometry (DEXA) scans.
Objectives: The aim of this study is to assess the predictors of one vs multiple fractures in males routinely referred for DEXA scans, in an observational cohort.

Methods: Data was obtained from patients referred to secondary care in the northwest of England who subsequently were assessed for low BMD via DEXA. Males referred between 2004 and 2019 were selected and data collected at attendance included patients' full medical history and body habitus. Logistic models reporting odds ratio were used to examine the predictive factors for one versus multiple fractures in the cohort.
Results: A total of 5390 male patients were included in this analysis, the median age at scan was 66 years and the mean age was 76.6 +/- 13.7 (SD). A total of 1853 fractures occurred in our population of males. Varying modifiable and non-modifiable factors were identified as predictors of fractures. Modifiable factors included those who drank excess alcohol. Patients who had a history of excess alcohol consumption were more likely to have multiple fractures OR: 1.260 (CI: 1.02-1.26) (p= 0.030). Furthermore, BMD at the left neck of femur was protective for multiple fractures OR: 0.938 (CI: 0.89-0.99) (p= 0.018). Interestingly the BMD at the right neck of femur was not predictive of multiple fractures. In terms of non-modifiable risk factors, height was statistically significant in being protective against fractures in this cohort OR: 0.991 (CI: 0.98-0.99) (p= 0.016). Rheumatoid arthritis, steroid use, family history and coeliac disease all produced insignificant results when predicting one versus many fractures in this male cohort. A summary of the results can be seen in Table 1.

Table 1. A summary of the predictors of fractures in males referred for BMD assessment.

Predictor	Odds Ratio	Confidence Interval	p-value
Excess Alcohol	1.260	1.02-1.26	0.030
BMD L NOF	0.938	0.89-0.99	0.018
BMD R NOF	0.966	0.91-1.03	0.255
Height	0.991	0.98-0.99	0.016

Conclusion: This study identifies factors predictive of multiple fractures among males referred for BMD assessment. Our analysis shows that a history of excess alcohol consumption, altered BMD results at the left neck of femur, and height were statistically significant in the prediction of multiple fractures. Our previous study also found a relationship between excess alcohol consumption and patterns of fractures in males. Further research is required to better understand both this link and alcohol's importance in the pathophysiology of osteoporosis in men. Such research is also imperative in hypothesising specific factors relating to fractures adjusted and unadjusted for age.
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POS0502 IMPLEMENTATION OF A CLINICAL CARE PATHWAY FOR SYSTEMATIC BONE FRAGILITY ASSESSMENT AT THE INITIATION OF ANDROGEN DEPRIVATION IN PROSTATE CANCER PATIENTS (HORMOS PROJECT)

Keywords: Osteoporosis, Bone diseases, Best practices

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Background: Androgen deprivation therapy (ADT) in prostate cancer (PCa) is associated with an increased risk of bone fragility including bone loss, osteoporosis and fractures. Although international recommendations suggest performing dual-energy x-ray absorptiometry (DXA) at the initiation of treatment, less than 10% of patients do it. The implementation of a standardised clinical care pathway could help prevent bone-related complications in patients starting ADT.
Objectives: To improve screening for bone fragility in patients starting ADT for PCa by setting up a clinical care pathway. To describe the characteristic of patients with PCa starting ADT.
Methods: The radiation oncologists, medical oncologists or urologists from a tertiary center systematically referred all patients starting any ADT for PCa to our rheumatology department for a bone-health assessment including a DXA and clinics with a bone specialist. The effectiveness of the pathway was assessed by the number of patients who performed DXA at the initiation of ADT.
Results: Between March and December 2022, 116 of the 119 patients (97%) referred to our department were able to have a bone assessment within an average of 36 +/- 15 days. The three patients not seen in the care pathway did not wish to come for a new medical appointment. Among the 116 patients, mean age at first visit was 75+/-7 years old, mean BMI 26.9 +/- 4.7 kg/m^2, 56% were previous or current smoker and Charlson Comorbidity Index was 4.75 +/- 2.5 with 20% diabetes, 15% peripheral vascular disease, 11% coronaropathy and 10% chronic kidney disease. Regarding PCa, 65% were on a localized or locally-advanced stage while 35% were metastatic and overall, 44% presented with a high risk histo-pronostic score (ISUP 4 or 5). Sixty-four patients (55%) were scheduled to concomitant prostatic external beam radiation, as initial or salvage therapy. Median PSA at diagnosis was 16 ng/ml (8.8-38.5) At inclusion, 70% of patients were newly-diagnosed PCa while 30% were recurrent PCa. ADT was prescribed alone for 65% of patients or in combination with new hormone-therapy (NHT) for 35% of patients and 26% with concomitant corticosteroids with a mean dose of 10 +/-4 mg. The mean duration of previous ADT for relapsing patients was 16 +/- 20 months. Regarding bone disease, 11% patients had previous bone fracture mainly in the spine, 15% had familial history of hip fracture and 20% reported a fall within the past year. Forty-two percent of patients had vitamin D supplementation but only one was previously treated with an anti-osteoporotic agent. Finally, 114 patients had a DXA. A lumbar BMD T-score ≤-2.5 was found for 9 patients, ≤ -2 for 17 patients. A hip BMD T-score ≤ -2.5 was found for 12 patients and ≤ -2 for 35 patients. A T-score ≤ -2.5 to at least one site was found in 18 patients (16%) and ≤ -2 for 41 patients (35%). After BMD assessment, an anti-osteoporotic treatment was prescribed in 40% of patients with bisphosphonate (71%) or denosumab (29%).
Conclusion: This clinical care pathway allowed 97% of patients to have a bone assessment when starting ADT for PCa. This cohort of 116 patients confirms the high prevalence of low BMD among these patients and the need to screen and treat patients to prevent bone-related complications.
Acknowledgements: I thanks Mioranirainy DERAHARIJAONA and Catherine LE BOURLOUT for their help in collecting clinical data.
Disclosure of Interests: None Declared.
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POS0503 RISK OF CARDIOEMBOLIC ISCHAEMIC STROKE AMONG NEW USERS OF ORAL BISPHOSPHONATES: A NESTED CASE-CONTROL STUDY

Keywords: Cardiovascular disease, Osteoporosis, Epidemiology

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Background: Bisphosphonates have been associated with atrial fibrillation, but studies carried out thus far have not shown that they are also associated with an increased risk of ischaemic stroke (IS). None, however, separated by IS subtype (cardioembolic vs non-cardioembolic).
Objectives: The present study aimed to test the hypothesis that use of oral bisphosphonates (oBs) increases specifically the risk of cardioembolic IS.
Methods: A nested case-control study was performed using the Spanish primary healthcare database BIFAP (period: 2002-2015). Incident cases of IS were identified and classified as cardioembolic or non-cardioembolic. Five controls per case were randomly selected, matched for exact age, sex, and index date (first recording of IS). The association of IS (overall and by subtype) with the use of oBs within the last year before index date was assessed by computing the adjusted odds ratios (AOR) and their corresponding 95%CI using conditional logistic regression. Only oBs initiators were considered. (Figure 1).
Results: A total of 4,568 cardioembolic IS cases (matched with 21,697 controls) and 9,213 non-cardioembolic IS cases (matched with 44,212 controls) were included. For cardioembolic IS, the use of oBs was associated with an AOR of 1.35(1.10-1.66), in a duration dependent manner (AOR≤1year=1.10;0.82-1.49; AOR>1-3years=1.41;1.01-1.97; AOR>3years=1.81;1.25-2.62; p for trend=0.001). Such increased risk only appeared when patients used concomitantly calcium supplements and was completely blunted by anticoagulants. No increased risk was observed for non-cardioembolic IS (AOR=1.03;0.88-1.21).
Conclusion: The long-term use of oBs with calcium supplements increases the risk of cardioembolic IS, while leaves materially unaffected the risk of non-cardioembolic IS.

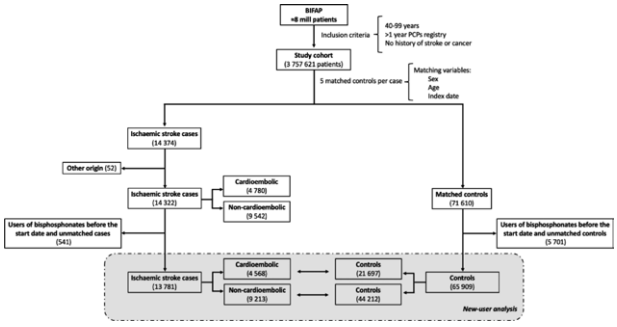


Figure 1.

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Disclosure of Interests: None Declared.
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POS0504 COMPARISON BETWEEN « SYSTEMATIC » VERSUS « RECOMMENDATION-BASED » VERTEBRAL FRACTURE ASSESSMENT REALIZATION DURING DUAL ENERGY X-RAY ABSORPTIOMETRY EXAMINATION

Keywords: Osteoporosis, Bone diseases

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Background: Realization of a thoraco-lumbar lateral view X-ray (Vertebral Fracture Assessment, VFA) when performing Dual Energy X-ray Absorptiometry (DEXA) is proposed in international guidelines to detect asymptomatic vertebral fractures. However, there is no clear consensus regarding indications of its realization.
Objectives: First, we compared the efficiency of a systematic VFA realization during DEXA versus its realization according to different criteria available in literature. Second, we looked after risk factors associated with vertebral fractures.
Methods: 401 successive patients underwent DEXA with a thoraco-lumbar lateral view X-ray (VFA). Medical files were retrospectively reviewed to determine if the patient should have benefited from a VFA according to the ISCD (International Society for Clinical Densitometry) 2007 criteria, ISCD 2015, NOF (National Osteoporosis fundation) 2014, SFR (French Society of Rheumatology), NHG (Nederlands Huisartsen Genootschap) 2nd revision or NHG 3rd revision.
Results: Among 401 successive patients who underwent systematic VFA, a vertebral fracture was observed in 71 patients (17.7%). 74, 54, 62, 73, 12 and 53% of patients should have undergone a VFA according to the ISCD 2007, ISCD 2015, NOF 2014, SFR, NHG criteria 2nd revision and NHG 3rd revision respectively. With the exception of the NGH 2nd revision criteria which only identified 28.2% of fractures, there was no significant difference in fracture detection between "systematic VFA" and "VFA realized following the recommendations" groups. Criteria sensitivity varied between 81.7 and 91.6% of detection, with the best detection performance for SFR criteria. The ISCD 2015 criteria presented the best sensitivity/ specificity ratio of detection. The NHG2 criteria were the most specific (40.8% of VFA positive for fracture) but they lack of sensitivity, compared to systematic use, missed the detection of 51 fractures (12.7%). The detection of a vertebral fracture was significantly more frequent in patients with low bone mineral density at lumbar spine, femoral neck, but also wrist. Age, menopause, height loss, hip fracture in a parent, back pain, COPD, active smoking and inhibitor of proton pump (PPI) use were also associated with higher fracture detection.
Conclusion: VFA realization based on literature criteria has a detection sensitivity between 82 and 92% (with the exception of the NHG 2nd revision criteria), with the SFR criteria having the best detection capacity and the ISCD 2015 criteria the best sensitivity/ specificity ratio. Use of the VFA realization criteria may help to better determine the selection of patients requiring a VFA: VFA realization based on these criteria did not detect significantly less fracture that the systematic VFA realization. Low bone density, loss of height and history of hip fracture in parents were associated with vertebral fracture. Among medical history, attention should be paid to COPD, smoking and PPI use, also associated with the demonstration of a vertebral fracture.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1729

POS0505 FREQUENCY OF DYSMOBILITY SYNDROME IN PATIENTS WITH RMD AND ITS RELATIONSHIP WITH FRACTURES AND FRAILTY

Keywords: Sarcopenia, Comorbidities, Osteoporosis

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Background: Dysmobility Syndrome (DS) is a novel concept to characterize musculoskeletal (MSK) health. DS includes parameters for osteoporosis, sarcopenia and falls [1]. It has been associated with fractures and mortality in community dwelling older adults [2-4] but has never been applied to patients with rheumatic and musculoskeletal diseases (RMD).
Objectives: To study the prevalence of DS and the association of DS with frailty and major osteoporotic fractures (MOF) in patients with inflammatory and non-inflammatory RMD.
Methods: Patients with inflammatory and non-inflammatory RMD aged 65 and older were recruited at a tertiary rheumatology hospital. DS was defined using published cut-offs [1, 2] of the following parameters: Osteoporosis (DXA T-score ≤ -2.5), obesity (DXA % body fat > 30% in men; > 40% in women), low appendicular lean mass (ALM/height^2 <7.26 kg/m^2 in men; < 5.45 kg/m^2 in women), low grip strength (< 30kg in men; < 20kg in women), slow gait speed (< 1.0 m/s) and falls (history of one or more falls within last year). A score of ≥ 3 was defined as having DS. The FRAIL-scale[5] was used to quantify frailty. Historical data on MOF as defined by FRAX (https://frax.shef.ac.uk/frax/) was collected.
Results: 141 patients (103 women/38 men) were included in the analysis. Mean age was 73 years. Of the total population, 80% had an inflammatory RMD (of those 45% had Rheumatoid Arthritis) as their primary diagnosis. Patients with non-inflammatory diseases had either degenerative spine and/or joint disease and/or fibromyalgia. Mean disease duration was 5 years. Mean DS score was 2.8 (for more demographic data see Table 1). 81/141 (57.5%) participants met DS criteria. DS was more common in women compared to men (63.1 vs. 42.1%, p= 0.0252) and in inflammatory RMD compared to non-inflammatory (61,1 vs. 42.9%, p=0.0811). Patients with DS reported fractures twice as often as those without DS (33,3 vs. 16.6%, p=0.0261). The frequency of individuals with a history of MOF increased with DS score (see Figure 1). Additionally, there was a significant association between DS and FRAIL scores in a univariate linear regression analysis (R^2=0,22, p<0.001).
Conclusion: This primary study to explore the prevalence of DS in patients with RMD showed that more than half of participants met DS criteria. Similar to studies of community dwelling older adults, fractures were more common in patients with DS. Importantly, a positive association of frailty and DS was seen. Further studies are needed to examine whether DS can be used clinically to better characterize overall MSK health in patients with RMD and whether a standardized management of DS will improve outcomes in these patients.
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Table 1. Study demographics

Variable	Total n = 141	Females n = 103	Males n = 38	p-value
% Inflammatory RMD	80.1	77.7	86.8	0.226
Age [years] (SD)	72.9 (5.2)	73.0 (5.1)	72.7 (5.6)	0.737
Height [cm] (SD)	165.3 (9.0)	161.5 (6.2)	175.6 (6.9)	**< 0.001**
Weight [kg] (SD)	77.9 (15.1)	76.1 (15.5)	82.8 (12.9)	**0.019**
ALM/height^2 [kg/m^2] (SD)	6.99 (1.17)	6.79 (1.07)	7.51 (1.28)	**0.001**
Body fat [%] (SD)	41.5 (7.91)	44.7 (6.40)	33.0 (4.72)	**< 0.001**
Lowest BMD T-score (SD)	-1.6 (1.16)	-1.7 (1.21)	-1.4 (1.01)	0.227
Grip strength [kg] (SD)	19.0 (10.2)	14.8 (6.79)	30.3 (9.38)	**< 0.001**
Gait speed [m/s] (SD)	0.95 (0.31)	0.89 (0.27)	1.11 0.36	**< 0.001**
Dysmobility Score (SD)	2.8 (1.30)	2.9 (1.30)	2.5 (1.25)	0.054
Simple Frail Score (SD)	2.6 (1.35)	2.7 (1.28)	2.3 (1.49)	0.085

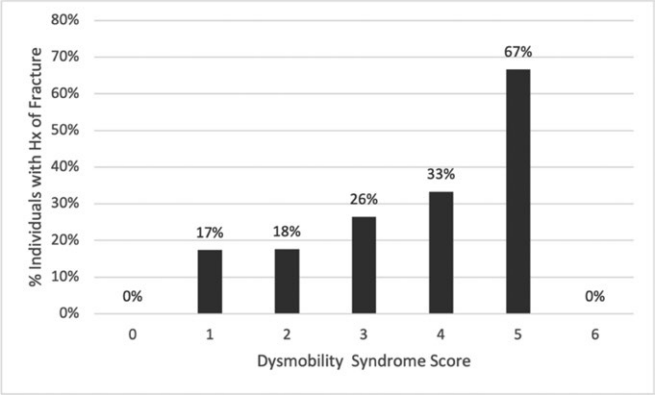


Figure 1. Frequency of individuals with history of MOF by Dysmobility Syndrome (DS) Score. The frequency of individuals with a history of MOF increased with the DS Score (p=0.0509). Note: Only 3 individuals had a DS score of 0 and only 2 had a DS score of 6.

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Disclosure of Interests: Bjoern Buehring Speakers bureau: Alexion, Biogen, Boehringer-Ingelheim, Gilead/ Galapagos, MSD, Sanofi Genzyme, UCB, Consultant of: Amgen, Gilead/ Galapagos, Theramex, UCB, Roshnak Parvaee: None declared, Celina Mueller: None declared, Ioana Andreica: None declared, David Kiefer: None declared, Uta Kiltz: None declared, Styliani Tsiami: None declared, Maryam Pourhassan: None declared, Timm Westhoff: None declared, Rainer Wirth: None declared, Xenofon Baraliakos: None declared, Nina Babel: None declared, Juergen Braun: None declared.

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POS0506 RISK FACTOR ANALYSIS OF FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Bone diseases, Osteoporosis

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Background: Patients with rheumatoid arthritis (RA) commonly develop osteoporosis and fragility fractures due to differentiation and induction of osteoclast, steroid use, and inactivities of daily life [1-3]. The prevalence of osteoporosis during long-term RA has been reported to be as high as 19-32%, and RA patients have 1.5-2.3 times the risk of fracture as non-RA patients. However, the relationship between bone mineral density and fracture risk in RA patients is not clear, and there are few reports on bone mineral density and fracture location in RA patients.

Objectives: To investigate the incidence of fracture and fracture site in RA patients, and to explore the risk factors for fragility fractures in RA patients.

Methods:

1. A total of 4785 RA patients were included. We extracted new incidence of fracture from medical record and investigated the location of fractures.
2. A total of 4270 patients including non-RA patients who had dual-energy X-ray absorptiometry (DEXA) were analyzed. The RA group was divided into two groups: RAfx+ group with fracture and RAfx- group without fracture. Young Adult Mean (YAM) values were compared between groups based on DEXA data from 3634 patients in the non-RA group, 147 patients in the RAfx+ group, and 489 patients in the RAfx- group.
3. The demographics, and clinical characteristics of 636 RA patients who had DEXA were investigated. Bone mineral density (YAM value), osteoporosis treatment intervention, steroid use, biologic drug use, the levels of anti-CCP (cyclic citrullinated peptide) antibody, and BMI (body mass index) were analyzed between two groups.

Results:

1. Of the 4785 RA patients, a total of 550 fractures occurred in 384 patients (8.0%). The mean age was 70.5 and 63 years old in the fracture and non-fracture groups, respectively, and was significantly higher in the fracture group (p<0.01). The most common fracture sites were vertebral (205 fractures), following 57 proximal femur fractures, 55 thoracic fractures, and 41 pelvic fractures.
2. The %YAM of femur was 73.9% in the non-RA group, 67.7% in the RAfx+ group, and 76.0% in the RAfx- group, and %YAM of lumber spine was 85.5% in the non-RA group, 81.0% in the RAfx+ group, and 88.1% in the RAfx- group, with the RAfx+ group having significantly lower values (p < 0.01). After age and sex matching, 147 patients were allocated to each group, respectively. Young adult mean (YAM) values of femur were 67.7/73.7% and those of lumbar spine were 81.0/86.0% in group A/B, both of which were significant (p<0.01, 0.01, respectively).
3. In univariate analysis, a history of osteoporosis intervention, especially denosumab use, and a history of steroid use were associated with fracture incidence (p = 0.02, 0.002, 0.03, respectively) significantly. In multivariate analysis, YAM value of femur (OR: 0.386), a history of steroid use (OR: 2.04), and osteoporosis intervention (OR: 0.413) were significantly associated with the incidence of fractures.

Conclusion: New fractures occurred in 8.0% of RA patients, with vertebral fractures being the most common. RA patients with fractures had significantly lower femoral/lumbar YAM values than RA patients without fractures. steroid use, low femoral bone density, and lack of osteoporosis intervention were factors significantly associated with fracture occurrence in RA patients.

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Disclosure of Interests: None Declared.

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POS0507 OSTEOPOROSIS IN SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY IN A MONOCENTRIC CENTER. ANY ROLE FOR CALCINOSIS?

Keywords: Bone diseases, Systemic sclerosis, Osteoporosis

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Background: Systemic sclerosis (SSc) is a rare and progressive autoimmune disease, that has been associated with an increased risk of osteoporosis (OP), but risk factors are still debated [1,2].

Objectives: The aim of our study was to investigate the risk factors for osteoporosis in SSc and to evaluate if any feature of the disease could increase the risk of osteoporosis.

Methods: In this cross-sectional study we included 60 consecutive patients, fulfilling the 2013 ACR/EULAR classification criteria of SSc[3], attending our Rheumatology Unit from July to December 2022. All the 60 patients performed a Dual-energy X-ray absorptiometry (DXA) between 2020 and 2022. Osteoporosis was defined as a T score less than -2.5 SD and osteopenia as a T-score between -1.0 and -2.5 SD, according to WHO definitions. We divided patients in two groups according to the diagnosis of osteoporosis (OP+) and non osteoporosis including osteopenia (OP-). We collected the main clinical-demographic and laboratory features of the patients and we assess the presence of any association with OP.

Results: All 60 patients were women with an average age (mean±SD) of 70.5±10.1 years, 35 had a diagnosis of osteoporosis (OP+ group) and 25 patients were included in OP- group, in which 17 patients had osteopenia. The two groups were comparable for age, disease duration, menopause and smoking habit. We found statistically significant differences between the two groups with BMI (21.97±3.47 in OP+ vs 24.04±3.63 in OP-, p=0.04), modified Rodnan Skin Score (mRSS) (8.91±12.19 vs 3.20±4.71, p=0.03) and presence of calcinosis (12 in OP+ vs 1 in OP-, p=0.005), pitting scars (17 vs 5, p=0.03) and telangiectasia (28 vs 13, p=0.02). Performing simple logistic regression analyses we confirmed the association of calcinosis (OR 12.52, CI 2.2-237.3, p=0.02), pitting scars (OR 2.02, CI 1.08-11.97, p=0.04) and telangiectasia (OR 2.24, CI 1.21-12.09, p=0.02) with the presence of OP. There was no difference between the two groups for NVC scleroderma pattern, autoantibodies and presence of digital ulcers. (Table 1).

Conclusion: This retrospective study confirms the association of OP with lower BMI in SSc. An increased mRSS and the presence of calcinosis, telangiectasias and pitting scars were also associated to OP in our patients. These SSc features deserve to pinpoint an early evaluation of bone health in our patients and an early referral to DXA, independently from the traditional risk factors of OP. Of interest, in our opinion, is the rather high prevalence of calcinosis in the OP+ group, confirming data from other authors[4] and suggesting a possible common pathogenically pathway in calcinosis development.

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Table 1.

	OP + (N=35)	OP – (N=25)	p
Sex (f/m)	35/0	25/0	ns
Age (years) (mean±SD)	70.03±11.56	70.52±8.18	ns
BMI (mean±SD)	21.97±3.47	24.04±3.63	**0.04**
Current smoking (N, %)	3 (8)	2 (8)	ns
Menopause (N, %)	33 (94)	24 (96)	ns
Disease duration (years) (mean ± SD)	13.97±9.15	11.68±7.19	ns
mRSS (mean ± SD)	8.91±12.19	3.20±4.71	**0.03**
DU (N, %)	13 (37)	6 (24)	ns
Pitting scars (N, %)	17 (49)	5 (20)	**0.03**
Calcinosis (N, %)	12 (34)	1 (4)	**0.005**
Telangiectasia (N, %)	28 (80)	13 (26)	**0.02**
NVC Scleroderma pattern (N, %)	32 (91)	20 (80)	ns
ACA (N, %)	16 (46)	13 (52)	ns
ATA (N, %)	9 (26)	7 (28)	ns
PPI therapy (N, %)	29 (83)	21 (84)	ns
Lumbar spine (T Score) (mean±SD)	-2.33±0.81	-0.69±1.18	**<0.0001**
Total hip (T Score) (mean±SD)	-2.49±0.75	-0.93±1.00	**<0.0001**
OP under treatment (N, %)	31 (88)	0 (0)	**<0.0001**
Pathological bone fractures (N, %)	11 (31)	0 (0)	**0.001**

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Crystal diseases, metabolic bone diseases other than osteoporosis

POS0508

A RANDOMISED CONTROLLED TRIAL COMPARING ANAKINRA VERSUS STEROIDS FOR THE TREATMENT OF GOUT ATTACKS IN PEOPLE WITH RENAL DISEASE (ASGARD): A FEASIBILITY STUDY

Keywords: Gout, Randomized control trial, Kidneys

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Background: Title: A study to determine the feasibility of undertaking a definitive randomised multi-centre, double-blind, double-dummy controlled study of Anakinra vs. intramuscular methylprednisolone acetate for acute gout attacks in patients with chronic kidney disease. Gout is common in people with chronic kidney disease (CKD) where effective treatments like non-steroidal anti-inflammatory drugs are contra-indicated. Anakinra, an IL-1 receptor antagonist, could be an important treatment option for treating gout flares in people with CKD (eGFR<60mls/min/1.73m2).
Objectives: Aim: to assess the feasibility of the design and procedures for a future definitive randomised trial of anakinra in people with moderate to severe CKD. Specific objectives were to: test recruitment and retention; test eligibility criteria; collect outcome data to inform sample and power calculations for a future trial; collect economic data to inform a future economic evaluation; and assess capacity for to scale up to a larger trial.
Methods: Design: two-parallel group, double-blind, double-dummy, multicentre randomised feasibility trial comparing subcutaneous anakinra 100mg for 5 days with a single injection of intramuscular methylprednisolone acetate 120 mg for treating gout flares in people with CKD (eGFR <60mls/min/1.73m2). Participants were planned to be recruited from five sites in the South East region of the UK over 15 months, the target sample size was 32. Proposed primary outcome was self-assessed pain intensity using Visual Analogue Scale (VAS) (0–100mm) and 5-point Likert scale. Proposed secondary outcome measures consisted of physician assessment of joint; assessment of activity limitation and quality of life using Health Assessment Questionnaire Disability Index, 36-Item Short Form Survey, Five-level EuroQol Five-Dimensional Questionnaire and Lower Extremity Functional Scale.
Results: 21 patients were randomised (anakinra 10, depo-Medrone 11), 3 were lost to follow-up. Mean age was 72 years and mean eGFR was 43.6 mls/min/1.73m2. The first metatarsophalangeal joint was the commonest joint affected (10/21). 2 participants were taking urate-lowering therapy although 16 reported previous flares. Mean overall change in pain from baseline was 35.88 by VAS and 1.69 by Likert scale. Functional assessment and quality of life assessment was highly completed. The baseline assessment was low for the SF-36 and HAQ-DI, the LEFS showed a trend of improvement and the HAD-QI showed a decline from day 7 to week 8. Health resource use was higher when assessed by health records compared to self-reporting. Qualitative feedback from participants alluded to high questionnaire burden and delays in receiving treatment. There were no serious adverse events or reactions. One patient needed rescue medication 10 days later for recrudescence of flare in the anakinra arm. We met three out of its four success criteria: recruiting at least 70% of eligible patients; 85% of participants completing 5 out of 7 pain outcome measure; and ≤10% treatment cross-over or failure.
Conclusion: Our study did not meet its entire feasibility target due to poor recruitment. This was compounded by various factors which may be possible to overcome. Aspects to rationalise the study would be utilising VAS and patient reported Likert, without physician assessment of joints. Functional assessment and quality of life assessment could be reconciled to using EQ-5D-5L and SF-36 at day 1, day 7 and week 8 minimising the questionnaire burden. We did not find good functional assessment with the LEFS and HAQ-DI, the gout flare score may be a possible alternative, bearing in mind the impact of questionnaire burden. A future definitive trial may be feasible if we are able to overcome challenges in recruitment, better ways of case finding, and initiating randomised treatment during gout flare. Our study is the first gout study looking specifically at people with advanced CKD and showed good safety and efficacy with these agents for this group of patients.

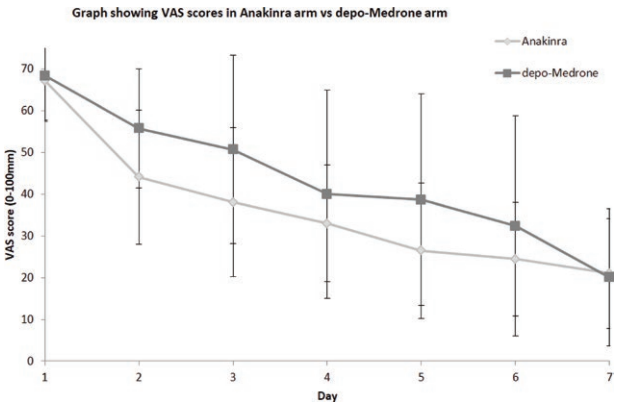


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0509

PROJECTING THE FUTURE HEALTH AND ECONOMIC BURDEN OF CONTROLLED AND UNCONTROLLED GOUT IN THE CHRONIC KIDNEY DISEASE POPULATION IN THE US: PRELIMINARY RESULTS USING MICROSIMULATION MODELLING METHODS

Keywords: Kidneys, Gout, Epidemiology

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Background: Chronic kidney disease (CKD) and gout are major public health concerns. The prevalence of gout (4%) and hyperuricemia (20%) is high in the general population and progressively increases as kidney function decreases [1,2]. An increasing number of people in the US are living with both gout and

CKD, posing a significant health and quality of life (QoL) burden to patients while putting economic pressure on the healthcare system. Moreover, current gout management in the US is sub-optimal, with a large number of gout patients remaining untreated, undertreated, or uncontrolled [3].

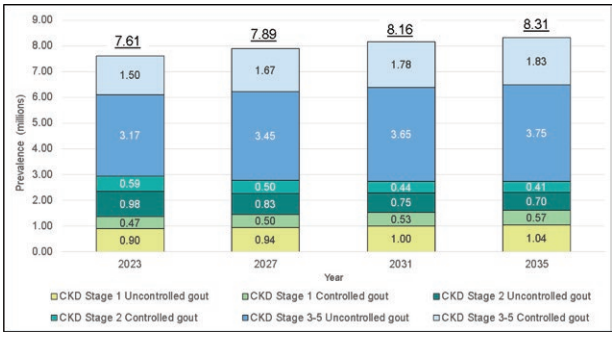
Objectives: To quantify the2023-2035 health and economic burden of controlled and uncontrolled gout in the US CKD population.

Methods: A validated microsimulation model was used to project gout burden in the US CKD population, which was reproduced virtually using United Nations data [4]. Each individual was assigned estimated glomerular filtration rate (eGFR), albuminuria, and serum urate (SU) values, which were extracted through analysis of the US NHANES (2011 to 2018). The prevalence of self-reported gout by age, sex, and CKD stage was also examined. Controlled and uncontrolled gout costs, eGFR decline rates, tophi and flare probabilities were drawn from the literature. Uncontrolled gout was defined as SU >6 mg/dL and ≥2 flares/yr or the presence of tophi. The microsimulation was run between2023 and 2035.

Results: The simulation predicts a 9.2% growth in the prevalence of gout and CKD in the US between2023 and 2035, from 7.6 million to 8.3 million patients, respectively. By 2035, 10.2% of CKD patients (5.5 million) are projected to have uncontrolled gout (**Graph 1**), an annual average increase of 37,000 patients each year to 2035. This compares with 5.2% of CKD patients (2.8 million) with controlled gout by 2035. The number of people living with gout and advanced CKD (stages 3-5) is projected to grow by 19.4%, from 4.7 million patients in2023 to 5.8 million patients by 2035, of which the majority (67.2%) will have uncontrolled gout. Factors driving this increase are predominantly population growth and ageing. Tophi and flare occurrence are similarly projected to increase. The resulting combined direct and indirect costs of gout in CKD patients are projected to increase from $43.5 billion in2023 to $47.5 billion by 2035. This equates to a cumulative cost of $594.4 billion over the next 12 years, of which 76% is due to uncontrolled gout **(Table 1)**. If all gout in CKD was controlled, the US could save $169.9 billion between2023 and 2035.

Table 1. Annual costs of controlled and uncontrolled gout in CKD (2023 US$, Billions)

Year	Cost of controlled gout	Cost of uncontrolled gout
2023	10.5	33.1
2029	11.1	34.8
2035	11.5	36.0
Cumulative (2023 – 2035)	143.7	450.7



Graph 1. Gout prevalence, by CKD stage (1, 2, and 3-5), in the US, between2023 and 2035

Conclusion: In US CKD patients, gout prevalence and symptoms (tophi, flares) are projected to rise markedly between2023 and 2035, posing a substantial and increasing health, economic, and QoL burden. Uncontrolled gout is projected to contribute most to the health and economic burden of gout in CKD. Urate-lowering interventions may help reduce this burden by lowering the proportion of uncontrolled gout. Such measures would therefore reduce costs and healthcare utilisation while leading to QoL improvements in CKD patients with gout.

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Disclosure of Interests: Joshua Card-Gowers Employee of: HealthLumen, Laura Webber Employee of: HealthLumen, Lise Retat Employee of: HealthLumen, Marek Piotrowski Employee of: HealthLumen, Brian LaMoreaux Shareholder of: Horizon, Employee of: Horizon, Brad Marder Shareholder of: Horizon, Employee of: Horizon, Ada Kumar Shareholder of: Horizon, Employee of: Horizon.

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POS0510 INTERMITTENT FASTING REDUCES CRYSTAL-INDUCED INFLAMMATION

Keywords: Gout, Crystal arthritis, Diet and nutrition

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Background: Inflammation induced by monosodium urate (MSU) and calcium pyrophosphate (CPP) crystals depends on interleukin (IL)-1β activated by the NLRP3 inflammasome. The inflammatory response can be modulated by diet, fasting, and caloric restriction.

Objectives: To determine whether intermittent fasting reduces MSU and CPP crystal-induced inflammation.

Methods: Crystal-induced inflammation was assessed using both types of crystals *in vivo* in the air pouch model in 8-week-old wild-type male mice fed either with a normal ad libitum diet or intermittent fasting (IF) (every over day fast, 2 days during 1 week). Inflammatory cytokine production (IL1β and CXCL-1) was assessed in the pouch lavages and the cellular infiltrate analyzed by histology (H&E staining). Metabolomic analyses were performed by high-performance liquid chromatography coupled to high-resolution mass spectrometry (LC-HRMS) on air pouch membrane, serum, and liver samples. Changes in metabolites associated with diet interventions were studied by the Metaboanalyst platform and we established the metabolic profiles for each experimental condition. In vitro, human monocytes THP-1 were stimulated by sterile synthetic crystals of MSU and CPP while the production of inflammatory cytokines was quantified by ELISA. To assess the role of glutamine/glutamate metabolism pathway related to IF in microcrystalline disease, the concentrations of glutamine/glutamate in synovial fluids (SF) from patients with gout, CPP-related disease and osteoarthritis (OA) were quantified by ultra-performance liquid chromatography coupled to tandem mass spectrometry (UPLC-MS/MS).

Results: Inflammation induced by MSU and CPP crystals was drastically decreased by IF compared with normal diet: IL-1β (MSU 0.0 vs. 30.0 pg/ml; CPP 0.0 vs. 47.5 pg/ml p<0.0001); CXCL-1 (MSU 67.5 vs. 186.8 pg/ml, CPP 156.1 vs. 549.5 pg/ml, p<0.005); as were cell infiltration assessed by number of cells in the air pouch lavages (MSU 0.2 x 10^6 vs. 1.1 x 10^6; CPP 0.4 x 10^6 vs 2.9 x 10^6; p<0.0001) and membrane histology semi-quantitative score (MSU 0.6 vs 3.0; CPP 0.8 vs 2.7; p<0.0001). Reduction of inflammation by IF was associated with significant changes in membrane, serum and liver metabolites. IF increased ketone bodies (hydroxybutyric acid) as well as cholic acid, acetyl glycine, hydroxy caproic acid. In contrast, IF decreased carbohydrate metabolites, as well as glutamate and succinic semi-aldehyde. Many metabolic pathways were altered by IF such as galactose, starch, sucrose, aspartate, glutamate, alanine and arginine metabolism. Interestingly, the glutamine and glutamate metabolic pathway was enriched in serum, membrane and liver compartments. Glutamine/glutamate involvement in microcrystal-induced inflammation was evidenced in SFs. SF concentration of glutamine was decreased during gout and CPP flares compared to OA effusion (gout 352.3 µM and CPP 357.5 µM vs OA 509.3 µM, p<0.0001 and p<0.0001 respectively) while the concentration of glutamate increased in gout (gout 212.5 µM vs 58.0 µM, p<0.0001; CPP 66.1 vs 58.0 µM, p=0.4). The glutamine/glutamate ratio was decreased in synovial fluids of crystal-related diseases compared to OA (gout 1.4 and CPP 6.1 vs OA 9.4, p<0.0001 and p<0.05 respectively). *In vitro*, crystal-induced inflammatory cytokine production was decreased by overnight serum deprivation (IL-1β: MSU 1446 vs 5464 pg/ml; CPP 3670 vs 7797 pg/ml, p<0.005; TNF-α: MSU 7.0 vs 47.0 pg/ml; CPP 15.6 vs 89.3 pg/ml, p<0.05; IL-8: MSU 2896 vs 9781 pg/ml; CPP 3984 vs 6820 pg/ml, p<0.01). The inhibition of crystal-induced IL-1β production by serum deprivation was abrogated when cells were treated with 3-MA, an autophagy inhibitor (MSU 1446 vs 4912 pg/ml; CPP 3670 vs 9367 pg/ml, p<0.005).

Conclusion: Intermittent fasting alleviates crystal-induced inflammation by altering many metabolic pathways, particularly those associated with glutamine and glutamate. Further studies are needed to determine how IF modulates metabolism to dampen crystal-induced inflammation.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0511 LIFESTYLE MODIFICATION FOR THE PREVENTION OF CARDIOVASCULAR DISEASE IN PATIENTS WITH GOUT

Keywords: Lifestyles, Gout, Cardiovascular disease

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Background: High morbidity and mortality of cardiovascular (CV) disease in patients with gout draw attention to CV risk management in daily clinical practice.
Objectives: To evaluate the effect of a favorable lifestyle on the incident CV events in patients with gout.
Methods: We identified 9,110 patients with gout from UK Biobank Cohort based on the combination of self-report and/or hospital diagnostic codes. Lifestyle behaviors defined by smoking status, physical activity, obesity and diet were categorized into favorable (≥ 3 healthy factors), intermediate (2 healthy factors), and unfavorable patterns (0-1 healthy factor). CV risk was estimated in participants with and without gout according to serum uric acid (SUA) levels and lifestyle patterns.
Results: Incidence rate of CVD was significantly higher in patients with gout than in participants without gout (11.38 vs 5.49 per 1000 person-year). A positive correlation was observed between SUA level and CV risk in the general population, whereas CV risk was consistently high in gout population, regardless of SUA level. A favorable lifestyle was associated with lower CV risk in both patients with gout and participants without gout. In all categories of SUA levels (< 6mg/dL, normal; 6-8.9 mg/dL, high; ≥ 9mg/dL, very high), CV risk was significantly lower in gout patients with a favorable lifestyle than in those with a unfavorable lifestyle.
Conclusion: Patients with gout are at high risk of CVD even with SUA levels in the normal range. Lifestyle modification can be an effective and inexpensive therapeutic strategy to prevent CV events in patients with gout.

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Disclosure of Interests: None Declared.
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POS0512 DIAGNOSTIC AND DIFFERENTIAL BIOMARKERS IDENTIFIED BY METABOLOMIC ANALYSIS IN PATIENTS WITH PSEUDOGOUT

Keywords: Biomarkers, Crystal arthritis, -Omics

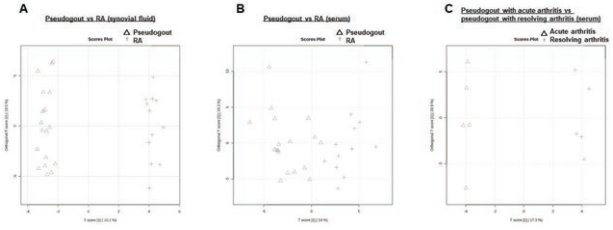
S. Takahashi[1,2], M. Takahashi[2], Y. Tanimoto[1], T. Yamaoka[1], M. Katayama[1], S. Hatachi[1], M. Shinohara[3,4], S. Kumagai[1,2]. *[1]Shinko Hospital, The Center for Reumatic Disease, Kobe, Japan; [2]Shinko Hospital, The Shinko Institute for Medical Research, Kobe, Japan; [3]Kobe University Graduate School of Medicine, The Integrated Center for Mass Spectrometry, Kobe, Japan; [4]Kobe University Graduate School of Medicine, Division of Molecular Epidemiology, Kobe, Japan*

Background: Pseudogout is an acute arthritis induced by calcium pyrophosphate dehydrate crystal deposition (CPPD) [1]. Pseudogout most commonly involves one or several large joints, such as the knee or wrist, typically tender and swollen [2]. The pathogenic mechanism of CPPD is partially understood, and the etiology of attacks is unclear. There is no diagnostic serum biomarker for pseudogout. CPPD disease is best diagnosed by identifying positively birefringent, typically rhomboid-shaped crystals in the synovial fluid of affected joints. However, CPPD disease and rheumatoid arthritis (RA) often coexist, and the similarity of pseudogout with acute flares of RA might lead to misdiagnosis.
Objectives: To identify the metabolites which characterize pseudogout compared with RA and to identify serum biomarkers of pseudogout using metabolomic analysis of serum and synovial fluid.
Methods: We collected serum and synovial fluid from 18 pseudogout patients and 12 RA patients with acute flares. We also collected serum from five pseudogout patients after resolving arthritis. We performed a metabolomic analysis of the samples using gas chromatography-mass spectrometry (GC-MS). Metabolites contributing to the differentiation between pseudogout with acute arthritis, pseudogout with resolving arthritis, and RA were determined by analysis of the orthogonal partial least-squares discriminant analysis (OPLS-DA) weightings (variable importance in the projection (VIP)>1, the absolute value of modeled correlation (|p(corr)|) > 0.5 in the S-plot) and Wilcoxon rank sum test ($p < 0.05$).
Results: A total of 123 metabolites from synovial fluid and 101 metabolites from serum were identified by GC-MS. By using OPLS-DA (Figure 1) and Wilcoxon rank sum test, nine metabolites from synovial fluid and 19 metabolites from serum were selected as the metabolites that contributed to the differentiation between pseudogout and RA, and nine metabolites from serum were selected as the metabolites that contributed to the differentiation between pseudogout with acute arthritis and pseudogout with resolving arthritis. Among the selected metabolites, we identified five metabolites which characterized pseudogout compared with RA and two metabolites which elevated in pseudogout with acute arthritis compared with both RA and pseudogout with resolving arthritis.
Conclusion: By metabolomic analysis, we identified metabolites that differentiate pseudogout from RA and the potential serum diagnostic biomarkers for pseudogout.

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Fig. 1



Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0513 QUALITY OF LIFE AND CLINICAL GOUT ASSESSMENT CHANGES IN UNCONTROLLED GOUT PATIENTS UNDERGOING PEGLOTICASE THERAPY AS PART OF THE MIRROR RANDOMIZED CONTROLLED TRIAL

Keywords: Quality of life, Gout, Randomized control trial

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Background: Refractory/uncontrolled gout can severely limit physical function and impact patient quality of life [1,2]. Unfortunately, limited treatment options exist for patients intolerant of or refractory to oral urate-lowering therapies. Pegloticase can lower serum urate (SU) in these patients [3] with demonstrated quality of life and physical function benefits [4]. The MIRROR RCT trial showed increased SU-response rates (71.0% vs. 38.5%) with lower infusion reaction risk (4.2% vs. 30.6%) when pegloticase was co-administered with methotrexate (MTX) vs. placebo (PBO), but patient-reported outcomes (PROs) from this study have not been reported [5].
Objectives: To report the prespecified PROs and gout-related clinical measures through Month 12 of pegloticase + MTX/PBO co-therapy in MIRROR RCT trial participants.
Methods: Patients with uncontrolled gout (sUA≥7 mg/dL, ULT failure/intolerance, and ≥1 of the following: ≥1 tophus, ≥2 flares in past year, chronic gouty arthritis) were administered pegloticase (biweekly 8 mg infusion) plus either oral MTX (15 mg/wk) or PBO. The study included 2-wk MTX tolerance, 4-wk blinded MTX/PBO Run-in, and 52-wk pegloticase+MTX/PBO Treatment periods. Key

exclusion criteria were being immunocompromised, G6PD deficiency, eGFR <40 ml/min/1.73m^2, or MTX contraindication. PROs included change from baseline (CFB) to Wk 52 in Health Assessment Questionnaire (HAQ) indices (secondary endpoints in ranked order: Disability [DI, score 0-3, MCID=0.22[4]], Pain [score 0-100, MCID=10[4]], Health [score 0-100, MCID=10[4]]). Physician Global Assessment of Gout (PhGA; score 0-10, MCID=1[4]), and tender [68 count]/swollen [66 count] joint counts [TJC/SJC], with decreases in measures reflecting improvement. Analyses were performed on the intent-to-treat population (ITT; all randomized patients). Least-square mean (±SE) CFB to Wk 52 was analyzed using a mixed-model for repeated measures, adjusting for baseline score, baseline tophi presence, treatment group, visit, visit by treatment group interaction, and visit by baseline interaction.

Results: 152 patients made up the ITT (100 randomized to MTX, 52 randomized to PBO). At baseline (before MTX exposure, Wk -6) HAQ scores indicated some disability, high pre-therapy pain, and somewhat poor overall health (mean [±SD] DI, Pain, Health: MTX: 0.7±0.7, 43.7±30.3, 44.9±28.6, respectively; PBO: 0.8±0.8, 40.5±28.6, 39.1±27.4, respectively). Baseline PhGA was similar between groups (MTX: 5.5±2.1, PBO: 5.4±2.2) but the MTX group had fewer affected joints (TJC: 6.7±8.4 vs. 11.0±15.9, SJC: 5.4±7.8 vs. 8.3±12.2). All HAQ measures progressively improved during treatment (**Figure 1**), but the treatment group difference in the Wk 52 CFB in HAQ-DI was not statistically significant, making further PRO analyses exploratory in nature. PhGA score improved (mean[±SE] Wk 52 CFB: -4.2±0.2 vs.-3.8±0.3), with a median observed score of 1.0 and 1.0 in the MTX and PBO groups, respectively, at Wk 52. TJC and SJC markedly declined during Treatment (mean[±SE] CFB TJC: -6.1±0.5 vs. -7.0±0.8, SJC: -5.1±0.4 vs. -6.0±0.6; MTX vs. PBO, both p >0.21), declining to a mean (±SD) TJC at Wk 52 of 1.4±4.6 and SJC of 1.4±4.5 in the MTX group and a TJC of 0.6±1.0 and SJC of 1.1±2.9 in the PBO group.

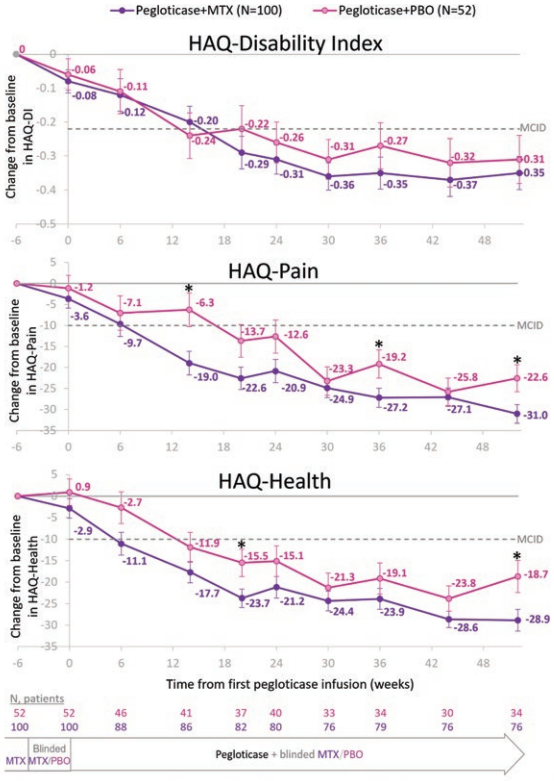


Figure. Change from baseline in HAQ-DI (**Top**), Pain (**Middle**), and Health (**Bottom**) during pegloticase+MTX and pegloticase+PBO co-therapy. Baseline was defined as prior to MTX exposure (Week -6), with Day 1 defined as first pegloticase infusion. Data points represent least-square mean change from baseline estimated analyzed using a mixed-model for repeated measures, adjusting for baseline score, baseline tophi presence, treatment group, visit, visit by treatment group interaction, and visit by baseline interaction. The dotted line represents MCID for each measure. Error bars represent standard error. *treatment group difference p<0.05. HAQ, Heath Assessment Questionnaire; CFB, change from baseline; DI, disability index; MCID, minimum clinically important difference; MTX, methotrexate; PBO, placebo.

Conclusion: Pegloticase treatment resulted in meaningful improvements in both clinical measures and quality of life in patients with uncontrolled gout. Patients co-treated with MTX experienced greater improvements in HAQ-Pain and Health scores after 52 wks of therapy, likely reflective of the higher urate-lowering response rate observed in the presence of MTX immunomodulation [5].

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POS0514

BONE EROSION REMODELING AFTER DEPLETION OF MONOSODIUM URATE DEPOSITION WITH INTENSIVE URATE-LOWERING WITH PEGLOTICASE IN PATIENTS WITH UNCONTROLLED GOUT: MIRROR RCT DUAL-ENERGY CT FINDINGS

Keywords: Imaging, Gout

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Background: Monosodium urate (MSU) crystal deposits can be visualized and quantified with dual-energy CT (DECT) [1], with DECT studies showing an association between MSU deposition and bone erosion [2]. Pegloticase rapidly lowers serum urate (SU) to near zero in uncontrolled gout patients (pts), with methotrexate (MTX) co-therapy recommended to increase SU lowering response rate (71% vs 39% with pegloticase+placebo [PBO]) and decrease infusion reaction risk (4% vs 31%; MIRROR RCT) [3]. MIRROR open-label trial (pegloticase+MTX co-therapy for ≤52 wks) DECT findings showed rapid, progressive MSU deposition volume (V_{MSU}) reduction with subsequent bone erosion remodeling in the 2 imaged pts [4]. The MIRROR RCT trial had a larger number of pts who underwent serial DECT imaging during pegloticase+MTX/PBO co-therapy, the findings of which are reported here.

Objectives: To examine V_{MSU} and bone erosion imaging findings of MIRROR RCT participants who underwent serial DECT imaging.

Methods: Pts were randomized 2:1 to receive oral MTX (15 mg/wk) or PBO as co-therapy to pegloticase (8 mg biweekly infusions). Serial images were obtained at DECT-capable sites using a standard acquisition protocol at prespecified time points during the 52-wk treatment period (Day 1 [first pegloticase infusion]; Wks 14, 24, 52). Bilateral hand/wrist, elbow, foot/ankle, and knee images were obtained. Images were post-processed using default settings and interpreted by an independent central reader blinded to treatment group and SU lowering response. V_{MSU} was measured in each scan. Up to 3 of the largest bone erosions per imaged region were assessed for evidence of remodeling, defined as a decrease in size, recortication, and/or new bone formation. Erosion size was evaluated as the product of the largest longitudinal and axial slice dimensions. Pts with baseline and Wk 52 images were included in analyses, excluding imaged regions with a baseline V_{MSU} <0.5 cm^3 to prevent large contributions of potential DECT artifacts [5]. DECT-imaged regions were also radiographed and photographed.

Results: 6 pts receiving pegloticase+MTX co-therapy and 2 pts receiving pegloticase+PBO co-therapy were included in analyses. In the MTX group, 5 pts had SU <6 mg/dL during Month 6 and received 52 wks of pegloticase+MTX co-therapy; 1 pt discontinued pegloticase+MTX at Wk 6 due to SU rise, continuing on allopurinol (mean SU on allopurinol = 4.6 mg/dL). In the PBO group, 1 pt had sustained SU-lowering through Month 6 and received 42 wks of pegloticase+PBO, continuing on febuxostat (mean SU on febuxostat = 5.2 mg/dL); 1 pt discontinued pegloticase+PBO at Wk 6 due to SU rise, continuing on allopurinol (mean SU on allopurinol = 3.0 mg/dL). V_{MSU} markedly decreased during therapy in both treatment groups (Wk 52, MTX: -94% ±9% [9 imaging regions of 6 pts], PBO: -96% ±3% [4 imaging regions of 2 pts]). Evidence of concomitant bone erosion remodeling (**Figure 1**) was observed in 69% (29/42) of evaluated erosions (9/12

[75%] imaged regions; 6/8 [75%] pts). Of the 29 erosions with remodeling, 100% had a decrease in size (mean: -7% change at Wk 52), with recortication (4 erosions [14%]) and new bone formation (3 erosions [10%]) also observed in some erosions.

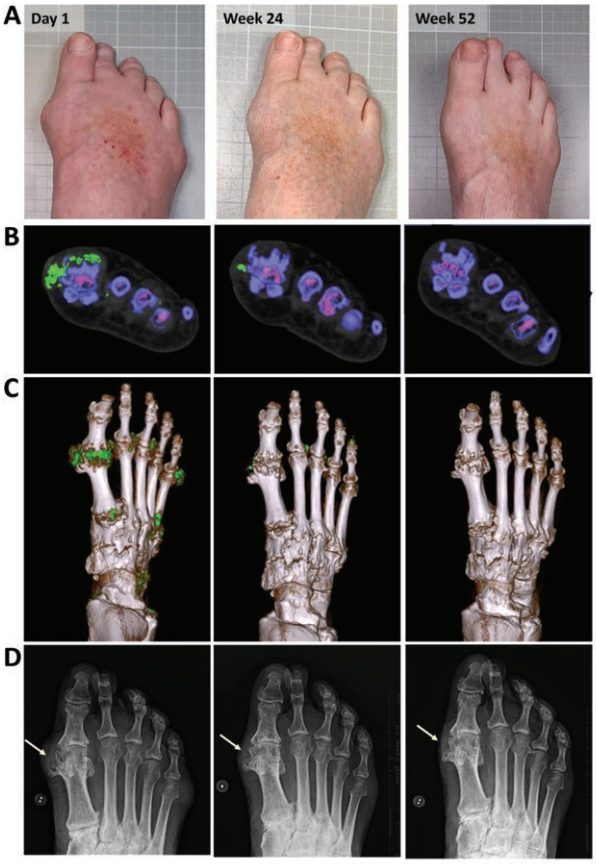


Figure. Serial photographs (**A**), DECT images (**B, C**), and radiographs (**D**) of the right foot of a patient who received 52-weeks of pegloticase (8mg biweekly infusion) and methotrexate (15 mg/week orally) co-therapy. The patient had sustained intensive urate-lowering during Month 6 and Month 12 (SU <1.0 mg/dL at Weeks 24, 52) and, by Week 52, bilateral feet monosodium urate crystal deposition volume had decreased to 0.3 cm^3 from a baseline of 23.5 cm^3 (**C**). Arrows indicate bone erosion remodeling at the first metatarsophalangeal joint.

Conclusion: In agreement with a prior serial DECT study [4], rapid and near complete V_{MSU} depletion was observed within 1 year of initiating pegloticase therapy. Concomitant bone erosion remodeling was also observed after 52 wks of intensive urate-lowering therapy. In these limited cases, DECT findings were similar between treatment groups. It is likely that SU-lowering, not MTX use, resulted in DECT changes, but further study is needed. However, these analyses suggest that bone remodeling is possible following MSU crystal depletion.

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Disclosure of Interests: Nicola Dalbeth Speakers bureau: Arthrosi, AstraZeneca, Dyve Biosciences, Hikma, Horizon, JPI, JW Pharmaceutical Corporation, LG Chem, PK Med, PTC Therapeutics, Protalix, Selecta, Unlocked Labs, Consultant of: Arthrosi, AstraZeneca, Dyve Biosciences, Hikma, Horizon, JPI, JW Pharmaceutical Corporation, LG Chem, PK Med, PTC Therapeutics, Protalix, Selecta, Unlocked Labs, John Botson Speakers bureau: AbbVie, Amgen, Aurinia, Chemocentryx, Horizon, Lilly, Novartis, Consultant of: AbbVie, Amgen, Aurinia, Chemocentryx, Horizon, Lilly, Novartis, Grant/research support from: Horizon, Allena, Radius Health, Kenneth Saag Grant/research support from: Alinea, Horizon, Lg, Sobi, Ada Kumar Shareholder of: Horizon, Employee of: Horizon, Lissa Padnick-Silver Shareholder of: Horizon, Employee of: Horizon, Brian LaMoreaux Shareholder of: Horizon, Employee of: Horizon, Fabio Becce Consultant of: Horizon, Grant/research support from: Siemens Healthineers (DECT research agreement).

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POS0515

THE POTENTIAL CAUSAL RELATIONSHIP BETWEEN PHYSICAL ACTIVITY, LEISURE SEDENTARY BEHAVIORS, AND GOUT

Keywords: Genetics/epigenetics, Gout

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Background: Gout is a type of inflammatory arthritis caused by the deposition of monosodium urate crystals onto diverse body joints [1]. Physical activity (PA) can reduce patients' pain caused by gout and Leisure sedentary behaviors (LSB) do harm to even normal people [2]. However, the genetic causality between PA/LSB and gout remains to be seen.

Objectives: In this study, we aimed to systematically evaluate the causal relationship between PA/LSB and gout.

Methods: We performed a two-sample Mendelian Randomization (MR) analysis to investigate the potential causality between PA/LSB and gout susceptibility. PA included five phenotypes: accelerometer-based PA, vigorous physical exercise (VPA), moderate to vigorous physical activity (MVPA), moderate physical activity 10+ minutes, and vigorous physical activity 10+ minutes. The summary data of PA were obtained from a genome-wide association study (GWAS) in UK Biobank [3]. LSB included four phenotypes: time spent watching television (TV), time spent using a computer, time spent driving, and time spent using a mobile phone. And the data of LSB was also derived from the GWAS of the UK Biobank. The gout GWAS (2,115 cases and 67,259 controls) was derived from the Global Urate Genetics Consortium. Single nucleotide polymorphisms (SNPs) that were independent ($r2 < 0.001$) and strongly related to PA/LSB ($p < 1 \times 10\text{-}7$, $F>10$) were selected as instrumental variables (IVs). Besides, we removed confounding IVs associated with alcohol, neutrophils, and BMI. The inverse variance-weighted (IVW), MR-Egger, and weighted median methods were employed to evaluate the causal effect between PA/LSB and gout. Among them, IVW is the principal method. Pleiotropic and heterogeneity assessment and sensitivity analyses were implemented with Cochran's Q test, MR-Egger intercept analysis, and the leave-one-out analysis.

Results: After removing confounders, the causality between genetically predicted accelerometer-assessed PA and risk of gout was indicated by IVW [OR=1.15, 95%CI: 1.02—1.31, p=0.0242]. No obvious causal relationship was observed between other PA/LSB and gout. (P>0.05) MR-Egger and weighted median were consistent with IVW results. No pleiotropy or heterogeneity of the IVs was found. Details of the results are shown in Figure 1.

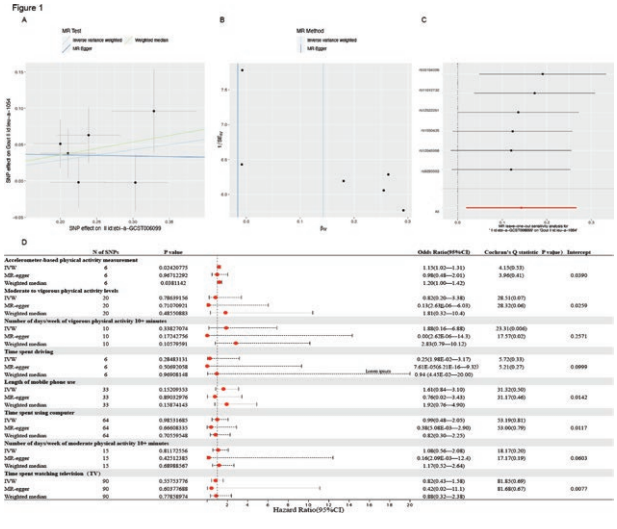


Figure 1. The causal associations between physical activity (PA), leisure sedentary behaviors (LSB), and gout were evaluated by the odds ratio (OR) values of IVW, MR-Egger, and Weighted median. Scatter plots (A), funnel plots (B), and leave-one-out analysis (C) from genetically predicted accelerometer assessed PA on gout.

Conclusion: Our findings supported a causal effect of accelerometer-measured PA on the increased risk of gout. No associations between other PA/LSB and gout were observed. Further research is needed to explore how physical activity affects gout.

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Disclosure of Interests: None Declared.

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POS0516 PERFORMANCE OF NURSE-LED GOUT CARE IN A PRIVATE HEALTHCARE SYSTEM. A RANDOMISED CONTROLLED TRIAL

Keywords: Non-pharmacological interventions, Gout, Randomized control trial

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Background: Nurse-led gout care has been studied mainly in managed healthcare systems [1].

Objectives: To investigate the effectiveness of a structured nurse-led gout programme in a private healthcare system.

Methods: A randomised single-blinded controlled trial with two study arms was performed. The inclusion criteria were the fulfilment of the 2015 ACR/EULAR gout classification criteria(2) and the indication for urate-lowering therapy (ULT). The inclusion period lasted 2 years and the intervention period 6 months. Physician FU visits took place at 6 and 12 months from baseline (BL). The achievement rate of the target serum acid level (SUA, ≤ 360 µmol/l) at the 6-month-FU served as the primary endpoint. In the intervention group, during the first six months after inclusion, a structured treat-to-target (T2T)-programme led by trained nurses was performed. In both groups, the patients were followed by their treating physicians without specific recommendations. We performed descriptive statistics. Categorical variables were reported as frequencies and compared using Fisher's exact test. Continuous variables were compared using Student's t-test or the Mann-Whitney U test in case of non-normal distribution.

Results: A total of 46 patients were included, of which 19 were randomised to the intervention group and 27 to the control group. Dropouts occurred in 6 patients in the intervention group and 3 in the control group. The median age was 69 years, and a pronounced male overrepresentation was found. 38% of the patients in the intervention group vs 53% in the control group were obese. Alcohol consumption was frequent in both groups (63% vs 59% of the patients). At BL, most patients were under an anti-inflammatory treatment (colchicine, steroids, NSAIDs). ULT was similar in both groups with a low median dosage of Allopurinol (250 mg/day at the 12 m FU). BL characteristics and outcomes are presented in *Table 1.*

Table 1. Baseline Characteristics and Outcome

Medians, (IQR), frequencies in %	BL		6-month-FU		12-month- FU	
Intervention (I)/ Controls (C)	I	C	I	C	I	C
n pat	19	27	16	23	17	24
Acute flare/arthritis	15(78.9%)	19(70.3%)	5 (31.3%)	7 (41.1%)	2 (12.5%)	4 (16.6%)
Oligo-/Polyarthritis	7	5	1	0	1	0
n pat with tophi	8 (42.1%)	5 (18.5%)	1	1	1	0
SUA [µmol/l]	**534.0(390.5; 606.3)**	487.0(411.0; 532.0)	**339.0 (285.8; 407.8)**	360.0 (304.0; 445.0)	342.5 (295.8; 415)	375.0 (268.5; 451.0)
GFR CKD EPI [ml/min/1.73m2]	**57.0** (44.8; 87.5)	**67.0** (43.0; 88.5)	65.5(51.3; 90.8)	75.0(56.0; 93.0)	65.5(53.0; 85)	70.0(62.0; 90.0)

Conclusion: There was no significant advantage over the standard of care regarding SUA reduction. However, the intervention patients showed twice as often impaired kidney function (grade 3-5) and tophaceous gout. Nevertheless, these patients reduced SUA levels better after 6 months (36% vs 26% reduction) and 64% of them achieved the SUA target after 12 months (vs 47% in the control group).

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Disclosure of Interests: None Declared.

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POS0517 ANTINUCLEAR ANTIBODIES IN GOUT: VICTIMS OF MODERN IMMUNOLOGY TECHNIQUES (A NEW VOMIT)

Keywords: Gout, Autoantibodies, Crystal arthritis

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Background: Non-rational prescription of tests in clinical practice may induce inefficient performances, misdiagnosis, and inappropriate consultations.

Objectives: We analyzed the prescription and results of antinuclear antibodies (ANA) prescription before first consultation to a rheumatology unit in a disease with commonly high diagnostic accuracy based on clinical findings: gout.

Methods: In the decade 2013-2022 the prescription and results of ANA testing prior to first rheumatology visit was added to the database, along with general data and variables related to comorbid conditions and clinical characteristics of gout. We made an analysis of variables plausibly associated with ANA prescription and biennial changes through n the rate of prescription.

Results: From Jan 2013 to Dec 2022, 504 patients gave written consent for data inclusion, 66 (13.7%) women and 415 men (86.3%), with mean age at entrance in the cohort of 73±14 and 65±14 years, respectively. ANA had been prescribed to 114 (23.7%) subjects, in 28/66 (42.4%) women and 86/415 men (p<0.001). No differences for prescription were observed in other variables, such as age, time from onset, flares per year, tophi, or polyarticular distribution. The rate of ANA prescription was not related to the diagnostic for consultation: arthralgia (24.4%), arthritis (21.7%) or gout (25.3%). 31/114 (27.2%) ANA tests were positive (90% with title <1/400), but only led to a new diagnosis (autoimmune hepatitis), and two had a previous diagnosis (Sjögren´s Syndrome and Systemic Lupus). The rate of positive ANA was much higher in women (12/28, 42.9%) than in men (8/86, 22.1%). The rate of ANA prescriptions showed a biennial and significative increase during the last decade (p= 0.007): 11.3% in 2013-14, 21.4% in 2015-16, 34.9% in 1016-2017, and 31.1% in 2021-22. A valley in ANA prescriptions was observed during SARS-COV2 pandemia 2019-2020 (19.7%).

Conclusion: In a rheumatic disease with quite typical clinical presentation as gout, the rate of ANA prescription prior to rheumatology consultation is unexpectedly high, and the highest in women, despite old age and absence of systemic clinic. The rate of positive ANA in the elder in our setting is quite high, especially in women, and may lead to misdiagnosis and inefficient management: a new VOMIT.

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Disclosure of Interests: Ana Maria Herrero-Beites: None declared, Cristina Vazquez-Puente: None declared, Maria del Consuelo Modesto-Caballero: None declared, Fernando Perez-Ruiz Speakers bureau: Menarini, Astellas, Consultant of: Arthriti, Alnylam, LG, Protalix, Selecta.

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POS0518 TREATMENT OF GOUT AND ITS EFFECTS ON METABOLIC SYNDROME

Keywords: Gout, Cardiovascular disease, Crystal arthritis

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Background: There is a known relationship between elevated serum urate (SUA) levels and renal, cardiovascular (CV), and metabolic disease. However, the precise reasons for this remain poorly defined. The CANTOS trial found a significant decrease in nonfatal MI, stroke, or CV death in patients (PTs) treated with canakinumab vs placebo. The LoDoCo2 trial found a decrease in CV death, nonprocedural MI, ischemic stroke, and ischemia-driven need for coronary revascularization in PTs treated with colchicine vs placebo. This suggests that inflammation is an independent risk factor for CV disease. The GOSPEL 4 trial found that French PTs with early-onset gout (EOG), a diagnosis (DX) < age 40, had slightly more arthritis, significantly less chronic stage 3 or 4 kidney disease (CKD) compared to common gout (CG) PTs, DX ≥ age 40. Metabolic syndrome was significantly more prevalent in the CG group. To our knowledge, no study has investigated the effects of EOG vs CG on incidence of metabolic-related diseases in a rural population in the US.
Objectives: To investigate whether early DX and control of gout results in lower incidence of metabolic-related diseases in a rural setting.
Methods: We conducted a retrospective analysis of PTs with gout at a rural tertiary care center. We identified PTs seen Jan 2016-Dec 2020 with a gout DX. Charts were reviewed for: sex; age at DX; age at the time of gout DX and at the last medical encounter; HbA1c level; SUA level; and BMI. Charts were reviewed for urate-lowering therapy (ULT) prescriptions, atherosclerotic cardiovascular disease (ASCVD)/peripheral arterial disease (PAD), diabetes mellitus (DM), hypertension (HTN), and CKD. We compared demographic and clinical characteristics between EOG and CG PTs using chi-square tests for categorical data and the Kruskal-Wallis test. All analyses were performed using SAS version 9.4.
Results: For baseline demographics, see Table 1. Of 12,362 charts reviewed, 692 had EOG, and 11,670 had CG. More PTs in the CG group had ASCVD/PAD (4.6% vs 0.3%, p <.0001), DM (38.2% vs 15.5%, p <.0001), HTN (83.8% vs 44.9%, p <.0001), CKD (43.4% vs 7.1%, p <.0001), and tophi (5.3% vs 0.0%, p <.0001). CG PTs had higher mean initial HbA1c (6.5 vs 6.1, p <.0001) and last HbA1c (6.1 vs 5.6, p <.0001). PTs in the EOG group had higher mean initial SUA levels (8.2 vs 7.1, p <.0001) and last SUA levels (7.5 vs 6.3, p <.0001). There was no significant difference in ULT use (72.6% vs 71.1%, p = 0.3856).
Conclusion: Our study suggests PTs with EOG had significantly lower rates of ASCVD/PAD, DM, CKD, tophi and lower A1c levels. Given that EOG and CG patient's ULT use was similar, this shows that EOG PTs on ULT are less likely to develop the comorbidities associated with gouty arthritis. We further intend to look at EOG time to comorbidity DX event.

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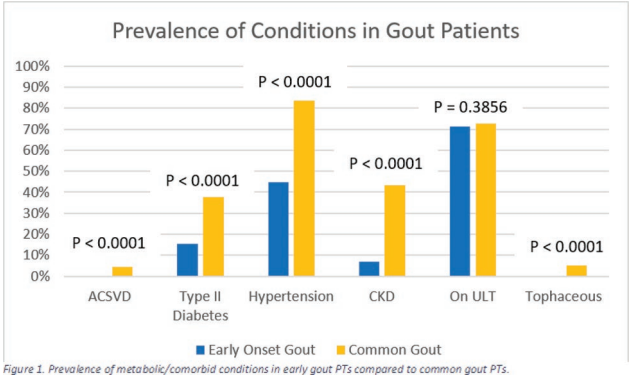


Figure 1. Prevalence of metabolic/comorbid conditions in early gout PTs compared to common gout PTs.

Table 1. Baseline Demographics

	CG N = 11,670	EOG N = 692	Total N = 12,362
Age, First Visit			
Mean (SD)	66.5 (12.16)	33.4 (4.40)	64.6 (14.09)
Median (IQR)	67.0 (58.0, 76.0)	34.0 (31.0, 37.0)	66.0 (56.0, 75.0)
Age, Gout DX			
Mean (SD)	67.0 (12.16)	33.9 (4.41)	65.1 (14.09)
Median (IQR)	67.9 (58.2, 76.3)	34.7 (31.2, 37.4)	66.9 (56.0, 75.8)
Sex			
Female	2,872 (24.6%)	42 (6.1%)	2,914 (23.6%)
Male	8,798 (75.4%)	650 (93.9%)	9,448 (76.4%)
BMI, Initial			
BMI < 18.5	48 (0.5%)	1 (0.2%)	49 (0.4%)
18.5 ≤ BMI < 25	1,020 (9.8%)	22 (3.5%)	1,042 (9.4%)
25 ≤ BMI < 30	2,974 (28.6%)	88 (14.2%)	3,062 (27.8%)
30 ≤ BMI	6,365 (61.2%)	510 (82.1%)	6,875 (62.3%)
BMI, Last			
BMI < 18.5	50 (0.5%)	1 (0.2%)	51 (0.5%)
18.5 ≤ BMI < 25	1,077 (10.3%)	22 (3.5%)	1,099 (10.0%)
25 ≤ BMI < 30	2,949 (28.3%)	88 (14.2%)	3,037 (27.5%)
30 ≤ BMI	6,331 (60.8%)	510 (82.1%)	6,841 (62.0%)

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0519

THE ANALGESIC EFFICACY OF THERAPIES USED FOR COMPLEX REGIONAL PAIN SYNDROME: A SYSTEMATIC REVIEW

Keywords: Quality of life, Systematic review, Pain

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Background: Complex regional pain syndrome (CRPS) is a multifactorial chronic pain condition which arises following commonplace injuries such as fractures. Pharmacological and non-pharmacological treatments including physiotherapy have been used to reduce pain but there is an unmet need for novel effective therapies.
Objectives: To review clinical trials for CRPS and evaluate effectiveness for reducing pain.
Methods: A PICO approach was used to search MEDLINE, PubMed, COCHRANE LIBRARY, EMBASE, CINAHL and Web of Science for studies published between 2003 to 2022. Keywords such as "Complex Regional Pain Syndrome", and its previous label "Reflex Sympathetic Dystrophy" were used, alongside "pharmacological" and "non-pharmacological interventions". The studies included were confined to adults clinically diagnosed with CRPS, that were written in English. Additional studies were also found via citation searching of references from eligible reports.
Results: The search strategy generated 41 RCTs in total (Figure 1). Pharmacological interventions such as bisphosphonates showed consistently significant improvement in pain, in addition to ketamine and steroids which yielded some successful outcomes. Interventional therapies such as local anaesthetics, sympathetic blocks, and nervous system stimulations also demonstrated potential. Finally, mirror therapy, motor imagery programs and virtual reality revealed partial improvement. Conversely, Pain Exposure Physical Therapy (PEPT), immunosuppressant drugs, free radical scavengers, anti-convulsants, calcitonin, immunoglobulins, Fluidotherapy and occlusal splints had no significant effects on pain outcomes. The Cochrane risk of bias tool was used to assess the quality of studies involved, for which the lower quality RCTs were those lacking full blinding or selectively reporting outcomes.

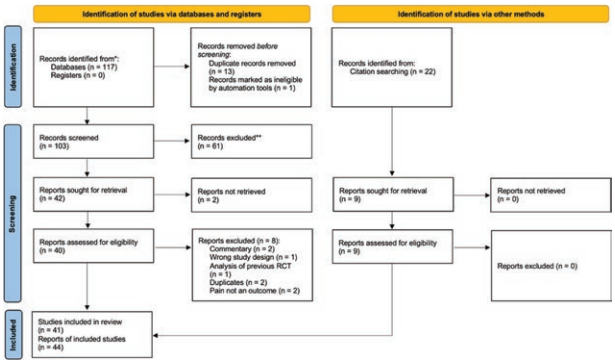


Figure 1. PRISMA flow diagram depicting the screening precesses used from database searching and citation searching.

Conclusion: Bisphosphonates provide the most consistent benefit in pain reduction in CRPS with larger effects than other interventions. Many studies of other interventions were small or of lower quality. Overall, larger, high-quality trials are required to validate any promising findings for other pharmacological and non-pharmacological therapies.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Charlotte Shekarsarai: None declared, Nicola Gullick Speakers bureau: Speaker fees: Abbvie, Eli Lilly, Janssen, Novartis, UCB, Consultant of: Consultancy fees: Abbvie, Janssen, Novartis, UCB, Grant/research support from: AstraZeneca, Abbvie, Eli Lilly, Izana, Novartis.

DOI: 10.1136/annrheumdis-2023-eular.3213

POS0520 CARDIOVASCULAR SAFETY OF FEBUXOSTAT IN PATIENTS WITH GOUT OR HYPERURICEMIA: A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS

Keywords: Gout, Crystal arthritis

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Background: To this date, a causal relationship between febuxostat and cardiovascular disease remains controversial as comparison between trials can be challenging and may lead to misleading conclusions especially when facing heterogeneous cardiovascular outcomes.

Objectives: We aimed to compare the cardiovascular outcomes in the most pertinent trials of Febuxostat compared to controls.

Methods: We searched electronic databases using a PICOS-style approach search strategy of randomized controlled trials on cardiovascular outcomes of Febuxostat in patients with gout or hyperuricemia. We conducted a quality and risk of bias assessment of the included clinical trials. The definition of MACE as well as all reported cardiovascular outcomes were retrieved from every involved trial.

Results: Of the 1173 records identified from all sources, 20 RCTs were included in the analysis. Mean duration of follow-up was 69.7 ± 81.5 weeks and Febuxostat dose ranged from 10 to 240 mg with 80 mg being the most commonly used dosage. Overall, the quality of evidence deriving from all RCTs showed concerns in most studies (65%). Major cardiovascular event (MACE) was defined in 7 of the 20 RCTs (35%) and cardiovascular outcome reporting was very heterogeneous. Overall, data of cardiovascular safety of Febuxostat were reassuring.

Conclusion: Our systematic review showed no alarming increase of cardiovascular mortality and outcomes in Febuxostat treated patients except for the CARES trial in which the credibility of the results is biased by the high rate of drug discontinuation and of most importantly, withdrawal from follow-up. FAST trial results, backed up with real-world data cohort studies, were robust and reassuring with regard to the cardiovascular safety of Febuxostat in most white males with gout including elderly patients. This should lead the regulatory agencies to reconsider the limitations imposed on the use of Febuxostat in patients with non-severe CV burden.

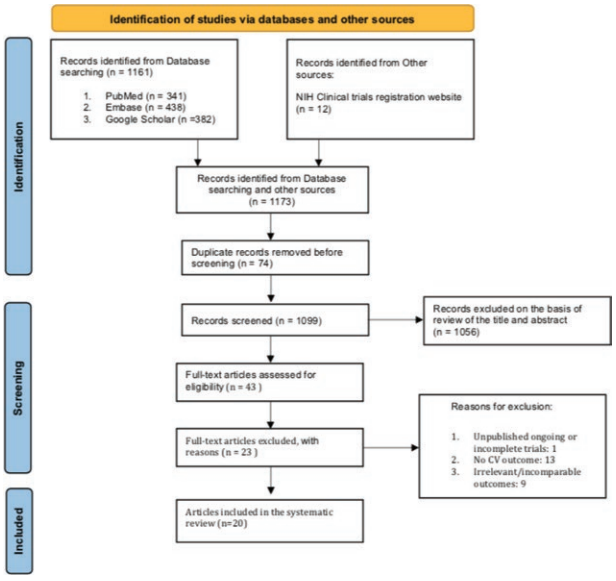


Figure 1. Flowchart of the included studies. NIH: National Institutes of Health; CV: Cardiovascular

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0521 MORTALITY RATE OF GOUT PATIENTS HAS BEEN INCREASED IN KOREA

Keywords: Gout

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Background: Many epidemiologic studies support an association between gout and increased premature mortality. However, there has been no study on mortality and cause of death in Korean patients with gout with large scale data. Therefore, we intended to investigate the risk of death, the change of mortality rate over time, and main cause of death in Korean patient with gout with the national insurance database.

Objectives: The purpose of this study is to assess the mortality rate, trends of mortality rate over time, and cause of death of gout patients in Korea.

Methods: Using Korean National Health Insurance Service data, we conducted a cohort study on gout patients. Gout patients were defined as those aged ≥ 20 years who were diagnosed as gout between 2002 and 2014, and control patients were matched with gout patients (1:1 ratio) after frequency matching for age, sex and index year. Primary outcome was all-cause mortality and observation period was between 2007 and 2015. Covariates were age, sex and comorbidities (hypertension, diabetes, chronic renal failure, ischemic heart disease, cerebrovascular disease and cancer). We calculated standardized mortality rate (SMR), and hazard ratio (HR) in Cox regression, adjusting potential confounders.

Results: This study included 18,406 gout patients and an equal number of matched controls. Baseline characteristics of gout and control patients are displayed in Table 1. Total 1,926 deaths occurred, and SMR of gout patients showed increasing tendency from 2007 to 2015 (Figure 1). The most common cause of death in Korean gout patients was chronic renal failure. Multivariate Cox regression analysis showed that gout patients showed increased risks of all-cause mortality (HR 1.182, 95% CI 1.098-1.274) after adjusting age, sex, and comorbidities.

Conclusion: Gout patients were associated with higher risk of all-cause mortality. The mortality rate of gout patients showed increasing tendency between 2007 and 2015, and most common cause of death was chronic renal failure.

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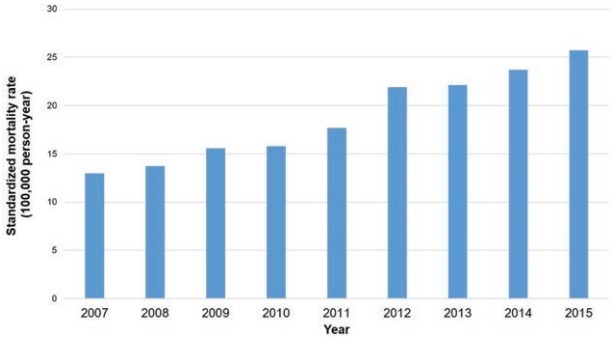


Figure 1. Standardized mortality rate of gout patients between 2007 and 2015

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0522 UTILIZATION OF A GOUT ANALYZER (U-GAN) FOR CRYSTAL EXAMINATION IN CLINICAL PRACTICE

Keywords: Diagnostic tests, Crystal arthritis

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[1]Regional Independent Administrative Corporation Naha City Hospital, Department of Nephrology and Rheumatology, Naha, Okinawa, Japan; [2]Tokyo Metropolitan Tama Medical Center, Department of Rheumatic Diseases, Fuchu, Tokyo, Japan

Background: Synovial fluid (SF) crystal analysis performed with a compensated polarized microscopy is the gold standard for identifying calcium pyrophosphate (CPP) and monosodium urate (MSU) crystals. Since a fully equipped compensated polarized microscope is not widely available, a gout analyzer (U-GAN, Olympus) is alternatively used in many countries. By attaching the analyzer in a slider-compatible revolving nosepiece, examination using compensated polarization can be easily performed by operating the lever.
Objectives: To evaluate the utility of crystal examination using U-GAN®.
Methods: We prospectively performed different crystal identification methods in 30 patients with knee joint effusion at Tokyo Metropolitan Tama Medical Center from February 2020 to March 2021. Rheumatologists who routinely use compensated polarized microscope blindly evaluated the non-centrifuged SF using three methods: 1) morphologic identification under ordinary light, 2) use of U-GAN®, and 3) use of fully-equipped compensated microscope (MT9300, Meiji Techno) in this order. In addition, in-hospital commercial laboratory technicians evaluated the sediment using U-GAN® after centrifugation (3000 rpm for 5 min).
Results: Total 30 SF were evaluated. By compensated polarized microscope, 15 were found crystal-positive (11 for CPP and 4 for MSU). The detection of both CPP and MSU by the in-hospital laboratory technician were in perfect agreement. Before centrifugation, the sensitivity of ordinal microscope and U-GAN® were 73.3% (11/15) and 80.0% (12/15), respectively (specificity 100% in both). When using U-GAN®, 3 (2 CPP and 1 MSU) were additionally detected after centrifugation.
Conclusion: U-GAN® can be used for detection of both CPP and MSU in clinical practice.

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Acknowledgements: NIL.
Disclosure of Interests: Takayasu Kise Grant/research support from: Daiichi Sankyo Co. Ltd., Naoto yokogawa Grant/research support from: Daiichi Sankyo Co. Ltd., Yuji Miyoshi Grant/research support from: Daiichi Sankyo Co. Ltd., Masako Utsunomiya Grant/research support from: Daiichi Sankyo Co. Ltd., Yoshiki Nagai Grant/research support from: Daiichi Sankyo Co. Ltd., Kota Shimada Grant/research support from: Daiichi Sankyo Co. Ltd.
DOI: 10.1136/annrheumdis-2023-eular.4262

POS0523 FEASIBILITY STUDY OF AN ELECTRONIC HEALTH RECORD-BASED GOUT REGISTRY

Keywords: Registries, Gout

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Background: Gout is the most common inflammatory rheumatism worldwide. Despite guidelines on acute and chronic management, it remains largely undertreated [1]. To evaluate the current standard of gout care, there is an unmet need for gout registers, especially in the non-rheumatology setting. The vast clinical information available in electronic health record (EHR) allows the implementation of registers to assess clinical indicators and monitor them following quality improvement programs. The Geneva University Hospitals (HUG), a 2000-beds tertiary hospital, provides multi-specialty in- and outpatient services, including care to vulnerable population (inmate, uninsured) with a unified EHR and thus represent an ideal setting for this purpose.
Objectives: To establish an EHR-based gout registry, to assess the correct identification of gout patients by manual chart review, and to evaluate the objective validity of gout diagnosis based on the ACR-EULAR 2015 gout classification criteria [2].
Methods: EHR of patients > 18 years old admitted to or consulting at the HUG between 01.01.2013 and 15.11.2022 were screened based on the presence of at least one of four criteria: ICD-10-GM gout diagnosis (M10), gout-related terms (gout, tophi or podagra) in the list of diagnosis, prescription of urate-lowering therapy (allopurinol, probenecid, febuxostat) among non-leukemia or lymphoma-suffering patient (ICD-10-GM code C81 to C96 were excluded), or uric acid crystal in synovial fluid. For each criterion, a sample of 20 medical charts were fully reviewed. The positive predictive value (PPV) to detect a true gout was established if a gout diagnosis was mentioned by any doctor in any part of the EHR. To further assess the validity of the gout diagnosis, the 2015 ACR-EULAR gout criteria was scored. Gout patients without any acute arthritis during any encounter with the HUG were classified as having an antecedent gout.
Results: The four criteria identified 7'046 patients suffering from gout, among which 33.4% were deceased. Most patients were identified by the drugs criterion (Figure 1). A large proportion of patients (43.2% of outpatients and 72,8% of inpatients) were identified by the presence of urate-lowering therapy only, without the mention of any gout diagnosis. Furthermore, 9.7% and 2.6% in the out- and inpatient setting respectively had a positive punction that wasn't associated with a documented diagnosis. PPV were 100% for ICD-10-GM code, list of diagnosis and punction, and 75% for urate-lowering therapy, while PPV based on a combined query (any criterion) was 93.8% to detect a gout patient in the charts. Among the 80 charts reviewed, 55 patients had at least one documented gout attack and 25 had an antecedent gout. Of the 55 patients with an acute gout, which allowed the use of the ACR-EULAR 2015 classification, 39 patients (70.9%) had a positive articular punction for uric acid or the presence of tophus as observed by a trained examiner. The remaining 16 patients (29.1%) had a mean score (SD) of 5.5 (2.39) for the ACR-EULAR 2015 classification (threshold to classify as gout is ≥8). The lack of clinical information available (documented presence of tophus, precise clinical course of symptoms) and lack of diagnostic imaging to assess gout complication might explain the low score, among these patients with a high probability of gout according to the chart review.
Conclusion: We demonstrate the feasibility of an EHR-based gout registry, with good positive predictive value and the ability to identify patients without a documented gout diagnosis in their EHR. The next step is to expend the queries to look for gout diagnosis in all of the patient's documents and imaging reports and to estimate the negative predictive value in a sample of patients without any criteria, yet with risk factors of gout.

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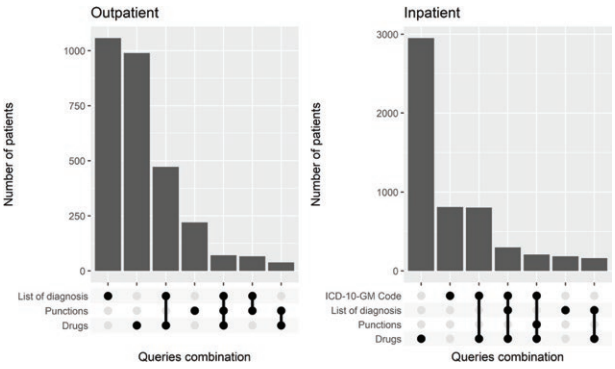


Figure 1. Upset-Plot of the four criteria identifying gout patient in the out- and inpatient setting of the Geneva University Hospital's EHR. ICD-10-GM code are available only for hospitalized patient.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0524 CXCL12 AND CXCR4 AS NOVEL BIOMARKERS IN PATIENTS WITH GOUTY ARTHRITIS

Keywords: Gout, Biomarkers, Inflammatory arthritides

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Background: CXCR4 binds to its ligand CXC chemokine CXCL12 and plays a role in induction of recruitment of inflammatory cells including leukocytes and endothelial cells. The CXCL12/CXCR4 axis has been implicated in the pathogenesis of some types of inflammatory arthritis and autoimmune diseases including rheumatoid arthritis, osteoarthritis, systemic lupus erythematosus, and ankylosing spondylitis. Evidence of the pathogenic role of CXCR4 and CXCL12 in uric acid-induced inflammation has not been presented.
Objectives: The aim of this study is to evaluate the expression of chemokine receptor CXCR4 and its ligand CXCL12 in patients with gout and uric acid-induced inflammation.
Methods: Forty patients with intercritical gout and 27 controls were consecutively enrolled. Serum levels of interleukin-1β (IL-1β, IL-18, CXCL12, and CXCR4 were assessed using enzyme-linked immunosorbent assay. Gene and protein expression for these target molecules was measured in human U937 cells incubated with monosodium urate (MSU) crystals using real-time reverse transcription polymerase chain reaction and Western blot analysis.
Results: Patients with intercritical gout showed higher serum IL-1β, IL-18, and CXCL12 levels than those in controls, but not serum CXCR4 level. Serum CXCR4 level in gout patients was associated with serum IL-18 level, uric acid level, and uric acid/creatinine ratio (r = 0.331, p = 0.037; r = 0.346, p = 0.028; r = 0.361, p = 0.022, respectively). U937 cells treated with MSU crystals significantly induced CXCL12 and CXCR4 mRNA and protein expression, in addition to IL-1β and IL-18. In cells transfected with IL-1β siRNA or IL-18 siRNA, CXCL12 and CXCR4 expression was downregulated compared to non-transfected cells in MSU crystal-induced inflammation. Receiver operator characteristic (ROC) curve analysis showed that serum CXCL12 for the diagnosis of gout was an area under roc curve (AUC) of 0.690 (p = 0.009).
Conclusion: This study reveals that CXCL12 and CXCR4 are involved in the pathogenesis of uric acid-induced inflammation and gouty arthritis.

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5261

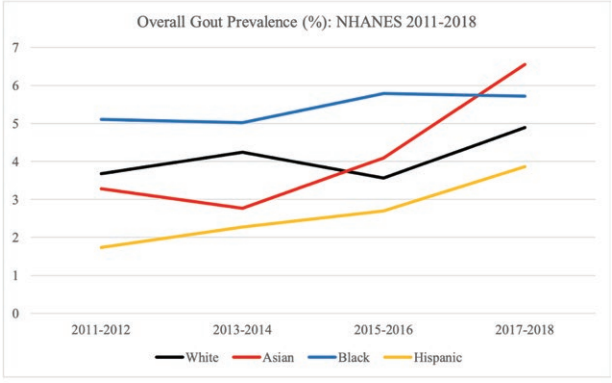
POS0525 WORSENING BURDEN OF GOUT AMONG ASIAN AMERICAN ADULTS – GENERAL POPULATION-BASED STUDY (2011-2018)

Keywords: Gender/diversity issues, Gout, Epidemiology

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Background: Asian Americans are the fastest-growing racial/ethnic group in the US. Gout disparities in Black Americans have been explained by socio-clinical factors; however, no data are available among Asians living in Western countries, despite their disproportionately worsening metabolic health.
Objectives: To determine the prevalence of gout and serum urate concentrations according to race/ethnicity and the potential impact of social determinants of health and clinical factors.
Methods: Using data from the latest NHANES cycles (2011-2018) in which Asian race data were collected, we determined the prevalence of gout and serum urate concentrations according to race/ethnicity and the potential impact of social determinants of health and clinical factors. We sought to replicate the Asian-White differences in the UK Biobank.
Results: Gout now affects 12.1 million Americans, with its prevalence increasing from 3.6% (95% CI, 2.8, 4.5) in 2011-2012 to 5.1% (4.2, 5.9) in 2017-2018 (p-trend=0.03); this trend nullified after excluding Asians (p-trend, 0.11) or after age adjustment (p-trend, 0.06). During the same period, age- and sex-adjusted prevalence among Asian Americans doubled from 3.3% to 6.6% (p-trend=0.007) to exceed all other racial/ethnic groups in 2017-2018 (**Figure 1**), with age- and sex-adjusted odds ratio (OR; Asian vs. White) of 1.61 (1.03, 2.51) and socio-clinical-factor-adjusted multivariable OR of 2.62 (1.59, 4.33) (**Table 1**). The latest gout prevalence among Americans ≥65 years was 10.0% among Whites and 14.8% among Asians (including 23.6% of Asian men). Serum urate concentrations also increased between 2011-2018 among Asian Americans (p-trend=0.009). The Asian-White disparity was also present in the UK Biobank (**Table 1**).
Conclusion: Gout now affects >12 million US adults due to an aging population and rising prevalence among Asian Americans, which surpassed all other racial/ethnic groups in 2017-2018. This Asian-White disparity does not appear to be driven by socio-clinical factors.

Figure 1. Trends in Gout Prevalence* by Race/Ethnicity: NHANES 2011-2018**



*Age-standardized prevalence

**Data are presented incorporating sample weights and adjusted for clusters and strata of the complex sample design of NHANES 2011-2018.

Table 1. Step-by-Step Regression for Potential Risk Factors for the Association between Asian Race and Odds of Gout and Serum Urate Concentration Compared to White Race, NHANES 2017-2018 and UK Biobank

	NHANES 2017-2018 (US)		UK Biobank, 2006-2021	
	OR for Gout, 95% CI	Serum Urate Concentration Difference (mg/dL), 95% CI	OR for Gout, 95% CI	Serum Urate Concentration Difference (mg/dL), 95% CI
Age- and Sex- adjusted	1.61 (1.03, 2.51)	0.21 (0.08, 0.35)	1.16 (1.05, 1.29)	0.12 (0.10, 0.15)
+Education[a]	1.61 (1.03, 2.52)	0.22 (0.08, 0.36)	1.18 (1.07, 1.32)	0.13 (0.10, 0.15)
+Poverty[b]	1.68 (1.07, 2.63)	0.22 (0.08, 0.36)	1.14 (1.02, 1.26)	0.11 (0.09 to 0.13)
+ Active health insurance[c]	1.67 (1.07, 2.63)	0.22 (0.08, 0.36)	-	-
+Alcohol consumption[d]	1.70 (1.08, 2.68)	0.23 (0.09, 0.37)	1.28 (1.14, 1.42)	0.17 (0.15, 0.19)
+DASH diet score[e]	1.78 (1.11, 2.83)	0.26 (0.13, 0.39)	1.33 (1.19, 1.48)	0.20 (0.18, 0.23)
+BMI[f]	2.37 (1.45, 3.86)	0.46 (0.33, 0.59)	1.64 (1.47, 1.83)	0.31 (0.29, 0.33)
+Diuretic use[g]	2.37 (1.45, 3.87)	0.47 (0.34, 0.60)	1.64 (1.47, 1.84)	0.30 (0.28, 0.33)
+CKD[h]	2.62 (1.59, 4.33)	0.50 (0.37, 0.62)	1.63 (1.46, 1.82)	0.30 (0.28, 0.33)

BMI=body mass index; CKD=chronic kidney disease; DASH=Dietary Approaches to Stop Hypertension; OR=odds ratio.Active health insurance not included in the UKBB models due to the universal publicly funded healthcare system in the UK.

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POS0526

PAIN PROCESSING IS ALTERED ABOVE PAGETIC BONE

Keywords: Pain, Bone diseases

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Background: Pain is the most common symptom of Paget's Disease of Bone (PDB) and affects between 60% and 70% of patients who present to clinic in the UK, but its mechanisms are incompletely understood [1]. Quantitative sensory testing (QST) has historically been used in the assessment of neuropathic pain [2]. but has precedent in patients with bone metastases and osteoarthritis [3,4]. In this study we used QST to dissect the mechanisms of pain in PDB, taking advantage of the disease's focal nature which allows the participant to act as their own control by testing at a contralateral site.

Objectives: To explore the sensory profiles of PDB patients with and without musculoskeletal pain.

Methods: All study data was collected and stored on the secure web-based software platform Research Electronic Data Capture (REDCap). Quantitative sensory testing (QST) measured the sensory response to various stimuli applied to the skin overlying the Pagetic bone and compared this to an unaffected site in 120 study participants. Differences between QST assessments in sites overlying Pagetic bone and control sites were assessed by the Mann-Whitney test.

Results: Significantly higher pain scores were reported above the site of PDB when compared to the control site, irrespective of whether the patient complained of musculoskeletal pain. The differences were apparent for hot roller testing ($p = 0.047$), pain threshold testing ($p = 0.007$), pin prick testing ($p = <0.001$) (see Figure 1), and wind-up pinprick testing ($p = <0.001$). Pain thresholds were significantly reduced above Pagetic bone ($p = 0.007$). Additionally, temporal summation scores were significantly higher ($p = 0.007$) in the pain subgroup compared with the no pain subgroup which could indicate higher levels of central sensitisation in patients who experience pain.

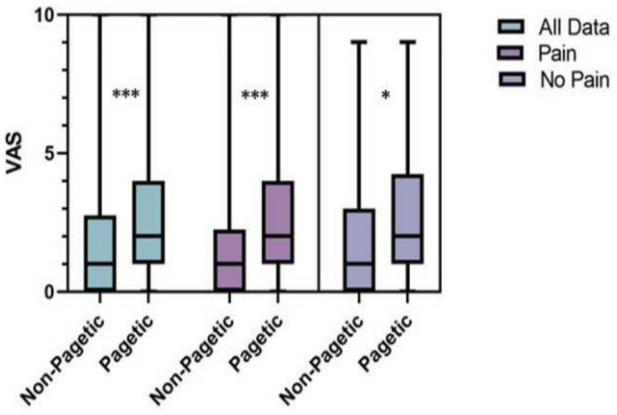


Figure 1. Visual Analogue Scale (VAS) scores reported following Single Pin Prick Testing. Data is split in to the full dataset, the 'Pain' reporting subgroup, and the 'No Pain' reporting subgroup.

Conclusion: This study illustrates that there are significant differences in the way that sensation is processed above Pagetic bone when compared to unaffected contralateral sites, regardless of the presence of current musculoskeletal pain. Our data suggest that patients who experience pain may do so, in part, because of higher levels of central sensitisation.

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POS0527 THE PRESENCE OF MONOSODIUM URATE DEPOSITS IN THE JOINTS OF PATIENTS WITH ASYMPTOMATIC HYPERURICEMIA IS ASSOCIATED WITH A HIGHER CARDIOVASCULAR RISK, BUT NOT WITH MORE ADVANCED KIDNEY DAMAGE

Keywords: Kidneys, Crystal arthritis, Ultrasound

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Background: Epidemiological studies conducted in patients (pts) from the general population and pts with chronic renal failure have shown that uric acid is an independent risk factor for the development and progression of kidney disease. Uric acid damages the kidneys by causing systemic and glomerular hypertension. Hyperuricemia is connected to arteriolosclerosis, characterized by arterial wall thickening and hyalinosis.
Objectives: To evaluate the association between asymptomatic hyperuricemia and renal damage and to establish whether the presence of monosodium urate (MSU) deposits in the joints of these pts is related to more advanced renal alterations.
Methods: This was a single-center cross-sectional study, including 73 consecutive pts divided into 34 pts with osteoarthritis (controls), 25 subjects with asymptomatic hyperuricemia and no ultrasound (US) evidence of MSU crystals in the joints and 14 individuals with asymptomatic hyperuricemia and MSU deposits in the joints. Pts underwent bilateral US examination of the joints of the hands, elbows, knees, ankles, feet and the kidneys. Measurements of the joints were conducted with a high-frequency linear transducer 4-15 MHz. The existence of double contour sign, intra-tendinous MSU aggregates, "snow storm", tophi, tophi with erosions, or a combination of these US features was assessed. Kidneys were examined with 3.5 MHz transducer, working with pulse Doppler frequency of 2.5 MHz. Renal length, parenchymal thickness and echogenicity were determined. The presence or absence of nephrolithiasis was reported. By means of the value of renal resistive index (RRI) we judged for intrarenal blood flow. Statistical analyzes were done by One-Sample Kolmogorov-Smirnov, t-test, Chi-square or Fisher`s exact test.
Results: The distribution of males and females (p=0.441), smokers and non-smokers (p=0.147), pts with arterial hypertension and normotensive individuals (p=0.298) as well as subjects with diabetes and without diabetes (p=0.775) and pts with dyslipidemia and normal lipid levels (p=1.000) was similar among the groups. The proportion of pts who had suffered with cardiovascular event was the highest in the group of asymptomatic hyperuricemia with MSU deposits in the joints (21.4%) compared to the group of osteoarthritis (14%) and hyperuricemia without MSU crystals in the joints (0%), (p=0.048). In the group of osteoarthritis the share of pts with eGFR < 90 ml/min was the lowest (5.9%) in comparison to the group of hyperuricemia without MSU deposits in the joints (29.2%) and hyperuricemia with crystals in the joints (46.2%), (p=0.005). The percentage of obese pts was the highest in hyperuricemia with MSU crystals in the joints (57.1%), but without reaching a significant difference with hyperuricemia without crystals in the joints (40%) and the group of osteoarthritis (29.4%), (p=0.195). The echogenicity of the kidneys (p=0.630) and the distribution of nephrolithiasis (p=0.596) was equal among the groups. Pts with hyperuricemia and MSU deposits in the joints compared to those with osteoarthritis had higher BMI (mean±SD; 31.79±5.92 kg/m^2 vs 28.06±4.27 kg/m^2, p=0.018) and smaller kidney size (mean±SD; 55.36±5.58 mm vs 59.58±5.12 mm, p=0.015). The comparison of hyperuricemia without MSU deposits in the joints to osteoarthritis group demonstrated a significant difference only in the age (mean±SD; 49.7±16.4 years vs 61.5±9.4 years, p=0.001). Finally, the comparison of the two groups with hyperuricemia showed that subjects with MSU deposits in the joints had higher BMI (mean±SD; 31.79±5.92 kg/m^2 vs 28.26±4.41 kg/m^2, p=0.041) with no difference in the age (p=0.072), kidney size (p=0.141), RRI (p=0.296), eGFR (p=0.528) and thickness of renal parenchyma (p=0.232).
Conclusion: Hyperuricemia independently of the presence of articular crystals is associated with similar kidney damage. Cardiovascular risk is higher when MSU crystals are found by US in the joints.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0528 PATIENT EXPERIENCES WITH CHRONIC REFRACTORY GOUT AND ITS IMPACT ON HEALTH-RELATED QUALITY OF LIFE

Keywords: Patient reported outcomes, Quality of life, Gout

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Background: Gout is a common inflammatory rheumatic disease, with elevated uric acid leading to deposition of monosodium urate crystals within joints [1]. Chronic refractory gout (CRG), also known as refractory or uncontrolled gout, is associated with unexpected disease flares characterized by severe and debilitating pain. Long-term symptoms include painful inflammatory arthritis, impaired physical function, and health-related quality of life (HRQoL), and tophi-related joint destruction [1].
Objectives: This study aimed to 1) develop and refine a conceptual model of patient-identified CRG symptoms and their impact on HRQoL; and 2) confirm that the 36-item Short Form Health Survey V2.0 (SF-36) and Health Assessment Questionnaire-Disability Index (HAQ-DI) are relevant to patients with CRG by mapping items to the CRG conceptual model.
Methods: A targeted literature review of the 10 years prior to August 2021 was conducted to assess the symptoms and impacts of CRG, alongside the use of SF-36 and HAQ-DI in previous clinical trials. The review results contributed to an initial conceptual model of signs, symptoms and impacts of CRG. This model was then refined using concept elicitation interviews (CEI) conducted with patients who have clinically confirmed CRG (≥3 gout flares within 18 months of screening; or presence of ≥1 tophus; or current diagnosis of gouty arthritis [defined as joint damage due to gout]). Interviews contained open-ended questions and patients were asked about duration, frequency, and severity for each concept; bothersome impacts were rated on a scale of 0–10. The refined model was then assessed against SF-36 and HAQ-DI to determine their suitability for evaluating disease burden in patients with CRG.
Results: Findings from the literature review identified the following commonly referenced symptoms, signs and impacts of gout that served as the basis of the draft conceptual model: bodily pain, joint swelling/inflammation, tophi, joint pain, joint tenderness, anxiety, depression, sleep effects, and work effects. Impacts were organized into five domains: activities of daily living (e.g., difficulty dressing), emotional (e.g., anxiety), physical (e.g., decreased mobility), social (e.g., stigma), and work/school (e.g., productivity). Twenty patients were interviewed. Most were male (70%) and non-Hispanic white (55%), with a mean (standard deviation) age of 55.9 (±12.1) years. Most patients (60%) reported having multiple (>3) and/or severe gout flares within the past 6 months, and most commonly 1–3 tophi (45%). The most frequently reported signs and symptoms included bodily pain, joint swelling, and tenderness (90% each). Others included joint pain (80%), joint stiffness (70%), and tophi (70%). Joint pain was rated as the most bothersome symptom (mean = 9.1). The most frequently reported impacts were difficulty climbing one or several flights of stairs (100% each), followed by completing chores, running errands and shopping, climbing five steps, putting on shoes, walking outdoors on flat ground, and emotional impacts (95% each). Impacts reported varied depending on the affected joints. The most bothersome impact reported was walking outdoors (mean = 9.6). All concepts discussed in the interviews were reviewed to determine whether they reflected the items included in SF-36 and HAQ-DI. Each assessed item from the two instruments was reported as relevant by at least 25% of participants and thus mapped consistently to concepts elicited by participants. Results of the CEI were used to revise the conceptual model (Figure 1).

Conclusion: Symptoms and associated impacts of CRG on HRQoL are multi-faceted, revealing a burden of disease that affects most aspects of a patient's life (Figure 1). Based on the interview data, all assessed items of SF-36 and HAQ-DI mapped directly to the domains and concepts included in the conceptual model, providing evidence that both questionnaires are suitable for assessing the burden of CRG.

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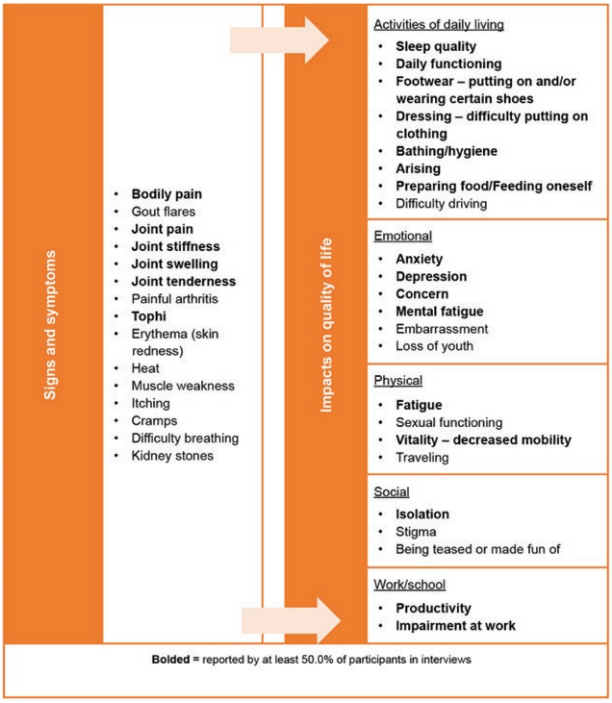


Figure 1.

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POS0529 USING SOCIAL MEDIA CONVERSATIONS TO UNDERSTAND PATIENT CARE: FACTORS DRIVING PROACTIVE VS REACTIVE MANAGEMENT OF GOUT

Keywords: Gout, Patient reported outcomes, Quality of care

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Background: To understand the needs of a particular community, it is imperative to actively listen to and interpret the patient experience. We used a proprietary artificial intelligence (AI) analytics engine that uses natural language processing to evaluate social media conversations in online gout communities. Gout is a chronic disease defined by uric acid crystal deposits which induce painful arthritis flares/flare-ups [1]. Managing gout can be characterized by two approaches: proactive and reactive management. Proactive management refers to scheduled, prophylactic care (e.g., regular doctor visits, treating underlying illness), whereas reactive management is spontaneous care driven by symptom onset (e.g., urgent care/walk-in clinic visits). The ideal management strategy is debated. Subspecialty groups recommend a proactive "treat-to-target" strategy focused on uric acid. The American College of Physicians recommends "treat-to-symptom control" without a "treat-to-uric acid-target" strategy. We assessed patient views on each to improve our understanding of these management methods.

Objectives: The current study aimed to identify gout symptoms associated with reactive management. We also wanted to contrast the sentiment of online gout community conversations when describing proactive vs reactive therapeutic experiences.

Methods: We evaluated 2 social media sources: a private Facebook group, The Gout Support Group of America (1000+ members, 99 countries), which had 50,000 posts/comments gathered in 2021-2022; and a public subreddit (r/gout) (9000+ members) with 125,000 posts/comments from 2011-2022. Our AI engine first tagged all posts/comments discussing proactive or reactive care experiences. Entity recognition was then used to identify the most frequently mentioned clinical findings in conversations by care type. We then fit a logistic regression model in which clinical finding mentions predicted care type. To characterize the general sentiment of conversations, the engine scored all posts/comments from –1 (most negative) to 1 (most positive) using a pretrained sentiment tagger.

Results: Flares, pain, uric acid, and swelling were the most frequently mentioned in both proactive and reactive conversations. Reactive care gout conversations (n = 1253 posts/comments from 624 users) were associated with a significantly higher probability of mentioning 'pain' and 'swelling' and a significantly lower probability of mentioning 'uric acid' than were proactive care conversations (n = 1205 posts/comments, 521 users). Mentioning 'flares' did not significantly impact the probability of mentioning either care type. Sentiment analysis showed that reactive care statements had a significantly lower mean sentiment score; indicating discussions about reactive care experiences tended to be more negative than those about proactive care.

Conclusion: In analyzing gout social media posts, we found that flares, pain, swelling, and concerns related to uric acid were primary motivators for individuals seeking gout care. Conversations mentioning 'pain' were twice as likely to mention reactive care compared to proactive gout conversations. Analysis also showed that reactive care gout conversations tended to be more negative, supporting the position that proactive management may be more beneficial for individuals with gout overall. This type of information can be used to identify and address patients' areas of concern or dissatisfaction. Future work should continue exploring these patient-reported perspectives and experiences so clinicians, caregivers, and patients can better understand and guide care-based management decisions.

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Our clients are pharmaceutical and biotechnology companies including, but not limited to Horizon Therapeutics, Chiesi Global Rare Disease, Novartis, Harmony Biosciences, and Avadel. TREND Community: owner, E. Robert Wassman Grant/research support from: Our clients are pharmaceutical and biotechnology companies including, but not limited to Horizon Therapeutics, Chiesi Global Rare Disease, Novartis, Harmony Biosciences, and Avadel. TREND Community: employee.

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POS0530 ANALYSIS OF APPROPRIATE DURATION OF COLCHICINE PROPHYLAXIS TO MAXIMIZE THE PERSISTENCE OF XANTHINE OXIDASE INHIBITORS AS THE FIRST-LINE URATE LOWERING THERAPY IN PATIENTS WITH GOUT USING THE KOREAN HEALTH INSURANCE REVIEW AND ASSESSMENT SERVICE DATABASE: DOES 6 MONTHS' DURATION MATTER?

Keywords: Gout, Crystal arthritis, Epidemiology

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Background: International guidelines for gout recommend at least 3 to 6 months of prophylaxis against gout attack for gout patients who start urate lowering therapy (ULT) [1-3], but there is lack of strong evidences supporting whether up to 6 months duration of gout flare prophylaxis is associated with the improvement the long-term adherence of ULT in real-world clinical settings.
Objectives: We aimed to investigate the appropriate duration of colchicine prophylaxis to maximize the long-term persistence of xanthine oxidase inhibitors (XOIs) as the first-line ULT in patients with gout using nationwide claim database. In particular, we attempt to compare which one is more effective in adherence to ULT between 6 months and 3 months duration of colchicine prophylaxis.
Methods: This is a nationwide population-based retrospective cohort study using the Korean Health Insurance Review and Assessment (HIRA) database. Gout patients ≥ 20 years who newly initiated allopurinol or febuxostat as the first-line ULT from July 2015 and June 2017 and received XOIs for ≧6 months were analyzed. Patients were followed-up to Jun 2019. Persistence of ULT was defined as continuation of allopurinol or febuxostat without an interruption for a period longer than 60 days (permissible gap), the time duration from the index date to the discontinuation of ULT. XOIs persistence was compared according to the 6 months of duration of colchicine prophylaxis such as (1) ≥6 months and proportion of days covered (PDC) ≥0.8 ("≥ 6 months group") and (2) <6 months or PDC <0.8 ("< 6 months group"). For additional subgroup analysis, we also compared the persistence of XOIs according to the 3 months of duration of colchicine prophylaxis ("≥ 3 months group" vs "< 3 months group").
Results: A total of 43,926 eligible gout patients (colchicine prophylaxis ≥6 months: n=2,784, colchicine prophylaxis <6 months: n=41,142 and colchicine prophylaxis ≥3 months: n=3,333, colchicine prophylaxis <3 months: n=40,593) were identified in HIRA database. The majority was male (82.6%) and the mean age was 58.6 years. Allopurinol (65.2%) was more frequently prescribed than febuxostat (34.8%). During the study period, 23,475 (53.4%) patients stopped XOIs. XOIs discontinuation occurred in 1,498 (53.8%) and 21,977 (53.4%) gout patients in the ≥ 6 months group and < 6 months group, respectively. In addition, 1,777 (53%) and 21,698 (53.5%) patients in the ≥ 3 months group and < 3 months group stopped XOIs, respectively. In multivariable Cox regression models revealed that colchicine prophylaxis ≥6 months did not significantly reduce the risk for discontinuation of XOIs compared with colchicine prophylaxis <6 months (HR=0.961, p=0.139). Otherwise, colchicine prophylaxis ≥3 months was significantly associated with a lower risk of non-persistence to XOIs after adjusting confounding factors (HR=0.95, p=0.041).
Conclusion: Our data suggest that at least 3 months of colchicine prophylaxis may be more appropriate than at least 6 months' duration in terms of maximizing the persistence of XOIs in gout patients.
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Disclosure of Interests: None Declared.
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POS0531 EVALUATION OF THE KNOWLEDGE OF INTERNAL MEDICINE PHYSICIANS, FINAL-YEAR MEDICAL STUDENTS AND RHEUMATOLOGISTS REGARDING THE DIAGNOSIS AND MANAGEMENT OF GOUT IN SWITZERLAND

Keywords: Quality of care, Gout

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Background: Gout is the most common inflammatory rheumatism in adults [1]. Its prevalence and incidence have doubled in the last two decades. However, it is commonly undertreated despite numerous therapeutic options and the availability of international recommendations.
Objectives: To explore the reasons why gout is undertreated, we aimed to assess and compare the knowledge of primary care physicians (internists), rheumatologists, and final-year medical students regarding the diagnosis and management of gout in Switzerland with mandatory continuing education for physicians.
Methods: We conducted a multicenter cross-sectional study between December 2021 and August 2022. All primary care physicians and hospital internists practicing in academic hospitals in Switzerland, rheumatology specialists, and final-year medical students from all 6 Swiss faculties of medicine were invited to complete an online questionnaire based on the EULAR 2016, 2018, and ACR 2020 recommendations. This multiple choice questionnaire consisted of 28 questions including 68 positive answers (since more than one positive answer was possible for each question) on gout diagnosis, management of an acute attack, indication to start hypouricaemic treatment and management of patients with renal failure. Participants were considered as having responded successfully to the questionnaire with at least 2/3 (45) correct answers.
Results: In total, we received approval for participation from 16 academic hospitals, 4 faculties of medicine, and the Swiss Society of Rheumatology. We included a total of 378 participants: 97 medical students, 210 internists and 71 rheumatologists.

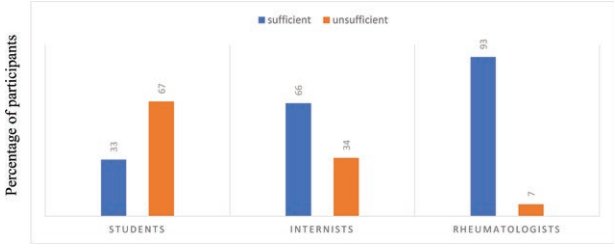


Figure 1. Percentage of participants who responded successfully to the questionnaire

Only 33% of final-year medical students demonstrated sufficient knowledge about how to manage gout, compared to 66% of internists and 93% of rheumatologists. 55%, 48% and 14% in the student, internist and rheumatologist groups respectively did not know what type of crystals were found during a gout attack. The majority of participants in the different groups were familiar with at least one of the treatments that should be used for the management of a first acute attack of gout. Most participants in all 3 groups did not know the indications for initiation of hypouricaemic therapy. 80% of students, 62% of internists and 18% of rheumatologists were unaware of the target urate serum level to aim for when introducing hypouricaemic therapy and more than three-quarters of the students and internists thought that 300 mg was the maximal possible dose of allopurinol.
Conclusion: These results suggest that knowledge about the diagnosis and management of gout is sub-optimal among final-year medical students and primary care physicians across Switzerland. Although most rheumatologists demonstrated good knowledge about the management of gout, a surprising proportion did not, despite being experts in this field. Knowledge about the diagnosis and management of gout needs to be improved.
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Infection-related rheumatic diseases

POS0532 GLOBAL ULTRASOUND SYNOVITIS SCORE MAY REFLECT DEVELOPMENT OF CHRONIC POST-CHIKUNGUNYA RHEUMATISM

Keywords: Infection-related RMDs, Outcome measures, Ultrasound

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Background: Chronic musculoskeletal (MSK) symptoms such as arthralgia and arthritis develop in up to half of patients after acute chikungunya virus (CHIKV) infection. While MSK complaints are common during the acute infection, chronic post-CHIKV rheumatism represents a more severe outcome and is usually assessed by joint counts, laboratory markers and patient-reported outcomes (PROs). Ultrasound (US) may be a practical tool for predicting and confirming the development of chronic CHIKV.
Objectives: To evaluate the clinical relevance of MSKUS findings in post-chikungunya rheumatism.
Methods: 80 patients with acute CHIKV infection were enrolled in a prospective cohort study in Jaén, Peru. Clinical exam, US scans using grey-scale and power Doppler (PDUS), and serum inflammatory markers were performed at inclusion and at 3-month follow-up. Patients completed the RAPID3 outcome assessment and a MSK stiffness questionnaire. Joint counts and PDUS scans included 20 pairs of joints. Global synovitis and tenosynovitis scores were calculated following the EULAR-OMERACT recommendations for rheumatoid arthritis (GLOESS).
Results: 59 patients (mean age 35 years, 68% female) were assessed both in the acute infection stage and at 3-month follow-up. 21 patients (35%) met strict criteria for defining chronic CHIKV rheumatism with a mean 4.4 (±2.2) tender joints and RAPID3 scores >6. In the acute infection phase, global PDUS synovitis and tenosynovitis scores correlated moderately with tender joint count and with pain severity, joint stiffness and RAPID3 scores, but were not strongly predictive of patients who went on to develop chronic arthralgia. After 3 months, global PDUS synovitis scores correlated more strongly with tender joint count (r=0.53, p<0.0001), pain severity (r=0.60, p<0.0001), joint stiffness (r=0.53, p<0.0001) and RAPID3 scores (r=0.60, p<0.0001) (Table 1).
Conclusion: Global PDUS synovitis and tenosynovitis scores may be an objective measure of disease severity in patients developing chronic CHIKV rheumatism. Further validation with longer-term follow-up is needed.

Table 1. Correlation of synovitis and tenosynovitis PDUS scores with clinical examination and patient-reported outcomes (n=59).

Period	Assessment	Variable	Synovitis correlation	P-value	Tenosynovitis correlation	P-value
Inclusion	Clinical exam	Tender joint count	0.35	0.0068	0.30	0.0210
	MSK stiffness	Severity score	0.41	0.0011	0.36	0.0048
	RAPID3	Disability index	0.39	0.0024	0.33	0.0119
		Pain severity	0.36	0.0052	0.29	0.0277
		Patient's global health	0.35	0.0060	0.21	0.1045
		Overall RAPID3 score	0.42	0.0010	0.31	0.0187
Month 3	Clinical exam	Tender joint count	0.53	<.0001	0.52	<.0001
	MSK stiffness	Severity score	0.54	<.0001	0.62	<.0001
	RAPID3	Disability index	0.48	0.0001	0.35	0.0070
		Pain severity	0.60	<.0001	0.56	<.0001
		Patient's global health	0.56	<.0001	0.59	<.0001
		Overall RAPID3 score	0.60	<.0001	0.57	<.0001

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POS0533 RISK OF SEVERE INFECTIONS IN IMMUNE MEDIATED INFLAMMATORY DISEASES WITH IMMUNOGLOBULIN DEFICIENCY UNDER RITUXIMAB THERAPY

Keywords: Infection-related RMDs, Adaptive immunity, bDMARD

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Background: Rituximab (RTX) is effective in treating immune-mediated inflammatory diseases (IMID). Hypogammaglobulinemia may occur under RTX and may increase infection risk.
Objectives: Since data are controversial, we evaluated the risk of severe infection in patients with IMID and hypogammaglobulinemia under RTX therapy.
Methods: We conducted a retrospective single-center study retrieving all patients treated with RTX for IMID. We calculated the incidence of RTX-induced immunoglobulin (Ig) deficiency, the type of Ig deficiency, the incidence of severe infection, and risk factors for severe infection.
Results: 311 patients were analyzed. Mean follow-up was 62.6 months. Exposure was 1623.7 patient-years. 15% of patients developed at least 1 severe infection. Incidence rate was 2.77/100 PY. 29 patients had prevalent Ig deficiency before being treated with RTX. 68 patients developed hypogammaglobulinemia, mainly for IgM (12%) and IgG (8%). Severe infection rate was higher in patients with prevalent Ig deficiency (RR 1.73; 95% CI 0.85-3.53), with significant difference in survival model (Log-Rank test: p=0.033). On the other hand, no excess risk of infection was observed in patients developing Ig deficiency under RTX in univariate analysis (RR 0.68; 95% CI 0.31-1.47) or in survival analyses after adjustment for confounding factors (type of IMID (RA versus other IMID), cumulative dose of RTX, presence of chronic pulmonary comorbidities, use of an immunosuppressive drug at inclusion, and mean dose of GCs collected at each cycle of RTX during follow-up) (Log-Rank test: p=0.399). Chronic lung disease and glucocorticoids (GCs) use during follow-up were associated with an increased risk of severe infection.
Conclusion: We did not observe an increased risk of severe infection in RTX-induced Ig deficiency. However, we found an increased risk of severe infection in case of prevalent Ig deficiency prior to RTX. In case of Ig deficiency, RTX management should be discussed on a case-by-case basis, according to an individual assessment of the infectious risk, especially when GCs therapy is used and chronic lung diseases are present.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0534 PREDICTORS OF SERIOUS INFECTIONS IN RHEUMATOID ARTHRITIS – A PROSPECTIVE BRAZILIAN COHORT

Keywords: Real-world evidence, Rheumatoid arthritis, Infection-related RMDs

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Background: Infectious intercurrences increase mortality and morbidity and often limit immunosuppressive treatment in rheumatoid arthritis (RA) patients [1].The risk of infection in this population may be influenced by factors related to treatment, the characteristics of rheumatic disease and the clinical and social conditions of patients [2].
Objectives: This study aims to evaluate the incidence and factors related to the occurrence of serious infections, defined as the need for hospitalization or the use of intravenous antibiotics for the treatment, among patients with rheumatoid arthritis in Brazil.
Methods: We analyzed data from the REAL [3], a prospective observational study, that evaluated Brazilian RA patients, with clinical and laboratory data

collected over a year in eleven tertiary health care centers. Were included patients with 18 years or older, who fulfilled classification criteria for RA and were previously followed up in rheumatology services for at least 6 months prior to inclusion. Exclusion criteria was the absence of information regarding the occurrence of infections in two or more visits. Univariate and multivariate analyses were performed from the adjustment of the logistic regression model *Generalized Estimating Equations* (GEE), with the primary outcome being the occurrence of serious infection. We assessed the corticosteroid dose that was most associated with the occurrence of serious infections, maximizing sum of sensitivity and specificity.

Results: 841 patients were included with an average follow-up time of 11,2 months (SD 2,4). Eighty-nine serious infections occurred, corresponding to 13 infections per 100 patient-years. The association between corticosteroid use and severe infections was dose-dependent until daily doses equal to or higher than 15 mg of prednisone (or equivalent) in which the highest association was found. Pulmonary fibrosis, chronic kidney disease (CKD) and central nervous system disease increased the chances of serious infection by 3.2 times (95% CI: 1.5 to 6.9), 3.6 times (95% CI: 1.2 to 10.4) and 2.4 times (95% CI: 1.2 to 5.0), respectively. The use of corticosteroids in moderate doses increased the chances by 5.4 times (95% CI: 2.3 to 12.4), and for each increase of 1 unit in the health assessment questionnaire (HAQ), the chance increased 60% (95% CI: 20 to 120%).

Table 1. Multivariable analysis

	Coef.	Value-p	OR	95% CI
Time (Visit)	0,81	<0,001	2,2	(1,8-2,8)
Pulmonary fibrosis	1,17	0,003	3,2	(1,5-6,9)
Chronic kidney disease	1,27	0,02	3,6	(1,2-10,4)
CNS Diseases	0,89	0,015	2,4	(1,2-5,0)
Prednisone (or equivalent) dose (≥ 15 mg)	1,68	<0,001	5,4	(2,3-12,4)
HAQ	0,46	0,005	1,6	(1,2-2,2)

Legend: Coef - coefficients. OR - Odds Ratio. 95%CI - 95% confidence interval. CNS - Central nervoussystem diseases. HAQ - health assessment questionnaire

Conclusion: We observed a high incidence rate of serious infections in this Brazilian cohort compared with cohorts from developed countries. The factors that were independently associated with them were neurological and pulmonary comorbidities, reduced kidney function, use of corticosteroids in moderate doses and reduced functionality. These findings may affect therapeutic decisions in RA patients.

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POS0535 IS THERE A DECREASED RISK OF DEVELOPING CF ARTHROPATHY IN CF PATIENTS UNDERGOING TREATMENT THAT TARGETS THE F508DEL MUTATION?

Keywords: Inflammatory arthritides, Lungs, Ultrasound

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Background: Cystic fibrosis (CF) is characterized by mutations within the CFTR (cystic fibrosis transmembrane conductance regulator) gene that result in a defect of the chloride transporter protein in different organs, particularly in the lung. Musculoskeletal symptoms have been reported in up to 29% of CF patients [1], most frequently as recurrent episodes of mono- or polyarthritis in joints of hands and feet. Recently, potent CFTR modulator therapies targeting the F508del mutation in CF have become available (i.e., Trikafta© - consisting of a triple combination of elexacaftor, tezacaftor, and ivacaftor) that increase CFTR protein availability and function at cell surfaces.

Objectives: To characterize musculoskeletal symptoms in a cohort of consecutive CF patients.

Methods: 25 CF patients were enrolled in this monocentric, prospective, and cross-sectional cohort study. Rheumatologic evaluation included clinical and laboratory parameters. Data were analyzed by covariance (ANCOVA) models, using the general linear model approach. Correlation analyses were performed calculating nonparametric Spearman correlation rank coefficients.

Results: Baseline characteristics are outlined in Table 1. 22/25 CF patients were under CFTR modulator treatment with a mean treatment duration of 13 + 4 months. Arthralgias and myalgias were reported in 48% and 20% of patients, respectively. Arthritis, mainly involving small joints, was clinically detected in 6/25 (24%) patients and confirmed by ultrasound (US) in 3/6 patients. Self-reported myalgias, but not self-reported arthralgias, were significantly associated with the presence of swollen joints ($r = 0.7452$, $p < 0.0001$), tender joints, ($r = 0.6674$, $p = 0.0003$), a positive squeeze test ($r = 0.5898$, $p = 0.0019$) and morning stiffness ($r = 0.6556$, $p = 0.0004$) (Table 1). Disease activity as assessed by the Simplified Disease Activity Index (SDAI) was moderate (mean 18 + 3). CCP and rheumatoid factor (RF) were detected in one patient not on CFTR modulator therapy (with US synovitis of PIP). Two patients on CFTR modulator therapy tested positive for RF. Another patient was seronegative but synovitis was confirmed by US.

Of note, longer duration of CFTR modulator therapy was significantly associated with a lower number of tender joints ($r = -0.410$ $p = 0.054$), swollen joints ($r = -0.400$, $p = 0.048$) and a lower CRP ($r = -0.509$, $p = 0.048$) (Figure 1).

Conclusion: The current cohort study confirms that musculoskeletal symptoms are frequent in adult CF patients. Self-reported myalgias were significantly associated with arthritis mainly involving small joints. Interestingly, longer duration of CFTR modulator therapy was associated with a decreased number of tender and swollen joints in line with the assumption that amelioration of mucosal airway inflammation may decrease the risk of developing CF arthropathy.

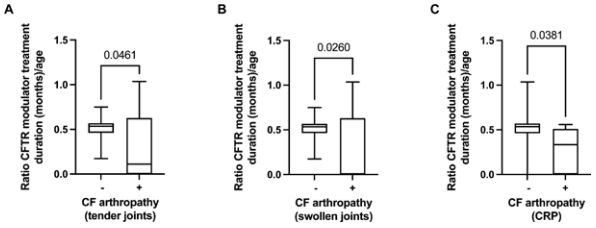
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Table 1. Baseline characteristic of cystic fibrosis (CF) patients, PGA = Patient global assessment, RF = Rheumatoid factors

	CF patients n = 25	CF +Arthropathy n = 6	CF - Arthropathy n = 19	P
Age (years), mean (±SD)	26 ± 5	28 ± 7	25 ± 3	NS
BMI (kg/m2), mean (±SD)	23 ± 4	24 ± 5	22 ± 3	NS
Female sex, n (%)	13/25 (52)	3/6 (50)	10/19 (53)	NS
CF disease characteristics				
PGA (0-10) Tiredness, mean (±SD)	2.6 ± 1.7	2.8 ± 1.5	2.2 ± 1.6	NS
Productive cough ejection > 1 Tablespoon, n (%)	3/25 (12)	2/6 (33)	1/19 (5)	0.038
CFTR modulator n (%)	22/25 (88)	3/6 (50)	0/19 (0)	0.001
Clinical joint characteristics				
PGA (0-10) Pain, mean (±SD)	1.9 ± 2.4	3.2 ± 0.9	0.8 ± 0.8	0.001
Arthralgia, n (%)	12/25 (48)	5/6 (83)	7/19 (37)	0.047
Myalgia, n (%)	5/25 (20)	4/6 (67)	1/19 (5)	0.001
Swollen Joint, n (%)	5/25 (20)	5/6 (83)	0/19 (0)	<0.0001
Tender Joint, n (%)	6/25 (24)	6/6 (100)	0/19 (0)	<0.0001
Morning stiffness, n (%)	6/25 (24)	3/6 (50)	3/19 (16)	NS
Squeeze test, n (%)	2/25 (8)	2/6 (33)	0/19 (0)	0.008
ACPA, n (%)/	1/25 (4)/	1/6 (17)/	0/19 (0)/	NS/ 0.001
RF, n (%)	3/25 (12)	3/6 (50)	0/19 (0)	
Laboratory parameters				
ESR (mm/h), mean (±SD)	9 ± 11	22 ± 14	5 ± 4	0.045
CRP (mg/L), mean (±SD)	4.2 ± 5.1	8.3 ± 3.4	2.8 ± 4.7	0.014

Fig 1



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Disclosure of Interests: None Declared.
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COVID-19

POS0537

SAFETY OF BIVALENT SARS-COV-2 VACCINES AS A SECOND BOOSTER DOSE IN ARTHRITIS PATIENTS ON IMMUNOSUPPRESSIVE THERAPIES

Keywords: Vaccination/immunization, Safety, COVID

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Background: Safety and efficacy of updated bivalent vaccines, containing both the original vaccine variant of SARS-CoV-2 Spike and either Omicron variants BA.1 or BA.4/5, are of particular interest in arthritis patients on immunosuppressive therapies. With the continuous emergence of new viral variants, it is important to evaluate whether updated vaccines induce more adverse events in this patient group.
Objectives: To examine if a second booster dose with updated bivalent vaccine increases the risk of adverse events, compared to the first booster dose with monovalent vaccines.
Methods: The prospective Nor-vaC study investigates vaccine responses in patients with immune mediated inflammatory diseases using immunosuppressive therapies (1). The present analyses included arthritis patients who received two booster doses. Patients received available vaccines according to the Norwegian vaccination program. The current recommendation in the Norwegian arthritis population is a three-dose primary vaccination series followed by two booster doses. Adverse events following vaccines doses were self-reported through questionnaires. Adverse events following the first (monovalent) and second (bivalent) booster were compared with McNemar's test.
Results: Between 7th of July 2021 and 6th of December 2022 a total of 243 arthritis patients (127 rheumatoid arthritis, 65 psoriatic arthritis, 51 spondyloarthritis) on immunosuppressive therapies (Table 1) received a first, monovalent (BNT162b2, mRNA-1273) and a second, bivalent booster dose (BNT162b2 (WT/OMI BA.1), mRNA-1273.214, BNT162b2 (WT/OMI BA.4/BA.5)). Adverse events were recorded within 2 weeks in all patients (Figure 1). In total, 45 vs 49 (19% vs 20 %) patients reported any adverse event after a second, bivalent booster dose, compared to the first, monovalent booster, respectively. There was no significant difference in adverse events overall (p= 0.57). The most common adverse events after the second booster were pain at injection site (12 %), flu-like symptoms (9 %) and headache (6 %). No new safety signals emerged. A total of 15 (6 %) patients reported a disease flare after receiving the second, bivalent booster, compared to 21 (8 %) after the first, monovalent booster.
Conclusion: There was no difference in adverse events between the monovalent, first booster, and the bivalent, second booster, indicating that bivalent vaccines are safe in this patient group.

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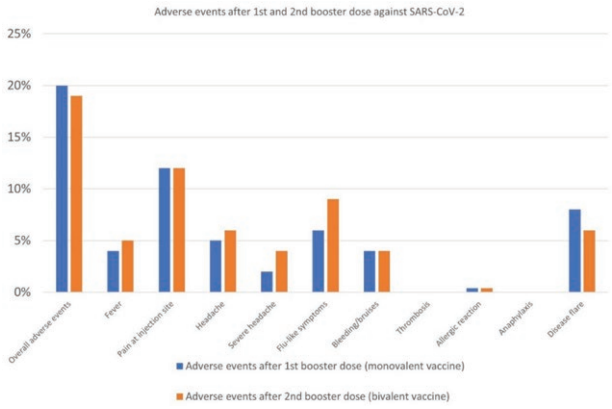


Figure 1. Adverse events after bivalent vaccine as a 2nd booster dose compared to a monovalent vaccine as a 1st booster dose.

Acknowledgements: We thank the patients and health-care workers who have participated in the Norwegian study of vaccine response to COVID-19. We thank the patient representatives in the study group, Kristin Isabella Kirkengen Espe and Roger Thoresen. We thank all study personnel, laboratory personnel, and other staff involved at the clinical departments involved, particularly Synnøve Aure, Margareth Sveinsson, May Britt Solem, Elisabeth Røssum-Haaland, and Kjetil Bergsmark.
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Table 1. Demographic characteristics and immunosuppressive medication in patients receiving a 1st monovalent and a 2nd bivalent booster dose.

Characteristics	Patients, n (%)
Total	243
Age (years), median (IQR)	61 (52-67)
Female	152 (63)
Immunosuppressive medication	
TNFi mono[a]	75 (31)
TNFi combo[a+b]	72 (30)
Methotrexate	62 (26)
Rituximab	9 (4)
IL-inhibitors[c]	6 (2)
JAK-inhibitors[d]	11 (5)
Other[e]	8 (3)
1st booster	
BNT162b2	106 (44)
mRNA-1273	137 (56)
2nd booster	
BNT162b2 (WT/OMI BA.1)	65 (25)
BNT162b2 (WT/OMI BA.4/BA.5)	120 (47)
mRNA-1273.214 (WT/OMI BA.1)	58 (23)

Results in n (%) unless otherwise specified.[a]Tumor necrosis factor inhibitors: infliximab, etanercept, adalimumab, golimumab, certolizumab pegol.[b]Combination therapy: methotrexate, sulfasalazine, leflunomide, azathioprine.[c]Interleukin inhibitors: tocilizumab, secukinumab.[d]Janus kinase inhibitors: filgotinib, baricitinib, upadacitinib, tofacitinib.[e]Other: abatacept, sulfasalazine, leflunomide, azathioprine.

POS0538

THE IMPACT OF IMMUNOMODULATING TREATMENT ON THE SEROLOGICAL IMMUNOGENICITY FOLLOWING THREE DOSES OF COVID-19 VACCINE AND PERSISTENCE OF IMMUNOGENICITY OF TWO VACCINE DOSES IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES - A SWEDISH STUDY (COVID19-REUMA)

Keywords: Vaccination/immunization, COVID, Adaptive immunity

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Background: Data on serological immunity after three doses and the long-term immunogenicity (persistence) of COVID-19 vaccine in patients with inflammatory rheumatic diseases (IRD) treated with different immunomodulating drugs are still limited.

Objectives: To elucidate if 1) a third dose COVID-19 vaccine improves antibody responses, compared to two doses, in patients with IRD treated with biologic or targeted synthetic DMARD (b/tsDMARDs) treatment given as monotherapy or in combination with conventional synthetic DMARDs (csDMARDs) compared to controls, and 2) the persistence of antibody response after two doses of COVID-19 vaccine in IRD patients.

Methods: Antibody levels to two antigens representing Spike full length protein and Spike S1 and a Nucleocapsid C-terminal fragment (used to confirm previous COVID-19 infection) were measured in serum samples collected 2-12 and 21-40 weeks after the second vaccine dose and 2-12 weeks after the third dose using a multiplex bead-based serology assay. A sufficient antibody response (seropositivity) was defined as having antibodies over the cut-off level for both spike antigens (1). WT (wild type) anti-Spike IgG and omicron BA.1 and BA.2 variants were measured. Patients with IRD receiving immunomodulating treatment, regularly followed at a rheumatology department and a group of controls were recruited from five Swedish region.

Results: In total, 323 of 414 patients with IRD and 36 controls who received three vaccine doses participated in this part of the study. Following treatment groups were included: rituximab (n=118; 68% female; mean age 67 years), abatacept (n=18; 72% female; mean age 64 years), IL6r inhibitors (n=60; 73% female; mean age 64 years), JAK-inhibitors (n=44; 80% female, mean age 52 years), TNF-inhibitors (n=59; 70% female; mean age 47 years;), IL12/23/17 inhibitors (n=24; 46% female; mean age 54 years) and controls (n=36; 75% female, mean age 51 years). b/ts DMARD treatment was given as monotherapy or in combination with csDMARD, methotrexate (MTX) being the most frequently used csDMARD (32.5%). Compared to results after two vaccine doses, proportion (%) of seropositivity after three vaccine doses increased significantly in groups rituximab +/- DMARD (p=0.003 and p=0.004, respectively), IL6r inhibitors +DMARD (p=0.02), and abatacept+DMARD (p=0.01). However, the proportion of seropositivity after three vaccine doses was still significantly lower in rituximab treated patients (52%) compared to other treatment groups or controls (p<0.001) (Figure 1A/B). Antibody response to WT, omicron sBA.1 and sBA.2 showed similar pattern with the lowest levels among patients treated with rituximab. When antibody response was compared between 2-12 weeks and 21-40 weeks after second dose, the proportion of seropositive rituximab treated patients decreased from 34.9 % to 32.6%. All patients with JAK inhibitors and with JAK-inhibitors and IL6r-inhibitors seropositive 21-40 weeks after the second vaccine dose. Patients treated with other bDMARDs were not included in this analysis due to limited number participants.

Conclusion: In this Swedish study including IRD patients receiving different b/t DMARDs, a sufficient immunogenicity of the third dose of COVID-19 vaccine was observed in all treatments with exception for rituximab. However, the increased proportion of seropositivity after the third COVID-19 vaccine doses in rituximab and other patients with insufficient response to two doses including response to the omicron variants, supports the current recommendations on additional booster doses. The immunogenicity of two vaccine doses was preserved to 40 weeks in majority of patients treated with different immunomodulating treatment with exception for rituximab.

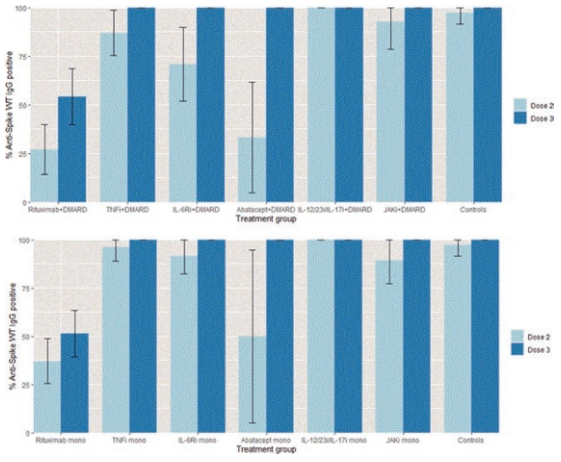


Figure 1.

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POS0539

CELLULAR AND HUMORAL IMMUNOGENICITY OF THE NEOANTIGEN S1 FROM SARS-COV-2 VACCINES IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES

Keywords: Adaptive immunity, Inflammatory arthritides, COVID

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Background: Data on cellular and humoral immunogenicity triggered by SARS-CoV-2 vaccines in patients with autoimmune rheumatic diseases (ARDs) are limited. While current vaccine efforts have focused on the induction of neutralizing antibodies against SARS-CoV-2, T-cell immunity may also provide protection against infection. Experimental data suggest that CD8+ T cell responses may have a protective role in the presence of decreasing or sub protective antibody titers [1].

Objectives: The aim of this project is to describe the serological and T cell responses to the third dose of vaccine (either with BNT162b2 mRNA or ChAdOx1 nCoV-19 replication-deficient adenoviral vector vaccines) in a cohort of patients with ARDs (rheumatoid arthritis and spondyloarthropathies) treated with biologic therapies, to describe the impact of these treatments on vaccine response in this patient population. As a second objective, we will describe the characteristics of patients who did not present an adequate immunogenic response.

Methods: Case-control study. We studied in 79 patients with ARDs and in 31 healthy controls, anti-SARS-CoV-2 specific interferon-gamma (IFN-γ) production measured by IGRA between 8-12 weeks after the third dose of anti-SARS-CoV-2 vaccine. In addition, humoral response was measured by anti-S1 IgG antibody production measured by chemiluminescent microparticle immunoassay. Statistical comparison between categorical variables was performed by Fisher's or $\chi 2$ test. For quantitative variables by Kruskal-Wallis test or Mann-Whitney test.

Results: 79 patients with ARDs (48 women, 31 men; mean age 58±11.4) 43 (54%), with rheumatoid arthritis and 36 (45.6%) with spondyloarthropathies. 32 (49.5%) of them were on glucocorticoid treatment (mean dose 4.92 mg/day), 25

(31.6%) on methotrexate and 56 (70.9%) on anti-TNF. Post-vaccination results showed positive T-cell immune responses in 68 of 79 (86.1%) ARDs patients with mean IFN- γ anti-SARS-CoV-2 titers of 1,606.85 mUI/ml. 7 (8.9%) of ARDs patients showed negative IFN-γ SARS-CoV-2 levels, while 4 (5%) had borderline titers. 100% of patients with previous COVID 19 disease had positive cellular responses. Within the group of negative or borderline cellular responses, 7 of 10 were men (70%), with no significant differences in terms of diagnosis, comorbidities or immunosuppressive treatments used. In the control group, 100% presented positive cellular responses. Anti-Spike IgG antibodies were detectable in all patients with ARDs as in the control group.

Conclusion: Our preliminary data show that most patients with ARD were able to generate an adequate specific cellular response after vaccination against SARS-CoV-2, emphasizing the relevance of vaccination in this group. Specific antibody responses secondary to anti-SARS-CoV-2 vaccination were detected in all patients with ARD. Our data could support the relevance of these immune responses to personalize prevention, vaccination decision-making and treatment in this subgroup of patients.

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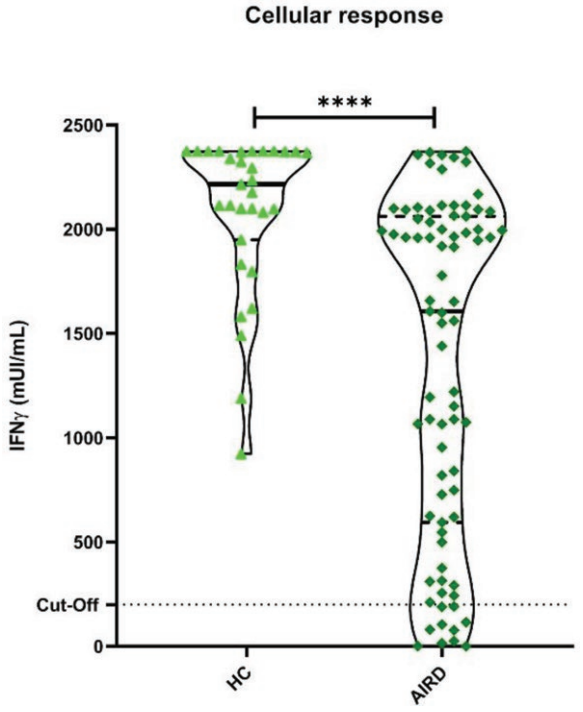


Figure 1. Specific anti-SARS-CoV-2-IFN- γ responses measured by IGRA. Dotted lines represent positivity cut-off: ≥200mUI/ml. HC: Healthy controls. AIRDs: Autoimmune rheumatic diseases.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2851

POS0540

PERFORMANCE OF COMMERCIAL SARS-COV-2 WILD-TYPE AND OMICRON BA.1 ANTIBODY ASSAYS COMPARED WITH PSEUDOVIRUS NEUTRALIZATION TESTS

Keywords: Diagnostic tests, COVID, Vaccination/immunization

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Background: Commercially available ELISA-based antibody tests are used to evaluate vaccination success against SARS-CoV-2 as recommended for immunocompromised and at-risk patients by medical committees in Germany and Austria [1,2], but it is unclear whether they correlate with neutralization of the Omicron variant.

Objectives: The objective was to compare the test performance of different ELISA-based SARS-CoV-2 wild-type or adapted Omicron BA.1 antibody test systems with wild-type and BA.1 virus neutralization as measured by pseudovirus neutralisation tests (pVNT).

Methods: 269 serum samples of a cohort of 44 non-immunosuppressed participants and 65 MTX-treated rheumatic patients taken before and after COVID-19 booster vaccinations were measured using COVID-19 antibody testing systems with wild-type and Omicron BA.1 antigens developed by three different manufacturers (surrogate virus neutralization test cPass, and binding antibody tests QuantiVac and SeraSpot), as well as with a pVNT. The pVNT was considered the gold standard for determining the presence and level of anti-SARS-CoV-2 antibodies.

Results: All three wild type ELISAs showed excellent test performance compared with wild type neutralization in pVNT. However, out of 56 samples without Omicron BA.1 neutralization in pVNT, 71.4% showed positive results in at least one and 28.6% in all three wild-type ELISAs at the manufacturer-defined cut-offs. Omicron ELISAs showed either decreased specificity (57.1% and 55.4% for binding ELISAs) or sensitivity (51.2% in cPass) compared to Omicron neutralization in pVNT. The proportion of any false positive results among all samples decreased from 26.5% before to 3.2% after booster vaccination, however binding antibody test specificities remained below 70%. Detailed results for all test systems can be found in Table 1 and Figure 1.

Conclusion: Decisions for booster vaccination or passive immunization of at-risk patients should not be based solely on antibody tests, because they do not indicate neutralization of Omicron as reliably as they did against wild-type.

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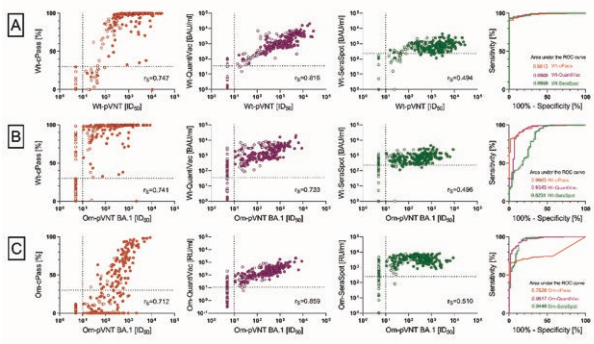


Figure 1. Scatter plot and ROC analysis of wild-type and Omicron antibody tests compared with wild-type and Omicron pVNT. Dotted horizontal and vertical lines mark manufacturer's cut-offs. Om, Omicron BA.1; r_S, Spearman's rank correlation coefficient; Wt, wild-type; white dots: measurement before first booster; dark dots: measurement after first booster

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Table 1. ELISA test performances with regard to pVNT results

Test comparison	At manufacturer's cut-off			At max. Youden index			At >99% specificity	
	Cut-off	Sensitivity [%]	Specificity [%]	Cut-off	Sensitivity [%]	Specificity [%]	Cut-off	Sensitivity [%]
A) Compared with Wt-pVNT								
Wt-cPass	≥ 30 %	90.8	100	> 30.4 %	90.8	100	> 30.4 %	90.8
Wt-QuantiVac	≥ 35.2 BAU/ml	98.8	72.2	> 109.8 BAU/ml	92.8	100	> 109.8 BAU/ml	92.8
Wt-SeraSpot	≥ 230 BAU/ml	90.4	100	> 180.5 BAU/ml	93.6	100	> 180.5 BAU/ml	93.6
B) Compared with Om-pVNT								
Wt-cPass	≥ 30 %	99.1	69.6	> 90.7 %	82.2	98.2	> 98.5 %	63.9
Wt-QuantiVac	≥ 35.2 BAU/ml	100	28.6	> 389.4 BAU/ml	90.6	85.7	> 3062 BAU/ml	29.6
Wt-SeraSpot	≥ 230 BAU/ml	95.8	58.9	> 281.0 BAU/ml	90.6	66.1	> 1278 BAU/ml	16.4
C) Compared with Om-pVNT								
Om-cPass	≥ 30 %	51.2	100	> 11.9 %	65.3	100	> 11.9 %	65.3
Om-QuantiVac	≥ 11.0 RU/ml	99.1	57.1	> 32.3 RU/ml	93.0	87.5	> 206.8 RU/ml	40.4
Om-SeraSpot	≥ 247 RU/ml	99.5	55.4	> 1139 RU/ml	93.0	87.5	> 4651 RU/ml	32.9

BAU, binding antibody units; Om, Omicron BA.1; pVNT, Pseudovirus neutralization assay; RU, relative units; Wt, wild-type

POS0541

INFLAMMATORY RHEUMATIC DISEASES (IRD) WITH ONSET AFTER SARS-COV-2 INFECTION OR COVID-19 VACCINATION: A COHORT STUDY FROM THE COVID-19 & ASD COLLABORATIVE STUDY GROUP

Keywords: COVID, Vaccination/immunization

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Background: A growing number of articles describe new-onset inflammatory rheumatic diseases (IRD) - including inflammatory joint diseases (IJD), polymyalgia rheumatica (PMR), connective tissue diseases (CTD) and vasculitis - in close temporal association with SARS-CoV-2 infection (1). On the other hand, also the exposure to vaccines may elicit autoimmunity and reports of IRD following vaccination with anti-COVID-19 vaccines appeared in literature since the earliest phases of the vaccination campaign (2,3).

Objectives: The aim of the present study was to contribute to the knowledge on the spectrum of new-onset post-COVID-19 and post-vaccine IRD with a comparative analysis from a large multicentric observational study.

Methods: In the present cohort study, we collected consecutive cases of IRD or acrosyndrome encountered during routine clinical practice from November 2021 to October 2022 (12 months) satisfying one of the following inclusion criteria: a) onset of the rheumatic manifestations within four weeks from SARS-CoV-2 infection, confirmed by nasopharyngeal swab OR, b) onset of the rheumatic manifestations within four weeks from the administration of one of the COVID-19 vaccines approved for administration in Italy during the collection period. Exclusion criteria were a past history of any IRD or acrosyndrome.

Results: A total of 270 cases were entered in the database. Three records were excluded because identified as mechanical pain (n = 1) or fibromyalgia (n = 2). The final analysis cohort comprised a total of 267 patients, of which 122 (45.2%) patients in the post-COVID-19 (age 54 ± 17 years, 69.7% females) and 145 (54.8%) patients (age 58 ± 16 years, 66.2% females) in the post-vaccine cohorts. Mean delay between COVID-19 diagnosis or vaccine administration and rheumatic manifestations development was 14.5 ± 7.8 vs 13.9 ± 8.5 days, respectively (p = 0.59). Distribution of various IRD categories differed between the two cohorts (Figure 1): the post-COVID-19 cohort had a higher percentage of patients classified as having IJD (52.5% vs 37.2%, p = 0.013) while the post-vaccine cohort had a higher prevalence of patients classified as PMR (33.1% vs 21.3%, p = 0.032). No differences were detected in the percentage of patients diagnosed with CTD (19.7% vs 20.7%, p = 0.837) or vasculitis (6.6% vs 9.0%, p = 0.467).

Conclusion: Although temporal association does not imply causation, our study reports the largest cohort of post-COVID-19 and post-vaccine IRD described to date and supports the hypothesis that new-onset IRD may be triggered by SARS-CoV-2 infection or COVID-19 vaccines. The spectrum of possible clinical manifestations is broad and includes different IJD, PMR, CTD and vasculitis in both cohorts. Our data also suggest a differential pattern of expression: while IJD are the most common IRD following SARS-CoV-2 infection, PMR is relatively more frequent after vaccine administration.

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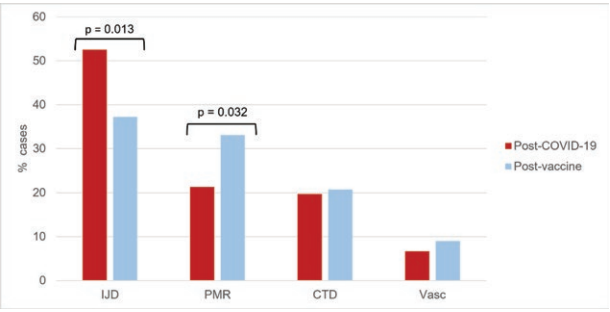


Figure 1.

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Disclosure of Interests: None Declared.

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POS0542 LYMPHOCYTES POPULATIONS AND AUTOANTIBODIES, IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS: A LONG-TERM STUDY OF COVID-19 CASES AND NON-COVID-19 CONTROLS

Keywords: COVID, Rheumatoid arthritis

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Background: COVID-19 infection favors multiple chronic disparities in the base health status, currently known as post-COVID syndrome (PCS), that can be related to immunological variations. It is important to determine if these alterations (both clinical and immunological) exist in a long-term period in patients with rheumatoid arthritis (RA) who have suffered from this infection.
Objectives: The aim of this study was to assess the immunological [Lymphocyte populations (LP) and Autoantibodies (Ab)] and clinical profile of RA patients who suffered from COVID-19 and compare it with non-COVID-19 RA patients.
Methods: A nested Case-control study of RA patients evaluated under a multidisciplinary model and strict follow-up with a treat to target strategy (T2T). Cases: RA patients and confirmed COVID-19 infection in the last 24 months and Controls: RA patients with no history of this infection. Subgroups in cases: a) Long covid (LC): symptoms after infection that persist for ≥4 weeks; b) PCS: symptoms persist for ≥12 weeks and c) symptoms < 4 weeks. Sociodemographic, clinical, and paraclinical variables of RA and COVID-19 infection (in cases) were captured. Antinuclear antibodies (ANAS), anticardiolipin antibodies, LP (BD FACSDuet™ - BD FACSLyric™ multiparameter flow cytometry) T, C, and NK were evaluated. Univariate and bivariate analyzes (STATA 17) were performed. Approval ethics committee was obtained.
Results: A total of 300 patients were included (148 cases and 152 controls; 87.3% women). Median age 59 years (Interquartile range -IQR 11), disease duration 12 years (IQR 12). The 71.86% were in low disease activity. There were no significant differences in sociodemographic and clinical characteristics between cases and controls. Cases had a time since infection of 18.5 months (IQR 7). Of the total cases, 69% presented LC and 63% with PCS. No significant differences were found between cases and controls in the LP T, B and NK, nor in the Abs evaluated. Similarly, there were no differences in the immune profile evaluated when comparing patients with LC and PCS with those with symptoms < 4 weeks after COVID-19 infection.

Table 1. Profile of autoantibodies and lymphocyte populations.

Laboratories	Total group (300) (n %)	Controls (152) (n %)	Cases (148) (n %)	P value[a]
ANAs	240(80)	126(82.8)	114(77.0)	0.204
ANAs Current title				0.413
160	46(19.17)	23(18.25)	23(20.18)	
320	97(40.42)	47(37.30)	50(43.86)	
640	58(24.17)	37(29.37)	21(18.42)	
1280	33(13.75)	16(12.70)	17(14.91)	
2560	6(2.50)	3(2.38)	3(2.63)	
Anticardiolipin IgG	21(7)	12(7.8)	9(6.0)	0.538
Anticardiolipin IgM	150(50)	77(50.6)	73(49.3)	0.817
[b]Lymphocyte events	2532.5(426.5)	2518(281)	2584(500)	0.050[c]
CD3+	72.3(11.9)	71.975(11.8)	72.775(11.4)	0.365
CD3+CD8+	24.16(11.9)	23.45(12.2)	24.775(11.6)	0.073
CD3+CD4+	45.13(12.5)	45.775(12.4)	43.995(13.2)	0.337
CD3+CD4+CD8+	0.76(0.8)	0.76(0.8)	0.74(0.8)	0.506
CD16+CD56+	12.64(9)	12.93(8.1)	12.4(9.3)	0.890
CD19+	12.4(8.8)	12.4(9.2)	12.3(8.4)	0.239
[b]CD45+	2013.9 (1024.9)	2023.3(846.6)	2007.9 (1072.5)	0.456[c]
4/8 Ratio	1.915(1.345)	1.98(1.305)	1.84(1.295)	0.133

[a] Chi-square Pearson [b] Median-IQR [c] U Mann-Whitney Test

Conclusion: The results propose a general description of a specific population of patients with RA with low disease activity, under treatment in a strict follow-up model, in which no differences were found in the behavior of the immunological profile (independent of symptoms of LC and PCS) evaluated long-term after infection with those who did not have COVID-19. This suggest that they return to their basal homeostatic state, something that has not yet been reported up to now. These results should forwardly be replicated in populations with other characteristics of RA.
REFERENCES: NIL.
Acknowledgements: NIL.

Disclosure of Interests: Julián Arias-Aponte: None declared, Arley Gómez-López: None declared, Paula Daniela Nieto-Zambrano: None declared, Maria Camila Cortés-Osma: None declared, Hector Fabio Restrepo-Guerrero: None declared, María Lorcy Monsalve-Córdoba: None declared, Edgar Garavito-Rodríguez: None declared, Rafael Parra-Medina: None declared, Laura Villarreal: None declared, Adriana Rojas-Villarraga: None declared, Pedro Santos-Moreno Speakers bureau: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi, Grant/research support from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi.
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POS0543 DETECTION OF SARS COV-2 ANTIBODIES FOLLOWING VACCINATION IN PATIENTS WITH RHEUMATIC MUSCULOSKELETAL DISEASE (DECODIR) – A REPORT FROM A DANISH PROSPECTIVE COHORT STUDY

Keywords: Inflammatory arthritides, Autoantibodies, COVID

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Background: The COVID-19 pandemic caused concerns whether patients with rheumatic musculoskeletal disease (RMD) treated with conventional (cs) or biologic (b) disease modifying drugs (DMARDs) and/or prednisolone exhibit an adequate immune response to the applied SARS-CoV2 vaccines.
Objectives: We established the DECODIR study to assess and compare the efficacy of the SARS-CoV2 vaccines administered as part of the national vaccine rollout: BNT162b2 vaccine (Pfizer/BioNTech) and mRNA-1273 vaccine (Moderna). The vaccines were offered as two doses four weeks apart; followed by a booster vaccination six months later. This national regimen included inflammatory rheumatic patients regardless of their respective anti-inflammatory treatment. We used patients' SARS-CoV2 IgG serum level as proxy for vaccination response (1).
Methods: The study was conducted as a longitudinal prospective cohort study. Patients with rheumatoid arthritis (RA), spondyloarthropathies (SpA) or psoriatic arthritis (PsA) receiving their outpatient treatment at the Danish Hospital for Rheumatic Diseases, Sonderborg, and monitored in the Danish DANBIO registry, were included. Blood samples, Disease activity and treatment information (cs/bDMARD, prednisolone) were collected at baseline (i.e. prior to vaccination), after six weeks, six and twelve months. SARS-CoV-2 IgG levels in serum were assessed by ELISA (Thermo-Fischer), and manufacturer's cut-off (>=10 EliA U/mL) selected as definition of sufficient IgG response. Antibody response was measured and compared at all four time points. Associations between antibody response, age, gender, disease (RA/PsA/SpA), treatment (none, cs/bDMARD or prednisolone) and disease activity were tested using proportional odds regression and bootstrapped tests of medians. Results were reported using mean, median (IqR) and bootstrapped 95% confidence interval (CI) of the median.
Results: A total of 243 patients were included at baseline and all were followed-up after six weeks; data from 233 patients were available at six months and for 229 patients at twelve months' follow-up. Those 229 patients had completed the national vaccination programme. The measurements performed 6 months after baseline demonstrated a *per se* decrease of IgG levels for the whole study population (median of 2.08 EliA U/mL at 6 months vs. 16 EliA U/mL at 6 weeks). The final measurements performed after twelve months demonstrated a significant increase of IgG levels. Thus, the completed vaccination programme, was followed by a significant increase in IgG levels (median of 100 EliA U/mL at twelve months vs. 16.5 EliA U/mL at six months, $p < 0.001$). Sufficient response rates were now recorded in all treatment scenarios, also in patients treated with prednisolone or combination of csDMARD and bDMARD. These two groups were at 6 months characterized by significant lower response rates, when compared with patients without any DMARD treatment.
Conclusion: Completed vaccination programme defined as two doses plus booster vaccination resulted in a sufficient vaccination response as measured by IgG levels regardless of RA treatment. It is noteworthy that IgG levels increased markedly in patients treated with a combination of cs/bDMARD or oral prednisolone, who had low IgG levels (below manufacturer's cut-off >=10 EliA U/mL) after 6 months. Our results strongly support the efficacy of the complete vaccination

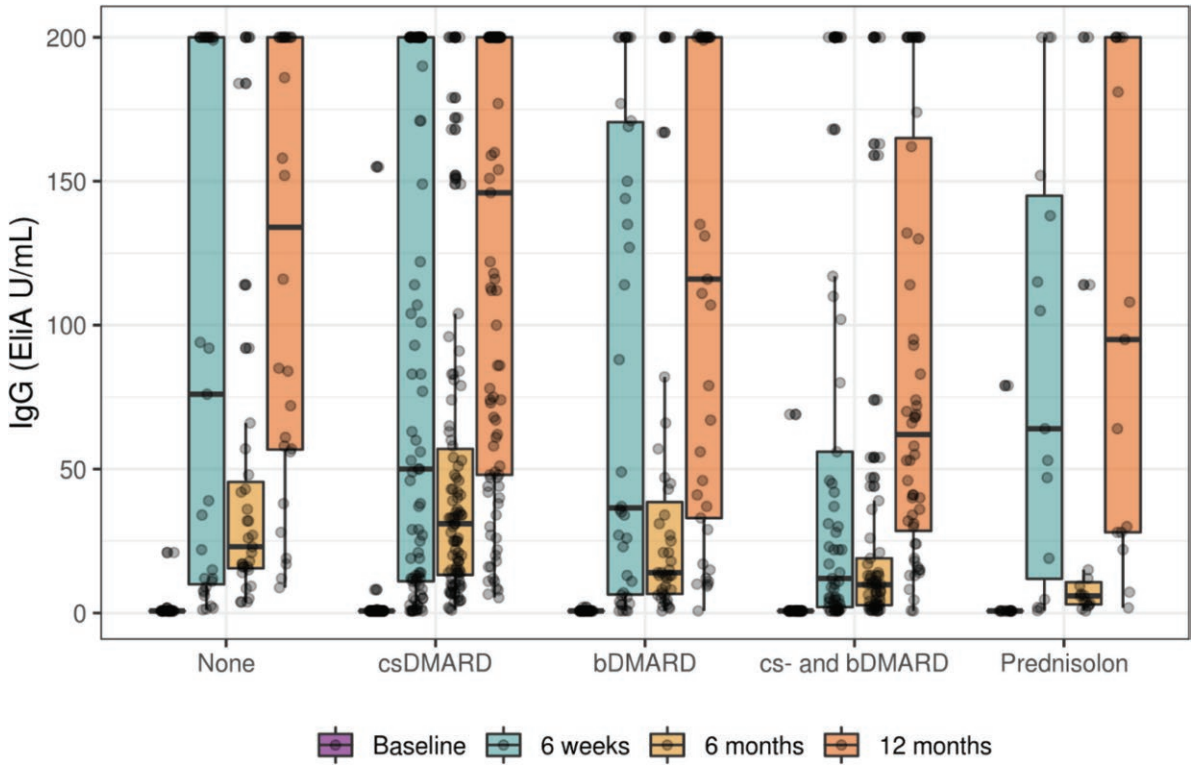


Figure 1. Serum IgG-levels at baseline, 6 weeks, 6 months and 12 months; stratified by antirheumatic treatment. (*Box plot showing median and interquartile range*).

programme including the 3rd booster vaccine in patients with inflammatory rheumatic diseases.

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[1] Schreiber K. et al. Reduced Humoral Response of SARS-CoV-2 Antibodies following Vaccination in Patients with Inflammatory Rheumatic Diseases—an Interim Report from a Danish Prospective Cohort Study. Vaccines 2022, 10(1), 35; https://doi.org/10.3390/vaccines10010035

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POS0544

THE CONTRIBUTION OF THE 3RD AND 4TH BOOSTER BNT162B2 MRNA VACCINES TO PREVENT SEVERE COVID-19 AMONG AUTOIMMUNE INFLAMMATORY RHEUMATOID DISEASES (AIRD) PATIENTS DURING THE OMICRON OUTBREAKS

Keywords: Vaccination/immunization, bDMARD, COVID

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Background: The 3rd booster of mRNA vaccines against SARS COV2 was highly efficient against delta variant but data regarding the efficacy of the 3rd and 4th boosters against the omicron variants, among AIRD pts are scarce.

Objectives: We aimed to assess the effect of the 3rd and 4th booster mRNA vaccines against SARS CoV2, in preventing severe COVID-19, in AIRD patients (pts) treated with immunomodulating drugs.

Methods: 212 pts (mean age(SD) 57(13), disease duration 11.2(7.4), who received the 3rd booster (Pfizer) were included in the study. We performed serology tests 24 weeks after the second dose of vaccine and 4-8 weeks after the 3rd booster. IgG Antibodies (Ab) against SARS COV2 virus were detected using the SARS-Cov-2 IgG II Quant (Abbott) assay. The test was considered positive above 50 AU/ml. Data regarding COVID-19 infection during the 5th outbreak (omicron) were collected from the medical files. The length of observation period was defined as the time from the 3rd booster to the last hospital visit or COVID 19 diagnosis, whichever occurred first.

Results: The 3rd booster administration (Pfizer) significantly augmented the humoral response (from mean(SD) 1121(4723) AU/ml to 12153(13687)). 58 patients received the 4th booster and 18 the 5th booster. COVID-19 was diagnosed in 103 pts (49%) within mean(SD) 224.8(106.5) days after the 3rd booster vaccination. 109 pts remained free of disease during mean(SD) follow-up 230.6(133.9). Following the 4th booster, 26 (45%) out of 58pts contracted COVID-19 within mean(SD) 97.6(78.7) days after the vaccination. One 70 year old patient (vaccinated 3 times) died and 2 other pts (rituximab treated) had severe COVID-19. The IgG Ab titer after the 3rd booster was lower in pts who contracted COVID 19 compared to those uninfected (mean(SD), median 8777.9(11716.4),3475 AU/ml vs 15348.1(14649.1),10801, p=0.004). There were no statistically significant differences between the pts with COVID-19 and those without, regarding age, type of disease, treatment and humoral response 24 weeks after the 2nd vaccination.

Conclusion: Despite an enhanced humoral response obtained after the 3rd booster, 49% of AIRD pts vaccinated with 3 doses and 45% of pts vaccinated with 4 doses had COVID-19 during the omicron outbreaks. Higher humoral response to the 3rd booster was associated with a lower rate of COVID19. The booster vaccines conferred 99% protection against severe COVID-19.

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Disclosure of Interests: None Declared.

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POS0545

PRE-EXPOSURE PROPHYLAXIS OF COVID-19 WITH TIXAGEVIMAB AND CILGAVIMAB IN RHEUMATOLOGIC PATIENTS TREATED WITH RITUXIMAB: DATA FROM A SINGLE-CENTRE COHORT

Keywords: COVID, bDMARD

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Background: Rheumatologic patients treated with Rituximab (RTX) are at higher risk of severe COVID-19 and death. The B-cell depletive treatment significantly affects B cell functions involved in anti-SARS-CoV-2 response, leading to relevant impacts on the clinical and serological course of infection, long-term immunity, and vaccine responses. In light of these observations, pre-exposure prophylaxis (PrEP) of COVID-19 with Tixagevimab and Cilgavimab (TGM/CGM) was recently approved in Italy for all patients treated with RTX in the previous year, independently of their serological status against SARS-CoV-2.
Objectives: We aimed to evaluate the efficacy and safety of TGM/CGM in a single-centre cohort of rheumatologic patients treated with RTX.
Methods: From October 2022, all patients who had been treated with RTX in the previous 12 months and who underwent clinical assessment at our rheumatologic tertiary centre were screened for eligibility to PrEP of COVID-19 with TGM/CGM. According to the indications of the Italian Medicines Agency (AIFA), we excluded subjects with major cardiovascular risk factors and/or coagulation abnormalities; those who reported a previous allergic reaction to any anti-COVID19 vaccine were referred to an allergologist for an evaluation before TGM/CGM administration. Patients who agreed to be treated with TGM/CGM signed an informed consent. Clinical and demographic features were collected at baseline, and follow-up phone assessment was performed the day after and 1 month after TGM/CGM administration, to assess treatment tolerability and new COVID-19- related events. A descriptive analysis was performed.
Results: From 1 October 2022 to 31 December 2022, 90 subjects were screened for eligibility to TGM/CGM. Among them, 11 were excluded for contraindications due to comorbidities and 55 refused TGM/CGM administration. Among patients who agreed to receive PrEP of COVID-19, 21 received TGM/CGM before 31 December 2022 and 3 were scheduled for January2023. Patients treated with TGM/CGM had a mean age of 54 years (standard deviation: 17) and 19 (90.5%) were female; 9 were affected by rheumatoid arthritis and 12 by other rheumatologic diseases (3 systemic lupus erythematosus, 2 systemic sclerosis, 1 Sjögren syndrome, 1 juvenile idiopathic arthritis, 3 anti-synthetase syndrome, 2 vasculitides). Most of them had completed the vaccination schedule against COVID-19 (19, 90.5%) and 9 (42.8%) reported an infectious event by SARS-CoV-2 in the previous year. One month after TGM/CGM administration, no patient reported adverse events related to TGM/CGM nor COVID-19 related symptoms.
Conclusion: PrEP of COVID-19 with TGM/CGM was well tolerated in our population of rheumatologic patients treated with RTX in the previous year and no COVID-19 related symptoms were observed in the month of follow-up after TGM/CGM administration. Future observations may provide further data on long-term efficacy of TGM/CGM in preventing COVID-19.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Maria Manara Speakers bureau: Novartis, Angelini, Consultant of: Lilly, MSD, Manuel Sette: None declared, Laura Giudice: None declared, Martina Biggioggero: None declared, Nicoletta Del Papa Speakers bureau: Janssen, Boehringer-Ingelheim, Actelion, Ennio Giulio Favalli Speakers bureau: AbbVie, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Consultant of: AbbVie, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Maria Gerosa: None declared, Francesca Ingegnoli: None declared, Roberto Caporali Speakers bureau: AbbVie, Amgen, BMS, Celltrion, Fresenius, Galapagos, Janssen, Lilly, Novartis, Pfizer, UCB, Consultant of: AbbVie, Fresenius, Galapagos, Lilly, Novartis, Pfizer, UCB.
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POS0546

REVACCINATION OF PATIENTS WITH SLE OR RA WITHOUT AN INITIAL COVID-19 VACCINE RESPONSE ELICITS SEROCONVERSION IN HALF OF THE PATIENTS

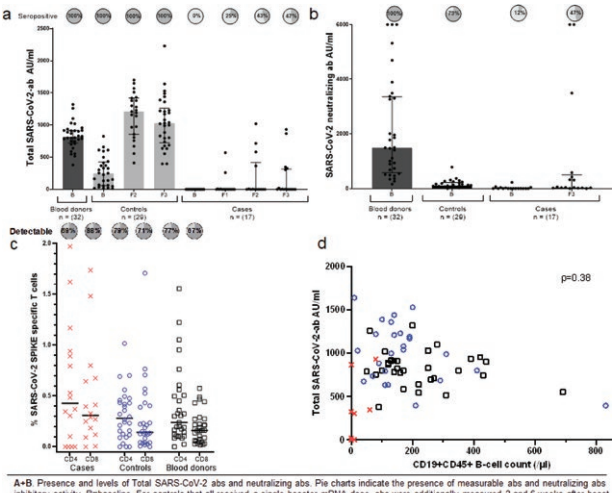
Keywords: COVID, Real-world evidence, Vaccination/immunization

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Background: Treatment with Rituximab (RTX) in patients with rheumatic diseases (RD) has presented a challenge during the COVID-19 pandemic, as RTX leads to markedly reduced and often undetectable antibody responses after COVID-19 vaccination (1).
Objectives: To investigate the effect of COVID-19 mRNA revaccination (two doses) on the antibody response in patients with RD who were initial vaccine non-responders. Further, to examine if B-cell levels or T-cell responses before revaccination predicted seroconversion.
Methods: From a RD cohort (COPANARD) vaccinated with the standard two-dose COVID-19 vaccinations, we enrolled cases without detectable antibody responses (n=17) and controls with detectable antibody response (n=29). Blood donors (n=32) were included as additional controls. Samples were collected before and six weeks after completed revaccination. Total antibodies (abs) and specific IgG, IgA, and IgM against SARS-CoV-2 spike protein, SARS-CoV-2 neutralizing abs, and SARS-CoV-2 reacting CD4+ and CD8+ T-cells were measured before and after revaccination. B-cells (CD19+CD45+) were quantified before revaccination. This study was funded by the Danish Rheumatism Association.
Results: Patient demographics are given in Table 1. Forty-seven percent of cases had detectable total SARS-CoV-2 abs and neutralizing abs after revaccination. However, antibody levels were significantly lower than in controls and blood donors ($p<0.008$), Figure 1A+B. Revaccination induced an antibody class switch in cases with a decrease in detectable IgM abs (Baseline 11/17, Followup 3/17) and increase in IgG. No significant difference was observed in T-cell responses before and after revaccination between the three groups, Figure 1C. The proportion of cases with detectable CD4+ T cells increased from 69% to 88% ($p=0.25$), and for CD8+ T cells, the proportion decreased from 88% to 82% ($p=1.00$). Only 29% of cases had measurable B-cells compared to 100% of controls and blood donors, Figure 1D. Fifty percent of revaccinated cases who seroconverted had measurable B-cells before revaccination, Figure 1D. Univariate logistic regression analysis was performed to analyze if active RTX treatment, the presence of B-cells, or a positive T-cell response prior to revaccination predicted seroconversion of total SARS-CoV-2-abs in the patient cohort. We did not find a significant explanatory effect of either variable in the univariate logistic models, data not shown.

Table 1. Demographics

	Cases Revaccination, n=17		Controls Boost, n=29	
Female sex, no(%)	14	82%	21	72%
Age, median (IQR)	65	49 - 70	67	62 - 72
Disease duration, years	15	10 - 18	22	9 - 31
Rheumatoid Arthritis/SLE	13/4		10/19	
None DMARD	5	29%	8	28%
Prednisone	4	24%	1	3%
Methotrexate	7	41%	12	41%
Hydroxychloroquine	2	12%	4	14%
None biologic treatment	4	24%	9	31%
Rituximab	12	71%	0	
TNF-inhibitors	1	6%	7	24%
JAK-inhibitors	0		6	21%
IL-6-inhibitors, Abatacept, Benlysta	0		7	24%
Previous rituximab treatment				
Any rituximab treatment	16	94%	1	3%
RTX within the last 15 months, no	14	88%	0	
Cumulative total dose, mg	13	4-24	2	
Time from RTX to revaccination, months	9	5-12	49	



A+B. Presence and levels of Total SARS-CoV-2 abs and neutralizing abs. Pie charts indicate the presence of measurable abs and neutralizing abs inhibitory activity. B=baseline. For controls that all received a single booster mRNA dose, abs were additionally measured 2 and 6 weeks after boost (F2 and F3 under controls). For cases receiving full two-dose revaccination, abs were measured 2 weeks after the 3rd and 2 + 6 weeks after the 4th dose (marked F1, F2, and F3, respectively, under cases) C SARS-CoV-2 SPIKE specific CD4+ and CD8+ T-cells in cases, controls, and blood donors D Correlation between CD19+CD45+ B-cells pre-revaccination and antibody levels.

Figure 1.

Conclusion: In conclusion, forty-seven percent of initial non-responders were able to seroconvert after two-dose revaccination. However, plasma concentrations of the antibodies against SARS-COV-2 and the levels of neutralizing capacity remained significantly lower than in immunocompetent blood donors. B-cell levels or T-cell responses before revaccination did not predict seroconversion. Our study suggests that patients with RDs who did not mount a detectable serological response to a COVID-19 mRNA vaccine have a T cell response similar to immunocompetent controls. Future studies should establish the antibody levels that identify RD patients without sufficient protection against SARS-CoV-2 infection.

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POS0547 RISK OF SARS-COV-2 INFECTION FOLLOWING THREE DOSES OF BNT162B2 OR MRNA-1273 IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES

Keywords: COVID, Inflammatory arthritides, Vaccination/immunization

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Background: We recently performed a long-term, model-based comparison of the humoral immunogenicity following two-dose vaccination with BNT162b2 and mRNA-1273 in individuals from SCQM, the Swiss cohort for patients with inflammatory rheumatic diseases (IRD). Vaccination with mRNA-1273 resulted in higher humoral immunogenicity compared to BNT162b2 throughout 24 weeks post second vaccine dose [1]. In booster vaccinations, the dose of mRNA-1273 was reduced and it is currently unknown if there was a difference in SARS-CoV-2 infections in BNT162b2 and mRNA-1273 recipients with IRD after the third vaccine dose.

Objectives: To investigate the risk of test-positive SARS-CoV-2 infection after three doses of BNT162b2 or mRNA-1273 in IRD patients.

Methods: Adult patients from the SCQM registry who previously participated in an observational cohort study comparing vaccine-induced humoral immune responses following two doses of BNT162b2 or mRNA-1273 were invited to participate in the next phase of the study. Participants answered study questionnaires via the mySCQM patient app, including on subsequent vaccine doses and SARS-CoV-2 infections, here taken as patient-reported positive PCR or antigen tests. Pre and post third vaccination anti-SARS-CoV-2 IgG (anti-S1) levels were quantified by testing self-collected capillary blood samples using the EUROIMMUN ELISA as previously described [1]. To analyze the risk of infection, we used a Cox proportional hazards model. The time of the third mRNA COVID-19 vaccine dose administration was taken as the baseline. Patient follow-up ended on the minimum date of the following events: testing positive for SARS-CoV-2 infection after the third mRNA COVID-19 vaccine dose, receiving a fourth vaccine dose, last data entry in the mySCQM patient app, or study end (2022-12-01). Patients whose follow-up ended in the first 14 days after the third vaccine dose were excluded from the analysis.

Results: 445 patients were included in the study (67% female; mean age 54 yrs; 36% RA, 36% axSpA, 21% PsA, 7% undifferentiated arthritis). Patients received their third dose of mRNA COVID-19 vaccine between 2021-08-06 and 2022-04-04 (BNT162b2: mRNA-1273 51%:49%; homologous vaccination applied in 95% of patients). Between 2021-12-08 and 2022-11-24, 175 patients reported a positive SARS-CoV-2 test occurring at least 14 days after the third vaccine dose (Figure 1A), only 3 of whom required hospitalization. We found no statistically significant difference in the risk of SARS-CoV-2 infection post third dose due to the vaccine received (mRNA-1273 vs BNT162b2) (Figure 1B). Higher anti-S1 levels at baseline were statistically significantly associated with a lower risk of infection post third vaccine dose. A prior SARS-CoV-2 infection also statistically significantly reduced the risk of infection post third vaccine dose.

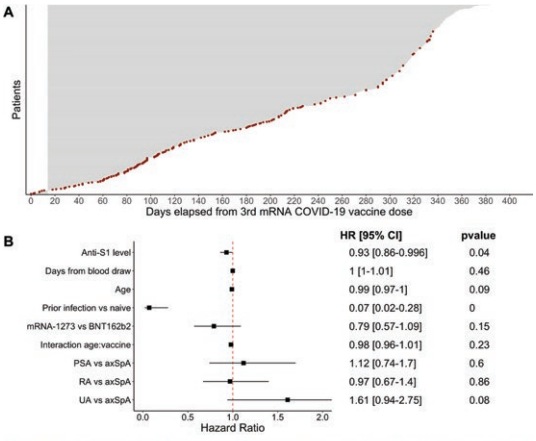


Figure 1. A) **Follow-up time (time at risk) for study** participants sorted by the individual end of follow-up as a function of days elapsed from third mRNA COVID-19 vaccine dose. Ten patients whose follow-up ended within the first 14 days post third vaccine dose were excluded from the analysis. Red dots indicate events, i.e. reporting of SARS-CoV-2 infection. B) **Hazard ratios** with 95% confidence intervals for SARS-CoV-2 infection post third mRNA COVID-19 vaccine dose for model covariates. 'Anti-S1 level': the humoral antibody level at the blood draw taken closest and prior to the date of the third vaccine dose; 'Days from blood draw': the days elapsed from the date of the last blood draw closest to the that of the third vaccine dose and the date of the third vaccine dose; 'Age': the age at baseline (date of third vaccine dose); 'Prior infection vs naïve': prior reported SARS-CoV-2 infection vs none reported; 'Interaction age:vaccine': interaction term showing how the HR of mRNA-1273 vs BNT162b2 changes with increasing age; RA: rheumatoid arthritis; axSpA: axial spondyloarthritis; PsA: psoriatic arthritis; UA: undifferentiated arthritis.

Conclusion: The risk of SARS-CoV-2 infection did not statistically significantly differ between mRNA-1273 and BNT162b2 recipients following a third vaccine dose. Higher anti-S1 levels at the time of the third mRNA COVID-19 vaccine dose, as well as a prior infection, were associated with a statistically significant lower risk of test-positive SARS-CoV-2 infections during follow-up in patients with IRD.

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Disclosure of Interests: Catherine Elizabeth Raptis Grant/research support from: This study was investigator-initiated and received independent financial support from an anonymous donation from a research foundation and Moderna Switzerland GmbH. The study sponsors had no role in the study design or in the collection, analysis and interpretation of the data, the writing of the abstract or the decision to submit it., Christos Polysopoulos: None declared, Christoph Berger: None declared, Adrian Ciurea: None declared, Diego Olivier Andrey: None declared, Pierre Lescuyer: None declared, Tanja Maletic: None declared, Myriam Riek: None declared, Almut Scherer: None declared, Isabell von Loga: None declared, Judith Safford: None declared, Kim Lauper Speakers bureau: Honoria/speakers fees for Pfizer, Viatris, Celltrion outside of the submitted work, Burkhard Moeller: None declared, Nicolas Vuilleumier: None declared, Axel Finckh Speakers bureau: AbbVie, BMS, Pfizer, Eli-Lilly, Sandoz outside of the submitted work, Consultant of: AbbVie, Novartis, Pfizer, MSD, Eli-Lilly outside of the submitted work, Grant/research support from: AbbVie, BMS, Galapagos, Lilly, Pfizer outside of the submitted work, Andrea Rubbert-Roth Speakers bureau: Honoraria for consultation and lectures from Abbvie, Amgen, Pfizer, Gilead, Novartis, Janssen, Eli-Lilly, Sanofi, Roche, UCB, BMS outside of the submitted work, Consultant of: Honoraria for consultation and lectures from Abbvie, Amgen, Pfizer, Gilead, Novartis, Janssen, Eli-Lilly, Sanofi, Roche, UCB, BMS outside of the submitted work.

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POS0548 HUMORAL AND CELLULAR IMMUNOGENICITY OF THE THIRD DOSE OF MRNA VACCINES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ON BELIMUMAB

Keywords: Systemic lupus erythematosus, COVID, Diagnostic tests

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Background: SARS-CoV-2 vaccination with mRNA vaccine (mRNA-1273 e BNT 162b2) represented the cornerstone of the pandemic strategy to prevent severe complications of infection. Immunosuppressive therapies potentially reduce both humoral and cellular-mediated response to vaccination, undermining its protective effect [1].
Objectives: To evaluate humoral and T-cell cellular-mediated immune response after three doses of SARS-CoV-2 mRNA vaccines in patients with systemic lupus erythematosus (SLE) under Belimumab.
Methods: 12 patients on Belimumab and 13 age-matched healthy volunteers were recruited. Patients were in remission or in low disease activity, and they were taking no corticosteroids or only low doses. None of the patients and controls had detectable anti-SARS-CoV-2 antibodies due to previous exposure to the virus. All the patients received three doses of mRNA anti-SARS-CoV-2 vaccines and the humoral and cellular-mediated response were tested 4 weeks after the second dose (T0), 6 months after the second dose (T1) and 4 weeks after the third dose (T2). Comparison with the control group was performed only at time T0 (i.e., 4 weeks after the second dose) since healthy controls didn't attend the third vaccine dose with an overlapping timing Total anti-SARS-CoV-2 RBD antibodies were analyzed using a diagnostic assay, while cellular-mediated response was evaluated using the interferon-gamma release assay (IGRA).
Results: A humoral response was documented in all the patients at T0 (median 459; IQR 225.25-758.5), but the antibody titer significantly declined from T0 to T1 (median 44.7; IQR: 30.3-202; p=0.0066). At T2, the antibody titer significantly increased from T1 (median 2500; IQR: 2500-2500), and it was not different from T0 (respectively p<0.0001, p=0.66). Cellular-mediated response significantly declined from T0 to T1 (p=0.003) but not from T0 to T2 (p=0.3) (Figure 1). No differences were found between patients and controls at T0 as regards both humoral and cellular responses (p=1.0 and p=0.09 for humoral and cellular responses, respectively).
Conclusion: Even if the low number of patients cannot establish definitive conclusions, the third dose of mRNA COVID-19 vaccine can restore both humoral and cellular immune response in SLE patients on Belimumab. In addition, the comparison with a control group of healthy people provided by our study, even if restricted to the T0, showed a similar vaccine response in SLE Belimumab-exposed patients. Overall, our results confirm the concept that in immunocompromised patients the third vaccine dose is not a booster dose, but it is a necessary completion of a regular vaccination cycle. Indeed, the significant decline of the antibody titer after 6 months from the second dose and the incomplete T-cell-mediated cellular response after the third dose in a percentage of patients support the potential role of a fourth dose as a booster dose for those patients exposed to B-cell targeted therapies, like Belimumab or Rituximab.

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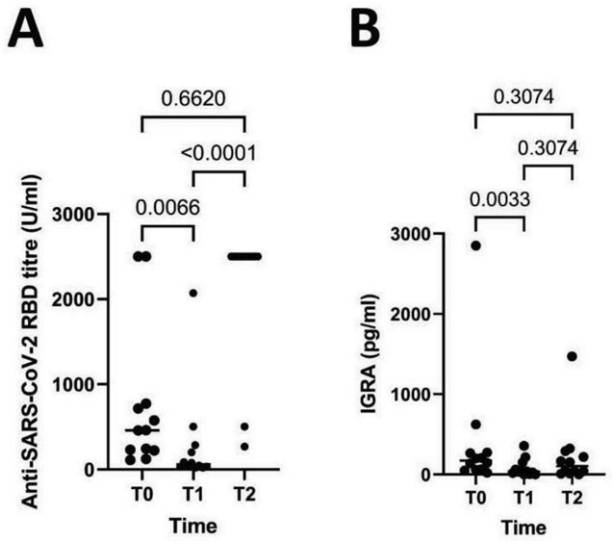


Figure 1.

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Disclosure of Interests: None Declared.
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POS0549

BREAKTHROUGH SARS-COV-2 INFECTION IN FULLY VACCINATED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM THE COVID-19 VACCINATION IN AUTOIMMUNE DISEASE (COVAD) STUDY

Keywords: COVID, Systemic lupus erythematosus, Vaccination/immunization

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Background: Although many studies have been conducted on COVID-19 in recent years, there are still unanswered questions regarding breakthrough infections (BTIs), particularly in patients with systemic lupus erythematosus (SLE).
Objectives: This study aimed to determine the occurrence of breakthrough COVID-19 infections in patients with SLE versus other autoimmune rheumatic diseases (AIRDs), non-rheumatic autoimmune diseases (nrAIDs), and healthy controls (HCs).
Methods: The study was based on data from the COVAD questionnaire which amassed a total of 10,783 complete responses from patients with SLE, AIRD, or

nrAIRD, and HCs. After exclusion of individuals who were unvaccinated, those who received one vaccine dose only, and those with uncertain responses regarding the vaccine doses, a total of 9,595 patients formed the study population of the present investigation. If a COVID-19 infection occurred after the initial two vaccine doses and at least one booster dose (at least three doses in total, herein termed full vaccination), it was considered a BTI. Data were analysed using multivariable regression models. Statistically significant results were denoted by *p* values <0.05.

Results: A total of 7,016/9,595 (73.1%) individuals were fully vaccinated. Among those, 1,002 (14.2%) reported at least one BTI, and 166 (2.3%) reported at least two BTIs. Among SLE patients, 867/1,218 (71.2%) were fully vaccinated. Among fully vaccinated SLE patients, 137 (15.8%) reported at least one BTI while 28 (3.2%) reported at least two BTIs. BTI frequencies in fully vaccinated SLE patients were comparable to those of other AIRDs (OR: 1.0; 95% CI: 0.8–1.3; *p*=0.447) and nrAIDS (OR: 0.9; 95% CI: 0.6–1.3; *p*=0.856) but higher compared with HCs (OR: 1.2; 95% CI: 1.0–1.6; *p*=0.022). For SLE patients with three vaccine doses, 113/137 (82.5%) reported at least one BTI while the corresponding number for four vaccine doses was 24/137 (17.5%). Compared with HCs (OR: 10.6; 95% CI: 1.2–93.0; *p*=0.032) and other AIRDs (OR: 3.5; 95% CI: 1.08–11.5; *p*=0.036), SLE patients showed higher frequencies of hospitalisation. AID multimorbidity was associated with a 15-fold increased risk for a need of advanced treatment for COVID-19 (OR: 15.3; 95% CI: 2.6–88.2; *p*=0.002).

Conclusion: COVID-19 BTIs occurred in nearly 1 every 6th fully vaccinated patient with SLE, and 20% more frequently in this patient population compared with fully vaccinated HCs. Moreover, BTIs in SLE patients were more severe compared with BTIs in HCs or patients with AIRDs other than SLE, resulting in a greater need for hospitalisation. AID multimorbidity contributed to a more severe COVID-19 BTI requiring advanced management. These insights call for greater attention to vaccination in the vulnerable group of SLE patients, with appropriate risk stratification towards optimised vaccination strategies.

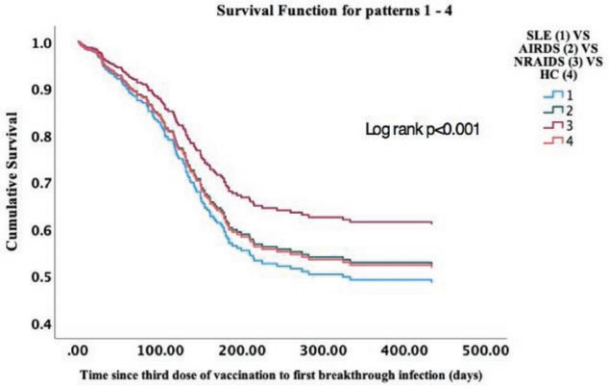


Figure 1. Survival analysis across patients with SLE, AIRDs, or nrAIDs, and HCs. SLE: systemic lupus erythematosus; AIRD: autoimmune rheumatic disease; nrAID: non-rheumatic autoimmune disease; HC: healthy control.

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POS0550 IMMUNE RESPONSE AFTER VACCINATION AGAINST SARS-COV2 IN PATIENTS WITH IMMUNOMEDIATED DISEASES (RIM-COV PROJECT)

Keywords: COVID, Vaccination/immunization

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Background: It is known that patients with immunomodulatory treatment may have less immune response to vaccines. Since SARS-CoV2 infection appeared, several vaccines have been developed. In previous studies, it has been observed that some subgroups of patients has a lower antibody response after SARS-Cov2 vaccination, especially patients treated with Rituximab (an anti-CD20 monoclonal antibody); but also in those treated with Mycophenolate Mofetil, Abatacept, JAK inhibitors, anti tumor necrosis factor (TNF) α, Methotrexate or Glucocorticoids. In some studies, an absence of humoral response but the presence of a T-cell response after vaccination has been observed in patients with B-cell depletion, even without finding differences between patients treated with rituximab compared with other immunomodulatory therapies or healthy controls. As well, it has been described a lower T-cell response in patients treated with anti-CTLA4, anti-interleukin 6 or antiTNFα.

Objectives: Our objective is to identify factors that influence humoral and cellular immune responses to SARS-CoV-2 vaccines in patients with immune-mediated rheumatic diseases (IMRDs) in treatment with disease-modifying anti-rheumatic drugs (DMARDs) and in healthy subjects as a control.

Methods: A total of 140 consecutive patients and 24 healthy controls were included in this observational cross-sectional single-centre study. Two months after second or third COVID-19 vaccine dose (BNT162b2 [Pfizer/BioNTech], mRNA-1273 [Moderna] or AZD1222 [AstraZeneca]), we quantified IgG anti-SARS-CoV-2 antibodies by chemiluminescent immunoassay of micro-particles and Interferon (IFN)-gamma production by T cells stimulated with SARS-CoV-2 peptides using an IFN-gamma release assay test. IgG anti-SARS-CoV-2 levels below 1800 AU/ml or IFN-gamma levels below 0.15 IU/ml were considered as a suboptimal humoral or cellular immune response, respectively. Multivariate analyses were used for exploring influence of different factors in these suboptimal immune responses.

Results: Of the140 patients, 101 were women and 39, men, with a median age of 55.9 (46.1-69.7) years and a disease duration of 13 years (6-20.8). 106 patients had a diagnosis of autoimmune arthropathy and 34, of systemic autoimmune disease. The higher risk of having a poor humoral response after the vaccination was shown in those patients receiving only two vaccine doses (OR: 7.83 (2.94-20.83);

p<0.0001), patients with diagnosis of systemic autoimmune disease (OR: 4.73 (1.47-15.21); p=0.009) or patients receiving treatment with Rituximab (OR: 13.17 (3.68-47.11); p<0.0001). There was a moderate association between suboptimal cellular immune response and older age (OR: 1.03 (1.01-1.05); p < 0.01). Receiving only two vaccine doses (OR: 4.02 (1.7- 9.5); p<0.001) and older age (OR: 1.04 (1.01-1.07); p<0.006) were associated with both suboptimal antibody and cellular immune responses to SARS-CoV2 vaccines, without agreement between both immune responses (kappa factor=0.198).

Conclusion: This study allows the early identification of suboptimal responders to SARS-CoV2 vaccines among patients with IMRDs who receive immunomodulatory therapy, and shows the need of a booster dose in elderly patients and, maybe, in patients with systemic autoimmune disease or those who are treated with Rituximab. Future studies demonstrating if these suboptimal immune responses are associated to more severe COVID-19 are required.

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Disclosure of Interests: None Declared.

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POS0551 SARS-COV-2 BREAKTHROUGH INFECTION IN COVID-19-VACCINATED ADOLESCENTS AND YOUNG ADULTS WITH CHILDHOOD-ONSET RHEUMATIC DISEASES

Keywords: COVID, Vaccination/immunization

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Background: Although robust humoral immune response after 2-dosed COVID-19 mRNA vaccination was demonstrated in adolescents and young adults (AYAs) with childhood-onset rheumatic diseases (cRDs) [1], data on prevalence and risk factors of SARS-CoV-2 breakthrough infection are limited.

Objectives: To describe the clinical characteristics and risk factors for SARS-CoV-2 breakthrough infection in vaccinated AYAs with cRD from our prospective and ongoing cRDs COVID-19 vaccination cohort.

Methods: Patients were recruited from March 2021 – December 2022 at KK Women's and Children's Hospital, Singapore. Breakthrough infections were defined as symptomatic infections occurring ≥14 days after the second dose in a two-dose series [2]. Humoral immunogenicity was assessed at 2-3 weeks after first vaccine dose and 1, 3, and 6 months after the second dose by the cPass™ SARS-CoV-2 Neutralisation Antibody (nAb) Assay and calibrated against the World Health Organisation International Standard for SARS-CoV-2 antibodies (WHO-nAb).

Results: 170 fully COVID-19 mRNA vaccinated patients (71% Chinese, 47% male) were included, Table 1. 141 patients received 3rd vaccine, 6 months after the full series. 51% had breakthrough infection at a median of 5.6 (IQR 4.0-6.8, n=22) and 3.7 (IQR 1.3-5.4, n=55) months after 2nd or 3rd vaccines, respectively, with mainly mild symptoms (5% admission). The median WHO-nAb was significantly lower in those with breakthrough infection (987.3 IU/ml, IQR 361.0 - 2083.4 vs 1892.1 IU/ml, IQR 1052.5 - 2657.7, p<0.001). Older patients had decreased risk of breakthrough SARS-CoV-2 infection (OR 0.83, 95% CI 0.739-0.936, p=0.002). A WHO-nAb titre of < 1000 IU/ml increased the risk of breakthrough SARS-CoV-2 infection (OR 4.16, 95% CI 1.964-8.794, p<0.001). Significantly more patients with infection were taking anti-TNF. Withholding methotrexate or mycophenolate mofetil did not impact the breakthrough infection risk.

Conclusion: Despite a robust humoral immune response to COVID-19 mRNA 2-dosed vaccination, one-half of the AYAs with cRDs had breakthrough infections, albeit mild disease. Younger patients and WHO-nAb < 1000 IU/ml increased the risk of infection. Additional vaccine is needed sooner than 6 months after the 2nd dose to prevent infection. Longitudinal data are being collected to determine the vaccine booster interval in our cohort.

Table 1. Clinical characteristics of vaccinated AYA with cRD

Clinical characteristics	Total	No infection, n=83	Infection, n=87	p
Male	80 (47.1)	40 (48.2)	40 (46.0)	0.772
Age (yrs)	16.7 (14.7-19.5)	17.6 (15.1-20.0)	16.3 (14.1-19.2)	0.022
Diagnosis				0.742
Juvenile Idiopathic Arthritis	98 (57.6)	47 (56.6)	51 (58.6)	
Systemic Lupus Erythematosus	30 (17.6)	14 (16.9)	16 (18.4)	
Other Connective tissue diseases	21 (12.4)	13 (15.6)	8 (9.1)	
Others	21 (12.4)	9 (10.8)	12 (13.8)	
Medication				
Prednisolone	32 (18.8)	14 (16.9)	18 (20.7)	0.524
Anti-TNF	57 (33.5)	21 (25.3)	36 (41.1)	0.026
Hydroxychloroquine	43 (25.3)	24 (28.9)	19 (21.8)	0.289
Azathioprine	6 (3.5)	5 (6.0)	1 (1.1)	0.111
Mycophenolate mofetil (MMF)	22 (12.9)	13 (15.7)	9 (10.3)	0.302
Methotrexate (MTX)	42 (24.7)	18 (21.7)	24 (27.6)	0.373
Holding MTX	34 (81.0)	14 (77.8)	20 (83.3)	0.650
Holding MMF	7 (41.2)	4 (36.4)	3 (50.0)	0.644
Patients with WHO-nAb* titer < 1000 IU/ml (before infection or after vaccination)	54 (36.0)	20 (24.1)	34 (50.7)	0.001

*WHO-nAb: WHO International standardized neutralizing antibodies

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POS0552 NEUTROPHIL EXTRACELLULAR TRAPS AND B-CELL ACTIVATING FACTOR AS MARKERS TO PREDICT AND MONITOR ADVERSE EFFECTS AFTER COVID-19 VACCINES

Keywords: Disease-modifying Drugs (DMARDs), Vaccination/Immunization, Biomarkers

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Background: Vaccine-induced immune thrombotic thrombocytopenia (VITT) has also been reported to be related to NETosis. However, whether non-VITT adverse events(AE) and AEs due to non-adenovirus vectors-COVID-19 vaccines are related to NET formation has not been confirmed.

Objectives: We hypothesized that COVID-19 Vaccine could induce circulating products of NETosis in fashion similar to the SARS-CoV-2.

Methods: Citrullinated histone H3 (citH3) and B-cell activating factor(BAFF) serum levels were check in healthy donors(HD) who received two doses of mRNA-1273(Moderna) or ChAdOx1 nCoV-19 vaccines in National Taiwan University Hospital, a tertiary medical center in northern Taiwan. Serial blood tests were done on the day before COVID-19 vaccination(Day 0), before mRNA-1273 boosters (booster Day 0) and 30 days after the boosters (booster Day 30). Therefore, two cohorts, MM-M and AA-M were enrolled from March 2021 to Jan 2022. A REDCap online survey of adverse effects 0-7 days after each vaccination was also performed. Grading of AEs were defined as the previous COVID-19 vaccine trial(KidCOVE trial) described. In addition to HD cohorts, serial antiphospholipid antibodies and citH3 serum titers were also monitored in a case series of three anti-BAFF(belimumab) treated patients, who were hospitalized due to severe AEs after COVID-19 vaccines. We had excluded concomitant COVID-19 infections since all HDs and hospitalized patients were negative for serial SARS-CoV-2 nucleocapsid antibody.

Results: We analyzed two HD cohorts as a whole(n=34), the serum citH3 on booster Day 0 were lowest among the HDs who experienced no AEs from booster Day 0 to Day 7(2.8±1.4 v.s. 12.3±10.8ng/ml(HD with Grade 1 to Grade 3 AEs), p<0.01, U test). Only serum citH3 on booster Day 0 but not on other time points could predict AEs due to COVID-19 vaccines. In addition, the serum BAFF on booster Day 0 were lowest among the HDs who reported no AEs from booster Day 0 to Day 7(1646.1±794.7 v.s. 723.4±218.5pg/ml(HD with ≥Grade 1 AEs), p<0.01). For the three hospitalized AZ-mRNA vaccine experienced patients, two patients suffered fatigue due to hypoperfusion at multiple area brain SPECT, and

one experienced refractory abdominal pain due to mesenteric vein thrombosis soon(eight, 24, and 67 days) after the last doses of COVID-19 vaccinations. Two of them had moderate clinical improvement and both citH3/IgM anticardiolipin decreased after belimumab monthly administration while one needed further IVIG treatment and salvage plasma exchange. In HDs who received two doses of ChAdOx1 vaccines(AZ) and a Moderna booster(AA-M cohort), citH3 increased most significantly after two doses of AZ (p=0.01, U test, cohort AA-M, n=26, Figure 1A) BAFF also increased significantly after two doses of AZ (p<0.001, Figure 1B) Brown-Forsythe heteroscedasticity test indicated their values of three time points were unequal(p=0.04). However, in HDs who received three doses of Moderna, citH3 only numerically increased after two doses of Moderna (p=0.13, U test, cohort MM-M, n=8, Figure 1C.) BAFF did not fluctuate after two doses of Moderna and even after the third dosage of Moderna. Brown-Forsythe test indicated BAFF were equal(p=0.87, Figure 1D.) A trend of higher NET formation and BAFF induction due to adenovirus vectors-COVID-19 vaccine were observed in comparison with mRNA-1273. It has been hypothesized antiplatelet factor 4 may occur after heparin or AZ vaccines due to similarity shared by anionic surfaces in adenoviral vector and heparin molecule. Further profiling of autoantibodies after various COVID-19 vaccines and *in vitro* platelet-neutrophil axis activation test may elucidate the mechanism by which induce NETosis as demonstrated in our cohort.

Conclusion: Dynamic serum citH3 level revealed that neutrophil extracellular traps may play important roles in AEs due to COVID-19 vaccines.

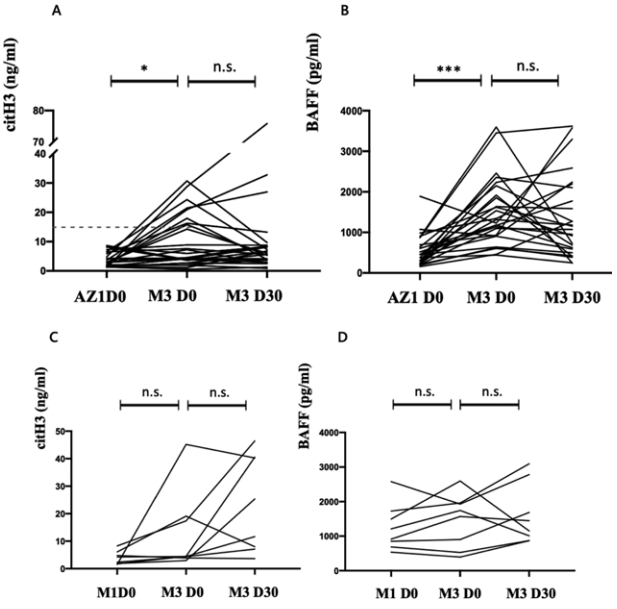


Figure 1.

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POS0553 TIXAGEVIMAB AND CILGAVIMAB IN RITUXIMAB-TREATED RHEUMATOLOGIC PATIENTS: A REAL-LIFE EXPERIENCE

Keywords: COVID, Real-world evidence

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Background: Rheumatologic patients receiving B cell-depleting therapy (BCDT), such as Rituximab (RTX), have relevant defects in humoral responses to a variety of vaccines. Moreover, RTX-treated patients appear vulnerable to breakthrough infections often showing worst outcomes. Monoclonal antibodies have been developed to provide passive immunity against SARS-CoV-2 in patients with depressed immune systems. Tixagevimab-Cilgavimab (TIX/CIL) is a monoclonal antibody that has been shown to reduce the risk of COVID-19 infections in immunocompromised patients and could be administered as pre-exposure prophylaxis or as targeted anti-SARS-CoV-2 treatment. Few data on real-life evidence on TIX/CIL in RTX-treated rheumatologic patients have been documented.

Objectives: The objectives of this study were to identify breakthrough COVID-19 infections and to evaluate outcomes in RTX-treated rheumatologic patients who underwent pre-exposure prophylaxis or treatment with TIX/CIL.

Methods: In this retrospective cohort study, we included 13 rheumatologic patients referring to the 3rd level Rheumatology Unit at the Tor Vergata University Hospital in Rome (Italy) who were treated with RTX for remission induction and/or maintenance and received TIX/CIL dose of 600 mg (300 mg Tixagevimab-300 mg Cilgavimab), between February and December 2022. A review of medical records was completed. Data on the rheumatologic disease, immunosuppressive treatment, COVID-19 vaccine status, TIX/CIL administration, peripheral blood CD19 cells and IgG levels before and after TIX/CIL administration were registered.

Results: The mean (±SD) age of included patients was 69 (±9) years, with 92.3% women. The cohort was diagnosed with Rheumatoid Arthritis (RA, 76.9%), Sjogren Syndrome (7.7%), Systemic Sclerosis (7.7%), Dermatomyositis (7.7%); one subject received RTX also for concomitant Multiple Sclerosis. Most patients received COVID-19 vaccines, and all but one received a third dose. All patients received a TIX/CIL dose of 600 mg (300 mg Tixagevimab-300 mg Cilgavimab), the majority (84.6%) of them as pre-exposure prophylaxis, while in 2 patients (15.4%) TIX/CIL was administered as a targeted anti-SARS-CoV-2 treatment. At the time TIX/CIL was administered, patients had a disease duration of 16±8 years. In patients undergoing pre-exposure prophylaxis, serum IgG levels before and after TIX/CIL administration were variable. Pre-TIX/CIL IgG levels were normal (54.5%), low (27.3%), and not available (18.2%). Post-TIX/CIL IgG levels were normal (72.7%), not available (18.2%) and low (9.1%). In those with documented pre- and post-TIX/CIL IgG levels, the levels did not change except for one patient with a normal post-TIX/CIL IgG level compared to a low pre-TIX/CIL IgG level. In addition, before getting TIX/CIL, CD19 was depleted (54.5%) and unavailable (45.5%) among patients. Post-TIX/CIL, CD19 was depleted (63.6%) and unavailable (36.4%). In those with documented pre-TIX/CIL and post-TIX/CIL CD19, the number of cells did not change. Among the 84.6% of patients who received TIX/CIL as a pre-exposure prophylaxis, one patient (9.1%) developed breakthrough COVID-19 disease, with mild symptoms (fever<38°C lasting<2 days, cough, fatigue) and no need of hospitalization. Among the 15.4% of patients who received TIX/CIL as a targeted treatment, none of them required hospitalization. The mean time from the onset of COVID-19 disease to TIX/CIL administration was 3±1.4 days. Regarding rheumatologic diseases, all patients continued RTX-therapy with a mean duration of treatment of 4±0.5 months and remained in remission.

Conclusion: Our findings, including mainly RA-patients, highlight the role of an adequate passive immunity in immunosuppressed patients. However, pre-exposure treatment can be crucial as well as the need to use early anti-viral agents/anti- SARS-CoV-2 mAb in most fragile patients. Larger cohorts and further measures are needed to support that challenge and to better investigate the interplay between RTX and monoclonal antibodies in treated patients.

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POS0554 ANTIPHOSPHOLIPID ANTIBODIES AND VASCULAR THROMBOSIS IN PATIENTS WITH THE MOST SEVERE FORMS OF COVID-19

Keywords: Autoantibodies, Anti-phospholipid syndrome, COVID

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Background: The presence of antiphospholipid antibodies (aPL) has been observed in patients with COVID-19 (1,2), suggesting that they may be associated with deep vein thrombosis, pulmonary embolism, or stroke in severe cases

(3). Antiphospholipid syndrome (APS) is a systemic autoimmune disorder and the most common form of acquired thrombophilia globally. At least one clinical criterion, vascular thrombosis (arterial, venous or microthrombosis) or pregnancy morbidity and at least one laboratory criterion- positive aPL two times at least 12 weeks apart: lupus anticoagulant (LA), anticardiolipin (aCL), anti-β2-glycoprotein 1 (anti-β2GPI) antibody, have to be met for international APS classification criteria(4). Several reports also associate anti-phosphatidylserine/prothrombin antibodies (aPS/PT) with APS.

Objectives: To combine clinical data on arterial/venous thrombosis and pregnancy complications before and during hospitalisation with aPL laboratory findings at 4 time points (hospital admission, worsening of COVID-19, hospital discharge, and follow-up) in patients with the most severe forms of COVID-19 infection.

Methods: Patients with COVID-19 pneumonia were consequetively enrolled, as they were admitted to the General hospital Pancevo. Exclusion criteria were previous diagnosis of inflammatory rheumatic disease and diagnosis of APS. Clinical data were obtained from the medical records. Laboratory results, including LA, aCL, anti-β2GPI, and aPS/PT antibodies were taken at hospital admission, worsening (defined as cytokine storm, connection of the patient to the respirator, use of the anti-IL-6 drug- Tocilizumab), at hospital discharge and at 3-months follow-up and sent to University Medical Centre Ljubljana, Slovenia for analysis. Statistics was performed by using SPSS 21.

Results: 111 patients with COVID-19 pneumonia were recruited; 7 patients died during hospitalisation (none were aPL-positive on admission and at the time of worsening), 3 due to pulmonary artery embolism. All patients were treated according to a predefined protocol which included antibiotics, corticosteroids, anticoagulation therapy and specific comorbidity drugs; patients with hypoxia were supported with oxygen. During hospitalisation, pulmonary artery thrombosis occurred in 5 patients, one was aPL-positive at all time points (was diagnosed with APS), others were negative. In addition, 9/101 patients had a history of thrombosis (5 arterial thrombosis (coronary and cerebral arteries), none of whom was aPL-positive on admission and at follow-up, and 4 venous thrombosis, one of which was aPL-positive at all time points and received an APS diagnosis). Among 9/101 patients with a history of thrombosis, 55.6% were transiently positive at the time of discharge, compared to patients without prior thrombosis, in whom 26.1% were transiently positive at the hospital release (p=0.074). Two patients had a history of pregnancy complications (both had miscarriage after 10th week of gestation), but did not have aPL positivity at any time point.

Conclusion: Although aPL was expected to be associated with vascular disease in the most severe forms of COVID-19, all patients that have died in our cohort were aPL negative. At hospital discharge, 56% of patients with a history of arterial or venous thrombosis had positive aPL that became negative at the 3-months follow-up (were transienlty positive), which should be considered when prescribing therapy after hospitalisation.

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POS0555

HIGH DOSE INTRAVENOUS ANAKINRA TREATMENT IS SAFE AND EFFECTIVE IN SEVERE AND CRITICAL COVID-19 PATIENTS: A PROPENSITY SCORE MATCHED STUDY IN A SINGLE CENTER

Keywords: COVID, bDMARD, Real-world evidence

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Background: In COVID-19 severe disease course such as need of intensive care unit (ICU) as well as development of mortality is mainly due to cytokine storm.

Objectives: In this study, we aimed to evaluate the high dose intravenous anakinra treatment response and outcome in patients with severe and critical COVID-19 compared to standard of care.

Methods: This retrospective observational study was carried out at a tertiary referral center. The study population consisted of two groups as follows; the patients receiving high dose intravenous anakinra (anakinra group) between 01.09.2021 and 01.02.2022 and the patients treated with standard of care (SoC, control group) as historical control group who were hospitalized between 01.07.2021 and 01.09.2021.

Results: After the propensity score 1:1 matching 79 patients in anakinra and 79 patients in SoC matched and included into the analysis. Mean±SD patient age was 67.4±16.7 and 67.1±16.3 years in anakinra and SoC group, respectively (p=0.9). Male gender was 38 (48.7 %) in anakinra and 36 (46.2 %) SoC (p=0.8). Overall, ICU admission was in 14.1 % (n=11) and 30.8 % (n=24) (p=0.013; OR: 6.2), intubation in 12.8 % (n=10) and 16.7 % (n=13) patients (p=0.5), 14.1 % (n=11) and 32.1 % (n=25) patients died in anakinra and control group, respectively (p=0.008; OR: 7.1)

Conclusion: In our study mortality was lower in patients receiving anakinra compared to SoC. Intravenous high dose anakinra is safe and effective treatment in patients with severe and critical COVID-19.

Table 1. Baseline clinical and laboratory features of patients receiving standard of care (SoC) and Anakinra before and after propensity score (PS) matching

	Before PS matching			After PS matching		
Variables	**Anakinra (n=148)**	**SoC (n=114)**	**p value (OR)**	**Anakinra (n=78)**	**SoC (n=78)**	**p value (OR)**
Age (years) (mean±SD)	66.8±17	63.1±17	0.09	67.4±16.7	67.1±16.3	0.9
Gender, male (n, %)	78 (52.7)	45 (39.5)	***0.033 (4.5)***	38 (48.7)	36 (46.2)	0.8
Duration of hospitalization (days) (median, IQR)	11 (12)	9 (7.3)	***0.02***	7.5 (9)	11 (8)	***0.01***
Comorbidities (n, %)						
Diabetes mellitus	41/146 (28.1)	39 (34.2)	0.3	18 (23)	31 (39.7)	***0.025 (5)***
Hypertension	84/143 (58.7)	64 (56)	0.7	30 (61.5)	50 (64)	0.7
Coronary heart disease	27/143 (19)	24 (21)	0.7	18 (23)	20 (25.6)	0.7
Heart failure	18/143 (12.6)	23 (20)	0.1	14 (18)	20 (25.6)	0.24
Chronic renal failure	31 (21)	6 (5.3)	***<0.001 (13.06)***	15 (19)	6 (7.7)	***0.035 (4.5)***
Chronic obstructive lung disease	23/144 (16)	19 (16.7)	0.9	14 (18)	15 (19)	0.8
Dementia	15/117 (12.8)	2 (1.8)	***0.001 (10.4)***	3/61 (5)	2 (2.6)	0.5
Malignancy	16/146 (11)	8 (7)	0.3	9 (11.5)	6 (7.7)	0.4
Immunosuppressive usage	18/146 (12.3)	2 (1.8)	***0.001 (10.08)***	5 (6.5)	2 (2.6)	0.2
Disease severity (n, %)						
NIH score 3 (severe)	57 (38.5)	68 (59.6)	***0.001 (11.5)***	48 (61.5)	44 (56.4)	0.5
NIH score 4 (critical)	91 (61.5)	46 (40.4)		30 (38.5)	34 (43.6)	
mcHIS score (mean±SD)	3.4±1.2	2.64±1.5	***<0.001***	2.9±1	3.1±1.3	0.2

PS: Propensity score, SoC: Standard of care, OR: Odds ratio, SD: Standard deviation, IQR: Interquartile range, mcHIS: Modified Covid hyperinflammatory syndrome score, NIH: National Institute Health, ALT: Alanin aminotransferase, AST: Aspartate aminotransferase

Table 2. Outcomes of patients receiving SoC and Anakinra before and after PS matching

	Before PS matching			After PS matching		
Variables (n, %)	**Anakinra (n=148)**	**SoC (n=114)**	**p value (OR)**	**Anakinra (n=78)**	**SoC (n=78)**	**p value (OR)**
Pneumothorax	3/134 (2.2)	0	0.25*	2/73 (2.7)	0	0.5*
Myocardial infarction	3/132 (2.3)	6 (5.3)	0.3	2/72 (2.8)	2/56 (3.6)	1
Pulmonary embolism	4/134 (3)	11 (9.6)	***0.034 (4.8)****	3/73 (4.1)	7 (9)	0.3*
Intensive care unit	60 (40.5)	25 (22)	***0.001 (10.2)***	11 (14.1)	24 (30.8)	***0.013 (6.2)***
Intubation	54 (36.5)	13 (11.4)	***<0.001 (21.3)***	10 (12.8)	13 (16.7)	0.5
Mortality	56 (37.8)	27 (23.7)	***0.015 (5.96)***	11 (14.1)	25 (32.1)	***0.008 (7.1)***

PS: Propensity score, SoC: Standard of care, OR: Odds ratio

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0556 LONG COVID IN RHEUMATOID ARTHRITIS AND IN PSORIATIC ARTHRITIS: CLINICAL PATTERN AND GENDER-BASED DIFFERENCES FROM A SINGLE-CENTRE CASE-CONTROL STUDY

Keywords: COVID, Rheumatoid arthritis, Psoriatic arthritis

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Background: Long Covid (LC) refers to prolonged symptoms after Sars-CoV2 infection not explained by alternative diagnosis lasting 4-12 weeks as defined by the National Institute for Health and Care Excellence. Few studies explored LC in rheumatic diseases patients (RD) concluding that they present persistent symptoms after infection, although lacking a healthy control (HC) group.
Objectives: To evaluate incidence and clinical features of LC on patients affected by Rheumatoid (RA) or Psoriatic arthritis (PsA) as well as infection's influence on disease activity.
Methods: A monocentric retrospective case-control study was conducted on consecutive outpatients affected by RA or PsA in Low Disease Activity or remission, referring to the Rheumatology Unit of University of Tor Vergata (Rome, Italy) between Sep '21 - Sep '22. Inclusion criteria: age ≥ 18 years, proven Sars-CoV2 infection between Jun '21 – Jun '22, 3 doses anti Sars-CoV2 vaccination, recovered for at least 12 weeks, diagnosis of PsA/RA before Feb '20. Exclusion criteria: symptoms explained by other diagnosis (as fibromyalgia, COPD ecc), hospitalization for Sars-CoV2. Patient were evaluated at 12 weeks after infection: demographic data, baseline comorbidities, ongoing therapy at infection and symptoms during and after infection were recorded; disease related data were recorded referred to the last clinical assessment too. Clinical features were compared among RA and PsA and with HC than among females and males patients.
Results: 120 (60 PsA/60 RA) patients and 60 HC were enrolled (Table 1). Patients compared to HC reported higher incidence of dyspnoea during infection while at resolution: lower VAS general health (GH), higher asthenia, joint pain and higher incidence of dyspnoea, chest pain, sleep disturbances and depression. All patients continued their therapy during infection and no differences were found about baseline comorbidities and ongoing therapy. No statistical differences emerged between PsA and RA patients among them but when compared with HC both presented higher VAS fatigue, joint pain, lower GH and a longer duration of anosmia and anageusia after infection. Moreover, PsA presented higher incidence of chest pain after infection and headache during and after infection; RA reported higher incidence of chest pain and headache after infection and dyspnoea during and after. Regarding gender: females reported higher VAS disease activity, asthenia and higher incidence of joint pain, dyspnoea, depression and sleep disturbances at infection resolution. Lastly, female PsA patients presented higher DAPSA score after infection than man. Disease related items were compared before and after infection (Figure 1): statistical significant differences emerged regarding VAS disease activity, asthenia, joint pain and GH in RA and PsA patients.
Conclusion: Here, we documented that RD patients – particularly females - suffer from a higher burden after Sars-Cov2 infection showing statistical significant higher incidence of symptoms than HC and a worsening of disease activity although no disease flare were registered. Thus, LC carrying a significant burden is becoming an urgent health issue that needs immediate prioritization to prevent another *national health disaster* that could be a further blow to health systems.

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Table 1. *: p <0,05; **: p<0,01

	Total RD	HC	p	Psa	RA	p PsA vs HC	p RA vs HC	Males	Females	P
Patients	120	60		60	60			48	72	
Disponea during	26,60%	11,60%	*	20%	33,30%	-	.	22,90%	35%	-
after	25%	8,30%	**	18,30%	31,60%	-	-	14,50%	38,3	*
Chest pain during	24,10%	16,60%	-	20%	28,30%	-	-	20,80%	31,60%	-
after	12,50%	0	-	10%	15%	**	*	10,40%	16,60%	-
Sleep disturbance during	43,30%	16,60%	**	41,60%	45%	**	**	27%	65%	**
after	38,30%	26,60%	-	35%	41,60%	-	-	18,70%	61,60%	**
Headache during	42,50%	28,30%	-	46,60%	38,30%	*	**	39,50%	53,30%	-
after	21,60%	11,60%	-	35%	38,30%	*	**	14,50%	31,60%	-
Depression										
after	35,80%	15%	*	35%	36,60%	-	-	20,80%	53,30%	**

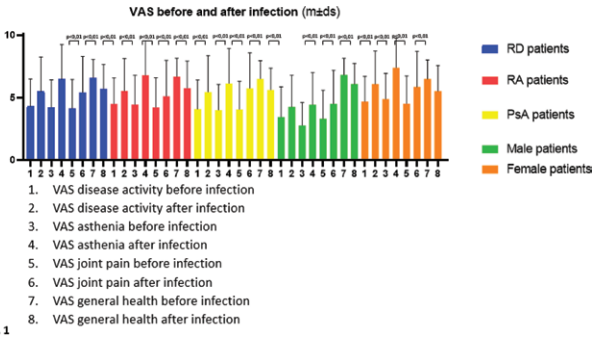


Fig. 1

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POS0557 COVID-19 OUTCOMES IN KOREAN PATIENTS WITH GOUT

Keywords: Crystal arthritis, COVID

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Background: Patients with autoimmune inflammatory rheumatic diseases are at higher risk for coronavirus disease (COVID)-19 hospitalization and worse clinical outcomes compared with the general population. However, data on the association between COVID-19 outcomes and gout, or gout-related medications are still lacking.
Objectives: We aimed to compare COVID-19 related clinical outcomes in gout vs. non-gout patients.
Methods: We conducted a retrospective cohort study using the electronic health record-based databases of Seoul National University hospital (SNUH) from January 2021 to April 2022 mapped to a common data model. Patients with gout and without gout were matched using a large-scale propensity score (PS) algorithm. The clinical outcomes of interest were COVID-19 infection, severe COVID-19 outcomes defined as the use of mechanical ventilation, tracheostomy or extracorporeal membrane oxygenation, and death within 30 days of COVID-19 diagnosis. The hazard ratio (HR) for gout vs. non-gout patients derived by Cox proportional hazard models were estimated utilizing a 1:5 PS-matched cohort.
Results: 2,683 patients with gout and 417,035 patients without gout were identified among the patients who visited SNUH. After 1:5 PS matching, 1,363 gout patients and 4,030 non-gout patients remained for the analysis. The risk of COVID-19 infection was not significantly different between patients with gout and those without gout (HR 1.07 [95% CI 0.59-1.84]). Within the first month after the COVID-19 diagnosis, there was also no significant difference in the risk of hospitalization (HR 0.57 [95% CI 0.03-3.90], severe COVID-19 outcomes (HR 2.90 [95% CI 0.54-13.71]), or death (HR 1.35 [95% CI 0.06-16.24]).
Conclusion: Patients with gout did not have an increased risk of COVID-19 infection or worse clinical outcomes. Updates of temporal trends of COVID-19 outcomes in gout patients are yet warranted as new SARS-CoV-2 variants emerge.

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Table 1. Clinical outcomes of COVID-19 infection in patients with gout

Outcomes	Unmatched population		Population with PS stratification using 10 strata		1:5 PS matched population	
	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value
COVID-19 infection	1.68 (1.03-2.57)	0.03	1.20 (0.72-1.87)	0.46	1.07 (0.59-1.84)	0.82
Hospitalization due to COVID-19	1.92 (0.32-6.05)	0.39	1.63 (0.26-5.77)	0.54	0.57 (0.03-3.90)	0.66
Severe COVID-19 infection	4.72 (1.44-11.28)	**<0.01**	4.22 (1.17-12.21)	**0.02**	2.90 (0.54-13.71)	0.20
Death due to COVID-19	1.15 (0.07-5.18)	0.90	0.77 (0.04-3.81)	0.82	1.35 (0.06-16.24)	0.84

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Disclosure of Interests: None Declared.
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POS0558

FLARES OF AUTOIMMUNE RHEUMATIC DISEASE FOLLOWING COVID-19 INFECTION: OBSERVATIONS FROM THE COVAD STUDY

Keywords: COVID, Patient reported outcomes, Real-world evidence

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Background: Viral infections can trigger flare of autoimmune rheumatic diseases through upregulation of interferon axis. However, global data on flares of AIRDs following COVID-19 infection is scarce.
Objectives: We aimed to study the prevalence and characteristics of patient-self reported flare of AIRDs following COVID-19 infection as part of the ongoing COVID-19 Vaccination in Autoimmune Diseases (COVAD) study.
Methods: The COVAD study, a cross-sectional patient-self reported electronic survey (157 collaborators, 106 countries) collected data on COVID-19 infection, vaccination and flares among AIRDs. The flares were patient self-reported. AIRDs with flare and without flare were compared. Descriptive stats and binary logistic regression (BLR) (adjusting for age, gender, ethnicity, vaccine type, type of immunosuppression, comorbidities, COVID-19 antibody status, and clinical features during previous COVID-19 infection) were performed.
Results: Of the 15165 respondents, 824 patients with AIRDs who contracted COVID-19 infection were identified. Most of the respondents were Caucasians (53.8%), females (86.5%), and had received the Pfizer-BioNTech vaccine (42.8%). Less than half were on glucocorticoids (41.0%), and methotrexate was the most commonly used immunosuppressant (29.9%). One-third (n=324, 36.9%) of patients with AIRDs reported flare following COVID-19 infection. Women and patients with comorbidities such as asthma, chronic obstructive pulmonary disease, diabetes mellitus, mental health disorders, and those with AID comorbidities had higher odds of flare compared to others (Table 1). Notably, certain features of COVID-19 disease such as joint pain (3.1; 2.0-4.9; <0.001), cough (1.5; 1.04-1.2; 0.030), and abdominal pain (2.5; 1.2-5.0; 0.011) were associated with increased risk of flares in BLR while the vaccine type, number of vaccine doses and autoantibodies against COVID-19 were not predictive. Patients who reported flares had worse PROMIS PF10 physical health scores (p=0.038), pain VAS (p<0.001), and lower mental health scores (p<0.001) compared to those who did not report flares.
Conclusion: One in three patients with AIRDs reported post-COVID-19 disease flares. A past history of asthma, comorbidities and those with certain acute COVID-19 symptoms were at higher risk.
REFERENCES: NIL

Table 1. Patient-reported flares following COVID-19 infection among AIRD patients who contracted COVID-19

	Total AIRDs (n=824) N (%)	AIRDs with flare following infection (n=304) N (%)	AIRDs without flare following infection (n=520) N (%)	OR (95%CI)	p
Age (median, IQR) years	46.0 (36.0-55.0)	45.0 (37.0-55.0)	46.0 (36.0-57.0)	-	0.121
Gender				1.6 (1.04- 2.5)	0.032
Male	105 (12.7)	29 (9.5)	76 (14.6)		
Female	713 (86.5)	274 (90.1)	439 (84.4)		
Comorbidities					
Any comorbidity	361 (43.8)	151 (49.7)	210 (40.4)	1.2 (1.06-1.5)	0.010
Asthma	96 (11.7)	46 (15.1)	50 (9.6)	1.6 (1.09-2.5)	0.017
Chronic obstructive lung disease	18 (2.2)	12 (3.9)	6 (1.2)	3.5 (1.3-9.4)	0.008
Diabetes Mellitus	42 (5.1)	22 (7.2)	20 (3.8)	1.9 (1.04-3.6)	0.033
Mental health disorders	258 (31.3)	126 (41.4)	132 (25.4)	1.5 (1.3-1.8)	<0.001
Non-rheumatic AID comorbidities					
Yes	218 (26.5)	98 (32.2)	120 (23.1)	1.5 (1.1-2.1)	0.004
COVID-19 antibody status					
Antibodies present	124/150 (82.6)	48/58 (82.7)	76/92 (82.6)	1.0 (0.4-2.4)	0.981
PROMIS PF Global 10a (median, IQR)					
Global physical health score	13.0 (12.0-15.0)	14.0 (12.0-15.0)	13.0 (12.0-15.0)	-	0.038
Global mental health score	13.0 (10.0-15.0)	12.0 (9.0-14.0)	13.5 (11.0-16.0)	-	<0.001
Fatigue VAS	3.0 (3.0-4.0)	3.0 (2.0-3.0)	4.0 (3.0-4.0)	-	0.003
Pain VAS	4.0 (2.0-6.0)	5.0 (3.2-7.0)	2.0 (1.0-5.0)	-	<0.001

Chi-Square for Categorical variables, Mann Whitney U for scale variable comparisons.AIRDs: Autoimmune rheumatic diseases, IQR: Interquartile range, OR: Odd's ratio,

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POS0559 **ACCELERATED WANING OF HUMORAL IMMUNE RESPONSE TO A THIRD COVID-19 VACCINATION IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES**

Keywords: Vaccination/immunization, COVID

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Background: A 3rd COVID-19 vaccination is currently recommended for patients under immunosuppression. However, a fast decline of antibodies against the SARS-CoV-2 receptor-binding domain (RBD) of the spike protein has been observed.
Objectives: It remains unclear whether immunosuppressive therapy affects kinetics of humoral and cellular immune responses.
Methods: 50 patients under immunosuppression and 42 healthy controls (HCs) received a 3rd dose of an mRNA-based vaccine and were monitored over a 12-weeks period. Humoral immune response was assessed 4 and 12 weeks after 3rd dose. Antibodies were quantified using the Elecsys Anti-SARS-CoV-2 Spike immunoassay against the receptor-binding domain (RBD) of the spike protein. SARS-CoV-2-specific T cell responses were quantified by IFN-γ ELISpot assays. Adverse events, including SARS-CoV-2 infections, were monitored over a 12-week period.
Results: At week 12, reduced anti-RBD antibody levels were observed in IMID patients as compared to HCs (median antibody level 5345 BAU/ml [1781 – 10208] versus 9650 BAU/ml [6633 - 16050], p < 0.001). Reduction in relative antibody levels was significantly higher in IMID patients as compared to HCs at week 12 (p < 0.001). Lowest anti-RBD antibody levels were detected in IMID patients who received biological diseases modifying anti-rheumatic drugs (DMARDs) or a combination therapy with conventional synthetic and biological DMARDs. Number of SARS-CoV-2-specific T cells against wildtype and Omicron variants remained stable over 12 weeks in IMID patients. No serious adverse events were reported.
Conclusion: Due to a fast decline in anti-RBD antibodies in IMID patients an early 4th vaccination should be considered in this vulnerable group of patients.
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Public health, health services research, and health economics

POS0560 **OUTCOME OF NEONATES BORN TO PATIENTS WITH RHEUMATIC DISEASES COMPARED TO HEALTHY CONTROLS**

Keywords: Pregnancy and reproduction

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Background: In general, more women are affected by rheumatic diseases and often during their reproductive age. Due to disease activity and/or specific autoantibodies autoimmune diseases might lead to impaired fetal outcome. Data from large registries help to improve information on the risks for patients and infants and thus enable us to better advise our patients.
Objectives: To analyse fetal outcome of babies born to patients with rheumatic diseases by different parameters and compare to healthy controls.
Methods: This study compares registry data from 2012–2022 from a specialized centre. We included 351 pregnancies from patients with rheumatic diseases and 1298 from age-matched HC.
Results: Patients with rheumatic diseases were distributed as follows: 58% CTD, 15% RA, 13% SpA, 5% autoinflammatory diseases and 4% vasculitis. Spontaneous abortion rate with 5% was comparable to the general population [1], APGAR, and umbilical cord pH were comparable to HC. Babies born to patients with rheumatic diseases have a significantly different outcome compared to HC: they present with lower birth weight (3245g vs 3038g; p<0.001) and length (50.7cm vs.49.7cm; p<0.001), higher number of intrauterine growth retardation (IUGR; 3% vs 7%; p<0.05) and are more often preterm (10% vs 16%; p<0.01). There is also a difference in the delivery mode, with a significant higher rate of scheduled caesarean birth rate (12%vs.32%;p<0.001),however not of unplanned caesarean birth. We also observed higher number of congenital anomalies (6%vs.12%;p<0.01) usage of postpartal continuous positive airway pressure (CPAP) therapy (4%vs.12%;p<0.001) and transfer to specialized neonatal care (10%vs.19%;p<0.001).When comparing different groups of rheumatic diseases, our analysis shows mainly abnormalities for CTD (especially SLE, Sjogren's syndrome and undifferentiated CTD),with high rates of small for gestational age (SGA; SLE:19%, SS:28%; UCTD:28%), high proportion of planned caesarean birth (SLE:44%).However, congenital anomalies were also more prominent in the group of patients with SpA. Interestingly, in the age group >35years patients and HC assimilated, eg we did not observe significant differences for birth weight anymore.
Conclusion: Fetal outcome of neonates born to patients with rheumatic diseases in general is favourable, as we observed a live birth rate of 95%. This is also supported by important parameters as APGAR and umbilical cord pH, which did not differ in between groups. However, the number of children born before 37gw and lower birth weight/length is significantly higher compared to HC. This has been suggested by us and other groups [2-4], but we here compare the fetal outcome of patients to an age-matched HC group from the same hospital, and therefore more comparable and valid data. One might speculate, that higher rates of preterm births explain the higher admission rate to neonatal care and CPAP therapy. Our data reveal, however, that these differences mainly affect patients with CTD, especially SLE, SS, UCTD, which is of special interest for the risk assessment in the treatment of pregnant patients with rheumatic diseases. Even though spontaneous abortion rates do not differ to the general population, we observed a significantly higher number of congenital anomalies. Further studies are necessary to determine the underlying cause, as both, disease activity and immunosuppressant medication might be responsible.
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POS0561 THE LEAKY PIPELINE IN CLINICAL RHEUMATOLOGY ACROSS EUROPE – RESULTS FROM AN ONLINE SURVEY

Keywords: Work-related issues, Health services research, Gender/diversity issues

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Background: While more than 50% of medical students and residents are women, their proportion drastically diminishes within higher ranks and leadership roles, a phenomenon also known as the "leaky pipeline".

Objectives: We aimed to evaluate the leaky pipeline among rheumatologists across Europe and to assess determinants inducing rheumatologists to leave hospitals.

Methods: Experts in the field of economics developed a questionnaire (50 thematic blocks, containing 172 single items) with relevance to the leaky pipeline. with scientific focus on the leaky pipeline among rheumatologists, which was distributed electronically by national scientific societies of EULAR countries and by individual contacts. We performed common factor analysis, univariate t-tests and multivariate regression analyses to appraise our dataset using Stata Version 17 (StataCorp, Texas, USA).

Results: 311 hospital-based rheumatologists from 23/45 EULAR countries (52.7% females, 47.3% males) responded to the questionnaire. The phenomenon of the leaky pipeline was present for the entire sample. Of 64% female rheumatologists only 34.2% departments' directors were female, with noteworthy regional differences (Table 1). Female doctors reported higher intentions to leave their hospitals ($\beta = 0.28$, $p < 0.05$) and lower commitment towards their current organization ($\beta = -0.34$, $p < 0.05$) when compared to males. Additionally, women reported lower levels of job satisfaction ($\beta = -0.26$, $p < 0.10$), promotion justice ($\beta = -0.55$, $p < 0.01$), and career perspectives ($\beta = -0.15$, $p < 0.10$, one-tailed) than men, explaining their lower organizational commitment.

Conclusion: Female rheumatologists perceive worse job opportunities and satisfaction than males. Many reasons for the leaky pipeline are beyond the control of organizations. By our results, organizations should be encouraged to reconsider and adjust their performance management practices enabling an equitable work environment.

Table 1. Leaky pipeline among rheumatologists working in hospitals across Europe

Overall Sample (n = 311)	
Percentage of female doctors in department	64.0%
Percentage of female doctors employed as senior physicians in department	49.2%
Percentage of female department heads	31.8%
Germany/Austria/Switzerland (n = 91)	
Percentage of female doctors in department	51.0%
Percentage of female doctors employed as senior physicians in department	42.2%
Percentage of female department heads	7.7%
Northern European Countries (n = 19)	
Percentage of female doctors in department	56.4%
Percentage of female doctors employed as senior physicians in department	50.5%
Percentage of female department heads	47.4%
Southern European Countries (n = 58)	
Percentage of female doctors in department	62.9%
Percentage of female doctors employed as senior physicians in department	36.4%
Percentage of female department heads	24.1%
Eastern European Countries (n = 133)	
Percentage of female doctors in department	73.4%
Percentage of female doctors employed as senior physicians in department	57.0%
Percentage of female department heads	45.9%

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POS0562 FREQUENCY OF IN-PERSON AND VIRTUAL VISITS FOR RHEUMATOID ARTHRITIS: ANALYSIS OF THREE YEARS OF VISIT DATA BEFORE AND AFTER THE COVID PANDEMIC

Keywords: COVID, Telemedicine, Rheumatoid arthritis

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Background: Few data have been published regarding appropriate visit frequency in rheumatoid arthritis (RA). While guidelines suggest more frequent visits early in disease and when disease is active, there are few descriptions of visit frequency. Also, visit frequency may have changed during the COVID pandemic.

Objectives: We examined visit frequency and types of visits (in-person versus virtual) for patients with RA seen at one US academic medical center during the 18 months before COVID lockdown, 3 months of lockdown, and 18 months after.

Methods: We extracted data from 11 clinically focused rheumatologists' practices at an academic medical center and created a sample of 257 patients with rheumatologist-diagnosed RA. The study period of interest encompassed the 18 months prior to COVID pandemic (Nov 2018 – Feb 2020), the 3 months of COVID lockdown (rheumatology clinic closed except emergencies, March – May 2020), and the 18 months after lockdown (June 2020 – Sept 2021); patients were required to have ≥1 visit prior and ≥1 visit after the lockdown to be included. We estimated: 1) monthly volume of in-person and virtual visits (telephone-only or video) for the RA study cohort, and 2) annual median patient visit frequencies. In addition, we assessed predictors of a patient's visit volume using multivariable linear regression over the pre- and post-lockdown periods. Variables tested included RA disease characteristics (CRP, serologic status, and DMARD use), patient demographics and comorbid conditions, and rheumatologist.

Results: Patient characteristics are shown in the **Table 1**. Patients' median age was 58y, 84% were female; 82% used any DMARD; 20% used only csDMARDs; and 61.5% used a t/bDMARD. Visit volume over 39 months is illustrated by visit type in the **Figure 1**. In the 18 months prior to the COVID pandemic, median annual visit frequency per patient was 2.7 (IQR 2.0, 3.3), with an overall median monthly visit volume of 61 (IQR 51, 58). Overall visit volume remained consistent post-lockdown: median annual visit frequency per patient 2.7 (IQR 2.0, 3.3), with an overall median monthly visit volume of 68 (50, 73). As expected, median monthly visit volume was reduced during the lockdown period: 58 (IQR 51, 65); but it rebounded to pre-pandemic levels within 9 months. During the first 3 months post-lockdown, virtual visits comprised 61% of all visits (51% video,

Table 1. Baseline Characteristics of 257 Patients with Rheumatoid Arthritis Followed in this Cohort

Patient Characteristics	N (%) or median (interquartile range)
Age, years	58.2 (48.7, 65.8)
Female sex	216 (84.0%)
Charlson-Deyo comorbidity index	1.0 (1.0, 1.0)
Race	
Black	11 (4.3%)
Other	21 (8.2%)
White	225 (87.5%)
Seropositive (n = 128)	87 (68.0%)
hsCRP, mg/L	2.0 (0.7, 5.0)
Disease modifying anti-rheumatic drug (DMARD) use	
csDMARD	147 (57.2%)
t/bDMARD	158 (61.5%)
Both	95 (37.0%)
Neither	47 (18.3%)
Non-steroidal anti-inflammatory drugs (NSAID) use	61 (23.7%)
Glucocorticoid (oral) use	84 (32.7%)
Opioid use	38 (14.8%)

*rheumatoid factor or anti-CCP antibody

10% telephone only). By the 12th month post-lockdown, virtual visits comprised 11% of all visits; all were video. The following variables associated with increased patient visit volume during the pre- and post-lockdown periods (36 months): older age and fewer comorbidities. When specific rheumatologists were added as fixed effects, these variables strengthened in their significance; additionally, several rheumatologists were associated with significant increases in visit volume.
Conclusion: The COVID pandemic caused a disruption in rheumatology practice with a rapid substitution of virtual visits. Office visit volume for RA rebounded relatively quickly in one US-based academic practice. Virtual visits were common during and immediately after lockdown but became less common over time. Several variables, unrelated to RA, were associated with visit volume.
References: None.

Figure: Longitudinal Pattern of Monthly Visit Volume Across 257 Patients with Rheumatoid Arthritis

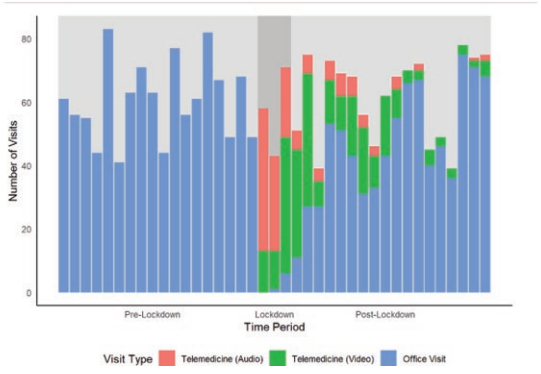


Figure 1. Longitudinal Pattern of Monthly Visit Volume Across 257 Patients with Rheumatoid Arthritis

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POS0563

USE OF A DIGITAL SOLUTION TO MONITOR CHRONIC INFLAMMATORY RHEUMATIC MUSCULOSKELETAL DISEASES: FINAL RESULTS OF THE DIGIREUMA STUDY

Keywords: Outcome measures, Self-management, Health services research

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Background: Patients with rheumatic and musculoskeletal diseases (RMDs) require a tailored follow-up, which may be limited by the healthcare resources. Innovative tools that save time need to be implemented effectively in the clinical care of patients with RMDs.
Objectives: To test the feasibility of a digital solution for real-time monitoring of electronic patient reported outcomes (ePROs) in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA).
Methods: Digireuma was a bicentric 6-month prospective study including patients with RA and SpA, using a digital solution, namely Adhera Rheumatology Digital Program. During follow-up, patients had a hybrid follow-up: face-to-face -baseline and 6 months visits-and digital. In the digital follow-up, patients were asked to report disease specific ePROs on a pre-established basis in the mobile solution- including at least one assessment per week. In addition, flares and incidences with medication were available to be reported at any time. Four rheumatologists monitored these outcomes, and contacted patients when deemed necessary (**Figure 1**). Assessment measures included patient global assessment (PGA) of disease activity, (self-reported) tender joint count (TJC) and swollen joint count (SJC), Health Assessment Questionnaire (HAQ) and pain visual analogue scale (VAS), for patients with RA; PGA, TJC, SJC, BASDAI, and ASAS-Health Index, for patients with SpA. All measures were delivered every two weeks. Engagement at 3 and 6 months was assessed.
Results: Out of 56 recruited patients, 51 (24/27 (89%) RA, 27/29 (93%) SpA) downloaded and used the mobile solution and 47 (84%) submitted at least one ePROs entry. Median age (IQR) was 47 (13.2) and 40 (16.0) years in the RA and SpA groups, respectively. 20/27 (74%) patients with RA and 14/29 (48%) with SpA were female. In the RA group there were a total of 2156 digital solution accesses (57 per patient) in 6 months, while patients with SpA had a total of 1644 accesses (29 per patient). ePROs measurements outcomes at baseline and 6 months are shown in **Table 1**. Patients with RA completed a median of 6710 ePROs interactions during follow-up, whereas patients with SpA completed a median of 4315. Regarding alerts, among a total of 52 notifications, 47 were deemed necessary to be contacted (5 cases were assessed directly in a programmed consultation, due to time-proximity). Among all alerts, 45 were flares (31 RA, 14 SpA) and 4 problems with the medication (3 causes were not registered). Of the 47 cases that were contacted, 36 (77%) were managed remotely, 9 (19%) required a face-to-face intervention and in 2 (4%) cases it was not possible to reach patients before consultation. Regarding engagement, at three months 26 patients (55%)- 15 with RA and 11 with SpA- continued submitting data periodically, while at six months 22 patients (47%)- 13 with RA and 9 with SpA- continued submitting any data.
Conclusion: This study shows that ePROs can be used to monitor disease activity, flares, and medication issues in patients with RA and SpA, with three out of four alerts being managed remotely. After six months, more than half of the patients showed non-adherence to the monitoring plan/digital solution. The participation of both healthcare professionals and patients is critical for the successful implementation of mobile health in clinical practice, specially to identify long term usage strategies.

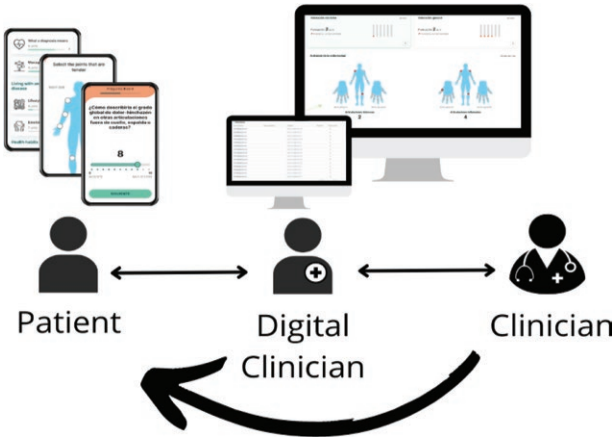


Figure 1. Digital monitoring in the study

Table 1. Onboarded patient outcomes

	DAS-28	BASDAI	TJC	SJC	HAQ	PtGA	VAS pain
Baseline, Face-to-face							
RA	2.6 (1.6, 3.6)	-	1 (0, 3.25)	0.5 (0, 2.5)	0.13 (0, 0.9)	2 (1, 5)	4 (2, 5)
SpA	-	2.1 (0.8, 3.8)	0 (0, 1)	0 (0, 1)	-	2 (1, 4)	2.5 (1, 4)
Baseline, Digital							
RA	-	-	1 (1, 3)	1 (1, 2.5)	0.2 (0, 0.5)	2 (1.8, 3.5)	3 (1, 6)
SpA	-	3.3 (1.5, 7)	1 (1, 2.75)	3 (1.2, 4.75)	-	1 (1, 2.5)	-
6 months, Face-to-face							
RA	1.6 (1.1, 2.9)	-	0 (0, 2)	0 (0, 2)	0.13 (0, 0.63)	1.5 (0.5, 4)	1.35 (0.75, 3)
SpA	-	2.2 (1.2, 4.8)	0 (0, 2)	0 (0, 0.25)	-	2 (1, 5)	2 (1, 4.25)
6 months, Digital							
RA	-	-	1 (1, 1.8)	1 (1, 1.8)	0.25(0.1, 0.5)	2 (2, 2.8)	2 (1, 2)
SpA	-	2.2(1.9, 2.5)	2.5(2.2, 2.8)	5 (3, 7)	-	2.5(1.5, 3.3)	-

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Disclosure of Interests: Diego Benavent Speakers bureau: Janssen, Roche, Galapagos., Grant/research support from: Novartis, Abbvie., Luis Fernández-Luque Employee of: Employee of AdheraHealth Inc., María Sanz: None declared, Victoria Navarro-Compán Speakers bureau: AbbVie, Eli Lilly, Janssen, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie and Novartis, Marta Novella-Navarro Speakers bureau: Galapagos, UCB, Lilly and Janssen, Grant/research support from: UCB, Lilly and Janssen, Ioannis Bilionis Employee of: Employee of AdheraHealth Inc, Enrique Calvo-Aranda Speakers bureau: Abbvie, LETICIA LOJO: None declared, Alejandro Balsa Speakers bureau: Pfizer, Abbvie, Lilly, Galapagos, BMS, Sandoz, Nordic Pharma, Gebro, Roche, Sanofi, UCB, Consultant of: Pfizer, Abbvie, Lilly, Galapagos, BMS, Nordic Pharma, Sanofi, UCB, Grant/research support from: Pfizer, Abbvie, BMS, Nordic Pharma, Gebro, Roche, UCB, Chamaida Plasencia Speakers bureau: Pfizer, Abbvie, Lilly, Sandoz, Sanofi, Biogen, Roche, Novartis, Grant/research support from: Pfizer and Abbvie.
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POS0564 THE IMPACT OF BIOSIMILAR SWITCHING POLICIES IN INFLAMMATORY ARTHRITIS ON UPTAKE AND SPENDING IN BRITISH COLUMBIA, CANADA

Keywords: bDMARD

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Background: The uptake of biosimilars has been suboptimal in North America. In response, in 2019, British Columbia (BC) became the first jurisdiction in North America to require patients with inflammatory arthritis to switch to a biosimilar version of infliximab and etanercept to maintain public coverage through the 'Biosimilars Initiative' policy. In 2021 this policy was extended to include adalimumab. The Biosimilars Initiative extended a previous policy which required people starting a biologic to use a biosimilar. Large commercial insurers which provide supplementary drug coverage also introduced biosimilars policies in line with the BC provincial government. Under both biosimilar switching policies, exceptional coverage to reference products was allowed if medically needed.
Objectives: To quantify the impact of the Biosimilars Initiative and the initial policy requiring new initiators to a biologic to use a biosimilar on uptake and spending on biosimilar infliximab, etanercept, and adalimumab in British Columbia (BC).
Methods: Administrative claims data in BC from January 2013 through March2023 were analyzed using interrupted time series analysis, a quasi-experimental study design commonly used to evaluate policy changes. Two policy interventions were evaluated: (1) *new starts*, whereby individuals initiating infliximab, etanercept, or adalimumab for the first time were required to start the biosimilar (implemented between Feb 2016 and July 2017), and (2) *mandatory switching*, which required those already receiving infliximab or etanercept (implemented between May and Nov 2019), or adalimumab (implemented between April and October 2012) to switch to the biosimilar version in order to maintain coverage. A segmented linear regression was used to model the level and trend change in biosimilar etanercept and infliximab utilization and spending before and after the two policy interventions.
Results: We identified 208,984 BC residents ≥18 years who qualified for public drug coverage, were treated with etanercept or infliximab, and were eligible for analysis between January 2013 and November 2020. After the *new start* policy, we detected a small gradual increase in the proportion of biosimilar etanercept prescriptions dispensed of 0.65% (95%CI 0.44, 0.85) per month. The monthly trend related to the proportion of total spending on biosimilar etanercept also increased (0.51, 95%CI 0.28, 0.73). After the *mandatory switching* policy (the Biosimilars Initiative), there was a sustained increase in the proportion of biosimilar etanercept and infliximab prescriptions dispensed of 76.98% (95%CI 75.56, 78.41) and 58.43% (95%CI 52.11, 64.75), respectively. Similarly, there was a persistent increase in spending on biosimilar etanercept and infliximab of 78.22% (95%CI 76.65, 79.79) and 71.23% (95%CI 66.82, 75.65), respectively. Similar results were seen for adalimumab which was switched later.

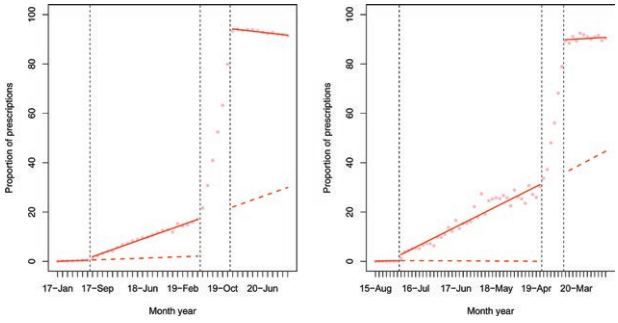


Figure 1. Overall proportion of prescriptions dispensed that were biosimilar etanercept and infliximab

Conclusion: Our study found *new start* policies resulted in small, gradual increases in biosimilar utilization. However, the *mandatory switch* policy, the Biosimilars Initiative, resulted in a marked immediate and sustained impact on uptake. Further analysis will examine changes in other health utilization, and long-term impact on prescribing patterns. These findings may be particularly relevant to areas with a more concentrated insurance system where mandatory switching policies could lead to greater savings.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0565 TOLERABILITY AND SAFETY OF RECOMBINANT ZOSTER VACCINE IN PATIENTS WITH INFLAMMATORY RHEUMATIC MUSCULOSKELETAL DISEASES - A PROSPECTIVE LONGITUDINAL STUDY OVER 6 MONTHS

Keywords: Safety, Vaccination/immunization, Infection-related RMDs

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Background: Herpes zoster (HZ) is common in the elderly with a lifetime risk of 25% (1). The primary risk factors for HZ are advanced age and immunosuppression. The recombinant zoster vaccine (RZV) contains recombinant glycoprotein E, the main target of CD4+T-cells.
Objectives: To describe the safety of RZV in patients with inflammatory rheumatic and musculoskeletal diseases (RMD).
Methods: Adult patients with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and giant cell arteritis (GCA) who had an indication to receive RZV were prospectively included. Data on demographics, vaccination, RMD diagnosis, disease activity, immunosuppressive treatments, flares, adverse events (AEs) and zoster breakthrough infections were collected at month 0, 2, 3 and 6. A flare was defined as change in ASDAS ≥ 0.9 for axSpA, change in DAS-28>1.2 for RA, or clinical signs for GCA and/or CRP ≥ 0.5 mg/dl and/or ≥30 mm. Descriptive analyses were performed.
Results: 50 patients were included of whom 18 (36.0%) had a history of HZ (Table 1). All patients received RZV at month 0, and 49 patients also at month 2. Safety assessments were performed in 49, 48 and 36 patients in months 2, 3 and 6, respectively. A total of 62, 35, 11 AE in 38, 33, and 10 patients, respectively, were reported (Figure 1). Localized AE (n=69 (63.9%)) were far more common than generalized AE (n=28 (25.9%)). Pain at the site of injection in 46 (42.6%) patients was the most frequent AE followed by fatigue (12 (11.0%)), redness at the injection site in (9 (8.3%)), swelling at the injection site (7 (6.4%)) and fever (5 (4.6%)). Serious AEs were reported in 6 patients (2 RA, 4 GCA). None of them with causal relation to RZV. No patient reported an AE of special interest. Out of 6, 4 and 4 flares reported by patients at month 2, 3 and 6, respectively, no one fulfilled predefined flare criteria and were rated as mild to moderate. However, 3 patients (2 GCA, 1 RA) were hospitalized due to flares. No episodes of HZ occurred.
Conclusion: The majority of patients tolerated RZV well with only a few reports of flare and serious AEs. Majority of AEs occurred within few days after vaccination. These findings are reassuring for rheumatologists and potential vaccine recipients and support confidence in RZV safety in patients with RMD.
REFERENCES:
[1] Thomas SL, Hall AJ. What does epidemiology tell us about risk factors for herpes zoster? Lancet Infect Dis. 2004;4(1):26–33.
Funding: The study was funded by GSK.

Table 1. Patients and disease characteristics

Variable	RA (n=18)	AxSpA (n=12)	GCA (n=20)
Age	55.4 (11.6)	46.6 (9.6)	73.3 (6.8)
Sex, female (No., %)	9 (50.0)	2 (16.7)	14 (70.0)
History of zoster (No., %)	5 (27.8)	2 (16.7)	11 (55.0)
CRP, mg/dl	0.5 (0.8)	0.8 (1.2)	0.2 (0.3)
Prednisolone, mean dosage mg/dl	(n=6 (33.3%))	0	(n=9 (45.0%))
	3.2 (1.7)		14.1 (15.6)
csDMARD(No., %)	18 (100.0)	0	8 (40.0)
bDMARD(No., %)	13 (72.2)	6 (50)	8
tsDMARD(No., %)	3 (16.7)	6 (50)	0
Physician global	0.9 (1.7)	2.3 (1.5)	0.8 (1.5)
Patient global	3.8 (2.2)	3.5 (2.1)	3.9 (2.6)
Pain	3.8 (2.28)	3.1 (2.08)	3.6 (2.6)
Disease activity	DAS-28	ASDAS	NA
	2.4 (1.3)	2.0 (1.1)	
Physical function	FFbH	BASFI	FFbH
	76.6 (20.9)	4.1 (2.0)	71.2 (23.3)

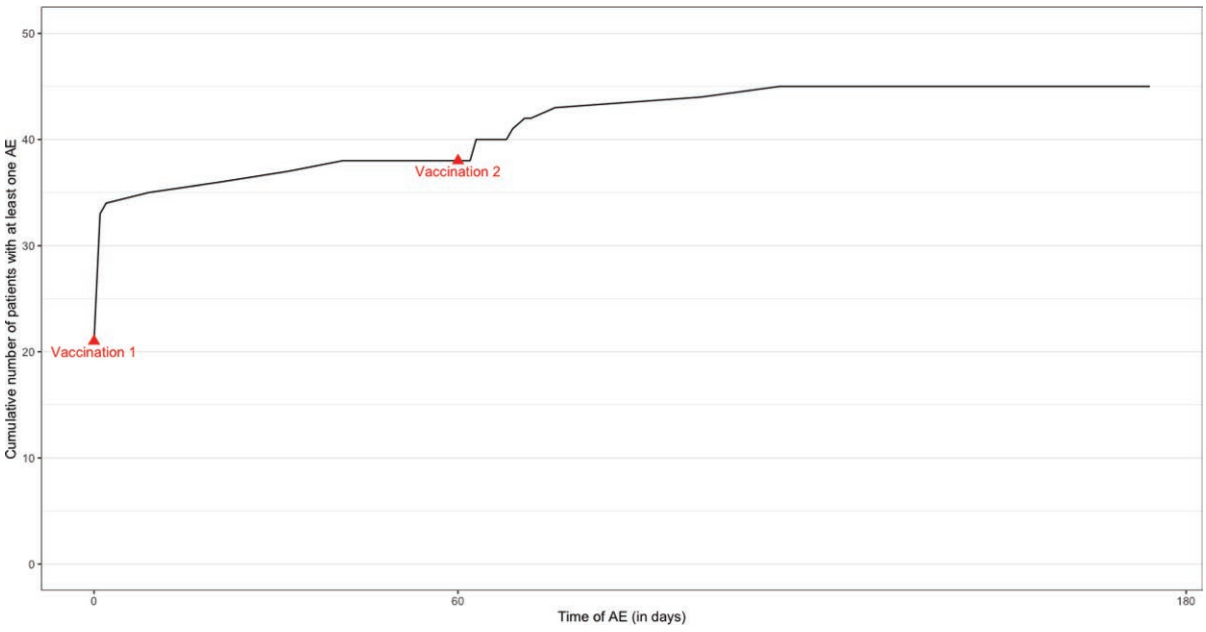


Figure 1. Cumulative number of patients with at least one adverse event

Disclosure of Interests: Ioana Andreica Speakers bureau: Abbvie, Chugai, Novartis, UCB, MSD, Lilly, Sobi, Astrazeneca, Amgen, Pfizer, Gilead, Paid instructor for: Astrazeneca, UCB, Consultant of: Abbvie, Chugai, Novartis, UCB, Galapagos, Takeda, Astrazeneca, Lilly, Boehringer Ingelheim, Amgen, Sobi, Stefania Reale: None declared, Gianna Intini: None declared, Benjamin Wilde: None declared, David Kiefer Speakers bureau: Abbvie, BMS, Roche, Chugai, Novartis, UCB, Sanofi, MSD, Merck, GSK, Janssen, Boehringer Ingelheim, Galapagos, Consultant of: Abbvie, BMS, Roche, Chugai, Novartis, UCB, Sanofi, MSD, Merck, GSK, Janssen, Boehringer Ingelheim, Galapagos, Grant/research support from: Novartis, Philipp Sewerin: None declared, Hilal Kavruk: None declared, Dimitra Karagkiozidou: None declared, Barbara Guminski: None declared, Andreas Kribben: None declared, Xenofon Baraliakos: None declared, Jürgen Braun: None declared, Uta Kiltz Speakers bureau: Abbvie, Novartis, Janssen, Hexal, Gilead, MSD, Roche, Consultant of: Abbvie, Novartis, Lilly, Janssen, Gilead, UCB, Onkowissen, Grant/research support from: Biogen, Abbvie, Novartis, Hexal, Fresenius, Amgen.

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POS0566

SURVIVAL ON TREATMENT AFTER SWITCHING TO A BIOSIMILAR: POPULATION-BASED EVIDENCE FROM A NATURAL EXPERIMENT DUE TO A POLICY CHANGE

Keywords: Health services research, bDMARD, Inflammatory arthritides

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Background: In the province of British Columbia (BC), Canada, a health policy implemented in July 2017 mandated that all new anti-TNF prescriptions for which a biosimilar exists, i.e., etanercept and infliximab at the time, be dispensed a biosimilar rather than the originator, for universal cost coverage by BC PharmaCare. In May-December 2019, a further policy mandated that current users of anti-TNF agents be switched to the corresponding biosimilar.

Objectives: The objective of this study is to compare the survival on treatment (as a surrogate marker of effectiveness and safety), between biosimilar switchers vs. users of originator Anti-TNF for inflammatory arthritis, after and before the health policy change.

Methods: Study Cohort: Using administrative data and validated definitions, we identified etanercept and infliximab users with rheumatoid arthritis (RA), psoriasis or psoriatic arthritis (Pso/PsA), or ankylosing spondylitis and other spondyloarthritis (SpA). Biosimilar switchers were current biologic users who switched to the corresponding biosimilar during the period of May to December 2019. Historical controls were randomly selected from all new users of originator etanercept and infliximab before July 2017, matched to biosimilar switchers on sex, previous number of biologics used, and disease. Controls were assigned an index date such that duration of originator anti-TNF therapy was the same at switching/index date for switchers and controls. Outcomes: Discontinuation was defined as no prescription renewal for at least 6 months. Statistical method: We followed patients from switching/index date to discontinuation, or for two yearsor until last health care utilization (if moving out-of-province), or end date of the follow-up (April 30, 2019 for originators, and December 31, 2021 for switchers), whichever occurred first. Weighted Cox proportional hazards models with propensity score overlap weighting estimated the HR of discontinuing anti-TNF agents for controls and switchers, adjusting for duration of of anti-TNF agent use at switch/index date, age, sex, socio-economic status (low income subsidy), rural vs urban residence, health authority, arthritis type, number of prior biologic agents, comorbidities, and other IA drugs used (MTX, non MTX DMARDs and glucocorticosteroids), all measured at time of switching/index date.

Results: A total of 1631 biosimilar switchers (1402 eternercept; 229 infliximab) were included in this study: 556(67.2%) RA, 178(21.5%) SpA, 93(11.2%) Pso/PsA patients. Table 1 shows numbers, rates (per 100 person-years), and hazard ratio of discontinuation among biosimilar switchers compared with originator users. Figure 1 shows survival on treatment. The discontinuation rates for the biosimilar eternacept users was similar to the originator users (15.42 vs 15.63) per 100 PYs: HR (95% CI) 1.02 (0.87, 1.19 [p=0.718]). The biosimilar infliximab switchers had a slightly lower discontinuation rate than the originator users, however the difference in rate and risk of discontinuation were not statistically significant (8.76 vs 11.29) per 100 PYs: HR (95% CI) 0.85 (0.54, 1.36 [p=0.503]).

Conclusion: Population-based data on real-world experience mandating switching from originator to biosimilar etanercept and infliximab for IA revealed the biosimilar switchers have comparable duration of treatment to the original medications.

Table 1. Discontinuation of anti-TNF in biosimilar switchers and originator controls.

Anti-TNF Drug	Cohort	discontinuation/ sample (N)	Median Follow-up, Years	Rate Per 100 PYs	Weighted CoxPH HR (95% CI)	p
Etanercept	Originator	347/1402	1.58	15.63	1.00	
	Biosimilar	354/1402	1.64	15.42	1.02(0.87,1.19)	0.820
Infliximab	Originator	44/229	1.70	11.29	1.00	
	Biosimilar	36/229	1.80	8.76	0.85(0.54,1.36)	0.503

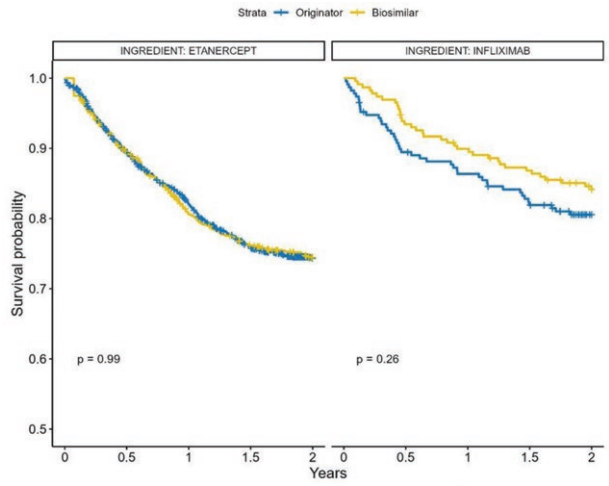


Figure 1 Kaplan Meier Survival Curve on Biologic after switching/index date

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POS0567

COMPARISON OF SURVIVAL ON TREATMENT AMONG NEW USERS OF BIOSIMILAR VS. ORIGINATOR BIOLOGICS IN INFLAMMATORY ARTHRITIS: POPULATION-BASED EVIDENCE FROM A NATURAL EXPERIMENT DUE TO A POLICY CHANGE

Keywords: Health services research, bDMARD, Inflammatory arthritides

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Background: British Columbia (BC) health policy mandated the use of biosimilars, when available, for all new anti-TNF prescriptions after June 2017.
Objectives: To compare drug survival (surrogate marker of effectiveness and safety) after initiation of etanercept and infliximab for inflammatory arthritis in new users of biosimilars vs. originators, using historical controls pre-policy change.
Methods: Using administrative health data, we identified all incident users of a new anti-TNF with rheumatoid arthritis (RA), psoriasis or psoriatic arthritis (Pso/PsA), or ankylosing spondylitis (AS). The biosimilar cohort started etanercept or infliximab between 07/01/2017 and 12/31/2019, were followed until 12/31/2020 (post-policy period). Historical controls started etanercept/infliximab originators between 01/01/2014 and 06/30/2016, were followed until 06/30/2017 (pre-policy period). To control for potential temporal trends, new users of adalimumab (no biosimilar available then) served as comparators. Discontinuation was defined as no prescription renewal for ≥6 mos. Individuals were followed from anti-TNF initiation until discontinuation or censoring due to death, moving out-of-province, or follow-up end, whichever occurred first. We applied weighted Cox Proportional Hazard Models that handle non-proportional hazards combined with propensity overlap weighting to estimate the adjusted hazard ratio (aHR) of discontinuing anti-TNFs, in people who started a biosimilar vs. the respective originator, after controlling for potential confounders. To control for temporal trend, we employed the difference-in-difference (DID) method, comparing drug survival among new biosimilar vs. originator etanercept/infliximab users with adalimumab users post- vs. pre-policy change, computed as the difference between the logarithms of aHRs for etanercept/infliximab and for adalimumab. We report the exponential of DID estimates (i.e. the ratio of the two aHRs).
Results: Our sample included 827 biosimilar etanercept users (RA:576, AS:171, Pso/PsA:80) and 271 infliximab users (RA:150, AS:54, Pso/PsA:67); 1312 etanercept and 230 infliximab originator users; and 2213 adalimumab originator users post- and 1773 pre-policy change. Discontinuation rates per 100 PY are shown in Table 1A. After adjusting for baseline covariates (Table 1B), and accounting for temporal trends (Table 1C), the risk of discontinuation was similar for biosimilar vs. originator etanercept and infliximab users.
Conclusion: Real-world population-based data in BC shows that incident users of biosimilar etanercept and infliximab for inflammatory arthritis have comparable duration of treatment to users of originators.

Table 1. Discontinuation of biosimilar and originator anti-TNFs before and after policy change

1A. Discontinuation rates

Drug	Period	Discontinuation/Follow-up N	Years	Rate (per 100 person-year)
ADALIMUMAB	Pre-policy	808/1773	2454	32.92
	Post-policy	1076/2213	2959	36.36
ETANERCEPT	Originator	650/1312	1752	37.10
	Biosimilar	381/827	1029	37.02
INFLIXIMAB	Originator	103/230	344	29.97
	Biosimilar	138/271	364	37.96

1B. Hazard Ratio (post- vs. pre- policy change)

Drug	Univariate Cox PH cHR (95%CI)	p value	Multivariable Cox PH* aHR (95%CI)	p value
ADALIMUMAB	1.08(0.98,1.18)	0.11	1.08(0.98,1.19)	0.11
ETANERCEPT	0.97(0.84,1.10)	0.60	0.97(0.85,1.11)	0.65
INFLIXIMAB	1.10(0.84,1.43)	0.50	1.11(0.86,1.45)	0.42

1C. Ratio of Hazard Ratio**

	Univariate Cox PH Ratio of cHR (95%CI)	p value	Multivariable Cox PH* Ratio of aHR (95%CI)	p value
ETANERCEPT	0.90(0.76,1.05)	0.19	0.90(0.76,1.06)	0.20
INFLIXIMAB	1.02(0.77,1.35)	0.91	1.03(0.78,1.37)	0.83

*Adjusted for age, sex, socioeconomic status, rural vs. urban, health authority, arthritis type, arthritis duration, no. prior biologic agents, comorbidities, steroid and DMARDs use, measured at anti-TNF start.**Ratio of Hazard Ratios of etanercept or infliximab to adalimumab.

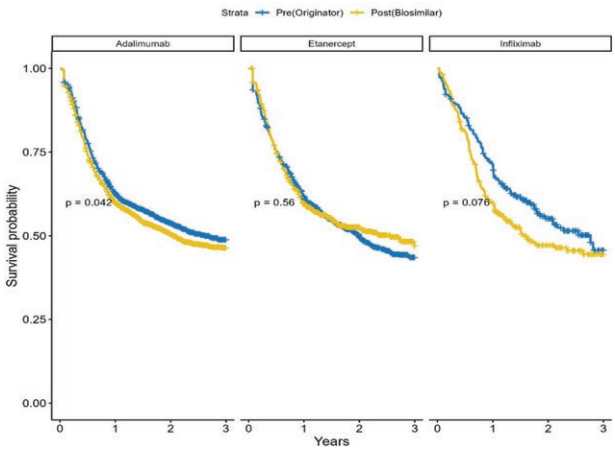


Figure 1. Kaplan Meier Biologics Survival Curve

Acknowledgements: This research received funding from the Canadian Initiative for Outcomes in Rheumatology cAre (CIORA) via the Canadian Rheumatology Association. Dr. Lacaille is supported by the Mary Pack Chair in Arthritis Research from the University of British Columbia and The Arthritis Society of Canada. Dr. Antonio Avina Zubieta is a BC Lupus Society Research Scholar and a Walter & Marilyn Booth Research Scholar. Dr. Hui Xie is supported by the Milan Ilich/ Merck Chair in Statistics for Arthritis and Musculoskeletal Diseases from Simon Fraser University.
Disclosure of Interests: None Declared.
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POS0568

THE RATIO BETWEEN BIOLOGICAL AND GLUCOCORTICOID USE IN VARIOUS COUNTRIES WORLDWIDE: RESULTS FROM THE METEOR REGISTRY

Keywords: Rheumatoid arthritis, Real-world evidence, Geographical differences

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Background: Previously a study in the QUEST-RA database, based on rheumatoid arthritis (RA) patients included between January 2005 and June 2006, has shown that the ratio between biological disease modifying antirheumatic drug (bDMARD) use and glucocorticoid (GC) use strongly differs between countries. Considering the difference in affordability between bDMARDs and GCs, it may be hypothesized, that when less bMDARDs are used, glucocorticoid use increases.
Objectives: To investigate globally, in more recent data, the ratio between bDMARD and GC use, and to assess whether this relates to a country's socio-economic status (SES).
Methods: Data on bDMARD and GC use between 1-1-2007 and 28-12-2020 were extracted from the METEOR registry: an international database capturing daily clinical practice data from patients with a clinical diagnosis of RA. The ratio between the proportion of patients who had ever used a bDMARD and the proportion of patients who had ever used a GC, with no concomitant bDMARD use, during a total follow up duration of two years (bDMARD/GC ratio) was calculated per country. Univariable linear regression was used to analyze the bDMARD/GC ratios according to publicly available country-level indicators of SES (Worldbank, OECD).
Results: Data from 10,856 patients covering eight countries showed varying proportions of bDMARD use. The number of patients included ranged from 64 (Spain) to 8484 (India). Baseline characteristics varied per country (Table 1) The percentage of patients who used a bDMARD (with or without a GC) during two years follow up ranged from 1% (South Africa, India) to 26% (United States, state of Massachusetts) and for those who used a GC at some time during two years follow up ranged from 19% (Great Britain) to 94% (South Africa). Higher country-level wealth measured in GDP per capita, health expenditure and household net adjusted disposable income were related to a higher bDMARD/GC ratio. For every 10,000 Intl$ increase in GDP per capita, household net adjusted disposable income and health expenditure per capita, the bDMARD/GC ratio (range 0 to 1) was observed to increase by a value of β 0.1 (Figure 1A, 95% CI 0.05;0.1, p<0.05), β 0.2 (Figure 1B, 95% CI 0.08;0.3, p<0.05) and β 0.6 (Figure 1C, 95% CI 0.4;0.8, p<0.05), respectively.
Conclusion: In this analysis based on a worldwide cohort capturing 8 countries, we show that the bDMARD/GC ratio differs across countries. These differences are significantly related to general country-level indicators of level of wealth, where greater wealth went with a higher proportion of patients using bDMARDs and/or a smaller proportion of patients using GCs.

Table 1. Baseline characteristics and proportions of bDMARD and GC use per country

	US	NL	Portugal	South Africa	Spain	UK	India	Mexico
N Included patients	215	369	334	754	64	466	8484	170
Female, %	74	68	73	82	86	64	85	84
Rheumatoid factor +, %	44	49	61	93	83	66	82	48
ACPA +, %	39	46	51	75	81	62	51	28
BMI, median (IQR)	29 (25;33)	25 (22;28)	27 (23;29)	28 (24;33)	25 (22;7.2)	27 (24;32)	25 (22;29)	28 (24;31)
Current or ever smoker,%	47	27	24	24	36	55	2	14
Age at diagnosis, mean (SD)	53 (15)	57 (16)	55 (15)	50 (13)	52 (15)	58 (15)	46 (12)	48 (14)
Symptom duration at baseline (years), mean (SD)	2.0 (3.8)	1.3 (3.5)	1.7 (3.1)	3.6 (4.6)	0.7 (0.8)	1.1 (2.3)	5.5 (6.1)	1.4 (3.3)
DAS28, mean (Sd)	5.1 (1.4)	4.5 (1.5)	5.1 (1.5)	5.5 (1.4)	4.8 (1.5)	5.1 (1.3)	6.3 (1.3)	5.1 (1.6)
GC use only,%								
Within 1 year	49	30	71	93	75	19	60	77
2 years	47	29	70	94	70	19	64	77
bDMARD and GC use, %								
Within 1 year	12	3	3	1	5	0	0	1
2 years	14	4	6	1	6	0	0	2
bDMARD use only, %								
Within 1 year	9	6	2	0	5	1	1	1
2 years	19	11	4	0	9	2	1	1

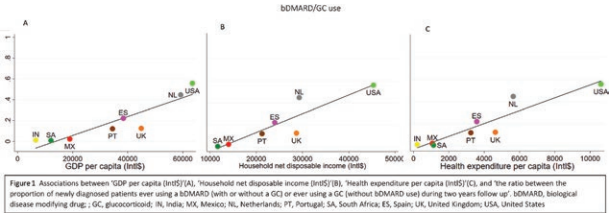


Figure 1 Associations between 'GDP per capita (Intl$)'(A), 'Household net disposable income (Intl$)'(B), 'Health expenditure per capita (Intl$)'(C), and 'the ratio between the proportion of newly diagnosed patients ever using a bDMARD (with or without a GC) or ever using a GC (without bDMARD use) during two years follow up'. bDMARD, biological disease modifying drug; ; GC, glucocorticoid; IN, India; MX, Mexico; NL, Netherlands; PT, Portugal; SA, South Africa; ES, Spain; UK, United Kingdom; USA, United States

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POS0569 IDENTIFYING THE IMPACTS OF ARTHRITIS ON LABOUR MARKET PARTICIPATION: AN OBSERVATIONAL STUDY IN BRITAIN

Keywords: Health services research, Rheumatoid arthritis, Work-related issues

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Background: Existing evidence of the impacts of rheumatic and musculoskeletal diseases (RMDs), including those with arthritis, compared to those without RMDs on labour market participation is limited. Furthermore, most studies are cross-sectional.
Objectives: To compare labour market outcomes in people with arthritis versus those without.
Methods: We utilise 10 waves of the UK Household Longitudinal Survey (2009-2019) which contains annual observations of a representative sample of individuals in Britain. The data contain labour market participation measures (employment, unemployment, non-participation due long-term sickness, and retirement) and data for those employed including whether the respondent has been off work for health reasons, job sector type and employing sector. These are observed over time, enabling assessments of changes in activity. Arthritis was self-reported (type of arthritis is not identifiable). Multivariable linear and non-linear probability regression models were estimated for: i) sickness absence (employed individuals), ii) transitions to unemployment (employed individuals), iii) transitions to long-term sick (employed, unemployed individuals), and iv) transitions to retirement (employed, unemployed, long-term sick individuals). The sample concerns those aged 30-64. The key covariate of interest is an indicator for whether the respondent has reported arthritis. The panel nature of the data permits accounting for unobserved heterogeneity (fixed-effects). A range of potentially confounding factors were adjusted for including: age (40-49, 50-59, 60-64, ref: 30-39), job sector (intermediate, routine, ref: managerial), employing sector (public sector, ref: private sector), year indicators, and the presence of other long-term conditions. Additional analyses interacted arthritis with age, job sector and employing sector, and other long-term conditions to test whether the impact of arthritis differs between these groups.
Results: The results were robust to linear or non-linear probability model specifications. Sample sizes representing individual-year observations for the sickness absence, and transitions to long-term sick, unemployment, and retirement were 166,878, 167,681, 166,994, and 169,811 respectively. 1.06% reported sickness absence and 8.31% reported arthritis. Those with arthritis had a greater probability of sickness absence than those without arthritis (1.35 percentage points (pp), p-value <0.001). The effects of arthritis did not vary by age, job sector, public sector employment, or for those with other long-term conditions. 0.04% transition to unemployment and 8.31% reported arthritis. Those with arthritis were no more likely to become unemployed (0.01 pp, p-value=0.148). The effects of arthritis was no different by age, employing sector, job sector, or for those with other long-term conditions. 0.36% transition to long-term sick and 8.38% reported arthritis. Those with arthritis were more likely to move into long-term sick (0.64 pp, p-value<0.001). The effects of arthritis did not differ by age or by whether the individual's employing sector was public nor by job sector; but was greater for those with other long-term conditions (8.92 pp, p=0.030). 1.22% transition to retirement over the period and 8.56% reported arthritis. Those with arthritis were more likely to retire in the following year (1.43 pp, p-value <0.001). The effects of arthritis was greater with age (40-49 (0.51 pp, p<0.001), 50-59 (1.90 pp, p=0.004) and 60-64 (4.69 pp, p<0.001)); was less for those in routine job role sectors (-1.16 pp, p=0.052), but not different for those in public sector jobs or for those with other long-term conditions.
Conclusion: The findings provide evidence of the detrimental impacts arthritis has on labour market participation and highlights those groups of the population for which the impacts of arthritis are greater, providing insight into where targeted support may be required by employers and policymakers to support labour market participation for those with arthritis.
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Disclosure of Interests: None Declared.
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POS0570

IMPACT OF CLINICIAN-RELATED FACTORS ON PHONE CONSULTATIONS IN RHEUMATOLOGY – ANALYSIS OF MEDICAL VS NON-MEDICAL CLINICIANS' OUTCOMES FROM A COVID-19 INITIATIVE

Keywords: Telemedicine, COVID, Health services research

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Background: Since COVID-19 pandemic, there have been changes in clinical practice to limit transmission, such as switching to remote consultations. Our department switched to delivering remote consultations during lockdown without suspending service. Patients were offered choice of either video or phone consultation. It is unclear if the medical vs non-medical status of clinicians has any influence on remote consultations.
Objectives: We aimed to study the influence of medical vs non-medical status of clinicians on phone consultations in our experience during the pandemic.
Methods: Between 15/10/2020 and 09/11/2020, 12 clinicians in our service completed data collection forms after each remote consultation, recording the technology used (video vs phone); technical problems encountered; discharge and subsequent appointment status; and technical aspects of the consultation itself using 11-point numerical rating scales (NRS) (Time Adequate; Relevant History; Physical Exam; Management Plan; and Communication Quality). Data were analysed in SPSS version 25 using chi-square tests and Mann-Whitney U tests for comparisons..
Results: Six medical clinicians (3 consultant rheumatologists, 2 Specialty Trainee Registrars and 1 Foundation Year 2 doctor) and six non-medical clinicians (3 Specialist Nurses, 1 Advanced Rheumatology Practitioner and 2 Senior Rheumatology Pharmacists) completed 285 forms. As non-medical clinicians didn't do new patient consultations, and as some clinicians did not do video consultations, these consultations were excluded. The remaining were follow-up patient phone consultations (n=196). Medical vs non-medical clinician appointments were 34.7% (n= 68), vs 65.3% (n=128). Medical and non-medical clinicians had a similar proportion of female patients (72.1%, n=49 vs 63.3%, n=81; p=0.22); similar mean age of their patients (63 vs 62 years; p=0.53); similar rates of technical problems reported (13.1%, n=8 vs 16.4%, n=19; p=0.57); and similar rates of interpreter use (3%, n=2 vs 3.5%, n=4; p=0.86). Medical clinicians had lower mean scores compared to the non-medical clinicians on NRS for Time Adequate (8.37 vs 8.57; p=0.013); Relevant History (8.55 vs 9.02; p<0.001); Management Plan (6.91 vs 8.17; p<0.001); and Communication Quality (7.85 vs 8.81, p<0.001); and had no significant difference in scores for Physical Exam (0.63 vs 1.75; p=0.19). Medical clinicians had a non-significant trend for higher rate of subsequent face-to-face appointments (21.9%, n=11 vs 11.6%, n=14; p=0.10); and a higher rate of discharge outcome compared with non-medical clinicians (23.5%, n=16 vs 1.6% n=2; p<0.001).
Conclusion: There were no significant differences between medical and non-medical clinicians in distributions of patients' gender or age, and rates of technical problems and interpreter use. While there was a non-significant trend for lower scores on Physical Exam NRS for medical clinicians, both mean scores were low reflecting the difficulty of this assessment in a phone consultation. Medical clinicians rated their consultations significantly lower in four of the NRS, potentially reflecting the complexity of medical problems of patients booked into medical clinicians' clinics compared to potentially patients with more stable disease in non-medical clinicians' clinics. Similarly, the lower discharge rate from non-medical clinicians' clinics could reflect a higher proportion of patients on established disease needing long-term follow-up. Further studies with larger numbers would help clarify these issues.
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POS0571

ASSOCIATION BETWEEN DIAGNOSIS DELAY AND DISEASE ACTIVITY WITH BURDEN OF THE DISEASE IN 4150 EUROPEAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Patient reported outcomes, Systemic lupus erythematosus, Quality of life

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Background: Despite significant improvements in diagnosis delay and treatment strategies, the burden of Systemic Lupus Erythematosus (SLE) remains high.
Objectives: The objective of the study was to assess the association between diagnosis delay, disease activity and burden on daily life (BoDL) in a large sample of European patients with SLE.
Methods: In May 2020, Lupus Europe, the European umbrella patient association for SLE, conducted a multilingual anonymous online cross-sectional study to individuals with a self-reported physician's diagnosis of SLE living in Europe. The BoDL score was computed using 1 to 5 Likert scales on 5 domains (mobility, anxiety/depression, self-care, daily activities and pain/discomfort) and the sum was transposed on a 0 (minimum Burden on daily life) to 100 (maximum BoDL) scale. Comparisons between independent groups were made using the Mann-Whitney test for continuous outcomes and the Chi-2 test (or Fisher's exact test) for quantitative data.
Results: Data of 4,150 SLE patients from 35 European countries were analysed. The mean (±SD) BoDL score in the study population was 37.8 (±18.7) with a modest downward trend of the BoDL based on age (from 33.4% to 42.1% from age less than 25 to age 65 - a loss of up to 9% points over up to 40 years). The diagnosis delay was reported to be <2 years in 1903 participants (47.5%), between 2 and <5 years in 1056 (26.3%) and ≥5 years or more in 1049 (26.2%). 142 did not answer.. Those with a diagnosis of SLE within 2 years of first symptoms had significantly lower mean Burden on daily life scores than those diagnosed after 5 years (33.6 versus 44.0, p<0.001). This trend is deemed robust as it was found across almost all European countries. These results highlight the importance of improving current diagnosis delay for SLE as a way to improve the burden of the disease on daily life. A total of 2980 (71.8%) patients felt that their "lupus has been under control over the last 3 months" while 1166 (28.1%) did not. 4 did not answer. The Burden on daily life score was significantly better in SLE patients feeling that their lupus had been under control during the past 3 months versus the others (34.0% versus 47.6%, p<0.001). Again, this trend was found across almost all European countries.
Conclusion: This large patient survey reveals both the importance of prompt SLE diagnosis as well the relationship between disease activity and disease burden upon the daily life of European lupus patients. Further improvements should focus on reducing the diagnosis delay and identifying new therapeutic strategies for those with uncontrolled disease. Healthcare pathways, which may accelerate diagnosis and optimize therapeutic management, are necessary to improve patients' outcomes in SLE.
REFERENCE:
[1] Cornet A, Andersen J, Myllys K, et al Living with systemic lupus erythematosus in 2020: a European patient survey Lupus Science & Medicine 2021;**8:**e000469. doi: 10.1136/lupus-2020-000469
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POS0572

IMMUNOGENICITY AND SAFETY OF ADJUVANTED RECOMBINANT ZOSTER VACCINE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

Keywords: Vaccination/immunization, Adaptive immunity, Rheumatoid arthritis

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Background: Herpes zoster (HZ) is caused by the reactivation of latent varicella-zoster virus (VZV) due to a decline in VZV-specific cell-mediated immunity (CMI) with increasing age and immunocompromised conditions [1]. Patients with rheumatoid arthritis (RA) treated with disease-modifying anti-rheumatic drugs (DMARDs) are at a high risk of developing HZ [2, 3]. An adjuvanted recombinant VZV glycoprotein E (gE) subunit vaccine (RZV) has been shown to be effective in preventing HZ in immunocompetent elderly populations. However, its efficacy and safety profile remain largely unknown in RA patients.
Objectives: This study aimed to determine the immunogenicity and safety of RZV in patients with RA treated with DMARDs.
Methods: This longitudinal prospective study enrolled 53 RA patients treated with DMARDs (csDMARDs, n=20; bDMARDs, n=23; and tsDMARDs, n=10) and 10 individuals with no history of immunosuppressive treatment as controls. All the participants were aged ≥50 years. The participants received two intramuscular RZV injections 2 months apart. VZV-specific CMI and humoral immunity (HI)

were assessed at 0 and 3 months after the first vaccination using flow cytometry and enzyme immunoassay. To assess CMI, the frequencies of VZV gE-specific $CD4^+$ $CD40L^+$ T cells expressing at least one activation cytokine (CD4[2+] T cells): IFN-γ, IL-2, and TNF-α were examined by flow cytometry. CMI responders were defined as a CD4[2+] T cell frequency ≥320 per 10^6 $CD4^+$ T cells counted (for participants with pre-vaccination frequencies below 320 per 10^6 $CD4^+$ T cells counted) or a ≥2-fold increase in CD4[2+] T cells (for those CD4[2+] T cells were already ≥320 per 10^6 $CD4^+$ T cells counted at the time of pre-vaccination). CMI and HI response rates were compared between all patients with RA (n=53) and controls (n=10). The participants were followed up for 6 months after the first RZV administration for HZ onset. Baseline characteristics and information regarding adverse events were collected.

Results: Patients' age and disease duration were 70 years old and 11 years, respectively. DAS28-CRP and CDAI scores at enrollment were 1.4 and 2.1, respectively. Thirty-six percent of RA patients had a history of HZ before the administration of RZV. VZV-specific CMI (controls: p=0.002, csDMARDs: p=0.012, bDMARDs: p=0.001, and tsDMARDs: p=0.002) (Figure 1A) and HI (controls: p=0.002, csDMARDs: p<0.001, bDMARDs: p<0.001, tsDMARDs: p=0.002) were significantly increased in DMARDs-treated RA patients after RZV administration, and the magnitudes of those responses were not significantly different between DMARDs-treated RA patients and controls. However, the vaccine response rate of CMI of DMARDs-treated RA patients was significantly lower than that of the controls (51% vs. 90%, p=0.034) (Figure 1B), whereas the response rate of HI was not (66% vs. 70%, p>0.999). In addition, no significant baseline factors affecting CMI responses, including DMARDs use, were identified between RA patients with and without CMI responses. RZV-related adverse events were generally mild, and all participants received two doses of RZV. RZV-induced RA flares occurred in two patients (3.8%) but were also mild and controllable.

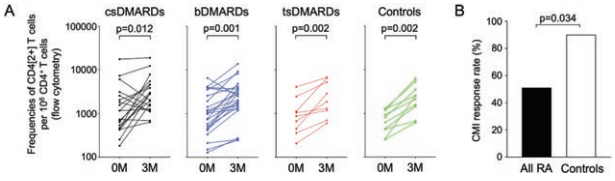


Figure 1. CMI responses to VZV in patients with RA and controls before and after RZV administration.

(A) The frequencies of VZV gE-specific CD4[2+] T cells were examined by flow cytometry.

(B) Vaccine response rate of CMI in all participants.

Conclusion: RZV is robustly immunogenic and has a clinically acceptable safety profile in elderly RA patients receiving DMARDs.

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POS0573

COMORBIDITIES, COMPLEX MULTIMORBIDITY AND PROMIS HEALTH OUTCOMES AMONGAUTOIMMUNE RHEUMATIC DISEASES: DATA FROM THE COVAD STUDY

Keywords: Comorbidities, Patient reported outcomes, COVID

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Clinical Immunology and Rheumatology, Lucknow, United Kingdom; [40]King's College London, Centre for Rheumatic Diseases, London, United Kingdom; [41]King's College Hospital, Rheumatology Department, London, United Kingdom

Background: Comorbidities have a profound impact on the QoL of patients living with autoimmune rheumatic diseases (AIRDs). Unfortunately, global data on the burden of comorbidities and its impact on health outcomes in this vulnerable group is scarce.

Objectives: We studied the prevalence, distribution and clustering of comorbidities and multimorbidity among patients with AIRDs and healthy controls (HCs) and its impact on health outcomes, utilizing data from the ongoing 2nd COVAD study.

Methods: The COVAD study is a global e-survey that embodies patient voice while empowering collaborators and young researchers. The study group of 157 physicians across 106 countries from February-June 2022 captured details of AIRDs, autoimmune and non-autoimmune comorbidities, and validated patient reported outcomes. Human Development Index (UNDP 2021-22) of country of residence was taken as a surrogate marker for socioeconomic status (SES). Basic multimorbidity (BM), Complex multimorbidity (CM), Autoimmune multimorbidity (AM) are defined as the co-occurrence of ≥2 non-rheumatic comorbidities, ≥3 non-rheumatic chronic conditions affecting ≥3 different organ systems [1] and ≥3 autoimmune diseases (AIDs) in an individual respectively. PROMIS global physical health (PGP), mental health (PGM), fatigue 4a (F4a) and physical function short form (SF10) scores were calculated for the different groups and compared using descriptive statistics, linear regression and cluster analysis (hierarchical followed by K means).

Results: Of 17,612 total respondents, 6149 (62.7%) had underlying AIRDs and 3652 (37.3%) were HCs, with female (80.8%) and Caucasian (53.9%) predominance in the former. All types of multimorbidity were more frequent in AIRDs than HCs, including any comorbidity (77.1% versus 25.0%; OR: 2.9; 2.7-3.2), BM (21.0% vs 6.2%; 4.0; 3.4-4.6), and CM (3.1% vs 0.5%; 6.4; 3.9-10.4), and with prevalence increasing with age (p<0.001) (Figure 1A, B). Comorbidity prevalence was the highest among Americans and Australians (72% each). Patients with AIRDs had poorer health outcomes than HCs, including lower PGP, PGM, SF10, F4a scores (all p<0.001). Among AIRDs, those with comorbidities had lower physical function and PROMIS scores (PGP, PGM, and SF10), and reported fatigue more often (all p<0.001). Female gender, and underlying BM and AM particularly predisposed patients to worse physical health (lower PGP, lower SF10a) and mental health outcomes (lower PGM). While advanced age (-1.815; <0.001), and lower SES (0.871; 0.027) specifically predicted poorer physical function (lower SF10a). Fatigue (higher F4a) was seen more frequently among women (1.711; <0.001), and those with BM (1.142; 0.002); AM (1.768; 0.011), and higher SEC (0.478; 0.016). Cluster analysis of patients with AIRDs revealed 2 clusters (Figure 1C 1D); cluster 1 with low PGP, PGM, SF10 and high F4a; cluster 2 with high PGP, PGM, SF10 and low F4a. The clusters differed predominantly based on the frequency of comorbidities; any comorbidity (59.7% vs 41.8%; p<0.001), BM (28.5% vs 14.7%; 0.001); CM (4.5% vs 1.9%; <0.001), and AM (10.0% vs 4.0%; <0.001).

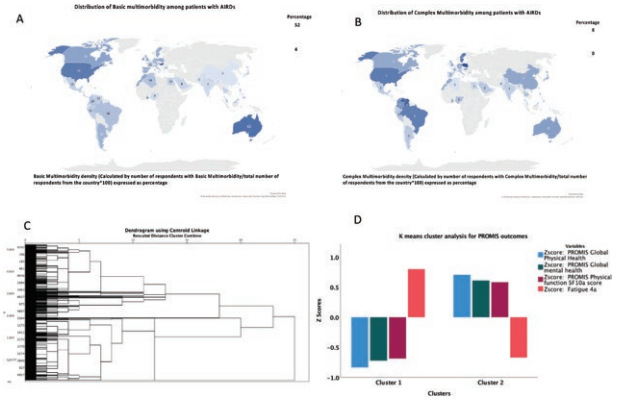


Figure 1. A, B Distribution of basic multimorbidity, complex multimorbidity among patients with AIRDs (expressed as percentage), C, D Hierarchical and K means cluster analysis of PROMIS outcomes among AIRDs.

Conclusion: Comorbidities complicate three-quarters of individuals living with AIRDs, and have an outsized impact on self-reported physical function, perceived fatigue, and QoL. Substantial regional differences call for further exploration of key drivers of this important aspect to allow optimized multidisciplinary and holistic care in anticipation of poorer outcomes.

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Educational cases

POS0574 **THE GREAT MASQUERADER OF RHEUMATOLOGICAL SYMPTOMS: A CASE REPORT**

Keywords: Imaging, Vasculitis, Cardiovascular disease

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Background: Primary cardiac tumors are extremely rare,and out of those atrial myxoma is the most common benign tumor (75%).Around 75% of the atrial myxoma cases arise from left side of the heart and present differently from right sided. Due to its varied presentation in regard to constitutional,embolic and obstructive features it mimics vasculitis.
Objectives: To create awareness about the atrial myxoma, the great mimicker of vasculitis and comment upon its clinical course and complications if not treated timely.
Methods: Case report and Discussion.
Results: 34 year old female with no past medical history came to the Rheumatology Department after failure to be diagnosed. She had 8 months history of pain in her finger tips, toes, small joints and Raynauds phenomenon. Intermittent fever associated with chills, palpitations, sweating and significant weight loss was noted during the course of illness. Before visiting our clinic, she was treated for Typhoid fever but she didn't respond. At presentation, her vitals and physical examination including auscultation was unrevealing.Her blood counts showed Hb at 8g/dL, metabolic panel,LFTs,coagulation profile were normal.But had high ESR levels in multiple reports ranging from 60-168mm/hour. CRP was also positive. Hypocomplementmia and increase in alpha-globulins were observed.ANA positive,dsDNA negative APLA, P and C-ANCA and Cryoglobulins were also negative. PET-CT was negative for avid FDG uptake in any organ. Patient was given iron formulations intravenously and was advised to cardiology in view of significant palpitations which was not given much attention before.Echo showed 4.1x 3.3cm, pedunculated mass arising from inter-atrial septum and anterior mitral leaflet (Figure 1).Patient was started on ecosprin and advised surgery which got postponed due to patient having complications of acute limb ischemia and stroke in right fronto-parietal lobe (Figure 1.) subsequently. She had multiple embolectomies of right brachial and bilateral femoral arteries, later followed by craniectomy and decompression from the hemorrhage with subsequent cranioplasty and at lastly removal of mass. The surgical pathological report of mass showed features characteristic of myxoma which concluded the diagnosis.After surgeries,the patient is doing much better.Her Hb levels have improved to 12g/dL and the ESR level came back to normal.Though there is residual weakness due to stroke but she has shown significant recovery in terms of modified Rankin scale of 3.No more systemic complaints like fever, fatigue, Raynauds phenomenon and digital pain are observed.In this case, duration from onset of symptoms to hospitalization for life threatening was complete one year with added 6 months to significant recovery from complications.

from complications.

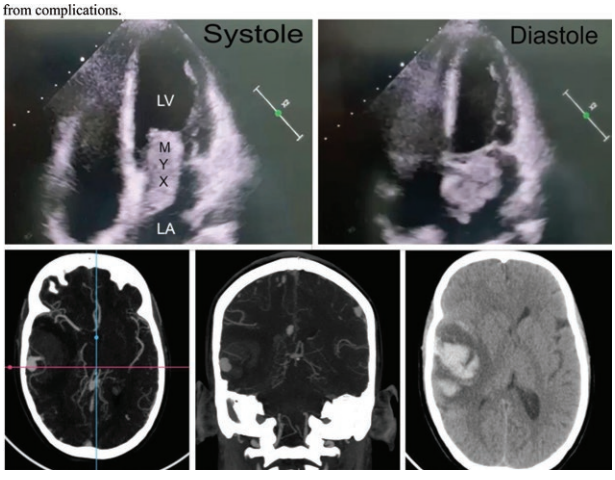


Figure 1. *Top Left and Right, Echocardiography during systole and diastole demonstrating dynamic myxoma propulsion into the left atrium.Bottom Left to Right, CT angiography- multiple saccular aneurysm from distal cortical branches of bilateral cerebral arteries with large aneurysm in close relation to the right temporal hematoma, likely ruptured.NCCT head- Right frontal bleed* LA- left atrium, LV= left ventricle, Myx - Myxoma

Conclusion: Myxoma, a rare intracardiac benign neoplasm due to release of inflammatory cytokines like IL-6 and embolic mechanism can present as inflammatory rheumatic disease. Diagnosing this great masquerader can be challenging even for a specialist but timely ordering of certain non-invasive tests could be life saving for the patient. For example in this case, Echocardiography or Cardiac MRI are critical. Therefore, having high diagnostic suspicion is very important when dealing with vasculitis and its mimics.

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POS0575 **OSTEOMALACIA INDUCED BY HYPOPHOSPHATEMIA – ROLE OF FGF 23: TWO CLINICAL CASES REPORT**

Keywords: Osteoporosis, Education, Bone diseases

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Background: Osteomalacia is a bone disorder characterized by decreased bone mineralization. Vitamin D deficiency and hypophosphatemia are the most frequent causes. Fibroblast growth factor 23 (FGF23) is a hormone secreted by osteocytes in response to increased calcitriol and serum phosphate levels. FGF23 main function is phosphate serum levels regulation, decreasing sodium-phosphate cotransporter expression on the proximal convoluted tubule. Thus, FGF23 reduces calcium reabsorption and increases urine phosphate excretion. FGF23 may also suppress 1α-hydroxylase, reducing vitamin D activation and calcium reabsorption.
Objectives: To increase the awareness of hypophosphatemia-induced osteomalacia.
Methods: Case reports and discussion.
Results: Case 1 – A 63-year-old man, hospitalized for total hip arthroplasty secondary to non-traumatic bilateral femoral neck fracture was evaluated by rheumatology on suspicion of osteoporosis. Medical history was relevant for a progressive paraparesis of lower limbs 6 years ago and which etiological investigation revealed a mesenchymal tumor in the body of the ninth dorsal vertebrae compressing the spinal cord. A multidisciplinary discussion concluded that the tumor was unresectable, but the patient underwent decompressive surgery to relieve neurological symptoms one year later. The patient also reported a history of multiple non-traumatic fractures in the past five years, including ribs, ankle, pelvis, femoral neck, and scapula, and denied any articular or bone pain. In laboratory evaluation, serum phosphate levels were below the laboratory detection limit, calcium and vitamin D were decreased, parathormone (PTH) was in the normal range and serum alkaline phosphatase (AF) was increased. Serum FGF23 levels were 6 times above the upper limit of normal (ULN). Thus, the diagnosis of oncogenic osteomalacia induced by an FGF23-producing mesenchymal tumor was made. The patient started intravenous phosphate repositioning in the intermediate care unit and then he continued oral phosphate, calcium, and vitamin D supplementation at home. Currently, the patient is in the oncology outpatient clinic, and he was proposed to initiate treatment with burosumab (anti-FGF23 antibody). **Case 2 –** A 57-year-old woman with Rendu-Osler-Weber syndrome and iron deficiency anemia, chronically supplemented with ferric carboxymaltose, was referred to the rheumatology outpatient clinic because of a right second metatarsal bone fracture associated with hypophosphatemia, vitamin D deficiency, AF and PTH elevation (above 3 times the ULN and 2 times the ULN, respectively), and normal calcium levels. Measurement of FGF23 serum levels revealed an elevation of 3 times the ULN. The diagnosis of FGF23-induced hypophosphatemia was made. The patient started oral phosphate and vitamin D supplementation and the formulation of intravenous iron was changed. Six months after the initial evaluation, the previously abnormal analytical values were within the normal range.
Conclusion: Osteomalacia has multiple identified causes like vitamin D deficiency, hypophosphatemia, chronic kidney disease, renal tubular acidosis, and hypophosphatasia. FGF23 is a hormone that regulates phosphate metabolism. There are several types of genetic and acquired FGF23-related hypophosphatemia, like X-linked hypophosphatemia and FGF23-producing mesenchymal tumors, respectively. In case 2, it is thought that the key mechanism responsible for the effect of iron results from the disproportionate inhibition of FGF23 degradation by the carbohydrates present in intravenous formulations with a consequent increase in its concentration and activity. The risk of hypophosphatemia and osteomalacia appears to be greater with iron carboxymaltose than with other intravenous iron formulations.

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POS0576 **ANTI-TIF1-Γ POSITIVE DERMATOMYOSITIS WITH SEVERE OROPHARYNGEAL INVOLVEMENT AFTER IMMUNE CHECKPOINT INHIBITORS**

Keywords: Myositis, Malignancy, Autoantibodies

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Background: Anti-TIF1-γ antibody is specifically associated with paraneoplastic dermatomyositis (DM) [1], but this serum marker has seldom been reported after cancer immunotherapy. Immune checkpoint inhibitors frequently cause immune-mediated endocrine, gastrointestinal, and cutaneous syndromes [2] and de novo DM cases have also been described and successfully treated using glucocorticoids and intravenous immunoglobulin (IVIG) [3].
Objectives: We report the case of a man developing anti-TIF1-γ positive DM following immunotherapy with progressively worsening dysphagia refractory to glucocorticoids, immunosuppressants, and IVIG.
Methods: Case report.
Results: In February 2021 a 47-year-old man was diagnosed with skin melanoma that was surgically resected and treated with adjuvant ipilimumab and nivolumab, leading to complete remission. After three months, he developed *de novo* thyroiditis, hepatitis, colitis, and experienced rapid progression of previous vitiligo, along with muscle weakness and 5X CK elevation. His rheumatological workup included positive ANA at indirect immunofluorescence (1:640 titer, speckled pattern), and high-titer anti-TIF1-γ antibodies. Inflammatory myositis was diagnosed and treated with glucocorticoids (prednisone 1 mg/kg) and mofetil mycophenolate (MMF, 3 g/d) with initial benefit on muscle function. In September 2021, the patient had a metastasis-negative lymph node evaluation and suspended MMF for surgery with a subsequent rapidly progressive deterioration of muscle function, with dysphonia, dysphagia, and typical DM skin lesions (**Figure 1**) with pancytopenia (hemoglobin 9 g/dL, white blood cells 1500/mmc, platelets 40.000/mmc). Further oncological evaluation (total body CT scan, brain MRI) was negative for the recurrence of malignancy or the presence of myasthenia gravis and neuropathy. Methylprednisolone pulses (500 mg for 3 days) were started, followed by high dose IVIG (5 g/kg), with marginal improvement on muscle function, normalization of CK levels, but no effect on dysphagia which required PEG tube placement. MMF was restarted but rapidly stopped because of septic shock requiring intensive care unit admission, followed by recurrent severe infections, contraindicating further immunosuppression. Six monthly high-dose IVIG infusions were continued [4] with minimal effect. Worsening tetra-paresis, absolute dysphagia, impaired cough, and inability to manage salivary secretions led to massive aspiration pneumonia. The man developed acute respiratory insufficiency, septic shock, and multiorgan failure, and died 13 months after the onset of DM.
Conclusion: Worsening myopathy, typical skin lesions, and concomitant immune-related adverse events should raise suspicion of DM in patients receiving immune checkpoint inhibitors [3]. Balancing the risks of DM disease flare, malignancy, and severe infections is of paramount importance when choosing the most appropriate therapy. Patients with anti-TIF1-γ DM following immunotherapy may also manifest tetra-paresis, dysphagia, and severe pancytopenia.
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Figure 1. Skin lesions. Heliotrope rash involving the face including the nasolabial folds, V-neck sign, vasculitis with microhemorrhages, periungual erythema, Gottron's papules, extensive vitiligo.

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Patient information and education

POS0577-PARE **EVALUATION OF PATIENT SATISFACTION WITH REMOTE SELF-INJECTION TRAINING: A SINGLE-CENTRE PATIENT-REPORTED SURVEY**

Keywords: Inflammatory arthritides, Patient reported outcomes, Patient information and education

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Background: Subcutaneous self-injection of methotrexate (SC MTX) is used for the treatment of several inflammatory diseases. All newly initiated patients should be educated and trained in the proper injection technique by their healthcare provider (HCP), with the first injection performed under medical supervision. This training has typically been conducted during face-to-face consultations, however since the start of the COVID-19 pandemic it has been necessary to conduct training remotely due to the cancellation of clinics.
Objectives: To understand patient-reported experiences and satisfaction with remote SC MTX self-injection training.
Methods: A cross-sectional electronic survey was administered between 11 October 2022 and 30 November 2022 to patients at Southern Health and Social Care Trust who had recently been trained via telephone or video conference [VC] on how to self-inject methotrexate using a pre-filled, auto-injector pen. Patients were aged ≥18 with a range of arthritis types, including rheumatoid, psoriatic, polyarticular juvenile idiopathic and chronic reactive inflammatory arthritis. Remote training was delivered by the patient's nurse as per routine practice (independently of this survey). Patients were sent a patient information pack (PIP) prior to the training consultation. During the training, the nurse discussed the process of injecting with the auto-injector pen before virtually supervising the first injection. The survey consisted of 14 questions; topics included experiences and satisfaction with preparation for the HCP appointment, the training consultation itself and post-training experiences and preferences. The responses were analysed descriptively on an item-by-item basis.
Results: In total 73 patients completed the survey; 77% (n=56/73) were female, and 96% (n=70/73) had no prior experience with a SC MTX auto-injector pen. The training was completed by telephone for 92% (n=67/73) of patients and by VC for 8% (n=6/73). 99% (n=72/73) received a PIP in advance of their training consultation and 92% (n=67/73) received this by post. 67% (n=49/73) of patients

strongly agreed and 26% (n=19/73) agreed that they felt prepared for the training after receiving the PIP; 78% (n=57/73) of patients strongly agreed and 22% (n=16/73) agreed that it was easy to read and understand, whilst 52% (n=38/73) strongly agreed and 32% (n=23/73) agreed that the PIP was helpful and did not require additional instructions before the appointment. 84% (n=61/73) took 15 minutes or less to complete the training with their HCP. None of the participants felt confused or did not understand the training instructions from their HCP, 78% (n=57/73) strongly agreed and 19% (n=14/73) agreed that the remote training was helpful and made them feel more confident to use the injector pen on their own and 97% (n=71/73) did not need to contact their HCP for more training or advice following their appointment. When asked about the main advantages of remote training, 32% (n=23/73) agreed it was more convenient, 25% (n=18/73) agreed that it was time saving and 30% (n=22/73) agreed that not having to attend the hospital was beneficial. 85% (n=62/73) strongly agreed and 14% (n=10/73) agreed that they were satisfied with the remote training provided and 82% (n=60/73) strongly agreed and 18% (n=13/73) agreed that they would recommend the remote training to another patient.

Conclusion: These findings provide new insight into patients' experiences with self-injection training when delivered remotely by their HCP. The patient information pack and training consultation were well received as most patients found it helpful, convenient and time saving.

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POS0578-PARE IMPROVED EDUCATION IS NEEDED FOR INDIVIDUALS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: INSIGHTS FROM A SOCIAL MEDIA LISTENING QUALITATIVE ANALYSIS

Keywords: Systemic lupus erythematosus, Descriptive Studies, Patient information and education

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease affecting multiple organs, including the kidneys in lupus nephritis (LN) [1]. Individuals living with SLE have impaired quality-of-life compared with the general population [1]. and a growing number are using social media for health-related information [2]. Thus, social media is a useful source of data to examine their experiences and concerns [3].

Objectives: To understand the perspective of individuals living with SLE/LN on their disease management and to assess where they seek information, how their personal perspective impacts their care, and what may be needed to improve care/experience.

Methods: This qualitative analysis used the Sprinklr social media listening tool to search historical posts across 11 countries, including the USA, the UK and Japan, between May 2021 and February 2022, using predefined keywords. Main data sources were Twitter, Instagram, Reddit, Facebook, Weibo and SLE-specialised websites. Publicly shared posts relating to SLE/LN were captured and key themes were analysed.

Results: Overall, 23,084 posts were exported; of these, 12,037 were in scope and mentioned SLE/LN disease and/or therapeutics. Of the 12,037 posts, 6424 were related to SLE/LN disease alone (diagnosis and management) and 5387 to therapeutics. The remaining 226 posts did not add any value to the analysis and were not considered. From analysis of the posts, many individuals with SLE/LN appeared to understand their condition and could identify symptoms (e.g., SLE: pain, fatigue, rash; LN: foamy urine, blood creatinine). However, there was a lack of knowledge of diagnostic and disease monitoring tests such as anti-nuclear antibodies. Individuals with SLE/LN also described not receiving enough explanation of their laboratory results. Based on the posts, physician focus on measurable disease activity and clinical trial data did not resonate with individuals with SLE/LN. Quality-of-life and patient-reported outcomes would be the preferred focus of discussion and may improve perception of their care. Individuals with SLE/LN reported being busy and symptoms of their disease (e.g. too tired or forget to take their medication) as reasons for poor adherence.

According to the posts, the most used SLE/LN drugs included methotrexate, hydroxychloroquine (HCQ), prednisolone, mycophenolate mofetil and azathioprine. Individuals with SLE/LN generally had positive sentiment towards their individual standard therapies (except for HCQ). Awareness of long-term side effects was generally high; however, some individuals with SLE/LN were not aware that long-term use of steroids may contribute to organ damage. Individuals with SLE/LN reported many barriers preventing them from focusing on long-term goals of disease management and achieving better outcomes, including diagnosis delays, daily disease impact, concerns with treatment effectiveness, safety, onset of response, and due to misleading information on social media.

Conclusion: Insights from this analysis suggest that improved education for individuals with SLE/LN on disease-specific tests/tools, laboratory results, treatments, and treatment effects could improve shared decision-making, including a needed shift in focus from short-term to long-term improvements. It could also help address discordance between physicians and individuals with SLE/LN on medication decision-making and adherence [4]. It is vital to consider known health disparities when providing education, as barriers such as racial discrimination have been associated with increased SLE disease activity and organ damage [5]. A change in care and clinical trials towards more collaborative and patient-centric care could also improve adherence and outcomes.

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POS0579-PARE REUMA REGIE, SELF-MANAGEMENT TRAINING BY AND FOR PATIENTS

Keywords: Patient information and education, Self-management

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Background: No self-management training for people with RMDs exists yet in Belgium. In its vision, ReumaNet is convinced that patients' expertise adds great value in several areas. This includes self-management. Instead of consulting external organisations, ReumaNet developed a self-management training by the patient experts themselves. The training is based on the major themes identified in the study by J. Ammerlaan, et al "Self-management in patients with RA: a qualitative study from the patient's perspective" and takes into account the recommendations for the implementation of self-management strategies drawn up by EULAR in June 2021.

Objectives: The aim of the training is for participants to gather the ability to understand their disease and cope with practical, physical and psychological consequences linked to their RMD.

Methods: The training is structured based on the patient journey: each person with an RMD goes through a number of stages as part of coping with his/her condition. This patient journey is the common thread throughout the training; a simple and efficient tool to guide patients towards their final goal. Via reflection and exercises, participants can identify their personal obstacles and challenges and are empowered to face daily challenges, due to their RMD. The training takes the form of a four-day training with an overnight stay, because we are convinced that 'taking a break from the daily routine' can provide sufficient distance, both literally and figuratively, for self-reflection. Moreover, there is then extra space for informal contact, which can enhance the group atmosphere. There is also the possibility of delving deeper into certain topics during a short evening session, should participants feel the need. During this four-day course in March2023, we provide 18 hours of training, using professional insights (f.e. webinars with specialists, certified return to work coordinator

ReumaNet, lifestyle coach,…) and personal experience. The training itself is developed by three patient experts and will be delivered to a group of up to 12 participants. The training is a collaboration with Samana, a Christian health organisation in Belgium. They provide logistical and financial support. Before implementation, the training content was reviewed by a group of trained patient experts from ReumaNet.

Results: During the training, the participants get enough tools to be able to steer their mindset in a more positive way, by actively dealing with challenges linked to their specific condition, f.e. good sleep quality, self-care, dealing with stress, fatigue and pain. Also provided tools in the context of communication, bringing in necessary help and social support, sexuality and professional reintegration empower participants to take matters into their own hands. Over all, participants are empowered to face their own challenges in daily life. They gather the ability to understand their disease and cope with practical, physical and psychological consequences.

Conclusion: No such training exists yet in Belgium and there is a high demand for it. We will repeat this self-management training annually. In addition, we are looking for other ways to organise this training: online, or via (semi-) daily training days for example.

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POS0580-PARE PATIENT ADHERENCE TO OSTEOPOROSIS TREATMENT IS HIGHER WITH CAREGIVER EDUCATION

Keywords: Patient information and education, Best practices, Osteoporosis

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Background: Treatment adherence to osteoporosis treatment remains low. Additional factors: the elderly age of patients, congestive disorders, high comorbidity, fears of side effects of drugs, fear of calcium deposits in the vessels, kidneys and gallbladder, the absence of obvious clinical manifestations of the disease lead to refusal or unreasonable interruptions in therapy for osteoporosis.

Objectives: Eo analyze the Treatment adherence to osteoporosis therapy of single patients, patients living in a family and patients coming to an appointment with a caring relative.

Methods: The analysis of outpatient records of 300 patients observed in the center for the diagnosis and treatment of osteoporosis was carried out. The study included all patients who visited the center in the period from the beginning of 2020 until reaching the enrollment of 100 people according to the ranked criterion. A total of 3 groups were recruited: 1st - single patients, N=100, 2nd - living in a family N=100, 3rd - coming to an appointment with a caring relative/social worker, N=100. The following were assessed: the completeness of the examination, the frequency of subsequent visits, adherence to therapy and the result of treatment according to densitometry data and repeated fractures. The observation period is 3 years. Patients who did not come to the follow-up examination (DXA) after 3 years were excluded from the study.

Results: 15.7% (47 people) withdrew from the study due to non-appearance for return visits. When calling patients, it was found that 6% (18 people) were going to start treatment, but did not start for various reasons, 9.7% (29) started taking vitamin D and continued to take it until the package was over, 5% (15 people) started taking vitamin D preparations (patients from 9.7% of the above) and calcium preparations were taken from 1 to 3 months, after which they stopped taking them, considering that the course of treatment was completed. 2.3% (7 people) died within 3 years from various causes (4 out of 1 gr, 1 out of 2, 2 out of 3). The final statistical analysis included 246 people. The results are presented in Table 1.

Table 1.

N=246	Single patients, N=65, 100%	Living in a family, N=87, 100%	With a caring relative/ social worker, N=94, 100%
Have passed a full examination	31; 47,7%	60; 69%	89; 94,7%
Attended all consultations or called/ wrote to the doctor	20; 30,7%	56; 64,4%	92; 97,9%
Treatment adherence to basic therapy	18; 27,7%	61; 70,1%	84; 89,4%
Treatment adherence to pathogenetic therapy	32; 49,2%	76; 87,4%	92; 97,9%
Positive dynamics, including DRA	27; 36,9%	52; 59,8%	76; 80,8%
A new fracture in 3 years	4; 6,2%	1; 1,2%	1; 1,1%

Conclusion: As a result of the analysis, it was confirmed that the highest adherence to examination and therapy was in patients who applied with a caregiver. Caregivers perceive verbal information better, seek repeated clarifications more often when questions arise about therapy and examination results, help patients solve technical problems (get to the center, purchase medicine, calculate dietary calcium, find a physical education video course). As a result of higher adherence to non-pharmacological and pharmacological treatment, the increase in bone mineral density in the 3rd group of patients was maximum. In the 1st group of patients, due to low adherence to therapy and the worst arrangement of life, by the 3rd year of observation, a higher percentage of fractures (6.2%) was revealed, differences in the frequency of fractures in the 2nd and 3rd groups over 3 years observation was not detected (1.2% and 1.1%) due to the short observation period and a relatively small sample of patients.

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POS0581-PARE VACCINATIONS IN PATIENTS WITH CHRONIC INFLAMMATORY DISEASES, PATIENT KNOWLEDGE AND AWARENESS: RESULTS FROM A NORDIC SURVEY

Keywords: Vaccination/immunization, Health services research, Patient information and education

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Background: Patients with chronic inflammatory diseases (CID) have an increased risk for contracting infections. For patients with rheumatic diseases EULAR recommends protecting them from vaccine-preventable diseases.

Objectives: To assess the knowledge and awareness of common vaccinations and extent of immunization among patients with CID in Denmark, Finland, Norway, Sweden (Nordics), and to identify gaps between the existing EULAR vaccination recommendations and current practice as experienced by patients.

Methods: A structured anonymous online survey for patients with CID ((rheumatological disease (RD), inflammatory bowel disease (IBD) and dermatological diseases (DD)) was conducted in 2022. The survey was answered by 1748 respondents (1031 patients with RD, 543 with IBD and 563 with DD).

Results: Among respondents, 89% were female and 58% had disease duration of above 10 years. In total, 56% were treated in specialised and 32% in primary care. Majority had ongoing systemic immunosuppressive treatment (IT) (65%). Majority of RD (59%) and IBD (66%) patients were treated in specialised care whereas minority of DD patients (38%) were treated in specialised care. Forty-nine percent (49%) responded that their healthcare professional (HCP) did not inform them about the increased risk of infection – however, 55% of the respondents believed

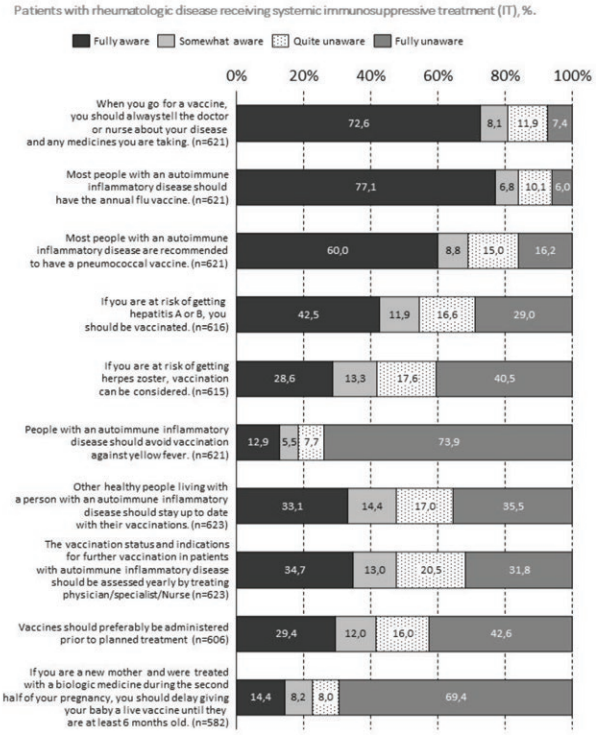
they are somewhat or much more likely to suffer from infections than those without CID or treatment, 33% thought there is no difference and 13% did not know there is a difference. In total 68% of respondents considered it important to get vaccinated due to CID or IT. The number was particularly high in RD group (74%), although 63% stated they had not received any information regarding vaccinations at the start of their treatment. Commonly recommended vaccinations by the HCP were COVID 19 (66%), influenza (63%) and pneumococcal (45%) vaccination. When comparing respondents ≥65 and <65 years, there was a difference in how often the influenza (71% vs. 57%) and pneumococcal (57% vs. 38%), but not COVID 19 vaccination (68% vs. 65%), were recommended. In addition, 74% and 75% of respondents receiving IT were recommended influenza and COVID 19 vaccination, respectively. In total, 22% had their vaccination status checked before initiating treatment; the lowest percentage was in DD (16%) and the highest in RD (25%). However, 44% of respondents received influenza vaccination before initiation of treatment. Moreover, 62% and 74% of respondents received influenza and COVID 19 vaccination while on treatment, respectively. Eighty-six percent (86%) did not receive a vaccination plan in relation to their CID and treatment. Moreover, 64% of the respondents (RD 57%; DD 71% and IBD 66%) did not have vaccination status assessed on a regular basis. Forty-three percent (43%) were dissatisfied with the follow-up of vaccination status by their HCP. Respondents of age ≥65 years were more satisfied than the younger ones (34% vs. 25% very satisfied) and respondents with RD were more satisfied than those with IBD or DD (33% vs. 25% vs. 20%). Forty-four percent (44%) responded that the information on vaccinations related to their CID and treatment was difficult to find and 71% would like to receive more information. The respondents with RD had different level of awareness regarding EULAR vaccination recommendations. The degree of awareness among patients with RD treated with IT are presented in Figure 1.

Conclusion: This Nordic survey provides insights on patients' information needs, information sources and own experiences related to recommendations on vaccinations in relation to their CID and IT. The results confirm a gap between patients' expectations and needs vs. the information they actually receive. Our findings demonstrate a need for increased awareness among patients, providers and HCP regarding EULAR vaccination recommendations in patients with RD.

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Figure 1. Awareness among patients with rheumatic diseases on EULAR overarching principles and recommendations selected from the lay version of the EULAR recommendations for the vaccination of adults with autoimmune inflammatory rheumatic diseases.



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Building patient led organisations

POS0582-PARE MEASURES FOR IMPROVING FEEDBACK TO PATIENT RESEARCH PARTNERS IN PARTICIPATORY RESEARCH PROJECTS

Keywords: Patient information and education

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Background: The acceptance of participatory research has increased in recent years. However, discussions during the meeting of the EULAR Study Group for Collaborative Research (EULAR conference 2022, Copenhagen) revealed the risk of mere "tokenism" in participatory research projects. In Germany, with more than 60 participatory research projects in the field of rheumatology, "tokenism" is also a matter of discussion in this country.

Objectives: One aspect of tokenism is that patient research partners (PRPs) are involved in the preparation of the application at the beginning of a research project, but they are neglected after the funding application has been submitted, resulting in a lack of feedback from the research projects. The German Rheumatism League (Deutsche Rheuma-Liga, DRL) tried to find ways to improve and uphold continuous communication between scientists and PRPs during all phases of research projects.

Methods: In May 2022, the DRL conducted a survey among the active PRPs on (a) how regularly the PRPs are informed about the status of the research projects, (b) whether contact is usually unsolicited and (c), how the communication was rated overall. Based on the evaluation, measures were discussed to improve communication, and supporting tools were developed. A new survey will be carried out after one year.

Results: In May 2022, the PRPs had not received any information from the research projects for an average of 124 days. However, the timelines varied greatly between ongoing projects (on average 77 days) and for those projects whose applications were only under submission and were waiting for the confirmation of funding ("application phase"; on average 280 days). In about 40% of all projects, the overall flow of information was rated as "bad" or "very bad". Based on these results, the DRL discussed measures with the PRPs as to what adequate communication looks like and how it can be guaranteed that it takes place. Supporting tools were developed and incorporated into the process of coordinating the PRPs. In addition, the DRL discussed what appropriate consequences might be put in place for projects that hesitate to adapt their communication behaviour.

Conclusion: The long absence of any communication, especially during the "application phase", was assessed as unacceptable. In a follow-up survey with PRPs, in May2023, we shall evaluate the impact of the developed tools and discuss and act upon the findings.

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HPR Epidemiology and public health (including prevention)

POS0584-HPR PROS AND DISEASE ACTIVITY IN YEAR PRIOR TO COVID PREDICT TRAJECTORIES OF DEPRESSION IN ADULTS WITH RA IN FIRST 2 YEARS OF PANDEMIC: DATA FROM THE CANADIAN EARLY ARTHRITIS COHORT

Keywords: COVID, Mental health, Rheumatoid arthritis

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Background: Growing evidence points to considerable mental health impacts of the prolonged COVID-19 pandemic, though data from longitudinal studies in rheumatic diseases are sparse.
Objectives: We explored distinct trajectories ofdepressive symptoms in the year prior to and throughout the first 2-years of the COVID-19 pandemic inadults with RA.
Methods: CATCH is a prospective multi-center study of adults with early RA (symptoms <1 year; 81% met 2010 ACR/EULAR criteria at enrolment) who receive care from rheumatologists across Canada. Prior to the pandemic, participants completed PROs and rheumatologists conducted RA assessments during scheduled in-person study visits. After March 2020, ongoing collection of PROs continued at in-person and remote visits. We used group-based trajectory modeling to identify latent groups with at least mild depression (PROMIS 4a depression score ≥55) in participants with ≥1 visits in the year prior to the pandemic (3/19-2/20) and ≥1 visits during pandemic (3/20-1/22) and identified prepandemic individual and clinical characteristics and PROs associated with each trajectory.
Results: The analytic sample included 989 participants with a mean (SD) age of 60 (14) and disease duration of 6 (4) years. 73% were women, 84% white, 60% had completed some post-secondary education, and 77% were in CDAI REM/LDA at visit closest to the start of pandemic. The best model included 4 groups (posterior probabilities ≥0.80 for each group): 1) **Resilient** (none-minimal depression throughout: N=594; 60%); **Worsening** (none/minimal to mild: N=222;22%); **Improving** (mild-resilient: N=80;8%); and **Persistent** (moderate-severe throughout: N=93;9%)(Figure 1). As compared with the Resilient group, those with Worsening Depression were more likely to be female, have a higher prepandemic CDAI, MD and patient global, and report worse pain, disability, anxiety, depression, fatigue, sleep disturbance, and lower participation (Table 1).

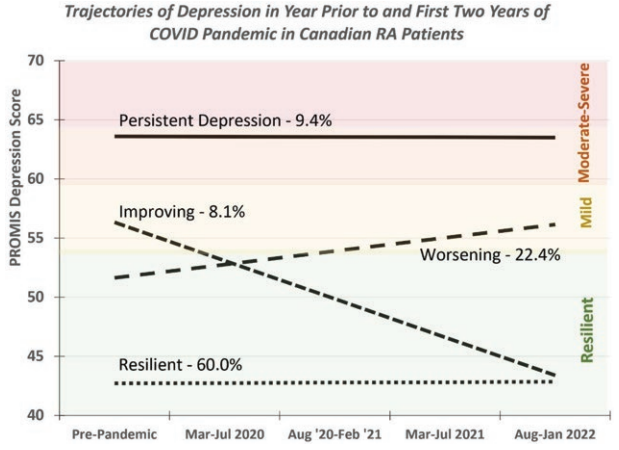


Figure 1.

Table 1.

Mean(SD); N(%)	Worsening N=222 (22%)	Resilient N=594 (60%)	Improving N=80 (8%)	Persistent N=93 (9%)	SIG
Age	60 (15)	61 (13)	59 (13)	61 (13)	0.538
Female	173 (78%)	406 (68%)	57 (71%)	74 (80%)	0.016
White	194 (87%)	533 (90%)	67 (84%)	71 (76%)	0.004
Education > high school	143 (64%)	388(65%)	56 (70%)	42 (45%)	0.001
RDCI (excl depression)	1.2 (1.2)	1.0 (1.2)	1.0 (1.1)	1.0 (1.1)	0.174
CDAI	6.7 (8.2)	5.4 (8.5)	11.3 (13.9)	13.0 (13.1)	<0.001
csDMARDs ±MTX	198 (89%)	547 (92%)	73 (91%)	67 (94%)	0.513
MTX only	153 (69%)	436 (73%)	62 (78%)	67 (72%)	0.443
Biologic or JAK	43 (19%)	102 (17%)	12 (15%)	26 (28%)	0.073
Corticosteroids	36 (16%)	86 (14%)	26 (33%)	20 (22%)	0.001
Patient Global	3.1 (2.4)	1.2 (2.1)	3.9 (2.9)	5.3 (2.7)	<0.001
PROMIS Anxiety >55	97 (44%)	44 (7%)	58 (73%)	86 (92%)	<0.001
PROMIS Depression >55	83 (37%)	13 (2%)	70 (88%)	90 (97%)	<0.001
PROMIS Fatigue >55	83 (37%)	94 (16%)	42 (53%)	74 (80%)	<0.001
PROMIS Pain >55	125 (56%)	187 (31%)	55 (69%)	76 (82%)	<0.001
PROMIS Physical Function <45	132 (59%)	238 (40%)	51 (64%)	78 (84%)	<0.001
PROMIS Participation <45	107 (48%)	141 (24%)	49 (61%)	72 (77%)	<0.001
PROMIS Sleep Problems >55	62 (28%)	88 (15%)	33 (41%)	so (54%)	<0.001

Conclusion: Although 60% of Canadian RA patients had consistently good mental health during the first 2 years of the COVID-19 pandemic, more than 1 in 5 reported deteriorating mood suggesting a cumulative impact over time; 9% had persistent depression and 8% improving mood. The proportion of adults with RA with at least mild symptoms of depression may be more than twice that reported for the general Canadian population. Participants with worsening depressive symptoms during the pandemic were more likely to be female, have higher prepandemic disease activity, symptoms, disability, and higher impairments in participation. Given the impact of depression on quality of life, inflammation, and disease management, vulnerable groups may benefit from more frequent evaluation and additional support from rheumatology providers.
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Disclosure of Interests: Susan J. Bartlett Speakers bureau: Janssen, Merck, Organon, Pfizer, Sandoz, Consultant of: Janssen, Merck, Organon, Orit Schieir: None declared, Marie-France Valois: None declared, Janet Pope Speakers bureau: UCB. Sandoz, Consultant of: AbbVie, Actelion, Amgen, Bayer, BMS, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead, Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Grant/research support from: Abbvie, BMS, Eli Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Louis Bessette Speakers bureau: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Gilles Boire Speakers bureau: Merck, BMS, Pfizer, Janssen, Consultant of: Amgen, BMS, Celgene, Eli Lilly, Pfizer, Grant/research support from: Amgen, Abbvie, BMS, Eli Lilly, Merck, Novartis, Pfizer, Sandoz, Carol Hitchon Grant/research support from: Pfizer, UCB, Edward Keystone Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb, F. Hoffmann-La Roche Inc., Janssen Inc., Merck, Pfizer Pharmaceuticals, Sanofi Genzyme, UCB, Consultant of: AbbVie, Amgen, AstraZeneca Pharma, Bristol-Myers Squibb Company, Celltrion, Myriad Autoimmune, F. Hoffmann-La Roche Inc, Genentech Inc, Gilead, Janssen Inc, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, Sandoz, Sanofi-Genzyme, Samsung Bioepsis, Grant/research support from: AbbVie, Amgen, Gilead Sciences, Lilly Pharmaceuticals, Merck, Pfizer Pharmaceuticals, PuraPharm, Sanofi, Carter Thorne Speakers bureau: Medexus/Medac, Consultant of: Abbvie, Amgen, Celgene, Centocor, Janssen, Lilly, Mexexus/Medac, Merck, Novartis, Pfizer, Sanofi, Grant/research support from: Abbvie, Celgene, CaREBiodam, Diane Tin: None declared, Glen Hazlewood: None declared, Vivian Bykerk Grant/research support from: Amgen, BMS, Genzyme, Pfizer, Regeneron Sanofi Aventis, UCB.
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HPR Interventions (educational, physical, social and psychological)

POS0585-HPR

EFFECTIVENESS OF INSPIRATORY MUSCLE TRAINING ON AEROBIC CAPACITY, RESPIRATORY FUNCTIONS AND RESPIRATORY MUSCLE STRENGTH IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A SINGLE-BLINDED RANDOMISED CONTROLLED TRIAL

Keywords: Physical therapy/physiotherapy, Randomized control trial, Lungs

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Background: Children with juvenile idiopathic arthritis (JIA) may present lower aerobic capacity, lung volumes, and respiratory muscle strength compared to their healthy peers [1].
Objectives: This study aimed to investigate the effectiveness of inspiratory muscle training (IMT) on aerobic capacity, lung volumes, respiratory muscle strength, functional capacity, and quality of life in children with JIA.
Methods: Thirty-three children with JIA who were on the same biologic disease modifying anti-rheumatic drugs for at least three months were included and divided into two groups as exercise group (n=17, mean age: 15.1±2.2 years, 12 male) and control group (n=16, mean age: 15.7±1.6 years, 11 male). Exercise group performed IMT daily for eight weeks. Initial IMT load was set as the 60% of maximal inspiratory pressure (PI_{max}) and was increased by %10 every two weeks. Control group received no additional intervention. Forced vital capacity

(FVC), forced expiratory volume in one second (FEV_1), FVC/FEV_1 ratio, PI_{max}, and maximal expiratory pressure (PE_{max}) were evaluated using a portable pulmonary function test device (Cosmed Pony FX, Rome, Italy). Participants performed a maximal Cardiopulmonary Exercise Test to measure maximal oxygen consumption (VO_{2peak}), metabolic equivalent (MET) and maximal heart rate. Six-minute walking distance (6MWD) was used to evaluate lower-extremity related functional capacity. The Pediatric Quality of Life Inventory (PedsQL) 3.0 Arthritis Module was used to evaluate the quality of life. Participants were evaluated at baseline and at the end of eight weeks.

Results: The groups were similar at baseline. FVC, FEV_1, PI_{max}, PE_{max}, VO_{2peak}, and MET significantly improved at the end of eight weeks in the exercise group ($p<0.05$), while no significant differences were observed in the control group ($p>0.05$). The difference over time in FVC, FEV_1, PI_{max}, VO_{2peak}, and MET were significantly higher in the exercise group compared to control group ($p<0.05$, Table 1). No other between group differences were detected ($p>0.05$).

Conclusion: IMT seems beneficial for improving respiratory functions in children with JIA.

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Table 1. Comparison of change-over-time values between groups

	Mean Differences (95 %CI)			
	Exercise Group (n=17)	**Control Group** (n=16)	**p***	**ES**
Lung Volumes				
FVC (l)	0.20 (0.07/0.32)	-0.01 (-0.11/0.09)	**0.010**	0.96
FEV_1 (l)	0.14 (0.02/0.25)	0.02 (-0.11/0.14)	0.124	-
FEV_1/FVC (%)	0.16 (-1.96/2.30)	1.74 (-1.50/4.98)	0.389	-
Respiratory Muscle Strength				
PI_{max} (cmH_2O)	19.11 (9.52/28.71)	1.56 (-3.37/6.50)	**0.002**	1.18
PE_{max} (cmH_2O)	12.41 (3.09/21.72)	5.06 (-1.55/11.68)	0.187	-
Cardiopulmonary Exercise Test				
VO_{2peak} (ml/min)	158.2 (63.8/252.7)	16.8 (-68.9/102.6)	**0.026**	0.81
VO_{2peak}/Body weight	3.28 (1.14/5.42)	0.33 (-1.47/2.14)	**0.034**	0.78
METs (ml/kg/min)	0.92 (0.34/1.49)	0.06 (-0.35/0.48)	**0.015**	0.88
HR_{peak} (pulse/min)	3.47 (0.17/6.76)	1.18 (-3.0/5.37)	0.367	-
HRR (pulse)	-3.47 (-6.76/-0.17)	-1.18 (-5.37/3.0)	0.367	-
VO_{2peak}/HR_{peak}	0.59 (0.18/1.00)	-0.02 (-0.37/0.34)	**0.024**	0.82
Lower Extremity Related Functional Status 6MWD (m)	9.52 (-15.53/34.58)	4.25 (-9.78/18.28)	0.704	-
Quality of Life PedsQL 3.0 (score: 0-100)	2.0 (-1.0/6.0)	0.5 (0.0/4.0)	0.470	-

*Student's t test, ES: Effect size (Hedge's g), CI: Confidence Interval, FVC: Forced vital capacity, FEV_1: forced expiratory volume in the first second, l: litres, %: percent, PI_{max}: maximal inspiratory pressure, PE_{max}: maximal expiratory pressure, cmH_2O: centimeters water, VO_{2peak}: peak oxygen consumption, m: meters, ml: milliliters, min: minute, kg: kilograms, MET: Metabolic Equivalent, HR_{peak}: peak heart rate, HRR: heart rate reserve, 6MWD: six-minute walk distance, PedsQL 3.0: The Pediatric Quality of Life Inventory 3.0 Arthritis Module

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

POS0586-HPR SARCOPENIA IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS OLDER THAN 65 YEARS: PREVALENCE AND PREDISPOSING FACTORS

Keywords: Sarcopenia, Spondyloarthritis

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Background: Sarcopenia is a muscle disease that presents as a loss of skeletal muscle mass and function. It is a condition associated with chronic diseases and aging that predicts disability, hospitalization and death.

Objectives: To describe the prevalence of sarcopenia and identify risk factors associated with sarcopenia in patients with spondyloarthritis (SpA) older than 65 years.

Methods: Design: Case-control study. Participants: Cases: They were recruited by simple random sampling among patients over 65 years of age with SpA (ACR/EULAR 2010 criteria) treated at 2 university hospitals. Controls: They were recruited for convenience by asking the cases to attend a consultation with a person of the same age (+/- 5 years) and sex. Variables: The main variable: sarcopenia, defined according to the European Working Group on Sarcopenia in Older People (EWGSOPII) 2019 criteria. The risk factors for sarcopenia evaluated were: economic level, malnutrition, measured with the Mini Nutritional Assessment (MNA), toxic habits, comorbidities and Charlson index, physical activity measured with the Global Physical Activity Questionnaire (GPAQ) and Short Physical Performance Battery (SPPB), muscle assessment measured by ultrasound. Other variables were: hemoglobin, calcium, vitamins D and B12, albumin, C-reactive protein, BMI (body mass index), polypharmacy (≥5), quality of life (EQ-5D) and factors related to SpA: activity of disease measured with BASDAI and ASDAS, physical function measured with BASFI, and treatments. Statistical analysis: descriptive and multivariate analysis was performed to identify factors associated with sarcopenia in SpA.

Results: 36 patients and 36 controls were recruited, of whom 54 (75%) were men, with a mean (± SD) age of 70 years (±4.37). Of the 36 patients with SpA, 20 (55.6%) had axial SpA and 15 (44.5) had SpA with axial and peripheral involvement with a mean of 32 years (±10.9) of disease. The prevalence of sarcopenia in patients with SpA is 8.3%. No differences were found in sarcopenia between patients [3(8.3%) and controls [1(2.8%)], p=0.614.Patients with SpA who had sarcopenia, compared with those who did not, had a mean years of evolution of their major disease [45.6 (±3.1) Vs 31.06 (± 10.5)], p=0.24; worse performance tests in the Short Physical Performance Battery (p=0.26), in relation to ultrasound parameters, a lower thickness was observed in the right forearm 75% radial and left forearm 66% radial [11.1(0.2) Vs 14, 7(2.4)], p=0.17 and left rectus femoris area [11.5(1.2)Vs15.4(2.8)], p=0.26, greater thigh fat right to 50% [25.6(4.7) Vs 15.2(8.3)], p=0.041 and lower albumin levels [7.17(21.5) Vs 19.02(608, 5)] p=0.053. On the other hand, no significant differences were found in the rest of the parameters studied for disease activity, disability, quality of life (EQ-5D), malnutrition, toxic habits, comorbidities or physical activity. In the multivariate model, the years of disease evolution (p=0.041) Table 1 were identified as an independent predictor of sarcopenia in patients with SpA. This model would explain 33% of sarcopenia in RA (R2=0.37).

Conclusion: In our study we found no differences in sarcopenia in patients older than 65 years with SpA compared to controls. The longer evolution time of their disease in patients with SpA is associated with a greater risk of sarcopenia.

Table 1. Multivariate analysis (VD: Sarcopenia) in patients with SpA

	OR(IC)	*p-valor*
Evolution of SpA (years)	***1,172 (1,002-1,363)***	***0,047***

R2=0,33

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0587-HPR IMPACT OF COMBINED INTERVENTION WITH CLINICAL NURSE SPECIALIST IN THE MANAGEMENT OF CARDIOVASCULAR RISK IN PATIENTS WITH GOUT

Keywords: Cardiovascular disease, Gout, Non-pharmacological interventions

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Background: Gout is associated with increased cardiovascular risk (CVR). Traditional CVR factors (CVRF) are frequently present in patients with gout, further worsening the prognosis. Several studies have shown that clinical nurse specialist (CNS) contributes effectively to the management of gout.

Objectives: To analyze the detection of CVRF in patients with gout in a rheumatology consultation with CNS and to evaluate short-term changes after a targeted approach.

Methods: Patients with gout according to ACR/EULAR 2015 criteria referred from Primary/Specialized Care due to poor control of the disease. At the first visit, demographic and clinical variables were collected: age, sex, smoking, alcohol consumption, duration of gout, tophi, comorbidities, urate-lowering treatment

(ULT) and concomitant drugs. A blood test and review of previous tests from the last year were performed, as well as measurement of blood pressure (BP), weight and abdominal circumference. Nurse-managed calls were made to monitor home measurements and check adherence/tolerance to pharmacological (start/adjustment of ULT, antihypertensive, lipid-lowering and anti-diabetes drugs) and non-pharmacological approach (gout education, dietary/lifestyle recommendations) initiated at the first visit, according to the Spanish gout guideline and EULAR recommendations for CVR management in rheumatic diseases. We count on multidisciplinary collaboration with other specialists. After 6 months, an in-person visit was made with the same measurements to determine potential changes. A descriptive analysis of the sample was performed. The Wilcoxon test was used to evaluate the variation in the parameters studied. The outcome variable was determined as improvement versus no improvement of the dependent variable. Chi-square and Mann Whitney U tests were used to evaluate the differences.

Results: Forty patients who met the inclusion criteria were included. 98% were male, with a median age of 66 (58-75) years, severe gout (83% tophaceous, median duration 7 years) and marked presence of CVRF (smoking 23%, hypertension 78%, dyslipidemia 55%, diabetes 23%), some of them previously undetected (10% hypertensive, 3% dyslipidemic, 3% diabetic), and related comorbidities (ischemic heart disease 8%, cerebrovascular disease 5%, chronic kidney disease 20%). Fifty-five percent were not taking ULT and 53% used non-steroidal anti-inflammatory drugs (NSAIDs) on a regular basis. At the first visit, ULT was started/adjusted in 95% of patients, antihypertensive in 15%, lipid-lowering drugs in 13%, and anti-diabetes drugs in 8%. At 6 months, there was a significant improvement in sUA and BP, and a non-statistically significant weight reduction (Table 1). Serum uric acid (sUA) target was achieved in 93% of patients (37/40 <6 mg/dl, 29/40 <5 mg/dl). The use of NSAIDs was reduced to 5%. Four out of 9 smokers quit. Systolic BP improved in 73% of patients and diastolic BP in 70%. Dietary and habit modifications, therapeutic adjustments and multidisciplinary care were significantly associated with improved BP (p=0.02).

Conclusion: In patients with difficult-to-treat gout and high CVR, combined intervention with CNS allows substantial short-term changes in CVRF, a drastic reduction in NSAID consumption and a high percentage of success in achieving the sUA target.

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Table 1. Anthropometric, blood pressure and serum uric acid changes 6 months after the first visit.

	Basal	6 months	p
Weight (kg)	87 (77.3-99)	85.4 (77-96.3)	0.79
Abdominal circumference (cm)	107 (102-116)	108 (103-116)	0.81
Systolic BP (mm Hg)	151 (133.3-162.5)	142.5 (124.8-155)	0.02
Dyastolic BP (mm Hg)	88.5 (76.3-95)	78.5 (70-86.8)	0.01
sUA (mg/dl)	7.7 (6.6-8.8)	4.5 (4.1-5.2)	<0.01

All variables expressed as median/IQR. BP: blood pressure; sUA: serum uric acid

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HPR Measuring health (development and measurement properties of PROs, tests, devices)

POS0588-HPR

DISCOVERING THE POTENTIAL OF DIGITAL BIOMARKERS IN THE WORK PROCESS OF THE RHEUMATOLOGY HEALTHCARE PROFESSIONALS, A DESIGN THINKING APPROACH. PRELIMINARY RESULTS OF THE HEALTHCARE PROFESSIONALS PERSPECTIVE

Keywords: Biomarkers, Health services research, Qualitative research methods

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Background: During times of social-distancing, in-person outpatient visits were greatly reduced. Health care professionals (HCPs) were dependent on the patient's reported experience of their disease activity in their assessments of the wellbeing and inflammatory state, due to lack of physical assessments. *Digital biomarkers* can support real-world continuous measurements and offer a method for remote quantification of inflammatory joint disease. They are defined as objective, quantifiable, physiological and behavioural data that are collected and measured with digital devices [1].

Objectives: This study uncovers the HCPs perspective on current manners of disease activity monitoring, easing their workload and the potential of digital biomarkers.

Methods: A Design Thinking approach is followed for digital biomarker development. It is a human-centered problem solving approach that leverages iteration, empathy and collective idea generation to tackle complex challenges [2]. Semi-structured online focus group discussions were conducted. Pilot 1-1 interviews were executed to assess the interview script. The script is underpinned by the graphical framework for clinical decision making [3] and the theoretical domain framework [4]. One moderator and three alternating observers facilitated the sessions. All interviews were audio-recorded, transcribed to verbatim and coded.

Results: In total 6 focus groups were organised, with a total of 28 HCPs. Participants were rheumatologists (N= 19, age 47 ± 9, 50% male) and rheumatology nurses (N = 9, age 51 ± 6, 0% male). The main findings from the interviews about digital biomarkers in relation to current practices were: *Trust;* HCPs felt self-assured about their own abilities of physical evaluation, reading patients and their gut feeling. Trust in flare detection with digital biomarkers and machine learning was low. It was expected that much disease activity is missed and many false-positive flares are detected. Biomarkers should be valid, reliable and sensitive to change. *Innovation should improve quality of care;* No consensus about a golden standard of care exists. HCPs were afraid that with digital biomarkers personal interaction recedes to the background and quality of care is compromised. Personal interaction was marked as essential to raise sensitive topics and stimulate therapy adherence. *Benefits of digital biomarkers;* HCPs enjoyed the delivery of efficient and effective care. They disliked repetition and the high administrative burden. In the HCPs opinion digital biomarkers could establish disease activity prior to the consultation, so time could be spent on what matters to the patient. New technologies should however not add to frustrations and make way for things that really matter.

Conclusion: The following problem statement from the HCPs perspective can be formulated: "In limited time we take many actions. We spend time on both disease and emotional support of our patients. Our workload is high and trivial tasks such as administration take too much of our time. Instead we want to focus on what's relevant to the patient. We are confident about our own abilities and, only if technology is proven to be valuable, valid, reliable and accepted by our patients it can be used in clinical practice."

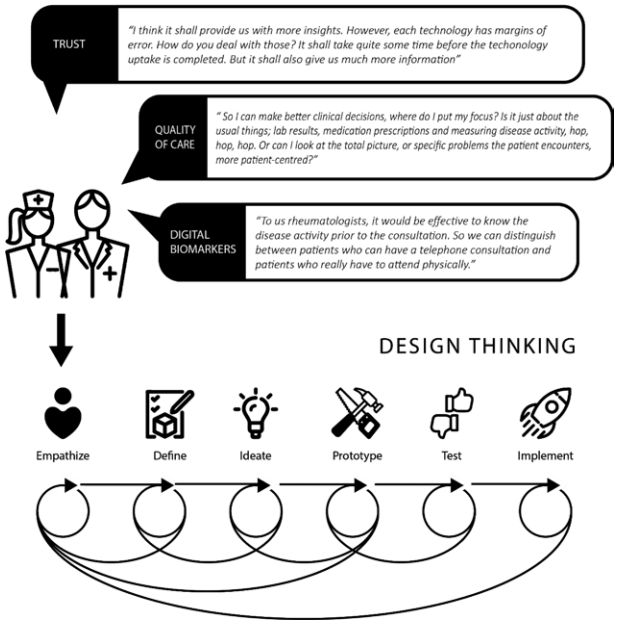


Figure 1. Interview Quotes of the HCP and the Design Thinking Process

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POS0589-HPR NATURE AND SEVERITY OF FUNCTIONAL LIMITATIONS ACCORDING TO THE HEALTH ASSESSMENT QUESTIONNAIRE DISABILITY INDEX IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SEVERE FUNCTIONAL DISABILITY

Keywords: Rheumatoid arthritis, Patient reported outcomes, Outcome measures

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Background: Despite the availability of effective medical treatment, there is still a subgroup of people with Rheumatoid Arthritis (RA) who have considerable functional limitations due to persistently high disease activity, joint destruction or deformities and/or comorbidities. More insight into the nature and severity of these functional limitations is important to provide adequate treatment matching the needs of this specific subgroup.
Objectives: To describe the nature and severity of functional limitations in patients with RA and severe functional limitations, identified by the Health Assessment Questionnaire Disability Index (HAQ-DI).
Methods: Baseline data from people with RA and severe limitations in physical functioning participating in a randomized controlled trial on the (cost-)effectiveness of longstanding physical therapy as compared to usual care [1] were used. Patients completed the HAQ-DI (Dutch version)[2, 3], a reliable, valid and widely used questionnaire reflecting problems in activities of daily living and consisting of 20 items divided over eight domains (Dressing and grooming, Arising, Eating, Walking, Personal hygiene, Reaching, Gripping and Usual activities). Each item is scored on a 4-point scale ranging from 0 to 3 (no difficulty - unable to perform), with the total HAQ-DI score ranging from 0 to 3 (no disability - severe disability). This preliminary data analysis does not yet take into account the use of assistance/assistive devices. Gender, age, sex and disease duration were recorded, and the EuroQol 5 Dimensions 5 Levels (EQ-5D-5L) administered for health related quality of life (HRQoL) (Single index score (-0.446-1.000), and visual analogue scale (EQ-VAS, 0-100), higher scores indicating better HRQoL).
Results: From 2020-2021, 215 people with RA were included (n=194; 90% women, mean age (standard deviation) of 58.8 (12.9) years and median disease duration (Interquartile Range (IQR)) of 19 (9-27) years (n=166)). The median EQ-5D-5L index and EQ-VAS were 0.6 (0.3-0.7) and 59 (41 -70), respectively. The median total HAQ-DI score was 1.5 (1.1-1.9). The majority (83%, n=179) had a total HAQ-DI score ≥1 indicating moderate to severe activity limitations. The mean HAQ-DI domain scores and the percentage of patients within each domain reporting no/some/much difficulty or inability to perform everyday activities are shown in Figure 1.The median number of domains with a score ≥1 was 8 (range 3-8, IQR 7-8, mean 7.1). More than half of the participants had a domain score ≥1 in all 8 domains (52%, n=111), almost a quarter in 7 domains (24%, n=52), 13% (n=28) in 6 domains and the minority (11%, n=24) in 5 or less domains. The highest proportion of patients with a maximum score of 3 were seen in the domains Personal hygiene (42%) and Reaching (28%), followed by Usual activities and Eating (15% and 14%, respectively). For Gripping, Arising, Walking and Dressing and grooming the proportions of patients with the maximum score was less than 8%.
Conclusion: In a subgroup of patients with RA and severe functional disability, the majority had limitations in almost all the domains of the HAQ-DI. Most severe limitations were seen in Reaching and Personal hygiene and the least severe for Arising and Dressing and grooming. In daily clinical practice, a comprehensive assessment of all areas of daily activities in this subgroup of RA patients is necessary, and because the functional limitations are present and significant in all domains, extensive support from multiple healthcare professionals may be indicated.
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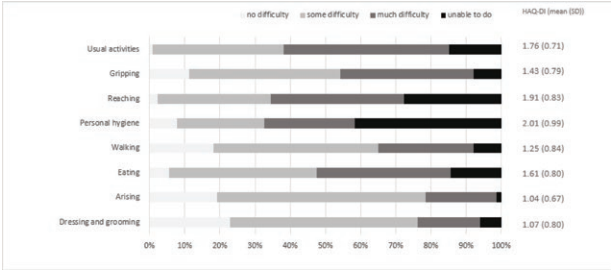


Figure 1. Mean HAQ-DI scores for each HAQ-DI domain and the percentage of patients that reported to have either no/some/much difficulty or unable to perform everyday activities represented for each domain.

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POS0590-HPR IDENTIFICATION OF RESPONDER AND DISEASE ACTIVITY THRESHOLDS FOR THE PSORIATIC ARTHRITIS IMPACT OF DISEASE-12 (PSAID-12) QUESTIONNAIRE USING POOLED DATA FROM TWO PHASE 3 TRIALS OF BIMEKIZUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Clinical trials, Patient reported outcomes

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Background: Psoriatic arthritis (PsA) can significantly impact patients' (pts) quality of life due to pain, fatigue and reduced physical function [1]. The PsA Impact of Disease-12 (PsAID-12) questionnaire is a 12-item pt-reported outcome measure developed to assess the impact of PsA on 12 physical, social and psychological domains [2,3].
Objectives: To determine responder thresholds (clinically meaningful within-pt improvement) and disease activity thresholds for the PsAID-12 total and single-item domain scores for pts with active PsA to complement preliminary thresholds published for the total score [2,4].
Methods: Pooled data from two phase 3 trials (BE OPTIMAL [NCT03895203] and BE COMPLETE [NCT03896581]) of subcutaneous bimekizumab 160 mg every 4 weeks (wks) were used to estimate responder and disease activity thresholds for the PsAID-12 in pts with moderate-to-severe PsA. Each study included a 16-wk double-blind, placebo-controlled phase; BE OPTIMAL included an adalimumab reference arm. Data used were observed scores at baseline (BL) and Wk 16 for all randomised pts with ≥1 non-missing PsAID-12 single-item domain score at any

scheduled visit. Anchor-based analyses (using the American College of Rheumatology [ACR] response criteria and PsA Disease Activity Score [PASDAS]) and distribution-based analyses (one standard error of measurement, and half of the baseline standard deviation [SD]) were used to determine responder thresholds at Wk 16. The maximum Youden index values from the receiver operating characteristic (ROC) curve analyses (using PASDAS and Disease Activity Index for PsA [DAPSA] scores as anchors; **Figure 1**) were used to determine disease activity thresholds.

Results: In 1,252 pts, mean (SD) PsAID-12 total score decreased from 4.19 (1.94) at BL to 2.65 (2.02) at Wk 16. Single-item domain scores ranged from 1.34 (2.13) for depression to 5.56 (2.26) for pain at BL and from 0.91 (1.80) for depression to 3.76 (2.51) for pain at Wk 16. The Wk 16 responder threshold for the PsAID-12 total score was identified as a 2-point decrease. For 8 PsAID-12 single-item domain scores, Wk 16 responder thresholds were identified as 3-point decreases. For the remaining 4 single-item domains (anxiety, fear and uncertainty; embarrassment and/or shame; social participation; depression), responder thresholds could not be determined due to floor effects at BL (absence of these symptoms in a high proportion of pts). Disease activity thresholds for the PsAID-12 total score were identified: ≤1.15, >1.15–≤1.95, >1.95–≤3.60 and >3.60 for Remission, Low, Moderate and High Disease Activity, respectively (**Figure 1**). Disease activity thresholds for PsAID-12 single-item domain scores are reported in the **Table 1**.

Conclusion: This analysis defined responder and disease activity thresholds for the PsAID-12 total score and most single-item domain scores, which can be used to assess treatment efficacy and disease impact in pts with PsA.

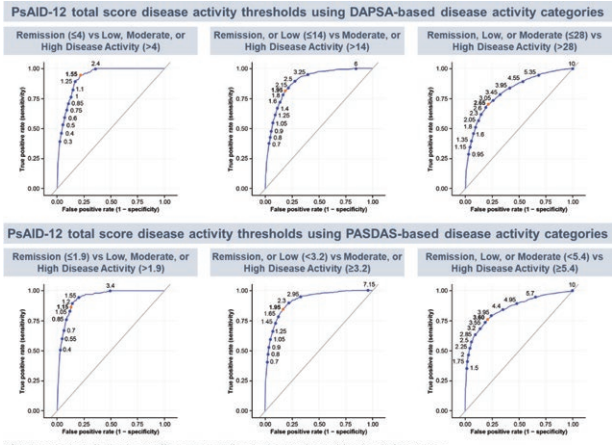
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Table 1. Disease activity threshold estimates for PsAID-12 total and single-item domain scores

	Remission	Low Disease Activity	Moderate Disease Activity	High Disease Activity
Total score	**≤1.15**	**>1.15–≤1.95**	**>1.95–≤3.60**	**>3.60**
Single-item domain score				
Pain	≤2	3	4	≥5
Fatigue	≤1	2	3 or 4	≥5
Skin problems	≤1	2	3 or 4	≥5
Work and/or leisure activities	≤1	2	3 or 4	≥5
Functional capacity	≤1	2	3 or 4	≥5
Discomfort	≤1	2	3 or 4	≥5
Sleep disturbance	≤1		2 or 3	≥4
Coping	≤1	2	3 or 4	≥5
Anxiety, fear and uncertainty[a]	-	-	-	-
Embarrassment and/or shame[a]	-	-	-	-
Social participation	≤1		2	≥3
Depression[a]	-	-	-	-

[a]Cutoffs for disease activity thresholds could not be determined as these domains did not demonstrate good discriminant power (area under curve <0.70). PsAID-12 score ranges from 0–10 (higher scores indicate worse status).



Orange markers indicate cutoffs corresponding to the maximum Youden index values.

Abbreviations: DAPSA: Disease Activity Index for Psoriatic Arthritis; PASDAS: Psoriatic Arthritis Disease Activity Score; PsAID-12: Psoriatic Arthritis Impact of Disease-12; ROC: Receiver Operating Characteristic.

Figure 1.

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POS0591-HPR THE UTILITY OF NOVEL ACCELEROMETER METRICS FOR CHARACTERISING CLINICAL FEATURES IN PATIENTS LIVING WITH RHEUMATOID ARTHRITIS

Keywords: Outcome measures, Rheumatoid arthritis

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Background: Research-grade accelerometers are commonly used to measure physical activity (PA) in rheumatology research, demonstrating superior reliability and validity relative to self-report methods. Several accelerometers offer manufacturer software and embedded proprietary algorithms to reduce the complexities of data processing. However, algorithms vary between device brands, and hinder standardisation of data processing and analysis. Best practice in PA research is now therefore considered to be the collection and analysis of raw accelerometer data, to which transparent and replicable data transformation methods can be carried out post-processing. Novel metrics include average acceleration, intensity gradient, and MX metrics, which represent PA volume, intensity and patterns, and have not been examined in rheumatic diseases.

Objectives: To explore the utility of novel accelerometer metrics for characterising clinical features in Rheumatoid Arthritis (RA), i.e. disease activity and severity, cardiovascular disease (CVD) risk.

Methods: People living with RA (n = 104) provided demographic data, medical history, a fasted blood sample, and completed the health assessment questionnaire (HAQ, disease severity). Disease activity was measured using the Disease Activity Score 28-CRP (DAS28-CRP), and CVD risk determined using the QRISK3. Participants wore a GT3X Actigraph accelerometer on their right hip for 7-days during waking hours. Accelerometer data were analysed using GGIR (v.2.1-1) to determine average acceleration (AA, m*g*, proxy for daily volume of PA), intensity gradient (IG = distribution of PA across the day) and MX metrics (acceleration above which a person's most active "X" mins are accumulated e.g., M5 = most active 5 mins). A higher AA and more positive IG indicate a

favourable activity profile. *Statistical analyses:* Participants were grouped according to DAS28-CRP (remission = <2.6, low = 2.6 - 3.1, moderate = 3.2 – 5.1, high = >5.1) disease severity (HAQ; low = <1, moderate = 1 – 1.9, high = ≥2) and QRISK3 (low = <10%, moderate = 10 - 19%, high = ≥20%. Between group differences in AA and IG were analysed using analysis of variance, adjusted for accelerometer wear time. Radar plots were produced in R, to illustrate differences in MX metrics according to clinical features.

Results: Valid accelerometer data (≥10hr on ≥4 days), were available for n = 102 participants (M ±SD, AA = 13.7 ±5.2 m*g*, IG = -2.91±.36). Participants in remission and with low CVD risk, demonstrated a better activity profile (i.e. [M ±SE, all p<.05] significantly higher AA [DAS28-CRP = 17.9 ±1.1; QRISK3 = AA = 15.4 ±0.6] and more positive IG [DAS28-CRP = -2.62 ±0/07, QRISK3 = 2.80 ±0.04], compared to patients with moderate or high disease activity and CVD risk (DAS28-CRP [moderate, AA = 12.8 ±0.6, IG = -2.99±.04] and [high, AA = 11.2 ±1.1, IG = -3.07±.08], QRISK3 [moderate, AA = 12.0 ±1.0; IG = -3.0 ±0.07] and [high AA = 10.3 ±1.1; IG = -3.16 ±0.08]). For disease severity IG was significantly more positive in patients with low (-2.78 ±0.05) vs. high (-3.10 ±0.08) HAQ scores. Radar plots (**Figure 1**) showed the intensity of the most active accumulated 2-45 mins (M2-M45) was greater (with M10 exceeding 75m*g*) among participants with better disease profiles (i.e. remission/low DAS28-CRP, HAQ and QRISK3 scores vs. moderate/high).

Conclusion: This is the first study to demonstrate the clinical utility of novel accelerometer metrics in RA. Results suggest higher AA, more positive IGs, and accumulating ≥10 mins at an intensity indicative of a slow walk (M10 >75m*g*), is characteristic of more favourable disease profiles. Future studies utilising these raw accelerometer metrics could provide valuable, standardised accelerometer data that can be used to deliver more personalised care (i.e. precision medicine).

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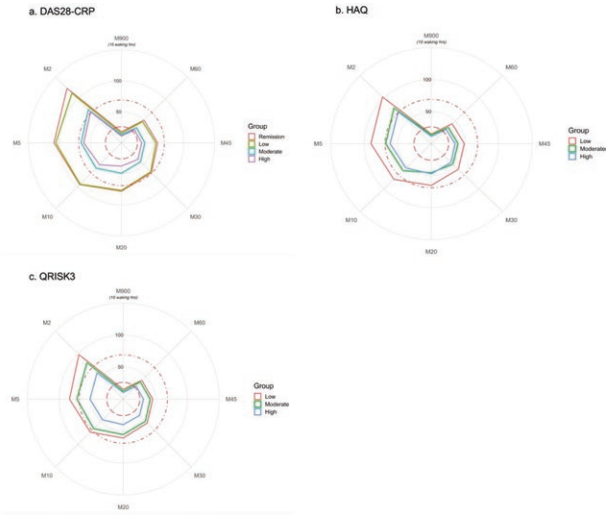


Figure 1.

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POS0592-HPR

IDENTIFYING IMPORTANT CLINICAL FEATURES FOR PREDICTING REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICS USING MACHINE LEARNING MODEL

Keywords: Pain, Rheumatoid arthritis, Artificial intelligence

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Background: Biologic disease-modifying antirheumatic drugs (bDMARDs) offer promising results for rheumatoid arthritis (RA) patients in general, but a substantial percentage of patients do not respond to them. It is important to predict the response before the treatment so that unnecessary adversities for the patients and costs for the healthcare system can be avoided. We developed a model to predict remissions in patients treated with bDMARDs and to identify important clinical features associated with remission using several machine learning (ML) models system that works with readily-available demographic and clinical factors for prediction of response to DAS-28.

Objectives: In this study, we established a machine learning model using data from the Kuwait Registry for Rheumatic Diseases (KRRD) and show its application to identifying clinical variables predictive of remission in RA patients treated with biologics.

Methods: We gathered the follow-up data of 1,000 patients treated with bDMARDs (etanercept, adalimumab, golimumab, infliximab, abatacept, and tocilizumab) from KRRD. Patients were recruited from public hospitals in Kuwait between February 2013 to September 2022. Remission (DAS-28 less than 2.6) was predicted at 1-year follow-up using baseline clinical data obtained at the time of enrollment. Machine learning methods system (including: lasso, ridge, support vector machine, random forest, XGBoost, and Shapley additive explanation (SHAP)) were used for the predictions.

Results: The ranges for accuracy and area under the receiver operating characteristic of the newly developed machine learning model for predicting remission were 52.8–72.9% and 0.463–0.719, respectively. The Shapley plot in XAI showed that the impacts of the variables on predicting remission differed for each bDMARD. The most important features were age for adalimumab, rheumatoid factor for etanercept, erythrocyte sedimentation rate for infliximab and golimumab, disease duration for abatacept, and C-reactive protein for tocilizumab, with mean SHAP values of – 0.250, – 0.234, – 0.514, – 0.227, – 0.804, and 0.135, respectively.

Conclusion: Our proposed machine learning model system successfully identified clinical features that were predictive of remission in each of the bDMARDs. This approach may be useful for improving treatment outcomes by identifying clinical information related to remissions in patients with rheumatoid arthritis.

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Disclosure of Interests: None Declared.
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POS0593-HPR

PRELIMINARY EVALUATION OF THE RHEUMATOID ARTHRITIS FOOT DISEASE ACTIVITY INDEX (RADAI-F5) AS A SCREENING TOOL FOR FOOT-RELATED DISABILITY

Keywords: Outcome measures, Patient reported outcomes, Rheumatoid arthritis

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Background: Impaired foot function in patients with rheumatoid arthritis (RA) can contribute to impairment and disability during daily activities [1]. RA foot disability has been studied extensively, although foot disease activity and its association with future foot impairment have not. The Rheumatoid Arthritis Foot Disease Activity Index (RADAI-F5) is a clinically feasible, valid, and reliable patient-reported outcome measure (PROM) that can be employed with the DAS-28 to evaluate RA foot disease activity [2]. Existing evidence supports the construct validity of the RADAI-F5, however predicative validity must be demonstrated for any newly created screening instruments.

Objectives: This study aims to evaluate the predictive validity of the RADAI-F5 for foot-related disability in RA.

Methods: This study drew its data from a randomised controlled trial comparing prefabricated versus customised foot orthoses for RA patients [3]. At baseline, six months, and 12 months, the patients' disability levels were examined using the Foot Function Index disability subscale (FFIdis). The newly created RADAI-F5 was gathered at baseline, one week, and six months. In the absence of recognised threshold cut-off values, the median split method was utilised to dichotomize FFIdis scores for poor and mild foot disability at 12 months. Two consecutive occurrences of moderate-high foot disease (RADAI-F5 > 3.45) at baseline and six months constituted poor foot disease activity. The predictive value of foot disability at 12 months was investigated using IBM SPSS bivariate binary logistic regression analysis controlling for baseline foot disability scores. The odds ratios (OR) and 95% confidence intervals (CI) were obtained, and a significance level of $P < 0.05$ was established.
Results: 51 patients, 36 of whom were female, with a mean [standard deviation, ±SD] age of 53.5 [±12.18] and disease duration of 8.34 [±6.57] years completed the 6-month and 12-month FFI follow-ups. At baseline and 6 months, mean [±SD] RADAI-F5 scores were 5.56 [± 2.07] and 4.12 [± 2.54], respectively. At 0 and 6 months, 75.2% and 52.5% of the sample, respectively, had moderate-high foot disease activity, whereas at 12 months, the prevalence of poor foot disability was 48.6%. Binary logistic regression identified that having two consecutive episodes of moderate-high foot disease was an independent predictor of poor foot disability at 12(OR=3.44, 95% CI= 1.04-11.40, $p < 0.05$).
Conclusion: The RADAI-F5 is an accurate predictor of foot-related disability. In clinical practice, the RADAI-F5 may be used as a screening tool to identify individuals who are at risk for persistent foot disability. Combining the RADAI-F5 with common physical outcome measures can improve the prediction of foot impairment.
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POS0594-HPR PSYCHOMETRIC AND CROSS-CULTURAL VALIDITY OF THE MEASURE OF ACTIVITY PERFORMANCE OF THE HAND (MAP-HAND) ACROSS THREE EUROPEAN COUNTRIES (SWITZERLAND, TURKEY AND THE UK)

Keywords: Patient reported outcomes

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Background: The MAP-Hand scale comprises 18 patient-generated items which assess hand activity among people with rheumatoid arthritis (RA). All items are scored on a 0–3 scale and are summed into a total score (0 to 54).
Objectives: The MAP-Hand is already fully validated within a UK population [1], and this study aims to assess the validity, stability and comparability across German-speaking Swiss and Turkish RA samples.
Methods: The MAP-Hand was assessed using Rasch model psychometric assessment methodology. Within the original UK validation, all items were assessed individually, then combined into four testlets (super-items) in order to account for observed local dependency among the items. This analytic strategy was replicated, where the psychometric properties of the scale items were assessed separately within each country-specific samples, and then across a merged sample of all three countries. A differential item function (DIF) analysis was used to assess scale stability across countries.
Results: When the countries are considered separately, although slight differences are apparent, the operation of the instrument appears to be very similar across Switzerland, Turkey, and the UK. Although there is a degree of scale misfit in all countries, the scale-sample targeting and the scale reliability are both excellent (Person Separation Index = 0.93-0.95; Cronbach's Alpha = 0.96-0.97), and the response categories function well across all items. However, there is a large degree of inter-item dependency present, and the MAP-Hand displays apparent multidimensionality within all three countries. Additionally, some individual items display Rasch model misfit to some extent, although these items are variable across the three countries. When the items were re-configured into four testlets, this accounted for the inter-item dependency, also improving the model fit and unidimensionality of the scale within all three countries separately, as well as when the data is merged into a single dataset. Some significant country-DIF was observed on the 'Dressing' testlet (comprised of items 1-3), but this was found to have no significant effect on total person score estimates. Despite the testlet re-structuring creating a narrower scale range, the scale-sample targeting and scale reliability remain high (Person Separation Index = 0.86-0.91; Cronbach's Alpha = 0.93).
Conclusion: It is recommended that the four-testlet structure is implemented across all three countries, as this offers a pragmatic approach to the utility and comparative scoring of the MAPHAND across the UK, Switzerland and Turkey. Although the re-structuring creates a narrower scale range and apparent reduction in the reliability, this is indicative of the initial dependency that is present, and suggests that the original reliability values are over-inflated.
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POS0595-HPR WILLINGNESS TO USE REMOTE CARE AMONG PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Patient reported outcomes, Telemedicine

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Background: Remote care is an alternative to standard care for patients with axial spondyloarthritis (axSpA) and may facilitate accurate and timely management of disease. However, there is limited knowledge on factors related to the patients' willingness to use remote care.
Objectives: To assess the willingness to use remote care among patients with axSpA and compare characteristics of patients at different levels of such willingness.
Methods: We used baseline data from a randomised controlled trial on remote care of axSpA (ReMonit). Patients with a clinical axSpA diagnosis fulfilling ASAS-criteria for axSpA, treated with TNFi and with low disease activity (ASDAS<2.1) were recruited at a single outpatient clinic. Years since diagnosis were retrieved from medical records, and self-reported education and work status. Willingness to use remote care was measured by scoring the statement "I want to use remote care" using a 4-point Likert scale (strongly disagree – strongly agree). Patients were then divided into three groups (disagree/agree/strongly agree) based on their willingness to use remote care. eHealth Literacy was measured using three scales of the eHealth Literacy Questionnaire (eHLQ) using a 4-point Likert scale (1=strongly disagree – 4=strongly agree, 4=best score). Bath Ankylosing Spondylitis Functional Index (BASFI, 0-10, 0=best score), and a single item from the Work Productivity and Activity Impairment (WPAI) Questionnaire scored 0-10, 0=best score) were used to measure self-reported physical function. Differences between groups on baseline characteristics were assessed using Kruskal Wallis tests with Dunn's post-hoc test.
Results: 242 patients were included, mean age 43 years (SD 11.7) and 75 % male. Most patients were willing to use remote care (strongly agree: 53.3%, agree: 43.0% and disagree: 3.7%). Descriptive and comparative analyses between groups show a trend toward younger males with higher education and full-time employment being more willing to use remote care. Moreover, patients

with higher willingness to use remote care had good physical function, fewer years since axSpA diagnosis and high eHealth literacy (Table 1).
Conclusion: Nearly all patients included in this trial of remote care of axSpA wanted to use remote care. Significant differences in baseline characteristics were revealed between the three groups according to their willingness to use remote care. However, precaution must be taken due to a small number of participants in the "disagree"-group.

Table 1. Sample characteristics grouped by willingness to use remote care

	Statement: "I want to use remote care"		
	Disagree (n=9)	Agree (n=104)	Strongly agree (n=129)
Age, mean (SD)	50.1 (16.1)	45.2 (11.7)$	41.5 (11.1)
Males, n (%)	7 (77.8)	77 (74.0)	98 (75.9)
Education level[1], n (%)			
Primary school	2 (22.2)	3 (3.0)	3 (2.3)
High school	1 (11.1)	19 (18.4)	18 (14.0)
University level	6 (66.6)	81 (78.6)	108 (83.7)
Work status, n (%)			
Full time	5 (55.6)	80 (77)	109 (84.5)
Age retired	1 (11.1)	5 (4.8)	4 (3.1)
Disability benefit	1 (11.1)	4 (3.8)	4 (3.1)
Other[2]	2 (22.2)	15 (14.4)	12 (9.3)
Years since axSpA diagnosis, mean (SD)	19.7 (19.9)	14.9 (10.4)	13 (9.7)
BASFI, mean (SD)	1 (1.5)	0.9 (0.9)$	0.5 (0.9)
WPAI Item 6, mean (SD)	1.7 (1.5)†	1.2 (1.4)$	0.7 (1.1)
eHLQ Scale 1[3], mean (SD)	2.8 (0.8)†	2.9 (2.9)$	3.5 (3.5)
eHLQ Scale 3[4], mean (SD)	3.0 (0.8)†	3.2 (0.4)$	3.8 (0.2)
eHLQ Scale 5[5], mean (SD)	2.5 (0.6)†	2.9 (0.4)$	3.6 (3.6)

$: Significant difference (p=<0.05) between Agree and Strongly agree, †: Significant difference (p=<0.05) between Strongly Agree and Disagree, [1]n=241 due to 1 missing, [2]Other: receiving social benefits, on sick leave, student/housekeeping, part time work and unemployed, [3]Using technology to process health information, [4]Ability to actively engage with digital services, [5]Motivated to engage with digital services, [6]Ability to perform daily activities, BASFI: Bath ankylosing spondylitis functional index; eHLQ: eHealth literacy Questionnaire, WPAI: Work Productivity and Activity Impairment.

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POS0596-HPR GOUT PATIENTS' PERSPECTIVE ON CONTINUATION OR DISCONTINUATION OF URATE-LOWERING THERAPY WHEN REMISSION HAS BEEN ACHIEVED: A MIXED METHODS STUDY

Keywords: Gout, Qualitative research methods, Remission

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Background: Long-term gout management is based on reducing serum urate by using urate-lowering therapy (ULT) [1, 2]. A lifelong treat-to-target approach is advocated, though a ULT (taper to) stop attempt can be considered (treat-to-avoid symptoms approach) during remission[1]. It is yet unclear if either is a superior strategy when remission has been achieved. Exploring gout patients' beliefs on these long-term ULT strategies is important for optimising gout management.
Objectives: To identify factors that influence the decision for continuation (treat-to-target) or discontinuation (treat-to-avoid symptoms) of ULT and to determine their perceived relative importance in gout patients in remission.
Methods: A mixed methods design was used. First, semi-structured interviews (substudy 1 EULAR POS1477 2020) were held to identify barriers and facilitators for continuation and discontinuation of ULT using inductive thematic analysis. These items were then summarized by a multidisciplinary team (including a patient partner) in neutrally formulated items. These items were subsequently used in a Maximum Difference Scaling study (MaxDiff, substudy 2) to rank them and to determine their relative importance based on utility scores (preference score). A rescaled probability score (RPS) was generated with a 0-100 range (the higher the score, the more important the item). For example, an item with an RPS of 8 is twice as important as an item with an RPS of 4. Patients of both studies were recruited from general practitioners and from the rheumatology department of the Sint Maartenskliniek (both in the Netherlands). The semi-structurered interviews as well as the MaxDiff experiment have been pilot tested.
Results: Substudy 1 and 2 included 18 and 156 patients, respectively (see Table 1). The semi-structured interviews yielded 46 barriers/ facilitators and were summarized in 22 items, divided into 10 overarching themes (logistics, lifestyle, role of serum urate, physician role, scientific knowledge, general medication use, anti-inflammatory use, gout flares, ULT use and long-term gout effects). Figure 1 shows their ranking (substudy 2). The 'risk of joint damage' (RPS 8.77) was the most important item, and is 26 times more important than the least important item, 'cost of my gout treatment' (RPS 0.34).
Conclusion: In particular, items concerning (control of) disease activity (flares, joint damage) play a role when gout patients in remission consider (dis)continuation of ULT. Costs, logistics and monitoring by physician were deemed less important. These results provide a basis for shared decision making between physicians and patients, and show which items should at least be discussed when considering ULT (dis)continuation in the remission phase.

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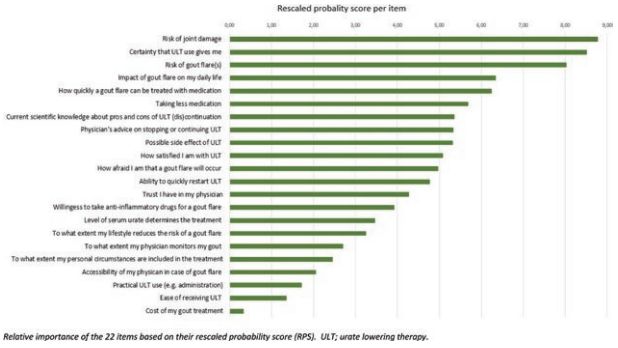


Figure 1. Relative importance of items of the maximum difference scaling study

Relative importance of the 22 items based on their rescaled probability score (RPS). ULT; urate lowering therapy.

Table 1. Patient characteristics semi-structured interviews (sub study 1) and MaxDiff (sub study 2)

Characteristic	Sub study 1 (n=18)	Sub study 2 (n=156)
Sex, male (%)	16 (89)	147 (94)
Age, mean (s.d.), years	67 (9)	66 (10)
Disease duration, median, years	8.4 (6)	10 (6)
Currently or previously treated by rheumatologist (%)	14 (78)	132 (85)
Current ULT use (%)	None 2 (11) Allopurinol 14 (78) Benzbromarone 0 (0) Febuxostat 2 (11)	None 24 (15) Allopurinol 116 (74) Benzbromarone 9 (6) Febuxostat 6 (4) Allopurinol + benzbromarone 1 (1)
Experience with ULT discontinuation (%)	Yes 4 (22) No 14 (78)	Yes 45 (29) No 106 (68) Don't know 5 (3)

%; percentage, s.d.; standard deviation; ULT: urate lowering therapy

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POS0597-HPR HEALTH LITERACY IN INDIVIDUALS WITH KNEE PAIN - A MIXED METHOD STUDY

Keywords: Pain, Self-management, Osteoarthritis

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Background: Health literacy (HL) is the ability to access, understand, appraise, and apply health information [1]. A low level of HL is associated with worse pain problems, poorer self-care, and an obstacle for health-promoting interventions among individuals with chronic pain and radiographic knee osteoarthritis (rKOA).
Objectives: To examine 1) the level of HL and associations with chronic pain, rKOA, lifestyle habits and health status, and 2) to explore the individuals' experiences of HL.
Methods: The study has a convergent parallel mixed-method design, including 221 individuals with knee pain (148 women, mean age 56±8 years). A purposeful sample of 19 individuals (11 women, 8 men) was selected for interviews. Quantitative data were general HL (GHL) assessed by HLS-EU-Q16, electronic HL (eHL) by eHEALS, pain distribution by a pain figure, rKOA by x-rays, lifestyle habits, and health status via SF-36. GHL and eHL were merged into one variable, "HL", where sufficient HL was defined as having a sufficient level of GHL or eHL. Statistical analyses were Chi^2 test, Mann-Whitney U-test, univariate and multivariate logistic regressions. Qualitative data consisted of individual semi-structured interviews that were analysed using manifest qualitative content analysis with an abductive approach based on the HLS-EU health literacy matrix [2].
Results: Of the 221 participants, 29% reported limited HL. Those with limited HL reported lower education, less usability and importance of the internet for accessing health information and making informed health-related decisions, and lower general health (GH) compared to the group with sufficient HL (data not shown). Higher education, CRP, a healthier diet, and minor alcohol consumption were associated with sufficient HL (Table 1). Only higher education and GH remained associated when adding GH to the multivariate analysis. Individuals' experiences of HL were described as 1) Searching for information influences the decision-making process by being an active searcher or passive receiver; 2) Processing of information influences the decision-making process by having light, moderate or high processing of the information; and 3) Taking a stand on the information influences the decision-making process based on trust and/or motivation (Figure 1).
Conclusion: Limited HL was found in one-third of the individuals with knee pain. CRP and healthy lifestyle habits were associated with sufficient HL, but higher education and health status had the strongest association. The search, level of process and standpoint on the health information influenced the decision on action. More research on HL is needed to gain knowledge of how to develop health promotion to prevent worsening pain problems in individuals with knee pain.

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Table 1. Two models with multivariate logistic regression analysis of associations with sufficient HL.

		Sufficient health literacy			
		Model 1		Model 2	
	n	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age	221	0.99 (0.95-1.04)	0.778	0.99 (0.95-1.04)	0.749
Education	221	1	0.002	1	<0.001
Compulsory school		4.39 (1.75–10.99)	0.001	4.85 (1.90-12.40)	<0.001
Secondary		4.65 (1.83–11.84)		5.41 (2.06-14.22)	
University					
Pain distribution	220	1	0.022	1	0.213
CWP		2.81 (1.16–6.80)	0.269	1.85 (0.70–4.87)	0.875
CRP		1.81 (0.63–5.15)		0.91 (0.27–3.02)	
NCP					
rKOA	216	1	0.371	1	0.417
Yes		1.37 (0.69–2.74)		1.35 (0.66–2.76)	
No					
Diet	221	1	0.035	1	0.091
Less healthy diet		2.53 (1.07–5.98)		2.14 (0.89–5.15)	
Healthy diet					
Alcohol intake	219	1	0.131	1	0.263
≥5 units/week		1.94 (0.82–4.59)	0.049	1.66 (0.68–4.05)	0.058
1-4 units/week		2.51 (1.00–6.29)		2.48 (0.97–6.34)	
<1 unit/week					
General health *(scoring 0–100, worst-best)*	216			1.02 (1.00–1.04)	0.019

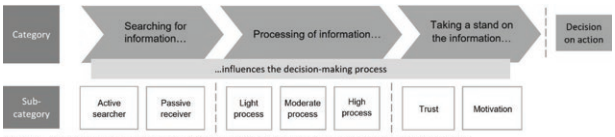


Figure 1. Overview of the results exploring the experiences of HL in individuals with knee pain.

Figure 1. Overview of the results exploring the experiences of HL in individuals with knee pain.

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POS0598-HPR WHAT DO USERS OF RHEUMATOID ARTHRITIS ONLINE FORUMS TALK ABOUT? APPLYING A DEEP LEARNING APPROACH TO UNCOVER COMMON THEMES

Keywords: Rheumatoid arthritis, Artificial intelligence, Descriptive Studies

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Background: Social media platforms have become a vital resource for individuals seeking information and support regarding health issues, including rheumatoid arthritis (RA). As such, the content generated on these platforms represents a valuable source of data for gaining insight into patients' perspectives on RA. However, previous research in this area has primarily relied on qualitative analyses of small sample sizes, limiting the ability to extract meaningful insights from social media content related to RA. With the advancement of machine learning techniques, it is now possible to analyze and extract insights from large volumes of social media posts related to RA.
Objectives: The purpose of this study was to identify the most common topics discussed in a large dataset of submissions about RA on Reddit, one of the world's largest online forums.
Methods: The data for this study was collected from the two largest Reddit forums ("subreddits") dedicated to RA, r/rheumatoid arthritis and r/rheumatoid, which have 18.9k and 7.6k members respectively. We retrieved all submissions but excluded responses in our analyses. All deleted or duplicate submissions and those with fewer than 10 words were removed, retaining 11,094 submissions from over 5,000 users for the analysis. To identify common themes, we applied topic modeling, a technique in natural language processing that identifies underlying themes or topics in a collection of documents. We used the Bertopic Python package (Grootendorst, 2022), which employs deep learning techniques to perform the topic modeling.
Results: The data indicates a significant increase in submissions to the two subreddits, rising from 113 in 2014 to 2892 in 2021 and 1928 in the first 8 months of 2022. Upon analysis, 65 topics were identified, with 4162 submissions (37.5%) remaining unclassified. A topic specifically dedicated to requests to participate in surveys was removed as it did not pertain to the experiences of forum users. Among the remaining topics, the top 10 accounted for 44.90% of all submissions. To better understand each topic, a sample of 10 submissions with the highest probability for that topic were examined (Table 1).

Table 1. Top 10 most frequent topics

Topic	n of submissions	Share of total*
Side effects of methotrexate	526	8.02%
COVID & vaccines	462	7.04%
Mental health	438	6.68%
RF and anti CCP test results	331	5.04%
RA of friends, partners, and close relatives	262	3.99%
Complaints about rheumatologist	212	3.23%
Questions about Humira	188	2.87%
Questions about prednisone	182	2.77%
Diets and RA	175	2.67%
Early symptoms of possible RA	170	2.59%
Exercise and RA	168	2.56%

* After excluding unclassified topics

Three of the ten topics pertained to specific medications - methotrexate, Humira, and prednisone, accounting for 12.71% of the total. The most prevalent topic, at 8.02%, focused on the side effects of methotrexate, with many submissions inquiring about symptoms such as nausea. The second most common topic, at 7.04%, primarily revolved around COVID-19 and related issues, with some

pre-COVID vaccine discussions also included. In 2021, COVID-related discussions were the most prevalent topic. The third most frequent topic (6.68% of total), dealt with mental health and the emotional struggles faced by those living with RA.

Conclusion: The surge in submissions on Reddit demonstrates its growing popularity as an online forum for discussing topics related to RA. Utilizing deep learning-based topic modeling has proven to be an effective method for extracting meaningful topics from the questions and experiences shared by users. The vast amount of data generated by Reddit, in combination with advanced machine learning techniques, enables both an overview of the various topics discussed and a detailed examination of specific topics. This makes the use of social media data a valuable source of insight into the concerns of RA platform users.

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Disclosure of Interests: None Declared.

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POS0599-HPR QUALITY OF REPORTING OF HARMS IN CLINICAL TRIALS ON EXERCISE THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS OR AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW

Keywords: Safety, Inflammatory arthritides, Systematic review

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Background: Exercise therapy has proven effective for people with rheumatic and musculoskeletal diseases (RMDs), including those with inflammatory arthritis such as rheumatoid arthritis (RA) or axial spondyloarthritis (axSpA) [1-2]. Exercise therapy is generally considered safe for people with RMDs, although the evidence is scarce. A few reviews reported on the nature and risk of harms of exercise therapy in RMDs, but none of them specifically addressed the quality of reporting of harms of exercise therapy in studies including people with inflammatory arthritis.

Objectives: This study aimed to describe the quality of reporting of harms in clinical studies on the effectiveness of exercise therapy in people with RA or axSpA.

Methods: RCTs with at least one treatment arm consisting of supervised exercise therapy in people with RA or axSpA were included. Eight electronic databases were searched up to November 2021. Two researchers independently selected studies for inclusion and extracted data and in case of disagreement a third researcher was consulted. Data extraction included study characteristics and fulfillment of a set of quality aspects derived from the Consolidated Standards of Reporting Trials (CONSORT) Extension for Reporting Harms Outcomes [3], predefined on the basis of consensus among authors (Table 1). Harms outcomes were defined as adverse events reported on individual level irrespective of causality or negative effects on group level (only if explicitly designated as measurement of potential harm). We considered the reporting on harms outcomes of sufficient quality if the authors reported at least 1) the methodology for active surveillance of harms outcomes (item 2a); and 2) the observed number and the nature of harms (items 3b and 3c).

Results: The search yielded 5921 records, of which 64 studies (n= 41 RA, n=23 axSpA; described in 83 papers) were included. Of those studies in RA and axSpA, 34 (83%) and 15 (65%) included any information on harms, with 12 (29%) and 3 (13%) reporting active surveillance and 22 (54%) and 5 (22%) reporting on harms outcomes in the results section, respectively (see Table 1). In total, 10 of the 41 (24%) RA studies and 2 of the 23 (9%) axSpA studies fulfilled the predefined criteria for sufficient quality of reporting.

Conclusion: The quality of reporting on harms outcomes is insufficient in the majority of RCTs on exercise therapy in people with RA or axSpA, with overall poorer quality in studies on axSpA which impedes substantiated conclusions about harms of exercise therapy. Our findings stress the need for consensus on the definition, classification, assessment and reporting of harms outcomes in trials on the effects of exercise therapy.

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Table 1. Quality of reporting of harms in in RA and axSpA; 9 Items based on CONSORT Extension for Reporting Harms Outcomes [3]

	RA (N=41) N (%)	axSpA (N=23) N (%)
Any information on harms (1 and/or 2 and/or 3 and/or 4)	34 (83)	15 (65)
Studies meeting sufficient quality of reporting of harms (2a & 3b & 3c)	10 (24)	2 (9)
1. Harms-related information in title, abstract or introduction section(s) (1-2)	25 (68)	9 (39)
2. Harms-related information in methods section (3-5)	16 (39)	4 (17)
a Data collection on harms on the basis of active surveillance (4)	12 (29)	3 (13)
3. Harms-related information in results section (6-8)	28 (68)	9 (39)
a Withdrawals due to AEs or health-related reasons (6)	22 (54)	9 (39)
b Number of participants with AEs and number of AEs (7)	15 (37)	6 (26)
c Nature of observed harms (8)	22 (54)	5 (22)
d Details on observed AEs: severity, timing and/or duration (8)	8 (20)	2 (9)
e The results section reports on what the method section promises (8)	6 (15)	1 (4)
4. Harms-related information in discussion section (10)	23 (56)	8 (35)

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POS0600-HPR WHAT TRADE-OFFS ARE ACCEPTABLE TO RHEUMATOID ARTHRITIS PATIENTS DURING TREATMENT SELECTION?

Keywords: Rheumatoid arthritis, Disease-modifying drugs (DMARDs)

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Background: The rheumatoid arthritis (RA) treatment landscape is diverse, with multiple therapies available that differ in several attributes such as mode of administration and benefit-risk profile. Patients and prescribers face challenging trade-offs during treatment selection to accommodate patients' circumstances in order to ensure comprehensive disease management. EULAR recommendations for RA management emphasize the need to recognize patient preferences in shared decision-making (SDM). Therefore, it is essential to understand how preferences differ in the RA patient population.

Objectives: This study elicited trade-offs that RA patients were willing to make during treatment selection while accounting for preference heterogeneity.

Methods: An online discrete choice experiment (DCE) was conducted from September to October 2021 in which RA patients were required to elicit their preferences for attributes of treatments for RA (Figure 1) and make trade-offs between them. Attributes were selected and defined based on literature review and

qualitative patient interviews, and were then tested in a quantitative pilot. Main data collection consisted of an online survey in which participants were asked to repeatedly choose between hypothetical treatments. Eligible patients were ≥18 years old, diagnosed with RA, currently received systemic disease-modifying anti-rheumatic drug therapy for RA, and were residents of France, Germany, Italy, Spain, United Kingdom, or United States. Male patients were oversampled to support subgroup analysis of preferences for effects on sperm parameters. Data were analyzed using a correlated mixed logit model and differences in preferences between sex and age were explored. Relative attribute importance (RAI) scores and maximum acceptable risk (MAR) measures were derived from the estimates.

Results: A total of 2,090 patients participated; 42% were female with predefined oversampling of male patients, with a mean age of 45.2 years (range 18–83). Estimated effects were significant for all attributes (p<0.001), implying that they all influenced treatment choices and suggesting preferences differed between participants. Average RAI scores revealed different priorities (p<0.001) between males and females (Figure 1). While reducing pain and negative effect on semen parameters was most important to male patients, female patients were most concerned by risk of blood clots and serious infections. The remaining attributes were of lower importance but were still relevant. However, no single attribute explained treatment preferences by more than 30%. Preferences were also affected by patients' age: patients aged 18-44 years placed less importance on frequency and mode of treatment administration (p<0.05) than older age groups. Patients were willing to make benefit-risk trade-offs; they accepted extra risks of blood clots (male: 1.8%; female: 0.8%), serious infections (male: 2.5%; female: 1.0%), or negative effects on sperm (male: 7.4%) for an oral pill every day instead of injection once a week. They also accepted extra risks of blood clots (male: 2.3%; female: 1.2%), serious infections (male: 3.2%; female: 1.6%), or negative effects on sperm (male: 10.4%) for reducing amount of pain from 30% to 10%. Similar observations were made for improved performance of daily activities. However, acceptable trade-offs varied between patients (p<0.05).

Conclusion: Preferences of RA patients were driven by benefits and risks of RA treatments, with no single attribute dominating the decision making. Patients were willing to accept higher risk of serious infections and blood clots in exchange for improvements in pain, daily activities, or administration convenience. These findings emphasize the importance of considering the entire treatment profile, including benefits, risks, and administration to support SDM between providers and patients.

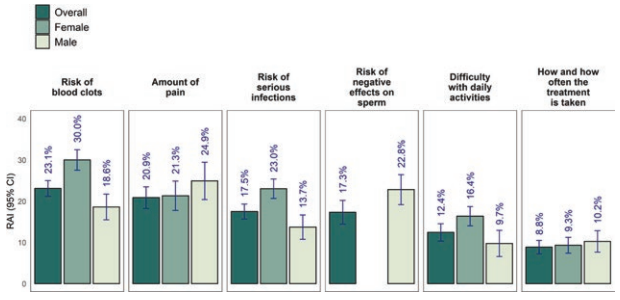


Figure 1. RAI overall and by sex

Preference drivers: males – pain, blood clots; females – blood clots, infections, pain. Sperm risk data are based on male responses only.

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POS0601-HPR DOING EVERYTHING POSSIBLE TO PRIORITIZE WORK: LIVED WORK EXPERIENCE OF YOUNG ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Qualitative research methods, Systemic lupus erythematosus, Work-related issues

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Background: Young adulthood (18-30 years) is a critical life-stage when individuals launch into independence, establishing employment. Failure to establish employment during young adulthood is associated with reduced lifetime socioeconomic achievement. A few studies focused on studying employment outcomes in young adults with systemic lupus erythematosus (YASLE) showed less full-time work than general population, substantial absenteeism and productivity loss. Studying the lived work experience of YASLE can broaden our understanding in this area from the patients' perspectives.

Objectives: To describe the early work experiences of YASLE and explore their perceptions of SLE influences on their work.

Methods: This was a qualitative descriptive study. Young adults with childhood- or adult onset SLE were recruited from 2 adult rheumatology clinics (Oct 2021-Aug 2022) in Manitoba and Ontario. Inclusion criteria: YASLE who were employed, unemployed (looking for work or not), or work disabled. Potential participants were purposely sampled for diversity in: sex/gender, age of onset, major organ disease, occupation groups. All completed a pre-interview questionnaire to provide demographic, SLE and work-related information. Semi-structured interviews were conducted individually via video conference, focusing on their work experiences, future aspirations and perceived SLE influences. Interviews were audio-recorded, transcribed verbatim and analyzed using a reflexive thematic analysis.

Results: Of 18 participants, 13 identified as females, 1 as non-binary; median age 25 (22- 29, 25-75th percentile) years. Participants' identified ethnicities: 7/18 Asian, 5/18 White, 2/18 Indigenous, 4/18 other. 7/18 were childhood-onset SLE, 9/18 had major organ disease. 12/18 were employed full-time, 3/18 unemployed/ looking for work, 3/18 unemployed/ not looking to work. 6/18 worked in managerial/ professional jobs. Three have current work accommodations, 2/3 for SLE. 13/18 report highest education to be university/ postgraduate. Most participants perceived themselves to be functioning relatively well at work despite modest physical, cognitive limitations. Two main themes emerged:

1) "Getting by, with some help" describes many factors that participants cited as critical in helping them stay in the workforce. Most of the factors mapped to the underlying construct of control over their work. Participants who have the flexibility to manage their time, physical positions and environment perceived fewer issues staying in work Participants also reported increasing recognition (over time) of the importance of medication adherence in disease control, which helped them to stay in work. Other frequently cited facilitators also included sedentary jobs and the availability of social support.
2) "Tough choices: work or health over everything else" describes how participants struggled to find a balance between their health, work and social life. Many described multiple strategies to prioritize work while trying to preserve their health: rest more, avoid commute, avoid stress, help or transfer responsibility for chores, limiting social activities. A few however deemed the costs of work to be too great and chose to prioritize their health by avoiding work altogether.

Conclusion: Most YASLE report being employed and setting a high priority on work. They recognized the importance of their health in helping them to work. They diverted considerable energy/ resources from other aspects of life to maintain work. This begs

the question of whether this approach could be sustainable beyond this life stage. However, this work on YASLE patients also identified multiple potential targets of interventions to help them continue working. By focusing on young adulthood, this will ensure that our strategies will be most appropriate for their life-stage, maximizing impacts.

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POS0602-HPR MORE ACTIVITY LIMITATIONS AND LOWER QUALITY OF LIFE IN PERSONS WITH SYSTEMIC SCLEROSIS WITH THREE OR MORE SYMPTOMS THAN IN THOSE WITH TWO SYMPTOMS

Keywords: Patient reported outcomes, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is an inflammatory rheumatic disease affecting skin and internal organs (1). Little is known about how many symptoms persons with SSc (pwSSc) report ever and currently and how they impact activities and quality of life (QoL).

Objectives: To investigate what symptoms pwSSc report as most troublesome ever and currently and how the number of current symptoms affect activities and QoL.

Methods: In an SSc study at Karolinska University Hospital data were collected using open ended questions of what symptoms pwSSc considered most troublesome ever and currently. The self-reported answers were analyzed using qualitative analysis and categorized with an inductive approach. Participants answered Scleroderma Health Assessment Questionnaire, SHAQ, with the symptom severity Visual Analogue Scales, VAS, and Quality of Life, QoL, measured with EuroQoL, EQ VAS. Analysis was done to investigate what categories/symptoms pwSSc reported most troublesome ever and currently and if the number of symptoms currently present impact activities and QoL. Differences in reported symptoms ever and currently were analyzed with non-parametric tests when investigating differences between participants with 0-2 and ≥3 reported symptoms currently.

Results: A total of 291 pwSSc, median age 60 yrs, 83% women, participated. 254 (87.3%) pwSSc reported symptoms ever and 260 (89.3%) symptoms currently. 38,5% of the participants had three or more symptoms currently present. These pwSSc also perceived more activity limitation (p=0.006) and less QoL (p=0.023) than those with fewer symptoms. The median score of SHAQ (activity limitation) was 0,0 (0-3) and EQ VAS (QoL) was 62 (0-100) in the whole group. Among pwSSc with 0-2 symptoms currently the score of SHAQ was 0.38 and EQ VAS was 70 and in those with ≥3 symptoms the median score of SHAQ was 0,63 and EQ VAS was 70, p=0.006 and p=0.023.

Conclusion: PwSSc and ≥3 self-reported symptoms have a higher disease severity, more activity limitations and a lower QoL than persons with fewer symptoms. Health professionals need to focus resources on pwSSc with more reported symptoms to lessen activity limitations and improve QoL in pwSSc.

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Table 1. Self-reported symptoms ever and currently, EQ VAS, SHAQ and SHAQ VAS.

Symptoms	Ever n=254		Current n=260					p-value*
Musculoskeletal	74.8%		69.6%					ns
Circulatory	46.1%		29.6%					<0.001
Pain	36.6%		35.0%					ns
Fatigue	27.2%		28.1%					ns
Lungs	22.9%		15.8%					<0.002
Skin	22.8%		14.6%					<0.001
Gastrointestinal	22.0%		18.1%					ns
Number of symptoms currently	**EQ VAS, median, n=18**	**SHAQ, median score, n=29**	**SHAQ VAS**					
0-2 symptoms	70	0.38	**dyspnea, median score, n=20**	**global, median score, n=19**	**gastro-intestinal, median score, n=26**	**Raynaud, median score, n=20**	**pain, median score, n=30**	**digital ulcers, median score, n=15**
≥3 symptoms	60	0.63	7	20	9	38	16	1
p-value#	0.023	0.006	24	43	27	55	40	5
			0.001	<0.001	0.019	0.022	<0.001	0.016

*= Wilcoxon, EQ= EuroQoL, VAS=Visual Analogue Scale, SHAQ=Scleroderma Health Assessment Questionnaire, #=Mann-Whitney U

Systemic sclerosis, myositis and related syndromes - aetiology, pathogenesis and animal models

POS0603

AUTOANTIBODIES AGAINST A SUBUNIT OF MITOCHONDRIAL RESPIRATORY CHAIN COMPLEX I IN INCLUSION BODY MYOSITIS

Keywords: Autoantibodies, Myositis

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Background: Autoantibodies are found in up to 80% of patients with idiopathic inflammatory myopathies (IIM) and are associated with distinct clinical phenotypes [1]. Autoantibodies targeting cytosolic 5´-nucleotidase 1A (anti-cN1A) are currently the only known serum biomarker for the subgroup inclusion body myositis (IBM) (2), although detected even in other autoimmune diseases.
Objectives: To identify new autoimmune targets in IIM by antigen bead array assay.
Methods: In a first cross-sectional exploratory study, 357 antigens representing 268 proteins were incubated with plasma samples from 219 IIM (108 Polymyositis (PM), 80 Dermatomyositis (DM) and 31 IBM) patients, 349 Systemic Lupus Erythematosus (SLE) patients and 306 population controls for screening of IgG reactivity by antigen bead array. All samples were identified in the local biobank of the Rheumatology clinic, Karolinska University Hospital. Interesting results obtained for the IBM subgroup were then validated in an independent larger cohort of 287 patients with IBM followed at nine European rheumatological or neurological centers. IBM serum samples were explored by antigen bead array and results validated by western blot. As controls, serum samples from 30 patients with PM and 30 with DM, HLA-matched with the IBM Swedish cohort, were included. Demographics, laboratory, clinical, and muscle biopsy data of the IBM cohort was retrieved.
Results: In the exploratory study IgG reactivity towards NADH dehydrogenase 1 α subcomplex 11 (NDUFA11), a subunit of the membrane-bound mitochondrial respiratory chain complex I, was discovered with higher frequency in the IBM (9,7%) than PM (2,8%) and DM samples (2,5%), although the difference was not statistically significant. Anti-NDUFA11 IgG was also found in 2,3% of SLE and 2,6% of population control samples. In the validation study anti-NDUFA11 autoantibodies were detected in 11/287 IBM patients (3,8%), 0/30 PM and 0/30 DM patients. Reactivity against NDUFA11 could be confirmed by western blot (Table 1, Figure 1). The eleven anti-NDUFA11 positive patients showed a trend of lower frequency of wheelchair/walker ever use and higher creatine kinase levels at time of IBM diagnosis compared to the anti-NDUFA11 negative group. Ragged red fibers were significantly more prevalent in anti-NDUFA11 positive than negative patients (p=0.04). Anti-cN1A autoantibodies were detected in 98/287 (34,1%) of IBM, 3/30 (10%) DM and 9/29 (31%) PM patients, p=0.03. Coexistence of anti NDUFA11 and anti-cN1A antibodies was observed in 3 IBM patients.
Conclusion: Our results reveal a new autoimmune target in the mitochondrial respiratory chain complex I that might be specifically associated with IBM. This is of particular interest as mitochondrial abnormalities are known histological findings in muscle biopsies of IBM patients.

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Table 1. NDUFA11 protein fragments (PrESTs)

NDUFA11	Amino acid sequence (excluding His6ABP)	PrEST molecular weight (Da) (including His6ABP)
PrEST 1	ASLVKMGRLEGWEVFAKPKV	19833,4
PrEST 2	MAPKVFRQYWDIPDGTDCHRKAYST	20574,06
PrEST 3	TLNPPGTFLEGVAKVGQYTFT	19828,23

Legend: Amino acid sequence and molecular weight of the protein fragments loaded on the western blot gel. NDUFA11, NADH dehydrogenase 1 α subcomplex 11; His6ABP, six histidine and albumin binding protein.

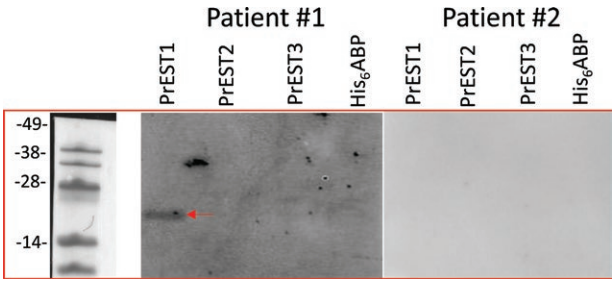


Figure 1. Validation of bead array assay results with western blot

Legend: Western blot showing the reactivity of two IBM patients against the NDUFA11 protein fragments (PrEST1,2,3) expressed with a His6ABP tag. Patient#1 was reactive to PrEST1 and not to PrEST2 and 3 in the bead array assay while patient#2 did not display any reactivity. NDUFA11, NADH dehydrogenase 1 α subcomplex 11; His6ABP, six histidine and albumin binding protein.
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POS0604

ACTIVATION OF TYPE I INTERFERON PATHWAY IN SERA OF PATIENTS WITH ANTI-MELANOMA DIFFERENTIATION-ASSOCIATED GENE 5 ANTIBODY-POSITIVE DERMATOMYOSITIS

Keywords: Myositis, Cytokines and chemokines

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Background: We have previously reported that anti-melanoma differentiation-associated gene 5 (MDA5) antibodies are more frequently associated with rapidly progressive ILD (RP-ILD) and amyopathic dermatomyositis (DM) than anti-aminoacyl-tRNA synthetase (ARS) antibodies and that serum ferritin levels are higher in anti-MDA5-positive patients and serve as a relevant biomarker for RP-ILD [1]. Thus, it is speculated that anti-MDA5 DM and anti-ARS idiopathic inflammatory myopathies (IIMs) have distinct pathomechanisms. It was reported that type I interferon (IFN) gene signature was upregulated in the peripheral blood mononuclear cells and the skin tissues from the anti-MDA5 DM patients [2]. However, the role of type I IFN in anti-MDA5 DM has yet to be fully elucidated.
Objectives: We aimed to determine the activity of IFN-α/β and IFN regulatory factor (IRF) in sera of patients with anti-MDA5 antibody-positive DM with ILD,

compare them to those of patients with anti-ARS antibody-positive polymyositis (PM) and DM with ILD, and investigate their association with clinical features.
Methods: Serum samples were collected from clinically active adult patients with anti-MDA5 antibody-positive DM (MDA5, *n* = 22), and anti-ARS antibody-positive PM and DM (ARS, *n* = 21) as well as healthy controls (HCs, *n* = 32). PM/DM were classified according to the 2017 EULAR/ACR classification criteria for IIMs. Only patients with ILD diagnosed on high-resolution computed tomography findings and HCs were included. Patients complicated by infection or malignancy were excluded. The reporter cell lines (purchased from InvivoGen) which secrete embryonic alkaline phosphatase (SEAP) in response to IFN-α/β and those secrete luciferase and SEAP in response to activation of IRFs and nuclear factor kappa B (NF-κB), respectively, were incubated with 20% (v/v) serum samples. The levels of SEAP and luciferase in supernatants were measured using a multi-mode microplate reader and their association with clinical features was statistically analyzed. IFNAR2-knockout reporter cells were also used.
Results: The sera of MDA5 patients demonstrated significantly higher IFN-α/β and IRF activities than those of ARS patients and HCs ($p < 0.001$ in all the comparisons), whereas no significant difference was detected in the NF-κB activities (Figure 1). The assays using IFNAR2-knockout reporter cells showed no significant difference in IRF or NF-κB activities. The serum ferritin levels in MDA5 patients were significantly higher than those in ARS patients (mean 679.7 ng/mL vs. 321.3 ng/mL, $p = 0.03$). The IFN-α/β and IRF activities induced by the MDA5 patients sera were correlated with the serum ferritin levels ($r = 0.53$ and 0.54, respectively), whereas they did not significantly correlate with the serum KL-6 levels, percent-predicted forced vital capacity (%FVC), or percent-predicted diffusing capacity of the lung for carbon monoxide (%DLCO).
Conclusion: IFN-α/β and IRF activities and their association with ferritin were demonstrated in sera of anti-MDA5-positive DM patients with ILD but not in those of anti-ARS-positive PM/DM patients with ILD. The present study suggests that activation of type I interferon pathway may be involved in the pathomechanisms of anti-MDA5 DM with ILD.
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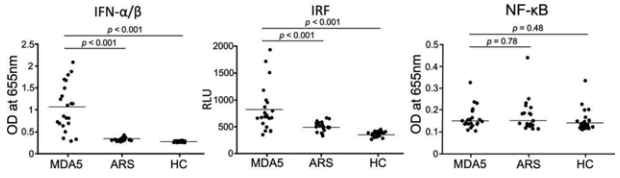


Figure 1. IFN-α/β, IRF and NF-κB activities measured using reporter cell lines in serum of anti-MDA5 and anti-ARS positive IIM patients. *P*-values were determined by Tukey-Kramer multiple comparisons test. Horizontal bars represent mean values.

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POS0606 DETECTION OF HISRS SPECIFIC AUTOREACTIVE CD4+ T CELLS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Keywords: Cell biology, Adaptive immunity, Myositis

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Background: Idiopathic inflammatory myopathies (IIM) or myositis are a group of chronic autoimmune disorders represented by lesions in muscle, skin, joints and lung. One of the most common autoantibodies with a prevalence of 25-35 % is anti-Jo1, targeting histidyl-transfer RNA synthetase (HisRS). Importance of T-cells in disease is established by their presence at sites of inflammation such as the muscle. We have shown that upon stimulation of PBMC with HisRS, $CD4^+$T-cells are activated and produce inflammatory cytokines. Genetic association of HLA-DRB1*03:01 further implicates the recognition of autoantigens by $CD4^+$T-cells. However, the presence of antigen specific $CD4^+$T-cells has not yet been shown in patients with IIM.
Objectives: The aim of this project is to identify HisRS $CD4^+$T-cells using HLA Class-II tetramers (Tmr) and single T cell receptor (TCR) sequencing.
Methods: HLA-DRB1*03:01 monomers with selected HisRS- and tetanus peptides as controls were produced in E.coli. The peptides were covalently linked to the HLA b-chain via a flexible peptide linker. HLA-tetramers were assembled using a commercial APC or PE labeled streptavidin. The efficacy of Tmrs was validated upon stimulation of PBMCs from HLA-matched healthy controls with tetanus peptide. In parallel, upregulation of T cell activation markers such as PD-1, CD69, CD137 was also investigated. Next, we stimulated PBMCs from anti-Jo1 positive patients with IIM that were HLA-DRB1*03 (n=10) with both tetanus and HisRS peptides and cultured the cells for 6 days followed by tetramer staining. Fluorospot was performed for the detection of IFNg and IL2 secreting cells and culture supernatants were collected for cytokine analysis using cytokine bead arrays. Summary of the workflow is presented in Figure 1.
Results: We detected HisRS+$CD4^+$T cells from 5 out of 10 patients using tetramers upon stimulation with HisRS peptide. We detected increased IFNg levels in the supernatants where Tmr+ cells were detected further supporting the activation of T cells. HisRS$^+CD4^+$T cells from patients (n=5) were single cell sorted and TCR a/b chains were sequenced (n=538). A bioinformatics pipeline for the alignment and assembly of the TCR sequences, was developed and the clonality analysis revealed presence of expanded T cell clones in 4 out of 5 patients. Expanded T cells had high mean fluorescent intensity values (MFI) for HisRS tetramers, suggesting the responsiveness of autoreactive T-cells to HisRS.
Conclusion: IIM are rare, chronic autoimmune disorders with no available cure. Previous studies indicate the importance of T cells in this disease. However, the phenotype and role of these cells in the disease pathogenesis has not been fully established. Our results indicate the presence of HisRS+$CD4^+$T-cells in IIM which will introduce the possibility of new targeted treatment approaches.

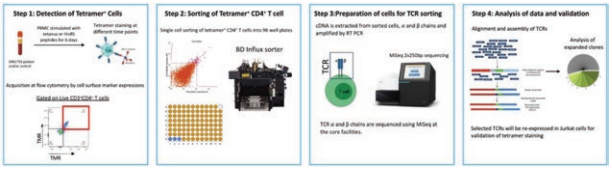


Figure 1. Summary of experimental setup starting from the stimulation of PBMCs and tetramer staining (Step 1), sorting of tetramer+ cells (Step 2), preparation of cells for TCR sequencing (Step 3) and analysis of TCRs (Step 4).

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POS0607 BREPOCITINIB PREVENTS TYPE-I INTERFERON INDUCED DAMAGE IN CULTURED MYOCYTES AND ENDOTHELIAL CELLS INDICATING A POTENTIAL ROLE IN THE TREATMENT OF DERMATOMYOSITIS

Keywords: Myositis, Targeted synthetic drugs, Cytokines and chemokines

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Background: Dermatomyositis (DM), an idiopathic inflammatory myopathy, is a chronic and often debilitating condition characterized by a hallmark skin rash (e.g., Gottron's sign and heliotrope rash) with perifascicular atrophy and subsequent muscle weakness [1]. The pathogenesis of DM involves dysregulation of Type I interferon (IFN-I) signalling and other cytokines (IFN-γ, IL-12, and IL-23). The kinases, TYK2 and JAK1, are essential for the signalling pathway of these cytokines. Brepocitinib, a selective and potent dual TYK2/JAK1 inhibitor is in development for the treatment of DM and is expected to reduce signalling of these cytokines, particularly IFN-I, and ameliorate the symptoms of disease.
Objectives: To evaluate the efficacy of brepocitinib in preventing IFN-I induced pathological changes characteristic of DM in human skeletal muscle and microvascular endothelial cells in vitro.
Methods: Human skeletal muscle myoblasts were cultured and differentiated into myotubes then treated with vehicle control or IFN-I (recombinant Human IFN

alpha A and Human IFN alpha D) to induce cellular damage. Myotubes were also preincubated for 1 hour with brepocitinib (1 μM or 130 nM, the latter is equivalent to the average free plasma concentration after administration of 30 mg once-daily) prior to IFN-I treatment. Immunofluorescence staining followed by image analysis to determine myosin 4 surface area were conducted after 48 hours of IFN-I treatment. Human dermal microvascular endothelial cells (HMEC-1) were cultured and, once vascular networks were established, cells were treated with IFN-I or vehicle control. Cells were also preincubated for 1 hour with brepocitinib as described above. Under light microscopy 9 hours after treatment, the number of nodes, master segment length, and total mesh area were analyzed. To determine statistical significance, one-way ANOVA followed by Tukey's multiple comparison post-hoc analyses were performed.

Results: Myosin surface area was reduced by ~40%, relative to vehicle treated control, in myotubes exposed to IFN-I ($p<0.0001$). This cytokine induced damage was almost completely prevented by brepocitinib preincubation (both 130 nM and 1 μM) with mean myosin surface areas of 96% and 100% of the vehicle control, respectively. The differences between IFN-I treatment alone and brepocitinib were significant ($p<0.0001$ [1 μM] and $P<0.001$ [130 nM]). Similarly, HMEC-1 exposure to IFN-I significantly reduced the mean number of nodes, mean master segment length, and mean total mesh area by 47 to 50% relative to vehicle control ($p<0.0001$ nodes and segments, $p<0.001$ mesh area). With brepocitinib preincubation, this damage was prevented with the mean number of nodes, master segment lengths, and total mesh area ranging from 89 to 111% of vehicle control. These differences were statistically different from the IFN-I treatment at both brepocitinib concentrations and all endpoints ($p<0.001$ for all conditions).

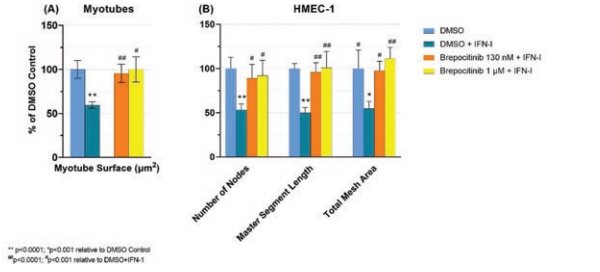
Conclusion: One of the most debilitating aspects of DM is muscle weakness resulting from perifascicular atrophy leading to significant impacts on quality of life for these patients[2]. We report here the ability of brepocitinib to prevent IFN-I induced damage in both myocytes and microvasculature in culture at clinically relevant concentrations, providing further pharmacologic rationale for brepocitinib in the treatment of DM.

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Figure 1.
(A) Brepocitinib Effects on IFN-I Induced Myotube Damage and (B) Brepocitinib Effects on IFN-I Induced Endothelial Cell Damage



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POS0608 TARGETING THE JAK/STAT PATHWAY IN MYOSITIS INHIBITS B CELL PROLIFERATION, DIFFERENTIATION AND ANTIBODY PRODUCTION

Keywords: Autoantibodies, Adaptive immunity, Myositis

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Background: Idiopathic inflammatory myopathies (IIM) or myositis are characterized as inflammatory, autoimmune disorders with a wide spectrum of symptoms and affected tissues. The presence of circulating autoantibodies and B-lineage cells in affected tissues, point towards an essential role of B cells in the pathogenesis of IIM. This sparked interest in the B cell depleting anti-CD20 antibody rituximab as a new treatment opportunity in IIM. However, despite its beneficial effects, rituximab results in long-term B cell depletion and does not target CD20-negative, long-lived plasma cells, which may maintain the autoimmune response. Hence, further research aimed at more specific and reversible therapies targeting B and plasma cells is warranted. The Janus kinase (JAK)-signal transducer and activator of transcription (STAT) signalling pathway is essential for several aspects of B cell biology, making it an attractive novel target for patients with IIM.

Objectives: To study whether targeting the JAK-STAT signalling pathway using tofacitinib, a small molecule inhibitor specific for JAK1/JAK3, impairs essential functions of B cells isolated from patients with IIM.

Methods: B lineage cell phenotyping was performed by flow cytometry, using PBMCs obtained from 3 IIM phenotypes (dermatomyositis, overlap-myositis, anti-synthetase syndrome) and healthy donors (HD). Functional assays were performed culturing PBMCs in the presence of tofacitinib, and the stimuli IL-21/anti-CD40 or IL-2/CpG to activate JAK/STAT signalling in a T cell-independent or T cell-dependent manner, respectively. After a 6-day culture, the effects of tofacitinib on B cell proliferation, differentiation, and antibody production were assessed by flow cytometry and ELISA.

Results: Peripheral blood B cell composition from patients with IIM showed reduced fractions of memory B cells, and an increase in transitional and naive B cells in comparison to HD reference values. Targeting JAK/STAT signalling using tofacitinib significantly reduced IL-21/anti-CD40 induced B cell proliferation, plasmablast differentiation and antibody production in B cells of patients with IIM and HD. However, this effect was observed to a lesser extent upon stimulation with IL-2/CpG. Interestingly, tofacitinib exerted its effects irrespective of the IIM phenotype.

Conclusion: Our data demonstrate that the composition of the peripheral B cell compartment in IIM patients is altered. Furthermore, tofacitinib treatment *in vitro* results in the inhibition of functional B cell responses, including proliferation, plasmablast differentiation, and antibody production, which was irrespective of the clinical phenotype. Consequently, targeting of JAK/STAT signalling may represent a novel treatment modality in myositis.

REFERENCES: NIL.

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Disclosure of Interests: None Declared.

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POS0609 EXPANDED CYTOTOXIC CD8+ T CELL CLONES CHARACTERIZE THE BLOOD OF INCLUSION BODY MYOSITIS PATIENTS

Keywords: Myositis, -Omics, Rare/orphan diseases

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Background: Inclusion body myositis (IBM) is an inflammatory myopathy, characterized by CD8+ T cell infiltration of muscle and patients present with progressive muscle weakness and atrophy, leading to disability due to no FDA-approved therapies. Patients with IBM have been noted to frequently exhibit aberrant expansion of circulating CD8+ T cells, even satisfying classification criteria for T cell large granular lymphocytic leukemia (T-LGL) in >50% of cases, in one study[1]. However, high-resolution profiling of the transcriptome and TCR repertoire in IBM are lacking.

Objectives: To evaluate the TCR repertoire of circulatory CD8+ T cells, allowing us to simultaneously define the transcriptomes of expanded and non-expanded clonotypes in blood of IBM patients and healthy age-matched blood donors.

Methods: 13 IBM patients and 9 age-matched healthy controls were sorted for either non-naïve CD8+ T cells and/or CD8+CD57+ T cells by flow cytometry. Single-cell RNA and TCR sequencing was performed to profile the whole gene expression, coupled with paired TCRa and TCRb chains, at single-cell resolution. Additional markers during flow cytometry allowed for further identification of aberrant populations in IBM compared to age-matched healthy controls.

Results: Our results found IBM CD8+ T cell were highly expanded compared to age-matched healthy controls. These CD8+ T cells were identified in both the broad non-naïve T cell population, as well as the specific CD8+ CD57+ T cell subset. Enrichment of T-LGL leukemia genes, in addition to CD8+ effector function, cytotoxicity and inflammatory chemokines and cytokines were found in expanded clonotypes, with a higher gene expression found in hyperexpanded clones compared to minimally expanded clonotypes. Absence of common TCR clonotypes between patients in IBM was found, a pattern also seen in T-LGL

leukemia. GSEA analysis also confirmed a downregulation of cell apoptosis processes in hyperexpanded clonotypes, a feature of T-LGL leukemia clones.
Conclusion: Significant clonal expansion of CD8+ T cells in the blood was found in our IBM cohort compared to our age-matched healthy controls. Additionally, these hyperexpanded clonotypes have various T-LGL leukemia gene markers, in addition to elevated cytotoxic and T cell activation genes in comparison to their minimally expanded counterparts. These results highlight how the blood compartment of IBM, a progressive muscle disease, is important in IBM and how future studies and therapies should be targeting these aberrant blood CD8+ T cell clones.

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Disclosure of Interests: None Declared.
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POS0610 NEW INSIGHTS IN HISTOPATHOLOGICAL CHARACTERIZATION AND PATHOPHYSIOLOGICAL MECHANISMS OF KU-POSITIVE MYOSITIS

Keywords: Undifferentiated connective tissue disease, Autoantibodies, Myositis

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Background: Ku-antibodies are one of the myositis-associated antibodies linked with muscle involvement in many connective tissue diseases. The histopathological pattern of Ku$^+$ myositis is described diversely with inflammatory and necrotic aspects, however, a detailed morphological characterization of Ku$^+$ myositis is still missing.
Objectives: The aim of the study was to analyze histopathological and transcriptional aspects of patients with Ku$^+$ myositis to gain new insights in possible pathophysiological mechanisms.
Methods: 23 biopsy samples from patients with clinical and morphological signs of myositis and positive Ku-antibodies were studied by histopathology, immunohistochemistry, and quantitative polymerase chain reaction (qPCR) and compared with biopsies derived from non-disease controls (NDCs) and immune-mediated necrotizing myopathy (IMNM) at the Department of Neuropathology of Charité university hospital Berlin.
Results: Mean patient's age was 55 years, 91% were women and the most common rheumatological diagnosis was overlap with systemic sclerosis (30%), followed by isolated myositis (26%) and overlap with primary sjögren's syndrome or rheumatoid arthritis (13% respectively). Creatine kinase elevation was present in 91% of the patients. Histopathologically, we noticed a broad phenotype spectrum with mild to severe myositis with predominantly MHC class I overexpression and milder MHC class II overexpression. 87% of the biopsies showed necrosis combined with inflammatory aspects of variable degree. Infiltrates were mainly CD68$^+$ cells (average of 213 cells per 10 high power fields (HPF)), followed by CD3$^+$ cells (76 cells/10 HPF), whereas CD20$^+$ or CD138$^+$ cells were rare (8 respectively 14 cells/10 HPF). Furthermore, we detected small vacuoles in 59% and large areas of p62$^+$ aggregates in 62% of the biopsies. Similarly, aggregates of LC3 and myotilin were found in 60% and 76% respectively. Immunofluorescence staining showed co-localization of p62 and myotilin indicating protein aggregates and induction of autophagy pathways. *P62* gene expression was neither elevated in Ku$^+$ patients nor in IMNM patients compared to NDC (*Figure 1A*). *SIGLEC1* gene expression was significantly elevated in Ku$^+$ patients compared to IMNM patients and NDC (*Figure 1B*).
Conclusion: In this study, we defined a histopathological pattern of Ku$^+$ myositis with predominant MHC class I expression, necrosis, small vacuoles and inflammation as well as peculiar p62$^+$ and LC3$^+$ aggregation in severely inflammatory biopsy samples. Whilst there definitely is a broad spectrum of presentation, MHC class I expression, necrosis and p62/LC3$^+$ aggregates seem to be the defining aspects of the histopathological presentation.

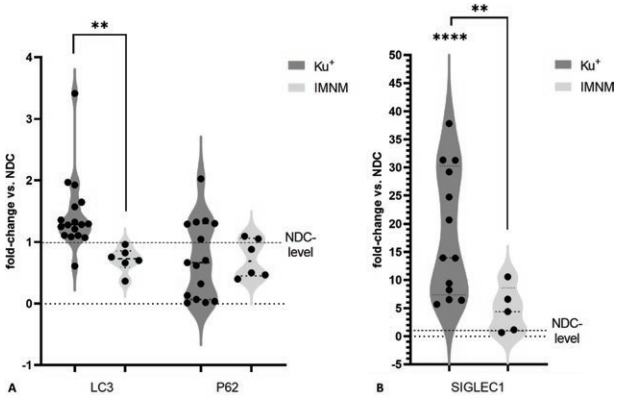


Figure 1. Transcriptional analysis of *LC3*, *P62* and *SIGLEC1* Quantitative polymerase chain reaction was used to analyze the gene expression of *LC3*, *P62* and *SIGLEC1*. Violin plots display fold-change versus non disease controls (NDC), calculated by [2^-(ΔCT Ku$^+$ patients/immune-mediated necrotizing myositis (IMNM) -ΔCT NDC)].
A *LC3* gene levels are elevated in Ku$^+$ patients compared to IMNM (p=0.0015), whilst *P62* levels do not differ from NDC.
B *SIGLEC1* gene expression is significantly elevated in Ku$^+$ patients compared to IMNM patients (p=0.0026) and NDC (p<0.0001).

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POS0611 SHARED MONOCYTE CYTOKINE SIGNATURE INDUCED BY SERUM FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTI-MDA5 ANTIBODY-POSITIVE DERMATOMYOSITIS THROUGH TYPE I INTERFERON PATHWAY

Keywords: Systemic lupus erythematosus, Cytokines and chemokines, Myositis

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Background: Type I interferon (IFN) plays a pivotal role in the pathogenesis of systemic lupus erythematosus (SLE) and dermatomyositis (DM)/polymyositis (PM) as typically evidenced by upregulation of type I IFN-stimulated genes (ISGs) in peripheral immune cells [1]. In addition, a distinct monocyte cytokine signature, which was induced by plasma from pediatric SLE patients and abrogated by Janus kinase (JAK) inhibition, was reported [2]. However, contribution of serum factors to expression of ISGs was not fully elucidated.
Objectives: To investigate the cytokine induction profile in multiple myeloid lineages by serum from patients with SLE or DM/PM using the whole blood stimulation system and identify the signaling pathway relavant to the monocyte cytokine signature.
Methods: Serum was collected from newly diagnosed, untreated, and clinically active adult patients with SLE (SLE group), anti-MDA5 antibody-positive DM (MDA5 group), and anti-aminoacyl-tRNA synthetase (ARS)

antibody-positive DM/PM (ARS group), and healthy controls (HCs) (n = 10 for each group). Heparinized whole blood from healthy donors was incubated with control serum (10 v/v%), patient serum (10 v/v%), or IFN-β in the presence of protein transport inhibitor cocktail for 6 hours. Red blood cells were lysed, and then leucocytes were fixed at a single step. Intracellular staining was performed and expression of 11 cytokines in $CD14^+$ monocytes, $CD1c^+$ dendritic cells (DCs), and $CD123^+$ DCs were analyzed using flow cytometry. A cut-off level was determined by 2% positivity of each cytokine in unstimulated condition. For transcriptomic analyses, sorted $CD14^+$ monocytes from healthy donors were incubated with serum (SLE, MDA5, ARS, or HCs), or IFN-β (n = 3 for each group) for 4 hours, and bulk RNA-sequencing was performed using the Illumina NextSeq 500 platform. RNA-seq raw sequence reads analysis and pathway analysis were performed using the Strand NGS software. To evaluate significance of JAK-signal transducer and activator of transcription (STAT) pathway, whole blood from healthy donors was pre-incubated with upadacitinib, a JAK1 inhibitor, stimulated with patient serum for 6 hours, and analyzed for cytokine expression as described above.

Results: Serum from SLE and MDA5 groups induced significantly higher monocyte chemoattractant protein-1 (MCP1) and interleukin-1 receptor antagonist (IL-1RA) expression in $CD14^+$monocytes than serum from HCs (Figure 1). These monocyte cytokine signatures were closely resembled that induced by IFN-β stimulation. Serum from ARS group did not induce any significant cytokine expression in $CD14^+$ monocytes. No significant cytokine expression was observed in $CD1c^+$ DCs or $CD123^+$ DCs. RNA-seq demonstrated that 612 and 462 genes were upregulated (fold change >2 relative to control) following stimulation with serum from SLE and MDA5 groups, respectively. In these upregulated genes, 383 genes were commonly upregulated across SLE and MDA5 groups and IFN-β. Pathway analysis revealed similar transcriptional profiles in SLE and MDA5 groups: upregulated genes were most frequently involved in IFN-αβ signaling pathway including multiple ISGs and STAT1/2. Upadacitinib significantly abrogated the monocyte cytokine signature, and MCP1 and IL-1RA expression induced by serum from SLE and MDA5 groups in a dose-dependent manner (p < 0.001 in all analyses).

Conclusion: These results suggest that serum factors in patients with active SLE and anti-MDA5 antibody-positive DM can induce shared monocyte cytokine signature through type I IFN pathway. $CD14^+$ monocytes 'primed' by serum might contribute to the pathogenesis of these diseases.

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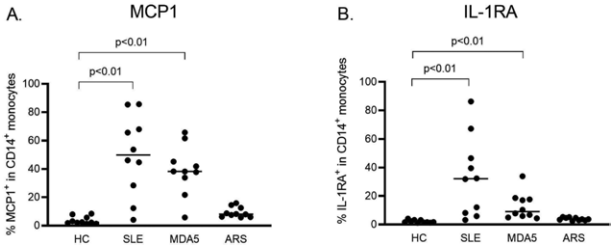


Figure 1. MCP1 (A) and IL-1RA (B) expression in $CD14^+$ monocytes induced by serum from SLE and anti-MDA5 antibody-positive DM. Horizontal bars represent median values. P-values were calculated using Kruskal-Wallis test followed by Dunn's multiple comparisons test.

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POS0612 GENE ANALYSIS REVEALED THE USEFULNESS OF TRIPLE THERAPY WITH BARICITINIB, RITUXIMAB AND TACROLIMS FOR ANTI-MDA5 ANTIBODY POSITIVE DERMATOMYOSITIS (MDA5-DM)

Keywords: Myositis

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Background: Anti-MDA5 antibody positive dermatomyositis (MDA5-DM) is characterized by high mortality due to rapid progressive ILD. MDA5 is a cytosolic protein and a family of RIG-I like receptor, which functions as a virus RNA sensor and induces the production of such as type-1 IFN. Although little is known about the pathogenesis of MDA5-DM, it is notable that the similarities were reported between COVID-19 infection and MDA5-DM. It may suggest that there is a common underlying autoinflammatory mechanism. We reported that in MDA5-DM, (1) RIG-I-like receptor signaling is enhanced and (2) antiviral responses such as type 1 IFN signaling are also enhanced as compare with anti-ARS-antibody positive DM, and (3) the key for survival is suppression of RIG-I-like and IFN signaling (EULAR2022, POS0390). We also found that a significant role for uncontrolled macrophage in the pathogenesis of ILD by our autopsy case. Recently, it has been reported that tacrolimus (TAC) and cyclophosphamide (CY) combination therapy (TC-Tx) has improved the prognosis of cases with early onset of the disease, but there are cases that cannot be saved. Therefore, we devised BRT therapy (BRT-Tx). The Tx combines baricitinib (BAR), which inhibits GM-CSF and IFN-mediated signaling and effectively suppresses uncontrolled macrophages, with rituximab (RTX) and TAC, which rapidly inhibits B and T cell interaction and ultimately prevents anti-MDA5 antibody production.

Objectives: To determine the differences in gene expression between BRT and TC-Tx for MDA5-DM in peripheral blood.

Methods: Total of 6 MDA5-DM (TC: 3, BRT: 3) were included and all of them had multiple poor prognostic factors. Peripheral whole blood was collected at just before and 2-3 months after the treatment. RNA was extracted, and quantified using a next-generation sequencer. Differentially Expressed Genes (DEGs) were identified by pre vs. post treatment. Gene Ontology (GO), clustering and Gene Set Variation Analysis (GSVA) were performed to DEGs. As one BRT case was added since our last year's report, we also reanalyzed the surviving vs. fatal cases. The IFN signature was scored separately for Types 1, 2, and 3, and the changes between pre- and post-treatment were investigated.

Results: Two of three cases with TC died during treatment, while all three cases on BRT recovered. The cluster analysis of the DEGs separated deaths from survivors, not by type of treatment. Comparing surviving and dead cases, GO analysis revealed that the immune system via immunoglobulins and B cells was significantly suppressed in surviving cases. GO analysis of DEGs in each therapeutic group showed that expression of B cell-related genes such as lymphocyte proliferation and B cell receptor signaling pathway were significantly suppressed in BRT-Tx. On the other hand, TC-Tx significantly suppressed such pathways as cell proliferation and cell surface receptor signaling, and was less specific for the target cells than BRT-Tx. The changes in IFN signature score after treatment showed an increase in type 2 and 3 IFN scores in all fatal cases and an increase in type 1 IFN score in one fatal case.

Conclusion: BRT-Tx significantly suppressed gene expression associated with B cells, while TC-Tx was characterized by low specificity of therapeutic targets and suppression of total cell proliferation. Comparison of surviving and dead cases revealed that the combination of RTX contributed to the success of treatment, as suppression of the immune system mediated by immunoglobulins and B cells is the key for survival. Analysis of the IFN signature revealed an increase in IFN score after treatment in fatal cases, indicating that the combination of BAR is beneficial. The superiority of BRT-Tx seems clear from the fact that all patients survived with BRT-Tx while only one/three patients survived with TC-Tx.

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POS0613 THE ROLE OF MICROBIOTA IN DIFFERENT DISEASE STAGES OF SYSTEMIC SCLEROSIS: A POSSIBLE IMPACT IN GASTROINTESTINAL TRACT DISEASE ACTIVITY?

Keywords: Gastrointestinal tract, Biomarkers, Systemic sclerosis

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Background: Gastrointestinal tract (GIT) is affected in approximately 90% of systemic sclerosis (SSc) patients from the earliest disease stages. Microbiota has recently emerged as an important environmental factor in SSc pathogenesis.
Objectives: to test differences in the taxa composition of the fecal microbiota of very early SSc (VEDOSS) and established SSc patients.
Methods: Twenty-nine SSc patients classified according to the ACR/EULAR 2013 criteria (27 female, mean ± SD disease duration 13.1±9.2 years) and 21 VEDOSS patients (19 female, mean± SD disease duration 6.4±5.2 years) were consecutively enrolled. For each patient, demographic, clinical and laboratoristic data were recorded and stool samples were collected. GI involvement and quality of life were investigated with UCLA-Gastrointestinal Tract Questionnaire (GIT)2.0 and Short Form Health Survey-36 (SF36). Microbiota was assessed through 16S rRNA Next Generation Gene-Sequencing analysis.
Results: We found a different fecal microbiota profile between SSc and VEDOSS. In particular, classes of *Bacilli* and *Choriobacteria*, orders of *Desulfovibrionales* and *Lactobacillales,* the family of *Eggerthellaceae*, the genera *Enterococcus, Lactobacillus*, *Streptococcus*, *Sutterella* and *Uncultured-Rhodospirillales* were statistically significant increased in SSc, while the class of *Clostridia*, the family of *Oscillospiraceae* and the order *UCG-002* were statistically significant increased in VEDOSS (Figure 1).

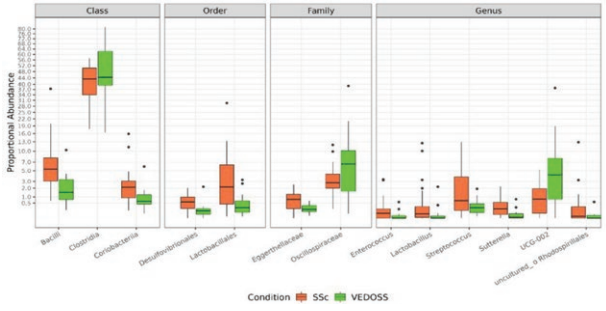


Figure 1. Boxplot showing the results of taxa-level differential abundance analysis between SSC and VEDOSS patients in fecal samples. Plot titles report the shrinked Log2 fold change (according to the DESeq2 function lfcShrink). All results have a p-value < 0.05.

VEDOSS patients had significantly higher SF-36-physical component score than SSc, a trend for higher SF-36-mental component summary (MCS), while no difference in the UCLA-GIT2.0 score (Table 1).

Table 1. SF 36 and UCLA GIT 2.0 score in VEDOSS and SSc patients

	VEDOSS (M ± DS)	SSc (M ± DS)	p-value
SF-36-physical component summary	47,8 ± 8,3	40,7 ± 8,3	<0,01
SF-36-mental component summary	46,3 ± 9,2	40,4 ±11,6	0,06
UCLA-GIT 2.0	0,3 ± 0,3	0,4 ± 0,4	NS

In SSc patients, we observed a significant positive association between the genus *Uncultured-Rhodospirillates* and MCS, and between both genera *Lactobacillus* and *Uncultured-Rhodospirillates* and UCLA-GIT 2.0 score. In VEDOSS we found a significant positive correlation between both *Bacilli* class and *Lactobacillus* genus and MCS.
Conclusion: Our data show, for the first time, a different microbiota composition in SSc and VEDOSS patients. In particular, we observed an increased abundance of genus *Lactobacillus* in SSc patients. However, no significant differences in the UCLA GIT score between the two groups were observed, confirming that GI symptoms also affect VEDOSS patients. Both these findings could suggest that the increased *Lactobacillus* values in SSc patients should raise the suspicion of more severe GIT involvement. This may account for the poor result of a lactobacillus-based probiotic treatment, usually observed in literature. It is necessary to confirm these data on larger groups of patients in the two phases of the disease.
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POS0614 INTERLEUKIN-17 MEDIATED INFLAMMATORY AND PRO-FIBROTIC ACTIVITY OF SKIN FIBROBLASTS DERIVED FROM SYSTEMIC SCLEROSIS PATIENTS (SSC) COMPARED WITH HEALTHY CONTROLS (HC)

Keywords: Cytokines and chemokines, Innate immunity, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is an autoimmune connective tissue disease defined by fibrosis of skin an internal organs as well as vascular impairment. Furthermore, in addition to the fibrosis several autoimmune features of SSc often show a phenotype of auto-inflammation. As recently published T-cell proliferation and, in particular, T helper 17 (Th17) cells with their cytokine interleukin-17 seem to play an important role in the pathogenesis of the fibro-inflammatory environment of the tissue in SSc.
Objectives: Here we investigated cultures of skin fibroblasts derived from SSc and healthy controls (HC) to evaluate the different expression of pro-inflammatory and pro-fibrotic proteins and cytokines (defined as biomarkers) after stimulation of interleukin-17 (IL-17) and tumor growth factor-beta (TGF-β), measured by concentrations in the cellular supernatant.
Methods: The current study was approved by the Ethics Committee at the Saarland University, all participants of the study gave their written informed consent for their participation in the study. SSc patients (n = 8, aged 43 to 65 years) and healthy controls (n = 4, aged 40 to 53 years) underwent a skin biopsy of the lateral abdominal wall. Fibroblasts isolated from the surgical samples were cultured for 5-8 passages according to standard procedures. The cells were stimulated by 25 ng/ml of IL-17 or 2.5 ng/ml of TGF-β for 48 h. The supernatant of the different fibroblast cultures was analysed for the following biomarkers: pro-inflammatory cytokines such as interleukin-1-beta, interleukin-6 (IL-6), interleukin-8 (IL-8), preferentially anti-fibrinolytic and/or pro-fibrotic proteins such as matrix metalloproteinase-1 (MMP-1), monocyte chemotactic protein 1 (MCP-1), procollagen, insulin-like growth factor-binding protein 3 (IGFPB-3), and Lysyloxidase-1 (LOX-1). The concentrations of these biomarkers were analysed applying commercial ELISA standard tests (IL-1β, IL-6, IL-8, MCP-1, MMP-1, procollagen, and IGFBP-3). The differences between SSc and HC (without and after stimulation with IL-17 or TGB-β, respectively) were statistically analysed by t-test (with fisher`s correction).
Results: IL-6, MCP-1 and procollagen secreted by native fibroblasts showed a significant higher concentration in SSc compared to HC in unstimulated conditions. In contrast, the anti-fibrotic efficient protein MMP-1 reached a significant lower concentration in SSc-derived fibroblasts, the significant differences between SSc and HC could also be reproduced after IL-17 stimulation (Table 1), whereas after stimulation with TGF-β the differences between SSc and HC were only significant for IL-6 and MCP-1. The remaining proteins and cytokines which were investigated (IL-1-β, IGFPB-3, LOX-1) do not resulted in significant differences.

Table 1. biomarkers cell culture supernatants of fibroblasts derived from SSc patients and HC

Growth	IL-6		MCP-1		MMP-1		Procollagen	
condition	SSc	HC	SSc	HC	SSc	HC	SSc	HC
Native	**0.22***	**0.03**	**0.37***	**0.12**	**13.53***	**35.96**	**885.3***	**333.0**
+/- SE	0.04	0.01	0.04	0.02	1.36	4.89	32.6	50.9
after IL-17	**3.95***	**1.57**	**6.20***	**2.99**	**77.41****	**162.22**	**957.2****	**323.8**
+/- SE	0.75	0.13	0.71	0.51	8.16	24.74	37.49	41.7
after TGF-β	**0.81**	**0.60**	**0.47**	**0.37**	**9.67***	**17.83**	**875.4****	**525.8**
+/- SE	0.10	1.70	0.06	0.10	2.34	2.13	43.3	50.3

Biomarker concentrations given in ng/ml; significant differences of concentrations between SSc and HC without or after stimulation (with TGF-β or IL-17, respectively) with * p-value p < 0.05 or ** p-value < 0.01

Conclusion: Skin fibroblasts in SSc patients showed significantly stronger pro-inflammatory and pro-fibrotic properties compared with healthy controls as an indication of the fibro-inflammatory character of the disease. Furthermore, the significant increase of the expression of IL-6, MCP-1, procollagen and the decrease of the anti-fibrotic efficient protein MMP-1 after IL-17 stimulation suggests IL-17 as a well promising target in SSc.

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POS0615 CLINICAL PERFORMANCE OF A MULTIPARAMETRIC AUTOANTIBODY PROFILE IN SYSTEMIC SCLEROSIS PATIENTS

Keywords: Biomarkers, Systemic sclerosis, Autoantibodies

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Background: Systemic Sclerosis (SSc) is an autoimmune disease characterized by excessive fibrosis, inflammation and vasculopathy of the skin and internal organs. Interstitial lung disease (ILD) is the most important cause of mortality. Multiple autoantibodies (Abs) against nuclear proteins are present in >95% of patients. Anti-Topoisomerase-I (ATA), anti-CENP-B (ACA) and anti-RNA-polymerase-III (RNAP3) Abs are included in the 2013 SSc ACR/EULAR classification criteria. The detection of additional Abs is of interest to identify seronegative cases or specific clinical phenotypes. The particle-based-multi-analyte technology (PMAT) is a multiplexed system based on antigen covered paramagnetic particles with unique signatures. It allows to simultaneously obtain different autoantibody results.

Objectives: The aim of this study was to evaluate the clinical performance of PMAT-Aptiva in a cohort of SSc patients from Hospital Clínic de Barcelona.

Methods: Study cohort includes serum samples of patients with SSc (n=138), disease controls with other autoimmune diseases (n=205) and healthy blood donors (n=25). Demographic characteristics and clinical manifestations of patients were collected. SSc specific (ATA, ACA or RNAP3) or SSc associated (Ro52, U1-RNP, Ku, Th/To (Rpp25 and Rpp38), Fibrillarin, Pm/Scl, BICD2, MIT3, Mup44, PUF60 (isoforms 1, 2 and 6), RNPC3r, RNPC3 (peptide 1, 2, 3, 4 and 5), RuvBL1/2, SMN1 and TERF1) Abs were tested on Aptiva by PMAT technology (Werfen, San Diego, USA). The prevalence of Abs was measured based on the manufacturer's recommended cut-offs. CTD-Essential has calibrated units (FLU) whereas other novel biomarkers were RUO (MFI). Associations between categorical variables were determined with Fisher's exact test. The relative measure of an effect was expressed as the odds ratio and the 95% CI when considering Ab positivity as the exposure. Results with p values <0.05 were considered statistically significant.

Results: From SSc patients, 109/138 (79.0%) were positive for ACA (n=71; 51.4%), ATA (n=29; 21.0%), RNAP3 (n=7; 5.1%) or double positive ACA-ATA (n=2; 1.4%) Abs, while the remaining 29/138 (21.0%) were negative for these three Abs. Nineteen of the 29 (65.5%) negative patients were also negative for all tested novel biomarkers. In 10/29 (34.6%) either single or multi-positivity was observed for anti-Pm/Scl, U1-RNP, Th/To (Rpp25 and Rpp38), TERF1 and Ro52 Abs. Specificity for all SSc related biomarkers was over 93.0%. MIT3 and Ro52 were the most prevalent non SSc criteria Abs (17.4% and 16.6%, respectively). As expected, ACA, ATA and RNAP3 previously known associations with specific cutaneous phenotype and ATA and RNAP3 with the presence of ILD were confirmed (Table 1). Interestingly, Rpp38 and RuvBL1 were more frequently found in patients with ILD. Additionally, PUF60 isoform 6 was associated with the presence of diffuse cutaneous phenotype whereas TERF1 was more prevalent in patients with diastolic dysfunction. We did not find association between any of the Abs studied and neoplasia, cardiac arrhythmias or conduction disturbances, pericarditis or myocardial damage, myositis, pulmonary hypertension or esophageal motility disorders.

Conclusion: In our SSc cohort, PMAT-Aptiva showed a proper specificity and represents a suitable option for patients' evaluation. Confirmation of promising clinical associations for novel markers PUF60 (isoform 1 and 6), FHL1, RuvBL1 and TERF1 in larger SSc cohorts is warranted.

Table 1. Significant associations (odds ratio) between clinical manifestations and markers.

		SSc specific biomarkers			SSc associated biomarkers								
	n	ACA	ATA	RNAP3	Ro52	U1-RNP	Rpp38	FHL1	MIT3	PUF60	PUF60	RuvBL1	TERF1
		73	31	7	23	10	3	4	24	10	7	3	2
Cutaneous phenotype													
Diffuse SSc	25		8.4	6.5					0.15		20		
Limited SSc	65				0.29								
Sine scleroderma	37	3.1	0.21		2.9					4.4			
Clinical manifestations													
ILD	50	0.07	6.6	27.7			10.9		0.28			10.9	
Severe ILD	12	0.03	5.8	9.9									
Raynaud phenomenon	126						0.03		0.14				
Telangiectasias	86							0.06					
Digital ulcers	30	0.41		10.2							5.2		
Diastolic dysfunction	30												14.9
Calcinosis	27			29.7									
Arthritis	4					15.4							
Scleroderma Renal Crisis	2		14.2										

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POS0616 THE CHARACTERISTICS OF PROGRESSIVE FIBROSING INTERSTITIAL LUNG DISEASE IN CONNECTIVE TISSUE DISEASES WITH SINGLE-CELL RNA SEQUENCING OF BRONCHOALVEOLAR LAVAGE FLUID

Keywords: -Omics, Comorbidities, Lungs

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Background: Connective tissue disease-associated interstitial lung disease (CTD-ILD) is a severe complication of rheumatic and musculoskeletal diseases, e.g. rheumatoid arthritis (RA), dermatomyositis (DM), systemic sclerosis (SSc) and so on. CTD-ILD is a heterogeneous syndrome driven by different diseases and cell types. This complexity provides a challenging field for elucidating the mechanism of the disease. Although some patients with CTD-ILD develop progressive fibrosing interstitial lung disease (PF-ILD) like as other ILD despite immunosuppressive treatment, it is difficult to predict which patients develop PF-ILD before treatment.

Objectives: The objective of this study is to find characteristics of immune cells and predictive biomarkers of PF-ILD in CTD-ILD patients.

Methods: We collected BALF and blood from 30 CTD-ILD and 12 idiopathic interstitial pneumonia (IIP) patients before treatment. Twelve out of 42 patients fulfilled PF-ILD criteria[1] in 1 year period. PF-ILD patients included 3 RA, 2 DM, 2 Sjögren syndrome, 1 ANCA-associated vasculitis, and 4 IIP patients. We applied Seq-Well, a portable platform of single-cell RNA sequencing[2], to analyze gene expressions in immune cells in BALF and blood. We compared the distribution of immune cells and differential gene expressions in BALF and blood between PF-ILD patients and patients without PF-ILD in CTD-ILD and IIP patients.

Results: We found that alveolar macrophages are the most abundant cell types in BALF of PF-ILD patients. We further classified alveolar macrophages and neutrophils into more detailed subsets based on their gene expression patterns and compared them between PF-ILD and patients without PF-ILD. In PF-ILD patients, we found increased $CXCL10^+$, $CXCL8^+$ alveolar macrophages and complement activation associated genes were upregulated in BALF. Moreover, we found increased interferon-induced proteins with tetratricopeptide repeats $(IFIT)^+$, $MMP\text{-}9^+$ and immature neutrophils, which were reported to be associated with severe COVID-19 pneumonia[3], in the blood of PF-ILD patients. Differentially expressed gene analysis revealed high levels of high mobility group box (HMGB)-2, IL-1β, and complement activation associated genes in alveolar macrophages in PF-ILD patients.

Conclusion: Alveolar macrophage phenotypes were changed in BALF while neutrophil phenotypes were changed in the blood of PF-ILD in CTD-ILD and IIP patients, which are consistent with the characteristics of severe COVID-19 pneumonia patients, suggesting common pathological pathways of lung fibrosis. We propose the hypothesis that alveolar macrophage phenotypic changes lead to complement and cytokine/chemokine mediated neutrophil activation and progression of PF-ILD (Figure 1). These cell subpopulations and up-regulated genes would be potential biomarkers or therapeutic target of PF-ILD in CTD-ILD patients.

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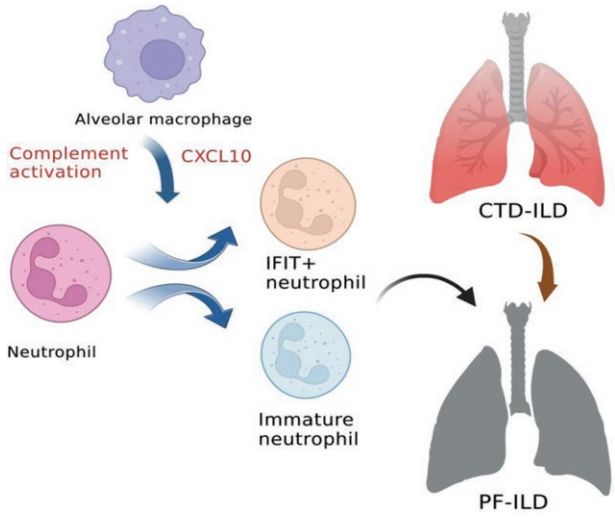


Figure 1.

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POS0617 THE GASOTRANSMITTER HYDROGEN SULFIDE PROTECTS AGAINST CALCIFIC TENDINOPATHY VIA INHIBITION OF LYSYL OXIDASES

Keywords: Cell biology, Animal models

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Background: Pathological calcification ((PC), *i.e.* the deposition of calcium-containing crystals) in tendons is a hallmark of calcific tendinopathy (CT), a disease associated with pain, tendon rupture, and disability. Currently, only symptomatic treatments exist for CT and none of them target specifically calcification. Intriguingly, the gasotransmitter H_2S has recently emerged as a potential anti-calcifying molecule [1].

Objectives: To establish in CT the potential anti-calcifying effect of hydrogen sulfide (H_2S) and of the H_2S-producing enzyme cystathionine gamma lyase (CSE), and the underlying mechanisms involved.

Methods: Wild type (WT) and CSE knock-out (KO) tenocytes were isolated from adult mice Achilles' tendons. Tenocyte were cultured in αMEM + 10% FBS + 50µg/ml ascorbic acid (Control medium) in presence of 10% calciprotein particles (calcification medium, CM). Spontaneous Achilles' tendon CT in old mice (35 weeks old) and surgery-induced Achilles' tendon CT in8-12 weeks old mice were quantified by micro computed tomography. Dynamic Young's modulus was measured in 35 weeks old mice as previously described [2]. Immunohistochemistry was performed on human and murine tendon sections with anti-CSE and anti-LOX and anti-LOXL2rabbit polyclonal antibodies. LOX expression was analyzed by qPCR and by Western-blot. LOX(L) activity was quantified in cells supernatants and lysates.

Results: *In vitro*, tenocyte calcification (in CM) was inhibited by exogenous H_2S-donors, while it was exacerbated in CSE KO tenocytes, producing as expected less H_2S than WT. Reduced calcification in tenocytes exposed to H_2S was accompanied by decreased expression of genes coding for BMP2, BMP4 and decreased activation of the BMP signaling pathway (pSMAD1/5/8).

Accordingly, BMPs expression and BMPs-pathway activation were exacerbated in CSE KO tenocytes compared to WT tenocytes. The protective role of CSE-H_2S was confirmed *in vivo.* Indeed, in aged mice, micro computed tomography revealed exacerbated Achilles' tendon calcification in CSE KO mice compared to WT. Interestingly, CSE deficiency led to reduced biomechanical strength, as the dynamic Young's modulus was significantly decreased upon increased tendon displacement. Furthermore, using a tenotomy model of CT, we found an inverse correlation between CSE expression and calcification in tendons. This was confirmed in human tendons from CT patients, which exhibited decreased CSE expression where calcification was present. In parallel experiments, we found that calcification in tenocytes was significantly reduced by addition of BAPN, a pan-inhibitor of lysyl oxidases (LOX(L)) enzymes. LOX(L) family includes 5 enzymes LOX and LOX1-4, catalysing elastin and collagen cross-links. We next investigated if the anti-calcfiying effect of H_2S in CT could be mediated by inhibition of LOX(L). Indeed, in CM-stimulated tenocytes we found that H_2S impacts both LOX/LOX2 expression (as CSE deficiency increased significantly LOX/LOX2 gene expression) and LOX(L) activity (as CSE deficiency increased LOX(L) activity and conversely H_2S dose-dependently inhibited LOX(L) activity in WT tenocytes. Finally, *in vivo* we discovered that, CSE was inversely correlated with calcification and LOX and LOXL2 expression in mouse and human tendons.
Conclusion: Altogether, our results suggest that increasing H_2S levels in tenocytes could represent a future strategy to prevent or decrease calcification in CT, likely via down-modulation of LOX(L) expression and activity.
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POS0618 QUANTITATIVE RADIOMIC RISK SCORE STRATIFIES RESPONSE TO ANTI-FIBROTIC TREATMENT IN A PRECLINICAL LUNG FIBROSIS MODEL

Keywords: Imaging, Lungs, Animal models

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Background: Anti-fibrotic drugs aim at slowing disease progression in patients with fibrosing interstitial lung disease (ILD). Currently, only repeated pulmonary function tests and/or serial chest high resolution computed tomography (HRCT) scans spanning long periods can identify treatment responders. Imaging omics data («radiomics») from HRCT scans, which integrate pathophysiological information of the whole lung, may provide a powerful tool not only for prediction of disease progression as shown previously, but also for timely stratification of treatment response on an individual base[1].
Objectives: To explore the potential of HRCT-based radiomics for stratification of treatment response to an established anti-fibrotic drug in a preclinical model of fibrosing ILD.
Methods: Fibrosing ILD was induced in mice by intratracheal instillation of 2 U/kg bleomycin on day 0. Treatment with (a) the (non)receptor tyrosine kinase inhibitor nintedanib at 60 mg/kg q.d. (n=10) or (b) vehicle-only (n=13) q.d. was administered by gavage from day 7 to 21. Lung pre- and post-treatment MicroCT scans were acquired at 35 µm resolution from each mouse. Lung tissue was collected post-mortem on day 21. Radiomic features (n=1'386) were calculated from semi-automatically defined 3D lung volumes using the in-house developed software Z-Rad. Calculation of our composite quantitative radiomic risk score (qRISSc), developed for risk stratification of systemic sclerosis patients with ILD, was performed as previously described[1]. Changes between pre- and post-treatment conditions (=delta qRISSc) were used to stratify treatment response. Ashcroft scoring was used to evaluate severity of fibrosis. Markers of fibrosis and inflammation, as well as drug-associated targets, were assessed by gene expression profiling and immunostainings. Lung proteome profiles were acquired by mass spectrometry in data-independent acquisition mode using a nanoLC-MS/MS workflow. Analysis of differentially expressed proteins and pathway enrichment were performed using R packages «limma» and «clusterProfiler», respectively.
Results: Post-treatment, non-omics readouts showed that response to treatment was heterogeneous with varied inter-individual responses. Yet, time-resolved radiomics analysis, capturing the individual pre- and post-treatment disease status, reliably allowed the detection of treatment response. A delta qRISSc threshold was established to distinguish responders from non-responders. Immunostainings of corresponding tissue revealed reduced infiltrates of αSMA+ myofibroblasts and F4/80+ macrophages in responders. In addition, transcriptional levels of fibrotic (*Col1a1*, *Col3a1*, *Fn1*), inflammatory (*Ccl2*, *Il6*), and nintedanib-associated (*Tgfb1*, *Timp1*, *Cxcl1*) targets were lower in these samples. Differential protein expression analysis demonstrated that proteins downregulated in responders were enriched in pathways related to fibrosing ILD pathophysiology (Figure 1A). To identify a molecular basis of delta qRISSc, we performed correlation analysis to the proteome profiles of all samples, including controls. Thereby, qRISSc increase (=non-response) strongly correlated with activation of pathways related to fibrosis and nintedanib mode of action (Figure 1B). These results indicate that radiomic signature changes reflect drug response on a molecular level.

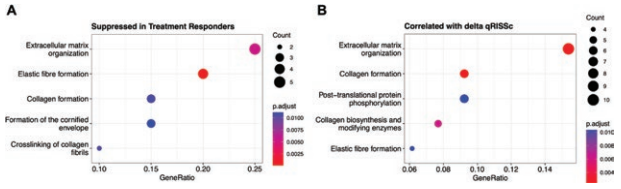


Figure 1. Reactome pathway enrichment analysis. (**A**) Differentially expressed proteins downregulated in treatment responders ($log_2FC<-0.3$, $p<0.05$). (**B**) Proteins correlated with delta qRISSc (Spearman's $\rho>0.5$, $p<0.05$).

Conclusion: Upon clinical validation, HRCT-based radiomics may provide a powerful tool for early distinction of patients benefiting from anti-fibrotic therapy and thus serve as a foundation for a more individualized and improved patient management.
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Disclosure of Interests: David Lauer Shareholder of: Roche, Employee of: Roche (until 2020), Hubert Gabrys: None declared, Malgorzata Maciukiewicz: None declared, Matthias Brunner: None declared, Thomas Frauenfelder: None declared, Stephanie Tanadini-Lang: None declared, Manfred Heller: None declared, Anne-Christine Uldry: None declared, Kerstin Klein: None declared, Oliver Distler Speakers bureau: Bayer, Boehringer Ingelheim, Janssen, Medscape, Consultant of: 4P-Pharma, Abbvie, Acceleron, Alcimed, Altavant Siences, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos, Glenmark, Horizon, Inventiva, Kymera, Lupin, Miltenyi Biotec, Mitsubishi Tanabe, MSD, Novartis, Prometheus, Redxpharna, Roivant, Sanofi, Topadur, Grant/research support from: Kymera, Mitsubishi Tanabe, Boehringer Ingelheim, Janine Schniering: None declared, Britta Maurer Speakers bureau: Boehringer-Ingelheim, GSK, Novartis. Congress support from Medtalk, Pfizer, Roche, Actelion, Mepha, MSD, Consultant of: Novartis, Boehringer Ingelheim, Janssen-Cilag, GSK, Grant/research support from: AbbVie, Protagen, Novartis Biomedical.
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POS0619 HIGH SERUM CXCL10 PREDICTS NEW ONSET OF SYSTEMIC SCLEROSIS-INTERSTITIAL LUNG DISEASE

Keywords: Biomarkers, Lungs, Cytokines and chemokines

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Background: Systemic sclerosis-interstitial lung disease (SSc-ILD) is a severe complication that affects most SSc patients causing one-third of SSc-related

deaths [1]. There is an unmet need for predictive biomarkers of ILD to identify patients at risk, prior to clinical manifestation. Activated IFN-induced chemokines and proteins are implicated in the early inflammatory phase of SSc-ILD [2]. CXCL10 is an IFN-induced chemokine that is important in the chemoattraction of inflammatory cells in SSc-affected tissue [3,4].

Objectives: We investigated CXCL10 serum levels in SSc, SSc-ILD, and healthy controls (HCs) to understand whether CXCL10 levels differ between groups and potentially play a role in ILD pathogenesis. We also sought whether CXCL10 levels in serum mirror those in the lungs to investigate whether systemic levels reflect those of the affected organ locally. The transcriptomic study investigated CXCL10 expression in inflammatory SSc-ILD lung sections compared to fibrotic sections to show whether CXCL10 is more prominent in early disease. We also assessed whether CXCL10 could serve as a predictive biomarker for the new onset of SSc-ILD. Finally, to better comprehend the clinical observations, *in vitro* studies aimed to reveal the inflammatory/fibrotic effects of local and systemic fluids of SSc-ILD patients compared to SSc without ILD and controls.

Methods: One-hundred sixty-five SSc patients (SSc-ILD = 41) and 13 age- and sex- matched HCs were retrospectively followed from 2013 to 2020. Furthermore, 15 SSc patients (SSc-ILD = 7) were prospectively recruited for bronchoalveolar lavage (BAL) procedure. CXCL10 mRNA and protein levels were measured on various levels (serum, BAL, and SSc-ILD lung tissues) by ELISA and nanoString transcriptomic assay. Spearman's correlations were performed between CXCL10 levels in serum and lungs. Kaplan-Meier analyses were performed to evaluate predictability of SSc-ILD using CXCL10 levels at baseline. Human primary lung fibroblasts were treated with BAL fluid or serum from SSc without ILD or SSc-ILD patients. After stimulation, inflammatory (IL-6 and CXCL10)/fibrotic (α-SMA and TGF-β) genes were assessed using qPCR.

Results: At baseline, serum CXCL10 was significantly higher in SSc-ILD patients compared to SSc without ILD [Median (IQR): 126 (66-282) vs 79 (50-122), p = 0.004] and HCs [Median (IQR): vs. 4 (4-9), p < 0.0001]. BAL fluid CXCL10 levels in SSc-ILD patients were not significantly higher than those in SSc without ILD [Median (IQR): 457 (42-725) vs 134 (72-333), p = 0.2). However, BAL CXCL10 levels significantly correlated with serum levels (r = 0.7, p = 0.007). The nanoString showed that CXCL10 gene expression is significantly higher in inflammatory lung tissue compared to fibrotic tissue (fold change = 2.3, p = 0.029). Kaplan-Meier survival analysis (Figure 1) revealed that CXCL10 levels >3rd quartile at baseline in SSc patients significantly predicted new onset of ILD (p = 0.023). The *in vitro* studies showed that CXCL10 and IL-6 were significantly overexpressed in lung fibroblasts treated with SSc-ILD BAL fluid or serum compared to SSc without ILD [(CXCL10: p = 0.0043; p = 0.0087), (IL-6: p = 0.0022; p = 0.0043), respectively) and controls (all: p = 0.0022). On the contrary, TGF-β and α-SMA expression did not change after treatment in all groups.

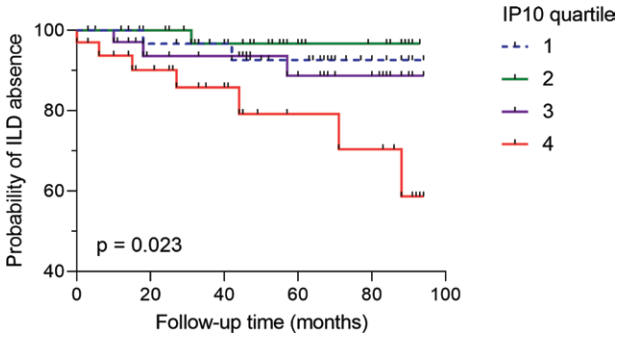


Figure 1. Kaplan-Meier survival curve according to baseline CXCL10 levels quartiles.

Conclusion: CXCL10 is a potential predictive biomarker for new onset of ILD in SSc patients. Further longitudinal studies with larger sample sizes are needed to verify the capability of CXCL10 to predict ILD. Additionally, our nanoString and *in vitro* data suggest that CXCL10 may play a significant role in the early development of SSc-ILD which might be amenable to therapeutic interventions.

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Disclosure of Interests: Yehya Al-Adwi: None declared, Isabella M. Atzeni: None declared, Berber Doornbos- van der Meer: None declared, Marcel Van der Leij: None declared, Bart-Jan Kroesen: None declared, Alja J. Stel: None declared, Harry van Goor: None declared, Tji-Joong Gan: None declared, Wim Timens: None declared, Johanna Westra: None declared, Douwe J Mulder Grant/research support from: Dr DJ Mulder as an employee of the UMCG received research grants from Sanofi which were paid to the UMCG.

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POS0620

BI 685509: A POTENT ACTIVATOR OF SOLUBLE GUANYLATE CYCLASE (SGC) AS A NOVEL TREATMENT OF VASCULOPATHY AND FIBROSIS IN SYSTEMIC SCLEROSIS (SSC)

Keywords: Systemic sclerosis, Animal models, Cell biology

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Background: SSc is an autoimmune disease characterized by vasculopathy and tissue fibrosis. Oxidative stress is prominent in affected organs and is hypothesized to contribute to inflammatory and fibrotic damage. sGC is a heterodimeric enzyme that binds nitric oxide (NO) to a prosthetic heme group and catalyzes the production of cGMP. Released cGMP acts as a second messenger to regulate processes including tissue remodeling and immune/inflammatory response [1]. Pharmacologic modulation of sGC with a class of compounds called sGC stimulators have been shown to exert anti-fibrotic and anti-inflammatory effects in models of SSc [2]. In a phase II study in SSc, patients treated with the sGC stimulator Riociguat showed a trend towards clinical efficacy [3]. The action of sGC stimulators is dependent on NO-sGC complexes bearing a reduced heme molecule. In environments of oxidative stress, as seen in SSc, altered redox balance may limit efficacy of sGC stimulators due to heme oxidation and the formation of a pool of NO-insensitive sGC. A second class of sGC compounds, called sGC activators, are heme-independent and can act as a substitute for the heme-NO complex and in turn activate the sGC enzyme. Thus, sGC activators may show enhanced activity vs. sGC stimulators in conditions of compromised redox balance.

Objectives: To evaluate the efficacy of the potent sGC activator BI 685509 in cellular and in vivo models of SSc pathobiology.

Methods: Human dermal microvascular endothelial cells (HDMVEC) were cultured in normoxic or 1% O_2 conditions in the presence of BI 685509 ranging in doses from 0.04 to 10 µM. After 48 hrs, culture supernatant was collected and the concentration of TGFβ2 was determined. Human platelet rich plasma (PRP) was isolated and activated for 5 minutes with ADP in the presence of BI 685509 or Riociguat at doses of 0.1, 1 or 10 µM. Following activation, supernatants were collected and the level of CXCL4 was measured. For the bleomycin indued skin and lung fibrosis studies, adult female C57Bl/6 mice were used. Mice received intradermal injections of bleomycin every other day for six weeks or a single intratracheal injection. Mice were treated with BI 685509, Riociguat or Nintedanib daily beginning at day 21 (dermal) or 14 (lung) after initiation of bleomycin injection. At 6 (dermal) or 4 (lung) weeks post treatment initiation, skin or lung samples were analyzed via histologic analysis for various cellular and biochemical markers of tissue fibrosis.

Results: In HDMVEC, hypoxia induced production of the tissue remodeling factor TGFβ2 was significantly inhibited upon treatment with BI 685509 (10 µM). In the mouse model of bleomycin induced skin and lung fibrosis, activation of sGC via BI 685509 treatment at 1 mg/kg resulted in significant amelioration of skin thickness and lung fibrosis that was equivalent to mice treated with the standard of care Nintedanib (60 mg/kg) or the sGC stimulator Riociguat (1 mg/kg). Lastly, to mimic a NO deficient environment seen in SSc, human PRP was utilized. Induction of the SSc relevant chemokine

CXCL4 was effectively inhibited in activated PRP treated with the sGC activator BI 685509 whereas minimal inhibition was observed in samples treated with the sGC stimulator Riociguat. Inhibition of CXCL4 production in activated human platelet rich plasma treated with the sGC activator BI 685509

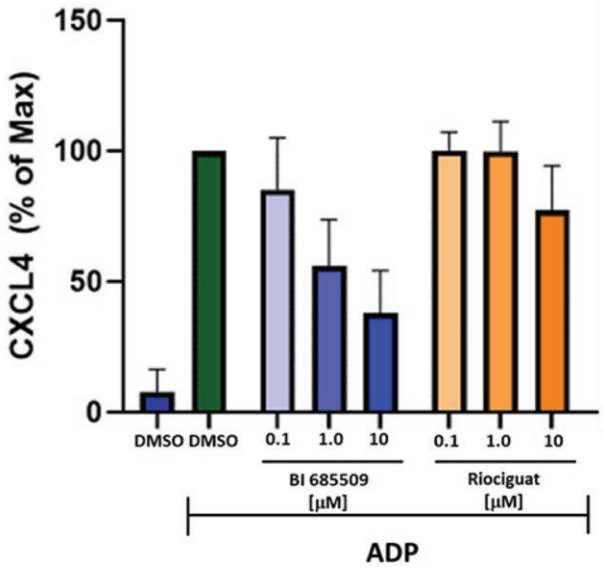


Figure 1.

Conclusion: Collectively, these results point to the use of the sGC activator BI 685509 as a novel treatment for SSc and suggests potential superior effects vs. sGC stimulators like Riociguat in this autoimmune disease.

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Disclosure of Interests: Gerald Nabozny Employee of: Boehringer Ingelheim Pharmaceuticals Inc., Chao-Ting Wang Employee of: Boehringer Ingelheim Pharmaceuticals Inc., Leeanne Daley Employee of: Boehringer Ingelheim Pharmaceuticals Inc., David Ebenezer Employee of: Boehringer Ingelheim Pharmaceuticals Inc., Denis Delic Employee of: Boehringer Ingelheim, Tom Bretschneider Employee of: Boehringer Ingelheim, Thuong Trinh-Minh: None declared, Cuong Tran-Manh: None declared, Joerg Distler: None declared, Julia Kaufman Employee of: Boehringer Ingelheim Pharmaceuticals Inc.

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POS0621 EFFECTS OF B CELL DEPLETION BY CD19-TARGETED CAR-T CELLS IN A MURINE MODEL OF SYSTEMIC SCLEROSIS

Keywords: Animal models, Systemic sclerosis

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Background: Chimeric antigen receptor (CAR)-T cells represent a potentially curative strategy for B cell malignancies. A first successful clinical experience has been reported in systemic lupus erythematosus, suggesting that CD19-targeted CAR-T cell transfer was feasible and tolerable [1].

Objectives: Since systemic sclerosis (SSc) and SLE are both severe diseases sharing B cell implication in their pathogenesis, we aimed at assessing the efficacy and tolerance of two B cell depletion strategies, including one with CD19-targeted CAR-T cells, in a preclinical model mimicking the severe lung damages observed in SSc.

Methods: B cell depletion strategies were evaluated in the Fra-2 transgenic (Tg) mouse model. We considered a first group of 16 untreated mice, a second group of 15 mice receiving a single intravenous (IV) dose (50 µg) of anti-CD20 monoclonal antibody (mAb) at day 1 and a third group of 8 mice receiving 50 µg anti-CD20 mAb IV at day 1 followed by the IV injection of $20*10^6$ CD19-targeted CAR-T cells at day 3. After 6 weeks, different validated markers of inflammation, lung fibrosis and pulmonary vascular remodeling were assessed.

Results: Following treatment with anti-CD20 mAb, CD19 expression was significantly decreased in peripheral blood and lesional lungs of Fra-2 Tg mice by 59% ($p<0.001$) and 40% ($p=0.019$), respectively, compared to control Fra-2. B cell depletion was even more pronounced in mice treated with CD19-targeted CAR-T cells: CD19 expression was decreased in peripheral blood and lungs of Fra-2 Tg mice by 92% ($p<0.001$) and 85% ($p<0.001$), respectively, compared to control Fra-2. CAR-T cell infusion increased mortality in Fra-2 Tg mice (**Figure 1A**). In line with the above findings, mice receiving CD19-targeted CAR-T cells displayed a significant increase in lung density (mean difference of 55±28 Hounsfield Units, $p=0.038$) (**Figure 1B-C**) and a marked reduction of functional residual capacity (mean difference of 25±9%, $p=0.041$) as compared to control Fra-2 when assessed by chest micro-CT imaging. CAR-T cell infusion significantly increased lung collagen content (mean difference of 11.93±4.44 µg/mL, $p=0.020$) (**Figure 1D**), histological fibrosis score (mean difference 1.74±0.48, $p=0.002$) (**Figure 1E-F**) and right ventricular systolic pressure mean difference 8.52±2.70 mmHg, $p=0.013$) (**Figure 1G**). CAR-T cells accumulated in lesional lungs and promoted T infiltration and activation: a significant increase of CD4+ effector memory T cells was observed in CD19-targeted CAR-T cell-treated Fra-2 Tg mice compared to Fc control Fra-2 Tg mice (mean difference of 32±%, $p=0.001$). Moreover, the fraction of CD69 and PD1-expressing cells was significantly increased within the CD4+ and CD8+ subsets in the lung of CD19-targeted CAR-T cell-treated Fra-2 Tg mice. Treatment with anti-CD20 mAb in monotherapy had no impact on lung inflammation-driven fibrosis and pulmonary hypertension.

Conclusion: B-cell therapies failed to show efficacy in the Fra2 transgenic mice. The exacerbated Fra-2 lung inflammatory burden stimulated accumulation and expansion of activated CD19-targeted CAR-T cells, secondarily inducing T-cell activation and systemic inflammation, finally leading to disease worsening.

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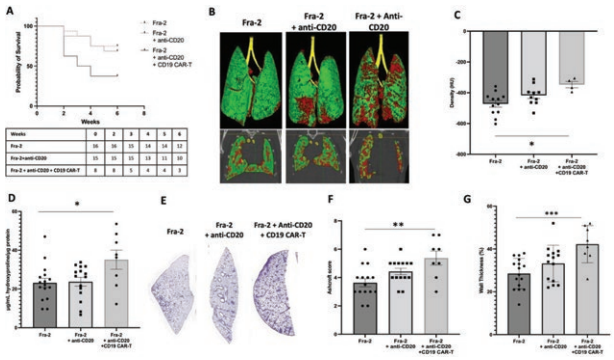


Figure 1. Effects of B cell depletion by anti-CD20 mAb in association or not with CD19-targeted CAR-T cells in Fra-2 Tg mice

A, Survival curves of Fra-2 mice after anti-CD20 mAb and CD19-targeted CAR-T cell infusion. Significance was determined by log rank (Mantel-Cox; $p=0.031$). **B,** Representative pictures of micro-computed tomography. **C,** Y-axis shows the lung density at micro-computed tomography. **D,** Y-axis shows the content of collagen in a lung fragment (µg) evaluated by Sircol assay. **E,** Representative HES 4-µm lung sections (magnification × 8). **F,** Y-axis shows the Ashcroft histological score. **G,** Y-axis shows the right ventricular systolic pressure (RVSP). All data are shown as the mean ± SEM. * $p<0.05$, ** $p<0.01$, ***$p<0.001$ determined by one-way analysis of variance with Tukey's *post hoc* test.

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POS0622 BIFIDOBACTERIUM LONGUM RAPO AMELIORATES DERMAL AND PULMONARY FIBROSIS THROUGH THE MODULATION OF GUT MICROBIOTA AND IMMUNE RESPONSE IN BLEOMYCIN-INDUCED SYSTEMIC SCLEROSIS IN MICE

Keywords: Systemic sclerosis, -Omics, Lungs

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Background: Systemic sclerosis (SSc) is a chronic autoimmune disorder characterized by immune abnormalities, vasculopathy, and fibrosis of the internal organs[1]. Because the etiology of SSc is uncertain, drugs that improve the course of the disease and symptom are lacking. Recent data have highlighted the importance of the microbiome and its relevance to SSc. The microbiome can trigger an exacerbation of SSc. On the other hand, it may relieve symptoms. *Lactobacillus* and *Bifidobacterium* strains have been reported to alleviate gastrointestinal symptoms of SSc[2,3]. However, there are no study on the microbiome that improves the major symptoms of SSc, such as dermal and lung fibrosis.
Objectives: This study aims to screen SSc-associated microbiome at the species level using serum and to explore potential microbial targets for SSc treatment. And we evaluated whether the candidate microbial species ameliorate dermal and lung fibrosis.
Methods: We performed an immunoglobulin (Ig) M antibody microarray against 384 microbial species in the serum from SSc patients and healthy control (HC). Then, the antifibrotic effect of candidate microbial species was investigated using a bleomycin (BLM)-induced fibrosis model in mice.
Results: *Bifidobacterium (B.) longum* RAPO, which was less abundant in the serum of patients with SSc than HC, alleviated BLM-induced skin and lung fibrosis in mice. The administration of *B. longum* RAPO normalized fecal microbial diversity with an increase in short-chain fatty acid-producing bacteria. Moreover, infiltrated inflammatory monocytes or macrophages in the spleen, the skin, and bronchoalveolar lavage of BLM-injected mice were significantly reduced by treating *B. longum* RAPO. In vitro, *B. longum* RAPO downregulated LPS-induced inflammatory cytokines gene expression in mouse macrophage cell Raw 264.7.
Conclusion: *B. longum* RAPO could have an antifibrotic effect on skin and lung fibrosis through gut microbial restoration and macrophage regulation in BLM-induced fibrosis mice. Microbial intervention would be a potential option for SSc treatment.

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POS0623 INTEGRATED SERUM PROTEOMIC AND METABOLOMIC PROFILES IN SYSTEMIC SCLEROSIS PATIENTS CHARACTERIZE NEW BIOMARKERS ASSOCIATED TO RELEVANT PATHOLOGICAL FEATURES

Keywords: Biomarkers, -Omics, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is a heterogeneous multisystemic autoimmune disease, characterized by extensive skin fibrosis, vascular abnormalities, and autoantibodies against various cellular antigens. The integrated analysis of proteomic and metabolomic in SSc might shed light in the pathogenesis of the disease and reveal novel biomarkers.
Objectives: The aim of this study was to characterize the circulating proteomic and metabolomic profiles in SSc and their association with key clinical features.
Methods: Serum NMR metabolomics (Nightingale; 250 metabolites covering glycolysis metabolites, amino acids and lipid measures), and proteomics, involving the analysis of 92 organ damage-related proteins [by proximity extension immunoassay (PEA, Olink)] were performed on serum from 72 SSc patients and 43 age-matched healthy donors (HD).
Main disease complications in the SSC cohort, including lung fibrosis, skin fibrosis, renal, vascular, and esophageal involvement were assessed, and prevalence of circulating autoantibodies, along with standard demographic and inflammatory parameters were analyzed by multiple t-test. Unsupervised hierarchical clustering methodologies were applied using Metaboanalyst software to identify subgroups of patients based on their proteomic profiles. Gene ontology enrichment was used to interrogate the biological meaning of the distinctive molecular signatures identified.
Results: Sixteen circulating proteins related to organ damage (9 increased and 7 reduced) as well as 143 metabolites (37 increased and 101 reduced) were found altered in SSc patients in relation to HD. Unsupervised clustering analyses differentiated 3 patients clusters presenting different proteomic profiles. Clinically, patients belonging to cluster 1 (C1) were characterized by a significant prevalence of multiple organ involvement (84%) in relation to C2 (52%) and C3 (43%), mostly encompassing lung and skin fibrosis and esophageal dysmotility. Immunologically, C1 further displayed the highest percentage of positivity for anti-scl70 antibodies. Nineteen proteins were identified as significantly altered in cluster 1 (C1) in relation to C2 and C3, mostly involved in biological processes such as cell proliferation, apoptosis, cell adhesion, migration, and immune response. Among them, two were functionally linked with cutaneous diseases (CALR and BANK1), two with digestive disorders (FGR and STXBP3) and three with lung disfunction (FOSB, SMAD1 and FOXO1). Levels of some overexpressed proteins in C1 (BID, INPPL1, BANK1 and FOSB) were further related to the positivity for anti-scl70, the specific SSC-autoantibody mostly associated to a bad prognosis and multiple organ involvement in SSC. Interestingly, thirty-five metabolic markers were found deregulated when comparing those proteomic clusters of SSC, comprising lipoprotein subsets, sphingomyelins, cholesterol, lactate, and albumin. Moreover, significant correlations were identified among the levels of proteins and metabolites found deregulated, pointing at a concordance on their involvement in mechanisms underlying the disease process.
CONCLUSION:
1) Serum proteomic and metabolomic signatures are significantly altered in SSC patients and associated to relevant clinical profiles.
2) Clinical classification of SSc patients could be improved based on serum proteomic and metabolomic profile, adding new insights to the underlying pathophysiological mechanisms.

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POS0624 BAG3 PROTEIN: A PROMISING NOVEL BIOMARKER OF FIBROSIS IN SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Biomarkers, Lungs

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Background: Systemic Sclerosis (SSc) is a rare autoimmune disease characterized by an abnormal remodelling of tissue matrix, leading to fibrosis of skin and internal organs. Despite progresses made in terms of knowledge of pathogenic mechanisms, no study has yet identified specific biomarkers useful for assessing disease evolution and response to therapies. Bcl2-associated athanogene 3 (BAG3) protein is a member of a family of co-chaperones that interact with the ATPase domain of the heat shock protein (Hsp) 70 through their BAG domain. BAG3 is constitutively present in a few normal cell types and some tumours, while its expression is induced by stressful stimuli in a wide variety of cells. BAG3 interacts with several partner proteins regulating different pathways, including apoptosis, autophagy and motility. Recent studies have demonstrated a pivotal role of extracellular BAG3 in pro-tumor cell signaling in the tumor microenvironment, as well as its involvement in the development of fibrosis in tumor tissues

[1]. In addition, a strong correlation between *bag3* gene expression and patients' survival was found in several types of fibrotic tumors [1].

Objectives: Our aim was to evaluate the presence of BAG3 in the serum of patients with SSc and to investigate whether circulating levels of BAG3 could have any relationship with different SSc subsets and disease features.

Methods: We enrolled SSc patients, all classified according to the ACR-EULAR criteria. Videocapillaroscopy (NCV) was performed at the time of serum collection. Lung involvement was assessed by spirometry and high-resolution chest CT. Patients were classified into 3 subgroups (no ILD, limited ILD, and extensive ILD) according to the diagram described by Goh et al.[2]. SSc disease activity was assessed according to the activity indices defined by the EUSTAR score [3]. Evaluation of BAG3 protein in serum samples was performed by a sandwich ELISA assay.

Results: The study cohort included 106 SSc patients (47 were classified with lcSSc and 59 with dcSSc) and 100 sex and age matched healthy controls (HC). Serum levels of BAG3 were significantly higher in SSc patients (mean value 85,3 pg/mL, 95% confidence interval CI 47,2-123,4) when compared with HC (0,68 pg/mL, 95%CI 0,13-1,23) (p=0.001). When analyzed according to disease subset, dcSSc patients showed values (143,3 pg/mL, 95%CI 78-208,5) significantly higher and lcSSc patients (8,7 pg/mL, 95%CI 1,64-15,9,5) (p=0.001). No correlation was found between BAG3 levels and digital ulcers, mRSS and disease activity. Conversely, BAG3 values positively correlated with the extent of lung damage (237,8 pg/mL, 95%CI 131,2-344 in the extensive lung disease vs 16,3 %CI 7,5-25,3 in the limited). Finally, BAG3 values were significantly higher in patients with late NVC pattern in comparison with NVC pattern early/active (p=0.0008).

Conclusion: Recent studies have highlighted a central role of extracellular BAG3 in maintaining the tumour microenvironment, as well as in the development of fibrosis in neoplastic tissues. To our knowledge, the presence of BAG3 in the serum of patients with SSc has never been described in the literature.

Serum levels of BAG3 were found to be significantly higher in the dcSSc, mostly in those with lung involvement. This is not surprising since the diffuse form of disease has more extensive fibrosis, both in the skin and lung, than lcSSc. Accordingly, BAG3 values correlated with the late pattern at NVC, the one most frequently associated with the more advanced and fibrotic stages of the disease. Conversely, serum BAG3 values did not correlate with disease activity, since these scores reflect the evolution and progression of disease rather than the extent of fibrosis. Indeed, the close correlation between BAG3 levels and the more fibrotic features of the disease, suggests that BAG3 might be a new promising marker of fibrosis.

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POS0625 EFFECTS OF DIFFERENTIATION STAGES OF HEALTHY AND SSC MACROPHAGES ON THE 3D HUMAN CARDIAC FIBROSIS MODEL

Keywords: Cardiovascular disease, Heart, Systemic sclerosis

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Background: Activated cardiac fibroblasts, key regulators of cardiac fibrosis, control contraction of human fibrotic cardiac microtissues (MT)[1]. Macrophages regulate fibrotic process by interfering with the extracellular matrix (ECM) turnover. The heart is one of the primary organs affected in systemic sclerosis (SSc).

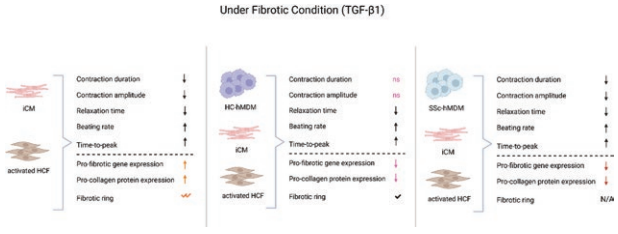
Objectives: To study the role of healthy donor- and SSc patient-derived macrophages in the functions of 3 dimensional (D) human cardiac MT fibrosis model.

Methods: CD14$^+$ blood-derived monocytes from healthy controls (HC) and SSc patients were isolated and differentiated into human monocyte-derived macrophages (hMDM) using human monocyte colony-stimulating factor (hM-CSF). A timeline of macrophage differentiation stages was performed by incubation of the CD14$^+$ cells for 1,3,5 and 7 days (d) with hM-CSF. One MT was generated by 4'000 human induced pluripotent stem cell-derived cardiomyocytes (iCM), 1'000 human cardiac fibroblasts (HCF) and 1'000 HC or SSc hMDM, mixed in a ratio 4:1:1 (HC-hMDM:iCM:HCF-MT or SSc-hMDM:iCM:H-CF-MT), and formed by self-assembling in plates with ultra-low-attachment surface. Control MTs were composed with iCM/HCF in a ratio 4:1/4:2 (iCM:H-CF-MT). Two days after MT assembly, the fibrotic condition was induced with transforming growth factor β1 (TGF-β1) for 10d. Contraction of each MT was assessed by recording videos, applying MUSCLEMOTION[2] and subsequent evaluation by relaxation time (ms), contraction amplitude (a.u.), contraction duration (ms), time-to-peak (ms) and beating rate (bpm). The level of fibrosis was analysed on several levels: mRNA by qPCR, ELISA to measure secreted pro-collagen-Iα1, immunohistochemistry (IHC) using Sirius Red to visualize collagen depositions and degree of fibrosis. Apoptosis was assessed using Caspase-3/7 assay.

Results: Control-iCM:HCF-MTs (n=23-49), following TGF-β1 stimulation, revealed a shorter contraction duration (p<0.01) and a lower contraction amplitude (p<0.0001) but not altered contraction duration (p=0.5095) and contraction amplitude (p=0.7298) compared to untreated-iCM:HCF-MTs. Interestingly, untreated-SSc-hMDM:iCM:HCF-MTs showed a shorter time-to-peak (p<0.0001), lower beating rate (p<0.01) and higher contraction amplitude (p<0.01) compared to untreated-HC-hMDM:iCM:HCF-MTs (n=41-81, both conditions 3d). Next, TGF-β1-stimulated SSc-hMDM:iCM:HCF-MTs exhibited a lower contraction duration (p<0.01) and contraction amplitude (p<0.0001), shorter relaxation time (p<0.0001), and higher beating rate (p<0.0001) compared to TGF-β1-stimulated HC-hMDM:iCM:HCF-MTs (n=33-42, both conditions 1d). Upon TGF-β1-stimulation, control-iCM:HCF-MTs showed significantly increased profibrotic genes: *ACTA2* (p<0.001) and *COL1A1* (p<0.01) (n=4-5), secreted human pro-collagen Iα1 (n=9-10, p<0.0001), and formed visible collagen-rich fibrotic ring. Remarkably, under fibrotic conditions, addition of HC or SSc hMDM into iCM:HCF-MTs resulted in lower mRNA expression of *ACTA2* (n=4-5, p<0.05, both conditions 7d) and *COL1A1* (n=4-5, p<0.05, both conditions 7d), lower excretion of human pro-collagen Iα1 protein (n=9-10, p<0.0001, both conditions 7d) and lack of collagen-rich fibrotic ring compared to control-iCM:HCF-MTs. Importantly, independently of culture duration of HC or SSc hMDM, before MT assembly, a similar reduction in profibrotic gene and protein expression was observed. Lastly, the level of apoptosis was similar in all three undifferentiated or TGF-β1-stimulated MTs types.

Conclusion: For the first time, the combination of iCM, HCF and hMDM in a 3D fibrotic cardiac MT model has been established and investigated. Under fibrotic conditions, addition of HC- but not SSc-hMDM into iCM:HCF-MTs influenced MT contractility. Importantly, both HC- and SSc-hMDM reduced TGF-β1-induced fibrotic responses.

Scheme 1: Graphical abstract



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Scheme 1: Graphical abstrac.t.

Disclosure of Interests: Laila Provenzale: None declared, Amela Hukara: None declared, Ievgeniia Kocherova: None declared, Elena Pachera: None declared, Andrea Laimbacher: None declared, Oliver Distler Speakers bureau: Oliver Distler has/had relationships with the following companies in the area of potential treatments for systemic sclerosis and its complications in the last three calendar years: Bayer, Boehringer Ingelheim, Janssen, Medscape. Consultant of: Oliver Distler has/had relationships with the following companies in the area of potential treatments for systemic sclerosis and its complications in the last three calendar years: 4P-Pharma, Abbvie, Acceleron, Alcimed, Altavant Sciences, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos, Glenmark, Horizon, Inventiva, Kymera, Lupin, Miltenyi Biotec, Mitsubishi Tanabe, MSD, Novartis, Prometheus, Redxpharna, Roivant, Sanofi and Topadur, Grant/research support from: Oliver Distler has/

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POS0626 PERTURBED LIPID METABOLISM IS A CENTRAL METABOLIC REPROGRAMMING HUB IN SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, -Omics, Skin

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Background: Perturbed cellular metabolism has been increasingly associated with fibroblast activation in fibrosis. A deeper understanding of metabolic rewiring might help to unravel the interplay between the metabolic and fibrotic pathways in systemic sclerosis (SSc).

Objectives: We aimed to identify transcriptomic alterations in metabolic pathway-related genes in fibrotic SSc skin and unravel whether fibroblasts could contribute to the perturbed skin metabolic networks in SSc.

Methods: We integrated transcriptomic microarray data from skin (clinically affected forearm and non-affected back skin) of 76 SSc patients and 26 healthy controls (HC, forearm skin) from three distinct cohorts (GSE:45485, 59785, 9285/32413). Differentially expressed (DE) genes (FDR<0.05) between healthy and SSc skin were identified using the limma package. The supervised gene set enrichment analysis (GSEA) was based on DE genes using the clusterProfiler package, focusing on metabolic pathways. Transcriptional changes in SSc skin were compared to the TGFβ-induced changes in transcriptomes of primary human skin fibroblasts, measured by RNA-seq and scRNA-seq. For these experiments, cultured healthy skin fibroblasts were treated or not with TGFβ for 24h.

Results: Pathway enrichment analysis of DE gene in skin transcriptomes identified multiple alterations of metabolic pathways in SSc skin (Figure 1A) compared to healthy skin, pointing to enhanced pyrimidine/folate metabolism and suppressed lipid metabolism in SSc skin. Steroid hormone biosynthesis (*AKR1, DHRS11, CYP1A2, SULT2B1, HSD1, EHTM2, HSD11B2*), fatty acid synthesis (*FASN1, FADS1, FADS2, ELOVL, SCD5, PTPLB*), and fatty acid degradation (*ACAT1/2, ACADS, ACAA1/2, ACADM, ACSL3*) were the main downregulated lipid metabolism pathways in SSc skin, particularly in patients with the inflammatory intrinsic gene expression subset. The latter changes were detected in the affected and non-affected SSc skin, suggesting that altered lipid metabolism is a generalized feature of the SSc skin. Furthermore, pathway enrichment analysis of TGFβ-induced transcriptional changes in skin fibroblasts, as detected by RNA-seq and scRNA-seq, suggested that TGFβ-driven reprogramming could significantly contribute to the lipid metabolism perturbations in SSc skin (Figure 1B, C). Specifically, STRING analysis revealed that TGFβ suppressed metabolic networks of glycerophospholipids, arachidonic acid, and fatty acids in cultured skin fibroblasts (Figure 1D).

Conclusion: Our data suggest perturbed lipid metabolic networks in SSc skin and identify skin fibroblasts, exposed to profibrotic milieu, as likely contributors to the altered lipid metabolism in SSc. These results might pave the way to a deeper understanding of the interplay between the metabolic and fibrotic pathways in SSc. Integrating these data with future metabolomic and single-cell studies could accelerate the discovery of potential metabolic targets in SSc.

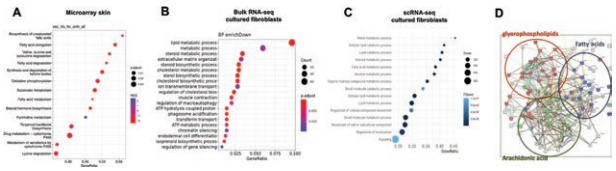


Figure 1. A) Enriched metabolic pathways in SSc skin compared to healthy skin based on DE gene expression. Downregulated GO biological processes in TGFβ-treated cultured healthy skin fibroblasts based on RNAseq (B) and scRNAseq (C) analyses. D) STRING pathway enrichment analysis of downregulated genes (RNA-Seq) linked to lipid metabolism in TGFβ-stimulated skin fibroblasts.

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POS0627 BLOOD-BASED PROTEIN BIOMARKERS ARE ASSOCIATED WITH SUBCLINICAL CARDIOVASCULAR ABNORMALITIES AS DEFINED BY CARDIOVASCULAR MAGNETIC RESONANCE IMAGING IN SYSTEMIC SCLEROSIS (SSC) PATIENTS

Keywords: Biomarkers, Systemic sclerosis, Cardiovascular disease

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Background: Systemic sclerosis-primary heart involvement (SSc-pHI) accounts for up to one-third of SSc-related deaths and clinically apparent pHI portends poor outcome. Early detection of SSc-pHI is therefore crucial. We have previously shown cardiovascular magnetic resonance (CMR)-detected subclinical myocardial abnormalities. Identifying robust blood biomarkers of SSc-pHI would facilitate diagnostic testing, help to resolve the biological mechanisms underpinning SSC-pHI and potentially identify new targets for drug development.

Objectives: To identify protein biomarkers associated with subclinical cardiovascular abnormalities as defined by CMR measures in SSc patients, and predominant inflammatory and cardiometabolic pathways implicated.

Methods: Seventy-eight patients from CONVAS ('CONnective Tissue Disease and VASculitis Cohort') and ELCASA ('ELectrophysiology and CArdiac imaging in SclerodermA')1 study cohorts underwent CMR imaging. Using Olink Proximity Extension Assay, normalised protein expression (NPX) across cardiometabolic, cardiovascular II/III and inflammation panels was measured in these patients at the time of CMR. Generalised linear regression with Benjamini Hochberg correction for multiple testing was used to identify significant proteins associated with CMR parameters of myocardial oedema/fibrosis [native T1, myocardial extracellular volume (ECV) and late gadolinium enhancement (LGE)] and vascular stiffness [aortic distensibility]. Subsequently, an expanded protein-protein interaction (PPI) network was created using an induced network approach (String-DB) with k-means clustering applied to identify enriched functional clusters that were then subjected to Gene Ontology (GO) and KEGG enrichment analysis.
Results: Of 355 proteins analysed, 70 proteins were associated with myocardial tissue oedema/fibrosis (64 proteins; 26 positively, 38 negatively) and vascular stiffness (6 proteins; 2 positively, 4 negatively). 2 overlapping proteins that associated with focal (LGE) and diffuse fibrosis (ECV) were identified. *Proteins identified include those involved in coagulation cascade (estimate = -1.97, 95%CI = -3.63 to -0.31, adj.p = 0.039), carbohydrate binding and opsonisation activities (estimate = -1.31, 95%CI = -2.19 to -0.43, adj.p = 0.006); and cancer and neovascular inflammatory conditions (estimate = -75.79 95%CI = -119.81 to -31.76, adj.p = 0.002). K-means clustering of the expanded PPI network (enrichment p.value < 1.0e-16) identified 4 clusters (Figure 1) with roles in TNF receptor superfamily binding and NF-kappa B signalling pathway (red); Vascular endothelial growth factor-activated receptor activity and Rap1 signalling pathway (yellow); IL-10 receptor activity and JAK-STAT signalling pathway (blue); and FGF activated class receptor binding and ErbB signalling pathway (green). Proteins associated with CMR detected subclinical myocardial tissue oedema/fibrosis mainly mapped to yellow and blue clusters.
Conclusion: In this first proteomic study of SSc-pHI, we have identified 70 protein biomarkers, with myocardial tissue oedema/fibrosis associated with inflammation and vascular pathways. The next step is to validate these proteins and test the utility of network proteins in an independent patient cohort that could aid detection and diagnosis of SSc-pHI. *Proteins names not disclosed as subject to Intellectual Property discussions via Innovation Factory, University of Manchester.

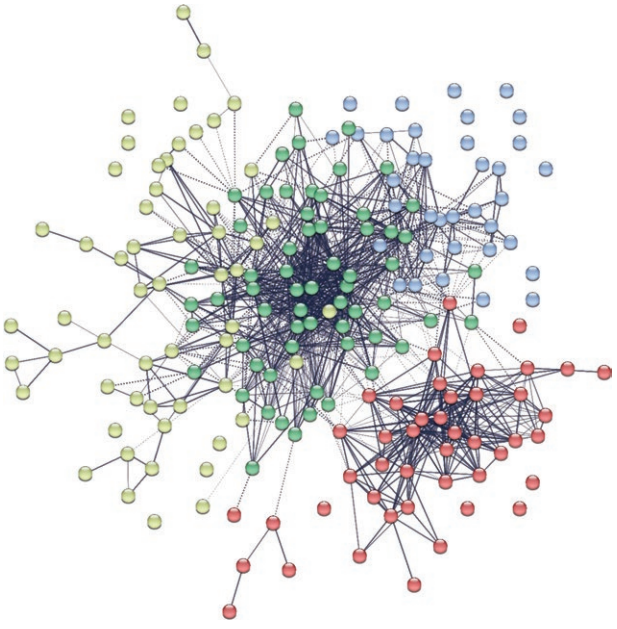


Figure 1. K-means clustering of the expanded PPI network. Four enriched functional clusters were identified using STRINGdb.

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POS0628 BARICITINIB AMELIORATES BLEOMYCIN-INDUCED PULMONARY AND SKIN FIBROSIS VIA JAK 1/2 INHIBITON

Keywords: Lungs, Animal models, Systemic sclerosis

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Background: Signal transducer and activator of transcription 3 (STAT3) protein is activated in lung fibroblasts and alveolar type II cells (AT-II) and is thought to contribute to fibrosis in lung tissue. Significant JAK/STAT activation was demonstrated in fibroblasts, skin biopsies and scleroderma animal models of patients with Systemic Sclerosis (SSc) [1].
Objectives: The aim of this study was to determine whether inhibition of JAK2/STAT3 in the experimental model of scleroderma is a potential therapeutic strategy for this disease and to investigate the effects of the JAK 1-2 inhibitor Baricitinib (BAR) on the experimental model of dermal and pulmonary fibrosis.
Methods: Thirty-two healthy 6-8 weeks old female C57BL mice with an average weight of 22±3 grams were included in our study. Before the treatment (baseline), day 15 and day 30 (day 30) the same back area was shaved in all mice and skin thickness was measured under the guidance of skin Ultrasound Biomicroscopy (US). US measurements were chosen to be at least >1 cm from the injection area. Whole lung Computed Tomography (CT) scans of each animal were acquired at post-treatment (day 30). H&E and Masson's Trichrome staining were performed to evaluate skin thickness, pulmonary alveolitis, and fibrosis. The Ashcroft score was assessed on Sirius Red stained lung sections post-treatment. For the molecular evaluation of tissue fibrosis, collagen and α-SMA levels were measured in skin and lung tissues by qRTPCR.
Results: We found that BAR resulted in favorable therapeutic outcomes by affecting the inflammation infiltration and collagen deposition both lung and skin tissues. Immunohistochemical results showed that BAR downregulated the levels of COL1A1 and COL1A2.Treatment with JAK 1-2 selective BAR has been shown to ameliorate BLM-induced skin and lung fibrosis at radiological, pathological and molecular measurements.
Conclusion: As a result of our study, the effect of JAK1-2 selective inhibitor baricitinib treatment on reducing skin and lung fibrosis in a mouse model created with BLM was demonstrated with radiological and pathological examinations. We conclude that JAKinh treatments will be an important research area for the treatment of SSc and other fibrotic diseases in the future.

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Table 1. Skin and lung measurements

	BLM (I)	BLM+BAR (II)	BLM+PBO (III)		Pairwise comparison		
	Mean (SD.)	Mean (SD.)	Mean (SD.)	P	I vs II	I vs III	II vs III
Dermal thickness (with H&E and MT) (µm)	430.29 (54.66)	308.00 (26.79)	452.50 (75.48)	**0.001** [a]	**<0.001**	0.721	**<0.001**
Dermal thickness (with UBM) (µm)	524.86 (116.21)	304.20 (61.45)	505.67 (88.09)	**<0.001** [a]	**<0.001**	0.919	**<0.001**
		Median (min-max)	**Median (min-max)**	**Median (min-max)**			
Ashcroft Score (0-8)	5 (2-7)	1 (0-4)	3 (2-5)	**0.001** [k]	**0.002**	0.630	0.176
	n (%)	**n (%)**	**n (%)**				
SSc-ILD in CT				0.215 [ff]			
Absent	2 (28.6)	7 (70)	2 (33.3)		ns.	ns.	ns.
Present	5 (71.4)	3 (30)	4 (66.7)		ns.	ns.	ns.

[a] OneWay ANOVA (Robuts Statistic:Brown-Forsythe); Post Hoc Test: Tukey HSD, [k] Kruskal Wallis Test (Monte Carlo); Post Hoc Test: Dunn's Test, [ff]Fisher Freeman Halton (Monte Carlo), ILD: Interstitial lung disease, UBM: Ultrasound biomicroscopy, H&E: hematoxylin and eosin staining, MT: Masson's Trichrome staining, ns.: non significant, min.: minimum, max.: maximum, SD.:Standard deviation, BLM: Bleomycine induced SSc group, BLM+BAR: Bleomycine with Baricitinib group, BLM+PBO: Bleomycine with Placebo group

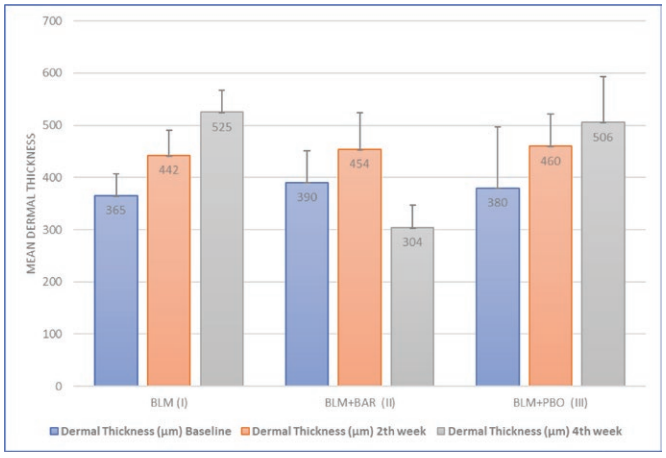


Figure 1. Dermal thickness change with UBM baseline, 2th and 4th week.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0629

DIFFERENT GUT MICROBIOME PROFILES AMONG PATIENTS WITH SYSTEMIC SCLEROSIS COMPARED TO RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Gastrointestinal tract, Systemic sclerosis

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Background: A growing body of evidence suggests that the gut microbiota plays a significant role in the development of autoimmune diseases. An altered microbiota composition has been associated with gastrointestinal and extraintestinal features in systemic sclerosis (SSc) patients.
Objectives: To characterize differences in the gut microbiota between SSc patients and rheumatoid arthritis (RA) patients and to look for associations between microbial profiles and SSc subtypes, disease manifestations and treatment.
Methods: SSc and RA patients seen at our center were recruited in a prospective study. The exclusion criteria included antibiotic or probiotic treatment during the month prior to recruitment, recent hospitalizations, BMI>30, diabetes mellitus or concomitant inflammatory bowel disease. Fecal samples were collected and processed and 16S rRNA gene sequences were analyzed using the QIIME2 package. Microbiome composition was determined, beta diversity and alpha diversity were calculated and ANCOM analyses was performed.
Results: During 7/2018-4/2022, 49 SSc patients (mean age [SD] 53.5[13.8] and disease duration 9.4 [8.0] years) and 21 RA patients (mean age [SD] 57.1[10.4] and disease duration 15.1[10.0] years) fulfilled the criteria and were willing to participate in the study. Significant differences in beta diversity (Unweighted q=0.019, and Weighted UniFrac q=0.005) were found between RA and SSc patients' stool microbiota, but not in alpha diversity. Composition analysis revealed higher abundance of Actinomyces and relative paucity of Coprococcus Eutactus among SSc patients compared to RA. Significant variations in beta diversity (unweighted and weighted) were associated with the subtype of SSc (diffuse - 27 vs limited - 22 patients, p [weighted] = 0.01), occurrence of interstitial lung disease (22 patients, p=0.011), renal crisis (3 patients, p=0.016), immunomodulatory treatment (33 patients, p=0.018) and biological treatment (11 patients, p=0.017). Composition analysis revealed higher relative abundance of Firmicutes in patients with GAVE [12]. Patients on biologicals (11) had higher abundance of Synergistaceae and lower of Firmicutes. The changes were consistent in recurrent fecal samples.
Conclusion: Significant differences on beta diversity were found between RA and SSc patients' gut microbiota, but not on alpha diversity. Diffuse SSc, interstitial lung disease, renal crisis and immunomodulatory treatment were associated with shifts in the microbiome of SSc patients. The impact of these changes on SSc disease progression needs further elucidation.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4363

Rheumatoid arthritis - biological DMARDs

POS0630

ANTIDRUG ANTIBODIES ARE NEGATIVELY ASSOCIATED WITH RESPONSE TO BIOLOGICAL DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS OF THE ABIRISK STUDY

Keywords: Prognostic factors, bDMARD, Rheumatoid arthritis

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Background: Anti-drug antibodies (ADAb) may be involved in loss of response or primary failure of bDMARDs in rheumatoid arthritis (RA). However, evidence in prospective clinical studies of diminished response to treatment in presence of ADAb is rare and restricted to monoclonal anti-TNF antibodies[1].
Objectives: In this analysis of the prospective European trial ABIRISK we aimed to analyze how ADAb might influence response to several bDMARDs in RA.
Methods: RA patients resistant to methotrexate and starting a bDMARD (anti TNF, anti IL-6 R and anti CD20) were included in 4 countries (ABIRA, NCT02116504). They had a clinical assessment and ADAb quantification at 6, 12, and 15 to 18 months. ADAb were detected using mesoscale discovery (MSD) technology. They were defined as transient if they were negative after a positive time point and persistent positive if they were positive at two sequential visits without negative timepoints afterwards. ADAb positivity was defined as having been ADA positive at least in one visit in the first 12 months. The primary endpoint was the EULAR response at 12 months. Association with ADAb was analyzed using univariate logistic regression. Patients withdrawing for side effects or for inefficacy were considered as non-responders. We also performed a univariate and a multivariate analysis through a generalized estimating equation (GEE) model that analyzes the EULAR response and ADAb status for each visit starting at 6 months. This allows taking advantage of all the data available in the study. The effect of methotrexate on ADAb was also studied. Finally, we performed drug concentration measurements for anti-TNF drugs.
Results: 230 patients were included treated with: adalimumab or infliximab = monoclonal TNFi (mTNFi, N=68); etanercept (ETN, N=82), rituximab (RTX N=30) or tocilizumab (TCZ N=50). ADAb were positive in 38,2% of the mTNFi-treated patients, 50% of the RTX-treated and 20% of the TCZ-treated patients. ADAb positivity was negatively associated with EULAR response at 12 months for all drugs OR=0.20 [0.10-0.42]. Only persistent and not transient ADAb were negatively associated with EULAR response at 12 months (persistent ADAb vs ADAb negative OR 0,17 [0.06-0.43] transient ADAb vs ADAb negative, p=0.57). This was also the case for mTNFi alone (persistent ADAb vs ADAb negative OR 0,1; p=0,0051; transient ADAb vs ADAb negative, p=0,99). 6% of ETN patients presented ADAb, always transient. In the GEE longitudinal analysis there was a negative association between ADAb positivity and response to all treatments (OR 0,36 [0.20-0.64]) and individually for TCZ (OR=0.18 [0.04-0.83]) and mTNFi (OR 0,44; p=0,097 trend). In the multivariate analysis, the ADAb status remained independently associated with non-response to treatment (Figure 1). Methotrexate co treatment at baseline was negatively associated with ADAb (OR=0.5 [0.25-1.00]). There was a significantly lower concentration of adalimumab and infliximab in ADAb positive patients compared to ADAb negative. There was a significantly higher concentration of adalimumab and etanercept in EULAR responder patients compared to EULAR non-responders.
Conclusion: This prospective multicenter study demonstrates that ADAb are frequently detected and associated with non-response to bDMARDs in RA. It is the first study demonstrating the association between ADAb and non-response to TCZ. Monitoring of ADAb should be considered in the personalized management of RA patients particularly in non-responder patients.

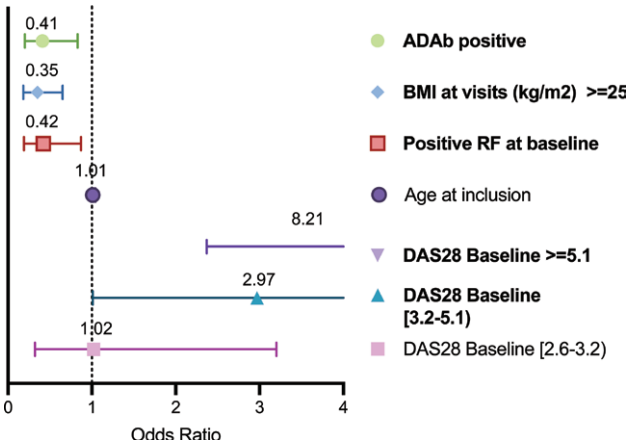


Figure 1. Multivariate analysis of parameters associated with EULAR response in the GEE analysis from M6 onwards.

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POS0631

TNF INHIBITOR USE AFFECTS BIRTH WEIGHT INDEPENDENTLY OF THE SFLT-1/PLGF RATIO IN PREGNANT WOMEN WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Pregnancy and reproduction, Biomarkers

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Background: TNF inhibitor (TNFi) use during pregnancy is associated with increased birthweight of the offspring of women with Rheumatoid Arthritis (RA). However, the underlying mechanism of the increased birthweight due to TNFi use is unknown. Prior studies demonstrated an association between biomarkers of placental function such as soluble fms-like Tyrosine Kinase-1 (sFlt-1) and placental growth factor (PlGF) and fetal growth restriction (FGR). We hypothesize that the increased birthweight in the offspring of women with RA treated with TNFi can be explained by better placentation by affecting the levels of biomarkers of placental function or by modulating the impact of these biomarkers on birthweight.

Objectives: To study the modulating impact of sFlt-1 and PlGF on birthweight and the use of TNFi in a cohort of pregnant women with RA.
Methods: Making use of the PreCARA cohort, in which pregnant women with RA are treated according to a treatment protocol aimed at remission. Biomarkers of placental function sFlt-1, PlGF and sFlt-1/PlGF ratio were measured in the first, second and third trimester of pregnancy.
Results: A total of 158 women were included. 52.5% of all patients ever used TNFi during pregnancy. 29.1% used TNFi during all trimesters of pregnancy. The sFlt-1/PlGF ratio is different in each trimester. After correction for confounders, there was no significant difference in sFlt-1 or the sFlt-1/PlGF ratio between patients that did, and did not use TNFα inhibitors (sFlt-1: β-0.000, 95% CI -0.063; 0.063 p = 0.997, PlGF β -0.014, 95% CI -0.06; 0.093 p = 0.721 and sFlt-1/PlGF ratio: β-0.014, 95% CI -0.107; 0.078 p = 0.757). When correlating sFlt-1 and birthweight, we found the previously established correlation in the group that did not use TNFα inhibitors during pregnancy (r = -0.462, p <0.001). However, this correlation disappeared in the group that did use TNFα inhibitors during pregnancy (r = 0.076, p = 0.522).
Conclusion: Our study shows that in pregnant women with RA, the biomarkers of placental function sFlt-1, PlGF and the sFlt-1/PlGF ratio are not related to the use of TNFi. In case of using TNFi, the negative correlation of sFlt-1 on birthweight disappeared, whereas this negative correlation on birthweight persists in the patients not using TNFi. This suggests that TNFi has a downstream effect on sFlt-1 or has an effect separate from sFlt-1. The underlying mechanism of this effect of TNFi on sFlt-1 in relation to birthweight, should be explored in future research.

Table 1. sFlt-1. PlGF and sFlt-1/PlGF ratio values per trimester for all patients that did not use TNFi during pregnancy and patients that used TNFi during pregnancy.

	TNFi -	TNFi +	TNFi all trimesters
Angiogenic marker values	N = 75	N = 83	N = 46
Trimester 1			
sFlt-1	1188 (816 - 1542)	1110 (574 - 1379)	1063,0 (617,8 - 1289,0)
PlGF	31,4 (19,8 - 50,4)	27,8 (16,2 - 46,6)	27,9 (16,7 - 46,1)
sFlt-1/PlGF	33,4 (17,0-51,2)	33,0 (17,8 - 45,9)	31,0 (18,9 - 40,0)
Trimester 2			
sFlt-1	1321 (1051 - 1761)	1557 (1038,5 - 2210,5)	1440,5 (921,8 - 2114,8)
PlGF	346 (240 - 461,5)	360 (247 - 596,5)	351 (195,8 - 541,0)
sFlt-1/PlGF	4,1 (2,3 - 5,9)	4,9 (2,3 - 7,1)	5,7 (2,0 - 8,2)
Trimester 3			
sFflt-1	1933 (1379,5 - 2682)	2011 (1453 - 2820,5)	1771,0 (1278,0 - 2541,0)
PlGF	497 (299,5 - 765)	644 (406,5 - 979,3)	562,0 (365,0 - 869,0)
sFlt-1/PlGF	3,8 (1,8 - 7,3)	3,2 (1,8 - 5,5)	3,1 (1,7 - 5,6)

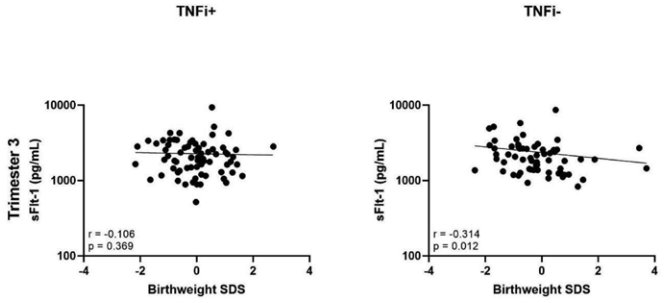


Figure 2. Correlation of sFlt-1 and birthweight SDS in the third trimester of pregnancy for all patients with and without ever-use of TNFi during pregnancy

REFERENCES: NIL.
Acknowledgements: NIL.
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POS0632

TARGETING NET FORMATION IN EARLY RA PATIENTS; A SPIN-OFF STUDY FROM THE NORD-STAR

Keywords: bDMARD, Comorbidities, Rheumatoid arthritis

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Background: The formation of neutrophil extracellular traps (NETs) with extrusion of nuclear, granular and cytosolic components from a dying neutrophil, has been described extensively in patients with rheumatoid arthritis (RA), and linked to generation of autoantigens (e.g. citrullinated proteins), inflammation and organ damage. Thus far there have been very few studies describing the effect of treatment in patients with RA on NET formation, and no studies comparing the effects of treatment strategies in (very) early RA.
Objectives: To assess the effects of different initial treatments on NET formation in patients with early RA.
Methods: NORD-STAR is an international, multicenter, open-label, assessor-blinded, phase 4 study where patients with newly diagnosed RA started methotrexate (MTX) and were randomized 1:1:1:1 to a) conventional treatment (either prednisolone tapered to 5mg/day, or sulfasalazine combined with hydroxychloroquine and intra-articular corticosteroids), b) certolizumab pegol, c) abatacept, or d) tocilizumab [1]. This study is a spin-off from the main NORD-STAR study measuring neutrophil biomarkers MPO-DNA (Myeloperoxidase-DNA; NETs) and calprotectin in 24 consecutive Dutch participants and 94 Swedish patients at baseline, 12 weeks and 24 weeks after the start of the treatment. Statistical analysis was done using the Wilcoxon Signed Rank test for paired samples and independent samples median test to compare patients to healthy controls in SPSS version 28.
Results: At baseline patients had elevated levels of NETs and neutrophil activation compared to healthy controls as indicated by calprotectin (median 1080ng/ml vs 133ng/ml, p<0.001) and elevated MPO-DNA (median 7185pM vs 3976pM, p<0.001). Both of the biomarkers decreased significantly at 12 and 24 weeks after treatment in the total group demonstrating reduced neutrophil activity and NET formation. After 24 weeks of treatment, calprotectin was significantly reduced in all groups by up to 93% (Table 1). MPO-DNA showed a more modest reduction of up to 13%, and was relatively similar in all groups, although the reduction in MPO-DNA did not reach statistical significance in the tocilizumab group.

Table 1. Results are reported as median (IQR) due to skewedness of the data. Reductions are reported as a percentage reduction compared to baseline. Measurements are marked with * if p<0.05, ** if p<0.01, * if p<0.001.**

	Baseline	Week 12	Reduction	Week 24	Reduction
Calprotectin (ng/mL)	1080 (1718)	231 (326) ***	-79%	214 (274) ***	-80%
Conventional treatment	1222 (2197)	354 (554) ***	-71%	285 (357) ***	-77%
Certolizumab pegol	1166 (1927)	213 (486) ***	-88%	157 (281) ***	-93%
Abatacept	850 (1323)	269 (313) ***	-68%	220 (354) ***	-74%
Tocilizumab	757 (1346)	169 (195) ***	-54%	184 (168) ***	-53%
MPO-DNA (pM)	7185 (2567)	6503 (2694) ***	-9%	6612 (2542) ***	-8%
Conventional treatment	7057 (4052)	6396 (2878) **	-11%	6629 (3092) **	-8%
Certolizumab pegol	7183 (2733)	6492 (3308) *	-10%	6549 (2608) *	-9%
Abatacept	7727 (2512)	7562 (4708)	-2%	6688 (3882) **	-13%
Tocilizumab	6904 (2168)	6120 (1921)	-11%	6509 (2113)	-6%

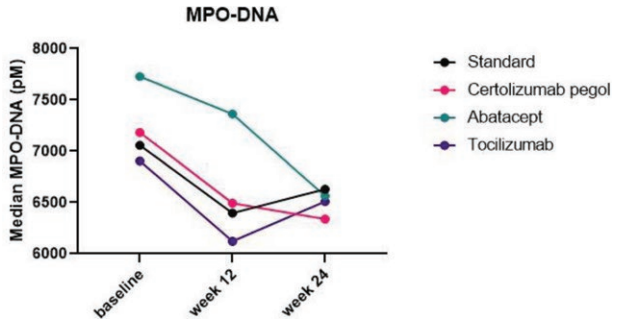


Figure 1. Median MPO-DNA over time (pM)

Conclusion: These results indicate highly elevated neutrophil activation and NET formation in recently diagnosed RA patients. All four treatments studied here reduced these detrimental processes within 3 months. The calprotectin reduction seen in this study is in line with an earlier spin-off study [2]. The rapid decline in these markers may have contributed to the minimal radiological progression that was seen in the NORD-STAR trial.

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POS0633 SAFETY OF GENETICALLY PROXIED TNF INHIBITION ON PREGNANCY RELATED OUTCOMES

Keywords: bDMARD, Pregnancy and reproduction, Epidemiology

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Background: TNF inhibitors (TNFi) have greatly improved the management of rheumatoid arthritis and several immune mediated inflammatory diseases. Although these diseases commonly start during childbearing age, the safety of TNFi in pregnancy is unclear, and is unlikely to change as clinical trials continue to exclude pregnant women for concern of harm to the foetus. Lack of scientific evidence to inform treatment decisions can contribute to maternal anxiety and suboptimally controlled disease. Naturally occurring variations in the genes that encode the protein drug target can provide population-level insights into safety, without exposing pregnant women to these drugs.

Objectives: To investigate the association between genetically proxied TNFi and pregnancy related outcomes, namely, spontaneous abortion, preterm birth, pre-eclampsia or eclampsia, gestational hypertension, gestational diabetes mellitus, and birthweight of the firstborn child.

Methods: To proxy TNFi, we selected uncorrelated (r^2>0.1) genome-wide significant ($p<5x10^{-8}$) single nucleotide polymorphisms within the gene encoding TNF receptor 1 (*TNFRSF1A*, build GRCh37/hg19: chromosome 12:6437923-6451280) from a genome wide association study (GWAS) of CRP among 337,199 individuals. CRP was (inverse rank-normal) transformed, with estimates scaled to per standard deviation (SD=4.35 mg/L) change in CRP. We selected CRP as the biomarker because clinical data show its suppression with TNFi. We estimated the F statistics of the instrument (square of the beta divided by square of the standard error) with F >10 being suggestive of adequate instrument strength. Genetic association data for spontaneous abortion (15,073 cases 135,962 female controls), preterm birth (7,678 cases 14,8153 controls), pre-eclampsia or eclampsia (6,436 cases 176,113 controls), gestational hypertension (7,503 cases 176,113 controls) and gestational diabetes (7,676 cases 130,424 controls) were derived from the FinnGen study. Data for firstborn birth weight (grouped into <7, 7 or >7 pounds (~3.2kg)) was obtained from 200,272 women in the UK Biobank. We included a positive control outcome, ankylosing spondylitis, and a negative control, multiple sclerosis. We used ratio method and, where an association was found, applied colocalization to test for genetic confounding.

Results: We identified one variant, rs1800693, to instrument TNFi. The F statistic was 65 suggesting adequate instrument strength. We found no evidence of associations between genetically proxied TNFi and any pregnancy related outcome (Figure 1) except gestational diabetes (OR 0.12 per SD reduction in CRP; 95%CI 0.03 to 0.57; p=0.007). The posterior probability of colocalization between CRP and gestational diabetes in the *TNFRSF1A* gene region was 99% conditional on the presence of a causal variant for the outcome, which provide evidence against genetic confounding.

Conclusion: We found no genetic evidence to suggest that TNFi is harmful for the selected outcomes relating to pregnancy. These results are reassuring and concur with observational data where women were exposed to TNFi during pregnancy. There was evidence that TNFi may be associated with lower risk of gestational diabetes. Further studies are needed to examine whether this is specific to diabetes during pregnancy or more generally. It is important to note that subtle differences in CRP levels through genetic variation may not be comparable to effects of pharmacological inhibition, and life-long exposure studied herein may differ from shorter duration of pharmacological intervention.

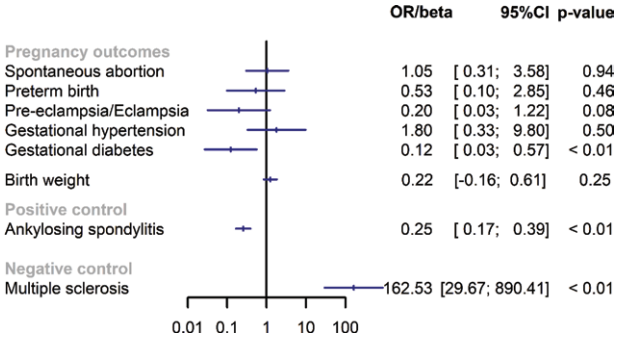


Figure 1.

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POS0634 EVALUATION OF THE SAFETY SKILLS OF PATIENTS WITH BIOLOGICAL DMARDS AFTER A THERAPEUTIC PATIENT EDUCATION PROGRAM

Keywords: bDMARD, Patient information and education

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Background: Biological DMARDs (bDMARDs) are well known cause a number of specific complications, including infectious ones. Patients receiving bDMARDs

must know them and acquire self-care and safety skills in order to take charge of themselves in risky situations. This is only possible thanks to therapeutic patient education (TPE) programs in chronic Inflammatory arthritis such as rheumatoid arthritis (RA), spondyloarthritis (SpA) and Psoriatic arthritis (PsA).

Objectives: To evaluate the impact of the therapeutic patient education program "EST-RIC" on the safety skills in patients treated with bDMARDs and on clinical parameters (Disease activity scores, compliance, number of infectious events, number of treatment stops, vaccination rate).

Methods: Non-randomized clinical trial comparing the knowledge and safety skills between two cohorts of patients with RA, SpA or PsA receiving bDMARDs for at least three months in the day hospital center of CHU of Constantine: group TPE (patients joined the "EST-RIC" therapeutic education program) versus group TPE-naive (patients who did not wish to participate).The primary outcome was the acquisition of safety skills at 3 and 6 months measured by the Biosecure questionnaire (0-100 scale), a 55 item validated questionnaire assessing competences to deal with fever, infections, vaccination, and other daily life situations [1]. The secondary outcomes were disease activity scores (DAS 28 for RA and BASDAI for SpA) at 6 months, compliance (Morisky score), number of infectious events, number of treatment stops, vaccination rate at 12 months.

Results: 450 patients were included, with mean age 41,6 ± 12,1 years old; 235 (52,2%) women; 192 (42,7%) had RA; mean disease duration 9,9 ± 6,6 years, 269 (60%) received subcutaneous bDMARDs. 240 patients in group TPE versus 210 patients in group TPE-naive. The median Biosecure score was significantly higher in the group TPE than in the group TPE-naive (75.7/100 versus 57.9/100; p<0.001) at 6 months (Table 1). There was a significant difference in disease activity scores: DAS28 and BASDAI, in rates of vaccination and discontinuation of treatment by forgetfulness. Regarding the observance to treatment or incidence of infectious events, there was no significant difference between the groups TPE and TPE-naive.

Conclusion: Safety is an important issue in the management of inflammatory arthritis treated with bDMARDs. In this trial, therapeutic patient education improves knowledge and safety skills of arthritis patient receiving bDMARDs, and disease activity scores.

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Table 1. The median Biosecure score at 6 months.

	Group TPE	Group TPE-naive	*P*
			<0,0001
Median Biosecure score	75,66	57,92	
Interquartile range	(70,98 - 78,72)	(50,96 - 65,28)	
MIN	52,78	28,80	
MAX	87,36	80,08	

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0635 METHOTREXATE MAINTENANCE ONE YEAR AFTER INITIATION OF A FIRST TARGETED THERAPY: RESULTS OF THE PROSPECTIVE STRATEGE 2 STUDY

Keywords: Rheumatoid arthritis, Treat to target, Disease-modifying drugs (DMARDs)

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Background: Methotrexate (MTX) is the first line standard of care for the management of rheumatoid arthritis (RA). In the event of an inadequate response to MTX and the presence of a poor RA prognosis factor, recommendations include initiation of biological (bDMARD) or synthetic (tsDMARD) targeted therapy in combination with MTX.

Objectives: STRATEGE 2 aims to establish the maintenance of MTX within two years of initiating a first targeted therapy.

Methods: STRATEGE 2 is a non-interventional study including RA patients treated with MTX for at least 3 months and requiring initiation of a first b/tsDMARD due to disease activity. The primary endpoint is maintenance of MTX unchanged within 12 months of initiation of targeted therapy. Non-maintenance is defined as: permanent discontinuation of MTX and/or dose reduction and/or transition from the subcutaneous route (SC) to oral (PO). Then, univariate and multivariate analysis was applied to identify potential predictors of MTX maintenance.

Results: Between Feb. 2019 and Dec. 2020, 53 French sites included 186 RA patients. Among them, data from 180 patients were analysable: 73.4% female, mean age 56.4 ±13.6 years, mean diagnostic oldness of 5.6 ±7.2 years, MTX treatment since 4.3 ±5.3 years, 71.7% via SC and the average dose was 19.9 ±3.9 mg/wk. The mean DAS28 score was 4.3 ±1.2 and the mean HAQ score was 1.0 ±0.7. At the end of the inclusion consultation, rheumatologists initiated a first targeted therapy: 8.6% by bDMARDs (anti-TNF: 58.4%, anti-IL6: 12.7%, Abatacept/Rituximab: 18.5%) and 10.4% by tsDMARDs. MTX was maintained unchanged in 76.1%, changed in 21.7% and stopped in 2.2% of the cases. The changes consisted of a dose reduction to 13.8 ±3.8 mg/wk for 19.4% of patients and a pathway change for 31.4% (from SC to PO). Approximately 12 months (377.8 ± 41.5 days) after initiation of targeted therapy, 95% of patients completed a follow-up visit (N=171). Of these patients, 6.4% had discontinued targeted therapy, 85.9% were on bDMARD (anti-TNF: 50.3%, anti-IL6: 12.8%, Abatacept/Rituximab: 22.8%) and 14.1% on tsDMARD. The average MTX dose was 18.0 ±4.2 mg/wk and MTX was administered SC for 59.4% of patients. According to the composite endpoint definition, MTX was maintained for 40.9% of patients. Non-maintenance was represented by 30% discontinuation, 44% of patients with a dose decrease only, 3% of patients with only a change in route of administration (from SC to PO) and 23% of patients with the two strategies. Using univariate analysis, three factors were selected for the multivariate: age (p=0.009), physicians' mode of practice (p=0.096) and patients who estimate having completely participated in the decision-making for the targeted therapy (p= 0.197). Only age was significative (OR=1.06, 95%CI [1.03,1.10], p<0.001), decision-making shows a strong trend (p=0.052) and both characteristics were adjusted on the mode of practice (p=0.256).

Conclusion: There are many therapeutic adaptations in the year following the initiation of b/tsDMARD. Twelve months after the introduction of b/tsDMARD, more than 8 out of 10 patients retained MTX as a combination therapy. Nearly 46% of patients had an adaptation of this treatment (dose reduction and/or return to the PO route). These practices are in line with the latest EULAR guidelines [1] which recommend the association of b/tsDMARDs with MTX.

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POS0636 SHOULD COMPLETE B-CELL DEPLETION BE SUSTAINED IN RITUXIMAB LONG-TERM TREATED PATIENTS FOR RHEUMATOID ARTHRITIS?

Keywords: bDMARD, Disease-modifying drugs (DMARDs), Rheumatoid arthritis

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Background: Complete peripheral B cell depletion has been considered as a relevant indicator of short-term response to rituximab (RTX) in rheumatoid arthritis (RA) [1,2]. However, no information is available to validate this observation in RA patients long-term treated with RTX.

Objectives: To determine whether sustained complete B cell (BC) depletion is associated with a better clinical response in RA patients long-term treated with RTX.
Methods: Retrospective routine care study conducted in the Rheumatology department of Cochin hospital. We included consecutive patients fulfilling the ACR/EULAR 2010 classification criteria for RA hospitalized in 2021 for a new RTX infusion. All recruited patients had received at least 3 prior RTX infusions and had disease activity assessment (DAS28 and DAS28-CRP) and CD19 counts (Aquios, Beckman Coulter) available during each of the 4 last infusion visits. The primary endpoint was the course of DAS28 and DAS28-CRP, calculated the day of the last 4 infusion visits according to sustained complete (mean CD19 counts <18/µL) or incomplete (mean CD19 counts ≥18/µL) BC depletion. Secondary endpoints were the frequency of end-of-dose effect and patient self-reported RA flares at each infusion visit, as well as the course of pain/fatigue VAS, CRP and gammaglobulin levels according to complete or incomplete B cell depletion.
Results: We included 126 patients (105 women, 83%) with a mean age of 64±12 years and a mean disease duration of 22± 5 years. Only 43 patients (34%) had maintained complete BC depletion during the last 4 infusions (mean CD19 counts 13±4/µL) (**Figure 1A-B**). Patients with incomplete BC depletion (n=83, mean CD19 counts: 77±73/µL, p<0.001) did not differ from those who maintained complete BC depletion in terms of age, gender, disease duration, structural damages and concomitant treatment. Patients with incomplete BC depletion had a higher frequency of rheumatoid factor (92% vs. 77%, p=0.018) and ACPA (84% vs. 72%, p=0.11); these patients had received RTX for a longer period (99±57 months vs. 69±47 months, p=0.003), with significantly higher number of infusions (14±7 vs. 12±6 infusions, p=0.037) and increased cumulative dose (10±6 g vs. 8±5 g, p=0.10) compared to patients with sustained complete BC depletion. On the other hand, their interval between 2 infusions was significantly longer (8±3 months vs. 6±1 months, p<0.001). The course of DAS28 and DAS28-CRP during the last 4 infusions was not different between the 2 groups (**Figures 1C-D**). The mean DAS28 and DAS28-CRP calculated at the time of last 4 infusion visits did not differ between patients with incomplete or sustained complete BC depletion (DAS28: 2.71±1.06 vs. 3.01±1.10, p=0.33 and DAS28-CRP: 2.53±0.88 vs. 2.88±0.84, p=0.095). The frequency of an end-of-dose effect and self-reported flares was similar between the 2 groups, as well as the evaluation of pain VAS, asthenia VAS, CRP and gammaglobulin levels (**Figures 1E-H**).
Conclusion: Maintaining complete BC depletion is not a therapeutic target to achieve in RA patients in long-term maintenance therapy with RTX. These results show that it is possible to space out RTX infusions to 8 months without loss of clinical benefit, which remains identical to that of patients treated every 6 months with sustained BC depletion. This result may have clinical implications during the COVID-19 pandemic since the antibody response to SARS-CoV-2 vaccination is preferentially obtained in patients with detectable B cells [3].
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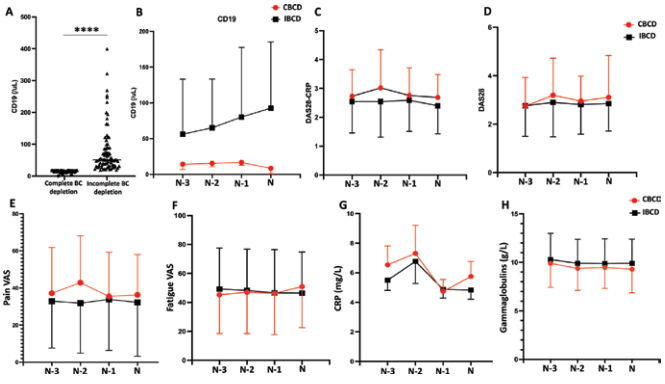


Figure 1. Course of mean (±SD) CD19, DAS28, DAS28-CRP, pain and fatigue VAS, CRP and gammaglobulins at the last 4 RTX infusion visits according to sustained complete or incomplete B cell depletion (CBCD and IBCD respectively).

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Disclosure of Interests: None Declared.
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POS0637

USING THE "POTENTIAL-OUTCOMES FRAMEWORK" TO PREDICT ADDED VALUE OF MORE INTENSIVE INITIAL THERAPY FOR INDIVIDUAL EARLY RA PATIENTS

Keywords: Treat to target, Clinical trials, Rheumatoid arthritis

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Background: DMARDs are the cornerstone of early RA treatment with Methotrexate (MTX) typically used as a first line treatment. More intensive initial combination therapy has been evaluated in clinical trials showing limited added value with longer follow-up in a treat-to-target (T2T) strategy [1,2]. Such studies report the treatment effect on group level, however, precision medicine requires information on which individuals will respond relevantly better to a more intensive therapy compared to MTX.
Objectives: The aim of this study was to identify whether clinically relevant heterogeneity in treatment effect exist, utilizing a "potential-outcomes framework" approach and to explore whether individual added value of more intensive therapy can be predicted.
Methods: We used data from U-Act-Early. This RCT compared initiating MTX monotherapy, tocilizumab (TCZ), and MTX + TCZ treatment in a T2T strategy in early RA with monthly disease activity assessment [1]. Time averaged CDAI score over 6 months was the primary endpoint. As physician VAS was missing a previously reported modified (m) CDAI was used [2]. Time-averaged mCDAI over 24 months and DAS28 over 6/24 months were secondary outcomes. For each patient we predicted outcomes of the treatments that they were not allocated to using multiple imputation (150 imputations using a random forest method). Predicted Individual Treatment effects (PITE) for each treatment comparison were calculated and the variation in PITEs between patients was evaluated. We used logistic regression to predict added value of more intensive treatment.
Results: Figure 1A shows the average PITE for TCZ + MTX versus MTX monotherapy as initial treatment over 6 months. 134 of 299 patients (45%) would relevantly benefit from MTX + TCZ (green part Figure 1). We defined sufficient added value for an individual patient as Cohen's effect size ≥0.8. Added value of MTX + TCZ could be predicted to a limited extent with the same variables used for imputation (AUC-ROC 0.65 (95% CI 0.56-0.73); Table 1 and Figure 1B). At 24 months 36% could be defined as benefitting from more intensive initial treatment. When using DAS28 as outcome measure 87% and 82% of patients benefitted respectively at 6 and 24 months. Added value could also be predicted to a limited extent (AUC-ROC 0.63 (0.54-0.71); 0.66 (0.56-0.75) and 0.63 (0.54-0.71) respectively) using logistic regression.
Conclusion: Relevant added value of more intense initial treatment for individual early RA patients could be defined and predicted to some extent using clinical predictors. However, thresholds for relevant clinical benefit as well as prediction should be improved and validated.
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Table 1. Prediction of added value of MTX+TCZ: results of logistic regression analysis

Predictor	Odds-Ratio	95% CI
mCDAI	1.02	0.98-1.06
HAQ	1.26	0.60-2.67
ln(CRP)	1.12	0.72-1.67
ln(BSE)	1.14	0.66-1.95
tender-swollen joint difference	1.01	0.97-1.08
VAS disease activity	0.99	0.97-1.01
age	0.99	0.97-1.02
Gender (male)	1.05	0.48-2.31
BMI	0.99	0.92-1.07
Smoking (no)	1.02	0.48-2.17
Alcohol (amount)	1.0	0.95-1.06
Rheumatoid factor presence	1.17	0.53-2.57

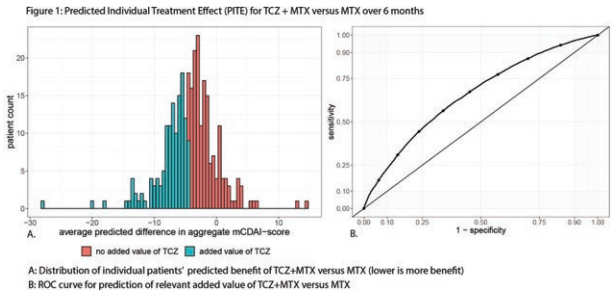


Figure 1.

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POS0638 SURVIVAL OF BIOSIMILAR ANTI-TNFA BLOCKERS COMPARED TO ORIGINATOR MOLECULES IN RHEUMATOLOGY: RESULTS FROM THE BIOBADASER COHORT

Keywords: Disease-modifying drugs (DMARDs), Real-world evidence, bDMARD

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Background: Recent data from a large cohort showed that biosimilars had no shorter survival than their originator molecules [1]. Although the survival of biological therapies in real practice has been recently analyzed in Spanish patients with rheumatic diseases (2), we do not know if there are differences in treatment survival, depending on whether the patients receive an originator or a biosimilar molecule.
Objectives: The main objective of this study was to compare the retention rate between subcutaneous biosimilar TNFα-blocker molecules and their originators. The secondary objective was to analyze the factors associated to drug survival.
Methods: Retrospective analysis of BIOBADASER cohort, the Spanish multicenter prospective registry of patients with rheumatic diseases with biological disease-modifying anti-rheumatic (bDMARD) or targeted drugs. We included patients who received originator or biosimilar molecules of etanercept or adalimumab for at least 6 months until December 2020. To avoid the *nocebo* effect, patients who had switched from the innovative molecule to the same biosimilar molecule were excluded. The drug retention rate was calculated considering all reasons for discontinuation as completion events, and analyzed using Kaplan-Meier curves for first and subsequent lines of treatment, adjusting for the use of concomitant conventional synthetic DMARD (csDMARD) and corticosteroids (CS). Hazard ratios (HR) were estimated using a Cox regression model, to identify factors associated to differences in the survival rates of biosimilar compared to originator molecules.
Results: A total of 4566 courses of treatment (2543 of adalimumab and 2023 of etanercept) and 4106 patients were included for this analysis. Biosimilars were used as 1st treatment in 51.1% of patients, as 2nd line in 39.2% and 3rd or subsequent lines in 37.7%. The use of csDMARD occurred in 63.8% of the cases and CS in 37.3%. Demographic and basal clinical characteristics of the patients are shown in Table 1. The main reason for discontinuation was inefficacy or loss of efficacy (58.1%), followed by adverse events (18.8%), pregnancies (3.5%), and remission (3.3%). The survival was higher for biosimilars (HR 0.68, 95% CI 0.53-0.98; p=0.002). Neither the disease type, sex, age, disease duration nor the concomitant treatments with CS or csDMARD influenced the retention rate. The survival was lower in smokers (HR 1.23, CI1-1.52; p=0.046), patients with overweight (HR 1.3, 95% CI 1.1-1-6; p=0.006) and 3rd line of treatment (HR 1.34, 95% CI 1.1-1.7; p=0.014). Among patients with adalimumab, survival was associated with JIA (HR 0.37, CI 0.16-0.85; p=0.015) and AS (HR 0.63, CI 0.43-0.91; p=0.015).
Conclusion: In real world practice, the survival of biosimilar TNFα-blocker molecules adalimumab and etanercept is higher compared to their originator molecules. Smoking, overweight and drug use in 3rd or subsequent lines of treatment are associated with a lower retention rate.
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Table 1.

	Alimumab	+ Etanercept	
	Originator(%)	**Biosimilar(%)**	**Total(%)**
Age at start, years, *mean (SD)*	48.2 (9.4)	51.4 (8.5)	8.50 (9)
Disease duration, years *mean (SD)*	14.6 (8.7)	13.7 (9)	9.00 (8.8)
Men	874 (52.1)	805 (47.9)	1679 (47.9)
Women	1247 (51.4)	1180 (48.6)	2427 (48.6)
RA	826 (47.5)	912 (52.5)	1738 (100.0)
JIA	138 (66.3)	70 (33.6)	208 (100.0)
AS	543 (52.7)	487 (47.3)	1030 (100.0)
PsA	614 (54.3)	516 (45.7)	1130 (100.0)
Overweight	471 (41.5)	664 (58.5)	1135 (100.0)
Smoker	420 (49.1)	436 (50.9)	856 (100.0)
Chronic CS	909 (53.4)	794 (46.6)	1703 (100.0)
csDMARD	1573 (54%)	1340 (46%)	2913 (100.0)
1st line treatment	1244 (48.9)	1299 (51.1)	2543 (100.0)
2nd line treatment	732 (60.8)	472 (39.2)	1204 (100.0)
3rd or subsequent line	510 (62.3)	309 (37.7)	819 (100.0)

csDMARD: conventinal synthetic disease-modifying anti-rheumatic drugRA: rheumatoid arthritisJIA: juvenil idiopatic arthritisAS: Ankylosing SpondylitisPsA: psoriatic arthritis

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Disclosure of Interests: None Declared.
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POS0639 SWITCHING FROM IL-6R ANTAGONISTS TO OLOKIZUMAB, A DIRECT IL-6 INHIBITOR

Keywords: bDMARD, Rheumatoid arthritis

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Background: Olokizumab (OKZ), an IL-6 ligand inhibitor in doses of 64 mg every two weeks (q2w) or every 4 weeks (q4w) demonstrated significant improvements in signs and symptoms of RA. Due to lack of availability of the IL-6 receptor antagonists tocilizumab and sarilumab in the pandemic COVID-19 situation, RA patients (pts) were switched to OKZ as a registered drug in Russia in 2022.
Objectives: To investigate safety and efficacy of OKZ after switching from an IL-6 receptor inhibitor in clinical practice.
Methods: This retrospective cohort study included available efficacy and safety data of OKZ in pts with RA after switching from tocilizumab (IV or SC) or sarilumab (SC) from 11 of participating centers. Efficacy assessments and routine biochemical data were analyzed using descriptive statistics – mean with standard deviation for continuous parameters and absolute and relative frequency for binary variables. AE were reported by participating centers according to pt's files. The statistical significance of data of the analyzed variable at a particular visit compared with previous visits or with the Switch visit was determined using paired t-test. Fisher's exact test or chi-square test was used to compare the proportion of pts with improvement/no change and worsening. All tests were 2-tailed, and a p-value <0.050 was considered statistically significant. As this is an observational study, the statistical criteria have not been pre-specified and therefore the data presented cannot be considered definitive but should be confirmed in future analyses.
Results: Efficacy and safety results were collected for 110 RA pts with a mean age of 47.8 (15.7) years, including 87 (79.1%) women. 77 (70.0%) pts were RF/ACPA positive. Mean RA duration was 13.1 (8.9) years and mean duration of treatment with an IL-6 receptor antagonist was 47.8 (30.0) months. Mean interval before switching was 54.7 (35.4) days with the main reason of unavailable IL6-R antagonist. Pts were treated with OKZ 64 mg q4w SC. Before initiation of OKZ, an increase of DAS28-CRP was observed due to a prolonged period after the last injection of the IL-6R inhibitor from 2.8 to 3.1 weeks in 32 pts on monotherapy who were transferred to OKZ faster (on average after 41.6 (23.8) days), and

from 2.7 to 3.3 weeks in 73 pts on concomitant sDMARDs (60.0 (38.0) days). DAS28-CRP was improved to 2.8 on the second OKZ visit (S+1) in both groups. Response to OKZ was maintained over a period of 2 months with no difference between pts previously receiving an IL-6 R antagonist. Of note, lower disease activity based on DAS28-CRP of 2.5 and 2.6 was achieved after 8 weeks (S+2) of OKZ therapy compared to the previous IL-6R inhibitors treatment S-1 visit (P less 0.05) (Figure 1).

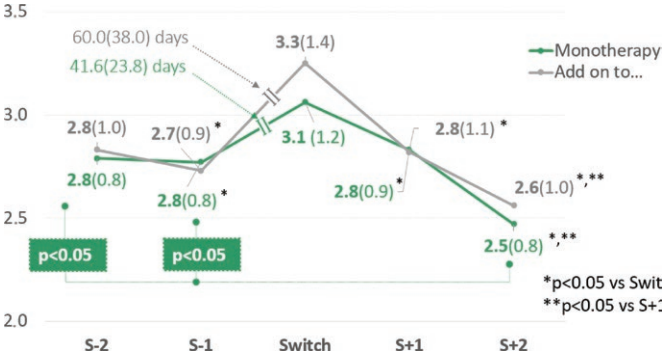


Figure 1. Mean DAS28CRP over time, M(SD)

Abbreviation: S-2 and S-1 last visits before switching– S+1 and S+2 visits after switching, Treatment emergent AE occurred in 7 (6.4%) pts, the most common AE in 3 pts (2.7%) included arthralgia of hands and feet and transient leukopenia in 2 (1.8%) pts. Serious AE were reported by 1 (0.9%) pt (exacerbation of herpes infection that led to treatment discontinuation). No deaths were reported. There were no apparent differences in safety and efficacy outcomes between pts on OKZ monotherapy compared to combined treatment with csDMARDs. Only one pt was switched back to tocilizumab when it became available.

Table 1. Summary of treatment emergent adverse events (safety population)

N	OKZ 64 mg q4w with MTX N=78	OKZ 64 mg q4w monotherapy N=32
Any AE	5	1 carpal canal syndrome
Any serious AE	1	0
Any AE leading to discontinuation of study drug	1	0
Any death	0	0
Any AE of special interest	1	0
Infections	1	0
Laboratory abnormalities	Hyperbilirubin-emia	ALT, AST elevation less than 3 ULN

ALT, alanine transaminase; AST, aspartate transaminase; ULN, upper limit of normal

Conclusion: In pts with RA responding to an IL-6R antagonist, switching to OKZ was safe and well tolerated in clinical practice. The treatment response was maintained and in some pts disease activity moderately decreased in comparison to baseline level both in OKZ mono and combination therapy.

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POS0640

OLOKIZUMAB IMPROVED PATIENT REPORTED OUTCOMES IN MTX AND TNF INCOMPLETE RESPONDER RHEUMATOID ARTHRITIS PATIENTS: RESULTS FROM THE LONG TERM EXTENTION TRIAL

Keywords: Patient reported outcomes, Clinical trials, Rheumatoid arthritis

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Background: Olokizumab (OKZ) is an interleukin-6-inhibitor for treatment of RA. We present patient reported outcomes (PROs) reported in a long-term extension trial (OLE) (ClinicalTrials number NCT03120949).

Objectives: To assess long-term effect of OKZ treatment in patient global assessment of disease activity (PtGA), pain, physical function (HAQ-DI), fatigue (FACIT-F) and health related quality of life (SF-36 physical (PCS) and mental (MCS) component summary and domain scores).

Methods: Patients (pts) who completed phase III core studies (within 24 weeks) were continued on OKZ 64 mg q2w or q4w, or were randomized 1:1 to receive OKZ 64 mg q2w or q4w following placebo (PL) or adalimumab (ADA) in RCTs with an OLE period of up to week 82. PROs through CORE and OLE phases are summarized as observed data by treatment groups using descriptive statistics.

Results: Baseline demographics and disease characteristics of 2104 enrolled pts were comparable between groups. The achieved improvement from CORE baseline to OLE baseline in PtGA, Pain, HAQ-DI, FACIT-F, SF-36 PCS, MCS and all domains under treatment with OKZ q2w and q4w was maintained over the full observation period of 106 weeks (Table 1, Figure 1). SF-36 improvements reported from OLE BL continued (in 5 domains) or increased (in 3 domains: PF, RE and RP) with OKZ until week 82.

Table 1. Patient reported outcomes dynamics

Mean (SD)	OKZ q2w N= 745			OKZ q4w N= 783			Adalimumab → OKZ N= 462			Placebo → OKZ N= 455		
	Core BL	OLE BL	Week 82	Core BL	OLE BL	Week 82	Core BL	OLE BL	Week 82	Core BL	OLE BL	Week 82
PtGA-VAS (mm)	67.6 (19.6)	32.3 (21.4)	31.4 (24.0)	67.4 (19.5)	32.0 (21.4)	30.7 (22.6)	66.7 (21.0)	31.3 (22.7)	29.5 (23.3)	68.8 (18.6)	42.7 (22.3)	32.6 (23.3)
Change from OLE BL			-0.2 [-2.1 -1.7]			0.1 [-1.8 -2.0]			-0.1 [-3.8 -1.4]			-10.0 [-13.1 -6.8]
Pain-VAS (mm)	68.6 (19.6)	30.4 (22.3)	29.4 (25.0)	67.6 (20.1)	29.9 (21.6)	28.5 (22.7)	66.8 (21.5)	30.5 (23.1)	27.7 (23.6)	67.6 (20.0)	41.2 (23.2)	30.0 (23.3)
Change from OLE BL			-0.4 [-2.4; 1.6]			0.2 [-2.1; 1.6]-			2.0 [-4.6; 0.5]-			10.4 [-13.7; -7.2]
HAQ-DI	1.74 (0.55)	1.03 (0.64)	0.99 (0.67)	1.70 (0.58)	1.02 (0.62)	0.94(0.66)	1.72 (0.57)	1.03 (0.67)	0.95 (0.68)	1.74 (0.58)	1.29 (0.67)	1.03 (0.67)
Change from OLE BL			-0.03 [-0.1; 0.0]			-0.04 [-0.1; 0.0]			-0.04 [-0.1; 0.0]			-0.24 [-0.3; -0.2]
SF-36 PCS score	31.7 (6.8)	41.1 (8.4)	42.0 (9.2)	31.7 (7.1)	41.1 (8.0)	42.4 (8.8)	31.4(7.4)	40.8 (8.6)	42.4 (9.3)	31.7 (6.9)	37.7 (8.0)	41.6 (9.1)
Change from OLE BL			0.8 [0.2; 1.5]			1.0 [0.4; 1.6]			1.2 [0.3; 2.0]			3.8 [2.9; 4.7]
SF-36 MCS score	43.1 (11.6)	49.1 (10.1)	48.7 (10.3)	43.5 (11.1)	49.7 (9.8)	49.4 (10.0)	44.1 (11.4)	49.8 (10.1)	50.1 (9.9)	42.8 (10.2)	46.4 (10.8)	46.2 (10.7)
Change from OLE BL			0.5 [-0.3; 1.2]			0.3 [-0.5; 1.0]			-0.2 [-1.2; 0.7]			2.0 [0.9; 3.1]
FACIT-F	26.8 (10.3)	36.4 (9.7)	37.2 (10.4)	27.1 (10.1)	36.8 (9.6)	37.7 (10.2)	27.4 (11.3)	36.7 (10.0)	38.0 (10.6)	27.1 (9.6)	33.0 (10.3)	37.2 (10.0)
Change from OLE BL			0.7 [-0.1; 1.4]			0.7 [-0.03; 1.4]			0.9 [0.04; 1.8]			3.6 [2.5; 4.7]
EQ-5D	43.8 (21.5)	67.8 (20.5)	70.1 (22.3)	44.7 (21.4)	68.6 (19.8)	70.3 (21.0)	45.2 (22.1)	68.7 (20.9)	72.6 (21.2)	44.4 (22.8)	59.7 (21.6)	69.7(20.4)
Change from OLE BL			2.1 [0.1; 4.1]			1.3 [-0.5; 3.0]			3.5 [0.9; 6.0]			9.7 [6.9; 12.5]

[95% CI]. **Abbreviations**: CI, confidence interval; EQ-5D, Health Questionnaire 5 Dimension; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire Disability Index; MCS, Mental Component Summary; PCS, Physical Component Summary; PtGA, Patient Global Assessment of disease activity; SD, standard deviation; SF-36, Short Form-36 Health Survey; VAS, visual analogue scale.

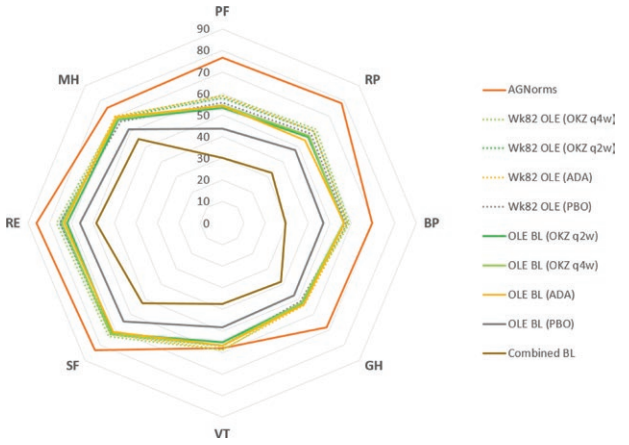


Figure 1. SF-36 domain changes from baseline to week 82.

Abbreviations: AGNorms, age- and gender-matched normative values; BL, baseline; BP, bodily pain; GH, general health; MH, mental health; OLE-open label extension; PF, physical functioning; q2w, every 2 week; q4w, every 4 week; RE, role emotional; RP, role physical; SF, social functioning; VT, vitality.

Conclusion: Treatment with OKZ resulted in sustained improvement of PROs in MTX and TNF-IR RA pts over a period of up to 106 weeks.

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POS0641

MACHINE LEARNING AND EXPLAINABLE AI METHODS CAN HELP TO PREDICT THE INEFFECTIVENESS OF INDIVIDUAL BIOLOGICAL DISEASE MODIFYING ANTIRHEUMATIC DRUGS (BDMARDS) – DATA FROM THE AUSTRIAN BIOLOGICAL REGISTRY BIOREG

Keywords: bDMARD, Artificial intelligence, Rheumatoid arthritis

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Background: The continuous development of biological disease modifying antirheumatic drugs (bDMARDs) in recent years has significantly improved the treatment options for patients suffering from rheumatoid arthritis. Selecting the most effective biologic remains a challenge, since therapy-response is highly individual depending on the patient history, laboratory values and demographics.

Objectives: The aim of this study was to investigate, if non-responders can be detected before therapy start using machine learning models and explainable artificial intelligence to provide a probability of non-response and to identify the most impactful contributing factors to the model output.

Methods: Data from the Austrian Registry for bDMARDs and tsDMARDs in Rheumatic Diseases – BIOREG were obtained. BIOREG provides a real-world data set, which covers rheumatology hospitals and practices throughout Austria. According to EULAR-guidelines the observation time window for treatment response is 6 months and the prediction time horizon was set at 6 months as well. Different machine learning models were trained for Abatacept (ABA), Adalimumab (ADA), Certolizumab (CERT), Etanercept (ETA) and Tocilizumab (TOC) to predict the risk of non-response per treat to target (ttt)-course. Nested cross-validation and hyperparameter tuning (iteration over fixed parameter grid) were applied. To evaluate the prognostic quality per model the area under the receiver operating characteristic (AUROC) was collected and the model with the highest score was selected for further evaluation. By applying the Explainable AI method SHAP (SHapley Additive exPlanations; a game-theoretic approach to evaluate variable importance) to each final model, the most contributing factors and direction of impact were evaluated.

Results: Data from 1397 patients, 2004 (baseline) visits and 22 variables (19 after cleaning) with at least 100 ttt-courses per drug were included in the study. The best models per biologic achieved an AUROC-score of: CERT: 0.76 (95% CI, 0.67–0.86). TOC: 0.72 (95% CI, 0.69–0.79), ABA: 0.71 (95% CI, 0.65–0.77), ADA: 0.67 (95% CI, 0.62–0.76), ETA: 0.68 (95% CI, 0.53–0.85). The explainable AI interpreted visual analytic scores (VAS) as most important variables for ABA, ETA and TOC. High scores were associated with high risk of non-response for these drugs. For ADA, co-therapy with glucocorticoids was the most important and risk-increasing factor. For CERT, the dosage of the prescribed drug was ranked as the most influential variable; high dosages were associated with lower risk of non-response. Interestingly, some variables displayed opposite impacts in different drugs: Male gender was interpreted as risk-increasing for ABA and risk-decreasing for ETA. Moreover, negative rheumatoid-factor was interpreted as risk-decreasing for ABA/ETA, but risk-increasing for ADA/CERT.

Conclusion: The results of our study show that non-responders of biological drugs can be detected with moderate to even good prognostic quality **before** starting a ttt-course, comparable to similar research with different prediction time horizons [1]. The opposite impact of some variables in different bDMARDs as well as the difference in variable importance per bDMARD indicate, that selecting the right drug is highly dependent on the individual patient characteristic. Machine Learning could be of additional support for rheumatologists and patients by providing not only a prediction of ineffectiveness per drug, but also an explanation for the prediction.

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Epidemiology, risk factors for disease or disease progression

POS0642

TREATMENT PATTERNS OF RHEUMATOID ARTHRITIS DURING TWO DECADES 2000-2020: REAL-WORLD DATA FROM A LARGE ISRAELI HEALTH MAINTENANCE ORGANIZATION

Keywords: bDMARD, Rheumatoid arthritis, Real-world evidence

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Background: Rheumatoid arthritis (RA) is the most common autoimmune inflammatory arthritis in adults. In recent years, the availability of therapeutic options for RA management has significantly increased. Yet, not all patients receive the recommended therapy (1 and real-world data on RA treatment patterns are limited.

Objectives: We aimed to identify and characterize RA patients, to examine their past and current treatment patterns, and identify factors associated with non-treatment.

Methods: We conducted a retrospective study using the computerized database of Maccabi Healthcare Services (MHS), a large health maintenance organization. Prevalent RA patients on Dec 31 2020 were defined by: ICD-9 code 714.X (≥2 diagnoses by a rheumatologist and/or ≥2 diagnoses by a primary care physician [PCP] and/or ≥1 diagnoses from a hospital with one diagnosis from a PCP); ≥1 rheumatoid factor (RF) test performed; age ≥18 years on the first diagnosis; first diagnosed before Dec 31 2018; MHS members for ≥12 months before and after the first RA diagnosis. RA patients also had to meet at least one of the following criteria: ≥1 purchase of disease modifying anti-rheumatic drugs (DMARDs) and/or ≥2 separate RA diagnoses by a rheumatologist and/or ≥1 positive RF test or anti-cyclic citrullinated peptide antibodies (anti-CCP) test. Patients were characterized according to socio-demographic and clinical factors. Treatment patterns with DMARDs were examined during 2000-2020. Multivariate logistic regression model was used to identify factors associated with current DMARDs treatment in 2020.

Results: We identified 8301 eligible RA patients (Table 1). The proportion of patients initiating treatment with any DMARDs within 12 months of diagnosis gradually increased from 37.8% in 2000 to 69.3% in 2010 and reached 80.0% for those first diagnosed in 2018. During 2000-2009, 60.0%-63.4% of the RA patients were not treated and during 2010-2020 53.8%-57.9% were not treated. Following the introduction of bDMARDs, the proportion of those using bDMARDs and/or tsDMARDs increased (Figure 1). The median time to treatment with the first bDMARDs decreased during follow-up, from 9 years (IQR 6.0-13.0) among those diagnosed in 2000 to 3 years (IQR 1.0-5.0) in those diagnosed in 2009, and to 1 year in those diagnosed in 2018 (IQR 0-1.0). In 2020, only 44.3% of the RA patients were treated with any DMARD. Patients with disease duration of 5-<10 years and disease duration of ≥10 years, were less likely to be treated with any DMARD in 2020 compared to those with disease duration of <5 years (OR 0.7, 95% CI 0.6-0.8; OR 0.6, 95% CI 0.5-0.7, respectively). Seropositive patients and those who initiated treatment with any DMARD within the first 12 months of diagnosis were more likely to be treated (OR 1.8, 95% CI 1.7-2.0; OR 3.5, 95% CI 3.2-3.9, respectively).

Conclusion: We observed an increase in the proportion of RA patients initiating treatment with any DMARD in the first year after diagnosis over the last two decades. Yet, about 55% of all RA patients were untreated in 2020, especially those with longer disease duration. Efforts should be made to optimize the disease management.

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Table 1. Baseline characteristics of RA patients (n=8301)

Age, Dec 31 2020 (SD)	63.6 (14.0)
Sex, Female	6,183 (74.5%)
Socio-economic status	
Low	1,487 (17.9%)
Medium	4,430 (53.4%)
High	2,384 (28.7%)
Age at diagnosis (SD)	50.9 (14.1)
Disease duration in years, Dec 31 2020 (SD)	12.2 (6.2)
Disease duration	
<5 years	1207 (14.5%)
5-<10 years	1901 (22.9%)
≥10 years	5193 (62.6%)
Seropositive, ever (rheumatoid factor and/or anti-CCP test)	4,429 (53.4%)
Oral corticosteroids use, 2020	222 (2.7%)
Comorbidities	
Ischemic heart disease	719 (8.7%)
Dyslipidemia	975 (11.7%)
Hypertension	4035 (48.6%)
Diabetes	1,806 (21.8%)
Osteoporosis	2,973 (35.8%)
Malignancy	1,582 (19.1%)

[1] **Mean (SD); n (%)**

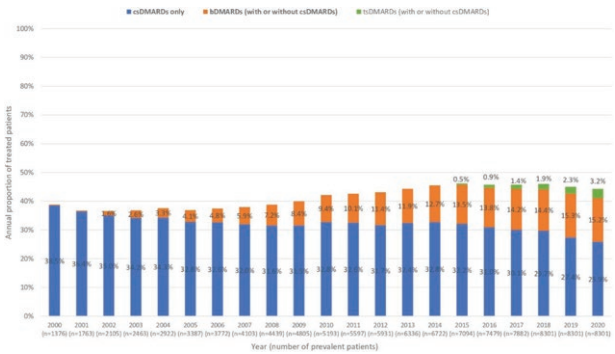


Figure 1. Treatment pattern among prevalent RA patients 2000-2020

Acknowledgements: NIL.

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POS0643

RITUXIMAB-ASSOCIATED HYPOGAMMAGLOBULINEMIA IN PATIENTS WITH RHEUMATIC DISEASES: A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY

Keywords: Safety, bDMARD, Real-world evidence

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Background: Rituximab (RTX) is a murine/human chimeric monoclonal antibody directed against the CD20 receptor expressed on pre-B and mature B cells. Rituximab is used effectively in the treatment of different rheumatic diseases, but it can induce hypogammaglobulinemia as a side effect.

Objectives: To analyze the prevalence of hypogammaglobulinemia and its association with infections in patients with rheumatic diseases treated with RTX.

Methods: Multicenter, retrospective, observational study. Patients with rheumatic diseases treated with RTX in 4 centers in Madrid, in which serum immunoglobulin counts were available, were included. Demographic and clinical variables of the sample were analyzed, and changes in immunoglobulin G concentrations during treatment from baseline were assessed. The chi-square test was used to examine the relationship between variables, considering a P value <0.05 as statistically significant. Logistic regression models were used to analyze the association between hypogammaglobulinemia and sample characteristics.

Results: One hundred and seven patients were included: 18 men (16.8%) and 89 women (83.2%), with a mean age of 55.9 (±13.9) years, a mean disease duration of 13.1 (±0.8) years, and a mean age of 51 (±14.4) years at the start of treatment. The most prevalent diagnoses were rheumatoid arthritis (RA) (50.5%), primary Sjogren's syndrome (pSS) (10.3%), and systemic lupus erythematosus (SLE) (10.3%). Fourteen (13%) patients were treated with RTX monotherapy. The rest

of the patients received concomitant treatment with other immunomodulators such as corticosteroids (64.5%), methotrexate (29%), hydroxychloroquine (27%), leflunomide (9.3%), sulfasalazine (1.9%), or mycophenolate mofetil (2.8%). Twelve (11.21%) patients developed hypogammaglobulinemia (IgG<600 mg/dl): 6 (50%) had RA, 1 (8.3%) SLE, 1 (8.3%) ANCA vasculitis, 1 (8.3%) leukocytoclastic vasculitis, 1 (8.3%) IgG4-related disease, 1 (8.3%) dermatomyositis, and 1 (8.3%) pSS. Patients with hypogammaglobulinemia had significantly lower mean serum IgG concentrations at the start of treatment (876.3 vs 1249.4 mg/dl; p=0.05). In the multivariate analysis, no variable related to hypogammaglobulinemia was found. Fifty-three (49.5%) patients presented infection, of which 17 (15.9%) were serious infections (those that required admission). The distribution of infection cases by groups (patients with and without hypogammaglobulinemia) is shown in Table 1. No significant differences were found in the development of infections or serious infections between patients with and without hypogammaglobulinemia. Only corticosteroid doses equivalent to ≥7.5 mg/day of prednisone were found as a risk factor for the development of infections (OR 3.48, 95% CI: 1.20-0.11; p=0.02).

Table 1. Hypogammaglobulinemia and infections in patients with rheumatic diseases treated with Rituximab.

	No infection (N, %)	Mild infection (N, %)	Serious infection (N, %)
Patients **without** hypogammaglobulinemia	55 (58.51)	24 (25.53)	15 (15.96)
Patients **with** hypogammaglobulinemia	7 (58.33)	3 (25)	2 (16.67)
p value		p=0.991	p=0.950

Conclusion: Patients with hypogammaglobulinemia had significantly lower mean IgG concentrations at the start of treatment with Rituximab than those who did not develop it. No greater frequency or severity of infections was observed between patients with and without hypogammaglobulinemia. Prednisone equivalent daily dose ≥7.5 mg/day was a risk factor for occurrence of infections. Larger sample size studies are needed to confirm these findings.

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POS0644 UNDERSTANDING REASONS INFLUENCING PATIENTS' PREFERENCES FOR THE MODE OF ADMINISTRATION OF ANTI-RHEUMATIC DRUGS IN INFLAMMATORY ARTHRITIS. A QUALITATIVE STUDY

Keywords: Patient information and education, Disease-modifying drugs (DMARDs)

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Background: The mode of administration is the third most important factor influencing patient preferences for the choice of antirheumatic drugs, after treatment benefit and risk of adverse events (ref1), with 30% of patients placing route and frequency of administration as their top choice (ref2).

Objectives: To understand the reasons of preferences of the patients with inflammatory arthritis (IA) towards the mode of administration of DMARDs (disease modifying anti-rheumatic drugs).

Methods: A qualitative study was conducted to explore the patients' perceptions and practices of DMARDs. The interviews were conducted by 3 anthropologists using in-depth semi directive and biographical methods, registered, transcribed and analysed using a thematic content analysis approach. Six domains were explored: (i) daily life with IA, (ii) practices of pharmacological and non-pharmacological treatments, (iii) the patient's social and work relationships, (iv) history of the patient pathway, (v) the patient–doctor relationship, decision-making, and (vi) medication daily management. The themes and subthemes related to the mode of administration (route and frequency of administration) were individualized.

Results: Overall 42 patients were included: 33/42, (33/42), with median age 51 years (17-82): 33 had rheumatoid arthritis (RA), 7 spondyloarthritis (SpA) and 2 psoriatic arthritis (PsA); 22 treated by cDMARDs, 19 by bDMARDs, 12 by JAK inhibitors (JAK-i), in monotherapy or combotherapy, 31 patients having more than 1 line of treatment. Four domains were found to influence patients' preferences: constraints and mental load, rituals and habits, empowerment versus a passive role, representation of disease for the patient and close ones. Subthemes are in Table 1.

Table 1. 8 subthemes associated with preference of patients for mode administration.

Subthemes	Intravenous	Subcutaneous	Oral
Time constraints	Half a day each month or more	Once a week or more	Every day/week
Logistical constraints	To stay available for appointments in hospital	Refrigerator storage, cold chain	No constraints in storage
Mental load	To stay available	Think about medication each week or more	Think about medication each day (for Jak-i)
Rituals	Rituals are managed and imposed by the hospital	Needs specific rituals from the patient	Integrated to existing rituals (i.e. meals)
Risk of forgetting treatment		Know what to do in case of skipped dose	Forgetting is a common phenomenon
Transfer of a medical procedure	Total medicalization, patient has a passive role	A medical procedure needs to be learnt	Tablets are more commonplace
Feeling ill	To go to the hospital makes you feel sick	Seeing the nurse makes you feel sick	Taking the tablets is more routine
The disease is made visible to others	To go to the hospital	« Sharing the fridge » An injection means a more serious disease	Tablets are more unobtrusive

Conclusion: Although many studies have looked for patients preferences, the reasons of the patients' choices for the mode of administration of targeted DMARDs were not well known. The reasons go beyond the simple "fear of needles" and reflect the integration of the treatment in the patients' representations and daily life and the visibility of the disease. This study brings clues that will help shared decision-making.

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POS0645 REAL LIFE SAFETY AND SURVIVAL OF TARGETED THERAPIES IN ARTHRITIS PATIENTS OVER AGE OF 65

Keywords: bDMARD, Targeted synthetic drugs

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Background: Prognosis for chronic inflammatory arthritis is drastically improved over previous decades and older patients are treated with targeted therapies (TTs) (biological or synthetic targeted therapies). Clinical trials provide mainly information about TTs in patients below the age of 65, so real-life studies are needed to provide more information about TTs in patients over 65 years of age.

Objectives: To compare clinical and therapeutic profile of arthritis patients undergoing TTs and to analyze safety and therapeutic survival according to different age groups.

Methods: We performed an observational cross-sectional study in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) patients, older than 40 years old, who started biological or anti-JAK therapy between 2000 and 2022 in the Rheumatology Department of HUP La Fe. A comparative analysis and a Kaplan-Meier survival analysis was performed.

Results: 938 patients (62% female) were included in the study, of which 20.3% are PsA, 55.6% RA and 24.1% AS, with a mean age at the beginning of treatment of 57 (10) years and a mean duration of treatment of 68 (64) months. Patients were classified according to the age at the beginning of treatment: 40-65 years and ≥ 65 years of age. 219 patients (23.3%) were over 65 years of age. In the Table 1 we show the comparative analysis between both groups. Higher proportion of arterial hypertension, diabetes mellitus and dislipemia in patients older than 65 years was observed. Using a logistic regression model, an association between conventional DMARD prescription and patients older than 65 years was found (P<0.001), being the methotrexate the most used (44.8%). Anti-TNF therapy was the most extended treatment in both groups of patients,

and an association between anti-IL6 therapy and older patients than 65 years was observed (P<0.001). Previous TTs were more frequent in older patients (P=0.002) and treatment duration was lower in those patients (P<0.001). Adverse events were more commonly found in patients older than 65 years as the reason to TT discontinue (P=0.008), being infections the more frequent.

Table 1. Comparative analysis of clinical profile of different age groups at the beginning of TTs.

Variable	40-65 years N=719	≥65 years N=219	P-value
	Mean (SD)/ n (%)	Mean (SD)/ n (%)	
Age at diagnosis (years)	43 (11)	56 (14)	< 0.001
Age at the beginning of treatment (years)	53 (7)	72 (5)	< 0.001
Time from the diagnosis to the beginning of treatment (years)	10 (10)	17 (12)	< 0.001
Treatment duration (months)	73 (66)	52 (52)	< 0.001
Female sex	425 (59.1%)	156 (71.2%)	0.001
Diagnosis:			
• RA	359 (49.93%)	163 (74.43%)	< 0.001
• PsA	168 (23.37%)	22 (10.05%)	< 0.001
• AS	192 (26.7%)	34 (15.53%)	< 0.001
Arterial hypertension	130 (29%)	84 (57.9%)	< 0.001
Diabetes mellitus	47 (10.5%)	32 (22%)	< 0.001
Dislipemia	124 (27.7%)	61 (42.1%)	< 0.001
Malignancy	54 (13%)	27 (22.5%)	0.016
DMARD concomitant			
• No DMARD	355 (49.4%)	79 (36.1%)	< 0.001
• Methotrexate	246 (34.2%)	98 (44.8%)	0.006
• Leflunomide	72 (10%)	22 (10.1%)	0.999
• Others	37 (5.2%)	20 (9.1%)	0.045
Targeted therapies:			
• ANTI-TNF	399 (55.5%)	86 (39.3%)	< 0.001
• ANTI-JAK	114 (15.9%)	33 (15.1%)	0.862
• ANTI-IL17	84 (11.7%)	12 (5.5%)	0.012
• ANTI-IL6	55 (7.7%)	32 (14.6%)	0.003
• Others	67 (9.3%)	56 (25.6%)	< 0.001
Continuing treatment			
Discontinued treatment by:	559 (77.9%)	158 (72.1%)	0.746
Primary non-response	10 (1.4%)	3 (1.4%)	0.895
Secondary non-response	27 (3.8%)	5 (2.3%)	0.401
Other causes	57 (7.9%)	18 (8.2%)	0.999
Adverse events	65 (9.1%)	35 (15.9%)	0.005
• Infection	11 (1.5%)	8 (3.7%)	0.093
• Malignancy	26 (3.6%)	7 (3.2%)	0.932

Conclusion: The use of conventional DMARDs, adverse events as the reason of treatment suspension and lower therapeutic survival are more frequent in patients older than 65 years of age.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0646 RISK FACTORS FOR POSTOPERATIVE COMPLICATIONS IN PATIENTS WITH RHEUMATIC DISEASES

Keywords: Outcome measures, Epidemiology, Inflammatory arthritides

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Background: Some patients with rheumatic diseases (RD) can require major surgical intervention. There are several risk factors for perioperative complications that must be addressed during de preoperative process [1,2].

Objectives: identify associated factors related to postoperative complications in patients with RD.

Methods: We performed a cohort study of patients with RD that required an elective or an emergency surgery from 2019-2021. We used as controls, patients with No-Rheumatic Diseases (NRD). All patients had preoperative assessment using Lee surgery index and the American College of Surgeons National Quality Improvement Program score (NSQIP), and we estimated disease activity of all RD according to the disease-specific activity scores. We follow-up patients until hospital discharge or death. Univariate and multivariate models were used to determine risk factors for postoperative complications (composite outcome: cardiac or lung complications, blood transfusion, infection, surgery reintervention, respiratory failure, use of vasopressors).

Results: We included 299 patients, 53 patients with RD and 246 NRD. The median age was 49 years in RD. Most patients with RD were women (85%). At baseline NRD patients had higher serum glucose levels, more use of insulin, and had higher rate of acute kidney injury. In the RD-group, 26 had rheumatoid arthritis, 13 systemic lupus erythematosus and 9 others (spondylitis, autoimmune hepatitis, antiphospholipid syndrome, polyarteritis nodosa). Active rheumatic disease was present in 21 patients. Most of the patients with RD (54%) had moderate to high risk of any complication, pneumonia, and risk of wound infection according the NSQIP score. The postoperative complications were higher in RD 37% vs NRD 16% (p=0.0003). Infection developed in 17% of RD patients vs 2.4% of NRD (p < 0.0001), uncontrolled hypertension was present in 3% in RD vs 0.4% in NRD, while hypovolemic shock was more frequent in NRD 4% vs 0%. One patient with RD died. Of the patients with RD, 58% continued with in-hospital glucocorticoid and 22% with another non-glucocorticoid immunosuppressor in-hospital. In the logistic regression analysis, the presence of active RD at the time of surgery (OR 4.9, IC95% 1.4-18) acute preoperative kidney injury (OR 3, IC95% 1.2-7.3) were predictors of post operative complications; type of surgery performed (elective or urgent), and in-hospital use of glucocorticoid, and immunosuppressors were not significant.

Conclusion: We observed higher post operative complications in RD patient's vs controls. The main prognostic factors were active rheumatic disease, preoperative kidney injury, while the type of surgery performed and in-hospital glucocorticoid or immunosuppressors were not associated to post operative complications.

Table 1. Baseline characteristics

	Rheumatic Disease (n=53)	No-Rheumatic Disease (n=246)	*p*-value
Age, median (IQR)	49 (19)	53 (18)	0.04
Female, n (%)	45 (85)	122 (49)	
Diabetes mellitus, n (%)	9 (17)	84 (34)	0.01
Systemic arterial hypertension, n (%)	22 (42)	90 (37)	0.46
Preoperative acute kidney injury, n (%)	1 (1.9)	27 (11)	0.03
NSQIP-Any risk, n (%)			<0.0001
High	13 (24)	17 (7)	
Moderate	16 (30)	37 (15)	
Low	24 (45)	192 (78)	
NSQIP-Serious risk, n (%)			<0.0001
High	13 (24)	14 (5)	
Moderate	7 (13)	28 (11)	
Low	33 (63)	204 (83)	
NSQIP-Surgical site infection risk, n (%)			<0.0001
High	13 (24)	12 (5)	
Moderate	16 (30)	28 (11)	
Low	24 (45)	206 (84)	
Surgery type, n (%)			
Elective	39 (74)	215 (88)	0.03
Urgent	14 (26)	31 (12)	
Glucocorticoids in-hospital, n (%)	31 (58)	4 (1.6)	<0.0001
Pre-hospital immunosuppressor, n (%)	12(22)		
Any complications, n (%)	20 (37)	40 (16)	0.0003

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Disclosure of Interests: None Declared.

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POS0647 A COMPARISON OF 20 YEAR DISABILITY OUTCOMES IN VALIDATED CASES OF RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS IN THE NORFOLK ARTHRITIS REGISTER

Keywords: Psoriatic arthritis, Rheumatoid arthritis, Outcome measures

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Background: Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are common inflammatory rheumatic diseases with distinct clinical phenotypes, that can

both result in significant disability. Whilst some data in selected samples report no difference in Health Assessment Questionnaire scores (HAQ) between RA and PsA(1), there is a lack of definitive long term population based data. The Norfolk Arthritis Register (NOAR) is an inception cohort of early inflammatory arthritis established in 1989, with over 4,500 cases of new onset inflammatory arthritis. Cases were recruited in primary care or from hospital clinics, and inclusion criteria were age >16 years with 2 swollen joints lasting ≥4 weeks. Data was collated on demographics and disability through Health Assessment Questionnaires (HAQ) over variable years of follow up (0-20 years); HAQ scores values range from 0 to 3, and the higher the score the greater the disability [2].

Objectives: Our aim was to compare differences between both baseline and follow-up HAQ scores in RA and PsA, in cases selected from the same base population and followed continuously for over 20 years.

Methods: Cases included in this study were recruits into NOAR, who were followed at intervals of 1, 2, 3, 4, 5, 7, 8, 10, 12, 15, 18 and 20 years. Cases of RA were defined using American College of Rheumatology (ACR) criteria; cases of PsA were classified by retrospective clinical record review. Cases with RA were compared to cases with PsA, and data analysis was carried out in R. Independent samples t-tests were used to assess statistical significance of unadjusted HAQ scores.

Results: A total of 1,812 cases of RA (85.4%) and 308 cases of PsA (14.5%) were identified with complete data on sex and age within the NOAR cohort who had recorded HAQ scores. The mean age of onset for RA was 56.3 years (min 18.6 – max 88.6; SD 13.9), and 47.3 years for PsA (min 16 – max 79.9, SD 13.1). Baseline HAQ: Mean baseline HAQ scores were higher for RA at 0.854 (SD 0.704) when compared with PsA at 0.706 (SD 0.688) (p<0.001). Females had higher baseline HAQ scores than males (0.915 vs 0.677) consistent across both disease types which was statistically significant (RA – 0.919 vs. 0.716, p <0.001: PsA – 0.885 vs. 0.533, p <0.001). Follow-up HAQ: Cases were followed up to 20 years. 1,812 cases of RA were identified at baseline, decreasing to 1552 with 1-year follow up (85.6%) and 165 cases with 20-year follow up (9.1%). 308 PsA cases were identified at baseline, 248 followed up at 1-year (80.5%) and 21 cases for 20-years (6.8%). Figure 1 illustrates that cases with RA had higher mean HAQ scores than PsA throughout a follow up period of up to 20 years. Mean HAQ scores accumulated over the follow up period for RA, whilst there was a decrease in HAQ scores after 12 years of follow up for those with PsA before increasing after 18 years.

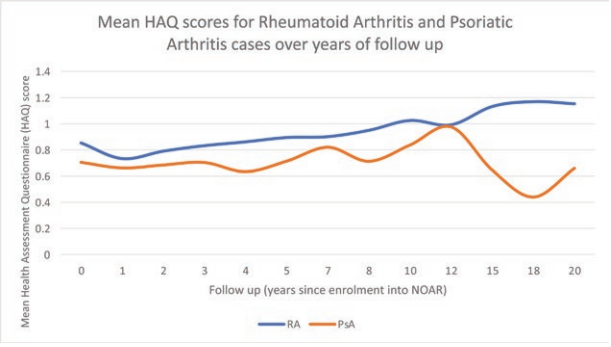


Figure 1. A comparison of the mean Health Assessment Questionnaire scores between Rheumatoid Arthritis and Psoriatic arthritis

Conclusion: The NOAR cohort is unique in its long follow up period of up to 20 years, allowing for the assessment of HAQ longitudinally. The relationship between higher HAQ scores in RA than PsA holds for both baseline HAQ scores and follow-up HAQ scores throughout the follow-up period, supporting the association of RA with greater disability. We hypothesise that this may be due to the nature of joint damage and other comorbidities associated with RA. We also demonstrate from this data that females present with statistically higher baseline HAQ scores than males within both diseases. In conclusion, there are evident trends with higher HAQ scores in RA over PsA consistent over time.

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Disclosure of Interests: None Declared.

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POS0648

EFFECT OF OBESITY ON DISEASE ACTIVITY OF PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: DATA FROM A NATIONWIDE COHORT

Keywords: Prognostic factors, Lifestyles, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic, multifactorial, inflammatory disease, and obesity is one of the risk factors implicated in RA development. Although obesity has been recently reported to be related to disease activity and clinical response of RA, the association between obesity and disease activity of RA is still controversial.

Objectives: This study aimed to investigate the effect of obesity on baseline disease activity and clinical response of patients with early RA.

Methods: Of 5,077 patients with RA enrolled in the Korean observational study network for arthritis (KORONA) registry, a nationwide RA-specific cohort, we identified 1,178 patients with disease duration of <2 years who had both baseline and 2-year follow-up data. Patients were grouped according to their body mass index (BMI): obese (BMI ≥25) and non-obese (BMI <25). Baseline and 2-year follow-up disease activity markers including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), swollen and tender joints, patient global assessment (PGA), evaluator global assessment (EGA), clinical disease activity index (CDAI), and health assessment questionnaire-disability index (HAQ-DI) were compared between two groups.

Results: Among early RA patients, 282 (23.9%) obese and 896 (76.1%) non-obese patients were identified. The non-obese group showed higher ESR than the obese group at baseline (29.9±0.9 vs 25.6±1.6, p=0.019), and other disease activity variables showed no difference according to the obesity status. When comparing the group who maintained obese (n=176) and non-obese (n=660) for two years, the obese group had higher CRP positivity (37.4% vs 26.9%, p=0.009) while other variables including CDAI showed no significant difference between the two groups.

Conclusion: Obesity was not associated with baseline disease activity and treatment response of patients with early RA. As obesity was related to CRP positivity in 2-year follow-up measurements, the use of disease activity tools containing CRP requires careful attention.

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Table 1. 2-year follow-up disease activity variables of obese and non-obese patients with RA

	Obese (n=176)	Non-obese (n=660)	p-value
ESR, mm/hr	22.5±1.7	23.5±0.8	0.606
CRP positivity	61 (37.4)	166 (26.9)	0.009
Tender joint count	2.15±0.25	1.86±0.18	0.305
Swollen joint count	1.79±0.15	1.50±0.08	0.100
PGA (0-100)	16.7±1.1	16.0±0.6	0.584
EGA (0-100)	33.1±1.8	33.0±0.9	0.975
CDAI score (0-76)	8.9±0.5	8.2±0.3	0.249
CDAI status			0.273
LDA	123 (70.3)	460 (70.4)	
MDA	42 (24.0)	172 (26.3)	
HDA	10 (5.7)	21 (3.2)	
CDAI remission, n (%)	19 (10.9)	65 (9.9)	0.716
HAQ-DI	0.42±0.04	0.41±0.02	0.840
Newly start of biologics	6 (3.4)	37 (5.6%)	0.241

Data are presented as number (%) or mean ± standard deviation, adjusted for gender, age, smoking status, income status, education levels, diabetes mellitus, and hypertension

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0649

WHEN DOES OBESITY EXERT ITS EFFECT IN CONFERRING RISK OF DEVELOPING RA – A LARGE STUDY IN COHORTS OF SYMPTOMATIC PATIENTS AT RISK

Keywords: Rheumatoid arthritis, Outcome measures

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Background: Case-control studies have identified body mass index (BMI) as a risk factor for development of rheumatoid arthritis (RA). However, it is unclear when BMI exerts its effect of increased risk, being either in the asymptomatic stage or in the symptomatic phase of Clinically Suspect Arthralgia (CSA) thereafter.

Objectives: To investigate this, we compared BMI of CSA-patients with the general population and we analyzed associations of BMI with progression to inflammatory arthritis (IA) within CSA-patients.

Methods: Firstly, 602 patients consecutively presenting with CSA were studied and followed during 2 years for development of IA. Their baseline BMI was compared to the mean BMI (corrected for age/gender) of the Dutch population (Statistics Netherlands,CBS,2012-2020). Secondly, cross-sectional associations between BMI and measures of inflammation, tender joint count (TJC-68) and C-reactive protein (CRP), were studied. Finally, the association of BMI and IA development was studied via cox-regression. Findings were validated in 295 additional comparable patients with CSA included in the SONAR (n=178) and TREAT EARLIER trial (placebo arm, n=117)); a pooled analysis was performed.

Results: CSA-patients had a higher mean BMI compared to the general population (26.5 vs 25.3 kg/m^2, p<0.001). Likewise, CSA-patients were more often obese (BMI ≥ 30 kg/m^2) than the general population (22.3 vs 13.8%, Figure 1A); this applied to both ACPA-positive and ACPA-negative patients and was confirmed in the validation cohorts. At baseline, obese CSA-patients had higher TJC-68(β 1.26(1.04;1.52)) and CRP (1.37(1.20;1.57)) than CSA-patients with a normal weight. However, obese CSA-patients did not have an increased risk of IA development (HR 0.66(95%CI 0.39;1.11), Figure 1B). Similarly in the validation cohorts, higher BMI was not associated with RA-development (OR per point BMI 0.98(0.95;1.01) for both cohorts together, Figure 1C)

Conclusion: Obesity is more frequent in CSA compared to the general population. Moreover, obesity is associated with higher inflammation at presentation with CSA but did not entail a higher risk for progression from CSA to IA. Hence, obesity primarily seems to exert its effect in the asymptomatic risk-stage of RA-development.

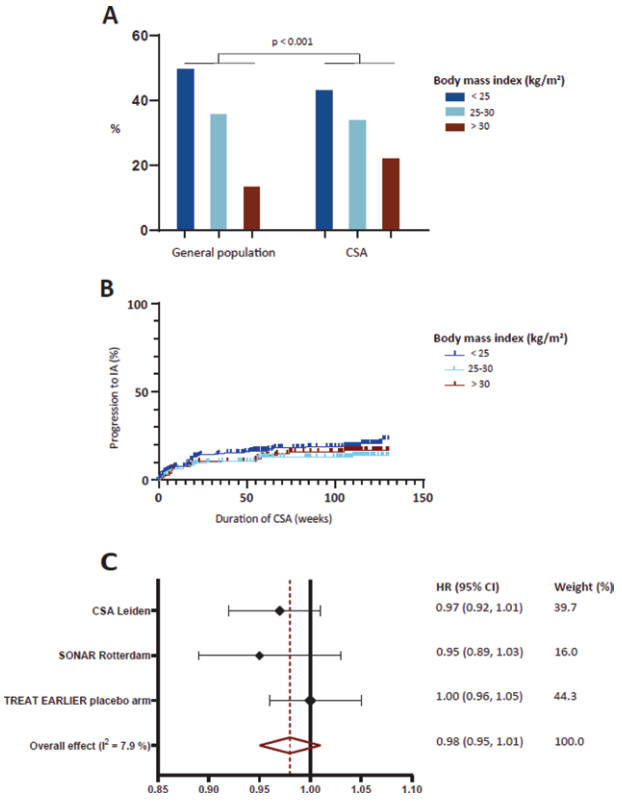


Figure 1. CSA-patients are more often obese than the general population (A); obesity in CSA-patients is not associated with IA development, studied via Kaplan-Meier analysis (B) or via pooled analysis of different cohorts (C).

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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Spondyloarthritis - clinical aspects (other than treatment)

POS0650

FACING THE ISSUES OF CHANGE IN ENTRY VISIT DIAGNOSIS AND LOST OF FOLLOW-UP OVER TIME IN INCEPTION COHORTS: DATA FROM THE AXIAL SPONDYLARTHRITIS (AXSPA) DESIR COHORT

Keywords: Spondyloarthritis, Epidemiology

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Background: Inception cohorts can be defined as long term follow-up of patients suffering at entry visit from a recent onset disease. Despite their huge advantage to better approach the truth in terms of long term prognosis of the disease, they are usually facing 2 issues: a) the possibility of a change in the entry visit (initial) diagnosis b) the missing data due to patients lost of follow-up.
Objectives: To evaluate both the frequency and the baseline predisposing factors of a) a change in the initial diagnosis b) the risk of loss of follow-up in the DESIR axSpA cohort.
Methods: *Study design*:DESIR is an ongoing (10 year follow-up completed for all the patients) multicenter cohort of recent onset axSpA. *Diagnosis*: At entry visit and during the 10 year follow-up period, this diagnosis was based on the opinion of the treating rheumatologist with the requirement of a highly suspected diagnosis of axSpA at entry visit and after the first 2 years of follow-up the possibility to exclude the patients in case of a change in the initial axSpA diagnosis. *Statistical analysis*: Multiple imputation was used to address missing data and estimates the probabilities of a change in initial axSpA diagnosis for each patient lost of follow up. Predisposing factors of an unchanged initial axSpA diagnosis were then evaluated using a multivariate logistic regression model on imputed data sets. A multivariate cox survival analysis exploring factors associated to the overtime risk of loss of follow-up was also performed.
Results: Of the 708 enrolled patients, 45 were excluded from the cohort because of a documented change in the initial axSpA diagnosis (mechanical low back pain n = 30, fibromyalgia n = 13, chronic inflammatory rheumatic disease (n = 1 and no information n = 1).The classification criteria were fulfilled by 16/45 (36%) versus 413/663 (63%) and 21/45 (47%) versus 522/663 (81%) patients with a documented change versus no change in their entry visit diagnosis according to the ASAS ax-SpA and the AMOR criteria respectively. During the 10 year follow-up period, 300 patients were lost of follow-up. Based on imputation, among these 300 patients, 19 patients were systematically suspected to have a change in their initial axSpA diagnosis in all imputations while 173 patients were never "suspected" for this change; 42 patients were considered as suspected for a change in their initial axSpA diagnosis in at least 70% of imputations. Predisposing factors of an unchanged initial axSpA diagnosis were (odds ratio [95% CI]): radiographic SIJ structural damage: 17.0 [4.1; 71.0]; past or present psoriasis: 5.3 [2.0; 14.3]; CRP ≥ 6 mg/l: 2.7 [1.3; 5.3]; good response to NSAID: 2.5 [1.5; 4.2]; HLA B27 positivity: 2.0 [1.3; 3.3]; anterior chest wall pain: 2.0 [1.2; 3.3] and female gender: 1.9 [1.2; 3.0]. Predisposing factors of the risk of loss of follow-up were: Age at back pain initiation< 45 years old: 1.8 [1.2; 2.9]; CRP < 6 mg/l: 1.5 [1.1; 1.9]; HLA B27 negativity: 1.4 [1.1; 1.8]; educational level < university: 1.4 [1.1; 1.8]; smoker: 1.3 [1.0; 1.6].
Conclusion: These data suggest that a) a change in the entry visit diagnosis and the risk of follow-up have to be considered in inception cohorts b) statistical models including multiple imputations could facilitate the evaluation of long term prognosis of the disease.
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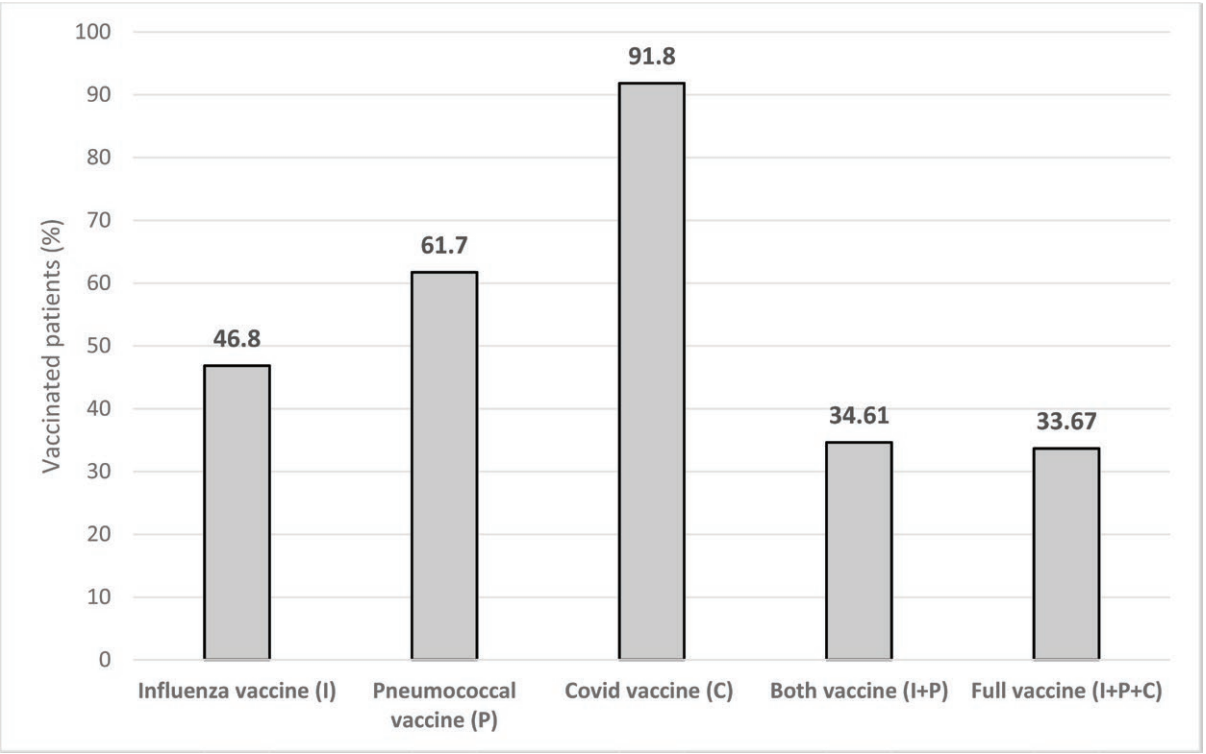
POS0651

VACCINATION RATE AND FACTORS ASSOCIATED WITH NON-VACCINATION IN AXIAL SPONDYLOARTHRITIS: A CROSS SECTIONAL PROSPECTIVE MULTICENTRIC OBSERVATIONAL STUDY

Keywords: Vaccination/immunization, Spondyloarthritis, COVID

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Background: Patients receiving biological therapy for auto-immune diseases are considered immunodepressed and multiple recent recommendations highlight the need for vaccination against influenza and pneumococcal infections.
Objectives: To evaluate influenza and pneumococcal vaccine coverage in patients receiving biological therapy for spondyloarthritis (SpA), and to identify factors associated with vaccination completion in this population.
Methods: We conducted a prospective cross-sectional study of a cohort of 500 patients taking biological therapy for axial spondyloarthritis between june 2021 and june 2022 in five teaching hospitals in France (university hospital centers Bordeaux, Clermont-Ferrand, Limoges, Montpellier-Nimes and Toulouse). Influenza and pneumococcal vaccine coverage rates were collected using a self-administrated questionnaire. Patients were queried about knowledge and opinions about these vaccines. We also investigated the respective role of physicians and rheumatologists in the care and reasons for not proposing the vaccines. SARS- COV 2 impact and vaccine rates were also assessed. To identify factors associated with influenza vaccination and with pneumococcal vaccination, we performed a univariate and multivariate analysis.
Results: Influenza vaccination was received by 46.8 % (n = 234) of patients. Pneumococcal vaccine had been previously administered to 61.7% (n = 307) of patients. Vaccination coverage against SARS-CoV-2 was high with 91.8% of vaccinated patients. Overall vaccine coverage rates were 34.6% for patients who received both influenza and pneumococcus vaccines and were 33% for those who received influenza, pneumococcus and Sars-COV2 vaccines. Factors associated with vaccinated status were a higher level of education (OR =1.66 (1.03-2.68), p=0.038) and taking part in educational therapy session (OR = 1.85 (1.12-3.06), p= 0.016) for pneumococcus, affiliation to a patients' association (OR=4.10 (1.10-15.2), p=0.035) and intravenous administration of bDMARD (OR = 3.12 (1.76-5.54), p=0,0001) for influenza. Patients reported that they did not seek vaccination (influenza, pneumococcus or both) because (1) they did not receive appropriate information on vaccination and (2) fear possible side effects.
Conclusion: This study showed insufficient vaccine coverage rates in a population at high risk because of exposure to biological therapy. Reasons for not being vaccinated included fear of adverse effects and lack of information and recommendations. Patient information by healthcare professionals about influenza and pneumococcal vaccination has a major impact and physicians should inform patients about vaccination as often as possible.
REFERENCES: NIL.
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Disclosure of Interests: AMORY Charlotte: None declared, Thomas Barnetche Paid instructor for: Biogen, Claire Rempenault: None declared, DESPRES Jerome: None declared, Jessika BERNARD: None declared, Maxime Vandersmissen: None declared, Justine LANDRIN: None declared, Adeline Ruyssen-Witrand Speakers bureau: AbbVie, Amgen, Biogen, Bristol Myers Squibb, Fresenius-Kabi, Galapagos, Janssen, Lilly, MSD, Mylan, Nordic-Pharma, Novartis, Pfizer, Roche Chugai, Sanofi, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Mylan, Novartis, Pfizer Inc, Sanofi Genzyme, Grant/research support from: AbbVie, Amgen, Mylan, Pfizer Inc, Pascale Vergne-Salle Speakers bureau: Abbvie, Fresenius, Grünenthal, Janssen, Pfizer, Roche Chugai, Sanofi, Novartis, Mylan, UCB, Lilly, Consultant of: anssen, Abbvie, UCB, Cécile Gaujoux-Viala Speakers bureau: bbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Gilead, Janssen, Lilly, Medac, MSD, Mylan, Nordic Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi et UCB, Consultant of: bbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Gilead, Janssen, Lilly, Medac, MSD, Mylan, Nordic Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi et UCB, Jacques Morel Speakers bureau: Abbvie, Amgen, Biogen, BMS, Fresenius Kabi, Galapagos, Lilly, Médac, Novartis, Pfizer, Sandoz, Sanofi, Consultant of: Abbvie, BMS, Boerhinger Ingelheim, Galapagos, GSK, Lilly, Novartis, Sanofi, Anne Tournadre Speakers bureau: Abbvie, Fresenius, Janssen, MSD, Pfizer, Roche Chugai, Sanofi, Paid instructor for: Fresenius, Consultant of: Abbvie, Fresenius, Lilly, Novartis, Sanofi, Grant/research support from: Fresenius, Novartis, Pfizer, UCB, Cédric Lukas Speakers bureau: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Consultant of: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Grant/research support from: Pfizer, Novartis and Roche-Chugai,
DOI: 10.1136/annrheumdis-2023-eular.3933



Graph 1. Comparison between vaccine coverage groups

Table 1. Reasons for non-vaccination

Reasons for non-vaccination (%)	Influenza	Pneumococcus	Both vaccine
Lack of proposal	40%	33%	23%
Fear side effect	17%	16%	9%
Advise against the vaccine by medicine	2%	2%	8%
Useless	5%	6%	3%
Non indication	2%	3%	1%
Forget or lack of time	9%	7%	5%

POS0652

INTEROBSERVER RELIABILITY AND SENSITIVITY TO CHANGE OF A COMPOSITE OCULAR INFLAMMATORY ACTIVITY INDEX: UVEDAI

Keywords: Uveitis, Validation, Outcome measures

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Background: Standardized and validated outcome measures of disease activity are lacking in the treatment and assessment of uveitis, making it difficult to compare efficacy and response to treatment. In 2014, this working group developed a composite index of ocular inflammatory activity, UVEDAI, which includes 7 variables. The index was validated in a subsequent study conducted in 2019.
Objectives: To determine the interobserver reliability and to demonstrate the sensitivity to change of the UVEDAI index in patients with anterior and non-anterior uveitis who undergo pharmacological treatment.
Methods: The design is an observational, longitudinal, prospective, multicentre study in 7 Spanish hospitals. Patients over 18 years of age diagnosed with active uveitis were included. A complete baseline visit was performed by two ophthalmologists who determined ocular inflammatory activity with the UVEDAI index independently and without contact between them. Ophthalmologist 1 made a new visit at 4 weeks to determine the change in the level of uveal inflammatory activity using the UVEDAI index. The interobserver reliability analysis was performed by calculating the Intraclass Correlation Coefficient (ICC), with the values of the variables and the UVEDAI index obtained by ophthalmologist 1 and ophthalmologist 2 in the most inflamed eye at the baseline visit. Sensitivity to change in the UVEDAI index was assessed at 4 weeks from the start of pharmacological treatment by determining the Clinically Relevant Change (CCR) defined as a change in UVEDAI of 0.8 points between the baseline visit and the 4-week visit.
Results: A total of 111 patients were included, 54.1% were male and the mean age at the time of the visit was 49.9 years. 36.9% of uveitis were idiopathic uveitis, and 58.6% were anterior uveitis. The UVEDAI value was calculated from the score obtained in the 7 variables of the index. The mean value recorded in the most inflamed eye at the baseline visit by ophthalmologist 1 was 1.9, being 1.2 points for anterior uveitis and 2.8 points for intermediate/posterior uveitis. In the interobserver reliability analysis, the ICC for the UVEDAI value was 0.9, and when compared to the mean UVEDAI values obtained by the two ophthalmologists for the most inflamed eye at the baseline visit, no statistically significant differences were found (p-value>0.05), neither for the total sample nor differentiating by anatomical location. As for sensitivity of UVEDAI change, statistically significant differences (p-value=0.00) were found when comparing the mean values of the index measured by ophthalmologist 1 at the baseline visit and at 4 weeks, both in the overall sample and differentiating by anatomic location of uveitis. In all cases, the index value decreased significantly by more than 1 point at the 4-week visit after pharmacological treatment.
Conclusion: The interobserver reliability of the UVEDAI was high in the total sample and in the different variables. Furthermore, the index was sensitive in determining the change in inflammatory activity after treatment in both anterior uveitis and intermediate/posterior uveitis/panuveitis. We believe it is an index of activity that could be used both in routine clinical practice and in clinical studies and trials to compare results objectively.

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Figure Interobserver Reliability: Differences obtained in the UVEDAI index score by ophthalmologist 1 and 2 at the baseline visit.

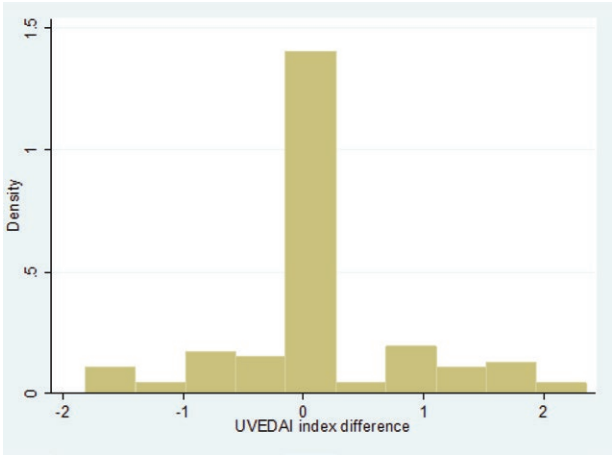


Figure 1.

Table Sensitive to Change: Mean value and difference in UVEDAI index value measured by ophthalmologist 1 in the active eye at baseline and at 4 weeks.

Table 1.

Anatomical Location	Anterior	Intermediate/ Posterior/Panuvetis	Total
UVEDAI INDEX baseline.opht.1*	1,2 ± 1,6	2,8 ± 1,8	1,9 ± 1,8
UVEDAI INDEX visit 4 wks.opht1*	0,2 ± 0,5	1,2 ± 1,5	0,6 ± 1,1
UVEDAI difference	1.04	1.54	1.25
p-value	0.00	0.00	0.00

*mean ± standard deviation

Disclosure of Interests: None Declared.
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POS0653 DIAGNOSTIC VALUE OF COMPUTER TOMOGRAPHY FEATURES OF SACROILIITIS FOR ANKYLOSING SPONDYLITIS

Keywords: Imaging, Spondyloarthritis, Diagnostic tests

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Background: Radiologic evidence of sacroiliitis is important for the diagnosis, classification, and management of patients with ankylosing spondylitis (AS)[1]. Conventional radiography (CR) has been the most widely utilized imaging modality for the assessment of sacroiliac involvement in axial spondyloarthritis (AxSpA) because of the low radiation dose, ease of operation, and low expenses. CR is used in both the 1984 modified New York criteria and ASAS criteria for classifying AS and AxSpA but lacks sensitivity for early changes. Though MRI detects early changes of the sacroiliac joints, as well as chronic structural changes, its use is limited by the associated cost, procedural time and certain contraindications. Computed tomography (CT) is a modality that enables visualization of erosions, sclerosis, and new bone formation, with the added benefit of multiplanar cross-sectional imaging.
Objectives: We aimed to analyze the diagnostic value of computer tomography (CT) features of sacroiliitis for ankylosing spondylitis in patients with inconclusive CR evidence for sacroiliitis.
Methods: In this retrospective monocentric observational study, 50 patients with chronic low back pain (LPB) with a duration longer than three months in the lumbosacral region were included. Using the patient record data were extracted on age, pain duration, and plain radiography. Eligible patients should have had plain radiography without evident radiographic sacroiliitis. All the patients had undergone a CT scan of the sacroiliac joint that a radiologist and rheumatologist evaluated for subchondral osteosclerosis, erosions, joint space narrowing (JSN), subchondral cysts, and ankylosis. Based on the clinical and instrumental findings, including structural changes characteristic of radiographic sacroiliitis, a final decision by a certified rheumatologist was made and a diagnosis of ankylosing spondylitis was set or ruled out.
Results: The mean age and duration of LBP of the patients were 44.7 (14.7) years and 63.9 months, respectively. Of the 50 included patients, 28 (56%) were females. The mean values of c-reactive protein and erythrocyte sedimentation rate were 13.9 mg/l and 39.4 mm/h. Subchondral osteosclerosis was found in 44 patients (88%), JSN – in 21 patients (42%), erosions – in 17 patients (34%), subchondral cysts – in 10 patients (20%), ankylosis – in 18 patients (36%). Definite CT data for sacroiliitis was seen in 24 patients (48%) and the diagnosis of ankylosing spondylitis was set in 23 patients (46%) of the study group. The likelihood ratios (LR+) for diagnosis of AS were high for erosions (18.4), subchondral cysts (11), ankylosis (6.9) and low for JSN (LR+ 1.9) and ankylosis (LR+ 1.1).
Conclusion: Nearly half of the patients with inconclusive CR evidence for sacroiliitis were diagnosed with AS after CT imaging. Erosions seen on CT increase the likelihood of assuming AS diagnosis. Computed tomography is a useful tool in diagnosing AS, but it is associated with higher ionizing radiation doses.
REFERENCE:
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Acknowledgements: NIL.
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POS0655 HLA-B27 POSITIVITY IN A LARGE MISCEGENATED POPULATION OF 5,389,143 HEALTHY BLOOD MARROW DONORS IN BRAZIL

Keywords: Genetics/epigenetics, Spondyloarthritis, Epidemiology

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Background: The prevalence of HLA-B27 gene positivity in healthy Caucasian communities varies between 8-14%. However, there is a lack of information in countries with a high rate of miscegenation, such as Brazil.
Objectives: To estimate the prevalence of HLA-B27 positivity in the Brazilian general population using a large national registry.
Methods: This is a cross-sectional ecological study using the Brazilian Registry of Volunteer Bone Marrow Donors (REDOME) database on HLA-B27 allelic frequency and proportion of positives from healthy donors (18-60 years old). Data were analyzed according to race (by self-reported skin color, according the predetermined five terms used by Brazilian Institute of Geography and Statistics [IBGE]), and geographic region of residence.
Results: From 1994 to 2022, a total of 5,389,143 healthy bone marrow donors were included. The overall positivity for HLA-B27 was 4.35% (CI 95% 4.32-4.37%). There was a difference according to race (Table 1): 4.85% in Whites; 2.92% in Blacks; 3.76% in Pardos (Browns i.e. miscigenated between blacks and whites); 3.95% in Amarelos (Yellows i.e. Asian Brazilians, predominantly of Japanese descent); and 3.18% in Indigenous, p<0.0001. There was also a difference regarding geographic region as shown in Figure 1 (North: 3.62%; Northeast: 3.63%; Southeast: 4.29%; Midwest: 4.5% and 5.25% in South, p<0.0001). The homozygosity rate for the HLA-B27 was 1.32% of all the positives and only 0.06% in the general population.
Conclusion: Our findings provide the first Brazilian national prevalence for HLA-B27 in 4.35%, with differences between races, similar to previously published in another miscegenated population [1]. There is a positivity gradient from North/Northeast (Pardos/Brown predominant population) to South (White predominant population), suggesting that the genetic background related colonization and internal migratory flows, could explain our findings.
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Table 1. HLA-B27 prevalence of positivity, according to races (defined by self-reported skin color) in Brazil, according to the REDOME database.

Race	HLA-B27 positivity % (95%CI)
Whites	4.85 (4.81 – 4.88)
Blacks	2.92 (2.85 – 3.00)
Pardos (Browns)	3.76 (3.71 – 3.80)
Amarelos (Yellows)	3.95 (3.82 – 4.08)
Indigenous	3.18 (2.85 – 3.52)

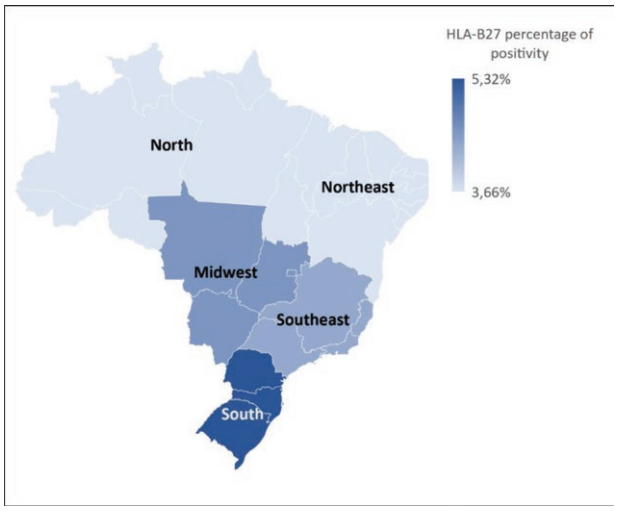


Figure 1. HLA-B27 percentage of positivity in healthy general population by region in Brazil, according to the REDOME database.

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POS0656

DOES RADIOGRAPHIC STATUS IMPACT SECUKINUMAB EFFECTIVENESS IN EUROPEAN AXIAL SPONDYLOARTHRITIS PATIENTS TREATED IN ROUTINE CARE?

Keywords: Spondyloarthritis, Real-world evidence, Imaging

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Background: The impact of radiographic status on real-world secukinumab treatment effectiveness in axial spondyloarthritis (axSpA) patients is unknown.
Objectives: To compare the treatment effectiveness of secukinumab in radiographic (r-) *vs.* non-radiographic (nr-) axSpA patients treated in routine care across Europe.
Methods: Prospectively collected data on secukinumab-treated axSpA patients with known radiographic status followed in routine care in the EuroSpA collaboration [1] were pooled from 9 countries. Patients were listed as r-axSpA if registered to fulfil the modified New York [2] or the radiographic ASAS classification [3] criteria. If patients were registered to fulfil neither criterion or if they did not fulfil one criterion and the other was unknown, patients were registered as nr-axSpA. Patient-reported outcome (PRO) remission rates including pain (VAS≤20), Bath Ankylosing Spondylitis Disease Activity (BASDAI≤20) and Functional Index (BASFI≤ 20) (all in the form of 0–100 visual analogue scale), and Ankylosing Spondylitis Disease Activity Score-CRP (ASDAS inactive disease <1.3) after 6, 12 and 24 months of secukinumab treatment were calculated. Remission rates in r-axSpA *vs.* nr-axSpA patients were compared by logistic regression analyses in an unadjusted model (MODEL1), a model adjusted for age/gender (MODEL2) and a model adjusted for age/gender/country/previous bDMARD (yes/no)/baseline CRP/years since diagnosis to secukinumab initiation (MODEL3). For MODEL3, parameter estimates (CRP) from 100 imputed data sets were pooled using Multivariate Imputation by Chained Equations.
Results: Patients with r-axSpA had longer disease duration at secukinumab initiation, were more frequently males and HLA-B27 positive compared to nr-axSpA patients. PROs at baseline were largely similar between groups, while CRP and ASDAS-CRP were higher in r-axSpA patients. A higher percentage of nr-axSpA patients had received previous bDMARDs compared to r-axSpA patients. Crude PRO remission rates at 6/12/24-months were significantly lower in nr-axSpA compared to r-axSpA patients (Table 1, Figure 1 (MODEL1)) as were percentages of patients in ASDAS inactive disease (Table 1). However, when adjusting for age/gender (MODEL2) the difference in PROs diminished, and when adjusting for multiple possible confounders (MODEL3), no significant differences were found between the two groups (Figure 1). Differences in percentages of patients in ASDAS inactive disease in r-axSpA *vs.* nr-axSpA patients were almost unaffected by adjustments (Figure 1).
Conclusion: While crude remission rates in European secukinumab-treated patients followed in routine care were higher in r-axSpA compared to nr-axSpA patients, this difference disappeared after adjusting for multiple confounders, and, thus, appeared to be related to other factors than radiographic status.

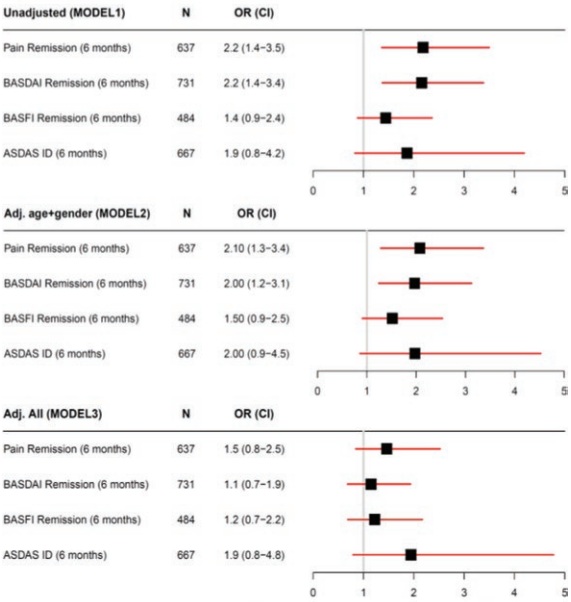
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Table 1. Baseline characteristics and remission rates for European secukinumab treated r- and nr-axSpA patients.

	Radiographic axSpA (n=899)		Non-radiographic axSpA (n=236)	
BASELINE	**Value** (%/ median (IQR))	**N available**	**Value** (%/ median (IQR))	**N available**
Age (years)	47 (38–55)	899	46 (36–55)	236
Male (%)	61	899	36	236
HLA–B27 pos (%)	80	754	55	214
Years from diagnosis	7 (3–14)	886	4 (2–8)	231
bDMARD naïve (%)	40	899	26	236
Pain (VAS, 0-100)	70 (55–85)	614	70 (51–80)	128
BASDAI (0-100)	64 (50–76)	685	67 (49–76)	139
BASFI (0-100)	55 (35–73)	476	54 (30–73)	118
CRP (mg/L)	16 (5–31)	680	5 (2–15)	151
ASDAS–CRP	4.0 (3.2–4.7)	623	3.6 (2.9–4.2)	123
FOLLOW-UP	**Remission rates** (6m/ 12m/ 24m)	**N available** (6m/ 12m/ 24m)	**Remission rates** (6m/ 12m/ 24m)	**N available** (6m/ 12m/ 24m)
Pain remission (≤ 20), (%)	39.2/ 46.1/ 47.7	523/ 360/ 174	22.8/ 25.0/ 27.6	114/ 76/ 29
BASDAI remission (≤ 20), (%)	37.6/ 41.2/ 49.7	603/ 408/ 197	21.9/ 19.3/ 19.4	128/ 83/ 31
BASFI remission (≤ 20), (%)	31.4/ 36.2/ 40.9	376/ 240/ 110	24.1/ 28.2/ 33.3	108/ 71/ 27
ASDAS inactive disease (<1.3), (%)	11.4/ 12.5/ 18.9	559/ 383/ 190	6.5/ 5.7/ 7.7	108/ 70/ 26

Figure: Comparison of 6 months PRO remission rates and ASDAS inactive disease in European secukinumab treated r-axSpA *vs.* nr-axSpA patients



Participating registries: SCQM (Switzerland), ATTRA (Czech Republic), DANBIO (Denmark), ICEBIO (Iceland), reuma.pt (Portugal), RRBR (Romania), biorx.si (Slovenia), TURKBIO (Turkey), BSRBR–AS (United Kingdom).
Logistic regression analyses adjusted for: MODEL2 age and gender; MODEL3 Age, gender, baseline disease activity (CRP), country/registry, years since diagnosis to secukinumab initiation and previous bDMARD (yes/no).
PRO, patient reported outcome; VAS, visual analogue scale pain (0–100); BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; ASDAS, Ankylosing Spondylitis Disease Activity Score-CRP; ID, inactive disease; OR, Odds Ratio; CI, Confidence Interval (95%).

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POS0657

LONG-TERM SAFETY OF UPADACITINIB IN PSORIATIC ARTHRITIS, ANKYLOSING SPONDYLITIS, AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS UP TO 5 YEARS

Keywords: Safety, Spondyloarthritis, Psoriatic arthritis

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Background: The efficacy and safety of upadacitinib (UPA), an oral JAK inhibitor, has been demonstrated in phase 3 trials for PsA, [1,2] AS, [3,4] and non-radiographic axial spondyloarthritis (nr-axSpA) [5].

Objectives: To provide a safety update for UPA across PsA, AS, nr-axSpA, and pooled axSpA from the SELECT program.

Methods: Safety data (cut-off: 15 Aug 2022) from 5 UPA trials in PsA (2), AS (2), and nr-axSpA (1) were compiled. Treatment-emergent adverse events (TEAEs; onset on or after first dose and ≤30 days for UPA 15 mg [UPA15], or ≤70 days for adalimumab [ADA], after last dose) were summarized for PsA (pooled UPA15 and ADA [1 study only]), AS (pooled UPA15), nr-axSpA (UPA15), and pooled axSpA (pooled UPA15 from AS and nr-axSpA trials). TEAEs are reported as exposure-adjusted event rates (events/100 patient-years [E/100 PY]). Age-gender adjusted standard incidence ratios (SIRs) using the SEER database and standardized mortality ratios (SMRs) were calculated.

Results: A total of 1789 patients (PsA, n=907; AS, n=596; nr-axSpA, n=286) received ≥1 dose of UPA15, totaling ~3690 PY of exposure (**Table 1**). Overall AEs and serious AEs were highest in PsA, and numerically higher with UPA15 vs ADA; rates were generally similar between AS and nr-axSpA. AEs leading to discontinuation were generally similar across treatment groups and diseases and were numerically lowest in AS. Rates of malignancy excluding non-melanoma skin cancer (NMSC), MACE, and VTE were similar between UPA15 and ADA in PsA and were generally similar across diseases (**Figure 1**). In PsA, higher rates of serious infection, herpes zoster (HZ), lymphopenia, and NMSC were observed with UPA15 vs ADA. The SIR (95% CI) for malignancy excluding NMSC with UPA15 was 0.94 (0.54-1.53) in PsA and 0.58 (0.12-1.69) in pooled axSpA; SIRs for AS (1 case) and nr-axSpA (2 cases) were not calculated separately due to low events. In PsA, the SMR (95% CI) with UPA15 was 0.71 (0.40-1.18), and 0.33 (0.13-0.69) with COVID-19 deaths excluded, suggesting no increased risk of death vs the general population. SMRs were not calculated for AS, nr-axSpA, or pooled axSpA due to low events. Data from this analysis should be interpreted with caution, as it was not enriched for AEs and duration of exposure was more limited for AS and nr-axSpA.

Conclusion: Higher rates of serious infection, HZ, lymphopenia, and NMSC were observed with UPA15 vs ADA in PsA; slightly elevated rates for most of these TEAEs were also observed with UPA15 in PsA vs axSpA. Apart from these differences, UPA15 demonstrated a generally consistent safety profile across disease states, with no new safety signals identified from previous reports.

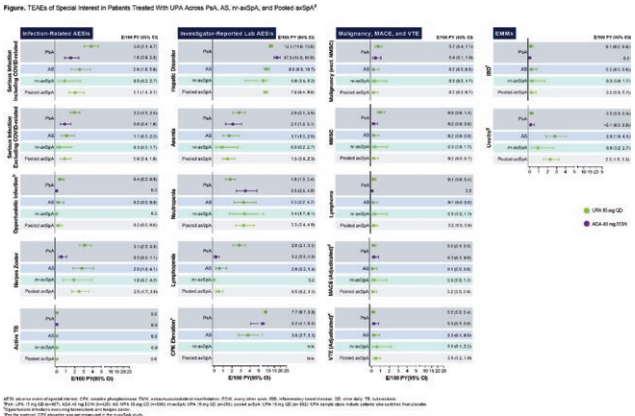
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Table 1. TEAEs in Patients Treated With UPA Across PsA, AS, nr-axSpA, and Pooled axSpA

	PsA		AS	nr-axSpA	Pooled axSpA[a]
	UPA 15 mg QD n=907	ADA 40 mg EOW n=429	UPA 15 mg QD n=596	UPA 15 mg QD n=286	UPA 15 mg QD n=882
Exposure					
Total, PY	2426.4	1146.4	939.1	323.9	1263.0
Median (min, max), years	2.9 (0.0, 5.0)	3.1 (0.0, 4.8)	1.7 (0.0, 3.8)	1.0 (0.0, 2.2)	1.6 (0.0, 3.8)
E/100 PY (95% CI)					
Any AE	232.9 (226.9, 239.1)	221.2 (212.7, 230.0)	185.9 (177.3, 194.9)	195.1 (180.2, 211.0)	188.3 (180.8, 196.0)
Any serious AE	10.9 (9.6, 12.3)	8.9 (7.3, 10.8)	8.1 (6.4, 10.1)	8.6 (5.7, 12.5)	8.2 (6.7, 10.0)
Any AE leading to discontinuation of study drug	5.2 (4.3, 6.2)	5.0 (3.8, 6.4)	3.7 (2.6, 5.2)	5.2 (3.1, 8.4)	4.1 (3.1, 5.4)
All deaths incl. COVID-related[b]	0.8 (0.5, 1.3)	0.2 (0.0, 0.6)	0.1 (0.0, 0.6)	0	0.1 (0.0, 0.4)
All deaths excl. COVID-related[b]	0.5 (0.3, 0.9)	<0.1 (0.0, 0.5)	0.1 (0.0, 0.6)	0	0.1 (0.0, 0.4)

EOW, every other week; QD, once daily.[a]Includes AS and nr-axSpA.[b]Includes non-treatment-emergent deaths. PsA: 16 deaths with UPA15 (most common cause was COVID-19), 2 deaths with ADA (accident and COVID-19 pneumonia);AS: 1 death (suicide).



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Disclosure of Interests: Gerd Rüdiger Burmester Speakers bureau: AbbVie, Eli Lilly, Galapagos, Janssen, MSD, Pfizer, Roche, and UCB, Consultant of: AbbVie, Eli Lilly, Galapagos, Janssen, MSD, Pfizer, Roche, and UCB, Jayne Stigler Shareholder of: Employee of AbbVie and may hold stock or options, Employee of: AbbVie, Andrea Rubbert-Roth Speakers bureau: AbbVie, Amgen, BMS, Chugai, Eli Lilly, Gilead, Janssen, Novartis, Roche, and Sanofi, Consultant of: AbbVie, Amgen, BMS, Chugai, Eli Lilly, Gilead, Janssen, Novartis, Roche, and Sanofi, Yoshiya Tanaka Speakers bureau: AbbVie, Asahi-kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, GSK, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer, Sanofi, and YL Biologics, Grant/research support from: AbbVie, Asahi-Kasei, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, and Takeda, Valderilio F Azevedo Speakers bureau: AbbVie, Amgen, Bristol-Meyers Squibb, Celltrion, Eli Lilly, Fresenius Kabi, GSK, Janssen, Novartis, Organon, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol-Meyers Squibb, Celltrion, Eli Lilly, Fresenius Kabi, GSK, Janssen, Novartis, Organon, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Bristol-Meyers Squibb, Celltrion, Eli Lilly, Fresenius Kabi, GSK, Janssen, Novartis, Organon, Pfizer, and UCB, Derek Coombs Shareholder of: Employee of AbbVie and may hold stock or options, Employee of: AbbVie, Reva McCaskill Shareholder of: Employee of AbbVie and may hold stock or options, Employee of: AbbVie, Ralph Lippe Shareholder of: Employee of AbbVie and may hold stock or options, Employee of: AbbVie, Peter Wung Shareholder of: Employee of AbbVie and may hold stock or options, Employee of: AbbVie, Lianne S. Gensler Consultant of: AbbVie, Fresenius Kabi, Gilead, Janssen, Eli Lilly, MoonLake, Novartis, Pfizer and UCB Pharma, Grant/research support from: Novartis and UCB Pharma.
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POS0658 ANKYLOSING SPONDYLITIS IS ASSOCIATED WITH INCREASED PREVALENCE OF VALVULAR HEART DISEASES: A POPULATION BASED STUDY

Keywords: Spondyloarthritis, Heart, Epidemiology

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory arthritis primarily affecting the sacroiliac joint and axial skeleton with associated extraarticular involvement including cardiovascular system disease including aortic value disease with variable reported prevalence.
Objectives: The aim of this study is to determine the prevalence of heart valve disorders in AS patients.
Methods: A retrospective, population-based, cross-sectional study retrieved from the Clalit Health Services (CHS) registry. Cases were defined as having AS, whereas controls were age- and sex- frequency matched in a ratio of 5:1. The prevalence of valvular heart diseases was compared between the two groups, a multivariate logistic regression model was applied to estimate the association after controlling for potential confounders.
Results: We included 4,082 AS patients and 20,397 age- and sex- frequency matched controls. AS patients had a significantly higher prevalence of cardiovascular risk factors (p<0.001) and a higher prevalence of valvular heart disease. In the multivariate logistic regression model, adjusting for multiple confounding factors, AS was independently associated with aortic stenosis (OR 2.25, 95% CI 1.57-3.23, p<0.001), aortic insufficiency (OR 2.44, 95%CI 1.5-3.94, p<0.001), mitral insufficiency (OR 1.75, 95%CI 1.17-2.61, p<0.001) but not mitral stenosis (OR 1.31, 95% CI 0.6-2.7, p=0.47).
Conclusion: Our study reports the increased risk of valvular heart diseases in patients with AS possibly due to the inflammatory milieu associated with the disease process and the result of biomechanical stress affecting the enthesis-like valvular structures.

Table 1. Characteristics of the study population of the present study

	Control (N=20397)	Ankylosing spondylitis (N=4082)	p-value
Age	56.5 (41.0-66.0)	54.9 (42.0-67.0)	0.065
Sex			
Male	13032 (63.9%)	2608 (63.9%)	0.999
Female	7365 (36.1%)	1474 (36.1%	
Smoking	3647 (17.9%)	1873 (45.9%)	
Comorbidities			
Obesity	2124 (10.4%)	1196 (29.3%)	<0.001
Hypertension	3021 (14.8%)	1499 (36.7%)	<0.001
Diabetes	1800 (8.8%)	885 (21.7%)	<0.001
Hyperlipidemia	4513 (22.1%)	2237 (54.8%)	<0.001
Ischemic heart disease	1290 (6.3%)	574 (14.1%)	<0.001
Pulmonary Hypertension	130 (0.6%)	47 (1.2%)	<0.001
Treatment			<0.001
NSAIDs	7881 (98.5%)	2257 (56.4%)	
DMARDS	101 (1.3%)	538 (13.4%)	
Anti-TNF	19 (0.2%)	1210 (30.2%)	
Valvular heart disease			
Aortic Stenosis	71 (0.3%)	61 (1.5%)	<0.001
Aortic Insufficiency	71 (0.3%)	46 (1.1%)	<0.001
Mitral Stenosis	28 (0.1%)	11 (0.3%)	0.053
Mitral Insufficiency	80 (0.4%)	46 (1.1%)	<0.001

Abbreviations – NSAIDs- non-steroidal anti-inflammatory drugs; anti-TNF – anti-tumour necrosis factor; DMARDs – disease modifying antirheumatic drugs

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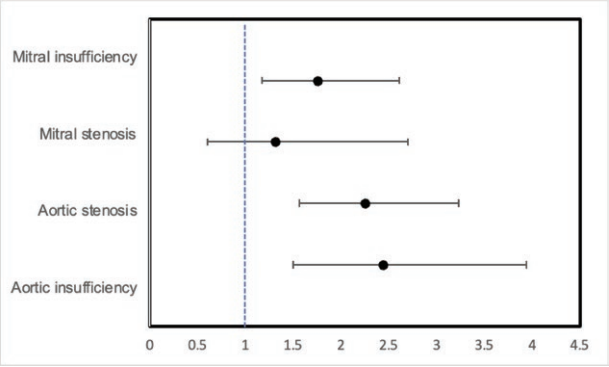


Figure 1. Logistic regression model showing the association of Ankylosing spondylitis with various heart valvular disease

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0659 COMPARISON OF METROLOGICAL PROPERTIES OF THE S-SCAISS VERSUS THE SPARCC SCORING SYSTEM FOR THE DETECTION/QUANTIFICATION OF INFLAMMATION AT MRI-SIJ IN SPONDYLARTHRITIS: DATA FROM THE DESIR COHORT

Keywords: Diagnostic tests, Spondyloarthritis

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Background: Different tools to quantify inflammatory changes in sacroiliac (SI) MRI have been developed. The Spondyloarthritis Research Consortium of Canada (SPARCC) appears to be the most sensitive to change, as it has demonstrated a good discriminating capacity. In a previous work of our group, we described the development of a fast, easy and reliable method to quantify the bone marrow edema (BME) in MRI-SIJ, through a semi-automatic process with a computer tool called SCAISS. SCAISS uses both semi-axial and semi-coronal slices from the MRI-SIJ. Since many centres only perform semi-coronal slices, we developed a simplified tool (s-SCAISS) that only requires the assessment of semi-coronal slices.
Objectives: To compare inter-rater reliability, discriminative validity and sensitivity to change using the s-SCAISS system, and compared to the SPARCC system, in patients presenting with inflammatory low back pain suggestive of axial spondyloarthritis from the DEvenir des Spondylarthopathies Indifférenciées Récentes (DESIR) cohort.
Methods: MRI-SIJ image of 206 patients collected at baseline of the DESIR cohort and after a first one year follow-up were analyzed (46.6% male, mean age 33.6 ± 8.8 years). Inter-reader reliability (3 readers for s-SCAISS and 2 central core readers for SPARCC) was assessed using intraclass correlation coefficients (ICC). Discriminative validity testing was performed by calculating the Area Under the Curve (AUC), sensitivity, specificity and likelihood ratios for different cut-off points for the classification of presence/absence of BME in SI, using positive/negative MRI as the gold standard according to DESIR core readers. Sensitivity to change was evaluated in subjects with improvement in illness activity testing

differences between paired measures. Three different criteria were considered to define activity improvement: a change in ASDAS score at 12 months of 1.1 (Clinical Important Improvement -CII-) and 2 points (Major Improvement -MI-) and a reduction ≥ 50% of the initial BASDAI score (BASDAI50).

Results: Inter-rater reliability: Both s-SCAISS and SPARCC showed good inter-reader reliability: In baseline MRI: ICC 0.95 and 0.82, respectively; At 1 year MRI: ICC 0.80 and 0.79, respectively.

Discriminative validity: Of the 206 patients included in our study, 70 (34%) fulfilled the ASAS criteria for presence of Inflammation on MRI, The AUC for EMO detection was excellent for both systems (0.88 and 0.98 for SCAISS and SPARCC, respectively). The optimal cut-off point for s-SCAISS was 60 u (Sens 83%, Esp 80%) and for SPARCC 1.25 u (Sens 93% and Esp 94%). Using the s-SCAISS cut-off point of 60 u, and the one 1.25 for SPARCC, 165 patients (81.3%) and 189 patients (93.1%), respectively were classified in accordance with the ASAS definition of the presence or absence of inflammation at MRI evaluated by the human central readers. Sensitivity to change: Of the 206 patients included, at 1 year after baseline assessment, 48 (23.3%), 17(8.3%) and 54 (26.2%) patients had a CII, MI and BASDAI50, respectively. In these patients with improved disease activity, the mean (SD) s-SCAISS score at baseline was 404.1 (SD 1055.1), 185.7 (262.7) and 375.3 (SD1008.8), respectively. While at 12 months it decreased to 72.6 (SD134.8), 46.1 (SD72.1) and 76 (SD151.7). The means of paired differences were 331.4 (SD 1019.6), 139.7 (SD 240.8) and 298.3 (SD 976.9), respectively, all of them with $p<0.05$. As expected, the AUC for the detection of CII, MI and BASDAI50 for both systems were poor (s-SCAISS 0.61, 0.63 and 0.58 and for SPARCC 0.7, 0.66, 0.60, respectively).

Conclusion: The MRI-SIJ EMO quantification system with s-SCAISS is as reliable and sensitive to change as SPARCC. The apparent advantage of SPARCC over s-SCAISS is artefactualised by the fact that the definition of the presence or absence of ASAS criteria for sacroiliitis is determined by the same readers who assess SPARCC.

Acknowledgements: We thank all DESIR-cohort patients and all individuals involved with creating and maintaining the cohort. The DESIR cohort was sponsored by the Département de la Recherche Clinique et du Développement, Assistance Publique Hôpitaux de Paris. We are also grateful to the heads of the participating regional centres.

Disclosure of Interests: None Declared.

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POS0660 FACET JOINT INFLAMMATION IS RARE, BUT WHEN PRESENT IT IS ASSOCIATED WITH FACET JOINT ANKYLOSIS IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS PATIENTS FROM THE SIAS COHORT

Keywords: Imaging, Spondyloarthritis

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Background: There is still little known on posterior element (PE) inflammation and ankylosis in the facet joints (FJ) of patients with axial spondyloarthritis (axSpA).

Objectives: To assess whether PE inflammation, in particular in the FJ, is associated with new FJ ankylosis on MRI one year later, in patients with radiographic axSpA (r-axSpA).

Methods: Patients with a diagnosis of r-axSpA recruited from Germany (Herne) and the Netherlands (Leiden) were included in the Sensitive Imaging in Ankylosing Spondylitis (SIAS) observational cohort when ≥1 inflammatory lesion on MRI of the spine and 1-18 syndesmophytes were present. Spinal MRIs were performed at baseline, 1 and 2 years. PE inflammatory lesions and FJ ankylosis were both assessed on MRI, per vertebral unit (VU) level by 3 readers independently. FJ inflammation in the cervical spine was not assessed. The probability of developing FJ ankylosis after one year was described conditional on the presence or absence of PE/FJ inflammation at baseline. Multilevel time-lagged auto-regressive GEE was used for the association between PE (or FJ) inflammation and the development of FJ ankylosis one year later, taking the reader and VU levels into account.

Results: In 58 patients MRI scores of at least 2 readers were available. Patients' average age was 49±10) years and 85% was male. Inflammation in PE or FJ at baseline was seen in 34 (59%) and 14 (24%) patients respectively. PE inflammation was distributed throughout the whole spine but most prevalent in the lower part of the thoracic spine (9%-16%). FJ inflammation was infrequently present and was more often reported in the upper thoracic spine (2%-5%) (Figure 1). FJ ankylosis was reported in 15 patients (26%) at baseline and 17 patients (29%) with follow up visits. FJ ankylosis was mainly present in the upper half of the spine (Figure 1). In 19 patients (33%) the development of new FJ ankylosis over 1 or 2 years was seen by at least 1 reader. Of the VU levels with PE or FJ inflammation only very few showed new FJ ankylosis after one year: 2 and 1 VU levels, respectively (Table 1). There was no association between PE inflammation and the development of new FJ ankylosis in the same level after one year (OR=1.15, 95%CI 0.55-2.42). However, FJ inflammation was associated with new facet joint ankylosis one year later (OR=3.79, 95%CI 1.47-9.75).

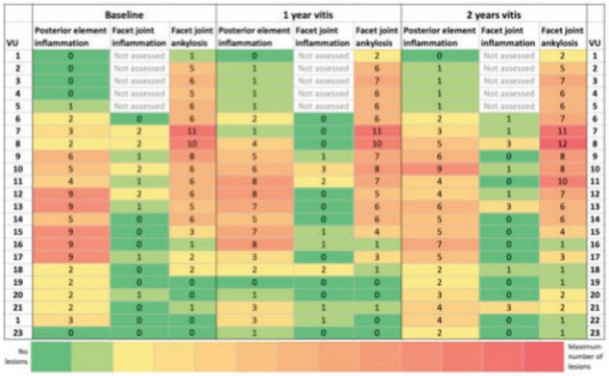


Figure. The extent of posterior element lesions on MRI across the 23 vertebral units (VU) in radiographic axial spondyloarthritis patients with 2 years follow-up.

Table 1. Probability of developing facet joint ankylosis with and without posterior element inflammation present one year before, in r-axSpA patients from the SIAS cohort

Inflammation in any part of the posterior elements			
PE inflammation	New facet joint ankylosis after one year	N*	P (FJ ankylosis | PE inflammation)
0	0	7195	P (FJ ankylosis | 0) = 43/7238 =
0	1	43	0.0059
1	0	511	P (FJ ankylosis | 1) =2/513 =
1	1	2	0.0039
Inflammation only in the facet joint			
Facet joint inflammation	New facet joint ankylosis after one year	N#	P (FJ ankylosis | FJ inflammation)
0	0	5934	P (FJ ankylosis | 0) = 38/5972 =
0	1	38	0.0064
1	0	93	P (FJ ankylosis | 1) =1/94 =
1	1	1	0.0106

PE; posterior elements, *; number of VU levels with inflammation in at least 1 part of the posterior elements (pedicle, facet joint, processes spinosi, soft tissue), #; number of facet joints, FJ; facet joint, P; probability

Conclusion: PE inflammation and FJ ankylosis on MRI were infrequently observed in patients with r-axSpA. No association was found between inflammation in the PE and the development of FJ ankylosis. However, when inflammation in the FJ is present the likelihood of developing FJ ankylosis after 1 year is over 3 times higher compared to FJ without inflammation. This finding adds to the pathophysiological relationship between inflammation and ankylosis at the same anatomical location of the axial skeleton in patients with axSpA.

REFERENCES: NIL.

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Disclosure of Interests: Manouk de Hooge Consultant of: UCB, Rosalinde Stal: None declared, Alexandre Sepriano Consultant of: Abbvie, UCB and Lilly, Xenofon Baraliakos Consultant of: AbbVie, BMS, Celltrion, Eli Lilly, Galapagos, MSD, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, MSD, Novartis, UCB, Monique Reijnierse: None declared, Juergen Braun: None declared, Désirée van der Heijde Consultant of: AbbVie, Bayer, BMS, Cyxone, Eisai, Galapagos, Gilead, Glaxo-Smith-Kline, Janssen, Lilly, Novartis, Pfizer, UCB Pharma, Floris A. van Gaalen Consultant of: Novartis, MSD, Abb Vie, Bristol Myers Squibb, Grant/research support from: Stichting vrienden van Sole Mio, Stichting ASAS, acobus Stichting, Novartis, UCB, Sofia Ramiro Consultant of: AbbVie, Eli Lilly, MSD, Novartis, Pfizer, UCB, Sanofi, Grant/research support from: AbbVie, Galapagos, MSD, Novartis, Pfizer, UCB.

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POS0661

A RADIOMICS MODEL DERIVED FROM T1-WEIGHTED IMAGES FOR EVALUATING STRUCTURAL LESIONS OF THE SACROILIAC JOINT USING LOW-DOSE CT AS THE REFERENCE STANDARD

Keywords: Imaging, Spondyloarthritis

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Background: Detection of structural lesions of the sacroiliac joint (SIJ) in patients with chronic low back pain is crucial for the diagnosis and classification of axial spondyloarthritis (axSpA). With MRI becoming a part of a routine diagnostic approach of axSpA, the question about the value of T1-weighted images (T1WI) evaluating structural lesions raised.
Objectives: To construct and validate a radiomics model based on T1WI to assess SIJ structural lesions in patients with suspected axSpA.
Methods: A total of 266 patients with clinical suspicion of axSpA between December 2016 and January 2022 were enrolled. Structural lesions were assessed by low-dose CT (ldCT) and MRI, respectively. Radiomics features, extracted from SIJ T1WI, were included to generate the radiomics model. Performance of the radiomics model was evaluated by the receiver operating characteristic curve. Point-biserial correlation analysis was used to interpret the associations between the radiomics features and structural lesions.
Results: Structural lesions were found in 122 of 187 patients (65.2%) in the training cohort and 52 of 79 patients (65.8%) in the validation cohort. Using ldCT as the gold standard, the area under the curves (AUCs) of the radiomics model and MRI experienced raters were 0.82 (95% CI: 0.76, 0.88) vs 0.73 (95% CI: 0.67, 0.79) in the training cohort, and 0.82 (95% CI: 0.72, 0.91) vs 0.74 (95% CI: 0.66, 0.83) in the validation cohort. The seven radiomics features included showed significant correlation with various structural lesions (*P* all <0.05). Among them, Wavelet.LHL_firstorder_90Percentile showed the strongest association with fat lesion (r = 0.48, *P*<0.05).
Conclusion: The radiomics analysis with T1WI could effectively detect SIJ structural lesions and each radiomics feature was correlated with different structural lesions significantly, which might inform radiomic-based applications for axSpA intelligent diagnosis.

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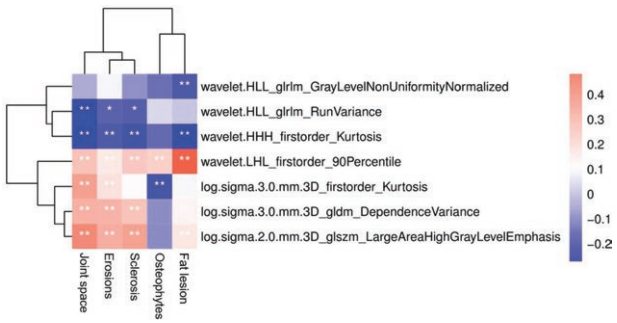


Figure 1. The heatmap depicting the correlation between the included radiomic features and structural lesions. Intensities indicate high positive (red) and negative (blue) correlations.**: P<0.05; *: P<0.01.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0662

THE SOCIOECONOMIC PROFILE OF PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IS ASSOCIATED WITH THE SEVERITY OF THE DISEASE AND WITH THE PERMANENT DISABILITY. A CLUSTER ANALYSIS IN A NATIONAL SPANISH REGISTRY

Keywords: Work-related issues, Spondyloarthritis, Outcome measures

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Background: Previous studies have demonstrated that male gender and higher level of education are independently associated with a lower hazard of sick leave in patients with axial Spondyloarthritis (axSpA), while female gender has a disadvantageous effect on employment. However, few studies have identified socio-economic profiles of patients and their association with the severity of the disease and disability.
Objectives: a) to identify clusters of patients with r-axSpA according to their socio-economic characteristics; b) to evaluate the association of these clusters with the severity of the disease and permanent disability.
Methods: REGISPONSER (Spanish Registry of Spondyloarthritis) was a cross-sectional and multicentre study including Spanish patients with spondyloarthritis (SpA) according to the ESSG criteria. Patients considered by their treating rheumatologist as suffering from radiographic axSpA (r-axSpA) or ankylosing spondylitis (AS) were included in this specific analysis. A cluster analysis was conducted using information on sociodemographic (age, sex, race, marital status, education) and socioeconomic characteristics (employment, profession, housing conditions and social level). Multiple correspondence analyses and k-means clustering methods were used. The clinical characteristics, burden of the disease and permanent disability were compared between the different clusters adjusting for disease duration.
Results: A total of 866 patients with r-axSpA were included in the analysis. Two clusters were found according to the socio-economic characteristics (Table 1). Cluster 1 (n=476) showed a profile of patients predominantly married, with secondary/elementary studies, unemployed/housekeepers, nonskilled workers, with good or deficient housing conditions and low-middle social level. On the other hand, cluster 2 (n=479) showed a profile of patients with predominantly university/bachelor studies, employed, with university/technician professions, optimal housing conditions and upper-middle social level. In terms of clinical characteristics and burden of the disease, after adjusting for disease duration, patients from cluster 1 showed older age at the diagnosis (37.9 vs. 32.6), a longer diagnosis delay (7.8 vs. 6.8 years), higher body mass index (27.6 vs. 25.9) and greater structural damage in comparison with cluster 2 (BASRI total (5.7 vs. 4.6) and BASRI cervical (6.9 vs. 5.7)). No differences were found regarding smoking, peripheral and extra-musculoskeletal manifestations. The access to biologic modified antirheumatic drugs (bDMARDs) was similar between the two groups (30.6% vs. 27.5%, p=0.376, for cluster 1 and 2, respectively). However, patients from cluster 1 showed a higher prevalence of permanent disability in comparison with cluster 2 after adjusting for disease duration [30.8% vs. 13.2%, OR 2.58 (95%CI 1.76 - 3.83), p<0.001].
Conclusion: This study suggests that the socio-economic profile of patients with r-axSpA may have implications in the severity of the disease and in permanent disability despite a similar use of bDMARDs.

Table 1. Comparison of the socioeconomic characteristics between the two clusters.

	Cluster 1 N = 476	Cluster 2 N = 390
Sex male vs. Female	75.2%	74.1%
Race white vs. Others	98.5%	99.7%
Married vs. single/ divorced/ widowed	81.5%	71.0%
University/ bachelor studies vs. secondary/ elementary studies/ illiterate	4.4%	73.1%
Employed/ retired vs. unemployed/ housekeeper	51.0%	67.4%
University/ technician profession vs. employee/ skilled/ non-skilled worker	0.4%	49.0%
Luxury/ optimal housing conditions vs. good/ deficient/ inadequate	27.9%	65.9%
Upper/ Upper-middle/ middle social level vs. low-middle/ underclass	8.4%	99.5%

REFERENCES: NIL.

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Disclosure of Interests: Clementina López-Medina Speakers bureau: UCB, Eli Lilly, Abbvie, Janssen, Novartis and MSD, Consultant of: Eli Lilly, Novartis and Eli Lilly, Grant/research support from: UCB, Abbvie and Eli Lilly, Desiree Ruiz: None declared, María Ángeles Puche Larrubia: None declared, María Lourdes Ladehesa Pineda: None declared, M. Carmen Ábalos-Aguilera: None declared, Font Ugalde Pilar: None declared, Alejandro Escudero Contreras Speakers bureau: Galapagos, Abbvie and Eli Lilly, Eduardo Collantes Estevez Speakers bureau: Eli Lilly and Novartis, Consultant of: Eli Lilly, Grant/research support from: UCB, Abbvie and Eli Lilly.

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POS0663 GUT INFLAMMATION ASSOCIATED WITH MORE STRUCTURAL DAMAGE IN THE SPINE IN AXIAL SPONDYLOARTHRITIS. RESULTS FROM THE SPARTAKUS COHORT

Keywords: Imaging, Gastrointestinal tract, Spondyloarthritis

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Background: While 5-10% of axial spondyloarthritis (axSpA) patients have diagnosed inflammatory bowel disease (IBD), 50-60% display microscopic gut inflammation upon examination of mucosal biopsies. Gut inflammation, as measured by faecal calprotectin (F-calprotectin), is more frequent in radiographic (r-axSpA) than non-radiographic axSpA (nr-axSpA) and has been linked to more active disease [1] – a known risk factor for structural damage progression. How gut inflammation relates to the degree of structural damage in the spine, however, remains sparsely studied.

Objectives: To assess if gut inflammation, as measured by elevated F-calprotectin, is associated with more structural damage in the spine in patients with axSpA.

Methods: Patients with clinical axSpA from a defined area of southern Sweden were cross-sectionally examined and classified as nr-axSpA (ASAS criteria; n=85) or r-axSpA (modified NY or ASAS criteria; n=171). Twenty-four (9.4%) subjects had comorbid IBD. Spinal structural damage was quantified by the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS; one experienced reader scored all examinations), and gut inflammation by F-calprotectin (Calpro AS ELISA). mSASSS scores of patients with normal F-calprotectin (<50 mg/kg) were compared to those with elevated (≥50 mg/kg) or substantially elevated (≥150 mg/kg) values, respectively (Mann Whitney U-test). Furthermore, to explore if presence of gut inflammation (F-calprotectin ≥50 mg/kg) was associated with an mSASSS score above the median, logistic regression analysis was used, adjusting for sex, symptom duration, HLA-B27-status, smoking (ever/never), CRP, NSAID (ASAS 3-month NSAID-score) and anti-TNF therapy (yes/no) use. Apart from assessing the overall axSpA group, analyses were also performed limited to subjects with r-axSpA, since both mSASSS and F-calprotectin values were expected to be higher in r-axSpA. Finally, analyses were also repeated after exclusion of patients with IBD as a sensitivity analysis.

Results: Characteristics of the included patients are displayed in the **Table 1**. In the overall axSpA group, mSASSS scores were significantly higher among patients with elevated F-calprotectin, and even more so among those with substantially elevated F-calprotectin, as compared to subjects with normal values (**Figure 1**). Similar results were seen when limiting the assessment to r-axSpA, although here mSASSS was significantly higher only among those with substantially elevated F-calprotectin (**Figure 1**). F-calprotectin ≥50 mg/kg was associated with having an mSASSS score above the median (>2 in the overall axSpA and >5 in the r-axSpA groups, respectively) in both study populations – all axSpA: adjusted odds ratio (OR) 2.2 (95%CI 1.1-4.3), p=0.019; r-axSpA: adjusted OR 2.7 (1.1-6.7), p=0.028. Excluding patients with comorbid IBD rendered similar results.

Conclusion: Presence of gut inflammation, as measured by elevated F-calprotectin, is associated with more structural damage in the spine in patients with established axSpA, as well as specifically in r-axSpA, even after adjustment for known risk factors of spinal damage development. This calls for prospective studies, assessing gut inflammation as a potential predictor of radiographic progression.

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	All AxSpA n=256	Radiographic axSpA n=171
Male sex	54%	61%
Age, years	51 (13)	53 (14)
Symptom duration, years	25 (14)	28 (14)
Nr-axSpA	33%	0%
mSASSS, mean (SD); median (IQR)	9.8 (17); 2.0 (8.8)	14 (20); 5.0 (21)
HLA-B27 positive	87%	85%
Smoking, ever	37%	43%
ASDAS-CRP	1.8 (0.9)	1.8 (0.9)
BASFI	2.0 (2.1)	2.1 (2.2)
CRP, mg/L	3.7 (7.2)	4.3 (8.5)
ASAS 3-month NSAID score	31 (41)	31 (41)
Ongoing anti-TNF therapy	42%	44%
IBD	9.4%	12%
F-calprotectin, mg/kg, mean (SD); median (IQR)	66 (113); 30 (51)	80 (132); 32 (70)

Mean (SD) if not otherwise stated. F-calprotectin missing in 11%, otherwise missing ≤5%.

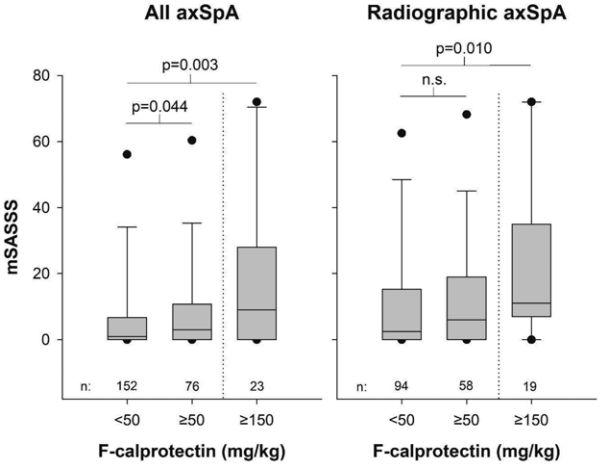


Figure. Box plots showing the distributions of mSASSS (modified Stoke Ankylosing Spondylitis Spinal Score) among all axSpA (nr-axSpA and r-axSpA combined) patients, as well as limited to those with r-axSpA, stratified according to F-calprotectin status: normal F-calprotectin (<50 mg/kg, reflecting no gut inflammation); elevated F-calprotectin (≥50 mg/kg, reflecting at least some gut inflammation); substantially elevated F-calprotectin (≥150 mg/kg, reflecting distinct gut inflammation). Note that patients with substantially elevated F-calprotectin (≥150 mg/kg) are also included among those with elevated values (≥50 mg/kg). The box plot lines represent medians, boxes 25th and 75th percentiles, whiskers 10th and 90th percentiles and dots 5th and 95th percentiles. P-values from comparisons by Mann Whitney U-test. n.s. non-significant.

Acknowledgements: Tor Olofsson and Elisabet Lindqvist contributed equally.

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POS0664 DEFINING THRESHOLDS OF PRESENTEEISM MEASURES FOR UNACCEPTABLE WORK PARTICIPATION IN AXSPA

Keywords: Patient reported outcomes, Outcome measures, Spondyloarthritis

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Background: Presenteeism is associated with lower work satisfaction and future sick leave in patients with axial spondyloarthritis (axSpA). It is generally assessed as a continuous variable; however, despite a lower precision, categorical variables are more clinically relevant in routine practice.
Objectives: 1) To identify thresholds of presenteeism instruments that reflect unacceptable work status in axSpA and whether those thresholds could predict future adverse work outcomes, 2) to compare the performance of these thresholds with thresholds from traditional outcomes for axSpA and 3) to understand whether thresholds are stable across contextual factors.
Methods: We used data from the 1-year multinational prospective study on Patient-Reported Outcomes in Employment Study in Ankylosing Spondylitis (AS-PROSE). Thresholds to determine when patients consider themselves in 'unacceptable work status' were calculated at baseline for 4 presenteeism instruments (Work Productivity and Activity Impairment questionnaire -WPAI-, Quality and Quantity method -QQ-, Workplace Activity Limitations Scale -WALS- and Work Limitations Questionnaire -WLQ 25-); and for BASDAI and BASFI. We performed receiver operating characteristic (ROC) analysis using as external criteria the Patient Acceptable Work State (PAWS) question 1, addressing ability to perform the current job satisfactorily. We used different approaches (75th percentile, Youden index, Liu method, nearest to 0.1) to determine the optimal cut-off, while balancing over-under diagnosis. Temporal validation was assessed by applying the thresholds in different timepoints. Influence of context (age, gender, nature of work, symptom duration) was explored in subgroup analyses. Finally, accuracy of thresholds to predict "future adverse work outcome" throughout 12 months (defined as sick leave or long-term disability) was assessed.
Results: A total of 366 patients were included: 72% males, mean age 43 (SD 10), with a mean symptom duration of 18.2 (11) years. 15% of the patients considered themselves in an unacceptable work status, and 6% had at least one adverse work outcome during the 12 months. The optimal thresholds of the presenteeism instruments that reflect an unacceptable work status are expressed in the Table 1. BASDAI and BASFI performed similarly to the presenteeism instruments (Figure 1). Across numerous contextual factors the thresholds were stable, except for some underdiagnoses among women and persons with a physical loading job by WPAI-, QQ-, BASDAI- and BASFI-thresholds. The threshold accuracy to predict adverse work outcome over 12 months was similar across all the presenteeism instruments (68-76% of correctly classified patients), except for the QQ (<60%). BASDAI and BASFI also performed slightly worse (66-67%).
Conclusion: Thresholds for presenteeism and health status representing unacceptable work status have been established, showing stability across contextual factors. The capacity of these thresholds to predict future adverse work outcome was somehow lower for all instruments. BASDAI and BASFI had a similar performance.

Table 1. Optimal thresholds for presenteeism measures and patients correctly classified for unacceptable work status and adverse work outcome at 12 months.

	Optimal threshold (SE/SP)	Correctly classified for unacceptable work status n (%)	Correctly classified for AWO at 12 months n (%)
WPAI presenteeism (0-100)	**≥40 (70/86)**	283 (83)	215 (76)
QQ method (0-10)	**≥3 (81/62)**	218 (65)	160 (57)
WALS (0-3)	**≥0.75 (86/75)**	255 (76)	193 (68)
WLQ 25	**≥29 (77/80)**	266 (79)	201 (71)
BASDAI (0-10)	**≥4.7 (81/71)**	245 (73)	290 (67)
BASFI (0-10)	**≥3.5 (81/67)**	232 (69)	185 (66)

SE, Sensibility; SP, Specificity; AWO, adverse work outcomes

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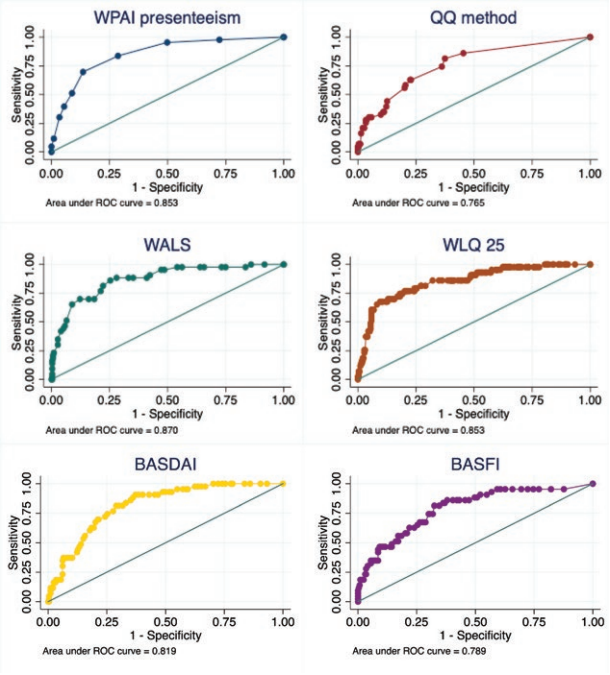


Figure 1. ROC curves for excessive presenteeism and health state from different measurement instruments according to unacceptable work status

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POS0665 **INCIDENCE RATE AND FACTORS ASSOCIATED WITH FRACTURES AMONG ADULTS WITH ANKYLOSING SPONDYLITIS IN THE UNITED STATES**

Keywords: Spondyloarthritis

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Background: Adults with ankylosing spondylitis (AS), also known as radiographic axial spondyloarthritis, are at a significantly increased risk of fracture relative to the general population. While some studies have evaluated the risk of fracture in AS, we do not have European or U.S. population-level studies assessing different fracture types performed within the last three decades.
Objectives: We evaluated the incidence rate and factors associated with fractures among those with AS using linked data from the national U.S. Rheumatology Informatics System for Effectiveness (RISE) registry and Medicare claims.
Methods: Data were derived from RISE, a large, national electronic health record-based registry, which was linked to Medicare claims from 2016-2018. Patients were required to have at least two visits for AS with a rheumatology provider, ≥ 30 days apart, prior to the baseline period of the study and at least one Medicare claim. One year of baseline characteristics was collected from both RISE and Medicare claims. Subjects were considered to have a historical

fracture (vs. an incident fracture) if a fracture occurred prior to the index date. Patients were followed over time for incident fractures after the index date. Fractures were defined by ICD codes. We examined all fractures, including those of the vertebrae, sternum/ribs, shoulder/clavicle/upper arm/elbow, distal forearm/wrist/hand, pelvis/hip/femur, knee/lower leg, and ankle/foot. First, we calculated the combined incidence of fracture and incidence by fracture type. Second, logistic regression models were constructed to identify factors associated with fracture, including age, sex, race or ethnic group, national area deprivation index, dual-eligibility for Medicare (healthcare for adults aged 65+ and some people with certain conditions/disabilities) and Medicaid (healthcare for those with limited income and resources), Charlson comorbidity index, body mass index, smoking status, osteoporosis diagnosis, historical fracture (fracture prior to index date), and use of glucocorticoids and opioids.

Results: We identified 1,426 adults with AS in RISE who were also observable in Medicare. The mean (SD) age was 69.4 years (9.8), 44.3% were female, and 77.3% were non-Hispanic White. Fractures occurred in 197 AS adults (**Table 1**). The overall incidence rate of fractures among adults with AS was 76.7 (95% CI 66.4-88.6) per 1,000 person-years. The most common fracture was vertebral with an incidence rate of 23.9 per 1,000 person-years (95% CI 18.6-30.7), followed by distal forearm/wrist/hand with an incidence rate of 17.4 per 1,000 person-years (95% CI 13.0-23.4). Age 85+ (OR 3.64, 95% CI 1.79-7.40), historical fracture (OR 5.18, 95% CI 3.40-7.89), and use of opioid drugs (OR 2.20, 95% CI 1.52-3.19) conferred increased odds of fracture; sex did not (**Figure 1**).

Conclusion: In this large U.S. sample of older adults with AS, vertebral fractures were the most common followed by distal forearm/wrist/hand fractures. Those who were older, had a historical fracture and used opioids had higher odds of fracture. Men and women were equally likely to have a fracture. Since chronic opioid use was associated with fracture in AS, this high-risk population should be considered for interventions to mitigate risk.

Table 1. Incidence rate of fractures by type.

First Fracture	N (%)	Incidence Rate per 1,000 person-years	95% CI
Any Fracture	197/1,426	76.7	66.4-88.6
By Fracture Type*			
Vertebral	61 (25.7)	23.9	18.6-30.7
Distal forearm/wrist/hand	45 (19.0)	17.4	13.0-23.4
Ankle/foot	33 (14.0)	12.8	9.1-18.0
Pelvis/hip/femur	29 (12.2)	11.2	7.8-16.1
Sternum/ribs	25 (10.5)	9.6	6.5-14.3
Shoulder/clavicle/upper arm/elbow	24 (10.1)	9.3	6.2-13.8
Knee/lower leg	20 (8.4)	7.7	5.0-11.9

*Subject's first fracture within a category were included in the counts by fracture type. Subjects can appear in more than one fracture type category if another fracture occurred in a different location. Data displays 237 unique fractures in 197 participants.

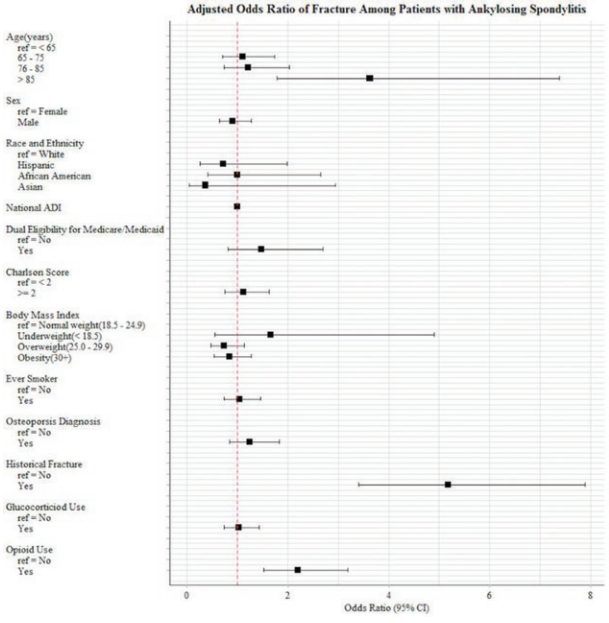


Figure 1.

Model adjusted for all variables shown in the Figure 1.

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Acknowledgements: NIL.

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POS0666 COSTOVERTEBRAL JOINT INVOLVEMENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Imaging, Spondyloarthritis

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Background: Several previous studies have reported that patients with axial spondyloarthritis (axSpA) presented with thoracic pain due to costovertebral joint arthritis. However, little is known about the prevalence and clinically relevant factors of costovertebral joint involvement in patients with axSpA.

Objectives: To evaluate costovertebral joint involvement in patients with axSpA and to assess its association with disease features.

Methods: We included 150 patients from the Incheon Saint Mary's axSpA observational cohort who underwent whole spine low-dose computed tomography (ldCT). Costovertebral joint abnormalities were scored by two readers on a scale of 0-48 based on the presence or absence of erosion, osteophyte, and ankylosis. The interobserver reliability of costovertebral joint abnormalities was assessed using intraclass correlation coefficients (ICCs). Associations between costovertebral joint abnormality scores and clinical variables were evaluated using a generalized linear model.

Results: Two independent readers found costovertebral joint abnormalities in 74 (49%) patients and 108 (72%) patients. The ICCs of scores for erosion, osteophyte, ankylosis, and total abnormality were 0.85, 0.77, 0.93, and 0.95, respectively. For both readers, total abnormality score was correlated with age, symptom duration, Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath AS functional index (BASFI), CT syndesmophyte score (CTSS), and number of bridging spines. Multivariate analyses showed age, ASDAS, CTSS to be independently associated with total abnormality scores in both readers. The frequency of ankylosed costovertebral joint was 10.2% (reader 1) and 17.0% (reader 2) in patients without radiographic syndesmophytes (n = 62), and 10.3% (reader 1) and 17.2% (reader 2) in patients without radiographic sacroiliitis (n = 29).

Conclusion: Costovertebral joint involvement was common in patients with axSpA, even in the absence of radiographic damage. LdCT is recommended for evaluating structural damage in patients with clinically suspected costovertebral joint involvement.

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Disclosure of Interests: None Declared.

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POS0667

KNOWN AND LESS KNOWN COMORBIDITIES IN AXIAL SPONDYLOARTHRITIS – WHAT ARE WE OVERLOOKING? RESULTS FROM THE SPARTAKUS COHORT

Keywords: Spondyloarthritis, Comorbidities, Epidemiology

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Background: It is well-established that axial spondyloarthritis (axSpA) is associated with extra-musculoskeletal manifestations such as anterior uveitis, psoriasis, and inflammatory bowel disease (IBD). Although relevant data exists also regarding other specific comorbid diseases, less is reported on the overall comorbidity burden in relation to the background population.
Objectives: To assess the frequency of a wide range of comorbidities, covering most important organ-domains and conditions, in a population-based axSpA cohort, including both non-radiographic (nr-axSpA) and radiographic (r-axSpA) disease, and to compare this to frequencies among matched general population comparator-subjects.
Methods: We included 246 well-characterised axSpA patients (mean age 52 years; 55% male) with established disease from the SPARTAKUS cohort, comprising patients from a defined area of southern Sweden. All patients had undergone a thorough clinical assessment and were classified as nr-axSpA (fulfilling ASAS nr-axSpA criteria; n=82) or r-axSpA (meeting modified New York/ASAS r-axSpA criteria; n=164). Furthermore, for each axSpA patient, 5 comparator-subjects from the general population, matched on sex, age, and residence area, were randomly drawn from the Swedish Population Register (n=1230). The frequency of 55 different comorbidities, covering most important organ-domains, were then investigated through ICD-10 diagnostic codes retrieved from the Skåne Healthcare Register (covering both primary and specialised care) and collected during a 10-year period preceding inclusion in the cohort (for the index cases; and during the same period for their respective comparator-subjects). Univariate logistic regression was used to compare frequencies of the various comorbidities between axSpA patients and comparator-subjects, while employing the Benjamini-Hochberg procedure to account for multiple tests. Comorbidities with <5 events in either group were excluded from the analysis (n=12).
Results: Characteristics of the included patients are displayed in the **Table 1**. Numerically, almost all investigated comorbidities were more frequent among axSpA patients than comparator-subjects (**Figure 1**). The patients showed a significantly higher frequency of known extra-musculoskeletal manifestations: anterior uveitis (28% vs. 1% for comparator-subjects, p<0.001), IBD (10% vs. 1%, p<0.001), and psoriasis (10% vs. 3%, p<0.001). Also, previously less investigated conditions such as degenerative disc disease (17% vs. 6%, p<0.001), fibromyalgia (12% vs. 3%, p<0.001) and nephrolithiasis (8% vs. 3%, p<0.001) were clearly overrepresented. In addition, patients displayed higher proportions of well-known side-effects of NSAIDs: gastritis (21% vs.10%, p<0.001) and hypertension (31% vs. 19%, p<0.001); as well as glucocorticoids (GC): cataract (11% vs. 7%, p=0.010), glaucoma (7% vs. 3%, p=0.008) and vertebral compression (4% vs. 1%, p=0.002); and more patients had been hospitalised for infections (10% vs. 5%, p=0.006).
Conclusion: When assessing a wide range of comorbidities, contemporary axSpA patients have markedly more morbidity than the background population, with an expected overrepresentation of known extra-musculoskeletal manifestations, but also of less explored conditions such as fibromyalgia and nephrolithiasis, that warrant attention and proper management. Although oral GCs are generally not recommended in axSpA, our results underscore that conditions known as side-effects of such medications are common also in this diagnosis, and that treatments need to be closely monitored.

	AxSpA n=246
Male sex	55%
Age, years	52 (13)
Symptom duration, years	26 (14)
Nr-axSpA	33%
HLA-B27 positive	86%
BMI, kg/m^2	27 (5)
Smoking, ever	39%
ASDAS-CRP	1.8 (0.9)
BASFI	2.1 (2.2)
CRP, mg/L	3.8 (7.2)
ASAS 3-month NSAID score	32 (41)
Ongoing csDMARD therapy	20%
Ongoing b/tsDMARD therapy	44%

Mean (SD) if not otherwise stated. Missing ranging from 0-5%.

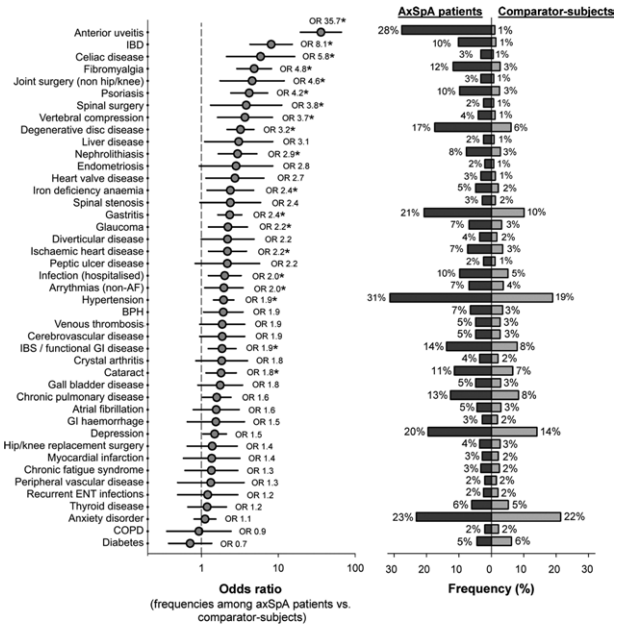


Figure. Odds ratios for frequencies of various comorbidities comparing axSpA patients with matched comparator-subjects from the general population (left) and the actual comorbidity frequencies for patients and comparator-subjects (right).
* Statistically significant after Benjamini-Hochberg procedure.
Note the logarithmic scale of the x-axis for the left panel of the figure.
Due to <5 events in either group, the following comorbidities were excluded from the analysis: congestive heart failure / cardiomyopathy, aortitis / large-vessel vasculitis, aortic aneurysm, microscopic colitis, kidney disease, tuberculosis, HIV/AIDS, infection associated with reactive arthritis, demyelinating disease, septic arthritis, osteonecrosis, hypermobility / Ehlers-Danlos syndrome
AxSpA, axial spondyloarthritis; OR, odds ratio; IBD, inflammatory bowel disease; AF, atrial fibrillation; BPH, benign prostate hyperplasia; IBS, irritable bowel syndrome; GI, gastrointestinal; ENT, ear-nose-throat; COPD, chronic obstructive pulmonary disease.

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Disclosure of Interests: Jonas Sagard: None declared, Elisabeth Mogard Speakers bureau: AbbVie, Novartis, Elisabet Lindqvist: None declared, Anna Jöud: None declared, Mats Geijer Speakers bureau: AbbVie, UCB, Johan K Wallman Speakers bureau: AbbVie, Amgen, Grant/research support from: AbbVie, Amgen, Eli Lilly, Novartis, Pfizer, Tor Olofsson Consultant of: Eli Lilly, MSD.
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POS0668

LOW UVEITIS RATES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED WITH BIMEKIZUMAB: POOLED RESULTS FROM PHASE 2B/3 TRIALS

Keywords: Spondyloarthritis, Safety, Uveitis

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Background: Acute anterior uveitis ('uveitis'), or 'iritis', is a common extra musculoskeletal manifestation among patients (pts) with axial spondyloarthritis (axSpA). The prevalence of uveitis varies with HLA-B27 positivity, axSpA subtype and disease duration, reaching >50% in radiographic (r)-axSpA (i.e., ankylosing spondylitis) [1] pts with >40 years symptom duration [2]. Interleukin (IL)-17 has been implicated in the pathogenesis of uveitis; however, inhibition of IL-17A alone may not be optimal for the management of uveitis [3]. Here, we report the incidence of uveitis following inhibition of IL-17A in addition to IL-17F with bimekizumab (BKZ).
Objectives: To compare incidence rates of uveitis in pts with axSpA treated with placebo (PBO) or BKZ 160 mg every four weeks (wks; Q4W) to Wk 16 of the phase (ph)3 trials BE MOBILE 1 and 2. To evaluate incidence rates of uveitis in pts with axSpA treated with BKZ 160 mg Q4W, using pooled ph2b/3 data.

Methods: The ph3 studies BE MOBILE 1 (NCT03928704; non-r-axSpA) and 2 (NCT03928743; r-axSpA) comprised a 16-wk double-blind treatment period (DBTP; subcutaneous BKZ 160 mg Q4W or PBO) followed by a 36-wk maintenance period (all pts received BKZ 160 mg Q4W) [5]. Upon entry to the ongoing BE MOVING open-label extension (OLE; [NCT04436640; cut-off 4 Jul 2022]) at Wk 52, all pts remained on BKZ 160 mg Q4W. The ph2b study BE AGILE (NCT02963506; r-axSpA) comprised a 12-wk double-blind, dose-ranging period followed by a 36-wk randomised period (BKZ 160 or 320 mg Q4W) [4]. Upon entry to the ongoing BE AGILE OLE (NCT03355573; cut-off 4 Jul 2022) at Wk 48, all pts received BKZ 160 mg Q4W. Data were pooled for all pts treated with BKZ 160 mg Q4W in the ph2b/3 trials listed above. Data were pooled separately for pts randomised to BKZ or PBO in the DBTP of BE MOBILE 1 and 2. Uveitis treatment-emergent adverse events (TEAEs) were identified using the preferred terms "autoimmune uveitis", "iridocyclitis", "iritis", and "uveitis", and were reported as both incidence and exposure adjusted incidence rates (EAIRs) per 100 pt years (PY) for all pts who received ≥1 BKZ dose.

Results: Baseline characteristics were reflective of a pt population with moderate-to-severe axSpA **(Table 1)**. In the DBTP of BE MOBILE 1 and 2, uveitis TEAEs occurred in 11/237 (4.6%; EAIR/100 PY [95% CI]: 15.4 [7.7, 27.5]) and 2/349 (0.6%; 1.8 [0.2, 6.7]) of pts randomised to PBO and BKZ (% difference [95% CI]: 4.07 [1.71, 7.60]), respectively **(Figure 1)**. In the 45 PBO-randomised (19.0%) and 52 BKZ-randomised (14.9%) pts with history of uveitis, uveitis TEAEs occurred in 20.0% (EAIR/100 PY [95% CI]: 70.4 [32.2, 133.7]) and 1.9% (6.2 [0.2, 34.8]) of pts, respectively. In the pooled ph2b/3 trial data, total BKZ exposure was 2,034.4 PY (N=848), 130 (15.3%) pts had history of uveitis. Uveitis TEAEs occurred in 25 (2.9%; EAIR/100 PY [95% CI]: 1.2 [0.8, 1.8]) and 14 (10.8%; 4.6 [2.5, 7.7]) pts overall and with history of uveitis, respectively **(Figure 1)**. All uveitis TEAEs were mild/moderate, one event led to discontinuation.

Conclusion: The incidence rate of uveitis TEAEs was lower to Wk 16 in axSpA pts randomised to BKZ 160 mg Q4W vs PBO. In the largest pool of ph2b/3 data available at the time of this report, the incidence rate of uveitis with BKZ 160 mg Q4W remained low at 1.2/100 PY.

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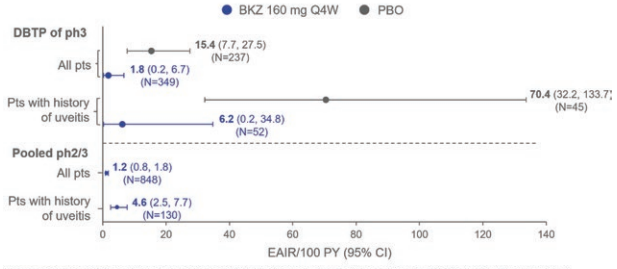
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Table 1. Baseline characteristics

	Pooled ph3		Pooled ph2b/3
	PBO (N=237)	BKZ 160 mg Q4W (N=349)	BKZ 160 mg Q4W (N=848)
Age (years), mean ± SD	38.8 ± 12.1	40.0 ± 11.8	40.3 ± 11.9
Male, n (%)	145 (61.2)	233 (66.8)	606 (71.5)
HLA-B27 positive, n (%)	187 (78.9)	294 (84.2)	717 (84.6)[a]
Caucasian, n (%)	200 (84.4)	286 (81.9)	746 (88.0)
r-axSpA, n (%)	111 (46.8)	221 (63.3)	604 (71.2)
Time since first axSpA symptoms (years), mean ± SD	10.3 ± 8.9	12.4 ± 10.5	12.4 ± 9.9
History of uveitis, n (%)	45 (19.0)	52 (14.9)	130 (15.3)
Baseline concomitant synthetic DMARDs, n (%)	51 (21.5)	77 (22.1)	197 (23.2)

[a]n=6 missing.

Figure. Pooled incidence of uveitis TEAEs (EAIR/100 PY [95% CI]) stratified by history of uveitis in pts randomised to BKZ 160 mg Q4W or PBO in the DBTP (Weeks 0 –16) of the ph3 trials BE MOBILE 1 and 2, and all pts treated with BKZ 160 mg Q4W in ph2b/3 trials.



Abbreviations: axSpA: axial spondyloarthritis; BKZ: bimekizumab; CI: confidence interval; DBTP: double-blind treatment period; DMARD: disease-modifying antirheumatic drug; EAIR: exposure adjusted incidence rate; HLA-B27: human leukocyte antigen B27; PBO: placebo; ph: phase; pts: patients; PY: patient years; Q4W: every 4 weeks; r-axSpA: radiographic axSpA; SD: standard deviation; TEAE: treatment-emergent adverse event.

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POS0669

CROSS-SECTIONAL ANALYSIS OF CARDIOVASCULAR DISEASE AND RISK FACTORS IN PATIENTS WITH SPONDYLOARTHRITIS: A REAL-LIFE EVIDENCE FROM BIOSTAR NATIONWIDE REGISTRY

Keywords: Spondyloarthritis

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Background: Association between spondyloarthritis and cardiovascular (CV) diseases is a complex issue with variable outcomes.

Objectives: This study aimed to assess the prevalence rates of CV diseases and to analyze the impact of CV risk factors on CV disease in patients with spondyloarthritis.

Methods: A multi-center cross-sectional study using BioSTAR (Biological and Targeted Synthetic Disease-Modifying Antirheumatic Drugs Registry) database was performed on patients with spondyloarthritis. Socio-demographic, laboratory and clinical, data were collected. Patients with and without major adverse

cardiovascular events (MACE) were grouped as Group 1 and Group 2.The primary outcome was the prevalence rates of CV disease and CV risk factors in the overall group. The secondary outcome was the difference in socio-demographic and clinical characteristics between the groups and predictive risk factors for CV disease.

Results: There were 1457 patients with a mean age of 45.7±10.9 years. The prevalence rate for CV disease was 3% (n=44). The distribution of these diseases was coronary artery disease (n=42), congestive heart failure (n=4), peripheral vascular disorders (n=6), and cerebrovascular events (n=4). Patients in Group 1 were significantly older than those in Group 2 (p<0.001). There were significantly more patients with hypertension, diabetes mellitus, chronic renal failure, dyslipidemia, and malignancy in Group 1 than in Group 2 (p<0.05). Smoking (36.7%), obesity (24.4%), and hypertension (13.8%) were the most prevalent traditional CV risk factors. Hypertension (HR=4.994, 95% CI:1.966-12.683, p=0.001) and dyslipidemia (HR=1.960, 95% CI:1.155-6.676, p=0.024) were the independent predictors for CV disease.

Conclusion: The prevalence rate of CV disease was 3.0% in patients with spondyloarthritis. Hypertension and dyslipidemia were independent CV risk factors for CV disease in patients with spondyloarthritis.

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Table 1. Socio-demographic and clinical characteristics of the study groups.

		Overall (n=1457)	Group 1 (n=44)	Group 2 (n=1413)	p
Age (year) †		45 (18-83)	54 (41-83)	44 (18-83)	<0.001
Age group ‡	≥40 years	1021 (70.1)	44 (100.00)	977 (69.1)	<0.001
	<40 years	436 (29.9)	0 (0)	436 (30.9)	
Comorbidities ‡					
	Hypertension	201 (13.8)	27 (61.4)	174 (12.7)	<0.001
	Diabetes mellitus	105 (7.2)	10 (22.7)	95 (6.9)	0.001
	Chronic renal failure	24 (1.6)	5 (11.6)	19 (1.4)	0.001
	Dyslipidemia	61 (4.2)	15 (48.4)	46 (6.9)	<0.001
	COPD	46 (3.2)	3 (6.8)	43 (3.1)	0.160
	Malignancy	7 (0.5)	2 (4.5)	5 (0.4)	0.018
	Valvular heart disease	10 (0.7)	1 (2.3)	9 (0.6)	0.265

Table 2. Univariate and multivariate analysis for MACE during the duration of the diseases.

			Univariate	Multivariate	
Parameter	Reference	Risk factor	p	HR (95% CI)	p
Age			0.007	1.001 (0.956-1.049)	0.956
Smoking	Non-/ex-smoker	Smoker	0.128	0.598 (0.223-1.601)	0.306
Alcohol	Non-/ex-consumer	Consumer	0.158	0.703 (0.231-2.142)	0.535
Hypertension	Absent	Present	<0.001	4.994 (1.966-12.683)	0.001
Diabetes mellitus	Absent	Present	0.297	0.629 (0.206-1.920)	0.416
Chronic renal failure	Absent	Present	0.013	1.241 (0.182-8.445)	0.826
Dyslipidemia	Absent	Present	<0.001	2.960 (1.155-6.776)	0.024
Chronic obstructive pulmonary disease	Absent	Present	0.330	0.809 (0.131-4.982)	0.819
Malignancy	Absent	Present	0.003	2.293 (0.131-40.212)	0.570
Phenotypes of SpA	Diagnoses other than r- axSpA	r- axSpA	0.365	0.788 (0.309-1.930)	0.581
BASDAI group	Non-high risk	High-risk	0.404	0.750 (0.325-1.727)	0.498
ASDAS-CRP group	Non-high risk	High-risk	0.063	2.158 (0.834-5.587)	0.113

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Disclosure of Interests: None Declared.

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POS0670

DIAGNOSTIC DELAY IS ASSOCIATED WITH WORSE OUTCOMES IN TERMS OF STRUCTURAL DAMAGE IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS. RESULTS FROM REGISPONSER-AS

Keywords: Descriptive Studies, Outcome measures, Spondyloarthritis

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Background: Diagnostic delay in axial Spondyloarthritis (axSpA) is longer than in many other rheumatic diseases. It has been demonstrated to be associated with socioeconomic factors, disease presentation [1], HLA-B27 negativity, female sex, psoriasis and younger age at onset [2]. Prolonged delay is associated with poorer long-term outcomes, including functional impairment and quality of life.

Objectives: To evaluate whether diagnostic delay in patients with radiographic axSpA (r-axSpA) is associated with poorer short-term outcomes after two years of follow-up.

Methods: Observational, longitudinal and prospective study including patients from the REGISPONSER-AS study (Spondyloarthritis Registry of the Spanish Rheumatology) with a diagnosis of r-axSpA according to the modified NY criteria. At baseline, the patients were divided into two groups according to the median of diagnosis delay (<5 years, ≥5 years). Binary logistic regression models adjusted for disease duration were constructed to evaluate the association between the diagnosis delay and disease outcomes at two years. The retention rate of the first anti-TNF treatment across the groups was evaluated using a log-rank test.

Results: A total of 729 patients were included. Outcomes at two years according to diagnosis delay are presented in the Table 1. Characteristics related with structural chronic damage (BASRI, occiput wall distance), inflammatory bowel disease (IBD), dactylitis, SF-12 mental component and inability to work were associated with longer diagnosis delay. No differences were found in the retention rate of the first anti-TNF antibody between the groups.

Conclusion: Diagnostic delay is associated with poorer short-term outcomes in terms of structural damage, prevalence of IBD, dactylitis, SF-12 mental component and inability to work in patients with r-axSpA.

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Table 1. Outcomes at 2 years adjusted by disease duration

	Diagnosis delay <5 years (N = 364)	Diagnosis delay 5 or more years (N = 365)	OR (95% CI)	p-value*
Age (years) at diagnosis	30.95 (10.53)	39.42 (11.59)	1.09 (1.07 – 1.1)	**<0.001**
Sex (male)	274 (75.3)	279 (75.8)	1.28 (0.89 – 1.86)	0.19
HLA-B27 positive	282 (81.3)	292 (81.6)	1.24 (0.81 – 1.88)	0.321
Psoriasis	41 (11.5)	39 (11)	1.02 (0.61 – 1.73)	0.926
IBD	19 (5.4)	27 (7.6)	0.41 (0.21 – 0.78)	**0.007**
Uveitis	82 (23.2)	83 (23.2)	1.28 (0.87 – 1.88)	0.215
CRP (mg/dL)	9.11 (14.62)	9.43 (11.78)	0.99 (0.99 – 1.01)	0.796
ASDAS-CRP, mean (SD)	2.49 (0.99)	2.67 (1.04)	1.06 (0.9 – 1.25)	0.47
BASDAI, mean (SD)	3.58 (2.15)	4.07 (2.36)	1.06 (0.99 – 1.14)	0.109
BASFI, mean (SD)	36.63 (27.55)	44.38 (27.1)	1 (0.99 – 1.01)	0.832
VAS (cm)	4.04 (2.55)	4.4 (2.61)	1.03 (0.97 – 1.1)	0.333
SF - 12 physical component	36.76 (9.45)	34.86 (9.97)	0.99 (0.97 – 1)	0.137
SF - 12 mental component	49.31 (9.85)	48.46 (11.3)	0.98 (0.97 – 0.99)	**0.04**
Radiographic sacroiliitis	347 (96.7)	356 (97.5)	1.35 (0.54 – 3.4)	0.523
Spine BASRI	6.55 (3.34)	7.33 (3.03)	0.94 (0.88 – 0.99)	**0.042**
Total BASRI	7.32 (3.97)	8.28 (3.65)	0.94 (0.89 – 0.99)	**0.02**
Magnetic resonance	11 (3)	11 (3)	1.07 (0.39 – 2.93)	0.9
Enthesitis	133 (38.4)	148 (41.2)	1.03 (0.67 – 1.58)	0.886
Dactilytis	39 (11.3)	18 (5.1)	0.47 (0.25 – 0.89)	**0.02**
Hip arthroplasty	19 (5.5)	18 (5.1)	4.02 (1.86 – 8.69)	**< 0.001**
Schober (cm)	3.23 (1.72)	2.89 (1.62)	1.09 (0.98 – 1.2)	0.099
Chest expansion (cm)	4.24 (2.1)	3.7 (2)	0.99 (0.91 – 1.07)	0.796
Distance to ground (cm)	18.02 (14.26)	21.6 (13.95)	1 (0.99 – 1.01)	0.687
Occiput wall distance (cm)	4.13 (6.43)	5.36 (6.64)	0.97 (0.94 – 0.99)	**0.015**
Lumbar lateral flexion (cm)	20.96 (18.01)	19.06 (18.19)	0.99 (0.99 – 1)	0.778
Inability to work				
-Transitory	14 (4.1)	13 (3.8)	1.5 (1.07 – 2.27)	**0.02**
-Permanent	90 (26.5)	110 (31.9)		

* Binary logistic regression

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Disclosure of Interests: None Declared.

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POS0671

VALIDATION OF TWO RESPONSE AND ONE STATUS MEASURES OF THE ASAS HEALTH INDEX VERSUS EXTERNAL ANCHORS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Validation, Outcome measures

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Background: Improvement in functioning and health as assessed by the ASAS Health Index (HI) is an important outcome of interventions in patients with axial spondyloarthritis (axSpA). The ability of various ASAS HI thresholds to discriminate between treatment arms of an active comparator trial have been demonstrated recently by our group with absolute improvement in the ASAS HI in general being superior to relative changes [1, 2].

Objectives: To assess whether ASAS HI response measures (absolute improvement of ≥3.0 and relative improvement of ≥30%) and reaching a status of good global functioning (ASAS HI ≤5.0) adequately discriminate between the changes and states in relevant external outcomes.

Methods: In this post-hoc analysis from the tight-controlled, treat-to-target (T2T) trial TICOSPA (2), data of active axSpA patients randomized to either the T2T arm (visits every 4 weeks, prespecified strategy of treatment intensification until achieving low disease activity) or usual care (UC; visits every 12 weeks, treatment at the rheumatologist's discretion) were used. The performance of ASAS HI response- and status scores against change (ASAS-40/ BASDAI-50 response, change in patient global/ BASDAI, and ASDAS improvement) and external status scores (ASAS partial remission, ASDAS status) was assessed, respectively. Analysis were performed by comparing the mean values and proportion of responses of continuous and dichotomous response outcomes, by t-tests. Missing data on outcomes was handled by non-responder imputation (NRI).

Results: ASAS HI was available in 160 patients, both at baseline and at week 48. At w48, an ASAS HI improvement of ≥30%, improvement of ≥3 points and ASAS HI ≤5.0 was achieved by 56 (35%), 51 (31.9%) and 54 (33.7%) patients, respectively. Patients with a meaningful improvement in global functioning had a larger reduction in patient global and disease activity as well a greater chance to reach remission compared to patients with no significant improvement in global functioning (Table 1). Health outcomes were not different between the two response measures of ASAS HI. Patients who achieved ASAS partial remission, ASDAS inactive disease or ASDAS low activity at week 48 were more likely to have an ASAS HI ≤ 5.0 compared with patients who did not achieve such states (Figure 1).

Conclusion: We demonstrated discriminant capacity of both, the relative and the absolute response measures of the ASAS HI. Both thresholds proved to have external validity and were able to discriminate between active treatment arms.

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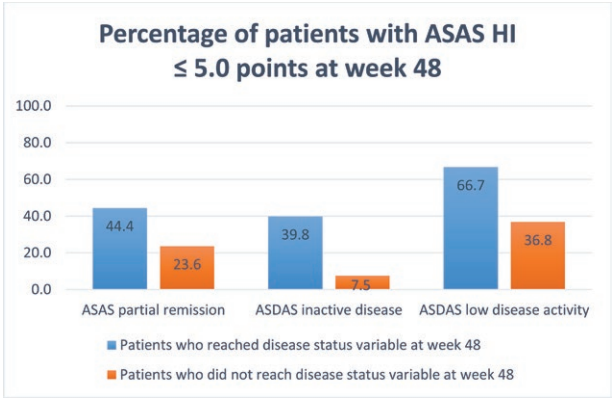


Figure 1. Proportion of patients reaching status of good global functioning at week 48

Table 1. Comparison of clinical outcomes and ASAS HI response at follow up

		ASAS HI response = > 30% improvement (NRI)			ASAS HI response = > 3 points improvement (NRI)		
		Yes (n=56)	No (n=104)	*p*	YES (n=51)	No (n=109)	*p*
ASAS40 response at w48		**48.2%**	**21.2%**	**<0.001**	**51.0%**	**(21.1%**	**<0.001**
BASDAI 50 at w48		**71.4%**	**28.8%**	**<0.001**	**68.6%**	**32.1%**	**<0.001**
ASDAS Major improvement (0 to 48w)		**23.2%**	**6.7%**	**0.005**	23.5%	7.3%	0.008
ASDAS Clinically Important Improvement (0 to 48w)		**62.5%**	**24.0%**	**<0.001**	**60.8%**	**26.6%**	**<0.001**
Change in Patient Global (0 to 48w)	Mean (SD)	**-3.54 (2.77)**	**-1.81 (2.61)**	**<0.001**	**-3.73 (2.85)**	**-1.80 (2.53)**	**<0.001**
	Median	**-4.00**	**-1.00 [-8.00.**		**-4.00**	**-1.00 [-8.00.**	
	[Min. Max]	**[-10.0. 6.00]**	**3.00]**		**[-10.0. 6.00]**	**3.00]**	
	Missing	**0 (0%)**	**18 (17.3%)**		**0 (0%)**	**18 (16.5%)**	
Change in BASDAI (0 to 48w)	Mean (SD)	**-2.79 (2.09)**	**-1.42 (2.04)**	**<0.001**	**-2.95 (2.17)**	**-1.40 (1.96)**	**<0.001**
	Median	**-2.60**	**-1.25 [-8.60.**		**-3.00**	**-1.20 [-8.60.**	
	[Min. Max]	**[-8.90. 1.40]**	**3.00]**		**[-8.90. 1.40]**	**3.00]**	
	Missing	**0 (0%)**	**18 (17.3%)**		**0 (0%)**	**18 (16.5%)**	

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POS0672

RHEUMATOLOGISTS OVERCALL SACROILIITIS ON X-RAY AND MRI IN AXIAL SPONDYLOARTHRITIS PATIENTS: DATA FROM THE BELGIAN INFLAMMATORY ARTHRITIS AND SPONDYLITIS COHORT (BE-GIANT)

Keywords: Imaging

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Background: Imaging of the sacroiliac joints, especially with magnetic resonance imaging (MRI), is an important tool for early diagnosis of axial spondyloarthritis (axSpA). Interpretation of sacroiliac joint imaging can vary according to readers' experience, but it is currently unknown if and how imaging assessment differs between academic hospitals and community based rheumatological care.

Objectives: To investigate (1) agreement between local and central reading of sacroiliac joint images (X-ray and MRI) from axSpA patients, and (2) to explore potential differences between patients diagnosed in an academic hospital compared to community centres.

Methods: The BelGian Inflammatory Arthritis and spoNdylitis cohort (Be-GIANT) includes newly diagnosed biological-naïve axSpA patients, that fulfil the ASAS classification criteria, at the outpatient clinic of an academic hospital and eight community centres in Flanders. X-ray and MRI of the sacroiliac joints (SIJ) of patients enrolled between November 2010 and August 2020 were assessed by the local rheumatologist ('local reading') and two calibrated central readers ('central reading') for definite radiographic sacroiliitis according to the modified New York criteria (X-SIJ) and active sacroiliitis according to the ASAS/OMERACT definition of a positive MRI (MRI-SIJ). Central readers resolved discrepant cases by consensus. Inter-reader reliability was assessed with Cohen's Kappa, and % overall, positive and negative agreement.

Results: Among the 271 included patients (n=205 academic hospital, n=66 community hospital), 231 X-SIJ and 208 MRI-SIJ were available for central reading (Table 1). Central readers disagreed with local readers on 30/231 (13%) X-SIJ images (κ=0.44, moderate); 4/231 (1.7%) were reclassified as radiographic sacroiliitis and 26/231 (11.3%) as not showing radiographic sacroiliitis. Overall agreement was higher between central readers and academic rheumatologists

compared to community rheumatologists (90.5% vs. 70.7%, p<0.001). 53/208 (25.4%) MRI-SIJ images were reclassified by central readers (κ=0.36, fair); the majority as negative for active sacroiliitis (51/208, 24.5%). Central readers agreed on the assessment of MRI-SIJ in a higher proportion with academic rheumatologists versus community rheumatologists (77.2% vs. 63.4%, p=0.07).
Conclusion: In newly diagnosed axSpA patients, the prevalence of radiographic sacroiliitis is low. Sacroiliitis on MRI is overcalled by rheumatologists both in academic and non-academic settings, underscoring the need for continuous educational trainings.

Table 1. Agreement between local and central readers on X-SIJ and MRI-SIJ of axSpA patients in academic and community centers.

	All axSpA patients		Academic hospital		Community centres	
	Local reading	**Central reading**	**Local reading**	**Central reading**	**Local reading**	**Central reading**
X-SIJ (N=231)						
X-SIJ +	41 (18%)	19 (8%)	30 (16%)	14 (7%)	11 (27%)	5 (12%)
X-SIJ -	190 (82%)	212 (92%)	160 (84%)	176 (93%)	30 (73%)	36 (88%)
Overall agreement	87.0%		90.5%		70.7%	
Positive agreement	50.0%		59.1%		25.0%	
Negative agreement	92.5%		94.6%		81.8%	
Kappa (95% CI)	0.44 (0.28 – 0.60)		0.55 (0.37 – 0.72)		0.10 (-0.20,0.40)	
MRI-SIJ (N=208)						
MRI-SIJ +	181 (87%)	132 (63%)	151 (90%)	115 (69%)	30 (73%)	17 (41%)
MRI-SIJ -	27 (13%)	76 (37%)	16 (10%)	52 (31%)	11 (27%)	24 (59%)
Overall agreement	74.5%		77.2%		63.4%	
Positive agreement	83.1%		85.7%		68.1%	
Negative agreement	48.5%		44.1%		57.1%	
Kappa (95% CI)	0.36 (0.25 – 0.48)		0.35 (0.20 – 0.49)		0.32 (0.10 – 0.55)	

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POS0673 ARE PATIENTS WITH AXIAL SPONDYLOARTHRITIS WHO WERE BREASTFED LESS PRONE TO MORE ACTIVE AND SEVERE DISEASE?

Keywords: Spondyloarthritis

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Background: Breast milk is the first source of microorganisms that colonize the gastrointestinal tract and a key factor in shaping the intestinal microbiome. It is currently believed that alterations in the intestinal microbiota are key in the pathogenesis of spondyloarthritis (SpA). It has been postulated that breastfeeding could reduce the risk of ankylosing spondylitis, although this claim needs further support [1].
Objectives: To analyze the potential effect of having received breastfeeding on activity and other disease outcomes in patients with axial SpA (axSpA).
Methods: Retrospective longitudinal study of 105 consecutive patients with axSpA. Only patients with reliable information about a history of breastfeeding were included. The following disease outcomes were collected: BASDAI, ASDAS-CRP, BASFI, structural damage (syndesmophytes), and ASAS-HI. The group was divided according to the history or not of breastfeeding, as well as its duration. Both groups were compared by univariate and multivariate regression methods.
Results: Forty-six women and 59 men were included, mean age 43.3 ± 12.5 years, mean age at diagnosis 34.3 ± 10.9 years. Fifty-eight percent had been breastfed for a mean of 5.5 ± 4.6 months, while 42% had not received breast milk. The main characteristics of both groups are shown in Table 1. In the raw estimate, all disease outcomes analyzed were significantly better in patients who had been breastfed. Regardless of sex, disease duration, family history, HLA-B27, use of biologics, obesity, and smoking, patients who were breastfed had a mean 1.13 points less (95% CI: -2.04, -0.23) in the estimate of BASDAI, p < 0.05, and an average of 0.38 points less (95% CI: -0.72, -0.04) in the ASDAS estimate, p < 0.05. After these same adjustments, no association was found between BASFI or structural damage and lactation. Regarding ASAS HI, breastfeeding was associated with a lower impact of the disease with 1.43 points less on average (95% CI: -2.98, 0.11), although the significance was borderline, p = 0.06. Breastfed patients were associated with less severe disease, severity being understood as a sustained combined outcome of BASDAI >4 and/or ASDAS > 2.1 + ASAS-HI > 5 + BASFI > 4 [OR 0,22 (95% CI 0.08-0.57), p < 0.01].
Conclusion: This study points to a potential benefit of breastfeeding on certain disease outcomes (activity and disease impact) in patients with axSpA. This potential beneficial effect of breastfeeding should be confirmed with larger and prospective studies.
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Table 1. Characteristics of the study population based on breastfeeding.

	Breastfeeding: no N=44	**Breastfeeding: yes N=61**
Age, years (mean ± SD)	44.4 (11.7)	42.5 (13.1)
Male	56.8%	55.7%
Radiographic axSpA	75%	49.2%
Non-radiographic axSpA	13.6%	32.8%
Mixed forms	6.8%	6.6%
HLA-B27	79.5%	70.5%
Age at diagnosis, years (mean ± SD)	34.8 (10.8)	33.9 (11)
Family history	45.5%	32.8%
Smoking	50%	27.9%
Obesity	15.9%	11.5%
Uveitis	18.2%	18%
IBD	13.6%	6.6%
BASDAI (mean ± SD)	4.41 (2.24)	3.06 (2.53)
ASDAS (mean ± SD)	2.31 (0.8)	1.84 (0.9)
ASAS HI (mean ± SD)	6.3 (4.2)	4.3 (4.1)
BASFI (mean ± SD)	3.2 (2.2)	2.4 (2.5)
Syndesmophytes (% of patients)	27.3%	19.7%
NSAIDs	81.8%	78.7%
Biologics	56.8%	60.7%

IBD: inflammatory bowel disease. The other acronyms and abbreviations as usual.

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POS0674 RENAL SAFETY OF LONG TERM NSAID USE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

Keywords: Spondyloarthritis

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Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) are the basis of treatment for patients with ankylosing spondylitis (AS) to reduce pain and inflammation. However, long-term NSAID use may cause deterioration of renal function.
Objectives: We aimed to investigate the renal safety from long-term NSAID exposure in patients with AS.
Methods: We extracted clinical information from the electronic medical records of patients with newly diagnosed AS with an observation period of more than one year who were treated at Asan Medical Center from January 1, 2000, to December 31, 2020, excluding patients with chronic kidney disease Stage 4–5, known kidney disease, and malignancy. Renal function was determined by calcuation of the estimated glomerular filtration rate (GFR) using the Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. Patients were stratified into three groups according to initial GFR: Stage 1 (GFR≥90), Stage 2 (60≤GFR<90), and Stage 3 (30≤GFR<60). The GFR values for every 3-year interval were imputed by the linear interpolation method using the measured values before and after each point, and NSAID use in each interval was estimated as the medication possession rate (MPR). To evaluate the association between NSAID use and annual changes in GFR, linear mixed effects models were used and adjusted for key covariates including age, sex, body mass index, baseline GFR, relative dosage of NSAIDs, comorbidities, and comedications.
Results: Among 1,838 patients with AS, the mean age was 38.0 (SD, 13.8) years with a median 6.1 years of follow-up. The majority of 1,386 (75.4%) patients belonged to the Stage 1 group, and the number of patients in the Stage 2 and Stage 3 groups was 442 (24.0%) and 10 (0.5%), respectively. In the multivariable models, the mean annual decrease in GFR was significant (model 1: β=-0.684, 95% CI -0.980 to -0.389, p<0.001; model 2: β=-0.387, 95% CI -0.770 to -0.004, p=0.048), and the MPR of NSAID use was significantly associated with an additional decrease in GFR (model 1: for 100% vs. 0% of MPR, β =-0.5, 95% CI, -0.8 to -0.1, p=0.008; model 2: for highest vs. lowest tertile of MPR, β=-0.519, 95% CI -0.906 to -0.132, p=0.009) in the Stage 1 group but not in patients in the Stage 2 group (Table 1).

Conclusion: This study suggested that long-term use of NSAIDs was associated with a small but significant decrease in GFR in patients with AS with normal initial renal function.

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Table 1. Effect of covariates on eGFR decline

		Model 1†				Model 2‡			
		Beta	95% CI		p-value	Beta	95% CI		p-value
			LB	UB			LB	UB	
Stage 1	Intercept	-0.684	-0.980	-0.389	**<0.001**	-0.387	-0.770	-0.004	**0.048**
	Baseline GFR	-0.066	-0.080	-0.053	**<0.001**	-0.066	-0.080	-0.053	**<0.001**
	NSAID MPR	-0.005	-0.008	-0.001	**0.008**				
	NSAID MPR tertile								
	1st tertile (<12)								**0.030**
	2nd tertile (≥12, <96)					-0.352	-0.720	0.016	0.061
	3rd tertile (≥96)					-0.519	-0.906	-0.132	**0.009**
Stage 2	Intercept	-0.297	-3.155	2.561	0.837	0.378	-2.473	3.229	0.794
	Baseline GFR	-0.063	-0.144	0.017	0.122	-0.064	-0.145	0.017	0.117
	NSAID MPR	-0.010	-0.025	0.006	0.211				
	NSAID MPR tertile								
	1st tertile (<12)								**<0.001**
	2nd tertile (≥12, <96)					-1.257	-2.024	-0.489	**0.001**
	3rd tertile (≥96)					-1.862	-2.676	-1.049	**<0.001**

†Model 1 consisted of GFR at baseline, NSAID MPR, other covariates and random effect for patient‡Model 2 consisted of GFR at baseline, tertile of NSAID MPR, other covariates and random effect for patient

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Disclosure of Interests: None Declared.

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POS0675 LOW RATE OF SWITCHING FROM NR-AXSPA TO R-AXSPA AFTER 10 YEARS OF FOLLOW UP IN EARLY AXIAL SPONDYLOARTHRITIS. DATA FROM DESIR COHORT

Keywords: Imaging, Spondyloarthritis, Prognostic factors

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Background: Previous evidence suggests that radiographic progression occurs slowly in the sacroiliac joints (SIJ) of patients with axial spondyloarthritis and that bone marrow edema (BME) on MRI-SIJ can, at least in part, explain such progression. However, information about the long-term course of radiographic structural damage at the SIJ level in patients with early axSpA is still scarce.

Objectives: To evaluate the proportion of patients switching from non-radiographic axSpA (nr-axSpA) to radiographic axSpA (r-axSpA) after 10 years of follow-up and whether BME on MRI-SIJ at baseline is associated with the r-axSpA status over time.

Methods: Patients with ≤3 years axSpA onset (according to the treating rheumatologist) from the DESIR cohort were included. The radiographic status of the patients (r-axSpA versus nr-axSpA) was based on the fulfillment of the mNY criteria (i.e. at least a bilateral grade 2 or a unilateral grade 3 on pelvic radiographs according to 2 out of 3 central readers). BME on MRI-SIJ was defined as positive ASAS definition according to 2 out 3 central readers at baseline. Information on mNY criteria was obtained in four reading waves: wave 1 (baseline (BL), wave 2 (BL and 2Y), wave 3 (BL, 2 and 5Y) and wave 4 (BL, 5 and 10Y). Images were scored by 3 trained central readers (wave 1: 2 readers + adjudicator), all of them unaware of the chronology of the images and the results of the other modality. A "progressor" was defined as a patient switching from nr-axSpA to r-axSpA. A "regressor" was defined as a patient switching from r-axSpA to nr-axSpA. The % of mNY net progressors (i.e. number of "progressors" minus number of "regressors" divided by the total number of patients) was assessed in "completers" (i.e., with pelvic radiographs available at BL and 10y in wave 4). A sensitivity analysis was conducted using a multilevel GEE model ('integrated analysis') that included all waves from all patients with at least one available mNY score from at least one reader available ("intention-to-follow" population). From this model, we estimated the absolute change per year in the percentage of mNY-positive cases with and without adjusting for the use of anti-TNF drugs. Finally, the effect of BME on MRI-SIJ at baseline on mNY positivity over 10 years, adjusting for potential confounders (Figure 1) were evaluated in a multivariable GEE model in the "intention-to-follow" population.

Results: Completers included 299 patients (mean age 34.5Y and 48.2% males), while the intention-to-follow population included 704 participants (mean age 33.7Y and 46.2% males). In the completers, the net % of progressors (switch from nr-axSpA to r-axSpA) was 5.7%. In the intention-to-follow population, there was a 0.91% (95%CI 0.60-1.20) increase per year in the probability of being mNY-positive (i.e. a progression of 9.1% after 10Y). After adjusting for anti-TNF use, this percentage decreased to 0.48% (95%CI 0.15-0.82) per year. The HLA-B27 status modified the association between BME on MRI-SIJ at baseline and mNY-positivity over 10 years (interaction p-value: <0.001). BME on MRI-SIJ was associated with being mNY positive over time in both HLA-B27 positive (OR 6.25 (95%CI 5.36-7.30)) and HLA-B27 negative patients (OR 3.03 (95%CI 2.42-3.80)), but the association was stronger in the former (Figure 1). In addition, male sex, symptom duration >1.5Y, ASDAS >2.1 (in HLA-B27 negatives) and smoking (in HLA-B27 positives) were also associated with being mNY-positive over 10 years.

Conclusion: Patients with early axSpA have a low likelihood of changing from nr-axSpA to r-axSpA over 10 years, especially when considering the use of anti-TNF. Local inflammation on MRI-SIJ is strongly associated damage accrual in the SIJ over time, in particular in patients who are HLA-B27 positive.

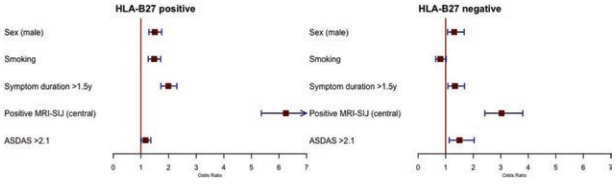


Figure 1. Baseline characteristics associated with radiographic sacroiliitis after 10 years of follow-up in axSpA patients with early onset (multivariable integrated analysis using four DESIR reading waves and stratified on HLA-B27).

REFERENCES: NIL.

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POS0676 THE CHALLENGE OF IDENTIFYING DIFFICULT-TO-TREAT AXIAL SPONDYLOARTHRITIS IN CLINICAL PRACTICE: RESULTS FROM LA PAZ-SPA COHORT

Keywords: Treat to target, Spondyloarthritis

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Background: Despite pharmacological options for axial spondyloarthritis (axSpA) have increased recently, still one out of three patients do not achieve the recommended target [1].

Objectives: To determine patient and disease characteristics in patients with "difficult to treat" (D2T) axSpA in comparison with "good responders" (GR) and to identify predictive factors of D2T-axSpA.

Methods: Data from an observational prospective cohort recruiting consecutively patients diagnosed of axSpA initiating the first bDMARD from La Paz Hospital between 2004-2019 were analysed. Patients who fulfilled one of the following definitions were included: i) D2T: failure to at least two b/tsDMARDs, ii) GR: patients

remaining treated with the first bDMARD for at least 3 years or stopping it due to disease control. Clinical characteristics, laboratory tests, concomitant treatment and disease activity measures prior to starting the first bDMARD and after 6 months were collected. Also, b/tsDMARD courses were registered. Chi-square or Fisher test were used for qualitative variables and unpaired t-student was used for quantitative variables. Univariable and multivariable logistic binary regression analyses were used.

Results: Out of 101 patients included, 41.6% were classified as D2T and 58.4% as GR. When initiating the first bDMARD, compared with GR, D2T patients had statistically significant shorter symptom duration and more frequently enthesitis, inflammatory bowel disease (IBD), concomitant NSAIDs, smoking habit and comorbidities (hypertension, dyslipidemia, depression or anxiety and fibromyalgia), all p<0.05 (Table 1). However, no significant differences were found in age, sex, BMI, subtype of axSpA, dactylitis, peripheral arthritis, uveitis, psoriasis, concomitant csDMARDs, diabetes mellitus or cardiopathy. While no differences were found for disease activity composite measures (ASDAS, BASDAI) and CRP or ESR, D2T patients had greater scores in BASDAI questions for pain and morning stiffness, TJC, PtGA and PhyGA. After 6 months of starting the first bDMARD, the scores for all disease activity measures, including ASDAS, BASDAI, CRP and ESR were significantly higher in D2T patients. Reasons for b/tsDMARDs discontinuation in D2T patients are shown in Figure 1. In multivariable analysis, smoking habit (OR=6.5, p<0.05), HLAB27 negative (OR=5.8, p<0.05), enthesitis (OR=48.1, p<0.01), baseline TJC (OR=1.2, OR<0.05) and baseline PhyGA (OR=1.05, p<0.05) were independently associated with D2T.

Conclusion: Compared with GR, patients with D2T-axSpA have more frequently poor prognostic factors for therapy response (smoking and HLAB27 negative) and worse response to first bDMARD after 6 months. Further strategies to implement recommendations for not smoking and control of comorbidities should be implemented.

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Table 1. Stratified characteristics. Results are shown as absolute numbers (%) or mean ± standard deviation.

	GR (n=59)	D2T (n=42)	p value
Symptom duration until first bDMARD (year)	10.5±10.7	5.5±7.7	<0.01
Current smoking habit	7 (11.9)	13 (31)	<0.05
HLAB27 +	48 (82.8)	27 (64.3)	<0.05
Enthesitis	35 (59.3)	40 (95.2)	<0.001
IBD	2 (3.4)	6 (14.3)	<0.05
Comorbidities			
Hypertension	15 (25.4)	20 (47.6)	<0.05
Dyslipidemia	23 (39)	28 (66.7)	<0.01
Depression or anxiety	14 (23.7)	23 (54.8)	<0.01
Fibromyalgia	1 (1.7)	6 (14.3)	<0.05
Concomitant NSAIDs	43 (81.1)	35 (97.2)	<0.05
Baseline			
ASDAS	3.3±1	3.6±0.9	0.2
BASDAI	5.6±2.1	6.4±1.7	0.06
BASDAI-spinal pain	6.4±2.7	7.5±2.1	<0.05
BASDAI-stiffness severity	5.9±2.8	7.1±2.5	<0.05
BASDAI-stiffness duration	4.7±2.7	6.1±2.8	<0.05
TJC	1.1±2.7	4.4±6.7	<0.01
PtGA	59.9±22.4	70.4±18.7	<0.05
PhyGA	39.9±19.7	50±20.2	<0.05
6-month			
ASDAS	1.6±0.9	2.8±1.1	<0.001
BASDAI	3.3±2.1	5.4±2	<0.001
CRP (mg/L)	1.7±2.7	5.9±7.9	<0.01

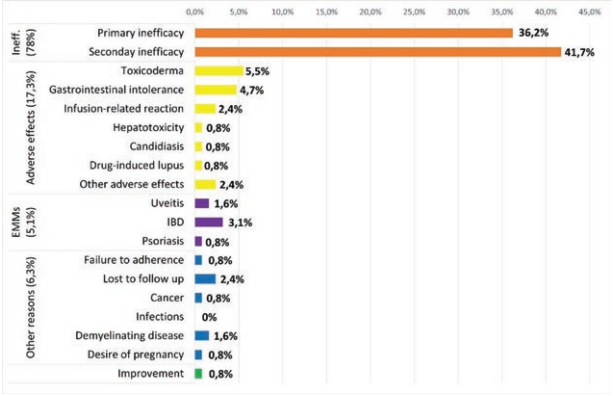


Figure 1. Reasons for b/tsDMARD discontinuation in D2T-axSpA.

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POS0677 THE DEVELOPMENT OF AN OPTIMAL MODEL FOR AUTOCALCULATION OF MSASSS USING DEEP LEARNING IN PATIENTS WITH ANKYLOSING SPONDYLITISDS

Keywords: Spondyloarthritis, Artificial Intelligence, Imaging

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Background: At present, to detect the structural changes of the spine in ankylosing spondylitis (AS), the most commonly used tool is spine X-ray photography and interpretation by a physician, and a score (modified Stoke Ankylosing Spondylitis Spinal Score, mSASSS) is given. However, because there is more than one spine (12 in total) and each spine joint disease includes at least 5 items, it takes at least 60 minutes to interpret the results of mSASSS and produce scores for each patient's spine. Therefore, because the manual calculation of mSASSS is time-consuming and may introduce interpretation errors, the study aimed to use deep learning to develop an optimal model for auto-calculation of mSASSS in patients with AS.

Methods: We collected 1056 pairs of cervical spine and lumbar spine radiographs in 646 patients with AS at Taichung Veterans General Hospital (TCVGH) from Aug 1, 2001, to Dec 30, 2020. We designed software for annotation (yes, no) of the mSASSS-related characteristics (erosion, sclerosis, squaring, syndesmophyte, bony bridging, spur, blurring) over the anterior corners of the cervical (C) and lumbar (L) spines from lateral views of radiographs. One radiologist (Lan-HHC) and two rheumatologists (Chen-HH, Chen-DY) annotate the characteristics and the final judgement was determined by a majority vote. We use PoseNet model develop a localization system identify spines (from second C-spine to first thoracic spines [C1-T1], from twelveth thoracic spine to first sacrum [T12-S1]). We developed a classification system using DenseNet model to identify the mSASSS-related specific characteristics and then calculate mSASSS.

Results: We randomly selected 211 pairs of radiographs as testing set. The remaining 845 (80%) pairs of images were used for model trainning and testing. Because the number of positive findings of erosion, sclerosis and squaring was quite low in both C-spine and L-spine, we combined radiographs of C-spine and L-spine for AI taining to score erosion, sclerosis and squaring. For detection of C-spine characterisitics, the area under curve (AUC)/specificity/sensitivity/accuracy for bridge, syndesmophyte and osteophyte were 99.8%/98.82%/97.44%/98.48%, 95.7%/94.2%/77.78%./91.67% and 97.5%/95.86%/84.16%/93.75%, respectively. For detection of L-spine chracteristics, the AUC/specificity/sensitivity/accuracy for bridge, syndesmophyte and osteophyte were 99.4%/98.46%/94.02%/97.36%, 94.00%/91.48%/77.97%./89.36% and 96.60%/91.08%/89.69%/90.82%, respectively. For detection of C/L-spine characteristics, the AUC/specificity/sensitivity/accuracy for sclerosis and squaring were 95.60%/93.91%/79.79%/91.58% and 94.40%/92.24%/77.56%./88.55%, respectively. We failed to develop an AI model to detect erosion due to its rarity (2 in C-spine and 8 in L-spine). Using the testing set of 211 paired C-spine and L-spine radiographs, the overall accuracy to detect mSASSS-related characteritics was 86.47%.

Conclusion: At this stage, the accuracy of the AI-assisted mSASSS scoring based on the perspective of the end user was 86.47%, which is expected to have good clinical practicability in TCVGH. Further testing of this mSASSS autocalculation AI model using radiographs from other hospitals is warranted for future clinical implementation in other hospitals.

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Disclosure of Interests: None Declared.

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POS0678

PERFORMANCE OF CLINICAL, LABORATORY AND IMAGING FEATURES FOR THE DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS - A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

Keywords: Spondyloarthritis, Systematic review

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Background: The Berlin algorithm for axial spondyloarthritis (axSpA) diagnosis was developed more than 15 years ago. New evidence suggests that the diagnostic performance of some SpA features might not be as good as initially thought.

Objectives: To review the evidence on the performance of SpA features for axSpA diagnosis.

Methods: Systematic literature review and meta-analysis of studies (2004-2021) reporting data on ≥1 SpA feature. The population was defined as adults (≥16 years) with a suspicion or definite clinical diagnosis of axSpA. The diagnostic performance of each SpA feature was tested against the physician diagnosis of axSpA. For each feature, if ≥2 studies analysed the same cohort, the one with the highest number of patients was included. Pooled sensitivity, specificity, positive and negative likelihood ratios (LR+ and LR-) were calculated. Sensitivity analyses were performed to assess the effect of covariates, like feature prevalence in the studies, on the diagnostic performance of SpA features.

Results: In total, 21 studies (19 cohorts) were included, comprising 8574 patients (4089 [48%] with axSpA). Table 1 shows the results of the meta-analysis. Inflammatory back pain (IBP) and good response to nonsteroidal anti-inflammatory drugs (NSAIDs) have low LR- (0.3), meaning that the diagnosis of axSpA is less likely when absent; however, if present they are not helpful in making a diagnosis (LR+ ~1). Peripheral features, extra-musculoskeletal manifestations (EMM) and preceding infection may help in the diagnosis of axSpA when present (LR+ 1.7-4.2), but have little value in its exclusion when absent (LR- 0.8-1.0). Imaging features, elevated C-reactive protein (CRP) and HLA-B27 have good diagnostic performances, reflected by their high LR+ (2.7-17.7) and (relatively) low LR- (0.5-0.7). In a sensitivity analysis the specificity of IBP was lower in studies with high prevalence of this feature (24% versus 78% in studies with low prevalence). The same was observed for buttock pain, peripheral features, uveitis, good response to NSAIDs, elevated CRP and HLA-B27.

Conclusion: Imaging features, HLA-B27 and elevated CRP have high diagnostic value, even though circularity cannot be ruled out. However, HLA-B27, with a LR+ of 2.7, has a worse diagnostic performance than earlier considered. When present, peripheral features and EMM importantly increase the probability of axSpA, while IBP and good response to NSAIDs do not, but are helpful in ruling out the disease when absent. The diagnostic value of most SpA features is somewhat lower compared to previous data.

Table 1. Performance of SpA features for axSpA diagnosis

SpA Feature	Sensitivity % (95% CI)	Specificity % (95% CI)	LR+ (95% CI)	LR- (95% CI)
IBP	84 (73; 91)	51 (31; 71)	1.7 (1.2; 2.5)	0.3 (0.2; 0.5)
Buttock pain	49 (32; 66)	71 (56; 82)	1.7 (1.2; 2.4)	0.7 (0.57; 0.9)
Heel enthesitis	21 (15; 28)	91 (85; 95)	2.3 (1.3; 3.9)	0.9 (0.8; 0.9)
Peripheral arthritis	21 (15; 29)	92 (84; 96)	2.7 (1.4; 5.2)	0.9 (0.8; 0.9)
Dactylitis	5 (3; 7)	99 (98; 99)	3.9 (2.2; 6.9)	1.0 (0.9; 1.0)
Uveitis	9 (7; 11)	98 (96; 99)	3.8 (2.1; 6.9)	0.9 (0.9; 1.0)
Psoriasis	8 (4; 13)	96 (93; 97)	1.7 (1.1; 2.8)	1.0 (0.9; 1.0)
Inflammatory bowel disease	4 (2; 6)	99 (97; 100)	4.2 (1.2; 14.9)	1.0 (1.0; 1.0)
Any EMM	29 (21; 38)	87 (81; 91)	2.2 (1.5; 3.4)	0.8 (0.7; 1.0)
Family history	20 (14; 27)	91 (84; 96)	2.3 (1.2; 4.3)	0.9 (0.8; 0.9)
Good response to NSAIDs	80 (57; 92)	60 (46; 72)	2.0 (1.2; 3.2)	0.3 (0.1; 0.9)
Elevated CRP	37 (35; 40)	90 (81; 96)	3.9 (1.6; 5.1)	0.7 (0.6; 0.8)
HLA-B27	61 (52; 69)	78 (68; 85)	2.7 (2.0; 3.8)	0.5 (0.4; 0.6)
BME on MRI (ASAS definition)	47 (35; 60)	97 (94; 98)	13.6 (7.9; 23.3)	0.6 (0.4; 0.7)
mNY+ on X-SIJ	31 (23; 40)	98 (95; 99)	17.7 (6.7; 46.9)	0.7 (0.6; 0.8)
Any enthesitis	21 (13; 32)	94 (88; 97)	3.3 (1.8; 6.2)	0.9 (0.8; 0.9)
Preceding infection	3 (2; 4)	99 (98; 99)	3.0 (1.8; 5.1)	1.0 (1.0; 1.0)
Age at symptom onset <45	87 (80; 92)	26 (15; 41)	1.2 (0.9; 1.5)	0.5 (0.3; 1.0)

BME on MRI: bone marrow edema on magnetic resonance imaging of the sacroiliac joints (SIJ); **mNY+ on X-SIJ:** positive modified New York criteria on SIJ radiography.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0679

COMPARISON OF ESTABLISHED AND NEW, PRELIMINARY PROPOSED ASAS CUT-OFFS FOR INFLAMMATORY MRI LESIONS IN THE SACROILIAC JOINTS OF AXIAL SPONDYLOARTHRITIS PATIENTS AND IMPLICATIONS FOR RECRUITMENT IN CLINICAL STUDIES

Keywords: Imaging, Clinical Trials, Spondyloarthritis

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Background: The Assessment of SpondyloArthritis international Society (ASAS) recently proposed preliminary, more stringent, data-driven definitions for active and structural MRI lesions of the sacroiliac joint (SIJ) typical of axial spondyloarthritis (axSpA) [1].

Objectives: To assess clinical outcomes of patients (pts) receiving certolizumab pegol (CZP) in the C-OPTIMISE trial who were MRI-positive (MRI+) or negative (MRI–) according to the existing and newly proposed definitions, as well as those who were MRI+ by the existing definition but MRI– by the newly proposed definition (discordant group).

Methods: C-OPTIMISE (NCT02505542) enrolled 736 pts with active axSpA who received 400 mg CZP at Weeks 0, 2, and 4, then 200 mg CZP every two weeks to Week 48 [2]. We report: percentage of pts achieving ASAS ≥40% improvement (ASAS40) response; mean BASDAI change from baseline (CfB) and percentage of pts achieving Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease (ID, ASDAS <1.3) to Week 48. In this post hoc analysis, outcomes were stratified by axSpA subgroup (radiographic [r-]/ non-radiographic [nr]-axSpA) and MRI definition. Missing values were imputed using non-responder imputation for ASAS40 and last observation carried forward for continuous variables.

Results: Baseline MRI data were available for 657/736 (89.3%) pts, 358/657 (54.5%) of whom had r-axSpA and 299/657 (45.5%) nr-axSpA. 386/657 pts (58.8%) were classified as MRI+ according to the existing definition compared with 333/657 pts (50.7%) using the newly proposed definition; the discordant group comprised 53/657 pts (8.1%; nr-axSpA: 35/299 [11.7%]; r-axSpA: 18/358 [5.0%]; **Table 1**). A numerically higher proportion of newly proposed definition MRI+ pts achieved ASAS40 at Week 48 vs those fulfilling the existing MRI+ definition; pts in the discordant group responded similarly to those originally classified as MRI– (**Figure 1**). Similar results were observed for mean BASDAI, with significant differences in responses between nr-axSpA pts in the newly proposed MRI+ definition and discordant groups (**Figure 1**). At Week 48, a lower proportion of pts in the discordant group achieved ASDAS inactive disease (ID, ASDAS <1.3) vs those classified as MRI+ according to either the existing or newly proposed definitions; differences between subgroups were more notable among pts with nr-axSpA (discordant group: 15/35 [42.9%]; existing definition MRI+: 112/191 [58.6%]; newly proposed definition MRI+: 97/156 [62.2%]) than with r-axSpA (discordant group: 10/18 [55.6%]; existing definition MRI+: 118/195 [60.5]); newly proposed definition MRI+: 108/177 [61.0%]).

Conclusion: In C-OPTIMISE, 11.7% fewer nr-axSpA pts would have been classified as MRI+ at baseline using the newly proposed definition vs the existing definition. Application of the preliminary MRI definition needs to be evaluated in future clinical trials to confirm its translation into fewer false-positive recruited pts.

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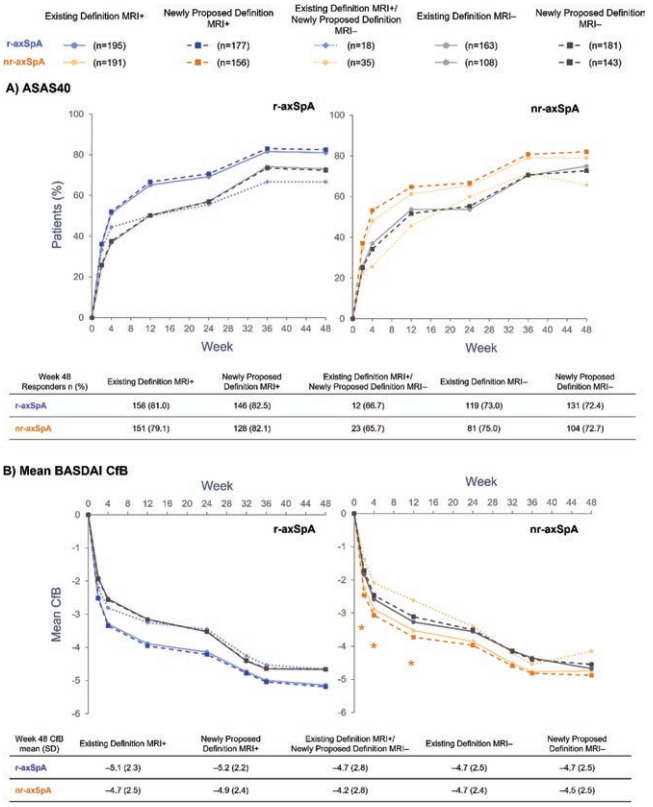
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Table 1. Baseline demographics and characteristics for MRI+ patients

	Existing Definition MRI+		Newly Proposed Definition MRI+		Existing Definition MRI+/ Newly Proposed Definition MRI–	
	r-axSpA (n=195)	nr-axSpA (n=191)	r-axSpA (n=177)	nr-axSpA (n=156)	r-axSpA (n=18)	nr-axSpA (n=35)
Age, years, mean (SD)	32.7 (6.8)	31.9 (7.0)	32.7 (6.9)	31.1 (6.5)	32.4 (5.5)	35.4 (8.0)
Sex, n (%) Male	154 (79.0)	123 (64.4)	138 (78.0)	109 (69.9)	16 (88.9)	14 (40.0)
CRP, mg/L, mean (SD)	17.3 (17.7)	11.0 (18.5)	17.1 (17.1)	11.5 (19.0)	19.6 (23.3)	8.6 (15.9)
HLA-B27, n (%) Positive	169 (86.7)	148 (77.5)	153 (86.4)	127 (81.4)	16 (88.9)	21 (60.0)
Symptom duration, years, mean (SD)	3.5 (2.1)	2.9 (1.6)	3.6 (2.2)	2.9 (1.6)	3.2 (1.3)	3.2 (1.8)
BASDAI, mean (SD)	6.8 (1.4)	6.6 (1.4)	6.8 (1.4)	6.5 (1.4)	6.2 (1.7)	6.9 (1.4)
ASDAS, mean (SD)	4.0 (0.8)	3.5 (0.8)	4.0 (0.7)	3.5 (0.8)	3.8 (1.0)	3.5 (0.7)

Figure. Proportion of patients achieving **A)** ASAS40 and **B)** change from baseline in mean BASDAI scores stratified by both existing and newly proposed ASAS SIJ MRI definitions



Missing ASAS40 data imputed using non-responder imputation; BASDAI missing data imputed using last observation carried forward. One sample t-tests were performed to identify significant differences between Existing Definition MRI+/Newly Proposed Definition MRI– and Newly Proposed Definition MRI+ patients' BASDAI scores. *p<0.01. ASAS:Assessment of SpondyloArthritis international Society; ASAS40: ASAS ≥40% improvement; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index;CfB: change from baseline; CRP: C-reactive protein; HLA-B27: human leukocyte antigen B27; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; r-axSpA: radiographic axial spondyloarthritis; SD: standard deviation; SIJ: sacroiliac joint.

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POS0680

DISEASE COURSE OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN KOREAN PATIENTS: DATA FROM A LONG-TERM RETROSPECTIVE OBSERVATIONAL COHORT

Keywords: Epidemiology, Descriptive Studies, Spondyloarthritis

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Background: Disease course of non-radiographic axial spondyloarthritis (axSpA) has been extensively studied in non-Asian population. However, there are limited data on the disease course of non-radiographic axSpA in Asian population. It is well known that clinical features of non-radiographic axSpA differ according to ethnicities. Therefore, the disease course of non-radiographic axSpA studied in non-Asian population cannot be generalized to Asian population.

Objectives: This study aimed to evaluate the long-term disease course of non-radiographic axSpA in Asian patients and identify factors associated with progression to radiographic axSpA.

Methods: A total of 56 Korean patients with non-radiographic axSpA were included. Disease course was assessed by the rate of progression to radiographic axSpA. Factors associated with the risk of progression to radiographic axSpA were assessed using multivariable Cox proportional hazard regression analysis.

Results: Over a mean observation period of 8.4 ± 3.7 years, 28 of 56 (50.0%) patients progressed to radiographic axSpA. In multivariable Cox proportional hazard regression analysis, the presence of syndesmophytes at diagnosis (adjusted hazard ratio [HR]: 4.50, 95% confidence interval [CI]: 1.54–13.15, p = 0.006) and active sacroiliitis on magnetic resonance imaging (MRI) at diagnosis (adjusted HR: 5.88, 95% CI: 2.05–16.82, p = 0.001) were significantly associated with a higher risk of progression to radiographic axSpA, whereas longer exposure to tumor necrosis factor inhibitors (TNFis) was significantly associated with a lower risk of progression to radiographic axSpA (adjusted HR: 0.89, 95% CI: 0.80–0.98, p = 0.022).

Conclusion: During long-term follow-up, a substantial proportion of Asian patients with non-radiographic axSpA progressed to radiographic axSpA. The presence of syndesmophytes and active sacroiliitis on MRI at the time of non-radiographic axSpA diagnosis were associated with a higher risk of progression to radiographic axSpA, while longer exposure to TNFis was associated with a lower risk of progression to radiographic axSpA.

References: None.

Table 1. Factors associated with progression to radiographic axSpA

	Univariable analysis		Multivariable analysis	
	Unadjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Age	1.01 (0.98–1.04)	0.604		
Male sex	0.72 (0.33–1.56)	0.400		
Symptom duration	1.14 (1.02–1.27)	0.018	1.06 (0.95–1.19)	0.276
Current smoker	0.79 (0.10–5.94)	0.817		
BMI, kg/m^2	0.90 (0.78–1.03)	0.117		
HLA-B27 positive	1.22 (0.49–3.05)	0.673		
Peripheral symptoms	0.73 (0.34–1.58)	0.423		
Uveitis	0.33 (0.09–1.14)	0.079		
Psoriasis	0.05 (0.00–7642.29)	0.617		
IBD	0.68 (0.09–5.07)	0.706		
Elevated ESR	1.62 (0.75–3.51)	0.222		
Elevated CRP	1.45 (0.67–3.15)	0.345		
Presence of syndesmophytes	4.70 (1.89–11.70)	0.001	4.50 (1.54–13.15)	0.006
Active sacroiliitis on MRI	3.97 (1.54–10.23)	0.004	5.88 (2.05–16.82)	0.001
NSAID intake score	1.00 (0.99–1.02)	0.817		
Use of sulfasalazine	0.53 (0.25–1.14)	0.106		
Use of TNFi	0.67 (0.31–1.44)	0.303		
Exposure duration of TNFi	0.88 (0.80–0.98)	0.014	0.89 (0.80–0.98)	0.022

BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HLA, human leukocyte antigen; HR, hazard ratio; IBD, inflammatory bowel disease; MRI, magnetic resonance imaging; NSAIDs, non-steroidal anti-inflammatory drugs; TNFi, tumor necrosis factor inhibitor; axSpA, axial spondyloarthritis

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POS0681

REVISION IN TREATMENT DECISION MIGHT BE NECESSARY IN SEEMINGLY INACTIVE AXSPA PATIENTS ACCORDING TO BASDAI

Keywords: Spondyloarthritis

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Objectives: To determine the frequency of inconsistency between the BASDAI and ASDAS-CRP cut-off values in disease activity categorization in patients with axial spondyloarthritis (axSpA) and to characterize the reasons for the discordance.
Methods: In total 575 axSpA patients (mean age: 40.2 ± 11.5; male gender: 358, 62.3%) followed up in a single center and who had both BASDAI and ASDAS-CRP scores at the same visit were included in this analysis. Of them 369 (64.2%) were classified as radiographic axSpA (r -axSpA). A BASDAI score of ≥4 and an ASDAS score of ≥2.1 were used as the cut-off value for the differentiation of inactive/active disease state. The demographic, disease related characteristics of the patients including structural damage were obtained.
Results: Inconsistency in the definition of the disease state according to two composite disease activity measures was found in 146 (25.4%) patients. As a consequence, the concordance rate of the two scales was calculated as 74.6% and corresponding κvalue was 0.458. Of the 274 patients who has inactive disease according to BASDAI, 46.4% were classified as active according to ASDAS-CRP (Figure 1). In our whole group; discordant patients for the disease state distinction according to two measures **had higher CRP values, lower percentage of heel pain, and they were using less biologics**. These patients also **had lower BASFI, HAQ-S, and overall pain scores** (Table 1). When we evaluated inactive patients according to BASDAI, discordant patients were significantly **older, had lower education, higher serum CRP levels, and more frequently peripheral arthritis**. Baseline mSASSS scores were higher in those discordant patients and more patients had syndesmophyte, additionally the progression rate according to mSASSS was higher.
Conclusion: In daily clinical practice discordance in the disease activity definition might be observed in around 25% of axSpA patients according to two widely used composite measures. The results of the present study suggested that patients with high serum CRP levels could be easily classified as inactive according to BASDAI and those patients might have developed more structural damage in disease course. Our results suggest that those patients misclassified according to BASDAI scale had worse functional status and quality of life. In conclusion ASDAS-CRP might be more appropriate disease activity measure in treatment decision.

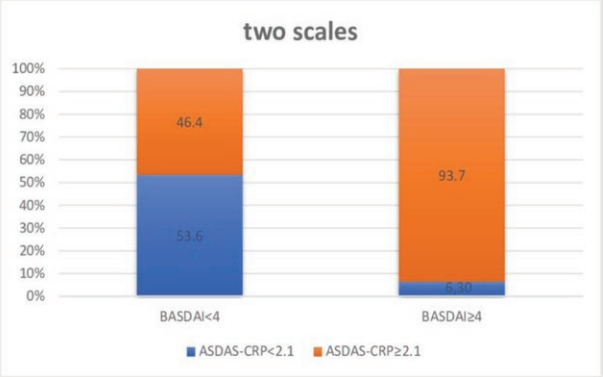


Figure 1.

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Disclosure of Interests: None Declared.
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POS0682

IDENTIFICATION OF A DIAGNOSTIC MODEL FOR AXIAL SPONDYLOARTHRITIS IN DAILY CLINICAL PRACTICE USING A RANDOM FOREST MACHINE LEARNING APPROACH

Keywords: Spondyloarthritis

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Background: In axial spondyloarthritis (axSpA), early diagnosis plays a key role in preventing disease progression. However, a validated diagnostic algorithm does not exist, while classification criteria are frequently misused diagnostically.
Objectives: To identify which decision model is being used for diagnosing patients with axSpA based on evaluations made in daily practice.
Methods: Complete clinical data of 399 patients who presented with chronic back pain in a specialized university clinic were retrospectively evaluated. All patients received complete rheumatologic examination. The total dataset was randomly split into training and test datasets at a 7/3 ratio. A model was built to classify patients into axSpA and non-axSpA based on the random forest algorithm, an ensemble machine learning technique which allows computing the importance of each variable in the statistical modelling process. The Mean Decrease Gini measure was used for the variable importance. The overall accuracy, sensitivity, specificity, and the area under the receiver operating characteristic (ROC) curve (AUC) in the test dataset were calculated.
Results: In total, 183 patients were diagnosed with axSpA and 216 with non-SpA (Table 1). In the test dataset, the model reached an accuracy of 0.9315, a sensitivity of 0.9634, a specificity of 0.8906, and an AUC of 0.9868 (Figure 1A). HLA-B27 positivity, erosion on SIJ MRI, and elevated CRP played the most important role in the statistical modelling process followed by awakening at second half of

	All patients			Patients with BASDAI<4		
Variables	Discordant Patients (n=146)	Concordant Patients (n=425)	P	Discordant Patients (n=127)	Concordant Patients (n=147)	P
Age, years	41.3±10.9	39.8 ± 11.7	0.262	41.0±10.6	36.9±10.5	**0.001**
Male, n (%)	93 (63.7)	285 (61.8)	0.678	86;67.7	101;68.7	0.861
Symptom duration, years	12.6 ± 10.4	12.4 ± 10.4	0.851	13.4 ±10.6	9.6 ±8.7	**0.001**
Diagnostic subtype (% r— axspa)	99 (67.8)	270 (62.9)	0.289	93 (73.2)	80 (54.4)	**0.001**
Smoking, n (%)	108 (74.0)	290 (67.8)	0.160	96 (75.6)	81 (55.5)	**0.001**
Education, year	9.8±4.4	10.0±4.5	0.651	9.4 ±4.4	11.5 ±4.6	**<0.001**
Presence of peripheral arthritis, n (%)	48 (33.8)	148 (35.6)	0.702	40 (32.3)	30 (21.1)	**0.040**
Presence Baseline heel pain	55; 37.7	195; 50.5	**0.043**	42;35.6	62;43.4	0.202
CRP, mg/dl	19.0 ± 23.7	12.2 ± 20.2	**<0.001**	21.7±24.3	3.4±3.6	**<0.001**
Basal mSSASS	8±17.0	8.2±16.9	0.443	9.4±17.7	5.4±14.1	**0.005**
Presence Baseline syndesmophyte, n (%)	57/121 (47.1)	145/367 (39.5)	0.141	54/106 (50.9)	29/127 (22.8)	**<0.001**
mSSASS progression, n (%)	14/41 (34.1)	30/149 (20.1)	0.06	14/38 (36.8)	8/54 (14.8)	**0.015**
Biological Treatment, n (%)	23 (16.0)	108 (25.4)	**0.020**	21 (16.8)	26 (17.8)	0.827
BASFI	2.5 ± 2.0	4.0 ± 3.1	**<0.001**	2.3±2.0	1.2±1.4	**<0.001**
ASQOL	7.1 ± 4.5	4.2 ± 2.2	**<0.001**	7.0±4.7	4.6±3.9	**<0.001**
HAQ-S	0.62 ± 0.5	0.9 ± 0.7	**<0.001**	0.6±0.5	0.3±0.4	**<0.001**
BAS - General Pain	3.4 ± 2.5	4.9 ± 3.0	**<0.001**	3.2±1.2	2.0±1.8	**<0.001**
BASMI	3.2 ± 1.7	3.4 ± 1.8	0.420	3.3±1.8	2.4 ±1.3	**<0.001**

* Continuous variables mean ±SD; categorical variables are expressed as n (%).

night due to back pain and bone marrow edema and fat metaplasia on SIJ MRI (Figure 1B).

Conclusion: Machine learning-based random forest classifier revealed a high performance in diagnosing patients with chronic back pain with axSpA and excluding patients with non-SpA using clinical, laboratory and imaging characteristics as evaluated in a daily practice scenario of a SpA-specialized clinic. External validation of the model is needed to investigate its clinical utility as a diagnostic decision support tool.

Table 1. Patient characteristics

	no axSpA, N = 216[1]	**axSpA**, N = 183[1]
Male	105 (49%)	111 (61%)
Age	35 (28, 43)	36 (27, 47)
Symptom duration	1.5 (0.5, 5.0)	2.0 (1.0, 5.0)
Insidious onset of back pain	94 (44%)	177 (97%)
Improvement with exercise of back pain	119 (55%)	140 (77%)
Morning stiffness of back pain	61 (28%)	103 (56%)
Awakening at second half of night due to back pain	87 (40%)	24 (13%)
Arthritis	24 (11%)	52 (28%)
Uveitis	4 (1.9%)	33 (18%)
Dactylitis	15 (6.9%)	9 (4.9%)
Psoriasis	18 (8.3%)	21 (11%)
Inflammatory bowel disease	6 (2.8%)	11 (6.0%)
Good NSAID response	100 (46%)	151 (83%)
Elevated CRP	36 (17%)	108 (59%)
HLA-B27 positivity	35 (16%)	125 (68%)
Bone marrow edema on SIJ MRI	76 (35%)	140 (77%)
Erosion on SIJ MRI	4 (1.9%)	88 (48%)
Sclerosis on SIJ MRI	71 (33%)	110 (60%)
Fat metaplasia on SIJ MRI	17 (7.9%)	81 (44%)
Ankylosis on conventional radiograph	1 (0.5%)	28 (15%)
Family history for axSpA	18 (8.3%)	59 (32%)

[1] n (%); Median (IQR). axSpA: axial spondyloarthritis; MRI: magnetic-resonance-imaging; NSAID: non-steroidal anti-inflammatory drug; SIJ: sacroiliac-joints

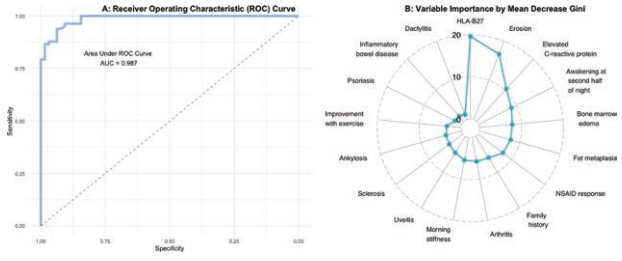


Figure 1.

REFERENCES: NIL.

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Disclosure of Interests: None Declared.

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POS0683

AN EXPLORATORY ANALYSIS OF THE POTENTIAL DISCONNECT BETWEEN OBJECTIVE INFLAMMATORY RESPONSE AND CLINICAL RESPONSE FOLLOWING CERTOLIZUMAB PEGOL TREATMENT IN PATIENTS WITH ACTIVE AXIAL SPONDYLOARTHRITIS

Keywords: Outcome measures, Spondyloarthritis, Clinical trials

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Background: In clinical trials of axial spondyloarthritis (axSpA), composite measures such as Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) response criteria, Assessment of Spondyloarthritis international Society (ASAS) response criteria, Ankylosing Spondylitis Disease Activity Score (ASDAS) disease activity states and ASDAS response criteria are used. However, these validated measures are largely based on patient (pt)-reported symptoms, which are likely to be confounded by other factors. In pts with active axSpA, certolizumab pegol (CZP) has demonstrated sustained clinical efficacy in clinical outcomes over 204 weeks [1]. However, we hypothesise that reduction of sacroiliac joint (SIJ) and spinal inflammation following treatment with CZP, as measured by MRI and C-reactive protein (CRP) levels, may not necessarily translate into clinical response [2].

Objectives: A post-hoc analysis to evaluate the relationship between objective signs of inflammation (OSI), as measured by MRI/CRP, and clinical outcomes following 12 weeks of CZP treatment in pts with active axSpA.

Methods: Data were analysed from the phase 3 RAPID-axSpA study (NCT01087762) [1]. To improve precision of pt-level estimates, data from two independent readers were pooled in a Mixed Model for Repeated Measures for each response variable; Manhattan plots are presented for ASDAS, BASDAI, CRP, Ankylosing Spondylitis spine MRI (ASspiMRI) Berlin Score and Spondyloarthritis Research Consortium of Canada (SPARCC) MRI SIJ score. Outcomes are reported for pts (initially randomised to either CZP, or to placebo before switching to CZP) prior to CZP treatment (pre-CZP treatment) and following 12 weeks (wks) of treatment (post-CZP treatment).

Results: 136 pts (radiographic axial spondyloarthritis [r-axSpA]: 76; non-radiographic axial spondyloarthritis [nr-axSpA]: 60) had a pre-CZP and ≥1 post-CZP MRI. Pre-CZP demographics for the r-axSpA and nr-axSpA populations are presented in **Table 1**. Following CZP treatment, CRP, ASspiMRI Berlin score, and SPARCC MRI SIJ score were reduced by >50%, in the majority of pts (CRP: 136/136 [100.0%]; BERLIN: 73/136 [53.7%]; SPARCC: 71/136 [52.2%]), and often by >75% (CRP: 18/136 [13.2%]; BERLIN: 53/136 [39.0%]; SPARCC: 50/136 [36.8%]) irrespective of pre-CZP value. However, only a minority of both r-axSpA and nr-axSpA pts (**Figure 1**), showed a >50% reduction in clinical responses (ASDAS: 66/136 [48.5%]; BASDAI: 64/136 [47.1%]). These results were also observed at the individual pt level; >50% improvements in MRI/CRP inflammatory measures did not translate into similar improvements in clinical responses for the majority of pts.

Conclusion: This analysis revealed a potential disconnect between OSI, as measured by MRI and CRP, and clinical outcome responses. In most pts, CZP treatment resulted in a reduction of objective measures of inflammation, irrespective of improvements in clinical symptoms and measures of disease activity. The use of clinical response measures as clinical trial endpoints may therefore underestimate anti-inflammatory treatment effects.

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Table 1. Baseline demographics and characteristics

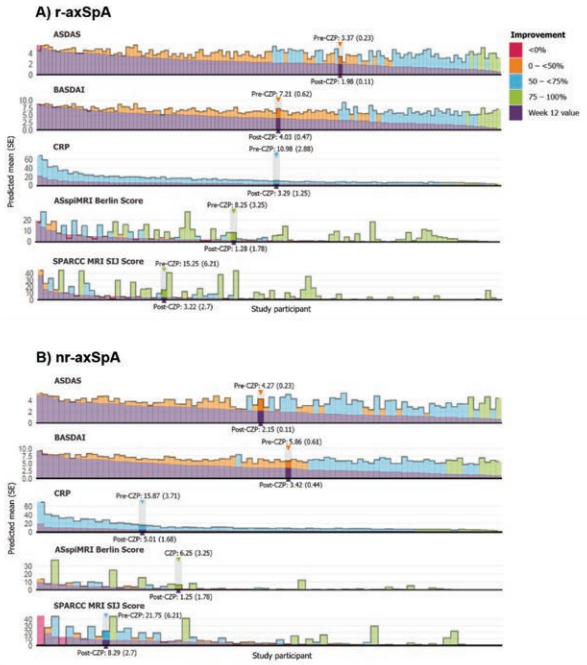
	r-axSpA (N=76)	**nr-axSpA (N=60)**
Age, years, mean (SD)	40.4 (11.6)	37.3 (13.0)
Male, n (%)	52 (68.4)	31 (51.7)
BMI, kg/m^2, mean (SD)	27.0 (5.2)[a]	26.8 (6.0)[a]
Symptom duration, years, median (min–max)	10.3 (0.3–50.9)	5.9 (0.3–39.6)
Symptom duration ≥5 years, n (%)	51 (67.1)	32 (53.3)
HLA-B27 positive, n (%)	59 (77.6)[b]	46 (76.7)[c]
ASDAS, mean (SD)	4.0 (0.9)	3.8 (0.9)
BASDAI, mean (SD)	6.8 (1.5)	6.6 (1.5)
CRP, mg/L	21.2 (27.5)	16.2 (17.0)
Mean (SD)	14.2 (0.8–159.9)	12.5 (0.1–76.7)
Median (min-max)		
CRP, n (%)	44 (57.9)	37 (61.7)
≤15 mg/L	32 (42.1)	23 (38.3)
>15 mg/L		
MRI status, n (%)	76 (100)	37 (61.7)
MRI+	0	18 (30.0)
MRI–	0	5 (8.3)
Unknown		

MRI set. [a]Data missing for 1 patient; observed case imputation used; [b]Data missing for 1 patient; [c]Data missing for 3 patients.

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Disclosure of Interests: Martin Rudwaleit Speakers bureau: AbbVie, Boehringer Ingelheim, Chugai, Eli Lilly, Janssen, Novartis, Pfizer and UCB Pharma, Consultant of: AbbVie, Eli Lilly, Novartis, and UCB Pharma, Filip van den Bosch Speakers bureau: AbbVie, BMS, Celgene, Janssen, Merck, Novartis, Pfizer and UCB Pharma, Consultant of: AbbVie, Amgen, Eli Lilly, Galapagos, Janssen, Merck, Novartis, Pfizer and UCB Pharma, Helena Marzo-Ortega Speakers bureau: AbbVie, Eli-Lilly, Janssen, MSD, Novartis, Pfizer and UCB Pharma, Grant/research support from: AbbVie, Eli-Lilly, Janssen, MSD, Novartis, Pfizer and UCB Pharma, Victoria Navarro-Compán Speakers bureau: AbbVie, Eli Lilly, Janssen, MSD, Novartis, Pfizer and UCB Pharma, Consultant of: AbbVie, Eli Lilly, Galapagos, Moonlake, MSD, Novartis, Pfizer and UCB Pharma, Grant/research support from: AbbVie and Novartis, Rachel Tham Employee of: Veramed statistical

Figure. Change following 12 weeks of CZP treatment in clinical response and measures of objective signs of inflammation in patients with **A)** r-axSpA and **B)** nr-axSpA



Patient treatment sequence: CZP 400 mg at Week 0. Each bar represents a single patient in the cohort of 76 patients (for r-axSpA) or 60 patients (for nr-axSpA). Across all five endpoints, the same patient is indicated by an arrow. The pre- and post-CZP states are indicated by the step-line (the "skyline") and the dark purple line within each bar (Week 12 value), respectively; the space between these points reflects the change in response. Change in response has been grouped into four categories based on the percentage reduction, as shown by the figure legend. Data presented were obtained from a Mixed Model Repeated Measures that was applied to each response variable: for SPARCC MRI SIJ score, ASspiMRI Berlin score, and ASDAS response variables a linear mixed effect model was used to estimate EBLUP with random effects of: reader j overall, reader j in reading campaign k overall, reader j for subject i and reader j for subject i in reading campaign k; for CRP and BASDAI response variables, a linear mixed effects model was used to estimate EBLUP with spatial autocorrelation (using nearby visits to estimate response variable values). ASDAS: Ankylosing Spondylitis Disease Activity Score; ASspiMRI: Ankylosing Spondylitis spine MRI score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BMI: body mass index; CRP: C-reactive protein; CZP: certolizumab pegol; EBLUP: empirical best linear unbiased predictor; HLA-B27: human leukocyte antigen B27; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; OSI: objective signs of inflammation; r-axSpA: radiographic axial spondyloarthritis; SD: standard deviation; SE: standard error; SIJ: sacroiliac joints; SPARCC: Spondyloarthritis Research Consortium of Canada.

consultant for UCB Pharma, Thomas Kumke Shareholder of: UCB Pharma, Employee of: UCB Pharma, Lars Bauer Shareholder of: UCB Pharma, Employee of: UCB Pharma, Mindy Kim Shareholder of: UCB Pharma, Employee of: UCB Pharma, Lianne S. Gensler Consultant of: AbbVie, Acelyrin, Eli Lilly, Fresenius Kabi, Janssen, Novartis, Pfizer, and UCB Pharma, Grant/research support from: Novartis and UCB Pharma paid to institution.

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POS0684

INFLAMMATION IS ASSOCIATED WITH INCIDENT HYPERTENSION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A LONGITUDINAL COHORT STUDY

Keywords: Real-world evidence, Spondyloarthritis, Prognostic factors

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Background: HT is the most prevalent comorbidity in axSpA (1), and is one of the strongest predictors for accelerated atherosclerosis and atherosclerotic vascular events in the general populations [2]. However, the association between time-varying inflammatory markers, disease activity and drug use and the development of incident hypertension (IHT) remain unknown.

Objectives: To elucidate the tiem-varying risk factors for the development of IHT in patients with axial spondyloarthritis (axSpA).

Methods: We conducted a long-term retrospective cohort study in axSpA patients who were recruited from 2001-2019 from a university clinic in Hong Kong. Patients with HT and/or anti-hypertensive drug use at baseline were excluded. They were followed until the end of 2020. The outcome was IHT, defined by a diagnosis and/or a prescription for an antihypertensive drug. Baseline and time-varying Cox regression analyses adjusting for age, sex, and body mass index (BMI), were used to assess the relationship between inflammatory burden, drug use and IHT.

Results: 413 patients [age: 34(25-43) years, male: 319 (77.2%)] were recruited. After a median follow up of 12 (6-17) years, 58 patients (14%) developed IHT (IHT+group). Among all the baseline variables, disease duration (BLDD) was the only independent predictor for IHT based on the Cox regression model. In the time-varying multivariate Cox regression analysis, ESR level as an inflammatory marker and BLDD longer than 5 or 10 years, remained as the significant independent predictors to increase risk of future IHT (Table 1a and 1b), while ESR≥20, the use of csDMARDs, sulfasalazine or paracetamol were no longer statistically significant. The Kaplan-Meier curve showed the survival probability were significant lower in groups with BLDD longer than 5 or 10 years (Figure 1).

Conclusion: Higher inflammatory burden as reflected by BLDD longer than 5 or 10 years were predictors associated with IHT after adjusting for inflammation marker and traditional CV risk factors. Higher ESR level may also play a role in the development of IHT in these patients.

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Table 1. Multivariable analysis with time-dependent Cox proportional hazard regression for the predictors of incident hypertension stratified by baseline disease duration.

Table 1a.	Model 1		Model 2	
	Time-dependent HR (95%CI)	p-value	Time-dependent HR (95%CI)	P-value
ESR	1.03 (1.00, 1.06)	0.035*		
ESR≥20			4.14 (0.75, 22.75)	0.102
csDMARDs	1.18 (0.24, 5.88)	0.838	1.56 (0.33, 7.332)	0.572
BLDD<5y	Ref	Ref	Ref	Ref
10>BLDD≥5y	5.82 (1.06, 31.77)	0.042*	4.97 (0.94, 26.27)	0.059
BLDD>10y	2.84 (4.46, 180.27)	<.001*	3.54 (4.51, 277.82)	<.001*
Paracetamol	8.20 (0.21, 3.18)	0.774	8.14 (0.21, 3.13)	0.764
Age	1.05 (0.99, 1.10)	0.077	1.05 (1.00, 1.10)	0.062
Sex	2.74 (0, ∞)	0.998	1.94 (0, ∞)	0.998
BMI	1.12 (1.00, 1.27)	0.060	1.10 (0.97, 1.24)	0.127
Table 1b.	Model 1		Model 2	
	Time-dependent HR (95%CI)	p-value	Time-dependent HR (95%CI)	P-value
ESR	1.03 (1.00, 1.06)	0.035*		
ESR≥20			3.96 (0.74, 21.32)	0.109
SULF	1.14 (0.18, 7.37)	0.891	1.31 (0.24, 7.19)	0.760
BLDD<5y	Ref	Ref	Ref	Ref
10>BLDD≥5y	6.02 (1.17, 31.04)	0.003*	5.22 (1.02, 26.78)	0.048*
BLDD>10y	2.80 (4.43, 177.25)	<.001*	3.28 (4.39, 245.63)	<.001*
Paracetamol	8.23 (0.21, 3.30)	0.758	8.36 (0.21, 3.40)	0.731
Age	1.05 (0.99, 1.10)	0.089	1.05 (1.00, 1.10)	0.076
Sex	2.77 (0,∞)	0.998	2.01 (0, ∞)	0.998
BMI	1.12 (0.99, 1.27)	0.070	1.11 (0.98, 1.25)	0.110

HR, Hazard ratio; BLDD: baseline disease duration; ESR: Erythrocyte Sedimentation Rate; BMI: Body mass index; y, years.

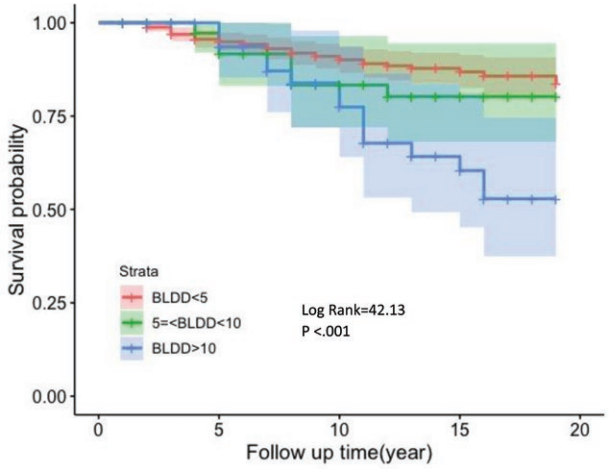


Figure 1. The Kaplan-Meier curve for the survival probability of groups stratified by baseline disease duration over time.BLDD: baseline disease duration.

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Disclosure of Interests: None Declared.
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POS0685

MONITORING PHYSICAL ACTIVITY OF PATIENTS WITH ANKYLOSING SPONDYLITIS IN THE SELECT-AXIS 2 PHASE 3 TRIAL: BASELINE USAGE AND ADHERENCE RESULTS FROM A WEARABLE DEVICE STUDY

Keywords: Spondyloarthritis, Clinical trials, Outcome measures

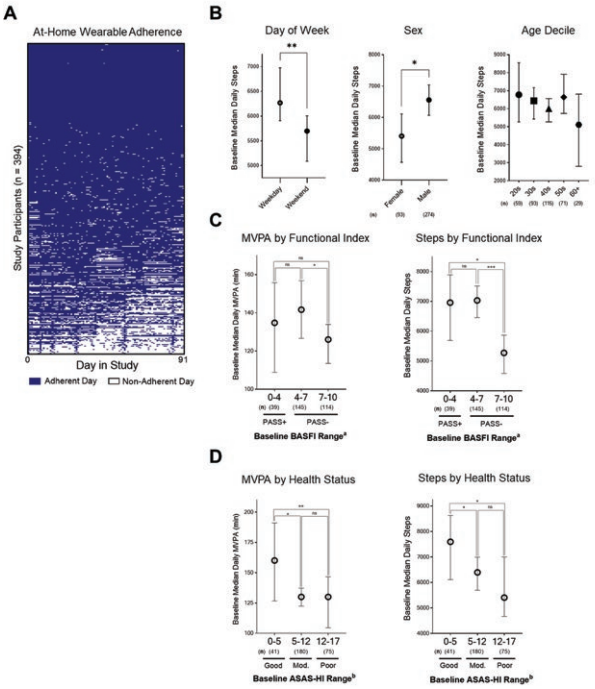
P. J. Mease[1], R. Grainger[2], D. Webster[3], M. Crouthamel[3], J. Shen[3], Y. Xing[3], A. Shmagel[3], H. Jones[3], J. Curtis[4]. [1]*Swedish Medical Center, Providence St Joseph Health, and University of Washington, Rheumatology Research Division, Seattle, WA, United States of America*; [2]*University of Otago, Wellington, Department of Medicine, Wellington, New Zealand*; [3]*AbbVie Inc, Immunology, North Chicago, IL, United States of America*; [4]*The University of Alabama at Birmingham, Division of Clinical Immunology and Rheumatology, Birmingham, AL, United States of America*

Background: Exercise can improve the symptoms of axial spondyloarthritis (axSpA) and is recommended as a cornerstone of management for axSpA [1]. Wearable devices can objectively measure physical activity and device-generated data may support development of digitally measured novel endpoints that correlate with treatment response.
Objectives: To report device usage and adherence with wearable technology used to assess the physical activity of people with active ankylosing spondylitis (AS) and inadequate response to biologic DMARD therapy (bDMARD-IR) in the SELECT-AXIS 2 trial, as well as evaluate the association between baseline physical activity and patient-reported measures of functional ability and health.
Methods: Patients in the SELECT-AXIS 2 bDMARD-IR study (NCT04169373), a 1:1 randomized, double-blind, phase 3 trial of upadacitinib vs placebo [2], were required to wear a medical-grade wrist-worn actigraphy device that monitored physical activity during the 14-week, placebo-controlled portion of the study. Eligibility criteria included a diagnosis of active AS and inadequate response to bDMARDs. Wearable device adherence, defined as at least 16 hours per day usage, was evaluated through 14 weeks. Baseline physical activity measurements, including median daily steps and time spent in moderate to vigorous physical activity (MVPA), were defined as those in the first week of device usage after trial entry. Median daily steps at baseline were compared by sex and day of the week (weekend vs weekday) across the entire patient cohort using the Mann–Whitney test; differences in physical activity by age were assessed with the Kruskal–Wallis test. For inclusion in all other baseline analyses, patients were required to have at least 3 out of 7 days with sufficient device use, and average physical activity was calculated over these adherent days. Finally, the comparison between baseline physical activity and functional index (BASFI) or health status (ASAS Health Index [ASAS-HI]) was calculated using the Mann-Whitney test; previously established cutoffs were used to distinguish patients into groups with low, moderate, or high functional ability or health [3,4].
Results: Of 420 total patients, physical activity data was collected from 394 participants, and 312 patients met minimal adherence criteria at baseline (first week). Through 14 weeks, adherence was demonstrated for 83.5% of study days (**Figure 1A**). At baseline, physical activity was higher in men than women and on weekdays than weekends; median daily steps were not significantly different based on age (**Figure 1B**). Baseline mean BASFI and ASAS-HI in the SELECT-AXIS 2 bDMARD-IR AS trial were 6.3 and 9.3 respectively, suggesting relatively high functional limitation. Patients with higher baseline functional impairment (BASFI score >7) did not statistically differ in median daily time spent in MVPA (p=0.366) but took an average of 1690 fewer steps per day (p=0.021) than patients with BASFI scores ≤4 who met the Patient Acceptable Symptom State (PASS) [3] (**Figure 1C**). Patients reporting "poor" health status [4] (ASAS-HI score ≥12 to 17) spent 30.0 fewer minutes in MVPA (p=0.005) and took 2186 fewer steps per day (p=0.010) than those with "good" health status [4] (ASAS-HI scores ≤5; **Figure 1D**).
Conclusion: bDMARD-IR patients with AS in SELECT-AXIS 2 had high adherence with use of a wearable activity monitoring device over 14 weeks. Lower physical activity was generally associated with higher disability scores and poor health status at baseline. These data support the utility of wearable devices for assessing physical activity in people with AS, suggesting the possibility to use such devices to evaluate the impact of targeted therapeutics on passively collected physical activity and functional ability outcomes.

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Figure 1. Wearable device adherence over 14 weeks and baseline physical activity characteristics of the SELECT-AXIS 2 bDMARD-IR study



(A) Heat map showing patient adherence to wearing the device at least 16 hours per day over 91 days, ranked from highest adherence at the top to lowest adherence at the bottom. Clinical visit days were censored from the analysis. (B) Comparisons of baseline physical activity by sex, day of the week, and age group across the entire patient cohort. (C, D) Baseline average daily number of steps and minutes spent in moderate to vigorous physical activity (MVPA) according to baseline functional index (BASFI) or health status (ASAS Health Index [ASAS-HI]) among patients with at least 3 of 7 days with sufficient device use. Nominal $^{*}P < 0.5$ and $^{**}P < 0.01$; ns, nonsignificant.
[a]BASFI range cutoffs were 0 to ≤4 for those who met the Patient Acceptable Symptom State (PASS) and dived into two groups (>4 to ≤7 and >7 to 10) for those who did not meet the PASS threshold, as previously defined (Zochling J, *Arthritis Care Res [Hoboken]* 2011;63:S47–58).
[b]ASAS-HI range cutoffs were 0 to ≤5 for "good", >5 to <12 for "moderate", and ≥12 to 17 for "poor" health status (Kiltz U, et al., *Ann Rheum Dis* 2018;77:1311–17).

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POS0686

GENDER DIFFERENCES IN THE MANAGEMENT OF SPONDYLOARTHRITIS (SPA) PATIENTS

Keywords: Spondyloarthritis

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Background: Spondyloarthritis (SpA) is a family of arthritic rheumatic diseases, including axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA), that primarily affects the spine and joints. It causes inflammation of the spinal and peripheral joints that can lead to severe, chronic pain and discomfort. Diagnosing SpA has proven challenging, particularly for women who are found to be underdiagnosed in AS despite the disease affecting men and women both equally, as there are no current diagnostic criteria for axSpA [1]. Disease activity can be measured through tests such haematology and joint count measurements.

Objectives: The objective of this study was to examine any gender differences in the management of SpA patients and highlight any nuances in treating these patients.
Methods: A multi-centre online medical chart review study of patients with PsA and Axial SpA was conducted between July 2022 – September 2022 among UK, FR, DE, IT & ES rheumatologists practicing across hospital and private practices. Physicians were screened for practice duration and patient volume. Charts of patients prescribed with biologics/tsDMARDS were included in the analysis.
Results: 262 sampled physicians collectively reported 1387 SpA patients. From the reported SpA patients, 812 were recorded as male and 575 as female. The female cohort were recorded with higher instances of co-existing conditions of depression (11.5% vs 5.3%) and anxiety (13.2% vs 8.1%) than men. When evaluating extra articular manifestations, female cohort were recorded with higher nail dystrophy (12.7% vs 8.6%) and psoriasis (36.7% vs 26.4%) than men. In assessing areas the AS patient suffers from, female cohort were recorded with higher peripheral involvement (49.6% vs 34.0%) and males more axial involvement (50.9% vs 28.0%). In assessing disease scores, female cohort were recorded with higher joint counts, haem scores, and PASI score. Physician-defined status of disease severity reported female cohort with higher current severity (48.4% vs 41.5% moderate and severe) and lower remission rates (45.4% vs 36.7% not in remission) in comparison to men.

Table 1. Reported patient disease and haematology scores (mean)

Reported SpA patients	Tender joint count (TJC)	Swollen joint count (SJC)	C-reactive protein (CRP)	Erythrocyte Sedimentation Rate (ESR)	Psoriasis area and severity index (PASI)
Female	3.5	2.0	12.1	21.5	14.2
Male	2.3	1.3	6.8	16.9	11.9

Length of time on current biologic and/or tsDMARD recorded male cohort on treatment for longer timeframe vs females (mean months: 50.2 vs 46.5). The most prominent biologics to treat the two patient groups are TNFis (72.2% male, 68.6% female); alternate modes of action, such as IL-17is and JAKis, are more prominently recorded in females vs males (31.2% vs 27.7%). Drivers of treatment choice – specified by sampled physicians - prioritised efficacy in skin (23.3% vs 19.3%), efficacy in manifestations of PsA beyond skin and joint (13.6% vs 9.6%), and reduction of peripheral joint inflammation (17.0% vs 10.3%) in female cohort versus male cohort.
Conclusion: From the sample surveyed, current disease activity is higher in reported female patients than males in SpA. Additionally, males are more likely to stay on the same bio/tsDMARD versus females, suggesting a disparity in efficacy or unmet needs when evaluating the two cohorts. It is possible that key differentiating identifiers, such as co-existing comorbidities outside axSpA or PsA or extra articular manifestations, can be used when deciding how to treat a patient. Discussion is necessary about gender-specific treatment plans in SpA, as well as factoring in possible mental health burden (anxiety and depression) disparities across gender cohorts. Further investigation using comparator cohort is warranted.
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POS0687 LONG TERM (10 YEAR) CLINICAL OUTCOME OF RECENT ONSET AXIAL SPONDYLOARTHRITIS (AXSPA): DATA FROM THE DESIR COHORT

Keywords: Prognostic factors, Spondyloarthritis, Epidemiology

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Background: The information related to the long term outcome of a disease is of huge interest for the clinicians in daily practice to facilitate the information of the patients recently diagnosed as axSpA. The data from inception cohorts are better approaching the truth of this long term prognosis in comparison to the conventional retrospective cohorts mainly conducted in patients with advanced and severe disease managed in tertiary referral centers.
Objectives: To evaluate the 10 year clinical outcome (and its predisposing factors) of patients suffering from recent onset axSpA in the DESIR cohort.
Methods: *Study design*: DESIR is an ongoing (10 year follow-up completed for all the patients) multicenter cohort of recent onset axSpA. *Diagnosis*: At entry visit and during the 10 year follow-up period, the diagnosis was based on the opinion of the treating physician with a requirement of a diagnosis of axSpA at entry and the possibility to exclude the patients after the first 2 years follow-up period in case of a change in this diagnosis. *Management during the 10 year period*: the investigators were in charge of the data collection required by the protocol but the management (treatment regimens) was only based on the decision of the treating rheumatologist. *Statistical analysis*: Data presented here are the ones issued a)from the analyses on the completers (observed data) and b) after multiple imputations considering the missing data due to the patients lost of follow-up (imputed data).
Results: Of the 708 enrolled patients, 45 were excluded from the cohort because of a change in the entry visit diagnosis, 3 patients died (suicide n = 1, colorectal cancer n = 1, sudden death n=1), 300 were lost of follow-up and 360 patients completed the 10 year period. *A -Based on the analyses of the 10 year completers (n=360)* No patient necessitated a spinal vertebrotomy, one single patient had a bilateral total hip replacement. A pension from the national health care system was provided to 16% patients because an invalidity related to the axSpA disease. A csDMARD (methotrexate and/or sulfasalazine) has been prescribed in 32% and a biotherapy in 55%. The prevalence of the main extra-musculoskeletal features increased from 18 to 30%, 10 to 18% and 5 to 10% from baseline to year 10 for psoriasis, acute anterior uveitis and inflammatory bowel disease respectively. The prevalence of the main comorbidities increased from 3 to 8%, 0 to 3%, 5 to 15%, 0 to 4%, 1 to 3% and 0 to 2%, from baseline to year 10 respectively for severe GI events, MACE, hypertension, diabetes, tuberculosis and other severe infections respectively. B- *Based on the analyses of the 10 year completers (n=360) (observed data) and the 663 patients with unchanged initial axSpA diagnosis (imputed data)* An acceptable status at year 10 was observed in 77%,70 [63; 77]%,;49% 43 [37; 49]%; 55% 48 [41; 56]% considering an acceptable PASS, BASDAI < 30, ASDAS < 2.1 for the observed (%) and imputed (% and [95%CI]) data respectively. The impact of the disease on the daily life of the patients was evaluated by different parameters: ASAS HI ≤ 5 (41 [35; 47]%, SF36 physical score (42 [40; 44]) and SF36 mental score (43 [40; 46]). The multivariate analysis of the baseline predisposing factors of an acceptable status at year 10 defined as an ASDAS score<2.1 picked-up the following variables: short (<1.5year)delay between the first symptoms and the baseline visit: OR= 1.46[0.93;2.29],socio-professional level (white collar): OR=1.87[1.20;2.90] and baseline BASDAI score<40, OR=1.91[1.23;2.94]
Conclusion: These data are suggesting a favorable 10 year outcome in terms of stringent measures such as the requirement to surgery contrasting with a relatively less favorable outcome with regard to patient reported outcomes. These data should improve and facilitate the information provided to the patients at the time of their diagnosis.
Acknowledgements: The authors would like to thank all the investigators of the 25 participating centers as well as all the 708 enrolled patients.This study has been financially supported via unrestricted grants from PFIZER and the French Society of Rheumatology.
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POS0688 COMPARING THE CONSTRUCT VALIDITY AMONG MEASURES OF PAIN AND STIFFNESS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Patient reported outcomes, Spondyloarthritis, Outcome measures

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Background: In the context of the recent update of the ASAS core outcomes set (COS), the preferred comparative validity of the measurement instruments to assess the domains 'Pain' and 'Stiffness' has been questioned as for each domain responsiveness of instruments was comparable. Group discrimination across various external constructs can help provide useful insights and represents unmet need.
Objectives: To compare the group discriminatory capacity, as part of the construct validity, of three instruments to assess pain and three questions of morning stiffness.

Methods: Data from the 8-year visit of patients with r-axSpA from the multinational OASIS cohort was assessed. The available instruments for pain assessment were: i) total spinal pain, ii) spinal pain at night, iii) spinal pain from BASDAI Q2 (addressing neck, back or hip pain); and for morning stiffness: i) severity of morning stiffness (BASDAI Q5), ii) duration of morning stiffness (BASDAI Q6), iii) the combined score between severity and duration of morning stiffness (average BASDAI Q5/6). Data from 8 year-visit were used as the first time-point where all the instruments were obtained on a 0–10 numeric rating scale (as currently used). The discriminatory capacity was assessed through the standardised mean difference (SMD) that is calculated as the difference of the group means divided by the pooled SD of the group means, with a higher value reflecting a higher discriminatory capacity. The external constructs used to compare the ability to discriminate between subgroups of patients were: ASDAS, BASDAI (dichotomized into inactive/active disease), PGA, PhGA, fatigue, BASFI, BASMI and mSASSS (dichotomized by the median).
Results: 98 patients were included: 71% males, mean age 54 (SD 11), with a mean symptom duration of 31 (11) years. The mean (SD) scores for pain were 3.7 (2.3), 2.9 (2.3) and 4.6 (2.6) for spinal pain, spinal pain at night and BASDAI Q2, respectively. The mean (SD) scores of morning stiffness were 3.7 (2.6), 3.3 (3.1) and 3.5 (2.7) for BASDAI Q5, Q6 and Q5/6, respectively. Spinal pain by BASDAI Q2 and total spinal pain had higher SMDs compared to spinal night pain across all group comparisons, with spinal pain BASDAI Q2 performing mostly slightly better (Table 1). Regarding morning stiffness, the severity question (BASDAI Q5) had consistently higher SMDs across all the clinical external constructs, while duration of morning stiffness (BASDAI Q6) performed worse.
Conclusion: Spinal pain from BASDAI Q2 and severity of morning stiffness (BASDAI Q5) are, respectively, the pain and morning stiffness instruments that best discriminate subgroups of patients classified according to disease activity, functional ability, fatigue or spinal mobility. The recommended ASAS COS pain instrument spinal pain BASDAI Q2, was confirmed to discriminate best. In the case of stiffness, the ASAS COS stiffness measure (BASDAI Q5/6) performed well although slightly less than the severity of morning stiffness (BASDAI Q5).

Table 1. Discrimination between subgroups of patients

Assessment measure	ASDAS <2.1 vs ≥2.1 SMD	BASDAI <4 vs ≥4 SMD	Fatigue <5 vs ≥5 SMD	BASFI <4 vs ≥4 SMD	BASMI <4 vs ≥4 SMD	mSASSS <15 vs ≥15 SMD
Total spinal pain	1.57	1.92	1.62	0.92	0.27	-0.32
Spinal night pain	1.07	1.39	1.27	0.78	0.07	-0.20
Spinal pain BASDAI Q2	1.88	2.37	1.65	0.89	0.31	-0.29
Morning stiffness severity BASDAI Q5	1.52	2.14	1.58	0.99	0.26	-0.11
Morning stiffness duration BASDAI Q6	1.18	1.80	1.09	0.83	0.09	-0.14
Morning stiffness average BASDAI Q5/6	1.40	2.14	1.38	0.95	0.17	-0.13

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POS0689

DIAGNOSTIC DELAY IN PATIENTS INCLUDED IN THE INTERNATIONAL MAP OF AXIAL SPONDYLOARTHRTIS: ASSOCIATIONS WITH GEOGRAPHIC, SOCIO-DEMOGRAPHIC AND DISEASE-RELATED FACTORS

Keywords: Patient reported outcomes, Spondyloarthritis, Diagnostic Tests

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Background: Despite efforts for early detection, delayed diagnosis in axial spondyloarthritis (axSpA) remains an unresolved challenge.
Objectives: This analysis aimed to assess diagnostic delay and its associated factors around the world in a large sample of patients included in the International Map of Axial Spondyloarthritis (IMAS).
Methods: IMAS is a cross-sectional online survey (2017-2022) including 5,557 unselected axSpA patients from 27 countries. Diagnostic delay was calculated as the difference between age at diagnosis and age at symptom onset reported by patients. The independent factors evaluated were: age at symptom onset, disease duration, gender, education level, diagnosed by rheumatologist, number of healthcare professionals (HCPs) seen before diagnosis, HLA-B27, uveitis, and inflammatory bowel disease. The factor world region was introduced as a dummy variable taking Europe as the reference region due to its larger sample size and diagnostic delay close to the overall mean. The Mann-Whitney, Kruskal-Wallis test and Pearson correlation were used to evaluate the differences in diagnostic delay and independent variables. Associations between diagnostic delay and regions, sociodemographic characteristics, as well as disease-related factors were explored through univariable and multivariable linear regression analysis.
Results: Data from 5,327 patients who reported data to calculate diagnostic delay in IMAS survey were analyzed: 3,231 were from Europe, 770 from North America, 600 from Asia, 548 from Latin America, and 146 from Africa. Overall, patients reported a diagnostic delay of 7.4 years (median: 4.0) since symptom onset, with substantial variation across regions, being the highest in South Africa and the lowest in Asia **(Figure 1)**. Furthermore, mean disease duration was 17.1 ± 13.3. Patients with longer diagnostic delay were more frequently female, younger at symptom onset, with more years with the condition, more commonly diagnosed by the rheumatologist, with a higher number of HCPs seen before diagnosis, had experienced uveitis, and inflammatory bowel disease. The variables independently associated with longer diagnostic delay in the final multivariable regression model were: younger age at symptom onset (b=-0.100), more disease duration (b=0.363), female gender (b=2.274), being diagnosed by rheumatologist (b=1.163), higher number of healthcare professionals (HCPs) seen before diagnosis (b=1.033), and presence of uveitis (b=1.286; **Table 1**).
Conclusion: In this global sample of axSpA patients, the mean diagnostic delay was 7.4 years, and had significant differences across regions. Younger age at symptom onset, longer disease duration, female gender, diagnosed by rheumatologist, higher number of HCPs seen before diagnosis, and the presence of uveitis were the parameters associated with a longer diagnostic delay in axSpA patients.

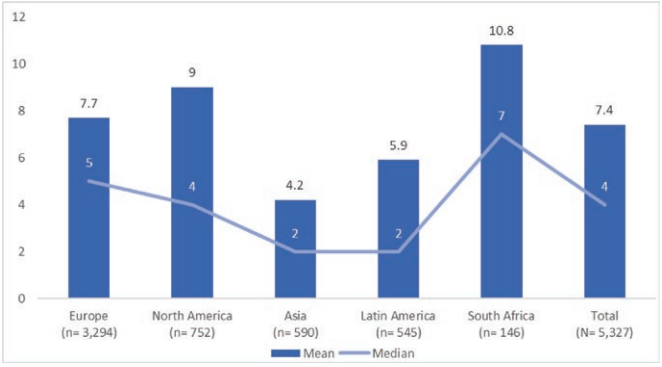


Figure 1. Mean and median diagnostic delays by region (N= 5,327)

Table 1. Univariable and multivariable linear regression analysis of the association between diagnostic delay and independent variables in patients with axial spondyloarthritis (N= 4,595)

Variables	Ref.	Univariable analysis		Multivariable analysis	
		B	95% CI	B	95% CI
Age at symptom onset, years	-	**-0.306**	**-0.326, -0.287**	**-0.100**	**-0.120, -0.080**
Disease duration	-	**0.401**	**0.386, 0.416**	**0.363**	**0.346, 0.380**
Female gender	Male	**2.324**	**1.843, 2.804**	**2.274**	**1.860, 2.687**
Diagnosed by rheumatologist, yes	No	**2.410**	**1.868, 2.952**	**1.163**	**0.710, 1.615**
No. of HCPs seen before diagnosis	-	**1.696**	**1.520, 1.873**	**1.033**	**0.877, 1.189**
Uveitis	No	**1.580**	**0.996, 2.165**	**1.286**	**0.808, 1.764**
Inflammatory bowel disease	No	**0.834**	**0.117, 1.550**	-0.043	-0.610, 0.525
Region, Asia	Europe	**-3.511**	**-4.241, -2.781**	**1.003**	**0.334, 1.673**
Region, North America		**1.228**	**0.499, 1.958**	**1.470**	**0.902, 2.039**
Region, Latin America		**-1.792**	**-2.583, -1.000**	0.626	-0.045, 1.297
Region, South Africa		**3.015**	**1.549, 4.481**	**3.356**	**2.170, 4.541**

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POS0690 IN AXIAL SPONDYLOARTHRITIS, NON-STEROIDAL ANTI-INFLAMMATORY DRUGS REDUCE MRI-APPEARANCE OF SACROILIITIS

Keywords: Imaging, Spondyloarthritis

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Background: MRI evidence of active sacroiliitis (sacroiliac joint bone marrow oedema (BMO)) is commonly used to assist diagnosis and classification of axial spondyloarthritis (axSpA). Non-steroidal anti-inflammatory drugs (NSAIDs) are used as first-line therapy, and for persistent clinical symptoms continuous treatment is recommended. Prescribed in primary care, and widely available over-the-counter, many patients are already taking NSAIDs when they first present to rheumatology.

Objectives: To determine whether NSAID use leads to an underestimation of sacroiliac joint BMO.

Methods: Adults with axSpA were recruited from NHS rheumatology clinics and asked to discontinue their NSAIDs for 1-2wks before undergoing a sacroiliac joint MRI (Scan 1) using a standardised protocol. All participants then re-started their NSAIDs. Those who scanned positive for BMO lesions, as determined using internationally recognised (ASAS) definitions, underwent a second scan 6wks after restarting NSAIDs. Scans were read independently by 2 readers (adjudicated by a 3rd, if required), blinded to participants' clinical characteristics and timepoint. We determined the proportion of participants who scanned negative at Scan 2 (on NSAIDs) who had previously scanned positive at Scan 1 (off NSAIDs).

Results: 311 participants were recruited from 34 centres. Table 1 shows participants' baseline characteristics. Almost all participants (296; 95%) completed the NSAID washout and underwent Scan 1. However, 135 (50%) reported an increase in spinal pain (median increase: 2 points on a 0-10 numerical rating scale; inter-quartile range: 1-3), and 166 (61%) reported worsening of disease activity (median increase in BASDAI: 0.9; 0.5-1.6). At Scan 1, 149 (50%) were positive for BMO lesions. 131 (88%) participants underwent the six-week follow-up scan, of whom 31 scanned negative (24%; 95%CI: 17-32%).

Conclusion: These findings suggest that NSAIDs influence sacroiliac BMO and, where sacroiliiitis is present, around one-in-four show resolution of lesions in the presence of NSAIDs. This has important implications for axSpA diagnosis and classification. If patients with axSpA (or suspected axSpA) are willing to attempt NSAID washout prior to MRI, this should be considered. There may be concerns about increases in disease activity or spinal pain, but we also provide evidence that almost all patients who attempt washout can successfully achieve it.

Table 1. PARTICIPANTS' BASELINE CHARACTERISTICS (N=311) (BEFORE NSAID WASHOUT)

		Median (inter-quartile range) or N (%)	
Demographic characteristics			
Age	Years	42	(32 to 52)
Sex	Male	194	(62%)
Ethnicity	White	271	(87%)
Disease classification			
Ankylosing spondylitis – modified New York criteria	93	(30%)	
ASAS axSpA criteria – imaging arm	186	(60%)	
ASAS axSpA criteria – clinical arm	155	(50%)	
Other clinical characteristics			
Symptom duration	Years	9	(4 to 20)
Time since diagnosis	Years	1	(0 to 7)
Disease activity	BASDAI	4.5	(2.8 to 6.2)
Function	BASFI	3.1	(1.5 to 5.6)
HLA-B27 status	Positive	171	(55.2%)
	Negative	71	(22.9%)
	Unknown	68	(21.9%)
C-reactive protein *	Elevated CRP (>4 mg/dL)	143	(46.0%)
	Value (mg/dL) **	6	(2.5 to 11)
NSAID use pre-washout[2]		266	(86%)

* Missing data for N=119. ** All participants started NSAIDs after Scan 1.

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POS0691 ANALYSIS OF GAIT IN LONGSTANDING AXIAL-SPONDYLOARTHRITIS: A MONOCENTRIC PILOT STUDY

Keywords: Descriptive Studies, Spondyloarthritis, Motor function

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Background: Progression of radiographic damage in axial-spondyloarthropaties is related to higher functionality impairment in longstanding patients, resulting in poorer quality of life and autonomy. Its impact on gait has not been extensively studied yet. Time-up and go (TUG) test and GAIT analysis (GA) are currently used in neurological and musculoskeletal diseases to evaluate changes in patients gait and stance.

Objectives: The aim of this study is to evaluate with standardized procedures modifications of gait in patients with inactive longstanding axSpa with radiographic damage, comparing them with a cohort of sex, age and BMI matched healthy controls.

Methods: Patients followed at Rheumatology Unit of the University Hospital of Cagliari were enrolled. Inclusion criteria were: 1) having a diagnosis of axSpa, 2) having an inactive disease (BASDAI<4, PtGA<20, PhGA<20), 3) evidence of radiographic damage in the most recent spine x-ray available (mSASSS >20), 4) ability to walk autonomously. Exclusion criteria were: 1) deafness, 2) any medical condition that, according to investigators, could expose patients at any excess risk or interfere with the procedures of the study. Patients underwent a TUG test and a gait analysis at the Department of Mechanical, Chemical and Materials Engineering, University of Cagliari. For TUG Test the following parameters were recorded: TUG time, sit-to-stand time, first and second rotation time, stand-to-sit time, walking time. Walking speed and mean step length were recorded using GAIT analysis. Statistical analysis was performed with MANOVA (Pillai's Trace, Wilk's Lambda, Hotelling's Trace, Roy's Largest Roots). Level of statistical significance was set at<0,05.

Results: Fifteen patients and fifteen HC were enrolled in this study. Mean age was 60,1±7,8 years for patients and 61,3±7,8 for HC. Weight and height were similar in both groups (axSpa 76,7 ± 16,8kg vs HC 72 ±7,2kg; axSpa 169,33 ± 8,8cm vs HC 170,4 ± 5,2cm). Disease duration was 27.61±9,67 years, mean mSASSS was 46,33±16,84. All patients were inactive, but showed clinical signs of disease progression (BASMI 5,9±1,19). Thirteen patients were on treatment with bDMARDs (TNF inhibitors), while 2 were off treatment. MANOVA revealed differences between axSPa patients and HC for TUG test (p<0,05). TUG time and walking time were significant longer in axSpa (TUG time 12,88±1,92s vs 10,44±2,18s, p=0,003; walking time 5,69±1,17s vs 3,68±0,8, p<0,001), while other parameters were not different between groups. Finally, axSpa patients were slower (0,95±0,16 m/s vs 1,18±0,17 m/s; p<0,05), and had a shorter step (0,52±0,65 m vs 0,65±0,69 m; p<0,05).

Conclusion: Patients with longstanding axSpa showed a different gait when compared with matched HC: we found that axSpa patients walk slower than HC, and with shorter steps. This could be interpreted as a compensatory behaviour as walking speed slower than 1 m/s has been reported as a risk factor for falling in elderly. In conclusion, we found that disease progression in axSpa patients could interfere with walking speed. Clinical relevance of these findings should be confirmed in future studies, as well as if some medical intervention (e.g. physical therapy) could minimize the impact of disease progression on posture control and walking.

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Table 1. Demographic and clinical features of patients and HC. Results of TUG and GA.

	axSpa	HC	p
Age (years)	60,1 ± 7,8	61,3 ± 7,8	ns
Sex	15 M	15 M	
Height (cm)	169,33 ± 8,8	170,4 ± 5,2	ns
Weight (kg)	76,7 ± 16,8	72 ±7,2	ns
Disease duration	27,6±9,67		
BASMI	5,9±1,19		
mSASSS	46,33±16,84		
TUG Test – Total time (s)	12,88±1,92	10,44±2,18	0,003
Sit-stand time (s)	1,53±0,42	1,38±0,34	ns
Stand-sit time (s)	1,26±0,37	1,36±0,62	ns
first turn time (s)	2,49±0,53	2,22±0,65	ns
second turn time (s)	1,9±0,47	1,79±0,75	ns
walking time (s)	5,69±1,17	3,68±0,8	<0,001
GA - walking speed (m/s)	0,95±0,16	1,18±0,17	<0,05
Step length/m	0,52±0,65	0,65±0,69	<0,05

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POS0692

CAN THE ASSESSMENT OF DIAGNOSTIC CONFIDENCE BE USED AS A PARAMETER FOR IMAGE READER'S PERFORMANCE IN AXIAL SPONDYLOARTHRITIS? FIRST RESULTS OF THE DAMACT STUDY

Keywords: Imaging, Spondyloarthritis

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Background: Early and accurate diagnosis is essential for the further outcome of patients with axial spondyloarthritis (axSpA). The confident interpretation of image data sets plays a special role in the clinical practice is crucial for diagnosing axSpA. Therefore, the own assessment of the diagnostic confidence (DC) in the evaluation of images plays an increasingly important role. For this reason, the current guidelines from the ASAS working group recommend reporting the diagnostic confidence in the radiological report.

Objectives: The aim of this study was to investigate the validity of self-reported DC on the performance of readers in the diagnosis of axSpA using sacroiliac joint (SIJ) images in X-ray, computed tomography (CT) and magnetic resonance imaging (MRI).

Methods: In total, 163 subjects were included in this retrospective study. In all subjects, X-ray, CT and MRI of the SIJ were available. In total, 9 readers scored the images for the presence or absence of axSpA. The readers were divided into three equal groups according to their experience in musculoskeletal imaging: inexperienced (0 to 1 year of experience), semi-experienced (3 to 8 years of experience) and experienced group (over 8 years of experience). All readers were blinded to clinical data. The DC was collected during the evaluation of the images on a scale from 0 (not sure) to 10 (very sure). Contingency table analysis was performed to assess the reader's performance using the clinical diagnosis (axSpA or non-axSpA) as standard of reference. The mean DC's and standard deviation (SD) were calculated for the correct and incorrect axSpA diagnosis for each readers group separately for X-ray, CT and MRI and their differences were assessed using the unpaired t-tests.

Results: Overall, 89 patients were diagnosed with axSpA and 56 patients with degenerative SIJ disease previously to the scoring. We included 18 healthy subjects in the scoring. The cumulative correct (right-positive) and incorrect (false-positive) axSpA diagnoses were evaluated separately for the different reader groups with the mean DC values, see also Table 1. We showed that the DC differs significantly for the correct and incorrect diagnosis of axSpA in the semi-experienced and in the experienced group in all modalities. However, in the inexperienced group, no significant difference was obtained between the DC's in X-ray and CT.

Conclusion: In this study, we were able to show for the first time that diagnostic confidence is a predictive measurement of the diagnostic performance respective reader in the evaluation of patients with axSpA. This is especially true for the interpretation of MRIs, which showed significant differences in all reader groups. Based on these findings, we hypothesize that the addition of diagnostic confidence in radiological findings is a reliable tool to predict diagnostic performance.

Table 1. Results. DC = diagnostic confidence. SD = standard deviation. n = cumulative number of correct or incorrect axSpA diagnosis.

	Correct axSpA diagnosis	**Incorrect** axSpA diagnosis	**P value**
X-ray	n	n	
Unexperienced (mean DC ± SD)	109 (6.29 ± 1.89)	60 (6.20 ± 1.71)	0.75
Semi experienced (mean DC ± SD)	164 (6.65 ± 2.65)	64 (5.81 ± 2.10)	0.007
Experienced (mean DC ± SD)	173 (7.94 ± 1.82)	61 (6.79 ± 2.24)	<0.0001
CT	n	n	
Unexperienced (mean DC ± SD)	166 (7.15 ± 1.74)	21 (6.78 ± 1.72)	0.10
Semi experienced (mean DC ± SD)	206 (8.38 ± 1.53)	22 (6.77 ± 2.22)	<0.0001
Experienced (mean DC ± SD)	202 (9.16 ± 1.43)	11 (7.18 ± 2.10)	<0.0001
MRI	n	n	
Unexperienced (mean DC ± SD)	184 (6.97 ± 1.85)	55 (5.80 ± 1.95)	<0.0001
Semi experienced (mean DC ± SD)	210 (8.18 ± 1.48)	54 (6.30 ± 1.68)	<0.0001
Experienced (mean DC ± SD)	208 (9.14 ± 1.67)	25 (6.72 ± 2.32)	<0.0001

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Vasculitis - large vessel vasculitis

POS0693 ULTRASOUND SHOWS ONGOING VESSEL WALL REMODELING IN GIANT CELL ARTERITIS FOR TWO YEARS AFTER DISCONTINUATION OF TOCILIZUMAB - FOLLOW-UP OF THE GUSTO TRIAL

Keywords: Imaging, Ultrasound, Vasculitis

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Background: The GUSTO (Giant cell arteritis (GCA) treatment with Ultra-Short glucocorticoids and TOcilizumab) trial evaluated the efficacy and safety of Tocilizumab (TCZ) monotherapy after a 3-day glucocorticoid-pulse in new-onset GCA [1]. Ultrasound measurements of the intima-media thickness (IMT) demonstrated a slow and steady decrease in the temporal arteries and a smaller and delayed effect on the axillary and subclavian arteries with TCZ monotherapy over 52 weeks [2]. Recently, a new Outcome Measures in Rheumatology (OMERACT) GCA ultrasonography score (OGUS) for monitoring disease activity in GCA has been proposed [3].
Objectives: To investigate the evolution of the IMT after discontinuation of TCZ at week 52 in the GUSTO trial. Data up to week 156 are presented (two-year drug-free follow-up).
Methods: Eighteen patients with new-onset GCA were enrolled in the GUSTO trial. [1] Patients received 500mg methylprednisolone intravenously for 3 consecutive days. Thereafter, glucocorticoid treatment was discontinued and TCZ (8mg/kg bodyweight) was administered intravenously, followed by weekly subcutaneous TCZ injections (162mg) from day 10 until week 52. Patients in clinical remission stopped TCZ at week 52 and entered the follow-up study. The maximum IMT of the temporal arteries (common superficial temporal artery, parietal and frontal branch) and IMT at landmarks of the axillary and subclavian arteries were measured bilaterally at weeks 52, 78, 104 and 156. The OGUS is calculated as follows: IMT divided by the rounded cut-off values of IMTs for each segment; the sum of these values is then divided by the number of segments available (maximum of 8 segments; axillary and temporal arteries considered). [3]
Results: At week 52, 13/18 patients were in relapse-free remission and entered the follow-up study. 1/13 patients presented with a minor relapse during the 104 weeks follow-up period. At week 156, 12/13 patients were in relapse-free and drug-free remission. The OGUS showed a steady decline with mean values of 0.90 (standard deviation (SD) 0.19) at week 52, 0.87 (SD 0.16) at week 78, 0.84 (SD 0.15) at week 104, and 0.79 (SD 0.12) at week 156. IMT measurements of one patient after restarting TCZ therapy were excluded (weeks 104 and 156).
Conclusion: After 52 weeks of treatment with TCZ, the IMT in GCA continues to decline during a drug-free period of up to or possibly more than two years. It can take more than one year after treatment discontinuation for the OGUS to become smaller than 1, indicating an average IMT below the rounded diagnostic cut-off values. Our results suggest a long-lasting remodeling phase of the vessel wall after treatment discontinuation.
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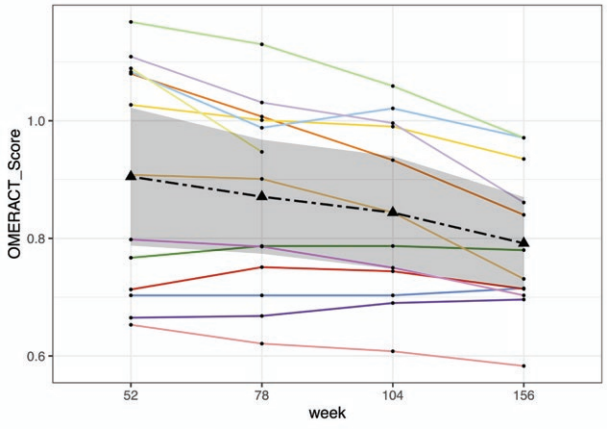


Figure 1. OMERACT-Score (OGUS) of 13 patients from the time of discontinuation of tocilizumab monotherapy (at week 52) and two years of follow-up without immunosuppressive therapy. Black dashed line (OGUS mean), grey area (95%-Confidence interval of OGUS mean).

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POS0694 MOLECULAR PHENOTYPING OF GIANT CELL ARTERITIS PATIENTS: ANALYSIS OF THE SERUM PROTEIN PROFILE USING A HIGH THROUGHPUT METHOD

Keywords: Biomarkers, -Omics, Vasculitis

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Background: There is a lack of biomarkers to profile phenotypes in giant cell arteritis (GCA) and predict potential complications. Serum protein profiling may identify molecular-based phenotypes and facilitate personalized medicine approaches.
Objectives: To investigate the serum protein signature of clinically defined GCA phenotypes and to evaluate whether serum protein-based profiling identified distinct patient clusters.
Methods: We analyzed baseline serum samples from 16 patients with new-onset GCA enrolled in the GUSTO trial (NCT03745586) [1]. Serum samples were collected prior to treatment or with the lowest prior GC-exposure. In total, 1436 differentially expressed proteins (DEPs) were assessed based on proximity extension assay technology. T-test (threshold, adjusted p-value <0.05) was performed with adjustment for multiple testing (Benjamini-Hochberg) to identify DEPs. Supervised and unsupervised cluster analyses were performed. Supervised analysis was stratified based on the three following clinical phenotypes: presence or absence of (i) cranial and (ii) polymyalgia rheumatica (PMR) symptoms, and (iii) response to treatment within the GUSTO trial.
Results: Differences in the serum protein profile were observed based on the presence of cranial GCA and treatment response within the GUSTO trial. We identified 18 DEPs for cranial vs. non-cranial GCA, covering proteins involved in endothelial function (ECE1) or Th17 signaling (IL17RA), and 24 DEPs for response vs. non-response. GCA patients with non-response displayed among others a pronounced Th1 (IL2, IL12) and altered BAFF/APRIL signature. We found no difference based on the presence or absence of PMR-symptoms. Unsupervised hierarchical cluster analysis of the serum protein profile revealed three distinct patient clusters (Figure 1). There was no separation between patients based on clinical parameters except for a tendency to separate GCA patients with (cluster 2) from patients without PMR-symptoms (cluster 1).
Conclusion: Upon further validation, in GCA, molecular profiling of patients based on serum protein signatures has great potential for future individualization of patient management. This is the first study to phenotype new-onset GCA based on the serum protein signature. GCA patients with cranial symptoms and treatment response display a distinct serum protein signature. We found a tendency to cluster GCA patients with concomitant PMR-symptoms. Our findings of different protein signatures might facilitate personalized treatment approaches in GCA.
REFERENCE:
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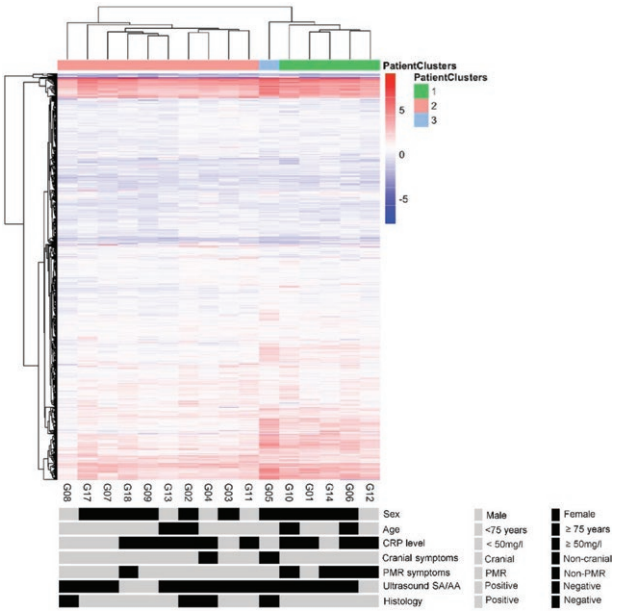


Figure 1. Hierarchical clustering using euclidean distance and complete linkage method.SA=subclavian artery. AA=axillary artery.

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POS0695

A PROSPECTIVE STUDY EVALUATING A PRE-TEST PROBABILITY SCORE IN THE DIAGNOSIS OF GIANT CELL ARTERITIS

Keywords: Diagnostic tests, Vasculitis, Ultrasound

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Background: Temporal Artery Ultrasound (TAUS) has been increasingly used in recent years to diagnose Giant Cell Arteritis (GCA) but has shown widely disparate results in studies to date [1-3]. A Pre-Test Probability Score (PTPS) has been developed to standardise the estimation of clinical probability of having GCA which, to date, has been validated in only one prospective study [4].

Objectives: To evaluate the diagnostic utility of the PTPS and to investigate whether its use can improve the sensitivity of US.

Methods: We performed a prospective multicentre study of all new referrals to our Rapid Access GCA clinic over 18 months. US of all branches of the Superficial Temporal (STA) and Axillary Arteries (AA) was performed using a GE P9 device. Sonographic abnormalities considered indicative of vasculitis included the halo sign and non-compressible arteries with a thickened intima-media complex [5]. The PTPS (scale 0-30) incorporates a number of variables to quantify the likelihood of having a diagnosis of GCA (Table 1) [4]. We compared results to a clinical diagnosis of GCA at 6 months, verified by 2 rheumatologists. We performed Chi-Square tests with ROC analyses and logistic regression to determine the diagnostic performance of the PTPS, US and of both tools combined.

Table 1. The Pre-Test Probability Score of having a diagnosis of GCA incorporates patient demographics, symptoms, examination findings, laboratory results and relevant false negatives, with a maximum score 30. Y = Yes (present), N = No (absent).

Score	-3	0	+1	+2	+3
Age (years)		≤49	50-60	61-65	≥66
Sex			Male	Female	
Duration of symptoms		>24 weeks	12-24 weeks	6-12 weeks	<6 weeks
CRP		0-5mg/L	6-10 mg/L	11-25mg/L	≥25mg/L
Headaches		N	Y		
Polymyalgia		N		Y	
Constitutional		N	Single		Combination
Ischaemic		N			Y
Visual (AION, CRAO, Field loss, RAPD)		N			Y
TA abnormality		N	Tender	Thick	Pulseless
Extra-cranial artery abnormality		N	Thick	Bruit	Pulseless
Cranial nerve palsy		N			Y
Infection	Y				
Cancer	Y				
Systemic rheumatic disease	Y				
Head and neck pathology	Y				

Results: 72/149 patients had a diagnosis of GCA with a mean age of 73.3 years of whom 58% were males. The PTPS AUC for a diagnosis of GCA was 0.807 (95% CI 0.736-0.875). At scores <10, the PTPS correctly refuted the diagnosis in 91.67%, with lower scores having even higher sensitivities. At scores >13, it correctly identifies the diagnosis in 93.51%, with higher scores having even higher specificities. The TAUS AUC for a diagnosis of GCA was 0.865 (95% CI 0.810- 0.920). A model which combines both PTPS and TAUS out-performs both individual tools with an AUC 0.912 and is illustrated in Figure 1. In the case of positive US, a PTPS ≥6 infers a >60% likelihood of having GCA. In cases of negative US, a PTPS ≤12 infers a <20% likelihood of having GCA.

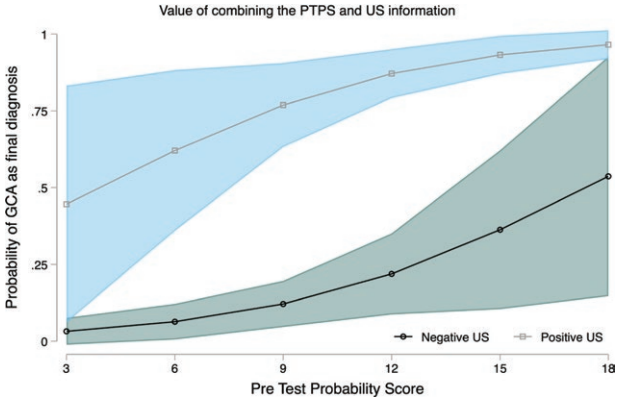


Figure 1. Probability of having a diagnosis of GCA at various PTPS in US-positive (above, blue) and US-negative (below, green) patients, with confidence intervals.

Conclusion: Our study demonstrates a strong correlation between baseline PTPS and a clinical diagnosis of GCA at 6 months, in a large prospective cohort. Although US is superior to PTPS for diagnosis of GCA, a model which combines both tools achieves a sensitivity of 91%, higher than that for US alone. This model can form the basis of an algorithm to guide early corticosteroid use in cases of suspected GCA.

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Disclosure of Interests: None Declared.
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POS0696 TREATMENT OF GIANT CELL ARTERITIS PATIENTS WITH ULTRA-SHORT GLUCOCORTICOIDS AND TOCILIZUMAB: ROLE OF IMAGING IN A PROSPECTIVE STUDY

Keywords: Vasculitis, Imaging

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Background: The full glucorticoid (GC)-sparing potential of Tocilizumab (TCZ) and its effect on vascular inflammation in giant cell arteritis (GCA) is currently unknown.
Objectives: To explore the efficacy of TCZ monotherapy after ultra-short pulse GC administration in new onset and relapsing large vessel GCA (LV-GCA).
Methods: This is a single-arm, single-center, open-label proof-of-concept trial (NCT05394909). Patients aged older than 50 years with newly diagnosed or relapsing LV-GCA were enrolled according to the following: PET/CT showing vascular FDG uptake ≥2 in at least one vascular district and considered consistent with active vasculitis and at least one among. 1.ESR >40 mm/h or CRP >10 mg/l 2.Cranial or systemic manifestations of GCA or polymyalgia rheumatica (PMR) Patients taking more than 10 mg/day of prednisone for more than 10 consecutive days in the previous 3 months were excluded. All patients received 500 mg per day methylprednisolone intravenously for 3 consecutive days and weekly subcutaneous TCZ injections from day 4 until week 52. PET/CT was performed in all patients at baseline and at weeks 24 and 52. PETVAS was calculated by a nuclear medicine specialist, and the diameters of the aorta were measured by a radiologist at 4 different levels. Any change of ≥5mm on serial CT was considered a significant progression of aortic damage. Remission was defined by all the following: absence of any clinical signs and symptoms directly attributable to GCA; normalization of acute phase reactants; absence of new/worsened aortic damage at CT; vascular FDG uptake <2 in all vascular districts at PET/CT or overall PET image interpretation of non-active vasculitis by nuclear medicine physician. Relapse was defined as one or more of the following: recurrence of signs or symptoms of GCA or PMR; CRP values greater than 10 mg/L, or ESR values greater than 40 mm/h if these were considered by the investigator to be due to GCA; evidence of worsening vascular FDG uptake at PET/CT. The definition of relapse included the necessity for the introduction of prednisone. The primary endpoints were the reduction of PETVAS at weeks 24 and 52 compared with baseline and the proportion of patients with relapse-free remission at weeks 24 and 52. The secondary endpoint was the proportion of patients with new aortic dilation at weeks 24 and 52.
Results: From March 2019 to November 2020 18 patients were included. The baseline characteristics are reported in the Table 1. A significant reduction of PETVAS was observed at weeks 24 and 52, mean (95% CI) reductions -8.6 (-11.5 to -5.7) and -10.4 (-13.6 to -7.2), p =0.001 and 0.002, respectively. The proportion of patients with relapse-free remission at weeks 24 and 52 was 10 out of 18 (56%, 95% CI 31-78) and 8 out of 17 (47%, 95% CI 23-72), respectively. At weeks 24 and 52 no patient showed new aortic dilation. However, 3 dilated patients at baseline showed a significant increase in aortic diameter (≥5 mm) at week 24, and 1 dilated patient showed a significant increase in aortic diameter at week 52. One patient underwent an aortic aneurysm surgical repair at week 44. 2 (11%) of 18 patients did not respond to treatment, and rescue GC treatment was necessary.
Conclusion: TCZ monotherapy after ultra-short GCs controlled the clinical symptoms of GCA, lowered acute phase responses, and significantly reduced vascular inflammation. 4 of 18 patients (22%) showed significant increase in aortic diameters on serial CT. The effect of TCZ on progression of aortic damage needs larger prospective studies.

Table 1. Baseline characteristics of the patients

Study population (n=18)	
Age, years	68.5 (10.6)
Female	13 (72%)
Newly-diagnosed LV-GCA	9 (50%)
Relapsing LV-GCA	9 (50%)
Glucocorticoid pretreatment	13 (72%)
CRP, mg/L	35 (36)
ESR, mm/h	56 (41)
Symptoms of active vasculitis	15 (83%)
Systemic symptoms	11 (61%)
Polymyalgia rheumatica symptoms	7 (39%)
Signs or symptoms of vascular insufficiency	4 (22%)
Cranial symptoms	1 (6%)
Visual symptoms	0 (0%)
Active vasculitis on PET/CT	18 (100%)
PETVAS	17.3 (5.1)
Aortic dilation	8 (44%)

Data are mean (SD) or n (%)

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0697 OUTCOME FOR PATIENTS WITH GIANT CELL ARTERITIS (GCA) TREATED WITH TOCILIZUMAB ACCORDING TO NICE GUIDANCE IN A SINGLE TERTIARY UK CENTRE

Keywords: Real-world evidence, Vasculitis, bDMARD

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Background: In 2018 NICE and NHS England approved one year of weekly subcutaneous tocilizumab for use in relapsing or refractory GCA [1, 2]. During the COVID pandemic NHS England allowed extended use of tocilizumab in selected high risk patients [3]. This extension ended in March 2022. This has created a cohort of patients who are now no longer treated with tocilizumab and may be at risk of GCA flare. Currently, NHS England does not allow retreatment with tocilizumab.
Objectives: This service evaluation used an intention-to-treat approach to retrospectively evaluate patients, who were ratified to receive tocilizumab for GCA according to the NICE guidance. We aimed to describe this cohort of patients for whom the use of tocilizumab had been approved, and their outcomes in terms of complications and disease control.
Methods: 49 patients were ratified to receive tocilizumab between May 2019 and April 2022 by a specialist multidisciplinary team at a single tertiary rheumatology center. Their response was assessed in terms of relapse rates, steroid usage and complications as described below.
Results: 80% of the 49 cohort of patients consisted of females (Table 1). 55% of patients were diagnosed with GCA on combination of clinical history, laboratory and temporal artery duplex findings. 94% (46/49) had at least a week's course of tocilizumab. Around half (51%) had relapsing disease. 6% had first dose as intravenous due to critical ischaemia. 27% (13/49) of patients developed complications whilst on treatment. Six developed cytopenia, 3 acquired infections and 4 stopped due to other reasons. As per guidelines, tocilizumab was stopped after 12 months in 25 patients (51%). 16% stopped treatment early due to complications. 18% had incomplete information. 10% had ongoing treatment. One patient died several months after finishing tocilizumab. 47% had methotrexate as DMARD therapy added prior to tocilizumab commencement (Figure 1). Out of 25 patients who completeted treatment, 24% (6/25) relapsed. 83% of these relapses were diagnosed on recurrence of symptoms and high inflammatory markers. In addition, 3 patients, who had tocilizumab suspended relapsed. 2/3 of these patients had treatment suspended due to infection. 5/9 relapse patients did not have preceding DMARD therapy. 22% (2/9) of relapse patients had PET-CT due to involvement of extra-cranial disease. 56% (5/9) relapsed following a median follow-up of 11 months. Of relapsed patients, seven were treated with increased dose of prednisolone and two patients received 6 months extension of tocilizumab with adequate tolerance and efficacy.
Conclusion: Our data shows good tolerability of tocilizumab and a 24% flare rate amongst patients who completed treatment. This is less than the 50% rate seen in GiACTA and other cohorts, where the majority of which occurred within 6 months of stopping treatment [4]. DMARD treatment may reduce relapse rate, but this will require further study. The data describing the efficacy of treatment beyond one year is limited [3]. However, with no established guidance for treating patients following tocilizumab, extension of treatment is a plausible option.

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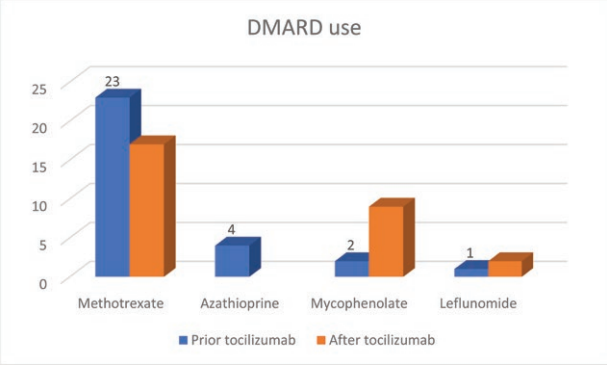


Figure 1.

Table 1.

Gender		Age at time of diagnosis				Indication for stopping treatment			
Male	Female	50-59	60-69	70-79	80-89	Completed treatment	Complications	Ongoing treatment	Incomplete information
18	31	3	16	20	10	25	10	5	8

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0698 REAPPRAISAL OF LARGE ARTERY INVOLVEMENT IN GIANT CELL ARTERITIS, A POPULATION-BASED COHORT OVER 70 YEARS

Keywords: Epidemiology, Vasculitis, Imaging

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Background: Screening for large artery manifestations in patients with Giant Cell Arteritis (GCA) has been adopted in clinical practice. However, the effect of recent use of imaging studies on incidence and mortality of large artery manifestations remains unclear.

Objectives: In this study, we aimed to investigate incidence trends and outcomes of large artery manifestations in a population-based cohort of patients with GCA over a span of seven decades.

Methods: The study cohort included patients with incident GCA between 1950-2016 in a defined geographical area. Incident large artery manifestations were defined as aortic aneurysm, aortic dissection, stenosis in the aorta or any of its main branches diagnosed within 1 year prior to the diagnosis of GCA or anytime afterwards. Patients were followed till December 31st, 2020, death, or migration. Cumulative incidence of large artery manifestations adjusted for the competing risk of death was estimated. Cox proportional hazards models adjusted for age and sex were used to assess the association of clinical characteristics with large artery manifestations.

Results: The study included 289 patients with GCA: 222 (77%) females; temporal artery biopsy was positive in 235 patients (81%); mean follow up period was 10.4 ± 7 years; mean age at diagnosis was 76.4 ± 8.2 years. Incident large artery manifestations developed in 104 patients throughout the follow up period, the majority (76%) were found incidentally. Cumulative incidence rates of large artery manifestations at 5 years were 7.3% (95% CI 2.4-22.1%), 15.9% (95% CI 10.6-23.8%) and 27.2% (95% CI 20.2-36.6) for patients diagnosed in 1950-1974, 1975-1999 and 2000-2016, respectively. Moreover, cumulative incidence of large vessel manifestations at 15 years was 14.8% (95% CI 7.0-31.6%), 30.2% (95% CI 23.1-39.4%) and 48.8% (95% CI 38.8-61.3%) for patients diagnosed in 1950-1974, 1975-1999 and 2000-2016, respectively (Figure 1). Patients with GCA diagnosed in 2000-2016 and 1975-1999 had more than 3.5-fold and 2-fold increase in incidence of large artery manifestations (HR:3.49 95%CI 1.67-7.3 and HR: 1.98 95% CI 0.97–4.07, respectively) compared to 1950-1974. However, there was no significant increase in aortic aneurysm or dissection (Table 1). Mortality risk has decreased significantly in patients with large artery manifestations diagnosed in the latest cohort 2000-2016 (HR 0.38 95% CI 0.17–0.81) following non-significant improvements in 1975-1999 (HR 0.61 95% CI 0.29-1.30) compared to 1950-1974 (reference). Clinical predictors for large artery manifestations included weight loss, fatigue, arm claudication, ever smoker and bruit on physical examination. Cranial symptoms were negatively associated with large artery manifestations.

Conclusion: Incidence of large artery manifestations (mainly large artery stenosis) has increased over time likely from increased use of imaging studies. However, the incidence of aortic aneurysm/dissection has been stable over the last 7 decades. Mortality improvement in the recent years may be due to earlier detection of large artery involvement.

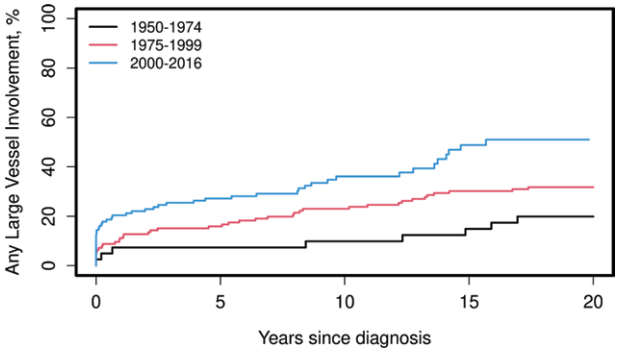


Figure 1. Cumulative incidence for time to any large artery manifestation (large artery stenosis, aortic aneurysm, aortic dissection) in patients with incident GCA 1950-2016 adjusted for the competing risk of death.

Table 1. Cox proportional hazards model showing Age- and Sex-adjusted risk of large artery manifestation among patients with incident GCA 1950-2016

Event Type	GCA Year	Total (Events)	HR (95% CI)
Large artery stenosis	1950-1974	41 (3)	Reference
	1975-1999	128 (21)	2.63 (0.78-8.88)
	2000-2016	**118 (39)**	**7.66 (2.30-25.5)**
Aortic Aneurysm/Dissection	1950-1974	41 (7)	Reference
	1975-1999	127 (34)	1.65 (0.73-3.75)
	2000-2016	119 (16)	1.29 (0.51-3.25)
Any Large Vessel manifestation	1950-1974	41 (9)	Reference
	1975-1999	126 (47)	1.98 (0.97-4.07)
	2000-2016	**118 (48)**	**3.49 (1.67-7.30)**

REFERENCES: NIL.
Acknowledgements: NIL.
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POS0699 GIANT CELL ARTERITIS CLINICAL DISEASE ACTIVITY MEASURES: RECOMMENDATIONS FOR USE IN CLINICAL PRACTICE

Keywords: Outcome measures, Ultrasound, Vasculitis

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Background: Although the systematic measurement of disease activity facilitates clinical decision making in Giant Cell Arteritis (GCA), no recommendations currently exist on which measures should be applied in clinical practice.
Objectives: To comprehensively evaluate the validity, feasibility, and acceptability of available GCA disease activity measures and derive recommendations for their use in clinical practice.
Methods: This was a 6-phases process which included a combination of a systematic literature review, psychometric analyses, validated group methods, and physician surveys. In phase 1, The GCA clinical Disease Activity Measures Working Group conducted a systematic review of the literature to identify GCA disease activity measures. Applying exclusion criteria: measurement tools were excluded from further consideration if they: (1) measured imaging only; (2) did not report a continuous value; (3) had insufficient information (e.g. not yet published in manuscript form.). Phase 2: Expert panel were asked to rank the remaining measures via an electronic survey. For each measurement tool, expert panel members were asked to indicate whether they were familiar with the measure (yes, no), whether they had ever used the measure (yes, no), and whether they would recommend the measure for clinical use (yes, no). The survey instructed the expert panel to apply the Outcome Measures for Arthritis Clinical Trials (OMERACT) filter of truth, discrimination, and feasibility as a guide when ranking their top five choices for use in clinical practice. The panel members were encouraged to identify additional measures not listed. Phase 3: following teleconferences the list of measures was reduced based on their rankings and panel comments. Phase 4: included comprehensive examination of the psychometric properties (reliability, validity, and responsiveness) of the remaining GCA disease activity measures. Phase 5 included an electronic survey to score the usefulness and feasibility in clinical practice and acceptance to use the tool on a regular basis when caring for patients. Phase 6: the final list of GCA disease activity measures was prepared.
Results: Using the list of specific disease activity measures as keyword searches, the systematic review of the literature resulted in identification of 21 GCA disease activity measures. Application of exclusion criteria and ratings by the expert panel narrowed the list to 10 measures for further evaluation. Practicing rheumatologists rated 7 of these 10 measures as most useful and feasible. From these 7 measures, the working group selected 6 with the best psychometric properties for inclusion in the final set of recommended GCA disease activity measures.
Conclusion: The GCA Clinical Disease Activity Index, has been developed including severity of headache (using 0-100 VAS), acute visual deficit (0-100 VAS), functional disability (0-3), Lab disease activity measures: ESR and CRP, patient global assessment (0-100 VAS), physician global assessment (0-100 VAS). These were identified as they are accurate reflections of disease activity; are sensitive to change; discriminate well between low, moderate, and high disease activity states; have remission criteria; and are feasible to perform in clinical settings.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0700

METABOLIC AND MORPHOLOGIC PET/MR FEATURES IN CRANIAL GIANT CELL ARTERITIS

Keywords: Descriptive Studies, Vasculitis, Imaging

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Background: Accurate and timely diagnosis is crucial for patients suspected of having cranial giant cell arteritis (C-GCA) as prompt treatment with high-dose glucocorticoids may prevent severe ischemic complications, such as vision loss. However, the use of high-dose glucocorticoids in patients without proven C-GCA should also be done with caution due to potential side effects. Currently, multiple diagnostic (imaging) tests are required to establish an accurate diagnosis as single tests lack sufficient diagnostic sensitivity. Next to ultrasonography, 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (FDG-PET/CT) and Magnetic Resonance Imaging (MRI) are used in clinical practice but carry a significant risk of false negative results. Since FDG-PET imaging measures metabolic activity, while MRI demonstrates morphological changes, combining these modalities may result in a composite hybrid diagnostic test with higher diagnostic accuracy.
Objectives: To describe the metabolic and morphologic imaging features of FDG-PET/MR in patients with diagnosed C-GCA.
Methods: Patients diagnosed with new-onset C-GCA underwent FDG-PET/CT and FDG-PET/ MR at 1 and 2 hours after FDG administration, respectively. Patients who had received treatment with glucocorticoids for more than 3 days prior to imaging were excluded from participating. Diagnosis of C-GCA was determined based on clinical information and the results from ultrasonography and FDG-PET/CT. On FDG-PET/MR imaging, thirteen arteries were evaluated bilaterally. Time-of-Flight (TOF) MR angiography was used to detect arterial stenoses or occlusions which were visually graded as either absent or present. To assess vessel wall thickness, T1-weighted contrast-enhanced (T1WCE) MRI images were visually graded on a scale of 0-3, with 0 indicating no mural enhancement or thickening, 1 indicating slight mural enhancement but no thickening, 2 indicating significant mural enhancement and thickening, and 3 indicating mural and perivascular enhancement and thickening. FDG uptake was visually graded on a scale of 0-2, with 0 indicating no vascular uptake, 1 indicating uptake slightly above background, and 2 indicating uptake significantly above background.
Results: The study included 12 patients with new-onset C-GCA with a median age of 74 years (range 61-84 years), of which 9 were female. The mean C-reactive protein (CRP) concentration was 63.2 (SD 41.0) mg/L, and one patient was receiving daily 60 mg prednisolone at the time of imaging (Figure 1, patient 12). Cranial artery ultrasonography was positive in 9 patients, and FDG-PET/CT was positive in the cranial arteries in 10 patients. All patients had at least one positive artery on T1WCE MRI (score ≥ 2) and all but one patient showed at least one arterial stenosis or occlusion on TOF MR angiography. One patient without FDG uptake FDG-PET/MR did also not show any FDG uptake on FDG-PET/CT. Figure 1 shows a heatmap of (a) presence of stenoses/occlusions, (b) the vessel wall thickening score (0-3), (c) the FDG uptake score (0-2), and (d) the overlap of FDG-PET positivity (score ≥ 1), T1WCE MRI positivity (score ≥ 2), and TOF MR angiography positivity. Data for each patient (1 to 12) is shown for each map in rows and data for each artery (Right and Left) are shown in columns. Vessel wall thickening and FDG-uptake were most seen in the vertebral, maxillary, and occipital arteries. Stenosis was most observed in the maxillary arteries. TOF MRA, T1-weighed contrast-enhanced MRI, and FDG-PET/CT scores agreed in 60% of all arteries, however just 10% of all positive arteries were positive on all three modalities. Agreement was highest (74%) between FDG-PET/CT and T1WCE MRI.
Conclusion: The study found an overlap in morphologic and metabolic features in affected arteries in patients with C-GCA using hybrid FDG-PET/MR. However, it also revealed that these features can occur independently of each other. This suggests that the use of hybrid morphologic and metabolic imaging may provide complementary information, potentially increasing diagnostic accuracy for C-GCA.

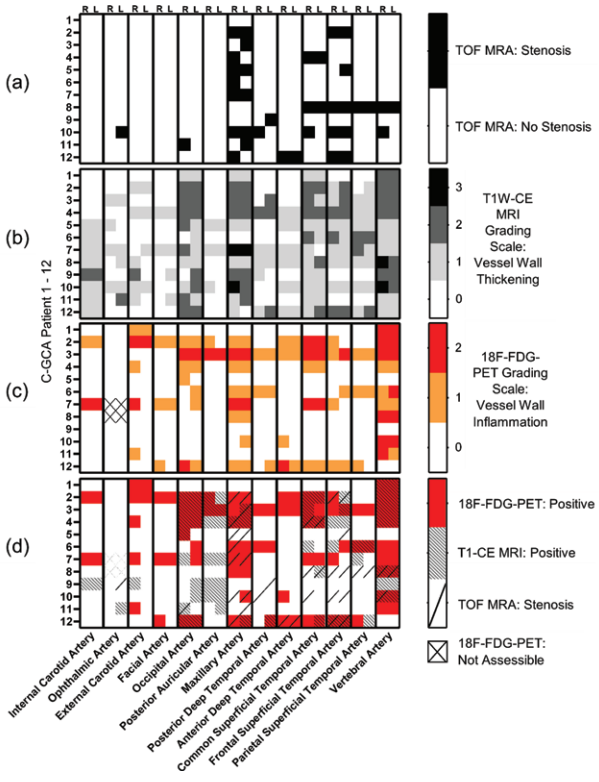


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0701 LONG-TERM EFFICACY OF TOCILIZUMAB MONOTHERAPY AFTER ULTRA-SHORT GLUCOCORTICOID ADMINISTRATION TO TREAT GIANT CELL ARTERITIS – TWO YEAR FOLLOW-UP OF THE GUSTO TRIAL

Keywords: Vasculitis, Clinical trials

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Background: Two randomised controlled trials (RCT) [1, 2] demonstrated a glucocorticoid (GC)-sparing effect of tocilizumab (TCZ) of at least 50% in the treatment of giant cell arteritis (GCA). The GUSTO (GCA treatment with Ultra-Short glucocorticoids and TOcilizumab) trial was set up to evaluate the efficacy and safety of TCZ-monotherapy after a 3-day GC-pulse in new-onset GCA.
Objectives: The objectives of this analysis were to explore the maintenance of remission 2 years after discontinuation of TCZ treatment (drug-free remission) and the effectiveness or retreatment with TCZ after relapse. Data up to week 156 are presented.
Methods: Eighteen patients with newly diagnosed GCA were enrolled in this investigator-initiated, single-arm, single-center, open-label clinical trial [3]. Patients received 500 mg methylprednisolone intravenously for 3 consecutive days. Thereafter, GC treatment was discontinued and TCZ (8 mg/kg body-weight) was administered intravenously, followed by weekly subcutaneous TCZ injections (162 mg) from day 10 until week 52. Patients in clinical remission stopped TCZ at week 52 and entered the follow-up study. Maintenance of efficacy at week 156 included the proportion of patients with complete relapse-free remission of disease at week 156, and time to first relapse after week 52.
Results: At baseline there were 12/18 female patients, and the median age was 72 (range 67-75) years. Overall, 15/18 complained of cranial symptoms (10/18 jaw claudication, 6/18 visual symptoms), 10/18 suffered from polymyalgia rheumatica symptoms, 16/18 had positive ultrasound findings of the cranial arteries, and in 13/18 temporal arterial biopsies showed a characteristic histopathology. At week 52, 13/18 patients were in relapse-free remission and entered the follow-up study. One out of 13 patients presented with a minor relapse at week 72. Remission was achieved after restart of TCZ-monotherapy. At week 156, 12/18 patients were in relapse-free remission.
Conclusion: After a 3-days pulse of methylprednisolone followed by 52 weeks of TCZ monotherapy, drug-free remission was maintained until week 156 in all but one patient entering long-term extension (12/13, 92%). This relapse rate is substantially lower than reported in the RCTs [1,2]. It may – at least in part – be explained by the patient characteristics (exclusively new diagnoses), and presumably by the intensive initial treatment consisting of a 3-day GC pulse, immediately followed by TCZ. As a proof-of-concept study, the protocol is not intended to be used in everyday clinical practice.

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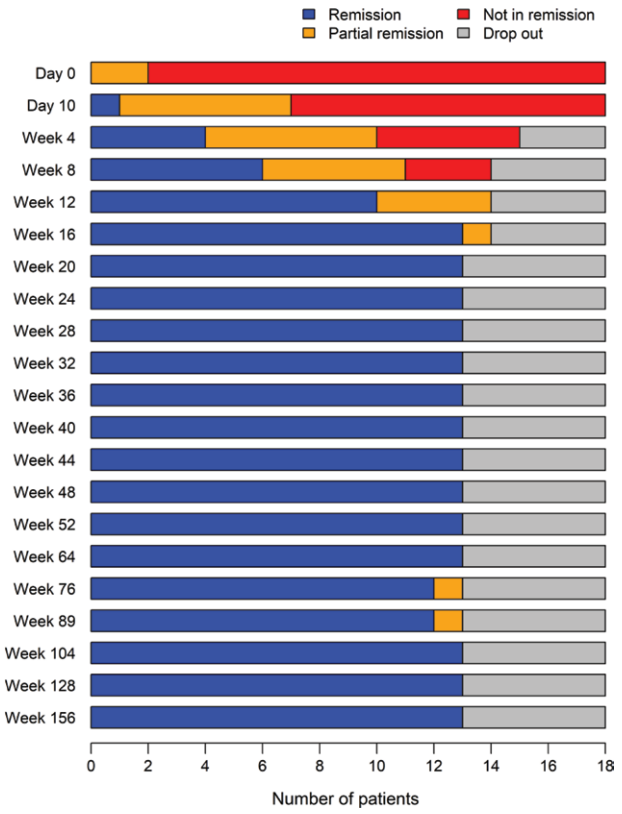


Figure 1. Disease status of patients at each visit (Day 0 – week 156, n=18)

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POS0702 TREATMENT EFFICACY AND SAFETY OF ADALIMUMAB VERSUS TOCILIZUMAB COMBINED WITH METHOTREXATE AND GLUCOCORTICOIDS IN PATIENTS WITH ACTIVE AND SEVERE TAKAYASU ARTERITIS: A RANDOMIZED, OPEN-LABEL, HEAD-TO-HEAD STUDY

Keywords: Clinical trials, Vasculitis, Treat to target

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Background: Takayasu's arteritis (TAK) is a rare large-vessel vasculitis characterized by granulomatous inflammation in the aorta and its major branches.[1] The affected arteries may become narrowed or even occluded, resulting in ischemia of the corresponding tissue or organs and threatening patient survival.[2] However, effective treatment strategies for TAK are lacking. Although TCZ and TNF-α inhibitors are commonly applied in the treatment of refractory TAK, a formal head-to-head study evaluating their efficacy is lacking. According to retrospective studies,[3, 4] the complete response rate associated with TCZ was slightly better than those associated with TNF-α inhibitors at 6 months (70% vs. 66%; 70% vs. 61%). However, another study indicated a better 3-month complete remission rate associated with TNF-α inhibitors than with TCZ (30% vs. 18%) [5]. Thus, the data are inconclusive regarding which medication is more effective. Furthermore, the 6-month nonresponse and 12-month relapse rates associated with these treatments were approximately 25% and 19%, respectively.[3] Thus, given the inconsistent results obtained thus far in this context, we conducted this randomized, open-label, head-to-head study to compare the efficacy and safety of the TNF-α antibody adalimumab (ADA) and TCZ combined with GCs and MTX in patients with active and severe TAK.
Objectives: This study was aimed at investigating the efficacy and safety of adalimumab (ADA) and tocilizumab (TCZ) in patients with active and severe Takayasu arteritis (TAK) concomitantly treated with glucocorticoids (GCs) and methotrexate (MTX).

Methods: Forty patients were randomized into ADA and TCZ groups (n = 21 and 19, respectively). They were treated with ADA or TCZ combined with GCs and MTX, respectively. The planned follow-up duration was 12 months. The primary end point was the efficacy rate (ER) at 6 months.
Results: The intention to treat (ITT) population included 21 and 19 patients from the ADA and TCZ groups, respectively. In this population, the ERs at 6 months were higher in the ADA group (85.71% *vs.* 52.63%, P = 0.02). Similar tendencies were also noted in per-protocol set (89.47% vs. 62.50%, P = 0.06). At the 6-month time point, the percentages of patients receiving a GC dose of ≤10 mg/day and the cumulative GC dose were similar between the ADA and TCZ groups (47.37% *vs.* 43.75%, P = 0.83; 4200 mg *vs*. 4100 mg, P = 0.15, respectively). Imaging improvement or stabilization was observed in most patients in both groups (ADA *vs.* TCZ: 19/19 *vs.* 15/16, P = 0.27). Adverse event incidence was comparable between the two groups (ADA *vs.* TCZ: 38.10% *vs.* 47.37%, P = 0.55).
Conclusion: ADA probably was more effective than TCZ in combined treatment with GCs and MTX among patients with active and severe TAK.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0703 RENAL ARTERY STENOSIS IS NOT ASSOCIATED WITH WORSE SURVIVAL IN TAKAYASU ARTERITIS – DATA FROM A SINGLE-CENTER RETROSPECTIVE COHORT OF 195 PATIENTS

Keywords: Epidemiology, Registries, Vasculitis

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Background: Renal artery stenosis (RAS) is more frequent in Asian patients with Takayasu arteritis (TAK). Few studies have assessed the impact of RAS on the presentation and prognosis of TAK using adjusted analysis.
Objectives: To compare the presentation and prognosis between TAK with or without RAS.
Methods: We compared the clinical presentation and vascular involvement (including angiographic subtypes by Hata's classification) between patients with TAK with or without RAS, with bilateral versus unilateral RAS, and with bilateral RAS versus those without RAS using multivariable-adjusted odds ratios (aOR) with 95% confidence intervals (95%CI) derived after logistic regression. We compared survival between these groups using hazard ratios (HR) with 95%CI adjusted for gender, age at disease onset, delay to diagnosis, baseline disease activity, and inter-group differences. The institute ethics committee provided a waiver of consent for retrospective data retrieval. The institute ethics committee provided a waiver of consent for retrospective data retrieval.
Results: Out of 195 TAK with imaging data available, 106 had RAS [58 bilateral, 48 unilateral; mean(±SD) follow-up 41.50(±43.35) months]. TAK with RAS (mean age 22.99 years) or bilateral RAS (mean age 22.83 years) were younger than without RAS (mean age 28.00 years). TAK with RAS had more hypertension (aOR 4.46, 95%CI 1.81 – 10.99), lower limb claudication (aOR 2.72, 95%CI 1.08 – 6.88), and less frequent upper limb claudication (aOR 0.43, 95%CI 0.19-0.99) and syncope or dizziness (aOR 0.35, 95%CI 0.14 – 0.85) than TAK without RAS. TAK with bilateral RAS had more frequent hypertension (aOR 11.83, 95%CI 1.38-101.16), blurring of vision (aOR 5.97, 95%CI 1.02 – 34.83), and less frequent constitutional symptoms (aOR 0.18, 95%CI 0.06 – 0.51) than those with unilateral RAS. TAK with bilateral RAS had more frequent hypertension (aOR 8.73, 95%CI 1.90-40.06), vascular bruits (aOR 2.94, 95%CI 1.03 – 8.34), and heart failure (aOR 4.16, 95%CI 1.00 – 17.32), and less frequent constitutional symptoms (aOR 0.23, 95%CI 0.09 – 0.62), pulse loss (aOR 0.29, 95%CI 0.11 – 0.77), and syncope or dizziness (aOR 0.21, 95%CI 0.06-0.73) than those without RAS. Hata's type IV and type V were more frequent in TAK with versus without RAS (OR 4.01 and 13.40, respectively), and in those with bilateral RAS versus no RAS (OR 5.97 and 10.94, respectively). Adjusted survival was similar between TAK with or without RAS, with unilateral or bilateral RAS, or with bilateral RAS vs those without RAS (Table 1).
Conclusion: RAS is associated with specific clinical and angiographic features but not with a greater risk of mortality in TAK.

Table 1. Risk estimates for the association of RAS with mortality in TAK

Exposure	Cox regression models*	Hazard ratio (95%CI)
With (n=101) vs without RAS (n=86)	Unadjusted	3.55(0.75–16.83)
	A, B, C, PGA	6.33(0.60–67.06)
	A, B, C, DEI.Tak	3.48(0.37–33.18)
	A, B, C, ITAS2010	4.00(0.42–37.96)
Bilateral (n=56) vs unilateral RAS (n=45)	Unadjusted	2.82(0.56–14.23)
	A, D, PGA	2.47(0.26–23.59)
	A, D, DEI.Tak	2.39(0.29–19.75)
	A, D, ITAS2010	2.57(0.33–20.32)
Bilateral RAS (n=56) vs without RAS (n=86)	Unadjusted	5.04(1.01–25.22)
	A, E, F, PGA	7.46(0.25–226.04)
	A, E, F, DEI.Tak	7.95(0.48–131.12)
	A, E, F, ITAS2010	9.52(0.57–160.30)

*Covariates adjusted forA – Chosen *a priori* - Gender, age at disease onset, delay to diagnosisB – Distinct clinical features-syncope/dizziness/vertigo, upper limb claudication, lower limb claudication, hypertensionC – Distinct vascular involvement–left carotid artery, abdominal aorta, or the superior mesenteric artery.D – Distinct clinical features– Constitutional symptoms, blurring of vision, hypertensionE – Distinct clinical features– Constitutional symptoms, syncope/dizziness/vertigo, pulse loss, vascular bruits, hypertension, heart failure.F – Distinct vascular involvement-left subclavian artery, abdominal aorta, superior mesenteric artery.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0704 RISK FACTORS OF DEPRESSION AND ANXIETY IN PATIENTS WITH TAKAYASU ARTERITIS

Keywords: Vasculitis, Mental health, Cytokines and chemokines

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Background: Takayasu arteritis (TA) is associated with an increased risk of developing complicated comorbidities, which can bring both psychological and physical burdens to the patients. Most cases are young female patients with an onset age of 10 to 40 years [1]. Psychological disorders have long been recognized as important comorbidities of immune diseases. In the case of rheumatoid progress, comorbid depression and anxiety would increase the mortality and heighten the medication, prognostic and economic burden. In patients with TA, there haven't been identified whether comorbid depression and anxiety may lead to an inaccurate evaluation of disease status and lower quality of life [2-5]. The emotional state generated by the TA should not be ignored. The primary aim of this study was to investigate the risk factors of comorbid depression and anxiety in patients with TA.
Objectives: The research is to investigate risk factors of comorbid depression and anxiety in patients with Takayasu arteritis.
Methods: In this observational, longitudianl cohort study, 86 TAK cases were respectively divided into two groups with or without depression and anxiety to identify the risk factors. The Zung Self-Rating Depression and Anxiety Scale (SDS/SAS) are widely applied in many medical researches related to mental health, which displays convincing results and a remarkable degree of consensus on the diagnosis of mood disorders.
Results: Individual patient data were available from 86 subjects, of whom 23 had depression, and 15 had anxiety. Depression was independently associated with Carotidynia, elevated IL-6, and decreased Hb (OR [95%CI] 7.116 [11.508–33.586], p=0.0010; OR [95%CI] 6.669 [1.746–25.470], p=0.005; OR [95%CI] 3.882[1.214–12.420], p=0.020) respectively. We used correlation analysis to find out the association between the level of IL-6 with SDS, SAS scores (r=0.337, p=0.002; r=0.280, p=0.010). The levels of Completement 3, NIH, ITAS.A and ITAS2010 were similarly correlated with SDS score (r=0.232, p=0.032; r=0.280, p=0.009; r=0.332, p=0.002; r=0.323, p=0.002), which wasn't seemed in SAS score.

Conclusion: Clinicians should be alert to risk factors for predisposing patients to mood disorders. TA patients comorbid depression and anxiety should be given more positive treatment to essentially control the disease to improve their emotional state and quality of life.

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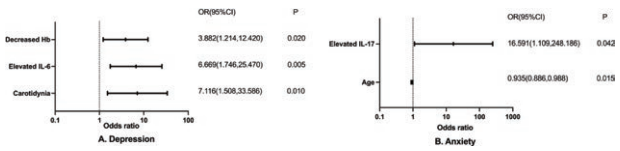


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1070

POS0705

PEDIATRIC-ONSET TAKAYASU ARTERITIS ASSOCIATES WITH WORSE SURVIVAL THAN ADULT-ONSET TAKAYASU ARTERITIS – DATA FROM A SINGLE-CENTER MATCHED RETROSPECTIVE COHORT STUDY OF 191 PATIENTS

Keywords: Vasculitis, Epidemiology, Registries

D. P. Misra[1], D. Thakare[1], P. Mishra[2], U. Rathore[1], K. Singh[1], M. Behera[3], N. Jain[4], M. Ora[5], D. Bhadauria[3], S. Gamhbir[5], S. Kumar[6], V. Agarwal[1]. [1]*SGPGIMS, Clinical Immunology and Rheumatology, Lucknow, India*; [2]*SGPGIMS, Biostatistics and Health Informatics, Lucknow, India*; [3]*SGPGIMS, Nephrology, Lucknow, India*; [4]*SGPGIMS, Radiodiagnosis, Lucknow, India*; [5]*SGPGIMS, Nuclear Medicine, Lucknow, India*; [6]*SGPGIMS, Cardiology, Lucknow, India*

Background: A subset of Takayasu arteritis (TAK) begins in the pediatric age group (≤18 years). Differences in prognosis between pediatric-onset and adult-onset TAK are unclear.

Objectives: To compare the presentation and prognosis between pediatric-onset and adult-onset TAK.

Methods: The clinical presentation, angiographic features, treatment patterns, disease activity on follow-up, and survival were compared between pediatric-onset and adult-onset TAK. Categorical variables were compared using odds ratios (OR between pediatric-onset and adult-onset TAK, with 95% confidence intervals). Survival for pediatric-onset and adult-onset TAK were presented using Kaplan-Meier plots and compared using log-rank test. Hazards ratios (HR, with 95% confidence intervals) were calculated, both crude and adjusted for prognostic factors. Propensity-score matched analyses adjusted for prognostic factors were conducted to assess adjusted differences in survival between pediatric-onset and adult-onset TAK. A previous meta-analysis of the risk of mortality with pediatric-onset vs adult-onset TAK [1] was updated with the findings from this study. The study was approved by the institutional ethics committee., which waived the requirement for informed consent in view of the retrospective review of chart records.

Results: Heart failure [odds ratio (OR) for pediatric-onset vs adult-onset TAK 2.76, 95%CI 1.12–6.80] and chest pain (OR 3.03, 95%CI 1.11-8.34) were more common in pediatric-onset TAK, and stroke or transient ischemic attack was more frequent in adult-onset TAK (OR 0.31, 95%CI 0.10-0.93). Hata's angiographic type V (OR 1.95, 95%CI 1.00-3.78) was commoner in pediatric-onset TAK, as opposed to Hata's type I in adult-onset TAK (OR 0.18, 95%CI 0.04-0.79). Disease activity at baseline, 6, 12, and 24 months, the use of glucocorticoids and disease-modifying antirheumatic drugs (DMARDs) were similar between pediatric-onset and adult-onset TAK. The unadjusted hazard ratio for mortality with pediatric-onset versus adult-onset TAK was 6.13 (95%CI 1.51-24.91), and after adjustment for prognostic covariates (gender, delay to diagnosis, baseline disease activity, number of conventional and biologic/targeted synthetic DMARDs used), was 4.97 (95%CI 1.20-20.58) (Table 1). Survival was worse for pediatric-onset than adult-onset TAK on unadjusted analyses (Figure 1) and after propensity score matching for these covariates (54 pairs, log rank p value 0.026). Risk ratio for mortality with pediatric-onset vs adult-onset TAK across studies was 2.27 (95%CI 1.05-4.85) after updating a meta-analysis of four observational studies [1] by including the present study.

Conclusion: Pediatric-onset TAK associates with greater mortality than adult-onset TAK. Greater vigilance is required while managing pediatric-onset TAK.

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Table 1. Risk estimates for the association of pediatric-onset TAK (compared with adult-onset TAK) with mortality

Covariates adjusted for using Cox proportional hazards model	Hazard ratio (95% confidence intervals)
None	6.13 (1.51 – 24.91)
Gender (male or female)	5.93 (1.46 – 24.08)
Gender (male or female), Delay to diagnosis	5.56 (1.36 – 22.67)
Gender (male or female), Delay to diagnosis, disease active at baseline assessment or not	5.84 (1.45 – 23.50)
Gender (male or female), delay to diagnosis, disease active at baseline assessment or not, number of conventional DMARDs used	5.70 (1.42 – 22.920
Gender (male or female), delay to diagnosis, disease active at baseline assessment or not, number of conventional DMARDs used, number of biologic DMARDs used	4.97 (1.20 – 20.58)

n=182 for all modelsDMARDs – Disease-modifying anti-rheumatic drugs

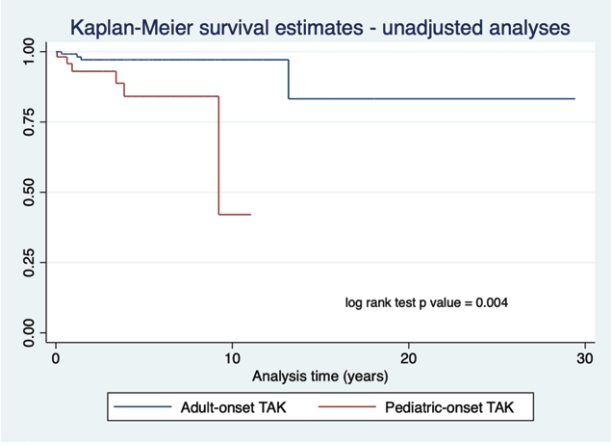


Figure 1. Survival of patients with pediatric-onset and adult-onset Takayasu arteritis

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POS0706

INCREASED ARTERIAL STIFFNESS AND ACCELERATED ATHEROSCLEROSIS IN TAKAYASU ARTERITIS

Keywords: Vasculitis, Cardiovascular disease

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Background: Cardiovascular diseases are the leading causes of morbidity and mortality in patients with Takayasu arteritis (TAK). Arterial stiffness and accelerated atherosclerosis contribute to the increased risk for cardiovascular morbidities in several inflammatory diseases. Although morphological changes have been well recognized, studies related with functional characteristics in TAK have been few. Shear wave elastography (SWE) is a non-invasive method of ultrasonography (US) to evaluate elasticity of biological tissues, by real time tracking and capturing the pace of the shear waves induced in response to the primary US waves.

Objectives: To evaluate arterial stiffness, as well as intima media thickness (IMT) and atherosclerotic plaques in the carotid arteries using US and SWE among patients with TAK and suitable controls.

Table 1. Linear regression analysis for carotid artery intima media thickness and shear wave values across study groups

			Reference category: healthy controls			
Measurement	Study groups	Mean± SD, mm	Unadjusted ß (95% CI)	P value	Adjusted* ß (95% CI)	P value
Right CCA IMT, mean± SD, mm	TAK	0.96±0.39	0.432 (0.326-0.539)	**<0.001**	0.325 (0.188-0.462)	**<0.001**
	SLE	0.53±0.12	0.003 (-0.041-0.048)	0.879	-0.028 (-0.067-0.012)	0.169
	HC	0.52±0.10	-	-	-	-
Left CCA IMT, mean± SD, mm	TAK	1.05±0.45	0.525 (0.402-0.647)	**<0.001**	0.434 (0.278-0.590)	**<0.001**
	SLE	0.56±0.15	0.028 (-0.021-0.077)	0.254	0.025 (-0.017-0.066)	0.236
	HC	0.53±0.09	-	-	-	-
SWE value, kPa	TAK	30.21±19.30	20.617 (15.471-25.762)	**<0.001**	18.189 (11.649-24.729)	**<0.001**
	SLE	11.54±4.72	1.947 (0.366-3.528)	**0.016**	1.925 (0.114-3.737)	**0.038**
	HC	9.60±3.23	-	-	-	-

ß: unstandardized beta coefficient, CI: confidence intervals for unstandardized beta coefficient, SD: standard deviation, kPa: kilopascal, IMT: intima-media thickness, CCA: common carotid artery, SWE: shear wave elastography, TAK: Takayasu arteritis, SLE: systemic lupus erythematosus, HC: healthy controls. *adjusted for cardiovascular risk factors

Methods: Consecutive patients with TAK (50, 40F/5M; mean age: 39.8±8.2 years) and systemic lupus erythematosus (SLE) (43, 38F/5M; 38.0±7.9 years) attending a single tertiary university hospital were studied in addition to apparently healthy hospital workers (57, 50F/7M: 39.5±7.1 years). Carotid artery IMT and SWE values were assessed using carotid artery B-mode US and SWE. Atherosclerotic plaques were noted. Disease duration, clinical characteristics and information related to immunosuppressive drug use were obtained from the patient's charts. Cardiovascular risk factors were determined.

Results: Study groups were balanced according to the most of the variables including mean age, gender ratio, BMI, past and current smoking history, post-menopausal status, the frequency of diabetes mellitus, the mean total, LDL, and HDL cholesterol levels and the median hsCRP levels (evaluated only in TAK and SLE). The mean systolic and diastolic blood pressure levels were significantly higher in both TAK and SLE patients compared to healthy controls (HC's). As shown in Table 1, the mean IMT in the right and left carotid arteries was significantly higher among patients with TAK, when compared to SLE and HCs. On the other hand, the mean SWE in the carotid artery was significantly increased among both TAK and SLE patients when compared to HCs, whereas patients with TAK had the highest values. After adjusting for cardiovascular risk factors, the significances remained robust. Only patients with TAK were found to have significantly increased frequency of carotid artery plaques (TAK: 22.0%, SLE: 4.7%, HC's: 5.3%, p=0.006). IMT and diastolic blood pressure levels were found to be associated independently with SWE.

Conclusion: Our study indicates that among patients with TAK, both atherosclerosis and arterial stiffness are increased and appear to be closely related. Arterial stiffness along with severe hypertension and accelerated atherosclerosis could contribute to the increased risk for cardiovascular morbidities in TAK. Furthermore, SWE could be an indicator of cardiovascular risk that can be surveyed in TAK.

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POS0707 EFFECTIVENESS AND SAFETY OF INTRAVENOUS VERSUS SUBCUTANEOUS TOCILIZUMAB IN TAKAYASU ARTERITIS: MULTICENTER RETROSPECTIVE STUDY

Keywords: Rare/orphan diseases, Vasculitis, Remission

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Background: Recently, the effectiveness of biological therapies such as inhibitors of tumor necrosis factor-α (TNF-α) and IL-6 receptor (tocilizumab) in TAK patients who were refractory to other immunosuppressive therapies has been reported in several studies. We have recently reported a French nationwide registry that showed quite similar effectiveness of TNF-α antagonists and tocilizumab, with acceptable safety profile and significant steroid sparing effect. A recent phase 3, randomized, double blind, placebo-controlled trial of tocilizumab *versus* placebo in TAK failed to reach its primary intention-to-treat analysis, but tocilizumab was favored in a secondary per-protocol analysis regarding TAK time to relapse. Besides its role on refractory patients, intravenous tocilizumab was also evaluated in treatment-naïve TAK patients in the French TOCITAKA prospective multicenter open-labeled trial, showing 6-month remission rates of 80%, of whom 54% were in glucocorticoid-free remission at 6 months.

Objectives: In this large multicenter study, we compared the effectiveness and safety of tocilizumab IV *versus* SC in 109 TAK patients.

Methods: We conducted a retrospective multicenter study in referral centers from France, Italy, Spain, Armenia, Israel, Japan, Tunisia, and Russia regarding biological-targeted therapies in TAK, since January 2017 to September 2019.

Results: A total of 109 TAK patients received at least 3 months tocilizumab therapy and were included in this study. Among them, 91 and 18 patients received IV and SC tocilizumab, respectively. A complete response (NIH<2 with less than 7.5 mg/day of prednisone) at 6 months was evidenced in 69% of TAK patients, of whom 57 (70%) and 11 (69%) patients were on IV and SC tocilizumab, respectively (p=0.95). The factors associated with complete response to tocilizumab at 6 months in multivariate analysis, only age < 30 years (OR = 2.85, 95% CI 1.14; 7.12; p=0.027) and time between TAK diagnosis and tocilizumab initiation (OR = 1.18, 95% CI 1.02; 1.36; p=0.034). During the median follow-up of 30.1 months [0.4; 105.8] and 10.8 [0.1; 46.4] (p<0.0001) in patients who received tocilizumab in IV and SC forms, respectively, the risk of relapse was significantly higher in TAK patients on SC tocilizumab (HR = 2.55, 95%CI 1.08;6.02; p=0.033). The overall cumulative incidence of relapse at 12 months in TAK patients was at 13.7% (95%CI 7.6; 21.5), with 10.3% (95%CI 4.8;18.4) for those on IV tocilizumab *versus* 30.9% (95%CI 10.5;54.2) for patients receiving SC tocilizumab. Adverse events occurred in 14 (15%) patients on IV route and in 2 (11%) on SC tocilizumab.

Conclusion: In this study, we confirm that tocilizumab is effective in TAK, with complete remission being achieving by 70% of DMARDs-refractory TAK patients at 6 months.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0708 VALIDATION OF THE REVISED 2022 AMERICAN COLLEGE OF RHEUMATOLOGY/ EULAR CLASSIFICATION CRITERIA FOR TAKAYASU ARTERITIS

Keywords: Diagnostic tests, Vasculitis, Validation

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Background: The 2022 American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) classification criteria for Takayasu arteritis (TAK) were recently published [1].

Objectives: To validate and evaluate the 2022 ACR/EULAR TAK classification criteria in the light of the 1990 ACR TAK classification criteria [2].

Methods: Clinical data of TAK patients from four referral centers (two from Italy and two from India) were reviewed to assess the fulfillment of 2022 ACR/EULAR and 1990 ACR TAK criteria. Control subjects included large-vessel giant cell arteritis (LV-GCA), large vessel vasculitis (LVV) other than TAK or GCA, or non-inflammatory arterial disorders. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratio of a positive test (LR+), likelihood ratio of a negative test (LR-), area under the receiver operating characteristics curve (AUC) at the cut-offs of ≥3 points for 1990 ACR criteria and ≥5 points for 2022 ACR/EULAR criteria were calculated. AUC was also calculated using the actual scores for the 2022 ACR/EULAR criteria. Secondary analyses

were conducted on the basis of sex (male/female), using only LV-GCA as controls, using subjects ≤60 years, and stratified on age (<40, 40-60, >60 years).
Results: 504 TAK [404 females, mean (SD) age at diagnosis 31.7 (12.6) years] and 222 controls [144 LV-GCA, 151 females, mean (SD) age at diagnosis 61.9 (15.4) years] were identified. The 2022 ACR/EULAR criteria had better sensitivity and NPV but had poorer specificity, PPV, LR+, LR-, and AUC at predetermined cut-offs than the 1990 ACR criteria (Table 1). Similar performance of 2022 ACR/EULAR criteria was observed with only LV-GCA as controls (sensitivity 95.83%, specificity 60.42%, AUC 0.781) or in subjects ≤60 years old (sensitivity 95.81%, specificity 61.90%, AUC 0.789). The 2022 ACR/EULAR criteria had a greater specificity (76.06% vs 57.62%) and AUC (0.845 vs 0.771) with similar sensitivity (93% vs 96.53%) in males than in females. Stratified for age [<40 years, n=399, 374 TAK, 25 controls; 40-60 years, n=186, 127 TAK, 59 controls; >60 years, n=141, 3 TAK, 138 controls], sensitivity remained similar (96.26%, 94.49%, 100%, respectively), whereas, specificity was higher for older age groups (52%, 66.10%, 64.49%, respectively). Cut-offs of ≥6 (sensitivity 91.87%, specificity 82.88%) and ≥7 (sensitivity 86.71%, specificity 86.49%) greatly improved balance between sensitivity and specificity (Figure 1).
Conclusion: In this first validation study, the 2022 ACR/EULAR TAK criteria had poorer specificity in real-life than in the development cohort. Higher cut-offs (6 or 7) might improve the performance of these criteria. Higher PPV but lower NPV in the Indian than in the Italian cohort might reflect the different performance of the criteria in different ethnic groups.

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Table 1. Performance of the criteria

	Overall (n=726, 504 TAK, 222 controls)		Italian cohort (n=401, 201 TAK, 200 controls)		Indian Cohort (n=325, 303 TAK, 22 controls)	
	ACR 1990 criteria	ACR EULAR 2022 criteria	ACR 1990 criteria	ACR EULAR 2022 criteria	ACR 1990 criteria	ACR EULAR 2022 criteria
Sensitivity	82.94%	95.83%	75.12%	94.53%	88.12%	96.70%
Specificity	90.54%	63.51%	93.50%	63.50%	63.64%	63.64%
PPV	95.22%	85.64%	92.07%	72.24%	97.09%	97.34%
NPV	70.03%	87.04%	78.90%	92.03%	28.00%	58.33%
LR+	8.77	2.63	11.56	2.59	2.42	2.66
LR-	0.19	0.07	0.27	0.09	0.19	0.05
AUC (95% CI)	0.867 (0.842 – 0.893)	0.797 (0.764 – 0.830)	0.843 (0.809 – 0.878)	0.790 (0.753 – 0.827)	0.759 (0.654 – 0.863)	0.802 (0.698 – 0.905)
Correctly classified (%)	85.26%	85.95%	84.29%	79.05%	86.46%	94.46%

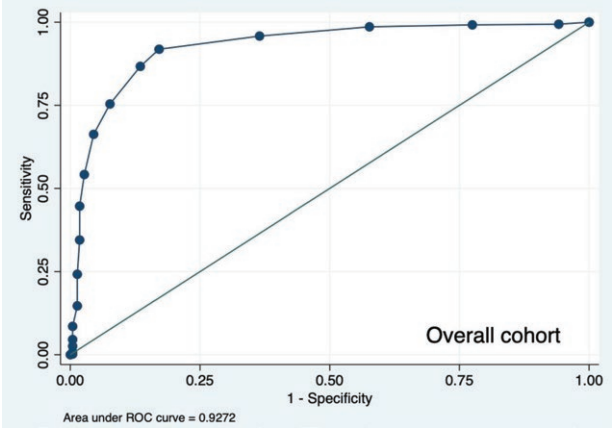


Figure 1. AUC using actual 2022 ACR/EULAR scores.

Disclosure of Interests: None Declared.
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POS0709

COMPARATIVE EFFICACY OF SECUKINUMAB VERSUS TUMOR NECROSIS FACTOR INHIBITORS FOR THE TREATMENT OF TAKAYASU'S ARTERITIS

Keywords: Vasculitis

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Background: Takayasu's arteritis (TAK) is a large-vessel vasculitis that mainly involves the aorta and its primary branches. Glucocorticoids (GCs) are the mainstay of treatment of TAK, especially for the induction of remission. However, the majority of patients experience relapses when the dose of GCs is reduced. Many patients fail to respond to synthetic conventional immunosuppressive drugs. IL-6 and TNF-α have been shown to be involved in the pathogenesis of TAK. Biologic drugs that target IL-6 or TNF-α (TNFis) have been reported to be effective and are recommended for the treatment of TAK refractory to low-dose GC combined with conventional treatment. Recently, Th-17 cells and its related cytokines IL-17A, IL-21, and IL-23 have also been identified as involved in the pathogenesis of TAK, suggesting that targeting IL-17A might be an effective treatment for this disease.
Objectives: This study aimed to investigate the efficacy of secukinumab, an anti-IL-17A monoclonal antibody, compared to treatment with TNFis for the induction of remission of patients with a relapse of TAK.
Methods: This was a prospective, single center, open-label cohort study. Patients with active TAK who failed to respond to treatment with glucocorticoids combined with 2 immunosuppressive agents were treated with either secukinumab or TNFi as an add-on therapy without increase of the dosage of GCs. Complete response was defined as full resolution of signs and symptoms of active disease, normal values of inflammatory markers, no progression on imaging of involved arteries, and dose of glucocorticoid <15mg/d. Partial response was defined as the same as complete response except ESR <40mm/hour and CRP <20mg/L.
Results: Nineteen patients in the secukinumab group and 34 patients in the TNFi group were enrolled. The demographic data and inflammatory markers of the two groups were comparable at baseline. The baseline dose of GC (prednisone) was ≤ 15mg/day in all patients in both treatment groups. The combined complete and partial responses at 3 months for patients treated with secukinumab and TNFi were 31.6% and 58.8% (P =0.506) respectively, and at 6 months were 52.6% and 64.7% (P= 0.389), respectively. Similar responses to both secukinumab and TNFi we also seen for time to initiation of GCs and time to achieving a dose of prednisone ≤ 5mg/day (Figure 1). The ESR, serum CRP, and IL-6 levels were significantly reduced compared with the baseline after 1, 3, and 6 months of treatment in both secukinumab and TNFis treatment groups. In the secukinumab treatment group 6 of 19 (31.6%) patients had their GC dosage tapered and 2 patients reduced the dose of conventional immunosuppressive agents at 6 months. In the TNFi treatment group 18 of 34 (52.9%) patients had their GC dosage tapered and 4 patients reduced the dose of conventional immunosuppressive agents at 6 months. There was no significant difference of the median dose of GC in either treatment group. No arterial structural changes were observed in patients in either the secukinumab or TNFi treatment group at 6 months. Two patients had infectious events in the secukinumab treatment group, one lead to discontinuation of the medication. Two patients in the TNFi treatment group had events leading to withdrawal from the study: one with a severe infection and one with a severe rash.
Conclusion: These results suggest that secukinumab and TNFi are effective treatments for patients with TAK who fail to respond to oral GCs and conventional immunosuppressive agents, with similar response rates at 3 and 6 months.

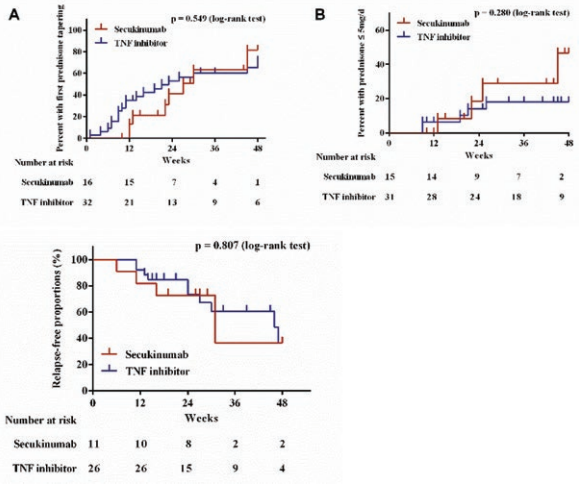


Figure 1.

Table 1. Comparison of different disease activity parameters

Parameter	Cut-off	Sensitivity	Specificity	Correctly classified	LR+	LR-	PPV	NPV	AUC (95% CI)
SUV_{max}	≥1.8	83.33%	91.67%	86.67%	10.00	0.18	93.75%	78.57%	0.875 (0.755–0.955)
SUV_{mean}	≥1.5	83.33%	91.67%	86.67%	10.00	0.18	93.75%	78.57%	0.875 (0.755–0.955)
TBR	≥1.125	83.33%	91.67%	86.67%	10.00	0.18	93.75%	78.57%	0.875 (0.755–0.955)
TLR	≥0.7	83.33%	91.67%	86.67%	10.00	0.18	93.75%	78.57%	0.875 (0.755–0.955)
MIV	≥1.8	88.89%	91.67%	90.00%	10.67	0.12	94.12%	84.62%	0.903 (0.792–1.000)
TIG	≥2.7	88.89%	91.67%	90.00%	10.67	0.12	94.12%	84.62%	0.903 (0.792–1.000)
PETVAS	5.5	50%	100.00%	70.00%	-	0.50	100.00%	57.14%	0.750 (0.631–0.869)
PETVAS	10	27.78%	100.00%	56.67%	-	0.72	100.00%	48.00%	0.639 (0.542–0.745)
PETVAS	15	11.11%	100.00%	46.67%	-	0.89	100.00%	42.86%	0.556 (0.481–0.630)
CRP	6 mg/L	83.33%	75.00%	80.00%	3.33	0.22	83.33%	75.00%	0.792 (0.636–0.947)
ESR	40 mm/hr	72.22%	90.91%	79.31%	7.94	0.31	92.86%	66.66%	0.816 (0.677–0.954)

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3440

POS0710

METABOLIC INFLAMMATORY VOLUME AND TOTAL INFLAMMATORY GLYCOLYSIS: NOVEL PARAMETERS TO EVALUATE DISEASE ACTIVITY ON PET-CT IN TAKAYASU ARTERITIS

Keywords: Vasculitis, Imaging

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Background: 18-fluorodeoxyglucose (FDG) Positron emission tomography-computed tomography (PET-CT) has only moderate concordance with C-reactive protein (CRP) in Takayasu arteritis (TAK).
Objectives: We propose and evaluate the diagnostic accuracy of two new PET-CT parameters, metabolic inflammatory volume (MIV) and total inflammatory glycolysis (TIG) to quantify arterial FDG uptake for active TAK.
Methods: Images of PET-CT of TAK were reviewed to calculate mean standardized uptake value (SUV_{mean}) and maximum standardized uptake value (SUV_{max}), target-to-blood pool ratio (TBR), target-to-liver ratio (TLR), and PET Vasculitis Activity Score (PETVAS) [1]. ESR, CRP, disease activity [using physician global assessment (PGA, active/inactive), Indian TAK Clinical Activity Score 2010 (ITAS2010), ITAS2010 with ESR (ITAS-A-ESR) or CRP (ITAS-A-CRP), Disease Extent Index in TAK (DEI.TAK)] were extracted from clinic files. Regions of interest (ROI) were drawn to calculate MIV in areas of FDG uptake ≥1.5-times SUV_{max} on syngo.via. MIV was semiautomatically calculated after excluding areas of physiological tracer uptake. TIG was calculated by multiplying MIV with SUV_{mean}. MIV and TIG for all areas of arterial FDG uptake were added. Area under the receiver operating characteristics (ROC) curves (AUC, with 95%CI) to predict active disease using PGA with absolute values of SUV_{max}, SUV_{mean}, TBR, TLR, MIV, TIG, PETVAS, CRP, ESR, ITAS2010, ITAS-A-ESR, ITAS-A-CRP, and DEITAK were calculated. Dichotomized cut-offs for active disease [PETVAS ≥5.5 [2],≥10,≥15,or≥20 [1]; CRP≥6 mg/L; ESR≥40 mm/hr; for the remaining parameters, cut-offs correctly classifying disease activity in most patients) were used to calculate sensitivity, specificity, likelihood ratio of a positive test (LR+), likelihood ratio of a negative test (LR-), positive predictive value (PPV), negative predictive value (NPV), and AUC (with 95%CI).Concordance between CRP and PET-CT parameters were assessing kappa statistic. Analyses were performed using STATA 16.1 I/C.
Results: PET-CT of 30 TAK [mean (SD) age 29.9 (11.5) years, 22 females, 29 immunosuppressive-naive) were reviewed. AUC using absolute values ranged between 0.852 to 0.926 (Figure 1). Using dichotomized optimal cut-offs for SUV_{max}, SUV_{mean}, TBR, TLR, MIV, and TIG, MIV and TIG performed better than SUV_{max}, SUV_{mean}, TBR, TLR, PETVAS (at cut-offs 5.5, 10, and 15 – none had PETVAS≥20) to detect active TAK (Table 1). Agreement with CRP for active TAK was similar for MIV (70%) and TIG (70%) with SUV_{max}, SUV_{mean}, TBR, and TLR (each 66.67%), and better than PETVAS [≥5.5 (56.67%), ≥10 (50%), ≥15 (40%), ≥40 (40%)].
Conclusion: Novel PET-CT parameters, MIV and TIG, had comparable performance to established PET-CT parameters and better performance than PETVAS for active TAK, and require further exploration in LVV.

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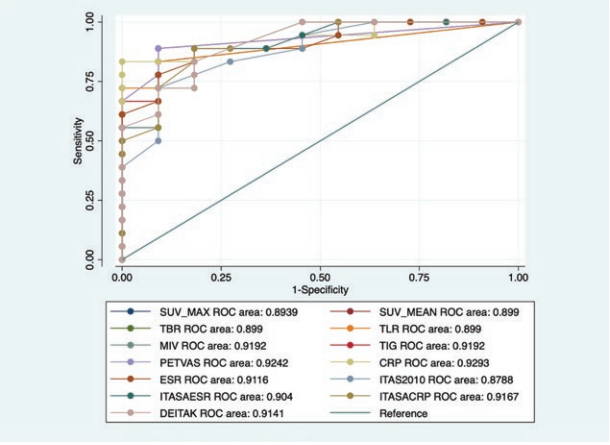


Figure 1. AUC using actual values of different parameters to distinguish active TAK by PGA

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0711

DEVELOPMENT OF THE TAKAYASU'S ARTERITIS INTEGRATED DISEASE ACTIVITY INDEX

Keywords: Vasculitis, Imaging

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Background: Disease activity indices that accurately assess inflammation in Takayasu's arteritis (TAK) are needed [1]. While clinical assessment is often considered the gold standard, determining if a symptom represents active vasculitis or damage can be challenging in TAK. FDG-PET can directly assess vascular inflammation but specificity of imaging findings, especially in absence of corresponding clinical symptoms, is questionable.
Objectives: The aim was to develop an index to assess disease activity in TAK called TAK Integrated Disease Activity Index (TAIDAI).
Methods: Clinical symptoms associated to TAK were derived from a comprehensive literature review [2]. TAIDAI was assessed in an observational cohort with a stepwise approach. All the symptoms present within 7 days of clinical evaluation were recorded by two clinicians, without determining whether the symptom reflected active disease or damage. Physician global assessment (PhGA) (scale 0-10) and certainty of the assessment (certain vs uncertain) were collected for every visit. Each patient underwent FDG-PET 24 hours after the clinical assessment. Active vasculitis, defined as arterial FDG uptake > liver, was recorded in specific arterial

territories and quantified using the PET Vascular Activity Score (PETVAS) [3]. To score TAIDAI, clinical symptoms are paired with specific arterial territories and only scored if there is active vasculitis by FDG-PET in a corresponding arterial territory. Constitutional symptoms are scored only if CRP ≥10mg/L or ESR≥40mm/hour. To determine content validity, correlations were performed between PhGA, patient-reported global assessment (PtGA, 0-10 scale), ESR, CRP, PETVAS, and TAIDAI. To determine criterion validity, performance characteristics of TAIDAI were calculated relative to clinical assessment, restricted to cases of assessment certainty. To determine responsiveness, TAIDAI scores were assessed longitudinally in patients initiated on tumor necrosis factor inhibitors (TNFi) or tocilizumab (TCZ). Complete response was defined as resolution of all symptoms of active vasculitis plus a daily prednisone dose not exceeding >50% of the pre-treatment visit.

Results: 17 clinical symptoms were identified for inclusion in the index. TAIDAI was calculated for 96 patients over 204 visits. Clinically active disease was present in 62 (30%) visits, with uncertainty of assessment in 82 (40%) visits. Inter-rater agreement for PhGA was poor (45%). At baseline, median TAIDAI was 1 (range 0-9), and 48 (50%) patients had a TAIDAI of 0. TAIDAI > 0 defined active disease with 96% sensitivity and 77% specificity compared to clinical assessment. TAIDAI score correlated most strongly with all other assessments (Table 1). Complete response was observed in 15/20 patients treated with TNFi and 8/11 patients treated with TCZ. A TAIDAI score of 0 was achieved by 21/23 (91%) responders, and TAIDAI remained > 0 for 5/8 (63%) treatment failures.

Conclusion: TAIDAI is a novel disease activity index focused on scoring clinical symptoms only when supported by relevant imaging or laboratory data. TAIDAI should be tested in other cohorts and future clinical trials in TAK.

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Table 1. Spearman's Correlations between different assessment domains of disease activity in Takayasu's Arteritis

	By Variable	p value	Spearman ρ
TAIDAI	PhGA	<.0001*	0.5523
TAIDAI	PETVAS	<.0001*	0.4742
PETVAS	PhGA	<.0001*	0.3686
TAIDAI	CRP	<.0001*	0.3128
TAIDAI	PtGA	0.0002*	0.3026
ESR	PhGA	0.0003*	0.2535
ESR	PtGA	0.0076*	0.2158
PtGA	PhGA	0.0110*	0.2058
TAIDAI	ESR	0.0043*	0.1991
CRP	PhGA	0.0489*	0.1384
ESR	CRP	0.0819	0.1221
CRP	PETVAS	0.1223	0.1085
ESR	PETVAS	0.2475	0.0813
CRP	PtGA	0.7259	-0.0287
PETVAS	PtGA	0.3454	-0.0771

TAIDAI = Takayasu's arteritis integrative disease activity assessment; PhGA = physician global assessment; PtGA = patient global assessment; PETVAS = PET vascular activity score; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.

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Disclosure of Interests: None Declared.
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POS0712 WHAT IS THE OUTCOME OF PATIENTS WITH OR WITHOUT SUBCLINICAL GIANT CELL ARTERITIS IN POLYMYALGIA RHEUMATICA? PRELIMINARY DATA OF AN OBSERVATION STUDY

Keywords: Ultrasound, Vasculitis

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Background: Subclinical giant cell arteritis (GCA) in polymyalgia rheumatica (PMR) is found in the 22.8% of patients on ultrasound examinations. The outcome and the optimal management of subclinical giant cell arteritis (GCA) in patients with polymyalgia rheumatica (PMR) have not been defined yet.

Objectives: The aim of this study was to investigate the short-term outcome of PMR patients with concurrent subclinical GCA that were included in our multicenter project on the prevalence, characteristics and outcome of subclinical GCA (diagnosed by vascular ultrasound) in PMR [1].

Methods: We analyzed follow up data at 3, 6, 12 and 18 months of consecutive PMR patients from 7 European rheumatology centers. All patients fulfilled 2012 EULAR/ACR Provisional Classification Criteria for Polymyalgia Rheumatica and they had not symptom of clinical GCA. Patients were stratified into two groups: pure PMR and PMR with subclinical GCA, and the outcome between these two groups were compared. A relapse was defined as clinical and/or laboratory worsening of the disease after the initial remission and minor and major relapse EULAR definition was used [2].

Results: We included 116 PMR patients (47 with concurrent subclinical GCA and 69 with pure PMR) followed for a median (IQR) of 21 (17; 23) months. We observed relapses in 35/116 patients (30.2%), 27/47 (57.4%) in PMR with subclinical GCA and 8/69 (11.6%) in pure PMR group (p<0.001). All relapses in the pure PMR group were minor relapses, whereas we observed 2 major relapses in the subclinical GCA group. The dose of corticosteroids used at the baseline visit was significantly higher in the GCA subclinical group, but tapering of steroids occurred faster than recommended by clinical guidelines [2]. Prednisone dose was significantly higher in patients with PMR and subclinical GCA than in patients with pure PMR both at baseline and at month 6 (Table 1). In patients with PMR with subclinical GCA mean starting dose of prednisone was 32.2±16.1 mg in those who relapsed and 36.2±12.8 in those who maintained remission (p=0.166); at 3 months, it was 13.2±7.1 and 18.2±7.9, respectively (p<0.05). Three patients in the PMR with subclinical GCA group received biological therapy at diagnosis; one of them had a minor relapse.

Table 1. Patients characteristics

	Pure PMR (n=69)	Subclinical GCA/PMR (n=47)	p
Age years (mean ± SD)	71.2±8.0	74.8±7.6	0.079
Sex (females %)	59%	52%	0.526
Relapses n (%)	8/69 (11.6%)	27/47 (57.4%)	0.001
Minor Relapses n (%)	8/69 (11.6%)	25/47 (53.2%)	0.001
Major Relapses n (%)	0	2/47 (4.2%)	
Steroids basal (mean ± SD))	18.3±9.1	34±14.8	0.001
Steroids month 3 (mean ± SD)	9.9±5.1	14.6±8.3	0.001
Steroids month 6 (mean ± SD)	5.6±2.1	8.8±6.8	0.037
Steroids month 12 (mean ± SD)	1.7±2.1	8.0±14.2	0.062
Steroids month 18 (mean ± SD)	1.1±1.8	3.6±5.6	0.09

Steroids = mg prednisone; SD = standard deviation; n= number of patients

Conclusion: PMR patients with subclinical GCA had a significantly higher number of relapses during the follow-up than pure PMR group. These results suggest that subclinical GCA in PMR should be treated in the same manner as clinically overt GCA.

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POS0713 A HISTORY OF POLYMYALGIA RHEUMATICA IS ASSOCIATED WITH ADVANCED SUPRA-AORTIC VASCULAR DAMAGE AT DIAGNOSIS OF GIANT CELL ARTERITIS

Keywords: Vasculitis, Ultrasound

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Background: Subclinical giant cell arteritis (GCA) can be found in imaging studies at diagnosis of polymyalgia rheumatica (PMR) in up to 30% of patients [1]. Newly diagnosed GCA patients with a preceding PMR diagnosis may therefore present with more advanced vasculitic vessel alterations than GCA patients without prior PMR.
Objectives: To compare vascular ultrasound (US) findings in newly diagnosed GCA patients with and without a history of PMR.
Methods: Retrospective analysis of patients with GCA diagnosed at the University Hospital Basel between 12/2006 and 05/2021.
Results: 49 of 311 newly diagnosed GCA patients (15.8%) had a preceding diagnosis of PMR a median of 2.5 (IQR 0.6-5.6) years earlier. US revealed vessel wall alterations typical for vasculitis in the supraaortic vessels (carotid, vertebral, subclavian and/or axillary arteries) more often in patients with prior PMR than without PMR (51% vs 25%, p<0.001). Additionally, patients with prior PMR had more often significant vascular stenoses in the supraaortic vessels that were affected by vasculitis (37.5% vs 13.6%, p=0.03). Patients with and without prior PMR did not differ in terms of ischemic complications of stroke or vision loss at GCA diagnosis nor in the number of vascular segments with atherosclerosis (Table 1). In multivariable analysis, prior PMR was significantly associated with vasculitic vessel wall alterations (OR 4.28, 95% CI 1.92–9.85, p<0.001) adjusted for sex, headache, scalp and temporal artery tenderness. Furthermore, prior PMR was associated with vascular stenoses (4.97, 95% CI 1.4–19.12, p=0.015) adjusted for age, sex, arteriosclerosis, cerebrovascular and coronary heart disease.

Table 1. Patient characteristics

Characteristics	All (n=311)	GCA without history of PMR (n=262)	GCA with history of PMR (n=49)	p-value
Age (years), mean±SD	73.8 (7.6-78.8)	73.5 (67.3-79.2)	74.4 (70.0-78.0)	0.678
Female	196 (63.0)	166 (63.4)	30 (61.2)	0.776
Hypertension	156 (50.2)	128 (48.9)	28 (57.1)	0.301
Diabetes mellitus	57 (18.3)	49 (18.7)	8 (16.3)	0.733
Dyslipidemia	78 (25.1)	64 (24.4)	14 (28.6)	0.539
Smoking	101 (32.5)	91 (34.7)	10 (20.4)	0.038
Arteriosclerotic segments*	1 (0.0-2.0)	1 (0.0-2.0)	0.0 (0.0-2.0)	0.078
Coronary artery disease	44 (14.1)	39 (14.9)	5 (10.2)	0.354
Cerebrovascular disease	29 (9.3)	22 (8.4)	7 (14.3)	0.282
ESR (mm/h)	70 (40.0-88.0)	72 (41.5-90.0)	50.0 (28.0-72.0)	0.002
CRP (mg/dl)	55.7 (24.1-109.3)	57.6 (25.6-110.3)	52.8 (17.3-102.5)	0.336
Headache	188 (60.5)	164 (62.6)	24 (49.0)	0.091
Jaw claudication	126 (40.5)	110 (42.0)	16 (32.7)	0.3
Scalp tenderness	112 (36.0)	102 (38.9)	10 (20.4)	0.02
Polymyalgic symptoms	119 (38.3)	94 (35.9)	25 (51.0)	0.053
Stroke	14 (4.5)	10 (3.8)	4 (8.2)	0.249
Permanent vision loss	45 (14.5)	38 (14.5)	7 (14.3)	0.968
Vasculitis in supraaortic vessels**	90 (28.9)	65 (24.8)	25 (51.0)	<0.001
Vascular stenoses (≥50%)†	17/83 (20.5)	8/59 (13.6)	9/24 (37.5)	0.032

n (%); median (interquartile range) for numeric values.CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, GCA: giant cell arteritis, PMR: polymyalgia rheumatica.*Number of vascular segments with atherosclerosis on ultrasound examination in both carotid, vertebral, subclavian and axillary arteries.**Number of patients with vasculitis in the carotid, vertebral, subclavian and/or axillary arteries.†Number of patients with vascular stenoses in the internal carotid, axillary and/or vertebral arteries affected by vasculitis (n=83).

Conclusion: GCA patients with prior PMR had a more extensive vascular involvement on ultrasound than those without prior PMR at diagnosis. Presence of stenoses could not be explained by arteriosclerosis. Undiagnosed subclinical GCA in patients with previous PMR may be a cause of more advanced vascular changes. These data support the need for screening strategies for GCA in patients with PMR.

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POS0714

TREAT-TO-TARGET RECOMMENDATIONS IN GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA

Keywords: Vasculitis, Remission, Treat to target

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Background: The treat-to-target (T2T) concept is not yet a recognized treatment approach in giant cell arteritis (GCA) and polymyalgia rheumatica (PMR). Developing such recommendations is an unmet medical need.
Objectives: To determine therapeutic targets and develop treat-to-target (T2T) recommendations in GCA and PMR.
Methods: We conducted a systematic literature review to retrieve data on treatment targets and outcomes in GCA/PMR as well as to identify the evidence for the effectiveness of T2T-based management approaches in these diseases. Based on evidence and expert opinion, the task force [29 participants from 10 countries (physicians, healthcare professional and patient)] developed recommendations, with consensus obtained through voting. The final level of agreement was provided anonymously.
Results: Five overarching principles and six specific recommendations were formulated (Table 1). Key messages are that the management of GCA and PMR should be based on shared decisions between patient and physician, underpinning the need for urgent treatment of GCA to avoid ischemic complications, and that it should aim at maximizing health-related quality of life in both diseases. The treatment targets are the achievement and maintenance of remission (still in need of ultimate validation), as well as prevention of tissue ischemia and vascular damage. Comorbidities should be considered when assessing disease activity and selecting treatment.
Conclusion: These are the first T2T recommendations for GCA and PMR. Treatment targets and strategies to assess, achieve and maintain these targets have been defined. The research agenda highlights the evidence-gaps and needs for future research.

Table 1. Treat-to-Target (T2T) recommendations in GCA and PMR

Overarching principles	LoE	LoA
A. Clinical management of GCA and PMR should be driven by the awareness that they are closely interrelated conditions in a common spectrum of inflammatory disease and can occur separately, simultaneously or in temporal sequence to each other.	n.a.	9.8 96.3% >8
B. GCA is a medical emergency because of the imminent risk of sight loss and other ischemic events and therefore requires immediate treatment; management usually requires multidisciplinary collaboration.	n.a.	9.9 100% >8
C. Patients should be offered access to information about GCA and PMR, including clinical disease features, patient reported outcomes, potential complications, treatment related benefits and risks, as well as relevant comorbidities.	n.a.	9.7 96.3% >8
D. Management of GCA and PMR should be based on shared decision making between the informed patient and the physician.	n.a.	9.8 100% >8
E. Treatment of GCA and PMR should aim at maximizing health-related quality of life through control of symptoms, preventing disease-related damage and minimizing treatment-related adverse consequences, taking relevant comorbidities into account.	n.a.	9.9 100% >8
Recommendations		
1. The treatment target of GCA and PMR should be remission; remission is the absence of clinical symptoms and systemic inflammation.	5	9.6 96.3% >8
2. Treatment of GCA should also aim to prevent tissue ischemia and vascular damage.	5	9.9 100% >8
3. Treatment selection in GCA and PMR should be based on disease severity and activity, presence of relevant comorbidities and potential predictors of outcome; treatment should be modified as needed during follow-up.	5	9.9 100% >8
4. Comorbidities may influence the assessment of the treatment target and should be considered before modifying treatment.	5	9.8 100% >8
5. Once remission is reached, it should be maintained with the minimal effective dose of medication[#]; drug-free remission may be achieved in a proportion of patients[##].	5[#] - 2[##]	9.9 100% >8
6. Disease activity in GCA and PMR should be monitored regularly, as frequently as every 1-4 weeks until remission has been achieved, and at longer monitoring intervals (for example between 3 and 6 months) in patients in stable remission on therapy; monitoring of patients off therapy should be discussed on an individual basis.	5	9.8 100% >8

LoE: Level of Evidence; LoA: Level of Agreement

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POS0715

SUSTAINED REMISSION FROM WEEKS 16 TO 52 AND WEEKS 24 TO 52 IN PATIENTS TREATED WITH SARILUMAB: POST-HOC ANALYSIS OF SAPHYR TRIAL IN PATIENTS WITH POLYMYALGIA RHEUMATICA

Keywords: Clinical trials, Remission

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Background: The SAPHYR study (NCT03600818) in patients with polymyalgia rheumatica (PMR) who were resistant to glucocorticoid (GC) taper met the primary endpoint with a significantly higher proportion of patients in the sarilumab arm versus the comparator arm achieving sustained remission from weeks 12 to 52 (28.3% vs 10.3%; P=0.0193) [1]. Sarilumab, when administered to patients with rheumatoid arthritis at a dose of 200 mg subcutaneously, achieved a steady state within 14 to 16 weeks [2]. Patients treated with sarilumab in SAPHYR may not have reached steady state concentrations by week 12 when disease remission was assessed for the primary endpoint of sustained remission.

Objectives: This post-hoc analysis of the SAPHYR study assessed the proportion of patients achieving sustained remission up to week 52 from week 16 and from week 24.

Methods: Patients were randomized (1:1 ratio) to 52 weeks of treatment with sarilumab 200 mg every 2 weeks (Q2W) + 14 week GC tapered regimen (sarilumab arm) or placebo Q2W + 52 week GC tapered regimen (comparator arm). Here, we assessed the proportion of patients achieving sustained remission and each of the sustained remission components from week 16 and from week 24 to the end of study. Sustained remission was defined as having met all of the following: disease remission at 16 weeks and 24 weeks (no PMR signs and symptoms + CRP normalization [<10 mg/L]); absence of disease flare from weeks 16 to 52 and weeks 24 to 52; sustained reduction of CRP (to <10 mg/L, with no successive elevations to ≥10 mg/L) from weeks 16 to 52 and weeks 24 to 52; and successful adherence to protocol specified GC taper dose from weeks 16 to 52 and weeks 24 to 52. Patients who did not achieve remission, received rescue treatment with open label prednisone (or equivalent), withdrew from the study before week 52, or had missing data that prevented assessment of the primary endpoint were considered as non-responders.

Results: Between Oct 2018 and Jul 2020, 60 patients were randomized to the sarilumab arm and 58 patients to the comparator arm (intent to treat population). A higher proportion of patients in the sarilumab arm, versus the comparator, achieved sustained remission from weeks 16 to 52 (30.0% vs 8.6%; difference [95% CI]: 21.4 [7.7, 35.0]; P=0.0047) and from weeks 24 to 52 (31.7% vs 10.3%; difference [95% CI]: 21.3 [7.2, 35.5]; P=0.0063). This improvement in sustained

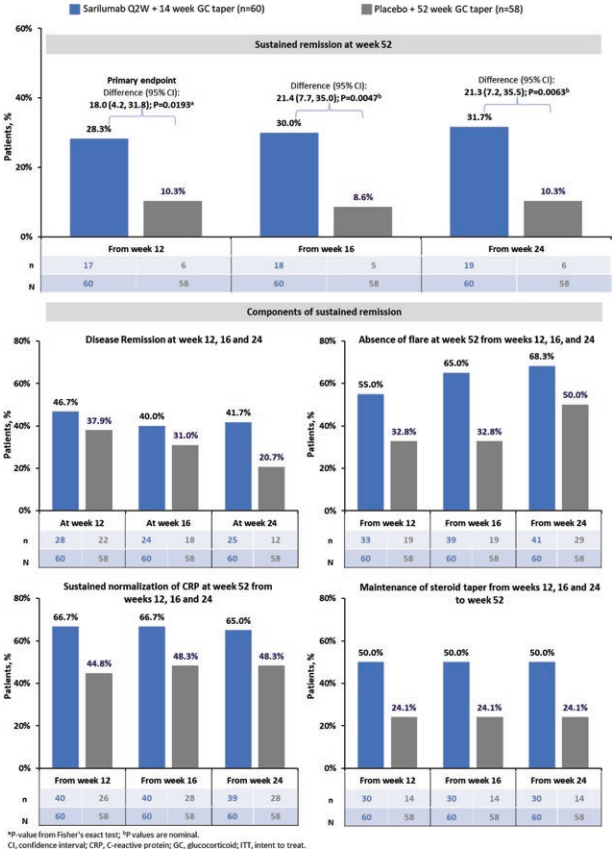
remission rate in the sarilumab arm was due to additional responses seen between weeks 12 to 24 **(Figure 1)**. Similarly, all the independent components of the sustained remission were achieved by a higher proportion of patients in the sarilumab arm, versus the comparator arm, during each assessment period. In both the sarilumab arm and the comparator arm, the disease remission rates decreased slightly at weeks 16 and 24 compared with week 12; sarilumab arm 40.0% and 41.7%, respectively vs 46.7% and comparator arm 31.0% and 20.7%, respectively vs 37.9%. Disease remission rates declined due to missing or abnormal CRP, as the proportion of patients with no PMR signs and symptoms increased over time. In the sarilumab arm, the proportion of patients with no disease flare increased from weeks 12 to 52 assessment to weeks 16 to 52 and weeks 24 to 52 assessments, whereas the proportion of patients with sustained CRP normalization or those who adhered to protocol-defined GC taper remained the same during the three assessment periods **(Figure 1).** Safety data were consistent with the know profile of sarilumab and were presented previously [1].

Conclusion: This post-hoc analysis showed that a higher proportion of patients in the sarilumab arm, versus the comparator arm, achieved sustained remission when assessed from week 16 and week 24 up to week 52. Most patients who achieved sustained remission did so rapidly by week 12 with some additional responses seen between week 12 and 24.

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Figure. Sustained remission and components of sustained remission at week 52, assessed from week 12, week 16 and week 24 (ITT)



*P-value from Fisher's exact test; bP values are nominal.
CI, confidence interval; CRP, C-reactive protein; GC, glucocorticoid; ITT, intent to treat.

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POS0716

DIFFERENCES IN CLINICAL AND ULTRASOUND CHARACTERISTICS OF POLYMYALGIA RHEUMATICA PATIENTS WITH SUBCLINICAL GIANT CELL ARTERITIS COMPARED TO THOSE WITH CLINICAL GIANT CELL ARTERITIS

Keywords: Vasculitis, Ultrasound

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Background: It has been reported that more than a quarter of patients with polymyalgia rheumatica (PMR) have subclinical giant cell arteritis (GCA) [1]. Risk markers for subclinical GCA in PMR have not been clearly established and it is unclear if the pattern of vascular involvement on ultrasound differs from that seen in GCA.

Objectives: To identify the characteristics of PMR patients that have subclinical GCA and to compare the ultrasound features of subclinical GCA in PMR to a GCA cohort.

Methods: 58 newly diagnosed PMR patients who met a clinical diagnosis for PMR were examined with ultrasound of their temporal and axillary arteries at time of diagnosis. US of all 6 branches of the superficial temporal arteries and both axillary arteries was performed using a GE P9 device. Sonographic abnormalities considered indicative of vasculitis in the temporal arteries included the halo sign and non-compressible arteries with a thickened intima-media complex. In the axillary arteries, a halo sign, and an intima-media thickness of >1.0mm was considered positive. Clinical and laboratory characteristics were recorded. Halo scores were calculated for positive cases. Ultrasound findings were compared to a cohort of 57 GCA patients.

Results: Our cohort consisted of 58 patients with newly diagnosed PMR. The mean age was 68 years and 48% were male and 53% were female. ACR/EULAR classification criteria were met in 46/58 patients (primarily due to prior corticosteroid use in primary care resulting in normal ESR/CRP). 15 patients (25.8%) were identified as having subclinical GCA on ultrasound. Of these, 12 were male and 3 were female (p=0.0201). The mean ESR at baseline for those with isolated PMR was 35, compared to 53 for those with subclinical GCA (p=0.0419). The mean baseline ESR for our GCA cohort was 58. There was no significant difference in the baseline CRP levels, between those with subclinical GCA and isolated PMR (p=0.1150). The extent of involvement of the temporal and axillary arteries of the 58 patients in the subclinical GCA group was compared to a cohort of 57 GCA patients. The total halo count was the similar for both subclinical GCA and clinical GCA at 4.33 and 4.36. However, GCA patients had higher halo scores in both temporal and axillary vessels of 13.17 and 13.28 respectively, compared to those with subclinical GCA with scores of 5 and 9.6.

Table 1.

	Isolated PMR (43)	Subclinical GCA (15)	GCA (57)
Age (mean + range)	67 (50-84)	70 (53-84)	74 (56-92)
Female	27	3	24
Male	16	12	33
BMI	28.3	27.9	27.8
Mean ESR at baseline (mm/h)	35	53	58
Mean CRP at baseline (mg/l)	24	40	66
Mean Halo count	0	4.33	4.36
Mean temporal artery halo score	0	5	13.17
Mean axillary artery halo score	0	9.60	13.28

Conclusion: PMR patients with subclinical GCA have a similar halo count to patients with clinical GCA suggesting a similar pattern of vascular involvement. However, those with clinical GCA have higher halo scores indicating more advanced vessel oedema which may be a key factor in causing headache symptoms. Male gender and a higher ESR at the time of PMR diagnosis appear to be risk markers for subclinical GCA though this requires analysis in larger cohorts of patients.

REFERENCE:

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POS0717

COMPARISON BETWEEN ORAL AND INTRAMUSCULAR GLUCOCORTICOID THERAPEUTIC SCHEME IN POLYMYALGIA RHEUMATICA: INTERIM ANALYSIS OF PROSPECTIVE SINGLE-CENTRE STUDY

Keywords: Vasculitis

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Background: Many patients with polymyalgia rheumatica (PMR) require prolonged glucocorticoid (GC) treatment, resulting in high cumulative GC doses. Treatment with intramuscular (IM) methylprednisolone (MP) injections results in considerably lower cumulative dose than conventional oral GC.
Objectives: We aimed to evaluate clinical and laboratory response and relapse frequency between PMR patients treated with oral or IM GC regimens.
Methods: This prospective study included patients with newly diagnosed PMR between October 2021 and September 2022. At diagnosis, patients were randomly allocated to IM or oral MP dosing groups in 1:2 ratio. Both groups followed a predefined MP tapering regimen. IM injections of 120 mg of MP were given every 3 weeks for the first 16 weeks, then every 4 weeks with dose reduction by 20 mg every 12 weeks until 60 mg, then by 20 mg every 16 weeks. Oral MP was started at 16 mg/day then, every 4 weeks, the dose was reduced to: 12 mg, 8 mg, 6 mg and 4 mg. Follow-up visits were performed adhering to protocol. The remission rate and other measures of disease activity were recorded and compared between IM MP and oral MP groups. Descriptive statistics were used to analyse the studied population.
Results: Of the 39 PMR patients (72% female, median (IQR) age 71 (66, 76) years) 26 patients received oral MP and 13 IM MP. Results are presented in Table 1. During follow-up we observed higher ESR values in the IM MP group. We observed slower clinical response in IM MP group at 4 weeks of follow-up. There was no difference between the two groups in clinical response measures at 12 and 24 weeks. During 24 weeks of follow-up, we identified 2 relapses in the oral MP group: 1 patient relapsed when lowering the MP dose to 6 mg/day at 16 weeks and 1 relapsed after discontinuing MP at week 24 due to patient's choice and presented with symptoms of giant cell arteritis. In the IM MP group, we observed no relapses in the first 24 weeks of follow-up, but there were 4 patients with inadequate response to treatment: 2 at week 4 and 2 at week 12. In these cases, we switched to oral MP. Due to the low number of patients in our study, results should be interpreted with caution.
Conclusion: In our cohort, treatment with IM MP compared to oral MP was effective in the majority of patients with PMR, but was associated with higher inadequate response rate and overall slower clinical and laboratory response.

Table 1. Comparison of follow-up data of IM and orally treated PMR patients

Characteristic	Follow-up week	IM MP	oral MP
ESR	0 (N = 39)	58 (50,72)	54 (39, 72)
	4 (N = 39)	31 (20, 43)	10 (7, 14)
	12 (N = 39)	28 (9, 35)	14 (8, 21)
	24 (N = 28)	22 (8, 28)	9 (7, 25)
CRP	0 (N = 39)	40 (26, 57)	46 (28,76)
	4 (N = 39)	0 (0, 9)	0 (0, 13)
	12 (N = 39)	0 (0, 17)	0 (0, 16)
	24 (N = 28)	0 (0, 0)	0 (0, 10)
Morning stiffness duration	0 (N = 35)	60 (52, 98)	60 (30, 60)
	4 (N = 39)	15 (5, 30)	0 (0, 15)
PGA	0 (N = 34)	6 (5, 7)	8 (6, 9)
	4 (N = 35)	3.5 (1.8, 5.0)	1.0 (0.0, 3.5)
MHAQ score	0 (N = 26)	1.0 (0.8, 1.4)	1.1 (0.9, 1.3)
	4 (N = 30)	0.4 (0.1, 0.7)	0.0 (0.0, 0.0)

Legend: PMR polymyalgia rheumatica; IM intramuscular; MP methylprednisolone; ESR erythrocyte sedimentation rate [mm/h]; CRP C-reactive protein [mg/L]; Morning stiffness duration [minutes]; PGA patient global assessment [0-10]. Results are presented as median (IQR).

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POS0718

IS IT POSSIBLE TO EVALUATE POLYMYALGIA RHEUMATICA WITHOUT CRP? CONCORDANCE AND AGREEMENT BETWEEN DIFFERENT PMR-AS ACTIVITY SCORES IN POLYMYALGIA RHEUMATICA

Keywords: Validation, Outcome measures

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Background: The main treatment of polymyalgia rheumatica (PMR) is based on corticosteroid, but sparing agents are a major unmet need and many new treatments are evaluated to avoid corticosteroid side effects in PMR. To monitor the disease, one disease activity score has been developed specifically for polymyalgia rheumatica (PMR), the PMR-AS (activity score) also called CRP-PMR-AS. It is a composite index built as an algebraic sum of morning stiffness, elevation of the upper limbs, physician's global assessment, patient's pain assessment and the C reactive protein (CRP). However, treatments of PM such as IL-6 antagonists or corticosteroid can normalize CRP level. Derived PMR-AS have been described to avoid such bias: erythrocyte sedimentation rate (ESR) PMR-AS, Clinical PMR-AS and CRP-imputed PMR-AS but the concordance and the correlation between these scores are unknown.
Objectives: Our primary objective was to measure the correlation and concordance of the PMR-AS and the other activity scores and our secondary objective was to evaluate the weight of CRP in the PMR-AS.
Methods: The SEMAPHORE trial (Safety and Efficacy of tocilizumab versus Placebo in Polymyalgia rHeumatica with glucocORticoid dEpendence), a superiority randomized double-blind parallel placebo-controlled trial in patients with active PMR despite corticosteroid treatment, investigated whether tocilizumab resulted in higher rates of low disease activity compared to a placebo, after 24 weeks. Four different PMR-AS have been measured. Using kappa coefficient, intra class correlation coefficient, scatter plots and Bland Altman graphics, we evaluated the concordance and correlation between CRP-PMR-AS, ESR PMR-AS, Clinical PMR-AS and imp-CRP PMR-AS across the entire population and by treatment group (placebo versus Tocilizumab) for different cut offs (1.5; 7; 10; 17) at each visit (inclusion, week 4, 8, 12, 16, 20 and 24).
Results: 100 patients received at least one dose of tocilizumab (49 patients) or placebo (51 patients) and were included in the analyses from inclusion to week 24. The correlation between the different PMR activity scores were excellent in the global analysis (Figure 1) but also in the two groups of treatment. Intraclass coefficients were all higher than 0.9 (Table 1). Bland Altman graphics using PMR-AS as a reference showed that differences between scores are low regardless of PMR-AS. Kappa coefficients between CRP-PMR-AS and the other three scores showed a good agreement (>0.8) (Table 1) at week 24.

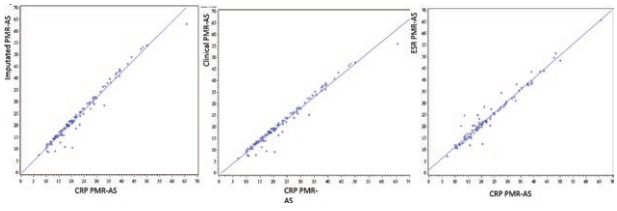


Figure 1. Scatter plots for the whole population at inclusion

Table 1. ICC and kappa between different PMR activity scores for the whole population

ICC (all patients all visits)	ICC (95% CI)
CRP PMR-AS and ESR PMR-AS	0.991 (0.990-0.992)
CRP PMR-AS and Clin PMR-AS	0.991 (0.990-0.992)
CRP PMR-AS and Imp PMR-AS	0.988 (0.987-0.989)
Kappa at week 24 (cut off 10)	**Kappa**
CRP PMR-AS and ESR PMR-AS	0.9562 (0.8961-1)
CRP PMR-AS and Clin PMR-AS	0.9133 (0.8304-0.9962)
CRP PMR-AS and Imp PMR-AS	0.8529 (0.7581-0.9577)

Table 1. Maternal and perinatal outcomes in women with vasculitis followed at a rheumatology-obstetric clinic

Main diagnosis	N (%)	Gestational age at delivery (mean ± SD weeks)	BW (mean ± SD grams)	SGA N (%)	Miscarriages N (%)	FGR N (%)	Preterm births N (%)	Pregnancy flares N (%)	Post-partum flares N (%)
Behçet's disease	18 (58)	38.3 ± 1.5	3013± 494	4/14 (29)	1/18 (6)	0	3/17 (18)	4/17 (24)	4/14 (29)
Polyarteritis nodosa	4 (13)	37.4 ± 0.6	2783± 175	1/4 (25)	0	0	0	2/4 (50)	0
Takayasu arteritis	4 (13)	38.0 ± 2.1	2725± 364	1/4 (25)	0	1/4 (25)	1/4 (25)	1/4 (25)	1/4 (25)
IgA vasculitis	1 (3)	40.3	3435	0	0	0	0	0	0
ANCA-PR3 cutaneous vasculitis	1 (3)	40.9	2845	1	0	0	0	1	0
Relapsing polychondritis	1 (3)	36.0	2040	1	0	1	1	1	1
Cryoglobulinemic vasculitis	1 (3)	35.9	3020	0	0	0	0	0	0
Cryoglobulinemic vasculitis associated with Sjögren's syndrome	1 (3)	39.0	3000	0	0	0	0	0	0
	31 (100)	**38.2 ± 2.1**	**2925± 566**	**8/27 (30)**	**1/31 (3)**	**2/31 (6)**	**5/30 (17)**	**9/25 (36)**	**6/27 (22)**

BW: birthweight; SD: standard deviation; SGA: small for gestational age; FGR: fetal growth restriction

Conclusion: The correlation between different PMR activity scores using or not CRP are excellent reflecting the low weight of CRP in the baseline composite index. In clinical trial using drugs that have an impact on CRP, CRP-PMR-AS or others, including clinical PMR-AS, can be used.

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POS0719 MATERNAL AND PERINATAL OUTCOMES IN WOMEN WITH VASCULITIS - A 13-YEAR EXPERIENCE FROM A PORTUGUESE TERTIARY CENTRE

Keywords: Vasculitis, Pregnancy and reproduction

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Background: The vasculitides are rare conditions that may affect women of childbearing age. These women seem to be at increased risk for developing adverse pregnancy outcomes (APO). Maternal and perinatal outcomes as well as their optimal management during pregnancy remain poorly understood in this population.

Objectives: To describe maternal and perinatal outcomes in women with vasculitis.

Methods: Observational retrospective study including pregnant women with vasculitis followed at a rheumatology-obstetric clinic from 01/2009 to 06/2022.

Results: We identified 31 pregnancies in 24 women with vasculitis. Table 1 summarizes demographic and clinical data. The most frequent diagnosis were Behçet's disease (BD) (18; 58%), polyarteritis nodosa (PAN) (4; 13%) and Takayasu arteritis (TAK) (4; 13%). The mean ± SD age at conception was 33 ± 6 years with a median disease duration of 6 (IQ range 3-12) years, 29 (94%) were in remission by the time of conception. We documented 30 live births, 1 early miscarriage (BD) and there was no perinatal mortality or birth defect. The mean ± SD gestational age at delivery was 38.2 ± 2.1 weeks. Five (17%) viable pregnancies resulted in preterm births - 3 BD, 1 TAK and 1 relapsing polychondritis (RP). Fetal growth restriction was detected in 2 (6%) pregnancies (TAK and RP). Eight (30%) newborns were small for gestational age (SGA), most of them from mothers with BD (4; 29%). Cesarean section (CS) was performed in 8 (26%) patients – 2 (TAK) due to vasculitis activity. Nine (36%) patients relapsed during pregnancy (4 BD; 2 PAN; 1 TAK; 1 RP; 1 ANCA-PR3 cutaneous vasculitis) while 6 (22%) relapsed during the post-partum period (4 BD; 1 TAK and 1 RP). A total of 24 (77%) patients were treated with glucocorticoids (GC), most of them (63%) at low doses (≤5mg/day of prednisolone or equivalent). Seven (23%) patients were treated with conventional DMARDs: 2 TAK and 3 BD with azathioprine and 2 PAN with azathioprine and hydroxychloroquine. Biological DMARDs were prescribed in 2 (6%) patients, both with the diagnosis of TAK: one with a multisegmental aortic disease who received tocilizumab during the first 30 weeks of gestation (WG) and had an uneventful pregnancy, and another patient with an ascending aortic aneurism (AAA) who also received tocilizumab, but from the 24th week onwards showed a gradual worsening of the AAA dimensions (maximum 56 mm). An elective CS at 32 WG was performed in the latter case due to the high risk of aneurysm rupture and a healthy baby with 1900g was born. The occurrence of flares during pregnancy increased the risk for APO (OR 13, 95 CI 2-80; p=0.007). No association was found concerning maternal age or use of DMARDs/GC and the risk of APO (p>0.05).

Conclusion: Most pregnant women with vasculitis managed at out multidisciplinary unit had successful gestations. However, they may still be at risk for developing APO, namely if they experience disease flares during gestation. SGA was the main APO recorded.

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POS0720 MEASURING FUNCTIONAL DISABILITY IN GIANT CELL ARTERITIS: THE VALIDITY, RELIABILITY AND RESPONSIVENESS OF THE GCA-DISABILITY INDEX (GCA-DI)

Keywords: Quality of life, Patient reported outcomes, Vasculitis

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Background: Giant cell arteritis (GCA) is the most frequent systemic vasculitis, typically affecting patients over 50. The disease burden includes a chronic course and a subsequent prolonged treatment, especially because of a high risk of relapse that affects approximately half of patients. Taken together, the disease and its symptoms, the chronic course and the treatment probably have an impact on the patients' functional ability as well as quality of life. Though functional disability has been identified as a core outcome measure in GCA, few studies have been dedicated to assess for the patients for this core measure.

Objectives: To test the GCA-disability index (GCA-DI) questionnaire for validity, reliability and responsiveness in patients with Giant Cell Arteritis.

Methods: The psychometric properties of GCA-DI were tested in 57 patients with GCA, mean age 63.6 (+/- 5.4), 77.2% women, mean disease duration 2.1 weeks

(+/- 3.1 days). At baseline, all the patients completed the GCA-DI, and the Health Assessment Questionnaire (HAQ). The patients were then asked to return to the clinic after having their blood tests and X-rays done to complete another copy of the questionnaire. Also, all the patients were asked to complete another copy of the questionnaire in their follow up visit in 4-weeks' time. This facilitated the assessment for validity, reliability and responsiveness. In addition, all the patients were asked to complete a copy of multidimensional Patient Reported Outcomes for GCA. Patient global assessment for functional disability was also recorded (0-100 VAS). Of the 57 patients who completed the health status instruments on two occasions, 53 were included in the responsiveness analyses. The test-retest reliability of the GCA-DI questionnaire was calculated using intraclass correlation coefficients (ICCs). Criterion validity was assessed using Spearman's correlations, while responsiveness was evaluated by 3 different methods: (1) effect size (the mean difference between the baseline scores and the follow-up scores divided by the standard deviation of the baseline scores); (2) standardized response mean (the mean change in scores divided by the standard deviation of the change in scores).

Results: GCA-DI fulfilled the established criteria for validity, reliability and responsiveness. Significant correlations were seen between GCA-DI scores and HAQ scores (rho = 0.672), Patient Global Assessment functional disability (rho = 0.629), pain (rho = 0.633), Test-retest reliability was satisfactory, with ICCs of 0.935. The results of responsiveness analysis indicated that the GCA-DI was sensitive to change. Standardized effect size was 2.84 after 4-weeks.

Conclusion: Our data suggest that the GCA-disability index can be considered as a reliable, valid and responsive tool for measuring physical functioning in GCA patients. It is suitable for use in clinical trials and daily clinical practice. Its generalizability and utility for assessing treatment and functional outcomes should be evaluated in larger settings.

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POS0721 DIFFERENT PATTERNS OF VASCULAR ULTRASOUND ARE ASSOCIATED WITH DIFFERENT ISCHEMIC COMPLICATIONS IN PATIENTS WITH GIANT CELL ARTERITIS

Keywords: Imaging, Vasculitis, Ultrasound

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Background: Patients with giant cell arteritis (GCA) can present ischemic complications (IC). Recognizing patients at risk of IC may help to improve GCA long-term outcomes. However, previous studies have failed to identify consistent risk factors for IC in this population, being mainly low systemic inflammation or atherosclerotic risk factors the main findings in some cohorts.

Objectives: Our objective is to determine if a specific pattern of vascular inflammation by ultrasound (US) is associated with different types of IC in patients with GCA.

Methods: A retrospective observational study of patients referred to the US fast track clinics of two academic centres with GCA clinical confirmation over a 4-years period. All patients underwent baseline US of cranial and extracranial arteries (carotid, subclavian and axillary) at the time of referral, and were classified in two categories; cranial or large vessel (LV)-GCA, according to US findings. IC was defined as the occurrence of acute anterior ischemic optic neuropathy (AION) or non-AION (including stroke, acute coronary syndrome, pulmonary embolism or peripheral artery disease) within 3 months after diagnosis, and after excluding other potentially implicated causes. Chi-squared and analysis of variance were performed to explore the association between clinical or US variables with the occurrence of different types of IC.

Results: A total of 42 (22.9%) patients over 188 patients with GCA clinical confirmation evaluated at our clinics had an IC within 3 months after diagnosis, 24 (12.8%) an AION and 19 (10.1%) a non-AION IC (10 stroke, 5 acute coronary syndrome, 4 peripheral artery disease, 2 pulmonary embolism and one case of ischemic colitis). Patient characteristics according to IC type are shown in Table 1. Patients with AION showed more frequently findings of US cranial involvement (100%) versus patients with non-AION IC (63.2%) and without IC (79.3%), p=0.009. In contrast, patients with non-AION IC presented more frequently signs of US LV-GCA (63.2%) versus patients with AION (25%) and without IC (55.2%), p=0.014).

Conclusion: Different patterns of vascular US involvement are associated with different IC in GCA patients. Predominantly cranial-GCA patients have more frequently AION, while predominantly LV-GCA patients have more frequently non-AION IC, as stroke, acute coronary syndrome, pulmonary embolism or peripheral artery disease.

Table 1. Characteristics of patients according to the type of IC.

	Total n=188	No ischemic complications n=145 (77.1%)	AION n=24 (12.8%)	Non-AION IC n=19 (10.1%)	p
Demographics					
Age, mean (SD)	78.2 (8.5)	77.7 (8.9)	81.1 (5.8)	78.6 (8.5)	0.183
Female, n (%)	88 (46.8%)	69 (47.6%)	10 (41.7%)	9 (47.4%)	0.864
Clinical variables					
Headache, n (%)	147 (78.2%)	115 (79.3%)	18 (75%)	14 (73.7%)	0.788
Jaw claudication, n (%)	47 (25%)	37 (25.5%)	6 (25%)	4 (21.1%)	0.915
Constitutional symptoms, n (%)	100 (53.2%)	81 (55.9%)	10 (41.7%)	9 (47.4%)	0.376
Fever, n (%)	29 (15.4%)	25 (17.2%)	0 (0%)	4 (21.1%)	0.074
SCORE CVR, mean (SD)	21.8 (14.7)	20.9 (14.8)	25.5 (13)	24 (15.4)	0.275
Laboratory					
CRP (mg/L), mean (SD)	36.4 (54.3)	40.3 (57.6)	26.3 (48.8)	20.1 (24.6)	0.194
ESR (mm/h), mean (SD)	58.1 (34.2)	56.1 (35.1)	73.7 (25.8)	54.4 (32.5)	0.072
Haemoglobin (g/dL), mean (SD)	13.4 (11)	13.8 (12.5)	12 (1.8)	12 (2)	0.658
Platelets 10^9/L, mean (SD)	326.5 (128.1)	334.7 (126)	297.1 (151.4)	302.6 (108.1)	0.288
Histology					
Temporal artery biopsy positive n=50, n (%)	21 (42%)	15 (39.5%)	6 (75%)	0 (0%)	**0.037**
US					
Positive US, n (%)	183 (97.3%)	140 (96.6%)	24 (100%)	19 (100%)	0.467
Positive cranial ACG US, n (%)	151 (80.3%)	115 (79.3%)	24 (100%)	12 (63.2%)	**0.009**
Isolated positive cranial ACG US, n (%)	85 (45.2%)	60 (41.4%)	18 (75%)	7 (36.8%)	**0.007**
Positive LV-GCA US, n (%)	98 (52.1%)	80 (55.2%)	6 (25%)	12 (63.2%)	**0.014**
Isolated positive LV-ACG US, n (%)	32 (17%)	25 (17.2%)	0 (0%)	7 (36.8%)	**0.006**

AION: acute anterior ischemic optic neuropathy; PMR: polymyalgia rheumatica; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; CVR: cardiovascular risk; SD: standard deviation.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0722 EFFECTS ON SOLUBLE IMMUNE CHECKPOINTS INDUCED BY TOCILIZUMAB MONOTHERAPY AFTER ULTRA-SHORT-TERM GLUCOCORTICOIDS IN LARGE VESSEL – GIANT CELL ARTERITIS PATIENTS

Keywords: Cytokines and chemokines, Biomarkers, Vasculitis

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Background: The most affected vessels in Giant cell arteritis (GCA) are the temporary arteries, but in some patients extracranial large vessels are also involved (LV-GCA). Tocilizumab (TCZ), a monoclonal anti-interleukin-6 receptor1 antibody, has been approved as glucocorticoid (GC) sparing agent in patients with GCA. Recently, new therapeutic protocols that combine rapid GC tapering and TCZ are emerging, but their effects on circulating immune cells and mediators are scarcely known [1]. Another clinical need in LV-GCA management is the lack of a gold standard to define disease state. The role of immune checkpoint molecules is tuning the activation of the immune system. They are expressed on the surface of immune cells, but also soluble forms exist. Active GCA patients showed a reduction of CD4+ T cells expressing PD1 and VISTA in comparison to controls [2,3]. We hypothesize that soluble immune checkpoints are modulated by the TCZ and GC combined treatment and that they are biomarkers able to differentiate active from inactive LV-GCA patients.

Objectives:

1) To evaluate the effects of TCZ monotherapy after ultra-short-term GC treatments on soluble immune checkpoints.
2) To identify plasma biomarkers able to discriminate between LV-GCA patients in the active phase from those in remission.

Methods: We included 16 patients with active LV-GCA enrolled in the single-arm open-label clinical trial (NCT05394909) performed at AUSL-IRCCS at Reggio Emilia. Inclusion criteria: PET/CT with FDG uptake ≥2 in at least one vascular district and at least one among ESR >40 mm/h (or CRP >10 mg/L); cranial or systemic manifestations of GCA or polymyalgia rheumatica. Exclusion criteria: more than 10 mg/day of prednisone for more than 10 consecutive days in the previous 3 months. Remission was defined by all the following: absence of any clinical signs and symptoms directly attributable to GCA; normalization of CRP and ESR values; absence of new/worsened vascular damage at CT; vascular FDG uptake <2 in all vascular districts at PET/CT or overall PET image interpretation of non-active vasculitis. All patients received 500 mg per day of methylprednisolone intravenously for three consecutive days and weekly subcutaneous TCZ injections from day 3 until week 52. Plasma samples were collected at baseline before treatment and after GC injections. For 10 patients plasma samples were also collected at week 52. Laboratory data were collected at the same time points. Concentrations of CD137L, CD137, CD27, CTLA4, CD80, CD40, CD40L, GITR, GITRL, ICOSL, IDO, LAG3, MICA, MICB, PD1, PDL1, PDL2, PTX3, TIM3 and VISTA were evaluated in plasma samples by a multiplex bead-based assay with the MAGPIX instrument. Wilcoxon test was used for comparison between groups, Spearman test was used for correlation analysis. $P < 0.05$ was considered statistically significant.

Results: Soluble CD137L, CTLA4, CD40, CD40L, GITR, IDO, PD1 and PDL1 were not detected in almost all of the samples irrespective of treatment and disease phase. Intravenous injections of GC determined a significant reduction of soluble CD137, CD80, GITRL, ICOSL, LAG3, MICA, and MICB and an increase of PTX3 and VISTA levels. After 52 weeks of TCZ as monotherapy, an increase in plasmatic ICOSL and a reduction in LAG3, PTX3, and VISTA were observed compared to baseline. At 52 weeks, 7 patients were classified in remission phase of the disease and 3 patients were active. Changes in immune checkpoint levels occurred irrespective to disease phase. Levels of soluble immune checkpoints did not correlate with ESR and CRP concentrations, markers currently used in clinical practice to evaluate systemic inflammation.

Conclusion: Ultra-short-term GC treatments and TCZ monotherapy modulate the levels of soluble immune checkpoints. The evaluation of the investigated panel of immune checkpoints did not allow to discriminate between LV-GCA patients in different disease phases.

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POS0723 ANALYSES OF PLASMA METABOLIC PROTEINS REVEAL BIOMARKERS PREDICTIVE OF SUBSEQUENT DEVELOPMENT OF GIANT CELL ARTERITIS; A PROSPECTIVE STUDY

Keywords: Biomarkers, Vasculitis

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Background: Incident cases of of giant cell arteritis (GCA) have a significantly reduced prevalence of diabetes at time of diagnosis (1) and lower fasting blood glucose, lipid levels and body mass index compared to controls have been found years before clinical diagnosis [2,3]. This implicates metabolic pathways in the development of GCA.

Objectives: To investigate the relation between plasma proteins associated with metabolism and subsequent development of GCA.

Methods: Participants in a population-based survey (N=30447), who were subsequently diagnosed with GCA, were identified in a structured process. GCA-free controls, matched for sex, year of birth, and year of screening were selected from the study cohort. Baseline plasma samples were analyzed using the antibody-based OLINK proteomics metabolism panel (92 proteins). Analyses were pre-designated as hypothesis-driven or hypothesis-generating. In the latter, principal component analysis was used to identify groups of proteins that explain the variance in the proteome.

Results: There were 95 cases with a confirmed incident diagnosis of GCA (median 11.4 years after inclusion). Among biomarkers with a priori hypotheses, Adhesion G protein-coupled receptor E2 (ADGRE2) was positively associated and Fructose-1,6-bisphosphatase 1 (FBP1) negatively associated with subsequent GCA (Table 1). In particular, ADGRE2 levels were elevated compared to controls in the subset sampled <8.5 years before diagnosis (Table 1). For meteorin-like protein (Metrnl), the highest impact on the risk of GCA was observed in those sampled closest to diagnosis, with a decreasing trend with longer time to GCA (p=0.03). In the hypothesis generating analyses, elevated levels of receptor tyrosine-like orphan receptor 1 (ROR1) were associated with subsequent GCA.

Conclusion: Our results indicate that changes in levels of plasma proteins that have regulatory effects on the immune system might precede clinical onset of GCA by many years. Among the biomarkers found to be predictive of subsequent GCA, both Metrnl and ADGRE2 are associated with macrophage activation. ROR1 mediated activation of NFkB may be relevant in this context. The negative association with FBP1, which is a rate-controlling enzyme in the gluconeogenic pathway, is compatible with a protective role for glucose metabolites.

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Table 1. Potential biomarkers of subsequent giant cell arteritis, from a priori hypotheses. Overall and stratified for time from screening to diagnosis.

	All	Quartile 1 (0.3-8.5 years) (N*=45)	Quartile 2 (8.50-12.0 years) (N*=49)	Quartile 3 (12.0-15.5 years) (N*=46)	Quartile 4 (15.5-19.1 years) (N*=48)	
	OR (CI)	OR (CI)	OR (CI)	OR (CI)	OR (CI)	P for trend
METRNL	1.42 (0.90-2.23)	2.40 (0.98-5.85)	3.13 (0.92-10.63)	0.90 (0.38-2.15)	0.74 (0.29-1.89)	**0.03**
FBP1	**0.59 (0.35-0.99)**	0.29 (0.06-1.39)	0.84 (0.43-1.65)	1.13 (0.38-3.30)	0.09 (0.02-0.48)	0.24
GAL	0.98 (0.66-1.45)	2.32 (0.83-6.51)	0.65 (0.29-1.49)	0.38 (0.15-0.97)	2.17 (0.92-5.13)	0.98
GHRL	0.83 (0.55-1.25)	1.20 (0.52-2.78)	1.38 (0.66-2.88)	0.39 (0.16-0.96)	0.55 (0.20-1.48)	0.06
ADGRE2	**1.67 (1.08-2.57)**	**3.91 (1.45-10.60)**	1.17 (0.52-2.64)	0.94 (0.44-2.00)	2.90 (0.83-10.16)	0.26
NECTIN2	1.33 (0.88-2.01)	1.47 (0.66-3.32)	1.64 (0.71-3.82)	1.40 (0.63-3.11)	0.84 (0.34-2.09)	0.38

*Total of cases and controlsConditional logistic regression analysis of biomarkers with a priori hypothesis. Odds ratios (OR) per standard deviation with 95 % confidence intervals (CI).

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POS0724 TRANSORBITAL ULTRASOUND IN NEWLY DIAGNOSED GIANT CELL ARTERITIS – A PROSPECTIVE STUDY

Keywords: Diagnostic tests, Vasculitis, Ultrasound

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Background: Giant cell arteritis (GCA) is an immune-mediated, granulomatous vasculitis that primarily affects the elderly and results in local vascular changes of

middle-sized and large arteries. A protracted diagnosis delaying high-dose corticosteroid therapy may result in permanent visual loss. Therefore, invasive and time-consuming biopsy of the superficial temporal artery has been replaced by high-resolution vascular ultrasound of the temporal and axillary artery to evaluate extracranial inflammation. Intracranial involvement of the ophthalmic vessels can be visualized by magnetic resonance imaging. Transorbital Ultrasound (TOS), as a simple and inexpensive diagnostic method, could be an option for assessing the optic nerve and the central retinal artery (CRA) and might improve diagnostic sensitivity in GCA, especially in anterior optic neuropathy (AION).

Objectives: The purpose of this study was to assess the utility of TOS in patients with untreated and newly diagnosed GCA.

Methods: Patients with new GCA diagnosed by a board-certified rheumatologist who also met the expanded ACR-EULAR classification criteria were enrolled in the study between October 1, 2018, and May 31, 2022. Each participant underwent TOS to assess the CRA and optic nerve diameter (OND). The eyes of the patients with GCA were categorized as eyes with or without visual impairment (VI), which was defined as transient or persistent visual field loss, diplopia, amaurosis, and blurred vision. Peak systolic velocity (PS), end diastolic velocity (ED), resistance index (RI) of the CRA and OND were recorded.

Results: A total of 54 GCA patients were prospectively enrolled in the study, 27 of whom had VI in at least one eye. To account for repeated measures within a patient, associations between TOS and VI were evaluated using linear mixed-effect models (LME). PS and ED values of the CRA were statistically significant lower in the eyes with GCA manifestation (ß=-1.93; p<0.001 for PS; ß=-0.61; p=0.003 for ED). The RI of the CRA was statistically significant reduced in the eyes with GCA associated VI (ß=-0.04; p=0.007). OND was lower in the eyes with VI, too (ß=-0.36; p=0.06) (Table 1, Figure 1).

Conclusion: In TOS, eyes affected by VI exhibited significantly reduced PS, ED, and RI indicating an inflammatory process of the intracranial vessels leading to impaired blood flow to the optic nerve and contributing to ischemia-associated optic neuropathy. The shown decrease in OND is probably due to reduced blood flow and the resulting lessened vessel diameter and, in the case of a persistent depletion of blood flow, due to atrophic alterations of the optic nerve suggestive of irreversible damage. Therefore, VI in combination with decreased PS, ED, RI and OND may constitute a specific finding in the diagnosis of optic affection in GCA. Our study was the first to prospectively demonstrate the diagnostic value of TOS in untreated and new diagnosed GCA patients as a complementary diagnostic tool to assess GCA associated intracranial inflammation.

Table 1. Mean values of central retinal artery flow velocity, resistance index, optic nerve diameter in patients with/ without visual impairment

	GCA without VI	GCA with VI	LME (ß)	p-value
Peak systolic velocity (SD); cm/s	12.95 (± 3.84)	10.16 (± 4.10)	- 1.93	<0.001
End diastolic velocity (SD); cm/s	3.91 (± 0.12)	3.18 (± 1.27)	-0.61	0.003
Resistance Index (SD)	0.69 (± 0.10)	0.64 (± 0.17)	-0.04	0.007
Optic nerve diameter (SD); mm	5.3 (± 0.99)	4.93 (± 1.1)	-0.36	0.06

Eyes affected by VI exhibited reduced flow velocity and resistance index of the central retinal artery and decreased optic nerve diameter. Abbrev.: GCA: Giant Cell Arteritis, VI: Visual impairment, LME: Linear mixed-effects model, SD: standard deviation

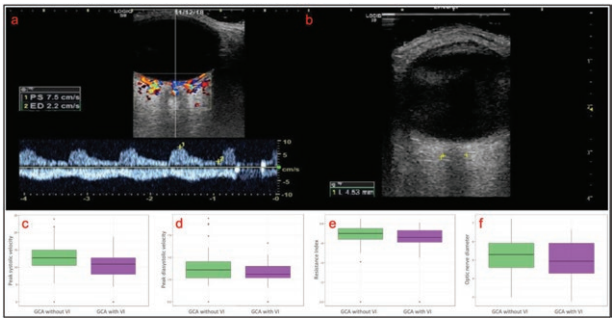


Figure 1. Assessment of central retinal artery/ optic nerve diametera, b: Measurement of central retinal artery flow velocity/ optic nerve diameter; c, d: Central retinal artery flow velocity (cm/s), e: Resistance Index, f: Optic nerve diameter (mm). Abbrev.: GCA: Giant Cell Arteritis, VI: Visual impairment, PS: Peak systolic velocity, ED: End diastolic velocity

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POS0725

CRANIAL, EXTRACRANIAL AND MIXED INVOLVEMENT IN GIANT CELL ARTERITIS: ANALYSIS OF THE CLINICAL DIFFERENCES

Keywords: Ultrasound, Descriptive studies, vasculitis

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Background: giant cell arteritis (gca) is a systemic vasculitis that affects large vessels, with a higher incidence in patients aged 70 years. It is known that GCA involves temporal arteries and the aorta and its branches either concomitantly or in isolation. Differentiating the characteristics in the expression of these disease subtypes will be relevant for the initial treatment, prognosis and the follow up.

Objectives: To analyze the different clinical and laboratory between the patterns of GCA involvement.

Methods: Retrospective study of new consecutive patients diagnosed with GCA for four years. 90.9% were diagnosed by Color Doppler ultrasound, measuring the superficial temporal arteries, common trunk, their frontal and parietal branches, and the extracranial arteries (axillary, subclavian, and carotid arteries). 9.1% were diagnosed by PET-CT or temporal artery biopsy. Ultrasound diagnosis was according to the OMERACT definitions of the halo sign and an intima-media cut off a thickness of ≥0.34 mm for the temporal arteries, ≥0.42 in the common superficial temporal artery and ≥ 1 mm for the axillary, subclavian, and carotid arteries. Clinical records were reviewed and their demographic, clinical and laboratory data were compared between patterns of ultrasound involvement. The EULAR recommendations of 2018 [1] were used to the remission and relapse.

Results: A total of 163 patients were included, 50.3% women, with a mean age of 79 years. Regarding the GCA subtypes, 78 patients had exclusive involvement of cranial arteries (CGCA), 36 patients had isolated involvement of extracranial giant cell arteritis (LVGCA) and 49 patients had mixed forms with both cranial and extracranial involvement (MGCA) Table 1. The analysis showed that patients with LVGCA present constitutional syndrome more frequently, less anterior Ischemic optic neuropathy (AION) (p<0.001) and less ESR values (p<0.01) than patients with CGCA. Extracranial artery involvement in any of the subtypes showed a significant association with polymyalgia rheumatica (PMR), although this was not exclusive to LVGCA. CGCA was associated with more AION-type ischemic manifestations than LVGCA. Remission maintained for at least 6 months together with corticosteroid-free remission is higher in LVGCA. No statistically significant differences in relapses, both major and minor.

Table 1. Clinical and laboratory characteristics between GCA subtypes

	GCA 163	CGCA 78	LVGCA 36	MGCA 49	CGCA -MGCA p	CGCA -LVGCA p	LVGCA - MGCA p
Female sex, n (%)	82 (50.3)	41 (52.6)	21 (58.3)	20 (40.8)	0.378	0.565	0.134
Age years, mean ± SD	79 ± 7.8	79 ± 7.5	77.6 ± 10	79.2 ± 6.7	0.883	0.435	0.403
ESR, mm/h mean ± SD	57 ± 34	63 ± 37.3	42.2 ± 27.6	47.4 ± 35	**0.019**	**0.003**	0.467
CRP mg/dL mean ± S.D.	52.6 ± 54	54 ± 55.4	43.2 ± 56	49.4 ± 49.4	0.631	0.335	0.588
PMR, n (%)	88 (53.6)	32 (41)	23 (63.9)	33 (66)	**0.005**	**0.023**	0.839
Constitutional symptoms, n (%)	87 (53)	38 (48.7)	25 (69.4)	24 (48)	0.936	**0.038**	**0.047**
AION, n (%)	38 (23)	25 (32)	3 (8.3)	10 (20)	0.135	0.006	0.136
Remission 6 months, n (%)	45 (27.4)	14 (17.9)	15 (41.7)	16 (32)	0.057	0.006	0.393
Glucocorticoid free-remission, n (%)	28 (17)	8 (10.3)	9 (25)	11 (22)	0.068	**0.039**	0.745
Major relapse, n (%)	7 (4.2)	3 (3.8)	3 (8.3)	1 (2)	0.947	0.679	0.751
Minor relapse, n (%)	52 (31.7)	25 (32)	11 (30.6)	16 (32)	0.943	0.947	0.378

CGCA Cranial giant cell arteritis; LVGCA Large vessel giant cell arteritis; MGCA Mixed giant cell arteritis; SD standard deviation; AION anterior Ischemic optic neuropathy; PMR polymyalgia rheumatica; CRP C reactive protein; ESR erythrocyte sedimentation rate.

Conclusion: Clinical features are different between the different GCA patterns. Patients with LVGCA have a greater constitutional syndrome and lower ESR than patients with CGCA. CGCA was associated with more NOIA-type ischemic manifestations than LVGCA. PMR is more frequent in cases with large vessel involvement. There is more maintained and corticosteroid-free remission in patients with LVGCA.

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POS0726 RITUXIMAB VERSUS CYCLOPHOSPHAMIDE FOR ANCA- ASSOCIATED VASCULITIS: A COST ANALYSIS

Keywords: Vasculitis

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Background: Cyclophosphamide (CYC) and Rituximab (RTX) have been found to be of equivalent effectiveness in remission induction of severe ANCA-associated vasculitis (AAV) (1); [2]. American College of Rheumatology in 2019, and more recently EULAR guidance on treatment of AAV, has recommended the use of RTX first-line due to a more favorable side-effect profile [3]. In the UK, in the absence of contraindications, our current guidance still advocates the use of CYC first-line. While RTX biosimilars are available at reduced cost compared to the originator molecule, the drug cost of RTX is far greater than CYC. A change in UK guidance could have significant cost-implications to healthcare services.
Objectives: The objective of this study was to compare the cost RTX and CYC induction regimens for patients with AAV and calculate the cost difference to our department of the two regimens.
Methods: Drug costs for CYC and the current preferred (cheapest) RTX biosimilar was provided by our pharmacy team. Exact drug costs are considered commercially sensitive and are hence not reported here. The Hospital Business Intelligence Unit provided total visit cost data and an average total visit cost for both RTX and CYC was calculated using worked examples. This accounts for cost differences due to in drug administration and the need for medical review. Data was available on the number of patients with AAV who started induction treatment with CYC from January 2022 and December 2022. We were able to calculate a total cost for this and an equivalent cost if these patients had all received RTX induction.
Results: As expected, drug costs for RTX were significantly greater than for CYC. Total visit costs were however similar. The increased total costs for CYC likely largely due to our policy of consultant and multidisciplinary team review prior to each infusion. The total visit cost approximations for cyclophosphamide for patients with AAV treated with CYC between January 2022 to December 2022 was £44,000. When RTX total visit costs were considered, the annual costs for RTX induction for these patients would have been approximately £14,000. Furthermore, as a standard CYC induction is administered as 6 cycles, while RTX is administered as two 1g infusions, if patients treated with CYC had received RTX this would have created an additional 143 hours of availability on our biologics day unit. Other potential time and cost savings we did not measure would include nadir monitoring bloods for CYC done prior to each infusion and pharmacy time in preparing the drugs and associated other medications such as anti-emetics.
Conclusion: The annual net saving if our hospital trust had treated the patients with AAV who received CYC induction with RTX instead, would have equated to £30,000. While this does not take into account subsequent maintenance treatment choices, we can be reassured that a shift towards RTX induction first-line in AAV, is likely to lead to significant cost-savings and would not place an additional financial burden on healthcare resources.

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POS0727 DEVELOPMENT OF POSTERIOR UVEITIS IN BEHÇET'S SYNDROME PATIENTS WITH VITREOUS CELLS WITHOUT ANY OTHER POSTERIOR INVOLVEMENT

Keywords: Vasculitis, Uveitis, Behcet's disease

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Background: A considerable number of patients with Behçet's syndrome (BS) have vitreous cells on slit lamp examination at the time of diagnosis. However, the prognostic importance of vitreous cells (VC) and their association with the development of posterior uveitis (PU) requiring immunosuppressive treatment is unknown.
Objectives: We aimed to determine the prognostic importance of VC in BS patients.
Methods: The charts of 572 consecutive BS patients fulfilling ISG criteria who were registered between 2010 and 2012 were reviewed. At baseline visit 164 patients had VC in one eye or both eyes. Among the remaining patients, 229 had no eye involvement, 116 patients had bilateral pan or posterior uveitis, 14 had unilateral pan or posterior uveitis and no eye involvement in the other eye, 20 had isolated anterior uveitis, and 29 had insufficient data in their medical records. Among the 164 patients with VC, 110 patients with a follow-up of ≥2 years were included in this study (Figure 1).
Results: At baseline, among the 111 included patients (68 men, mean ± SD age: 31±9 years), 61 had VC in both eyes, 34 had VC in only one eye, and 15 had VC in one eye and PU in the other eye. There was anterior uveitis (AU) in addition to VC in the same eye in 13 patients at baseline (Figure 1).
New PU developed in 26 (24%) patients during a mean follow-up of 1.9±1.1 years.7 patients that developed PU in the eye with VC had had PU in the contralateral eye at baseline. This means 7 of 15 patients with VC in one eye and PU in the contralateral eye developed bilateral PU despite treatment. 2 of these 7 patients had developed AU before they developed PU. Additionally, 6 patients that developed PU in the eye with VC had anterior uveitis in the same eye at baseline.
Conclusion: Careful follow-up is required for patients with VC since one quarter developed PU within 2 years. The presence of PU in the contralateral eye and AU in the same eye may be risk factors for the development of PU in patients with VC.

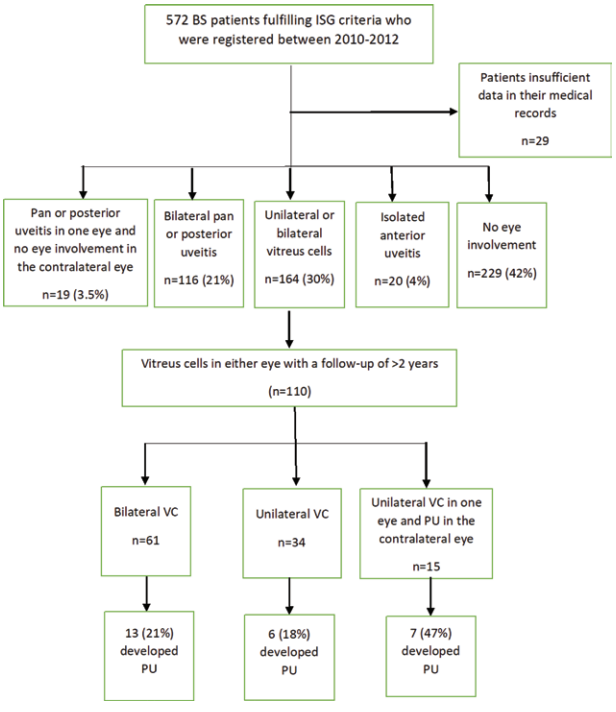


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0728 EFFECTIVENESS AND SAFETY OF A 26 WEEK TAPER REGIMEN OF GLUCOCORTICOID IN NEWLY-DIAGNOSED GCA PATIENTS: A REAL LIFE EXPERIENCE

Keywords: Vasculitis

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Background: The GiACTA [1] was the first trial comparing two standardized prednisone (PDN)-taper protocols (52 week and 26 week) in GCA. Sustained remission rate at week 52 was similar. Patients enrolled in the placebo group with a 26 week taper protocol experienced lower PDN cumulative dose but more flares than those enrolled in the 52 week one.
Objectives: To assess the effectiveness and safety of the 26 week taper regimen of glucocorticoids (GC) used in the GiACTA trial in a prospective cohort of treatment-naive, biopsy-proven GCA.
Methods: Patients with a new diagnosis of biopsy-proven GCA enrolled in the GC arm of the START project (molecular stratification of patients with GCA to tailor GC and tocilizumab therapy) were included [2]. All patients were treated with the 26 week taper regimen of GC used in the GiACTA trial. Disease assessment was performed at baseline and every 12 weeks. In case of disease relapse, GC was increased or restarted with or without adjunctive immunosuppressive treatment. PET/CT was performed in 18 patients at baseline. Large vessel involvement was defined by evidence of vascular FDG uptake ≥liver in at least one vascular district. CT angiography was performed after at least 52 weeks of follow-up in all patients and was compared with baseline CT of the PET scan. The diameter of the aorta was measured at 4 different levels. Aortic dilation was defined by a diameter >40 mm in the ascending aorta, ≥40 mm in the descending aorta and ≥30 mm in the abdominal aorta. Any change of ≥5mm on serial CT was considered significant progression of aortic damage. Remission was defined as the absence of any clinical symptoms attributable to GCA, including a normalization of the acute phase reactants. Relapse was defined as one or more of the following: recurrence of signs or symptoms of GCA or PMR; CRP values greater than 10 mg/L, or ESR values greater than 40 mm/h if these were considered by the investigator to be due to GCA. The definition of relapse included the necessity for intensification of treatment. The primary endpoint was the rate of relapse-free remission at week 52. Secondary endpoints were the rate of remission at the end of follow-up and the proportion of patients with new aortic dilation or worsened aortic damage.
Results: 22 patients were included between December 2018 and February 2022. The baseline characteristics are reported in the Table 1. At week 52, 10 patients (46%, 95% CI 24-68) were in relapse free-remission. After a median (IQR) follow-up of 27.5 (18.5-34) months, 7 patients (32%, 95% CI 14-55) remained in relapse-free remission. 18 patients with baseline PET/CT underwent CT angiography at the end of the follow-up. No patients had evidence of new aortic dilation, significant progression of aortic damage or large vessel stenosis. 15/22 patients (68.2%) had at least one relapse during follow-up. No patients developed visual or cerebrovascular manifestations during relapses. Mean (SD) prednisone cumulative dose was significantly lower in non-relapsing than in relapsing patients at week 52 and at the end of follow-up [3.7 (1.3) vs 4.8 (8.7) g, p=0.017, and 4.3 (2.6) vs 6.8 (1.7) g, p=0.014, respectively]. However, 19/22 (83.4%) patients had at least one GC-related adverse event.
Conclusion: A 26 week taper regimen of GC was effective and safe in inducing and maintaining remission in a sizeable proportion of newly diagnosed cranial GCA patients. If confirmed in larger trials, this faster taper regimen could allow sparing GC, and should be considered as initial treatment in all newly-diagnosed GCA patients, reserving immunosuppressive treatment only in relapsing patients.
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Table 1. Baseline characteristics of the population

Study population (n=22)	
Age (years)	74.8 (7.3)
Female	19 (86%)
Cranial symptoms	21 (96%)
Visual symptoms	9 (41%)
Systemic symptoms	8 (36%)
PMR	8 (36%)
Halo sign at US	15 (68%)
LVV at PET CT	10/18 (56%)
Aortic dilation	3/18 (17%)

Data are mean (SD) or n (%).

Acknowledgements: Foundation for Research in Rheumatology (FOREUM) for funding the project.
Disclosure of Interests: None Declared.
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POS0729 DIFFERENCES BETWEEN GLUCOCORTICOIDS, CONVENTIONAL DMARDS AND TOCILIZUMAB IN ACHIEVING DISEASE REMISSION AND IN PREVENTING THE PROGRESSION OF DAMAGE IN GIANT CELL ARTERITIS PATIENTS

Keywords: Vasculitis, Outcome measures, Treat to target

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Background: Patients with Large Vessel Vasculitis (LVV) may experience severe consequences of the disease, caused by underlying vasculitis and prolonged treatment. A validate damage tool specific to LVV is lacking. Moreover, despite new evidence, the overall assessment of the activity is still an unmet need.
Objectives: The aim of the present study is to evaluate the efficacy of different regimens in achieving clinical, laboratory and imaging disease remission and in preventing the progression of disease-related damage and treatment-related damage, especially glucocorticoids induced, in Giant Cell Arteritis (GCA).
Methods: Consecutive inpatients and outpatients, classified as GCA with LVV involvement, were prospectively enrolled. We included all patients with new diagnosis or relapsing disease who underwent to at least 2 consecutive 18F-FDG PET-CT or MR scan between March 2011 and September 2022. Before every PET scan demographic, clinical data and disease activity were assessed. Remission was defined as absence of signs and symptoms attributable to GCA and normalization of acute phase reactants (ESR <30 mm/H and CRP <1 mg/dL) [1]. For each PET scan the vessel's metabolic activity was evaluated using the Meller's grading and the PETVAS score [2]. The damage was evaluated using the Large-Vessel Vasculitis Index of Damage (LLVDI) and the Composite Glucocorticoid Toxicity Index (GTI), distinct in Cumulative Worsening Score (GTI-CWS) and Aggregate Improvement Score (GTI-AIS) [3,4]. GCA patients were compared according to current treatment regimen: glucocorticoid (GC) monotherapy versus conventional disease modifying anti-rheumatic drug (cDMARDs), and tocilizumab (TCZ).
Results: The study included 49 LV-GCA patients (age 28 [21-48], 71.4% female) exposed to a total of 76 treatment regimens (n = 39 GC monotherapy, n = 21 cDMARDs, n = 16 TCZ). All the treatment led to significant reduction of acute phase reactants (GC-treated: ESR p < 0.001, CRP p < 0.001; cDMARDs - treated: ESR p = 0.033, CRP p = 0.01, and TCZ-treated: ESR p = 0.006, CRP p = 0.003). Significant improvement in PETVAS was observed in all patients: GC treated 12 4-21 vs 7 2-14 (p=0.033), cDMARDs treated 16 5-20 vs 4 3-10.5 (p = 0.039), and TCZ - treated 12 9-20.2 vs 3 1-9 (p < 0.001). Daily prednisone dose at last examination was 5 [0-7.25] mg/d in the cDMARDs group vs 0 [0-5] mg/d in the TCZ group (p = 0.148). GC withdrawal was observed in 82% of TCZ-treated patients, while 58% in the GC group (p=0.112). At last evaluation LLVDI was similar in the three groups (2 [1-6] vs 2 [1-3] vs 3 [2.25-5], p = 0.073). Baseline GTI resulted higher in the TCZ group, when compared to DMARDs and GC (75 [48- 101] vs 49 [35-64] vs 32 [10-74], respectively, p = 0.008). At the last follow-up TCZ-treated patients showed higher GTI-CWS (97 [77-127] vs 72 [48-81] vs 65 [48-103], p = 0.025) than those treated with DMARDs and GC, while no differences were observed in GTI-AIS (0 [- 19 to 33] vs 0 [77.5 to 127] vs 0 [-16 to 18.7], p = 0.154). When considering only those patients who received TCZ as a first line treatment (n=4), GTI-AIS at last follow-up resulted significantly lower compared to DMARDs and GC treated individuals (-30 [-71 to-5.5] vs 0 [77.5 to 127] vs 0 [-16 to 18.7], p = 0.0249).
Conclusion: Tocilizumab treatment significantly reduce vessel's metabolic activity over time, when compared to conventional treatment. None of the three

different treatment regimen reduce the progression of the damage caused by both the vasculitis and the glucocorticoid treatment. TCZ as a first line treatment reduced significantly the GTI-AIS at the last follow up, when compared to the other treatment.

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Disclosure of Interests: None Declared.

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POS0730

PROGNOSTIC FACTORS AND EFFICACY OF DMARD USE IN GCA: RESULTS FROM THE PROSPECTIVE, LONGITUDINAL,MULTI-CENTRE HAS-GCA STUDY

Keywords: Vasculitis, Ultrasound, Imaging

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Background: GCA is a critically ischemic large vessel vasculitis, varying in extent, severity and outcomes, hence requires disease stratification using clinical, laboratory and imaging parameters, for targeted management. Although DMARDs are used, the effectiveness in real life, such adjuvants remain un-elucidated. We performed a prospective, multi centre cohort study of new GCA stratified into remitting, relapsing, refractory, ischemic disease.

Objectives: We assessed prognostic factors and compared critical outcomes such as remission with glucocorticoid (GC) monotherapy versus GC plus DMARDs in the first 12 months.

Methods: HAS GCA study (1) recruited consecutive patients with new onset GCA from 7 centres (UK, Italy, Spain, Netherlands). diagnosis was confirmed used a modified GiACTA criteria at 6 months follow up. All underwent ultrasound (bilateral common, parietal, frontal temporal arteries, and axillary arteries) using accepted standard cut-off values [2]. GCA patients had US at baseline,1,3,6,12 months and halo count (HC) and Halo score (Temporal TAHS, axillary AAHS, total THS) assessed [3]. The primary outcome- remission at 12 months (absence of signs/symptoms, CRP<5 mg/dl, prednisolone < 5 mg daily). Results are reported as descriptive statistics.

Results: 229 participants included in the study (GCA- 84 (36.68 %) (Figure 1). Study recruited during Covid pandemic,73 completed,11 lost to follow-up (died -7, withdrawn-4). The deceased/withdrawn patients (compared to completers) were older (80 v74 yrs, p=0.018), preponderantly male (73% v 36%, p=0.043) with visual symptoms (91% v 49%, p=0.010) partial/total sight loss (55% v 21%, p=0.024), lower CRP (21 v 68, p=0.061) and ESR (42 v 62, p= 0.317). Of 73 completers 36 required early DMARDs (<12 weeks) for refractory/relapsing/ischemic/GC related AEs. This group had more LV involvement (50% v 11%, p=0.0003), Remission attained at 12 months 32/36 (89%) in DMARD group was comparable to the remitting GC monotherapy group 33/37 (89%) with comparable cumulative GC doses (Figure 1, Table 1). At 12-months follow up, median TAHS, AAHS and THS reduced from 13 to 3, 12 to 9 and 21.5 to 12, respectively.

Conclusion: Our study suggests, elderly males with visual symptoms, sight loss, lower CRP are a high-risk group with increased mortality within GCA. Difficult to treat disease is seen in half of all patients especially with LV involvement. This group responds well to early DMARD use achieving remission comparable to the remitting group at 12 months. Current therapies fail to achieve remission in 9.5 % of cases. HS and HC show significant improvement mirroring clinical outcomes during first 12 months of therapy.

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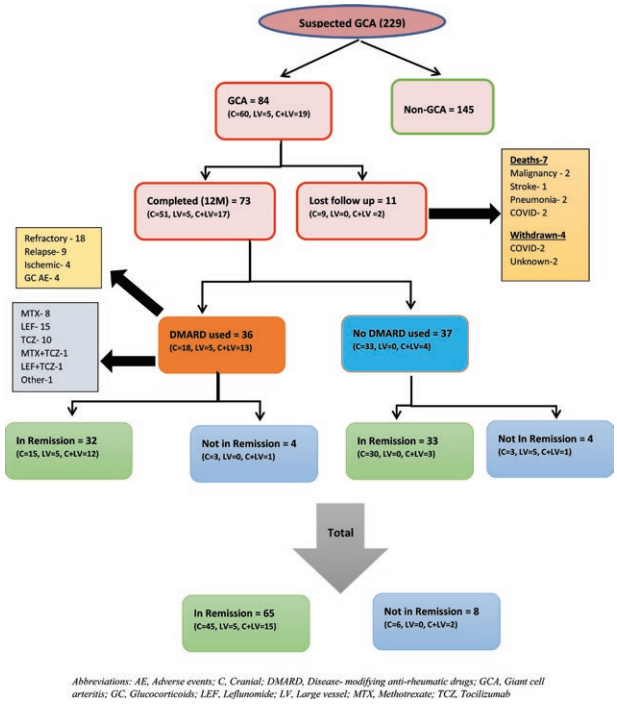
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[2]' Schafer VS et al. Rheumatology 2017

[3]' van der Geest KSM et al. ARD 2020

Table 1. comparison between the DMARD-used group and only GC group in all the GCA completed the 12 months follow up

Patients' characteristics	GCA with completed follow-up (n=73)	
	GCA treated with DMARD=36	**GCA not treated with DMARD=37**
Age, median (range) years	73.5 (60-89)	76 (60-89)
Sex, Females, n (%)	23 (64)	24 (65)
US halo score (HS)/IMT median (range)		
Temporal artery HS	11 (0-23)	13 (1-22)
Axillary artery HS	12 (0-21)	12 (0-18)
Axillary artery IMT (mm)	0.77 (0.33-2.6)	0.82 (0.39-1.21)
Total HS	22.5 (2-41)	21 (5-40)
Clinical features, n (%)		
Temporal headache	25(69)	30 (81)
Scalp tenderness	17 (47)	19 (51)
Jaw & Tongue claudication	22 (61)	24 (65)
Polymyalgic symptoms	21 (58)	13 (35)
Constitutional symptoms	21 (58)	18 (49)
Any visual disturbance	15 (42)	21 (57)
Partial or complete vision loss	8 (22)	7 (19)
History of PMR	6 (17)	3 (8)
Exam findings, n (%)		
Temporal artery abnormality	24 (67)	30 (81)
AION/ CRAO	8 (22)	6 (16)
Ocular nerve palsy	1 (3)	3 (8)
Lab markers at baseline, median (range)		
CRP mg/dL,	72.2 (6.4-292)	59 (6-206)
ESR mm/hr	67 (9-130)	57 (2-120)
GC treatment, median (range)		
GC starting dose, (baseline)	45 (0-60)	50 (0-60)
GC dose at 12m,	5 (0-25)	2.5 (0-10)
Cumulative GC dose at 12m	4627.5 (2600-10260.5)	4622.5 (944-10737.5)
Remission with prednisolone dose ≤5 mg at 12m, n (%)	32 (89)	33 (89)



Abbreviations: AE, Adverse events; C, Cranial; DMARD, Disease- modifying anti-rheumatic drugs; GCA, Giant cell arteritis; GC, Glucocorticoids; LEF, Leflunomide; LV, Large vessel; MTX, Methotrexate; TCZ, Tocilizumab

Acknowledgements: NIL.

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None declared, Edoardo Conticini: None declared, Muhammad Khurshid: None declared, Sue Inness: None declared, Jo Jackson: None declared, Alwin Sebastian: None declared.
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POS0731

SOUTHEND GCA PROBABILITY SCORE (GCAPS) AND ULTRASOUND HALO SCORE (HS) AS MARKERS FOR DIAGNOSIS AND MONITORING OF GCA: RESULTS FROM THE PROSPECTIVE, MULTICENTER HAS-GCA STUDY

Keywords: Vasculitis, Ultrasound, Imaging

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Background: Ultrasound (US) is recommended as the first-line imaging test in patients with suspected Giant Cell Arteritis (GCA). Traditionally, the US halo sign has been used for diagnosis. We have described a composite Halo Score that allows quantifying vascular inflammation on US. Prospective studies on response and disease monitoring are lacking.
Objectives: To prospectively assess the role of the US and Southend GCA pretest probability score (GCAPS) in diagnosing and monitoring GCA patients. We report 12-month follow-up data on our current recruitment.
Methods: HAS GCA (IRAS#264294) is a prospective, multicentre study recruited from 7 European centres, referrals of suspected GCA to fast-track clinics. Based on the GCAPS [1], patients were stratified in to low, intermediate and high risk categories [2]. Temporal and axillary US Halo Scores were calculated from the halo thickness and extent in bilateral temporal arteries, parietal and frontal branches (TAHS) and axillary arteries (AAHS). These scores were summed (TAHS x1 plus; AAHS x3) to generate a Total Halo Score (THS) [3]. Remission defines as the patient on prednisolone ≤ 5mg at 12 months follow up. Mann Whitney U test was used to compare baseline features between GCA and controls. Wilcoxon signed rank test was used to evaluate disease features at baseline and at 12 months in GCA patients. Sensitivity (Sn), Specificity (Sp) and ROC curve were calculated, where applicable. P value <0.05 is statistically significant.
Results: 229 patients (84 GCA, 145 controls) have been recruited from 7 European centres: 73 completed 12-month follow-up assessments; 11 were lost to follow-up (7 died, 4 withdrew consent due to pandemic). 65 achieved remissions at 12months. Demographics, clinical features, and US results are shown (**Table 1**). Among GCA patients, 60 had cranial, 5 large-vessel and 19 mixed phenotypes. Diseases were diagnosed by US and additional tests such as PET CT. Jaw claudication (54%) and constitutional symptoms (52%) were the dominant features in GCA patients compared to controls. Median age was 75 years in GCA (60% females) and 68 years in controls (69% females). GCA and controls were stratified by GCAPS to Low risk (0% vs 46%; Sn-undefined, Sp-99), Intermediate risk (21% vs 38%; Sn-83, Sp-98) and High risk (79% vs 16%; Sn-99, Sp-91). Optimal GCAPS cut-off point was ≥12 (Sn-89, Sp-78). Median THS was 21.5 in GCA and 8 in controls. Optimal cut-off Halo Score in diagnosis was TAHS ≥6 (Sn-86, Sp-92), AAHS ≥11 (Sn-52, Sp-75), THS ≥17 (Sn-76%, Sp-91%). Baseline Halo Score and CRP levels showed positive correlation (spearman rank correlation). at 12-months follow up, median TAHS, AAHS and THS reduced from 13 to 3, 12 to 9 and 21.5 to 12, respectively (**Figure 1**).
Conclusion: Along with GCAPS, Halo Score successfully discriminates GCA from non GCA mimics and. HS is effective in showing 12-month response. This score may be a useful marker to monitor GCA disease activity.

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Table 1. Patient characteristics at baseline:

Patients' characteristics	Patients with GCA (n=84)	Patients without GCA (n=145)	P Value
Age, median (range) years	75 (60-92)	68 (44-96)	0.001
Sex, Females, n (%)	50 (60)	100 (69)	0.15
GCAPS category, n (%)			
Low risk	0 (0)	67 (46)	<0.001
Intermediate risk	18 (21)	55 (38)	0.01
High risk	66 (79)	23 (16)	<0.001
Halo Score (HS) median (range)			
Temporal artery HS	13 (0-24)	2 (0-17)	<0.0001
Axillary artery HS	12 (0-21)	6 (0-18)	<0.0001
Total HS	21.5 (2-41)	8 (0-29)	<0.0001
Clinical features, n (%)			
Temporal headache	62 (74)	102 (70)	0.65
Scalp tenderness	42 (50)	46 (32)	0.007
Jaw claudication	45 (54)	10 (7)	<0.0001
Polymyalgic symptoms	37 (44)	38 (26)	0.008
Constitutional symptoms	44 (52)	30 (21)	<0.0001
Any visual disturbance	46 (55)	62 (43)	0.10
Partial or complete vision loss	21 (25)	9 (6)	<0.0001

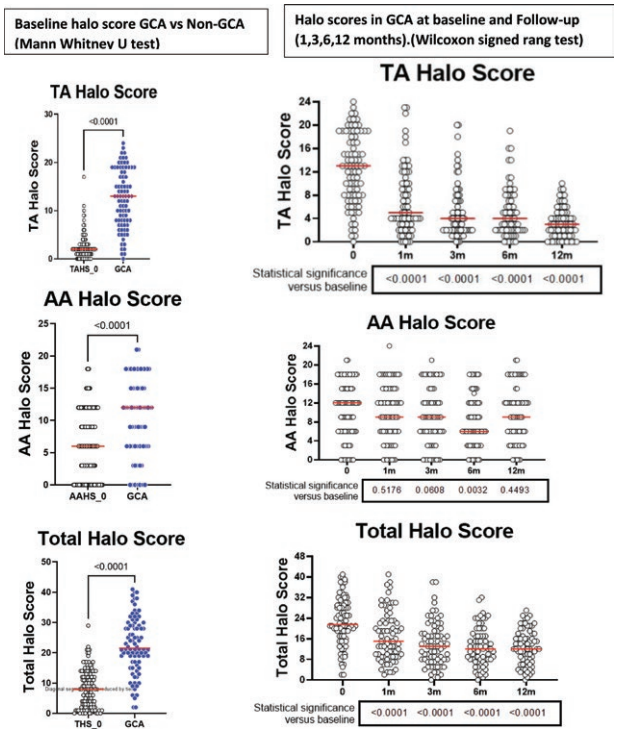


Figure 1.

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POS0732

PERFORMANCE OF THE 2022 ACR/EULAR CLASSIFICATION CRITERIA FOR GIANT CELL ARTERITIS IN ROUTINE CLINICAL CARE

Keywords: Ultrasound, Vasculitis, Imaging

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Background: The 2022 ACR/EULAR giant cell arteritis (GCA) classification criteria have been designed to improve diagnostic accuracy incorporating vascular

imaging modalities and potential large vessel (LV) involvement. These new criteria have been validated in an independent set of patients and controls, with a sensitivity of 87.0% and a specificity of 94.8%, but not tested in routine care.

Objectives: Our objective is to examine the performance of the new 2022 ACR/EULAR GCA classification criteria in this clinical scenario.

Methods: Multicentric retrospective observational study of patients referred to our ultrasound (US) fast track clinic over a 4-year period. The gold standard for GCA diagnosis was clinical confirmation after 6 months of follow-up. Patients with GCA were compared with unselected controls referred to our clinic with suspected GCA. All patients underwent US exam of temporal and extracranial arteries (carotid, subclavian and axillary) within 24-48 hours at baseline. FDG-PET/CT was performed according to standard clinician criteria. Following the new 2022 GCA ACR/EULAR classification criteria, the total score for the 10 items included in the criteria was calculated, with a total cut-off ≥ 6 for the classification of GCA. The performance of these criteria was evaluated in all GCA patients across different subsets of the disease.

Results: A total of 319 patients (188 cases and 131 controls) were included for analysis (mean age 76 years, 58.9% females). Patients with GCA and controls differed in age (78.2 vs 72.9, p<0.001) and sex (females 53.2% vs 67.2%, p=0.013). The diagnostic accuracy of the 2022 ACR/EULAR GCA classification criteria and the previous 1990 ACR GCA classification criteria in different subsets of patients is shown in Table 1. Overall, the new criteria had a sensitivity of 92.6% and a specificity of 74%, using GCA clinical diagnosis as an external criterion and the area under the curve (AUC) was 0.932 (95% CI 0.903 to 0.960). Isolated LV-GCA showed a sensitivity of 62.2% and a specificity of 74% (AUC 0.696 [0.596 – 0.796]) and biopsy-proven GCA showed a sensitivity of 100% and a specificity of 74% (AUC 0.992 [0.981 – 1]).

Conclusion: The new 2022 ACR/EULAR GCA classification criteria showed good diagnostic accuracy of patients with suspected GCA under routine care, and a substantial improvement upon the sensitivity and specificity of the 1990 ACR GCA classification criteria in all patients subsets.

Table 1. Diagnostic accuracy of the new 2022 ACR/EULAR GCA and the 1990 ACR/EULAR classification criteria, with clinical diagnosis serving as the external criteria in all GCA, patients with isolated cranial GCA, isolated LV-GCA, all LV-GCA and biopsy proven GCA. GCA, giant cell arteritis; LV, large vessel; Sens, sensitivity; Spec, specificity; LR+, positive likelihood ratio; LR–, negative likelihood ratio; AUC: area under the ROC curve analysis

		Sens	Spec	LR+	LR-	AUC (95% CI)
All GCA (n = 188) vs controls (n = 131)	2022 ACR/EULAR criteria	92.6%	74%	3.56	0.1	0.932 (0.903 – 0.960)
	1990 ACR criteria	53.2%	80.2%	2.68	0.58	0.719 (0.663 – 0.775)
Isolated cranial GCA (n = 83) vs controls (n = 131)	2022 ACR/EULAR criteria	96.4%	74%	3.71	0.05	0.965 (0.933 – 0.996)
	1990 ACR criteria	61.4%	80.2%	3.1	0.48	0.764 (0.699 – 0.829)
Isolated LV-GCA (n = 37) vs controls (n = 131)	2022 ACR/EULAR criteria	62.2%	74%	2.39	0.51	0.696 (0.596 – 0.796)
	1990 ACR criteria	18.9%	80.2%	0.95	1.01	0.554 (0.455 – 0.653)
Biopsy proven GCA (n = 21) vs controls (n = 131)	2022 ACR/EULAR criteria	100%	74%	3.85	0	0.992 (0.981 – 1)
	1990 ACR criteria	95.2%	80.2%	4.81	0.06	0.931 (0.877 – 0.985)
LV-GCA (with or without cranial GCA) (n = 105) vs control (n=131)	2022 ACR/EULAR criteria	89.5%	74%	3.44	0.14	0.905 (0.865 – 0.946)
	1990 ACR criteria	46.7%	80.2%	2.36	0.66	0.683 (0.616 – 0.751)

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Disclosure of Interests: None Declared.

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POS0733 REPEATING TEMPORAL AND AXILLARY ARTERY ULTRASOUND SCANS IN PATIENTS WITH SUSPECTED GIANT CELL ARTERITIS WITH NEGATIVE SCAN AT PRESENTATION

Keywords: Real-world evidence, Ultrasound, Vasculitis

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Background: Giant cell arteritis (GCA) is a medical emergency due to its risk of severe ischaemic complications such as irreversible blindness [1]. Treatment with systemic glucocorticoids (GC) should be initiated to prevent these complications promptly. However, this can compromise the confirmation of the diagnosis by decreasing the sensitivity of the temporal and axillary artery ultrasound scan (TA and AX US) recommended for GCA diagnosis [1-3]. One possible strategy for managing patients with symptoms suggestive but not typical of GCA, who have an initial negative TA and AX US on GC treatment, is weaning the GC rapidly and performing a second ultrasound off GC, within six weeks of their initial ultrasound. This practice aims to increase the diagnostic yield of the second ultrasound and safely rule out GCA without submitting the patient to unnecessary GC treatment.

Objectives: To assess the safety of repeating a TA and AX US after a rapid GC taper in patients with suggestive but not typical symptoms of GCA and a negative first ultrasound on a high dose GCs.

Methods: This is a retrospective study that included patients with suspected GCA referred to the Rheumatology department at Nuffield Orthopaedic Centre - Oxford, from Oct 2020 to June 2022. The inclusion criteria were: i) negative first TA and AX US while on treatment with GCs ≥30mg/d; ii) first ultrasound performed at least 6 months prior to the data collection; iii) second ultrasound performed within 6 weeks of the first one. The TA and AX US was considered positive when a non-compressible halo sign was present. Data regarding patient demographics, clinical manifestations, treatment, and outcomes was collected using Electronic Patient Records (EPR). The patients' records were also reviewed to check for any subsequent diagnosis of large vessel vasculitis (LVV) within 6 months of the first TA and AX US.

Results: Twenty-nine patients were included, 19/29 (65.5%) were females and the median age at the time of the referral was 65 (range 51-87). The most frequent clinical manifestation at presentation was temporal headache in 23/29 (79.3%) patients, followed by scalp tenderness in 18/29 (62.3%) and visual disturbance in 15/29 (51.7%). Patients were on GC treatment for a median duration of 10 days (range 3-35) with a median cumulative dose of 480mg (range 120 – 1400mg). All patients were on high doses of GCs, of whom 8/29 (27.6%) were on 60mg of prednisolone, 2/29 (6.9%) on 50mg, 17/29 (58.6%) on 40mg and 2/29 (6.9%) on 30mg. GCs were weaned over an average of 12 days (range 0-28). The second ultrasound was performed after stopping GC treatment for a median of 11 days (range 3-30) and the median interval between the two scans was 23 days (range 6-42). Regarding the second ultrasound, 28/29 (96.5%) patients had a negative and 1/29 (3.4%) had a positive TA and AX US. Moreover, 2/29 (6.9%) patients were found to have LVV on subsequent Positron Emission Tomography (PET) scans that were requested due to clinical suspicion of extra-cranial GCA.

Conclusion: This study shows that for patients presenting with symptoms suggestive but not typical of GCA, who were already on GC treatment, rapid taper of GCs and a negative second TA and AX US safely ruled out GCA in 26/29 (89.6%) patients. Although more studies are needed to confirm these preliminary results, this practice should maintain a good diagnostic ability but prevent unnecessary GC toxicity.

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POS0734 ANALYSIS OF IMPROVEMENT IN GIANT CELL ARTERITIS: DEFINING THRESHOLDS FOR GCA-RESPONSE

Keywords: Outcome measures, Ultrasound, Vasculitis

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Background: The creation of instruments for the structured assessment of disease activity has facilitated the effective use of DMARDs to control disease activity in patients with inflammatory arthritis. Composite measures for Giant Cell Arteritis (GCA) incorporating several key clinical and laboratory variables which allow for a standardized quantitative assessment of GCA disease activity has been recently introduced. These assessment tools for measuring disease activity are of particular benefit in helping to achieve therapeutic goals in patients with GCA, including amelioration of the symptoms and signs of active disease, and the consequent avoidance of functional impairment and restoration of physical function.

Objectives: To identify the preliminary definition of improvement in GCA and the higher thresholds for improvement reflecting significant and major improvement as well as remission.

Methods: In developing criterion for improvement of individual GCA patients, consideration was restricted to the 6 variables identified as outcome measures: severity of headache (0-100), acute visual deficit (0-100), functional disability (0-3), Patient Global Assessment (0-100), Physician global assessment (0-100), ESR and CRP levels. For each variable, the value at baseline were compared with the value at 4-weeks and 12-weeks of treatment to determine the degree of improvement or deterioration that occurred. The percentage of improvement was calculated directly for each of the 6 variables in 51 patients. Using the 6 variables, preliminary analysis was performed to determine the percentage of improvement. Preliminary definition of improvement required >x% improvement in >y of the 6 variables, where "x" was set at 20%, 30%, 40%, 50%, 70%, 90% and 100%, and "y" was set at 2,3,4,5, or 6 variables. To assess the discriminating power of high response percentages (70%, 90% and 100%) the percentage of improvement in the headache severity (as the main outcome measure reflecting the disease activity status) was compared to the change of the rest of the core set measures. The individual improvement criterion identified was then applied prospectively to a cohort of 25 patients diagnosed to have GCA and starting their therapy.

Results: A definition of >50% improvement in 4 or more variables produced the largest difference between patient's assessment at 4-weeks and 12-weeks in comparison to the baseline. Sharpening the cut-offs to 70% or 90% means that the patient should nearly or completely reach a status of remission in order to fulfil such an impressive improvement criterion. Reaching 100% means that the patient has achieved remission. Outcome of the prospective study revealed that 100% of the patients achieved 50% GCA response. Assessing the higher response rates, revealed that 10% of the patients achieved 70%, 30% achieved 90% whereas 60% achieved 100%.

Conclusion: Core sets of valid outcome measures have been defined. GCA response criteria have been developed and showed comparable validity. The 70% (significant improvement), 90% (major improvement) and 100% (remission) GCA improvement criteria showed good discriminating capacity though less than the 50% criteria. GCA response can be used in standard clinical practice to identify disease activity status and response to therapy. Calculation of GCA-N index would be the next step to attain a continuous variable rather than at arbitrary 20%, 50%, and 70% levels. A second advantage is that a continuous index can include recognition of possible deterioration in addition to improvement.

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Disclosure of Interests: None Declared.

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POS0735 PREDICTORS OF RELAPSE IN PATIENTS WITH GIANT CELL ARTERITIS: RESULTS FROM A MULTICENTER, PROSPECTIVE PATIENT COHORT

Keywords: Vasculitis, Prognostic factors

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Background: Despite significant advances in the diagnosis and therapy of giant cell arteritis (GCA), relapses during the disease course are common. The exact predictors for their occurrence at diagnosis or during the disease course have not been defined.

Objectives: To evaluate the frequency and predictors of relapses in a real-life GCA cohort.

Methods: Data were derived from an ongoing, multicenter, prospective cohort study of patients with GCA. Patients were evaluated at baseline and approximately 2 years later. Data regarding their demographics, clinical characteristics, treatment patterns, co-morbidities and relapses were retrospectively and prospectively collected and analyzed. Predictors of relapse were examined by logistic regression analyses.

Results: At the 1st cross-sectional evaluation, 254 patients with GCA were included; 68% were women with a mean age of 72.3 years at diagnosis and a mean disease duration of 2 years. Diagnosis had been established by temporal artery biopsy in 67% (n=171) and by ultrasound of temporal arteries in 21% (n=53) of patients. At the 2nd evaluation (median follow-up: 2.02 years), data were available for 199 patients (78%). All patients had been treated initially with glucocorticoids (GCs, mean prednisolone dose = 40 mg/day) and during the disease course additionally with non-biologic (39%, n=59) and/or biologic (16%, n=25) agents. At the 2nd evaluation time point, 73% of patients were still on therapy with GCs (60%) and/or GC-sparing agents (29%: non-biologics: 16%, biologics: 13%). During the prospective follow-up phase of 2 years, 27% (n=43) of patients had at least one disease relapse. Relapsing patients had shorter disease duration at 1st evaluation (1.4 *vs.* 4 years, p=0.015), more frequent large vessel involvement at diagnosis (21% *vs.* 8%, p=0.019) and cardiovascular events (CDV) during follow-up (14% *vs.* 4.2%, p=0.032), and had received a higher GC daily dose at diagnosis (mean 46.2 *vs.* 39.9 mg, p=0.01) compared to the non-relapsing ones. By multivariable logistic regression analysis, large vessel involvement at diagnosis [odds ratio (OR) (95% confidence intervals) = 4.22 (1.14, 15.58)], a cardiovascular event (CVD) during follow-up [OR = 4.60 (1.11, 19.13)] and a higher GC daily dose at diagnosis [OR = 1.04 (1.00, 1.08)] were associated with disease relapses.

Conclusion: In this large, real-life, long -term GCA cohort, despite continued treatment with GCs and/or GC-sparing agents, relapses occurred in 27% of patients. Factors associated with relapses included large vessel involvement and high GC dose at diagnosis as well as cardiovascular events during follow up. These are novel findings that could be useful in the design of the appropriate monitoring and therapeutic strategies in these patients.

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POS0736 SYSTOLE AND DIASTOLE ULTRASOUND WALL THICKNESS SHOWS SIGNIFICANT DIFFERENCES THAT AFFECT THE DIAGNOSIS AND ASSESSMENT OF GIANT CELL ARTERITIS

Keywords: Ultrasound, Vasculitis, Comorbidities

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Background: In the last few years, several cut-off points for the intima-media thickness (IMT) of temporal arteries (TA) and large vessels (LV) have been proposed for the ultrasound (US) diagnosis of giant cell arteritis (GCA). It has usually been recommended to use the average measure of the higher IMT, but there is currently a lack of consensus on this. We have observed some changes in the IMT measurements depending of if they are performed in systole or diastole.

Objectives: The main objective of this study is to confirm if there are differences in the IMT measurement taken in systole or diastole and if they are clinically relevant.

Methods: Observational retrospective study on consecutive patients of our GCA fast track clinic. The gold standard diagnosis was the opinion of the clinical doctor after at least 6 months of follow-up. US recorded videos, of every explored vessel temporal (common trunk, frontal and parietal branches), subclavian and axillary arteries were reviewed and the IMT of each of them was measured in systole and diastole peaks for comparison. We define an ultrasound result as positive with cut-off values of IMT ≥ 0.34 mm for frontal and parietal branches, ≥ 0.42 mm for the common trunks of TA, and ≥ 1 mm for the axillary and subclavian arteries. Demographic data of the included patients were also collected.
Results: We have included 72 cases, 36 with GCA diagnosis and 36 without GCA (controls). The mean values of age and sex, as well as the IMT in systole and diastole of each vessel are shown in Table 1. There were not significant differences in sex but patients without GCA were younger (p<0.01). The US IMT measurements at the systolic and diastolic times showed statistically significant differences in all the explored vessels, as in patients with GCA as in the control non GCA group. All the IMT measured in diastole showed higher and statistically significant values than those measured in systole, with a mean increment of measurement of 5.3% and 6.5% in TA and 6.4% and 5.6% in LV, respectively in the GCA and control group. This result can be of clinical relevance because if we used diastolic measures, instead of systolic measures, 5/36 (13.8%) cases in controls had halo sign in one isolated vessel (2 cases in parietal right, 1 in common trunk right, 1 in subclavian right, 1 in subclavian left). However, in GCA patients, the number of patients with halo sign did not change, but the number of pathological vessels was increased when the measured was performed in diastole (1 frontal right branch, 1 common trunk right, 4 frontal left branches, 5 common trunks left and 2 axillary right), so this could have influence in the assessment of the disease.
Conclusion: There are significant differences between the IMT measured in systolic and diastolic peaks, with higher values in diastole. The differences are relatively small but may increase the number of false positives (13.8%) in controls, and the number of affected vessels in the GCA group. This should be considered in the diagnosis and assessment of GCA.

Table 1. Changes in the IMT values in systole and diastole in GCA and non GCA patients

Category	No GCA			GCA		
N	36			36		
Sex ♂ / ♀ (n)	14/22			17/19		
Age years (mean ± SD)	74.4±9.4			80.8±6.6		
	Systole	**Diastole**	p	**Systole**	**Diastole**	p
TA Frontal (right)	0.23±0.56	0.24±0.60	0.001	0.36±0.15	0.39±0.16	0.001
TA Frontal (left)	0.21±0.44	0.23±0.46	0.001	0.37±0.18	0.39±0.18	0.010
TA Parietal (right)	0.21±0.40	0.23±0.41	0.001	0.42±0.21	0.44±0.21	0.001
TA Parietal (left)	0.21±0.45	0.23±0.43	0.001	0.38±0.20	0.40±0.21	0.001
TA Common (right)	0.25±0.76	0.26±0.74	0.001	0.48±0.26	0.52±0.28	0.001
TA Common (left)	0.23±0.50	0.23±0.50	0.001	0.44±0.20	0.44±0.20	0.001
Axillary (right)	0.57±0.14	0.60±0.14	0.001	0.76±0.30	0.82±0.29	0.001
Axillary (left)	0.54±0.13	0.57±0.13	0.001	0.72±0.29	0.76±0.32	0.010
Subclavian (right)	0.64±0.15	0.68±0.15	0.001	0.79±0.27	0.85±0.30	0.001
Subclavian (left)	0.61±0.16	0.64±0.16	0.001	0.80±0.33	0.85±0.34	0.001

GCA= giant cell arteritis; N= number of patients; SD= standard deviation; TA temporal artery. Measures are showed in mm.

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POS0737

AGE AND SEX BIAS OF ULTRASOUND SCORES FOR DIAGNOSIS OF GIANT CELL ARTERITIS: INSIGHTS FROM THE PROSPECTIVE, LONGITUDINAL HAS-GCA STUDY

Keywords: Ultrasound, Imaging, Vasculitis

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Background: Giant cell arteritis (GCA) is an age-linked, critically ischaemic vasculitis where ultrasound (US) serves as an important tool enabling urgent diagnosis and therapy. US scores have been developed to quantify the arterial inflammation in GCA [1,2], but optimal diagnostic cut-off points and potential bias of age and sex on these values remain un-elucidated.
Objectives: To compare the diagnostic accuracy of previously reported US scores for GCA, and to determine whether these scores require correction for age and sex.
Methods: The HAS-GCA study, with a prospective, multicentre, cohort design, recruited 229 consecutive patients with suspected, new-onset GCA from 7 sites located in the UK, Italy, Spain and the Netherlands. All cases underwent bilateral US evaluation of the three temporal artery segments (common superficial, parietal, frontal) and axillary arteries. Intimal-medial thickness (IMT) was measured in each segment. Three ultrasound scores were calculated based on the IMT: halo count (HCount) [1], Halo Score (HScore) [2] and the OMERACT GCA US Score (OGUS) [2]. The definition of halo was based on previously reported IMT cut-off values [3]. The reference standard was the final clinical diagnosis after 6 months follow-up. ROC with AUC analysis was performed. Optimal cut-off points were determined by Youden Index. Group comparisons were made by Mann Whitney U test and correlations by Spearman's rank correlation coefficient. P values < 0.05 were considered statistically significant.
Results: A final diagnosis of GCA was made in 84 patients, whereas 145 cases received an alternative diagnosis (i.e. non-GCA patients). HCount, HScore and OGUS were significantly higher in GCA patients than non-GCA patients. In non-GCA patients, all three scores were significantly higher in men than women, and showed a statistically significant, positive correlation with age. In GCA patients, the US scores showed a positive correlation (HCount and OGUS) or strong trend for a positive correlation (HScore) with age; and the HCount was significantly higher in men. All scores effectively discriminated GCA from non-GCA patients as indicated by ROC analysis: AUC for halo count 0.936 (0.899-0.974), Halo Score 0.894 (0.848-0.939) and OGUS 0.937 (0.902-0.973). The optimal diagnostic cut-off points were: 2 for HCount (sens 86%, spec 92%), 17 for HScore (sens 76%, spec 91%) and 0.80 for OGUS (sens 87%, spec 93%). These diagnostic cut-off points differed in sensitivity and specificity within different age- and sex-defined groups with the highest sensitivity and lowest specificity observed among old (>81yr) male patients. Alternatively, age- and sex-stratified cut-off points could be established for the US scores (Table 1).
Conclusion: All previously reported US scores show excellent diagnostic accuracy for GCA, but are prone to over-diagnose GCA in older males. Our data highlight the need for age- and sex-specific diagnostic cut-off points. The excellent comparative performance of the simple HCount in GCA diagnosis suggests an exciting role in future clinical practice.
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Table 1. Ultrasound scores in different age and sex groups. Age cut-offs were based on 25th percentile and 75th percentile of age in female and male patients with GCA.

Category	Score	AUC in ROC analysis	Optimal cut-off point	Sensitivity (%)	Specificity (%)
Women	Halo count	0.897	2	75	98
Age <67	Halo Score	0.883	12	83	90
	OGUS	0.925	0.66	83	85
Women	Halo count	0.927	1	88	93
age 67-79	Halo Score	0.873	16	72	93
	OGUS	0.933	0.80	80	98
Women	Halo count	0.938	2	92	94
Age >79	Halo Score	0.889	16	92	88
	OGUS	0.928	0.83	92	94
Men	Halo count	0.919	1	100	68
Age <74	Halo Score	0.877	15	88	74
	OGUS	0.911	0.87	75	97
Men	Halo count	0.972	3	94	88
Age 74-81	Halo Score	0.837	20	72	100
	OGUS	0.972	0.76	100	88
Men	Halo count	0.958	4	100	83
Age >81	Halo Score	0.885	19	88	83
	OGUS	0.896	0.90	100	83

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POS1603

TREAT-TO-TARGET STRATEGIES IN GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA: A SYSTEMATIC LITERATURE REVIEW INFORMING AN INTERNATIONAL TASKFORCE

Keywords: Remission, Vasculitis, Treat to target

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Background: Polymyalgia rheumatica (PMR) and Giant cell arteritis (GCA) are chronic inflammatory diseases. Despite the progress made in the management of these conditions, new unmet needs have emerged particularly in terms of prevention of disease- and treatment-related complications. A treat-to-target (T2T) strategy, which has been well established in other rheumatic diseases, has not yet been developed for PMR and GCA.
Objectives: To retrieve current evidence on T2T strategies in PMR and GCA to inform an international task force (TF) developing T2T recommendations.
Methods: A systematic literature review (SLR) was conducted. Medline, EMBASE, Cochrane Library and clinicaltrials.gov (from inception until May 2022), as well as EULAR/ACR abstract databases were searched (2019-2021). Randomized controlled trials (RCTs) and non-randomized interventional studies published in English and answering at least one of the eleven PICO questions on treatment targets and outcomes, were identified (Table 1). The study selection process, data extraction, data synthesis and risk of bias assessment were conducted independently by two investigators.
Results: Of 7809 screened abstracts, 397 were selected for detailed assessment and 76 papers were finally included (31 RCTs, 8 subgroup/exploratory analyses of RCTs and 37 non-randomized interventional studies). No study comparing a T2T strategy against standard of care was identified. In PMR RCTs, treatment-related outcomes were most commonly used (90.9% of RCTs), specifically in terms of the glucocorticoids (GC) cumulative dose and GC tapering, followed by clinical, laboratory and safety targets (63.3% each). Conversely, the most frequently reported outcomes in RCTs in GCA were prevention of relapses (72.2%), remission, treatment, and safety (66.7 % each). Remission and relapses were variably defined in PMR and GCA RCTs but, in most cases, they comprised a combination of clinical and laboratory parameters (Figure 1). The following predictors of poor treatment response were identified: for GCA, data from RCTs yielded female sex, initial prednisone dose <30mg/day, bad baseline patient-reported outcomes, increased inflammatory markers after the achievement of clinical remission and absence of PMR symptoms at baseline as risk factors for treatment failure and an increased relapse rate. In PMR, no high-quality data predicting clinical outcomes were identified. Finally, in RCTs comparing the outcomes of GCA patients with new onset versus established disease, no differences were found, given that treatment was equal in both groups.
Conclusion: This SLR informed an international TF developing T2T recommendations in PMR and GCA. It provides up-to-date evidence while simultaneously highlighting the gaps in current knowledge about T2T strategies in these diseases.

Table 1. Clinical key questions

1. What are the treatment targets and outcomes in GCA/PMR, and how can they be measured (imaging, lab parameters, clinical, PRO)?
2. Is coming-off GC a treatment target in GCA/PMR, and how quickly should it be achieved?
3. What should be the frequency of monitoring disease state/ adapting therapy? How fast and to what extent should disease activity change before requiring treatment modification?
4. How do comorbidities influence T2T outcomes in GCA/PMR?
5. What are comorbidities related to uncontrolled disease activity?
6. Do targets need to be adapted based on the presence of comorbidities?
7. Is residual disease activity acceptable, and to what extent?
8. How can reaching disease targets, reducing/ preventing treatment side effects, and long-term consequences of disease be balanced in GCA/PMR? What is more important: control of disease activity or prevention of treatment related adverse effects?
9. Can treatment success be predicted?
10. What are the predictors of successful treatment reduction (e.g., duration on target)?
11. Do treatment targets differ over time (early vs. established disease)?

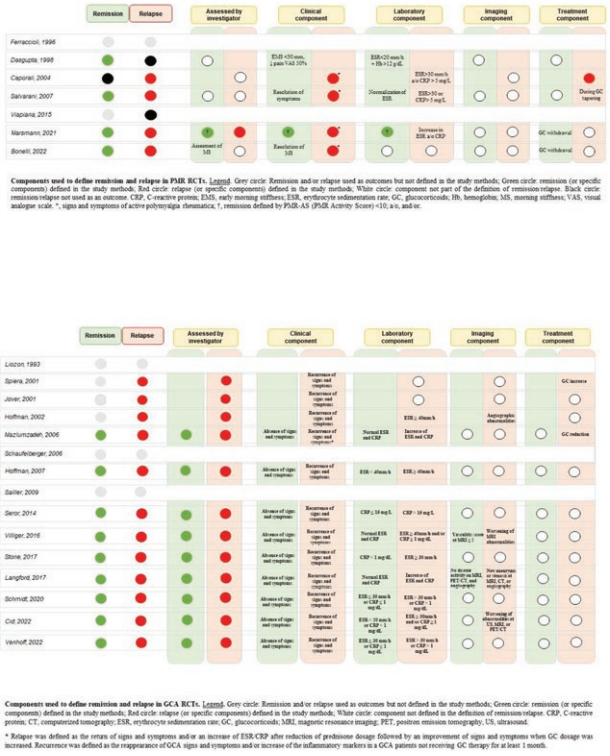


Figure 1. Components used to define remission and relapse in PMR and GCA RCTs

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Basic and translational science in paediatric rheumatology

POS0738 CHILDHOOD ABDOMINAL/PELVIC PAIN AS A PREDICTOR OF RECURRENT MUSCULOSKELETAL PAIN IN ADOLESCENT BOYS AND GIRLS: A PROSPECTIVE POPULATION-BASED STUDY

Keywords: Epidemiology, Pain

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Background: Primary musculoskeletal pain conditions interfere greatly with the quality of life and are challenging to manage, from the patient's and clinician's perspectives. Susceptibility to chronic musculoskeletal pain syndromes in adulthood can be traced back to childhood when prevention might be most effective. Population-based longitudinal studies in pediatric ages allow for testing different predictors of pain trajectories to assist risk stratification. Recurrent pain experiences in non-musculoskeletal sites are common in young children and may be red flags for future musculoskeletal pain susceptibility [1].
Objectives: We aimed to quantify the prospective association of non-musculoskeletal pain experiences at ages 7 and 10 with recurrent musculoskeletal pain at age 13 in a large population-based cohort of boys and girls.
Methods: We used data from Generation XXI, a population-based birth cohort setup in 2005-06 in the public maternities of Porto, Portugal. Participants were invited to regular follow-up visits at ages 7, 10, and 13 years. In each wave, pain history in the previous 3 months was assessed using the Luebeck Pain Screening Questionnaire, applied to caregivers (ages 7 and 10) and adolescents (age 13). We included only the main pain identified in the questionnaire, and only if it occurred more than once in the previous 3 months. Musculoskeletal pain sites comprised upper/lower limbs, back, neck, shoulders, hips, and generalized musculoskeletal. Non-musculoskeletal sites were head, abdomen/pelvis, or other. We calculated relative risks and 95% confidence intervals for the association between pain sites at ages 7 and 10 and recurrent musculoskeletal pain at age 13. The analysis was stratified by sex at birth.
Results: We included 3833 participants (47.9% girls). Recurrent pain was reported in 28.4% of children at age 7 (25.7% of boys, and 31.3% of girls), 26.6% at age 10 (23.3% of boys, and 30.2% of girls), and 35.1% at age 13 (28.8% of boys, and 41.9% of girls). For girls, the most reported recurrent pain sites before adolescence were abdomen/pelvis (10.3% at 7, and 9.7% at 10), musculoskeletal (8.1% at 7, and 9.0% at 10), and head (7.7% at 7, and 7.3% at 10). In boys, recurrent pain was more frequent in musculoskeletal sites (9.0% at 7, and 9.6% at 10), followed by abdomen/pelvis (7.7% at 7, and 5.0% at 10), and head (5.1% at 7, and 6.0% at 10). As shown in the Figure 1, in 7-year-old girls, only abdominal/pelvic pain was predictive of future musculoskeletal pain at age 13 RR 1.43; (95%CI 1.07, 1.87). At age 10, musculoskeletal pain became predictive of musculoskeletal pain at age 13 [1.44 (1.07 - 1.84)]. In boys aged 7 years, both musculoskeletal and abdominal/pelvic pain were predictive of future musculoskeletal pain at age 13 [1.49 (1.13, 1.91) and 1.40 (1.02, 1.86), respectively]. At age 10 only musculoskeletal pain remained predictive of musculoskeletal pain at age 13 [1.45 (1.11, 1.84)].
Conclusion: In this population-based cohort, musculoskeletal pain in adolescents was preceded by non-musculoskeletal pain experiences - especially abdominal/pelvic pain - during childhood in both boys and girls. Widening the scope to non-musculoskeletal sites may contribute to the early detection and risk stratification of individuals who are more susceptible to developing chronic musculoskeletal pain trajectories.
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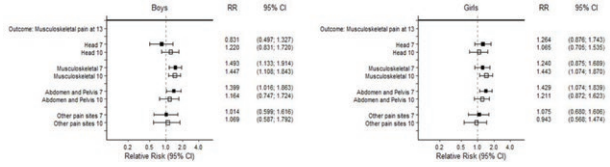


Figure 1. Association between recurrent pain sites at ages 7 and 10, and recurrent musculoskeletal pain at age 13.

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POS0739 LEUCOCYTE ABNORMALITIES AND CYTOKINE LEVELS IN SYNOVIAL FLUID OF JUVENILE IDIOPATHIC ARTHRITIS PATIENTS: A PRELIMINARY STUDY

Keywords: Cell biology, Cytokines and chemokines, Uveitis

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Background: Juvenile idiopathic arthritis (JIA) is a heterogeneous group of diseases characterized by joint inflammation and uveitis is the most frequent extra-articular manifestation [1,2]. Although several studies evaluated the differences between the different types of JIA, no specific markers have been identified which would allow early stratification of patients and predict the future disease course. Recently, it has been suggested that rheumatic diseases might be associated with genomic instability and increased sensitivity to DNA damage (3), but it has not yet determined in JIA.
Objectives: To investigate cell populations, cytokine levels, and signs of genotoxicity in synovial fluid (SF) of patients with different JIA subtypes.
Methods: SF was collected from the knees of 24 patients, untreated for at least 6 months prior to enrollment, and fulfilling ILAR criteria (4): 9 with polyarticular (poly)-JIA (age:6.56±4.67 years) and 15 with oligoarticular (oligo)-JIA (age:8.33±5.15 years). Six poly-JIA and 8 oligo-JIA patients were at disease onset. Among the oligo-JIA patients, 12 had positive antinuclear antibodies (ANA+) and 5 had uveitis. SF was examined under optical light microscopy. White cell count (WBC) and the polymorphonuclear cell (PMN) percentage were determined in SF according to standard procedures. May-Grünwald-Giemsa staining was used to determine the percentage of hypo- or hypersegmented PMN, binucleated monocytes, and cells with micronuclei (MN), pyknosis, necrosis, apoptosis and nuclear buds, which are considered biomarkers of genotoxic events. SF IL-1β and IL-8 levels were assayed by ELISA.
Results: WBC count and PMN percentage were higher in SF of patients with poly-JIA than in those with oligo-JIA, albeit not significantly. Comparison between the two groups at disease onset showed that WBC levels and PMN percentage were significantly greater in SF from poly-JIA (poly-JIA WBC:10500±4580.32 cells/mm^3, PMN:59.83±13.75%; oligo-JIA WBC:4850±1050 cells/mm^3, PMN:41.5±16%; $p<0.05$). IL-1β and IL-8 levels were higher in children with poly-JIA, but the difference reached statistical significance only for IL-8 in patients at disease onset (poli-JIA:1253.19±264.4 pg/ml; oligo-JIA:519.67±468.34 pg/ml; $p<0.01$). This group also showed a percentage of cells with MN significantly greater as compared to that in oligo-JIA (poli-JIA:7.1±2.42%; oligo-JIA:1.75±2.05%; $p<0.001$). Although SFs from oligo-JIA-ANA+ patients had higher WBC and PMN percentage than those from oligo-JIA-ANA-, no significant differences were observe between the 2 groups. SFs from oligo-JIA patients with uveitis showed higher but not significant IL-8 levels (554.06±520.26 pg/ml), significantly greater IL-1β concentrations (100.94±76.05 pg/ml; $p<0.05$) and percentage of cells with MN (5.73±3.06%; $p<0.05$), and significantly lower hypersegmented PMN percentage (11.06±8.45%; $p<0.05$) than those from oligo-JIA patients without uveitis (IL-8:280.88±310.11 pg/ml; IL-1β:6.04±15.4 pg/ml; cells with MN:1.96±2.36%; hypersegmented PMN:22.79±8.07%). There was no significant difference in the other studied parameters between the different patient groups.
Conclusion: This study shows that poly-JIA SFs have higher inflammation marker levels than oligo-JIA SFs, and this is observed mostly at the disease onset. The presence of MN may be associated with SF genotoxic effects, and trigger the induction of inflammatory pathways that contribute to disease complications. As hypersegmented PMN suppress T cell proliferation, a low cell number with this phenotype may reflect a persisting antigenic stimulus.
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Paediatric rheumatology

POS0740 VALIDATION OF THE PEDIATRIC BEHÇET DISEASE CRITERIA (PEDBD): A REAL LIFE CONSENSUS-BASED APPROACH

Keywords: Vasculitis, Behcet's disease

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Background: Behçet's syndrome (BS) is an autoinflammatory disease characterized by a variable vessel vasculitis. In children, BS may start early in life, mimicking other autoinflammatory diseases and making the diagnosis challenging. In the past, several criteria have been created for adult BS classification. In 2015, the first set of BS paediatric classification criteria, the PEDBD, was proposed by an international Expert consensus [1].
Objectives: to perform an external validation of the PEDBD criteria in a cohort of internationally validated paediatric BS patients.
Methods: 210 patients (70BS, 40 PFAPA, 35 FMF, 26 MKD, 22 TRAPS, 17 UND/ SURF) were randomly selected from the Eurofever Registry (patients excluded if > 16 years and if included in first PEDBD study). A set of 11 Experts blinded to original diagnosis, were chosen to evaluate the patients: in the 1st round, clinical and serological data were evaluated; in the 2nd round genetic data were added; in the 3rd round the other Experts' votes and comments were shown. Using the expert consensus as gold standard (agreement>80%), the PEDBD, the ISG and the ICBD criteria were applied to BS patients and to the confounding diseases in order to define the sensitivity, specificity and accuracy.
Results: At the end of the 3rd round, a consensus on the initial diagnosis was reached in 112/210 patients (53.3%), with an additional consensus on a different final diagnosis in 27 patients. The BS patients with an agreement (24) were classified as confirmed-BS, and those with an agreement of 60-70% (10) as probable-BS. In confirmed-BS patients, oral ulcers were present in all the patients, genital ulcers in 77%, skin manifestations in 50%, a positive pathergy reaction in 39%, anterior and posterior uveitis in 29 and 27%, retinal vasculitis and papillary oedema in 8% of patients, with a resulting impaired vision in 17%. Venous thrombosis was present in 2 patients (8%). The patients with ocular and vascular involvement were all males. Cranic nerve palsy (17%) was the most frequent neurologic symptom. Abdominal pain was present in 33%, diarrhoea and gastrointestinal bleeding in 13% and anal/perianal ulcers in 8%. 29% presented arthralgia, and 13% arthritis. Fever was present in 50% of patients. HLA-B51 was positive in 69% of patients. When comparing these patients with the confounding diseases, an older age at disease onset, the presence of oral and genital ulcers, skin papulo-pustular lesions, a positive pathergy test and posterior uveitis were BS distinctive elements. The ISG, ICBD and PEDBD criteria were applied to confirmed and probable-BS and to the confounding disease controls, resulting in the following test characteristics (Table 1).

Table 1.

Criteria	Sensitivity	Specificity	Accuracy
ISG	0.50	1.0	0.90
ICBD	0.79	0.98	0.95
PEDBD	0.58	0.99	0.91

Conclusion: the PEDBD criteria were extremely specific but had a lesser sensitivity than ICBD which had a better accuracy. One limitation is that specific monogenetic BS mimics were not included as disease controls, thus the true accuracy of all these criteria may be lower in practice. The complexity of childhood BS suggests that genotyping (incorporating autoinflammatory diseases, BS mimics, and HLA-type) combined with clinical features are likely to yield the most accurate classification criteria, which would require further validation in a larger cohort.
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Disclosure of Interests: None Declared.
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POS0741 CLINICALLY UNSUSPECTED JOINT INFLAMMATION DETECTED BY WBMRI IS MORE FREQUENT IN JIA PATIENTS THAN CONTROLS

Keywords: Inflammatory arthritides, Outcome measures, Imaging

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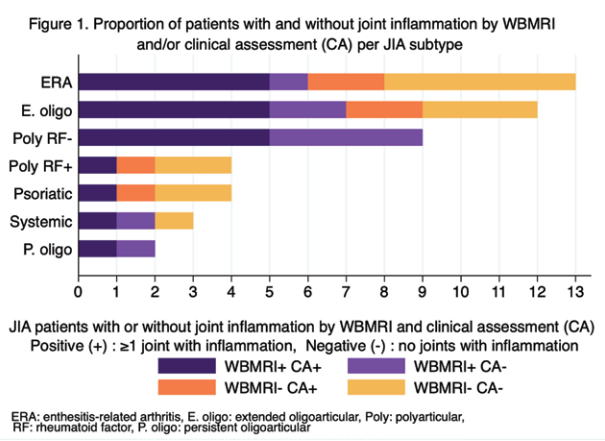
Background: Whole-body MRI (WBMRI) enables a comprehensive assessment of joint inflammation in children and young people (CYP) with juvenile idiopathic arthritis (JIA). The clinical relevance of WBMRI-detected inflammation in joints requires further assessment.
Objectives: To evaluate the frequency of WBMRI-detected subclinical joint inflammation in CYP with JIA and without inflammatory arthritis. To explore the relationship between WBMRI-detected and clinically detected joint inflammation in patients with JIA.
Methods: CYP aged 14-24 with JIA (any subtype) or non-inflammatory joint pain (controls) were prospectively recruited in a cross-sectional study. All participants underwent a Dixon-based WBMRI scan after being clinically assessed. Based on clinical findings, the CYP with JIA were divided into the active (≥1 active joint or sacroiliitis) and inactive group (no active joints or sacroiliitis). Three musculoskeletal radiologists blindly and independently reviewed the post-contrast images for joint inflammation, and this was considered present if detected by ≥2 radiologists. Peripheral joint inflammation was defined as above-normal intensity synovial enhancement with ≥1 additional feature (synovial hypertrophy, subarticular osteitis, joint effusion or periarticular soft tissue oedema). The frequency of subclinical joint inflammation (WBMRI-detected inflammation in ≥1 clinically inactive joint per participant) was compared between the control and JIA groups, and between the JIA subgroups using unpaired proportions.
Results: 47 CYP with JIA and 13 controls were included. The median age of participants was 17 years (IQR 16 to 20) with 62% and 85% female in JIA and controls respectively. Twenty-seven (57%) participants with JIA were treated with biologic disease-modifying anti-rheumatic drugs (DMARDs) and 29 (62%) with conventional synthetic DMARDs. The frequency of WBMRI-detected joint inflammation was higher in active than inactive JIA patients (Table 1). A higher percentage of patients with JIA were detected to have subclinical inflammation by WBMRI (49%, 23/47) compared to controls (15%, 2/13), difference of 34% (95% CI: 9, 58)). One joint with inflammation was detected by WBMRI in both controls, respectively. Fifty-six per cent (14/25) of JIA patients labelled active clinically had WBMRI-detected subclinical inflammation, compared to 41% (9/22) of clinically inactive JIA patients [difference: 15% (95% CI:-13, 43)]. The proportions of patients classified as active or inactive by both clinical and WBMRI assessment varied between JIA subtypes (Figure 1).
Conclusion: This study demonstrated that WBMRI-detected subclinical joint inflammation is a common finding in JIA, but rare in controls. Inflammation is more common in patients with clinically active compared with inactive disease.

This suggests that inflammation seen on WBMRI is a reflection of disease and not artefactual.

Table 1. Frequency of WBMRI-detected joint inflammation [n (%)] compared to clinical assessment

		Active JIA	Inactive JIA	Difference (95% CI)
WBMRI	**+**	19 (76%)	9 (41%)	35% (9%,62%)
	-	6 (24%)	13 (59%)	
	Total	25	22	

WBMRI +: participants with inflammation in ≥1 joint by WBMRI, WBMRI -: participants without joint inflammation on WBMRI. CI: confidence interval.



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POS0742 CLUSTERS OF JUVENILE PSORIATIC ARTHRITIS IDENTIFIED AT INITIAL PRESENTATION TO PAEDIATRIC RHEUMATOLOGY IN A NATIONWIDE UK COHORT

Keywords: Epidemiology, Artificial Intelligence, Psoriatic arthritis

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Background: The heterogenous presentation and variable clinical response of juvenile psoriatic arthritis (JPsA) to disease-modifying therapies suggests undiscovered subgroups within this disease. Nevertheless, JPsA is often studied under the umbrella of juvenile idiopathic arthritis (JIA), with few studies interrogating JPsA separately. To improve stratified treatment of this rare disease, such subgroups must be uncovered.
Objectives: To identify novel, phenotypically consistent subgroups of children and young people (CYP) with JPsA at the point of first contact with paediatric rheumatology.
Methods: CYP were initially selected if enrolled between January 2001 and December 2019 to the Childhood Arthritis Prospective Study, a UK, multicentre, prospective inception cohort of JIA. Those who had a physician's diagnosis of JPsA at any time point through the 10-year follow-up were included, to allow for onset of psoriatic signs after initial diagnosis. At initial presentation to paediatric rheumatology, clinical features within the ILAR classification criteria for JPsA were collected: an active joint count and the presence or absence of psoriasis, dactylitis and nail abnormalities. Latent class analysis used these features to identify clusters of disease. Between one and ten clusters were tested and an optimal model selected based on statistical fit.
Results: Of 1,753 CYP with JIA recruited to CAPS within the study period, a total of 161 CYP had ever had a diagnosis of JPsA (n=97 diagnosed as JPsA at initial presentation to paediatric rheumatology). The majority were female (61%), of white ethnicity (94%) and the median age at initial presentation was 10 years (IQR 6, 13). The optimal latent class model identified two clusters of JPsA. An oligoarticular cluster (90%, median active joint count (IQR): 2 (1,5)) had a higher proportion of CYP affected by psoriasis (Cluster 1: 29%, Cluster 2: 14%). A polyarticular cluster (10%, median active joint count (IQR): 20 (16, 27)) had a higher proportion with nail abnormalities (Cluster 1: 8%, Cluster 2: 27%). There were similar proportions of dactylitis among the clusters (Cluster 1: 18%, Cluster 2: 15%) (Figure 1).
Conclusion: This study identifies two clusters of JPsA at initial presentation to paediatric rheumatology with differences in key features used to classify this disease. Such subgroups may have different experiences of disease, and future analysis will explore characteristics, alongside disease impact and response to therapy for these groups.

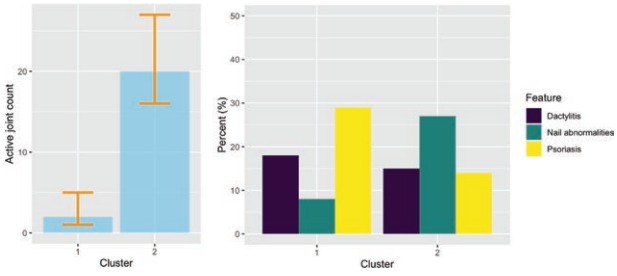


Figure 1. Characteristics of two JPsA clusters identified at initial presentation to paediatric rheumatology

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POS0743 THE DIAGNOSTIC AND PROGNOSTIC ROLE OF SYNOVIAL TISSUE ANALYSIS IN JUVENILE IDIOPATHIC ARTHRITIS: A MONOCENTRIC STUDY

Keywords: Synovium, Prognostic factors, Inflammatory arthritides

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Background: Juvenile idiopathic arthritis (JIA) refers to arthritis persisting for more than 6 weeks and presenting before 16 years. Once the diagnosis of JIA has been formulated, clinicians face challenges in tailoring the therapeutic approach upon each patient's clinical features. To date, no study has addressed the role of synovial pathobiology to support the diagnostic approach and guide clinical management in children.
Objectives: This study aimed at investigating the diagnostic role of synovial biopsy in children presenting with arthritis and assess the prognostic significance of synovial histology in predicting clinical outcomes among patients with JIA.
Methods: Medical records of pediatric patients undergoing synovial biopsy between 1995 and 2020 were retrospectively reviewed. Synovial samples were analyzed histologically and immunohistochemically.
Results: Of 99 patients included, synovial biopsy was performed for diagnostic purposes in 65 cases allowing to correctly classify 79% of patients. At histological

analysis on 42 JIA samples, any difference emerged between JIA subsets (Table 1) or treatment-naïve and treatment-experienced subjects. Tissue analysis predicted subsequent disease course: higher number of layers of synovial lining predicted a worse disease course (>4 flares during follow-up) (median 4.5 [IQR 3.0] vs. 3.0 [IQR 2.5], p=0.035), even after adjusting for age at diagnosis and observation time (OR 2.2, 95% CI 1.3-3.9, p=0.007); subjects who had switched >2 bDMARDs had higher prevalence of subsynovial elementary lesions (55.6% vs 10.3%, p=0.005) and fibrin deposits in synovial lining (60.0% vs 22.6%, p=0.049), even after adjustment for observation time and age at diagnosis (OR 8.1, 95% CI 1.03-64.2, p=0.047). At immunohistochemistry on 31 JIA samples, higher CD3 expression was described in polyarticular compared to oligoarticular subset (p=0.040), while no differences were found between persistent and extended oligoarticular subsets (p=0.670). Patients with severe disease course had higher CD20+ cells percentage (OR 7, 95% CI 1.4–35.5, p=0.023), regardless of JIA subset and treatment exposure (Figure 1).

Conclusion: The present study offers several novel insights into the potential role of synovial pathobiology in JIA. Synovial tissue analysis might support the clinicians in the diagnostic approach of pediatric patients presenting with arthritis and guide the clinical management of JIA.

Table 1. Synovial morphological and immunohistochemical features in the overall population and within JIA subtypes.

	Oligo	Poli RF-	ERA	PsA	Systemic	Overall population
Morphologic						
Layers of synovial lining (score), median (IQR)	3.0 (2.0) (n=26)	2.8 (2.4) (n=6)	6.0 (3.0) (n=4)	5.5 (0.0) (n=1)	4.0 (1.0) (n=3)	3.5 (2.6) (n=40)
Subsynovial elementary lesions, % (n)	n=24	n=6	n=4	n=1	n=3	n=38
Edema	33 (8)	50 (3)	25 (1)	0 (0)	0 (0)	32 (12)
Fibrosis	50 (12)	50 (3)	50 (2)	0 (0)	33 (1)	47 (18)
Edema+fibrosis	17 (4)	0 (0)	25 (1)	100 (1)	67 (2)	21 (8)
Fibrin deposit, % (n/N)	33 (9/27)	17 (1/6)	25 (1/4)	0 (0/1)	67 (2/3)	32 (13/41)
Krenn synovitis score, median (IQR)	6.0 (1.5) (n=24)	5.0 (3.5) (n=6)	6.0 (2.3) (n=4)	7.0 (0.0) (n=1)	7.0 (2.5) (n=3)	6.0 (3.0) (n=38)
Inflammatory infiltrate (score), median (IQR)	2.0 (1.0) (n=27)	1.5 (1.0) (n=6)	2.0 (1.0) (n=5)	2.0 (0.0) (n=1)	2.0 (1.0) (n=3)	2.0 (1.0) (n=42)
Immunohistochemistry	n=22	n=5	n=3	n=1	n=0	n=31
CD3 ≥40% % (n)	41 (9)	100 (5)	33 (1)	0 (0)	-	48 (15)
CD20 ≥40% % (n)	32 (7)	20 (1)	67 (2)	0 (0)	-	32 (10)
CD69 ≥40% % (n)	23 (5)	40 (2)	0 (0)	0 (0)	-	23 (7)
CD103 ≥40% % (n)	5 (1)	0 (0)	0 (0)	0 (0)	-	3 (1)

JIA= juvenile idiopathic arthritis; Oligo= oligoarticular; Poly FR -= polyarticular rheumatoid factor negative; ERA= enthesitis arthritis; PsA= psoriatic arthritis.

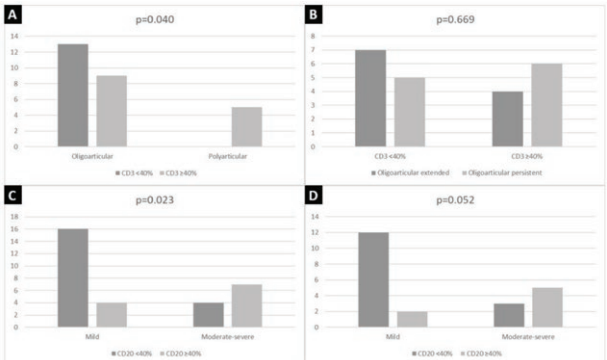


Figure 1. (A) CD3+ infiltrate in oligoarticular and polyarticular JIA; **(B)** CD3+ infiltrate in persistent and extended oligoarticular JIA; **(C)** Correlation between the percentage of CD20+ B cells and the severity of disease in all JIA subtypes; **(D)** Correlation between the percentage of CD20+ B cells and the severity of disease in oligoarticular group only.

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POS0744

MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN ACROSS 16 LATIN AMERICAN COUNTRIES: A MULTICENTER STUDY FROM THE REKAMLATINA NETWORK

Keywords: COVID

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Background: Multisystem Inflammatory Syndrome in Children (MIS-C) is one of the most feared complications following SARS-CoV2 infection in children and adolescents. Few multinational multicenter studies from Latin America have been published.
Objectives: To describe the clinical presentation, management, and outcomes of MIS-C in Latin America.
Methods: Observational, prospective and retrospective, multicenter study to gather information from 84 participating centers across 16 Latin American countries, between August January 1, 2020 and June 30, 2022.
Results: Of the 1,239 reported cases of MIS-C, 84.2% were previously healthy. The most frequent clinical manifestation in our studied population was abdominal pain (N=804, 64.9%), followed by conjunctival injection (N=784, 63.3%). The median days of fever at the time of hospital admission was 5 and a significant number of subjects required admission to an intensive care unit (N=589, 47.8%). A total of 538 (47.2%) patients had an abnormal initial echocardiogram. Most of the subjects (N= 1,096, 88.7%) were treated with intravenous immunoglobulin

(IVIG), while 76.7% (N= 947) were treated with steroids, of which 10.6% (N= 100) did not receive IVIG. The death rate attributed to MIS-C was 4.88%, with a rate of 3.39% for those initially diagnosed with MIS-C and 8.85% for those whose admission diagnosis was not MIS-C (*P= 0.00001)*.

Conclusion: One of the most significant findings from our study was the death rate, especially in those not initially diagnosed with MIS-C, in whom it was higher. This highlights the importance of increasing awareness and making an earlier diagnosis of MIS-C in Latin America.

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Disclosure of Interests: None Declared.

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POS0745 THE INCIDENCE AND PREVALENCE OF JUVENILE IDIOPATHIC ARTHRITIS DIFFERS BETWEEN ETHNIC GROUPS IN ENGLAND

Keywords: Epidemiology, Gender/diversity issues

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Background: Juvenile Idiopathic Arthritis (JIA) is a heterogenous group of autoimmune disorders characterised by chronic joint inflammation, affecting children and young people (CYP) under the age of 16. Recent analysis in the UK has updated estimates of the incidence and prevalence of JIA, but the association between ethnicity and JIA has not been investigated in the UK context. Differential rates between ethnic groups could be indicative of underlying biological differences and/or health inequities. Health inequities (avoidable systemic differences in health outcomes for different population groups) may lead to specific ethnic groups being less likely to be referred resulting in delays in diagnosis and apparent differences in incidence rates.

Objectives: To calculate and compare the incidence and prevalence rates of JIA in different ethnic groups in England.

Methods: CYP with JIA were identified in anonymised electronic primary care records (the Clinical Practice Research Datalink (CPRD) Aurum database) using pre-defined read code lists between 1995 and 2011. Cases were further validated through linked Hospital Episode Statistics (HES) data with either >=3 outpatient specialist care (rheumatology/paediatric rheumatology) appointments or a HES inpatient admission coded with JIA, prior to age 16. Ethnic group was extracted from CPRD/HES records and aggregated to broad ethnic groups, as defined by the Office for National Statistics (ONS). Incidence and prevalence rates by broad ethnic group were calculated using CYP under the age of 16 in CPRD, as of December 2011. Indirect standardisation was performed by age and region using ONS Census 2011 data, to account for varying ethnic make-up across different age groups and regions of England. The distribution of observed JIA cases across ethnic groups was subsequently compared with the expected distribution based on population statistics using Chi2.

Results: A total of 314 incident cases were identified in CYP <16y between January 1995 and December 2011 using code lists. The overall age and region indirectly standardised incidence rate was 4.3 per 100,000 population age <16y, varying from 4.7 for White CYP to 1.1 for CYP with Mixed ethnic group. A total of 268 HES-validated cases were identified, giving an indirectly standardised incident rate of 4.3 per 100,000 population age <16y, varying from 4.8 for White CYP to 0.9 for CYP with Mixed ethnic group. In December 2011 there were 471 prevalent cases from code lists (381 validated using HES). The indirectly standardised prevalence rate was 35 per 100,000 CYP under the age of 16 (31 for validated cases), varying from 38 (34) for White CYP to 11 (11) for CYP with Mixed ethnic group.

Table 1. Standardised incidence and prevalence of JIA in CYP by ethnic group in England

Ethnic group	All	White	Mixed	Asian	Black
Proportion of CYP <16y:					
England general 2011, %	-	78.1	5.4	10.2	5.0
JIA, % (95% CI) †	-	86.9 (83.2, 90.7)	1.3 (0.0, 2.5)	7.0 (4.2, 9.8)	1.9 (0.4, 3.4)
Observed:Expected ratio		1.1	0.3	0.7	0.4
Incidence per 100,000 person years CYP <16y, 2011 (95% CI)	4.3 (3.8, 4.8)	4.7 (4.1, 5.3)	1.1 (0.3, 2.8)*	3.0 (1.9, 4.6)	1.7 (0.6, 3.7)*
Prevalence per 100,000 CYP <16y, 2011 (95% CI)	35.1 (32.0, 38.5)	38.3 (34.7, 42.3)	10.8 (4.6, 21.4)*	24.3 (16.8, 33.9)*	24.1 (14.0, 38.6)

* Statistically significant when compared to 'White' ethnic group (p<.05). † Statistically significant when compared to ethnic group distribution in general population, p<.001 Chi-Square.

Conclusion: The incidence and prevalence of JIA amongst CYP in England differs by ethnic group, being highest amongst 'White' CYP and lower amongst other ethnic groups, and is not in keeping with the known distribution of ethnic groups in the <16y England population. Understanding whether this reflects a health inequity or differences in the underlying biology of JIA needs further evaluation.

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Disclosure of Interests: None Declared.

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POS0746 CONTRIBUTION OF GENETIC VARIANTS ASSOCIATED WITH PRIMARY IMMUNODEFICIENCIES IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS

Keywords: Systemic lupus erythematosus, Genetics/epigenetics

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Background: Dysregulated immune response is the hallmark of autoimmune disorders[1]. Evidences suggested that systemic autoimmune diseases and primary immunodeficiency disorders (PID) may be similar diseases with alternative clinical phenotypes[2].

Objectives: This study aimed to investigate the burden of PID associated genetic variants in the childhood-onset systemic lupus erythematous (cSLE) patients.

Methods: One hundred and eighteen cSLE cases regularly followed at Chang-Gung memorial hospital were enrolled. Targeted next-generation sequencing was applied searching for PID genetic variants. Genetic variants were compared to those of 1,475 unrelated healthy individuals and further filtered by allelic frequency and various functional score systems. Customized immune assays were applied to test the function of the identified variants.

Results: Upon filtration, 36 (30.5%) patients harbored rare variants in PID-associated genes predicted to be damaging. One homozygous *TREX1* (c.294dupA) mutation and four heterozygous variants with possible dominant PID traits, including *BCL11B* (c.G1040T), *NFKB1* (c.T695G), and *NFKB2* (c.G1210A, c.G1651A), were discovered. With recessive traits, variants were found across all PID types; one-fifth involved phagocyte number or function defects. Predicted pathogenic PID variants were more predominant in those with a family history of lupus regardless of infection susceptibility. Moreover, mutational loads were greater among cSLE patients than controls despite sex or age at disease onset. While greater mutational loads were observed among cSLE patients with peri-pubertal disease onset, no significant difference in sex or phenotype were noted among cSLE patients.

Conclusion: Our findings suggest that cSLE is mostly not a monogenic condition. Gene-specific analysis and mutational load investigations suggested that while rare and predicted damaging variants in immunodeficiency related genes may contribute to cSLE susceptibility, genetic investigations of PID disorders may not be warranted for cSLE patients with recurrent infections.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0747 CORRELATIONS BETWEEN CAPILLARY DENSITY AND DEGREE OF SKIN PIGMENTATION IN HEALTHY CHILDREN ANALYSED BY NAILFOLD VIDEO CAPILLAROSCOPY

Keywords: Skin, Imaging, Diagnostic tests

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Genova, IRCCS Polyclinic San Martino Hospital, Laboratory of Experimental Rheumatology and Academic Division of Clinical Rheumatology, Department of Internal Medicine and Medical Specialties, Genova, Italy

Background: Nailfold Video Capillaroscopy (NVC) is a simple, non-invasive diagnostic tool but studies with normal values for capillary density in healthy children are rare. Ethnic background seems to play a role in capillary density; however, this is not well substantiated yet [1,2].
Objectives: In this work, we set out to evaluate influence of ethnic background/skin pigmentation and age on capillary density reading in healthy children. Secondary aim was to investigate whether there is a significant difference in density between different fingers within the same patient.
Methods: Capillaroscopic images from healthy children were obtained in a one-time visit videocapillaroscopy (x200 magnification) addressing the capillary density (i.e. number of capillaries per linear millimeter in the distal row). This parameter was compared to age, sex, ethnicity, skin pigment grade (I-III) and between eight different fingers, excluding the thumbs.
Results: We investigated 145 healthy children with mean age of 11.03 years (SD 3.51). The range of capillary density was 4-11 capillaries per millimetre. We observed a lower capillary density in the 'grade II' (6.4 ± 0.5cap/mm, p<0.001) and 'grade III' (5.9 ± 0.8 cap/mm, p<0.0001) pigmented-classified groups compared to the 'grade I' group (7.0 ± 0.7 cap/mm). We did not find a significant correlation between age and density in the overall group. The fifth fingers on both sides had a significantly lower density compared to the other fingers.
Conclusion: Healthy children <18 years with higher degree of skin pigmentation show a significantly lower nailfold capillary density. In subjects with an African/Afro-Caribbean and North-African/Middle-Eastern ethnicity, a significantly lower mean capillary density was observed compared to subjects with the Caucasian ethnicity (p<0.0001, and p<0.05, respectively. There were no significant differences between other ethnicities. No correlation was found between age and capillary density. The fifth fingers on both hands displayed lower capillary density compared to the other fingers. This needs to be taken into account when describing lower density in paediatric patients with connective tissue diseases.
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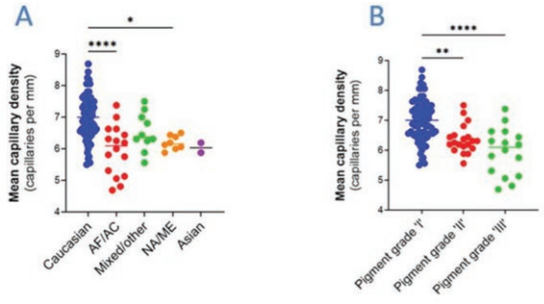


Figure 1. Differences in capillary density between ethnicities and pigment grades.

A) Mean capillary density for each ethnicity depicted as categorical variable.

B) Mean capillary density per pigment group (ordinal variable). Individual data points represent mean capillary density scores for each included subject.

* p < 0.05, ** p<0,005, *** p <0.001, **** p < 0.0001, calculated by Sidak's corrected ANOVA.

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POS0748 TOWARD THE DEFINITION OF CUTOFF VALUES FOR DISEASE ACTIVITY STATES IN SYSTEMIC JADAS

Keywords: Outcome measures, Treat to target

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Background: Systemic juvenile idiopathic arthritis (sJIA) accounts up to 15 % of all patients with JIA and is distinct from the other disease categories due to the association of articular and extraarticular manifestations. The systemic Juvenile Arthritis Disease Activity Score (sJADAS) is a composite disease activity score validated specifically for use in sJIA that includes, beside the four components of the original JADAS, a fifth item aimed to quantify the burden of systemic features. The interpretation of scores on sJADAS requires criteria that identify the states of disease activity. These criteria can be used to monitor the disease course over time and to define therapeutic targets.
Objectives: To compare the clinical and laboratory data of each disease activity state in patients enrolled in the multinational study aimed to define the sJADAS cutoffs.
Methods: Data were extracted from a multinational cross-sectional dataset that included patients diagnosed as sJIA by ILAR criteria, recruited between February 2022 and November 2022. At study visit, each patient was categorized subjectively by the caring physician into one of the following disease activity states: inactive disease (ID), low (or minimal) disease activity (LDA), moderate disease activity (MDA), or high disease activity (HDA). Study data was collected through a standard case report form and entered into an electronic database.
Results: A total of 231 patients were enrolled in 29 centers in 12 countries. The mean age at diagnosis was 5.63 years. 87 patients (37.7%) were judged as having ID, 39 (16.9%) LDA, 46 (19.9%) MDA and 59 (25.5%) HDA. The comparison of the main clinical and laboratory features across patients with the four disease activity states is shown in the Table 1. Overall, the presence of extraarticular manifestations was more common in patients with MDA and HDA (P<0.00001), whereas fever, rash, hepatosplenomegaly, and lymphadenopathy were more frequent in HDA patients (<0.00001). The count of active joints increased progressively from ID to HDA (p<0.00001). The mean values of physician global assessment of disease activity and systemic manifestations, as well as the mean values of acute phase reactants, were highest in patients with HDA, with gradual decrease from MDA to LDA to ID.
Conclusion: This preliminary analysis of the study data indicates that the subjective assessment of disease state by the caring physicians led to discriminate reliably patients with different level of disease activity. This evaluation will, then, serve well as reference for the subsequent analyses aimed to identify the cutoffs for the main disease activity states in sJIA.
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Table 1. Comparison of clinical and laboratory features across disease activity states (n = 231). ID=inactive disease; LDA= low (or minimal) disease activity; MDA=moderate disease activity; HDA=high disease activity; MD global VAS=physician global assessment of disease activity; MD systemic VAS= physician global assessment of systemic disease activity; ESR= erythrocyte sedimentation rate; CRP= C-reactive protein; NAJ=Number of active joints.

	ID	LDA	MDA	HDA
Number of patients (n, %)	87 (37.7)	39 (16.9)	46 (19.9)	59 (25.5)
Age at onset, years (mean, SD)	6.17 (4.24)	5.44 (3.06)	5.11 (3.42)	5.36 (4.06)
MD global VAS (mean, SD)	1.08 (2.64)	2.5 (2.59)	5.03 (2.59)	6.61 (2.91)
MD systemic VAS (mean, SD)	0.06 (0.23)	0.88 (1.13)	3.08 (2.69)	7.52 (2.17)
Systemic features (n,%)	1 (1.1)	7 (17.9)	22 (47.8)	56 (94.9)
• Fever	0 (0)	0 (0)	19 (41.3)	55 (93.2)
• Rash	0 (0)	4 (10.3)	9 (19.6)	29 (49.2)
• Hepatomegaly	0 (0	0 (0)	2 (4.3)	21 (35.6)
• Splenomegaly	0 (0)	1 (2.6)	4 (8.7)	14 (23.7)
• Lymphadenopathy	1 (1.1)	2 (5.1)	5 (10.9)	20 (33.9)
• Serositis	0 (0)	0 (0)	4 (8.7)	9 (15.3)
ESR, mm/h (mean, SD)	8.46 (7.63)	16.26 (14.43)	46.11 (34.53)	66.85 (32.4)
CRP, mg/dl (mean, SD)	0.39 (0.85)	0.88 (1.93)	5.17 (7.03)	7.89 (6.06)
NAJ > 1 (%)	1 (1.1)	13 (33.3)	34 (73.9)	53 (89.8)

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POS0749 TRANSITION READINESS AMONG FINNISH ADOLESCENTS WITH JIA

Keywords: Patient information and education, Self-management, Outcome measures

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Background: Juvenile idiopathic arthritis (JIA) is the most common persistent rheumatic condition in children [1]. It's nature is chronic (2) and in our own study 40% of patients were transferred to adult clinic when they reached the transition age [3]. A successful transition requires sufficient self-management skills to manage one´s chronic condition and all the tasks involved in it [4]. There are multiple practices to establish the transition readiness and self-management among the adolescents [5].

Objectives: The purpose of our study was to evaluate transition readiness in Finnish patients with JIA and estimate the usefulness of a specific questionnaire. We aimed to find forecasting values for a successful transition and study the possible consequences of an unsuccessful transition to the disease outcome.

Methods: Our questionnaire was inspired by the Canadian Good2Go questionnaire (www.sickkids.ca/en/patients-visitors/transition-adult-care), and it was part of the routine rheumatological visits in our clinic. Eighty-three patients filled it in between June 2011 and December 2013. The questionnaire was given to patients who were likely to be transferred into an adult clinic, that is patients with a long history of ongoing disease activity and ongoing medication. The questions evaluate the self-management in several aspects, e.g., independence in the disease management (medication, appointments, pain control), everyday life (school, future educational plans, mental support, exercise, sexual health), and substance abuse. We used 13 questions with three answer options (yes =2, partly= 1, or no= 0), higher score indicating better readiness. Patients filled in the questionnaire in the pediatric site. We also gathered information from the first adult visit to assess the success of the transition and its relation to disease activity. The transition was defined successful when the patient attended the first visit at an adult care independently, as scheduled, and the medication was carried out as agreed at last pediatric visit.

Results: The cut-off score for a successful transition by ROC-analysis was 24 (OR 6.11 (95% CI: 1.71 to 1.43)). That is, the best estimate for successful transition is when the score is 24 or more. We were able to receive all necessary information to define the success of the transition from 77 patients. In 55 (71%) patients the transition was estimated as a successful. The mean score 22,5 (SD 2,2) in the transition readiness questionnaire is shown in the Figure 1. Seven patients (9 %) received the maximum score.

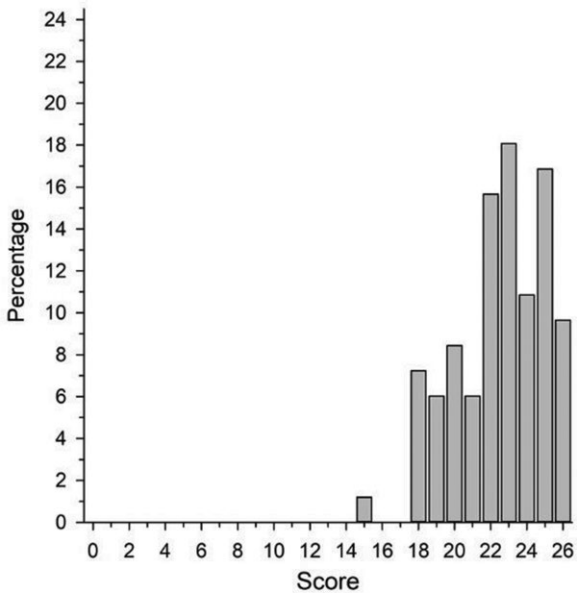


Figure 1. The distribution of scores in the transition readiness questionnaire

At the first adult visit, the DAS28 was assessed in 58 patients. If the transition was defined as unsuccessful (score<24), the DAS28 was higher, mean 2.21 (SD 1.14) and if the transition was defined as successful (score≥24) the DAS28 was better, mean 1.35 (SD 0.48), p<0.001.

Conclusion: We found this questionnaire a useful tool to evaluate transition readiness. Determination of a successful transition helps us to discover those adolescents who need more profound support to improve their self-management skills and thus enhance their transition process. An unsuccessful transition has also impact on disease outcome.

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POS0750 RELATIONSHIP OF CLINICAL AND PATIENT-REPORTED OUTCOMES WITH IMAGING MEASURES OF SYNOVITIS IN JUVENILE ARTHRITIS

Keywords: Patient reported outcomes, Inflammatory arthritides, Ultrasound

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Background: In children with JIA, the use of outcomes measures for the assessment of disease course and health-related quality of life (HRQL) contribute to improvement of the quality of care provided. However, these subjective outcome measures do not always accurately reflect the inflammatory disease burden and may be influenced by comorbid conditions. Musculoskeletal ultrasound (MSUS) and contrast-enhanced MRI imaging measures of synovitis provide an objective assessment of JIA disease activity. A novel MSUS score for knee arthritis (MSUS-knee score) showed strong correlation with the combined Juvenile Arthritis MRI Scoring (JAMRIS) system in children with JIA[1].
Objectives: To determine the relationship of clinical and patient-reported outcomes (PROs) measures with the MSUS-knee score and the JAMRIS system in children with JIA.
Methods: Children with a diagnosis of JIA who received a MSUS of the knee(s) were enrolled. Data collected included knee physical examination findings, disease activity assessment, the Child Health Assessment Questionnaire (CHAQ) and the pediatric PROMIS Mobility measure (t-score mean 50, standard deviation 10). The following measures were asked to the patients specifically for the examined knee: pain, swelling and morning stiffness. A comprehensive knee MSUS examination was performed on all participants by MSUS certified pediatric rheumatologist. MSUS images were scored by pediatric MSUS experts, who were blinded to clinical information using a semiquantitative scoring system (0-normal to 3-severe)[1]. The MSUS-knee score was calculated by adding the abnormal B-mode MSUS scores (score 2 or 3) and the power doppler MSUS scores (score 1 to 3) from the 3 views of MSUS-knee (MSUS-knee score range: 0-15)[1]. A subset of participants received an MRI with and without contrast of the knee. MRI of the knee was scored for presence and severity of synovial thickening and joint effusion as per JAMRIS system[2]. Associations between clinical and PROs outcome measures and imaging measures were assessed using Spearman's Correlation Coefficient.
Results: Forty-eight children (mean age of 12.1 years) contributed 60 visits. Twenty-four knee MRIs were obtained following MSUS of the knee. Patient reported presence of knee swelling was strongly correlated with the MSUS-knee score and moderately correlated with the JAMRIS system. No other significant statistically associations were found between PROs assessing lower extremity pain and physical function, and overall disease status with imaging measures (Table 1).
Conclusion: Imaging measures of JIA disease activity could provide a more accurate assessment of JIA disease state, given low correlation with commonly used outcome measures. Integration of imaging measures into the shared decision-making in daily clinical practice may improve the quality of medical care. Future studies with a larger population are required.

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Table 1. Correlations of Outcomes Measures with Imaging Measures of Synovitis in JIA

		MSUS-knee score	JAMRIS system
cJADAS10[a]		0.24 (0.102)	0.15 (0.501)
Md Global[b]		0.11 (0.547)	-0.04 (0.917)
PGA[c]		0.12 (0.414)	0.18 (0.425)
CHAQ		-0.11 (0.393)	0.17 (0.438)
PROMIS Mobility		0.13 (0.439)	-0.14 (0.523)
Knee-specific symptoms	**Pain (0-10)**	0.00 (0.990)	-0.03 (0.898)
	Joint swelling (y/n)	0.62 (<0.001)	0.53 (0.011)
	Morning stiffness (<15, 15-30, 31-60, >60 min)	0.08 (0.557)	0.10 (0.669)

[a] Clinical-Juvenile Arthritis Disease Activity Score-10: sum of the scores of the [b]physician's global assessment of disease activity (Md global: 0- no activity to 10- maximum activity), [c]patient/parent global assessment of well-being (PGA: 0- very well to 10- very poor), and the active joint count (AJC) up to 10 joints.

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POS0751

PHARMACOKINETICS OF UPADACITINIB IN PEDIATRIC PATIENTS WITH POLYARTICULAR COURSE JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Targeted synthetic drugs, Clinical trials, Disease-modifying drugs (DMARDs)

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Background: Upadacitinib is a Janus kinase inhibitor with preferential inhibition of JAK1 over other JAK isoforms that has been approved for the treatment of adults with moderate to severe rheumatoid arthritis (RA). Children with polyarticular course juvenile idiopathic arthritis (pcJIA) have similar clinical presentations compared to adult RA. In Phase 3 RA studies in adult patients, the median (5^{th}, 95^{th} percentiles) model-estimated area under the plasma upadacitinib concentration curve AUC over 0-24 hours (AUC_{0-24}) at steady state were 362 (216, 785) and 720 (434, 1531) ng·h/mL after multiple 15 mg and 30 mg once daily (QD) doses, respectively.
Objectives: The objective of this analysis was to characterize upadacitinib pharmacokinetics from a Phase 1 study in children with pcJIA.
Methods: Patients (N = 51) diagnosed with pcJIA were enrolled into one of four groups in an open-label, multiple-dose study (Group 1, 12 to < 18 years, low dose; Group 2, 12 to < 18 years, high dose; Group 3, 6 to < 12 years, low dose; Group 4, 2 to < 6 years, low dose). The low and high doses were selected to provide comparable plasma exposures in pediatrics to 15 mg and 30 mg QD doses of ER tablet formulation in adults, respectively. Patients received bodyweight-based upadacitinib doses either as twice-daily (BID) immediate-release (IR) oral solution or QD extended-release (ER) tablet formulation. Pharmacokinetic assessment was performed at steady state on Study Day 7, after which all patients might continue the study with low dose.
Results: Summary of the demographics of the enrolled patients are shown in Table 1. Pharmacokinetic results from 49 patients with evaluable drug concentrations on Study Day 7 were reported. In Group 1, the geometric mean upadacitinib maximum plasma concentration (C_{max}) and AUC_{0-24} at steady state were 35.1 ng/mL and 269 ng·h/mL, respectively. In Group 2, the geometric mean upadacitinib C_{max} and AUC_{0-24} were 69.8 ng/mL and 553 ng·h/mL, respectively. In Group 3, the geometric mean upadacitinib C_{max} and AUC_{0-24} were 51.0 ng/mL and 346 ng·h/mL, respectively. In Group 4, the geometric mean upadacitinib C_{max} and AUC_{0-24} were 46.6 ng/mL and 369 ng·h/mL, respectively. The median time to maximum upadacitinib concentration was approximately 3 hours and 1 hour; and the harmonic mean functional half-life was approximately 5 hours and 2 hours for the QD ER tablet and the BID IR solution regimens, respectively. Upadacitinib apparent oral clearance increased in pcJIA patients with increasing bodyweight. The mean upadacitinib plasma concentration-time profiles of each group are presented by dosing regimen in Figure 1.
Conclusion: Upadacitinib plasma exposures in pediatric patients with pcJIA were comparable to adult RA patients at the evaluated dosing regimens with the ER tablet or IR solution and at both low and high dose levels. These results support the use of the current bodyweight-based dosing regimen in upadacitinib pediatric studies.

Table 1. Demographics Summary of Enrolled Pediatric pcJIA Patients

		Group 1 (N = 9)	Group 2 (N = 9)	Group 3 (N = 19)	Group 4 (N = 14[a])
Age[b] (years)	Mean ± SD	14.9 ± 1.5	13.9 ± 1.2	9.5 ± 1.6	3.6 ± 1.5
	(Range)	(13 – 17)	(12 – 16)	(6 – 12)	(2 – 6)
Weight (kg)	Mean ± SD	61.3 ± 14.6	51.7 ± 13.0	37.8 ± 14.4	15.1 ± 3.2
	(Range)	(42.0 – 92.9)	(32.5 – 71.5)	(19.7 ± 72.1)	(11.0 ± 22.5)
Sex	Male, N (%)	2 (22.2)	1 (11.1)	4 (21.1)	3 (21.4)
	Female, N (%)	7 (77.8)	8 (88.9)	15 (78.9)	11 (78.6)
Dose Form	Oral Solution, N (%)	0 (0.0)	0 (0.0)	7 (36.8)	14 (100.0)
	Tablet, N (%)	9 (100.0)	9 (100.0)	12 (63.2)	0 (0.0)

a.Two patients were excluded from pharmacokinetic analysis. One patient mistakenly received half dose and the other patient had incomplete PK sample collection.b.Age was determined at the time of screening.

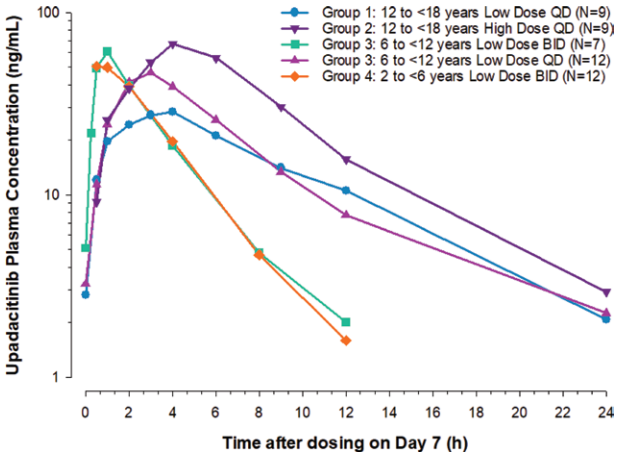


Figure 1. Mean Upadacitinib Plasma Concentration-Time Profiles in Pediatric pcJIA Patients

REFERENCES: NIL.
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POS0752 MUSCULOSKELETAL INVOLVEMENT IMPAIRS QUALITY OF LIFE IN JUVENILE PSORIATIC ARTHRITIS

Keywords: Quality of life, Psoriatic arthritis, Ultrasound

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Background: Juvenile psoriatic arthritis (JPsA) is one of the least common subtypes of JIA. Information on JPsA is mainly clinical, but scarce regarding the impact of musculoskeletal involvement on children's quality of life.
Objectives: To describe the clinical and ultrasound (US) characteristics of children with JPsA, and to assess their impact using a composite quality of life index, the PsAID (Psoriasis Arthritis Impact of Disease).
Methods: A multicentre cross-sectional observational study recruited consecutive JPsA patients, from January-2020 to May-2022. Inclusion criteria: 1/ age at onset ≤ 16 years, 2/ diagnosis by the prescribing physician based on one of the 2 JPsA diagnostic classification systems (ILAR or Vancouver). All were assessed clinically and US (independently) and completed two questionnaires: PsAID (1) and Child Health Assessment Questionnaire (CHAQ, to measure physical disability). Statistics included correlation Spearman (rho) and PsAID was identified as the dependent variable.
Results: The 48 children included (mean age at inclusion 11±4 years), 71% girls, 67% had oligoarthritis and 80% psoriasis in a first or second-degree relative. Mostly arthritis started before the psoriasis. The median time lag between the diagnosis and the onset of specific musculoskeletal manifestations was 1 year; interquartile range 0.5-2. ANA and HLAB27 were present in 19 (40%) and 5 (10%) of the children, respectively. A history of axial inflammatory symptoms was present in 3 (5%) patients, and unilateral sacroiliitis was confirmed by MRI in only one patient. Psoriasis and dactylitis were the most frequent manifestations identified (≥50%), while uveitis was less common (12%). Twenty-eight (58%) patients used methotrexate, 21 used anti-TNF agents and 14 needed corticosteroid infiltration. The population showed low clinical activity in the DAPSA composite activity index (md 3.5; range 0-25). Similarly, US showed a low number of affected joints but US was slightly superior to clinical examination, while US was clearly superior to detect enthesitis and tenosynovitis, particularly tendons of the fingers. The PsAID index (median 0.4; range 0-9.2) showed low correlation with CHAQ (r 0.3) and high with DAPSA (r 0.7); however, the correlation between PsAID and total joint count was low for both clinical and US assessment (r 0.4). The correlation between PsAID and total joint count was moderate for clinical (r 0.5) and low for US (r 0.4). Children with the presence of enthesitis and clinical dactylitis had a higher mean PsAID score than those without (dactylitis; p=0.002, and enthesitis; p<0.001).
Conclusion: The study supports the existence of an atypical pattern of late-onset JPA characterised by a predominance of girls with peripheral involvement and little uveal involvement. Based on our results, dactylitis and enthesitis have a greater impact on the child's quality of life than joint involvement per se. Studies with a larger sample size and/or disease activity are needed to confirm these findings.
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Acknowledgements: Sociedad Española de Reumatología Pediátrica (SERPE)
Disclosure of Interests: None Declared.
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POS0753 TIF1-GAMMA IGG2 ISOTYPE IS ASSOCIATED WITH ETHNICITY IN JDM PATIENTS

Keywords: Myositis, Autoantibodies, Descriptive studies

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Background: Dermatomyosis is an autoimmune disease that can present in children, adolescents (juvenile dermatomyosis JDM), and adults (adult dermatomyositis DM). The pathological hallmarks of DM are similar between JDM and adult DM, including skin rashes and proximal muscle weakness, however, the manifestations and prevalence of associated autoantibodies vary, depending on age of onset. Myositis specific antibodies (MSA) have been used as a prognostic tool to aid management of disease in both adult DM and JDM. In JDM, anti-TIF1γ is highly prevalent, and is the most common MSA in Caucasian patients. This MSA is associated with malignancy in adult DM [1]. We have previously shown that adult DM patients with cancer have significantly higher frequency and serological level of anti-TIF1γ IgG2 isotype [2]. However, there are limited data on anti-TIF1γ isotypes in JDM.
Objectives: To investigate anti-TIF1γ isotypes as a potential biomarker for clinical manifestations in JDM.
Methods: We conducted a retrospective study to evaluate clinical features of anti-TIF1γ positive patients. This cohort includes 20 patients from French healthcare centres and 11 patients from the UK healthcare centres. Serum samples were first tested for anti-TIF1γ using either lineblot or immunoprecipitation. Within those with anti-TIF1γ antibodies, anti-TIF1γ isotypes including IgG1, IgG2, IgG3 and IgG4 were measured using a multiplex ALBIA assay developed by Aussy et al. (2019) [2].

Results: Out of 31 children, 54.8% (17) were Caucasian, followed by North African (25.8%, n=7), and other minority groups. Male to female ratio was 14/17. All 31 patients had IgG1 isotype, and 14 had more than one isotype of anti-TIF1γ antibody. Although IgG2 isotype of anti-TIF1γ has been shown to be a biomarker for malignancy and mortality in adult DM, there were no reports of malignancy in this paediatric cohort. In our JDM cohort, the rate of IgG2-positive was 25.8% (8/31) which is lower than observed in adult DM of 55% [2]. Two cases in this JDM cohort died: both were positive for IgG4, but both were negative for IgG2.
Interestingly, there were significant differences regarding IgG2 isotype of anti-TIF1γ antibody presence between ethnic groups (p = 0.008). Specifically, although Caucasian patients were the majority, only 1 out of 8 IgG2 positive cases was Caucasian. Between Caucasian and non-Caucasian groups, significant differences were observed when comparing the groups' means (p = 0.02) and variances (p = 0.01). Notably, 4/8 IgG2 positive were found in North African population, making up 44.4% (4/9) of this ethnic group. We also showed that anti-TIF1γ isotypes can change over time. Specifically, of 6 patients tested for anti-TIF1γ isotypes at a second time point, 4 cases had changes in serological levels of anti-TIF1γ isotypes: 2 had lower titer levels, 1 lost positive status for IgG2 and IgG3, and 1 gained positive status for IgG4.
Conclusion: Our study indicates that there may be a relationship between anti-TIF1γ IgG2 isotype and ethnicity. Importantly, although IgG2 is a biomarker for cancer in adult DM, it is not associated with severe onset or manifestations such as mortality or malignancy in JDM patients.
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POS0754 PROTEASOME ACTIVITY TEST AS A POTENTIAL CLINICAL TOOL FOR THE DIAGNOSIS OF CHRONIC ATYPICAL NEUTROPHILIC DERMATOSIS WITH LIPODYSTROPHY AND ELEVATED TEMPERATURE (CANDLE) SYNDROME AND RELATED PROTEASOME DISORDERS

Keywords: Diagnostic tests, Rare/orphan diseases, Genetics/epigenetics

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Background: Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) syndrome, is an interferonopathy caused by proteasomal dysfunction. Clinical characteristics include early onset inflammation, nodular rashes, hepatosplenomegaly, myositis, panniculitis, lipodystrophy and basal ganglion calcifications. CANDLE and associated syndromes are gouped into the proteasome-associated autoinflammatory syndromes (PRAAS). Our patient presented at age of 3 months with features strongly suggestive of PRAAS. Genetic testing revealed a novel proteasome variant classified as a variant of unknown significance (VUS).
Objectives: Functional testing of the proteasome was undertaken in order to support the suspicion of PRAAS. Our aims are to describe the potential role of this test for aiding in the diagnosis of PRAAS.
Methods: First, interferon signature was obtained and whole exome sequencing was analyzed for the patient and her parents. Nest, samples of whole blood were taken from the patient, parents and 3 healthy controls. PBMC were lysed using activity preserving methods (active extraction). Samples were normalized using BCA enzymatic assay. Activity of the proteasomal subunits was measured using peptides specific to different subunits (caspase, chymotrypsin and trypsin activity).
Results: Interferon signature was abnormally high, suggestive of an interferonopathy. Whole exome sequencing revealed a novel heterozygous variant in a PSMB4, the gene that encodes for β7, a structural non –catalytic subunit of the proteasome classified as a variant of unknown significance (VUS). A pilot analysis of proteasome activity showed a 50% reduction in the catalytic activity of proteasome subunit β1, indicating severe impairment of proteasomal activity, with compensatory hyper-activation of the immunoproteasome subunit β1i (Figure 1). The apparent dysfunction of β1 and hyper activation of β1i suggested a proteasomal assembly dysfunction. Using the above findings, the patient commenced JAK inhibitor (baricitinib) with remarkable clinical improvement (Figure 2).
Conclusion: Proteasomal activity testing may serve as a useful tool for the diagnosis of CNDLE/PRASS in suspicious cases. Since JAK inhibitors may provide an adequate therapeutic response, it is of great importance to timely diagnose this disease in cases where the genetic results are equivocal.
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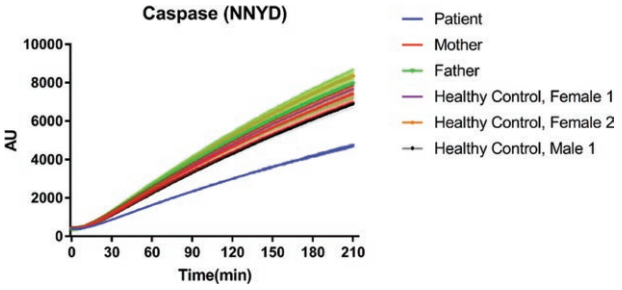


Figure 1. Reduced β1 proteasomal subunit activity as measured by caspase reaction, compared to healthy conrtols



Figure 2. The patient, before (A) and 2 weeks after (B) starting the treatment with JAK inhibitor (baricitinib)

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0755 TOWARDS THE DEVELOPMENT OF COMPOSITE PARENT-CENTERED DISEASE ACTIVITY SCORES FOR JUVENILE DERMATOMYOSITIS

Keywords: Outcome measures, Myositis, Patient reported outcomes

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Background: In recent years, increasing attention has been paid to the development of parent- and child-centered composite disease activity scores for the assessment of health status of children with rheumatic diseases.

Objectives: This study is aimed to develop and test an entirely parent-centered composite disease activity score for JDM, named parent Juvenile DermatoMyositis Activity Index (parJDMAI). Two versions of the score, which differed in the fourth item included, were evaluated.
Methods: Both parJDMAI1 and parJDMAI2 include the following items: 1) parent assessment of skin disease activity (Parent Skin Scale) on a 0-5 scale, by giving 1 point to the presence of each of the following: i) rash on eyelids, ii) nose/cheeks, iii) knuckles, iv) trunk/arms, v) skin ulceration; 2) parent assessment of muscle disease activity (Parent Muscle Scale) on a 0-5 scale, by giving 1 point to the presence of each of the following: i) fatigue/discomfort, ii) muscle weakness, iii) muscle pain, iv) voice change, v) difficulty swallowing; 3) parent assessment of child's fatigue on a 0-10 visual analog scale (VAS) (0 = no fatigue; 10 = maximum fatigue). As fourth item, the parJDMAI1 includes the parent global assessment of child's wellbeing, measured on a 0-10 VAS (0 = best; 10 = worst), whereas the parJDMAI2 includes the parent global assessment of disease activity, measured on a 0-10 VAS (0 = no activity; 10 = maximum activity). To give the four components of the tools the same weight, the scores of the Parent Skin and Muscle Scales were doubled. Thus, the total score of both instruments ranges from 0 to 40. Initial validation was conducted on a multicentric sample of 213 patients followed in standard clinical care and evaluated prospectively (number of visits = 577), and on a monocentric sample including 50 patients, all assessed at baseline and 32 also assessed after a median of 3.9 months (number of visits = 82). Validation analyses included calculation of the correlations between individual parJDMAI items and physician-centered JDM outcome measures, and between the total score of parJDMAI1 and parJDMAI2 with that of the global composite disease activity scores for JDM named JDMAI1 and JDMAI2. Because both JDMAI1 and JDMAI2 include the parent global assessment of child's wellbeing, which is also part of parJDMAI1, we also tested the correlations of parJDMAI1 with reduced versions of JDMAI1 and JDMAI2, that included only the 3 physician-centered items. Spearman correlations were defined as low, moderate or high when r_S was < 0.4, ≥ 0.4 and ≤ 0.7, or > 0.7, respectively.
Results: Correlations between individual components of parJDMAI1 and parJDMAI2 and physician-centered JDM outcome measures were low-to-moderate in the multicentric sample, but moderate in the monocentric sample. Likewise, correlations between the scores of parJDMAI1 and parJDMAI2 and that of original and reduced versions of JDMAI1 and JDMAI2 were strong in the monocentric sample, but moderate in the multicentric sample.
Conclusion: The new parent-centered composite disease activity scores revealed satisfactory measurement properties. That correlations with physician-centered outcome measures and original and reduced JDMAI versions were higher in the monocentric sample than in the multicentric cohort indicates that the proposed tools should be further tested in different clinical and cultural environments before their widespread use can be recommended.
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Table 1. Spearman correlation between parJDMAI1 and parJDMAI2 and other outcome measures.

	Multicentric sample		Monocentric sample	
	Spearman r	**N**	**Spearman r**	**N**
Parent JDMAI1 vs JDMAI1	0.70	402	0.83	68
Parent JDMAI1 vs JDMAI2	0.69	350	0.82	65
Parent JDMAI2 vs JDMAI1	0.69	394	0.80	71
Parent JDMAI2 vs JDMAI2	0.67	347	0.79	68
Parent JDMAI1 vs DAS total	0.51	395	0.72	69
Parent JDMAI2 vs DAS total	0.51	400	0.71	72
Parent JDMAI1 *vs* Physician Global VAS	0.48	419	0.73	71
Parent JDMAI2 *vs* Physician Global VAS	0.49	420	0.74	74
Parent JDMAI1 *vs* JDMAI1-3-Items	0.49	402	0.72	68
Parent JDMAI1 vs JDMAI2-3-Items	0.49	350	0.67	65

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POS0756

EFFICACY AND SAFETY OF ADALIMUMAB IN PEDIATRIC NON-INFECTIOUS NON-ANTERIOR UVEITIS: REAL-LIFE EXPERIENCE FROM AIDA INTERNATIONAL REGISTRY

Keywords: Real-world evidence, Uveitis, Registries

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Background: Evidence about the effectiveness of the tumor necrosis factor inhibitor adalimumab (ADA) in pediatric patients with non-infectious intermediate uveitis/pars planitis, posterior uveitis and panuveitis is still limited.
Objectives: Aim of this study is to investigate the therapeutic role of ADA in a cohort of pediatric patients with non-anterior uveitis.
Methods: This is an international multicenter study based on real-life data from pediatric patients treated with ADA due to non-anterior uveitis. Data were drawn from the retrospective branch of the AutoInflammatory Disease Alliance (AIDA) registry dedicated to uveitis. Figure 1 provides the flow diagram describing the selection of the patients enrolled on October 1st, 2022.
Results: 21 patients (36 affected eyes) were enrolled. Eleven patients (19 affected eyes) did not experience further ocular inflammation after ADA introduction; 10 cases (17 affected eyes) showed a partial response with reduced frequency of relapses (3 cases), reduced severity of relapses (3 cases) or reduced frequency and severity of relapses (4 cases). The number of ocular flares dropped from 3.91 to 1.1 events/patient/year after ADA introduction (p=0.0009). Macular edema and retinal vasculitis were respectively observed in 18 eyes and 20 eyes at the start of ADA and in 4 eyes and 2 eyes at the last assessment. The mean daily glucocorticoids dosage significantly decreased at the last assessment (p=0.005). As observed in Table 1, intermediate uveitis/pars planitis (p=0.01) and posterior uveitis (p=0.03) were more frequent among patients with full response to ADA; panuveitis was significantly more frequent among patients continuing to experience uveitic flares (p=0.001). Regarding the safety profile, a case of generalized adenopathy was observed.
Conclusion: ADA had a role in all pediatric patients with non-anterior uveitis with a significant glucocorticoid sparing effect. Panuveitis seems to be more frequent among patients continuing to experience uveitic flares.

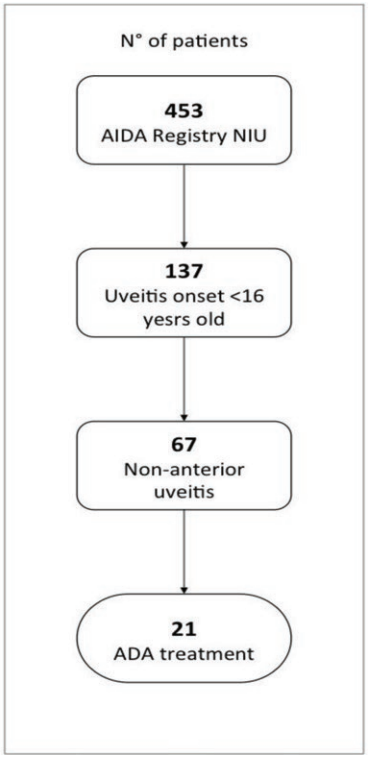


Figure 1. Study flow diagram illustrating the process leading to the selection of patients. *Abbreviations: ADA, adalimumab; AIDA, AutoInflammatory Disease Alliance; NIU, non-infectious uveitis.*

Table 1. Baseline features of patients showing a full control of ocular relapses (group 1) and those experiencing ocular relapses despite the improvement in the frequency and/or the severity of ocular flares. ***Abbreviations: IBD: inflammatory bowel disease; IQR, interquartile range JIA: juvenile idiopathic arthritis; VKH: Vogt-Koyanagi-Harada syndrome; CS: corticosteroids.***

	Group 1 – no further uveitis flares	Group 2 – reduced frequency or severity of relapses	*p* value
N° patients/eyes	11/19	10/17	
Male/Female, N°	6/5	7/3	0.96
Mean age at uveitis onset, years (mean ± SD)	10.8 ± 3.8	7.7 ± 3.6	0.08
Unilateral/bilateral involvement at the onset	3/8	2/5	0.83
Mean duration from uveitis onset at ADA introduction, months – median (IQR)	11 (24)	12 (17)	0.97
Mean duration of follow-up, months – median (IQR)	11 (15)	27 (28.5)	0.08
Anatomical classification, N° eyes (%)	Pars planitis, 10 (52.6) Posterior, 5 (26.3) Panuveitis, 5 (26.3)	Pars planitis, 2 (11.8) Posterior, 0 (0) Panuveitis, 14 (82.4)	0.01 0.03 0.001
Uveitis presentation, N° eyes (%)	Sudden, 9 (47.4) Insidious, 9 (47.4) Unknown, 1 (5.3)	Sudden, 12 (70.6) Insidious, 5 (29.4) Unknown, 0 (0)	0.16 0.28
Uveitis course, N° eyes (%)	Acute, 2 (10.5) Recurrent, 3 (15.8) Chronic, 12 (63.2) Unknown, 2 (10.5)	Acute, 0 (0) Recurrent, 10 (58.8) Chronic, 7 (41.2) Unknown, 0 (0)	0.18 0.008 0.19
Concomitant systemic diseases, N° eyes (%)	Idiopathic, 7 (63.6) Behçet's disease, 2 (18.2) IBD, 1 (9.1) Scleroderma, 1 (9.1)	Idiopathic, 6 (60) JIA, 2 (20) VKH syndrome, 1 (10) Behçet's disease, 1 (10)	0.92
ADA molecule used, N° eyes	Originator, 5 (45.5) ABP501, 3 (27.3) SB5, 2 (18.2) GP2017, 1 (9.1)	Originator, 6 (60%) ABP501, 2 (20) SB5, 1 (10) GP2017, 1 (10)	0.52
Concomitant CS treatment at the start of ADA, N° patients (%)	8 (73.7)	6 (60)	0.55
Concomitant cDMARDs at the start of ADA, N° patients (%)	7 (63.6)	9 (90)	0.17

REFERENCES: NIL.
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POS0757 UVEITIS AS PREDICTORS OF RELAPSE AFTER ANTI-TNF TREATMENT WITHDRAWAL IN JUVENILE IDIOPATHIC ARTHRITIS: AN ITALIAN MULTICENTRIC EXPERIENCE

Keywords: bDMARD, Inflammatory arthritides, Prognostic factors

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood. TNF inhibitors (TNFi) have dramatically changed the prognosis of this disease, but once achieved disease remission, it is not clear how and when stop therapy.
Objectives: Our purpose is to describe a multicentric cohort of JIA patients treated with the first course of Adalimumab and Etanercept in whom therapy was discontinued to persistent remission and identify predictors of relapse.
Methods: In a multicentric Italian retrospective study (Florence, Brescia, Trieste and Bari), patients with oligoarticular and polyarticular JIA were enrolled if they stopped therapy for persistent remission after the first course of Adalimumab and Etanercept. We collected demographic, clinical and laboratory data at onset and during biologic treatment.
Results: 136 patients were enrolled (102 female, median age at onset 3 years (R1-15)), of whom 76 (55.9%) had oligoarticular JIA and 55 (40.4%) had uveitis. ANA positivity was found in 99(72.8%) (Table 1). TNFis were started at median age of 6 years (R1-16), with a median time intercourse between TNFi initiation and diagnosis of 12 months (0-127m). Seventy-nine (59.3%) were treated with ADA, and 57 (40.7%) with ETA. Remission was achieved after a median time of 4 months (R 1-32) and TNFi was discontinued after a median time of 30 months (R 6-90). TNFi were stopped in the 76.5% increasing the interval of administration, 18.4% reducing the dose, and 16.9% abrupt discontinuation. 106 patients (79.4%) relapsed after a median time of 6 months (R 0.5-96) for arthritis in 71 (66.9%), uveitis in 19 (17.9%), both in 18 (16.9%). Patients who relapsed were more frequently female (χ^2 5.9 p<0.014), had history of uveitis (χ^2 7.4 p<0.006), younger at onset (median 3 vs 7, p<0.001) and when TNFi was started (6 vs 9.5, p 0.002). Moreover, the time intercourse between diagnosis and TNFi initiation was longer (13 vs 8.5 months, p 0.02) and the weaned of therapy happened in shorter time (6 vs 9 m, p 0.005) (Table 1). Patients who not-relapse suspended TNFi more frequently lengthening intervals of administration (χ^2 5.2 p0.015). Relapse free survival curve after withdrawal evaluated with Kaplan-Meier showed that patients with uveitis had a significantly earlier relapse (Log Rank χ^2 = 12.8 p <0.0001)
Conclusion: Although this is a retrospective study, we highlighted that early age at onset and at TNFi initiation, presence of uveitis and a long time to start biologics seem to be significantly more frequent in subjects who relapse, while stop therapy lengthening the interval of drug administration might be protective.

Table 1. Characteristics of JIA patients after drug withdrawal (relapse Vs no-relapse)

	Entire cohort (136) n (%)	*Not relapse (28)*	*Relapse (108)*	*Test and p value*
Female n, %	102 (75%)	16 (57.1%)	86 (79.1%)	**χ^2 5.9 p 0.014**
Age at diagnosis, years, m (R)	3 (1-15)	7 (1-15)	3 (1-11)	**p<0.001**
Uveitis history, n (%)	55 (40.4%)	5	50	**χ^2 7.4 p<0.006**
Type of JIA	55 (40.4%)	12	43	**ns**
pOligo n (%)	21 (15.4%)	3	18	
eOligo n (%)	60 (44.1%)	13	47	
Poli n (%)				
ANA positivity	99 (72.8%)	16	83	**χ^2 4.3 p 0.03**
Comorbdity n	29	10	19	**$\chi^2$4.35 p 0.037**
HLA B27	14	6	7	**$\chi^2$3.9 p 0.048**
Type of Biologics	ADA 79 ETA 57	ADA 13 ETA 15	ADA 66 ETA 42	ns
Characteristics at biologic starting and withdrawal				
Age at B initiation years, m, R	6 (1-16)	9.5 (1-15)	6 (1-16)	**p0.002**
Concomitant therapy	111 MTX (81.6%)	20(71.4%)	91(84.2%)	**χ^2 6.58 p 0.03**
Time between diagnosis and B (months)	12 (0-127)	8.5 (0-117)	13 (1-127)	**p0.021**
Time free from relapse out of therapy months	6 (0.5-96)	16 (4-96)	5 (0.5-66)	**p<0.001**
Type of flare	71 (66.9%)	-	71	ns
Arthritis	19 (17.9%)		19	
Uveitis	18 (16.9%)		18	
Both				
Continuation of concomitant therapy after stop B	6	33	39	**χ^2 0.68 p 0.43**
N of months to stop B	6 (0-22)	9 (0-22)	6 (0-22)	**p 0.005**
Modality to stop B	104 (76.5%)	26(92.8%)	78 (72.2%)	**χ^2 5.2 p0.02**
Lengthening intervals	25 (18.4)	4	21	
Reduction of dose	16 (11.8%)	1	15	
Abrupt				

Abbreviations: n number, m median, R range, pOligo persistent oligoarthritis, eOligo: extended oligoarthritis, Poli polyarticular, B biologic, ns: non significant

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0758 ON DEMAND CANAKINUMAB THERAPY FOR COLCHICINE RESISTANT FAMILIAL MEDITERRANEAN FEVER (FMF) PAEDIATRIC PATIENTS – A MULTICENTER STUDY

Keywords: Quality of care

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Background: Familial Mediterranean fever (FMF) is the most common autoinflammatory disease.

Without therapy, it may lead to the development of secondary amyloidosis. Treatment with colchicine leads to long-term remission in ~70% of patients. 5% are resistant to colchicine therapy (crFMF) and may be treated with monthly dose of canakinumab (anti IL-1beta). However, colchicine, the only drug proved to prevent secondary amyloidosis. Canakinumab is immunosuppressive as well as expensive.
Objectives: To compare on demand canakinumab (COD) dosage policy vs. canakinumab fixed frequency (CFF) policy.
Methods: Data from 3 pediatric rheumatology centers (Schneider, Sheba, Rambam) were collected regarding crFMF patients treated with canakinumab. crFMF patients treated according to the COD policy were given 1 dose of sc-canakinumab injection 4mg/kg (max 150mg), with subsequent doses administered only after an additional attack. CFF patients were given fixed 4 weekly doses according to the manufacturer instructions.
Results: Overall, 51 crFMF (25 COD vs. 26 FCC) with mean follow-up of 22.6 months were included. There were no significant demographic, clinical or genetic differences between the groups. The COD group received significantly lower cumulative canakinumab dosage during the follow-up period (15.68±8.95mg/kg vs.32.5±8.05mg/kg;P<0.001). There were no differences between groups in mean FMF attacks nor in mean CRP levels at the end of follow-up period. None the less, the COD group necessitated higher colchicine doses (0.05±0.01mg/kg vs. 0.03±0.01mg/kg;P<0.001).
Conclusion: COD treatment in crFMF patients is as effective as CFF treatment. Using COD can reduce drug expenses and decrease immunosuppression exposure without negatively influencing the disease control.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0759 MONOGENIC DISORDERS IN THE MAIDEN COHORT OF PEDIATRIC RHEUMATOLOGICAL DISEASES OF NEPAL- A SPECK OF IMPRINT ON EVEREST.

Go to page 2159.

POS0760 LONG-TERM PROGNOSTIC FOLLOW-UP OF PATIENTS WITH REFRACTORY SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS AFTER THE CLINICAL TRIAL OF TOCILIZUMAB AS A FIRST-LINE BIOLOGIC TREATMENT

Keywords: bDMARD, Prognostic factors, Inflammatory arthritides

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Background: Tocilizumab (TCZ) was approved for systemic juvenile idiopathic arthritis (sJIA) as an intravenous formulation in 2008 after its effectiveness and safety were shown in a world-leading clinical trial performed in Japan in 2002–2008.
Objectives: This study aimed to understand the long-term prognosis of patients participating in phases II (Study MRA011JP), III (Study MRA316JP), and III/IV (Study MRA324JP). There were 149 participants in the clinical trial.
Methods: Information on eligible patients was obtained from 12 cooperating institutions approved by the Ethics Committee of Tokyo Women's Medical University and each institution. Patients who could be followed-up were referred and transferred to other hospitals or departments. The following long-term prognoses were assessed: treatment status, including the continuation of TCZ administration during the long-term course of sJIA, disease status (remission rate and clinical phenotype), complications, social adjustment, employment status, and *health-related* quality of life (HRQOL) scale.
Results: Results were collected for 132 cases from ten centers by December 2022. We examined 125 patients (58 males and 67 females) whose medical records were still available and whose final diagnosis was sJIA. The age of the study participants was 18.6 years at the time of the study, 4.3 years at onset, 8.8 years at first TCZ administration, 3.8 years from onset to the first TCZ administration, and 9.1 years from TCZ initiation (all median values). Of the 125 patients, 28 (22.4%) were in medication-free remission and were either under or completely followed-up. Of the 93 patients (74.4%) who continued therapy, 10 (10.8%) were moved to a subcutaneous version of TCZ, which is not yet licensed for the treatment of sJIA in Japan. Ten patients (10.8%) were switched to canakinumab (CAN) due to TCZ primary failure (5 patients), secondary failure (2 patients), side effects (1 patient developed anaphylaxis), or other reasons. Of the 124 patients, 44 (35.5%) changed from acute febrile sJIA to chronic arthritic sJIA, in which chronic arthritis was the primary pathology without systemic inflammation, and 17 of these patients still had active arthritis at the last observation. Corticosteroids were prescribed in 54 of 93 patients (58.1%). Except in one case of sudden death, the causes of death in the four cases that resulted in fatalities were macrophage activation syndrome, sJIA-related interstitial pneumonia, and disseminated aspergillosis. The most commonly observed complications were osteoporosis in 68 (54.4%), infection requiring hospitalization in 32 (25.6%), and hypertension in 25 (20%). The EQ-5D-5L score was 0.91 (mean). The final mean height of the patients whose information was available after the age of 18 years (n = 62) was 157.7 cm for males (mean 170.4 cm in Japanese) and 144.3 cm for females (mean 156.7 cm in Japanese), showing a significant short stature. The college/university enrollment rate was as high as 68.4% (Japanese statistical data: 58.9%), and all but five students were employed.
Conclusion: Seventy-four percent of the patients continued treatment with TCZ or CAN, and conversion to chronic arthritic sJIA was observed in 35.5%. Despite issues such as growth retardation, social adjustment and employment status were promising, suggesting a contribution of treatment.
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POS0761 UVEITIS IN OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS PATIENTS AND IN JUVENILE SPONDYLOARTHRITIS/ENTHESITISRELATED ARTHRITIS – IS THERE ANY DIFFERENCE?

Keywords: Uveitis

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Background: Juvenile idiopathic arthritis (JIA) is the most common systemic disease causing uveitis in childhood and adolescence. JIA-associated uveitis has an estimated prevalence ranging from 11% to 30%, being higher in patients with oligoarticular JIA (oJIA), and to a lesser degree, in patients with juvenile spondyloarthritis/enthesitis related arthritis (jSpA-ERA), especially in HLA-B27 positive patients.
Objectives: To compare the demographic and laboratory characteristics and clinical outcomes of uveitis in oJIA and jSpA-ERA patients.
Methods: A retrospective single-center study of patients with oJIA and jSpA-ERA followed in a tertiary Hospital was conducted. ILAR classification criteria were fulfilled and sociodemographic, clinical and treatment data were collected from the Portuguese Rheumatic Diseases Register (Reuma.pt) and medical records. Age at onset of uveitis, disease duration, acute-phase reactant proteins at diagnosis, and characteristics of uveitis including complications, medical and surgical treatments were collected. Statistic was performed with independent samples t-test, Mann-Whitney U test, chi-square test and Fisher's exact test. Statistical significance was set at a p-value <0.05.
Results: A total of 75 patients with oJIA (57 females, 76.0%) and 23 patients with jSpA-ERA (6 females, 26.1%) were included. Thirty-five of 98 patients (35.7%) developed uveitis, 28 patients had oJIA (80.0%) and 7 patients had jSpA-ERA (20.0). There were more females in the oJIA with uveitis group (p=0.006) and the age at diagnosis of JIA was lower in oJIA patients (p=0.005). ANA positivity was significantly higher in the oJIA with uveitis group (0.012) and HLA-B27 positivity was significantly higher in the jSpA-ERA with uveitis group (0.002). No significant differences were found in the ESR and CRP values at diagnosis and csDMARD/bDMARD use. Uveitis appeared in younger age in patients with oJIA than in patients with jSpA-ERA (8.4 ± 5.9 years vs 17.8 ± 7.2 years, p=0.001). In addition, the uveitis in the majority of oJIA patients was asymptomatic and the diagnosis was made during eye screening (n=21, 75.0%), as opposed to jSpA-ERA patients, in which the uveitis was symptomatic in the majority of patients (n=6, 85.7%, p=0.003). Concerning uveitis characteristics, anterior uveitis was the most frequent type in the 2 groups (and the only one in jSpA-ERA patients). In oJIA patients, panuveitis occurred in 8 patients (28.6%). However, no significant differences were found regarding the type of uveitis in the 2 groups. Patients with jSpA-ERA had more frequently unilateral alternating uveitis (n=4), followed by unilateral uveitis (same eye, n=3). No one developed bilateral uveitis. In oJIA patients, uveitis was more frequently unilateral (same eye, n=7), followed by bilateral involvement (n=9, 32.1%) and unilateral alternating (n=6, 21.4%). Complications were more frequent in oJIA group (n=15, 53.6%) than in jSpA-ERA (n=1, 14.3%, p=0.62). The most common complications in the oJIA group were cataracts (n=12, 42.9%), band keratopathy (n=8, 28.6%), ocular hypertension (n=8, 28.6%) and synechiae (n=6, 21.4%). Twelve patients (42.9%) with oJIA were submitted to eye surgery. On the contrary, no patient with jSpA-ERA was submitted to eye surgery.
Conclusion: In our study, uveitis manifested in 35.7% of the included patients with oJIA and jSpA-ERA. Uveitis in oJIA patients had poorer outcomes, such as complications and eye surgery requirement. Uveitis seems to have different characteristics depending on the JIA subtype, which leads us to think that possibly different immunologic mechanisms may be involved.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0762 ASSOCIATIONS BETWEEN POWER DOPPLER ULTRASOUND FINDINGS AND B-MODE SYNOVITIS AND CLINICAL ARTHRITIS IN JUVENILE IDIOPATHIC ARTHRITIS USING A STANDARDIZED SCANNING APPROACH AND SCORING SYSTEM

Keywords: Ultrasound, Imaging, Inflammatory arthritides

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Background: Ultrasound is a valuable tool in the evaluation of synovitis in patients with juvenile idiopathic arthritis (JIA). However, interpretation of Doppler signals in children is challenging due to physiologic vascularization that can be misinterpreted as pathologic findings. Definitions for synovitis in children, including B-mode (BM) and Doppler findings, have been developed and emphasize that only Doppler signals within synovial hypertrophy should be considered as synovitis [1]. So far, few studies have implemented this definition in the evaluation of Doppler findings in children.
Objectives: To describe power Doppler (PD) ultrasound findings in joint regions with BM synovitis in patients with JIA using a standardized scanning protocol and scoring system. Further, to examine associations between PD findings and BM synovitis, clinical arthritis, patient characteristics and disease activity.
Methods: In this cross-sectional study one rheumatologist with broad ultrasound experience, blinded to clinical findings, performed ultrasound examinations in 27 patients with JIA aged 2 to 17 years old with suspected clinical arthritis using the same ultrasound machine with standardized settings. The elbow, wrist, metacarpophalangeal 2-3, proximal interphalangeal 2-3, knee, ankle and metatarsophalangeal 2-3 joints were assessed bilaterally and scored for BM and PD findings using a joint-specific scoring system (grades 0-3) with reference atlas [2]. Pathologic BM and PD findings were defined as grades ≥1. Multilevel mixed-effects ordered logistic regression models were used to explore associations between PD findings and BM synovitis, clinical arthritis, age, sex, JIA subgroup, disease duration and measures of disease activity (Juvenile Arthritis Disease Activity Score (JADAS10), (range 0-40).
Results: Overall, 971 joint regions were evaluated by ultrasound, 129 had BM synovitis and were assessed for PD. PD findings were detected in 45 joint regions (34.9%), most frequently in the lateral parapatellar recess of the knee joint (24.4%) (**Figure 1**). Increasing PD grades were associated with higher BM grades (OR=5.0, 95% CI: 2.7-9.1, p<0.001) and with the presence of clinical arthritis (OR=7.4, 95% CI: 2.7-21.7, p<0.001). PD findings were not associated with age, sex, JIA subgroups, disease duration or JADAS10.
Conclusion: Increasing severity of PD findings were significantly associated with BM synovitis and with the presence of clinical arthritis. These findings suggest that PD signals detected using a standardized ultrasound examination and scoring system can reflect active disease in patients with JIA.
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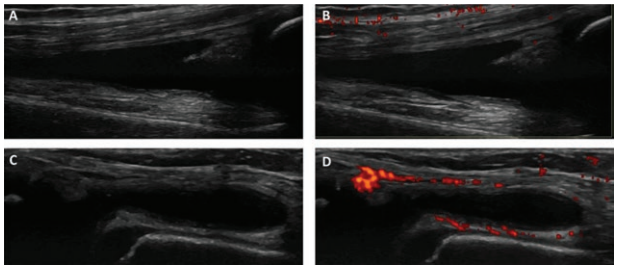


Figure 1. Illustration of variations in power Doppler (PD) ultrasound findings in two joint regions of the knee in a 10-year-old child with juvenile idiopathic arthritis (JIA). **A**: Longitudinal dorsal scan of the knee joint (suprapatellar recess) showing B-mode (BM) synovitis, **B**: and BM synovitis without abnormal PD signals (grade 0). **C**: Longitudinal dorsal scan of the knee joint (lateral parapatellar recess) showing BM synovitis, and **D**: BM synovitis with abnormal PD signals (grade 3).

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POS0763

AN EVALUATION OF THE EFFICIENCY OF METHOTREXATE IN THE TREATMENT OF JUVENILE ENTHESITIS RELATED ARTHRITIS

Keywords: Disease-modifying drugs (DMARDs), Spondyloarthritis, Enthesitis

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Background: Methotrexate (MTX) is quiet commonly used to treat all subtypes of juvenile idiopathic arthritis (JIA). Despite that, there are no studies on the efficiency of MTX treatment in juvenile enthesitis related arthritis (ERA).
Objectives: This study aims to evaluate the efficacy of MTX treatment in children with juvenile arthritis of the ERA subtype.
Methods: We conducted a retrospective chart review from January 2017 to December 2021 of all patients who received MTX for at least 3 months. The clinical manifestation of the ERA was determined by using JADAS and the JSpADA. Good therapeutic response was defined by a reduction of the JSpADA by 0,8 points or more. A JADAS under < 2 was considered minimal disease activity, whereas a JADAS < 1 was interpreted as inactive disease.
Results: We found 188 patients in whom MTX was initiated, 117 (62,23 %) of these patients were treated with MTX for at least three months and therefore fulfilled the criteria for this analysis. At all follow-ups, the patients showed a significant reduction in both scores compared to the start (see Table 1). After three months 49,57 % of the participating patients were considered good responders, after twelve months it was 70 %. Half of the followed patients achieved the state of remission after twelve months, another 12,82 % showed only minimal disease activity at this point.
Conclusion: This study shows the efficacy of MTX as a first-line therapy for the treatment of children with ERA. A comparative study with Sulfasalazine would be interesting.

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Table 1.

	0 months	3 months	6 months	12 months
Number of patients	n = 117	n = 117	n = 95	n = 70
JADAS 10				
Median [Q1; Q3]	9.0 [6.0;11.5]	5.5 [2.5, 9.5]	5.0 [1.5, 8.0]	1.8 [0.1, 6.5]
Mean (SD)	9.2 (4.5)	6.5 (5.0)	5.6 (4.8)	3.6 (3.9)
JSpADA				
Median [Q1, Q3]	2.50 [2.00, 3.50]	2.50 [2.00, 3.50]	1.50 [0.50, 2.50]	1.00 [0.00, 1.50]
Mean (SD)	2.67 (1.27)	1.88 (1.35)	1.71 (1.31)	1.13 (1.21)

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POS0764

IMPACT OF TOFACITINIB TREATMENT ON HEIGHT IN JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Inflammatory arthritides, Targeted synthetic drugs, Randomized control trial

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Background: Diminished growth can be a consequence of juvenile idiopathic arthritis (JIA).[1] Growth hormone signals through a Janus kinase (JAK)2 tyrosine kinase-coupled receptor.[2] Tofacitinib, an oral JAK inhibitor approved for JIA, preferentially inhibits signalling by heterodimeric receptors associated with JAK1 and/or JAK3 and has less functional selectivity for JAK2.
Objectives: To evaluate the growth of patients (pts) with JIA treated with tofacitinib.
Methods: This post hoc analysis of the Phase 3 trial of tofacitinib in pts with JIA (NCT02592434; a 44-week, 2-part, double-blind [DB], withdrawal study in 225 pts aged 2–<18 years) enrolled 212 pts (pts with systemic JIA were excluded). In part 1, pts received open-label tofacitinib 5 mg twice daily (BID; or weight-based oral solution) for 18 weeks/flare. In the DB phase, pts achieving JIA/American College of Rheumatology improvement ≥30% by Week 18 were randomised to receive tofacitinib or placebo until Week 44/flare. Pts could then receive tofacitinib in a long-term extension study. Height Z-scores were calculated for pts at baseline (BL), Weeks 18, 44, 68 and 92 using age- and sex-matched reference data from the World Health Organization. A repeated measures mixed-effects analysis of pts who received continuous tofacitinib assessed change in height Z-scores over time. The impact of JIA category, age, sex, race, ethnicity, biologic disease-modifying antirheumatic drug (bDMARD)/conventional synthetic DMARD (csDMARD) use, and C-reactive protein (CRP; normal/elevated) on BL height Z-score was also assessed. A separate analysis assessed the impact of treatment on change in height Z-scores during the DB phase. Growth velocity (cm/year) from BL to Week 44 was calculated.
Results: Ethnicity was the only characteristic associated with BL height Z-score (Table 1). For 83 pts who received continuous tofacitinib, mean (95% confidence intervals [CI]) BL height Z-score was -0.4 (-0.7, -0.1), and was stable up to Week 92 (Figure 1). Mean (95% CI) change in height Z-score from BL of the DB phase (Week 18) to Week 44 was not different for pts receiving tofacitinib (N=56; -0.03 [-0.1, 0.04]) vs placebo (N=36; -0.04 [-0.1, 0.04]). Growth velocities in the 56 pts who received tofacitinib for 44 weeks was within normal range for age and sex with peak values at ages 9–10 years and 11–12 years for females and males, respectively (data not shown).

Table 1. BL Z-score by pt characteristics

Characteristic		n	Median height Z-score (IQR)	Mean height Z-score (SD)	p value[a]
JIA category	Enthesitis-related arthritis	21	0.3 (-0.4–0.9)	0.2 (0.9)	0.17
	Extended oligoarthritis	28	0.1 (-0.6–0.6)	0.1 (1.1)	
	Juvenile psoriatic arthritis	20	-0.1 (-0.8–0.7)	-0.1 (1.0)	
	RF- polyarthritis	104	-0.3 (-1.1–0.4)	-0.4 (1.4)	
	RF+ polyarthritis	39	-0.1 (-1.1–0.6)	-0.3 (1.1)	
Age	2–<6 years	20	-0.4 (-1.3–0.2)	-0.6 (1.0)	0.09
	6–<12 years	58	0.1 (-0.6–0.7)	0.0 (1.2)	
	12–<18 years	134	-0.3 (-1.0–0.6)	-0.3 (1.2)	
Sex	Female	164	-0.3 (-1.0–0.5)	-0.3 (1.2)	0.25
Race	Black/African American	5	0.3 (0.2–0.3)	0.0 (0.8)	0.1
	Other	22	-0.6 (-1.7–0.1)	-0.8 (1.4)	
	White	185	-0.2 (-0.8–0.6)	-0.2 (1.2)	
Ethnicity	Hispanic/Latino	60	-0.6 (-1.5–0.1)	-0.8 (1.5)	<0.001
	Not Hispanic/Latino	152	0.0 (-0.7–0.7)	0.0 (1.0)	
Previous bDMARDs	bDMARD naïve	169	-0.1 (-0.9–0.6)	-0.2 (1.2)	0.49
csDMARDs[b]	Yes	191	-0.3 (-0.9–0.6)	-0.2 (1.2)	0.74
CRP category	Normal	112	0.0 (-0.7–0.6)	-0.1 (1.1)	0.15

[a]Calculated using Kruskal-Wallis rank sum test[b]Methotrexate or otherIQR, interquartile range; n, number of pts with characteristic; RF, rheumatoid factor; SD, standard deviation

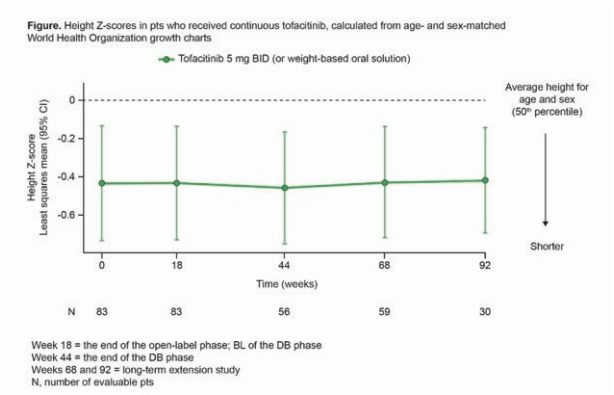


Figure. Height Z-scores in pts who received continuous tofacitinib, calculated from age- and sex-matched World Health Organization growth charts

Week 18 = the end of the open-label phase; BL of the DB phase
Week 44 = the end of the DB phase
Weeks 68 and 92 = long-term extension study
N, number of evaluable pts

Conclusion: In this post hoc analysis, pts with JIA began with near normal height Z-scores and tofacitinib had no negative impact on height Z-scores after 92 weeks. Growth velocity was within the normal range for age up to Week 44. Catch-up growth was not observed, possibly due to the study duration being too short and the BL height Z-scores being near normal.

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Disclosure of Interests: Hermine Brunner Speakers bureau: Novartis and Pfizer Inc, Consultant of: AbbVie, AstraZeneca/MedImmune, Bayer, Biocon, Boehringer Ingelheim, Bristol Myers Squibb, Cerecor, Eli Lilly, EMD Serono, Janssen, Novartis, Pfizer Inc, Roche, R-Pharm and Sobi, Grant/research support from: Bristol Myers Squibb, Novartis and Pfizer Inc, Employee of: Cincinnati Children's Hospital Medical Center, Halley Wasserman Consultant of: Endocrine Society Pediatric Self-assessment program, NIH-funded trial for skeletal health and bone marrow composition, Grant/research support from: Calcilytix, Ultragenyx, Michelle Saul Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Douglas Robinson Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Edward Nagy Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Annette Diehl Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Mahta Mortezavi Shareholder of: Pfizer Inc, Employee of: Pfizer Inc.

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POS0765 SERUM BASIC FIBROBLAST GROWTH FACTOR IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Biomarkers, Disease-modifying drugs (DMARDs), Rheumatoid arthritis

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Background: Patients with rheumatic diseases are at high risk for poor outcomes and gaps in care when severe fibrosis occur, as a result of tissue damage caused by chronic phase of persistent inflammation. Only limited data also controversial results are available on the fibrosis predictors in patients with juvenile idiopathic arthritis (JIA) on long-term methotrexate (MTX) treatment [1,2]

Objectives: To evaluate serum levels of basic fibroblast growth factor (bFGF) in children with juvenile idiopathic arthritis treated with methotrexate.

Methods: 104 patients with polyarthritis (50,96%) and oligoarthritis (40,38%) variants JIA (mean age 13.3 yrs, 59,62 % female, mean age of JIA onset 7.2 yrs, mean disease duration 5.06 yrs) were included in this 4-years prospective study. In 104 children with JIA were treated with MTX 75.96 % (vs. 24.04 % not treated with MTX, 16,35 % were prescribed MTX, but they didn't receive any dose yet on investigation day). Among patients treated with MTX 4.81 % had dose less than 10 mg/m^2/week, 32.69 % 10-12.5 mg/m^2/week, 31.73 % 12.6 - 15 mg/m^2/week, 6.73 % over 15 mg/m^2/week. bFGF levels were determined by bFGF ELISA kits (Elabscience, USA). Serum levels of bFGF were analyzed depending on patients' gender, age, and age of JIA onset, its variant, duration, activity, and presence of MTX in treatment and its dose. Levels of erythrocyte sedimentation rate (ESR), C-reactive protein (C-RP), circulating immune complex (CIC) and antistreptolysin-O (ASL-O) were analyzed in this study.

Results: We evaluated bFGF level for children with JIA (min: 4171.56 pg/ml; Me:7089.28 pg/ml; max: 18011.25 pg/ml). The average level of bFGF significantly increased in children with age of JIA onset from 15 to 18 years versus age of JIA onset up to 3 years ($p = 0.009$) and 11–14 years ($p = 0.014$). It was also found higher bFGF in patients with an average activity according JADAS-27 pattern versus a low one ($p = 0.0005$). Activity according JADAS-27 pattern, levels of ESR, CIC and ASL-O was associated with bFGF level. Mostly bFGF was correlated with with ASL-O (among: boys r=0.45, patients with oligoarthritis r=0.49, moderate disease activity according to JADAS-27 r=0.58, MTX treatment r= 0.38, dose of MTX, 12,5-15mg/m2/week r=0.50 $p < 0.05$), with CIC (among: patients with polyarthritis r=0.37, low disease activity according to JADAS-27 r=0.34, dose of MTX, less 10mg/m2/week r=0.96 $p < 0.05$), with ESR (among: girls r=0.37, patients with polyarthritis r=0.38, $p < 0.05$).

Conclusion: Children with JIA had a higher bFGF level in patients with JIA onset after 15 years old and moderate disease activity. CIC and ESR were corresponded with high bFGF level. Presence of additional streptococcal infection impact on fibrosis formation in children with JIA.

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POS0766 CIRCULATING SOLUBLE UROKINASE PLASMINOGEN ACTIVATOR RECEPTOR (SUPAR) ASSOCIATES WITH JOINT DESTRUCTION IN JUVENILE IDIOPATHIC ARTHRITIS: A CASE-CONTROL STUDY WITH LONGITUDINAL FOLLOW-UP

Keywords: Inflammatory arthritides, Prognostic factors, Biomarkers

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Background: Reliable biomarkers in the early stages of juvenile idiopathic arthritis (JIA) are scarce. The disease heterogeneity makes it clinically challenging to predict the risk of future permanent joint damage. Some indicators of poor outcome have been identified, e.g. rheumatoid factor (RF) and antibodies against cyclic citrullinated peptides (anti-CCP), but additional biomarkers with predictive potential are warranted in order to start optimal treatment before tissue damage occurs. The soluble urokinase plasminogen activator receptor (suPAR) has been reported as an easily measurable biomarker for prognosis and severity in several diseases, including adult rheumatoid arthritis, systemic lupus erythematosus and other inflammatory conditions [1]. However, to our knowledge, suPAR has never been studied in JIA.

Objectives: We asked whether suPAR could predict a more severe course with erosions in JIA.

Methods: 51 well-characterized patients with recent-onset or established JIA and 50 age- and sex-matched healthy control subjects were included. Blood sampling was performed at inclusion and sera were stored for later analysis of suPAR by suPARnostic ELISA (Virogates, Birkeröd, Denmark). The patients were carefully followed over 3 years and erythrocyte sedimentation rate, C-reactive protein, RF, anti-CCP and antinuclear antibodies were analyzed as part of clinical routine. Signs of joint destructions were evaluated by radiographic investigation of affected joints. Data was evaluated using non-parametrical statistical methods.

Results: Overall, the levels of suPAR did not differ significantly between JIA and controls (Figure 1). Still, the subgroup of subjects with polyarticular disease showed higher suPAR than the controls (p=0.013). In addition, elevated suPAR levels were associated with joint erosions (p=0.022). In two individuals with erosions, high levels of suPAR were found despite absence of RF and anti-CCP.

Conclusion: We present new data on the biomarker suPAR in JIA. The results indicate that, in addition to RF and anti-CCP, analysis of suPAR could be of additional value in predicting the risk of joint erosions. Early analysis of suPAR could potentially guide treatment decision-making in JIA, but our findings call for confirmation in larger cohorts.

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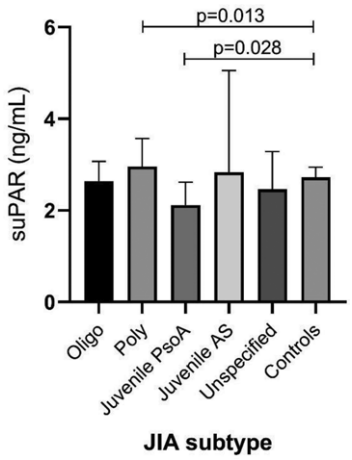


Figure 1.

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POS0767 THE EVALUATION AND IMPORTANCE OF TRANSITION FROM PEDIATRIC TO ADULT RHEUMATOLOGY CARE IN RHEUMATOLOGICAL DISEASES

Keywords: Patient information and education, Descriptive Studies

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Background: The transition from pediatric to adult health care often challenging for young adults with rheumatic diseases. During the transition period, disruptions, diagnostic changes, and treatment differences may occur. The successful transition of the young adult patient to adult care is an important milestone in pediatric rheumatology.
Objectives: In this study, we aimed to examine the diagnosis and treatment changes of transition patients and the characteristics of the transition period in our clinic.
Methods: This was retrospective observational study was carried out in Dokuz Eylul University Pediatric and Adult Rheumatology Department. Patients who followed-up in Pediatric Rheumatology Department transferred to the Adult Rheumatology Department within the last ten years and continued to visit at least once a year were included in this study. If the transition period of the patients was less than three months, it was defined as early transition. Demographic features and educational status, parental divorce, diagnosis changes, and diagnosis-specific treatment changes were recorded.
Results: In total, 962 transitional patients scanned and 210 of them met follow-up criteria. Of the patients, 117 (55.7%) were female, with a median age of 24 (IQR, 21 – 28). Most of patients followed-up juvenile rheumatoid arthritis (JIA) (n=79, 37.6%) and familial Mediterranean fever (FMF) (n=79, 37.6%). Median duration of pediatric rheumatology follow-up was 52 months (IQR, 23 – 87) and 47 (22.%) patients have been treated with biological agent (Table 1). Median transition time was 4 months (1-13 IQR) and the rate of early transition was 46.7%. We found that receiving biological therapy associated with early transition (59.6% vs 40.4%, p=0.040). We also found that Bachelor's degree or higher educational status associated with late transition (40% vs 60%, p=0.025). Rheumatologic diseases were not associated with late transition except FMF, patients with FMF were prone to late transition (32.9% vs 67.1%, p=0.015). Gender and parents' divorce did not associate with transition time (Table 1). The diagnoses of 13% of the participants were changed after they were followed-up in adult rheumatology. The median follow-up period for adult rheumatology was 40 months (15-75 IQR). Biological therapy was started for the first time in 21 patients, the biological therapy of 5 patients was changed, and the biological therapy of 7 patients was discontinued during adult rheumatology follow-up.
Conclusion: We found that most of the patients who were followed-up in pediatric rheumatology in our center did not transition to the adult rheumatology in the same center. Less than half (46.7%) of the patients started to be followed up in adult rheumatology within the first 3 months. Treatment with biological agents was found associated with early transition. Since patients who were treated with biological agent need for a doctor's visit to reach the treatment was considered the main reason for these patients' early transition. We found that Bachelor's degree or higher educational status was associated with late transition. Patients often move to other cities for university may be the reason of the late transition. Transition time did not associate with the rheumatologic diseases except FMF. The reason for the late transition in FMF can be explained by the admission to the hospital frequently with attacks. Transition may be challenging in pediatric rheumatology. The ideal transition to adult rheumatological care should start in the early adolescence period of the patients, planned transition visits may increase the rate of follow-up.

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Table 1. Factors associated with transition duration

	All Participants (n=210)	Early Transition (n=98)	Late Transition (n=112)	P value
Age, years, median (IQR)	24 (21 – 28)	24 (21 – 29)	25 (21 – 28)	0.40
Gender, female, n (%)	117 (55.7)	55 (56.1)	62 (55.4)	0.91
Parents' divorce, n (%)	23 (10.9)	9 (10.7)	14 (13.3)	0.58
Diagnose in Pediatric Rheumatology, n (%)				
JIA	79 (37.6)	42 (53.2)	37 (46.8)	0.015
FMF	79 (37.6)	26 (32.9)	53 (67.1)	
FMF+JIA	6 (2.9)	2 (33.3)	4 (66.3)	
SLE	18 (8.6)	12 (66.7)	6 (33.3)	
Behcet's Disease	9 (4.3)	5 (55.6)	4 (44.4)	
Others	19 (9.0)	8 (42.1)	11 (47.9)	
Duration of Pediatric Rheumology Followed-up, months, median (IQR)	52 (23 – 87)	50 (21 – 85)	55 (24 – 88)	0.48
Duration of transition	4 (1 – 13)	1 (0 – 2)	13 (8 – 28)	<0.001
Education status, n (%)				
Under Bachelor's degree	90 (42.9)	50 (55.6)	40 (44.4)	0.025
Bachelor's degree or higher	120 (47.1)	48 (40)	72 (60)	
Treatment with biological agents at pediatric rheumatology, n (%)	47 (22.4)	28 (59.6)	19 (40.4)	0.040

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Disclosure of Interests: None Declared.
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POS0768 CHARACTERISTICS OF PATIENTS WITH DIFFICULT-TO-TREAT JUVENILE IDIOPATHIC ARTHRITIS AT ADULTHOOD IN FRANCE

Keywords: bDMARD, Descriptive studies, Prognostic factors

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Background: An effort to unify the variability of juvenile idiopathic arthritis (JIA) phenotypes was initiated in 1994 resulting in the current categories of systemic JIA, oligoarthritis (persistent or extended), rheumatoid factor (RF)-negative polyarthritis, RF-positive polyarthritis, psoriatic JIA, and enthesitis related arthritis. Recently, EULAR has proposed a definition of difficult-to-treat rheumatoid arthritis (D2TRA) and the concept was later extended to spondyloarthritis and psoriatic arthritis.
Objectives: The aim of this study was to describe difficult-to-treat JIA (D2TJIA) at adulthood based on the EULAR definition of D2TRA.
Methods: We stratified consecutive JIA patients treated at Cochin Hospital in Paris into two groups, a D2TJIA group and a non-D2TJIA group. Based on EULAR definition of D2TRA, we defined D2TJIA as JIAs failing at least two targeted therapies, with a different mechanism of action.
Results: In total, we identified 18 D2TJIA patients (mean age 27.4 years, 67% female) and 88 non-D2TJIA patients (mean age 29.1 years, 70% female). Regarding JIA subtypes, we observed significantly more systemic JIA in the D2T group (39% vs 14%, p=0.02). D2TJIA patients were more likely to have erosions on X-rays (82% vs. 55%, p=0.038). Regarding auto-antibodies, positive anti-CCP

(6.7% vs. 35%, p=0.048) were less common in D2TJIA than in non-D2TJIA patients, and no difference was observed for RF and anti-nuclear antibody positivity (**Table 1**). Compared with non-D2TJIA, patients with D2TJIA had a significantly reduced duration of exposure to the first line of bDMARD (6.5 vs 32 months, p<0.01) (**Table 1**).

Table 1. Characteristics of JIA patients

	Non-D2TJIA (n = 88)	D2TJIA (n = 18)	p
Age, mean (SD)	29.1 (3.53)	27.4 (4.50)	0.14
Female, n (%)	62 (70%)	12 (67%)	0.75
JIA type, n (%)	12 (14)	7 (39)	0.02
Systemic JIA	18 (20)	3 (17)	1
RF-positive polyarthritis	13 (15)	3 (17)	0.7
RF-negative polyarthritis	19 (22)	3 (17)	0.8
Persistent oligoarthritis	4 (5)	1 (5)	1
Extended oligoarthritis	1 (1)	1 (5)	0.3
Psoriatic JIA	21 (24)	1 (5)	0.1
Enthesitis related arthritis			
Age at diagnosis, median [Q25-75]	9.00 [4.00; 13.0]	7.00 [3.00; 8.00]	0.11
Duration of bDMARD 1 (in months), median [Q25-75]	32.0 [16.0; 79.0]	6.50 [4.25; 31.5]	<0.01
Duration of bDMARD 2 (in months), median [Q25-75]	21.0 [7.00; 50.2]	10.0 [4.00; 23.2]	0.17
Duration of bDMARD 3 (in months), median [Q25-75]	6.00 [2.50; 19.0]	13.0 [4.00; 30.0]	0.32
Duration of bDMARD 4 (in months), median [Q25-75]	5.00 [1.00; 28.5]	6.00 [4.00; 15.0]	0.67
Number of used bDMARD, median [Q25-75]	2.00 [1.00; 2.00]	4.00 [3.00; 4.00]	<0.001
Prosthesis, n (%)	11 (12%)	5 (28%)	0.14
Coxitis, n (%)	27 (35%)	9 (53%)	0.16
Inflammatory bowel disease, n (%)	1 (1.2%)	0 (0%)	1
Psoriasis, n (%)	4 (4.7%)	2 (11%)	0.28
Uveitis, n (%)	22 (26%)	3 (17%)	0.55
Erosions, n (%)	47 (55%)	14 (82%)	0.038
Anti-nuclear antibody positive, n (%)	27 (44%)	5 (33%)	0.47
Anti-CCP positive, n (%)	17 (35%)	1 (6.7%)	0.048
RF positive, n (%)	21 (35%)	4 (25%)	0.45

Conclusion: Our work is the first to describe D2TJIA in France. It seemed interesting to raise the question of whether D2T JIA exists, and if so, what could be its potential definition and management. This may serve as a hypothesis and a basis for future reflections. As observed in rheumatoid arthritis, we report significantly more patients with erosions on X-ray in the D2TJIA group compared to the non-D2TJIA patients which supports such stratification. However, D2TJIA patients did not differ from non-D2TJIA patients in terms of demographic data. Interestingly, patients with D2TJIA had a significantly reduced duration of exposure to the first line of bDMARD suggesting early treatment escape and supporting the importance of temporality in defining difficult-to-treat patients. Our work suggests the relevance of identifying patients with D2TJIA. As showed in other inflammatory rheumatic diseases, this can open the door to a better stratification and personalized management. The definition of D2TJIA needs to be validated and temporality seems to be an essential element to consider.

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Disclosure of Interests: None Declared.
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POS0769 VISCERAL ADIPOSE TISSUE AND ADIPOKINES/ CYTOKINES IN JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Inflammatory arthritides, Biomarkers

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Background: Increased visceral adipose tissue (VAT) associates with markers for rheumatic inflammatory and cardiovascular diseases, but knowledge is sparse in juvenile idiopathic arthritis (JIA).
Objectives: To compare VAT mass, lipid profile and selected adipokines/cytokines in patients with JIA with matched controls, and to explore the role of VAT in disease associated inflammation and cardiovascular risk. Moreover, to explore the differences in circulating biomarkers between poly- and oligoarticular disease.
Methods: 60 patients with JIA (50 girls) age between 10–16 years were consecutively recruited at Oslo University Hospital and 60 age-and sex-matched controls were randomly drawn from the National Registry. The JIA group included 30 patients with persistent oligoarticular JIA (oligo disease) and 30 patients with extended oligoarticular or polyarticular disease RF +/- (poly disease). VAT (g) was estimated by dual-energy x-ray absorptiometry. Lipid profile, CRP and adipokines/cytokines (by ELISA) were analyzed. Differences between groups were tested with parametric or non-parametric analyses as appropriate and associations with univariate and multiple linear regression analyses.
Results: VAT (g) was comparable between patients and controls [median (25^{th} – 75^{th} percentile) 64 (23-149) vs 66 (30-99), p=0.98] and between patients with oligo disease and poly disease [46 (22-123) vs 80 (23-167), p=0.32]. Patients presented lower serum levels of APOA1 and RBP4, and elevated serum levels of IL-6, progranulin and MCP-1 (Table 1) as compared to the controls. Patients with poly disease had lower plasma levels of LDL-C, LILA, IL-1RA, progranulin and VEGF, and elevated serum levels of IL-1b and IL-1b/IL-1RA ratio (Table 1) as compared to patients with oligo disease. No statistically significant differences were seen between neither patients and controls nor patients with oligo disease and poly disease for TC, HDL-C, APOB, CRP, leptin, adiponectin, NGAL, angpl4, angiopoietin, chemerin and resistin. In patients, higher IL-6 [unstandardized B (95% CI) 48.7 (25.1, 72.2), p<0.001], resistin [8.5 (5.1, 11.8), p<0.001] and leptin [2.5 (0.9, 4.0), p=0.002] were identified as correlates for higher VAT. In controls, only higher leptin [unstandardized B (95% CI) 5.3 (3.7, 6.9), p<0.001] was identified as correlate for higher VAT.
Conclusion: Despite similar mass, VAT seems to be closely related to IL-6 and resistin suggesting an active metabolic role in JIA. In addition to IL-6, several pro-inflammatory adipokines/cytokines were increased in JIA potentially playing a role in disease activity. Novel biomarkes, among them IL-1b/IL-1RA system, were identified for differentiating between oligo vs poly disease.

Table 1. Adipokines/cytokines in patients and controls

	Patients (n=60)	Controls (n=60)	p-value patients vs controls	Oligo disease (n=29-30)	Poly disease (n=30)	p-value oligo vs poly disease
TC (mmol/L)	3.9 (0.7)	4.2 (0.6)	0.05	4.1 (0.7)	3.8 (0.7)	0.07
LDL-C (mmol/L)	2.2 (0.6)	2.3 (0.6)	0.23	2.4 (0.5)	2.0 (0.6)	**0.02**
APOA1 (g/L)	1.3 (0.2)	1.4 (0.2)	**0.01**	1.3 (0.2)	1.3 (0.2)	0.89
LILA (nmol/L)	15 (7-37)	20 (7-74)	0.29	26 (8-79)	10 (7-22)	**0.03**
IL-6 (pg/mL)	0.42 (0.29-0.67)	0.34 (0.27-0.46)	**0.01**	0.39 (0.24-0.53)	0.48 (0.37-0.71)	0.055
IL-1b (pg/mL)	1.00 (0.84-1.14)	0.99 (0.86-1.22)	0.53	0.91 (0.75-1.01)	1.06 (0.94-1.19)	**0.01**
Progranulin (ng/mL)	82.3 (61.7-104.2)	69.3 (58.5-87.8)	**0.03**	103.2 (37.4)	72.4 (24.1)	**<0.001**
IL-1RA (ng/mL)	0.50 (0.33-0.95)	0.62 (0.34-1.02)	0.59	0.68 (0.44-1.30)	0.39 (0.30-0.77)	**0.003**
RBP4 (ng/mL)	12989 (2792)	15421 (4877)	**0.001**	13111 (2718)	12867 (2905)	0.74
VEGF (ng/mL)	21 (15-34)	23 (15-32)	0.61	24 (17-42)	17 (13-27)	**0.03**
MCP-1 (ng/mL)	63.0 (54-75)	57 (46-70)	**0.02**	63 (55-77)	62 (54-74)	0.79
IL-1b (pg/mL)/ IL-1RA (ng/mL)	1.85 (0.98-3.08)	1.76 (0.86-3.07)	0.71	1.15 (0.67-2.31)	2.83 (1.56-4.14)	**<0.001**

Numbers are mean (SD) or median (25^{th} – 75^{th} percentile).Oligo disease *persistent oligoarticular juvenile idiopathic arthritis (JIA)*; poly disease *extended oligoarticular JIA or polyarticular disease*.

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POS0770 CAREGIVER BURDEN IN INDIAN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS: A SINGLE HOSPITAL-BASED STUDY

Keywords: Descriptive studies, Patient reported outcomes, Mental health

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Background: Caring for a child with juvenile idiopathic arthritis (JIA) negatively impacts caregivers. There are no studies on caregiver burden in JIA from South Asia.
Objectives: To assess the caregiver burden in children with JIA from India.
Methods: We conducted this observational study in a Tertiary care center in North India. We translated and culturally adapted the CAREGIVER QUESTIONNAIRE[1] into Hindi and administered it to 145 caregivers of JIA patients age ≤ 18 years from November 2021 to December 2022. We collected their

socio-economic data, clinically examined the child and reviewed their clinic records for disease characteristics including activity and damage. The Juvenile Arthritis Multidimensional Assessment Report was used to assess the physical function and health related quality of life. The CAREGIVER QUESTIONNAIRE was scored[2] to determine impact in various domains.

Results: One hundred and forty-five caregivers participated with median age of 39 (32-45) years. This included 68 (47.9%) fathers, 34 (23.4%) mothers, 22 (15.2%) brothers, 18 (12.4 %) uncles and 1 (0.7%) sister, grandfather and grandmother. The JIA patients had median age of 15 (12-17) years and the male: female ratio 2.4:1. Enthesitis related arthritis was the predominant subtype (65.5%) followed by systemic onset JIA (11.7%), RF+ polyarthritis (9.0%), RF- polyarthritis (6.9%), oligoarticular JIA (6.2%) and extended oligoarticular (0.7%). Majority (69.7%) expressed sadness at diagnosis, and one fourth (28.3%) continued to express sadness. Half (53.4%) of the caregivers neglected their health and one tenth (9.7%) became sick. Two thirds (64.8%) had to borrow money to meet the expenses. Emotional impact scored 12.9 ± 2.3 (range 4-18). Social impact scored 6.1 ± 1.9 (range 2-9), economic impact 2.6 ± 1.0 (range 0-5), labour impact 7.0 ± 4.2 (range 0-15), family impact 6.8 ± 1.6 (range 4-16) relationship impact 0.6 ± 0.5 (range 0-0.8). Impact on spirituality was 0.9 ± 0.6 (range 0-5) and impact of social networks was 0.8 ± 0.8 (min= 0, max=8). Total score was 37.8 ± 9.2 (range 10-84).

Conclusion: JIA has significant emotional, social, economic and labor impact on caregivers. Social support needs to be given to caregivers for caring for children with JIA.

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Table 1. Characteristics of 145 children with juvenile idiopathic arthritis

Characteristic	N= 145
Age in years	15 (12-17)
Sex M:F	103 (71.0): 42 (29.0)
Duration of illness in years	3 (2-6)
Height of patients in cms	158 (142- 166)
Weight of patients in kgs	43 (31-51)
Children with JIA siblings	5 (3.4)
Children with at least 1 school year lost	51 (35.2)
Children with hospitalization in past	51 (35.2)
Time required to reach hospital in hours	6 (4-8)
Income in last 12 months	100000 (48000-150000)
Disease associated direct costs in last 12 months, in INR	26375 (10800-50100)
Disease associated indirect costs in last 12 months, in INR	11250 (6000-24000)
Juvenile arthritis disease activity score-27	9 (3-17)
Children with Juvenile arthritis damage index- articular ≥ 1	23 (15.9)
Children with Juvenile arthritis damage index- extraarticular ≥ 1	31 (21.4)
Juvenile arthritis functionality scale	3 (0.75-6.625)
Paediatric Rheumatology Quality of Life Scale	7 (2-14)

Frequency represented as n(n%). Continuous variables expressed as median(interquartile range)

Image: Emotional burden in 145 caregivers of JIA patients

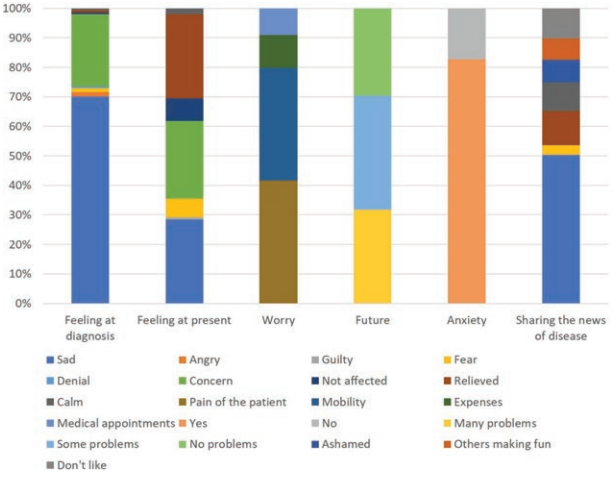


Figure 1.

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POS0771

JAK INHIBITORS AS TREATMENT OF ADULT PATIENTS WITH PEDIATRIC-ONSET JUVENILE IDIOPATHIC ARTHRITIS: A MONOCENTRIC EXPERIENCE

Keywords: Inflammatory arthritides, bDMARD

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Background: JAK inhibitors (JAKi), small molecules that inhibit the Janus kinase enzymes, are increasingly used to treat children with rheumatologic diseases. Clinical experience of JAKi in the management of adult patients with pediatric-onset rheumatic conditions is still scarce.

Objectives: The aim of this study consists in evaluating efficacy and safety of JAKi in a monocentric cohort of adult patients with juvenile idiopathic arthritis (JIA).

Methods: Clinical records of patients attending the rheumatology transition clinic at our centre were retrospectively reviewed; patients were included in case of: i) JIA diagnosis according to current classification criteria (1); ii) age ≥18 years and iii) treatment with JAKi for at least 3 months.

Results: 17 patients that met the inclusion criteria were included in this study. Their demographics and clinical features are detailed in **Table 1**. 9 patients were treated with tofacitinib (52.9%) and 8 subjects (47.1%) received baricitinib. At 3 months, 4 patients (23.5%) achieved disease remission on JAKi: 3 patients achieving remission were treated with baricitinib and 1 with tofacitinib (37.5 vs. 16.7%, p=0.29). None of the patients with systemic JIA and enthesitis-related arthritis obtained remission; the remission rate at 3 months was higher, although not significantly, in the oligoarticular subset compared to the polyarticular subset (37.5 vs. 20%; p=1.0). Disease duration, age at onset and at JAKi start were similar between patients achieving remission and those with active disease (p=0.94, p=0.58 and p=0.72, respectively). Patients with ≤1 active joint involvement at JAKi start had higher remission rate (50 vs. 22.2%; p=0.58). Subjects who achieved remission on JAKi had a significantly lower pre-treatment DAS28 compared to those with still active disease (median DAS28 (IQR) 2.17 (1.9-2.4) and 4.54 (3.8-4.9), respectively; p=0.01, Mann-Whitney U=4). A pre-treatment DAS28 <3.76 predicted response to JAKi with 100% sensitivity and 84.6% specificity (AUC 0.88, p=0.02, 95%CI 0.71-1.05). Concomitant treatment with methotrexate did not significantly affect the remission rate (16.7 vs. 37.5%; p=1.0). This was lower among patients who had been treated with ≥2 biological drugs before JAKi start (9 vs. 66.7%; p=0.05). None of the patients developed side effects during JAKi treatment.

Conclusion: JAKi could represent an effective and safe treatment option for adult JIA patients with low/moderate disease activity, particularly in case of oligoarticular involvement.

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Table 1. Demographics and clinical features of enrolled JIA subjects.

	O-JIA (n=8)	P-JIA (n=5)	ERA (n=2)	S-JIA (n=2)	Total cohort (n=17)
Age at JIA onset, median (IQR)	4.5 (9)	13 (6)	15 (1)	10 (6)	10 (13)
Age at JIA diagnosis, median (IQR)	4.5 (10)	14 (8)	15 (1)	10 (6)	11 (13)
Age at starting treatment with JAKi, median (IQR)	28.8 (6.7)	26 (12)	40.8 (1.8)	37 (10)	31 (13.6)
Gender (F, %)	75% (6)	100% (5)	100% (2)	50% (1)	83.4% (14)
ANA positivity, % (n)	75% (6)	60% (3)	50% (1)	0% (0)	58.8% (10)
Disease duration at JAKi start in years, median (IQR)	27.1 (11.2)	18 (3)	26.25 (1.2)	28 (4)	25 (11.3)
DAS28 at starting treatment with JAKi, median (IQR)	3.76 (1.07)	5 (1)	4.86 (0.25)	3.0 (1)	4 (1.57)
Iridocyclitis, % (n)	50% (4)	20% (1)	0.0 (0)	0.0 (0)	29.4 (5)
N of pre-JAKi sDMARDs, median (IQR)	2 (1.0)	2.0 (1.0)	3.0 (2.0)	4.5 (0.5)	3 (2.0)
Ongoing MTX, % (n)	12.5% (1)	60%(3)	50%(1)	50%(1)	35.2 (6)
Median dose (IQR)	15mg/wk	10 mg/wk	7,5 mg/wk	7.5 mg/wk	15mg/wk
Ongoing LEF, % (n)	25%(2)	20%(1)	0% (0)	0% (0)	17.6% (3)
Median dose (IQR)		20mg die			
Ongoing oral steroids, % (n)	0% (0)	40%(2)	0%(0)	0% (0)	11.7% (2)
Median dose (IQR)		10mg die			
N of pre-JAKi bDMARDs, median (IQR)	2.5 (2.25)	3 (2)	5 (1)	2 (2)	2 (2)
N of involved joints at JAKi discontinuation, median (IQR)	0.5(0)	1 (2)	4 (1)	1 (1)	1 (2)
Days of duration of treatment with JAKi, median (IQR)	324.5 (345)	297(149)	95 (5)	574.5 (513.5)	297 (315)

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POS0772 ´´EPIDEMIOLOGY OF JUVENILE IDIOPATHIC ARTHRITIS IN ARGENTINA: A RETROSPECTIVE STUDY´´

Keywords: Epidemiology

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Background: The term juvenile idiopathic arthritis (JIA) represents a heterogeneous group of disorders, all manifesting joint inflammation, but with different clinical phenotypes, disease course, and outcomes [1,2]. In Argentina, information about patients with JIA is scarce. In our country, different factors such as the diversity of sociodemographic conditions and the disparities in the access to health care, could influence the JIA subtypes prevalence and prognosis of these patients.
Objectives: Describe the sociodemographic and clinical characteristics of patients with different subtypes of JIA.
Methods: Descriptive, retrospective, chart review and multicenter study. Patients were included with a diagnosis of JIA, according to ILAR criteria (2001) and onset of symptoms ≤ 16 years, diagnosis within the last 3 years and with at least 12 months of follow-up since diagnosis by the same physician or treating team. Sociodemographic variables, clinical variables prior to diagnosis by the pediatric rheumatologist, time to specialist consultation, treatments prior to diagnosis and variables at the time of diagnosis by the specialist were recorded: JIA subtype; serological, articular, ocular, and systemic manifestations; associated complications and treatments given.
Results: 320 patients from 17 specialized care centers in Argentina (11 public and 6 private) were included. The mean age at symptom onset was 6.9 years (SD 4.09) and 65.6% of the patients were girls. 94.4% of the patients were in school according to their chronological age. 37.2% and 36.9% of the patients belonged to lower-middle socio-economic strata respectively as measured by the Graffar scale. 96.9% had urban residence and the place of residence in decreasing order were: Province of Buenos Aires, Gran Buenos Aires, CABA, Córdoba, Santa Fe, Jujuy; Salta, Tucumán, Entre Ríos, Catamarca, Chubut, Río Negro, Santiago del Estero, San Juan, Formosa, Chaco, La Pampa, La Rioja, Mendoza, Neuquén and Santa Cruz. 49.1% had private medical insurance and 41.6% public. The mean education (in years) of the parents was 13.6 years (SD 4.16). 54.5% of the cases the first professional visited was the orthopedist. 57.% of patients had received previous treatment: 90.9% non-steroidal anti-inflammatory drugs (NSAIDs) and 5.11% corticosteroids. At diagnosis, JIA subtypes were represented by persistent oligoarthritis (37.8%); polyarthritis FR -(20%); systemic (15%); polyarthritis FR +(12.1%); enthesis-related (6.8%); extended oligoarthritis (2.5%); psoriatic (1.8%) and undifferentiated (0.3%). The median delay by subtype was persistent oligoarthritis (3.00[2.00,4.50]); polyarthritis FR -(3.00[2.00,6.00]); systemic (1.00[100,2.00]); polyarthritis FR +(3. 00 [2.00,6.00]); enthesis-related (7.00 [3.25,12.0]); extended oligoarthritis (3.5 [1.00,4.25]); psoriatic (11.5 [4.75,13.8]) and undifferentiated (1.00 [1.00,1.00]). Articular and serological manifestations were the most frequent. Ocular involvement (12.5%) was more frequent in the oligoarticular subtype. Macrophage activation syndrome was observed in the systemic subtype (2%) and FR - polyarthritis (1.5%). The most used treatments were NSAIDs, cDMARDs, with methotrexate being the first choice. Patients belonging to the systemic (18.7%) and FR+ polyarthritis (5.0%) subtypes were treated with cDMARDs (Anti TNF and IL6 inhibitors).
Conclusion: This is the first national multicenter study of patients with JIA, and the results provide data that should be prioritized, such as shortening the time to specialist consultation. The comprehensive approach to children with JIA should be coordinated by pediatric rheumatologists and supported by a multi- and interdisciplinary team.

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POS0773 PRESCRIPTION PATTERNS AND EFFICACY OF THE SECOND BIOLOGIC AGENT IN JUVENILE IDIOPATHIC ARTHRITIS

Keywords: bDMARD, Real-world evidence, Disease-modifying drugs (DMARDs)

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Background: Biologic agents (bDMARDs) have dramatically changed the disease course of juvenile idiopathic arthritis (JIA). TNF-α inhibitors (TNFi) are frequently used as first-line treatment, while there are no clear recommendations on the choice of the second bDMARD.
Objectives: We aim to describe the prescription pattern of the second bDMARD in a cohort of non-systemic JIA patients.
Methods: This retrospective cohort study included non-systemic JIA patients treated with at least two bDMARDs followed in two Rheumatology Pediatric tertiary centers in Milan, Italy. Analyses were performed with R commander.
Results: The study cohort included 39 patients; general features of the cohort are reported in Table 1. The median age at the first bDMARD was 5.9 [(interquartile range (IQR) 5.3] years. The prescription pattern of bDMARD is shown in Figure 1. Etanercept and adalimumab were the most frequently prescribed bDMARD (16 and 15 times, respectively). The causes of the first bDMARD discontinuation were the following: articular flare (43%), uveitis flare (33%), both articular and uveitis flare (6%), and adverse events (18%). Discontinuation of the first bDMARD due to articular flare was significantly more frequent in patients treated with adalimumab than with etanercept (73% vs. 25%; p=0.01). Conversely, the rate of bDMARD withdrawn due to active uveitis was higher in etanercept-treated patients than in adalimumab ones (38% vs. 20%; p=0.4). The discontinuation rate due to uveitis was significantly higher in the infliximab group than in the adalimumab group (80% vs. 20%; p=0.03). The median age at the second bDMARD was 9.4 (IQR 7.3) years. The majority of the cohort (80%) received a TNFi as the second bDMARD. Adalimumab was the most prescribed second bDMARD (55%) followed by infliximab (29%); the most frequent switch was from etanercept to adalimumab (13 times) (Figure 1). To note, the concomitant use of MTX decreased significantly between the two bDMARDs courses (85% vs. 64%; p = 0.04). The rate of clinical inactive disease (CID) at 3, 6, and 12 months did not differ significantly between the first and the second bDMARD. The general CID (defined as the ever achievement of CID) rate was lower during the first bDMARD course compared to the second (79% vs. 95%; p=0.04). A non-TNFi was prescribed as the second bDMARD in 8 patients (20%): 4 subjects received abatacept (2 for articular disease and 2 for adverse effects), and 4 subjects were treated with tocilizumab (all for articular disease). Uveitis activity represented the main reason for discontinuation in almost half of the patients who switched to a TNFi as the second bDMARD. No significant differences in efficacy were observed during the second course of bDMARDs between patients treated with TNFi or non-TNFi. Eighteen patients discontinued the second bDMARD: 16/31 (52%) from the TNFi group and 2/8 (25%) from the non-TNFi group. The reasons for discontinuation were articular flare (60%), uveitis flare (22%), both articular and uveitis flare (6%), and adverse events (12%).
Conclusion: Most of the patients in our cohort received a TNFi as the second bDMARD, with a significant proportion of patients being treated without MTX. No

apparent differences were seen between the non-TNFi and TNFi for the achievement of clinical inactive disease. Larger studies are needed to explore the choice of the second bDMARD in JIA.

Table 1. Demographic and clinical features of patients

Clinical features	Switch to TNFi (n=31)	Switch to non-TNFi (n=8)	Overall population (n=39)	p-value
Gender, %F (n)	87 (27)	88 (7)	87 (34)	1
Age at onset of symptoms, median (IQR)	2 (3.7)	3 (5.2)	3 (4)	0.651
Uveitis, % (n)	52 (16)	50 (4)	51 (20)	1
JIA subtype, % (n)				
Oligoarticular	58 (18)	38 (3)	54 (21)	0.432
Polyarticular RF-	19 (6)	50 (4)	25 (10)	0.167
Polyarticular RF +	3 (1)	13 (1)	5 (2)	0.372
Enthesitis-related arthritis	8 (3)	0 (0)	8 (3)	1
Psoriatic arthritis	12 (4)	0 (0)	8 (3)	1
Duration of I bDMARDs, median (IQR)	14 (35)	29.5 (16.8)	18 (31)	0.347
Follow-up time (months), median (IQR)	112 (112)	110.5 (82)	112 (103.5)	0.944



Figure 1. Prescription pattern of biologic agents (bDMARDs) in the cohort

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5093

POS0774 CESAREAN SECTION IN WOMEN WITH JUVENILE IDIOPATHIC ARTHRITIS – A POPULATION-BASED STUDY

Keywords: Quality of care, Pregnancy and reproduction, Registries

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Background: The literature on delivery methods in women with juvenile idiopathic arthritis (JIA) is insufficient. Active inflammation is a risk factor for cesarean section (CS) in other arthritic diseases. A CS entails a higher risk for complications than vaginal delivery and a restricted physical activity the first weeks after birth.
Objectives: To explore a possible association of inflammatory active disease and the proportion of CS in women with JIA.
Methods: Data from the Norwegian nationwide observational register RevNatus were linked with data from the Medical Birth Registry of Norway (MBRN). Cases comprised singleton births in women with JIA (n= 196) included in RevNatus 2010 to 2019. Singleton births registered in MBRN during the same period of time and excluding mothers with rheumatic inflammatory diseases (n = 575 798), served as population controls. Disease activity was assessed using Disease Activity Score with CRP (DAS28-CRP-3). We defined inactive JIA as DAS28-CRP-3 < 2.6 and active JIA as DAS28-CRP-3 ≥ 2.6.
Results: CS was more frequent in women with JIA (20.4%) than in population controls (15.6%) and occurred most frequently in inflammatory active JIA (30.0%). Women with JIA had similar risk for elective CS (risk difference 1.1%, 95% CI-1.7 to 5.4) and higher risk for emergency CS (risk difference 3.8%, 95% CI -0.4 to 9.3) compared with population controls. Active disease increased the risk for emergency CS (risk difference 14.0%, 95% CI 4.3 to 27.4).
Conclusion: Women with active JIA had higher risk for emergency CS compared with population controls.
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Table 1. Characteristics of patient group and population controls, reported as n (%) unless specified as mean (SD)

Characteristic	Population controls	JIA	p-value [α]
Singleton births 2010 – 2019	575 798	196	
Maternal age (years), mean (SD)	30.6 (5.1)	29.7 (4.7)	**0.009**
≥35 years	115 077 (20.0)	25 (12.8)	
missing	0	0	
Nullipara	244 354 (42.4)	97 (49.5)	0.054
missing	0	0	
Smoking in pregnancy	34 237 (6.7)	8 (4.3)	0.24
missing	67 663	10	
BMI first trimester, mean (SD)	24.4 (4.8)	24.3 (4.5)	0.90
≥25.0	138056 (34.5)	53 (34.4)	1.0
≥30.0	49167 (12.3)	20 (13.0)	0.89
missing	176 090		
Previous CS	55 992 (9.7)	25 (12.8)	0.19
missing	0	0	
Diabetes[β]	25924 (4.5)	9 (4.6)	1.0
missing	0	0	
ART	20121 (3.5)	9 (4.6)	0.52
missing	0	0	

JIA = juvenile idiopathic arthritis, BMI = body mass index, CS = cesarean section, ART = assisted reproductive technology [α] p-value for patient group compared to population controls, [β] pregestational or gestational

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0775 ASSESSMENT OF SCHOOLING OUTCOMES OF CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Education, Patient reported outcomes, Inflammatory arthritides

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Background: Juvenile idiopathic arthritis (JIA) is the most common inflammatory arthropathy in childhood. It can often be disabling, have an impact on the child's integration, and affect school attendance to varying degrees.
Objectives: The objective of this study was to assess the impact of juvenile idiopathic arthritis (JIA) on children's educational outcomes.
Methods: This is a cross-sectional monocentric study including school-age children with JIA diagnosed according to the International League of Associations of Rheumatology (ILAR) classification criteria. Data were collected for all children on their school level, school difficulties, attendance, and absenteeism. Academic failure was defined by either dropping out of school or grade retention. To evaluate disease activity we used the Disease activity score (DAS-28) for oligoarticular and polyarticular forms, and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score for axial forms. The Childhood Health Assessment Questionnaire (C-HAQ) was used to assess functional disability.
Results: Thirty-six patients were enrolled. The average age was 13.5 ± 5.9 with a female percentage of 55.6 %. The polyarticular form was the most frequent (52.8%) meanly seronegative, followed by the Oligoarticular form (13.9%), then the enthesitis-related form (12.4%). None of our patients was illiterate. Eight children (22.2%) dropped out of school because of their functional disability. Students with JIA who attended school had an absenteeism rate of 67.8%. Slightly more than half of the JIA patients (57.1%) failed at least one grade. Academic failure was associated with a high disease activity (p=0.003), the presence of joint deformities (p=0.002), a high C-HAQ score (p=0.01), and an erythrocyte sedimentation rate: ESR ≥100 mm/h (p=0.02). The absenteeism rate was associated with rural origin (p=0.004), pain level (p=0.02), high disease activity (p=0.01), hip involvement (p=0.001), and a high C-HAQ score (p=0.03).
Conclusion: Our study shows that the schooling of children with JIA was negatively influenced by this disease. Proper control of the disease activity and inflammation will guarantee better school attendance and increase academic performance.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5972

POS0776

STUDY OF GROWTH AND DEVELOPMENT IN INDIAN PATIENTS WITH ENTHESITIS RELATED ARTHRITIS CATEGORY OF JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Inflammatory arthritides

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Background: Juvenile Idiopathic Arthritis (JIA) is an umbrella term for chronic arthritis with onset before 16 years of age. According to ILAR classification criteria it is subdivided in 6 category. Growth failure is a well observed phenomenon in JIA and more so in Systemic onset and polyarticular variants. Except from western literature, in Asian countries Enthesitis Related arthritis (ERA) is more prevalent. In our study, we have studied the growth and development of patients with Enthesitis Related arthritis variant.
Objectives: To assess the prevalence of growth failure and sexual maturity in patients with JIA-ERA and possible association with disease activity, damage and drug therapy.
Methods: We have enrolled all patients of JIA-ERA, visiting rheumatology outdoor patient service in KGMU, Lucknow, from July 2021 to Dec 2021. All the patients must qualify Revised ILAR classification criteria for ERA. Those who have concomitant developmental disorders, secondary amyloidosis and macrophage activation syndrome were excluded from the study. All patients were clinically examined and previous medical records were thoroughly checked. Anthropometric measurement and tanner staging was done at baseline. Growth velocity was observed at follow up visit. This is a Prospective observational study with follow up at 3 and 6 months.
Results: 50 patients of JIA-ERA were enrolled. Majority of them were boys with a male to female ratio of 4.5:1 and mean age of 15.5 years. Mean age of onset was 11.5 years with a mean disease duration of 41.25 months. 32% had family history of SpA in first degree relatives and 12 % had history of uveitis in parents. Only 3 patients (6%) had history of other autoimmune diseases in family. There was no developmental delays in children with JIA-ERA and 47 patients (94%) were vaccinated for their age. 76% patients had inflammatory back pain with significant early morning stiffness at baseline and 18% had purely axial involvement. 20% had active or past history of uveitis, 12% had dactylitis and 30% had enthesitis (predominantly Achilles enthesitis). 76% had achieved age appropriate linear growth with 20% were 2SD above their mid parental height. 12 patients (24%) had significant limb length discrepancies. 64% were underweight for their age with low BMI. 30% patients had delayed sexual maturity in terms of sparse axillary and pubic hair with low tanner stage for that age. In majority of cases growth velocity of 4cm/6month was observed which was quite similar to the pubertal growth spurt of normal reference value. No significant association of growth failure was observed with prior corticosteroid use, disease duration, disease activity (JSPADA and JADAS27) and damage (JADI) score.
Conclusion: Growth failure wasn't well observed in JIA-ERA variants. One third had delayed sexual maturity for their age. Growth velocity was similar to age matched healthy population. No significant association was found with prior corticosteroid use, disease duration, disease activity or damage score.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6439

POS0777

ADALIMUMAB AND ANTI-DRUG ANTIBODIES IN A COHORT OF CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A SINGLE-CENTER EXPERIENCE

Keywords: Inflammatory arthritides, Targeted synthetic drugs, Outcome measures

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Background: Adalimumab (ADA), a fully humanized antibody against tumor necrosis factor (TNF)-α, has revolutionized treatment of patients with juvenile idiopathic arthritis (JIA). Although most of these respond within the first weeks, a minority may show loss of response (LOR) after continued exposure. Many studies demonstrate the influence of anti-adalimumab antibodies (AAA) on serum drug concentrations and clinical outcome in adults. However, little information about AAA and LOR is available for children with JIA.
Objectives: To describe demographic and clinical features in a single-center cohort of JIA patients treated with ADA, grouped according to frequency of drug administration (1W vs 2W); to assess ADA levels versus AAA titer and, finally, to investigate possible correlation between LOR to ADA and AAA.
Methods: Records of JIA patients on ADA treatment were retrospectively reviewed with focus on medical history and ELISA (enzyme-linked immunosorbent assay) ADA/AAA levels in a 12-month-period (Feb 2021-Feb 2022). Children with idiopathic uveitis were excluded. Samples furthest from last drug administration was defined as "trough level". Data were analyzed via descriptive statistics (STATA 15.1).
Results: Of 61 JIA patients treated with ADA (49% females), 38 had ANA positive oligoarthritis with almost one large joint involvement at disease onset (T0). None of them presented RF-positive polyarthritis, nor systemic JIA (s-JIA). The median age at T0 was about 3 years. Half of study cohort was b-DMARDS naive at ADA start (T1), while all children were on c-DMARDs. Chronic recurrent uveitis was the main reason for ADA starting, followed-by tenosynovitis and spine or hip active arthritis. At the first ADA/AAA sampling (T2), approximately 15% of patients had active disease, with elbows or wrists as the most frequently involved. Extreme variability was observed between AAA titers (median 7.4 AU/ml) and ADA levels (median 15.4 micrograms/ml), regardless from 1 or 2-weekly administration. ADA levels, compared to the days from last drug administration, reached plateau values corresponding to a pharmacokinetic steady state. Among both study groups, a possible inverse correlation between ADA and AAA was found. We identified 30 JIA patients with clinical (presence of arthritis or uveitis) or laboratory (ESR ≥15 mm/h; CRP> 0.5 mg/dL) disease activity. Among these in only 6 we found very high AAA titers (350.0 - 113.4 AU/mL). In the subgroup of 37 patients with "trough-level" sampling heterogeneous data about AAA titers and drug level distribution were observed.
Conclusion: Our preliminary data showed a possible association between occurrence of AAA and lower ADA levels. However, a targeted risk analysis about high AAA titers and LOR incidence was not available. Monitoring of drug immunogenicity should be implemented in daily practice and become subject of future studies JIA.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6465

Clinical cases

POS0778

METASTATIC ANGIOSARCOMA MASQUERADING AS SYSTEMIC INFLAMMATORY DISEASE WITH REFRACTORY PERICARDITIS

Keywords: Malignancy, Heart

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Background: Rheumatologists are frequently asked to evaluate patients with acute pericarditis. The majority of cases are idiopathic with systemic autoimmune disease underlying maybe 7% or less of cases in developed countries.[1-2] It is critical to recognize the presence of systemic symptoms or poor prognostic pericarditis features, such as tamponade physiology or poor response to non-steroidal anti-inflammatories, that raise concern for a malignant etiology of pericarditis.[1-2]
Objectives: A case report of a patient presenting with refractory pericarditis caused by metastatic angiosarcoma.
Methods: A 46 year old male presented for evaluation of unresolving pericarditis. Five months prior, he had developed abrupt-onset pericarditic chest pain with associated dyspnea. Initial ED evaluation was notable for normal troponins and non-specific T wave abnormality on ECG. CT chest angiogram revealed a trace pericardial effusion and isolated right axillary lympadenopathy. The patient declined further evaluation. He presented a week later with persistent pericarditic pain. Echocardiogram showed enlargement of the pericardial effusion with possible early tamponade. Respiratory viral testing was negative. C-reactive protein (CRP) was elevated to 20.83mg/dL (Ref ≤0.5mg/dL) and ferritin to 2344.4ng/

mL (Ref 21.8-274.7ng/mL). Soluble IL-2 receptor and blood counts were normal. Rheumatoid factor was weakly positive with ANA, anti-DNA, anti-CCP, and ANCA returning negative. Core needle biopsy of an axillary lymph node was negative for malignancy. Pericardiocentesis was deferred due to patient preference and stability. He was started on colchicine for autoimmune versus idiopathic pericarditis without significant improvement. He was transitioned to prednisone with improvement in his chest pain, effusion, and CRP; dyspnea and hyperferritinemia persisted. Attempts to taper prednisone failed due to flaring of pericarditis. The patient was referred to our center for evaluation of refractory pericarditis and possible systemic inflammatory disease. No signs or symptoms of RA or CTD were present. The patient endorsed recent night sweats, 11 kg of weight loss, and new bone pain. Full body PET/CT was pursued and demonstrated two FDG avid masses adjacent to the right side of the heart along with multiple lytic bone lesions of the spine and pelvis.

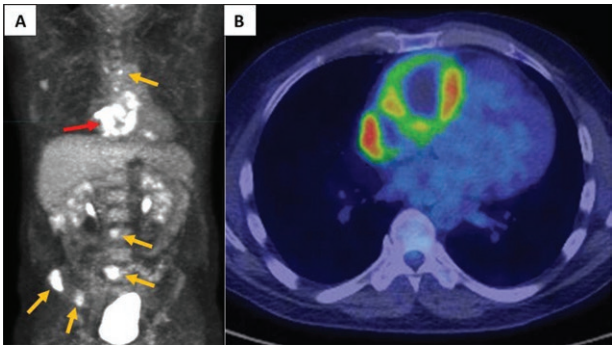


Figure 1. (A) PET Maximum intensity projection showing large cardiac mass (red arrow) and multiple FDG avid bone lesions (yellow arrows). (B) PET Axial fused image showing large FDG avid cardiac mass.

Results: Cardiac CT confirmed malignant-appearing, centrally necrotic mass along the right side of the heart extending to involve the pericardium. Iliac bone biopsy confirmed a diagnosis of metastatic angiosarcoma. He was not a candidate for cardiac tumor resection and was referred to oncology for palliative chemotherapy.

Conclusion: Primary malignant cardiac tumors are a rare cause of pericarditis. Cardiac angiosarcomas are the most common type of primary malignant cardiac tumor. They most commonly arise from the right atrium or pericardium and may present with pericarditis-like symptoms.[3]

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Disclosure of Interests: None Declared.

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POS0779

BRAIN TUMOR-LIKE LESIONS AS FORM OF PRESENTATION OF NEUROPSYCHIATRIC LUPUS

Keywords: Systemic lupus erythematosus, Imaging

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Background: Neuropsychiatric (NP) systemic lupus erythematosus (SLE) encompasses a broad spectrum of syndromes.[1] The attribution of the NP manifestations to the disease itself is a challenge and is critical to select the correct treatment. [2]

Objectives: To present a case of a woman with SLE who developed brain tumor-like lesions.

Methods: The clinical manifestations, complementary tests, treatment are described.

Results: 28-year-old woman with a history of SLE with moderate disease (constitutional, cutaneous, musculoskeletal, hematologic and serological) and frequent flares despite treatment with hydroxychloroquine and doses of prednisone up to 20mg/day. She was admitted to the rheumatology service due to a severe flare-up of SLE, with headache, fever, worsening of lesions in photo-exposed areas, lymphadenopathy, arthralgia, nausea, and vomiting. Blood tests showed platelets 60,000/μL, elevated ESR, abnormal liver biochemical, decreased C3, normal urine, with no data of infectious etiology. After treatment with iv methylprednisolone (250mg x 3) and iv belimumab (600mg), she presented clinical and analytical improvement and was discharged from the hospital. Three days later, the patient presented persistent headache and fever, and decreased level of consciousness; laboratory tests showed leukocytosis, anemia, abnormal liver function tests, elevated ESR and CRP. She was referred to the emergency room. On the neurological exam: patient disoriented in time and space, opened her eyes only after painful stimulus, signs of dysarthria, and facial paralysis. CT scan revealed a space-occupying lesion (3 x 2cm), at the level of the right basal nuclei with perilesional edema and collapse of the anterior horn of the right lateral ventricle, discreet mass effect with displacement midline, and similar contralateral involvement. The patient was admitted to the hospital due to a probable primary neoplasm of the central nervous system, without being able to initially exclude infectious, vascular, and inflammatory pathologies. Treatment was started with iv dexamethasone and empiric therapy for bacteria, viruses, fungi, and parasites. The following day, brain MRI (Figure 1, A - B) showed lesions in the right and left basal ganglia, with a mass effect in the right basal ganglia and images of their interior with artifact related to hemosiderin or deoxyhemoglobin, related to history of bleeding from the lesions. Alteration of thickness and irregular subependymal signal in the occipital horns. The stereotaxic brain biopsy showed parenchyma with intense acute inflammatory changes, with necrosis and vascular inflammation, without histopathological features of etiological specificity, and no evidence of neoplasia. The lumbar puncture did not show alterations, cytology without malignant cells, antibodies against onconeuronal proteins negative. Ruled out infectious etiology. Slow progressive improvement in clinical and laboratory manifestations and in imaging tests improvement was seen in response to the therapy with high doses of glucocorticoids and cyclophosphamide pulses. After prolonged hospitalization, she was discharged from the hospital, her neurological status being normal. Brain MRI (Figure 1, C-D), two months after discharge, showed a clear decrease in the size of the brain lesions.

Conclusion: To the best of our knowledge, no brain space-occupying lesions (simulating neoplasms) attributed to SLE have been described. The context of concomitant activity, the negative results for infectious/malignant diseases, and the favorable response to immunosuppressive treatment, support the neuroinflammatory etiology.

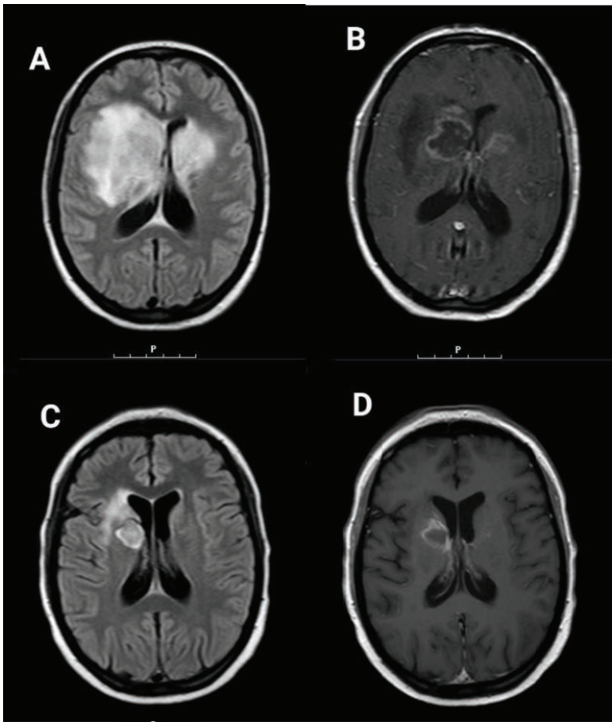


Figure 1.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0780 PSEUDOGOUT OF THE TEMPOROMANDIBULAR JOINT: A CASE REPORT

Keywords: Pain, Ultrasound, Crystal arthritis

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Background: Deposition of calcium pyrophosphate dihydrate crystals occurs in crystalline arthropathies, such as gout and chondrocalcinosis. Occasionally, crystal deposits may affect the temporomandibular joint (TMJ), especially involving the articular cartilage and fibrocartilage, causing pain and jaw claudication, mimicking giant cell arteritis (GCA). Ultrasound (US) images reveal spotted hyperechoic signals in the articular disk and sometimes a marked destruction of the condyle with erosive changes.
Objectives: To highlight and discuss the potential role of TMJ US in guiding differential diagnosis of orofacial pain syndrome (frontal headache and jaw claudication), arousing the suspicion of GCA.
Methods: Case-report describing an old patient presenting with severe headache and jaw claudication with particular reference to the role of TMJ US in differential diagnosis of an initially suspected GCA.
Results: An 85-year-old woman presented to the Emergency Department with a 2-days history of progressively worsening frontal headache and jaw claudication. She reported no visual loss or polymyalgia rheumatica symptoms. Right temporal artery tenderness was appreciated on clinical examination, without reduced temporal artery pulse. No axillary, brachial, or carotid bruits were appreciated. Neurologic examination was normal; brain computed tomography (CT) revealed no intracerebral hemorrhage or intraparenchymal lesions. Her erythrocyte sedimentation rate was 67 mm per hour, and C-reactive protein level 3.30 mg per deciliter. Temporal artery US revealed no abnormalities (absence of halo sign or arterial stenosis). Since patient complained of chewing pain and given that temporomandibular disorders may be misdiagnosed as GCA, TMJ US was performed revealing the presence of extensive calcifications around the right temporomandibular head and in the meniscus (Figure 1, Panel A). Brain CT images were then carefully reviewed: in the right TMJ massive calcifications surrounding the right temporomandibular head were appreciable (Figure 1, Panel B). Moreover, coronal CT scan of the atlantoaxial region showed calcifications of the alar ligaments, particularly evident on the superior-left side (Figure 1, Panel C). High dose glucocorticoid regimen was then started (Methylprednisolone 40 mg once daily). The patient's pain rapidly improved, steroid was rapidly tapered until withdrawal, with a complete resolution of symptoms within few weeks.
Conclusion: Crowned dens syndrome is characterized by recurrent neck pain related to radiodense deposits of hydroxyapatite or calcium pyrophosphate dihydrate in ligaments around the odontoid process, which create the appearance of a crown or halo surrounding the odontoid process on radiographic imaging. Evidence of inflammation (e.g., fever or elevated levels of C-reactive protein) is usually observed. A short course of steroids, followed by administration of non-steroidal anti-inflammatory medication, usually completely alleviates symptoms. Rarely, temporal arteritis headache may mimic TMJ irradiation pain, or present as jaw claudication. In this case, temporal arteries and TMJ US can enable to discern a halo sign, as a hallmark of giant cell arteritis, from suspicious signs of TMJ disorder. Rapid diagnosis can prevent misdiagnosis, invasive and unnecessary investigations (temporal artery biopsy) and inappropriate treatment (long term steroid regimen, leading to cardiovascular risk and increased bone loss).
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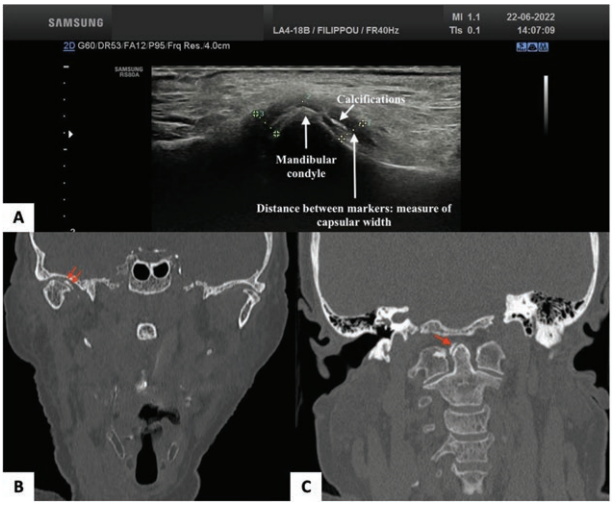


Figure 1.

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Disclosure of Interests: None Declared.
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Arthritis research

POS0781-PARE RETROSPECTIVE STUDY OF VITAMIN D DEFICIENCY IN RHEUMATOLOGIC PATIENTS DURING THE COVID-19 PANDEMIC IN POLAND

Keywords: COVID, Best practices, Vitamin D

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Background: Before the COVID-19 pandemic it was estimated that nearly 70% of the population is deficient in vitamin D - 25(OH)D <20ng/ml in Poland [1]. The percentage was expected to increase due to indoor isolation during the COVID-19 pandemic. Vitamin D has a positive effect on the condition of the bones, affects the course of autoimmune diseases, the course of neurological diseases, in type 2 diabetes, vitamin D supplementation improves glucose tolerance and reduces insulin resistance [2,3,4].
Objectives: The aim of the retrospective study was to determine what percentage of rheumatology clinic patients suffer from vitamin D deficiency and whether this condition is effectively treated.
Methods: In January 2023, a retrospective analysis of the documentation of 172 patients treated at the Rheumatology Outpatient Clinic in Bełżyce (Poland) in 2022 was conducted.
Results: Results: The mean age of the 172 patients whose documentation was analyzed was 60.43 years (min 19, max 88). There were 132 women (76.8%) and 40 men (23.2%) in this group. The mean concentration of vitamin D was 25.57ng/ml±SD11.9 (min 5.7, max 75, Me 22.8). Vitamin D deficiency was found in 44% (serum concentration <20mg/ml), suboptimal concentration (20-30ng/ml) in 31%, optimal concentration (30-50ng/ml) in 21%, and high concentration (>50ng/ml) ml) in 4%. All those with a deficit or deficiency (75 people) were prescribed cholecalciferol in a dose of 20,000 units orally, 1 capsule twice a week after breakfast for 2 months [5]. Patients with optimal vitamin D levels were advised to take a dose of 2,000 units per day. Among the patients with deficit or deficiency, 48 people came for a follow-up visit to check the level of vitamin D (64% of the group with too low vitamin D concentration; 28% of the entire group whose documentation was analyzed). In the follow-up examination, the mean concentration of vitamin D was 37.14±9.8ng/ml (min 28, max 84, Me 35.3). Therefore, a statistically significant increase in the concentration of vitamin D in the blood was noted ($p<0.05$). In the group of people who came for the follow-up examination, there were 35 women, whose mean age was 60.7 years and 13 men (mean age 68.2 years).

Conclusion:
1. During the COVID-19 pandemic in the group of outpatient rheumatology patients, 75% had a deficiency or suboptimal level of vitamin D.
2. Treatment with cholecalciferol in a dose of 20,000 IU twice a week orally for 2 months is effective treatment of vitamin D deficiency.
3. Too low percentage of patients diagnosed with vitamin D deficiency come for visits and check-ups.

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Disclosure of Interests: None Declared.
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POS0782-PARE MANAGING PSORIATIC ARTHRITIS: PATIENTS' VIEWS AND ATTITUDES TO USING AN ONLINE WELLNESS PROGRAM

Keywords: Psoriatic arthritis

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Background: Patients diagnosed with psoriatic arthritis (PsA) confront decisions about how to optimize treatment of their chronic disease including patient physician interaction and modifying their own lifestyle choices that may impact their disease outcomes.
Objectives: To examine PsA patients' views and attitudes of managing their disease using a guided online wellness program to address lifestyle behaviors such as nutrition, exercise, sleep, and stress management.
Methods: A cross-sectional online survey was developed with patient and clinician input and administered to US adults with a self-reported diagnosis of PsA in the ArthritisPower registry. Survey questions assessed participant (pt) experience with, and motivations to participate in, an online wellness program through various mechanisms to address nutrition, exercise, sleep and stress management. E-coaching is a validated tool using email coaching as an individualized tailored communication on wellness strategies to improve lifestyle behaviors.
Results: 312 pts completed the survey, of whom 83.0% were female, 91.0% white, mean age 57.1 (SD 11.4) years, and 10.0 (SD 10.2) years since PsA diagnosis. Most pts (93.6%) were diagnosed by a rheumatologist for their PsA. Over 90% of pts reported being 'somewhat likely' or 'very likely' to interact with an online coach at least twice a week or spend one to two hours a week learning about nutrition, exercise, sleep and stress management (90.4% and 92.6%, respectively) if they had the opportunity to take part in a wellness program. However, only 8.7% of pts are currently participating in a structured wellness program. Feeling better was the top motivator for participating in a wellness program (179, 57.4%) followed by the want to improve PsA symptoms (145, 46.5%). About a third of pts would prefer to participate in a wellness program by interacting with an online trained professional (34.0%), followed by attending an online course (16.4%) and reading written material (16.0%) (Table 1). In reporting barriers to wellness changes, cost and not having the energy to make changes were selected by about half of pts (both 47.1%) (Figure 1). Over one-tenth (13.1%) of pts reported having no barriers to participation in wellness programs.
Conclusion: The overwhelming majority of patients report willingness to be involved in a wellness program. Feeling better is a top motivator, while cost and lack of energy to make changes were top barriers to adopting wellness behaviors. Our study results support the use of guided online participation in wellness programs over alternatives such as online courses and written materials. Further studies are needed to elucidate how e-coaching wellness platforms may improve and sustain lifestyle changes in PsA patients.

Table 1. Participation Preferences for a Wellness Program, N=312

	n (%)
Interacting with an online coach (trained professional)	106 (34.0)
Attending an online course	51 (16.4)
Reading written material	50 (16.0)
Watching videos	46 (14.7)
In-person consultation and coaching from a trained professional	45 (14.4)
Attending an in-person class	14 (4.5)

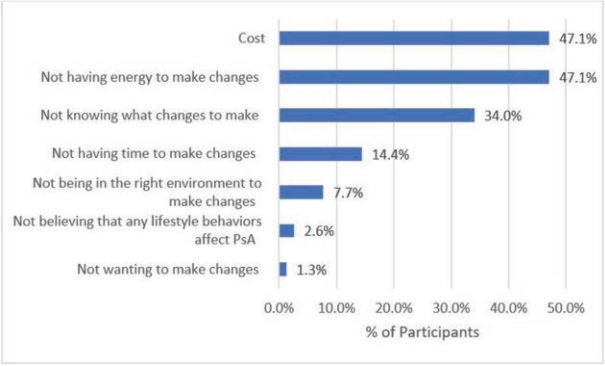


Figure 1.

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Disclosure of Interests: W. Benjamin Nowell Grant/research support from: AbbVie, Amgen, Janssen and Scipher Medicine, Angela Degrassi: None declared, Shilpa Venkatachalam: None declared, Kelly Gavigan: None declared, Ashley Krivohlavek: None declared, Esteban Rivera: None declared, M Elaine Husni: None declared.
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POS0783-PARE WITHDRAWN

POS0784-PARE **RHEUMATOID ARTHRITIS (RA) PATIENT CONCERNS REGARDING ADVERSE EFFECTS OF TREATMENT AND ISSUES OF ADHERENCE**

Keywords: Self-management, Safety, Patient reported outcomes

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Objectives: To explore whether rheumatoid arthritis (RA) patients' concerns regarding adverse events (AEs) during their treatment are adequately collected and considered in making treatment decisions.
Methods: Using pilot focus groups,and after obtaining voluntarily 12 RA patients (8 women, 4 men, duration RA 1 to > 20 years) met in groups of 4 and described their concerns regarding how they experience being treated for RA. All patients were from Southern California and spoke and understood english fluently.We recorded/ transcribed three 90-120 minute focus groups. Participants completed an 18 item Beliefs about Medications Questionnaire (BMQ), which included 10 specific arthritis medication questions and 8 questions about doctors. They examined a table describing 75 AEs of concern to oncology patients - the PRO-CTCAE (Patient Reported Outcome-Common Terminology for Adverse Events), and checked AEs they had experienced or were of concern. Data were recorded and transcribed from all 90-120 minutes sessions.. Using Dedoose software, transcriptions were inductively coded and analyzed to identify specific áreas of associated with RA medications. A total of 225 excerpts were extracted to which a total of 607 codes were applied.
Results: AEs associated with medications were the expilicit objective of this study and so we could not estimate the percent of patients with medication-related AE concerns Of the 36 excerpts in which participants discussed AEs while discussing particular types of medications, conventional synthetic DMARD(csDMARD) were more likely to be discussed than biologics/ targeted synthetic DMARD(b/tsDMARD) (58% csDMARDS, 28% b/tsDMARDs, 14% corticosteroids). 42 unprompted comments emphasized self-management strategies 10/42 specificied the context of medications, such as modifying dosages (40%) or stopping medication altogether (60%); of these, 8/10 comments specified csDMARDs or corticosteroids. Four of 12 voiced uncertainty about whether AEs were related to RA, medications, or something else. On the BMQ, participants generally agreed that their health depended on their medications, which protected them from becoming worse and that the medicines did more good than harm. Nevertheless, their medications disrupted their lives, and they worried about long-term effects. Generally, participants did not think doctors used too many medications or placed too much trust in the medications.. In each focus group, participants found the PRO-CTCAE bewildering and raised the specter of cancer due to their medications. The 10 most commonly marked AEs were dry mouth, mouth sores, nausea, bloating, diarrhea, abdominal pain, hair loss, bruising, general pain and fatigue.
Conclusion: Medications were generally viewed positively but AE concerns were more common among those using csDMARD than b/tsDMARDS or corticosteroids. Concerns about AEs triggered self-management strategies, potentially affecting adherence. We suggest that a robust mechanism for patients to explicitly *report the impact* of AEs that they are experiencing could facilitate clinical communication and positively impact adherence.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6393

Psychosocial support

POS0785-PARE **NEWLY DIAGNOSED WITH INFLAMMATORY ARTHRITIS – PATIENTS' EXPERIENCES, THOUGHTS, AND CONCERNS: A QUALITATIVE STUDY**

Keywords: Patient information and education, Inflammatory arthritides, Qualitative research methods

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Background: To be diagnosed with inflammatory arthritis (IA) is challenging for the individual, who may experience uncertainty and anxiety [1,2]. We need more knowledge on how health professionals can support patients that have been diagnosed recently. Previous studies have focused on patients' experience of living with IA, but few have aimed to focus on the newly diagnosed.
Objectives: This study aimed to explore patients' experiences, thoughts, and concerns after being diagnosed with IA.
Methods: Participants were patients newly diagnosed with IA (rheumatoid arthritis or psoriatic arthritis) recruited from a feasibility study to a self-management intervention [3]. Data was collected through semi-structured interviews. The analysis was based on reflexive thematic analysis method, which provides a rich and complex understanding of patterns within data [4].
Results: Twelve adults (six men and six women, aged 25-77) diagnosed with rheumatoid arthritis (n=8) or with psoriatic arthritis (n=4) within the last three months, were interviewed at an outpatient rheumatology clinic in Denmark. We identified four main themes: 1) *The intrusiveness of arthritis.* Symptoms affected patients physical and emotional state. The initial symptoms were experienced very differently. For some, symptoms were acute and explosive. In others, disease progression was slow, and participants became more and more invalidated with time. However, all experienced that arthritis affected their mood, and in general, patients were overwhelmed to being diagnosed with arthritis. 2) *Getting familiar with arthritis and its treatment*. Patients requested information about how to manage IA, and several were already seeking information about non-pharmacological treatments such as different diets, meditation, and exercises. The participants paid great attention to how they responded to the pharmacological treatment and how their bodies reacted in different situations. Furthermore, the newly diagnosed also strove to become acquainted with their new body with arthritis. 3) *Adapting to life with arthritis*. Some felt it natural to tell family members about their arthritis. In contrast, others thought it was none of their concern and did not like to bother them. The participants did not want arthritis to be an issue for other people to worry about. 4) *Worries about the future*. Overall, the pharmacological treatment had a profound focus immediately after diagnosis. Worries about the potential lack of effect contributed to great concern and frustration. The worries were related to all aspects of life, including work and family life. However, the newly diagnosed also hoped that symptoms would be acceptable so that everyday life could be restored. Nevertheless, they also realized that they had to rethink how they wanted to prioritize in the future.
Conclusion: The results of this study highlight the complexity of being newly diagnosed with IA. Time after diagnosis is dominated by worries about the benefit and harms of pharmacological treatment and the future. However, the participants did not want to perceive themselves as being sick. Instead, they strove to comfort themselves with hope for successful pharmacological treatment together with taking their own non-pharmacological initiatives.
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Disclosure of Interests: None Declared.
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POS0786-PARE CONNECTING THROUGH SHARING - PUBLISHING A BOOK FOR YOUNG PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES (RMDS) BY YOUNG PEOPLE WITH RMDS

Keywords: Quality of life, Mental health, Self-management

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Background: Research has shown that adolescents with chronic conditions such as rheumatic and musculoskeletal diseases (RMD) are more prone to developing psychiatric conditions. Reasons for this could be the common stigmatization that they encounter in their daily life and the feeling of being the only odd one out. Youth-R-Well.com, the Dutch organization for youth (18-30 years) with RMDs, responded to this by providing monthly columns from their peers with RMDs. These columns show the daily life and struggles of young arthritis patients with a touch of humor, thus providing some of the much needed recognition.
Objectives: The main objective of this project is to provide information, recognition and awareness about the daily life and struggles of young RMD patients. By reading the columns that were written lightly humorous, it will be easier for young people to find the much needed recognition that they often lack in their own environment. These columns do not only recognize the often experienced pain and (chronic) fatigue, but also recognize the insecurities that come with living with a RMD, and show ways to face them. By describing their daily life, these young people provide tips on how to approach certain situations. Therefore, besides providing information and recognition, these columns can also function as a tool that increases the self-management of their disease.
Methods: To provide these columns, different young people with a RMD (18-30 years) were asked over the years to regularly write columns that were published on the website of Youth-R-Well.com. To draw more attention to the columns and reach more people, e.g., by distributing the books in hospitals, the columns of one of the writers will be published in a book.
Results: Since 2012, approximately 150 columns have been published on the website of Youth-R-Well.com, from nine different writers. Youth-R-Well.com has received, and still receives, many thankful messages from young people with RMDs, saying that they benefited a lot from the tips and recognition that the columns provided. The book has not been published yet, but Youth-R-Well.com is right now talking to self-publishing companies, and has also received commitments from parties that will take partial responsibility for the costs of publishing.
Conclusion: Publishing columns on a regular basis has helped a lot of young RMD patients in the Netherlands to feel recognized in their struggles with living with a RMD. They have said to have learned a lot about how to cope with certain issues that come with having a RMD. This is something Youth-R-Well.com will definitely continue with. The book is unfortunately not published yet, but will be in the near future.
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Disclosure of Interests: None Declared.
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HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

POS0787-HPR PHYSICAL ACTIVITY GUIDANCE IN THE RHEUMATOLOGY CLINIC – PATIENT EXPERIENCES AND PREFERENCES. A QUALITATIVE STUDY

Keywords: Qualitative research methods, Lifestyles, Rheumatoid arthritis

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Background: Evidence of the positive health effects of physical activity (PA) and exercise in patients with rheumatoid arthritis (RA) is well established. Nonetheless, higher proportions of patients with RA are physically inactive compared to the general population [1]. Besides disease-related barriers to engaging in health-enhancing PA, a significant barrier may be the lack of specific PA guidance from healthcare professionals [2].
Objectives: The present national qualitative study aimed to explore daily PA levels and the patients' perspectives on the current and future support from health professionals (HPRs) in promoting PA in patients with RA.
Methods: We recruited participants from five rheumatology departments in Denmark. Recruitment was based on results from an earlier register-based cross-sectional study [3], which aimed to identify socio-demographic and clinical differences between participants and those declining participation in a RCT focusing on promoting light-intensity PA in patients with RA [4]. Accordingly, we used a purposive sampling method to ensure that interview participants variated in age, educational level, smoking status, PA levels, and disease history. Due to COVID-19, the interviews were conducted by telephone, physically, or through online platforms. Data analysis was based on reflexive thematic analysis [5].
Results: Of the 20 participants, 13 were female, and the mean age was 55 years (range 22-77). We generated four themes; 1) *Accept of arthritis is a process*, which was attributed to acknowledging RA as part of life as an essential mental step before the participants could fully adapt PA levels and exercise. 2) *Daily physical activity – motivation and barriers,* where participants described how they generally perceived PA. Also, they described their preferred intensities and types of activities as well as motivations and barriers for engaging in PA. 3*) Experiences with physical activity guidance – your own responsibility?* This theme reflected how participants missed to have more comprehensive and detailed discussions with HPRs in the rheumatology outpatient clinics about PA, - in other words not making it a matter of their own insistence and curiosity. 4*) How, when and where physical activity guidance is provided is essential*, which referred to the participants' preferences and needs for future PA guidance in the rheumatology clinic, including timing, content and location.
Conclusion: The study results emphasize that treating patients with RA should hold an integrated and strengthened focus on PA and exercise in routine care. However, to optimize this focus, HPRs may need adequate training in how to prioritize, guide, and motivate patients towards initiating and maintaining PA in their everyday lives.

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POS0788-HPR "IT'S LIKE LISTENING TO THE RADIO WITH A LITTLE INTERFERENCE" - MANAGEMENT OF PAIN AMONG PATIENTS WITH PSORIATIC ARTHRITIS

Keywords: Qualitative research methods, Pain, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is an inflammatory rheumatic disease, associated with the skin disease psoriasis. Health-related quality of life is severely affected and is suggested to be so since these people have two chronic diseases at the same time, a skin disease that causes cosmetic changes and a joint disease that causes functional limitations [1]. Both international collaborations [2] and single studies of outcome measures, disease consequences and experiences of pain in PsA emphasize that pain is one of the most important areas to focus on in the assessment and treatment of this patient group [3]. To the best of our knowledge, no studies with a qualitative design exploring the management of pain from the perspectives of patients with PsA exist.
Objectives: To explore and describe approaches towards pain and its management among patients with PsA.
Methods: A descriptive design with a qualitative inductive approach was used. Semi structured interviews were conducted with 11 participants with PsA (3 men and 8 women) recruited from one outpatient rheumatology clinic in the middle region as well as from a university hospital rheumatology clinic in the northern region of Sweden. Variation in gender, age, disease duration, activity limitation, perceived pain, fatigue, and general health was aimed at by using strategic sampling. Qualitative content analysis was used, and a pattern of theme of meaning, descriptive subthemes, and categories was constructed based on the participants' experiences and perceptions [4, 5].
Results: A main overarching theme of meaning and three subthemes describing participants' management of pain were identified. They were 'Taking charge of life despite the constant murmur of pain' through 'Sorting out vulnerability', 'Reaching acceptance and engagement' and 'Directing focus to change'. Nine categories further described the components of the management; 'face uncertainty for the future', 'consider restrictions', 'illuminate the invisible', 'increase awareness', 'find permissive environment and social support', 'enhance inner endurance', 'reformulate emotions and thoughts ', 'use distracting activities' and 'adjust activities' (Figure 1).

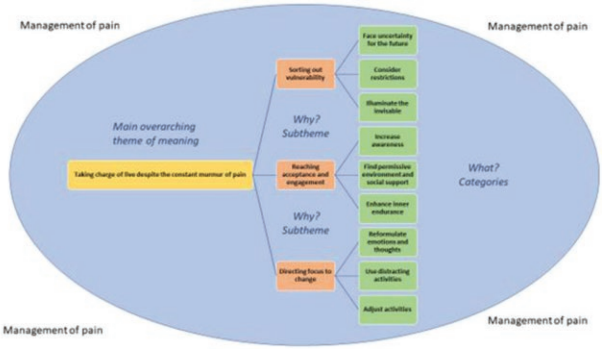


Figure 1.

Conclusion: Dealing with and regulating feelings and thoughts within oneself as well as altering behavior and finding new solutions outside oneself seem to be significant for management of pain among patients with PsA. Grasping an understanding of this complex reality of living with a constant murmur of pain has the potential to improve and enhance the overall care. To support patients in taking charge of life health professionals should be able to provide team-based interventions that are underpinned by self-regulation skills and include cognitive, behavior and affective components.

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HPR Service developments, innovation and economics in healthcare

POS0789-HPR STRUCTURES THAT FACILITATE PATIENT ENGAGEMENT IN THE DEVELOPMENT AND DELIVERY OF HEALTH CARE SERVICES: A SYSTEMATIC SCOPING REVIEW

Keywords: Quality of care, Systematic review, Health services research

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Background: System-level patient engagement (PE) is required to improve future healthcare services. Structures that facilitate PE are likely to be diverse and complex, but are scarcely explored and described.
Objectives: To identify, summarize and map research about system-level PE structures in healthcare services.
Methods: A systematic scoping review was conducted, searching the MEDLINE, EMBASE, Cochrane, and PsycINFO databases. Key search elements were identified using the Population, Context, and Concept framework [1]. The population was patient representatives, healthcare professionals, managers, and leaders. The context includes practices, motives, and outcomes, and the concept was PE in the development and delivery of healthcare services. Studies published between 2005 and 2022 were included. The coding of extracted characteristics was inspired by a PE-adapted model to evaluate the quality of healthcare services [2]. Data was collapsed into structural attributes such as organisation, consistency, and timing of PE initiatives (Table 1), in addition to representativeness, PE knowledge, and finances.
Results: Of 8588 identified records, 37 studies were found to be eligible. Studies aimed to explore the impact of PE initiatives (n=8), increase knowledge and understanding about PE (n=15), and experience, attitudes, or opinions (n=9). Standing committees or panels were the most consistent PE initiatives, often acting as an established part of the structure (Table 1). Lack of PE knowledge was mentioned as a barrier in eighteen studies. Of these, eight reported that multiple stakeholders such as patients, healthcare professionals, and/or managers could benefit from increasing their PE knowledge. In twelve studies, lack of time and/or finances were listed as a barrier. High age, small numbers of patient representatives with time to spare, and professionals repeatedly recruiting the same patient representatives were described as a restriction for sufficient representativeness.
Conclusion: The findings indicate that the PE process may flourish through education, training, experience, and diversity among all PE stakeholders. Sufficient representativeness and PE knowledge were reported as essential structural attributes to facilitate equality and a meaningful co-creation process. Earmarked funds, sufficient to facilitate the PE structure are described as a cornerstone of integrating system-level PE in any environmental and healthcare setting.

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POS0790-HPR THE EFFECT OF A GOAL SETTING STRATEGY WITH INTEGRATED FEEDBACK ON GOAL ATTAINMENT IN INFLAMMATORY ARTHRITIS PATIENTS: A MIXED METHOD STUDY

Keywords: Self-management, Patient reported outcomes, Quality of life

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Background: Healthcare is increasingly shifting towards a person-centered care(PCC) approach. Unfortunately, in daily practice, outpatient consultations focus mainly on medical topics, ignoring the impact of the disease on daily life. To understand the impact on patients' daily lives, Patient Reported Outcomes(PROs) can be used. However, it is not enough to only use PROs when offering PCC, because the patient's true values and goals can only be ascertained during a good conversation, in which both medical and patient goals should be addressed.
Objectives: The aim of this study is to evaluate the effect of a goal management strategy with integrated feedback on goal attainment and Health-Related Quality of Life(HRQoL) in inflammatory arthritis(IA) patients. We also explored what type of goals were set.
Methods: Data were used from the Immune Mediate Inflammatory Disease(IMID) registry, a prospective cohort study in which IMID patients were followed with online PRO questionnaires. IA patients with active disease were asked to formulate up to 3 achievable goals within 3 months of follow-up. They could work independently on their goals. Every 2 weeks, patients received an automatically generated e-mail reminder asking them how well they had worked on their goals for the previous 2 weeks. After 3 and 6 months, it was evaluated whether the goals were achieved. If the goals were achieved after 3 months, new goals could be formulated for the next 3 months. Patients' goals were classified into the 14 domains of the Self-management

Table 1. Organisation, consistency, clarity, and timing of PE tasks described in the included studies, related to development and delivery of healthcare services.

Organisational structure			**PE[a] phase**						
	PE task		**PE timing**				**Consistency of PE initiatives**		**Total[c] n= 48 (N =150)**
Organisation of PE initiatives	*Clearly defined/ operationalized*	*Undecipherable*	*Idea/ planning*	*Delivery*	*Evaluation/ feedback*	*Unspecified*	*Consistent PE initiative*	*Inconsistent PE initiative*	
Focus groups/workshops/ forum	n=10	n = 7	n=9		n=3	n=6	n= 7	n=10 [b]	**17 (51)**
Committee/board/panel	n=11	n=4	n=6	n=1	n=2	n=6	n=12	n=3	15 (45)
Consultation/discussion meeting.	n=1	n=1	n=2	n=1	n=1			n=2	2 (8)
Survey/ interview	n=7	n=3	n=4		n=5	n=2	n=1	n=9	10 (30)
Action research, Experienced-based co-design, Mystery patient)	n= 3		n= 2		n=1			n=3	3 (15)
Delphi Technique Experiment	n=1		n=1					n=1	1 (3)
Total n = 113 (N=150)	**24 (32)**	11 (14)	**19 (24)**	2 (2)	10 (12)	8 (14)	15 (20)	**24 (28)**	

[a]PE: Patient engagement, [b]Ten studies reported diverse PE initiatives and are reported in more than one PE initiative, [c]N = occurrences, n = primary studies. Light colour indicates few studies, darker indicates more studies.

Web, extended with the domains pain and energy. At each visit (baseline, 3 and 6 months) patients also filled out online questionnaires on goal setting, shared decision making(SDM) and PROs. PRO questionnaires included HRQoL, patient satisfaction(VAS-PS), pain(VAS-pain), general health(VAS-GH) and daily functioning(HAQ). At baseline also a questionnaire on coping styles was filled out.

Results: Ninety-two patients participated in the study. The mean age was 51 years and the most common diagnosis was rheumatoid arthritis. A total of 302 patient goals were set, of which 32% were achieved. Most goals were formulated in the domains lifestyle(14%), pain(13%) and symptoms & side-effects(13%). Fewer goals were formulated in the domains intimate relationships & sexuality(0.6%) and finances(0.3%). In the entire population, HRQoL, VAS-PS, VAS-pain, VAS-GH and HAQ scores did not change over time. However IA patients who did not achieve their goals tended to score worse on HRQoL, VAS-PS and HAQ after 6 months. In contrast, VAS-pain and VAS-GH showed no relation with goal attainment. The patients' most common coping styles were active approach and comforting thoughts.

Conclusion: This study has raised awareness off the importance of patients goal setting. However, the goal-setting process is time consuming and, therefore, health professionals should be trained in goal setting. An online support tool which can be used in preparation for an outpatient clinic visit, can circumvent aforementioned problems. An example of such a tool is the Self-management Web, which help patients organize and prioritize perceived problems in different domains and subsequently helps them to formulate their goals. As a result patients' goals can be concretized immediately during the consultation, which can save time and, therefore, lower the threshold for implementation. Moreover, the incorporation of a feedback mechanism into a goal-setting intervention also seems to have a positive effect on goal attainment. Unfortunately, our intervention showed no effect on HRQoL. However, a general HRQoL measurement may not be sensitive or specific enough to detect change at this point. Possibly self-management and self-efficacy are better outcome measures. These may improve if patients actively address their problems in daily life, set goals to overcome them, and thereby better manage the disease. Therefore, we recommend using more specific outcomes, or qualitative assessment of outcomes, in goal setting studies.

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Acknowledgements: NIL.

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HPR Professional education, training and competencies

POS0791-HPR

NURSE EDUCATION ON METHOTREXATE FOR PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES: A SCOPING REVIEW TO INFORM EDUCATIONAL STANDARDS

Keywords: Patient information and education, Disease-modifying drugs (DMARDs), Nursing

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Background: Patient education (PE) is a key role of nurses,[1] which includes providing information, training, and support about methotrexate (MTX), an anchor drug in rheumatology. However, there is wide variation in the access to rheumatology nurse consultations in Europe and no standard strategy about when, what, and how nurses should provide PE to these patients.

Objectives: The objective of this scoping review was to provide a comprehensive overview of the existing research on nurse education on MTX for children/youth and adults with Rheumatic and musculoskeletal diseases (RMDs).

Methods: We searched PubMed (MEDLINE), Scopus and Cochrane Database, and CINAHL complete, from inception until march of 2022. Articles on patient education with a focus on MTX exclusively were included. Two independent reviewers performed standardized data extraction and synthesis.

Results: From 292 references identified, 14 fulfilled the inclusion criteria (Figure 1). A Summary of study methods and results are presented in Table 1.

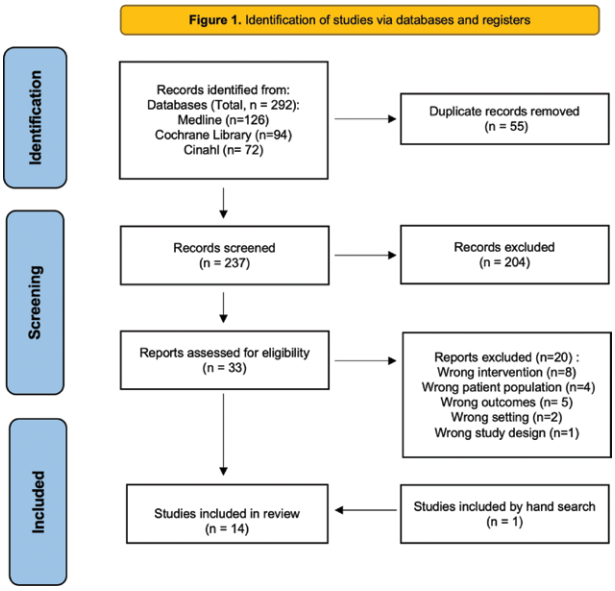


Table 1. Characteristics of included studies

1st Author (year), Country	Study design	Study sample[a]	Results
Burma (1996), EUA	Non-randomised experimental	183	Addition of a supplemental "MTX pocketcard" improve knowledge on MTX
Homer (2009), UK	RCT	62	Better adherence and satisfaction to MTX after nursing counselling
Livermore (2003), UK	Non-randomised experimental	18 families	Teaching families to manage MTX administration at home is feasible
Sowden (2012), UK	Cross-sectional	51	Despite consistent baseline patient education, end-user knowledge and awareness pertinent to MTX safety are limited
Barton (2013), EUA	Cohort	135	Age > 55, less than high school education, better function, and biologic use were independently associated with poor knowledge on MTX
Ciciriello (2014), Australia	Cohort	31	Multimedia patient education program about MTX treatment for RA found to be user-friendly and easily implementable. A validated scale to evaluate MTX-related knowledge was developed.
Katz (2015), Canada	RCT	29	An education video may be a good supplement to standard in-person nurse education for MTX self-injection
Rittberg (2016), Canada	Cross-sectional	60 youtube videos (adults, nurses)	Videos may be a useful additional educational tool
Robinson (2017), UK	Cross-sectional	104 nurses	Nurses' confidence correlated with knowledge about MTX and time in the role of the nurses. The amount of training received correlated with confidence but not with knowledge.
Robinson (2018), UK	Qualitative	6 rheumatology nurses	Nurses described a lack of confidence when they first started counselling patients commencing MTX, with a wide variation in training.
Sørensen (2020), Norway	Qualitative	8 children 11 parents 7 nurses	When clinicians used an acknowledge communication and offered sufficient coping strategies, children seemed to become involved in the procedure and acted with confidence. The initial educational training session may have a great impact on long-term outcomes.
Otón (2021), Spain	Qualitative	12 adult representatives	Barriers and facilitators of adherence to MTX involve: drug-related aspects, patient-physician relationship, social environment, and medication and medical care practicalities.
Robinson (2021), UK	Mixed-methods	10 consultations (adults, nurses)	Consultations generally consisted of communication from nurse to patient rather than a dialogue, with an 'overloading' of the patient with information.
Fayet (2021), France	Retrospective	66	A therapeutic education session improves patients' knowledge about MTX.

a. Adult patients unless stated otherwise

Conclusion: Through this scoping review, we identify that knowledge of MTX improves when education by nurses is provided. Patient education about MTX can be de delivered in different forms and can result in better satisfaction and adherence. More RCTs with powered samples are required.

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HPR Interdisciplinary research

POS0792-HPR LIVING WITH RA GIVES NEW INSIGHTS TO LIFE - PATIENTS' EXPERIENCES AFTER 1-2 YEARS OF DMARD TREATMENT

Keywords: Rheumatoid arthritis, Qualitative research methods, Lifestyles

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Background: Rheumatoid arthritis (RA) is a disease that greatly impacts all aspects of life. Living with RA affects patients' physical, emotional, psychological, and social health. Patients with RA are treated with disease-modifying anti-rheumatic drugs (DMARDs) and monitored with tight control to achieve low disease activity or remission. Nevertheless, RA can be life-changing when the patients need long-term treatment to control the disease activity. The goal of treatment for patients with chronic diseases such as RA is to achieve optimal health and normal life. It is therefore important to gain knowledge about how patients experience everyday life a short period after the initiation of DMARD treatment.

Objectives: The purpose of the study was to describe patients' experiences of living with RA after 1-2 years of DMARD treatment.

Methods: The study has a qualitative design with an inductive approach. Focus groups (n=17) and individual (n=5) interviews were conducted with 22 patients with RA. The participants consisted of 15 women and 7 men with a mean age of 57 years and a disease duration of 12-21 months. The participants were treated with conventional or biological DMARDS for 12-20 months. The main questions were: "Can you tell me how RA impacts your daily life?" "Which outcomes of your RA are important to you?" The interviews were analyzed with latent qualitative content analysis[1,2], and five categories with an overarching theme emerged (Table 1).

Results: Patients' experiences of living with RA after 1-2 years of DMARD treatment gives new insights to life and were expressed as 1) Surrendering to disease limitations due to being restricted by pain, fatigue, and in function; 2) Adapting to disease limitations by adjusting one´s work balance and one's social life; 3) Transitioning in self-identity due to disease limitations by not recognizing oneself and experiencing a change of bodily appearance and mood; 4) Fighting disease limitations by experiencing joy through exercise, promoting health by exercise and dietary habits, and; 5) Feeling humility despite disease limitations by being grateful for the treatment and seizing the day.

Conclusion: Although patients have been living with RA and treated with DMARD for 1-2 years, they are still struggling to make everyday life work. Although patients adapt their lives to the new conditions, they are affected by symptoms such as fatigue, pain, stiffness, and side effects such as nausea, hair loss, and weight gain. However, patients highlight the positive impact of how exercise influences their health and how living with RA gives new insights to life.

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Table 1. Overview of the theme, categories, and sub-categories showing patients' experiences living with RA after 1-2 years of DMARD treatment.

Theme	**Living with RA gives new insights to life**				
Categories	**Surrendering to disease limitations**	**Adapting to disease limitations**	**Transitioning in self-identity due to disease limitations**	**Fighting disease limitations**	**Feeling humility despite disease limitations**
Sub-categories	To be restricted by pain	To adjust one´s work balance	To not recognize oneself	To experience joy through exercise	To be grateful for the treatment
	To be restricted by fatigue	To adjust one's social life	To experience change of bodily appearance	To promote health by exercising	To seize the day
	To be restricted in function		To experience change of mood	To promote health through dietary habits	

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Disclosure of Interests: None Declared.

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POS0793-HPR OBSERVATIONAL STUDY IN REAL CLINICAL PRACTICE OF THE TREATMENT OF NON-INFECTIOUS UVEITIS

Keywords: Uveitis, Spondyloarthritis, Treat to target

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Background: Uveitis is an ocular disease that is a major cause of morbidity and blindness in the developed world. Although Immunosuppressive drugs and biologic therapy have been shown to be effective in their treatment there are no clear protocols for their use.

Objectives: To describe the characteristics of patients with uveitis associated with immunologic or idiopathic disease who require immunosuppressive treatment and their response in real clinical practice.

Methods: Observational, descriptive, longitudinal, and retrospective study of a cohort of patients diagnosed with uveitis associated with immunologic or idiopathic diseases attended in a multidisciplinary consultation between January 2011 and February 2022. To assess the response to treatment, we evaluated the change in visual acuity and vitritis and the presence of macular edema.

Results: We included 356 patients (mean age at diagnosis 42.8 ± 15.8 years, 50% female). Of the total, 157 (44%) had a single flare and 164 (46%) more than three. The involvement was bilateral in 85 patients (24%) and anterior (73%) and idiopathic (43%) were the most frequent. Twelve percent required treatment with systemic corticosteroids and 66 patients (18.5%) immunosuppressive/biological treatment, methotrexate being the most used (55%). Ten patients of the 66 (15%) started treatment with biologics and 34 (48%) required them at some point during the disease, adalimumab being the most used. Thirty-five patients (53%) needed to change drug due to lack of response. There were no differences between different drugs in the resolution of vitritis and improvement of vision. Disappearance of macular edema was achieved in all patients treated with tocilizumab.

Conclusion: The use of systemic corticosteroids and immunosuppressive/biologics was necessary in a high number of patients with non-infectious uveitis. In our series tocilizumab proved to be significantly more effective in the resolution of macular edema.

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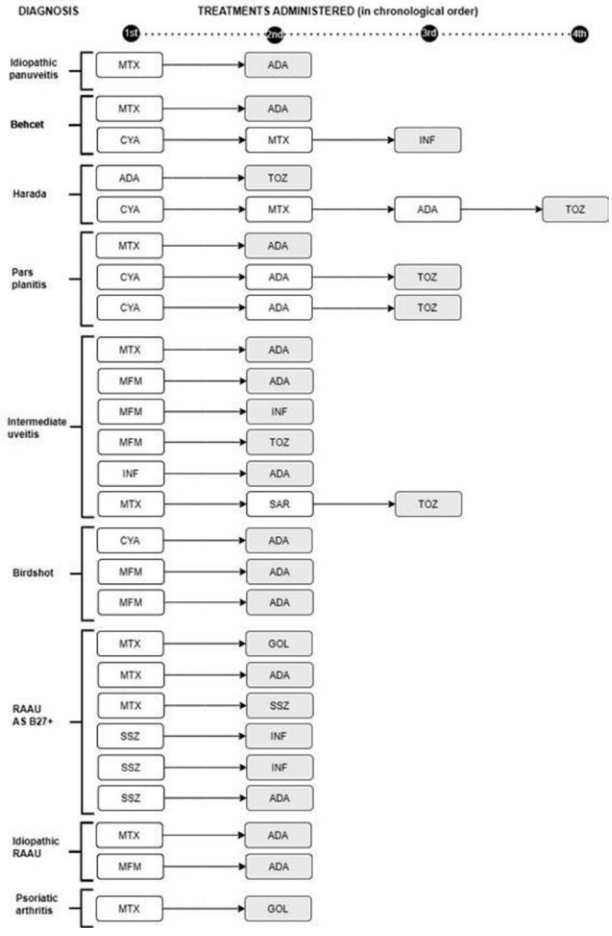


Figure 1. Timeline of immunosuppressive treatments and/or biologics administered in patients with non-infectious uveitis who required at least two treatments, according to diagnosis. Shaded: treatment that resolved the uveitis. RAAU: recurrent acute anterior uveitis AS: axial spondyloarthropathy MTX: Methotrexate. ADA: adalimumab MFM: mycophenolate mofetil IFX: infliximab TCZ: tocilizumab SAR: sarilumab CYA: Cyclosporine. SSZ: sulfasalazine

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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HPR Epidemiology and public health (including prevention)

POS0794-HPR **SNAPS JIA - SURVEY OF ADOLESCENTS' NEEDS AND PARENTS' VIEWS ON SEXUAL HEALTH IN JUVENILE IDIOPATHIC ARTHRITIS**

Keywords: Education, Inflammatory arthritides, Patient information and education

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Background: According to the world health organization, sexual health (SH) is "a state of physical, emotional, mental and social well-being in relation to sexuality". Studies on the impact of juvenile idiopathic arthritis (JIA) on SH are scarce especially during the critical phase of adolescence. We can ask ourselves: are health professionals (HP) "good" interlocutors for JIA patients?
Objectives: We aimed to determine the expectations of JIA adolescents (10-19 years) and the perceptions of their parents regarding exchanges with HP in the field of SH.
Methods: A multicenter survey was performed in nine French rheumatology centers and three patient associations from September 2021 to April 2022, among JIA patients, aged 18-45 years and their parents. On the advice of two child psychologists and a psychiatrist, we interviewed an adult population to obtain convincing data about their adolescence with the necessary hindsight on the subject. Self-administered questionnaires were designed (for JIA patients and parents) after an extensive literature review and experts' consensus and distributed to participants.
Results: 76 patients and 43 parents completed the anonymous questionnaires. Most patients were women (75%), with a mean age of 26 (7.2) years and an education level higher than high school (89%). Parents were mainly mothers (88%), with a mean age of 54 (5.6) years and an education level higher than high school (56%). Half the patients considered that JIA impacted their love life. The main causes were body complexes (46%) and low self-esteem (40%). The impact on their sex life was not clear-cut. Love life was discussed with parents for 52% and sexual life for 20% of patients. 59% of patients reported they were comfortable to discuss SH with an HP (yet, only 26% had done). Their main sources of information were referees (at school (46%), family (43%)) or social networks (34%). If patients reported that SH has been discussed, it was mainly when the HP was proactive (56%), with the hospital rheumatologist (50%), from a biomedical perspective. Focusing the needs for optimal care, patients and parents agreed to address SH during an individual patient education session in hospital (51% vs 35%), a regular consultation (47% vs 53%) or a dedicated consultation by request of the adolescent without parents being informed (38% vs 21%). Most patients and parents agreed that the HP should be proactive (78% vs 70%). At hospital, for patients, the most competent or the most affordable HP were the gynecologist (68%; 47%, respectively), the rheumatologist (55%; 41%), and the psychologist (53%; 39%). Patients and parents both considered that a peer expert would make patients feel more comfortable (38% vs 37%); however, contrary to patients, fewer parents point out their skills (46% vs 25%, p>0.0276). The opportunity of a suitable moment (64% of patients vs 53% of parents), an HP comfortable with the subject (59% vs 53%), and availability of brochures (45% vs 49%) seemed to be helpful for both. The only statistically significant difference concerned HP gender, less cited by parents (7% vs 43%, p <0.0001). The use of digital resources was significantly more cited by patients than parents (video information (29% vs 9%, p=0.0127); smartphone application (25% vs 9%, p=0.0372)). 79% of patients were looking for general information (impact of JIA and treatments on sexuality), discussion (68%), reassurance (65%), and listening (51%). General information (58%, p=0.0158) and discussion (39%, p=0.0022) were significantly less cited by parents.
Conclusion: To our knowledge, this is the first study to address the SH needs of adolescents with JIA. HPs should take up this real need about SH, especially in hospital for adolescents and their parents. Indeed, there are expectations directly linked to the specifics of the disease. The main difference between patients and parents would be the use of digital tools. There could be an interesting vector of communication with adolescents if the sources are reliable and parents reassured about their content.
Acknowledgements: This work has obtained the financial support of the French Society of Rheumatology.
Disclosure of Interests: None Declared.
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POS0795-HPR **STAGE 1 HYPERTENSION CARRIES EXCESSIVE CARDIOVASCULAR RISK IN AXIAL SPONDYLOARTHRITIS PATIENTS: A 12-YEAR LONGITUDINAL COHORT STUDY**

Keywords: Self-management, Cardiovascular disease, Spondyloarthritis

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Background: Hypertension (HT) is one of the modifiable risk factors for the development of CV event (CVE) [1,2]. The American College of Cardiology/American Heart Association (ACC/AHA) recommended a new definition for arterial HT in adults since 2017 [3]. Whether this new definition of HT is associated with increased CV risk in patients with axSpA remains unknown.
Objectives: To ascertain whether stage 1 hypertension at baseline is a predictor of future cardiovascular event (CVE) in patients with axial spondyloarthritis (axSpA).
Methods: We conducted a retrospective cohort study in axSpA patients who were recruited from 2001-2017. Patients with at least 2 years of follow-up and without prior CVE were divided into three groups according to the calculated mean BP over the first 2-year period (adjusted mean BP) (≥140/90mm Hg, 130-139/80-89mm Hg and <130/80mm Hg). They were followed from baseline until the end of 2020 or occurrence of a first CVE. Multivariate Cox regression analyses adjusting for baseline and time-varying variables were used to assess the relationship between mean BP and with CVE.
Results: Out of the 458 patients fulfilling the inclusion criteria, 56 (12.2%) and 141 (30.8%) had an adjusted mean BP ≥140/90mm Hg and 130–139/80–89mm Hg respectively, and 261 (57.0%) were normotensives. After a median follow-up of 12 [7-18] years, 56 (12.2%) CVE were documented. The incidence rates were 21.4, 14.2 and 5.9 per 1000 patient-years for the three groups respectively. A adjusted mean BP of 130–139/80–89 mm Hg was independently associated with the occurrence of CVE after adjusting for the baseline covariates (Figure 1) as well as time-varying inflammatory burden (Table 1). This association was not significant after adjustment for time-varying traditional CV risk factors.
Conclusion: Stage I hypertension at baseline is associated with increased risk of developing CVE in axSpA patients. This association may be mediated by other traditional CV risk factor.s.
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Table 1. Multivariable Cox regression analysis of the 3 BP groups stratified by age group after excluding patients who are older than 60 years.

	Model 1		Model 2		Model 3	
	Time-dependent HR (95%CI)	p-value	Time-dependent HR (95%CI)	P-value	Time-dependent HR (95%CI)	P-value
<130/80	Ref	Ref	Ref	Ref	Ref	Ref
130-139/80-89	2.60 (1.07, 6.31)	0.035*	1.90 (0.98, 3.69)	0.057	2.16 (0.87, 5.35)	0.098
≥140/90	4.39 (1.66, 11.63)	0.003*	2.15 (0.98, 4.69)	0.055	3.52 (1.28, 9.67)	0.015*
Age group						
Age<30	Ref	Ref	Ref	Ref	Ref	Ref
30≤Age<40	2.46 (0.47, 12.80)	0.284	1.70 (0.56, 5.13)	0.345	2.55 (0.49, 13.29)	0.266
40≤Age<50	8.04 (1.81, 35.62)	0.006*	4.69 (1.73, 12.70)	0.002*	7.12 (1.58, 32.15)	0.011*
50≤Age<60	11.40 (2.36, 55.19)	0.002*	7.91 (2.69, 23.29)	<.001*	8.65 (1.70, 43.86)	0.009*
ESR ≥20	2.27 (1.07, 4.82)	0.033*			2.07 (0.97, 4.44)	0.061
LP ever			1.78 (0.80, 3.98)	0.160	1.33 (0.47, 3.79)	0.595
DM ever			1.62 (0.91, 2.87)	0.099	2.19 (1.09, 4.40)	0.029*

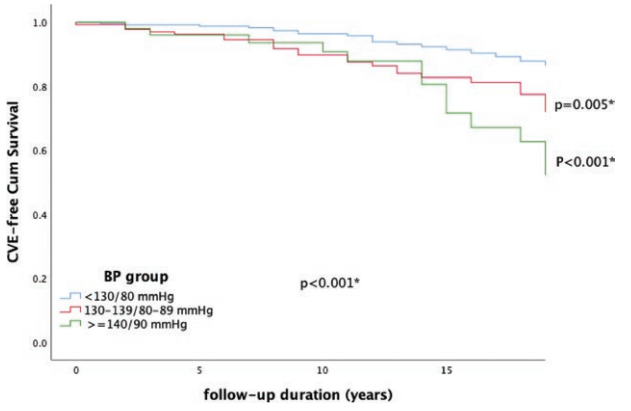


Figure 1. Kaplan-Meier analysis for CVE-free cumulative survival among the three patient groups (green line: ≥140/90mm Hg, red line: 130–139/80–89 mm Hg, blue line <130/80mm Hg).

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Disclosure of Interests: None Declared.
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POS0796-HPR

ASSOCIATIONS BETWEEN PAIN REDUCTION AFTER PARTICIPATION IN FIRST-LINE OSTEOARTHRITIS MANAGEMENT PROGRAMS AND PROGRESSION TO JOINT REPLACEMENT: A REGISTER-BASED STUDY OF 44588 PATIENTS WITH HIP OR KNEE OSTEOARTHRITIS

Keywords: Registries, Physical therapy/physiotherapy

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Background: First-line treatment for people with hip and knee OA is education, exercise, and if needed weight control. It has been shown that people participating in first-line treatment experience positive effects on outcomes such as pain (1-3), health-related quality of life, self-efficacy, and function (3), and may postpone the need for total joint replacement [4]. However, it is still unclear if the results from first-line treatment are associated with progression to joint replacement.
Objectives: To investigate the association between changes in pain after participation in first-line OA management programs and progression to joint replacement in persons with hip and knee OA.
Methods: An observational register-based study. Data from the BOA register was merged with data from the Swedish Arthroplasty Register. The primary prognostic factor was the change in pain between baseline and 3-month follow-up. The pain was measured on a numeric rating scale (NRS). The NRS pain comprises an 11-point scale where 0 indicates no pain and 10 indicates the worst possible pain during the last week. In the current study, pain change was categorized into a) much better (≥2 steps of improvement), b) slightly better (1 step of improvement), c) no change in pain, d) slightly worse (1 step of deterioration) and e) much worse (≥2 steps of deterioration). The main outcome was progression to joint replacement. A Cox regression model was applied to investigate the association between changes in pain and progression to joint replacement and presented with Hazard ratios (HR).
Results: Among patients with hip and knee OA, respectively, 26% (n=3555/13876) and 9% (n=2686/30712) progressed to joint replacement. An improvement in pain was associated with a lower probability of progression to surgery while patients who got worse in pain had an increased probability (Table 1).
Conclusion: Progression to joint replacement after participation in first-line treatments for hip and knee OA is influenced by the change in pain intensity. This implies that patients should participate in first-line treatment before being referred to joint replacement.
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CHARACTERS FROM TABLE CONTENT INCLUDING TITLE:

Table 1. Progression to joint replacement among patients participating in first-line OA intervention, depending on the effect of treatment on change of pain from baseline to 3 months follow-up.

	Hip OA		Knee OA	
Pain change on NRS	**Crude HR** (95% CI)	**Adjusted HR[a]** (95% CI)	**Crude HR** (95% CI)	**Adjusted HR[a]** (95% CI)
No change in pain	Reference	Reference	Reference	Reference
Much better	0.5 (0.4-0.5)	0.4 (0.3-0.4)	0.6 (0.6-0.7)	0.5 (0.4-0.5)
Slightly better	0.7 (0.7-0.8)	0.6 (0.6-0.7)	0.9 (0.8-1.0)	0.9 (0.8-1.0)
Slightly worse	1.1 (1.0-1.2)	1.1 (1.0-1.3)	1.3 (1.1-1.5)	1.5 (1.3-1.7)
Much worse	1.2 (1.1-1.3)	1.7 (1.5-1.9)	1.3 (1.1-1.5)	1.9 (1.6-2.1)

Disclosure of Interests: Kristin Gustafsson: None declared, Anna Cronström: None declared, Ola Rolfson Consultant of: Yes, Novartis advisory board, Grant/research support from: Yes, instituational support, Eva Ageberg: None declared, Therese Jönsson: None declared.
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POS0797-HPR PREVALENCE AND ASSOCIATIONS WITH DEVELOPMENT OF RADIOGRAPHIC KNEE OSTEOARTHRITIS IN INDIVIDUALS WITH KNEE PAIN – A 2-YEAR FOLLOW-UP

Keywords: Osteoarthritis

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Background: Pain and functional impairment form the basis for a clinical knee osteoarthritis (KOA) diagnosis according to the National Institute for Health and Care Excellence (NICE) guidelines [1]. Enhanced knowledge of the progression from knee pain to radiographic KOA (RKOA), may enable early identification of individuals at risk.
Objectives: To study the development of radiographic knee osteoarthritis in individuals with knee pain over time, and its associations to baseline variables.
Methods: In all 172 individuals (30-67 years) with knee pain, from the Swedish HALLOA cohort (2) were studied from baseline to 2-year follow-up. The individuals were at baseline coded as clinical KOA according to NICE guidelines or not. None had RKOA at baseline. At follow-up they were dichotomised as RKOA or not (Ahlbäck grade 1 or more). Self-reported knee symptoms (the Knee injury and Osteoarthritis Outcome Score (KOOS)), and knee pain intensity (numerical rating scale (NRS)) were assessed. Body composition, functional performance and clinical examination were also assessed. The Chi-Square-test or Mann-Whitney U-test was used for comparisons between groups, and logistic regression for analysis of associations between baseline variables and RKOA at follow-up adjusted for age.
Results: The mean age of the group was 51 (SD 8) years, 67% were women, Body Mass Index (BMI) was 26 (SD 5). The prevalence of RKOA at follow-up were 13% (n=23), and all of them had clinical KOA at baseline according to NICE guidelines. Furthermore, those with RKOA at follow-up had significantly higher BMI median 28.8 (IQR 8.6) vs. 25.1 (5.7), p=0.011, visceral fat area (VFA) 130.7 (88.7) vs. 84.7 (62.4), p=0.009, and knee pain; KOOS sub score Pain 69 (28) vs. 78 (19), p=0.016, and pain intensity 5.0 (5.0) vs. 4.0, (3.0) p=0.039, at baseline. Higher BMI and VFA, worse knee pain intensity, and worse KOOS sub scores for Pain, Symptoms, ADL, and QOL at baseline, were associated with RKOA at follow-up (Table 1). Sex, self-reported morning knee stiffness and restricted knee motion, functional performance tests and clinical examined crepitus, were not associated to RKOA and thus not included in the final analysis (p-value 0.477 - 0.930).
Conclusion: More than one out of ten individuals with clinical KOA developed RKOA already in 2 years. In individuals with knee pain, variables associated with RKOA at follow-up can be detected early through NICE guidelines, assessment of BMI, VFA and self-reported symptoms with KOOS questionnaire as a support to start with early management.

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Table 1. Development of radiographic knee osteoarthritis (Ahlbäck grade 1 or more in painful knee) at a 2-year follow-up and associated baseline variables (n=172), analysed with logistic regression models adjusted for age.

	Odds ratio (OR)	95% CI	p-value
Body Mass Index *(kg/m²)*	1.132	1.034-1.240	**0.007**
Visceral fat area *(cm²)*	1.009	1.001-1.018	**0.024**
Knee pain intensity, *(NRS 0-10, best to worst)*	1.230	1.022-1.480	**0.028**
Bony enlargement	1.788	0.683-4.686	0.237
One-Leg Rising, *(number)*	0.966	0.921-1.012	0.146
KOOS (Pain 0-100, *worst to best*)	0.964	0.937-0.991	**0.011**
KOOS (Symptoms, 0-100, *worst to best*)	0.968	0.940-0.996	**0.028**
KOOS (ADL, 0-100, *worst to best*)	0.969	0.941-0.998	**0.039**
KOOS (Sport/Rec, 0-100, *worst to best*)	0.984	0.966-1.002	0.088
KOOS (QOL, 0-100, *worst to best*)	0.970	0.944-0.997	**0.030**

NRS = Numeric Rating Scale knee pain intensity. **KOOS =** Knee injury and Osteoarthritis Outcome Score. **ADL** = Function, daily living. **Sport/Rec** = Function, sports and recreational activities. **QOL** = Quality of Life.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0798-HPR PREVALENCE OF RISK FOR ANXIETY AND DEPRESSION IN PATIENTS WITH RHEUMATIC DISEASES

Keywords: Mental health, Comorbidities, Epidemiology

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Background: Patients with chronic diseases have a higher prevalence of anxiety and depression. The complex relationship between chronic diseases and mental health disorders can influence each other negatively. (1)
Objectives: To determine anxiety and depression symptoms prevalence in an out-patient rheumatology clinic, and its associated factors.
Methods: This was a cross-sectional study. Patients > 16 years old with a rheumatologic disease were included. Data from medical history were collected. The Hospital Anxiety and Depression Scale (HADS) was applied from March to November 2022. A score from 0-7 points is classified as low risk, 8-10 as intermediate risk, and >11 as high risk. Patients with high risk were referred to an evaluation by Psychiatry in the same clinic. We compared groups according to HADS scores using Kruskal-Wallis or Chi-square test.
Results: A total of 705 patients were included, 658 women, demographic characteristics in Table 1. Most common diagnosis was RA, followed by systemic lupus erythematosus (SLE). High anxiety risk was found in 125 patients, median disease duration of 6 years. Sixteen patients had high risk for depression, median disease duration of 10 years. Intermediate risk of depression was assessed in 15 patients, median disease duration of 10 years. We received 38 patients that accepted to be referred to a psychiatric evaluation. An association was found between high risk of anxiety and gender (p=0.019), no association was found with age or menopause. High risk of anxiety was more prevalent (n=125) than depression (n=16), and patients with intermediate risk for depression showed a higher prevalence of intermediate and high risk for anxiety (p=.000).

Conclusion: We found that high risk of anxiety was more prevalent than depression. Higher risk of anxiety was found in female patients. Almost 1 of every 5 patients with rheumatic diseases has an intermediate risk for anxiety. The implementation of a mental health screening tool can help patients receive earlier attention by a specialist.

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Table 1. Demographic, clinical and rheumatic disease characteristics.

Characteristics	HADS A low	HADS A inter	HADS A high	*p*	HADS D low	HADS D inter	HADS D high	*p*
	(n= 477)	(n=103)	(n=125)		(n= 674)	(n=15)	(n=16)	
Age, years, median (iQR)	51.0 (42.5-61.0)	51.0 (45.0-61.0)	56.0 (45.0-64.0)	NS	52.0 (43.0-61.0)	60.0 (38.0-63.0)	59.5 (40.5-69.0)	NS
Women, n (%)	437 (91.6)	98 (95.1)	123 (98.4)	**0.019**	628 (93.1)	98 (100)	15 (93.7)	NS
Disease duration, years, mean	5.0 (1.0-10.0)	4.0 (1.00-10.0)	6.0 (2.25-12.0)	NS	5.0 (1.0-10.0)	10.0 (1.00-20.0)	10.0 (4.25-20.0)	NS
Age of diagnose, years, median (iQR)	45 (32.0-53.5)	45.9 (35.0-54.0)	48.0 (37.0-56.7)	NS	45.0 (33.5-54.0)	45.0 (31.0-59.0)	47.0 (28.3-58.5)	NS
Comorbidities, #, median (iQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	NS	0.0 (0.0-1.0)	1.0 (0.0-1.0)	1.0 (0.0-1.0)	NS
RA, n (%)	249 (52.2)	52 (50.4)	53 (42.4)	NS	341 (50.5)	6 (40.0)	7 (43.7)	NS
LES, n (%)	67 (14.0)	12 (11.6)	15 (12.0)		89 (13.2)	1 (6.6)	4 (25.0)	
FM, n (%)	14 (2.9)	2 (1.9)	3 (2.4)		18 (2.6)	1 (6.6)	0 (0)	
SS, n (%)	10 (2.0)	4 (3.8)	5 (4.0)		18 (2.6)	1 (6.6)	0 (0)	
SCLERODERMA, n (%)	10 (2.0)	2 (1.9)	1 (0.8)		12 (1.7)	1 (6.6)	0 (0)	
OP, n (%)	15 (3.1)	2 (1.9)	7 (5.6)		22 (3.2)	1 (6.6)	1 (6.2)	
Overlap, n (%)	31 (6.4)	10 (9.7)	21 (16.8)		57 (8.4)	3 (20.0)	2 (12.5)	
Other, n (%)	81 (16.9)	19 (18.4)	19 (15.2)		116 (17.2)	1 (6.6)	2 (12.5)	

iQR interquartile range, RA reumathoid arthritis, SLE systemic lupus erytemathosus, FM fibromyalgia, SS Sjogren´s syndrome, OP osteopenia

Disclosure of Interests: None Declared.

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HPR Interventions (educational, physical, social and psychological)

POS0799-HPR

EFFECTIVENESS OF AN INTERDISCIPLINARY HEALTH PROMOTION EDUCATIONAL PROGRAM IN IMPROVING THE QUALITY OF LIFE OF INDIVIDUALS WITH FIBROMYALGIA IN BRAZIL: A RANDOMIZED CLINICAL TRIAL OF AMIGOS DE FIBRO

Keywords: Patient information and education, Fibromyalgia, Self-management

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Background: "Amigos de Fibro" (Fibro Friends), is a recent and innovative program created from the joint action of patients and health professionals, which can be an effective educational tool to be implemented in primary health care centers, promoting self-care, quality of life and health promotion in individuals with fibromyalgia in Brazil.

Objectives: Evaluate the effectiveness of an interdisciplinary health promotion educational program called "Amigos de Fibro" in improving pain intensity, symptom severity, quality of life, sleep quality and self-care agency in individuals with fibromyalgia in Brazil.

Methods: A randomized clinical trial was carried out with 24 participants divided into two groups: the experimental group (EG) and the control group (CG). The EG group held online meetings through the Google Meet platform with an interdisciplinary team (10 professionals) that worked in primary health care in Brazil, where they gave lectures and held debates and dynamics on the importance of health promotion and self-care in fibromyalgia. In addition, participants performed a physical exercise protocol. The "Amigos de Fibro" protocol has been previously published and showed good agreement. The control group (CG) received an education and self-care e-book for fibromyalgia that addressed information similar to the EG (*http://www.amigosdefibro.com.br*). Participants were assessed pre and post-intervention. A descriptive analysis of the data was performed, as well as the differences of the independent variables between the intervention and control groups were studied using Student's t test for independent samples. A significance level of 5% was adopted.

Results: The mean age of the participants was 38.7±9.4 years for the EG and 44.9±10.6 for the CG, all (100%) of whom were female in both groups. Compared to the baseline, all EG variables and only the FIQ symptoms domain of the CG showed significant improvements (p<0.005), however, the other CG variables showed improvements, but they were not significant (Table 1).

Table 1. Results of the variables studied in both groups.

	EG			CG		
	Pre-intervention	Post-intervention	p-value	Pre-intervention	Post-intervention	p-value
	Mean±SD	Mean±SD		Mean±SD	Mean±SD	
GDI	14±3,2	8,3±3,0	**<0,001***	13,8±2,5	11,5±3,7	0,066
SS	10,3±1,8	6,9±2,7	**0,001***	10,8±1,0	10,1±1,4	0,244
FIQ-R						
Function	21,0±4,6	10,6±4,8	**<0,001***	21,4±4,7	19,3±5,4	0,128
Global	16,1±5,1	8,1±4,2	**0,002***	16,5±2,6	13,8±3,6	0,016
Symptoms	37,3±5,7	23,2±8,1	**<0,001***	39,4±5,1	34,3±7,8	**0,004***
Total score	74,6±12,8	42±15,1	**<0,001***	77,3±9,6	67,5±14,6	0,006
VAS	7,8±1,0	4,7±2,2	**<0,001***	7,7±1,5	6,9±2,4	0,193
Sleep	16,7±2,0	11,9±4,2	**0,001***	16,2±2,6	15,8±4,2	0,664
Self-care	51,3±6,8	63,6±5,6	**0,001***	53,1±7,3	49,1±11,1	0,251

Caption: EG: Experimental Group; CG: Control Group; SD: Standard deviation; GDI: Generalized Pain Index; SS: Severity of Symptoms; FIQ-R: The Revised Fibromyalgia Impact Questionnaire; VAS: Visual Analog Pain Scale.

Conclusion: "Amigos de Fibro", a light technology in health, was considered with good results and improvement of all studied variables that address the main aspects that promote the health of individuals with fibromyalgia and, therefore, being considered valid for use by health professionals with the target public in primary health care in Brazil, enabling them to act as health promoting agents. Our next steps are to expand knowledge of this program to other countries.

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Disclosure of Interests: None Declared.

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POS0800-HPR

START WITH THE END IN MIND- EMBEDDING AN INTEGRATED SELF MANAGEMENT APPROACH WITHIN ROUTINE CLINICAL CARE FOR NEWLY DIAGNOSED PATIENTS WITH INFLAMMATORY ARTHRITIS

Keywords: Inflammatory arthritides, Prognostic factors, Self-management

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Background: Long term outcomes of inflammatory arthritis patients are not only dependent on early identification of symptoms and tight control of disease, but also on the person's abilities to manage the impact of their condition. (1-2) In 2019 Fife Rheumatology Service focussed on early identification of patient's assets for self managment (SM) and those at risk of poorer outcomes with the aim of targeting supported SM resources. EULAR 2021 recommendations endorse the implementation a self management approach within routine care[3].

Objectives:

1. Implement a SM approach as part of routine clinical care.
2. Establish baseline patient characteristics data set to evaluate the effectiveness SM interventions on long term outcomes.

Methods: Identified priorities of the re-design were:

1. Additional investment in psychology to lead the re-design.
2. SM database.
3. SM screening and triage tool, and, a SM check list.
4. Stepped model of care including referral to patient organisations.
5. Feedback from patients, staff and patient organisations.
6. Virtual weekly patient disease and SM virtual multidisciplinary team (VMDT) clinic.
7. SM Digital App.
8. Patient Initiated Review (PIR) system for disease stable and self managing patients.

Results: All 8 priorities were implemented and 315 patients have been referred to the pathway since 25/08/2022. Positive feedback about the pathway and the App has been received from patients, staff and patient organisations. Six patients at 5 months post diagnosis are discussed weekly at our VMDT clinic. Of the total patients referred, 42% were male and 58% were female. The mean age was 56 years, range 16-85 years. Twenty one percent of patients at baseline had low to moderate confidence in managing their inflammatory arthrtis across the 4 subsets of *Emotions, Activities of daily Living (ADLS), Social Interactions* and *Symptoms* of the Patient-Reported Outcomes Measurement Information System-managing chronic conditions.(4) Lowest scores were found in the *Emotions* and *ADLs subsets*. Nineteen percent of patients of working age were not working. Twenty eight percent of patients had moderate to severe disability on the Modified Health Assessment Questionnaire and 54% had moderate to severe depression on the Patient Health Questionnaire-9. Forty two percent of patients fell into the deprived or most depvied categories of the Scottish Index of Multiple Deprivation.

Conclusion: The implementation of a self management approach as per EULAR Recommendations has been well received by key stakeholders and has helped with the early identification of patients' SM needs and highlighted those at risk of poorer outcomes. This data will act as a basis for the application of improvment methodology to assess the effectivness of future interventions and measure long term outcomes. Early indications would suggest targeting resources on improving patients' confidence in managing their mental mealth and ADLs.

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Disclosure of Interests: None Declared.

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POS0801-HPR GREAT EXPECTATIONS: A FATIGUE MANAGEMENT PROGRAMME CAN ALSO IMPROVE SLEEP QUALITY AND MENTAL WELL-BEING IN RHEUMATIC DISEASE PATIENTS

Keywords: Self-management, Non-pharmacological interventions, Mental health

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Background: Fatigue is a significant problem for patients with Rheumatic diseases and yet remains overlooked and undertreated[1-3]. It is known to be associated with increased sleep disturbance in this patient group[4] and with poorer mental health[5]. A fatigue management programme (FMP) was developed with the aim of reducing the impact of fatigue on patients. Outcome measures were used to determine whether an improvement in fatigue scores also resulted in an improvement in sleep and mental health.

Objectives: The primary objective was to evaluate whether a reduction in fatigue corresponded with an improvement in sleep quality following attendance at a virtual FMP. The secondary objective was to evaluate the impact of the FMP on patient mental well-being.

Methods: The FMP was based on the RAFT study[6] and patient-reported outcome measures (PROMs) were assessed before and after enrolment to the FMP. The Visual Analogue Scale (Fatigue) (VAS-F) was used to evaluate fatigue scores. The Pittsburgh Sleep Quality Index (PSQI) was used to assess changes in sleep quality. The Patient Health Questionnaire 9-Item (PHQ-9) and the Generalised Anxiety Disorder Assessment (GAD-7) were used to measure depression and anxiety scores respectively.

Results: Gender ratio 5:1 females to males, age range 25-81 with a mean of 51.6 ± 12.3. Patient's diagnoses were equally divided between Rheumatoid Arthritis, Systemic Lupus Erythematosus and other Rheumatic Diseases. Both primary and secondary objectives have been met.

Table 1. PROM scores reported before and after the FMP. Data is shown as mean and standard deviation.

n = 43	Pre-FMP	Post-FMP	p value
VAS-F	74.3 ± 18.4	52.3 ± 22.1	<0.0001
PSQI	11.8 ± 4.8	9.1 ± 4.1	<0.0001
PHQ-9	13.8 ± 6.2	8.9 ± 5.4	<0.0001
GAD-7	8.5 ± 6.4	5.7 ± 5.3	0.0005

Patient's scores significantly improved in all of the PROMs collected for the purposes of this service evaluation (see Table 1). There was a correlation between improvements in VAS-F scores and improvements in PSQI scores (r = 0.365) which was statistically significant (p = 0.016).

Conclusion: An FMP is effective at significantly reducing fatigue, improving sleep quality and mental wellbeing. We have shown that there is a correlation between a reduction in fatigue and an improvement in sleep and this work highlights the importance of such a programme as part of routine care and management of these chronic conditions.

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POS0802-HPR

SELF-MANAGEMENT SUPPORT NEEDS OF PATIENTS WITH INFLAMMATORY ARTHRITIS AND THE CONTENT OF SELF-MANAGEMENT INTERVENTIONS: A SCOPING REVIEW

Keywords: Inflammatory arthritides, Self-management, Rehabilitation

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Background: Studies show varying but beneficial effects of self-management interventions on self-efficacy, symptoms or burdens, such as pain, fatigue, illness perception, and quality of life, supporting the need of multi-disciplinary interventions in rheumatology (1, 2). However, the content of the self-management interventions differs widely [2]. There is a need for an overview of the existing evidence of self-management support needs in patients with inflammatory arthritis (IA) to inform the development of relevant and effective interventions.

Objectives: 1) to identify the evidence for self-management support needs among patients with IA, and 2) to identify the content (theory/theoretical approach, mode of delivery, duration and frequency) of self-management interventions that target patients with IA.

Methods: In May 2021, we performed a scoping review (protocol published at the Open registries network, no. DOI 10.17605/OSF.IO/TVX82)) and conducted a systematic literature search (from 2000 onward) in five databases.

Results: Out of 11,748 records identified, we included 31 articles describing patients' support needs and 33 articles describing the content of self-management interventions (Figure 1). Patients' self-management support needs were categorized into six topics: 1) Disease impact and the pharmacological treatment, 2) Care continuity and relations with health professionals, 3) The importance of non-pharmacological treatment, 4) The need for support from family and friends, 5) Support needs related to work issues, and 6) Contextual preferences for self-management support. Content of the self-management interventions varied widely and the descriptions of the content were deficient and needed clarification (Table 1). The identified topics for support needs were compared with the described content in the included articles (Table 1). Only few self-management interventions focused on patients' need for support concerning work, family, and friends.

Conclusion: Health professionals provided self-management support to patients with IA in various ways. There were gaps between the patients' support needs and the identified interventions. The self-management concept needs to be clearly defined when developing self-management interventions. Further studies are required to investigate various modes of delivery, frequency, and duration to develop effective interventions that meet patients' self-management support needs.

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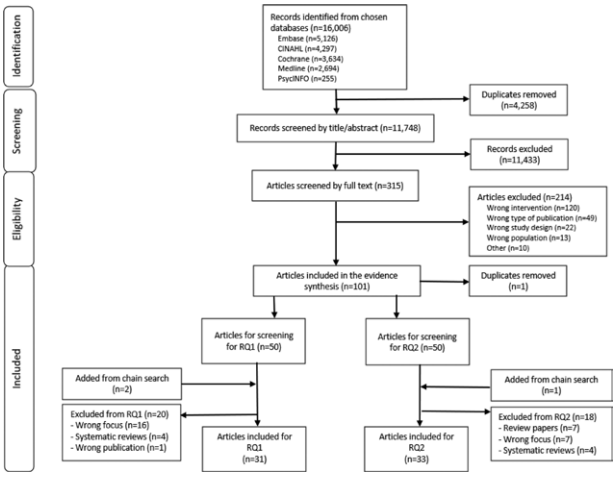


Figure 1. Flowchartn – number of records or articles; RQ1 - Research question 1; RQ2 - Research question 2.

Table 1. Numerical summary of patients' support needs and corresponding content of self-management interventions

Topics on patients' support needs	Content			
	n	**Theory/theoretical approaches** (n)	**Mode of Delivery** (n)	**Duration & Frequency** (n)
1 Disease impact and pharmacological treatment	24	Patient-centered, SM, self-efficacy, self-care behavior and patient education (14; no clear theory) Cognitive behavioral theory (8) Cognitive restructuring techniques (5) Self-efficacy theory and autonomous motivation (3) The Health Belief Model (2) Problem focused and action-oriented (1) The Social Learning Theory (1) The Transtheoretical Model of Behavior Change (1) The social cognition theory (1) Behavioral change theory (1)	**Face-to-face:** Group meetings (14) Group plus one-to-one meetings (6) One-to-one meetings (6) **Remote:** Individual, online (5) Group sessions, online (2) By mail, single intervention (3)	1-32 hours in total Delivered during 3 weeks to 9 moths, or as a single assessment (26) Unknown (6) On-line access anytime (3)
2 Care continuity and relations with health professionals	8			
3 The importance of non-pharmacological treatment	31			
4 The need for support from family and friends	11			
5 Support needs related to work issues	2			
6 Contextual preferences for SM support (single/ multiple mode of delivering SM support)	21 (single) 12 (multiple)			

n= number of articles; SM=self-management

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POS0803-HPR

DEVELOPMENT OF A PATIENT-CENTERED MULTIMODAL DISEASE MANAGEMENT PLATFORM FOR THE FIBROMYALGIA-LIKE POST-COVID19 SYNDROME

Keywords: Fibromyalgia, COVID, Patient reported outcomes

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Background: About 30% of patients with post-COVID19 syndrome satisfy the ACR survey criteria for fibromyalgia. The most common symptoms are chronic fatigue, generalized pain, sleep impairment, anxiety and depression. A substantial part of the patients already suffered from similar symptoms before infection. Digital health solutions have shown efficiency for fibromyalgia, offering specific disease monitoring and multimodal interventions and thus may work in patients with post-Covid19 syndrome.
Objectives: To develop a multimodal, multi-interventional self-management platform for post-COVID19 and potentially other post-viral syndromes patients. To ensure a patient-centric development and evaluate the usability of this solution by performing qualitative user experience research.
Methods: We developed a web-based user interface with a horizontal basic navigation menu consisting of patient reported outcomes, symptoms evolution and interventions. The therapeutic content was created by rheumatologists, psychiatrists, physiotherapists and occupational therapists and included educational content, physical-, respiratory- and olfactory exercises, cognitive behavioral therapy, mindfulness, relaxation training, therapeutic stories and art therapy. Usability and satisfaction surveys have been conducted among 53 post-COVID19 patients and qualitative interviews have been performed.
Results: The frontend design of the platform is shown in Figure 1. 90% of the patients preferred a regular symptoms list questionnaire over a chatbot to collect patient reported outcomes. Longitudinal symptom evaluation is shown in the 'my results' section. 81% of patients expressed their wish that their symptoms are displayed with a benchmark of all other patients and to learn what has helped other patients with similar symptoms. A majority of them were also interested in links to patient communities (63%), so an anonymized discussion forum has been added. Patients preferred active training programs (63%) and information (59%) over interactive and gamified content like quizzes (15%). Interactivity on the web-app was created by accordion function and horizontal navigation within each treatment module. An administrator content management dashboard has been implemented to ensure a flexible and reactive supervision of the platform.
Conclusion: We present a functioning, patient-centered app tailored for patients with post-COVID19 syndrome. Further clinical studies on user experience, adherence, adoption driving factors and efficacy are ongoing.

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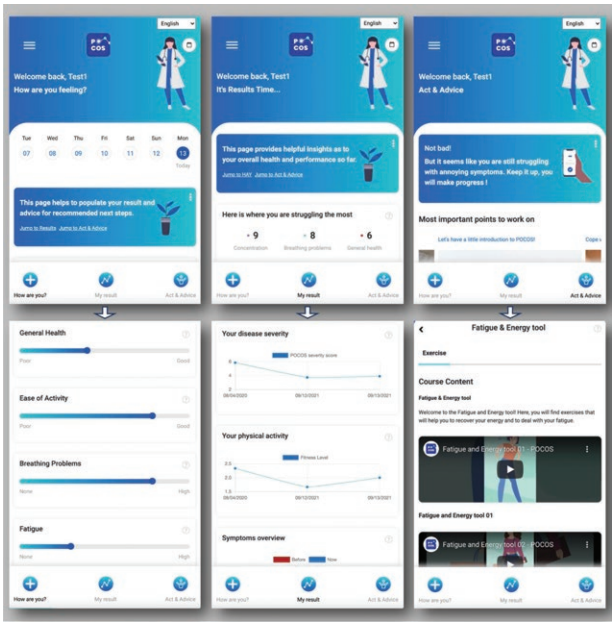


Figure 1. POCOS user interface (app): Left side: '*How are you?*', with electronic patient reported outcomes and activity. Middle: '*My result*', with monitoring of symptom's activity and health conditions. Right side: '*Act & Advice*', with personalized training program, adapted to the user's symptoms.

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Disclosure of Interests: Marc BLANCHARD Shareholder of: ATREON SA (board member), Thomas Hügle Shareholder of: ATREON SA (Scientific board member), Pedro Ming Azevedo: None declared.
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HPR Measuring health (development and measurement properties of PROs, tests, devices)

POS0804-HPR

INVESTIGATION OF THE VALIDITY AND RELIABILITY OF THE STEP UP AND DOWN TEST IN PATIENTS WITH TOTAL KNEE ARTHROPLASTY SURGERY

Keywords: Physical therapy/physiotherapy, Outcome measures, Osteoarthritis

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Background: Stair climbing has been showed as the first changing activity in patients with knee osteoarthritis (KOA) [1]. Stair climbing and step tests of patients with KOA are used as measurement tools to determine the functional level of patients and to determine the effectiveness of treatment. Patients with KOA undergoing total knee arthroplasty (TKA) show asymmetrical patterns and slower climbing stairs when the affected limb is compared to the healthy limb [2]. Therefore, unilateral evaluation of the extremity undergoing TKA is important. There are many tests that evaluate stair climbing function in patients with TKA. However, the Step Up and Down (StUD) test, which was previously found to be valid and reliable in knee osteoarthritis, is a 15-second test that can evaluate the affected limb unilaterally, requires only one stair, and is similar to the daily living activities of the patients [3]. For this reason, it would be useful to use it as a criterion in the evaluation of the physical functions of individuals with TKA. However, there is no study on the validity and reliability of the StUD test in patients with TKA.
Objectives: The aim of the study is to measure the validity and reliability of the StUD test in patients with TKA.
Methods: Forty patients (Mean age; 6,87 ± 8,01) with primary TKA included in this study. The test-retest reliability of the StUD test was measured with a 1-hour interval to prevent fatigue. Validity was assessed by testing predefined hypotheses. Therefore, the 30s Chair Stand Test (30sCS), the Hospital for Special Surgery score (HSS) and Short Form-12 Quality Life Questionnaire (SF-12) were used as comparator instruments.
Results: The StUD test showed good correlation with 30sCS test (r=0,706, p<0,001), moderate to low correlation with HSS score (r=0,4, p<0,001), moderate correlation with SF12 score (r=0,508, p<0,001). Test-retest reliability was excellent (ICC= 0,93, %95 CI= 0,87-0,96). Standard error of measurement and smallest real difference at the 95% confidence level for StUD test were respectively 0,34 and 0,94. There was no significant difference in the mean VAS scores measured after the tests or between the first and the second trials (p >.05)
Conclusion: According to the results of our study the StUD test excellent reliability, good validity and high sensitivity in patients with TKA. Additionally, there was no significant increase in pain levels at the end of the test. This result suggests that StUD test can be used the safely without increasing pain levels, and this test can also be tolerated by patients with TKA. The SRD_{95} of StUD test was 0,94. According this, it can be interpreted that the STUD test can be used reliably to monitor small changes in patients' function.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0805-HPR **FACE VALIDITY AND RELIABILITY TEST OF THE DANISH VERSION OF THE COMPLIANCE QUESTIONNAIRE RHEUMATOLOGY**

Keywords: Validation, Outcome measures, Patient reported outcomes

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Background: Medication adherence in inflammatory arthritis has been reported to vary from 30% to 80%, despite the fact that non-adherence may cause worsening of symptoms and disease severity [1]. Hence, supporting adherence to medication is an essential part of the treatment and care of patients with rheumatic and musculoskeletal diseases [1]. The Compliance Questionnaire Rheumatology (CQR) measures adherence in rheumatic diseases through 19 items covering drug-taking behaviour to identify the factors that contribute to suboptimal adherence [2].
Objectives: To present the translation of the CQR into Danish and the face validity and reliability test.
Methods: The CQR was translated into Danish according to the International Quality of Life Assessment method (3), which involved forward and backward translations by four independent translators, followed by a face validity test among 10 patients with rheumatoid arthritis. The test–retest reliability of the Danish CQR was evaluated in 49 patients with rheumatoid arthritis using the standard error of the measurement (SEM) converted into the minimally detectable change (MDC) and the intraclass correlation coefficient (ICC). Questionnaires were administered with a minimum of 10 days between assessments.
Results: The face validity test did not lead to substantial corrections. The participants in the reliability test had a mean age of 57.4 years (SD 16.1) and a mean disease duration of 1.13 years (range 2 months–2 years). The mean CQR score in the test and retest was 62.69 (confidence interval (CI) 58.76; 66.63) and 62.51 (CI 58.91; 66.12), respectively, with a SEM of 8.59 (7.16; 10.73) and a MDC of 16.83. A satisfactory test–retest reliability was confirmed by an ICC value of 0.79 (CI 0.68; 0.89) (Table 1).
Conclusion: The Danish CQR has satisfactory test–retest reliability in patients newly diagnosed with rheumatoid arthritis and is thus considered a reliable tool to measure adherence in this group.
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Table 1. Reliability and agreement parameters for the Compliance Questionnaire Rheumatology (CQR) in 49 patients with rheumatoid arthritis

	Mean (95% CI) test Mean (95% CI) retest	Difference (95% CI)	LOA	SEM (95% CI)	ICC (95% CI)	MDC
CQR19	62.69 (58.76; 66.63) 62.51 (58.91; 66.12)	0.18 (–2.29; 2.65)	–16.66–17.01	8.59 (7.16; 10.73)	0.79 (0.68; 0.89)	16.83

LOA = limits of agreement, *SEM* = standard error of measurements, *MDC* = minimal detectable change, *ICC* = intraclass correlation coefficient model 2.1

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Disclosure of Interests: Line Raunsbæk Knudsen Speakers bureau: Novartis, Phizer, Eli Lilly, Annette de Thurah: None declared.
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SLE, Sjön's and APS - aetiology, pathogenesis and animal models

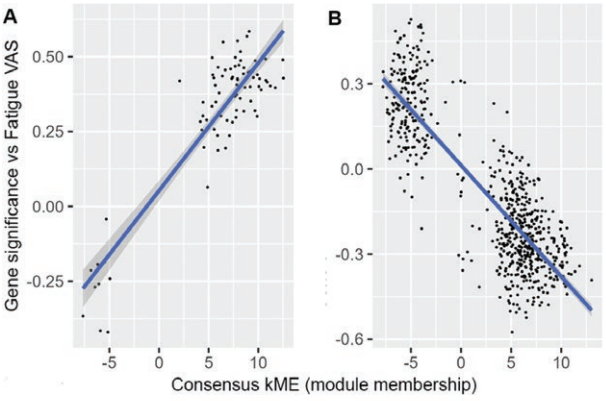
POS0807

A TRANSCRIPTIONAL PROFILE OF FATIGUE IN PRECLINICAL AUTOIMMUNITY WHICH IS PRESERVED IN SLE AND SJOGREN'S SYNDROME

Keywords: Systemic lupus erythematosus, -omics, Sjögren syndrome

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Background: Fatigue is a prevalent and debilitating symptom in autoimmune connective tissue diseases (CTDs). Its immunological mechanisms are poorly understood. Although targeted therapies can improve fatigue, the effect is modest and variable. This is likely because, in established disease, immunological drivers of fatigue may be obscured by multifactorial effects from glucocorticoids, accrued damage and comorbidity. However, fatigue frequently pre-dates formal diagnosis or end-organ manifestations, suggesting immunological mechanisms may be better interrogated in the preclinical phase. SLE and primary Sjogren's syndrome (pSS) are preceded by a preclinical phase of anti-nuclear antibody (ANA) positivity with no or non-specific symptoms years before clinically manifest inflammation. Although only a minority ultimately develop overt CTDs, ANA-positive individuals demonstrate complex immune dysregulation including increased interferon (IFN) pathway activation [1]. We hypothesise that immune disturbances underlying fatigue in SLE and pSS are i) established during the earlier ANA-positive preclinical phase; ii) contribute to the symptom burden among ANA-positive individuals, and (iii) are differentially modulated in established disease states.
Objectives: To investigate unique and conserved peripheral blood immune cell transcriptional signatures associated with symptomatic fatigue in ANA-positive preclinical patients and established SLE and pSS.
Methods: Bulk RNASeq was performed on peripheral blood mononuclear cells isolated from 35 ANA-positive preclinical individuals demonstrating ≤1 clinical criterion for classifiable CTD, symptom duration <12 months and naive of therapy, of whom 15 later progressed to SLE/pSS and 20 did not progress. Disease controls with SLE (n=18), pSS (n=10) were also analysed. Weighted gene co-expression network analysis was used to identify gene expression modules associated with fatigue in preclinical subjects. Consensus networks were constructed for Preclinical:SLE and Preclinical:pSS to identify fatigue-associated modular signatures which are retained in established CTDs. Gene ontology enrichment was evaluated using g:profiler.
Results: Within the preclinical transcriptomic network 5 module eigengenes showed significant and specific association with patient fatigue VAS. A type-I IFN signature, centred upon canonical ISGs, *MX1*, *IRF7* and *IFIT5*, was positively correlated with fatigue score (R=0.48, p=0.003) and conserved across preclinical, SLE and pSS networks, with subtly different modular organisation. One further module, enriched for tRNA modification was significantly correlated with fatigue in preclinical subjects (R=0.41, p=0.01) but with no counterpart preserved in either SLE or pSS networks. The modular signature with strongest negative association with fatigue (R= -0.35, p=0.004) in preclinical subjects was enriched for mitogen-activated protein kinase (MAPK) cascades, heat shock and protein folding chaperone activity, and included transcription factors *JUN* and *ATF3*. This signature was retained in pSS patients, but did not persist in the SLE consensus network.
Conclusion: We describe novel modular transcriptomic signatures associated with fatigue in the preclinical phase of autoimmunity which demonstrate differential persistence and activity in SLE and pSS. These pathways may help identify individuals with immune-mediated fatigue most amenable to therapy, and could provide insights into new therapeutic targets for fatigue across a range of autoimmune diseases.



Scatterplot of Gene Significance for fatigue vs. Module Membership (MM) for genes located in two preclinical transcriptomic modules. One module with significant positive association with fatigue (A) is conserved across preclinical, SLE and pSS networks. Another module (B) negatively associated with fatigue was conserved in preclinical and pSS networks but not in SLE.

Figure 1.

REFERENCE:
[1] Psarras et al. 2020 Nat Commun 11: 6149

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POS0808

MICA/B-DEPENDENT ACTIVATION OF CYTOTOXIC NATURAL KILLER CELLS BY INFLAMMATORY CDC2 CONTRIBUTE TO PRIMARY SJÖGREN´S SYNDROME PATHOLOGY

Keywords: Animal models, Innate immunity, Sjögren syndrome

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Background: Primary Sjögren´s syndrome (pSS) is an example of an inflammatory autoimmune disorder largely mediated by IFN responses, leading to damage of exocrine glands that has been linked to autoreactive adaptive immune cells, such as Th17, CD8+ T cell and B cell [1, 2, 3]. However, the potential contribution of different innate immune cells such as Natural Killer (NK) cells and dendritic cells (DC) to pSS pathology remains understudied.
Objectives: We identify the molecular mechanisms regulating pathogenic crosstalk between NK and DC in pSS using samples from pSS patients and an experimental *in vivo* SS model.
Methods: Phenotypical analysis of myeloid and NK cell subsets in PBMCs from 47 pSS patients and 56 healthy donors (HD) was performed by flow cytometry. Histological analysis of SG from n=7 pSS was performed by confocal microscopy. Cytotoxic function of NK cells was assessed by culture with a K562-GFP target cell line. Transcriptional analysis of sorted Mo, CD1c+ and CD141+ cDC from four pSS patients and four HD was performed by RNA-seq. Co-culture between sorted NK cells, Mo and CD1c+ or CD141+ cDCs was used for test functional interactions. Regulation of ligands for NK cell receptors on cDC was analyzed by FACS after stimulation with poly I:C in the absence or the presence of specific siRNAs. Finally, altered DC and NK cell phenotypes and interactions with Th17 and B cells were analyzed in a murine Sjögren-mouse model induced by poly I:C intraperitoneal injections [4] in which we used a depleting anti-NK1.1 antibody or an isotype control each 4 days.
Results: Here, we identified an enriched transitional CD16^{+} CD56^{hi} NK cell subset in pSS individuals associated with higher NK cell cytotoxic function *in vitro*. In addition, elevated proportions of inflammatory CD64^{+} cDC2 exhibiting increased levels of MICa/b (p= <0,01), the ligand for the activating receptor NKG2D, were observed in the blood of these patients. Circulating cDC2 from pSS were capable of efficiently inducing activation of cytotoxic NK cells *ex vivo* and were found near CD56^{+} NK cells in salivary glands (SG) from pSS patients. Interestingly, cDC2 from pSS were characterized by preferential transcriptional activation of IFN signatures associated to the RIG-I/DDX60 pathway and its target genes. These sensors regulate the expression of MICa/b ligands on cDC2. Finally, increased proportions of CD64^{hi} cDC2 (p=<0,0001) expressing RAE-1 (p= <0,01), a murine activating NKG2D ligand, and transitional NKG2D^{+} CD11b^{+} CD27^{+} NK cells (p=<0,001) were present *in vivo* in the SG of an *in vivo* model of

pSS. Remarkably, depletion of NK cells during the inflammation onset prevented subsequent induction of IL-17^{+} CD4 (p= <0,01) and memory IgD^{-} IgM^{-} CD38^{hi} B cells (p=<0,0001) in the SG.

Conclusion: Thus, our study provides novel innate immune cellular and molecular mechanisms contributing to pSS pathology and identifies new potential therapy targets.

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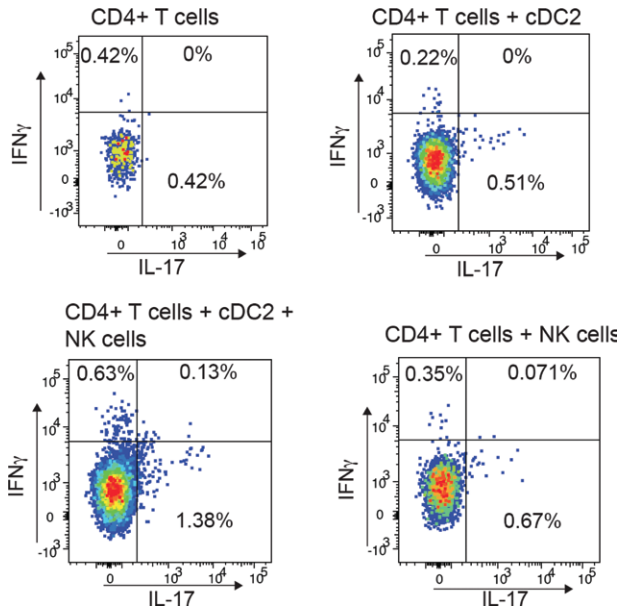


Figure 1.

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POS0809 HARNESSING CELL ENERGY METABOLISM TO SUPPRESS SALIVARY GLAND INFLAMMATION IN SJÖGREN SYNDROME

Keywords: Sjögren syndrome

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Background: SG epithelial cells (SGEC) play a key role in sustaining inflammation in Sjögren Syndrome (SS), which is indeed termed an 'autoimmune epithelitis'. However, the mechanisms responsible for the inflammatory activation of SGEC remain largely undetermined. Our line of research indicates that SGECs in SS exhibit profound changes in cell energy metabolism as indicated by aberrant expression of autophagy [1]. Inhibitions of autophagic process results in a down regulation of SGECs activation [1], thus indicating a crucial role of SGEC energy metabolism in the induction of autoimmune epithelitis.

Objectives: Aim of this study is to characterize metabolic changes occurring in SS SGECs and dissect the link between these changes and their acquired pro-inflammatory function.

Methods: SGECs were isolated from minor SG biopsies deriving from patients with SS and sicca. Intracellular metabolomic analysis was performed on direct ex vivo isolated primary SGECs. As read out of functional activation of SS SGECs, supernatants from SGECs coltures were collected to perform ELISA test in order to evaluate the expression of the pro-inflammatory mediator IL-6.

Results: Principal component analysis (PCA) of high-throughput metabolomics analysis of sicca (n=7) and SS (n=7) SGECs revealed a separation along the component 1 axis (46.6% of variance) indicating profound differences in the intracellular metabolome (**Figure 1a**). Unsupervised clustering analysis of metabolites revealed profound metabolic differences between SS and (n=7) sicca (n=7) SGECs (**Figure 1b**). Analysis of selected metabolites confirmed a shift towards increased glycolysis and TCA cycle activation in SS SGECs (**Figure 1c**). Supernatant concentrations of IL-6 were higher in SS (n=21) compared to sicca (n=14) SGECs (**Figure 1d**).

Conclusion: SGECs from SS patients display altered cell energy metabolism with evidence of increased glycolysis and activated TCA cycle. A metabolic driven pro-inflammatory status of SS SGECs seems confirmed by increased basal expression of IL-6. Validation of our metabolomic results, along with transcriptomic and epigenetic studies, is currently ongoing in SGECs from SS and sicca to dissect the link between changes in cell energy metabolism and their acquired pro-inflammatory phenotype.

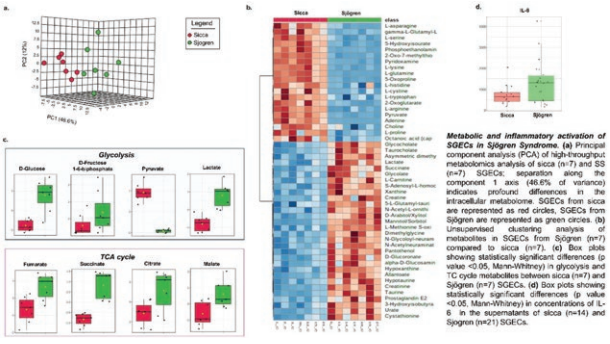


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POS0810 T FOLLICULAR HELPER CELLS IN BLOOD MIRROR SALIVARY GLAND-INFILTRATING T CELLS IN PRIMARY SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Adaptive immunity

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Background: Although clonal expansion of autoreactive T cells have been identified in the peripheral blood and salivary gland of primary Sjögren's syndrome (pSS) (1), the relationship between peripheral immune environments and inflammatory organs remains still unclear.

Objectives: Here, we examined which T cell subsets in blood share the same T cell receptor (TCR) αβ with T cells infiltrated at labial salivary gland (LSG) in patients with pSS, and evaluated mechanisms of their differentiation.

Methods:

1) TCR repertoires of each effector memory T cell subset (Th1, Th17, Tfh1, Tfh2, Tfh17) in blood, and LSG-infiltrating T cells obtained from the same pSS patient were analyzed by TCR sequence (*n*=1).
2) The proportion of each T cell subset in blood was compared between patients with pSS (*n*=30) and healthy controls (HC) by flow cytometry (*n*=20).

3) The proportion of each T cell subset between blood and LSG was evaluated in patients with pSS by flow cytometry (*n*=7).
4) Based on the above results, by focusing on Tfh cells, Tfh-related gene mRNA expressions (CXCR5, Bcl6, TGF-β, IL-6, IL-12, IL-21) were evaluated in LSG of pSS (*n*=11) and HC (*n*=3).
5) The conditions of Tfh cell differentiation in pSS were examined.
6) Cytokine production from $CD4^+$ T cells cultured under determined Tfh cell differentiation condition in pSS were examined.
7) pSS derived peripheral $CD4^+$ T cells were co-cultured with HC derived naïve B cells under Tfh cell differentiation condition, and effect on B cells differentiation was analyzed.

Results:

1) LSG-infiltrating T cells, and blood Th1, Tfh1, and Tfh2 cells showed higher clonality than Th17, and Tfh17 cells (Figure 1). Blood Tfh1, and Tfh2 cells were the two most frequent subsets comprised by the same T cell clones infiltrating in LSG.
2) Blood Tfh subsets were all significantly increased in patients with pSS than in HC. Among Tfh subsets, both PD-1 and ICOS expression was highest in Tfh1 subsets. Furthermore, the proportion of $PD\text{-}1^+ICOS^+$Tfh1 cells correlated with titers of anti-nuclear antibody, anti-SS-A antibody, and anti-SS-B antibody in pSS.
3) The proportions of memory Tfh subsets, especially Tfh1, was significantly increased in LSG compared with matched peripheral blood in pSS.
4) Expression levels of CXCR5, IL-6, IL-21, and TGF-β in LSG were significantly higher in pSS than HC. TGF-β positively correlated with CXCR5 expression in pSS.
5) $CD4^+$ T cells cultured under CD3/28 and TGF-β stimulation significantly increased CXCR5 expression, and Tfh1 population.
6) Production of IL-21, IL-2, and TNF-α were significantly increased after CD3/28 and TGF-β stimulation.
7) HC derived naïve B cells after co-culturing with pSS derived $CD4^+$ T cells, under Tfh differentiation condition (CD3/28 and TGF-β stimulation) expressed higher CD19, and $CD19^+CD38^+$ B cell population was increased.

Conclusion: Tfh1 cells in blood not only frequently showed high clonal expansion, but also highly shared the same TCRαβ with LSG-infiltrating T cells in pSS. Tfh1 cell proportion was expanded among pSS at both peripheral blood and LSGs, and furthermore, they positively correlated with autoantibody production. They proliferated under TGF-β-enriched environment, such as seen in LSG of pSS. Thus, we conclude that blood Tfh1 subsets has the potential to reflect inflammatory organ immune environment, possibly taking a role on autoantibody production at LSG.

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Figure1:

T cell clonality of each sample, is shown. LSG infiltrating T cells, blood Th1, Tfh1, and Tfh2 shows higher clonality compared to blood Th17, and Tfh17 population.

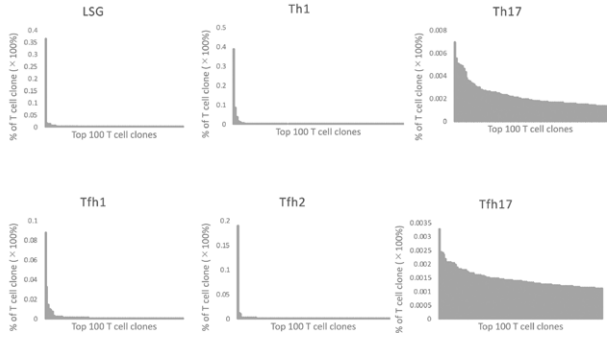


Figure 1. T cell clonality of each sample, is shown. LSG infiltrating T cells, blood Th1, Tfh1, and Tfh2 shows higher clonality compared to blood Th17, and Tfh17 population.

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POS0811

HIGH DIMENSIONAL CARTOGRAPHY OF LYMPHOCYTES USING SINGLE-CELL MASS CYTOMETRY DIFFERENTIATES SYSTEMIC LUPUS ERYTHEMATOSUS AND PRIMARY SJÖGREN`S SYNDROME

Keywords: Systemic lupus erythematosus, Sjögren syndrome, Qualitative research methods

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Background: Autoimmune conditions such as primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE) share clinical and serological features characterized by IFN signature (1), autoantibody formation (2), post-activated phenotype (3) and chronic inflammation. Although the 2019 SLE EULAR/ACR classification criteria facilitate a more precise clinical discrimination between SLE and pSS (4), a better understanding of the distinct immunological patterns of both diseases is required for developing fine-tuned immune modulations as therapeutic interventions.

Objectives: In this study we aimed at characterizing and deep phenotyping of lymphocytes and innate immune cells of patients with SLE and pSS for a better differentiation and understanding of immunological abnormalities.

Methods: Peripheral PBMCs of patients with SLE (n=21) or pSS (n=13) as well as from healthy controls (HD, n=15) were isolated. PBMCs were stained with both a B and a T/innate panel and analyzed using mass cytometry. After manual pre-gating of CD19+, CD3+ and innate immune cells, unbiased clustering analysis was performed and visualized as UMAPs. Clusters were identified and subsequently annotated according to median expression of lineage markers.

Results: Altogether, we identified 13 clusters in the B cell, 12 cluster in the T cell and 13 clusters in the innate compartment with disease dependent variations in frequencies and marker expression. B cell abnormalities were characteristic of SLE while striking T cell abnormalities were more prominent in pSS. IgD-CD27- double negative (DN) B cell sub-clusters were increased in SLE. Among the DN subsets the frequency of the cluster that presented with a lower CD19 expression correlated with PB frequencies. A Comparison of activation markers revealed increased CD86 expression on various B cell clusters of patients with SLE. Further, a memory B cell cluster expressing IgA stood out by higher KI-67 and CD45RO expression. In pSS patients, PD1+ ICOS+ CD4+ T follicular helper cell, CD8 effector memory and terminal differentiated effector memory CD8 T cell clusters were expanded. Notably, checkpoint molecules ICOS, TIGIT and PD1 were upregulated on various T cell clusters. Finally, intermediated monocytes that express CD226 were reduced in SLE when compared to pSS.

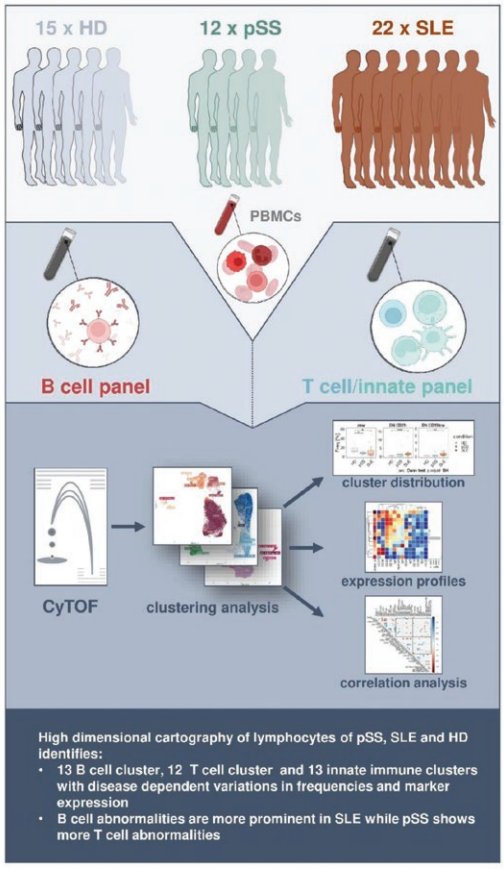


Figure 1. *Workflow of the study to characterize lymphocytes using single-cell mass cytometry in SLE and pSS. (Created with BioRender.com)*

Conclusion: High dimensional characterization of B, T and innate immune cells of patients with SLE or pSS illustrated immunological differences between diseases. SLE showed more B cell abnormalities while T cell alterations were more prominent in pSS consistent with distinct activation pathways driving these diseases. The immunologic abnormalities, distinct for pSS and SLE, might contribute to a better disease monitoring and selective treatment approaches.

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POS0812 BINDING OF CXCL13 WITH HEPARAN SULFATE OF SYNDECAN-1 PLAYS AN IMPORTANT ROLE IN PATHOGENESIS OF SJÖGREN'S SYNDROME

Keywords: Cytokines and chemokines, Sjögren syndrome

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Background: Sjögren's syndrome (SS) is a chronic autoimmune disorder with lymphocytic infiltration in exocrine and non-exocrine epithelia, in which epithelial cells play a critical role in the initiation and amplification of inflammatory processes. Syndecan-1 (SDC-1) is a transmembrane heparan sulfate proteoglycan predominantly expressed on epithelial cells and binds to and regulates heparan sulfate-binding molecules, such as chemokines.

Objectives: In this study, we investigated the expression of SDC-1 and homeostatic chemokines and the colocalization and association of SDC-1 and B cell chemokines in mouse model of primary SS to define the role of SDC-1 in the pathogenesis of SS.

Methods: Female NOD/ShiLtJ between 6 and 12 weeks of age and sex-, and age-matched C57BL10 mice were used. Stimulated salivary flow rates (SFRs), histopathologic findings and expression of growth factor and chemokines were evaluated. Inflammation of the submandibular glands (SMGs) was assessed by the ratio index (the ratio of the area of inflammation to the total area of glandular tissue). SDC-1 level in SMGs and blood were analyzed using dot blot method. Immunofluorescence staining was performed for detection of colocalization of CXCL13 and SDC-1. For SDC-1 and CXCL13 coassociation experiments, immunoprecipitation assay was performed.

Results: The mean SFR was significantly reduced in 12-week-old NOD mice (p=0.013). Periductal inflammatory cell infiltration was detected in the SMGs in 1 of 8 (12.5%) of the 6-week-old and in all of 12-week-old NOD mice. The mean ratio index was 0.1, 4.0, 7.1, and 10.2 in the 6-, 8-, 10-, and 12-week-old NOD mice, respectively. The expression of SDC-1 in inflamed SMGs of NOD mice was elevated, especially on the ductal epithelial cells, and tended to increase as the glandular inflammation progressed. Compared to controls, the concentration of SDC-1 in the SMGs and blood of NOD mice began to increase significantly from the age of 6 weeks (SMGs, 15.6±3.6 vs. 3.5±1.2, p=0.049; Blood, 17.4±1.3, 9.7±1.6, p=0.005). In the NOD mice, the concentration of SDC-1 of SMGs and blood began to be significantly different from the age of 10 weeks (6-week-old vs. 10-week-old mice, SMGs, 15.6±3.6 vs. 25.8±2.7, p=0.033; Blood, 17.4±1.3 vs. 27.7±1.2, p<0.001). Compared to controls, the expression of growth factors in NOD mice was reduced, while the expression of chemokines (CXCL12, CXCL13 and IL-7) and chemokine receptors (CXCR4, CXCR5) was increased. CXCL13 and SDC-1 were detected together on the surface of glandular epithelial cells in the SMGs by immunofluorescent staining. Furthermore, colocalization of SDC-1 and CXCL13 was confirmed by immunofluorescent staining using NMuMG cells which express SDC-1 abundantly. Immunoprecipitation studies demonstrated that SDC-1 formed complexes with CXCL13, which suggested that SDC-1 binds with CXCL13 directly through heparan sulfate on the surface of glandular epithelial cells and participates in an inflammatory pathway through B cell chemotaxis.

Conclusion: These results suggested that increased SDC-1 expression in submandibular glands plays a role in the inflammatory processes through binding of SDC-1 with CXCL13 in pathogenesis of SS.

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POS0813 ALTERATION OF ILC HOMEOSTASIS MAINLY CONCERNS SALIVARY GLANDS IN PRIMARY SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Innate immunity

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Background: Little is known about the early stages leading to the autoimmune process in primary Sjögren's syndrome (pSS). Some data suggest the involvement of the innate immunity both in disease initiation and maintenance of autoimmunity in pSS, but more studies are needed to dissect the role of innate immune cell actors. Innate lymphoid cells (ILC) are a recently discovered cell population divided into three groups including type 1, 2 and 3 ILC subsets. While ILC are normally involved in the maintenance of tissue homeostasis, they can also contribute to generate tertiary ectopic lymphoid structures [1], as observed in some patients with pSS, and potentiate inflammatory processes in different chronic inflammatory diseases [2].

Objectives: The aim of this study was to analyze the frequencies of ILC subsets in the peripheral blood (PB) and quantities and location in minor salivary glands (MSG) of pSS patients.

Methods: The frequencies of ILC subsets were analyzed in the PB of 21 pSS patients and 28 healthy controls (HC) by flow cytometry. ILC were identified as CD45+, lineage (CD1a, CD3, CD4, CD14, CD16, CD19, CD34, CD303, FcεRI)- and CD127+. Within the ILC gate, ILC1 were identified as c-kit+ and CRTH2-, ILC2 as CRTH2+, and ILC3 as c-kit+ and CRTH2–. The amounts and location of ILC subsets were studied in the MSG of 13 pSS patients and 5 controls (SC) using immunofluorescence. ILC were defined as lineage (CD3, CD14, CD19)- and CD127+ cells. The expressions of T-bet (nuclear) and CRTH2 (cytoplasmic) were used to distinguish between ILC1 (T-bet+), ILC2 (CRTH2+) and ILC3 (T-bet– and CRTH2-) subsets.

Results: In PB, the frequencies of total circulating ILC and ILC subsets did not differ in pSS patients compared to HC. There was a significantly higher number of circulating ILC1 in pSS patients with positive anti-SSA antibodies (p=0.03) and a lower number of circulating ILC3 in pSS patients with glandular swelling (p=0.01). The proportions of ILC subsets in PB did not correlate with systemic disease activity measured by ClinESSDAI. Most of the ILC identified in MSG of pSS patients were ILC3 (91.1%). The amount of ILC3 was higher in tissues with lymphocytic infiltrates compared to non-infiltrated tissues in pSS patients (p=0.0002) and to normal glandular tissues in SC (p=0.0005). No difference was observed when comparing the quantity of ILC1 and ILC2 in the MSG between pSS patients and SC. ILC3 were preferentially located at the periphery of the infiltrates and were inversely correlated with the surface of T/B lymphocyte infiltrates (r=-0.42, p=0.002). ILC3 were inversely correlated with time since diagnosis (r=-0.69, p= 0.01).

Conclusion: Alteration of ILC homeostasis mainly concerns salivary glands in pSS. The majority of ILC in MSG is composed by ILC3, located at the periphery of lymphocytic infiltrates. ILC3 are more abundant in smaller infiltrates and in

recently diagnosed pSS patients. ILC3 might play a pathogenic role in the development of T and B lymphocyte infiltrates in the early stages of pSS.

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POS0814 UNTARGETED METABOLOMICS ANALYSIS OF SEBUM: A NON-INVASIVE STRATEGY THAT SHOWS POTENTIAL TO IDENTIFY NEW BIOMARKERS IN PRIMARY SJÖGREN'S SYNDROME AND SYSTEMIC SCLEROSIS

Keywords: Biomarkers, Sjögren syndrome, -omics

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Background: Saliva and tears are easy accessible fluids for biomarker analyses but a major drawback is that a substantial proportion of patients with primary Sjogren's syndrome (pSS) suffers from severe dryness, with limited or no saliva or tear to donate. Thus, novel non-invasive strategies applying state-of-the-art technologies should be welcomed.

Objectives: To evaluate if metabolome analysis of sebum can be used as a non-invasive method to identify skin metabolic signatures in patients with primary Sjogren's syndrome (pSS) as compared to healthy controls and other systemic autoimmune diseases.

Methods: Untargeted metabolomics of sebum samples collected from sebutapes placed on the forehead for 5 minutes was performed using mass spectrometry. Sebum metabolomes of healthy controls (HCs, n=17) and 32 pSS patients were compared (for this abstract only ions from the negative ionization mode are discussed, for the positive ionization mode similar results were found). Additionally, the metabolomes of two other systemic autoimmune diseases, i.e. systemic sclerosis (SSc, n=21) and systemic lupus erythematosus (SLE, n=8), were compared to pSS and HCs. The human biological samples were sourced ethically and their research use was in accord with the terms of the informed consents under an IRB/EC approved protocol.

Results: Modest significant differences were observed between the sebum metabolome of pSS patients as compared to HCs. Unsupervised dimensionality reduction using UMAP showed no strong differences between metabolic signatures of pSS patients and HCs. However, correlation analyses of metabolic changes and disease activity markers did identify several metabolite ions with a good correlation with disease activity. A total of 335 metabolite ions significantly correlated to the European Sjogren's Syndrome Disease activity index (ESSDAI) score, 13 metabolite ions correlated with sIgG and 41 metabolite ions with lymphocytic focus scores (LFS, all spearman r <- 0.50 or >0.50, p<0.05). To understand if pathways in disease activity-associated metabolites may underlie the observed changes we performed pathway enrichment analyses to investigate potential group function of the metabolite ions identified in these comparisons. Two significantly enriched pathways were identified correlating to the ESSDAI score: alpha-linolenic acid metabolism and phenylalanine metabolism. More robust significant differences were identified in patients with systemic sclerosis as compared to healthy controls, indicating metabolites significantly enriched for pathways associated with neurotransmission, including metabolite ions with annotations as L-glutamic acid, noradrenaline, dopamine and 3'-AMP. Interestingly, when analyzing differentially expressed metabolite ions of pSS and SSc patients relative to HCs highly significant and strong correlations were observed (R=0.78 for negative ionization mode), indicating that these diseases might have common metabolic dissimilarities.

Conclusion: This pilot study demonstrates that sebum metabolomics might be a novel strategy to identify biomarkers in pSS and other (systemic) autoimmune diseases. Larger follow-up studies using more targeted metabolomics strategies that take into account potential confounding factors and optimize sebum collection should demonstrate the feasibility of this novel non-invasive monitoring method in molecular profiling of disease.

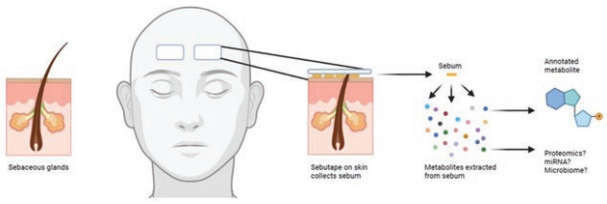


Figure 1. Application of sebutapes to collect sebum from the skin of the forehead for metabolomics analysis. All participants avoided using facial products for 24 hours and did not wash their forehead up to 3 hours prior to sample collection. Before sebum collection the participant's forehead was systematically cleaned with soap and water and 2 Sebutape Adhesive Patches for collecting sebum were applied to the forehead for 5 minutes and stored at -80 °C until analyses.

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Disclosure of Interests: None Declared.

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POS0815 CD40L BLOCKADE WITH DAZODALIBEP (VIB4920/HZN4920) REDUCES BLOOD BIOMARKERS OF T AND B CELL COSTIMULATION IN SUBJECTS WITH SYSTEMIC SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Randomized control trial, Biomarkers

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Background: Dazodalibep (DAZ) is a non-antibody biologic antagonist of CD40L. In several autoimmune diseases, the CD40/CD40L pathway is activated on a variety of cell types, including T cells, B Cells, antigen-presenting cells, and activated epithelial cells. DAZ blocks costimulatory signals between T cells and CD40-expressing B cells, disrupting the development of germinal centers, pathogenic B cells, plasma cells, and autoantibodies that are hallmarks of Sjögren's Syndrome (SS).

Objectives: To evaluate the impact of DAZ on blood biomarkers of B and T cell costimulation in adult SS subjects with moderate-to-high systemic disease activity.

Methods: This was a randomized, double-blind, placebo-controlled, crossover study to evaluate DAZ therapy in adult SS subjects with moderate-to-high systemic disease activity, as defined by a EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) score ≥ 5. Subjects were randomized 1:1 to receive intravenous DAZ 1500 mg or placebo (PBO) Q2W x 3 doses, then Q4W x 4 additional doses (Stage 1). Starting on Day 169, subjects initially randomized to DAZ received PBO Q4W x 5 doses and subjects initially randomized to PBO received DAZ Q4W x 5 doses and were then followed for 12 weeks (Stage 2). B cell subsets downstream of T cell stimulation (Ki67+CD27+ memory, CD27 high CD38 high plasmablasts, and CD11c high atypical memory cells) were assayed via FACS throughout the study period. Serum CXCL13 concentrations, a chemokine essential for GC formation produced by activated follicular T cells, and rheumatoid factor (RF) autoantibodies were also measured.

Results: Concomitant with DAZ-related reductions in ESSDAI observed at Stage 1, significant and rapid reductions were observed in Ki67+CD27+ memory B cells, plasmablasts, CD11c^{high} memory B cells, CXCL13 and RF antibodies from day 15 onwards in subjects who received DAZ as compared to PBO. In Stage 2, similar reductions were found in these biomarkers when PBO-treated subjects were transitioned to DAZ treatment. In DAZ-treated subjects who were transitioned to PBO in stage 2, these biomarkers returned to baseline values while sustained reductions were observed in ESSDAI from baseline through the duration of stage 2.

Conclusion: CD40-CD40L blockade with DAZ in patients with SS reduces systemic disease activity by inhibiting T and B cell costimulation, as evidenced by treatment related reductions in blood biomarkers downstream of these pathways.

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Table 1. The Impact of DAZ on Blood Biomarkers of B and T Cell Costimulation in Adult Sjogren's Syndrome Subjects

Median (-/+ IQR) FC of baseline in Placebo-Dazodalibep group				
	Days from study start			
	Phase 1 (Placebo)		Phase 2 (Dazodalibep)	
Analyte Name	**85**	**169**	**253**	**365**
CXCL13 (pg/mL)	1.01 (0.87, 1.21)	1.06 (0.8, 1.24)	0.62 (0.45, 0.83)	0.69 (0.53, 0.85)
Rheumatoid Factor (IU/mL)	1.23 (0.97, 1.31)	1.27 (1.13, 1.49)	0.55 (0.45, 0.92)	0.45 (0.38, 0.65)
%Ki-67+ (of post-sw memory B cells)	1.07 (0.67, 1.68)	1.32 (0.69, 1.82)	0.58 (0.29, 1.05)	0.47 (0.26, 0.96)
%Plasmablasts (of CD19 B cells)	1.19 (0.63, 1.87)	0.89 (0.68, 1.97)	0.58 (0.43, 1.12)	0.57 (0.33, 0.74)
%CD11c^{high} (of CD19 B cells)	2.37 (1.19, 3.48)	1.43 (0.95, 2.64)	1.09 (0.7, 2.07)	1.06 (0.51, 4.29)
ESSDAI Total Score	0.6 (0.34, 0.87)	0.58 (0.34, 0.84)	0.41 (0.18, 0.66)	0.49 (0.25, 0.71)
Median (-/+ IQR) FC of baseline in Dazodalibep-Placebo group				
	Days from study start			
	Phase 1 (Dazodalibep)		Phase 2 (Placebo)	
Analyte Name	**85**	**169**	**253**	**365**
CXCL13 (pg/mL)	0.62 (0.55, 0.89)	0.71 (0.48, 0.85)	1.08 (0.84, 1.21)	1.02 (0.78, 1.15)
Rheumatoid Factor (IU/mL)	0.41 (0.27, 0.74)	0.29 (0.27, 0.54)	0.97 (0.77, 1.21)	0.91 (0.81, 1.32)
%Ki-67+ (of post-sw memory B cells)	0.45 (0.16, 0.63)	0.44 (0.25, 1)	1.59 (1.1, 2.36)	1.14 (0.94, 2.07)
%Plasmablasts (of CD19 B cells)	0.56 (0.3, 0.72)	0.61 (0.34, 0.84)	1.85 (0.53, 3.11)	1.84 (0.72, 3.45)
%CD11c^{high} (of CD19 B cells)	0.65 (0.47, 2.04)	0.92 (0.56, 2.01)	1.41 (0.81, 3.83)	1.3 (0.92, 2.91)
ESSDAI Total Score	0.6 (0.41, 0.85)	0.46 (0.26, 0.57)	0.5 (0.34, 0.67)	0.42 (0.16, 0.57)

FC, fold-change; IQR, interquartile range

Therapeutics plc, Employee of: Horizon Therapeutics plc, E. William St. Clair Consultant of: Horizon Therapeutics plc, Bristol Myers Squibb, CSL Behring, Resolve Therapeutics, Sonoma Biotherapeutics, and receives royalties from UpToDate.
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POS0816 ALTERATIONS IN THE IMMUNE AND STROMAL CELL LANDSCAPE OF THE SALIVARY GLAND AND PERIPHERY IN PRIMARY SJÖGREN'S SYNDROME

Keywords: Cell biology, Sjögren syndrome

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Background: Primary Sjögren's syndrome (pSS) is a heterogeneous, chronic, complex systemic autoimmune disease. Patients with pSS exhibit focal lymphocytic sialadenitis in the salivary gland (SG), supporting the SG as the pathogenic center and primary damaged organ in pSS. As of today, but the knowledge of existing pSS disease heterogeneity is still limited and the immune mechanisms of SG injury have been challenging to clarify.
Objectives: To give a comprehensive understanding of cellular heterogeneity in the SG and to define commonalities and discrepancies between the SG and peripheral blood immune cell populations, we performed droplet-based single cell mRNA sequencing (scRNA-seq) (10X Genomics) in pSS patients and non-SS controls.
Methods: 11 patients and 5 non-pSS controls were recruited from the The First Affiliated Hospital of USTC. The non-pSS were subjects who had experienced subjective symptoms of dryness, but no not meet any of the classification criteria of pSS. After resection, SG tissue samples were obtained after labial gland biopsy, rapidly digested to a single-cell suspension and subjected to scRNA-seq using the 10X platform. After rigorous quality control (QC) definition, low-quality cells were filtered. we applied principle component analysis on genes variably expressed across all 72,853 SG cell. In addition, we collected another cohort for blood single-cell RNA sequencing, including an additional 5 pSS patients who fulfilled the same selection criteria and 3 healthy individuals.
Results: A total of 72,853 cells were obtained from all SG samples. Seurat was applied to normalize and cluster the gene expression data, subsequently generating a matrix that identified 11 unique, major cell subpopulations, including epithelial cells, ionocytes, fibroblasts, smooth muscle cells (SMC), endothelial cells, pericytes, melanocytes, T cells, B cells, plasma cells, and myeloid cells. As expected, lymphocytes (T and B cell populations) were significantly increase in the SG of patients with pSS. In addition, epithelial cells of pSS samples had obviously higher numbers of differentially expressed genes (DEGs) than other cell types. Gene ontology (GO) analysis of down-regulated DEGs in SG epithelial cells of pSS patients related to 'salivary secretion' and 'epithelial cell differentiation'. We identified a disease-associated epithelial subpopulation, myoepithelial cell, with characteristically low expression of SOX9, which leads to impaired regeneration of epithelial cells. Our results identified three distinct endothelial subtypes according to the differentially expressed cell markers. We also found that pSS patients have a strikingly increased number of ACKR1^{+} endothelial cells that could potentially promote transendothelial migration from peripheral blood monocyte populations. Using a reciprocal principal component analysis method for the integration of PBMCs and SG scRNA-seq data, we obtained a total of 79,596 immune cell transcriptomes. Among these, we identified five major populations and 36 immune cell clusters, including 4 B cell clusters, 4 plasma cell clusters, 19 T cell clusters, 8 myeloid cell clusters, and natural killer (NK) cells. Additionally, pseudotime trajectory analysis defined a bifurcated differentiation pathway for peripheral B cells and a trajectory leading to three distinct subtypes for peripheral CD4^{+} T cells enriched in the SG of pSS patients. Finally, we provide a series of detailed maps of the global interactions between immune cells and stromal cells, and among stromal cells. Fibroblasts were identified as the center of a stromal-immune interaction network likely responsible for disrupting extracellular matrix formation, impairing epithelial regeneration, and inflammatory progression.
Conclusion: In conclusion, our study provides a preliminary cellular atlas for the SG in Sjögren's Syndrome, opening new avenues of research for therapeutic development to treat this disease.

Figure 1

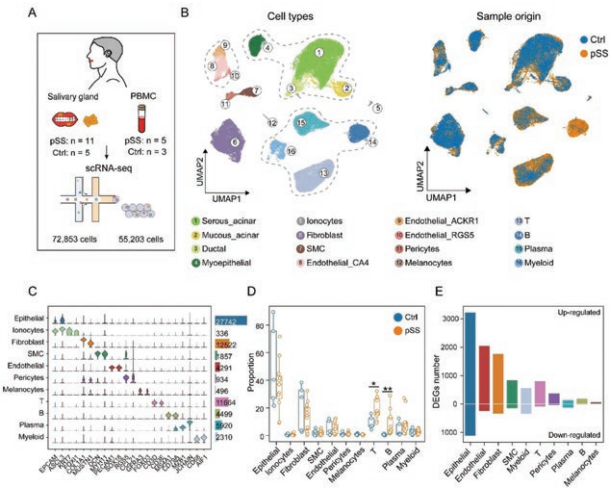


Figure 1.

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POS0817 THE ROLE OF IGG N-LINKED SIALYLATION AND GALACTOSYLATION IN PRIMARY SJÖGREN'S SYNDROME IN ITS POTENTIAL AS A MARKER OF DISEASE STATE AND DISEASE ACTIVITY

Keywords: Adaptive immunity, Sjögren syndrome, Autoantibodies

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Background: Primary Sjögren's Syndrome (pSS) is characterized by the presence of antibodies (Ab). Their effector function mainly depends upon the glycan structures attached to their Fc-fragment. Our study is the first to address the value of IgG glycosylation profiles in relation to disease state, salivary gland ultrasound (SGUS) and auto-Ab in patients with probable (prob pSS) and definite pSS (def pSS).
Objectives: To investigate N-glycosylation of IgG in patients from the Belgian Sjögren's Syndrome Transitial Trial (BeSSTT) in relation to pSS state, disease activity, SGUS and the presence of Ab to SSA/Ro52, SSA/Ro60 and SSB.
Methods: The relative amount of sialylated (sial) and galactosylated (gal) IgG was determined by capillary electrophoresis after the endo-S glycosidase assay. 314 sera of the BeSSTT, an observational cohort of patients with def pSS, fulfilling the 2016 ACR/EULAR classification criteria, and of patients with suspected pSS due to presence of either objective sicca or one immunological criterion, were used. Groups were made based on the presence or absence of sicca complaints, objective sicca, anti-SSA Ab and histopathology focus score. SGUS by Hocevar was categorized in negative (0-14), low positive (15-26) and high positive (27-48)[1]. Disease activity using the Eular Sjögren's Syndrome disease activity index (ESSDAI) was categorized in low (0-4), moderate (5-13) and high (14-123). Differences in sial and gal IgG levels were determined using One-way ANOVA and Kruskal-Wallis testing. P-values ≤0.05 were considered statistically significant. Bonferroni correction was applied.
Results: Disease state was addressed in well-defined groups: patients with only sicca complaints, patients with only objective sicca, patients with only anti-SSA/SSB reactivity (prob pSS) and patients with def pSS. Def pSS patients had a significantly lower median percentage of sial and gal IgG compared to patients with only sicca complaints, only objective sicca or only anti-SSA Ab. No significant difference in sial and gal IgG was seen between the latter three groups (Figure 1). Patients with high ESSDAI had a significantly lower percentage of sial and gal IgG versus those with low ESSDAI. In high positive SGUS-score, a significantly lower median percentage of sial IgG and a lower percentage of gal IgG was noted compared to negative or low positive Hocevar score (Figure 1). Mono-anti-Ro52 reactivity, double-anti-Ro52Ro60 reactivity or triple-anti-Ro52Ro60 SSB reactivity had a significantly lower percentage of sial and gal IgG compared to anti-SSA/SSB negative. Strikingly, anti-Ro5260+ and anti-Ro52Ro60 SSB+ had a significantly lower percentage of sial and gal IgG compared to mono anti-Ro60 (Figure 1).
Conclusion: These results indicate that disease state, disease activity, salivary gland involvement and serology profile is strongly associated with different levels of sial and gal IgG in pSS. This highlights the potential role for glycosylation as diagnostic marker and biomarker and its potential role in the pSS pathophysiology.
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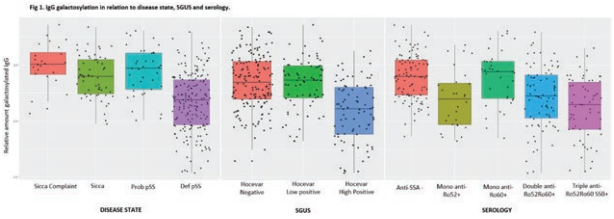


Figure 1.

Table 1.

	N	Relative area of sial	Relative area of gal	P-values (α=0.05)	
				Sial	Gal
Disease state		**Mdn**	**Mdn**		
Sicca complaint	24	0.080	0.60	<0.001	<0.001
Sicca	58	0.067	0.56		
Prob pSS	37	0.075	0.59		
Def pSS	183	0.057	0.47		
SGUS		**Mdn**	**M**		
0-14	160	0.064	0.538	<0.001	<0.001
15-26	72	0.067	0.532		
27-48	82	0.050	0.434		
ESSDAI		**M**	**M**		
0-4	264	0.062	0.52	<0.01	<0.001
5-13	31	0.055	0.48		
14-123	5	0.022	0.35		
SEROLOGY		**M**	**M**		
No anti-SSA/SSB	104	0.070	0.56	<0.001	<0.001
Mono anti-Ro52	28	0.055	0.48		
Mono anti-Ro60	35	0.073	0.56		
Double anti-Ro52Ro60	79	0.056	0.48		
Triple anti-Ro52Ro60 SSB	62	0.045	0.45		

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POS0818 IN PRIMARY SJÖGREN'S SYNDROME CCR9/CXCR5 CO-EXPRESSING EFFECTOR CD4 T CELLS ARE INCREASED AND ARE ENRICHED IN PD-1/ICOS-EXPRESSING T CELLS

Keywords: Sjögren syndrome

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Background: Primary Sjögren's syndrome (pSS) is an autoimmune disease characterized by B cell hyperactivity. CXCR5+ follicular helper T cells (Tfh), CXCR5-PD-1hi peripheral helper T cells (Tph) and CCR9+ Tfh-like cells have been implicated in driving B cell hyperactivity in pSS (1-3), however, their potential overlap has not been evaluated.
Objectives: To study the overlap between the two CXCR5- cell subsets and to study their PD-1/ICOS expression, hall mark markers, as compared to "true" CXCR5/PD-1/ICOS-expressing Tfh cells.
Methods: We defined Tph cells as CXCR5-PD-1hi memory (CD45RO+), CCR9+ Tfh-like as CXCR5-CCR9+, and CCR9+ Tfh as CXCR5+CCR9+ memory CD4 T cells, as previously described. CXCR5+CCR9+ co-expressing cells were not specified on memory phenotype. Tfh cells were defined as CXCR5+ memory, and "true" Tfh cells as CXCR5+PD-1+ICOS+ memory cells. CXCR5- Tph and CCR9+ Tfh-like cell populations from peripheral blood mononuclear cells of pSS patients (n=12) and age- and gender-matched healthy controls (HC, n=11) were compared by flow cytometry. PD-1/ICOS expression from these cell subsets was compared to each other and to CXCR5+ Tfh cells, taking into account their differentiation status.
Results: In pSS patients the number of Tph cells was significantly increased compared to HC (median 0.53% versus 0.23% of CD4 T cells, p=0.049). Also the number of CCR9+ Tfh-like cells was significantly elevated in pSS patients as compared to HC, i.e. approximately 2.7% in pSS patients versus 1.7% in HC (medians, p=0.019). CCR9 expression was equally distributed between pSS patients and HC in Tph cells. Only a modest number of 2.1% (1.2-3.2%) of Tph cells expressed CCR9 (median with interquartile range), indicating limited overlap. CXCR5+ (Tfh) cells were characterized by the highest frequency of PD-1hi cells, either with or without CCR9 co-expression (PD-1hi expression differed between CXCR5+ T cell subsets compared to CXCR5-CCR9- and CXCR5-CCR9+ T cells, both p<0.0001.) No difference in PD-1hi expression was seen between CXCR5+CCR9- and CXCR5+CCR9+ cells (p=0.57). Within the PD-1hi populations, cells expressing either CXCR5 and/or CCR9 of pSS patients showed a trend of higher ICOS expression compared to HCs, but this was only significant in CCR9+ Tfh-like cells (28.6% and 55%, medians for HC and pSS respectively, p=0.02) PD-1/ICOS expression was higher in memory cells expressing CXCR5 or CCR9. However, the highest expression was found in CXCR5/CCR9 co-expressing T cells, which are enriched in the circulation of pSS patients. PD-1, ICOS, and PD-1/ICOS co-expression was significantly higher on CCR9+ Tfh cells than on CCR9- Tfh cells (in all three comparisons p<0.05).
Conclusion: CXCR5- Tph and CCR9+ Tfh-like cells are two distinct cell populations that both are enriched in pSS patients and can drive B cell hyperactivity in pSS. The known upregulated expression of CCL25 and CXCL13, ligands of CCR9 and CXCR5, at pSS inflammatory sites suggests concerted action to facilitate migration of CXCR5+CCR9+ T cells, which are characterized by the highest frequencies of PD-1/ICOS positive cells. Hence, these co-expressing effector T cells may significantly contribute to the ongoing immune responses in pSS.
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POS0819

ALTERED EXPRESSION OF RNA METHYLATION AND DEAMINATION ENZYMES IN SALIVARY GLANDS FROM SJÖGREN'S SYNDROME PATIENTS

Keywords: Sjögren syndrome, Cytokines and chemokines, Genetics/ epigenetics

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Background: Primary Sjögren's syndrome (pSS) is an autoimmune disease characterized by an overactivation of the type I interferon pathway (IFNs I) and differential microRNAs expression in the salivary glands (SG) [1]. In these patients, hsa-miR-145-5p downregulation was found to be associated with increased levels of IFNs I and the overactivation of its pathway [2]. IFNs I can alter miRNA biogenesis by reducing the processing of some primary microRNAs (pri-miRNAs) through diminished interaction with the microprocessor complex, leading to decreased mature microRNA levels [3]. Although the mechanisms involved are not fully understood, changes in adenosine deamination that lead to adenosine to inosine (A-to-I) editing or methylation of the N6-position of adenosines (m6A) in the pri-miRNAs could be participating.
Objectives: To evaluate the expression of pri-miR-145 and the enzymes that methylate (METTL3 and METTL14), demethylate (FTO and ALKBH5), and deaminate (ADAR1p110 and ADAR1p150) adenosines in RNAs of labial SG (LSG) from pSS-patients.
Methods: LSG from 9 pSS-patients and 6 controls as well as HSG cells stimulated with IFNs I (IFN-α or IFN-β) were analyzed. pri-miR-145 levels were determined by TaqMan assays. Enzymes transcript and protein levels were measured by qPCR and Western blot, respectively. The enzymes localization was determined by immunofluorescence.
Results: LSG from pSS-patients showed increased pri-miR-145 levels, which directly correlated with the IFNs I score, a measure of the activation of the IFNs I pathway. LSG from pSS-patients also showed increased METTL3, ALKBH5 and ADAR1p150 levels, with no changes in METTL14 and FTO. ADAR1p150 levels also correlated directly with the IFNs I score. All the enzymes were mainly observed in the nuclei of LSG acinar cells. Finally, stimulation of HSG cells with IFNs I upregulated ADAR1p150
Conclusion: Increased pri-miR-145 levels suggest accumulation of this precursor in LSG of pSS-patients due to lack of processing, which could contribute to the hsa-miR-145-5p downregulation found previously (2) and could be associated to the overactivation of the IFNs I pathway. The overexpression of METTL3, ALKBH5 and ADAR1p150 could lead to changes in RNA methylation or deamination, particularly in pri-miRNAs that alter their processing, which needs further study. Finally, the functional assays suggest an association between the IFNs I overactivation and the ADAR1p50 overexpression observed in SS-patients.
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POS0820

SEX-EQTL ANALYSIS REVEALS A SIGNIFICANT SEX-BIAS IN THE EFFECTS OF SJÖGREN'S SYNDROME ASSOCIATED ALLELES ON GENE TRANSCRIPTION

Keywords: Genetics/epigenetics, Sjögren syndrome

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Background: Primary Sjögren's syndrome is a systemic autoimmune disease that affects exocrine glands, particularly the salivary- and lacrimal glands, leading to the hallmark symptoms of mucosal dryness. Patients commonly also experience fatigue, joint and muscle pain. Sjögren's syndrome predominantly affects women, with a female-to-male ratio of 14:1. Genetic risk factors associated with Sjögren's syndrome have been identified, however, the mechanisms behind the profound sex-bias remain incompletely understood.
Objectives: The aim of this study was to analyze whether the sex of a carrier of genetic variants associated with Sjögren's syndrome affects the expression of genes in associated loci.
Methods: Genetically regulated gene expression differences between sexes were identified by identifying expression quantitative trait loci (eQTLs). Databases including the Genotype-Tissue Expression project (GTEx, version 8), and the NHGRI-EBI Catalog of human genome-wide association studies (GWAS catalog) as well as a literature review were utilized to extract information about variants significantly associated with Sjögren's syndrome, and their sex-specific eQTL effects.
Results: Out of 22 non-*HLA* loci identified as associated with Sjögren's syndrome at the genome-wide level, 4 independent loci had one or more significant sex-eQTL effects in the GTEx database in any tissue. These included variants near *IRF5*, *TNIP1*, *SYNGR1* and the *BLK-FAM167A* loci. Additionally, variants in 4 Sjögren's syndrome associated loci within the *HLA* region on chromosome 6 were found to have one or more sex-eQTL effects in the GTEx database. Of the 14 identified sex-eQTLs for Sjögren's associated loci, 10 were female biased.
Conclusion: Sjögren's syndrome is a female biased disease and genetic variants associated with Sjögren's syndrome have discordant effects on gene expression in females compared to males. A majority of the identified effects point towards a more severe effect of these variants in female carriers than male carriers, indicating that females could be more profoundly affected by these genetic risk factors than males. This suggests a mechanism where genetic risk factors could disproportionately increase disease risk in one sex compared to the other.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Gudny Ella Thorlacius: None declared, Albin Björk: None declared, Marie Wahren-Herlenius Grant/research support from: Janssen Pharmaceutica NV and Merck KGaA.
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POS0821

DIFFERENTIALLY EXPRESSED GENES (DEGS) OVERLAPPED FROM DATASETS FROM PATIENTS WITH SJÖGREN'S SYNDROME (SS) THROUGH INTEGRATIVE BIOINFORMATICS ANALYSIS DISPLAY INTERFERON SIGNATURE

Keywords: Biomarkers, -omics, Sjögren syndrome

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Background: Sjögren's Syndrome is an autoimmune disease comprised by oral and ocular dryness due to destruction of lacrimal and salivary glands. It may be associated with other rheumatological pathologies such as Rheumatoid Arthritis or Systemic Lupus Erythematosus [1]. Bioinformatics has been used to elucidate the pathophysiology underlying rheumatological diseases [2]. Key findings include an Interferon (IFN) signature common to rheumatic diseases and aberrant activation of B and T cells [3]. Nonetheless, they are inconclusive since several studies propose different DEGs.
Objectives: We aimed to identify overlapped genes across datasets of gene expression from patients with primary SS doing an integrative bioinformatics metanalysis.
Methods: A search strategy was designed in the Gene Expression Omnibus platform to identify datasets of gene expression profiling by array experiments in patients with SS. The inclusion criteria were: 1) Assays performed in humans, 2) Inclusion of healthy controls in each dataset, and 3) Data analysis with GEO2R. The exclusion criteria were: 1) Incomplete information of the genes, and 2) Gene expression by RNAseq. DEGs were selected when $p < 0.05$ and log fold change > 2 or < -2. Functional enrichment analysis was realized with free-access platforms GeneMania and DAVID from the significant overlapped genes. A protein-protein interaction (PPI) analysis was constructed with STRING. A topologic interaction network using CytoHubba to find the genes with the highest interaction within the cluster was realized.
Results: 8 datasets qualified to be analyzed. 260 DEGs were identified. 10 DEGs overlapped among the datasets. Prediction analysis yielded 21 co-expressed pairs. Functional enrichment analysis showed 3 biological processes in which those genes participate (Table 1): 20 genes in defense response to virus, 14 in response to virus, and 10 in the negative regulation of the viral genome replication. Most of them belong to the type I IFN signature. PPI analysis showed a cluster of 27 genes and the topological analysis yielded 10 genes (Figure 1).

Table 1. Top 3 biological processes in which the genes participate.

Functional Enrichment Analysis		
Process	**Gene count**	*p Value*
Defense response to virus (Type I IFN Response)	20	1,0E-31
Response to virus	14	3,5E-23
Negative regulation of the viral genome	10	3,2E-18

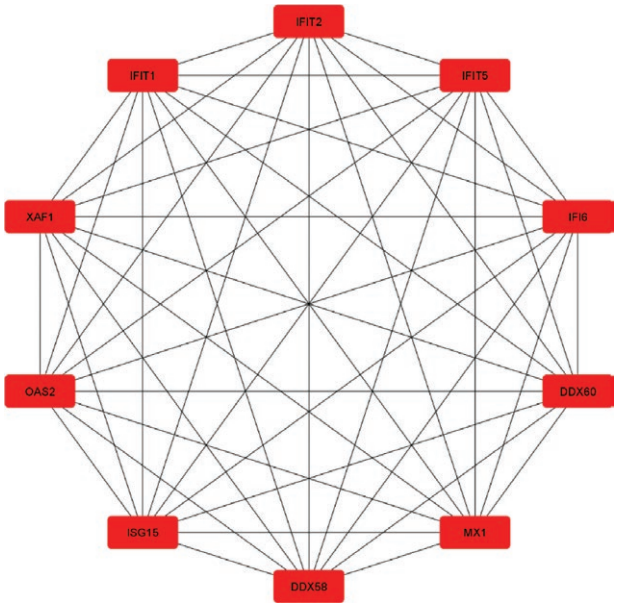


Figure 1. Topologic analysis displaying the Interferon Signature.

Conclusion: We identified DEGs through bioinformatic and functional enrichment analysis. 10 genes appeared in different datasets, while 21 were listed as their co-expressed pairs. These genes play a fundamental role in the processes of Defense response to virus, Response to virus and Negative regulation of the viral genome replication. Most of them belong to the type I IFN signature. An in vivo analysis in patients with primary SS is needed to validate these genes as possible diagnostic biomarkers and even possible therapeutic targets.

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Rheumatoid arthritis - non biologic treatment and small molecules

POS0822

DOES CONCOMITANT/NON-CONCOMITANT USE OF MTX WITH BIOLOGICS AND JAK INHIBITORS AFFECT ULTRASOUND FINDING OF INTRA-ARTICULAR SYNOVITIS?

Keywords: Ultrasound, Disease-modifying drugs (DMARDs), bDMARD

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Background: Biological disease-modifying antirheumatic drugs (bDMARDs) and janus kinase inhibitors (JAKi) are generally more effective combined with methotrexate (MTX) in patients with rheumatoid arthritis (RA). However, in clinical practice, bDMARDs/JAKi is sometimes used without MTX for such as elderly patients with poor renal function. To date, there are few reports evaluating ultrasound finding of intra-articular synovitis in patients with RA treated bDMARDs/JAKi with or without MTX.

Objectives: Ultrasound finding of intra-articular synovitis in patients with RA treated bDMARDs/JAKi with or without MTX was compared by using propensity score matching.

Methods: A total of 750 RA patients who underwent ultrasound examination were included. Ultrasond examination was performed at the of bilateral first to fifth metacarpophalangeal (MCP) joints, first interphalangeal (IP) and second to fifth proximal interphalangeal (PIP) joints, wrist joints (three part of radial, medial and ulnar) and first to fifth metatarsophalangeal (MTP) joints. Of all 750 RA patients, 517 RA patients (68.9%) who treated bDMARDs/JAKi were divided into with or without MTX. Then, patients were matched using the propensity score adjusted for age, sex, duration of RA, disease activity (CDAI), CRP level, and MMP-3 level. The total gray scale (GS) and power Doppler (PD) score (GSUS/ PDUS) were compared between bDMARDs/JAKi treated patients without and with MTX.

Results: There were 159 (30.8%) patients without MTX and 358 (69.2%) patients with MTX. The 151 patients in each group were matched. The mean MTX dose of bDMARDs/JAKi with MTX group was 8.8±3.5 mg/week. Patients' characteristic of bDMARDs/JAKi without MTX and bDMARDs/JAKi with MTX were shown in Table 1. Ultrasound synovial findings were significantly suppressed in the MTX combined group, GSUS 11.6 ± 11.8 vs 8.5 ± 8.0 (p = 0.009) and PDUS 8.3 ± 9.9 vs 5.5 ± 6.2 (p = 0.004). Moreover, US findings were compared in TNF user, non-TNF user and JAKi user. Notably, ultrasound findings were worse in non-TNF inhibitor users without MTX.

Table 1. Patients' characteristic of bDMARDs/JAKi without MTX and bDMARDs/JAKi with MTX.

	bDMARDs/JAKi without MTX (n=151)	bDMARDs/JAKi with MTX (n=151)	p value
Age, y	70.2±10.8	68.4±12.8	0.186
Female, %	82.1	77.5	0.390
BMI, kg/m2	21.9±3.4	22.7±3.4	0.029
Disease duration, y	16.7±11.6	16.2±13.3	0.756
RF+, %	91.4	90.1	0.843
CCP+, %	87.3	85.4	0.728
DAS28 ESR	3.2±1.3	3.3±1.5	0.393
DAS28 CRP	2.8±1.2	2.8±1.2	0.949
SDAI	11.9±10.5	11.2±10.7	0.552
CDAI	11.7±10.4	10.9±10.5	0.499
HAQ	0.76±0.72	0.80±0.87	0.645
ESR mm/h	16.1±19.3	21.3±21.5	0.028
CRP, mg/dL	0.18±0.45	0.26±0.71	0.204
MMP-3, ng/mL	128.0±160.1	114.1±184.9	0.488

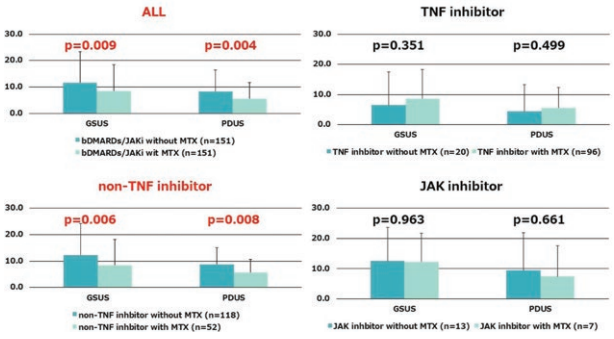


Figure 1. Ultrasound findings of bDMARDs/JAKi without MTX and bDMARDs/JAKi with MTX.

Conclusion: Ultrasound synovial findings in patients with bDMARDs/JAKi was more suppressed with MTX. It was considered necessary to keep in mind that synovitis may persist in patients who are not concomitant with MTX and are using non-TNF inhibitors.

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POS0823 UPTAKE OF INFLIXIMAB BIOSIMILARS AMONG U.S. RHEUMATOLOGY PRACTICES THROUGH 2022

Keywords: Registries, bDMARD, Epidemiology

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Background: The first infliximab biosimilar (infliximab-dybb) entered the U.S. market in 2016 and two additional products are now available (infliximab-axxq and infliximab-abda). Biosimilars have significant potential to slow drug spending; however, biosimilar uptake in the U.S. has lagged. Little is known about the impact of additional infliximab biosimilar approvals on market penetration or about patterns of use among rheumatologists.

Objectives: We used the national RISE registry 1) to examine uptake of infliximab biosimilars between 2016 and 2022 and 2) to study physician prescribing of these drugs. For the latter, we analyzed patterns of biosimilar drug use across a national sample of practices and analyzed characteristics of patients who were prescribed biosimilars vs. bio-originator infliximab.

Methods: Data from RISE, a national registry that includes electronic health records from one-third of U.S. rheumatology practices, was used. All bio-originator or biosimilar infliximab administrations (of any dose) between April 2016 and March 2022 were analyzed. We included patients 18 years or older who had at least one visit with a rheumatologist; all infliximab bio-originator or biosimilar users, regardless of diagnosis, were included. To assess the uptake of biosimilar infliximab, we examined the proportion of patients using each formulation (infliximab, infliximab-dybb, infliximab-abda and infliximab-axxq) in 2-month intervals during the study period. Patients were included in multiple time windows if they received different products during the study period. Next, we examined practice-level uptake of biosimilars among practices with ≥ 20 new infliximab users after 2019. Finally, we examined the characteristics of patients who were prescribed biosimilars. For this analysis, we calculated standardized mean differences (SMDs) to permit comparisons of the characteristics of users of bio-originator infliximab and each biosimilar. In cases where more than one infliximab product was prescribed, patients were classified based on their most recent infliximab prescription.

Results: During the study period, 32,916 individuals used bio-originator infliximab, 3,999 used infliximab-dybb, 1,369 used infliximab-abda, and 1,099 used infliximab-axxq. **Figure 1** demonstrates that uptake of biosimilar infliximab formulations remained below 20% and rose only minimally with the introduction of new biosimilar formulations in 2017 and 2020. Among 102 rheumatology practices with ≥ 20 new infliximab users, we observed significant variability in biosimilar use. 16.6% of practices had no patients on biosimilars, 27.4% had between one and ten percent of patients on biosimilars; only 15.6% had more than half of patients on biosimilars. SMDs for age, sex, race and ethnicity, insurance, region, and rheumatic disease diagnosis were all ≤0.5, indicating only small differences in patient characteristics across different formulation groups when comparing bio-originator infliximab to biosimilar versions.

Conclusion: Uptake of biosimilar infliximab drugs has been slow and minimally impacted by the introduction of additional biosimilar formulations in the U.S over the last six years. Only a small percentage of rheumatology practices use biosimilars for most patients, and a substantial proportion do not use biosimilars at all. We noted only small differences in patient characteristics between bio-originator and biosimilar infliximab users, suggesting that patient demographic characteristics, geographical region, diagnosis and insurance are not major drivers of prescribing differences. These findings suggest that in the absence of mandatory switching policies or other incentives, the U.S. has largely failed to achieve a robust biosimilars market, stymieing efforts to increase competition and reduce cost.

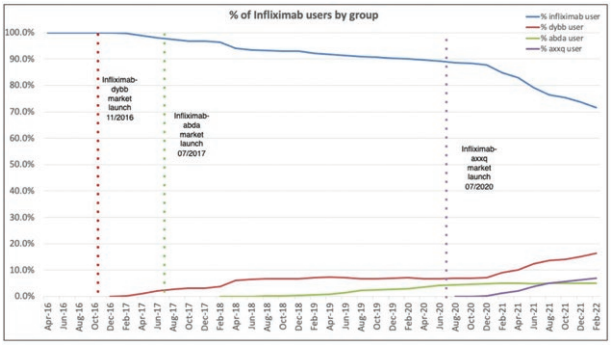


Figure 1. Proportion of patients in the RISE registry using infliximab bio-originator or biosimilars between 2016 and 2022.

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POS0824 CARDIOVASCULAR (CV) AND MALIGNANCY EVENTS IN THE FILGOTINIB (FIL) RHEUMATOID ARTHRITIS (RA) CLINICAL DEVELOPMENT PROGRAM UP TO 8.3 YEARS

Keywords: Safety, Targeted synthetic drugs, Rheumatoid arthritis

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Background: FIL is a Janus kinase (JAK) 1 preferential inhibitor for the treatment of RA. Data from the ORAL Surveillance post-marketing study (NCT02092467) suggest that in patients with active RA aged ≥50 years with ≥1 CV risk factor, the risks of cancer and major adverse cardiovascular events (MACE) are higher with the pan-JAK inhibitor tofacitinib vs tumor necrosis factor inhibitors, with higher rates in those aged ≥65 vs <65 years.[1]

Objectives: To assess the incidence of malignancies excluding non-melanoma skin cancer (NMSC), NMSC, MACE and venous thromboembolism (VTE) in patients treated with FIL 200 mg (FIL200) and FIL 100 mg (FIL100) in RA clinical trials.

Methods: Data were pooled from patients treated with FIL200 or FIL100 from DARWIN 1–3 (NCT01888874, NCT01894516, NCT02065700) and FINCH 1–4 (NCT02889796, NCT02873936, NCT02886728, NCT03025308). Data cuts used for the ongoing DARWIN 3 and FINCH 4 studies were May 2, 2022, and May 6, 2022, respectively. Exposure-adjusted incidence rates (EAIRs) per 100 patient-years of exposure (PYE) were calculated for MACE, VTEs, malignancies

excluding NMSC, NMSC and treatment-emergent adverse events (TEAEs) leading to death, according to FIL dose (200 vs 100 mg) and age (<65 vs ≥65 years); no statistical testing was performed, so all differences are numerical. MACE and VTE were adjudicated by an independent committee; the cutoff for adjudication was April 3, 2022.

Results: Overall, 3691 patients were treated with FIL for a total of 12,541 PYEs. Median (max) PYE was 3.8 (8.3) years for FIL200 and 3.3 (7.8) years for FIL100. Baseline characteristics are shown in the **Table 1**. A greater proportion of those aged ≥65 years vs <65 years had a CV medical history in both the FIL200 (75.7% vs 36.1%) and FIL100 (71.8% vs 40.9%) groups. Overall EAIRs (95% confidence interval [CI]) were 0.40 (0.3, 0.5) for MACE, 0.19 (0.1, 0.3) for VTEs, 0.69 (0.6, 0.9) for malignancy excluding NMSC, 0.29 (0.2, 0.4) for NMSC and 0.65 (0.5, 0.8) for TEAEs leading to death. EAIRs of MACE and VTE were higher in patients aged ≥65 vs <65 years but were generally similar for FIL200 and FIL100 within each age group (**Figure 1**). EAIRs of malignancies, NMSC and TEAEs leading to death were also higher in the ≥65- vs <65-year group. Within the ≥65-year group, EAIRs (95% CI) of these events were numerically higher in the FIL200 vs FIL100 group: 2.0 (1.3, 2.9) vs 0.99 (0.5, 1.9) for malignancies, 1.38 (0.8, 2.2) vs 0.44 (0.1, 1.1) for NMSC, and 1.59 (1.0, 2.5) vs 1.20 (0.6, 2.2) for TEAEs leading to death, respectively.

Conclusion: Rates of MACE and VTE in FIL-treated patients were low and similar for FIL200 and FIL100. There was a higher proportion of patients aged ≥65 years vs <65 years with a CV medical history. In patients aged ≥65 years, EAIRs of malignancies, NMSC and TEAEs leading to death were higher with FIL200 vs FIL100, although CIs overlapped.

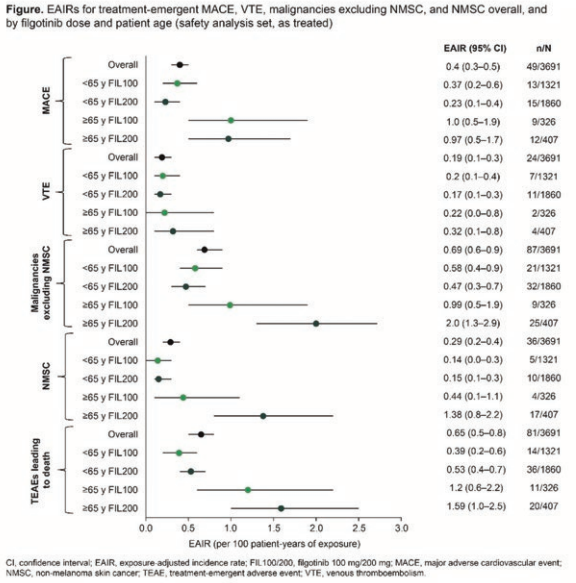
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Table 1. Baseline characteristics

	FIL200		FIL100	
	<65 y (n=1860)	≥65 y (n=407)	<65 y (n=1321)	≥65 y (n=326)
Age, y, mean (SD)	48.8 (10.7)	70.0 (4.4)	49.0 (10.5)	70.2 (4.5)
Female, n (%)	1506 (81.0)	322 (79.1)	1075 (81.4)	244 (74.8)
BMI, kg/m^2, mean (SD)	27.5 (6.3)	28.1 (5.9)	27.7 (6.4)	27.2 (5.1)
Creatinine clearance, mL/min, mean (SD)	122 (37.4)	84 (23.4)	122 (38.1)	83 (22.5)
CRP, mg/L, mean (SD)	19.0 (24.3)	18.4 (25.2)	18.9 (25.9)	17.2 (24.7)
Current smoker, n (%)*	207 (14.4)	37 (10.9)	165 (15.3)	28 (9.7)
CV family history, n (%)†	43 (3.0)	10 (2.9)	47 (4.3)	12 (4.2)
Any CV medical history, n (%)	672 (36.1)	308 (75.7)	540 (40.9)	234 (71.8)
Current alcohol use, n (%)*	296 (20.6)	78 (22.9)	213 (19.7)	54 (18.7)

*FIL200 <65 y: n=1436, ≥65 y: n=340; FIL100 <65 y: n=1081, ≥65 y: n=289.†FIL200 <65 y: n=1434, ≥65 y: n=339; FIL100 <65 y: n=1081, ≥65 y: n=289.BMI, body mass index; CRP, C-reactive protein; CV, cardiovascular; FIL100/200, filgotinib 100 mg/200 mg; SD, standard deviation.



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POS0825

CANCER RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH JANUS KINASE INHIBITORS: A NATIONWIDE DANISH REGISTER-BASED COHORT STUDY

Keywords: Targeted synthetic drugs, Malignancy, Real-world evidence

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Background: Concerns regarding the risk of cancer with janus kinase inhibitor (JAKi) use in patients with rheumatoid arthritis (RA) escalated after the release of results from Pfizer's clinical trial, *ORAL Surveillance*.[1] The trial showed increased risks of major adverse cardiovascular events and cancer in tofacitinib compared with tumour necrosis factor inhibitor recipients. Precautionary considerations on JAKi use in high-risk subsets of patients with RA have since been issued by the European Medicines Agency.

Objectives: We aimed to investigate the risk of first primary cancer in patients with RA treated JAKi (tofacitinib and baricitinib) compared with those who received biologic disease-modifying anti-rheumatic drugs (bDMARDs) in a real-world setting.
Methods: We performed an observational cohort study using the nationwide registers in Denmark. Patients with RA aged 18+ years, without a previous cancer diagnosis, and who initiated treatment with JAKi or bDMARDs from 1 January 2017 to 31 December 2020 were identified in the Danish Rheumatology Quality Register (DANBIO) and followed for any cancer (except non-melanoma skin cancer). We applied inverse probability of treatment weighting (IPTW) to account for covariate differences between treatment groups. IPTW-generated weights were used with cause-specific Cox (CSC) models to calculate hazard ratios (HRs) for cancer incidence in JAKi-treated compared with bDMARD-treated patients with RA. Multiple subgroup and sensitivity analyses were performed.
Results: We identified 875 and 4247 RA patients treated with JAKi and bDMARDs, respectively. The JAKi group contributed with 1315 person years (PYRS) and 19 cancers, while the bDMARD group contributed with 8597 PYRS and 111 cancers. The corresponding crude incidence rates per 1000 PYRS for cancer were 14.4 (JAKi) and 12.9 (bDMARD). Comparing the two groups using weighted CSC models, a HR of 1.41 (95%CI 0.76 to 2.37, 95% confidence intervals) was seen for JAKi- versus bDMARD-treated patients with RA.
Conclusion: JAKi treatment in real-world patients with RA was not associated with a statistically significant increased risk of first primary cancer compared with those who received bDMARDs. However, risk estimates were elevated in many analyses, and an excess risk of cancer with JAKi treatment cannot be ruled out. More studies investigating JAKi and cancer risk in patients with RA are highly warranted.
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Table 1. Number of patients, person years (PYRS), cancers, crude incidence rates (IR), and hazard ratios (HRs) for cancer by type of analysis, by choice of statistical model, and by groups of JAKi- and bDMARD-treated patients with rheumatoid arthritis

	N patients	N PYRS	N Cancers (except NMSC)	Crude IR (per 1000 years)	HR (95%CI)
JAKi vs bDMARD (all patients)					
JAKi group	875	1315	19	14.4	
bDMARD group	4247	8597	111	12.9	
IPTW + CSC [a]					1.41 (0.76 to 2.37)
CSC model 1 [b]					1.17 (0.72 to 1.91)
CSC model 2 [c]					1.37 (0.81 to 2.32)
Age 50+					
JAKi group [d]	653	-	≥15	18.3	
bDMARD group	3099	6274	103	16.4	
IPTW + CSC					1.37 (0.75 to 2.30)
CSC model 1					1.19 (0.72 to 1.97)
CSC model 2					1.40 (0.81 to 2.42)
Age 65+					
JAKi group	268	401	11	27.4	
bDMARD group	1364	2711	65	24.0	
IPTW + CSC					1.34 (0.55 to 2.81)
CSC model 1					1.20 (0.62 to 2.29)
CSC model 2					1.25 (0.61 to 2.56)

NotesJAKi: janus kinase inhibitors, bDMARDs: biological disease-modifying anti-rheumatic drugs, N: number of, 95%CI: 95% confidence intervals, NMSC: non-melanoma skin cancer, IPTW: inverse probability of treatment, CSC: cause-specific Cox proportional hazard regression with death as the competing risk.a: IPTW weights combined with CSC.b: CSC model 1 unweighted with age as underlying timescale and adjustment for sex.c: CSC model 2 as CSC model 1 but with adjustment for all covariates (not shown in this abstract) with no missing information. d: PYRS and N cancers not shown according to Danish data legislation on indirect anonymisation.

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POS0826

SAFETY PROFILE OF UPADACITINIB UP TO 6.5 YEARS OF EXPOSURE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Targeted synthetic drugs, Safety

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Background: Upadacitinib (UPA) is an oral JAK inhibitor that has demonstrated safety and efficacy in patients (pts) with moderate-to-severe active RA in the phase 3 SELECT clinical program.[1–6]
Objectives: To describe the long-term integrated safety profile of UPA relative to active comparators in pts with RA from the SELECT clinical program through the cutoff date of 15 August 2022.
Methods: Pooled safety data were analyzed from 6 randomized controlled trials evaluating UPA in RA.[1–6] Treatment-emergent adverse events (TEAEs) and AEs of special interest were summarized for the following groups: pooled UPA 15 mg once daily (QD; UPA15, 6 trials), MTX (1 trial), and adalimumab (ADA) 40 mg every other week (EOW; 1 trial). TEAEs were defined as AEs with an onset after the first dose and ≤ 30 days (UPA and MTX) or ≤ 70 days (ADA) after the last dose of study drug and reported as exposure-adjusted event rates (EAERs) per 100 patient-years (PY; E/100 PY). The standardized mortality ratio (SMR) was estimated for the general population using World Health Organization country-age-gender specific mortality rates through 2016.
Results: 3209 pts received ≥ 1 dose of UPA15 with 10 782.7 PY of exposure. EAERs of AEs, serious AEs (SAEs), and AEs leading to discontinuation on UPA15 were comparable to MTX and ADA (**Table 1**). COVID-19 pneumonia was the most common SAE with UPA15 (0.7 E/100 PY). Rates of serious infections were similar between UPA15 and ADA but higher compared with MTX (**Figure 1**). Herpes zoster (HZ) rates were higher with UPA15 vs MTX and ADA. Most HZ cases with UPA15 were non-serious (95%) and affected a single dermatome (75%) or unilateral multiple dermatomes (16%); 8% of cases were reported as disseminated and none involved the central nervous system. Creatine phosphokinase elevations were transient and more common with UPA15 than MTX or ADA. Anemia and neutropenia rates were similar between UPA15 and ADA. Most hepatic disorders were mild or moderate transaminase elevations. Treatment discontinuation due to these lab events was rare (≤ 0.1 E/100 PY). Similar rates of adjudicated MACE, adjudicated VTE, and malignancy (excluding non-melanoma skin cancer [NMSC]) were observed across treatment groups. The rate of NMSC was numerically higher with UPA15 vs ADA; no cases occurred with MTX. SMR analysis indicated that the mortality rate among pts with RA treated with UPA15 was not higher than what would be expected among the general population (SMR [95% CI]: 0.67 [0.52, 0.86] including COVID-19 deaths; 0.41 [0.29, 0.56] excluding COVID-19 deaths).
Conclusion: The integrated safety profile of UPA in pts with RA remained consistent with previous findings,[7] with no new safety risks identified up to 6.5 years of exposure. Similar rates of AEs of special interest were observed for UPA15 and ADA, except for higher rates of HZ, CPK elevations, and NMSC with UPA.

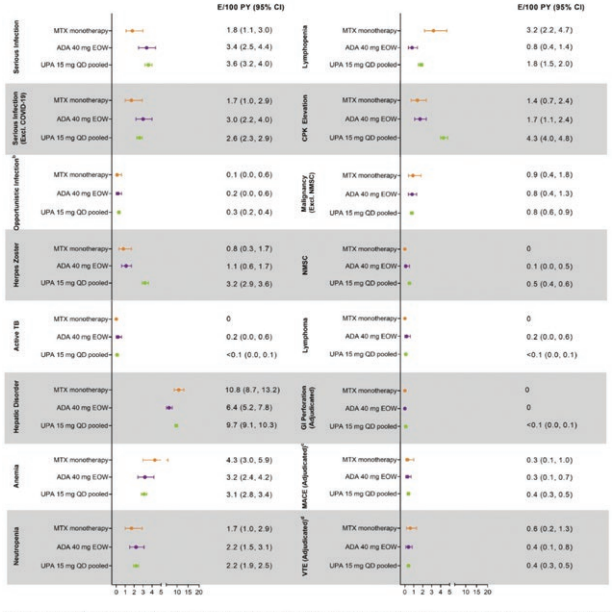
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Table 1. Treatment-emergent Adverse Events in Patients Treated with UPA, ADA, and MTX

	UPA 15 mg QD	ADA 40 mg EOW	MTX
n (number of subjects)	3209	579	314
Exposure			
Total PY	10 782.7	1573.2	865.1
Mean (SD), years	3.4 (1.9)	2.7 (2.3)	2.8 (2.0)
Median (range), years	4.0 (0.0, 6.6)	2.2 (0.0, 6.6)	2.6 (0.0, 5.4)
E/100 PY (95% CI)			
Any AE	206.1 (203.4, 208.8)	195.5 (188.6, 202.5)	203.2 (193.8, 212.9)
Any SAE	12.8 (12.2, 13.5)	13.5 (11.7, 15.4)	9.0 (7.1, 11.3)
Any AE leading to study drug discontinuation	4.8 (4.4, 5.2)	5.5 (4.4, 6.8)	5.5 (4.1, 7.4)
Any COVID-19-related AE	4.6 (4.2, 5.0)	4.7 (3.7, 5.9)	2.4 (1.5, 3.7)
Deaths[a]	0.8 (0.7, 1.0)	1.0 (0.5, 1.6)	0.9 (0.4, 1.8)

ADA, adalimumab; E/100 PY, exposure-adjusted event rates per 100 patient-years; QD, once daily; SAE, serious AE; UPA, upadacitinib.[a]Includes treatment-emergent, non-treatment-emergent, and COVID-related deaths.

Figure. Treatment-emergent Adverse Events of Special Interest in Patients Treated with UPA, ADA, and MTX[a]



ADA, adalimumab; CI, confidence interval; CPK, creatine phosphokinase; E/100 PY, exposure-adjusted event rates per 100 patient-years; EOW, every other week; GI, gastrointestinal; NMSC, non-melanoma skin cancer; QD, once daily; TB, tuberculosis; UPA, upadacitinib.
MTX: n = 314, PY = 865.1; ADA 40 mg EOW: n = 579, PY = 1573.2; UPA 15 mg pooled: n = 3209, PY = 10 782.7.
[a]Patients who switched from placebo, ADA, or MTX to UPA were included in the UPA 15 mg QD group from the start of UPA, while those who switched from UPA to ADA were included in the ADA group from the start of ADA and were censored at the time of switch. MTX monotherapy was censored at the time of rescue to combination therapy (addition of UPA).
[b]Opportunistic infections excluding TB and herpes zoster.
[c]MACE was defined as cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke.
[d]VTE was defined as deep vein thrombosis and pulmonary embolism.

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POS0827

CLINICAL OUTCOMES OF PATIENTS WITH RHEUMATOID ARTHRITIS WHO DISCONTINUED TOFACITINIB OR TUMOUR NECROSIS FACTOR INHIBITORS: RESULTS FROM ORAL SURVEILLANCE

Keywords: Targeted synthetic drugs, Safety, Rheumatoid arthritis

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Background: Switching or discontinuing therapy may occur in patients (pts) with rheumatoid arthritis (RA) with an inadequate response/intolerance to treatment. In ORAL Surveillance, a post-authorisation safety study of tofacitinib vs tumour necrosis factor inhibitors (TNFi) in pts with RA despite methotrexate aged ≥50 years with ≥1 additional cardiovascular risk factor,[1] pts could discontinue the assigned study drug and switch to local standard of care (SOC) treatment and, in contrast to previous randomised controlled trials, were encouraged to remain in the study.
Objectives: To assess efficacy/safety in the SOC period in pts who discontinued study drug and started SOC treatment.
Methods: This post hoc analysis included randomised pts from ORAL Surveillance (NCT02092467) who received ≥1 dose of study drug (tofacitinib 5 or 10 mg twice daily [BID], or TNFi) and initiated SOC treatment per-protocol after discontinuing study drug. SOC treatment could include disease-modifying antirheumatic drugs (DMARDs; biologic, targeted synthetic, or conventional synthetic [cs]), or glucocorticoids. Efficacy outcomes included mean observed and change from randomisation/SOC baseline (BL; Δ) in Simplified Disease Activity Index (SDAI) over time. Adverse events (AEs) and serious AEs (SAEs) were reported; incidence rates (IRs; pts with events/100 pt-years [PY]) were estimated for AEs of

special interest (AESI). Data were analysed for the periods in which pts who discontinued study drug received 1) tofacitinib or TNFi (randomised period) and 2) SOC treatment (SOC period). Pts were analysed in their original treatment group (ex-tofacitinib 5/10 mg BID, or ex-TNFi). Analyses were descriptive.

Results: Of 4362 randomised and treated pts, 718 (16.5%) stopped study drug (50.7, 59.3 and 47.8% due to AEs; 15.1, 5.8 and 21.9% due to insufficient clinical response for tofacitinib 5 mg BID, 10 mg BID and TNFi, respectively); most received csDMARDs only in the SOC period (73.1–79.6% across groups). In general, BL characteristics in pts who switched to SOC treatment were numerically similar across groups. Mean duration of randomised and SOC periods was 21.9–26.0 and 15.0–18.6 months, respectively. ΔSDAI over time was similar across groups in the randomised period (data not shown) with modest improvements in the SOC period (Figure 1) and with SDAI score generally reflecting moderate disease activity (data not shown). In general, AE and SAE rates were similar across groups but numerically higher in the randomised vs SOC period (data not shown). AESI rates were generally similar across groups in the SOC period (Table 1).

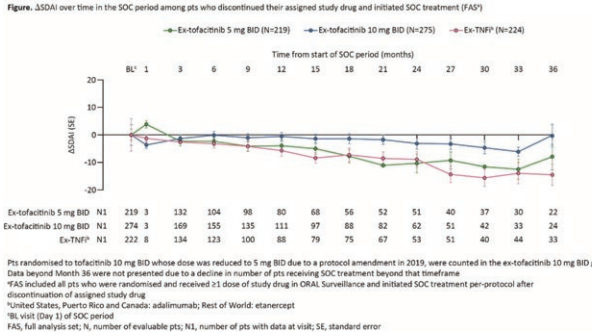


Table 1. IRs (95% CIs) of AESI in the SOC period (SAS[a], total On-SOC time)

	Ex-tofacitinib 5 mg BID (N=219)	Ex-tofacitinib 10 mg BID (N=275)	Ex-TNFi[b] (N=224)
Major adverse cardiovascular events[c]			
n (%), PY	3 (1.4), 285.7	8 (2.9), 394.8	5 (2.2), 357.5
IR (95% CI)	1.1 (0.2, 3.1)	2.0 (0.9, 4.0)	1.4 (0.5, 3.3)
Malignancies excluding NMSC[c]			
n (%), PY	4 (1.8), 286.1	9 (3.3), 391.7	4 (1.8), 359.3
IR (95% CI)	1.4 (0.4, 3.6)	2.3 (1.1, 4.4)	1.1 (0.3, 2.9)
NMSC[c]			
n (%), PY	1 (0.5), 286.6	2 (0.7), 395.4	2 (0.9), 357.7
IR (95% CI)	0.4 (0.0, 1.9)	0.5 (0.1, 1.8)	0.6 (0.1, 2.0)
Venous thromboembolism[c]			
n (%), PY	1 (0.5), 287.1	2 (0.7), 395.4	1 (0.5), 361.1
IR (95% CI)	0.4 (0.0, 1.9)	0.5 (0.1, 1.8)	0.3 (0.0, 1.5)
Serious infections			
n (%), PY	16 (7.3), 276.2	15 (5.5), 375.6	17 (7.6), 332.4
IR (95% CI)	5.8 (3.3, 9.4)	4.0 (2.2, 6.6)	5.1 (3.0, 8.2)
All-cause deaths			
n (%), PY	7 (3.2), 288.8	13 (4.7), 396.3	8 (3.6), 361.2
IR (95% CI)	2.4 (1.0, 5.0)	3.3 (1.8, 5.6)	2.2 (1.0, 4.4)

[a]Same as FAS[b]United States, Puerto Rico and Canada: adalimumab; Rest of World: etanercept[c]AdjudicatedCI, confidence interval; n, number of pts with event; NMSC, non-melanoma skin cancer; SAS, safety analysis set

Conclusion: In ORAL Surveillance, pts with RA who discontinued tofacitinib or TNFi and switched to SOC treatment had modest improvements in efficacy over time without increased risk of AEs. Limitations included that this analysis was post hoc.

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POS0828

IMPACT OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE RISK IN PATIENTS TREATED WITH UPADACITINIB VERSUS COMPARATORS: POST HOC ANALYSIS OF THE SELECT RHEUMATOID ARTHRITIS PROGRAM

Keywords: Safety, Targeted synthetic drugs, Cardiovascular disease

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Background: In ORAL Surveillance, a post-approval safety study conducted in RA patients aged ≥50 years with ≥1 cardiovascular (CV) risk factor, non-inferiority was not shown for MACE and malignancy (excluding nonmelanoma skin cancer) for tofacitinib versus TNF inhibitor (TNFi) therapy.[1] A post hoc analysis of the ORAL Surveillance data suggested that patients with a history of atherosclerotic cardiovascular disease (ASCVD) were most at risk relative to TNFi.[2] Whether these findings are characteristic of the entire JAK inhibitor class is unclear.

Objectives: To evaluate the impact of baseline ASCVD risk on the incidence of MACE with upadacitinib (UPA) versus TNFi and MTX in an RA population similar to ORAL Surveillance from the SELECT RA clinical program.

Methods: Post hoc analysis of adjudicated MACE was performed in two patient populations pooled across six SELECT phase 3 studies: the overall population and the higher CV risk subset (patients aged ≥50 years with ≥1 CV risk factor). Patients received UPA 15 mg once daily (with or without conventional synthetic DMARDs), adalimumab (ADA) 40 mg in combination with MTX, or MTX monotherapy. CV risk factors used to identify the higher-risk patients included prior CV event, hypertension, diabetes mellitus, current or former tobacco/nicotine use, and baseline HDL-C levels <40 mg/dL. Patients were further stratified based on medical history of ASCVD, which included coronary artery disease and other relevant events (e.g., arteriosclerosis, ischemic stroke, and carotid artery disease). In patients without a history of ASCVD, 10-year ASCVD risk categories were calculated with a 1.5 multiplier applied.[3] Exposure-adjusted incidence rates (EAIRs) per 100 patient-years were summarized based on the treatment received; 95% CIs were determined based on the exact method for the Poisson mean.

Results: Of 4102 enrolled patients (UPA 15 mg, n=3209; ADA, n=579; MTX monotherapy, n=314), approximately half were aged ≥50 years with ≥1 CV risk factor (n=2199 total; UPA 15 mg, n=1717; ADA, n=320; MTX monotherapy, n=162). In the overall SELECT population, EAIRs of adjudicated MACE were 0.3, 0.3, and 0.2 n/100 PY for UPA, ADA, and MTX groups, respectively (**Figure 1**). Rates of MACE were higher in UPA-treated patients with a history of ASCVD (1.9 n/100 PY) compared to those without a history of ASCVD (0.2 n/100 PY) in the overall population; no occurrences of MACE were reported with ADA or MTX in patients with a medical history of ASCVD, possibly due to the limited patient numbers in these groups. Among patients with no history of ASCVD in the overall population, higher rates of MACE were observed for patients in the high or intermediate 10-year ASCVD risk categories versus the low or borderline risk category, irrespective of treatment. In the higher CV risk subset of the SELECT population, rates of MACE were numerically higher than the overall population but were similar between treatment groups (0.6, 0.5, and 0.5 n/100 PY for UPA, ADA, and MTX groups, respectively). Consistent with the overall population, the incidence of MACE was higher among UPA-treated patients with a history of ASCVD relative to those without a history of ASCVD. The rates of MACE in the higher-risk population were also generally similar across treatment groups for patients within each of the different 10-year ASCVD risk groups.

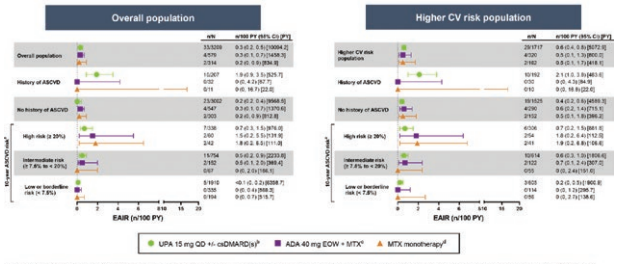
Conclusion: In this post hoc analysis, higher rates of MACE were observed in UPA-treated patients with a history of ASCVD versus those with no history of ASCVD. In both the overall SELECT population and the higher CV risk subset, rates of MACE were generally comparable between UPA and ADA in the

different ASCVD risk categories. However, given the low sample size and limited patient-years of exposure in ADA and MTX treatment groups, results should be interpreted with caution.

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Figure. Exposure-adjusted incidence of MACE by history of atherosclerotic cardiovascular disease and 10-year predicted risk assessments



ADA, adalimumab; ASCVD, atherosclerotic cardiovascular disease; csDMARD, conventional synthetic DMARD; EAIR, exposure-adjusted incidence rate; EOW, every other week; MTX, methotrexate; QD, once daily; UPA, upadacitinib.
[a]In patients without a history of ASCVD, 10-year ASCVD risk calculations were derived as previously described (Golf DC, et al. *J Am Coll Cardiol*. 2014; 63:2935-59), with a 1.5 multiplier applied (Agca R, et al. *Ann Rheum Dis*. 2017;76:17-28).
[b]Upadacitinib data were from patients with any upadacitinib 15 mg exposure, including those randomized to upadacitinib 15 mg in all six trials and those who switched from other randomization groups (i.e., placebo, adalimumab, or abatacept) to upadacitinib.
[c]Adalimumab data were from patients enrolled in SELECT-COMPARE who were initially randomized to adalimumab or rescued to adalimumab from upadacitinib.
[d]MTX monotherapy data were from patients starting MTX monotherapy in SELECT-EARLY, censored at the time of rescue to upadacitinib.
The cutoff date for data analysis was February 15, 2022.

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POS0829

SAFETY AND EFFICACY OF FILGOTINIB: AN UPDATE FROM THE DARWIN 3 PHASE 2 LONG-TERM EXTENSION WITH A MAXIMUM OF 8.2 YEARS OF EXPOSURE

Keywords: Rheumatoid arthritis, Safety

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Background: DARWIN 3 (NCT02065700) is a long-term extension (LTE) study assessing the safety and efficacy of filgotinib (FIL) in patients with rheumatoid arthritis (RA) and an inadequate response to methotrexate (MTX).[1] In the DARWIN 1 (NCT01888874) and DARWIN 2 (NCT01894516) parent studies, patients received FIL in combination with MTX or FIL monotherapy, respectively.

Objectives: To provide an update on the safety and efficacy of FIL 200 mg (FIL200) in patients with RA, with or without MTX, with a maximum of 8.2 years of exposure.

Methods: Patients completing the DARWIN 1 (FIL + MTX) and DARWIN 2 (FIL monotherapy) phase 2 studies could enter DARWIN 3, receiving FIL200. The proportion of patients experiencing treatment-emergent adverse events (TEAEs) were reported using the safety analysis set, comprising data from both the parent and LTE studies. Efficacy was assessed from LTE baseline using the American College of Rheumatology (ACR) 20/50/70 improvement criteria and Disease Activity Score in 28 joints–C-reactive protein (DAS28-CRP), up to 264 weeks. Low disease activity and remission were defined as DAS28-CRP ≤3.2 and <2.6, respectively.

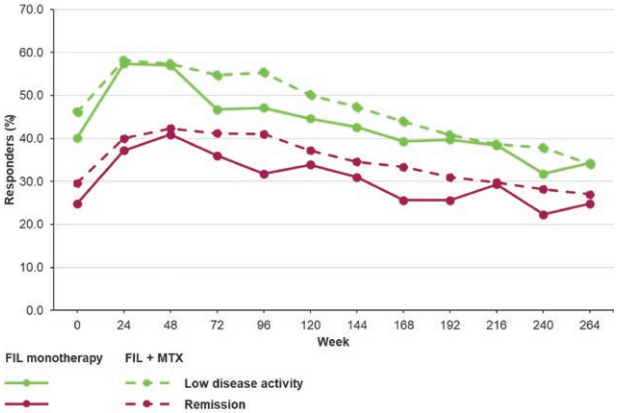
Results: In total, 739 patients were enrolled in DARWIN 3. Mean (standard deviation; SD) FIL exposure was 4.89 (2.72) years in the FIL + MTX group and 4.78 (2.79) years in the FIL monotherapy group. In the FIL + MTX vs FIL monotherapy groups, TEAEs were reported for 90.9% and 92.1% of patients, respectively (**Table 1**). The most common TEAE was infection. In both treatment groups, 8 patients had a TEAE leading to death (1.6% and 3.3%, respectively). Exposure-adjusted incidence rates, censored at time of first event for major adverse cardiovascular event, venous thromboembolism, herpes zoster, infections, serious infections, non-melanoma skin cancer (NMSC), malignancies excluding NMSC, gastrointestinal perforations and TEAEs leading to death, will be reported. Through 5 years, ACR20/50/70 responses were maintained in 86.3%/66.7%/50.7% of the FIL + MTX group and 90.8%/74.8%/51.4% of the FIL monotherapy group, respectively (observed data). DAS28-CRP low disease activity and remission rates (non-responder imputation) at DARWIN 3 baseline were 46.1%/40.1% (FIL + MTX) and 29.6%/24.8% (FIL monotherapy) (**Figure 1**). At Week 264, the proportion of patients achieving low disease activity and remission were 34.0%/34.3% (FIL + MTX) and 27.0%/24.8% (FIL monotherapy).

Conclusion: With a maximum of 8.2 years of exposure in patients with RA, the FIL safety profile is similar between the background MTX and monotherapy treatment arms. Both arms show sustained efficacy over time.

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Figure. Proportion of patients achieving DAS28-CRP low disease activity and remission, from LTE baseline to Week 264



N=497 (FIL + MTX); N=242 (FIL monotherapy). Non-responder imputation. Denominators are fixed for each timepoint.
DAS28-CRP, Disease Activity Score in 28 joints–C-reactive protein; FIL, filgotinib; LTE, long-term extension; MTX, methotrexate.

Table 1. TEAEs of interest

	FIL + MTX N=497	FIL monotherapy N=242
Any TEAE	452 (90.9)	223 (92.1)
MACE	4 (0.8)	3 (1.2)
VTE	3 (0.6)	0
Herpes zoster	30 (6.0)	14 (5.8)
Infections	317 (63.8)	140 (57.9)
Serious infections	28 (5.6)	19 (7.9)
NMSC	6 (1.2)	2 (0.8)
Malignancies excluding NMSC	12 (2.4)	8 (3.3)
GI perforations	1 (0.2)	0
TEAEs leading to death	8 (1.6)	8 (3.3)

Data are n (%).FIL, filgotinib; GI, gastrointestinal; MACE, major adverse cardiovascular event; MTX, methotrexate; NMSC, non-melanoma skin cancer; TEAE, treatment-emergent adverse event; VTE, venous thromboembolism.

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POS0830 BARICITINIB VERSUS TNF-INHIBITORS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO CSDMARDS: 12 WEEKS RESULTS OF A PRAGMATIC, MULTICENTER, OPEN LABEL, NONINFERIORITY TRIAL

Keywords: Randomized control trial, Targeted synthetic drugs, Real-world evidence

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Background: The EULAR guidelines for RA recommend that treatment should be aimed at reaching a predefined disease activity target (T2T). If this treatment target is not achieved with csDMARD, adding a TNFi or a JAK-inhibitor are advised options in patients with poor prognostic factor, obviously considering contraindications. While randomized clinical trials have provided relevant data on the relative efficacy and safety of TNFi and JAKi under ideal conditions, the extent to which such results can be generalized to real-life clinical practice conditions remains unclear.

Objectives: To demonstrate non-inferiority (NI) and, in case NI could be shown, subsequent superiority of a T2T strategy in which csDMARDs refractory RA patients are subsequently treated with baricitinib versus TNFi.

Methods: Biologic or targeted synthetic DMARD-naïve RA patients failing to respond to csDMARDs were eligible if they were pretreated according to T2T principles, had a disease duration <5 years and no contraindications to b/tsDMARD. All included patients were treated open label at the discretion of their attending rheumatologist with either TNFi (any type) or baricitinib. Patients were seen at baseline and 12-weekly until final follow-up (48 weeks). Full clinical assessment was performed at each visit. Self-report questionnaires, including PROMs, were collected as well. The primary endpoint was defined as NI of baricitinib versus TNFi in the proportion of patients achieving ACR50 response at week 12, with subsequent superiority testing in case non-inferiority was shown. For the primary efficacy analysis, the proportion of patients achieving ACR50 response were compared, using 95% confidence intervals calculated using the Wilson score method. The non-inferiority margin for baricitinib was set at -12%.

Results: 199 patients who received a first dose of either TNFi (102) or baricitinib (97) were included. Baseline characteristics were comparable between both groups (see Table 1). At 12 weeks, the lower bound of the 95% confidence interval for the difference in proportions of patients meeting the ACR50 response is to the right of zero in both the per-protocol and intention-to-treat analysis (see Figure 1). Hence, baricitinib was found to be non-inferior and statistically superior to TNFi in the analysis of the primary endpoint. Moreover, DAS28 remission (DAS28-CRP <0.6) was achieved in 74% of baricitinib patients compared with 46% of TNFi patients (p<0.001) at 12 weeks.

Conclusion: Baricitinib was found to be non-inferior and superior to TNFi in terms of ACR50 response at 12 weeks in real-world csDMARD refractory RA patients. Analysis of secondary endpoints, disease activity across other measurement points, PROMs, radiology, safety and costs is currently ongoing.

Table 1. Baseline characteristics

	TNFi	Baricitinib	p
	N=102	N=97	
Age	55.2 (13.4)	54.8 (12.0)	0.833
Gender			0.796
F	68 (66.7%)	62 (63.9%)	
M	34 (33.3%)	35 (36.1%)	
Smoking			0.963
never	38 (37.3%)	37 (38.9%)	
Stopped	39 (38.2%)	36 (37.9%)	
Yes	25 (24.5%)	22 (23.2%)	
BMI	27.5 (4.91)	26.5 (5.03)	0.178
Disease duration (years)	2.00 [1.00;3.00]	2.00 [1.00;3.00]	0.766
Erosions			0.537
No	71 (69.6%)	74 (76.3%)	
Unknown	12 (11.8%)	10 (10.3%)	
Yes	19 (18.6%)	13 (13.4%)	
CV			0.432
No	74 (72.5%)	76 (78.4%)	
Yes	28 (27.5%)	21 (21.6%)	
RF			0.576
Neg	33 (32.4%)	27 (27.8%)	
Pos	67 (65.7%)	66 (68.0%)	
Unknown	2 (1.96%)	4 (4.12%)	
ACCP			0.262
Neg	37 (36.3%)	27 (27.8%)	
Pos	65 (63.7%)	70 (72.2%)	
MTX			1
No	31 (30.4%)	30 (30.9%)	
Yes	71 (69.6%)	67 (69.1%)	
DAS28ESR	4.41 (1.06)	4.43 (1.14)	0.919
DAS28CRP	4.17 (1.02)	4.12 (1.07)	0.741
TJC28	4.00 [2.00;7.00]	4.00 [2.00;7.00]	0.662
SJC28	3.00 [1.00;5.00]	3.00 [2.00;4.00]	0.805
BSE	24.0 (19.7)	25.0 (22.1)	0.738
CRP	13.7 (19.1)	12.8 (17.6)	0.728
HAQ	12.2 (5.66)	10.9 (6.35)	0.13
SDAI	21.2 (8.97)	21.1 (9.00)	0.933

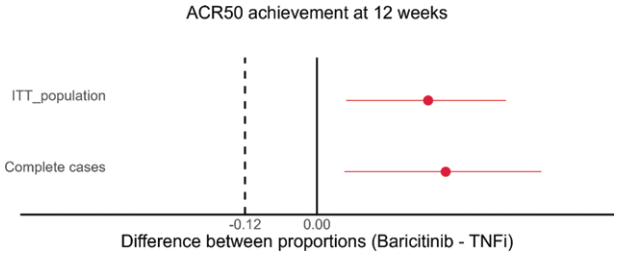


Figure 1.

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POS0831 MALIGNANCIES RISK IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB OR TNF INHIBITORS, A NATIONAL STUDY: RELATION STUDY

Keywords: Targeted synthetic drugs, Rheumatoid arthritis

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Background: Patients with IMID, and notably patients with rheumatoid arthritis RA, are at increased risk of cancer compared with the general population [1,2]. It is hence paramount to assess the impact of biological or targeted DMARD (e.g.., tofacitinib and TNFi) on the risk of cancer outcome in patients already at-risk, particularly in the context of ORAL Surveillance which showed a higher risk for malignancies (excluding nonmelanoma skin cancer, NMSC) with tofacitinib, in comparison with TNFI, in RA patients [3].
Objectives: To assess the impact of tofacitinib and TNFi on the risk of malignancies in patients with RA treated in real-world clinical practice.
Methods: The RELATION study is a retrospective observational cohort study using the French nationwide healthcare database (SNDS). Patients aged 18 years or older, affiliated to the national health insurance with a diagnosis of RA and initiating tofacitinib after November 1, 2017 or TNFi after January 1, 2010 (including adalimumab, etanercept, or other TNFi, without previous exposure to tofacitinib) were followed from treatment initiation to December 31, 2020. Patients with a previous history of a malignancy (excluding NMSC) in the 4 years preceding cohort entry were excluded. All malignancies events were defined by the first hospitalization for malignancy during follow-up. Comorbidities and traditional cardiovascular (CV) risk factors were identified using hospitalizations, procedures, or medication dispensing in the 4 years prior cohort entry. The unadjusted incidence rate (IR) of malignancies (excluding NMSC) was assessed in patients initiating either tofacitinib or a TNFi (with associated 95% confidence intervals (95% CI)). A 1:3 PS matching was conducted to balance the baseline characteristics of patients initiating tofacitinib and TNFi. Cox proportional hazards regression models were used to compare the risk of malignancy with tofacitinib vs TNFi during the follow-up period.
Results: Between 2010 and 2020, a total of 39,578 patients with RA were included in the study. Among these, 2,811 initiated tofacitinib and 36,767 initiated a TNFi (adalimumab: 10,621, etanercept: 16,512, other TNFi: 9,634). Patients had a mean age of 53 years at cohort entry, and 72% to 81% were women. Around 61% of the cohort had at least one CV risk factor (66.3%for tofacitinib compared to 60.9% for TNFi). The two major co-medications at treatment initiation in the two groups were methotrexate (60.9%) and corticosteroids (50.8%).
After PS matching, the tofacitinib cohort included 2,628 patients, and the TNFi cohort included 7,884 patients. Over a median follow-up period of 11.31 months (tofacitinib: 8.56 months, TNFi: 12.52 months), 15 incident malignancy events occurred in the tofacitinib group (IR: 5.89 (3.55–9.77) per 1,000 patient-year (PY)) and 135 occurred in the TNFi group (8.03 (6.78–9.50)). The risk of malignancies was similar with tofacitinib vs TNFi (adjusted HR 0.76 [95%CI 0.44, 1.32]; p=0.3347). Similar results were found for other (other than breast, melanoma, colorectal, lung cancer or lymphoma) active cancers (HR 0.97 [95% CI 0.50, 1.89]; p=0.9382). For other specific cancer types (cited above), the number of events was too low to perform these analyses.
Conclusion: In this large population-based study, tofacitinib was not associated with an increased risk of malignancies (excluding NMSC) in comparison with TNFI in patients with RA treated in real-world settings. Studies with longer follow-up durations may be necessary to understand the long-term implications of tofacitinib vs TNFi on the risk of malignancies.
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Disclosure of Interests: Jacques-Eric Gottenberg Consultant of: AbbVie, Bristol Myers Squibb, Galapagos, Gilead, Lilly, MSD, Novartis, Pfizer, Grant/research support from: Pfizer, Bristol Myers Squibb, Meriem Kessouri Shareholder of: Pfizer, Employee of: Pfizer, Jeremie Rudant Shareholder of: Pfizer, Employee of: Pfizer, Nada Assi Employee of: Heva, Fanny Raguideau Employee of: Heva, Julien Kirchgesner Speakers bureau: Pfizer, Consultant of: Gilead, Pfizer, Roche.
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POS0834 LONG-TERM EXTENSION STUDY OF THE SAFETY AND EFFICACY OF NEUROIMMUNE MODULATION USING A VAGUS NERVE STIMULATION DEVICE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Non-pharmacological interventions, Rheumatoid arthritis, Randomized control trial

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Background: The inflammatory reflex is a centrally integrated physiological mechanism whereby vagus nerve signaling regulates the production of proinflammatory cytokines that mediate systemic inflammation. The safety and efficacy of a neuroimmune modulation device were assessed in a first-in-human, double-blind pilot study in subjects with multi-drug refractory rheumatoid arthritis (RA). Previously reported data showed that vagus nerve stimulation (VNS) for 12 weeks using the neuroimmune modulation device, a miniature, leadless neurostimulator that is surgically implanted in the neck on the left vagus nerve, improved clinical outcomes, was safe and well-tolerated.[1] We now report 36-month long-term data from this pilot study.
Objectives: Determine the long-term safety and efficacy of neuroimmune modulation using a novel neuroimmune modulation device.
Methods: Subjects (N=14) with active RA and prior insufficient response to ≥2 biological or targeted synthetic (b/ts) DMARDs with ≥2 modes of action were implanted with the neuroimmune modulation device.[1] All subjects who completed Week 12 (N=14) were enrolled in an open-label, long-term extension study where subjects continued or if assigned to the sham group, began to receive treatment. Of these subjects, 11 completed 36 months of treatment as follows: VNS for 1 minute either once per day (QD, N=4) or four times per day (QID, N=3); subjects randomized to sham treatment during the first 12 weeks were crossed over to active VNS for 1 minute, randomized to either QD (N=3) or QID (N=1). The addition of a concomitant b/tsDMARD to study treatment was allowed at the discretion of the investigator and the subject. The safety and clinical effectiveness of VNS using the Clinical Disease Activity Index (CDAI) were evaluated.
Results: The 11 subjects completing the Month 36 visit had previously failed, on average, five different agents, with 73% (8/11) having failed a tsDMARD. The average CDAI change from baseline (i.e., initiation of stimulation) for the 11 subjects completing Month 36 was -17.8 (SD 16.3). At Month 36, 64% (7/11) of subjects achieved a CDAI MCID response from baseline (by the 12pt/6pt/1pt criteria[1]), of whom two (2) were treated with VNS monotherapy and five (5) were on continuous VNS with concomitant b/tsDMARD. The number of subjects in low disease activity (LDA) increased from 9% (1/11) at baseline to 45% (5/11) at Month 36, while the number of subjects in high disease activity (HDA) decreased from 64% (7/11) at baseline to 36% (4/11) at Month 36. Through Month 36, 81% (9/11) subjects elected to combine VNS with a b/tsDMARD, with 8/11 continuing concomitant b/tsDMARD at Month 36. Two adverse events related to VNS therapy occurred during the long-term follow-up period. These events were non-serious, anticipated, and reported by the same subject. One event was a mild sore throat, and the other was moderate tenderness near the implant site. Both events resolved without sequelae following a reduction in stimulation strength. There were no related infections, surgical revisions, or device explantations.
Conclusion: Despite small numbers, data demonstrate long term use of VNS was safe and effective treatment for RA to maintain or lower disease activity including when added to a b/tsDMARD.
REFERENCE:
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Acknowledgements: NIL.
Disclosure of Interests: Norman Gaylis: None declared, David Sikes: None declared, Alan Kivitz: None declared, Diane M Horowitz: None declared, Melissa Evangelista Shareholder of: SetPoint Medical, Employee of: SetPoint Medical, Yaakov Levine Shareholder of: SetPoint Medical, Employee of: SetPoint Medical, David Chernoff Shareholder of: SetPoint Medical, Employee of: SetPoint Medical, Mark C. Genovese: None declared.
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POS0835 EFFECTIVENESS AND SAFETY OF JAK INHIBITORS IN RHEUMATOID ARTHRITIS-INTERSTITIAL LUNG DISEASE. NATIONAL MULTICENTER STUDY OF 57 PATIENTS

Keywords: Rheumatoid arthritis, Lungs, Disease-modifying drugs (DMARDs)

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Background: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). Abatacept and rituximab are the recommended drugs **[1-2].** JAK inhibitors (JAKi) have demonstrated efficacy in RA. However, in clinical trials patients with active ILD were usually excluded. Moreover, a warning on ILD toxicity is included in SmPC (Summary of Product Characteristics) with tofacitinib (TOFA). Nonetheless, evidence on efficacy of JAKi in RA-ILD is growing **[3].**

Objectives: to assess **a)** the effectiveness and **b)** the safety of JAKi in AR-ILD patients.

Methods: National multicenter study of 57 RA-ILD patients on treatment with JAKi. We analyzed from baseline the following outcomes: **a)** forced vital capacity (FVC), **b)** diffusing capacity of the lungs for carbon monoxide (DLCO), **c)** chest high resolution computed tomography (HRCT), **d)** dyspnea (modified Medical Research Council scale), **e)** arthritis activity (DAS28-ESR or clinical records), and **f)** sparing corticosteroids effect.

Results: We studied 57 patients (37 women/ 20 men; mean age 66 ±10 years) from clinical practice on treatment with JAKi [baricitinib (BARI)= 42 (74%), TOFA= 6 (11%), upadacitinib (UPA)= 8 (14%), filgotinib (FILGO)= 1 (2%)]. Baseline demographic and clinical characteristics are shown in **Table 1**. All patients had received disease-modifying antirheumatic drugs (DMARDs) before JAKi [Methotrexate (49,86%), Leflunomide (37, 65%), Sulfasalazine (14, 25%), Hydroxychloroquine (13, 23%), Abatacept (32, 56%), Tocilizumab (14, 25%) and Rituximab (10, 18%)]. Since most patients were on BARI we focused on this group (n=42). Median [IQR] ILD duration up to BARI initiation was of 42 [13-62] months. Mean baseline values of FVC and DLCO (% predicted) were 87±22 and 71±21, respectively. Patients were followed-up for a mean of 37 ±37 months. The evolution of FVC and DLCO remained stable during the first 12 months (**Figure 1).** At the end of the follow-up, available chest HRCT images improved/ stabilized in 82% of patients. Stabilization or improvement of dyspnea was found in 87% of patients. Most patients showed articular remission or low activity. BARI was withdrawn in 12 (29%) patients due to articular inefficacy (n=11) and development of hypersensitivity pneumonitis (n=1).

Conclusion: JAKi, especially BARI, may be useful and safe in controlling the course of both pulmonary and joint disease in RA-ILD patients, even in refractory cases.

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Table 1. Baseline characteristics of RA-ILD patients treated with JAKi.

	RA-ILD with JAKi (n=57)
Age, years mean±SD	66 ± 10
Women, n (%)	37 (64,9)
Smoker ever, n (%)	36 (63)
Time since ILD diagnosis, months, median [IQR]	49 [14-63]
RF// ACPA, n (%)	56 (98)
FVC (% of the predicted), mean±SD	90 ±22
DLCO (% of the predicted), mean±SD	71 ±19
UIP-like fibrotic pattern on HRCT, n (%)	30 (55)
Joint activity n (%)	41 (89)
Type of JAKi, n (%)	
Baricitinib (BARI)	42 (74)
Tofacitinib (TOFA)	6 (11)
Upadacitinib (UPA)	8 (14)
Filgotinib (FILGO)	1 (2)
Previous immunosuppressive therapy, n (%)	
Conventional/ biologic DMARD	57 (100)/ 47 (82)
Concomitant immunosuppresive therapy, n (%)	
Conventional/ biologic DMARD	19 (33)/ 0 (0)
Concomitant antifibrotic therapy, n (%)	5 (9)

ACPA, anti-citrullinated protein antibodies; DLCO, diffusing capacity of the lung for carbon monoxide; DMARD, disease-modifying antirheumatic drug; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; JAKi, JAK inhibitor; RA, rheumatoid arthritis; RF, rheumatoid factor; UIP, usual interstitial pneumonia.

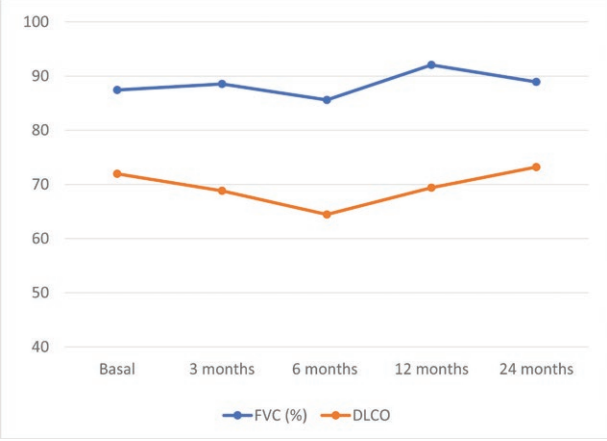


Figure 1. Evolution of pulmonary function tests (mean % of the predicted FVC and DLCO) in RA-ILD patients with BARI therapy at baseline and 24 months.

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POS0836 RISK OF INFECTIONS BETWEEN JAK INHIBITORS AND TNF INHIBITORS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Safety, Rheumatoid arthritis, Disease-modifying drugs (DMARDs)

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Background: With the increasing number of treatment options for rheumatoid arthritis (RA), safety is one of the important consideration for decision-making.
Objectives: To compare infectious risk between JAK inhibitors (JAKi) versus TNF inhibitors (TNFi) among patients with RA in Korea.
Methods: Using 2009-2019 Korea National Health Insurance Service database, we conducted a cohort study on RA patients initiating JAKi or TNFi. The outcomes of interest were 1) serious bacterial, 2) opportunistic, and 3) herpes zoster infections. Propensity-score fine-stratification (PSS) based weighting was applied to adjust for >60 baseline covariates. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazard models comparing JAKi versus TNFi users.
Results: Among 2,967 JAKi initiators and 13,152 TNFi initiators, 2,963 JAKi initiators PSS-weighted on 5,169 TNFi initiators were included. During a mean follow-up of 1.16 years, the most frequent type of infections was herpes zoster with an incidence rate (IR) per 100 person-years of 11.54 and 4.88 in JAKi and TNFi users, respectively, followed by serious bacterial infections with an IR of 1.39 and 1.32, respectively. The opportunistic infection was rare with a majority being tuberculosis, and showed an IR of 0.12 and 0.49 in JAKi and TNFi users, respectively. The PSS-weighted HR [95% CI] for individual types of infections was 2.37 [2.00-2.80] for herpes zoster, 1.04 [0.71-1.52] for serious bacterial infections, and 0.25 [0.09-0.73] for opportunistic infections, comparing JAKi to TNFi initiators. The risk of hospitalized herpes zoster was even higher among JAKi than TNFi initiators with a HR of 7.43 [3.91-14.11].
Conclusion: In this nationally-representative cohort study on RA patients, we found an exceptionally high IR of herpes zoster among JAKi initiators in Korea, showing a doubled risk compared to that in TNFi initiators. Although the risk of serious bacterial infections was comparable between the two treatment groups, the risk of opportunistic infections, particularly tuberculosis, was less among JAKi than TNFi initiators.

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Table 1.

	JAK inhibitor n = 2 963			**TNF inhibitor** (Ref) **n = 5 169**			HR [95% CI]
	Events	PY	[a]IR [95% CI]	Events	PY	[a]IR [95% CI]	
As-treated analysis							
Serious bacterial infection	48	3445	1.39 [1.03-1.85]	61	4629	1.32 [1.01-1.69]	1.04 [0.71-1.52]
Opportunistic infection	4	3489	0.11 [0.03-0.29]	23	4686	0.49 [0.31-0.74]	0.25 [0.09-0.73]
Herpes zoster	361	3128	11.54 [10.38-2.80]	221	4528	4.88 [4.26-5.57]	2.37 [2.00-2.80]
Serious zoster	62	3435	1.81 [1.38-2.31]	11	4682	0.24 [0.12-0.42]	7.43 [3.91-14.11]
365-day ITT							
Serious bacterial infection	36	2260	1.59 [1.12-2.21]	61	4133	1.48 [1.13-1.90]	1.08 [0.72-1.63]
Opportunistic infection	3	2274	0.13 [0.03-0.39]	16	4155	0.39 [0.22-0.63]	0.35 [0.10-1.20]
Herpes zoster	242	2173	11.14 [9.78-12.63]	211	4072	5.18 [4.51-5.93]	2.15 [1.79-2.59]
Serious zoster	37	2263	1.64 [1.15-2.25]	12	4156	0.29 [0.15-0.50]	5.77 [3.00-11.12]

[a]IR is per 100 person-years.

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Disclosure of Interests: None Declared.
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POS0837 IMPACT OF JAKI, TOFACITINIB, ON CV RISK IN RHEUMATOID ARTHRITIS: JAKI CV RISK IMPACT STUDY

Keywords: Targeted synthetic drugs, Rheumatoid arthritis, Cardiovascular disease

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Background: Cardiovascular disease, that includes CAD & Stroke, is the leading cause of premature mortality and sudden death in RA. Classical CV risk & disease specific risk factors all contribute to the enhanced CV risk in RA. Endothelial dysfunction (ED), the " sine qua non" for atherosclerosis appearance, is the key promoter of CVD. ED is a barometer for CV health and a seminal target for reducing cardiovascular (CV) risk in RA. Given the magnitude of the problem, therapeutic armamentarium for CV risk reduction in RA is limited.
Objectives: To prospectively investigate the impact of Tofacitinib (TOFA) on CV risk in active RA.
Methods: 81 consecutive RA patients (Table 1) meeting 2010 Rheumatoid Arthritis Classification Criteria median age 54 years, 81% female, disease duration 14 years, moderate to high activity (DAS28-5.3) who were non-responders to MTX at least 15 mg/week and/or other synthetic DMARDs free of clinical overt cardiovascular disease were randomized 1:1 to receive TOFA 5 mg bid (n=41) or placebo (n=41) for 12 weeks as an adjunct to existing stable antirheumatic drugs. Primary endpoints included endothelial dysfunction assessed by Flow Mediated Dilatation (FMD), using Angiodefender, at baseline and after 12 weeks of treatment and occurrence of MACE and VTE throughout the study. The secondary end points included: DAS28, ESR, CRP, HAQ-DI.

Table 1. Demographic, clinical and biochemical characteristics of 81 rheumatoid arthritis patients

Clinical Parameters	**Tofacitinib (n=41)**	**Placebo (n=40)**	**P value**
Age (years)	56.13± 7.95	54.8 ± 8.4	0.34
Gender: M/F (n)	06/35	06/34	0.84
BMI (kg/m^2)	26.71 ± 3.23	25.08 ± 4.17	0.79
Disease Duration (yrs)	14.28 ± 6.85	13.7 ± 6.6	0.48
RF Positive	29 (48.33%)	30 (50.84%)	--
Anti CCP	15 (25%)	13 (22%)	--
Systolic Blood Pressure (mm Hg)	124.3± 7.52	122.2 ± 6.89	0.47
Diastolic Blood Pressure (mm Hg)	78.38 ± 5.16	76.84 ± 4.52	0.56
ESR (mm 1sthr)	38.84 ± 16.03	39.2 ± 17.14	0.56
CRP (mg/dl)	20.15± 20.82	18.16 ± 12.25	0.33
DAS-28	5.4 ± 2.18	5.48 ± 2.3	0.88
HAQ-DI	0.52 ±0.54	0.59 ± 0.70	0.32

Values presented as mean ± SD, except gender which is expressed as a number of female and male. F: female, M: male, SBP: systolic blood pressure, DBP: diastolic blood pressure, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, DAS-28: disease activity score in 28 joints, HAQ-DI

Results: At baseline, endothelial function was impaired and levels of inflammatory measures were elevated and HAQ-DI was impaired in both groups. After treatment, FMD improved significantly in the tofacitinib group from (6.64 ± 2.13 to 8.17 ± 2.69, p=0.0001) as compared to placebo (6.36 ± 3.01% to 6.84 ± 2.95%, p=0.68) (Figure 1A). DAS28 (Figure 1B), ESR and CRP levels improved significantly in tofacitinib group as compared to placebo (p≤0.05). TOFA significantly decreased HAQ-DI (Figure 1C) values as compared to placebo. There was no MACE or VTE event during the study period in either group. After 12 weeks of treatment, FMD increased by 23.04% where as DAS28, ESR and CRP decreased by 31.23%, 29% and 60% respectively in the TOFA group (Figure 1D). Significant negative correlation was observed between FMD and CRP (0.32, p≤0.05) before and after (r= -0.34, p≤0.05) treatment with TOFA whereas no such correlations were found in placebo group.

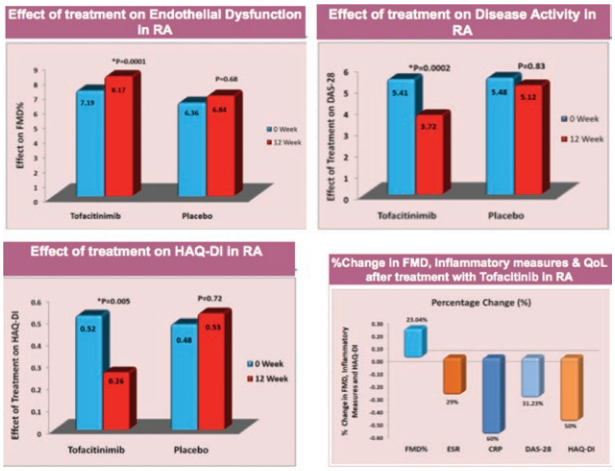


Fig 1. Effect of Tofacitinib treatment on (A) Endothelial dysfunction (B) Disease activity (C) HAQ-DI and (D) % Change

Conclusion: TOFA, apart from its anti-inflammatory activity, improves endothelial dysfunction and cardiovascular risk in active RA without clinical overt cardiovascular disease. Thus, JAK inhibition with TOFA has vasculoprotective and cardioprotective effect mediated through anti-inflammatory and probably other mechanisms.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0838 AGOMELATINE IDENTIFIED FROM THE FDA-APPROVED DRUG LIBRARY IS THERAPEUTIC AGAINST COLLAGEN INDUCED ARTHRITIS

Keywords: Rheumatoid arthritis, Cytokines and chemokines

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Background: Treatment effect of tumor necrosis factor α (TNFα) inhibitors is still low in patients with rheumatoid arthritis (RA), around 50%-70%. Thus more drugs by targeting proliferation of synovial fibroblasts (FLS) and TNFα induced inflammatory cytokine production are needed. Repurposed use of drugs that have been used in clinic is a quick and cost-effective way to find new drugs.

Objectives: This study aims to screen drugs that could inhibit the proliferation and inflammation induced by TNFα in FLS from FDA approved on market drug library, then to assess the treatment effect of the identified drugs on collagen-induced arthritis (CIA) mouse model.

Methods: CCK8 assay was performed to screen the drugs that could inhibit FLS proliferation, followed by qRT-PCR and ELISA to select the drugs that could suppress TNFα induced inflammatory cytokine production. Then, treatment effects of the identified drugs were assessed in CIA mouse model.

Results: The first and second round drug librabry screening aimed to select out the drugs that could inhibit the proliferation of FLS. Results showed, from 1815 drugs, 372 drugs were indentified at the initial screening (Figure 1A) and 121 drugs were identified from the second screening (Figure 1B). The third round screening was performed to screen the drugs that could inhibit TNFα-induced inflammation, and results showed that a total of 77 drugs could inhibit mRNA expression levels of both IL-6 and IL-8 by over 50%, and 64 drugs could suppress secretion levels of both IL-6 and IL-8 for more than 20% (Figure 1C-F). Then a total of 14 drugs that were not anti-cancer drugs were used to further confirm the inhibitory effect on the TNFα induced inflammation, and results showed only Agomelatine (AOM), Cinacalcet (CCC), Amlodipine (ALM), Simvastatin (SV), and Pindolol (PDL) could suppress mRNA expression and secretion levels of IL-6, IL-8 (Figure 1G-J). As highly proliferated FLS and inflammatory cytokines play a critical role in the pathology of rheumatoid arthritis (RA), we tested the treatment effect of AOM, CCC, ALM, SV, and PDL in the CIA mose model. Results showed ALM (5mg/kg), CCC (10mg/kg), and PDL (10mg/kg) had a trend to reduce the clinical score but did not reach statistical meaning while SV (10mg/kg) did not show any treatment effect. Whereas, AOM (10mg/kg) could effectively alleviate the swelling of the the joint, which was as effective as the positive control drug methotrexate (MTX) (Figure 1K). ALM, AOM, as well as MTX could reduce the pathological score of inflammation and bone erosion at both the knee and the anke while PDL could only reduce the inflammation and relieve bone erosion at the knee(Figure 1L-N).

Conclusion: Agomelatine indentified from the FDA approved drug library could inhibit FLS proliferation and TNFα induced inflammation, and was therapeutic against CIA mouse model.

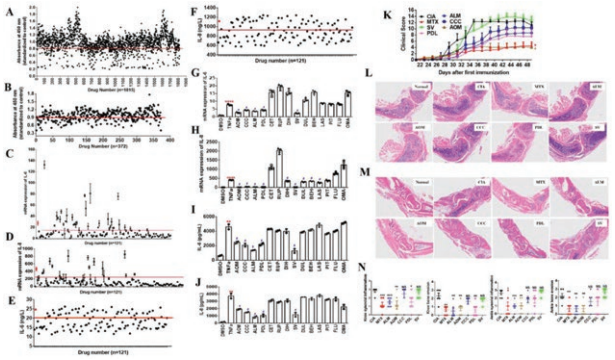


Figure 1. Agomelatine identified from the FDA-approved drug library is therapeutic against collagen induced arthritis. (A) The first round screening by CCK8 assay. The drugs could inhibit more than 20% absorbance at 450nm, under the red lines, were the target ones, n=372. (B) The second round screening. The drugs could inhibit more than 10% absorbance at 450nm, under the red lines, were the target ones, n=121. (C-F) The third round screening. (C-D) mRNA expression levels of IL-6 and IL-8. (E-F) the secretion levels of IL-6 and IL-8. (G-J) The confirmation of drugs' inhibitory effect on the inflammation cytokine production. Red asterisk indicated the conparison between TNFα group and DMSO group and blue pound signs suggested the conparison between drugs and TNFα group. (G-H) the mRNA expression levels of IL-6 and IL-8. (I-J) the secretion levels of IL-6 and IL-8. CIA mouse model was established to test the treatment effect of SV (10mg/kg), PDL (10mg/kg), ALM (5mg/kg), CCC (10mg/kg), and AOM (10mg/kg), and MTX (2mg/kg) was set as the positive control. (K) clinical score of joint swelling (L) H&E staining of knee joint (M) H&E staining of ankle joint (N) pathological scoring of H&E staining for joint inflammation and bone erosion.

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POS0839 THE COMPARISON OF MALIGNANCY RISK BETWEEN JAK INHIBITORS AND TNF INHIBITORS IN MULTI-CENTER COHORT STUDY

Keywords: Targeted synthetic drugs, Rheumatoid arthritis, Safety

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Background: Ytterberg et al. demonstrated the concern about the incidence of malignancy during treatment with tofacitinib [1]. However, there is few published data of such adverse events in clinical settings.

Objectives: We aimed to compare the incidence of malignancies in RA patients treated with JAK inhibitors and TNF inhibitors in real-world settings.

Methods: We enrolled 499 RA patients treated with JAK inhibitors (tofacitinib, n=192 or baricitinib, n=104) or TNF inhibitors (adalimumab, n=88 or etanercept, n=115). The standardized incidence ratio (SIR) of malignancies were determined using the general Japanese population. After adjusting the clinical characteristic imbalance by propensity score weighting, we compared the risk of malignancy between JAK inhibitors and TNF inhibitors using Cox proportional hazard models.

Results: Observational period was 961.9 patient-years (PY), and median observational period was 1.3 years. We identified 11 cases (3.7%) of malignancies in JAK inhibitors and 4 cases (2.0%) in TNF inhibitors. The SIR for overall malignancies in TNF inhibitors was comparable with general population (0.94, 95%CI: 0.26–2.41), and the SIR in JAK inhibitors was higher than the general population but no significant difference (1.61/100PY, 95%CI: 0.80-2.88). The adjusted hazard ratio was 0.38 (95%CI: 0.09-1.55) between JAK inhibitors and TNF inhibitors in the risk of malignancies (Figure 1).

Conclusion: We demonstrated that the incidence of malignancy in JAK inhibitors was numerically high but not significant compared with general population and TNF inhibitors.

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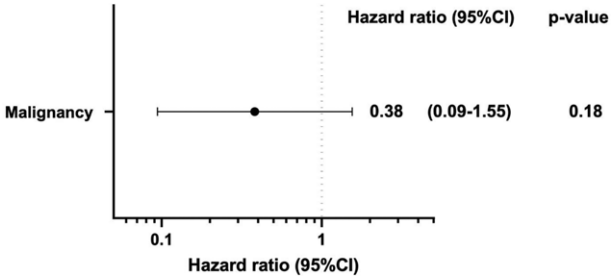


Figure 1. The adjusted hazard ratio of the duration for the incidence of malignancy of the RA patients treated with TNF inhibitors to JAK inhibitors

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0840 THE DIFFERENCE IN CREATINE KINASE ELEVATION CAUSED BY JAK INHIBITORS AND IL-6 INHIBITORS IN RHEUMATOID ARTHRITIS

Keywords: Comorbidities, Rheumatoid arthritis

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Background: Cases of creatine kinase (CK) elevation caused by Janus kinase inhibitor (JAKi) treatment for rheumatoid arthritis (RA) have been reported in clinical trials[1]. IL-6 signals via the JAK-STAT pathway. However, it is not known whether the CK elevation is due to JAKi alone or to IL-6 inhibitor (IL-6i) as well.
Objectives: The objective was to examine whether the CK elevation is specific to JAKi therapy or similar to IL-6i therapy by propensity score (PS)-matching.
Methods: A multicenter database of JAKi (n=168) and IL-6i (n=113) treatment was used. All cases were followed-up at 24 weeks, and their CK levels were evaluated. A total of 71 cases in each group were extracted by the PS-matching method (using age, sex, BMI, and CK at 0 weeks (W)). The percentage abnormal from the standard titer was compared for the JAKi and IL-6i groups. The factors related to an elevated CK at 24 weeks were investigated using patients' background characteristics at the time of starting treatment by univariate analysis.
Results: The patients' median age was 66 years, CK at 0W was 57I U/L, and mean BMI was 22.5 kg/m^2. There were no significant differences between the groups at the time of starting treatment (Table 1). The changes in CK by JAKi and IL-6i treatments are shown in the Figure 1. The CK at 4W with JAKi treatment was significantly higher than that with IL-6i treatment (83 vs 72 IU/L; P=0.018). The same tendency was seen at 12W and 24W. The outlier rate (Grade 1: 1 < titer < 2.5 times) with JAKi treatment increased significantly over time (0W: 4.2%, 4W: 18.1%, 12W: 21.7%, 24W: 18.3%, P=0.015), whereas that with IL-6i treatment increased slightly (0W: 5.6%, 4W: 9.2%, 12W: 8.6%, 24W: 8.5%, P=0.745), with a significant difference between the groups (P=0.035). Of all the patients, only three showed Grade 2 (2.5 < titer < 5 times). No RA patients discontinued treatment due to myalgia or renal dysfunction. The factors significantly positively related to elevated CK at 24W were male and creatine, and those significantly negatively related were stage, class, mHAQ, eGFR, and PSL dosage.
Conclusion: CK elevation was greater with JAKi treatment at 4W and maintained until 24W than with IL-6i treatment in RA patients with adjustment for background characteristics. The CK elevation might be specific to JAKi treatment. The mechanism needs to be clarified in the future.

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Table 1. Characteristics at the time of starting JAKi or IL-6i treatment by the PS- matching method

	JAKi (n-71)	IL-6i (n=71)	P value
Female, %	83.1	81.7	1.000
Age, y	66 (53, 74)	67 (56, 74)	0.943
Disease duration, y	15 (7.6, 25.7)	11.3 (3.4, 21.4)	0.106
BMI, kg/m^2	22.5 ± 3.8	22.5 ± 3.7	0.999
Creatinine kinase, IU/L	56, (41, 87)	58 (40, 84)	0.886
RF, %	77.9	81.8	0.668
CRP, mg/dL	1.23 (0.34, 2.98)	1.34 (0.42, 3.45)	0.673
DAS28ESR	5.06 ± 1.45	5.00 ± 1.36	0.797
mHAQ	0.625 (0.125, 1.250)	0.5 (0.125, 1.125)	0.419
eGFR, mL/min/1.73 m^2	75.1 (60.8, 88.3)	71.4 (54.4, 89.1)	0.638
Glucocorticoid, % (mg)	38.0 (4.3 ± 2.6)	36.6 (5.3 ± 3.0)	1.000

Data are shown as means ± standard deviation (SD) or medians (25th, 75th percentile).

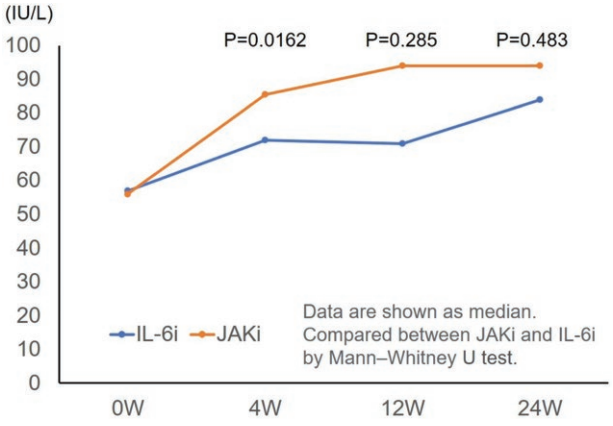


Figure 1. Changes of CK with JAKi treatment and IL-6i treatment

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0841 EFFECTIVENESS AND SAFETY OF UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PRIOR TNF-THERAPY IN GERMANY. FINAL RESULTS FROM A POST-MARKETING OBSERVATIONAL STUDY

Keywords: Targeted synthetic drugs, Real-world evidence, Rheumatoid arthritis

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Background: The efficacy and safety of Upadacitinib (UPA), a selective Janus kinase inhibitor, have been evaluated in the SELECT clinical trial program [1-6]. The UPwArds study was designed to further elucidate UPA's real-world effectiveness in daily clinical practice.
Objectives: To assess UPA effectiveness and safety after a treatment period of 12 months in three different RA patient groups: i) the total patient population, ii) patients with previous failure of TNFi (prior TNFi), and iii) patients naïve to targeted-synthetic or biological disease-modifying anti-rheumatic drugs (ts/bDMARDs naïve).
Methods: UPwArds is a prospective, open-label, multicenter, post-marketing observational study including adult patients with moderate-to-severe RA and an inadequate response or intolerance to at least one previous disease-modifying anti-rheumatic drug. At month 12 of the observational period, improvement of the DAS28(CRP), CDAI and the 0-10 numerical rating scale for overall pain (NRS pain) were assessed for the different patient populations specified above. In addition, the three patient population groups were evaluated regarding safety data concerning adverse events that were collected over the study period. Respective comparisons are presented as number of events per 100 patient-years, including

confidence intervals. Data analysis was conducted as observed without imputation of missing values.

Results: From all initially enrolled patients (n_{total} = 533, $n_{prior\ TNFi}$ =262, $n_{ts/bDMARDs\text{-}naïve}$ = 209), 371 completed the study (70%), of whom 175 and 148 were prior TNFi or ts/bDMARDs-naïve patients, respectively. At month 12, the proportion of patients achieving DAS28 < 2.6, DAS28 ≤ 3.2, CDAI ≤ 2.8, CDAI ≤ 10, and NRS pain reduction ≥ 50% reflected comparable outcomes in all three patient groups (Figure 1). Although the number of any AE per 100 patient years was higher in prior TNFi patients, no significant differences were found in any particular AE category, including serious AEs or other AEs of particular interest (Table 1).

Conclusion: In a real-world setting, UPA demonstrated comparable effectiveness and safety in prior TNFi patients, ts/bDMARDs-naïve patients and the overall patient population.

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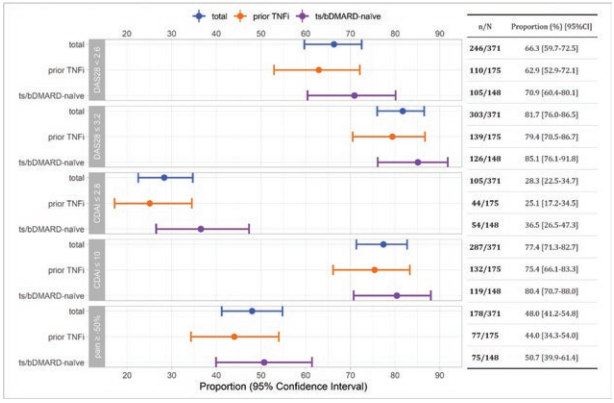


Figure 1. Proportion of patients attaining specified effectiveness criteria after 12 months

Table 1. Frequency of categorized adverse events

	Number of AEs (total)	Events/100 PY (total, N=533) [95%CI]	Events/100 PY (prior TNFi, N=262) [95%CI]	Events/100 PY (ts/bDMARD-naïve, N=209) [95%CI]
Any AE	467	104.4 [95.1 – 114.3]	117.3 [103.5 – 132.5]	84.9 [71.8 – 99.7]
SAE	65	14.5 [11.2 – 18.5]	14.9 [10.2 – 20.9]	14.3 [9.3 – 21.2]
AE leading to discontinuation (total)	121	27.0 [22.4 – 32.3]	30.2 [23.4 – 38.4]	21.8 [15.4 – 29.9]
-Discontinuation due to AE	87	19.4 [15.6 – 24.0]	21.7 [16.0 – 28.7]	17.2 [11.6 – 24.6]
-Discontinuation due to lack of efficacy	34	7.6 [5.3 – 10.6]	8.6 [5.2 – 13.4]	4.6 [2.0 – 9.0]
Serious infections	13	2.9 [1.5 – 5.0]	2.7 [1.0 – 5.9]	3.4 [1.3 – 7.5]
Herpes zoster	12	2.7 [1.4 – 4.7]	3.6 [1.6 – 7.1]	0.6 [0.0 – 3.2]
Malignancy (other than NMSC)	4	0.9 [0.2 – 2.3]	0.9 [0.1 – 3.3]	1.1 [0.1 – 4.1]
Major adverse cardiovascular events[a]	3	0.7 [0.1 – 2.0]	0.5 [0.0 – 2.5]	0.6 [0.0 – 3.2]
Venous thromboembolism[b]	1	0.2 [0.0 – 1.2]	0 [0.0 – 1.7]	0.6 [0.0 – 3.2]
Death[c]	1	0.2 [0.0 – 1.2]	0.5 [0.0 – 2.5]	0 [0.0 – 2.1]

[a]defined as cardiovascular death, non-fatal myocardial infarction (n = 1), non-fatal stroke (n = 2), [b]deep vein thrombosis (n = 1), [c] recurrence of breast cancer (n = 1) - considered unrelated to study medication; mean exposure days were 307 (126) for the total patient sample, 309 (123) for prior TNFi patients, and 305 (130) for ts/bDMARD-naïve patients

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POS0842

GLUCOCORTICOID USAGE AFTER JANUS KINASE INHIBITOR (JAKI) AND OTHER BIOLOGIC DMARDS INITIATION AND IMPACT OF COMEDICATION OF CONVENTIONAL DMARDS ON TREATMENT PERSISTENCE IN RHEUMATOID ARTHRITIS PATIENTS: RETROSPECTIVE STUDY IN THE AUSTRALIAN POPULATION

Keywords: Disease-modifying drugs (DMARDs), Rheumatoid arthritis, Epidemiology

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Background: Janus Kinase inhibitors (JAKi) and biologic disease modifying anti-rheumatic drugs (bDMARDs) are routinely used in the management of rheumatoid arthritis (RA) patients for whom conventional (c)DMARDs have failed. The usage of glucocorticoids after DMARD initiation and the influence of comedication on treatment persistence, used as a surrogate for treatment effectiveness, remains unkown.

Objectives: To assess glucocorticoids usage after treatment initiation and to compare the impact of comedication on the persistence of JAKi and bDMARDs in Australian RA patients.

Methods: A retrospective observational study was conducted among 4,521 RA patients in the Australian Medicare Database (from 2011 to 2022), aged ≥18 and for whom a JAKi or bDMARDs were dispensed. A deidentified 10% sample of the database was taken as a random representation of RA patients in Australia. Kaplan-Meier analysis was used to calculate drug persistence rates, defined as the time from treatment initiation until the date of the last dose when there had not been a script dispensed for 6 months. Wilcoxon Singed Rank test was used to compare glucocorticoid dose changes from 1-year prior to 1 and 1 – 2 years after initiation of the DMARDs. Only patients who had persisted on DMARDs for 2 years were included for analysis. Log-rank test was used to compare time on a particular DMARDs treatment between the following sub-groups: (a) monotherapy; (b) combination MTX; and (c) combination cDMARDs.

Results: A total of 634 met the inclusion criteria for the glucocorticoids analyses, average dose of glucocorticoids decreased from 4.1mg/day at 1 year prior to initiation of DMARD, to 2.9mg/day and 2.0mg/ day at 1- and 1–2-years post-initiation, respectively (**Figure 1**). Daily dose changes were statistically significant for all RA DMARDs combined, tofacitinib and baricitinib combined (1–2 years post initiation only), TNFi, abatacept, and tocilizumab. The proportion of patients with a decrease in glucocorticoids dose from 1 year prior to 1 and 1–2 years after DMARD initiation was 62% and 70% for 'all DMARDs' (*n*=634), 35% and 52% for baricitinib (*n*=23), 58% and 63% for tofacitinib, 59% and 61% for abatacept (*n*=87), 65% and 78% for tocilizumab (*n*=148), and 62% and 70% for TNFi (*n*=387), respectively. For each drug individually, treatment persistence rates were higher in combination with MTX and in combination with other cDMARDs, compared to monotherapy (**Table 1**). Statistical significance was only reached when comparing baricitinib combined with cDMARD to monotherapy baricitinib (65% [*p*=0.04] *vs* 52%), tofacitinib combined with MTX and combined with other cDMARDs to monotherapy tofacitinib (56% [*p*=<0.01] and 55% [*p*=<0.01] vs. 45%); and TNFi combined with MTX and combined with other cDMARDs to monotherapy TNFi (63% [*p*=<0.0001] and 65% [*p*=<0.0001] vs. 43%).

Conclusion: This real-world data showed that among Australian RA patients glucocorticoids dosage decreased with JAKi and bDMARD use. When treatment was combined with MTX or other cDMARDs persistence rates were not sig. different when comparing upadacitinib, baricitinib and TNFi. Tofacitinib had similar persistence rates to TNFi.

Average daily glucocorticoids usage.

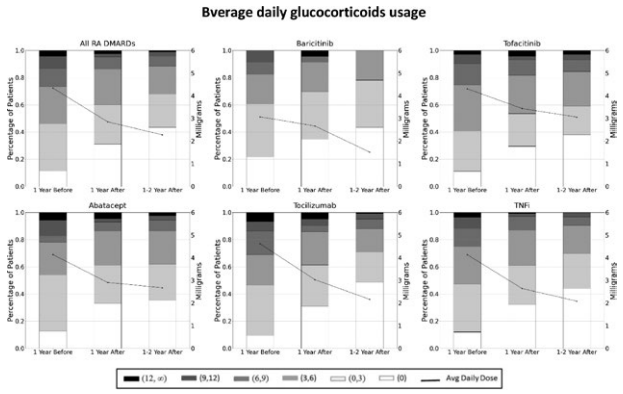


Figure 1.

Table 1.

Persistence rates at 12 months post-initiation, based on KM-estimates

	All			Monotherapy			Combination methotrexate			Combination cDMARD		
	n	Estimate	95% CI	*n*	Estimate	95% CI	*n*	Estimate	95% CI	*n*	Estimate	95% CI
Baricitinib	553	61%	(58 – 67)	86	52%	(44 – 65)	199	64%	(58 – 72)	373	65%	(61 –71)
Tofacitinib	1230	53%	(68 – 76)	161	45%	(38 – 54)	480	56%	(52 – 61)	813	55%	(52 –59)
Upadacitinib	574	72%	(68 – 76)	78	70%	(60 – 82)	236	75%	(69 – 81)	371	74%	(70 –79)
Abatacept	941	49%	(46 – 53)	165	44%	(38 – 53)	421	49%	(45 – 55)	671	49%	(47 –55)
Tocilizumab	1139	55%	(54 – 60)	273	52%	(47 – 59)	423	56%	(52 – 62)	748	58%	(57 –64)
TNFi*	3501	58%	(57 – 61)	899	43%	(41 – 48)	1381	63%	(62 – 67)	2169	65%	(63 –67)

* Subcutaneous anti-tumor necrosis factor, including adalimumab, certolizumab, etanercept, and golimumab

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POS0843

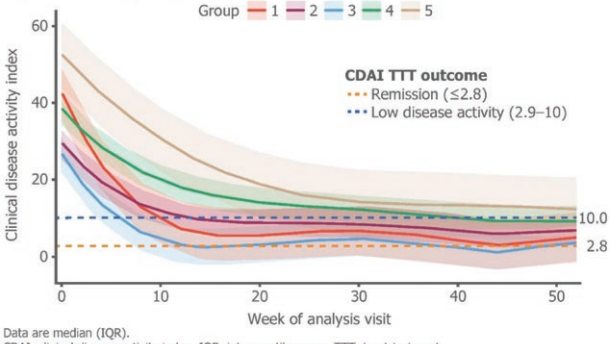
DISTINCT TREATMENT RESPONSES IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING FILGOTINIB 200 MG OVER 12 MONTHS: A POST HOC ANALYSIS OF FINCH 1

Keywords: Remission, Rheumatoid arthritis

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Background: FINCH 1 (NCT02889796) was a Phase 3 randomized controlled trial evaluating filgotinib (FIL) in patients with rheumatoid arthritis and an inadequate response to methotrexate (MTX).[1] Patients received background MTX and were randomized 3:3:2:3 to FIL 200 mg (FIL200), FIL 100 mg, adalimumab or placebo.
Objectives: To identify patterns of response trajectory over 12 months in patients from FINCH 1 receiving FIL200.
Methods: Group-based trajectory modeling is a statistical method which groups individuals based on similar patterns of change in an outcome over time.[2] A group-based trajectory modeling approach was applied to identify five distinct phenotypic groups in terms of observed clinical disease activity index (CDAI) outcomes (and components) over a 12-month period (**Figure 1**). Responders were recorded as either low disease activity (LDA) or remission, defined as CDAI between 2.9 and 10, or ≤2.8, respectively, at 6 or 12 months.
Results: Mean age, the proportion of females and disease duration were similar across all groups. Improvements in efficacy outcome measures were seen for all groups. Baseline (median interquartile range [IQR]) CDAI was highest (worst) in Group 5 (52 [48, 60]), followed by Group 1 (48 [44, 55]). Groups 1 and 3 showed a rapid reduction in CDAI in the first 6 months and sustained response over 12 months. Groups 2, 4 and 5 demonstrated slower response trajectories, with continued improvements in the proportion of CDAI responders between 6 and 12 months; of note, Group 5 constituted 16.8% (80/475) of the total analysis population. **Table 1** shows that despite substantial and comparable improvements in CDAI components across all 5 groups over 12 months, Group 5 demonstrated some residual disease activity.
Conclusion: A group-based multivariate trajectory model identified 5 distinct CDAI disease activity trajectories in patients from FINCH 1 receiving FIL200. Patients in all groups demonstrated either fast and sustained response or slower and continued improvements, with no or low numbers of swollen or tender joints at Month 12. The current analysis suggests that patients who do not achieve CDAI LDA within 6-months may still benefit from treatment continuation and informs a range of expectations for times to clinical response. Future work will assess biomarker profiles that may be used to predict the observed clinical response patterns.
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[1] Combe B, et al. Ann Rheum Dis 2021;80:848–58
[2] Nagin DS, et al. Stat Methods Med Res 2018;27:2015–23

Figure. CDAI trajectory in patients from FINCH 1 receiving FIL200



Data are median (IQR).
CDAI, clinical disease activity index; IQR, interquartile range; TTT, treat-to-target.

Table 1. Efficacy outcomes from baseline to Month 12 in phenotypic patient groups receiving FIL200: CDAI components.

	Group 1 N=94	Group 2 N=103	Group 3 N=131	Group 4 N=67	Group 5 N=80
PtGADA					
Baseline	72 (60, 84)	67 (52, 78)	60 (46, 72)	77 (66, 85)	76 (67, 89)
12-month abs change	58 (44, 70)	31 (20, 50)	50 (33, 65)	40 (21, 56)	46 (20, 59)
12-month value	9 (3, 21)	25 (12, 43)	6 (3, 13)	33 (23, 50)	36 (21, 46)
PhGADA					
Baseline	71 (61, 80)	62 (52, 71)	60 (49, 68)	73 (63, 82)	77 (64, 88)
12-month abs change	66 (51, 71)	48 (36, 58)	51 (42, 62)	53 (43, 63)	51 (36, 62)
12-month value	5 (1, 10)	10 (4, 17)	4 (1, 9)	22 (8, 31)	23 (9, 36)
SJC28					
Baseline	14 (11, 18)	8 (6, 9)	8 (6, 11)	10 (8, 12)	16 (12, 20)
12-month abs change	14 (10, 18)	7 (5, 8)	8 (6, 10)	9 (7, 12)	13 (10, 17)
12-month value	0 (0, 0)	0 (0, 1)	0 (0, 0)	0 (0, 2)	2 (0, 3)
TJC28					
Baseline	20 (16, 24)	10 (8, 14)	11 (7, 13)	15 (13, 18)	22 (18, 26)
12-month abs change	18 (15, 22)	9 (7, 12)	11 (7, 13)	13 (10, 16)	16 (12, 22)
12-month value	0 (0, 2)	1 (0, 2)	0 (0, 0)	3 (1, 5)	5 (2, 9)
CDAI responders (LDA and remission), n (%)					
6-months	79 (92)	66 (78)	122 (99)	11 (21)	14 (23)
12-months	75 (91)	75 (90)	119 (99)	27 (52)	20 (34)

Data are median (IQR) unless otherwise stated.abs, absolute; CDAI, clinical disease activity index; IQR, interquartile range; LDA, low disease activity; PhGADA, Physician's Global Assessment of Disease Activity; PtGADA, Patient's Global Assessment of Disease Activity; SJC28, swollen joint count 28; TJC28, tender joint count 28.

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Disclosure of Interests: Peter C. Taylor Speakers bureau: AbbVie, Consultant of: AbbVie, Biogen, Fresenius, Galapagos, Gilead, GlaxoSmithKline, Janssen, Lilly, Nordic Pharma, Pfizer, Sanofi, UCB, Grant/research support from: Galapagos, Yoshiya Tanaka Speakers bureau: AbbVie, AstraZeneca, BMS, Boehringer-Ingelheim, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, GlaxoSmithKline, Mitsubishi-Tanabe, Pfizer, Grant/research support from: Asahi-Kasei, AbbVie, Boehringer-Ingelheim, Chugai, Daiichi-Sankyo, Eisai, Takeda, Emily Aiello Consultant of: Galapagos, Janssen, Pfizer, UCB, Employee of: Cytel, Inc., Thomas Debray Consultant of: Biogen, Galapagos, Gilead, Chris Watson Shareholder of: Galapagos, Employee of: Galapagos, Kristina Harris Shareholder of: Galapagos, Employee of: Galapagos, Gerd Rüdiger Burmester Speakers bureau: AbbVie, Amgen, BMS, Chugai, Galapagos, Lilly, Pfizer, Sanofi, Consultant of: AbbVie, Amgen, BMS, Galapagos, Lilly, Pfizer, Sanofi.

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POS0844

INTEGRATED SAFETY ANALYSIS OF FILGOTINIB IN PATIENTS WITH MODERATE TO SEVERE ACTIVE RHEUMATOID ARTHRITIS WITH A MAXIMUM EXPOSURE OF 8.3 YEARS

Keywords: Rheumatoid arthritis, Safety

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Background: Filgotinib (FIL) is an oral Janus kinase 1 preferential inhibitor, approved for the treatment of moderate to severe active rheumatoid arthritis (RA). In previous analyses, comparable incidence of selected adverse events (AEs) occurred in FIL 200 mg (FIL200) and 100 mg (FIL100) dose groups, except for herpes zoster.[1]

Objectives: To provide an update on FIL selected AEs up to a median (max) exposure of 3.8 (8.3) years.

Methods: Integrated FIL RA data from 7 clinical trials are reported: phase 2 (NCT01888874, NCT01894516), phase 3 (NCT02889796, NCT02873936, NCT02886728), and the long-term extension studies DARWIN 3 phase 2 (NCT02065700) and FINCH 4 phase 3 (NCT03025308). Exposure-adjusted incidence rates (EAIRs)/100 patient-years of exposure (PYE), censored at time of first event, were determined for major adverse cardiovascular event (MACE), venous thromboembolism (VTE), arterial systemic thromboembolism, non-melanoma skin cancer (NMSC), malignancies excluding NMSC, herpes zoster, serious infections and deaths. Data were as of May 2, 2022 (DARWIN 3) and May 6, 2022 (FINCH 4). MACE and VTE only include positively adjudicated events with a data cutoff of April 3, 2022.

Results: The as-treated population included 3691 patients with 12,541 PYE. Median (max) exposure was 3.8 (8.3) in the pooled FIL group; 3.8 (8.3) years for FIL200 and 3.3 (7.8) years for FIL100. Baseline demographics and disease characteristics were balanced between groups.[2] Small numerical differences were observed between FIL doses for EAIRs of selected AEs. Numerically higher incidences of NMSC, herpes zoster and all-cause mortality were reported with FIL200 vs FIL100; incidences of MACE and serious infections were numerically lower with FIL200 vs FIL100, with overlapping confidence intervals (**Table 1**). Over 240 weeks, the risks of MACE and VTE were comparable for FIL100 vs FIL200; low event numbers make interpretation difficult. The risk of herpes zoster was higher with FIL200 vs FIL100, and generally similar for serious infection or all-cause mortality (**Figure 1**).

Conclusion: Over a maximum of 8.3 years, FIL200 and FIL100 continued to show small numerical differences in EAIRs of selected AEs between dose groups in the overall RA population. Slightly higher incidence rates for NMSC, herpes zoster and all-cause mortality were reported in the FIL200 than FIL100 group, with a higher incidence of MACE and serious infections with the lower dose; confidence intervals overlapped between the dose groups.

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[1] Winthrop KL, et al. Arthritis Rheumatol 2022;74(S9): abstract 0273

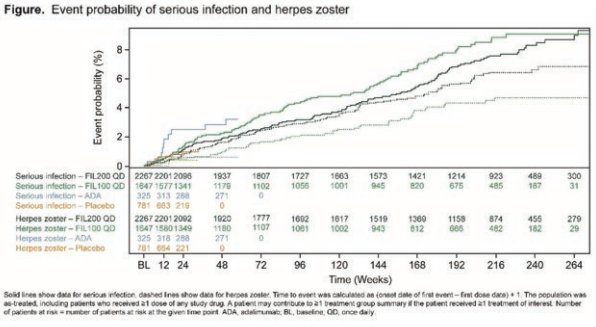
[2] Winthrop KL, et al. Ann Rheum Dis 2022;81:184–92

Table 1. Frequencies and EAIRs of selected AEs in parent and ongoing long-term extension RA clinical trials

	FIL100 (PYE= 4532.4) (n=1647)	FIL200 (PYE= 8008.6) (n=2267)
	n (%), EAIR per 100 PYE (95% CI)	
MACE*	22 (1.3), 0.49 (0.3, 0.7)	27 (1.2), 0.34 (0.2, 0.5)
VTE*	9 (0.5), 0.20 (0.1, 0.4)	15 (0.7), 0.19 (0.1, 0.3)
ASTE	1 (<0.1), 0.02 (0.0, 0.1)	1 (<0.1), 0.01 (0.0, 0.1)
NMSC	9 (0.5), 0.20 (0.1, 0.4)	27 (1.2), 0.34 (0.2, 0.5)
Malignancies (excluding NMSC)	30 (1.8), 0.66 (0.4, 0.9)	57 (2.5), 0.71 (0.5, 0.9)
Herpes zoster	49 (3.0), 1.10 (0.8, 1.5)	114 (5.0), 1.48 (1.2, 1.8)
Serious infections	97 (5.9), 2.18 (1.8, 2.2)	149 (6.6), 1.88 (1.6, 2.2)
All-cause mortality	26 (1.6), 0.57 (0.4, 0.8)	57 (2.5), 0.71 (0.5, 0.9)

*Positively adjudicated MACE/VTE.AE, adverse event; ASTE, arterial systemic thromboembolism; CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL100/200, filgotinib 100/200 mg; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; PYE, patient-years of exposure; RA, rheumatoid arthritis; VTE, venous thromboembolism.

Figure. Event probability of serious infection and herpes zoster



Solid lines show data for serious infection, dashed lines show data for herpes zoster. Time to event was calculated as (onset date of first event – first dose date) + 1. The population was as-treated, including patients who received ≥1 dose of any study drug. A patient may contribute to ≥1 treatment group summary if the patient received ≥1 treatment of interest. Number of patients at risk = number of patients at risk at the given time point. ADA, adalimumab; BL, baseline; QD, once daily.

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Disclosure of Interests: Kevin Winthrop Consultant of: Pfizer, AbbVie, UCB, Eli Lilly & Company, Galapagos, GSK, Roche, Gilead, BMS, Regeneron, Sanofi, AstraZeneca, Novartis, Grant/research support from: BMS, Pfizer, Daniel Aletaha Speakers bureau: AbbVie, Gilead, Galapagos, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sandoz, Sanofi, Consultant of: AbbVie, Gilead, Galapagos, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sandoz, Sanofi, Grant/research support from: AbbVie, Gilead, Galapagos, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sandoz, Sanofi, Roberto Caporali Speakers bureau: AbbVie, Galapagos, Lilly, Pfizer, UCB, BMS, Fresenius, Novartis, Celltrion, Janssen, Amgen, Consultant of: AbbVie, Galapagos, Lilly, Pfizer, UCB, Fresenius, Novartis, Yoshiya Tanaka Speakers bureau:

Boehringer Ingelheim, Eli Lilly, AbbVie, Gilead, AstraZeneca, BMS, Chugai, Daiichi-Sankyo, Eisai, Pfizer, Mitsubishi-Tanabe, GSK, Grant/research support from: Asahi-Kasei, AbbVie, Chugai, Eisai, Takeda, Daiichi-Sankyo, Boehringer Ingelheim, Tsutomu Takeuchi Speakers bureau: AbbVie GK, AYUMI, BMS, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Gilead Sciences Inc., Janssen Pharm K.K., Mitsubishi-Tanabe, Pfizer Japan, Sanofi K.K., Consultant of: AbbVie GK, Astellas, Chugai, Eli Lilly Japan, Gilead Sciences Inc., Janssen Pharm K.K, Mitsubishi Tanabe, Pfizer Japan, Grant/research support from: Astellas, AYUMI, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, AbbVie GK, Asahi Kasei Pharma, Mitsubishi Tanabe, Nippon Kayaku, UCB Japan, Paul Van Hoek Consultant of: AOP Health, Aspen, Astellas, Galapagos, Sanofi-Genzyme, Employee of: Janssen, MSD, Schering-Plough, Pieter-Jan Stiers Employee of: Galapagos, Vijay Rajendran Shareholder of: Galapagos, Employee of: Galapagos, Katrien Van Beneden Shareholder of: Galapagos, Employee of: Galapagos, Jacques-Eric Gottenberg Consultant of: AbbVie, BMS, Galapagos, Gilead, Lilly, MSD, Novartis, Pfizer, Grant/research support from: BMS, Pfizer, Gerd Rüdiger Burmester Speakers bureau: AbbVie, Amgen, BMS, Chugai, Galapagos, Lilly, Pfizer, Sanofi, Consultant of: AbbVie, Amgen, BMS, Galapagos, Lilly, Pfizer, Sanofi.

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POS0845 EFFECTS OF NINTEDANIB ON CIRCULATING BIOMARKERS IN PATIENTS WITH PROGRESSIVE FIBROSING AUTOIMMUNE DISEASE-RELATED INTERSTITIAL LUNG DISEASES

Keywords: Clinical trials, Lungs, Biomarkers

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Background: Data from the randomised placebo-controlled INBUILD trial in subjects with progressive fibrosing interstitial lung diseases (ILDs) other than idiopathic pulmonary fibrosis suggested that nintedanib may have effects on circulating levels of biomarkers of epithelial injury, inflammation and extracellular matrix (ECM) turnover.

Objectives: We investigated the effects of nintedanib on circulating biomarkers in subjects in the INBUILD trial who had pulmonary fibrosis due to autoimmune disease.

Methods: Subjects in the INBUILD trial had diffuse fibrosing ILD of >10% extent on HRCT and met criteria for progression of ILD within the prior 24 months, despite management in clinical practice. Subjects were randomised to receive nintedanib or placebo, stratified by fibrotic pattern on HRCT (usual interstitial pneumonia-like fibrotic pattern or other fibrotic patterns). Blood samples were taken at baseline and at weeks 12, 24, 36 and 52. Fold changes in adjusted mean levels of biomarkers were analysed using a linear mixed model for repeated measures. Data were log10 transformed before analysis and estimates of change from baseline were back-transformed.

Results: Of 663 subjects, 170 had autoimmune disease-related ILDs; 82 of these subjects received nintedanib and 88 received placebo. Over 52 weeks, there were treatment-related decreases in fold changes from baseline in levels of Krebs von den Lungen-6 (KL-6), surfactant protein D (SP-D), CA-125 (markers of epithelial injury) in subjects who received nintedanib versus placebo (Figure 1). The most pronounced difference between nintedanib and placebo was in CA-125. The effect of nintedanib on CA-125 was observed as early as week 12. Small decreases in fold changes from baseline in soluble intercellular adhesion molecule (s-ICAM) (a marker of inflammation) and in C3M and pro-C6 (markers of ECM turnover) were observed in subjects who received nintedanib versus placebo (Figure). No notable trends were observed for the other biomarkers assessed.

Conclusion: In subjects with progressive fibrosing autoimmune disease-related ILDs, nintedanib reduced circulating levels of markers of epithelial injury, with the most pronounced effect observed on CA-125. The treatment-related decreases in these markers in subjects with autoimmune disease-related ILDs were similar to those observed in subjects with other ILDs.

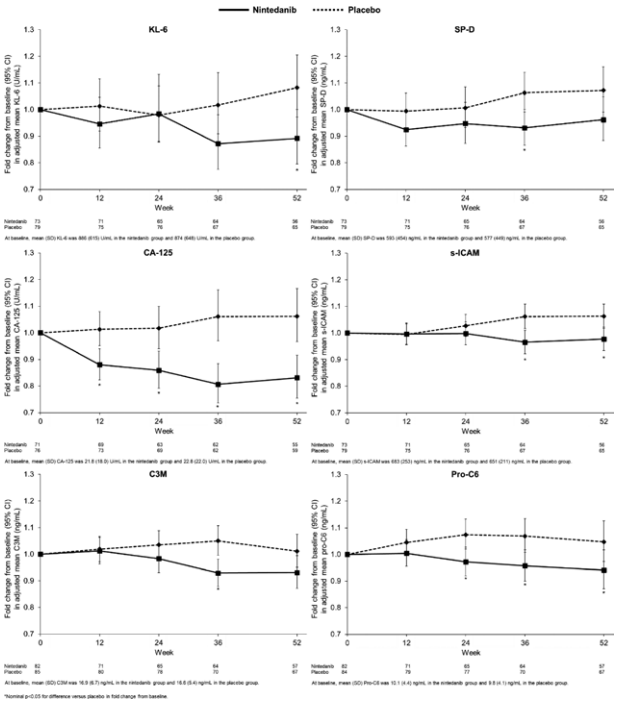


Figure 1. Fold changes from baseline in circulating biomarkers over 52 weeks in subjects with progressive fibrosing autoimmune disease-related ILDs in the INBUILD trial.

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Disclosure of Interests: Toby Maher Speakers bureau: Boehringer Ingelheim, Roche/Genentech, United Therapeutics, Consultant of: AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, GlaxoSmithKline, MSD, Roche/Genentech, United Therapeutics, UCB, Grant/research support from: AstraZeneca, GlaxoSmithKline, UCB, Francesco Bonella Speakers bureau: Boehringer Ingelheim, Roche, Sanofi, Consultant of: Boehringer Ingelheim, Roche, Sanofi, Shervin Assassi Speakers bureau: Integrity Continuing Education, Consultant of: Abbvie, AstraZeneca, aTyR, Boehringer Ingelheim, CSL Behring, TeneoFour, Grant/research support from: Boehringer Ingelheim, Janssen, Momenta, Imre Noth Consultant of: Boehringer Ingelheim, Genentech, Sanofi, Grant/research support from: Veracyte, Claudia Diefenbach Employee of: Boehringer Ingelheim, Carina Ittrich Employee of: Boehringer Ingelheim, Klaus Rohr Employee of: Boehringer Ingelheim, Martin Kolb Speakers bureau: Boehringer Ingelheim, Roche, Consultant of: Abbvie, Algernon Pharmaceuticals, Bellerophon Therapeutics, Boehringer Ingelheim, CSL Behring, DevPro Biopharma, Horizon Therapeutics, LabCorp, MitoImmune Therapeutics, Nitto Denko, Pieris Pharmaceuticals, Roche, ShouTi, United Therapeutics, Grant/research support from: Boehringer Ingelheim, Pieris Pharmaceuticals, Roche, ShouTi.

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POS0846 EFFICACY, SAFETY, AND RECURRENCE OF IGURATIMOD COMBINED WITH CSDMARDS TREATMENT IN RHEUMATOID ARTHRITIS: A PROSPECTIVE REAL-WORLD STUDY

Keywords: Disease-modifying drugs (DMARDs), Clinical trials, Rheumatoid arthritis

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Background: Iguratimod (IGU) is widely used in the treatment of rheumatoid arthritis (RA) and has been considered the first-line treatment option in many countries. The efficacy and safety of IGU combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) therapy have been

confirmed by many studies [1]. Only a few studies focused on the long-term efficacy and safety of IGU treatment, and the maintenance strategy after short-term remission (REM) still needs to be explored.

Objectives: To observe the long-term efficacy, safety, and recurrence of IGU combination with csDMARDs in the treatment of active RA and the characteristic of patients who obtain the most benefit from IGU.

Methods: The study was conducted in China (ClinicalTrials.gov ID: NCT03855007). Patients who matched the 2010 ACR/EULAR RA criteria or the 2014 early rheumatoid arthritis (ERA) criteria [2] were recruited. According to patientsicalTrials.gov ID: NCT03855007). Patients who matched the 2010 ACR/EULAR RA criteria or the 2014 early rheumatoid arthritis (ERA) criteria enefit from IGU.on with conventiond follow-up from baseline to week 96 regularly. We divided them into three groups according to whether and when to reduce the drugs: maintained (MA), reducing the dose of IGU, MTX, and LEF after (AF) or before (BF) low disease activity (LDA), or REM was achieved. The proportion of LDA or REM of DAS28-ESR achieved at week 96, the ratio of ACR20, ACR50, ACR70, the recurrence (loss of LDA status and the increase of DAS28-ESR ≥ 0.6 [3]), and the occurrence of adverse events (AE) were investigated. The chi-square test or long-rank test analyzed the corresponding statistical differences.

Results: A total of 246 patients were enrolled in this study, and 131 (53.3%) participants completed the 96-week follow-up. Efficacy analysis found that the proportion of achieving ACR20 reached a plateau after 24 weeks, while there was a sustained increase in the LDA and REM ratio of DAS28-ESR (week 24: 57.25% vs. week 96: 68.70%, p = 0.06), ACR50 (66.41% vs. 77.86%, p = 0.01) and ACR70 (22.90% vs. 41.98%, p < 0.01) (**Figure 1 A, B**). Further subgroup analysis revealed the expected effects of age, gender, and disease duration on whether achieved the LDA or REM at 96 weeks. Moreover, the time of IGU, MTX, and LEF reduction also played an essential role in long-term treatment. There was no difference in the improvement of DAS28-ESR between the MA (n=15) and reduction (AF+BE) groups. We found that patients in the AF group (n=73) were able to achieve and maintain LDA or REM and ACR50 responses better than the BE group (n=43) (**Figure 1 C**). There was no statistical difference in the incidence of AE between BE and AF groups (p = 0.44). During the follow-up period, 48 patients had a relapse of the disease in the AF and BE groups. The subgroup analysis found that drug reduction after REM was more recommended in patients with a diagnosis of RA (vs. ERA), disease duration ≥ 2 years, age < 45 years, and morning stiffness <1 hour (**Figure 1 D**) for maintaining long-term LDA or REM (p < 0.05).

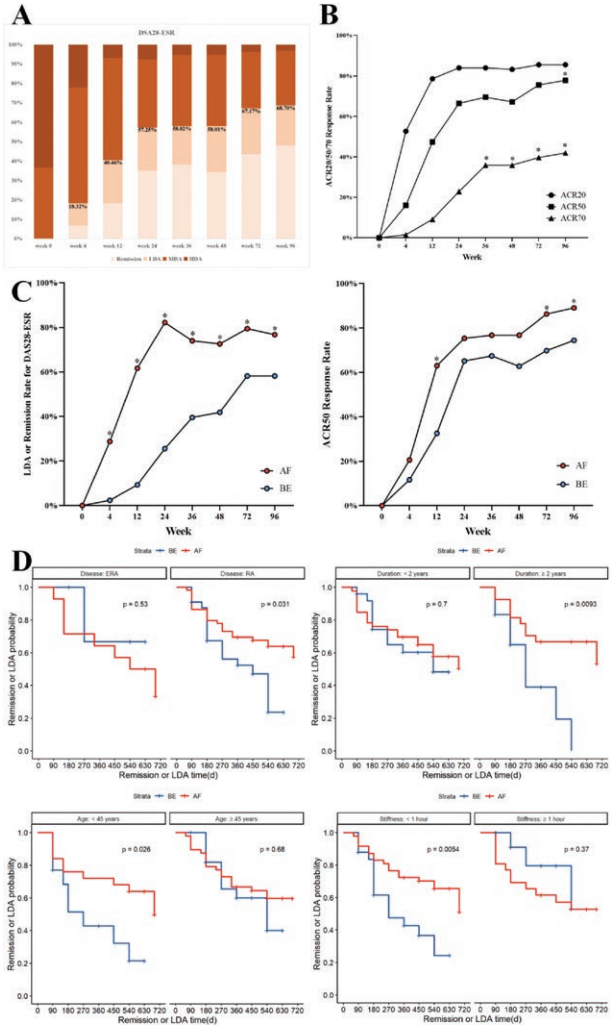


Figure 1. The efficacy and recurrence of IGU combination treatment for patients who completed the 96-week follow-up. (A) The rate of achieving LDA or REM of DAS28-ESR; (B) The rate of achieving ACR20, ACR50, and ACR70, * p < 0.05, compared to week 24; (C) The rate of achieving LDA or REM of DAS28-ESR, ACR50 in AF and BE groups, * p < 0.05, compared to the BE group; (D) The Kaplan-Meier curves of AF and BE subgroup analysis according to the disease stage, duration, age and morning stiffness.

Conclusion: The RA patients could achieve deeper REM and sustained after long-term treatment of IGU combination with csDMARDs. LDA or REM should be achieved before reducing the dose of IGU and csDMARDs, especially for the long-course, younger, with shorter morning stiffness RA patients.

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POS0847

UPADACITINIB AS MONOTHERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PRIOR INADEQUATE RESPONSE TO METHOTREXATE: RESULTS AT 260 WEEKS FROM THE SELECT-MONOTHERAPY STUDY

Keywords: Rheumatoid arthritis, Targeted synthetic drugs, Safety

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Background: Upadacitinib (UPA), an oral JAK inhibitor, was shown to be safe and effective in improving the signs and symptoms of moderate-to-severe RA through 84 weeks (wks) when administered as monotherapy in patients (pts) with a prior inadequate response to MTX in the phase 3 SELECT-MONOTHERAPY trial (NCT02706951).[1]

Objectives: To evaluate the efficacy and safety of UPA monotherapy up to wk 260 from the long-term extension (LTE) of SELECT-MONOTHERAPY.

Methods: Pts with active RA on stable MTX were randomly assigned to either continue MTX (cMTX) or switch to UPA monotherapy at 15 mg (UPA15) or 30 mg (UPA30) once daily (QD) during the 14-wk randomized, double-blind treatment period. From wk 14, the start of the LTE, pts receiving cMTX were switched to UPA15 or 30 per pre-specified assignment at baseline; pts randomly assigned to UPA15 or 30 continued their initial treatment assignment. After the study protocol was amended (13 December 2019), all pts treated with UPA30 were eventually switched to UPA15 (approved dose). Efficacy outcomes through wk 260 are presented by randomized treatment group and reported as observed and using non-responder imputation. Safety results are presented based on actual treatment received with treatment-emergent adverse events (TEAEs) summarized per 100 pt years (PY) of exposure through a cut-off date of 10 August 2022, when all pts completed wk 260.

Results: Of 648 pts randomized, 299 (46%) discontinued the study drug by wk 260 primarily due to AEs (16%), consent withdrawal (12%), or other reasons (11%). At wk 260, pts on UPA maintained or further demonstrated clinical improvement across various endpoints; similar efficacy outcomes were also observed among pts who switched from cMTX to UPA15 or 30 (**Table 1**). As observed, over three-quarters of pts achieved low disease activity based on CDAI and DAS28(CRP) at wk 260. Total PY of exposure were 1111.0 for UPA15, 812.5 for UPA30, and 300.2 for UPA15

switched from UPA30. The most frequently reported TEAEs were urinary tract infection, creatine phosphokinase (CPK) elevation, upper respiratory tract infection, nasopharyngitis, bronchitis, and RA worsening/flare. COVID-19 pneumonia was the most common serious AE. Pts on UPA30 had higher rates of herpes zoster (HZ), hepatic disorder, neutropenia, lymphopenia, and CPK elevation than pts on UPA15; rates of serious infection and malignancy excluding non-melanoma skin cancer (NMSC) were similar between UPA doses (**Figure 1**). Most HZ events affected 1–2 dermatomes with 2 ophthalmic (UPA15; 0.2 E/100 PY) and 1 disseminated (UPA30; 0.1 E/100 PY) cases reported. Eleven adjudicated MACE (UPA15: 0.5 E/100 PY; UPA30: 0.7 E/100 PY) and 10 adjudicated VTE (UPA15: 0.6 E/100 PY; UPA30: 0.4 E/100 PY; UPA15 switched from UPA30: 0.3 E/100 PY) all occurred in pts with ≥ 1 cardiovascular risk factor. Through wk 260, 16 deaths were reported (10 treatment-emergent) with 5 related to COVID-19 infection.

Conclusion: UPA monotherapy continued to be effective in treating RA signs and symptoms through wk 260. No new safety signals were identified with longer-term exposure to UPA, consistent with prior findings[1–3] and the established safety profile of UPA across indications.

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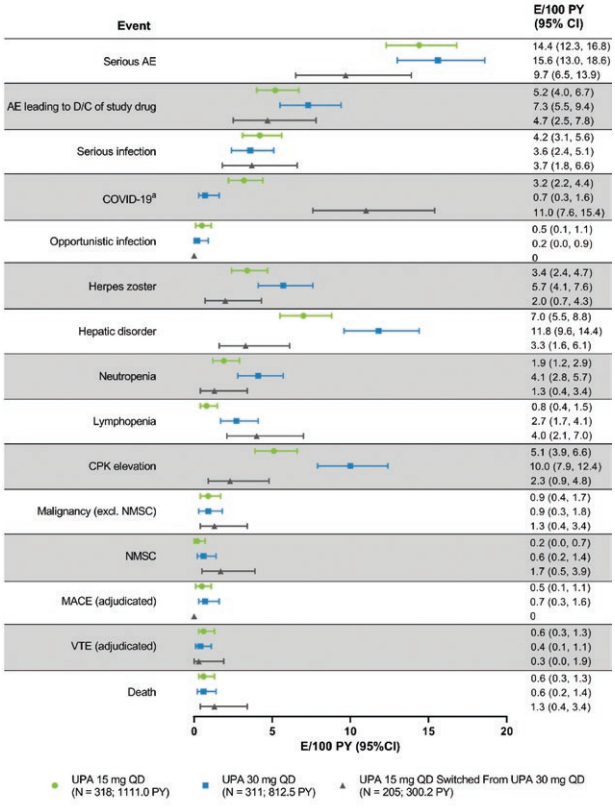
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Table 1. Efficacy Endpoints at Week 260 (AO and NRI)

Response, %	cMTX -> UPA 15 mg		cMTX ->UPA 30 mg		UPA 15 mg		UPA 30 mg	
	AO [a] N=57 – 65	NRI N=108	AO [a] N=54 – 56	NRI N=108	AO [a] N=107 – 114	NRI N=217	AO [a] N=117 – 123	NRI N=215
ACR20/50/70	89/82/61	48/43/32	86/75/57	43/39/30	90/76/59	50/42/32	93/80/63	50/44/34
DAS28(CRP) ≤3.2/< 2.6	86/72	43/36	84/67	41/33	89/71	42/34	84/76	44/40
CDAI ≤10/≤2.8	88/49	48/28	82/40	40/20	86/42	43/21	79/54	42/29
Boolean Remission	39	21	32	17	32	16	42	23

AO, as observed; cMTX, continue MTX; NRI, non-responder imputation; UPA, upadacitinib.[a]AO response rate was calculated from patients with observed records only.

Figure. TEAEs Through 260 Weeks (E/100 PY, 95% CI)



CI, confidence interval; CPK, creatine phosphokinase; D/C, discontinuation; E/100 PY, events per 100 patient-years; NMSC, non-melanoma skin cancer; QD, once daily; TEAEs, treatment-emergent adverse events; UPA, upadacitinib.
[a]Most patients were already switched to UPA 15 mg QD during the pandemic and hence there was a higher rate of COVID-19 observed with UPA 15 mg QD vs UPA 30 mg QD.

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POS0848

DISCONTINUATION AND EFFECTIVENESS OF BARICITINIB IN RHEUMATOID ARTHRITIS ACCORDING TO PATIENT AGE AND PRIOR TREATMENT: 2-YEAR DATA FROM THE EUROPEAN COHORT OF THE RA-BE-REAL STUDY

Keywords: Rheumatoid arthritis, Registries, Real-world evidence

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Background: Baricitinib (BARI), an oral selective JAK1/2 inhibitor, is approved for treating adults with moderate to severe active rheumatoid arthritis (RA). RA-BE-REAL is an ongoing 3-year, multinational, prospective, observational study of adult patients with RA starting BARI or any biologic or other targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD).

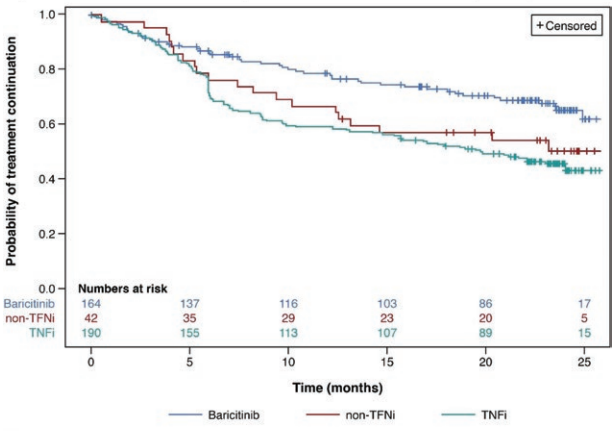
Objectives: To report treatment discontinuation and effectiveness in patients with RA receiving BARI or b/tsDMARD, based on prior b/tsDMARD use (experienced/naïve) and age <65 years versus ≥65 years, in Europe.

Methods: Patients with RA initiating treatment with BARI 2 or 4 mg (cohort A) or any b/tsDMARD (cohort B) for the first time were included. The primary outcome is time to discontinuation (TTD) for any cause (excluding sustained response) at 2 years; TTD at 6 months has been published [1]. Discontinuation (Kaplan-Meier analyses and rates) and effectiveness (Clinical Disease Activity Index [CDAI] low disease activity [LDA] and remission rates) of treatment to 2 years, based on prior b/tsDMARD status (experienced/naïve) and age (<65/≥65 years) were analysed post-hoc and descriptively for cohort A and subgroups of cohort B.
Results: Key baseline characteristics of 1008 RA patients and effectiveness at 2 years for the subgroups in this analysis are shown in the Table 1. Numerically more BARI-treated patients were receiving monotherapy (Table 1). By 2 years, 31.1%, 54.7% and 47.6% of b/tsDMARD-naïve patients aged <65 years receiving BARI, tumour necrosis factor inhibitors (TNFi) and non-TNFi, respectively, had discontinued treatment; corresponding discontinuation rates for b/tsDMARD-naïve patients aged ≥65 years were 28.4%, 65.6% and 44.0%, b/tsDMARD experienced patients aged <65 years were 47.9%, 59.0% and 65.5% and b/tsDMARD experienced patients aged ≥65 years were 42.0%, 78.3% and 66.7%. An example of TTD is presented in the Figure 1. Consistent CDAI LDA and remission rates were observed with BARI regardless of age and prior treatment (Table 1).
Conclusion: Two-year discontinuation rates and effectiveness with BARI in a real-world setting were consistent irrespective of previous treatment or patient age.

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Figure. Time to discontinuation over 2 years in b/tsDMARD-naïve patients aged <65 years



Patients with sustained clinical response were not included in this analysis

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POS0849

LONG-TERM SAFETY AND EFFICACY OF UPADACITINIB OR ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: 5-YEAR DATA FROM THE SELECT-COMPARE STUDY

Keywords: Safety, Rheumatoid arthritis, Targeted synthetic drugs

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Background: Upadacitinib (UPA) is an oral reversible Janus kinase inhibitor. In patients (pts) with RA, UPA 15 mg once daily (QD) demonstrated better clinical responses at 12 weeks (wks) vs adalimumab (ADA) 40 mg every other week (EOW) in the phase 3 SELECT-COMPARE study; these were maintained through 3 years (yrs) in the ongoing long-term extension (LTE), along with an acceptable safety profile.[1,2]
Objectives: To assess the safety and efficacy of UPA vs ADA through 5 yrs in the SELECT-COMPARE LTE.
Methods: Pts receiving background methotrexate were randomized 2:2:1 to UPA 15 mg QD, placebo (PBO), or ADA 40 mg EOW. Rescue (PBO to UPA, UPA to ADA, or ADA to UPA) was mandated for lack of response (<20% improvement in tender or swollen joint counts at wks 14, 18, or 22), or failure to achieve Clinical Disease Activity Index (CDAI) low disease activity (LDA) at wk 26. All remaining PBO pts switched to UPA at wk 26. Pts who completed the 48-wk double-blind period could continue to receive open-label UPA or ADA in the LTE for up to 10 yrs total. Rates of treatment-emergent adverse events (TEAEs) and AEs of special interest were calculated per 100 pt-yrs through 5 yrs for all pts receiving UPA or ADA. Efficacy assessments at 5 yrs were performed by original randomized group for CDAI LDA (≤10) and remission (≤2.8), and disease activity score for 28-joints C-reactive protein (DAS28[CRP]) ≤3.2 and <2.6. Radiographic progression (change from baseline in modified total Sharp score [mTSS]) and proportion of pts with no radiographic progression (change from baseline in mTSS ≤0) were assessed at 192 wks (latest available timepoint; data collected at wks 96/192/520 only) by treatment sequence. No formal statistical comparisons were performed.

Table 1. Baseline data and effectiveness of treatment at 2 years in subgroups based on b/tsDMARD-naïve and -experienced patients aged <65 and ≥65 years[a]

			Age, years[b]	Female[c]	Duration of RA, years[b]	Monotherapy[c]	Baseline CDAI[b]	2-year CDAI remission[d]	2-year CDAI LDA[d]
Naïve <65 years	Cohort A (N=164)	BARI	50.8±9.5	120 (73.2)	5.8±6.4	66 (40.2)	23.0±11.0	20/86 (23.3)	42/86 (48.8)
	Cohort B (N=251)[e]	TNFi (N=192)	49.5±11.0	142 (74.0)	4.9±6.1	48 (25.0)	24.8±13.3	34/130 (26.2)	47/130 (36.2)
		Non-TNFi bDMARD (N=42)	53.1±9.6	32 (76.2)	9.0±8.6	11 (26.2)	20.5±10.5	4/25 (16.0)	10/25 (40.0)
Naïve ≥65 years	Cohort A (N=81)	BARI	73.3±5.7	63 (77.8)	8.9±9.8	49 (60.5)	23.4±11.5	12/37 (32.4)	16/37 (43.2)
	Cohort B (N=93)[e]	TNFi (N=61)	72.7±4.7	37 (60.7)	10.8±11.0	14 (23.0)	24.3±13.1	8/32 (25.0)	16/32 (50.0)
		Non-TNFi bDMARD (N=25)	74.4±5.8	17 (68.0)	8.8±11.5	5 (20.0)	24.8±11.6	4/13 (30.8)	4/13 (30.8)
Experienced <65 years	Cohort A (N=165)	BARI	52.3±9.4	131 (79.4)	11.8±8.5	88 (53.3)	23.9±11.9	21/92 (22.8)	33/92 (35.9)
	Cohort B (N=142)[e]	TNFi (N=61)	48.5±12.4	48 (78.7)	8.6±8.9	29 (47.5)	20.4±11.4	7/37 (18.9)	15/37 (40.5)
		Non-TNFi bDMARD (N=58)	51.6±9.8	51 (87.9)	11.3±10.2	16 (27.6)	21.5±8.9	3/27 (11.1)	14/27 (51.9)
Experienced ≥65 years	Cohort A (N=100)	BARI	72.7±5.6	77 (77.0)	15.1±9.7	55 (55.0)	24.2±11.6	11/51 (21.6)	26/51 (51.0)
	Cohort B (N=77)[e]	TNFi (N=23)	72.7±5.6	14 (60.9)	12.4±12.8	10 (43.5)	24.9±13.0	2/9 (22.2)	3/9 (33.3)
		Non-TNFi bDMARD (N=36)	71.5±4.4	25 (69.4)	16.4±11.9	16 (44.4)	26.4±13.2	2/16 (12.5)	8/16 (50.0)

[a] Effectiveness data were not available for all patients[b] Mean±standard deviation[c] n (%)[d] n/N (%)[e] An additional 65 patients in total received other tsDMARDs (7–23 per group); data for these patients are not shown because of the small numbers

Results: Through 5 yrs, 1417 pts were exposed to UPA (4497 pt-yrs) and 579 to ADA (1472 pt-yrs). UPA was generally well tolerated, with similar rates of TEAEs, serious TEAEs, TEAEs leading to discontinuation of study drug, and COVID-related TEAEs vs ADA (**Figure 1**). Rates of most AEs of special interest with UPA were similar vs ADA, except for numerically higher rates of herpes zoster, creatine phosphokinase elevation, lymphopenia, and hepatic disorder (mainly transaminase elevations) with UPA. In the 651 and 327 pts originally randomized to UPA and ADA, respectively, greater proportions of pts achieved CDAI LDA and remission, and DAS28(CRP) scores ≤3.2 and <2.6, with UPA vs ADA (**Table 1**). Through 192 wks, similar proportions of pts treated with UPA vs ADA had no radiographic progression; mean changes from baseline in mTSS were similar, except for a numerically smaller change with continuous UPA (**Table 1**).

Conclusion: The safety profile of UPA over 5 yrs was consistent with the 3-yr results and the integrated phase 3 safety analysis.[1,2] Consistent with the 3-yr analyses,[2] UPA continued to show numerically better clinical responses than ADA at 5 yrs. Radiographic progression remained similarly low through 192 wks with UPA and ADA.

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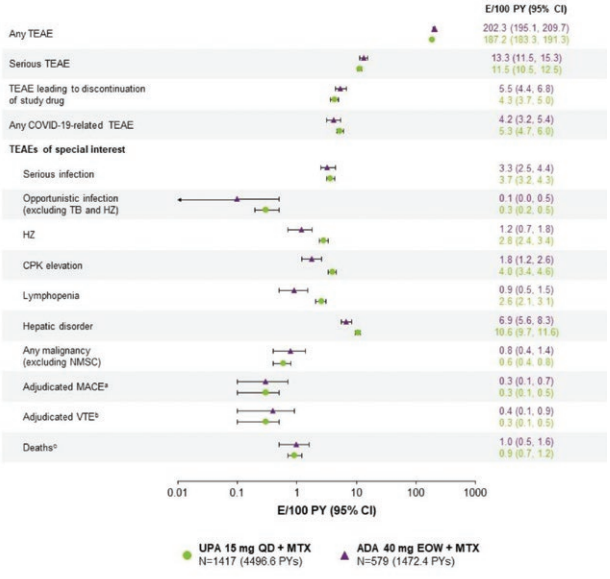
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Table 1. Efficacy endpoints

At 5 yrs, by original randomized group (non-responder imputation)	UPA N=651[a,b]		ADA N=327[a,c]		
CDAI ≤10	36.4 (32.7, 40.1)		26.9 (22.1, 31.7)		
CDAI ≤2.8	24.6 (21.3, 27.9)		18.7 (14.4, 22.9)		
DAS28(CRP) ≤3.2	34.7 (31.1, 38.4)		24.8 (20.1, 29.4)		
DAS28(CRP) <2.6	31.8 (28.2, 35.4)		23.2 (18.7, 27.8)		
At 192 wks, by treatment sequence (as observed)	**PBO to UPA N=442**	**UPA N=288**	**UPA to ADA N=150**	**ADA N=109**	**ADA to UPA N=111**
Radiographic progression (change from baseline in mTSS, mean [95% CI])	1.3 (0.8, 1.7)	0.5 (0.2, 0.9)	1.7 (0.7, 2.8)	1.2 (0.5, 1.9)	0.9 (0.2, 1.5)
No radiographic progression (mTSS change from baseline ≤0)	77.1 (73.2, 81.1)	80.9 (76.4, 85.4)	74.0 (67.0, 81.0)	78.0 (70.2, 85.8)	77.5 (69.7, 85.2)

Data are % of pts (95% confidence interval) unless otherwise stated. [a]Pts rescued at or before wk 26 were considered non-responders. [b]252 rescued. [c]159 rescued.

Figure. Exposure-adjusted event rates of TEAEs through 5 yrs



Data for all pts receiving UPA or ADA, including exposure to rescue treatment after switching, with assignment based on drug exposure at the time of event.
[a]Includes cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke.
[b]Defined as deep vein thrombosis and pulmonary embolism (fatal and non-fatal).
[c]Includes treatment-emergent deaths (occurring ≤30 days after last dose of UPA or ≤70 days after last dose of ADA) and non-treatment-emergent deaths (occurring >30 days after last dose of UPA or >70 days after last dose of ADA).

CI, confidence interval; CPK, creatine phosphokinase; E, event; HZ, herpes zoster; MACE, major adverse cardiovascular event; MTX, methotrexate; NMSC, non-melanoma skin cancer; TB, tuberculosis; VTE, venous thromboembolic event.

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POS0850 **WITHDRAWN**

POS0851

REAL-WORLD EXPERIENCE WITH FILGOTINIB (FIL) FOR RHEUMATOID ARTHRITIS (RA) IN GERMANY: A RETROSPECTIVE CHART REVIEW

Keywords: Rheumatoid arthritis, Real-world evidence, Targeted synthetic drugs

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Background: Randomized controlled trials have demonstrated the efficacy and safety of FIL for moderate to severe RA;[1–3] however, real-world evidence is lacking.
Objectives: To evaluate the rationale for starting FIL in patients (pts) with moderate to severe RA in Germany. Secondary objectives were to describe pt characteristics, concomitant use of glucocorticoids (GCs) and/or methotrexate (MTX), and prior treatment with disease-modifying antirheumatic drugs (DMARDs). Disease activity was an exploratory objective.
Methods: This multicenter retrospective chart review included pts aged ≥18 years with confirmed moderate to severe RA, who initiated FIL before 1 December 2021, with medical records available for ≥6 months prior to initiating FIL (index date) or since initial diagnosis. Data were collected using electronic case report forms; collection was completed on 2 May 2022. Reasons for starting FIL were recorded at index, based on pre-set response categories. Disease activity was assessed in pts with available data using the Clinical Disease Activity Index and Disease Activity Score for 28 joints with C-reactive protein, 3 and 6 months after the index date. Discontinuation of FIL (including reasons) was assessed during the available follow-up of 12 months.
Results: This study included 301 pts with RA from 20 practices across Germany. Selected baseline pt characteristics and comorbidities are summarized (**Table 1**). Overall, pts had previously been treated with conventional synthetic (cs) DMARDs (n=282, 93.7%), GCs (n=241, 80.1%), biologic (b) DMARDs (n=199, 66.1%), and targeted synthetic (ts) DMARDs (n=113, 37.6%). One, two, and ≥3 prior advanced DMARDs were received by 87 (28.9%), 51 (16.9%), and 90 (29.9%) pts, respectively; 73 pts (24.3%) were advanced DMARD-naïve. Last treatments before initiating FIL included csDMARDs (n=120, 43.0%), bDMARDs (n=97, 34.8%), GCs (n=88, 31.5%), and tsDMARDS (n=63, 22.6%). Most pts received FIL as monotherapy (n=220, 73.1%); pts received FIL + GCs (n=32, 10.6%), FIL + MTX (n=26, 8.6%), and FIL + MTX + GCs (n=23, 7.6%). Reasons for initiating FIL included oral administration (n=236, 78.4%), fast onset of action (n=201, 66.8%), administration as monotherapy (n=197, 65.4%), good controllability (n=176, 58.5%), good benefit/risk ratio (n=155, 51.5%), low potential for drug-drug interactions (n=97, 32.2%), dosage adjustment in elderly pts (n=35, 11.6%), lower risk of herpes zoster (n=45, 15.0%), and inefficacy of previous therapies (n=10, 3.3%). Disease activity during the follow-up is shown (**Figure 1**). In total, 43 pts (14.3%) discontinued FIL during the follow-up because of: lack of efficacy (n=26, 8.6%), intolerance or adverse drug reaction (n=12, 4.0%), lack of drug adherence (n=4, 1.3%), and remission (n=1, 0.3%).
Conclusion: In this real-world setting in Germany, reasons for initiating FIL were related to general Janus kinase inhibitor, as well as FIL-specific, attributes. Most pts received FIL as monotherapy. FIL was effective and generally well tolerated; however, longer-term data are needed.

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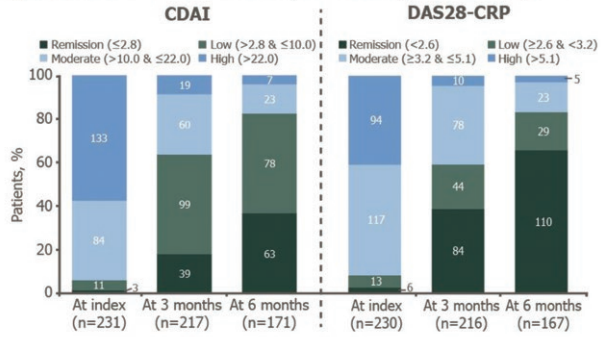
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Table 1. Selected baseline patient characteristics and comorbidities

	Total N=301
Age at index date, mean (SD)	59.2 (12.4)
Age groups, n (%)	
<65 years	202 (67.1)
≥65 to 74 years	62 (20.6)
≥75 years	37 (12.3)
Female sex, n (%)	244 (81.1)
CDAI, mean (SD)	25.4 (10.9), N=231
DAS28-CRP, mean (SD)	4.8 (1.1), N=230
Disease duration, years, n (%)	
<1	11 (3.7)
1–5	86 (28.6)
5–10	89 (29.6)
>10	115 (38.2)
Follow-up, months, mean (SD)	7.9 (4.0)
Current/ex-smoker, n (%)	43 (14.3)/46 (15.3)
Any cardiovascular risk factor,* n (%)	140 (46.5)
Obesity [BMI ≥30 kg/m^2], n (%)	35 (11.6)
Cancer, n (%)	12 (4.0)
Inflammatory bowel disease, n (%)	6 (2.0)

*Patients may have ≥1 cardiovascular risk factor.BMI, body mass index; CDAI, Clinical Disease Activity Index; DAS28-CRP, Disease Activity Score for 28 joints with C-reactive protein; SD, standard deviation.

Figure. Distribution of disease activity scores during the follow-up period



Values in bars are number of patients.
CDAI, Clinical Disease Activity Index; DAS28-CRP, Disease Activity Score for 28 joints with C-reactive protein.

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Disclosure of Interests: Olaf Schultz Speakers bureau: Abbott, BMS, Galapagos, MSD, Novartis, Pfizer, Christoph Fiehn Speakers bureau: AbbVie, AstraZeneca, Boehringer Ingelheim, Celgene, Galapagos, Janssen, Lilly, Medac, MSD, Novartis, Pfizer, Sanofi, UCB, Consultant of: Boehringer Ingelheim, Galapagos, Lilly, Christian Kneitz Speakers bureau: AbbVie, Berlin-Chemie, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Chugai, Galapagos, Gilead, GSK, Janssen, Lilly, Medac, MSD, Novartis, Oxford Immunotec, Pfizer, Roche, Sanofi, Takeda, UCB, Consultant of: AbbVie, Boehringer Ingelheim, Galapagos, Janssen, Novartis, Nils Picker: None declared, Daniel Kromer: None declared, Monia Zignani Shareholder of: Galapagos, Employee of: Galapagos, Francesco De Leonardis Employee of: Galapagos, Hans-Dieter Orzechowski Shareholder of: Gilead Sciences, Employee of: Galapagos Biopharma GmbH Germany, Margot Gurrath Shareholder of: Gilead Sciences, Employee of: Galapagos Biopharma GmbH Germany, Klaus Krueger Speakers bureau: Galapagos, Gilead, Consultant of: Galapagos, Gilead.

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POS0852

REAL LIFE DATA OF FILGOTINIB IN RHEUMATOID ARTHRITIS PATIENTS: DATA FROM ITALIAN GISEA REGISTRY

Keywords: Targeted synthetic drugs, Rheumatoid arthritis, Registries

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Background: In the age of targeted-synthetic disease-modifying antirheumatic drugs (tsDMARDs), filgotinib represents the last JAK inhibitor available in Europe for rheumatoid arthritis (RA). Filgotinib is characterized by predominantly inhibition of JAK1 and its efficacy and safety have been highlighted by phase 2/3 studies, but no real-life data in RA are currently available.

Objectives: The aim of this study was to evaluate the effectiveness and safety profile of filgotinib in real-life setting in RA patients included in Italian GISEA (Group for the Study of Early Arthritis) registry.

Methods: For this study, data from RA patients treated with filgotinib recorded in Italian GISEA registry were analysed. Disease activity scores and patients reported outcomes (PROs) were compared at baseline and six months follow-up using paired t-tests. The retention rate was estimated by the Kaplan-Meier method, while a cox regression model was used to search for possible factors influencing drug survival.

Results: One hundred and seventy-nine patients (female 89.4%, age 57.8±12 years, FR/ACPA+ 64.3%, current/former smoker 31.8%) included in GISEA registry started filgotinib for active RA. Most patients were taking filgotinib as second (23.5%) or further (43%) b/tsDMARDs line of treatment. Filgotinib was used in monotherapy in 66.5% of patients, while 52% were not on treatment with glucocorticoids (GCs) at baseline. All demographic and clinical data are reported in Table 1. A follow-up visit was available for 122 patients (mean time of first follow-up visit: 4±2 months). As shown in table 1, we observed a decrease of all disease activity scores and PROs. At first follow-up visit, 67.8% of patients were in remission/low disease activity according to CDAI and 65.4% according to SDAI. Kaplan-Meyer analysis highlighted that drug persistence was similar either in monotherapy or combination therapy (Figure 1a), and irrespective of GCs at

Table 1. Demographic and disease characteristics at baseline and at first follow-up visit (T1) of RA patients treated with Filgotinib.

Variables		baseline (n. 179)	T1 (n. 122)
Age	mean (SD), years	57.8 (12.7)	58 (12.6)
Gender	n. (%), female	160 (89.4)	110 (90.2)
	n. (%), man	19 (10.6)	12 (9.8)
BMI	n. (%), underweight	4 (3.8)	4 (5.3)
	n. (%), heathy weight	50 (48.1)	36 (47.4)
	n. (%), overweight	21 (20.2)	15 (19.7)
	n. (%), obese	29 (27.9)	21 (27.6)
Smokers	n. (%), currently smoker	13 (13.8)	8 (13.5)
	n. (%), former smoker	17 (18)	12 (20.3)
	n. (%), never smoker	64 (68.1)	39 (66.1)
IgG RF/ACPA +	n. (%)	74 (64.3)	54 (71.1)
VAS pain	mean (SD)	63.1 (29.1)	35 (30.7)***
VAS PtGA	mean (SD)	60 (26.7)	35 (29)***
VAS PhGA	mean (SD)	44 (25.4)	20.9 (23)***
TJC28	mean (SD)	5.4 (5)	2.7 (3.8)**
SJC28	mean (SD)	3.3 (3.5)	1.3 (2.2)***
DAS28-ESR	mean (SD)	4.6 (1.3)	3.3 (1.4)**
CDAI	mean (SD)	19.1 (11.3)	9.6 (9.5)**
SDAI	mean (SD)	20.5 (12)	10.3 (10)**
HAQ-DI	mean (SD)	1.3 (0.7)	0.9 (0.7)***
glucocorticoid	n. (%)	86 (48)	47 (38.5)**
Prednisone (equivalent), mg/die	mean (SD)	5.8 (3.7)	3.4 (2.6)*
csDMARD (in corso)	n. (%)	60 (33.5)	31 (25.4)
b/tsDMARD line	n. (%), 1^ line	60 (33.5)	/
	n. (%), 2^ line	42 (23.5)	
	n. (%), 3^ line or others	77 (43)	

Mean time of first follow-up visit: 4±2 months*p<0.05, **p<0.01, ***p<0.001

baseline (Figure 1b). However, a better persistence was observed in RA patients on first line treatment with filgotinib (Figure 1c). Thirty-five patients stopped filgotinib during follow-up, 10 for lack of efficacy, 4 for loss of efficacy, 4 for adverse events, while for the remaining cases the cause of drug discontinuation was unknown. No major cardiovascular events were reported. Finally, univariate Cox-regression model showed that b/tsDMARD naïve patients had a lower risk of drug discontinuation (naïve vs other lines: HR 0.37, 95%CI 0.20-0.86).
Conclusion: In Italian real-life setting, filgotinib confirms a good effectiveness and safety profile.

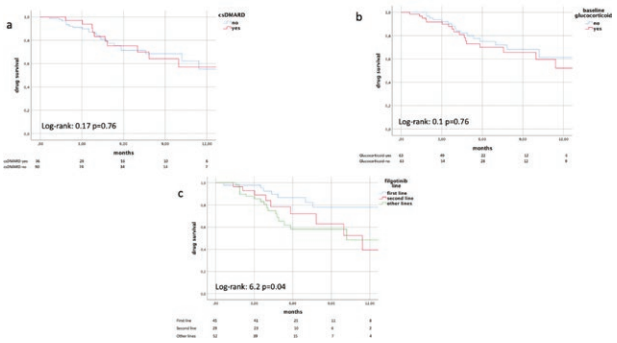


Figure 1. Survival analysis in RA patients treated with Filgotinib.

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Disclosure of Interests: None Declared.
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POS0853

EFFICACY OF FILGOTINIB (FIL) IN PATIENTS (PTS) WITH RHEUMATOID ARTHRITIS (RA): WEEK (W) 156 RESULTS FROM A LONG-TERM EXTENSION (LTE) STUDY

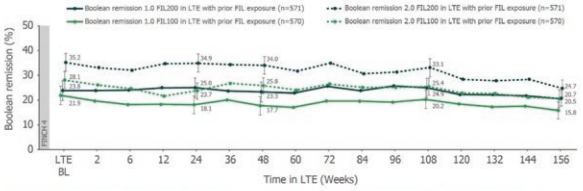
Keywords: Remission, Clinical trials, Rheumatoid arthritis

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Background: In the treatment of RA, JAK inhibitors are a valuable option to meet remission or low disease activity (LDA) treatment targets following an inadequate response (IR) or intolerance to ≥1 conventional synthetic disease-modifying antirheumatic drug (DMARD). FIL is a JAK1 preferential inhibitor available in two doses for the treatment of moderate to severe RA.
Objectives: To evaluate long-term efficacy of two doses of FIL in clinically relevant pt populations.
Methods: In this interim analysis, efficacy (non-responder imputation) of FIL 200 mg (FIL200) and 100 mg (FIL100) was assessed from LTE baseline (BL) to W156 in pts with an IR to methotrexate (MTX-IR) and biologics (bDMARD-IR), enrolled from FINCH 1 (NCT02889796) and 2 (NCT02873936) parent studies (PS), respectively, receiving ≥1 FIL dose in FINCH 4 (NCT03025308).
Results: Study design, BL characteristics and W48 outcomes for MTX-IR[1] and bDMARD-IR[2] pts were reported previously. For MTX-IR and bDMARD-IR pts who received FIL200 or FIL100 in the PS, W156 remission rates using Boolean 1.0 criteria were 20.5% and 15.8%, and 18.2% and 8.9%, respectively. Adopting the Boolean 2.0 criteria slightly increased remission rates for FIL200 and FIL100 at W156: +4.2% and +4.9% for MTX-IR pts, and +1.5% and +2.4% for bDMARD-IR pts, respectively. For pts rerandomized to FIL on entering the LTE, Boolean 2.0 criteria also increased remission rates vs Boolean 1.0. Both MTX-IR (**Figure 1**) and bDMARD-IR pts maintained long-term Boolean remission through W156 with FIL200 and FIL100, irrespective of prior FIL. Results for Disease Activity Score 28 with C-reactive protein (DAS28-CRP) <2.6, Clinical Disease Activity Index (CDAI) ≤2.8, and Simplified Disease Activity Index (SDAI) ≤3.3, and mean change from PS BL in Health Assessment Questionnaire–Disability Index (HAQ-DI) and pain are shown (**Table 1**). Similar trends in efficacy were seen for LDA and ACR response criteria.
Conclusion: In FINCH 4, both FIL200 and FIL100 showed sustained efficacy up to W156 in clinically relevant pt populations. Boolean 2.0 criteria classified more pts in remission, in line with the range reported in the validation study.[3]

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Figure. Boolean remission 1.0 and 2.0 for MTX-IR pts in FINCH 4 LTE through W156 (safety analysis set, non-responder imputation)



Safety analysis set includes enrolled pts who received ≥1 dose of study drug. Error bars are 95% confidence intervals.
Non-responder imputation: subjects with missing outcomes were set as non-responders for binary response measurements.

Table 1. Efficacy in MTX-IR and bDMARD-IR pts through W156 in FINCH 4 (safety analysis set; non-responder imputation)

		n*	DAS28-CRP <2.6 n (%)	CDAI ≤2.8 n (%)	SDAI ≤3.3 n (%)	Pain mean change (SD)	HAQ-DI mean change (SD)
				MTX-IR			
LTE BL	FIL200/ FIL200	571	344 (60.2)	190 (33.3)	195 (34.2)	–43 (26.5)	–0.95 (0.648)
	FIL100/ FIL100	570	301 (52.8)	159 (27.9)	158 (27.2)	–41 (26.1)	–0.81 (0.641)
	ADA/FIL200	128	77 (60.2)	32 (25.0)	40 (31.3)	–43 (24.4)	–0.82 (0.630)
	ADA/FIL100	130	70 (53.8)	39 (30.0)	38 (29.2)	–38 (27.4)	–0.86 (0.642)
LTE W156	FIL200/ FIL200	571	253 (44.3)	153 (26.8)	151 (26.4)	–42 (27.0)	–0.94 (0.666)
	FIL100/ FIL100	570	216 (37.9)	125 (21.9)	121 (21.2)	–38 (27.6)	–0.77 (0.645)
	ADA/FIL200	128	50 (39.1)	29 (22.7)	28 (21.9)	–40 (25.6)	–0.81 (0.642)
	ADA/FIL100	130	38 (29.2)	24 (18.5)	25 (19.2)	–33 (26.3)	–0.78 (0.639)
				bDMARD-IR			
LTE BL	FIL200/ FIL200	132	46 (34.8)	29 (22.0)	25 (18.9)	–34 (28.4)	–0.68 (0.627)
	FIL100/ FIL100	124	37 (29.8)	23 (18.5)	25 (20.2)	–31 (31.2)	–0.54 (0.063)
	PBO/FIL200	59	8 (13.6)	3 (5.1)	3 (5.1)	–17 (29.4)	–0.26 (0.583)
	PBO/FIL100	55	10 (18.2)	6 (10.9)	4 (7.3)	–21 (28.6)	–0.38 (0.604)
LTE W156	FIL200/ FIL200	132	42 (31.8)	32 (24.2)	29 (22.0)	–39 (30.4)	–0.76 (0.741)
	FIL100/ FIL100	124	31 (25.0)	17 (13.7)	14 (11.3)	–35 (28.3)	–0.70 (0.713)
	PBO/FIL200	59	15 (25.4)	9 (15.3)	8 (13.6)	–27 (30.1)	–0.67 (0.866)
	PBO/FIL100	55	12 (21.8)	7 (12.7)	8 (14.5)	–27 (25.9)	–0.58 (0.734)

*Pain and HAQ-DI: MTX-IR LTE BL FIL200/200 (n=569); LTE W156 FIL200/200 (n=414), FIL100/100 (n=405), ADA/FIL200 (n=87), ADA/FIL100 (n=83). bDMARD-IR LTE BL FIL100/100 (n=123); LTE W156 FIL200/200 (n=80), FIL100/100 (n=74), PBO/FIL200 (n=38), PBO/FIL100 (n=38). ADA, adalimumab; PBO, placebo; SD, standard deviation.

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POS0854

DRUG RETENTION OF BIOLOGIC AND TARGETED SYNTHETIC DMARDS IN KOREAN SEROPOSITIVE RHEUMATOID ARTHRITIS (RA) PATIENTS: A REAL-WORLD SINGLE-CENTER RETROSPECTIVE STUDY

Keywords: Rheumatoid arthritis, Targeted synthetic drugs, bDMARD

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Background: Despite the approval of the new janus kinase inhibitors (JAKi) for rheumatoid arthritis (RA) treatment, the real world data on the drug effectiveness of biologic DMARDs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs) including recently approved JAKi is scarce, especially in Asia.

Objectives: The purpose of this single center, retrospective study was to compare the short and long-term retention rates of b/tsDMARDs including recently approved JAKi in Korean seropositive RA patients.

Methods: This study was conducted with total 1,538 treatment courses of 1063 seropositive RA patients who started b/tsDMARDs between 2008 and 2020 at Seoul St. Mary's Hospital [adalimumab (ADA; n = 332), etanercept (ETN; n = 369), infliximab (IFX; n = 146), abatacept (ABT; n = 152), tocilizumab (TCZ; n = 299), tofacitinib (TOF; n = 136), and baricitinib (BAR; n = 104)]. Discontinuation after 1 year and 3 years from the first prescription of each drug was investigated. Kaplan–Meier estimates of time to discontinuation were conducted to compare the difference in drug retention rate for each drug in b/tsDMARDs-naïve and experienced group, respectively. Patient-level predictors for drug discontinuation were evaluated by a Cox proportional hazard model.

Results: Overall 1-year drug retention rate was as follows: from 60.1% of ADA to 90.0% of TOF in the b/tsDMARDs-naïve group & from 55.2% of IFX to 84.8% of TOF in the b/tsDMARDs-experienced group. And 3-year drug retention rate was as follows: from 36.9% of IFX to 86.5% of TOF in the b/tsDMARDs-naïve group & from 31.0% of IFX to 65.4% of TCZ in the b/tsDMARDs-experienced group. The drug discontinuation seems to be affected by several factors including previous treatment history, starting year, and specific type of b/tsDMARDs, and baseline level of erythrocyte sedimentation rate.

Conclusion: Compared to before 2015, the overall drug retention rate of b/tsDMARDs increased in Korean seropositive RA patients. TCZ and JAKi are as widely used as tumor necrosis factor-alpha inhibitors, and they were less often discontinued at 1 year and 3 years from the first prescription. Especially, drug with the highest 3-year retention rate was TOF in b/tsDMARDs-naïve group, and TCZ in b/tsDMARDs-experienced group.

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Table 1. Hazard ratio of drug discontinuation in the b/tsDMARDs-naïve and b/tsDMARDs-experienced treatment courses. (3-year follow-up group)

Variables	3-year follow-up group			
	Naïve		Experienced	
	Univariable HR (95% CI)	Multivariable HR (95% CI)	Univariable HR (95% CI)	Multivariable HR (95% CI)
Age (years), per year	0.99 (0.98-1.00)	0.99 (0.98-1.00)	1.01 (1.00-1.02)	1.01 (1.00-1.02)
RA disease duration, per year	0.99 (0.98-1.00)	0.99 (0.98-1.00)	1.01 (0.99-1.02)	
High CCI (over 4)	0.97 (0.79-1.19)		1.34 (1.02-1.75)*	1.15 (0.77-1.72)
MTX combination	1.16 (0.84-1.59)		1.10 (0.74-1.64)	
Corticosteroid combination	1.20 (0.87-1.64)		1.30 (0.87-1.93)	1.34 (0.90-2.00)
Elevated ESR (over 40mm/h)	1.60 (1.26-1.93)***	1.33 (1.06-1.67)*	1.42 (1.07-1.88)	1.28 (0.94-1.74)
Elevated CRP (over 1mg/dL)	1.09 (0.89-1.33)		1.10 (0.84-1.45)	
Type of b/tsDMARDs				
ADA	Ref	Ref	Ref	Ref
ETN	0.70 (0.54-0.89)*	0.70 (0.54-0.90)**	0.72 (0.49-1.04)*	0.66 (0.45-0.96)*
IFX	1.09 (0.82-1.45)	1.17 (0.87-1.56)	0.87 (0.49-1.53)	0.79 (0.45-1.41)
ABT	0.56 (0.37-0.84)**	0.78 (0.50-1.22)	0.62 (0.37-1.04)	0.66 (0.39-1.12)
TCZ	0.65 (0.47-0.90)**	0.81 (0.57-1.17)	0.37 (0.25-0.55)***	0.36 (0.24-0.55)***
TOF	0.16 (0.07-0.39)***	0.25 (0.10-0.62)**	0.39 (0.24-0.63)***	0.52 (0.29-0.92)*
Starting year of b/tsDMARDs				
2008-2014	Ref	Ref	Ref	Ref
2015-	0.58 (0.46-0.73)***	0.74 (0.55-0.98)*	0.58 (0.43-0.77)***	0.73 (0.50-1.07)

* p < 0.05, ** p < 0.01, *** p < 0.001.

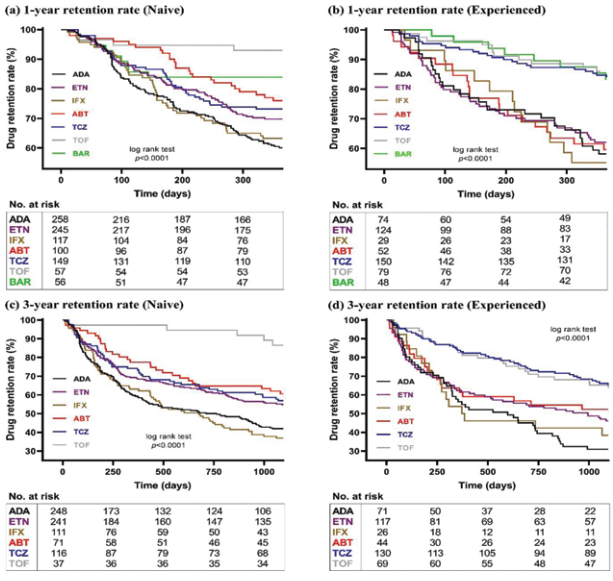


Figure 1. 1 & 3-year retention rates of each drug in b/tsDMARDs naive and experienced treatment courses with seropositive RA.

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Disclosure of Interests: None Declared.
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POS0855

EVOLUTION OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE IN PATIENTS TREATED WITH JAK INHIBITORS: A MULTICENTER RETROSPECTIVE STUDY

Keywords: Safety

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Background: The treatment to adopt when (Interstitial Lung Disease)ILD is detected in Rheumatoid Arthritis (RA) patients has always been a matter of debate. The management and treatment of RA-ILD is challenging because there is still little information available on this topic, and the main literature comes from observational studies. No clinical trials have been dedicated to this topic, however its consideration is increasing in guidelines. There is relatively limited data on the use of JAKi in patients with RA-associated ILD.
Objectives: The aim of this multicenter retrospective study was to investigate the effectiveness and safety of the available JAKi in patients with RA-ILD.
Methods: We retrospectively analyzed patients with classified RA and RA-ILD undergoing JAKi in 6 Italian tertiary centres from April 2018 to June 2022. We included patients with at least 6 months of active therapy and one high-resolution chest tomography (HRCT) carried out within 3 months before the start of JAKi treatment. The HRCT was then compared to the most recent one carried out within 3 months before the last available follow-up appointment. We also kept track of the pulmonary function tests.
Results: We included 43 patients with RA-ILD, 23 males (53.48%) with median age (interquartile range, IQR) of 68.87 (61.46-75.78) treated with JAKi. Clinical and disease characteristics have been reported in Table 1. The median follow-up was 19.1 months (11.03–34.43). The forced vital capacity remained stable in 22/28 (78.57%) patients, improved in 3/28 (10.71%) and worsened in 3/28 (10.71%). The diffusing Capacity of Lung for Carbon Monoxide showed a similar trend, remaining stable in 18/25 (72%) patients, improving in 2/25 (8%) and worsening in 5/25 (20%). The HRCT remained stable in 37/43 (86.05) cases, worsened in 4/43 (9.30%) and improved in the last 2 (4.65%) (Figure 1).

Table 1. Patient characteristics at Treatment Baseline

	Av Obs.	Baseline
Age, years, median (IQR)	43	68.87 (61.46-75.78)
Male, n (%)	43	23 (53.48)
Disease Duration, years, median (IQR)	43	12.66 (7.61)
ILD duration, years, median (IQR)	43	5.55 (5.13)
Follow-up, months, median (IQR)	43	19.1 (14.92)
Rheumatoid factor positivity, n (%)	43	38 (88.37)
ACPA positivity, n (%)	43	35 (81.40)
HRCT pattern, n (%)	43	
UIP		25 (58.14)
NSIP		5 (11.62)
LIP		2 (4.65)
CPFE		1 (2.33)
Indeterminate		10 (23.26)
Baseline DLCO, mean (SD)	27	65.81 (16.92)
Baseline FVC, mean (SD)	30	88.76 (24.03)
Prescribed JAKi, n/%)	43	
Baricitinib		28 (65.12)
Filgotinib		3 (6.98)
Tofacitinib		9 (20.93)
Upadacitinib		3 (6.98)
Use of DMARD before JAKi, n (%)	43	
Methotrexate		32 (74.41)
Leflunomide		3 (6.97)
TNFalpha inhibitors		19 (44.19)
Rituximab		12 (27.91)
Abatacept		16 (38.10)
Tocilizumab		13 (30.23)
JAKi + Methotrexate, n (%)	43	16 (37.21)
Glucorticoids n(%)	43	26 (60.47)

Conclusion: This study seems to confirm that JAKi therapy might be a safe therapeutic option for patients with RA-ILD.

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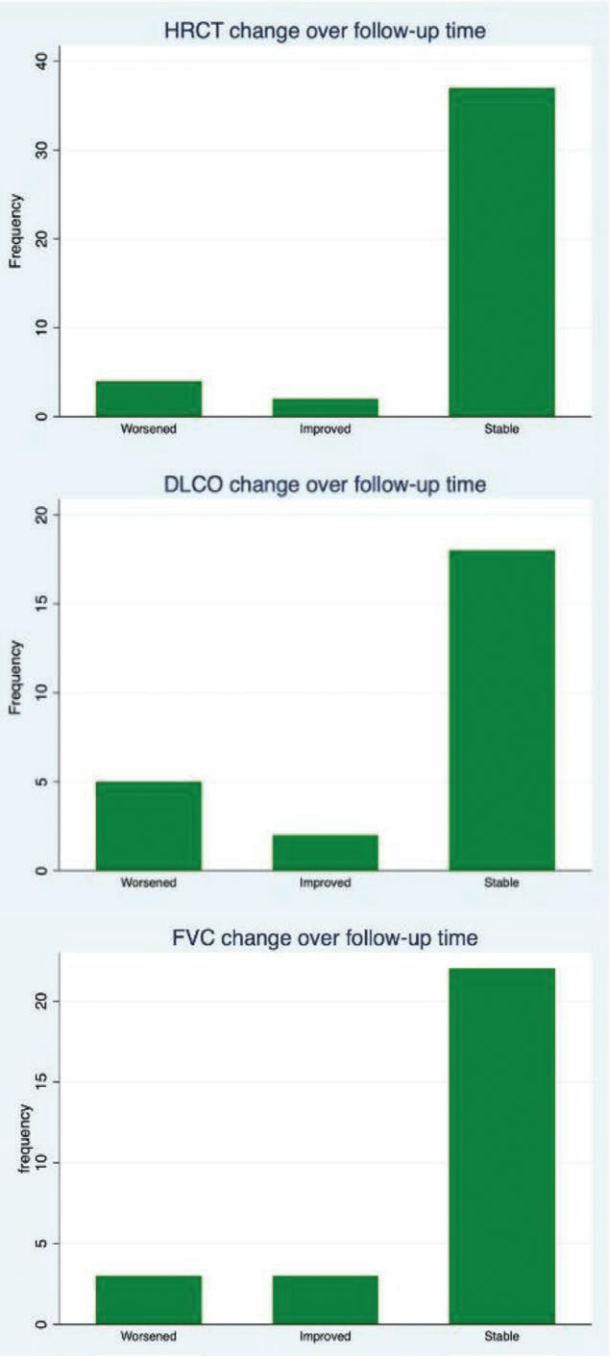


Figure 1. Pulmonary Function Tests and High-Resolution Computed Tomography (HRCT) evolution. Upper Panel: ILD evolution at HRCT, Middle Panel:.Diffusing Capacity of Lung for Carbon Monoxide (DLCO). Lower Panel: Forced vital Capacity (FVC).

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POS0856

MONOTHERAPY AND FIRST LINE USE ARE ASSOCIATED WITH HIGHER JAK-INHIBITOR RETENTION RATES IN PATIENTS IN BOTH RHEUMATOID AND PSORIATIC ARTHRITIS: A RETROSPECTIVE REAL-WORLD STUDY

Keywords: Psoriatic arthritis, Rheumatoid arthritis, Targeted synthetic drugs

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Background: Janus kinase inhibitors (JAKi) have been licensed for the treatment of rheumatoid (RA) and psoriatic arthritis (PsA) and currently there is limited evidence of differences among the four available molecules while real-world data are needed for safety and efficacy.
Objectives: To investigate the efficacy and safety of approved JAKi and analyze the relationship between the patients' baseline characteristics and drug survival.
Methods: This is a retrospective study on patients treated in 2021-2022 with tofacitinib, baricitinib, upadacitinib, or filgotinib for RA or with tofacitinib, baricitinib or upadacitinib for PsA as first or subsequent line of therapy after the failure of one or more conventional DMARD. We collected demographic and clinical data including clinimetric indices and registered the presence of comorbidities, smoking, and previous DMARDs.
Results: The study included 205 patients (81% women) who started or continued a JAKi for RA or PsA between January 2021 and October 2022 (**Table 1**) and were followed until the cutoff on October 31, 2022 for a median of 24 (interquartile range 12-40) months for a total observation of 431 patients-years. One hundred-two (50%) patients received the JAKi as first-line treatment and 108 (53%) as monotherapy. At the last available observation, 144 (72%) patients were still on JAKi, with 27% of patients (54/205) reporting a temporary discontinuation of the therapy, in 69% of cases due to bacterial or viral infections of the upper respiratory tract. Forty-one (20%) patients stopped the JAKi for inefficacy, in 18 (44%) being a primary failure. Eighteen serious adverse events were observed; e.g. 12 major infections, mainly pneumonia, 2 venous thrombotic events, 3 ischemic cardiovascular events and one rhabdomyolysis. Among the 5 patients reporting thrombosis or myocardial infarction, 4 were older than 65 and all had at least one cardiovascular risk factor, mostly obesity and arterial hypertension. Non-disseminated Herpes zoster reactivation was registered in 19 patients but none required the discontinuation of the JAKi. Better retention rates were registered at univariate analysis in bio-naïve patients (p=0.002) and in patients on JAKi monotherapy (p=0.026), while no significant correlation was found with disease duration, comorbidities, and smoking habits. The multivariate analysis confirmed that receiving JAKi as monotherapy (p=0.04, odds ratio 2.01, 95% confidence interval 1.03-3.94) is associated with a longer treatment duration, opposite to having failed one bDMARD before receiving a JAKi (p=0.001, odds ratio 0.29, 95% confidence interval 0.14-0.6), irrespective of gender, age, and disease duration. Having RA or PsA did not impact the treatment duration.

Table 1.

	Total (n=205)	RA (n=187)	PsA (n=18)
Age (years) (median; IQR)	62 (53-71)	61.9 (54-72)	56.6 (48.7-62.0)
Female gender [n (%)]	166 (81%)	152 (81%)	14 (77%)
Rheumatoid Factor positive [n (%)]	117 (57%)	117 (63%)	0 (0%)
ACPA positive [n (%)]	121 (59%)	121 (65%)	0 (0%)
Therapies			
Duration of JAKi therapy (median; IQR)	24 (12-40)	28 (13-41)	8.6 (4-14.5)
bDMARDs naive [n (%)]	102 (50%)	97 (52%)	11 (61%)
JAKi monotherapy [n (%)]	108 (53%)	99 (53%)	3 (17%)
Baricitinib [n (%)]	123 (60%)	122 (65%)	1 (6%)
Upadacitinib [n (%)]	46 (22%)	16 (9%)	2 (11%)
Tofacitinib [n (%)]	18 (9%)	31 (17%)	15 (83%)
Filgotinib [n (%)]	18 (9%)	18 (10%)	0 (0%)
Comorbidities			
Previous or current smoker [n (%)]	61 (30%)	58 (31%)	3 (17%)
Obesity [n (%)]	45 (22%)	37 (20%)	8 (44%)
Hypertension [n (%)]	69 (34%)	65 (35%)	4 (22%)
Diabetes [n (%)]	13 (6%)	13 (7%)	0 (0%)
Previous Venous Thromboembolism [n (%)]	5 (2%)	4 (2%)	1 (6%)
Coronary Arthery Disease [n (%)]	19 (9%)	18 (10%)	1 (6%)

Conclusion: Irrespective of the diagnosis of RA or PsA, JAKi cumulatively have the best treatment duration when are used as monotherapy or as first line before a bDMARD. The safety and efficacy profiles did not differ significantly between RA and PsA, albeit a limited number of patients were included in the latter group.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Nicoletta Luciano Speakers bureau: Abbvie, BMS, Ely-Lilly, Janssen, Consultant of: Galapagos, Elisa Barone: None declared, Enrico Brunetta: None declared, Maria De Santis: None declared, Angela Ceribelli: None declared, Marta Caprioli: None declared, Giacomo Maria Guidelli Speakers bureau: Janssen, Eli-Lilly, Novartis, Abbvie, Galapagos, Consultant of: Janssen, Arianna Sonaglia: None declared, Daniela Renna Speakers bureau: Janssen, Natasa Isailovic: None declared, Carlo Selmi Speakers bureau: Abbvie, Amgen, Alfa-Wassermann, Biogen, Eli-Lilly, Galapagos, Novartis, Janssen, Pfizer, SOBI, Consultant of: Abbvie, Amgen, Alfa-Wassermann, Biogen, Eli-Lilly, Galapagos, Novartis, Janssen, Pfizer, SOBI, Grant/research support from: Abbvie, Amgen, Pfizer.
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POS0857

EFFECTIVENESS AND SAFETY OF BIOLOGIC AND TARGET SYNTHETIC DRUGS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS IN THE ERA OF JAK INHIBITORS: A REAL-LIFE STUDY FROM BIOPURE REGISTRY

Keywords: Rheumatoid arthritis, Targeted synthetic drugs, Registries

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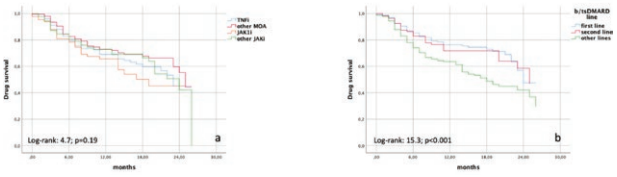
Background: Nowadays, rheumatoid arthritis (RA) patients can benefit from several drugs classified as biologic (b) or JAK inhibitors (JAKi). Four JAKi are now available, whose two JAKi, with predominantly JAK1 selectivity (JAK1i), came onto the market in 2020.
Objectives: The aim of this study was to compare the effectiveness among RA patients included in BIOPURE registry on treatment on TNF inhibitors (TNFi) JAK1i, other JAKi (oJAKi), and other mechanisms of action (oMOA) bDMARD.
Methods: Data of RA patients who started a new line of treatment with a b/tsDMARD were prospectively collected from October 2020, when JAK1i was first prescribed, to May 2022. Demographics and disease characteristics were evaluated using standard descriptive statistics. Patients were divided in four groups: patients on TNFi therapy, patients on JAK1i (upadacitinib and filgotinib), patients on oJAKi (tofacitinib and baricitinib) and patients on oMOA (abatacept, tocilizumab and sarilumab). The drug survival was evaluated by Kaplan– Meier analysis. Estimated hazard ratios (HRs) of discontinuing therapy were assessed by multivariate regression models.
Results: Since October 2020, 580 RA patients started a new line treatment with b/tsDMARDs (171 TNFi, 192 oMOA, 88 oJAKi and 120 JAK1i). Overall cohort characteristics are reported in Table 1. As expected, monotherapy was more used in patients treated with JAK1i (73.6%), oJAKi (63.6%) and oMOA (54.7%) compared to TNFi (30.4%). Patients treated with JAK1i and oJAKi were more likely to be refractory to previous b/tsDMARDs, 76% of JAK1i and 76.2% of oJAKi had received prior treatment with ≥2 bDMARDs or other tsDMARDs. Patients treated with JAK1i presented higher disease activity compared to other b/tsDMARD and higher grade of disability at baseline compared to TNFi. Drug survival was similar between the four groups, being 66.7% for TNFi, 71.9% for oMOA, 64.8% for oJAKi and 69.8% for JAK1i (log-rank test:4.69, p=0.19) (Figure 1a). Multivariate cox regression model and K-M analysis (Figure 1b) showed that the main predictor of b/tsDMARDs discontinuation was a previous treatment with >2 b/tsDMARDs (HR: 1.85, 95% CI 1.21-2.85) Finally, a comparable number of adverse events causing drug discontinuation was observed: 10 (5.8%) in TNFi, 12 (6.3%) in oMOA, 9 (10.2%) in oJAKi and 10 (8.3%) in JAK1i.

Table 1. Characteristics of RA patients treated with b/tsDMARDs

Variables	TNFi (171 pt.)	Other MOA (192 pt.) (84 ABA, 88 TCZ, 20 sarilumab)	Prevalent JAK1i (129 pt.) (78 upadacitinib, 51 filgotinib)	Other JAKi (88 pt.) (55 baricitinib, 33 tofacitinib)
Age, mean (SD)	56 (13)	58 (12)	55 (12)	58 (11)
Female, n(%)	143 (83.6)	156 (81.3)	114 (88.4)	71 (80.7)
Seropositivity, n. (%)	108 (74)	123 (81.5)	100 (90.9)*^	50 (67.6)
Erosive arthritis	80 (46.8)	99 (51.6)	69 (53.5)	48 (54.5)
Comorbidities count, median (IQR)	0 (0-1)	1 (0-2)*	1 (0-2)*	0 (0-2)
csDMARD, n. (%)	119 (69.6)	87 (45.3)*	34 (26.4)*	32 (36.4)*°
Glucocorticoid, n. (%)	99 (57.9)	132 (68.8)	87 (67.4)	55 (62.5)
Glucocorticoid dose daily, mean (SD)	5.9 (3.3)	6.2 (4.0)	6.2 (3.9)	5.5 (2.0)
Biologic line, n. (%)	99 (57.9)	83 (43.2)*	31 (24)*°	21 (23.9)*°
1	29 (17)	34 (17.7)	32 (24.8)	16 (18.2)
2	43 (25.1)	75 (39.1)*	66 (51.2)*	51 (58)*°
other				
DAS28-ESR, mean (SD)	4.2 (1.3)	4.1 (1.5)	4.5 (1.5)°^	4 (1.2)
CDAI, mean (SD)	17 (10)	18 (11)	20 (12)^	16 (8)
VAS-pain, mean (SD)	56 (25)	53 (24)	61 (25)	57 (26)
VAS-phGA, mean (SD)	35 (18)	41 (22)	44 (22)*	37 (22)
VAS-pGA, mean (SD)	56 (23)	55 (24)	61 (22)	56 (21)
HAQ-DI, mean (SD)	1 (0.7)	1.3 (0.8)*	1.3 (0.7)*	1.1 (0.8)

phGA: physician global assessment; pGA: patient global assessment; VAS: visual analogue scale*p<0.05 vs TNFi; °p<0.05 vs other MOA, ^p<0.05 vs other JAKi

Figure 1. a: drug persistence of RA patients according to different b/tsDMARDs. B: drug persistence of RA patients according to different lines of treatment



Conclusion: Our study highlighted good effectiveness and safety of new and old b/tsDMARDs in Apulian cohort of RA patients included in BIOPURE registry. Of note, despite more than half patients starting JAK1i or oJAKi were multi-failure, they showed a similar drug survival compared to those on TNFi who were predominantly biologic-naïve.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0858

THE LONG-TERM RETENTION RATE OF JAK INHIBITORS IN RHEUMATOID ARTHRITIS: DATA FROM THE NATIONAL ITALIAN REGISTRY GISEA

Keywords: Registries, Targeted synthetic drugs, Rheumatoid arthritis

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Background: The efficacy of Janus Kinase inhibitors (JAKis) in Rheumatoid Arthritis (RA) has been established in the last years through numerous randomized clinical trials. Recently, the safety profile of this drug class has come under the spotlight, questioning the actual use in clinical practice and making real-life data even more crucial.

Objectives: The purpose of this study is to evaluate the long-term retention rate of JAKis and to estimate the influence of baseline population characteristics on treatment persistence.

Methods: Data of all RA patients who started a JAKi were prospectively collected in the Italian multicentric GISEA registry. The 3-year retention rate of JAKis was calculated by the Kaplan-Meier method and compared by a log-rank test after stratification according to different baseline population characteristics. A descriptive analysis of reasons for discontinuation was performed.

Results: The study population included 1361 patients (females 83.5%, mean age [±SD] 57.3 [±12.3] years, over 65 years 30%, mean disease duration 12.7 [±9.7] years, mean baseline SDAI 20.6 [±11.7], ACPA positive 68%, RF positive 66%, current smokers 19%, past smokers 13%) who received a JAKi (baricitinib=763, tofacitinib=321, upadacitinib=151, filgotinib=126) as first (n=491) or subsequent line (n=870) targeted drug. The overall 3-year retention rate was 46%. Drug survival was significantly higher in ACPA positive compared with negative patients (51.6 vs 41.8%, p=0.0051) (Figure 1A) and in first-line versus second or further lines of therapy (50.6 vs 43.3%, p=0.0013) (Figure 1B). No difference was found according to age (< or ≥65 years), concomitant methotrexate, smoke, history of diabetes, or at least one cardiovascular comorbidity (hypertension, stroke, or heart failure). Therapy was discontinued in a total of 523 patients because of ineffectiveness (67.5%), adverse events (25.8%), or compliance/other reasons (0.3%). Of relevance, adverse events included cancer (0.7%), major adverse cardiovascular events (MACE) (0.4%), deep vein thrombosis (DVT) (0.6%), and herpes zoster virus (HZV) infections (1.5%).

Conclusion: Our data confirmed in a real-life setting a favorable 3-year retention rate of JAKis in RA. ACPA positivity and use as first-line targeted drug significantly improved persistence of JAKis. Discontinuations of JAKis because of adverse events (including MACE, DVT, HZV, and malignancy) were very uncommon, suggesting an overall favorable safety profile.

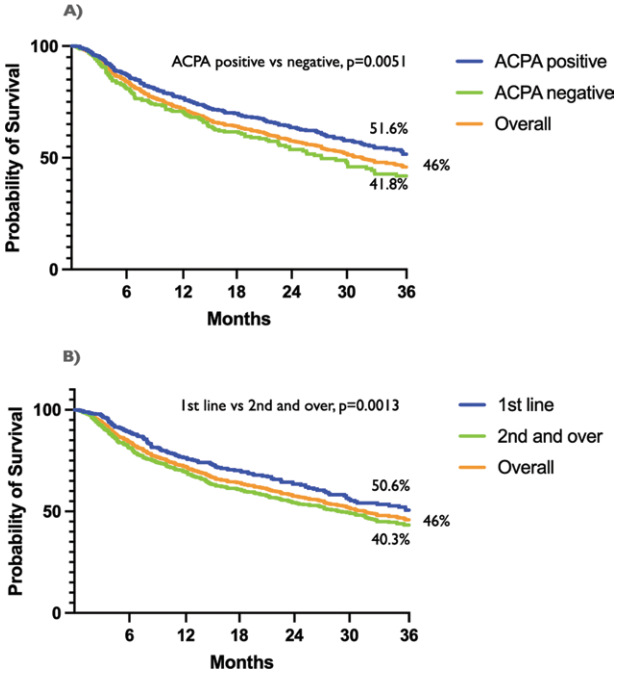


Figure 1. A) Retention rate in ACPA positive versus ACPA negative patients. B) Retention rate in first-line versus second or further lines of therapy.

Acknowledgements: We thank the physicians and patients who participated in these studies.

Disclosure of Interests: Martina Biggioggero Speakers bureau: Galapagos, Elisa Gremese: None declared, Serena Bugatti: None declared, Andreina Manfredi: None declared, Simone Parisi: None declared, Chiara Bazzani: None declared, Antonio Carletto: None declared, Carlo Garaffoni: None declared, Angelo Semeraro: None declared, Addolarata Corrado: None declared, Rosario Foti: None declared, Alberto Cauli: None declared, Francesca Romana Spinelli Speakers bureau: Amgen, AbbVie, Eli Lilly, Galapagos, Consultant of: Amgen, AbbVie, Eli Lilly, Galapagos, Florenzo Iannone: None declared, Ennio Giulio

Favalli Speakers bureau: AbbVie, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Consultant of: AbbVie, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB.
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POS0859 VENOUS AND ARTERIAL THROMBOEMBOLIC RISK OF JAK INHIBITORS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Systematic review, Safety, Randomized control trial

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Background: JAK inhibitors (JAKi) are a new class of drugs developed for the treatment of different immune-mediated inflammatory diseases (IMIDs). Thrombotic events have been reported in some long-term extension studies as adverse effects. As a consequence, in 2017 the Food and Drug Administration (FDA) inserted a black box warning in the Summary of Product Characteristics (SPC) for Baricitinib, stating that it should be used with caution in patients at increased risk of thrombosis [1]. A similar warning was issued by the European Medicines Agency (EMA) in 2019 for Tofacitinib 10 mg [2].
Objectives: To perform a systematic review of randomized controlled trials (RCTs) with the aim to estimate the risk of venous and arterial thromboembolic (TE) events in patients with IMIDs treated with JAKi.
Methods: RCTs on the efficacy and safety of JAKi in IMIDs patients were identified by electronic search of the MEDLINE and EMBASE database until October 2021. Risk of bias was assessed according to Cochrane criteria. All JAKi and all IMIDs were included in the main analysis. Venous and arterial TE events (deep vein thrombosis, pulmonary embolism, unusual site thrombosis, superficial venous thrombosis, stroke, transient ischemic attack, coronary ischaemic events and peripheral artery ischaemia) and major adverse cardiovascular events (MACE) were extracted from the reported safety analysis of the different RCTs. Studies which did not report any information on the cardiovascular safety profile in the paper or supplementary materials were excluded. Differences in thrombotic outcomes among groups were expressed as pooled odds ratio (OR) and corresponding 95% confidence interval (CI), using both a fixed-effects and a random-effects model. Statistical heterogeneity was evaluated using the I^2 statistic.
Results: One phase I, 21 phase II, 3 phase II-III and 36 phase III RCTs on Rheumatoid Arthritis (32.8%), Atopic Dermatitis (22.9%), Psoriasis (11.5%), Inflammatory Bowel Disease (11.5%), Psoriatic Arthritis (9.8%), Ankylosing Spondylitis (6.6%) and Lupus Erytheratosus (4.9%) were included, for a total of 19443 patients in the JAKi group (Abrocitinib, Baricitinib, Brepocitinib Deucravacitinib, Filgotinib, Ivarmacitinib, Peficitinib, Tofacitinib and Upadacitinib) and 9073 in the placebo group. Thirty-one (unweighted rate 0.16%) TE events were reported in the JAKi group and 20 (unweighted rate 0.22%) in the control group in an unweighted mean follow-up of 16.8 weeks. IMIDs patients treated with JAKi had not an increased TE risk compared to IMIDs patients treated with placebo (OR 0.69 [95% CI, 0.44–1.10, I^2 0%] at fixed-effect model) (Figure 1). No clinically relevant results were seen among different IMIDs and drugs. The ORs of venous and arterial TE events were respectively 0.61 (95% CI, 0.32–1.15, I^2 0%) and 0.78 (95% CI, 0.41–1.48, I^2 0%) at fixed-effect model. The incidence of MACE was similar among the groups (OR 0.82 [95% CI, 0.48–1.40, I^2 0%] at fixed-effect model).
Conclusion: Despite our study has some limits like the short duration of the RCTs, the different inclusion criterias, permitted concomitant therapies, mean age and mean disease activity, we did not find any evidence that JAKi increase the risk of venous and arterial TE events and MACE. The performed sub-analysis did not find any correlation between the use of any JAKi and TE events in any considered IMID, even if the meta-analysis is likely underpowered (i.e. β error) to highlight statistically significant differences of the incidence of TE events between different diseases and different JAKi. JAKi do not increase TE risk compared to placebo in IMIDs patients enrolled in phase I/II/III RCTs.
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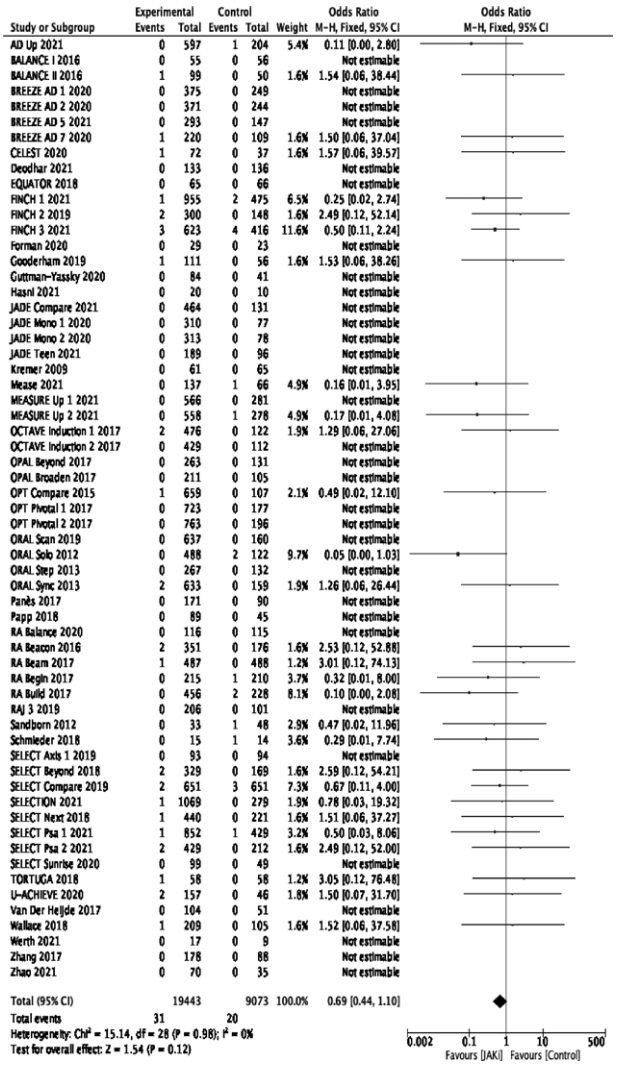


Figure 1.

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Disclosure of Interests: None Declared.
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POS0860 COMPARING THE EFFICACY OF THE BDMARD SWITCHER GROUP AND JAK CYCLER GROUP IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH FAILURE TO THE JAK INHIBITORS

Keywords: Targeted synthetic drugs

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Background: Patients benefiting from the advent of JAK inhibitors has increased in the treatment of rheumatoid arthritis(RA). However, it is also known that there are RA cases that do not respond sufficiently to JAK inhibitors(JAKi). In order not to increase the number of refractory rheumatoid arthritis cases, it is necessary to establish the following treatment methods for JAKi-resistant cases.
Objectives: We analyzed the efficacy of the bDMARD switcher group and the JAKi cycler group as the next treatment for JAKi- refractory cases.
Methods: Cases were recruited to SHin-yokohama Arthritis REgister (SHARE) between 2015 and 2022 (n=4,056). 347 Patients were diagnosed according to ACR/EULAR 2010 classification criteria and treated with JAKi. Efficacy analysis was evaluated by continuation rate and CDAI improvement rate.

Results: JAKi were administered to 347 patients for an average of 64.5 weeks. There were 75 cases (21.6%) who discontinued the JAKi due to insufficient effect. Of the cases in which JAKi were discontinued, 45 (60.0%) were in the bDMARD switcher group, 22 (29.3%) were in the JAK cycler group, and 8 (10.7%) were switched to csDMARD alone. The continuation rate of the next treatment in the bDMARD switcher group and the JAK cycler group was 77.8% and 89.0% at week 12, respectively, with no significant difference (Log-rank p=0.2806). The CDAI improvement rates in switcher group and the JAK cycler group were 43.5% and 46.2%, respectively, at week 12, with no significant difference (Wilcoxon p=0.6397). There was no significant difference in the CDAI improvement rate according to the treatment class and the number of b/tsDMARDs between the two groups (p>0.05). CDAI improvement rate with each of following b/tsDMARs were TNFi=48.2%, IL-6i=30.0%, abatacept=42.4%, JAKi=49.9%. Especially for IL-6 inhibitors, 50.2% CDAI improvement rate was obtained when sarilumab was selected as the following DMARD.

Conclusion: JAK cycler, as well as bDMARD switcher, may be useful as the next treatment for patients who discontinue JAKi.

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Disclosure of Interests: MASAOMI YAMASAKI Speakers bureau: Lilly, Abbvie, Asahi-Kasei, Eisai,

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POS0861 EFFECT OF JAK1 INHIBITION ON EROSION REPAIR IN RHEUMATOID ARTHRITIS: A PILOT HR-PQCT STUDY

Keywords: Targeted synthetic drugs

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Background: Blockade of JAK, preferably JAK1, by upadacitinib is a feasible approach to achieve erosion repair as it 1) is approved for the treatment of rheumatoid arthritis (RA), 2) effectively controls the inflammation and 3) targets pathogenic pathways that influence local bone homeostasis in the joint.

Objectives: To evaluate whether inhibition of JAK1 could lead to erosion repair on high-resolution peripheral quantitative computer tomography (HR-pQCT) in patients with active RA.

Methods: This was a 24-week, single-centered, prospective, non-randomized pilot study. We enrolled 20 adult patients with active RA (Disease activity score 28-C-reactive protein [DAS28-CRP] > 3.2) and ≥1 bone erosion on HR-pQCT. They were given upadacitinib 15mg once daily for 6 months. HR-pQCT of the 2-4 metacarpophalangeal (MCP) head was done at baseline and 6 months. The serum inflammatory cytokine profile and bone-cartilage interface biomarkers were also checked before and after treatment. The primary outcome was the change of erosion volume on HR-pQCT. Secondary outcomes included change in RA disease activity and serum biomarkers, as well as predictors of response to treatment. Erosion regression was defined as decrease in volume exceeding the smallest detectable change.

Results: The baseline clinical characteristics of the recruited patients were shown in **Table 1**. Of the 20 patients, 11 (55%) patients failed to respond to 3 or more csDMARDs. At 24-week, there was significant improvement in mean DAS28 (-1.75, p<0.001). Erosion regression was seen in 8 (40%) patients on HR-pQCT. Although no significant change in overall median erosion volume before and after upadacintinib (0.07 [-0.90-0.76mm3] mm3, p=0.904) was noted, the deterioration was less obvious compared to a historic cohort of 20 patients with similar age and disease activity on csDMARDs (median erosion volume change in 6 months: 0.67 mm3). There was significant reduction in the serum level of bone resorption marker C1M before and after treatment, which was not seen in the historic cohort. Significant reduction in various inflammatory cytokines (e.g. TNF-α, IL-6) was also noted after treatment. When patients were stratified according to whether or not they had failed multiple csDMARDs, significantly high proportion of patients in the non-multiple-DMARDs failure group had volume regression in at least one erosion compared to those in the failure group (75% vs 25%, p=0.04). There was improvement in mean total erosion volume in the non-failure group (-0.33±1.33 mm3), whereas mean erosion volume in the failure group worsened (2.09±7.62 mm3). One patient developed chest infection requiring hospitalization and withdrew from the study. No other serious adverse event was noted.

Conclusion: The results of the study suggested upadacitinib was clinically efficacious in refractory RA disease and could retard erosion progression. Regression of erosion was possible, particularly in those with limited csDMARDs exposure. Whether earlier JAK1 inhibition could lead to better structural outcome warrants further investigations.

Table 1. Baseline Demographic and Clinical Characteristics of the Patients

	N=20
Age, years	52±12
Female sex, number (%)	14 (70)
Disease duration, years	3.5±5.9
RF, number (%)	17 (85)
Anti-CCP, number (%)	17 (85)
Failure to 3 or more csDMARDs, number (%)	11 (55)
TJC	8.6±6.4
SJC	3.4±2.7
DAS28-CRP	4.50±0.98
HAQ	1.1±0.7

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Ho SO Speakers bureau: Abbvie, Boehringer Ingelheim, Fosun Industrial, GSK, Janssen, Pfizer, Consultant of: Abbvie, GSK, Grant/research support from: Fosun Industrial, Isaac T. Cheng: None declared, Martin Li: None declared, Chun Kwok Wong: None declared, Lai-Shan Tam Consultant of: AbbVie, AstraZenaca, Boehringer Ingelheim, Eli Lilly, Janssen, Pfizer, and Sanofi, Grant/research support from: Amgen, Boehringer Ingelheim, GSK, Janssen, Novartis and Pfizer.

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POS0862 PRESCRIPTION PATTERN OF JAK INHIBITORS OVER 5 YEARS IN ITALY: DATA FROM THE ITALIAN NATIONAL GISEA REGISTRY

Keywords: Registries, Disease-modifying drugs (DMARDs), Targeted synthetic drugs

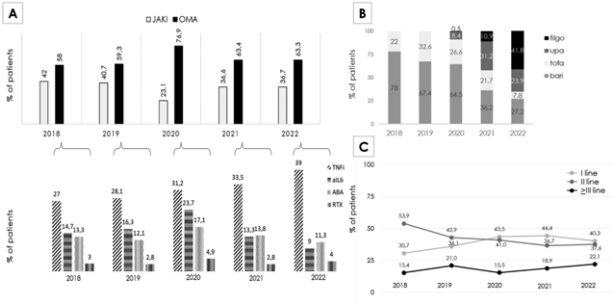
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Background: Since 2018, JAK inhibitors became available in Italy for the treatment of adult patients with moderately to severely active Rheumatoid Arthritis (RA) and an inadequate response to methotrexate (MTX).

Objectives: This analysis aimed to characterize the prescription pattern of JAK inhibitors in patients with RA over the last 5 years.

Methods: Patient demographics, disease characteristics and medication history were collected. Patients starting treatment either with biological Disease Modifying Anti-Rheumatic Drugs (bDMARDs) or targeted synthetic (ts)DMARDs (baricitinib, tofacitinib, upadacitinib and filgotinib) were included in the analysis. Data were extracted from the GISEA (Gruppo Italiano di Studio sull'Early Arthritis) registry.
Results: From January 2018 to December2022 overall 4424 patients with RA were included in the GISEA registry (3622 F: 802 M, mean age 57.9±12.8 years, mean disease duration 12.9±9.9 years). Overall, the number of patients starting bDMARDs and tsDMARDs in 2018, 2019, 2020, 2021 and 2022 was 729, 784, 1204, 794 and 913, respectively; 306 (42%), 319 (40,7%), 278 (23%), 291 (36.6%) and 335 (36.7%) started a JAK inhibitor. Figure 1 summarizes the prescription pattern of bDMARDs and tsDMARDs during the 5 years of observation (A) and the percentage of patients starting each JAK inhibitor (B). The prescription of JAK inhibitors was stable from 2018 to 2022 with the only exception of 2020 (coinciding with the beginning of the pandemic) when we recorded a significant decrease in JAK inhibitors prescribed (p<0.00001 vs 2019) and a significant increase in the number of patients treated with abatacept (from 12.1% to 17.1%, p=0.0024) and anti-IL-6R (from 16.3% to 23.7%, p=0.000067). Conversely, in 2021 the number of patients who started JAK inhibitors significantly increased (0<0.00001 vs 2020) and those starting anti-IL-6R significantly decreased (from 23.7% to 13.4%). From 2018 to 2022 the percentage of bDMARD-naıve patients increased, without reaching a statistical significance, from 30.7%, 36%, 43.5%, 44.4%, 40.3% of patients starting a JAK inhibitor after MTX-failure (Figure 1C).
Conclusion: The use of JAK inhibitors for treating RA of patients in Italy is stable from 2018 onward with a shift towards an earlier line of treatment and a significant change in the prescription pattern within the class over time.

Figure. Prescription pattern of bDMARDs and tsDMARDs during the 5 years of observation (A),and prescription patterns of the four available JAK inhibitors in the same period (B). Prescription of JAK inhibitors according to treatment line (C)



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Disclosure of Interests: Francesca Romana Spinelli Speakers bureau: Amgen, Abbvie, Eli Lilly, Galapagos, Consultant of: Abbvie, Eli Lilly, Galapagos, Florenzo Iannone Speakers bureau: Abbvie, Galapagos, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, UCB, Consultant of: Abbvie, Galapagos, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, UCB, Ennio Giulio Favalli Speakers bureau: BMS, Lilly, Roche, MSD, UCB, Pfizer, Sanofi-Genzyme, and Abbvie, Consultant of: BMS, Lilly, Roche, MSD, UCB, Pfizer, Sanofi-Genzyme, and Abbvie, Elisa Gremese Speakers bureau: Abbvie, BMS, Eli Lilly, Galapagos, Consultant of: Abbvie, BMS, Eli Lilly, Galapagos, Serena Bugatti Speakers bureau: bbVie, Bristol-Myers Squibb, Eli Lilly, Galapagos, Pfizer and Sanofi, Consultant of: Abbvie, Grant/research support from: Pfizer, cristina garufi Speakers bureau: Eli Lilly, Fabiola Atzeni: None declared, Alberto Cauli: None declared, Marco Sebastiani Speakers bureau: Eli Lilly, BMS, Pfizer, Antonio Carletto: None declared, Marcello Govoni: None declared, Angelo Semeraro: None declared, Rosario Foti: None declared, Francesco Paolo Cantatore: None declared, Chiara Bazzani Consultant of: Abbvie, Simone Parisi: None declared, Maria Sole Chimenti Speakers bureau: Abbvie, Eli Lilly, Galapagos, Bruno Frediani Speakers bureau: Abbvie, ELi Lilly, Galapagos, Roberto Caporali Speakers bureau: Abbvie, BMS, Eli Lilly, Galapagos, Pfizer, Roche, UCB, Consultant of: AbbVie, Accord, BMS, Celltrion, Ely Lilly, Fresenius-Kabi, Galapagos, Pfizer, Roche, Sandoz, Fabrizio Conti Speakers bureau: Abbvie, BMS, Eli Lilly, Galapagos, UCB.
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POS0863 BARISUR STUDY: DESCRIPTIVE STUDY OF BARICITINIB SAFETY IN SPANISH PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Safety, Rheumatoid arthritis, Descriptive studies

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Background: Baricitinib (BCT) and tofacitinib (TFC) are the most widely used JAK inhibitors worldwide and both were approved in Spain in 2017. Data from Oral Surveillance study showed in 2021 an increased risk of malignancies and major adverse cardiovascular events (MACEs) in patients treated with TFC versus anti-TNF drugs. However, there is no clear position among rheumatologists regarding the risk of MACE, thromboembolic events (TEE) or other safety concerns of JAK inhibitors. Although JAK inhibitors have a common mechanism of action, each drug has specificities such as selective affinity to different targets, pharmacodynamics, metabolism and dosing, conferring differences between drugs. Therefore, it is to be expected that the safety profile may be different.
Objectives: The aim of this study is to collect real world data from Spanish patients to analyze efficacy trends, daily use patterns and a descriptive analysis of the safety profile of rheumatoid arthritis treatments in southern Spain.
Methods: A multicenter, observational, retrospective study was conducted, collecting data from patients with rheumatoid arthritis previously treated with methotrexate (MTX) and other prior biologic therapies.
Results: Data from 270 patients were analyzed, 73% were female, the mean age was 58 years (SD: 12,7) and the mean age at diagnosis was 47 years (SD:14,33). Of the population, 95,1% had some risk factor for MACE or TEE; specifically 7,5% had previous cardiac events, 2,6% and 9,4% had previous TEE and malignancies, respectively. The distribution of baseline treatment is shown in the Table 1. Median use of prior disease-modifying treatments (DMT) was 1 for the total population, but 2 for BCT patients. BCT patients had 10,5 (SD: 9,0) mean years of disease progression and initiated treatment at 57 (SD: 12,25) years mean age. After the first 12 months of follow-up, there was a trend towards reduce the use of NSAIDs (28,9% to 24,2%), prednisone 85% to 58,4%) and MTX (46,2% to 36,6%). Simultaneously, Disease Activity Score 28 (DAS28), VSG and PCR also decreased during the period from 4,92 (SD:0,84), 24,41 (SD: 15,78) mm/h and 11,89 (SD: 9,69) mg/l to 3,06 (SD: 1,13), 20,79 (SD: 13,31) mm/h, and 8,21 (SD: 9,14) mg/l respectively. BCT safety profile was well tolerated, with 33 adverse events at 6 months of follow-up and 3 serious adverse events (TEE, pneumonia and stroke) during the period. Of BCT population, 57,6% stopped treatment due to toxicity or lack of efficacy.
Conclusion: Taking into account the heterogenicity and the age of our population, these preliminary results showed low risk of MACE and cancers with BCT for the Spanish cohort. Future analysis is guarantee in order to understand the safety profile in the long term.
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Acknowledgements: NIL.
Disclosure of Interests: Esteban Rubio Romero Speakers bureau: Lilly, Galapagos, Abbvie, Paid instructor for: Lilly, Galapagos, Abbvie, Consultant of: Lilly, Galapagos, Abbvie, Grant/research support from: Lilly, Adela Gallego Speakers bureau: Lilly, Galapagos, Abbvie, Paid instructor for: Lilly, Galapagos, Abbvie, Consultant of: Lilly, Galapagos, Abbvie, Marta Llanes Speakers bureau: Lilly, Galapagos, Abbvie, Paid instructor for: Lilly, Galapagos, Abbvie, Consultant of: Lilly, Galapagos, Abbvie, ELOY DELGADO VIDAL: None declared.
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POS0864 EFFECTIVENESS OF ANTIFIBROTICS IN RHEUMATOID ARTHRITIS-INTERSTITIAL LUNG DISEASE. NATIONAL MULTICENTER STUDY OF 50 PATIENTS IN CLINICAL PRACTICE

Keywords: Lungs, Rheumatoid arthritis, Descriptive studies

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Background: Interstitial lung disease (ILD) is a severe complication of rheumatoid arthritis (RA). Abatacept and rituximab are the preferred disease-modifying antirheumatic drugs (DMARDs) for RA-ILD **[1-4]**. However, progression of ILD despite its use is not uncommon. A subgroup analysis of the INBUILD trial has shown a slower decline in forced vital capacity (FVC) in patients with progressive fibrosing autoimmune disease-related ILDs with the antifibrotic nintedanib (NINTE) **[5]**.

Objectives: A) To assess the efficacy of antifibrotic drugs, NINTE and pirfenidone (PIRFE), in Spanish RA-ILD patients with a progressive phenotype in clinical practice. **B)** To compare the profile of clinical practice RA-ILD patients with the RA-ILD patients included in the INBUILD trial **[5]**.

Methods: National multicenter study of RA-ILD patients to whom NINTE or PIRFE were added due to progressive fibrosing ILD. Demographic and clinical variables were collected from all patients. These features were compared with those of RA-ILD patients included in the INBUILD trial (n=89, 42 treated with NINTE and 47 with placebo). Forced vital capacity (FVC) evolution was the primary endpoint. Results are expressed as percentage, mean±SD or median [IQR].

Results: A total of 50 patients (19 women/31 men) from clinical practice were collected (NINTE=45, PIRFE=5), mean age 70±8 years. Median ILD duration up to antifibrotic initiation was of 45 [19-72] months. Mean FVC one year before antifibrotic start was 81±20 (% pred.), whilst mean baseline FVC was 72±23 (% pred.). Comparison of baseline characteristics of RA-ILD patients treated with NINTE in clinical practice (n=45) and RA-ILD patients of the INBUILD trial is shown in **Table 1**. The evolution of FVC and DLCO in our patients from the previous year of antifibrotic initiation is shown in **Figure 1.** After a median follow-up of 16 [5-24] months, no decline in mean FVC and DLCO values was observed. Stabilization or improvement of dyspnea was found in 83% of patients. NINTE was withdrawn in 8 patients due to: gastrointestinal adverse events (GAE) (n=6), death (n=1) or hemorrhage risk (n=1). PIRFE was withdrawn in 2 patients due to GAE.

Conclusion: Antifibrotics, specially NINTE, seem to slow ILD progression in patients with RA-ILD. In clinical practice, patients are treated later in the evolution of the disease, but results are satisfactory. Combination of antifibrotics and DMARDs in RA-ILD is possible and safe.

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Table 1. Baseline characteristics of RA-ILD patients treated with NINTE in clinical practice and RA-ILD patients of the INBUILD trial.

	Clinical practice (n=45)	INBUILD trial (n=89, 42 NINTE vs 47 PCB)
Age, years mean±SD	70±8	67±10
Women, n (%)	18 (40)	35 (39.3)
Smoker ever, n (%)	34 (76)	57 (64)
Time since ILD diagnosis, years mean±SD	4.6±4.4	3.6±3.2
RF, n (%)	40 (89)	-
ACPA, n (%)	37 (82)	
FVC (% pred) mean±SD	72±24	72±16
DLCO (% pred) mean±SD	51±15	48±16
Dyspnea mMRC median [IQR]	2 [2-3]	-
UIP-like fibrotic pattern on HRCT, n (%)	31 (69)	77 (86)
Concomitant IS therapy, n (%)	45 (100)	79 (89)
Glucocorticoids	34 (76)	-
cDMARD	14 (31)	
bDMARD	19 (42)	
JAKi	4 (9)	

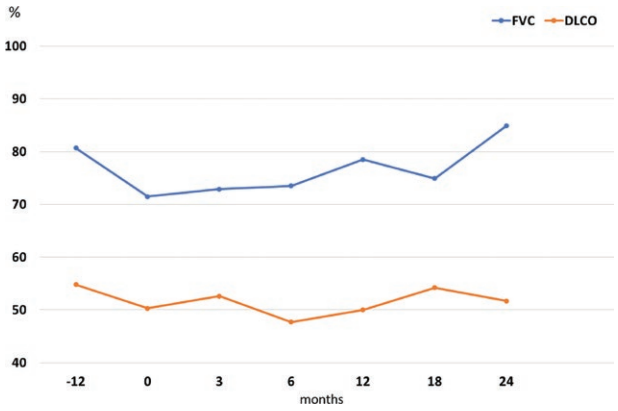


Figure 1. Evolution of FVC and DLCO in patients with RA-ILD treated with antifibrotics in clinical practice from the previous year of initiation.

Members of the Spanish Collaborative Group of Antifibrotics in RA-ILD: Juan Ramón de Dios (HU Araba), Libe Ibarrola (HU de Navarra), Carmen Gonzalez Montagut (HCU de Valladolid), Sergi Ordoñez (H. Arnau de Vilanova), Anahy Mª Brandy (HU Cabueñes), Fernando Lozano (HCD Gómez Ulla), Maria López Lasanta (HU Vall d'Hebron), Cristina Campos (CHGU de València), Marta Garijo (H. de Sagunto), Ivette Casafont (HU Germans Trias i Pujol), Mónica Calderón (H. José Molina Orosa), Carlota Iñiguez (HU Lucus Augusti), Francisco Ortiz-Sanjuán (HUP La Fe), Emilio Giner (H. Royo Villanova), Ignacio Braña (HU Central de Asturias).

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POS0865 THE CORRELATION BETWEEN FOUR ADHERENCE MEASUREMENTS METHODS IN PATIENTS WITH RHEUMATOID ARTHRITIS USING METHOTREXATE

Keywords: Rheumatoid arthritis, Disease-modifying drugs (DMARDs)

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Background: Methotrexate (MTX) is the cornerstone in the pharmacological treatment of rheumatoid arthritis (RA) patients. However, medication adherence to MTX is not ideal, which might lead to suboptimal treatment outcomes. Consequently instruments to assess medication non-adherence are warranted to detect and intervene on non-adherence. To date there is no consensus on the best method to determine adherence to MTX.

Objectives: The aim of this study was to assess the correlation between compliance measured with MEMS (gold standard) versus pill count, MTX-polyglutamate (PG) concentration and Compliance Questionnaire Rheumatology (CQR) in patients with established RA. Second, correlations between these methods and the Disease Activity Scores of 28 joints (DAS28) were examined.

Methods: Adult patients with established RA treated with MTX were included. Multivariable linear and logistic regression were used, with taking compliance assessed with MEMS as dependent variable versus pill count, MTX-PG concentrations, CQR, as independent variables, and DAS28 score versus each of the 4 adherence measurements methods. Comedication, age and use of corticosteroids and NSAIDs were included as covariates in the analysis.

Results: 190 consecutive RA patients were included. Median follow-up time was 4.9 months (IQR 3.6 – 6.2). Pill count correlated with taking compliance assessed with MEMS (linear regression, β =.690, p = <.001), whereas MTX-PG concentrations and CQR were not. Logistic regression only confirmed the correlation between dichotomized taking compliance MEMS and pill count (β = 5.64,

p =.001). No other correlations were found. Between adherence outcomes and DAS28 scores no correlations were seen.

Conclusion: Taking compliance measured with MEMS was correlated with pill count, whereas other methods were not correlated with MEMS, nor with DAS28. Pill count can be used to estimate adherence to MTX therapy, when MEMS is not feasible.

Table 1. Results of multiple imputation linear regression analyses (pooled).

Dependent variable: MEMS		β	p	95% confidence interval forβ	
				Lower bound	Upper bound
IV	Pill count	0.690	<0.001*	0.377	1.004
	MTX-PG concentration	0.000	0.341	0.000	0.001
	CQR	0.035	0.399	-0.046	0.116
Dependent variable: DAS28					
IV	MEMS	0.001	0.748	-0.003	0.004
	Pill count	-0.180	0.544	-0.761	0.402
	MTX-PG concentration	0.000	0.262	0.000	0.001
	CQR	0.118	0.087	-0.017	0.253

Missing data was imputed with 50 imputations. MEMS: Medication Event Monitoring System, LN transformed; CQR: Compliance Questionnaire Rheumatology; IV: independent variable; beta: unstandardized coefficient; * Significance at 0.05. For MEMS, the following covariates were included in the final model: age, treatment centre, amount of other medication, corticosteroid-use, and the use of NSAIDs or COX-2 inhibitors. For DAS28, included covariates were: age, way of living status (e.g., alone, with a partner), educational level, biological-use, corticosteroid-use, other comedication and baseline DAS28.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0866 OLIVE OIL AND NUTS IN RHEUMATOID ARTHRITIS DISEASE ACTIVITY

Keywords: Rheumatoid arthritis, Diet and nutrition

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Background: Rheumatoid arthritis (RA) is a chronic, autoimmune arthropathy affecting around 1% of the general population. Though the availability of many synthetic and biologic DMARDs (disease modifying anti-rheumatic drugs), a non-negligible portion of patients still does not reach the remission. Increasing interest is raising about dietary interventions, in order to optimize disease control: scientific literature suggests that Mediterranean diet could exert an anti-inflammatory role in many rheumatologic conditions, including RA.

Objectives: In this cross-sectional analysis of RA patients from Italy, where extra virgin olive oil is traditionally used, we aim to assess if consumption of two food groups, one including olive oil and olives, and the other considering six types of nuts, might improve RA disease activity, through the related higher intake of vegetable-source fatty acids.

Methods: Within a recent Italian cross-sectional study (365 patients, median age: 58.46 years, 78.63% females), we focused on two food groups, olive oil and nuts, representing vegetable sources of fatty acids. Disease activity was measured with Disease Activity Score on 28 joints (DAS28-CRP) and the Simplified Disease Activity Index (SDAI). Robust linear and logistic regression models included tertile-based consumption categories of each food group and several confounders. Stratified analyses were performed by disease severity or duration.

Results: Higher consumption of both food groups exerted a beneficial effect on disease activity, significant only for olive oil (Beta: -0.33, p-value: 0.03) in the linear regression on the overall sample. This effect was stronger in the more severe or long-standing forms of RA (p-value for heterogeneity<0.05, especially for disease severity). Significant ORs were as low as ~0.30 for both food groups, strata, and disease activity. Mean DAS28 significantly decreased by ~0.70 for olive oil and ~0.55 for nuts in the two strata; mean SDAI significantly decreased by 3.30 or more for olive oil in the two strata.

Conclusion: In this cross-sectional study on Italian RA patients, higher consumption of olive oil and nuts generally led to an improvement of disease activity, but, in most cases, in the absence of statistical significance. The beneficial effect was, however, stronger for those patients with a more severe RA form or a long-standing RA activity, in the presence of significant heterogeneity across strata, especially for disease severity.

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Table 1.

Overall analysis				
Logistic regression				
Food Groups	Tertile categories	OR	95% CI	
DAS				
Olive oil	II	0.93	0.52	1.64
	III	0.60	0.31	1.17
Nuts	II	0.71	0.38	1.30
	III	0.57	0.31	1.06
SDAI				
Olive oil	II	0.99	0.51	1.91
	III	0.69	0.34	1.40
Nuts	II	1.24	0.63	2.43
	III	1.05	0.54	2.05
Robust linear regression				
Food Groups	Tertile categories	Beta	SE	p-value
DAS				
Olive oil	II	-0.14	0.13	0.30
	III	-0.33	0.15	0.03
Nuts	II	-0.07	0.14	0.64
	III	-0.20	0.14	0.15
SDAI				
Olive oil	II	-0.53	0.77	0.50
	III	-1.27	0.87	0.15
Nuts	II	0.25	0.81	0.76
	III	-0.26	0.81	0.75

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Disclosure of Interests: None Declared.

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Psoriatic arthritis - clinical aspects (other than treatment)

POS0867

B-CELL SUBSETS IN PERIPHERAL BLOOD ACROSS DISEASE PHASES OF PSORIATIC ARTHRITIS AND THEIR CORRELATION WITH SYNOVIAL TISSUE FEATURES

Keywords: Synovium, Biomarkers, Remission

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Background: Psoriatic Arthritis (PsA) has been historically considered as a T-cell driven disease, with the role of B-cells generally under investigated since common seronegativity. However, over the years new insights have come to light on B-cells in PsA, focusing on the presence of ectopic lymphoid structures as well as on the presence of specific anti-carbamylated/citrullinated cathelicidin LL37 antibodies in psoriatic SF and plasma.
Objectives: The aim of the study was to examine the frequencies of distinct peripheral blood (PB) B-cell subsets in across different disease phases, evaluating their potential correlation with synovial tissue (ST) heterogeneity in terms of inflammatory degree and microanatomical organization.
Methods: 150 patients fulfilling the CASPAR criteria for PsA were recruited (81 naive to cDMARDs or bDMARDs, 45 c- and/or b-DMARDs resistant and 24 in clinical and US sustained remission, respectively) and underwent US-guided ST biopsy and PB withdrawal. 22 patients with psoriasis (PsO) and arthralgia were included as comparison group. All ST FFPE specimens were routinely processed and stained with H&E and classified by a pathologist, blinded to clinical characteristics, using a H&E based semiquantitive score (KSS) integrated with the presence/absence of lymphocytes, plasmacells, granulocytes and myxoid degeneration, respectively. [1] Frequencies of PB B-cell subpopulations were determined by FACS using the CD27/IgD classification as follows: naïve B-cells ($CD27^{neg}IgD^{pos}$), IgM memory ($CD27^{pos}IgD^{pos}$), switched memory ($CD27^{pos}IgD^{neg}$), late memory ($CD27^{neg}IgD^{neg}$), plasmablasts ($CD27^{pos}CD38^{pos}$) and plasmacells ($CD138^{pos}$).
Results: In PsA cohort, the distribution of synovitis score was significantly different among patients with distinct disease phases (ANOVA p<0.001). In particular, KSS was contingent on disease phase being significantly lower in PsA in remission (2.04 ± 1.39) compared to naive (3.20 ± 1.77, p=0.02) and resistant PsA (3.78 ± 2.22, p<0.001), while there was no significant difference between remission PsA and at risk PsO group in terms of synovial hyperplasia, stromal density, and lymphocyte infiltrate respectively. ST of c- and/or b-DMARDs resistant PsA was enriched of plasmacells than remission PsA (p=0.03). Considering B-cell subpopulations, PB of c- and/or b-DMARDs resistant PsA was enriched of plasmablasts and plasmacells compared to PsO at risk of PsA development (p=0.01 for plasmablasts and p=0.001 for plasmacells, respectively). Conversely, c- and/or b-DMARDs resistant PsA showed, at PB level, lower rates of switched memory and naïve B-cells compared to PsO at risk of PsA development (p= 0.02 for switched memory and p=0.039 for naive, respectively). Finally, stratifying PsA based on KSS category, remission PsA with persistent high grade synovitis (KSS ≥ 5) showed lower rates of PB plasmablasts compared to remission PsA with low grade or without residual synovial inflammation (p=0.045).
Conclusion: Disease state across PsA course significantly impacts PB B-cell subsets distribution mirroring ST residual inflammation at the time of sustained disease remission and supporting the tight dynamic connection between PB and ST environments.
REFERENCE:
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POS0868

NOT ALL SYNDESMOPHYTES ARE EQUAL: THE IMPACT OF BODY MASS INDEX ON THE PRESENCE, LOCATION AND TYPE OF SYNDESMOPHYTES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Comorbidities, Imaging

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Background: New bone formation is a hallmark of Axial spondyloarthritis (axSpA). Body mass index (BMI) is associated with the presence of syndesmophytes, especially in males. To date, it is not clear whether obesity impacts the axSpA through adipokines or biomechanical forces.
Objectives: We aimed to investigate the relation between BMI and the presence and types of syndesmophytes at different spine levels, to better understand the impact of biomechanical forces in AxSpA.
Methods: AxSpA patients who had cervical and lumbar spine x-rays as their standard of care were included (n=144). The cervical and lumbar spine xrays were scored separately, for the presence and type (thin vs bulky) of syndesmophytes. The factors associated with syndesmophytes were investigated, using a multivariate logistic regression.
Results: The mean±SD age of the patients was 45.2±14.0. Syndesmophytes were seen in 48 (33.3%) patients of the cervical and 43 (29.9%) of the lumbar spine. Older and male patients had more frequent syndesmophytes on both levels. While the BMIs of patients with lumbar syndesmophytes were higher than those without (28.4 (8.2) vs 26.8 (7.0), p=0.015), patients with and without cervical syndesmophytes had similar BMIs (27.1 (8.3) vs 28.2 (7.5), p=0.177). Patients with cervical syndesmophytes had higher frequency of uveitis (47.9% vs 20.8%, p=0.001) than those without, which could not be detected for lumbar syndesmophytes. In regression analysis, age and male gender were associated with syndesmophytes in both the cervical and lumbar spine, whereas uveitis was associated only with syndesmophytes in the cervical spine (Table 1). BMI was associated only with syndesmophytes in lumbar spine, but not the cervical spine. The only factor that was found to be associated with bulky (vs thin) syndesmophytes was BMI for the lumbar spine, but not for the cervical spine (Table 1). Presence of PsA was not linked to the bulky type syndesmophytes.
Conclusion: Higher BMI increases the risk of syndesmophytes in the lumbar spine as well as impacting its shape; but not in the cervical spine. Abdominal obesity (apple-shaped) is more common among men in general. We hypothesize that the obesity may be increasing the risk of lumbar syndesmophytes as well as bulkiness in males due to the mechanical forces, which may not be seen in generally "pear-shaped" women, where the fat tissue and mechanical forces spare the lumbar spine.
REFERENCES: NIL.

Table 1. Multivariate logistic regression for the presence and type of syndesmophytes

Independent variables	Presence of Cervical syndesmophytes			Presence of Lumbar syndesmophytes		
	All	Male	Female	All	Male	Female
Age	**1.06 (1.03-1.10)*****	**1.08 (1.03-1.14)$^{+++}$**	1.06 (0.99-1.14)	**1.05 (1.02-1.09)***	**1.05 (1.00-1.09)$^{\#\#\#}$**	1.06 (0.97-1.15)
Sex (male)	**3.80 (1.43-10.15)$^{++}$**	-	-	**4.95 (1.72-14.22)****	-	-
BMI	1.04 (0.96-1.13)	0.99 (0.87-1.13)	1.08 (0.95-1.22)	**1.12 (1.02-1.20)$^{\#}$**	**1.16 (1.00-1.34)$^{+}$**	1.09 (0.96-1.23)
Smoking (ever)	0.89 (0.36-2.22)	0.56 (0.16-1.92)	1.36 (0.28-6.69)	0.86 (0.34-2.15)	0.44 (0.13-1.50)	1.36 (0.21-8.92)
Uveitis (yes)	**4.75 (1.82-12.43)*****	**6.97 (1.91-25.47)****	3.82 (0.69-21.06)	0.65 (0.24-1.79)	1.29 (0.39-4.30)	.000 (.000-.)
Elevated ESR (a)	1.96 (0.75-5.13)	1.05 (0.28-3.97)	2.82 (0.53-15.03)	2.29 (0.89-5.90)	1.81 (0.54-6.12)	3.86 (0.61-24.38)
Proportion of exposure to biologics (b)	1.01 (0.99-1.02)	0.99 (0.97-1.01)	1.02 (0.998-1.04)	0.99 (0.98-1.01)	0.98 (0.96-1.01)	1.00 (0.98-1.03)

Independent variables	Presence of bulky-shaped syndesmophytes in cervical spine	Presence of bulky-shaped syndesmophytes in lumbar spine
Age	0.996 (0.94-1.06)	1.01 (0.93-1.09)
Sex (male)	1.59 (0.34-7.39)	1.53 (0.29-7.95)
BMI	1.09 (0.97-1.23)	**1.17 (1.02-1.34)$^{\#\#}$**
PsA Diagnosis	2.00 (0.50-8.00)	2.06 (0.45-9.37)
Uveitis (yes)	0.67 (0.17-2.62)	-

*p=0.005; **p=0.003; ***p=0.001; $^{\#}$p=0.017; $^{\#\#}$p=0.030; $^{\#\#\#}$p=0.042; $^{+}$p=0.045; $^{++}$p=0.008; $^{+++}$p=0.002Numbers are given as OR (95%CI)(a) ESR elevated in at least two occasions (positive)(b) years on biologic therapies/total disease duration x100

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POS0869 **WITHDRAWN**

POS0870 **PROTEIN BIOMARKERS ASSOCIATED WITH ENTHESITIS IN PSORIATIC ARTHRITIS**

Keywords: Psoriatic arthritis, Enthesitis, Biomarkers

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Background: The presence of enthesitis in PsA may provide clues to disease pathogenesis, aid diagnosis and contribute to poor prognosis. Ultrasound is an invaluable tool in assessing entheseal disease, but it requires training and is time consuming. We investigated whether enthesitis may be measured by changes in serum proteins and as such allow us to better understand, diagnose and treat the condition.
Objectives: To use mass spectrometry (MS) based proteomics to identify protein biomarkers that may be associated with those PsA patients who suffer from enthesitis.
Methods: Serum was collected as part of a prospective observational study from PsA patients who fulfilled the CASPAR criteria and were ≥ 18 yrs. All patients were biologic naive and due to commence biologic treatment. We utilised the MAdrid Sonographic Enthesitis Index (MASEI) to assess US confirmed enthesitis with a score of ≥ 18 suggesting significant enthesitis and <18 determined to be non-significant. The samples were analysed using targeted MS multiple reaction monitoring (MRM) analysis with > 200 candidate proteins. The MRM data was analysed in 3 ways: 1) Raw with no normalisation 2) Normalisation to 7 stable isotopically labelled peptide spike-ins (SIL7) correcting for fluctuations in sample injections/mass spectrometry loading; and, 3) Normalisation to a set of endogenous peptides that represent total serum protein abundance (TSPA) correcting for different amounts of total serum across samples. Univariate analyses and multivariate machine learning Random Forest (RF) modelling were performed.
Results: 80 samples were analysed. 29 patients had a MASEI score of < 18 [36.25%] and 51 had a score > 18 [63.75%]. We identified 35 candidate proteins from all data sets that are included in Figure 1. RF multivariate analysis of all data revealed a set of peptide signatures with the ability to differentiate between MASEI scores < 18 vs ≥ 18. RF models generated from the peptide data had a testing and training AUC of 0.789 [95% CI 0.65, 0.93] 0.953 [95% CI 0.92, 0.98] (Raw), 0.83 [CI 0.74, 0.94], 0.972 [95% CI 0.96, 0.99] (TSPA7) and 0.845 [95% CI 0.72, 0.97]0.966 [95% CI 0.94, 0.99] (SIL7) respectively.
Conclusion: We have identified serum proteins, within this small cohort, which are associated with enthesitis in PsA. Verification of these findings in a larger, independent dataset is the next required step. Proteins related to peptide sequences for univariate + multivariate analysis. Blue (all data sets) Green (all univariate data sets and at least one multivariate) Yellow (all multivariate data sets and at least one univariate) Grey (all multivariate data sets) Red (all Univariate data sets) Pink (2 Multivariate data sets) ANT3: Adenine nucleotide translocase 3 AGT:Angiotensinogen A2HSGP: Alpha 2 HS glycoprotein ALAI: Apolipoprotein A-I ARP3: Angiopoietin related protein 3 AT3: Antithrombin III CNCC: Carboxypeptidase N catalytic chain CBG:Corticosteroid binding globulin GP3: Glutathione peroxidase 3 HSPB: Heat Shock Protein HSP 90-beta HRG: Histidine rich glycoprotein IGFBPC Insulin-like growth factor-binding protein complex acid labile subunit PEDF: Pigment epithelium derived factor SHBG: Sex hormone binding globulin PGSPD: Phosphatidylinositol-glycan-specific phospholipase D TX: Tenascin-X VDBP Vitamin D binding protein.

RAW		TSPA7		SIL7	
Univariate	Multivariate	Univariate	Multivariate	Univariate	Multivariate
SHBG	SHBG	SHBG	SHBG	SHBG	SHBG
AGT		AGT		AGT	AGT
AT3		AT3	AT3	AT3	
VDBP	VDBP	VDBP	VDBP	VDBP	
CBG		CBG	CBG	CBG	
Calumenin		Calumenin		Calumenin	Calumenin
ARP3	ARP3	ARP3	DmX-like protein	ARP3	
GP3		GP3	GP3	GP3	
	PEDF	PEDF	PEDF		PEDF
PGSPD	ANT3	PGSPD	Thyroid hormone recepter beta	PGSPD	ANT3
IGFBPC	HRG	IGFBPC	Agglutinin like protein	IGFBPC	HRG
A2HSGP		A2HSGP	Pleckstrin homology like domain	A2HSGP	
ALAI		ALAI	Beta 2 microglobulin antigen	ALAI	
CNCC		CNCC	Complement factor B	CNCC	
TX		TX	Complement component 4 binding protein alpha	TX	
HSPB		HSPB	Immunoglobulin J chain	HSPB	
Protein S100-A8		Complement factor H	Alpha 1-antichymotrypsin	CRP	
		Immunoglobulin heavy variable 3-7	Heparin cofactor 2	Prothrombin	
		Serum amyloid P component	Cadherin 13		

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POS0871

ROLE OF INFLAMMATORY BURDEN AND TREATMENT ON JOINT SPACE WIDTH IN PSORIATIC ARTHRITIS-A HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY STUDY

Keywords: Outcome measures, Psoriatic arthritis

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Background: Psoriatic Arthritis (PsA) is associated with enthesitis and synovitis which lead to bone erosions, cartilage loss, and new bone formation. High-resolution peripheral quantitative computed tomography (HR-pQCT) enables the quantitative 3D assessment of joint space width (JSW) with superior resolution compared to radiography. Whether disease-specific parameters are associated with JSW on HR-pQCT in PsA remains uncertain.

Objectives: To assess HR-pQCT joint space outcomes by comparison with radiographs and investigate the relationship between disease-related variables and JSW on HR-pQCT in PsA patients.

Methods: PsA patients who underwent HR-pQCT examination (XtremeCT I, SCANCO Medical AG, Brüttisellen, Switzerland) of the second to fourth metacarpophalangeal joint (MCPJ 2-4) were recruited in this cross-sectional study. The joint space metrics included joint space volume (JSV), mean, minimum (Min) and maximum (Max) JSW, JSW asymmetry (Asymm) and distribution (SD). Volumetric joint space was quantified using an algorithm developed by consensus from the Study group for eXtreme Computed Tomography in Rheumatoid Arthritis (SPECTRA). The joint space domain on standard radiography was scored using the Sharp/van der Heijde (SvdH) joint space score. A generalized estimating equation (GEE) was used to estimate the ability of HR-pQCT to predict SvdH scores. Linear regression models were used to determine the association between disease-related variables and JSW.

Results: 67 patients [47 (55.2%) males; median age: 57.0 (53.0, 63.0); median disease duration: 21 (16, 28) years] were included in this analysis. Most had mild disease activity [Disease Activity index for PsA (DAPSA): 10.1 ± 6.6]. 56/67 (84%) were on conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) while 27/67 (40%) were on biologic DMARDs (bDMARDs). 11 MCPJ 2, 9 MCPJ 3 and 7 MCPJ 4 were excluded due to poor image quality. Individual MCP joint space parameters were presented in Table 1. Subluxations were detected more frequently by HR-pQCT than radiographs. SvdH score was negatively associated with a lower mean, Max and Min JSW; and higher JSW SD and Asymm (all p<0.05). Multivariable linear regression analysis showed that males had larger JSV (MCPJ 2-4), mean (MCPJ 4) and Max JSW (MCPJ 3). Longer disease duration (MCPJ 2-3) and higher ESR level (MCPJ 3) were negatively associated with mean and Max JSW, while higher damage joint count was negatively associated with mean and Min JSW (MCPJ 2) (Figure 1). Use of csDMARDs was negatively associated with Min JSW (MCPJ 3); while use of bDMARDs was positively associated with Min JSW (MCPJ 2).

Conclusion: HR-pQCT could be widely used for assessing joint damage prior to evidence of radiographic joint damage in PsA patients. Higher inflammatory burden as reflected by longer disease duration, higher ESR levels, and damage joint count was negatively associated with mean, Max, and Min JSW, while suppression of inflammation using bDMARDs seems to prevent a decline in JSW.

Table 1. Joint space analysis in PsA patients

JS parameters	MCPJ 2	MCPJ 3	MCPJ 4
JS volume (mm^3)	87.1 ± 18.8	94.1 ± 22.7	66.1 ± 15.0
Mean JSW (mm)	1.8 ± 0.2	1.7 ± 0.2	1.6 ± 0.2
JSW SD (mm)	0.3 (0.3, 0.3)	0.3±0.0	0.3±0.1
Max JSW (mm)	2.9 (2.7, 2.9)	2.7 (2.5, 2.9)	2.6 (2.5, 2.7)
Min JSW (mm)	1.1 (0.8, 1.4)	1.1 (0.2, 1.3)	1.0 (0.9, 1.2)
JSW Asym	2.4 (2.1, 3.2)	2.5 (2.2, 15.8)	2.4 (2.1, 3.0)

PsA, psoriatic arthritis; MCPJ, metacarpophalangeal joint; JS, joint space; JSW, joint space width; SD, standard deviation; Max JSW, maximum JSW; Min JSW, minimum JSW; Asym, joint asymmetry.

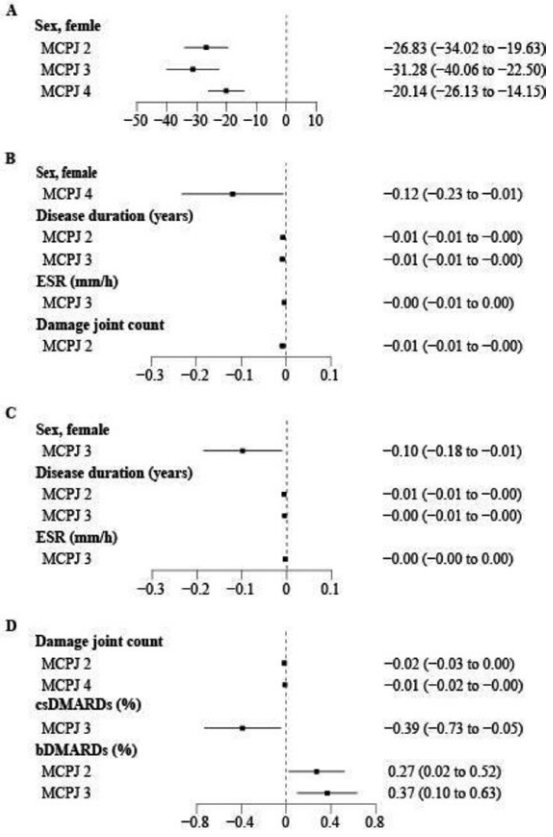


Figure 1. Forest plot demonstrating multivariable linear regression analysis between demographic and disease-related variables and JSW parameters at MCPJ 2 to 4A, Joint space volume; B, Mean joint space width (JSW); C, Maximum JSW; D, Minimum JSW.MCPJ, metacarpophalangeal joint; ESR, erythrocyte sedimentation rate; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs, biologic disease-modifying anti-rheumatic drugs.

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POS0872 CHARACTERIZATION AND RISK FACTORS FOR LUNG INVOLVEMENT IN PSORIATIC ARTHRITIS: DATA FROM A SINGLE RHEUMATOLOGIC CENTRE

Keywords: Prognostic factors, Lungs, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory systemic disease associated with several comorbidities. Few data are available concerning the association between psoriasis (PsO) and lung disease (LD), such as chronic obstructive pulmonary disease (COPD)[1] and interstitial lung disease (ILD)[2]. This association has also been hypothesized in PsA. Therefore, evaluating distinct lung manifestations in PsA could be an important driver to improve patients' management.
Objectives: To assess the prevalence and clinical features of PsA, to examine the co-occurrence of different LDs patterns and to evaluate their impact on clinical outcomes.
Methods: We performed a cross sectional observational study including patients with diagnosis of moderate to severe PsA and at least one chest imaging (as CT scan) performed at the beginning of bDMARD therapy, referred to our Rheumatologic Unit. Demographic, clinical data and concomitant comorbidities were collected. We used Chi-square test for categorical variables and Student's T test for continuous variables.
Results: 288 PsA patients were evaluated. Patients' characteristics are shown in *Table 1.* We observed 28 patients affected by COPD (9.7%) and 7 by ILD (2.4%). About 20% of patients had radiological abnormalities without a distinct clinical diagnosis. In particular, 27 patients presented aspecific nodules (9.4%), 19 signs of bronchitis or emphysema (6.6%) and 17 interstitial thickening (5.9%). Notably, smoke (HR 2.2, p 0.04), higher age at PsA diagnosis (53.8 ± 8.5, p<0.001), higher BMI (28.6 ± 5.6, p 0.05) and recurrent infections (HR 12.3, p<0.001) were associated to COPD. Among comorbidities, cardiovascular diseases (HR 3.8, p 0.005), dyslipidaemia (HR 3.6, p 0.007) and diabetes (HR 4.1, p 0.001) were associated to COPD. Both COPD patients (HR 3.3, p 0.01) and patients with other LDs (HR 2.9; p 0.002) had a history of bDMARDs failure of at least >3 bDMARDs underwent, significantly more than patients without LD. Even in ILD patients, we observed an older age at PsA diagnosis (58 ± 12.2, p 0.01) and a higher prevalence of diabetes (HR 4.1, p <0.001) compared to patients without LD. Furthermore, nail psoriasis (HR 4.7, p 0.05) and malignancy (HR 7.1, p 0.01) were related to ILD.
Conclusion: Our results confirm the prevalence of COPD in PsA[3] and add evidence about the co-occurrence of other LDs in PsA. Risk factors associated with the presence of LD emerged from our analysis, highlightening an occult unmet need in PsA patients. Moreover, we observed as LDs could influence bDMARDs failure. Otherwise, focusing on pulmonary comorbidities could improve therapeutic response and clinical outcomes.
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Table 1.

	Cohort	LD (N=85)		No LD (N=206)	*P value*	
		COPD	ILD		p1	p2
No. of patients, N (%)	288	28 (9.7)	7 (2.4)	206 (71.5)	-	-
Female, N (%)	185 (64.2)	19 (67.8)	2 (28.6)	131 (63.6)	0.6	0.06
BMI, mean ± SD	27 ± 5.7	28.6 ± 5.6	27.7 ± 3.7	26.5 ± 5.2	**0.05**	0.6
Smoke, N (%)	151 (52.5)	16 (57.1)	5 (71.4)	102 (49.5)	**0.04**	0.06
Age at diagnosis, mean ± SD	44.7 ± 13.1	53.8 ± 8.5	58 ± 12.2	42.1 ± 12.7	**<0.001**	**0.01**
Psoriasis, N (%)	240 (83.3)	21 (75)	6 (85.7)	174 (84.5)	0.1	0.9
Nail psoriasis, N (%)	106 (36.8)	8 (28.6)	5 (71.4)	72 (34.9)	0.5	**0.05**
Dactylitis, N (%)	75 (26)	8 (28.6)	3 (42.8)	23 (11.2)	0.7	0.3
Enthesitis, N (%)	99 (34.4)	11 (39.3)	1 (14.3)	71 (34.5)	0.6	0.2
CV, N (%)	114 (39.6)	15 (53.6)	5 (71.4)	74 (35.9)	**0.005**	0.06
Dyslipidaemia, N (%)	104 (36.1)	13 (46.4)	3 (42.8)	67 (32.5)	**0.007**	0.5
Diabetes, N (%)	50 (17.4)	9 (32.1)	4 (57.1)	29 (14.1)	**0.001**	**<0.001**
Hyperuricemia, N (%)	52 (18)	7 (25)	1 (14.3)	36 (17.5)	0.3	0.8
Malignancy, N (%)	19 (6.6)	3 (10.7)	2 (28.6)	11 (5.3)	0.2	**0.01**
bDMARDs ≥3, N (%)	37 (12.8)	7 (25)	0	19 (9.2)	**0.01**	-

p1: *p value* between COPD and No LDp2: *p value* between ILD and No LD**Legend:**BMI Body Mass Index; bDMARDs biologic Disease Modifying Anti-Rheumatic Drugs; COPD Chronic Obstructive Pulmonary Disease; CV Cardiovascular; ILD Interstitial Lung Disease; LD Lung Disease.

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POS0873 SYNOVIAL TISSUE FEATURES ASSOCIATED WITH POOR PROGNOSIS IN INFLAMMATORY ARTHRITIS

Keywords: Rheumatoid arthritis, Synovium, Psoriatic arthritis

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Background: Rheumatoid arthritis (RA), Psoriatic arthritis (PsA), and undifferentiated arthritis (UA) are chronic immune-mediated inflammatory diseases characterized by joint inflammation. However, the prognosis related to progression to chronic and erosive disease or to an autolimited outcome could be different between those clinical phenotypes. Synovial lymphoid neogenesis (LN) has been previously studied as a prognostic factor in RA but results were conflicting between studies [1,2].
Objectives: To evaluate the potential association of inflammatory cell infiltrates and the expression of ectopic LN structures in synovial tissue (ST) with poor prognosis factors (PPF) in patients with RA, PsA, and UA.
Methods: This is a retrospective study including patients with active RA, PsA, and UA who had ST obtained by rheumatological arthroscopy in our department. We evaluated clinical data and synovial LN and the cellular infiltrate by immunohistochemistry, as previously detailed [1]. Patients who were on Biologic Disease-modifying Antirheumatic Drug (bDMARDs) at the time of arthroscopy were excluded. PPF in patients with RA and UA were defined by anti-cyclic citrullinated peptide/protein antibodies (ACPA) and/or rheumatoid factor (RF), development of erosive disease or the initiation of bDMARDs during the follow-up. PPF in patients with PsA were defined by high levels of acute phase reactants (ESR and/or CRP), dactylitis or nail involvement at the time of arthroscopy and/or the initiation of bDMARDs. Statistical analysis was done with SPSS Statistics 27 program. For the analysis of LN and PPF, we performed x^2, T-test to compare PPF with the cellular density and Spearman's rank correlation coefficient for cellular density and disease activity score 28 (DAS28).
Results: A total of 87 patients were included: 26 RA, 32 PsA and 29 UA. Demographic characteristics are detailed in Table 1. Seventeen out of 26 (65.38%) RA patients had LN and 14 (53.84%) had PPF. Twelve patients (46%) had LN and PPF. LN was associated with PPF (p 0.038). In PsA group, we found LN in 16 out of 32 (50%) and PPF in 42.4%. Polyarticular PsA (58.5%) was the most frequent phenotype and 15.2% of patients had onychopathy. Nevertheless, LN was not associated with PPF. Patients with PPF had a higher CD15+ polymorphonuclear cell density (477.63 [SD 410.68] vs 99.63 [SD 93.23] cells/cm2 in patients without PPF, p 0.031). Thirteen out of 29 (44.82%) UA patients had LN and 55.17% had PPF. The final diagnosis for these patients were: 12 RA; 4 PsA; 8 peripheral SpA and 5 remained as UA. LN was not associated with PPF. Synovial CD68+ macrophages cells density (lining, sublining and total) was negatively correlated with DAS28 CRP (r= -0.27, p 0.024).

Table 1.

	RA	PsA	UA
N	26	32	29
Female, n (%)	20 (76.9)	14 (42.4)	18 (41.4)
Smoker, n (%)	5 (19.2)	3 (9.1)	5 (17.2)
Age, mean years (SD)	53.19 (14.4)	51.40 (13.7)	47.24 (16.5)
Disease duration, mean months (SD)	83.30 (113.2)	60.70 (70.9)	29.50 (50.8)
Anti-CCP positive, n (%)	19 (73.7)	-	8 (27.6)
RF positive, n (%)	16 (61.5)	-	8 (27.6)
HLAB27 positive, n (%)	-	9 (27.3)	6 (20.7)
DAS28 CRP, mean (SD)	3.44 (1.1)	2.65 (0.6)	3.00 (0.92)
DAS28 ESR, mean (SD)	4.37 (1.5)	3.46 (1)	4.34 (1.2)
Initiation bDMARd, n (%)	13 (50)	10 (30.3)	12 (41.4)

Conclusion: Synovial LN was associated with PPF only in patients with RA, suggesting the specific pathogenic role that these well-compartmentalized lymphoid aggregated play in RA. However, in PsA, PPF was associated with synovial CD15+ neutrophils density, probably related to the pathogenic relevance of myeloid cells in this disease. Finally, synovial CD68+ macrophages negatively correlated with disease activity in UA patients, probably reflecting the heterogeneity of pathogenic mechanisms occurring in this group. Although this study is retrospective and with relatively small cohorts, the findings suggest a great heterogeneity of the ST features and its pathogenic implications in the subtypes of inflammatory arthritis studied.
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POS0874 DO PATIENTS WITH PSORIATIC ARTHRITIS EXPERIENCE MORE FEELINGS OF SHAME AND GUILT THAN PATIENTS WITH RHEUMATOID ARTHRITIS?

Keywords: Psoriatic arthritis, Quality of life, Mental health

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Background: Patients with rheumatoid arthritis (RA) may experience feelings of guilt and shame related to the impact of the disease on their quality of life. However, patients with psoriatic arthritis (PsA) face an aesthetic problem in addition to the functional disability.
Objectives: The purpose of this study was to determine whether patients with PsA experience more feelings of shame and guilt than patients with RA.
Methods: We conducted a cross sectional study including patients with RA (ACR/EULAR criteria) and PsA (CASPAR criteria). Feelings of guilt and shame were assessed using the Experience of Shame Scale (ESS) [1] and the Test of Self Conscious Affect- Version 3 (TOSCA-3S) [2]. ESS is a self-report scale assessing 3 areas: (1) characterological shame (2) behavioral shame and (3) bodily shame. Each item was rated in a 4-point Likert scale. Higher scores indicate higher levels of shame. TOSCA-3S is composed of 11 scenarios, each followed by 4 possible responses. Each item was rated in a 5-point Likert scale. This score measures shame-proneness, guilt-proneness, detachment and externalization (blaming others). Only the shame and guilt subscales of the TOSCA-3S were used for the statistical analysis. A $p<0.05$ was considered significant.
Results: A total of 40 RA patients (36 women, 4 men) and 30 PsA patients (12 women and 18 men) were included. The mean age was 54 years [25-75] and 51 years [21-80], respectively. The mean disease duration was 12 years [3-33] in RA patients and 13 years [2-20] in PsA patients. Illiteracy was noted in 22% of RA patients and in 5% of PsA patients. Regarding the professional status, 42% of RA patients and 50% of PsA patients were employed. High disease activity was noted in 42% of RA patients and in 13% of PsA patients. The mean total score of ESS was 45 [27-80] in RA and 65 [31-98] in PsA. There was a significant difference between the groups ($p<0.001$). The mean subscale scores were significantly higher among PsA patients: the characterological shame (29 vs 19, $p=0.05$), the behavioral shame (25 vs 18, $p=0.001$), and the bodily shame (10 vs 7, $p<0.001$). For the TOSCA-3S, the mean "shame self-talk Total" score was higher in PsA patients, but the difference was not significant (35 vs 33, $p=0.453$). The mean "guilt self-talk Total" score was 48 in RA and 47 in PsA ($p=0.341$).
Conclusion: Feelings of guilt and shame are experienced by both PsA and RA patients. However, PsA may have a higher psychosocial impact. Therefore, effective management of the dermatological and psychological aspects is necessary.
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POS0875 AUTOANTIBODIES DIRECTED TO G-PROTEIN COUPLED RECEPTORS CORRELATE WITH DISEASE ACTIVITY SCORES IN PATIENTS WITH PSORIATIC ARTHRITIS

Keywords: Comorbidities, Autoantibodies

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease that affects the skin, nails, tendons and joints. In addition, several comorbidities have been identified with PsA. In particular, a frequent occurrence of fatigue and mental disorders such as depression have been described in patients with PsA. Key cellular players in pathophysiology of PsA are T cells. However, in recent years, various autoantibodies such as anti-LL37 and anti-Pso-p27 have been identified in PsA as well [1]. Autoantibodies targeting G protein-coupled receptors (GPCRs) have been identified in several diseases and are involved in disease pathophysiology [2]. Many of these autoantibodies are agonists that enhance the effect of the natural ligand at the receptor [3].
Objectives: The aim of this study was to investigate the association between autoantibodies directed to distinct GPCRs and disease activity as well as comorbidities in PsA.
Methods: In a prospective observational study forty-five patients with an active PsA according to CASPAR criteria and 24 healthy controls (HCs) matched according to age and sex were included in this study. The serum-concentrations of 20 autoantibodies directed to GPCRs involved in the renin-angiotensin-aldosterone system, the sympathetic and parasympathetic nervous system as well as chemokine, complement and scavenger receptors, were measured by the company CellTrend GmbH (Luckenwalde, Germany). Autoantibodies measured in patient's sera at baseline were transformed and adjusted for age as confounder for further analyses. To compare autoantibody concentrations between PsA and HCs we applied Two-Way-ANOVA. Correlation analyses were performed using Pearson correlation. Autoantibody concentrations between patients with and without depression were analyzed by Student's T test and binary logistic regression.
Results: Patients were equally distributed according to sex (male 51.1%, female 48.9%) and of a mean age of 47.5 ± 13.2 years. Mean arthritic disease manifestation assessed by DAPSA was 44.4 ± 21.2. Patients displayed a disease activity with a mean PASI of 6.19 ± 6.33, and high impact on patient reported outcomes with a mean DLQI of 10.3 ± 7.4 and a mean HAQ of 1.0 ± 0.8. Autoantibody concentrations did not differ significantly between patients with PsA and HCs. Further analysis revealed significant correlations between autoantibody levels, disease activity scores and treatment response of cutaneous disease manifestation after 16 weeks of treatment (Δ PASI), **Figure 1**. Moreover, the levels autoantibodies directed to the MAS receptor, CXCR3, PAR1 and stabilin were significantly higher in patients with PsA suffering from depression compared to patients without depression (MASR: $p=0.035$; CXCR3: $p=0.011$; PAR1: $p=0.047$; stabilin: $p=0.035$), although binary logistic regression did not prove any predictive value for these four antibodies.
Conclusion: Autoantibodies directed to GPCRs correlated with disease activity scores in patients with PsA. Further larger analyses regarding the functional role of these autoantibodies in PsA are required.
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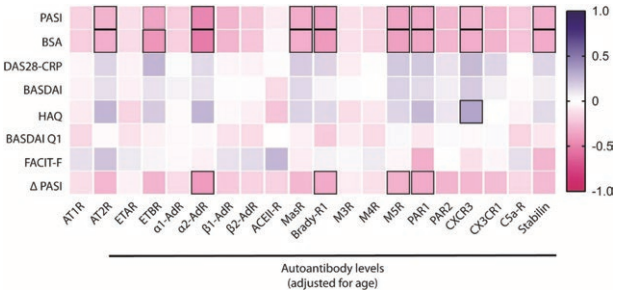


Figure 1. Heatmap displaying Pearson's correlation coefficient of correlation analyses between diseases activity scores and autoantibody concentrations adjusted for age at baseline. Pearson correlation analyses with a p-value <0.05 are marked with a box.

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POS0876 ASYMPTOMATIC HELL ENTHESITIS IN PSORIASIS PATIENTS: AN ULTRASOUND STUDY

Keywords: Enthesitis, Ultrasound, Psoriatic arthritis

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Background: Enthesitis is a common clinical feature of psoriatic arthritis (PsA) especially in lower limb. Clinical screening for enthesitis in patients with psoriasis before developing PsA may be non-specific. Ultrasound has shown its value in the study of entheses.

Objectives: To asses heel entheses of asymptomatic psoriasis patients and healthy control using ultrasound.

Methods: We conducted a cross-sectional case-control study including psoriasis patients with no rheumatic symptoms and sex and age-matched healthy controls. We assessed the affected skin surface (SC) and the psoriasis severity score (PASI). Ultrasound evaluation of the calcaneal enthesis (CE) and the plantar fascia enthesis (PFE) was performed. Ultrasound abnormalities sought were: hypoechogenicity, enthesis thickening, bursitis, cortical erosion, calcification, enthesophyte, and presence of Doppler signal.

Results: A total of 76 patients (38 cases and 38 controls) were recruited with a mean age of 51.9±15 [19-76] years and male predominance (60%). On clinical examination, pressing pain was present at the CE and PFE in, respectively, 17.5% and 12.5% of psoriasis patients but with no significant difference comparing to controls (10% EC; 10% PFE respectively) (p=0.777; p=0.259 respectively). On ultrasound, 60% of psoriasis patients had at least one ultrasound abnormality at the CE versus 17.5% of controls (p<0.001). The most observed ultrasound abnormalities at the CE were: enthesophyte (n=17), enthesis thickening (n=15), erosions (n=11) and hypoechogenicity (n=5). The PFE was less affected on ultrasound, presenting abnormalities in 42.5% of psoriasis patients versus 12.5% of controls (p=0.410). Erosions (n=13) and enthesis thickening (n=12) were the most observed abnormalities. The presence of ultrasound abnormalities at the PFE in psoriasis patients was correlated with age (p=0.012) and disease duration (p=0.015). Psoriasis severity according to SC and PASI was not associated with the presence of ultrasound abnormalities at CE (p=0.860; p=0.417 respectively) and PFE (p=0.399, p=0.156 respectively).

Conclusion: Our study showed that psoriasis patients could have asymptomatic heel enthesitis with greater involvement of the CE. Psoriasis patients need regular monitoring and screening for early symptoms of PsA.

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Disclosure of Interests: None Declared.

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POS0877 A COMPARISON OF PSA AND RA PATIENT PROFILES REQUIRING ADVANCED THERAPIES: PSA PATIENTS ACCESS TO THE ADVANCED THERAPIES EARLIER THAN RA

Keywords: bDMARD, Psoriatic arthritis, Rheumatoid arthritis

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Background: International guidelines recommend switching to advanced therapy (AT) in patients with Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA), when conventional synthetic disease modifying antirheumatic drugs (csDMARD) fail. There are several factors playing a role in that decision, including patients' comorbidities and choices as well as the availability of the treatments.

Objectives: Here we present the results of a comparison of PsA and RA patient profiles requiring advanced therapies, from our pilot biologics clinic. Better patient outcomes in one disease may help us to recognize what can be improved in the other.

Methods: Biologics clinic is a new initiative at Ottawa Hospital aiming to improve the long-term outcomes. Patients who are about to start or switch advance therapy are evaluated at the biologics clinic. Extensive data regarding disease history, medication exposure and disease activity are collected in a standardized fashion; the comorbidity burden is documented. A protocoled ultrasound (US) is conducted at baseline and three-month intervals, until reaching remission. The data presented here represent a pilot exploratory comparative analysis.

Results: PsA (n=18) and RA(n=42) patients had similar demographic features, other than RA patients being older (table 1). The majority of the comorbidities were similar in both groups, although PsA patients had more frequent liver disease numerically (5 (27.8 %) vs 5 (11.9%), p= 0.149) and less alcohol use (19 (38.9%) vs 7 (45.2%), p= 0.649). PsA patients had more frequent moderate/severe depression using the PHQ (61.1% of PsA vs 26.2% of RA; p=0.01). For disease activity, PsA patients tend to have higher disease activity based on the TJC, HAQ and physician global; in addition to significantly longer morning stiffness then RA (Table 1). Conversely, the disease activity within the joints based on the US scores of RA patients were higher. Disease duration at the time of initiation of the first advanced therapy was significantly shorter in PsA (median (IQR) 1.0 (7.75) years) compared to RA (6 (12.5), p=0.005) and PsA patients were treated with less numbers of csDMARD.

Conclusion: According to our preliminary data, PsA patients access to advanced therapy earlier than the RA. This may be due to the heterogeneity of PsA, such as manifestations other than the joint inflammation (enthesitis and axial disease) determining treatment decisions. PsA patients also had more frequent liver disease, which also may have prevented initiation of csDMARD and led to expediated initiation of the advance therapy- as early as at diagnosis. Whether earlier access leads to better patient outcomes in PsA, will be investigated with long-term follow up. PsA patients having more tender joints despite less severe US scores may be due to the proximity of the enthesis to the joints and difficulties to differentiate entheseal pain from joint involvement by the physical exam. The use of US may improve the assessment of the domains in PsA leading to choosing the right treatments.

Table 1. Comparison of PsA and RA patient profiles

		RA (N:42) N (%)	PSA (N:18) N (%)	p
Demographics	**Sex: Female**	30 (71.4 %)	12 (66.7 %)	0.712
	Age; Mean±SD	59.3±14.9	50.3±13.6	**0.033**
	Smoking (ever)	27 (64.3 %)	12 (66.7 %)	0.859
Disease Features	**RF positive**	30 (73.2 %)	2 (12.5 %)	<0.001
	anti-CCP positive	23 (57.5 %)	2 (14.3 %)	0.005
	CRP positive	16 (38.1 %)	6 (33.3 %)	0.726
	ESR positive	16 (38.1 %)	7 (38.9 %)	0.954
	Disease duration (years)*	14.0 (19.8)	5 (13.8)	**0.036**
Previous therapies*	**Previous number of csDMARDs**	3 (1)	2 (2)	**0.005**
	Previous number of advanced therapies	0.5 (2)	0.5 (2)	0.945
	Time to first biologics initiation from diagnosis	6 (12.5)	1 (7.75)	**0.005**
Disease activity/ Clinical*	**Duration of morning stiffness (hours)**	1 (1.4)	2 (5.5)	**<0.001**
	Swollen joint count (44)	8 (5)	5 (5.5)	0.199
	Tender joint count (44)	8.5 (13)	14 (17)	0.244
	Patient VAS	5.5 (4)	6 (3)	0.648
	Physician VAS	5 (3)	6 (2)	0.066
	HAQ	1.125 (1.125)	1.625 (1.094)	0.087
Disease activity/US*	**Ultrasound: GLOESS score**	36 (28)	22 (28)	**0.025**
	Ultrasound: Doppler score	8 (18)	3.5 (7.8)	0.058

* Median (IQR)

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POS0878 SCREENING FOR THE EARLY IDENTIFICATION OF PSORIATIC ARTHRITIS WITH AXIAL INVOLVEMENT (AXPSA) IN A COHORT OF ITALIAN PATIENTS AFFECTED BY PSORIASIS: RESULTS OF A DERMO-RHEUMATOLOGIC CROSS-SECTIONAL STUDY (ATTRACT)

Keywords: Diagnostic tests, Psoriatic arthritis, Spondyloarthritis

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Background: Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease characterized by different domains.[1] Interest is growing towards early diagnosis of axial PsA (AxPsA), to allow better disease characterization and well-timed targeted therapeutic strategies.

Objectives: In this study, we report preliminary results of a rheumatological screening strategy settled in a dermatological centre. Primary objective is to validate the screening tool in a cohort of Italian patients affected by psoriasis, improving early diagnosis of AxPsA. Secondary objectives are: 1. classification and characterization of axial involvement; 2. profiling of patients' characteristics and comorbidities.

Methods: Patients were enrolled in the ATTRACT study (**A**xial psoria**T**ic ar**T**hritis sc**R**eening **A**n**C**ona i**T**aly) according to the following inclusion criteria: **1.** age > 18 years; **2.** diagnosis of psoriasis (Pso) by a dermatologist; **3.** capacity to understand and sign the informed consent. Patients who assumed any DMARD 12 weeks prior to screening were excluded. Study design is shown in Figure 1. The Dermatologic-Centred Screening (DCS) tool[2], recently validated for early identification of AxPsA, was translated in Italian and administered to outpatients in the dermatological clinic. Patients were divided in the following groups based on answers to the Inflammatory Back Pain (IBP) related questions of the DCS: **A.** no affirmative answers (low AxPsA probability); **B.** all affirmative answers (high probability); **C.** only two affirmative answers (intermediate probability). Group B & C patients underwent complete rheumatological examination comprehensive of clinimetric, laboratoristic and genetic data; Xray and MRI imaging of the whole spine and pelvis were performed in all of them classifying in: **a.** confirmed AxPsA; **b.** peripheral PsA involvement only; **c.** PsA excluded.

Results: N.366 patients were screened; n.101 met exclusion criteria. N.91 (34.3%) were classified as group A, n.125 (47.2%) as group B, n.49 (18.5%) as group C. Following characteristics were notable: a. female sex more represented in group B; b. mean age higher in group C; c. onichopathy more represented in group A & C. List of patients' clinical characteristics is shown in Table 1 Among group B patients, n.28 (22.4% - B1) were classified as PsA excluded; n.22 (17.6% - B2) as isolated per-PsA (according to CASPAR criteria), n.39 (31.2% - B3) as AxPsA (n.34 fulfilling ASAS criteria, n.31 with concomitant per-PsA). Among group C, n.15 (30.6% - C1) as PsA excluded; n.3 (6.1% - C2) as isolated per-PsA, n.5 (10.2% - C3) as AxPsA (n.4 fulfilling ASAS, n.5 with concomitant per-PsA). N.13 patients are still awaiting results of imaging; n.49 (n.24 group B, n.25 group C) refused to undergo imaging and were considered lost at follow-up.

Conclusion: The DCS tool may be useful for PsA screening in a real-life cohort of Pso patients, an Inflammatory Back Pain was reported by about half of the screened Pso patients. This tool helped to identify a substantial number of naïve patients not only affected by AxPsA but also by peripheral PsA in a purely dermatological setting.

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Table 1. Comparison between clinical characteristics of patients in groups A, B and C.

	Group A (n.91)	Group B (n.125)	Group C (n.49)	p
Gender (F/M), n(%)	35(38.5)/56(61.5)	76(60.8)/49(39.2)	20(40.8)/29(59.2)	**0.002**
Age, yrs	51.49±17.33	49.15±15.65	59.57±17.9	**0.0012**
PASI*	3.71±5.38	3.33±6.35	1.73±2.73	0.171
Onichopathy, y/n, n(%)	30 (46.2)/35 (53.8)	76(69.7)/33(30.3)	24(66.7)/12(33.3)	**0.007**
Cardiovascular diseases	32 (59.3)	36 (42.9)	22 (59.5)	0.124
Metabolic diseases	33 (61.1)	52 (61.9)	23 (62.2)	0.476
Infections	1 (1.9)	3 (3.6)	0 (0.0)	0.670
Neurologic/Psychiatric	4 (7.4)	7 (8.3)	3 (8.1)	0.877
Back pain duration > 3 months (question 3a), n(%)	0 (0.0)	125(100)	34(69.4)	**< 0.001**
Back pain start before age of 45 (question 3b), n(%)	0 (0.0)	125(100)	15(30.6)	**< 0.001**

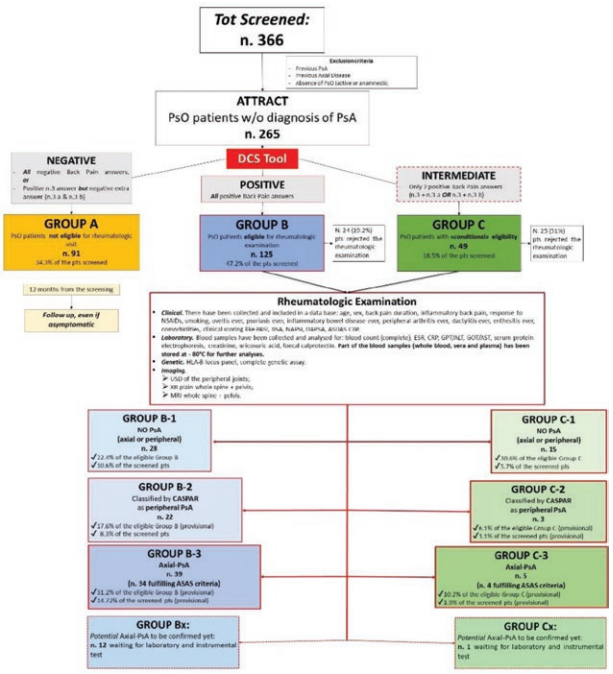


Figure 1. Design of the study

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POS0879

THE IMPACT OF 6-MONTH DELAY IN DIAGNOSIS ON CLINICAL AND FUNCTIONAL STATUS IN THE PSA PATIENTS UNDER BDMARD TREATMENT: RESULTS FROM TREASURE DATABASE

Keywords: Registries, Psoriatic arthritis, Real-world evidence

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Background: The impact of delay in diagnosis on the disease severity and functional loss has been shown previously In Psoriatic arthritis (PsA) patients.

Objectives: This study aimed to evaluate the impact of 6 month-delay in diagnosis on patients` clinical outcomes and functional outcomes in the PsA patients under bDMARD therapy using a national database.

Methods: TReasure is a national, multicentre, longitudinal, and observational database, initiated in Turkey in 2017 and now includes 17 centres [1]. PsA patients with/out more than 6 months from the onset of symptoms to diagnosis were evaluated. Demographic characteristics of the patients (age, gender, delay in diagnosis), smoking (ever), BMI, and CCI score were calculated. PsA and associated disease characteristics; dactylitis, enthesitis, uveitis, IBD, sacroiliitis by mNY, disease activity at bDMARD initiation; SJC (66 joints), TJC (68 joints), ASDAS-CRP, ASDAS-ESR, BASDAI, ESR, CRP, VAS (physician global, patient global), function and quality of life; BASFI (>40 mm), HAQ-DI (<0.5, 0.5-1.0, >1.0), EQ5D, were assessed and compared between two groups.

Results: In TReasure database, the time between symptom to diagnosis was known in 865/911 (94.9%) of PsA patients. More than 6 months of delay in diagnosis was present in 627/865 (72.4%) patients. In delayed-diagnosis group time from symptom onset to initiation of bDMARD was longer (6.1 (3.3-6.1) vs 2.4 (0.8-7.1) years, p<0.001). Patients with delay in diagnosis of PsA had more sacroiliitis (57.3% vs 46.2%, p=0.014) according to mNY criteria. However, dactylitis was more common in patients with less than 6 months of delay in diagnosis (31.2% vs 19.1%, p<0.001).Patients' ASDAS-CRP and VAS-Physician Global score were slightly higher, while other activity parameters were similar; (ASDAS-ESR, BASDAI, BASMI, VAS patient global, SJC and TJC) (Table 1). There was no difference between the median (IQR) BASFI and HAQ-DI scores in delayed-diagnosis group, whereas BASFI and HAQ-DI categories showed worse function and quality of life. EQ5D showed similar result with slightly worse scores in delayed-diagnosis group.

Conclusion: Approximately three-quarters of PsA patients using bDMARDs have a delay of at least 6 months in diagnosis. Delay in diagnosis significantly prolongs the time until bDMARD initiation. The most important clinical finding in earlier diagnosis group is dactylitis. Axial involvement may be a reason, perhaps the result, of the delay in diagnosis. Since the delay in diagnosis is related to poor function and quality of life, efforts should be made for early diagnosis at every stage.

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Table 1. Demographic and Clinical Characteristics of Patients with/without diagnostic delay

	Patients with diagnostic delay < 6 months n=238	Patients with diagnostic delay > 6 months N=627	P
Current Age (y)	45 (38-57)	47 (40-57)	0.09
Gender (male) n, (%)	89 (37.4)	200 (31.9)	0.13
Delay in diagnosis, month	3.0 1.0-4.9)	24.0 (11.9-61.0)	**<0.001**
Disease duration (symptom-bDMARD initiation)	2.4 (0.8-7.1)	6.1 (3.3-6.1)	**<0.001**
Disease duration (diagnosis-bDMARD initiation)	2.3 (0.6-7.1)	2.5 (0.7-6.2)	0.61
BMI	28.1 (24.6-32.0)	28.0 (24.9-31.9)	0.62
Smoking (ever)	119 (50.6)	289 (47.2)	0.37
CCI (≥1), n (%)	47 (19.7)	127 (20.3)	0.62
ASDAS-CRP	3.45 (2.77-4.08)	3.62 (3.14-4.25)	**0.011**
BASFI Score (0-10)	4.6 (2.2-6.2)	4.7 (3.4-5.9)	0.52
BASFI category > 4	92 (61.7)	307 (71.4)	**0.028**
EQ5D score	11 (9-11)	11 (10-12)	**0.026**
HAQ-DI score	0.64 (0.40-1.0)	0.63 (0.50-0.80)	0.76
HAQ-DI category	37 (28.0)	68 (17.6)	**0.002**
<0.5	58 (43.9)	241 (62.4)	
0.5-1.0	37 (28.0)	77 (19.9)	
> 1.0			
VAS-Physician global	70 (50-80)	70 (60-80)	**0.003**
Sacroliitis according to mnY, n (%)	80 (46.2)	238 (57.3)	**0.014**
Dactylitis, n (%)	64 (31.2)	105 (19.1)	**<0.001**

Continious variables were presented as median (%25-75),BMI: Body mass index (n=856), CCI: Charlson Comorbidity Index (n=865), BASFI: The Bath

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Disclosure of Interests: None Declared.

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POS0880

COMPARATIVE DISEASE BURDEN IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS OR ANKYLOSING SPONDYLITIS: DATA FROM COVAD PATIENT-REPORTED E-SURVEY

Keywords: Psoriatic arthritis, Rheumatoid arthritis, Spondyloarthritis

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Background: Rheumatoid arthritis (RA) and spondyloarthritis, including either Psoriatic Arthritis (PsA) and Ankylosing Spondylitis (AS), are some of the most diagnosed autoimmune rheumatic diseases (AIRDs) in rheumatologists' routine clinical practice [1]. Understanding patients' health and functional status is crucial to provide personalized management strategies to optimize disease control and enhance the quality of life.

Objectives: We aimed to compare disease burden in patients with RA, PsA or AS by assessing Patient-Reported Outcome Measurement Information System (PROMIS) Physical Health, Global Mental Health, Physical Function and Fatigue 4a together with VAS Pain.

Methods: Data were obtained in the international COVID vaccination in autoimmune rheumatic diseases study second e-survey (COVAD study). Demographics, AIRD diagnosis, disease activity, PROMIS Global Physical health, PROMIS Global Mental Health, PROMIS Physical Function SF10 and PROMIS Fatigue 4a score were extracted from the COVAD study database. For this study, we only included patients with self-reported RA or spondyloarthritis (either PsA or AS) undergoing active treatment with conventional synthetic disease-modifying drugs (DMARDs) and/or biologic DMARDs, who answered all the survey questions. Active disease was defined as the patient's perception of their disease as active in the four weeks before their first COVID-19 vaccine shot. Analysis of Variance with Bartlett's and Tukey's test was used to compare continuous variables between groups.

Results: From January to June 2022, n.1907 patients with RA, female 87.62% (1671/1907), with mean age (±SD) 50.95 ±13.67, n.311 patients with PsA, female 67.20% (209/311), with a mean age of 50.42 ±12.70, and n.336 patients with AS, male 51.31% (209/311), with a mean age of 43.13 ±12.75 years, responded to the COVAD e-survey. In those with active disease, neither physical health, global mental health, physical function, fatigue, nor pain were different among groups

(Table 1, Figure 1). Patients with inactive AS had higher mean global physical health scores than RA patients (13.13 ±2.93 VS RA 12.48 ±2.90, p=0.01, Table 1). Those with inactive RA or PsA showed more severe fatigue (PsA 10.58 ±2.22, RA 10.45 ±4.08 VS 9.4 ±4.13, p =0.01 for both). Patients with inactive RA also reported poorer physical function and more residual pain than those with AS (37.79 ±8.86 VS 41.13 ±7.79, p<0.001; 3.87 ±2.45 VS 3.34 ±2.39, p=0.01, respectively). Similarly, residual pain was perceived as higher in patients with inactive PsA than those with AS (4.04 ±2.50 VS 3.34 ±2.39, p=0.01)

Conclusion: Disease burden is roughly comparable in patients with active RA, PsA or AS. Patients with inactive RA and PsA suffer higher disease burden than those with inactive AS.

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Table 1. Patient-Reported Outcome Measures between groups.

Inactive disease							
	AS (n.185)		PsA (n.179)		RA (n.1167)		
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	
PROMIS Global Physical Health	13.13*	2.95	12.43	3.27	12.48	2.90	p=0.01, VS RA
PROMIS Global Mental Health	13.31	3.36	12.97	3.33	12.84	3.17	
PROMIS Fatigue 4a	9.4	4.13	10.58*	4.22	10.45*	4.08	p=0.01, both
PROMIS Physical Function SF10 Score	41.13	7.39	39.27	9.01	37.79*	8.86	p<0.001, VS AS
VAS Pain	3.34	2.39	4.04*	2.50	3.87*	2.45	p=0.01, both
Active Disease							
	AS (n.35)		PsA (n.38)		RA (n.189)		
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	
PROMIS Global Physical Health	11.05	3.19	10.10	2.76	11.24	3.41	
PROMIS Global Mental Health	11.31	3.26	10.84	3.63	11.89	3.30	
PROMIS Fatigue 4a	12.94	4.87	12.84	4.42	11.75	4.68	
PROMIS Physical Function SF10 Score	35.82	9.62	33.52	8.76	34.90	9.80	
VAS Pain	4.68	2.77	5.0	2.54	4.68	2.61	

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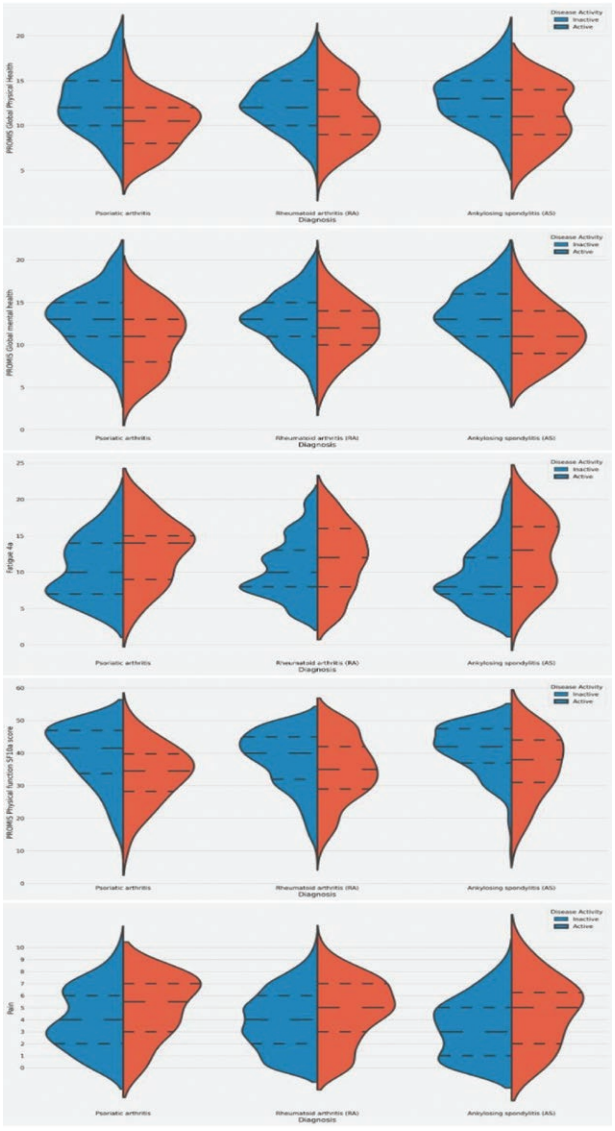


Figure 1. Violin plots showing kernel densities, quartiles and median for Patient-Reported Outcome Measures for patients with RA, PsA and AS, stratified by disease activity status.

POS0881

SPECIFIC AI-GENERATED PATTERN OF TENDER JOINTS AND TENDERNESS AT ENTHESIAL SITES ARE PREDICTIVE FOR OBJECTIVE DETECTION OF MUSCULOSKELETAL INFLAMMATION IN PSORIASIS PATIENTS

Keywords: Artificial intelligence, Psoriatic arthritis

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Background: Psoriasis (Pso) is one of the most common chronic inflammatory skin diseases in Europe. Psoriatic arthritis (PsA) is closely associated to Pso. Up to 30% of the Pso patients will develop PsA during skin disease course. Defined and validated approaches for early detection are still missing. Beside biomarkers from blood or imaging, clinical characteristics of the patients may be of value to detect PsA patients in the transition state early.

Objectives: To perform an AI-based cluster analysis in a cohort of Pso patients at-risk for development of PsA to assess clinical characteristics as markers for early PsA.

Methods: Clinical data sets from the recently published XCITING study [1] were used to perform an AI based analysis using the attributes “tenderness of joints

(68 TJC)" "tenderness at entheses (LEI)" to detect clinical profiles for early detection of inflammatory musculoskeletal (MSK) processes defined as positive findings in clinical examination (SJC, PsA diagnosis), MSUS or fluorescence optical imaging. Main criteria for inclusion into XCITING as at-risk study were Pso without PsA diagnosis, nail involvement and/or MSK complaints within the last 6 months. For clustering the patients, the AI-based analysis contained three steps: (1) Reducing random noise by performing Non-Negative Matrix Factorization, (2) embedding into 2D using t-SNE and (3) clustering using DBSCAN.

Results: Characteristics of the XCITING cohort were described previously [1]. After performance of the cluster analysis, seven different cluster types were identified (cluster 0-6) according to the clinical data sets of the cohort by use of the attributes and tested for their significance to predict the presence or absence of MSK inflammation in Pso (swollen joints, positive MSUS or positive FOI). Three "tenderness clusters" out of 7 were identified with significant correlation: while as expected cluster 2 (no major findings in LEI and TJC) is associated with no inflammation, "feet- type" involvement (cluster 4) and dominance at PIP and DIP joints (cluster 6) (Figure 1, Table 1) are associated with MSK inflammation at the hands.

Conclusion: Markers for early detection of Pso patients who will develop PsA are missing. Within this analysis we show, that by use of clinical data sets only, risk profiles developed from finding of tenderness at different anatomical regions might be helpful for detection of inflammatory MSK processes. Interestingly, the feet tenderness can also predict MSK inflammation at the hands. A combination of both, clinical data sets and liquid/imaging biomarkers may be identified on base of this observation to increase the potential to detect Pso patients with high-risk profiles for PsA early.

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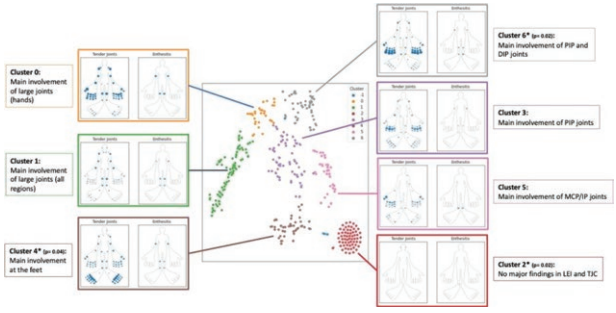


Figure 1. Cluster analysis of patients with psoriasis only but increased risk for PsA according to the attributes "tenderness of joints (68 TJC)" and "tenderness at entheses (Leeds enthesitis index)"

Table 1. Results of the cluster analysis

Cohort	Cluster	P-Value	Odds Ratio	CI	n=402
No major findings in LEI and TJC	Cluster 2	**0.02**	0.53	[0.31, 0.91]	64
Main involvement at the feet	Cluster 4	**0.04**	2.0	[1.03, 4.06]	48
Main involvement of PIP and DIP joints	Cluster 6	**0.02**	2.2	[1.10, 4.31]	50
Combination of other clusters	0+1+3+5	0.53	0.87	[0.58, 1.31]	240

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Disclosure of Interests: None Declared.

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POS0882 SCREENING/REFERRAL STRATEGIES FOR THE EARLY RECOGNITION OF PSA AMONG PATIENTS WITH PSORIASIS: RESULTS OF A GRAPPA SURVEY

Keywords: Psoriatic arthritis, Diagnostic tests

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Background: Diagnostic delay in psoriatic arthritis (PsA) is associated with poorer outcomes, and early screening/ referral strategies are important to reduce the delay. Implementation of early screening approaches demands cooperation between rheumatologists, dermatologists and primary care providers (PCPs).

Objectives: To explore the experiences of dermatologists and rheumatologists in the early recognition of PsA and suggest improvements to the current shared-care model.

Methods: A 24-question survey addressing referral strategies was constructed within GRAPPA (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis) and sent to all members (n=927). Questions addressed the use of screening tools, interspecialty involvement in therapeutic decision making, and suggestions for earlier recognition.

Results: Surveys were completed by 113 rheumatologists from 37 countries (across six continents) and 26 dermatologists from 16 countries (across 4 continents), with a mean of 21.7 ± 10.7 and 18 ± 12.3 years experience, respectively. Of dermatologists, 81% use PsA-specific screening instruments. Conversely, rheumatologists reported that only 27% of patients referred to them from all sources had been assessed with screening tools. Across both specialties, "PEST" was reported to be the most used tool. Whilst dermatologists reported that 67% ± 28% of their suspected PsA cases were confirmed, rheumatologists felt ~48% ± 24% of suspected PsA cases were confirmed. Both specialties (n=137) reported similar views regarding optimisation of the diagnostic process: 78% believed that the best approach involved combining patient-reported and physician-confirmed findings (see Figure 1A). Moreover, the education of PCPs was seen as the greatest priority to improve screening with 76% raising this as an unmet need (Figure 1B).

Conclusion: The survey indicated the current unmet needs in the early recognition of PsA. Accordingly, important areas to address include improving the use of validated screening instruments, increasing the education of community-based dermatologists and PCPs, and utilising a combination of patient-reported and physician-confirmed findings to identify patients with a high probability of PsA among those with psoriasis.

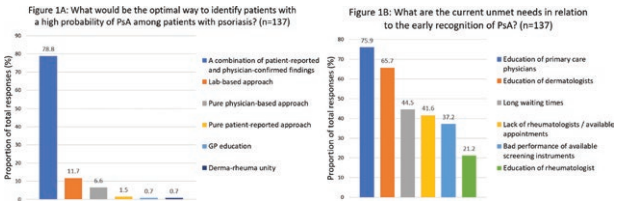


Figure 1. Clinicians' views on optimising early PsA recognition.

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POS0883 PREDICTORS OF PATIENT-REPORTED TREATMENT SUCCESS IN PATIENTS WITH PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis

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Background: Determinants of patient-reported treatment success in psoriatic arthritis (PsA) have not been defined.

Objectives: To determine predictors of patient-reported treatment success in PsA.

Methods: Rheumatologist-diagnosed PsA patients, who met the CASPAR classification, were recruited from a single center. PsA outcome measures included 68/66 joint counts, enthesitis, dactylitis, psoriasis body surface area (BSA), patient reported outcomes including PROMIS CAT. The study primary outcome was patient-reported treatment success: "Today, considering the level of control of your psoriatic arthritis and psoriasis, do you consider your treatment has been successful?" with response options Yes/No. Multivariate logistic regression analyses were performed to determine

predictors of patient-reported treatment success in PsA. We hypothesized that disease activity measures, including arthritis, psoriasis, enthesitis, and dactylitis, symptoms, and treatment type would contribute to patient-reported treatment success. We did not include multiple patient-reported outcomes in a model due to collinearity.
Results: A total of 178 participants had a baseline visit. Mean (SD) CASPAR score was 3.7 (0.9) age 51.7 (13.5) years, BMI 31.3 (7.2), while 52.2% were women, and 86.0% Caucasian. Treatment success was reported by 116 patients (65%). Overall, 105 participants had complete data for all the variables included in the logistic regression models. The total joint swelling 66, total joint tenderness 68, PROMIS pain interference, and PROMIS fatigue were significantly negatively associated with treatment success while controlling for age, race, gender, and BMI. Each additional swollen joint was associated with a 23% decreased odds of treatment success, each tender joint was associated with 17% decreased odds of success, each additional point on the PROMIS fatigue and on the PROMIS pain interference was associated with 6% and 15% decreased odds of success, respectively (Table 1). Patients receiving a tumor necrosis factor inhibitor (TNFi) had approximately 11-13 times increased odds of reporting treatment success compared to patients on a classical synthetic DMARD alone, while controlling for age, race, gender, and BMI.
Conclusion: Patient-reported treatment success was independently associated with control of tender and swollen joints, pain, fatigue, and with receiving a TNF-inhibitor medication. This supports the use of biological treatments as standard of care in PsA.

Table 1. Two models of predictors of patient-reported treatment success

	Model 1				Model 2		
Variable	Odds Ratio	95% Confidence Interval	P-value	Variable	Odds Ratio	95% Confidence Interval	P-value
Total joint swelling 66	**0.77**	**0.604-0.991**	**0.04**	**Total joint tenderness 68**	**0.83**	**0.70-0.97**	**0.02**
SPARCC Enthesitis Index	1.78	0.479-6.591	0.39	SPARCC Enthesitis Index	2.22	0.53-9.26	0.28
Psoriasis BSA	0.85	0.71-1.020	0.08	Psoriasis BSA	0.83	0.69-1.00	0.05
LDI Total Score	2.61	0.265-25.639	0.41	LDI Total Score	1.67	0.21-13.40	0.63
PROMIS pain interference	**0.85**	**0.772-0.931**	**0.00**	**PROMIS fatigue**	**0.94**	**0.88-0.99**	**0.03**
Medication MOA	Ref	Ref	Ref	*Medication MOA*	Ref	Ref	Ref
Classical synthetic	**12.86**	**1.497-110.47**	**0.02**	Classical synthetic	**10.61**	**1.3-86.9**	**0.03**
DMARD	12.53	0.64-245.168	0.10	DMARD	13.22	0.80-219.5	0.07
(reference)	1.90	0.332-10.847	0.47	(reference)	1.16	0.31-8.31	0.57
TNFi	2.17	0.227-20.824	0.50	**TNFi**	0.84	0.10-7.08	0.87
PDE4i	6.74	0.792-57.295	0.08	PDE4i	3.27	0.41-25.95	0.26
IL-17i	0.34	0.002-49.204	0.67	IL-17i	0.46	0.01-14.34	0.66
IL-23i				IL-23i			
Multiple MOAs				Multiple MOA			
No MOA				No MOAs			
BMI	1.06	0.977-1.154	0.16	BMI	1.05	0.97-1.14	0.19
Age at enrollment	1.01	0.966-1.064	0.57	Age at enrollment	1.00	0.95-1.04	0.90
Gender	Ref	Ref	Ref	*Gender*	Ref	Ref	Ref
Female (reference)	0.90	0.258-3.150	0.87	Female (reference)	0.70	0.21-2.37	0.57
Male				Male			
Race	Ref	Ref	Ref	*Race*	Ref	**Ref**	**Ref**
White	0.24	0.017-3.359	0.29	White (Reference)	0.38	**0.03-4.28**	**0.44**
Black	0.81	0.035-18.923	0.90	Black	1.18	**0.07-19.37**	**0.91**
Asian				Asian			

Ref, reference group; i = inhibitorModel 1: N=105; R^2 = 0.36Model 2: N=104, R^2=0.32

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POS0884

THE REAL IMPACT OF AGE ON PSORIATIC DISEASE: A PORTUGUESE MULTICENTER COHORT STUDY

Keywords: Psoriatic arthritis

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Background: Psoriatic Arthritis (PsA) is an immune-mediated disease that additionally to the predominant skin and musculoskeletal features, comorbidities such as metabolic syndrome are common. This type of comorbidities increases significantly the burden of the disease, reduces quality of life, and affects negatively the clinical response to the treatment. Ageing adds another variable to this composite as there appears to be evidence of clinical, genetic, and histopathological differences between early and late-onset PsA.
Objectives: To compare the socio-demographics and clinical data in PsA patients with a younger-onset (YOPsA) and late-onset (LOPsA) of disease and to evaluate disease activity and function at presentation and during a follow-up of two years.
Methods: A multicenter cohort study including adult PsA patients with peripheral involvement registered in the Rheumatic Diseases Portuguese Register (Reuma.pt) up to December 2022 was performed. Patients were divided into 2 groups according to the onset age of PsA: YOPsA (<50 years) and LOPsA (≥50 years). Univariate analysis was performed followed by multivariate analysis.
Results: A total of 543 [YOPsA, 301 (55.4%); LOPsO, 242 (44.6%)] patients with peripheral PsA were included. Demographic and clinical data is represented in Table 1. Compared to patients with LOPsA, PsA patients with early onset showed more frequently dactylitis and nail involvement (p<0.001). Regarding the comorbidities, there was a higher frequency of arterial hypertension, dyslipidemia, diabetes mellitus and hyperuricemia in LOPsA patients (p<0.05). After 2 years of follow-up, LOPsA patients had a worse Disease Activity Score-28 with Erythrocyte Sedimentation Rate (DAS-ESR) (2.8 vs 2.5, p=0.006), higher Patient Global Assessment (PGA) (40.5 vs 35, p=0.05), higher levels of C -Reactive Protein (CRP) (0.9 vs 0.7, p=0.038) and ESR (18.9 vs 14.2, p=0.001) and higher Health Assessment Questionnaire (HAQ) (0.7 vs 0.5, p=0.005). LOPsA patients were treated with more biologic DMARDs (p<0.0001). Adjusting for age, the late onset of PsA was associated with the presence of traditional cardiovascular risk factors.

Table 1.

	YOPsA (n=301)	LOPsA (n=242)	*p*
Current age, years (mean±SD)	48.2±9.3	68.4±7.7	**<0.001**
Sex (M/F), n	165/136	135/106	0.516
Age of diagnosis, years (mean±SD)	37.8±7.9	58.7±6.5	**<0.001**
Disease duration, years (mean±SD)	10.5±5.2	9.7±4.6	0.193
Comorbidities, n (%)			
Arterial Hypertension	38 (12.6)	69 (28.5)	**<0.001**
Dyslipidemia	29 (9.6)	61 (25.2)	**<0.001**
Diabetes Mellitus	11 (3.7)	38 (15.7)	**<0.001**
Obesity	8 (2.7)	9 (3.7)	0.468
Hyperuricemia	2 (0.7)	10 (4.1)	**0.007**
Smoking status, n (%)	41 (13.6)	26 (10.7)	**0.013**
Psoriasis, n (%)	211 (70.1)	165 (68.2)	0.425
Nail involvement, n (%)	85 (28.2)	36 (14.9)	**<0.001**
Axial involvement, n (%)	76 (25.2)	59 (24.4)	0.919
Dactylitis (ever), n (%)	102 (33.9)	44 (18.2)	**<0.001**
Enthesitis (ever), n (%)	78 (25.9)	47 (19.4)	0.093
Positivity HLA-B27, n (%)	30 (10)	25 (10.3)	0.084
Family history, n (%)	55 (18.3)	42 (17.4)	0.909
Type of clinical pattern, n (%)			**0.001**
Asymmetric oligoarthritis	93 (31)	69 (28.5)	
Symmetric polyarthritis	162 (53.8)	154 (63.6)	
Predominant distal interphalangeal joint	22 (7.3)	1 (0.4)	
Mutilans arthritis	3 (1.0)	4 (1.7)	
DAS28-CRP at baseline, mean±SD	3.6±1.4	3.6±1.1-	0.909
DAS28-ESR at baseline, mean±SD	3.9±1.4	3.9±1.3	0.339
ESR at baseline, mean±SD	29.3±28.1	14.2±14.8	0.061
CRP at baseline, mean±SD	2.1±3.5	2.3±2.6	0.115
PGA at baseline, mean±SD	52.1±27.8	58.1±21.4	0.365
HAQ at baseline, mean±SD	0.6±0.7	0.7±0.6	0.531
DAS28-CRP, mean±SD*	2.4±1.1	2.4±1.1	0.339
DAS28-ESR, mean±SD*	2.5±1.4	2.8±1.3	**0.006**
ESR, mean±SD*	14.2±14.8	18.9±16.6	**0.001**
CRP, mean±SD*	0.7±1.5	0.9±3.55	**0.038**
PGA, mean±SD*	35.0±25.8	40.5±26.9	**0.05**
HAQ, mean±SD*	0.5±0.7	0.7±0.6	**0.005**
Therapeutic, n (%)			
cDMARDs	202 (67.1)	178 (73.5)	0.084
bDMARDs	84 (27.9)	117 (48.3)	**<0.001**

*after two years of follow-up

Conclusion: Our study suggests that the age at onset of PsA seems to be an important covariate that might affect the clinical and laboratory manifestations of the disease and its clinical outcomes.
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Diagnostics and imaging procedures

POS0885 CARDIAC INVOLVEMENT IN SYSTEMIC SCLEROSIS - THE ADDED VALUE OF CARDIAC MAGNETIC RESONANCE

Keywords: Systemic sclerosis, Imaging, Heart

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Background: Cardiac complications of systemic sclerosis (SSc) are frequently subclinical or insidious and may affect up to 80% of patients [1], remaining one of the leading causes of death in, usually in the mechanism of life-threating arrythmia, heart failure or sudden cardiac arrest [2]. Diagnostic tools that can be used for heart involvement in SSc include ECG, echocardiography, serum markers (troponin, CK-MB, BNP, NT-proBNP) and, recently, magnetic resonance imaging. Cardiac magnetic resonance (CMR) with advanced tissue characterization techniques (including parametric mapping of T1 and T2 relaxation times as well as extracellular volume [ECV] fraction of the myocardium) can provide unique non-invasive insight into early (inflammation, oedema) and late (fibrosis, necrosis) stages of heart involvement in those patients [3].
Objectives: To assess cardiac involvement in unselected systemic sclerosis patients in both diffuse (DSSc) and localized (LSSc) clinical subgroups, using contemporary cardiac magnetic resonance imaging techniques.
Methods: In this prospective single-centre study, we included 20 consecutive systemic sclerosis patients (51+/- 14 years, 14 [70%] female) in whom CMR was performed between 2013 and 2022. Their baseline CMR results, clinical presentation of SSc, medical history, laboratory tests, lung function tests, and follow-up were analyzed with special attention to CMR features of heart involvement in the course of SSc in both clinical subgroups. Moreover, CMR findings were compared to a group of healthy controls (N= 37).
Results: Systemic sclerosis patients had significantly lower LVEF (56,6% vs 61,6%, p<0,002), higher LVESVI (38,9 ml/m2 vs 31,6 ml/m2, p=0,002), longer T1 and T2 relaxation times (1029,3 ms vs 993 ms and 48,1 ms vs 44 ms, respectively; p<0,001), and higher ECV (27,9% vs 26,0%, p<0,05) as compared to healthy controls. Overall, 13 (65%) patients had at least one abnormal finding in CMR, of which in 7 (35%) baseline ECG and echocardiogram were normal or borderline normal. Additionally, heart involvement was more frequent among DSSc patients (11/13), with more severe manifestations including greater extent of dysfunction and more pronounced tissue alterations than in LSSc patients (2/7). Of note, CMR allowed for detection of subtle tissue abnormalities in 3 (15%) of patients with normal ECG and normal echocardiogram, as well as added new tissue information (edema/abnormal T1/T2/ECV and/or non-ischemic fibrosis) in 4 (20%) others, in whom borderline unspecific echo abnormalities were detected. During a median follow up of 3,4 (1,9-5,5) years, three patients (15%) died (heart failure - 1, gastrointestinal complications - 1 and breast cancer - 1). Treatment escalation and deescalation were required in 8 and 5 patients, respectively. Two patients had their treatment changed over the follow up period, in 5 the treatment remained unchanged.
Conclusion: SSc patients frequently present heart involvement, especially in DSSc type. This complication is often late diagnosed or misdiagnosed by conventional methods. Cardiac magnetic resonance with modern tissue characterization techniques, provides detailed insight in heart involvement in systemic sclerosis. Modern quantitative techniques allow for early diagnosis, thus prompting closer follow up and/or treatment decisions in a proportion of patients in whom other diagnostic tests were inconclusive.
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POS0886 18F-FDG PET-CT OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH EARLY SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Lungs, Imaging

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Background: Patients with systemic sclerosis associated interstitial lung disease (SSc-ILD) have a highly variable disease course, which makes clinical management challenging [1]. Hence, there is a clinical need for new tools to improve patient monitoring and stratification. ^{18}F-Fluorodeoxyglucose (FDG) PET-CT of the lungs has previously shown promising results in patients with SSc-ILD by reflecting ILD activity and contributing to the prediction of lung function decline [2,3]. However, as most studies have been performed in patients with longstanding and severe ILD, there is limited information concerning the value of ^{18}F-FDG PET-CT in the first two years after SSc diagnosis and the recognition of early ILD.
Objectives: To prospectively investigate the presence and severity of ILD as detected by ^{18}F-FDG PET-CT in patients with early SSc.
Methods: Included patients fulfilled the 2013 ACR-EULAR classification criteria for SSc, had a disease duration ≤ 2 years (from onset of first non-Raynaud's symptoms) and diffuse cutaneous disease. All patients underwent a high-resolution CT scan of the lungs to evaluate the presence of ILD, as part of routine clinical care, as well as pulmonary function tests. ^{18}F-FDG PET-CT was performed in 13 patients (ILD n=9; no ILD n=4). For quantitative analysis, six volumes of interest (VOIS) of 2cm were placed in pre-specified dorsobasal lung areas, as described previously [3]. The six standardized uptake values (SUV) were processed and averaged to obtain a total SUV for the dorsobasal lung fields. To correct for inter-individual differences, all uptake values were corrected for ^{18}F-FDG uptake in the mediastinal blood pool [3]. Statistical analysis was performed using a Mann-Whitney U test to compare for between-group differences.
Results: In the ILD group, 7/9 (78%) of the patients were male with an average age of 53.2 years. In the non-ILD group 2/4 patients were male (50%), with an average age of 41.3 years. All patients received immunosuppressive treatment with either Mycophenolate Mophetil (ILD 100%; no ILD 50%) or Methotrexate (ILD 0%; no ILD 50%) before inclusion. Quantitative analysis of ^{18}F-FDG PET-CT revealed that SUVmax corrected in the dorsobasal lung fields was higher in the patients with ILD (median [range] 0.90 [0.65]) than in patients without ILD (median [range] 0.63 [0.15]; p=0.03). The higher ^{18}F-FDG uptake in patients with ILD compared to those without ILD is visually illustrated in Figure 1. The relationship between the uptake of ^{18}F-FDG, high-resolution CT scan of the lungs and pulmonary function tests at baseline is currently under analysis (and will be presented during the meeting).
Conclusion: Our results suggest that in early disease stages, within two years of SSc diagnosis, ^{18}F-FDG uptake in the dorsobasal lung fields is higher in patients with ILD compared to patients without ILD. Further analysis is warranted to investigate ^{18}F-FDG uptake in other lung regions, its relationship to conventional tools and with regard to treatment outcomes. As such, we will investigate repeated ^{18}F-FDG PET-CT and clinical outcomes after 1 year of follow-up in patients with SSc-ILD.
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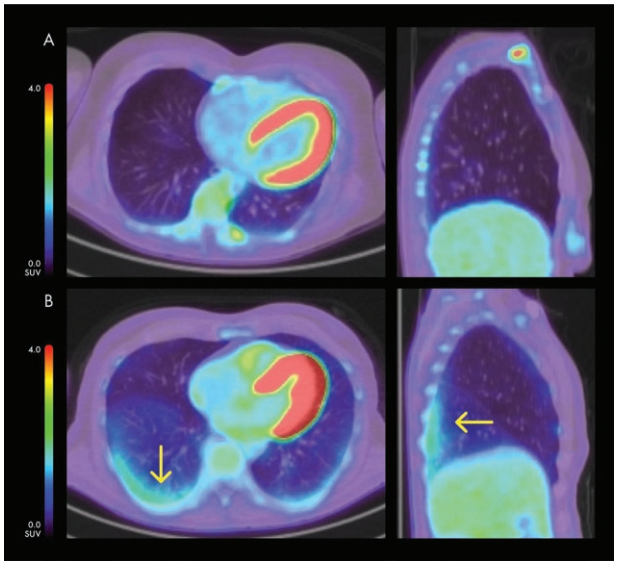


Figure 1. Pulmonary uptake of ^{18}F-FDG in patients with diffuse cutaneous SSc without ILD (A) and with ILD (B). ^{18}F-FDG uptake is indicated by the yellow arrows.

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POS0887 INFLUENCE OF CONTEXTUAL FACTORS AND RELIABILITY OF ULTRASOUND SKIN MEASURES IN PERSONS WITH SYSTEMIC SCLEROSIS AND HEALTHY CONTROLS

Keywords: Systemic sclerosis

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Background: Skin involvement is a cardinal feature for the diagnosis and prognosis of systemic sclerosis (SSc) and is associated with worse functional ability and quality of life.[1] Gender and age have been found to influence ultrasound dermal thickness and skin stiffness, and preliminary normal reference percentile curves for these ultrasound measures have been proposed.[2] The possibility that contextual factors, like room temperature, may influence these measurement is of crucial importance, but it has been very scarcely addressed.[3]
Objectives: To examine the influence of contextual factors upon the evaluation of skin thickness and stiffness by ultrasound and to assess the reliability of these parameters.
Methods: Ultrasound dermal thickness (by B-mode, 18MHz) and skin stiffness (by shear-wave elastography, 9MHz) were assessed in persons with systemic sclerosis (SSc) and in healthy controls. The influence of contextual factors upon repeated measures was evaluated: (i) room temperature (16-17°C *vs* 22-24°C); (ii) time of day (morning *vs* afternoon), and (iii) menstrual cycle phase (menstrual *vs* ovulatory). Differences were analyzed using the related-samples Wilcoxon signed-rank test. Inter- and intra-rater reliability of ultrasound skin thickness and stiffness were evaluated in the 17 skin Rodnan sites of 20 persons with SSc and 20 healthy controls, under stable contextual conditions.
Results: A significant increase in dermal thickness values was observed between the morning and afternoon evaluations, at the leg 6.96% (SD3.39), p=0.007, and 7.39% (8.42), p=0.018, in SSc patients and in controls, respectively (Table 1).No significant changes were observed in association with room temperature and menstrual cycle. Intra- and inter-rater-reliability was good to excellent for ultrasound dermal thickness and stiffness, both in SSc and healthy controls.
Conclusion: The timing of the ultrasound procedure within each day seems to influence the ultrasound measures at the legs and feet, and this aspect should deserve attention when designing and reporting future trials. Our study corroborates that ultrasound dermal thickness and skin stiffness are reliable domains to quantify skin involvement in SSc.

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Table 1. Skin ultrasound measures, dermal thickness, and skin stiffness, measured at the five Rodnan skin sites, in the morning (08.30-10.30am) and in the afternoon (4.30-6.00pm) periods of the same day.

	SSc patients (n=10)				Controls (n=10)			
	Morning	Afternoon	Diff. (%)	p	Morning	Afternoon	Diff. (%)	p
Dermal thickness (mm)								
Forearm	0.99 (0.20)	0.96 (0.19)	-1.64	0.767	0.87 (0.14)	0.87 (0.12)	2.40	0.878
Hand	0.84 (0.14)	0.87 (0.25)	0.35	0.953	0.74 (0.07)	0.74 (0.09)	0.99	0.778
Finger	0.87 (0.16)	0.88 (0.25)	-0.12	1.00	0.70 (0.07)	0.72 (0.06)	1.47	0.148
Leg	1.03 (0.18)	1.08 (0.20)	**6.96**	**0.007**	1.05 (0.17)	1.14 (0.17)	**7.39**	**0.018**
Foot	0.77 (0.09)	0.79 (0.10)	1.05	0.766	0.79 (0.71)	0.86 (0.08)	10.20	0.080
Skin stiffness (m/s)								
Forearm	1.78 (0.69)	1.87 (0.75)	2.24	0.477	1.36 (0.17)	1.39 (0.19)	0.78	0.838
Hand	2.02 (0.47)	2.17 (.78)	-0.25	0.475	1.73 (0.31)	1.76 (0.23)	1.03	0.635
Finger	2.94 (1.28)	2.91 (1.37)	-4.71	0.333	1.84 (0.27)	1.90 (0.23)	3.08	0.859
Leg	1.92 (0.37)	2.53 (0.90)	**18.21**	**0.047**	2.10 (0.47)	2.46 (0.79)	11.53	0.139
Foot	1.83 (0.32)	2.09 (0.39)	**11.77**	**0.037**	1.69 (0.26)	2.01 (0.29)	**14.42**	**0.021**

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POS0888 NORMAL PERCENTILE REFERENCE CURVES FOR SKIN ULTRASOUND THICKNESS AND STIFFNESS AT RODNAN SITES

Keywords: Systemic sclerosis

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Background: Skin involvement is a hallmark of systemic sclerosis and an important marker of disease activity, severity and prognosis.[1] The modified Rodnan skin score (mRSS), the current gold standard for the evaluation of the skin in SSc, both in clinical trials and in practice, has several limitations.[2] This highlights the need for more sensitive and objective measures of skin involvement, not only support the evaluation and development of new treatments, but also to facilitate the earlier diagnosis of SSc. Normal reference curves for skin ultrasound parameters, considering relevant influential factors seem of pivotal importance to fully exploit the potential of these new techniques as reliable tools for diagnostic and follow-up purposes.
Objectives: Our primary objective was to establish preliminary normal reference curves for ultrasound dermal thickness and skin stiffness, in the 17 Rodnan skin sites, considering the effect of gender and age on these measures. As an exploratory objective, we investigated the effect of body mass index and the menopause on skin ultrasound measures.
Methods: A cross-sectional study was conducted involving 140 healthy volunteers, aged 20-79 years. Recruitment was stratified for age (10-year categories) and gender to guarantee a balanced distribution of these factors in the sample. participants were excluded if they had any of the following conditions: (1) diagnosis of any skin or connective tissue or rheumatic inflamma- tory disease, (2) history of insulin treated diabetes, (3) history of anticancer chemo/radiotherapy treat- ments, (4) exposure to organic solvents, (5) past glucocorticoid treatment for more than 4 months or (6) recent (<4 weeks) treatment with glucocorticoids, regardless of dose, clinical indication and timing. Ultrasound dermal thickness and skin stiffness were assessed by high-frequency ultrasound (18MHz) and shear-wave elastography (9MHz), respectively, at the 17 Rodnan skin sites. All ultrasound measures were performed in the morning (between 9:00 and 13:00 hours) in the same room and at stable temperature. Outcomes were evaluated through a mixed linear model, univariate, and multivariate regressions. Normal reference curves were derived for both ultrasound measures in each Rodnan skin site, for females

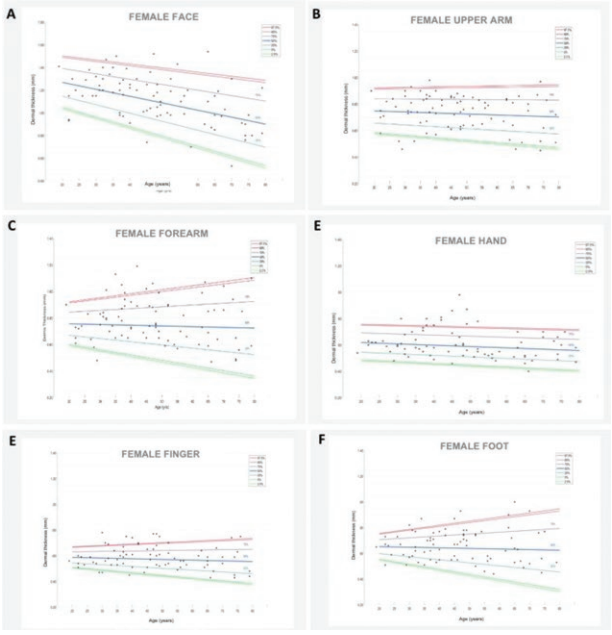


Figure 1. Ultrasound dermal thickness in females: percentile curves. (A) Face; (B) Upper arm; (C) Forearm; (D) Hand; (E) Finger; (F) Foot.

and males (Example in Figure 1). An online calculator of the percentiles of skin ultrasound measures was also developed. A radar chart showing these values and the percentile for each site is automatically drawn, allowing the clinician to export the results obtained.

Results: A total of 140 caucasian participants, i.e., 80 females, mean (SD) age of 47.2 (16.0) years; and, 60 males, 49.5 (17.3) years were included. Ultrasound dermal thickness and stiffness measures were higher in males than females, in all Rodnan skin sites (except in chest for ultrasound-dermal thickness). Age had also a significant impact in both ultrasound measures, but only in some skin sites. Gender and age percentile curves (97.5th, 95th, 75th, 50th, 25th, 5th, 2.5th) were plotted for each of the measures in each skin site.

Conclusion: Gender and age are strongly associated with skin ultrasound parameters, imposing the need for gender- and age-specific reference values. Normal reference percentile curves for skin ultrasound measures are promising tools to support earlier diagnosis and refine sensitivity to time- or drug-induced changes. These reference percentile curves are provided as a basis for future cooperative work to strengthen its evidence-basis, representativeness and refinement regarding potentially influential factors.

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[3] doi:10.1002/acr.2359

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POS0889 ASSESSMENT OF MYOSITIS-RELATED INTERSTITIAL LUNG DISEASE BY ^{68}GA-DATA.SA.FAPI PET-CT

Keywords: Lungs, Myositis, Imaging

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Background: Idiopathic inflammatory myopathies (IIM) are a group of heterogeneous autoimmune disorders marked by skeletal muscle inflammation and extra-muscular complications including pulmonary involvement. Interstitial lung disease (ILD) is a common manifestation affecting up to 78% in IIM patients. Methods and means for in-vivo visualization of ongoing tissue remodeling in affected organs are scarce.

Objectives: To quantify and compare fibroblast activation in the lungs between IIM-patients and control subjects using ^{68}Ga-labelled inhibitor of Fibroblast-Activation-Protein based positronic emission tomography-computed tomography (^{68}Ga-DATA.SA.FAPI PET-CT) imaging.

Methods: Patients with IIM recruited prospectively from the rheumatology outpatient clinic, and control subjects without rheumatic conditions or ILD recruited from the cardiology outpatient clinic underwent ^{68}Ga-FAPI PET-CT imaging. Pulmonary FAPI accumulation was assessed by measuring the maximal standardized uptake value (SUVmax) and mean SUV (SUVmean) over the whole lung (wl), respectively. Values of SUV were compared across IIM patients with and without ILD and controls using analysis of variance (ANOVA) test and displayed as mean ±standard deviation (SD).

Results: The clinical characteristics of patients with IIM (15 patients with ILD confirmed by CT and 4 non-ILD patients with primary muscular affection) and control subjects (n=17) are displayed in the Table 1. Subtypes of IIM included antisynthetase syndrome (57.9%), dermatomyositis (15.8%), overlap myositis (15.8%), and immune-mediated-necrotizing-myositis (10.5%). In individuals with IIM-related ILD, whole-lung ^{68}Ga-DATA.SA.FAPi uptake was significantly increased as compared to both, the non-ILD IIM patients and the control group: wlSUVmax (6.63 [±2.05] vs. 3.74 [±0.71] and 4.74 [±1.24] respectively, both p<0.001) (Figure 1A) and wlSUVmean (1.50 [±0.48] vs. 0.94 [±0.22] and 1.11 [±0.34] respectively, both p<0.05) (Figure 1B). No differences of wlSUVmax or wlSUVmean were observed between non-ILD IIM patients and the control group.

Conclusion: This study demonstrates enhanced tracer uptake in ^{68}Ga-DATA.SA.FAPi PET-CT in patients with IIM. Thus, FAPi PET-CT may provide a useful tool for the assessment of lung disease in IIM. Further discriminatory and diagnostic testing approaches are needed to integrate this novel imaging method into clinical decision making.

Table 1. Demographic and clinical characteristics of participants at baseline.

	IIM patients	Controls
No. (n)	19	17
Sex (female)	11 (57.9%)	13 (76.5%)
Mean age (years ± SD)	49.0 ± 16.7	79.0 ± 3.8
Ethnicity (Caucasian)	18 (94.7%)	19 (100%)
Disease subtype		
Antisynthetase Syndrome	11 (57.9%)	-
Dermatomyositis	3 (15.8%)	-
Overlap Myositis	3 (15.8%)	-
Immune-mediated necrotizing myopathy	2 (10.5%)	-
Interstitial lung disease (ILD)		
Yes	15 (78.9%)	-
ILD-Subtype		
NSIP	8 (53.3%)	-
UIP	1 (6.7%)	-
OP	3 (20%)	-
NSIP and OP	3 (20%)	-
Autoantibodies		
Aminoacyl-tRNA synthetase	11 (57.9%)	-
Ro-52	3 (15.8%)	-
MDA5	2 (10.5%)	-
Mi-2	1 (5.3%)	-
Seronegative	2 (10.5%)	-
Pulmonary function tests		
FVC % (mean ± SD)	81.9 ± 21.4	-
DLCO % (mean ± SD)	66.1 ± 21.3	-

Abbreviations: No./n, number; SD, standard deviation; NSIP, nonspecific interstitial pneumonia; UIP, usual interstitial pneumonia; OP, organizing pneumonia; FVC, forced vital capacity; DLCO, diffusion capacity of the lungs for carbon monoxide.

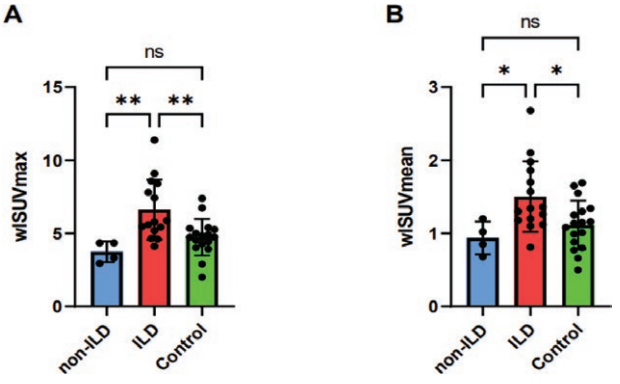


Figure 1. ^{68}Ga-FAPI-04 uptake in the lungs of IIM-patients and controls. A) whole lung maximal standardized uptake value; B) whole lung mean standardized uptake value in myositis patients with or without interstitial lung disease and control subjects. P values <0.05 were considered statistically significant. Abbreviations: wlSUVmax, whole-lung maximal standardized uptake value; wlSUVmean, whole-lung mean standardized uptake value; ILD, interstitial lung disease; ns, not significant. P values <0.05 are marked with one asterisk; p values <0.001 are marked with two asterisks.

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POS0890 USING POLYGENIC RISK SCORES TO AID DIAGNOSIS OF PATIENTS WITH EARLY INFLAMMATORY ARTHRITIS: RESULTS FROM THE NORFOLK ARTHRITIS REGISTER

Keywords: Epidemiology, Inflammatory arthritides, Genetics/epigenetics

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Background: There is growing evidence that genetic information can offer valuable information to a clinician in a diagnostic setting, and that it is feasible that

genetic data would be of benefit to the rheumatology outpatient setting by aiding early diagnosis. A genetic probability tool (G-PROB) has recently been developed to aid diagnosis using existing knowledge of disease-associated genetic variants but has only been tested in a limited capacity.

Objectives: Our aim was to assess whether G-PROB could aid diagnosis in the rheumatology outpatient setting using data from the Norfolk Arthritis Register (NOAR), a large prospective observational cohort of patients presenting with early inflammatory arthritis where diagnosis at baseline is unclear.

Methods: Genotypes and follow-up clinician diagnoses were obtained from patients from NOAR. Six G-probabilities (0-100%) were created for each patient based on known disease-associated odds ratios (ORs) of published genetic risk variants, each corresponding to one disease of rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), psoriatic arthritis (PsA), spondyloarthropathy (SpA), gout or "other rheumatological diseases". Performance of the G-probabilities compared with the final (follow-up) clinician diagnosis was assessed.

Results: G-PROB was tested on 972 patients from NOAR. Calibration of G-probabilities with clinician diagnosis was high, with regression coefficients of 1·03, where 1·00 represents perfect calibration. G-probabilities discriminated clinician diagnosis with pooled areas under the curve (95% CI) of 0·84 (0·81 to 0·86). G-probabilities <5% corresponded to a negative predictive value (NPV) of 96% where it was possible to suggest at least one unlikely diagnosis for 99·9% of patients, two or more diseases for 94% of patients, and three or more diseases for 54% of patients. G-probabilities >50% corresponded to a positive predictive value (PPV) of 74%. In 57% of patients, the disease with the highest G-probability corresponded to clinician diagnosis.

Conclusion: G-PROB successfully converts complex genetic information into meaningful, and interpretable conditional probabilities which may be especially helpful at suggesting unlikely diagnoses in the rheumatology outpatient setting.

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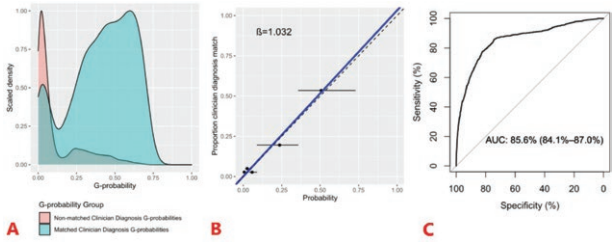


Figure 1. (A) Distribution of G-probabilities which match and those which do not match clinician diagnosis. Ideally the correct diagnosis should have higher probabilities, and the distribution should be skewed to the right, with incorrect diagnoses having lower probabilities with a distribution skewed to the left. (B) Linear regression without intercept showing concordance of G-probabilities with clinician diagnosis match, where x-axis shows G-probabilities, and y-axis shows binary outcome of concordance with clinician diagnosis (y=1) and non-concordance (y=0). A β of one indicating exact calibration is shown as a dashed black line. For visualisation, G-probabilities were placed into five equally sized bins and plotted the proportion of instances where predicted disease is concordant with clinician diagnosis. (C) ROC analysis of correspondence of G-probabilities with clinician diagnosis, where AUC shows pooled data for all diseases (microAUC).

Table 1. Performance of G-probabilities in suggesting likely and unlikely diagnoses at different thresholds

G-probability threshold	# of patients with at least one G-probability at the given threshold (n=972) (%)	# of G-probabilities at the given threshold (n=5,832) (%)	NPV or PPV at the given threshold in %
A) Thresholds suggesting unlikely diagnoses			
<5%	971 (100)	2410 (41)	NPV 96
<20%	972 (100)	3857 (66)	NPV 96
B) Thresholds suggesting likely diagnosis			
>20%	972 (100)	1975 (34)	PPV 41
>50%	470 (48)	470 (8)	PPV 74

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POS0891 AUTOMATIC COMPUTATION OF KNEE OSTEOARTHRITIS SEVERITY USING KNEE X-RAYS AND CONVOLUTIONAL NEURAL NETWORKS

Keywords: Imaging, Artificial intelligence, Osteoarthritis

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Background: Knee osteoarthritis is a heterogeneous and complex degenerative pathology, characterized by a progressive deterioration of bone cartilage and structural modifications of the joint [1]. The precision of the diagnosis and the rating of the severity are major criteria for the therapeutic management and its follow-up. They are based on three criteria: the assessment of the pain, of the functional impairment and of the structural modifications. For this last criterion, the standard protocol in routine care remains the interpretation of X-ray images using standardized scales. The Kellgren-Lawrence (KL) score, which assesses both the joint space and the presence of osteophytes, allows a classification of the stages of osteoarthritis, but it relies on subjective manual interpretation and is time consuming for practitioners [2].

Objectives: In this study, we have developed artificial intelligence algorithms to automatically measure the tibia-femur joint spacing (or joint space width JSW) and determine the Kellgren-Lawrence (KL) score.

Methods: We constituted a retrospective cohort of 19,560 patients. Using all their images, we trained different neural networks in order to select just knee AP X-rays without prosthesis nor artifacts. Our work explores two approaches: the prediction of the stage of osteoarthritis according to the KL scale and the measurement of the JSW. For the prediction of the KL score, 2,081 X-rays annotated by 3 radiologists were used to train a convolutional neural network (CNN). The measurement of the JSW required the realization of 3 different annotations: the positioning of the joint, of the two condyles (medial and lateral) and the contouring of tibia and femur. Three neural networks were optimized to reproduce these annotations before calculating the JSW for each condyle. For each individual task, we decomposed the datasets into training, validation, and test sets, used different data augmentation techniques, and researched the best possible architecture.

Results: The Kellgren-Lawrence score prediction obtained the following performances: an accuracy of 0.92, a sensitivity of 0.84 and an average area under the ROC curve (AuC) of 0.97. To evaluate the measurement of the JSW, we calculated the correlation between the area measured by the annotators and the area predicted by the algorithms, obtaining a Pearson correlation of 0.84.

Conclusion: This study highlights the relevance of the use of artificial neural networks for the assessment of osteoarthritis. Their performance opens the way to a tool assisting in the precise and standardized gradation of the severity of joint degradation.

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Disclosure of Interests: None Declared.

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POS0892 AN END-TO-END MACHINE LEARNING PIPELINE FOR THE AUTOMATED DETECTION OF RADIOGRAPHIC HAND OSTEOARTHRITIS: A NO-CODING PLATFORM EXPERIENCE

Keywords: Osteoarthritis, Artificial intelligence, Imaging

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Background: Machine learning's performances in the field of radiology have been constantly increasing in recent years such that nowadays many algorithms equals human performances and are FDA approved.[1,2] Non-coding platforms have recently emerged and allow healthcare professionals with no programming experience to play an active role in the development of machine learning (ML) algorithms according to existing or emerging clinical needs.

Objectives: We aimed to evaluate the feasibility of ML algorithm generation using a no-coding platform by clinicians without ML experience. By using such a platform, we developed a model for automated recognition and grading of radiographic distal interphalangeal osteoarthritis (DIP-OA) with subsequent user experience (UX) testing of the algorithm.
Methods: 13690 hands x-rays from 2863 patients within the Swiss Cohort of Quality Management (SCQM) and an external control dataset of 346 non-SCQM patients were collected and scored for DIP-OA by the modified Kellgren and Lawrence Score (K/L). 48892 DIP joints were extracted and classified according to the K/L score. GIOTTO (L2F, Lausanne) was used as a no-coding platform for training of 2 convolutional neural networks, the first one for segmentation of hand joints and subsequent DIP-joints extraction, and the second one for classification of KL scores according to the presence of osteophytes and joint space narrowing on the previously extracted DIP-joints. The classification model's performance was tested by an internal test set (SCQM database) and an external test set (non-SCQM). User experience (UX) of a web app developed from the platform as a provisory user interface (UI) was investigated in rheumatologists and radiologists. The usability of heat maps was also investigated.
Results: The sensitivity and specificity of this model for detecting DIP-OA, was 79% and 86%, respectively. The accuracy for grading the K/L score was 75% with a kappa score of 0.76. A similar sensitivity (79%) and specificity (80%) for detecting DIP-OA was found in an independent external test set. The accuracy per DIP-OA class differed with 79% for no OA (defined as K/L 0 and 1), 65% for K/L2, 40% for K/L3, and 70% for K/L4. On the external test set overall accuracy was 66% and the kappa score 0.75. The platform was intuitive and easy to use, but support from data scientists was still required for upload of the data set exceeding the drag and drop process, DIP-joints extraction, heatmap generation and episodic debugging of the platform. UX testing of the web app revealed a moderate demand by rheumatologists (notably for differential diagnosis and evolution over time) and a low demand by radiologists for the automated scoring of DIP-OA. Conversely, adding heat maps to the UI was considered of high added value.
Conclusion: No-coding platforms are an opportunity to develop end-to-end AI-prototypes for further testing. Their use by clinicians without experience in programming and machine learning is possible. Here, automated radiographic DIP-OA detection is both feasible and usable, whereas grading between individual KL scores, e.g. for clinical trials, remains challenging, partly because of the inter-observer variability inherent to the scoring method.

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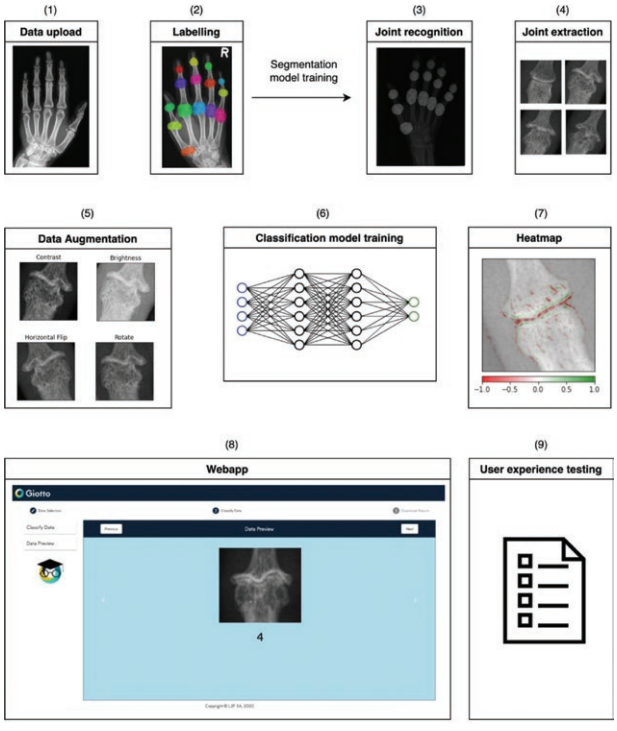


Figure 1. Making of an algorithm for detection and grading of distal hand osteoarthritis using a no-coding platform: end-to-end process.

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Disclosure of Interests: Leo Caratsch: None declared, Christian Lechtenboehmer: None declared, Matteo Caorsi Employee of: Chief Scientific Officer at L2F, Lausanne. L2F produces the platform Giotto., Karine Oung: None declared, Fabio Zanchi: None declared, Yasser Aleman: None declared, Patrick Omoumi: None declared, Thomas Hügle: None declared
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POS0893

SIGNIFICANT OVERLAP OF INFLAMMATORY AND DEGENERATIVE FEATURES ON SPINAL IMAGING AMONG PATIENTS WITH DEGENERATIVE SPINAL DISEASE, DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS AND RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

Keywords: Imaging, Bone diseases

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Background: Degenerative changes of the spine (DC), diffuse idiopathic skeletal hyperostosis (DISH) and radiographic axial Spondyloarthritis (r-axSpA) may present with overlapping inflammatory and degenerative findings on imaging, which, next to the general symptom of chronic back pain might, represent a challenge for an accurate diagnosis.
Objectives: To evaluate the distribution of spinal imaging features in a real-life cohort of patients with chronic back pain referred to a tertiary university rheumatology center and identify those associated with DC, DISH or r-axSpA.
Methods: In a cross-sectional analysis of patients with chronic low back pain, demographic and disease data were collected. Imaging of the spine (thoracic or lumbar) and sacroiliac joints was performed per the clinical indication. All images were evaluated by two independent trained readers including erosions, sclerosis, squaring, osteophytes and syndesmophytes on conventional radiographs (CR) and bone marrow edema (BME) or degenerative changes on magnetic resonance imaging (MRI). The final diagnosis made by the rheumatologist at discharge was the gold standard. Data were presented descriptively and compared among the three diagnosis groups (DC, DISH and axSpA).
Results: Among 136 referred patients, 71 had DC, 38 DISH, and 27 r-axSpA. Mean age was 63.2±11.4 (p=0.135 among the three groups), and 86 (63.2%) were males (88.9% in axSpA, p=0.003). Patients had high levels of comorbidities: 91 (72.8%) had hypertension (higher in the DC group, 52 (82.8%), p=0.04), 37 (27.6%) had diabetes (higher in DISH, 39.5%, p=0.012) and 31 (23.3%) were current smokers (higher in axSpA, 53.8%, p<0.001). Although axSpA-related spinal changes on CR were expectedly more prevalent in the axSpA group (thoracic 14.1%, p=0.024; lumbar 93.9%, p=0.034), they were also present in DISH (27.8% and 21.9%) and DC (7.6% and 22.6%, respectively). DC were present in the three groups in 93.0% in the thoracic and in 93.9% in the lumbar spine, without a statistically significant differences (Table 1). Similarly, on thoracic and lumbar spine MRI, BME was present in DISH in 33.3% and 41.7% and in DC in 20.4% and 32.7% lumbar spines, respectively.
Conclusion: A significant overlap of inflammatory and degenerative features on spinal imaging among patients with DC, DISH or axSpA was found in this older group of patients. Particularly, r-axSpA-related spinal CR features were found in a fourth of patients with DISH, while MRI BME was found in a third of them.

Table 1. Thoracic and Lumbar Spinal Imaging features in a cohort of 136 patients referred for low back pain.

	DISH	DEGENERATIVE	AS	All	p-value
Total number of patients	**38**	**71**	**27**	**136**	
Thoracic Spine Xray					
Presence of SpA changes, N patients/ All patients in the group (%)	10/36 (27.8)	5/66 (7.6)	3/26 (11.5)	18/128 (14.1)	0.024
Presence of degenerative changes, N patients/ All patients in the group (%)	36/36 (100)	58/66 (87.9)	25/26 (96.1)	119/128 (93.0)	0.055
Lumbar Spine Xray					
Presence of SpA changes, N patients/ All patients in the group (%)	7/32 (21.9)	14/62 (22.6)	11/22 (50.0)	32/116 (27.6)	0.034
Presence of degenerative changes, N patients/ All patients in the group (%)	30/32 (93.8)	58/62 (93.5)	21/22 (95.5)	109/116 (93.9)	1.000

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POS0894 DIFFERENTIAL DIAGNOSIS BETWEEN HAND OSTEOARTHRITIS AND PSORIATIC ARTHRITIS USING INDOCYANINE GREEN-BASED FLUORESCENCE OPTICAL IMAGING

Keywords: Imaging, Osteoarthritis, Psoriatic arthritis

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Background: Fluorescence optical imaging (FOI) provides a measure of inflammation in finger joints and wrists [1,2]. Recognizing specific joint signals and morphologic patterns in FOI may be helpful in differential diagnosis of hand osteoarthritis (OA) and psoriatic arthritis (PsA).
Objectives: To analyze the diagnostic value of the established FOI Activity Score (FOIAS) and predefined morphologic patterns in the differentiation between hand OA and PsA.
Methods: FOIAS has been validated for inter- and intra-reader reliability[3]. FOI sequences were examined by one trained reader (BD). Cases with physician-based diagnosis of hand OA (n=47) and PsA (n=54) were randomly mixed and the reader was blinded to diagnosis. In total, 16 joints (wrist, thumb base, MCP1-5, (P)IP1-5, DIP2-5) in each hand were evaluated on a semiquantitative 0-3 scale in five images during the FOI sequence (composite image PrimaVista Mode (PVM), phase 1, phase 2 (first and middle image), and phase 3). Additionally, predefined morphologic patterns were observed ('streaky signals'[2], 'green/blue nail sign'[4], 'Werner sign'[1,5] and 'bishop's crozier sign'[3]). A collection of example images for joint signals and morphologic findings was previously compiled into an atlas for reference and training[3]. Based on joint signals and morphologic findings, the reader matched each case to diagnosis OA or PsA. Agreement on diagnosis was calculated using Cohen's kappa (κ). Mean sum signals for different joint groups were compared by T test for independent samples. Morphologic pattern distribution was assessed with Pearson Chi-Square.
Results: 78.2% of cases (79/101) were diagnosed correctly by reading FOI, showing moderate agreement (κ=0.57, p<0,001). For PIP2-5, we found overall statistically significantly higher mean joint sum scores in OA cases (39.0 in OA vs. 20.0 in PsA, p<0.001) as well as for each of the 5 phases (PVM, phase 1, phase 2 first and middle, phase 3). DIP2-5 displayed overall statistically significantly higher mean joint sum scores in OA (16.5 in OA vs. 8.4 in PsA, p<0.001) as well as in PVM, phase 2 first and middle images. Other joint groups (MCP1-5, wrist) did not present any statistically significant differences between OA and PsA. Regarding morphologic patterns, the 'Werner sign' was presented significantly more often in PsA patients (55.6% in PsA vs. 21.3% in OA, p<0.001).
Conclusion: There was moderate agreement between the physician-based diagnosis of OA and PsA and the diagnosis that was proposed based on FOI findings. OA cases presented more pronounced signal enhancement in PIP and DIP joints when compared to PsA cases. Additional morphologic criteria and pattern recognition might be needed to expand the diagnostic capability of FOI.
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Disclosure of Interests: Benedict Drude: None declared, Øystein Maugesten: None declared, Stephanie Gabriele Werner: None declared, Jörn Berger Employee of: Xiralite GmbH, Jens Klotsche: None declared, Gerd Rüdiger Burmester: None declared, Ida K. Haugen Grant/research support from: Pfizer/Lily (paid to institution) and personal fees from Abbvie, Novartis and GSK, outside of the submitted work, Sarah Ohrndorf: None declared
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POS0895 ANKLE RETINACULA ABNORMALITIES AS FEATURES OF PSORIATIC ARTHRITIS: AN ULTRASOUND STUDY

Keywords: Psoriatic arthritis, Ultrasound

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Background: Ankles are frequently involved in rheumatoid arthritis (RA) and psoriatic arthritis (PsA) and can be observed in both diseases. The detection of enthesitis may support the diagnosis for PsA and help to distinguish theses 2 rheumatic diseases. At ankle level, retinacula can be analyzed with ultrasonography (US) and their insertions into bones can be considered as enthesitis.
Objectives: The aim of the present study was to compare the US assessment of the retinacula of ankles in a population of RA and PsA patients with painful ankle.
Methods: This was an observational cross-sectional study. We analyzed consecutive RA or PsA patients with ankle pain. We also analyzed healthy controls (HC), without rheumatic disorders nor ankle pain. The following US features were assessed: presence of synovitis of tibiotalar or talonavicular joints, presence of tenosynovitis of peroneal or posterior tibial tendons. Two retinacula: the superior peroneal retinaculum (SPR) and the flexor retinaculum (FR) were also evaluated in mode B (thickness, echogenicity and presence of malleolar periostosis) and the vascularization at their insertion into bone by using power Doppler (PD).
Results: We analyzed data for 80 consecutive patients (60% women; median age 56 years). Among these patients, 37 (46%), 23 (29%) and 20 (25%) were RA, PsA and HC patients, respectively. A total of 160 ankles were assessed. The evaluation of SPR did not show difference between the two diseases. Regarding the FR, we observed that FR was thicker in PsA patients than in RA (0.96mm ± 0.39 vs. 0.64mm ± 0.15, P<0.001) and HC (0.96mm ± 0.39 vs. 0.56mm ± 0.12, P<0.001) without difference between RA patients and HC. The following US features were more frequently found in PsA than in RA ankles: hypoechogenicity (46% vs 7%, P<0.001), positivity of PD (43% vs 8%, P<0.001) and malleolar periostosis (43% vs 8%, P<0.001). By using ROC curve analysis, we determined that a cut-off of 1mm of FR thickness provided a sensitivity of 49% and specificity of 97% for the diagnosis of PsA. The association of a thickness ≥1mm with hypervascularization of the malleolar insertion of FR, named as "retinaculitis", was observed in 39% and 3% of ankles in PsA and RA, respectively. The proportion of retinaculitis of SPR was not different between the two diseases.
Conclusion: US abnormalities of FR were more frequently observed in PsA than in RA patients and appear to be specific for PsA. Thus, US assessment of FR might be useful to distinguish RA and PsA in patients with painful ankles.
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Disclosure of Interests: None Declared.
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POS0896 ANALYSIS OF THE PERFORMANCE OF AN ARTIFICIAL INTELLIGENCE ALGORITHM FOR THE DETECTION OF RADIOGRAPHIC SACROILIITIS IN AN INDEPENDENT COHORT OF AXSPA PATIENTS INCLUDING BOTH NR-AXSPA AND R-AXSPA

Keywords: Artificial intelligence, Imaging, Spondyloarthritis

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Background: Conventional radiography of the sacroiliac joints is the first imaging method if axial spondyloarthritis (axSpA) is suspected. The presence of definite radiographic sacroiliitis is needed to classify as radiographic (r-axSpA) based on the modified New York Criteria (mNYc). However, the reliability of radiographic sacroiliitis assessment is low, especially if performed locally. Expert central reading for classification purposes in clinical trials is time-consuming and still has high inter-reader variability. A possible solution to detect radiographic sacroiliitis with consistent reproducibility, could be the use of an artificial intelligence analysis of radiographs. Recently an artificial neural network showed an expert-level performance for classification and diagnostic settings[1,2].
Objectives: The aim of this study was to evaluate the performance of this previously trained artificial network in a completely new cohort of patients previously evaluated as r-axSpA or nr-axSpA by central readers.

Methods: Baseline radiographs of sacroiliac joints from RAPID-axSpA (NCT01087762, N=277) were evaluated by 3 central reader experts and the majority decision of fulfillment the mNYc was used as a reference. None of the patients nor any of the central readers participated in the studies used to pre-train the artificial network. For performance evaluation of the neural network, the area under the receiver operating characteristic curve (AUROC) was calculated. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the prediction cut-offs were calculated along with their 95% Confidence Intervals (CI) using accelerated bootstrapping. Cohen's Kappa and the absolute agreement were used to assess the agreement between the neural network and the human readers.

Results: Baseline characteristics are presented in Table 1. Sensitivity and specificity for the cut-off weighting both measurements were 0.82 (95% CI: 0.78, 0.86) and 0.81 (95% CI: 0.75, 0.87). The Cohen's kappa between the neural network and the reference judgements was 0.61 (95% CI: 0.51, 0.70), and the absolute agreement on the classification yielded 82% (95% CI: 0.78, 0.85). The neural network achieved an 0.89 (95% CI: 0.86, 0.93) PPV and a 0.70 (95% CI: 0.64, 0.77) NPV in recognition of definite radiographic sacroiliitis with AUROC of 0.88 (Figure 1).

Table 1. ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BMI: body mass index; CRP: C-reactive protein; HLA-B27: human leukocyte antigen B27; nr-axSpA: non-radiographic axial spondyloarthritis; r-axSpA: radiographic axial spondyloarthritis; SD: standard deviation.

Baseline characteristics	All (N = 277)		r-axSpA (N = 181)		nr-axSpA (N = 96)	
Age, years, mean (SD)	39.5	(12.1)	39.2	(11.6)	40	(13.0)
Sex (Male), n (%)	165	(59.6)	122	(67.4)	43	(44.8)
Symptom duration, years, mean (SD)	10.2	(9.4)	10.6	(9.6)	9.5	(9.2)
Disease duration, years, mean (SD)	6.3	(7.0)	7.1	(7.5)	5	(5.8)
HLA-B27 (+), n (%)	210	(75.8)	150	(82.9)	60	(62.5)
BMI, kg/m^2, mean (SD)	28.0	(6.0)	27.9	(5.5)	28.2	(6.8)
BMI class (kg/m^2), n (%)						
< 18.5	6	(2.2)	2	(1.1)	4	(4.2)
18.5 - < 25	89	(32.1)	56	(30.9)	33	(34.4)
25 - < 30	89	(32.1)	67	(37)	32	(33.3)
>= 30	88	(31.8)	54	(29.8)	34	(35.4)
Missing	5	(1.8)	2	(1.1)	3	(3.1)
CRP, mg/L, mean (SD)	18.6	(23.0)	20.5	(24.3)	14.9	(19.8)
CRP category, mg/L, n (%)						
<= 15 mg/L	163	(58.8)	101	(55.8)	62	(64.6)
> 15 mg/L	114	(41.2)	80	(44.2)	34	(35.4)
ASDAS, mean (SD)	3.9	(0.9)	4.0	(0.9)	3.7	(0.8)
BASDAI, mean (SD)	6.5	(1.6)	6.5	(1.6)	6.4	(1.5)
BASFI, mean (SD)	5.3	(2.2)	5.5	(2.2)	5.1	(2.3)
BASMI, mean (SD)	3.8	(1.7)	4.1	(1.8)	3.4	(1.5)

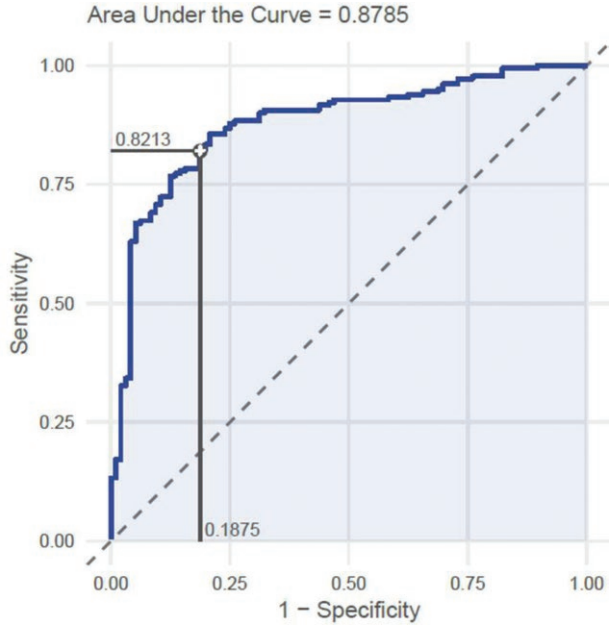


Figure 1. Area Under the Receiver Operating Characteristic Curve for Evaluating Performance of the Neural Network to Detect Radiographic Sacroiliitis

Conclusion: A pre-trained artificial neural network can enable the accurate detection of definite radiographic sacroiliitis relevant for the diagnosis and classification of axSpA close to expert performance. In the present study, the previously trained network showed an excellent ability to generalize data that was completely new to the network. Our results show the potential for classification purposes in multi-center axSpA trials in the future, providing a reproducible and cost-effective tool without unnecessary time delays.

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POS0897

THE PERFORMANCE OF COMBINING EYE SIGN AND FUNCTIONAL MAGNETIC RESONANCE IMAGING IN DIAGNOSING PATIENTS WITH NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Diagnostic tests, Systemic lupus erythematosus, Imaging

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Background: The diagnosis of NPSLE becomes challenging for rheumatologists, both at a diagnostic and therapeutic level. The 1999 ACR criteria had a high sensitivity (91%), but a low specificity (46%) [1].

Objectives: To investigate the alterations of eye sign and functional magnetic resonance imaging (fMRI) in patients with neuropsychiatric systemic lupus erythematosus (NPSLE) and to explore the performance of combining eye sign and MRI in diagnosing NPSLE.

Methods: In phase 1, SLE patients were consecutively recruited Sep 2017 to Sep 2018 including NPSLE patients and non-NPSLE patients. Eye sign examination for bulbar conjunctival microvascular were performed for all SLE patients and fMRI scanning for NPSLE patients. Demographic and clinical data were compared between two groups and to identify potential predictors for NPSLE by using multivariable logistic regression analysis. In phase 2, NPSLE patients in phase 1 were enrolled, and a new diagnostic algorithm including predictors and changed fMRI parameters was designed with the 1999 NPSLE ACR classification as comparison. Expert opinion was considered as golden standard. Double-blind clinical diagnosis from expert were recorded using new algorithm and 1999 ACR classification, respectively. Area under the curve (AUC) under receiver operating characteristic (ROC) curve, sensitivity and specificity were calculated and compared between these two diagnostic methods.

Results: 120 SLE patients were recruited (32.99±1.03 years) including 45 NPSLE and 90 non-NPSLE. NPSLE had higher disease activity (reflected as SLEDAI and ESR). Compared with Non-NPSLE group, fMRI showed changed fALFF and ReHo in brain regions relevant to cognition and emotion ($p<0.01$). Eye sign examination showed NPSLE group had significantly higher scores of ramified loops, vascular tone, microangioma, wound point and had higher total scores than non-NPSLE group ($p<.001$). In multivariable logistic analysis, SLEDAI, ramified loop, microangioma, wound point and presence of antiphospholipid antibodies were predictors of NPSLE (Table 1). the AUC of the ACR classification under ROC curve was 0.775, sensitivity was 75.0%, specificity was 80.0% ($p=0.002$), the AUC of new algorithm under ROC curve was 0.815, sensitivity was 75.0%, specificity was 88.0% ($p<.001$) (Figure 1).

Conclusion: This proposed new algorithm showed not to be inferior to the 1999 ACR classification and need to be confirmed in further studies.

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Table 1. Multivariable logistic regression analysis of predictors for developing NPSLE.

	HR (95%CI)	P-value
SLEDAI	1.34 (1.03-1.75)	0.029*
Ramified loop	7.42 (1.58-34.79)	0.011*
Microangioma	2.78 (1.45-5.33)	0.002*
Wound point	4.17 (1.07-16.32)	0.040*
Antiphospholipid antibodies	18.59 (1.87-185.31)	0.013*

SLEDAI: Systemic Lupus Erythematosus Disease Activity Index.

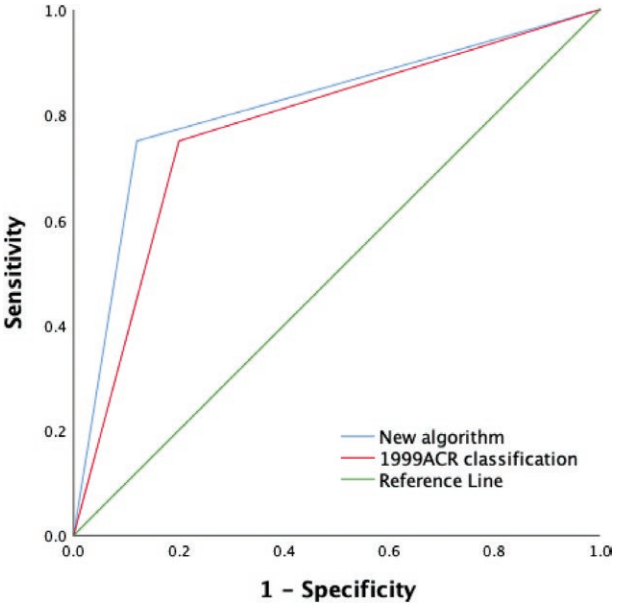


Figure 1. ROC curve of new algorithm and 1999 ACR classification in diagnosing NPSLE.ROC: receiver operating characteristic; AUC: area under the curve.

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POS0898

EARLY DETECTION OF ANTI-TNF INDUCED CHANGES IN NEW BONE FORMATION IN PSORIATIC ARTHRITIS PATIENTS BY ^{18}F-FLUORIDE PET-CT

Keywords: Imaging, Psoriatic arthritis

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Background: New bone formation in psoriatic arthritis (PsA) can be observed in all musculoskeletal disease domains and can lead to disability due to ankylosis and bridging syndesmophytes [1, 2]. The positive effect of anti-tumor necrosis (anti-TNF) therapy on radiographic damage (e.g. erosion and joint space narrowing) is well known, but there are contradictory findings on its effects on new bone formation [3, 4]. Imaging of new bone formation in PsA is pivotal in order to ascertain the extent and potential therapeutic effects on structural changes at an early stage of treatment. Our group recently demonstrated that molecular new bone formation can be observed in all PsA disease domains, using ^{18}F-Fluoride PET-CT scans. Moreover, the ability of this imaging technique to detect early therapeutic effects in ankylosing spondylitis patients was also demonstrated by our group [5].
Objectives: To investigate whether ^{18}F-Fluoride PET-CT scans can detect a change in ^{18}F-Fluoride uptake, reflecting a change in new bone formation, after 12 weeks of anti-TNF therapy in clinically active PsA patients.
Methods: Nine patients (male 4/9, median age 47 (IQR 19)) with PsA fulfilling CASPAR criteria or a clinical diagnosis according to the treating rheumatologist and clinically active disease including ≥1 clinically active enthesitis site were included. In each patient, a whole body ^{18}F-Fluoride PET-CT scan was performed prior to and 12 weeks after starting anti-TNF therapy. Scans were independently assessed for PET-positive lesions (dichotomous) by two readers (blinded for clinical data). Fixed sized volumes of interest were drawn on top of visual PET positive lesions as well as on locations where visual PET positive lesions appeared or disappeared before or after treatment. Standardized uptake values corrected for individual integrated whole blood activity concentration (SUV_{AUC}) were used for quantitative analysis. CT was used for anatomical reference.
Results: Combining all PET-positive lesions of all patients, a total of 153 lesions were observed at baseline (89, 30 and 34 in peripheral joints, entheses and spine, respectively). At week 12, a total of 119 PET-positive lesions were observed (69, 13 and 37 in peripheral joints, entheses and the spine, respectively). Grouping all lesions of all patients, there was a decrease in the mean SUV_{AUC} between baseline (1.578, SD 0.99) and week 12 of anti-TNF treatment (1.230, SD 0.85) (Figure 1A). Similar results were observed when grouping all lesions of all patients for separate disease domains. Mean SUV_{AUC} changes between baseline and 12 weeks were -0.294 (SD 0.88), -0.357 (SD 0.69) and -0.300 (SD 0.67) for respectively peripheral joints (Figure 1B), entheses (Figure 1C) and the spine (Figure 1D).
Conclusion: ^{18}F-Fluoride PET-CT detected a change in new bone formation in PsA domains during anti-TNF therapy as early as 12 weeks post-treatment. The data point at a mean decrease of new bone formation in peripheral joints, entheses and axial skeleton.

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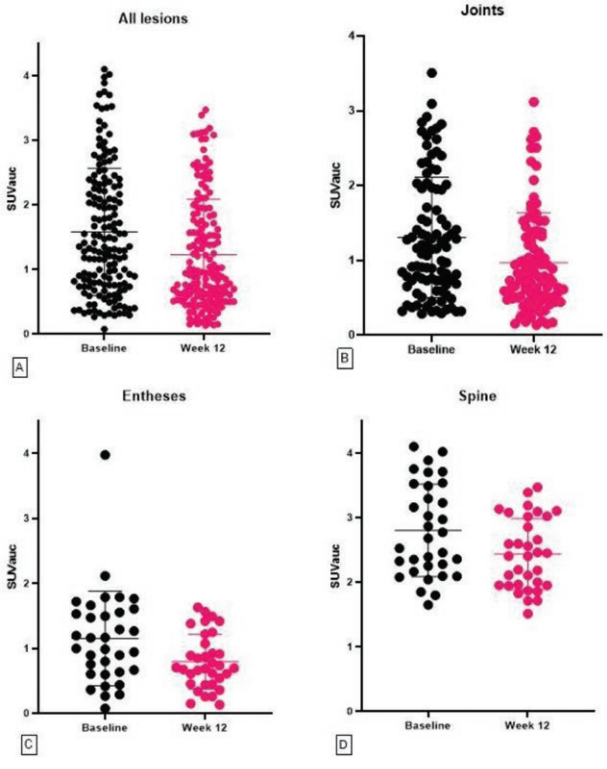


Figure 1. SUV_{AUC} at baseline and week 12 when grouping all lesions of all patients (A), peripheral joints (B), entheses (C) and spine (D)

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Disclosure of Interests: Jerney de Jongh: None declared, Gerben C.J. Zwezerijnen: None declared, Robert Hemke: None declared, Maqsood Yaqub: None declared, Marleen G.H. van de Sande Speakers bureau: UCB, Novartis, Janssen, Consultant of: UCB, Novartis, Abbvie, Eli Lily, Grant/research support from: UCB, Novartis, Eli Lily, Arno Van Kuijk Consultant of: UCB, Janssen, Grant/research support from: Janssen, Novartis, Pfizer, Alexandre Voskuyl Consultant of: GSK, Astra Zeneca, Grant/research support from: Boehringer Ingelheim, Conny J. van der Laken Speakers bureau: Janssen, Abbvie, Pfizer, Novartis, UCB Pharma, Galapagos, Paid instructor for: Lilly, Galapagos, Consultant of: UCB Pharma, GSK, Novartis, Grant/research support from: Pfizer, Abbvie, Novartis, GSK, UCB Pharma
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POS0899 SPECIFICITY OF SALIVARY GLAND ULTRASOUND IN THE DISCRIMINATION OF PRIMARY SJOGREN'S SYNDROME FROM UNDIFFERENTIATED CONNECTIVE TISSUE DISEASES

Keywords: Imaging

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Background: Recently, compelling data have been published on the value of salivary gland ultrasound (SGUS) in differentiating between primary Sjögren's Syndrome (SS) from nonimmune-mediated sicca syndrome. Limited data are available regarding the diagnostic accuracy of SGUS to distinguish SS from undifferentiated connective tissue diseases associated with sicca syndrome.
Objectives: The aim of this study was to evaluate the power of SGUS to distinguish patients with SS from those with xerostomia and/or xerophthalmia and suffering from undifferentiated connective tissue diseases.
Methods: Our cross-sectional study consecutively recruited 95 patients with either SS (according to the American European Consensus Group criteria) or undifferentiated connective tissue diseases associated with sicca syndrome. Immunological assessment and salivary gland biopsies were performed in all patients. Ultrasonography of the parotid and submandibular glands on both sides were assessed for size, parenchymal echogenicity, and inhomogeneity, by the same blinded rheumatologist. A second ultrasound reading was performed blinded by another rheumatologist, with inter-observer Kappa calculation. Ultrasound abnormalities of the salivary glands were graded according to the OMERACT score ranging from 0 to 3 (threshold ≥2).
Results: The study included 95 patients; 51 with SS and 44 with undifferentiated connective tissue disease. Patients with SS showed a higher SGUS score compared with those with rheumatism with sicca syndrome [mean 1.69 (SD=1.17) versus 0.18 (SD= 0.44), P < 0.0001]. The SGUS threshold showed a sensitivity of 60%, a specificity of 98%, a positive predictive value of 97% and a negative predictive value of 67% for the diagnosis of SG. A significant correlation was also found between the SGUS score and the minor salivary gland biopsy/focus score (r=0.64, P<0.0001). Finally, the inter-observer Kappa coefficient ranged from 0.61 to 0.70.
Conclusion: Our study confirmed the good sensitivity and high specificity of SGUS in differentiating SS from other undifferentiated connective tissue diseases with sicca syndrome.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0900 AUTOMATIC SCORING OF EROSION, SYNOVITIS AND BONE OEDEMA IN RHEUMATOID ARTHRITIS USING DEEP LEARNING ON HAND MAGNETIC RESONANCE IMAGING

Keywords: Artificial intelligence, Imaging, Rheumatoid arthritis

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Background: Rheumatoid Arthritis (RA) Magnetic Resonance Imaging (MRI) scoring system (RAMRIS) [1] is used to manually assess severity of disease activity and monitor treatment response, but it is dependent on observer variability and is time-consuming. Deep learning techniques have the potential to improve the reproducibility and efficiency of RAMRIS scoring by automating the analysis of hand MRI scans, however, there are limited data on an automated assessment approach.
Objectives: To investigate whether a deep neural network (DNN) can be trained to automatically detect erosion, synovitis, and oedema in RA patients using hand MRI scans and RAMRIS.
Methods: We used 1,5 Tesla hand MRI (Siemens Magnetom Vida and Aera) from the BARE BONE trial, a prospective, single-arm, interventional, open-label, phase 4 trial (EUDRACT 2018-001164-32) in which RA patients were treated with baricitinib (4 mg/day) for 48 weeks. One of the objectives of BARE BONE was to assess the effect of baricitinib on joint damage and synovial inflammation. Participants of BARE BONE received hand MRI at week 0, 24, 48 following a standardized scanning protocol [2]. All images were scored according to RAMRIS. DNNs were applied on coronal T1 (pre/post contrast enhancement) and T2 MR images. 3-D landmarks for each location for RAMRIS scoring were identified and a region of interest (ROI) around each landmark was extracted to train a DNN. Three separate DNNs were trained, one for each of the RAMRIS subcomponents (erosion, synovitis, oedema). Each DNN is based on a ResNet-3D [3] architecture that was pretrained on a video classification task [4]. The networks were trained to predict the severity scores of each disease characteristic into three classes ranging from 0 (no pathological change) to 2 (high disease burden). The performance of the DNNs was evaluated using the area under the receiver operating characteristic curve (AUROC) and the area under the precision-recall curve (PR-AUC). Three-fold cross-validation were used and the network performance on a hold-out test set was evaluated.
Results: In total, we obtained 212 coronal MR images with both T1 and T2 weighting from 30 RA patients (24 woman/6 men, age 53.5±12.6 years, disease duration 4.3±4.4 years). The overall RAMRIS score decreased from 20.6 (CI95% 14.4 to 27.8) to 18.3 (CI95% 11.5 to 26.5) at week 48. For the evaluation of erosions and oedema, 23 landmarks respectively were used per hand, and 7 landmarks for synovitis. In total 4608 landmarks for erosion and oedema were available, and for synovitis 1152 landmarks. The AUROC for predicting erosions was 86±2% with a PR-AUC of 83±4%. For the prediction of oedema the AUROC was 78±14% and PR-AUC was 83%±10%. Despite a low number of ROI for synovitis scoring, the respective AUROC was 60±4% and PR-AUC was of 69±3%.
Conclusion: This proof-of-concept study demonstrated that fully automated extraction of synovitis, bone oedema, and erosion is feasible. In the future, our deep neural network approach may help to automatically assess MRI data of the hand in routine clinical practice and trials with high accuracy while keeping costs and human resources manageable.
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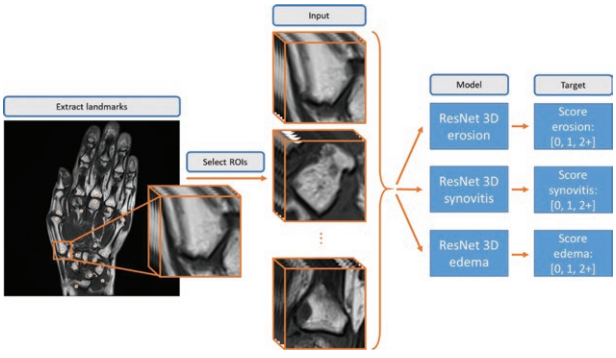


Figure 1. Neural network pipeline. Region of interests required required for RAMRIS scoring are extracted from hand MR images. All region of interests required are fed into a ResNet 3D to detect erosion, synovitis and bone oedema, respectively.

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POS0901 CAN B-MODE OCULAR ULTRASOUND ASSESS VITRITIS IN PATIENTS WITH AXIALSPONDYLOARTHRITIS AND PSORIASIC ARTHRITIS?

Keywords: Ultrasound, Inflammatory arthritides, Uveitis

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Background: Vitritis is the presence of cellular infiltration in the vitreous body, resulting from inflammation of the vitreous cavity itself or from the extension of the anterior chamber inflammatory process[**1**]. Uveitis is the most frequent extra-articular manifestation of axial spondyloarthritis and psoriatic arthritis, and may occur in any uveal topography[**2**]. B-mode ultrasound can useful for confirming uveitis, especially in those conditions in which there is opacification of the light-conducting medium and the vitreous cavity and the rest of the globe cannot be visualized by ophthalmological examination[**3**]. In the case of vitritis, the vitreous appears on the ultrasound screen in the form of thin, confluent and mobile images[**4**].
Objectives: To detect the presence of vitritis in patients with axial spondyloarthritis and psoriatic arthritis using a B-mode ocular ultrasound and comparing it with the slit lamp ophthalmologic examination.
Methods: Observational and cross-sectional study with 6 patients with non-radiographic axial spondyloarthritis according to the ASAS criteria; 24 with radiographic axial spondyloarthritis according to the modified New York criteria and 34 with psoriatic arthritis according to the CASPAR criteria, selected for convenience between the months of August and December 2021, from the Rheumatology outpatient clinic of the Pontifical Catholic University of Campinas Hospital. One hundred and twenty-six eyes were evaluated by an ophthalmologistby slit lamp biomicroscopy. B-mode ocular ultrasound machine (EsaoteSpA, São Paulo, Brazil) was performed with a high frequency linear probe of 12MHz. A total of 127 eyes were evaluated, categorizing vitritis semi-quantitatively through the intensity of echovitreous in grades 0 (absent), 1 (mild), 2 (moderate) and 3 (severe) **(Figure 1)**. Sensitivity, specificity, negative (NPV) and positive (PPV) predictive values and the ROC curve were calculated for B-mode ultrasound in relation to the ophthalmological evaluation.
Results: The mean age of patients with axial spondyloarthritis was 46.3±13 years, with a BASDAI of 4.10±2.84. The mean age among patients with psoriatic arthritis was 55.2±12.5 years, with a DAPSA of 24.27±22.15. Ophthalmic examination detected vitritis in 3.33% of the eyes. B-mode ultrasound identified grade 0 echovitreous in 39.37% of the eyes, **grade 1** in 25.98%, **grade 2** in 29.92%, and **grade 3** in 4.73% of the eyes. Sensitivity, specificity, NPV and PPV are described in **Table 1**. The ROC curve: area under the curve of **0.58 (95% CI: 0.41-0.74)**.
Conclusion: B-mode ocular ultrasound showed an excellent negative predictive value for detecting vitritis, constituting an important complementary tool in the evaluation of uveitis in patients with axial spondyloarthritis and psoriatic arthritis.
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Table 1. Performance according to the intensity of B-mode ultrasound echovitreous:

Echovitreous grades	Sensitivity (IC95%)	Specificity (IC95%)	NPV (CI95%)	PPV (CI95%)
1+2+3	0.69 (0.44-0.94)	0.41 (0.32-0.50)	0.12 (0.05-0.19)	0.92 (0.84-1.00)
2+3	0.46 (0.32-0.50)	0.67 (0.59-0.76)	0.14 (0.04-0.24)	0.92 (0.86-0.98)
3	0.08 (0.00-0.22)	0.96 (0.92-0.99)	0.17 (0.00-0.46)	0.90 (0.85-0.95)

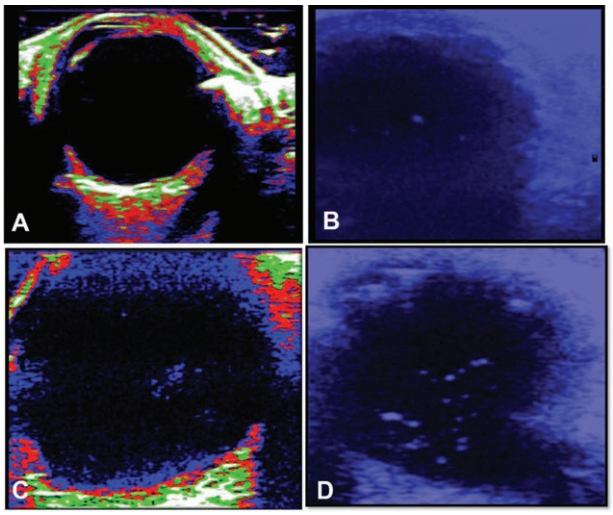


Figure 1. Patients with axial spondyloarthritis and psoriatic arthritis: Echovitreous intensity by B-mode ultrasound through color map and histogram: **A.** grade 0; **B.** grade 1; **C.** grade 2; D. grade 3.

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POS0902 ANTI-SSA RO52 AND ANTI-RO60 AUTOANTIBODIES: ASSOCIATION WITH CLINICAL PHENOTYPES

Keywords: Diagnostic tests

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Background: Anti-SSA autoantibodies can be differentiated according to their antigenic target proteins as anti-Ro60 (60 kDa) or anti-Ro52 (52 kDa). Anti-SSA(Ro60) are clearly associated with Connective Tissue Diseases (CTD), but the clinical significance of anti-SSA(Ro52) remains unclear.

Objectives: To analyze the disease phenotype of patients with anti-Ro52 and/or anti-Ro60.

Methods: Multicenter, cross-sectional study of anti-Ro52 and/or Ro60 positive patients followed at 10 Rheumatology centers from January 2018 until December 2021. Patients were categorised into 3 groups: group 1 (Ro52+/Ro60-); group 2 (Ro52-/Ro60+); group 3 (Ro52+/Ro60+). Antinuclear antibodies were evaluated by indirect immunofluorescence assay and further screened for anti-extractable nuclear antigen (ENA) antibodies. Demographics and clinical data were compared between the 3 groups, by patients' medical chart review. Univariate analysis was performed using chi-square, Fisher's exact or Kruskall-Wallis test. Subsequently, the Bonferroni test was used to identify intergroup differences (level of significance: p<0.0167). Univariate logistic regression was used to calculate the odds ratio with a 95% confidence interval (CI).

Results: We included 776 patients [female: 83.1%; median age: 59 (46-71) years]. Groups 1, 2 and 3 comprised 31.1%, 32.6%, and 36.3% of the patients, respectively. Characteristics of the groups are presented in Table 1. Anti-Ro52 alone is more frequently associated with non-rheumatic diseases, older age, and men (p<0.05). Among patients with CTD, the diagnosis of systemic lupus erythematosus is 3 and 2 times more prevalent in groups 2 and 3, respectively, than in group 1 [OR 2.8 (95% CI 1.60, 4.97),p=<0.001; OR 2.2 (95% CI 1.28, 3.86), p=0.007]. In group 2, the diagnosis of undifferentiated connective tissue disease is more frequent than in the other groups. The presence of isolated Ro52+ is more frequently associated with inflammatory myositis than in group 2 [OR 0.09 (95% CI 0.01, 0.33), p=<0.001] or group 3 [OR 0.08 (95% CI 0.01, 0.29), p=<0.001]. Group 1 was also more frequently associated with arthritis (p=0.006), interstitial lung disease (p=0.002), and myositis (p=0.009).

Table 1. Characteristics of the study population according to the groups of anti-SSA(Ro) positivity.

	Group 1 (n=241)	Group 2 (n=253)	Group 3 (n=282)	*p*
Age, median (IQR)	64 (52-76)	56 (44-67)	57 (44-69)	**<0.001**
Female, n (%)	185 (76.8)	214 (84.6)	246 (87.2)	**0.005**
Other anti-ENA, n (%)				
Anti-La	24 (10)	50 (19.8)	114 (40.4)	**<0.001**
Anti-RNP	11 (4.6)	23 (9.1)	17 (6.0)	0.115
Anti-Scl70	3 (1.2)	4 (1.6)	6 (2.1)	0.146
Anti-Jo1	7 (3)	1 (0.4)	3 (1.1)	0.070
Anti-Sm	1 (0.4)	7 (2.8)	6 (2.13)	0.098
Anti-dsDNA	11 (4.6)	39 (15.4)	37 (13.1)	**<0.001**
Anti-centromere	12 (5)	3 (1.2)	6 (2.1)	**0.026**
Lupus anticoagulant	10 (4.2)	32 (12.7)	23 (8.2)	**0.008**
Anti-cardiolipin	8 (3.3)	10 (3.9)	23 (8.2)	**0.024**
Anti-β2 glycoprotein 1	6 (2.5)	10 (3.9)	10 (3.6)	0.736
Rheumatoid Factor	46 (19.1)	44 (17.4)	81 (28.7)	**0.001**
Anti-CCP	11 (4.6)	15 (5.9)	19 (6.7)	0.327
Non-rheumatologic disease, n (%)	77 (32)	35 (13.8)	30 (10.6)	**<0.001**
Infections	11 (14.3)	2 (5.7)	1 (3.3)	0.192
Neoplasms	22 (28.6)	3 (8.6)	6 (20.0)	0.057
Interstitial lung disease	5 (6.5)	4 (11.4)	0	0.168
Other diseases	46 (59.7)	25 (71.4)	22 (73.3)	-
Immune-mediated rheumatologic disease, n (%)	164 (68.1)	218 (86.2)	252 (89.4)	**<0.001**
Sjögren syndrome	92 (56.1)	88 (40.3)	150 (59.5)	**<0.001**
Systemic lupus erythematosus	20 (12.2)	61 (28)	59 (23.4)	**0.001**
Systemic sclerosis	11 (6.7)	7 (3.2)	8 (3.2)	0.150
Inflammatory myositis	15 (9.2)	2 (0.9)	2 (0.8)	**<0.001**
Rheumatoid arthritis	18 (11)	17 (7.8)	16 (6.4)	0.234
Undifferentiated connective tissue disease	11 (6.7)	35 (16.1)	21 (8.3)	**0.004**
Mixed connective tissue disease	6 (3.7)	6 (2.8)	4 (1.6)	0.406
Other diseases	9 (5.5)	8 (3.7)	10 (4.0)	-

Conclusion: Anti-Ro52+ alone is frequently found in patients with non-rheumatic diseases. In addition, anti-Ro52+ is also prevalent in patients with CTD and associated with clinical phenotypes that are different from anti-Ro60+.

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Disclosure of Interests: None Declared.

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POS0903

DIFFUSE GENERALIZED VENULITIS AS THE PRIMARY PATHOLOGY OF BEHÇET'S DISEASE: A COMPREHENSIVE MAGNETIC RESONANCE VENOGRAPHY STUDY

Keywords: Behcet's disease

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Background: Behçet's Disease (BD) is a chronic multisystem vasculitis that manifests with recurrent oral/genital ulcerations and destructive inflammation affecting eyes, central nervous system, and blood vessels. Venous thrombosis is observed in up to 40% of patients, however pathology of vein involvement in BD is poorly characterized [**1].** Recently, demonstration of wall thickening in posterior wall of common femoral vein with an ultrasound (US) was reported to be a reliable auxiliary diagnostic tool in BD. Magnetic resonance (MR) venography may give more comprehensive information about deep veins and adjacent tissues.

Objectives: In this study, we aimed to characterize vein involvement in BD and evaluate diagnostic utility of MR venography.

Methods: Sixty-five BD patients who fulfilled the International Study Group (ISG) criteria and 20 healthy control subjects were enrolled. BD patients were separated into two groups based on previous history of vascular involvement. Inferior vena cava (IVC), common iliac veins (CIV), external (EIV) and internal iliac veins (IVV), common femoral veins (CFV), femoral veins (FV), and greater saphenous veins (GSV) of BH patients and healthy controls were evaluated with MR venography and ultrasonography for the presence pathologic features, luminal thrombi, vessel wall changes and perivascular abnormalities.

Results: 33 vascular and 32 non-vascular BD patients (mean age 39.3±11.3 years and 48 [73.8%] male) were enrolled. MR venography revealed diffuse concentric thickening of the walls of IVC, CIV, EIV, IIV, CFV, FV and GSV in BD (healthy controls vs BD p<0.05 for all the vein segments). **(Table 1).** There was no significant difference between vascular and non-vascular BD groups in terms of vein diameter and wall thicknesses, while both groups had significantly thicker veins than healthy controls (p<0.05). US examination revealed similar results. MR venography provided additional information about veins and perivascular tissues like contrast enhancement, enlarged lymph nodes and seminal vesicle vascularization which were significantly more frequent in vascular BD than non-vascular BD and healthy controls.

Conclusion: The results of our study suggest that the involvement of the venous system is diffuse and generalized in BD, and demonstration of venulitis might help diagnose the disease. Further studies are needed to elucidate prognostic role of wall thickening, venulitis, in terms of anticipation of future thrombosis and treatment response.

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Table 1. Comparison of magnetic resonance (MR) venography findings with respect to vascular and non-vascular involvements of Behçet's disease

	Control group (n=20)	BD all group (n=65)	BD vascular (n=33)	BD non-vascular (n=32)	p1	p2
Inferior vena cava						
Wall thickness	1.19±0.11	1.43±0.31	1.44±0.31	1.42±0.32	**0.001***	0.768
Diameter	18.93±3.02	20.00±4.34	20.26±5.09	19.74±3.55	0.31	0.647
Common iliac vein						
Wall thickness	0.98±0.07	1.17±0.25	1.17±0.25	1.17±0.24	**0.001***	0.97
Diameter	11.88±1.50	12.31±2.33	12.74±2.42	11.87±2.20	0.33	0.14
External iliac vein						
Wall thickness	0.87±0.11	0.96±0.17	0.99±0.18	0.93±0.15	**0.006***	0.16
Diameter	10.00±1.25	10.61±2.28	11.17±2.27	10.07±2.19	0.12	0.05
Internal iliac vein						
Wall thickness	0.58±0.08	0.66±0.20	0.66±0.19	0.65±0.20	0.01	0.76
Diameter	0.69±1.61	0.69±1.75	7.14±1.59	6.64±0.19	0.99	0.26
Common femoral vein						
Wall thickness	0.62±0.08	0.74±0.22	0.77±0.30	0.71±0.87	**0.001***	0.28
Diameter	7.30±1.25	8.86±2.38	8.80±2.13	8.91±2.57	**0.001***	0.85
Deep femoral vein						
Wall thickness	0.56±0.08	0.63±0.26	0.68±0.34	0.58±0.10	**0.05**	0.11
Diameter	6.42±1.49	6.67±1.56	6.79±1.55	6.53±1.59	0.53	0.54
Greater saphenous vein						
Wall thickness	0.25±0.06	0.35±0.15	0.38±0.17	0.32±0.10	**0.001***	0.11

All values are mean ± SD in millimeters. p1: Control group vs BD all group, p2: BD vascular vs non-vascular involvements.

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Disclosure of Interests: None Declared.

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POS0904

INTENSIVE TRAINING PROGRAM FOR ULTRASOUND-GUIDED MINIMALLY INVASIVE SYNOVIAL TISSUE BIOPSY PROCEDURE ON SMALL AND LARGE JOINTS IN DIFFERENT PHASES OF JOINT INFLAMMATION

Keywords: Synovium, Education, Rheumatoid arthritis

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Background: Ultrasound (US)-guided minimally invasive technique has improved the availability of soft tissue specimens, as synovial tissue (ST), to be used for basic and translational studies. However, to date, there is a lack of standardized programs to systematically train rheumatologists in its performance on joints in different disease stages of inflammation.
Objectives: (i) to develop an intensive training program for US-guided ST biopsy on large and small joints across inflammatory arthritis phases; (ii) to assess the learning curve, sample quality and trainees' expectations and perceptions.
Methods: Rheumatoid arthritis (RA) patients with active disease or in sustained remission were included in the study. Eight trainees in rheumatology with basic skills on musculoskeletal US joined the training program consisting of 4 sequential phases: (i) observation of the procedure performed by the trainer, (ii) performance of guided step-by-step phases of the procedure, (iii) execution of the whole procedure on small and large joints in parallel with the trainer as reference (each one carried out on paired joints with comparable US-defined joint inflammation on the same patient) and (iv) performance of the complete procedure autonomously. ST specimens were processed for histology (H&E) to assess sample quality in terms of anatomical representativity given by lining and sublining layers presence, required for the semiquantitative assessment of synovitis degree using Krenn score. Before and after the program, trainees' expectations and perceptions were collected using a questionnaire.
Results: 236 ST biopsy procedures were included in the analysis. After completing the observational and guided step-by-step phases, trainees conducted complete procedures (n=44) in parallel with the trainer performing the procedure on the contralateral joint [n=36 knees (n=24 inflamed and n=12 in remission) and n=8 inflamed wrists] showing comparable rate of informative samples recovered by trainees on knees in terms of lining (91.4% and 83.3% for active and remission knees, respectively) and sublining (100% for both) presence, compared to the trainer's procedures ($p>0.05$). Conversely, the rate of informative samples retrieved from active wrists by trainees was lower in terms of lining layer (62.5%), but not sublining layer (100%) presence, compared to the trainers (100% for both, $p=0.05$). Then, trainees performed n=148 procedures without the trainer guidance (n=74 on active and n=43 remission knees respectively, and n=31 on active wrists) achieving an excellent rate of informative samples of 93.3% and 90.3% on active knees and wrists respectively but lower (72.1%, $p=0.0017$) on remission knees, always due to the lack of lining layer retrieval. After the training completion, the trainees' expectation about the invasiveness and pain infliction related to the procedure decreased ($p=0.0625$ and $p=0.0156$, respectively). However, after the training program, trainees' perception of the difficulty of executing the procedure decreased only for large joints regardless to the inflammatory status ($p=0.0312$) remaining unchanged for small joints ($p=0.0625$).
Conclusion: This intensive multi-step program is an effective training system for developing advanced skills in the performance of US-guided ST biopsy on large and small joints, providing high quality specimens to be used for basic and translational studies on chronic inflammatory joint diseases as RA. The intensity and the timing of the training needed to reach acceptable success rates, might be adjusted according to the inflammatory status and the location of the procedure.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0905 AXILLARY ARTERIES ULTRASOUND IN THE DIAGNOSIS OF GIANT CELL ARTERITIS WITH PREDOMINANTLY CRANIAL SYMPTOMS

Keywords: Diagnostic tests, Imaging, Vasculitis

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Background: Giant cell arteritis (GCA) is the most common form of primary systemic vasculitis in patients aged >50 years. It predominantly affects the cranial arteries; however, extra-cranial disease involving the aorta and its major branches can also be present. According to the 2018 EULAR recommendations, the ultrasound of temporal arteries (TAs), with or without axillary arteries (AXs), should be the first imaging modality performed in patients with suspected predominantly cranial GCA [1]. This recommendation reflects that the value of the AXs ultrasound in GCA diagnosis is still questionable, especially in patients who present with cranial symptoms of the disease.
Objectives: To assess the value of AXs ultrasound in the ultrasonographic diagnosis of GCA, particularly in patients with predominantly cranial symptoms of GCA.
Methods: Observational retrospective study involving the Rheumatology Departments of Centro Hospitalar Universitário Lisboa Norte (CHULN), Lisbon-Portugal, and the Nuffield Orthopaedic Centre (NOC), Oxford-UK. We included patients with a clinical diagnosis of GCA and a positive ultrasound for GCA at diagnosis, i.e., the presence of a non-compressible halo sign in the TAs or AXs. Information regarding the demographics, clinical manifestations at disease presentation, and therapeutics were collected. Cranial symptoms included headache, temporary or permanent loss of vision, diplopia, blurred vision, jaw or tongue claudication, scalp tenderness or paraesthesia, stroke, or transient ischaemic attack (TIA).
Results: We included 230 patients, 139 (60.4%) from the NOC and 91 (39.6%) from CHULN. One hundred and thirty-six (59.1%) patients were females, and the mean ± standard deviation age at diagnosis was 75.3 ± 8.5 years. The ultrasound was performed after ten days of treatment with prednisolone ≥30mg/day in 70/230 (30.4%) patients. The presence of halo sign in the TAs was found in 207/230 (90.0%) patients and in the AXs in 57/230 (24.8%) patients. According to the ultrasound pattern presented, 173/230 (75.2%) patients had positive TAs and negative AXs ultrasound, 23/230 (10.0%) had negative TAs and positive AXs ultrasound, and 34/230 (14.8%) had both positive TAs and AXs ultrasound. Cranial symptoms were reported in 207/230 (90.0%) patients, in whom AXs involvement on ultrasound was detected in 43/207 (20.8%) of cases. Concerning only the patients with negative TAs and positive AXs ultrasound, 13/23 (56.5%) reported cranial symptoms. Headache was reported in 10/23 (43.5%), visual symptoms in 6/23 (26.1%), jaw or tongue claudication in 4/23 (17.4%), scalp tenderness or paraesthesia in 4/23 (17.4%), and stroke or TIA in 1/23 (4.3%) patients. Constitutional symptoms were present in 13/23 (56.5%), polymyalgia rheumatica in 9/23 (39.1%), and limb claudication in 1/23 (4.3%) patients. A total of 10/23 (43.5%) patients were on glucocorticoid treatment at the time of the diagnosis, but only 4/23 (17.4%) were on prednisolone ≥30mg/day for at least ten days.
Conclusion: Axillary involvement in GCA is frequent, affecting around 1/4 of the patients at diagnosis. The additional assessment of the AXs improved the ultrasound diagnostic sensitivity by 10% compared to only assessing the TAs. Patients with AXs involvement were reported to have cranial symptoms in 43/57 (75.4%) of cases. More than half of the patients with negative TAs and positive AXs ultrasound presented with cranial symptoms. Our results support the need to assess the AXs in patients with suspected GCA, regardless of the presence or absence of cranial symptoms.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0906 ULTRASONOGRAPHY AND FDG-PET/CT FOR SUSPECTED POLYMYALGIA RHEUMATICA: DIAGNOSTIC PERFORMANCE IN TREATMENT-NAÏVE VERSUS ALREADY TREATED PATIENTS

Keywords: Diagnostic tests, Ultrasound, Imaging

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Background: Polymyalgia rheumatica (PMR) is a common rheumatic, inflammatory disease in the elderly. Traditionally, the diagnosis is based on clinical and laboratory findings, which are not specific for PMR. Although most patients initially respond well to glucocorticoid (GC) treatment, a refractory or relapsing disease course is not uncommon and may cause doubt about the initial diagnosis. This usually prompts additional diagnostic evaluation for PMR with imaging tools such as ultrasonography and FDG-PET/CT, usually after GC tapering. However, it is unclear whether these tests perform equally well in patients already treated under the presumed diagnosis of relapsing or refractory PMR, when compared to treatment-naïve patients, suspected of new PMR.
Objectives: To compare the diagnostic accuracy of ultrasonography and FDG-PET/CT for PMR in treatment-naïve and already treated patients
Methods: Retrospective study including 144 consecutive patients that were referred to the Rheumatology and Clinical Immunology department for suspected PMR, including 63 treatment-naïve patients, and 81 already treated patients with or without still ongoing treatment. Patients were referred by general practitioners (n=107) or other medical specialist. Bilateral ultrasonographic evaluation of the shoulders and hips was performed in 135 patients. The presence of biceps tenosynovitis, subacromial bursitis, glenohumeral synovitis, hip synovitis and trochanteric bursitis was assessed. A sum score of the latter abnormalities was constructed (score range 0-10), and termed total ultrasound score. FDG-PET/CT from skull to upper legs was performed in 72 patients. FDG uptake was visually scored at 12 key sites in order to calculate the Leuven PMR-PET score (score range 0-24) [1,2]. The final clinical diagnosis at 6 months was the reference standard.
Results: A clinical diagnosis of PMR was made in 94/144 (65%) patients. The provisional ACR/EULAR criteria for PMR were fulfilled in 67/94 (71%) patients with PMR and in 19/50 (38%) patients without PMR. More specifically, PMR was diagnosed in 42/63 (67%) treatment-naïve patients and 52/81 (64%) already treated patients. Among the already treated patients, 24 patients were still on GC treatment during the ultrasound scan (median prednisolone dose 6.25 mg daily, range 1.25-30), while 2 patients were taking methotrexate (n=1) or leflunomide (n=1). Only 2 patients were on GC treatment during the FDG-PET/CT scan (prednisolone dose 1 and 2.5 mg), while 1 patient was treated with leflunomide. The total ultrasound score and Leuven PMR-PET score showed good diagnostic accuracy in treatment-naïve patients as indicated by the AUC in the ROC analysis (Table 1). The diagnostic accuracy of the total ultrasound score was poor in patients that had already been treated, even when GC treatment had been fully tapered. In contrast, the diagnostic accuracy of FDG-PET/CT remained good in already treated patients.
Conclusion: FDG-PET/CT shows equal diagnostic accuracy for already treated PMR as for treatment-naïve PMR, if GC therapy is fully tapered. However, ultrasonography for suspected PMR is best performed before initiation of treatment. A simple sum score of inflammatory lesions in the shoulders and hips aids the interpretation of ultrasonography in PMR.
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Table 1.

Patient group	Imaging score	AUC in ROC analysis	Optimal cut-off point	Sensitivity (%)	Specificity (%)
Treatment-naïve	Total ultrasound score (n=61)	0.792 (0.661-0.922)	2	88	62
	Leuven PMR-PET score (n=29)	0.795 (0.592-0.998)	11	100	63
Already treated (all)	Total ultrasound score (n=74)	0.628 (0.487-0.770)	1	77	58
	Leuven PMR-PET score (n=43)	0.837 (0.695-0.979)	11	75	82
Already treated (treatment fully tapered before imaging)	Total ultrasound score (n=50)	0.680 (0.517-0.843)	1	81	63
	Leuven PMR-PET score (n=41)	0.845 (0.706-0.985)	11	80	82

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POS0907 ULTRA-HIGH FREQUENCY ULTRASOUND TO ASSESS SKIN INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS: PRELIMINARY DATA FROM A MONOCENTRIC COHORT

Keywords: Skin, Ultrasound, Systemic lupus erythematosus

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Background: The assessment of cutaneous involvement in Systemic Lupus Erythematosus (SLE), particularly the differential diagnosis between active lesions and damage, might be a challenge for the clinicians. Ultra-high frequency ultrasound (UHFUS), with a sub-millimeter resolution, is a promising tool in the evaluation of superficial structures. In recent years its use has grown in the field of dermatology, where UHFUS finds application in the study of normal anatomy, differentiation of cutaneous lesions (bullous and inflammatory disease), diagnosis of skin malignancies and pre-surgical mapping, increasing diagnostic sensitivity and accuracy in guiding medical and surgical therapies.
Objectives: The aim of the study was to explore a possible role of UHFUS assessment in the evaluation of skin involvement in a monocentric cohort of SLE patients and to evaluate the relationship with patients' perception of their skin disease.
Methods: Consecutive adult SLE patients (1997 ACR criteria) regularly followed at our Lupus Clinic were prospectively enrolled during a scheduled outpatient visit in presence of skin lesions. Demographical, clinical, laboratory and treatment data were collected at enrolment. Disease activity and organ damage were evaluated with the SELENA-2K and SLICC-DI, respectively. Clinical assessment of skin lesions was done by an experienced rheumatologist using the Cutaneous LE Disease Area and Severity Index (CLASI); at the same time, UHFUS evaluation of skin lesions was performed with a 70 MHz probe by an experienced dermatologist. The Skindex-16 questionnaire was used to assess the impact of the skin involvement on patients' quality of life.
Results: We included 70 assessments in 55 SLE patients with skin lesions (5/55 evaluated twice, 5/55 three times). Cutaneous disease subtypes were distributed as follows: acute 37.5%, subacute 12.5%, chronic 50.0%. The characteristics of the cohort are shown in Table 1. The most frequent UHFUS alteration was the presence of power Doppler (51/70, 72.9%), followed by dermal oedema (37/70, 52.9%), dermal inhomogeneity (33/70, 47.1%), follicular plugging (32/70, 45.7%), vascular ectasia (27/70, 38.6%) and thinning of the epidermis (10/70, 14.3%). The CLASI activity score was significantly higher in cutaneous areas with power Doppler signal (p=0.032). Dermal oedema was also found to be associated with

Table 1. Characteristics of the cohort

N° of patients	55
Female	49 (89.1%)
Age[1] [years]	45 (35-55)
Disease duration[1] [years]	11 (7-19)
Ethnicity: Caucasian/ Asian/ African-American	51 (92.7%)/ 3 (5.5%)/ 1 (1.8%)
Organ involvement *[cumulative/ ongoing]*	
Mucocutaneous	55 (100%)/ 55 (100%)
Haematological	20 (36.4%)/ 6 (10.9%)
Renal	7 (12.7%)/ 2 (3.6%)
Articular	33 (60.0%)/ 8 (14.5%)
Serositis	2 (3.6%)/ 0
Neuropsychiatric	3 (5.5%)/ 0
SLEDAI-2K[1]*	4 (2-6)
SLICC-DI[1]*	0 (0-1)
CLASI activity[1]* *[global/ UHFUS area]*	5 (3-8)/ 2 (1-3)
CLASI damage[1]* *[global/ UHFUS area]*	1 (0-5)/ 0 (0-2)
Skindex-16 global[1]*	53.9 (31.3-83.3)
Skindex-16 symptoms[1]*	50.0 (25.0-85.7)
Skindex-16 emotions[1]*	61.9 (28.6-97.6)
Skindex-16 functioning[1]*	33.3 (13.3-86.7)

[1] Median (IQR)* data on 70 assessments

higher CLASI activity scores, considered both globally (p<0.001) and at the level of the US-evaluated region (p=0.002), and with higher damage scores of the evaluated area (p=0.034), while vascular ectasia was only associated with higher damage scores of the evaluated area (p=0.036). Skindex-16 symptoms subscale scores were significantly higher in patients with thinning of the epidermis (p=0.01) and dermal inhomogeneity (p=0.049). Regarding the subtype of cutaneous involvement, vascular ectasia was significantly more frequent in chronic cutaneous LE (p=0.029), while no other UHFUS alterations were found to differ between the three groups.

Conclusion: Although preliminary, our data seem to suggest UHFUS as a promising tool not only for assessing skin involvement in SLE, but also for monitoring disease activity over time with a view to optimising the management of these patients.

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Disclosure of Interests: None Declared.

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POS0908 NAILFOLD CAPILLAROSCOPY FINDINGS OF INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES (IPAF)

Keywords: Lungs, Imaging

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Background: Objectives: We evaluated nailfold capillaroscopy (NFC) of interstitial pneumonia with autoimmune features (IPAF) and compared it with that of patients with CTD-ILD and idiopathic interstitial pneumonia (IIP).

Methods: Patients with newly diagnosed as ILD were evaluated using NFC. Baseline demographic, clinical, serological, and high-resolution CT findings were collected. NFC was semi-quantitatively scored with six domains ranging from 0 to 18. In addition, the overall patterns (scleroderma/non-scleroderma patterns) were determined.

Results: A total of 81 patients (31 with CTD-ILD, 18 with IPAF, and 32 with IIP) were included. The non-specific interstitial pneumonia pattern was the most common ILD pattern in the CTD-ILD and IPAF groups, whereas the usual interstitial pneumonia pattern was the most common in the IIP group. The semi-quantitative score of the CTD-ILD group was higher than that of the IPAF or IIP groups (5.8 vs 4.2 vs 3.0, p < 0.001, respectively). Giant capillaries and haemorrhages were more frequently present in the CTD-ILD and IPAF groups than in the IIP group. A scleroderma pattern was present in 27.8% of the IPAF group, whereas none of the IIP patients showed a scleroderma pattern.

Conclusion: NFC findings may be useful in classifying patients with ILD into CTD-ILD/IPAF/IIP.

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Disclosure of Interests: None Declared.

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POS0909 IS IT NECESSARY TO STOP NOVEL ORAL ANTICOAGULANT THERAPY PRIOR TO MUSCULOSKELETAL ULTRASOUND GUIDED INTERVENTIONAL MANEUVERS?

Keywords: Comorbidities, Ultrasound, Inflammatory arthritides

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Background: Anticoagulation is common in patients undergoing arthrocentesis or joint/ periarticular injections. Previous retrospective studies have established the safety of continuing anticoagulation with Novel Oral Anticoagulant Therapy (NOAC) when performing such kind of interventional maneuvers [1]. Indeed, ultrasound guided interventional maneuvers have shown a superior safety profile compared to blind anatomical maneuvers [2].

Objectives: To evaluate the post-procedural bleeding complications in patients diagnosed with inflammatory/ degenerative rheumatologic pathology.

Methods: Consecutive patients diagnosed with inflammatory/ degenerative rheumatologic pathology requiring interventional articular/ periarticular maneuvers were prospectively recruited. Patients were divided in two groups – Group 1 treated with NOACs and Group 2 (control group) without anticoagulation. NOAC therapy was administered in a continuous regimen prior to the interventional maneuver, in therapeutic regimens dictated by the underlying anticoagulation indication. Demographics, laboratory analysis, systemic medication, local administered medication (corticosteroids/ viscosupplementation), interventional maneuver location, type of needle, the occurrence/ absence of bleeding accidents in the anatomic structures submitted to needle penetration were recorded. The written informed consent was obtained. Post-procedural control was performed at 30 minutes, 48 hours and 7 days.

Results: Results are presented in Table 1. No articular/ intra- tendon sheath/ bursa or muscular bleeding event occurred in patients treated with NOAC regardless of their type and dosage, local medication administration/ needle size/location and number of interventions per individual. Several patients in both groups developed small superficial ecchymoses at injection site.

Table 1. Demographics, laboratory analysis, systemic medication, interventional maneuver location, type of needle, the occurrence/ absence of bleeding accidents.

Parameter	Group with NOAC	Group with No NOAC
Number patients	79	156
with 2 interventions	25	40
Age (median +/- IQR)	65 ± 11.4	69 ± 12.3
Gender (number F/M)	44/35	99/57
GFR (median ± IQR)	79 (50-99)	74 (66-103)
NOAC type		
Apixaban (5mg/day)	40	0
Rivaroxaban (15-20 mg/day)	38	0
Dabigatran (75mg/day)	1	0
Vitamine K antagonists	0	0
Aspirine 100mg/d	12	10
Injection number	104	196
Ultrasound guided injections (%)	100	100
Needle size (Gauge)	15	43
G18 (for viscosupplementation)	70	123
G21	19	30
G24		
Injection site		
Knee joint	55	70
Shoulder (SASDb)*	28	69
Hip joint	2	27
Tendon sheath	9	19
Paravertebral	10	11
Bleeding events in the targeted anatomic structure	0	0

*SASDb = subacromial subdeltoid bursa, GFR-glomerular filtration rate

Conclusion: Our results suggest that NOACs are safe to be used in a continuous regimen prior to joint/periarticular ultrasound guided injections, even in combination therapy with aspirin. The use of lower gauge needles, chosen for viscosupplementation therapy, was not burdened with adverse effects on the procedural outcome.

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POS0910 A MULTIPLEX RT-QPCR KIT FOR EXPRESSION ANALYSIS OF INTERFERON-STIMULATED GENES AS A USEFUL TOOL FOR MOLECULAR STRATIFICATION IN LUPUS AND OTHER AUTOIMMUNE DISEASES

Keywords: Validation, Diagnostic tests, Systemic lupus erythematosus

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Background: It is recognized that the expression of interferon (IFN)-stimulated genes (IFN signature) plays a significant role in several autoimmune diseases (AIDs) [1], such as systemic erythematosus lupus (SLE), idiopathic inflammatory

myopathies (IIM) and rheumatoid arthritis (RA). A quick and ready-to-use method to differentiate IFN activation state is clinically needed.

Objectives: This study aimed to conduct analytical validation of the Multiplex ISGs RT-qPCR Kit in clinical practice

Methods: We designed a multiplex RT-qPCR method to provide IFN score covering both type I IFN and type II IFN by simultaneously detecting the expression of 3 IFN stimulated genes (ISGs), IFI44, MX1(type I ISGs), and IRF1(type II ISG), relative to one housekeeping gene (HPRT1). Measurements were performed on mRNA extracted from the peripheral blood cells of patients with multiple AIDs. The relative expression of each target gene (T/R) was calculated via 2^-ΔCT. The T/R of each target gene was then normalized as the following: $T/R_{subject}$ - Mean $_{HC}$/ SD_{HC}. IFN score was calculated as the mean of the normalized T/R of three target genes. Scores higher than the mean of HC plus two SD were designated IFN score high; otherwise, IFN score low. Analytical validation was performed to assess compliance rate, accuracy and method detection limit.

Results: Significantly elevated IFN scores were found in SLE(n=116), IIM(n=118), and RA(n=17) compared to other AIDs and HC. Four distinct subpopulations of SLE patients were observed: Thirty-five percent of SLE patients exhibited elevation of all three genes, indicating both type I and type II IFN pathways were activated. 44% of SLE patients had elevated expression of type I ISGs but no change in the type II ISG suggesting only type I IFN pathway was activated. 15% SLE patients presented no elevated expression of ISG gene. And 6% SLE patients only showed increased expression of IRF1 without overexpression of other 2 Type I ISGs, suggesting they probably only had type II IFN pathway activated. We repeated the tests. The compliance rate was 100% and accuracy was 100% with a CV of 0.36%. The method detection limit was 0.61 ng/μL.

Conclusion: Using the Multiplex® ISGs RT-qPCR Kit, we assessed the IFN score in multiple AIDs. The analytical validation of the kit reveals that it is a reliable, reproducible diagnostic tool that will be useful in clinical practice but may require confirmation in larger-scale trials.

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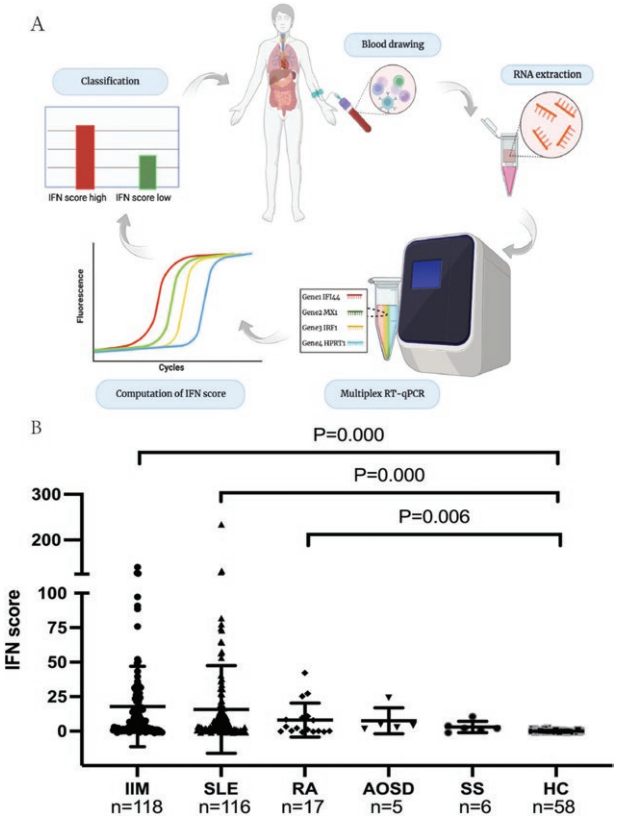


Figure 1. The IFN score obtained by the Multiplex® ISGs RT-qPCR Kit among various AIDs

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Disclosure of Interests: None Declared.

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POS0911 **ULTRASOUND-DETECTED SYNOVITIS AMONG INDIVIDUALS AT RISK OF RHEUMATOID ARTHRITIS INCREASES THE RISK OF DEVELOPING CLINICAL ARTHRITIS IN THE FUTURE**

Keywords: Rheumatoid arthritis

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Background: During the transition to rheumatoid arthritis (RA) patients pass through several phases. In the preclinical phase, the presence of anti-citrullinated protein antibodies (ACPA) can be detected [1]. A set of clinical characteristics for patients with arthralgia who are at risk of progression to RA was established (clinically suspected arthralgia; CSA) [2]. Ultrasound (US) is more sensitive diagnostic tool in detecting synovitis than clinical assessment and was recommended to use in diagnostics of RA.

Objectives: To test if ultrasound-detected synovitis among patients at risk of progression to RA increases the risk of developing clinical arthritis (CA) in the future.

Methods: ACPA+ individuals with arthralgia and/or those fulfilling CSA criteria were enrolled into the study and were assessed in 3 months interval (routine clinical investigation with laboratory tests, 68-joint count, US assessment). Tender and swollen joint counts were provided by an independent investigator. Sonographer was blinded to all clinical and laboratory data. CA was defined as clinically swollen and tender joint. All US assessments were provided by a single experienced investigator. Thirty joints US score was assessed bilaterally in wrist, MCP I-V, PIP II-V (dorsal and palmar approach), MTP II-V (dorsal approach), ankle (dorsal, medial and lateral approach). US synovitis was defined according the EULAR-OMERACT and scored separately in grey-scale (GS; 0-3) and Power Doppler (PD; 0-3), and combined GS+PD score GLOESS (Global OMERACT-EULAR Score System) was used. For the statistical analysis, we used GraphPad Prism 8.0.0 software (Wilcoxon-Mann-Whitney test), and relative risk ratio (RR).

Results: 159 patients were enrolled into the study (93% female). 95 individuals were ACPA+ (38% fulfilled the CSA criteria additionally), 64 individuals fulfilled the CSA criteria and were ACPA-. At baseline, GS≥1 was detected in 109 patients (67%), PD≥1 was found in 30 individuals (19 %). Single erosion was found by US only in 4 patients (3%) at baseline. 33 patients (21%) developed CA during follow up (mean 13 months after enrolment into the study). No statistical difference in US synovitis score was found between ACPA+ vs. ACPA- and CSA+ vs. CSA- groups at baseline. RR to develop CA at the patient level in patients with GS≥2 at baseline was 1.58 (95% CI 1.16- 2.18; p<0.01), in PD≥1 the RR was 3,14 (95% CI 1.74-5,7; p<0.001), in PD≥2 RR was 7,64 (95% CI 3,1-18,82; p<0.0001). GLOESS score>5 showed RR 3,82 (95% CI 1,74-8,4; p<0,001). US-detected synovitis preceded clinical finding of arthritis by 3 months (SD 1,2).

Conclusion: US-detected synovitis in patients at risk of RA further increases the risk of developing clinical arthritis in a larger prospective study. US detected synovitis in joints appears about 3 months prior synovitis detected by routine clinical assessment.

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Table 1. Relative risk of developing clinical arthritis according to US-detected synovitis at baseline in patients with clinically suspected artralgia. (grey-scale (GS), Power-Doppler (PD), and GLOESS score)

	Relative Risk	95% CI	P value	Odds Ratio	95% CI	P value
GS≥1	1,59	0.60 to 4.20	0,35	1,86	0.75 to 4.63	0,18
PD≥1	**3,14**	**1.74 to 5.70**	**<0,001**	**4,72**	**2.00 to 11.15**	**<0,001**
GS≥2	**1,58**	**1.16 to 2.18**	**<0,01**	**2,75**	**1.23 to 6.17**	**<0,05**
PD≥2	**7,64**	**3.10 to 18.82**	**<0,0001**	**11,43**	**3.87 to 33.79**	**<0,0001**
GLOESS>3	1,84	1.11 to 3.07	0,019	2,46	1.10 to 5.51	0,028
GLOESS>4	2,33	1.22 to 4.45	0,01	3,00	1.25 to 7.23	0,014
GLOESS>5	**3,82**	**1.74 to 8.40**	**<0,001**	**5,04**	**1.89 to 13.50**	**<0,01**

Acknowledgements: Project NU22-05-00226.

Disclosure of Interests: None Declared.

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POS0912 **SARCOPENIA IN SPONDYLOARTHRITIS. ULTRASOUND EVALUATION**

Keywords: Spondyloarthritis, Ultrasound, Sarcopenia

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Background: Spondyloarthritis are a group of chronic inflammatory rheumatic diseases that share clinical and imaging characteristics. Sarcopenia is characterized by loss of muscle mass and function associated with impairment of quality of life and adverse outcomes such as fractures and death. Patients with Spondyloarthritis had a prevalence of up to 25.7% of sarcopenia. The available imaging techniques for the detection of low muscle quantity and quality are: dual-energy X-ray absorptiometry (DXA), bioelectrical impedance analysis (BIA), and recently muscular ultrasound (US). Ultrasound estimate muscle quantity using prediction equations based on muscle thickness that have shown to be highly reliable in healthy population. Among the models used, the following equations are applicable in different ethnicities to predict muscle mass Abe 2018, Barbosa Silva 2021, Tang 2022.

Objectives: To evaluate the prevalence of sarcopenia in Spondyloarthritis and to determine which of the three ultrasonographic predictive models correlates best with BIA and DXA in our population.

Methods: Observational, cross-sectional study. We included 42 patients with spondyloarthritis (according to ASAS criteria for ankylosing spondylitis or CASPAR criteria for psoriatic arthritis). Appendicular skeletal muscle mass (ASMM) was evaluated by DXA and predicted by BIA and US. We performed a US examination with a GE LOGIQ^{TM}e, equipped with a broadband linear probe to measure muscle thickness (MT) at seven sites. Based on ultrasound prediction models, we use age, sex, height, and MT to estimate ASMM (Abe-2018, Barbosa-2021, and Tang-2022). A bivariate analysis was performed to assess the differences between patients with and without decreased ASMM. Pearson´s correlation coefficient was calculated to evaluate the correlation of the ultrasonographic predictive models with DXA and BIA. Finally, a ROC curve analysis was performed to determine the area under the curve of the models.

Results: We included 42 patients, composed mainly of men (24/42, 57.1%), with ankylosing spondylitis (AS) in 35 (83.3%) and psoriatic arthritis in 7 (16.7%). The prevalence of sarcopenia was about 33% (10/14 sarcopenia y 4/14 severe sarcopenia). When comparing patients with and without decreased ASMM, differences were only found in ultrasonography measurements of the quadriceps and anterior tibial muscles (p=0.003 y 0.00). On the other hand, the ultrasound prediction models had a moderate to strong correlation with DXA and BIA (0.80, 0.87, 0.53 and 0.88, 0.74, 0.66 for Abe-2018, Barbosa-2021, and Tang-2022). Nevertheless, in the ROC curve, the ABE-2018 model expresses a better diagnostic performance (AUC 0.80 p=0.002).

Conclusion: Results indicated a low ASMM in 30% of the patients with Spondyloarthritis (sarcopenia 24.4%, severe sarcopenia 9.8%). This study supports the use of ultrasound and shows a good correlation with DXA and BIA for ASMM evaluation in Spondyloarthritis, particularly with the Abe-2018 predictive model.

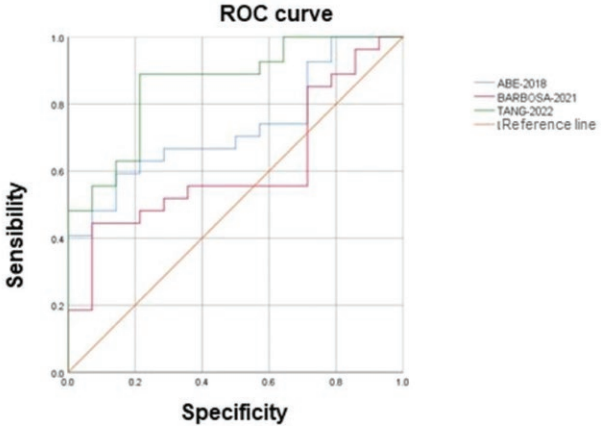
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Table 1. General characteristics of patients

Variable	Normal ASMM N (%)	Low ASMM N (%)	*p
Men	14 (58.3)	10 (41.6)	.22
AS	21 (60)	14 (40)	.19
Age	48.85+12.67	49.92+17.38	.82
HLA-B27	16 (66.7)	9 (90)	.13
Arthritis	8(66.6)	4(33.3)	.93
Enthesis	6 (75)	2 (25)	.60
Low grip strength	8(30.8)	4 (33.3)	.87
Gait speed 6 m <1 m/s	16 (61.5)	10 (83.3)	.16
Ultrasound†‡	3.81+.52	3.47+.46	.
Quadriceps	4.67+.45	3.97+.46	00
Tibialis anterior			.00
Predictive models US†*	7.36+1.02	6.58+.67	.015
ABE 2018	7.91+.95	7.56+.92	.268
BARBOSA 2021	8.72+.60	7.72+.63	.000
TANG 2021			

AS, Ankylosing spondylitis; PsA, Psoriatic arthritis;†= Mean, standard deviation; ‡ = Presented in cm; *= Presented in kg/m^2, IQR= Interquartile range



Graph 1. Area under de curve

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6242

POS0913 **LOW ADDITIVE VALUE OF A REPEAT MRI EXAMINATION OF THE SACROILIAC JOINTS WHEN THE FIRST MRI IS INCONCLUSIVE**

Keywords: Imaging, Inflammatory arthritides, Spondyloarthritis

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Background: Diagnosing sacroiliitis on MRI of the sacroiliac joints (SIJ) is not always straightforward. It is common practice in inconclusive cases to repeat the MRI after a variable period of time with an expectation that more conclusive acute/structural lesions will develop and allow for an irrefutable diagnosis of sacroiliitis.

Objectives: To evaluate the diagnostic utility of a repeat SIJ MRI following an initial inconclusive MRI examination.

Methods: Subjects with >1 SIJ MRI examinations, where the index scan was inconclusive for sacroiliitis and ≥ 6 months' interval has elapsed between scans, were included. Repeat scans were evaluated for the presence of structural/acute SIJ lesions and were accordingly diagnosed with either sacroiliitis or another applicable diagnosis. Clinical data was extracted from the patients' clinical files and by a telephone questionnaire. Diagnoses and scores were compared between index and follow-up examinations (t test).

Results: 71 subjects were included in the study; 77.4% females, mean age 41.0±15 years. Mean time interval between exams 30.4 ± 25.24 months. 12 subjects performed >2 scans. Clinical information was available in 63 subjects (86%) and is summarized in Table 1. In only two subjects (2.81%), both females, MRI diagnosis changed from inconclusive to definite sacroiliitis on the follow-up scan; a 41-year-old patient that had inflammatory back pain for two years prior to the index MRI, had peripheral arthritis but no family history of SpA and a 39-year-old patient with inflammatory back pain since the age of 23 years and an elevated CRP but no family history of SpA or other clinical rheumatic involvement. Final diagnosis after the 2nd MRI was osteitis condensans illi in 29 patients, DISH in 3 patients, degenerative changes in 6 patients (two accompanied by enthesitis) and enthesitis in 1 patient. In 10 patients (14.1%) diagnosis was still inconclusive after the 2nd MRI examination. No major abnormality was found in the follow-up MRI examination in 20 subjects. None of the subjects with >2 scans, had evidence of sacroiliitis in any of the following MRI examinations.

Conclusion: Repeating SIJ MRI examination when index MRI is inconclusive is of minimal additive value. When MRI findings are inconclusive, decision making should be based on clinical data.

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Table 1. Patients' characteristics*

Average back pain onset	32.4 years (sd=14.0 years)
Average pain duration	23.3 months (sd=17.6 months)
Bach pain awakens at night	61 patients (84%)
Back pain improves with activity	39 patients (62%)
Swollen large joint	20 patients (40%)
Dactilitis	20 patients (40%)
Psoriasis	9 patients (15%)
IBD	5 patients (8%)
First degree relative with psoriasis	12 patients (19%)
First degree relative with IBD	2 patients (3%)
Elevated CRP	37 patients (59%)
HLAB27 positive	7 patients (11%)
NSAIDS treatment	57 patients (90%)
Good response to NSAIDS	30 patients (48%)

*Data from 63/71 patients

Acknowledgements: NIL.

Disclosure of Interests: Iris Eshed Speakers bureau: Novartis, Abbvie - lecture fees, Tamar Goitein: None declared, Merav Lidar Speakers bureau: Abbvie, Novartis.

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POS0914

ULTRASONOGRAPHIC EVALUATION OF ENTHESEAL FIBROCARTILAGE IN PATIENTS WITH PSORIATIC ARTHRITIS, HEALTHY CONTROLS AND ATHLETES: A COMPARISON STUDY

Keywords: Enthesitis, Psoriatic arthritis

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Background: Enthesitis is the hallmark Psoriatic Arthritis (PsA), with the enthesseal fibrocartilage (EF) found to be the possible target tissue of inflammation [1]. With the development of feasible and more accurate imaging modalities, the *in vivo* study of this important tissue has become more precise.

Objectives: The aim of this study was: 1) to evaluate the EF at Achilles tendon insertion by using power Doppler ultrasound (PDUS) in PsA 2) to assess the intra and inter-reader reliability in the evaluation of EF thickness 3) to compare EF thickness of healthy controls (HC) and athletes; 4) to evaluate the association of EF abnormalities with other entheseal abnormalities and disease activity and functional indices in PsA.

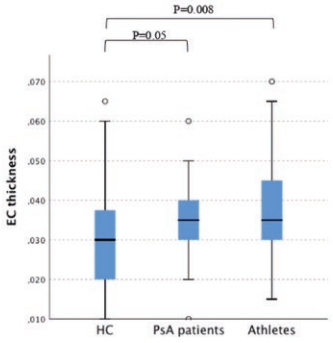
Methods: Consecutive PsA patients attending our unit with age < 50 years were asked to participate. HC and agonist athletes (basketball and soccer players with a minimum of 10 hours training per week) were enrolled as control group. Bilateral PDUS evaluation of Achilles tendons was performed in order to evaluate the EF in all patients and controls. EF was defined as the thickness of the anechoic layer just above the cortical bone and was measured at its thickest point in the longitudinal scan, as previously described [2]. All PsA patients underwent a complete clinical examination.

Results: 30 PsA patients, 20 HC and 40 athletes were enrolled. Female/male ratio was balanced among the three group. Median age (IQR) was higher in PsA patient (49; 41-54) than HC (26; 21-29) and athletes (24; 21-27). Four (13.3%). No patients had clinical heel enthesitis. Median (IQR) EF thickness between PsA, athletes and HC was 0.035 (0.03-0.04) cm, 0.035 (0.03-0.04) cm and 0.03 (0.02-0.04) cm respectively (p=0.05 between PsA and HC; Kruskall-Wallis analysis, see Figure 1). The intra-reader reliability was excellent [intraclass correlation coefficient-ICC (95% confidence interval-CI) of 0.91 (0.88-0.95)] and the inter-reader reliability good [ICC (95% CI) of 0.80 (0.71-0.86)]. At PDUS, no statistically significant differences were found in entheseal abnormalities. However, 3 PsA patients showed erosions at entheseal site in respect to HC and athletes which did not show erosive changes. We did not find correlations between EF thickness and BMI, age, disease duration, disease activity (assessed by DAPSA), LEI and impact of disease (assessed by PsAID) and duration of sport activities in athletes. A trend toward a correlation between EF thickness and body weigh was found (Table 1). Assessment of EF was feasible with a mean time of 2 minutes.

Figure 1. Comparison of the median EF thickness among the three groups (Kruskal-Wallis Test)

Independent-Samples Kruskal-Wallis Test Summary

Total number 180; p= 0.025



*HC: healthy controls; PsA: Psoriatic arthritis

Table 1. Spearman's rho correlations (by site) between EF thickness and clinical characteristics in Psoriatic arthritis (PsA) patients, healthy controls (HC) and athletes.

EF thickness (right)		
	rho	P value
All (PsA+ HC+ Althletes)		
Age	-0.144	0.177
Weight	0.193	0.072
BMI	0.117	0.277
PsA patients		
DAPSA	0.194	0.364
Disease duration (months)	-0.171	0.375
LEI	0.109	0.545
PsAID	0.232	0.234
EF thickness (left)		
	rho	P value
All (PsA+ HC+ Althletes)		
Age	-0.091	0.398
Weight	0.156	0.148
BMI	0.149	0.165
PsA patients		
DAPSA	0.036	0.868
Disease duration (months)	-0.094	0.635
LEI	0.129	0.455
PsAID	0.034	0.643

BMI: body mass index; DAPSA: disease activity index for psoriatic arthritis; LEI: Leeds enthesitis index; PsAID: psoriatic arthritis impact of disease

Conclusion: The assessment of EF is a feasible and reproducible test. Furthermore, our data suggest an increased thickness of EF in PsA patients in respect to HC with similar values in respect to agonist athletes and may open the way to further large studies on this peculiar aspect.

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Ennio Lubrano Speakers bureau: Lilly, Pfizer, AbbVie, Novartis, Janssen, Amgen, Consultant of: Lilly, Pfizer, AbbVie, Novartis, Janssen, Amgen.
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POS0915

ATP-BINDING CASSETTE G1 MEMBRANE TRANSPORTER-MEDIATED CHOLESTEROL EFFLUX CAPACITY INFLUENCES CORONARY ATHEROSCLEROSIS AND CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS

Keywords: Cardiovascular disease, Rheumatoid arthritis

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Background: Cholesterol efflux capacity CEC measures the ability of high-density lipoprotein (HDL) to remove cholesterol from arterial wall macrophages upon interaction with membrane transporter proteins and reduce the lipid content of atherosclerotic plaques. CEC inversely associated with cardiovascular risk in general patients independently of HDL levels. CEC through the ATP-binding-cassette G1 (ABCG1) membrane transporter is impaired in RA, yet, its relationship to atherosclerosis and cardiovascular risk is unknown.
Objectives: We here evaluated associations of ABCG1-mediated CEC with coronary atherosclerosis burden, plaque progression and incident cardiovascular event risk in RA.
Methods: Coronary atherosclerosis was evaluated with computed tomography angiography in 140 patients without cardiovascular disease and reassessed in 99 after 83.6±4.0 months. ABCG1-mediated CEC was measured in Chinese hamster ovary cells, not transfected or transfected with ABCG1 gene, as percentage of effluxed cholesterol over total intracellular cholesterol content. Logistic and negative binomial regression tested associations of ABCG1 with binary and count plaque outcomes respectively. Cox regression evaluated the association of ABCG1 with long-term cardiovascular event risk.
Results: Mean (standard deviation [SD]) of ABCG1 was 4.71 (0.92)%. At baseline, ABCG1 inversely associated with likelihood of extensive atherosclerosis (≥5 plaques) (odds ratio 0.50 [95% CI 0.28-0.88]) and numbers of partially-calcified (rate ratio [RR] 0.71 [95% CI 0.53-0.94]) and low-attenuation plaques (RR 0.63 [95% CI 0.43-0.91]) independently of ASCVD score and statin use. There were no main effects of ABCG1-CEC in adjusted plaque progression models. However, higher ABCG1-CEC predicted decreased noncalcified and calcified plaque progression exclusively in patients with higher time-weighted mean prednisone dose (Figure 1A,B). Furthermore, ABCG1-CEC inversely associated with progression of partially-calcified plaque at lower time-averaged CRP levels (Figure 1C). ABCG1-CEC did not have a main effect on cardiovascular event risk after adjusting for ASCVD score. However, higher ABCG1 associated with lower risk in patients with any versus no prednisone exposure during follow-up (Figure 1D,G), ≥1 versus no noncalcified plaques (Figure 1E,H), and low (<median) versus higher baseline CRP (Figure 1F,I) after adjustments including for ASCVD score (p-for-interaction=0.008, 0.021 and 0.033 respectively)
Conclusion: ABCG1-mediated CEC inversely associated with coronary plaque burden and number of high-risk plaques at baseline. It further predicted decreased plaque progression conditionally on cumulative inflammation and prednisone dose. Notably, ABCG1-mediated CEC inversely associated with cardiovascular risk specifically in prednisone users, patients with noncalcified plaques at baseline and those with lower inflammation.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: George Karpouzas Speakers bureau: Sanofi/Genzyme/Regeneron, BMS, Consultant of: Sanofi/Genzyme/Regeneron, Janssen, Scipher, Grant/research support from: Pfizer, Bianca Papotti: None declared, Sarah Ormseth: None declared, Marcella Palumbo: None declared, Elizabeth Hernandez: None declared, Maria Pia Adorni: None declared, Francesca Zimetti: None declared, Matthew Budoff: None declared, Nicoletta Ronda: None declared
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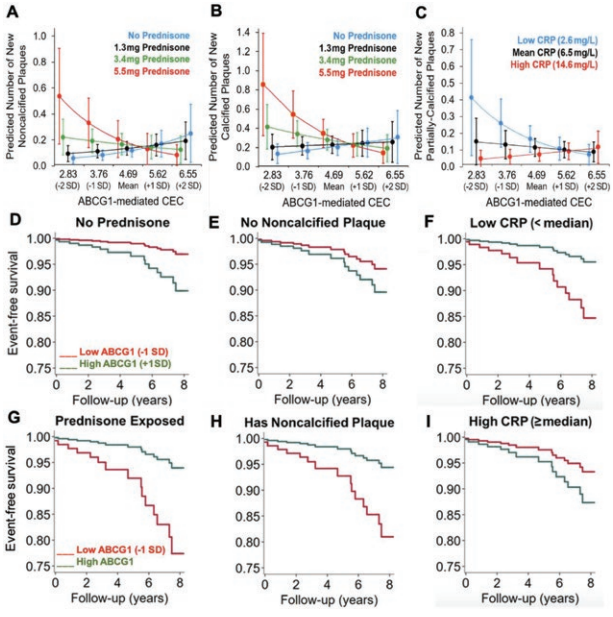


Figure 1. ABCG1-CEC significantly decreases formation of new **(A)** noncalcified and **(B)** fully calcified atherosclerotic lesions exclusively in patients with higher daily average prednisone dose and **(C)** partially calcified plaques in patients with low CRP. ABCG1-CEC further attenuates cardiovascular risk in patients with any vs. no prednisone exposure during follow-up **(D,G)**, ≥1 versus no noncalcified plaques **(E,H)**, and low (<median) vs. high CRP **(F,I)**

POS0916

THE CURRENT SITUATION OF MUSCULOSKELETAL ULTRASOUND EDUCATION - A SYSTEMATIC LITERATURE REVIEW

Keywords: Ultrasound, Education

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Background: The use of musculoskeletal ultrasound improves patient care by increasing diagnostic and therapeutic safety. With its growing application and increasing evidence of its value, the demand for standardized training in musculoskeletal ultrasonography (MSUS) rises rapidly.
Objectives: In this systematic literature review, we aim to provide a general overview of the various aspects of musculoskeletal ultrasound education worldwide, including target groups, teaching staff, didactic methods, and course formats, as well as to reflect on existing problems and future opportunities. No restrictions were made regarding the educational level of the course recipients nor the specialization of the course instructors.
Methods: In our methodological approach, we followed the PRISMA statement for reporting systematic reviews and meta-analyses of studies[1]. In January 2022, the databases Embase, PubMed, and Google Scholar were considered with all publications to date and were filtered for relevant publications using previously defined keywords. Title and abstract were then screened independently by two authors for inclusion using relevant study characteristics determined in advance according to the PICO scheme[1]. Finally relevant information was filtered from the full text version of the sixty-seven included publications.
Results: The range of training programs has increased greatly in recent years, primarily aiming at residents in rheumatology, radiology and physical medicine and rehabilitation. However, MSUS is also receiving more attention as a training tool for medical students. Due to the COVID pandemic, didactic approaches using distance learning via simulators and handheld devices have gained additional importance. Given the existing lack of sufficient equipment and trained teaching staff, those approaches should continue to be explored post-pandemic. Another still existing problem is the low international comparability of MSUS training and competency assessment. Therefore, several international institutions, including the European League Against Rheumatism (EULAR) and the Pan-American League of Associations for Rheumatology (PANLAR) have proposed guidelines for training curricula to promote standardized ultrasound training.
Conclusion: There is a broad consensus that the development of standardized curricula improves training and facilitates the implementation of new training centers. The development of alternative teaching methods incorporating e-learning, peer teaching, and distance learning on mobile ultrasound devices and the determination of international guidelines could facilitate overcoming the remaining major obstacles still to be passed.

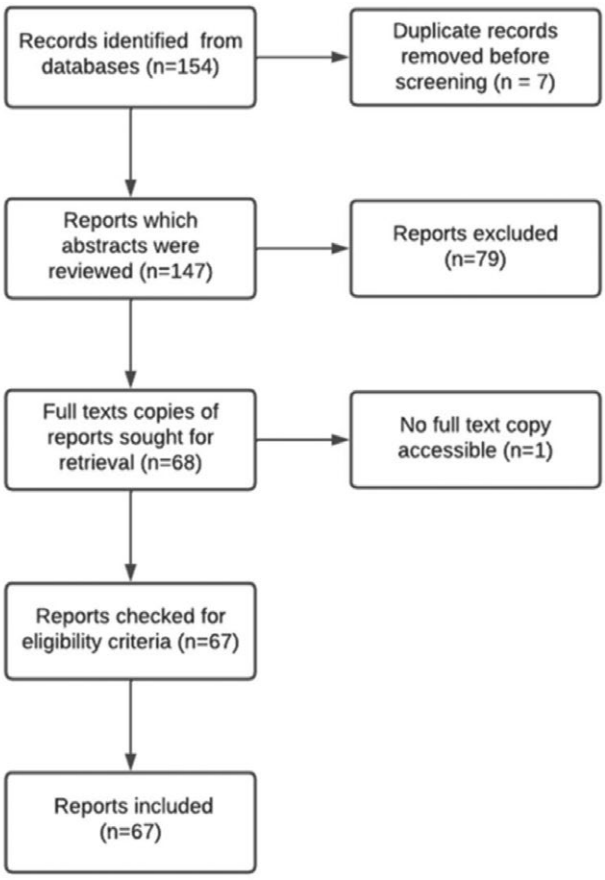


Figure 1: Literatur selection process

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Disclosure of Interests: None Declared.

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POS0917 **ULTRASOUND GUIDED SACROILIAC JOINT INJECTIONS IN MANAGEMENT OF ACTIVE SACROILIITIS: ONE YEAR DATA**

Keywords: Spondyloarthritis, Ultrasound, Imaging

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Background: Active sacroiliitis represent the radiological hallmark of Ankylosing Spondylitis (Ax-SPA) and manifest as low back pain accompanied by morning stiffness (MS). The pain at rest as well as MS represent the main symptoms that impair patients' quality of life. The treatment of Ax-SPA rely on non steroidal anti-inflammatory drugs (NSAIDs), monoclonal antibodies as Anti-TNF-α, anti interluekine-17/23 and, recently, on Janus Kinase Inhibitors; such compounds modify the disease natural history and reduce inflammation, thus restoring patient's well being and quality of life. However, despite a full treatment regimen, sometimes it is not possible to reach a low disease activity or remission.

Objectives: In rheumatological practice, corticosteroids (GCs) injections are successfully exploited in the every-day scenario to treat oligo-articular inflammatory disorders. In this context, we decided to evaluate the long-term efficacy of ultrasound-guided sacroiliac joint injections (US-SIJIs) of GCs in the treatment of active sacroiliitis and to understand whether local therapy has a role in the management of active sacroiliitis.

Methods: We enrolled patients affected by Ax-SPA with active sacroiliitis from our outpatient clinic. Some were treated with an US-SIJI when starting a biological disease modifying rheumatic drug (bDMARD) while others were treated with conventional therapy (bDMARD + NSAIDs) and used as controls. Variables such as age, gender, disease duration, type of bDmard, visuo-analogic pain scale (VAS) and MS were collected at baseline. VAS and MS were collected at each follow up visit that were scheduled at 24 and 48 hours, then after 7 days, 14 days, 1, 3, 6, 9 and 12 months. Each patient treated with SIJI received an explanation of the technique and informed written consent was obtained; subsequently, each patient was invited to lay pronated on a medical bed while a musculoskeletal sonographer individuated sacroiliac joints (SIJ) with a convex probe and demarcated the needle entry site with a dermographic pen. A sterile hood was put on the probe, the skin was accurately disinfected, then a 2,5 mL syringe was loaded with 40 mg of triamcinolone acetonide and a spinal needle of 22 gauge was used to reach SIJ. Each SIJI involved crossing the posterior sacroiliac ligament and each injection was carried out following real time the needle trajectory. All of the US-SIJI patients received a bilateral SIJI. The statistical analysis exploited descriptive statistics to define baseline anthropometric variables, ANOVA test and Test U of Mann were used to compare the means between groups. The $p<0,05$ was considered significant. The present study was conducted in accordance to the Declaration of Helsinki and was approved by the local ethical committee.

Results: We enrolled 33 subjects: 12 received an US SIJI and 21 were treated with a standard therapy according the most up-to-date recommendations. Both groups were comparable for age and VAS pain at baseline. In US-SIJI group after 24 h was documented a significant reduction of VAS pain that lasted up to 1 year displaying always a persistent significant lower value compared to baseline; in SIJIs group the higher VAS pain reduction from baseline was documented after 7 days (- 71%); in the control group VAS pain reduction reached significance after 3 months from baseline and the higher VAS pain reduction was documented at end of study (-32 %). In the US-SIJI group MS dropped significantly after two weeks from SIJI while in the controls after 3 months from baseline. At the end of study the patients treated with US-SIJI displayed a higher VAS pain (-50 % in SIJIs vs. -32 %, $p<0,05$) as well as MS reduction compared to controls (- 71 % in SIJIs vs – 42%, $p<0,05$). Any serious adverse event was recorded.

Conclusion: The US-SIJIs represent a safe and useful tool to control the symptoms of an active sacroiliitis and they should be performed concomitantly to the beginning of a bDMARD therapy to guarantee a rapid restoration of patients' quality of life.

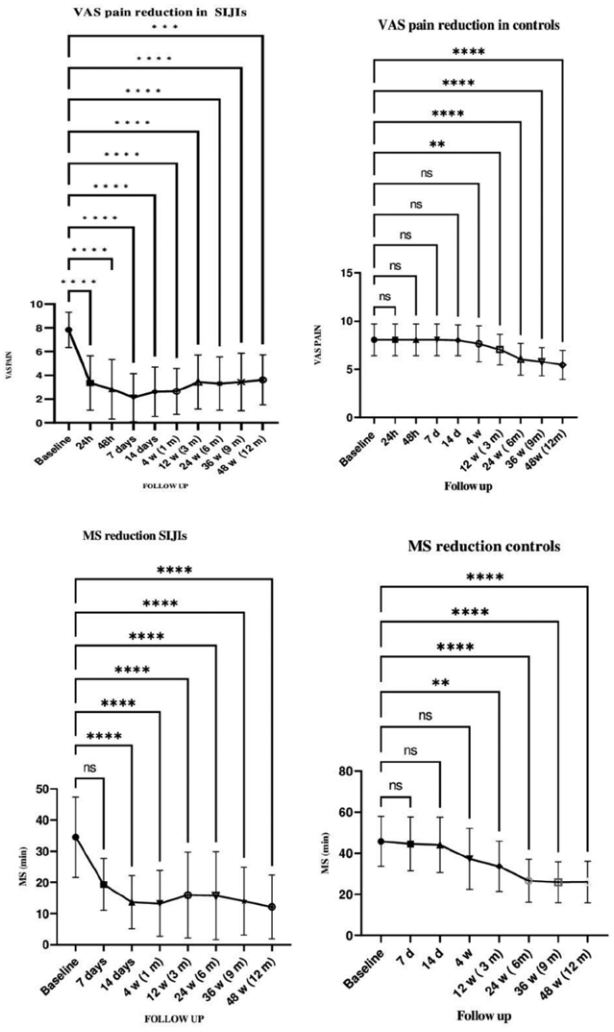


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1860

POS0918 **VALIDATION OF A MODIFIED NEW YORK CRITERIA RETIC E-TOOL FOR INCREASING SCORING PROFICIENCY OF RADIOGRAPHS OF THE SACROILIAC JOINTS IN AXIAL SPONDYLOARTHRITIS**

Keywords: Imaging, Spondyloarthritis, Validation

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Background: Radiographic assessment of the sacroiliac joints (SIJ) according to the modified New York (mNY) criteria is essential in the classification of ankylosing spondylitis, but low to moderate inter-reader agreement and limited improvement by calibration have been reported [1]. A web-based real-time iterative calibration (RETIC) module for scoring SIJ radiographs according to the mNY criteria has been developed by experienced readers to allow remote standardized calibration.
Objectives: To test the performance of this online RETIC calibration module in enhancing scoring proficiency with an expert reader as gold standard reference.
Methods: This RETIC module consisted of 50 cases with radiographs of the SIJ at one timepoint with an integrated scoring interface with real time feedback to the reader's grading compared to the expert readers' grading. The mNY grade (0-4) was assessed for each joint. Reliability for fulfilling versus not fulfilling the mNY criteria was assessed in real-time by kappa data being provided every 10 cases, until proficiency targets (kappa > 0.5) were achieved. In this study, 19 readers from the EuroSpA Imaging project were randomized to one of two reader calibration strategies (groups A and B) that comprised of 3 calibration steps, each followed by a reading exercise (Exercises 1-3; 25 patients per exercise). Calibration steps were as follows: Group A; 1. Review of original manuscripts describing the mNY method. 2. Review of PowerPoint summary of mNY method and video with grading examples PLUS completion of mNY_{RETIC} module. 3. Re-review of PowerPoint summary and video. Group B; same 3-step strategy as group A except that the mNY_{RETIC} module was completed at step 3, i.e. immediately before Exercise 3. The reliability of scoring was compared to an expert radiologist (RL) using kappa statistics for positivity of mNY criteria and intraclass correlation coefficients (ICCs) for the grades of the mNY criteria.
Results: The mean agreement for all readers on fulfillment of the mNY criteria with kappa was 0.69 in exercise 1, 0.72 in exercise 2 and 0.83 in exercise 3. Corresponding ICCs for mNY scoring 0-4 were 0.77, 0.77 and 0.82 in exercises 1, 2 and 3, respectively, see Table 1 and Figure 1. For Reader Group A, kappas for exercises 1-3 were 0.65, 0.76 and 0.83, respectively and ICCs 0.71, 0.82 and 0.81 (exercise 3). Interestingly, the main increase in agreement occurred between Exercises 1 and 2, i.e. after the RETIC module was performed. For Reader group B, corresponding kappas were 0.71, 0.77 and 0.83 and ICCs 0.80, 0.72 and 0.80, for exercises 1-3, respectively. Similarly, agreements predominantly improved directly after the RETIC module was performed.
Conclusion: Agreement on scoring radiographs of the SIJ according to the mNY criteria was noticeably improved when using a systematic online calibration module and in general readers achieved very good agreement with experts implying that systematic calibration of readers before scoring of images can enhance scoring proficiency.
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Table 1. Reader agreement versus expert radiologist, after different training steps.

	All Readers (n=19)	Reader Group A (RETIC before exercise 2) (n=8)	Reader Group B (RETIC before exercise 3) (n=11)
Agreement mNY+ vs mNY- (Kappa)			
Exercise 1	0.69	0.65	0.71
Exercise 2	0.72	0.76#	0.67
Exercise 3	0.83	0.83	0.77#
Agreement mNY score 0-4* (ICC)			
Exercise 1	0.77	0.71	0.80
Exercise 2	0.77	0.82#	0.72
Exercise 3	0.82	0.81	0.80#

#: Reading performed right after doing the RETIC module.*Grading per sacroiliac jointICC: Intra-class correlation coefficient (two-way, single measurement, absolute agreement), mNY+: Fulfilling radiographic part of Modified NY criteria; mNY-: Not fulfilling radiographic part of Modified NY criteria.

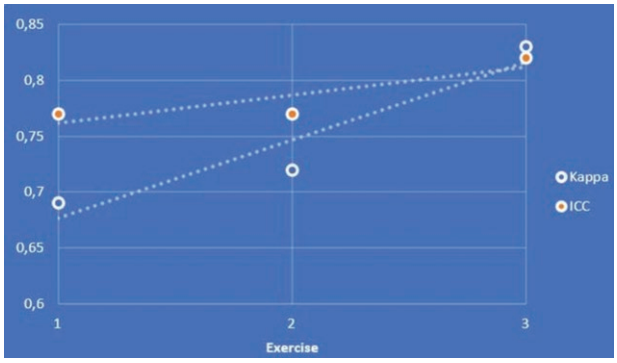


Figure 1. Reader agreement for all readers combined

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POS0919 [18F] POSITRON EMISSION COMPUTED TOMOGRAPHY ([18F] FDG PET/CT) IS ABLE TO PREDICT ULTRASOUND-DEFINED REMISSION IN RHEUMATOID ARTHRITIS

Keywords: Inflammatory arthritides

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Background: Assessing joint inflammation in rheumatoid arthritis (RA) is of high importance because associated with structural damage. In addition to clinical examination and ultrasound (US), joint inflammation can also be quantified by [18F] positron emission computed tomography ([18F] FDG PET/CT). Nowadays, PET/CT is widely used for cancer evaluation and systemic inflammation work-up and it can be used for opportunistic joint evaluation in RA patients. In addition, PET/CT allows a whole-body articular evaluation in one examination. We, and others, have previously demonstrated that PET/CT is significantly correlated with US parameters, but with a weak correlation coefficient.
Objectives: We investigated the ability of PET/CT to predict US-defined remission at the joint level and at the patient level.
Methods: 61 RA patients were included and underwent [18F] FDG PET/CT and US evaluations. For PET/CT, standardized uptake value (SUV) was determined on 22 joints (wrists, PIP and MCP of both hands). At the patient level, the maximum SUV (SUVmax), the number of PET positive joints (SUV>0) and the sum of all SUVs (cumulative SUV) were evaluated. US evaluation included gray-scale and Power Doppler imaging, according to OMERACT.
Results: At the joint level, PET/CT activity (SUV) was significantly different when the joint was under US remission or not (OR 0.411, p<0.0001 with remission defined as "no synovitis grade ≥ 2 with no PDI "). ROC-curves identified SUV thresholds to define joint remission with a high predictive positive value (95.2; confidence interval (CI): 93.8-96.4), but with low negative predictive value (28.9; CI: 21.7-36.8). When wrists, MCP and PIP were evaluated separately, AUC was higher for wrists. Predictive positive value was high for each sub-type (93.4, 94.2, 96.3% respectively). Negative predictive value was low for MCP and PIP (34.0 and 22.2%) but better for wrist (71.4%). At the patient level, SUVmax was significantly different when the patient was under US remission or not (p=0.0023 with remission defined as "no synovitis grade ≥ 2, no PDI, no tenosynovitis"). Cumulative SUV was also different (p=0.045) while there was no difference for the number of PET-positive joints. SUVmax threshold was determined with ROC-curves and demonstrated a high negative predictive value for determining US remission (92.9, CI: 66.1-99.2), while the positive predictive value was lower (67.4, CI: 52.0-80.5). For cumulative SUV threshold, negative and predictive value for determining US-defined remission were 73.1 and 73.5 respectively.
Conclusion: PET/CT is able to predict US-defined remission in RA patients. In addition to its well-known role in cancer evaluation and systemic inflammation work-up, PET/CT is also a promising tool in RA metrology. When considering US remission at the joint level, the predictive positive value is high, while the predictive negative value is better when predicting US remission at the patient level. Among PET/CT parameters, the maximum SUV (SUVmax) and the cumulative SUV exhibit the highest performances to predict US remission.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2190

POS0920 QUANTIFICATION OF TENOSYNOVITIS IN RA FROM WRIST MRIS, BASED ON DEEP LEARNING

Keywords: Artificial intelligence, Rheumatoid arthritis, Imaging

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Background: To assess tenosynovitis in wrist MRI scans from patients suspected of developing rheumatoid arthritis (RA), visual scoring (RAMRIS) is usually applied. As this time-consuming and requires rigorous training, we propose a method for the wrist that is based on Deep Learning (DL) combined with post-processing. This method detects all structures (a process called 'segmentation'), including all tendons, and measures inflammation around each tendon (group).
Objectives: To develop a method that automatically segments tendons together with all other anatomical structures of the wrist, and perform automatic tenosynovitis quantification as an alternative to the RAMRIS score.
Methods: Post-contrast axial MR scans of the wrist of 1216 patients with early-onset synovitis from the early arthritis clinic (EAC) cohort were used. From 28 EAC patients, ground truth manual segmentations were obtained as atlases. This dataset contains 33 labels: 14 flexor/extensor tendon groups; 10 carpal, 5 metacarpal bones; 1 label for all main vessels; 2 labels for skin and remaining tissue; and 1 air label. We normalized each input image using the Z-score. For segmentation of the wrist (see Figure 1a), our method utilizes a U-Net. For data augmentations we used intensity scaling (0.8-1.25) and added normally distributed noise (μ= 0, σ=0.06). We used softmax cross-entropy as a loss function, Adam optimization for 200 epochs, with a constant learning rate of 0.001. After 1-fold cross-validation evaluation, we trained on all 28 atlases. For validation we compared the automated tenosynovitis score against the manual RAMRIS score for tenosynovitis. From 10 RAMRIS tenosynovitis scores defined by two clinicians, we computed the mean score (Tμ). To define starting and end MRI slices for the scoring area we followed the RAMRIS definition. Starting from the slice where radius and ulna are closest to each other, ending with the hook of the hamate. The scoring areas were computed 3 mm around tendons, using a Euclidean distance transform, while excluding bones and vessels. Subsequently we computed histograms of the image intensities in the blood vessels and used the 25th percentile point as threshold to define inflamed areas within the scoring area (see Figure 1b). The final tenosynovitis quantification (Tq) was defined as the ratio between the number of 'inflamed pixels' and the total scoring area.

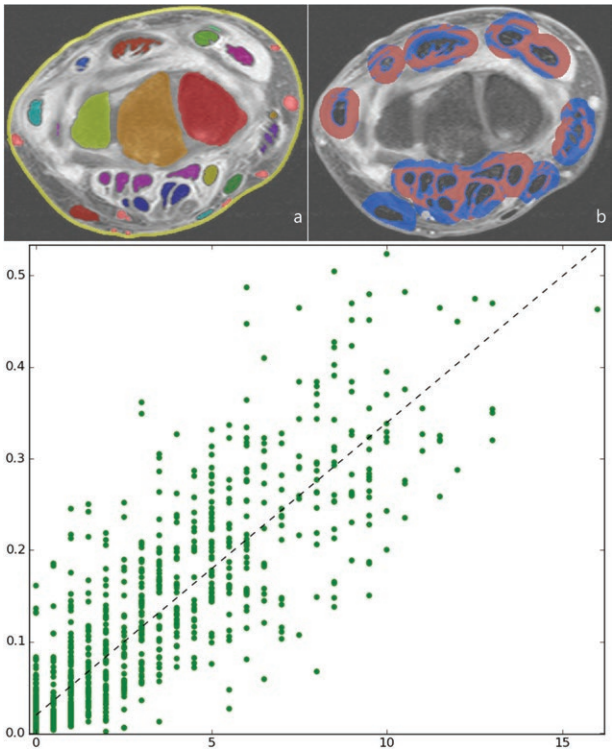


Figure 1. The upper left image shows the result of the segmentations using the U-net, 33 labels for each structure. The upper right image shows the scoring area at 3 mm (in blue), and detected inflamed areas (in pink). The tenosynovitis mean score was Tμ=11.5, the computed quantification value Tq=0.46. The tenosynovitis scores from RAMRIS were: expert 1 (VI:2, V:1, IV:1, III:1, II:2, I:1, 1:0, 2:2, 3:1, 4:1); expert 2 (VI:2, V:1, IV:0, III:1, II:2, I:1, 1:0, 2:2, 3:1, 4:1).

Bottom image: Scatter plot of total quantitative measurements of tenosynovitis versus total visual scores for 1216 patients. Pearson correlation r=0.87, p<0.001. The dashed line represents linear regression fit.

Results: In this work, we presented an alternative automatic quantification of tenosynovitis on MRI of the wrist. The results provide sufficient quantitative measurements compared to RAMRIS visual scores. The quantitative measurement was computed for 1216 patients, with Pearson correlation coefficient r = 0.87 and p < 0.001 (see the scatter plot in Figure 1).

Conclusion: Our DL-method provides a way to automate the quantification of tenosynovitis with MRI. It is very fast (~10 sec per patient) as compared to manual visual scoring. We illustrate the cumulative measurement of all synovial areas, while computing per tendon is also feasible. The accomplished results provide a solid basis for automatic tenosynovitis quantification.

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Disclosure of Interests: Denis Shamonin Grant/research support from: Bristol-Myers Squibb and Pfizer contributed to this project, through a grant from the Dutch Research Council (NWO), Applied and Engineering Sciences., Yanli Li: None declared, Tahereh Hassanzadeh Grant/research support from: Bristol-Myers Squibb and Pfizer contributed to this project, through a grant from the Dutch Research Council (NWO), Applied and Engineering Sciences., M. Els Bakker: None declared, Monique Reijnierse Grant/research support from: Bristol-Myers Squibb and Pfizer contributed to this project, through a grant from the Dutch Research Council (NWO), Applied and Engineering Sciences., Annette van der Helm – van Mil Grant/research support from: Bristol-Myers Squibb and Pfizer contributed to this project, through a grant from the Dutch Research Council (NWO), Applied and Engineering Sciences., Berend Stoel Grant/research support from: Bristol-Myers Squibb and Pfizer contributed to this project, through a grant from the Dutch Research Council (NWO), Applied and Engineering Sciences.

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POS0921

INFLUENCE OF HLA-B27 STATUS ON MR IMAGING FINDINGS IN PATIENTS WITH LOW BACK PAIN

Keywords: Imaging, Gender/diversity issues, Spondyloarthritis

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Background: The knowledge of factors influencing the susceptibility to and extent of changes at the sacroiliac joints (SIJs) are of great importance in the understanding of pathophysiological processes in axial spondyloarthritis (axSpA)[1]. Recent studies showed that previous delivery and the HLA-B27 status have a special role in the expression of bone marrow edema at the SIJs in the general population. Furthermore, the influence of HLA-B27 differed in men and women[1 2].

Objectives: The aim of this study was to investigate the sex-specific influence of the HLA-B27 status on the SIJ lesions such as ankylosis, erosion, fat metaplasia and bone marrow edema and its distribution and extent in patients with low back pain of non-inflammatory origin.

Methods: In this post-hoc analysis, 139 patients (90 women and 49 men) with low back pain of mechanical/ non-inflammatory origin (after exclusion of axSpA) were included. The MR images of the sacroiliac joints were scored by two trained readers separately for the presence of axSpA features: ankylosis, erosions, sclerosis, fat metaplasia and bone marrow edema. The scoring was performed for the three SIJ regions (ventral/middle/dorsal) differentiated for the sacral and iliac sides. Frequencies of lesions per joint region were compared between HLA-B27 positive and negative individuals using Chi-squared tests. Extent of lesions, expressed as sum scores were compared using T-tests. All analyses were carried out for the entire group and for men and women separately.

Results: A total of 90 women and 49 men were included in this post-hoc-analysis. HLA-B27 was positive in 33/90 women (36.7%), while this was the case in 23/49 men (46.9%) (further clinical data is given in Table 1). There was no difference in frequency of overall occurrence of erosion (22.9% vs. 16.1%; p = 0.392), sclerosis (48.2% vs. 48.2%; p > 0.999), fat metaplasia (12.0% vs. 7.1%; p = 0.403), bone marrow edema (28.9% vs. 32.1%; p = 0.710) and ankylosis (2.4% vs. 3.6%; p > 0.999) between HLA-B27 negative and positive individuals, respectively. A detailed graphical representation of spatial distribution of lesion within the joint is given in Figure 1.

Conclusion: In our cohort of pre-selected patients with chronic low back pain and after exclusion of axSpA, the HLA-B27 status did not determine extent or pattern of imaging lesions in either men or women. These results somewhat contradict previously published data on healthy volunteers. This indicates that further studies are needed especially in the investigation of the sex-specific influence of HLA-B27 status on imaging lesions.

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Table 1. Patient characteristics by HLA-B27 status. Group differences were investigated by chi-squared tests or T-test

	HLA-B27 positive	HLA-B27 negative	p
Women [n,%]	33 (58.9)	57 (68.7)	0.279
Age [mean, SD]	40.2 (11.2)	38.8 (10.0)	0.435
BMI [mean, SD]	22.9 (2.7)	24.8 (4.3)	0.061
CRP [mean, SD]	2.6 (5.4)	2.6 (4.3)	0.968
BASDAI [mean, SD]	4.0 (1.9)	4.3 (1.8)	0.455
Months symptom duration [mean, SD]	109.9 (111.7)	85.5 (89.9)	0.206

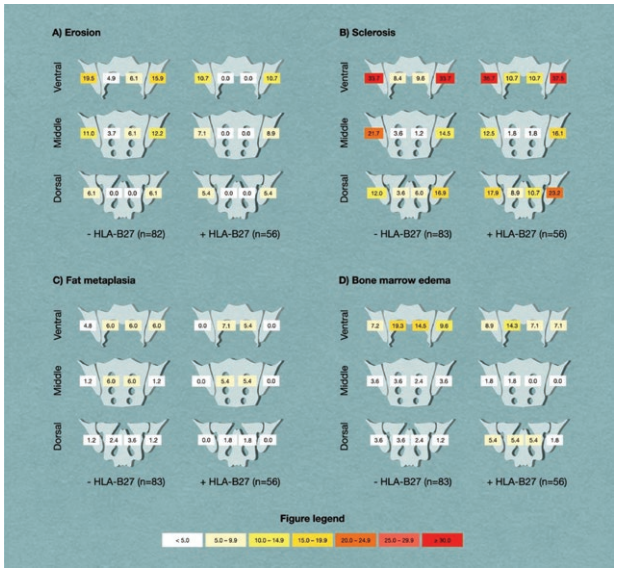


Figure 1. Distribution of lesions by HLA-B27 status. Frequencies are given as percentages; chi-squared tests revealed no statistically significant differences in frequencies.

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Disclosure of Interests: Sevtap Tugce Ulas Grant/research support from: STU reports funding from the Berlin Institute of Health (BIH) during the conduct of this study (Junior Digital Clinician Scientist Programme)., Fabian Proft Speakers bureau: FP reports grants and personal fees from Novartis, Lilly and UCB, as well as personal fees from AbbVie, AMGEN, BMS, Hexal, Janssen, MSD, Pfizer and Roche., Grant/research support from: FP reports grants and personal fees from Novartis, Lilly and UCB, as well as personal fees from AbbVie, AMGEN, BMS, Hexal, Janssen, MSD, Pfizer and Roche., Torsten Diekhoff Speakers bureau: TD reports personal fees from MSD, Novartis and Eli Lilly., Grant/research support from: TD reports funding from the Berlin Institute of Health (BIH) during the conduct of this study., Valeria Rios Rodriguez Speakers bureau: VRR reports personal fees from AbbVie and Falk e.V., Judith Rademacher Grant/research support from: JR reports funding from the Berlin Institute of Health (BIH) during the conduct of this study (Clinician Scientist Programme)., Mikhail Protopopov Speakers bureau: MP reports personal fees from UCB and Novartis., Denis Poddubnyy Speakers bureau: DP reports personal fees from AbbVie, Eli Lilly, MSD, Novartis, Pfizer, Bristol-Myers Squibb, Roche, UCB, Biocad, GlaxoSmithKline and Gilead outside the submitted work., Grant/research support from: DP reports grants from AbbVie, Eli Lilly, MSD, Novartis, Pfizer and personal fees from Bristol-Myers Squibb, Roche, UCB, Biocad, GlaxoSmithKline and Gilead outside the submitted work., Katharina Ziegeler Grant/research support from: KZ reports funding (research grant) from the Assessment of Spondyloarthritis international Society (ASAS) during the conduct of this study.

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POS0922

DIFFERENTIAL DIAGNOSIS OF FOCAL IMMUNOGLOBULIN G4-RELATED SIALADENITIS AND BENIGN SALIVARY MASSES: THE VALUE OF CONTRAST-ENHANCED ULTRASOUND

Keywords: Diagnostic tests, Ultrasound

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Background: Immunoglobulin G4 related disease (IgG4-RD) is a newly recognized immune-mediated fibroinflammatory disease characterized by involvement of multiple organs, among which salivary gland is one of the most commonly involved sites. Immunoglobulin G4-related Sialadenitis (IgG4-RS) presents itself as focal or diffuse lesions, of which focal lesions are difficult to differentiate from salivary gland masses [1], especially benign masses with a high clinical incidence. Differential diagnosis of both sets of disorders has significant clinical implications due to different treatment modalities.

Objectives: The aim of this study was to clarify the effectiveness of contrast-enhanced ultrasound (CEUS) in differential diagnosis of focal IgG4-RS and benign salivary masses.

Methods: We retrospectively included 13 patients with diagnosis of focal IgG4-RS according to the Comprehensive Diagnostic Criteria for IgG4-RD (20 foci) and 32 patients with pathologically confirmed benign salivary masses (32 foci). Ultrasonography [grey scale (GS), color Doppler flow imaging (CDFI) and CEUS] of the bilateral parotid and submandibular glands were performed by two experienced radiologists in all patients. We compared the characteristics of ultrasonography and determined the diagnostic value for differentiating between focal IgG4-RS and benign salivary masses.

Results: Of the 13 focal IgG4-RS patients, 7 were female and mean age was 57.46 (± 9.90) years, which was older than that of patients with benign salivary masses (41.03 ± 13.52 years) ($p < 0.001$). Focal IgG4-RS patients were more frequently presented with gland enlargement and elevated serum levels of IgG4 and IgE ($p < 0.001$). These two groups of patients showed localized hypoechoic masses on gray-scale ultrasound, with homogeneous or heterogeneous internal echo, while focal IgG4-RS may have unclear boundaries. CDFI revealed more abundant blood flow signals of patients with IgG4-RS, mostly grade II-III. Compared with benign salivary masses, patients with focal IgG4-RS more often showed iso-enhancement, blurred enhancement margins, whereas unenhanced area was less frequently present. The detail ultrasonography characteristics of patients were compared in Table 1. The AUC of CEUS and conventional ultrasound for differentiating focal IgG4-RS and benign salivary masses were 0.973 and 0.891, respectively, of which CEUS is superior to conventional ultrasound ($p < 0.05$).

Conclusion: CEUS was remarkably effective in differentiating focal IgG4-RS and benign salivary masses, its discriminatory value was superior to conventional ultrasound. The diagnostic accuracy can be more improved by effectively combing clinical data and laboratory findings.

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Table 1. Ultrasonography characteristics of focal IgG4-RS and benign salivary masses.

Characteristics	IgG4-RS (n=20)	Benign Masses (n=32)	*P*	Characteristics	IgG4-RS (n=20)	Benign Masses (n=32)	*P*
Grey scale							
Internal echo			0.065	Shape			0.930
Homogeneous	10 (29.4)	24 (70.6)		Regular	11 (37.9)	18 (62.1)	
Heterogeneous	10 (55.6)	8 (44.4)		Irregular	9 (39.1)	14 (60.9)	
Boundary	13 (28.9)	32 (71.1)	0.001	Cystic change	0 (0.0)	5 (100.0)	0.143
Clear				Yes			
Not clear	7 (100.0)	0 (0.0)		No	20 (42.6)	27 (57.4)	
Color Doppler	0 (0.0)	4 (100.0)		II grade	4 (66.7)	2 (33.3)	<0.001
0 grade	2 (8.0)	23 (92.0)		III grade	14 (82.4)	3 (17.6)	
I grade							
CEUS							
Enhancement degree	14 (51.9)	13 (48.1)	0.039	Enhancement margin	1 (3.1)	31 (96.9)	<0.001
Hyper/isoenhancement				Clear			
Hypoenhancement	6 (24.0)	19 (76.0)		Blurred	19 (95.0)	1 (5.0)	
Eenhancement pattern			0.143	Peripheral enhancement			0.071
Centripetal	0 (0.0)	5 (100.0)		Yes	0 (0.0)	6 (100.0)	
Non-centripetal	20 (42.6)	27 (57.4)	0.216	No	20 (43.5)	26 (56.5)	0.005
Enhancement homogeneity	11 (47.8)	12 (52.2)		Unenhanced area	0 (0.0)	12	
Homogeneous	9 (31.0)	20 (69.0)		Yes	20 (50.0)	(100.0)	
Inhomogeneous				No		20 (50.0)	

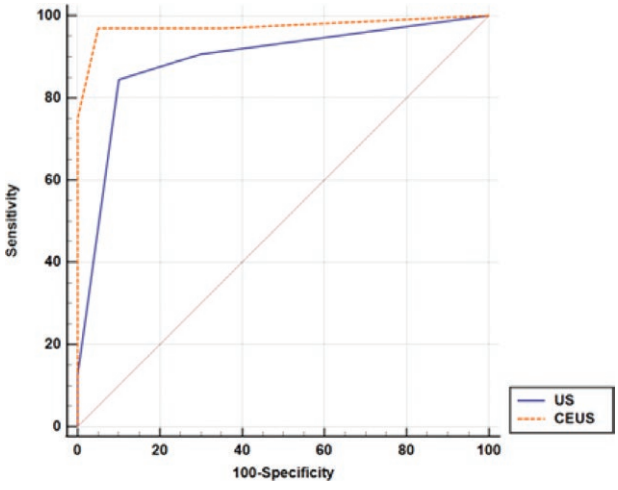


Figure 1. The ROC curve of ultrasound and CEUS for differentiating focal IgG4-RS and benign salivary masses.

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Disclosure of Interests: None Declared.
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POS0923

THE TRANSITION FROM ACTIVE LESIONS TO STRUCTURAL CHANGES ON SACROILIAC MRI AND ITS ASSOCIATED FACTORS

Keywords: Spondyloarthritis, Real-world evidence, Registries

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Background: Both active and chronic lesions can be seen on sacroiliac MRI.
Objectives: Aim was to compare the demohraphic and disease characteristics of patients with active and structural lesions on sacroiliac MRI in a bDMARD cohort of Spondyloarthritis (SpA) patients.
Methods: TReasure is a national, multicentre, longitudinal, and observational database, initiated in Turkey in 2017 and now includes 17 centres [1]. 1230/7015 (17.5%) patients with SpA [including Psoriatic arthritis (PsA)] had findings consistent with sacroiliitis on MRI that was recorded by the radiologist at each center for the presence of active and structural lesions. Demographic characteristics of the patients, SpA associated characteristics; dactylitis, enthesitis, uveitis, IBD, SpA family history, hip involvement, hip replacement, sacroiliitis by mNY, syndesmophyte. disease activity during bDMARD initiation; ASDAS-CRP, ASDAS-ESR, BASDAI, ESR, CRP, VAS (physician global, patient global), function and quality of life; BASFI (>40 mm), HAQ-DI (<0.5, 0.5-1.0, >1.0), EQ5D, were assessed and compared between groups with active/ active and structural/structural lesions.
Results: Of 1230 patients with sacroiliac MRI, 548 (44.5%) had only active lesions, 418 (33.9%) had both active and structural lesions, and 264 (21.5%) had only structural lesions. The diagnoses of the patients were r-SpA 833 (67.7%), peripheral SpA 329 (26.7%), nr-SpA 321 (26.1%), enteropathic SpA 79 (6.4%), PsA 64 (5.2%). From `only active lesion` to `only structural lesion` on MRI, age was older, disease duration was longer, meeting mNY criteria and hip involvement was more common, HLA-B27 positivity was more common, syndesmophyte was more common, uveitis was more common, and metrological indices (BASMI and Schober`s test) was worse (Table 1). Multivariate analysis showed factors associated with the development of structural lesions from active lesions, disease duration with OR 1.09 (CI 95% 1.04-1.14), mNY positive sacroiliitis with OR 3.36 (95% CI 1.52-7.40) and uveitis with 3.80 (95% 1.23-11.8).
Conclusion: Transition from active lesions to structural lesions in sacroiliac MRI may be time-related, and chronicity develops in approximately 5 years. As expected, when structural lesions develop on MRI, the rate of meeting the mNY criteria increases around 3 times. There is a relationship between uveitis and the development of structural damage. The relationship of metrological indices with structural damage should also be considered. However, the lack of central reading in MR is a limitation in this assessment.
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Table 1. Characteristics of patients with active/active and structural/ structural lesions on MRI

	MRI with active lesion n=548	MRI with active and chronic lesion n=418	MRI with chronic lesion n=264	P
Current Age (y)	40 (33-48)	41 (35-50)	45 (38-52)	**<0.001**
Gender (male) n, (%)	279 (50.9)	200 (47.8)	146 (55.3)	0.16
Disease duration (symptom-bD-MARD initiation)	5.1 (2.4-9.0)	5.9 (2.7-10.3)	7.5 (3.1-14.7)	**<0.001**
Disease duration (diagnosis-bDMARD initiation)	1.6 (0.5-4.4)	2.2 (0.6-5.9)	2.9 (0.7-7.4)	**<0.001**
AS n=833	301 (36.1)	323 (38.8)	209 (25.1)	NA
Peripheral SpA n=329	176 (53.5)	91 (27.7)	62 (18.8)	
nr-AxSpA n=321	204 (63.6)	76 (23.7)	41 (12.8)	
Enteropathic arthritis n=79	41 (51.9)	24 (30.4)	14 (17.7)	
PsA n=64	31 (48.4)	25 (39.1)	8 (12.5)	
BMI	25.9 (23.4-29.4)	27.6 (23.4-30.6)	26.7 (23.9-30.9)	0.011
mNY criteria	301 (56.9)	323 (80.0)	209 (81.3)	**<0.001**
BASMI	1.8 (1.0-2.6)	3.0 (1.8-3.8)	3.4 (1.9-4.6)	**<0.001**
Schober`s test ≤ 2 cm n (%)	11 (4.2)	23 (12.6)	19 (19.2)	**<0.001**
HAQ-DI score	0.50 (0.20-0.90)	0.63 (0.35-0.98)	0.63 (0.30-1.0)	**0.025**
HAQ-DI <0.5, n (%)	126 (45.3)	66 (28.4)	40 (31.0)	**0.001**
HAQ 0.5-1.0, n (%)	84 (30.2)	105 (45.3)	53 (41.1)	
HAQ > 1.0, n (%)	68 (24.5)	61 (26.3)	36 (27.9)	
Syndesmophyte, n (%)	57 (12.1)	62 (17.4)	56 (24.3)	**<0.001**
Enthesitis, n (%)	155 (34.9)	70 (21.2)	64 (31.2)	**<0.001**
Uveitis, n (%)	45 (8.3)	34 (8.3)	42 (16.2)	**0.001**
Hip involvement, n (%)	45 (9.3)	69 (18.3)	49 (20.4)	**<0.001**

Continious variables were presented as median (%25-75)

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Disclosure of Interests: None Declared.
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POS0924

USEFULNESS OF LOW-DOSE CT IN PSORIASIS AND PSORIATIC ARTHRITIS PATIENTS WITH NON-SPECIFIC AXIAL SYMPTOMS

Keywords: Imaging, Psoriatic arthritis

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Background: Low-dose CT (ldCT) has been shown advantegous over conventional radiography (CR) in showing spinal structural changes in Axial Spondyloarthritis (AxSpA) [1,2]. There is no data on the value of ldCT in psoriatic arthritis (PsA) patients.
Objectives: The aim of this study is to determine the contribution of spinal ldCT to the diagnosis and disease severity in patients with psoriasis (PsO) and PsA with non-spesific axial symptoms.
Methods: 143 PsO patients referred from the Dermatology Outpatient Clinic in the last 9 months were evaluated; patients with any axial symptoms (116) were included. 47 of 116 patients (40.5%) had ldCT. Patients were evaluated with pelvis CR, lumbar/cervical CR and whole spinal ldCT. Age, gender, PsO and PsA disease duration were recorded. Patients were divided into four groups according to CR findings; 1. Modified New York criteria (mNY) not met, 2. Only sacroiliitis (SI) according to mNY, 3. SI and syndesmophyte (SIN) present, 4. Only SIN (according to the consensus of two rheumatologists UK and LK). All spinal CTs (coronal and sagittal planes) were evaluated by two rheumatologists. Syndesmophytes were determined between C2-S1 and it was also noted if bridging was present (according to the consensus of two rheumatologists UK and GA). The contribution of spinal ldCT to axial involvement was evaluated.
Results: 47 patients (n=15 (32%) with inflammatory, n=32 (68%) non-specific axial symptoms) were evaluated in this study. The mean age of the patients (68.1% female, 31.9% male) was 47.4 years. Median duration of PsO was 15 years. Median disease duration of 10 patients with a previous diagnosis of PsA was 4.5 years. 12 (25.5%) patients had only PsO and 35 (74.5%) patients had PsA. 25/35 (71%) of those with PsA had axial involvement (SI and/or SIN) according to CR, CR was normal in 10/35 (29%) patients (Figure 1). When the whole spinal ldCT was evaluated, SIN was detected in 8/12 (66.7%) of patients with only PsO (8 thoracic, 4 lumbar, 2 cervical). On the other hand, 30/35 (85.7%) of PsA patients had SIN (Figure 1). The distribution of SIN in ldCT is shown in Table

1. Bridging SIN and Andersson lesion were detected in 1/12 (8.3%) and 2/12 (16.7%) of PsO patients versus 17/35 (48.6%) and 8/35 (22.9%) of PsA patients, respectively. In 15/22 (68%) of those with normal CR, 7/9 (77.7%) of those with only SI in CR, 5/5 (100%) of those with SI and SIN in CR, 11/11 (100%) of those with only SIN in CR were found to have syndesmophyte on ldCT. Accordingly, 38/47 (80.8%) patients had at least one syndesmophyte on ldCT (Table 1).

Conclusion: When PsO and PsA patients with non-specific axial symptoms were evaluated with spinal ldCT, new syndesmophytes were found in a significant proportion of patients (2/3 of patients with only PsO), additionally an increased distribution of syndesmophytes was observed. The thoracic vertebra is one of the most frequently involved area in psoriatic disease similar with SpA. Comparative studies with a healthy control group are needed to determine the potential role of ldCT.

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Table 1. Distribution of SIN detected by ldCT

	All patients n=47	Only SI* n=9	SI and SIN n=5	Only SIN** n=11	SI and SIN negative n=22
C2-L5 at least on one vertebrae	38 (80.9)	7 (77.8)	5 (100)	11 (100)	15 (68.2)
C2-L5 at least on two region***	28 (59.6)	5 (55.6)	5 (100)	10 (90.9)	8 (36.4)
C2-L5 at least on three region***	10 (21.3)	1 (11.1)	1 (20)	7 (63.6)	1 (4.5)
C2-C7 at least on one vertebrae	19 (40.4)	3 (33.3)	2 (40.0)	10 (90.9)	4 (18.2)
C2-C7 at least on two vertebrae	7 (14.9)	0	1 (20)	6 (54.5)	0
T1-T12 at least on one vertebrae	37(78.7)	7 (77.8)	5 (100)	10 (90.9)	15 (68.2)
T1-T12 at least on two vertebrae	34 (72.3)	7 (77.8)	5 (100)	10 (90.9)	12 (54.5)
T1-T12 at least on three vertebrae	24 (51.1)	4 (44.4)	5 (100)	8 (72.7)	7 (31.8)
L1-L5 at least on one vertebrae	20 (42.6)	3 (33.3)	4 (80)	7 (63.6)	6 (27.3)
L1-L5 at least on two vertebrae	14 (29.8)	3(33.3)	4 (80)	5 (45.5)	2 (9.1)

*SI: Sacroiliitis**Syndesmophyte***Region: either cervical or thoracic or lumbar

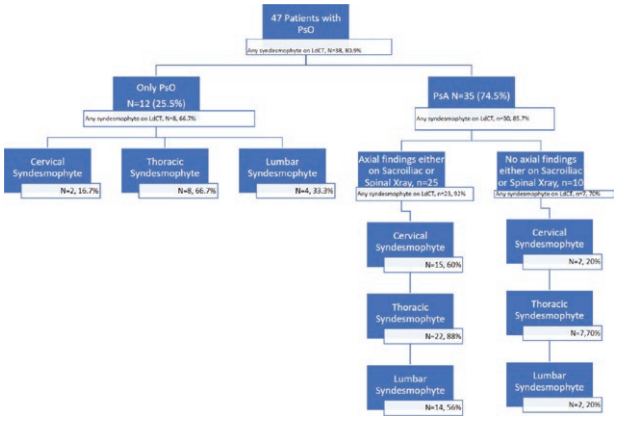


Figure 1. Distribution of ldCT findings with CR results

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0925 AUTOMATIC SCORING OF ULTRASOUND SYNOVIAL HYPERTROPHY IN RHEUMATOID ARTHRITIS THROUGH INTEGRATING MULTIPLE CONVOLUTIONAL NEURAL NETWORK MODELS

Keywords: Rheumatoid arthritis, Artificial intelligence, Ultrasound

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Background: The OMERACT-EULAR Synovitis Scoring (OESS) system is worldwide used to evaluate arthritis severity on ultrasound (US) images. Because of inter-observer and intra-observer variability, deep learning (DL) has been applied in high-quality image interpretation and analysis. Previous studies mostly focused on Doppler US (DUS) classification by convolutional neural network (CNN), which could provide objective assessment. However, the reports of DL intervention in grey scale (GS) US image automatic measurements are limited.

Objectives: The aim of this study was to develop an integrated multiple CNN model in precise scoring GS US images from rheumatoid arthritis (RA) patients.

Methods: The standard US images from patients of RA were retrospectively selected by three 10-years US experienced rheumatologist together and were graded according to the OESS system. Six different joints data were taken, including proximal interphalangeal, metacarpophalangeal, wrist, elbow, knee and ankle joints. We conducted the DL model integrating three binary CNNs to predict four-class GS US scoring (Figure 1). The accuracy of the trained model was tested by an independent test data.

Results: Total 678 images from 447 patients of RA were used in this study. These images were divided into training (n=611) and testing (n=67) sets. The integrated multiple CNNs model could achieve a four-class accuracy of 77.6%. The individual accuracy of grades 0, 1, 2 and 3 were 68.4%, 77.3%, 73.3% and 100%, respectively (Table 1). Furthermore, we found that adding on anatomic site parameters or labeling areas of interest would establish a better average area under curve (AUC) with 92.6% and 89.0%.

Conclusion: Our study suggests the possibility of using the integrated multiple CNNs model in grading synovial hypertrophy of RA, which is critical in RA healthcare. External validation would be required to confirm the predictive ability of this model.

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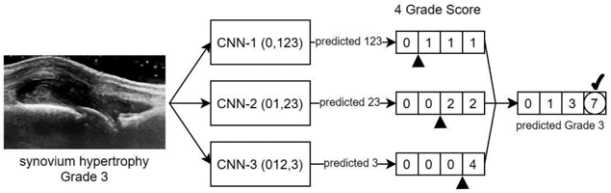


Figure 1. The proposed integrated multiple CNNs model to predict grade 3 synovium hypertrophy in rheumatoid arthritis. CNN: convolutional neural network.

Table 1. Prediction results of the integrated model for grey scale ultrasound scores

	Integrated model					Accuracy
Rheumatologist	0	1	2	3	Total	(%)
0	13	4	2	0	19	68.4
1	4	17	1	0	22	77.3
2	1	2	11	1	15	73.3
3	0	0	0	11	11	100
Total	18	23	14	12	67	77.6

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0926 OPTICAL SPECTRAL TRANSMISSION IN THE DIAGNOSIS OF HAND OSTEOARTHRITIS: CLINICAL ASSOCIATIONS AND EVALUATION OF A NEW DIAGNOSTIC ALGORITHM INCLUDING ALL FINGER JOINTS

Keywords: Osteoarthritis, Imaging

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Background: Optical spectral transmission (OST) is a modern diagnostic technology able to quantify joint inflammation in a non-invasive, rapid and examiner-independent manner [1-3]. The vast majority of studies on OST have been performed in patients with rheumatoid arthritis (RA) [1-3]. No sufficient data on the diagnostic value of OST regarding other arthropathies have been published. However, our study group and others could show that concomitant to RA joint pathologies, such as primary or secondary (post-arthritic) osteoarthritis (OA) could have an influencing effect on OST results [1,4].

Objectives: Aim of this study was therefore to investigate the performance of OST in the diagnosis of OA and to evaluate its ability to identify activated OA changes.

Methods: Patients from two large Rheumatology departments with diagnosed finger and/or wrist OA and without any inflammatory joint disease, as well as healthy controls, were recruited in the context of this study. All study subjects were evaluated via clinical (counts of tender and swollen joints) and OST examinations. Moreover, OA-patients underwent laboratory (C-reactive protein, erythrocyte sedimentation rate) and X-ray examinations of both hands and the extent of osteoarthritic changes was evaluated by an established radiographic score [Kellgren-Lawrence (KL) score]. To evaluate OA activity, joint ultrasound (US) examinations [Grey-scale (GSUS), power Doppler (PDUS) scores] were performed in a subset of patients. Moreover, a new diagnostic algorithm including the distal interphalangeal joints (DIP) was examined next to the established algorithm concerning only wrists, MCP and PIP joints.
Results: *2,134* joints of OA patients [n=97; 80.4%♀; 68 years (58-76, IQR)] and *2,200* joints of healthy controls [n=100; 80%♀; 49 years (33.5-56, IQR)] were examined via OST. OA patients showed statistically significantly higher OST scores compared to control subjects [13.73 (11.19-16.51, IQR) vs. 10.19 (8.05-14.31, IQR); p<0.001] during the evaluation of the algorithm including wrist, MCP and PIP joints. This difference remained significant also after adjusting for age and sex (p=0.033). The novel diagnostic algorithm including additionally DIP joints (next to MCP, PIP and wrists) showed also a statistically significant difference between patients and controls (p<0.001, after adjustment p=0.021). Interestingly, receiver operating characteristics revealed an improved diagnostic performance when including DIP joints in the algorithm [Area under the curve (AUC) 0.718; 95%CI (0.645-0.792) (with DIP) vs AUC 0.698; 95%CI (0.625-0.771) (without DIP)]. OST did not correlate with GSUS/PDUS or KL-Score (all; p>0.05). However, it did correlate moderately-significantly with patient hand-size (without DIPs: rho=0.337; p<0.001; with DIPs: rho=0.363; p< 0.001).
Conclusion: Hereby we could show that presence of OA can indeed influence OST values and that OA changes should be taken into account when interpreting OST results. Moreover, we found that inclusion of DIP joints can lead to an improvement of diagnostic performance of OST. To our knowledge, this the largest study examining the diagnostic value of OST in OA and the first external exploration of this specific DIP-associated algorithm. Value of OST in the follow up examinations of OA patients should be investigated in studies with longitudinal design.

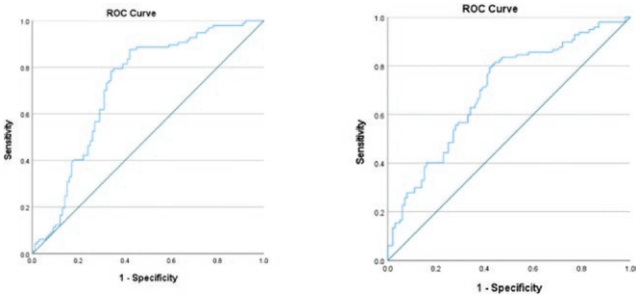


Figure 1. Receiver operating characteristics (patients vs. controls) of two different algorithms: **A.** with DIP joints **B.** without DIP joints.

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Acknowledgements: NIL.
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POS0927 COMBINED BRAIN/HEART MAGNETIC RESONANCE IMAGING REVEALS SUBCLINICAL BRAIN LESIONS IN PATIENTS WITH INFLAMMATORY ARTHRITIDES AND CARDIAC SYMPTOMS

Keywords: Imaging, Inflammatory arthritides, Diagnostic tests

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Background: Inflammatory arthritides (IA) can affect diverse body tissues beyond joints, including the heart [1,2]. Particularly in chronic inflammatory states, circulating immune mediators can also induce central nervous system inflammation [3]. Nevertheless, little is currently known about the consequences of cardiac inflammation on the occurrence of brain lesions in these patients.
Objectives: We hypothesized that patients with IA and cardiac symptoms would show evidence of brain lesions, and that the presence of cardiac inflammation would be associated with the presence of brain lesions. We thus investigated patients with IA and compared them to a cohort of disease-controls using combined brain/heart magnetic resonance imaging (MRI).
Methods: Patients with IA and shortness of breath, chest pain and/or palpitations (n=25) were compared to age-matched disease-controls with non-autoimmune cardiovascular disease (CVD) (n=30) using a 1.5T MRI system. The presence of white matter hyperintensities (WMHs) was investigated in subcortical/deep/periventricular white matter, the basal ganglia, pons, brainstem, or mesial temporal lobe. Cardiac function and inflammation were investigated using standard protocols. Patients with IA were diagnosed with rheumatoid arthritis [14 (56%)], ankylosing spondylitis [5 (20%)], juvenile rheumatoid arthritis [3 (12%)], mixed connective tissue disease [2 (8%)] or enteropathic arthritis [1 (4%)]. Disease controls had various CVDs including coronary artery disease [5 (17%)], myocarditis [5 (17%)], hypertension [3 (10%)], Duchenne muscular dystrophy [3 (10%)], and others.
Results: Patients with IA and disease-controls respectively had a median (IQR) age of 45 (39, 51) vs. 53 (40, 57) years (p=0.269), and 16 (64%) vs. 7 (23%) were women (p=0.002). WMHs were detected in ≥1 brain area in 15 (60%) patients with IA and 15 (54%) disease-controls (p=0.620). The majority of participants had WMHs in subcortical [29 (53%)], periventricular [5 (9%)], or deep WM [11 (20%)]. Some also had cortical lesions [5 (9%)], while basal nuclear, brainstem and mesial temporal lesions were rare [1 (2%) for all]. Amongst subjects with WMHs, the median (IQR) number of brain lesions in patients with IA and disease-controls was 1 (1, 2) for both groups (p=0.635). There were no significant differences in the distribution of brain lesions between groups. Amongst patients with IA, each 0.1-unit increase in cardiac T2-ratio was associated with an increased probability of WMH occurrence [odds ratio (95%): 1.29 (1.05-1.59), p=0.016] and higher cardiac T2-ratio (per 0.1-unit change) and extracellular volume fraction (ECV) were associated with a higher WMH lesion burden in linear regression analysis [Beta (95% confidence interval): 0.08 (0.01-0.15), p=0.021 and 0.22 (0.03-0.41), p=0.027, respectively]. MRI-derived left/right-ventricular ejection fraction, early/late-gadolinium enhancement and T1/T2 mapping were not associated with the presence of WMHs.
Conclusion: In patients with IA and cardiac symptoms, 60% showed evidence of subclinical brain lesions, which was on average as prevalent as in age-matched disease-controls with non-autoimmune CVD. Higher myocardial T2-ratio, an MRI-derived surrogate of myocardial edema, was associated with the presence of WMHs, and higher T2-ratio as well as myocardial ECV values were predictive of higher WMH burden. Further research is required to determine the clinical relevance of these findings.
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POS0928 DEEP LEARNING BASED ASSESSMENT OF SALIVARY GLAND ULTRASONOGRAPHY IMAGES FOR SUPPORTING THE DIAGNOSIS OF PRIMARY SJOGREN'S SYNDROME

Keywords: Artificial intelligence, Sjögren syndrome, Ultrasound

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Background: Salivary gland ultrasound (SGUS) has proven to be a promising tool for diagnosing primary Sjögren's syndrome (pSS). However, the widespread use of it as standardized diagnostic tools is limited by inter/intra operator variability.

Objectives: The aim of this study was to evaluate the utility of deep learning-based SGUS image assessment in the diagnosis of pSS.
Methods: Between Sep 2021 and Oct 2022, 1133 SGUS images of 137 patients from one center were included in this retrospective study. Among them, 61 patients with 480 images were diagnosed as pSS and 76 patients with 653 images were non-SS. All the SGUS image data were randomly divided into training dataset (50%), validation dataset (20%) and testing dataset (30%). The SGUS automatic classification model was developed by using a deep residual convolutional network architecture (RESNET). The predictive performance was validated by sensitivity, specifcity and area under reciver operating characteristic curve (ROC).
Results: When applying deep learning-based SGUS image assessment, it showed better performance than operator based SGUS score system by improving the specifcity (86.9% vs. 80.1%), while similar sensitivity (59.4% vs. 61.4%). The area under the ROC were comparable between them (0.800 vs 0.775).
Conclusion: Deep learning-based SGUS image assessment maybe an objective and promising tool compared to expert-based scoring of SGUS in the diagnosis of pSS. This may support SGUS as an effective and prospective diagnostic tool to supplement current diagnostic methods.
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POS0929 VALUE OF LUNG ULTRASOUND FOR THE DETECTION OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Lungs, Ultrasound

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Background: Interstitial lung disease (ILD) is an extra-articular manifestation of rheumatoid arthritis (RA) associated with increased morbidity and mortality. High-resolution computed tomography (HRCT) is the gold standard for ILD diagnosis, but it has high cost and risk of ionizing radiation. Lung Ultrasound (LUS) is a non-invasive, low-cost, non-ionizing and easily performed diagnostic tool.
Objectives: To establish the diagnostic value of LUS in ILD in patients with RA, using chest HRCT as the gold standard.
Methods: A cross-sectional study was performed at the Hospital Italiano de Buenos Aires, Argentina. Consecutive patients with RA (ACR/EULAR-2010 criteria), who had a chest HRCT performed at least 12 months previous to inclusion.Demographic, clinical, laboratory and therapeutic data were recorded. Each patient underwent a LUS with a simplified examination (14 bilateral lung intercostal spaces -LIS-), with assessment of B-lines (BL) and pleural irregularities (PI). Additionally, a 6MWT was performed on each patient. For the diagnosis of ILD, HRCT was the gold-standard, taking as a threshold an extension of interstitial involvement ≥10%, scored by an expert lung specialist. ROC curves were made to test the ability of LUS findings (BL and PI), and 6 MWT, to discriminate patients with ILD.
Results: A total of 104 RA patients were included, 21,8 % with ILD, 82.7% (95% CI 74.0-89.4) were women, with a median age at diagnosis of RA of 57.5 years (IQR 47.3 -67.2) and a median disease duration of 8.7 years (IQR 3.3-15.8). 96.2% of patients (95% CI 90.5-98.9) were seropositive for rheumatoid factor (RF) and/or anti-citrullinated protein antibodies (ACPA), and median DAS28-ESR was 3.19 (IQR 2.6-4.6). Methotrexate had been used at some point of the disease in 94.2% patients (95% CI 87.9-97.8), and 46.2% (95% CI 36.3-56.2) were under bDMARD or tsDMARD treatment at inclusion. Patients with ILD were older at the time of RA diagnosis (64 vs 54 years, p=0.002) and had higher erythrocyte sedimentation rate (ERS) and C-reactive protein (CRP) (48 vs 29 mm/h and 5.9 vs 3 g/L p=0.002) than patients without ILD. In LUS, patients with ILD had more BL (median 26 vs. 1, p <0.001), (Figure 1) and PI (median 12 vs. 4, p <0.001) than patients without ILD.The diagnostic accuracy in ROC curves was: AUC 0.88 - 95% CI 0.78-0.93 for BL and AUC 0.82 - 95% CI 0.74-0.89 for PI (Figure 3 and 4). The best cut-off point for ILD detection was 8 BL and 7 PI.The performance of LUS was more sensitive than 6 MWT (Table 1).
Conclusion: The presence of 8 BL and/or 7 PI in the LUS showed an adequate diagnostic performance for ILD, with a good negative prognostic value.

Table 1. Diagnostic performance of LUS and 6MWT for the detection of ILD

Test	Sensitivity	Specificity	LLR positive	LLR negative	Positive Prognostic Value	Negative Prognostic Value	AUC
	80,95%	79,52%	3,95	0,24	50	94,30	0,88 (0,78-0,93)
Pleural irregularities (≥7 spaces)	80,95%	75,90%	3,36	0,25	45,95	94,03	0,82 (0,74-0,89)
6MWT	36,84%	92,31%	4,70	0,68	53,85	85,71	-

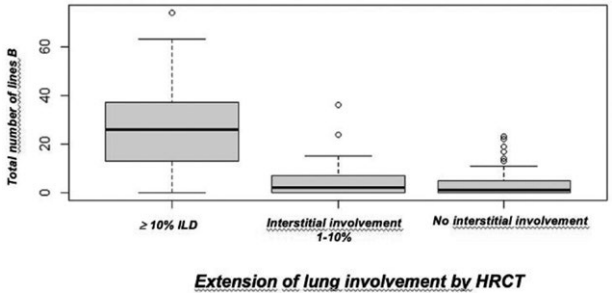


Figure 1. Number of B lines according to the extension of pulmonary interstitial involvement measured by HRCT.

REFERENCES: NIL.
Acknowledgements: NIL.
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POS0930 SUBCLINICAL SYNOVITIS OF THE KNEE REMAINED IN ONE-THIRD OF CASES IN PATIENTS WITH RHEUMATOID ARTHRITIS AFTER TOTAL KNEE ARTHROPLASTY: MUSCULOSKELETAL ULTRASONOGRAPHY STUDY

Keywords: Rheumatoid arthritis, Ultrasound

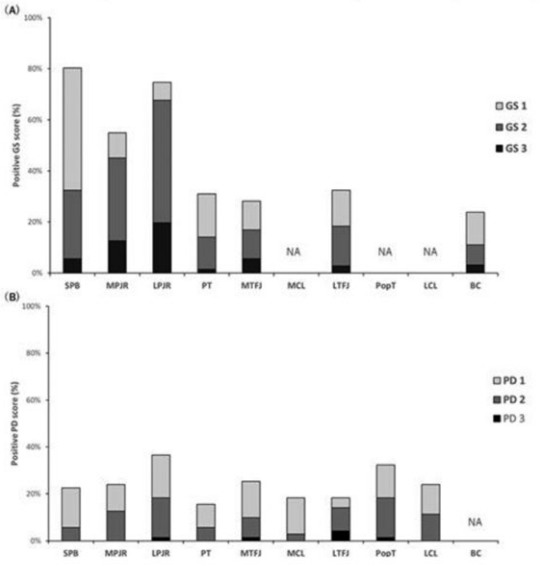
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Background: There is no report investigating the prevalence, sites, and risk factors of knee synovitis in patients with rheumatoid arthritis (RA) after total knee arthroplasty (TKA).
Objectives: This study aimed to clarify the prevalence, anatomical distribution, and risk factors of knee synovitis in RA patients after TKA.
Methods: This study was a retrospective cross-sectional study. Subjects were patients who met the 2010 ACR/EULAR RA classification criteria and underwent TKA at Tokyo Metropolitan Tama General Medical Center. Knee joints on surgically treated sides were assessed by musculoskeletal ultrasonography (MSUS) from April 1, 2020, to March 31, 2022. Knee US-synovitis was defined as the presence of PD 2 or higher at joint synovium (suprapatellar bursa, medial/lateral parapatellar joint recess, medial/lateral tibiofemoral joint space).
Results: Forty-five patients with RA after TKA underwent MSUS, with a total of 71 knee joints (38 right, 33 left). Patient background: age (years) 74.4±10.0, female(%) 84%, disease duration (years) 20.6±10.4, TKA postoperative period (years) 5.7±4.0, ACPA positivity 77%, RF positivity 79%, DAS28(ESR) 3.17±1.03, mHAQ 0.8±0.8, PSL users 44%, MTX users 64%, csDMARDs users 87%, BioDMARDs users 44%, tsDMARDs users 0%, Knee injury and Osteoarthritis Outcome Score-pain (KOOS-P) 82.5±17.2. The number of joints with GS 2 or higher

was more prevalent than that with PD 2 or higher (Figure 1). The number of post-TKA knee joints with PD 2 or higher was 18 (25.3%) out of 71. The knee joints assessed within one year from TKA were more likely to have joint synovitis detected by MSUS than those over one year (5 joints (62.5%) vs 13 (20.6%)). Fifteen (33.3%) patients had US-synovitis at post-TKA knee joints. There was no difference in disease activity scores (DAS28-CRP, DAS28-ESR, SDAI, CDAI), patient pain Visual Analogue Scale, or KOOS-P in patients with knee US-synovitis (n=15) compared with those without knee US-synovitis (n=30). There was no significant correlation between PD grades and KOOS-P (p=0.73).

Conclusion: Subclinical US-synovitis of the knee still remained in one-third of cases in patients with RA after TKA. US-synovitis at post-TKA knee joints did not correlate with knee pain scores. The knee prosthesis would have a protective effect on synovitis-induced pain at post-TKA knee joints in RA.

Fig.1 Prevalence of positive US scores at each site on the post-TKA knee joint of RA patients.



Shown are the frequencies of positive GS scores (A) and power Doppler scores (B) at each site on the post-TKA knee joint of RA patients. SPB: suprapatellar bursa; MPJR: medial parapatellar joint recess; LPJR: lateral parapatellar joint recess; PT: patellar tendon; MTFJ: medial tibiofemoral joint space; MCL: medial collateral ligament; LTFJ: lateral tibiofemoral joint space; PopT: popliteal tendon; LCL: lateral collateral ligament; BC: Baker's cyst, NA; not applicable.

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POS0931 USEFULNESS OF MUSCULOSKELETAL ULTRASOUND IN CLINICAL DECISION-MAKING IN RHEUMATOLOGY CLINICAL PRACTICE

Keywords: Ultrasound, Descriptive studies, Work-related issues

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Background: Ultrasound (US) has proven to be a useful technique in the routine clinical practice of rheumatologists. Due to its low cost, accessibility, and the large amount of information it provides us, more and more ultrasound studies tend to be carried out. However, we wonder about the real clinical-ultrasound correlation and whether, after a given result, the clinician made decisions based on said result.

Objectives: To describe the reason for request of the sonographic studies in our department and the effect of its result in the decision-making in the clinical practice.

Methods: Cross-sectional, observational analytical study. We enrolled all the patients that were cited in the ultrasonography agenda from march to august 2022. Variables for identification of request-exploration-review management times, motivation for the request, topography of the exploration performed, correlation with clinical suspicion and effect on decision-making were collected. Data extraction was performed by four different observers. Quality control was performed by a fifth observer.

Results: Records of 462 medical actions were included in the US agenda over 6 months. Including double requests (211 were bilateral scans), the results of 673 US scans performed were reviewed. Of the requests made, 118 (25.5%) were from patients with known diagnoses of inflammatory diseases. The attached Table 1 summarizes the reasons for the request and topography of the exploration of the studies carried out. The waiting time and standard deviation (SD) until the test was performed from its request was 85.4 SD 54.3 days (0;574) and until the reassessment in the office was 37.5 SD 43.4 days (0;217). The diagnostic correlation of US and clinical suspicion was confirmed in 277 studies (59.2%), it was not demonstrated in 161 (34.4%) and did not apply in the rest. The frequency of bilateral studies whose result could have been obtained with a unilateral exploration was 37/211 (17.5%). In 72 studies we could not determine to what extent US examination changed clinical decision (review query not available or not applicable). In 132 studies (33.8%) the clinician intensified the treatment, in 40 (10.2%) the clinician de-intensified the treatment, and in 63 (16.1%) the clinician indicated the discharge of the patient. Among those cases in which US modified the clinical decision, the time between test-requesting and decision-making was 120.1 SD 64.3 days, while in cases in which there was no effect on the clinical decision it was 160.9 SD 61.3. (p=.0031). Evaluating only the US scans indicated in inflammatory pathology, the times were 66.5 DE 32.5 and 84.3 DE 29.5 days, respectively (p=.0012).

Conclusion: Our study is limited to identifying bivariate associations between decision making and the result of a complementary test. The authors recognize that clinical decisions are made considering all available information, including those from specific complementary test. US proves to be a useful test in clinical decision-making and presumably more so the less time elapses between its request and its interpretation. In addition, performing bilateral US scans seems justified as less than a fifth of the requests would have given the same result with a unilateral scan.

Table 1. Topography of the explorations and reason of the ultrasound request

Topography	Bilaterality	Reason of the ultrasound request				
		Diagnostic uncertainty	Activity assessment	Ultrasound-guided procedure	Diagnostic + Procedure	Activity assessment + Procedure
Hand (50%)	Unilateral	45	15	9	24	8
	Bilateral	75	48	-	8	2
Foot	Unilateral	35	13	5	6	2
(19.4%)	Bilateral	23	6	-	1	-
Shoulder	Unilateral	26	5	3	14	-
(11.5%)	Bilateral	4	-	-	2	-
Knee	Unilateral	8	2	1	5	2
(4.9%)	Bilateral	3	1	-	1	-
Hip	Unilateral	5	2	3	-	1
(2.8%)	Bilateral	2	-	-	-	-
Salivary gland	Unilateral	2	-	-	-	-
(4.1%)	Bilateral	16	1	-	-	-
Elbow (3.8%)	Unilateral	2	2	3	4	1
	Bilateral	5	1	-	-	-
Vascular (1.7%)	Bilateral	5	3	-	-	-
Total scans		259	102	26	63	16

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POS0932 ULTRASOUND-DEFINED GRADE I SYNOVITIS IN PATIENTS WITH INFLAMMATORY-SUSPECTED ARTHRALGIA AND ITS ROLE IN DIAGNOSIS A YEAR LATER

Keywords: Ultrasound, Inflammatory arthritides, Diagnostic tests

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Background: Musculoeskeletal ultrasound is frequently used in several rheumatology units to detect subclinical inflammation in patients with joint symptoms suspected for progression to inflammatory arthritis.

Objectives: The main goal is to investigate the correlation between synovitis grade I (EULAR-OMERACT combined score) and the diagnosis of established inflammatory arthropathy that is carried out after a follow-up period of one year since the first ultrasound findings. The assessment is done in an ultrasound-specialized unit of a Rheumatology Department

Methods: We conducted a descriptive, retrospective and unicentric study where 135 patients were selected from the ultrasound-specialized unit of our rheumatology department from July 2018 to December 2021. Patients that presented synovitis grade 0,2 and/or 3 on combined score were excluded. Collected baseline data included age, sex, immunological profile, acute phase reactants and physical examination previous to the ultrasound findings, as well as the

diagnosis made by the rheumatologist a year after said findings. To achieve that, the patients are divided into two groups: those who were diagnosed with inflammatory arthropathy and those who were not. In addition, non-parametric statistical tests for comparing means were used.

Results: The mean age was 55 years and 75% of the patients were females. At the beginning, clinical examination revealed a median of one tender joints and none swollen. Previous diagnosis of psoriasis was present in 18 (13,3%) patients while inflammatory bowel disease was present in 6 patients (4,4%). Of the 135 patients, after a year follow-up, 46 (34,1%) received the diagnosis of inflammatory arthropaty after a follow-up of one year: 15 (32,6%) psoriatic arthritis, 8 (17,4%) rheumatoid arthritis, 8 (17,4%) undifferentiated arthritis, 4 (8,7%) spondyloarthritis, 4 (8,7%) calcium pyrophosphate dehydrate crystal-related joint disease, 3 (6,5%) reactive arthritis, 2 (4,3%) systemic sclerosis, 1 (2,2%) Sjögren syndrome and 1 (2,2%) polymyalgia rheumatica. Non-inflammatory arthropathies were also found 89 (65,9%), of which 64 (71,9%) were osteoarthritis, 20 (22,5%) Carpal tunnel syndrome and 5 (5,6%) had other soft tissue disease. In the group of patients who did not developed an autoimmune arthropathy, 3 were Rheumatoid factor-positive and 10 were AAN-positive, none of them were aCCP- positive; The HLA B-27 and Cw6 test resulted in 5 patients testing positive in HLA-B27 and none in Cw6. Among the group of patients that developed an inflammatory arthropathy the median of joints with ultrasound involvement was 2. Grade I power Doppler signal was detected in one case. 7 (15,2%) patients were RF- positive, and 6 (13%) aCCP-positive. AANs were positive in 13 cases (28,3%). There were no significant differences for clinical variables and acute phase reactants (Age, sex, SJC, TJC, RCP, ESR) between both groups. Comparing the immunological profile through a Fisher's exact test, we obtained a statistically significant association for RF (p=0,033), aCCP (p=0,001) and AAN (p=0,014) in the group who finally received the diagnosis of inflammatory arthropathy. No other significant differences were found (Total joints GSUS, total joints PDUS, HLA B27 and HLA Cw6)

Conclusion: Despite the limitations and possible statistical bias that might appear in a retrospective study, there are a remarkable number of patients with ultrasound-defined grade I synovitis who develop inflammatory arthropaty a year later. Rheumatoid factor, aCCP and AAN positivity were the only factors statistically associated with progression.

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POS0933 NAILFOLD VIDEOCAPILLAROSCOPY AS A POSSIBLE BIOMARKER TO DETECT ABERRANT PLACENTAL MICROCIRCULATION IN PREGNANT WOMEN: A PILOT STUDY

Keywords: Pregnancy and reproduction, Biomarkers, Imaging

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Background: During pregnancy, exchanges between mother and fetus are provided by the placenta. Defects in the early stages of placentation prevent the creation of a high-flow, low-resistance circle resulting in an impaired maternal-fetal exchange. The development of aberrant microcirculation leads to placental abnormalities, detectable by placental histologic examination [1].

Objectives: To assess whether nailfold videocapillaroscopy (NVC), in combination with umbilical artery doppler ultrasound (UA-dU), can detect microvascular status during pregnancy [2]; and to evaluate if NVC follow-up during pregnancy might operate as a red flag biomarker of placental microcirculation abnormalities.

Methods: We conducted a longitudinal observational exploratory study on 54 healthy pregnant women (age range 26-46 y) within the 16th gestational week, excluding those with cardiovascular comorbidities. We performed clinical, UA-dU and NVC evaluation with an optical probe (200x magnification) at each trimester of pregnancy and post-partum [3]. We performed an after-birth placenta histology (abPH) in a subgroup of 20 women (among the 54 women) who developed complications during pregnancy (e.g., gestational hypertension) evaluated through optical microscopic technique, according to Amsterdam criteria [4].

Results: We noticed over time, in the whole cohort, a statistically significant increase in neo-angiogenesis ($p<0.05$), considering the absolute count of microvessel ramifications (abnormal shapes) (**Figure 1a**). Conversely, we did not observe any statistically significant variation in capillary density (n/linear mm), microhaemorrhages or dilated capillaries over time. Besides, a statistically significant difference in the absolute number of capillaries in the first trimester between subjects with and without areas of placental dysmaturity (aberrant placental microcirculation) was detected at abPH (7.0/mm ± 0.82 vs 8.2/mm ± 0.62; $p=0.030$), (**Figure 1b**). A receiver operating characteristic curve was drawn for calculating the Area Under the Curve (AUC: 0.87; 95%CI: 0.66–1.00), identifying the optimal discriminatory cut-off value for prediction of placental dysmaturity areas (≤7.50/mm capillaries, sensitivity: 88.9%; specificity: 75.0%). Of note, a similar difference was confirmed at the third trimester, although not reaching statistical significance ($p=0.06$). Not any significant association was found between UA-dU and any of the assessed NVC parameters.

Conclusion: This study confirms, in a large cohort of pregnant women, the NVC detection of increased neoangiogenesis over time, even during post-partum. In addition, this is the first report suggesting the possible role of NVC (capillary density) for the early detection of aberrant placental microcirculation noticeable at abPH. A study in pregnant patients affected by autoimmune connective tissue diseases has already started, using those findings as reference parameters.

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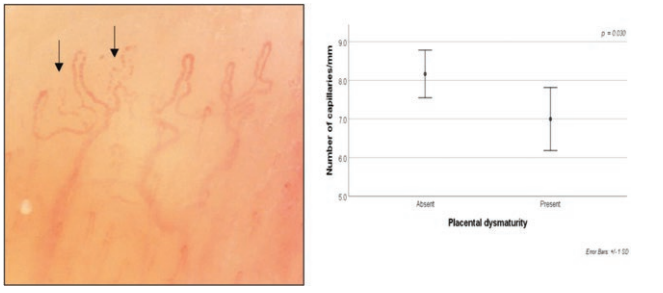


Figure 1. a. Neo-angiogenesis (arrows) at the 3rd trimester (magnification 200x). b. Difference in the absolute number of capillaries in the 1st trimester between women with and without areas of placental dysmaturity at abPH.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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Epidemiology, risk factors for disease or disease progression

POS0934

PREVALENCE AND TRENDS OF PULMONARY HYPERTENSION IN AUTOIMMUNE DISEASES

Keywords: Lungs, Comorbidities, Epidemiology

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Background: Pulmonary hypertension (PHTN) is a known complication of connective tissue diseases such as Systemic lupus erythematosus (SLE), Scleroderma (Scl), and Mixed connective tissue disease (MCTD).[1] The underlying mechanism for development of PHTN is remodeling and vasoconstriction of pulmonary arteries and arterioles.[2] There have been cases of severe PHTN in SLE patients that have shown improvement with immunosuppressive therapy, hence accentuating the role of inflammation in pathogenesis.[3] The Prevalence of PHTN is not well studied, and there are no large cohort studies available. This study was undertaken to capture the trend in the prevalence of PHTN in the aforementioned diseases.

Objectives: To determine the prevalence of PHTN in SLE, Scl, and MCTD, analyze the trend over a 15-year period as well as identify racial predisposition, length of stay (LOS), and cost of hospitalization in these patients.

Methods: We used the Nationwide Inpatient Sample database (years 2003-2018) and extracted patients with PHTN using validated International Classification of Disease (ICD) codes. Data from 2015 was excluded from the study considering the transition of the coding system from version 9 to 10. We identified cases having the diagnosis of SLE, Scl, and MCTD. Prevalence, as well as demographics, cost of hospitalization, and length of stay (LOS), were analyzed and charted. Data were analyzed using statistical analysis system 9.4 software.

Results: Over the period of 15 years, we identified 2,155,750 cases of PHTN. As seen in the graph, patients with SLE had the highest prevalence of PHTN. The prevalence rate of SLE in PHTN cases in 2003 was 0.92% which significantly increased to 1.05% in 2018, with a peak of 1.15% seen in 2014 (p <0.0001). Prevalence rate of Scl in PHTN decreased from 1.07% in 2003 to 0.80% in 2018 (p< 0.0001). It was seen that the prevalence rate of MCTD in cases with PHTN significantly increased from 0.06% in 2003 to 0.23% in 2018, (p<0.0001). It was observed that the average age of PHTN cases was significantly younger in SLE (55.60 vs 70.80 years, p <0.0001), Scl (62.94 vs 70.72 years, p < 0.0001), and MCTD (58.49 vs 70.66 years, p <0.0001). On examining the racial distribution, African Americans, Hispanics, and Native Americans were more likely to have underlying SLE, Scl, and MCTD, respectively. PHTN was more prevalent in females in all 3 diseases. The average cost of hospitalization was significantly higher in PHTN cases with MCTD ($76,696.7 vs $65,643.3, p<0.0001) and SLE ($69,106.5 vs $65,620.6, p<0.0001), while it was not significantly lower in PHTN cases with Scl ($65,272.9 vs $65,659.9, p = 0.65). Average LOS was significantly longer in PHTN with MCTD (7.02 vs 6.64 days, p = 0.0119). Though not significant, average LOS was longer in PHTN with SLE (6.73 vs 6.64 days, p = 0.0812) and shorter in PHTN with Scl (6.62 vs 6.64 days, p = 0.7917).

Conclusion: Improved survival, seen secondary to increased awareness, better diagnostic testing, multidisciplinary team approach, and newer treatment modalities has led to an increase in the prevalence of patients living with PHTN. Interestingly, our study shows that the prevalence of PHTN in SLE and MCTD is increasing while decreasing for Scl. Racial predisposition becomes evident, which demands a higher index of suspicion for the early diagnosis of PHTN in the respective races. There is a higher socioeconomic burden for patients with PHTN and autoimmune disease, as reflected by the increased LOS and cost of hospitalization.

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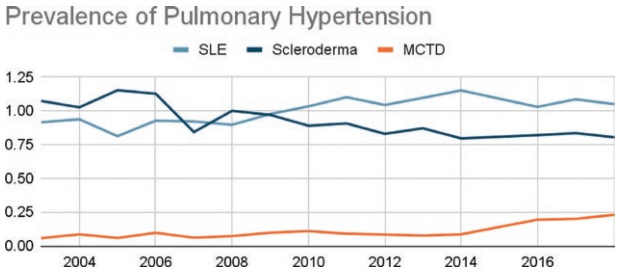


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.433

POS0935

THE COURSE OF CYTOKINE AND CHEMOKINE GENE EXPRESSION IN CLINICALLY SUSPECT ARTHRALGIA PATIENTS DURING PROGRESSION TO INFLAMMATORY ARTHRITIS

Keywords: Rheumatoid arthritis, Cytokines and chemokines

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Background: Autoantibody-responses rise years before onset of inflammatory arthritis (IA) and are stable during transitioning from clinically suspect arthralgia (CSA) to IA. Cytokine and chemokine levels also rise years before IA-onset. However, the course in the at-risk stage of CSA during progression to disease or non-progression is unknown.

Objectives: To increase the understanding of processes mediating disease development, we studied the course of cytokine, chemokine and related receptors gene expression in CSA-patients during progression to IA, and in CSA-patients who ultimately did not develop IA.

Methods: Whole-blood RNA-expression of 37 inflammatory cytokines/chemokines/related receptors was determined by dual-colour reverse-transcription multiplex ligation-dependent probe amplification, in paired samples of CSA-patients at CSA-onset and either at IA-development or after 24-months without IA-development. ACPA-positive and ACPA-negative CSA-patients developing IA were compared at CSA-onset and during progression to IA. GEE-models tested changes over time. A false discovery rate approach was applied.

Results: None of the cytokines/chemokine genes significantly changed in expression between CSA-onset and IA-development (Figure 1A). In CSA-patients without IA-development, G-CSF expression decreased (p=0.001), whereas CCR6 and TNIP expression increased (p<0.001 and p=0.002, respectively) over a 2-year period (Figure 1B). Expression levels in ACPA-positive and ACPA-negative CSA-patients who developed IA were similar.

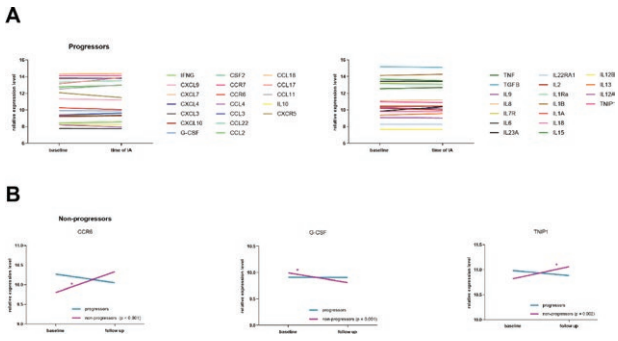


Figure 1. (A) Modelled course of gene expression of 37 cytokines/chemokines/related receptors in CSA-patients that progressed to IA. Cytokines, chemokines and related receptors were measured at baseline and at time of IA-development and for reasons of clarity presented in two plots. No statistically significant changes were observed during follow-up. (B) Modelled course of gene expression of CCR6, G-CSF and TNIP1 in CSA-patients that did not progress to IA. Cytokines, chemokines and related receptors were measured in paired samples from each patient with 2-year intervals. For comparison, the course of patients that progressed to IA was included, here the 2nd samples was collected at IA-development. CSA, clinically suspect arthralgia; IA, inflammatory arthritis.

Conclusion: Whole-blood gene expression of assessed cytokines/chemokines/related receptors did not change significantly from CSA to IA-development. This suggests that changes in expression of these molecules may not be related to the final process of developing chronicity and may have occurred preceding CSA-onset. Changes in gene expression in CSA-patients without IA-development may provide clues for processes related to resolution.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0936 TUMOUR NECROSIS FACTOR INHIBITORS USE AND DISCONTINUATION AMONG PREGNANT WOMEN WITH CHRONIC INFLAMMATORY DISEASES

Keywords: Pregnancy and reproduction, bDMARD, Descriptive studies

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Background: Previous guidelines (2006) recommended that tumour necrosis factor inhibitors (TNFi) be discontinued during pregnancy. Despite new guidelines (2016 & 2020) now recommending against this, the choice to stop TNFi pre-conception is patient- and provider-dependent. Observational studies have evaluated use of disease-modifying anti-rheumatic drugs (DMARDs) during pregnancy, but few have specifically assessed TNFi discontinuation pre-conception. Understanding trends and predictors of TNFi discontinuation pre-conception may help inform initiatives to improve care and optimize maternal and fetal outcomes.

Objectives: We examined trends in TNFi discontinuation pre-conception over time, and evaluated the characteristics of pregnant women with chronic inflammatory diseases who stopped using TNFi pre-conception (without resuming in pregnancy) compared with those who used TNFi at any time during pregnancy.

Methods: We created a cohort of pregnant women with rheumatoid arthritis (RA), ankylosing spondylitis, psoriatic arthritis (PsA), psoriasis (PsO), and/or inflammatory bowel diseases (IBD) who delivered between 2011 and 2019, using the MarketScan commercial database. TNFi use was defined as at least 1 filled prescription or infusion procedure claim, categorized according to the timing of the filled prescription or infusion procedure date in relation to the gestational period: 1) TNFi pre-conception only (i.e. at least 1 prescription filled or infusion procedure claim in the 12 weeks preceding the gestational period but none within the gestational period) or 2) TNFi use at any time during pregnancy (i.e. any prescription filled or infusion procedure claim during the gestational period, including restarts, new starts, and those continuing from pre-conception).

Results: We identified 3,372 pregnancies; 13% discontinued TNFi in the 12 weeks before conception and did not restart, and 86% were exposed to TNFi during pregnancy. Pregnancies in IBD patients accounted for 47% of all pregnancies. Nearly all pregnancies with IBD were exposed to TNFi during pregnancy (95%). Compared to those with IBD, more patients with RA (difference of 18%, 95% CI 15-21%) and PsA/PsO (20%, 95% CI 16-24%) discontinued their TNFi. Corticosteroid use was similar in both TNFi exposure groups, while patients who took TNFi during pregnancy were more likely to use non-biologic DMARDs concomitantly. Over time, a lower proportion of patients stopped TNFi pre-conception (2011-2013 19% vs 2014-2016 13% vs 2017-2019 10%; p-value for trend <0.0001).

Conclusion: In our sample, 13% discontinued TNFi in the 12 weeks before conception and did not restart. The proportion of patients stopping TNFi pre-conception between 2017-2019 decreased compared to earlier years, possibly reflecting updated guidelines. Further research on TNFi discontinuation in the years after the 2020 ACR guidelines is warranted.

Table 1. Characteristics of pregnant women with chronic inflammatory diseases who stopped TNFi pre-conception and those who took TNFi at any time during gestation (n=3,372).

	Total (n=3372)	TNFi pre-conception only (n=470)	TNFi any time during pregnancy (n=2902)
Maternal Diagnosis, n (%)		470/3372 (14)	2902/3372 (86)
All	1588 (47)	82/1588 (5)	1506/1588 (95)
IBD only	807 (24)	187/807 (23)	620/807 (77)
RA only	530 (16)	132/530 (25)	398/530 (75)
PsA/PsO only			
Corticosteroids, n (%)	1085 (32)	149/470 (32)	936/2902 (32)
Non-biologic DMARDs, n (%)	713 (21)	66/470 (14)	647/2902 (22)
Delivery Year, n (%)			
2011-2013			
All	1202 (36)	224/1202 (19)	978/1202 (81)
IBD only	510 (15)	36/510 (7)	474/510 (93)
RA only	345 (29)	96/345 (29)	249/345 (72)
PsA/PsO only	200 (6)	61/200 (30)	139/200 (70)
2014-2016			
All	1138 (34)	148/1138 (13)	990/1138 (34)
IBD only	549 (16)	20/549 (4)	529/549 (96)
RA only	266 (8)	60/266 (23)	206/266 (8)
PsA/PsO only	157 (5)	41/157 (26)	116/157 (74)
2017-2019			
All	1032 (31)	98/1032 (9)	934/1032 (91)
IBD only	529 (16)	26/529 (5)	503/529 (95)
RA only	196 (6)	31/196 (16)	165/196 (84)
PsA/PsO only	173 (5)	30/173 (17)	143/173 (83)

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Disclosure of Interests: None Declared.

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POS0937 FACTORS ASSOCIATED WITH HOSPITAL ADMISSIONS DUE TO OPIOID-RELATED HARMS IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

Keywords: Osteoarthritis, Fibromyalgia, Prognostic factors

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Background: Hospital admissions due to opioid-related toxicity have doubled in the United Kingdom over the last decade. Rheumatic and musculoskeletal diseases (RMDs) are some of the most common indications for prescribing opioids in primary care. Little is known about what individual factors are associated with serious opioid-related harms in this population. A better understanding of these risks is imperative for safe prescribing of opioids in patients with RMDs.

Objectives: To assess patient factors associated with opioid-related hospitalisations in new opioid users with the following RMDs: rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), systemic lupus erythematosus (SLE), osteoarthritis (OA), and fibromyalgia.

Methods: This retrospective cohort study evaluated new adult opioid users without cancer between 01-Jan-2006 and 31-Aug-2021 using data from the Clinical Practice Research Datalink Aurum diagnosed with one or more of the six RMDs. Patient-level data were linked to Hospital Episodes Statistics (HES). The main outcome of opioid-related hospitalisations within five years of first opioid prescription, were defined using ICD-10 codes from HES. Logistic regression and random forest classification were used to assess patient characteristics associated with opioid-related hospitalisations. To identify the most relevant variables we used "Boruta" feature selection, a wrapper algorithm built around the random forest classifier that compares the importance of the real predictor variables with those of permuted copies of the original features using statistical testing and several iterations of random forests. Feature importance is ranked by the Boruta algorithm using mean Z-scores (the number of standard deviations from the mean a data point

is). The higher the Boruta importance score, the stronger the impact the particular input variable has on the outcome variable.
Results: The cohort comprised 1,329,698 new opioid users (801,533 women [60.3%]; 992,542 White patients [88.2%]), with a mean age of 60 years [SD 17]. The proportion patients with different RMDs in order of frequency were OA: 1,246,574 (93.7%); RA, 50,000 (3.8%)], fibromyalgia [47,708, 3.6%], PsA [11,181 (0.8%)], SLE [6,757 (0.5%)] and AS [6,560 (0.5%). Of our study population, 4,016 individuals (0.3%) experienced a hospitalization for opioid-related harms within our follow-up period of five years after first prescription date. Logistic regression and random forest models showed consistent results when ranking the most important variables associated to opioid-related hospital admissions. The main risk factor identified consistently across both methods was history of alcohol excess, with an odds ratio (OR) of 10.7, 95% confidence interval (95% CI): 8.1–14.2 and Boruta Importance (Imp) of 93.6. Other main risk factors included history of attempted suicide and self-harm (OR 7.5, 95% CI: 5.6–9.9, Imp: 80.3), major depression (OR 2.0, 95% CI: 1.7–2.3, Imp: 39.7) and lower socioeconomic status (OR: 10.4, 95% CI: 4.6–23.4, Imp: 34.0).
Conclusion: Patients with a documented history of alcohol excess, severe psychological problems and those most socioeconomically deprived were found to have a higher risk of opioid-related hospitalisations. Medical providers should be made aware of psychosocial factors associated with opioid hospital admissions when prescribing opioids to patients with RMDs. By determining patient subgroups most vulnerable to opioid-related harms and further analysing patient risk factors, we hope to contribute to the development of targeted interventions for safer future clinical care.
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Disclosure of Interests: Carlos Ramirez Medina: None declared, David Jenkins: None declared, Niels Peek: None declared, Belay Birlie Yimer: None declared, Joyce (Yun-Ting) Huang: None declared, Mark Lunt: None declared, William Dixon Consultant of: WGD has received consultancy fees from Google unrelated to this work, Meghna Jani: None declared.
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POS0938

PROLONGED PHYSICAL STRAIN AT WORK CONFERS RISK FOR DEVELOPMENT OF RHEUMATOID ARTHRITIS IN PATIENTS WITH CLINICALLY SUSPECT ARTHRALGIA: CUES FOR MECHANICAL FACTORS AS FINAL PATHOPHYSIOLOGICAL HIT

Keywords: Rheumatoid arthritis, Epidemiology, Work-related issues

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Background: Some case-control studies have identified physical workload as a risk-factor for rheumatoid arthritis (RA).
Objectives: To better understand its influence on the pathophysiological trajectory of RA-development, we studied the relation of work-related physical strain with MRI-detected joint-inflammation in clinically suspect arthralgia (CSA) and the general population, and with progression from CSA to clinical arthritis.
Methods: 501 consecutively presenting CSA-patients and 155 symptom-free persons filled out questionnaires on their occupation. Physical strain was determined using the International Standard Classification of Occupations (ISCO) per subject-reported occupation. Contrast-enhanced hand-MRIs were evaluated for synovitis/tenosynovitis/osteitis (summed as joint-inflammation) using the RAMRIS-method. CSA-patients were followed on clinical arthritis development (median follow-up 25 months). Analyses included interaction with age as proxy for prolonged physical strain.
Results: In CSA-patients, the degree of physical strain was associated with the severity of subclinical joint-inflammation, independent of BMI/smoking/education-level: there was a positive interaction between age and physical strain; p=0.007. Plotting the age-dependent effects showed a positive relation in CSA-patients aged ≥50 years (Figure 1A), suggesting the effect relates to prolonged physical strain. Especially tenosynovitis was increased in relation to higher physical strain. Prolonged physical strain in symptom-free persons was not associated with MRI-detected joint-inflammation. Older (≥ 50 years) CSA-patients with higher physical strain developed clinical arthritis more often (Figure 1B; HR 1.17 (95%CI 1.00–1.35) per 10 percentage-points physical strain increase; p=0.043). This was partially mediated by subclinical joint-inflammation. Moreover, physical strain partially mediated the known association between low educational attainment and clinical arthritis development.
Conclusion: Prolonged work-related physical strain increases the risk of developing RA in CSA-patients, which is partially mediated by an effect on increased subclinical joint-inflammation. This points to mechanical factors as a final hit in the pathophysiology of RA-development.

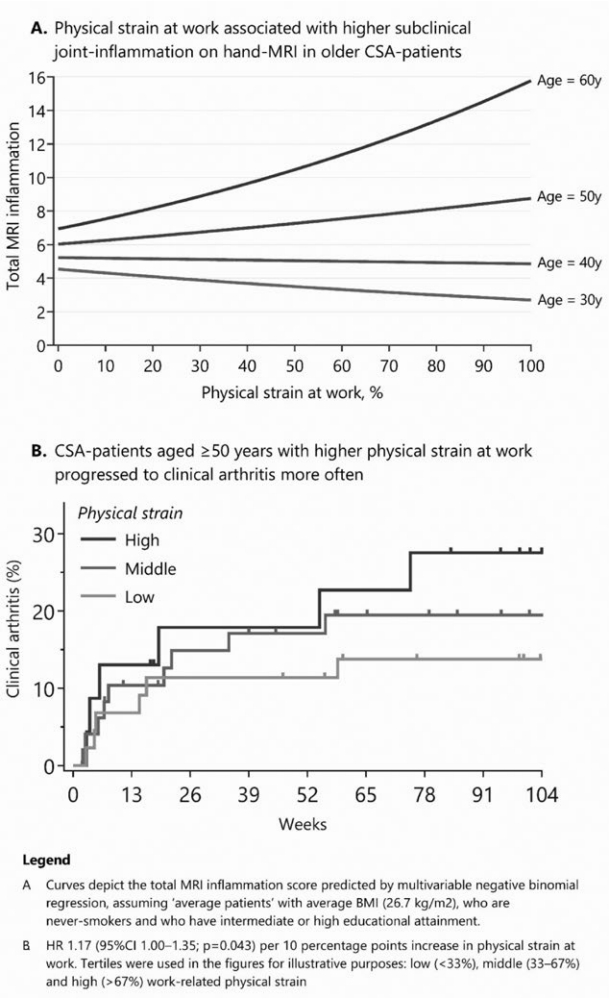


Figure 1.

Acknowledgements: We thank dr. B. Ravesteijn for sharing occupation-specific physical strain data (see Ravesteijn et al., Health Econ. 2018, and www.bastian-ravesteijn.com).
Disclosure of Interests: None Declared.
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POS0939

PLEUROPARENCHYMAL FIBROELASTOSIS: A SPECIAL CLINICAL SITUATION IN PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH CONNECTIVE TISSUE DISEASES. DESCRIPTIVE STUDY FROM A REFERRAL CENTRE

Keywords: Comorbidities, Lungs

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Background: Pleuroparenchymal fibroelastosis (PPFE) is a rare interstitial lung disease (ILD) that can be idiopathic or associated with a variety of different conditions, including connective tissue diseases (CTD) **[1-2]**. In this regard, the presence of PPFE has been reported as an independent predictor of worse

prognosis in CTD-ILD patients **[3]**. Approximately one third of the patients with ILD meet criteria for a CTD **[4]**.

Objectives: A) To determine the prevalence of PPFE in a cohort of Spanish patients with CTD-ILD, and **B)** to compare the characteristics between CTD-ILD patients with and without PPFE.

Methods: A total of 99 patients with CTD-ILD (31 rheumatoid arthritis (RA), 31 systemic sclerosis (SSc), 21 idiopathic inflammatory myositis (IIM), 6 primary Sjögren's syndrome (SS), 4 systemic lupus erythematosus (SLE) and 6 with other CTDs) from the Hospital Universitario Marqués de Valdecilla (Santander, Spain) were included in this study. The presence of PPFE was confirmed by experienced radiologists evaluating chest high-resolution computed tomography images from all patients. In addition, demographic, clinical and radiological characteristics were collected.

Results: The presence of PPFE was found in 9 (9.1%) of the 99 CTD-ILD patients, whereas the remaining 90.9% had no signs of PPFE. In particular, it was confirmed in 4 patients with RA (12.9%), 2 with SSc (6.5%), 1 with IIM (4.8%), 1 with primary SS (16.7%) and 1 with SLE (25.0%) (**Figure 1**). The prevalence of bronchial dilation was statistically higher in CTD-ILD patients with PPFE compared to those without PPFE (44.4% *versus* 6.74%, respectively, p=0.006, **Table 1**). There were no significant differences in age at CTD or ILD diagnosis, sex, smoking history, body mass index and pulmonary function tests at ILD diagnosis between both groups (**Table 1**).

Conclusion: We provide the prevalence and clinical data of PPFE in patients with CTD-ILD from a national referral centre. Approximately 1 out of 10 of our patients presented associated PPFE, closely correlated to bronchial dilation. The identification of this condition in CTD-ILD patients should be considered routinely since it may worsen their prognosis.

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Table 1. Demographic, clinical and radiological characteristics between CTD-ILD patients with and without PPFE.

Characteristics	CTD-ILD patients with PPFE	CTD-ILD patients without PPFE	p
Age at CTD diagnosis (years), mean ± SD	57.4 ± 11.3	53.0 ± 12.6	0.35
Age at ILD diagnosis (years), mean ± SD	54.9 ± 12.6	56.4 ± 12.5	0.73
Sex (men/women), n (%)	3/6 (37.5/62.5)	43/47 (47.8/52.2)	0.50
Smoking history, n (%)	4 (50.0)	52 (62.7)	0.48
Body mass index	23.5 ± 5.5	26.2 ± 4.6	0.14
PFTs at ILD diagnosis			
FVC ml, mean ± SD	2196 ± 1268	2740 ± 945.3	0.16
FVC (% predicted), mean ± SD	71.3 ± 38.1	84.1 ± 25.4	0.22
DLCO (% predicted), mean ± SD	36.2 ± 19.3	47.0 ± 16.0	0.15
DLCO/VA (% predicted), mean ± SD	66.8 ± 18.8	72.9 ± 23.2	0.57
Radiological features			
Any bronchial dilatation, n (%)	4 (44.4)	6 (6.74)	**0.006**

CTD: connective-tissue disease; DLCO: diffusing capacity of the lung for carbon monoxide; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; ILD: interstitial lung disease; PFTs: pulmonary function tests; PPFE: pleuroparenchymal fibroelastosis; SD: standard deviation; VA: alveolar volume.Significant results are highlighted in bold.

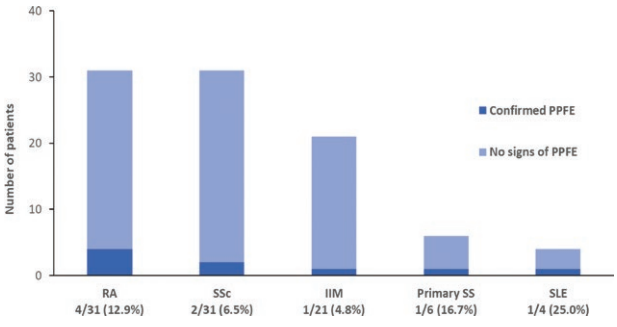


Figure 1. Prevalence of PPFE in each CTD-ILD.

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POS0940 CHRONIC PAIN IN MULTIPLE SITES AND WIDESPREAD PAIN IS ASSOCIATED WITH VASCULAR AND HEART FUNCTION: A PROSPECTIVE COHORT STUDY

Keywords: Cardiovascular disease, Heart, Pain

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Background: Chronic pain is highly prevalent in the general population and has been considered a disease entity in itself. Recent studies including our own have shown that chronic pain in multiple sites was associated with a higher risk of cardiovascular disease (CVD) and the relationship may be causal. Early changes in vasculature and heart function such as arterial stiffness, carotid intima thickness (CIMT), cardiac index (CI) and ventricular ejection fraction (LVEF), have been strong and independent predictors of CVD risk; however, whether chronic pain is associated with early signs of vasculature and heart function changes has not been investigated.

Objectives: To examine the associations of chronic pain in multiple sites and widespread pain with arterial stiffness index (ASI), CIMT, CI and LVEF.

Methods: This study utlised data from the UK biobank study which is a prospective cohort study with over 500,000 participants aged 40–69 years recruited at baseline, and some participants attending the subsquent three followups including two imaging visits. Pain sites (including hip, knee, back, neck/shoulder or 'all over the body') and duration were measured via a questionnaire at each visit. Chronic pain was defined if pain had lasted for ≥3 months. Participants were categorised into six groups: no chronic pain, chronic pain in 1, 2, 3 and 4-site and 'all over the body'. ASI (in m/s) was measured by using finger photoplethysmography at each visit. CIMT, CI and LVEF were assessed at the two imaging visits. CIMT (in micrometres) was measured using ultrasound. CI (in litres/min/m2) and LVEF (in percentage) were obtained from heart MRI. Linear mixed-effects model was used for the analyses.

Results: A total of 97,774, 12,213, 28,326, and 2,903 participants who had complete data were included in the ASI analysis over a median follow-up of 11.4 years (interquartile range [IQR]: 10.6–12.3), while 22,851 and 607 participants were included for CIMT and heart function analyses over a median follow-up of 2.3 years (IQR: 2.2–2.5) (Figure 1). At baseline, the participants were 56.5 [8.1] years (Mean [SD] age) and 51% were females. Greater number of chronic pain sites was associated with a higher ASI and lower LVEF in a dose-response relationship (both P for trends <0.05) after adjustment for all covariates. Participants with chronic pain 'all over the body' had the highest ASI (β=0.24, 95%CI 0.06–0.43) and lowest LVEF (β=-1.21, 95%CI -2.21—0.22). No statistically significant association was found for CIMT and CI. No significant interaction between chronic pain and follow-up time with all outcomes was observed, indicating that the effect of chronic pain on vasculature and heart function did not change over time.

Conclusion: This study found a dose-response relationship between number of chronic pain sites and ASI and LVEF, with participants with chronic widespread pain having the highest ASI and lowest LVEF. These findings suggest that chronic pain may have a detrimental effect on vasculature and heart function.

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Disclosure of Interests: None Declared.

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POS0941 SYSTEMIC SCLEROSIS IS A RISK FACTOR OF INCIDENT PSORIASIS: RESULTS FROM A NATIONWIDE COHORT STUDY

Keywords: Epidemiology, Systemic sclerosis, Real-world evidence

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Background: Co-existing psoriasis (PsO) in patients with systemic sclerosis (SSc) has been reported. However, it is unclear whether SSc contributes as a risk factor for development of PsO.
Objectives: We aimed to assess whether SSc is associated with the risk of incident PsO.
Methods: From the Korean National Health Insurance Service database, 4,933 patients with SSc and 24,665 age- and sex-matched controls were selected. Hazard ratios (HRs) and 95% confidence intervals (CIs) for incident PsO were estimated using multivariable Cox proportional hazard models adjusted for known risk factors of PsO. Further, we selected individuals whose health check-up data were available (2,355 patients with SSc and 11,775 age- and sex-matched controls). In this population, we further adjusted for additional risk factors of PsO using the health check-up data.
Results: In the analysis of 4,933 patients with SSc and 24,665 age- and sex-matched controls, incidence rates of PsO in patients with SSc and controls were 10.26 and 3.20 per 1,000 person-years, respectively. After adjusting for risk factors of PsO, patients with SSc had a significantly higher risk of incident PsO (adjusted HR: 3.055 [95% CI: 2.597, 3.594]). Moreover, in the analysis of individuals who had health check-up data, additional risk factors of PsO were further adjusted; the result also showed that patients with SSc have a significantly higher risk of incident PsO (adjusted HR: 2.820 [95% CI: 2.207, 3.603]).
Conclusion: In this large cohort study, SSc was associated with a 3-fold higher risk of incident PsO than controls, independent of known risk factors of PsO. This observation advances our knowledge by showing that a risk relationship exists between SSc and PsO, beyond a simple co-existence between the two conditions.

Table 1. Comparison of risk of incident psoriasis between patients with systemic sclerosis and controls.

	N	Incident PsO	Duration, pyrs	Incidence rate /1,000 pyrs	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Total cohort						
Controls	24,665	463	144,671.7	3.20	1 (Ref.)	1 (Ref.)
Patients with SSc	4,933	272	26,507.0	10.26	3.198 (2.753, 3.715)	3.055[a] (2.597, 3.594)
Health check-up cohort						
Controls	11,775	210	60,965.5	3.44	1 (Ref.)	1 (Ref.)
Patients with SSc	2,355	111	11,391.9	9.74	2.821 (2.241, 3.551)	2.820[b] (2.207, 3.603)

[a]Adjusted for age, sex, income, hypertension, type 2 diabetes, dyslipidaemia, MI, stroke, CHF, COPD, ESRD, and cancer.[b]Adjusted for age, sex, income, smoking status, alcohol consumption, physical activity, obesity, hypertension, type 2 diabetes, dyslipidaemia, CKD, MI, stroke, CHF, COPD, and cancer.PsO, psoriasis; pyrs, person-years; HR, hazard ratio; CI, confidence interval; SSc, systemic sclerosis; CKD, chronic kidney disease; MI, myocardial infarction; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease

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Disclosure of Interests: None Declared.
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POS0942 THE SIGNIFICANCE OF PRE-SCREENING OF SUBCLINICAL MALIGNANCIES BEFORE THE TREATMENT OF BIOLOGIC AGENTS OR JAK INHIBITORS TO CONNECTIVE TISSUE DISEASE PATIENTS

Keywords: Targeted synthetic drugs, bDMARD, Malignancy

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Background: Malignancies under the treatment of biologic agents (Bio) or JAK inhibitors (JAKi) are attracting public attention[1] [2]. It is important to administer Bio or JAKi safely to the patients, it seems to be absolutely necessary of the screening of cancer. Intensive pre-screening examinations for malignancies before the treatment of Bio or JAKi has been performed in our department since 2016.
Objectives: To elucidate the utility of the intensive pre-screening examination and the prevalence of malignancies prior to the therapy of Bio or JAKi to the patients of connective tissue diseases (CTD).
Methods: Three hundred thirty-six CTD patients (RA:254, SLE:27, SpA:25, Vasculitis:13, Overlap syndrome:6, others:11) before the administration of Bio or JAKi were enrolled from April 2016 to September 2021. Upper gastric intestinal endoscope, fecal occult blood test (twice), thyroid and abdominal ultrasound, chest and abdominal non-contrast enhanced CT, serum prostate-specific antigen (only for male) and screening for the cancer of the cervix and mammography (only for female) were performed to all patients above as an intensive pre-screening examination. Herein, we retrospectively analyzed the prevalence of both benign and malignant tumors including species before the therapy of Bio or JAKi, and the patient-treatment outcomes with cancers.
Results: The patient characteristics were as follows: Median age: 68 yr.(n=336). (RA:69 yr., SLE:48yr., SpA:63yr., Vasculitis:73yr., Overlap syndrome:70yr., others:57yr.). The prevalence of benign tumors and malignant tumors were 24.7% (n=83, median age:68yr.) and 5.1% (n=17, median age:74yr.<Max:89yr. Min:50yr.>), respectively. The details of the malignancies were prostate cancer (n=6, 35.3%), uterus or ovarian cancer (n=3, 17.6%), gastric cancer (n=3, 17.6%), colon cancer (n=2, 11.8%), breast cancer (n=1,5.9%), lung cancer (n=1, 5.9%) and thyroid cancer (n=1, 5.9%). Most of the age complicated with cancers was 80yr (median) except for those of uterus or ovarian cancer:50yr(median). Eleven patients (64.7%) among cancer bearing patients (n=17) successfully administered Bio or JAKi after radical operation such as endoscopic or surgical resection and all of the 11 patients achieved clinical remission.
Conclusion: Subclinical malignancies were detected by means of intensive pre-screening examinations. The most common cancer was prostate cancer, subsequently uterus or ovarian cancer and gastric cancer. It is important to perform pre-screening examinations before an aggressive therapy such as Bio or JAKi to CTD patients.
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[2] Rheumatol Ther 2017;4:333-347
Acknowledgements: NIL.
Disclosure of Interests: Kenta Misaki Speakers bureau: Astellas, Bayer, Boehringer Ingelheim, Eli Lilly, Chugai, Sanofi, Kyowa-Kirin, Abbvie, Kowa, Pfizer, Ono Pharmaceutical, UCB, Mitsubishi-Tanabe, Gilead Sciences, Nippon Shinyaku, Novartis, Eisai, Janssen, Taisho, Teijin, VIATRIS and Asahi-kasei; and has received research grants from Ono Pharmaceutical, Grant/research support from: ONO PHARMACEUTICAL CO., LTD, Yamamoto Mako: None declared, Takuya Okada: None declared, Yusuke Tarutani: None declared, Moemi Yabe: None declared, Kenshi Inoue: None declared, Naofumi Dobashi: None declared, Yasuhiko Imaizumi: None declared.
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POS0943 A GENETIC STUDY ABOUT POTENTIAL CAUSAL RELATIONSHIP BETWEEN SEDENTARY ACTIVITY AND PSORIASIS

Keywords: Genetics/epigenetics, Psoriatic arthritis

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Background: Psoriasis is a common, chronic, immune-mediated skin disorder, which is characterized by clearly demarcated areas of erythematous plaques with overlying silvery scales appearing on the skin [1]. Previous studies have shown that plenty of psoriasis patients are engaged in less physical activity (PA), however, the genetic causal association between PA and psoriasis is of scarce evidence [2].
Objectives: In this study, we aimed to evaluate the causal association between PA and psoriasis.
Methods: We used genome-wide association study (GWAS) data to conduct a Two-Sample Mendelian randomization (MR). MR utilizes single nucleotide polymorphisms (SNPs) as instrumental variables (IVs) to examine the causality of an observed association between exposure and outcome [3]. SNPs that were independent ($r2 < 0.001$) and without linkage disequilibrium and strongly related to PA ($p < 1e\text{-}08$, F>10), were selected as IVs. PA was divided into two parts including sedentary and physically active activities. Physically active behaviors include accelerometer-based physical activity, vigorous physical activity, moderate to vigorous physical activity, moderate physical activity 10+ minutes, and vigorous physical activity 10+ minutes. GWAS summary data of four types of sedentary behavior and five types of physically active behaviors were acquired from the UK biobank. The GWAS data of sedentary behavior includes watching TV (N=437,88), using computer(N=360,895), mobile phone use (N=310,555), and driving(N=456,972). The FinnGen collaboration provides summary statistics for psoriasis, which included 216,752 European individuals (4,510 cases and 212,242 non-cases). Inverse-variance weighted (IVW), MR-Egger, and the weighted median were used to assess causality. IVW was a key method to estimate. Cochran's Q test and egger-intercept analysis were used as auxiliary analyses to assess pleiotropy and heterogeneity.
Results: There were strong genetic causal relationships between psoriasis and TV watching. Watching TV was identified as the risk factor of psoriasis by

IVW (OR =2.11; 95% CI, 1.35-3.30, P=1.02E-03), identical to MR-Egger and the weighted median analysis. Pleiotropy and heterogeneity were not found by Cochran's Q (P =0.140)and egger-intercept (P=0.43), suggesting these findings were reliable. In contrast, there was no causal relationship between the other activities and psoriasis (P > 0.05).

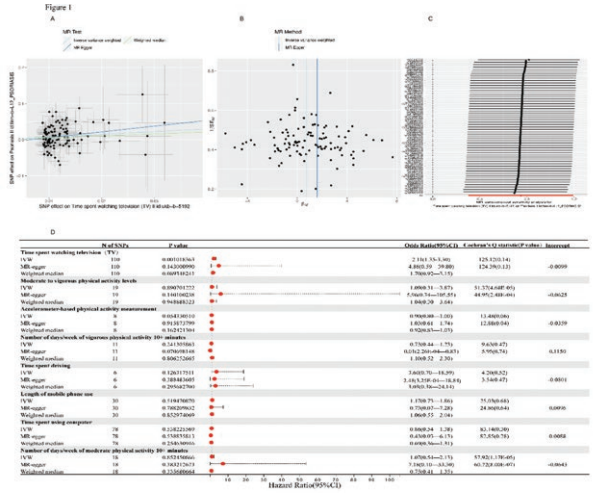


Figure 1: Mendelian randomization results for gene-level causality between physical activity (PA) and psoriasis were evaluated by the odds ratio (OR) values of IVW, MR Egger, and Weighted median. Scatter plots (A), funnel plots (B), leave-one-out analysis (C), and forest plot (D) present TV watching as a risk factor for psoriasis. IVW, inverse-variance weighted; CI, confidence interval; SNP, single nucleotide polymorphisms.

Figure 1. Mendelian randomization results for gene-level causality between physical activity (PA) and psoriasis were evaluated by the odds ratio (OR) values of IVW, MR Egger, and Weighted median. Scatter plots (A), funnel plots (B), leave-one-out analysis (C), and forest plot (D) present TV watching as a risk factor for psoriasis. IVW, inverse-variance weighted; CI, confidence interval; SNP, single nucleotide polymorphisms.

Conclusion: Our findings reveal that TV watching is an apparent risk factor for psoriasis. It provides psoriasis patients with a piece of advice that they should lessen extended sedentary time and boost physical activity.

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POS0944 DIETARY PATTERNS AND FOOD GROUPS IN RELATION TO DISEASE ACTIVITY AND FATIGUE IN PATIENTS WITH INFLAMMATORY ARTHRITIS

Keywords: Inflammatory arthritides, Diet and nutrition

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Background: Recently, diet and nutrients have received considerable attention as potential precipitating factors and exacerbation triggers of inflammatory arthritis.

Objectives: To evaluate the associations of diet with disease activity and fatigue in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA, including psoriatic arthritis [PsA]).

Methods: Data of German patients with RA, SpA/ PsA were prospectively collected by the Mida Rheuma App (CE-certified mobile application, Midaia GmbH, Germany) from Jan 2022 to Dec 2022. Anonymized data of patients were extracted for retrospective analysis. We assessed demographic parameters, major dietary patterns, and food groups by each patient's consumption intensity. Consumption of dairy products, fruits, vegetables, sausages, meat, oily fish, white fish, sugar, and alcohol was collected. For each group, participants were asked how often, on average, they had consumed the foods and beverages, with four or five responses ranging from "never" to '4–5 times per day/per week or every day'. The presence of lactose, gluten, and fructose intolerance was also assessed. Disease activity was measured by Patient's Global Assessment of Disease Activity (PtGADA, scored from 0 to 100 mm) and Patient's Global Assessment of Pain Intensity (PPAIN, scored from 0 to 100 mm). Fatigue was assessed by The Brief Fatigue Inventory (BFI, scored from 0 to 10 points). Patients were divided into subgroups to evaluate associations depending on the food group, and the high-consumption group (HCG) was compared with the low-consumption group (LCG). Patients on a specific diet were compared with the 'eat all group' (EAG). The differences in the data sets were examined for their significance using t-test, p-value ≤ 0.05 was considered statistically significant.

Results: Of 1564 extracted patients, 774 completed diet questionnaires. These were included in the analysis (480 RA, SpA: 180 axSpA, 61 PsA, 53 - combination of two arthritis). 79.8% of patients were female, 19.5% - male, and 0.7% - another gender; the mean age was 42.8±12.6 years. The mean PtGADA, PPAIN, and BFI were 55.7±26.7, 52.6 ±26.5, and 5,17±1,98. According to dietary patterns, 432 (55.8%) patients were included in EAG, 21.6% were on a vegan/vegetarian diet (4.8%/16.8%), 15,5% - Mediterranean, and 7.1% - low-carb diet; 8.4% had lactose, gluten, fructose intolerance or their combinations. The Mediterranean diet group had statistically significant lower PtGADA and PPAIN (by 8.98%, p=00.4 and 14.3%, p=0.007 respectively), compared with EAG. Vegan/vegetarian and low-carb diet groups demonstrated only positive trends for PtGADA, PPAIN, and BFI vs. EAG. At the same time, fruit and vegetable HCGs showed negative trends for all outcomes compared with LCGs. Negative trends were also found for dairy products, meat, and sugar, with the most substantial difference for sugar (10.1%, 7.92% and 8.67% for PtGADA, PPAIN and BFI, respectively). Statistically significant higher PtGADA, PPAIN and BFI were in sausage HCG vs. LCG: 16.4%, p=0.01, 15.6%, p=0.02, and 11.8%, p=0.03 for PtGADA, PPAIN and BFI respectively. Statistically significant lower PtGADA and PPAIN were in oily fish HCG vs. LCG (18.1%, p=0.01, and 17.1%, p=0.03, respectively). However, for white fish, this difference was not demonstrated.

Conclusion: According to the presented data high processed meat consumption is potentially associated with higher disease activity and fatigue, while the Mediterranean diet and high oily fish consumption – with low disease activity. These findings highlight the importance of future research and the potential of dietary interventions in patients with inflammatory arthritis.

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POS0945 ILD PROGRESSION ON STANDARD OF CARE VARIES IN PATIENTS WITH CONNECTIVE TISSUE DISEASE

Keywords: Prognostic factors, Organ damage, Lungs

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Background: A subset of patients with connective tissue disease associated interstitial lung disease (CTD-ILD) progresses. These patients have been included in clinical ILD trials as a group despite their different underlying diseases. It has not been studied whether this basket approach of pooling different CTD-ILDs is valid, e.g., if the disease course of the ILDs depends on the underlying CTD. In addition, the impact of immunosuppressive treatment, which CTD-ILD patients receive for ILD or other organ manifestations as a standard of care, is not fully understood.

Objectives: To assess ILD progression in patients with CTD-ILDs on standard of care treatment.

Methods: CTD-ILD patients (N=504) from a Norwegian and Swiss cohort fulfilling the respective classification criteria of the underlying CTD with ILD diagnosed on HRCT were included. Data were extracted from prospectively collected local registries. Additional data were extracted from electronic patient records. Change in absolute FVC% predicted over 12 months was calculated. In addition, ILD progression was assessed over 12 months on standard of care treatment, defined as:

(I) Absolute decline of FVC (% predicted) ≥10%
(II) 2022 ATS/ERS/JRS/ALAT guideline criteria including 2/3 of (1) worsening of respiratory symptoms; (2) absolute decline in FVC ≥ 5% or in DLCO ≥ 10% and (3) disease progression on HRCT over 12 months

Multivariable logistic regression and descriptive statistics were applied. Analyses were adjusted for underlying CTD and immunosuppressive treatment (including corticosteroids any dose, csDMARDs, mycophenolate, cyclophosphamide, CD-20/TNF/ JAK/IL6-inhibitors).

Results: The total CTD-ILD cohort of 504 patients included 231 (46%) systemic sclerosis (SSc)-ILD, 91 (19%) anti-synthetase syndrome (ASS)-ILD, 82 (16%) rheumatoid arthritis (RA)-ILD, 57 (11%) primary Sjögren syndrome (pSS)-ILD and 43 (9%) mixed connective tissue disease (MCTD)-ILD patients (Table 1). Mean absolute change in FVC% over 12 months was for the entire cohort -0,74% (range -34 to +42%), 57 (13,7%) had an FVC decline ≥10% and 47 (12%) fulfilled the guideline criteria. ILD progression varied between the diagnoses, with SSc-ILD and pSS-ILD showing the strongest absolute FVC decline over 12 months and the highest percentage of progressive patients defined by the 2022 guideline. Additionally, patients with SSc-ILD and MCTD-ILD had more frequent FVC ≥10% events (Table 1). Overall, 240 (62,8%) patients were treated with immunosuppressives (table 1). There was no difference between patients treated and not treated in absolute FVC decline (OR 1.00, 95%CI 0.98-1.02, p= 0.705), and in the percentage of progressive patients according to the guideline criteria (OR 1.00, 95%CI 0.54-1.86, p= 0.995). However, there was less FVC decline ≥10% (OR 0.51, 95% CI 0.28-0.90, p= 0.022) in patients treated with immunosuppressives. Patients with SSc-ILD (11% vs 20%, p=0.059) and pSS-ILD (8% vs 19%, p=0.329) showed numerically less FVC decline ≥10%. The different CTD diagnoses had different patterns of treatment with immunosuppressives, with the majority of RA and ASS-ILD being treated (Table 1).

Table 1.

	pSS (N = 57)	ASS (N= 91)	SSc (N = 231)	RA (N = 82)	MCTD (N = 43)
Male sex, n (%)	10 (18)	29 (32)	55 (24)	37 (45)	14 (33)
Age at diagnosis, yrs (SD)	52 (14,9)	49 (15,4)	48 (15,0)	54 (15,3)	39 (17,4)
Disease duration, yrs (SD)	9,8 (8,7)	10,1 (8,2)	10,4 (12,4)	11,3 (13,2)	13,3 (9,7)
Immunosuppression, n (n with valid data) (%)	28 (46) (60,9)	62 (69) (89,9)	86 (228) (37,7)	47 (50) (94)	17 (23) (73,9)
Baseline FVC% (SD)	91,5 (17,8)	79,6 (23,1)	88,6 (20,0)	73,0 (19,1)	85,5 (18,2)
Δ FVC% (SD) after 12 months	- 2,39 (9,2)	-0,37 (10,3)	-1,18 (9,3)	1,67 (9,0)	-0,64 (11,9)
FVC decline ≥ 10 %, n (%)	5 (13)	7 (11)	38 (17)	3 (5)	4 (18)
Guideline criteria, n (%)	5 (12,8)	5 (8,1)	34 (14,9)	2 (4,5)	1 (5,3)

Conclusion: In this CTD-ILD cohort, both underlying CTD and immunosuppressive treatment seemed to be associated with different patterns of ILD progression over a 12-month period. This has implications for the enrichment for progressive disease and inclusion of CTD-ILD patients into clinical trials.

REFERENCES: NIL.

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POS0946

ASSOCIATION BETWEEN PARENTAL AUTOIMMUNE DISEASE AND ATOPIC DERMATITIS IN THEIR OFFSPRING VARIED BY SEX: A NATIONWIDE CASE–CONTROL STUDY

Keywords: Pregnancy and reproduction, Epidemiology

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Background: Association of parental autoimmune diseases and offspring atopy is unknown.

Objectives: Our study explored the association between paternal and maternal autoimmune diseases and occurrence of atopic dermatitis in their children in Taiwan.

Methods: The birth data between 2006 and 2012 from National Birth Registry was linked with National Health Insurance Research Database (2003-2017) in this study. We enrolled 312,329 mother-parent linkages when the children were diagnosed with atopic dermatitis before 5 years old, and compared them with 862,612 control parent-child linkages. Conditional logistic regression was utilized to calculate adjusted odds ratio (aOR) and 95% confidence interval (CI) when investigating the association between parental diseases and AD in their offspring.

Results: After adjusting for infant's characteristics, perinatal factors, and other parental illnesses, the odds ratio of developing AD was 2.269 (95% CI 1.333-3.861) with parental rheumatoid arthritis and 1.610 (95% CI,1.094-2.369) with parental psoriasis. Parental allergic diseases such as AD (aOR 2.071, 95% CI 1.952-2.198) and asthma (aOR 1.494, 95% CI 1.400-1.594) were also significant predictors for childhood AD before 5 years old. Thus, parental autoimmune diseases could be one of the risk factors for subsequent AD development in their offspring. The subgroup analysis presented the different odds ratios of parental autoimmune diseases between children's sex. Parental rheumatoid arthritis showed aOR of 3.070(95% CI, 1.532-6.154) in boys with AD, while parental psoriasis showed1.945(95% CI, 1.129-3.350) in girls with AD.

Conclusion: Parental autoimmune diseases were found to induce subsequent atopic dermatitis in their children before 5 years old, and there were different risk factors for atopic dermatitis between boys and girls.

Table 1. Adjusted odds ratios of risk factors for childhood atopic dermatitis by using multivariate logistical regression analysis

	The parental diseases existed in			
Parental diseases	Neither maternal nor paternal	Only maternal	Only paternal	Both maternal and paternal
Obstetric complications				
Preeclampsia	Reference	1.001(0.977-1.027)		
GDM	Reference	**1.164(1.146-1.181)**		
Cervical incompetence	Reference	**1.168(1.058-1.290)**		
Autoimmune disease				
RA	Reference	**1.212(1.131-1.300)**	**1.153(1.062-1.252)**	**2.269(1.333-3.861)**
SLE	Reference	**1.177(1.093-1.267)**	Nil[α]	Nil
SS	Reference	**1.181(1.130-1.234)**	**1.127(1.053-1.206)**	**1.140(0.949-1.369)**
AS	Reference	**1.300(1.189-1.420)**	**1.187(1.130-1.247)**	1.152(0.629-2.111)
Psoriasis	Reference	**1.243(1.164-1.327)**	**1.118(1.055-1.186)**	**1.610(1.094-2.369)**
Systematic diseases				
Anemia	Reference	1.030(1.018-1.043)	1.042(1.010-1.074)	1.090(1.051-1.130)
HTN	Reference	1.066(1.030-1.102)	1.115(1.092-1.139)	**1.259(1.128-1.404)**
DM	Reference	1.105(1.079-1.131)	1.116(1.081-1.152)	**1.358(1.216-1.518)**
COPD	Reference	1.186(1.150-1.224)	1.170(1.138-1.201)	**1.213(1.110-1.325)**
Hyperthyroidism	Reference	1.187(1.158-1.217)	1.148(1.091-1.207)	1.164(0.932-1.454)
OSA	Reference	1.265(1.145-1.398)	1.208(1.154-1.264)	0.700(0.417-1.178)
Allergic disease				
Asthma	Reference	**1.286(1.258-1.315)**	**1.211(1.182-1.241)**	**1.494(1.400-1.594)**
AD	Reference	**1.474(1.454-1.495)**	**1.328(1.288-1.369)**	**2.071(1.952-2.198)**

NOTE:"Because the prevalence of SLE was largely higher in female, (female: male=14:1 in Taiwan, 2011) we only calculated the odds ratio of maternal SLE rather than taken the few male patients into consideration.The ORs of Obstetric complications was compared between maternal exposure and non-exposure.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0947 SUBCLINICAL SYNOVITIS IN ANTI-CCP POSITIVE INDIVIDUALS AT-RISK OF RA: HOW LIKELY IS IT TO RESOLVE?

Keywords: Prognostic factors, Rheumatoid arthritis, Ultrasound

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Background: Subclinical synovitis is a relatively common ultrasound (US) finding in individuals at-risk of rheumatoid arthritis (RA) (33%) [1]. It is associated with the development of inflammatory arthritis (IA); which often results in physicians prescribing disease modifying anti-rheumatic drugs (DMARDs) in the absence of clinical inflammation. Prediction of resolution of these changes may prevent overtreatment in a number of these patients.

OBJECTIVES:

1) To assess reversibility of subclinical synovitis in individuals at risk of RA, within 12 months' time.
2) To investigate factors associated with resolution of subclinical synovitis.

Methods: A single centre, prospective, observational study recruited anti-cyclic citrullinated peptide (anti-CCP) antibody positive at-risk individuals with a new musculoskeletal complaint, but no clinical synovitis. US scans of wrists, metacarpophalangeal joints, proximal interphalangeal joints and metatarsophalangeal joints were performed at baseline. Those with subclinical synovitis [grey scale (GS) ≥1 and power doppler (PD) ≥1] in at least one joint were then selected. The following variables were collected: gender, age, smoking exposure, anti-CCP titre, the presence of rheumatoid factor, antinuclear antibodies (ANA) and shared epitope, levels of CRP (mg/dL) and ESR (mm/h), minutes of early morning stiffness (EMS), number of tender joints, number of painful joints reported by the patient, number of joints with subclinical synovitis and number of bone erosions. Another US scan was performed after 12 months. If participants had been diagnosed with an IA by then, they were considered to have persistent synovitis and the US scan was not repeated. Univariate analysis was used to identify relevant factors for resolution of subclinical synovitis. Multivariable binary logistic regression and ROC curves were performed to identify the best prediction model.

Results: A total of 91 individuals presented with subclinical synovitis on US. This resolved in 47.3% (43/91) of cases, whereas US changes persisted in 52.7% (48/91) of participants [out of which 62.5% (30/48) developed an IA within 12 months]. Univariate analysis showed that a low anti-CCP titre [<3x upper limit of normality (ULN)], a negative rheumatoid factor, no smoking exposure, age ≤55, ESR≤13, absence of bone erosions and <2 joints with subclinical synovitis at baseline were associated with resolution of subclinical synovitis within 12 months (p<0.05). ROC curves were performed to identify the best cut-offs for continuous variables. Statistically significant factors were included in a multivariate binary logistic regression analysis, which was also adjusted for confounders (age, smoking status and gender). The ROC curve (Figure 1) of the final multivariate prediction model showed AUC=0.819 (p<0.001), with anti-CCP low titre having an odds ratio (OR) of 3.43 for resolution of subclinical synovitis [95%CI (1.07-11.05); p=0.039] and ESR≤13 having OR=3.41 [95%CI (1.22-9.56) p=0.019].

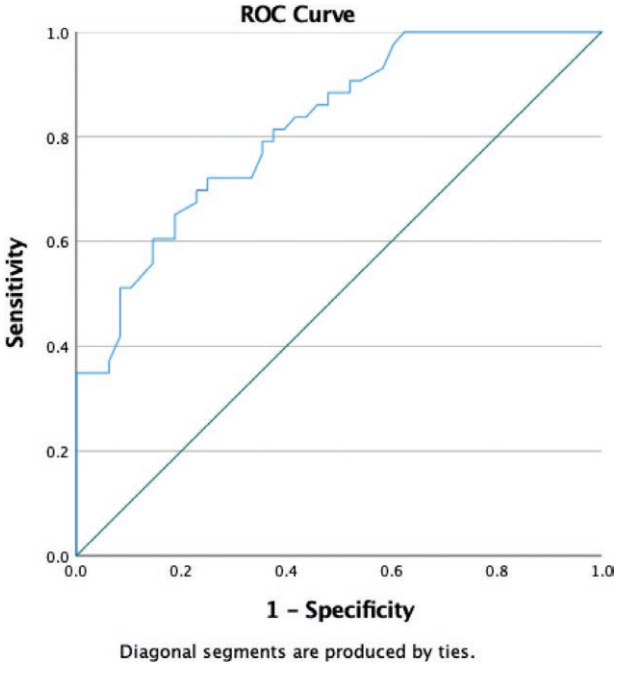


Figure 1. ROC curve of the multivariate predictive model.

Conclusion: Subclinical synovitis is a common finding in anti-CCP positive at-risk individuals, which has shown association with progression to IA. However, by 12 months' time, these US changes disappear in approximately half of the patients, with ESR≤13 and a low anti-CCP titre being the most significant predictors of resolution. Considering the risks associated with immunosuppressants, these data may prevent unnecessary treatment in these patients.

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[1] *Rakieh C. et al. Predicting the development of clinical arthritis in anti-CCP positive individuals with non-specific musculoskeletal symptoms: a prospective observational cohort study. Ann Rheum Dis. 2015 Sep;74(9):1659-66.*

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0948 PATTERNS OF DISEASE PROGRESSION IN SYSTEMIC SCLEROSIS PATIENTS WITH INTERSTITIAL LUNG DISEASE

Keywords: Systemic sclerosis, Lungs, Prognostic factors

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Background: Interstitial lung disease (ILD) is a severe complication of systemic sclerosis (SSc) that may lead to irreversible loss of lung function and increased mortality. Patterns of disease progression (PODs) in SSc-ILD are poorly characterized.

Objectives: To define PODs in SSc-ILD patients that may have clinical implications for patient stratification and clinical trial design.

Methods: Patients with SSc at risk for ILD were recruited in 6 tertiary referral centers. Inclusion criteria were: a) Disease duration < 5 years at the time of the first pulmonary function test (PFT); b) absence of anti-centromere antibodies; c1) diffuse cutaneous subset (dcSSc) OR c2) limited cutaneous subset (lcSSc) with either presence of anti-topoisomerase (Topo I) antibodies or evidence of ILD at high-resolution computed tomography (HRCT). Analyses were restricted to those with ILD at HRCT. PODs at 5 years, defined by absolute changes in forced vital capacity (FVC) % of predictd values, were explored by latent class mixed models (LCMM). Survival analysis (lung-related events) was also conducted on evolution data.

Results: 473 patients at risk for SSc-ILD were identified, of those 424 (89.6%) had evidence of ILD at HRCT and were selected for in-depth analyses. Baseline demographic and clinical characteristics are reported in the Table 1. Multivariable Cox regression showed that FVC values (HR = 0.953, CI95 = 0.956 – 0.982, p < 0.001) as well as the yearly change in FVC (HR = 0.961, CI95 = 0.932 - 0.992, p < 0.05) were predictive of 10-years mortality. LCMM analysis discovered 5 PODs (Figure 1); the majority of patients showed a stable FVC or slow decline in lung function. Patients with sharp improvement had higher age and shorter disease duration compared to patients with sharp deterioration (55 ± 10.5 vs 47 ± 15.3 and 0.88 ± 1.1 vs 1.03 ± 1.5 years, both p < 0.05) and a lower exposure to immunosuppressants (68.4% vs 85.3%); no other difference in clinical or demographic variables was observed among classes. Ten-years survival estimates were lower in patents with sharp (75.1%) or slowly-declining lung function (79.8%) compared to the other groups (>90%) with no event in the sharp improvement class (log-rank p = 8*10-4). The predictive capability of LCMM classes was 0.766 ± 0.03 as measured by Harrel's C-index.

Table 1. Baseline characteristics

Variable	SSc-ILD (n = 424)
dcSSc, n (%)	229 (54%)
F, n (%)	354 (83.5%)
Scl70, n (%)	331 (78.1%)
SSA, n (%)	93 (21.9%)
Deaths 10 yrs	32 (7.5%)
FVC, % pred	88.8 ± 18.8
DLco, % pred	64.4 ± 19.9
Age at first PFR, yrs	49.5 ± 13
Disease duration at first PFR, years	0.91 (0.19 - 2.26)
Patients exposed to immunosuppressants, n (%)	291 (68.6%)
Number of visits	5713
Exposure to CYC, n visits (%)	441 (7.7%)
Exposure to MMF, n visits (%)	729 (12.8%)
Exposure to AZA, n visits (%)	533 (9.3%)
Exposure to TCZ, n visits (%)	26 (0.5%)
Exposure to RTX, n visits (%)	134 (2.3%)
Exposure to csDMARDs, n visits (%)	1703 (29.8%)
Exposure to bDMARDs, n visits (%)	160 (2.8%)

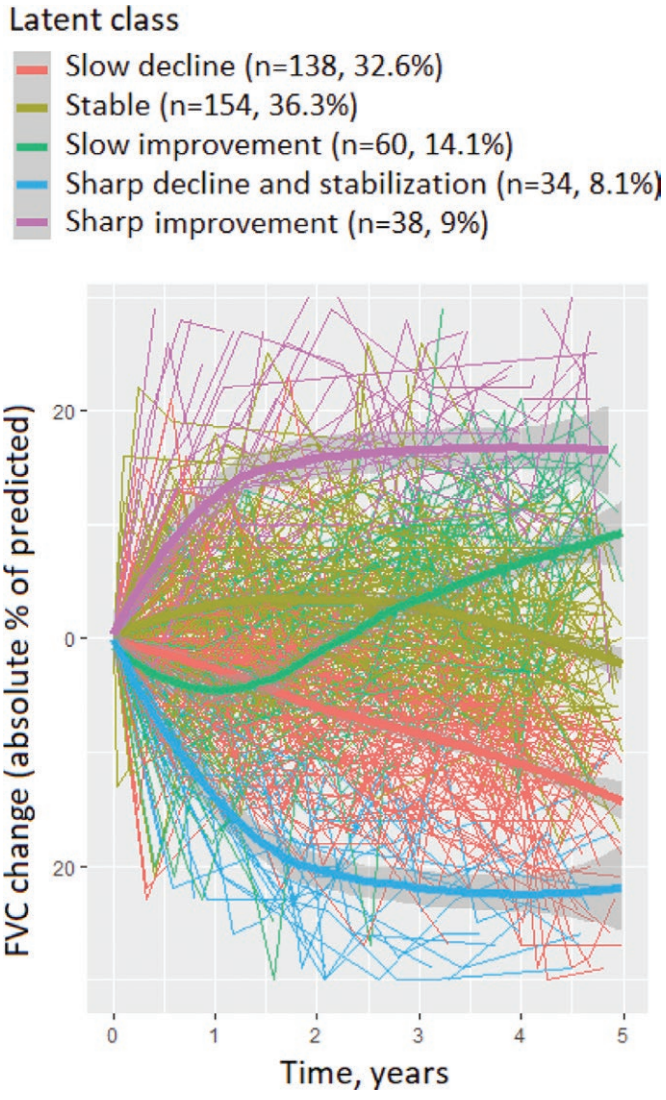


Figure 1. Latent classes of disease progression

Conclusion: PODs in SSc-ILD are associated with mortality with an increased risk for those with a sharply or slowly declining lung function. The use of PODs for patients' stratification may be useful for prognostication and patient counselling as well as for clinical trial design.

REFERENCES: NIL.

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Disclosure of Interests: None Declared.

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POS0949

CLINICAL FACTORS ASSOCIATED WITH PNEUMOCYSTIS PNEUMONIA DESPITE ITS PRIMARY PROPHYLAXIS: A CASE-CONTROL STUDY

Keywords: Infection-related RMDs

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Background: Previous studies have suggested that primary prophylaxis against pneumocystis pneumonia (PCP) using trimethoprim-sulfamethoxazole (TMP-SMX) is beneficial in patients with rheumatologic diseases receiving immunosuppressive drugs[1]. However, there is little evidence for an optimal prophylaxis duration or a time point of prophylaxis withdrawal.

Objectives: This study aims to investigate the risk factors that are associated with PCP occurrence despite its primary prophylaxis, and, ultimately, to provide evidence regarding the ideal schedule for primary PCP prophylaxis.

Methods: This case-control study included treatment episodes of patients with rheumatic diseases who received prophylactic TMP-SMX with immunosuppressive treatment between 2010 and 2022 in a tertiary referral center in South Korea. The index date was defined as the date of starting the prophylactic dose of TMP-SMX. We captured PCP cases that occurred within 1 year from the index date based on the review of the medical record by two independent expert investigators. The effect of clinical factors, such as demographics, underlying disease, immunosuppressive treatment, and pattern of prophylaxis on the PCP occurrence was examined using binary logistic regression.

Results: A total of 1,379 treatment episodes were analyzed, and eleven cases of PCP occurred during the observation—a one-year PCP incidence of 0.80 (95% CI=0.40-1.43) per 100 person-years. In 10 cases (90.9%), PCP occurred after discontinuation of TMP-SMX prophylaxis, with a mean (SD) interval of 185.6 (90.9) days. The mean (SD) duration of prophylaxis in the PCP group was 108.5 (132.3) days. The main reasons for prophylaxis withdrawal in the PCP group were adverse events (5 cases) and treating physicians' decisions (5 cases). The dose of glucocorticoid at the time of prophylaxis cessation was the most critical risk factor for PCP. Patients who were receiving glucocorticoid more than 15 mg/day of prednisone equivalent at the time of TMP-SMX discontinuation showed a significantly higher odds of developing PCP (OR=15.06; 95% CI=1.92-117.94). The prophylaxis duration and presence of structural lung disease were not associated with PCP. This result was consistent in the multivariable analysis adjusted for age, underlying disease, rituximab treatment, azotemia, and lymphopenia (adjusted OR=12.21; 95% CI=1.52-98.24) (Table 1).

Conclusion: Discontinuation of TMP-SMX during glucocorticoid treatment greater than 15 mg of prednisone equivalent significantly increases the risk of PCP, which suggests that a time when glucocorticoids are tapered to less than 15mg/day of prednisone dosage equivalent may be a reasonable time to consider withdrawing PCP prophylaxis.

REFERENCE:

[1] Park JW, Curtis JR, Moon J, Song YW, Kim S, Lee EB. Prophylactic effect of trimethoprim-sulfamethoxazole for pneumocystis pneumonia in patients with rheumatic diseases exposed to prolonged high-dose glucocorticoids. Ann Rheum Dis. 2018;77(5):644-9.

Table 1. Factors associated with PCP despite primary prophylaxis

	Univariable		Multivariable	
	OR (95% CI)	P	OR (95% CI)	P
Age	**1.06 (1.01-1.11)**	**0.02**	1.05 (0.10-1.10)	0.08
Sex, female	0.71 (0.22-2.35)	0.58		
SLE	0.34 (0.04-2.64)	0.30		
AAV	**4.19 (1.27-13.84)**	**0.02**	0.50 (0.08-3.07)	0.46
Other vasculitis	0.65 (0.14-3.02)	0.58		
Inflammatory myopathies	0.55 (0.07-4.33)	0.57		
Rheumatoid arthritis	3.01 (0.38-24.03)	0.30		
Others	3.81 (0.47-30.57)	0.21		
Rituximab	**6.03 (1.82-19.99)**	**<0.01**	4.06 (0.87-18.99)	0.08
Cyclophosphamide	1.55 (0.41-5.87)	0.52		
Mycophenolate mofetil	0.99 (0.13-7.76)	0.99		
Azathioprine	1.00 (0.13-7.90)	1.00		
Prophylaxis duration	0.10 (0.99-1.00)	0.16		
Last Gc dose ≤ 15 mg	**15.06 (1.92-117.94)**	**0.01**	**12.21 (1.52-98.24)**	**0.02**
Azotemia	9.88 (2.13-45.94)	**0.00**	**7.04 (1.31-37.71)**	**0.02**
Lymphopenia	5.18 (1.51-17.81)	**0.01**	3.13 (0.86-11.39)	0.08
Structural lung disease	2.34 (0.71-7.70)	0.16		

* Adjusted for clinical factors with relevant association (P < 0.1) in univariable analysisAAV, ANCA associated vasculitis; Gc, glucocorticoid; SLE, systemic lupus erythematosus

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0950 THE BURDEN OF TEMPOROMANDIBULAR DISORDERS AMONG IMMUNE-MEDIATED RHEUMATIC DISEASES OF THE ADULT: A SYSTEMATIC REVIEW

Keywords: Patient reported outcomes, Pain, Systematic review

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Background: The temporomandibular disorders (TMDs) encompass a heterogenous group of inflammatory and degenerative diseases which impair the masticatory function causing local pain and dysfunctional consequences of the temporomandibular joint (TMJ) [1].
Objectives: To systematically review the literature concerning TMDs in immune-mediated rheumatic diseases (IMRDs) of the adult and synthetize their burden in multiple domains of clinical interest: patient-reported outcomes (PROs), frequencies of signs on physical examination, imaging features, histological findings, and risk factors for their development in patients with IMRDs.
Methods: A literature search on PubMed Central, Embase and Cochrane Library databases was performed, until June 2022, for studies including TMJ outcomes in IMRDs patients compared with healthy controls, other rheumatic diseases or in the assessed IMRDs patients after follow-up and treatment. Among the IMRDs of the adult, original articles investigating TMJ involvement in inflammatory polyarthritides and/or autoimmune connective tissue diseases were considered. The TMJ outcomes used in clinical studies, the prevalence of TMDs in IMRDs and the risk factors for their development were qualitatively synthetized.
The quality of the studies was scored using the Newcastle-Ottawa scale (NOS).
Results: Of the 3259 screened abstracts, 56 papers were included in the systematic review. All of them were evaluated as of fair quality, at least. Most of the papers (77%) investigated TMDs in rheumatoid arthritis (RA) with a prevalence of signs and symptoms varying from 8% to 70% **(Table 1).** The risk factors for TMDs development in RA were female sex, younger age, anti-citrulline peptide antibodies (ACPA) positivity, higher disease activity, cervical spine involvement, cardiovascular and neuropsychiatric comorbidities **(Figure 1).** Ten papers (18 %) evaluated TMDs in spondylarthritides (SpA) reporting a prevalence of symptoms and signs in 12%-80% of patients with higher TMDs prevalence in patients with radiographic spine involvement, skin psoriasis and HLADRB1*01 positivity. Among autoimmune connective tissue diseases (CTDs), systemic sclerosis (SSc) displayed the highest evidence of TMDs PROs and clinical findings (20-93%), followed by systemic lupus erythematosus (SLE) in 18-85%, mixed connective tissue disease (MCTD) in 31-63%, primary Sjögren's syndrome (pSS) in 24-54% and idiopathic inflammatory myopathies (IIMs) in 4-26%. In SSc and SLE, TMDs were more frequent in patients with higher disease activity and duration, correlating with the extent of skin fibrosis in SSc and with renal involvement in SLE.
Conclusion: TMDs in IMRDs display a significant relevance in the rheumatological clinical practice even if they are often overlooked. This burden is epidemiologically important in terms of PROs and clinical findings which correlate with disease activity in RA, SpA, SSc and SLE. The early recognition and multidisciplinary management of TMDs is warranted and should be aimed at hindering the TMJ structural damage maximizing the quality of life of patients.

Table 1. Prevalence of TMJ findings across multiple clinical domains in different IMRDs.

IMRD Domains of TMJ involvement	RA	SpA	SSc	SLE	pSS	MCTD	IIMs
Number of studies investigating TMJ involvement	43/56 (77%)	10/56 (18%)	5/56 (9%)	4/56 (7%)	4/56 (7%)	3/56 (5%)	1/56 (2%)
Prevalence of TMJ PROs	8-70%	12-80%	20-93%	31-66%	24-54%	31%	17-26%
Prevalence of TMJ signs on physical examination (i.e., reduced mouth opening)	30-54%	17-68%	44-71%	41-85%	24-44%	50-63%	4-13%
Imaging findings on X-ray of TMJ	50-66%	30-38%	NA	22%	NA	19%	NA
Imaging findings on computerized tomography of TMJ	61-76%	NA	NA	NA	NA	NA	NA
Imaging findings on magnetic resonance imaging of TMJ	11-95%	6-67%	67-94%	NA	NA	13-93%	NA
Histological findings of TMJ	Synovitis and degenerative changes	NA	NA	NA	NA	NA	NA

Legenda. NA: not assessed. See the text for the other abbreviations.

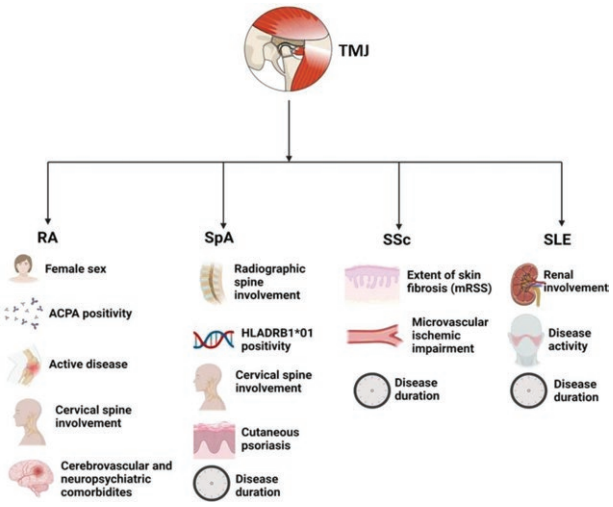


Figure 1. Risk factors for TMJ involvement in RA, SpA, SSc and SLE (created with biorender.com)

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0951 BASELINE PREDICTORS OF SEVERE OUTCOMES IN IMMUNE CHECKPOINT INHIBITOR-INDUCED INFLAMMATORY ARTHRITIS

Keywords: Malignancy, Inflammatory arthritides

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Background: Immune checkpoint inhibitor-induced inflammatory arthritis (ICI-IA) is the most common rheumatic adverse effect of cancer immunotherapy. Patients have dramatically different trajectories; some have a mild self-limited course, while others have severe IA requiring immunosuppression[1]. Additionally, some patients may have persistent IA beyond ICI cessation[1]. Risk factors for severe disease are unknown.
Objectives: To determine which clinical features at baseline rheumatology visit predict severe outcomes such as requirement of immunosuppression in ICI-IA.
Methods: Participants were drawn from a prospective longitudinal study of rheumatic immune related adverse events and had rheumatologist diagnosed ICI-IA. Demographics, cancer history and prior treatment, clinical (e.g.synovitis, tenosynovitis, inflammatory back pain determined by clinician) and laboratory features of arthritis and outcomes were collected at clinic visits. Descriptive statistics were calculated for demographic and clinical features of the whole cohort and for the two groups by primary outcome. The primary binary outcome was requirement of either csDMARDs and/or bDMARDs (determined by failure to wean to < 10 mg prednisone/day); other outcomes were persistence of IA at least 6 months after ICI cessation and requirement of corticosteroids. T-tests or Wilcoxon rank sum tests and Fisher's exact tests were used to compare clinical characteristics by outcome categories. Logistic regression models evaluated univariate associations between clinical features and primary and secondary outcomes. Next, multivariable logistic regression was used to further evaluate these associations, adjusting for potential confounders.
Results: 126 patients with ICI-IA were included. The average age was 60; the majority were female (N=70 56%). The most common cancers were melanoma and lung cancer. Patients were primarily treated with anti-PD-(L)1 agents (N=78 62%) or combination anti-CTLA-4/PD-1 therapy (N=28 22%). Average clinical disease activity index (CDAI) was 17. Of the 126 patients, 53 (42%) required a csDMARD or bDMARD. In univariate logistic regression, higher baseline CDAI (OR 1.05 p=0.01) and presence of tenosynovitis (OR 4 p=0.005) were significantly associated with a higher likelihood of requiring DMARDs; there was a trend toward those treated with prior chemotherapy for cancer being less likely to need DMARDs for IA (OR 0.52 p=0.09). When adjusted for age, gender,

and prior steroid use, tenosynovitis and higher CDAI remained associated with requiring DMARDs and prior chemotherapy was associated with lower likelihood of DMARDs (Table 1). Higher CDAI was also associated with higher likelihood of requiring corticosteroids (1.11 p=0.012). Those positive for rheumatoid factor had a lower likelihood of requiring steroids (0.168 p=0.013). Combination anti-CTLA-4/PD-1 (5.07 p=0.036) therapy and being on steroids at baseline (5.28 p=0.031) were associated with a higher likelihood of persistent IA; there were trends for higher CDAI and tenosynovitis associating with persistence.

Conclusion: Higher levels of disease activity and having tenosynovitis were associated with a higher likelihood requiring immunosuppression beyond corticosteroids for ICI-IA while those treated previously with chemotherapy were less likely to require additional immunosuppression. The presence of risk factors for severe disease at baseline may indicate higher initial steroid dose or earlier adoption of immunosuppression to improve outcomes.

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Table 1. Unadjusted and adjusted odds ratios (OR) for outcome of requiring csDMARDs and/or bDMARDs

	Unadjusted OR	p-value	Adjusted OR	p-value
Age	1.00	0.977	0.99	0.989
Female gender	1.61	0.198	1.41	0.43
Prior Chemotherapy	0.52	0.085	**0.38**	**0.026**
Already on steroids at baseline visit	1.99	0.094	1.74	0.237
Presence of tenosynovitis	**4**	**0.005**	**3.39**	**0.046**
CDAI	**1.05**	**0.01**	**1.05**	**0.028**

Acknowledgements: NIL.

Disclosure of Interests: Laura Cappelli Grant/research support from: Bristol-Myers Squibb, Omer Kamal: None declared, Clifton Bingham Grant/research support from: Bristol-Myers Squibb, Ami Shah Grant/research support from: Kadmon Corporation, Eicos Sciences, Medpace LLC, Arena Pharmaceuticals.

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POS0952 ASSOCIATION BETWEEN SARCOPENIA AND RISK OF MAJOR ADVERSE CARDIAC AND CEREBROVASCULAR EVENTS IN A POPULATION FROM THE UK BIOBANK DATABASE

Keywords: Sarcopenia, Prognostic factors, Comorbidities

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Background: Few studies on the risk of incident major adverse cardiac and cerebrovascular events in presarcopenic and sarcopenic patients have been reported, with contradictory results [1].

Objectives: The objective was to assess the association between presarcopenia and sarcopenia, and higher risk of major adverse cardiac and cerebrovascular events.

Methods: It was a retrospective analysis of the UK Biobank prospective cohort, using data collected between 2006 and 2021. Community-dwelling Caucasian participants aged 37 to 73 years were included if values for Handgrip Strength and Skeletal Muscle Index were available, and if no history of a major adverse cardiac and cerebrovascular event was reported. Exposure was assessed using the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) criteria [2]. Muscle strength was measured using Handgrip Strength, and muscle mass using the Skeletal Muscle Index (from bioimpedance data). Presarcopenia was defined as low Handgrip Strength with normal Skeletal Muscle Index, whereas sarcopenia was defined as low Handgrip Strength with low Skeletal Muscle Index. Participants with presarcopenia and sarcopenia were merged to form a single group (PreSarc) and were compared against a group of non-sarcopenic participants (NonSarc). To determine whether sarcopenia and/or presarcopenia were predictors of major adverse cardiac and cerebrovascular events (composite events: acute myocardial infarction, angina pectoris, ischemic or hemorrhagic stroke, and transient ischemic attack, whether fatal or non-fatal).

Results: A total of 406,411 participants (women: 55.7%; median age: 58.0 (IQR: [50.0; 63.0]) years) were included. At baseline, 18,612 participants (4.6%) were allocated to the PreSarc group. Over a median follow-up of 12.1 years (IQR: [11.4; 12.8]), 28,300 participants (7.0%) were diagnosed with at least one event. Compared to NonSarc, PreSarc was significantly associated with a higher risk of major adverse cardiac and cerebrovascular events (fully adjusted HR=1.25, 95%CI=[1.20; 1.31]). When presarcopenia and sarcopenia were considered independently, they were still associated with a higher risk of all major adverse cardiac and cerebrovascular events (fully adjusted HR=1.24, 95%CI=[1.18; 1.30]) and HR=1.58, 95%CI=[1.31; 1.90], respectively).

Conclusion: In a community-dwelling population, the risk of major adverse cardiac and cerebrovascular events was higher in both presarcopenic and sarcopenic participants.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0953 PROGRESSIVE PULMONARY FIBROSIS IN CONNECTIVE TISSUE DISEASE ASSOCIATED INTERSTITIAL LUNG DISEASES

Keywords: Lungs, Outcome measures

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Background: Progressive pulmonary fibrosis (PPF) is characterized by deterioration of respiratory symptoms, lung function decline and progressive fibrosis on high-resolution computed tomography (HRCT). It is associated with poor prognosis. Patients with connective tissue disease-related interstitial lung disease (CTD-ILD) may also develop PPF and need intensified clinical management. However, different criteria for PPF are used in trials (i.e. INBUILD and RELIEF) and the ATS/ERS/JRS/ALAT 2022 guideline.[1-3] This variety in criteria complicates study comparison and clinical implication.

Objectives: To explore the prognostic relevance for mortality of different PPF criteria in patients with CTD-ILD.

Methods: This is a single center retrospective cohort study in patients with CTD-ILD or interstitial pneumonia with autoimmune features between 2005 and 2021. The prognostic relevance was compared between the INBUILD criteria[1], the ATS/ERS/JRS/ALAT 2022 criteria[3], and the simplified progressive fibrosing (simplified PF) criteria used in a previous cohort (≥10% relative decline in FVC, ≥15% relative decline in DLCO, or progression of fibrosis on HRCT within two years)[4] in the time-dependent receiver operator characteristic model.

Results: The cohort consisted of 230 patients. The median age was 63 years (IQR 54—69), and 122 (53%) were female. The most prevalent CTD was rheumatoid arthritis (n=77, 33%), followed by 38 (17%) patients with idiopathic inflammatory myopathies and 33 (14%) with primary Sjögren's syndrome. Various HRCT patterns were observed at baseline: UIP in 63 (27%) patients, fibrotic NSIP in 21 (9%), cellular NSIP in 25 (11%), mixed NSIP in 79 (34%), OP in 34 (15%), two (1%) mixed NSIP/OP, and other patterns in six. The median follow-up period was 6 (3—9) years. Mortality risk was independently associated with age (adjusted HR 1.07, $p < 0.001$), smoking history (adjusted HR 1.90, $p = 0.045$), extent of fibrosis on HRCT at baseline (adjusted HR 1.05, $p = 0.018$) and baseline DLCO % of predicted (adjusted HR 0.97, $p = 0.013$). PPF was observed in 61 (27%) patients meeting INBUILD criteria, 53 (23%) meeting ATS/ERS/JRS/ALAT 2022 criteria, 136 (59%) meeting simplified PF criteria and 125 (54%) when using simplified PF criteria with a threshold for HRCT ≥ 5% increase in the extent of fibrosis. The prognostic relevance for mortality did not differ between simplified PF criteria, INBUILD and ATS/ERS/JRS/ALAT 2022 criteria; the prognostic relevance improved when the simplified PF criteria defined HRCT progression with a ≥5% increase in fibrosis. (Figure 1)

Conclusion: Higher age, smoking, increased extent of fibrosis and low baseline DLCO were associated with poor prognosis. The prognostic value was similar between the different PPF criteria and increased during the first three years and achieved a plateau thereafter.

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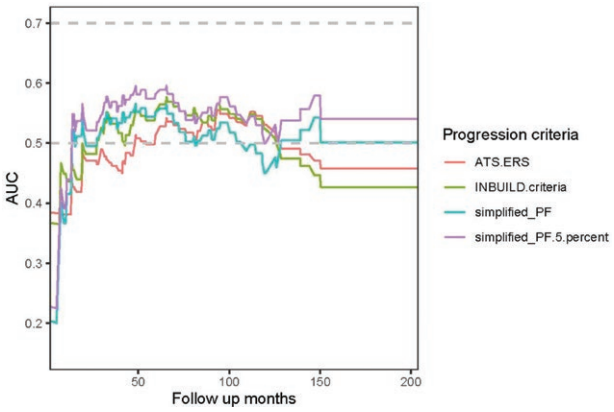


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: Yu-Hsiang Chiu: None declared, Maaike Koops: None declared, Mareye Voortman: None declared, H. Wouter van Es: None declared, Lucianne Langezaal: None declared, Paco Welsing: None declared, Anna Jamnitski: None declared, Anne Wind: None declared, Jacob M. van Laar Grant/research support from: Grant from Boehringer, Astra Zeneca, MSD, Roche, J.C. Grutters: None declared, Julia Spierings Grant/research support from: A grant from Boehringer.
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POS0954 CLINICAL FEATURES AND GENOMIC LANDSCAPE OF MYELOPROLIFERATIVE NEOPLASM (MPN) PATIENTS WITH AUTOIMMUNE AND INFLAMMATORY DISEASES

Keywords: Outcome measures, Genetics/epigenetics, Descriptive studies

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Background: Autoimmune and inflammatory diseases (AID) are associated with myeloid malignancies[1], and include both organ-specific diseases and systemic inflammatory disorders. While the occurrence of associated AID reaches up to 15-20% in myelodysplastic neoplasms (MDS) patients[2,3], its prevalence in the context of myeloproliferative neoplasm (MPN) remains unknown. In patients with a history of AID, the risk of developing MPN was increased[4], suggesting a correlative link between the two disorders, but data regarding the characterization of AID in MPN patients remain scarce and the lack of studies prevents from identifying potential risk traits that may underline a common physiopathology.
Objectives: We conducted a single center retrospective study to describe the prevalence, clinical and biological features of AID in MPN patients. We also reported the mutational landscape of MPN with associated AID, along with its prognostic impact.
Methods: All patients with a diagnosis of Philadelphia-negative MPN according to the World Health Organization's criteria, followed between January 2011 and January 2021 in our center were included. Clinical and biological characteristics at the time of diagnosis and follow-up were collected. Next-generation targeted sequencing was performed targeting a panel of 36 genes involved in myeloid malignancies. AID diagnosis was based on recommended international criteria specific to each AID. Patients with interferon-alpha-induced AID were excluded from this study.
Results: A total of 1541 MPN patients were included, including 95 (6%) patients with AID who were compared to the remaining 1446 (94%) patients without AID. Median age was 51.6 [6.6; 98.3] years at MPN diagnosis in the whole cohort. Female patients were predominant within the AID group (62 (65%) versus 773 (54%), p=0.03). Within the AID cohort, a total of 103 diagnoses of AID were reported in 95 patients, including 48 organ-specific AID (47%) (autoimmune hypothyroidism (n=33), inflammatory bowel diseases (IBD, n=7), neuroinflammatory disorders (n=4), autoimmune cytopenia (n=2), glomerulonephritis (n=1) and pernicious anemia (n=1)), 13 inflammatory arthritis (13%), 9 connective tissue diseases (9%), 9 dermatosis (9%), 6 systemic vasculitis (6%) and 18 unclassified AID (17%). Molecular sequencing was performed in 998/1541 (65%) patients and the prevalence of driver and additional mutations did not differ between the MPN with or without AID. The prevalence of *TET2* mutations was higher in the AID cohort (21/65, 32% versus 208/993, 22%), although not reaching statistical significance (p=0.08). After a median follow-up of 8.3 $_{IQR}$[3.7-14.3] years, the association with AID did not impact overall survival (p= 0.67), MDS/AML transformation free survival (p=0.37) or secondary myelofibrosis-free survival (p=0.91).
Conclusion: Our data suggest that the prevalence of AID is similar in MPN patients to that of the general population, and that the distribution and presentation of AID in MPN patients is also similar. *TET2* mutations are highly prevalent in MPN patients with AID suggesting a shared physiopathology. Additional mechanistic studies are needed to further decipher a potential TET2-mediated common physiopathology. The association with AID did not impact MPN patients' outcome.
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Acknowledgements: The authors thank the clinical care team of the Comprehensive Myeloproliferative neoplasms Center for samples and data collection, and the staff of the cellular biology laboratory for excellent technical assistance. The authors also thank the French Intergroup for Myeloproliferative neoplasms (FIM) for insightful discussions.
Disclosure of Interests: None Declared.
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POS0955 PREGNANCY IN CONNECTIVE TISSUE DISEASES: A 30 YEAR FOLLOW-UP STUDY OF 465 PREGNANCIES FROM A SPANISH MONOCENTRIC REGISTRY

Keywords: Pregnancy and reproduction, Sjögren syndrome, Systemic lupus erythematosus

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Background: Pregnancy in patients with connective tissue diseases are known to be at high risk for the occurrence of adverse pregnancy outcomes.
Objectives: To evaluate the pregnancy outcomes in patients with systemic autoimmune diseases, including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), primary Sjögren's syndrome (pSS) and undifferentiated connective tissue disease (UCTD).
Methods: A retrospective and descriptive study was conducted from 1990 to 2020. All data were collected from the medical records of childbearing age women with SLE, SSc, SS and UTCD enrolled in our clinic at the time of their pregnancy and childbirth. The obstetric, maternal and fetal outcomes were collected and compared regarding diagnosis and adverse outcomes.
Results: The study group included 295 patients, 125 patients (42%) with SLE, 50 patients (17%) with SSc, 80 patients (27%) with Sjogren's, 40 patients (14%) with UCTD. A total of 465 pregnancies were registered. The maternal and fetal outcomes are detailed in Table 1 and Figure 1. The mean age at delivery was 31.5±8.5 years and the mean duration of disease was 7.2±5.6 years. Pregnancy loss occurred in 21% of patients, live births in 66% of pregnancies, preterm delivery in 8%, postpartum haemorrhage in 6%, preeclampsia in 5%, placental abnormalities in 4%, ectopic pregnancy in 3%, premature rupture of membranes in 2%. Treatment with HCQ was received in 115 pregnancies in SLE (59%), 21 pregnancies in SSc (24%) 62 pregnancies in pSS (52%) and 32 pregnancies in UCTD (49%). Exposure to corticosteroids and biologics during pregnancy was 23 (18.4%), 6 (12%), 15 (19%) and 3 (7.5%), respectively. Patients with SLE had a higher risk of fetal morbidity, including abortion (p=0.03), mean abortion rate (p=0.03), preeclampsia (p=0.04), ectopic pregnancy (p=0.03), preterm delivery (p=0.02) and postpartum haemorrhage (p=0.01) than patients without SLE. The multivariate model adjusted for age, nulliparity, active disease activity during pregnancy, smoking and exposure to biologics, HCQ and corticosteroids found an association between unfavourable pregnancy outcomes and disease activity (OR 2.4 95% CI (1.3-7.2), p 0.003), whilst HCQ during pregnancy (OR 0.23 95% CI (0.03-0.82) had a protective effect.
Conclusion: 66% of pregnancies in patients with autoimmune diseases resulted in live births. Patients with SLE had higher rates of fetal and maternal morbidity than SSc, pSS and UCTD. Disease activity was associated with unfavourable pregnancy outcomes. Exposure to HCQ had a protective effect during pregnancy. Pregnancy planning and counselling prior to conception of patients with connective tissue diseases leads to a reduction in maternal and perinatal complications.

Table 1. Fetal and maternal morbidity outcomes in SLE, SSc, pSS and UCTD

	SLE	SSc	pSS	UCTD	P value
Total of pregnancies	192	88	120	65	
Age at pregnancy	32.4±4.5	29.5±7.2	30.4±3.5	33.5±2.7	0.45
Smokers	32 (26%)	17 (34%)	25 (31%)	12 (30%)	0.27
Birth	103 (67%)	68 (77%)	90 (75%)	47 (72%)	0.28
Abortion	57 (37%)	12 (14%)	18 (15%)	10 (15%)	**0.03**
Mean abortion number	2.7±0.7	1.1±0.6	2.4±0.3	0.9±0.5	**0.03**
Preeclampsia	15 (9.8%)	3 (3%)	2 (2%)	2 (3%)	**0.04**
Ectopic pregnancy	10 (6.5%)	0	1 (1%)	1 (2%)	**0.03**
Placental abnormalities	8 (5%)	5 (5.7%)	2 (2%)	3 (5%)	0.21
Premature rupture of membranes (PROM)	5 (3.3%)	0	2 (2%)	1 (2%)	0.24
Preterm delivery	20 (13%)	0	8 (6%)	5 (8%)	**0.02**
Postpartum haemorrhage	21 (14%)	0	4 (4%)	1 (2%)	**0.01**

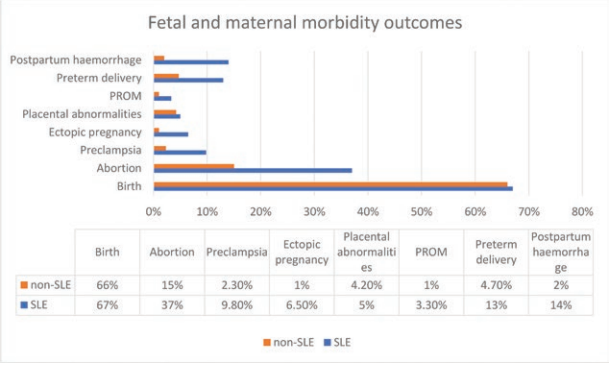


Figure 1. Fetal and maternal morbidity outcomes in SLE and non-SLE patients.

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Disclosure of Interests: None Declared.

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POS0956 **WITHDRAWN**

POS0957 **EPIDEMIOLOGY OF NEUROSARCOIDOSIS DISEASE IN NORTHERN SPAIN 1999-2019: A POPULATION-BASED STUDY**

Keywords: Registries, Lungs, Epidemiology

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Background: Neurosarcoidosis (NS) is a serious and relative uncommon complication of sarcoidosis [**1**]**.** Data on incidence is scarce and varies worldwide.
Objectives: To estimate NS epidemiology in Northern Spain.
Methods: Patients diagnosed with sarcoidosis at a University hospital in Northern Spain, between January 1999 and December 2019 were assessed. Sarcoidosis diagnosis was established according to ATS/ERS/WASOG criteria as follows: compatible clinical and radiological presentation, histopathologic confirmation, and exclusion of other granulomatous diseases. NS was diagnosed according to the NS Consortium Consensus Group [**2**]**.** Demographic and clinical data were collected. The incidence of sarcoidosis between 1999-2019 was estimated by gender, age, and year of diagnosis.
Results: NS was observed in 30 of 234 (12.8%) (19 women/ 11 men) (mean age: 55.0±15.8 years) patients with sarcoidosis. The underlying neurological manifestations were chronic headache (n=13, 43.4%), peripheral neuropathy (n=6, 20.0%), cranial neuropathy (n=5, 16.7%), spinal cord abnormalities (n=3, 10.0%) and aseptic meningitis (n=3, 10.0%). A comparison between different geographical areas is summarized in **Table 1**. There are wide variations in frequency (US:4.8% to France:33.9%), gender predominance and age at diagnosis (31 to 55 years) depending on the geographical area. Nevertheless, most of the patients were diagnosed in the 5th decade of life. Annual incidence of NS in our population area in the 1999-2019 period was 0.11 per 100,000 people, 95% (CI:0.11-0.26); 0.08 (0.07-0.24) in men, 0.13 (0.09-0.24) in women. There were variations in annual incidences, ranging from a minimum value of 0.08 in 2013-2014 to a maximum of 0.19/100,000 people in 1999-2000. A downward trend in annual incidence over time was observed. Nevertheless, the correlation was weak (r^2=0.1135) (**Figure 1**).
Conclusion: The epidemiological characteristics of NS is very different in frequency. Frequency estimated in this study was similar to that of other countries.
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Table 1. Main clinical features and treatment of neurosarcoidosis in different geographical areas

Author, year	Country	cases			Male n (%)		Age at onset years mean ± SD	
		S	NS	%	S	NS	S	NS
Gascón-Bayarri et. al., 2011	Spain	445	30	6.7	ND	10 (33.4)	ND	48.3±ND
Leonhard et. al, 2016	The Netherlands	ND	52	ND	ND	22 (48.0)	44±ND	43.0±ND
Joubert et. al, 2017	France	690	234	33.9	ND	117 (50.0)	ND	31.5±ND
Dorman et. al, 2019	USA	1706	82	4.8	691 (40.6)	43 (52.4)	49±10.8	45.0±11.4
Arun et. al, 2020	UK	ND	80	ND	ND	35 (44.0)	ND	47.8±ND
Goel et al., 2020	India	ND	12	ND	ND	4 (33.4)	ND	44.0± 9.2
Sambon et. al, 2022	Belgium	180	22	12.2	ND	14 (64.0)	ND	40.5±ND
Byg et al., 2022	Denmark	ND	20	ND	ND	11 (55.0)	ND	51.6±ND
Present study, 2023	Spain	234	30	12.8	105 (44.9)	11 (36.7)	48.4±14.8	55.0±15.8

Abbreviations: ND: non data, NS: neurosarcoidosis, S: Sarcoidosis



Figure 1. Trends in age at neurosarcoidosis diagnosis in Cantabria, Spain, in 1999-2019 by gender

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POS0958

PREVALENCE AND RISK FACTORS OF OSTEONECROSIS OF THE FEMORAL HEAD IN PATIENTS WITH ADULT-ONSET STILL'S DISEASE

Keywords: Inflammatory arthritides, Quality of life, Epidemiology

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Background: Adult-onset Still's disease (AOSD) is a rare systemic autoinflammatory disease, characterized by symptoms such as spiking fever, arthralgia, sore throat, and skin rashes. The detailed pathogenesis of AOSD is not yet understood, hence the management often involves the use of corticosteroids. Among glucocorticoid-associated complications, osteonecrosis of the femoral head (ONFH) is rare and not immediately life threatening, however, delayed diagnosis can lead to a significant reduction in patients' quality of life and often requires surgical treatment. Although it is of great importance for rheumatologists to understand ONFH, little is known about ONFH in patients with AOSD because most studies on ONFH in adult have focused on systemic lupus erythematosus (SLE) despite AOSD being heavily glucocorticoid-exposable similar to SLE.
Objectives: To investigate the prevalence of ONFH complications among AOSD patients and explore its risk factors.
Methods: We reviewed all consecutive patients with AOSD who have visited the Keio University Hospital from 2012 to 2022 retrospectively. We investigated the development of ONFH after treatment and assessed relevant clinical features and laboratory data. To compare the frequency of ONFH in patients with AOSD with that in those with other rheumatic diseases, we also investigated prevalence of OFNH in patients with other rheumatic musculoskeletal diseases including SLE, idiopathic inflammatory myopathy (IIM), and vasculitis who had a history of treatment with high-dose (0.8 – 1mg/kg) glucocorticoid. All statistical analyses were performed using JMP 15 (SAS Institute Inc., Cary, NC, USA).
Results: We included 108 AOSD patients in the analysis and collected information from their charts. The mean age of onset was 44 years old, and 77% of the patients were female. Out of 108 patients, 9 (8.3%) developed OFNH throughout the mean observation period of 12.8 years. All 9 patients with OFNH had a history of high-dose corticosteroid therapy, and 8 of 9 (88.9%) received glucocorticoid pulse therapy. Univariate analysis revealed that male and complication of serositis or remarkable leukocytosis (>15000/μL) were associated with development of ONFH in AOSD patients, in addition to the history of treatment with high-dose glucocorticoid and pulse therapy (Table 1.) Next, we compared the frequency of ONFH development among 60 AOSD patients with high-dose corticosteroid treatment history with that of patients with other rheumatic diseases including SLE (n=312), IIM (n=84), small-vessel vasculitis (n=123), and large-vessel vasculitis (n=59). We identified that AOSD patients were second most likely to develop ONFH, following SLE; ONFH prevalence was 15.0% in AOSD, 20.5% in SLE 6.0% in idiopathic inflammatory myopathy, 1.6% in small-vessel vasculitis, and 1.6% in large-vessel vasculitis (Figure 1).
Conclusion: The complication of ONFH is frequent in patients with AOSD, the second highest after SLE in rheumatic musculoskeletal diseases. Glucocorticoid pulse therapy, high-dose glucocorticoid therapy, male sex, and remarkable leukocytosis and serositis are risk factors for developing ONFH.
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Table 1. Risk factors of osteonecrosis of femoral head in patients with Adult-onset Still's Disease

	Odds Ratio	95%CI	p-value
Steroid pulse therapy	31.6	(3.7, 268.1)	<.0001
High-dose glucocorticoid therapy (PSL > 0.8mg/kg/day)	9.9	(1.2, 82.4)	0.0112
Serositis	4.3	(1.0, 19.3)	0.0405
White blood cell count > 15000μL	N.A	N.A	0.0172

N.A: not applicable

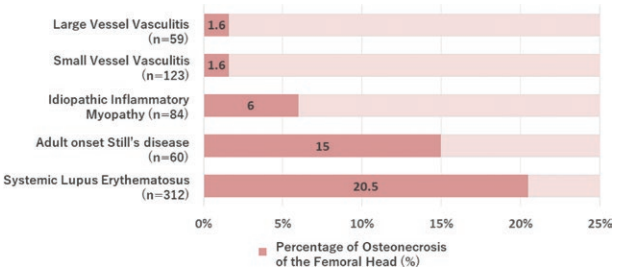


Figure 1. Frequency of osteonecrosis of femoral head among rheumatic musculoskeletal diseases

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0959 **WITHDRAWN**

POS0960 **INCREASED INCIDENCE OF SJÖGREN'S SYNDROME IN THE FEMALE PATIENTS WITH HASHIMOTO THYROIDITIS: A LARGE PROPENSITY SCORE-MATCHED COHORT STUDY**

Keywords: Epidemiology, Sjögren syndrome, Comorbidities

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Background: In clinical practice, we notice that **S**jögren's syndrome (SS) usually coexists with Hashimoto thyroiditis (HT). There were a lot of case reports regarding the coexistence of SS and HT.
Objectives: To determine whether Hashimoto thyroiditis (HT) is a risk factor of Sjögren's syndrome (SS) longitudinally in a very large cohort.
Methods: We conducted a cohort study using TriNetX (Cambridge, MA, USA), a global federated health research network that provides real-time electronic medical record datasets. The diagnosis of HT or SS was based on ICD10 codes. We analyzed the incidence of newly diagnosed SS in the female patients with HT within ten years. Propensity score matching including 38 factors was performed to adjust for demographic variables, comorbidities, and medication use. Kaplan-Meier analysis was used to estimate the probability of the outcome of interest. The hazard ratio (HR) and associated confidence intervals (CI) were calculated along with the proportionality test using R's Survival Package v3.2-3.
Results: We identified 101,590 female patients aged 20-64 years with HT among 54,801,179 patients in the database with ≥ 2 visits between 2012/01/01~2021/12/31. Of these patients, 100,027 were included after exclusion those diagnosed with SS before index date. The control cohort was selected from those females without thyroid disorders or related therapy. After 1:1 propensity score matching, 100,027 patients in either HT or control cohort were analyzed for comparison. After one-year follow-up, the incidence (0.51%) of new cases of SS in the HT cohort was higher than that (0.098%) in the control cohort (HR 4.324, 95% CI 3.483-5.368). During the study period, higher incidence of SS in the HT cohort (1.16%) than in the control cohort (0.36%) was found (HR 3.557, 95% CI 3.151-4.016). Increased incidences of SS in HT cohort were also confirmed in the subgroups of different ages, races and smoking status, and subgroups with or without diabetes mellitus, overweight/obesity, sleep disorder, depression, hypertension and asthma (Figure 1).
Conclusion: This study underlines that HT is a risk factor for developing SS, which implies that SS and HT are 2 autoimmune diseases closely related, and may share some underlying pathophysiological mechanisms.

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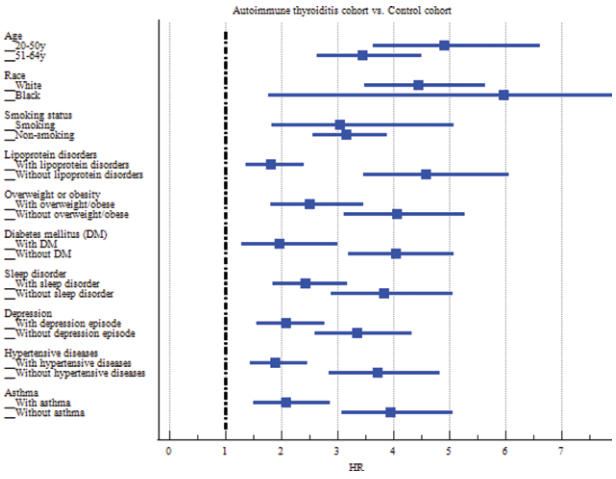


Figure 1. Forest plot_subgroup analyses

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0961

ASSOCIATION BETWEEN AIR POLLUTANTS AND INITIATION OF BIOLOGICAL THERAPY IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A NATIONWIDE, POPULATION-BASED CASE-CONTROL STUDY

Keywords: Epidemiology, bDMARD, Spondyloarthritis

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Background: Ankylosing spondylitis (AS) is a systemic inflammatory disease and the first-line pharmacological therapy includes non-steroidal anti-inflammatory drugs (NSAIDs) for spinal and peripheral joint involvement and immunosuppressants including methotrexate (MTX) and sulfasalazine (SSZ) for peripheral arthritis[1]. Biological therapy under National Health Insurance (NHI) reimbursement is indicated for AS patients without adequate response to first-line therapy in Taiwan. Initiation of biologics such as tumor necrosis factor inhibitors and interleukin-17 inhibitors may act as a proxy for high disease activity. Outdoor air pollution has been found to trigger a systemic inflammatory response[2]. Therefore, we hypothesized that air pollutants may be associated with biologics use in AS patients.
Objectives: To investigate the association between air pollutants and initiation of NHI-reimbursed biologics indicated for high disease activity in patients with AS.
Methods: We conducted a nationwide case-control study using the Taiwan National Health Insurance Research Database, and incidental AS patients from 2003 to 2013 were identified. We excluded those with visits with a diagnosis of rheumatoid arthritis, those treated with biologics including etanercept, adalimumab, and golimumab before the first date of visit with AS diagnosis, and those without outpatient visits after 2009. We identified all AS patients initiating biologics for active AS as biologics cases, and non-biologics controls for those who didn't. Index date was designated as the date of initiation of first biologics for cases and the date of first outpatient department visits each year for controls. We matched both groups at a 1:4 ratio for gender, age at first biologic initiation (± 3 years), year of first AS diagnosis, and disease duration (± 0.3 year), and finally included 584 biologics cases and 2336 matched controls. With aid of a spatio-temporal model built by a deep-learning approach, we used the hourly concentrations of ambient air pollutants from 60 air quality censoring stations to estimate the mean exposed levels of air pollutants, including PM2.5, PM10, NO2, CO, SO2, and O3, at 374 residential locations in Taiwan within one year before index date. We examined the association of biologics initiation and air pollutants using conditional logistic regression analyses shown as adjusted odds ratio (aOR) with 95% confidence intervals (CIs) adjusting for potential confounders within one year before index date including disease duration, urbanisation level, monthly income, Charlson comorbidity index (CCI), extra-articular manifestations (i.e., uveitis, psoriasis, and inflammatory bowel disease), and use of medications for AS.
Results: The initiation of NHI-reimbursed biologics was associated with disease duration (aOR, 8.97; 95% CI, 5.99–13.46), CCI (aOR, 1.31; 95% CI, 1.12–1.53), psoriasis (aOR, 25.06; 95% CI, 9.47–66.35), use of NSAIDs (aOR, 23.66; 95% CI, 8.96–62.46), MTX (aOR, 4.53; 95% CI, 2.93–7.00) and SSZ (aOR, 12.15; 95% CI, 8.98–15.45), prednisolone equivalent dose (mg/day) (aOR, 1.11; 95% CI, 1.05-1.18). After adjusting for potential confounders, it was associated with exposure to CO (per 1 ppm) (aOR, 8.58; 95% CI, 2.02–36.35), and NO2 (per 10 ppb) (aOR, 0.23; 95% CI, 0.11–0.50).
Conclusion: Use of NHI-reimbursed biologics, a proxy for high disease activity, in AS patients was positively associated with CO level, but negatively associated with NO2 level. Further studies are warranted to confirm our findings and elucidate the mechanisms.

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POS0962

DIFFERENCE IN CLINICAL AND SEROLOGICAL CHARACTERISTICS OF ADULT ONSET STILL'S DISEASE BETWEEN ELDERLY-ONSET AND YOUNG-ONSET PATIENTS

Keywords: Rare/orphan diseases, Epidemiology

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Background: Adult-Onset Still's Disease (AOSD) is a systemic autoinflammatory disease of unknown etiology characterized by fever, skin rash, and arthritis. AOSD generally develops in young adults, with the mean age at onset in the 30 to 40 years old and female dominant. However, the distribution of age at diagnosis has recently shifted towards older in patients with AOSD, as well as other rheumatic musculoskeletal diseases. The clinical manifestations of patients with elderly-onset AOSD have not been characterized yet, and understanding the characteristics of patients with elderly onset AOSD is essential for appropriate management.
Objectives: To clarify the clinical manifestations of patients with elderly onset AOSD.
Methods: We reviewed consecutive patients with AOSD who had visited Keio University Hospital from 2012 to 2022 retrospectively. We divided them into two groups according to the onset age. The age for elderly-onset AOSD was defined as ≥ 65 years. We compared their clinical characteristics, laboratory findings, and image examination data. All statistical analyses were performed using JMP 15 (SAS Institute Inc, Cary, NC, USA).
Results: We included 103 patients with AOSD in the analysis. Among them, 20 (19%) developed AOSD at age 65 or older and were categorized as elderly-onset. The median age of the elderly-onset and young-onset patients was 78 and 47 years, and female proportion was 75% and 82%, respectively. The proportion of elderly-onset AOSD patients significantly increased from 2000s, with the highest of 30% after 2010s (Figure 1). In the elderly-onset group, the frequency of serositis, interstitial lung disease, and median Pouchot Score were significantly higher than the young–onset group (70% vs 8%, p<0.001; 26% vs 6%, p=0.009; 7 vs 6, p=0.014, respectively). On another front, typical rash, sore throat, and splenomegaly were less frequent (40% vs 74%, p=0.039; 40% vs. 67%, p=0.026; 21% vs 50%, p=0.025, respectively, Table 1). The duration of hospitalization was longer (48 vs 30 days, p=0.03), and the yearly incidence of hospitalization was significantly higher in the elderly-onset group (0.86/year vs 0.24/year, p<0.001). Hospitalization for AOSD flare or recurrence was comparable between the groups (44% vs 50%, p=0.632), while hospitalization due to infectious complications was more frequently observed in the elderly-onset group.

Table 1. Clinical characteristics of young and elderly-onset AOSD

	Younger-onset AOSD (n=83)	Elderly-onset AOSD (n=20)	p Value
Age at diagnosis (years)	**47**	**78**	**<0.001***
Sex (Female %)	62(75%)	14(82%)	0.501
Death (n (%))	4(4.8%)	2(10.0%)	0.330
Observation period (year)	**7.8(3.4-14.7)**	**3.5(1.9-5.8)**	**0.008***
Length of Hospitalization (Day)	**27(0, 56)**	**79(36.5, 169.5)**	**<0.001**
Clinical Characteristics			
High fever (>39℃)	46(92%)	17(85%)	0.399
Pharyngalgia	**53(67%)**	**8(40%)**	**0.026***
Typical rash	**57(74%)**	**8(40%)**	**0.004***
Myalgia	30(65%)	8(44%)	0.128
Arthralgia	72(87%)	19(95%)	0.302
Lymphadenopathy	58(88%)	14(70%)	0.058
Hepatomegaly	53(94.6%)	16(80.0%)	0.073
Splenomegaly	**33(50%)**	**4(21%)**	**0.025***
Serositis	**6(8%)**	**14(70%)**	**<0.001***
Pleuritis	**6(8%)**	**14(70.0%)**	**<0.001***
Pericarditis	**6(8%)**	**7(35%)**	**0.003***
Interstitial lung disease	**4(6%)**	**5(26%)**	**0.009***
White blood cell (/μL)	15450 (11700-19335)	16250 (10978-19958)	0.838
CRP (mg/dL)	15.8(7.9-19.7)	14.1(7.1-24.0)	0.620
Ferritin (ng/mL)	3373 (990-9020)	4565 (1306-13640)	0.747
Pouchot score	**6(4-6)**	**7(5-7.8)**	**0.013***

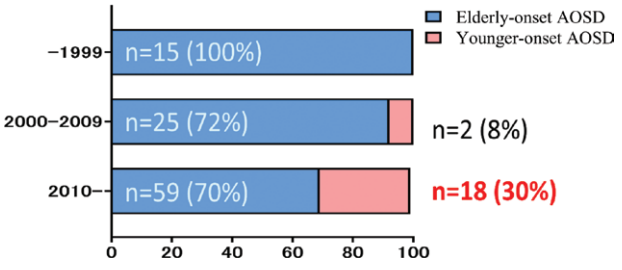


Figure 1. Trends in the proportion of young and elderly-onset AOSD

Conclusion: The frequency of patients with elderly-onset AOSD has been increasing in recent years. Patients with elderly-onset AOSD had significantly characteristic clinical features in comparison with those with young-onset AOSD. Attention should be made for infectious complications as well as AOSD flare in patients with elderly-onset AOSD.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0963 PERINATAL DEATHS IN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES

Keywords: Mental health, Pregnancy and reproduction

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Background: The grief over the death of a baby around the date of birth registers becomes a traumatic event and generates emotional distress, changes in sleep and eating patterns, vulnerability to illness and an increased risk of maternal mortality up to two years following the loss [1]. In México during 2021, 23,000 fetal deaths were registered: 83.5% were before birth, 15.3% during birth and 1.2% was not specified [2]. Women with autoimmune rheumatic diseases (ARDs) have greater risk of perinatal loss, the correct psychological approach is fundamental in the grieving process when these events occur.

Objectives: Describe the frequency and characteristics of the perinatal loss (PL) in women with ARDs.

Methods: A descriptive, observational, cross-sectional study was conducted; we selected patients with history of PL from 2017 to date. Clinical records from the Pregnancy and Rheumatic Diseases Clinic (CEER) from the Hospital University "Dr. José Eleuterio González" in México were revised to obtained ARDs, obstetric clinical history, socioeconomic studies and the Edinburgh Postnatal Depression Scale (EPDS) scores.

Results: From the 79 patients that have been admitted to the clinic, 16 (20%) had PL. The ARDs more frequent was Rheumatoid Arthritis (RA) with 7 (43.8%) patients, Systemic Lupus Erythematosus (SLE) with 6 (37.5%) and other diagnosis (Dermatomyositis, Antiphospholipid Syndrome and UCTD) with 3 (18.9%), other characteristics are displayed in **table 1**. Twelve of these patients have their ARDs active during their pregnancy, 4 of them didn't continue with their rheumatic treatment after the event. Regarding the PL; 6 (37.5%) experienced the loss during the first trimester, 3 (18.7%) in the second trimester and 1 (6.2%) in the third trimester and 6 (37.5%) were neonatal losses. From all the pregnancies, 9 were not planned and 13 were desired. Grieving counseling was offered to the patients, only 5 (31.2%) get the counseling for an unspecified period of time. All the patients were asked to respond the EPDS; only 11 (69%) of them answered it and 3(27%) got a score greater than 13 (need for follow up of possible depressive symptoms). Of this deaths, one was in the second trimester and two were after birth. Scores greater than 13 were correlated with education, marital status, total number of PL and agreeing to the grieving counseling. No statistically significant correlation was found.

Conclusion: We have a 20% loss rate in our population. Women with ARDs that experienced one or more perinatal deaths could have greater risk to develop physical and emotional complications after the event. It's necessary to develop a proper guideline to treat our patients and prevent physical and emotional struggles.

Table 1. Clinical characterization

	Loss during pregnancy (n=10)*	Neonatal loss(n=6)*
Age(mean)	33.7	24.33
Years of education, n(%)		
<9 years	5(50%)	1(17%)
High School	5(50%)	5(83%)
Marital Status, n(%)		
Single	2(20%)	-
Married	3(30%)	1(17%)
Common law marriage	5(50%)	5(83%)
Occupation, n(%)		
Student	-	1(17%)
Housewife	9(90%)	2(33%)
Employed	1(10%)	3(50%)
Total of Deaths (mean)+	1.5	1.5
Rheumatic Diagnosis		
Rheumatoid Arthritis	6(60%)	1(17%)
Systemic Erythematosus Lupus	3(30%)	3(50%)
Other diagnosis	1(10%)	2(33%)

***Two groups: losses during pregnancy and after birth+Total of perinatal deaths in their life**

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Disclosure of Interests: None Declared.

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POS0964 RELATIONSHIP BETWEEN PM2.5 PARTICLE FROM HOUSEHOLD AIR POLLUTION AND INFLAMMATORY AND EPIGENETIC MARKERS IN RHEUMATIC PATIENTS FROM AN INDIGENOUS COMMUNITY IN CHIAPAS: BASELINE STUDY

Keywords: Cytokines and chemokines, Genetics/epigenetics, Lifestyles

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Background: Chronic exposure to household air pollution (HAP) from cooking by biomass leads to noncommunicable diseases as chronic obstructive pulmonary disease or lung cancer (1), but it is less well known if it could promote epigenetic or proteomic changes leading to autoimmune susceptibility. HAP remains a serious health problem for poor and marginalized indigenous communities. Recent studies have shown a high prevalence of rheumatic disease in Latino American indigenous people (2), but it is unknown if HAP and the PM2.5 particles, could be a risk factor for the pathogenesis of rheumatic diseases.

Objectives: To evaluate the relationship between the levels of PM2.5 derived from HAP and levels of inflammatory and epigenetic markers in rheumatic patients from an indigenous community in Chiapas, México.

Methods: Cross-sectional study nested in a cohort of patients with rheumatic disease in a Tzotzil indigenous community in Chiapas (Southern Mexico). Following the COPCORD methodology and employing an instrument adapted and translated into the local language, people with chronic pain were identified from the adult inhabitants of the community. Rheumatic disease diagnosis was made by a certified rheumatologist. Baseline blood samples were collected from rheumatic patients and controls without rheumatic disease. PM2.5 particle ($\mu g/m^3$) were measured in house indoor air continuously for 37 hours and the mean and accumulated levels calculated. Blood levels of cytokines IL-6, IL-8 and MCP-1 and epigenetic markers (H3K18ac and 5-methylcitosine%) were determined by ELISA. Comparisons between groups were analyzed using the Mann-Whitney U tests. Spearman correlation testing was employed to correlate PM2.5 particle and baseline markers levels. Statistical significance was set at 0.05%.

Results: The indigenous community is made up of 123 adults who live in 53 houses, with an average age of 38.3±16.2 years, where 61.2% are women and 43% only speak local language. Of a total of adult inhabitants, 69 people with chronic pain and 14 patients with different rheumatic diseases (11.4%) were identified. Additionally, 25 biological samples were collected from volunteers without rheumatic disease. When comparing the inflammatory levels and epigenetic markers in the baseline blood samples between these two groups, no significant differences were found. The mean PM2.5 particle inside the houses was 114.5±140.1 $\mu g/m^3$ (8.23-462.9), while for control measurements outside it was 9.1±5.5 $\mu g/m^3$ (4-14.9). However, when comparing PM2.5 levels at homes of patients and controls, no significant differences were found (40.99 vs. 65.19 $\mu g/m^3$). Likewise, no significant correlation was observed between inflammatory markers or epigenetic markers, either when evaluating as group or as a whole. It is necessary to complete the baseline study by evaluating citrullination levels in sputum and blood samples, as well as perform a deeper analysis of exposure time to high levels of the PM2.5 particle.

Conclusion: We found no relationship between PM2.5 levels and the levels of inflammatory or epigenetic markers, suggesting that HAP could have a more complex pathogenesis than expected on rheumatic health.

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Disclosure of Interests: None Declared.

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POS0965 SEVERITY AND PROGRESSION OF RADIOGRAPHIC HAND OA IS NOT ASSOCIATED WITH PROGRESSION OF RADIOGRAPHIC KNEE OA: THE IMI-APPROACH COHORT

Keywords: Prognostic factors, Bone diseases, Osteoarthritis

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Background: Osteoarthritis (OA) frequently affects multiple joints including the knees and hands. Currently, it is unknown which patients with knee OA have the highest risk to progress, and how these patients can be identified.

Objectives: To investigate the association of radiographic hand OA and its progression with radiographic knee OA progression over two years of follow-up.

Methods: We used baseline and two-year follow-up data from the Applied Public-Private Research enabling OA Clinical Headway (IMI-APPROACH) cohort. This cohort consists of participants fulfilling the American College of Rheumatology clinical knee OA classification criteria who were likely to have radiographic joint space width loss and/or knee pain progression based on machine learning. Participants and OA characteristics were collected using validated questionnaires and tests. Radiographs of both knees and both hands were scored paired in known time order. Joints were scored according to Kellgren and Lawrence (KL) assessing both knees and both hands (DIPJs, PIPJs, IPJs, MCPJs and CMC1Js (range 0-4 for each joint)). Osteophytes and joint space narrowing (JSN) were scored on 0-3 scales in the bilateral DIPs, PIPs and CMC1s and as absent/present in the IPJs and STTs according to the OARSI atlas, bilateral medial and lateral femoral and tibial osteophytes were scored (0-3 scale), as well as medial and lateral tibiofemoral JSN (0-3 scale). Radiographic knee and hand OA progression were defined as a difference larger than the minimal detectable difference (MDD; based on repeated scoring of 30 radiographs) for the concerning score. Participants that had a knee replacement during follow-up (n=22) were considered as progressors. Logistic regression analyses were used to assess the association of the severity (sum score) or progression of hand OA with knee OA progression for osteophytes, JSN and KL score separately, adjusted for potential confounders (age, sex, BMI and radiographic hand and knee baseline scores).

Results: There were 222 participants with radiographic data on both knees and both hands at baseline and two years (mean baseline age 66 (standard deviation (SD) 7), 171 (77%) women, mean BMI 27.7 (SD 5.0)). Any radiographic abnormality at baseline (osteophyte, JSN or KL score >0) was present in 195 participants (88%) in any knee and for 217 (98%) in any hand. Baseline and two-year radiographic outcomes are shown in **Table 1**. Radiographic hand OA features at baseline were not associated with knee OA progression of the same features (adjusted odds ratio (95% confidence interval (OR (95% CI)) for osteophytes 0.98 (0.95;1.01), for JSN 1.01 (0.98;1.04) and for KL score 1.00 (0.97;1.02)). Osteophyte and KL score progression in the hands were not associated with knee progression of the same features (adjusted ORs 0.62 (95%CI 0.30;1.23) and 0.94 (95%CI 0.42; 2.00), respectively). Those with hand JSN progression had a crude OR of 2.45 (95%CI 1.01;5.70) for knee JSN progression (adjusted: 2.24 (0.88;5.42)).

Conclusion: Radiographic hand OA severity and progression was not associated with a higher risk of progression of radiographic knee OA. These data indicate that radiographic hand OA does not add to identify radiographic knee OA progressors, and suggest different underlying pathogenetic mechanisms playing a role in these two phenotypes.

Table 1. Radiographic hand and knee osteoarthritis scores (n=222)

Score (range)	Baseline (median, interquartile range)	Two years (median, interquartile range)	Minimal detectable difference	Number of participants with progression (%)
Knees				
Osteophyte sum score (0;24)	4 (1;7)	5 (2;9)	1.1	81 (38%)
JSN sum score (0;12)	1 (0;3)	2 (1;4)	1.24	32 (15%)
KL sum score (0;8)	3 (1;4)	3 (2;5)	0.65	53 (25%)
Hands				
Osteophyte sum score (0;58)	10 (5;27)	10.5 (6;19)	1.7	60 (28%)
JSN sum score (0;58)	4 (1;9)	5 (1;11)	1.98	39 (18%)
KL sum score (0;120)	16 (9;27)	17 (10;29)	1.73	55 (26%)

Progression was defined as a change larger than minimal detectable difference. Abbreviations: JSN = joint space narrowing, KL = Kellgren and Lawrence.

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Acknowledgements: NIL.

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POS0966 THE RISK OF INFLUENZA IN PATIENTS WITH SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES-FOCUS ON PRIMARY SJOGREN'S SYNDROME, POLYMYOSITIS/DERMATOMYOSITIS AND SYSTEMIC SCLEROSIS

Keywords: Sjögren syndrome, Systemic sclerosis, Myositis

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Background: Influenza vaccine is recommended in patients with most systemic autoimmune rheumatic diseases (SARDs). However, the risk of influenza was less studied in the SARDs other than rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).

Objectives: This study aimed to investigate the risks of influenza-related hospitalization in patients with SARDs, including primary Sjogren's syndrome (pSS), polymyositis/dermatomyositis (PM/DM), systemic sclerosis (SSc), RA and SLE.

Methods: This is a nationwide population-based cohort study analyzing the National Health Insurance Database in Taiwan. Patients with catastrophic certification of each SARD were identified. The risks of influenza-related hospitalization in patients with each SARD were compared with their age- and sex-matched non-AIIRD cohort (1:2). Incidence rates (IR) with incidence rate ratios (IRR) in various AIIRDs were analyzed.

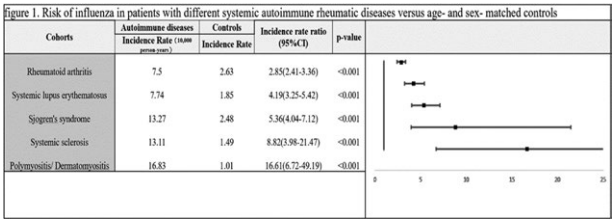
Results: Totally, 48,905 patients with RA, 24,143 patients with SLE, 16,891 patients with pSS, 2,633 patients with SSc and 2561 patients with PM/DM were identified, with basic characteristics shown in table 1. The IR of hospitalization due to influenza was highest in patients with PM/DM (Figure 1) followed by pSS, SSc, SLE and RA. In comparison with their age- and sex-matched controls,

the risk was highest in patients with PM/DM with an IRR of 16.83, followed by patients with SSc, pSS, SLE and RA.

Conclusion: Patients with PM/DM, SSc, pSS, RA and SLE had significant increased risk of influenza-related hospitalization. In comparison with each matched controls, PM/DM, SSc and pSS cohorts had even higher IRR than that of the SLE and RA cohorts, whose risks of influenza and the benefit of vaccination were well-known. Considering the risk, patients with these SARDs should follow the recommendations to have influenza vaccine every year and further study about the benefit of vaccine in patients with DM/PM, SSc and pSS are needed.

Table 1. Clinical characteristics of systemic autoimmune rheumatic diseases and the age- and sex-matched cohorts

Variables	Patients with autoimmune diseases	Age- and sex-matched controls	*p* value
Rheumatoid arthritis	**n =48905**	**n =97810**	
Mean age (SD), years	52.50(15.61)	52.52(16.61)	0.813
Female, n (%)	37659(77.0%))	75318(77.0%)	1
Influenza, n (%)	291(0.60%)	297(0.30%)	<0.001
Systemic lupus erythematosus	**n =24143**	**n =48286**	
Mean age (SD), years	35.56(15.84)	35.56(15.84)	0.952
Female, n (%)	21308(88.3%)	42616(88.3%)	1
Influenza, n (%)	170(0.70%)	99(0.21%)	<0.001
Systemic sclerosis	**n =2633**	**n =5266**	
Mean age (SD), years	50.04(49.44)	50.02(49.60)	0.965
Female, n (%)	1979(75.2%)	3958(75.2%)	1
Influenza, n (%)	25(0.95%)	9(0.17%)	<0.001
Sjogren's syndrome	**n =16891**	**n =33782**	
Mean age (SD), years	54.21(14.35)	54.19(14.35)	0.848
Female, n (%)	15025(89.0%)	30050(89.0%)	1
Influenza, n (%)	108(0.64%)	97(0.29%)	<0.001
Polymyositis/Dermatomyositis	**n =2561**	**n =5122**	
Mean age (SD), years	46.56(18.09)	46.57(18.10)	0.969
Female, n (%)	1714(66.9%)	3428(66.9%)	1
Influenza, n (%)	27(1.05%)	6(0.12%)	<0.001



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POS0967

MORTALITY-RELATED HEALTH METRICS IN RHEUMATIC AND MUSCULOSKELETAL DISEASES AN EPIDEMIOLOGICAL ANALYSIS OF A NATIONWIDE REGISTER-BASED COHORT

Keywords: Geographical differences, Registries, Epidemiology

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Background: Rheumatic and musculoskeletal diseases (RMDs) have become leading causes of death (CODs)[1,2]. However, few study has provide an integrated overview of mortality burdens, leaving a care gap between regions[3]. Therefore, estimates on mortality burdens of RMDs and their relationships with socioeconomic factors are essential for prioritizing health policies, especially in low-to-middle income countries (LMICs).

Objectives:

- To provide an integrated atlas of mortality-related health metrics of 9 RMDs, including RA, SpA, SLE, SS, IIM, SSc, BD, TAK, and AAV.
- To illustrate the associations between disease burdens of RMDs and development indicators from multiple aspects.

Methods: A nationwide multicentre cohort was linked to Nation Mortality Surveillance System. RMD ascertainment was based on classification criteria, death case ascertainment was following ICD-10 codes. Data collection was conducted, followed by a 3-phase imputation and sensitivity analyses. CODs, SMRs, and life expectancies were estimated. A composite indicator, human development index (HDI), and indicators in economy, healthcare, and education were adopted as area-level socioeconomic status indicators. Mixed-effects meta-regression models were established to explore impacts of socioeconomic indicators.

Results: Between 2008 and 2021, 175 846 individuals were included (Figure 1). AAV, IIM, and SSc ranked top 3 diseases with the highest fatality rates over 10% and lowest survival rates within 10 years after the first diagnosis of RMDs. Principal immediate CODs in patients with RMDs are shown in Figure 1. Adjusted SMR was highest for TAK, followed by IIM, SSc, SLE, AAV, BD, and SS (Figure 1). The mortality risk of patients with RA was generally comparable with overall population. Early disease-onset is a risk factor of excess death in both male and female patients with CTDs. Higher HDI was associated with significant increases in mortality risks in both RA and SLE (SMR ratio 12.24 and 5.15 for 1-unit increase in HDI, p<0.001 and p=0.080) patients compared with region-specific general population. More medical institutions (SMR ratio 0.95 for 1 more medical institution per 10 000 resident population, p=0.005) and hospital beds (SMR ratio 0.35 for 1 more hospital bed per 100 resident population, p=0.131) were protect factors of excess mortality in SLE. In overall patients, SS, SLE and AAV, IIM and SSc, had mild, moderate, and strong associations with the loss in life expectancy, respectively (Figure 1).

Conclusion: This study relied on the biggest nationwide register-based cohort of more than 170 000 patients with RMDs confirmed by rheumatologists. We observed that mortality risk (up to 4.5 times) and loss of life years (up to 25 years at the age of 10) in patients with RMDs can be in substantial excess versus general population. Additionally, our study provides the first systematic account that the mortality burdens of RMDs have a complicate relationship with the level of regional deprivation. Increasing mortality burdens associated with RMDs implied the relative insufficiency of capacity building of diagnosis and treatment in RMDs in LMICs.

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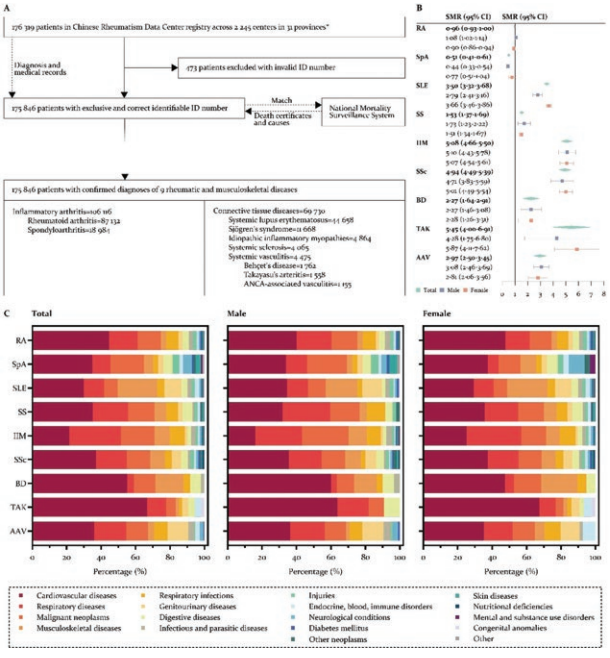


Figure 1. Patient flow chart, standardized mortality ratios (SMRs) of rheumatic and musculoskeletal diseases (RMDs), and immediate causes of death (CODs). **(A)** Patient flow chart. **(B)** SMRs and **(C)** immediate CODs in total, male, and female patients with 9 RMDs.ID=national identification number. SMR=standardized mortality ratio. *31 provinces: 31 provinces, municipalities, and autonomous regions.

Disclosure of Interests: None Declared.

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POS0968

ANCA-ASSOCIATED VASCULITIS INCIDENCE IN A NORTHERN SPANISH HEALTH REGION, 1994-2022: A POPULATION-BASED STUDY

Keywords: Descriptive studies, Vasculitis, Epidemiology

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Background: Anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) includes granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA) or microscopic polyarteritis (MPA). Precise estimation of the incidence of AAV has been difficult due to the absence of reliable diagnostic criteria.
Objectives: To estimate the incidence in a Northern Spanish population-based cohort.
Methods: Population-based study of 132 patients diagnosed with small vessel vasculitis between 1994 and 2022 in a tertiary hospital. Finally, 98 patients were included as AAV according to ACR/EULAR 2022 criteria [1]. Incidence was estimated by gender, age, and year of diagnosis.
Results: AAV was diagnosed in 98 (49 women/ 49 men) patients: GPA (n=47, 48%) MPA (n=37,37.8%) and EGPA (n=14, 14.3%). Annual incidences were estimated in AAV (Figure 1). GPA annual incidence in our population area in the 1994-2022 period was 2.81 per 1,000,000 people, 95% CI: 3.77-1.85 (2.82 [4.35-1.29] in males and 2.80 [4.50-1.09] in females). An upward trend in annual incidence over time was observed with rates ranging from 1.88 in 1994 to 6.84 in 2022 (weak correlation; r 2=0.2729). On the other hand, MPA annual incidence was 2.23 per 1,000,000 people (1.92 [3.55-0.27] in males and 2.46 [4.07-0.85] in females). Rates ranged from 1.88 in 1994 to 1.71 in 2022 with an upward trend over time (very weak correlation; r 2=0.0746). In the case of GEPA, annual incidence was 0.83 per 1,000,000 people, 95% CI: 1.72-0.06 (1.22 [2.74-0.30] in males and 0.46 [2.29-1.37] in females). As in the other types of AAV, there was an upward trend over time with variations of from 1.88 in 1999 to 3.42 in 2022 (weak correlation; r 2=0.3335). A comparison between different geographical areas is summarized in Table 1. Wide varia-tions in annual incidence per million were observed in all AAV (GPA 2.1-34; MPA 2.23-10.4; EGPA 0.64-2.7). The highest annual incidence of all AAV was observed in nordic countries and central Europe while the lowest in Southern Europe.
Conclusion: There seems to be a progressive increase in incidence of AAV over the years in the studied population. Annual incidence in our population was similar to that of other south-ern European countries.

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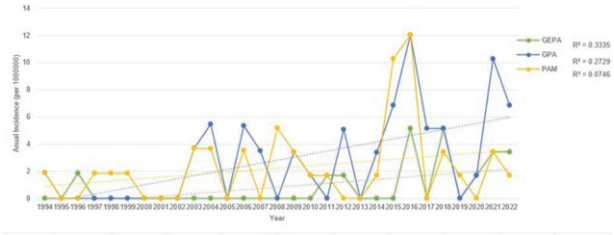


Figure 1. Annual incidence of AAV in 1994-2022.

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POS0969

PREDICTIVE FACTORS OF FAVOURABLE EVOLUTION IN GLUCOCORTICOIDS-DEPENDENT POLYMYALGIA RHEUMATICA

Keywords: Clinical trials, Prognostic factors, Randomized control trial

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Background: The main treatment of polymyalgia rheumatica (PMR) are glucocorticoids (GC) with a 6-month decrease target, but 45% of patients have an unfavourable evolution with relapses or glucocorticoids dependence. Poor prognostic factors in PMR are understudied and controversial.
Objectives: The aim of this work was to identify predictive factors of favourable evolution in GC-dependent PMR patients to optimize its management.
Methods: This work used data from the phase III study SEMAPHORE, which compared tocilizumab with placebo in combination with a standardized decrease in oral GC in patients with GC-dependent PMR. Response to treatment was assessed at week 24 after 6 administrations of tocilizumab 8 mg/kg or placebo. The favourable outcome criterion was a PMR-AS < 10 with a dose of glucocorticoids ≤ 5 mg/day of prednisone equivalent or a dose reduction of ≥ 10 mg/day between inclusion and week 24. The prediction of a favourable outcome based on the inclusion parameters was evaluated in univariate and then multivariate analysis for the variables with a p <0.2 in univariate in the whole of the population and in both treatment arms (tocilizumab and placebo).
Results: At week 24, 49% of the 100 patients included had fulfilled the favourable outcome criterion. In the whole population, being treated with tocilizumab was the main predictor of favourable evolution (OR: 6.28 (2.49-17.27), p=0.0002). In the tocilizumab group, the absence of anemia, the absence of renal impairment and a low HAQ-DI at inclusion were predictive of favourable evolution (OR: 13.2

Table 1. AAV incidence cases reported in the literature.

Study, year	Country, data source	Time period	Incident cases per million population GPA	Incident cases per million population MPA	Incident cases per million population EGPA
Pearce, F. A. et al. 2016	Nottingham, UK, population register	1656-1663	8.2	13.4	1.5
Nilsen, A. T. et al. 2020	Tromso, Norway, population register	1999-2013	15.6	10.4	2.7
Mohammad, A. J et al. 2009	Lund, South Sweden, population register	1997-2006	9.8	10.1	0.9
Takala, J. H et al. 2008	Finland, analysis national discharge data	1996-2000	9.3	NA	NA
Hellmich, B. et al. 2021	Germany, analysis insurance claims database	2013-2016	34	13	NA
Dadoniene, J. et al 2005	Vilnius, Lithuania, analysis hospital database	1990-1999	2.1	3	1.3
Panagiotakis, S. H. et al. 2009	Crete, Greece, analysis hospital database	1995-2003	6.6	10.2	NA
Romero-Gómez, C. et al. 2004	Malaga, Spain, retrospectiva population.	1994-2010	2.1	3.4	0.64
Catanaso, M. et al. 2014	Reggio Emilia, Italia, analysis hospital discharge database	2004-2009	3.4	NA	NA
Vinit, J. et al. 2006	Burgundy, France, analysis hospital discharge database	1998-2008	NA	NA	1.2
Kanecki, K. et al. 2018	Poland, analysis hospital discharge database	2008-2013	NA	NA	1.5
Kanecki, K. et al. 2018	Poland, analysis hospital discharge database	2011-2015	7.7	NA	NA
Present study, 2023	Northern Spain.	1999-2022	2.81	2.23	0.83

(1.62-166.5613.2), 8.78 (1.19-91.23) and 10.16 (2.03-78.66) respectively). No variable was related to favourable outcome in the placebo group.
Conclusion: In patients with an active disease despite GC, a favourable outcome was predict by tocilizumab treatment. In the population treated by tocilizumab, the absence of comorbidities such as anemia or renal impairment and a better functional activity with a low HAQ-DI were associated with favourable outcome. No predictive factors were identified in patients trated with GC only.
REFERENCES: NIL.
Acknowledgements: NIL.
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POS0970 PSYCHO-COGNITIVE FACTORS AND ADHERENCE IN AXIAL SPONDYLOARTHRITIS: A MULTICENTER CROSS-SECTIONAL STUDY

Keywords: Spondyloarthritis, bDMARD, Descriptive studies

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Background: There is a lack of data on adherence in axial Spondyloarthritis (axSpA). It is estimated between 28.2 et 70.6% by the largest study currently available [1]. Many factors may influence adherence, among them psychological factors.
Objectives: The objectives were to assess the adherence to biological disease-modifying anti-rheumatic drug (bDMARDs) and the impact of catastrophizing, fibromyalgia, anxiety, and depression in a cohort of patients with axSpA.
Methods: A multicenter cross-sectional study was conducted in five departments of Rheumatology in France. Inclusion criteria were axSpA according to the ASAS criteria, and treatment by bDMARDs. Patients completed an anonymous self-questionnaire including demographic data, disease activity scores, Girerd score (GS) measuring adherence, and psycho-cognitive scores such as the Fibromyalgia Rapid Screening Tool (FIRST), Hospital Anxiety and Depression Scale (HAD) and the Pain Catastrophizing Scale (PCS). Rheumatologists completed an independent medical questionnaire collecting the disease-related data.
Results: 500 patients with axSpa were enrolled into the study between June 2021 and June 2022. Patients had a mean age of 49.5 ±13.8 and 53.2% were male. They were treated by anti-TNF, anti-IL 17 or anti-IL 12-23 in 85.8%, 13.2% and 1% of cases, respectively. Forty-nine point two percent were adherent (GS=0) and 50.8% were non-adherent (GS ≥1). The prevalence of catastrophizing, fibromyalgia, anxiety and depression in our study was 17.2%, 21.4%, 25.6% and 11.0%, respectively. Patients with best adherence were older (mean age: 53.26 ± 13.3 with GS=0 vs 45.85 ± 13.4 with GS ≥1; p<0.0001), pensioners (26.4 % with GS=0 vs 12.6% with GS ≥1; p<0.001) and had a lower education level (OR 1.84; 95% CI 1.23-2.75; p=0.03). Patients with anxiety and catastrophizing had a lower adherence (OR 1.53; 95% CI 1.02-2.30; p=0.04 and OR 1.61; 95% CI 1.00-2.58; p=0.05, respectively). Adherence was not different between male and female patients, although female patients with axSpA had more catastrophizing (OR 1.84; 95% CI 1.15-2.95; p=0.015), fibromyalgia (OR 3.27; 95% CI 2.07-5.16; p<0.0001) or anxiety (OR 2.26; 95% CI 1.50-3.41; p<0.0001). In multivariate analysis, lower adherence was associated with younger age (OR 0,96; 95 CI 0,95-0,98; p<0,001) and anxiety (OR 1,72; 95% CI 1,05-2,81; p=0,03).
Conclusion: Half of axSpA patients were non-adherent to bDMARDs, especially among young people, catastrophizers and patients with anxiety. We recommend that practitioners screen for these psycho-cognitive factors and manage them very carefully.
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POS0971 A COMPARISON OF MYOSITIS AUTOANTIBODY AND CLINICAL CHARACTERISTICS AMONG RACIAL GROUPS IN ASIA AND AUSTRALASIA – A COLLABORATIVE MULTICENTRE EFFORT BY THE APLAR MYOSITIS SIG

Keywords: Autoantibodies, Myositis

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Background: Idiopathic inflammatory myopathies (IIM) are a group of systemic autoimmune conditions with predominant skeletal muscle involvement. Major subsets of disease recognised by the EULAR/ACR Classification Criteria include dermatomyositis (DM), amyotrophic dermatomyositis (ADM), inclusion body myositis (IBM) and polymyositis (PM) and immune mediated necrotising myositis (IMNM). Myositis-specific antibodies (MSA) more so than myositis-associated antibodies (MAA) are associated with distinct clinical phenotypes of disease and can aid in predicting the risk for extra-muscular manifestations, such as interstitial lung disease (ILD). Racial differences in autoantibody profile and clinical phenotypes have been described, though pooled intergroup comparisons are limited.
Objectives: We characterised the autoantibody profiles in IIM patients of different racial groups and identified relationships with IIM subsets and select extra-muscular manifestations.
Methods: Pooled data for adult IIM patients who had been tested for MSA and MAA was analysed. IIM subtypes were diagnosed by histology and/or EULAR/ACR criteria. Demographic, autoantibodies, clinical data, and mortality data, where available, was collected and analysed retrospectively in STATA. MSA includes autoantibodies directed against Jo1, PL-7, PL-12, EJ, OJ, Mi-2, SRP, NXP-2, TIF1-gamma, MDA5 and anti-HMGCR. MAA include autoantibodies against PM-Scl, Ku, U1RNP, and Ro52. Using multivariate logistic regression, we analysed the relationship of racial groups and autoantibodies, with (i) IIM subtypes, (ii) ILD and(iii) mortality.
Results: 787 (Australia (n=243), India (n=241), Japan (n=134), Malaysia (n=99), Singapore (n=51), Thailand (n= 19)) patients with IIM were analysed; 543 (67%) patients were female. The median age of diagnosis was 52 years (IQR 39, 64) with the following racial distribution: 26.7% identified as Caucasian, 37.2% East and Southeast Asian (SEA), 33.4% South Asian, and 3% other. The most frequent disease subsets were DM (n = 259) and PM/ IMNM (n = 264). MSA or MAA were detected in 351/787 patients (44.6%); of these 54.7% (192/351) were positive for MSA, 33.9% (119/351) were positive for MAA, and 11.4% were positive for both (40/351). DM was most frequently diagnosed in the East and SEA and South Asian racial groups. Controlling for demographics and autoantibodies, IIM patients of East and SEA descent were five times more likely to be diagnosed with DM (OR 5.52, 95% CI 3.19, 9.56) compared with Caucasians; South Asians were nine times more likely to be diagnosed with DM (OR 8.89, 95% CI 4.83, 16.36). Conversely in PM/IMNM, East and SEA (OR 0.20, 95% CI 0.12, 0.33) and South Asian (OR 0.34, 95% CI 0.20, 0.58) groups were much less likely to be diagnosed compared with Caucasians. Specific MSA and MAA were infrequently associated with racial groups. However, anti-SRP antibodies were 3 times more likely to be detected in the East and SEA groups (OR 2.84, 95% OR 1.04, 7.74) compared with Caucasians. Patients with anti-HMGCR antibodies were four times more likely to be diagnosed with PM and IMNM (OR 4.24, 95% CI 2.16, 8.33). MSA (OR 6.66, 95% CI 4.25, 10.43) and MAA (OR 3.06, 95% CI 1.76, 5.35) were more likely to be detected in

patients with ILD; no gender difference was evident. Compared with Caucasians, East and SEA (OR 5.14, 95% CI 2.59, 10.21) patients were up to 10 times more likely to be diagnosed with ILD. Controlling for racial groups, age and gender, IIM patients with ILD had significantly higher odds of mortality (OR 1.84, 95% CI, 1.02, 3.32), though the odds were significantly lower in the South Asian racial group (OR 0.37, 95% CI 0.14, 0.92) compared with Caucasians.

Conclusion: Our study is the first of its kind to demonstrate an association between racial groups, clinical profiles, autoantibodies, and the subtypes of IIM. There is heterogeneity in MSA and MAA positivity among racial groups. Importantly, we show that race appears to have a possible role in the predilection for IIM subtypes and ILD.

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POS0972 INCREASED RISK FOR STROKE IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER, RESULTS FROM A LARGE POPULATION-BASED STUDY

Keywords: Rare/orphan diseases, Real-world evidence, Innate immunity

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Background: The association between chronic inflammatory conditions and cardiovascular disease is well established. Considering Familial-Mediterranean-Fever (FMF), few studies exist investigating the risk of ischemic heart disease, and none address the risk of stroke.

Objectives: To evaluate the incidence and risk for stroke in FMF patients compared to the general population.

Methods: A retrospective cohort study using the electronic database of Clalit Health Services (CHS), the largest health organization in Israel. All FMF patients diagnosed between 2000-2016 were included and matched with control according to age, gender, and place of residence. Follow-up continued until the first diagnosis of stroke or death. The incidence of stroke was compared between the groups using univariate and multivariate models adjusting for cardiovascular risk-factors.

Table 1. Comparison of rates and risk for stroke in FMF patients compared to controls

Group	Variables	FMF	Controls
FMF (n=9,769 ¥)	Stroke events, n	208	148
	Age at stroke, mean ±SD	59.8 ± 15.9**	65.3 ±14.9
	Follow-up time, person-years	104,967	106,080
	Follow-up time, median (IQR)	12.4 (6.9-14.5)	12.5 (7.1-14.6)
	Incidence rate per 10,000 person-years, (95%CI)	19.8 (17.2 to 22.7)	13.9 (11.8 to 16.4)
	Unadjusted HR (95%CI)	1.42 (1.15 to 1.76) **	reference
	Age-and-sex adjusted HR (95%CI)	1.46 (1.18 to 1.80) **	reference
	Multivariate¶ HR (95%CI)	1.44 (1.16 to 1.78) **	reference
FMF with complications† (n=418 ¥)	Stroke events, n	53	30
	Age at stroke, mean ±SD	65.6 ±12.6*	70.3 ±11.6
	Follow-up time, person-years	4,140	4,976
	Follow-up time, median (IQR)	11.8 (6.5-14.6)	14.0 (9.7-15.5)
	Incidence rate per 10,000 person-years, (95%CI)	128.0 (95.9 to 167.5)	60.3 (40.7 to 86.1)
	Unadjusted HR (95%CI)	2.16 (1.38 to 3.38) **	reference
	Age-and-sex adjusted HR (95%CI)	2.32 (1.48 to 3.64) **	reference
	Multivariate¶ HR (95%CI)	2.19 (1.38 to 3.48) **	reference
FMF without complications† (n=9,351 ¥)	Stroke events, n	155	118
	Age at stroke, mean ±SD	57.5 ±16.4**	63.8 ±16.4
	Follow-up time, person-years	100,827	101,104
	Follow-up time, median (IQR)	12.4 (6.9-14.5)	12.4 (7.0-14.6)
	Incidence rate per 10,000 person-years, (95%CI)	15.4 (13.1 to 18.0)	11.7 (9.7 to 14.0)
	Unadjusted HR (95%CI)	1.32 (1.04 to 1.67) *	reference
	Age-and-sex adjusted HR (95%CI)	1.28 (1.01 to 1.63) *	reference
	Multivariate¶ HR (95%CI)	1.30 (1.02 to 1.66) *	reference

† Including amyloidosis, chronic renal failure, dialysis, and kidney transplant.¶ Adjusted for age, sex, and cardiovascular baseline risk factors.¥ Compared to a similar number of matched controls.

Results: 9,769 FMF patients and a similar number of controls were followed up for a median period of 12.5 years. The mean age at the beginning of the follow-up was 25.7 years. 208 FMF patients were diagnosed with stroke compared to 148 controls, resulting in an incidence rate (per 10,000 persons-years) of 19.8 (95%CI 17.2-22.7), and 13.9 (95%CI 11.8 to 16.4) respectively, and a crude HR of 1.42 (95% CI 1.15 to 1.76; p<0.001). In a multivariate analysis, FMF patients who developed amyloidosis with related or non-related renal failure demonstrated significant stroke risk (HR=2.16; 95%CI 1.38 to 3.38; P<0.001), as well as for those who did not develop these complications (HR=1.32; 95%CI 1.04 to 1.67; P<0.05).

Conclusion: FMF patients are at increased risk for stroke regardless of known complications.

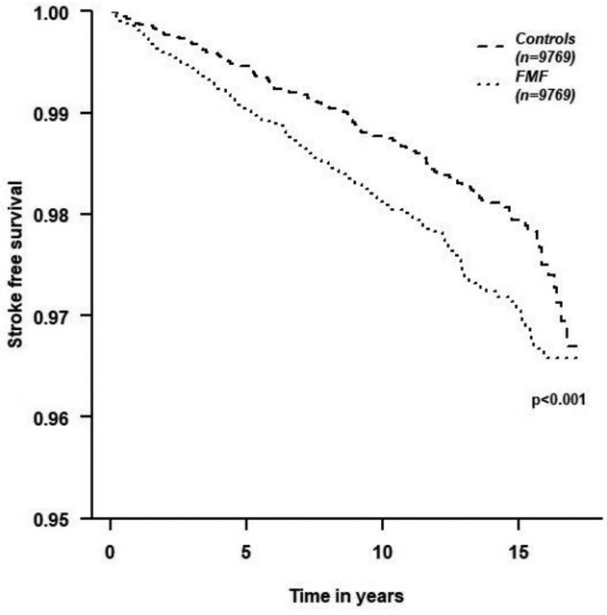


Figure 1.

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POS0973 EFFECT OF RENAL AND EXTRARENAL FLARES ON DEVELOPMENT OF CKD AND EXTRARENAL ORGAN DAMAGE IN PATIENT WITH LUPUS NEPHRITIS

Keywords: Organ damage, Systemic lupus erythematosus, Kidneys

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Background: Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease with a plethora of manifestations potentially affecting every organ system. Lupus nephritis (LN) is recognized as one of the most common and fearsome manifestations presenting in up to 35-60% of SLE patients, usually during the first 5 years from disease onset[1]. LN and LN flares are associated with nephron loss and chronic kidney disease (CKD)[1,2,3], which on its own is a major risk factor for overall morbidity and mortality[1,4]. However, the association between extrarenal disease flares and CKD and the contribution of LN and extrarenal flares to overall damage accrual are less investigated.

Objectives: To assess the impact of disease flares on development of CKD and extrarenal organ damage in lupus nephritis.

Methods: We performed a multicentric retrospective cohort study on biopsy-proven LN patients in whom we evaluated the impact of disease flares on CKD development and damage accrual. Disease flares were divided into renal (doubling of serum creatinine or persistent increase in proteinuria with normal GFR) and extra-renal (cSLEDAI>0 across extrarenal domains). Renal-extrarenal clinical remission was defined as serum creatinine <1mg/dl, eGFR>60ml/min/1.73m2, proteinuria <0.5g/24h and cSLEDAI=0 lasting for at least one year.

CKD as serum creatinine >1.0mg/dl with eGFR <60ml/min/1.73 m2 and inactive urinary sediment, confirmed by at least three determinations for at least 3 months, and damage was measured by the SLICC damage index (SDI). Non-parametric tests were used for comparisons.

Results: 303 LN patients were included (females 86.5%, mean follow-up 14.8 (9.8-22.0) years). 257 patients (84.8%) achieved remission after a median of 1.44 (0.69-3.58) years from initial treatment, which persisted throughout follow-up in 115 patients. Among 142 patients who had their remission interrupted, 39 (27.5%) did so due to extrarenal flares, while 103 (72.5%) experienced renal flares (creatinine or proteinuria). Loss of remission due to extrarenal flares was less frequently associated with CKD development than remission lost to renal flares (5.1% vs. 28.2%, respectively; OR95%CI 0.14 (0.031-0.61), p=0.003), while the ultimate median annual SDI increase was comparable between patients experiencing either renal or non–renal flares (renal vs. extrarenal flares: +0.05 (0-0.1) vs. +0.06 (0-0.14), p=0.8).

Conclusion: Patients experiencing renal flares are at greater risk of CKD, yet more than 5% of patients undergoing extrarenal flares develop CKD. Renal and extrarenal flares both contribute comparably to damage accrual across other organ domains. Extra-renal flares deserve attention and should not be regarded as mild by definition.

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POS0974

CARDIOVASCULAR OUTCOMES OF ANTI-TNF ALFA AND JAK INHIBITORS IN PATIENTS WITH RHEUMATOID AND PSORIATIC ARTHRITIS. REAL WORLD EVIDENCE AND INSIGHTS OF BIOBADASAR 3.0 REGISTRY

Keywords: Real-world evidence, Registries, bDMARD

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Background: Major Cardiovascular Adverse Events (MCAE) are a concern in autoimmune diseases. Rheumatoid Arthritis (RA) and psoriasis arthritis (PsA) are diseases where inflammation plays a vital role in developing the disease and producing short- and long-term damage.

The TNF alpha plays a significant role in inflammation. The JAK/STAT signaling pathway is an essential regulatory signaling cascade of intracellular processes used in treating these conditions. It is crucial to evaluate the effect of these treatments on long-term comorbidities associated with these diseases.

Objectives: This study aims to provide real-world evidence on the influence of Anti-JAK, Anti-TNFa, and cs-DMARDs therapy on cardiovascular events in RA and PsA.

Methods: Data from the BIOBADASAR 3.0 registry of patients diagnosed with RA and PsA (ACR-EULAR 2010/ CASPAR 2006) from June 2010 to May 2022. This data was recollected from patients treated with cs-DMARDs (control group), Anti-TNF alpha, and JAK inhibitors. The history of specific comorbidities and the appearance of AE were recorded. Kaplan Meier curves evaluated event-free survival time, and the comparison between the different treatments was performed by Log Rank analysis. Additionally, to account for alternative explanations, a propensity score (PS) was estimated, which assigned a value to each observation according to the probability of incorporating all the information available to estimate this probability and making the groups associating similar patients more comparable.

Results: Of 6,209 patients, 4,817 (77.6%) with RA and 510 (8.2%) with PsA were studied. The overall frequency of MCAE was 48 (2.2%) in the Anti-TNFa group, 5 (2.37%) in the Anti-JAK group, and 38 (1.84%) in the control group (p=0.6). MCAE-free survival was a median in years of 3.02 for the Anti-TNFa group (HR 1.3 95%CI 0.8-384), 5.1 for the control group (HR 1.5 95%CI 0.32-651), and 1.8 for the group with JAK inhibitors (HR 3.02 95% CI 0.2-0.8), The results of the regression model adjusted by PS to present MCAE were for the Anti-TNFa group HR 1.28 IC95% 0.77-2.13 p 0.34, for the non-exposed group HR 1.48 IC95% 0.82-2.67 and the JAK inhibitor group 3.12 IC95% 1.48-6.6 p < 0.001.

Conclusion: In conclusion, we found no statistically significant difference between the RA and APS groups appearance of adverse events of interest. In this study, we observed a higher MCAE-free survival time in the not exposed group than in the Anti-TNFa group and considerably low in the Anti-JAK group with a statistically significant difference. These differences persist in the multivariate model adjusted by propensity score.

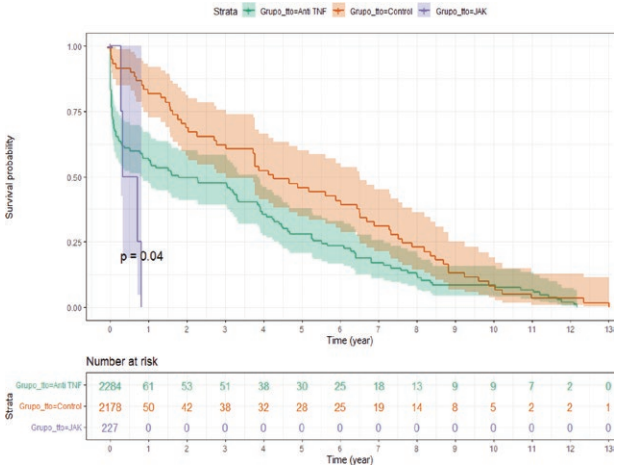


Figure 1. MCAE free-survival time according to treatment.

REFERENCES: NIL.

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Validation of outcome measures and biomarkers

POS0975

VALIDATION OF INTERFERON STIMULATED GENE SCORES, PREVIOUSLY DEVELOPED IN PERIPHERAL BLOOD MONONUCLEAR CELLS, IN WHOLE BLOOD SAMPLES

Keywords: Rheumatoid arthritis, Cytokines and chemokines, Systemic lupus erythematosus

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Background: A recent EULAR Task force identified critical variability in interferon (IFN) assay methods and defined a research agenda to improve and harmonise assays. IFN scores A and B, developed using IFN stimulated genes (ISG) measured in peripheral blood mononuclear cells (PBMC) differentiate between clinical subsets of patients with autoimmune disease [1]. Whole blood (WB) samples are more commonly used in clinical practice and trials. Regardless of sample type, real time polymerase chain reaction (RT-PCR) experiments require a suitable reference gene (RG) which is uniformly expressed across different experimental conditions in order to normalise target gene expression quantities [2].
Objectives: (i) To determine whether sample type affects the previously defined IFN scores; (ii) if so, to develop revised IFN scores in WB; (iii) to identify the best RG for future RT-PCR experiments.
Methods: Samples were collected from participants enrolled in 5 studies; DEFINITION, CONVAS, USEFUL, MASTERPLANs and BRAGGSS. PBMCs were separated from blood using leucosep tubes and WB was collected using Tempus™ Blood RNA Tubes. Undetected delta Ct values were singly imputed. IFN scores A and B were calculated in paired WB and PBMC samples and agreement between the sample types was assessed via the Bland-Altman (BA) method. New IFN scores for WB were derived via exploratory factor analysis (EFA) of 31 ISG as per the original work [1]. Separation of clinical subgroups was visualized using violin plots and effect sizes calculated using Hedges' g. RG identification from 16 candidates used online software.
Results: We used samples from 342 participants with systemic lupus erythematosus (SLE), 6 ANA positive at risk progressors, 7 at risk non-progressors, 30 with rheumatoid arthritis (RA) and 10 healthy controls (HC). Subsets were used for sample comparison (n=45) and RG work (n=22). Comparing score A in PBMC versus WB matched samples resulted in bias of -1.44, limits of agreement (LOA 0.08, -2.96), the spread of data on BA plot showed a systematic difference. The same comparison in score B gave bias of -1.23 (LOA 0.26, 2.73), data on BA plot suggested differences were not systematic. EFA in WB produced a two-factor solution which explained 97% of the variation. The first (score C) contained 3 ISG and the second (score D) contained 4 (Table 1), compared with score A (12 ISG) and score B (14 ISG) [1]. Both scores showed potential to differentiate between HC and those with SLE or RA, but neither separated SLE from RA as the original PBMC scores A and B had done (Figure 1). YWHAZ, PGK1 and GUSB were the most stable RG. Others such as ACTB performed poorly as RG.
Conclusion: PBMC and WB may be used interchangeably to calculate IFN score A, but not score B. This suggests an influence of neutrophils, including the demethylation of neutrophil ISG cytosine-guanine sites, on Score B genes [3]. In WB we derived a further two scores which differentiated SLE or RA from HC, although neither score distinguished between SLE and RA. Further work is needed to assess the performance of scores A-D in WB samples. The Minimum Information for Publication of Quantitative Real-Time PCR Experiments recommend using ≥3 RG to avoid bias[4]; we found that YWHAZ, PGK1 and GUSB were the most stable genes across a range of experimental conditions.

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Table 1. Interferon stimulated genes selected in two-factor solution derived via exploratory factor analysis in whole blood.

Variable	Score C	Score D
CCL8	1.01	
IFI27	0.84	
CXCL10	0.80	
LAMP3	0.73	
ISG15	0.66	
CASP1		0.93
CEACAM1		0.89
TRIM38		0.73
SOCS1		0.58

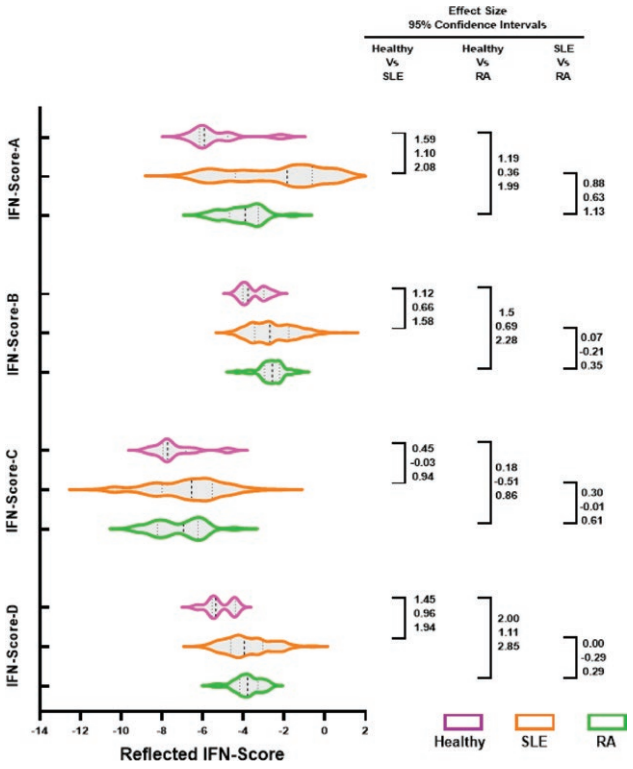


Figure 1. Violin plots (bold dashed line = median, dotted lines = upper and lower quartiles) and effect sizes presented as top value and lower and upper 95% CI presented underneath.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0976

HAND FUNCTION IS ALREADY REDUCED BEFORE RA-DEVELOPMENT AND REFLECTS SUBCLINICAL TENOSYNOVITIS

Keywords: Imaging, Rheumatoid arthritis, Motor function

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Background: Clinically suspect arthralgia (CSA) is characterized by arthralgia of small joints and considered a risk stage for development of rheumatoid arthritis (RA). However, it remains unknown if the function of the hands is already affected and what mechanisms underlie impaired hand function in CSA.
Objectives: We aimed to study to what extent the function of the hands is affected in CSA-patients, whether that would reflect underlying subclinical inflammation, and if it can be of value in clinical practice.
Methods: We studied various measures of hand function in two CSA-populations. CSA-patients in the TREAT-EARLIER-trial (n=236) were evaluated at baseline for: grip strength on a dynamometer, patient-reported difficulties in the grip-domain of the HAQ-questionnaire and incomplete fist-closure at physical examination. Contrast-enhanced MRI of the hands measured synovitis/tenosynovitis/osteitis (summed as subclinical inflammation). Findings were validated in an independent CSA-cohort (n=600) where hand-function was measured as: grip strength evaluated by squeezing the examiner's fingers, grip-domain of the HAQ-questionnaire, and fist-closure.
Results: Grip strength (on a dynamometer) was reduced in 75% compared to reference-values in healthy-controls (1), 60% reported grip-difficulties and 13% had incomplete fist-closure. Reduced grip strength was associated with subclinical inflammation (-0.38 kg per point inflammation, 95%CI -0.68;-0.08). Studying separate MRI-features, grip strength reduction was independently associated with tenosynovitis, decreasing with -2.63kg (-2.26; -0.33) per point tenosynovitis (range of observed tenosynovitis scores: 0-20). Similar relations with tenosynovitis were seen for patient-reported grip-difficulties (OR 1.12 per point, 1.07;1.42) and incomplete fist-closure (OR 1.36 per point, 1.03;1.79). In the validation-cohort, 36% had decreased examiner-assessed GS, 51%

reported grip-difficulties, and 14% incomplete fist-closure: all were associated with tenosynovitis. Decreased dynamometer-measured grip strength was most sensitive for detecting tenosynovitis (75%), while incomplete fist-closure was most specific (88-90%).

Conclusion: Hand function is already often affected before RA-development, reflecting subclinical inflammation. In practice, testing hand-function in CSA-patients could conveniently objectify functional limitations and reveal subclinical tenosynovitis.

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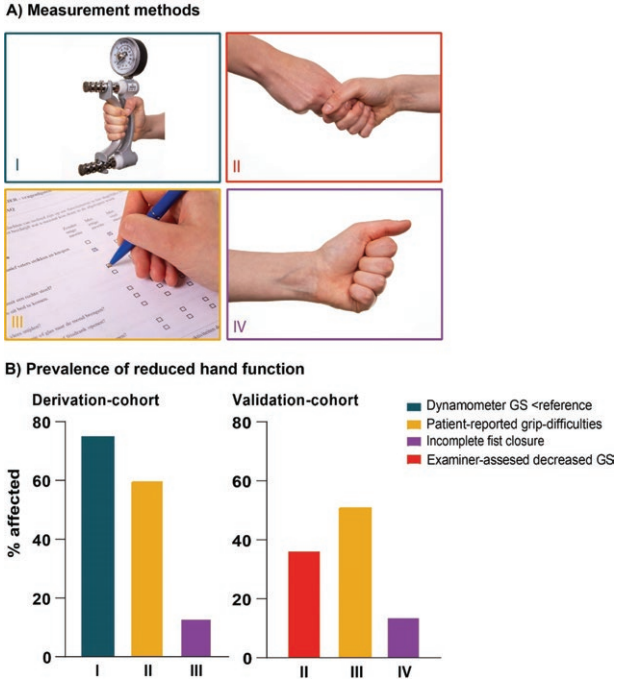


Figure 1. Assessment and prevalence of reduced hand function in the CSA-phase Legend Figure 1.A depicts the different measures of hand function used: I Dynamometer-measured grip strength (GS), II patient-reported grip-difficulties in the HAQ grip-domain, III fist-closure, IV Examiner-assessed. In B, dynamometer-measured grip strength was compared to the mean grip strength in healthy individuals of the same age and sex as reported by Gunther et al.(1) Patient-reported grip-difficulties were defined as a score of 1 or higher (i.e. individuals indicating some difficulty, much difficulty or unable to perform a task) in the HAQ grip domain.I, III and IV were assessed in the derivation-cohort, II, III and IV in the validation-cohort. GS: grip strength.

Acknowledgements: We thank G. Kracht (medical photographer) for preparing Figure 1.

Disclosure of Interests: None Declared.

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POS0977 **WITHDRAWN**

POS0978 EXPLORING SMARTPHONE-BASED DIGITAL ENDPOINTS FOR RHEUMATIC CONDITIONS

Keywords: Outcome measures, Telemedicine, Validation

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Background: The care of rheumatic diseases is currently episodic, based on visits every 3-6 months at the rheumatologist, which may fail to characterize the condition state. To address this issue, the research community is investigating ways to use smartphones and sensors to monitor conditions passively.

Objectives: Explore associations between smartphone-generated data, standardized functional tests, and Patient Reported Outcome Measures (PROMS) to support the creation of digital endpoints.

Methods: Participants from Portugal and Austria participated in a Data Collection that included: (i) physical activities, such as walking with a smartphone in the pocket; (ii) hand dexterity exercises, such as copying text sentences with the smartphone keyboard; (iii) downloading and processing sociability data from the participants' smartphone; (iv) performing functional tests, such as Moberg Pickup Test (Moberg) and Timed Up-and-Go (TUG); and (v) answering validated PROMS, such as MD-HAQ, EQ-5D-5L, and visual analogue scale (VAS) for pain, fatigue, and disease activity. Statistical analysis focused on the correlation between smartphone-collected data and functional tests or PROMs, and independent t-test for between-group comparison.

Results: We collected data from 59 participants (76% female, 24% male). From this set, 31 were patients diagnosed with osteoarthritis (45%), rheumatoid arthritis (26%), or psoriatic arthritis (29%). The remaining 28 were age-matched healthy controls. In terms of age, 17% of participants were under 41 years old, 52% were between 41 and 60, and 31% were 61 or older. Most patients reported stiffness or pain in the upper (90%) and lower (83%) parts of the body. Subjective health status was high (M=77.95, SD= 16.31) in the VAS of EQ-5D-5L. Independent t-tests (Table 1) showed significant differences between patient and control groups regarding Mobility (M= 1.90, SD= 0.77), Pain/Well-Being (M= 2.48, SD= 0.81), and Mental Health (M= 1.68, SD=0.83) with higher difficulty levels reported by rheumatic patients compared to controls. Rheumatic patients also rated worse in HADS anxiety (M= 5.90, SD= 3.74) but not depression. We found significant differences between patients and controls in the variability of key pressing time (ms), with less variability among patients than controls (M= 30.71, SD= 11.99). The inter-key typing time was lower in participants below 50 years than above. A moderate correlation was found between the number of character deletions and the Moberg test (r= 0.44, p = 0.02) in patients with hand joint pain. Regarding Mobility associations, TUG total time (s) was positively correlated with the number of total steps (r=0.81, p <.001), the average duration (s) of each step (r= 0.35, p <.001), the average speed (m/s) of walking (r= -0.92, p <.001), as well as the standing up (r= 0.59, p <.001) and sitting down (r=0.55, p <.001) times (s).

Table 1. – Group comparison through independent t-test applied to some of the collected variables.

Dimension	Variable	Significance	Effect Size (*d*)	Patient Group (mean±SD)	Control Group (mean±SD)
Functional and disease assessment (EQ-5D-5L)	Mobility	0.018	-0.63	1.90±0.77	1.32±0.77
	Self-Care	0.981	-	1.39±0.76	1.39±1.10
	Daily Activities	0.116	-	1.71±0.78	1.36±0.91
	Pain/Well-Being	<.001	-1.02	2.48±0.81	1.68±0.82
	Mental Health	0.014	0.39	1.68±0.83	1.25±0.59
	Subject H. Status	0.200	-	75.10±16.31	81.22±19.67
Mental health (HADS)	Anxiety	0.005	-0.68	5.903±3.744	3.75±2.40
	Depression	0.124	-	3.83±3.10	2.43±3.75
TUG	Standing time (s)	0.001	-0.72	1.26±0.364	0.98±0.24
	Sitting time (s)	0.045	-0.53	2.215±0.922	1.80±0.58
	Avg. number of steps in curves	0.035	-0.56	3.419±0.847	2.93±.90
Moberg	Dominant hand time (s)	0.004	-7.20	19.813±6.21	15.856±4.58
Transcriptions	Key pressing time variability (ms)	0.005	0.78	30.71±11.99	22.996±7.71

Conclusion: Data collection with smartphone appears to have face, construct and discriminative validity, able to support future trials in patients with rheumatic diseases, to validate smartphone-based data vs objective measures of disease activity and quality of life over time.

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POS0979 THE GLUCOCORTICOID TOXICITY INDEX-METABOLIC DOMAINS: AN ABRIDGED VERSION OF THE GLUCOCORTICOID TOXICITY INDEX

Keywords: Outcome measures

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Background: Measurement of glucocorticoid (GC) toxicity is critical to efforts to reduce it. In clinical trials, the Glucocorticoid Toxicity Index (GTI)[1] measures toxicity effectively using two scores, the Cumulative Worsening Score (CWS) and the Aggregate Improvement Score (AIS). In clinical practice, high patient volumes limit time available to perform the full GTI. An abbreviated GTI version – the GTI-Metabolic Domains (GTI-MD) – may address this issue by including only data that are collected routinely at clinic visits, requiring no additional physician time. The GTI-MD includes four domains: Body Mass Index, Glucose Tolerance, Blood Pressure, and Lipid Metabolism.

Objectives: We evaluated the correlations between the GTI-MD, overall GTI scores, and the remaining GTI domains to determine if the GTI-MD differentiates patients effectively according to GC toxicity.

Methods: We used data from ADVOCATE[2], a phase 3 trial in which avacopan replaced a standard GC taper in ANCA-associated vasculitis, to test the correlation of the GTI-MD with overall GTI scores. We evaluated the ability of the GTI-MD to differentiate the treatment groups by GC toxicity, comparing GTI-MD scores between groups at weeks 13 and 26.

Results: The abilities of the full GTI domains to differentiate the treatment groups according to GC toxicity have been reported[3]. The Spearman rank correlation coefficient for the GTI-MD CWS with GTI CWS was 0.78 (p<0.0001). The corresponding correlation for the AIS was 0.73 (p<0.0001). The GTI-MD distinguished the two groups by GC toxicity at both 13 and 26 weeks (**Table 1**). The mean GTI-MD CWS was lower in the avacopan group, consistent with less toxicity (15.9 versus 23.0 at 13 weeks [p=0.001]; 26.7 versus 31.7 at 26 weeks [p=0.009]). The GTI-MD AIS values were also consistent with less toxicity in the avacopan group (2.5 versus 13.0 at 13 weeks [p=0.0003], 4.4 versus 10.1 at 26 weeks [p=0.03]). Contributions of the four GTI-MD domains were balanced (**Figure 1**). A GTI-MD score of zero correlated with low toxicity in other domains.

Table 1. Differentiation of the two treatment groups in ADVOCATE by glucocorticoid toxicity, as measured by the Glucocorticoid Toxicity Index-Metabolic Domains.

GTI-MD Score	Week	Treatment Group	N	Mean Score	Standard Deviation	P-value
AIS	13	Avacopan	160	2.5	23.4	0.0003
		Prednisone	161	13.0	27.3	
	26	Avacopan	154	4.4	25.7	0.03
		Prednisone	153	10.1	26.1	
CWS	13	Avacopan	160	15.9	15.7	0.001
		Prednisone	161	23.0	19.2	
	26	Avacopan	154	26.7	20.1	0.009
		Prednisone	153	31.7	20.3	

GC, glucocorticoid; GTI-MD, Glucocorticoid Toxicity Index-Metabolic Domains; AIS, Aggregate Improvement Score; CWS; Cumulative Worsening Score

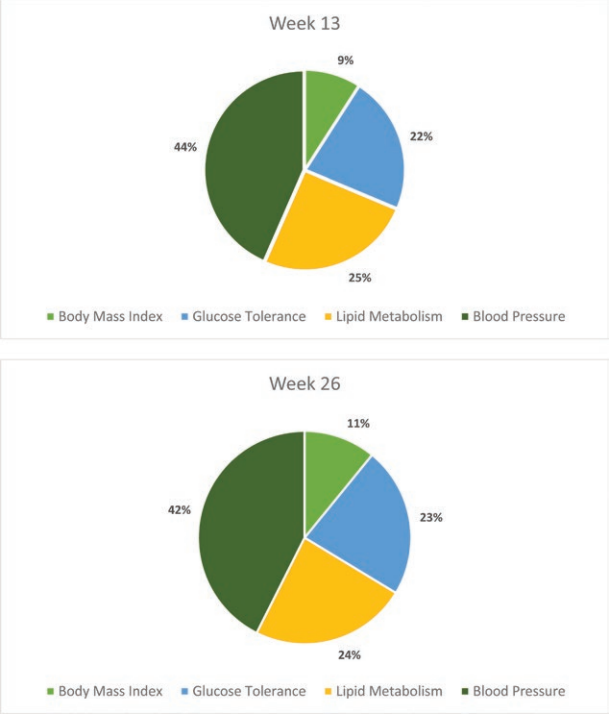


Figure 1. Percentage of the Glucocorticoid Toxicity Index-Metabolic Domains score contributed by each domain at 13 and 26 weeks, as reflected by the Aggregate Improvement Score values adjusted for weight.

Conclusion: The GTI-MD correlated well with the full GTI in ADVOCATE and may be incorporated readily into routine clinic workflows. Additional studies will be required to determine how effectively the GTI-MD predicts certain long-term GC toxicities such as osteonecrosis, bone fractures, infection, and death, and to understand how the instrument performs in other types of settings and study designs. Utilization of the GTI-MD may help clinicians monitor GC toxicity longitudinally, with the goals of preventing the burden of chronic, treatment-related morbidity, and reducing long-term costs to health systems.

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POS0980

WHICH ACR RESPONSE DEFINITION SHOULD BE USED FOR DISEASE ACTIVITY CLAIMS IN APPROVAL STUDIES OF RHEUMATOID ARTHRITIS? A SYSTEMATIC EVALUATION

Keywords: Outcome measures, Validation, Rheumatoid arthritis

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Background: An accurate evaluation of efficacy is key in any trial of novel pharmaceutical compounds. For rheumatoid arthritis (RA), the American College of Rheumatology 20, 50 and 70 response criteria (ACR20/50/70) were reported in all major clinical trials since 1995. Although clinically irrelevant, the ACR20 response still remains the primary endpoint required by the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA).

Objectives: In this analysis we explored how the stringency of the ACR response definitions (20%, 50% or 70%) differs with respect to their observed frequency and timing to inform potential future trial designs and regulatory decisions on required claims during the drug approval process in RA.

Methods: We conducted a systematic literature search in EMBASE, Medline and the Cochrane Library for multi-national, multi-center, phase 3 randomized drug trials (RCTs) investigating biological and targeted synthetic disease modifying anti-rheumatic drugs (bDMARDs/tsDMARDs) in adult RA patients. We included full articles published in English and reporting ACR responses for ≥3 time points over a 24-week study period. Baseline characteristics as well as ACR responses were extracted. For direct comparison of the response dynamics over time, we visualized ACR response rates on scales normalized to their maximum numerical responses observed during the respective trial (for details see legend). Calculation of p-values per outcome and timepoint for each treatment arm against placebo (Fisher's Exact test; α=0.05) allowed us to compare the discriminative capacity of the ACR responses between active treatment and placebo across all timepoints. Statistical analyses were done using R (V4.2.1, 2022, Vienna, Austria).

Results: We screened 12.457 articles (AK and VK) and selected 313 articles for full-text reading; we included 44 articles in the final analysis, which allowed for comparison of 95 treatment arms against placebo, investigating 8 different modes of action in DMARD-naïve patients as well as csDMARD and bDMARD insufficient responders (IR). The discriminative capacity of the ACR20 was highest across all timepoints analyzed (week 1 to 24), on average reaching 70% of the maximum response rate in the trial as early as by week 2 ('normalized' ACR response, Figure 1, Panel A). In contrast, ACR50 and 70 responses reached rates comparable to the ACR20 close to or at week 24, thus exhibiting slower response dynamics (Figure 1,

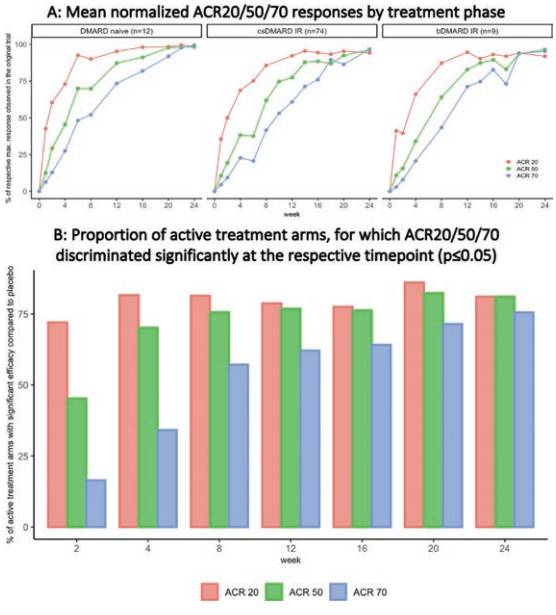


Figure 1. Mean normalized ACR responses. ACR responses were normalized to the respective maximum response achieved during the course of the trial; for example, if the maximum ACR20 response rate was observed at week 16 and amounted to 76% responders, then this was the normative 100% in the respective trial; and if the maximum ACR70 response rate was observed at week 20 and amounted to 28%, then this was taken as 100% for the ACR70 response. These data are summarized in panel A for DMARD naïve patients (n=12), csDMARD IR (n=74) and bDMARD IR (n=9) (n=number of treatment arms); Panel B: Percentage of treatment arms (n=95) from 44 different trials with significant (p≤0.05) ACR20, 50 and 70 response (active treatment vs. placebo) per timepoint (week 0-24).

Panel B). This effect was seen across all treatment arms (N=95) and independent of the mode of action, but slower for trials including treatment-IR patients compared with those assessing DMARD-naïve patients (Figure 1, Panel A).
Conclusion: The ACR20 response definition continues to be the most powerful discriminator between active treatment and placebo at early timepoints during trials; however, the discriminative capacity of the ACR50 and 70 definitions increases over the course of time. Our findings therefore support the use of these clinically more relevant response definitions at later but not early timepoints.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0981

PRECISION MEDICINE IN RHEUMATOID ARTHRITIS. EVALUATION OF TWO NOVEL TESTS TO PREDICT CLINICAL RESPONSE TO METHOTREXATE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

Keywords: Disease-modifying drugs (DMARDs), Rheumatoid arthritis, Biomarkers

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Background: The main goal of treatment in patients with early Rheumatoid Arthritis (RA) is to achieve a clinical remission. Methotrexate (MTX) should be the first treatment strategy in naïve patients, but about one third will not respond to this therapy. There is a lack of tools to predict the individual response to MTX. Pre-treatment number of circulating monocytes may predict clinical response to MTX (1) and ROS production may be related to the pharmacological action of MTX (2, 3).
Objectives: To evaluate the feasibility of 2 novel tests (ROS and Monocytes Tests) to measure in vitro the sensitivity to MTX in patients with new-onset RA and the association of MTX response with clinical remission at 6 months.
Methods: This is an observational, longitudinal Proof-of-Concept with a follow-up of 6 months. 33 adult patients with early RA according EULAR criteria and with a DAS28 ≥2.6 were included before treatment with a disease-modifying antirheumatic drugs disease (DMARD). 26 patients had a valid sample for tests performance. At baseline a patient blood sample was collected, where PBMCs were isolated and frozen. After 3 weeks, PBMCS were defrost, placed in a plate p96, activated with phytohemagglutinin, and exposed to MTX. In the ROS test, Reactive Oxygen Species were measured by means of a specific vital probe with fluorimetry. In the Monocytes test, monocytes metabolic activity was determined with resazurin and measured with fluorimetry. Clinical and analytical variables were registered along patients´ follow-up and DAS28<2.6 was used as criteria for clinical remission. Results of both tests were compared in patients with and without clinical remission at 6 months.
Results: ROS levels as determined with the ROS test showed to be increased in patients with clinical remission when compared with patients without remission (p<0.001) (Figure 1). Monocytes number determined with the Monocytes test was decreased in the patients with clinical remission vs patients without remission (p<0.05) (Figure 1). The predictive capacity of these models was analyzed with the area under the operating characteristics curve (ROC), showing for ROS Test an AUC of 0.919 (CI95% 0.813- 1.025) (p<0.0001) and for Monocytes test 0.826 (CI95% 0.664-0.989) (p<0.0001).

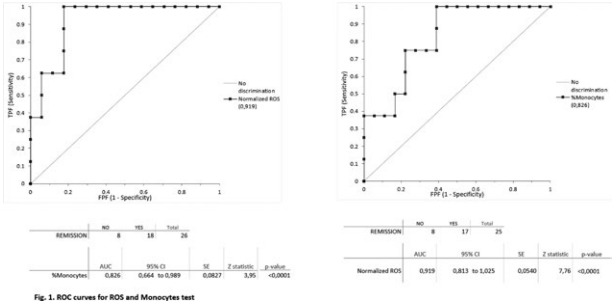


Figure 1.

Conclusion: In naïve patients with new-onset RA, the pharmacological response to MTX can be measured in vitro by the quantification of total monocytes and ROS production from PBMCs. Low monocyte percentages and high levels of ROS production are associated with patients´ clinical remission at 6 months.

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Acknowledgements: NIL.
Disclosure of Interests: Alejandro Escudero Contreras: None declared, Francisco J. Blanco: None declared, Mercedes Alperi-López: None declared, Ana Isabel Turrión: None declared, Chary Lopez-Pedrera: None declared, Tatiana Yebra Employee of: Biohope Scientific Solutions for Human Health, Gema Cordero Employee of: Biohope Scientific Solutions for Human Health, Teresa Diez Employee of: Biohope Scientific Solutions for Human Health, Isabel Portero Shareholder of: Biohope Scientific Solutions for Human Health, Employee of: Biohope Scientific Solutions for Human Health.
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Clinical cases

POS0982

UNUSUAL PRESENTATION OF LEWIS-SUMNER SYNDROME IN ELDERLY SIMULATING POLYMYOSITIS AND POLYMYALGIA RHEUMATICA

Keywords: Rare/orphan diseases

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Background: Lewis-Sumner syndrome (LSS) or multifocal acquired demyelinating sensory and motor neuropathy (MADSAM) is an atypical form of chronic inflammatory demyelinating polyneuropathy (CIDP). This rare disease is characterized by a predominantly distal, asymmetric weakness mostly affecting the upper limbs and motor dysfunction with adult onset. Diagnosis can be difficult to establish if the clinical presentation is atypical and frequently simulates inflammatory myopathy.
OBJECTIVES:
Methods: We report a rare case of LSS in an old patient with unusual clinical aspects.
Results: A 70-year-old female patient with a history of atrial fibrillation complicated by pulmonary embolism, presented with myalgia and muscle weakness of the shoulders, upper arms, hips and thighs. This involvement was bilateral, symmetrical and evolving since 3 months, causing difficulties in climbing stairs, standing or walking. Physical examination showed a proximal muscle deficiency affecting proximal muscles of the upper and lower limbs. In this stage we suspected a poly yositis or polymyalgia rheumatica. We completed by biological assessment that showed a biological inflammatory syndrome (ESR at 90 mm at first hour; CRP at 80 mg/L) and elevated lactate dehydrogenase level at 490 IU/L. The immunoblot polymyositis profile (anti-Mi2, anti-Ku, anti Pm/SCL, anti-Jo1, anti-PL12, anti-PI7, anti-SSA 52kDa, anti-EJ, anti-OJ and anti-SRP) was negative. The MRI of lower limbs revealed a signal abnormality in the gluteus medius muscles on both sides with inflammatory appearance. The Electromyography revealed sensorimotor neuropathy affecting the four extremities with motor nerve conduction blocks. This aspect was in favor of LSS, so we completed by a cerebrospinal fluid study which revealed a proteinorachia at 0.4g/l with normal glycorachia and normal cell counts. These results confirmed the diagnosis of LSS. The patient was treated by corticosteroids at dose of 1 mg/ kg/ day during 2 months, with a progressive decrease of treatment. The evolution was marked by a spectacular clinical and biological response.
Conclusion: LSS is a very rare disease that can simulate inflammatory myopathy and polymyalgia rheumatica in elderly. So, it should be suspected in old patients suffered from proximal muscle deficiency.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0983

TET2 MOSAICISM IN HUMAN IS ASSOCIATED WITH A COMPLEX PHENOTYPE INCLUDING LYMPHOPROLIFERATION, AUTOIMMUNITY, IMMUNODEFICIENCY, AND HEMATOLOGIC MALIGNANCY

Keywords: Autoantibodies, Genetics/epigenetics, Malignancy

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Background: The TET2 gene encodes ten-eleven translocation methylcytosine dioxygenase 2 (TET2). TET2 is an epigenetic regulator that converts 5-methylcytosine to 5-hydroxymethylcytosine and also interacts with histone-modifying enzymes and transcription factors. Somatic mutations in TET2 are early events in clonal expansion and are found in association with myeloid and lymphoid haematological diseases. Germline mutations in TET2 have only been described in 3 children of consanguineous parents. These mutations led to immunodeficiency and lymphoma and early mortality in childhood.
Objectives: To assess the clinical and immunological consequences of a combination of a germline and a somatic mutation in *TET2*.
Methods: Genetic analysis was done by whole exome sequencing. An in-depth immunological analysis was performed.
Results: Clinical phenotype: The patient of non-consanguineous parents presented at the age of 38 with axial spondyloarthritis. Apart from trace homogeneous fluorescence on the HEp2 cell his immunologic work-up was unremarkable. After start of a TNF-inhibitor he developed persisting fever, serositis, interstitial lung disease, peripheral arthritis and a pronounced lymphadenopathy/splenomegaly. His condition improved after the TNF-inhibitor was changed to an IL-17-inhibitor combined with prednisone (up to 40 mg/d), but lymphadenopathy persisted and the patient recurrently suffered from fevers, fatigue and pleurisy. Lymphnode biopsies showed no signs of malignancy. The patient had recurrent episodes of pancytopenia that spontaneously improved and he developed two episodes of pneumonia. Furthermore, he suffered from recurrent episodes of herpes zoster.
Immunological results: On immunologic work-up the patient had a polyclonal hypergammaglobulinemia and autoantibody testing revealed a homogenous ANA (1:1600), and positive anti-nucleosomen-, anti-PM-Scl75-, anti-SRP-, anti-PL-12-, anti-phospholipid-, anti-dsDNA- and anti-MPO-autoantibodies. Despite of increased amounts of immunoglobulins the patient developed a progressive and persistent loss of B cells (Figure 1), with an increased expression of CD80/86 on the remaining memory B cells. Within the T cell compartment double-negative T cells were increased.
Results of whole exome sequencing: Whole exome sequencing revealed a germline mutation in TET2 with the variant c3641G>A; pArg1214Gln in the heterozygous state (NAF 0.53; NM_001127208.3). This mutation affects a phylogenetically conserved amino acid and is classified as predominantly pathogenic in the in silico prediction. Another variant identified is the mutation c.1864C>T; p.Gln622, which leads to the emergence of a stop codon (NAF 0.41). This variant was only detectable as a low-grade mosaic (5-10%) in the buccal mucosa in the control, possibly as a result of lymphocytic infiltration into the buccal mucosa. In leukocytes, this mutation was detectable in 83% of cells in the heterozygous state. Both mutations have a low frequency in the population (1-2/125000-150000; gnomAD).
Hematogical malignancy: 5 years after the progessive loss of B cells had started, the patient was diagnosed with a follicular B cell lymphoma and shortly after with AML with myelodysplasia-associated changes (AML-MRC). A familial-allogeneic peripheral blood stem cell transplantation was performed. During the now 6 months follow-up no relapse occurred.
Conclusion: Combined heterozygous germline and somatic mutations in TET2 are associated with a very complex phenotype combining autoimmunity, lymphoproliferation and hematological malignancy, may present in adulthood and thus clinically differ from combined heterozygous germline mutations with early onset in childhood.

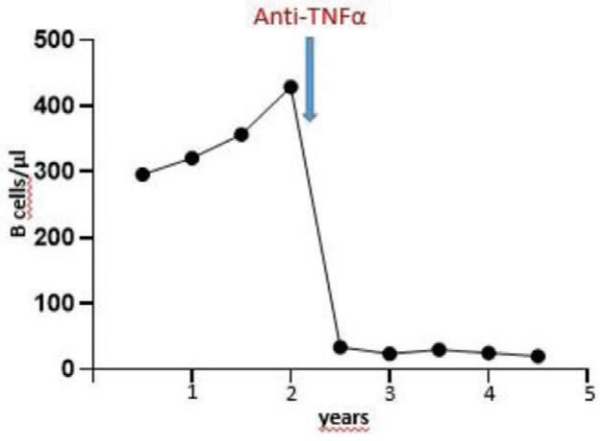


Figure 1.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0984 DARATUMUMAB RESCUE THERAPY IN A PATIENT WITH ANTI-MDA5 ASSOCIATED ARDS

Keywords: Myositis, Lungs, Autoantibodies

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Background: MDA5-associated dermatomyositis is often associated with rapid progressive interstitial lung disease resulting in acute respiratory distress syndrome (ARDS). Patients that progress to require mechanical ventilation or extracorporeal membrane oxygenation (ECMO) generally have a high mortality despite intensive combined immunosuppressive treatment. (1) Daratumumab, an anti-CD38 monoclonal antibody has been successfully used in the treatment of refractory autoantibody-associated diseases with the intention of targeting autoantibody-producing CD38+ plasma cells. (2)
Objectives: Rescue treatment of anti-MDA5 antibody associated ARDS with Daratumumab combination therapy.
Methods: We treated an ECMO-dependent patient with refractory anti-MDA5 dermato-pulmonary syndrome with a combination treatment of four weekly doses of 1800mg daratumumab s.c. as well as tofacitinib, ciclosporin and prednisolone.
Results: A 55-year-old patient was transferred to our hospital with ARDS of unknown origin combined with a short history of oligoarthritis and Gottron's papules. She required mechanical ventilation and ECMO. Autoantibodies showed strong positivity for anti-MDA5 and -Ro52, so she was diagnosed with MDA5+ dermatopulmonary syndrome. She initially received treatment with cyclophosphamide, tofacitinib, ciclosporin, intravenous immunoglobulins and high-dose steroids. However, her interstitial lung disease showed no improvement. We escalated the immunosuppressive therapy with daratumumab. The pulmonary function improved approximately four weeks after daratumumab initiation and the patient was consequently weaned from ECMO and respirator. The clinical course was complicated by an ischemic stroke and a blood stream infection with enterococci which would have made a lung transplantation impossible. We were able to discharge the patient to rehabilitative care with only low-flow supplemental oxygen.
Conclusion: Rescue immunosuppressive therapy of MDA5-antibody associated ARDS with daratumumab in addition to tofacitinib, ciclosporin and prednisolone was associated with remarkable clinical improvement in this case. More clinical data and long-term follow-up are needed to investigate safety and efficacy of this treatment regimen in MDA5-antibody-associated disease.
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Acknowledgements: We thank the patient and her family for allowing us to present this case.
Disclosure of Interests: Lennard Ostendorf Speakers bureau: Speaker for Roche, unrelated to the abstract., Frédéric Münch: None declared, Lena Thormählen: None declared, Jens Nee: None declared, Udo Schneider: None declared.
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Psychosocial support

POS0985-PARE FACTORS ASSOCIATED WITH FEELINGS OF GUILT AND SHAME IN PATIENTS WITH PSORIATIC ARTHRITIS

Keywords: Mental health, Skin, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease that can have a major impact on patients' quality of life with functional and psychological impairment.
Objectives: We aimed to investigate feelings of shame and guilt among patients with PsA and to determine its associated factors.
Methods: We conducted a cross-sectional study including patients with peripheral PsA according to the CASPAR criteria. Sociodemographic data, clinical, and therapeutic modalities were collected. Patients were asked to respond to the Experience of Shame Scale (ESS) [1] and to the Test of Self Conscious Affect- Version 3 (TOSCA-3S) [2]. ESS is a self-report scale assessing 3 areas: (1) characterological shame (2) behavioral shame and (3) bodily shame. Each item was rated in a 4-point Likert scale. Higher scores indicate higher levels of shame. TOSCA-3S is composed of 11 scenarios, each followed by 4 possible responses. Each item was rated in a 5-point Likert scale. This score measures shame-proneness, guilt-proneness, detachment and externalization (blaming others). Only the shame and guilt subscales of the TOSCA-3S were used for the statistical analysis. A $p<0.05$ was considered significant.
Results: We included 30 patients with PsA: 12 females (40%) and 18 males (60%). The mean age was 51±14years [21-80]. Five percent of patients were illiterate and 95% of them had an educational level. Twenty seven percent of patients were unemployed, 50% were employed, and 23% were retired. Seventy seven percent of patients were married. The mean disease duration was 13±5 years [2-20]. The mean DAS28 ESR and DAS28 CRP were 5.34±1.84 and 4.75±2.06, respectively. The mean Psoriatic area severity index (PASI) was 10.2 [0-70]. For the ESS, the mean total score was 63 [31-98] with mean subscale scores of: 28 [14-45] for characterological shame, 25 [12-35] for behavioral shame and 9 [5-20] for bodily shame. For the TOSCA-3S, the mean "shame self-talk Total" score was 33 [17-44], and the mean "guilt self-talk Total" score was 47 [37-55]. A significant correlation was found between guilt self-talk Total score and disease activity: DAS 28 ESR ($p=0.028$) and DAS28 CRP ($p=0.039$). The guilt self-talk Total score was significantly higher in women (49 vs 46, $p=0.025$) and among unemployed patients ($p=0.08$). The shame self-guilt Total score was associated with educational level ($p=0.027$). The Bodily shame subscale was associated with the educational level ($p=0.028$). A significant positive correlation was noted between the PASI and the bodily shame score ($p<0.001$, $r=0.673$).
Conclusion: Feelings of guilt and shame were frequent among PsA patients. Associated factors were mainly disease activity, PASI, and sociodemographic parameters.
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Acknowledgements: NIL.
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Best practice campaigning

POS0986-PARE **IMPACT OF EDUCATIONAL CAMPAIGNS ON RMD IN SOCIAL NETWORKS**

Keywords: Education, Self-management, Quality of life

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Background: Panama's prevalence of rheumatoid arthritis lies within the global range (.24 to 1%). To improve the quality of life of RMD patients in the country, FUNARP was created over 18 years ago to educate and support patients, caregivers, and civil. FUNARP decided to focus its efforts on digital campaigns since 2020 taking advantage of its coverage, low costs, and ease of usage. Further, the mobile penetration of Panama is 136% of its population [1] making social media the best distribution channel for this purpose.
Objectives: To expand educational coverage, especially for those with limited mobility or living in hard-to-reach areas. Another objective is to measure the effectiveness of digital media campaigns (paid vs organic growth), as well as to identify the most effective social network for these purposes.
Methods: Social media campaigns complement FUNARP's annual education plan which consists of monthly onsite and virtual lectures/seminars. The educational approach is based on the physician's perspective and the patient's experience. The campaigns consist of a mixed scheme: selected ad investment and in-house content creation; and full-fledged campaigns with professional content development and paid ads. In 2022, a total of five campaigns were launched following this process: a) selection of the campaign theme, b) professional advice on content, c) sponsorship, d) hiring of the marketing agency, e) approval of design and publications, and f) analysis of results to the board of directors and sponsors.
Results: "*Early Diagnosis and Motivation to Consult a Rheumatology Specialist*" was the most successful campaign - developed by a marketing agency with videos supporting the message, and paid ads on both Instagram and Facebook, see Figure 1. Salient results: 110,488 accounts reached and 25,975 interactions, see Table 1.



Figure 1. Best performing campaign.
Campaigns with professional content creation and paid ads in social media ads had more than 50% reach and 90% interaction than the ones without them. Videos have a higher acceptance vs. static images, see Table 1:

Table 1. Salient KPI of social media campaigns in 2022 (reach vs. engagement)

	Campaign	Facebook	Instagram	Images	Videos	Paid Ads	Non-paid Ads
Reach (110,488 accounts)	Arthritis remission, is it possible?	9%	91%	81%	19%	24%	76%
	Self-care in rheumatic diseases	37%	63%	74%	26%	0%	100%
	Prepare your visit to the rheumatologist	68%	33%	94%	6%	93%	7%
	Myths around rheumatic diseases	21%	79%	87%	13%	20%	80%
	Early diagnosis and motivation to consult a rheumatology specialist	18%	82%	13%	87%	87%	13%
Interactions (25,975)	Arthritis remission, is it possible?	9%	91%	88%	12%	31%	69%
	Self-care in rheumatic diseases	37%	63%	76%	24%	0%	100%
	Prepare your visit to the rheumatologist	68%	33%	92%	8%	91%	9%
	Myths around rheumatic diseases	21%	79%	98%	2%	29%	71%
	Early diagnosis and motivation to consult a rheumatology specialist	18%	82%	2%	98%	89%	11%

Qualitative results have been observed by rheumatologists who have indicated that patients who have had access to information from our foundation are more informed and involved in their treatment. They perceive that these patients have a better quality of life compared to those who do not have access to information about their pathology.
Conclusion: Working with marketing companies, and rheumatologists, as well as investing in advertising directly influences the effectiveness of health awareness and literacy campaigns. Publications where real patients appear as protagonists had higher acceptance vs. those with stack images and videos, or models. Instagram appears to have a better impact than Facebook. The early diagnosis campaign managed to overcrowd first-time consultations with rheumatologists in the public health system (less than 20 rheumatologists for a 4.2 MM population in Panama). FUNARP observed an increase in requests for information and orientation in the navigability of the system to obtain care with rheumatologists and advice on various health issues from the community through social media messaging services.

FUNARP will continue to conduct digital campaigns to expand the educational coverage of the Panamanian population. It is recommended to have advertising investments of more than U.S.$100.00 per publication of each campaign and to have content generated by specialists and advertising agencies. In addition, sponsorship will continue to be sought to increase literacy in patients with RMD. For the next campaigns, the WhatsApp button will be made available to easily address requests and questions from the community. A marketing and advertising commission has been created within FUNARP to keep more detailed metrics and measure other variables in the campaigns that have not been measured so far.

REFERENCE:

[1] Panamanian Public Services Authority 2022

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POS0987-PARE **SPONDYREPORT: A REPORT SENT TO ALL GPS IN NORWAY, TO PROVIDE KNOWLEDGE ABOUT THE DIFFERENT SPONDYLOARTHRITIS DIAGNOSES**

Keywords: Spondyloarthritis

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Background: The report provides brief and precise knowledge of spondyloarthritis diagnoses, axial spondyloarthritis, psoriatic arthritis, IBD associated arthritis and juvenile spondyloarthritis.

Objectives: The aim of sending this report to all GPs in Norway is to give knowledge gaps around the different spondyloarthritis diagnoses. To give knowledge gap in this report, we want to reduce the diagnostic delay of SpA.

Methods: Information about the diagnoses axial spondyloarthritis, psoriatic arthritis, IBD arthritis and juvenile spondyloarthritis, is written and quality assured by rheumatologists. This report provides information on what the referral should contain when sent to a rheumatologist if suspected spondyloarthritis. It provides information that MRI is the most important tool for setting axSpA diagnosis and ASAS criteria for SpA. It provides information where both healthcare professionals and patients can turn to when planning pregnancy and rheumatic diseases. Provides information about physical activity, where patients can get help for this. These patients have several health challenges in addition to their Spondyloarthritis diagnosis, this report gives knowledge about heart disease, dry eyes and exhaustion fatigue. In addition, we have included patients' stories about their experiences with their GP, both what help they get and don't get from their GP.

Results: The spondyreport has been physically sent to all (5071) GPs in Norway in January 2023. In order to reach as many GPs as possible, it was decided to send it out physically to all GPs. This report is a pilot project, where the goal is to send it yearly to GPs and other relevant physicians.

Conclusion: By sending this report to all GPs in Norway, it provides knowledge about symptoms and referrals to rheumatologists, to make this work easier for the GP and at the same time provide knowledge to a patient group who lives a lifetime with burden of their diseases.

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HPR Measuring health (development and measurement properties of PROs, tests, devices)

POS0988-HPR **SENSITIVITY TO CHANGE OF THE SCLEROID COMPARED TO THE UCLA GIT SCORE IN A COHORT OF SSC PATIENTS WITH LOWER GI SYMPTOMS**

Keywords: Patient reported outcomes, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is a multi-organ disease and patient-reported outcome measures (PROMs) are important to better understand the complexity and impact of the disease. This heterogeneous disease has a wide specter of symptoms, and there are several different PROMs in use for this disease-group to assess all possible symptoms. Recently, a SSc-specific patient-derived questionnaire The Systemic Sclerosis Impact of Disease (ScleroID) has been developed and validated. Longitudinally, the questionnaire performed better than other comparators with regard to change over time. The ScleroID has so far not been used in a clinical study, nor been compared with the Scleroderma Clinical Trials Consortium Gastrointestinal Scale (UCLA GIT score) 2.0.

Objectives:

i: To estimate the sensitivity to change in ScleroID with the UCLA GIT score as comparator.

ii: To assess association between upper and lower GI in ScleroID and the UCLA GIT score.

Methods: We assessed the ScleroID and the UCLA GIT score in a 20 weeks randomized clinical trial, including patients with predominantly lower GI symptoms and without severe cardiopulmonary complications. The ScleroID includes questions about the severity of Raynaud`s phenomenon, hand function, upper and lower GI symptoms, life choice and mobility. It is scored using a 10 points Likert scale, with scores ranging from 0 (no impairment) to 10 (extreme impairment). The UCLA GIT score is a seven –item scale asking for frequency of experienced reflux, distention/bloating, diarrhea, fecal soilage, constipation, emotional well-being and social functioning, where all scales are scored from 0 (none of the days) to 3 (5-7 days a week). Changes in the scores from baseline to week 20 were analyzed by Paired- Samples T test. The Standardized response mean (SRM) was computed and interpreted according to Cohen's effect size index, in which 0.2 refers to a small difference, 0.5 to a moderate difference, and 0.8 or more to a large difference. Correlation were determined by the Spearman correlation coefficient at baseline.

Results: The study cohort included 67 SSc patients with mean age of 61 years and mean disease duration of 10 years (table 1). After week 20, the ScleroID and UCLA GIT total score showed low sensitivity to change, with SRM 0,42 (95% CI 0,10-0,68) and 0,45 (95%CI 0,18-0,77), respectively (Figure 1). Upper GI score of the ScleroID showed a strong correlation with UCLA reflux (r=0.799, p< 0.001). Lower GI of the ScleroID correlated moderately with UCLA reflux (r=0.399, p=0.008), constipation (r=0.306, p=0.031) and distention/bloating (r=0.444, p<0.001). In total, 54% of the patients reported an improvement in upper GI symptoms and 51% in lower GI symptoms of ScleroID. For the UCLA GIT score 56% reported improvement in reflux, 59% in bloating/distention and 33% in diarrhea.

Conclusion: The ScleroID and UCLA GIT score showed a low sensitivity to change after 20 week in a lower GI predominant SSc-cohort without severe organ involvement. The majority of the patients reported improvement in upper and lower GI symptoms in both questionnaires.

Table 1. Demographics

	SSc patients (n = 67)
Age at assessment, years, mean, (SD)	61 (11.5)
Disease duration at assessment, years, mean (SD)	10 (7.2)
Female sex, n (%)	62 (93)
Limited cutaneous SSc, n (%)	60 (89)
Anti-centromere AB, n (%)	51 (76)
Organ involvement	
Interstitial lung disease, n (%)	11 (16)
Pulmonary arterial hypertension, n (%)	1 (1)
Gastrointestinal involvement, n (%)	67 (100)
Bloating	44 (66)
Diarrhea	23 (34)
Treatment	
Immunosuppresives, n (%)	13 (19)

Disclosure of Interests: Maylen N Carstens: None declared, Torhild Garen: None declared, Henriette Didriksen: None declared, Håvard Fretheim Speakers bureau: Boehringer Ingelheim, Consultant of: Bayer, Grant/research support from: GSK/Actelion, Imon Barua: None declared, Inger-Lise Knutsen: None declared, Tone Karaaslan: None declared, Tove Hatletveit: None declared, Maiju E Pesonen: None declared, Øyvind Midtvedt: None declared, Øyvind Molberg: None declared, Anna-Maria Hoffmann-Vold Speakers bureau: Boehringer Ingelheim, Jannsen, Medscape, Merck Sharp & Dohme and Roche, Consultant of: ARXX,

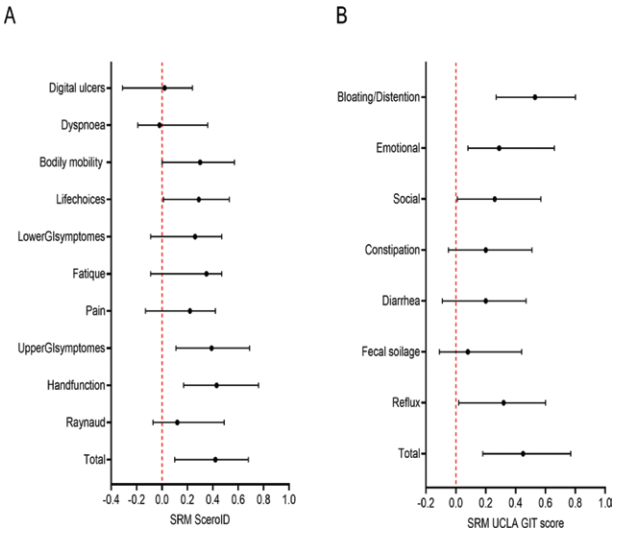


Figure 1.

Boehringer Ingelheim, Genentech, Jannsen, Medscape, Merck Sharp & Dohme and Roche, Grant/research support from:? Boehringer Ingelheim, Jannsen.
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POS0989-HPR REAL-WORLD INDUCTION DMARD THERAPY IN RHEUMATOID ARTHRITIS; INSIGHTS IN THE DUTCH SANTEON BENCHMARK FRAMEWORK TO IMPROVE PATIENT CARE

Keywords: Real-world evidence, Disease-modifying drugs (DMARDs), Rheumatoid arthritis

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Background: Methotrexate (MTX) is the cornerstone therapy for rheumatoid arthritis (RA) patients, with well-established safety and efficacy profiles and support in international guidelines. Guidelines state that the maximal effect of MTX in a dose around 25 mg/wk can be seen after 3-6 months of therapy. However, older studies showed that the maximum dosage usually is up to 15 mg/wk and <40% had started treatment with MTX within 3–6 months from the diagnosis.[1,2,3] Santeon hospitals showed by analysis that disease activity score (DAS 28 CRP) of newly diagnosed RA patients was comparable after 6 months of treatment. However, initial treatment protocols showed large variation leading to difference in MTX dosage, mono and/or combination csDMARD therapy[4]. This suggests that under and/or overtreatment might be the fact.
Objectives: To get insight in the actual induction DMARD treatment strategies in newly diagnosed RA patients based on real world data.
Methods: We used data of the Santeon RA program[4] Maasstad Hospital, Medisch Spectrum Twente, St. Antonius Hospital treat over 4,500 RA patients/year. Although there are no (inter)national protocols for induction dose of MTX, all hospitals had a protocol but they varied between the hospital.[4] We included all newly diagnosed RA patients during Jan 2016 – June 2021. For analysis we assessed the initial conventional DMARD therapy and MTX dose at baseline, at 3 months and 6 months.
Results: In total 1238 new RA patients (714 Maasstad, 284 MST, 240 Antonius) were diagnosed during a 5.5 year period. A large variation in initial MTX dosages was seen (Figure 1). Data shown are of all Santeon hospitals combined, but differences within hospitals varied even more (data not shown). In 551 of 1238 patients (44%) does not start with MTX within 3 weeks after diagnosis. 931 (74%) started MTX treatment within 3 months after the diagnosis. Of those 921 MTX users, 253 (27%) started with a dose of 15mg/week. At three months the MTX dosages differed between the hospitals: in two of the three hospitals the most patients used 25 mg/week while in the other 15 mg/week (data not shown). Overall at 6 months 29% (361/1238) Santeon RA patients were on a dose of 25mg MTX. Of all 258 patients that did not start with MTX during 6 months, 216 (84%) started with other csDMARD where hydroxychloroquine (HCQ) was most frequent. The prescription of HCQ in combination with MTX varied strongly between the centers (69% vs 33% and13% per center) 3.3% of all new RA patients no csDMARD was started. The top 3 was 1. missing data (n= 19) 2. patients decision (n=7) and 3. unclear diagnosis (n=3).
Conclusion: We can conclude from real-world benchmark data from Dutch Santeon hospitals that a large variance in MTX dose was observed within and between hospitals. Moreover a large group of new RA patients did not start with MTX, within 3 months but with other csDMARD like HCQ. Our findings rise the urgency of an international induction protocol since the DAS28 did not vary after 3 and 6 months. Moreover this raises the urgency for precision treatment based on patients characteristics (gender, rheumafactor, anti CCP) can achieve similar outcomes (low disease activity) using a lower dose of MTX. To identify these characteristic is topic for further analysis.

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		MTX dose (mg) after 6 months														
		0	2,5	5	6	7,5	8	10	12,5	15	18,75	20	22,5	25	30	
MTX dose (mg) at baseline (within 3 weeks after diagnosis)	0	314	2	0	1	1	0	21	4	68	0	49	0	85	6	551
	2,5	0	1	0	0	1	0	0	0	0	0	0	0	3	0	5
	5	2	0	1	0	0	0	0	0	6	0	1	0	5	0	15
	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	7,5	8	0	0	0	2	0	0	0	1	0	1	0	12	0	24
	10	10	0	0	0	3	0	16	1	7	0	17	0	12	0	66
	12,5	0	0	0	0	0	0	3	2	2	0	0	0	0	0	7
	15	40	0	0	0	0	0	14	3	89	0	24	0	81	2	253
	17,5	1	0	0	0	0	0	0	0	0	0	0	0	1	0	2
	20	34	0	0	0	0	0	5	1	14	1	50	1	106	17	229
	25	7	0	0	0	0	0	1	1	10	0	8	0	56	1	84
	30	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2
		416	3	1	1	7	0	60	12	197	1	150	1	361	28	1238

Figure 1. MTX dosages (mg)

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POS0990-HPR COMPARISON BETWEEN THE CLINIMETRY MEASUREMENTS MADE BY THE PATIENTS AND BY THE RHEUMATOLOGIST UNDER DIFFERENT EDUCATIONAL CONTEXTS

Keywords: Outcome measures, Patient reported outcomes

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Background: Rheumatoid arthritis (RA) is a chronic disease that affects different spheres of the patient, compromising their quality of life. Patient education for self-knowledge and active participation in follow-up is essential. Through the present study, the clinimetry performed by the rheumatologist (RC) was compared with that performed by the patient (PC) when educated through different strategies.
Objectives: Compare the clinimetry measurements made by the patients with the rheumatologist measurements under different educational contexts.
Methods: A Cross-sectional study was designed. Inclusion criteria: Patients older than 18 years with RA, in follow-up under treatment of a T2T (Treat to target) strategy and access to digital tools. Three groups were included: Group 1 education under an RA program with thematic deepening in three levels and duration of 12-14 months, Group 2 with short education carried out in digital format through original video, duration of 75 minutes, in Spanish containing 7 talks (10 - 20 minutes each one). Group 3 without any educational intervention. The three groups performed the PC by means of a digital form and a maximum of one week later they were evaluated by the rheumatologist who developed the RC in a blind manner. Disease activity scales, functional class and quality of life were measured. Univariate and bivariate analyzes (Chi-square and Wilcoxon for paired data) were performed to compare the RC and PC measurements in the three groups. The project was approved by the ethics committee.

Table 1.

	Total n=91		**Group 1 n=28**			**Group 2 =26**			**Group 3 n=37**		
Variable [a]	RC	PC	RC	PC	P-value [c]	RC	PC	P-value [c]	RC	PC	P-value [c]
Global VAS [b]	5 (4)	5 (4)	4.5 (3)	5 (3)	0.302	5.7 (1.4)	6 (3)	***0.042***	5 (4)	6 (4)	*0.074*
Pain VAS [b]	5 (3)	6 (3)	5 (2.9)	5 (4)	0.767	5.5 (2.6)	6 (2)	***0.040***	5 (4.5)	6 (3)	***0.039***
Fatigue [b]	4 (6)	5 (5)	4 (7)	5 (6)	***0.021***	3.5 (6)	4 (4)	0.198	5 (5)	6 (5)	***0.023***
MDHAQ [b]	2.7 (2.7)	2 (2.6)	1.7 (2.9)	1.3 (2.5)	0.303	3 (2.1)	2 (2.5)	***0.010***	2.7 (2.3)	2.3 (2)	***0.008***
HAQ [b]	0.79 (0.76)	0.597 (0.769)	0.50 (0.83)	0.41 (0.72)	0.387	0.89 (0.60)	0.60 (0.72)	***0.012***	0.79 (0.68)	0.69 (0.59)	***0.007***
RAPID 3	12.7 (7.7)	13.7 (7.7)	11 (6.4)	11.5 (8.7)	0.597	13.3 (4.3)	14.1 (7)	0.684	12.2 (9.2)	14.7 (8.3)	0.844
PAS	4.23 (2.51)	4.57 (2.5)	3.6 (2.1)	3.8 (2.8)	0.569	4.42 (1.41)	4.7 (2.3)	0.638	4 (3)	4.8 (2.8)	0.792
TTO EQ5 SCORE [b]	0.71 (0.302)	0.64 (0.300)	0.812 (0.259)	0.710 (0.338)	0.100	0.665 (0.267)	0.675 (0.240)	0.322	0.648 (0.267)	0.640 (0.605)	0.140
VAS EQ5 SCORE [b]	0.645 (0.242)	0.590 (0.240)	0.722 (0.203)	0.645 (0.275)	0.306	0.614 (0.208)	0.617 (0.190)	0.256	0.594 (0.204)	0.590 (0.415)	0.169

[a] Median (Interquartile range) [b].Signifficant differences in the total group [c] Wilcoxon test for paired samples. RC: Rheumatologist Clinimetry. PC: Patient Clinimetry.

Results: 28 patients were included in Group 1, 26 in Group 2, and 37 in Group 3. 100% were women. 51.6% presented erosivity, 81.3% positivity for rheumatoid factor and 79.1% for anti-citrulline antibodies. 46.2% had secondary level studies (higher proportion in Group 1). In group 1, there were no significant differences between the RC variables and those PC, except for fatigue (Table 1). In group 2, significant differences were found in 4 variables, as in Group 3. The RAPID 3 and PAS variables did not have significant differences when analyzing the total group or when analyzing by intervention subgroups.

Conclusion: When the clinimetry performed by the rheumatologist is compared with that performed by the patient, no differences are found in the group of patients who have in-depth educational training; while when the education is short, differences are found between the measurements of the rheumatologist and the patient, in a similar way to when there is no such education. These results deserve to be corroborated in other contexts.

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POS0991-HPR ADHERENCE TO THE MEDITERRANEAN DIET IS ASSOCIATED WITH A REDUCED DAS-28 INDEX AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Diet and nutrition, Health services research

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Background: The Mediterranean diet (MedDiet) has been shown to have protective effects against the development and activity of Rheumatoid Arthritis (RA). It is hypothesized that changes in lifestyle which include diet may lead to the reduction of RA activity and progression. Dietary manipulations are commonly used to minimize RA symptoms by lowering inflammation.

Objectives: The aim of the present study was to assess the adherence of adult patients with RA from Kuwait to the MedDiet and its association with RA activity.

Methods: Adult patients who satisfied the American College of Rheumatology (ACR) classification criteria for RA from major hospitals in Kuwait were evaluated. A cross-sectional study conducted on 187 RA patients aged (35-82) years. DAS-28 scores were obtained in those patients. A validated 14-item Questionnaire (paper-based or web-based) given to the patients to measure adherence to MedDiet. Multivariate and univariate statistical techniques were utilized to analyze data. Statistical comparison and correlation were made in terms of MedDiet levels and RA disease activity by multivariant logistic regression.

Results: A total of 187 patients were included (median age 54 years; 140 males) with a median DAS-28 of 2.616. Out of 187 RA patients, 103 (55.1%) had lower MedDiet scores (MedDiet ≤ 5). Based on the logistic regression function, we found that The multivariable-adjusted odds ratio of RA patients with high adherence to the MedDiet (MedDiet ≥ 6) had lower DAS-28 scores (OR 5.34, 95% CI 1.176 - 24.230, P-value = 0.030) and improved lipid profiles compared to patients with low adherence.

Conclusion: Higher adherence to the MedDiet among Kuwaiti adults with RA may lead to improved DAS-28 scores. Lifestyle and dietary manipulations may be one of the non-pharmacological methods to control RA activity scores.

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Disclosure of Interests: None Declared.

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POS0992-HPR THE EFFECT OF CENTRAL SENSITIZATION ON DISEASE SEVERITY LEVELS AND PRESENTEEISM-RELATED PRODUCTIVITY LOSS IN FEMALE WORKERS WITH RA

Keywords: Patient reported outcomes, Rheumatoid arthritis

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Background: Patients with RA experience a decline in health-related quality of life, which is associated with increased illness severity and impairment of work abilities. Central sensitization (CS) emerges as an accurate predictor and correlate of poor pain experience.

Objectives: The purpose of this cross-sectional, multicentric study is to investigate the mediating role of CS in unfavorable relationships with disease activity levels, CS and work productivity loss due to presenteeism in women with RA, with the goal of identifying potential new targets for preventive interventions.

Methods: The study used a cross-sectional design and included 101 female workers with RA classified according to 2010American College of Rheumatology (ACR)/Europenan League Against Rhumatisms (EULAR) classification criteria. All patients filled out the italian version of the RAID, an assessment and evaluation tool that measures RA patient disease activity, progress, and outcomes. The Central sensitization Inventory (CSI) was used to measure CS, and the Work Productivity and Activity Impairment questionnaire-RA (WPAI-RA) was used to evaluate patients' employment status. RA patients were grouped into categories, based on their RAID total score. Multiple regression analysis was used to find out which factors were most likely to presenteeism.

Results: The patients' age ranged from 25 to 65 years, with a disease duration of 5.4 (SD 6.1) years. The CSI score was ≥ 40 in 39/101 patients (38.6%). 70 patients (69.3%) worked full-time, while 31 (30.7%) worked part-time. The

majority of respondents (64.5%) reported a high degree of presenteeism with an average level of 31.8%. On the other hand, absenteeism was uncommon, with just 7.3% of respondents reporting it. %. Presenteeism was associated with higher CSI score (0.049), increased disease activity (0.0007), disease duration (0.0072) and age (0.0019) (Table 1).

Conclusion: CS disease activity and age were the factor most significantly associated with presenteeism-related productivity loss in RA patients. our findings have implications for health policy and emphasize the significance of identifying high-risk RA patients by monitoring CS as an indicator of presenteeism and severe disease activity.

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Table 1. Multiple Regression Equation: Coefficients, Standard Errors and p values

Independent variables	Coefficient	Std. Error	t	P
(Constant)	*39.8907*			
mRDCI comorbidity score	0.1049	0.1609	0.652	0.5153
DASS-21	0.06935	0.08491	0.817	0.4151
CSI score	2.8830	1.2640	1.994	0.0498
ROAD score	0.8098	1.3899	0.583	0.5609
RAID score	4.4737	1.2903	3.467	0.0007
Kihon score	-0.3921	0.5589	-0.702	0.4838
Age, yrs	-0.6624	0.2100	-3.155	0.0019
Disease duration	-0.03542	0.01303	-2.719	0.0072

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0993-HPR NAILFOLD VIDEOCAPILLAROSCOPIC CHANGES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHROPATHY ON ANTI-TNF-ALPHA THERAPY

Keywords: Disease-modifying drugs (DMARDs), Rheumatoid arthritis, Psoriatic arthritis

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Background: It is known that systemic inflammation in rheumatic diseases was associated with microvascular involvement that can determine the severity and prognosis of the disease [1]. Videocapillaroscopy is an easy and non-invasive method with high sensitivity and specificity, that allows the study "in vivo" of nailfold capillaries.

Objectives: To assess the changes in capillary morphology in rheumatoid arthritis and psoriatic arthritis patients after anti-TNF-alpha treatment using nailfold videocapillaroscopy.

Methods: We performed a retrospective study on 80 patients (rheumatoid arthritis (RA) – 30 patients, psoriatic arthritis (PsA) – 31 patients and a control lot – 19 healthy subjects). Inclusion criteria: patients with high disease activity with RA (who met the EULAR/ACR 2010 criteria), and patients with PsA (who met CASPAR criteria). Exclusion criteria: age under 18 years old, Raynaud's syndrome, history of smoking or alcoholism, patients with history of biological treatment. Patients received anti-TNF-alpha therapy (Infliximab – 33.3% of RA patients and 25.8% PsA patients, Adalimumab - 36.7 % of RA patients and 38.7% of PsA patients, Etanercept- 33.3% of RA patients and 35.5% of PsA patients). In the RA group, 86% of the patients were females, and the mean age of the group was 42 ± 12. In the PsA group, 57% of the patients were females and the mean age of the group was 46 ± 19. We used a videocapillaroscope (VideoCap 3.0) with a magnification of 200x before (T0) and after 6 months of anti-TNF-alpha treatment (T1). We analyzed the capillaroscopic abnormalities such as bushy, tortuous capillaries, dilated capillaries, megacapillaries, hemorrhages, angiogenesis and avascular areas.

Results: We observed a significant correlation between the use of anti-TNF agents and improved. capillary density in RA patients (p=0.00001) and PsA patients (p=0.00002). Moreover, significant correlation was observed between the improvement of avascular areas and Adalimumab use in both groups (p=0.001). We also observed a significant correlation between the lack of angiogenesis and six months use of anti-TNF agents in RA group (p=0.00001) and PsA group (0.00003). A significant correlation was observed between the use of Infliximab and the lack of dilated capillaries (p=0.00005) in the RA group and the use of Etanercept (p=0.00001) and Infliximab (p=0.00001) in the PsA group. Also, strong correlation was observed between the lack of giant capillaries at 6 months and the use of TNF-alpha inhibitors in RA group (p=0.00003) and PsA group (p=0.00001). Significant correlation was found between the lack of hemorrhages and the use of 6 months of Adalimumab and Etanercept in the RA (p=0.00003) and the use of Adalimumab, Etanercept and Infliximab in the PsA (p=0.00001). No significant correlations were observed between videocapillaroscopic changes and age and sex. Also, no significant correlations were observed between the use of TNF-alpha inhibitors and elongated, tortuous and ramified capillaries in both groups.

Conclusion: According to our findings, after six months of anti-TNF treatment we observed a decrease in the incidence of dilated/giant capillaries, angiogenesis, hemorrhages and avascular areas in RA and PsA patients. Nailfold capillaroscopy could be useful in monitoring the efficacy of the biological treatment in patients with inflammatory arthritis.

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POS0994-HPR CONVERGENT VALIDITY OF SIX MINUTE STEPPER TEST TO EVALUATE FUNCTIONAL EXERCISE CAPACITY IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Physical therapy/physiotherapy, Validation

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Background: Exercise capacity is impaired in systemic sclerosis (Ssc) patients due to respiratory and cardiovascular involvements, muscle weakness, arthritis/arthralgia, and joint contractures. Various tests are employed to assess submaximal and maximal exercise capacity in Ssc. Maximal exercise tests, the gold standard for assessing exercise capacity, are challenging since they require expensive equipment and qualified personnel. The 6-minute walk test (6MWT) is a commonly used submaximal field exercise test to assess functional exercise capacity and is shown to be associated with the prognosis in SSc patients. The 6-minute stepper test (6MST) is a low-cost, space-friendly submaximal field test that has been demonstrated to be valid, reliable, and sensitive in assessing exercise capacity in various diseases.

Objectives: No research hasn't been done on the validity of 6MST in Ssc patients. Given that it mimics stair climbing, the 6MST may be more helpful in evaluating lower extremity functions in Ssc. Therefore, the aims of this study were (1) to assess the convergent validity of the 6MST in Ssc; and (2) to compare physiological responses, dyspnea and fatigue perception obtained in 6MST and 6MWT.

Methods: Thirty female patients with Ssc (52.13 + 11.83 years) were enrolled. Demographic and clinical characteristics were recorded. 6MST was performed twice (6MST-1 and 6MST-2) to eliminate learning effect and because the hydraulic jacks become more flexible after they have warmed up. The 6MST-2 was performed after a resting time of at least 20 minutes after 6MST-1. The 6MWT was carried out three hours after the 6MST-2 to minimize fatigue on outcomes. To test the convergent validity of the 6MST, correlation between the 6MWT and 6MST-2 was assessed. In addition, the association between 6MST and the level of physical activity, dyspnea and fatigue severity in Ssc patients was investigated. International Physical Activity Questionnaire (IPAQ), modified British Medical Research

Council Questionnaire (mMRC) dyspnea scale, Fatigue Severity Scale (FSS) were used to assess physical activity, dyspnea and fatigue severity, respectively. The heart rate (HR), peripheral oxygen saturation (SpO_2), blood pressure (BP), modified Borg scale score for dyspnea, general and leg fatigue were recorded before and after 6MWT and 6MST. Changes between their final and initial values (Δ) for HR, SpO_2, BP, and modified Borg score were calculated.

Results: The number of steps in 6MST-2 was significantly higher than 6MST-1 ($p<0.001$). The number of steps in the 6MST-2 was significantly correlated with the distance walked in the 6MWT ($r=0.616$, $p<0.0001$). Additionally, significant correlations were observed between 6MST-2 and mMRC dyspnea scale score ($r=-0.733$, $p<0.0001$), FSS score ($r=-0.575$, $p\leq0.001$), IPAQ score ($r=0.330$, $p<0.05$). ΔBP, Δdyspnea, Δgeneral and Δleg fatigue perception were higher in the 6MST-2 than the 6MWT ($p<0.0001$). ΔHR and ΔSpO_2 were similar in 6MST and 6MWT ($p<0.05$).

Conclusion: The 6MST is a valid test to evaluate functional exercise capacity in Ssc patients. The 6MST might be more appropriate for evaluating perceived exertion, functioning, and lower extremity capacity. To assess the exercise capacity in Ssc patients, 6MST can be done with ease in all settings, including primary care to hospital settings with limited space and home-based telerehabilitation.

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POS0995-HPR SLE-DAS AS AN ALTERNATIVE TOOL TO MEASURE ACTIVITY OF SYSTEMIC LUPUS ERYTHEMATOSUS: COMPARISON WITH SLEDAI-2K, IN A POPULATION FROM THE DOMINICAN REPUBLIC. PILOT STUDY

Keywords: Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that mainly affects women. Efforts are currently being made to validate the Systemic Lupus Erythematosus Disease Activity Score (SLE-DAS), since it allows quantifying the magnitude of the findings as opposed to an arbitrary value of present or absent in the renal, joint, hematological and serological spheres. [2]

Objectives: To evaluate the activity of Systemic Lupus Erythematosus with the SLE-DAS tool, comparing it with SLEDAI2-K.

Methods: Descriptive, observational, transversal. Patients from the Rheumatology Service of the Padre Billini Teaching Hospital were evaluated between October-December 2022. Inclusion criteria: > 18 years, SLE according to the EULAR/ACR 2019 classification criteria. Exclusion criteria: diagnosis of another autoimmune disease, patients with cognitive deficits. SLE-DAS tool: Inactive ≤2.08, mild 2.08 - 7.64, moderate/severe >7.64, SLEDAI: Inactive: <3, Mild to moderate: 3/12, severe >12. Descriptive analysis and Spearman's rho (ρ) correlation using SPSSv23.

Results: 92 patients met inclusion criteria. 95.7% (88) female, mean age 41.5 ± 12 years, mean SLE 8.2 years. AHT 29.3% (27), DM 7.6% [7], lupus nephritis 35.8% (33), Obesity 7.6% [7], musculoskeletal 20.6% (19), Vasculitis 6.5% [6], Neuro Lupus 4.3% [4], antimalarials 96.7% (89), glucocorticoids 39.1% (36), Mycophenolate Mofetil 40.2% (37), Rituximab 7.6% [7], Methotrexate 5.4% [5], Azathioprine 4.3% [4], Tacrolimus 2.1% (2), Cyclophosphamide 1.1% [1]. SLE-DAS inactive: 81.5% (75) vs SLEDAI inactive: 88% (81), SLE-DAS inactive: 81.5% (75) vs SLEDAI inactive: 88% (81) (Spearman's rho (ρ)= -0.11), a gradient difference of 6.5% [6].

Conclusion: Our study demonstrated a significant inverse correlation in the correlation between SLE-DAS vs. SLEDAI in inactive patients, supporting that the use of the SLE-DAS may be more sensitive to assess activity or changes in the clinical course of patients with SLE. More studies are needed to validate this tool and standardize it for our population.

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Disclosure of Interests: None Declared.

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HPR Epidemiology and public health (including prevention)

POS0996-HPR THE PREVALENCE OF PULMONARY ARTERIAL HYPERTENSION IN PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Epidemiology, Systematic review, Mixed connective tissue disease

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Background: The prevalence and outcome of mixed connective tissue disease-associated pulmonary arterial hypertension (MCTD-PAH) has not been well understood.

Objectives: Our aim was to review the current knowledge on the prevalence, severity, and mortality of MCTD-PAH. We also aimed to examine the trend of the prevalence of MCTD-PAH over the years.

Methods: PubMed/Medline, Embase, Scopus and Web of Science electronic databases were searched for the published randomized controlled clinical trials (RCTs) and observational/original studies on PAH in patients with MCTD from January 1972 – December 2020.

Results: The results were pooled using random-effects meta-analysis based on the DerSimonian and Laird method. A total of 983 patients from eight studies were included in the meta-analysis (K=8, N=983). Pooled prevalence of PAH in MCTD patients was 12.53% [95% CI 8.30%-18.48%] with significant level statistical heterogeneity tau2=0.30, tau=0.55, I2 83.3%, H=2.13 Q(df,7) =31.90, P=0.001. There was no association between PAH and female gender or age. The percentage of deaths in MCTD patients due to PAH varied and reached up to 81.8%.

Conclusion: This is the first systematic review and meta-analysis investigating the prevalence of PAH in patients with MCTD and it revealed an overall prevalence of PAH in patients with MCTD of 12.53%. Our results showed trends of reduced prevalence of MCTD-PAH over the years, reconfirmed the lower prevalence rate in the recent studies, but revealed increased mortality rate. We also determined the low impact of the age, gender, and interstitial lung disease on MCTD-PA.H.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS0997-HPR LUPUS MORTALITY IN RELATION TO THE OVERALL ENVIRONMENTAL QUALITY INDEX AND ITS FIVE DOMAINS

Keywords: Geographical differences, Prognostic factors

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Background: Growing evidence suggests a role of exposure to chemicals and industrial pollutants, such as hydrocarbons, silica, mercury, organochlorines and trichloroethylene, particulate air pollution, UV radiation, infectious agents, living in certain geographic regions, and sociodemographic factors in increasing the risk and/or affecting the outcome of systemic lupus erythematosus (SLE). We utilized the environmental quality index (EQI) developed by the U.S. Environmental

Protection Agency (EPA) to represent environmental quality to better understand the association between environmental factors and lupus deaths. Five domains including air, water, land, built and sociodemographic comprised the EQI.
Objectives: Here, we summarize the descriptive statistics between environmental exposures and lupus death and compared them to accidental deaths, heart disease and malignant neoplasm.
Methods: The study population comprises all individual U.S. deaths from 2006 to 2011. We describe mean/median EQI in lupus deaths versus those who died of other leading causes of death, namely accident, heart disease, and malignant neoplasm. Cause-specific death counts were obtained using ICD 10 codes: lupus (M321, M328, M329), accident (V, W, X0-5, Y85-86), heart disease (I0, I11, I13, I2-4, I50-51), and malignant neoplasm (C0-8, C90-97).
Results: There were 5,430 lupus deaths and 398,382 accidental deaths in the US from 2006 to 2011. The total EQI was significantly worse in lupus decedents than in accidental deaths ($p<0.001$), but not when compared to deaths attributed to heart disease and malignant neoplasm. Of the five EQI domains, air and built, but not the other three domains, were higher in lupus decedents than in accident ($p<0.001$), heart disease ($p <0.05$), and malignant neoplasm ($p<0.05$) decedents.
Conclusion: Total environmental quality as well as its air and built domains were worse in lupus decedents than in accidental deaths, suggesting a possible role of environmental exposure in contributing to lupus outcome. Further analysis is needed to identify the specific environmental determinants, which are potentially modifiable to improve lupus outcome.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS0998-HPR THE EPIDEMIOLOGY OF PRIMARY SJOGREN'S SYNDROME: IS IT A RARE DISEASE?

Keywords: Sjögren syndrome, Real-world evidence, Epidemiology

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Background: Sjogren's syndrome (SSj) is a systemic disease with autoimmune pathogenesis, with prevalent involvement of the lacrimal and salivary exocrine glands, classified as primary or secondary on the basis of the association with other rheumatic diseases.
The epidemiological data in the literature are variable due to the heterogeneity of the populations examined and the different classification criteria used.
In a recent systematic review by Baodon Qin et al. In a recent systematic review by Baodon Qin et al. the average incidence rate was 7 cases every 100,000 people/year (range 5-9) with higher values in the Caucasian and Asian populations, with a women/men ratio of 9.3 (95% CI 3.35 to 13.18), while the prevalence rate was 61 cases per 100,000 inhabitants (range 10-90) with a female/male ratio of 10.7 (95% CI 7.35-15.62).
Objectives: The aim of the study was to estimate the prevalence rate of primary SSj in real-life, through analysis of administrative data.
Methods: An epidemiological research was carried out as at 31 December 2020, through the analysis of all adult patients residing in Piedmont (northwest of Italy) with exemption code (EC) for SSj (code 030) and any association with other ECs for rheumatological pathologies or for pathologies considered according to the 2016 EULAR/ACR classification criteria; specifically, the EC were considered for rheumatoid arthritis, ulcerative colitis and Crohn's disease, chronic hepatitis (active), HIV infection, affected subjects from malignant neoplastic pathologies, tumors of uncertain behavior, systemic lupus erythematosus, Hashimoto's thyroiditis, undifferentiated connective tissue disease; mixed cryoglobulinemia, antiphospholipid antibody syndrome (primary form), primary and familial amyloidosis, hereditary/familial autoinflammatory syndromes, microscopic polyangiitis, polyarteritis nodosa, sarcoidosis, dermatomyositis, polymyositis, mixed connective tissue disease, progressive systemic sclerosis.
Results: There were 3889 patients with EC for SSj as at 31 December 2020, of which 2611 with active EC. The number of assisted people alive with the aforementioned exemption was 2601, while those with other exemptions in the list were 1020. Of these patients, 1581 had only the exemption from code 030 as at 31 December 2020; the distribution of the other pathologies analyzed is shown in the tables below (Table 1). Of the total number of patients with active exemption, 2442 were female, while 159 were male, with a female/male ratio of 15.3; the distribution by gender is shown in Figure 1. Considering that the Piedmont population on 31 December 2020 was 4 274 945 inhabitants (ref: National Institute of Statistics), the estimated prevalence rate was 4.7 cases per 10 000 inhabitants.

Table 1. Distribution of EC in patients residing in Piedmont as at 31/12/2020

Diseases with EC	N of patients
Rheumatoid Arthritis	250
Ulcerative colitis and Crohn's disease	18
chronic hepatitis	52
HIV infection	2
Systemic Lupus Erythematosus	122
Subjects affected by malignant neoplastic pathologies	330
Hashimoto's thyroiditis	280
Undifferentiated Connective Tissue Sisease	86
Mixed Cryoglobulinemia	6
Antiphospholipid Antibody Syndrome	8
Primary And Familial Amyloidosis	3
Hereditary/Familial Autoinflammatory Syndromes	1
Microscopic Polyangiitis	2
Polyarteritis Nodosa	1
Sarcoidosis	5
Dermatomyositis	2
Polymyositis	5
Mixed connective tissue disease	25
Progressive systemic sclerosis	56

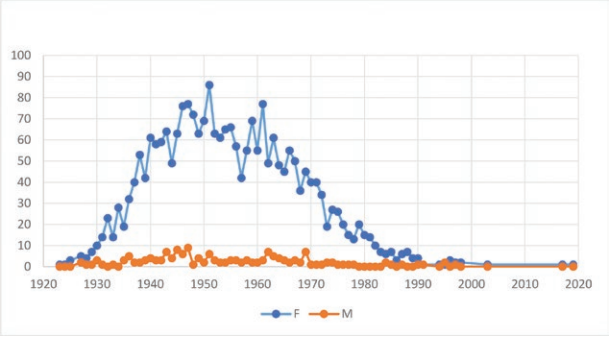


Figure 1. Distribution by gender of patients residing in Piedmont with exemption for Sjogren's Syndrome. F: Female; M: Male

Conclusion: This research has some limitations, including the retrospective design and the use of administrative data which may be affected by the aforementioned difficulty of classification as well as incorrect attributions of exemption, both for SSj and for associated pathologies. Our research highlights a number of patients with primary SSj lower than the prevalence figure that defines a rare disease, i.e. a prevalence of less than 5 cases per 10,000 inhabitants. Further studies are needed to confirm these preliminary data.
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Disclosure of Interests: None Declared.
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POS0999-HPR THE IMPACT OF THE COVID-19 PANDEMIC ON REFERRALS TO MUSCULOSKELETAL SERVICES FROM PRIMARY CARE AND SUBSEQUENT INCIDENCE OF INFLAMMATORY RHEUMATIC MUSCULOSKELETAL DISEASE: AN OBSERVATIONAL STUDY

Keywords: Rheumatoid arthritis, Epidemiology, COVID

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Background: Inflammatory rheumatic and musculoskeletal diseases (iRMDs), including rheumatoid arthritis (RA) and juveneille inflammatory arthritsi (JIA), are common and cause a high disease burden globally. Early diagnosis of iRMDs and subsequent timely access to disease modifying therapies is associated with improved health and socio-economic outcomes. However, the COVID-19 pandemic meant that the way healthcare was delivered changed abruptly as all consultations were 'remote by default' was widely implemented, replacing traditional 'face-to-face' healthcare.
Objectives: To describe the impact of the COVID-19 pandemic upon referral patterns and incident diagnosis of iRMDs.

Methods: Data from the Clinical Practice Research Datalink Aurum were analysed from 01/04/17 to 01/10/2021 to describe episodes of care for patients with musculoskeletal (MSK) conditions, in a primary care setting, for pre-COVID-19 (01/04/2017–31/03/2020), early-COVID-19 (01/04/2020–31/07/2021), and late-COVID-19 pandemic (01/08/2020–31/10/2021) periods. Prevalent and incident MSK consultations were determined. Referrals were matched to these consultations. Trends in referrals to MSK services and further incident diagnoses of iRMDs were described using Joinpoint regression and comparisons made between time-periods. Negative binomial regression was used to compare incident rates between time-periods: first MSK consultation to RA/JIA/iRMD diagnosis; first MSK consultation to first referral; first referral to RA/JIA/iRMD diagnosis. The number of consultations between first MSK consultation and referral/diagnosis were described. Results were adjusted for age and sex and further stratified by geographical region and deprivation.
Results: The incidence of RA and JIA reduced by -13.3% (from 32.0 to 17.2 per 100,000) and -17.4% (from 1.8 to 0.97 per 1,000,000) per month respectively between January 2020 and April 2020, and then increased by 1.9% (from 17.2 to 25.2 per 100,000) and 3.7% (from 0.97 to 1.3 per 1,000,000) per month respectively between April 2020 and October 2021. The incidence of all diagnosed iRMDs was stable until October 2021. Referral incidence decreased between February 2020 and May 2020 by -16.8% (from 4.8 to 2.4 per 100) per month in patients presenting with a MSK condition. After May 2020, referrals increased significantly (16.8% per month from 2.4 to 4.5 per 100) to July 2020. Time from first MSK consultation to RA diagnosis, and referral to RA diagnosis increased in the early-pandemic period (rate ratio (RR) 1.11, 95% confidence interval (CI) 1.07-1.15; RR 1.23, 95%CI 1.17-1.30) and remained consistently higher in the late-pandemic (RR 1.13, 95%CI 1.11-1.16; RR 1.27, 95%CI 1.23-1.32) periods respectively, compared to the pre-COVID-19 period.
Conclusion: Patients with underlying RA/JIA that developed during the pandemic may be yet to present, or in the process of being referred and/or diagnosed. Primary care clinicians should remain alert to this possibility and consider the use of fast-track referral pathways where indicated. It is apparent that patients developing incident episodes of inflammatory arthropathies may display a prodrome of other MSK symptoms and conditions, which alone may not warrant referral but in combination require further investigation. Commissioners should be alert to these findings to allow for the appropriate planning and commissioning of services.

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Disclosure of Interests: None Declared.
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POS1000-HPR CORRELATION OF ABNORMAL DIET AND ABNORMAL LIFESTYLE WITH INFLAMMATORY MARKERS AND RAPID 3 SCORE IN AUTOIMMUNE RHEUMATIC DISEASE-RELATED ARTHRITIS (RA, SPA AND PSA) AFTER TREATMENT

Keywords: Inflammatory arthritides, Lifestyles, Diet and nutrition

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Background: It is considered that unhealthy diet and unhealthy lifestyle has a possible role in inflammation of patients with Rheumatoid arthritis (RA), Spondyloarthritis (SpA) and Psoriatic arthritis (PsA).
Objectives: We set out to find out the role of unhealthy diet and unhealthy lifestyle in the regulation of inflammation after treatment in our patients with autoimmune arthritides such as RA, SPA, PSA.
Methods: A retrospective analysis was carried out using a questionnaire on diet and lifestyle for our defined study population. Our source data was analyzed for inflammatory markers such as CRP, ESR and RAPID 3 scores post-treatment for the patients who filled the questionnaire. A total of 56 patients participated who visited our clinic. After obtaining informed consent, data was gathered through interview method and was further correlated with ESR, CRP and RAPID 3 scores post treatment. Based on consensus, unhealthy diet was defined as consuming red meat anytime, having more than two teaspoons of sugar per day, smoking any amount or in any frequency, and daily alcohol consumption beyond the usual acceptable standard daily limits. Unhealthy lifestyle was defined as spending more than 6 hours per day sitting without taking any break and never engaging in any physical exercises. All the parametric measures were represented as mean ± SEM, and categorical variables were represented in contingency tables as number of incidences/occurrences. The continuous variables were compared by One-way Anova, categorical variables were analyzed by Chi-square test (non-parametric test) and correlation analysis was performed using Pearson's correlation test. The $p<0.05$ was considered as statistically significant.
Results: Average age of our study group of 56 patients was 48 years, 64% were female, 50% were homemakers, mean duration of treatment was 51 months, predominance of RA (42%), PsA patients (25%), SPA (31%) and a few overlaps. Mean weight was 67.6kg and mean height was 158.76cms. 77% were on combination of CS DMARDS + TS DMARDS. 46% reported they consumed red meat any time, 68% consumed sugar more than 2 teaspoons per day, 9% were smokers while 21 % consumed alcohol daily above the usual defined daily limits. 34% of study population were sedentary, 17% sitting for long hours without break, while 38% with minimal or no exercise. We observed no statistically significant (p 0.5798) correlation between unhealthy diet and RAPID 3 scores post treatment. Similarly, there was no statistically significant correlation between unhealthy diet and ESR (P 0.09) and CRP (p 0.7). There was again no statistically significant correlation between unhealthy lifestyle and CRP (p 0.539), ESR (p 0.164) and RAPID 3 scores (p 0.7) post treatment. However when we analyzed the unhealthy lifestyle parameter sitting for more than 6 hours without break separately we found the correlation of sitting for more than 6 hours without break and RAPID 3 scores to be statistically significant in our study population (p 0.04).
Conclusion: In our study group with limited number of patients we found no statistically significant correlation of unhealthy diet or unhealthy life style in regulation of inflammation post treatment in patients with inflammatory arthritides (RA, SpA and PsA). However, we found that sitting for 6 hours without break and RAPID 3 scores statistically correlated well. This possibly indicates that those patients with inflammatory arthritides (RA, SpA, PsA) who did not move from one place beyond 6 hours in a day had persisting poor quality of life even after treatment suggesting that "Sitting beyond 6 hours without a break could be deemed as the new smoking". But, more patient numbers would be required to retest the same hypothesis at a later stage.
Unhealthy Lifestyle vs Rapid 3 scores Correlation.
Criteria: Sitting for More than 6 Hours.
p value 0.04

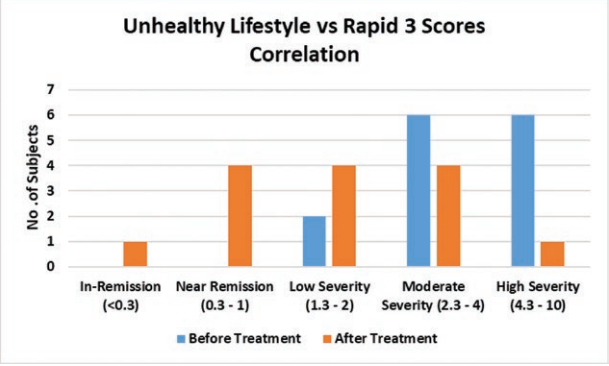


Figure 1.

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Disclosure of Interests: None Declared.
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POS1001-HPR THE IMPACT OF FRAILTY ON FEAR OF FALLING, QUADRICEPS MUSCLE STRENGTH AND FUNCTIONAL PERFORMANCE IN OLDER ADULTS WITH TOTAL KNEE ARTHROPLASTY DUE TO KNEE OSTEOARTHRITIS

Keywords: Osteoarthritis, Outcome measures

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Background: Frailty has been linked with poor quality of life, mortality, and readmission to the hospital. Also, frailty may have an impact on patients' capacity to enhance their functional ability which may be revealed by impaired muscle strength and increased fear or risk of falling. The presence of frailty is generally investigated before the arthroplasty surgery, however, patients may be at risk of future adverse health outcomes during the post-surgical period.
Objectives: To investigate the impact of frailty on fear of falling, quadriceps femoris muscle strength, and functional performance among older adults who had undergone total knee arthroplasty due to knee osteoarthritis.
Methods: A total of 70 patients were evaluated aged between 60 to 90 years, had undergone total knee arthroplasty surgery at least one year before the study. Patients were categorized according to their frailty status based on the FRAIL scale. The FRAIL scale includes 5 items as fatigue, resistance, ambulation, illness, and loss of weight (scoring: ≥3/5 criteria as frail, 1-2/5 as pre-frail, and 0/5 as robust). The Falls Efficacy Scale (FES) was utilized to determine the fear of falling. Bilateral isokinetic quadriceps femoris muscle strength was evaluated at 180 deg/sec. The Timed Up and Go (TUG) test was used to assess functional performance. A between-group comparison with post hoc analysis was performed to reveal the effects of frailty on outcome measures.
Results: The mean age of patients was 71.04±6.43 years with 87.1 % being female. According to the FRAIL scale, 30.0 % of the patients were frail, 44.3 % were pre-frail, and 25.7 % were robust. The frail group had higher fear of falling and lower functional performance compared to pre-frail and robust individuals ($p<0.05$). The peak torque of the quadriceps femoris muscle at 180 deg/sec was lower in the frail group compared to pre-frail and robust patients ($p<0.05$). No differences were detected between robust and pre-frail patients ($p>0.05$).
Conclusion: Our findings indicate that frailty status should be considered during the routine assessment of patients who had undergone total knee arthroplasty. Concomitant frailty during the post-surgical period may decrease functional performance, increase fear of falling, and deteriorate muscle strength which may result in increased fall risk and adverse health outcomes. Patients may need a multimodal intervention including muscle strengthening and postural balance exercises to reverse the effects of frailty.
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Table 1. Comparison of patients according to their frailty status.

	Robust (n = 18)	Pre-frail (n = 31)	Frail (n = 21)	P
Age, mean (SD) years	69.0 (4.35)	70.2 (6.68)	73.9 (6.81)	0.039*
BMI, mean (SD), kg/m2	32.81 (5.96)	34.75 (5.66)	34.71 (7.16)	0.531
Falls Efficacy Scale, mean (SD)	21.16 (9.30)	32.23 (17.90)	44.47 (15.46)	0.001**
TUG, mean (SD), sec	11.77 (2.55)	14.58 (4.70)	17.02 (4.05)	0.001**
Knee extension peak torque (affected extremity), mean (SD), Nm	34.07 (9.78)	31.28 (10.50)	24.27 (7.72)	0.003**
Knee extension peak torque (non-affected extremity), mean (SD), Nm	37.13 (12.06)	30.54 (9.80)	26.81 (9.47)	0.022**

*Significant differences between frail and robust patients.** Significant differences between frail to pre-frail and robust patients.

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POS1002-HPR PREDICTIVE FACTORS FOR MAJOR ADVERSE CARDIOVASCULAR EVENTS IN SERBIAN ANTIPHOSPHOLIPID SYNDROME PATIENTS– A 10-YEAR FOLLOW-UP STUDY

Keywords: Anti-phospholipid syndrome, Cardiovascular disease

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Background: Non-valvular cardiac disease in antiphospholipid syndrome (APS) has been modestly evaluated.
Objectives: We wanted to assess the prevalence and evolution of major adverse cardiovascular events (MACE) in a cohort of APS patients.
Methods: From a large cohort of 181 APS patients included in a study from 2011-2012.year at University Clinical Hospital Center Bezanijska kosa, Belgrade, Serbia, data for the occurrence of MACE in 10 years of follow-up were evaluated in 82 patients (86.6% females, 62.2% with primary (PAPS), and 37.8% patients with APS associated with systemic lupus erythematosus (SLE) (sAPS)). At the inclusion in all patients, a transthoracic echocardiography study for the assessment of dimensions and functionality of the left and right heart along with valvular functions and morphology has been performed along with color doppler scan of carotid arteries for the intima-media thickness and presence of plaques, and flow-mediated dilatation of the brachial artery (FMD) as markers of subclinical atherosclerosis. Standard atherosclerotic risk factors prevalence was analyzed. Antiphospholipid antibodies (aPL) analysis included the detection of aCL (IgG/IgM), ß2GPI (IgG/IgM), and LA, and all patients were treated according to the valid guidelines by the rheumatologist. Data regarding the occurrence of new myocardial infarction (MI), cerebrovascular events (CVI), arterial and/or venous thrombosis, heart failure (HF), and cardiovascular death (considered as MACE) have been collected 10 years after inclusion.
Results: The prevalence of standard atherosclerotic risk factors was less than 40% in both study groups. Left ventricle ejection fraction (LVEF) was over 45% in more than 90% of patients in both groups (p=0.246) with valvular dysfunction present in 49% of PAPS and 58.1% of sAPS patients (p=0.426). FMD was lowered in 29.4% of PAPS and 29% of sAPS (p=0.971) and carotid atherosclerotic plaques were present in 41.2% of PAPS and 64.5% of sAPS patients (p=0.040). 9.8% PAPS and 12.9% sAPS had coronary artery disease (CAD) (p=0.724) and HF was present in 7.8% PAPS and 3.2% sAPS (p=0.645). MACE occurred in 17.6% of PAPS and 22.6% of sAPS (p=0.585). The new MI occurred in 9.8% of PAPS and 9.7% of sAPS (p=1.000), CVI in 5.9% of PAPS and 3.2% of sAPS (p=1.000), HF in 5.9% of PAPS and 3.2% of sAPS (p=1.000) and cardiovascular death in 9.8% of PAPS and 12.9% of sAPS (p=0.724). New thrombotic events (arterial and/or venous) occurred in 15.7% of PAPS and 17.2% of sAPS (p=1.000). During the follow-up period, 66.7% of PAPS and 55.2% of SAPS (p=0.313) were treated with aspirin, 25.5% of PAPS and 25.0% of sAPS with warfarin, and chloroquine was administered in 46.8% of PAPS and 53.6% of sAPS (p=0.571). Age (p=0.008), gender (p=0.034), thrombotic APS (p=0.033), hypertension (p=0.003), diabetes mellitus (p=0.043), and cardiovascular manifestations present at the time of APS diagnosis (p=0.035), namely CAD (p=0.001) and HF (p=0.005) were significantly associated with 10y MACE. In our cohort, aPL type and category were not associated with 10y MACE. In a multivariate logistic model, age. hypertension, and HF were independent predictors for 10y MACE (p=0.012, OR 8.406, p=0.032, OR 4.588, p=0.019, OR 20.377, respectively for CI 95%).
Conclusion: APS patients develop new cardiovascular events despite optimal medical therapy. Cardiovascular evaluation at the time of diagnosis and proper cardiologist follow-up with the rigorous treatment of standard atherosclerotic risk factors is of utmost importance.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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HPR Interventions (educational, physical, social and psychological)

POS1003-HPR EFFECTS OF VIRTUAL REALITY IN PATIENTS WITH CHRONIC REFRACTORY PAIN SYNDROMES UNDERGOING A MULTIMODAL PAIN PROGRAM

Keywords: Health services research, Fibromyalgia, Pain

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Background: Virtual reality (VR) has shown efficacy and safety in reducing pain in various indications. Our department has been using virtual reality applications for several years in the multimodal pain program, where patients also undergo a detailed physical and psychological evaluation, allowing for distinct phenotyping.
Objectives: The aim of this study was to investigate the quantitative and qualitative analgetic and anxiolytic effect of a virtual reality (VR) procedure, and to identify patient clusters with a positive response to virtual reality.
Methods: 201 patients with refractory chronic pain syndromes (mainly back pain, primary or secondary fibromyalgia) who participated in a two-week multimodal treatment were included. Of those, 43 performed VR sessions under supervision. Pain (0-10) and anxiety (0-10) were assessed before and directly after a 10-minute VR session (Healthy Mind, France). Multivariate analysis with clinical variables and unsupervised machine learning for clustering analyses by hierarchical agglomerative clustering using the Ward variance minimization algorithm was performed (Python 3.10). In 40 patients, we performed qualitative user experience (UX) assessment of VR by telephone interviews.

Results: Overall, 51% patients experienced a reduction of pain (mean -1.03, baseline 6.15) and 49% a reduction of anxiety (mean -1.36, baseline 4.25) directly after the VR intervention. In 14% pain reduction was ≥3 points (25% for anxiety). Pain increased after the intervention in 15% and anxiety in 7% of the patients. The overall experience with VR was rated as positive in 76%, neutral in 9%, and negative in 14%. Qualitative assessment revealed that several of the non-responders expect a positive outcome in case of a more frequent application of VR. Unsupervised learning indicated the highest positive response in 2/5 clusters. One cluster was characterized by peri-menopausal women with moderate depression and systemic low-grade inflammation. The second cluster was mainly young to middle-aged men with low BMI, hypermobility, anxiety and somatoform pain. Other clusters characterized by failed-back surgery or post-traumatic stress disorders responded less to VR.

Conclusion: Overall, VR was well tolerated and showed a positive short-term response on pain and anxiety. Machine learning algorithms trained in larger cohorts may confirm the prediction of VR response in specific patient subgroups.

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POS1004-HPR INVESTIGATING THE EFFECTS OF COGNITIVE EXERCISE THERAPY APPROACH ON FUNCTIONING, ANXIETY, DEPRESSION AND BIOPSYCHOSOCIAL STATUS OF INDIVIDUALS DIAGNOSED WITH SYSTEMIC SCLEROSIS: A CONTROLLED PILOT STUDY

Keywords: Systemic sclerosis, Physical therapy/physiotherapy, Rehabilitation

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Background: Systemic Sclerosis (SSc) with heterogeneous involvement limits the functionality of individuals. Anxiety-depression and biopsychosocial effects are observed due to these functional limitations. Therefore, a biopsychosocial approach is recommended in the disease management of individuals with SSc [1, 2]. The Cognitive Exercise Therapy Approach (BETY) developed on individuals with rheumatism has been presented to the literature as a biopsychosocial-based exercise approach [3].

Objectives: The aim of this study was to investigate the effects of BETY on functionality, anxiety-depression and biopsychosocial status of individuals diagnosed with SSc.

Methods: 24 individuals diagnosed with SSc, 12 of who participated in BETY exercise sessions (Group 1) and 12 in the control group (Group 2) were included in the study. BETY exercise sessions were applied as group exercises 3 days a week for 12 weeks. At the beginning of the sessions and at the end of 12 weeks, functionality was evaluated with the Scleroderma Health Assessment Questionnaire (SHAQ) [4], anxiety-depression status with the Hospital Anxiety Depression Scale (HADS) (2) and biopsychosocial status with the BETY-Biopsychosocial Questionnaire (BETY-BQ) [3].

Results: The mean age of the individuals in the exercise group (44.50 ± 10.16 years) and the control group (47.75 ± 13.63 years), other demographic information and first evaluation parameters were similar (p>0.05). Individuals who participated in all BETY exercise sessions showed a significant improvement in all parameters (p<0.05). In the control group, depression score worsened (p<0.001) while other parameters did not change (p>0.05) (Table 1).

Table 1. Within and between group changes of individuals with SSc

		Pre-treatment (n=12)	Post-treatment (n=12)	Wilcoxon Signed Ranks Test	Mann-Whitney U Test
		Median (Min-Max)	Median (Min-Max)	p value	p value
SHAQ-Global (0-3)	Grup 1	0,54 (0-2,2)	0,2 (0-1,5)	0,019	0,006
	Grup 2	0,84 (0,1-1,7)	1,2 (0,3-2)	0,117	
HADS-Anxiety (0-21)	Grup 1	6,5 (0-18)	4,5 (0-16)	0,003	<0,001
	Grup 2	10 (5-15)	12 (5-18)	0,065	
HADS-Depression (0-21)	Grup 1	5 (0-12)	1 (0-12)	0,011	<0,001
	Grup 2	7 (2-12)	10 (3-19)	0,014	
BETY-BQ (0-120)	Grup 1	43 (8-93)	24 (3-68)	0,003	0,003
	Grup 2	56 (27-87)	61 (13-95)	0,875	

Conclusion: Individuals with SSc who participated in BETY exercise sessions showed improvements in functionality, anxiety-depression and biopsychosocial features which were not seen in the control group. The results obtained from the study were interpreted as an example that BETY, an innovative exercise method on the basis of the biopsychosocial model, can meet this need in the disease management of individuals with SSc, where the importance of biopsychosocial approach is emphasized. It was aimed to investigate the contribution of BETY to the literature by evaluating it on more individuals with SSc and with objective measurement parameters as well as scales.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1005-HPR RELIABILITY AND VALIDITY OF THE CONE EVASION WALK TEST IN KNEE OSTEOARTHRITIS

Keywords: Cartilage, Comorbidities, Clinical trials

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Background: Knee osteoarthritis (OA) can cause a variety of dysfunctions leading to limitations in mobility, gait, and balance that predisposes them to increased fall risk [1,2]. Falls are the leading cause of injury and fracture [3], putting a significant financial burden on the healthcare system. The fall risk is even higher in people with knee OA with a prevalence between 23 and 63% [4]. Another study reported that almost 50% of patients with knee OA experienced falls [5]. Therefore, the identification of fall predictors is essential to minimize fall incidence [6]. The Cone Evasion Walk Test (CEW) evaluates fall risk by the ability to evade obstacles and walking, which provides a versatile assessment including attentional, perceptual, seeing, and several neuromusculoskeletal and movement-related functions and can be performed with or without a walking aid [7].

Objectives: The study aimed to investigate the reliability, validity, and minimal clinically important difference (MCID) of the CEW in people with knee OA.

Methods: Thirty-three patients with knee OA were included. Patients performed trials for the CEW and the Timed up and Go Test on the same day. Between the trials, patients waited for an hour in a sitting position to prevent fatigue.

Results: The CEW was shown to have excellent test-retest reliability and moderate validity (p<0.001). The relative (ICC coefficient) and absolute (SEM and SRD95) reliability of the CEW were 0.97, 0.73, and 2.02 respectively. The Pearson correlation coefficient between the CEW and the TUG was 0.72.

Conclusion: The measurements support the use of the CEW to evaluate dynamic balance and obstacle avoidance of knee OA patients. The analysis demonstrated excellent reliability and moderate validity. The low MCID value (2.02) indicated that it is a responsive test to identicate small changes in a patient's status. The CEW can be used for a global evaluation of the function and mobility of knee OA patients with little space and equipment, easily and quickly.

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HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

POS1006-HPR DOES FIBROMYALGIA AFFECT OCCUPATIONAL PRODUCTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS?

Keywords: Work-related issues, Fibromyalgia, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) may have a negative impact on patients' autonomy, quality of life and work productivity. Associated fibromyalgia may further accentuate this issue.
Objectives: We aimed to assess the impact of RA-associated fibromyalgia on occupational productivity.
Methods: We conducted a cross-sectional study including RA patients (2010 ACR/EULAR criteria). Patients were divided into two groups: group 1 (G1) including patients with fibromyalgia associated to RA, and group 2 (G2) including patients with RA. Fibromyalgia screening was based on the Fibromyalgia Rapid Screening Tool (FIRST). All patients completed the following questionnaires: Workplace Activity Limitations Scale (WALS) which is composed of 11 items (total score varying between 0 and 33), Work Productivity and Activity Impairment (WPAI) and Euro-Qol (EQ-5D). We compared the two groups of patients using the Student's t-test. The significance threshold was set at a p value of 0.05.
Results: Our study included 80 patients (G1: N=40 and G2: N=40) with an average age of 59±9 years [42-77] for G1, and 53 ±10 years for G2 [37-74]. The gender-ratio was 0.05. All the patients in G1 and 80% of patients in G2 held a job. The mean RA duration was 11.29±6.24 years. RA was erosive and ACPA/RF positive in 90% and 85% of cases, respectively. The mean delay between fibromyalgia and RA diagnosis was 49±7 months. The mean Disease Activity Score 28 (DAS_{28} ESR) was 5 in G1, and 3.97 in G2. The reduction of work activity was greater in G1 compared to G2: the mean WALS in G1 was 18±2.7 vs 10.2±1.5 in G2; p= 0.01. The WPAI showed that the mean number of work hours missed due to RA was significantly higher in G1 compared to G2: 10.2±8 hours vs 4.3±0.8 hours (p< 0.01). The mean absenteeism rate was higher in G1 compared to G2: 17.5 ±1.9% in G1 vs 10.2 ±0.5% in G2 (p= 0.02). The percentage of overall impairment of health related-activity was higher in G1 compared to G2: 50±8.6% in G1 vs 30±4.4% in G2 (p= 0.01). The mean self-rated health status using the EQ-5D VAS was 72.08 ±7% in G1 and 48 ±3.5% in G2 (p=0.05). The most affected dimensions in the EQ-5D for both groups were in the first place pain and discomfort, and secondly mobility. Loss of autonomy was found in 7 patients (37.5%) in G1 and 3 patients (7.5%) in G2. Depression and/or anxiety occurred in 45% of cases in G1, and 22.5% of cases in G2, respectively.
Conclusion: Our study showed that RA-associated fibromyalgia has a negative impact on work performance and productivity. This association also seems to alter the quality of life.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1007-HPR EXPERIENCES OF PARTICIPATION IN GOAL SETTING PRIOR TO RHEUMATIC TEAM REHABILITATION – A JOINT VENTURE

Keywords: Qualitative research methods, Rehabilitation

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Background: Patient involvement in the goalsetting process and use of shared decisions increases adherence to rehabilitation and support patients' motivation to achieve the goals (1). However, the shared decisions that are essential for goal setting during a rehabilitation process may be compromised by patients' lack of ability to participate actively in setting goals, inadequate skills among health professionals (HPs) to facilitate goal setting and poor organizational conditions such as insufficient time [2]. This study focuses on a Danish multi-professional team rehabilitation context where, over several years, work has been done to improve the prerequisites for goal setting, both by organizational changes and by educating and preparing HPs as well as patients for the goal setting process.
Objectives: To understand how patients with rheumatic musculoskeletal diseases (RMDs) perceive participation in the goal setting process prior to multi-professional team rehabilitation.
Methods: Individual semi-structured interviews were performed with 22 patients (median 49 years, 17 female), who were to be admitted to multi-professional team rehabilitation for patients with RMDs at one of two Danish rehabilitation centres. We applied qualitative content analysis with an inductive approach. All participants had received information about goal setting prior to admission and the team used supportive tools and motivational interviewing to facilitate the goal setting process.
Results: The analysis derived one overarching theme, goal setting was viewed as a *joint venture* between the patients and the team, where capacities and resources were shared in order to formulate one or more goals. Three subthemes emerged from the analysis (Table 1): 1) *Responsibility during goal setting* was experienced as a shared responsibility between the patient and the team, where active involvement in the goal setting process added to patients' feeling of responsibility. For others, goal setting was perceived as a responsibility that solely rested with the team of HPs, who were considered to be the experts. 2) *Being dressed for goal setting* reflected whether patients felt prepared to take part in goal setting. Written and oral information prior to rehabilitation evoked thoughts on potential goals and previous experiences with rehabilitation made patients feel more qualified for setting goals. Others perceived goal setting as very difficult, partly because it felt like a huge commitment or due to lack of information.3) *Being an equal member of the team* referred to the interaction with the HPs. Patients felt they were seen as whole persons, and they felt acknowledged and respected. On the other hand, some felt as outsiders and considered HPs as authorities, causing a feeling of nervousness and insecurity related to the validity of the patients' wishes and expectations.
Conclusion: Despite a clinical practice where key areas of importance to successful patient-centred goal setting has been implemented, goal setting is still perceived as a challenge for some patients with RMDs. Future studies should uncover whether the level of health literacy among patients with RMDs bears importance for shared decisions and goal setting prior to rehabilitation.
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Table 1. Overview of the theme, subthemes and categories that describe patients' perceptions of participation in the goal setting process.

Theme	A joint venture					
Subthemes	Responsibility during goal setting		Being dressed for goal setting		Being an equal member of the team	
Categories	Goal setting is a shared responsibility	The health professionals are the experts	Feeling well prepared	Goal setting is challenging	Feeling like a part of the team	Feeling as an outsider

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

POS1008 INVESTIGATING ANTIGEN SPECIFIC T CELLS AND THEIR CITRULLINATED PROTEIN TARGETS IN SYNOVIAL TISSUE

Keywords: Adaptive immunity, Rheumatoid arthritis, Synovium

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Background: Rheumatoid arthritis (RA) is a T cell mediated autoimmune disease in which citrullinated self-antigens are recognized by anti-citrullinated protein antibodies (ACPA) and T cells. To date, the majority of T cell studies have been performed using peripheral blood and have focused on well-documented ACPA targets. Studies of disease-affected tissue are needed to confirm and extend observations that have been made through study of peripheral blood T cells.
Objectives: T cell subsets and targets that have not been observed in peripheral blood are likely to comprise an important (but as yet, understudied) component of the antigen specific responses that underlie RA. We sought to generate novel insights about T cell phenotypes and antigenic targets by performing multicolor flow cytometry analysis and HLA peptidomics studies of synovial tissue samples from subjects with RA.
Methods: Synovial tissue was obtained from 7 subjects with seropositive RA, 4 subjects with seronegative RA, and 8 subjects with osteoarthritis, all of whom had undergone arthroplasty procedures. Synovial cell suspensions were obtained from tissue through mincing, digestion in collagenase I, and filtration. These were subjected to multicolor flow cytometry analysis to gain insights about the lymphocyte and non-lymphocyte cell subsets present. After confirming leukocyte antigen (HLA) protein expression by flow cytometry, additional tissue was solubilized in lysis buffer and HLA class I and HLA-DR complexes were captured (separately) on affinity columns. HLA-bound peptides were eluted, concentrated, and peptide spectra were identified by LC-MS/MS analysis. The resulting datasets were assigned sequences by searching against a human protein database. Mass shifts associated with each assigned sequence were utilized to identify post-translational modifications – most notably citrullination of native arginine residues. Comprehensive libraries of the HLA-Class I- and HLA-DR-bound peptides from each individual were imported into a custom database, which was then used to catalogue the most prevalent self-proteins for each patient type. T cell assays were then performed to demonstrate the immunogenicity of novel targets and probe T cell antigen specificity in tissue.
Results: Flow cytometry analysis of synovial tissue derived cells demonstrated that fibroblasts (including fibroblast-like synoviocytes), monocytes, and B cells were all present in tissue. In particular, fibroblasts and monocytes showed evidence of inflammation, including upregulated levels of HLA-DR expression. Similar numbers of CD4+ and CD8+ T cells were present in tissue, with phenotypes that included various memory subsets but essentially no naïve cells. In comparison with peripheral blood, T cells from synovial tissue showed evidence of recent activation, expressing higher levels of CD95, CD71, PD-1, ICOS, and CD69. The most prevalent self-proteins in the HLA-DR-bound peptidome from the synovial tissue of RA subjects included expected targets such as vimentin, alpha-enolase, fibrinogen, collagen, histones, and BIP but also contained novel targets such as fibronectin, gelsolin, and proteoglycan 4. Prevalent self-proteins in the HLA-Class I-bound peptidome included well-studied CD4+ T cell targets such as vimentin, alpha-enolase, and collagen but also contained more novel targets such as caspase-14, stromelysin-1, and filamin-A. T cell assays supported the immunogenicity of expected targets and the new candidate antigen gelsolin. In particular, a comparatively robust population of aggrecan specific T cells was present in tissue.
Conclusion: Our findings demonstrate that flow cytometry and HLA peptidomic analysis of synovial tissue can provide novel insights about the phenotype and antigen specificity of T cells in RA. Further characterization of T cell response in tissue, including those that recognize novel antigens, has the potential to provide important new insights about the character of antigen specific T cell responses that promote the development of RA.
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Innate immunity in rheumatic diseases

POS1009 RADIOGRAPHIC AIRWAY ABNORMALITIES IN UNTREATED EARLY RHEUMATOID ARTHRITIS ARE ASSOCIATED WITH PERIPHERAL NEUTROPHIL ACTIVATION

Keywords: Lungs, Innate immunity, Rheumatoid arthritis

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Background: The role of the lung for the initiation and progression of rheumatoid arthritis (RA) is still unclear [1]. Up to 10% of RA patients develop severe treatment resistant lung disease [2]. Understanding early disease mechanisms is of great importance. Neutrophils are key players in RA pathogenesis and are recruited to the lungs early in the disease [3]. In RA, circulating neutrophils display an activated phenotype and neutrophil activation markers predict joint destruction and development of extra-articular nodules [4]. Neutrophil activation status has not been studied in relation to pulmonary abnormalities (PA) in early untreated RA (ueRA).
Objectives: To determine whether there is an association between peripheral neutrophil phenotypes and presence of PA on chest high-resolution computed tomography (HRCT) in ueRA.
Methods: Clinical data and blood were collected, and HRCT performed at diagnosis on 30 consecutive anti-citrullinated protein antibody (ACPA) and/or rheumatoid factor (RF) positive ueRA patients. HRCTs were evaluated for the presence and extent of RA-associated parenchymal, airway and/or pleural abnormalities. Expression of phenotype markers on neutrophils separated by density was determined by flow cytometry. Levels of calprotectin, ACPA and RF were measured using immunoassays. An initial principal component analysis was used to visualize the relationships of the multidimensional data followed by univariate analysis of the strongest associations.
Results: The median patient-reported symptom duration was 6 months, 20 % of the patients were current smokers and the mean disease activity was moderate in this seropositive ueRA cohort. The frequency of having any PA detected by HRCT was 60 %. Airway abnormalities were present in 50%, nodules in 43 % and interstitial lung abnormalities (ILA) in 10 %. Unsupervised multivariate factor analysis showed clustering of "any PA" with neutrophil activation, parameters of inflammation and RF titres (Figure 1A). Univariate analysis confirmed a significantly increased CD11b and decreased CD62L expression on neutrophils indicating activation in patients with PA as compared to no PA. Titres of RF, but not ACPA, correlated with expression of the neutrophil activation marker CD11b. A stratified analysis demonstrated that airway involvement was the PA subtype with the strongest association with neutrophil activation (CD11b 1.3-fold, p=0.014 and CD62L 0.6-fold, p=0.003 in patients with airway abnormalities as compared to no PA) and with RF IgM titres (8.8-fold, p=0.0002) (Figure B-E).
Conclusion: We report a significant association between radiographic airway findings and activation of circulating neutrophils in early RA supporting a role of innate immunity and the lung in disease onset. Our results also indicate different contributions of RF and ACPA in the RA pathogenesis. Parts of this abstract was presented 15 September 2022 on a national rheumatology meeting in Gothenburg, Sweden.

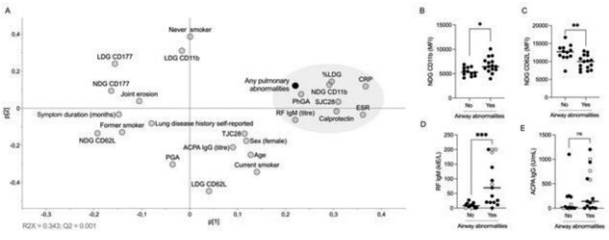


Figure 1. Principal component analysis showing the relationship between the presence any pulmonary abnormalities by HRCT, neutrophil phenotypes, disease activity measures and demographic data in ueRA patients (n=30) (A). Univariate analysis of CD11b (B) and CD62L (C) expression, RF (D) and ACPA titres (E) in patients with airway abnormalities vs no PA. Bars show median. NDG=normal density granulocytes, LDG=low density granulocytes. Smokers open circles.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1010 MACROPHAGE EXTRACELLULAR TRAPS PROMOTE FIBROBLAST-LIKE SYNOVIOCYTES PROLIFERATION AND PROINFLAMMATORY CYTOKINE IN RHEUMATOID ARTHRITIS

Keywords: Innate immunity, Synovium, Rheumatoid arthritis

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Background: Macrophage Extracellular Traps (METs) play an important role in the promotion of tissue injury, inflammation progression and autoimmune diseases.
Objectives: This study aims to investigate the effects of METs on the proliferation and expression of proinflammatory cytokines in fibroblast-like synoviocytes (FLS) in patients with rheumatoid arthritis (RA).
Methods: Synovial tissues of RA patients and traumatic controls undergoing joint replacement in our hospital were collected, and FLS of RA patients were cultured in vitro. Peripheral blood mononuclear cells (PBMC) were isolated from RA patients and differentiated into macrophages by M-CSF. The macrophages were co-cultured with serum of RA patients and healthy controls. SYTOX green, which stained the DNA released from cells and was a common method for detecting ETs, was added to observe the formation of METs. The expressions of CD68 and CitH3 in synovium were detected by immunofluorescence. METs were isolated and purified from THP-1 derived macrophages and co-incubated with FLS. The RNA expressions of proinflammatory cytokines TNF-a and IL-1β of RA-FLSs were detected by qPCR. The proliferation ability of RA-FLSs was detected by CCK-8 assay.
Results: We found the enrichment of macrophages labeled with CD68 and CitH3 in RA synovial tissues but not in traumatic controls. Immunofluorescence co-localization assay displayed that most CitH3 were distributed around CD68, suggesting that macrophages may be the main source of ETs (Figure 1A). PBMC induced macrophages co-incubated with serum from RA patients showed the formation of strip-like METs, while no obvious METs were observed with serum from healthy controls (Figure 1B). Purified METs were isolated and co-incubated with RA-FLSs for 48h. TNF-a and IL-1β were significantly overexpressed, and the proliferation of RA-FLSs was promoted (Figure 1C-D).
Conclusion: METs were detected in RA synovium but not in traumatic controls. The autoantibodies or inflammatory cytokines presented in the serum or RA patients may be associated with the increased METs formation in RA. In vitro experiments, METs could promote the proliferation and proinflammatory cytokines expression of RA-FLSs, suggesting that clearing or blocking the formation of METs may be a new therapeutic target for RA.

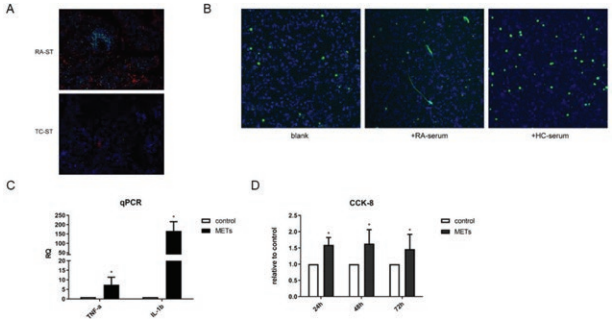


Figure 1. A, Immunofluorescence of synovium in RA and traumatic controls. Immunofluorescence showed the areas stained with anti-CD68 (red), anti-CitH3 (green) and DAPI (blue). RA: rheumatoid arthritis, ST: synovial tissue, TC: traumatic controls. B Formation of METs in human monocyte-derived macrophages with serum SYTOX green showed the formation of METs in macrophage with RA-serum. SYTOX green (green) and Hoechst 33342 (blue). C-D The promotion of METs in biologic behaviors of RA-FLSs. METs could promote the proliferation (C) and proinflammatory cytokines expression (D) of RA-FLSs.

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POS1011 DIFFERENT SYNOVIAL MACROPHAGE AND FIBROBLAST SUBSETS, EXPRESSION PROFILES AND CELL-CELL INTERACTIONS CHARACTERISE SEX DIFFERENCES IN CHRONIC INFLAMMATORY JOINT DISEASES

Keywords: Synovium, Inflammatory arthritides, -omics

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Background: Chronic inflammatory joint diseases differ between males and females in terms of disease manifestation, treatment response and radiographic progression. A molecular basis that could explain these differences has yet to be identified.
Objectives: The study aimed to find differences in synovitis at histology and transcriptome level between males and females with chronic inflammatory joint diseases.
Methods: Synovial tissue was obtained by ultrasound-guided biopsy from inflamed joints from 5 males and 5 age- and disease-matched females. Histological analysis included Krenn score and synovial pathotype. Single-cell RNA-sequencing (scRNA-seq) libraries were prepared with 10X Genomics and sequenced with NovaSeq 6000. We performed additional histological analyses (Krenn score and CD68 staining) on synovial tissue samples obtained from joint replacement surgery in 13 males and 13 age- and synovial pathotype-matched females with rheumatoid arthritis. The following R packages were used for bioinformatic analysis: Cell Ranger, Seurat, Harmony and CellChat. KEGG gene set enrichment analysis was performed with ClusterProfiler.
Results: We included 4 psoriatic arthritis, 2 rheumatoid arthritis, 2 undifferentiated arthritis and 2 peripheral spondyloarthritis patients. Females and males did not significantly differ in baseline characteristics: mean age was 46.2 years in females, 46.8 years in males; 2 knees and 3 wrists were biopsied per sex; mean swollen joint count was 6.8 in females and 8.2 in males. Histological analysis between the sexes showed no significant differences: synovitis was moderate in both sexes (mean Krenn total score 4.0) and pathotypes were balanced in males (1 diffuse-myeloid, 2 lympho-myeloid, 2 pauci-immune) and females (1 diffuse-myeloid, 1 lympho-myeloid, 1 pauci-immune, 2 ungradable). 41,014 cells were integrated for scRNA-seq analysis (female 21,636 and male 19,378 cells). Pseudobulk variance analysis showed a significant correlation of sex with principal component (PC) 3, accounting for 12.6% of the sample variation (Figure 1A). In addition to the sex-specific genes XIST and PRS4Y1, the following genes were main drivers of the PC3 variation: H19, CXCL9 and CXCL10. Diagnosis was not significantly associated with any PC. Comparison of the individual cell cluster proportions showed that LYVE1^{pos} macrophages (MC) were significantly more prevalent in females (4.9% in males versus 13.7% in females, p = 0.03) (Figure 1B). In confirmatory histological analysis, consistent with the known location of LYVE1^{pos} MC in the lining layer, both Krenn lining score (mean (SD) score in males 1.85 (0.69) and 2.08 (0.76) in females) and CD68 lining score (mean (SD) score in males 1.77 (1.17) and 2.08 (0.95) in females) were higher in females but did not reach statistical significance. Differential gene expression analysis showed that mainly in synovial fibroblasts (SF) genes were differentially expressed between males and females (n = 1944). In SF, upregulated genes in males led to a significant enrichment of proinflammatory pathways (TNF pathway, NF-kappa B pathway, IL-17 pathway). In contrast, upregulated genes in females were significantly associated with ECM-receptor interaction, focal adhesion, protein digestion and absorption pathways (Figure 1C). In cell-cell interaction analyses, most outgoing signaling was observed in SF while MC represented most receiving cells; IL6 and CXCL signaling pathways were significantly enriched in males, and COLLAGEN and THY1 signaling pathways in females (Figure 1 D/E).
Conclusion: Our study shows potential important differences in synovitis between males and females with chronic inflammatory joint diseases. In females, synovitis was characterized by abundance of LYVE1^{pos} MC and SF expressing

extracellular matrix-associated genes. In contrast, male SF showed a proinflammatory transcriptional profile. These sex-specific differences should be considered in research studying synovitis and may warrant sex-specific therapeutic approaches.

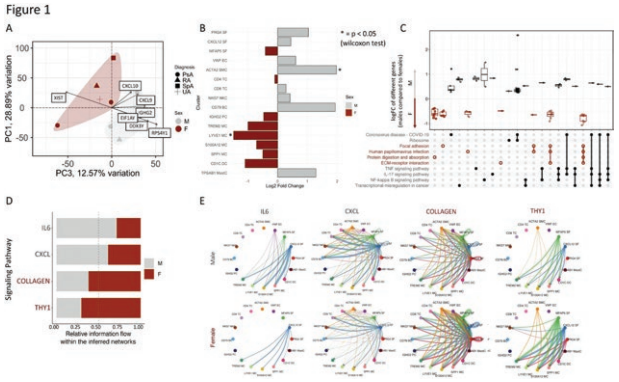


Figure 1.

REFERENCES: NIL.

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Rheumatoid arthritis - aetiology, pathogenesis and animal models

POS1012

SINGLE CELL RNA SEQUENCING REVEALS DISTINCT B CELL CHARACTERISTICS IN ANTI-CCP POSITIVE AT-RISK INDIVIDUALS WITH IMMINENT RHEUMATOID ARTHRITIS

Keywords: -omics, Genetics/epigenetics, Rheumatoid arthritis

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Background: Anti-cyclic citrullinated peptide (CCP) antibody positive individuals with musculoskeletal (MSK) symptoms but no clinical synovitis are at elevated risk of developing rheumatoid arthritis (RA) [1]. Whilst risk stratification is possible, specific immunological changes underpinning the transition from pre-RA to clinical arthritis remain unclear.

Objectives: We aimed to define markers of rapid progression across immune-cell subsets to enable early differentiation of those who will progress to arthritis in 'high-risk' anti-CCP positive individuals.

Methods: Peripheral blood mononuclear cells (PBMCs) were collected from anti-CCP positive individuals with MSK symptoms but no clinical synovitis (CCP+ at-risk). We performed single cell RNA sequencing (scRNAseq) of PBMCs from 10 CCP+ at-risk individuals (6 CCP+ progressors, 4 CCP+ non-progressors) collected at baseline and follow-up time points (i.e. progression to arthritis in the CCP+ progressors). All subjects had high positive anti-CCP levels (>3x ULN) and were HLA-DR shared epitope positive with median time to progression in progressors being 4 months. Analysis was performed in R using SingleR for subset annotation and Seurat for differential gene expression analysis between progressors and non-progressors and across time points.

Results: Examining all subsets, we noted a generalised increased Type 1 interferon response in non-progressors, with B cells (n=8,659) showing the most prominent divergence between groups. Within B cells we observed 334 differentially expressed genes (DEG) in CCP+ progressors versus non-progressors at baseline and 143 DEG at follow up (padj<0.05), with 77 DEG consistent across timepoints. At baseline, CCP+ progressors demonstrated upregulation of genes associated with B cell antigen-presentation, including Class II MHC molecules, CD83 and CD74. Conversely, interferon stimulated genes (ISG) were enriched in the CCP+ non-progressor DEG. Notably, this ISG signature ceased at follow-up (median 14 months). Examining the DEG per B cell subset, we noted that upregulation of genes associated with B cell antigen-presentation is found across naïve, unswitched memory and switched memory B cells in CCP+ progressors at baseline. In contrast, ISG upregulation is specific to a separate subset of interferon-responsive B cells. At baseline, these cells form a significantly greater proportion of all B cells in the CCP+ non-progressor group versus the progressor group (17.8% versus 2.6%, p<10-5). At follow-up, the proportions are comparable between the two groups (2.5% in non-progressor versus 3.4% in progressor, p=0.08), reflecting the transient nature of ISG upregulation.

Conclusion: CCP+ at risk individuals with imminent arthritis demonstrate a distinct B cell gene expression profile. Imminent progression is associated with markers of B cell mediated antigen presentation across multiple subsets whereas non-progressors demonstrate transient over-expression of ISGs driven by expansion of a subset of interferon-responsive B cells. These data reveal mechanistic insights into the early divergence between these groups and the development of RA.

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POS1013

EARLY LOW DOSE IL-2 REDUCED THE INITIATION OF COLLAGEN-INDUCED ARTHRITIS THROUGH RESTORING TFH/TFR BALANCE

Keywords: Rheumatoid arthritis, Adaptive immunity, Animal models

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Background: To date,there are also exploratory studies of partial prevention of RA, including dexamethasone,methotrexate, hydroxychloroquine, abatacept and so on[1].But no interventions have been proven to prevent the clinical onset of RA, and only some drugs may delay the appearance of clinical symptoms. Early restoration of immune tolerance and interruption an autoimmune response that is not yet well established may help prevent the occurrence of RA or achieve drug-free remission.Low-dose IL-2 is a new therapeutic strategy for many autoimmune diseases, including RA.However, no studies have focused on its preventive effect in Pre-RA.

Objectives: The aim of this study was to observe the preventive effect of low-dose IL-2 in collagen-induced arthritis, and to characterize the cellular mechanism underlying such an effect.

Methods: CIA is induced by primary immunization of bovine type II collagen (CII) and complete Freund's adjuvan and a booster injection of CII in incomplete Freund's adjuvant (day 21)in DBA/1 mice. CIA mice were intraperitoneally injected with 30000 IU rhIL-2 every other day at 0, 7, 14 and 21 days after primary immunization, lasted for 28 days.In addition CIA control, healthy control and Control-IL-2 were set up.Arthritis index was assessed after booster immunization.At the end of the experiment(d56 after the initial immunization), splenic mononuclear detected by flow cytometry.

Results: (1)The results showed that incidence rate of arthritis of the 0d-IL-2 group was lower than the 7d, 14d, 21d and CIA model groups (p=0.0012, p=0.0003, p<0.0001,p=0.0013). The arthritis index(AI) of 0d-IL-2 group was lower than that of 14d, 21d and CIA groups (p=0.0224, 0.0389, 0.0498), showing a trend of delayed arthritis.The AI of the 21d-IL-2 group had a decreased tendency compared with CIA group, but there was no significant difference. (2)At the end of the experiment, Flow cytometry was used to evaluate the proportions of Tfh($CD4^+CXCR5^+$) and Tfr($CD4^+CXCR5^+CD25^+Foxp3^+$) cells in spleen.The Tfh had no significant changes among all groups. The 14d-IL-2 group showed an increased trend of Tfh compared with other groups, but there was no statistical difference.The proportion of Tfr cells in both 0d-IL-2 and 14d-IL-2 group was significantly increased than that of CIA and healthy control group.By comparing the proportion of Tfh/Tfr in each

group, the proportion of Tfh/Tfr in CIA group was significantly higher than healthy control group. Compared with CIA model group,Tfh/Tfr in all intervention groups (0d,7d,14d,21d-IL-2) were significantly lower.

Conclusion: Early administration of low-dose IL-2 may help reduce the incidence of arthritis and disease activity in CIA by restoring Tfh/Tfr balance,but it has time heterogeneity.

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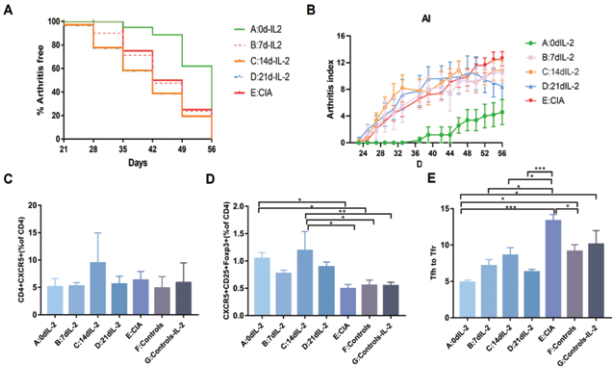


Figure 1. Early intervention of CIA with low dose of IL-2 at different time points. **(A)**The percentage of mice that remained arthritis free over time. **(B)**Arthritis scores of each experimental group over time. **(C)** Comparison of Tfh ($CD4^+CXCR5^+$)cells percentage and **(D)**Tfr($CD4^+CXCR5^+CD25^+Foxp3^+$) cells of $CD4^+$T cells in different groups. **(E)**The Tfh to Tfr ratio in different group.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1014 INVESTIGATING THE SYNOVIAL PATHOLOGY RELATED TO TREATMENT RESISTANCE IN JAPANESE RHEUMATOID ARTHRITIS PATIENTS USING SINGLE-CELL ANALYSIS

Keywords: Rheumatoid arthritis, Synovium

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Background: Despite of recent developments in therapeutic agents for rheumatoid arthritis (RA) patients[1], it is reported that half of the patients are unable to achieve remission even with existing drugs[2]. Therefore, there is an urgent need to gain mechanistic insight into treatment resistance. Nowadays, single-cell RNA sequencing (scRNA-seq) technology have dramatically improved our understanding of the heterogeneity in synovial cells. However, it has not been fully elucidated how the cell clusters are related to treatment response, especially in Asian races[3].

Objectives: We intend to analyze the RA synovium from Japanese patients based on single-cell transcriptomics to explore the pathological key players related to treatment resistance.

Methods: Synovial specimens were collected from 31 RA patients using an ultrasound-guided needle biopsy. The proportion of 5 immune cell subsets ($CD4^+$ T cells, $CD8^+$ T cells, B cells, NK cells, monocytes) and mesenchymal cells (synovial fibroblasts (SF), endothelial cells, mural cells) were analyzed by flow cytometry. $CD45^+$ and $CD45^-$ live cells were isolated, and scRNA-seq libraries were prepared using the 10x chromium system.

Results: We classified the patients into the following three groups based on treatment status at the time of biopsy; treatment-naïve, inadequate response to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs-IR), or biological DMARDs (bDMARDs-IR). The proportion of $CD8^+$ T cells, especially *GZMB*$^+$ *GZMK*$^+$ $CD8^+$ T cells, was significantly lower in csDMARDs-IR patients compared to treatment-naïve patients. This population was characterized by enhanced expression of *IFNG* and *GZMK*, the cooperative inducers of IL-6 production from SF. Meanwhile, an increased proportion of SF, especially *THY1*^{low} sublining and *CD34*$^+$ sublining, was observed in csDMARDs-IR and bDMARDs-IR patients. Intriguingly, by integrating gene set variation analysis (GSVA) with transcriptomic data of cytokine-stimulated SF *in vitro*[4], *THY1*^{low} sublining was indicated to be activated independently of the effects of inflammatory cytokines (e.g., TNF-α, IL-1β, IFNs) (Figure 1). Collectively, this SF subpopulation was inferred to be less susceptible to cytokine-blocking agents such as IL-6 receptor or TNF-α inhibitors.

Conclusion: The synovial analysis has the potential to be useful in parsing the mechanism of treatment resistance in Japanese RA patients, and gaining insights into novel therapeutic targets.

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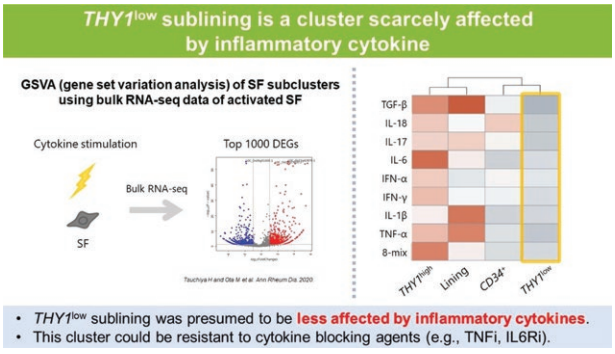


Figure 1.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1015 A NOVEL DRUG COMBINATION OF IGURATIMOD AND TOFACITINIB ALLEVIATES RHEUMATOID ARTHRITIS AND SECONDARY OSTEOPOROSIS

Keywords: Osteoporosis, Rheumatoid arthritis, Animal models

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Background: At present, specific immune targeted therapeutics including biologics and kinase inhibitors has made significant progress in Rheumatoid arthritis (RA). However, the irresponse to targeted therapies in some refractory RA patients suggests more attention should be paid on cell death pathways, such as pyroptosis. TNF-α is a proinflammatory cytokine that plays a fundamental role in the pathogenesis of RA, which could induce pyroptosis in monocytes and macrophages and cause the destruction of bone and cartilage. Iguratimod (IGU) has been confirmed as a highly efficacious and safe conventional synthetic disease-modifying

anti-rheumatic drug for RA in Asia. Whether the combination of IGU and Tofacitinib (TOF), the Janus kinase inhibitor, would be better partner need to be elucidated.
Objectives: To evaluate the therapeutic effect of IGU and TOF on active RA and secondary osteoporosis in collagen-induced arthritis (CIA)+TNF model.
Methods: In this study, hematoxylin and eosin (HE) staining were used to evaluate the pathological changes in ankle joints of CIA+TNF model. Immunohistochemistry (IHC) were used to evaluate the level of pyroptosis related proteins in synovial tissue. We performed Micro-computed tomography (Micro-CT), HE staining and IHC to analyze the trabecular bone changes in distal femoral metaphyses to investigate the destruction of knee joint.
Results: After 6 weeks treatment of IGU and/or TOF, the diameter of ankle joint and the level of interleukin (IL)-18, IL-1 of CIA+TNF model. Immunohistochemistry (IHC) were used to evaluate the level of pyroptosis related proteins in synovial tissue. We performed M group. HE staining showed that only a small amount of inflammatory cell infiltration and less pannus were seen in synovial tissue of both monotherapy and combination group, when compared with the CIA+TNF group. Of importance, the pyroptosis related proteins, such as gasdermin D (GSDMD), nucleotide-binding domain (NOD)-like receptor protein 3 (NLRP3), caspase-1, and IL-1β were significantly less expression in synovial tissue of combination group compared with the CIA+TNF group. Both the osteoblast bone formation and osteoclast bone absorption were sharply ruined in CIA+TNF model. However the bone destruction was significantly alleviated and bone turnover rate was remarkably increased in combination group, detected by Micro-CT, HE staining and IHC.
Conclusion: The TOF-IGU combination synergistically alleviated the disease severity of the CIA model, including relieving joint inflammation and bone erosion, with suppressing the activation of the NLRP3 inflammasome and reducing GSDMD-mediated pyroptosis. The combined application of TOF and IGU may have a stronger therapeutic effect on RA and secondary osteoporosis bone remodeling.

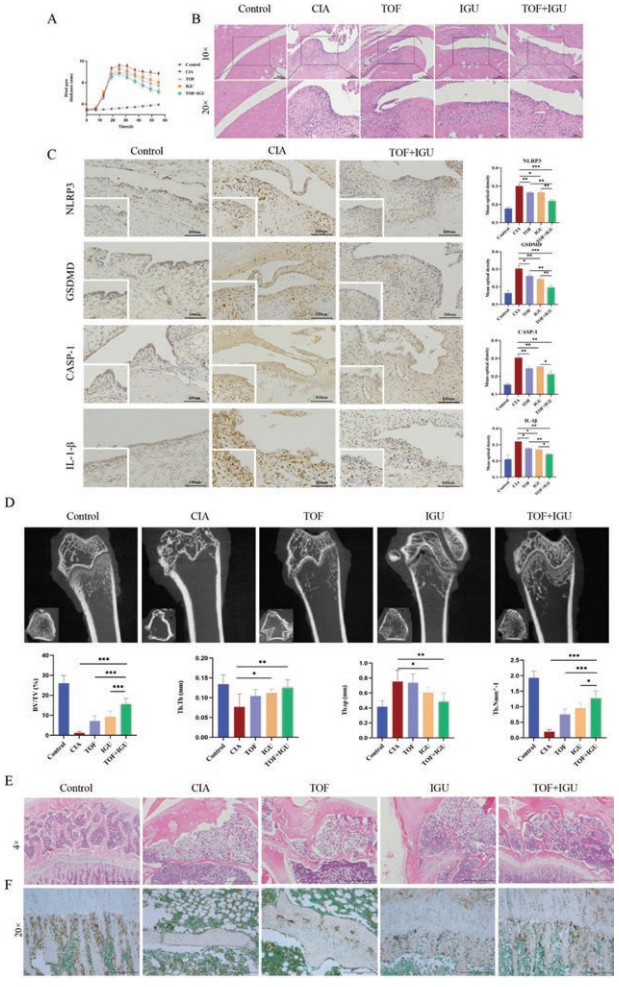


Figure 1. Therapeutic effects of TOF and IGU on the disease severity in CIA+TNF model. (A) The diameter of ankle joint; (B) HE staining in synovial tissue; (C) IHC staining of pyroptosis related proteins in synovial tissue; (D) Micro-CT analysis in distal femurs; (E) HE staining in knee joint; (F) IHC staining of ALP and TRAP staining in knee joint.

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2450

POS1016 **ANALYSIS OF GUT MICROBIOTA IN RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE**

Keywords: Rheumatoid arthritis

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Background: The gut microbiota has been related to rheumatoid arthritis (RA), inflammation, and its severity. Interstitial lung disease (ILD) causes high morbidity and mortality in RA patients. However, the association between gut microbiota and RA- associated ILD (RA-ILD) is still unknown.
Objectives: -To analyze the gut microbiota and gut permeability in RA-ILD patients. -To evaluate the association between gut microbiota and permeability, and the pulmonary progression.
Methods: Nested case-cohort study of 2 prospective cohorts of patients with RA with and without ILD. The cohorts were matched for age, sex, and time of RA evolution. All cases systematically underwent high-resolution computed tomography (HRCT) and pulmonary function testing (PFT) on the diagnosis of ILD. The ILD was defined according to the lung biopsy or HRCT based on the standard criteria of the American Thoracic Society/European Respiratory Society, the progression was defined as the worsening of the FVC > 10% or DLCO > 15%. The gut microbiota was measured by the 16S rRNA gene and the sequences were processed using the Quantitative Insights into Microbial Ecology (QIIME2). Serum lipopolysaccharide-binding protein (LBP) and lipopolysaccharide (LPS) were measured as markers of gut permeability. Demographic, clinical, laboratory, and treatment-related data were recorded. The disease activity was measured by Disease Activity Score-28 with Erythrocyte Sedimentation Rate (DAS28-ESR), and the function using the Health Assessment Questionnaire (HAQ). We performed a descriptive analysis and Cox regression analysis to identify prognostic factors for the time to progression of RA-ILD.
Results: Thirty-five RA-ILD and 35 RA without ILD were included. Table 1 shows the baseline characteristics. After a median (SD) period of 66,1 (47,2) months, pulmonary progression criteria had observed in 13 patients (37.1%). Compared with controls, RA-ILD had greater values of DAS28-ESR (p=0.032) and higher HAQ scores (p=0.003). They also had higher levels of serum LPS (p = 0.007) and more abundance of *Streptococcus* genus (p = 0.087), as well as a lower abundance of *Slackia* (p = 0.022) and *Paraprevotella* genera (p = 0.082). The RA-ILD with progression had a higher abundance of *Streptococcus* genus (p = 0.090) and a lower abundance of *Slackia* genus. In Cox regression analysis, the moderate-high activity of DAS28-ESR (HR [IC 95%], 3.53 [1.20-6.98]; p=0.017), LPS (HR [IC 95%], 1.12 [1.02-1.23]; p=0.018) and the *Slackia* genus (HR [IC 95%], 0.98 [0.97-0.99]; p=0.010) were associated with RA-ILD.
Conclusion: RA-ILD patients showed increased gut permeability and also displayed a different pattern of gut microbiota associated with ILD diagnosis and prognosis. These findings may enable the discovery of potential RA-ILD biomarkers.

Table 1. Clinical and demographic characteristics

VARIABLE	RA-ILD n=35	RA without ILD n=35	P-value
Age in years, mean (SD)	69.7 (9.3)	66.6 (7.0)	0.130
Male; n (%)	20 (57.1)	20 (57.1)	1.000
Smoking			0.760
Never smoked, n (%)	17 (48.6)	18 (51.4)	
Ex-smoker, n (%)	10 (28.6)	8 (22.9)	
Active smoker, n (%)	8 (22.9)	9 (25.7)	
Time since diagnosis RA, months, median (IQR)	149.8 (93.3-245.5)	133.7 (67.8-204.2)	0.384
Time since diagnosis of ILD, mean (SD)	66.1 (47.2)	-	-
RF+ (>10), n (%)	33 (94.3)	31 (88.6)	0.393
ACPA+ (>20), n (%)	32 (91.4)	31 (88.6)	0.690
Erosions, n (%)	21 (60.0)	19 (55.6)	0.705
DAS28-ESR, mean (SD)	3.1 (0.9)	2.6 (0.9)	0.032
HAQ, mean (SD)	1.2 (0.6)	0.8 (0.6)	0.003
FVC mean (SD)	63.0 (17.1)	83.4 (4.4)	<0.001
DLCO, mean (SD)	61.0 (15.2)	85.9 (7.9)	<0.001
UIP, n (%)	29 (82.9)	0 (0.0)	<0.001
NSIP, n (%)	6 (17.1)	0 (0.0)	<0.001

Abbreviations. ACPA: anticitrullinated peptide antibody; DAS28: Disease activity score; DLCO: diffusing capacity of the lung for carbon monoxide; ESR: erythrocyte sedimentation rate; FVC: forced vital capacity; HAQ: Health Assessment Questionnaire; IQR: interquartile range; NSIP: nonspecific interstitial pneumonia; RA: rheumatoid arthritis; RF: rheumatoid factor; SD: standard deviation; UIP: usual interstitial pneumonia.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1017 **WITHDRAWN**

POS1018 **ROLE OF THE SIGNALING LYMPHOCYTE ACTIVATION MOLECULE FAMILY IN RHEUMATOID ARTHRITIS COMPLICATED WITH INTERSTITIAL LUNG DISEASE**

Keywords: Rheumatoid arthritis, Cytokines and chemokines, Lungs

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Background: Interstitial lung disease (ILD) is the most common extra-articular complication of rheumatoid arthritis (RA). The prevalence of RA with ILD is approximately 20% and the risk of ILD is significantly higher in RA patients than in healthy controls [1]. The pathogenesis of RA-ILD has not been elucidated, although various genetic, immunological, and environmental factors have been suggested to be involved in its development and progression [2]. Therefore, it is crucial to explore new targets and predictors of RA-ILD pathogenesis.
Objectives: To explore the possible mechanisms involved in the initiation and progression of RA-ILD.
Methods: Synovial samples of RA (GSE55235), lung samples of ILD (GSE53845 and GSE81292) were extracted from the Gene Expression Omnibus (GEO) database. Differentially expressed genes (DEGs) analysis, weight gene co-expression network analysis (WGCNA) and Consensus Cluster were implemented with R language. Enrichment analysis and shared hub gene analysis were then performed. The function of selected gene signatures and hub genes were validated in external datasets (synovial tissues of RA (GSE55457) and RA-associated usual interstitial pneumonia (RA-UIP) (GSE199152)), in terms of single cells level, RA-ILD patients and our collagen-induced arthritis (CIA) relative ILD animal model.
Results: The ILD relative gene signatures which contained 90 shared genes was obtained (Figure 1 A). KEGG pathway enrichment analysis identified cytokine-cytokine receptor interactions and chemokine signaling pathways (Figure 1 B). CytoHubba selected 17 hub genes as shown Figure 1 C. Validated the 17 hub genes in lung tissue samples from three RA-UIP patients and four non-UIP controls with the external database (Figure 1 D). In single cell port, the surface molecules of B cells, CD19, CD27, CD38, CD79A, SLAMF1, SLAMF2 and SLAMF7 can be detected in RA synovial tissues and lung samples of ILD (Figure 1 E). The SLAMF1, SLAMF2 and SLAMF7 in PBMCs of RA-ILD patients were highly expressed (Figure 1 F). Furthermore, we constructed the CIA+TNF animal model , whose lung pathology showed ILD-like manifestations (Figure 1 G), together with an increased infiltration of B cells, especially those expressing SLAMF1, SLAMF2 and SLAMF7 in both synovial and pulmonary tissues (Figure 1 H).
Conclusion: Our study explored the common pathogenic mechanisms of RA and ILD, identified the shared 17 hub genes of RA-ILD. Especially the SLAMF1, SLAMF2 and SLAMF7 expressing B cells can migrate to pulmonary and take part in the development of fibrosis and ILD, with the guide of chemokines. This indicated a joint-lung axis hypothesis might play important roles in the development and progression of RA-ILD.

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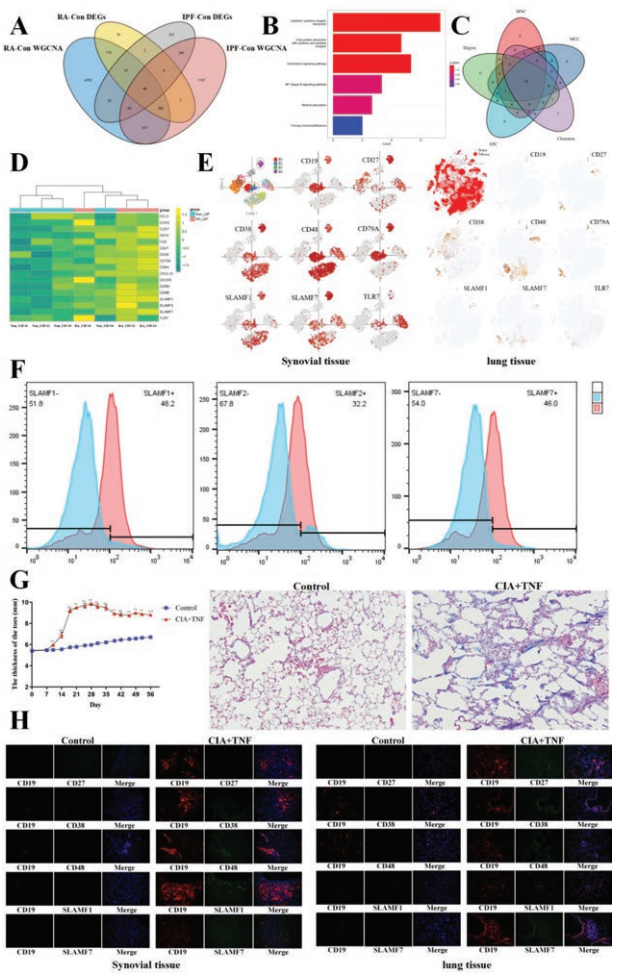


Figure 1. The exploration for the mechanisms of RA-ILD. (A) Venn diagram: showed the overlapped genes of relative DEGs and WGCNA modules; (B) The bar plot of KEGG analysis, the size of the dot means the number of genes involved; (C) Venn diagram: the overlapped genes of the five algorithms: MCC, MNC, Degree, EPC and Closeness; (D) The expression of the 17 hub genes in lung tissues of RA-UIP patients; (E) Expression of the key genes in synovial and lung tissues with Single Cell portal; (F) The expression of SLAMF in RA and RA-ILD patients by flow cytometry:SLAMF1, SLAMF2 and SLAMF7; (G) The construction of the CIA models and Masson staining (100×) in the lung tissue of CIA+TNF and control rat; (H) The immunofluorescence staining of joint tissues and lung tissue in CIA+TNF model: DAPI in blue, CD19 in red and target genes (CD27, CD38, SLAMF1, SLAMF2 and SLAMF7) in green, from left to right: CD19, target gene and merge.

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Disclosure of Interests: None Declared.
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POS1019 DIPYRIDAMOLE, A COMPOUND THAT INCREASES EXTRACELLULAR ADENOSINE LEVELS, AS A THERAPEUTIC AGENT FOR RHEUMATOID SARCOPENIA

Keywords: Rheumatoid arthritis, Animal models, Sarcopenia

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Background: In addition to joint damage, rheumatoid arthritis (RA) confers a higher risk of several comorbidities, including changes in body composition with reduced muscle mass and strenght (sarcopenia) with stable or increased fat mass. Adenosine and ATP are responsible for the maintenance of energy balance and activate cell signaling through selective receptors. Adenosine A2A receptor activation regulates bone turnover, targetting bone destruction in inflammatory diseases like RA. The use of dipyridamole (blocks adenosine uptaken by the cells increasing extracellular adenosine levels activating adenosine receptors) modulates the intracellular and extracellular levels of adenosine and ATP in murine C2C12 myoblasts, via activation of the adenosine A2B receptor, cAMP and AMPK pathways, counteracting deleterious effects on skeletal muscle differentiation.
Objectives: To determine if dipyridamole prevents sarcopenia in arthritis murine model.
Methods: 12-wk-old C57BL/6 male mice were injected with pooled K/BxN serum (100 µl, ip) on day 0 and 2. Dipyridamole 25mg/Kg was administered daily starting after the first serum injection. Clinical signs (joint swelling and thickness) were measured daily. DXA analysis and motor activity tests were performed prior to serum inoculation and at day 13. Mice were euthanized on day 16. Inflammatory cytokines and C-reactive protein (CPR) were measured in serum. Gastronemius was collected for protein and RNA extraction. Tibialis was frozen and embedded in OCT for histology.
Results: Serum transfer (RA mice) induced an increase in joint inflammation that was maximal 2wk after injection. Dipyridamole decreased the appearance of inflammation in the joints (clinical score of 5±3 vs 14±1 RA mice, p<0.005, n=7), and counteracted weight loss (p<0.01). Moreover, dipyridamole modulates the systemic inflammation found in RA mice promoting an signifficant increase on anti-inflammatory cytokines such as IL-10, and a signifficant reduction on pro-inflammatory citokines such as INFγ, IL1β, TNFα and IL6, with a non signifficant decrease in CRP. In motor tests, the RAmice had a reduced distance traveled when compared to healthy mice (sham) (830±37cm vs 1393±187cm Sham, p<0.001, n=4-7), as well as a reduce strength (22.4±7g vs 44.4±3g Sham, p<0.05, n=4-7) and endurance, while the rotarod test showed a loss of motor coordination with increase of latency to fall(43.3±5.4sec vs 75.9±3.3sec Sham, p<0.05, n=4-7). Dipyridamole treatment resulted in a revertion of physical development induced by serum transfer. Furthermore, RA mice had decreased lean mass, BMD and BMC, as well as an increased fat percentage, that were reverted in the presence of dipyridamole. RA mice muscle weights decreased when compared to sham mice, whereas dipyridamole reversed this effect. MHC protein expression was decreased in RA mice when compared to sham mice (60±7% vs 100% Sham, p<0.005, n=4-7) and reverted by dipyridamole (184±6%vs 60±7%RA mice, p<0.005,n=6-7), meanwhile PAX7 expression was enhanced by dipyridamole (274±11%dipyridamole,151±13% RA mice vs. 100%, p<0.005, n=6-7). AMPK activation decreased in RA mice (53±7% decreased vs Sham, p<0.05, n=4-7), whereas dipyridamole reversed this loss (152±5% dipyridamole vs 53±7% RA mice, p<0.001,n=6-7). Adenosine A2A and A2B receptors protein expression were decreased in RA mice (71±3% for A2A and 35±9% for A2B vs 100% Sham, p<0.005,n=4-7), been reverted by dipyridamole. Senescence markers p21and p16 were increased in RA mice (221±38% for p21 and 392±25% for p16 vs 100% Sham, p<0.001,n=4-7) and dipyridamole reduced their expression.
Conclusion: Arthritic mice developed sarcopenia accompanied by a loss of motor activity, strong systemic inflammation and an increased muscle senescence. Dipyridamole counteracted both systemic and joint inflammation as well as muscle loss, enhancing muscle regeneration. This indicate that the use of agents that increase extracellular adenosine levels might be interesting as a therapeutically approach forinflammatory sarcopenia.
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POS1020 A DIMINISHED EXPRESSION OF THE UBIQUITIN-PROTEASOME SYSTEM IN PATIENTS WITH RHEUMATOID ARTHRITIS AND DIABETES IS LINKED TO IL-1 PATHWAY HYPER-ACTIVITY

Keywords: Cytokines and chemokines, Rheumatoid arthritis, Comorbidities

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Background: A consistent connection between rheumatoid arthritis (RA) and type 2 diabetes (T2D) has been recently reported highlighting interleukin-1β (IL-1β) as shared pathogenic pathway and therapeutic target [1]. In a clinical trial

enrolling patient with RA and T2D, we demonstrated that IL-1 inhibition led to a marked reduction of glycated haemoglobin together with a decrease of RA disease activity [2].

Objectives: To evaluate the synovial expression of IL-1 related genes and the relationship to the ubiquitin-proteasome system in the synovial tissues of RA patients with and without T2D. To assess the effects of high concentration of insulin in vitro, mimicking the hyperinsulinism of the early phases of T2D, on ubiquitinated proteins in fibroblast-like synoviocytes (FLSs).

Methods: Early (<1 year) treatment-naïve RA patients with T2D (RA/T2D n=16) were compared with age- and gender-matched RA patients without T2D (n=16) enrolled in the Pathobiology of Early Arthritis Cohort (PEAC) [3]. Synovial tissue biopsies obtained under ultrasound guidance underwent RNA-sequencing as previously described [3], and we compared IL-1 pathway genes in patients without and with T2D. The synovial expression of ubiquitin in macrophages and synovial lining fibroblasts was assessed by immunohistochemistry/immunofluorescence and correlated with synovial pathotypes [4]. Finally, FLSs from RA patients (n=5) were isolated and treated with human insulin (200 and 500 nM) and ubiquitinated proteins were assessed by western blot.

Results: Synovial RNA-sequencing showed that one third of IL-1 pathway genes (41/138) were significantly different in RA/T2D patients compared to RA patients without T2D. In parallel, synovial tissues of RA/T2D patients were characterised by a consistent reduced expression of ubiquitin-proteasome genes. More specifically, ubiquitin genes (*UBB*, *UBC*, and *UBA52)* were significantly lower in T2D/RA patients. Furthermore, 22 genes codifying proteasome subunits were significantly lower in RA/T2D patients (*PSMA2*, *PSMA6*, *PSMA7*, *PSMB1, PSMB3, PSMB4, PSMB6, PSMB7, PSMB8, PSMB9, PSMB10*, *PSMC1, PSMC3, PSMC5, PSMC13*, *PSMD4, PSMD7, PSMD8, PSMD9*, *PSME1, PSME2*, and *PSMF1)*. Additionally, several genes regulating ubiquitin and proteasome system were significantly different in the synovial tissue of RA/T2D patients. Specifically, *APP*, *BAG4*, and *BTRC* were upregulated in RA/T2D patients. Conversely, *RACK1*, *RBX1*, *RPS27A*, *SEM1*, *SHARPIN*, and *SIGIRR* were significantly downregulated in RA/T2D patients. Immunohistochemistry showed a significant reduction of the percentage of ubiquitin-positive cells in synovial tissues of RA/T2D patients. The percentage of ubiquitin-positive cells was also increased in patients with a lympho-myeloid pathotype compared to diffuse myeloid or pauci-immune-fibroid. Despite its widespread expression in synovia, immunofluorescence showed that ubiquitin mainly colocalized with synovial macrophages and lining fibroblasts. Finally, *in vitro* experiments showed a reduction of ubiquitinated proteins in RA-FLSs treated with a high concentration of insulin (500 nM).

Conclusion: Increased IL-1 gene expression was observed in the synovial tissues of RA/T2D patients linked with decreased ubiquitin-proteasome system. These findings may provide a mechanistic explanation of the observed clinical benefits of IL-1 inhibition in patients with RA and concomitant comorbid T2D, as the reduction of the ubiquitin-proteasome system may enhance the levels of precursor IL-1β and the production of bioactive IL-1β.

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POS1021

HIGH THROUGHPUT MULTIPLEX PROTEOMICS IDENTIFIES BIOMARKERS AND NETWORKS ASSOCIATED WITH THE RHEUMATOID ARTHRITIS-CARDIOVASCULAR DISEASE (RA-CVD) MULTIMORBID AXIS

Keywords: Rheumatoid arthritis, Cardiovascular disease, Biomarkers

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Background: Rheumatoid arthritis (RA) patients have higher mortality rates compared to the general population, primarily due to excess cardiovascular (CV) disease (CVD). We have shown the earliest stages of RA are associated with CV abnormalities but blood biomarkers to identify CVD in early RA are lacking.

Objectives: In a treatment-naïve new-onset RA trial cohort, to identify (i) blood-based protein biomarkers that associate with cardiovascular magnetic resonance imaging (CMR) abnormalities, (ii) whether these biomarkers are sensitive to change; (iii) the predominant inflammatory and metabolic pathways implicated.

Methods: CADERA (Coronary Artery Disease in Early RA)[1] was an add-on study to a parent RCT of an early RA inception cohort where 81 patients underwent CMR at baseline and year 1. Proximity extension immunoassay (Olink) was used to measure normalised protein expression (NPX) across inflammation, CV II/III and cardiometabolic panels at time of CMR. Bayesian linear mixed effects regression was used to identify proteins associated with CMR parameters of myocardial oedema/fibrosis [MO/MF = native T1, myocardial extracellular volume (ECV) and late gadolinium enhancement (LGE)] and vascular stiffness [VS = aortic distensibility and stiffness index] at baseline, year 1 and those sensitive to change over time. An expanded protein interaction (PPI) network using baseline proteins was created using an induced network approach (String-DB) and clusters identified using k-means that were then subjected to Gene ontology (GO) and KEGG enrichment analysis.

Results: Of 340 proteins analysed using Olink, 108 proteins were associated with CMR markers of MO/MF (64 proteins; 28 positively, 36 negatively) and VS (44 proteins; 13 positively, 38negatively) at baseline. 46/108 proteins identified at baseline were sensitive to change over time and of these, 15 remained associated with CMR parameters at Year 1 (see Figure 1A & B). No overlapping proteins were identified that associated with focal (LGE) and diffuse fibrosis (ECV). Table 1 reports posterior estimates and 95% credible intervals for two top proteins. Figure 1C displays change in predicted NPX for 2 time-sensitive proteins associated longitudinally with CMR parameters. K-means clustering of the expanded baseline PPI network (enrichment $p < 0.0001$) identified 4 clusters (Figure 1D) with roles in IL27 receptor binding and NF-kB signalling pathway (red), vascular endothelial growth factor receptor binding and JAK-STAT signalling pathway (green); Macrophage CSF receptor binding and ErbB signalling pathway (blue); and IL10 receptor activity and complement and coagulation cascades (yellow).

Conclusion: This is the first study to identify sensitive protein biomarkers that may help with early diagnosis and monitoring of RA-CVD and inform on possible therapeutic targets. Treatment group differences and subgroup analyses with responders are ongoing. Further validation of these candidate biomarkers is needed in an independent cohort.

Table 1. Top proteins sensitive to change and longitudinally associated with CMR detected subclinical myocardial oedema(MO)/fibrosis(MF) and vascular stiffness (VS). PE = posterior estimate, CrI = credible intervals.

	Proteins	Role	Baseline PE(95%CrI)	Year 1 PE(95%CrI)
MO/MF	*Protein A	Lipid metabolism	-4.33(-8.07 to -0.6)	-52.18 (-97.4 to -6.8)
VS	*Protein G	Growth factor, heparin binding	0.84(0.12 to 1.58)	1.31(0.2 to 2.4)

*Proteins, clusters subject to intellectual property discussions via Innovation Factory, University of Manchester.

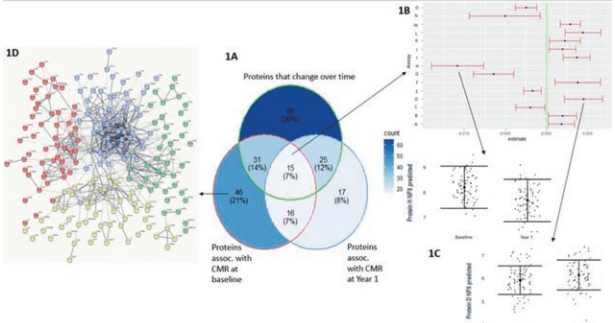


Figure 1. A(middle):Overlap of proteins associated with CMR parameters at baseline, year 1 and those sensitive to change. B(top right): Posterior estimate of 15 proteins from the intersect of figure 1A. C(bottom right): Predicted normalised protein expression of protein D(bottom) and H (top)at baseline and Year 1. D(left): Baseline PPI network analysis identifies 4 clusters.

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POS1022 A NEWLY DEVELOPED SMALL MOLECULE CD38 INHIBITOR EXERTS THERAPEUTIC EFFECTS IN A COLLAGEN-INDUCED ARTHRITIS MOUSE MODEL

Keywords: Disease-modifying drugs (DMARDs), Rheumatoid arthritis, Animal models

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Background: CD38 is a NAD+ consuming enzyme ubiquitously expressed on immune cells and its expression increases in several pathological conditions, including Rheumatoid Arthritis (RA) [1, 2]. Pre-clinical studies in CD38 *knock-out* models have demonstrated that CD38 deficient animals develop an attenuated form of Collagen-Induced-Arthritis (CIA) characterized by reduced inflammation and damage at the joint level suggesting a causal role of CD38 in the pathogenesis of CIA and, potentially, RA [3-5].
Objectives: This study investigated the efficacy of NTX-748, a newly developed, potent and orally available small molecule inhibiting the enzymatic activity of CD38, in reducing the inflammation, cartilage destruction, pannus formation, and bone resorption associated with developing CIA in mice, a well-established animal model for the study of RA.
Methods: Mice were injected intradermally (ID) with Freund's complete adjuvant (CFA) containing bovine type II collagen to induce arthritis on study days 0 and 21. Beginning on study day 18, the animals were dosed twice daily (BID) by the oral route (PO) with vehicle or NTX-748 (3, 10, or 30 mg/kg), or dosed PO once daily (QD) with Methotrexate (1 mg/kg) (n=12/group) for 18 days. One group served as a naïve control group (n=4). Efficacy evaluation was based on animal body weights, clinical arthritis scores (CAS) based on daily clinical scores of the paws (right front, left front, right rear, left rear) expressed as area under the curve (AUC), summed histopathology scores based on histopathologic evaluation performed on fore paws, hind paws, and knees, analysis of NTX-748 plasma concentrations and tissue metabolomic profile. The primary endpoint was day 36 CAS.
Results: Treatment with NTX-748 at 10 and 30mg/kg showed a statistically significant dose-dependent beneficial effect reducing day 36 CAS by 37% and 50% respectively relative to vehicle (p=0.13 and p=0.047), without showing any toxicity, including body and spleen weights. Histopathology analysis of joints, paws and knees confirmed NTX-748 efficacy. Strikingly, NTX-748 reduces incidence of CAS up to 50% in a dose-dependent manner (p = 0.0015). Plasma concentrations of NTX-748 increased approximately in proportion to dose. Mass Spectrometry-based tissue metabolomic analysis (liver and spleen) confirmed target engagement with dose dependent increases of NAD+ levels, the main substrate of CD38-mediated NAD+ hydrolysis, and decreases of NAM and ADPR, both products of the same enzymatic reaction. Methotrexate 1mg/kg also demonstrated efficacy (98% reduction in CAS) however significant splenomegaly (3-fold increase) indicated toxicity at this dose.
Conclusion: Our results demonstrated that NTX-748, a small molecule inhibiting the NADase enzymatic activity of CD38, is efficacious in the mouse CIA model, and thus potentially RA. These data confirm the potential of CD38 as druggable target in the treatment of inflammation-driven autoimmune diseases such as RA.
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POS1023 CHARACTERIZATION OF TRYPTOPHAN METABOLISM ALTERATION IN RHEUMATOID ARTHRITIS AND EVIDENCE FOR A THERAPEUTIC POTENTIAL OF AADAT ADMINISTRATION IN MICE

Keywords: Rheumatoid arthritis

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Background: Tryptophan metabolism alterations have been reported in inflammatory diseases, including rheumatoid arthritis. However, understanding whether these alterations participate RA development and can therefore be considered as putative therapeutic targets remain undetermined.
Objectives: In this study, we combined quantitative Tryptophan metabolomics in the serum of RA patients and corrective administration of a recombinant enzyme in experimental arthritis to address the question.
Methods: Targeted quantitative metabolomics was performed on the serum of 574 treatment naïve early untreated RA patients from the ESPOIR cohort and on 98 healthy subjects. Dosages were also conducted in serum of collagen-induced arthritis mice and controls. A proof-of-concept study evaluating the therapeutic potency of targeting the kynurenine pathway was performed in the collagen-antibody induced arthritis model.
Results: Differential analysis revealed drastic changes in Trp metabolites levels in RA patients compared to healthy controls. Amongst them, decreased levels of kynurenic (KYNA), xanthurenic (XANA) acids and indoles derivatives as well as an increased level of quinolinic acid in the serum of RA were positively correlated to disease severity (assessed by both circulating biomarkers and disease activity scores) and negatively correlated to quality-of-Life scores. Similar alterations of metabolites of the kynurenine pathway were observed in collagen-induced arthritis. Finally, the administration of the recombinant enzyme Aminoadipate Aminotransferase (AADAT), which is responsible for the generation of XANA and KYNA, was protective in collagen-antibody induced arthritis model.
Conclusion: Altogether, our clinical and experimental data indicate that Trp metabolism alterations play an active role in RA pathogenesis and might be considered as new therapeutic avenue.
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POS1024 TOFACITINIB TREATMENT AMELIORATES MUSCLE LOSS IN COLLAGEN-INDUCED ARTHRITIS MODEL

Keywords: Targeted synthetic drugs, Animal models, Sarcopenia

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Background: Sarcopenia is a muscle disease characterized by reduction of muscle strength and muscle mass. In RA, 25.9 to 43.3% of the patients present sarcopenia [1]. The loss of muscle mass observed in RA patients occurs either by activation of catabolic pathways or by inhibition of anabolic pathways [2]. Despite having a list of drugs capable of treating RA inflammation, the effect of these therapeutic interventions on muscle are not elucidated [3].

Objectives: To evaluate the effect of tofacitinib on muscle mass of collagen-induced arthritis (CIA) mice.
Methods: CIA was induced in male DBA/1J mice. Animals were randomized into 3 groups: I) CIA + tofacitinib (CIA-TOF; n=10); II) CIA + vehicle (CIA-VEH; n=10); III) healthy controls (CO; n=9). Vehicle (PBS) or tofacitinib 15mg/kg were administered twice a day, between days 18 and 45 after the disease induction. Clinical score, edema and body weight were evaluated during the experimental period. After euthanasia, tibio-tarsal joints were collected for assessment of disease histopathological score, and tibialis anterior (TA) and gastrocnemius (GA) muscles were weighed to assess muscle mass. Muscle atrophy was evaluated by measurement of TA myofiber cross-sectional area (CSA). Expression of proteins related to muscle regeneration or catabolism (Pax7, MyoD, myogenin and Murf-1) were evaluated by western blot in GA homogenates. Serum inflammatory markers (TNF and IL-6) were evaluated by ELISA. Statistical analysis included ANOVA followed by Tukey's or with Kruskal-Wallis. The statistical difference was assumed for $p<0.05$.
Results: As expected, tofacitinib treatment decreased arthritis severity by reducing clinical score ($p=0.03$) and hind paw edema ($p=0.04$) in comparison with CIA-VEH group. CIA-TOF showed weight gain ($p=0.02$), higher TA ($p=0.009$) and GA ($p=0.02$) weights, and increased CSA compared to CIA-VEH group ($p=0.01$). On day 45, CIA-TOF presented increased muscle strength compared to CIA-VEH group ($p=0.006$), however, no difference was found in the fatigue parameter among groups ($p>0.05$). The expression of Pax7 was unchanged ($p=0.07$), while MyoD expression showed an increase trend, and myogenin expression was significantly increased in CIA-TOF compared to CIA-VEH ($p=0.04$) and CO groups ($p=0.02$). The treatment did not significantly modify Murf-1 expression. Compared to CIA-VEH group, CIA-TOF mice showed decreased serum levels of TNF ($p=0.04$), and no difference in IL-6 serum levels ($p=0.08$).
Conclusion: Tofacitinib attenuated muscle loss in arthritic mice, as increased muscle weight and muscle CSA were detected in treated mice. Additionally, an increased activation of satellite cells regeneration, based on the expression of myogenin, is a potential mechanism involved in tofacitinib-protection against muscle loss.
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POS1025 COMBINATION OF BULK AND SINGLE CELL RNASEQ ANALYSES TO REVEAL MECHANISMS OF ABT-317 (JAK INHIBITOR) ON SYNOVIAL FIBROBLASTS

Keywords: Rheumatoid arthritis, -omics, Disease-modifying drugs (DMARDs)

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Background: Janus Kinase (JAK) inhibitors, including upadacitinib, are approved for clinical use, and show good therapeutic responses in Rheumatoid arthritis (RA) patients. In addition to impacts on cytokine signaling in immune cells, fibroblast-like synoviocytes (FLS) are also emerging as key cellular participants that contribute to the JAK- Signal transducer and activator of transcription (STAT) pathway guided cytokine-mediated interactions between FLS and immune cells. Despite the important role of FLS in RA pathogenesis, the mechanism of action of JAK inhibitors on FLS has not been extensively studied.
Objectives: The aim of this study is to characterize the molecular effects of a tool JAK1 selective inhibitor (ABT-317) on RA-FLS by performing bulk RNA-seq and single cell RNA seq (scRNA-seq) analysis on cell cultures following exposure to Staphylococcus enterotoxin B (SEB)-conditioned PBMC medium (CM) to mimic the RA inflammatory milieu +/- ABT-317.
Methods: RA-FLS cultures from 6 (Bulk RNA-seq) or 4 (ScRNA-seq) donors were pre-treated with various concentrations (0.1 and 1 μM) of ABT-317 with/without exposure to 30% SEB-conditioned PBMC medium. Total 36 Bulk RNA-seq library was prepared using NEB kit. EdgeR was used for differential expression gene (DEG) analysis, and DEGs (defined as padj < 0.1) were evaluated using Ingenuity Pathway Analysis (IPA). Total 24 ScRNA-seq libraries were prepared by 10x Genomics, and 87,108 cells were recovered. The data was analyzed with Cell Ranger, IPA, Seurat, and Harmony R packages. Gene Expression Omnibus (GEO) repository data sets (GSE12021 and GSE55457) from RA synovial tissue studies were used to compare with this study.
Results: The addition of ABT-317 to CM-stimulated FLS resulted in a downregulation of the same genes upregulated to the greatest degree by CM indicating that ABT-317 reverses a major portion of gene expression induced. IPA analysis demonstrated the expected impact of Jak inhibition on JAK/STAT and interferon signaling pathways that drive inflammation. Interestingly however, pathways unrelated to JAK signaling, such as the regulation of cell adhesion, complement activation and cytosolic DNA-sensing were also downregulated by ABT-317, suggesting that additional pathogenic mechanisms in synovial fibroblasts are also impacted by JAK inhibition. To determine whether specific fibroblast sub-populations are impacted by Jak inhibition, scRNA-seq was used to segregate FLS cells into distinctive clusters with and without CM and ABT-317 (1uM). We found that the pseudobulk data from scRNA-seq was highly correlated to the bulk RNA-seq data demonstrating consistency between our single cell and bulk datasets. We identified 9 clusters that only emerged following treatment of FLS with CM and upon addition of ABT-317 in a dose-dependent manner. ABT-317 reversed the elevated expression of cell migration related genes like ITGB8 after CM treatment in a specific cluster which suggests a potential for differential Jak responsiveness within subpopulations of fibroblasts. To establish the relevance of this in vitro data to patients, the relationship of FLS cultures stimulated with CM with public synovial tissue datasets from RA patients was explored. DE genes from the datasets (RA vs. OA) were positively correlated with the bulk and pseudobulk from the FLS culture scRNAseq (CM vs. UT), suggesting many of the same pathways are activated in vitro compared to patient synovial tissue.
Conclusion: We find that Jak inhibition is effective in downregulating several proinflammatory pathways induced by conditioned media stimulation in FLS cultures as well as additional mechanisms that could impact fibroblast pathogenesis in RA. These studies advance our understanding of Jak1 inhibitors and how they may contribute to clinical efficacy.
REFERENCES: NIL.
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POS1026 FUNCTIONALLY SELECTIVE IMMUNOMODULATOR SHOWS ROBUST EFFICACY IN A MURINE COLLAGEN-INDUCED-ARTHRITIS MODEL

Keywords: Rheumatoid arthritis, Innate immunity, Animal models

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Background: Activated monocytes play a key role in the initiation and progression of inflammatory synovitis in rheumatoid arthritis (RA), leading to cartilage destruction and, via invasive pannus development, loss of peri-articular bone.

ER000145 is a functionally selective immunomodulator derived from IT1t, a CXCR4 antagonist demonstrated to exert immunomodulating properties[1]. As an immunomodulating model compound, ER000145 previously showed increased potency by downmodulating several key pro-inflammatory cytokines in Toll-like receptor (TLR)7/8 stimulated immune cells and low/no CXCR4 antagonism *in vitro* as well as strong efficacy in a murine pristane-induced lupus model[2].

Objectives: The aim of the present study is to evaluate the potency of the functionally selective immunomodulator ER000145, both *in vitro* on murine and human immune cells as well as *in vivo* in a murine collagen-induced arthritis (mCIA) model.

Methods: *In vitro* immunomodulating potency of ER000145 was evaluated in fresh murine splenocytes and isolated primary monocytes from healthy volunteers (HV). After 1-hour incubation with ER000145 and 24-hour stimulation with TLR7/8 agonists (R848 or R837, 5 or 1 µg/mL respectively), supernatant was collected. Pro-inflammatory cytokines were detected by flow cytometry (LegendPlex). For the mCIA model, male DBA-1 mice (n=8 per group) were immunized with bovine collagen type 2 on Day 1 in Complete Freund Adjuvant (FA) and on Day 21 with Incomplete FA. Mice were randomized and dosed once daily (QD) intraperitoneally (IP) with either PBS (vehicle control), ER000145 at 3, 10 or 30 mg/kg, or IT1t at 30 mg/kg as of Day 28, for a duration of 14 days. As a positive control, mice received 10 mg/kg prednisolone QD orally. Blood samples were collected after single (Day 28) and 14-days of repeated dosing to evaluate exposure of ER000145. During the study, disease activity was monitored based on the extent of edema and erythema in each paw, and paw thickness was measured using a digital caliper. At study termination, all paws from the vehicle-treated and 30 mg/kg ER000145-treated mice were collected and prepared for histopathological scoring using hematoxylin and eosin (H&E) staining.

Results: ER00145 inhibited key pro-inflammatory cytokines (TNF-α/IL-6/IL-1β) in TLR7/8 agonist-stimulated HV primary monocytes as well as murine splenocytes. Daily IP administration of ER000145 in a mCIA model reduced significantly clinical scores in a dose-dependent manner: a dose of 3 mg/kg was not efficacious in contrast to both the 10 and 30 mg/kg QD doses. At efficacious doses, the average concentration (C_{avg}) of ER000145 in blood ranged between 14 and 33 ng/mL. In addition, no body weight loss was observed. Histologically, administration of 30 mg/kg of ER000145 QD was associated with significant suppression of the severity of articular pathology (synovitis, pannus infiltration and bone resorption) and reactive inflammatory responses (stromal cell reactions and bonne marrow cellularity).

Conclusion: The immunomodulator ER000145 showed significant *in vitro* potency by downmodulation of key proinflammatory cytokines in both human and murine cellular assays after stimulation. *In vivo* potency was further demonstrated in a therapeutic mCIA model where both 10 and 30 mg/kg daily IP doses prevented significant disease progression. Based on these promising efficacy data with ER000145, orally available immunomodulators are currently being developed as a potentially novel treatment option for chronic inflammatory autoimmune diseases like rheumatoid arthritis.

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Disclosure of Interests: Hélène ASNAGLI Employee of: presently employee of Ermium Therapeutics, Simon TESSIER Employee of: presently employee at Ermium Therapeutics, Martyn Foster Consultant of: consultant for Ermium Therapeutics, Sofies Denies Consultant of: consultant for Ermium Therapeutics, Eef HOEBEN Consultant of: consultant for Ermium Therapeutics, Jean-Philippe HERBEUVAL Consultant of: consultant for Ermium Therapeutics, Joël CROUZET Employee of: CEO of Ermium Therapeutics, Annegret Van der Aa Employee of: employee for Ermium Therapeutics.

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POS1027 THE LIPOPROTEIN AND LIPID PROFILE CAN PREDICT THE DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

Keywords: Biomarkers, Rheumatoid arthritis, -omics

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Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic and systemic synovial inflammation, cartilage erosion and subsequent joint destruction. Despite the existence of many targeted therapies, RA remains a disease with high morbidity, requiring monitoring with prognostic biomarkers. RA presents with abnormal lipoprotein levels, a phenomenon known as the "lipid paradox," which requires comprehensive characterization with -omics techniques [1].

Objectives: The purpose of this study is to describe the distinct lipoprotein and lipidomic profile in active and remission RA populations, in an effort to globally map the effect of inflammation and disease activity on the metabolome and obtain biomarkers with predictive capacity.

Methods: Plasma samples of 161 RA patients were collected under fasting conditions. Patients were classified based on their DAS28 as High (>5.1), Moderate (3.2-5.1), Low (2.6-3.2) and Remission (<2.6). Lipoproteins and their subclasses were detected and quantified using 1H NMR spectroscopy with the B.I.LISA method (Bruker), while lipid spieces detection was achieved with mass spectrometry (DMS-MS) using the Lipidyzer method (Sciex). Glycoproteins signals were acquired from 1H NMR led spectra. High Disease Activity (n=21) and Remission (n=33) were analysed pairwise with Multivariate models (OPLS-DA) and univariate t-test (boxplots). The correlation coefficient was calculated for the entire lipoprotein and lipid profiles with DAS28 for each experimental group.

Results: Patients with high disease activity showed relatively increased levels of VLDL (VLPN), IDL (IDPN), total Triglyceride (TPTG), Free fatty acids (FFA(18:1), FFA(16:0)) and Phosphatidylcholines (PC(16:0/20:4), PC(18:0/20:4)) compared to those in remission. RA patients in remission were characterized by high levels of LDL (LDPN, L4PN), HDL Apolipoprotein A1 (HDA1, H4A1), Cholesterol Esters (CE(18:2), CE(18:1)) and Phosphatidylcholines (PC(16:0/18:2), PC(18:0/18:2)). The entire lipoprotein and lipid profiles were correlated with DAS28 in Remission (R2=0.24; R2=0.40) and High disease activity (R2=0.26; R2=0.47) groups, indicating that the lipid profile is more predictive of the disease activity in both groups. Univariate analysis highlighted relatively higher concentration of large density HDL-4 subclasses (HDL-4 -Cholesterol (p=0.0003), ApoA1 (p=0.0003), ApoA2 (p=0.0018) and Phospholipids (p=0.0024)), Sphingomyelin (SM(24:0); p=0.0012), Hexosylceramide (HCER(22:0); p=0.0057), and Cholesterol Esters (CE(18:0); p=0.0025, CE(18:2); p=0.0121), but lower Glycoprotein A and B (p=0.0003; 0.0007) levels in Remission.

Conclusion: In summary, comprehensive lipoprotein and lipid analysis identifies markers that characterize RA in exacerbation and remission. Large density HDL-4 Apolipoprotein A1 and Cholesterol Esters are indicative of Remission, while VLDL, Triglycerides and Free fatty acids describe High disease activity in RA. The above markers will be evaluated in comparison with those already existing in clinical laboratory application.

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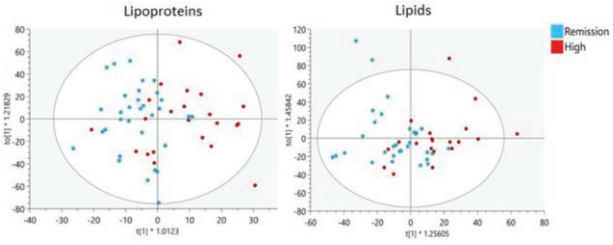


Figure 1. Multivariate supervised (OPLS-DA) models comparing the lipoprotein and lipid profiles of RA patients in Remission (blue) and with High Disease activity (red).

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Disclosure of Interests: None Declared.

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POS1028 SUCCESSFUL TREATMENT OF MURINE RHEUMATOID ARTHRITIS MODELS WITH CENERIMOD, A SELECTIVE S1P1 RECEPTOR MODULATOR, HIGHLIGHTS THE BENEFIT OF S1P IMMUNOMODULATION IN RHEUMATIC DISEASES

Keywords: Disease-modifying drugs (DMARDs), Rheumatoid arthritis, Animal models

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Background: Since the discovery of the sphingosine-1-phosphate (S1P) pathway and its potentially beneficial role of inducing lymphocyte retention and subsequent immunomodulation [1], several small molecule S1P receptor modulators have been approved for the treatment of diverse autoimmune diseases such as multiple sclerosis and ulcerative colitis. Cenerimod, a selective $S1P_1$ receptor modulator, has shown efficacy in preclinical models of systemic lupus erythematosus (SLE), systemic sclerosis and Sjögren's syndrome [2-4] and is now entering a Phase III clinical trial (OPUS; NCT05648500) in patients with moderate to severe SLE.

Objectives: We investigated the efficacy of cenerimod in modulating disease progression in preclinical models of rheumatoid arthritis (RA).

Methods: We analyzed the efficacy of cenerimod in several models of RA in mice and rats. Disease-relevant biomarkers such as autoantibody development and chemokine secretion were measured to gain a deeper understanding of the mode of action of $S1P_1$ receptor modulation in these RA models.

Results: In mouse RA models, prophylactic treatment with cenerimod inhibited the acute inflammatory response post antigen challenge and prevented autoantibody formation, thus completely preventing the initiation of disease. Cenerimod treatment at disease onset further showed a strong reduction of joint inflammation and significantly delayed clinical symptoms and the secretion of several pro-inflammatory chemokines. Although corticosteroid treatment is frequently administered as an adjunct treatment for interventional disease management in RA, its systemic toxic effects do not permit long-term usage to control disease activity in patients with rheumatic diseases [5]. In rats, cenerimod treatment prevented disease development dose-dependently when given directly at initiation of disease, while treatment at disease onset stopped further inflammation of the joints. Further, treatment with low-dose cenerimod limited joint inflammation to the same extent as low-dose corticosteroid treatment while not having a similar negative impact on body weight over the duration of the experiment.

Conclusion: S1P receptor immunomodulation is a highly effective treatment option for murine models of RA with translational value for rheumatological indications. Combined with the published data on rheumatic diseases, we believe that $S1P_1$ receptor modulation by cenerimod will benefit patients suffering from RA who are underserved by the current treatment landscape.

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Disclosure of Interests: Thomas Hoyler Shareholder of: Idorsia Pharmaceuticals Ltd., Employee of: Idorsia Pharmaceuticals Ltd., Maxime Bulle Shareholder of: Idorsia Pharmaceuticals Ltd., Employee of: Idorsia Pharmaceuticals Ltd., Jérémy Scherer Shareholder of: Idorsia Pharmaceuticals Ltd., Employee of: Idorsia Pharmaceuticals Ltd., Conrad Wyss Employee of: Idorsia Pharmaceuticals Ltd., Sylvie Froidevaux Shareholder of: Idorsia Pharmaceuticals Ltd., Employee of: Idorsia Pharmaceuticals Ltd., Marianne Martinic Shareholder of: Idorsia Pharmaceuticals Ltd., Employee of: Idorsia Pharmaceuticals Ltd.

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POS1029 MACROPHAGE MARKERS FOLATE RECEPTOR BETA AND CD206 ARE DIFFERENTIALLY EXPRESSED IN SYNOVIAL TISSUE OF RA PATIENTS WITH A DIFFUSE-MYELOID, LYMPHO-MYELOID AND FIBROID-PAUCI IMMUNOPATHOTYPE

Keywords: Rheumatoid arthritis, Prognostic factors, Imaging

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Background: Three different synovial immunopathotypes of rheumatoid arthritis (RA) have been identified: Fibroid-Pauci immune (FP, fibroblast-rich), Diffuse-Myeloid (DM, macrophage-rich) and Lympho-Myeloid (LM, lymphocyte- and macrophage-rich), and have been associated with treatment outcome to biologicals [1]. Therefore, identification of the synovial immunopathotypes before the start of therapy could be supportive for development of individualized treatment strategies. However, this currently requires invasive synovial tissue sampling. Novel whole-body molecular imaging with positron emission tomography (PET) and the use of specific PET tracers can non-invasively detect and quantify the presence of immune cells in RA inflamed synovium. Folate-receptor beta (FRβ) is a cell surface receptor on macrophages, shown clinical exploitation for high specificity PET imaging of arthritis [2]. However, it remains to be elucidated whether FRβ is a suitable marker for RA immunopathotype stratification. Furthermore, it is unclear whether FRβ is expressed on macrophages with a pro-inflammatory (M1) or homeostatic (M2) phenotype in the 3 immunopathotypes.

OBJECTIVES:

(1) Investigate FRβ expression across the three distinct RA immunopathotypes.
(2) Investigate FRβ expression in relation to the general macrophage marker CD68 and the mannose receptor CD206 (which is associated with M2-type macrophages [3]).

Methods: Synovial biopsies of the RA-affected ankle or knee (N=28) were retrieved from RA patients with clinically active disease defined by ACR RA criteria [4]. Subsequently, biopsy sections were immunohistologically stained in order to stratify each patient into one of three RA-immunopathotypes. Confocal microscopy was used to determine CD68, FRβ and CD206 expression (integrated density), and co-expression (comparing fold-change average expression) for all patients within each immunopathotype (N=8-10/ group).

Results: Out of 28 RA synovial biopsies 10 could be classified as FP, 9 DM and 9 LM immunopathotype. Average expression of CD68, FRβ and CD206 was significantly increased in the DM and LM compared to the FP immunopathotype (## $p<0.01$). Quantitative CD68, FRβ and CD206 expression was highest in the DM immunopathotype. FRβ expression correlated significantly with CD206 expression in all three pathotypes (Spearman $R_{FP}= 0.67$; $R_{DM}= 0.76$; $R_{LM}= 0.49$). On the contrary FRβ expression did not correlate with CD68 expression except in the DM pathotype (Spearman $R_{DM}= 0.46$).

Conclusion: The results of this study put forward that FRβ is a potential target for delineation of RA immunopathotypes, to be explored for non-invasive molecular imaging stratification. Furthermore, investigation of FRβ expression has an additive value over CD68 since it can be used to distinguish the presence of M2 macrophages in the RA synovium specifically.

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Disclosure of Interests: None Declared.

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POS1030 DNA-METHYLATION PROFILING IN THE BLOOD OF PATIENTS WITH RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

Keywords: Genetics/epigenetics, Lungs, Rheumatoid arthritis

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Background: Rheumatoid Arthritis-associated Interstitial Lung Disease (RA-ILD) is an extraarticular manifestation with clear clinical relevance because it impairs quality of life and survival. Despite this, RA-ILD etiology and pathogenesis are only partially understood. However, we know that fibrosis and collagen deposition, aging and telomere shortening, the expression of the mucin MUC5B gene, the RA autoantibodies and smoking are contributing elements. A better knowledge of RA-ILD pathogenesis will lead to improved outcomes for the patients.

Objectives: This study aims to identify CpG sites that are differentially methylated in the blood of RA-ILD patients compared to matched RA patients without ILD. These findings will point to genes and pathways of specific relevance to RA-ILD pathogenesis.

Methods: We compared two matched groups of 32 patients with RA: RA patients diagnosed with ILD less than one year before sample collection; RA patients without ILD. The two groups were assessed by High-Resolution Computed Tomography (HRCT) and matched by sex, age, smoking (ever/never), and anti-CCP status. Blood samples were used for DNA extraction. Methylation of 850000 CpG was measured with the Infinium Methylation Epic BeadChip (Illumina). Identification of the differentially methylated positions (DMP) and differentially methylated regions (DMR) was performed using the R application ShinyÉPICO [1]. Gene set enrichment analysis (GSEA) was done with the R package methylGSA [2].

Results: A total of 6679 DMP with ≥ 2 % difference and FDR < 0.05 were identified in the autosomal chromosomes. In addition, 119 DMR (72 in gene bodies, 32 in promoters, and 15 in CpG Islands) were discovered. Some of these DMP y DMR are associated with genes of known relevance (Figure 1): genes of mucins (*MUC6, MUC13*) and collagens (*COL9A3, COL21A1*), genes involved in telomere maintenance (*TERF, TERT1, POT1*), and some genes related to immunological processes (*HLA-DRA, VCAM1, TGFBR2…*). A systematic analysis of the associated genes with GSEA showed significant enrichment of 62 gene ontology (GO) terms and 49 Reactome pathways. Several of the top enriched GO terms referred to the detection of chemical stimuli involved in sensory perception, either by smell or taste. This finding was replicated in the enriched pathways. Other top GO terms identified chromosome changes during mitosis: centromeric duplication, chromosome segregation, and others. They corresponded to top-enriched pathways involved in the M phase of mitosis and cell cycle checkpoints. Another group of GO terms referred to post-translational modifications of proteins: deacylation of proteins, which coincided with top pathways involved in chromatin modifications, including acetylation and deacetylation of histones; and ubiquitination of proteins, also reflected in several top enriched pathways. Besides, enriched GO terms that referred to the catabolic process of nuclear-transcribed mRNA correlated with top pathways of mRNA metabolism. In addition, there were other significantly enriched gene sets, such as the involved in the transport of intracellular vesicles and the location in the cell of proteins, mitochondria, RNA, and chromosomes, the host interaction with viral infections, gene silencing by small RNA, SUMOylation, and the RHO GTPase cycle.

Conclusion: We observed significant differences in blood DNA methylation between matched RA-ILD and RA-control patients. Some of these differences were related to potentially interesting genes (mucins, collagen, telomere maintenance), and biological processes and pathways (detection of chemical stimuli, post-translational modifications of proteins, chromosome and intracellular vesicle localization, and transport) that will help us to better understand RA-ILD pathogenesis.

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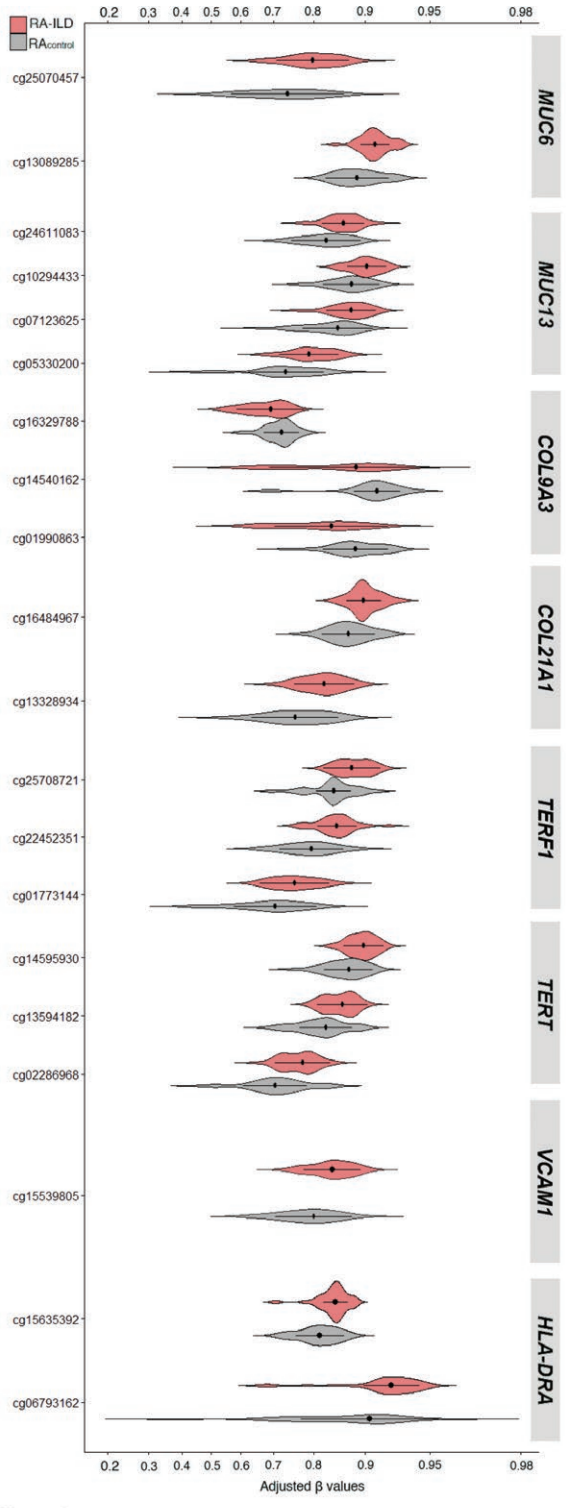


Figure 1. Violin plots of DNA methylation β values of individual CpG sites annotated to the selected genes comparing RA-ILD and RA control groups. X axis is in the logit scale (M values).

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POS1031

THERAPEUTIC EFFECTS OF GINGIVAL MESENCHYMAL STEM CELLS AND THEIR EXOSOMES IN A CHIMERIC MODEL OF RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Animal models

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease that leads to progressive joint destruction involving multiple joints. There is a large body of evidence that suggests a crucial role for activated synovial fibroblasts (RASF) in mediating both direct tissue injury and perpetuation of the complex disease process in RA [1]. RASF from RA patients are able to attach to articular cartilage and deeply invade and degrade the cartilage matrix [2] and have been shown to migrate to secondary joint locations *in vivo* and invade and degrade cartilage similarly to the primary site [3]. Human gingival-derived mesenchymal stem cells (GMSC) are promising therapeutic cell treatments for autoimmune diseases due to their immunomodulatory capacity [4]. Others have demonstrated the ability of GMSC, and exosomes derived from GMSCs (GMSCExo) to suppress the deleterious *in vivo* effects of the collagen induced arthritis model in mice [5].
Objectives: Our aim was to test whether the destructive invasive effects of RASF in an *in vivo* chimeric mouse model of RA could be modulated by the presence of GMSC or GMSCExo. In addition, we analyzed the effects of both GMSC and GMSCExo on the ability of RASF to migrate to secondary locations. Mechanistic studies were done to understand how the GMSC were inhibiting the invasiveness of the RASF.
Methods: A chimeric human/mouse model of synovitis was created by surgically implanting SCID mice with a small piece of human articular cartilage surrounded by RASF. Each mouse received two implants; the primary implant on the right flank of the mouse contained RASF, the secondary implant contained no RASF. Mice were retro-orbitally injected once with either GMSC or GMSCExo at 5-7 days post-implantation. The implants were removed after 60 days for evaluation. Histology and IHC were used to assess RASF invasion of the cartilage. Flow cytometry was used to understand the homing ability of GMSC *in vivo,* the incidence of apoptosis of RASF and the exchange of exosomes *in vitro.*
Results: We demonstrate that both GMSC and GMSCExo are potent inhibitors of the deleterious effects of RASF. Both treatments were effective in inhibiting the invasive destructive properties of RASF as well as the potential of these cells to migrate to secondary locations and attack the cartilage there. We also present evidence that GMSC home to the site of the implant and induce programmed cell death of the RASF through the direct transfer of exosomes.
Conclusion: Our results indicate that both GMSC and GMSCExo can block the pathological effects of RASF in this chimeric model of RA. A single dose of either GMSC or GMSCExo can inhibit the deleterious effects of RASF. These treatments can also block the invasive migration of the RASF, suggesting that they can inhibit the spread of RA to other joints. Because the gingival tissue is harvested with little difficulty, relatively small amounts of tissue are required to expand the cells, the fairly simple *in vitro* expansion process, and the increasing technological advances in the production of therapeutic exosomes, we believe that GMSCExo are excellent candidates as a potential therapeutic for RA.
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POS1032

ITACONATE – A GLUCOSE METABOLITE WITH ANTI-INFLAMMATORY PROPERTIES IN RHEUMATOID ARTHRITIS

Keywords: Biomarkers, Prognostic factors, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is the most prevalent autoimmune mediated joint disease. A complex dysfunction of the immune response is considered central for its pathogenesis as well as a dysregulated crosstalk between fibroblast-like synoviocytes (FLS) and monocytes.
Objectives: This project aims to examine and validate the anti-inflammatory effects of the natural glucose metabolite itaconate-derivative 4-octyl itaconate (4-OI) on stromal and immune cells from patients with active RA and evaluate the downstream effector molecule Heme-Oxygenase 1 (HO-1) as a potential biomarker.
Methods: Synovial fluid mononuclear cells (SFMC) from patients with chronic RA (cRA) were used to harvest RA FLS. Monocultures of synovial fluid derived FLS (SF-FLS) and autologous co-cultures of SF-FLS and peripheral blood mononuclear cells (PBMC) were cultured with and without 4-OI, corticosteroids, and anti-TNF (n=7). Subsequently, analyses by flow cytometry, Western Blotting, MTT assay, and ELISA were performed. The 4-OI target protein Nrf2 was knocked out in immortalized FLS (FLS-KO) generated by Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR). Furthermore, we measured HO-1 by ELISA in plasma samples from newly diagnosed, active and treatment-naïve early RA (eRA) patients at baseline and after 6 months of intensive treatment (the OPERA trial, n=80)[1] with a follow-up period of 24 months and plasma and in synovial fluid samples from patients with active, chronic RA (cRA, n=20) during disease activity flares. Plasma samples from age approximated and gender matched healthy controls (HC) (n=35) were also included.
Results: *In vitro* 4-OI significantly inhibited MCP-1 secretion in cultured SFMC, THP-1 (monocyte cell line), and FLS and resulted in a concomitant increased HO-1 production. 4-OI reduced the MCP-1 secretion by 84%, anti-TNF by 41% and corticosteroids by 54% (all $p<0.01$) in co-cultures consisting of autologous RA SF-FLS and PBMCs. In FLS we observed a linear decrease in pro-inflammatory cytokine production. 4-OI did not decrease collagen production, even in dosage of 500 µn FLS we observed a linear decrease in pro-inflammatory cytokine production. 4-OI did not decrease collagen production, even in dosage of 500 1 production. 4-OI reduced the MCP. In eRA plasma levels of HO-1 was significantly increased at baseline (2039 pg/mL, 95% CI [1619, 2460]) vs HC (1209 pg/mL, 95% CI [1047, 1370]). Treatment with MTX or MTX + anti-TNF, lowered levels of HO-1 (1704 pg/mL, 95% CI [1377, 2031]) after 6 months irrespective addition of anti-TNF treatment, reducing the difference to a no longer significantly different level from HCs. HO-1 was associated with number of swollen joints ($r=0.25$, $p<0.02$), tender joints ($r=0.24$, $p<0.02$) and Clinical Disease Activity Index ($r=0.23$, $p<0.02$). Baseline HO-1 predicted radiographic joint damage progression (change in Total Sharp-van der Heijde score (Δn eRA plasma levels of HO-1 was significantly increased at baseline (2039 pg/mL, 95% CI [1619, 2460]) vs HC (1209 pg/mL, 95% CI [1047, 1370]). Treatment with MTX or MTX + anti-TNF, lowered levels of HO-1 (1704 pg/mL, 95% CI [1377, 2031]) after 6 months irund ($r=0.75$, $p<0.001$). High levels of HO-1 in SF from inflamed joints were associated with CRP ($r=0.52$, $p<0.05$) during flares in cRA.
Conclusion: *In vitro* 4-OI decreased MCP-1 secretion and increased the HO-1 expression in cultures of monocytes and in RA FLS and PBMC without decrease in collagen production or cell growth. In total, 4-OI decreased MCP-1 in both immune and stromal dominated RA pathobiology. In eRA patients, pre-treatment-plasma HO-1 levels were increased and correlated with parameters for disease activity, treatment-effect after 6 months, and predicted radiographic progression after 24-month.
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POS1033

CHILDHOOD EXPOSURES AND RISK OF RHEUMATOID ARTHRITIS IN E3N FRENCH WOMEN COHORT

Keywords: Rheumatoid arthritis, Registries, Epidemiology

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Background: Rheumatoid arthritis (RA) results from a gene-environment interaction and is characterized by a preclinical, or asymptomatic, phase during which autoantibodies appear, in particular anti-citrullinated protein antibodies (ACPA) [1].This gene-environment interaction, occurs many years before the diagnosis of RA, possibly during childhood. Only smoking, in genetically predisposed patients (carriers of the shared HLA-DRB1 epitope), has been shown to be a reproducible risk factor for developing seropositive RA [2,3]. Other inhaled substances may play a role as many non-smokers develop RA, inducing inflammation of the lung mucosa and a systemic immune response, such as occupational exposure to silica, possibly pesticides and air pollution [4]. Early life exposures may play a major role in the pathophysiology of RA. All these elements lead us to study the impact of exposure to environmental factors in childhood on the risk of RA in adulthood, mainly airborne exposure.
Objectives: To assess the relationships between exposure to a rural lifestyle during childhood and the risk of RA in women involved in the E3N cohort.
Methods: E3N is an ongoing French prospective cohort that included 98,995 women aged 40-65 years. Women completed, every 2-3 years, mailed questionnaires on their lifestyle and health-related information. In 2002 a questionnaire on their childhood environment was assessed, including passive smoking, educational level, smoking during pregnancy and World War II deprivation scores, exposures to cats and dogs at home, whether women had lived on a farm for at least 3 successive months during childhood, and if so, the type of animals they were exposed to and their age at first pet or farm animal exposure. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of incident RA were estimated using multi-adjusted Cox proportional hazards regression models with age as the time scale.
Results: A total of 698 incident RA cases, among whom 77,754 non RA women were ascertained. Farming lifestyle was not associated with the risk of RA. In contrast, in a multivariable-adjusted Cox regression model including known risk factors of RA (age, active and/or passive smoking during adulthood, BMI, educational level), exposure to cats and/or dog between 1 and 2 years old was associated with a decrease risk of incident RA compared to children without pets: HR = 0.55 (95% CI 0.3-0.9), p= 0.031). Furthermore, as previously described, passive smoking in childhood [HR=1.24 (1.0-1.5) p=0.044] and high educational level ([HR=0.78 (0.6-0.9) p=0.037]; [HR=0.772 (0.6-0.9) p=0.0426] for up to 2 years and ≥3 years of university education, respectively versus no education) were shown to be associated with RA in the multi-adjusted model.
Conclusion: More than farming lifestyle or the type of pet, the very early exposition to cats and/or dog (1-2 years) seems to reduce the incidence of RA while passive smoking in childhood increases it. This supports the idea that the lung and thus airborne exposures in early childhood play an important role in the genesis of RA occurring in adulthood.
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Disclosure of Interests: None Declared.
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POS1034

IMMUNOLOGICAL PROFILING IDENTIFIED CLINICAL CORRELATES AND ABATACEPT TREATMENT RESPONSE PREDICTOR OF RHEUMATOID ARTHRITIS

Keywords: -omics, Rheumatoid arthritis, Biomarkers

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Background: Rheumatoid arthritis (RA) patients are heterogeneity in their clinical phenotype and in response to molecular targeted therapies. To date, only limited number of studies addressed the immunological changes that lie behind the clinical heterogeneity.
Objectives: To identify immunological correlates of clinical phenotypes and predictors of treatment response, we performed peripheral blood multi-omics profiling of patients initiating abatacept treatment.
Methods: In the PREDICTABA study, we have recruited 104 RA patients starting abatacept treatment at six hospitals in Japan (Figure 1A). Peripheral blood mass cytometry analysis was performed in discovery and validation cohorts (n=79 and 22). In total, 10 million T and B cells were clustered by cell surface protein expression (Figure 1B, 1C). After accounting for the effects of age, sex, CDAI disease activity, anti-CCP antibody titer, and donor batch effects, immune cell clusters were tested for their association with baseline treatment and future abatacept treatment response (CDAI improvement at 6 months) using mixed-effects modeling of association of single cells [1]. Peripheral blood RNA-seq identified immune cell signatures and immune pathway signatures.
Results: At baseline, median age was 73 years. 80% were female and 80% were seropositive. Median CDAI improved from 17 to 5 after 6 months of abatacept treatment. RNA-seq immune cell gene signatures validated mass cytometry immune cell cluster frequencies. Naive CD8 T cells were negatively associated with age (odds ratio (OR) 0.57 and 0.32, P-values<0.001). Naive B cells were negatively associated with baseline prednisolone use (OR 0.53 and 0.25, P-values<0.001). Plasmablasts were negatively associated with baseline methotrexate use (OR 0.59 and P-value<0.001, Figure 1B, 1D, 1E), and with IL6_JAK_STAT3 signaling gene signature (Rho=-0.36, P-value<0.001). Finally, CD8+CD25+ T cells showed suggestive association with CDAI improvement after abatacept treatment (OR 1.4 and 1.6, P-values 0.01 and 0.07, Figure 1C, 1F, 1G).
Conclusion: Through immunophenotyping analysis of RA patients, we have revealed that B cell subsets are associated with conventional RA treatments. Abundance of CD8+CD25+ T cells may be predicative of good abatacept response.
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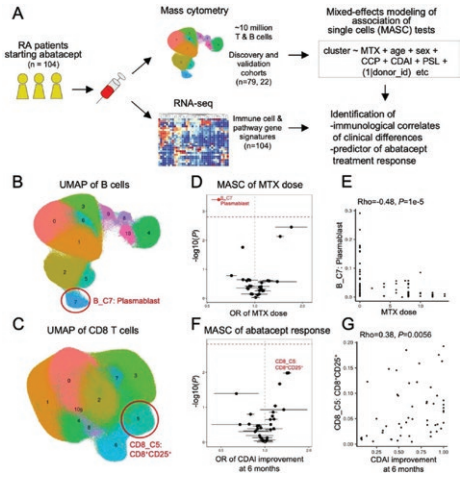


Figure 1. (A) Overview of the study. (B-C) UMAP visualization of B cells (B) and CD8 T cells (C) from mass cytometry analysis. (D) Mixed-effects modeling of association of single cells (MASC) between 32 mass cytometry T and B cell clusters and baseline methotrexate (MTX) dose. Red dashed line indicates Bonferroni corrected P-value threshold for P-value < 0.05. (E) Negative correlation between baseline MTX dose and B_C7 Plasmablast frequencies by the Spearman's rank correlation coefficient test. (F) MASC analysis of CDAI improvement rate at 6 months after the start of abatacept treatment. (G) The correlation between CDAI improvement rate at 6 months after abatacept treatment and CD8_C5: CD8+CD25+ T cells cluster by the Spearman's rank correlation coefficient test. (B-G) Discovery cohort data

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POS1035 FOCAL ADHESION PROTEINS KINDLIN-1, -2 AND TALIN-1 ARE REGULATED IN IL-1B-STIMULATED RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

Keywords: Synovium, Cytokines and chemokines, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a progressive chronic inflammatory autoimmune disease characterized by synovial hyperplasia, articular inflammation and excessive joint and bone erosion. Activated RA synovial fibroblasts (SF) are key players of cartilage erosion by attaching and invading into cartilage. The kindlin family of focal adhesion proteins consists of three members, whose function is to activate integrins and thereby enable focal adhesion. Integrins play a central role in regulating cell-matrix and cell-cell adhesion. The effects of integrin activation are cell adhesion and migration, which are known to be pathologically increased in RASF. It is well described that dysfunction of integrins and kindlins and their co-factor talin-1 are involved in the pathogenesis of certain diseases characterized by inflammation and malignant transformation. However, the role of kindlins and talin-1 in RA, and specifically RASF, remain unclear.
Objectives: To investigate the compartmental and cellular localisation of kindlin-1, -2, -3 and talin-1 in RA synovial tissue and RASF, and the impact of pro-inflammatory activation on their expression on mRNA and protein level.
Methods: Synovial fibroblasts were isolated from synovial tissue after joint replacement surgery (RA, osteoarthritis (OA)) or synovectomy of hand joints (non-arthritic controls). RASF were stimulated with 10 ng/ml IL-1β for 6, 17, 24 and 48 h. In a second approach, RASF were repetitively stimulated three times with 0.05 ng/ml IL-1β every 24 h. RNA was isolated, reverse-transcribed and qPCR performed for kindlin-1, -2, -3 and talin-1. Whole RNA sequencing was performed for the repetitive stimulation approach and evaluated using matrix combining pairwise contrasts (DESeq2 and DESeq) normalized counts and thresholds for significance of differential expression per contrast. Immunocytochemistry on RASF seeded on chamber slides was performed. Immunohistochemistry on synovial tissue was performed on 5 µm acetone-fixed cryosections. Biological replicates and Kruskal-Wallis-test with Dunn's multiple comparison were used for statistics.
Results: In RA synovial tissues, kindlin-2 and talin-1 protein were detectable adjacent to blood vessels, in the synovial lining layer and in the sublining. Kindlin-2 and talin-1 could be detected in cultured RASF with a consistent signal of the cell body without a nuclear signal. Kindlin-1 and -3 were neither detectable in synovial tissue nor in synovial fibroblasts. Relative mRNA levels (arbitrary units) of kindlins and talin-1 in RASF differed, with the strongest signal for talin-1 (663 ± 186), followed by kindlin-2 (88 ± 23), kindlin-1 (2.15 ± 2.06) and kindlin-3 (0.12 ± 0.08). In comparison to unstimulated controls, stimulation of RASF with IL-1β led to a temporary downregulation of kindlin-2 (-4.1-fold, p=0.0456) and talin-1 (-1.6-fold) after 17 h and returned to the baseline levels after 48 h. This time-dependent effect could also be observed by immunocytochemistry of IL-1β-stimulated RASF. Kindlin-1 mRNA expression was significantly upregulated after 6 h (2.9-fold, p=0.0178) of stimulation and downregulated after 17 h (-1.5-fold, p<0.0001), 24 h (-0.7-fold, p=0.0004) and 48 h (-1.2-fold, p<0.0001) compared to 6 h. After repetitive activation of RASF, kindlins and talin-1 were constantly regulated compared to the first stimulation (kindlin-1: 1.03-fold; kindlin-2: -1.06-fold; talin-1: 1.00-fold). In contrast, IL-6 showed an inflammatory adjustment to IL-1β leading to lower induction of IL-6 (49.1%) after repetitive IL-1β exposure.
Conclusion: Focal adhesion proteins kindlin-2 and talin-1, factors involved in integrin activation of cells, are present on RA synovial tissue and in RASF. As a time-dependent regulation of kindlin-2 and talin-1 after stimulation was observed, this effect may lead to a temporary and repetitive reproducible activation of RASF and activation of integrins, subsequently contributing to altered adhesion and migration of RASF under inflammatory arthritic conditions.
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POS1036 NF-ΚB SIGNALLING IS CRITICALLY IMPORTANT FOR FUNCTIONAL RESPONSES OF ACPA-PRODUCING B CELL CLONES FROM PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Cell biology

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Background: Anti-citrullinated protein antibodies (ACPA) play a role in rheumatoid arthritis (RA) pathogenesis, and their presence is associated with disease severity. Moreover, high serum levels of ACPA in the preclinical phase are one of the major risk factors for RA progression. Consequently, detailed analysis of ACPA^{pos} B cells is required to disentangle the role of these cells in RA. Multiple intracellular signalling pathways are involved in functional B cell responses. NF-κB signalling is one of the prime regulators of B cell proliferation, differentiation and (auto)antibody production. Moreover, NF-κB activation leads to pro-inflammatory cytokine and chemokine production. JAK-STAT signalling is induced after activation of the B cell receptor (BCR) and is also involved in B cell proliferation and maturation. Targeting NF-κB or JAK-STAT signalling may advance our understanding of the mechanisms involved in the activation of ACPA-producing B cells. We make use of ACPA^{pos} B cell clones, since peripheral ACPA^{pos} cells are present at low frequencies in the peripheral blood.
Objectives: To identify whether NF-κB or JAK-STAT signalling inhibition using small molecule inhibitors (SMIs) is effective in targeting functional responses of ACPA^{pos} B cell clones from RA patients, including survival, proliferation, differentiation, and antibody production.
Methods: Previously generated ACPA^{pos} and ACPA^{neg} B cell clones [1] (see Figure 1A for method) were expanded and cultured with anti-CD40 and IL-21. Canonical and non-canonical NF-κB signalling were targeted by validated SMIs of Inhibitor of κB kinase β (IKKβi, canonical NF-κB signalling) and NF-κB inducing kinase (NIKi, non-canonical NF-κB signalling), respectively. Tofacitinib (a JAK1/JAK3 specific small molecule inhibitor) was used to target JAK-STAT signalling. Cell viability, proliferation and differentiation were evaluated by flow cytometry. Antibody production was measured by ELISA.
Results: We observed a dose-dependent reduction in proliferation in ACPA-producing B cell clones treated with either IKKβi (12.5 µM IKKβi: 39.12±9.86% decrease, 25 µM IKKβi: 56.55±1.84% decrease, 50 µM IKKβi: 65.65±3.1% decrease; data normalised on DMSO) or NIKi (12.5 µM NIKi: 12.13±19.42% decrease, 25 µM NIKi: 26.63±17.37% decrease, 50 µM NIKi: 41.69±2.00% decrease; data normalised on DMSO) upon T cell-dependent stimulation with 2.25 µg/ml anti-CD40 and 1.0 ng/ml IL-21 (Figure 1B). Similarly, we observed a dose-dependent reduction in IgG production (Figure 1C). IKKβi treatment seemed to have a stronger effect than NIKi treatment on ACPA^{pos} B cell clones, while we did not observe a clear difference between IKKβi and NIKi in ACPA^{neg} B cells (12.5 µM IKKβi: 6.90±5.38% decrease, 25 µM IKKβi: 33.32±2.15% decrease, 50 µM IKKβi: 50.11±3.15% decrease; 12.5 µM NIKi: 6.09±3.61% decrease, 25 µM NIKi: 17.83±6.53% decrease, 50 µM NIKi: 54.67±20.37% decrease; data normalised on DMSO). These effects were not caused by cytotoxic effects as cell viability was not affected by IKKβi or NIKi treatment. In contrast to the effects of IKKβi and NIKi treatment, tofacitinib only had limited effects on ACPA^{pos} and ACPA^{neg} B cell proliferation and IgG production. At present these results are being corroborated in freshly isolated ACPA^{pos} B lineage cells of RA patients.
Conclusion: Our data point towards a critical role of the NF-κB signalling pathways in the functional responses of ACPA-producing B cells, whereas a limited role of JAK-STAT signalling was observed. Consequently, targeting NF-κB signalling may have beneficial effects in limiting (autoreactive) B cell responses in RA.
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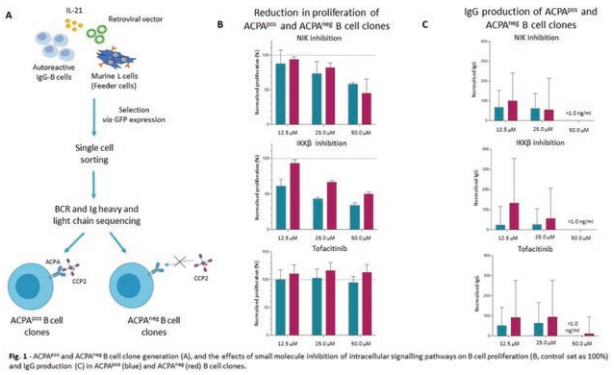


Fig. 1 - ACPA^{pos} and ACPA^{neg} B cell clone generation (A), and the effects of small molecule inhibition of intracellular signalling pathways on B cell proliferation (B, control set as 100%) and IgG production (C) in ACPA^{pos} (blue) and ACPA^{neg} (red) B cell clones.

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POS1037 THE GUT MICROBIOME IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS: FACTORS ASSOCIATED WITH COMPOSITION, AND ITS VALUE FOR PREDICTING TREATMENT RESPONSES

Keywords: bDMARD, Rheumatoid arthritis, -omics

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Background: The gut microbiota has been proposed to be an important environmental factor in the development of rheumatoid arthritis (RA). However, changes in the gut microbiome of RA patients who were already treated with disease-modifying anti-rheumatic drugs (DMARDs) have not been studied well.
Objectives: We aimed to investigate the gut microbiota of patients with established rheumatoid arthritis (RA) who have been managed with DMARDs for a long time. We focused on factors that might affect composition of the gut microbiota. Furthermore, we investigated whether gut microbiota composition predicts future clinical responses to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) in patients with an insufficient response to initial therapy.
Methods: We recruited 94 patients with RA and 30 healthy participants. Fecal samples were collected, and the gut microbiome was analyzed by 16S rRNA amplificon sequencing. Calypso online software was used to compare microbial composition between groups. For RA patients with moderate-to-high disease activity, treatment was changed after stool collection, and responses were observed 6 months later.
Results: The composition of the gut microbiota in patients with established RA was different from that of healthy participants. Young RA patients (< 45 years) had reduced richness, evenness, and distinct gut microbial compositions when compared with older RA patients and healthy individuals. Disease activity and rheumatoid factor levels were not associated with microbiome composition. Overall, biological DMARDs and csDMARDs, except sulfasalazine and TNF inhibitors, respectively, were not associated with the gut microbial composition in patients with established RA. However, the combination of *Subdoligranulum* and *Fusicatenibacter* genera was associated with a future good response to second-line csDMARDs in patients who showed an insufficient response to first-line csDMARDs.
Conclusion: Gut microbial composition in patients with established RA is different from that in healthy individuals. Thus, the gut microbiome has the potential to predict responses of some RA patients to csDMARDs.

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Disclosure of Interests: None Declared.
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POS1038 NAD+ BOOSTERS AS A NOVEL ANTI-INFLAMMATORY TOOL IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Rheumatoid arthritis

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Background:
Objectives: 1- To analyze the levels of NAD^+ and genes involved in its metabolism in Rheumatoid Arthritis (RA) patients. 2- To evaluate the effect of anti-TNF therapy in the NAD^+ metabolism. 3- To explore mechanistically the anti-inflammatory effects of NAD^+ boosters in leukocytes from RA patients.
Methods: Plasma and PBMCs were purified from 100 RA patients and 50 healthy donors (HDs). NAD+ levels were determined by using the NAD/NADH-Glo Assay. Gene expression analysis of markers related to the synthesis (NAMPT, NMNATs, etc), transport (Cx43), and consumption of NAD^+ (PARPs, SIRTs, CD38, etc) were performed in PBMCs by RT-PCR. Public datasets from GEO repository were used to validate the analyses. A panel of 92 inflammatory mediators was also analyzed in the RA serum using Olink platform. In a second cohort of 50 RA patients treated with anti-TNF therapy, NAD+ levels were analyzed before and after 6 months of treatment. PBMCs from a third cohort of 10 active RA patients were treated *ex vivo* with 1 mM of NAD^+ boosters including nicotinamide (NAM) and nicotinamide riboside (NR) in the presence of inhibitors of NAMPT (FK866) and Cx43 (GAP19). After 24 hours, the Olink inflammatory panel was used to evaluated anti-inflammatory effects.
Results: NAD+ levels were significantly reduced in the plasma of RA patients and the expression of genes involved in the consumption (PARPs, SIRTs, CD38, CD157) and biosynthesis (NMNATs) of NAD^+ were increased and reduced respectively in RA PBMCs. NAMPT and Cx43 were also upregulated in those patients. The results were validated in an independent dataset. Unsupervised clustering analysis of the inflammatory proteome identified 3 cluster of patients, where cluster 1 was characterised by higher levels of inflammatory mediators and disease activity (DAS28) and lower levels of NAD^+, and cluster 3 by lower levels of inflammatory mediators and DAS28 and higher levels of NAD^+. Cluster 2 showed intermediate profiles. Anti-TNF therapy restored the altered NAD^+ levels in RA patients towards those exhibited by HD. Moreover, changes in DAS28 and NAD^+ levels were correlated. In vitro, NAD^+ boosters promoted a significant increase in NAD^+ levels of RA PBMCs. The FK866 treatment highlighted the key role of NAMPT in the generation of NAD^+ promoted by NAM. The inhibition of the extracellular transport of NAD^+ with GAP19 further increased the intracellular NAD^+ content in the presence of NAM and NR. Both boosters reduced the levels of numerous secreted inflammatory mediators in the supernatant, which was enhanced by effect of GAP19. In parallel, the gene expression of key inflammatory mediators was deeply reduced along with markers of oxidative stress and apoptosis.
Conclusion: 1- The NAD^+ levels and its metabolism is altered in RA patients and directly linked to their inflammatory profile and disease activity. 2- Anti-TNF therapy restore NAD+ altered levels in line with the clinical response. 3- NR and NAM increase the NAD^+ levels in PBMCs from active RA patients, through a mechanism mediated in part by NAMPT, promoting an extensive anti-inflammatory effect which is enhanced by Cx43 inhibition. NAD^+ boosters might be considered as novel therapeutic approach to reduce inflammation in RA.

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POS1039 ANTI-CITRULLINATED PROTEIN ANTIBODY (ACPA) REACTIVITY TOWARDS NEUTROPHIL-DERIVED ANTIGENS: THE IMPACT OF CLONAL DIVERSITY AND INTER-INDIVIDUAL VARIATION

Keywords: Autoantibodies

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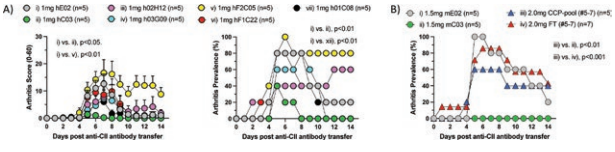
Background: Why the adaptive immune system turns against citrullinated antigens in rheumatoid arthritis (RA) and whether anti-citrullinated protein antibodies (ACPAs) contribute to pathogenesis are questions that have triggered intense research but still are not fully answered. Neutrophils may be crucial in this context, as sources of citrullinated antigens and also as targets of ACPAs.
Objectives: To better understand how ACPAs and neutrophils contribute to RA pathogenesis, we studied the reactivity of a broad spectrum of RA patient-derived ACPA clones to activated or resting neutrophils, and we also compared neutrophil binding using CCP2 captured polyclonal ACPAs from different patients.
Methods: Human neutrophils were isolated from the peripheral blood of healthy volunteers, individuals at risk for RA [1] and patients with established RA. The cells were activated using a Ca^{2+} ionophore, phorbol 12-myristate 13-acetate (PMA), nigericin, zymosan or IL-8. The binding of different monoclonal or polyclonal ACPA preparations to the cells was studied using flow cytometry and confocal microscopy. Neutrophil extracellular trap formation (NETosis) was analyzed using IncuCyteZOOM™. The role of protein arginine deiminase (PAD)2 and PAD4 was studied using neutrophils obtained from PAD-deficient mice or PAD4 inhibitors. Osteoclast cultures were established from human peripheral blood monocytes in the presence of M-CSF and RANK-L.
Results: ACPAs targeted NET-like structures in all tested conditions but did not bind to the surface of intact cells or influence NETosis. We observed a prominent clonal diversity in the capacity of ACPAs to bind to neutrophil-derived antigens. PAD2 was dispensable but the majority of the clones required PAD4 for neutrophil binding. When using polyclonal ACPA preparations from different patients, we observed high patient-to-patient variability in targeting neutrophil-derived antigens. Similar inter-individual variability was observed in another cellular effect of ACPAs: the stimulation of osteoclast differentiation.
Conclusion: Neutrophils can be important sources of citrullinated antigens under conditions that lead to PAD4 activation, NETosis and the extrusion of intracellular material. A substantial clonal diversity in targeting neutrophils and a high variability among individuals in both neutrophil binding and osteoclast stimulation suggest that ACPAs may influence RA-related symptoms with high patient-to-patient variability.
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Disclosure of Interests: Alexandra Cîrciumaru: None declared, Marcelo Gomes Afonso: None declared, Heidi Wähämaa: None declared, Akilan Krishnamurthy: None declared, Monika Hansson: None declared, Linda Mathsson-Alm Employee of: Thermo Fisher Scientific, Lena Israelsson: None declared, Ragnhild Stålesen: None declared, Charlotte de Vries: None declared, Miriam Shelef: None declared, Vivianne Malmström: None declared, Lars Klareskog: None declared, Anca Catrina: None declared, Caroline Grönwall: None declared, Aase Hensvold: None declared, Bence Réthi: None declared.
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POS1040 PATIENT-DERIVED ACPA CLONES DISPLAY BOTH PRO- AND ANTI-INFLAMMATORY POTENTIAL IN VIVO

Keywords: Animal models, Rheumatoid arthritis, Autoantibodies

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Background: Anti-citrullinated protein autoantibodies (ACPA) are known to associate with strong risk factors for rheumatoid arthritis (RA), as well as worse clinical prognosis[1]. Due to their high specificity in RA, ACPA are part of the classification criteria and regarded as being essential in the identification of individuals at risk of developing RA. However, not every ACPA-positive at-risk individual progresses to a clinical diagnosis[2], suggesting that the presence of ACPA per se does not dictate the clinical outcome. We have recently shown that ACPA are in fact predominantly anti-inflammatory and present different biological effects in a murine model of arthritis[3]. Having a wide diversity of ACPA clones isolated from different tissues of RA patients at our disposal, we have continued to analyze different monoclonal as well as polyclonal ACPA in their capacity to affect inflammatory processes in vivo.
Objectives: To determine whether ACPA with pathogenic features, i.e. capable of increasing or sustaining joint inflammation, can be found among different isolated ACPA clones from patients with established RA.
Methods: Immunoglobulin from single B cells from RA patients were sequenced and recombinantly expressed as monoclonal human (h)IgG1 in Expi293F cells, followed by validation of citrulline reactivity. Here, we tested 5 new monoclonal ACPA isolated based on anti-citrullinated tetramer staining of B cells[4]. Polyclonal ACPA IgG from 34 RA patients were enriched via a CCP2 affinity column. The unbound IgG fraction was used as the flow-through control. Arthritis was induced in BALB/c mice by i.v. transfer of 1.5mg of an arthritogenic cocktail of anti-type II collagen (CII) antibodies (Chondrex, USA) followed by administration of 25ug of LPS (*E. coli* strain O55:B5) 3 days later. Individually, 1mg of purified ACPA monomers, 2mg of ACPA-pool or 2mg flow-through IgG were transferred i.v. together with the arthritogenic antibody cocktail. An isotype control antibody and a previously identified anti-inflammatory ACPA clone (hE02 and hC03, respectively)[3] were used as experimental reference conditions. Arthritis development was monitored daily by a quantitative scoring system of inflamed joints – toes, knuckles, and wrist/ankle of front/hind paws. Statistical analysis was performed with repetitive-measure one-way ANOVA with Geisser-Greenhouse correction and Holm-Šidák's multiple comparisons test.
Results: Adding to our previous data with 8 monoclonal ACPA[3], where 3 of them did not alter the disease course, and 4 displayed strong anti-inflammatory properties, we observed an additional 4 newly tested ACPA clones that did not influence arthritis development. Furthermore, we identified one novel monoclonal ACPA (hF2C05) that displays a pro-arthritogenic effect ($p<0.01$). When assessing a polyclonal ACPA sample, we observed a dominant anti-inflammatory effect of the ACPA-pool in comparison to its non-ACPA flow-through IgG fraction, displayed by a significantly reduced disease prevalence ($p<0.001$).
Conclusion: Our preliminary data focusing on distinct monoclonal ACPA, as well as a new set of patient-derived polyclonal ACPA-pool, strengthens the notion that ACPA clones differ significantly between them, and within the same individual. Although we were able to identify an ACPA clone with arthritogenic potential, the majority of ACPA display no aptitude to affect joint inflammation or are anti-inflammatory. Together, this diversity of inflammatory effects calls for a re-evaluation of the proposed role of ACPA in RA, where their heterogeneity must be considered.
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POS1041 LIPID METABOLISM IS DEEPLY ALTERED IN ACTIVE RHEUMATOID ARTHRITIS PATIENTS AND REVERSED BY ANTI-TNF, ANTI-IL6R, AND JAK-INHIBITORS

Keywords: Rheumatoid arthritis, Artificial intelligence, -omics

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Background: Since lipid metabolism impact immune cell plasticity regulating cell activation, differentiation and function, the extensive analysis of the lipidomic profile using novel high-throughput metabolomic techniques in chronic inflammatory diseases such as Rheumatoid Arthritis (RA) might contribute to better characterise the pathogenesis of the disease.
Objectives: To analyse the whole lipidomic profile in the serum of RA patients, its association with the disease activity and its modulation by biological and targeted synthetic therapies.
Methods: Two hundred and fifty consecutive RA patients were included in this study. Serum samples and clinical data (disease activity, acute phase reactants, autoimmune profile, etc) were obtained from all subjects. The lipidomic profile was analysed by using nuclear magnetic resonance (NMR) spectroscopy from Nightingale LTD technology which included more than 200 lipid markers. In parallel, active RA patients from this cohort were prospectively followed up after 6 months of therapy with biologics [anti-TNF (n=50), anti-IL6R (n=15)], and JAK inhibitors (JAKi, n=20) and serum samples were obtained before and after those therapies where changes in the lipid and clinical profile were also evaluated.
Results: RA patients were stratified according to high (68), moderate (117) and low (65) disease activity and approximately 100 lipid markers were significantly altered in the serum of patients from these groups. Interestingly, most of the lipid markers were found reduced in the group of patients with high disease activity including apolipoproteins, cholesterol (free and in lipoproteins), fatty acids [saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), Omega 3 and 6, Linoleic acid (LA), Docosahexaenoic acid (DHA)], triglycerides (alone and in lipoproteins), cholines, phospholipids, lipoproteins [high-density lipoproteins (HDL), low-density lipoproteins (LDL), very low-density lipoproteins (VLDL)], and the total lipid content present in those lipoproteins. These alterations of the lipidomic profile might be associated with an abnormal liver function linked to an exacerbated inflammatory status. Furthermore, multiple correlations were also found among those lipids markers and inflammatory [C-reactive protein (CRP) and erythrocyte sedimentation rate CRP (ESR)] and autoimmune parameters [anti-citrullinated protein antibodies (ACPAS) and rheumatoid factor (RF)]. Interestingly, after six months of therapy, in parallel to the improvement in clinical and analytical profiles of RA patients, a significant upregulation of lipid markers was observed, including common and distinctive molecules reversed by each drug.
Conclusion: The circulating lipidomic profile of active RA patients is deeply reduced and directly linked to the activity of the disease, its inflammatory and autoimmune profile. In parallel to the clinical improvement of the disease, biological therapies and JAKi re-establish the altered lipid metabolism.
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Disclosure of Interests: None Declared.
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POS1042 JANUS KINASE INHIBITOR SUPPRESSES THE DIFFERENTIATION AND FUNCTION OF TUMOR NECROSIS FACTOR-ALPHA AND INTERLEUKIN-6-INDUCED OSTEOCLASTS IN PERIPHERAL BLOOD MONOCYTES FROM PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Cytokines and chemokines, Disease-modifying drug (DMARDs)

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Background: We have previously reported that stimulation of mouse bone marrow–derived macrophages with tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) induces differentiation of osteoclast-like cells having bone resorption ability[1]. Recently, we have shown that the combination of TNF-α and IL-6 can induce osteoclasts (OCs) from human peripheral blood mononuclear cells (PBMCs) via receptor activator of nuclear factor kappa-B ligand (RANKL)-independent pathways, and that there are functional differences between TNF-α and IL-6-induced OCs and RANKL-induced OCs. In particular, the number of TNF-α and IL-6-induced OCs differentiated from PBMCs in patients with rheumatoid arthritis (RA) positively correlated with the modified total Sharp score (mTSS). On the other hands, no such correlation was observed between the number of RANKL-induced OCs from RA PBMCs and mTSS[2].
Objectives: We undertook this study to clarify whether Janus kinase (JAK) inhibitors, a new class of disease modifying anti-rheumatic drugs, could inhibit the differentiation and function of TNF-α and IL-6-induced OCs using peripheral blood monocytes (PBMs) derived from patients with RA.
Methods: PBMs derived from RA patients and healthy donors were stimulated by TNF-α and IL-6 or RANKL with or without 10-1000 nM filgotinib, a JAK inhibitor. The number of tartrate-resistant acid phosphatase-positive multinucleated cells induced by TNF-α and IL-6 or RANKL and bone resorption activity using a pit formation assay were assessed. The examination was the number of TNF-α and IL-6-induced or RANKL-induced OCs differentiated from PBMs in RA patients before and 6 months after treatment with filgotinib.
Results: The number of TNF-α and IL-6–induced OCs and RANKL-induced OCs derived from PBMs in patients with RA was significantly increased compared to that derived from PBMCs in healthy donors (n = 5 each). Addition of filgotinib *in vitro* significantly inhibited the differentiation of TNF-α and IL-6-induced OCs derived from PBMs of RA patients in a dose-dependent manner. The same concentrations of filgotinib did not inhibit osteoclastogenesis induce by RANKL. Stimulation of RA PBMs by TNF-α and IL-6 in the presence of filgotinib significantly inhibited generation of resorption pits on dentin slices compared to findings in those PBMs in the absence of filgotinib. In contrast, stimulation of RA PBMs by RANKL with filgotinib showed generation of resorption pits in a manner similar to those generated by RANKL without filgotinib. Six months after treatment with filgotinib, the number of TNF-α and IL-6-induced OCs differentiated from PBMs was significantly decreased compared with those of before the treatment, whereas no significant change in the number of RANKL-induced OCs was observed in the same patients (Figure 1).
Conclusion: Our results suggest that the prevention effect of progressive bone destruction by JAK inhibitor in RA patients may involve inhibition of TNF-α and IL-6-induced OC differentiation, as well as suppression of osteoclastic bone resorption activity.
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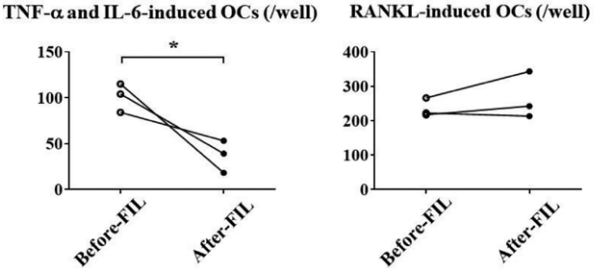


Figure. A JAK inhibitor, filgotinib (FIL), inhibits the differentiation of TNF-α and IL-6-induced osteoclasts (OCs) in peripheral blood monocytes (PBMs) from patients with rheumatoid arthritis. Left; Six months after treatment with FIL, the number of TNF-α and IL-6-induced OCs differentiated from PBMs was significantly decreased compared with those of before the treatment. Right; No significant change in the number of RANKL-induced OCs was observed in the same patients (n = 3 each). * = $P < 0.05$.

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Disclosure of Interests: Kazuhiro Yokota: None declared, Yoshimi Aizaki: None declared, Hiroshi Kajiyama: None declared, Yasuto Araki: None declared, Hiroaki Yazawa: None declared, Yuji Akiyama: None declared, Toshihide Mimura Grant/research support from: T.M. has received a research grant from Gilead Sciences.
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POS1043 SKELETAL MUSCLE PGC1A1 PREVENTS ARTHRITIS-INDUCED CAPILLARY RAREFACTION AND IMPAIRED GLUCOSE UPTAKE

Keywords: Sarcopenia, Comorbidities, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease with prevalent musculoskeletal complications (Steinz et al., 2019; Steinz, Santos-Alves, & Lanner, 2020), including metabolic disturbances. Patients with RA have a higher risk of developing type 2 diabetes (T2D) than the general population, however, the causality between RA and T2D is unknown. Skeletal muscle is essential for locomotor activity and the primary site for postprandial glucose disposal.
Objectives: Here we utilized a mouse model of arthritis and mice with chronic elevated expression of the transcriptional co-activator PGC1α1 to elucidate metabolic and functional alterations in skeletal muscle induced by chronic inflammation.
Methods: Arthritis was induced by complete Freund's adjuvant (CFA, ankle injection) in female wildtype or muscle-specific PGC-1α1 transgenic (MCK-PGC1α1) mice. Glucose uptake (*in vivo* and ex *vivo*), immunofluorescence staining, and immunoblotting were assessed 14 days post-CFA injection. Gene expression was analyzed 3 days after CFA induction.
Results: *In vivo* glucose uptake was reduced by 50-80% in limb muscle (extensor digitorum longus, tibialis anterior, soleus) of mice with arthritis as compared with control mice. Despite this, GLUT4 abundance and membrane translocation were enhanced by ~160% and ~70%, respectively, in limb muscle afflicted by CFA as compared with control. However, no difference was observed in *ex vivo* glucose uptake between the two groups, suggesting the reduction in glucose uptake was due to an alteration in muscle blood perfusion. Expression of angiogenesis-associated genes, including PGC1α (total and α1 isoforms), VEGF (A and B), and ERR (α and γ) was decreased by 50-70% in muscles afflicted by CFA, which was accompanied by a 25% reduction in muscle capillary density (capillary rarefaction). Muscle specific chronic elevation of PGC1α1 prevented the increase in GLUT4 abundance and capillary rarefaction induced by arthritis.
Conclusion: Induction of arthritis leads to reduced muscle capillary rarefaction and glucose uptake, which can advance the risk of developing metabolic disease. Strikingly, this pathophysiological development can be corrected by PGC-1α1.
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Acknowledgements: This study has been supported by The Swedish Research Council, The Promobilia foundation, The Swedish Rheumatism foundation, and The Royal King Gustaf V's memorial foundatio.n.
Disclosure of Interests: None Declared.
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POS1044

SINGLE CELL TRANSCRIPTOMICS ANALYSIS OF BLOOD IMMUNE CELLS IDENTIFIES GENE SIGNATURES AND CELL SUBSETS ASSOCIATED WITH DISEASE ACTIVITY IN A DIVERSE POPULATION OF RHEUMATOID ARTHRITIS PATIENTS

Keywords: -omics, Rheumatoid arthritis, Remission

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Background: Single cell transcriptional profiling has previously been used to identify gene signatures associated with rheumatoid arthritis (RA) pathophysiology, as well as characterize cell subpopulations. However previous studies have not adequately addressed potential comparison bias such as age and sex, or included patients from different ethnic backgrounds.
Objectives: This study leverages single cell sequencing of peripheral blood mononuclear cells (PBMCs) from patients with RA and matched healthy controls to identify disease relevant cell subsets and cell type specific signatures of disease in the periphery across a diverse cohort of patients.
Methods: PBMC samples from 18 RA patients and 18 healthy controls matched on age, sex, and ethnicity were sequenced at a single cell resolution using 10X Chromium protocols. Samples were processed using standard CellRanger and Scanpy pipelines, with HarmonyPy for batch correction. Differential gene expression was computed using DESeq2 and pathway analysis was carried out with GSEA. Cell proportion analyses were carried out within cell subsets using Mann-Whitney analysis between matched RA and control and in RA remission and low activity (DAS28 CRP < 3.2) versus moderate and high (DAS28 CRP ≥ 3.2).
Results: The final dataset consisted of 22,159 genes across 125,698 cells. The cohort was composed of 66.7% of females with a mean age of 54 years old, and was multi-ethnic with 11.1% of asian-american, 83.5 % of caucasian-american and 5.6 % of hispanic american, the mean DAS28-CRP for patients with RA was 3.33, 61.1 % had positive rheumatoid factor and 83.3 % had anti-citrullinated protein antibodies, 38.9 % were treated by DMARDs, only one patient had a biological. We identified 18 peripheral blood mononuclear cells (PBMC) subsets, including 5 CD4+ T cell subsets, 3 CD8+ T cell subsets, 2 Natural Killer (NK) cell subsets, 3 B cell subsets, and 5 monocyte subsets (Figure 1A). 70 genes were found to be significantly differentially expressed between RA and control CD4+ T cells, 98 genes in monocytes, 11 in B cells, 97 in CD8+ T cells, and 23 in NK cells (FDR ≤ 0.05) with some overlapping across cell types (Figure 1B). Enrichment analysis of genes significantly upregulated in RA-derived classical monocytes identified pathways associated with type 1 interferon signaling and cytokine production (p<0.001). Density plots revealed shifts in proportions of cell subsets between patients with high and moderate activity (DAS28 CRP ≥ 3.2;n=7), patients in low disease activity and remission (DAS28 CRP < 3.2; n=9), and healthy controls (n=18, Figure 1C). Non classical monocytes were significantly decreased in patients with low disease activity compared to control and high disease activity (p = 0.015 and 0.022). CD4 T central memory cells were also decreased in patients with high disease activity (p = 0.034) compared with controls.
Conclusion: Here we describe a dataset of single cell RNA sequenced PBMCs from a diverse population of patients with RA and matched healthy controls. We identified differentially expressed genes and new cell subsets linked to RA but also disease activity, providing potential new insight in non-remission mechanisms and pathophysiology in a diverse RA cohort.
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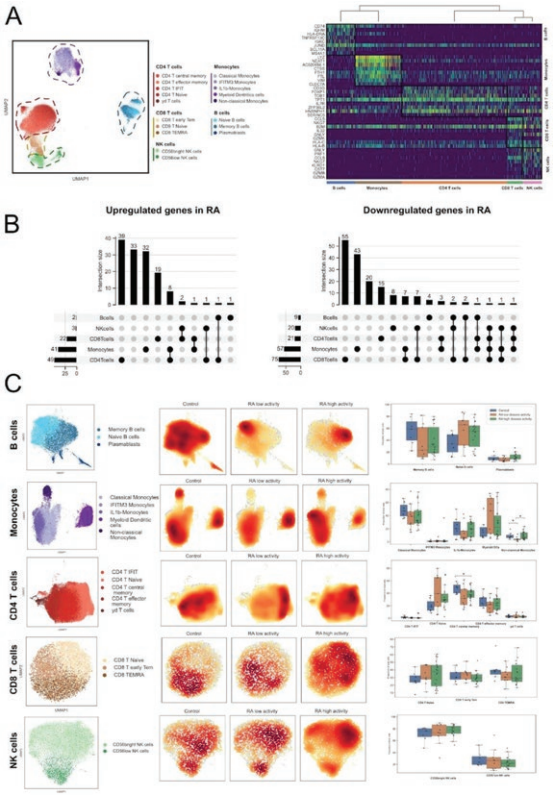


Figure 1. A) UMAP embeddings and subset annotations of single cell RNAseq dataset from patients with rheumatoid arthritis (RA) (n=18) and healthy controls (HC) (n=18) and heatmap with normalized expression of cell type specific gene markers are plotted in the heatmap. B) Significant up and down regulated genes in cell subsets in RA compared to HC matched on age, sex and ethnicity. C) UMAP embeddings of cell subsets with density plots and differential proportion analysis by Mann-U Whitney in HC samples (n=18), RA patients with low disease activity (DAS28 CRP < 3.2, n=9), and patients with moderate and high activity (n=7).

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POS1045

HISTOLOGICAL COMPOSITION OF (TENO)SYNOVIAL AND SYNOVIAL INFLAMMATION IN RHEUMATOID ARTHRITIS ACROSS DISEASE PHASES

Keywords: Synovium, Inflammatory arthritides, Rheumatoid arthritis

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Background: Subclinical tenosynovitis arose as a primary sign of inflammation already in the pre-clinical phases of Rheumatoid Arthritis (RA) and tenosynovitis is a common feature of active state and might persist although sustained remission is achieved.
Objectives: To assess the histological features of (teno)synovium from the extensor digitorum tendons of the hand across RA trajectory and to compare it with paired synovial tissue samples.
Methods: Thirty-seven patients underwent minimally invasive ultrasound (US)-guided biopsy of the tenosynovium of extensor digitorum tendons [n=16 with clinically suspected arthralgia (CSA), n=19 with RA (n=4 naïve, n=6 resistant to csDMARDS, n=8 to bDMARDs, and n=1 in sustained remission respectively)]. Twenty-three out of 37 patients presenting CSA or clinically evident synovitis in a peripheral joint (whether anatomically adjacent or not to the tendon of interest) underwent US-guided synovial tissue (ST) biopsy also in that location. The Krenn synovitis score (KSS) and the inflammatory infiltrate using CD68/CD21/CD3/CD20 immunohistochemical (IHC) analysis were assessed for each sample.
Results: Tenosynovium belonging to the extensor digitorum compartment of the wrist was successfully collected using a minimally invasive US-guided technique that enabled to retrieve representative samples in terms of lining and sublining layers presence in 86.5% and 100% of cases, respectively. Considering the pre-arthritis subgroup, KSS was similar in ACPA/RF^{pos} vs ACPA/RF^{neg} CSA (p=0.5814) and KSS was contingent with RA activity, being significantly higher in naïve or resistant RA (ANOVA p<0.001) compared to CSA. Moreover, the comparison between (teno)synovial and synovial tissue paired samples from two adjacent anatomical locations revealed a similar KSS value (p>0.999) and IHC showed comparable enrichment in terms of lining and sublining CD68^{pos}, sublining CD20^{pos} and CD3^{pos} cells (for all comparisons p>0.05) between the two sites, in naive and c- or b-DMARDs resistant RA patients. The procedure was well tolerated, and no tendon injury occurred within 10 months follow-up. One patient developed local hematoma that recovered after topic treatment.
Conclusion: (Teno)synovium is a retrievable tissue through a minimally invasive procedure across RA trajectory and its inflammation is directly related to the disease state. Semiquantitative analysis showed comparable inflammatory degree and inflammatory cellular composition in adjacent anatomical sites of the same person.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1046

IN ANTI-CCP POSITIVE AT RISK INDIVIDUALS, WHICH BIOMARKERS CHANGE PRIOR TO PROGRESSION TO INFLAMMATORY ARTHRITIS?

Keywords: Descriptive studies, Autoantibodies, Rheumatoid arthritis

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Background: The pre-clinical phase of inflammatory arthritis (IA) can be prolonged. Although many baseline biomarkers have shown predictive value for progression to IA, their evolution during the disease continuum remains unclear.
Objectives: To investigate which biomarkers change before progression to IA and assess their predictive value in the next 6 months.
Methods: In a single centre prospective cohort, 472 at-risk individuals were recruited with a positive anti-cyclic citrullinated peptide antibody (anti-CCP Ab) and a new musculoskeletal symptom, but without clinical arthritis. They were followed prospectively until IA occurred. Sequential data on early morning stiffness (EMS) duration, erythrocyte sedimentation rate (ESR), anti-CCP2 Ab value, rheumatoid factor (RF) value, number of small joints tender on examination, number of joints with power Doppler grade ≥1 (PD≥1), health assessment questionnaire (HAQ), visual analog scale for general health (VAS GH), global pain (VAS GP), and fatigue (VAS fatigue) were analysed. Three time-intervals were investigated within the progression (P) group: less than 6 months (P≤6M), 6 to 12 months (P 6-12M), and over 12 months before progression to IA (P>12M). Paired analysis (Wilcoxon signed rank and Mc-Nemar tests) were used to compare P≤6M and P >12M **(Pα)**, P≤6M and P6-12M **(Pβ)** within the P group. Independent analyses (Mann Whitney U and Fisher's tests) were used to compare the non-progression (NP) and P groups. Time-intervals for NP visits were adjusted to P visits by time elapsed since first visit. Multivariate predictive analysis of change in biomarkers were done using random effects panel data using robust standard errors, adjusted for age and gender. Significant difference was defined by p<0.05.
Results: Paired analysis within P group showed significant increase in **Pα** for RF, EMS, ESR, number of small joints tender, HAQ, and VAS GP, and in **Pß** for EMS and VAS GP (Figure 1). After dichotomisation, significant increases were also found for EMS ≥30min, ≥1 joint PD≥1, VAS GP ≥50mm, ESR positive, and ≥1 small joint tender. Analysis between P and NP groups showed significant differences in anti-CCP2 Ab, RF, ESR, number of joints PD≥1, number of small joints tender on examination, and HAQ at multiple time-intervals (Figure 1). EMS and VAS GP were only different at P≤6M. Multivariate panel data analysis showed predictive value in the change of anti-CCP2 Ab ≥3x upper limit of normal (ULN) (OR 51, p=0.041), positive RF (OR 7, p=0.002), EMS ≥30min (OR 9 p=0.004), and abnormal ESR (OR 7, p=0.046) for progression to IA within 6 months.
Conclusion: In anti-CCP2 Ab+ at-risk individuals, a change in predictive biomarkers occurs in the 6 months prior to IA development. Whilst EMS and VAS GP only show a late increase, multivariate panel data analysis suggest that anti-CCP2Ab ≥3xULN, positive RF, EMS ≥30min and positive ESR predict IA development within the next 6 months. These observations may be of value for monitoring at-risk individuals.

Table 1. Biomarkers characteristics

	NP group (N=330)	P group (N=142)	
		P >6M before IA	P ≤6M before IA
Anti-CCP2 Ab value ≥3xULN [A]	412/783 (53%)	170/206 (83%)	67/73 (92%)
RF positive [A]	183/778 (24%)	120/189 (63%)	53/68 (78%)
EMS minutes [B]	5 (0-30)	10 (0-30)	30 (3-67)
ESR abnormal [A]	435/1307 (33%)	150/330 (45%)	67/115 (58%)
Nb of small joint tender [B]	0 (0-2)	0 (0-2)	1.5 (0-5)
Nb of joint PD≥1 [B]	0 (0-0)	0 (0-1)	0 (0-1)
HAQ [B]	0.250 (0.0-0.875)	0.375 (0.0-1.0)	0.562 (0.125-1.250)
GH-VAS mm [B]	22(7-47)	21 (8-47)	28 (10-50)
GP-VAS mm [B]	27 (8-52)	27 (9-51)	35 (12-61)
GP-VAS ≥50 [A]	375/1311 (29%)	100/353 (28%)	49/124 (40%)

[A] n/N (%)[B] Median (IQR)N= number of visits with available data

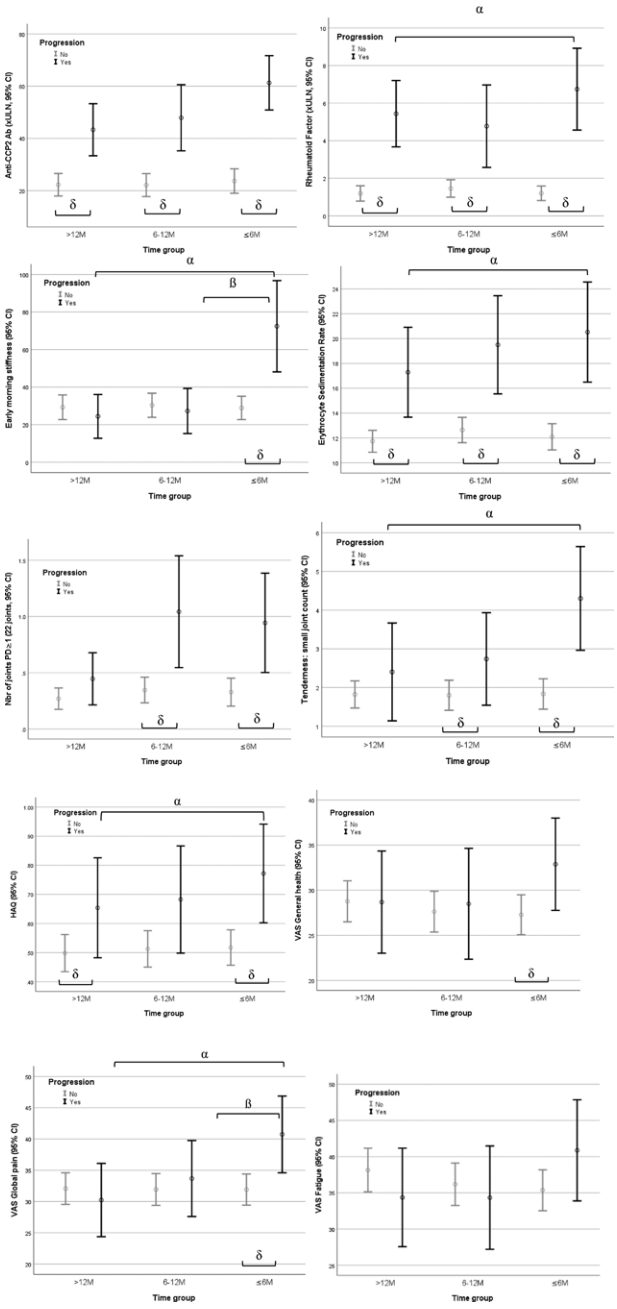


Figure 1. Biomarkers change through time. Un-paired 95% Confidence interval (95%CI) for the value of each biomarker with time; Progression (P) vs Non Progression (NP) groups. α Significant difference in paired analysis within P group between P>12M and P≥6M. ß Significant difference in paired analysis within P group between P 6-12M and P≥6M. δ Significant difference in independent analysis between P and NP groups.

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POS1047

RNA-SEQUENCING OF CLASSICAL MONOCYTES FROM RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT BONE EROSION

Keywords: Genetics/epigenetics, Inflammatory arthritides, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is an inflammatory autoimmune disease characterized by systemic and localized bone impairment. Bone erosions, the hallmark lesions of RA, are an important predictor of disability, disease severity, and mortality. The arising of bone erosions is triggered by chronic inflammation, mediated mainly by immune cells. Under inflammatory conditions, classical (CD14++CD16-) monocytes are the main source of osteoclasts precursors, the accountable cells responsible for bone resorption process. Although previous transcriptomic studies have shown that CD14++CD16- monocytes have high expression of genes involved in inflammation and in extracellular matrix degradation process, there is no data regarding the impact of CD14++CD16- monocytes on bone destruction in RA.

Objectives: To analyze CD14++CD16- monocytes transcriptomic profile from RA patients presenting bone erosions evaluated by high-resolution peripheral quantitative computed tomography (HR-pQCT), comparing with RA patients without bone erosions and healthy controls.

Methods: Thirty-nine premenopausal RA women were included in this study. Based on bone erosion identification on metacarpophalangeal and proximal interphalangeal joints of the dominant hand assessed by HR-pQCT, RA patients were classified into two groups according to the presence or absence of bone erosions. Twenty age- and body mass index-matched healthy subjects were enrolled in the control group. CD14++CD16- monocytes were indirectly isolated using the CD16 MicroBeads, and RNA-Sequencing was performed. Transcriptome analysis of CD14++CD16- monocytes from control group were used to account for background expression. The differentially expressed genes (DEGs) were identified and the analysis of the biological pathways was performed using bioinformatics tools.

Results: RNA-seq analysis revealed 1140 DEGs in RA patients with erosion, of which 89 were up-regulated and 1051 down-regulated compared to the group of patients without erosion. A top ranked genes suggested that the up-regulated genes were highly associated with immune response and cytokine activation. Interestingly, the down-regulated genes were associated with bone formation and wound healing (Table 1). Enriched pathways in patients with erosion were associated with substantial activation of immunity and inflammation. Pathways associated with osteoblast differentiation and the regulation of Wnt signaling were less activated in RA patients with erosion. Interesting, while the activity of immune pathways was positively correlated with the number of bone erosions, a negative correlation was observed between the number of erosions with osteoblast differentiation and regulation of cell matrix adhesion.

Table 1. Top differentially expressed genes identified in RA patients with bone erosion.

Genes	Ave FC	FDR	Main biological process
Up-regulated genes			
HSPA1B	9.26	0.0001	Ubiquitin-proteasome pathway
HLA-DQA2	6.35	0.0095	Adaptive immunity
KLF14	4.60	0.0416	Innate and adaptative immunity
IL18RAP	3.90	0.0317	Cytokine activity
CMTM1	3.83	0.0439	Chemokine activity.
Down-regulated genes			
LARP6	0.0026	0.0001	Collagen biosynthetic
PRRX1	0.0029	0.0004	Regulation of transcription by RNA polymerase II
RAB3B	0.0061	0.0001	Regulation of ion transport
AHNAK2	0.0065	0.0001	Wound healing
PAPPA	0.0072	0.0001	Bone formation

FC: Fold-change; Ave FC: average FC; FDR: False Discovery Rate.

Conclusion: These findings suggest that increasing of immuno-inflammatory activation and impairment of bone formation processes might potentially be a key driver of bone erosion in RA pathogenesis.

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Disclosure of Interests: None Declared.

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POS1048

SEMAPHORIN3B PROMOTES A RESOLVING-INFLAMMATION PHENOTYPE IN MACROPHAGES FROM RHEUMATOID ARTHRITIS PATIENTS

Keywords: Genetics/epigenetics, Rheumatoid arthritis, Cytokines and chemokines

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Background: Our group have recently shown that (Sema)phorin3B is reduced in RA patients and plays a protective role in an arthritis mouse model, through the reduction of inflammatory mediators and the synovial fibroblast invasiveness and was associated with a reduction of CD68 positive synovial macrophages (Igea, 2022). On the other hand, MerTK is a receptor protein kinase involved in the resolution of inflammation and plays a protective role in arthritis mice models (Waterborg, 2018). A recent study has shown that a population of synovial tissue macrophages characterized by the expression of MerTK are associated with remission maintenance and with an anti-inflammatory phenotype of RA FLS (Alivernini, 2020).
Objectives: The aim of this study is to determine the role of Sema3B in the phenotypic characteristics of RA macrophages and the implication of MerTK.
Methods: Peripheral blood monocytes from RA patients (n=10) were differentiated into macrophages by culturing in the presence of IFN-γ (10 ng/mL) for 6 days. Afterwards, macrophages were stimulated for 24 h with LPS (10 ng/mL), Sema3B (200 ng/mL) or the combination of both mediators. The expression of pro- and anti-inflammatory mediators was determined by quantitative PCR (qPCR) and ELISA. The expression of MerTK and macrophage surface markers was measured by flow cytometry.
Results: Sema3B did not modulate the macrophage expression of pro-inflammatory mediators *IL1B, IL6, IL12B, IL23, TNF, CCL2, CXCL10* and *CD86*, but significantly reduced the LPS-induced expression of these mediators (Figure 1A), as well as the protein secretion of IL6, IL12p70 and TNF. In addition, Sema3B alone, but not in combination with LPS, significantly induced the gene and protein expression of MerTK and the secretion of Resolvin D1, a MerTK-mediated lipid involved in resolution of inflammation (Figure 1B). Moreover, Sema3B reduced the expression of the M1 marker CD64, while induced the expression of the M2 marker CD163.

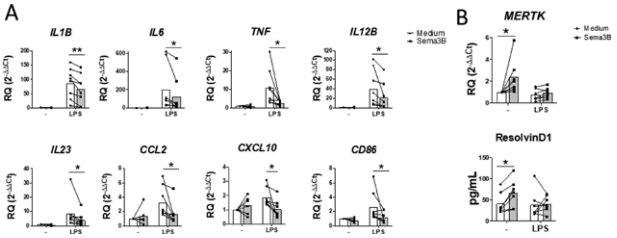


Figure 1. Sema3B enhances anti-inflammatory activity in macrophages of RA patients (n=6). (A) Significative reduction of the genetic expression of pro-inflammatory mediators. (B) Significative increase of *MERTK* and ResolvinD1. Macrophages differentiated from monocytes of RA patients during 6 days (IFN-γ 10 ng/mL) and stimulated with Sema3B (200 ng/ml), LPS (10 ng/mL) and their combination for 24 hours. Symbols represent individual patients; bars show the mean ± SEM. *P < 0.05 and **P < 0.01.

Conclusion: Our data demonstrate that Sema3B modulates the macrophage phenotype of RA macrophages, inducing a skewing towards an anti-inflammatory/pro-resolving phenotype, likely in a MerTK-dependent manner. Therefore, here we identified a new mechanism involved in the protective role of Sema3B in RA pathogenesis.

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POS1049

INTERLEUKIN 40 IS INCREASED IN THE SERUM OF INDIVIDUALS AT RISK OF RHEUMATOID ARTHRITIS AND STIMULATES AN INFLAMMATORY RESPONSE IN MONONUCLEAR CELLS VIA NFKB

Keywords: Cytokines and chemokines, Biomarkers, Rheumatoid arthritis

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Background: Interleukin 40 (IL-40) is a new cytokine implicated in the pathogenesis of several autoimmune disorders including rheumatoid arthritis (RA). Recently, we found an association of IL-40 with the early stages of RA and demonstrated the pro-inflammatory potential of IL-40 on neutrophils.
Objectives: As the period preceding clinically apparent RA has not yet been fully described with respect to clinical biomarkers, we aimed to investigate IL-40 in individuals who are at risk of RA and to assess its functional mechanism in immune regulation in peripheral blood mononuclear cells (PBMCs).
Methods: IL-40 was determined in the serum of individuals at risk of RA (defined as patients with arthralgia with no clinical arthritis at baseline who are either carriers of anti-citrullinated protein antibodies, ACPA, or meeting the EULAR definition of clinically suspect arthralgia) at baseline (n=179) and at the time of arthritis manifestation in patients who progressed to clinical arthritis (n=25). IL-40 was also analysed in the serum of age and sex-matched healthy controls (n=60). *In vitro* experiments were performed on PBMCs from at-risk individuals (n=10). PBMCs were exposed to recombinant IL-40 (10, 50, 100, and 250 ng/ml) and LPS. For inhibition studies, cells were pretreated with NFkB inhibitor prior to incubation with IL-40. Levels of IL-40 and IL-6 were measured by commercially available ELISA kits.
Results: Serum IL-40 was significantly up-regulated in at-risk individuals compared to healthy individuals (4.8 ± 0.2 vs. 1.5 ± 0.09 ng/ml, p<0.0001). Moreover, the levels of IL-40 were significantly higher in the serum of double-positive ($ACPA^+$/rheumatoid factor, RF^+) compared to double-negative at-risk individuals (6.4 ± 0.7 vs. 4.5 ± 0.5 ng/ml; p<0.05). Out of 175 at-risk individuals, only 25 developed clinical arthritis (within a median of 8,17 months of follow-up); however, we have not found a significant difference in the levels of IL-40 at baseline, and at the time of arthritis manifestation. To evaluate the pro-inflammatory effect of systemically elevated IL-40 in at-risk individuals, their PBMCs were exposed to recombinant IL-40 *in vitro*. We showed that IL-40 strongly enhances the secretion of IL-6 by PBMCs in a dose-dependent manner when compared to unstimulated cells (10 ng/ml of IL-40: p<0.05; 50, 100, 250 ng/ml of IL-40: p<0.01). Furthermore, the application of NFkB inhibitor to the PBMCs prior to the exposure to IL-40 significantly reduced the secretion of IL-6 when compared to IL-40 treated cells without NFkB inhibition (p=0.004).

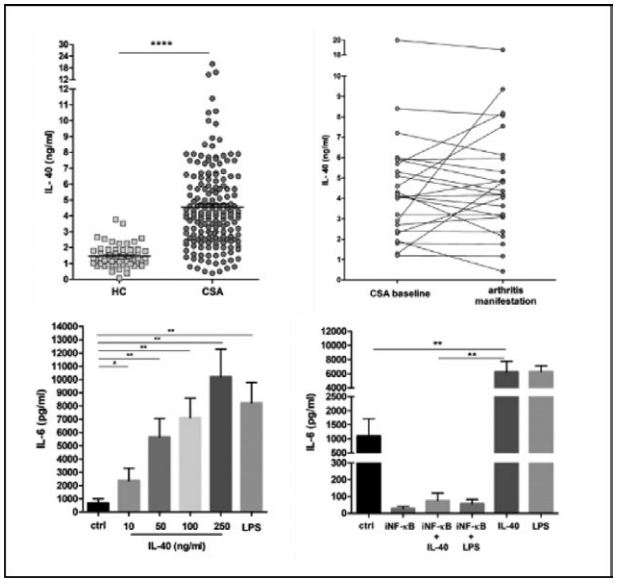


Figure 1.

Conclusion: This is the first study to demonstrate the up-regulation of IL-40 in the serum of individuals at risk of RA. Moreover, we showed that IL-40 induces the pro-inflammatory response in PBMCs at-risk individuals via NFκB dependent pathway.

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Rheumatoid arthritis - comorbidity and clinical aspects

POS1050

INCIDENCE RATES OF INTERSTITIAL LUNG DISEASE AMONG PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ABATACEPT: A POST HOC POOLED ANALYSIS FROM A COMPENDIUM OF CLINICAL TRIALS

Keywords: Rheumatoid arthritis, Lungs, Disease-modifying drug (DMARDs)

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Background: Interstitial lung disease (ILD) is a recognized complication of RA. Prior studies have suggested stabilization or improvement of ILD in patients with RA (RA-ILD) treated with abatacept.[1,2] Few studies have evaluated the background incidence rate of RA-ILD.

Objectives: To determine the incidence rate of clinically significant ILD in a cohort of patients with RA receiving abatacept + MTX versus placebo + MTX from multiple clinical trials.

Methods: This retrospective analysis examined pooled safety data from ten phase 3 clinical trials of patients with RA treated with background MTX in combination with abatacept or placebo. The term 'interstitial lung' was used to identify incidences of ILD reported as AEs in the safety data. The exposure period for each patient was censored at first incidence of clinically significant ILD, 56 days after last study drug administration, or 1 day prior to commencement of another study drug, whichever occurred first. Poisson regression models were used to estimate crude incidence rates per 100 person-years for baseline risk factors within treatment groups, and to estimate incidence rate ratios for the placebo + MTX versus abatacept + MTX treatment groups. Disease activity parameters, DAS28 (CRP) and HAQ-DI, were estimated from baseline to the time of ILD diagnosis (as reported by AEs).

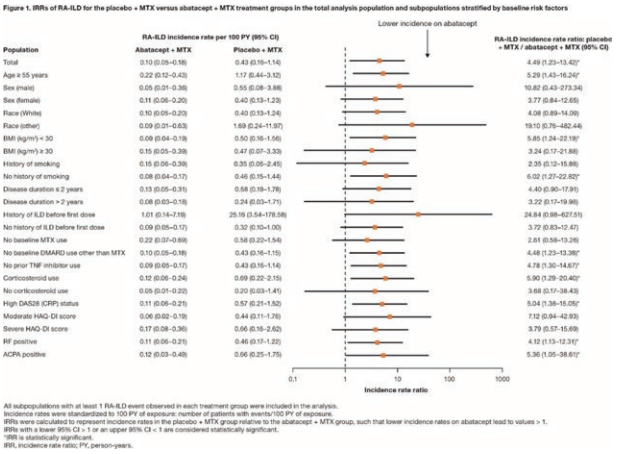
Results: In total, 3,708 patients (10,521 person-years) treated with abatacept + MTX and 999 patients (938 person-years) treated with placebo + MTX were included. Patients treated with placebo + MTX had a higher incidence rate of ILD per 100 person-years (95% CI) versus those treated with abatacept + MTX (0.43 [0.16–1.14] vs 0.10 [0.05–0.18], respectively; Figure 1). The incidence rate ratio of placebo + MTX versus abatacept + MTX treatment groups for the total population was 4.49 (95% CI, 1.23–13.42). For all subpopulations stratified by baseline risk factors (where ≥ 1 patient in each treatment group had an ILD event), incidence rate ratios were > 2. Patients with RA aged ≥ 55 years, BMI < 30 kg/m^2, no history of smoking, no baseline DMARD use other than MTX, no prior TNF inhibitor use, corticosteroid use, high DAS28 (CRP) status, and RF or anti-citrullinated protein antibody (ACPA) positivity were all significantly less likely to develop ILD if treated with abatacept + MTX versus placebo + MTX (Figure 1).

Conclusion: Incidence rates of ILD among patients with RA were significantly lower in those treated with abatacept + MTX than placebo + MTX, both in the total analysis population and subpopulations stratified by baseline risk factors. This suggests a possible protective benefit of abatacept on the incidence rate of RA-ILD. Limitations of this post hoc analysis include the different observation period lengths of the 2 treatment arms due to the original study designs, and the low number of patients with ILD events overall. However, the low incidence rate of ILD observed here is consistent with previously reported studies.[3]

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Figure 1. IRRs of RA-ILD for the placebo + MTX versus abatacept + MTX treatment groups in the total analysis population and subpopulations stratified by baseline risk factors



All subpopulations with at least 1 RA-ILD event observed in each treatment group were included in the analysis.
Incidence rates were standardized to 100 PY of exposure; number of patients with events/100 PY of exposure.
IRRs were calculated to represent incidence rates in the placebo + MTX group relative to the abatacept + MTX group, such that lower incidence rates on abatacept lead to values > 1.
IRRs with a lower 95% CI > 1 or an upper 95% CI < 1 are considered statistically significant.
*IRR is statistically significant.
IRR, incidence rate ratio; PY, person-years.

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POS1051

LUNG CLUSTERING ANALYSIS-BASED PHENOTYPES OF RHEUMATOID ARTHRITIS USING ARTIFICIAL INTELLIGENCE-BASED TECHNOLOGY FOR CHEST COMPUTED TOMOGRAPHY

Keywords: Rheumatoid arthritis, Artificial intelligence, Lungs

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Background: Lung involvement is a prevalent extraarticular manifestation of rheumatoid arthritis (RA) that remains a significant clinical challenge. Few studies have comprehensively quantified lung abnormalities of RA patients using artificial intelligence-based (AI) technology.

Objectives: The aim of this study was to quantify lung lesions in RA patients and classify them based on their lung parameters.

Methods: An AI-based quantitative computed tomography (CT) image analysis software (AIQCT) was applied to high-resolution CT scans of RA patients in a cross-sectional manner. AIQCT automatically classified and quantified 10 types of parenchymal image patterns, expressing the volumes as percentages of total lung volume [1]. Hierarchical Ward's linkage clustering based on these patterns identified five clusters. Visual assessments (ILD, and airway lesions) of HRCT and clinical phenotypes were assessed.

Results: A total of 408 RA patients were included in the study. The lung profiles of the five clusters were as follows: Cluster I (68.6%), characterized by nearly normal lungs; Cluster II (23.5%), characterized by slight lung lesions with honeycombs or ground-glass opacities (GGOs); Cluster III (5.6%), characterized by the

predominance of GGOs; Cluster IV (1.0%), characterized by a predominant hyperlucent area; and Cluster V (1.2%), characterized by extensive lung abnormalities (Figure 1, Table 1). The number of patients in each cluster with ILD and airway lesions, based on visual assessments, were as follows: [ILD] Cluster I, 11/280 (3.9%), Cluster II, 19/96 (19.8%), Cluster III, 5/23 (21.7%), Cluster IV, 0/4 (0%), and Cluster V, 5/5 (100%) ($p < 0.001$): [airway lesions] Cluster I, 31/280 (11.1%), Cluster II, 29/96 (30.2%), Cluster III, 6/23 (26.1%), Cluster IV, 0/4 (0%), and Cluster V, 1/5 (20%) ($p < 0.001$). Clinical characteristics of each cluster were described in Table 1. The disease activity of RA in each cluster were as follows: [DAS28ESR, mean (SD)] Cluster I, 2.4 (1.0), Cluster II, 3.0 (1.2), Cluster III, 2.8 (1.0), Cluster IV, 2.2 (0.7), and Cluster V, 3.0 (0.8) ($p < 0.001$); [HAQ, mean (SD)] Cluster I, 0.4 (0.6), Cluster II, 0.9 (0.9), Cluster III, 1.1 (0.9), Cluster IV, 0.3 (0.3), and Cluster V, 0.8 (0.9) ($p < 0.001$).

Conclusion: This study is the first to classify lung lesions in comprehensive RA patients using quantitative data derived from novel AI technology. The AIQCT-derived clustering of RA patients appears to be associated with their clinical backgrounds and characteristics.

REFERENCE:

[1] Ann Am Thorac Soc 2022;19:399-406

Table 1. Scores of ten lung parenchymal image patterns and clinical characteristics in each cluster.

Cluster	I (n=280)	II (n=96)	III (n=23)	IV (n=4)	V (n=5)	p value
AIQCT lung score (%), mean (SD)						
Normal	**92.6 (1.5)**	90.7 (2.5)	87.4 (1.8)	76.3 (5.1)	80.2 (1.6)	<0.001
GGOs	0.7 (0.3)	**1.0 (0.4)**	**2.9 (1.4)**	0.6 (0.3)	**2.4 (0.5)**	<0.001
Reticulation	0.1 (0.1)	0.4 (0.4)	0.5 (0.5)	0.2 (0.2)	**3.8 (3.3)**	<0.001
Consolidation	0.1 (0.05)	0.3 (0.3)	0.3 (0.2)	0.4 (0.6)	**1.6 (1.1)**	<0.001
Honeycombs	0 (0.02)	**0.08 (0.2)**	0.01 (0.02)	0.07 (0.05)	**1.7 (1.8)**	<0.001
Small nodules	0.1 (0.06)	0.3 (0.2)	0.5 (0.6)	0.1 (0.04)	0.5 (0.4)	<0.001
Interlobular septum	0.1 (0.06)	0.3 (0.2)	0.4 (0.3)	0.1 (0.07)	0.5 (0.3)	<0.001
Hyperluency	0.1 (0.3)	0.7 (1.6)	0.1 (0.1)	17.1 (3.9)	0.4 (0.4)	<0.001
Bronchi	1.8 (0.4)	2.3 (0.6)	2.5 (0.7)	1.9 (0.3)	**4.2 (1.4)**	<0.001
Blood vessels	4.4 (1.0)	4 (1.1)	5.5 (1.1)	3.3 (0.6)	4.7 (0.5)	<0.001
Age, mean (SD)	62.9 (12.0)	72.2 (8.0)	70.4 (9.9)	68.5 (4.8)	60.0 (8.0)	<0.001
Sex; female, n (%)	240 (86)	81 (84)	19 (83)	1 (25)	5 (100)	0.015
Smoking history, n (%)	94 (34)	25 (26)	8 (35)	4 (100)	0 (0)	0.019
RF titer, mean (SD)	94 (165)	151 (216)	184 (328)	120 (130)	288 (425)	0.012
ACPA titer, mean (SD)	132 (189)	181 (306)	132 (161)	92 (41)	677 (1018)	<0.001
MTX, n (%)	201 (72)	64 (67)	13 (57)	3 (75)	1 (20)	0.065
PSL, n (%)	45 (16)	32 (33)	8 (35)	1 (25)	4 (80)	<0.001
bDMARDs, n (%)	136 (49)	45 (47)	9 (39)	2 (50)	5 (100)	0.183

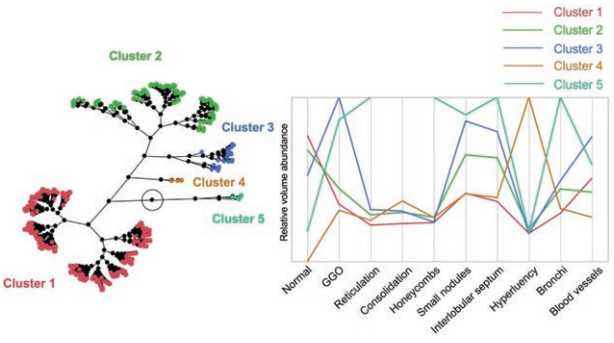


Figure 1. Clustering constellation tree diagram for ten lung parenchymal HRCT image patterns of rheumatoid arthritis.

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Disclosure of Interests: Yoichi Nakayama: None declared, Ran Nakashima: None declared, Tomohiro Handa: None declared, Kiminobu Tanizawa: None declared, Hideo Onizawa: None declared, Takayuki Fujii: None declared, Koichi Murata Speakers bureau: AbbVie GK, Eisai Co., Ltd., Pfizer Inc., Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Corporation, Pfizer Inc., Bristol-Myers Squibb, Daiichi Sankyo Co. Ltd., and Asahi Kasei Pharma Corp., Grant/research support from: Daiichi Sankyo Co. Ltd, Kosaku Murakami: None declared, Akira Onishi: None declared, Masao Tanaka: None declared, Mirei Shirakashi: None declared, Ryosuke Hiwa: None declared, Hideaki Tsuji: None declared, Koji Kitagori: None declared, Syuji Akizuki: None declared, Hajime Yoshifuji: None declared, Akio Morinobu: None declared.

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POS1052

RHEUMATOID ARTHRITIS ASSOCIATED INTERSTITIAL LUNG DISEASE ACROSS CONTINENTS

Keywords: Rheumatoid arthritis, Lungs, Comorbidities

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Background: Interstitial lung disease (ILD) is a spectrum of inflammatory and fibrotic lung diseases, and can be associated with RA (RA-ILD). The reported prevalence ranges from 1.8 to 58 percent, depending on the definition and diagnostics.

Objectives: To investigate the incidence and prevalence of RA-ILD in different countries worldwide.

Methods: Patients of 5 countries from 2 observational databases were studied. Patients from India, Mexico, South Africa (two clinics) and Colombia with a physician-based RA diagnosis were selected from the observational METEOR database. From the Leiden EAC in the Netherlands, patients with early RA (1987 ACR/ 2010 ACR/EULAR criteria) were included. A clinical diagnosis of RA-ILD was based on chest X-ray or CT. X-ray was performed at the first visit in India, South Africa and the Netherlands and on clinical indication in all countries. Prevalence of RA-ILD at the end of follow-up was calculated for each country. Incidence rates (IR) were calculated in patients with newly diagnosed RA and an available baseline visit. Patient characteristics were described, comparing patients with and without RA-ILD using appropriate statistical tests.

Results: Within the five countries 16,667 patients with RA, both newly diagnosed and with longer RA disease duration, were evaluated. Prevalence and incidence of RA-ILD differed per country. The prevalence of RA-ILD at the end of follow-up was 0.7% (84/11,733) in India (mean follow-up 12±20 months), 2.1% (9/427) in Mexico (mean follow-up 17±27 months), 2.0% (21/1,077) in the Netherlands (mean follow-up 83±71 months), 3.0% (19/629) in South Africa (mean follow-up 20±21 months) and 0.7% (18/2,747) in Colombia (mean follow-up 14±12 months). The IR of RA-ILD in newly diagnosed RA patients in India was 1.6 (95% CI 1.0-2.5) per 1000 person years. In the Netherlands the IR was 3.8 (95% CI 1.6-9.1) per 1000 person years. In South Africa the IR was 6.6 (95% CI 2.5-17.5) per 1000 person years. For Mexico and Colombia, no IR could be calculated. Patient characteristics are described in Table 1. In India and Mexico, patients with RA-ILD were older. In 4 of 5 countries RA-ILD patients were more often male. Higher inflammatory markers and more RF positivity were seen in RA-ILD patients in India and the Netherlands. In South Africa, patients with RA-ILD more often had a history of smoking. ACPA positivity was more frequent in RA-ILD patients from India, but less frequent in RA-ILD patients from South Africa.

Conclusion: Prevalence and incidence of RA-ILD varied between the four countries with the highest prevalence and incidence in South Africa. These differences might be partially explained by differences in diagnostic approaches, and potentially in patient populations, used therapies and comorbidity.

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Table 1. Patient characteristics at the first available visit

	India		Mexico		South Africa		Netherlands		Colombia	
	RA-ILD (n=84)	no RA-ILD (n=11,703)	RA-ILD (n=9)	no RA-ILD (n=418)	RA-ILD (n=19)	no RA-ILD (n=610)	RA-ILD (n=21)	no RA-ILD (n=1,077)	RA-ILD (n=18)	no RA-ILD (n=2,729)
Age (years)	**57.9±10.6**	**46.6±15.3**	**62.1±13.3**	**52.7±12.6**	52.8±10.2	50.5±12.8	57.4±9.2	55.8±14.5	61.2 (15.9)	59.1 (13.6)
p	**<0.001**		**0.027**		0.42		0.60		0.50	
Symptom duration (months)	47.9	59.9	108.4	68.2	25.0	45.3	4.0	4.0	89.1	111.2
	(18.0-95.9)	(23.9-143.9)	(49.3-206.8)	(46.7-159.6)	(8.3-58.4)	(13.1-92.5)	(1.9-7.8)	(1.6-8.0)	(37.9-180.9)	(67.6-140.6)
p value	**0.029**		0.32		0.18		0.98		0.38	
Sex (female)	**77%**	**85%**	**67%**	**90%**	84%	82%	48%	68%	78%	89%
p	**0.043**		**0.027**		0.84		0.055		0.12	
Ever smoker	3%	1%	11%	13%	**93%**	**28%**	65%	62%	*	
p	0.27		0.89		**<0.001**		0.81			
DAS28	6.3±1.3	6.0±1.4	4.5±1.7	4.6±1.4	4.9±0.9	5.2±1.4	5.2±0.7	5.1±1.3	*	
p	0.11		0.84		0.54		0.80			
ESR (mm/h)	**91.5±29.9**	**76.7±32.8**	30.7±16.6	9.0±13.3	45.0±22.8	37.1±28.8	**44.3±23.5**	**32.0±25.3**	*	
p	**<0.001**		0.77		0.26		**0.027**			
Patient global assessment	51.2±21.0	53.8±18.3	27.8±31.1	44.6±27.8	**42.6±12.0**	**60.1±24.9**	31.5±26.4	41.1±25.3	22.2±19.3	31.0±21.5
p	0.26		0.075		**0.004**		0.11		0.084	
ACPA positive	**94%**	**81%**	*		**83%**	**96%**	62%	54%	*	
p value	**0.011**		**0.008**	0.45						
RF positive	**95%**	**83%**	*		94%	98%	**86%**	**57%**	*	
p	**0.003**				0.31		**0.009**			

Data are presented as mean±SD, median (IQR), %.*Insufficient data available

POS1053

PREVALENCE OF FIBROSING PROGRESSIVE INTERSTITIAL LUNG DISEASE IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Lungs, Rheumatoid arthritis

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Background: Interstitial lung disease (ILD) related to rheumatoid arthritis (RA) significantly impacts on quality of life and survival of the patients. Data about prevalence and natural history of RA-ILD are only partially known and mainly based on retrospective studies. The recent introduction of antifibrotic drugs have allowed for the first time the opportunity to treat ILD in RA patients; in fact, INBUILD study demonstrated the efficacy of nintedanib in the treatment of progressive fibrosing ILD different than idiopathic pulmonary fibrosis (IPF), including RA-ILD, but the prevalence of RA-ILD patients that may potentially benefit from nintedanib therapy remain unknown.

Objectives: Aim of the present multicenter Italian study was to investigate the prevalence of fibrosing progressive patterns in a cross-sectional cohort of non-selected RA-ILD patients.

Methods: We enrolled in the study all RA patients according to 2010 EULAR/ACR classification criteria, with an ILD confirmed at high resolution computed tomography (HRCT) and with a follow-up of at least 24 months. According to the current indication of nintedanib, patients were defined as having a progressive fibrosing ILD in case of a relative decline in forced vital capacity (FVC) ≥10% predicted and/or an increased extent of fibrotic changes on chest imaging in a 24 month-period. Respiratory symptoms were excluded to reduce possible bias due to the retrospective interpretation of cough and dyspnoea.

Results: One hundred and thirty-four RA-ILD patients were enrolled in the study (males/females 54/80, mean age 72±9.5 years, mean RA and ILD duration 13.1±9.5 and 4.6±4.1 years, respectively. Anticitrullinated peptides antibodies (ACPA) and rheumatoid factor (RF) were recorded in 76.2% and 87.6% of cases, respectively. According to radiologic features, ILD was classified as probable or definite usual interstitial pneumonia (UIP) in 50.7% of patients, NSIP in 19.4% and other patterns in 29.8%. A fibrosing pattern was reported in 73.9% of cases (all patients with UIP pattern, 57.7% of patients with NSIP and 40% with other pattern). A relative decline of 6.8% of forced vital capacity (FVC) was recorded during the follow-up, without significant difference between fibrosing and non-fibrosing ILD (6.3%±13.8 vs 5.9%±21.3, respectively). A relative FVC decline ≥ 10% and/or a progression of radiologic fibrotic involvement was observed in 38.8% of patients. As expected, a significant difference in relative decline of FVC was recorded between progressive and non-progressive ILD (15.7%±16.4 vs -1.3%±8.3, respectively). Globally, a fibrosing progressive pattern was recorded in 35.8% of patients (48/134, 48.5% of patients with fibrosing pattern). Of interest, also 11.4% of patients with a non-fibrosing pattern showed a progressive behavior of disease (see Figure 1).

Conclusion: The recent introduction of nintedanib for the treatment of fibrosing progressive ILD different by IPF has potentially changed the paradigm for the treatment of RA-ILD. In fact, for the first time, rheumatologist has a therapy available with efficacy on RA related lung involvement. This study shows some limitations. The retrospective design and the need of serial HRCT and FVC could induce an overestimation of progressive disease (pulmonary function could not have been properly evaluated in asymptomatic patients). On the other hand, the exclusion of symptoms, such as a worsening of dyspnea and cough, might underestimate the prevalence of progressive lung disease. Finally, some patients were already treated with antifibrotic drugs, possibly influencing the evolution of lung disease in the last 2 years. In conclusion, about a third of RA-ILD patients shows a fibrosing progressive pattern of ILD and might benefit of antifibrotic treatment, alone or in combination with anti-rheumatic drugs. For RA patients with progressive non-fibrosing ILD, we need more studies to establish the best therapeutic approach.

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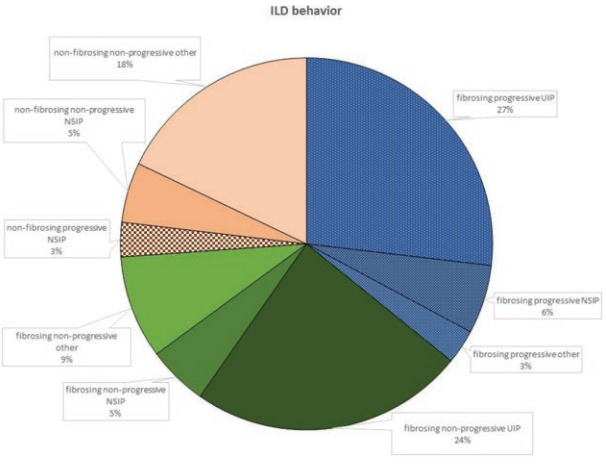


Figure 1.

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POS1054

FREQUENCY AND MODALITIES OF SCREENING FOR ILD: A SURVEY OF 1132 PATIENTS WITH RA

Keywords: Lungs, Rheumatoid arthritis, Patient-led research

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Background: Interstitial lung disease (ILD) can have a significant impact on the long-term outcome in patients with rheumatoid arthritis (RA) but international screening guidelines for early diagnosis of RA-ILD are lacking. It is unknown to date how RA patients are screened for ILD in clinical practice. An analysis of patients' experiences and perspectives will help identify current practice and guide future directions to optimize screening, management and patients care.

Objectives: To identify patients' experiences and unmet clinical needs regarding screening for RA-ILD.

Methods: An international multidisciplinary panel of 18 ILD experts developed and distributed an online-based survey in 12 languages for RA patients with and without ILD from August to December 2022 to receive self-reported data. User representatives of relevant patient associations and RA patients with and without ILD refined and piloted the survey questions. The survey covered management strategies, including information and awareness of ILD, screening for ILD and patient' perspectives on future directions. The study was approved by the Ethics committee of the University Clinic Heidelberg, Germany, and patients consented before starting the online survey.

Results: In total, 1132 RA patients from 11 countries answered the survey. Mean age was 57 (SD13.6) years, 129 (12%) were males, 690 (75%) had seropositive RA with a disease duration of 9.9 (SD7.9) years (Table 1). Of all, 434 (39%) were informed about the possibility of ILD development and 387 (35%) were screened for ILD, of which 75% by x-ray, 49% by high-resolution computed tomography (HRCT), 49% with pulmonary function test (PFT), 23% with respiratory symptoms, 40% with auscultation and 194/387 (59%) were screened with several modalities. Older age, male sex, presence of other lung comorbidities and treatment with Rituximab or Abatacept were associated with screening assessed by multivariable logistic regression (Figure 1). Of all RA patients, 138 (12.4%) were diagnosed with ILD. Screening was significantly associated with an ILD diagnosis (OR 8.87, 95%CI 5.61-14.03, p<0.001) driven by screening for symptoms (OR 1.77 (95% CI 1.06-2.94, p=0.028), PFT (OR 3.42, 95%CI 2.11-5.36, p<0.001) and HRCT (OR 7.17, 95%CI 4.16-12.34, p<0.001). Screening by auscultation or x-ray was not associated with a diagnosis of ILD. Of all RA patients, 89% sought more information about the risk of lung involvement in RA, 95% asked for better information about respiratory symptoms, 71% would prefer that increased attention be paid to potential lung involvement by their treating physician and 98% wanted more research in RA-ILD.

Conclusion: Based on this self-reported patient survey, information about ILD provided to RA patients is frequently limited. Only one third are screened for ILD. The majority of patients stated a clear need for more information on RA-ILD, increasing awareness of lung involvement in RA should be a priority in clinical practice and research.

Table 1. Disease characteristics of all RA patients, and patients screened and not screened for ILD

	All RA (N=1132)	Screened for ILD (n=387)	Not screened (n=611)
Male, n (%)	129 (12)	72 (19)	41 (7)
Age, years (SD)	57 (13.6)	59 (13.2)	55 (13.8)
Disease duration, years (SD)	9.9 (7.9)	10 (7.7)	9.7 (7.7)
Seropos RA, n (%)	690 (75)	260 (77)	347 (70)
RA activity, mean (SD)	4.4 (2.4)	4.4 (2.4)	4.5 (2.5)
Smoker, n (%)	499 (47)	182 (49)	261 (45)
Any comorbidity, n (%)	630 (58)	252 (66)	322 (54)
MTX, n (%)	693 (61)	244 (63)	380 (62)
bDMARD, n (%)	586 (52)	226 (58)	298 (49)

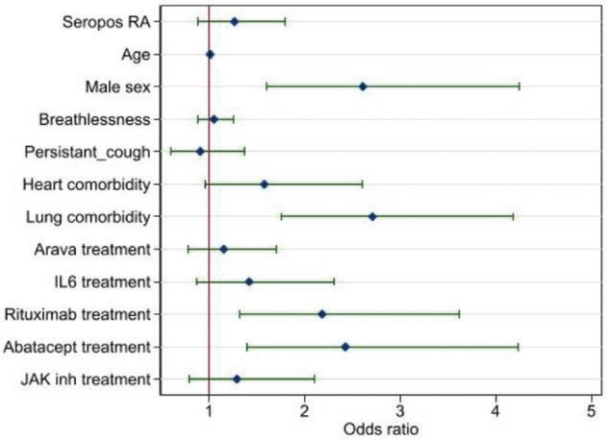


Figure 1.

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POS1055

ASSOCIATIONS AND MORTALITY IMPACT OF MACHINE LEARNING-DERIVED QUANTITATIVE PARENCHYMAL LUNG COMPUTED TOMOGRAPHY FEATURES IN RHEUMATOID ARTHRITIS AND NON-RA COMPARATORS IN A MULTICENTER PROSPECTIVE COHORT OF SMOKERS

Keywords: Rheumatoid arthritis, Lungs, Imaging

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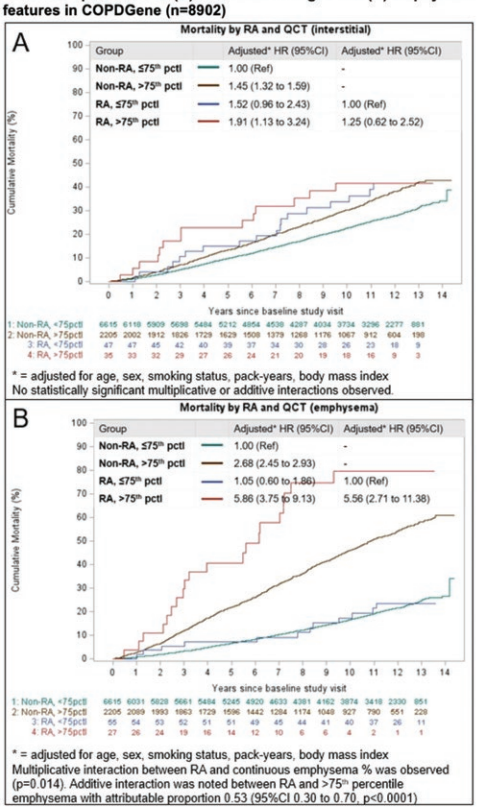
Background: Quantitative computed tomography (QCT) methods have been developed to automatically quantify parenchymal lung features on chest CT imaging. There have been limited investigations of QCT in RA participants and non-RA comparators or studies of the mortality impact of QCT features in RA.
Objectives: Determine the association and mortality impact of QCT features in RA and non-RA participants.
Methods: We analyzed associations between RA and QCT features in COPDGene, a multicenter cohort study of current or former smokers that excluded participants with known interstitial lung disease or bronchiectasis. We identified participants with and without RA using RA self-report and DMARD use. We assessed the lung parenchyma in each scan by categorizing regions of interest into normal lung, interstitial changes, or emphysema using the local tissue density and distance from the pleural surface. Interstitial changes were subclassified into reticular, subpleural line, linear scar, honeycombing, centrilobular nodule, nodular, and ground glass. Each feature was summed and standardized to total lung volume. We examined associations between QCT features and RA using multivariable linear regression. We dichotomized participants using the 75th percentile for each QCT feature among non-RA participants and investigated mortality associations by RA status and QCT features using Cox regression. We examined multiplicative interactions between RA and continuous interstitial and emphysema percentages and additive interactions between RA status and >75th percentile of QCT features using multiplicative interaction terms and attributable proportion.
Results: We identified 82 RA cases and 8820 non-RA comparators. RA was associated with a lower percentage of normal lung (85.8% vs. 91.0% p=0.0001), increased interstitial changes (7.0% vs. 4.8%, p<0.0001), and no statistical difference in emphysema (2.6% vs. 1.9%, p=0.09) compared to non-RA comparators. In linear regression analyses adjusted for age, sex, smoking status, pack-years, and body mass index, RA was associated with increased interstitial changes (β=1.7±0.5, p=0.0008) but not emphysema (β=1.3±1.7, p=0.44). The combination of RA and >75th percentile of emphysema had significantly higher mortality compared to both non-RA participants (HR 5.86, 95%CI 3.75-9.13) and RA participants (HR 5.56, 95%CI 2.71-11.38) with <75th percentile of emphysema. There were statistically significant interactions between RA and emphysema for mortality (multiplicative: p=0.014; additive: attributable proportion 0.53, 95%CI 0.30-0.70, p<0.0001).
Conclusion: Using machine learning-derived QCT data in a cohort of smokers, we found that RA was associated with increased interstitial changes, even after adjustment for smoking and other lifestyle factors. The combination of RA and emphysema conferred greater than 5-fold increased mortality.

Table 1. Quantitative CT features and multivariable linear regression by RA status in COPDGene (n=8902)

Feature (% of lung volume, median, IQR)	RA cases (n=82)	Non-RA comparators (n=8820)	Unadjusted p-value	Adjusted* β±SE (RA vs. non-RA)	Adjusted p-value
Normal lung	85.8 (77.3-92.4)	91.0 (82.7-94.7)	0.0001	-3.0±1.7	0.08
Interstitial	7.0 (4.0-9.7)	4.8 (3.0-7.8)	<0.0001	1.72±0.51	0.0008
Reticular	6.0 (3.6-8.8)	4.1 (2.6-6.8)	<0.0001	1.55±0.46	0.0008
Subpleural line	0.40 (0.22-0.64)	0.31 (0.18-0.51)	0.02	0.084±0.03	0.009
Linear scar	0.17 (0.09-0.30)	0.13 (0.06-0.24)	0.006	0.029±0.02	0.08
Honeycombing	0.05 (0.02-0.11)	0.03 (0.009-0.07)	<0.0001	0.058±0.02	0.003
Centrilobular nodule	0.005 (0.00-0.03)	0.008 (0.00-0.05)	0.47	-0.006±0.01	0.69
Nodular	0.008 (0.002-0.03)	0.004 (0.001-0.02)	0.007	-0.005±0.03	0.88
Ground glass	0.005 (0.001-0.01)	0.003 (0.00-0.007)	0.01	0.0016±0.02	0.93
Emphysema	2.6 (0.8-12.8)	1.9 (0.5-8.8)	0.09	1.3±1.7	0.43

* linear regression adjusted for age, sex, smoking status (current/former), pack-years, BMI

Figure: Cumulative mortality and hazard ratios stratified by RA/comparator status and < or >=75th percentile of (A) interstitial changes and (B) emphysema quantitative CT features in COPDGene (n=8902)



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POS1056 CYTOKINE ANALYSIS IN PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH RHEUMATOID ARTHRITIS

Keywords: Comorbidities, Cytokines and chemokines, Biomarkers

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Background: Interstitial lung disease (ILD) is the most frequent non-pleural pulmonary manifestation in rheumatoid arthritis (RA) and causes high morbidity and mortality [1-3]. Currently, there are no clinically useful serum markers for the diagnosis and prognosis of RA associated ILD (RA-ILD) [4].

Objectives: To identify soluble cytokines that work as biomarkers for diagnosis and prognosis in RA-ILD and explore whether there is an association between those and pulmonary progression.

Methods: Observational case-control study nested in a prospective cohort of cases of patients with RA (ACR/EULAR 2010) [5] with and without ILD, paired by sex, age, and time of RA evolution. All subjects underwent pulmonary function tests (PFTs) and high-resolution computed tomography (HRCT) on the inclusion date (protocol date) and, in cases of RA-ILD, also on diagnosis of ILD. The primary variable ILD was defined according to lung biopsy or HRCT according to the American Thoracic Society/European Respiratory Criteria [6], and pulmonary progression was defined as worsening FVC >10% or DLCO >15% [4]. Inflammation variables included inflammatory activity data measured by DAS28-ESR and a cytokine multiplex including Th1/Th2 function, inflammatory cytokines, and chemokines. Other clinical, RA severity and therapeutic variables were also studied: rheumatoid factors (RF), anti-cyclic citrullinated peptide antibodies (ACPA), radiological erosions, and Health Assessment Questionnaire (HAQ) values. A descriptive analysis and two Cox regression models were performed to identify factors associated with ILD and ILD progression in RA, adjusting for time to development of ILD-RA and to ILD progression, respectively.

Results: A total of 70 subjects were included, 35 RA-ILD cases and 35 RA controls without ILD (Table 1). A higher percentage of patients with RA-ILD, compared to the rest, presented elevated RF (p=0.089) and ACPA levels (p=0.031), higher DAS28-ESR values (p=0.032), number of swollen joints (p=0.040) and worse quality of life measured by HAQ (p=0.003). The variables that were independently associated with RA-ILD in the Cox regression adjusted for time of evolution of RA (Figure 1) were DAS28-ESR of moderate-high activity (OR [95% CI], 2,474 [1,173-5,220]; p= 0.017), elevated ACPA levels (OR [95% CI], 2.905 [1.244-6.786]; p=0.014), IL-18 (OR [95% CI], 1.063 [1.002-1.127]; p=0.044), MCP1CCL2 (OR [95% CI], 1.031 [1.001-1.064]; p=0.049) and SDF1 (OR [95% CI], 1.001 [1.001-1.002]; p=0.010). In the other COX regression model adjusted for time to ILD progression, the only variable associated with progression was IL18 (OR [95% CI], 1.254 [1.074-1.465]; p=0.004).

Table 1. Baseline characteristics of the study population

VARIABLE	RA-ILD n=35	RA without ILD n=35	*P*-value
RF+ (>10), n (%)	33 (94.3)	31 (88.6)	0.393
High RF (>60)	24 (68.6)	17 (48.6)	**0.089**
ACPA+ (>20), n (%)	32 (91.4)	31 (88.6)	0.690
High ACPA (>340), n (%)	22 (63.0)	14 (40.0)	**0.039**
Erosions, n (%)	21 (60.0)	19 (55.6)	0.705
DAS28-ESR, mean (SD)	3.1 (0.9)	2.6 (0.9)	**0.032**
Remission/low activity, n (%)	19 (54.3)	27 (77.1)	**0.044**
Moderate/high activity, n (%)	16 (45.7)	8 (22.9)	**0.044**
Number of swollen joints, median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	**0.040**
HAQ, mean (SD)	1.2 (0.6)	0.8 (0.6)	**0.003**

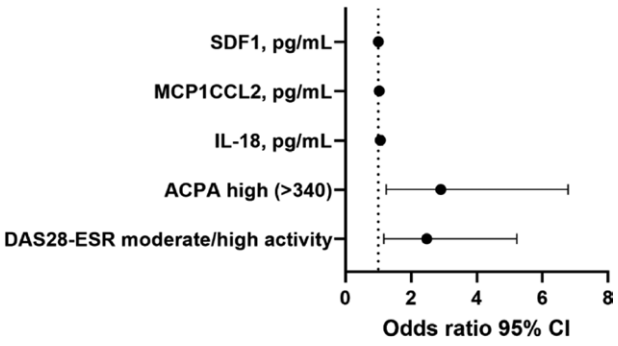


Figure 1. Cox regression analysis adjusted for time of evolution of RA

Conclusion: Patients with RA-ILD show higher inflammatory activity than RA patients without ILD. Some cytokines are associated both with diagnosis and with a worse prognosis in patients with RA-ILD, so they could be potential biomarkers for this entity. Future studies are needed to validate these data and confirm the findings.

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POS1057 LUNG ULTRASONOGRAPHY AS A SCREENING TOOL FOR INTERSTITIAL LUNG DISEASE IN RHEUMATOID ARTHRITIS: RESULTS FROM A SYSTEMATIC LITERATURE REVIEW

Keywords: Ultrasound, Rheumatoid arthritis, Systematic review

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Background: In rheumatoid arthritis (RA), interstitial lung disease (ILD) is a frequent pulmonary manifestation which is responsible for a high morbidity and mortality. Chest high resolution computed tomography (HRCT) is the imaging gold standard for the diagnosis and characterisation of ILD. Recently, the use of lung ultrasonography (US) has been suggested as a valid, less invasive and radiation-free tool in the pulmonary screening process.

Objectives: To review the reliability of lung US as a screening tool for the diagnosis of ILD in RA patients.

Methods: A systematic literature search in several databases was conducted following the PICO framework on July 2022. Two researchers independently screened abstracts and titles, and full texts were subsequently reviewed to determine eligibility (original research articles enrolling adult RA patients undergoing lung US and HRCT). Data from eligible articles were extracted and risk of bias (RoB) was assessed with validated tools. Owing to extensive interstudy heterogeneity, narrative summaries had to be used to present the data.

Results: Out of 690 retrieved papers, only 7 were eligible and only 5 of them enrolled a control group (Table 1). All studies had a cross-sectional design and no follow-up data were available. Although all studies relied on the US identification of B-lines, the number of intercostal spaces assessed as well as the threshold/score to classify the findings as ILD or no-ILD varied across studies. Furthermore, some studies also focused on the irregularities of the pleural line. The sensitivity of lung US ranged between 62.2 and 97.1% while specificity ranged between 89 and 100%. However, the studies' heterogeneity did not allow any comparison. In RA patients with neither respiratory symptoms nor previous ILD diagnosis, the concordance in identifying pathological findings between US and HRCT ranged between 90 and 100%.

Conclusion: Our Systematic Literature Review shows that lung US may have a role as screening tool for ILD in RA and also in asymptomatic patients. The implementation of the routine use of lung US in RA might allow an early identification and a prompt treatment of RA-ILD patients as well. However, the harmonization of US findings is required to allow either for the comparison of research studies and for a broad implementation of lung US in clinical practice.

Table 1. Characteristics and main findings of studies with a control group

	Patients N, type	Controls N, type	Comparator	US Se%	US Sp%	Thresholds for Se and Sp calculation
Gutierrez 2022	74 RA w/o ILD	74 NS	HRCT	92	89	≥ 6 B-lines in 14 ICS*
Fotoh 2021	75 RA-ILD	75 RA w/o ILD	HRCT	88	100	LUS score ≥ 5.5 in 14 ICS °
Mena-Vazquez 2020	35 RA-ILD	36 RA w/o ILD	HRCT, PFT	62.2	91.3	5.5 B-lines in 8 ICS
Moazedi-Furst 2015	25 RA w/o ILD	40 NS	HRCT	NR	NR	NA
Moazedi-Furst 2014	64 RA w/o ILD	40 NS	HRCT	97.1	97.3	Multiple B lines, irregularities of the pleural line > 2.8 mm

**Semi-quantitative scale of B-line number: 0 = normal (≤ 5 B-lines); 1 = slight (≥ 6 and ≤ 15); 2 = moderate, (≤ 16 and ≥ 30); 3 = severe (≥ 30).°LUS score= number of B lines contained in each ICSRA, rheumatoid arthritis; ILD, interstitial lung disease; NS, normal subjects; ICS, intercostal space; Se, sensitivity; Sp, specificity; US, ultrasonography, HRCT, high resoluation computed tomography; PFT, pulmonary function test; w/o, without; NR, not reported*

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1058

CORRELATION BETWEEN SERUM KL-6 AND ANTI-MODIFIED PROTEIN ANTIBODIES (AMPAS) IN RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

Keywords: Biomarkers, Lungs, Rheumatoid arthritis

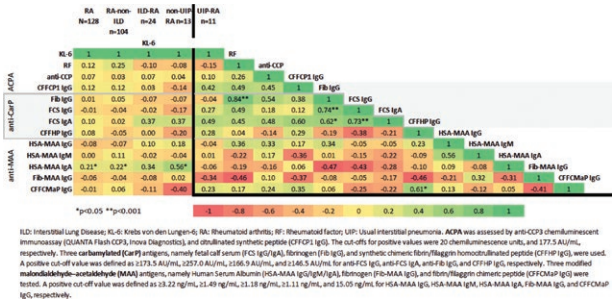
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Background: Some studies have shown that Krebs von den Lungen-6 (KL-6) may be a valuable biomarker for diagnosis and stratifying prognosis in Rheumatoid Arthritis-Associated Interstitial Lung Disease (RA-ILD). Citrullination and carbamylation are responsible for generating Anti-Modified Protein/Peptide Antibodies (AMPAs) and are associated with RA-ILD.
Objectives: To evaluate the correlation between serum KL-6 and AMPAs in patients with RA.
Methods: We conducted a cross-sectional study that included patients with RA (ACR/EULAR 2010 criteria) with available KL-6 and AMPAs data measured in blood serum at study enrolment. ILD was diagnosed by high-resolution computed tomography and confirmed by a multidisciplinary committee. Serum KL-6 levels were measured by Lumipulse G KL-6 Kit (Fujirebio, Japan), using Chemiluminescent enzyme immunoassay (CLEIA). The reference value for KL-6 in healthy subjects was 118-627 U/mL. The inter-assay variation coefficient of the reagent was ≤ 4.4%. AMPAs repertoire tested included ACPA, anti-carbamylated protein antibodies (anti-CarP), and autoantibodies to malondialdehyde–acetaldehyde (anti-MAA). ACPA, anti-CarP, and anti-MAA were determined by homemade ELISA tests. Antigens, cut-off values, and isotypes tested are depicted in Figure 1. Spearman's rank correlation coefficient was used to analyze the correlation between serological markers.
Results: A total of 128 patients were included (24 RA-ILD and 104 RA-non-ILD). Patient characteristics were as follows: female 73%, mean age 60.3 ± 12.4 years, mean disease duration 6.5 ± 4.7 years, RF positive 68%, anti-CCP positive 83.6%, erosive disease 54.7%, and mean DAS28 2.94. Most patients received treatment with methotrexate 84 (65.6%), glucocorticoids 72 (56.3%), and biological DMARDs 23 (18.0%). Among RA-ILD patients, the median FVC and DLco (% predicted value) were 79 (IQR 74.7–88.7) and 62.9 (IQR 53.1–70.6), respectively. Usual interstitial pneumonia (UIP) was found in 11/24 (45.8%) patients. The mean KL-6 level was 476.4 ± 400.9 U/mL. KL-6 levels were elevated in 22 patients (17.2%). Serum levels of KL-6 in the RA-ILD group were significantly higher than those in the RA-non-ILD group (756.0 ± 673.4 U/mL vs. 411.9 ± 273.0 U/mL; p<0.001). Serum KL-6 had a moderate positive correlation with HSA-MAA IgA (*r*=0.56; p=0.048) in patients with non-UIP pattern (**Figure 1**). Anti-CarP (Fib IgG: 81.8% vs. 54.7; p=0.019) and anti-MAA antibodies (HSA-MAA IgA: 36.4% vs. 10.4; p=0.018) were significantly associated with elevated KL-6 values (**Table 1**).
Conclusion: Serum KL-6 is a surrogate biomarker of ILD, elevated in a subgroup of patients with RA-ILD. KL-6 elevation correlated with some AMPAs, such as anti-CarP and anti-MAA. Whether AMPAs are potential biomarkers for RA-ILD requires further analysis.
Funding: Hospital Clinic of Barcelona (Grant # 37 933) and the Spanish Ministry of Economy and Competitiveness (Grant # RTI2018-094120-B-I00).
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Table 1. Anti-Modified Protein/Peptide Antibodies (AMPAs) distribution according to serum KL-6 status in RA patients.

Biomarker	All population N=128	High KL-6 n=22	Normal KL-6 n=106	*P*
Anti-Citrullinated Protein Antibodies (ACPA)				
anti-CCP3	107 (83.6)	16 (72.7)	91 (85.8)	0.130
CFFCP1 IgG	89 (69.5)	15 (68.2)	74 (69.8)	0.880
Anti-Carbamylated Protein Antibodies (anti-CarP)				
Fib IgG	76 (59.4)	**18 (81.8)**	58 (54.7)	**0.019**
FCS IgG	69 (53.9)	12 (54.5)	57 (53.8)	0.947
FCS IgA	39 (30.5)	10 (45.5)	29 (27.4)	0.093
CFFHP	33 (25.8)	6 (27.3)	27 (25.5)	0.860
Autoantibodies to Malondialdehyde–Acetaldehyde (anti-MAA)				
HSA-MAA IgG	9 (7.0)	2 (9.1)	7 (6.6)	0.830
HSA-MAA IgM	1 (0.8)	0	1 (0.9)	0.810
HSA-MAA IgA	19 (14.8)	**8 (36.4)**	11 (10.4)	**0.018**
HSA-MAA IgA, ng/mL	0.5 ± 0.7	**0.9 ± 0.2**	0.7 ± 0.07	**0.004**
Fib-MAA IgG	25 (19.5)	3 (13.6)	22 (20.8)	0.661
CFFCMaP IgG	26 (20.3)	5 (22.7)	21 (19.8)	0.864

Antigens and cut-off values are specified in Figure



ILD: Interstitial Lung Disease; KL-6: Krebs von den Lungen-6; RA: Rheumatoid arthritis; RF: Rheumatoid factor; UIP: Usual interstitial pneumonia. **ACPA** was assessed by anti-CCP3 chemiluminescent immunoassay (QUANTA Flash CCP3, Inova Diagnostics), and citrullinated synthetic peptide (CFFCP1 IgG). The cut-offs for positive values were 20 chemiluminescence units, and 177.5 AU/mL, respectively. Three **carbamylated (CarP)** antigens, namely fetal calf serum (FCS IgG/IgA), fibrinogen (Fib IgG), and synthetic chimeric fibrin/filaggrin homocitrullinated peptide (CFFHP IgG), were used. A positive cut-off value was defined as ≥173.5 AU/mL, ≥257.0 AU/mL, ≥166.9 AU/mL, and ≥146.5 AU/mL for anti-FCS IgG, anti-FCS IgA, anti-Fib IgG, and CFFHP IgG, respectively. Three modified **malondialdehyde–acetaldehyde (MAA)** antigens, namely Human Serum Albumin (HSA-MAA IgG/IgM/IgA), fibrinogen (Fib-MAA IgG), and fibrin/filaggrin chimeric peptide (CFFCMaP IgG) were tested. A positive cut-off value was defined as ≥3.22 ng/mL, ≥1.49 ng/mL, ≥1.18 ng/mL, ≥1.11 ng/mL, and 15.05 ng/mL for HSA-MAA IgG, HSA-MAA IgM, HSA-MAA IgA, Fib-MAA IgG, and CFFCMaP IgG, respectively.

Figure 1. Heatmap of correlation between serum KL-6 and AMPAs in patients with RA.

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POS1059

ASSOCIATION OF THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE WITH ARTERIAL INFLAMMATION, ASSESSED WITH ^{18}F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY, IN RHEUMATOID ARTHRITIS

Keywords: Cardiovascular disease, Biomarkers

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Background: Rheumatoid arthritis (RA) and atherosclerosis share many common inflammatory pathways. Reducing the activity of inflammatory pathways with immunomodulators may lessen the risk of cardiovascular disease in RA. As such, a multi-biomarker of RA disease activity (MBDA; AKA the Vectra Score) could serve as an indicator of treatment-associated improvements in atherosclerotic plaque inflammation.
Objectives: To prospectively evaluate the association of an MBDA score and its components with the change in arterial inflammation in RA patients enrolled in a clinical trial of two different RA treatment strategies.
Methods: In the TARGET Trial, patients with active RA despite methotrexate were randomly assigned to the addition of either a TNF inhibitor (TNFi) or sulfasalazine+hydroxychloroquine (triple therapy). Baseline and 24-week follow-up 18F-flourodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) scans were assessed for change in arterial inflammation measured as the maximal arterial target-to-blood background ratio (TBR) of FDG uptake in the most diseased segment (MDS) of either the carotid arteries or aorta (TBRmax MDS). The MBDA score, measured at baseline and weeks 6, 18, and 24, was assessed for its association with the change in arterial inflammation. The MBDA score was categorized as low, moderate, and high disease activity (LDA, MDA, and HDA; LDA<30, MDA 30-44, HDA>44 units).
Results: Among the 150 randomized TARGET participants, 112 had an interpretable TBR at baseline and trial conclusion (24 weeks) (mean age=60 years; 71% female; RA duration=1.4 years; baseline DAS28-CRP=4.8). The MBDA score at week 24 was significantly correlated with the change in TBRmax MDS (Spearman's rho=0.239; p=0.011), while the baseline and interim MBDA scores were less strongly and not significantly correlated with the change in TBRmax MDS. The week 24 MBDA score remained significantly associated after adjustment for relevant confounders. Neither the baseline, follow-up, or change in DAS28-CRP nor CRP significantly predicted the change in TBRmax MDS. There was no significant difference in the association of the MBDA score with the change in arterial inflammation between the two randomized treatment groups. Those achieving MBDA LDA at week 24 had a statistically significant adjusted reduction in TBRmax MDS of 0.35 TBR units, while no significant reductions in TBRmax MDS over time were observed in those remaining in MBDA MDA or HDA(Figure 1A). The component of the MBDA score with the strongest association with change in TBRmax MDS was serum amyloid A (SAA) (Figure 1B), with the largest reduction in TBRmax MDS occurring in those in the lowest tertile of SAA week 24 who also achieved DAS28-CRP LDA (-0.450 TBR units) vs. those in the highest tertile of SAA who had also achieved articular LDA (-0.019 TBR units; Figure 1C).
Conclusion: Achieving low disease activity by the MBDA at 24 weeks was associated with a clinically meaningful reduction in arterial inflammation, similar to high-intensity statins, in a way not predicted using other RA disease activity measures, suggesting that treatment-associated improvements in arterial inflammation may be indicated by specific biomarkers that overlap those used to track articular disease activity.

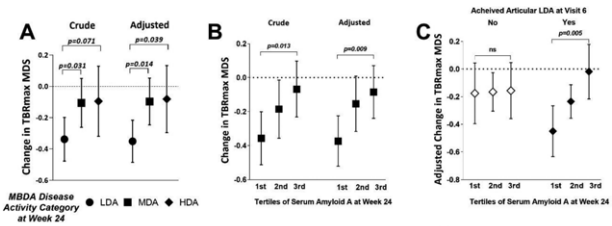


Figure. Associations of the MBDA Score at Week 24 with the Change in ^{18}F-FDG PET Detected Arterial Inflammation (Maximal Target-to-Background Ratio of the Most Diseased Arterial Segment; TBR_{max} MDS). Crude and adjusted means and 95% CIs presented. Adjusted for age, current and former smoking, and methotrexate dose.
MBDA=multi-biomarker disease activity score; FDG=fluorodeoxyglucose; PET=positron emission tomography; LDA=low disease activity; MDA=moderate disease activity; HDA=high disease activity; ns=non-significant

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POS1060

HUMORAL RESPONSES AGAINST HDL ARE LINKED TO LIPOPROTEIN TRAITS, ATHEROSCLEROSIS, INFLAMMATION AND PROTEOMIC PATHOGENIC PATHWAYS DURING EARLY ARTHRITIS STAGES

Keywords: -omics, Cardiovascular disease, Autoantibodies

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Background: cardiovascular (CV) risk excess in rheumatoid arthritis (RA) cannot be solely attributed to traditional CV risk factors. Chronic inflammation and immune dysregulation are crucial mechanisms for atherosclerosis development in RA. Recent evidence suggests a link via humoral responses against high-density lipoproteins (HDL) and its components. However, their exact specificity, clinical relevance and emergence along disease course are unknown, especially during the earliest phases of arthritis.
Objectives: to characterize the specificity and clinical relevance as predictors of anti-HDL responses along during the earliest phases of arthritis.
Methods: IgG and IgM serum levels of antibodies against HDL (anti-HDL) and Apolipoprotein A1 (anti-ApoA1) were measured in 82 early RA patients (EULAR/ACR classification criteria), 14 arthralgia individuals (EULAR definition) and 96 controls. Established RA patients (n=42) were included for validation. Atherosclerosis occurrence and vascular stiffness were measured by Doppler-ultrasound. Lipoprotein content, particle numbers and size were measured by H-NMR. Cytokines were measured by immunoassays. A cardiometabolic-related protein panel was evaluated using high-throughput targeted proteomics.
Results: IgG and IgM anti-HDL and anti-ApoA1 responses were increased in early RA compared to controls (both p<0.001) and were comparable to established disease. Only IgG anti-ApoA1 antibodies were increased in arthralgia compared to controls (p<0.050). IgG anti-HDL and anti-ApoA1 were associated with unfavourable lipoprotein traits (particle content, number and size distribution) in RA and arthralgia, respectively. A similar picture was observed for positive correlations with inflammatory mediators (IFNa, MIP-1a, IL-6, IL-8 and IFNg). No associations with clinical features or traditional risk factors were found. IgG anti-HDL were independently associated with atherosclerosis occurrence (p=0.012) and extension (r=0.274, p=0.016) in early RA. This association remained after adjusting for traditional CV risk factors in multivariate models (OR 1.001 [95% CI: 1.000 – 1.002], p=0.004). The addition to IgG anti-HDL to the mSCORE chart improved patient classification and outperformed patient stratification over mSCORE alone (Table 1). The addition of IgG anti-ApoA1 levels resulted in low-to-milder improvements (Table 1). IgG anti-HDL antibodies correlated with serum proteomic signatures involved in immune activation, remodelling, and lipid metabolism pathways in early RA (Figure 1).

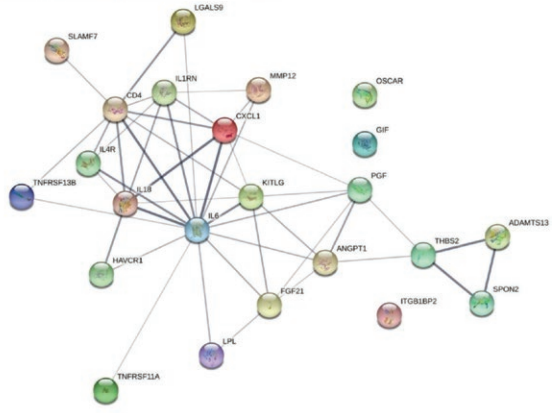
Table 1.

	mSCORE	mSCORE + IgG anti-HDL	mSCORE + IgG anti-ApoA1
AUC ROC (95% CI)	0.636 (0.514 – 0.759)	0.826 (0.731 – 0.922)	0.740 (0.627 – 0.852)
p-value	p=0.044	p<0.0001	p=0.0003
Mathews' Correlation Coefficient	0.319 p=0.003	0.514 p<0.0001	0.431 p<0.001
Hosmer-Lemeshow test	p=0.002	p=0.207	p<0.001
R2	0.173	0.510	0.297
OR (95% CI)	13.12 (1.62 – 106.00)	36.80 (7.67 – 176.93)	10.500 (3.14 – 35.05)
% Patients Correctly Classified	57.14 (45.37 – 68.19)	80.52 (69.60 – 88.34)	71.43 (59.83 – 80.86)
Likelihood Ratio (95% CI)	9.43 (1.31 – 68.13)	11.12 (2.87 – 43.01)	4.72 (1.84 – 12.12)
Sensitivity	30.43 (18.20 – 45.92)	71.74 (56.32 – 83.54)	60.87 (45.39 – 74.54)
Specificity	96.77 (81.49 – 99.83)	93.55 (77.16 – 98.87)	87.10 (69.52 – 95.92)
Positive Predictive Value	93.33 (66.03 – 99.65)	94.29 (79.48 – 99.00)	87.50 (70.07 – 95.92)
Negative Predictive Value	48.39 (35.66 – 61.32)	69.05 (52.76 – 81.69)	60.00 (44.37 – 73.94)
Youden Index (value)	0.632 (2.25)	0.685 (4.75)	0.634 (2.75)
NRI		0.381	0.207

Conclusion: humoral responses against HDL particles are an early event along arthritis course, although quantitative and qualitative differences can be noticed among stages. These differences informed distinct capacities as biomarkers (incremental value) and underlying pathogenic circuits. Anti-HDL but not anti-ApoA1 were robust predictors of lipoprotein features, inflammatory milieu and subclinical CV burden in early RA.

Figure 1

(A) Protein-protein interaction networks



(B) Proteomic pathways associated with IgG anti-HDL

Pathway	Enrichment FDR	Fold enrichment
Cell adhesion	$3.9 \cdot 10^{-7}$	7.9
Biological adhesion	$3.9 \cdot 10^{-7}$	7.8
Positive regulation of multicelular organismal process	$3.9 \cdot 10^{-7}$	8.0
Cytokine-mediated signaling pathway	$4.5 \cdot 10^{-6}$	10.3
Cellular response to cytokine stimulus	$4.5 \cdot 10^{-6}$	8.3
Hemopoiesis	$4.9 \cdot 10^{-6}$	9.6
Psotive regualtion of chemokine production	$4.9 \cdot 10^{-6}$	57
Response to cytokines	$5.3 \cdot 10^{-6}$	7.8
Hematopoietic or lymphoid organ development	$5.3 \cdot 10^{-6}$	9.3
Regulation of cell population proliferation	$5.3 \cdot 10^{-6}$	6.5

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Disclosure of Interests: None Declared.
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POS1061

RISK OF ACUTE MYOCARDIAL INFARCTION AND STROKE ASSOCIATED WITH ANTI-RHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONWIDE POPULATION-BASED STUDY

Keywords: Disease-modifying drug (DMARDs), Cardiovascular disease, Rheumatoid arthritis

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Background: The risk of acute cardiovascular events including acute myocardial infarction (AMI) and ischemic stroke in patients with rheumatoid arthritis (RA) is increased compared with the general population and is the leading cause of death in these patients.
Objectives: The present study aimed to investigate the risk of new-onset AMI/stroke following the initiation of different anti-rheumatic drugs for RA using a nationwide database.
Methods: This nested case–control study with a cohort of 35,133 AMI/stroke-naïve patients with RA was conducted using the Korean Health Insurance Review and Assessment (HIRA) database from 2011 to 2020. Cases with incident AMI/stroke were identified and individually matched to randomly selected controls (1:4). Anti-rheumatic drug use was measured for one year before the index date and stratified by exposure duration. The association of each anti-rheumatic drug with AMI/stroke risk was estimated using conditional logistic regression adjusted for comorbidities and concomitant drug use.
Results: Approximately 5.3% of patients (n=1,870) were newly diagnosed with AMI (n=484) or ischemic stroke (n=1,386). In total, 1,868 (excluding unmatched control [n=2]) AMI/stroke cases and 7,423 controls with newly diagnosed RA were included for analysis. In a multivariable-adjusted analysis, recent use (within three months) of leflunomide (adjusted odds ratio [aOR]=1.21, 95% confidence interval [CI]=1.06–1.37), glucocorticoids (aOR 1.84, 95% CI 1.61-2.11) and tocilizumab (aOR=2.04, 95% CI=1.11–3.75) were associated with increased AMI/stroke risk. The recent use of anti-TNF-alpha agents (aOR=0.72, 95% CI=0.52–0.99), sulfasalazine (aOR=0.79, 95% CI=0.66–0.93), and hydroxychloroquine (aOR=0.83, 95% CI=0.74–0.94) were associated with a significantly decreased AMI/stroke risk.
Conclusion: Anti-TNF-alpha agents, hydroxychloroquine, and sulfasalazine used to treat RA decreased the risk of AMI/stroke, whereas leflunomide, glucocorticoids, and tocilizumab increased this risk.

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Table 1. Risk of incident AMI/stroke according to anti-rheumatic drug use

	Case (n=1,868)	Control (n=7,423)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Hydroxychloroquine	573 (30.7%)	2407 (32.4%)	0.92 (0.82–1.03)	0.83 (0.74–0.94)
Methotrexate	1101 (58.9%)	4147 (55.9%)	1.15 (1.03–1.28)	0.99 (0.88–1.11)
Leflunomide	627 (33.6%)	1807 (24.3%)	1.61 (1.44–1.81)	1.21 (1.06–1.37)
Sulfasalazine	213 (11.4%)	1012 (13.6%)	0.82 (0.69–0.96)	0.79 (0.66–0.93)
Tacrolimus	156 (8.4%)	478 (6.4%)	1.34 (1.10–1.61)	1.17 (0.95–1.43)
Anti-TNF-alpha agents	51 (2.7)	254 (3.4%)	0.79 (0.58–1.07)	0.72 (0.52–0.99)
Abatacept	8 (0.4%)	37 (0.5%)	0.86 (0.40–1.84)	0.85 (0.38–1.90)
Tocilizumab	19 (1.0%)	37 (0.5%)	2.07 (1.18–3.62)	2.04 (1.11–3.75)
Rituximab	1 (0.1%)	8 (0.1%)	0.50 (0.06–4.00)	0.36 (0.04–2.92)
Janus kinase inhibitors	9 (0.5%)	19 (0.3%)	1.90 (0.85–4.25)	1.95 (0.82–4.63)
Glucocorticoid	1453 (77.8%)	4482 (60.4%)	2.37 (2.10–2.68)	1.84 (1.61–2.11)

TNF: Tumor necrosis factor

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1062

THE USE OF EXPANDED RISK SCORE IN RA (ERS-RA) FOR THE DEFINITION OF RISK FOR MAJOR CARDIOVASCULAR EVENTS IN PATIENTS CANDIDATES TO RECEIVE JANUS KINASES INHIBITORS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

Keywords: Cardiovascular disease, Rheumatoid arthritis, Targeted synthetic drugs

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Background: The observation in the ORAL SURVEILLANCE trial[1] of an increased rate of major cardiovascular (CV) events (MACE) in patients with rheumatoid arthritis (RA) treated with Janus kinase inhibitors (JAKis) recently prompted the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) to suggest significant restrictions on the use of this class of drugs in order to minimize CV risk.
Objectives: Assessing the performance of a CV risk chart developed and validated for RA (Expanded Risk Score in RA [ERS-RA[2,3]) in quantifying the risk for MACE in comparison with the PRAC recommendation in a real-life cohort of RA patients treated with JAKis.
Methods: A retrospective analysis on all RA patients treated with a JAKi in a tertiary care academic hospital was conducted. According to PRAC recommendation, the study population was stratified into patients at increased (>65 years old; current or former long-term smokers; patients carrying increased risk of MACE, defined according to ORAL SURVEILLANCE trial[1] inclusion criteria [>50 years old and having at least one CV risk factor]) or not CV risk. The same stratification was also calculated with the ERS-RA[2,3], using a 10% increase in 10-year risk of MACE as a cut-off for the definition of increased CV risk. The incidence of MACE was calculated over a mean follow-up period of 3 years and was correlated with the two different definitions of CV risk considered.
Results: The study population included 194 RA patients exposed to JAKis for a total of 337 patient/years. The baseline characteristics of enrolled population has been fully described in **Table 1**. According to PRAC definition, CV risk was considered increased in 80 (41.2%) patients (n=27 [33.8%] >65 years old; n=25 [31.2%] smokers). Calculated with the ERS-RA, the CV risk was found to be increased in 36 (18.6%) patients. Over the follow-up period, we observed only one MACE (a non-fatal stroke) in a patient who met the definition of increased CV risk according to both criteria. The specificity of ERS-RA score was 0.82 (positive predictive value 0.03), whereas the specificity of PRAC criteria was 0.59 (positive predictive value 0.01).
Conclusion: Our study shows that in a real-life setting the use of a validated score chart as ERS-RA allows CV risk to be calculated more accurately in RA patients undergoing JAKis than the strict application of the PRAC recommendation. Further prospective observational studies on larger populations are advocated to better define CV risk assessment in this scenario.

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Table 1. Baseline population characteristics.

	Study population (N=194)
Age, mean±SD (years)	57.94 ± 0.87
Male sex	N=29 (14.9%)
BMI, median (95% CI)	23.88 (21.36 – 26.59)
Current smokers	N=35 (18.0%)
Disease duration, mean±SD (years)	16.31 ± 0.77
RF and/or ACPA positive	N=121 (62.4%)
HAQ score, median (95% CI)	0.675 (0.125-1.25)
Corticosteroid use	N=79 (40.7%)
Arterial hypertension	N=59 (30.4%)
History of Ischemic heart disease	N=3 (1.6%)
Non-IHD heart disease	N=18 (9.3%)
Heart failure	N=4 (2.1%)
History of stroke	N=2 (1.0%)
History of venous thrombosis (VTE/PE)	N=2 (1%)
Thrombophilia	N=23 (11.9%)
Hyperlipidemia	N=71 (36.6%)
Diabetes	N=10 (5.2%)
History of solid malignancy	N=8 (4.1%)

SD, standard deviation; BMI, body mass index, 95% CI, 95% confidence interval, HAQ, Health Assessment Questionnaire, IHD, Ischemic heart disease

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Disclosure of Interests: Ennio Giulio Favalli Speakers bureau: AbbVie, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Consultant of: AbbVie, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Gilberto Cincinelli: None declared, Francesco Orsini: None declared, Maria Manara Speakers bureau: Novartis, Angelini, Consultant of: Lilly, MSD, Sabino Germinario: None declared, Martina Biggioggero Speakers bureau: Galapagos, Raffaele Di Taranto: None declared, Matteo Ferrito: None declared, Roberto Caporali Speakers bureau: AbbVie, Amgen, BMS, Celltrion, Fresenius, Galapagos, Janssen, Lilly, Novartis, Pfizer, UCB, Consultant of: AbbVie, Fresenius, Galapagos, Lilly, Novartis, Pfizer, UCB.
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POS1063

CARDIOVASCULAR AND THROMBOEMBOLIC EVENTS IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS OVER 3 YEARS BEFORE AND 3 YEARS AFTER INITIATION OF A FIRST ADVANCED THERAPY. DATA FROM THE UNIVERSITY OF SHERBROOKE REGISTRY OF ADVANCED THERAPIES (USRAT)

Keywords: Disease-modifying drug (DMARDs), Rheumatoid arthritis, Cardiovascular disease

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Background: Uncontrolled inflammation increases the risk for cardiovascular (CV) and venous thromboembolic (TE) events. Reducing inflammation using advanced therapies (AT) is expected to reduce these risks. Clinical registries are best for precise observations on diagnosis, reasons for drug withdrawal, and disease activity. Administrative databases are more comprehensive for comorbidities and outcomes.
Objectives: To compare the incidence of CV and TE events before and after AT initiation in the same rheumatoid arthritis (RA) patients, to explore specific toxicities or poorer protection of some ATs.
Methods: USRAT Registry combines administrative and clinical data. Our team is the single one treating rheumatology patients among over 500,000 people. All their inpatient episodes are recorded in the administrative system of one single multisite hospital. Since 2003, we developed a registry of 1800+ patients treated with AT. Episodes of inpatient care for these patients were extracted from our hospital's database from 1995 up to the end of 2021. Clinical charts were revised to confirm diagnosis and disease activity over time. We report severe CV and TE events occurring over the 3 years before and the 3 years after initiation of a first AT in patients for which chart revision is currently completed. We analyzed data according to initial AT, identifying a large subset remaining on first AT (First Persistent), a small subset who stopped first AT but did not switch (First-Stop), and others who switched AT over the period (Switch)
Results: RA was confirmed in 596 (66.3% women; mean age 59.1). Mean disease duration at first AT initiation (anti-TNF in 61%) was 7.3 years. First Stop patients trended to be men (47.6%) vs 34.8% (First Persistent) and 30.1% (Switch) (p = 0.074). Switch patients were younger (57.9 yo vs 59.8 First Persistent and 60.8 First Stop) (p = 0.04). Mean duration of first AT treatment was similar in Switch and First-Stop (0.94 vs 0.93 y), versus 5.3 in First Persistent.
Incidences of CV (1.57/100 person-years (py)) and TE (0.34/100 py) events before first AT were similar across First-Persistent, Switch and First-Stop subsets (Table 1). Over the 3 years after first AT initiation, we noted a numerical (non-significant) increase in new CV (2.35/100 py) and TE (0.67/100 py) events. CV incidence post-AT was significantly higher in the First-Stop subset, and not significantly different between First Persistent and Switch patients.
After initiation of a first AT, TE events were numerically higher in Switch (1.05/100 pt-y) and First Stop (2.33/100 pt-y) than First Persistent (0.26/100 pt-y) patients.
Conclusion: Prescribing an AT to patients with active RA appears insufficient to bring their 3-year risk for CV and TE events below their pre-AT levels. The worst CV and TE outcomes were seen in patients who stopped their first AT and did not switch (First-Stop) over the observation period, compatible with persistent poorly controlled inflammation. Numerically higher TE but not CV events were seen in Switch relative to First-Persistence patients. First-Stop patients did not have more CV or TE events before AT initiation; other characteristics of the more at risk First-Stop patients are to be defined.

Table 1. Incidence of events over the 3 years preceding and the 3 years following the initiation of a first advanced therapy in 596 RA patients

	Before		After	
	Events (n)	Incidence per 100 py	Events (n)	Incidence per 100 py
Cardiovascular (CV)	28	1,57	35	2,35
First-Persistent (n=305)	11	1,20	16	2,06
Switch (n=249)	14	1,87	13	1,95
First-Stop (n=42)	3	2,38	6	14,00 *
Thromboembolic (TE)	6	0,34	10	0,67
First-Persistent (n=305)	1	0,11	2	0,26
Switch (n=249)	4	0,54	7	1,05
First-Stop (n=42)	1	0,79	1	2,33

Person-years (py): **Before**: Total (1788); First-Persistent (915); Switch (747); First-Stop (126).**After**: Total (1487); First-Persistent (777); Switch (668); First-Stop (43).*p<0.05 Before vs After AT among First-Stop

Table 1. Multivariable Cox proportional hazards regressions using the demographic variables as time fixed in patients without any diabetic drug use (RA and PsA cohort)

	Model 1		Model 2	
Variables	Time-dependent HR (95% CI)	*p* value	Time-dependent HR (95% CI)	*p* value
Age	1.06(1.05-1.07)	<0.001*	1.06(1.05-1.07)	<0.001*
Male	1.57(1.26-1.95)	<0.001*	1.31(1.05-1.62)	0.014*
Disease duration	1.07(1.01-1.13)	0.013	1.07(1.01-1.12)	0.017*
Ever hypertension	3.50(2.58-4.74)	<0.001*	3.60(2.65-4.88)	<0.001*
Time-varying laboratory results				
ESR	1.01(1.00-1.01)	<0.001*		
CRP			1.10(1.08-1.13)	<0.001*
Atherogenic index log (TG/HDL)	3.40(1.50-7.71)	0.003*	3.45(1.52-7.79)	0.003*
FG <5.6	Ref	NA	Ref	NA
FG 5.6 - 6.9	2.54(1.50-7.71)	<0.001*	2.43(1.97-2.99)	<0.001*
FG >=7	4.47(3.25-6.16)	<0.001*	3.51(2.53-4.86)	<0.001*
Time-varying treatment				
bDMARDs				
Anti-TNF	0.70 (0.40-1.23)	0.214	0.70(0.40-1.23)	0.214
Non-anti-TNF	0.58(0.28-1.17)	0.127	0.54(0.27-1.11)	0.092
csDMARDs				
MTX	0.76(0.62-0.93)	0.008*	0.78(0.64-0.96)	0.016*
SLZ	1.18(0.96-1.45)	0.111	1.15(0.94-1.41)	0.168
NSAIDs				
COXII inhibitors	0.56(0.35-0.90)	0.016*	0.65(0.42-1.01)	0.055
Non-COXII inhibitors	0.83(0.67-1.01)	0.067	0.81(0.42-1.00)	0.048*
Steroid	2.16(1.77-2.64)	<0.001*	1.96(1.61-2.39)	<0.001*

*Statistically significant at $p \leq 0.05$.NA, not available; ESR, erythrocyte sedimentation rate; CRP, c-reactive protein; bDMARDs, biological disease-modifying anti-rheumatic drugs; TC, total cholesterol HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TG, triglycerides; FG, fasting glucose; TNF, tumor necrosis factor; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; MTX, methotrexate; SLZ, sulfasalazine; LEF, leflunomide; COXII, cyclooxygenase-2.

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POS1064 PRE-DIABETES INCREASED THE RISK OF MAJOR CARDIOVASCULAR EVENTS IN PATIENTS WITH INFLAMMATORY ARTHRITIS: A POPULATION-BASED COHORT STUDY

Keywords: Inflammatory arthritides, Cardiovascular disease, Comorbidities

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Background: Pre-diabetes was associated with an increased risk of all-cause mortality and cardiovascular disease (CVD) in the general population. However, data exploring the effect of pre-diabetes on the risk of CVD in patients with inflammatory arthritis (IA), including rheumatoid arthritis (RA) and psoriatic arthritis (PsA), were limited.

Objectives: To evaluate the effect of pre-diabetes on the risk of major cardiovascular events (MACE) in patients with IA.

Methods: A population-based cohort of IA patients was identified in the city-wide platform (The Hospital Authority Data Collaboration Lab) of the Hong Kong Hospital Authority. IA patients recruited from 2006 to 2015 were followed until the end of 2018. Time-varying Cox proportional hazard models with time-varying fasting glucose (FG) levels were analyzed to identify the risk of having MACE in IA patients.

Results: A total of 13,905 (12,233 RA and 1,672 PsA) patients with IA were recruited. After a total of 119,571 patient-years of follow-up, 934 (7.0 %) patients developed a first MACE. At baseline, the mean age of the entire cohort was 56.9±14.4 (RA: 57.7±14.4 vs. PsA: 51.0±12.8, p<0.001), mean disease duration was 0.6±1.5 (RA: 0.7±1.5 vs. PsA: 0.3±1.0, p<0.001) and the proportion of patients with diabetes was 3.6% (RA: 3.4 vs. PsA: 5.4, p<0.001). Using multivariable Cox regression analysis, in IA patients who were not on any anti-diabetic medications, the time-varying FG level of a prediabetic state (5.6-6.9 mmol/L) was found to be independently associated with a higher risk of MACE (HR 2.54, 95%CI 1.50-7.71, p<0.001 in the ESR model; HR 2.43, 95%CI 1.97-2.99, p<0.001 in the CRP model) (Table 1), after adjusting for age, sex, and baseline cardiovascular comorbidities and treatment. On the other hand, in patients already on anti-diabetic treatments, MACE risks were similar between patients with FG levels <5.6 mmol/L and prediabetes.

Conclusion: Pre-diabetes, as reflected by FG level at 5.6-6.9 mmol/L over time, was independently associated with an increased risk of MACE.

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POS1065 DAS28-GGT FOR THE PREDICTION OF MAJOR CARDIOVASCULAR EVENTS IN RHEUMATOID ARTHRITIS: RESULTS FROM THE ESPOIR COHORT

Keywords: Rheumatoid arthritis, Biomarkers, Cardiovascular disease

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Background: Patients with rheumatoid arthritis (RA) experience premature mortality that is largely due to cardiovascular disease (CVD). Ample evidence suggests that elevated γGT activity is associated with increased risk of CVD. We have previously showed that replacing ESR by γGT in DAS28 calculation (DAS28-γGT) allowed a combined evaluation of cardiovascular risk in patients with RA, in addition to joint disease activity [1].

Objectives: To validate the predictive value of the DAS28-γGT for the occurrence of major cardiovascular events (MACE) in the ESPOIR cohort.

Methods: We conducted a prospective observational study including patients with RA from the ESPOIR cohort fulfilling the 2010 ACR/EULAR criteria. Patients were recruited between 2002 and 2005 and were followed up to 10 years. Patients with a history of cardiovascular disease and not followed up to 1 year were excluded from the analysis. DAS28-γGT was calculated at baseline using the following formula: $0.56*\sqrt{TJ\text{-}28}+0.28*\sqrt{SJ\text{-}28}+2*ln(\gamma GT)+0.014*GH$. Our primary outcome was the occurrence of MACE during the observation period.

Results: 720 RA patients (77% females) were considered with a mean age of 48±13 years and a mean disease duration of 93±185 days. Disease activity was high, with a mean DAS28 of 5.1±1.3. At baseline, the DAS28-γGT correlated with age (r=0.26, p<0.001) and the Framingham risk score (r=0.31, p<0.001). The DAS28-γGT was also significantly increased in males (10.3±1.8 vs. 9.4±1.9, p<0.001) and in patients presenting the following conditions: high alcohol consumption (11.2±1.8 vs. 9.5±1.9, p<0.001), active smoking (9.72±1.93 vs. 9.44±1.86, p=0.036), blood hypertension (10.2±2.01 vs. 9.44±1.85, p<0.001), diabetes mellitus (10.67±2.20 vs. 9.53±1.87, p=0.001), hypercholesterolemia (9.95±1.97 vs.

9.50±1.88, p=0.017) and obesity (BMI > 30 kg/m^2) (10.01±1.90 vs. 9.26±1.83, p<0.001). No association was observed between DAS28-γGT and treatment with NSAIDs or corticosteroids. The DAS28-γGT steadily increased according to cardiovascular risk (**Figure 1A**) and was significantly increased in patients with at least 2 cardiovascular risk factors (**Figure 1B**). A total of 35 MACE was recorded during the observation period, with a mean time to event of 70±44 months. ROC curve analysis indicated that DAS28-γGT>9.4 had the best sensitivity (74%) and specificity (62%) for the diagnosis of MACE during the observation period. Increased DAS28-γGT (>9.4) was predictive of the occurrence of MACE, with a hazard ratio (HR) of 3.05 (95% confidence interval, CI 1.44-5.43) (**Figure 1C**). Multivariate Cox analyses confirmed increased DAS28-γGT together with age and diabetes mellitus as independent predictors of MACE (**Table 1**). The DAS28 was not predictive of the occurrence of MACE in this cohort.

Conclusion: The DAS28-γGT was identified in this large prospective cohort as an independent predictor of MACE in patients with RA. In addition to the assessment of disease activity, the DAS28-γGT is a simple and useful tool to evaluate CV risk in routine and warn the clinician about the CV risk burden in patients with RA.

REFERENCE:

[1] *Vergneault et al, J Rheumatol 2020*

Table 1. Multivariate COX analysis to identify independent predictors of MACE

Variable at baseline	Multivariate analysis (HR, 95% CI)	p-value
DAS28-γGT >9.4	2.36 (1.08-5.18)	0.032
Age	1.06 (1.01-1.08)	0.015
Male gender	1.16 (0.54-2.48)	0.71
Alcohol consumption	0.86 (0.19-3.78)	0.85
Active smoking	1.20 (0.59-2.42)	0.61
Blood hypertension	1.85 (0.83-4.12)	0.13
Hypercholesterolemia	0.89 (0.38-2.05)	0.78
Diabetes mellitus	4.06 (1.52-10.80)	0.005
Body mass index > 30	0.56 (0.26-2.16)	0.12

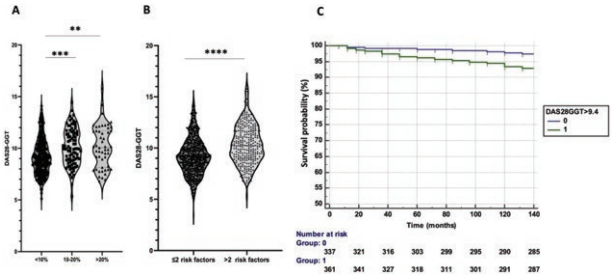


Figure 1. DAS28- 1:6-2.16)> 30s COX analysis to identA, DAS28-6-2.16)> 30s COX analysis to identify independent predictors of MA** p<0.01 and ***p<0.001 by ANOVA test with Dunnett1 by alysis to identify independent predictors of MACent predictor of MACE in patients ular risk factors (NO or > 2 risk factors), ****p<0.0001 by unpaired t test. C, MACE-free survival according to the DAS28- MAC(o or > 9.4).

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POS1066 WHERE HAVE ALL THE RHEUMATOID NODULES GONE?

Keywords: Rheumatoid arthritis, Epidemiology, Skin

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Background: The most common extraarticular manifestation of rheumatoid arthritis (RA) is the rheumatoid nodule, which is reported to affect about 30% of patients with RA.[1] The development of rheumatoid nodules has been associated most strongly with high disease activity, seropositive status, and more rapid progression of joint destruction. Despite significant changes in RA treatment and decreasing incidence of seropositive RA, no recent population-based studies have assessed the epidemiology of rheumatoid nodules.

Objectives: We aim to investigate changes in rheumatoid nodule incidence over time.

Methods: This study evaluated rheumatoid nodule incidence trends using an inception cohort that included all adult patients from a geographically well-defined area who met the 1987 American College of Rheumatology criteria for RA between 1/1/1985 and 12/31/2014. Patients were followed until the earlier of death, migration from the region, or 12/31/2000 (for patients with incident RA in 1985-1994) or 12/31/2008 (for 1995-2007 patients) or 10/15/2022 (for 2008-2014 patients). Patients were divided into two cohorts based on the incidence date of RA, an early cohort from 1985-1999 and a later cohort from 2000-2014. Medical records were reviewed manually, and the incidence date of rheumatoid nodules was recorded if determined to be present either by clinical judgment and/or histopathology. The 10-year cumulative incidence of rheumatoid nodules was estimated in each cohort. Cox proportional hazard models adjusted for age, sex and calendar year were used to determine associations between specific demographic and RA disease data with rheumatoid nodules.

Results: 907 patients were included in this study, 296 (67% female) in the 1985-1999 cohort and 611 (70% female) in the 2000-2014 cohort. The mean follow-up period between these cohorts, respectively, was 9.1 and 7.4 years. Baseline characteristics (earlier cohort, latter cohort) included rheumatoid factor (RF) positive (70%, 59%), joint erosions in the first year of RA (24%, 29%), and ever smoker (57%, 47%). The 10-year cumulative incidence of rheumatoid nodules was 31% in the 1985-1999 cohort and 16% in the 2000-2014 cohort (hazard ratio [HR] 0.52, 95% confidence interval [CI] 0.39-0.70). Identified risk factors for the development of rheumatoid nodules included RF positivity (HR 4.38, 95%CI 2.37-8.09), erosions (HR 2.53, 95%CI 1.64-3.91), current smoker (HR 2.09, 95%CI 1.30-3.37), male sex (HR 1.77, 95%CI 1.14-2.73), methotrexate use (HR 1.77, 95%CI 1.09-2.86) and other DMARDs (HR 2.07, 95%CI 1.14-3.74) (Table 1).

Conclusion: The incidence of rheumatoid nodules has decreased substantially over time. More research is needed to understand the drivers of this improvement and implications on RA disease outcomes.

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Table 1. Risk factors associated with rheumatoid nodules in the 2000-2014 cohort.

Variable	Rheumatoid Nodules HR (95% CI)
Age (per 10-year increase)	0.95 (0.82, 1.09)
Male sex	1.77 (1.14, 2.73)
Calendar year of RA incidence	0.88 (0.84, 0.93)
Cigarette smoking at baseline	
Ever	1.38 (0.90, 2.13)
Current	2.09 (1.30, 3.37)
BMI (per 1kg/m^2 increase) baseline	1.00 (0.97, 1.04)
RF positivity	4.38 (2.37, 8.09)
Highest ESR in the 1st year of RA (per 10 mm/h increase)	1.03 (0.95, 1.12)
Erosions/destructive changes on radiographs	2.53 (1.64, 3.91)
Medication usage	
Methotrexate	1.77 (1.09, 2.86)
Hydroxychloroquine	0.95 (0.61, 1.49)
Other DMARD	2.07 (1.14, 3.74)
Biologic response modifiers	1.64 (0.87, 3.11)
Corticosteroids (systemic)	1.11 (0.69, 1.77)

*Adjusted for age, sex, and calendar year.**RA, rheumatoid arthritis; BMI, body mass index; RF, rheumatoid factor; ESR, erythrocyte sedimentation rate; DMARD, disease-modifying antirheumatic drug

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POS1067 MORBIDITIES ASSOCIATED WITH SERIOUS INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Epidemiology

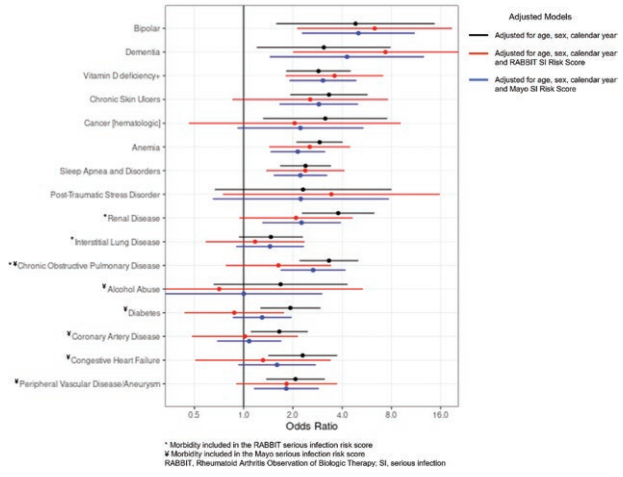
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Background: Patients with rheumatoid arthritis (RA) are at increased risk for serious infections (SI) and have a higher prevalence of multimorbidity. The increased risk for SI has led to the creation of multiple infection risk models over the last decade for patients with RA. These models often include combinations of patient demographics, medications, and a limited list of morbidities. However, the limited number of morbidities included in these models are not fully reflective of the morbidity burden seen in real-world practice. Thus, some morbidities that contribute to SI risk may be absent from the existing models.

Objectives: We aim to examine associations between a comprehensive list of morbidities and SI in patients with RA.
Methods: This population-based cohort study evaluated morbidities as risk factors for SI by including all adult patients from a geographically well-defined area from 1/1/1999 through 12/31/2013 who met the 1987 American College of Rheumatology criteria for RA. Patients were followed until the earlier of: death, migration from the region, or 12/31/2021. Fifty-five morbidities were evaluated as risk factors for SI and were ascertained from medical records using international classification of disease (ICD)-9 and ICD-10 codes, requiring 2 separate codes at least 30 days apart for inclusion. Serious infections were defined as infections requiring hospitalization and were identified using previously validated ICD-9 and ICD-10 codes where the primary diagnosis for hospitalization was infection. Conditional frailty models (a variation of Cox model that accounts for multiple events per patient) were used to analyze the association between each morbidity and SI. The first model adjusted for age, sex, and calendar year; the second model adjusted for age, sex, calendar year, and factors included in the Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) SI risk score;[1] the third model adjusted for age, sex, calendar year, and for factors included in the Mayo SI risk score.[2]
Results: 911 patients (70% female, mean age 56 years, 66% seropositive) were included. The most common morbidities (% of patients; % person-years) included hypertension (53.6%; 40.9%), hyperlipidemia (54.6%; 37.4%), and osteoarthritis (55.2%; 32.6%). There were 293 SI among 155 patients (17%), which corresponded to an incidence of 3.9 SI per 100 person-years. Nineteen SI were fatal. Risk of SI was significantly increased in 26 of 55 morbidities in the initial model adjusted only for age, sex, and calendar year. In the RABBIT and Mayo SI risk score adjusted models, 12 and 23 morbidities were associated with increased risk, respectively. Morbidities conferring high risk among the three adjusted models are included Figure 1. Specific morbidities included in the RABBIT and Mayo SI risk scores continued to have large and/or significant effect sizes despite adjustment (Figure 1). The number of morbidities was also associated with SI risk, leading to a 16% (initial), 11% (RABBIT), and 13% (Mayo) increase in SI risk per morbidity.
Conclusion: Several morbidities are associated with increased risk of SI in patients with RA, and this risk is not completely accounted for in two SI risk scores. Morbidity burden is an important clinical characteristic that may influence SI prevention strategies and treatment approaches in patients with RA.
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Figure 1. Risk of Serious Infection Among Selected Morbidities



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POS1068

HUMORAL IMMUNE RESPONSE TO 13 VALENT-CONJUGATE AND 23-VALENT POLYSACCHARIDE PNEUMOCOCCAL VACCINES IN RA PATIENTS TREATED WITH ABATACEPT: RESULTS OF THE OPEN RANDOMIZED CONTROLLED TRIAL VACINA (VACCINATION AGAINST PNEUMOCOCCAL IN NAÏVE ABATACEPT RHEUMATOID ARTHRITIS PATIENTS)

Keywords: Comorbidities, Randomized control trial, Rheumatoid arthritis

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Background: To prevent infections, EULAR recommends to vaccinate RA patients against streptococcal pneumoniae. It is recommended to vaccine with the conjugate vaccine (PCV13) followed by a dose of PPSV23 at least 8 weeks later. PCV13 is a T- cell dependent vaccine whereas PPSV23 induces a T-independent humoral response. Abatacept is a biological DMARD that inhibits T cell activation.
Objectives: We hypothesized that the humoral response may be more affected under abatacept after PCV13 vaccination than after PPSV23. To adress this question, we compared the humoral response four weeks after vaccination with PCV13 or PPSV23 in RA patients treated with abatacept.
Methods: We conducted a prospective, multicenter, randomized, open-label study in patients with RA according to ACR/EULAR 2010 criteria, and starting abatacept because of inadequate response to MTX or leflunomide (DAS28>3,2). Patients were randomized in 2 groups: the first group (G1) was vaccinated with the PPSV23 and the second group (G2) with PCV13 and PPSV23 8 weeks later. Abatacept was to be started on the same day as the first vaccine (PCV13 or PPSV23). Patients having been treated previously with rituximab within the last year were excluded. A patient was considered as responder if there was a two-fold increase in the antibodies titer measured by ELISA for at least 3 of 5 serotypes of interest (1, 3, 14, 7F, 19A) which are the most frequently involved in pneumococcal infections. For the primary endpoint, we compared the rate of responders at one month in G1 and G2 using a Chi-Square test. Sample size calculation based on alpha risk 5% and 80% power requirements resulted in 80 patients. Tolerance of the vaccines were collected within the first week and later in a patient booklet. Adverse events were also collected at 1, 2, 6 and 12 months.
Results: Eighty patients were included and randomized in the two groups: 40 in G1 and 40 in G2 (1 patient withdrew his consent before any treatment in G2). Characteristics of patients are described in Table 1. Female were more represented in G1 (82.5%) compared to G2 (64.1%). Lymphocyte count were significantly higher in G1 compared to G2: 1841/uL (+/-887) vs 1603/uL (+/-580). In the mITT, the rate of responders was 47.5% in in G1 and 38.46% in G2 (p=0.42) with a RR of 1.23 (IC95%: 0.73-2,06; when comparing responders in PPSV23 vs PCV13 groups. This absence of difference was confirmed with a per protocol analysis (p=1) and after adjusting for gender and lymphocytes count with a logistic regression test (RR=1.6 IC95% 0.6-4.2). 17 infections were reported in G1 and 28 in G2 with 3 severe infections but no pneumococcal infection.
Conclusion: In RA patients treated with abatacept combined with sDMARDs (MTX or LEF), the rate of responders is similar 28 days following vaccination with PCV13 or PPSV23. Although PCV13 is a T cell dependent vaccine, immunogenicity to PCV13 under abatacept is similar to PPSV23. There were no unexpected side effects after pneumococcal vaccines.

Table 1. Characteristics of patients at inclusion

Variable	Modality	All population N=79	Group1 PPSV23 N=40	Group 2 PCV 13 N=39
Age (years)	Mean (±SD)	59.61 (± 12.59)	58.08 (± 13.74)	61.18 (± 11.24)
Gender	Women	58 (73.42)	33 (82.50)	25 (64.10)
BMI (kg/m²)	Mean (±SD)	26.03 (± 5.09)	26.76 (± 6.17)	25.29 (± 3.62)
Previous pneumocccal vaccine	Yes/ (%)	17 (21.52)	10 (25.00)	7 (17.95)
DAS28 CRP	Mean (±SD)	4.33 (± 0.90)	4.20 (± 0.79)	4.46 (± 1.00)
RF positive	Yes/ (%)	55 (70.51)	30 (75.00)	25 (64.10)
ACPA positive	Yes/ (%)	55 (70.51)	31 (77.50)	24 (61.54)
Erosive RA	Yes/ (%)	47 (61.04)	24 (60.00)	23 (58.97)
Lymphocytes count n/uL	Mean (±SD)	1822.31 (± 778.25)	2029.73 (± 886.68)	1603.97 (± 579.90)
MTX	Yes/ (%)	63 (79.75)	32 (80.00)	31 (79.49)
MTX dose (mg/w)	Mean (±SD)	15.67 (± 4.52)	15.63 (± 5.12)	15.73 (± 3.88)
Leflunomide	Yes/ (%)	8 (10.13)	4 (10.00)	4 (10.26)
Steroids	Yes/ (%)	33 (41.77)	16 (40.00)	17 (43.59)
Steroid dose (mg/d)	Mean (±SD)	7.77 (± 2.42)	7.50 (± 2.58)	8.03 (± 2.30)

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POS1069

SYSTEMATIC LITERATURE REVIEW INFORMING THE EULAR POINTS TO CONSIDER TASK FORCE ON THE INITIATION OF TARGETED THERAPIES IN PATIENTS WITH INFLAMMATORY ARTHRITIDES AND A HISTORY OF CANCER

Keywords: Comorbidities, bDMARD, Malignancy

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Background: Potential associations between targeted therapies in patients with an inflammatory arthritis (IA)
and malignancy are a frequent concern in daily rheumatology practice. No specific framework has been proposed to evaluate the benefit/risk balance of initiating or reinitiating a targeted therapy (bDMARDs/tsDMARDs) in patients with IA and a history of cancer.
Objectives: To perform a systematic literature review (SLR) to inform the task force formulating.
the EULAR Points to Consider on the initiation of targeted therapies in patients. with IA and a history of cancer.
Methods: Specific research points were defined with the task force before formulating. the research questions with a librarian under supervision of two methodologists. The task force agreed to focus the SLR on clinical data in patients treated with any targeted therapy for an inflammatory or autoimmune rheumatic or skin or bowel disease. All studies up to. the 15th July 2022 were searched through Pubmed and Embase. Inclusion criteria required studies reporting on the initiation of a targeted therapy in patients with history of cancer, a control group. of patients treated with a conventional DMARDs or healthy controls, and report of a relative risk measure (e.g. Hazard Ratio (HR)) of cancer recurrence between groups. Two reviewers independently performed standardized article selection, data extraction, synthesis, and risk of bias assessment. The quality of the studies was graded according to the Newcastle-Ottawa quality assessment scale.
Results: A total of 1555 publications were identified of which 79 articles fulfilled inclusion criteria, including. 13 published articles and 1 EULAR abstract. All studies were high quality observational data from cohorts or registries, representing 4522 patients (13030 patient-years). Most of the patients included were treated for rheumatoid arthritis. The previous cancer was a solid cancer for more than 90% of the patients. The targeted therapy evaluated was a TNF inhibitor in all the studies, and 4 studies evaluated rituximab as well. The overall HR of cancer recurrence was 1.02 (0.83-1.26) in patients treated with a targeted therapy compared to those treated with a conventional DMARD (Figure 1). In patients treated with. a TNF-inhibitor, the HR was 1.01 (0.86-1.18). In patients treated with rituximab, the HR. was 1.10 (0.72-1.67). In subgroup analyses, no difference in cancer recurrence was observed if. the targeted therapy was initiated before or after 5 years since the diagnosis of the initial cancer; no difference in cancer recurrence was observed depending on the initial cancer type.
Conclusion: The SLR informing EULAR PTC show that overall, the targeted therapies and clinical context covered by the included studies were not associated with an increased risk of cancer recurrence when compared with conventional synthetic DMARDs. This SLR also shows the lack of data for other targeted therapies, for other clinical contexts, and for other conditions than RA.

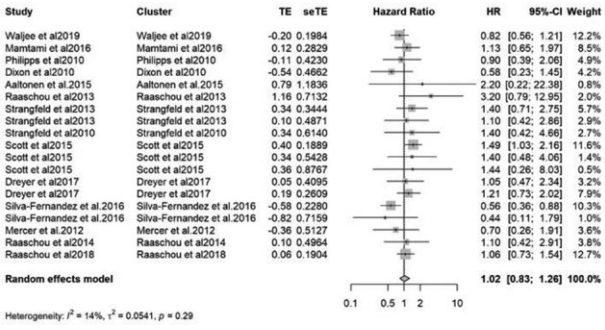


Figure 1. Relative risk of cancer between targeted therapies and csDMARDs in patients with a history of cancer

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POS1070

SLIGHTLY INCREASED INFECTION RISK FOR JAK INHIBITORS TOFACITINIB AND BARICITINIB COMPARED TO BDMARDS: A REAL-WORLD EVIDENCE STUDY

Keywords: bDMARD, Rheumatoid arthritis, Targeted synthetic drugs

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Background: Rheumatoid arthritis (RA) is treated with disease modifying anti-rheumatic drugs (DMARDs), including biological DMARDs (bDMARDs) and more recently, Janus kinase inhibitors (JAKi). Both JAKi and bDMARDs are safe and effective, however infection risk remains a concern. Recently, the ORAL Surveillance trial showed an increased risk of infections and especially herpes zoster (HZ) in JAKi compared to TNF-inhibitors (a type of bDMARDs).[1] However, clinical trials do not fully reflect the real-world population as they usually include younger and healthier patients and have a short follow-up time. Therefore, larger long-term observational studies also including more frail and older adults as seen in clinical practice are needed.

Objectives: The objective of this study was to compare infection risk between bDMARDs and JAKi in RA patients, with a special focus on HZ and older adults.

Methods: From a nationally representative prescription database, all adult RA patients starting a new JAKi or bDMARD between August 1st 2018 and January 31st 2021 were included. This database covers ~63% of all outpatient prescriptions dispensed in the Netherlands and contains coded prescription records including patient characteristics, medication and prescriber information. Prescriptions of antibiotic, antiviral or antifungal medication were used as proxy for infections. Infection incidence rates (IR) were compared between JAKi and bDMARDs and infection risks using multilevel Poisson regression adjusted for follow-up time and potential confounders and stratified for age < 65 and ≥ 65 years.

Results: In total, 14,989 patients were included, with 20,050 treatment episodes with either JAKi or bDMARDs. Most patients were female (72%) and median age was 61 years (IQR 52-70). Infection IRs were higher in JAKi (48/100 patient years) compared to bDMARDs (35/100 patient years, adjusted incidence rate ratio (IRR) 1.22, 95% CI 1.12-1.33). More HZ infections were seen in JAKi compared to bDMARDs (adjusted IRR 3.03, 95% CI 2.26-4.07) (Table 1). No significant differences in infection IRs were found between JAKi baricitinib and tofacitinib. In older patients, absolute infection IRs were higher (overall infection IR 42/100 patient years for age ≥ 65 versus 31/100 patient years for age < 65). However, comparing JAKi to bDMARDs, IRRs were similar for all ages (adjusted IRR for age ≥ 65 1.31 (95% CI 1.15-1.49), adjusted IRR for age < 65 1.17 (95% CI 1.05-1.30)).

Conclusion: JAKi are - compared to bDMARDs - associated with a slightly higher infection risk and a higher risk of HZ specifically. In older patients, absolute infection IRs are higher but relative infection risks for JAKi versus bDMARDs are similar in all age groups. No differences in infection risk between tofacitinib and baricitinib were found.

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Table 1. Number of infections and IRR for 1) bDMARD and JAKi users, 2) baricitinib and tofacitinib

Main analysis: bDMARD vs JAKi		
	bDMARDs	JAKi
N (treatment episodes)	18,085	1,965
% of DDD used, median (IQR)	102 (99-102)	100 (100-100)
All infections (n)	8,638	1,116
n/100 patient years	35	48
Adjusted IRR*	Ref 1.0	1.22 (95% CI 1.12-1.33)
Herpes zoster (n)	246	74
n/100 patient years	0.98	3.2
Adjusted IRR*	Ref 1.0	3.03 (95% CI 2.26-4.07)
Subanalysis: within JAKi		
	Baricitinib	Tofacitinib
N (treatment episodes)	991	885
All infections (n)	701	459
n/100 patient years	54	48
Adjusted IRR*	Ref 1.0	0.91 (95% CI 0.77-1.07)
Herpes zoster (n)	41	23
n/100 patient years	3.2	2.4
Adjusted IRR**	Ref 1.0	0.74 (95% CI 0.43-1.29)

* adjusted for age, sex, number of used DMARDs in the 2 years prior to the index date, concurrent use of csDMARDs and corticosteroids, comorbidities (diabetes mellitus and chronic obstructive respiratory diseases), dosage (as percentage of defined daily dose) and follow-up time**adjusted for age, sex, dosage (as percentage of defined daily dose) and follow-up time

POS1071

THE IMPACT OF COMORBIDITIES ON THE EFFICACY OF IL-6 INHIBITOR OLOKIZUMAB COMPARED TO ADALIMUMAB

Keywords: bDMARD, Comorbidities, Rheumatoid arthritis

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Background: Comorbid conditions may affect efficacy of treatment in patients with rheumatoid arthritis (RA).

Objectives: The aim of this analysis was to evaluate the impact of comorbidity burden on the efficacy of IL-6 inhibitor olokizumab (OKZ) and TNF-α inhibitor adalimumab (ADA) in the CREDO-2 clinical trial cohort of patients with active rheumatoid arthritis (RA).

Methods: Patients in the double-blind RCT (NCT02760407) who received OKZ 64 mg once every 2 weeks (q2w) or 4 weeks (q4w), or ADA 40mg q2w for 24 weeks were included. To assess the impact of comorbid conditions on efficacy, outcomes were stratified by patients with Low Charlson Comorbidity Index (CCI = 1; RA only) vs High (CCI ≥ 2; RA and at least 1 comorbidity). Age points in CCI were excluded from the analysis. The comparison of outcomes between the Low and the High CCI groups was performed using $\chi 2$-test in unadjusted analysis, and logistic regression in adjusted analysis. Baseline characteristics with an absolute standardized difference > 0.1 were identified as covariates for adjusted comparison. The impact of comorbidity was investigated separately for OKZ and ADA.

Results: A total of 1402 patients with RA were included in the analysis: 940 patients treated with OKZ 64 mg q2w or q4w and 462 patients treated with ADA 40mg q2w. All patients received background MTX therapy. The results are presented in the Table 1. There was no difference in efficacy results between the OKZ-treated groups with and without comorbid conditions during the study, except the achievement of SDAI ≤ 3.3 at Week 24, which was observed more frequently in the Low CCI group. However, the presence of comorbid conditions affected the efficacy of ADA therapy. In the group of High CCI, the proportions of patients who achieved ACR 20 response at Week 12, ACR 50 response (Weeks 12 and 24), SDAI ≤ 3.3 (Weeks 12 and 24) and CDAI ≤ 2.8 (Week 24) and CDAI ≤ 10 (Week 24) were significantly lower in comparison with the group of Low CCI.

Conclusion: High CCI (or presence of at least one comorbid disease) does not affect OKZ treatment efficacy in RA patients. In the same study, high CCI significantly reduces the efficacy of ADA treatment, including LDA and remission achievement.

Table 1. Impact of comorbidities on the efficacy parameters in the OKZ and ADA-treated patients

Variable	OKZ				ADA			
	Low, n(%) N=701	High, n(%) N=239	Adjusted Odds Ratio (95% CI)	p-value	Low, n(%) N=352	High, n(%) N=110	Adjusted Odds Ratio (95% CI)	p-value
ACR20								
Week 12	504 (71.9)	164 (68.6)	0.82 (0.54 – 1.23)	0.329	247 (70.2)	62 (56.4)	0.49 (0.31-0.79)	**0.003**
Week 24	518 (73.9)	168 (70.3)	0.77 (0.51 – 1.17)	0.211	249 (70.7)	70 (63.6)	0.63 (0.39-1.02)	0.060
ACR50								
Week 12	309 (44.1)	86 (36.0)	0.78 (0.53 – 1.15)	0.570	148 (42.0)	33 (30.0)	0.58 (0.35-0.93)	**0.026**
Week 24	362 (51.6)	112 (46.9)	0.87 (0.59 – 1.27)	0.473	178 (50.6)	36 (32.7)	0.48 (0.30-0.77)	**0.003**
SDAI ≤ 3.3								
Week 12	70 (10.0)	18 (7.5)	0.82 (0.40 – 1.59)	0.570	31 (8.8)	4 (3.6)	0.30 (0.08-0.84)	**0.037**
Week 24	108 (15.4)	26 (10.9)	0.54 (0.28– 0.96)	**0.044**	55 (15.6)	5 (4.5)	0.22 (0.07-0.54)	**0.003**
CDAI ≤ 2.8								
Week 12	61 (8.7)	12 (5.0)	0.64 (0.27 – 1.36)	0.272	32 (9.1)	5 (4.5)	0.40 (0.13-1.03)	0.080
Week 24	86 (12.3)	24 (10.0)	0.72 (0.36 – 1.34)	0.315	55 (15.6)	5 (4.5)	0.24 (0.08-0.57)	**0.004**
CDAI ≤ 10								
Week 12	278 (39.7)	75 (31.4)	0.72 (0.47-1.08)	0.117	148 (42.0)	34 (30.9)	0.63 (0.39-1.03)	0.067
Week 24	341 (48.6)	97 (40.6)	0.70 (0.47-1.02)	0.068	186 (52.8)	43 (39.1)	0.60 (0.37-0.96)	**0.033**
DAS28 (CRP) < 3.2								
Week 12	348 (49.6)	100 (41.8)	0.73 (0.50 – 1.07)	0.111	150 (42.6)	35 (31.8)	0.64 (0.39-1.03)	0.070
Week 24	387 (55.2)	126 (52.7)	0.87 (0.59 – 1.28)	0.476	176 (50.0)	43 (39.1)	0.67 (0.41-1.07)	0.093

Abbreviations: ACR 20, 20% improvement in the American College of Rheumatology criteria; ACR 50, 50% improvement in the American College of Rheumatology criteria; CDAI, Clinical Disease Activity Index; CI, Confidence interval; DAS28 (CRP), Disease Activity Score 28-joint count based on C-reactive protein; SDAI, Simplified Disease Activity Index. Bold font indicates statistical significance.

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POS1072 INSULIN INHIBITS ACTIVITY OF CD4+ T CELLS IN RHEUMATOID ARTHRITIS

Keywords: Adaptive immunity, Comorbidities, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) and diabetes mellitus (DM) have common genetic risk factors, while molecular mechanisms behind this commonality have not been studied.

Objectives: To study non-metabolic effects of insulin in CD4+ T cells of RA patients.

Methods: Incidental DM was studied in a consecutive cohort of 330 (256 female, 74 male) RA patients and 1011 (798 female, 213 male) gout patients matched to RA by age and gender (1 to 3) retrieved from the Health Care Register of Western Sweden during 10 years of follow-up. Insulin was measured at baseline and analyzed in relation to clinical and serological disease parameters. Transcriptomics by RNAseq was done on $CD4^+$T cells of 57 RA patients. Differentially expressed genes (DEG, nominal p<0.05) in patients with hyperinsulinemia (n=11, median 344 pmol/L) were identified using DESEq2 (R studio, Bioconductor) and analyzed for enrichment of biological processes and transcription factor (TF) families using GSEA (Broad Institute). To study direct effect of insulin on $CD4^+$T cell function, *in vitro* culture experiments were performed. Analysis of $CD4^+$Tcell phenotype for senescence, exhaustion and apoptosis was done by flow cytometry, transcriptomics and cytokine measurement.

Results: In total, 102 new cases of DM were registered, significantly less often in RA patients compared to gout patients (p=3.2e-4, OR=0.34 [0.18-0.64]). The new DM were more prevalent in men (p=0.012) with no difference between RA and gout patients (9.8 vs 7.5%, OR=1.34 [0.46-3.52] p=0.55). In females, RA patients developed significantly fewer cases of DM than gout patients (2.1 vs 9.4%, OR=0.21 [0.07; 0.47], p=3.2e-5). In RA patients, the insulin levels correlated positively to inflammation measured by serum levels of IL6, VEGF and IL8 followed by IFNγ total, 102 new cases of DM were registered, significantly less often in RA patients compared to gout patients (p=3.2e-4, OR=0.34 [0.18-0.64]). The new DM were more prevalent in men (p=0.012) with no difference between RA and gout patients (9.ol/L). Transcription profile of $CD4^+$T cells revealed 688 (131 upregulated, 557 downregulated) protein-coding DEG in patients with hyperinsulinemia. The down-regulated DEG showed enrichment for T cell activation (GO:0042110, FDR 2.6e-26) and inflammatory response (GO:0006954, FDR 2.9e-21). Analysis for TF families showed that the down-regulated DEG were controlled by TFs HMGB1, NFAT and NFκB (all FDR<e-6), which were significantly enriched for Th1 T cell markers including TBX21, EOMES, CXCR3 and IL2. The upregulated DEG were controlled by TFs MORC2, which regulates response to DNA damage, and ZBTB7B essential for differentiation and commitment of $CD4^+$T cells. DEG included GART gene controlling the folate biosynthesis and the transcription regulating proteins MRPL3 and DAP3. Patients with hyperinsulinemia had significantly higher serum levels of IL6, IL8 and VEGF (all p<0.05), suggesting an inflammatory environment. However, they were not different in DAS28, CRP, WBC and platelet counts. Stimulation of $CD4^+$T cell cultures with insulin (n=12) resulted in a significant suppression of IFNγ cell cultures with insulin (n=12) resulted in a significant suppression of IFNscription regulating proteins MRPL3 and DAP3. Patients with hyperinsulinemia had significantly higher serum levels of IL6, IL8 and VEGF (all p<0.05), suggesting an inflammatoryrichment for DNA ($7AAD^+$ cells) in flow cytometry, which does not support induction of senescence by insulin in $CD4^+$ cells. In contrast, $CD4^+$ cells of hyperinsulinemic RA patients expressed lower levels of CCL chemokines, IL2, and TNF, which suggests that insulin induced exhaustion of $CD4^+$T cells.

Conclusion: This study shows that hyperinsulinemia has non-metabolic functions under conditions of chronic inflammation. It could indicate residual RA activity. Insulin controls overactivation of adaptive immunity and causes exhaustion of pro-inflammatory Th1 cells in RA patients.

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POS1073 IMPACT OF COMORBIDITIES ON THE FIRST BDMARD EFFECTIVENESS AND RETENTION RATE AFTER 2 YEARS OF FOLLOW-UP IN PATIENTS WITH RHEUMATOID ARTHRITIS. DATA FROM THE SPANISH REGISTRY BIOBADASER

Keywords: Rheumatoid arthritis, Comorbidities, bDMARD

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Background: Patients with Rheumatoid Arthritis (RA) have a higher prevalence of comorbidities, compared to the general population. The presence of such comorbidities has been directly associated with an increased disease activity. However, little is known about the impact of comorbidities in the therapeutic response and in the retention rate.
Objectives: a) To evaluate the effect of comorbidities on the first biologic disease-modifying antirheumatic drug (bDMARD) effectiveness in patients with RA after 2 years of follow-up, and b) to determine the influence of such comorbidities on the first bDMARD retention rate.
Methods: The study population consisted of patients with a diagnosis of RA and exposed to a first bDMARDs, included in BIOBADASER. BIOBADASER is a prospective, large national drug safety registry of patients with rheumatic diseases exposed to b- or tsDMARDs. Patients were classified in two groups at baseline according to the Charlson Comorbidity index (CCI) score: <3 and ≥3. Patients achieving remission (DAS28<2.6) at 1 and 2-years timepoints after the anti-TNF initiation were compared between the two groups using chi-square test. The absolute DAS28 score over time was compared between both groups of patients using a linear regression model adjusted for sex and age, and considering the follow-up visit as covariate. Finally, the first bDMARD retention rate was compared between patients <3 and ≥3 using Log-Rank test and Kaplan-Meier curve.
Results: A total of 1253 patients initiating bDMARD were included (76.6% female and mean age 56 years at the beginning of therapy). Overall, 107 (9%) patients had a CCI ≥3, being diabetes the most frequent comorbidity (5.0%). No differences were found in DAS28<2.6 between patients with CCI<3 and CCI≥3 after 1 year of follow-up (48.2% vs. 44.2%, p-value=0.457), nor after 2 years (50.8% vs. 40.7%, p-value=0.135). The linear regression model showed significant higher scores in DAS28 over the two years in patients with a CCI ≥3 after adjusting for age and sex (beta coefficient 0.27, 95%CI: 0.02-0.51; p-value=0.034). Finally, no differences in the bDMARD retention rate were found between both groups (median 2.6 years [IQR: 1.5-4.1] in CCI<3 vs. 2.1 years [IQR: 0.6-3.7] in CCI≥3; log rank test p-value 0.467) (Figure 1).
Conclusion: These data suggest that a higher CCI in patients with RA is associated with greater DAS28 scores during the first two years after bDMARD initiation, although no differences in remission status were found. In addition, a slightly shorter retention rate was found in patients with CCI≥3, although the difference was non-significant. These results suggest a lower probability of disease activity control in patients with comorbidities after the initiation of bDMARD.

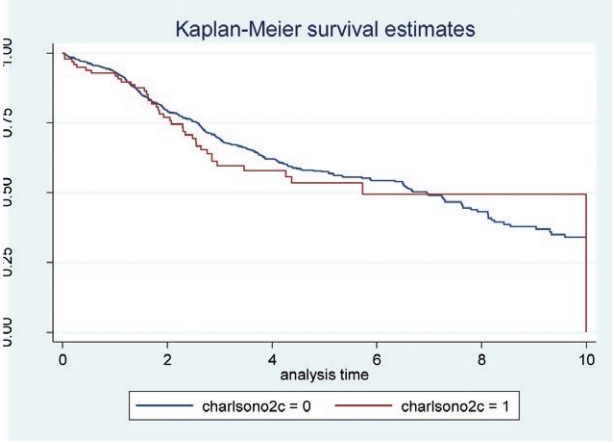


Figure 1. Kaplan Meier curve comparing the first bDMARD retention rate between the two groups.

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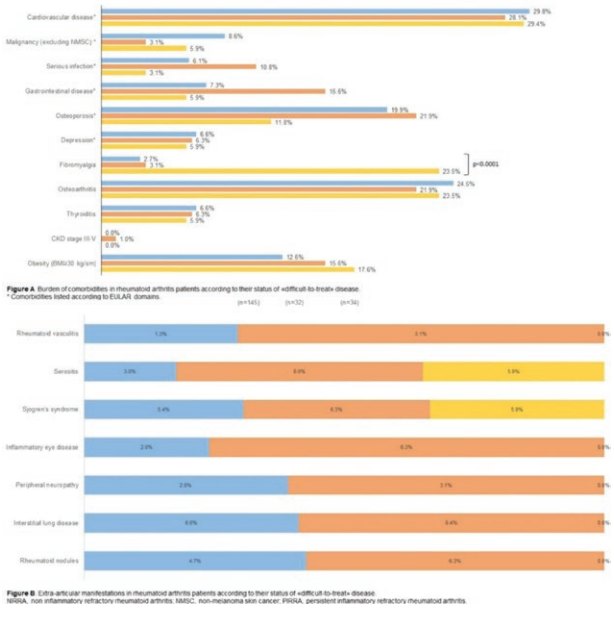
POS1074

COMORBIDITIES AND EXTRA-ARTICULAR INVOLVEMENT IN PERSISTENT INFLAMMATORY AND NON-INFLAMMATORY DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS AND CONTROLS

Keywords: Rheumatoid arthritis, Cardiovascular disease, Comorbidities

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Background: Comorbidities are prevalent among people with rheumatoid arthritis (RA). Some authors have postulated that there is a tight relationship between comorbidities and refractoriness to treatments and a status of difficult-to-treat (DT2) RA. Nevertheless, strong evidence for this association is lacking.
Objectives: We compared the frequencies and type of comorbidities and extra-articular RA manifestations in a cohort of patients previously assessed for D2TRA.
Methods: This was a cross-sectional study in a multicentre cohort of patients diagnosed with RA between 2000 and 2019 and with a disease duration of more than two years (established disease). Participants were stratified according to their fulfillment of the EULAR definition of DT2RA. We analyzed comorbidities according to EULAR domains (cardiovascular diseases, malignancies, depression, osteoporosis, gastrointestinal diseases, and serious infections) plus the following not included in EULAR domains: fibromyalgia, thyroiditis, osteoarthritis, chronic kidney disease (CKD), and obesity. We compared the frequencies of each comorbidity by Chi-squared test between three groups: non-D2TRA, DT2RA 'persistent-inflammatory refractory RA' (PIRRA[1]) and DT2RA 'non-inflammatory refractory RA' (NIRRA[1]). DT2RA-PIRRA and DT2RA-NIRRA were defined according to the presence (PIRRA) or absence (NIRRA) of active inflammation as detected by raised inflammatory markers, clinical or ultrasound-proven synovitis. We also assessed extra-articular manifestations of RA (serositis, secondary Sjogren's syndrome, inflammatory eye diseases, neuropathy, interstitial lung disease, vasculitis, and rheumatoid nodules). Correlations were assessed by the Spearman test. P-values were not corrected for multiplicity due to the exploratory nature of this analysis.
Results: This cohort included 211 RA patients: D2TRA-PIRRA (n=32), DT2RA-NIRRA (n=34), non-D2TRA (n=145). At least one EULAR comorbidity was present in 46% of patients (range 0 to 4). The most represented EULAR comorbidities were cardiovascular diseases (29.5%), osteoporosis (19.5%) and gastrointestinal diseases (8.0%). The number of EULAR comorbidities was similar across groups (p=0.581 by Kruskal-Wallis test), and it was moderately correlated with age at RA onset (r=0.439, p<0.0001). When separately analyzing each comorbidity, there were no significant differences yet a numerical increase in the prevalence of gastrointestinal diseases (15.6% vs 7.3% vs 0.0%, p=0.162) and serious infections (12.5% vs 6.0% vs 5.9%, p=0.328) in D2TRA-PIRRA compared to D2TRA-NIRRA and non-D2TRA patients (Figure 1A). With regard to comorbidities not encompassed in the EULAR domains, fibromyalgia was highly prevalent among D2TRA-NIRRA (23.5%) compared to DT2-RAPIRRA (3.1%) and non-D2TRA (2.7%) patients (p<0.0001; Figure 1A). Extra-articular manifestations were recorded in 27.2% of non-DT2RA, 25.0% of DT2RA-PIRRA and 17.62% of DT2RA-NIRRA (p=0.787), without significant differences in single manifestations. DT2RA-PIRRA patients had numerically more serositis, inflammatory eye disease, and interstitial lung disease than non-D2TRA, while D2TRA-NIRRA patients only showed features of serositis and Sjogren's syndrome (Figure 1B).



Conclusion: Fibromyalgia was associated with D2TRA-NIRRA. Otherwise, we did not find a strong association between comorbidities or extra-articular manifestations and D2TRA. There were trends for more serious infections, gastrointestinal diseases and extra-articular manifestations in D2TRA-PIRRA. Our results suggest that the current definition of D2TRA may not adequately identify DT2RA patients with a substantial burden of comorbidities.

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POS1075 RETENTION RATE OF BIOLOGIC AND TARGETED SYNTHETIC ANTI-RHEUMATIC DRUGS IN ELDERLY PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS: DATA FROM ITALIAN GISEA REGISTRY

Keywords: Safety, Comorbidities, bDMARD

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Background: An increased number of elderly patients with rheumatoid arthritis (RA) has been observed in the last years mainly due to the increase of life expectancy. In this group it is possible to include two different categories: patients with onset of RA in advanced age (60-65 years old), and patients with an early occurrence of RA aged with the disease. For all elderly patients many factors such as: comorbidities and polytherapy, extra-articular manifestations of RA, and the process of immune-senescence can increase frailty and difficulties for rheumatologist in management of RA. Although patients with late onset of RA frequently show more aggressive articular involvement and systemic manifestations, literature data suggest that rheumatologists tend to treat elderly patients less aggressively. Moreover, they delay treat to target approach with less frequent use of biologic drugs and prolonged use of steroids or NSAIDsThe improvement of knowledge about persistence of different drugs and associated patients' profiles could suggest more specific treatment strategies encouraging the correct management of RA elderly patients in clinical practice.

Objectives: Aim of the study was to evaluate the retention rate at two years of treatment with biologic or targeted synthetic (ts) DMARDs, namely TNF inhibitors, anti-IL6, anti-CD20, Abatacept and Janus kinases inhibitors (JAKis), in patients with RA who received a targeted therapy over 65 years of age.

Methods: Data were extracted from the GISEA registry (Gruppo Italiano Studio Early Arthritis), selecting RA patients in which biologic- or ts-DMARDs were prescribed over 65 years of age.

Global persistence in therapy and 2-year retention rate were evaluated by mean of Cox regression. Then, a multivariate analysis was performed to evaluate factors associated to the discontinuation of the treatment.

Results: We analysed data of 1221 patients (F/M ratio 966/255). Therapies prescribed were: TNFis in 362 pts (29.6%), anti-IL6 in 199 pts (16.3%), JAKi in 304 pts (24.9%), anti-CD20 in 53 pts (4.3%), abatacept in 303 pts (24.8%). Median time of persistence in therapy was 181 weeks (confidence interval 95% 158-205), with a significant difference among different classes of drugs (abatacept 254 weeks, CI95% 219-289; anti-CD20 221, 104-337; TNFis 184, 151-217; JAKis 139, 115-164; and anti-IL6 136, 105-167; p<0.001). Retention rate at two years was 66.3%± 3.8 for abatacept, 59.7%± 8.8 for anti-CD20, 54.9%± 3.7 for TNFis, 49.2%±0.5 for anti-IL6, 52.7%±3.7 for JAKis (Figure 1). A multivariate analysis including age, gender, class of drug, line of treatment, disease activity index on 28 joints (DAS28) was performed. Anti-citrullinated peptides antibodies, rheumatoid factor, combination therapy with glucocorticoids or methotrexate were excluded from the model, since not significant at univariate analysis. Multivariate analysis revealed that treatment with TNFis (HR 1.63 CI 1.01-2,63, p=0.044), treatment with anti-IL6 (HR 1.43 CI 1.11-1.85, p=0.006), an increase of 1 point of DAS28 (HR 1.21 CI 1.08-1.35, p=0.001) correlated with lower retention rate at two years. Among 1220 pts considered, 33.5% discontinued therapy. The most frequent cause of discontinuation for all drugs was a secondary loss of efficacy in 49.3% of cases.

Conclusion: In our study abatacept resulted the drug with the highest retention rate among drugs prescribed in elderly patients. On the other side, anti-IL6 showed the lowest persistence. Disease activity and the therapeutic choice may influence the retention rate. Our results on a very large population represent interesting points to consider for the choice of treatment for elderly RA patients. Prospective studies should be advisable to confirm these data.

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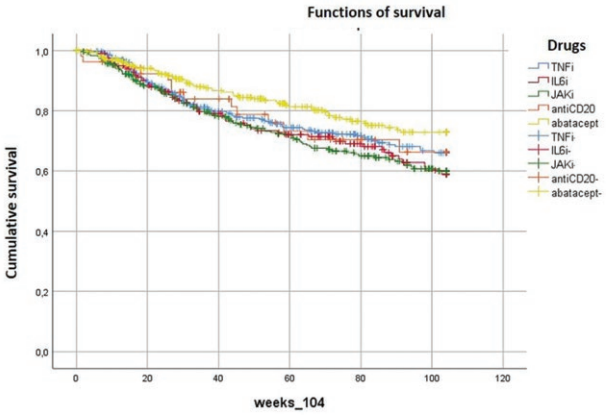


Figure 1.

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POS1076 ARE DISEASE-MODIFYING ANTIRHEUMATIC DRUGS FOR RHEUMATOID ARTHRITIS ASSOCIATED WITH A LOWER RISK OF DEMENTIA? A SYSTEMATIC REVIEW WITH META-ANALYSIS

Keywords: Comorbidities, Rheumatoid arthritis, bDMARD

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Background: Dysregulation of several inflammatory cytokines including tumor necrosis factor (TNF) in dementia patients has also been identified as a key factor in the pathogenesis of rheumatoid arthritis (RA). Existing epidemiologic evidence suggests an increased risk of incident dementia associated with RA. Modulating systemic inflammation with disease-modifying anti-rheumatic drugs (DMARDs) is hypothesized to attenuate the development of dementia.

Objectives: We aimed to investigate the association of DMARDs therapy for RA with risk of incident dementia.

Methods: Electronic database searches of PubMed, EMBASE and Cochrane Library were performed. Observational studies that assessed the association of dementia with DMARDs in RA were included. Pooled risk ratios (RRs) with 95%

confidence intervals (CIs) were used as summary statistic, with either fixed-effects or random-effects model. The certainty of evidence using the GRADE system.
Results: A total of 14 studies involving 940,442 patients with RA were finally included. Compared with conventional synthetic DMARDs, a 24% reduction in dementia risk was found with biological DMARDs overall (RR 0.76, 95% CI 0.72-0.80, n=9 studies), with 24% for TNF inhibitors (RR 0.76, 95% CI 0.71-0.82), 24% for non-TNF biologics (RR 0.76, 95% CI 0.70-0.83). There was a significant subgroup effect among different types of TNF inhibitors (RR 0.58, 0.65, 0.80 for etanercept, adalimumab, infliximab, respectively; P-value between groups=0.002). However, compared with nonusers of investigative treatment, no significant effect on dementia incidence was observed in those receiving conventional synthetic DMARDs overall (RR 0.84, 95% CI 0.59-1.20), methotrexate (RR 0.78, 95% CI 0.54-1.12), hydroxychloroquine (RR 0.95, 95% CI 0.63-1.44), except for sulfasalazine with its seemingly detrimental effect (RR 1.27, 95% CI 1.06-1.50).
Conclusion: Biological DMARDs for RA are associated with decreased risk of dementia, while the protective effect is not observed in conventional synthetic DMARDs. Future interventional studies may be worth considering.

Invetigative treatment	No. study	Risk ratio (95% CI)	I^2	Egger	Begg
Biological DMARDs	9	0.76 (0.72, 0.80)	14.4%	0.754	0.371
TNF inhibitors	7	0.76 (0.71, 0.82)	34.2%	0.552	0.902
Etanercept	3	0.58 (0.53, 0.65)	0.0%	0.461	1.000
Adalimumab	3	0.65 (0.59, 0.72)	0.0%	0.797	1.000
Infliximab	3	0.80 (0.72, 0.88)	0.0%	0.402	1.000
non-TNFi biologics	2	0.76 (0.70, 0.83)	0.0%	/	/
Conventional synthetic DMARDs	7	0.84 (0.59, 1.20)	94.6%	0.181	0.764
Methotrexate	5	0.78 (0.54, 1.12)	91.3%	0.213	0.806
Hydroxychloroquine	3	0.95 (0.63, 1.44)	81.3%	0.913	1.000
Sulfasalazine	3	1.27 (1.06, 1.50)	42.6%	0.441	1.000

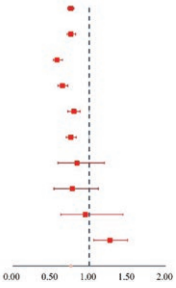


Figure 1. Meta-analysis of dementia risk associated with DMARDs in patients with rheumatoid arthritis.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1077

TIME TREND OF SEROPOSITIVITY IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS BETWEEN 2000 AND 2021: DATA FROM THE IORRA COHORT

Keywords: Rheumatoid arthritis, Real-world evidence

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Background: It has been reported that patients with rheumatoid arthritis (RA) differ in disease progression and responsiveness to treatment depending on their serological status. Examining time trends in serological status may lead to the recognition of changes in the phenotype of RA. Recent reports revealed that the incidence of rheumatoid factor (RF)-positive RA had been decreasing[1,2]. This needs to be further investigated in other registries and races; however, data from a large observational study of Japanese are lacking.
Objectives: We aimed to investigate the time trend of seropositivity in Japanese RA patients.
Methods: This is a retrospective study using data from the Institute of Rheumatology Rheumatoid Arthritis (IORRA) cohort. Among patients enrolled in the IORRA cohort between 2000 and 2021, patients with a disease duration of <3 years at enrolment were included. Seropositive status was defined as positive for rheumatoid factor (RF) (cut-off: 15 IU/mL) and/or anti-cyclic citrullinated peptide (CCP) antibody (second generation; cut-off: 4.5 U/mL). Patients with one negative and one unmeasured or both unmeasured were excluded. The time period was divided into 2000–2010 and 2011–2021. The effect of the time period on seropositivity was analyzed using multivariable analysis after adjusting for age, sex, smoking, and body mass index (BMI) at enrollment.
Results: Of 6,514 patients enrolled, 5,289 (81.2%) patients were female, and the median age was 54.9 (interquartile range: 44.0–64.5). 5,142 (88.2%) were seropositive, and the proportion of serological status differed between 2000–2010 (n=4,261) and 2011–2021 (n=2,004) (Figure 1). The proportion of seropositive patients was 90.2% in 2000–2010 and 84.0% in 2011–2021. The positivity for RF and anti-CCP antibody was decreased over time: 74.9% and 78.1% in 2000–2010 and 70.0% and 74.3% in 2011–2021, respectively. The time period (2011–2021) was associated with seronegativity (adjusted odds ratio [OR]: 1.51, 95% confidence interval [CI]: 1.24–1.83). Additionally, the time period (2011–2021) was also associated with RF negativity (adjusted OR: 1.44, 95% CI: 1.23–1.68) and anti-CCP negativity (adjusted OR: 1.30, 95% CI: 1.10–1.52).
Conclusion: Analysis of the IORRA cohort data revealed a decrease in seropositivity in Japanese patients with RA. The phenotype of RA in the clinical setting may have been changing over time.
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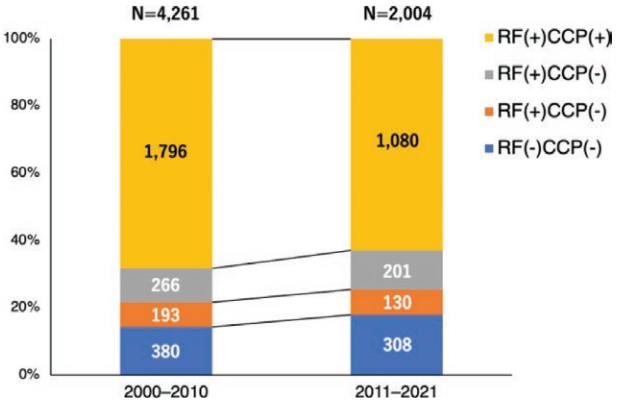


Figure 1. Time trend of the serological status in the study population. The number of each group was shown in the graph.

Acknowledgements: NIL.
Disclosure of Interests: Tomoaki Higuchi: None declared, Eiichi Tanaka Speakers bureau: AbbVie Japan GK; Asahi Kasei Corp.; Astellas Pharma Inc.; Ayumi Pharmaceutical Co.; Chugai Pharmaceutical Co., Ltd.; Eisai Co., Ltd.; Eli Lilly Japan K.K.; GlaxoSmithKline K.K.; Kyowa Pharma Chemical Co., Ltd.; Janssen Pharmaceutical K.K.; Mochida Pharmaceutical Co., Ltd.; Pfizer Japan Inc.; Takeda Pharmaceutical Co., Ltd.; and Teijin Pharma Ltd., Eisuke Inoue Speakers bureau: Bristol Myers Squibb Co., Ltd.; Pfizer Japan Inc.; Nippontect systems Co., Ltd.; RCR Co., Ltd., Mai Abe: None declared, Kumiko Saka: None declared, Eri Sugano: None declared, Naohiro Sugitani: None declared, Moeko Ochiai: None declared, Rei Yamaguchi: None declared, Katsunori Ikari Speakers bureau: Asahi Kasei Corp.; Astellas Pharma Inc.; AbbVie Japan GK; Ayumi Pharmaceutical Co.; Bristol Myers Squibb Co., Ltd.; Chugai Pharmaceutical Co., Ltd.; Eisai Co., Ltd.; Eli Lilly Japan K.K.; Janssen Pharmaceutical K.K.; Kaken Pharmaceutical Co. Ltd.; Mitsubishi Tanabe Pharma Co.; Pfizer Japan Inc.; Takeda Pharmaceutical Co. Ltd.; Teijin Pharma Ltd.; and UCB Japan Co. Ltd., Yamanaka Hisashi Consultant of: CorEvitas LLC, Masayoshi Harigai Speakers bureau: AbbVie Japan GK; AstraZeneca K.K.; Ayumi Pharmaceutical Co.; Boehringer Ingelheim Japan Inc.; Bristol Myers Squibb Co., Ltd.; Chugai Pharmaceutical Co., Ltd.; Eisai Co., Ltd.; Eli Lilly Japan K.K.; GlaxoSmithKline K.K.; Gilead Sciences Inc.; Janssen Pharmaceutical K.K.; Kissei Pharmaceutical Co., Ltd.; Nippon Kayaku Co., Ltd.; Nippon Shinyaku Co., Ltd.; Novartis Japan; Pfizer Japan Inc.; CIMIC Holdings Co., Ltd.; Mitsubishi Tanabe Pharma Co.; Teijin Pharma Ltd.; and UCB Japan Co. Ltd., Consultant of: AbbVie; Boehringer-Ingelheim; Bristol Myers Squibb Co.; Kissei Pharmaceutical Co., Ltd.; and Teijin Pharma Ltd., Grant/research support from: Grant/research support from: AbbVie Japan GK; Asahi Kasei Corp.; Astellas Pharma Inc.; Ayumi Pharmaceutical Co.; Boehringer Ingelheim Japan, Inc.; Bristol Myers Squibb Co., Ltd., Chugai Pharmaceutical Co., Daiichi-Sankyo, Inc., Eisai Co., Ltd.; Kaken Pharmaceutical Co., Ltd.; Kissei Pharmaceutical Co., Ltd.; Mitsubishi Tanabe Pharma Co.; Nippon Kayaku Co., Ltd.; Sekisui Medical; Taisho Pharmaceutical Co., Ltd.; and Teijin Pharma Ltd.
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POS1078

EFFECTS OF LONG-TERM LOW DOSE GLUCOCORTICOID TREATMENT FOR RHEUMATOID ARTHRITIS ON BODY WEIGHT AND BLOOD PRESSURE: A POOLED ANALYSIS OF INDIVIDUAL PATIENT DATA FROM FIVE RANDOMISED TRIALS

Keywords: Randomized control trial, Comorbidities, Rheumatoid arthritis

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Background: High-dose glucocorticoids (GCs) can cause weight gain and hypertension. It is unclear whether GCs at ≤7.5mg/d prednisone equivalent ("low dose"), administered for rheumatoid arthritis (RA), do as well. Prior studies could not definitively answer this research question: Observational studies are confounded by indication, and individual randomized trials (RCTs) are usually underpowered for small safety signals.

Objectives: To assess the effects of long-term treatment with low dose GCs in RA on body weight and blood pressure by pooling individual patient data from RCTs.

Methods: Data from five RCTs with two-year interventions were pooled.[1-5] All trials originated in Europe and allowed concomitant treatment with DMARDs. Intervention groups received GCs at a dose of ≤7.5mg/d prednisone equivalent, control groups received placebo or nothing. Co-primary outcomes were the difference in change from baseline in a) body weight (kg) and b) mean arterial blood pressure (MAP; mmHg). A secondary outcome was difference in the change of number of administered antihypertensive drugs. Several sensitivity and subgroup analyses were conducted. All analyses were based on analyses of covariance, trial ID was included as a random effects factor to account for clustering of patients within trials. Multiple imputation was used to account for missing data under the intention-to-treat approach. No imputations were performed for trials with no data collected or available for the given outcome. A detailed prespecified protocol (dx.doi.org/10.17504/protocols.io.x54v9y4d1g3e/v1) with a hierarchical statistical testing procedure was followed.

Results: 1,112 participants were included (mean ± SD age 61 ± 15 years; 68% female). A mean DAS28 of 4.87 ± 1.16 indicated moderate disease activity at baseline; disability was moderate to severe with a median (interquartile range) health assessment questionnaire score of 1.38 (0.80; 2.25). Median disease duration was 1 year (0.42; 7). Baseline values for weight and MAP were 73kg ± 14 and 98mmHg ± 12; median number of antihypertensive drugs was 0 (0; 1). After two years, patients on GCs gained mean 1.1kg (95%CI 0.5 to 1.8; p < 0.001; **Table 1**) more weight than patients in the control groups. Both groups increased MAP by 2-3mmHg, without difference between the groups (–0.4; 95% CI –3.0 to 2.2 mm Hg; p = 0.19; **Table 1**). The change in number of antihypertensive drugs was low and similar in both groups (**Table 1**). Results were consistent across sensitivity and subgroup analyses focusing on overweight or hypertensive patients, and when comparing GCs at 5mg/d with 7.5mg/d (data not shown).

Conclusion: We present robust evidence that low dose GCs, taken over two years for the treatment of RA, lead to about one additional kg of weight gain but do not cause changes in blood pressure.

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Table 1. Changes in weight and mean arterial blood pressure in GC and control groups over two years.

	n	GC group n		Control group	Contrast	P value
Weight, kg	547	1.9 (0.8)	565	0.7 (0.8)	1.1 (0.5 to 1.8)	<0.001
Mean arterial blood pressure, mmHg	429	2.3 (1.3)	433	2.7 (1.4)	–0.4 (–3.0 to 2.2)	0.19
Number of antihypertensive drugs*	276	0 (0;0)	282	0 (0;0)	0 (0 to 0)	**

Values are least squares mean changes (SE), and differences in least squares mean changes (95% confidence intervals), unless otherwise stated.* Non-normal distribution: the group estimates are median changes (inner quartiles), and effect estimate is the median of differences between the two groups with corresponding 95% CIs, with no imputation for missing data and ignoring the grouping within studies. Analysis on the studies separately, and separate analyses on each imputed dataset showed similar results.** In line with the study protocol, no significance test was performed for this secondary outcome.

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POS1079 COMPARISON OF CHOLESTEROL PROFILE CHANGES AFTER TREATMENT WITH BIOLOGICS OR JANUS KINASE INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, bDMARD, Comorbidities

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Background: Janus kinase inhibitor (JAKi) and tumor necrosis factor inhibitor (TNFi) both effectively reduce inflammation, and both increases serum lipid levels. However, in the recent phase 3b-4 trial, major adverse cardiovascular events were higher with tofacitinib than TNFi. Cholesterol is still primary to the development of atherosclerosis, which collaborates with inflammation. Even in the young population, mildly abnormal lipid levels were associated with an increased future risk of atherosclerotic cardiovascular disease events.

Objectives: To assess the effects of biological and targeted synthetic disease-modifying anti-rheumatic drugs (DMARDs) on lipid profiles in patients with moderate-to-severe rheumatoid arthritis (RA).

Methods: This retrospective single-center observational study included patients with RA who initiated and maintained tumor necrosis factor-α inhibitor (TNFi), abatacept, tocilizumab, and Janus kinase inhibitor (JAKi) for at least 6 months. Changes in lipid profile were assessed at months 3 and 6, and associations with clinical efficacy, concomitant medications, and co-morbidities were evaluated.

Results: This study included 114 patients treated with TNFi, 81 patients with abatacept, 103 patients with tocilizumab, and 89 patients with JAKi. Median percent change from baseline to 6 months in total cholesterol, low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C levels were higher in tocilizumab and JAKi versus TNFi and abatacept recipients (16% and 15% vs 6% and 3%, 19% and 24% vs 8% and 3%, 5% and 9% vs 3% and 0%, 19% and 19% vs 7% and 8%, respectively). The significant change in non-HDL-C was associated with JAKi (versus TNFi, OR, 2.671; 95% CI, 1.44–4.956), tocilizumab (versus TNFi, OR, 1.996; 95% CI, 1.087–3.665), concomitant glucocorticoids (OR, 2.802, 95% CI 1.344–5.843), and statin (OR, 0.419; 95% CI 0.230–0.765), and presence of rheumatoid factor (OR, 3.252, 95% CI, 1.029–10.276). However, the change in disease activity in 28 joints was not associated with a significant non-HDL-C change.

Conclusion: Regardless of disease activity changes, tocilizumab and JAKi-associated increases in serum non-HDL-C levels were observed. Combination with glucocorticoids may induce elevations in non-HDL-C, whereas statins may decrease in non-HDL-C.

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Disclosure of Interests: None Declared.

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POS1080

THE IMPACT OF SYNOVITIS OF INDIVIDUAL FINGER JOINTS ON GRIP FORCE OVER THE FIRST FIVE YEARS IN EARLY RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) has a major impact on hand function in many patients. Information on the contribution of individual joints to impaired grip strength may be helpful for guiding individualized management.
Objectives: The objective of this study was to investigate the relation between swelling and tenderness of individual finger joints and grip force over time in patients with early RA.
Methods: An inception cohort of patients with early RA (symptom duration ≤12 months), recruited in 1995-2005, was investigated and followed in a structured program, with follow-up evaluations after 1 and 5 years. All patients were examined by the same rheumatologist according to a structured protocol. Grip force (Newton) was measured using the electronic instrument Grippit (AB Detektor, Gothenburg, Sweden). Average grip force values of each hand were evaluated and compared to the expected, based on age- and sex-specific reference values from the literature [1]. Grip force was expressed as % of expected values. Generalized estimating equations were used to assess the relation between finger joint synovitis and grip force over time. With repeated measures of grip force as the dependent variable, we investigated whether time-varying synovitis of individual metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints were associated with reduced grip force over time. As wrist involvement, high erythrocyte sedimentation rate (ESR) and severe patient reported pain have been independently associated with reduced grip force in early RA (2), the analyses were adjusted for these parameters as time-varying covariates.
Results: A total of 215 patients with early RA (71 % women; mean age 60 years) were investigated. The median symptom duration at inclusion was 7 months; interquartile range 5-10. Clinical synovitis was most frequently observed in MCP I and MCP II (>60% at inclusion in both hands), and less in MCP IV and V (12-13% at baseline). Swelling of individual PIP joints was observed in 16-34% of patients at inclusion. Swollen joint counts (of 28 joints) decreased over time (median 7, interquartile range (IQR) 5-11 at diagnosis; median 4, IQR 4-7 after 5 years), and there was a parallel increase in grip force (mean 39% of expected for both hands at inclusion, 56% for the right hand and 55% for the left hand after 5 years). Synovitis of MCP I and MCP IV was significantly associated with reduced grip over time in both hands, with a similar finding for MCP V in the left hand only (Table 1). PIP synovitis had a lower impact on grip force (Table 1).

Table 1. Relation between synovitis of individual MCP and PIP joints and grip force (% of expected) over the first five years after diagnosis of RA; β (95 % CI), adjusted for wrist synovitis, ESR and VAS pain

	Right hand	Left hand
Synovitis		
MCP I	**-5.0 (-8.3 to -1.7)**	**-3.7 (-6.6 to -0.8)**
MCP II	-1.7 (-4.9 to 1.5)	-1.7 (-4.8 to 1.4)
MCP III	-1.2 (-4.4 to 2.0)	-0.4 (-3.3 to 2.4)
MCP IV	**-4.7 (-9.3 to -0.2)**	**-6.1 (-10.9 to -1.4)**
MCP V	-3.0 (-7.7 to 1.7)	**-6.0 (-10.2 to -1.8)**
PIP I	0.8 (-4.5 to 6.1)	-2.4 (-6.7 to 1.9)
PIP II	0.3 (-3.3 to 3.9)	-1.8 (-5.6 to 1.9)
PIP III	0.7 (-2.6 to 4.0)	-0.6 (-4.4 to 3.3)
PIP IV	-0.3 (-4.4 to 3.9)	0.1 (-4.2 to 4.3)
PIP V	-3.0 (-8.1 to 2.2)	1.1 (-4.6 to 6.9)

MCP: Metacarpophalangeal joint
PIP: Proximal interphalangeal joint

Conclusion: MCP synovitis of the thumb is common in early RA, and a major contributor to reduced grip force over the first 5 years. Although less frequent, involvement of MCP IV and MCP V may also have a significant impact on hand function. Despite improvement, grip force was still impaired 5 years after RA diagnosis. This underlines the importance of both efficient treatment of synovitis and structured hand training in early RA.
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POS1081

SERONEGATIVE RHEUMATOID ARTHRITIS (RA) – IS IT REALLY RA?

Keywords: Rheumatoid arthritis

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Background: The 2010 rheumatoid arthritis (RA) classification criteria are intended for research purposes and classification of the disease and not for diagnostic purposes. It is however a tool which clinicians commonly use in everyday practice when evaluating patients with arthritis. It is clearly stated in the criteria that the synovitis should not be better explained by another disease. However, some patients who are classified as seronegative RA might still have an alternative diagnosis, such as psoriatic arthritis, chronic gout or pseudogout, polymyalgia rheumatica etc. Misclassification has direct impact on treatment, prognosis and follow up of patients, but also on research projects. Increased attention and constant re-evaluation should be embraced in this group of patients to avoid misclassification and promote optimal treatment.
Objectives: To assess the frequency of patients classified as seronegative RA that have a potential alternative diagnosis that could better explain the arthritis.
Methods: This is an observational cohort study including adult patients classified as rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) negative RA (symptom duration < 1 year), based on ICD-10-SE (M06.0, M06.0M), and without typical RA radiographical changes, between 2015-2019 at Karolinska University hospital. Patients were identified from the Swedish Quality Rheumatology register (SRQ) and had a minimum of 2 years follow-up after RA diagnosis. Additional medical information was collected from the medical charts retrospectively. Patients were re-classified in 6 different groups: G1: presence of symptoms and signs typical for crystal arthritis (gout or pseudogout), and/or hyperuricemia and/or typical ultrasound and/or x-ray changes; G2: symptoms typical for PMR – fulfilment of PMR criteria at the time of RA diagnosis or before; G3: diagnosis of systemic inflammatory disease after RA diagnosis (SLE, myositis, systemic sclerosis, etc); G4: cancer diagnosis one year before or after RA diagnosis; G5: signs of seronegative spondylarthritis (i.e. diagnosis of psoriasis before or after RA diagnosis, development of inflammatory back pain, presence of dactylitis +/- enthesitis); G6: no other diagnosis than seronegative RA which can better explain the polyarthritis.
Results: A total of 229 patients received a diagnosis of RA and fulfilled the criteria (double-seronegativity and absence of radiographical changes) during 2015-2019 and were included in the study. Approximately 85% of the patients had at least 3 years and 50% at least 5 years of follow-up time. The percentage of patients who were re-classified in the 6 subgroups as described above were: G1 = 6.6%, G2 = 6.5%, G3 =3.1%, G4 =7.4%, G5 = 4.4% and G6 =72%.
Conclusion: In this observational study almost one third of patients who received a diagnosis of seronegative RA have an alternative diagnosis than RA that can explain the arthritis, with paramalignant phenomenon, PMR and crystal arthritis being the most common. Increased vigilance in the subgroup of seronegative, non-erosive RA patients is important and constant consideration of differential diagnoses is warrantied.
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Acknowledgements: NIL.
Disclosure of Interests: Emma Birgersson Wettersand: None declared, Katerina Chatzidionysiou Grant/research support from: Research grant: Galapagos.
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POS1082

JOINT INVOLVEMENT IN RA STARTS PREDOMINANTLY IN THE HANDS: FUNCTIONAL, CLINICAL AND IMAGING STUDIES IN CLINICALLY SUSPECT ARTHRALGIA AND DURING PROGRESSION TO RA

Keywords: Rheumatoid arthritis

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Background: At time of Rheumatoid arthritis (RA) diagnosis, patients typically present with clinical arthritis of hand and foot-joints. It is unknown whether RA starts in hands or feet.
Objectives: To investigate this, we performed functional, clinical and imaging studies during progression from clinically suspect arthralgia (CSA) to RA. We also studied whether functional disabilities of hands/feet in CSA contribute to predicting RA-development.
Methods: 600 CSA-patients were followed for development of clinical inflammatory arthritis (IA) during a median follow-up of 25 months, of whom 99 developed IA. Functional disabilities were measured at baseline/4/12/24 months with the Health Assessment Questionnaire Disability-Index (HAQ); HAQ-items assessing hand- and foot-disabilities were selected. The course of disabilities towards IA-development (here considered as t=0) was depicted by increasing incidences and analysed using linear mixed models. To evaluate robustness of findings, tender hand/foot joints and subclinical joint-inflammation (measured with CE-1.5TMRI of hand/foot) were additionally studied. Associations between disabilities at CSA-presentation (here t=0) and future IA-development were studied using Cox-regression in the total CSA-population.
Results: During IA-development, hand-disabilities occurred earlier and more frequently than foot-disabilities. Despite both hand- and foot-disabilities rose significantly towards IA-development, hand-disabilities were more severe during this course (mean difference over time: 0.41 units,95%CI=0.28-0.55,p<0.001, on a range 0-3). Similar to functional disabilities, tender joints and subclinical joint-inflammation occurred earlier in the hands than feet (Figure 1). In the total CSA-population, a single HAQ-question on difficulties with dressing (hand-functioning) was independently predictive for IA-development: HR=2.2,95%CI=1.4-3.5,p=0.001.
Conclusion: Evaluation of functional disabilities, supported by clinical and imaging findings, revealed that joint involvement starts predominantly in the hands during RA-development. Additionally, a single question on dressing-difficulties adds value to risk stratification in CSA-patients and is easy to use in clinical practice.

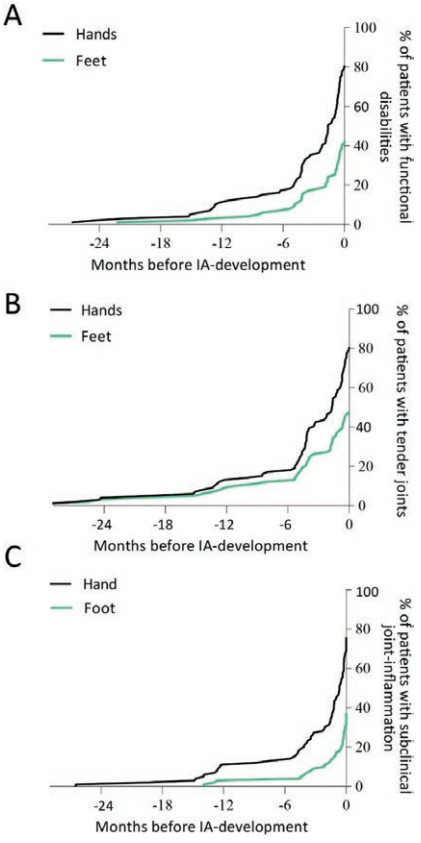


Figure 1. Functional disabilities (A), tender joints (B) and subclinical joint-inflammation (C) towards IA-development occur earlier and more frequently in the hands than in the feet lines depict the increasing incidence of functional disabilities (HAQ), tender joints (physical examination) and subclinical joint-inflammation (MRI-detected) in the hands and feet prior to development of inflammatory arthritis.Abbreviations: HAQ= Health Assessment Questionnaire; IA= inflammatory arthritis.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1083

DIFFICULT TO TREAT INFLAMMATORY ARTHRITIS: MAKING THE DEFINITION MORE PRECISE AND TIME FRAMED

Keywords: Outcome measures, Remission, Rheumatoid arthritis

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Background: Management of difficult to treat (D2T) inflammatory arthritis requires meticulous evaluation for the presence or absence of inflammation to support pharmacological and non-pharmacological management strategies. The challenge arises from the finding that D2T has been linked to a variety of characteristics. The EULAR Task Force has recently defined D2T rheumatoid arthritis as patients having persistency of symptoms and/or signs despite failure of at least two biological or targeted synthetic disease modifying anti-rheumatic drugs with different mechanisms of action. However, the proposed EULAR Task Force definition of D2T was based on just one assessment at one moment of time, during which flare up of the disease may not be reflective of the actual disease activity status.
Objectives: To address the unmet needs and derive a comprehensive, yet precise, approach to define the inflammatory arthritis patients who are "Difficult-to-Treat".
Methods: Five key clinical questions including 20 domains were identified by core scientific committee. Literature Review team performed a systematic review to summarize evidence advocating the D2T definition, assessment and management, as well as benefits and harms of available pharmacologic and non-pharmacologic therapies. Subsequently, recommendations were formulated. The level of evidence was determined for each section using the Oxford Centre for Evidence-based Medicine (CEBM) system. A 3-round Delphi process was conducted. All rounds were conducted online. Consensus, consequently, to become a recommendation, would be achieved if at least 80% of participants reached agreement (score 7-9). A consensus was achieved on the direction and the strength of the recommendations.
Results: The work proposed an inclusive definition of D2T in inflammatory arthritis based on 4 pillars: "persistent inflammation that continues to cause significant burden despite standard treatment as perceived by the treating rheumatologist and/or the patient". Two extra factors have been suggested to be added to the EULAR definition. These are "disease burden" and "timeframe" for the assessment of the disease activity status. "Continuous disease burden" has been defined as having difficulties in: Achieving treatment target, controlling disease progression, sustained elevation of the acute phase response over 3 months period attributed to the inflammatory joint disease, lack of functional restoration and poor quality of life despite good

symptomatic control, and treatment compliance due to: unacceptable tolerability or non-adherence or rejection of the treatment option. Time frame has been identified as: persistent joint inflammation (active/progressive disease") has been documented according to validated composite measures including joint counts in 2-readings, 3-months apart. Level of agreement was high and in the range of 8.17-8.83).

Conclusion: this study revealed a consensus that time factor is vital to consider inflammatory arthritis as persistent, hence meet the difficult to treat definition. Adding the "continuous disease burden has added another dimension to the management of D2T, advocating a more holistic approach toward the patient rather than observing a patient through the prism of the index disease.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1084 EFFECT OF RHEUMATOID ARTHRITIS ON TOTAL KNEE ARTHROPLASTY

Keywords: Rheumatoid arthritis

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Background: According to the results of previous studies, it has been reported that rheumatoid arthritis (RA) patients receive total knee arthroplasty (TKA) at a younger age than osteoarthritis (OA) patients. However, studies on the effect of RA on TKA are still insufficient.

Objectives: We conducted this study to find out how RA affects primary TKA and revision arthroplasty.

Methods: The data of OA and RA patients who underwent primary TKA and revision at Jeju National University Hospital between March 2003 and December 2022 were retrospectively analyzed. To exclude the effect of other connective tissue diseases, patients with SLE, Sjogren's syndrome, polymyalgia rheumatica, mixed connective tissue disease, undifferentiated connective tissue disease, Behcet's disease, systemic sclerosis, and vasculitis were excluded.

Results: A total of 5245 TKAs were performed, and the average age at primary TKA was 72.4 ± 6.4 years, and 2292 (85.7%) were female. When they were divided into OA group and RA group, RA knees were 159 (3.1%). The age at primary TKA in the RA group was significantly smaller (69.6 ± 6.8 vs 72.5 ± 6.4, p<0.001), and the female ratio was higher (91.9% vs 85.5%, P=0.031). Although the rate of revision surgery was not statistically significant, the RA group had more (5.6% vs 3.1%, p=0.111), and the period to revision tended to be shorter in the RA group (33.8 ± 49.2 months vs 67.7 ± 56.1 months). month, p=0.078). The cause of reoperation was not significantly different between the two groups, but the rate of infection was higher in the RA group (55.6% vs 43.7), and reoperation due to loosening was more common in the OA group (46.2% vs 22.2%). There was no difference in other test values at the time of surgery, but in the RA group, ESR (43.8 ± 31.7 mm/h vs. 26.6 ± 22.6 mm/h, P<0.001), CRP (1.8 ± 2.3 mg/dL vs. 0.8 ± 2.1 mg/dL, p<0.001) was significantly higher. The incidence of TKA was higher in the RA patients than OA patients (1436.2 per 100,000 Person-Years vs 1379.7 per 100,000 Person-Years). When comparing the risk of patients undergoing primary TKA during their lifetime by adjusting for gender, it was found that RA patients started receiving primary TKA at a younger age and had a significantly higher risk of undergoing TKA (HR 1.48, 95% CI 1.263–1.733, P<0.001). As a result of logistic regression analysis, the increase in ESR (OR 10.2, 95% CI 1.01-1.03, P=0.001) and CRP (OR 1.09, 95% CI 1.01-1.17, P=0.021) at the time of primary TKA increase risk of revision arthroplasty, but RA did not.

Conclusion: Patients with RA have a higher risk of primary TKA and start primary TKA at a younger age, and the increased inflammation level at the time of primary TKA increase risk of revision arthroplasty, so it is recommended to perform primary TKA after inflammation is controlled.

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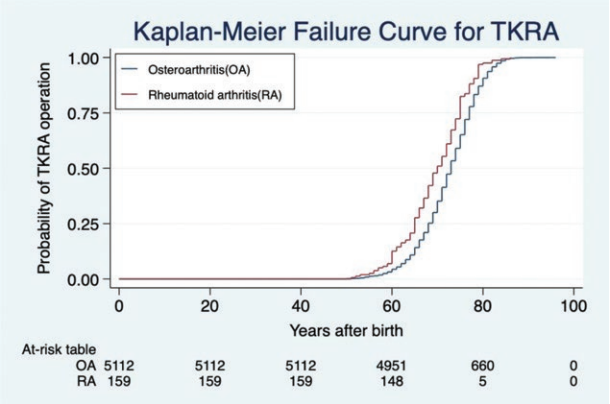


Figure 1.

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Disclosure of Interests: None Declared.

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POS1085 INITIATION OF A JANUS KINASE INHIBITOR BEFORE AND AFTER THE SAFETY WARNINGS: CHANGES IN CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Registries, Comorbidities, Disease-modifying drug (DMARDs)

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Background: In 2019, 2020 and 2021, the European and US-American regulatory agencies issued warnings about venous thromboembolism, major cardiovascular events and malignancy risks associated with the Janus kinase inhibitor (JAKi) tofacitinib and required changes in labelling.

Objectives: To investigate whether characteristics of patients with rheumatoid arthritis receiving a JAKi versus biologic therapy differed before and after the safety warnings.

Methods: Data from patients who started with any JAKi or biologics treatment in the German biologics register RABBIT between 01/2017 and 04/2022 were included. Multivariate logistic regression analyses were used to understand differences in characteristics of patients starting a JAKi treatment versus a biologic treatment in three annual cohorts: 2017 the year JAKis became available in Germany, 2019 before the EMA safety warnings and 2021. In each year, only the first treatment episodes of each JAKi, TNF inhibitor, interleukin-6 inhibitor or B/T-cell targeted therapy were considered. Prior treatment episodes were possible. The logistic regressions were corrected for clustering at the patient level. In 2017, we included 549 JAKi versus 2510 bDMARD treatment episodes, in 2019 674 versus 2233 and in 2021 700 versus 1296 episodes.

Results: Patient characteristics at treatment start have changed over time. In 2017, compared to patients receiving a biologic, patients starting a JAKi had been treated with a higher number of therapies, had a higher (worse) physician reported heath and were more likely to have comorbidities such as hypertension, coronary heart disease, diabetes, hyperlipoproteinaemia, thrombosis, malignancy or lymphoma. In 2019, patients initiating a JAKi therapy compared to a biologic were less likely to be women, had a worse physician reported health and were more likely to receive a dose of less than 10mg glucocorticoids than none. In 2021, after the safety warnings, compared to patients receiving a biologic, those who started a JAKi were older, had a worse physician reported health, had received a higher number of previous therapies, had poorer self-reported health and were less likely to receive a high dose of glucocorticoids. Although not significant, patients with comorbidities were less likely to receive a JAKi.

Conclusion: The analyses show that after the launch of JAKi treatment in 2017, comorbidities increased the likelihood to receive JAKis as a new treatment option. In 2021, patients with a high disease burden and with many other previous therapies were more likely to receive JAKis, but not those with comorbidities. This development shows that rheumatologists in Germany follow the safety recommendations and consider the patients' disease burden and risk factors when prescribing JAKis.

Table 1. Odds Ratios of the logistic regressions for treatment start of a JAKi compared to a bDMARD in 2017, 2019, 2021

	Year of treatment start		
	2017	2019	2021
	OR LogReg (95%CI)		
intercept	0.10	0.25	0.24
Ref: age <50			
50-65	1.00 (0.77-1.31)	1.27 (0.99-1.64)	1.50 (1.14-1.97)
65+	0.81 (0.60-1.10)	1.15 (0.86-1.53)	1.51 (1.11-2.05)
sex (m vs. f)	0.96 (0.76-1.20)	0.74 (0.60-0.91)	1.03 (0.83-1.26)
Relevant comorbidities*	1.37 (1.10-1.70)	1.16 (0.96-1.40)	0.86 (0.70-1.06)
Seropositivity	0.95 (0.76-1.19)	0.98 (0.13-1.20)	1.16 (0.93-1.45)
disease duration	0.99 (0.98-1.00)	0.99 (0.98-1.00)	1.00 (0.99-1.01)
#previous b/tsDMARDs	1.37 (1.30-1.44)	1.02 (0.98-1.07)	1.18 (1.12-1.25)
physician global health (0-10)	1.16 (1.10-1.22)	1.09 (1.04-1.14)	1.08 (1.03-1.13)
patient global health (0-10)	0.95 (0.89-1.01)	1.02 (0.97-1.08)	0.95 (0.90-1.00)
% of full physical function	1.00 (0.99-1.00)	1.00 (0.99-1.00)	1.00 (0.99-1.00)
Ref: 0 mg/d glucocorticoids			
>0-<10 mg/d	0.89 (0.70-1.12)	1.27 (1.05-1.54)	1.01 (0.83-1.24)
>=10 mg/d	0.75 (0.54-1.03)	1.01 (0.75-1.37)	0.70 (0.50-0.98)

*≥ 1 comorbidity mentioned in the safety warnings (hypertension, coronary heart disease, diabetes, hyperlipoproteinaemia, thrombosis, malignancy, lymphoma)

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POS1086 **WITHDRAWN**

Public health, health services research, and health economics

POS1087

EFFICACY OF PHARMACOLOGICAL INTERVENTIONS: A SYSTEMATIC REVIEW INFORMING THE 2023 EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF FATIGUE IN PEOPLE WITH INFLAMMATORY RHEUMATIC AND MUSCULOSKELETAL DISEASES

Keywords: Patient reported outcomes, Systematic review, bDMARD

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Background: There is evidence that pharmacological interventions, including biologic therapies, can improve inflammation, disease activity and function in inflammatory rheumatic and musculoskeletal diseases (I-RMDs), and fatigue has increasingly been included as a secondary outcome of I-RMDs clinical trials. However, no systematic review (SR) has established the evidence for the pharmacological management of fatigue in people with I-RMD [1,2].
Objectives: To identify the best evidence on the efficacy of pharmacological interventions in reducing fatigue in people with I-RMDs and to summarise their safety in the identified studies to inform EULAR recommendations for the management of fatigue in people with I-RMD.
Methods: Systematic review of adults with I-RMD conducted according to the Cochrane Handbook. Search strategy ran in Medline, Embase, Cochrane Library, CINAHL Complete, PEDro, OTseeker and PsycINFO. Assessment of risk of bias, data extraction, and synthesis performed by two reviewers independently. Data pooled in statistical meta-analyses.
Results: From a total of 4,150 records, 454 were selected for full-text review, 105 fulfilled the inclusion criteria, and 19 RCTs were included in meta-analyses. Adalimumab was superior to placebo in reducing fatigue at 52 and 12 weeks (wk) in rheumatoid arthritis (RA) (mean difference [MD]=-2.25, p=0.03; MD=-3.03, p<0.001; respectively) and psoriatic arthritis (MD=-3.16, p=0.26). Golimumab (24wk: MD=-5.27, p<0.001), baricitinib (24wk: MD=-4.06, p<0.001), sarilumab (24wk: MD=-3.15, p<0.001), tocilizumab (24wk: MD=-3.69, p<0.001) and tofacitinib (12wk: MD=-4.44, p<0.001) were also superior to placebo in reducing fatigue in RA. A dose/effect relationship was observed for sarilumab, tocilizumab and tofacitinib. In spondyloarthritis, secukinumab was superior to placebo in reducing fatigue at 16wk (MD=-4.15, p<0.001), with a dose/effect relationship also observed (**Figure 1**). The narrative results of the RCTs not included in the meta-analysis indicated that several other pharmacological interventions were efficacious in reducing fatigue, with reassuring safety results.
Conclusion: Pharmacological interventions are efficacious and safe for the management of fatigue in people with I-RMD.

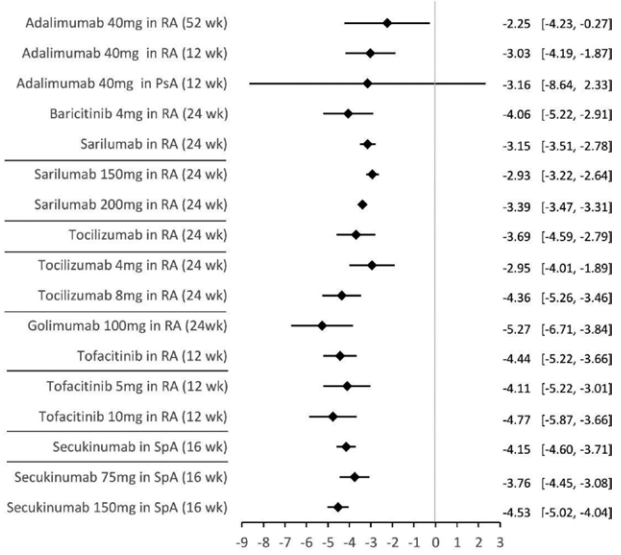


Figure 1. The summary of the meta-analyses, PsA: Psoriatic arthritis, RA: Rheumatoid arthritis, SpA: Spondyloarthritis, wk: weeks

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POS1088

THE PATIENT-PERSPECTIVE AND FEASIBILITY OF HOME FINGER PRICK TESTING TO COMPLEMENT AND FACILITATE LARGE SCALE DIGITAL DATA COLLECTION

Keywords: Health services research, Inflammatory arthritides, Patient reported outcomes

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Background: Previous studies have shown that using a finger prick as the primary method for blood withdrawal is an efficient way to collect blood samples remotely, and data on blood levels from a finger prick are directly comparable to that obtained by a venepuncture. During the COVID-19 pandemic, we therefore complemented our large digital research platform with serum collection via a home finger prick testing in order to collect samples without the need of visits to a hospital. This repeatedly enabled us to rapidly answer new and relevant clinical research questions about COVID-19, thereby showing the potential of the finger prick for research purposes. However, the use of finger pricks in a research or clinical practice setting is still uncommon, and not yet tested on a large scale. In addition, there is limited data on peoples' willingness and ability to successfully use the finger prick at home, especially in patients with inflammatory rheumatic diseases (iRD) who may have impaired hand function.
Objectives: To investigate the feasibility of finger prick testing in combination with a digital research platform by evaluating the success rate and patients' perspective towards the use of the finger prick.
Methods: Data were collected from an ongoing prospective cohort study including patients with iRD from the Amsterdam Rheumatology & immunology Center and healthy controls. Serum samples were collected up to eight times during follow-up via blood withdrawal by venepuncture at the local research institute or via a finger prick that could be performed at home. For the latter option, participants were instructed to collect three drops of blood, which would yield approximately 40-80 µL of serum after clotting. All study participants were questioned about their preference for a particular sampling method for individual healthcare and for scientific research. Participants who received a finger prick test before June 26, 2021, were asked to complete a digital evaluation questionnaire of the finger prick after their attempt. The finger prick was defined as failed when less than 10 µL of serum could be recovered from the collection device, or if no sample was returned to the laboratory and participants indicated in the questionnaires that they did not succeed in collecting the required amount of serum.
Results: A total of 3080 patients with iRD and 1102 healthy controls were included in the study. Of these, 2135 (69%) patients and 899 (82%) controls attempted to execute at least one finger prick, and 1439 (67%) patients and 712 (21%) controls executed multiple finger pricks. The first finger prick was successfully done by 92% (CI 90 – 93) of iRD patients, 94% (CI 92 – 95) of healthy controls, 93% (CI: 92 – 94) of all participants aged 70 years or younger, and 89% (CI 86 – 92) of all participants aged above 70 years (Table 1). Sex did not impact

these success rates. Repeated failure occurred in 11 of 1439 (0.8%) patients and 4 of 712 (0.6%) controls. The two most common reasons for perceived failure of the finger prick were related to insufficient blood yield when applying the finger prick. Finally, both patients and controls were less willing to perform a finger prick for individual healthcare compared to scientific research; 31% of patients and 61% of controls were willing to perform a finger prick for scientific research compared to 19% of patients and 39% of controls for healthcare. The most important reason for this was lower confidence in the execution and laboratory measurements when blood was drawn via a venepuncture compared to a finger prick.

Conclusion: In this study, we demonstrated that the vast majority of participants, among which elderly and patients of whom hand function may be impaired by an underlying rheumatic disease, were able to successfully draw the required amount of blood for serological analyses. This shows that the finger prick testing is suitable for a high-throughput implementation to monitor patients remotely, which will likely contribute to improving the efficiency and cost-effectiveness of both healthcare and scientific research.

Table 1. Success rate for the first, second and third execution of the finger prick

	First execution			Second execution			Third execution		
Patient characteristics	**No. successful executions**	**%**	**(95% CI)**	**No. successful executions**	**%**	**(95% CI)**	**No. successful executions**	**%**	**(95% CI)**
Disease status									
Healthy controls	842/899	**94**	(92 – 95)	681/712	**96**	(93 – 97)	473/481	**98**	(97 – 99)
Rheumatic IMID patients	1959/2135	**92**	(90 – 93)	1388/1439	**96**	(95 – 97)	888/902	**98**	(97 – 99)
Age									
< 70	2314/2488	**93**	(92 – 94)	1712/1774	**96**	(96 – 97)	1122/1137	**99**	(97 – 99)
≥ 70	487/546	**89**	(86 – 92)	357/377	**95**	(92 – 97)	239/246	**97**	(94 – 99)
Sex									
Male	932/1020	**91**	(89 – 93)	638/668	**95**	(94 – 97)	402/410	**98**	(96 – 99)
Female	1869/2014	**93**	(92 – 94)	1431/1483	**96**	(95 – 97)	959/973	**99**	(98 – 99)

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Rheumatoid arthritis - comorbidity and clinical aspects

POS1089

PSYCHOLOGICAL DISTRESS OVER 12 MONTHS POST-DIAGNOSIS IN A NATIONAL EARLY INFLAMMATORY ARTHRITIS COHORT

Keywords: Mental health, Inflammatory arthritides, Patient reported outcomes

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Background: In inflammatory arthritis patients, the concomitant decline of their mental wellbeing is an increasing concern[1,2]. It is important to not only describe the trajectory of psychological distress in early disease stages, but also understand which clinical outcome measures are most associated with these changes.

Objectives: Using data from the National Early Inflammatory Arthritis Audit (NEIAA), we assessed trends in psychological wellbeing over 12 months after initial diagnosis and mapped these against clinical outcomes to identify significant associations.

Methods: NEIAA collects data from patients referred with suspected early inflammatory arthritis in rheumatology services in England and Wales. We used data provided by 20,472 patients eligible for follow-up (diagnosis of inflammatory arthritis) between May 1st, 2018, and April 1st, 2022. Data items included baseline demographics e.g., age and gender, and clinical variables e.g., rheumatic disease comorbidity index (RDCI), DAS28, and patient reported outcomes. Psychological distress was measured by the sum score of Patient Health Questionnaire Anxiety and Depression Screener (PHQ4ADS). Using mixed effects regression models, we analysed the co-variability of PHQ4ADS with demographic factors and clinical outcomes over 12 months. Time was included as a dummy-coded covariant.

Results: The analysis included 36% of patients (7,378 out of 20,472) who completed the baseline patient outcome survey. In this cohort, PHQ4ADS scores decreased from a baseline average of 4.7 (CI: [4.6, 4.8]) to 2.62 (CI: [2.5, 2.8]) at 12 months post-diagnosis. The proportion of patients screening positive decreased from 50.0% (CI: [48.9, 51.1]) at baseline to 23.8% (CI: [21.8, 25.9]) at 12 months. At baseline, psychological distress correlated significantly with age, gender, ethnicity, RDCI, prior depression diagnosis, and baseline DAS28 (Figure 1). No significant correlations were found between psychological distress and working diagnosis, seropositivity, or the assessment being recorded after the start of the COVID-19 pandemic. Younger ages were nonlinearly associated with higher distress levels (coefficient per decade: -0.006; p<0.001; CI: [-0.009, -0.003]) (Figure 1a). Distress levels in females were higher than that of males (coefficient: 0.5; p<0.001; CI: [0.4, 0.7]) (Figure 1b). White patients reported lower PHQ4ADS scores compared to non-white patients (coefficient: -0.7; p<0.001; CI: [-1.0, -0.4]) (Figure 1c). Higher distress levels were also associated with higher RDCI (coefficient: 0.2; p<0.001; CI: [0.1, 0.3]) and prior diagnosis of depression (coefficient: 1.8; p<0.001; CI: [1.5, 2.2]) (Figure 1d, 1e). Furthermore, higher baseline DAS28 scores correlated with more severe psychological distress (coefficient: 0.8; p<0.001; CI: [0.7, 0.8]) (Figure 1f). By 12-months, psychological distress decreased significantly overall, which correlated significantly with ethnicity (coefficient: 0.8; p=0.005; CI: [0.3, 1.4]) and baseline DAS28 (coefficient: -0.5; p<0.001; CI: [-0.6, -0.4]). Compared to white patients, the reduction was significantly greater for non-white patients, but the level of distress was no longer different at 12 months (Figure 1c). While those with higher baseline DAS28 showed a greater reduction in psychological distress, the distress levels remained higher at 12 months (Figure 1f).

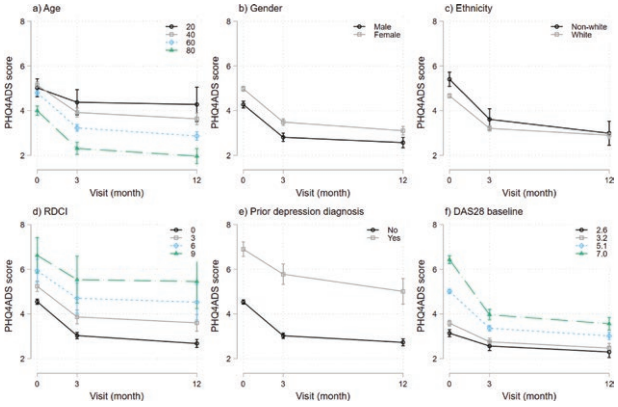


Figure 1. Changes in psychological distress correlated with age, gender, ethnicity, RDCI, prior depression diagnosis, and baseline DAS28.

Conclusion: In this early inflammatory arthritis cohort, mental health burden was high. Age, gender, ethnicity, RDCI, prior depression diagnosis and baseline DAS28 significantly correlated with psychological distress at baseline. Supporting mental health should be a focus of clinical care for this population and it may be beneficial to use an approach that is culturally valid for non-white patients and accounts for multimorbidity.

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POS1090

IMPLEMENTATION OF QUALITY STANDARDS FOR HEALTH CARE OF PATIENTS WITH RHEUMATOID ARTHRITIS: FIRST RESULTS FROM THE NATIONAL DATABASE OF THE GERMAN COLLABORATIVE ARTHRITIS CENTRES

Keywords: Health services research, Rheumatoid arthritis, Quality of care

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Background: Despite the establishment of national and international recommendations for the management of patients with rheumatoid arthritis (RA), remediable deficits in the quality of care (QoC) still exist. On behalf of the German Society for Rheumatology, with participation of the patient organization Deutsche Rheuma-Liga, eight Quality standards (QS) have been developed to improve the QoC in Germany. The QS can be used to determine and quantitative gaps in QoC in respect to time to diagnosis, use of glucocorticoids, rates of remission and impairments in physical function [1].

Objectives: To quantify gaps in QoC based on five QS in patients with RA for whom data from the National Database of the German Collaborative Arthritis Centres (NDB) exists.

Methods: In 2020, 4863 patients with RA from 12 Rheumatology centres were followed in the NDB. Five QS were reviewed: (QS1) How often was RA diagnosed within 8 weeks of symptom onset? (QS2) How many patients are in remission? (QS3) How many patients are in glucocorticoid-free remission? (QS4) How many patients who were not in remission had their medication adjusted? (QS5) How many patients with impairments in physical function received physiotherapy, functional training, and/or rehabilitation? Remission was investigated both by DAS28 and by CDAI cut-offs. Impairments in physical function were assessed with the FFbH (≤70% of full function). Switches, additions, or dose increases of disease-modifying antirheumatic drug (DMARD) were considered adjustment of medication. Individual components of the DAS28 are reported to determine reasons for not achieving remission.

Results: Fulfillment of QS (Figure 1) was investigated in 4863 patients (Table 1). In 2020, 76 patients had their first contact to rheumatologist and 30 were seen by a rheumatologist within 8 weeks (39%). Of 61 patients with available diagnosis date, 25 (41%) were diagnosed within 8 weeks. 1523 of 3410 patients with available DAS28 were in DAS28 remission (45%) and 933 of 4023 patients with available CDAI were in CDAI remission (23%). 1155 of 1520 patients in DAS28 remission and 789 of 930 RA patients in CDAI remission were glucocorticoid-free (76%/85%). 373 of 1676 patients who were not in DAS28 remission had adjustment of medication (22%). Patients without therapy adjustment had fewer clinical signs of inflammatory activity (SJC 1.3 vs. 2.6, TJC 2.6 vs. 3.7, ESR 25.7 vs. 27.4, Physician global 1.8 vs. 2.8, Patient disease activity 4.1 vs. 4.8) compared to patients with adjustment of medication. 68 of 149 patients with high disease activity (DAS28>5.1) had adjustment of medication (46%). 377 of 772 patients with impairments in physical function and information on physiotherapy received physiotherapy (49%), 32 of 767 patients with data on functional training received functional training (4%) and 117 of 1175 patients with data on rehabilitation received rehabilitation (10%).

Table 1. Patient characteristics, n=4863

Female sex (%)	74
Age, mean in years	63
Disease duration, mean, years	14
ACPA or RF positive (%)	72
DAS28, mean (n=3,410)	2.9
CDAI, mean (n=4,023)	7.7
TJC, mean	1.6
SJC, mean	1.0
ESR, mean in mm/h	19.1
Patient global disease activity, mean	3.5
Physician global disease activity, mean	1.5
Functional assessment (FFbH 0-100), mean (n=4526)	75.4
cs/bDMARDs (%)	70/ 29
Glucocorticoids (%)	35
First Rheumatology visit in 2020, n	76
Duration of symptoms, mean/median, months	20.2/4.0
Rheumatologist contact within 8 weeks, n (%)	30 (39%)
Diagnosis within 8 weeks, n (%) (n=61 with available diagnosis date)	25 (41%)

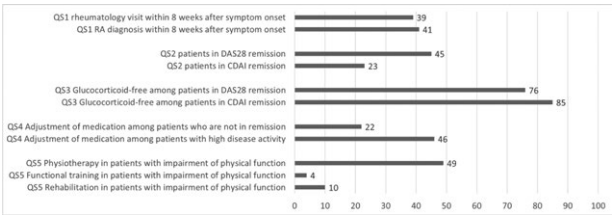


Figure 1. Fulfillment of quality standards (%)

Conclusion: With the new QS, QoC of patients with RA can be measured in a standardized form. While some results reflect high quality of care, other QSs point to opportunities for improvement. The implementation of the QS enables both a comparative evaluation at facility level and a general rheumatology health care outcome. This will help to optimize the QoC for patients with RA in Germany.

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[1] PMID 34652486

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POS1091

INFLAMMATION IS MORE PROMINENT THAN JOINT DAMAGE AT INITIAL VISITS OF PATIENTS WITH INFLAMMATORY ARTHRITIDES, BUT ORGAN DAMAGE AND PATIENT DISTRESS ARE AS PROMINENT IN OVERALL RHEUMATOLOGY CARE: DATA FROM A FEASIBLE PHYSICIAN RHEUMATIC CHECKLIST

Keywords: Inflammatory arthritides, Treat to target, Comorbidities

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Background: Patients consult rheumatologists for symptoms which may result from inflammatory activity (INF), joint or other organ damage (DAM) and/or distress (STR), e.g., fibromyalgia, depression. However, quantitative assessment in routine rheumatology care is directed primarily (often exclusively) to INF, e.g., DAS28, CDAI, SLEDAI, ASDAS, and DAPSA. DAM and STR are recognized in many patients, but generally recorded only as narrative descriptions, rather than as quantitative data. INF indices function effectively in clinical trials, but measures and indices designed to assess INF may be elevated in many unselected routine care patients by comorbid DAM and/or STR, often despite little or no INF. A RheuMetric checklist includes 4 0-10 visual numeric scales (VNS) for physician global assessment (DOCGL), DOCINF, DOCDAM, and DOCSTR, and estimates of the % of DOCGL attributed to INF, DAM, and STR.

Objectives: To analyze RheuMetric scores in unselected routine care patients with all diagnoses at initial or return visits to an academic rheumatology setting.

Methods: A retrospective cross-sectional study was performed of RheuMetric checklist 0-10 VNS estimates for DOCGL and estimates of %INF, %DAM, and %STR (total=100%) completed in routine care by the treating rheumatologist. Mean levels of these estimates were analyzed according to primary diagnosis, classified as INF (RA, SLE, SpA, vasculitis and gout), osteoarthritis (OA), primary fibromyalgia (FM), and "other," at initial or return visits, using descriptive and chi-square statistics.

Results: Highest DOCINF was in inflammatory diseases, DOCDAM in OA, and DOCSTR in primary FM (Table 1). The % of DOCGL attributed to INF, DAM, and STR was highest in INF diseases, OA, and primary FM, respectively

Table 1. Cross sectional analyses of mean (standard deviation) for 0-10 physician global estimate (DOCGL) and % of DOCGL attributed to inflammation (%INF), damage (%DAM), and patient distress (%STR) (Total=100%) at 244 first visits compared to 319 return visits

	Initial visits					Return visits				
Primary rheumatic physician ICD-10 diagnosis	N (%)	DOC GL	Mean (SD) % of DOCGL attributed to…			N(%)	DOC GL	Mean (SD) % of DOCGL attributed to…		
		DOC GL	% INF	% DAM	% STR		DOC GL	% INF	% DAM	% STR
Inflammatory diseases (RA, SLE, SpA, Vasc, Gout)	67 (27%)	4.3 (2.5)	62%Δ (33%)	24% (24%)	14% (24%)	127 (40%)	3.7 (2.6)	33%Δ (31%)	49% (35%)	18%* (27%)
Osteoarthritis	45 (18%)	4.4 (2.0)	14% (19%)	72%Δ (28%)	14% (18%)	69 (22%)	5.0 (2.2)	7% (14%)	69%Δ (30%)	24% (28%)
Fibromyalgia	32 (13%)	4.9 (2.6)	14% (22%)	12% (16%)	74%Δ (28%)	36 (11%)	5.0 (2.0)	12% (21%)	20% (21%)	68%Δ (26%)
Other diagnosis	100 (41%)	3.0 (2.1)	37% (33%)	35% (31%)	29% (33%)	87 (27%)	3.5 (2.4)	26% (29%)	52% (35%)	22% (30%)
TOTAL	244 (100%)	3.9 (2.4)	36% (35%)	36% (33%)	28% (34%)	319 (100%)	4.1 (2.5)	22% (28%)	51% (35%)	28%◊ (32%)

Δ32%)35%))nosisseases (RA, SLE, SpA, Vasc, Gout) at 244 first visits compared to 319 return visits

(p<0.001) (Table 1). At initial visits of patients with INF, mean DOCGL was 4.3, attributed 62% to INF, 24% to DAM and 14% to STR, respectively; at return visits, DOCGL was 3.7, attributed 33% to INF, 49% to DAM and 18% to STR (Table 1). In patients with all diagnoses, 36%, 36%, and 28% of DOCGL were attributed to INF, DAM, and STR, respectively, at first visits, vs 22%, 51%, and 28% at return visits (Table 1). RheuMetric estimates required 15-20 seconds to complete.

Conclusion: RheuMetric physician estimates for INF, DAM, and STR are feasibly assessed in routine care, with face validity documented by significantly higher INF in inflammatory diseases, DAM in OA, and STR in FM. DOCINF was higher at first vs return visits, reflecting highly effective anti-inflammatory treatments at this time, while %DOCDAM rose. At return visits, INF accounted for 22% of DOCGL vs 50% for DAM and 28% for STR, indicating that control of inflammation is not the primary activity in overall rheumatology care after the first visit.

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Rehabilitation

POS1092

PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR IN PATIENT WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES: A CASE CONTROL STUDY

Keywords: Lifestyles, Rehabilitation, Inflammatory arthritides

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Background: Engaging in regular physical activity (PA) is important in maintaining health and increasing the overall quality of life of patient living with chronic inflammatory rheumatic diseases (CIRD). Its is assumed that patients with CIRD reports low levels of physical activity. In the era of evidence-based medicine few studies compare PA levels and its predictors between patient with CIRD and healthy control.

Objectives: we aim to investigate PA levels of patients with CIRD, to examine predictors of PA and furthermore compare findings to healthy control.

Methods: A cross-sectional study was performed among patients with CIRD Aged between 18 and 65 years old who visited the outpatient clinic between April 2022 and October 2022. The diagnosis of spondyloarthritis was based on ASAS criteria and the diagnosis of rheumatoid arthritis was based on ACR/EULAR 2010 criteria. Healthy controls were recruited in a specialized consultation. Socio-demographic findings were collected. Patients were assessed for pain and disease activity using visual analogic scale (VAS), DAS28 CRP and ASDAS CRP. Physical activity levels were assessed using the international physical activity questionnaire (IPAQ-SF). Furthermore, all participants underwent screening for anxiety and depressive disorders using Patient health questionnaire (PHQ-9) and General anxiety disorder (GAD-7) respectively.

Results: The final study simple was made up of 172 patients (92 RA, 65 SpA and 15 Undifferentiated CIRD) and 159 healthy controls.

Table 1. socio-demographic informations, clinical findings and physical activity levels of patients with CIRD and healthy controls.

	Patients with CRID N= 172	Healthy controls N= 159	p Value
Age (Mean ±SD)	45,97 ± 12,063	45,53 ± 12,244	P= 0.787
Sexe (female pourcentage)	72,7%	70,3%	P= 0.654
BMI (Median percentiles)	25 [20.93, 28.08]	26.39 [23.63, 29.75]	P=0.033
Socioeconomic status:	Low: 50.6 %(n=87) Medium: 28.5 %(n=49) High: 1.7 % (n=3) Don't Know: 19,2 %(n=33)	Low: 28.9 % (n=46) Medium: 40.3 % (n=64) High: 11.3 % (n=18) Don't Know: 19,5 % (n=31)	P=0.007
IPAQ-SF: Met/min/week (Median percentiles)	936 [231, 4282]	1546 [864, 3612]	P= 0.001
IPAQ-SF: category	Low PA: 38.4% (n=63) Moderate PA: 32.9%(n=54) High PA: 28.7% (n=47)	Low PA: 17% (n=27) Moderate PA: 31.4% (n=50) High PA:51.6% (n=82)	P=0.000
Sedentary behavior: Min/day (IPAQ-SF)	120 [60, 240]	120 [60, 180]	P= 0.015
Depression PHQ-9 scale	8 [5, 14]	4 [1, 9]	P=0.000
Anxiety GAD-7 scale	8 [4.75, 12]	6 [3, 10]	P=0.001
Disease duration year	8 [3, 17]	N/A	N/A
Disease activity	Remission: 39 %(n=67) Low disease activity: 11.6% (n=20) Moderate disease activity: 24.4%(n=42) High disease activity: 25%(n=43)	N/A	N/A

In patients with CIRD uni and multivariate analysis showed no association between PA levels and disease related variables: Disease activity(OR (95%CI) = -0.032 (-0.160, 0.095); p=0.61), disease duration(OR (95%CI) = -0.013 (-0.028, 0.003); p=0.111) and comorbidities(OR (95%CI) = -0.013 (-0.109, 0.083); p=0.794) on the contrary PA levels were negatively associated with depression (OR (95%CI) = -0.011(-0.021,- 0.002); p=021)In healthy controls uni and multivariate analysis showed that PA levels were negatively associated with age (OR (95%CI) =-0.013 (-0.004, -0.023; p=0.007)), BMI (OR (95%CI) = -0.029 (-0.051, - 0.006; p=0.013)) and depression (OR (95%CI) =-0.029 (-0.049, - 0.009; p=0.004)).

Conclusion: Our study shows that patients with CIRD reports significantly low levels of PA and high level of SB compare to healthy controls. The unexpected finding in our study is that low levels of PA in patients with CRDI were not associated with disease activity nor disease duration. Depressive disorders are an important predictor of physical inactivity and sedentary behavior regardless of the presence of CRID. Depressive disorders are common among patients with CRID. Screening for depression and treating in time is essential to help overcome sedentary behavior in our patient and community.

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POS1093

WHO ARE THE PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASE IN NEED TO SPECIALISED MULTIDISCIPLINARY REHABILITATION?

Keywords: Rehabilitation, Non-pharmacological interventions

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Background: Patients with inflammatory rheumatic disease, while receiving highly effective disease-modifying antirheumatic drugs, are still referred to multidisciplinary rehabilitation in specialised centres. Although multidisciplinary rehabilitation only have small and short-term improvements in patients' outcome, it could benefit patients with specific disability and rehabilitation needs, indicating a more complicated disease [1].
Objectives: In order to identify the specific rehabilitation needs of patients with inflammatory rheumatic disease, it is of paramount importance to describe their clinical characteristics. The present study includes all patients with inflammatory rheumatic disease who were referred to multidisciplinary rehabilitation in Northern Norway between 2018 and 2021.
Methods: In Norway, the cost of multidisciplinary rehabilitation in specialised centres is covered by the national welfare system. However patients must be referred by a physician and the referral approved by the regional assessment office (rehabilitation regional vurderingsenhet) at the University Hospital of North Norway. All patients referred to multidisciplinary rehabilitation were included in this longitudinal study; the study was retrospective from January 1st 2018 to 31st December 2018 and afterwards prospective to June 10th 2021. Data were extracted from referrals and hospital discharge summaries. Age, gender, diagnosis, county and municipality, referring physicians were collected in all patients. Major symptoms and associated diseases were later included in the study.
Results: 786 patients out of 1028 referrals were referred to multidisciplinary rehabilitation during the study period. The referral rate was 0.39 and 0.56/1000 persons/year for respectively the counties of Nordland and Troms-Finnmark. Patients´ mean age was 54 and 76 % were women. 43 % of all patients were first time referral. 56 % had spondyloarthritis, 23 % rheumatoid arthritis, 15 % connective tissue disease and 3.3 % vasculitis including polymyalgia rheumatica. The most common associated diseases were osteoarthritis and obesity, respectively in 36 and 31 % (Table 1). 41 % complained of fatigue and 38 % had diffuse pain.
Conclusion: In Northern Norway, the referral rate to multidisciplinary rehabilitation is 0.47/1000 persons/year. The prototypical patient referred to multidisciplinary rehabilitation is a woman in her sixth decade with spondyloarthritis, often complaining of fatigue and diffuse pain. Although these patients have seldom major physical disability, they are mostly in need for coping strategies regarding fatigue and chronic pain.
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Characters from table content including title and footnotes.
BMI>30: obesity; DM: diabetes mellitus; FMS: fibromyalgia; MI: myocardial infarct; OA: osteoarthritis; PSY: depression and/or anxiety; T<-2.5: osteoporosis.

Table 1. Frequency of associated disease in patients with inflammatory rheumatologic disease referred to multidisciplinary rehabilitation in Northern Norway.

	OA	Prosthesis	BMI>30	FMS	PSY	T <-2.5	DM	MI	Malignancy
% of patients	36	11	31	17	17	11	8.6	4,6	5.8

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Disclosure of Interests: None Declared.
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Education

POS1094

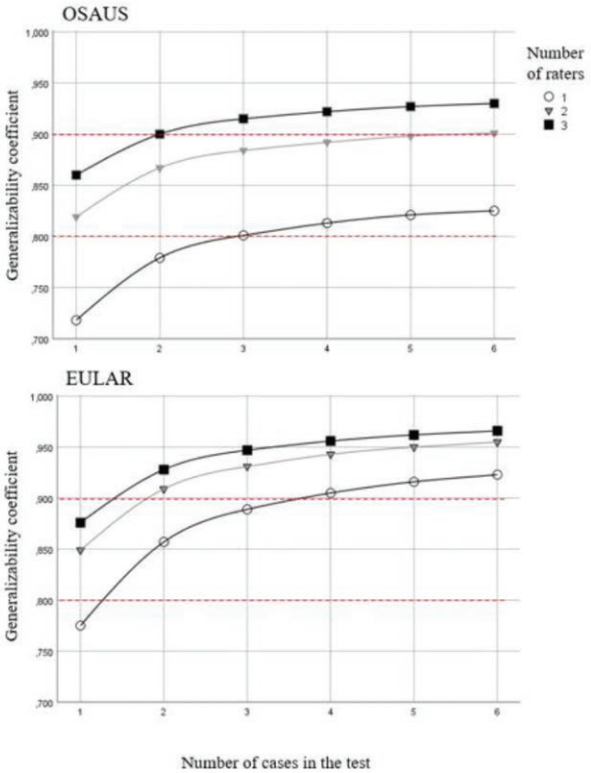
THE EULAR TOOL IS SUPERIOR TO A GENERIC TOOL IN THE ASSESSMENT OF MUSCULOSKELETAL ULTRASOUND COMPETENCE: A VALIDITY STUDY

Keywords: Ultrasound, Education

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Background: Musculoskeletal ultrasound (MSUS) is a widely implemented tool in rheumatological routine care. It has been established which competencies are relevant for rheumatologists[1], and competency levels have already been developed within European League Against Rheumatism (EULAR)[2] and European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB)[3]. Furthermore, the content and conduct of MSUS courses have been published [2]. Thus, the only component missing is an objective assessment tool supported by a contemporary validity framework to determine when residents have acquired the competencies relevant for independent practice[1]. A generic assessment tool for the assessment of ultrasound competence, The Objective Structured Assessment of Ultrasound skills (OSAUS)[4], has been developed and is already used in clinical practice in several other medical fields[5,6]. EULAR has developed another assessment tool specific for MSUS. Although both OSAUS and the EULAR tool are consensus-based, the tools' reliability and their discriminatory ability have not been explored.
Objectives: To explore the validity of the generic OSAUS tool and the EULAR tool for the assessment of MSUS operator performance. Moreover, to examine the optimal number of cases and raters needed to ensure a reliable assessment of residents.
Methods: We included 30 physicians, representing MSUS novices, intermediates, and experts. Validity evidence was gathered using the gold standard contemporary framework of Messick[8] All participants performed MSUS examinations of four joint areas: the wrist, fingers, ankle, and shoulder on the same patient with rheumatoid arthritis. All performances were video recorded and subsequently assessed in completely random order by two blinded raters using first the OSAUS assessment tool and then one month after, followed by new randomization of the videos, the EULAR tool.
Results: A total of 120 videos were assessed twice by two assessors. The inter-rater reliability was high for both tools: 0.807 (OSAUS) versus 0.848 (EULAR), and both tools demonstrated excellent inter-case reliability of 0.970 (OSAUS) versus 0.964 (EULAR). The ability to discriminate between different experience levels and MSUS performance was significant (p <0.001) for both the OSAUS and the EULAR tool. Moreover, by conducting a series of Decision-studies, we estimated the optimal number of cases and raters needed to ensure a reliable assessment (generalizability coefficient >0.8). A reliable assessment could be reached by using either one rater and three cases or two raters and one case (OSAUS), whereas the EULAR assessment tool only needed one rater assessing two cases or two raters assessing one case (Figure 1).

Figure 1: Number of raters and cases needed to make a reliable assessment of MSUS competences



The red-dotted lines illustrate the acceptance limit of 0.8 for normal supervision and examinations and the high-stake limit of 0.9 (e.g., obtaining final medical degree or postgraduate medical exams).

Conclusion: MSUS operator competences can be assessed in a reliable and valid way using either the OSAUS or the EULAR assessment tool, thereby allowing a uniform competency-based MSUS education in the future. Although both tools demonstrated high inter-rater reliability, the EULAR tool was superior to OSAUS. Using the EULAR tool in clinical practice will allow a single assessor to provide a reliable MSUS assessment of the trainee by observing only two different MSUS examinations.

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POS1095 E-LEARNING AND PRACTICAL PERFORMANCE IN MUSCULOSKELETAL ULTRASOUND - A MULTICENTER RANDOMIZED STUDY

Keywords: Education, Ultrasound, Randomized control trial

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Background: The COVID-19 pandemic has forced a change in the teaching approach when educating physicians. Several training programs have been digitally transformed, including complex procedures such as ultrasound [1]. Recent studies have suggested the possibilities for practicing theoretical and practical ultrasound skills using online platforms, e.g., e-learning [2]. Even though the effect of e-learning on theoretical knowledge is unquestionable, the impact on practical skills is unknown. Thus, it is essential to examine the effect of e-learning on the development of practical skills.

Objectives: To examine the effect of pre-course e-learning on residents' practical performance in musculoskeletal ultrasound (MSUS). Moreover, to examine the effect of pre-course e-learning on residents' satisfaction with the following face-to-face MSUS course.

Methods: We designed a multi-center randomized controlled study following the CONSORT statement. Residents with no or little MSUS experience were randomized to either an e-learning group or a traditional group. One week before a 2-day face-to-face MSUS course, the e-learning group received access to an interactive platform consisting of online lectures, assignments, and practical instruction videos aligned with the content of the following course. The traditional group only received standard pre-course information (program, venue, and time). All participants performed a pre- and post-course practical MSUS examination and were assessed by two individual raters, blinded to the group allocation, using the validated Objective Structured Assessment of Ultrasound skills (OSAUS) tool. Finally, the participants filled out a subjective satisfaction questionnaire, the Intrinsic Motivation Inventory (IMI).

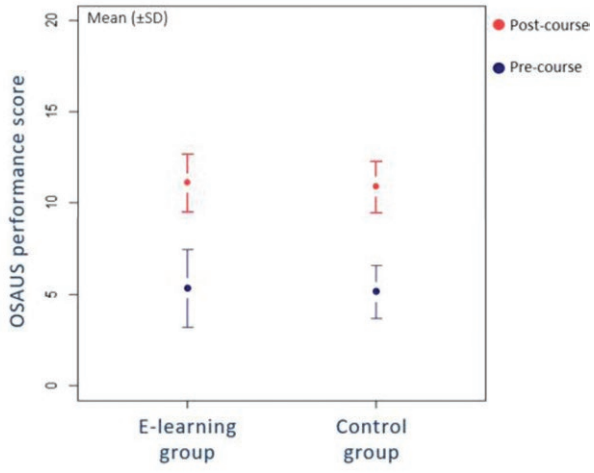
Results: Twenty-eight participants completed the study. There were no statistically significant differences in the pre- or post-course practical MSUS performance between the e-learning group and the traditional group; the mean pre-course OSAUS score (±SD) in the e-learning group was 5.4±3.7 compared to 5.2±2.4 in the traditional group, p=0.8, whereas the post-course OSAUS score in the e-learning group was 11.1±2.8 compared to 10.9±2.4 in the traditional group, p=0.8 (Figure 1). There was a significant difference between the mean pre- and post-course scores (p<0.001) for both groups. The OSAUS assessment tool demonstrated excellent inter-rater reliability (ICC=0.84). There were no significant differences between the groups regarding their subjective satisfaction with the course measured by the IMI score.

Conclusion: We found no significant impact of pre-course e-learning on novices' acquisition of practical MSUS skills or on trainees' satisfaction with the course. Hands-on training is of utmost importance and improves MSUS performance significantly. The OSAUS assessment tool is an applicable tool for the assessment of trainees' MSUS competences and demonstrated excellent interrater reliability.

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Figure 1. The effect of e-learning on novices' practical MSUS performance before and after the face-to-face course



Objective Structured Assessment of Ultrasound skills (OSAUS) performance score, presented as mean ± SD.

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POS1096 ASSESSMENT OF PERCEPTION OF BENEFITS AND BARRIERS TO EXERCISE PARTICIPATION AMONG PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES AND HEALTHY INDIVIDUALS: A CASE CONTROL STUDY

Keywords: Inflammatory arthritides, Education, Rehabilitation

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Background: Benefits of regular physical activity (PA) are well known and well publicized. Despite the many benefits of PA, patients with chronic inflammatory rheumatic diseases (CIRD) report low levels of PA and engage more in sedentary behavior.

Objectives: We aim to assess the perception levels of benefits and barriers to exercise participation among patients with CIRD and healthy individuals and examine the predictors of poor perception levels.

Methods: A cross-sectional study was performed among patients with CIRD Aged between 18 and 65 years old who visited the outpatient clinic. Healthy controls were recruited in a specialized consultation. Socio-demographic and clinical findings were collected. Physical activity levels were assessed using (IPAQ). Perceived benefits and barriers to exercise scale (PBBS) was used to assess the perception of patients and healthy controls toward exercise. Furthermore, all participants underwent screening for anxiety and depressive disorders using (PHQ-9) and (GAD-7) respectively.

Results: 172 patients were enrolled in the study (92 RA, 65 SpA and 15 Undifferentiated CIRD) and 159 healthy controls.

Table 1. Sociodemographic and clinical findings, PA levels and perception toward PA among patients and healthy individuals.

	Patients with CRID N= 172	Healthy controls N= 159	p Value
Age (Mean ±SD)	45,97 ± 12,063	45,53 ± 12,244	p= 0.787
Gender (female)	72,7%	70,3%	p= 0.654
Disease duration year	8 [3, 17]	N/A	N/A
Disease activity	Remission: 39 % LDA: 11.6% MDA: 24.4% HDA: 25%	N/A	N/A
IPAQ:	Low PA: 38.4% Moderate PA: 32.9% High PA: 28.7%	Low PA: 17% (n=27) Moderate PA: 31.4% (n=50) High PA:51.6% (n=82)	**p=0.000**
Top three Perceived benefits to exercise (Mean ±SD).	**1-**Exercise decreases feelings of stress and tension for me (3.49 ± 0.77) **2-**Exercise improve my mental health (3.48 ± 0.87) **3-** My disposition is improved with exercise (3.46 ± 0.79)	**1-**Exercising increases my level of physical fitness (3.69 ± 0.61). **2-**Exercise improves overall body functioning for me (3.65 ± 0.57) **3-** My disposition is improved with exercise (3.65 ± 0.678)	N/A
Top three Perceived barriers to exercise (Mean ±SD).	**1-** I'm fatigued by exercise (2.38 ± 1.19) **2-** Exercise tires me (2.21 ± 1.15) **3-** Places for me to exercise are too far away (2.13 ± 1.23)	**1-** Exercise tires me (1.97 ± 1.02) **2-** I'm fatigued by exercise (1.94 ± 1.06) **3-** Places for me to exercise are too far away (1.91 ± 1.19)	N/A
PBBS Total (Mean ±SD).	138.81 ± 23.36	147.87 ± 18.83	**p= 0.000**
PBBS of perceived Benefits (Mean ±SD).	94.30 ± 20.09	101.01 ± 15.27	**p= 0.001**
PBBS of perceived Barriers (Mean ±SD).	25.49 ± 7.46	23.14 ± 7.92	**p= 0.006**
Depression PHQ-9	8 [5, 14]	4 [1, 9]	**P=0.000**

In patients with CIRD, multivariate analysis showed a positive association between the PBBS scale and Socio-economic status:(OR (95%CI) = 4.960 (1.901, 8.019); **p=0.002**), and level of education (OR (95%CI) = 3.789 (0.833, 6.745); **p=0.012**).Poor perception of benefits towards exercise participation was associated with high levels of depression in both groups: - In patients with CIRD (OR (95%CI) = -0.792 (-1.395, -0.189); **p=0.010**) and in healthy controls (OR (95%CI) = -0.520 (-1.046, -0.001; **p=0.050**)).

Conclusion: We found that patients with CIRD perceive significantly less benefits and more barriers to exercise participation than healthy individuals. Barriers to physical activity in both groups are related to physical exertion, thus we highlight the role of adapted PA especially in patients with CRID. Depressive disorders is known to alter perception of reality in a negative way [1]. Education about the diagnosis and treatment of depressive disorders is essential to promote PA [2].

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POS1097 IMPROVED REFERRALS FROM PRIMARY CARE AND MANAGEMENT OF INFLAMMATORY ARTHRITIS THROUGH AN INTEGRATED COLLABORATIVE ACADEMY AND NETWORK USING BLENDED LEARNING, MENTORING AND ACTION LEARNING SETS

Keywords: Education, Inflammatory arthritides, Quality of care

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Background: Improving the delay to diagnosis in inflammatory arthritis remains an important challenge in rheumatology. The National Early Inflammatory Arthritis Audit (NEIAA) in the UK aims to reduce the time to diagnosis through early referral from primary care. In order to achieve this as well as improve the quality of referrals, we have created an integrated Rheumatology Academy and Collaborative Network (RheumACaN) for clinicians in primary care.

Objectives: RheumACaN aims to build confidence in primary care to refer and manage patients with inflammatory arthritis (RA, PsA, AxSpA) as well as other rheumatic diseases. Through integration of pathways from primary to secondary care, RheumACaN aims to reduce delays to diagnosis, improve referral from primary care and enhance management of patients.

Methods: RheumACaN was a 1 year rolling programme with face to face discovery day meetings sharing best practice, teaching and discussion on local referral pathways, guidelines and investigations. In between the face to face sessions there was active learning through virtual mentoring. Participants completed action learning sets, case discussion and the course workbook. The outcome was measured through metrics in the NEIAA, referral patterns and feedback from participants.

Results: RheumACaN was attended by 80 participants over 2 cohorts in 2021-2022 including general practitioners (GPs), community musculoskeletal (MSK) physiotherapists and first contact practitioners (FCPs). Prior to RheumACaN, the number and percentage of patients with suspected early inflammatory arthritis (EIA) referred to a specialist clinic within three working days which is a measure of primary care performance was 109/312 (32%) in 2018/19, 190/334 (57%) in 2019/20, 45/86 (52%) in 2020/21. Post RheumACaN, this increased to 140/201 (70%) in 2021/22. The national average for this metric was 47% in 2019/20 and 54% in 2021/22. Feedback from 2 cohorts was 100% scored 5/5 (excellent) for how well the purpose of the programme was communicated, 100% scored 5/5 for how organised and easy to follow the programme was, 98% scored 5/5 for how engaged the presenters were. All participants responded that they had learned from the programme and this would change their practice. Narrative feedback included: "Very interesting - diagnosis and management, and when to refer onwards, very clear", "Really helpful for future referrals, good tips what to look out for", "Clear criteria and management (onward referral)", "Enjoy discussing the cases and getting feedback, useful to hear other cases", "Great having group discussion, learned so much", "Fantastic afternoon, energising, positive, lots of new ideas/approaches."

Conclusion: We created RheumACaN, a knowledge-sharing model to bring together clinicians from primary and secondary care for a robust, holistic approach to manage rheumatic diseases. Similar models such as project ECHO with the hub and spoke model of 'moving knowledge not people' have been used[1]. Our collective understanding of how to disseminate and implement best practices across diverse disciplines resulted in the rapid increase of early referrals of inflammatory arthritis from primary care in our centre which is now above the national average in the UK. New referral quality and outcomes are continuously reviewed with an annual audit to assess impact in line with the NEIAA. RheumACaN has also a train the trainer ethos with participants in Cohort 1 coming back to share and teach Cohort 2. Cohort 1 graduates have also been doing peer to peer teaching sessions to help spread and ensure sustainability. This continuous loop of learning, mentoring and peer support makes this a unique programme, with a long-lasting impact far beyond that of a webinar, e-learning course or seminar, with knowledge which is tested and refined through a local lens.

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Spondyloarthritis - treatment

POS1103 BIMEKIZUMAB MAINTAINED IMPROVEMENTS IN EFFICACY ENDPOINTS AND HAD A CONSISTENT SAFETY PROFILE THROUGH 52 WEEKS IN PATIENTS WITH NON-RADIOGRAPHIC AND RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: RESULTS FROM TWO PARALLEL PHASE 3 STUDIES

Keywords: Randomized control trial, Clinical trials, Spondyloarthritis

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Background: Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, met all primary/secondary endpoints at Week (Wk) 16 in patients (pts) with active non-radiographic axial spondyloarthritis (nr-axSpA) and radiographic axSpA (r-axSpA; i.e., ankylosing spondylitis), in the parallel phase 3 BE MOBILE 1 and 2 studies, respectively.[1,2]
Objectives: To assess efficacy and safety of BKZ in these pts up to Wk 52.
Methods: BE MOBILE 1 (NCT03928704) and 2 (NCT03928743) both involved a 16-wk placebo (PBO)-controlled and 36-wk maintenance period.[1,2] Pts were randomised to subcutaneous BKZ 160 mg Q4W (BKZ) or to PBO then BKZ from Wk 16 (PBO/BKZ).
Results: 220/254 (86.6%) randomised pts with nr-axSpA and 298/332 (89.8%) with r-axSpA completed Wk 52. Efficacy was sustained to Wk 52 in both studies (**Table 1**). ASAS40 responses in BKZ-randomised pts increased from Wk 16 (nr-axSpA: 47.7%; r-axSpA: 44.8%; non-responder imputation [NRI]) to Wk 52 (60.9%; 58.4%; NRI) with high levels of efficacy across TNFi-naïve and TNFi-IR populations (**Table 1**). At Wk 52, ASDAS <2.1 was achieved by 61.6% and 57.1%, and ASDAS <1.3 by 25.2% and 23.4%, of BKZ-randomised pts with nr-axSpA and r-axSpA, respectively (**Figure 1**). Wk 16 reductions from baseline in objective signs of inflammation (MRI, hs-CRP), and improvements in function (BASFI) and ASQoL, were maintained through 52 wks. Efficacy at Wk 52 was similar in PBO/BKZ-treated and BKZ-randomised pts (**Table 1**). At Wk 52, 75.0% (183/244) of pts with nr-axSpA and 75.5% (249/330) of pts with r-axSpA had ≥1 treatment-emergent adverse event (TEAE) on BKZ; the most frequent (% pts) TEAEs by preferred term (MedDRA v19.0) were nasopharyngitis (nr-axSpa: 12.3%; r-axSpA 9.1%) and upper respiratory tract infection (9.4%; 6.4%); few COVID-19 infections were reported (7.0%; 2.1%). Incidence (pts/100 pt years) of serious TEAEs were low (4.4; 7.1); no major adverse cardiovascular events, active tuberculosis cases, serious COVID-19 infections, or deaths were reported. Most incidences of fungal infection (19.6; 14.9; none serious or systemic) were *Candida* (12.8; 8.3) and mild to moderate; two pts in both studies discontinued the study due to *Candida* infections. Incidence of IBD (1.0; 1.0) and uveitis (1.5; 2.4) were low.
Conclusion: Across the axSpA spectrum, BKZ resulted in sustained efficacy to Wk 52. No new safety signals were observed, consistent with the Wk 24 safety profile.[1,2]

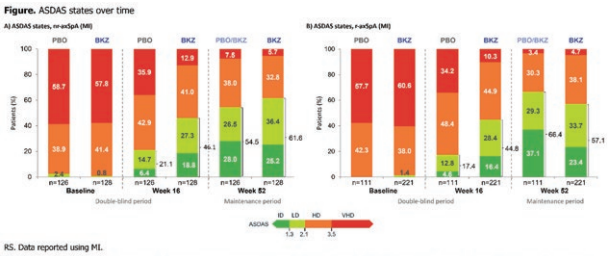
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Table 1. Efficacy at Wk 52

Mean (SE), unless stated	BE MOBILE 1		BE MOBILE 2	
	PBO→BKZ N=126	BKZ N=128	PBO→BKZ N=111	BKZ N=221
ASAS40 [NRI] n (%)	64 (50.8)	78 (60.9)	76 (68.5)	129 (58.4)
ASAS40 in TNFi-naïve [NRI] n (%)	58 (53.2)[a]	73 (61.9)[b]	67 (71.3)[c]	108 (58.7)[d]
ASAS40 in TNFi-IR[e] [NRI] n (%)	6 (35.3)[f]	5 (50.0)[g]	9 (52.9)[f]	21 (56.8)[h]
ASAS20 [NRI] n (%)	88 (69.8)	94 (73.4)	89 (80.2)	158 (71.5)
ASAS PR [NRI] n (%)	38 (30.2)	38 (29.7)	41 (36.9)	66 (29.9)
ASAS 5/6 [NRI] n (%)	65 (51.6)	71 (55.5)	74 (66.7)	124 (56.1)
BASDAI CfB [MI]	–3.5 (0.2)	–3.9 (0.2)	–4.0 (0.2)	–3.6 (0.1)
BASFI CfB [MI]	–2.6 (0.2)	–3.0 (0.2)	–2.8 (0.2)	–2.8 (0.1)
ASDAS-MI [NRI] n (%)	37 (29.4)	47 (36.7)	49 (44.1)	71 (32.1)
Nocturnal spinal pain CfB [MI]	–4.1 (0.2)	–4.3 (0.3)	–4.6 (0.3)	–4.1 (0.2)
ASQoL CfB [MI]	–5.3 (0.4)	–5.9 (0.4)	–5.6 (0.4)	–5.7 (0.3)
SF-36 PCS CfB [MI]	11.4 (0.9)	12.2 (0.9)	12.3 (0.9)	12.0 (0.6)
BASMI CfB [MI]	–0.4 (0.1)	–0.6 (0.1)	–0.7 (0.1)	–0.7 (0.1)
Total resolution of enthesitis[i] [NRI] n (%)	41 (44.6)[j]	51 (54.3)[c]	31 (46.3)[k]	67 (50.8)[l]
ASDAS-CRP CfB [MI]	–1.6 (0.1)	–1.8 (0.1)	–1.9 (0.1)	–1.7 (0.1)
SPARCC MRI SIJ score CfB [OC][m] Mean (SD)	–6.4 (10.7)[n]	–7.6 (10.5)[o]	–2.8 (6.1)[p]	–4.7 (8.2)[q]
Berlin MRI spine score CfB [OC][m] Mean (SD)	–0.4 (2.0)[k]	–0.7 (2.5)[r]	–2.1 (3.4)[p]	–2.4 (3.9)[s]
hs-CRP, mg/L [MI] Median	2.2	1.7	2.0	2.3

RS. n: [a]109, [b]118, [c]94, [d]184; [e]Max 1 TNFi; n: [f]17, [g]10, [h]37; [i]MASES=0 in pts with MASES >0 at BL; n: [j]92, [k]67; [l]132; [m]MRI sub-study; n: [n]70, [o]82, [p]48, [q]90, [r]79, [s]89.



Abbreviations: ASAS20/40: Assessment of SpondyloArthritis international Society 20/40 response; ASAS 5/6: ASAS 5/6 response; ASAS PR: ASAS partial remission; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score C-reactive protein; ASDAS-MI: ASDAS major improvement; ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BKZ: bimekizumab; BL: baseline; CfB: change from baseline; CRP: C-reactive protein; HD: high disease; hs-CRP: high sensitivity-CRP; ID: inactive disease; LD: low disease; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; MI: multiple imputation; MRI: magnetic resonance imaging; n: number; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; OC: observed case; PBO: placebo; r-axSpA: radiographic axial spondyloarthritis; pts: patients; Q4W: every four weeks; RS: randomised set; SD: standard deviation; SE: standard error; SF-36 PCS: Short Form-36 Physical Component Summary; SIJ: Sacroiliac Joints; SPARCC: Spondyloarthritis Research Consortium of Canada; TNFi: tumour necrosis factor inhibitor; Wk: week; VHD: very high disease activity.

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POS1104

BIMEKIZUMAB MAINTAINED STRINGENT CLINICAL RESPONSES THROUGH WEEK 52 IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE PHASE 3 STUDIES BE MOBILE 1 AND BE MOBILE 2

Keywords: Clinical trials, Spondyloarthritis, Outcome measures

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Background: Axial spondyloarthritis (axSpA) is a chronic rheumatic disease which requires optimal management and disease control. Assessment of SpondyloArthritis international Society ≥40% improvement (ASAS40) is a stringent efficacy outcome in clinical trials, while in clinical practice the focus is on the achievement of sustained remission or low disease activity (LDA) according to Ankylosing Spondylitis Disease Activity Score (ASDAS). Patients (pts) can

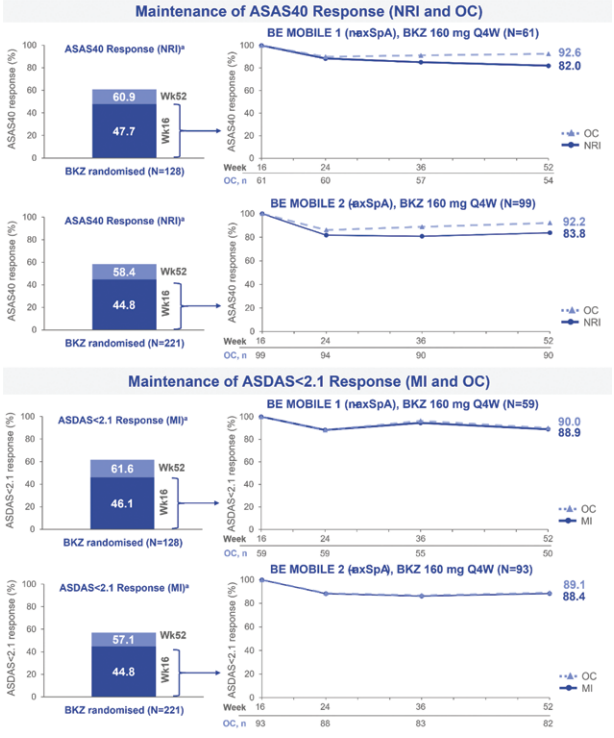
experience loss of response in the long term and maintenance of response is an internationally recommended treatment target.[1] Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A. BKZ has demonstrated consistent and sustained clinical efficacy to Week (Wk) 52 in pts across the full spectrum of axSpA in the phase 3 studies BE MOBILE 1 and 2.[2]

Objectives: To report the maintenance of stringent clinical responses through one year of treatment with BKZ in pts with non-radiographic axSpA (nr-axSpA) and radiographic-axSpA (r-axSpA, i.e., ankylosing spondylitis)[3] in phase 3 studies.

Methods: In BE MOBILE 1 (NCT03928704; nr-axSpA; pts met ASAS criteria for axSpA) and BE MOBILE 2 (NCT03928743; r-axSpA; pts fulfilled ASAS and modified New York criteria for r-axSpA), pts were randomised to receive subcutaneous BKZ 160 mg every 4 wks (Q4W) or placebo (PBO) to Wk 16. From Wks 16–52, all pts received BKZ 160 mg Q4W.[4,5] ASAS40 and ASDAS <2.1 (LDA) or <1.3 (inactive disease [ID]) responses to Wk 52 were assessed among BKZ-randomised pts who responded at Wk 16. Missing ASAS40 data were imputed using non-responder imputation (NRI), and multiple imputation (MI) was used for missing ASDAS data. MI was based on Markov Chain Monte Carlo (for intermittent missing data) followed by monotone regression (for monotone missing data). Observed case (OC) data are also reported. Wk 16 and Wk 52 responder rates for all BKZ-randomised pts are included for context (NRI or MI). The number of treatment-emergent adverse events (TEAEs) to Wk 52 are reported for pts who received ≥1 dose of BKZ, including pts who switched from PBO to BKZ at Wk 16.

Results: A total of 128 and 221 pts were randomised to BKZ 160 mg Q4W in BE MOBILE 1 and 2, respectively. At Wk 16, 47.7% and 44.8% of these pts achieved the primary endpoint, ASAS40, and this increased to 60.9% and 58.4% at Wk 52 (NRI, **Figure 1**). Of pts that achieved ASAS40 at Wk 16, 82.0% and 83.8% maintained this response at Wk 52 (NRI, **Figure 1**). ASDAS LDA was achieved by 46.1% and 44.8% of BKZ-randomised pts at Wk 16 of BE MOBILE 1 and 2, respectively; this increased to 61.6% and 57.1% at Wk 52 (MI, **Figure 1**). Of pts that achieved ASDAS LDA at Wk 16, 88.9% and 88.4% maintained this response at Wk 52 (MI, **Figure 1**). At Wk 16 of BE MOBILE 1 and 2, ASDAS ID was achieved by 18.8% and 16.4% of BKZ-randomised pts, respectively; and this increased to 25.2% and 23.4% at Wk 52 (MI). Among Wk 16 ASDAS ID responders, ASDAS ID was maintained by 79.2% and 75.1% at Wk 24, 85.3% and 71.7% at Wk 36, and 88.0% and 58.7% at Wk 52 (MI). To Wk 52 of BE MOBILE 1 and 2, 183/244 (75.0%) and 249/330 (75.5%) pts reported ≥1 TEAE whilst receiving BKZ, respectively; 9 (3.7%) and 20 (6.1%) reported serious TEAEs.

Figure. Maintenance of ASAS40 and ASDAS LDA (ASDAS <2.1) through 52 wks of BKZ 160 mg Q4W among Wk 16 ASAS40 and ASDAS LDA responders, respectively, from BE MOBILE 1 and 2



[a]Response at Wk 16 and Wk 52 in pts randomised to BKZ 160 mg Q4W at baseline.
Abbreviations: ASAS40: Assessment of SpondyloArthritis international Society 40%; ASDAS<2.1: Ankylosing Spondylitis Disease Activity Score <2.1; axSpA: axial spondyloarthritis; BKZ: bimekizumab; LDA: low disease activity; MI: multiple imputation; nr-axSpA: non-radiographic axSpA; NRI: non-responder imputation; OC: observed case; pts: patients; Q4W: every four weeks; r-axSpA: radiographic axSpA; wk: week.

Conclusion: Dual inhibition of IL-17F and IL-17A with BKZ provided robust maintenance of stringent clinical responses from Wk 16 to Wk 52 across the full axSpA disease spectrum. This is consistent with previously reported observations of BKZ treatment over three years in pts with r-axSpA in the phase 2b study BE AGILE and its open-label extension.[6]

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[**6**] Navarro-Compán V. Presented at EULAR 2022, POS0938.

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POS1106

ACHIEVEMENT OF LOW DISEASE ACTIVITY OVER 52 WEEKS IN PATIENTS WITH ACTIVE AXIAL SPONDYLOARTHRITIS ON BIMEKIZUMAB TREATMENT: RESULTS FROM THE PHASE 3 STUDIES BE MOBILE 1 AND BE MOBILE 2

Keywords: Spondyloarthritis, Clinical trials, Treat to target

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Background: Ankylosing Spondylitis (AS) Disease Activity Score (ASDAS) is the recommended instrument to assess disease activity in axial spondyloarthritis (axSpA).[1] However, the Bath AS Disease Activity Index (BASDAI) remains commonly used in clinical practice. The recommended treatment target for axSpA is remission or low disease activity (LDA) according to ASDAS levels,[1] while limited data exist to validate cut-offs for BASDAI.[2,3] However, remission is difficult to achieve for many patients (pts), especially in established disease. Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A. BKZ has demonstrated consistent and sustained efficacy up to Week (Wk) 52 in the BE MOBILE 1 and 2 phase 3 studies, including achievement of LDA according to ASDAS by >50% of pts with non-radiographic (nr-)axSpA and radiographic (r-)axSpA (i.e. AS).[4,5]

Objectives: To report achievement of LDA, as assessed by either ASDAS <2.1, BASDAI <4, or both, to Wk 52 with BKZ across the spectrum of axSpA in two phase 3 studies.

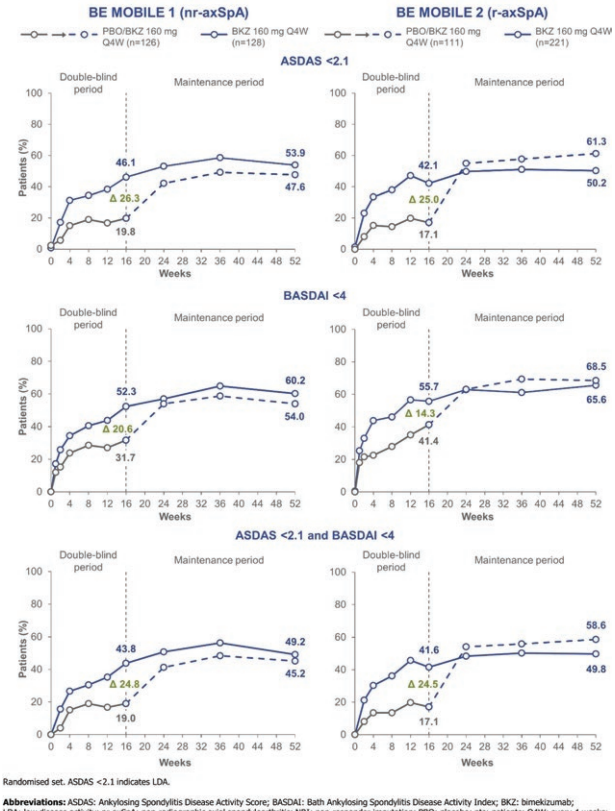
Methods: BE MOBILE 1 (NCT03928704) and BE MOBILE 2 (NCT03928743) each comprised a 16-wk placebo (PBO)-controlled and 36-wk maintenance period.[5] Pts with nr-axSpA in BE MOBILE 1 met Assessment of SpondyloArthritis international Society (ASAS) classification criteria and had objective inflammation as assessed by MRI and/or elevated C-reactive protein. Pts with r-axSpA included in BE MOBILE 2 met modified New York criteria and also fulfilled ASAS classification criteria. All pts had active disease (BASDAI ≥4 and spinal pain ≥4 as per BASDAI item 2) at baseline. Pts were randomised to subcutaneous BKZ 160 mg every 4 wks (Q4W) or PBO; all pts received BKZ 160 mg Q4W from Wk 16 onwards.[5] The PBO arm is therefore referred to as PBO up to Wk 16, and PBO/BKZ at later timepoints. Here, we present the proportion of pts achieving LDA to Wk 52, as defined by either ASDAS <2.1, BASDAI <4, or both, using non-responder imputation.

Results: A total of 254 pts with nr-axSpA (BKZ: 128, PBO: 126) and 332 with r-axSpA (BKZ: 221, PBO: 111) were randomised. Most pts had high (ASDAS ≥2.1–≤3.5) or very high (ASDAS >3.5) disease activity at baseline (nr-axSpA: BKZ: 99.2%, PBO: 97.6%; r-axSpA: BKZ: 98.6%, PBO: 100%). In pts with nr-axSpA, a greater proportion of BKZ vs PBO-treated pts achieved LDA at Wk 16 according to ASDAS <2.1 (BKZ: 46.1%, PBO: 19.8%), BASDAI <4 (BKZ: 52.3%, PBO: 31.7%), and both (BKZ: 43.8%, PBO: 19.0%). Separation from PBO was apparent from first post-baseline assessment for ASDAS <2.1 and both ASDAS <2.1 and BASDAI <4 (**Figure 1**). Results were similar for pts with r-axSpA (**Figure 1**). Across continuous BKZ-treated pts and PBO/BKZ switchers, achievement of LDA, according to ASDAS <2.1, BASDAI <4, and both, was sustained or improved in both studies to Wk 52 (**Figure 1**). Proportion of pts achieving BASDAI <4 was consistently higher compared with achievement of ASDAS <2.1, regardless of treatment arm.

Conclusion: Across the full axSpA disease spectrum, dual inhibition of IL-17A and IL-17F with BKZ resulted in rapid achievement of LDA vs PBO to Wk 16, as assessed by ASDAS <2.1, BASDAI <4, or both. Proportion of pts achieving LDA increased to Wk 52. These data suggest that ASDAS <2.1 is a more stringent criteria for LDA than BASDAI <4, and the majority of pts who achieved ASDAS <2.1 also achieved BASDAI <4. This is relevant for the consideration of BKZ in the context of a potential treat-to-target approach for pts with axSpA in daily practice.

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Figure. Proportion of pts achieving ASDAS <2.1, BASDAI <4, or both, over 52 wks in BE MOBILE 1 and 2 [NRI]



Randomised set. ASDAS <2.1 indicates LDA.

Abbreviations: ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BKZ: bimekizumab; LDA: low disease activity; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; PBO: placebo; pts: patients; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis; wks: weeks.

[**4**] Boel A. Ann Rheum Dis. 2019;78:1545–9;
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POS1107

BIMEKIZUMAB ACHIEVED SUSTAINED IMPROVEMENTS IN EFFICACY OUTCOMES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS, REGARDLESS OF PRIOR TNF INHIBITOR TREATMENT: WEEK 52 POOLED RESULTS FROM TWO PHASE 3 STUDIES

Keywords: bDMARD, Spondyloarthritis, Clinical trials

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Background: In patients (pts) with axial spondyloarthritis (axSpA), tumour necrosis factor inhibitors (TNFi) are the usual first line biologic treatment, yet many pts may experience loss of response over time, and some are intolerant to TNFis.[1] Typically, response to second line biologics is limited in TNFi-inadequate responders (IR). Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A. In the phase 3 BE MOBILE 1 and 2 studies, BKZ treatment resulted in rapid and sustained improvements in efficacy outcomes through 52 weeks (wks) in pts with active non-radiographic (nr-)axSpA and r-axSpA (i.e., ankylosing spondylitis [AS]).[2,3] In studies of BKZ in psoriatic arthritis, similar efficacy between TNFi-naïve and TNFi-IR pts were observed.[4]

Objectives: To assess the efficacy of BKZ in TNFi-naïve or -IR pts with active nr-axSpA and r-axSpA through Wk 52 across multiple key endpoints.

Methods: In BE MOBILE 1 (nr-axSpA; NCT03928704) pts met Assessment of SpondyloArthritis international Society (ASAS) classification criteria and in BE MOBILE 2 (r-axSpA; NCT03928743) pts fulfilled modified New York and ASAS criteria. Pts were randomised to receive subcutaneous BKZ 160 mg every 4 wks (Q4W) or placebo (PBO) then BKZ 160 mg Q4W from Wk 16. This post hoc analysis reports pooled mean efficacy data, including disease activity, MRI inflammation, physical function, and quality of life (QoL), through Wk 52 of BE MOBILE 1 and 2, stratified by TNFi status (naïve/IR). TNFi-IR pts are defined as those who experienced intolerance, or IR, to prior treatment given at an approved dose for ≥12 wks.

Results: This pooled analysis included 505 TNFi-naïve and 81 TNFi-IR pts. 302/505 (59.8%) TNFi-naïve and 47/81 (58.0%) TNFi-IR pts were randomised to BKZ. At Wk 16, the proportion of pts achieving ASAS40 and AS Disease Activity Score (ASDAS)<2.1 (low disease activity) were higher in BKZ-randomised TNFi-naïve/-IR pts vs PBO. In both TNFi-naïve/-IR continuous BKZ-treated pts, responses were similar and increased to Wk 52 (**Figure 1**). Similar substantial reductions from baseline in ASDAS-CRP and MRI inflammation by Wk 16 were also achieved with BKZ vs PBO in both TNFi-naïve and IR pts; in continuous BKZ-treated pts this was sustained or further improved through 52 wks. Comparable improvements in physical function, nocturnal spinal pain and ASQoL were observed through 52 wks with BKZ in TNFi-naïve/-IR pts (**Table 1**).

Conclusion: Across the full axSpA disease spectrum, BKZ treatment resulted in clinically relevant improvements in key efficacy outcomes vs PBO, including suppression of inflammation and improvements in physical function and QoL, regardless of prior TNFi exposure. The improvements with BKZ at Wk 16 were sustained to Wk 52.

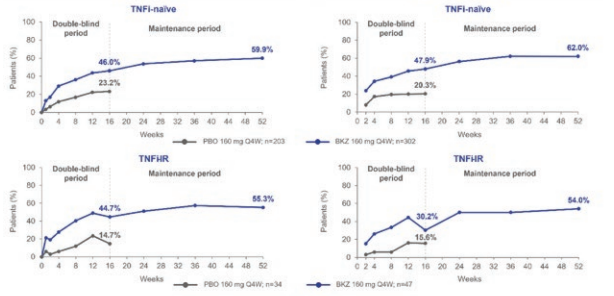
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Table 1. Pooled efficacy endpoints across BE MOBILE 1 and 2 in TNFi-naïve and -IR pts

	Wk 16				Wk 52	
	TNFi-naïve		TNFi-IR		TNFi-naïve	TNFi-IR
	PBO N=203	BKZ 160 mg Q4W N=302	PBO N=34	BKZ 160 mg Q4W N=47	BKZ 160 mg Q4W N=302	BKZ 160 mg Q4W N=47
ASDAS-CRP CfB [MI] mean (SE)	−0.7 (0.1)	−1.5 (0.1)	−0.6 (0.1)	−1.6 (0.1)	−1.8 (0.1)	−1.9 (0.2)
BASDAI CfB [MI] mean (SE)	−1.7 (0.1)	−3.0 (0.1)	−1.6 (0.4)	−2.7 (0.3)	−3.6 (0.1)	−3.7 (0.3)
SPARCC MRI SIJ CfB [OC] mean (SD)	−0.9 (7.3)[a]	−5.3 (8.4)[b]	1.4 (6.0)[c]	−5.6 (13.4)[d]	−5.9 (9.1)[e]	−6.9 (12.2)[d]
Berlin MRI Spine CfB [OC] mean (SD)	−0.2 (1.5)[f]	−1.4 (3.2)[g]	0.4 (1.3)[h]	−0.5 (1.9)[i]	−1.7 (3.6)[d]	−1.2 (2.1)[i]
BASFI CfB [MI] mean (SE)	−1.1 (0.1)	−2.3 (0.1)	−0.5 (0.3)	−2.2 (0.3)	−2.8 (0.1)	−2.9 (0.3)
Nocturnal spinal pain CfB [MI] mean (SE)	−1.7 (0.2)	−3.4 (0.2)	−2.1 (0.5)	−3.3 (0.3)	−4.1 (0.2)	−3.9 (0.3)
ASQoL CfB [MI] mean (SE)	−2.8 (0.3)	−5.1 (0.3)	−2.4 (0.6)	−4.2 (0.6)	−5.8 (0.3)	−4.7 (0.6)

Wk 52 data shown only for continuous BKZ pts. [a]n=95; [b]n=144; [c]n=13; [d]n=15; [e]n=130; [f]n=94; [g]n=140; [h]n=12; [i]n=127; [j]n=15.

Figure. Achievement of ASAS40 and ASDAS<2.1 (LDA) over 52 wks in TNFi-IR and TNFi-naïve pts, pooled across BE MOBILE 1 and 2



Abbreviations: ASAS40: Assessment of SpondyloArthritis international Society 40 response; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score C-reactive protein; ASDAS<2.1: Ankylosing Spondylitis Disease Activity Score <2.1; ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BKZ: bimekizumab; CfB: change from baseline; IR: inadequate responders; LDA: low disease activity; MI: multiple imputation; MRI: magnetic resonance imaging; n: number; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; OC: observed case; PBO: placebo; pts: patients; Q4W: every four weeks; SD: standard deviation; SE: standard error; SIJ: sacroiliac joints; SPARCC: Spondylarthritis Research Consortium of Canada; TNFi: tumour necrosis factor inhibitor.

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POS1108 EFFICACY OF UPADACITINIB IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN EARLY VERSUS ESTABLISHED DISEASE

Keywords: Spondyloarthritis

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Background: The phase 3 SELECT-AXIS 2 trial (NCT04169373) assessed the efficacy and safety of upadacitinib (UPA) in patients with non-radiographic axial spondyloarthritis (nr-axSpA). This subgroup analysis investigated the efficacy of UPA in early versus established disease.

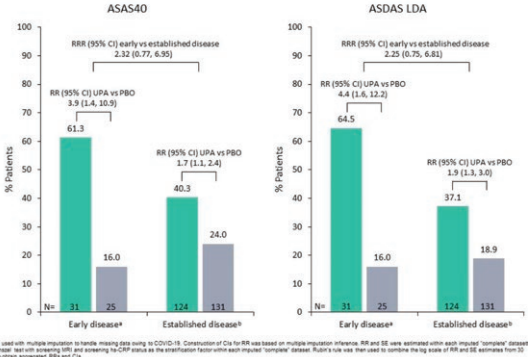
Objectives: This post hoc analysis evaluated the rates of achievement of ≥40% improvement in ASAS score (ASAS40 response) and Ankylosing Spondylitis Disease Activity Score (ASDAS) low disease activity (LDA; <2.1) at week 14 in early versus established disease (defined as symptom duration <2 versus ≥2 years).

Methods: In SELECT-AXIS 2[1], adult patients with or without prior biologic DMARD (bDMARD) exposure, with a clinical diagnosis of axSpA, fulfilling the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for nr-axSpA, and with objective signs of active inflammation on MRI of SI joints and/or high-sensitivity (hs)-CRP exceeding the upper limit of normal (2.87 mg/L) at screening, were randomized 1:1 to UPA 15 mg once daily or placebo (PBO) for 52 weeks. Response rate, relative risk (RR; UPA versus PBO), and RR ratio (RRR; early versus established disease) are reported. When interpreting RRRs, a 95% confidence interval (CI) that crosses 1 indicates no statistically significant difference between the groups being compared.

Results: Baseline characteristics were similar in patients with early versus established disease, although the proportion of females, mean age, and rates of prior bDMARD exposure were higher in established versus early disease **(Table 1)**. Mean symptom duration was 1.0 versus 10.9 years in patients with early versus established disease. ASAS40 and ASDAS LDA response rates at week 14 were significantly increased with UPA versus PBO in both early and established disease (ASAS40: 61.3% versus 16.0% and 40.3% versus 24.0%; ASDAS LDA: 64.5% versus 16.0% and 37.1% versus 18.9%; respectively) **(Figure 1)**. For ASAS40 and ASDAS LDA, the RR of response for UPA versus PBO was greater in early versus established disease (3.9 versus 1.7 and 4.4 versus 1.9, respectively). RRRs for ASAS40 and ASDAS LDA for early versus established disease were 2.3 (95% CI: 0.77, 6.95) and 2.3 (95% CI: 0.75, 6.81), respectively, reflecting no statistically significant difference in treatment response between early and established disease.

Conclusion: UPA 15 mg is more efficacious than PBO in reducing signs and symptoms of nr-axSpA, regardless of symptom duration. Although treatment responses were numerically higher in early disease, the differences versus established disease were not statistically significant.

Figure. Rates of Achievement of ASAS40 Response and ASDAS LDA at Week 14 (NRI-MI)



Non-responder imputation was used with multiple imputation to handle missing data owing to COVID-19. Construction of CIs for RR was based on multiple imputation inference. RR and SE were estimated within each imputed "complete" dataset using the Cochran-Mantel-Haenszel test with screening (vIR) and screening hs-CRP status as the stratification factor within each imputed "complete" dataset. Rubin's rule was then used to combine the log scale of RR and SE estimates from 30 imputed "complete" datasets to obtain aggregated RRs and CIs

[a]Defined as symptom duration <2 years. [b]Defined as symptom duration ≥2 years.

ASAS40, ≥40% improvement in Assessment of SpondyloArthritis international Society score; ASDAS LDA, Ankylosing Spondylitis Disease Activity Score low disease activity; CI, confidence interval; hs-CRP, high-sensitivity CRP; NRI-MI, non-responder imputation with multiple imputation; PBO, placebo; RR, relative risk; RRR, RR ratio; SE, standard error; UPA, upadacitinib

REFERENCE:

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Table 1. Baseline demographics and disease characteristics in patients with early versus established disease

Characteristic, mean (SD)[a]	Symptom duration	
	Early disease[b] (N=56)	Established disease[c] (N=255)
Female, n (%)	28 (50.0)	153 (60.0)
Age, years	35.7 (13.4)	43.4 (11.4)
Duration since axSpA diagnosis, years	0.7 (0.7)	5.3 (6.0)
Median (range) duration since axSpA diagnosis, years	0.5 (0.1, 4.8)	3.4 (0.1, 32.4)
Duration of axSpA symptoms, years	1.0 (0.4)	10.9 (7.8)
Median (range) duration of axSpA symptoms, years	1.0 (0.2, 2.0)	8.7 (2.0, 41.1)
HLA-B27 positive, n (%)	37 (66.1)	146 (58.2)[d]
Concomitant csDMARD use, n (%)	18 (32.1)	72 (28.2)
Concomitant oral corticosteroid use, n (%)	6 (10.7)	29 (11.4)
Prior bDMARD exposure, n (%)	7 (12.5)	95 (37.3)
ASDAS-CRP	3.7 (0.7)	3.6 (0.7)
BASFI (0–10)	5.5 (2.0)	6.0 (2.1)
MRI SPARCC score (SI joints)	4.8 (9.2)[e]	3.8 (8.0)[f]
Patients' assessment of total back pain (NRS 0–10)	7.0 (1.3)	7.3 (1.5)

[a]All data are mean (SD) unless otherwise stated. [b]Defined as symptom duration <2 years. [c]Defined as symptom duration ≥2 years. [d]N=251. [e]N=51. [f]N=237axSpA, axial spondyloarthritis; ASDAS, Ankylosing Spondylitis Disease Activity Score; bDMARD, biologic DMARD; csDMARD, conventional synthetic DMARD; NRS, numeric rating scale; SD, standard deviation; SPARCC, Spondyloarthritis Research Consortium of Canada

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POS1109

PUTATIVE ROLE OF THE HISTIDINE AND TRYPTOPHAN BIOCHEMICAL PATHWAYS IN THE MODE OF ACTION OF UPADACITINIB IN PATIENTS WITH ANKYLOSING SPONDYLITIS

Keywords: -omics, Spondyloarthritis, Clinical trials

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Background: Upadacitinib (UPA) 15 mg QD is efficacious in patients with active ankylosing spondylitis (AS) exhibiting inadequate responses to nonsteroidal anti-inflammatory drugs (NSAIDs-IR).[1]

Objectives: We determined the impact of UPA on the global metabolome in these patients.

Methods: Baseline (BL), weeks 4, and 14 serum samples were obtained from a subset of patients enrolled in SELECT-AXIS1 (PBO, n = 59 out of 94; UPA, n = 59 out of 93). Patients met the modified New York AS criteria and had active disease at BL. Samples were processed using dansyl-^{12}C-labeling kits or DmPA-^{12}C-labeling kits for each chemical-group channel and analyzed by LC-MS–based metabolomics. Data analysis was performed using a commercial software and metabolite identification was done using a commercial reference database.[2] Tier 1 and 2 metabolites matched single compounds from a labeled metabolite library and a linked identity library, respectively. Tier 3 metabolites matched more than 1 compound. Differentially modulated metabolites (DMM) were identified using a mixed linear model measuring change from BL for each treatment group (selection criteria, absolute Log10 fold change ≥ 0.079, and false discovery rate ≤ 0.1). Pathway enrichment analyses were conducted using a dedicated software.[3] Relationships between metabolite level changes, and clinical changes were assessed by Pearson's correlation.

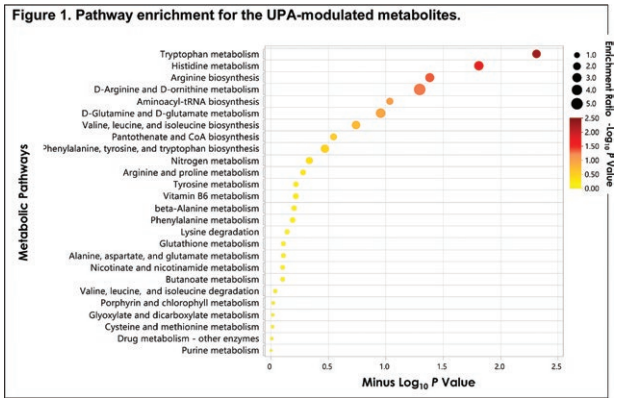
Results: We detected a total of 8020 distinct metabolites (ie, ≥ 80% detectability across timepoints within each treatment group) across the global metabolome. From these 8020 metabolites, we identified 289 and 221 DMM at weeks 4 and 14 in the UPA group vs 32 and 89 in the PBO group, respectively. Most DMM in the UPA group (187 and 144 at weeks 4 and 14, respectively) belonged to the Tier 3 identification category, and 51 and 40 at weeks 4 and 14, respectively, belonged to the Tier 1 and 2 categories. Pathway enrichment suggests UPA affects the histidine and tryptophan biochemical pathways (**Figure 1)**, consistent with increases in metabolites observed in the UPA group. Increases in histidine and tryptophan levels were significantly associated with an improvement in CRP levels and Ankylosing Spondylitis Disease Activity Score-CRP scores ($P \leq .05$). Increases in histidine levels were also associated with the improvement in MRI Spondyloarthritis Research Consortium of Canada Spine indices.

Conclusion: This is the first comprehensive metabolome analysis of serum samples collected from patients with AS treated with UPA. Data highlight the promise of advanced metabolomics to elucidate therapeutic agent's mode of action in AS. The putative effect of UPA on the tryptophan biochemical pathway is of particular interest because the tryptophan/kynurenine pathway is associated with chronic pain[4] and is perturbed toward the degradation of tryptophan in patients with AS.[5] We hypothesize that the increase in tryptophan and histidine may be related to the mode of action of UPA in NSAID-IR patients with AS.

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Figure 1. Pathway enrichment for the UPA-modulated metabolites.



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POS1110

PATIENT CLUSTERS IDENTIFIED BY MACHINE LEARNING: DATA FROM A POOLED ANALYSIS OF PHASE-3 TRIALS OF SECUKINUMAB IN PSORIATIC ARTHRITIS, ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS WITH AXIAL MANIFESTATIONS

Keywords: bDMARD, Spondyloarthritis

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Background: Universally acceptable criteria to define axial psoriatic arthritis (PsA) are lacking. Machine learning (ML) algorithms can detect patterns from large clinical datasets and identify clusters with potential therapeutic or prognostic significance in PsA patients (pts) with axial manifestations.[1]

Objectives: To identify pt clusters based on baseline (BL) demographics and clinical indicators to support characterisation of the axial PsA phenotype within the spondyloarthritis (SpA) spectrum.

Methods: Pooled BL demographics and clinical data of secukinumab (SEC)-treated pts from 10 Phase-3 studies: FUTURE 1–5 (PsA), MEASURE 1–4 (ankylosing spondylitis, AS) and MAXIMISE (PsA with axial manifestations) were analysed to identify pt clusters by ML.[2] Finite mixture model methodology was applied to the pooled dataset. Longitudinal responses of SEC 300 mg vs 150 mg were explored across the identified clusters and clinical indicators tender joint counts (TJC), swollen joint counts (SJC) and enthesitis.

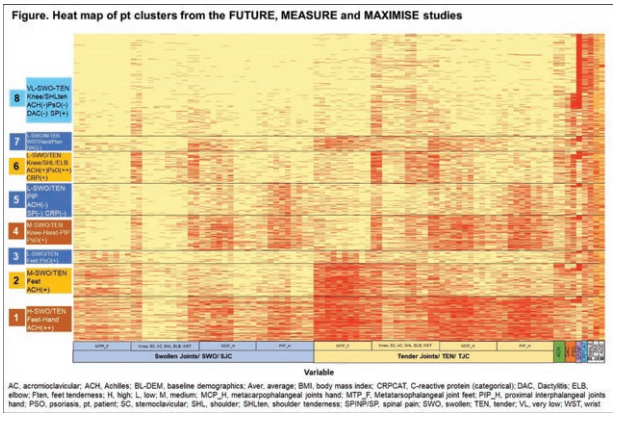
Results: Eight distinct clusters were identified (n=3907, **Figure 1 and Table 1**). Pts with PsA with axial manifestations (MAXIMISE) were overrepresented in clusters 6–8. Pts in cluster 6 (mean age 48 yrs; 46% male) were overweight with pronounced psoriasis (PsO), and high articular burden in large joints. Pts in cluster 7 (mean age 47 yrs; 53% male) were less overweight with lower polyarticular joint counts (mean 11 joints) and tenderness focused on the feet, wrists and hands. Pts in cluster 8 were mostly pts with AS (mean age 43 yrs; 64% male), less overweight with oligoarthritis and high prevalence of spinal pain. Pts with PsA (FUTURE) were overrepresented in clusters 1–5. Longitudinal analysis showed significant improvements with SEC 300 mg vs 150 mg in clusters 6 and 8 for TJC, and cluster 7 for SJC.

Conclusion: PsA clusters obtained by ML in the pooled dataset indicate phenotypical heterogeneity of pts with PsA with axial manifestations and overlapping features across the SpA spectrum.

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AC, acromioclavicular; ACH, Achilles; BL-DEM, baseline demographics; Aver, average; BMI, body mass index; CRPCAT, C-reactive protein (categorical); DAC, Dactylitis; ELB, elbow; Flen, feet tenderness; H, high; L, low; M, medium; MCP_H, metacarpophalangeal joints hand; MTP_F, Metatarsophalangeal joint feet; PIP_H, proximal interphalangeal joints hand; PSO, psoriasis, pt, patient; SC, sternoclavicular; SHL, shoulder; SHLten, shoulder tenderness; SPINP/SP, spinal pain; SWO, swollen; TEN, tender; VL, very low; WST, wrist

Table 1. Pt characteristics by cluster

	H-SWO/TEN ACH (++)	M-SWO/TEN ACH (+)	L-SWO/TEN PsO (+)	M-SWO/TEN PsO (+)	L-SWO/TEN ACH (-)	L-SWO/TEN ACH (+) PsO (++)	L-SWO/M-TEN DAC (-)	VL-TEN-SWO ACH/DAC/PsO (-)
Variables, mean (SD) unless specified	**Cluster 1 (n=567)**	**Cluster 2 (n=420)**	**Cluster 3 (n=164)**	**Cluster 4 (n=452)**	**Cluster 5 (n=403)**	**Cluster 6 (n=408)**	**Cluster 7 (n=193)**	**Cluster 8 (n=1300)**
Pt demographics								
Male, n (%)	225 (39.7)	183 (43.6)	98 (59.8)	193 (42.7)	239 (59.3)	187 (45.8)	103 (53.4)	829 (63.8)
BMI (kg/m^2)	30.0 (7.05)	29.6 (6.53)	28.5 (5.40)	30.3 (6.68)	28.1 (5.39)	30.2 (6.15)	28.6 (5.09)	27.3 (5.41)
Age (yrs)	51.3 (11.58)	47.8 (12.01)	46.5 (11.59)	49.9 (11.93)	48.4 (12.20)	48.2 (12.22)	46.9 (11.67)	42.9 (12.14)
Clinical indicators								
SJC	14.6 (8.44)	7.2 (4.49)	4.0 (1.93)	8.8 (4.00)	5.5 (2.80)	5.0 (2.43)	3.7 (2.78)	0.9 (1.30)
TJC	29.0 (7.22)	16.0 (4.87)	7.2 (2.67)	15.1 (4.48)	7.5 (3.21)	8.6 (2.76)	10.9 (3.12)	2.5 (2.40)
ACH tendon*	1 (0.91)	0.9 (0.90)	0.4 (0.66)	0.5 (0.76)	0.2 (0.57)	0.7 (0.88)	0.5 (0.75)	0.3 (0.64)
DAC, n (%)	247 (43.6)	156 (37.1)	76 (46.3)	171 (37.8)	139 (34.5)	150 (36.8)	48 (24.9)	206 (15.9)
PsO, n (%)	254 (44.9)	185 (44.0)	85 (51.8)	233 (51.5)	197 (48.9)	252 (61.8)	84 (43.5)	410 (31.5)
CRP >5 mg/L, n (%)	278 (49.0)	213 (50.7)	71 (43.3)	227 (50.2)	155 (38.5)	228 (55.9)	86 (44.6)	665 (51.2)
Spinal pain, n (%)	184 (32.5)	176 (41.9)	62 (37.8)	138 (30.5)	100 (24.8)	162 (39.7)	104 (53.9)	1035 (79.6)
Studies	Total, n (%)							
FUTURE	2453 (62.8)	493 (87.0)	323 (76.9)	130 (79.3)	386 (85.4)	354 (87.8)	303 (74.3)	121 (62.7)	343 (26.4)
MAXIMISE	485 (12.4)	45 (7.9)	43 (10.2)	19 (11.6)	45 (10.0)	29 (7.2)	65 (15.9)	40 (20.7)	199 (15.3)
MEASURE	969 (24.8)	29 (5.1)	54 (12.9)	15 (9.2)	21 (4.7)	20 (5.0)	40 (9.8)	32 (16.6)	758 (58.3)

*ACH tendon enthesitis for right or left footACH, Achilles; DAC, Dactylitis; H, high; L, low; M, medium; n, number of evaluable pts; SWO, swollen; TEN, tender; VL, very low

Acknowledgements: NIL.

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POS1111

TREATMENT WITH UPADACITINIB RESULTS IN THE INHIBITION OF A BROAD RANGE OF POTENTIALLY PATHOGENIC PATHWAYS IN NR-AXSPA AND BDMARD-IR AS PATIENTS: PROTEOMIC ANALYSIS FROM THE SELECT-AXIS 2 PHASE 3 STUDIES

Keywords: Clinical trials, Biomarkers, Spondyloarthritis

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Background: Upadacitinib (UPA) 15 mg QD, an oral Janus kinase inhibitor, demonstrated efficacy in patients with non-radiographic axial spondyloarthritis (nr-axSpA) and patients with ankylosing spondylitis (AS) with an inadequate response (IR) to biological disease-modifying antirheumatic drugs (bDMARD) in SELECT-AXIS 2[1,2] (NCT04169373).

Objectives: To identify biological pathways modulated by UPA in nr-axSpA and bDMARD-IR AS patients based on an extensive proteomic profiling, emphasizing those associated with disease activity at baseline.

Methods: A subgroup of patients from the SELECT-AXIS 2 program, with available biomarker samples, were selected for analysis (nr-axSpA PBO: n = 82; nr-axSpA UPA: n = 82; bDMARD-IR AS PBO: n = 111; bDMARD-IR AS UPA: n = 112). In addition, samples from 24 age- and gender-matched healthy volunteers (HVs) were included in the analysis. The levels of 1463 unique protein biomarkers (pBMs) were analyzed using proximity extension assay technology. Differences in pBMs levels between patients and HVs and their changes from baseline upon treatment were expressed as Log2 Fold Changes (Log2 FC). Relationships between pBMs levels and the Ankylosing Spondylitis Disease Activity Score using C-reactive protein (ASDAS-CRP) were derived using Pearson's correlation. A repeated measure mixed linear model identified pBMs differentially modulated by UPA. All tests were corrected for multiple testing using the Benjamini-Hochberg method. Significance threshold was defined as FDR ≤ 0.05. We used a commercially available software application for pathway analysis.

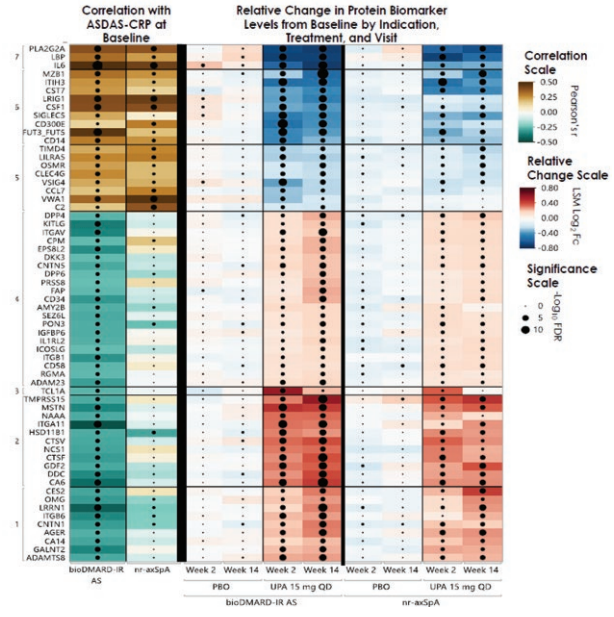
Results: At baseline, we identified 174 (nr-axSpA) and 178 (bDMARD-IR AS) pBMs that were significantly differentially expressed in patients compared to HVs. Only 24 out of 1463 pBMs tested were differentially expressed between the two patient populations. Notably, interleukin-6, matrix metalloproteinase-1, metalloproteinase-3, and interleukin 17 receptor A were significantly more elevated in bDMARD-IR AS patients than in nr-axSpA patients. The pathway enrichment analysis on the differential pBMs pointed to a dysregulation of the adaptive and innate immune systems, increase in endothelial activation, and damage to connective tissue in both patient groups, although more pronounced in bDMARD-IR AS patients. Baseline levels of 49 (4 negatives and 45 positives) and 178 (130 negatives and 48 positives) pBMs correlated with baseline ASDAS-CRP in the nr-axSpA and bDMARD-IR AS patients, respectively. Treatment with UPA resulted in a broad modulation of pBMs at weeks 2 and 14 in both patient groups, with a larger effect in bDMARD-IR AS patients than in nr-axSpA patients. Based on pathway prediction analysis, the effects of UPA on pBMs were consistent with the inhibition of the adaptive (T cell activation and migration, and antigen presenting cell activation) and innate (phagocyte and granulocyte migration and activation) immune pathways. The effects of UPA treatment on pBM correlating with ASDAS-CRP at baseline were consistent with UPA's broad activity on potential pathogenic pathways in both nr-axSpA and bDMARD-IR AS patients (**Figure 1**).

Conclusion: While presenting different degrees of axial skeletal involvement, nr-axSpA and bDMARD-IR AS patients share common pathogenic pathways, with a more pronounced dysregulation observed in the latter group as observed from our data. Treatment with UPA inhibited multiple potentially pathogenic pathways associated with disease activity at baseline in nr-axSpA and bDMARD-IR AS patients. These observations are consistent with prior analyses in bDMARD-naïve AS patients[3]. We propose that the clinical efficacy of UPA in these 2 patient populations may result, at least in part, from its broad biological activity observed at the protein level.

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Figure 1. *Effects of Treatment with UPA on the Relative Expression of pBMs Correlating Significantly with ASDAS-CRP at Baseline*



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Disclosure of Interests: Thierry Sornasse Shareholder of: May own stock or stock options of AbbVie, Employee of: AbbVie, In-Ho Song Shareholder of: May own stock or stock options of AbbVie, Employee of: AbbVie, Peter Wung Shareholder of: May own stock or stock options of AbbVie, Employee of: AbbVie, Yingtao Bi Shareholder of: May own stock or stock options of AbbVie, Employee of: AbbVie, Buvana Ravishankar Shareholder of: May own stock or stock options of AbbVie, Employee of: AbbVie, Hengcheng Alvis Hu Shareholder of: May own stock or stock options of AbbVie, Employee of: AbbVie, Walter P Maksymowych Consultant of: AbbVie, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Novartis, Pfizer, and UCB.

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POS1112 COMBINED BIOLOGICAL OR TARGETED THERAPY IN SPONDYLOARTHRITIS: EXPERIENCE FROM A MULTICENTER CASE SERIES IN SPAIN

Keywords: Spondyloarthritis

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Background: Combined biological or targeted therapy (CBTT) is rarely considered in clinical practice due to not being recommended in clinical guidelines, potential safety concerns and high costs. Successful experiences have been found with CBTT in refractory patients with inflammatory bowel disease (IBD). Previous early data in selected refractory spondyloarthritis (SpA) have shown encouraging results[1].

Objectives: Our aim was to assess real-world effectiveness and safety of CBTT in a wider SpA population.

Methods: This is a retrospective multicenter study. We identified patients with SpA and simultaneous combined use of two biological or targeted (excluding apremilast) agents with different therapeutic targets since 2017. All patients fulfilled axial or peripheral SpA ASAS criteria and signed written informed consent. Demographics, clinical, laboratory, and safety data were collected from electronic medical records. Cut-offs for remission/low activity criteria for axial-peripheral disease were ASDAS-CRP <1.3/<2.1 or DAS-28-CRP<2.6/<3.2 or DAPSA<4/<14, respectively. Major clinical improvement (MCI) was defined as a change in ASDAS-CRP>2 and DAS-28-CRP>1.2 units and improvement of >85% in DAPSA.

Results: A total of 39 CBTT courses were identified in 35 SpA patients (Table 1). The main indication for CBTT was active musculoskeletal disease (Table 2). Three patients presented remission or low SpA activity at baseline and were excluded in the efficacy SpA analysis. Most patients (89.7%) had previously failed at least one of the two therapies used in CBTT. The most common combination was TNF inhibitor plus IL12/23 inhibitor agent (n=20; 51.2%). Median exposure to CBTT was 16 months (IQR 11-24). At last follow-up, we observed a significant mean reduction in ASDAS-CRP (2.07; 95% CI: 1.31-2.83; p=0.001). Remission/low activity rates were 52.7%, and 61.1% (n=22) reached MCI. In a bivariate analysis, patients who reached MCI had a lower baseline ASDAS-CRP than those who did not (4.33 vs 6.20, p=0.052). Nine patients discontinued CBTT due to inefficacy, seven of them because of IBD activity. In 39 CBTT courses, 4 serious AE were identified in only 3 patients: non-infectious pulmonary infiltrates, a staphylococcal bacteremia and a patient with cytomegalovirus colitis and esophageal candidiasis.

Conclusion: Our preliminary results suggest that CBTT might be a feasible alternative in selected refractory multidomain SpA patients, with acceptable effectiveness/safety ratio. Prospective wider studies are warranted to confirm these data.

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[1] Valero-Martínez C et al. ARD. 2022;81(6):899-901.

Table 1. Baseline characteristics of the population and outcomes

Characteristics	N=35
Diagnosis, n (%)	
Axial + peripheral SpA	9 (25.7)
Axial SpA	9 (25.7)
Peripheral SpA	3 (8.5)
Psoriatic Arthritis	8 (22.8)
Juvenile Idiopathic Arthritis	6 (17.1)
Duration of SpA, years, median (IQR)	18 (8.5-20)
Extramusculoskeletal disease, n (%)	
Psoriasis	14 (40)
Uveitis	5 (14.2)
IBD	24 (68.5)
Number of prior bDMARDs/ tDMARDs, median (IQR)	3 (1.5-5)
Indication for CBTT, n (%)	
SpA	22 (56.4)
Psoriasis	1 (2.5)
IBD	7 (17.9)
IBD + SpA	8 (20.5)
Psoriasis + SpA	1 (2.5)
Dual treatment courses (n=39):	
●Secukinumab +	
○GOL 2, ETN 3, ADA 1	
●Ixekizumab +	
○ADA 1, GUS 1	
●Brodalumab + ADA 1	
●Ustekinumab +	
○ADA 9, GOL 2, CTZ 2, ETN 1, IFX 2, VED 1	
●Guselkumab +	
○ABT 1, VED 1, CTZ 1	
●Risankizumab + GOL 1	
●Vedolizumab +	
○GOL 1, ADA 1	
●Tofacitinib + IFX 1	
Clinical activity at last evaluation*	
SpA remission, n (%)	9/36 (25)
SpA low activity, n (%)	10/36 (27.7)
Discontinue glucocorticoids	11/20 (55)
Major clinical improvement SpA**	22/36 (61.1)

ABT: abatacept; ADA: adalimumab; bDMARDs: biological disease-modifying antirheumatic drugs;; CRP: C-reactive protein; CTZ: certolizumab ETN: etancercept; GOL: golimumab; GUS: guselkumab; IBD: inflammatory bowel disease; IQR: interquartile range; IFX: infliximab; n: number; SpA: spondyloarthritis; tDMARDs: targeted disease-modifying antirheumatic drugs; VED: vedolizumab

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Disclosure of Interests: None Declared.
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POS1113

PROFILING OF SYSTEMIC IMMUNE RESPONSES IN AXIAL SPONDYLOARTHRITIS PATIENTS REVEALS STRIKINGLY DISTINCT CELLULAR AND MOLECULAR MECHANISMS OF ACTION OF IL-17A INHIBITORS AND TNF-BLOCKERS

Keywords: bDMARD, Spondyloarthritis

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Background: IL-17A inhibitors (IL-17i) and TNF-inhibitors (TNFi) are currently the only biologic drugs available as first line treatment in axial spondyloarthritis (axSpA). While several studies have provided mechanistic insights into TNFi action, much less is known how IL-17i affect immune responses in patients.
Objectives: We have compared the effects of IL-17i and TNFi on immune cell frequencies and induced immune responses to obtain information about the mechanisms of action of these two drugs in axSpA patients *in vivo*.
Methods: Induced immune responses to microbial and pathway-specific stimuli were analyzed in peripheral blood samples from 40 axSpA patients before and after IL-17i or TNFi treatment, using highly standardized whole-blood stimulation assays. Changes in gene expression were determined by RNA sequencing and secreted molecules were measured using proximity ligation assays.
Results: IL-17A-blockade had very limited effects on systemic immune responses with no significant gene expression changes detectable in stimulated whole-blood cultures when comparing samples before and 16 weeks after treatment initiation. In contrast, anti-TNF therapy induced profound changes in patients' immune responses affecting the expression of more than 4000 genes. Pathways analysis revealed major effects of TNFi on the expression of genes involved in protection from bacterial (Tuberculosis, Legionellosis), viral (EBV, Influenza) and parasitic (Leishmaniasis, Toxoplasmosis) infections (Figure 1). Analysis of secreted inflammatory cytokines and chemokines showed that TNF-blockade also strongly affected innate and adaptive immune cell signaling, while only minor changes were observed in stimulation cultures from IL-17i-treated axSpA patients. Furthermore, we noted major effects of TNFi, but not of IL-17i, on neutrophil and monocyte counts in the circulation of treated patients.
Conclusion: We show that the two currently used biotherapies of axSpA act by strikingly distinct cellular and molecular mechanisms. While anti-TNF therapy has major effects on systemic immune responses with potential implications for increased susceptibility to infectious microorganisms, IL-17 inhibitors had a lesser impact on systemic immune responses compared to TNFi, suggesting that may rather act on non-immune cells and/or in inflamed tissues.

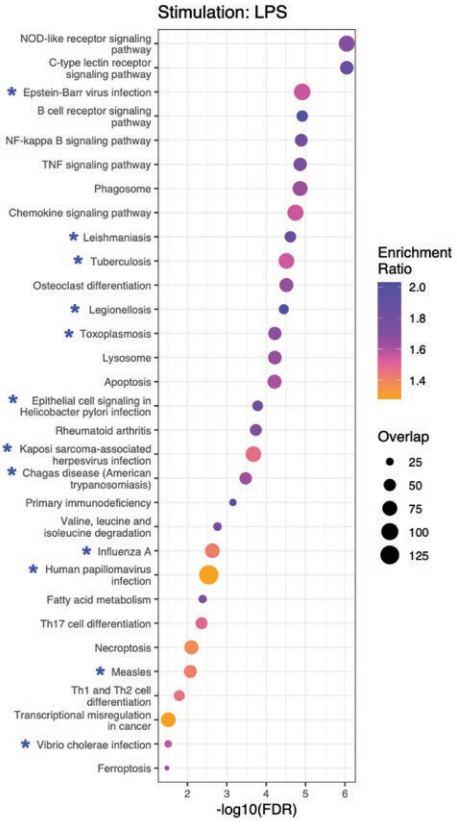


Figure 1: TNF-blockade affects multiple pathways associated with protection to infectious microorganisms. Pathway over-representation analysis (ORA) of differentially expressed genes from RNA-seq data generated from whole-blood stimulation (TruCulture) assays (LPS stimulus) performed before and 12 weeks after initiation of anti-TNF therapy. Pathway analysis was performed with the WEB-based gene set analysis toolkit (WebGestalt). Bubble plot representation of significant pathways with False Discovery Rate (FDR < 0.05, x-axis), enrichment ratio and gene counts (colors and bubble size, respectively). Blue asterisks mark infectious disease pathways.

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POS1114

CHARACTERISTICS OF DIFFICULT TO TREAT AXIAL SPONDYLOARTHRITIS: A COMPARATIVE ANALYSIS

Keywords: Spondyloarthritis, Real-world evidence, Disease-modifying drug (DMARDs)

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Background: The concept of difficult-to-treat rheumatoid arthritis (D2T RA) has recently emerged. It is defined by the persistence of disease activity and the failure of at least 2 b/tsDMARDs of 2 different mechanisms of action (MoA) [1]. In this definition, the period during which the treatments have failed is not included. The D2T concept has not yet been applied with consensus in axial spondyloarthritis (axSpA).
Objectives: To study the characteristics of patients with D2T axSpA to better identify the potential causes of treatment failure. The second objective was to study a sub-group of D2T axSpA patients with a predefined time criteria.
Methods: A multicentric retrospective longitudinal study was performed in secondary and tertiary centers. axSpA diagnosis was based on ASAS criteria. Patients were followed up from January 2016 to December 2021. Patients starting a b/tsDMARDs with a minimum of 2-year follow-up were included. D2T axSpA patients were defined as patients who received more than 2 b/tsDMARDs with different MoA among b/tsDMARD available. These patients were compared to non-difficult-to-treat axSpA patients (nD2T axSpA) using statistical tests. Very D2T axSpA patients were defined as patients who received at least 2 b/tsDMARDs in less than 2 years during the time of follow-up.
Results: 311 patients were included, 88 were D2T axSpA and 223 nD2T axSpA. Baseline characteristics are presented in the Table 1. No statistical difference was found between the 2 groups regarding main comorbidities, including fibromyalgia and depression. Among the D2T patients, 76 (86%) had presented a primary or secondary inefficacy from 2 drugs with different MoA and 12 (14%) presented a contraindication to TNFinhibitor or IL17 inhibitor (multiple sclerosis, inflammatory bowel diseases, recurrent uveitis, solid cancer less than 5 years old). Seven patients were categorized as very D2T axSpA. When compared to the rest of the D2T axSpA group, no significant difference was observed.
Conclusion: Significant differences were found between the characteristics of patients D2T axSpA and nD2T axSpA, which were the smoking status, axSpA duration, presence of arthritis, history of uveitis and baseline BASDAI. Limitations exist about applying the EULAR D2T RA definition to axSpA. The inclusion of a time should also be considered.

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Table 1. Baseline characteristics of patients

Parameters	N	D2T axSpA n = 88	N	nD2T axSpA n = 223	p value
Men	88	44 (50.0)	223	126 (56.5)	0.30
Age (years), mean ± SD	88	47.6 ± 12.5	223	46.4 ± 13.1	0.46
BMI, mean ± SD	70	26.3 ± 5.5	163	27.0 ± 6.1	0.41
axSpA duration (years), median (IQR)	83	8.0 (5.0; 13.0)	205	9.0 (7.0; 17.0)	**0.006**
Current smoker status	59	18 (30.5)	121	23 (19.0)	0.23
Clinical axSpA characteristics at baseline					
Radiographic axSpA	73	52 (71.2)	179	108 (60.3)	0.10
Arthritis	86	30 (34.9)	215	46 (21.4)	**0.015**
Enthesitis	66	14 (21.2)	207	33 (15.9)	0.32
Dactylitis	83	4 (4.8)	222	11 (6.0)	1.00
Psoriasis at baseline	81	17 (21.0)	208	42 (20.2)	0.88
IBD	86	5 (5.8)	191	6 (3.1)	0.33
Uveitis	85	18 (21.2)	191	21 (11.0)	**0.03**
Positive HLA B27 status	78	58 (74.4)	190	131 (68.9)	0.33
Baseline CRP (mg/L), median (IQR)	78	11.1 (3.0; 25.7)	168	12.4 (4.6; 22.8)	0.78
Baseline BASDAI, mean ± SD	80	58.6 ± 14.7	163	58.6 ± 14.7	**0.015**

Values are expressed as number (%) unless otherwise stated. axSpA: axial spondyloarthritis. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; bDMARD: biological disease modifying antirheumatic drug; BMI: body mass index; CRP: C-reactive protein; (n)D2T: (non) difficult-to-treat; HLA: human leukocyte antigen IBD: inflammatory bowel disease; IQR: interquartile range; N: number of available observations; NA: not applicable; SD: standard deviation

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POS1115

EFFECT OF SECUKINUMAB VERSUS ADALIMUMAB BIOSIMILAR ON RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: SUBGROUP ANALYSES BY BASELINE SYNDESMOPHYTES AND C-REACTIVE PROTEIN STATUS

Keywords: Spondyloarthritis, bDMARD

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Background: SURPASS, a phase IIIb randomised controlled study in patients (pts) with radiographic axial spondyloarthritis (r-axSpA), found low spinal radiographic progression over 2 years with no significant difference between the secukinumab (SEC) and adalimumab biosimilar (SDZ-ADL) arms.[1,2] Baseline (BSL) radiographic damage (presence of syndesmophytes) and elevated C-reactive protein (CRP) levels have been identified as predictors of radiographic progression in r-axSpA.[3]
Objectives: To evaluate the effect of SEC and SDZ-ADL on spinal radiographic progression in subgroups of pts based on the presence of syndesmophytes and elevated high-sensitivity CRP (hsCRP) levels at BSL, from the SURPASS study.
Methods: Biologic-naïve pts with active r-axSpA and with hsCRP ≥5 mg/L and/or ≥1 syndesmophyte(s) on spinal radiographs were randomised (1:1:1) to SEC (150 or 300 mg; dose-blinded) or SDZ-ADL (40 mg; open label). Pts were categorised into the following subgroups at BSL: hsCRP ≥5 mg/L (CRP+), hsCRP <5 mg/L (CRP–), presence of syndesmophyte(s) (Synd+), absence of syndesmophyte(s) (Synd–), and CRP+Synd+. The proportion of pts with no radiographic progression (change from baseline in modified Stoke Ankylosing Spondylitis Spinal Score [mSASSS] ≤0.5), mean change from BSL in mSASSS, and proportion of pts with no new syndesmophytes(s) in each subgroup at week 104 (all as observed) are reported.
Results: Of the 859 pts, 653 (76%) were CRP+, 627 (73%) were Synd+, and 466 (54%) were CRP+Synd+ at BSL. Demographic and BSL disease characteristics were largely balanced across subgroups and treatment arms, except for the Synd– group in which mean age, proportion of male pts, and mean time since diagnosis were lower than in other subgroups (**Table 1**).
All radiographic outcomes at week 104 were similar across treatment arms; however, differences were observed between subgroups irrespective of the treatment arm. The Synd– subgroup followed by the CRP– subgroup showed the least progression in all radiographic outcomes (as indicated by the higher proportion of pts with no radiographic progression and no new syndesmophytes, and lower mean change from BSL in mSASSS), across treatment arms (**Figure 1**). The CRP+Synd+ subgroup followed by the Synd+ subgroup and the CRP+ subgroup had higher radiographic progression compared with the Synd– and CRP– subgroups (**Figure 1**).
Conclusion: Spinal radiographic progression over 2 years was low with no notable difference between SEC and SDZ-ADL arms regardless of the presence or absence of specific predictive factors for progression (syndesmophytes/elevated CRP). Expectedly, pts from subgroups without predictive factors (especially Synd–, followed by CRP–) had lower rates of radiographic progression.

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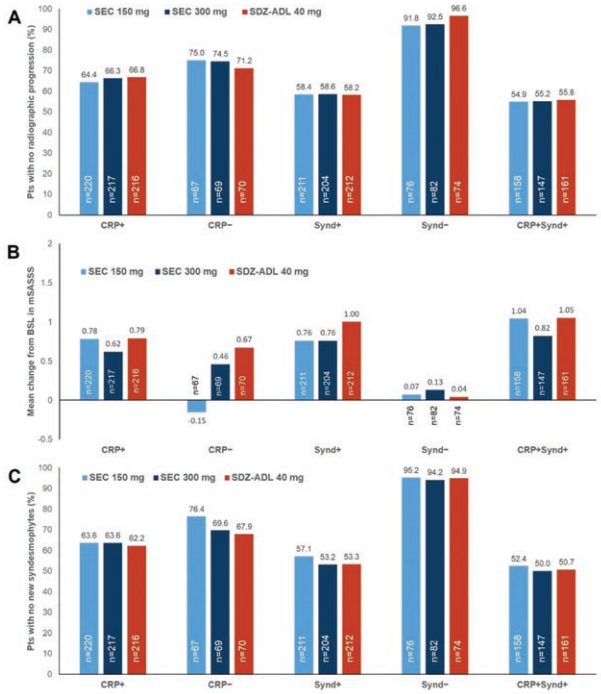
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Table 1. Demographic and baseline disease characteristics by subgroup

Characteristics, mean values unless specified otherwise	CRP+ N=653	CRP− N=206	Synd+ N=627	Synd− N=232	CRP+Synd+ N=466
Age (years)	40.7	46.4	45.0	34.2	43.4
Male, %	80.1	73.3	82.1	68.5	84.3
BMI (kg/m²)	27.3	27.2	27.6	26.4	27.6
Time since diagnosis of r-axSpA (years)	6.3	8.0	7.6	4.3	7.2
mSASSS	16.2	17.8	22.5	0.1	22.5
Number of syndesmophytes	6.8	7.6	9.6	0	9.5
BASDAI	7.2	6.9	7.1	7.2	7.2
hsCRP (mg/L)	26.1	2.6	19.9	22.0	25.8
HLA-B27 positive, %	82.4	77.7	81.2	81.5	82.0

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; HLA-B27, human leukocyte antigen B27; hsCRP, high-sensitivity C-reactive protein; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; r-axSpA, radiographic axial spondyloarthritis

Figure 1. Radiographic outcomes at week 104 by subgroup: A) Pts with no radiographic progression (change in mSASSS ≤0.5), B) Mean change from BSL in mSASSS, C) Pts with no new syndesmophytes



BSL, baseline; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; Pts, patients; SDZ-ADL, adalimumab biosimilar; SEC, secukinumab
A patient was considered to have a syndesmophyte if at least one reader assessed mSASSS score of ≥2 for any individual vertebral corner

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POS1116

TIME TO IMPROVEMENT OF PAIN, MORNING STIFFNESS AND DISEASE ACTIVITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TOFACITINIB

Keywords: Pain, Patient reported outcomes, Spondyloarthritis

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Background: Pain, morning stiffness and disease activity are core domains of ankylosing spondylitis (AS), relevant to patients (pts) and physicians. AS treatment guidelines recommend using the AS Disease Activity Score C-reactive protein ($ASDAS_{CRP}$) to assess disease activity. Greater improvements in pain, morning stiffness and disease activity were previously shown with tofacitinib vs placebo (PBO) in pts with AS.[1] There are limited data on time to improvement in these core domains in pts with AS receiving tofacitinib.

Objectives: To estimate the median time to improvement of pain, morning stiffness and disease activity in tofacitinib-treated pts with AS.

Methods: This post hoc analysis used data from a Phase 3 trial (NCT03502616)[1] in pts with AS receiving tofacitinib 5 mg twice daily (BID) or PBO to Week (W)16. After W16, all pts received open-label tofacitinib 5 mg BID to W48. Outcomes included nocturnal pain (numerical rating scale 0–10), morning stiffness (mean of Bath AS Disease Activity Index [BASDAI] Questions 5 and 6), BASDAI total score and $ASDAS_{CRP}$. Median time (weeks) to initial improvement events was estimated using non-parametric Kaplan-Meier models. Initial improvement event was defined as time to first post-baseline observation with an improvement of ≥30% (nocturnal pain ["much improved"][2]), ≥50% (nocturnal pain ["very much improved"],[2] morning stiffness and BASDAI total score) or $ASDAS_{CRP}$ ≥1.1 (clinically important improvement)/≥2.0 (major improvement) points.

Results: Overall, 269 pts (tofacitinib: n=133; PBO→tofacitinib: n=136) were assessed. Median times to initial improvement events were shorter with tofacitinib vs PBO→tofacitinib (p<0.05 [Table 1]). Median times to initial ≥30% and ≥50% improvement in nocturnal pain for tofacitinib were 4 and 8 weeks, respectively, and 24 weeks (8 weeks since switch to tofacitinib) for both thresholds for PBO→tofacitinib. Median time to initial ≥50% improvement in morning stiffness and BASDAI total score for tofacitinib was 12 weeks, and 32 weeks (16 weeks since switch to tofacitinib) for PBO→tofacitinib. Median time to $ASDAS_{CRP}$ improvement ≥1.1 for tofacitinib was 4 weeks, and 24 weeks for PBO→tofacitinib (not estimable [NE] for $ASDAS_{CRP}$ improvement ≥2.0 [both treatment arms]). Limitations: this was a post hoc analysis, there was no active treatment comparator, trial pt population may not reflect routine care pt population and comparisons with PBO were only possible to W16.

Table 1. Median times (weeks) to initial improvement events (Kaplan-Meier analysis)

	Median time (interquartile range)		
Improvement threshold	**Tofacitinib 5 mg BID (N=133)**	**PBO→tofacitinib[a] (N=136)**	**p value**
≥30% improvement			
Nocturnal pain	4 (2–24)	24 (8–32)	0.0003
≥50% improvement			
Nocturnal pain	8 (4–40)	24 (16–NE)	<0.0001
Morning stiffness	12 (4–NE)	32 (24–NE)	0.0091
BASDAI total score	12 (4–NE)	32 (16–NE)	0.0002
Improvement in $ASDAS_{CRP}$			
≥1.1 points	4 (2–20)	24 (12–40)	<0.0001
≥2.0 points	NE	NE	0.0361

p values are based on log-rank tests for differences in survival curves for tofacitinib vs PBO→tofacitinib[a]Switched to open-label tofacitinib at W16

Conclusion: In pts with AS, during the first month of tofacitinib treatment, it is expected that half of pts will experience ≥30% improvement in nocturnal pain ("much improved") and a clinically important improvement in $ASDAS_{CRP}$. During the first 2 and 3 months of tofacitinib treatment, it is expected that half of pts will experience ≥50% improvement in nocturnal pain ("very much improved") and morning stiffness, respectively. Improvements in pain, morning stiffness and disease activity occurred more rapidly with tofacitinib vs PBO→tofacitinib. This study informs physicians and pts receiving tofacitinib of when improvement in these core domains in AS may be anticipated.

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POS1117 DOWNSTREAM EFFECTS ON CYTOKINE EXPRESSION PROFILE OF SIX DIFFERENT JAK INHIBITORS IN AN IN VITRO MODEL OF IMMUNE MEDIATED INFLAMMATORY ARTHRITIS

Keywords: Cytokines and chemokines, Targeted synthetic drugs

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Background: Janus kinase inhibitors (JAKis) are a group of disease modifying antirheumatic drugs (DMARDs) used for the treatment of several immune mediated inflammatory arthritides (IMIAs) including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondyloarthritis (SpA). There are several JAK inhibitors (JAKis) with different selectivity already approved or in clinical and preclinical development[1]. Thus, tofacitinib is a JAK1/3 inhibitor, baricitinib is an JAK2/3 inhibitor, filgotinib and upadacitinib are selective JAK1 inhibitors, decernotinib is a selective JAK3 inhibitor[2] and deucravacitinib is a selective tyrosine kinase 2 (TYK2) inhibitor[3]. The downstream effects on cytokine expression profile of JAKis with different selectivity is not fully understood.

Objectives: Here we investigate whether JAKis with different selectivity show differences in downstream cytokine expression in an in vitro model of IMIA.

Methods: Synovial fluid mononuclear cells (SFMCs) from patients with peripheral SpA (n=3), PsA (n=3), juvenile idiopathic arthritis (n=4), and unspecified inflammatory arthritis (n=1). Synovial fluid was collected after therapeutic arthrocentesis. SFMCs from each patient were cultured for 48 hours with the JAKis priorly listed. Culture medium and DMSO were used as negative controls. In vitro drug response was assessed by MesoScale V-PLEX Proinflammatory Panel 1 Human Kit measuring interferon γ (IFN- γ), interleukin 1β (IL-1β), IL-2, IL-4, IL-6, IL-10, IL-12p70, IL-13 and TNFα.

Results: First, we tested whether JAKis with a similar selectivity had comparable effects on the secretion of cytokines. Indeed, JAKis with selectivity towards JAK1 and JAK3 clustered together in the hierarchical analysis. Then, we examined whether there was a difference between the six JAKis on mean cytokine expression merging all cytokines (mean merged cytokine expression). All JAKis with a JAK1 selectivity decreased the cytokine secretion more than the JAK2/3 inhibitor baricitinib (filgotinib vs. baricitinib, p<0.005; upadacitinib vs. baricitinib, p<0.05; tofacitinib vs. baricitinib, p<0.05). There was no difference between the JAKis with JAK1 selectivity and decernotinib (JAK3) or deucravacitinib (TYK2). After correcting for multiple comparisons using Tukey's test, there was also no difference in mean merged cytokine expression between JAKis with JAK1 selectivity and baricitinib. Finally, we studied differences between individual patients. Interestingly, JAKis with different selectivity were better at decreasing certain cytokine secretions compared to other JAKis on an individual level. E.g., SFMCs from patient H had a generally higher decrease in cytokine secretion after filgotinib treatment.

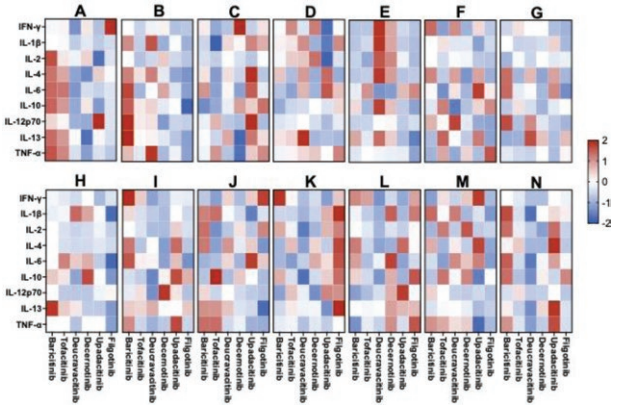


Figure 1. Cytokine secretion for each JAKi treatment relative to DMSO control for each patient (n=14). Data are z-normalized for each patient relative to each cytokine's level of secretion.

Conclusion: Similarities in mode of action for the six JAKis were reflected in drug response measured by multiple cytokine secretions. Generally, JAKis with JAK1 and JAK3 selectivity decreased total cytokine secretion the most. In selected patients, specific JAKis decreased total cytokine secretion considerably more than the remaining JAKis, while most patients had an equal response to all six JAKis.

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POS1118 DISCRIMINATING CAPACITY OF THE ASAS HEALTH INDEX IN PATIENTS TREATED WITH IXEKIZUMAB IN THE COAST PROGRAMME

Keywords: Spondyloarthritis, bDMARD, Clinical trials

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Background: The Assessment of SpondyloArthritis international Society Health Index (ASAS HI) is a validated health outcome measure used to assess functioning and health in patients (pts) with axial spondyloarthritis (axSpA) [1]. Two thresholds for clinical improvement have been recently proposed: improvement ≥3 points and a 30% improvement from baseline [1,2]. However, an exploration of the optimal threshold in an independent cohort has not been carried out to date.

Objectives: Using data from the COAST trials, this analysis aimed to test the discriminatory capacity of the ASAS HI at different thresholds of improvement.

Methods: This *post hoc* analysis included patients treated with either ixekizumab (IXE) 80 mg every 4 weeks (Q4W) or placebo (PBO) from the intent-to-treat populations of COAST-V (NCT02696785) and COAST-W (NCT02696798) for radiographic (r)-axSpA, and COAST-X (NCT02757352) for non-radiographic (nr)-axSpA over 16 weeks. To assess the discriminatory capacity of the ASAS HI, response rates at Week 16 were compared between IXE Q4W and PBO using Fisher's exact test. Phi coefficients (ranging from -1 to +1) were calculated to compare the degree of association between the level of improvement and treatment allocation. Missing data were handled using non-responder imputation.

Results: ASAS HI data at Week 16 were available for pts with r-axSpA from COAST-V (IXE Q4W, N=81; PBO, N=87) and COAST-W (IXE Q4W, N=114; PBO, N=104) and pts with nr-axSpA from COAST-X (IXE Q4W, N=96; PBO, N=105). Percentages of pts reaching improvement scores for different study arms are shown in Figure 1. Differences in response rates by the various absolute or

relative thresholds for improvement are shown in Table 1. Data demonstrated an inconsistent picture of the best performing threshold between the different COAST studies. While for COAST-V discriminatory capacity were demonstrated for higher values this was opposite to COAST-W, and there was no clear discriminating threshold in COAST-X (Table 1, Figure 1). The majority of Phi coefficients were below 0.2, suggestive of low discriminatory capacity.

Conclusion: In this post hoc analysis of pts from the COAST trials at Week 16, several thresholds of improvement of the ASAS HI seem to have discriminating capacity. However, there were some differences between the COAST trials and no single threshold worked best in the r-axSpA (bDMARD-naïve and experienced) and nr-axSpA populations.

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Table 1. Baseline ASAS HI scores presented as mean (SD) followed by the absolute difference in the proportion (%) of responders by the different ASAS HI improvement thresholds.

	COAST-V r-axSpA, bDMARD-nacor			COAST-W r-axSpA, TNFi-experienced			COAST-X nr-axSpA, bDMARD-naien		
Baseline	7.5 (3.3)			10.0 (3.7)			8.6 (3.4)		
IXE Q4W	8.1 (3.5)			9.0 (3.5)			9.0 (3.7)		
PBO									
ASAS HI Improvement (≥)	Trt Diff (%)	p-value	Phi	Trt Diff (%)	p-value	Phi	Trt Diff (%)	p-value	Phi
2.0 pt	2.3	0.876	0.023	25.5	*0.001*	*0.255*	9.8	*0.198*	*0.098*
2.5 pt	8.6	0.265	0.088	16.3	0.022	0.173	7.3	0.301	0.076
3.0 pt	8.6	0.265	0.088	16.3	0.022	0.173	7.3	0.301	0.076
3.5 pt	15.7	*0.024*	*0.187*	10.8	0.087	0.129	7.0	0.337	0.078
4.0 pt	15.7	*0.024*	*0.187*	10.8	0.087	0.129	7.0	0.337	0.078
20%	8.9	0.276	0.089	23.9	*0.001*	*0.242*	10.7	0.153	0.107
25%	10.6	0.210	0.106	23.1	0.001	0.237	10.5	0.150	0.107
30%	17.3	0.026	0.177	16.2	0.023	0.171	14.5	*0.040*	0.150
35%	16.7	0.031	0.177	11.6	0.075	0.131	12.3	0.092	0.131
40%	21.3	*0.004*	*0.232*	10.6	0.098	0.123	14.3	*0.042*	0.155
50%	15.9	0.030	0.183	11.1	0.064	0.142	14.1	*0.031*	*0.163*

Data are presented as non-responder imputation. Difference refers to the difference between IXE Q4W and PBO response rates. Best performing thresholds are italicized.

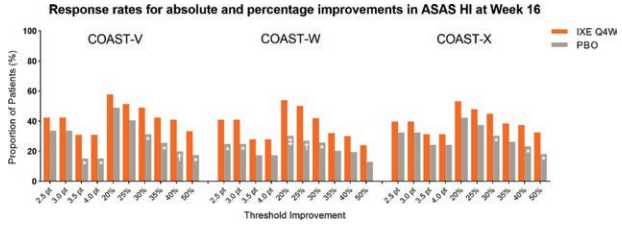


Figure 1. Data are presented as proportion (%) of patients.

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Disclosure of Interests: Uta Kiltz Speakers bureau: AbbVie, Biocad, Chugai, Eli Lilly and Company, Fresenius, Grünenthal, Hexal, Janssen, MSD, Novartis, Pfizer, Roche, UCB, Consultant of: AbbVie, Biocad, Chugai, Eli Lilly and Company, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche, UCB, Grant/research support from: AbbVie, Amgen, Biogen, Fresenius, GSK, Hexal, Novartis, Pfizer, Anna Moltó Consultant of: Abbvie, Biogen, BMS, Gilead, Eli Lilly and Company, MSD, Novartis, Pfizer, UCB, Grant/research support from: UCB, Pfizer, Désirée van der Heijde Speakers bureau: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly and Company, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, and UCB Pharma, Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly and Company, Galapagos, Gilead, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, and UCB Pharma, Louis Bessette Speakers bureau: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Eli Lilly and Company, Novartis, Sanofi, Sandoz, Fresenius Kabi, Teva, Organon, JAMP Pharma, Consultant of: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Eli Lilly and Company, Novartis, Sanofi, Sandoz, Fresenius Kabi, Teva, Organon, JAMP Pharma, Grant/research support from: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Eli Lilly and Company, Novartis, Gilead, JAMP Pharma, Annelies Boonen Speakers bureau: Eli Lilly and Company, Novartis, Abbvie, Consultant of: Galapagos, Grant/research support from: AbbVie, Rebecca Bolce Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Christophe Sapin Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Theresa Hunter Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Boris Janos Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Andris Kronbergs Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Soyi Liu Leage Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Juergen Braun Consultant of: AbbVie, Amgen, Celgene, Eli Lilly and Company, Janssen, MSD, Novartis, Pfizer, Sanofi, and UCB.

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POS1119

ARE WE TREATING-TO-TARGET IN SPONDYLOARTHRITIS (SPA)? A ONE-YEAR ANALYSIS FROM THE ASIA PACIFIC LEAGUE OF ASSOCIATIONS FOR RHEUMATOLOGY (APLAR) SPA REGISTRY

Keywords: Spondyloarthritis

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Background: Data on the extent to which internationally agreed treat-to-target (T2T) recommendations were applied in clinical practice in patients with spondyloarthritis (SpA) across the Asia-Pacific region is lacking. The APLAR SpA Registry is a multi-centre study aiming to assess the utility of early diagnosis and intensive protocolized treatment to patients with SpA on the long-term outcome.

Objectives: This analysis aimed to evaluate the extent of T2T achievement after 1-year intensive treatment in patients with SpA.

Methods: Patients who fulfilled the CASPAR 2006 classification criteria for psoriatic arthritis (PsA), and 2009 ASAS classification for axial spondylitis (AxSpA) were recruited. The current analysis included the first 99 patients reaching the 1-year timepoint across 6 Asia-Pacific regions.

Results: 49 patients with PsA (age: 52±11 years, 27(55%) male, disease duration: 6.0±7.9 years) and 50 patients with AxSpA (age: 40±14 years, 36(72%) male, disease duration: 5.9±7.6 years) were included. All of them were Asian. After 1-year treatment, there were significant improvements in disease activity (Disease Activity in Psoriatic Arthritis (DAPSA): 15.3±11.6 at baseline vs 10.1±11.2 at 1-year, p=0.002; Ankylosing Spondylitis Disease Activity Score (ASDAS): 2.4±1.0 at baseline vs 1.9±0.9 at 1-year, p=0.003). Other characteristics are shown in Table 1. Concerning medication use, there was an increase in the number of PsA patients receiving conventional synthetic disease-modifying drugs (csDMARDS, 65% at baseline to 72% at 1-year) and biologic DMARDS (bDMARDS, 24% at baseline to 43% at 1-year). For AxSpA, the prevalence of csDMARDs use decreased (30% at baseline to 18% at 1-year) while the prevalence of bDMARDs use increased (32% at baseline and 54% at 1-year). Patients in both groups required less NSAIDs (Figure 1). Regarding T2T, 63% and 51% of PsA patient achieved DAPSA-low disease activity (DAPSA-LDA) and minimal disease activity (MDA) respectively, while 66% of patients with Axial SpA achieved ASDAS-LDA. The MDA and ASDAS-LDA achievement rate was slightly higher than that of the tight control arm of TICOPA (41%)[1] and TICOSPA cohort (60%)[2] respectively. The bDMARDs use in TICOPA cohort was 37% and that in TICOSPA was 57%, both comparable to our APLAR SpA cohort (Figure 1). There was no significant difference in baseline demographics and clinical features between patients who could or could not achieve treatment target, except a lower patients' pain and global assessment, and lower functional disability in patients who achieved DAPSA-LDA at 1-year.

Conclusion: Implementing the T2T strategy in a patient with SpA is feasible in the selected sites of the APLAR SpA registry. We expect more long-term outcome data in the following years regarding other outcomes.

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[2] *Molto A et al. Ann Rheum Dis. 2021;80(11):1436-44.*

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Table 1. Clinical features and disease activity in patients with SpA in the APLAR region at baseline and 1-year

	PsA (n=49)			AxSpA (n=50)		
	Baseline	Year 1	p	Baseline	Year 1	p
Age, years	52 ± 11			40 ± 14		
NRS Patients' pain assessment, 0-10	4 ± 2	3 ± 2	*	4 ± 2	3 ± 2	*
NRS Patients' global assessment, 0-10	4 ± 2	3 ± 2	*	4 ± 2	3 ± 2	*
NRS Physicians' global assessment, 0-10	3 ± 2	2 ± 2	*	4 ± 2	3 ± 2	*
PASS, acceptable	33 73%	41 89%		31 67%	44 92%	*
TJ count, 0-68	4 ± 5	3 ± 6	*	1 ± 2	1 ± 2	
SJ count, 0-66	2 ± 4	1 ± 3	*	0 ± 0	0 ± 1	
Dactylitis digit	1 ± 2	0 ± 1	*	0 ± 0	0 ± 0	
PASI	3.81 ± 5.38	2.17 ± 3.27	*			
SPRACC, 0-15	0 ± 1	0 ± 1	*	0 ± 1	0 ± 1	
ESR, mm/h	20 ± 18	17 ± 12		25 ± 21	19 ± 13	
CRP, mg/L	7.3 ± 8.9	4.3 ± 4.9	*	20.9 ± 62.3	8.4 ± 19.4	
DAPSA	15.27 ± 11.60	10.06 ± 11.21	*			
ASDAS CRP				2.43 ± 1.00	1.93 ± 0.87	*
BASDAI				3.6 ± 2.2	2.6 ± 2.1	*
BASFI				2.8 ± 2.3	1.9 ± 2.2	*
BASMI				3 ± 2	3 ± 2	*
HAQ-DI	0.503 ± 0.614	0.372 ± 0.469		0.470 ± 0.471	0.318 ± 0.428	*

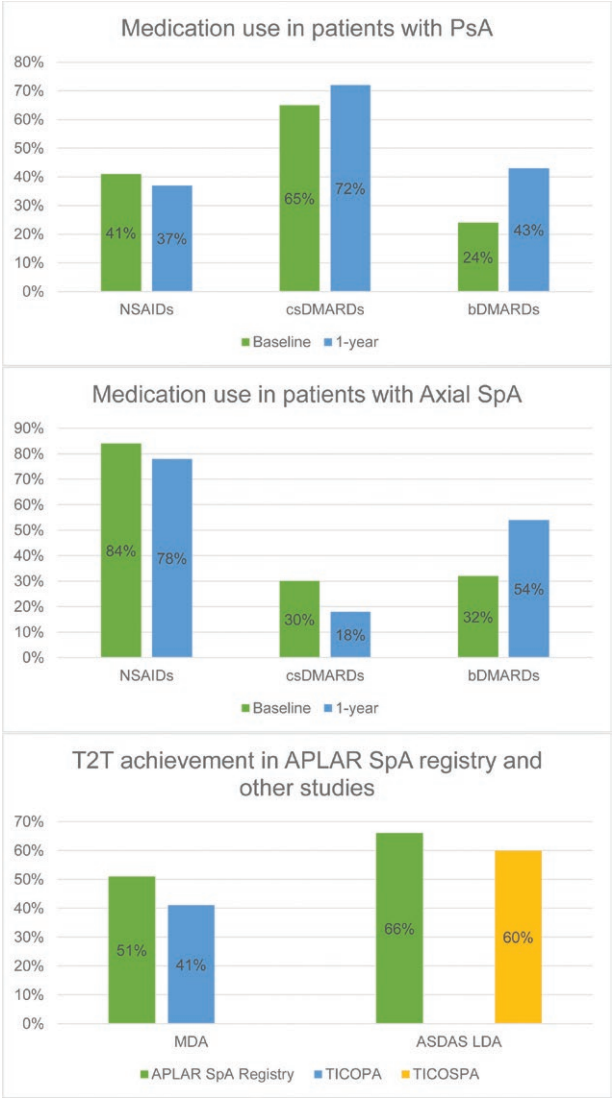


Figure 1. Medication use at baseline and 1-yr in patients with PsA (Upper panel)/ Axial SpA (middle panel) and T2T achievement in PsA and Axial SpA patients in APLAR SpA registry and other studies (lower panel)

Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Kyowa Kirin, Novartis, Ono Pharma, Pfizer, Tanabe-Mitsubishi, and UCB Pharma, James Cheng-Chung Wei Consultant of: Tsh biopharm, Abbvie, BMS, Celgene, Chugai, Eisai, Janssen, Novartis, Pfizer, Sanofi-Aventis and UCB pharma, Grant/research support from: Abbvie, Amgen, Astellas, BMS, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer Sun and UCB, Lai-Shan Tam: None declared.

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POS1120

IMPACT OF BASELINE CRP LEVEL ON SECUKINUMAB (SEC) RETENTION IN AXIAL SPONDYLOARTHRITIS (AXSPA): RESULTS OF THE FRENCH RETROSPECTIVE STUDY FORSYA

Keywords: Spondyloarthritis, Prognostic factors, Real-world evidence

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Background: While data on real-life SEC retention rate in patients (pts) with axSpA is accumulating, there are few data on predictive factors for this retention. Presence of objective sign of inflammation (OSI), especially increased baseline CRP level, is known to be predictive of efficacy of anti-TNFs and their retention in axSpA.

Objectives: To assess whether OSI, especially increased baseline CRP level, were predictive of SEC retention at 1 year in axSpA.

Methods: French retrospective study collecting between October 2019 and September 2020 data from axSpA pts a) having initiated and received at least one dose of SEC between August 11th 2016 and August 31st 2018, b) with at least a one-year follow-up period. Retention rate of SEC at 1 year was estimated by the Kaplan Meier (KM) method. OSI were defined by at least one of the following: CRP ≥5 mg/l or ESR ≥28 mm/h if CRP not available (CRP+) within the 3 months before initiation of SEC and MRI inflammation at the sacroiliac or spine level (MRI+) at any time. *The a priori selected potential predictive factors of the SECU 1 year retention* (CRP+, MRI+, age, sex, BMI, smoking, HLA B27, non-radiographic vs radiographic axSpA, past or present uveitis/Inflammatory Bowel Disease/psoriasis/arthritis or synovitis, diagnostic delay, disease duration, SEC line of biologic therapy, SEC maintenance dose, concomitant csDMARD/oral corticosteroids/proton pomp inhibitor at SEC initiation, history of depression/fibromyalgia) were analyzed by cox model regression. Only variables with <20% missing data were included in the model after imputation and stepwise selection (significance level for entering variables =20%; significance level for removing variables =10%), except for CRP and MRI which were forced into the model whatever their significance level or rate of missing data.

Results: In total, 906 pts from 47 centers (male: 42.2%, mean age: 46.2 ± 11.7 years, mean disease duration: 9.3 ± 9.1 years) were included in the analysis. The mean baseline CRP (± SD) was 11.1 ± 17.5 mg/L. At initiation of SEC, 86.3% of pts had ≥ 1 OSI (41.3% CRP+, and 69.4% MRI+) and respectively 8.0%, 14.9% and 77.1% were in 1st, 2nd and ≥ 3rd line (L) of biologic/targeted synthetic DMARD. The 1-year retention rate for SEC was 59% [95%CI: 55%-62%]. This retention at one year was 62.4% vs 59.1% and 57.4% vs 66% in patients with CRP+ vs CRP- and MRI+ vs MRI- respectively. In univariate cox regression, CRP+ was not predictive of SEC discontinuation at 1 year (HR = 0.90 [0.71-1.16]; p=0.422 nor was MRI+ (HR=1.29 [0.99; 1.68]; p=0.063). In multivariate cox analysis, after adjustment, these results were confirmed for CRP+ but MRI+ was identified as predictive of a worst SEC retention at 1 year (Table 1). In multivariate analysis lack of prior exposure to anti-TNF inhibitors, absence of IBD and absence of history of depression were also associated with a better SEC retention at 1 year (at 10%).

Conclusion: The overall retention of SEC at 1 year in daily practice in France was 59% for axSpA patients, independently of CRP level at SEC initiation.

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Table 1. Retention of secukinumab at 1 year according to components of at least one sign of inflammation with univariate and multivariate (after multiple imputation + stepwise selection) cox regressions

Predictive factor (*reference)	Modality (N)	Retention of SEC at 1 year (%)#	Univariate cox regression		Multivariate cox regression**	
			p	HR [95% CI]	p	HR [95% CI]
CRP ≥ 5 mg/l or ESR ≥ 28 mm/h (if CRP not available)	Yes (N=282)	62.4%	0.422	0.90 [0.71-1.16]	0.328	0.90 [0.73-1.11]
	No (N=398)*	59.1%				
MRI signs of inflammation at sacroiliac joint or spine	Yes (N=487)	57.4%	0.063	1.29 [0.99-1.68]	<.001	1.49 [1.18-1.89]
	No (N=214)*	66.0%				

without imputation for missing data**Adjustment on IBD, secukinumab treatment line, history of depression or anti-depressive concomitant treatmentInterpretation HR > 1: the hazard of discontinuation at 1 year is X times higher vs reference

Dougados Speakers bureau: Pfizer, Abbvie, Lilly, UCB, Merck, BMS, Roche, Biogen, Sanofi, Novartis, and Sandoz, Consultant of: Pfizer, Abbvie, Lilly, UCB, Merck, BMS, Roche, Biogen, Sanofi, Novartis, and Sandoz, Grant/research support from: Pfizer, Abbvie, Lilly, UCB, Merck, BMS, Roche, Biogen, Sanofi, Novartis, and Sandoz, Audrey Lardy-Cléaud: None declared, Emilie Desfleurs Employee of: Novartis employee, Pascal Claudepierre Speakers bureau: AbbVie, Janssen, Lilly, MSD, Novartis, Pfizer, Consultant of: Abbvie, Pfizer, Roche-Chugai, Bristol-Myers Squibb, MSD, UCB, Novartis, Janssen, Lilly, Celgene, Adeline Ruyssen-Witrand Speakers bureau: AbbVie, Amgen, Biogen, Bristol Myers Squibb, Fresenius-Kabi, Galapagos, Janssen, Lilly, MSD, Mylan, Nordic-Pharma, Novartis, Pfizer, Roche Chugai, Sanofi, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Mylan, Novartis, Pfizer Inc, Sanofi Genzyme, Grant/research support from: AbbVie, Amgen, Mylan, Pfizer Inc, Alain Saraux Speakers bureau: Abbvie, Biogen, Bristol Myers Squibb, Fresenius, Galapagos, GSK, Lilly, Merck Sharp, Nordic, Novartis, Pfizer, Roche-Chugai, UCB, Consultant of: Abbvie, Lilly, Novartis, Pfizer, Grant/research support from: Roche-Chugai, Lilly, Fresenius, Anne Tournadre Speakers bureau: Abbvie, Fresenius, Janssen, MSD, Pfizer, Roche Chugai, Sanofi, Paid instructor for: Fresenius, Consultant of: Abbvie, Fresenius, Lilly, Novartis, Sanofi, Grant/research support from: Fresenius, Novartis, Pfizer, UCB, Cédric Lukas Speakers bureau: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Consultant of: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Grant/research support from: Pfizer, Novartis and Roche-Chugai, Daniel Wendling Speakers bureau: AbbVie, BMS, MSD, Pfizer, Roche Chugai, Amgen, Nordic Pharma, UCB, Novartis, Lilly, Sandoz, Grunenthal, Janssen, Galapagos, Consultant of: Novartis.

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POS1121

IMPACT OF SUBCLINICAL ANKLE AFFECTION ON THE FUNCTIONAL STATUS OF RHEUMATOID ARTHRITIS PATIENTS: AN ULTRASOUND-BASED STUDY

Keywords: Ultrasound, Quality of life, Rheumatoid arthritis

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Background: Subclinical involvement of the ankles is common in rheumatoid arthritis (RA) and occurs even in patients in clinical remission[1]. Assessing the characteristics of ankle inflammation and its effect on the functional status will enable the clinician to target treatment interventions[2]. Ankle joint is underrepresented in many clinical, sonographic RA-scores, and there is little information available in the literature about ultrasound (US) evaluation of asymptomatic ankle pathologies in RA patients.

Objectives: To assess the impact of US diagnosed subclinical ankle pathologies on the functional status of RA patients.

Methods: The study included 52 RA patients without ankle pain and 52 healthy age, gender matched controls. Ankle joints were examined clinically then by US using gray scale (GS) and Power Doppler (PD) including tibiotalar (TTJ), subtalar (STJ), talonavicular (TNJ), calcaneo-cuboid joints. In addition, tibialis anterior (TA), extensor hallucis longus (EHL), extensor digitorum longus (EDL), tibialis posterior (TP), flexor digitorum longus (FDL), flexor hallucis longus (FHL), peroneus longus, brevis and achilles tendons (AT), retrocalcaneal bursa (RCB) and plantar fascia (PF) were assessed. Functional capacity was measured using Health Assessment Questionnaire (HAQ) and Foot Function Index (FFI)

Results: Data showed significantly more GSUS pathologies in the asymptomatic RA group than in the control group in TP (27.9% vs 3.8%) (P=0.043), FDL (3.8% vs 0%) (P=0.043), and peroneal tenosynovitis (26% vs 0%) (P<0.001), TTJ (23.1% vs 5.8%) (0.024) and TNJ synovitis (23.1% vs 3.8%) (P=0.024), AT tendinitis (19.2% vs 4.8%) (P=0.01), RCB bursitis (13.5% vs 1.9%) (P=0.002), STJ (13.5% vs 0%) (P=0.024), and calcaneo-cuboid joint synovitis (4.8% vs 0%) (P=0.024). Pathologies; see Figure 1. There was a trend to statistical significance of PDUS in TTJ and peroneal tendons in RA patients. Impaired functional activity as represented by higher HAQ and FFI scores was highly significantly associated to pathologies in TTJ, STJ, TNJ, AT, RCB, and PF; see Table 1.

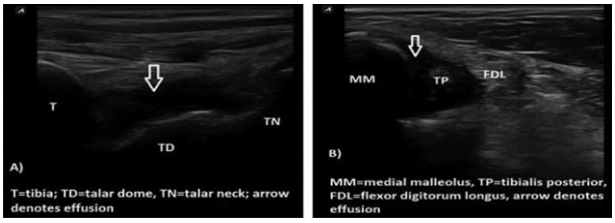


Figure 1. Asymptomatic ankle pathologies in RA by US. a) Tibiotalar synovitis, b) Tibialis posterior tenosynovitis)

Table 1. Impact of subclinical ankle pathologies on functional status of RA patients

Ultrasound pathology	Health assessment questionnaire				Foot function index			
	Low	Moderate	High	P	Low	Moderate	High	P
Tibiotalar synovitis	2(8.3%)	15(62.5%)	7(8.7%)	**0.05**	1(4.2%)	17(70.8%)	6(25%)	**0.002**
Subtalar synovitis	1(7.1%)	6(42.9%)	7(50%)	**0.001**	0(0%)	7(50%)	7(50%)	**<0.001**
Talonavicular synovitis	3(12.5%)	11(45.8%)	10(41.7%)	**<0.001**	1(4.2%)	15(62.5%)	8(33.3%)	**<0.001**
Calcaneo-cuboid synovitis	0(0%)	1(20%)	4(80%)	**<0.001**	0(0%)	5(100%)	0(100%)	0.125
TA tenosynovitis	0(0%)	0(0%)	0(0%)	.....	0(0%)	0(0%)	0(0%)	.....
EHL tenosynovitis	0(0%)	0(0%)	0(0%)	.....	0(0%)	0(0%)	0(0%)	.....
EDL tenosynovitis	0(0%)	0(0%)	0(0%)	.....	0(0%)	0(0%)	0(0%)	.....
TP tenosynovitis	4(14.3%)	17(60.7%)	7(25%)	0.233	4(14.3%)	18(64.3%)	6(21.4%)	**0.037**
FDL tenosynovitis	2(50%)	0(0%)	2(50%)	**0.018**	0(0%)	4(100%)	0(0%)	0.192
FHL tenosynovitis	0(0%)	0(0%)	0(0%)	.....	0(0%)	0(0%)	0(0%)	.....
Peroneal tenosynovitis	6(23.1%)	14(53.8%)	6(23.1%)	0.316	5(19.2%)	17(65.4%)	4(15.4%)	0.285
Achilles tendinopathy	3(15%)	7(35%)	10(50%)	**<0.001**	3(15%)	11(55%)	6(30%)	**0.016**
Retrocalcaneal bursitis	2(14.3%)	6(42.9%)	6(42.9%)	**0.009**	0(0%)	8(57.1%)	6(42.9%)	**<0.001**
Plantar fasciitis	2(20%)	3(30%)	5(50%)	**0.005**	2(20%)	2(20%)	6(60%)	**<0.001**

TA:tibialis anterior, EHL:extensor digitorum longus, EDL:extensor digitorum longus, TP:tibialis posterior, FDL:flexor digitorum longus, FHL:flexor hallucis longus

Conclusion: Asymptomatic RA ankles exhibited higher number of US alterations in comparison to healthy individuals and significantly impaired the functional status of patients with RA. Foot and ankle joints should be considered for future scores in assessing disease activity and follow-up.

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POS1122

EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS AND AN INADEQUATE RESPONSE TO BIOLOGIC DMARD THERAPY: ONE-YEAR RESULTS FROM A PHASE 3 STUDY

Keywords: Spondyloarthritis, Targeted synthetic drugs, Clinical trials

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Background: Upadacitinib (UPA), a Janus kinase inhibitor, has demonstrated efficacy and an acceptable safety profile in patients (pts) with ankylosing spondylitis (AS) in the phase 3 SELECT-AXIS 1 and 2 program, including pts with an inadequate response or intolerance to biologic disease-modifying antirheumatic drugs (bDMARD-IR).[1,2]

Objectives: To assess the 1-year efficacy and safety of UPA 15 mg once daily (QD) in bDMARD-IR pts with active AS in SELECT-AXIS 2.

Methods: The design of the SELECT-AXIS 2 AS bDMARD-IR study has been described previously.[1] Pts who completed the 14-wk placebo (PBO)-controlled period were eligible to enter an ongoing long-term extension and receive open-label UPA 15 mg QD for up to 90 wks. This analysis evaluated efficacy over 52 wks in pts who received continuous UPA, and those who switched from PBO to UPA at wk 14. Efficacy endpoints included proportion of pts achieving Assessment of SpondyloArthritis international Society 40 response (ASAS40), ASAS partial remission (PR), ASDAS (AS Disease Activity Score with C-reactive protein [CRP]) low disease activity (LDA; <2.1), ASDAS inactive disease (ID; <1.3), and changes from baseline in ASDAS and high-sensitivity CRP (hsCRP). As-observed (AO) and non-responder imputation with multiple imputation (NRI-MI) analyses are presented for binary endpoints and mixed model for repeated measures (MMRM) analyses for continuous endpoints. Safety was assessed through the cut-off date of May 19, 2022 in all pts who received ≥1 dose of UPA. Treatment-emergent adverse events (TEAEs) and TEAEs of special interest are presented as exposure-adjusted event rates (events/100 pt-years [E/100 PY]).

Results: A total of 420 pts were randomized and received study drug (PBO to UPA: n=209; continuous UPA: n=211). Response rates were maintained from wk 14 to wk 52 in the continuous UPA group, and responses were similar in the PBO to UPA group at wk 52. NRI-MI response rates at wk 52 for the PBO to UPA and continuous UPA groups, respectively, were: ASAS40 (64.6% and 65.9%), ASAS PR (29.2% and 30.3%), ASDAS LDA (55.3% and 56.9%), and ASDAS ID (25.2% and 26.0%) (**Figure 1**). Changes from baseline in ASDAS and hsCRP were also similar between groups (-1.9 and -2.0, and -10.6 and -10.0 for the PBO to UPA and continuous UPA groups, respectively). Safety was assessed in 414 pts (534.4 PY of exposure) who received ≥1 dose of UPA (**Table 1**). Rates of serious TEAEs and TEAEs leading to study drug discontinuation were 9.9 and 3.0 E/100 PY, respectively. Rates of malignancy, major adverse cardiovascular events, and venous thromboembolic events were low (0.2, 0.2, and 0.4 E/100 PY, respectively).

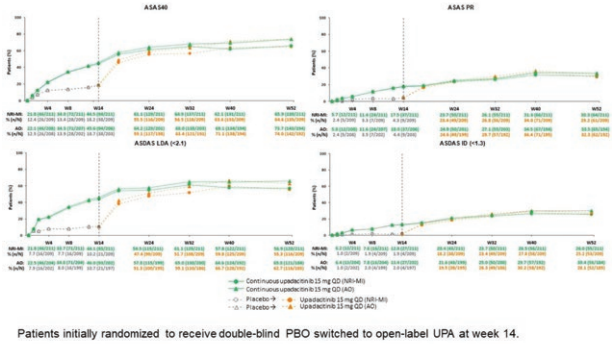
Conclusion: UPA 15 mg demonstrated sustained efficacy up to wk 52 in bDMARD-IR pts with active AS. Similar efficacy was observed at wk 52 in pts with continuous UPA exposure and those who switched from PBO to UPA. UPA 15 mg was generally well tolerated in this bDMARD-IR population, with no new safety signals identified.

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Figure. Efficacy over 52 weeks (NRI-MI and AO)



Patients initially randomized to receive double-blind PBO switched to open-label UPA at week 14.

AO, as observed; ASAS40, Assessment of SpondyloArthritis international Society 40 response; ASDAS, AS Disease Activity Score with C-reactive protein; ID, inactive disease; LDA, low disease activity; NRI-MI, non-responder imputation with multiple imputation; PBO, placebo; PR, partial remission; QD, once daily; UPA, upadacitinib; W, week.

Table 1. Treatment-emergent adverse events

Exposure-adjusted event rates, (E/100 PY)	Any upadacitinib 15 mg QD (n=414; PY=534.4)
Any AE	877 (164.1)
Serious AE	53 (9.9)
AE leading to discontinuation of study drug	16 (3.0)
Any death[a]	1 (0.2)
Infection	301 (56.3)
Serious infection	24 (4.5)
Herpes zoster	19 (3.6)
Malignancy other than NMSC	1 (0.2)
NMSC	2 (0.4)
Adjudicated MACE	1 (0.2)
Adjudicated VTE	2 (0.4)
Adjudicated gastrointestinal perforation	0
Renal dysfunction	1 (0.2)
Anemia	11 (2.1)
Lymphopenia	3 (0.6)
Neutropenia	19 (3.6)
Hepatic disorder	47 (8.8)
Uveitis	7 (1.3)
Inflammatory bowel disease	1 (0.2)
Psoriasis	2 (0.4)

[a]One patient died due to polytrauma.AE, adverse event; E, event; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; PY, patient-years; QD, once daily; VTE, venous thromboembolic event.

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POS1123

IMPACT OF THE TIME OF INITIATION AND LINE OF BIOLOGIC THERAPY ON THE RETENTION RATE OF SECUKINUMAB (SECU) IN AXIAL SPONDYLOARTHRITIS (AXSPA). DATA FROM THE FRENCH MULTICENTER RETROSPECTIVE FORSYA STUDY

Keywords: Prognostic factors, Spondyloarthritis, Real-world evidence

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Background: The characteristics of patients receiving a new therapy might differ overtime since its launch (date of its availability in a specific region/country); the differences in these characteristics might impact the efficiency of this treatment.

Objectives: To compare the one year retention rate of SECU in axSpA and its predisposing factors with regard to its time of initiation (e.g. right after its launch or later).

Methods: *Study design*: Retrospective multicenter French study of axSpA patients a) having initiated and received at least one dose of SECU b) with at least a one year follow-up. *Study periods*: Two cohorts were evaluated with regard to the time of initiation of SECU: *Cohort (C1)*: between August 11th, 2016 (time of the launch of SECU in France) and Aug 3st 2018; *Cohort 2 (C2)*: between sept 1st 2018 and Nov 13, 2020 (remotely from the launch). *Statistical analysis*: The one year retention rate of SECU was estimated using the Kaplan Meier technic and Cox models and was used to compare the retention rate performed in C1 and C2. Preselected factors of SECU retention at 1 year (≥1 Objective Sign of Inflammation [CRP> N, MRI-inflammation at the sacroiliac or spine level], age, sex, BMI, smoking, HLA B27, non-radiographic vs radiographic axSpA, past or present uveitis/ Inflammatory Bowel Disease (IBD)/ psoriasis/ arthritis or synovitis, diagnostic delay, disease duration, SEC line of biologic therapy, SECU maintenance dose, concomitant csDMARD/ oral corticosteroids/ proton pomp inhibitor at SECU initiation, history of depression/ fibromyalgia) were analyzed by univariate and multivariate cox model regression. Only variables with <20% missing data were included in the model after multiple imputation and stepwise selection (significance level for entering variables = 20%; for removing variables = 10%).

Results: In total, 906 pts in C1 and 758 pts in C2 from 50 centers were included in the analysis. Pts characteristics (male: 42.8%, mean age: 46.5 ± 11.9 years, mean disease duration: 9.2± 9.4 years) were similar between the 2 cohorts. The 1 year retention rate was better in C2 vs C1 (64% [61-68%] vs 59% [55-62%], Hazard Ratio (HR)=0.84 [0.72-0.98], p = 0.03). Between C1 and C2, the proportion of patients receiving SECU as the 1st or 2nd line of biologic therapy increased from 23% to 40%. In the multivariate analysis, line of biologic therapy was the single predictive factor of the 1 year retention rate of SECU in both cohorts with a better retention rate for the 1st line of biologic therapy (Table 1).

Table 1. Impact of SECU line on SECU retention rate at 1 year with regard of its time of initiation

SECU line (* reference)	Survival probability estimate at 1 year (95% CI)#	$HR_{adjusted}$ [95% CI]$	p vs ref	p type III
Cohort 1†				
1st L (n=68; 8%)*	70% [59%-81%]			0.084
2nd L (n=132, 15%)	62% [54%-70%]	1.53 [0.91; 2.57]	0.107	
≥ 3rd L (n=676, 77%)	57% [53%-61%]	1.67 [1.06; 2.62]	0.028	
Cohort 2†				
1st L (n=93, 13%)*	78% [69%-86%]			0.007
2nd L (n=192, 27%)	63% [56%-70%]	1.92 [1.18; 3.13]	0.009	
≥ 3rd L (n=437, 60%)	62% [57%-66%]	2.11 [1.32; 3.35]	0.002	

† See Methods for explanation# without imputation for missing data$ Adjustment on: C1 (OSI, IBD, History of depression or anti-depressive concomitant treatment); C2 (OSI, History of depression or anti-depressive concomitant treatment, disease duration, corticosteroids)Interpretation HR > 1: the hazard of discontinuation at 1 year is X times higher vs referenceL = Line of biologic therapy

Conclusion: These data showing a better retention rate at 1 year remotely from the launch of SECU, probably explained by its use at an earlier stage of the disease, suggest a change in the behavior of prescribing physicians probably reflecting a better confidence in this treatment. These data also underline the interest of iterative evaluations of treatments used in daily practice.

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SLE, Sjön's and APS - treatment

POS1124 LUPUS100.ORG A NEW TOOL FOR DOCTORS TO BUILD PATIENTS LUPUS KNOWLEDGE AND FIGHT POOR QUALITY WEB INFORMATION

Keywords: Education, Systemic lupus erythematosus, Best practices

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Background: Access to quality disease information is one of the cornerstones of therapeutic education and critical to help the doctor-patient dialog and adherence to treatment. Lupus patients and doctors alike lack the time in consultation to address the many questions patients have. As a result, patients often rely on poor quality or unverified information from the web. For non-English speakers, the language barrier is adding yet another obstacle to quality therapeutic education.
Objectives: To provide access to doctor verified SLE quality information on-line, in the mother language of 95%+ of the European population so that doctors can refer patients to quality information sources.
Methods: With the endorsement of ERN ReCONNET reference network, Lupus Europe and doctors from ReCONNET's SLE Working group have developed a multilingual Euro-wide website answering the top 100 questions patients have about lupus. The starting point to build the content has been the French book "lupus en 100 questions" authored by lupus experts from the French FAI2R. Working extensively with patients from Lupus Europe PAN, the list of questions has been adjusted, answers to existing questions have been checked and validated or adjusted for up-to-dateness. New patient questions have been answered by lupus specialised doctors in collaboration with patients. The resulting documents have been translated in English and the translations validated by both patients and doctors. This core English version has then received feedback from ERN ReCONNET SLE WG doctors. Finally, the end result has been translated in more than 15 languages, verified by native lupus doctors and patients prior to being put on line. This exercise is continuing at the time of writing the abstract, with the goal of covering more than 20 languages and 99% of European population by end 2023. The web site is managed and controlled by Lupus Europe, the European Lupus patients organisation. Aside from this "one-shot" effort, a process has been designed to collect questions and comments from patients and doctors. Those will then feed the on-going maintenance of the information. New developments or new questions will be used to systematically review the content and update it using a Delphi process within the ERN ReCONNET SLE Working group.
Results: lupus100.org website provides free of charge quality information on lupus for patients, relatives, doctors or students. Its multilingual character allows all people in Europe to have access to verified information in their own language, with lay terms. This non-commercial tool is available for doctors of all countries to grow their patients education on lupus and hence build a stronger therapeutic alliance, minimising the time lost in fighting wrong information.
Conclusion: A new tool is available for doctors and patients to build lupus education. The challenges are now (a) to maximise its reach by ensuring all patients and doctors are aware of the initiative, and (b) to ensure that currency is maintained medium to long term.
REFERENCE:
[1] www.lupus100.org
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1310

POS1125 HYDROXYCHLOROQUINE USE IN PREGNANT WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND MAJOR CONGENITAL MALFORMATIONS IN THE OFFSPRING

Keywords: Registries, Pregnancy and reproduction, Systemic lupus erythematosus

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Background: Hydroxychloroquine (HCQ) is currently recommended for all pregnant women with systemic lupus erythematosus (SLE) if tolerated. Some studies have reported an increased risk of malformations associated with HCQ, but others find no increased risk.
Objectives: To assess the risk of major congenital malformations (MCM) associated with exposure to HCQ during the 1st trimester in the offspring of women with SLE.
Methods: We conducted a population-based cohort study of pregnancies with a singleton birth from 2006 to 2020 among women with prevalent SLE in Sweden. Pregnancies were identified from the Medical Birth Register (MBR). Prevalent SLE was defined as having at least two ICD-coded visits in the National Patient Register before pregnancy, with at least one with an SLE specialist. The exposure was defined as filling at least one HCQ prescription during the 1st trimester (Prescribed Drug Register). The unexposed births were required to not have any HCQ dispensations from three months preconception to the end of the 1st trimester. The outcome was any ICD code for MCM in the offspring assessed at birth listed in the MBR, defined according to the European Surveillance of Congenital Anomalies classification. Inverse probability of treatment weighting (IPTW) using propensity score was applied to adjust for confounding. We included maternal characteristics, comorbidities (e.g., diabetes, other autoimmune diseases), and medication use (e.g., corticosteroids, other disease-modifying anti-rheumatic drugs) in the propensity score model as a priori variables. Risk ratios and 95% confidence intervals (RR 95%CI) were estimated using modified Poisson regression models in the weighted population with robust variance estimation.
Results: The study population comprised 407 exposed births and 520 unexposed births. The mothers' mean age at delivery was 32 (standard deviation ± 5). Overall, there were 21 births with at least one MCM, corresponding to an overall risk of 2.3%. The most common type of MCM was ventricular septal defect (n = 6). The unadjusted risks of MCM among the exposed and unexposed were 2.7% and 1.9%, respectively (unadjusted RR 1.42, 95%CI 0.60-3.28). The IPTW-adjusted population achieved a good balance across patient characteristics. The IPTW-adjusted RR was 1.59 (95%CI 0.67-3.75). The adjusted risk difference was 0.01 (95%CI -0.01-0.03). In a sensitivity analysis in which the exposure was defined as having at least one HCQ dispensation from three months preconception to the end of the 1st trimester, the IPTW-adjusted RR was 1.56 (95%CI 0.69-3.54). We could not examine different categories of HCQ daily dose due to very few events in each category.
Conclusion: In this birth cohort, our findings show an increased, but not statistically significant, risk of MCM at birth among births born to women with SLE exposed to HCQ during the 1st trimester compared to those without HCQ exposure. Our findings should be interpreted considering the lack of data on early pregnancy termination or loss induced by MCM. Future studies are warranted to investigate this association further and should utilize a longer follow-up for MCM ascertainment (i.e., within one year of birth). For managing SLE during pregnancy, the benefits of HCQ may still outweigh the risks.
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POS1126 THERAPEUTIC RANGE OF HYDROXYCHLOROQUINE BLOOD LEVELS CAN REDUCE ODDS OF HIGH LUPUS DISEASE ACTIVITY

Keywords: Treat to target, Systemic lupus erythematosus, Outcome measures

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Background: Hydroxychloroquine (HCQ) is the cornerstone of systemic lupus erythematous (SLE or lupus) treatment, yet, the optimal dosing of HCQ in SLE is unknown. Reducing HCQ dose to 5 mg/kg to limit toxicity, as suggested by the American Academy of Ophthalmologists (AAO),(1) also predicts increased flares.(2) One study showed six-fold higher risk of severe SLE flares in patients receiving AAO recommended HCQ dosing.(2) Therefore, establishing effective therapeutic ranges of HCQ blood levels may provide an opportunity to individualize HCQ dosing to maximize efficacy and limit toxicity.

Objectives: The objective of this study was to examine the association of HCQ blood levels with high lupus disease activity (HDA) in a prospective SLE cohort.
Methods: This cross-sectional study measured HCQ blood levels in unique SLE visits using liquid chromatography-tandem mass spectrometry. HCQ blood levels and SLE disease activity index (SLEDAI) scores were measured on the day of the visit for each patient. High lupus disease activity (HDA) was defined as SLEDAI scores of ≥6.(3) To identify significant HCQ blood levels that determined lower odds of HDA, we examined associations between HDA and every 50-100 ng/ml increase in HCQ blood levels starting at 100 ng/ml through 1500 ng/ml. Other factors that can affect HCQ levels, such as patient-reported adherence, kidney function, and HCQ dose and timing, were included in multivariable models.
Results: Among 143 SLE patients in whom HCQ blood levels were measured, 92% were women and 32% were of non-White race or Hispanic ethnicity. HDA was noted in 18% of patients. We noted a 75% reduction in the odds of HDA first at HCQ blood levels of ≥750 ng/ml (Adjusted OR 0.25, 95% CIs 0.066-0.89, p-value = 0.035; Figure 1). This effect peaked with HCQ blood levels ≥1100 ng/ml with 93% lower odds of HDA at this level (Adjusted OR 0.07, 95% CIs 0.005-0.61, p-value = 0.038; Figure 1). Interestingly, levels of 1150 ng/ml or higher did not further reduce the odds of HDA (Figure 1).
Additionally, we noted that female sex was associated with 88% lower odds of HDA (Table 1), while other factors including HCQ dose or timing were not associated with HDA (Table 1).
Conclusion: We report an effective therapeutic range of HCQ blood levels, 750-1100 ng/ml, that significantly correlated with reduced risk of high lupus disease activity (HDA) by 75-93% in patients with SLE. These findings could guide clinicians to individualize HCQ doses to achieve target blood levels within this range to maximize efficacy, while balancing safety.

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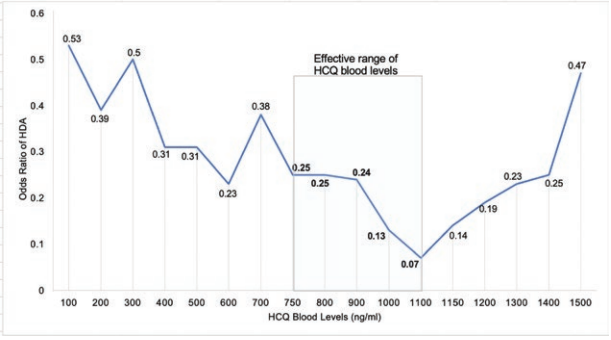


Figure 1. Effective range of HCQ levels (shaded box) that reduces odds of high SLE disease activity. Significant adjusted odds ratio shown in bold.

Table 1. Factors Associated with High SLE Disease Activity (SLEDAI ≥6), Multivariable Model

Variables	Adjusted Odds Ratio (95% CIs)	p-value
Age (per 10 years increase)	0.99 (1.03, 9.6)	0.89
Female	**0.11 (0.013, 0.83)**	**0.03**
Non-White race & Hispanic ethnicity	0.75 (0.23, 2.3)	0.61
Weight (per 5 kg increase)	0.97 (0.93-1.01)	0.13
CKD stage ≥2	1.077 (0.29, 3.9)	0.91
HCQ total dose		
200 mg daily	ref	
300 mg/d	1.8 (0.29, 22)	0.43
400 mg daily	3.0 (0.49, 22)	0.25
AAO-Guideline based dose, ≤5 mg/kg/day	1.4 (0.2, 12)	0.73
HCQ blood levels ≥1100 ng/ml	**0.07 (0.004, 0.45)**	**0.02**
Patient-reported adherence ≥80%	0.57 (0.16, 2.1)	0.38
Social Determinants of Health, Present	3.2 (0.86, 12)	0.99
HCQ dose timing		
<4 hours	ref	
4-6 hours	3.3 (0.15, 153)	0.48
6-8 hours	2.03 (0.1, 81)	0.66
>8 hours	0.15 (0.08, 60)	0.80

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POS1128

ZETOMIPZOMIB (KZR-616) TREATMENT RESULTS IN CLINICALLY MEANINGFUL RENAL RESPONSES IN PATIENTS WITH LUPUS NEPHRITIS

Keywords: Kidneys, Clinical trials, Systemic lupus erythematosus

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Background: Zetomipzomib, a first-in-class selective inhibitor of the immunoproteasome blocks multiple pathways involved in inflammatory cytokine production and immune effector cell activity – including macrophages, B cells and T cells leading to broad immunomodulation across both the innate and adaptive immune systems[1-3]. The MISSION Phase 1b/2, open-label study (NCT03393013; KZR-616-002) evaluated safety, tolerability, and exploratory efficacy of zetomipzomib in patients with systemic lupus erythematosus (SLE) +/- lupus nephritis (LN). In the Phase 1b portion, zetomipzomib was well-tolerated in patients with active SLE +/- LN and resulted in improvement across disease activity measures as well as biomarkers, including reduced proteinuria and urinary CD163 in 2 of 2 patients with LN[4].
Objectives: Results from the completed Phase 2 portion of the MISSION study are presented here.
Methods: MISSION Phase 2 evaluated zetomipzomib 60 mg SC QW in patients with active LN (Class III or IV ± Class V) with proteinuria, defined as urine protein to creatinine ratio (UPCR) >1 despite stable background therapy of ≥8 weeks. Patients received zetomipzomib for 24 weeks. Safety, tolerability, UPCR, other measures of renal function, SLE disease activity, and biomarkers were measured.
Results: 21 patients received ≥1 dose of zetomipzomib (safety population) and 4 patients discontinued before end of treatment (evaluable population, n=17). 90.5% were women with a mean age of 35.3 years; 52.4% were Hispanic/Latino. Patients had mean LN duration of 5.3 years with mean 24-hour UPCR of 2.6 mg/mg and mean eGFR of 104.7 mL/min/1.73 m^2. Concomitant medications included corticosteroids (100%, mean dose: 20.2 mg/d), MMF or mycophenolic acid (95.2%), HCQ (66.7%), and/or AZA (9.5%). Clinically meaningful renal responses were observed by the end of treatment (EOT) at Week (W) 25 with 11/17 evaluable patients demonstrating ≥50% reduction in UPCR from baseline and 6 of 17 patients achieving a Complete Renal Response*. Furthermore, renal responses were maintained or deepened through the end of study 12-weeks post-treatment at W37. eGFR levels remained stable throughout the study. Reduction of daily steroid dose to 10 mg/day was observed in 14/17 patients as early as W13 and at W25 while other background immunosuppressive doses remained stable throughout the study. Urinary CD163, a marker of inflammation, decreased with zetomipzomib treatment and was shown to be correlated with UPCR. Adverse events were generally mild to moderate (Grade 1/2) without evidence of immunosuppression (no serious/opportunistic infections or immune cell depletion). *Complete Renal Response: UPCR ≤0.5, eGFR ≥60 mL/min/1.73m^2 or no worsening of eGFR from baseline of ≥25%, prednisone (or equivalent) ≤10 mg and no use of prohibited medication.
Conclusion: In the MISSION Phase 2 study, treatment with zetomipzomib 60 mg SC QW for 24 weeks demonstrated strong activity against LN as evidenced by improvement in UPCR and has the potential to be a long-term, steroid-sparing immunomodulatory treatment for LN patients.

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POS1129 IN VITRO EVIDENCE DEMONSTRATES THAT AFIMETORAN (BMS-986256), AN EQUIPOTENT TLR7/8 DUAL ANTAGONIST, HAS STEROID-SPARING POTENTIAL IN THE CLINIC

Keywords: Systemic lupus erythematosus, Cytokines and chemokines, Targeted synthetic drugs

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Background: Systemic lupus erythematosus (SLE), a chronic autoimmune disease, is characterized by high clinical and molecular heterogeneity and the presence of autoantibodies with various specificities, including those against DNA and RNA. While steroids, such as prednisolone, are a part of the standard-of-care for SLE, alternative treatments that overcome steroid resistance and minimize the risk of numerous short- and long-term side effects associated with their use remain an important unmet need. Toll-like receptors 7 and 8 (TLR7/8), two endosomal receptors expressed in various immune cells, play key roles in innate immunity through recognition of single-stranded RNA and driving downstream signaling via the nuclear factor kappa B (NFkB) and interferon regulatory factor (IRF) pathways. Activation of the NFkB pathway via TLR7/8 along with inhibition of plasmacytoid dendritic cell (pDC) apoptosis via TLR7 are reported to contribute to steroid resistance.
Objectives: *In vitro* determination of the potency and modes of action of afimetoran in whole blood (WB) of healthy volunteers (HVs) and patients with SLE, as well as probing the modes of action for the steroid-sparing potential of afimetoran.
Methods: Afimetoran was evaluated *in vitro* for its ability to inhibit TLR7- and TLR8-mediated interleukin 6 (IL-6) induction in WB. Briefly, WB samples from HVs and patients with SLE were treated with afimetoran for 1 hour before the addition of the TLR7 or TLR8 agonists. Following overnight incubation, supernatants were collected, and IL-6 was quantified by ELISA. The same assay was used to determine the pharmacodynamic activity of afimetoran in WB from HVs in a phase 1 multiple ascending dose study (NCT03634995). The potency of afimetoran to inhibit TLR7 agonist-induced CD69 expression on B cells and TLR8 agonist-induced CD319 expression on monocytes from WB was assessed using flow cytometry. The steroid-sparing potential of afimetoran was evaluated *in vitro* in combination with prednisolone through inhibition of IL-6 induction in WB from HVs and reversal of TLR7 agonist-induced resistance to prednisolone-induced pDC apoptosis, which was measured by flow cytometry staining of annexin V.
Results: Afimetoran equipotently inhibited TLR7- and TLR8-mediated induction of IL-6 in WB from HVs and patients with SLE. Afimetoran also equipotently inhibited surface expression of CD69 on B cells and CD319 on monocytes with single-digit nM IC50 values. Afimetoran robustly and durably inhibited TLR7- or TLR8-mediated induction of IL-6 in HV WB samples from a phase I multiple ascending dose clinical trial. When combined with prednisolone, afimetoran had a synergistic effect in inhibiting TLR7- and TLR8-mediated induction of IL-6 in WB of HVs and reversed TLR7-mediated resistance to prednisolone-induced pDC apoptosis.
Conclusion: WB-based data show that afimetoran is an equipotent TLR7/8-dual antagonist with sub-nM to nM potency in blocking TLR7- and TLR8-mediated functions. WB- and cell-based evidence demonstrates that afimetoran in combination with prednisolone synergistically inhibits induction of IL-6, a NFkB-dependent cytokine, and reverses TLR7-mediated resistance to prednisolone-induced pDC apoptosis, thus supporting the steroid-sparing potential of afimetoran in patients with SLE.
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POS1130 DESIGNING OF A PHASE 2, MULTICENTER, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY TO ASSESS THE EFFICACY AND SAFETY OF NIPOCALIMAB, AN FCRN INHIBITOR, IN ADULTS WITH PRIMARY SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Safety, Autoantibodies

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Background: Dysregulated humoral immunity is a hallmark of primary Sjögren's Syndrome (pSS). This dysregulation involves aberrant B-lymphocyte activity resulting in abnormally high immunoglobulin G (IgG) levels and the production of autoantibodies, particularly those reactive with Ro/La ribonuclear complexes. pSS can affect almost any organ system, and current evidence-based therapies only offer some symptom relief, but no licensed therapy has been shown to alter the disease course. Nipocalimab is a high-affinity, fully human monoclonal antibody that reduces circulating IgG levels by selectively blocking the interactions of IgG, including pSS autoantibodies, with the neonatal Fc receptor (FcRn). Nipocalimab has previously induced rapid, safe, and durable serum IgG reductions in healthy volunteers (NCT02828046)[1] and in autoantibody-driven generalized myasthenia gravis (gMG) in adults (Vivacity-MG; NCT03896295)[2], suggesting that nipocalimab may treat a broad range of autoimmune disorders associated with autoantibodies, immune complexes and B-lymphocyte hyperactivity, including pSS.
Objectives: Here, we describe the key data from Vivacity-MG that illustrate the therapeutic potential of nipocalimab in IgG autoantibody-driven conditions and review the design of a phase 2 study evaluating the efficacy and safety of nipocalimab in patients with pSS (NCT04968912).
Methods: Study feasibility assessments involved evaluating results from the phase 2 placebo-controlled trial Vivacity-MG. Of the 68 patients enrolled, 54 patients were randomized 1:1:1:1:1 to 4 treatment groups or a placebo group.
Results: In Vivacity-MG, there were no discontinuations due to treatment-emergent adverse events (TEAEs), severe AEs, or related serious AEs with nipocalimab. The incidence of infections and headaches with nipocalimab were comparable to placebo (**Table 1**). Treatment with nipocalimab resulted in rapid

and dose-dependent reductions in serum total IgG levels and anti-AChR IgG autoantibodies (**Figure 1**), as compared to placebo. The safety and pharmacodynamic data from Vivacity-MG support the hypothesis that nipocalimab has the potential to treat pSS through lowering pathogenic IgGs. As such, we developed a phase 2, multicenter, randomized, placebo-controlled, double-blind study enrolling adults with moderately-to-severely active pSS. The pSS study consists of a ≤6-week screening period, a 24-week double-blind treatment period, and a 6-week follow-up period. Participants are randomized 1:1:1 to treatment every 2 weeks with intravenous nipocalimab (low or high dose), or placebo, through Week 22. The primary efficacy endpoint is change from baseline in Clinical European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (clinESSDAI) score at Week 24. Safety assessments include TEAEs, abnormal vital signs, and laboratory parameters.

Conclusion: Vivacity-MG demonstrated that nipocalimab has the potential to offer an important new and targeted treatment option for patients with IgG-mediated diseases. The ongoing phase 2 study evaluates the safety and efficacy of treatment with nipocalimab in patients with moderately-to-severely active pSS.

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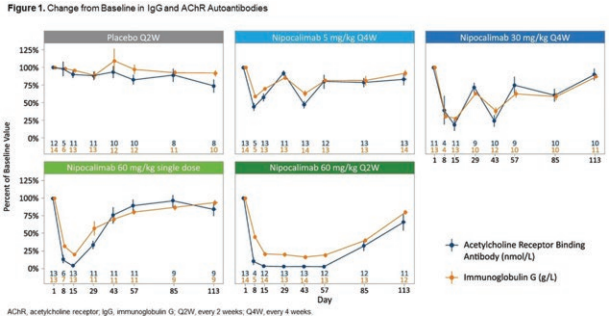
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Table 1. TEAE Overview

	Nipocalimab (n=54)	Placebo (n=14)
Patients with TEAE, n (%)	44 (81.5)	11 (78.6)
Patients with grade ≥3 TEAE, n (%)	0	4 (28.6)
Most frequent TEAEs, n (%)		
Exacerbation of MG	0	2 (14.3)
Headache	6 (11.1)	1 (7.1)
Nasopharyngitis	6 (11.1)	0
Diarrhea	6 (11.1)	1 (7.1)
Patients who discontinued due to TEAEs, n (%)	0	2 (14.3)
Patients with serious TEAE, n (%)	1 (1.9)*	2 (14.3)*
Patients with TEAEs deemed related to study drug by investigator, n (%)	21 (38.9)	1 (7.1)

MG, myasthenia gravis; TEAE, treatment-emergent adverse event.*Serious TEAE deemed unrelated to study drug.



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POS1131 SECRETAGOGUE EFFECT OF PDE4 INHIBITOR APREMILAST ON HUMAN SALIVARY GLAND ORGANOIDS OBTAINED FROM PRIMARY SJÖGREN'S SYNDROME PATIENTS

Keywords: Disease-modifying drug (DMARDs), Cell biology, Sjögren syndrome

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Background: in primary Sjögren's syndrome (pSS), salivary epithelial cells show an active role in the initiation and reiteration of the immunomediated damage. Epithelial saliva production is regulated by autonomic stimuli, intracellular calcium and cAMP concentration. The latter controls the action of cystic fibrosis transmembrane conductance regulator (CFTR), whose malfunction is postulated in sicca syndrome and pSS pathogenesis. (1) Forskolin is an activator of CFTR used in organoid swelling test in human salivary-gland derived organoid culture systems. Interestingly, also PDE4 is involved in intracellular cAMP deregulation: PDE4 inhibition might thus stimulate salivary function in pSS. (2-3) To the best of our knowledge, no data on the application of human salivary gland organoids specifically for testing drugs effective on xerostomia in pSS are found in literature.

Objectives: to culture vital salivary gland organoids obtained through labial or parotid biopsy of pSS patients; to evaluate the morphological structure and functional capacity of organoids in basal condition and after stimulation with forskolin or PDE4 inhibitor apremilast.

Methods: salivary gland tissues were harvested from 5 pSS patients through labial or parotid biopsy. After tissue processation and vital organoids obtainment, swelling essay and cell proliferation tests were performed after forskolin and apremilast application, compared to DMSO-treated controls. Immunohistochemistry evaluation on original salivary gland tissue and corresponding organoids was performed, by testing: alpha-amylase and AQP5 for acinar differentiation; EMA for ductal differentiation; calponin for myoepithelial differentiation and CK5 for basal differentiation; CK14, cKit and CD34 as markers of progenitor/stem cells.

Results: after application of forskolin or apremilast, we observed organoid swelling after 30 minutes, compatible with positive functional status and enhancement of saliva production. DMSO-treated controls were instead unaffected. In 3 cases apremilast induced proliferation of the organoids (Figure 1). All the cases were positive for CK14, most of the cases for CK5. All the cases were positive for Amylase; its secretion, and thus functional status of organoids, was confirmed by its high concentration in the culture medium. A focal ductal differentiation was found in some cases, highlighted by EMA positivity. The more differentiated EMA positive areas were negative for the staminal marker CK14, showing a sort of "complementary staining".

Conclusion: our data confirm that, from pSS epithelium, differentiated cells that escape senescence and vital and functional organoids that recapitulate the development of original salivary glands can be obtained from different target tissues of pSS. The direct stimulating effect of PDE4 inhibitor apremilast on pSS human salivary organoids is reported, opening new perspectives on targeting oral dryness with drugs that combine secretagogue and immunomodulatory effects.

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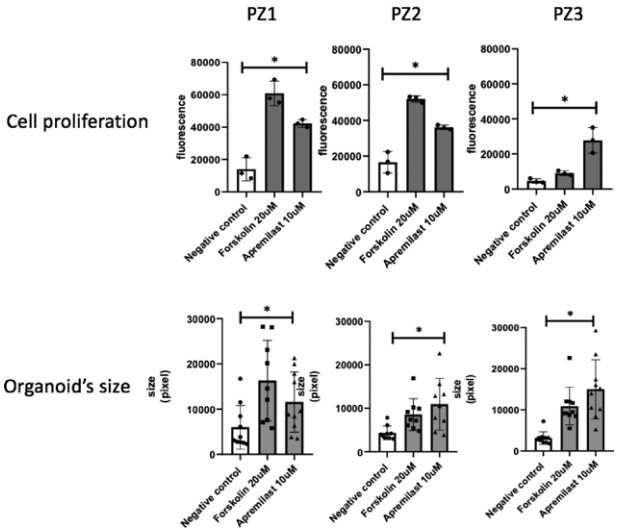


Figure 1. results on cell proliferation (upper graphs) and swelling essay (lower graphs) of salivary gland organoids after forskolin or apremilast application.

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POS1132

HYDROXYCHLOROQUINE, WHICH REGULATES IFN, IS HIGHLY EFFECTIVE IN SLE WITH ELEVATED SERUM S100 PROTEIN

Keywords: Systemic lupus erythematosus, Cytokines and chemokines

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Background: Background: Serum S100 protein, a damage-associated molecular pattern factor, has been associated with interferon (IFN) [1]. In a previous study, we found that hydroxychloroquine (HCQ), which regulates IFN activity, modulates serum S100 protein in SLE patients [2].
Objectives: This study determined if the therapeutic effect of HCQ is altered in SLE patients with different serum S100 protein levels.
Methods: This single-center, prospective, exploratory study evaluated patients before HCQ treatment and every 3 months for a year. SELENA-SLEDAI, SLE-DAS, and the Lupus Low Disease Activity State (LLDAS) scale measured disease activity. Serum cytokines (TNF-α, IL-6, IL-8, MCP-1, IL-1ra, VEGF-A, and MIP-1a) were measured by the multiplex Luminex assay, and serum S100A8 and S100A9 protein and adipokines (adiponectin, leptin, and resistin) by ELISA.
Results: Sixty-seven patients (63 females, mean age 41.8 years) were divided into three groups, namely, high, intermediate, and low, according to baseline S100A8 and S100A9 protein levels. The high and low groups were analyzed (Table 1). The S100A8 high group was more likely to have a history of lupus nephritis and active skin lesions. The S100A8 low group had a low serum complement titer (C3) and white blood cell count. The S100A8 high group was more likely to achieve LLDAS after HCQ treatment (high group, 76.9 % vs. low group, 56.3%). SLEDAI and SLE-DAS improved in the S100A8 high group after 3 months of HCQ treatment. There was no significant improvement in SLEDAI and SLE-DAS in the S100A8 low group (Figure 1). The C3 increase was greater in the S100A8 high group after 3 months of HCQ treatment. Regarding serum cytokines and adipokines, serum IL-1ra and resistin levels were significantly higher in the S100A8 high group. Cytokine changes after HCQ treatment were also greater than S100A8 low group. A trend similar to S100A8 was observed in S100A9.
Conclusion: SLE patients with high serum S100 protein levels respond better to HCQ therapy. This finding suggests that serum S100 protein levels may predict the response to IFN inhibitor therapy.

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Table 1. Characteristics of SLE patients.

Characteristic	All (N = 67)	S100A8 High (N = 22)	S100A8 Low (N = 22)	
Female, n (%)	63 (94.0)	22 (100)	21 (95.5)	0.235
Age, years, mean (SD)	41.8 (13.0)	43.5 (10.3)	44.8 (10.5)	0.972
Disease duration, years, mean (SD)	14.8 (11.1)	18.5 (12.5)	16.9 (11.1)	0.897
History of lupus nephritis, n (%)	30 (44.8)	15 (68.2)	7 (31.2)	0.015
Prednisone, n (%), median dosage, mg/day[#]	57 (76.1) 5 (3.0–7.3)	21 (95.5) 5 (4.5–10)	18 (81.8) 4 (2.4–6)	0.142 0.072
Disease activity				
Cutaneous lesion, n (%)	39 (58.2)	16 (72.7)	11 (50)	0.229
Joint lesion, n (%)	15 (22.4)	4 (18.2)	6 (27.2)	0.768
CLASI activity score[#]	2 (1–4) (n = 39)	2 (1–5)	1.5 (1–3)	0.260
SLEDAI score[#]	4 (2–6)	4 (2–4.3)	4 (2–6)	0.348
SLE-DAS score[#]	3.5 (1.1–5.2)	3.5 (1.3–5.1)	3.0 (1.1–6.1)	0.972
LLDAS, n (%)	18 (26.9)	7 (31.8)	4 (18.2)	0.294
Anti-dsDNA antibodies, IU/ml[#]	7.4 (5.0–16.3)	5 (5–13.3)	7.8 (5–19.5)	0.475
C3, mg/dL[#]	75 (63–94)	78.5 (66.5–96.3)	67 (51.8–83.3)	0.071
C4, mg/dL[#]	13 (10–20.6)	15(8.5–22)	11.5 (8–17.3)	0.495
CH50, U/mL[#]	33.8 (30.4–39.6)	33.9 (28.9–41.6)	32.2 (27.8–36.4)	0.245
White blood cells,/μL[#]	4650 (3750–5950)	5940 (5150–7337.5)	4290 (2897.5–4657.5)	<0.0001
Platelets, $\times 10^4$/μL[#]	21.0 (17.0–26.2)	23.1 (18.9–29.4)	19.8 (15.5–25.6)	0.170

The statistical analyses were conducted using the Mann-Whitney U test. [#]Nonparametric distributions are represented as medians (interquartile range).

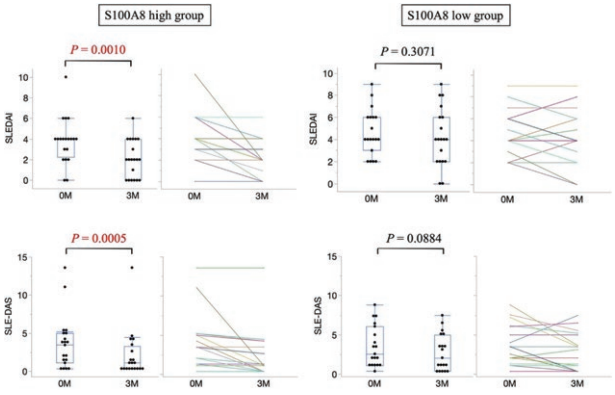


Figure 1. Association of serum S100 protein levels at baseline with SLE disease activity changes.

Changes in SLEDAI and SLE-DAS scores before and 3 months after HCQ administration were analyzed separately by baseline S100A8 levels. P-values were determined using Wilcoxon signed-rank sum test. 0M, 0 months; 3M, 3 months.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1133

TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH UPADACITINIB RESULTS IN THE COORDINATED INHIBITION OF TYPE 1 IFN-RELATED BIOMARKERS: BIOMARKER ANALYSIS OF THE M19-130 (SLEEK) PHASE 2 STUDY

Keywords: Cytokines and chemokines, Biomarkers, Systemic lupus erythematosus

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Background: Activation of Type I interferons (IFNs) and a wide array of innate and adaptive immune mediators are hallmarks of the pathogenesis of systemic lupus erythematosus (SLE) and activation of IFN pathways correlates with disease activity [1]. In a phase 2 study of SLE patients, upadacitinib (UPA, Janus kinase inhibitor) given alone or in combination with elsubrutinib (ABBV-599, Bruton's tyrosine kinase inhibitor) resulted in significant improvement in disease activity as measured by British Isles Lupus Assessment Group-Based Combined Lupus Assessment (BICLA) and SLE Responder Index-4 (SRI-4) at weeks 24 and 48.

Objectives: To evaluate the impact of UPA and ABBV599 on immunologic pathways associated with SLE pathogenesis.
Methods: SLE patients (n = 205) were randomized to (placebo [PBO]: n = 75; UPA 30 mg QD: n = 62; ABBV599: n = 68). At screening, patients were stratified by their SLE Disease Activity Index 2000 (SLEDAI-2K) score, corticosteroid dose (> 10-mg prednisone or not), immunosuppressant and IFN score. Proteomic analyses were performed on the plasma samples using a commercial proximity-extension immunoassay. A repeated mixed linear model was used to compare changes in biomarkers vs PBO and Pearson's correlation was tested to compare protein biomarkers, IFN score, and SLEDAI-2K score. All analyses were corrected for multiple testing using the Benjamini–Hochberg method. Enrichment analyses were performed to elucidate the biological pathways associated with changes in protein biomarkers.
Results: As expected, elevated IFN gene expression at baseline was associated with higher SLEDAI 2K disease activity scores, increased anti-double stranded DNA titers, and lower levels of complement components. Expression of serum proteins related to the IFN pathway, such as CXCL10, sialic acid binding immunoglobulin-like lectin 1, IFN gamma, and ZBP1, positively correlated with the IFN score. Treatment with UPA monotherapy or the combination ABBV-599 significantly reduced the IFN gene scores compared with PBO at weeks 4 and 24 ($P \leq .0001$). Proteomic analyses revealed 301 protein biomarkers differentially modulated at weeks 2, 12, and 24 compared with PBO, including significant downregulation of Type I IFN pathway proteins. There were additional impacts of UPA and ABBV-599 on T-cell–associated cytokines, B cells, macrophages, and innate response markers. These effects were similar with UPA and ABBV-599, suggesting that the main effect was attributable to activity of UPA.
Conclusion: These results suggest that the clinical benefit demonstrated by UPA in patients with SLE includes the modulation of Type I IFN with impact on several core pathogenic pathways involved in SLE. The main biomarker effects of UPA and ABBV-599 were driven by UPA.
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Disclosure of Interests: Marie-Claude Gaudreau Shareholder of: May hold AbbVie stock or stock options, Employee of: AbbVie, James Fann Shareholder of: May hold AbbVie stock or stock options, Employee of: AbbVie, Shalina Contrepois Shareholder of: May hold AbbVie stock or stock options, Employee of: AbbVie, Alan Friedman Shareholder of: May hold AbbVie stock or stock options, Employee of: AbbVie, Thierry Sornasse Shareholder of: May hold AbbVie stock or stock options, Employee of: AbbVie, Joan T Merrill Consultant of: AbbVie, Alexion, Alumis, Amgen, Astra Zeneca, Aurinia, Bristol Myers Squibb, EMD Serono, Genentech, Gilead, GlaxoSmithKline, Lilly, Merck, Pfizer, Provention, Remegen, Sanofi, UCB, and Zenas, Grant/research support from: Astra Zeneca, Bristol Myers Squibb, and GlaxoSmithKline.
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POS1134 NOVEL APPROACH TO TREAT SYSTEMIC LUPUS ERYTHEMATOSUS, BY TARGETING THE "ROOT CAUSE", B CELLS AND PLASMA CELLS, USING BCMA-CD19 COMPOUND CAR

Keywords: Autoantibodies, Systemic lupus erythematosus, Clinical trials

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Background: Systemic lupus erythematosus (SLE) is a heterogenous multi-system autoimmune disease characterized by presence of autoreactive antibodies produced by the "root" cause, B and plasma cells. Autoantibody depletion has been attempted by targeting B cells, however no such treatment addresses both B and plasma cells.
Objectives: We assess the safety and efficacy of dual resetting B and plasma cell populations using our novel BCMA-CD19 cCAR T (cCAR) in an open label phase I clinical trial.
Methods: We constructed a cCAR composed of a complete BCMA-CAR fused to a complete CD19-CAR, separated via self-cleaving P2A peptide. The cCAR functional activity was assessed in co-culture assays with multiple cell lines and mouse models. T cells from peripheral blood obtained via apheresis were transfected to create cCAR. Cessation of steroids and immunosuppressing medications was followed by conditioning. Patients received monthly IgG until B cells recovered. Patients were dosed from $1.5\text{-}3x10^6$ cCAR cells/kg body weight and monitored. P1 and P2: 20-year history of managed SLE and received cCAR as compassionate use for B cell lymphoma. P1 and P2achieved complete remission (CR). After 1-year follow up demonstrated CR of SLE, hospital approved additional SLE/Lupus Nephritis (LN) patients for treatment. Baseline Characteristics: 12 patients received cCAR as of 15 Jan 2023. Patient age range: 20-58. Ten of 12 were female. P1 and P2: SLEDAI-2K score 4, and 8, respectively. Patient 3-12: SLEDAI-2K baseline score mean 11 range 6 to 16. All of patients (3-12) had LN on kidney biopsy between IV to V with failure of standard therapy.
Results: Safety: Overall cCAR has been well tolerated to date. There have been no severe adverse events (SAE) or infections attributed to cCAR, no CRES and no CRS above Grade 1. All patients with >3 weeks follow up had a mild fever (CRS grade 1) which resolved with supportive care. Onset of mild fever occurred between days 3 to 14 and resolved within a week of onset. Efficacy: B cells were entirely depleted in peripheral blood 3-14 days post cCAR. Three patients treated >6 months in CR (SLEDAI-2K = 0, all autoantibodies negative, and normal complement). P1 and P2 maintain drug free CR and with no autoantibodies post-cCAR approximately 40 and 20 months respectively. All B cells recovered within 2-6 months with no indications of relapse. At ≥1-4 months post-treatment 9 patients were negative for, anti-dsDNA autoantibody, anti-nuclear autoantibody, anti-SSA/Ro52 autoantibody, anti-SSA/Ro60 autoantibody, anti-ribosomal P, and anti-U1-snRNP. Among 9 patients rapid improvement within 1 month after cCAR, mean SLEDAI-2K dropped from 8.7 mean at baseline to 2 at 1 month (7 patients no symptoms), and mean drop to 0.88 within 6 months (9 patients no symptoms). All patients achieved 100% response and are maintaining medication free recovery (no immunosuppressives or glucocorticoids). An immune "reset" was confirmed via flow cytometry showing that most of recurring cells are naïve B cells, and further observed in BCR deep sequencing (patients 3-4), whereby IgG and IgA clonotypes are absent and non-class-switched BCR repertoires are greater than 95% IgM heavy chain.
Conclusion: These data on the 12 patients treated with cCAR demonstrate that the intervention is well tolerated. Initial data suggests immune system "reset" with long-term remission is possible as cCAR treats the "root cause" of disease by depleting autoreactive antibodies produced by plasma cells and memory B cells. This approach can be extended to other B and/or plasma cell mediated autoimmune disorders. The full dataset will be updated at the meeting.
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POS1135 EFFECT OF IMMUNOMODULATORY THERAPIES ON ANTIPHOSPHOLIPID ANTIBODIES TITERS IN CHILDREN WITH ANTIPHOSPHOLIPID SYNDROME

Keywords: Anti-phospholipid syndrome, Autoantibodies

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Background: Pediatric Antiphospolipid Syndrome (APS) is an autoimmune disease characterized by venous and/or arterial thrombotic events (TE) associated with 2 consecutive positive determinations (at least 12 weeks apart) of antiphospholipid antibodies (aPL), IgG/IgM anticardiolipin (aCL), IgG/IgM β2-glycoprotein I (aβ2GPI) and/or lupus anticoagulant (LA). Recent data suggests that aPL levels may decrease over time due to the natural history of the disease or to treatments. Therefore, monitoring of aPL levels may represent a strategy to evaluate disease activity and response to therapies.
Objectives: To investigate the trend over time of aPL titers in children with APS, comparing patients under immunomodulatory therapies and those without them.
Methods: A descriptive, observational, cross-sectional study was carried out in children with APS. aPLs testing was carried out in all patients from diagnosis every 3-4 months for 2 years. Interferon Gene Signature (IGS) was assessed as described by Crow[1]. Laboratory parameters, clinical and demographic data was retrieved and analyzed. Statistical analysis was performed with software R_v. 4.0.3.

Results: Sixteen children with a diagnosis of APS were included in this study. The median age at disease onset was 11.5 years (range: 6 months – 17 years) and 62.5% were female; 87.5% Caucasians. Thirteen patients (81.2%) had a diagnosis of primary APS and 3 (18.8%) out of 16 of secondary APS. Regarding clinical manifestations, 11 children developed at least one TE (7 arterial and 5 venous). Cerebral territory was the most frequently involved with 5 thrombosis, followed by 3 deep vein thrombosis, 1 pulmonary thromboembolism and 2 arterial renal thrombosis. Most of the patients received an antiaggregant and/or anticoagulant therapy (13 and 8 patients, respectively). However, 1 patient presented a new TE after the antiaggregant withdrawal. A total of 12 (75%) children developed at least one non-criterion manifestation: 7 patients (44%) cardiac (Libman-Sacks endocarditis or valvular heart disease), 7 patients (44%) neurological (chorea or white matter lesions), 6 patients (37.5%) hematological (thrombocytopenia, hemolytic anemia or Evans syndrome) and 1 patient (3.8%) a renal thrombotic microangiopathy. Related to immunological parameters, 4 (25%) were positive for only 1 aPL, 5 (42%) for 2 aPL subtypes and 7 (44%) for all 3 aPL subtypes, showing the highest rates IgG aβ2GP (87.5%) and IgG aCL (81.25%). Lower rates were identified for LA (44%), IgM aCL (18.7%) and IgM aB2GP (12.5%). Four (25%) had ANA positivity (3 secondary and 1 primary APS). Regarding treatment, 13 children (81.25%) received at least one immunomodulatory drug (13 patients mycophenolate; 4 rituximab) and 3 (18.7%) were not treated with them. During the 2-year-follow-up, 11 patients (68.8%) showed a reduction of aPL titers compared to the onset, with becoming 9 negative (56.3%) at the end of follow-up (Figure 1A). Of those who were negative, 8 children were under immunomodulatory therapies and only 1 did not receive any treatment. Five patients (31.2%) showed stable titers of aPLs during follow-up. Of them, 2 were not treated with immunomodulatory therapies and 2 were under mycophenolate but with poor compliance (reduction of titers with the restart of therapy were observed). We also evaluated the presence of the IGS in 11 patients with APS for whom a whole blood RNA sample was available: the IGS was positive in 9 (81.8%) of 11 children (7 with primary APS and 2 with secondary APS).

Conclusion: Our data suggest the possible effect of immunomodulatory therapies in reducing antibody titers in APS. Therefore, it may represent a strategy to control the disease activity leading to a better prognosis. Further studies are needed to confirm and expand our data.

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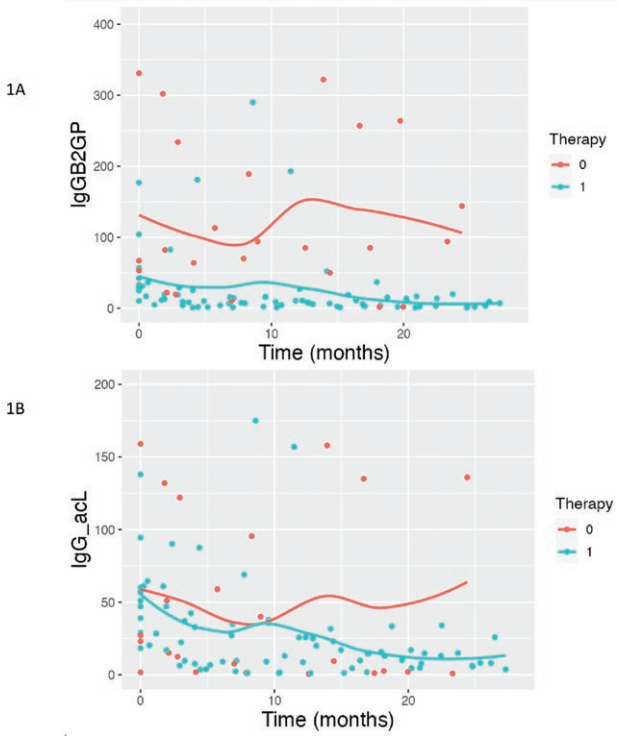


Figure 1. A. Trend of IgG aB2GP during 2 years of follow-up. B. Trend of IgG aCL during 2 years of follow-up.Red line (0): children without immunomodulatory (IMM) therapies; blue line (1): children with IMM therapies.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1136 DISEASE-MODIFYING EFFECT AND LONG-TERM SAFETY DATA OF BELIMUMAB IN PATIENTS WITH SLE: A SINGLE CENTRE RETROSPECTIVE ANALYSIS

Keywords: Systemic lupus erythematosus

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Background: Disease modification is an important concept for minimizing disease activity with the fewest treatment-associated toxicities when managing SLE. Belimumab has been used as a maintenance therapy for SLE; however, data on its disease-modifying effects are scarce.

Objectives: Therefore, we aimed to investigate the disease-modifying effects of belimumab in SLE patients.

Methods: This single-centre retrospective cohort study included SLE patients treated with belimumab at our institution. We analysed the changes in flare-free ratio, lupus low disease activity state (LLDAS) achievement ratio, glucocorticoid dosage, SLICC/ACR damage index (SDI) score, and drug retention rate after belimumab initiation.

Results: Of the 567 patients with SLE followed up in our hospital, 95 used belimumab and to 92 were included in the study. Fifty-two weeks after initiating belimumab, the flare rate decreased (82.6% to 14.1%) ($p<0.01$). At week 52 and day 1,000 after initiation of belimumab, >70% and approximately 90% of the patients achieved LLDAS, respectively. Belimumab administration also significantly decreased glucocorticoid demands, and at the end of the study period, 68.5% of patients achieved prednisolone ≤5 mg/day and 22.8% achieved glucocorticoid discontinuation. Furthermore, most patients were free of SDI progression (week 52, ±95%; end of study period, almost 90%), and belimumab showed a high drug retention rate (week 52, 90%; day 1000 after initiation >80%).

Conclusion: Most patients on belimumab achieved LLDAS, decreased flare rate and glucocorticoid demand, and a stable trend of SDI after its induction. Furthermore, belimumab had a high drug retention rate. Therefore, the introduction of belimumab may be a key element in disease modification.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Masato Okada Speakers bureau: Elli-Lilly, Janssen, Takehiro Nakai: None declared.

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POS1137 PHARMACOKINETICS AND EXPOSURE-RESPONSE RELATIONSHIPS OF UPADACITINIB OR ELSUBRUTINIB ALONE OR IN COMBINATION (ABBV-599) IN SYSTEMIC LUPUS ERYTHEMATOUS

Keywords: Systemic lupus erythematosus

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Background: ABBV-599 is a novel combination of upadacitinib (UPA), a reversible JAK inhibitor approved for the treatment of several autoimmune diseases, and elsubrutinib (ELS), a covalent BTK inhibitor being developed for the treatment of immune-mediated inflammatory diseases. The efficacy and safety profile of the monotherapies (UPA and ELS) and combination (ABBV-599) were evaluated in systemic lupus erythematous (SLE) in the global Phase 2 Study SLEek (NCT#03978520).

Objectives: The analyses presented here characterize the pharmacokinetics of UPA and ELS as well as exposure-response relationships for efficacy at Week 24 and Week 48 and safety endpoints through Week 48.

Methods: Phase 2 Study SLEek evaluated UPA 30 mg once-daily (QD), ELS 60 mg QD, ABBV-599 high dose (ELS 60 mg + UPA 30 mg) QD and ABBV-599 low dose (ELS 60 mg + UPA 15 mg) QD in a placebo-controlled manner. Pharmacokinetic, efficacy, and safety data from subjects with moderately to severely active SLE enrolled in the study were used to conduct the analyses (N = 341). UPA pharmacokinetics were described using a previously published population pharmacokinetic model[1] and ELS pharmacokinetics were characterized using Bayesian population pharmacokinetic analyses based on data from the healthy subjects, RA patients, and SLE patients. Exposure-response analyses for efficacy were conducted using logistic regression models to characterize the relationships for the monotherapies and combination average plasma concentration (C_{avg}) and the percentage of patients achieving SLE Responder Index-4 (SRI-4), SRI-4 and steroid dose ≤ 10 mg QD, and British Isles Lupus Assessment Group (BILAG)-Based Combined Lupus Assessment (BICLA) response at Week 24 and Week 48. Exposure-response analyses for safety were conducted using quartile plots and logistic regression modeling at or through Week 48.

Results: The previously developed population pharmacokinetic model for UPA showed that UPA pharmacokinetics were comparable in subjects with SLE and RA. A one-compartment model with a proportional error model best described the pharmacokinetics of ELS. Exposure-response analyses for efficacy based on logistic regression modeling demonstrated that at Week 24 and Week 48, statistically significant relationships were observed between UPA C_{avg} and SRI-4, SRI-4 and steroid dose ≤ 10 mg QD, and BICLA (Figure 1). No exposure-response trends were observed for ELS C_{avg} and the evaluated efficacy endpoints during the Week 24 analysis. Inclusion of ELS C_{avg} in the logistic regression models did not improve the model performance. Simulations based on the logistic regression models showed that UPA 30 mg QD is predicted to provide 8% to 17% higher response rates across the evaluated endpoints compared to UPA 15 mg QD. Exposure-response analyses for safety showed no clear trend for serious infections, lymphopenia, or neutropenia through Week 48. A shallow trend was observed for an increase in the percentage of subjects experiencing herpes zoster and a > 2 g/dL decrease in hemoglobin from Baseline at or through Week 48 with increasing upadacitinib C_{avg}.

Conclusion: Population pharmacokinetic and exposure-response analyses demonstrated that plasma exposures associated with UPA 30 mg QD were efficacious in subjects with SLE, while maintaining an acceptable safety profile. Addition of ELS, as part of ABBV-599, was not estimated to provide any additional efficacy benefit over UPA alone.

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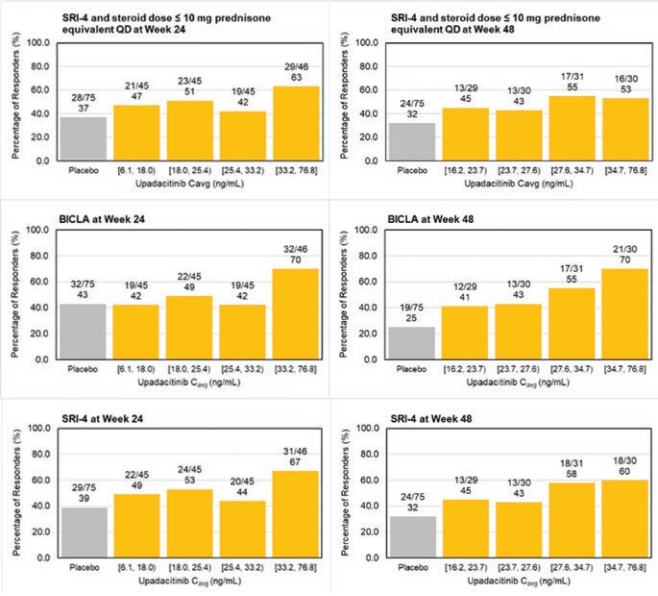


Figure 1. Graphical Assessment for Exposure-Response Relationships Between Upadacitinib Average Plasma Concentration and Evaluated Efficacy Endpoints at Week 24 (left) and Week 48 (right) C_{avg}: average plasma concentration; QD: once-daily

Acknowledgements: NIL.

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POS1138

SIROLIMUS VERSUS MYCOPHENOLATE MOFETIL FOR THE TREATMENT OF LUPUS NEPHRITIS: RESULTS FROM A REAL-WORLD CSTAR COHORT STUDY

Keywords: Systemic lupus erythematosus, Kidneys

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Background: The effectiveness and safety of sirolimus for the treatment of systemic lupus erythematosus (SLE) and lupus nephritis (LN) have been shown in some studies. However, a comparison of sirolimus with standard of care (SoC) for LN patients has not been reported.

Objectives: To compare the effectiveness and safety of sirolimus versus mycophenolate mofetil (MMF) for LN treatment.

Methods: A real-world cohort study based on the Chinese SLE Treatment and Research (CSTAR) registry was conducted. Excluded patients with LLDAS (lupus low disease activity state) or remission at baseline, LN patients who were prescribed sirolimus or MMF were enrolled. Propensity score matching was used to ensure equivalent disease conditions. SLE and LN disease activity indices, serological parameters, steroid doses, and adverse events were compared between the two groups at 3-month, 6-month, and 12-month visits.

Results: Data from 53 patients in each group were analyzed. The clinical effectiveness of sirolimus, including the proportion of patients with LLDAS/remission, or clinical response (SLEDAI-2K reductiongroups at 3-month, 6-month, and 12-month vSystemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) scores, physician's global assessment (PhGA) scores, the remission of LN, the change of 24 hours urine protein level, and the steroid tapering effect, were equivalent to those of MMF (P≥0.05). Greater improvements in complement levels were observed in the sirolimus group than the MMF group at 3, 6, and 12 months. Ten adverse events in the sirolimus group and one in the MMF group were recorded. None was severe or led to drug discontinuation.

Conclusion: Sirolimus was as effective as MMF in the treatment of LN and glucocorticoid tapering. Sirolimus had better effects on serological improvement. Sirolimus was well tolerated in LN patients.

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Table 1. Effectiveness of MMF vs. sirolimus for LN patients

	3 months			6 months			12 months		
	MMF (N=38)	Sirolimus (N=44)	P value	MMF (N=29)	Sirolimus (N=32)	P value	MMF (N=14)	Sirolimus (N=13)	P value
SLEDAI-2K change	-4.00 (-8.00 , 0.00)	-2.00 (-6.00 , 0.00)	0.228	-4.00 (-8.00 , -1.00)	-2.00 (-6.00 , 0.00)	0.141	-4.00 (-6.00 , -1.50)	-2.00 (-6.00 , -0.50)	0.532
PhGA change	-0.250 (-0.650 , 0.200)	-0.200 (-0.600 , 0.000)	0.928	-0.200 (-0.750 , 0.200)	-0.200 (-0.800 , 0.100)	0.743	-0.350 (-0.775 , 0.150)	-0.400 (-0.650 , -0.025)	0.908
Clinical response	51.4% (18/35)	47.4% (18/38)	0.729	64.0% (16/25)	50.0% (13/26)	0.313	66.7% (8/12)	50.0% (5/10)	0.429
LLDAS or remission	10.5% (4/38)	15.9% (7/44)	0.476	13.8% (4/29)	18.8% (6/32)	0.602	50.0% (7/14)	61.5% (8/13)	0.547
LN Remission (CR+PR)	68.4% (26/38)	65.9% (29/44)	0.809	72.4% (21/29)	56.3% (18/32)	0.189	85.7% (12/14)	76.9% (10/13)	0.557
24-hour urine protein level (g) change	-0.287 (-0.900 , -0.002)	-0.960 (-2.083 , 0.115)	0.284	-0.669 (-2.085 , -0.475)	-0.220 (-1.540 , 0.270)	0.121	-0.675 (-1.433 , 1.750)	-1.470 (-4.410 , 0.150)	0.44
Recovered hypocomplementaemia	41.7% (10/24)	74.1% (20/27)	0.019	30.0% (6/20)	75.0% (18/24)	0.003	0% (0/8)	71.4% (5/7)	0.003
Change in C3	0.075 (-0.063 , 0.196)	0.206 (0.084 , 0.321)	0.008	0.001 (-0.072 , 0.130)	0.219 (0.062 , 0.378)	0.001	-0.007 (-0.074 , 0.125)	0.259 (-0.003 , 0.570)	0.063
Change in C4	0.014 (-0.001 , 0.060)	0.033 (0.009 , 0.071)	0.25	-0.001 (-0.038 , 0.060)	0.054 (0.014 , 0.103)	0.011	-0.003 (-0.028 , 0.026)	0.020 (-0.008 , 0.101)	0.121
Change in GC dosage (mg/d)	0.00 (-5.00 , 0.00)	0.00 (-13.75 , 0.00)	0.174	0.00 (-6.25 , 0.00)	0.00 (-10.63 , 0.00)	0.771	-6.25 (-12.50 , -1.88)	-5.00 (-22.50 , 0.00)	0.961
GC dosage≤7.5 mg/d prednisone	34.2% (13/38)	31.8% (14/44)	0.818	37.9% (11/29)	46.9% (15/32)	0.481	64.3% (9/14)	84.6% (11/13)	0.228

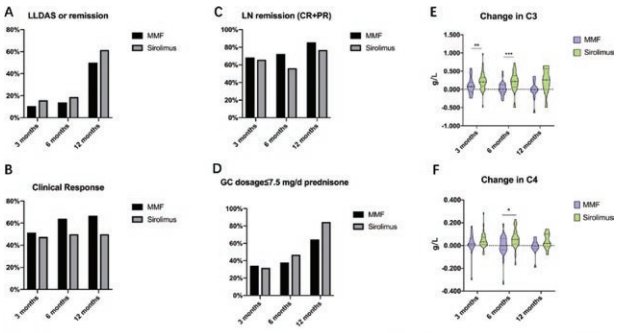


Figure. Clinical effectiveness of sirolimus versus MMF for lupus nephritis (LN). MMF, mycophenolate mofetil; LLDAS, lupus low disease activity state; GC, glucocorticoid; CR, complete remission; PR, partial remission.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1139 **WITHDRAWN**

POS1140

A NOVEL TLR7/8 ANTAGONIST BLOCKS PRO-INFLAMMATORY FUNCTION OF IMMUNE COMPLEXES FROM LUPUS PATIENTS AND ABROGATES LUPUS-LIKE DISEASE IN MICE

Keywords: Innate immunity, Disease-modifying drug (DMARDs), Systemic lupus erythematosus

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Background: Toll-like receptors (TLR) 7 and 8 are innate sensors of single stranded RNA (ssRNA). Genetic and *in vivo* evidence suggests that aberrant recognition of RNA-containing autoantigens by TLR7/8 drives autoimmune diseases (Junt and Barchet, 2015). More validation for a pathogenic effect of TLR7 in chronic inflammation comes from recent data showing that a TLR7 gain-of-function mutation is sufficient to drive lupus-like disease (Brown et al., 2022).
Objectives: Here we report on the preclinical characterization of MHV370, a highly selective, orally active TLR7/8 inhibitor for treatment of chronic inflammatory diseases.
Methods: We used a suite of in vitro profiling assays to investigate the effect of MHV370 on TLR responses. This included the stimulation of PBMCs by immune complexes from systemic lupus erythematosus patient sera. Furthermore we characterized MHV370 in different mouse models of acute and chronic TLR7-driven inflammation.
Results: *In vitro,* MHV370 interfered with TLR7/8-dependent production of cytokines in humans and mice, most notably of interferon alpha, a clinically validated driver of autoimmune diseases. MHV370 abrogates B cell, monocyte, and neutrophil responses downstream of TLR7/8. *In vivo*, prophylactic or therapeutic administration of MHV370 suppressed TLR7-dependent cytokines and interferon stimulated genes. In the NZB/W F1 mouse model of lupus, MHV370 prevented halted disease progression and glomerulonephritis. Unlike hydroxychloroquine, MHV370 interfered with cytokine production triggered by immune complexes between systemic lupus erythematosus patient sera and necrotic cell extract, suggesting differentiation from clinical standard of care.
Conclusion: The pharmacological data presented here support further development of MHV370 towards clinical proof of concept trials in man.
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Disclosure of Interests: Stuart Hawtin Shareholder of: Novartis, Employee of: Novartis, Cédric André Shareholder of: Novartis, Employee of: Novartis, Géraldine Collignon Zipfel Shareholder of: Novartis, Employee of: Novartis, Simone Appenzeller: None declared, Bettina Bannert: None declared, Lea Baumgartner Shareholder of: Novartis, Employee of: Novartis, Damian Beck Shareholder of: Novartis, Employee of: Novartis, Claudia Betschart Shareholder of: Novartis, Employee of: Novartis, Thomas Boulay Shareholder of: Novartis, Employee of: Novartis, Hermine Brunner Speakers bureau: Novartis, Pfizer, Roche, Grant/research support from: From Pfizer. The Cincinnati Children's Hospital where Dr. Brunner works as a full-time employee, has received contributions from the following industries in the past 2 years: AbbVie, Astra Zeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Celgene, Cerocor, horizon, Janssen, Eli Lilly, Idorsia, Cerocor, F. Hoffmann-La Roche, Merck, Novartis, and Sanofi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment to third parties, Melanie Ceci Shareholder of: Novartis, Employee of: Novartis, Jonathan Deane Shareholder of: Novartis, Employee of: Novartis, Kumquat Biosciences, Roland Feifel Shareholder of: Novartis, Employee of: Novartis, Enrico Ferrero Shareholder of: Novartis, Employee of: Novartis, GSK, Diego Kyburz Consultant of: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, Roche, Grant/research support from: Abbvie, Frederique Lafossas Shareholder of: Novartis, Employee of: Novartis, Pius Loetscher Shareholder of: Novartis, Employee of: Novartis, Christina Merz-Stoeckle Shareholder of: Novartis, Employee of: Novartis, Pierre Michellys Shareholder of: Novartis, Employee of: Novartis, Odyssey Therapeutics, Barbara Nuesslein-Hildesheim Shareholder of: Novartis, Employee of: Novartis, Friedrich Raulf Shareholder of: Novartis, Employee of: Novartis, James Rush Shareholder of: Novartis, Employee of: Novartis, Kling Bio, Giulia Ruzzante Shareholder of: Novartis, Employee of: Novartis, Thomas Stein Shareholder of: Novartis, Employee of: Novartis, Samantha Zaharevitz Shareholder of: Novartis, Employee of: Novartis, Grazyna Wieczorek Shareholder of: Novartis, Employee of: Novartis, Richard Siegel Shareholder of: Novartis, Employee of: Novartis, Peter Gergely Shareholder of: Novartis, Employee of: Novartis, Tamas Shisha Shareholder of: Novartis, Employee of: Novartis, Tobias Junt Shareholder of: Novartis, Employee of: Novartis.
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POS1141

SUBTHERAPEUTIC HYDROXYCHLOROQUINE CONCENTRATION IS ASSOCIATED WITH INCREASED DISEASE ACTIVITY AND GREATER ORGAN DAMAGE DURING 5-YEAR FOLLOW-UP IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus

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Background:
Objectives: Hydroxychloroquine (HCQ) is a cornerstone drug in patients with systemic lupus erythematosus (SLE), as it decreases the risk of flares and comorbidities and improves survival. This study investigated the effects of the serum HCQ concentration on clinical manifestations, disease activity, and organ damage in a longitudinal cohort of SLE patients.
Methods: The 338 SLE patients from the Korean Lupus Network registry were assessed with respect to their demographic data, clinical and laboratory findings, PGA score, and adjusted mean SLEDAI-2000 (AMS) and SLICC damage index scores annually for 5 consecutive years. Patients were divided into two groups according to their serum HCQ concentration at baseline: patients with a subtherapeutic level (< 500 ng/mL) and those with a therapeutic level (try were assessed with respect to their demographion the clinical outcomes was evaluated in a longitudinal analysis using a generalized estimating equation (GEE) and a logistic regression analysis.
Results: Of the 338 patients, 287 (84.9%) were in the subtherapeutic group at baseline. This group had a higher incidence of newly developed lupus nephritis (P = 0.036) and had been prescribed higher mean and cumulative doses of prednisolone (P = 0.003 and P = 0.013) than the therapeutic group. In multivariable analyses based on GEE, an association of the subtherapeutic group with both a higher PGA score (β coefficient = 0.328, 95% confidence interval [CI]: 0.215–0.441, P < 0.001) and a higher SLICC damage index score (β coefficient = 0.366, 95% CI: 0.061–0.671, P = 0.019) was determined across all 5 years. In the multivariate logistic regression analysis, subtherapeutic HCQ was significantly associated with the AMS (odds ratio [OR] = 1.142, 95% CI 1.022–1.276, P = 0.019), mean PGA (OR = 3.697, 95% CI 1.767–7.735, P < 0.001), and an annual increase in the SLICC damage index score (OR = 1.529, 95% CI 1.005–2.325, P = 0.047).
Conclusion: A subtherapeutic HCQ concentration may affect the development of new-onset LN, and had the significant association with higher disease activity and cumulative organ damage in these SLE patients over time.
REFERENCES: NIL.

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Disclosure of Interests: None Declared.
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POS1142

SPANISH NATIONAL REGISTRY OF BELIMUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Registries, Systemic lupus erythematosus

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Background: Belimumab (BLM) is a monoclonal antibody that inhibits B-lymphocyte stimulating factor (BlyS) approved as a specific treatment for systemic lupus erythematosus (SLE) in 2011. We present the experience with BLM in a Spanish cohort with more than 460 patients.

Objectives: To describe demographic characteristics, efficacy and safety of BLM in patients with SLE in Spanish population since its approval.

Methods: Descriptive, retrospective, multicenter study in patients diagnosed with SLE according to EULAR/ACR 2019, SLICC and/or ACR 1997 diagnostic criteria. Data regarding SLE patients treated with BLM were collected from medical records (2011-2022). Demographic features, efficacy, laboratory variables, SLEDAI, renal involvement, steroid dose, administration routes and safety were assessed. To see whether a trend in BLM prescription had changed or not over time, two periods of time were analyzed: 2011-2016 (period1) and 2017-2022 (period2).

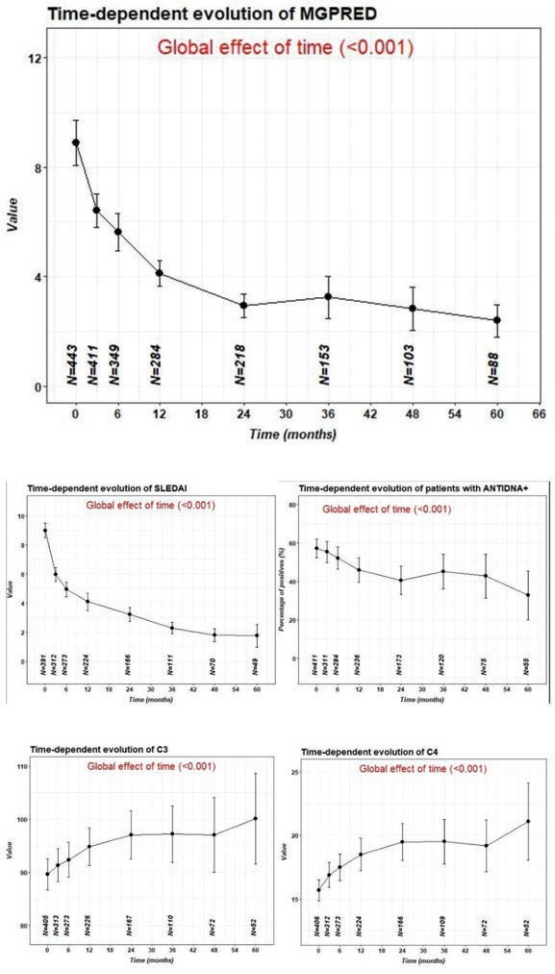
Results: Baseline characteristics of patients are summarized in Table 1. A total of 462 patients (36 hospitals) were included, 50.9% were on intravenous (IV), 34% on subcutaneous (SC) and 15.1% switched from IV to SC route. The median number of pre-BLM csDMARD use was 2.0 (2.0-3.0), being hydroxychloroquine (HCQ) the most frequently used (94.5%). Fifty-two patients were treated with IV cyclophosphamide with a median of 6 bolus received. At the time of BLM start, 443 patients were on prednisone with a median dose of 6.2 mg (5.0-10.0). Significant decreases in prednisone dose, SLEDAI and anti-DNA antibodies were observed from baseline until the last visit, whereas complement C3 and C4 values raised (Figure 1). A total of 118 patients (27.4%) had renal involvement with a median proteinuria of 1.0 g/day (0.5-2.4). Renal biopsy was done in 102 out of 118 patients, being class IV (33%), class III (21%) and class V (16%) the most frequently reported. After BLM, 73.3% of these patients improved (median proteinuria of 0.2 g/day (0.1-0.7). In period1, 100 patients started BLM compared to 362 in period2. The median time from SLE diagnosis to BLM begin was 7.1 (4.0-13.7) and 6.2 (2.1 -14.4) years in period1 and period2, respectively (p=0.454). We found a trend to use more csDMARD before BLM treatment in period1: 2.5 (2-3) vs. 2 (2-3) (p=0.088). A total of 143 (30.5%) patients discontinued treatment mostly due to inefficacy (55.9%) and infections (11.9%). In fact, 116 patients developed infections, mostly mild; 2 patients died, 16 had COVID-19 and 4 patients developed tumors requiring discontinuation of the drug.

Conclusion: In our cohort of SLE patients in a real-world setting, BLM has been effective, safe and seems to be a good choice to treat renal involvement.

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Figure 1: Prednisone, SLEDAI, DNA and complement time-dependent evolution.



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Disclosure of Interests: None Declared.

Table 1: Baseline characteristics of patients included in Belimumab Spanish registry.

Age at SLE diagnosis (years)**	34.4 (24.7 - 43.9)
Age at BLM starts (years)**	44 (35.8 - 52.8)
Gender (female) n, (%)	395 (85.5)
Time from diagnosis until BLM start (years)**	6.6 (2.3 - 14.3)
ANA title**	1/640 (1/320-1/1280)
ANA positive, n (%)	415 (89.8)
DNA positive, n (%)	378 (86.9)
Antiphospholipidic syndrome, n (%)	49 (11.2)
Antiphospholipidic antibodies, n (%)	123 (31.1)
("aB2GPI-", "ACL-", "AL+")	26 (6.6)
("aB2GPI+", "ACL+", "AL-")	16 (4.0)
("aB2GPI+", "ACL+", "AL+")	40 (10.1)
("aB2GPI-", "ACL+", "AL-")	24 (6.1)
("aB2GPI-", "ACL+", "AL+")	6 (1.5)
("aB2GPI+", "ACL-", "AL-")	7 (1.8)
("aB2GPI+", "ACL-", "AL+")	4 (1.0)
Renal involvement, n (%)	118 (27.4)
Articular involvement, n (%)	280 (78.9)
Hematologic involvement, n (%)	216 (51.4)
Skin involvement, n (%)	230 (54.0)
Cyclophosphamide, n (bolus)**	52 (6)
bDMARD, n (%)	79 (18.6)
- Rituximab	67 (84.8)
- Others	12 (15.2)
cDMARD pre BLM, n (%)	453 (100)
- Hydroxychloroquine	435 (96.0)
- Methotrexate	246 (54.3)
- Azathioprine	158 (34.9)
- Mycophenolate mofetil/mycophenolic acid	137 (30.2)
- Leflunomide	55 (12.1)

** Median (IQR)

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POS1143

URINARY CD163 PREDICTS COMPLETE RENAL RESPONSE WITH ZETOMIPZOMIB TREATMENT IN THE OPEN-LABEL MISSION PHASE 2 STUDY IN PATIENTS WITH LUPUS NEPHRITIS

Keywords: Biomarkers, Systemic lupus erythematosus, Clinical trials

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Background: Complete renal response (CRR) defined by ACR/EULAR guidelines is a desirable clinical outcome associated with long-term preservation of kidney function in patients with lupus nephritis (LN) as demonstrated in clinical trials when achieved after 1-2 years. Urinary CD163 (uCD163), a biomarker that correlates with LN histologic inflammation, has been observed to predict clinical response to therapy[1]. Results previously reported on MISSION, a Phase 2 open-label study evaluating the safety and tolerability of zetomipzomib in active, proliferative LN, demonstrated clinically meaningful renal responses along with reductions in uCD163 and strong correlation with UPCR[2]. Decrease in uCD163 at early timepoints and its prediction in proteinuria response may increase probability of achieving a meaningful treatment effect.

Objectives: Data from the MISSION Phase 2 study of zetomipzomib was used to evaluate uCD163 as a potential predictor of complete renal response (CRR) for patients with LN.

Methods: In the MISSON Phase 2 study, patients with active proliferative LN (Class III or IV ± V) received 60 mg of zetomipzomib subcutaneously once weekly (first dose 30 mg) in addition to stable background therapy for 24 weeks. End-of-treatment (EOT) was at Week (W) 25, and end-of-study (EOS) occurred at W37. uCD163 data at W13 and W25 were used to model a predictive association with CRR* at W25 & W37, respectively. A logistic regression model and the Youden Index were used to generate Receiver Operating Characteristics (ROC) curves to help evaluate accuracy and identify optimal cut-off points to differentiate responders and non-responders. *Complete Renal Response: UPCR ≤0.5, eGFR ≥60 mL/min/1.73m^2 or no worsening of eGFR from baseline of ≥25%, prednisone (or equivalent) ≤10 mg and no use of prohibited medication.

Results: Of the 21 patients enrolled in MISSION, 17 reached EOT and EOS. CRR was achieved in 35% and 41% of patients at W25 and W37. Anti-inflammatory potential of zetomipzomib was demonstrated by reduction of uCD163, which was strongly correlated with UPCR improvement at W13, W25 and W37 (Figure 1). For the thirteen patients who consented to urine biomarker analysis, baseline 24-hour UPCR was: mean=2.8 mg/mg, median=1.8 mg/mg, SD=3.3, range 0.93-13.4; uCD163: mean=1.7 mg/mmol, median=0.97 mg/mmol, SD=2.3, range 0.28, 8.9. ROC analysis results from the MISSION study suggests that LN patients with uCD163 values of ≤0.13 at W13 and ≤0.09 at W25 are more likely to achieve a CRR at W25 and W37 following treatment with zetomipzomib (Table 1).

Conclusion: This post-hoc analysis of zetomipzomib data generated from the MISSION Ph2 study suggests that in patients with proliferative LN, uCD163 levels might predict CRR achieved up to 3 months later and could therefore potentially help to guide optimal therapy. Further evidence is needed from larger randomized LN trials with zetomipzomib to confirm the utility and limits of uCD163 as a predictive biomarker.

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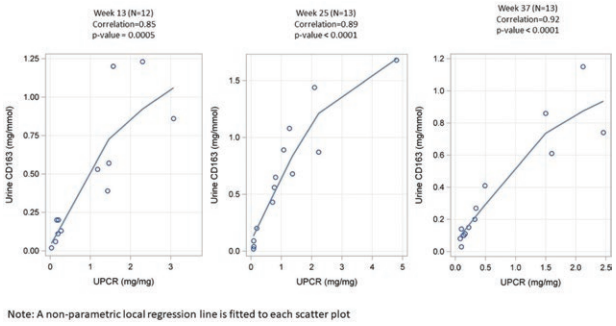


Figure 1. uCD163 and UPCR Correlation Plots

Table 1. Summary of ROC Analysis based on Logistic Regression Model

Predictor	Outcome	N used in ROC analysis	Youden Cutpoint	ROC AUC (max=1)	Sensitivity (0-1)	Specificity (0-1)	Predictive probability in CRR	Predictive probability in non-CRR
uCD163 at Week 13 (p=0.3615)	CRR at Week 25 (4 CRR)	12 (1 missing)	uCD163 =0.13	1.0	1.0	1.0	100%	100%
uCD163 at Week 25 (p=0.1218)	CRR at Week 37 (5 CRR)	13	uCD163 =0.09	0.8	0.6	1.0	100%	80%
			uCD163 =0.56*		0.8	0.75	67%	86%

*based on the criterion of smallest Δ=Sensitivity – Specificity.

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POS1144

EFFECTIVENESS OF BELIMUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS OF A MULTICENTER SPANISH COHORT

Keywords: Systemic lupus erythematosus, bDMARD, Real-world evidence

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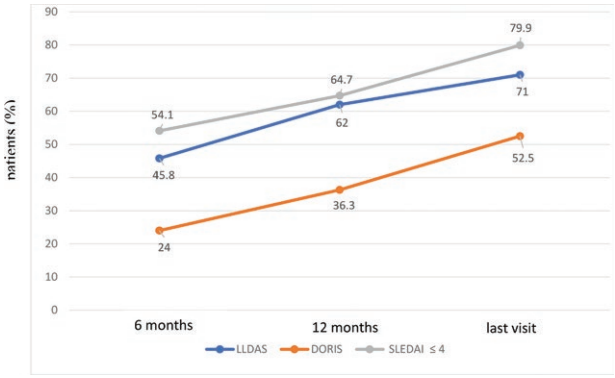
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Background: Belimumab (BLM) is a recombinant human IgG-1λ monoclonal antibody that inhibits B-cell activating factor. It is approved for the treatment of systemic lupus erythematosus (SLE). It is effective in reducing disease activity, flares, damage prevention and also as a steroid-sparing agent. A treat to target (T2T) approach in the care of SLE patients is important in terms of improving short and long-term outcomes.
Objectives: To evaluate belimumab (BLM) effectiveness in SLE patients from a Spanish multicenter registry.
Methods: A longitudinal retrospective multicenter cohort including SLE patients treated with belimumab from 18 Spanish rheumatology departments. Demographic, clinical and serological data were collected at baseline, 6, 12 and in the last visit available. Changes in SLEDAI-2K; LLDAS and DORIS 2021 states and global response according to physician criteria were compared between visits, as well as changes in damage and glucocorticoids used. T-test was used for numerical variables and the Fisher's test for categorical variables.
Results: 324 patients were included: 295 (91%) females with a mean (±SD) age of 42.4 (±12.9) years. Mean follow-up was 3,8 (±2.7) years and mean time with BLM was 2.7 (±2.4) years. At baseline, mean SLEDAI-2K was 10.4 (±5.25), 68.2% had elevated anti-double-stranded DNA (anti-dsDNA) antibodies and 69.8% had complement consumption. BLM was initiated concomitant to other DMARD in 67.9% (n=220) of patients. Mean reduction in SLEDAI-2K score was 5.0 (± 5.1), 6.1 (± 5.5) and 7.13 (± 5.3) points at 6, 12 months and in the last visit, respectively (p<0.05 for all comparisons). Rates of achievement of LLDAS, DORIS and clinical response according to physician criteria, significantly increased from baseline to 6, 12 months, and to the last visit (Table 1). Anti-dsDNA antibodies and inflammatory markers (ESR, CRP), significantly decreased from baseline to 6, 12 months and in the last visit. Complements increased over the follow up but without statistical significance. A total of 107 (45,9%) patients discontinued GC. At 6 months, 58.9% (n=155) of patients reduced the dose of GC with respect to baseline and 72.8% (n=131) of patients did it at the last visit. Mean (±SD) prednisone dose was significantly reduce over the visits: 12.3 (±12.16); 7.42 (±5.36); 5.8 (±4.42) and 4.7 (±3.7) mg/day at baseline, 6 and 12 months and in the last visit, respectively. Median (IQR) SDI score at the end of the observation period did not change from baseline visit: 0 (0-1) and 0 (0-1), respectively (p=0.97). Neither were changes observed in the percentage of patients with damage between the beginning and the end of the observation period: at baseline 47.5% (n=152) patients presented damage and, in the last visit, 45.6% (n=99).

Table 1. Clinical response and changes in GC dose.

Disease activity Mean (±SD) or number (%); n=324	Baseline	6 months	12 months	Last visit
SLEDAI reduction; mean (±SD)	10 (± 5.25)	5.0 (± 5.1) *	6.1 (± 5.5) *	7.13 (± 5.3) *
LLDAS	6 (1.9%)	137(45.8%) *	145 (62%) *	177 (73.1%) *
DORIS	6 (1.9%)	72 (24%) *	85 (36.3%) *	127 (52.5%) *
Response according to physician		212 (65.4%) *	185 (57.1%) *	165 (50.9%) *
Number of swollen joints; mean (±SD)	3.3 (±3.6)	1.2 (±2.8) *	0.69 (±1.95) *	0.55 (±1.82) *
Prednisone dose (mg/day); mean (±SD)	12.3 (± 12.16) *	7.4 (± 5,36) *	5.8 (± 4,42) *	4.75 (±3.74) *

SLEDAI: *Systemic Lupus Erythematosus Disease Activity Index*. cSLEDAI: clinical SLEDAI; LLDAS: *Lupus Low Disease Activity State*. DORIS: *Definition of remission in SLE*. *p<0.05



	6 months	12 months	Last visit
Discontinued	45	74	130
Ongoing	279	250	194

Figure 1. Rates of therapeutic targets attained by patients in treatment with Belimumab.

Conclusion: Real-world data of SLE patients confirm belimumab efficacy in real world, reducing clinical and serological activity in the short and medium-term. Add-on therapy with BLM leads to high rates of LLDAS and DORIS at 6 months, that continue increasing over time. BLM has an important GC sparing effect and prevents organ damage accrual. All these data shows that BLM is useful to achieve the therapeutic goals of a T2T strategy.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1145

FACTORS ASSOCIATED WITH SURVIVAL AND DISCONTINUATION OF ANTIMALARIAL AGENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM A SWEDISH LONGITUDINAL REGISTRY

Keywords: Disease-modifying drug (DMARDs), Systemic lupus erythematosus

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Background: Hydroxychloroquine (HCQ) and chloroquine, referred to as antimalarial agents (AMA), are cornerstone drugs in systemic lupus erythematosus (SLE), which inhibit type I interferon release via toll-like receptor binding and increasing the pH in plasmacytoid dendritic cell lysosomes [1]. AMA use has established benefits in SLE, such as improved prognosis and decelerated accrual of organ damage. Use of HCQ is safe for most patients and serious side-effects are uncommon, even during pregnancy. Medical therapy to prevent repeated disease flares is of essential weight in the treatment of SLE. However, it is well-known that non-adherence to prescription of AMA is a considerable problem [2].
Objectives: The aim of this cross-sectional study was to investigate the frequency of AMA prescription, and evaluate factors associated with ongoing use and discontinuation of AMA in a Swedish SLE population.
Methods: We retrieved data from the *Clinical Lupus Register in North-Eastern Gothia* (Swedish acronym: KLURING), a longitudinal research and quality registry, including all prevalent and incident cases of SLE in the Östergötland County from 2008 onwards. All included subjects fulfilled the validated 1982 American College of Rheumatology (ACR) and/or the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria and had been diagnosed from 1963 onwards. Factors associated with ongoing use and discontinuation of AMA were investigated using logistic regression analysis, Mann-Whitney U test and chi-square test.
Results: A total of 328 subjects were included in the analysis. The mean age at diagnosis was 40.0 years (range: 3–85; standard deviation [SD]: 17.7) and 85.7% were females. The mean SLICC/ACR damage index (SDI) score at last visit was 2.0 (range: 0—11; SD: 2.5). In total, 92.4% had used AMA at some point during their disease course ("ever" users; Table 1). Data from the last available visit indicated that 73.2% were currently prescribed AMA, exclusively HCQ, yielding a

daily mean HCQ dose of 228.0 mg (range: 100—400; SD: 71.0). Among individuals who had discontinued AMA, 25.9% had developed a contraindication, mostly on ophthalmological basis (33.3%). Less common reasons were cardiac conditions (19.0%) and renal failure (9.5%). Subjective side-effects were also common; the most frequently reported were gastrointestinal symptoms (n=20/37). Most common patient-related factor associated with discontinuation was intentional non-adherence (e.g., low motivation; 8/11). Patients who had discontinued AMA showed a higher SDI score at the last visit (mean: 2.9; SD: 2.8; mean follow-up: 20.0 years) compared with patients on AMA (mean: 1.4; SD: 1.8; p=0.001; mean follow-up: 15.3 years). Those who fulfilled the immunological disorder ACR criterion (ACR-10) were more likely to continue on AMA (p=0.003). No significant differences were found regarding gender or smoking status.

Table 1. AMA therapy

	N (%)
AMA, ever user	303 (92.4)
AMA, current use	222 (73.3)
AMA, discontinued user	81 (26.7)
Therapy related factors	58 (71.6)
Related to contraindication	21 (25.9)
Related to adverse events	37 (45.7)
Patient related factors	11 (13.6)
Unknown reason	12 (14.8)

Conclusion: The vast majority of patients in KLURING had been exposed to AMA, and approximately 25% discontinued AMA therapy during follow-up. The main reason for discontinuation were therapy-related factors, such as contraindications and experience of side-effects. Above 50% of the reported side-effects that led to discontinuation were gastrointestinal symptoms. The group of discontinued AMA users accrued more damage over time.

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POS1146 LOW MOLECULAR WEIGHT HEPARINS INTERFERE WITH NEUTROPHIL ACTIVATION AND NET GENERATION IN HIGH-RISK PREGNANT PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

Keywords: Cell biology, Pregnancy and reproduction, Innate immunity

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Background: Neutrophil activation and the generation of neutrophils extracellular traps (NETs) contribute to vascular damage and thrombosis in antiphospholipid syndrome (aPS). We reported that Low molecular weight heparin (LMWH) prevent neutrophil activation induced by P-selectin expressed by activated platelets [1, 2] and jeopardize in healthy subjects the ability of neutrophils to generate NETs and to mobilize granule contents [3].

Objectives: To investigate whether LMWH, used on empirical bases to in high-risk patients, regulate neutrophil/platelet interaction in pregnant women.

Methods: Here we report preliminary data from a prospective monocentric study in which the activation of platelets and neutrophils was assessed in sixteen pregnant women treated with LMWHs, with or without aPS at 12, 24 and 32 weeks of gestation. Patients were studied again when feasible after pregnancy completion. Sixteen healthy pregnant women, ten healthy women outside pregnancy and ten women with Systemic Lupus Erythematosus outside pregnancy served as controls.

Results: Platelets of pregnant healthy women were activated, as assessed by the increased expression of P-selectin and tissue factor. All patients successfully completed the pregnancy. Abnormalities were evident at the pathological assessment of the placentae despite the treatment with LMWHs. The treatment was associated with significantly reduced: i) platelet/neutrophil interaction, as assessed by heterotypic aggregates; ii) neutrophil expression of tissue factor; iii) platelet expression of the prototypic DAMP, HMGB1; iv) accumulation in the blood of byproducts of NET formation/catabolism, such as myeloperoxidase-DNA complexes. P-selectin expression was, in contrast, unaffected.

Conclusion: The results indicate that neutrophil and platelet activation/interaction, which may reflect detrimental intravascular immune events leading to pregnancy complications, abate in patients treated with LMWHs.

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POS1147 EFFICACY OF CENERIMOD IN PATIENTS WITH HIGH IFN-1 GENE EXPRESSION SIGNATURE AND HIGH ANTI-DSDNA ANTIBODY LEVELS: POST-HOC ANALYSIS FROM A PHASE 2 STUDY

Keywords: Clinical trials, Systemic lupus erythematosus

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Background: Cenerimod is an orally active, selective sphingosine 1-phosphate (S1P) 1 receptor modulator under investigation for the treatment of systemic lupus erythematosus (SLE). The Phase 2 CARE study (NCT03742037) did not meet its primary endpoint after adjustment for multiplicity, but patients treated with cenerimod 4 mg showed reduced disease activity versus placebo after 6 months.[1] Along with prior findings that type-1 interferon (IFN-1) activation is a robust biomarker of SLE disease activity and that an elevated IFN-1 signature associates with autoantibodies and more severe disease, cenerimod reduces plasma levels of IFN-α and leads to decreased circulating B and T cells in patients with SLE, suggesting effects on both innate and acquired immune responses.

Objectives: These post-hoc analyses evaluated the efficacy of cenerimod in subpopulations of patients with SLE.

Methods: CARE randomised 427 patients with SLE to once-daily cenerimod (0.5, 1, 2 or 4 mg) or placebo. At month (M) 6, patients receiving 4 mg cenerimod were re-randomised to placebo or cenerimod 2 mg for the subsequent 6 months, while all other groups continued their initially assigned treatment to M12. The primary endpoint was change from baseline to M6 in SLEDAI-2K score modified to exclude leukopenia (mSLEDAI-2K) due to the mechanism of action of cenerimod. Post-hoc analyses were performed in patients with high IFN-1 gene expression signature or anti-dsDNA levels ≥30 IU/mL. IFN-1 gene expression signature was based on the expression of four genes (*IFI27*, *RSAD2*, *HERC5*, *IFIT1*).

Results: Primary results from the CARE study were presented at ACR 2022.[1] The primary endpoint was not met (nominal P=0.0291 for cenerimod 4 mg vs placebo). At baseline, 207 patients (51%) in CARE had high IFN-1 gene expression signature, including 36 (45%) and 40 (50%) randomised to cenerimod 4 mg and placebo, respectively. Anti-dsDNA antibody levels ≥30 IU/mL were noted in 86 patients (20%), including 21 (25%) and 15 (17%) for cenerimod 4 mg and placebo, respectively. There was an association between high IFN-1 gene expression signature and high anti-dsDNA levels, with more than 75% of patients with anti-dsDNA levels ≥30 IU/mL having high IFN-1 gene expression signature. Reduction in mSLEDAI-2K from baseline to M6 for the cenerimod 4 mg group was greater in patients with high IFN-1 gene expression signature and high anti-dsDNA antibody levels versus the overall population (Figure 1A). Similarly, the proportion of SRI-4 responders at M6 was higher in patients with high versus low IFN-1 gene expression signature

(70% vs 41% for cenerimod 4 mg; 46% vs 43% for placebo). Patients with high IFN-1 gene expression signature treated with 4 mg cenerimod showed reduced IFN-α and anti-dsDNA levels at M6 versus baseline. At M6 resolution of alopecia was reported by more patients with high versus low IFN-1 gene expression signature (38% vs 26% for cenerimod 4 mg; 14% vs 7% for placebo), as were resolution of arthritis (57% vs 28% for cenerimod 4 mg; 38% vs 42% for placebo) and reduction in mucosal ulcers (80% vs 67% for cenerimod 4 mg; 41% vs 41% for placebo) on the mSLEDAI-2K. However, there was no treatment effect observed in rash.

Conclusion: Treatment with cenerimod 4 mg resulted in greater reductions of disease activity versus placebo at M6 in patients with high IFN-1 gene expression signature or high anti-dsDNA antibody levels at baseline. Cenerimod treatment also reduced levels of IFN-α protein and anti-dsDNA antibodies in these patients. Two Phase 3 studies of cenerimod 4 mg in SLE are underway.

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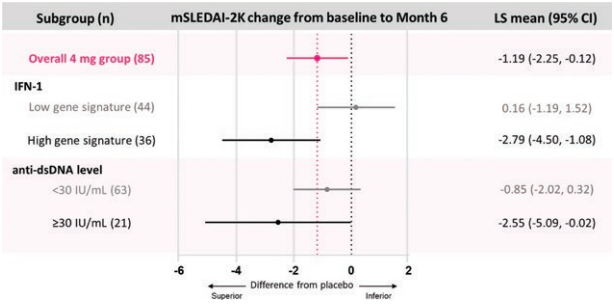


Figure 1. mSLEDAI-2K least-square mean (95% CI) change from baseline to Month 6 in the cenerimod 4 mg group.

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POS1148 OPTIMAL CUT-OFF POINT FOR ELECTROCARDIOGRAM IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ON HYDROXYCHLOROQUINE THERAPY

Keywords: Disease-modifying drug (DMARDs), Systemic lupus erythematosus

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Background: Hydroxychloroquine (HCQ) is a widely used drug in Systemic Lupus Erythematosus (SLE) that can cause cardiac alterations such as arrhythmic events in the short-term and dose-dependent cardiomyopathy in the medium to long-term. The cardiological implications of HCQ accumulation in these patients in the medium to long-term is unknown.

Objectives: To assess the optimal cut-off point for electrocardiogram (ECG) in patients with SLE on HCQ therapy to prevent arrhythmic complications.

Methods: Single university hospital observational study of all consecutive SLE patients who had an ECG at baseline and at least one ECG at follow-up. New conduction disturbances were assessed by ECG, defined as atrioventricular block, bundle branch block or QT interval prolongation. ECGs were extracted from the medical record and interpreted at baseline and for 15.2 years (95%CI 13.24-17.16) of follow-up. We defined cumulative HCQ (cHCQ) as the total grams of HCQ that had been administered. A Receiver Operating Characteristic (ROC) curve analysis was performed to determine the optimal cut-off point for sensitivity and specificity.

Results: We studied 105 (93 female/12 male) SLE patients with a mean (±SD) age of 61.8±14.9 years. The mean daily dose of HCQ in our sample was 256 mg per day (**Table 1**). The ROC curve showed a moderate diagnostic ability for new conduction disturbances with an area under the curve of 0.69 (95% CI 0.59 - 0.77) (**Figure 1**). The highest efficacy cut-off point was cHCQ: 4097g (Sensitivity 15%; Specificity 100%) and the optimal cut-off point was cHCQ: 901g (Sensitivity 85%; Specificity 52.9%). This cut-off point was reached with a mean HCQ treatment in our sample of 9.7 years. High grade atrio-ventricular block was found in 5 patients. In all of them the cHCQ dose was over 901g.

Conclusion: According to our study, 901g of cHCQ dose is a good cut-off point for performing a protocolized ECG to rule out cardiac conduction disturbances in patients with SLE and chronic HCQ treatment. This is equivalent to 9.7 years of treatment with the mean HCQ dose use in our sample.

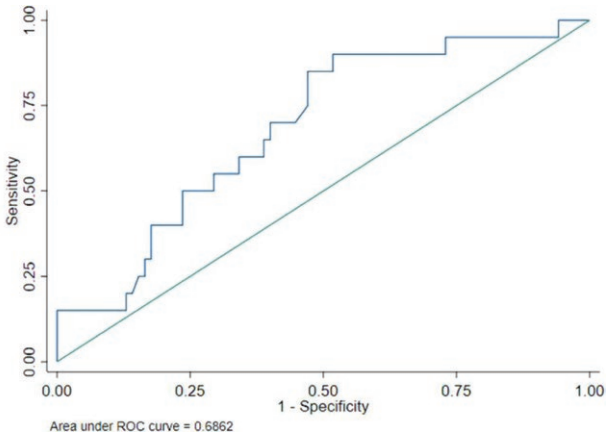


Figure 1. Receiver Operating Characteristic (ROC) curve on cumulative hydroxychloroquine dose and new conduction disturbances

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Disclosure of Interests: Alba Herrero-Morant: None declared, Jon Zubiaur-Zamacola: None declared, Adrián Margarida-de Castro: None declared, Raquel Pérez-Barquín: None declared, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Lilly, Bristol-Myers, Janssen, Galapagos and MSD, Consultant of: Abbvie, Pfizer, Roche, Lilly, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD, Novartis and Roche.

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Table 1. Clinical characteristics of Systemic Lupus Erythematosus patients

General characteristics	Global (N=105)
Current age (mean ± SD)	61.8 ± 14.9
Years of SLE evolution (mean ± SD)	16.3 ± 10.3
Sex, n (%)	93 (88.6)
Diabetes Mellitus, n (%)	15 (14.4)
Hypertension, n (%)	58 (55.2)
Dyslipidaemia, n (%)	47 (45.2)
Chronic renal failure, n (%)	10 (9.6)
Obesity, n (%)	8 (7.8)
Alcohol consumption, n (%)	3 (2.9)
Smoking history, n (%)	41 (39.0)
SLE treatment	
HCQ dose in mg/day (mean ± SD)	256 ± 87.2
Time in HCQ in months (mean ± SD)	149.8 ± 111.9
Cumulative HCQ dose in grams (mean ± SD)	1154.94 ± 946.10
Cumulative HCQ dose in grams, median (IQR)	913.1 (474, 1473)
Prednisone, n (%)	30 (28.6)
Prednisone dose in mg/day (mean ± SD)	17.3 ± 16.8
Other immunosuppressant, n (%)	14 (13.3)

Abbreviations: HCQ: Hydroxychloroquine, SLE: Systemic Lupus Erythematosus

POS1149

COMPARISON OF THE EFFICACY AND SAFETY OF TELITACICEPT VERSUS BELIMUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN REAL CLINICAL PRACTICE: ANALYSES WITH PROPENSITY SCORE-BASED INVERSE PROBABILITY OF TREATMENT WEIGHTING

Keywords: Treat to target, Real-world evidence, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a multi-system autoimmune disease characterized by aberrant expansion of B cells. The B cell-stimulating molecules, B cell activating factor/a proliferation-inducing ligand (BAFF/APRIL), are critical factors in promoting the proliferation and differentiation of B cells thus play a prominent role in the pathogenesis of SLE. There are two types of BAFF/APRIL-targeted biological agents being approved as an add-on therapy for patients with active SLE in China, including the BAFF/APRIL dual inhibitor, telitacicept and the BAFF inhibitor, belimumab. However, the differences of efficacy and safety between these two agents in real clinical practice has not been clarified.

Objectives: To compare the differences of efficacy and safety between the two types BAFF/APRIL inhibitors telitacicept and belimumab in the treatment of active patients with SLE.

Methods: Clinical features, laboratory data, SLE Disease Activity Index 2000 (SLEDAI-2K), treatment history, and adverse events (AEs) during the six months follow-up were collected. Propensity score based inverse probability of treatment weighting (IPTW) was used to reduce the selection bias.

Results: Active SLE patients who received telitacicept (N=52) and belimumab (N=77) from 2019 to 2022 at our rheumatology department were retrospectively reviewed. No significant differences were observed in patient characteristics between the two groups after adjustment by IPTW. Patients who received telitacicept have a significantly higher decrease of SLEDAI-2K score and Physician's Global Assessment (PGA) score at 24 weeks ($p<0.05$). Consistently, there was a higher elevation of complement (C) 3 and C4 levels at 4 and 12 weeks in telitacicept group ($p<0.05$). The telitacicept group acquire a higher frequency of primary efficacy renal response (PR) than belimumab at 12 weeks and no obvious differences were observed in complete renal response (CR) at 12 and 24 weeks according to the Belimumab International Lupus Nephritis Study (BLISS-LN) criteria. In addition, the improvement of anemia was better in the telitacicept group ($p<0.05$). Importantly, the telitacicept group had a lower incidence of AEs, including upper respiratory tract infections, diarrhea and leukopenia, than the belimumab group after IPTW ($p<0.05$).

Conclusion: Telitacicept showed a better efficacy and safety than belimumab for active SLE patients in a single center clinical practice. Further investigations in a larger cohort are required to testify these findings.

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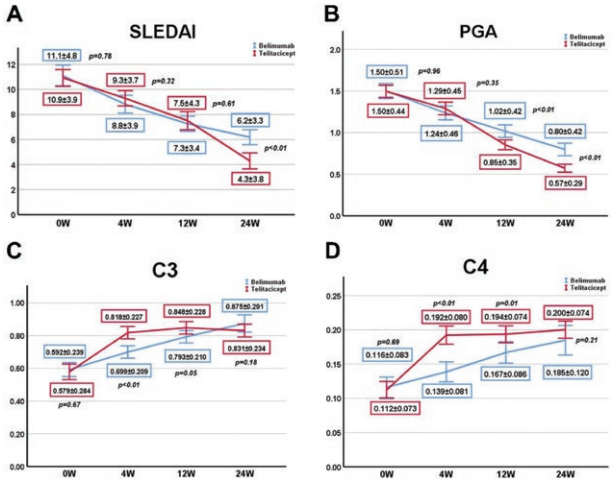


Figure 1. (A,B) The improvement of SLEDAI-2K and PGA scores after belimumab and telitacicept treatment at 4w, 12w, 24w by IPTW. (C,D)The elevation of complement (C) 3 and C4 levels after belimumab and telitacicept treatment at 4w, 12w, 24w by IPTW

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POS1150

ULTRASOUND-DETECTED EROSIONS COULD PREDICT THE EFFICACY OF BELIMUMAB IN ARTICULAR SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: bDMARD, Systemic lupus erythematosus, Ultrasound

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Background: Articular involvement (69-95%) in patients with systemic lupus erythematosus (SLE) is traditionally considered non-erosive. SLE arthritis with radiographic erosions with or without rheumatoid factor (RF) and/or anti-citrullinated peptide antibody (ACPA) positivity is often described as "rhupus" and is considered an overlap between SLE and rheumatoid arthritis (RA). While radiographic erosions are shown in about 5-15% of the patients, ultrasound and magnetic resonance imaging could reveal erosions in up to 40% of patients with SLE.

Objectives: The aim of this study is to assess if the presence of ultrasound-detected erosions can predict the efficacy of belimumab, a B lymphocyte simulator (BlyS) inhibitor, in the treatment of SLE-related articular manifestations.

Methods: We performed a spontaneous, monocentric, retrospective, and observational study. We enrolled patients with a diagnosis of SLE according with the 2019 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria with articular involvement treated with belimumab. Patients with ACPA- or RF-positivity, Jaccoud's arthropathy, or radiographic erosions were excluded. We collected laboratory and clinical data from the electronic records. Joint disease activity was assessed at baseline, 3- and 6-months follow-ups (FU) using disease activity score on 28 joints based on C-reactive protein (DAS28-CRP). At baseline, all patients underwent an ultrasound examination of the wrist, metacarpophalangeal, proximal interphalangeal, and metatarsal-phalangeal joints. Erosions were defined according with the outcome measures in rheumatology (OMERACT) definition (at least 1 mm). Student's T-test and Mann-Whitney's U-test were used to assess differences between means and Fisher's exact test to assess differences between proportions.

Results: We enrolled 23 patients (baseline characteristics in Table 1). Seven patients (30.4%) had bone erosions at baseline. They were generally older (61±16.1 vs 46.13±10.7 years, p=0.016), more frequently male (42.8 vs 6.2%, p=0.03), with higher CRP levels (10.29±11.6 vs 2.25±3.1 mg/L, p=0.015), and higher C4 (0.19±0.17 vs 0.1±0.04 g/L, p=0.05) than patients without erosions. DAS28-CRP decreased significantly at 6-months FU (2.95±0.89 vs 2.26±0.48, p=0.01) only in patients without erosions, as shown in Figure 1. The majority of patients (73.9%) achieved remission at 6-months FU (DAS28-CRP criteria), with a significant difference between patients with and without erosions (42.8 vs 87.5%, p=0.045).

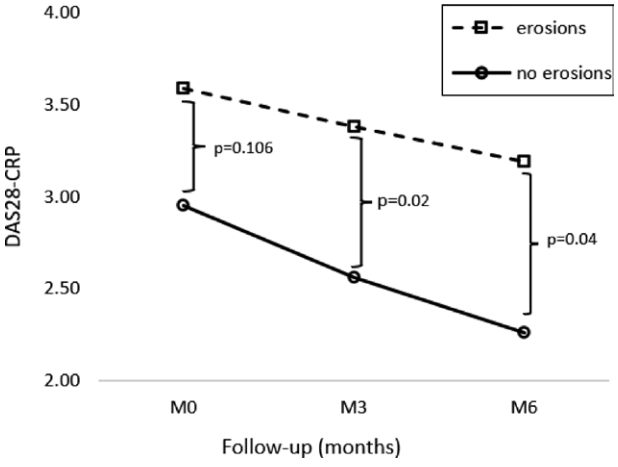


Figure 1. Mean DAS28-CRP levels at baseline and 3- and 6-months FU in patients with and without erosions Legend: DAS28-CRP = Disease Activity Score 28 joints count based on C-reactive protein, FU=follow-up

Table 1. Clinical, laboratoristic, and therapeutic characteristics of the cohort at baseline

Age (years), mean ± SD	50.65 ± 14.1
Female, n (%)	19 (82.6)
Disease duration (years), mean ± SD	12.74 ± 9.7
Smokers, n (%)	6 (26.1)
CRP (mg/L), mean ± SD	4.7 ± 7.6
Concomitant HCQ, n (%)	20 (87)
Glucocorticoid (PDN mg/day), mean ± SD	10.54 ± 10.5
Articular bone erosions, n (%)	7 (30.4)
Number of joints with erosions, mean ± SD	1.04 ± 2
Tender joints, mean ± SD	3.2 ± 2.4
Swollen joints, mean ± SD	1.04 ± 1.5
PGA, mean ± SD	9.2 ±.4
DAS28-CRP, mean ± SD	3.14 ± 0.9
SLEDAI-2K, mean ± SD	6.7 ± 2.8
Clinical SLEDAI-2K, mean ± SD	2.83 ± 2.5
SDI, mean ± SD	1.17 ± 1.3

Conclusion: The presence of ultrasound-detected erosions could be predictive of a decreased efficacy of belimumab in articular SLE. A possible explanation is a rheumatoid-like articular phenotype, despite the lack of ACPA-positivity and radiologic erosions. Our findings could help expand the "rhupus" spectrum and highlight the possible role of different SLE phenotypes in the therapeutic response.

REFERENCES: NIL.

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POS1151

THERAPEUTIC DRUG MONITORING OF AZATHIOPRINE AND TACROLIMUS IN SLE PREGNANCIES: PRELIMINARY RESULTS FROM THE LEGACY COHORT

Keywords: Disease-modifying drug (DMARDs), Pregnancy and reproduction, Systemic lupus erythematosus

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Background: Pregnant SLE women still face an unacceptably high risk of maternal and fetal morbidity, particularly when their disease is active. How to personalize SLE therapies to optimize pregnancy outcomes remains unknown. Though guidelines strongly recommend azathioprine (AZA) and tacrolimus (TAC) in specific SLE pregnancy scenarios, evidence to guide drug monitoring in this context is non-existent.

Objectives: In the prospective "Lupus prEGnAnCY (LEGACY)" cohort we evaluated AZA and TAC levels at the first pregnancy (baseline) visit.

Methods: LEGACY is a prospective cohort enrolling unselected SLE pregnancies ≤16 6/7 gestational weeks at 7 Systemic Lupus International Collaborating Clinics. We record demographics, disease activity, and drugs. In addition, whole blood samples are collected at baseline to determine AZA metabolites (e.g., erythrocyte-free 6-thioguanine, 6-TG) and trough TAC levels if applicable. The present study included Montreal LEGACY participants prescribed either AZA or TAC ≥3 months prior to their first pregnancy visit. We characterized AZA metabolite and TAC levels as continuous and categorical variables (i.e., non-adherent, sub-therapeutic, therapeutic, and supra-therapeutic, using established cut-offs in non-pregnant populations). We defined patients as non-adherent if they had undetectable or barely detectable levels despite appropriate dosing.

Results: Of 64 LEGACY pregnancies enrolled in Montreal, 23 (36%) and 6 (9%) were prescribed AZA and TAC, respectively. Among those prescribed AZA, only 9% had therapeutic levels, while 91% were sub-therapeutic or non-adherent. Compared to those with therapeutic levels, pregnancies with sub-therapeutic or non-adherent AZA levels were more likely to occur in women of non-Caucasian ethnicity/race, on steroids, with longer SLE duration, and with prior lupus nephritis (Table 1). Among those prescribed TAC, 50% (3/6) had therapeutic levels, while 33% (2/6) and 17% (1/6) were sub-therapeutic and supra-therapeutic, respectively. No patient on TAC were identified as non-adherent. Less than half (43%) of pregnancies non-adherent to AZA were in Lupus Low Disease Activity State (LLDAS) at baseline as opposed to 71% of those with higher AZA levels (i.e., sub-therapeutic or therapeutic). Of the pregnancies with sub-therapeutic TAC levels, 50% (1/2) were not in LLDAS, while all (4/4) pregnancies with therapeutic or supra-therapeutic TAC levels were in LLDAS at baseline.

Conclusion: We observed that most SLE pregnancies prescribed AZA had sub-therapeutic levels, with nearly a third identified as non-adherent. Pregnancies with lower AZA and TAC levels may be less likely to achieve LLDAS. Despite low numbers, our preliminary results suggest the value of personalized drug monitoring as a novel approach to precision medicine in pregnant SLE women, that might improve efficacy, safety, and adherence in a high-risk population.

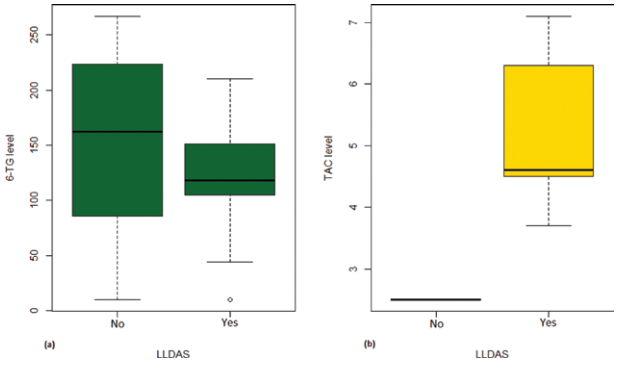


Figure 1. Boxplot of 6-TG levels [pmol/8×10^8 RBC] (a) and TAC trough levels [ng/ml] (b) according to LLDAS.

Table 1. Characteristics of pregnant women with SLE at baseline visit stratified according to AZA metabolites and TAC trough levels.

		AZA (n=23)				TAC (n=6)			
		Non-adherent	Sub-therapeutic	Therapeutic	Supra-therapeutic	Non-adherent	Sub-therapeutic	Therapeutic	Supra-therapeutic
Pregnancies, n (%)		7 (30)	14 (61)	2 (9)	-	-	2 (33)	3 (50)	1 (17)
AZA dose in mg/kg, mean ± sd		2.5 ± 0.5	1.9 ± 0.5	2.0 ± 0.2	-	-	-	-	-
TAC dose in mg/kg, mean ± sd		-	-	-	-	-	0.04 ± 0.02	0.04 ± 0.02	0.03 ± 0
Age in years, mean ± sd		34.0 ± 4.1	33.8 ± 3.9	29.0 ± 0.7	-	-	30.3 ± 3.3	31.3 ± 4.1	32.4 ± 0
Race/ Ethnicity, n (%)	Caucasian	1 (14)	4 (29)	2 (100)	-	-	2 (100)	2 (67)	1 (100)
	Hispanic	-	-	-	-	-	-	1 (33)	-
	Black	2 (29)	3 (21)	-	-	-	-	-	-
	Asian	2 (29)	5 (36)	-	-	-	-	-	-
	Arabic	1 (14)	-	-	-	-	-	-	-
Education in years, mean ± sd		15.7 ± 3.5	16.7 ± 3.1	17.0 ± 1.4	-	-	19.0 ± 1.4	14.3 ± 1.5	16.0 ± 0
Disease duration in years, mean ± sd		10.3 ± 6.5	10 ± 6.9	5.3 ± 0.7	-	-	9.3 ± 0	4.2 ± 1.1	3.8 ± 0
LLDAS, n (%)		3 (43)	10 (71)	-	-	-	1 (50)	3 (100)	1 (100)
Prior or current lupus nephritis, n (%)		5 (71)	5 (36)	-	-	-	2 (100)	1 (33)	-
Steroid use, n (%)		2 (29)	1 (7)	-	-	-	-	-	-

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POS1152 ATTAINMENT OF EULAR/ERA-EDTA TREATMENT TARGETS IN THE FIRST YEAR IN LUPUS NEPHRITIS: A MULTICENTER OBSERVATIONAL STUDY

Keywords: Systemic lupus erythematosus, Kidneys, Treat to target

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Background: The approval of two new drugs, belimumab and voclosporin, in lupus nephritis (LN) over the last years has raised questions regarding their place in the therapeutic algorithm of LN. Their use in initial regimens or in refractory/relapsed disease depends on disease outcomes with current standard of care (SoC) therapies.

Objectives: To calculate EULAR/ERA-EDTA renal response rates with SoC therapies at 3, 6 and 12 months, as well as rates of successful tapering to the recommended glucocorticoid use at 6 months in real-life clinical settings.

Methods: Combined retrospective and prospective (2015-today) cohort study of patients with histologically confirmed LN. Demographic, clinical, and laboratory data, as well as treatment administered at baseline and respective changes every 3 months, were collected. Renal response rates according to EULAR/ERA-EDTA goals of treatment were calculated: (at 3 months: proteinuria reduction by 25%, 6 months: 50% reduction to subnephrotic level, 12 months: proteinuria< 500-700mg/24h, all with stabilization or improvement in kidney function). The percentage of patients who received IV methylprednisolone (total recommended dose 500-2500mg), as well as mean prednisone dose per day at baseline (recommended dose 0.3-0.5mg/kg in class III and class IV and 20mg in class V) and thereafter (<7.5mg/day at 6 months in class III and class IV and <5mg/day at 3 months in class V). We also calculated the percentage of patients who had tapered prednisone to the recommended daily dose by 6 months.

Results: 110 patients were included, 83 completed a 12month follow up [81.8% female, median (IQR) age 36.5 (23) years]. One third (33.6%) of patients had nephrotic range proteinuria at diagnosis. Histologically, 16.7% had LN class III, 33.3% class IV, 18.5% class V and 27.8% mixed class (III/IV +V). With SoC therapy [initial therapy: 48.1% cyclophosphamide (CYC), 32.4% mycophenolic acid (MPA), followed by maintenance therapy], 76.7%, 82.6% and 71.1% achieved EULAR/ERA-EDTA renal response rates at 3, 6 and 12 months, respectively. No differences between CYC and MPA groups regarding response rates were noted. All patients received IV methylprednisolone at baseline [median (IQR) 2.0 (3.0) gr].

Regarding glucocorticoid use, in proliferative classes (III/IV), median (IQR) prednisone starting dose was 40.0 (20.0) mg/day, corresponding to a mean (SD) dose of 0.63 (0.27) mg/kg/day. At 6 months, median (IQR) daily dose was 10.0 (10.0) mg. In class V LN, median (IQR) daily starting dose was 32.5 (20.0) mg and 15.0 (10.0) mg at 3 months.

Conclusion: Although a significant number of LN patients achieve treatment target between 3-12 months, approximately 25-30% fail. Moreover, prednisone doses used in LN tend to be higher than those recommended by EULAR/ERA-EDTA. Predictive factors associated with suboptimal response can help to shape therapeutic decisions identify patients that may benefit from early use of novel therapies.

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POS1153 APPLYING THE WORKING DEFINITION OF THE DISEASE MODIFICATION CRITERIA TO SYSTEMIC LUPUS ERYTHEMATOSUS TREATMENTS FROM THE PUBLISHED LITERATURE

Keywords: Organ damage, Kidneys, Outcome measures

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Background: In our recently published working definition, we proposed that disease modification in systemic lupus erythematosus (SLE) requires 'minimising disease activity with the fewest treatment-associated toxicities and slowing or preventing organ damage progression'.[1]

Objectives: To apply the proposed non-renal disease modification criteria to SLE treatments.

Methods: Based on a review of a selection of clinical trial (n=31) and observational (n=42) data publications for 16 SLE medications across different treatment classes and, the authors' clinical experience, we evaluated their disease modification potential per the non-renal disease activity and organ damage criteria at three time points (**Table 1**).[1]

Results: Nine of the 16 SLE treatments met at least one disease modification criterion across all time points (**Table 1**). Hydroxychloroquine improved overall survival at >5 years, suggesting long-term disease modification, but with data per specific criteria lacking.[2] Belimumab met two of the three disease modification criteria at the first two time points, but was the only treatment to meet criteria at >5 years based on the current literature. While steroids unambiguously decrease disease activity at early timepoints, at doses higher than 7.5 mg/day the negative impact on damage accrual might hamper their disease modification potential >5 years.

Conclusion: This is the first attempt to determine which of the currently used treatments in patients with SLE fulfil the disease modification criteria at different time points. Belimumab and hydroxychloroquine showed evidence of disease modification up to and beyond 5 years; evidence for many other SLE therapies was incomplete, particularly at >5 years of follow up. The use of multiple agents, differences in study designs, patient populations, and definitions of treatment response pose challenges in categorising treatments as disease modifiers. Future studies will evaluate the minimum number of criteria required to designate disease modification at each of the three time points so that disease modification can be considered in the care of patients with SLE and in SLE trial design.

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Table 1. Application of the proposed matrix for non-renal immunoinflammatory and organ damage disease modification criteria

Product	DISEASE MODIFICATION POTENTIAL		DISEASE MODIFICATION CONFIRMED (BEYOND 5 YEARS)
	Outcomes Year 1	Outcomes Years 2–5	Outcomes Year >5
	❶ Significant reduction in disease activity measured using a validated tool (i.e., SELENA-SLEDAI, BILAG, SRI-4) ❷ Significant reduction in severe flare measured using a validated tool (i.e., SFI or BILAG) ❸ Reduction in use of steroids* and/or immunosuppressants	❶ Sustained improvement in multiple organ domains/no worsening in multiple organ domains ❷ Prevention of severe flares ❸ Continued reduction in use of steroids*and/or immunosuppressants	No change in SDI or delayed progression
Glucocorticoids	1 2 3	1† 2† 3	● †
Hydroxychloroquine	1 2 3	1 2 3	⊕
Azathioprine	1 2 3	1 2 3	●
Cyclophosphamide	1 2 3	1 2 3	●
Methotrexate	1 2 3	1 2 3	●
Mizoribine	1 2 3	1 2 3	●
Leflunomide	1 2 3	1 2 3	●
Mycophenolate mofetil	1 2 3	1 2 3	●
Cyclosporine	1 2 3	1 2 3	●
Tacrolimus	1 2 3	1 2 3	●
Voclosporin	1 2 3	1 2 3	●
Belimumab	1 2 3	1 2 3	●
Rituximab	1 2 3	1 2 3	●
Abatacept	1 2 3	1 2 3	●
Anifrolumab	1 2 3	1 2 3	●

●, criterion met; ⊕, insufficient evidence in the literature to meet the specific criterion, but strong general indications of met criterion; ●, inconclusive; ●, data not available in the literature

*≤7.5 mg/day per 2019 EULAR SLE treatment guidelines and LLDAS; ≤5 mg/day per DORIS remission definition

†Data were available in the literature but the criterion was not met

BILAG, British Isles Lupus Assessment Group; DORIS, definition of remission in SLE; LLDAS, Lupus Low Disease Activity State; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Disease Index; SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment - SLE Disease Activity Index; SFI, SELENA-SLEDAI flare index; SRI-4, SLE Responder Index-4

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POS1154

PRE-TREATMENT DIFFERENTIALLY EXPRESSED METAGENES CHARACTERIZE SYSTEMIC LUPUS PATIENTS WHO SUBSEQUENTLY ACHIEVE CLINICAL RESPONSE TO BELIMUMAB

Keywords: Clinical trials, -omics, Systemic lupus erythematosus

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Background: Belimumab, which targets the B Cell activator and survival factor BLyS, is an approved treatment for systemic lupus (SLE) and has demonstrated efficacy in multiple clinical trials around the world. Nevertheless, like other SLE treatments, belimumab can have disappointing results in a significant proportion of this heterogenous population, a problem further complicated by the unpredictable impact of various combination treatments used with belimumab in trials and clinical practice.

Objectives: Examination of gene expression variables in SLE patients prior to belimumab treatment with limited background medications in order to distinguish those who subsequently respond from those who do not.

Methods: A prospective open-label study of belimumab was conducted in 24 SLE patients with active but non-organ threatening disease, who were required to withdraw other immune suppressants (only antimalarials or low dose steroids allowed). At baseline, patients were given optional steroid injections for temporary relief, then followed for six months on intravenous belimumab (10 mg/kg). The primary endpoint was time to treatment failure compared to historical controls from the BOLD study which followed the same protocol but without treatment after initial steroids[1]. Response was also evaluated at six months by the SLE Responder Index (SRI-4) or the BILAG-based Combined Lupus Assessment (BICLA). Before and during treatment, Pax Gene tubes were collected, and RNA sequenced, using the same methods for healthy control samples. To maximally discriminate clinical responders from non-responders by baseline gene expression patterns in a small, heterogenous population, principal component analysis was conducted with modules (metagenes) comprised of differentially expressed genes (DEGs).

Results: Of 24 patients entering the study, 20 completed 6 months of treatment. The mean survival time without flare, treatment change, or study withdrawal was 18.4 weeks (CI 15.3-21.5) compared to the 41 BOLD participants with mean survival 9.829 weeks (CI 0.999-7.871) ($p<0.001$ by log rank test). At 6 months, 14 patients who received belimumab (58%) and 1 from the BOLD study (2.4%) remained free of flare. The SRI-4 was met by 7 patients in this study (29.2%), the BICLA by 9 (37.5%). SRI-4 response was used as the basis for modeling two metagenes comprised of the 25 most upregulated and 25 most downregulated genes at baseline in belimumab responders as compared to non-responders. There was no overlap between metagene scores of responders' vs non-responders (Figure 1). After 3 months of treatment with belimumab all metagene scores corrected towards levels in healthy controls. The most discriminatory DEGs included protein transcription factors and long non-coding RNA (transcription regulators).

Conclusion: When background immune suppressants are excluded, belimumab still achieves SRI 4 or BICLA response for some patients, and most do not flare for at least six months. A composite metagene model has been identified as a potential predictor of belimumab response. Confirmation studies should be prospectively conducted.

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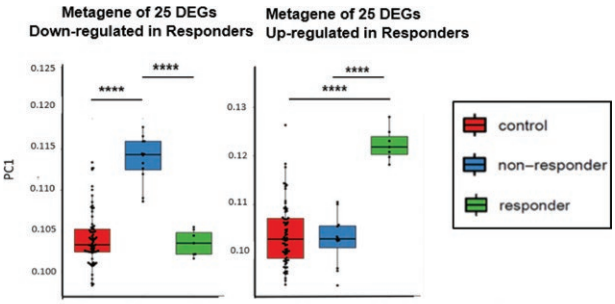


Figure: No overlap between pre-treatment metagene module scores in SLE patients who do or do not respond to belimumab

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POS1155

IMPACT OF HYDROXYCHLOROQUINE ON INTERFERON PATHWAY EXPRESSION OF SLE PHENOTYPIC SUBSETS IN THE ABSENCE OF BACKGROUND MEDICATIONS

Keywords: -omics, Systemic lupus erythematosus, Biomarkers

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Background: Chronic activation of interferon (IFN) pathways is a key driver of immune dysregulation in SLE. Hydroxychloroquine (HCQ) inhibits toll-like receptors 7 and 9 in plasmacytoid dendritic cells resulting in decreased release of interferon alpha[1]. Studies in SLE are limited by patient heterogeneity and the superimposed complexity of combined medications they receive.
Objectives: This project compared activation of Type I and II interferon (IFN) pathways in SLE patients with discrete immune phenotypes who were taking hydroxychloroquine or not (HCQ vs No Rx) without corticosteroids or any other SLE treatments.
Methods: 133 samples from 85 SLE patients (70 on HCQ, 63 on No Rx) and 37 healthy controls were studied. Characteristic clusters of patients who shared immune activation patterns were identified by Random Forest modeling of soluble mediators and gene co-expression module scores, as previously reported[2,3]. Samples from four of these immunologic clusters (C1, C4, C3, and C6), all with elevated expression of IFN modules (M1.2, M3.4, and M5.12) were examined for impact of HCQ on IFN pathway expression and compared to clusters with lower interferon signals. Dual samples from each of 21 patients when on HCQ vs on No Rx at different timepoints were also examined.
Results: As expected, expression of IFN pathway modules were increased in the overall SLE population vs healthy controls, driven by patient phenotype clusters 1,3,4 and 6. All IFN modules were decreased in SLE patients on HCQ vs. no Rx (M1.2 p=0.035, M3.4 p=0.009, and M5.12 p=0.005), again promulgated by changes in clusters 1,3,4 and 6 (Figure 1). In multilinear regression modeling, HCQ had independent effects on M1.2 (p=0.004), M4.3 ($p < 0.001$), and M5.12 ($p < 0.001$) after adjusting for cluster and race. Age and SLEDAI score had no confounding effects. Of the 21 patients with samples on HCQ vs No Rx, IFN scores were lower when on HCQ by Wilcoxon matched pairs signed rank test with Holm-Sidak correction (M1.2 p=0.0125, M3.4 p=0.0125, M5.12 p=0.0048).
Conclusion: This study confirms previous reports that hydroxychloroquine dampens interferon pathways in SLE patients, while addressing potentially confounding effects of polypharmacy and differing immune activation patterns in these patients. Limitations include inability to include more ill patients who inevitably require more complex treatment regimens and not having HCQ levels to improve data interpretability. These findings support the feasibility of strategies to improve patient selection for HCQ, optimize its dosing, and more rationally select combination treatments.

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Table 1. Characteristics of the SLE Population

	All Samples	Cluster 4	Cluster 1	Cluster 3	Cluster 6	Cluster 2,5,7
Number of Samples	133	2	21	29	30	51
Age (SD)	45.95 (12.30)	53.00 (4.243)	43.43 (12.00)	46.31 (11.43)	47.57 (16.80)	45.57 (9.892)
Race						
% Caucasian	53.33	66.67	53.85	33.33	51.28	62.90
% African	15.56	0	3.85	30.56	23.08	9.68
% Native American	14.07	0	23.08	16.67	10.26	12.90
% Asian	2.22	0	3.85	11.11	0	0
Ethnicity						
% Hispanic	14.81	33.33	15.38	8.33	15.38	14.52
% on HCQ	52.63	0	47.62	58.62	46.67	56.86
SLEDAI Score (SD)	3.99 (3.43)	6.00 (2.83)	2.86 (2.24)	4.35 (3.82)	4.70 (3.84)	3.77 (3.31)
M 1.2 (SD)	0.02495 (0.00374)	0.02866 (0.00365)	0.02651 (0.00383)	0.02539 (0.00311)	0.02834 (0.00213)	0.02190 (0.00216)
M 3.4 (SD)	0.02547 (0.00170)	0.02827 (0.00125)	0.02629 (0.00185)	0.02537 (0.00142)	0.02694 (0.00101)	0.02423 (0.00099)
M 5.12 (SD)	0.02554 (0.00096)	0.02765 (0.00069)	0.02626 (0.00101)	0.2518 (0.00077)	0.02631 (0.00055)	0.02491 (0.00057)

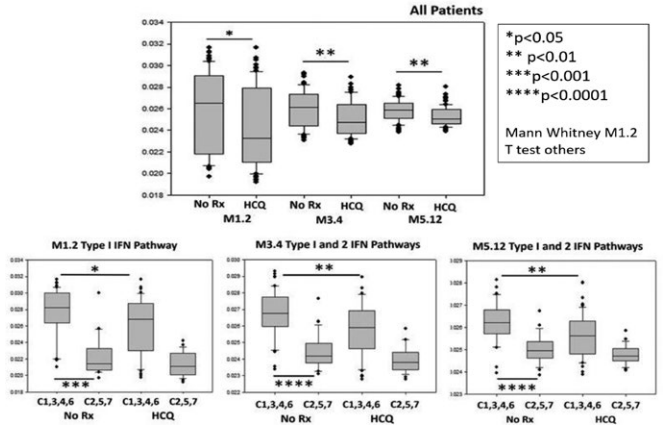


Figure 1. Expression of interferon modules M1.2, M3.4, and M5.12 in all patients (top row) and in subsets (bottom row) grouped by greater expression of IFN pathways (Clusters 1,3, 4,6) vs lower expression (Clusters 2,5,7)

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Disclosure of Interests: None Declared.
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POS1156

PREDICTORS OF DE NOVO RENAL FLARES IN SYSTEMIC LUPUS ERYTHEMATOSUS – TIME TO REVISIT BELIMUMAB DOSE FOR EXTRA-RENAL DISEASE? RESULTS FROM FIVE PHASE III CLINICAL TRIALS OF BELIMUMAB

Keywords: Clinical trials, Kidneys, Systemic lupus erythematosus

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Background: Each lupus nephritis (LN) flare causes nephron loss that equals a decade or more of reduction in renal function lifespan, making prompt initiation of therapy imperative and prevention of flares even more desirable. Identification of readily available signals of imminent flare is therefore expected to improve prognosis.
Objectives: In light of observed cases of *de novo* LN during belimumab treatment (1), we evaluated predictors of *de novo* renal flare occurrence in patients with systemic lupus erythematosus (SLE) and no prior history of renal disease undergoing standard therapy (ST) with or without add-on belimumab in clinical trial settings.
Methods: Data from five clinical trials of belimumab in SLE (BLISS-52 NCT00424476; BLISS-76 NCT00410384; BLISS-NEA NCT01345253; BLISS-SC NCT01484496; EMBRACE NCT01632241) were utilised. The study population comprised 1932 patients with a baseline renal British Isles Lupus Assessment Group (BILAG) score E. *De novo* renal flares were defined as a change from renal BILAG E to A or B within a 52-week follow-up. Comparisons of baseline data were made using the Mann-Whitney *U* test, Pearson's chi-squared (χ^2) test or Fisher's exact test as appropriate. Predictors of renal flare occurrence were investigated using univariable and multivariable Cox regression analysis. *p* values <0.05 were considered statistically significant.
Results: *De novo* renal flares were documented in 146 (7.6%) patients. Among patients who developed at least one renal flare, greater proportions were Asians (30.8% versus 20.2%; $p<0.003$), had positive baseline anti-dsDNA levels (74.0% versus 61.3%; $p=0.003$), and had low baseline levels of C3 (51.4% versus 38.2%; $p=0.002$) and C4 (45.2% versus 35.8%; $p=0.030$) compared with patients who did not flare. In univariable Cox regression analysis, azathioprine use was protective against renal flares (HR: 0.70; 95% CI: 0.49–0.99; $p=0.047$), while anti-Sm positivity at baseline showed a trend towards an association with imminent renal flare (HR: 1.68; 95% CI: 0.99–2.85; $p=0.057$). In multivariable Cox regression analysis adjusting for age, sex, ethnicity, serum creatinine, and variables that differed significantly in univariable analysis, Asian ancestry (HR: 1.60; 95% CI: 1.03–2.49; $p=0.036$), high mean prednisone dose from baseline until renal flare occurrence or throughout the follow-up (HR: 1.03; 95% CI: 1.02–1.05; $p<0.001$), and baseline serum creatinine (HR: 1.02; 95% CI: 1.01–1.03; $p=0.001$) were associated with imminent *de novo* renal flare, while extra-renal clinical SLE Disease Activity Index 2000 (cSLEDAI) showed a negative association (HR: 0.92; 95% CI: 0.86–0.98; $p=0.007$). Notably, use of belimumab 1 mg/kg by intravenous (IV) infusion yielded a nearly 3 times decreased hazard of renal flare (HR: 0.37; 95% CI: 0.20–0.68; $p=0.001$), whereas IV belimumab 10 mg/kg and belimumab 200 mg administered subcutaneously (SC) displayed no clear protection.
Conclusion: Asian patients appeared particularly susceptible to new-onset renal involvement, corroborating the substantial vulnerability of Asian SLE populations to renal affliction. Add-on low-dose IV belimumab on top of ST appeared protective against renal flares in SLE patients with no prior history of nephritis, while addition of the approved 10 mg/kg IV belimumab dose and SC belimumab yielded no clear protection. Discrepant results between low and high/approved belimumab doses warrant in-depth mechanistic exploration of underlying reasons e.g., potential effects of belimumab on B cell subsets that acquire regulatory properties.
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POS1157 WARFARIN VS DOACS IN A REAL-WORLD DATA

Keywords: Real-world evidence, Anti-phospholipid syndrome

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Background: Antiphospholipid syndrome (APS) is a syndrome which consists of vascular thrombotic events, arterial or venous, with the presence of persistent circulating antibodies. APS patients have a highly variable risk profile, derived from their different medical risk factors and diverse antiphospholipid antibodies (aPL) profile. The current mainstay for the treatment of APS is anticoagulation with Vitamin K antagonists (VKAs). The primacy of Warfarin has been challenged by the introduction of direct oral anticoagulants (DOACs), stems from DOACs convenience, constant dosing, without the need for blood test monitoring and almost no drug interactions. However, the TRAPS study that compared Rivaroxaban to Warfarin treatment in APS patients was terminated prematurely due to higher incidence of thrombotic events in the Rivaroxaban group [1]. Yet, all patients on the TRAPS trial were triple-aPL positive. Similar conclusions were demonstrated on the ASTRO study that compared Apixaban to Warfarin treatment [2]. Because the risk profile of APS patients is heterogeneous, both clinically and serologically, it is difficult to conclude that treatment with DOACs is generally inferior to VKAs for all APS patients, for instance in the low-risk patient population.
Objectives: We assume that under real-life circumstances, VKAs narrow therapeutic range and the constant need for repeated INR checkups may change the above studies outcomes. Hereby, the aim of this study is to compare real-life outcomes of APS patients treated with DOACs to patients treated with Warfarin from the aspect of thrombotic events reoccurrence on one hand and bleeding events on the other hand. We also checked the outcomes specifically for different APS risk profile subgroups under different treatments with either Warfarin or DOACs.
Methods: 139 non obstetric APS patients from "Meir" medical center were followed up retrospectively for a mean period of 16 years, since diagnosis time until 31/12/2022. We gathered data on patients SLE status, aPL profile and type of thrombotic event at the time of diagnosis. We checked for thrombotic events reoccurrence and bleeding events (including their types) with respect to the specific treatment at the time of each event.
Results: Of 139 followed-up patients, we report a total of 217 thrombotic and 60 bleeding events. From the Warfarin treated group, 178 (82%) thrombotic events were recorded, 130 (74%) of them occurred in the high risk serological profile patients. From the DOACs treated group, 39 (18%) thrombotic event were recorded, 23 (59%) of them occurred in the high risk serological profile patients. 59 (98%) bleeding events were recorded in the Warfarin treated group, 46 (82%) among the high risk profile group. only one bleeding event was recorded in the DOACs group.
Conclusion: According to our single center data gathered retrospectively form a follow up of real- life APS patient's treatment, Warfarin vs DOACs, we found higher incidence of thrombotic events (82%) in the Warfarin group compared to the DOACs group (59%). High risk profile patients had a higher thrombotic incidence in both groups. Moreover, patients taking Warfarin had a dramatically higher incidence of bleeding events comparing to DOACs (98% vs 0.01% respectively). These findings may raise the differences between real-life and controlled researches and may challenge the superiority of Warfarin. More researches are needed in order to answer this question.
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Vasculitis - small vessel vasculitis

POS1158

COMPARISON OF THE ACR/EULAR 2022 CLASSIFICATION CRITERIA AND THE EMEA (THE EUROPEAN MEDICINES AGENCY) ALGORITHM IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS (AAV)

Keywords: Validation, Vasculitis

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Background: The anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAVs) are a group of disorders involving systemic, small-vessel vasculitis. The diseases include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA). The diagnosis of vasculitis is challenging, due to the heterogeneous nature of these diseases. In 2022, ACR/EULAR proposed new internationally standardized classification criteria for AAV (ANCA-associated vasculitis). However, the performance of the new classification criteria have not been fully verified.
Objectives: To clarify the characteristics of the ACR/EULAR 2022 classification criteria (the 2022 criteria) in patients with AAV, by comparing those of the 2022 criteria with the existing European Medicines Agency (EMEA) algorithm.
Methods: All consecutive patients who had been newly diagnosed with AAV in Keio University Hospital between March 2012 and May 2022 were retrospectively reviewed. We reclassified them according to the EMEA algorithm and the 2022 criteria and identified their difference. We also analysed their clinical characteristics statistically.
Results: We included 114 patients in the analysis. The mean age at diagnosis of AAV was 67.2 ± 14.3, and 70 patients (61.4%) were female. According to the EMEA algorithm, the patients were classified as EGPA in 21 patients, GPA in 43, MPA in 29, and unclassifiable in 21, while according to the 2022 criteria, they were classified as EGPA in 24, GPA in 13, MPA in 62, EGPA-MPA overlap in 1, GPA-MPA overlap in 6, and unclassifiable in 8. All 21 EGPA patients with the EMEA algorithm met the EGPA-2022 criteria. Forty three GPA patients with the EMEA were classified as EGPA in 1, GPA in 11, MPA in 24, GPA-MPA overlap in 6, and unclassifiable in 1 with the 2022 criteria. Patients who were classified as GPA according to both criteria were significantly younger (53.0 ± 18.6 vs 74.5 ± 9.9 years old, respectively, P=0.003), female dominant (54.5% vs 20.8%, P=0.056), c/PR3-ANCA positive (90.9% vs 0%, P<0.001), had frequent epistaxis (45.5% vs 0%, P=0.001), and less with interstitial lung disease (9.1% vs 58.3%, P=0.007) compared to those who were reclassified from GPA to MPA with 2022 criteria. Among the 29 MPA patients with EMEA, 26 patients also met the MPA classification criteria with 2022 criteria, and among the 21 unclassifiable patients with EMEA, 12 patients were classified as MPA. Patients who were reclassified from unclassifiable to MPA with 2022 criteria were significantly older (75.2 ± 8.7 vs 57.7 ± 5.9 years old, P=0.002), had more p/MPO-ANCA (100% vs 11.1%, P<0.001), fewer ENT lesions (0% vs 55.6%, P=0.003), and tended to have more interstitial lung disease (75.0% vs 33.3%, P = 0.056) than 9 patients who did not meet the MPA-2022 criteria. During the average observation period of 3.95 ± 2.91 years, 16 patients deceased. The 16 deceased patients were classified as GPA in 7, MPA in 6, and unclassifiable in 3 with the EMEA algorithm, while they were classified as MPA in 14, GPA-MPA overlap in 1, and unclassifiable in 1 with the 2022 criteria. Overall survival was not significantly different with the EMEA algorithm (P=0.21), whereas it was significantly shorter in patients with MPA according to the 2022 criteria (P=0.023).

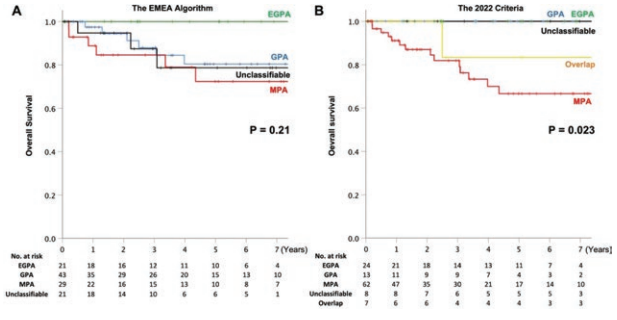


Figure 1. Overall Survival. (A) Based on the EMEA algorithm. (B) Based on the 2022 criteria.

Conclusion: Among the cases classified as GPA or unclassifiable by the EMEA algorithm, older cases with a high rate of p/MPO-ANCA and interstitial lung disease reclassified as MPA by the 2022 criteria were detected. The 2022 criteria is also useful for prognostic prediction compared to the EMEA algorithm.

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POS1159

GLUCOCORTICOID-SPARING EFFECT OF MEPOLIZUMAB: REAL LIFE EXPERIENCE IN A MONOCENTRIC COHORT OF PATIENTS AFFECTED BY EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

Keywords: Real-world evidence, Vasculitis, Tapering

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Background: Oral glucocorticoids (GC) are the mainstay of treatment for eosinophilic granulomatosis with polyangiitis (EGPA) but chronic exposure to GC is associated with serious comorbidities. Mepolizumab (MEPO) demonstrated to be an efficacious treatment for EGPA in the randomized controlled MIRRA trial [1]. ACR guidelines suggest treating non-severe EGPA with MEPO associated with GC as first choice and adding MEPO in non-severe relapses occurred while receiving other immunosuppressants. There are insufficient data to support dosages and duration of GC treatment during MEPO treatment, although guidelines suggest prescribing the minimum effective dose to minimize GC toxicity [2].
Objectives: The aim of the study was to evaluate the GC-sparing effect of MEPO in our cohort of patients affected by EGPA.
Methods: We enrolled 26 patients affected by EGPA according to MIRRA criteria and/or ACR criteria [1][3]. We compared cumulative GC dosage prescribed in the 6 months before beginning treatment with MEPO to the cumulative dosage prescribed in the 6 months after starting MEPO. We also analyse MEPO efficacy comparing median number of asthma attacks, BVAS and VDI.
Results: Twenty-six patients (M/F 16/10) affected by EGPA were diagnosed at a median age of 57 years (IQR 47-65) and started therapy with MEPO after a median disease duration of 6 (1.5-10) years. Overall clinical features of patients before MEPO starting, at MEPO starting (T0) and after 6 months of MEPO (T6) are described in Table 1a. At MEPO starting (T0), 24/26 (92.3%) were treated with GC and 13/26 (50%) were on treatment with other immunosuppressants (1 cyclosporine, 2 methotrexate, 3 mycophenolate, 7 azathioprine). The cumulative GC dosage administered to patients in the six months after MEPO starting was significant lower if compared with dosage in the prior six months. After MEPO starting, there was also a significant reduction of asthmatic flares number and BVAS score, with no increasing in VDI score (Table 1b and 1c). Eleven patients were treated with MEPO 300 mg monthly, and 15 with 100 mg monthly, with no statistically significant differences in clinical response.

Table 1.

1a. Clinical features

	Overall before T0 N(%)	T0 N(%)	T6 N(%)
General	12 (46%)	1 (4%)	1 (4%)
Cutaneous	9 (35%)	1 (4%)	0 (0%)
Ear, nose, throat	22 (85%)	9 (35%)	5 (19%)
Pulmonary	25 (96%)	18 (69%)	1 (4%)
Cardiac	6 (23%)	1 (4%)	0 (0%)
Digestive	4 (15%)	1 (4%)	0 (0%)
Neurological	14 (54%)	6 (23%)	2 (8%)
Renal	0 (0%)	0 (0%)	0 (0%)

1b. Disease activity before MEPO starting (T0) and after 6 months (T6)

	T0 N(%)	T6 N(%)	p value
BVAS: median (IQR)	2 (0-2)	0 (0-0)	0.0005*
VDI: median (IQR)	2 (1,25-3)	2 (1,25-3)	0.5716

1c. Comparison of asthma activity and GC therapy between the 6 months before and the 6 months after T0

	In the 6 months before T0	In the 6 months after T0	p value
GC cumulative dose (mg): median (IQR)	1376 (821-2045)	964 (521-1561)	0.0005*
GC daily dose (mg/day): median (IQR)	8 (5-11)	5 (3-9)	0.0007*
Cumulative Number of asthma attacks: median (IQR)	1 (0-1)	0 (0-0)	0.0211*

IQR: interquartile ratio, BVAS: Birmingham vasculitis activity index, VDI: Vasculitis damage index. *Significant p value

Conclusion: In our cohort MEPO had a significant GC-sparing effect and significantly reduced asthma attacks and disease activity.

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Disclosure of Interests: None Declared.
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POS1160 AGE, FRAILTY, AND OUTCOMES IN OLDER ADULTS WITH ANCA-ASSOCIATED VASCULITIS

Keywords: Epidemiology, Real-world evidence, Vasculitis

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Background: Older adults with ANCA-associated vasculitis (AAV) have differences in clinical presentation, as well as increased mortality and risk of infections, when compared to younger adults. Despite a high incidence of AAV in older adults, these individuals are underrepresented in clinical trials. Frailty, a geriatric syndrome associated with increased morbidity and mortality, has not been adequately studied in older adults with AAV. Better characterization of outcomes and risk factors in these patients is needed to inform treatment.

Objectives: To compare the risks of and factors associated with early (within 2 years) end-stage renal disease (ESRD), severe infection, and death in adults with a new diagnosis of AAV who are ≥ 75 years old vs 65-74 years old.

Methods: Patients ≥ 65 years were included from the 2002-2019 Mass General Brigham AAV cohort, a consecutive inception cohort. EGPA patients were excluded. Covariates including demographics, disease characteristics, and comorbidities (Charlson comorbidity index) were assessed at baseline. Disease activity at time of diagnosis was assessed using the Birmingham Vasculitis Activity Score (BVAS/WG). Frailty was measured at baseline using a claims frailty index, and pre-established cut-offs were utilized to define degrees of frailty (robust, pre-frail, mildly frail, and moderately/severely frail).[1] Death and ESRD were ascertained from linkage to national registries and/or medical records. Severe infections were identified utilizing inpatient data and/or death certificates. The cumulative incidence of death, ESRD and severe infections within 2 years were estimated. In univariate analyses, we assessed factors associated with outcomes within 2 years.

Results: 298 individuals were included. Most patients were female (61%), white (86%), MPO-ANCA+ (80%), and had renal involvement (72%). Patients ≥ 75 years old (n=156) had a median age of 81 years, while median age was 69 years in the 65-74 years group. The cumulative incidence at 2 years of the composite outcome of ESRD/death (23.1% [95% CI 16.5, 29.7]) vs 5.6% [95% CI 1.8, 9.4]) and severe infection (34.0% [95% CI 26.5, 41.4] vs 12% [95% CI 6.6, 17.3]) higher in AAV patients ≥ 75 vs 65-74 years old. Age ≥ 75 years was associated with an increased risk of ESRD/death (hazard ratio (HR) 4.42, 95% CI 2.05-9.51); frailty was not (HR 2.71, 95% CI 0.63,11.72) (Table 1). In contrast, frailty (HR 19.39, 95% CI 2.77,135.66) as well as age ≥ 75 years (HR 3.21, 95 CI% 1.87, 5.52), pulmonary involvement (HR 1.98, 95% CI 1.23, 3.18), and higher baseline comorbidity burden (HR 1.13, 95% CI 1.06, 1.20) were associated with severe infection risk.

Conclusion: Compared to AAV patients aged 65-74 years, AAV patients ≥ 75 years had a higher incidence of death/ESRD and severe infections. Older age but not baseline frailty was associated with ESRD/mortality risk whereas frailty was a very strong risk factor for severe infection. These findings highlight the need for innovative considerations beyond age when assessing outcome risks in AAV.

Table 1. Univariate analyses of factors associated with composite outcome and severe infections within 2 years

Factors	Composite outcome (ESRD/Death)	Severe infection
	HR (95% CI)	HR (95% CI)
Age ≥ 75 years (Ref, 65-74 years)	4.42 (2.05, 9.51)	3.21 (1.87, 5.52)
Female sex (Ref, male)	0.75 (0.41, 1.35)	0.70 (0.44, 1.12)
Comorbidities (CCI per 1 unit)	1.07 (0.97, 1.19)	1.13 (1.06, 1.20)
Frailty	REF	REF
Robust	1.85 (0.44, 7.80)	4.01 (0.56, 28.72)
Pre-frail	2.71 (0.63, 11.72)	19.39 (2.77,
Frail		135.66)
BVAS (per 1 unit)	1.14 (0.99, 1.31)	1.05 (0.94, 1.18)
Organ involvement	1.58 (0.76, 3.29)	1.26 (0.74, 2.16)
Renal (Ref, none)	1.75 (0.95, 3.20)	1.98 (1.23, 3.18)
Pulmonary (Ref, none)		
Induction Regimen (CYC-based vs not)	1.45 (0.72, 2.94)	1.07 (0.64, 1.78)

ESRD = end-stage renal disease, HR = hazard ratio, CI = confidence interval, CCI = Charlson Comorbidity Index, BVAS = Birmingham Vasculitis Activity Score, CYC = cyclophosphamide

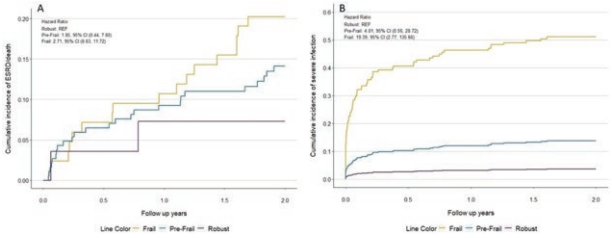


Figure 1. Composite outcome (A) and severe infections (B) by frailty status at baseline.

Acknowledgements: NIL.

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POS1161 RITUXIMAB VS. COMBINATION OF RITUXIMAB AND CYCLOPHOSPHAMIDE INDUCTION THERAPY FOR ANCA-ASSOCIATED VASCULITIS: A RETROSPECTIVE STUDY

Keywords: Real-world evidence, Quality of care, Vasculitis

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Background: In ANCA-associated vasculitis (AAV), the use of rituximab (RTX) according to the RAVE trial [1] or RTX in combination with cyclophosphamide (CYC) according to the RITUXVAS trial [2] showed noninferiority to CYC for the induction of remission. However, there is a lack of comparative real-world data between both therapy regimens.

Objectives: To compare the effectiveness of RTX with combined RTX/CYC for remission induction in AAV.

Methods: In this comparative effectiveness retrospective monocentric study, data of 166 patients with AAV (granulomatosis with polyangiitis [GPA] n=97; microscopic polyangiitis [MPA], n=69) were analyzed. Patients were treated first-line with RTX, RTX/CYC, or CYC between January 2012 and November 2022. The primary outcome was the relapse rate at 24 months. Clinical data (BVAS, therapy) and serologic markers (creatinine, protein excretion, CRP, immunoglobulin levels) were assessed at baseline and every 6 months up to 24 months.

Results: Of the 166 patients, 81 received first-line RTX (RAVE), 23 RTX/CYC (RITUXVAS), and 62 CYC according to CYCLOPS [3]. At baseline, there was no difference between RAVE and RITUXVAS treatment groups with respect to disease activity (BVAS; RAVE vs. RITUXVAS: 12.07±5.69 vs. 16.12±9.85, *P*=0.2083). In AAV, treatment according to RAVE and RITUXVAS was not inferior to treatment according to CYCLOPS (Figure 1). Moreover, RTX was not inferior to RTX/CYC (HR 0.61, P=0.1356, Figure 1). Interestingly, subgroup analysis showed RAVE was slightly superior to RITUXVAS in GPA (HR: 0.48, P=0.0408, Figure 1).

Conclusion: In AAV, RTX and the combination of RTX/CYC were not inferior to CYC. The combination of RTX and CYC was not superior to RTX alone.

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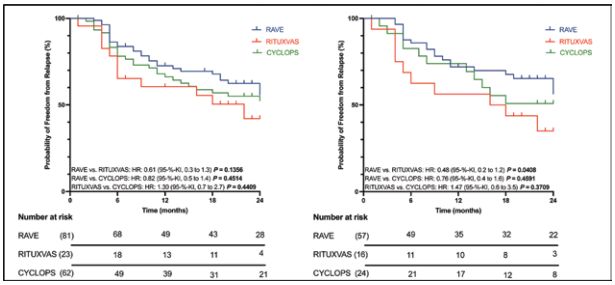


Figure 1. Kaplan-Meier survival analysis. RTX (RAVE) and RTX/CYC (RITUXVAS) were not inferior to CYC (CYCLOPS) in AAV. Specifically, RTX (RAVE) was slightly superior to RTX/CYC (RITUXVAS) in GPA.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1162 EVALUATION OF THE 2022 ACR/EULAR CLASSIFICATION CRITERIA FOR GPA AND MPA IN A EUROPEAN ANCA-ASSOCIATED VASCULITIS (AAV) COHORT

Keywords: Vasculitis, Validation

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Background: In 2022, the ACR and the EULAR proposed new classification criteria for granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) based on numerical item scoring for different manifestations in ANCA-associated vasculitis (AAV). Recently, a low concordance rate of only 73% in comparison with the 2012 revised International Chapel Hill Consensus Conference Nomenclature and the 2007 European Medicines Agency (EMA) algorithm [1] was reported in a Korean cohort of 65 GPA patients.
Objectives: We performed a retrospective classification according to the new 2022 classification criteria of patients from our multi-centric AAV cohort, using a computational algorithm that involved existing clinical, laboratory and histological entries. These results were compared to prior clinical diagnoses.
Methods: Data of AAV patients from four tertiary referral centers (Germany and Switzerland) were collected between 2000 and 2021. The 2022 ACR/EULAR criteria for GPA and MPA were applied by algorithmically analyzing (1) BVAS entries for organ manifestation, (2) laboratory results for ANCA/ ELISA testing and (3) histological data for detection of granuloma and/or pauci-immune glomerulo-nephritis. Twenty cases with inconclusive ANCA status were excluded from computed analysis. Results were compared to previously reported diagnoses; whereby renal limited disease was considered a distinct entity.
Results: The final dataset included 305 cases, 294 (96.4%) of Caucasian ethnicity, 161 males (52.8%), median age 61 years (IQR 50-70). Based on the 2022 ACR/EULAR criteria, 299 (98%) cases could be unambiguously categorized, 180 patients were classified as GPA and 119 as MPA (**Table 1**). Positive concordance, i.e. patients matching the novel classification criteria and clinical diagnosis, was higher in MPA than in GPA patients (98.8 vs. 90.8%). By contrast, negative concordance, i.e. proportion of cases negative for both clinical and novel classification-based diagnosis, was higher in GPA (97.3 vs. 84.1%). Twenty-seven cases of renal limited disease were mostly reclassified as MPA (92%). Taken together, alignment of matching both, positive and negative cases in relation to all cases was 93.1% in GPA and 88.2% in MPA. Six cases (2%) that were clinically diagnosed as GPA could not be classified due to competing findings of increased eosinophil cell count and anti-proteinase-3 positivity.
Conclusion: In the present multi-centric cohort, our computational algorithm applying the novel 2022 ACR/EULAR criteria based on existing clinical, laboratory and histological data performed well to categorize 98% of all cases. Our findings demonstrated overall positive and negative concordance rates above 88% and suggest a higher specificity for GPA, but higher sensitivity for MPA classification criteria.

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Table 1.

Entity	Clinical Diagnosis n (%)	2022 criteria-based n (%)		Cases n	Concordance (%)
GPA	195 (63.9)	180 (59)			
	+	+		177	90.8
	+	–		18	
	–	+		3	
	–	–		107	97.3
both positive and negative matching cases for GPA (284/305):					93.1
MPA	85 (27.9)	119 (32.8)			
	+	+		84	98.8
	+	–		1	
	–	+		35	
	–	–		185	84.1
both positive and negative matching cases for MPA (269/305):					88.2
Not classified	0	6 (2)			
		GPA	MPA		
Renal limited disease	25 (8.2)	2 (8)	23 (92)		

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Disclosure of Interests: Stefan Krämer: None declared, Thomas Rauen Consultant of: Vifor, Kristian Pruin: None declared, Teresa Anslinger: None declared, Martin Busch: None declared, Tobias Schmitt: None declared, Raoul Bergner Speakers bureau: Abbvie, Bristol Myers Squibb, Chugai, Glaxo Smith Kline, Galapagos, MSD, Novartis, Consultant of: Galapagos, Vifor, Sebastian Mosberger: None declared, Thomas Neumann Speakers bureau: Roche Pharma (Suisse) AG, GlaxoSmithKline AG, Celgene Switzerland, UCB-Pharma AG, Janssen-Cilag AG, Vifor Pharma Switzerland, Novartis Switzerland, Consultant of: Roche Pharma (Suisse) AG, GlaxoSmithKline AG, Celgene Switzerland, AstraZeneca GmbH, Janssen-Cilag AG, Amgen Switzerland AG, Vifor Pharma Switzerland, Grant/research support from: Vifor Pharma Switzerland.
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POS1164 WITHDRAWN

POS1165

UNBIASED PROTEOMIC APPROACH TO IDENTIFY NOVEL BIOMARKERS OF DISEASE ACTIVITY IN ANCA-ASSOCIATED VASCULITIS

Keywords: Vasculitis, Biomarkers, Prognostic factors

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Background: ANCA-associated vasculitis (AAV) carries excessive morbidity and mortality owing to the delay in diagnosis and limited prognostication. Identifying clinically useful biomarkers of disease activity that facilitate accurate prognostication would help personalize management decisions. Biomarkers used in day-to-day practice include PR3- or MPO-ANCA, CRP, and ESR, but these poorly predict future disease activity. Few studies have examined a limited number of circulating proteins as biomarkers, including BCA-1, MMP-3, TIMP-1[1-4]. We previously leveraged a high-throughput, unbiased approach to investigate 92 potential biomarkers for disease prognostication in AAV patients and identified 5 potential biomarkers.

Objectives: To further investigate the association of 5 novel protein biomarkers with AAV disease activity.

Methods: Serum samples from patients in the Mass General Brigham (MGB) AAV cohort were retrieved from the MGB Biobank following IRB approval. We chose a random 78 subjects who had AAV. We classified disease activity as "Active" or "Remission" at sample collection. The O-link high-throughput proteomic assay was used to measure the levels of 5 proteins of interest (MCP3, TNFSF-14, OSM, Flt3L, and SCF). For analysis, protein levels were first normalized. We compared protein levels in active disease vs remission. ESR, CRP, white blood cell (WBC) count and platelet levels were extracted for comparison. Using the mean value of each potential biomarker in the cohort as cut-off values, we determined the odds ratio (OR) and the area under the receiver operating curve (AUC) of the association of elevated biomarkers with active disease.

Results: Of n=78, the mean age was 57.3 +/- 17.6, 55% were female, and 28% had active disease at sample collection. When examining the outcome of active disease vs remission, abnormal levels of OSM, TNF-SF-14, Flt3L, and SCF differentiated disease states: OR of 5.10 (p=0.005), 3.71 (p=0.017), 0.13 (p=0.001), and 0.34 (p=0.040), respectively. AUC analysis indicated that TNF-SF-14 (0.731, CI 0.601-0.862), OSM (0.745, CI 0.622-0.867), and Flt3L (0.757, CI 0.644-0.871) were more strongly associated with active disease than other biomarkers, including WBC (0.703, CI 0.566-0.840), platelets (0.680, CI 0.551-0.809), CRP (0.549, CI 0.376-0.721), and ESR (0.547, CI 0.372-0.722).

Conclusion: Using a high-throughput, unbiased proteomics approach, we further investigated 5 novel candidate markers differentiating active AAV disease from remission. These proteins likely reflect different states of immune activation during active disease and outperform conventional inflammatory markers (e.g., CRP, ESR) as well as WBC and platelets. Our study has certain limitations, including sample size, a cross-sectional study design, and requires validation across diverse, longitudinal cohorts. The potential for biomarkers that accurately identify those individuals in remission compared to active disease may facilitate tailored, personalized therapeutic intervention, which avoids unnecessary exposure to the toxic side effects of immunomodulatory agents.

Table 1. Biomarker mean levels and characteristics for active disease.

Biomarker	Mean level Active vs. Remission	Odds Ratio (mean cutoff, CI, p-value)	AUC (CI)
OSM	7.39 ± 0.83 vs. 6.60 ± 1.01, p=0.002	5.1 (≥ 6.96, 1.64-15.85, p=0.005)	0.745 (0.622-0.867)
TNF-SF-14	7.59 ± 0.90 vs. 6.85 ± 0.91, p=0.001	3.71 (≥ 7.07, 1.26-10.93, p=0.017)	0.731 (0.601-0.862)
Flt3L	9.28 ± 0.48 vs. 9.74 ± 0.49, p=0.001	0.13 (≥ 9.64, 0.04-0.43, p=0.001)	0.757 (0.644-0.871)
MCP-3	3.51 ± 0.78 vs. 2.99 ± 0.73, p=0.008	1.24 (≥ 3.18, 0.46-.3.36, p=0.666)	0.628 (0.485-0.771)
SCF	9.73 ± 0.74 vs. 10.19 ± 0.38, p=0.001	0.34 (≥ 10.13, 0.12-0.95, p=0.04)	0.700 (0.570-0.830)

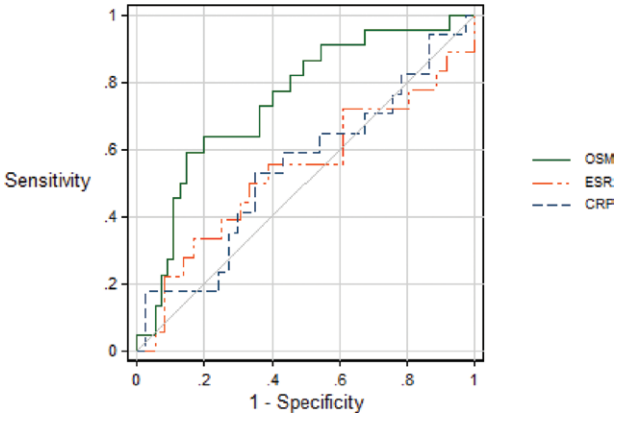


Figure 1. Area under the receiving operating curves for active disease.

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Disclosure of Interests: None Declared.
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POS1166

IDENTIFICATION OF KEY GENES AND IMBALANCE OF IMMUNE CELL INFILTRATION IN IMMUNOGLOBULIN A ASSOCIATED VASCULITIS NEPHRITIS BY INTEGRATED BIOINFORMATIC ANALYSIS

Keywords: Cell biology, Vasculitis, Genetics/epigenetics

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Background: Immunoglobulin A associated vasculitis (IgAV), also known as Henoch-Schonlein purpura, is a common systemic vascular inflammatory disease that chiefly manifests as skin purpura, arthritis, abdominal pain, gastrointestinal bleeding, and kidney involvement [1]. It is characterized by immunoglobulin A-dominant immune deposition in small blood vessels, and the excessive production of various inflammatory molecules [2]. Although the etiology and pathogenesis of IgAV are not fully understood, there is increasing evidence that infection, genetic susceptibility, and immune response disorders are closely related to the development and progression of IgAV [3,4]. Meawhile, abnormal expression of immune factors and imbalance of immune cell differentiation in general circulation may play crucial roles in the pathogenesis of IgAV [5]. Therefore, it is necessary to identify key pathways and immune cells in vasculitis, and to assess the significance of the immune microenvironment in the pathogenesis of IgAV.
Objectives: This study attempted to identify differentially expressed genes (DEGs) and find dysregulated immune cell types in IgAV to find the underlying pathogenesis for IgAV to the effective prediction of therapeutic targets in the future.
Methods: GSE102114 datasets were obtained from the Gene Expression Omnibus (GEO) database to identify DEGs. Then, the protein-protein interaction (PPI) network of the DEGs was constructed using the STRING database. And key hub genes were identified by cytoHubba plug-in, performed functional enrichment analyses and followed by verification using PCR based on patient samples. Finally, the abundance of 24 immune cells were detected by Immune Cell Abundance Identifier (ImmuCellAI) to estimate the proportions and dysregulation of immune cell types within IgAV.
Results: A total of 4200 DEGs were screened in IgAV patients compared to Health Donor, including 2004 upregulated and 2196 downregulated genes. Of the top 10 hub genes from PPI network, *STAT1*, *TLR4*, *PTEN*, *UBB*, *HSPA8*, *ATP5B*, *UBA52*, and *CDC42* were verified significantly upregulated in more patients. Enrichment analyses indicated that hub genes were primarily enriched in Toll-like receptor (TLR) signaling pathway, nucleotide oligomerization domain (NOD)-like receptor signaling pathway, and Th17 signaling pathways. Moreover, we found a diversity of immune cells in IgAV, consisting mainly of T cells. Finally, this study suggests that the overdifferentiation of Th2 cells, Th17 cells and Tfh cells may be involved in the occurrence and development of IgAV.
Conclusion: We screened out the key genes, pathways and maladjusted immune cells and associated with the pathogenesis of IgAV. The unique characteristics of IgAV-infiltrating immune cell subsets were confirmed, providing new insights for future molecular targeted therapy and a direction for immunological research on IgAV.
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Disclosure of Interests: None Declared.
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POS1167

SHORT-TERM OUTCOME OF ADULTS WITH IGA VASCULITIS – A SINGLE CENTER EXPERIENCE

Keywords: Vasculitis, Prognostic factors

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Background: Follow-up data on IgA vasculitis (IgAV) in adults are scarce compared to paediatric population.
Objectives: The aim of our study was to investigate the short-term outcome in a well-defined adult IgAV cohort.
Methods: We analyzed medical records of histologically proven adult IgAV cases diagnosed between January 2010 and July 2022, and followed at our rheumatology center for more than 3 months. The frequency and type of relapses were studied. In addition the information on renal function (creatinine, estimated glomerular filtration rate (eGFR)) and urine analysis was recorded. Persistent abnormal urinalysis was defined as persistent haematuria (>10x10^6 red blood cells/L) and/or daily proteinuria >300 mg. A significant worsening of renal function during follow-up was defined as eGFR decline >20% from baseline. Risk factors for relapsing IgAV and persistent abnormal urinalysis were studied using Cox regression analysis.
Results: We identified 362 IgAV patients (59.4% males, median (IQR) age 64.2 (45.4; 76.2) years). Four patients died during the acute IgAV. Of the remaining patients, 265 (73.2%) were followed for a median (IQR; range) 24.1 (12.5, 55.2; range 3.0 to 146.1) months, while 93 patients had either a follow-up time less than 3 months or were lost to follow up. Of 265 patients 38.9%, 29.8% and 44.5% had at baseline articular, gastrointestinal, and renal involvement, respectively; and 28.3% had skin limited IgAV. One hundred and eighty-nine (71.3%) patients received at baseline systemic glucocorticoid, and 32 (12.1%) additional immunomodulatory therapy. One patient transiently required haemodialysis. During the follow-up period 42 (15.8%) patients relapsed. Table 1 shows the frequency and type of relapses. As factors associated with relapses emerged age (HR 0.97 (95% CI 0.95; 0.99)), and the use of systemic glucocorticoid at initial presentation (HR 0.27 (95% CI 0.15; 0.50)). Seventy-four (27.9%) patients had persistent abnormal urinalysis during follow-up, and 12 (16.2%) of them had daily proteinuria >1g. As factors associated with persistent abnormal urinalysis emerged heart failure as comorbidity (HR 2.28 (95% CI 1.20; 4.32), articular involvement (HR 0.42 (95% CI 0.25; 0.70)) and baseline immunomodulatory treatment (HR 2.30 (95%CI 1.29; 4.10)). eGFR decline of >20% from baseline was recorded in 41 (15.5%) patients (in 18/74 (24.3%) patients with persistent abnormal urinalysis, and in 23/191 (12.0%) patients without clear IgAV associated renal pathology; p=0.022). Heart failure (HR 3.06 (95%CI 1.44; 6.52)) and age (HR 1.03 (95CI 1.01; 1.05)) were associated with eGFR decline during follow up. Two patients developed end-stage kidney disease in association with IgAV. Forty-eight (18.1%) patients died during follow-up period, and death of one patient was related to IgAV relapse.

Table 1. Frequency and type of relapses of IgAV

Number of relapses	Number (%) of patients	The type of relapse in 33 patients with up to 3 relapsing episodes *	
1	24 (57.1%)	Skin	23 (52.3%)
2	7 (16.7%)	Skin + kidney	14 (31.8%)
3	2 (4.8%)	Skin + joints	2 (4.53%)
≥4	9 (21.4%)	Skin + joints + GIT	1 (2.3%)
		Kidney	4 (9.1%)

Legend: GIT gastrointestinal tract; *patients with multiple (≥4) relapses had skin relapses.

Conclusion: Fifteen percent of our adults had relapsing IgAV course, with skin relapses being the predominant relapse type. Younger patients with symptomatically managed IgAV were more prone to relapse. Persistent abnormal urinalysis was recorded in a quarter of patients. Concurrent heart failure had an impact on the persistent renal pathology in adult IgAV.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1188

POS1168

NOMOGRAM FOR IDENTIFYING THE HIGH-RISK PATIENTS OF ORGAN INVOLVEMENT IN EARLY-STAGE ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

Keywords: Vasculitis

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Background: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is characterized by small-vessel vasculitis and systemic autoimmune inflammatory response [1, 2]. Although AAV is rare, the condition of AAV is relatively severe. The clinical manifestations of patients with AAV are different [3], ranging from mild non-specific symptoms to severe life-threatening organ involvement. Therefore, the clinical need to achieve accurate and quick identification for the high-risk groups of organ involvement in early-stage AAV remains strong.
Objectives: There is no study to identify the high-risk patients with organ involvement of early-stage of AAV. We aimed to develop a model to identify those high-risk patients at an early stage.
Methods: The data of the 74 new-onset patients with AAV (61 of whom had definite organ involvement) was collected in our retrospective study. The predictor variables for organ involvement in AAV were assessed by the logistic regression analysis. We developed the risk stratification model by nomogram. And the model was validated by concordance index, calibration curve, and decision curve analysis.

Results: The logistic regression analysis showed that BVAS, IL-17 and Treg cells were the predictor variables for organ involvement in AAV (Figure 1). We constructed a nomogram model consisting of BVAS, Treg cells and IL-17 (Figure 2A). In the nomogram, the value of each predictor was assigned a certain number of points, and the sum of the points for each predictor corresponded to the risk of organ involvement in AAV. Then we evaluated the nomogram model. The calibration curve in 1000 bootstrap replications revealed a good predictive accuracy between the predicted probability and observed probability of the nomogram model with a concordance index (C-index) of 0. 957 (95% CI = 0. 694–0.960) and bias-corrected C-index of 0. 937 (Figure 2B). And the chi-squares of Hosmer–Lemeshow test was 0.37(P = 0.83) indicating a good fitness of the model. Next, the receiver operating characteristic (ROC) curve of the model (Figure 2C) yielded the AUC of the curve was 0.9571 (95%CI =0.9124–1.000) showing it had a great ability for discriminating organ involvement in AAV. The decision curve analysis (DCA) showed a positive net benefit for patients with organ involvement (Figure 2D), which suggested that patients with organ involvement could benefit from interventions. And the clinical impact curve (Figure 2E) showed that the risk of organ involvement predicted by the nomogram model under threshold probability (red curve) was close to the actual value of organ involvement events under each threshold probability (blue curve).

Conclusion: The risk stratification nomogram model was effective to identify the high-risk patients of organ involvement in early-stage AAV, and it was validated with good discrimination, calibration as well as great application value in clinical.

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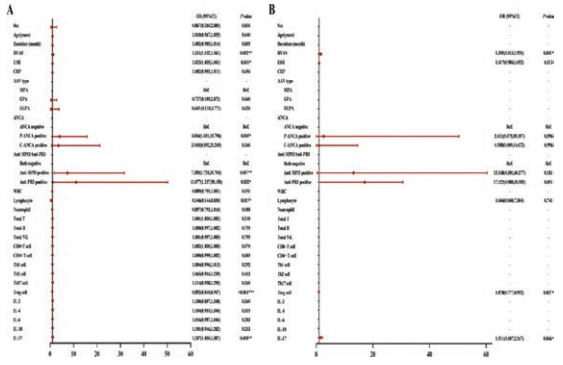


Figure 1. Forest plot of univariate and multivariate logistic regression analysis of AAV with organ involvement. (*P < 0.05, **P < 0.01, ***P < 0.001)

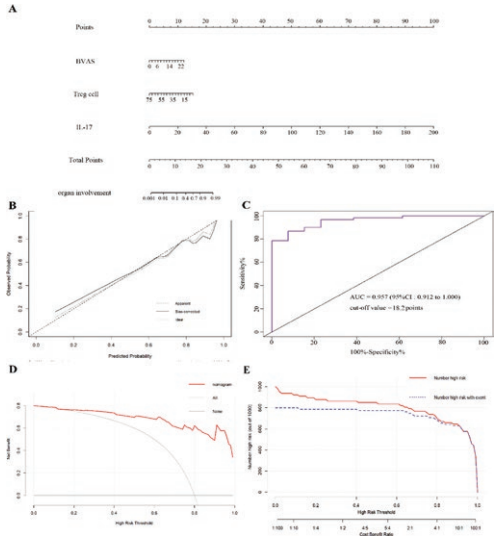


Figure 2. The development and validation of the nomogram model. (A) The nomogram model for identifying the high-risk patients of organ involvement in early-stage AAV. (B) The calibration curve of the nomogram model was obtained by comparing the observed and predicted risk of organ involvement in AAV. (C) ROC curve of the nomogram model. (D) DCA of the nomogram model. (E) The clinical impact curve of the nomogram.

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Disclosure of Interests: None Declared.

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POS1169

RECOVERY AND LONG-TERM RENAL OUTCOME OF PATIENTS WITH ANCA-ASSOCIATED VASCULITIS WHO ARE ON DIALYSIS AT PRESENTATION

Keywords: Vasculitis

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Background: Renal involvement in ANCA-associated vasculitis (AAV) can lead to severe renal dysfunction requiring dialysis at the time of diagnosis. Studies have demonstrated that a significant proportion of patients could discontinue dialysis after treatment, with dialysis recovery-associated factors including kidney pathology such as proportion of normal glomeruli and extent of tubular atrophy or interstitial fibrosis. However, these works focused on short-term outcomes within 6–12 months after AAV diagnosis (1, 2). Research reporting if patients who discontinued dialysis resumed during long-term follow-up are lacking.

Objectives: We assessed the clinical and pathologic characteristics of patients with AAV dependent on dialysis at presentation and the long-term renal outcomes of those who recovered after dialysis.

Methods: This retrospective study analyzed the data of patients diagnosed with AAV who were on dialysis at baseline from July 2005 to May 2021 at a single tertiary center in Korea. Medical records, including renal function and dependence on dialysis, were obtained.

Results: We included 34 patients on dialysis at the time of AAV diagnosis in this study. The median age was 64.5 years, and 61.8% were female. Among all patients, 13 discontinued dialysis and 21 remained dialysis dependent. The proportions of normal glomeruli (p<0.001) and interstitial fibrosis (p=0.024) were significantly different between the two groups. The multivariable analysis revealed that the proportion of normal glomeruli tended to be associated with dialysis discontinuation (OR=1.34, 95% CI 0.88–1.27, p=0.068). Treatment modalities, including plasmapheresis, were not significantly associated with dialysis discontinuation. In the follow-up analysis of 13 patients who had discontinued dialysis for a median of 81 months, 12 did not resume dialysis, and their glomerular filtration rate values had significantly increased at follow-up compared with at dialysis cessation (37.5 [28.5–45.5] vs. 24.0 [18.5–30.0] mL/min/1.73 m², p=0.008).

Conclusion: Approximately 38% of AAV patients discontinued dialysis, and the recovered patients had improved renal function without dialysis. Thus, patients with AAV on dialysis should be considered for dialysis discontinuation and renal recovery, especially those with normal glomeruli in kidney pathology.

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Table 1. Long-term follow-up of patients who discontinued dialysis

	All (n = 13)
Age, years	64.0 (60.069.5)
Female	7 (53.8)
Duration of follow-up, mo.	81.0 (21.5105.5)
Duration of dialysis, days	36.0 (33.5126.5)
Remission	10 (76.9)
Renal profile at the time of dialysis discontinuation	
Creatinine, mg/dL	2.60 (2.053.16)
eGFR, mL/min/1.73 m²	24.0 (18.530.0)
Induction therapy	
IV cyclophosphamide	3 (23.1)
PO cyclophosphamide	10 (76.9)
Rituximab	1 (4.8)
Maintenance therapy	
Azathioprine	10 (76.9)
Mycophenolic acid	2 (15.4)
Duration of therapy, days	594.0 (119.52160.5)
Renal profile at final follow-up	
Creatinine, mg/dL	1.85 (1.342.02)
eGFR, mL/min/1.73 m²	36.0 (27.545.0)

Values are median (interquartile range) or n (%); eGFR: estimated glomerular filtration rate, BVAS: Birmingham Vasculitis Activity Score

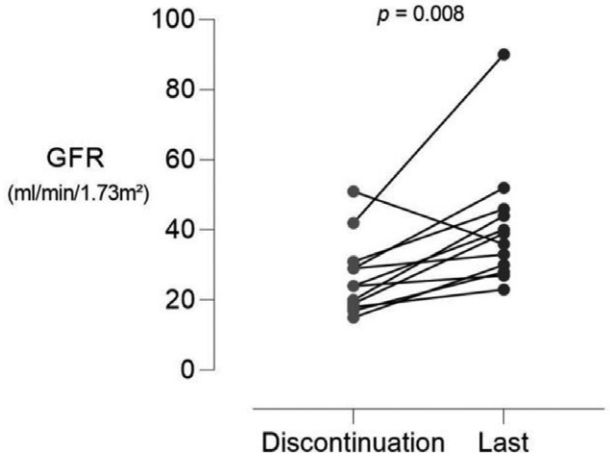


Figure 1. Comparison of values of estimated glomerular filtration rate (eGFR) of patients (n=12) with dialysis discontinuation between the time of dialysis discontinuation and time after the follow-up period

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1170

EXPLORING SUBCLINICAL MICROVASCULAR CHANGES IN ANCA-VASCULITIDES: THE OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY AND NAILFOLD CAPILLAROSCOPY IN THE EVALUATION OF DISEASE-RELATED DAMAGE

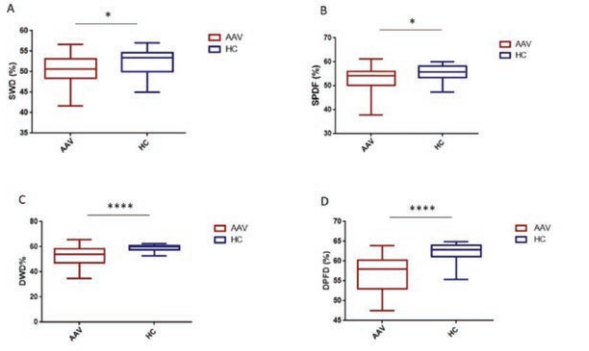
Keywords: Organ damage, Vasculitis

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Background: Both cardiovascular and complement-mediated disorders might lead to microvascular damage in anti-neutrophil cytoplasm autoantibodies (ANCA)-associated vasculitides (AAV). No evidence of subclinical microvascular retinal abnormalities neither their potential correlation with capillaroscopy anomalies has been reported in eosinophilic granulomatosis with polyangiitis (EGPA), granulomatosis with polyangiitis (GPA), and microscopic polyangiitis (MPA).
Objectives: We aimed at investigating subclinical microvascular abnormalities by analyzing retinal and nailfold capillary changes in an AAV cohort. Retinal plexi were investigated using optical coherence tomography angiography (OCT-A), while nailfold capillary changes with videocapillaroscopy (NVC). Potential correlations between OCT-A abnormalities and both disease damage and periungual capillaries change were also explored.
Methods: A monocentric observational study was conducted on consecutive AAV. Main inclusion criteria were a defined diagnosis of EGPA/GPA/MPA in accordance with International Criteria, age ≥18 ≤ 75 yrs, intraocular pressure (IOP) <21 mmHg by Goldmann, a best-corrected-visual-acuity (BCVA) ≥ 0,5 logMAR, and no ophthalmological and/or systemic disorders or treatment with known retinal involvement. Disease activity was assessed by Birmingham Vasculitis Activity Score (BVAS), damage by Vasculitis Damage Index (VDI), and poorer prognosis by the Five Factor Score (FFS). Moreover, OSDI and MIDAS questionnaires have been administered. Quantitative analysis of vessel density (VD) was performed by OCT-A in the superficial capillary plexi (SCP) and deep capillary plexi (DCP) for all subjects. For completeness, a structural analysis of retinal thickness was performed by OCT-scans. Figures and detailed analysis from NVC were performed for all AAV patients.
Results: From 47 consecutive AAV patients referring to the Rheumatologic Clinic, 23 consecutive patients who met the inclusion criteria were included and compared with 20 age/sex-matched healthy subjects (HC) (Table 1). In AAV, BVAS correlated directly with VDI (P=0.001) and FFS (P=0.01) while it was inversely related with disease duration (P=0.01). A total of 46 eyes from AAV patients were analyzed. Retinal VD in superficial whole (SWD) and parafoveal (SPFD) plexi were significantly decreased in AAV compared to HC (P=0.02 and P=0.01, respectively, Figure 1A-B). Furthermore, deep whole (DWD) and parafoveal vessel density (DPFD) were strongly reduced in AAV than HC (P ≤0.0001 for both, Figure 1C-D). In AAV patients, significant inverse correlations emerged between VDI and OCTA-VD in both the superficial (parafoveal, P=0.03) and the deep plexi (whole, P=0.003, and parafoveal P=0.02). The retinal thickness measured by OCT-scans was similar between AAV patients and HC. At NVC examination we found non-specific pattern abnormalities in 82% of AAV patients. Common abnormalities were pericapillary edema (73%), tortuosity (65%), while rare cases of ectasias and hemorrhages resulted (0.8%). No meandering capillaries nor empty dermal papillae were observed. Correlations between NVC changes and OCT-A abnormalities were not described.
Conclusion: Subclinical microvascular retinal changes occur in patients with AAV and correlate with the disease-related damage. In this context, the OCT-A can represent a useful tool in the early detection of vascular damage. AAV patients present microvascular abnormalities at NVC, whose clinical relevance requires further studies.

Table 1.

	AAV (n=23)
GPA, N/%	5/22
EGPA, N/%	9/39
MPA, N/%	9/39
Age at the study (yrs, mean ± SD)	60.9 ± 8.7
Disease duration (yrs, mean ± SD)	9.6 ± 9.1
ENT, N/%	15/65
Kidney, N/%	4/17
Heart, N/%	4/17
Lung, N/%	21/91
Skin, N/%	6/26
Joint, N/%	9/39
Peripheral Nervous System, N/%	13/57
ANCA positivity, N/%	16/69.6
BVAS (mean ± SD)	3.3 ± 2.5
VDI (mean ± SD)	4.5 ± 1.5
FFS (mean ± SD)	0.3 ± 0.4



AAV, Anti-neutrophil cytoplasm autoantibodies (ANCA)-vasculitides; HC, healthy controls; SWD, superficial whole density; SPFD, superficial parafoveal density; DWD, deep whole density; DPFD, deep parafoveal density. *p<0.05 ****p<0.0001

Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1171

NEW INDEX USING TRIGLYCERIDE-GLUCOSE-BODY MASS INDEX FOR PREDICTING MORTALITY IN PATIENTS WITH ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

Keywords: Vasculitis, Biomarkers, Diet and nutrition

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Background: The mortality rate of patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is relatively higher than that of those

with other vasculitides. Various biomarkers are developed to predict outcome of AAV. Recently, a novel index, triglyceride (TG) glucose-body mass index (BMI) (TyG-BMI) was introduced to predict insulin resistance (IR), cardiovascular disease, cerebrovascular accidents in general population. Given that IR and its related diseases such as CVD and CVA are generally major risk factors for all-cause mortality in the general population, it could be assumed that TyG-BMI could be a robust predictor of all-cause mortality in AAV patients.

Objectives: This study aimed to investigated whether TyG-BMI and a new index using TyG-BMI (NITGB) could predict all-cause mortality in nonobese patients with AAV.

Methods: The medical records of 78 nonobese AAV patients (BMI < 23.0 kg/m2 for Asian) were retrospectively reviewed. TyG-BMI was calculated by the equation: Ln [triglyceride × fasting glucose/2] × BMI. To develop NITGB, we assigned a weight of a number close to an 0.1 decimal integer to each variable according to the slopes for independent variables with P-value < 0.1 in the multivariable Cox analysis.

Results: The median age was 54.3 years and five patients died. When nonobese AAV patients were divided into two groups based on TyG-BMI ≥ 187.74, those with TyG-BMI ≥ 187.74 exhibited a significantly higher risk for all-cause mortality than those without (RR 9.450). Since age (HR 1.324), Birmingham vasculitis activity score (BVAS; HR 1.212), and TyG-BMI ≥ 187.74 (HR 12.168) were independently associated with all-cause mortality, NITGB was developed as follow: age + 0.2 × BVAS + 2.5 × TyG-BMI ≥ 187.74. When nonobese AAV patients were divided into two groups based on NITGB ≥ 27.36, those with NITGB ≥ 27.36 showed a significantly higher risk for all-cause mortality than those without (RR 284.000).

Conclusion: Both nonobese AAV patients with TyG-BMI ≥ 187.74 and those with NITGB ≥ 27.36 exhibited significantly higher cumulative rates of all-cause mortality than those without. NITGB along with TyG-BMI could predict all-cause mortality in nonobese AAV patients.

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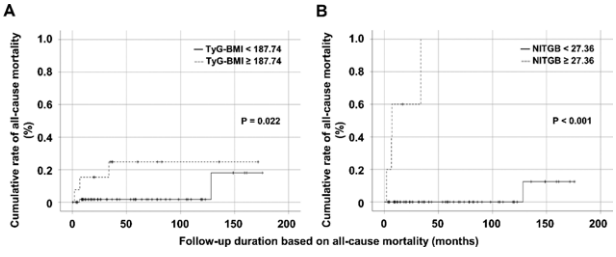


Figure 1.

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POS1172

GEOGRAPHICAL VARIABILITY OF ORGAN DAMAGE BURDEN IN A LARGE INTERNATIONAL MULTICENTER COHORT OF PATIENTS WITH BEHÇET'S SYNDROME: PRELIMINARY RESULTS OF THE PROBE STUDY

Keywords: Organ damage, Behcet's disease, Vasculitis

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Background: A remarkable variability in the clinical course of Behçet's Syndrome (BS) seems to arise by comparing cohorts from different geographical areas. However, no data are currently available on the possible variability of organ damage burden, although it is currently recognized as a major outcome in BS.

Objectives: To evaluate and compare the extent, characteristics, and associated factors of organ damage in patients from different World areas.

Methods: We analyzed demographic and clinical data of a multicenter cohort of 935 consecutive BS patients from 11 Countries clustered in 5 geographic areas: Europe (EU, n 345), North Africa (NA, n 278), Middle East (ME, n 227), Central Asia (CA, n 44), America (AM, 41). Organ damage was assessed by the BS organ damage index (BODI) [1]. Uni- and multivariate analysis was performed to evaluate the association between the geographical region and organ damage using demographic and clinical data as covariates.

Results: Demographics and clinical features are reported in the Table 1. The prevalence of any damage (BODI≥1) in the EU, ME, NA, CA, and AM areas

Table 1. Demographic and clinical characteristic of the patients form different geographical area.

	Europe	Middle East	North Africa	Central Asia	America
Males	37.1%	59.5%	80.2%	41.5%	40.9%
Age, yrs	46.3 (14.1)	37.4 (10.0)	37.7 (11.1)	36.2 (17.6)	44.1 (14.5)
Disease duration, yrs	14.6 (11.4)	12.1 (8.7)	8.6 (7.2)	11.6 (9.6)	14.3 (10.1)
Diagnosis delay, yrs	4.1 (7.2)	6.5 (7.4)	2.4 (4.8)	5.2 (6.1)	4.5 (6.5)
BODI domains					
Mucocutaneous	13.0%	14.5%	46.8%	92.7%	4.5%
Musculoskeletal	3.2%	0.4%	1.4%	7.3%	6.8%
Ocular	22.0%	31.3%	54.3%	68.3%	31.8%
Vascular	10.7%	12.3%	36.0%	7.3%	18.2%
Cardiovascular	11.9%	12.3%	37.4%	12.2%	18.2%
Neuropsychiatric	11.3%	4.8%	18.3%	46.3%	36.4%
Gastrointestinal	0.6%	1.3%	1.4%	0.0%	0.0%
Miscellaneous	10.4%	5.3%	4.0%	9.8%	9.1%
BODI score	1.1 (1.7)	1.2 (1.7)	3.5 (2.4)	4.5 (2.6)	1.9 (1.9)
In males	1.6 (2.1)	1.5 (1.8)	3.7 (2.3)	5.0 (2.9)	2.9 (2.2)
In females	0.8 (1.3)	0.9 (1.4)	2.6 (2.4)	4.2 (2.5)	1.7 (1.8)

Europe included patients from Italy. Portugal. Spain. Greece; North Africa: Morocco. Egypt; Middle East: Turkey. Iran; Central Asia: Kazakhstan; America: USA. Brazil. Continuous variables are reported as mean (SD).

was 47.0%. 54.6%. 91.7%. 97.6% and 77.3%, respectively, whereas the mean (SD) total BODI score was 1.1 (1.7), 1.2 (1.7), 3.5 (2.4), 4.5 (2.6), and 1.9 (1.9). The prevalence of different BODI domains is reported in the Table 1. Significant differences were recorded in NA vs. EU and ME cohorts (Figure 1) (CA and AM not included in the statistical analysis for the small sample size). In multivariate analysis, the geographical area was independently associated ($p < 0.001$) with damage (NA vs. EU OR 11.3; ME vs. EU OR 1.5). Male gender (OR 1.5; $p = 0.004$), age (OR 1.03 per year; $p = 0.002$), disease duration (1.03 per year; $p = 0.003$), ocular (OR 2.8; $p < 0.001$), vascular (OR 5.3, $p < 0.001$), and neuropsychiatric (OR 3.8, $P<0.001$) involvement were also associated with BODI≥1.

Conclusion: A variable prevalence of organ damage was observed in BS patients from different World areas. Further research is needed to understand the cause underlying such geographic variability, as it may unveil biological, environmental, or health-system factors driving damage accrual in BS. The BODI effectively captures damage independently from the studied cohort's geographical origin.

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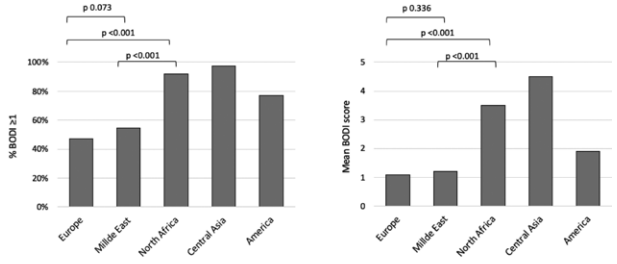


Figure. Comparison of prevalence of any damage (BODI≥1) and extent of damage (total BODI score) among different geographic areas. Chi-squared test and T-student test were used to compare prevalence of BODI≥1 and mean BODI scores. Cenrtal Asia and America not included in the statistical analysis for because the simple size.

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Disclosure of Interests: None Declared.

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POS1173 LONG-TERM ANALYSIS OF RELAPSE RATES IN A EUROPEAN ANCA-ASSOCIATED VASCULITIS (AAV) COHORT FOR GPA AND MPA

Keywords: Registries, Vasculitis

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Background: Therapeutic interventions for ANCA-associated vasculitides (AAV) dramatically changed over the last two decades. Especially the introduction of rituximab into the therapeutic portfolio significantly improved outcome data, whereby relapse rates in previous cohorts were mostly reported from only up to two-year periods.

Objectives: With the present study, we thought to retrospectively investigate the overall relapse rates in a large European AAV cohort.

Methods: Data of patients with newly diagnosed GPA and MPA (retrospectively classified on ACR/EULAR 2022 criteria) from four tertiary referral centers in Germany and Switzerland were collected between 2000 and 2021. Events were captured during routine out-patient visits and hospital admissions. A relapse was considered at the time of any increased vasculitis activity, i.e. therapeutic necessity to increase glucocorticoids ≥10 mg prednisolone per day. First relapse occurrence was analyzed as time-to-event analysis and number of cases for each group. Differences were compared by ANOVA- and X^2-test, respectively.

Results: Our data set comprised a total of 338 patients, 46.2% women (mean age of 59.2±14.7 years). Of these, 203 cases (60.1%) were classified as GPA and 135 (39.9%) as MPA. At initial presentation, 74.9% of patients exhibited renal, 50.9% pulmonary and 35.2% ENT involvement. Over a median follow-up period of 58.7 months (IQR 29.4 to 101.7) we observed an overall relapse rate of 35.8% in the entire cohort and median time to first relapse was 32.6 months (IQR 11.9 to 56.9). Following three years after initial diagnosis, we observed a significant difference, yielding 46 relapses (22.7%) in GPA and 19 (14.1%) in MPA patients at that time ($p<0.05$). Over the entire follow-up, 86 patients with GPA experienced at least one relapse (42.4%) whereas in MPA only 35 (25.9%) patients relapsed ($p<0.01$). In addition, log-rank test revealed a significant difference in relapse over time ($p<0.05$, Figure 1). The median time to the first relapse did not differ significantly between GPA and MPA patients (GPA: 27.9 months, IQR 13.6 to 55.9, vs. MPA: 35.1 months, IQR 8.6 to 55.9, $p=0.458$).

Conclusion: In our European AAV cohort, we observed an overall relapse rate of 35.8% for both AAV entities with the first relapse occurring after a median of 32.6 months. GPA patients exhibited consistently higher relapse rates than those with MPA over the entire observational period. We propose that future analyzes of relapse rates should cover a minimum of three years to capture roughly half of all expected events.

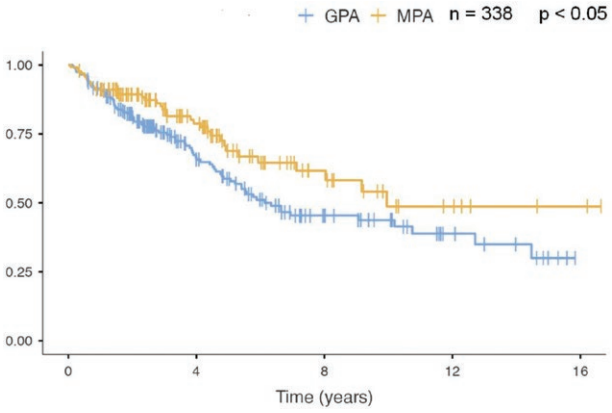


Figure 1. Kaplan Meier curve of relapses.

REFERENCES: NIL.

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Disclosure of Interests: Stefan Krämer: None declared, Thomas Rauen Consultant of: Vifor, Kristian Pruin: None declared, Teresa Anslinger: None declared, Martin Busch: None declared, Tobias Schmitt: None declared, Raoul Bergner Speakers bureau: Abbvie, Bristol Myers Squibb, Chugai, Glaxo Smith Kline, Galapagos, MSD, Novartis, Consultant of: Galapagos, Vifor, Sebastian Mosberger: None declared, Thomas Neumann Speakers bureau: Roche Pharma (Suisse) AG, GlaxoSmithKline AG, Celgene Switzerland, UCB-Pharma AG, Janssen-Cilag AG, Vifor Pharma Switzerland, Novartis Switzerland, Consultant of: Roche Pharma (Suisse) AG, GlaxoSmithKline AG, Celgene Switzerland, AstraZeneca GmbH, Janssen-Cilag AG, Amgen Switzerland AG, Vifor Pharma Switzerland, Grant/research support from: Vifor Pharma Switzerland.

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POS1174 IMPACT OF THE 2022 ACR/EULAR CLASSIFICATION CRITERIA ON CLINICAL DIAGNOSIS OF ANTINEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA) ASSOCIATED VASCULITIS

Keywords: Vasculitis, Real-world evidence

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Background: In 2022 the American College of Rheumatology (ACR) and European Alliance of Associations for Rheumatology (EULAR) presented new classification criteria for the three subsets of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV): granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and Eosinophilic Granulomatosis with Polyangiitis (EGPA).[1-3] The purpose of this classification was to ensure homogeneous populations for clinical trials and research. These criteria were developed based on a population of patients with a high certainty of diagnosis.[1-3] As with any novel criteria, these can potentially lead to re-classification of AAV patients which can impact selection of patients in future studies.

Objectives: To assess the impact of the new 2022 ACR/EULAR classification criteria for GPA, MPA and EGPA on re-classification of clinical diagnoses of AAV patients.

Methods: An established cohort of 337 patients of AAV patients at a single center, academic hospital was used to screen patient and disease characteristics and clinical data at the time of diagnosis and matched to the novel 2022 ACR/EULAR classification criteria for GPA, MPA or EGPA. Patients with an unspecified AAV diagnosis and patients with no clinical data or only ANCA serology available for the time of diagnosis were excluded.

Results: In total 249 patients, 160 (64%) and 89 (36%) females, with a median age of 66 (range 12-96) and a AAV diagnosis between 1983 to 2022, were included. 179 patients had a clinical diagnosis of GPA, 43 of MPA and 27 of EGPA. Of the 179 GPA patients, 155 (87%) met the classification criteria for GPA, 15 (8%) for MPA and 10 (6%) remained unclassified. One patient could be classified as both GPA and MPA. Of the 43 MPA patients, 33 (77%) classified as MPA, 8 (19%) as GPA and 3 (7%) patients remained unclassified. Again, one patient could be classified as GPA and MPA. Only 14 of 27 (52%) EGPA patients met the classification criteria for EGPA. Three (11%) EGPA patients classified as GPA, 4 (15%) as MPA and 6 (22%) remained unclassified. These results show a lower sensitivity than observed in the development study (87 vs 93% for GPA, 78 vs 93% for MPA and 52 vs 85% for EGPA).[1-3] When analysing our cohort based on ANCA specificity, from 67 MPO positive patients, 50 (75%) would classify as MPA, 9 (13%) as GPA and 4 (6%) as EGPA. Clinical diagnosis was MPA in only 40 (60%) of patients and GPA in 18 (27%) patients and EGPA in 9 (13%) patients. From 145 PR3 positive patients, 141 (97%) would classify as GPA, none as MPA and 1 (1%) as EGPA, compared to 140 (97%) clinical diagnosis of GPA, 1 (1%) of MPA and 4 (3%) of EGPA.

Conclusion: When comparing the EULAR/ACR classification criteria to real-life clinical diagnosis, 13% of GPA patients, 23% MPA patients and 48% of EGPA patients would not meet the criteria for the corresponding classification. Moreover, because the presence of ANCA auto-antibodies is highly weighted, the percentage of MPO positive GPA patients is diminished. We demonstrate using these new criteria will impact selection of patients in future studies, especially for EGPA studies.

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Disclosure of Interests: Jolijn van Leeuwen: None declared, Sophia Hafemann: None declared, Y.K. Onno Teng Consultant of: YKOT received an unrestricted research grant and consultancy fees from Vifor Pharma., Grant/research support from: The work of YKOT was supported by the Dutch Kidney Foundation (17OKG04) and by the Arthritis Research and Collaboration Hub Foundation. Arthritis Research and Collaboration Hub is funded by Dutch Arthritis Foundation (ReumaNederland).

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POS1175 ANTI-IL5 THERAPY IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS: DOSAGE, EFFICACY AND OUTCOME IN A LARGE COHORT OF PATIENTS IN REAL LIFE (REVAS STUDY)

Keywords: Targeted synthetic drugs, Descriptive studies, Vasculitis

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA), formerly Churg-Strauss syndrome, is a rare type of anti-neutrophil cytoplasm antibody-associated vasculitis, associated with asthma, nasal poliposis and rinosinusitis, in which eosinophils play a key role. Eosinophil targeted therapies alone or associated to conventional treatment with corticosteroids and immunosuppressant drugs may be useful in patients with refractory disease or asthma/ENT manifestations difficult to treat.

Objectives: To describe the indications, dosage, efficacy and safety, of eosinophil targeted therapies in patients with EGPA in a real practice.

Methods: Retrospective study evaluating all patients with EGPA included at REVAS Registry, treated with anti-IL5 therapy, in order to assess the effectiveness and safety of this therapy. Treatment response was evaluated from 3 months to the censoring data. Complete response (CR) was defined as the absence of asthma and/or sinonasal exacerbations with a prednisone dosage of ≤5 mg/day, and partial response (PR) when the prednisone dosage was ≥5 mg/day. Statistical analysis was performed using SSPS 21 package.

Results: Fifty patients (median age 47 years) were evaluated. Forty-five (90%) patients received mepolizumab (38 patients 100 mg every 4 weeks and 7 patients 300 mg every 4 weeks) for a mean period of 31 (1-68) months; 4 (8%) received benralizumab (30 mg every 4 weeks) for a mean of 33 (7-42) months, and 3 (6%) received resilizumab (n=3, 6%) for a mean period of 54,3 (43-67) month. Anti-Il5 therapy was indicated for severe steroid-dependent asthma (94%) and/or persistent sinonasal involvement (80%). 11 (22%) patients also had symptoms of active vasculitis (5 mononeuritis multiplex, 3 miocarditis, 2 infiltrative cutaneous lesions, 1 orbital pseudotumor). ANCA were positive in 27 (54%) cases with MPO specificity. All patients were receiving corticosteroids at the time of anti-IL5 therapy beginning, with a mean dosage of 11,5 mg/day. A total of 11 (22%) patients had previously received omalizumab, that was changed to mepolizumab in 9 cases, reslizumab in 1 and benralizumab in another, due to PR (n=5) or recurrence of asthma and/or sinusitis (n=6) after a long period of treatment (70.5 months). Anti-IL5 therapy was given concomitantly to AZA in 7 cases, MTX in 3, and RTX in 2. 38 (84,4%) patients treated with mepolizumab achieved a CR after 6-18 months of treatment. The median dosage of prednisone 6 months after mepolizumab, benralizumab and reslizumab initiation was 6 (5-15) mg/day, 5.3 (2.5-10) mg/day, and 3.3 (0-5) mg/day, respectively. The median dosage of prednisone 12 months after mepolizumab, benralizumab and reslizumab beginning was 3.5 (0-5) mg/day, 3.1 (0-5) mg/day and 2.5 (0-5) mg/day, respectively. The median number of exacerbations decreased from 2.5 over the 6 months previous to therapy beginning to 1 in the following 12 months. CS were stopped in 12 (24%) patients. All 3 drugs were safe and well tolerated. During the follow-up period, three patients experienced a major relapse of the disease, and were successfully treated with RTX in conjunction with mepolizumab, with no serious adverse events. Mepolizumab dosage was reduced to 100 mg every 6 weeks in 50% of cases. In one case mepolizumab was changed by benralizumab due to PR.

Conclusion: Mepolizumab at both 100 mg every 4 weeks and 300 mg every 4 weeks is effective for the treatment of EGPA. Both doses should be compared in the setting of a controlled trial. Benralizumab and reslizumab are also effective. Sequential therapy with anti-IL5 drugs and rituximab was safe and effective in achieving remission in patients with a major relapse of the disease.

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POS1176 HOSPITALIZATION RATES, FEATURES, AND DISCHARGE DIAGNOSES OF A LARGE NATIONWIDE COHORT OF ANCA-ASSOCIATED VASCULITIS

Keywords: Epidemiology, Real-world evidence, Vasculitis

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Background: Hospitalizations due to relapse or disease complications are major concerns during follow-up of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV).

Objectives: To determine rates of hospitalization in a large cohort of patients with AAV compared with the national general population, and to describe features and associated primary discharge diagnoses.

Methods: Between 2007 and 2018, we examined the hospitalization records of AAV patients from 13 Italian hospitals. Hospitalization dates, features, length of stay, primary discharge diagnoses and patient data were abstracted from charts. Age- and sex-standardized hospitalization rates (SHR) were calculated by an indirect method, per year and for the study period, using the 2007–2018 hospitalization data provided by the Italian Ministry of Health. Multivariable and survival models were used to explore associations between these outcomes, clinical parameters at diagnosis, and pre-existing comorbidities.
Results: A total of 610 hospitalizations occurred in 635 patients with AAV (19.4% microscopic polyangiitis, MPA; 34.6% granulomatosis with polyangiitis, GPA; 46.0% eosinophilic GPA, EGPA) during a 12-year observation; in 19.8% for life-threatening conditions and leading to death in 2.3%. The median time to first hospitalization was 504 days (25-75%IQR, 95-1497), and the median hospitalization length was 8 days (25-75%IQR, 8-14). The 2018 SHR (95%CI) was 1.14 (0.91, 1.43) for all AAV combined, 1.13 (0.68, 1.76) for MPA, 1.48 (1.02, 2.08) for GPA, and 0.90 (0.60, 1.31) for EGPA. These rates tended to a gradual increase from 2007 to 2018 in the whole AAV cohort of patients and in every disease subset (Figure 1A). The main causes of hospitalization in patients with AAV were infectious diseases (18.7%), followed by major relapse and diagnostic re-evaluation (17.2% each), and cardiovascular diseases (10.8%). Among those due to infections, the main site was the respiratory system (44.6%), followed by urinary tract (9.6%) and sepsis (6.3%). Among AAV patients hospitalized during follow-up (47.1%), 55.5% had only 1 hospitalization, 18.7% had 2, and 25.6% had 3 or more hospitalizations. Patients with a diagnosis of GPA or MPA (versus EGPA), higher vasculitis activity (assessed by BVAS), ANCA positivity at diagnosis, and hospitalization at diagnosis (all $p<0.001$), more pre-existing comorbidities and older age (both $p<0.05$), were more likely to be hospitalized during follow-up (Figure 1B).
Conclusion: Patients with AAV have a significant burden of hospitalization during the disease course. Approximately half of the patients is hospitalized during follow-up, with infections, relapses and cardiovascular diseases as the main causes of hospitalizations. Our findings showed the existence of risk profiles of patients more likely to be hospitalized, requiring more active vigilance.
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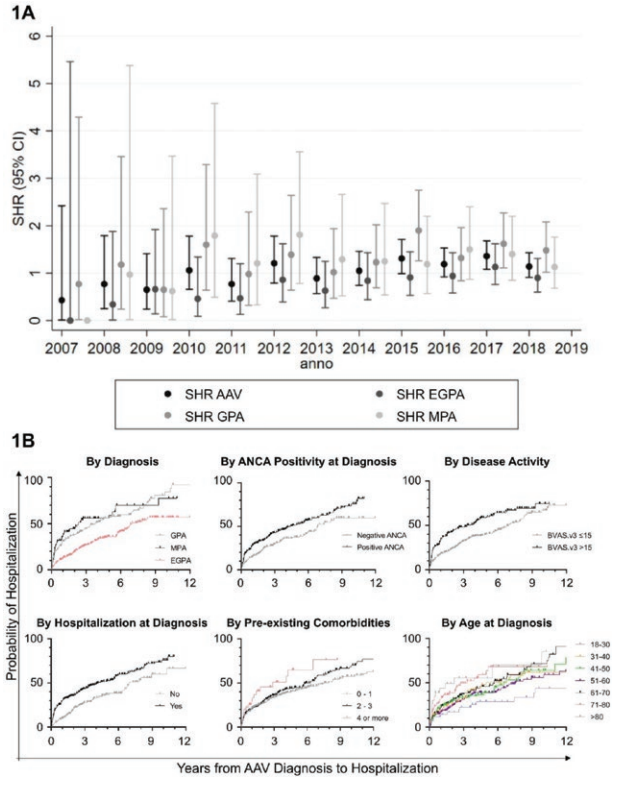


Figure 1. Age- and sex-SHR by year for patients with AAV, MPA, GPA and EGPA during 2007-2018 (A). Kaplan-Meier Plots of the probability of hospitalization after AAV diagnosis (B).

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POS1177

ROLE OF INTRATHECAL PRODUCTION OF IL-6 IN THE PATHOGENESIS OF CHRONIC PROGRESSIVE NEURO-BEHCET'S DISEASE

Keywords: Cytokines and chemokines, Behcet's disease

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Background: Behçet's disease (BD) is characterized by recurrent attacks of aphthous stomatitis, uveitis, genital ulcers, and skin lesions, including folliculitis, erythema nodosum like lesions, and superficial thrombophlebitis. Central nervous system (CNS) involvement is one of the most serious complications in BD and is called neuro-Behçet's disease (NB). There has been accumulating evidence that NB can be classified into acute type (ANB) and chronic progressive type (CPNB) based upon differences in the clinical courses as well as in responses to corticosteroid treatment. Thus, ANB responds well to corticosteroids and usually runs a self-limiting course. By contrast, CPNB is characterized by intractable neuro-behavior changes and cerebellar ataxia, which progress in spite of high doses of corticosteroids or immunosuppressive drugs, including azathioprine or cyclophosphamide.
Objectives: Previous studies have demonstrated that cerebrospinal fluid (CSF) IL-6 was elevated in patients with CPNB. However, little is known as to the mechanism of the elevation of CSF IL-6 in CPNB. The present study was designed in order to elucidate the mechanism of the elevation of CSF IL-6 in the pathogenesis in CPNB.
Methods: Paired serum and cerebrospinal fluid (CSF) samples were obtained from 19 patients with CPNB when they presented active neuropsychiatric manifestations and from 19 control patients with non-inflammatory neurological diseases. Among the 19 patients with CPNB, 5 patients received treatment with infliximab and followed up thereafter. The levels of albumin and IL-6 in CSF and sera were measured by ELISA. Blood-brain barrier (BBB) function was evaluated by Q albumin (CSF/serum albumin quotient x 1,000). The intrathecal production of IL-6 was evaluated by CSF IL-6 indices ([CSF IL-6 x serum albumin]/[serum IL-6 x CSF albumin]).
Results: Serum IL-6 and CSF IL-6 were significantly higher in 19 patients with CPNB compared with control patients with non-inflammatory neurological diseases. Among 19 CPNB patients, serum IL-6 levels were not significantly correlated with CSF IL-6 levels (r=0.0938). As for 5 patients with CPNB treated with infliximab, all of CSF IL-6, serum IL-6, Q albumin and CSF IL-6 indices were significantly elevated compared with control patients with non-inflammatory neurological diseases. Treatment of the 5 patients with infliximab dramatically decreased CSF IL-6 in the next day, but neither serum IL-6 nor Q albumin (Figure 1). Of note, CSF IL-6 indices were dramatically decreased on the next day of treatment with infliximab in the 5 patients with CPNB (Figure 1).

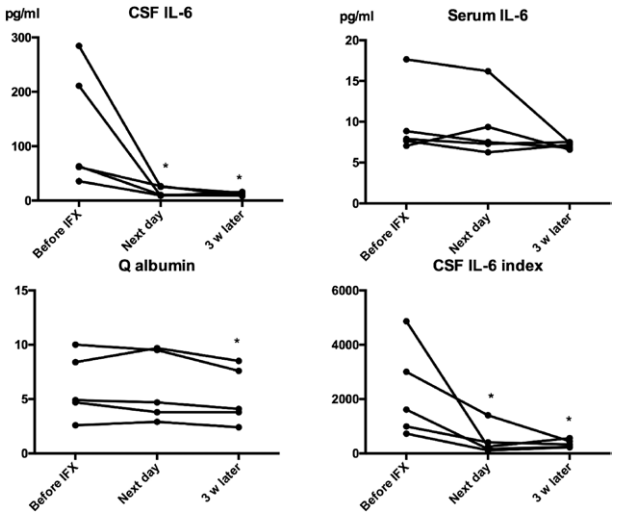


Figure 1.

Conclusion: These results indicate that serum IL-6 as well as CSF IL-6 is involved in the pathogenesis of CPNB. More importantly, the course of treatment of 5 CPNB patients with infliximab clearly indicated that the elevation of CSF IL-6 was not caused by blood-brain barrier breakdown, but by its intrathecal production in CPNB.

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Disclosure of Interests: None Declared.
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POS1178

IDENTIFYING THE NEW DISORDER "IDIOPATHIC HYPOCRYOGLOBULINAEMIA" IN PATIENTS WITH PREVIOUSLY UNIDENTIFIED CLINICAL CONDITIONS

Keywords: Rare/orphan diseases, Vasculitis, Kidneys

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Background: A considerable number of patients with high clinical suspicion for cryoglobulinaemic vasculitis either. show negative results for the detection of cryoglobulins or show only trace amounts which cannot. be characterized for composition.
Objectives: We aimed at establishing whether the failure to detect or the detection of trace amounts of cryoglobulin with conventional methods either identifes a peculiar subset of low level cryoglobulinaemia (from now on hypocryoglobulinaemia) or represents a separate entity.
Methods: Using a modifed precipitation technique in hypo-ionic medium, we prospectively identified between 2008 and 2021 237 patients (median age 60.8 years [22–97], 137 females) having < 0.5% cryocrit and clinical suspicion of autoimmune disorder.
Results: Of these 237 patients, only 54 (22.7%) had a history of HCV infection. One hundred and sixty-nine out of 237 patients (71%) had an established underlying disease, while 68 patients (28.6%) (median age 62.9 years [29–93], 35 females) did not show either laboratory markers or clinical symptoms consonant with an underlying aetiology. These 68 cases with only trace amounts of cryoglobulins were defned as having a putatively idiopathic hypocryoglobulinaemia. Nineteen of these 68 patients (27.9%) had a history of HCV infection. Twentyfour patients out of 68 (35.3%) were positive for rheumatoid factor (RF), while 25 (36.7%) patients had signs of complement consumption (i.e., C4< 15mg/dl and/or C3 < 80mg/dl), and 36 (52.9%) had increased infammatory indexes. Seven patients only had arthralgia and constitutional symptoms while 61 out of 68 (89.7%) presented with at least one of the three cardinal signs of cryoglobulinaemic vasculitis including skin lesions, peripheral nerve involvement, and glomerulonephritis. Seventy-fve percent of the subjects had type III hypocryoglobulins. In patients with hypocryoglobulinaemia the histologic features of glomerulonephritis (also examined by electron microscopy) resembled those of mixed cryoglobulinaemia-associated glomerulonephritis.
Conclusion: In conclusion, hypocryoglobulins are often polyclonal and are mainly unrelated to HCV infection. Patients who present high clinical suspicion for vasculitis, especially glomerulonephritis and yet test negative for cryoglobulinaemia detected by standard techniques, could require deeper investigation even in the absence of HCV infection, RF activity or signs of complement consumption.

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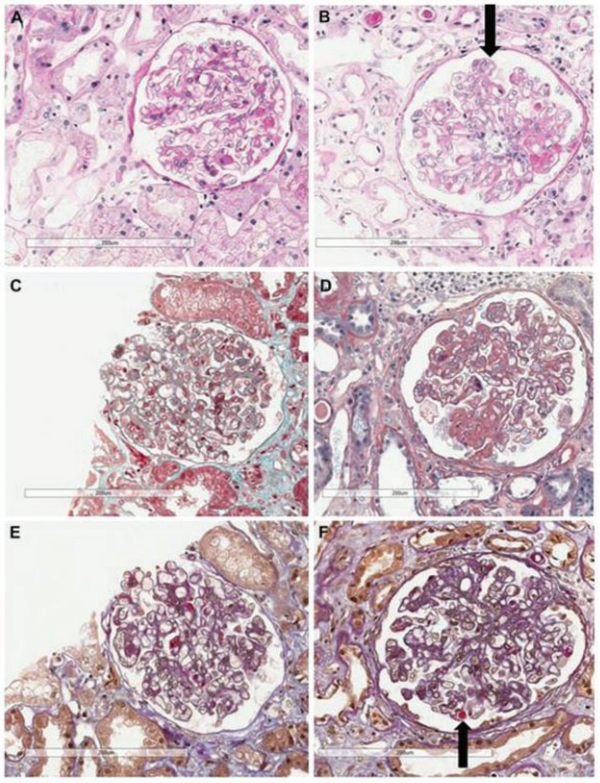


Figure 1. Light microscopy findings in hypocryoglobulinaemic glomerulonephritis. (**A**–**C**) PAS and Trichrome stains show mild thickening of basement membranes with segmental duplication (arrow in **B**), mild mesangial hypercellularity and increased matrix and eosinophilic refractile pseudothrombi (**A**, **B**), PAS original magnification × 200; (**C**) trichrome original magnification × 200. (**D**–**F**) Pseudothrombi appear respectively blue on PTAH stain and glassy pink (arrow in **F**) on AFOG sections (**D**, PTAH original magnification × 200; **E**, **F**, AFOG original magnification × 200).

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1179

USING ARTIFICIAL INTELLIGENCE TO IDENTIFY ANTI-NEUTROPHIL CYTOPLASMATIC ANTIBODY (ANCA)-ASSOCIATED VASCULITIS PATIENTS IN ELECTRONIC HEALTH RECORDS

Keywords: Vasculitis, Artificial intelligence

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Background: Anti-neutrophil cytoplasmatic antibody (ANCA) associated vasculitis (AAV) is a rare, life-threatening, systemic auto-immune disease.[1] Due to the low prevalence, multiple treating disciplines and poor registration, including ICD-10 classification, identifying AAV patients for (pre-)clinical studies, research and health care evaluation is challenging.[2, 3] Therefore, there is an urgent need to improve identifying these patients in health care organisations. Employing artificial intelligence (AI) – supported search engines are increasingly suggested to achieve this.

Objectives: Reliably identify AAV patients in electronic health records (EHR) using an AI-based tool that incorporates text mining and Natural Language Processing (NLP).
Methods: The identification method consists of a search strategy combined with NLP-based exclusion. A search strategy to optimally identify AAV patients within a single center EHR system of an academic hospital was developed using an established AAV cohort (n=203) as a gold-standard reference set. Patient records, identified by the search strategy outside of the reference set, underwent manual review to confirm newly-identified AAV patients. Then, improvement in performance by adding NLP to the text-mining search strategy was investigated. Validation was performed on an independent EHR system of a non-academic hospital with an established AAV cohort available for reference (n=84).
Results: The search strategy combined five queries based on disease description, laboratory measurements, medication and relevant specialisms. In the determination EHR, the search strategy identified 608 patients, including 197/203 (97.0%) AAV patients of the reference set and 149 newly-identified AAV cases confirmed by manual review. Employing NLP in the identification method improved the positive predictive value (PPV) from 57% (346/608 patients) to 78% (339/444 patients). These results were validated in an independent EHR system where the search strategy identified 333 patient, including 82/84 (97.6%) AAV patients of the reference set and 112 newly-identified AAV cases upon manual review. NLP improved PPV from 59% (194/333 patients) to 86% (192/223 patients). Negative predictive values and specificities were above 98% in all analyses.
Conclusion: We present an AI based identification method to identify low-prevalent AAV patients in EHR systems. We demonstrated improved performance when adding NLP to the text-mining search strategy. Successful validation in an independent health organisation supports the applicability and transportability of this method which can be an important accelerator for research efforts and health care evaluation in AAV patients.
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Acknowledgements: NIL.
Disclosure of Interests: Jolijn van Leeuwen: None declared, Erik Penne: None declared, Y.K. Onno Teng Consultant of: YKOT received an unrestricted research grant and consultancy fees from Vifor Pharma., Grant/research support from: The work of YKOT was supported by the Dutch Kidney Foundation (17OKG04) and by the Arthritis Research and Collaboration Hub Foundation. Arthritis Research and Collaboration Hub is funded by Dutch Arthritis Foundation (ReumaNederland).
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POS1180 CONCORDANCE IN THE CLASSIFICATION CRITERIA IN A PATIENT COHORT OF ANCA ASSOCIATED VASCULITIS

Keywords: Validation, Vasculitis

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Background: Despite existing of different classifications criteria for ANCA-associated vasculitis (AAV), early diagnosing AAV is still challenging. Previous classification criteria do not include some of important diagnostic tests (for example, ANCA) or surrogate clinical markers and had insufficient specificity. According to the Vasculitis Patient-Powered Research Network study, the median time to diagnosis of vasculitis amounts 7 months and 73% of patients are misdiagnosed initially. Recently the American College of Rheumatology (ACR) and European Alliance of Associations for Rheumatology (EULAR) have proposed the new classification criteria for AAV, but they have not yet wildly used in a clinical practice.
Objectives: to evaluate the 2022 ACR/EULAR classification criteria for AAV in a Ukrainian patient cohort and compare it with the ACR 1990 classification criteria/ European Medical Agency (EMA) algorithm.
Methods: The retrospective study included 42 patients diagnosed between 2010 and 2022 with GPA, EGPA, MPA and undifferentiated vasculitis (UN) in two rheumatology centers from Ukraine. All patients have serology conformation (positivity of antibodies against proteinase-3 and/or myeloperoxidase performed using the ELISA test) and surrogate clinical markers of vasculitis. All cases were classified according to the 1990 ACR criteria, the 2007 EMA algorithm and reclassified according to the new ACR/EULAR 2022 criteria. If the patients do not meet the criteria of EGPA, MPA, or GPA, they are classified as UN. Concordance between different classification criteria and diagnosis was performed using Cohen's kappa coefficient with determination of sensitivity and specificity.
Results: Among 42 patients (female: male ratio 1:0.6) with AAV with mean age at the time of diagnosis of 47.19±11.55 years, 25 patients were diagnosed with GPA, 7 patients with EGPA, 7 patients with MPA and UV – 3 patients. According to the classification criteria of ACR 1990 and EMA 2007, 31 patients were diagnosed with GPA, EGPA – 4 patients, MPA – 1 patient, UV – 3 patients. Three patients simultaneously met the criteria for GPA and EGPA. When applying the new classification criteria, 24 patients were diagnosed with GPA, 5 patients with MPA, 5 patients with EGPA, and 4 patients with UV. Four patients simultaneously met the criteria for GPA and MPA. In total, in 28 patients the established diagnosis corresponded to the diagnosis according to the previous and new criteria, in 8 patients the diagnosis corresponded only to the new criteria (6 MPA, 1GPA, 1 UV), in 5 patients the diagnosis corresponded only to the classification criteria of ACR 1990 and the EMA algorithm (3 EGPA, 1 UV, 1 GPA), and one patient has not met any criteria. The new classification criteria compared to the previous ones demonstrated better agreement with the established diagnosis of GPA (k 0.6 vs 0.3, sensitivity 88.0% vs 92.0%, specificity 70.6% vs 35.3 %) and MPA (k 0.5 vs 0.2, sensitivity 71.4% vs 14.3%, specificity 88.6% vs 100%), but worse agreement with the diagnosis of EGPA (k 0.8 vs 1.0, sensitivity 71.4% vs 100%, specificity 100% vs 100%). The observed agreement between the two classification criteria was slight for GPA (k 0.3) and MPA (k 0.2), but substantial for EGPA (k 0.8).
Conclusion: The new ACR/EULAR 2022 classification criteria for ANCA-associated vasculitis demonstrate a high diagnostic value in the Ukrainian patient population (for GPA, sensitivity - 88%, specificity - 71%, for MPA - 71% and 89%, respectively, and for EGPA - 71% and 100%, respectively) and an advantage over the previous classification criteria for GPA and MPA. However, about 10% of the patients are unclassified and the same amount are matched two diagnoses with the new criteria. There is a slight agreement between ACR/EULAR2022 criteria and ACR1990 criteria/EMA algorithm for GPA and MPA.
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Acknowledgements: I have no acknowledgments to declare.
Disclosure of Interests: None Declared.
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POS1181 VALIDATION OF THE 2022 - AMERICAN COLLEGE OF RHEUMATOLOGY/EUROPEAN ALLIANCE OF ASSOCIATIONS FOR RHEUMATOLOGY CLASSIFICATION CRITERIA IN INDIAN PATIENTS WITH ANCA ASSOCIATED VASCULITIS

Keywords: Vasculitis

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Background: 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology Classification Criteria for classification of ANCA associated vasculitis need to be validated in different cohorts.
Objectives: The purpose of this study was to validate the recently published 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology Classification Criteria for classification of ANCA associated vasculitis/AAV (Granulomatosis with Polyangiitis [GPA], Eosinophilic Granulomatosis with Polyangiitis [EGPA] and Microscopic Polyangiitis [MPA])
Methods: Patients with a diagnosis of AAV from Indian vasculitis registry (INVAR) cohort were included in the study. The new 2022 ACR classification criteria of AAV[1]–[3], 1990 ACR classification criteria for GPA and EGPA, and the EMA Algorithm were validated in our cohort to assess their performance. The level of agreement was assessed using Cohen's kappa. The clinician's diagnosis was considered as the gold standard.
Results: A total of 302 patients diagnosed AAV with mean age of 42.87 ± 14.7 years were included. 58.7% were female and 42.3 % were male. Figure 1 show the distribution of AAV patients classified according to various classification criteria. The new ACR 2022 criteria for GPA (kappa: 0.961; sensitivity: 99% and specificity: 99%), MPA (kappa: 0.992, sensitivity: 99.9% and specificity: 99.9%), EGPA (kappa:0.961, sensitivity: 92% and 100%) had almost perfect agreement with INVAR cohort. Table 1 shows performance of EMA algorithm and the ACR 1990 criteria compared to the new 2022 classification criteria for AAV in the INVAR

cohort. Furthermore, predominant CNS or ocular GPA (if PR3/MPO negative) were missed by the new ACR classification criteria. EMA Algorithm missed cases of ANCA vasculitis where histology was not possible or ANCA was positive by IIF.
Conclusion: The study showed the new criteria for AAV, had good performance in INVAR registry AAV patients. The new criteria had good sensitivity and specificity for classification of GPA, MPA and EGPA compared to EMA algorithm.
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Table 1. Table showing sensitivity and specificity of the EMA algorithm and the ACR 1990 Criteria compared to the new 2022 classification criteria for AAV in the INVAR cohort

		Sensitivity	Specificity	kappa
GPA	EMA ALGORITHM	87%	89%	0.332
	ACR 1990	69%	71%	0.081
MPA	EMA ALGORITHM	92%	99%	0.711
	ACR 1990	NA	NA	
EGPA	EMA ALGORITHM/ ACR 1990	69.2%	94%	0.451

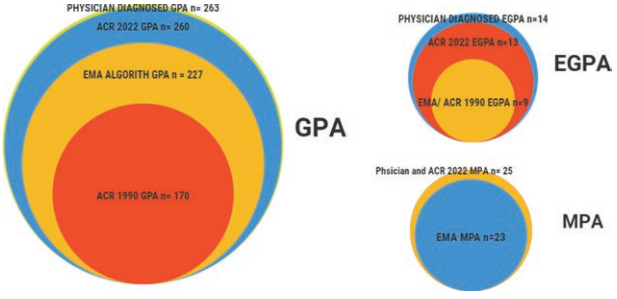


Figure 1. Venn Diagram showing classification of AAV in INVAR cohort according to various classification criteria

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1182 **GENDER IMPACT ON BASELINE PRESENTATION AND OUTCOME IN ADULT IGA VASCULITIS**

Keywords: Epidemiology, Gender/diversity issues, Vasculitis

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Background: It has been shown that patient's demographical characteristics may impact presentation and outcome in adult IgA vasculitis (IgAV). Aging was shown to negatively impact disease severity and outcome of adult IgAV. IgAV is also known to be more frequent in male, with a male to female gender ratio of 1.6. However, the potential impact of gender during vasculitis has been overlooked.
Objectives: We aimed to study the impact of gender on presentation and outcome of adult IgAV.
Methods: We retrospectively study the data of the French retrospective multicenter cohort (IGAVAS), including 260 IgAV adult patients. Comparison of presentation and outcome were performed according to gender status (male *vs*. female).
Results: Of the 260 patients included, data from 259 patients were analyzed: 95 female and 164 male (one missing data). Compared to female, baseline disease presentation in male was similar for cutaneous involvement (n=164 (100%) *vs.* n=95 (100%), p= 1.0), joint (n= 99/164 (60%) vs. n= 60/95 (63%), p= 0.7) involvement, gastrointestinal involvement (n= 93/164 (57%) *vs.* 43/95 (45%) p=0.093) and glomerulonephritis (n=120/164 (73%) *vs.* n=61/95 (64%) p=0.16)). However, compared to female, glomerulonephritis in male was more severe at baseline with lower glomerular filtration rate (median (IQR) 90 ml/min/1,73m2 (59-105) *vs.* 97 ml/min/1,73m2 (76-116), p = 0.015)), increased protein level excretion (0.84 g/day vs 0.58 g/day, p = 0.01) and a higher serum IgA level (3.6 g/l (2.5-4.8) *vs.* 3.3 g/l (2.3-4.6) p=0.03). However, among patients who had renal biopsy (n =47 female, n=97 male), no significant difference was observed. Male were more frequently and more aggressively treated than female. Pulses of methylprednisolone were more frequently prescribed in male (n=52/129 (40%) *vs.* n=14/64 (22%), p= 0.015). Immunosuppressants were more frequently given to male, especially cyclophosphamide (n=31/129 (24%) *vs*. n=4/64 (6%), p=0.0025) and azathioprine (10 % *vs* 2%, p = 0.038). Analysis of treatment response showed that male had more frequent refractory disease: lack of response was significantly higher in male compared to female (30 % *vs.* 13%, p = 0.004). Finally, baseline differences did not impact long term outcome such as mortality (7 % in male *vs.* 5 % in female, p = 0.77), neither progression to chronic kidney failure, dialysis transplantation.
Discussion: Interpretation of this study is tricky. There is a discrepancy between renal laboratory and pathological findings making difficult to affirm a greater severity of glomerulonephritis in male. Additionally or renal. data regarding comorbidities influencing renal function has not been gathered. However, in the literature, studies have shown differences between male and female in IgA nephropathy with more rapid progressive disease in male population. Moreover, a Slovenian group recently observed in a prospective cohort of 124 adults IgAV patients, that males had more severe disease than females.
Conclusion: Despite its limits, this study raises the question of a more severe disease in male in terms of glomerulonephritis. This hypothesis is sustained by the fact that male compared to female were strikingly more severely treated and present a poor short outcome whereas the long term outcome do not seem to differ. Altogether, these results raise the question of the gender as a new prognostic factor during the course adult IgAV.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Clinical cases

POS1183 **DIAGNOSTIC CHALLENGES IN A PREGNANT PATIENT WITH SLE AND SYSTEMIC SCLEROSIS OVERLAP – PREECLAMPSIA, ACTIVE LUPUS NEPHRITIS OR RENAL CRISIS?**

Keywords: Systemic lupus erythematosus, Pregnancy and reproduction, Systemic sclerosis

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Background: Pregnancy is an important issue for young women with inflammatory systemic disease and pose a clinical challenge.
Objectives: The aim of this case report is to underline the challenges to correctly diagnose pregnancy complications versus disease flare in pregnant women with overlap syndrome.
Methods: Clinical information collected from the patient's journal.
Results: A 26 years old woman was referred to Karolinska University Hospital because of Raynaud's phenomenon, sclerodactyly, skin rash, palate ulcerations and recurrent finger ulcerations with necrosis, infections and self-amputation of distal phalanges. Interstitial lung disease was confirmed by high resolution CT and a restrictive pattern on lung function tests. Immunological analyses detected autoantibodies against Scl-70, ribosomal-P, SS-A, SS-B, Ku, as well as dsDNA with immunofluorescence technique with varying titers over the years. Complement activation, anemia and lymphopenia were also present. The patient experienced muscle weakness and peripheral muscle MRI and muscle biopsy confirmed myositis. During follow-up she developed pericardial effusion and myocarditis. The patient was diagnosed with overlap syndrome with clinical and serological features of systemic sclerosis, SLE and myositis. The immunosuppressive treatment over the disease course comprised hydroxychloroquine, methotrexate, azathioprine, rituximab and low dose prednisolone. Later, treatment was switched to mycophenolate mofetil because of flares on the previous regimens. For the digital ulcers, she was treated with nifedipine, sildenafil and iloprost infusions. Despite medical advice on pregnancy risks during active disease, the patient stopped medication with mycophenolate at the age of 35 years and became pregnant. Enalapril, spironolactone and sildenafil were discontinued and she was referred to the specialist maternity care. The pregnancy evolved without complications until week 18 when the blood pressure (BP) began to rise.

In trying to avoid alpha blockers, because of recent finger ulcerations, nitrates and hydralazine were started without sufficient effect on the BP. Soon thereafter, she also developed marked trombocytopenia and hemolytic anemia. The titers of dsDNA antibodies were higher compared to the status before pregnancy and the creatinine and proBNP started to rise. Urine analysis revealed proteinuria and granular casts. Pre-eclampsia was suspected, though SLE flare with active nephritis, hemolysis and trombocytopenia could not be ruled out. Tacrolimus, intravenous immunoglobulin and methylprednisolone were started, as well as labetalol and diuretics. Plasmapheresis was applied twice. The BP remained uncontrolled and kidney function was deteriorating; therefore hemodialysis was started. Since the foetal growth was impaired and the patient's clinical status was not improving, decision was made to stop the pregnancy. The medical abortion with vaginal birth proceeded without complications and minimal hemorrhage. Since hypertension and hemolysis continued post-abortion despite several antihypertensive drugs and the patient developed lung edema, renal crisis was suspected and the patient was started on enalapril. BP, and later on the renal function, improved slowly. Two weeks postpartum dialysis was no longer needed. Renal biopsy revealed thrombotic microangiopathy without signs of nephritis.

Conclusion: We described a patient with overlap syndrome who developed serious pregnancy complications that ended up with pregnancy termination in week 20. This case illustrates the difficulty in differential diagnostics of preeclampsia-induced hypertension with renal and hematological changes versus active SLE and the importance of keeping in mind that renal crisis may complicate the clinical picture in SLE/ scleroderma patients. Also, this case underscores the significance of low disease activity when starting a pregnancy and that every effort should be made for shared decision making.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1184 A CASE OF DELAYED DIAGNOSIS OF MUCKLE WELLS SYNDROME- AN EXTREMELY RARE BUT IMPORTANT DIFFERENTIAL OF INFLAMMATORY ARTHRITIS IN A RHEUMATOLOGY CLINIC

Keywords: Rare/orphan diseases, Inflammatory arthritides

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Background: Muckle wells syndrome (MWS) is one of the rare clinical phenotypes of Cyropyrin associated periodic syndromes (CAPS), driven by Interleukin-1 mediated systemic inflammation.[1] A typical presentation includes episodic fever, urticarial rash and arthralgia but can also result in episodic inflammatory arthritis and sensorineural hearing impairment. Secondary amyloidosis is the most feared complication especially in patients with untreated active disease.[2]

Objectives: We present a case of a 32 years old male, with history of episodic pain and swelling of the right knee for 2 years before presentation to rheumatology clinic.

Methods: Over the years, prior to rheumatology review he was seen by multiple specialties for varied unexplained symptoms including ENT for progressive sensorineural hearing impairment, dermatology for intermittent childhood onset eczematous rash and by ophthalmology for episodic idiopathic iritis and uveitis. He was also seen by haematology for an episode of cervical lymphadenopathy with no definite cause identified. There was no history of inflammatory back pain, psoriasis or Inflammatory bowel disease. Of note, his father had severe sensorineural hearing loss and his brother had a diagnosis of undifferentiated inflammatory arthritis at a young age. On initial rheumatology assessment he had a moderate knee right knee effusion and an erythematous non-specific rash over his upper back. A review of previous investigations showed raised inflammatory markers (CRP 93). A prior MRI right knee showed areas of synovial hypertrophy with a moderate knee effusion.

Results: Subsequent investigations were negative for Rheumatoid factor, Anti-CCP Ab, ANA, ENA, ANCA, HLA B27 and HLA B-51. The initial rheumatology impression was of an isolated seronegative inflammatory arthritis of the right knee but given other unexplained symptoms and family history we investigated for autoinflammatory disorders. Subsequent genetic screen was positive for NLRP3 gene confirming Muckle Wells syndrome as the unifying diagnosis. This case was also discussed with the National Autoinflammatory Disease Centre, UCL London and he has recently been commenced on Anakinra.

Conclusion: Targeted IL-1 inhibitors can prevent secondary amyloidosis. Effect on hearing impairment is uncertain but can be reversed in some cases. The heterogeneity of presentation poses a significant diagnostic challenge, however given the clear efficacy of available treatment options, an early diagnosis is extremely important to improve symptoms and prevent serious organ damage from secondary amyloid.

2) Although episodic pyrexia is considered a hallmark of autoinflammatory disorders, its absence does not exclude CAPS, as was the case in our patient.

3) We recommend considering this diagnosis as a differential of seronegative inflammatory arthritis, especially in younger patients with unexplained multi systemic involvement and suspicious family history.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.526

POS1185 WITHDRAWN

HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

POS1186-HPR INVESTIGATION OF THE RELATIONSHIP BETWEEN ARTIFICIAL JOINT AWARENESS AND EMOTIONAL STATUS IN PATIENTS WITH TOTAL HIP ARTHROPLASTY

Keywords: Cognitive function, Outcome measures, Health services research

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Background: Patient-reported outcome measures, including joint-specific parameters of activities of daily living, such as joint awareness, are increasingly recognized as an important part of post-surgical outcome assessment [1].
Objectives: The aim of this study was to examine the relationship between artificial joint awareness and emotional status in patients who have undergone total hip arthroplasty (THA) surgery.
Methods: In this study, volunteer patients aged between 40-65 years who had undergone THA surgery and at least 1, a maximum 3 years after surgery were included. Artificial joint awareness was evaluated with the Forgotten Joint Score-12 (FJS-12) scale. It is a scale that questions awareness of artificial joint during various daily living activities from the patient's perspective in order to determine the ability of patients to forget artificial hip joints after THA surgery [2]. High scores indicate how much (%) the patient can forget the operated side of the patient and adapt to their life. In other words, a high score indicates a high degree of "forgetting" the artificial joint – i.e. a low degree of awareness. A 5-point Likert system is used in the scoring. The emotional status of patients was determined by Hospital Anxiety and Depression Scale (HADS). It includes anxiety (HADS-A) and depression (HADS-D) subscales. It consists of a total of 14 items, 7 of which are about anxiety and 7 of which are investigating symptoms of depression [3]. Pearson correlation analysis was used according to distribution of the data to determine relationship between the variables. The significance level was accepted as $p<0.05$.
Results: Sixty patients with THA, aged 53.46±7.9 years, were included in the study. Mean FJS-12, HADS-A, and HADS-D scores were 32.68±6.54, 7.27±3.2, and 5.27±2.5, respectively. A moderately and statistically significant correlation was found between FJS-12 and HADS-A and HADS-D ($r=0.466$, $p=0.004$; $r=0.483$, $p=0.003$ respectively).
Conclusion: The results of the current study showed that the adaptation of the artificial limb to daily life is poor and was correlated with emotional status. These results may show that worsening of patients' emotional status may contribute to development of artificial joint awareness. Therefore, also take into consideration the emotional state of patients with THA while applying therapeutic approaches aiming to decrease awareness of artificial joint and increase adaptation of artificial limb to daily life may increase the effectiveness of rehabilitation.

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POS1187-HPR PARTICIPANTS' VIEW ON THE FEASIBILITY OF INSELMA - A NEW INTERDISCIPLINARY NURSE-COORDINATED SELF-MANAGEMENT INTERVENTION TO PEOPLE WITH INFLAMMATORY ARTHRITIS AND SUBSTANTIAL DISEASE IMPACT - A QUALITATIVE EVALUATION

Keywords: Inflammatory arthritides, Qualitative research methods

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Background: Despite continuous improvements in antirheumatic pharmacological treatment, many people with inflammatory arthritis (IA) still report substantial disease impact. Based on the framework for complex interventions [1], we developed a self-management intervention (INSELMA)[2]. Based on shared decision-making, which included an initial assessment and a goal setting process a rheumatology nurse coordinated interdisciplinary support and available offers in primary care to achieve the patients' individual goals. A feasibility test of the six-month intervention encompassed 19 patients with IA and substantial impact of the disease.
Objectives: The objective of this study was to explore the participants' experience of feasibility, acceptability, and potential benefit from participation in the INSELMA intervention.
Methods: Individual semi-structured interviews were conducted with participants in INSELMA. Thematic analysis was applied [3].
Results: Fifteen participants were interviewed (9 women, 6 men, aged 44-75, 17-75 min.). The participants associated the benefits they experienced from the intervention to the impact IA had on their everyday lives.
The analysis derived four overall themes.
1) *A new opportunity*. Participation in INSELMA was experienced as an opportunity to improve, reduce challenges, or change issues they felt they had fought alone until now. Some expressed worries that their situation was too complex to be able to contribute to the study and some participated to contribute to scientific IA evidence.
2) *The importance of person-centred goals*. The individual goals encompassed both physical, social, and emotional life skills. When expectations and goals were aligned, it facilitated a positive outcome. The empathic support and coaching from the nurses, who listened, motivated, and understood their problems were considered especially valuable. Time between consultations to work with goals at home was pointed out as important to experience progress.
3) *A little nudging means everything.* Several participants expressed that the intervention had contributed with new or refreshed knowledge and motivation to change habits. Some would like continued follow-up with the nurse after the end of the study to stay committed. Also some suggested that this type of intervention should be a general offer for all patients with IA. Having access to a physiotherapist and an occupational therapist with rheumatology experience for exercise support adapted to the participants' needs and abilities was especially important for them.
4) *I got more than I wished for*. The intervention was experienced as feasible and meaningful, and the overall impression was positive. Several cried tears of joy and gratitude as they experienced decreased symptom load, improvement in physical strength, mobility, and sleep as well as increased energy and coping. Two had experienced no change, of which one had resumed physical activity after several years. The participants expressed hope for the future as they had new tools and habits to prevent problems and manage symptoms, which resulted in motivation to work towards new goals.
Conclusion: Patients found the INSELMA intervention feasible. They experienced decreased disease impact and increased activity level, facilitated by empathy and self-management support from the health professionals.

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POS1188-HPR EXPERIENCES OF TELEMONITORING PULMONARY FUNCTION IN SYSTEMIC SCLEROSIS ASSOCIATED INTERSTITIAL LUNG DISEASE – A QUALITATIVE STUDY

Keywords: Telemedicine, Qualitative research methods, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is a heterogeneous auto-immune disease with interstitial lung disease (ILD) being the leading cause of mortality [1]. Current practice is to treat patients with severe or progressive ILD with immunosuppression[2]. Therefore tight monitoring of the pulmonary function is of huge importance, which can be improved by telemonitoring.

Objectives: To analyse experiences, facilitators and barriers of telemonitoring the pulmonary function in SSc-ILD patients.
Methods: This study was embedded in a longitudinal study on the validity of detecting progressive ILD with weekly home spirometry in adult SSc patients, fulfilling the ACR-EULAR criteria with a disease-duration ≤ 5 years and a maximum of immunosuppressive treatment of 8 weeks. Using a bluetooth-enabled handheld spirometer, measurements are collected via a mobile application for smart devices with results being visible, as graphs and bar charts, for both physician and patient. The weekly measurements are evaluated by a physician and an extra hospital check-up will be scheduled if results decrease. This system has proven to be feasible in SSc patients in our pilot study [3].
In patients, who used home spirometry for at least 3 months, semi-structured interviews were conducted and audio-records were transcribed. Patients were selected using purposive sampling based on age, treatment for ILD and course of pulmonary function in telemonitoring (>5% decline/stable) till data-saturation was achieved (i.e. no new codes in the last 2 interviews). Interviews were coded by 2 researchers independently using inductive thematic analysis.
Results: In total 13 patients (8 female/5male) were interviewed from whom 3 patients had > 5% decrease in pulmonary function during the observation period. The age ranged from 36-75 with a median of 58 year. Five main themes were extracted: telemonitoring routine, impact of telemonitoring, trust in telemonitoring, contextual factors and implementation in regular healthcare (Figure 1).
Most patients perceived it as reassuring to see stable results weekly, though the moment itself might be tensive. Moreover, the possibility to detect progressive disease earlier was appreciated. One patient, however, preferred disease activity being monitored by the physician instead.
Some patients placed fluctuations of measurement within limits of normal in perspective, while others experienced negative feelings in case of a decreased value. Experienced advantages of telemonitoring were being in the lead, insight in disease course (for some resulting in less confronting hospital visit), increased trust in health, decreased fear of progression, and reduced dependence on hospital visits. Most patients trusted the results of telemonitoring, although some trusted the hospital measurements more, because of external guidance from an analyst (leading to more motivation and unbiased results), and the manner of measurement (during breathing cycle in hospital vs. single breath at home). Understanding the rationale behind telemonitoring is an important facilitator, whereas possible barriers to perform weekly home spirometry are excessive saliva production (as it hinders proper function of the spirometer), confrontation with the disease, and older age. Most patients advocated to implement telemonitoring in healthcare and appreciated an accompanied reduction in hospital visits, although others viewed the regular physical contacts and control of other disease features as important. It was recommended to provide information about limits of normal values or regular feedback.



Figure 1. Overview of general dimension, first-, and second-order themes.

Conclusion: In SSc telemonitoring the pulmonary function can contribute to patient empowerment, however it might not be suitable for every patients, as it might elicit negative feelings.

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POS1189-HPR

LUNG AND MYELOPROLIFERATIVE NEOPLASMS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH JANUS KINASE INHIBITORS: A REVIEW OF THE LITERATURE

Keywords: bDMARD, Malignancy, Rheumatoid arthritis

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Background: Janus Kinase inhibitors (JAKi) have been shown to be effective in the therapeutic strategy of rheumatoid arthritis (RA). However, an increased risk of developing malignancy has been reported in previous literature [1].
Objectives: This review aimed to investigate the risk of lung carcinoma and subsequent myeloproliferative neoplasm (MPN) in RA patients treated with JAKi.
Methods: We conducted a literature review in order to identify cases of lung carcinoma and MPN associated to JAKi in RA patients. A comprehensive search was conducted using *PubMed* and *Scopus*. The databases were searched from 2015 until date December 2022. No restrictions were applied in terms of study design, setting, country, or time frame. For *PubMed*, the search was carried out using a strategy employing the combination of synonyms of "pulmonary neoplasm," terms related to "JAK inhibitors," and terms related to "rheumatoid arthritis." For Scopus, the previous terms were searched in the article title, abstract, or key-words. We also did manual research on reference lists of retrieved relevant articles. Articles were eliminated if they had duplicate titles, did not contain the key-words, or included the words "review", "expert's opinion", or "qualitative." In this review, we included prospective or retrospective case reports and case series conducted on JAKi and lung carcinoma or MPN.
Results: The initial search yielded 153 papers. Following duplicate elimination, we screened for 119 papers. Only eight papers were finally selected for analysis and met inclusion criteria. The mean number of RA patients included was 2422 [486-6194]. Standardized incidence ratio of lung carcinoma and MPN ranged from 0.17 to 0.19 and 0.01 to 0.1, respectively. Most papers raised the possibility that RA patients treated with JAKi may have a markedly higher rate of development of lung carcinoma (95% CI [1.51 - 1.79]) or MPN (95% CI [2.05 - 2.96]) compared to patients who did not receive the treatment. The Table 1 exposes the main characteristics of the nine studies retained in this review.

Table 1. Studies assessing malignancy associated to JAKi therapy in RA patients

Authors	Year	Article type	Neoplasm	Number of cases/ SIR*	(95% CI**)
Curtis JR et al.	2015	Retrospective case series	Lung carcinoma	24 out of 5761/ 0.19	(1.39-3.29)
Hisashi Y et al.	2016	Prospective case series	Lung cancer	2 out of 486/ --	--
			Lymphoma	2 out of 486/ --	
Masayoshi H.	2019	Prospective case series	Lung cancer	24 out of 5677/ --	--
			Lymphoma	10 out of 5677/ --	
Taylor CT et al.	2021	Retrospective case series	Lung cancer	26 out of 3770/ 0.17	(0.11-0.25)
			Lymphoma	6 out of 3770/ 0.01	(0.01-0.09)
Eun BL et al.	2014	Prospective study	lymphoma	5 out of 958/ --	--
Curtis JR et al.	2015	Retrospective case series	lymphoma	10 out of 5761/ 0.08	(0.04-0.14)
Mariette X et al.	2018	Prospective study	Lymphoma	19 out of 6194/ 0.1	(0.06-0.15)
Josef S et al.	2019	Retrospective case series	lymphoma	6 out of 3492/ 0.09	(0.03-0.19)

***SIR: Standardized incidence ratio, **CI: confidence interval**

Conclusion: Our study showed that JAKi was associated with an increased risk of development of lung malignancy and lymphoma. Although the risk of malignancy is increased compared with the general population, it is still similar to that seen in the overall RA patients.

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POS1190-HPR WHY LUPUS? – PATIENTS' THOUGHTS OF TRIGGERS OF SYSTEMIC LUPUS ERYTHEMATOSUS AND PERCEIVED HEALTH

Keywords: Systemic lupus erythematosus, Patient information and education

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Background: It is well known that genetic factors and environmental triggers contribute to the inflammatory process and onset of systemic lupus erythematosus (SLE). Yet, other contributors may still be unknow, and few studies have to date systematically explored patients' views on what caused SLE onset. In a longer perspective, we also need to pay more attention to health literacy, and to patients' understanding of their disease since these aspects are important for treatment compliance, patients' perceptions of health and patient education.

Objectives: To explore patients' thoughts of the cause of SLE and to analyse their reports in relation to perceived health and quality of life.

Methods: Adult patients with SLE (≥ 4 ACR criteria) recruited to a cohort study in tertial care. The participants answered the written question *"Do you have any thoughts of why you got SLE?"* and additional questions of perceived SLE activity during the last three months (score 0-10, 0= no activity), SLE health last week (score 0-100, 0=good SLE health) and current general health (score 0-100, 100=full health). The participants' free written answers were categorized according to the content. We explored if patients' age, educational level, disease duration as well as perceived health differed between the categories.

Results: 375 patients were included. The main question regarding their thoughts of why they got SLE, was commented by 290 patients (77%), mean age 48 years, range 18-87, mean disease duration 15 ±14 years. The replies on the health scales ranged from minimum till maximum. SLE activity was low to moderate (mean 4.2 ±3), perceived SLE health mean 34.7 ±25.9 and current general health mean 63.1 ±21.0. The highest reported level of education was university education for 47% and high school for 36%. Among the patients who answered the main question (n=290), 33% (n=95) answered that they had no idea/thoughts of why they got SLE. Men (p = 0.041) and persons with lower educational level (p = 0.038) were more common in this group, also reporting slightly better general health (p= 0.050) than the group that had explicit thoughts of why they got SLE. Age, disease duration or perceived SLE parameters did not differ between the two groups. The answers of patients' thoughts of why they got SLE were sorted into categories: genetics (n=82), stress/trauma (n=65), infections/immunization (n=36), hormones/treatment (n=28), lifestyle behavior (n=28), treatment/disease other than SLE (=26) and environmental factors (n=5). A majority (n=135, 69%) wrote one potential factor of why they got SLE, two factors were reported by 49 patients (25%), one patient wrote five potential reasons. It was exclusively answers from women that could be categorized as "hormones/treatment" or "treatment/diseases other than SLE", and only one man wrote a statement of stress/trauma" as potential trigger of SLE. Patients in the category "hormones/treatment" had shorter disease duration (p=0.029), higher perceived SLE activity (p=0.011) and worse general health (p= 0.002) compared to those that had no statement that could be sorted into the category. Only five patients reported environmental triggers and these perceived worse SLE health (p= 0.022) and worse general health (p=0.038). Patients who reported stress/trauma as potential triggers of SLE onset had in a lager extent university education (p= 0.027) than those who did not report stress/trauma as a trigger.

Conclusion: Beside genetic factors, a prominent number of patients in this study reported stress/trauma or hormones as important triggers for developing SLE. In these groups perceived health and educational levels had different patterns. Additionally, infections/immunization were perceived as triggers for SLE but without the same difference in perceived health or educational level. Further studies should extend these results and investigate patients' perceptions of triggers for SLE flares, and high disease activity, information which can enhance our understanding of factors that may contribute to important aspects of SLE and patients' perceptions of health.

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POS1191-HPR ULTRASONOGRAPHIC AND FUNCTIONAL CORRELATION OF THE FEET IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Ultrasound, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a chronic immune-mediated disease with involvement of various organs[1,2]. El 95% of patients with SLE have musculoskeletal involvement[1], most often in the form of arthralgias or non-erosive arthritis affecting mostly the hands and knees. A subgroup of patients with SLE, which is seen with increasing frequency, late develops a deforming arthropathy as a result of laxity of ligaments and peritendinous apparatus resulting in joint subluxations and tendon ruptures which is part of the accumulated damage of the disease. The foot is a heavily affected structure that may initially go unnoticed, but results in significant disability.

Objectives: To determine the relationship between inflammatory activity measured by ultrasound in metatarsophalangeal (MTF) and questionnaires of foot functionality, hand deformities and SLE activity.

Methods: A cross-sectional study was performed. Thirty-six subjects with a diagnosis of SLE in the Rheumatology Unit were consecutively recruited between March and June 2022. Inclusion criteria were: patients with SLE diagnosis according to EULAR/ACR 2019 criteria, with at least one year of evolution and age equal or older than 18 years. A Rheumatology nurse collected information on socio-demographic data, questionnaires and ultrasound scans. The SLE activity questionnaires completed were: SLEDAI and SLICC, quality of life: EQ-5D, foot function: FFI (Foot Function Index), FAAM (Foot and Ankle Ability Measures Questionnaire), FPI (Foot Posture Index). As for hand malformations collected were: Jaccoud arthropathy, non-reducible arthritis, z-finger, grommet finger, non-reducible arthritis, burst finger and gooseneck finger. A descriptive, bivariate and R-Pearson correlation analysis was performed.

Results: Thirty-six SLE patients (97.2% female) with a mean (SD) age of 49.31 (11.4) years with a range 23-66 years participated. A total of 30 patients (83.3%) showed at least one MTF synovitis, the most frequent being 2nd MTF left (58.8%) and right (44.4%), followed by 1st MTF right and left (41.7%). The number of patients with and without ultrasound synovitis, as well as the degree of synovitis and Doppler signal in each joint are shown in Table 1. A significant direct correlation was observed between inflammatory activity with Doppler in the 1st MTF of the right foot with the SLICC (r=0.439; p=0.007) and SLEDAI (r=0.608; p<0.001) questionnaire; as well as an inverse relationship between synovitis in the 1st toe of the right foot with the FPI questionnaire of the right foot (r=-0.340; p=0.040) (Table 2). Likewise, a significant relationship was observed between deformity in the hands with the synovitis of 5 right (p=0.042) and left (p=0.005) MTFs.

Conclusion: Ultrasound synovitis in MTFs is common in SLE patients and is associated with disease activity, some deformities and functionality.

Table 1. Description of inflammatory activity by ultrasound in metatarsophalangeal joints of 36 patients with SLE.

Variable	Grade 1 Synovitis	Grade 2 Synovitis	Grade 3 Synovitis	Doppler 1	Doppler 2
Rigth Foot					
1º MTF	3(8,3%)	13(36,1%)		2 (5,6%)	1 (2,8%)
2º MTF	8 (22,2%)	6 (16,7%)	1(2,8%)	2 (5,6%)	
3º MTF	11 (30,6%)	3 (8,3%)			
4º MTF	3 (8,3%)	4 (11,1%)	1 (2,8%)	1 (2,8%)	
5º MTF	7 (19,4%)				
Left Foot					
1º MTF	6(16,7%)	9 (25%)		1 (2,8%)	
2º MTF	10 (27,8%)	9 (25%)			
3º MTF	14 (38,9%)	2 (5,6%)	1 (2,8%)		
4º MTF	3 (8,3%)	6 (16,7%)	1 (2,8%)		
5º MTF	3 (8,3%)	1 (2,8%)			

Table 2. R-Pearson correlation analysis.

	Doppler 1st right toe	
	R Pearson	**P value**
SLICC	0,439	0,007
SLEDAI	0,608	<0,001
	Synovitis 1st right toe	
	R Pearson	**P valor**
Rigth FPI	-0,341	0,04

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POS1192-HPR ASSESSMENT OF KNOWLEDGE AND ATTITUDE IN MOROCCAN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Best practices, Patient information and education

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Background: Rheumatoid arthritis (RA) is a chronic, disabling condition that impairs quality of life.

Objectives: The objective of the study was to evaluate the knowledge and attitude of Moroccan patients with rheumatoid arthritis, and to determine the factors associated with them. Thus, it will be possible to set up a targeted education program for a better adherence to treatments.

Methods: This is a descriptive and analytical monocentric study of patients followed up for RA at Al Ayachi University Hospital, Sale, Morocco; and of patients who are members of the Moroccan Association for the fight against Rheumatoid Arthritis (AMP), from December 2021 to July 2022. The consent of the study population was free and informed. The interview questionnaire was developed by the team of rheumatologists and included sociodemographic data, the patients' knowledge about their disease, the treatments and their side effects, the follow-up and the patients' attitude toward self-medication. A score was indicated between 0 and 10 and represents the rate of correct answers per patient.

Results: We recruited 200 patients. The mean age was 55.1 ± 12.0 years, and the majority were women (91%). More than half of the population (57.5%) was illiterate and only 5.5% of the patients had a university education. ¾ of the population was urban (74.5%), and 93% were not working. 64.5% correctly identified the nature of RA as an autoimmune disease, and 26% correctly recognized that RA has a genetic predisposition. 58.5% of patients do not use corticosteroids over the counter against medical advice, 78% do not discontinue corticosteroids abruptly. Whereas 49.4% of patients undergoing biotherapy do not discontinue methotrexate against medical opinion. Moreover, the majority of patients (85%) had a favorable attitude for not accepting paramedic's opinions. Only about a third of patients (30%) knew that pneumopathy could be a possible complication of Methotrexate. 56% did not know what a biomedical drug is, 82.1% did not know that infection is an adverse effect of a biomedical drug, and 98% had no idea what a biosimilar is. The study revealed that 67% of the patients had a total score of correct answers more than 5.0, and the remaining 33% had a score between 2.0 and 4.5.

Conclusion: The level of knowledge of the disease and attitudes among Moroccan patients with RA was globally satisfying. The maintenance and improvement of this level of knowledge and the acquisition of good practices remain fundamental, in particular by diversifying the sources of information: awareness campaign by direct doctor-patient contact, multimedia supports and patients' associations.

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POS1193-HPR AN EVALUATION OF PATIENT EXPERIENCE OF THE BELFAST HEALTH AND SOCIAL CARE TRUST RHEUMATOLOGY ETANERCEPT BIOSIMILAR SWITCH PROGRAMME

Keywords: Patient information and education, Best practices, Patient reported outcomes

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Background: The Belfast Health and Social Care Trust Rheumatology department commenced a biosimilar switch programme in July 2019, switching patients from Etanercept (Enbrel) to biosimilar (Benepali). Patients attended a bespoke switch clinic providing education and training before proceeding with biosimilar switch.

Objectives: To evaluate patients' experience of the Etanercept biosimilar switch programme including understanding of, attitudes towards and satisfaction with the switch process.

Methods: A service evaluation of patients invited to undergo biosimilar switch was undertaken. Ethical approval was not required. Patients' views were surveyed with a web-based questionnaire via text message/QR code or completed via telephone by an evaluator entering responses into the survey-tool.

Results: 182/342 patients responded (53%). Most [171 (94%)] reported discussing biosimilars with a healthcare-professional, received written information [174 (96%)] and felt adequately informed [172 (95%)]. 140 (77%) thought the reason for switching was to save money and 83 (45%) understood biosimilars as "*A highly similar but not identical copy of a biologic medicine*". Most [118 (65%)] reported a shared decision-making process but 52 (28%) thought "*Rheumatology team alone decided*". Most [126 (69%)] had no reservations about biosimilars, but 53 (29%) were concerned about its effectiveness. Mean visual analogue score for confidence in the biosimilar was 7.51 (median 8, 1-10). 168 (92%) reported switching to biosimilar agent. 103/168 (61%) reported no problems afterwards. Switch-back rate was 13% (22/168). 95% (161/168) rated support provided afterwards as adequate or better. Mean visual analogue score for satisfaction was 7.84 (median 8, 1-10).

Conclusion: The Etanercept biosimilar switch programme was successful with high switch rates, high levels of patient confidence and satisfaction. Recommendations for future include improving the process of shared decision-making during consultation to ensure fully informed patient consent.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1194-HPR EFFECTS OF RAMADAN INTERMITTENT FASTING ON RHEUMATIC DISEASES

Keywords: Spondyloarthritis, Rheumatoid arthritis

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Background: Intermittent fasting (IF) during the month of Ramadan is one of the 5 fundamental pillars of Islam. Many patients report that IF improves or worsens their symptoms during this month, however, few studies had assessed the impact of IF on rheumatic diseases.

Objectives: The present study was conducted to assess the impact of IF during the month of Ramadan on rheumatoid arthritis (RA) and spondyloarthritis (SpA) activity.

Methods: The study included 71 patients with RA or SpA who fasted during Ramadan of 2022. Patients were assessed in 2 visits: 4 months before the month of Ramadan and the second after fasting at least after 15 days.

Results: RA group: 49 patients were included. IF was associated with a significant decrease in VAS (Visual analogue Scale) pain (5.76± 2.16 to 3.14 ±1.47) ($p < 0.001$), duration of morning stiffness (47,76 ± 39,68 minutes to 11,73 ± 11,11 minutes) ($p < 0,001$), number of painful joints (13,35 ± 5,43 to 7,36 ± 0,71) ($p<0.001$), number of synovitis(12,84 ± 6,715 to 3,04 ± 3,6) ($p<0.001$), CDAI (18.29 ± 4.74 to 12.35 ± 3.48) ($p<0.001$), SDAI (20.39 ±4.86 to 10.32± 4.68) ($p < 0.001$), DAS28 ESR (4.003 ± 0.1 to 2.55 ± 1.39) ($p < 0.001$), and DAS 28 CRP (4.06 ± 0.89 to 2.15 ± 0.77) ($p < 0.001$). SpA group: 22 were included. IF was associated with a significant decrease in VAS pain (5,14 ± 1,93 to 3,05 ± 1,70) ($p < 0.001$), number of painful joints (10,91 ± 5,63 to 1,27 ± 4,24) ($p<0.001$), number of synovitis (12,41± 6,71 to 1,73± 1,38) ($p<0.001$), BASDAI (4.92 ± 0.88 to 2.28 ± 0.81) ($p<0.001$), ASDAS CRP (4.44 ± 0.69 to 2.49 ± 1.29) ($p< 0.001$), and ASDAS ESR (4.12± 0.83 to 2.55± 1.39) ($p<0.001$).

Conclusion: IF was associated with significant improvement in RA and SPA activity. It is a promising non-pharmacological therapeutic option for patients with RA and SpA. Larger sample studies with control groups are needed to confirm these findings.

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POS1195-HPR REPRODUCTIVE HEALTH IN AUTOIMMUNE RHEUMATIC DISEASES FROM THE PATIENT'S PERSPECTIVE: QUALITATIVE STUDY

Keywords: Pregnancy and reproduction, Descriptive studies, Quality of life

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Background: Reproductive health (RH), family planning (FP), and managing a high-risk pregnancy should be prioritized in the rheumatology consultation to achieve shared and respectful decision-making [1]. Lack of knowledge of reproductive health and poor communication during the consultation may lead to increased pregnancy complications in patients with ARDs.

Objectives: To describe and analyze patients' experiences with ARDs on reproductive health issues at the clinic of pregnancy and reproductive health in rheumatic diseases (CEER) in Mexico.

Methods: A descriptive qualitative study was conducted using semi-structured interviews following an interview guide. Women of childbearing age, suffering from ARD, with different socioeconomic, cultural, disability, and sexual diversity conditions were invited to participate. The face-to-face or virtual interviews were recorded and transcribed. A multidisciplinary team of researchers performed an independent and blinded thematic analysis.

Results: Twenty-one patients participated. The age media was 28 years (yrs.), 38% were married, 28.5% were free union and 28.5% were single; 33.3% were pregnant, 38% were in the preconception stage with the desire of pregnancy and 28.5% women who have already had children. The main rheumatologic diagnoses were rheumatoid arthritis (47.6%), systemic lupus erythematosus (47.6%), and mixed connective tissue disease (4.7%). Three main themes were identified: medications related to pregnancy and lactation, contraceptive methods, and pregnancy planning (Table 1).

Table 1. Themes and narratives of patients with ARDs on reproductive health issues

Theme	Subtheme	Quote
Medications/ Breastfeeding	**Medication**	*But I don't know, uh, which medications to take, no";"… the truth, and I don't remember". (27 yrs., AR, pregnant).*
	Breastfeeding	*"I know that there is much more myth about (breastfeeding), … I feel that there is a lot of misinformation about it and that there are minimal medications that interfere with breastfeeding" (34 yrs., RA, pregnant).*
Contraceptive Methods	**Contraception**	*"I'm not sure, and I don't know which ones do interfere. I've never wondered if arthritis interferes with any method" (23 yrs., RA, pregnant).*
	Factors influencing choice	*"My mom helped me to make the decision"*"She told me, "If you want to use that one, that's fine" (20 yrs., SLE, postpartum).*
Pregnancy planning	**Planning**	*"Because first, you have to check that everything is okay in your health, they have to make sure that your disease is asleep, that nothing is altered, that everything is under control" (22 yrs., SLE/RA, reproductive age).*
	Heredability	*"Well, there is a certain percentage, according to what the geneticist explained when I went to her office. Yes, I knew something about it because my mother has rheumatoid arthritis. … I don't think it is a fact that I will pass it on to my baby". (34 yrs., RA, pregnant).*
	Accompaniment	*"Well, that they have all the information about both arthritis and pregnancy because, for me at least, it gives me a lot of comfort to be in the clinic because I know that I have this communication…y then not being with one doctor and then with another and explaining to one what the other one told me. (23 yrs., RA, pregnant).*

All quotes were extracted from interviews conducted in Spanish. Quotes were further translated to English.

Conclusion: The experiences of patients with rheumatic diseases were diverse, and the amount of biomedical knowledge of RH issues was limited in FP, decision-making, and prenatal or postnatal care. The patients recognized the relevance of a multidisciplinary team led by their rheumatologist to generate confidence in the quality of information and allow better decision-making according to patients' beliefs, preferences, and reproductive rights.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1196-HPR WHAT OUTCOMES MATTER TO PATIENTS WITH FOOT AND ANKLE DISORDERS IN RHEUMATIC AND MUSCULOSKELETAL DISEASES? FINDINGS FROM A QUALITATIVE SYNTHESIS AND SCOPING REVIEW OF THE LITERATURE

Keywords: Qualitative research methods, Systematic review, Patient reported outcomes

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Background: Foot and ankle involvement is common and debilitating in rheumatic and musculoskeletal diseases (RMDs), but outcomes in research and clinical practice are often inconsistently measured and may not be meaningful to patients. Outcome inconsistency contributes to lack of high-quality evidence to determine the effectiveness of foot and ankle treatments [1].

Objectives: To understand what outcomes are important to patients living with foot and ankle disorders in RMDs through an exploration of symptoms and impact, and to establish how these compare to outcomes measured in existing research studies.

Methods: A qualitative systematic review of interview and focus group studies involving patients with foot and ankle disorders in RMDs (inflammatory arthritis, osteoarthritis, crystal arthropathies, connective tissue diseases and musculoskeletal conditions in the absence of systemic disease) was undertaken. A scoping review of clinical trials and observational studies comparing conservative, pharmacological or surgical interventions for these disorders was also performed. Seven databases (Ovid Embase; Ovid MEDLINE; CINAHL; Psycinfo; Cochrane Database of Systematic Reviews; CENTRAL; PEDro) were searched from inception to March 2022. All data from the results sections of qualitative studies were extracted, coded and synthesised to develop themes, whilst outcomes measured in quantitative studies were extracted and tabulated. Confidence in the qualitative findings was assessed using the GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative research) approach, incorporating Critical Appraisal Skills Programme quality appraisal [2]. Patient and public involvement contributors were involved throughout both reviews, in the design, analyses and discussions about the findings.

Results: Thirty-four studies were included in the qualitative review, whilst 150 studies (n=83 randomised trials) were included in the scoping review. The majority of studies included patients with foot and ankle disorders in rheumatoid arthritis (n=18 qualitative studies, n=43 quantitative studies) or osteoarthritis (n=5

qualitative, n=96 quantitative). Six themes were generated from the qualitative synthesis: pain, change in appearance, activity limitations, social isolation, work disruption and emotional distress. Themes were closely related; foot/ankle pain and appearance changes (e.g. deformity and subsequent limitations in footwear and clothing) affected emotions and led to restrictions in physical, social and work activities, which caused further distress. Based on grading of the evidence, we had moderate confidence that most of the review findings represented the experiences of patients with foot and ankle disorders in RMDs. Foot/ankle pain (n=117 studies) and foot/ankle function (n=102 studies) were the most commonly measured outcomes identified in the scoping review; social function, occupational function and emotional status were rarely reported.

Conclusion: This is the first study to explore patients' experiences of foot and ankle disorders in RMDs alongside outcomes currently measured by clinicians and researchers. Our findings highlight that these disorders impact on multiple areas of patients' lives, both physically and psychologically. Pain was the predominant symptom experienced by patients and the most commonly measured outcome in existing research, but other outcomes that are important to patients should not be overlooked by clinicians and researchers. Our findings can guide patient-centred care and measurement of outcomes within clinical practice and future research.

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POS1197-HPR HEALTH-RELATED MOBILE APPLICATIONS IN RHEUMATOID ARTHRITIS: WHAT ARE THE PATIENTS' EXPECTATIONS?

Keywords: Self-management, Rheumatoid arthritis, Telemedicine

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Background: The use of mobile phone applications for the management of rheumatic diseases (RD) has grown significantly these past few years [1]. Nevertheless, the success of these applications requires identifying the educational needs and interests of patients with RD.

Objectives: The purpose of our study was to investigate the expectations of rheumatoid arthritis (RA) patients regarding mobile applications in managing their disease.

Methods: We conducted a cross-sectional survey in our rheumatology department including RA patients, fulfilling the ACR/EULAR 2010 criteria. They were invited to respond to a questionnaire related to the utility of a mobile application in managing their disease. We evaluated their point of view on the desired functions of a smartphone app, the required content as well as the preferred design.

Results: The study included 40 RA patients: 36 females (90%) and 4 males (10%). The mean age was 52.25±14.4 years [21-78]. The mean disease duration was 11.97±6.69 years [1-29]. Two items were considered important and concerned the ability to contact the doctor when necessary and discuss their symptoms (72%), as well as the ability to check laboratory results (72%). Other features listed as useful were reminder date of clinic appointments (65%), and reminder of hours' medication intake (60%). Nearly half of the patients expected the app to include educational videos (52%), exercise strategies to feel better (52%), ways to improve lifestyle habits (sports, sleep, professional activity, and dietary habits) (52%) and information about alternative treatments (55%). When asked about "what kind of health-related information should be tracked or monitored using a smartphone application?", the most requested data to monitor concerned disease symptoms tracking (45%) using a validated measures of disease activity (43%), pain and fatigue (52%) using pain and general well-being questionnaires (41%) as well as arthritis-related functional scores (42%). Regarding the design, the application should be simple (68%), quick (63%), with clear font (44%). Moreover, it shouldn't require too much battery power (42%), and include frequent recall notices (42%).

Conclusion: Our study showed that RA patients prioritized information about medications and monitoring their disease. Surprisingly, the availability of lab results was considered an important component of the app. Identifying these needs will be the first step to ensure the success of the mobile phone applications.

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POS1198-HPR PREVALENCE OF INFLAMMATORY BACK PAIN IN PRIMARY SJOGREN'S SYNDROME IS INCREASED AND ASSOCIATED WITH ACUTE AND STRUCTURAL CHANGES OF THE SACROILIAC JOINT

Keywords: Sjögren syndrome, Pain, Spondyloarthritis

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Background: An increased prevalence of axial articular manifestations has recently been reported in primary Sjögren's syndrome (pSS).[1]Radiologic findings associated with inflammatory back pain (IBP) are not well documented in pSS patients.

Objectives: To assess the prevalence of IBP and its association with magnetic resonance imaging (MRI) detected acute inflammatory and structural changes of sacroiliitis in pSS patients with IBP.

Methods: In this cross-sectional study, consecutive pSS patients fulfilling ACR/EULAR classification criteria and age- and sex-matched healthy controls (HC) were screened for IBP according to the Calin, Rudwaleit and ASAS IBP criteria.[2] Sacroiliac MRI imaging of patients with IBP was performed and SpA features in the ASAS Classification Criteria for Axial Spondyloarthritis (SpA) were questioned. Two radiologists assessed sacroiliac joint MRIs (SIJ/MRI) for the cut-off values for a possible diagnosis of axSpA using ASAS defined lesion definitions. Cut-off values were defined previously by Maksymowych et al.[3]. The First questionnaire was used to evaluate the relationship between fibromyalgia and back pain.[4]

Results: A total of 202 pSS patients meeting the ACR/EULAR classification criteria and 124 healthy controls were included. The mean age [mean (SD)=52.8 (11.9)] and sex distribution in pSS (female/male: 198/4) was similar to HC [51.5 (9.2), (p=0.3) and female/male: 119/122? 5, (p=1), respectively] IBP was more prevalent in pSS (for pSS n(%): 51 (25.2), for HC n(%): 11 (8.8), p<0.001). SIJ/MRI was available in 49 patients with IBP. The mean (SD) age of onset of IBP was 33.6 (5.8). The mean (SD) duration of the IBP of the patients with pSS was 18.9 (10) years. pSS patients with IBP had significantly higher scores of the First questionnaire (patients with IBP mean (SD): 3.9 (1.7), patients without IBP: 2.8 (1.9), p=0.001). A total of 12 (24.5%) patients could meet the an axSpA diagnosis with a PPV of ≥95% as defined by Maxymowych et al. [3] Of these 12 patients, two with edema in the sacroiliac joint, nine with erosions, and four with fat metaplasia could be diagnosed as axSpA based solely on SIJ/MRI findings.

Conclusion: Low back pain meeting the IBP criteria is highly prevalent in pSS, and a quarter of these patients may have a radiologic diagnosis of axSpA. However, axSpA-associated features are absent in most patients, and very few meet the ASAS classification for axSpA. The presence of increased fibromyalgia may lead to an over-interpretation of radiologic features in the majority of these patients.

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Table 1. AxSpA associsted clinical and imaging features of pss patiens with an SIJ/MRI diagnosis of AxSpA

AxSpA classified according ASAS, n (%)	2 (16.7)
ASAS defined sacroiliitis, n (%)	2 (16.7)
Psoriasis, n (%)	0 (0)
Uveitis, n (%)	0 (0)
HLA-B27 positivity, n (%)	1 (8.3)
Heel enthesitis, n (%)	4 (33.3)

(AxSpA: Axial Spondyloarthritis)

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Disclosure of Interests: None Declared.

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HPR Service developments, innovation and economics in healthcare

POS1199-HPR **IMPROVING THE UPTAKE OF ELECTRONIC PATIENT REPORTED OUTCOME MEASURES IN A SPECIALISED AXIAL SPONDYLOARTHROPATHY CLINIC**

Keywords: Patient reported outcomes, Spondyloarthritis, Outcome measures

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Background: Sheffield Teaching Hospitals (STH), UK, has a specialised axial spondyloarthropathy (axSpa) clinic run by a rheumatology consultant and physiotherapist with special interest in this area. BASDAI and BASFI patient reported outcome measures are used to assess disease activity and response to treatment, in line with national guidelines. STH has invested in MyPathway (MP), an electronic patient messaging system used for patient information, appointments and electronic patient reported outcome measures (ePROMs). The data can also be viewed at a system level on a clinician dashboard. Prior to 2020 the uptake of ePROMs was low in the axSpa clinic. The move primarily to telephone consultations in March 2020, due to the COVID-19 pandemic, created an opportunity for increasing the use of MP for ePROMs collection to enable improved remote monitoring of patients with axSpa.
Objectives: This quality improvement project aimed to increase the use of electronic BASDAI and BASFI (ePROMs) in the axSpa clinic.
Methods: A multi-pronged approach has been taken since March 2020 to increase ePROMs completion and improve their use. Each appointment was used as an opportunity to discuss and recruit patients to MP. Clinicians invited each patient to join MP and sent them a link after their appointment. QR codes were then added to all rheumatology patient letters encouraging patients to register. A pathway was set up that automatically sent a prompt to patients registered on MP to complete their BASDAI and BASFI questionnaires prior to clinic appointments. Clinicians began logging into MP to view scores during appointments to provide patients with real-time feedback. A mixed methods approach was used to assess the uptake of ePROMs over time. We tracked MP registration rates and BASDAI completion rates as the key outcome measures, using a run chart to assess special cause variation. We undertook a patient focus group to explore attitudes towards ePROMs, key barriers and opportunities for further improvement.
Results: The total number of axSpa patients seen in the specialised clinic (named LADAS) who have registered with MP has increased from 56 (35.9%) in January 2019 to 200 (58.9%) in September 2022. There has been an improvement in the BASDAI completion rate, with 80% of patients completing more than one BASDAI in 2022, compared to 24% in 2019, as illustrated on a run chart (Figure 1). Patients can complete BASDAI forms sent to them in a previous month, therefore the completion rate some months exceeds 100%. In a dedicated focus group, patients reported that ePROMs were generally more convenient, and provided a useful record to refer back to. This could be further improved by development of a graph function to view scores over-time and the ability for patients to complete a questionnaire between appointments when they feel their disease is more active. A key theme for improving the use of ePROMs was the need for more discussion about their utility and around individual patient's scores. There is concern that the BASDAI and BASFI scores are arbitrary and lack nuance, and that the importance of these scores at an individual patient level is not clear. This may be rectified by more discussion with clinicians in appointments, to add meaning to these scores. There was also concern that sleep and other generic health measures are not covered in the BASDAI or BASFI. The EQ-5D, a generic questionnaire, is also sent to axSpa patients, but there seems to be a lack of patient awareness regarding it. There is an appetite to improve and standardise the amount of patient information accessible on MP, for example disease information and links to patient support groups.
Conclusion: There has been a clear improvement in the completion of ePROMs in the dedicated axSpa clinic at STH, over the last three years. Patient feedback has highlighted key areas for further improvement to maximise the potential of ePROMs, including more discussion around PROM scores to increase understanding and add individual patient meaning and nuance.

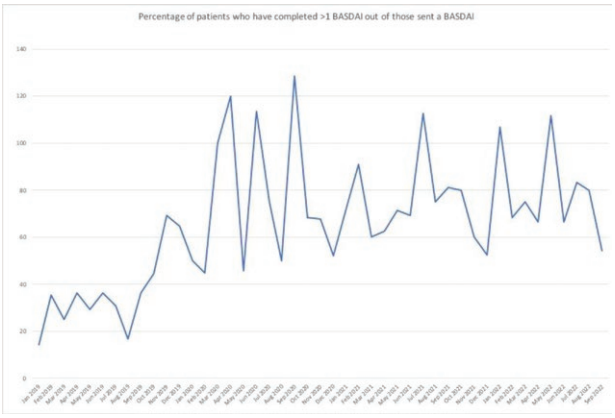


Figure 1.

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POS1200-HPR **IL-17 OR TNF INHIBITORS - REAL WORLD IMPACT OF SHARED DECISION MAKING IN A NURSE LED BIOLOGICS SERVICE**

Keywords: bDMARD, Spondyloarthritis, Real-world evidence

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Background: Since the availability of anti TNF biosimilars and the push from reimbursement panels to use them first line, real world data regarding therapeutic choice in biologic naive population is sparse.
Objectives: Evaluate the reasons for nurse led service choosing IL17 antagonists in biologic naïve SpA patients, in a shared decision making model, despite the availability of cheaper anti TNF biosimilar.
Methods: We conducted a retrospective analysis of our electronic register for people with PsA and AS from 1994 up to and including April 2022 at our university teaching hospital. We had access to full patient records including details on co-morbidities, drugs and disease management. All patients were evaluated in biologics service led by clinical specialist nurses.
Results: PsA. 90 patients were prescribed Secukinumab since its availability in the UK. Mean age was 51 yrs (24-80) and 56 (62%) were women. All were prescribed since the adoption of Adalimumab biosimilar. Median duration of therapy was 551 days (62-1284). Mean TJC and SJC were 8.14 (1-64) and 3.15 (1-57) at initiation which improved at six months to 6.28 (1-46) and 2.77 (1-18) respectively. 24 (27%) were biologic naïve; 18 had it for better efficacy (six had axial disease, four with enthesitis and eight with concomitant moderate to severe psoriasis) and six for relative anti TNF contraindications including three with treated solid organ neoplasms, one with BMI>35 and two for concurrent chronic infections including HIV. AS. 47 patients were prescribed Secukinumab. Mean age was 54 (27-79) and half were women. Median duration of therapy was 679 days (51-1154). Mean BASDAI was 3.3 (0-9.2) at initiation which improved to 2.1 (0-7.5). 11 (23%) were biologic naïve; five had it for better efficacy and six for relative anti TNF contraindications including three with treated cancers, two with latent TB and one for MS.
Conclusion: To our knowledge this is the first dedicated retrospective review of a large real world spondyloarthritis cohort evaluating reasons for biologic choice. Nearly a quarter of patients were prescribed Secukinumab prior to cheaper adalimumab biosimilar despite it being commissioned first choice agent in the region. Clinicians including nurse specialists chose it for better efficacy in various SpA domains. Relative contraindication to anti TNF drugs, which would not have been considered significant in the past, was the second reason. Efficacy and safety outcomes were comparable to other biologics. This confirms that shared decision

making process demands flexibility and limiting choice goes against clinical acumen and patient preference. Opting only for lower drug acquisition tariff is unlikely to be cost effective as the disease progresses whilst patients struggle with inappropriate prescription and thus delay biologics which are more likely to be efficacious and retained longer. Hence there is an urgent need to review prescribing guidelines to allow earlier employment of appropriate advanced therapies in the treatment paradigm with significant benefits to both patients and the health economy.

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POS1201-HPR ADVANCED PRACTICE RHEUMATOLOGY NURSING FOR PATIENTS WITH GOUT TARGETS URATE, KNOWLEDGE, AND LIFESTYLE TO ENHANCE CHRONIC DISEASE OUTCOME

Keywords: Gout, Patient information and education, Treat to target

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Background: Gout is the most common chronic inflammatory arthritis worldwide and the only curable. Yet, gout care remains suboptimal despite evidence of the benefits of a treat-to-target approach to normalise urate levels. The efficacy and cost effectiveness of nurse led care in this treat-to-target strategy has been well recognised (Fuller, 2020)

OBJECTIVES:

- To implement a patient centred treat-to-target urate lowering strategy within a holistic health promotion, secondary prevention model of advanced practice nursing.
- To engage, raise awareness and educate patients about:

i) the short and long-term health implications of hyperuricaemia and
ii) the merits of self-management strategies to improve their health outcome

Methods: With stakeholder agreement a gout clinic was established. The Making Every Contact Count (MECC) framework was used to implement the treat-to-target approach per the EULAR (European Alliance of Associations for Rheumatology) recommendations for the management of gout. Making every contact count, grounded in a behavioural change approach, promotes brief intervention therapy to support lifestyle behaviour change to make each routine contact with patients count in terms of chronic disease healtcare (Meade, 2022: Gwinnutt, 2023). The 12-question Gout Self-Management Knowledge Questionnaire was completed at baseline, followed by a nursing educational intervention through a planned gout programme and repeated at final visit (Fields, 2017).

Results: To date 102 patients have attended the clinic. Baseline and final clinic assessments are available for 42 patients. The number of clinic reviews per patient was 6. Thirty-five (83%) were male; mean age was 61 years (range 29-91); mean disease duration was 9 years (range 1-40). The mean time to diagnosis from symptom onset was 4 years (range 0-29). At baseline, 17 (40%) reported a family history and past experience of a urate-lowering therapy. The reported mean number of flares per-annum was 1-2 (n=20); 3-5 (n=17); >6 (n=5); 20 patients (48%) had podagra; 14 patients (33%) had tophi. Urate levels improved by 76%, falling from a baseline of 397 µmol/L to 301 µmol/L at final visit; an 83% improvement was seen in the Gout Self-Management Knowledge Questionnaire. The subjective numeric global health score (0-10, where 10 represents worst health status) showed a median score of 1.5 at baseline and 1 at final visit.

Conclusion: Findings demonstrated 1) normalisation of urate to target levels, 2) an improvement in patients' insight and 3) a parallel upgrading in patients reported global health score.

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POS1202-HPR ADDRESSING AXSPA DIAGNOSTIC DELAY BY IMPLEMENTATION OF ASYNCHRONOUS TELEMEDICINE AND MEDICAL STUDENT-SUPPORTED VISITS

Keywords: Spondyloarthritis, Health services research, Telemedicine

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Background: Axial Spondyloarthritis (axSpA) has one of the longest diagnostic delays in rheumatology [1]. Telemedical solutions and integration of medical students to support routine care may be promising to overcome current limitations and accelerate axSpA diagnosis and treatment.

Objectives: We aimed to test a novel diagnostic pathway and asynchronous report-based diagnostic assessments for patients with suspected axSpA.

Methods: 40 patients with chronic back pain for more than 3 months completed a pre-appointment visit (T-1) with a medical student prior to their planned actual first visit (gold standard, T0) (Figure 1). Findings were discussed with a rheumatologist to finalize diagnostics and initiate therapy. Patients also completed two digital symptom checkers (SC), started to continuously report ePROs (BASDAI) via an app and received upper-arm self-sampling devices to self-collect capillary blood at home for remote C-reactive protein (CRP) and HLA-B27 analysis. Two additional students and three additional tele-rheumatologists reviewed SC, laboratory and imaging results to investigate an asynchronous telemedical diagnostic approach. Acceptance was measured using the net promoter score (NPS) [2]. For this, patients were asked to rate on an 11-point scale ranging from 0 ('Very unlikely') to 10 ('Very likely') how likely they would recommend the applications to others. To calculate an overall NPS, the percentage of detractors (rating 0-6) was subtracted from the percentage of promoters (rating 9 or 10).

Results: N=36 patients completed the study. AxSpA was confirmed in 17 and ruled out in 19 cases. The student visit helped to complete diagnostic evaluations prior to the actual first visit and the diagnostic delay (T-1,T0) was significantly reduced by about two months (Med (IQR), 55.5 (67.3) days, p <0.0001). The diagnostic accuracy (DA, axSpA yes or no) for the two SC Ada and bechterew-check was 58% and 47%, respectively. The student with patient contact reached a DA of 86%, the mean DA ± SD of the students who did not have patient contact (asynchronous decision) was 75% ± 0%. Results of the three tele-rheumatologists showed a high sensitivity (98% ± 3%) and diagnostic accuracy (89% ± 3%). Imaging results turned out to be an essential part for asynchronous decision making, as they significantly increased the sensitivity of the decision of all three physicians. Unsupervised at-home self-collection of capillary blood was successfully conducted by 80% of the patients. For the first time, accuracy of self-sampled HLA-B27 was demonstrated. Patients expressed high acceptance regarding the pre-appointment student visit, self-sampling and ePRO, with NPS of +62%, +36% and +31%, respectively.

Conclusion: To our knowledge, this is the first study exploring the potential of self-sampling, medical students and asynchronous assessments to accelerate axSpA diagnosis. The investigated elements were well accepted among patients and significantly reduced axSpA diagnostic delay.

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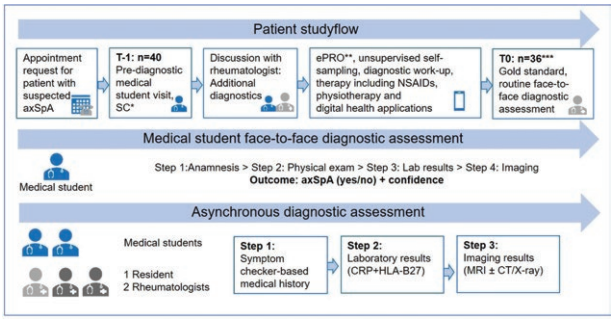


Figure 1. Study Flow

* SC, symptom checkers; Ada (www.ada.com) and OptiRef questionnaire (www.bechterew-check.de),

** BASDAI and flare questionnaire each two weeks,

*** Drop-outs: n=3 due to missed appointments, n=1 due to overburdening with the technical requirements

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POS1203-HPR EVALUATION OF TELENURSING FOLLOW-UP IN A COHORT OF STABLE/LOW DISEASE ACTIVITY PATIENTS WITH INFLAMMATORY ARTHRITIDES: A FEASIBILITY STUDY

Keywords: Telemedicine, Nursing, Inflammatory arthritides

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Background: Periodic follow-up (FU) is necessary for patients with Rheumatic Diseases (RDs). In the case of a stable clinical condition or low disease activity, FU can be carried out also by rheumatology nurses (RNs). Recent studies focusing on FUs led by RNs either in Rheumatology Clinics and with Telenursing (TN), showed promising results in terms of outcomes, cost reduction and users' satisfaction.

Objectives: To evaluate the feasibility of a Telenursing FU in a Rheumatology Centre in Florence, Italy.

Methods: In this pilot study, patients with stable inflammatory arthritis or low disease activity were contacted, after their first visit, through TN (T0) and then assessed during the following in-person visit (V12) by RNs for treatment adherence, for pain, for mental and physical health, for workability, for perception of disease activity and satisfaction concerning the TN service.

Results: Out of 27 interviewed patients, 59.3% (n=16/27) was affected by Rheumatoid Arthritis (RA), 18.5% (n=5/27) by Spondyloarthritis (AS), 14.8% (n=4/27) by Psoriatic Arthritis (PsA) and 7.4% (n=2/27) by Juvenile Idiopathic Arthritis. The mean age was 57.5±13.1 (M± DS) years and the treatment adherence level was optimal. 11.1% (n=3/27) of patients was referred for medical consultation because of the urgent clinical situation assessed by the RNs according to the clinical multidisciplinary checklist. After specialist consultation, 1 patient was revalued in presence for a transient ischemic attack; 1 patient was contacted by the rheumatologist following independent discontinuation of methotrexate therapy; 1 patient was redirected to urgent dermatology consultation because of a suspected cutaneous drug reaction. During the TN period (12 months), 33.3% (n=9/27) of the patients contracted SARS-CoV-2 infection and 11.1% (n=3/27) contracted urinary or upper respiratory tract infections. RA patients showed a mean Rheumatoid Arthritis Impact of Disease-RAID score of 2.4 at T0 and 2.5 at V12 (Range 0-10); AS patients showed a mean Assessment of Spondyloarthritis International Society-ASAS score of 0.3 in both periods and PsA showed a mean Psoriatic Arthritis Impact of Disease-PSAID score of 0.7 and 0.8 at T0 and V12, respectively. Among RA, AS and PsA patients, as a pain score of 3 was recorded in both periods. In order to attend the in-person FU visit, 68.4% (n=13/19) of the patients took work leave. 37% (n=10/27) of them waited 40.9±18.6 minutes at V12 control. The average distance between the Rheumatology Centre and patients' home was 29.3±25.6 km. 15.4% (n=5/13) of the respondents did not own a car and 23.1% (n=3/13) was accompanied to visit by their caregiver. All the included patients expressed high satisfaction for the TN service, corresponding to 5 point Likert scale.

Conclusion: The data show that TN FU is a valuable model for maintaining an adequate level of therapeutic adherence, reducing the travel time and working day loss, intercepting remotely clinical issues, as well as registering a high level of user acceptance and satisfaction. Further studies on larger samples are needed to confirm our findings.

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Disclosure of Interests: None Declared.

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POS1204-HPR PREVALENCE OF SATISFACTORY REPLACEMENT OF IN-PERSON RHEUMATOLOGY CONSULTATIONS WITH TELECONSULTATIONS IN A BRAZILIAN TELEHEALTH SYSTEM - THE TELESSAÚDERS-UFRGS EXPERIENCE

Keywords: Telemedicine, Quality of care, Health services research

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Background: TelessaúdeRS-UFRGS is a university-based telemedicine project in Brazil that receives support and resources from Brazil's Ministry of Health, and the State Health Department of Rio Grande do Sul. Since 2013, TelessaúdeRS has provided a synchronous toll-free telephone teleconsulting service that supports primary health care (PHC) physicians across the country. Family medicine, internal medicine, and rheumatology specialists answer clinical inquiries using the best evidence. (1)

Objectives: Describe the prevalence of specific rheumatology topics, recommendations provided in teleconsultations, and the change in the utilization pattern of this service over time.

Methods: In this cross-sectional study, we retrospectively extracted data from the TelessaúdeRS-UFRGS database. Teleconsultations were included from September 21, 2018, to January 25, 2022, addressing rheumatologic topics. Teleconsultations with incomplete data were excluded. Teleconsulting involves the discussion of clinical cases between patients' physicians and a rheumatologist or a trained PHC physician. All teleconsultations are registered in the TelessaúdeRS-UFRGS database. The teleconsultant formulates a diagnostic hypothesis, and a decision (based on referral protocols) is taken: referral to rheumatology, emergency care, stay in PHC or re-evaluation after a treatment course, or diagnostic tests. Criteria for referral to a rheumatologist were: diagnosis or high suspicion of systemic inflammatory disease, diagnosis still in doubt after re-evaluation, or non-inflammatory rheumatic diseases refractory to treatment. Besides the consultant's recommendation, the assistant doctor has the final decision about the referral. Chi-square test was used for statistical analysis.

Results: A total of 7715 teleconsultations were eligible for analysis after excluding 39 cases with incomplete data. The most frequent diagnostic hypotheses generated during teleconsultations were rheumatoid arthritis (RA), non-specific arthralgia/arthritis, and systemic lupus erythematosus (Table 1). Fibromyalgia, gout, and osteoarthritis were other diagnostic hypotheses commonly considered. Almost one-third (n=2219; 29% of total consultations) of the discussions referred to patients already waiting for rheumatology consultation, and teleconsulting replaced the in-person specialist evaluation in 32% (n=722) of these cases. Of the 5496 that were not waitlisted, 1369 (24.9%) were referred after teleconsulting. In total, 54.9% of the teleconsultations decided that the patients could be adequately managed in the PHC. The Figure 1 describes the utilization pattern of the rheumatology teleconsulting service during the time frame of this study. The utilization of the teleconsulting service increased significantly, and the proportion of patients referred to in-person rheumatology consultations reduced over the last years (P<0.001).

Table 1.

Diagnostic hypotheses formulated after teleconsulting, n=7715 (%)	
Rheumatoid arthritis	1665 (21.6%)
Undifferentiated arthralgia/arthritis	1298 (16.8%)
Systemic lupus erythematosus	830 (10.8%)
Fibromyalgia	570 (7.4%)
Laboratory test	547 (7%)
Gout	466 (6%)
Spondylarthritis	432 (5.6%)
Osteoarthritis	326 (4.2%)
Other connective tissue disease	431 (5.6%)
Other soft tissue diseases	396 (4.5%)
Osteoporosis	153 (1.9%)
Others	601 (7,7%)

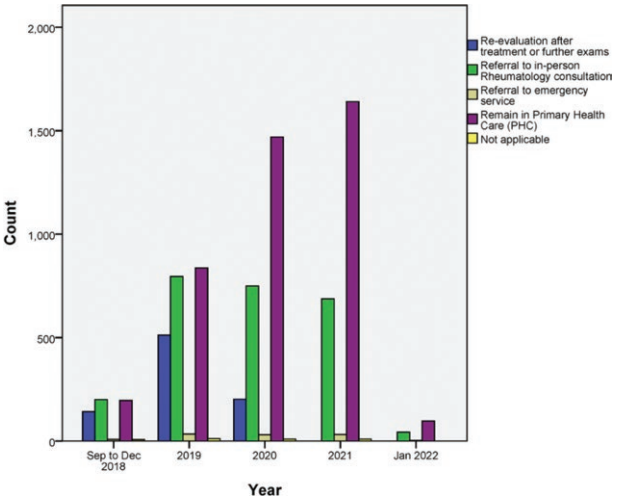


Figure 1.

Conclusion: Prevalent rheumatic diseases, especially RA, are frequent reasons for using teleconsulting support in our country. According to our study, after guidance, the PHC physician was considered able to manage most cases in rheumatology. This reduced the waiting list by approximately one-third. There was a progressive increase in teleconsultations over the years, but the proportion of patients referred to rheumatology reduced over time.

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HPR Professional education, training and competencies

POS1205-HPR **PRESCRIBING TRENDS OF METHOTREXATE IN RHEUMATOID ARTHRITIS: A TUNISIAN SURVEY**

Keywords: Disease-modifying drug (DMARDs), Rheumatoid arthritis

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Background: Methotrexate (MTX) remains the first line disease modifying antirheumatic drug (DMARD) in the course of treatment for rheumatoid arthritis (RA). There are wide variations in prescribing pattern among rheumatologists.

Objectives: We aimed to determine the prescribing practices of MTX by Tunisian rheumatologists.

Methods: We conducted a cross-sectional study including Tunisian rheumatologists. An online survey composed of 18 questions via Google Drive Forms was designed to analyse the prescription trends of MTX in RA patients.

Results: The online questionnaire was sent to 184 rheumatologists, 66 of whom (35.8%) responded. The majority of rheumatologists initiated MTX at therapeutic doses: 10 mg/week (34.8%) and 15 mg/week (36.3%). Ninety-eight percent of rheumatologists preferred the oral route during the initiation of MTX. Fifty-nine percent of rheumatologists advised their patients to take MTX on an empty stomach. Doctors preferred injectable MTX in case of digestive intolerance (96.9%) or in case of lack of efficacy (48.4%). Regarding the MTX escalation strategy, the majority of rheumatologists followed a conventional strategy with an increase in doses in steps of 2.5 mg (65%) and 5 mg (35%) every 02 (16.6%) to 04 (42.4%) weeks. The optimal dosage of MTX was reached after 08 and 12 weeks in 27.2% and 59% of cases, respectively. Sixty-eight percent of rheumatologists split doses of MTX, 60% of whom from a dose of 15 mg/week. The time interval between the two doses was 06 (27.2%) to 12 hours (27.2%). All rheumatologists systematically associated folic acid with MTX. The average dose of folic acid prescribed was 10 mg/week (72.7%). The doctors questioned advised patients to take acid folic 48 hours after MTX 51.5%. The maximum dose of MTX prescribed by rheumatologists before switching to biological (b) DMARDs was 20 mg/week (60.6%). In case of use of bDMARDs, 63.6% of doctors decreased the dose of MTX to 10 mg/week. Once remission is reached, 34.8% of doctors continued MTX at the same dose while 62% of them gradually reduced the dose (decrease of 2.5mg every 02 weeks in 27.2% of cases and 5 mg every 08 weeks in 34.8% of cases).

Conclusion: Our study showed that the majority of Tunisian rheumatologists prescribe MTX according to international recommendations. Indeed, the current therapeutic strategy for RA encourages powerful and effective treatment early in the course of the disease.

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Scleroderma, myositis and related syndromes

POS1206

SARCOPENIA IS A MARKER OF MUSCLE DAMAGE ASSOCIATED WITH DISEASE SEVERITY AND DISABILITY IN PATIENTS WITH INFLAMMATORY MYOPATHIES

Keywords: Biomarkers, Myositis, Sarcopenia

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Background: Inflammatory myopathies (IM) are autoimmune diseases characterized by muscle inflammation and weakness. Damage is a prognostic factor in IM, but its assessment in daily clinical practice represents an unmet need.
In other settings than IM, a low muscle mass and strength (referred as sarcopenia) have been linked with disability, decreased quality of life and increased mortality. Sarcopenia has never been studied in IM.
Objectives: To determine the prevalence and clinical significance of low muscle mass, strength and sarcopenia in inactive or low-activity IM.
Methods: Adult IM patients according to 2017 ACR/EULAR classification criteria with disease duration ≥12 months, creatine kinase (CK) serum level <500 U/l, >6-month stable medication and Physician Global Activity ≤3/10 were prospectively enrolled. Healthy age and sex-matched volunteers were enrolled as controls. Activity and damage were assessed according to the IMACS scores. Appendicular lean mass (ALM) and strength were measured by dual-energy X-ray absorptiometry (DXA), hand-held dynamometer and manual muscle testing (MMT). Physical performance, disability, respiratory volumes and maximum inspiratory (Pimax) and expiratory pressures (Pemax) were assessed. Sarcopenia was diagnosed according to the EWGSOP consensus[1]. Several myokines were measured in the blood.
Results: Forty IM patients (27 females, 68%) with an average age of 59.9 years (±14) and 30 healthy age and sex-matched volunteers (19 females, 63%) were prospectively enrolled. Eight patients suffered from dermatomyositis (DM), twelve from immune-mediated necrotizing myopathy (IMNM), eleven from anti-synthetase syndrome (ASS), nine from scleromyositis (SM) since 4.6 years (2.9 - 8.4). At the enrolment, MMT-8 was 140/150 (135.3-147), MMT-12 was 213/220 (203.3-216.8), CK were 122 U/l (87.5-195.5). ALM correlated with MMT-8 (r=0.4, p=0.01), MMT-12 (r=0.5, p=0.004), grip strength (r=0.3, p=0.05), 6-minute walking distance (6mWD) (r=0.6, p=0.0002), time to drink a 20 centilitre cup (r=-0.5, p=0.001), vital capacity (r=0.5, p=0.02), Pimax (r=0.6, p=0.03) and Pemax (r=0.6, p=0.04), severity (r=-0.5, p=0.003), extension (r=-0.4, p=0.007) and global (r=-0.6, p=0.0001) damage. Grip strength correlated with MMT-8 (r=0.5, p=0.003), MMT-12 (r=0.4, p=0.005), ALM (r=0.3, p=0.05), 6mWD (r=0.4, p=0.02), global damage (r=-0.4, p=0.008), HAQ score (r=-0.3, p=0.04). Seven out of forty myositis patients (17.5%) were sarcopenic (vs 0% in the control group). They suffered from IMNM (57% vs 24%), DM (29% vs 18%) and SM (14% vs 24%). No patient suffered from ASS (0% vs 33%). Sarcopenic patients had history of severe muscle involvement: loss of walking ability (vs 21%, p=0.0002), higher maximum CK values (5998 U/l (3488-6500) vs 1636 (626-5000), p=0.07), respiratory muscles impairment (29% vs 3%, p=0.02) and myocarditis (43% vs 3%, p=0.001); and they more frequently required intravenous immunoglobulins (86% vs 33%, p=0.03), plasmapheresis (29% vs 3%, p=0.02) and/or unconventional immunosuppressants (57% vs 27% p=0.1). By contrast, extramuscular involvements were less frequent (43% vs 76%, p=0.08). None of sarcopenic patients had inflammatory joint involvement during the follow-up (0% vs 49%, p=0.02). At the time of evaluation, sarcopenic patients had lower MMT-8 (131/150 vs 142/150, p=0.004) and MMT-12: 199/220 vs 215/220, p=0.004), reduced 6mWD (196 (±80) vs 478 (±89) meters, p<0.0001) and HAQ score (2.1 (1.2-2.8) vs 0.6 (0.3-1), p=0.0008).
Irisin and secreted protein acidic and rich in cysteine serum levels were lower in sarcopenic compared to non-sarcopenic patients (respectively p=0.008, p=0.001).
Conclusion: Muscle mass measurement by DXA and muscle strength measurement by hand held dynamometer are simple and relevant tools to assess muscle damage in IM. Sarcopenia is frequent in patients with inactive or low-activity IM. It is associated with important skeletal damage, poor function and disability.
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POS1207

EFFICACY AND SAFETY OF ANTI-IFNB-SPECIFIC MONOCLONAL ANTIBODY, PF-06823859, ON MYOSITIS: PHASE 2 STUDY IN PATIENTS WITH MODERATE-TO-SEVERE DERMATOMYOSITIS

Keywords: Myositis, Cytokines and chemokines, Rare/orphan diseases

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Background: Interferon (IFN) dysregulation is a key feature in the pathogenesis of dermatomyositis (DM). PF-06823859 is a potent, selective, humanised immunoglobulin 1-neutralising monoclonal antibody (mAb) directed against human IFNβ.
Objectives: To examine the efficacy and safety of IFNβ blockade with PF-06823859 in adult patients with muscle-predominant moderate-to-severe DM.
Methods: This DM cohort within the Phase 2 study randomised patients with DM with moderate-to-severe muscle disease activity to PF-06823859 600 mg or placebo (1:1) for 12 weeks. Patients were required to meet one of the following inclusion criteria: (1) Manual Muscle Testing (MMT-8) ≤136/150 and Physician Global Assessment (PhGA) ≥3 cm on a 0–10 cm visual analogue scale (VAS) or (2) the sum of PhGA, Patient Global Assessment (PtGA), extramuscular global assessment ≥10 cm (using 0–10 cm VAS for each), with refractory disease, defined as failure of at least two or more adequate courses of an immunosuppressive or immunomodulatory agent, including intravenous immunoglobulin. Endpoints included clinical efficacy assessments (mean Total Improvement Score [TIS], mean change from baseline [CFB] in MMT-8, and mean CFB in PhGA), patient-reported outcomes (mean CFB in PtGA and mean CFB in Health Assessment Questionnaire Disability Index [HAQ-DI]), muscle enzyme levels (mean CFB in creatine kinase [CK]), mean CFB in extra muscular activity, and safety and tolerability at Week 12.
Results: All 18 randomised patients completed the 12-week treatment. The least squares mean (LSM) TIS showed numerical advantage of PF-06823859 600 mg versus placebo with increasing trends over time (4–12 weeks) and no plateau at Week 12. The LSM (90% confidence interval [CI]) TIS at Week 12 for PF-06823859 600 mg and placebo were 56.4 (41.4, 71.4) and 36.9 (22.0, 52.0), respectively, with a placebo-adjusted difference of 19.4 (-1.8, 40.7). Sensitivity analyses, excluding a single efficacy observation for a placebo recipient who received prohibited concomitant medications, reached nominal statistical significance (p=0.0497). At Week 12, PF-06823859 600 mg had numerically better efficacy scores than placebo across other key muscle function endpoints (estimated mean [90% CI] CFB in MMT-8 21.2 [11.9, 30.6] for PF-06823859 600 mg and 11.7 [2.3, 21.0] for placebo; in PhGA -3.40 [-4.9, -1.9] for PF-06823859 600 mg and -2.05 [-3.56, -0.55] for placebo; in PtGA -4.6 [-5.9, -3.4] for PF-06823859 600 mg and -1.2 [-2.4, 0.1] for placebo; in HAQ-DI -0.54 [-0.87, -0.22] for PF-06823859 600 mg and -0.03 [-0.38, 0.32] for placebo; in CK -185.8 [-273.9, -97.6] for PF-06823859 600 mg and -39.9 [-125.7, 46.0] for placebo; in extra muscular activity -2.81 [-3.87, -1.76] for PF-06823859 600 mg and -1.62 [-2.68, -0.56] for placebo. The mean (90% CI) placebo-adjusted differences in CFB for MMT-8, PtGA and CK were 9.6 (-3.8, 23.0), -34.5 (-52.7, -16.2) and -145.9 (-269.4, -22.4), respectively, with nominal statistical significance for PtGA (p=0.0046) and CK (p=0.0282). Treatment-emergent adverse events (TEAEs) were similar between

the PF-06823859 and placebo groups, and mostly mild in severity. The most common TEAEs were gastrointestinal disorders. There were no cases of herpes zoster or herpes simplex.

Conclusion: Anti-IFNβ mAb PF-06823859 was generally safe and well tolerated, improved clinical parameters (TIS, MMT-8, PhGA), patient-reported outcomes (PtGA, HAQ-DI), extra muscular activity and significantly decreased muscle enzyme levels (CK) in patients with muscle-predominant refractory moderate-to-severe DM.

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POS1208

INCIDENCE, PREVALENCE & MORTALITY IN IDIOPATHIC INFLAMMATORY MYOPATHIES & ASSOCIATED INTERSTITIAL LUNG DISEASE IN ENGLAND: A NATIONAL COHORT USING ROUTINELY COLLECTED ADMINISTRATIVE DATA

Keywords: Lungs, Epidemiology, Myositis

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Background: Ethnicity, sex, age & socioeconomic deprivation can all lead to health inequity. Impact of these factors in epidemiology of Idiopathic Inflammatory Myopathies (IIM) has not been widely researched.

Objectives: In collaboration with National Congenital Anomaly & Rare Disease Registration Service (NCARDRS), we described national incidence, prevalence & mortality in IIM and associated Interstitial Lung Disease (IIM-ILD) according to demographics.

Methods: Hospital Episode Statistics (HES) collected at every NHS hospital admission in England, were used to create a national cohort of patients with IIM & IIM-ILD associated ICD-10 codes between 2006-2022. Cases were identified according to pre-validated methods.[1] Age, sex, ethnicity, Index of Multiple Deprivation (IMD) and death certification were collated. Denominator populations were extracted from Office of National Statistics publications. Incidence rates were calculated by multivariate Poisson regression, standardized mortality ratio (SMR) by indirect standardization, and survival analysis by multivariate Cox models. Incidence Rate Ratios (IRR) were mutually adjusted for age, sex & IMD (Ethnicity IRR was not adjusted for IMD due to lack of suitable denominator data). Cox models were adjusted for age, sex, ethnicity, IMD and ILD status.

Results: 14,891 incident IIM cases were identified giving an incidence rate of 1.72/100,000 person-years. Point prevalence was 17.9/100,000 in 2022. Mean age was 59.7 years with incidence peaking at 70-80 years. Multivariate models (Table 1) showed IIM incidence was higher in females IRR 1.30 (95%CI 1.25, 1.34), but mortality was lower (hazard ratio (HR) 0.78 (95%CI 0.74, 0.82)). Incidence was higher in Asian and Black ethnicities than White (IRR 1.56 and 2.77 respectively). Mortality was higher in White ethnicity (Asian HR 0.80 and Black HR 0.78). The most deprived population quintile had similar incidence IRR 1.06 (95%CI 1.02, 1.11), but higher mortality HR 1.34 (95%CI 1.25, 1.44) than less deprived populations. 17.2% of IIM cases had ILD. Incidence of IIM-ILD did not vary largely by socioeconomic deprivation, but incidence was substantially higher in Black, Other and Asian populations compared to White (IRR 5.11, 4.07, 2.48). Mortality of IIM-ILD was also lower in Asian HR 0.76 (95%CI 0.61, 0.95) and Black HR 0.73 (95%CI 0.57, 0.93) patients. SMR was 5.13 for IIM and 7.92 for IIM-ILD. Crude mortality increases with age, but standardized mortality is highest in younger patients with ILD. (Graph). Death certification was available in 7,159 cases. IIM was recognized as a contributory factor in 39%, and ILD in 10.6%. Malignancy was the most reported 'underlying cause of death' (24.7%), then cardiovascular disease (19.9%) and respiratory disease (15.8%). Asian and Black ethnicities were less likely to have malignancy mentioned on death certificates (IRR 0.48 and 0.61 respectively).

Table 1.

	Adjusted IRR (95%CI)		Adjusted mortality HR (95% CI)	
	IIM	IIM-ILD	IIM	IIM-ILD
Male	-	-	-	-
Female	1.30 (1.25, 1.34)	1.73 (1.60, 1.88)	0.78 (0.74, 0.82)	0.79 (0.70, 0.89)
IMD 1 (most deprived)	1.06 (1.02, 1.11)	1.04 (0.94, 1.15)	1.34 (1.25, 1.44)	1.37 (1.17, 1.61)
IMD 2-5	-	-	-	-
White	-	-	-	-
Asian	1.56 (1.47-1.66)	2.48 (2.19, 2.81)	0.80 (0.71, 0.91)	0.76 (0.61, 0.95)
Black	2.77 (2.59-2.96)	5.11 (4.51, 5.79)	0.78 (0.67, 0.90)	0.73 (0.57, 0.93)
Mixed	0.96 (0.82-1.14)	1.28 (0.89, 1.86)	0.81 (0.53, 1.23)	0.95 (0.42, 2.13)
Other	2.97 (2.63-3.35)	4.07 (3.16, 5.25)	0.79 (0.61, 1.02)	0.84 (0.54, 1.30)

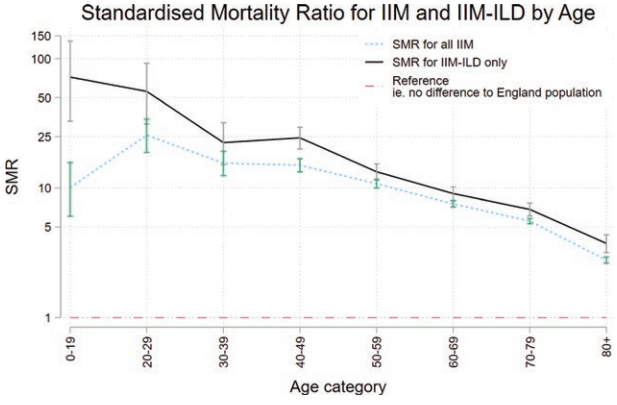


Figure 1.

Conclusion: We have defined national incidence, prevalence and SMR estimates for IIM and IIM-ILD. Incidence is higher in females, Black, Asian and Other ethnicities. Mortality is higher in White ethnicities, increased deprivation and males. Increased mortality in White ethnicities may partially relate to increased malignancy-associated disease.

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POS1209 INTERNET-BASED ENROLLMENT OF A MYOSITIS PATIENT COHORT

Keywords: Telemedicine, Myositis

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Background: Recruitment for myositis clinical research is challenging, due to the rarity of the disease and geographic considerations. Remote enrollment using digital health technologies, social media, and tele-medicine provide researchers with more optimal recruitment options. (1)
Objectives: To assess the effectiveness of various remote recruitment strategies in myositis patients.
Methods: "Myositis Patient Centered Tele-Research" (MyPacer) is an NIH-funded multi-center observational study assessing the feasibility, efficiency and acceptability of virtual research in myositis. Subjects were recruited from anywhere in the United States (U.S.) via online strategies: a) Patient organizations (e.g. The Myositis Association [TMA], Myositis Support and Understanding [MSU], etc.) posted a study link on their website, emailed members, and posted on social media; b) Targeted advertisements were posted on Google, Facebook and Twitter; c) Myositis physicians were emailed with a request to refer patients. Interested subjects reviewed study details, e-consented and enrolled via the study mobile application (app) or website. Adult patients who fulfilled self-reported eligibility criteria were enrolled (after physician verification of polymyositis [PM], necrotizing myositis [NM], or dermatomyositis [DM] and fulfillment of at least 4/6 disease criteria for PM/NM, or 3/6 for DM). Disease criteria included: muscle weakness, elevated CK, compatible EMG or biopsy (muscle or skin), DM rash, or a positive myositis associated auto-antibody. The diagnosis and disease criteria were confirmed by a physician via chart review.
Results: In 6 months, 94 participants were enrolled [71 (75.5%) females, median age of 54 years (SD +/- 13.9), and 76 (80.9%) White, 9 (9.6%) Black, and 3 (3.2%) Asian]. The most common diagnosis was DM (46, 48.9%), then PM (35, 36.2%), NM (7, 7.5%), and unspecified myositis (6, 6.4%). Primary myositis doctors were rheumatologists (80, 85.1%), neurologists (10, 10.6%), or dermatologists (2, 2.1%). We enrolled subjects from 30 states and 5 regions in the U.S., with higher participation from Virginia (n=13; 13.8%), Pennsylvania (n=11; 11.7%), Florida (n=8;8.5%), and California (n=7; 7.4%). Among the main recruitment sources, TMA was responsible for 63 (67%) participants, MSU for 20 (21.3%), and doctor referral for 9 (9.6%). Other recruitment sources (n=53; 56.4%) included 18 (19.1%) via Facebook, 6 (6.4%) via study website, 2 (2.1%) via Twitter, and 1 (1%) via Google advertisements. Participants recruited via Facebook were younger than those recruited via email (mean ages 47.39, SD +/- 10.66 and 56.59, SD +/- 13.63 respectively; 95% CI 2.15-16.25; p=0.01). For enrollment method, 62 (66%) individuals used the study app, and 32 (34%) used the study website. The app was the preferred method throughout the country, except in the Southeast where 51.7% of participants used the study website. The mean age of app and website users was 51.79 (SD +/- 12.43) and 60.12 (SD +/- 14.23) years, respectively (95% CI 2.68-13.98; p=0.004).
Conclusion: Online recruitment is a viable alternative for maximizing potential recruitment in myositis clinical studies. We remotely enrolled patients from every region in the U.S. Patient support organizations were very successful in augmenting recruitment. Moreover, Facebook was responsible for almost 20% of participants, especially within the younger (ages 30 to 66) population. Our study app appeared quite functional with 66% use of the enrolled subjects and a clear favorite in younger individuals compared to website use. We hope these findings will guide future online myositis studies and advance clinical research.

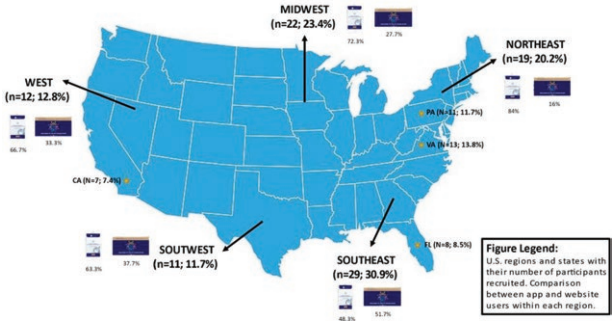


Figure 1.

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POS1210 PATIENTS WITH SUBCLINICAL HEART INVOLVEMENT AT DIAGNOSIS OF MYOSITIS ARE MORE LIKELY TO PRESENT CARDIOVASCULAR EVENTS THAN PATIENTS WITHOUT CARDIAC INVOLVEMENT IN A MONOCENTRIC RETROSPECTIVE STUDY

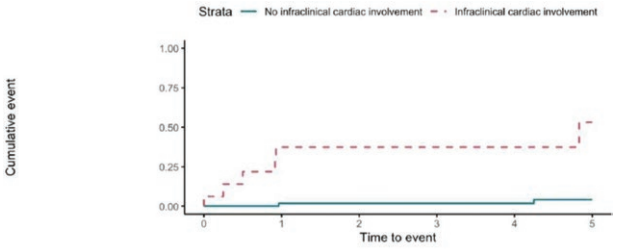
Keywords: Heart, Myositis

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Background: Idiopathic inflammatory myositis (IIM) is a group of rare and heterogeneous systemic diseases characterized by clinical muscle weakness and histological inflammation in skeletal muscles. Myositis classification distinguishes dermatomyositis (DM), inclusion body myositis (IBM), immune-mediated necrotizing myopathy (IMNM), anti synthetase syndrome (ASSD) and overlap myositis (OM) [1-2]. Patients with myositis are more likely to die younger than in general population [3]. Cardiovascular events (CVE) are one of the main causes of death during the disease's course [4].
Objectives: To investigate the occurrence of CVE and their link with features of cardiac involvement in a French myositis population.
Methods: We conducted a retrospective observational cohort study of patients with a diagnosis of DM, ASSD, IBM, IMNM or OM, from the department of internal medicine in Saint Antoine's hospital, Paris, France, between 1992 and 2020. Demographic and clinical data were collected at diagnosis, at the last follow up visit, and at the first CVE if one happened. Subclinical heart involvement was defined by electrocardiogram abnormality, transthoracic echocardiography abnormality or cardiac MRI abnormality. CVE were defined by the occurrence during the follow up of heart failure, inflammatory myocarditis or admission in resuscitation department. Descriptive, bivariate and survival analysis were performed.
Results: Among the 78 patients included, 52 (67%) were women. Thirty three patients (42%) had a DM, 18 (23%) an ASSD, 12 (15%) an OM, 11 (14%) an IMNM and 4 patients (5%) an IBM. Mean age at diagnosis was 49 years. Median follow up time was 72 months. Subclinical involvement was present at diagnosis for 17 (22%) patients; and 14 (21%) patients presented a CVE during the follow up period. Patients with subclinical cardiac involvement at diagnosis were more likely to present a CVE than patients without subclinical cardiac involvement. Three years after the diagnosis, 7 CVE occurred in the subclinical cardiac involvement group (event rate 37.5%; 95% CI 4.92-58.92) and only 1 CVE occurred in the no cardiac involvement group (event rate 1.89%; 95% CI 0-5.48). Time to CVE was significantly different between groups (log rank test p < 0,001, Graph 1). This difference remains significant at 5 years after myositis diagnosis.
Conclusion: Patients with subclinical cardiac involvement at myositis diagnosis are more likely to present CVE in the first 5 years of disease than patients without subclinical cardiac involvement. Clinical cardiac involvement is rare at diagnostic, but subclinical cardiac involvement seems to be a more frequent condition. Our results suggest that we should pay more attention to patient with subclinical cardiac involvement at myositis diagnosis, especially in the first years of the disease's course.

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Graph 1 : time to event (CVE) in patients with subclinical cardiac involvement at diagnostic compared to patients without subclinical cardiac involvement

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POS1211 CHARACTERISTICS OF MYOCARDIAL INVOLVEMENT OF POLYMYOSITIS/DERMATOMYOSITIS EVALUATED BY CARDIAC MAGNETIC RESONANCE: A PILOT STUDY

Keywords: Biomarkers, Imaging, Myositis

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Background: Polymyositis (PM) and dermatomyositis (DM) are autoimmune systemic diseases characterized by muscle weakness and inflammatory cell infiltration into skeletal muscle. Myocardial involvement is a common cause of death in PM/DM. It has been reported that myocardial involvement is observed in 9% to 72% of PM/DM [1], but it is still unclear. Electrocardiogram (ECG) and echocardiography are the most often used tests to evaluate cardiac abnormalities, but early detection of myocardial involvement in PM/DM is difficult. Cardiac magnetic resonance (CMR) is a noninvasive technique that has been efficiently evaluated in early myocarditis [2]. Late gadolinium enhancement (LGE) imaging evaluated at T1 remains one of the most important MRI techniques in the setting of suspected myocarditis [3], and the presence of LGE denotes tissue inflammation, necrosis, and early fibrosis [4,5]. Contrast-enhanced T1 mapping can calculate extracellular volume (ECV) fraction and is used for evaluation of myocardial fibrosis and scar [6]. T2 mapping is used for the evaluation of myocardial edema in association with myocardial inflammation [7]. T1, T2 and ECV are elevated in the setting of myocardial lesions. However, the evaluation of myocardial involvement in PM/DM by CMR still remains unclear and warrants investigation.
Objectives: This study aimed to investigate characteristics of myocardial involvement evaluated by CMR, and identify the clinical markers indicating the presence of cardiac complications in PM/DM.
Methods: PM/DM patients who visited our service between January 2014 to September 2022 were enrolled in this retrospective study. All patients met the 2017 EULAR/ACR classification criteria for idiopathic inflammatory myopathies, and patients with several elevated cardiac markers were included. Patients were excluded if they were complicated with other connective tissue diseases and cardiovascular diseases at the diagnosis of PM/DM. All patients performed ECG, echocardiography and CMR. Clinical and findings of CMR information were collected and statistically analyzed. The findings of CMR, such as T1, T2, LGE and ECV, were also analyzed.
Results: Twelve patients (3 patients with PM and 9 patients with DM) were enrolled in this study. ECG and echocardiography did not detect any abnormalities associated with PM/DM. However, in CMR, abnormalities indicating myocardial involvement were identified in 6 (3 patients with PM and 3 patients with DM) patients: 66.6% of patients had LGE, all patients had elevated ECV, and 33.3% of patients had elevated T2. Serum myoglobin levels were significantly elevated in patients with myocardial involvement (814.5±124.7 ng/mL vs 324.8±151.0 ng/mL, p=0.031). There were no significant differences in other cardiac markers, including serum CK, CK-MB and NT-pro-BNP, between with and without myocardial involvement. The following items were extracted as possible items for the presence of myocardial involvement: being PM (p=0.003) and anti-ARS antibodies positive (p=0.049).
Conclusion: Our results propose that myocardial involvement is more likely to develop in PM/DM patients even if the finding of echocardiography is normal. In addition, CMR should be performed in cases of PM/DM with high myoglobin levels, considering the possibility of myocardial involvement.

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POS1212 SERIAL IMAGING CHANGES IN SKELETAL MUSCLE COMPOSITION AND THEIR ASSOCIATION WITH CLINICAL OUTCOMES IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Keywords: Outcome measures, Myositis, Imaging

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Background: Muscle weakness in inflammatory myopathies (IIM) is due to muscle-edema, atrophy and fatty-infiltration among which edema is the predominant cause at baseline. Some IIM pateints donot achieve full muscle power even with immunosupressive treatment which mainly targets edema. Serial changes occuring in skeletal muscles visualized on thigh MRI can help understand the failure of complete recovery. Role of Dual energy X-ray Absorptiometry (DXA) assessed skeletal muscle compositon as outcome measure in IIM was not studied previously.
Objectives: To see the changes in skeletal muscle composition over 6 months in IIM patients using imaging and to assess the agreement of MRI and DXA scores with each other and with clinical outcome measures.
Methods: Patients satisfying 2017 ACR-EULAR classification criteria for IIM were prospectively enrolled. All patients underwent thigh MRI(t-MRI) STIR and T1 weighted sequences (axial and coronal) at baseline, 3 and 6 months and DXA scan at baseline and 6 months. Manual muscle testing-8(MMT-8), Functional index-3(FI-3), 2-minute walk distance (2MWD) were assessed at baseline, 3 and 6 months. t-MRI was scored using a semi-quantitative score for muscle edema, fascial edema, muscle atrophy and fatty infiltration. Friedman test was used to compare variables at baseline, 3 and 6 months and Spearman correlation was done for agreement of MRI and DXA scores with each other and clinical outcome measures.
Results: 17 patients (12 females) were enrolled and all of them completed 3 months follow-up while only 13 completed 6 months follow-up. Median (IQR) age was 38 (27-46) years, disease duration was 6 (2-24). The study group comprised of 10 dermatomyositis, 5 antisynthetase syndrome and 3 immune mediated necrotizing myopathy patients. MRI assessed muscle edema and fascial edema decreased significantly ($p<0.01$) and fatty infiltration increased significantly ($p=0.001$) from baseline to 3 months. Muscle atrophy did not change significantly from baseline to 3 months and 6 months. DXA assessed appendicular lean mass/ht^2($p=0.007$) and total lean mass/ht^2($p=0.021$) improved significantly from baseline to 6 months. Improvement in MMT-8 and 2MWD was significant only from baseline to 3 months($p=0.000$) whereas FI-3 continued to improve till 6 months($p=0.000$) (Table 1). At baseline MMT-8($R=-0.631$; $p<0.01$), FI-3($R=-0.698$; $p<0.01$) and 2MWD ($R=-0.485$; $p<0.05$) negatively correlated with only muscle edema. At 3 months MMT-8 and 2MWD (R1, R2) negatively correlated with muscle edema (R1=-0.673, R2=-0.591), atrophy (R1=-0.732, R2=-0.577) and fatty infiltration (R1=-0.575, R2=-0.743; $p<0.05$). FI-3 negatively correlated with only atrophy ($R=-0.488$; $p<0.05$). MRI fatty infiltration score and atrophy score did not correlate with DXA assessed leg fat percentage and appendicular mass/ht2 respectively at baseline but had significant correlation ($p<0.05$) at 6 months (Figure 1).
Conclusion: In IIM, edema decreased and muscle strength increased significantly in first 3 months but fatty infiltration increased. DXA assessment of fat and lean mass did not agree with MRI atrophy and fatty infiltration at baseline probably due to concomitant muscle edema.

Table 1 : Serial change in t-MRI scores, DXA assessed lean mass and clinical outcome measures

	Baseline	3 months	6 months	P-value
Muscle edema	17.03(7.4-32.4) *	0.37(0.00-11.11) *	0.00(0.00-5.37)	**0.000**
Fascial edema	46.66(15.0-57.7) *	7.77(0.00-25.55) *	4.44(0.00-23.88)	**0.004**
Muscle atrophy	0.00(0.00-1.67)	0.00(0.00-2.22)	0.00(0.00-2.22)	0.670
Fatty infiltration	6.66(0.00-15.00) *	8.88(2.22-21.66) *	8.88(2.22-23.33)	**0.001**
Appendicular lean mass/Ht^2	5.5(3.9-6.2) *	-	5.6(4.8-7.3) *	**0.007**
Lean body mass/Ht^2	12.6(10.7-14.4) *	-	13.4(11.1-15.6) *	**0.021**
Manual Muscle Testing-8	56(51.5-70.5) *	78(71.50-80) *	78(76-80)	**0.000**
Functional Index-3	33.88(9.7-57.2) *	56.6(29.4-77.2) *	72.2(50-83.3) *	**0.000**
2-Minute Walking Distance	122(40-141) *	142(126.5-177) *	150(138-161)	**0.002**

*indicates significant change between 2 time points

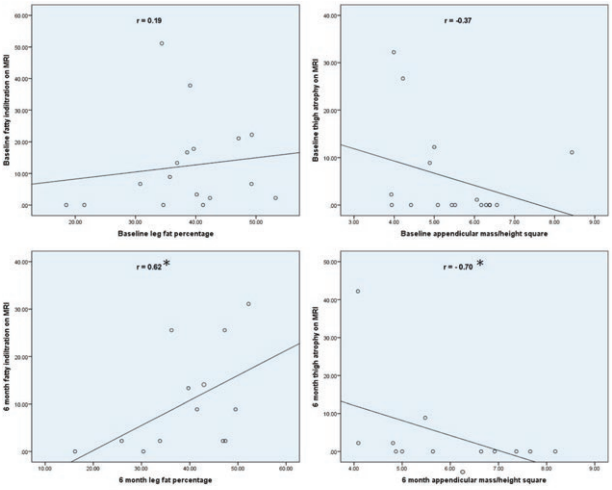


Figure 1: Correlation of MRI assessed fatty infiltration and atrophy with DXA assessed leg fat percentage and appendicular mass/height^2 at baseline and 6 months
* Indicates p<0.05

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POS1213

RISK OF ATHEROSCLEROSIS-RELATED DISEASES IN ADULTS WITH POLYMYOSITIS AND DERMATOMYOSITIS: A LARGE SCALE POPULATION-BASED STUDY

Keywords: Myositis

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Background: Select systemic autoimmune diseases show a predilection to Atherosclerotic and Cardiovascular Disease (ASCVD) largely attributed to proinflammatory cytokines supporting the role of the inflammatory hypothesis in endothelial dysfunction and subsequent clinical sequala. Dermatomyositis (DM) and polymyositis (PM) are polygenic autoimmune disorders involving mainly skeletal muscles. The association between DM/PM and ASCVD has not been well addressed and explored.
Objectives: To investigate the association between DM/PM and ASCVD events by exploring incidence, mortality, and interaction with respect to disease-modifying agents, autoantibodies, and traditional CVD risk factors in a large, population-based sample.
Methods: A retrospective cohort study using the electronic database of Clalit Health Services (CHS), the largest health organization in Israel. All DM and PM patients diagnosed between 2000-2016 were included with age- and sex-matched controls in a 1:5 ratio. Follow-up continued until the first diagnosis of ASCVD or death. The incidence of ASCVD was compared between the groups using univariate and multivariate models adjusting for baseline cardiovascular risk factors.
Results: The study population included 1,567 DM/PM patients and 7,676 controls. The mean age at the index date was 32.5 years (SD±19 years), and the female proportion was 60.3%, similar for both groups. Traditional cardiovascular risk factors were similar between both groups. Median follow-up time was 8.4 (3.6-12.8) in the PM/DM group compared to 8.6 (3.7-12.9) in the control group. 47 (3.0%) PM/DM patients were diagnosed with IHD compared to 140 (1.8%) controls, yielding an Unadjusted HR of 1.66 (1.19 to 2.30). Unadjusted HR for CVA in the PM/DM group was (95%CI) 2.76 (1.86 to 4.11). Unadjusted HR for ASCVD (95%CI) was 1.88 (1.46 to 2.43). APLA-associated antibody predicted ASCVD among PM/DM groups as compared to non-ASCVD PM and DM patients (OR- 2.33, 95% CI - 1.41 to 3.86, p<0.0001).
Conclusion: Our study demonstrates that PM and DM are both associated with an increased risk of MI and ischemic stroke. Furthermore, PM and DM patients positive for APLA-associated antibodies were associated with excessive rates of ASCVD. Taken together, these findings support the increased need for awareness and surveillance of cardiovascular outcomes in the DM/PM cohort.

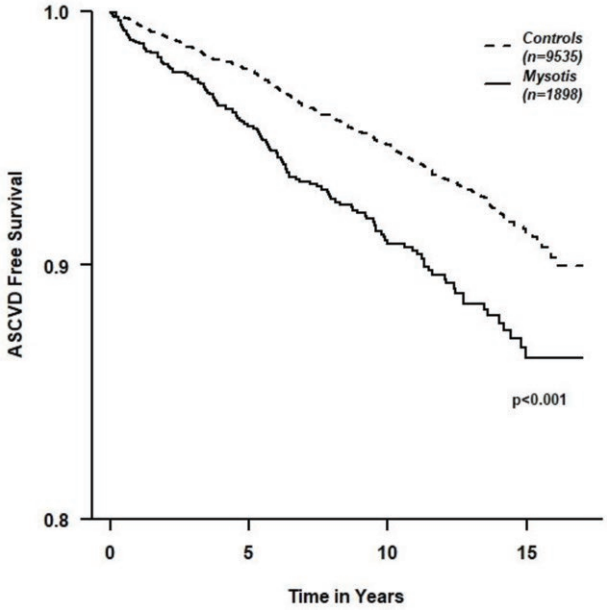


Figure 1. Kaplan Meyer survival analysis comparing All atherosclerotic related cardiovascular diseases (ASCVD) outcomes between inflammatory myositis patients and controls.

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POS1214

PATIENT REPORTED OUTCOME FOR PHYSICAL FUNCTION IN IDIOPATHIC INFLAMMATORY MYOPATHY

Keywords: Patient reported outcomes, Myositis

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Background: Patient-reported outcomes (PRO) measures provide direct and valuable information on treatment efficacy and quality of life. However, the commonly-used PRO measures in Idiopathic inflammatory myopathies (IIM) have several psychometric limitations. The Patient-Reported Outcomes Measurement Information System (PROMIS) is an NIH initiative, with several PROs developed and validated in different medical conditions.
Objectives: To (1) investigate the psychometric properties of PROMIS physical function-20 (PF-20) in a large US-wide IIM population, and (2) evaluate the feasibility and compliance of PRO measures administered in a local clinic compared to remote US-wide patients.
Methods: "Myositis Patient Centered Tele-Research" (My PACER) is a multi-center prospective 6-month observational study of U.S. IIM subjects, competitively recruited through traditional in-person clinic visits (Center-Based Cohort [CBC]), and remotely using smartphone technology, wearable devices, and

telemedicine principles (Tele-Research Cohort [TRC]). Data collection included baseline demographic and clinical parameters, PRO and other patient self-assessments at 6 monthly visits, including myositis core set measures (health assessment questionnaire [HAQ-DI], patient global disease activity), PROMIS PF-20, functional tests (six-minute walk, timed up-and-go [TUG] and sit-to-stand [STS] tests], and physical activity monitor. Physician-reported assessments including myositis core set measures (manual muscle testing [MMT], physician global disease activity, extra-muscular global disease activity, creatine kinase [CK]) were obtained at baseline and 6 months.

Results: 141 IIM patients were enrolled (94 TRC/47 CBC). Mean age was 55±13.4 years, female sex 106/141 (75.2%), and 113/141 (80.1%) Caucasians, with similar demographics between the two groups. 116 patients completed the PROMIS-PF form (79 (84%) and 37 (78.7%) in TRC vs. CBC group) with a mean of 6.6±1.7 vs. 6.3±1.5 times per patient (p=0.33) in TRC and CBC group, respectively. The PROMIS PF-20 score was not associated with age, gender or race. There was no difference between the mean PROMIS PF-20 score in the TRC and CBC groups (p=0.84). The mean PROMIS PF-20 score was 43.9 ± 9.5 in the whole cohort, with 26/116 (22.4%) with a mean t-score lower than 35, indicating severe functional limitation, which was similar between TRC and CBC groups. PROMIS PF-20 showed strong test-retest *reliability* with a high correlation when repeated at 1 month (r=0.94,p<0.0001). At baseline, PROMIS PF-20 was significantly associated with all core set measures except extra-muscular global and CK. In addition, PROMIS PF-20 was associated with myositis symptoms as well as functional tests and physical activity **(Table 1),** indicating good *validity.* Finally, absolute changes in the PROMIS-PF t-score (between the baseline and 6-month visit) were significantly associated with absolute changes in some of the core set measures as well as with the STS and physical activity.

Conclusion: PROMIS PF-20 demonstrates favorable psychometric properties in a large cohort of myositis patients, with similar compliance and results in patients recruited traditionally from clinics or remotely using social media and digital health technology.

Table 1 . Validity.Associations of PROMIS-PF 20 with legacy myositis outcome measures

Parameter	Coefficient	P value
CK level (Muscle Enzyme) *	-0.0004	0.65
Patient-reported		
Patient Global Disease Activity*	-2.40	**<0.001**
Muscle weakness	-10.14	**<0.001**
Muscle pain	-6.23	**<0.001**
Fatigue	-8.80	**<0.001**
Joint pain	-6.6	**0.002**
HAQ score*	-11.09	**<0.001**
Physician assessment		
Physician Global Disease Activity	-1.89	**<0.001**
MMT-8*	**0.31**	**<0.001**
MDAAT		
Fatigue	-9.31	**<0.001**
Myalgia	-8.48	**<0.001**
Myositis- mild	-7.54	**<0.001**
Constitutional Disease Activity	-2.83	**<0.001**
Skeletal Disease Activity	-4.64	**0.002**
Muscle Disease Activity	-2.37	**<0.001**
Physical Function tests		
Average steps per minute	0.73	**0.006**
Sit-to-stand (average score)	1.21	**<0.001**
Timed up and go (average score)	-0.45	**<0.001**

*Myositis Core Set Measure

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POS1215

FLARES AFTER COVID-19 INFECTION IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: RESULTS FROM THE COVAD STUDY

Keywords: Infection-related RMDs, Myositis, COVID

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Background: Viral infections are known triggers of disease flares in idiopathic inflammatory myopathies (IIMs). Reports of post-COVID-19 flares of IIMs have raised suspicion of a possible role of SARS-COV-2 in their onset [1,2]. However, despite rising flare rates in this vulnerable patient group during the pandemic, the risk factors for post-COVID-19 IIMs flares remain unknown [3,4].

Objectives: Disease flares among patients with idiopathic inflammatory myopathies (IIMs) can lead to significant disability, though are poorly explored in the post-COVID-19 period. We analysed risk factors for post-COVID-19 flares in a global sample of IIM patients in a subset analysis as part of the ongoing COVID-19 Vaccination in Autoimmune Diseases (COVAD) study.

Methods: A cross-sectional patient self-reporting survey was circulated by the international COVAD study group (157 collaborators, 106 countries) to patients with autoimmune diseases and healthy controls from February-June 2022. Data was collected on demographics, autoimmune disease details, treatment history, comorbidities, COVID-19 history and course and COVID-19 vaccination details. Patients with IIMs who flared post COVID-19 were compared to those who did not using the χ^2 test, factors found significant in univariate analysis and deemed clinically important, underwent multivariable analysis (binary logistic regression using the Enter method) with adjustment for age, gender, ethnicity, vaccine type, immunosuppression, autoimmune and non-autoimmune comorbidities, COVID-19 antibody status, and clinical symptoms of COVID-19. Statistical analyses were performed using IBM SPSS version 28.0, with statistical significance considered at p<0.05.

Results: 15,165 respondents completed the survey of whom 1,169 contracted COVID-19. Of these, 207 had IIMs [median (IQR) age 57.0 (47.0-67.0), 71% female, 74.4% Caucasian]. We noted with concern that nearly a third of patients with IIMs (63/207, 30.4%) reported experiencing a flare. A past medical history significant for Asthma, (34.9% vs 6.9%, multivariable OR: 7.1; 95%CI: 3.1-16.4, p<0.001) and specific clinical symptoms during COVID-19 including joint pains (multivariable OR: 6.05; 95%CI: 1.60-22.9, p=0.008), and difficulty in breathing (multivariable OR: 3.43; 95%CI: 1.09-10.8, p=0.036) were found to confer conferred a higher risk of flares (Table 1).

Table 1 Patient Reported Flares following COVID-19 infection among IIM patients

	Total IIMs (n=207)	IIMs with flare after COVID-19 (n=63)	IIMs without flare after COVID-19 (n=144)	OR (95%CI)	P
Age (median, IQR) years	57.0 (47.0-67.0)	53.0 (47.0-62.0)	59.0 (47.0-69.0)	-	0.024
Gender	60 (29.0)	7 (11.1)	53 (36.8)	0.2 (0.09-0.5)	<
Male	147 (71.0)	56 (88.9)	91 (63.2)		0.001
Female					
Comorbidities	32 (15.5)	22 (34.9)	10 (6.9)	7.1 (3.1-16.4)	<0.001
Asthma	31 (15.0)	11 (17.5)	20 (13.9)	1.3 (0.5-2.9)	00.508
ILD					
Clinical features in previous COVID-19 infection	134 (64.7)	52 (82.5)	82 (56.9)	3.5 (1.7-7.4)	<0.001
	94 (45.4)	44 (69.8)	50 (34.7)	4.3 (2.3-8.2)	<0.001
Fatigue	56 (27.1)	36 (57.1)	20 (13.9)	8.2 (4.1-16.4)	<0.001
Myalgia	41 (19.8)	27 (42.9)	14 (9.7)	6.9 (3.3-14.6)	<0.001
Arthralgia					
Difficulty in breathing					

Conclusion: We observed a high frequency of patients with IIM experiencing post-COVID-19 disease flares. A past history of Asthma and those with certain acute COVID-19 symptoms were at higher risk.

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POS1216

MULTIMORBIDITY AND PROMIS HEALTH OUTCOMES IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: DATA FROM A LARGE, GLOBAL E-SURVEY (COVAD STUDY)

Keywords: Myositis, Mental health, Patient reported outcomes

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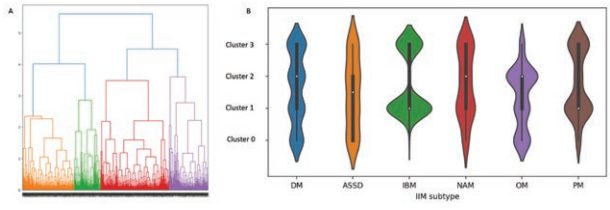
Background: Prevalence of comorbidities and their impact on health outcomes in Idiopathic inflammatory myopathies (IIMs) is limited.
Objectives: This study aimed to explore the prevalence of multimorbidity in patients with IIMs, other autoimmune rheumatic diseases (AIRDs) and Healthy controls (HCs). We further explore the impact of comorbidities on patients' physical, mental, and social health assessed by the Patient-Reported Outcome Measurement Information System (PROMIS instruments).
Methods: Data for this study were acquired from the COVAD 2 e-survey hosted by a study group consisting of 167 collaborators in 110 countries. Basic multimorbidity (BM) was defined as the co-occurrence of two or more comorbidities in an individual, while complex multimorbidity (CM) signified the co-occurrence of 3 or more chronic conditions affecting 3 or more different organ systems. PROMIS global physical health (PGP), mental health (PGM), fatigue 4a (F4a) and physical function short form (SF10) were analysed using descriptive statistics and linear regression models. Hierarchical Clustering on Principal Components was performed to outline the grouping.
Results: Of 10740 complete respondents, 1558 IIMs, 4591 AIRDs and 3652 HCs were analysed. Individuals with IIMs exhibited high burden of any comorbidity (OR: 1.62 vs AIRDs and 2.95 vs HCs,p<0.01), BM (OR 1.66 vs AIRDs and 3.52 vs HCs,p<0.01), CM (OR: 1.69 vs AIRDs and 6.23 vs HCs,p<0.01), and mental health disorders (MHDs) (OR 1.33 vs AIRDs and 2.63 vs HCs,p<0.01). IIM patients with comorbidities (and MHDs) had worse physical function (low PGP, PGM, SF10 and higher F4a scores, all p<0.001). Worse physical function (PGP) was predicted by age (0.35; 0.030), active disease (-1.51; <0.001), BM (-1.11; <0.001), and MHDs (-1.47; <0.001). PGM was impacted by age (0.51; 0.004), active disease (-1.34, <0.001), BM (-0.75; 0.001) and MHDs (-2.22; <0.001). Determinants of SF10a were age (-3.86; <0.001), active disease (-7.03, <0.001), female (2.85, <0.001), BM (-2.95; <0.001) and MHDs (-2.37; <0.001). Fatigue (F4a) was impacted by age (-0.96, <0.001), active disease (1.45, <0.001), country human development index (0.95; 0.036), BM (1.11; <0.001); and MHDs (2.17; <0.001). Four distinct clusters (Figure 1A, Table 1) were identified i.e., cluster 0: lower burden of comorbidities and good health status; cluster 1: older patients, whit higher burden of comorbidities and poor health status, cluster 2: patients with higher prevalence of MHDs, lower PGP and PGM; and higher F4a scores; and lastly Cluster 3 that comprised older patients with an average burden of comorbidities and overall good health status according to PROMIS scores. Dermatomyositis, anti-synthetase syndrome, necrotizing autoimmune myopathy were similarly represented in all clusters, whilst inclusion body myositis and polymyositis were more predominant in clusters 1 (40.6% and 17.2%) and 3 (32 % and 17.5%), while overlap myositis was more represented in cluster 2 (25.6%) and 0 (32.7%) (Figure 1B).

Table 1. Characteristics of clusters

	Cluster 0 (n. 219)	Cluster 1 (n.564)	Cluster 2 (n. 318)	Cluster 3 (n.422)
Female, n. (%)	189 (86.3)[a]	358 (63.5)[b]	288 (90.6) [a]	258 (61.1) [b]
Age, mean ±SD	44 ±13[a]	66 ±10[b]	45 ±12[a]	66 ±9[b]
BM, n. (%)	10 (4.6)[a]	330 (58.5) [b]	44 (13.8)[c]	156 (37)[d]
CM, n. (%)	4 (1.8)[a]	153 (27.1)[b]	27 (8.5)[c]	31 (7.3)[c]
MHDs, n. (%)	39 (17.8)[a]	241 (42.7)[b]	176 (55.3)[c]	61 (14.5)[a]
PROMIS Global Physical health, mean ±SD	15.8 ±2.1[a]	10.2 ±1.9[b]	10.5 ±2.3)[b]	14.5 ±1.7[c]
PROMIS Global Mental Health, mean ±SD	15.4 ±2.7[a]	11.2 ±2.7[b]	10.8 ±3.0[b]	15.2 ±2.4[a]
PROMIS Physical function SF10a, mean ±SD	45.8 ±4.5[a]	25.6 ±8.5[b]	34.3 ±8.6[c]	36.4 ±9.5[d]
PROMIS Fatigue 4a score, mean ±SD	7.2 ±2.4[a]	13.7 ±3.2[b]	13.8 ±3.3[b]	8.0 ±2.3[c]

Each superscript letter indicates a subset of the 4 groups analyzed for which the means or proportions showed no difference at a significance level of.05.

Figure 1A: Cluster dendrogram representation; Figure 1B: Violin plots of hierarchical cluster analysis in IIM subsets



Conclusion: Patients with IIMs have a higher burden of comorbidities that adversely impact physical and mental health, calling for optimized approaches for holistic patient management.
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POS1217 CCL-18 AS A BIOMARKER OF INTERSTITIAL LUNG DISEASE (ILD) AND PROGRESSIVE FIBROSING ILD IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Keywords: Biomarkers, Myositis, Lungs

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Background: Interstitial lung disease (ILD) is the most frequent organ involvement in patients with idiopathic inflammatory myopathies (IIMs). Some patients with connective tissue diseases including IIMs may develop a progressive fibrosing (PF-)ILD [1]. The chemokine CCL18 is constitutively expressed by dendritic cells and macrophages in lung tissues and may induce collagen synthesis in lung fibroblasts. Circulating CCL18 correlated with fibrosis severity in idiopathic pulmonary fibrosis and it predicts ILD progression in patients with systemic sclerosis (SSc) [2]. OX40 ligand (OX40L) is a glycoprotein expressed on activated antigen-presenting cells and in vivo OX40L blockade prevents inflammation-driven skin, lung, and vessels fibrosis in mouse models of SSc [3].
Objectives: To assess the potential role of CCL-18 and OX40L as biomarkers of ILD and PF-ILD in patients with IIMs.
Methods: Patients affected with IIMs (EULAR/ACR 2017 criteria) followed in our referral center were consecutively enrolled from September 2020 to March 2021. Clinical and serological variables, and organ involvement were recorded. Pulmonary involvement was investigated by high-resolution CT (HRCT) and pulmonary function tests (PFTs). CCL-18 (pg/ml) and OX40L (pg/ml) serum levels were measured by validated ELISA assays (according to the manufacturer's instructions) in patients and in 35 controls (matched for age and sex). Follow-up data including worsening of respiratory symptoms, and repeated PFTs and HRCT were recorded. PF-ILD was defined according to the INBUILD criteria [1].
Results: Ninety-three IIMs patients (64.5% females) with median age 62 (IQR 54.5-71) years and disease duration 3 (IQR 2-9) years were enrolled; ILD was detected in 52 (54.7%) patients. OX40L serum levels were similar between patients and controls, whereas CCL-18 serum levels were higher in IIMs patients than in controls (232.9 [IQR 134.7-399.07] vs. 48.4 [IQR 29.9-147.5], p<0.0001, **Figure 1A**). Among IIMs patients, those with ILD exhibited higher levels of CCL-18 than those without (305.6 [181.6-518] vs. 164.3 [79.6-270.7], p=0.001, **Figure 1B**). No association between CCL-18 values with autoantibodies, PFTs or any other clinical features was detected. During follow-up 16/52 (31%) patients developed a PF-ILD. At baseline, patients who developed PF-ILD had higher CCL-18 serum levels than non-progressors (306.4 [198.9-621.9] vs. 207.8 [102.6-376.8],

p=0.03]. Higher CCL-18 values, Anti-Ro52 and anti-MDA5 positivity, lower Creatine Kinase levels and diffusing capacity for carbon monoxide (DLCO) values were predictors of PF-ILD occurrence at univariate but not at multivariate analysis.

Conclusion: CCL-18 but not OX40L may be a useful biomarker in the assessment of patients with IIMs-ILD.

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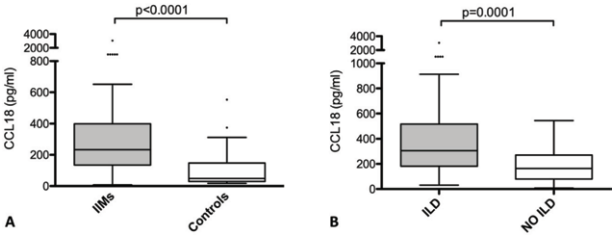


Figure 1.

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POS1218 A LARGE INCREASE IN ANTI-MELANOMA-DIFFERENTIATION-ASSOCIATED-GENE-5 (MDA5) ANTIBODY POSITIVITY AND ASSOCIATED DISEASE IN YORKSHIRE SINCE 2020

Keywords: Myositis

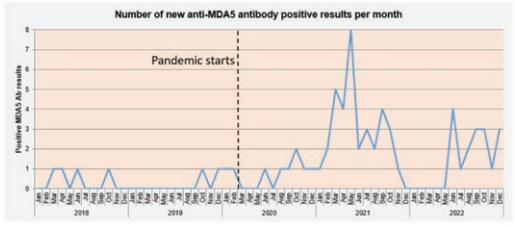
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Background: Melanoma differentiation-associated protein 5 (MDA5) is an intracellular detector of viral RNA. It is considered that viral infections are involved in the aetiology of autoimmune diseases, including autoimmune myositis. Previously we reported on a post-COVID-19 pandemic cluster of myositis occurring in the Yorkshire region (De Marco, 2022), despite the usually low frequency observed in the UK. More recently, we noticed increased anti-MDA5 positivity rate in myoblot tests.

Objectives: Our aim is to appraise the significance of the observed increased anti-MDA5 positivity recognized at our tertiary centre.

Methods: The Leeds Teaching Hospitals NHS Trust serves as an immunology laboratory reference for the wider Yorkshire region (3.6 million residents). We audited the increased anti-MDA5 positivity in relationship to other muscle-specific autoantibodies (Euroimmun immunoblot©) analysing retrospectively all tests performed between January 2018 and December 2022. Clinical notes review focused on: MDA5+ without disease; patterns of symptomatic MDA5 disease (including degree of ILD); muscle or other organs involvement; response to therapy. We also appraised the temporal associations between recent COVID-19 infection and SARS-CoV-2 vaccination.

Results: Requests for anti-MDA5 were stable between 2018 and 2020, but doubled thereafter. Anti-MDA5 positivity went from 0.6% to 4.9% in that period, dropping to 2.2% at the end of 2022 (Figure 1). Out of 66 individuals testing positive for anti-MDA5, clinical notes were available in 50 cases. Eleven had myositis without ILD (7 had dermatomysitis/"mechanic" hands rash). 18/50 cases developed ILD (12 had also myositis associated pathology, including 5 dermatomyositis rash and 5 "mechanic" hands). No cases of carditis were recorded. After treatment, outcome was stable/improved in 17 cases (6 ILD cases). Yet, 3 cases worsened and 6 died despite therapy (ILD cases). Twenty cases had signs described as within the connective tissues diseases spectrum (without any lung involvement), though no formal diagnosis. A minority of cases were associated with evidence of SARS-CoV-2 infection or vaccination, with 15 cases vaccinated before disease onset and 4 with preceding COVID-19 infection.



Summary per year	2018	2019	2020	2021	2022
Number of requests	364	535	459	812	1011
Number of patients	339	505	425	726	947
Total MDA5 Ab positive	4	3	10	40	22
New MDA5 Ab positive	4	2	9	35	17
Percentage positive (of total requests)	1.1	0.6	2.2	4.9	2.2

Figure 1.

Conclusion: Our data show an increased rate of anti-MDA5 positivity in the latter stages of the COVID-19 pandemic, as previously noted in the UK (Hannah J, ACR 2022). Most cases had MDA5 positivity without confirmed autoimmune disease and despite the MDA5 positivity occurrence in the face of the COVID-19 pandemic further longitudinal observation is needed to ascertain any potential links with either infection, vaccination or both.

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POS1219 INCIDENCE, FEATURES AND OUTCOME OF DISEASE RELAPSE AFTER COVID-19 VACCINATION IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Keywords: COVID, Myositis, Vaccination/Immunization

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Background: The approved COVID-19 vaccines showed clear safety and efficacy in reduction of severe SARS-CoV-2 disease. Patients with idiopathic inflammatory myopathies (IIM) were not well represented in these vaccine trials and there are limited data in the literature about development of confirmed disease flare after COVID-19 vaccination.

Objectives: To evaluate frequency, features and outcome of disease relapses in patients with IIM following SARS–CoV-2 vaccination.

Methods: A cohort of 176 IIM patients (mean age:57.6 years, 117 females, 59 males, 106 PM, 70 DM) were interviewed after the 3rd wave of COVID-19 pandemic and prospectively followed. Relapses were determined using the IMACS disease state criteria, outcome of the flares with myositis response criteria, calculating the total improvement score (TIS).

Results: A total of 146 (82.9%) patients received vaccination and 17/146 (11.6%) patients had relapse within 3 months and 13/146 (8.9%) patients within one month. The relapse rate of unvaccinated patients (1/30; 3.3%) was not significantly different (p>0.1). No fatal flare has been observed. Three months after the post-vaccination relapses, 70.6% of the patients (12/17) achieved improvement of disease activity (average TIS score:30±15.81; 7 minor, 5 moderate and 0 major improvement). Six months after flares improvement was detected in 14/16 (87.5%) of relapsed patients (average TIS score: 43±20.17; 3 minimal, 7 moderate and 4 major). Forward stepwise logistic regression analysis revealed that the active state of myositis at time of injection (p<0.0001; OR: 31.2 CI: 9.0 – 108) and the application of BNT162b2 vaccination (p=0.026; OR: 4.06 CI: 1.1 – 14.7) were significantly associated with the occurrence of relapse.

Conclusion: Minority of the vaccinated IIM patients had confirmed disease flare after COVID-19 vaccination and majority of the relapses improved after individualized treatment. Active disease state at the time of vaccination probably contributes to the increased risk of post vaccination myositis flare.

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Disclosure of Interests: None Declared.
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POS1220

TRANSITION IN SYMPTOMS, ORGAN INVOLVEMENT, AND CLINICAL DIAGNOSIS OF PATIENTS POSITIVE FOR ANTI-ARS ANTIBODIES

Keywords: Epidemiology, Myositis

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Background: Myositis-specific autoantibodies are useful biomarkers to make a diagnosis and predict prognosis of idiopathic inflammatory myopathies. Anti-aminoacyl transfer RNA synthetase antibodies (anti-ARS) is one of the most representative myositis-specific autoantibodies, however, organ involvement in patients positive for anti-ARS is not limited to the muscles but also skin, joints, and lungs, which constructs spectrums of idiopathic inflammatory myopathies called anti-synthetase syndrome. While individual anti-ARS antibodies have been known to form distinct clinical subsets, little is known regarding their chronological clinical presentation patterns and diagnosis during clinical course.
Objectives: To clarify the clinical characteristics of patients positive for anti-ARS and transition in manifestations and diagnosis during their clinical courses.
Methods: We reviewed consecutive patients with anti-ARS who had visited our hospital between 1998 and 2022 retrospectively. Anti-ARS antibodies were detected and categorized with RNA immunoprecipitation assays. We collected patient clinical characteristics and laboratory parameters including transition of diagnosis, manifestations and, organ involvement from their medical records chronologically. All statistical analyses were performed using JMP 15 (SAS Institute Inc., Cary, NC, USA).
Results: We included 97 patients positive for anti-ARS in the analysis. The mean age was 53.2 years old, and 73 (75%) were female. The types of anti-ARS Ab were anti-Jo-1 (37%), anti-EJ (32%), anti-PL-7 (11%), anti-PL-12 (12%), anti-KS (4%), and anti-OJ (3%). Half of the patients had co-existing other autoantibodies such as anti-SS-A/Ro, anti-SS-B/La, anti-dsDNA, anti-RNP, and/or rheumatoid factor, but the combination of antibodies was not different among each anti-ARS. The initial diagnoses of the patients were polymyositis (22%), dermatomyositis (33%), amyopathic dermatomyositis (13%), and interstitial pneumonia with autoimmune features (27%). Raynaud's phenomenon were observed in 25% of the patients; 19% in patients with anti-Jo-1, 36% in anti-EJ, 11% in anti-PL-7, 30% in anti-PL-12, 25% in anti-KS, and 33% in anti-OJ antibodies. Interstitial lung disease was observed in all patients except for three (two with anti-Jo-1 and one with anti-PL-12). Myositis was diagnosed initially in 72% of patients with anti-Jo-1, 50% with anti-EJ, 40% with anti-PL-7, 42% with anti-PL-12, none with anti-KS, and 67% with anti-OJ antibodies, but additional 6%, 4%, 40%, 8%, 0%, and 0% with those individual antibodies, respectively, were diagnosed with myositis during the mean observation period of 9.6 years. Acute or subacute exacerbation of interstitial lung disease requiring immunosuppressive treatment intensification were observed in 28% of patients with anti-Jo-1, 33% with anti-EJ, 40% with anti-PL-7, 8% with anti-PL-12, 33% with anti-KS, and 67% with anti-OJ antibodies.
Conclusion: Almost all patients positive for anti-ARS positive had interstitial lung disease irrelevant of myositis diagnosis. Patients with anti-Jo-1 were suffering from typical myositis complicated with interstitial lung diseases at initial diagnosis, while patients with anti PL-7 tended to have precedent interstitial lung disease followed by development of myositis during clinical courses. The incidence of acute exacerbation of interstitial lung disease was the lowest in patients with anti-PL12.
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POS1221

CLINICAL FEATURES OF PATIENTS WITH ANTI-SYNTHETASE SYNDROME AND DERMATOMYOSITIS-ASSOCIATED SKIN MANIFESTATIONS: RESULTS FROM THE MYONET REGISTRY

Keywords: Myositis, Skin, Epidemiology

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Background: Up to 28% of patients with anti-synthetase syndrome (AsyS) have dermatomyositis (DM)-type rashes. However, it is not clear whether ASyS patients with DM-type rashes should be treated similarly to patients with DM or classified as DM in a clinical trial setting. Furthermore, it is not known if presence of DM-type rashes confers an increased risk of DM-specific extramuscular manifestations, such as malignancy.
Objectives: To compare clinical characteristics, including the frequency of cutaneous, extramuscular features, and malignancy, between adults with ASyS and DM.
Methods: Using data from the MYONET registry, an adult cohort of DM patients with anti-Mi2/TIF1γ/NXP2/SAE/MDA5 autoantibodies, and an ASyS cohort of patients with anti-tRNA synthetase autoantibodies (anti-Jo1/PL7/PL12/OJ/EJ/KS), were identified. Patients with DM *sine* dermatitis and with dual autoantibody specificities were excluded. Sub-cohorts of ASyS patients with or without skin involvement were defined based on presence of DM-type rashes (heliotrope rash, Gottron's papules, violaceous rash, shawl sign, V sign, erythroderma, and/or periorbital rash).
Results: In total, 737 patients were included (DM, n=251; ASyS, n=486). Within the ASyS cohort, 34% (n=163) had DM-type skin involvement (ASyS-skin). A higher frequency of Raynaud's phenomenon differentiated ASyS-skin from DM (n=72, 44% vs n=34, 14%, p<0.01), whereas higher frequency of any of four DM-type rashes: heliotrope rash (n=155, 62% vs n=73, 45%), V sign (n=69, 28% vs n=22, 14%), periorbital rash (n=53, 21% vs n=27, 17%), and shawl sign (n=89, 36% vs n=15, 9%) differentiated DM from ASyS-skin (all p<0.01). Cancer-associated myositis (CAM) was more frequent in DM (17%) compared to ASyS (3%) and ASyS-skin (3%) cohorts (both p<0.01) (Table 1).
Conclusion: DM-type rashes are frequent in patients defined as having ASyS; however, certain clinical features differentiate these patients from classical DM. Skin involvement in ASyS does not necessitate increased malignancy surveillance or investigation. These findings will help to inform future ASyS-based classification criteria.
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Table 1 Clinical manifestations of disease

	DM (n=251)	ASyS (n=486)	ASyS-skin (n=163)	ASyS-without-skin (n=323)	DM vs ASyS Adjusted p-value	DM vs ASyS-skin Adjusted p-value	ASyS-skin vs ASyS-without-skin Adjusted p-value
DM-type rashes n (%)	155 (62)	73 (15)	73 (45)	0 (0)	<0.01	<0.01	<0.01
Heliotrope Rash							
Gottron's Papules or Sign	145 (58)	110 (23)	110 (68)	0 (0)	<0.01	0.66	<0.01
Violaceous Rash	94 (38)	51 (11)	51 (31)	0 (0)	<0.01	0.23	<0.01
Erythroderma	22 (9)	9 (2)	9 (6)	0 (0)	<0.01	0.11	<0.01
Periorbital Rash	53 (21)	27 (6)	27 (17)	0 (0)	<0.01	0.04	<0.01
V Sign Rash	69 (28)	22 (5)	22 (14)	0 (0)	<0.01	<0.01	<0.01
Shawl Sign	89 (36)	15 (3)	15 (9)	0 (0)	<0.01	<0.01	<0.01
Extramuscular manifestations n (%)	72 (29)	75 (15)	43 (26)	32 (10)	<0.01	0.045	<0.01
Periungual Erythema							
Calcinosis	7 (3)	9 (2)	6 (4)	3 (1)	0.62	0.81	0.15
Ulceration	11 (4)	5 (1)	3 (2)	2 (1)	0.04	0.65	0.72
Vasculitis	4 (2)	1 (0.2)	0 (0)	1 (0.3)	0.045	0.61	1
Mechanic's Hands	11 (4)	142 (29)	62 (38)	80 (25)	<0.01	<0.01	<0.01
Raynaud's Phenomenon	34 (14)	178 (37)	72 (44)	106 (33)	<0.01	<0.01	<0.01
Arthritis	29 (12)	221 (46)	77 (47)	144 (45)	<0.01	<0.01	1
Dysphagia	72 (29)	88 (18)	35 (22)	53 (16)	<0.01	0.25	0.22
Alopecia	24 (10)	26 (5)	12 (7)	14 (4)	0.17	1	0.21
Interstitial Lung Disease	28 (11)	320 (66)	100 (61)	220 (68)	<0.01	<0.01	0.11
Cardiac Involvement	4 (2)	30 (6)	14 (9)	16 (5)	0.03	<0.01	0.20
CAM n (%)	42 (17)	16 (3)	5 (3)	11 (3)	<0.01	<0.01	0.90

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POS1222 PROGRESSIVE PULMONARY FIBROSIS IN ANTI-SYNTHETASE SYNDROME: A SINGLE CENTER COHORT

Keywords: Lungs, Myositis

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Background: Interstitial lung disease (ILD) is one of the major causes of morbidity and mortality in patients with idiopathic inflammatory myopathies (IIM). [1] Within IIM, ILD is frequently found in patients with anti-synthetase syndrome (ASyS). Current treatment is based on a combination of high doses of glucocorticoids and other immunosuppressors such as cyclophosphamide, with progression of ILD despite the treatment. One anti-fibrotic drug, nintedanib, has recently been approved for patients with progressive fibrotic ILD.

Objectives: To explore if within patients with ASyS there is a group with worsening ILD that fits the definition of progressive pulmonary fibrosis (PPF)[2] and thus would be eligible for anti-fibrotic treatment.[3]

Methods: A single center based retrospective cohort of patients diagnosed with ASyS, ILD involvement, and positivity for specific autoantibodies anti-Jo1, anti-PL7, anti-PL12, anti-EJ and/or anti-OJ (ASyS-AB) was identified using the Swedish Myositis network register. We selected the latest computed tomography (CT) thoracic scans, pulmonary function tests (PFT) and the development of respiratory symptoms according to clinical records. Patients were evaluated based on the INBUILD study criteria[3] and the international thoracic and respiratory clinical practice guideline (CPG)[2] for the presence of PPF. An experienced thoracic radiologist reviewed the CT scans of those who met the criteria to confirm PPF.

Results: We identified 147 individuals positive for ASyS-AB; 66 of them were not included due to either a follow-up period of less than one year, lack of data in the national registry or absence of ILD. Finally, a cohort of 81 patients was included, 67.9% women, with a median (Q1,Q3) age at disease onset of 58 (48,67) years (Table 1). The median time from disease onset until assessment for PPF criteria was of 6 years. The most prevalent CT finding amongst all groups was fibrotic changes (n=28) neither fitting the usual interstitial pneumonia (UIP) (n=9) nor the fibrotic non-specific interstitial pneumonia (NSIP) (n=6) criteria; followed by inflammatory NSIP (n= 18). 14.8 percent or 19.8 percent (INBUILD and CPG, retrospectively) of the individuals with any type of lung fibrotic pattern on CT met the definition of PPF.

Table 1. Baseline characteristics of patients with anti-synthetase syndrome (ASyS) in the cohort

	Total	By antibody				
		PL7, n=8	**PL12**, n=8	**Jo1**, n=58	**EJ**, n=4	**OJ**, n=3
Women, n (%)	55 (67.9)	6 (75)	5 (62.5)	40 (69)	3 (75)	1 (33.3)
Median age at disease onset, years (Q1,Q3)	58 (48,67)	61 (35,68)	61 (48,67)	56 (47,65)	72 (46,76)	61 (55,74)
Time since disease onset at evaluation, years (Q1,Q3)	6 (3,11)	10 (3,22)	4 (2,5)	7 (3,13)	2 (2,15)	4 (1,7)
Patients meeting criteria for progressive fibrosis, n (%)						
INBUILD criteria	12 (14.8)	2 (25)	1 (12.5)	8 (13.8)	0 (0)	1 (33.3)
ATS/ERS/JRS Clinical practice guidelines	14 (17.3)	3 (37.5)	1 (12.5)	10 (17.2)	0 (0)	0 (0)
Time since disease onset at evaluation, years (Q1,Q3)	10 (5,21)	-	-	-	-	-

Conclusion: In this cross-sectional study, 15% of patients with ASyS fulfilled the definition of progressive fibrosis and thus could be eligible for anti-fibrotic treatment. To our knowledge, this is the first cohort to demonstrate a possible real-life target of anti-fibrotics in IIM-ILD.

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POS1223 ASSOCIATION BETWEEN NAILFOLD VIDEOCAPILLAROSCOPY FINDINGS AND SKL-6 LEVELS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES–RELATED INTERSTITIAL LUNG DISEASE

Keywords: Outcome measures, Cytokines and chemokines, Myositis

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Background: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of acquired muscle diseases with distinct clinical, pathological and histological features. interstitial lung disease (ILD) is a frequent pulmonary manifestation in IIM (IIM-ILD) and considerably influences morbidity and mortality. Krebs von den Lungen 6 (sKL-6) has been proposed as a potential biomarker reflecting the severity of ILD in connective tissue diseases. Raynaud's phenomenon is very

frequent and the presence of microvascular changes in IIM have been described however, the role of nailfold videocapillaroscopy (NVC) in diagnosis and prognosis in IIM is not clearly established.

Objectives: To determine if there is any association between NVC findings, sKL-6 levels and pulmonary involvement in patients with inflammatory myopathies.

Methods: We performed a retrospective study of IIM patients followed in a reference center and compared them according to the presence of ILD. Epidemiological, clinical and immunological data, pulmonary function tests (forced vital capacity and diffusing capacity for carbon monoxide), sKL-6 levels and NVC finding were retrieved. NVC findings including loss of capillary density, enlarged and giant capillaries, ramified capillaries, haemorrhages, thrombosis, avascular areas, disorganization of capillary architecture and subpapillary venous plexus presence were recollected, if present. Statistical analysis was performed by T-test and Fisher's exact test to compare qualitative and/or quantitative variables and multiple logistic regression modelling to identify correlation between pulmonary function tests, NVC findings and sKL-6 levels. Values of p<0.05 were considered statistically significant.

Results: 95 patients were included, 47 patients (49%) with ILD. 34% were male with a median age at inclusion of 55.3±24 years and a median disease duration of 6.8±7 years. Avascular areas and capillary loss showed a significant association with the presence of ILD (OR 2.43, 95% CI 1.3-5.7, p 0.004) and (OR 1.7, 95% CI 1.48-3.1, p 0.04). A negative correlation between capillary loss and enlarged capillaries was also found with FVC% (β=-0.46, p 0.001 and β=-0.57, p <0.0001) and DLCO% (β=-0.32, p 0.04 and β=-0.23, p 0.03), respectively. When we studied the correlation between sKL-6 levels, positive correlations with the presence of ILD (β=0.77, p 0.0004), the presence of hemorrhages (β =0.21, p 0.04) and avascular areas in NVC (β =0.64, p 0.03) and negative correlations with FVC% (β=-0.47, p 0.001) and DLCO% (β=-0.59, p, 0.005) were found. Multiple logistic regression identified as predictors for developing IIM-ILD are summarized in Table 1 and represented in the scatter plot in Figure 1. Male sex, respiratory symptoms, %FVC and %DLCO, sKL-6 levels, anti-Jo1 positivity and the presence of avascular areas and enlarged capillaries in NVC were identified as IIM-ILD predictors (R^2=0.974, p =0.006).

Conclusion: Capillary loss and avascular areas showed a significant association with the presence of ILD, worse FVC and DLCO values and sKL-6 levels. We identified 9 predictors for developing ILD in IIM. NVC assessment and sKL-6 levels can have a predictive role for studying pulmonary function and assessing the prognosis of IIM-ILD.

Table 1. Significant logistic regressions for predictors for IIM-ILD

Predictor	B value	P value
Male sex	0.186	0.036
Respiratory symptoms	0.40	0.002
%FVC	-0.322	0.01
%DLCO	-0.59	0.001
sKL-6 levels	0.53	0.002
Anti-Jo 1	0.28	0.03
Avascular areas	0.72	0.006
Enlarged capillaries	0.49	0.04

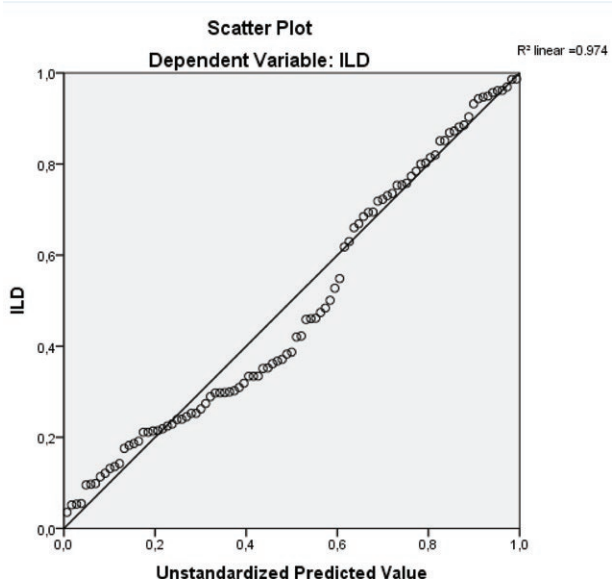


Figure 1 : Scatter plot

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POS1224

CLINICAL FEATURES AND PREDICTORS OF MYOCARDIAL INVOLVEMENT IN ANTI-SYNTHETASE SYNDROME PATIENTS

Keywords: Heart, Myositis, Biomarkers

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Background: Anti-synthetase syndrome (ASS) is a rare systemic connective tissue disease with protean clinical manifestations. Myocarditis is one of the most worrisome organ involvement[1].

Objectives: To investigate the features associated with myocardial involvement and the predictors of myocarditis in ASS patients.

Methods: ASS patients followed up at our Myositis Clinic were identified. Patients were classified as having myocarditis whether they had a positive cardiac magnetic resonance (CMR) and/or a positive endomyocardial biopsy (EMB). All patients underwent troponin T, NTproBNP and echocardiography at first evaluation at our

Table 1. Baseline features of ASS patients with and without myocarditis

	Myocarditis (n = 13)	**No Myocarditis** (n = 30)	**p-value**
Age (years)	60 ± 13	56 ± 15	0.641
Sex (female)	6 (46%)	26 (87%)	**0.009**
Cardiovascular risk factors	2 (15%)	3 (10%)	0.637
IMA	6 (46%)	7 (23%)	0.173
Smoking	4 (31%)	11 (37%)	0.739
Arterial Hypertension	2 (15%)	2 (7%)	0.589
Obesity/overweight	2 (15%)	4 (14%)	0.999
Dyslipidemia	1 (8%)	2 (7%)	0.999
Diabetes	0 (0)	1 (3%)	0.999
Sudden cardiac death familiarity			
Autoantibodies	7 (54%)	16 (53%)	0.999
Anti-Jo1	3 (23%)	4 (13%)	0.655
Anti-PL7	1 (8%)	5 (17%)	0.649
Anti-PL12	1 (8%)	2 (7%)	0.999
Anti-EJ	7 (54%)	13 (43%)	0.740
Anti-SSA			
Clinical features	9 (69%)	5 (17%)	**0.001**
Fever	8 (61%)	15 (50%)	0.526
Muscle weakness	6 (46%)	7 (23%)	0.163
Mylagias	5 (38%)	10 (33%)	0.742
Raynaud's phenomenon	0 (0)	1 (3%)	0.999
Calcinosis	10 (77%)	21 (70%)	0.727
ILD	7 (54%)	14 (47%)	0.747
Dyspnoea	3 (23%)	6 (20%)	0.999
Dysphagia	1 (8%)	2 (7%)	0.999
Gottron's sign	3 (23%)	6 (20%)	0.999
Mechanical hands	1 (8%)	3 (10%)	0.999
Heliotrope rash	5 (38%)	8 (27%)	0.485
Arthritis			
MMT8 score	83 ± 25	74 ± 7	0.564
Biochemistry	29 ± 19	25 ± 19	0.584
ESR (mm/1h)	21 ± 16	3 ± 2	**0.011**
CRP (mg/L)	2182 ± 792	1200 ± 401	0.249
CPK (U/L)	528 ± 279	358 ± 224	0.220
LDH (U/L)	136 ± 101	35 ± 30	**0.007**
AST (U/L)	133 ± 108	37 ± 27	**0.006**
ALT (U/L)			
Echocardiography	56 ± 9	22 patients	0.076
LVEF (%)	3 (23%)	62 ± 5	0.106
Hypokinesia	2 (15%)	1 (4%)	0.586
LVEF<55%	1 (8%)	2 (9%)	0.999
Pericardial effusion	4 (31%)	1 (4%)	0.148
Diastolic dysfunction		2 (9%)	
Cardiac enzymes	461 ± 351	41 ± 36	**<0.001**
Troponin T (ng/L)	1802 ± 1484	248 ± 198	**0.013**
NTproBNP (pg/mL)	1 (8%)	2 (9%)	0.999
Troponin T <2x	3 (23%)	0 (0%)	**0.044**
Troponin T between 2 – 5x	8 (61%)	6 (27%)	0.075
Troponin T > 5x			

centre. Those with palpitations and/or evidence of arrhythmias also underwent 24-hour Holter-ECG. Patients with abnormalities in one the above mentioned parameters underwent CMR +/- EMB. The presenting features and the prevalence of traditional cardiovascular risk factors were compared between the 2 groups. Univariate and multivariate logistic regression analyses were performed.

Results: 43 ASS patients were identified, 13 (30%) with myocarditis and 30 (70%) without myocarditis; of these baseline echocardiography data and troponin T and NTproBNP levels before immunosuppressive treatment introduction were available for all myocarditis patients and for 22 ASS patients without myocarditis. The clinical characteristics of patients are summarized in Table 1. At baseline myocarditis patients were more frequently male, had more raised levels of troponin T (although not always with values > 5 times upper limits of normality), NTproBNP, liver enzymes and CRP. Of note, for what concerns clinical features, only fever was more frequently observed in ASS patients with myocarditis (69% versus 17%, p = 0.001). At multivariate logistic regression analysis only the presence of fever at baseline (OR 7.707, 95%CI 1.026 – 57.917, p =0.047) was associated with myocarditis.

Conclusion: Myocarditis is not a rare, but likely, an overlooked manifestation in ASS. Myocarditis in ASS can be subtle as shown by the presence of only slightly raised cardiac enzymes in some patients and the absence of striking echocardiographic or clinical features. The presence of fever might suggest that a more inflammatory phenotype is associated with myocarditis in ASS.

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POS1225 PATIENT GLOBAL ASSESSMENT AND INFLAMMATORY MARKERS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES – A LONGITUDINAL STUDY FROM THE MYONET COHORT

Keywords: Myositis, Patient reported outcomes

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Background: Idiopathic inflammatory myopathies (IIM) constitute a heterogeneous group of diseases with systemic inflammation. Inflammation has previously been associated with poor subjective health appraisal in both acute and chronic inflammatory diseases [1-5].

Objectives: To explore if the patient-reported outcome measure "patient global assessment" (PGA) is associated with markers of inflammation over time and if associations could be explained by functional measures in patients with IIM.

Methods: PGA and inflammatory markers longitudinally collected over 5 years were retrieved for 1333 patients with IIM from the international MyoNet registry. Associations between PGA, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and creatine kinase (CK) were analyzed with mixed effect regression analyses. Mediation analysis was used to test if the associations between PGA and inflammatory markers could be explained by disease-associated symptoms and signs.

Results: PGA improved and inflammatory markers decreased during the first year of observation. High levels of ESR and CRP were associated with worse PGA in both men (ESR:*b*=0.21, 95%CI 0.10-0.32, p<0.001, CRP:*b*=0.16, 95%CI 0.04-0.29, p=0.012) and women (ESR:*b*=0.34, 95%CI 0.25-0.42, p<0.001, CRP:*b*=0.26, 95%CI 0.14-0.37, p<0.001) across time points, and CK was associated with PGA in women (*b*=0.70, 95%CI 0.48-0.93 p<0.001) but not in men (*b*=0.07, 95%CI -0.54-0.68, p=0.831). In men, the association between elevated inflammatory markers and poorer PGA was explained by disability and extra-muscular disease activity whereas in women this association could not be explained by any of the included functional measures. With a few exceptions, the association between reduced inflammatory markers and improved PGA during the first year of observation was partially mediated by improvements in all functional measures.

Conclusion: Higher levels of systemic inflammation were associated with poorer PGA in patients with IIM. In addition to known benefits of lowered inflammation, these findings emphasize the need to reduce systemic inflammation to improve subjective health.

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Longitudinal associations between PGA and inflammatory markers

Women	obs (n)	patients (n)	b PGA	CI	p-value	Men	obs (n)	patients (n)	b PGA	CI	p-value
ESR[1]	2447	545	0.34	0.25;0.42	<0.001***	**ESR[1]**	1035	254	0.21	0.10,0.32	<0.001***
CRP[2]	2720	733	0.26	0.14;0.37	<0.001***	**CRP[2]**	1107	308	0.16	0.04;0.29	0.012*
CK[3]	2823	821	0.70	0.48;0.93	<0.001***	**CK[3]**	1109	336	0.07	-0.54;0.68	0.831

*p<0.05, **p<0.01, ***p<0.001. 1.Erythrocyte sedimentation rate. 2.C-reactive protein. 3. Creatine kinase as ratio of upper limit normal.Mixed models with fixed effect coefficients (b) and 95% confidence intervals (bootstrapped based p-values, 20000 repetitions). All models were adjusted for age and included all available data points.

POS1226 CARDIOVASCULAR RISK IN PATIENTS WITH MYOSITIS COMPARED TO THE GENERAL POPULATION

Keywords: Myositis, Cardiovascular disease

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Background: Cardiovascular (CV) risk due to accelerated atherosclerosis and impaired metabolism can be increased in idiopathic inflammatory myopathies (IIM) on behalf of systemic inflammation, limited mobility, and glucocorticoid therapy.
Objectives: This study aimed to evaluate CV risk in patients with IIM in comparison to healthy controls (HC) and to assess its association with disease-specific features.
Methods: 90 patients with IIM (70 females; mean age 56.6; mean disease duration 5.95 years; dermatomyositis: n=29, polymyositis: n=12, immune-mediated necrotizing myopathy (IMNM): n=20, anti-synthetase syndrome: n=29) and 180 HC (130 females, mean age 54.3) were included. In both groups, subjects with a history of CV disease (angina pectoris, myocardial infarction, cerebrovascular, and peripheral arterial vascular events) were excluded. Muscle involvement, disease activity, and tissue damage were evaluated (by MMT-8, MITAX, MDI, respectively). Comorbidities and current treatment were recorded. All participants underwent examinations of carotid intima-media thickness (CIMT), pulse wave velocity (PWV), ankle-brachial index (ABI), and body composition (by densitometry (DXA) and bioelectrical impedance analysis (BIA)). The risk of fatal CV events was evaluated by the Systematic COronary Risk Evaluation (SCORE, charts for the European population) and its modifications: SCORE multiplied by the coefficient 1.5 (mSCORE), and SCORE2.
Results: Compared to HC, IIM patients had a significantly higher prevalence of traditional CV risk factors, carotid artery disease (CARD), abnormal ABI, and PWV ($p<0.05$ for all). After propensity score matching (PSM) using traditional CV risk factors, the prevalence of CARD and pathologic PWV remained significantly higher in IIM than HC ($p<0.05$ for all), but no significant difference in SCORE was observed. Overall CV risk based on calculated risk (modifications of SCORE) and ultrasound (US) examinations was comparable between IIM ad HC after PSM (CVR-SCORE $p=0.457$, CVR-SCORE2 $p=0.130$, CVR-US $p=0.126$). IMNM patients had the most unfavorable CV risk profile among IIM subtypes. The calculated CV risk scores by SCORE and SCORE2 (in both IIM and HC), and mSCORE (in IIM only) were reclassified according to CIMT and the presence of carotid plaques. SCORE was demonstrated to be the most inaccurate in predicting CV risk in IIM, while there was a significantly higher proportion of reclassified patients with underestimated CV risk evaluated by SCORE compared to SCORE2 and mSCORE ($p=0.020$). Age, disease activity, lipid profile, body composition parameters, and blood pressure were the most significant predictors of CV risk in IIM patients ($p<0.05$ for all variables in bivariate analysis). Moreover, the length of glucocorticoid therapy was positively associated with an increased count of carotid plaques and overall CV risk estimated by US examination ($p<0.05$ for both).
Conclusion: This cross-sectional cohort study in IIM patients demonstrated a significantly increased risk of subclinical atherosclerosis and CV risk, and also an increased prevalence of traditional CV risk factors compared to HC with comparable age and gender distribution. The most unfavorable findings were seen in patients with IMNM. All scoring systems for CV risk screening underestimated the CV risk in IIM when using the CV risk according to ultrasound findings. SCORE2 appeared to be the most accurate tool in IIM.
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Disclosure of Interests: None Declared.
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POS1227 CAPISAS PROJECT: INCIDENCE AND EPIDEMIOLOGY OF ANTISINTETASE SYNDROME IN CATALONIA (SPAIN) BETWEEN 2016 AND 2019

Keywords: Myositis, Autoantibodies

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Background: Antisynthetase syndrome (ASSD) is an autoimmune disease characterized by the presence of antiaminoacyl tRNA-synthetase antibodies (ARS) and clinical manifestations that may include interstitial lung disease (ILD), myositis, arthritis, Raynaud´s phenomenon (RP), fever and mechanic's hands (MHs). The incidence rate is unknown and no population epidemiological studies have been published.
Objectives: To determine the incidence and epidemiology of ASSD between 2016 and 2019 in Catalonia. Diagnostic criteria considered were: the positivity of ARS associated with at least one major clinical manifestation (myositis, ILD or arthritis)
Methods: Restrospective multicentrical observational study. All patients with a first ARS (Jo1, PL7, PL12, OJ, EJ) positive during the period study were selected. Patient identifacation was carried out through the immunology laboratories of all the hospitals of the public catalan network. We estimed the cumulative incidence in the average population of Catalonia betwen 2016-2019 (7.526.982 individuals) and collected demographic, epidemiologic, clinical and immunologic data.
Results: We identified 201 patients with ARS, 125 of them met ASSD criteria. The estimated cumulative incidence was 1.66 cases per 100,000 inhabitants. Most were women (62.9%) with a mean age at diagnosis of 59.8 years (DE 15.4) and 78.3% southern european caucasians. Sixty three per cent worked in the tertiary sector and 20.5% in the secondary. Some environmental exposure were recognized in 17.9%, being contact with animals and asbestos the most common, and 38.8% were smokers or ex-smokers. Anti-Jo1 was the most frequent ARS (39.2%), followed by PL7 (28.8%), PL12 (21.6%), EJ (5.6%) and OJ(4.8%). ANA were positive in 74%, mostly with a cytoplasmic pattern (59,3%). Another specific ANA was present in 58.4%, predominantly Ro52 (48%). Rheumatoid factor, ACPA and ANCA were positive in 13.6%, 4.6% and 4.3% respectively. The mean age at first symptom was 58.5 years (DE 15.6). All patients presented at least one major manifestation: 45.6% one, 40.8% two and 13.6% three. ILD was present in 90.3%: subacute/chronic dyspnea 39.3%, cough 22.3%, rapidly progressive dyspnea 18.8% and 17% asymptomatic. HRCT patterns observed were: NSIP 50.5%, OP 15.3%, NSIP+OP 11,7%, UIP 11.7% and unclassifiable pattern 9.9%. Myositis was present in 64 cases (51.6%). Muscle biopsy was available in 34 cases: 50% dermatomyositis pattern, 36% polymiositis pattern, 20% indeterminate pattern and 1% necrotizing myositis. Arthritis was present in 27.2% (polyarthritis 78.6%, oligoarthritis 21.4%), RP 11.2%, fever 25.4% and skin manifestations 49,6% (71% MH's, 27.4% Gottron'n papules, 12.9% heliotrope rash and 3.2% shawl rash). First manifestation was ILD in 58.9% of patients, followed by myositis (21.4%) and arthritis (19.6%). Fifteen patients (12%) presented cancer, 8 of them less than 3 years from AS diagnosis. Breast cancer was the most common. In 14 cases (11.2%) another autoimmune disease was associated, highlighting 6 cases with Sjögren's syndrome.
Conclusion: The estimated cumulative incidence of ASSD between 2016 and 2019 in Catalonia was 1.66 cases per 100,000 inhabitants. Despite the absence of diagnostic criteria for ASSD, the presence of ARS is a necessary condition to

establish it. We believe that identification of cases based on positive results of anti-ARS antibodies is a useful strategy to determine the incidence of ASSD in our territory.

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Disclosure of Interests: None Declared.

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POS1228 DETERMINANTS OF PATIENT GLOBAL DISEASE ACTIVITY IN ADULT MYOSITIS

Keywords: Myositis, Patient reported outcomes

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Background: Myositis is a heterogeneous rare autoimmune disorder with muscle weakness and many systemic features that contribute to morbidity and mortality. The myositis core set measures (CSM) were developed to capture myositis disease activity, and are useful in clinical practice and therapeutic trials [**1].** However, the CSM are primarily subjective physician assessments. Understanding the drivers of the patient global (PT global) disease activity assessment and the difference between the physician and patient perception of their disease activity is important to elucidate [**2].**

Objectives: To examine the determinants of the PT global, and the discordance between PT global and physician-global (MD global) disease activity in myositis.

Methods: Adults with myositis were enrolled at the University of Pittsburgh Myositis Center and the following outcome measures were collected: Manual muscle testing (MMT), HAQ, creatine kinase (CK), fatigue, pain, PROMIS physical function (PF-20), Short Form-36 (SF-36), sit-to-stand, timed up-and-go, six-minute walk, and Actigraph step per min/day count. PT- and MD global scores (10cm visual analog scale [VAS]) were recorded, and discordance was defined as ≥3 point difference between the scores based on published literature in other rheumatic diseases [**3].** The difference in both scores was also analyzed in myositis subjects with active vs inactive disease. A linear regression model was used to determine the contribution of each measure to the PT global.

Results: Fifty patients (60% females; mean age 51.6 [±14.9] years) with probable/definite myositis (24 dermatomyositis [DM], 6 polymyositis [PM], 9 necrotizing myositis [NM] and 11 anti-synthetase syndrome [ASyn]) according to the ACR/EULAR Classification Criteria were enrolled prospectively. PT global correlated strongly with muscle disease activity, MD global, MMT, HAQ-DI, PROMIS physical function, pain VAS, fatigue VAS, SF36 physical function, health, fatigue, social functioning, and pain subdomains, 6MWD and step per min/day count (r=0.57-0.75), moderately with STS, TUG and CK levels (r=0.36-0.46), and poorly with cutaneous, pulmonary, and extra-muscular disease activity (r=0.02-0.17). Correlations of PT global with pain, physical function, fatigue, quality of life and physical activity measures were overall stronger than the MD global, as opposed to muscle and extra-muscular disease activity which correlated better with the MD global. Physical function and fatigue measures contributed most to the PT global, followed by measures of pain, physical activity, quality of life, and muscle disease, while the MD global was primarily driven by muscle disease activity (**Figure 1**). The PT global was discordant with MD global in 30% (n=15) of the patients, where the PT global was higher than the MD global in 66% (n=10). Patients with a discordantly high PT global suffered from significantly higher levels of pain (p=0.03), fatigue (p=0.05), and more functional limitation as reflected by the HAQ (p=0.04).

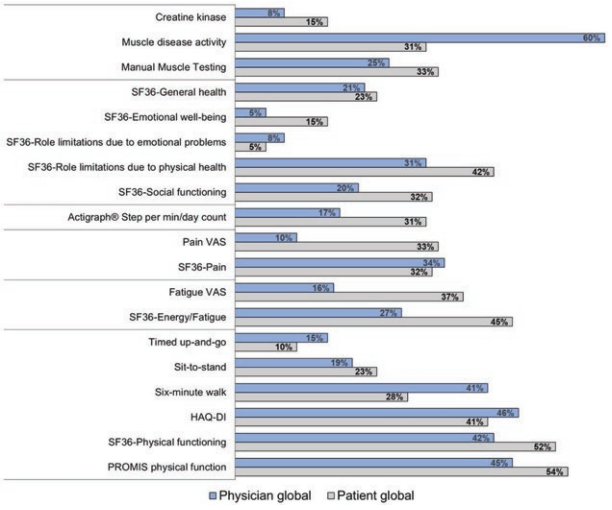


Figure 1. The determinants of patient-reported global disease activity (PT global) and physician-reported global disease activity (MD global).

Conclusion: Fatigue, pain, and physical activity are important driving factors of the differences observed in the patient vs. physician assessment of myositis disease activity. Understanding the gap between patient-physician perspectives may help provide patient-centered care.

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POS1229 DO MYOSITIS AUTOANTIBODIES PREDICT RESPONSE TO IVIG IN DERMATOMYOSITIS? A POST-HOC ANALYSIS OF THE PRODERM TRIAL

Keywords: Myositis, Randomized control trial, Autoantibodies

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Background: Dermatomyositis (DM) is an immune-mediated idiopathic inflammatory myopathy (IIM). Two subsets of autoantibodies have been identified in patients with IIM. The first includes myositis-specific antibodies (MSA) such as anti-Jo-1, anti-TIF-1 and anti-MDA-5. The second includes myositis-associated antibodies (MAA) such as anti-PM-SCL, anti-Ku and anti-Ro, which are also found in patients with other autoimmune diseases. MSA are highly specific for IIMs and represent a unique clinical phenotype and prognosis, and have also been associated with the pathogenesis of various subsets of IIM. The ProDERM study recently demonstrated the efficacy and safety of intravenous immunoglobulin (IVIg) in DM patients (1) but the potential role of MSA and MAA in the treatment responses of these patients has not yet been determined.

Objectives: Autoantibody status at baseline and its relationship to treatment response to IVIg were investigated in a post-hoc analysis of the randomized, placebo-controlled ProDERM study.

Methods: In the ProDERM study, dermatomyositis patients received 2 g/kg IVIg treatment (n=47) or placebo (n=48) every 4 weeks for 16 weeks. From week 16 onwards eligible patients (n=91) received IVIg for a further 24 weeks. The primary endpoint was a Total Improvement Score (TIS) of at least 20 (indicating at least minimum improvement) at week 16 and no confirmed deterioration up to week 16. Serum samples were taken at baseline and analysed for MSA (anti-Jo-1, PL-12, SRP, Mi-2, TIF-1, MDA5, MJ, SUMO) and MAA (anti-PM-SCL, Ku, U1RNP, Ro/SSA) by the Oklahoma Medical Research Foundation. Patients were stratified according to their antibody status as MSA-positive (including patients who were also MAA-positive), MAA-positive only, or antibody negative at baseline. The association of antibody status with treatment response measured by TIS was evaluated.

Results: At baseline, a total of 49 (52%) patients were MSA-positive, 13 (14%) were MAA-positive, and 33 (35%) were antibody negative. Demographics of patients in each group are shown in Table 1. Of patients who were MSA-positive, 10 were also positive for MAA. The numbers of patients from the ProDERM study with each specific MSA and MAA are shown in Figure 1.

In the MSA group, 71% (35/49) of patients had TIS response (score ≥20) at week 16, compared to 55% (18/33) in the autoantibody-negative group. In the MSA group 24 patients were randomized to IVIg and of these 83% (20/24) showed TIS response (score ≥20) at week 16 compared to 60% (15/25) in the group of MSA-positive patients receiving placebo. Additional analyses (including results for specific subgroups in the MSA-positive group) will be presented at the EULAR 2023 congress.

Conclusion: Myositis-specific antibodies were commonly identified in patients with dermatomyositis in the ProDERM study. Further analyses will determine if specific MSA, such as anti-TIF-1 and others, play a role in treatment response to IVIg.

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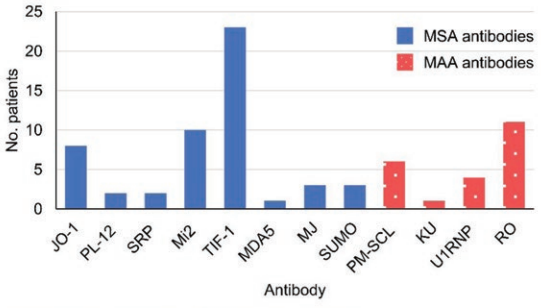
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Table 1. Patient demographics and baseline characteristics

	MSA-positive* (N=49)	MAA-positive** (N=13)	Antibody negative (N=33)
Mean (range) age, years	51 (22–79)	54 (33–70)	54 (28–77)
Mean (range) time since diagnosis, years	3.66 (0.16–15.6)	5.04 (0.39–18.4)	5.8 (0.09–48.7)
Sex, n (% female)	39 (79.6)	11 (84.6)	12 (63.6)
Race, n (% White)	42 (85.7)	13 (100.0)	32 (97.0)
Mean BMI, kg/m^2	29.8	27.0	26.5
Disease severity, n (%)	10 (20.4)	4 (30.8)	12 (36.4)
Mild	31 (63.3)	8 (61.5)	17 (51.5)
Moderate	8 (16.3)	1 (7.7)	4 (12.1)
Severe			
CDASI score	19 (38.8)	5 (38.5)	20 (60.6)
≤14	30 (61.2)	8 (61.5)	13 (39.4)
>14			
Randomised treatment	24	4	19
IVIg	25	9	14
Placebo			

BMI, body mass index; CDASI, Cutaneous Disease Area and Severity Index; IVIg, intravenous immunoglobulin; MAA, myositis-associated antibodies; MSA, myositis-specific antibodies.*10 patients positive for MSA were also positive for MAA.**MAA-positive group contains only patients with MAA (no MSA).

Figure 1. Numbers of dermatomyositis patients with myositis-specific antibodies (MSA) and myositis-associated antibodies (MAA) in the ProDERM trial*



*Patients may have been positive for more than one autoantibody

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POS1230

ASSOCIATION OF CANCER AND ANTISYNTHETASE SYNDROME: A RETROSPECTIVE MULTICENTER STUDY

Keywords: Myositis, Malignancy

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Background: Idiopathic inflammatory myopathies (IIM) are rare and heterogeneous conditions, associated with cancer in 10 to 30% of cases. While some features have been associated with cancer (age, male sex, dermatomyositis, anti-TIF1-γ antibodies), the association with cancer is more debated in antisynthetase syndrome (ASS). Few studies have assessed the prevalence of cancer during ASS meeting the criteria of cancer-associated myopathy (CAM)(cancer diagnosed within 3 years before or after the diagnosis of ASS) [1].

Objectives: The main objective was to assess the prevalence of CAM in patients with ASS. Secondary objectives were to describe clinical features, biological features and prognosis associated with CAM in ASS patients.

Methods: In this retrospective multicenter study, we included patients of the main tertiary care centers of Grand-Est and Bourgogne-Franche Comté regions (MyositEst network). Inclusion criteria were age ≥ 18 years old, and Connors criteria fulfilment. Patients with low antisynthetase antibodies levels were excluded.

Results: Among 212 patients screened, 122 patients were included, with a median age of 53.5 ± 14.5 years old, and a female predominance (68%) (Figure 1). The most frequent manifestations of ASS were interstitial lung disease, myositis, skin involvement and inflammatory rheumatism (81%, 69%, 65% and 57%, respectively), followed by fever and cardiac involvement (16% and 4%, respectively). The most frequent specific antibodies were anti-JO1, anti-PL12 and anti-PL7 antibodies (61%, 17% and 10%, respectively), followed by anti-EJ and anti-OJ antibodies (7% and 1.6%, respectively). Four patients were positive for both anti-JO1 and anti-PL12 antibodies, and 1 was positive for both anti-JO1 and anti-PL7 antibodies. Among patients included, 15 (12.3%) met CAM criteria. The diagnosis of cancer was made following whole-body imaging (n=10, either CT-scan or ^{18}FDG-positron emission tomography), systematic cancer screening (n= 3) and physical examination (n= 2). Patients with cancer were older (63.5 ± 8.27 *vs.* 52.1 ± 14.7 years-old, p = 0.0001), had lower CPK levels (541 ± 962 *vs.* 1628 ± 2404 U/L, p = 0.004), less frequently myalgia (20% *vs.* 46.7%, p = 0.05) and a higher MRC muscle scale (4.93 ± 0.25 *vs.* 4.6 ± 0.7, p = 0.0014). CAM patients had more frequent history of cancer (46.6% *vs.* 2.7%, p = 0.004) and had a higher mortality rate (33% *vs.* 5%, p = 0.003). Age above 55 years-old, fever and CPK below 500 U/L were associated with CAM both on bivariate and multivariate analysis (logistic regression model, entry p valule threshold of 0.2,

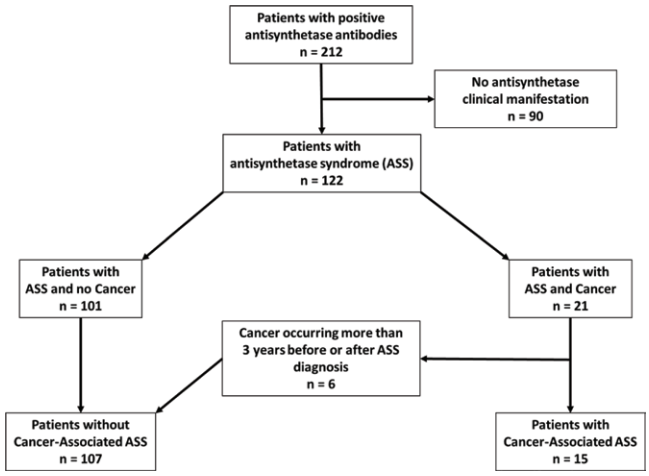


Figure 1 : Flow chart

OR = 7.3 [1.72 – 50.6], p = 0.01; OR = 4.12 [1.03 – 16.6], p = 0.04; and OR = 4.2 [1.1 – 21.1], p = 0.04, respectively)(Table 1).

Conclusion: In our study, CAM in ASS were more prevalent compared to literature data. CAM were independently associated with age, fever and low CPK levels. CAM patients had higher mortality. Careful physical examination, age and sex-based cancer screening, and whole-body imaging could be a relevant screening strategy.

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Table 1: Factors associated with Cancer-Associated Myopathy in patients with antisynthetase syndrome.

Characteristics		Event yes/no (%)	Bivariate analysis		Multivariate analysis	
			OR (95%CI)	p	OR (95%CI)	p
Age > 55 years	No	3/61 (5%)				
	Yes	12/46 (21%)	5.3 (1.41 to 19.89)	0.01	7.3 (1.72 to 50.6)	0.015
Female	Male	7/32 (18%)				
	Female	8/75 (9.6%)	2.1 (0.68 to 6.13)	0.2		
Fever	No	8/94 (7.8%)				
	Yes	7/13 (35%)	6.32 (1.96 to 20.35)	0.0034	12 (1.03 to 16.6)	0.042
CPK < 500 U/L	No	29/181 (16.5)				
	Yes	2/8 (25.0)	4.42 (1.15 to 16.9)	0.03	4.2 (1.1 to 21.1)	0.049
Inflammatory rheuamtism	No	8/45 (15.1%)				
	Yes	7/62 (10.1%)	0.63 (0.21 to 1.9)	0.4		
Interstitial lung disease	No	1/22 (4.3%)				
	Yes	14/85 (14.1%)	3.62 (0.45 to 29.1)	0.22		
Skin involvement	No	9/70 (11.4%)				
	Yes	6/37 (14%)	0.78 (0.26 to 2.39)	0.7		
Muscular involvement	No	8/76 (9.5%)				
	Yes	7/31 (18.4%)	0.47 (0.15 to 1.39)	0.2		
Cardiac involvement	No	14/103 (12%)				
	Yes	1/5 (16.6%)	1.83 (0.19 to 17.6)	0.5		

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POS1231

IMPAIRED HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: A CROSS-SECTIONAL ANALYSIS FROM AN INTERNATIONAL E-SURVEY

Keywords: Patient reported outcomes, Myositis, Quality of life

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Background: Comprehensive and large-scale assessment of health-related quality of life in patients with idiopathic inflammatory myopathies (IIMs) worldwide is lacking. The second COVID-19 vaccination in autoimmune disease (COVAD-2) study [1] is an international, multicentre, self-reported e-survey assessing several aspects of COVID-19 infection and vaccination as well as validated patient-reported outcome measures (PROMs) to outline patient experience in various autoimmune diseases (AIDs), with a particular focus on IIMs.

Objectives: To investigate physical and mental health in a global cohort of IIM patients compared to those with non-IIM autoimmune inflammatory rheumatic diseases (AIRDs), non-rheumatic AIDs (NRAIDs), and those without AIDs (controls), using Patient-Reported Outcome Measurement Information System (PROMIS) global health data obtained from the COVAD-2 survey.

Methods: Demographics, AID diagnoses, comorbidities, disease activity, treatments, and PROMs were extracted from the COVAD-2 database. The primary outcomes were PROMIS Global Physical Health (GPH) and Global Mental Health (GMH) scores. Secondary outcomes included PROMIS physical function short form-10a (PROMIS PF-10a), pain visual analogue scale (VAS), and PROMIS Fatigue-4a scores. Each outcome was compared between IIMs, non-IIM AIRDs, NRAIDs, and controls. Factors affecting GPH and GMH scores in IIMs were identified using multivariable regression analysis.

Results: A total of 10,502 complete responses from 1582 IIMs, 4700 non-IIM AIRDs, 545 NRAIDs, and 3675 controls, which accrued as of May 2022, were analysed. Patients with IIMs were older [59±14 (IIMs) *vs*. 48±14 (non-IIM AIRDs) *vs*. 45±14 (NRAIDs) *vs*. 40±14 (controls) years, p<0.001] and more likely to be Caucasian [82.7% (IIMs) *vs*. 53.2% (non-IIM AIRDs) *vs*. 62.4% (NRAIDs) *vs*. 34.5% (controls), p<0.001]. Among IIMs, dermatomyositis (DM) and juvenile DM were the most common (31.4%), followed by inclusion body myositis (IBM) (24.9%). Patients with IIMs were more likely to have comorbidities [68.1% (IIMs) *vs*. 45.7% (non-IIM AIRDs) *vs*. 45.1% (NRAIDs) *vs*. 26.3% (controls), p<0.001] including mental disorders [33.4% (IIMs) *vs*. 28.2% (non-IIM AIRDs) *vs*. 28.4% (NRAIDs) *vs*. 17.9% (controls), p<0.001]. GPH median scores were lower in IIMs compared to NRAIDs or controls [13 (interquartile range 10–15) IIMs *vs*. 13 (11–15) non-IIM AIRDs *vs*. 15 (13–17) NRAIDs *vs*. 17 (15–18) controls, p<0.001] and PROMIS PF-10a median scores were the lowest in IIMs [34 (25–43) IIMs *vs*. 40 (34–46) non-IIM AIRDs *vs*. 47 (40–50) NRAIDs *vs*. 49 (45–50) controls, p<0.001]. GMH median scores were lower in AIDs including IIMs compared to controls [13 (10–15) IIMs *vs*. 13 (10–15) non-IIM AIRDs *vs*. 13 (11–16) NRAIDs *vs*. 15 (13–17) controls, p<0.001]. Pain VAS median scores were higher in AIDs compared to controls [3 (1–5) IIMs *vs*. 4 (2–6) non-IIM AIRDs *vs*. 2 (0–4) NRAIDs *vs*. 0 (0–2)

controls, p<0.001]. Of note, PROMIS Fatigue-4a median scores were the highest in IIMs [11 (8–14) IIMs *vs*. 8 (10–14) non-IIM AIRDs *vs*. 9 (7–13) NRAIDs *vs*. 7 (4–10) controls, p<0.001]. Multivariable regression analysis in IIMs identified older age, male sex, IBM, comorbidities including hypertension and diabetes, active disease, glucocorticoid use, increased pain and fatigue as the independent factors for lower GPH scores, whereas coexistence of interstitial lung disease, mental disorders including anxiety disorder and depression, active disease, increased pain and fatigue were the independent factors for lower GMH scores.

Conclusion: Both physical and mental health are significantly impaired in patients with IIMs compared to those with non-IIM AIDs or those without AIDs. Our results call for greater attention to patient-reported experience and comorbidities including mental disorders to provide targeted approaches and optimise global well-being in patients with IIMs.

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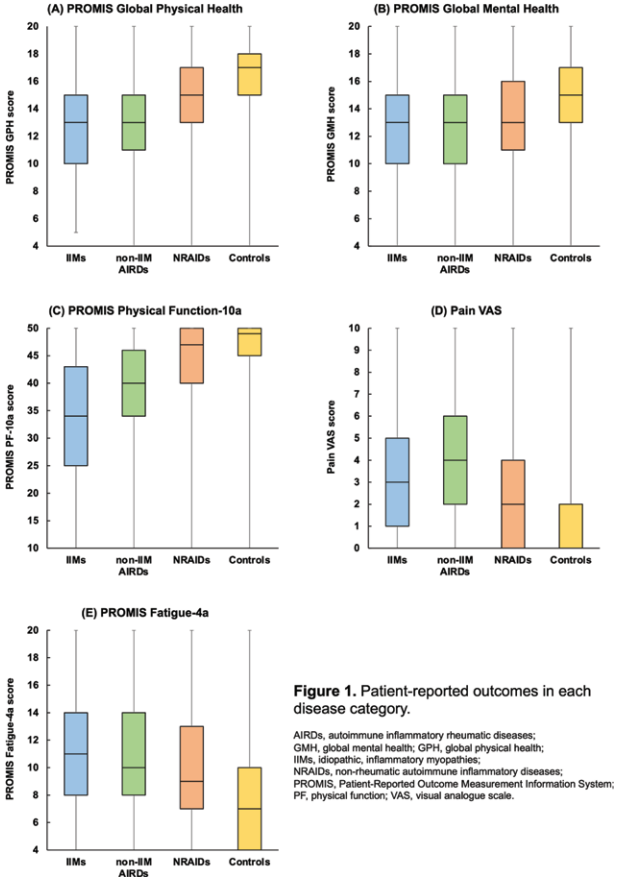


Figure 1. Patient-reported outcomes in each disease category.

AIRDs, autoimmune inflammatory rheumatic diseases; GMH, global mental health; GPH, global physical health; IIMs, idiopathic, inflammatory myopathies; NRAIDs, non-rheumatic autoimmune inflammatory diseases; PROMIS, Patient-Reported Outcome Measurement Information System; PF, physical function; VAS, visual analogue scale.

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POS1232

EFFECT MODIFICATION OF CANCER ON THE ASSOCIATION BETWEEN DYSPHAGIA AND MORTALITY IN EARLY IDIOPATHIC INFLAMMATORY MYOPATHIES

Keywords: Epidemiology, Malignancy, Myositis

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Background: The complex interactions amongst dysphagia, cancer, and mortality in idiopathic inflammatory myopathies (IIM) have never been studied.

Objectives: The aim of this study was to investigate the hypothesis that cancer can modify the effect of early dysphagia exposure on all-cause mortality in IIM patients.

Methods: A cohort of adult IIM patients with documented dysphagia exposure within 6 months of disease onset were identified from clinical registries in five countries (Sweden, Canada, Czech Republic, Denmark, and Norway). Mortality rates including 95% CI were calculated. Crude and adjusted mortality rates in IIM patients exposed to dysphagia or not were compared with Kaplan Meier curves and Cox proportional hazard models. To explore possible effect modification of cancer on the association between dysphagia and mortality, an adjusted Cox proportional hazard model stratified on cancer status and including an interaction term between dysphagia and cancer was performed.

Results: This study included 230 IIM adult individuals with a mean±SD age at diagnosis of 57±15 years and a mean±SD disease duration of 3±2 months. Of those, 146 (64%) were women, 122 (54%) had severe disease at baseline, 29 (13%) had cancer in the 3 years preceding IIM onset or within 6 months after IIM onset and 112 (49%) had dysphagia. When comparing the subjects unexposed or exposed to dysphagia, interstitial lung disease was less frequent (25 vs 58%), with more dermatomyositis (56 vs 28%) and less anti-synthetase syndrome (10 vs 36%) in the group exposed to dysphagia. Mortality rates per 100 person-years for IIM patients exposed to dysphagia were 2.3 (95%CI 1.0-4.5) in those without cancer compared to 33.3 (95%CI 16.6-59.2) in those with cancer. Crude survival curves for dysphagia exposure stratified by cancer status were significantly different (p <0.0001). The main effect of dysphagia exposure in IIM patients without cancer was HR 0.6 (95%CI 0.2-1.8) compared to HR 2.9 (95%CI 0.7-12.4) in those with cancer. Dual exposure to dysphagia and cancer significantly increased the risk of mortality relative to patients with neither condition (p-value interaction 0.05).

Conclusion: This is the first study to demonstrate effect modification of cancer on the association between dysphagia and mortality in IIM. This suggests that IIM patients with and without cancer are very different and that separate analyses for the 2 groups should be considered when the outcome of interest is mortality.
Reference: None.

Table 1. Crude and adjusted risk estimates for the association between dysphagia exposure and mortality

	Deaths	P-Y	Mortality rate per 100 p-y	Crude HR (95% CI)	Stratified Cox PH model[a] HR (95% CI)
Dysphagia					
No	11	367	3.0 (1.5-5.4)	Reference	Reference
Yes	19	384	5.0 (3.0-7.8)	1.7 (0.8-3.6)	0.6 (0.2-1.5)
Cancer					
No	15	681	2.2 (1.2-3.6)	Reference	-
Yes	15	67	22.4 (12.6-37.0)	9.4 (4.6-19.3)	-
No dysphagia/ no cancer	7	332	2.1 (0.9-4.3)	-	Reference
Dysphagia/ no cancer	8	349	2.3 (1.0-4.5)	-	0.6 (0.2-1.8)
Dysphagia/ cancer	11	33	33.3 (16.6-59.5)	-	5.0 (1.0-24.6)
No dysphagia/ cancer	4	34	11.9 (3.2-30.4)	-	Reference
Dysphagia/ cancer	11	33	33.3 (16.6-59.5)	-	2.9 (0.7-12.4)
Age at diagnosis (years)					
<50	2	257	0.8 (0.1-2.8)	Reference	Reference
51-66	14	275	5.0 (2.8-8.5)	6.4 (1.4-27.9)	6.2 (1.4-28.8)
>66	14	216	6.5 (3.6-10.9)	8.2 (1.9-35.9)	8.7 (1.9-40.7)
IIM subsets					
Non-DM	8	470	1.7 (0.7-3.4)	Reference	Reference
DM	22	278	7.9 (5.0-12.0)	4.3 (1.9-9.8)	5.5 (2.5-12.0)

[a]Model stratified on cancer status and adjusted for dysphagia, sex, age group at diagnosis, IIM subset and including an interaction term between cancer and dysphagia. P-Y, person-year.IIM, idiopathic inflammatory myopathy; DM, dermatomyositis.p <0.05 in bold.

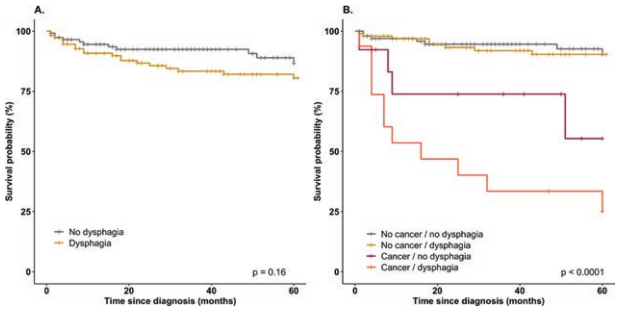


Figure 1. Unadjusted survival curves

Legend: Differences between survival probabilities compared using the log rank test.

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POS1233

CLINICAL, SEROLOGICAL AND MUSCLE SHEAR WAVE ELASTOGRAPHY ASSESSMENT IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Keywords: Ultrasound, Myositis, Imaging

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Background: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of systemic autoimmune disorders characterized by various degrees of muscle weakness and inflammation. Shear wave elastography may be as a potential noninvasive quantitative imaging biomarker.

Objectives: The objective of this work was to describe the demographic, clinical and serological characteristics of IIM patients, and to evaluate the role of shear wave elastography in detecting muscle damage.

Methods: We enrolled 14 patients with IIM fulfilling the EULAR/ACR 2017[1] and having muscle involvement. Shear wave elastography were performed on rectus femoris (RF), deltoid (DEL), biceps brachii (BB) and sternocleidomastoid (SCM) muscles in these patients and 20 healthy controls along the transverse and longitudinal axes, respectively. Demographic, clinical, and serological characteristics were collected from patients' medical records.

Results: The study included 14 patients with IIM (5 dermatomyositis, 7 immune-mediated necrotizing myopathy, 2 anti-synthetase syndrome). The mean age at diagnosis was 52.93 (±12.99) years, with 9 females (64.3%). The demographic, clinical, serological characteristics of the patients were summarized in Table 1. Muscle ultrasound of IIM patients revealed increased muscle and fascia echogenicity, indicating obvious edema (Figure 1). The shear wave velocity and dispersion slope of RF (1.39 vs. 1.60 m/s, 6.70 vs. 7.59 kHz/[m/s]; 1.82 vs. 1.95 m/s, 7.95 vs. 10.10 kHz/[m/s]), DEL (1.28 vs. 1.41 m/s, 7.01 vs. 7.37 kHz/[m/s]; 2.20 vs. 2.57 m/s, 11.05 vs. 14.39 kHz/[m/s]) and BB (1.29 vs. 1.43 m/s, 7.12 vs. 7.54 kHz/[m/s]; 2.28 vs. 2.60 m/s, 11.74 vs. 13.49 kHz/[m/s]) in myositis patients are significantly lower than those in healthy controls on transverse and longitudinal axes, while SCM (6.94 vs. 7.25 kHz/[m/s], 9.49 vs. 10.51 kHz/[m/s]) only has differences in the dispersion slope ($p < 0.05$). We further calculated the sum of viscoelasticity of these four groups of muscles. The overall shear wave velocity (10.82 vs. 11.83 m/s, 16.72 vs. 18.6 m/s) and dispersion slope (55.54 vs. 59.49 kHz/[m/s], 80.46 vs. 96.99 kHz/[m/s]) of myositis patients were lower than that of the healthy controls, which was consistent across transverse and longitudinal axes ($p < 0.05$). Correlation analysis identified significant negative correlation between CK and LDH and muscle viscoelasticity, with correlation coefficients of -0.56 to -0.60 and -0.57 to -0.71, respectively ($p < 0.05$).

Conclusion: The viscoelasticity of muscle in IIM patients was significantly decreased, which was moderately to strongly correlated with muscle injury markers. Shear wave elastography can quantitatively evaluate muscle injury, it may serve as an imaging marker for the diagnosis and activity evaluation of myositis.

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[1] Lundberg IE, et al. 2017 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies and Their Major Subgroups. Arthritis Rheumatol. 2017;69:2271-82.

Table 1. Demographic, clinical, and serological characteristics of IIM patients.

Characteristics	IIM
Age, mean (S.D.), years	52.93 (12.99)
Female/Male (n, %)	9 (64.3)/ 5 (35.7)
Duration of disease (median, IQR), months	10 (2.75-27)
Lung disease (n, %)	6 (42.9)
Skin disease (n, %)	7 (50.0)
CK (U/L), (median, IQR)	2114.50 (511.50-3302.00)
LDH (U/L), (median, IQR)	464.50 (332.25-643.75)
ALT (U/L), (median, IQR)	95.00 (28.50-138.25)
AST (U/L), (median, IQR)	93.50 (37.75-147.00)
ANA (n, %)	9 (64.3)
Anti Jo1 (n, %)	2 (14.3)
MTT-8 (0-150), (median, IQR)	144 (136-148)

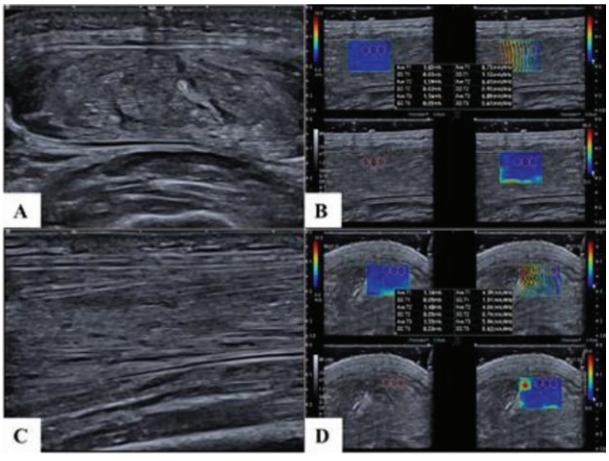


Figure 1. A 60-year-old male with dermatomyositis. B-mode ultrasound showed hyperechoic rectus femoris and thickened fascia on transverse axis (A) and longitudinal axis (C); Shear wave elastography measured the shear wave velocity and dispersion slope of the rectus femoris on transverse (B) and longitudinal (D) axes were 1.45 m/s, 4.79 kHz/[m/s] and 1.6 m/s, 6.67 kHz/[m/s], respectively, lower than those of healthy controls.

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Disclosure of Interests: None Declared.
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POS1234 CEREBROVASCULAR AND CARDIOVASCULAR RISK OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES IS INCREASED AND CAN BE PREDICTED BY ENA POSITIVITY

Keywords: Biomarkers, Cardiovascular disease, Myositis

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Background: Patients with idiopathic inflammatory myopathies (IIM) are under increased cardiovascular (CV) and cerebrovascular (CVB) risk [1-3]. Nevertheless, data on diagnostic tools that could assist CV and CVB patient screening in IIM are scarce. Surrogate markers of CV and CVB risk have been shown to improve risk stratification in the general population and have thus been endorsed by the European Society of Cardiology (ESC) for use in clinical practice. In particular, stiffness of the aortic vasculature and sonography of the carotid arteries are associated with high levels of evidence regarding their CV- and CVB-risk predicting value.
Objectives: Therefore, aim of this study was to examine an oscillometric marker of aortic stiffness and sonographic indices of carotid atherosclerosis and rigidity in a cohort of IIM patients. Moreover, we sought to investigate their relationships with patient- and disease-associated parameters.
Methods: Patients from two large Rheumatology Departments, who have been diagnosed with IIM according to the ACR/EULAR criteria, were recruited. Carotid-femoral pulse wave velocity (cfPWV; gold standard) was used for the examination of aortic stiffness. Moreover, B-mode and Doppler sonography examinations of the common- and internal carotid arteries (CCA, ICA) were performed to assess plaque presence and/or possible abnormalities of carotid intima media thickness (cIMT), as well as vascular resistance and pulsatility indices (RI, PI). The ESC-SCORE (Systematic Coronary Risk Evaluation) was also assessed in all eligible patients.
Results: 73 IIM patients [58.9%♀; age 58 (50-65, IQR)] and 88 healthy subjects [84.1%♀; age 51 (37-57, IQR)] underwent cfPWV examinations in the context of the study (Table 1). A subgroup of the patients (n=63) was additionally evaluated via carotid sonography. IIM patients showed statistically significantly higher cfPWV-[7.92 m/s (6.49-9.26, IQR), vs. 6.72 m/s (6.0-7.69, IQR); p<0.001] and cIMT-values [0.92 mm (0.77-1.1, IQR), vs. 0.8 mm (0.66-0.88, IQR); p<0.001], compared to controls. CCA- and ICA- resistance and pulsatility indices were also statistically significantly higher in the patient group (all; p<0.01). Almost all of these differences remained significant after adjusting for confounding factors, such as age, smoking, BMI, hypertensive treatment and cholesterol [cIMT (p_{adj}<0.001), CCA-PI (p_{adj}=0.002), CCA-RI (p_{adj}=0.004), ICA-PI (p_{adj}=0.02), ICA-PI (p_{adj}<0.001)]. Interestingly, patients with ENA positivity showed higher CCA-RI values compared to their counterparts [0.85 (0.765-0.88, IQR) vs. 0.77 (0.72-0.82, IQR), p=0.044].
Conclusion: Hereby, we could show that IIM patients have a higher level of carotid atherosclerosis, as well as increased vascular resistance and pulsatility, compared to healthy subjects. Thus, a higher CVB and CV risk can be postulated. To our knowledge, this is one of the largest surrogate marker studies in the field of IIM and the first one to show that positivity of myositis associated antibodies (MSA) can be an independent predictor of a higher carotid resistance index. Therefore, MSA-status should be taken into account during CV/CVB risk-stratification of IIM.

Table 1. Descriptive characteristics by group (selection).

	Controls *(n=88)*	**Patients** *(n=73)*	**Significance**
Age *(y)*	51 (37-57)	58 (50.5-65)	<0.001
Gender *(f)*	84.1%	58.9%	<0.001
Nicotine *(smokers)*	15.9%	20.3%	<0.001
Antihypertensive drugs	19.3%	46.5%	<0.001
BMI	23.91 (21.7-27.1)	27.74 (24.3-31.2)	<0.001
MAP *(mmHg)*	80 (66-93)	93 (88-100)	<0.001
Heart rate *(/min)*	66 (59-70)	74 (67-81)	<0.001
Cholesterol (mg/dl)	208.4 (178-239)	204 (168-246)	0.962
cfPWV *(m/s)*	6.72 (6-7.69)	7.92 (6.5-9.3)	<0.001
ANA	-	50%	-
ENA	-	22.1%	-
Myositis antibodies	-	55%	--
CPK	-	148 (64-318)	-
DMARD	-	47.9%	-
Carotid Plaques	14.8%	68.3%	0.002

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[2] Triantafyllias K, et al. Rheumatology (Oxford) 2021;60(3):1300-131
[3] Rai S K, et al. Rheumatology (Oxford) 2016;55(3):461-9.
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Disclosure of Interests: Konstantinos Triantafyllias Speakers bureau: Pfizer, Novartis, Galapagos, Janssen, Chugai, Sanofi, AbbVie, Svea Gauch: None declared, Lorenzo Cavagna: None declared, Andreas Schwarting Speakers bureau: GSK, Novartis, Grant/research support from: GSK, Pfizer, AbbVie, Novartis, and Roche.
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POS1235 ANTIBODY PREDICTORS OF PROGNOSIS IN IDIOPATHIC INFLAMMATORY MYOPATHY ASSOCIATED INTERSTITIAL LUNG DISEASE

Keywords: Autoantibodies, Myositis, Lungs

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Background: IIM-ILD follows a varied clinical course. Serological profile can help predict clinical phenotype, but impact on ILD prognosis is less clear.
Objectives: This multicentre UK cohort study examines whether serological profile can predict mortality and change in lung function over time.
Methods: Patients with IIM-ILD were identified in 3 NHS trusts from local databases. Adults with ILD meeting IIM diagnostic criteria or Interstitial Pneumonia with Autoimmune Features (IPAF) with Myositis Specific Antibodies (MSA) were included. Baseline characteristics from time of presentation were compared across antibody groups and across survivors/deceased at 2 years. Survival analysis looking at time to death (or lung transplant) for duration of available follow-up was modelled by Cox-Proportional Hazards comparing each antibody individually to all others. Models were adjusted for age, gender, ethnicity, presence of overlap CTD/malignancy, smoking and site. Regression models were also used to observe trends in lung function parameters over time.
Results: Of 430 included patients, 68% were female, 46% were of White ethnicity. 81% met IIM criteria, 19% were IPAF. Mean follow up duration was 4.3 years. Common antibodies were to Ro52, Jo1, PL12, MDA5 (n=195, 126, 44 & 32 respectively). 10% had evidence of pulmonary hypertension within 1 year of diagnosis, 4% had malignancy within 3 years. Baseline characteristics of survivors vs fatal cases at 2 years showed survivors were younger (51.4 vs 61.7 years), more likely to have never smoked (69% vs 44%), less likely to have been hospitalised at diagnosis (15% vs 52%) and had a lower Charleson Comorbidity Index. Survivors had lower CRP, higher CK & higher baseline FEV1/FVC/TLCO. Imbalance in age, BMI, CK and comorbidity status were seen across antibody groups. MDA5 had the highest adjusted hazard ratio (HR) for mortality of 4.59 (95%CI 2.10-10.01). Kaplan-Meier curve shows high early mortality in this group. Anti-synthetase antibodies (ARS) carried a reduced risk of mortality (HR 0.63), however individually Jo1 had low HR (0.61, 95%CI 0.4-0.87)

Table 1.

Antibody	n	Deaths/ Transplant	Univariate HR	p value	Multivariate HR	p value
Jo1	126	21	0.56 (0.35, 0.91)	**0.020**	0.61 (0.42, 0.87)	**0.006**
PL12	44	10	0.90 (0.47, 1.73)	0.748	1.06 (0.90, 1.26)	0.482
PL7	26	11	2.29 (1.22, 4.31)	**0.010**	2.07 (1.44, 2.99)	**<0.001**
EJ	16	*	0.63 (0.15, 2.56)	0.517	0.65 (0.30, 1.41)	0.271
OJ	9	*	0.51 (0.07, 3.68)	0.505	0.36 (0.01, 8.50)	0.529
Mi2	19	*	1.31 (0.48, 3.58)	0.603	0.89 (0.27, 2.90)	0.848
SRP	16	*	1.00 (0.32, 3.17)	1.000	0.82 (0.18, 3.73)	0.797
MDA5	32	11	2.90 (1.53, 5.49)	**0.001**	4.59 (2.10, 10.01)	**<0.001**
PMScl	40	8	0.89 (0.43, 1.85)	0.764	0.66 (0.40, 1.09)	0.105
RNP	30	12	1.48 (0.80, 2.72)	0.208	1.88 (1.25, 2.84)	**0.003**
Ku	13	*	1.16 (0.37, 3.66)	0.804	1.78 (0.36, 8.77)	0.477
Negative	32	7	0.96 (0.45, 2.08)	0.924	0.90 (0.49, 1.65)	0.740
Ro52	195	40	1.13 (0.75, 1.70)	0.568	1.15 (0.74, 1.80)	0.525
All ARS	215	39	0.58 (0.38, 0.87)	**0.009**	0.63 (0.52, 0.77)	**<0.001**

** counts of < 5 suppressed for anonymity*

and PL7 had high HR (2.07, 95%CI 1.44-2.99). RNP showed worse prognosis on adjusted analysis (HR 1.88, 95%CI 1.25-2.84) (Table 1). Regression models suggest that compared to other antibodies, %pred FVC in MDA5 improves over the first 3 years, in PL7 it drops, and in Jo1 it is no different (Figure 1). MDA5 % pred FEV1 also showed improvement, but in Ku it was lower than other antibodies from 21 months. There were no significant differences in % pred TLCO between antibodies.

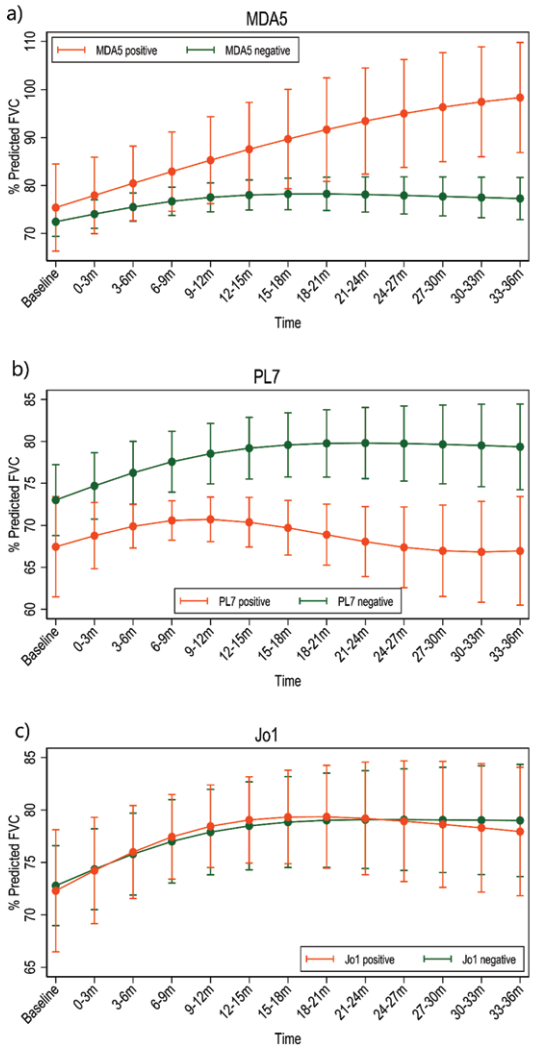


Figure 1.

Conclusion: There is strong evidence that antibody status associates with clinical outcomes, both in terms of progression of lung disease and mortality, suggesting pathogenetic differences. MDA5 predicts a high risk of death early on in disease course, whilst Jo1 associates with lower mortality. PL7 and RNP were additional antibodies associating with higher mortality. Difference between Jo1 and PL7 highlights variation within anti-synthetase syndrome. Paradoxically, if an MDA5 positive person survived the early disease phase, there was evidence that lung function can recover, which may reflect different MDA5 subpopulations.

REFERENCES: NIL.

Acknowledgements: NIL.

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POS1236

TREATMENT TRAJECTORIES IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Keywords: Myositis, Registries

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Background: Idiopathic inflammatory myopathies (IIM) are a group of rare, heterogeneous diseases in which the hallmark feature is chronic inflammation of skeletal muscle leading to muscle weakness. Initial conventional therapy is based on expert opinion and includes glucocorticoids in combination with methotrexate, azathioprine, or mycophenolate. If this therapy is not sufficiently effective, second line therapy (calcineurin inhibitors or IVIG) may be considered. If still insufficient, escalation to rituximab or cyclophosphamide is considered. Agents not included in conventional recommended therapies have also been used and are being studied in the management of IIM.

Objectives: To characterize real-world treatment trajectories among individuals with IIM.

Methods: Data were provided by adults with IIM enrolled in FORWARD, The National Databank for Rheumatic Diseases. Participants with a co-occurring RA, SLE, or SSc diagnosis were excluded. Participant characteristics were assessed at baseline (study entry) by treatment category and significance was assessed by one way ANOVA and Fisher's exact tests, as appropriate ($p<0.05$). Treatment category (none, steroid alone, first line without steroid, first line, second line, third line, and other DMARD) was assessed at baseline and for ultimate line of treatment reported during observation. First, second, and third line treatments were considered "conventional" and others were considered "nonconventional."

Results: A total of 126 participants met inclusion criteria. At baseline, 43% of participants were on first line therapy. Most of the remaining participants were either on a corticosteroid alone (23%) or were on first line therapy but without a corticosteroid (17%). A relatively small number of participants (2%) were on second line therapy, and none were on third line therapy at baseline. About 9% reported use of a nonconventional DMARD, and the remaining 6% reported no treatment. Those who reported no therapy were more likely to be male and had higher global severity scores. Across 504 person-years of observation, 47% reported first line treatment, 10% reported second line, and 3% reported third line as the most advanced conventional therapy received. The remaining 40% reported either nonconventional or no treatment.

Conclusion: Despite published recommendations to combine glucocorticoids with another immunosuppressive drug as part of first line therapy for IIM, many individuals with IIM are not prescribed concomitant DMARDs. In this cohort, there were no significant differences in IIM subtype, disease duration, or calendar year by conventional vs nonconventional therapy at study entry. A relatively small number of individuals with IIM reported receiving no treatment during observation, which may be due to significantly shorter follow up time in that subgroup. Future work should examine treatment response and changes in disease activity with changing lines of treatment.

Table 1. Characteristics of included participants at study entry by baseline treatment category.

	Conventional Therapy	Nonconventional Therapy	No Therapy	
	n=57	n=61	n=8	p
Age, years	54.6 (14.3)	57.2 (14.2)	57.0 (8.3)	0.61
Female sex, %	77.8	82.8	37.5	0.02
White race, %	90.6	88.5	75.0	0.62
IIM subtype				
DM	41.1	44.1	37.5	
PM	42.9	32.2	12.5	0.19
Unspecified	16.1	23.7	50.0	
Time since symptom onset, years	6.5 (6.0)	8.3 (6.3)	4.1 (5.2)	0.20
Study entry prior to 2010, %	55.4	66.1	37.5	0.50
Observation time, years	3.6 (3.4)	4.4 (4.8)	2.0 (2.4)	0.01
Rural residence, %	30.4	21.1	37.5	0.41
Hx smoking, %	42.9	40.7	75.0	0.18
Pain VAS, 0-10	3.1 (2.8)	3.2 (2.9)	5.1 (3.5)	0.71
Global severity, 0-10	3.6 (2.8)	3.4 (2.7)	6.3 (2.8)	0.03
HAQ-II, 0-3	1.0 (0.7)	0.9 (0.6)	1.2 (0.7)	0.48
PAS-II, 0-3	3.5 (2.3)	3.3 (2.3)	5.1 (2.6)	0.86

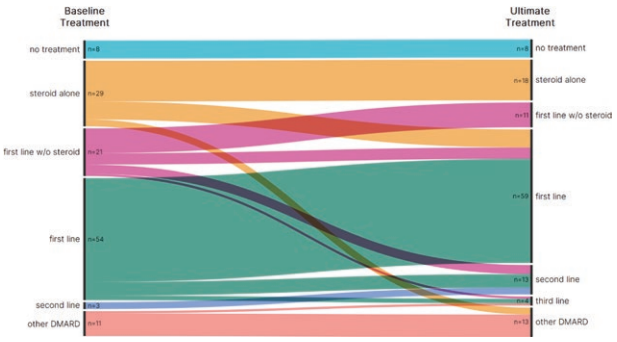


Figure 1. Treatment progression among individuals in FORWARD with IIM. Baseline (at study entry) treatment category is shown on the left, and ultimate treatment category (during observation) is shown on the right. First line = glucocorticoid + methotrexate, azathioprine, or mycophenolate. Second line = calcineurin inhibitors or IVIG. Third line = rituximab or cyclophosphamide.

REFERENCES: NIL.

Acknowledgements: NIL.

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POS1237 MICROVASCULAR DAMAGE IN AUTOIMMUNE CONNECTIVE TISSUE DISEASES: A CAPILLAROSCOPIC ANALYSIS FROM 20 YEARS OF EXPERIENCE IN A EULAR TRAINING AND RESEARCH REFERRAL CENTER FOR IMAGING

Keywords: Diagnostic Tests, Myositis, Systemic sclerosis

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Background: Nailfold videocapillaroscopy (NVC) safely allows the detection of microvascular damage which can vary in terms of extent and severity (validated NVC patterns) in patients with Raynaud's phenomenon (RP) secondary to autoimmune connective tissue diseases (CTDs).
Objectives: The prevalence of the morphological capillary findings was retrospectively evaluated in a wide cohort of patients with RP secondary to a CTD at the time of the first single NVC analysis, independently from their current treatment, autoantibody profile and comorbidities.
Methods: One-thousand-one-hundred-eighty-one (1181) patients affected by CTDs (1065 females, mean age 54.1 ± 16.2, mean disease duration 4.5 years ± 3) were analysed from 2001 to 2021. The considered CTDs, diagnosed through the classification criteria available at the time of the enrollment, included: systemic sclerosis (SSc, 51%), undifferentiated connective tissue disease (UCTD, 26%), mixed connective tissue disease (MCTD, 6%), dermatomyositis (DM, 3%), systemic lupus erythematosus (SLE, 9 %), Sjögren's syndrome (SS, 3%) and primary anti-phospholipid syndrome (aPS, 2%). The capillaroscopic parameters were classified according to the CAP Fast Track Algorithm and distinguished between scleroderma-pattern (specific NVC alterations) and non-scleroderma patterns (non-specific NVC alterations) [1]. The presence of specific NVC findings detectable with a progressive microangiopathy in SSc patients ("early", "active", "late" patterns) have been searched also in other CTDs, beyond SSc. The "scleroderma-like pattern" was defined when a concomitant mix of the specific abnormalities of the SSc-patterns (namely: giant capillaries, loss of capillaries, capillary dilations, microhaemorrhages, abnormal shapes) was detected without fitting the single definition of "Early", "Active" or "Late" pattern [2].
Results: Among CTDs, the mean capillary density (1 linear mm) was significantly lower in SSc, DM and MCTD (respectively, 7.04 ± 0.18 vs 6.5 ± 0.75 vs 7.7 ± 0.48) compared with other CTDs. "Early", "Active" and "Late" NVC scleroderma patterns were detected in 34%, 38% and 16% of SSc patients, whereas the scleroderma-like pattern was found significantly more frequent in DM (63 %) and MCTD (37%). Giant capillaries, capillary dilations and microhaemorrages were significantly more frequent in SSc and DM compared with other CTDs (respectively in 73%, 99% and 70% of SSc patients e in 73%, 96% e 70% of DM patients, Figure 1). The non-specific abnormalities of capillary morphology, such as the ramifications (abnormal shapes as expression of neoangiogenesis) were significantly more frequent in SSc, MCTD and APS among all the CTDs (respectively, in 48%, 41% and 36% of cases). Moreover, giant capillaries and abnormal shapes were detected in 61% and 41% of MCTD patients. In APS, the most significant prevalence of microhaemorrages (50%) was observed compared with other CTDs, to the exclusion of SSc and DM being detectable in 70% of cases. No significant damages were observed in SS and SLE patients (Figure 1).
Conclusion: This large sample size of CTDs patients, collected over 20 years of analysis, confirms the highest specificity and severity of the NVC microvascular damage respectively in SSc and DM patients, when compared to other CTDs. Those data will be used to implement easy algorithms to distinguish scleroderma patterns, from non-scleroderma and scleroderma-like patterns.

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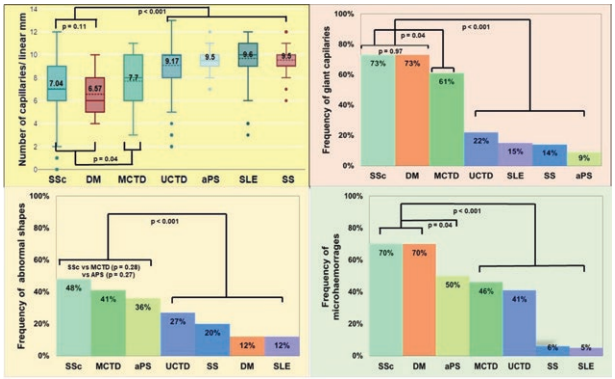


Figure 1. Frequency of capillary density, giant capillaries, abnormal shapes and microhemorrhages across different CTDs (see text)

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Disclosure of Interests: None Declared.

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POS1238 FIRST EVIDENCE FOR EFFICACY OF CAR-T CELL TREATMENT IN REFRACTORY ANTISYNTHETASE SYNDROME

Keywords: Treat to target, Myositis, Remission

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Background: We previously reported that deep B cell depletion using a single infusion with autologous CD19 chimeric antigen receptor (CAR) T cells induced drug-free clinical remission in patients with severe systemic lupus erythematosus [1,2]. Whether other forms of severe autoimmune disease are sensitive to treatment with CD19 CAR-T cells has been unknown to date. Antisynthetase syndrome (ASS) is a autoimmune disease that affects muscles, joints, skin and lung. ASS can be very severe and life-threatening needing effective and fast treatment. This abstract presents the first evidence that severe ASS is highly sensitive to treatment autologous CD19 CAR-T cells.
Objectives: To test whether administration of CD19 CAR-T cells is tolerable and effective in patients with severe refractory Antisynthetase syndrome.
Methods: Autologous CD19 CAR-T cells were prepared from leukapheresis specimen after enrichment of T cells and transfection with MB-CART19.1

lentiviral vector (Miltenyi) encoding for a 4-1BB based CAR targeting CD19. Cells were expanded for 12 days and 1 million CAR-T cells/kg body weight were administered as a single intravenous infusion after standard conditioning therapy with cyclophosphamide/fludarabine, as described previously [1,2]. All disease related treatments were stopped before CAR-T cell administration. Patients were followed up in inpatient care for the first 10 days after CAR-T cell administration, thereafter weekly until the end of the first month, then monthly for three months and every three months later. Tolerability was assessed by monitoring for Cytokine-Release Syndrome (CRS) and Immune-related effector Cell Neurotoxicity Syndrome (ICANS). Efficacy was assessed by CK levels, good response according 2016 ACR/EULAR total improvement score (TIS), imaging of muscles and lungs and successful cessation of all immunosuppressive treatments including glucocorticoids.

Results: Two anti-Jo1 ASS patients (patient 1: 41year old male, patients 2: 43year old female) were treated with CD19 CAR-T cells. Both patients presented with active myositis with CK levels of 9305 U/l (normal value <190U/l), and 3055U/l, respectively. Patient 1 showed involvement of the muscles, skin and lungs, patient 2 showed involvement of muscles, skin, joints and lungs. Patient 1 did not respond to 5 different immunosuppressive treatments including cyclophosphamide and rituximab, patient 2 did not respond to 10 treatments including cyclophosphamide, rituximab and ocrelizumab. CAR-T cell treatment was well-tolerated. Only mild CRS (grade I) was observed in both patients. Patient 2 had signs of mild self-limited ICANS (grade I discrete ataxia for a few days) two weeks after CAR-T treatment. In patient 1, CAR-T cells expanded to a maximum of 60cells/µl on day 8, in patient 2 to 1524cells/µl on day 8. Expansion of CAR-T cells paralleled with the complete depletion of circulating B cells. B cell aplasia lasted for 119 days in patient 1, while patient 2 is still in B cell aplasia (day 60). Both patients experienced normalization or significant reduction in CK levels (patient 1: CK+120 days: 70 U/l, patient 2: CK+60 days: 311 U/l), major clinical improvement according to the 2016 TIS and could stop all immunosuppressive therapy. Follow-up CT scans of the lung and MRI of the thigh muscles done in patient 1 showed resolution of alveolar inflammation as well as abrogation of inflammatory changes in the thigh muscles and the hamstrings. At the latest follow up (120days and 60days) both patients were in drug-free remission. Also, the highly positive anti-Jo1 antibodies (331 U/l) disappeared after CAR-T cell treatment (5 U/l; cut-off 25U/l, Orgentec ELISA, Mainz, Germany) in patient 1, while patient 2 awaits follow up measurement.

Conclusion: Taken together, these data suggest that CD19 CAR T-cell therapy provides a possibility to intercept with severe ASS leading to drug-free remission, resolution of muscle and lung inflammation and abrogation of disease-associated autoimmunity.

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POS1239

TYPE I INTERFERON SCORE IS ASSOCIATED WITH THE SEVERITY AND POOR PROGNOSIS IN ANTI-MDA5 ANTIBODY-POSITIVE DERMATOMYOSITIS PATIENTS

Keywords: Prognostic factors, Myositis

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Background: Anti-MDA5 antibody-positive dermatomyositis (anti-MDA5+DM) is a rare autoimmune disease associated with a high mortality rate due to rapid-progressive interstitial lung disease (RP-ILD), particularly in East Asia[1]. MDA5, acts as a cytoplasmic sensor of viral RNA, thus activating antiviral responses including the type I interferon (IFN) signaling pathway[2]. The involvement of type 1 IFN in the pathogenesis of MDA5+DM has been proposed based on the significantly elevated expression of its downstream stimulated genes(ISG) in muscle, skin, lung, and peripheral blood[3; 4]. Janus kinase inhibitor, which targets the IFN pathway, combined with glucocorticoid could improve the survival of early-stage MDA5+DM-ILD patients[5]. In clinical practice, there is still an urgent demand for sensitive biomarkers to facilitate clinical risk assessment and precise treatment.

Objectives: This study aimed to investigate the clinical significance of interferon score, especially IFN-I score, in patients with anti-MDA5+DM.

Methods: Different subtypes of idiopathic inflammatory myopathy, including anti-MDA5+DM(n=61), anti-MDA5-DM(n=20), antisynthetase syndrome(ASS,n=22),polymyositis(PM,n=6) and immune-mediated necrotizing myopathy(IMNM,n=9), and 58 healthy controls were enrolled.. A multiplex quantitative real-time PCR(RT-qPCR) assay using four TaqMan probes was utilized to evaluate two type I ISGs (IFI44, MX1, which are used for IFN-I score), one type II ISG (IRF1), and one housekeeping gene (HRPT1). Clinical features and disease activity index were compared between high and low IFN-I score groups in 61 anti-MDA5+DM patients. The association between laboratory findings and the predictive value of baseline IFN-I score level for mortality was analyzed.

Results: The IFN scores were significantly higher in patients with anti-MDA5+DM than in HC (Figure 1A). The IFN-I score correlated positively with serum IFN α(r = 0.335, P =0.008), ferritin (r = 0.302, P = 0.018), and Myositis Disease Activity Assessment Visual Analogue Scale (MYOACT) score(r=0.426, P=0.001). Compared with patients with low IFN-I scores, patients with high IFN-I scores showed increased MYOACT score, CRP, AST, ferritin, and the percentages of plasma cells (PC%) but decreased lymphocyte count, natural killer cell count, and monocyte count. The 3-month survival rate was significantly lower in patients with IFN-I score > 4.9 than in those with IFN-I score ≤ 4.9(72.9% vs. 100%, P=0.044)(Figure 1B).

Conclusion: IFN score, especially IFN-I score, detected by multiplex RT-qPCR, can be a valuable biomarker for monitoring disease activity and predicting mortality in anti-MDA5+DM patients.

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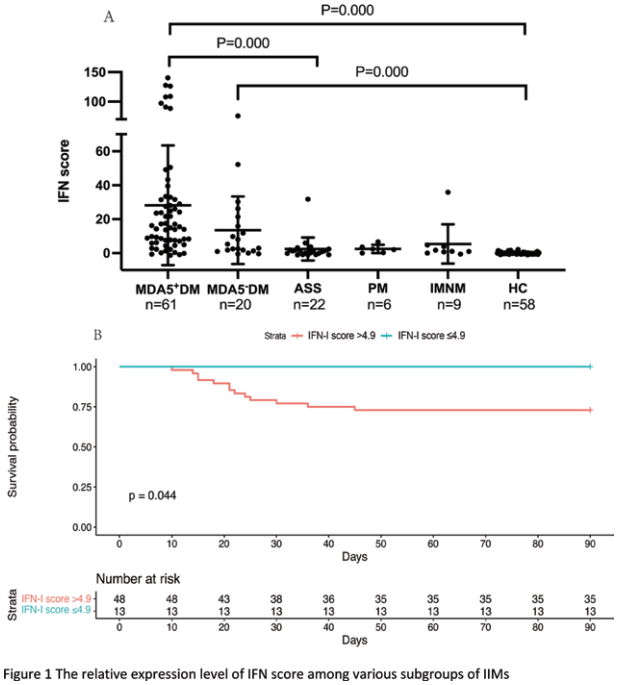


Figure 1 The relative expression level of IFN score among various subgroups of IIMs

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POS1240 **EFFICACY AND SAFETY OF ABATACEPT IN MYOSITIS ASSOCIATED INTERSTITIAL LUNG DISEASE**

Keywords: Myositis, Clinical Trials, Lungs

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Background: Interstitial Lung Disease (ILD) is the most common cause of mortality in myositis and there is lack of randomized clinical trials for myositis-associated ILD (MA-ILD). A T-cell mediated pathogenesis has been postulated for MA-ILD, and abatacept (ABA) is a T cell co-stimulatory modulator.

Objectives: Our primary objective was to evaluate the efficacy, safety and tolerability of ABA (125 mg SQ weekly) combined with standard of care (SOC) vs. placebo/SOC in MA-ILD patients in a multi-center, double-blind, randomized placebo-controlled proof of concept clinical trial.

Methods: 20 patients (pts) with anti-synthetase antibody (Anti-Syn Ab) were enrolled across 5 centers for 24 weeks in a randomized placebo-controlled phase (RCT) followed by an open label extension (OLE) for 24 weeks. Active myositis was not required but pts must have had active ILD (new onset or worsening requiring treatment) and previously failed ≥1 SOC drug for ILD. Pts were required to be on stable SOC [glucocorticoids (GC)/1 immunosuppressive (IS) agent (azathioprine or mycophenolate) prior to the trial as well as stable SOC IS throughout the trial]. A recommended GC taper was instituted. The primary endpoint was the change in Force Vital Capacity (FVC) (in ml) change from baseline to week 24. Secondary endpoints included FVC changes over 48 weeks, patient reported outcomes (PRO) of dyspnea (UCSD-shortness of breath questionnaire; range 0-120, MCID of 8) and DLCO corrected % predicted (DLCO) at 24 and 48 weeks. Mixed effect modeling was used for analysis and the study was not powered for primary or secondary outcomes.

Results: A total of 20 anti-Syn Ab positive pts (mean age of 57, 45% female and 85% Caucasian, Jo-1, 55%) were randomized to ABA (n=9) and placebo (n=11). All but 1 pts completed 48 weeks of the trial. There was no significant or clinically relevant difference in median FVC (ml) from baseline to week 24 between ABA (-40 ml) and placebo (30 ml), p = 0.97. However, the median FVC (ml) change from baseline to week 48 was 140 ml and -40 ml, in ABA vs. placebo (p=0.15), with a 180 ml difference in favor of the ABA group. FVC% predicted remained stable (±5%) or improved (>5%) without death or drug rescue in 75% (6/8) and 45% (5/11) at week 24 and week 48, in ABA vs. placebo, respectively. The median DLCO change from baseline was -4.5 and -10.5 at week 24; 6.5 and -2.7 at week 48, in ABA vs. placebo group, respectively. DLCO remained stable (±5%) or improved (>5%) without death or rescue in 57% (4/7) and 45% (5/11) at week 24; 62.5% (5/8) and 40% (4/10) at week 48, in ABA vs. placebo, respectively. Dyspnea improved by median of 1 and 3 at week 24; 13 and 5 at week 48 in ABA vs. placebo, respectively. Dyspnea improved by an MCID of 8 without requiring drug rescue or death in 22% (2/9) and 45.5% (5/11) at week 24; 50% (4/8) and 18% (2/11) pts at week 48 in ABA vs. placebo, respectively. There were 3 severe adverse events (1 in RCT, 2 in OLE) in 2 pts requiring hospitalization in the ABA group for progressive respiratory failure and 1 died (at 24 weeks). There were 36 and 23 adverse events among 9 placebo and 9 treatment group pts. ABA was well tolerated.

Conclusion: MA-ILD ABA-treated subjects showed similar FVC, DLCO and dyspnea PRO trends compared to placebo at 24 weeks but clinically and numerically meaningful trends were observed in ABA-treated subjects at week 48. These results suggest the need for a larger randomized study of ABA in MA-ILD. Abatacept was relatively safe and well tolerated in the cohort.

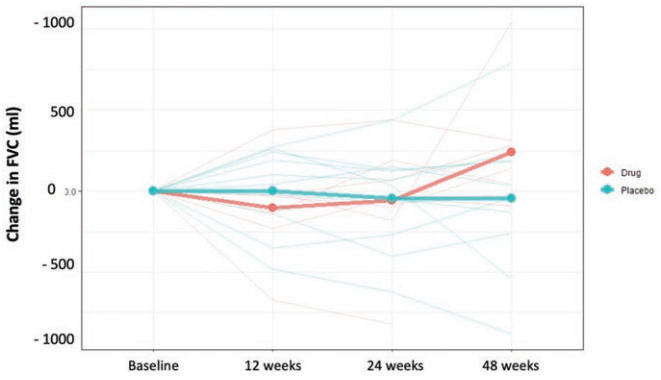


Figure 1 : Change from baseline in Forced Vital Capacity (FVC) in ml by treatment groups.

Table 1. Baseline demographics and clinical variables by treatment groups:

Clinical variable	Placebo (N=11)	Abatacept (N=9)
Age	57.7 [47.8-64.5]	49.7 [46.6-59.3]
Female	4 (36)	5 (56)
Non-Hispanic	11 (100)	9 (100)
Caucasian	10 (91)	7 (78)
Anti-synthetase antibody		
Jo-1	7	4
Non-Jo1	4	5
ILD status		
New onset	3 (27)	2 (22)
Chronic	8 (73)	7 (78)
Myositis status		
Inactive	5 (45)	2 (22)
Active	4 (37)	5 (56)
Not present	2 (18)	2 (22)
FVC%	61 [53-78]	66 [49-69]
DLCO%	49 [41-64]	47 [38-52]
Prednisone	11 (100)	8 (88)
Mycophenolate	8 (73)	8 (88)
Azathioprine	0 (0)	1 (11)

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Scleroderma, myositis and related syndromes

POS1241 IMAGING OF INFLAMMATION IN THE CONTEXT OF MYOPATHIES USING A NEAR-INFRARED FLUORESCENCE-BASED METHOD - A POSSIBILITY FOR THE DIAGNOSTIC SUPPORT OF POST-ACUTE SYMPTOMS AFTER VIRUS-RELATED DISEASES?

Keywords: Inflammatory arthritides, Imaging, Myositis

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Background: Myopathies with main symptoms of muscle pain and weakness can have a wide variety of triggers, be characterized by different courses and localizations, and occur as side effect of rheumatic diseases. They have also recently come into focus as sequelae after systemic viral infections, for example as post-acute Covid-19 syndrome. Inflammatory reactions (Polymyositis, PM) are often difficult to differentiate from non-inflammatory myalgias. Clinical examinations and analysis of serum parameters are helpful, but do not always lead to clear results due to overlapping syndromes. In addition to pathogen-related myositis (Lyme disease, LD), muscle inflammation can also occur in autoimmune-caused rheumatic diseases such as systemic sclerosis (SSc), rheumatoid arthritis (RA), or polymyalgia rheumatica (PMR). Furthermore, overexertion, degeneration, or psychosomatic influences (fibromyalgia, FM) can lead to the symptom of muscle pain.
Objectives: The present work investigates the potential of NIR-FOI feature assessment in diagnosing patients with muscle weakness and muscle pain to better explore therapy options.
Methods: NIR-FOI analyses of patients (n = 200) without clinical symptoms (Ref, n = 31), or the diagnosis of osteoarthritis (OA) (n = 35) were compared with PM patients (n = 9), and patients diagnosed with autoimmune RA (n = 35), SSc (n = 34), Sjögren Syndrome (SS, n = 20), or PMR (n = 5). In addition, patients with diagnoses of LD or primary FM (n = 31) were examined. Indocyanine green as fluorescence dye was injected and the FOI images of both hands were evaluated from 0-240s (Prima Vista Image, PVI), or in the late period P3 (150-240s). Signal intensities (SI) were created from the summation images. For characterization of the cohorts, serum parameters were determined.
Results: Since the detection of serum JO-1 antibodies can be considered as reliable evidence of myositis, patients with this verification were examined first. In addition to increase of SI in PVI ($p<0.0001$), 8/9 PM patients show stronger accumulation in P3 in the anatomical position of hand muscles, and in the tendon-muscle junction of the forearm compared to the Ref group (Figure1). In the cohort of patients with PMR, the PVI SI was also increased ($p<0.0001$). Stronger P3 accumulation was observed in 3/5 patients. However, besides accumulation in the joints as the main site of inflammation in this disease, signal increase was detected mostly in the muscle-tendon transition, which could be also attributed to degenerative changes due to the high age of this cohort. That is also true for the patients in the OA cohort, but with lower SI both in PVI and P3. In addition, increased PVI SI was detected in all other disease cohorts ($p<0.01$). However, increased accumulation in P3 can only be detected in some of the patients of these cohorts and predominantly in the muscle-tendon transition. Most frequently, patients with increased accumulation in P3 were identified in the groups of RA and SS. However, increased accumulation in P3 was also detected in 48% of patients diagnosed with fibromyalgia, but only in the muscle-tendon junction.
Conclusion: The study demonstrates that changes in the microcirculation in inflammatory processes in the context of myositis correlate with a late phase dye accumulation during a NIR-FOI examination. This could provide valuable information for differential diagnoses of inflammatory versus non-inflammatory myopathies to optimize therapy. NIR-FOI could also potentially be used for the screening of myositis in virus-related diseases (e.g., Covid-19).

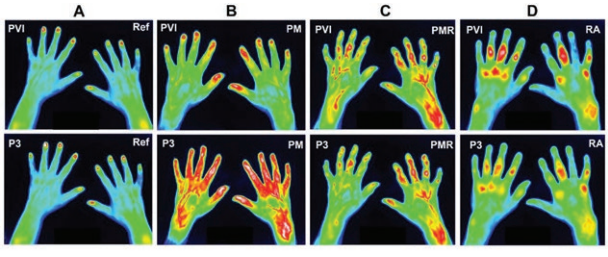


Figure 1: Examples of NIR-FOI images in patients: A. without clinical symptoms (Ref), B. JO-1 positive Polymyositis (PM), C. Polymyalgia rheumatica (PMR), or D. Rheumatoid arthritis (RA). Analysis of fluorescence dye distribution 0-240s (summations image, PVI), or in late phase 150-240s (P3). The figure demonstrates significant dye accumulations in inflammatory tissues with a focus in the areas of the muscles and tendons in PM, and in the joints in PMR and RA.

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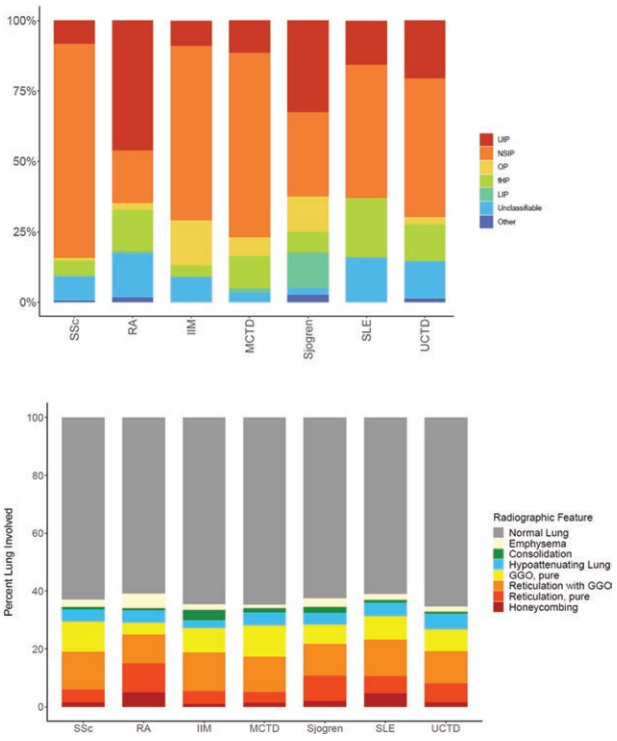
POS1242 COMPUTED TOMOGRAPHY FINDINGS IN CONNECTIVE TISSUE DISEASE RELATED INTERSTITIAL LUNG DISEASE

Keywords: Rheumatoid arthritis, Systemic sclerosis, Lungs

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Background: Lung imaging findings vary among subtypes of connective tissue disease-associated interstitial lung disease (CTD-ILD), leading to both diagnostic and therapeutic challenges.
Objectives: We performed a comprehensive assessment of ILD morphology across CTD-ILD subtypes by examining the presence of overall imaging patterns and specific morphological features.
Methods: High-resolution chest computed tomography (HRCT) of patients with CTD-ILD enrolled in the multicentre Canadian Registry for Pulmonary Fibrosis from their first ILD clinic visit were re-reviewed in standardized multidisciplinary discussion. All CTD diagnoses were rheumatologist-confirmed. An experienced chest radiologist blinded to clinical data quantified the percentage of lung parenchyma affected by honeycombing, reticulation, ground glass opacity (GGO), hypoattenuating lobules, consolidation, and emphysema. Gas trapping was evaluated on expiratory CT. Each case was categorized into an overall disease pattern including usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP), fibrotic hypersensitivity pneumonitis (fHP), lymphocytic interstitial pneumonia (LIP), and unclassifiable.
Results: 615 patients with CTD-ILD were assessed with 215 (33%) having systemic sclerosis (SSc), 127 (20%) rheumatoid arthritis (RA), 100 (16%) idiopathic inflammatory myopathy (IIM), 61 (9%) mixed connective tissue disease (MCTD), 40 (6%) Sjogren's syndrome (SS), 19 (3%) lupus (SLE), and 83 (13%) undifferentiated connective tissue disease (UCTD). NISP was most predominant in SSc (76%), IIM (62%), and MCTD (66%), while UIP was most common in RA (47%) and SS (33%). A fHP pattern was most common in RA (15%), SLE (21%), and MCTD (12%) (Figure 1a). There was substantial variability in the extent of fibrotic (honeycombing, reticulations) and non-fibrotic (pure GGO, consolidation) parenchymal features within and across each CTD (Figure 1b).
Conclusion: There is considerable variation in imaging features across subtypes of CTD-ILD, with NSIP generally most common, UIP most frequent in RA and SS, and fHP less frequent but most common in RA, SLE, and MCTD. This variability highlights the need for additional data on management of CTD-ILD that considers the potential for variable treatment responses across major CTD-ILD subtypes and phenotypes.
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Disclosure of Interests: Boyang Zheng: None declared, Daniel-Costin Marinescu: None declared, cameron hague: None declared, Nestor Muller: None declared, darra murphy: None declared, Andrew Churg: None declared, Joanne Wright: None declared, Amna Al-Arnawoot: None declared, Gerald Cox: None declared, Zachary Guenther: None declared, Amanda Grant-Orser: None declared, James Huynh: None declared, Tracy Elliot: None declared, Derek Fladeland: None declared, Jen Ellis: None declared, geoff karjala: None declared, Gillian Goobie Grant/research support from: Boehringer Ingelheim. Pulmonary Fibrosis Foundation, Kerri Johannson Paid instructor for: Boehringer-Ingelheim, Hoffman-La Roche Ltd, Consultant of: Boehringer-Ingelheim, Hoffman-La Roche

Figure 1. Presence of overall imaging patterns (A) and mean parenchymal involvement of specific imaging features (B) across different CTD-ILD subtypes



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POS1243

THE ROLE OF TAPSE/SPAP RATIO IN PREDICTING PULMONARY HYPERTENSION AND MORTALITY IN THE SYSTEMIC SCLEROSIS EUSTAR COHORT

Keywords: Heart, Lungs, Systemic sclerosis

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Background: Early pulmonary arterial hypertension (PAH) diagnosis and treatment are crucial to improve systemic sclerosis (SSc) patients' outcomes. In PAH the progressive pulmonary vascular remodelling leads to an increasing load on the contracting RV and an altered right ventricular - pulmonary arterial (RV-PA) coupling. The RV-PA coupling describes the RV adaptation to its afterload [1]. Tricuspid annular plane systolic excursion/systolic pulmonary artery pressure (TAPSE/sPAP) ratio is the validated non-invasive estimation of RV-PA coupling [2]. In the new 2022 pulmonary hypertension (PH) guidelines, TAPSE/sPAP ratio has been included among the additional echocardiographic signs suggestive of PH and the echocardiographic parameters for 1-year mortality risk assessment [3]. However, to date, the role of TAPSE/sPAP ratio in SSc is underinvestigated [4-6].

Objectives: The primary aim of the study was to assess the predictive role of TAPSE/sPAP ratio for PH diagnosis in the SSc European Scleroderma Trials and Research (EUSTAR) cohort. The secondary aim of the study was to evaluate the prognostic role of TAPSE/sPAP ratio in predicting mortality in the SSc EUSTAR cohort.

Methods: Eligible patients were systemic sclerosis (SSc) patients registered in the EUSTAR database with at least one visit recording TAPSE and sPAP data. Individual centres were required to provide TAPSE and sPAP data at 12 ± 3 months before right heart catheterization (RHC). Logistic regression analysis was applied to analyse the predictive ability of TAPSE/sPAP ratio for PH diagnosis. Cox regression analysis was performed to evaluate TAPSE/sPAP ratio as a predictive factor for all-cause mortality.

Results: 2555 SSc patients met the inclusion criteria for this study with 355 SSc patients having available RHC data at baseline. PH was confirmed by RHC in 195 SSc patients (54.9%). TAPSE/sPAP ratio <0.55 mm/mmHg [OR 0.251 (95% CI 0.084-0.753), p<0.05] and FVC/DLCO [OR 2.568 (95% CI 1.227-5.375), p<0.05] were significantly associated with PH diagnosis. In logistic regression analysis with echocardiographic parameters at 12±3 months before RHC, TAPSE/sPAP ratio <0.55 mm/mmHg [OR 0.265 (95% CI 0.102-0.685), p<0.01] and FVC/DLCO [OR 2.529 (95% CI 1.358-4.711), p<0.01] were significantly associated with PH diagnosis. In multivariate Cox regression analysis, TAPSE/sPAP ratio ≤0.32 mm/mmHg [HR 0.310 (0.164–0.585), p<0.001] was the most significant predictive factor for all-cause mortality.

Conclusion: TAPSE/sPAP ratio <0.55 mm/mmHg is a predictive risk factor for PH. TAPSE/sPAP ratio ≤0.32 mm/mmHg is a predictive risk marker for all-cause mortality.

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POS1244

RESULTS OF A PHASE 2A STUDY OF CILNIDIPINE, A NOVEL DAILY ORAL CALCIUM CHANNEL BLOCKER WITH N-CHANNEL SELECTIVITY, FOR THE TREATMENT OF RAYNAUD'S AND OTHER SYMPTOMS IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Clinical trials, Disease-modifying drugs (DMARDs)

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Background: Systemic Sclerosis(SSc) is a rare autoimmune disease with fibrosis, changes in the skin, vasculature, joints and internal organs. Diffuse disease involves lung, heart and kidney and 10-year mortality is >35%.[1] Raynaud's attacks occur in ~95% of SSc patients. Severe Raynaud's (RP) affects patients' health status more than depression, obesity, and heart disease.[2] No treatment for Raynaud's is approved, but calcium channel blockers (CCBs) are first-line treatment. Cilnidipine, a 4th generation CCB approved for hypertension in Asia, has been shown to be safer than other CCBs in treating hypertension, and has beneficial effects on the kidney and heart. Cilnidipine is more selective for N-type Ca channels, and improves analgesia, sympathetic, autonomic and endothelial function.[3] Cilnidipine might be repurposed for SSc-RP patients.
Objectives: We studied safety and preliminary efficacy of cilnidipine use in SSc-RP, dose response and co-administration of a low dose PDE-V inhibitor. Results are compared to a 2017 meta-analysis of CCB use in SSc-RP.
Methods: RECONNOITER-1 is a two-part, planned 76 patient trial. In Part 1, we evaluated safety, dose, efficacy and co-administration of tadalafil. Dose groups were cilnidipine 10mg and 20mg, alone and with tadalafil 5mg, tadalafil alone and placebo. The 1° endpoint was reduction in weekly frequency of RP. 2° endpoints included Raynaud's Condition Score (RCS), pain, severity, duration, and a validated PRO (SHAQ). The DSMB reviewed data on the first 27 patients in 8/2022.
Results: The ITT population was 27 patients, the mITT 24. Results are reported for the mITT population. Cilnidipine-only treated patients(n=7) had a reduction in weekly attacks of 42.2% versus 18.9% in placebo(n=4) Dose response was seen in weekly attack frequency and severity. Response was greater in the higher cilnidipine dose group on attack duration and RCS. Tadalafil increased treatment effect with 10 mg but not with 20 mg. Cilnidipine at either dose was well tolerated and only Grade 1 mild AEs were reported with cilnidipine (17.6%), with no treatment discontinuations due to AEs. The DSMB halted Part 1 early based on meeting study goals.
Conclusion: In this preliminary study, cilnidipine was well-tolerated and efficacy trends were seen. A published metanalysis of CCB use for RP finds AE's >46% and treatment discontinuation in >30% of patients.[4] Cilnidipine appears superior in safety to commonly used CCBs (P= 0.0247). Our results replicate the improved safety in hypertension treatment. PRO results (SHAQ) also favor the 20 mg dose of cilinidipine over placebo with significance over placebo, depsite the small numbers (p=0.0115). Increased N-type channel blockade may increase safety and efficacy with the drug. Part 2 will compare Cilnidipine 20mg daily to placebo in a crossover trial in 38 patients.

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PARAMETER	Placebo (n=4)	Cilnidipine (20mg) **(n=3)	Rirash 2017 Metanalysis (n=548)
Mean Weekly attacks @ baseline	16.7	12.7	16.4 (n=117 for 2°RP)
Mean % reduction in weekly attacks (1° Endpoint)	18.9*	43	24% (n=117 for 2°RP)
Mean Severity @ baseline	3.3	3.7	unknown
Mean % reduction in Severity	-16.2	35.5	10.2(n=138 for 2°RP)
Mean Duration of attack @baseline	164.2	19.4	unknown
Mean % reduction in Duration	12.3	20.0	6(n=138)
Mean Pain level @baseline	2.3	2.3	unknown
Mean % reduction in Pain	-3.9	-11.8	ns
Mean RCS at baseline	2.6	3.5	unknown
Mean % reduction in RCS	5.1	27.9	9(n=192)

Scleroderma Health Assessment Questionnaire (SHAQ)

	Mean change (SD)	Mean Change (SD)	Wilcoxon p-value	T-test p-value
VAS - PAIN Change	0.78(1.23)	-1.1 (0.79)	0.200	0.136
VAS - Raynaud's Change	-0.5(1.43)	-1.27(1.06)	0.686	0.436
VAS - Breathing Problems Change	-0.075	-0.83(1.15)	0.943	0.540
VAS - Overall Disease Severity Change	0.7(1.31)	-1.63(0.15)	0.029	0.0115

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POS1245

TREATMENT WITH METHYLPREDNISOLONE IN VERY EARLY SYSTEMIC SCLEROSIS: RESULTS OF THE HIT HARD AND EARLY RANDOMIZED CONTROLLED TRIAL

Keywords: Investor initiated trial, Systemic sclerosis, Randomized control trial

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Background: Accumulating evidence indicates that inflammatory mechanisms drive vasculopathy and fibrosis in Systemic Sclerosis (SSc), mainly in very early disease [1]. Therefore, anti-inflammatory therapies, such as glucocorticoids, might be effective in this early pathophysiological phase. According to the VEDOSS criteria, patients can be classified as very early SSc when a combination of Raynaud's phenomenon, SSc associated autoantibodies, early SSc nailfold capillary pattern and puffy hands are present [2]. We hypothesize that by inhibition of the inflammatory process, treatment with glucocorticoids will induce remission in patients with very early SSc.
Objectives: We performed a double-blind, randomized, placebo controlled, multicenter trial in patients who meet the VEDOSS criteria, to analyze the efficacy of high dose methylprednisolone.
Methods: The trial was initiated between January 2017 and February 2021 at the Department of Rheumatology of the Radboud University Medical Centre in Nijmegen, The Netherlands and the Department of Rheumatology of the University Hospital Gent, Belgium. Patients were randomly assigned (2:1) to methylprednisolone 1000 mg intravenously for 3 consecutive days monthly for 3 months, or placebo. Patients were stratified by sex, age, and center. The primary endpoint was difference in nailfold capillary density, measured by nailfold microscopy at week 13. Changes in capillary density after 52 weeks, change in number of mega capillaries, signs and symptoms of disease progression, time to disease progression and general health utilities were secondary outcomes.
Results: Baseline characteristics were comparable between the 2 groups. Thirty patients were randomly assigned to receive methylprednisolone (n= 21) or placebo (n=9). No significant difference in change in nailfold capillary density was found at week 13, mean -0.5 (95% CI 1.1 – 0.2) (Table 1). Moreover, no differences between groups in secondary outcomes were observed, except for a difference in Visual Analogue Scale gastrointestinal complaints assessed by the Gastrointestinal Tract questionnaire in favor of the methylprednisolone group. Thirty-seven percent of patients, 4 in the placebo group and 7 in the methylprednisolone group, had disease progression during the 1 year follow up with no difference between groups (Figure 1). A relevant pulmonary function decline was seen in 23% of patients, 2 in the placebo group and 5 in the methylprednisolone group, respectively. No serious adverse events were reported.
Conclusion: We report data from the first ever investigator initiated randomized, multicenter, double blinded, placebo controlled trial on treatment with methylprednisolone in very early SSc. We were not able to demonstrate a beneficial effect of methylprednisolone. However, we observed that a substantial proportion of patients showed disease progression underlining the importance of early identification and tight monitoring of signs and symptoms of disease progression early in the course of the disease to consequently start potential treatment in this category of patients. This study shows that it is feasible to perform an intervention study with patients with very early disease.

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Table 1. Primary endpoint at week 13. Values are presented as mean (SD).

	Placebo (n=9)		Methylprednisolone (n=21)		Mean difference between groups (95% CI)*
	Primary endpoint				
	Baseline	Week 13	Baseline	Week 13	
Density, mm	7.0 (1.1)	7.3 (1.6)	7.3 (1.6)	7.2 (1.7)	-0.5 (-1.1 – 0.2)

*Adjusted for baseline values and stratification variables.

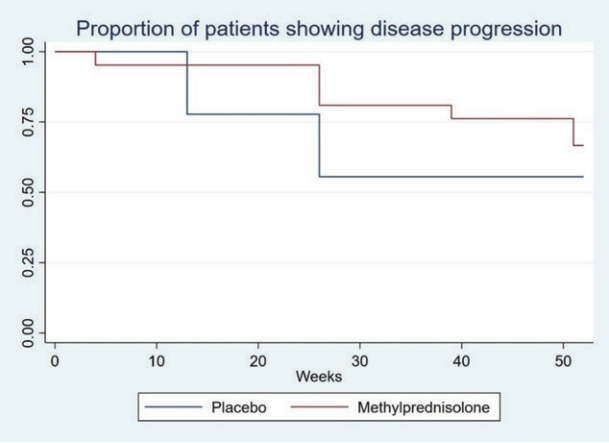


Figure 1. Kaplan Meier curve; proportion of patients with disease progression.

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Disclosure of Interests: None Declared.
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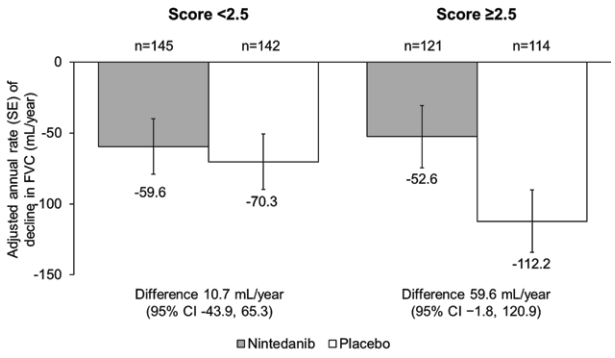
POS1246

EFFECTS OF NINTEDANIB IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD) IN SUBGROUPS BY DISEASE ACTIVITY INDEX

Keywords: Systemic sclerosis, Lungs, Clinical trials

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Background: The European Scleroderma Trials and Research group (EUSTAR) disease activity index was developed to assess disease activity in patients with systemic sclerosis (SSc).
Objectives: To assess disease activity using a modified version of the EUSTAR disease activity index, and compare outcomes in subgroups by disease activity, in patients with SSc-ILD in the SENSCIS trial of nintedanib versus placebo.
Methods: The SENSCIS trial enrolled patients with SSc with first non-Raynaud symptom in the prior ≤7 years and extent of fibrotic ILD on high-resolution computed tomography (HRCT) ≥10%. Patients were randomised to receive nintedanib or placebo. The EUSTAR disease activity index assesses SSc activity based on modified Rodnan skin score (mRSS), C-reactive protein (CRP) level, diffusing capacity of the lung for carbon monoxide (DLco), presence of digital ulcers, presence of tendon friction rubs, and worsening of skin fibrosis over the previous month (as assessed by the patient). A score ≥2.5 identifies patients with active/very active vs inactive/moderately active disease. For this analysis, a modified version of the index was developed that excluded worsening of skin fibrosis, as data prior to enrolment in the trial were not collected. The modified version had a maximum score of 8.5. We analysed the rate of decline in FVC (mL/year) and adverse events over 52 weeks in subgroups by score on the modified index (<2.5 or ≥2.5) at baseline. An exploratory interaction p-value was calculated to assess potential heterogeneity in the effect of nintedanib versus placebo between the subgroups.
Results: Among 523 patients, 55.1% and 44.9% had modified disease activity index scores of <2.5 and ≥2.5, respectively at baseline. Compared with patients with a score <2.5, those with a score ≥2.5 had a greater extent of fibrosis on HRCT (38.0% vs 34.8%) and lower mean FVC % predicted (69.1 vs 75.1); greater proportions had diffuse cutaneous SSc (70.2% vs 38.9%), were anti-topoisomerase I antibody positive (65.5% vs 56.3%) and were taking mycophenolate (54.0% vs 45.8%). In the placebo group, the rate of decline in FVC over 52 weeks was numerically greater in patients with a score ≥2.5 than <2.5 (Figure 1). The effect of nintedanib on reducing the rate of FVC decline was numerically greater in patients with a score ≥2.5 than <2.5, but the interaction p-value did not indicate heterogeneity in the effect of nintedanib between the subgroups (p=0.24). The adverse event profile of nintedanib was similar between the subgroups (Table 1).
Conclusion: Based on a modified version of the EUSTAR disease activity index, almost half of the patients in the SENSCIS trial had active/very active SSc. Nintedanib had a consistent effect on reducing the rate of FVC decline over 52 weeks in patients with low and high SSc disease activity at baseline.



Treatment-by-time-by-subgroup interaction p=0.24.

Figure 1. Rate of decline in FVC (mL/year) over 52 weeks in subgroups by modified disease activity index at baseline in the SENSCIS trial

Table 1. Adverse events in the SENSCIS trial in subgroups by modified disease activity index at baseline.

	Score <2.5		Score ≥2.5	
	Nintedanib (n=146)	Placebo (n=142)	Nintedanib (n=121)	Placebo (n=114)
Most frequent adverse events*				
Diarrhoea	78.8	27.5	71.1	33.3
Nausea	30.8	15.5	35.5	12.3
Skin ulcer	13.7	11.3	24.0	26.3
Vomiting	22.6	9.2	28.9	12.3
Cough	12.3	13.4	9.9	20.2
Nasopharyngitis	17.1	18.3	9.1	16.7
Upper respiratory tract infection	6.8	10.6	13.2	8.8
Abdominal pain	8.9	9.2	11.6	3.5
Fatigue	9.6	6.3	14.0	9.6
Weight decreased	11.0	5.6	12.4	3.5
Adverse event(s) leading to treatment discontinuation	17.8	9.9	14.0	8.8

*Adverse events were coded according to preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). Data are % of patients with ≥1 such adverse event reported over 52 weeks (or until 28 days after last trial drug intake in patients who discontinued trial drug before week 52). Adverse events reported in >10% of patients in either treatment group in the overall trial population are shown.

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POS1247

RIGHT VENTRICULAR MORPHOLOGY AND FUNCTION AFTER HIGH INTENSITY INTERVAL AND RESISTANCE TRAINING IN PEOPLE WITH SYSTEMIC SCLEROSIS: A RANDOMISED CONTROLLED PILOT STUDY

Keywords: Cardiovascular disease, Systemic sclerosis, Non-pharmacological interventions

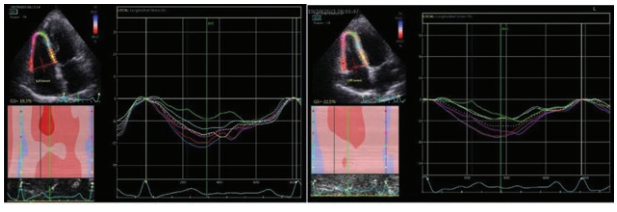
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Background: The presence of left ventricular (LV) remodeling and dysfunction in systemic sclerosis (SSc) have been well studied to date [1]. Cardiac deformation and impaired right ventricular (RV) free wall contractility patterns in SSc have also been described [2]. High intensity interval training (HIIT) has demonstrated to improve microvascular function in people with SSc [3]. However, the cardiac morphology and function after exercise training in people with SSc have not been studied yet. Echocardiographic indices of RV function [4] were found to be correlated with cardiorespiratory fitness, as assessed by peak oxygen uptake (VO_2peak) in people with SSc.

Objectives: The primary objective of the present study was to assess possible exercise-induced changes in RV morphology and function. A secondary objective was to explore the relationship between VO_2 peak and RV echocardiographic indices after exercise training in people with SSc.

Methods: Twenty-eight people with SSc (24 females, mean age 57.21 ± 10.76 yrs.) were randomized into groups A (exercise) and B (control group). Baseline and three-month follow up assessments included: medical history, anthropometrics, echocardiography, and an arm crank cardiopulmonary exercise testing (CPET). Following the baseline assessments, Group A performed a 3-month supervised exercise program (twice/week) adjunctive to the usual care, while Group B received only the usual care. The supervised exercise training consisted of aerobic and resistance exercises as described previously [5]. The aerobic protocol consisted of HIIT (30s at 100% of peak power output achieved during CPET following by 30s passive recovery) on an arm ergometer.

Results: The average compliance in the exercise program was 90% with no dropouts and no adverse effects. Group A demonstrated a statistically significant increase in VO_2 peak by 25.1% ($p<0.001$), global RV free wall longitudinal systolic strain by 6.69% ($p<0.03$), RV free wall longitudinal systolic strain of the basal segment by 13.5% ($p<0.001$) and global RV four-chamber longitudinal systolic strain by 6.76% ($p<0.03$) after exercise training (Figure 1). No statistically significant difference was observed in group B.



(a) (b)

Figure 1. RV strain measurements in a SSc patient (a) at baseline (RV4CLS = −18.5%) and (b) after exercise training (RV4CLS = −22.5%).

Conclusion: Our results support the significance of 2DSTE in clinical practice for the early detection of cardiac deformation in SSc patients. In conclusion, a combined exercise training program seems to be effective in improving cardiorespiratory efficiency and RV systolic function in people with SSc with subclinical RV dysfunction.

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POS1248

OVERALL SURVIVAL, PROGRESSION-FREE SURVIVAL AND RELAPSE RATES ARE SIMILAR IN FEMALES VERSUS MALES UNDERGOING AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) FOR AUTOIMMUNE DISEASE

Keywords: Safety, Real-world evidence, Registries

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Background: Autologous HSCT has been increasingly used for over 25 years to treat refractory autoimmune diseases (ADs). Multiple sclerosis (MS) and systemic sclerosis (SSc) cover around 80% of transplants performed for ADs[1], where HSCT has become an integral and standard-of-care part of treatment algorithms. In a first European Society for Blood and Marrow Transplantation (EBMT) analysis of HSCT performed between 2010 and 2015, there was chronological improvement in outcomes (i.e., progression-free survival, relapse/progression, and transplant-related mortality), strictly connected to the transplant center experience, patient selection and progress with supportive care.[2] Here, trends and outcomes have been updated to include HSCT performed for ADs between 2015 and 2020.

Objectives: To describe outcomes of autologous HSCT for ADs, 2 and 5 years from transplant.

Methods: This is a retrospective study on data routinely reported to EBMT's Autoimmune Diseases Working Party (ADWP) registry, based on 247 centers in 40 countries and others (Italy, Germany, Sweden, United Kingdom, Netherlands, Spain, France, and Australia account for ~75% of cases). We included adult patients (≥18 years) undergoing autologous HSCT for ADs between 2015-2020. Patients without information on follow-up after HSCT were excluded. The date of the transplant was the starting point for all time-to-event analysis, and individuals with no event were censored at the date of the last follow-up. Successful initial engraftment was defined as achieving a neutrophil white cell count ≥ 0.5×10^9/L for three consecutive days. We used Kaplan-Meier curves to evaluate overall survival (time until death) and progression-free survival (PFS) - defined as time to either relapse/progression or death. We also determined the cumulative incidence of AD relapse.

Results: We studied 1,389 individuals with ADs undergoing autologous HSCT from peripheral blood cell sources. The median follow-up was 26 months. Individuals were mostly female (58%), at a median age of 40 years (interquartile range

32.4-48.6). The main indications for HSCT included MS (68%) and SSc (21%). Successful initial engraftment occurred in the vast majority (98.5%), most times within 30 days from transplant. We observed 70 deaths (5% of 1,389), most (57, 81%) occurring within 2 years. Deaths were most often caused by AD relapse/progression (27%) or infection (24%). At 2 years post-transplant, overall survival was 95.5% (95% CI 94.2-96.5%), PFS was 82% (95% CI 79.6-84.2%), and relapse of AD occurred in 14.8% (95% CI 12.7-17.0%). Non-relapse mortality was 3.2% (2.3 - 4.3) at 2 years. Similar overall survival, PFS, and relapse rates were found for females versus males (biological sex at birth) at both 2 and 5 years post-HSCT (Table 1). Multivariate analysis was not done due to the heterogeneity of the population and the limited number of events.

Conclusion: Autologous HSCT for autoimmune disease results in high survival and moderately low relapse. Limitations include inadequate precision to stratify by autoimmune disease and transplant regimens.

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Table 1. Outcomes at 2 and 5 years after transplant, stratified by biological sex at birth

	Outcome	Male % (95 CI%)	Female % (95 CI%)
2 years	Overall survival	94.7% (92.4-96.4%)	96.0% (94.3-97.2%)
	Progression free-survival	79.9% (75.9-83.3%)	83.5% (80.5-86.2%)
	Non-relapse mortality	3.5% (2.2-5.3%)	3.0% (1.9-4.4%)
	Relapse	16.6% (13.3-20.2%)	13.5% (11.0-16.3%)
5 years	Overall survival	90.2% (85.9-93.3%)	95.1% (92.8-96.7%)
	Progression free-survival	61.5% (54.4-67.7%)	69.2% (63.9-73.8%)
	Non-relapse mortality	4.8% (2.8-7.5%)	3.9% (2.4-5.9%)
	Relapse	33.8% (27.3-40.3%)	26.9% (22.3%-31.8%)

Acknowledgements: The data originate from the EBMT registry.
Disclosure of Interests: None Declared.
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POS1249 LUNG ULTRASOUND CHANGES COMPARED WITH AUTOMATED QUANTITATIVE COMPUTED TOMOGRAPHY FOR DETECTING SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

Keywords: Ultrasound, Systemic sclerosis, Lungs

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Background: B-lines and pleural line (PL) changes represent lung ultrasound (LUS) findings for detection of systemic sclerosis-associated interstitial lung disease (SSc-ILD). The ≥10 B-lines cut-off was found to be closely related to moderate ILD on high-resolution chest tomography (CT). Recently proposed Fairchild's criteria for PL evaluation resulted in high accuracy and reproducibility and a low spending time. Semi-quantitative PL irregularity score by Pinal-Fernandez proved to be superior to total B-lines number to detect SSc-ILD. Although several evidence-based LUS scores have been presented, there is currently a lack of studies involving a comprehensive LUS assessment and comparing different LUS scores with CT, particularly with automated quantitative CT (qCT) assessment.

Objectives: To evaluate the accuracy of quantitative and qualitative LUS B-lines and PL changes for SSc-ILD detection compared to CT with qCT assessment.

Methods: Consecutive SSc patients according to 2013 ACR/EULAR classification criteria underwent LUS by two certified blinded operators using a 14-scans method. The ≥10 B-lines cut-off and Fairchild's criteria fulfilment were selected as qualitative findings. From quantitative point of view, total B-lines number and the sum of the PL score adapted from Pinal-Fernandez were collected. CT scans performed over a ±6 months period were recorded and evaluated by two thoracic radiologists, with further processing by automated texture analysis software.

Results: The study population consisted of 29 SSc patients (Table 1). Agreement between the two operators was almost perfect for Fairchild's criteria [Cohen's kappa (k) 0.84] and substantial for ≥10 B-lines cut-off (k 0.78). Both qualitative LUS scores were predictive of ILD presence on CT, with Fairchild's criteria resulting in slightly more accuracy (Figure 1A). Results were confirmed on multivariate analysis, introducing confounders like age, disease duration, ongoing immunosuppressant therapy, and current/ever smoking (Fairchild's criteria: p 0.0003 and B-line cut-off: p 0.03). All qualitative and quantitative LUS findings were found to be significantly associated with ILD extension on qCT ($p<0.05$). Total B-lines number correlated with extension of reticulations and PL quantitative score correlated with extension of both ground-glass and reticulations (Figure 1B and C). Lung bases PL quantitative score, but not B-lines number of the same site, was found to correlate with basal ILD extension on qCT (Figure 1D).

Conclusion: This study highlights the reliability and good accuracy of a comprehensive and systematic LUS assessment for SSc-ILD detection, compared to automated qCT. LUS is increasingly emerging as an accurate, feasible, low-cost, and radiation-free pre-CT screening tool. For these reasons, standardisation of LUS appears to be required, in order to achieve its wider use in clinical practice.

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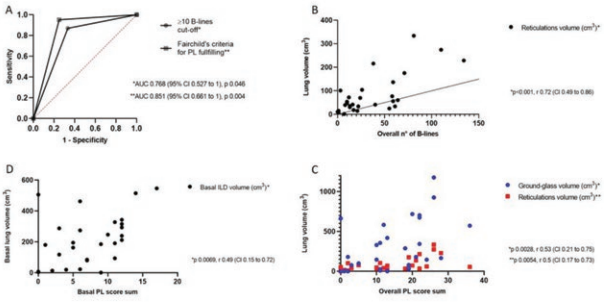
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Table 1 Data of study population, LUS assessment and qCT software analysis.

Female/male, N° (%)	26/3 (89.6/10.4)
Median age (years) [quartiles]	59 [49;70]
Median disease duration (years) [quartiles]	8 [4;12]
Diffuse/limited cutaneous disease, N° (%)	20/9 (69/31)
Immunosuppressive therapy, N° (%)	15 (51.7)
Interstitial Lung Disease (ILD), N° (%)	22 (75.9)
Fairchild's criteria for PL fulfilling, N° (%)	21 (72.4)
≥10 cumulative B-lines, N° (%)	21 (72.4)
Total B-lines (median [quartiles])	24 [8;57]
Total PL score sum (median [quartiles])	13 [4;22]
Ground-glass (cm^3/ %) (median [quartiles])	179 [30;578]/ 3.8 [0.65;15]
Reticulations (cm^3/ %) (median [quartiles])	47 [28;103]/ 1.2 [0.6;5.2]
Total ILD (cm^3/ %) (median [quartiles])	323 [70;652]/ 8.2 [1.6;19]
Basal ILD (cm^3) (median [quartiles])	191 [51;305]

LUS, lung ultrasound; qCT, quantitative chest tomography; PL, pleural line.

Figure 2 A) ROC curve of Fairchild's criteria and ≥10 B-lines cut-off accuracy to detect SSc-ILD as assessed by CT. B) Correlation of overall B-lines number with reticulations volume. C) Correlation of overall PL score sum with ground-glass and reticulations volumes. D) Correlation of basal PL score sum with corresponding basal ILD volume.



ROC, receiver operating characteristic; SSc-ILD systemic sclerosis-associated interstitial lung disease; CT, high resolution chest tomography; PL pleural line; CI, 95% confidence interval; AUC area under the curve.

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Disclosure of Interests: None Declared.
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POS1250 PROGRESSION OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS DOES NOT PREDICT FURTHER PROGRESSION

Keywords: Prognostic factors, Lungs, Systemic sclerosis

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Background: Interstitial lung disease (ILD) is a major cause of morbidity and mortality in systemic sclerosis (SSc). In clinical practice, physicians often wait for progression to initiate or escalate therapy. Similarly, progressive SSc-ILD patients

are recruited into trials to enrich for further progression. These strategies assume that patients with recent ILD progression have a higher risk for further progression. However, this has not been analyzed in SSc-ILD and there is currently no evidence to support such treatment and recruitment strategies.

Objectives: We assessed whether ILD progression predicts subsequent progression using four definitions of progressive disease in two well-characterized SSc-ILD cohorts.

Methods: We included all SSc patients from the Oslo and Zurich cohorts who had ILD on HRCT and at least three consecutive annual FVC measurements. For the primary analysis, ILD progression was defined as absolute FVC decline >5% over 12 months. Patients were grouped into progressors (FVC >5% decline) and non-progressors (all others). At the next annual follow up visit, all patients were again assessed for ILD progression. In secondary analyses, we applied other definitions of progression such as:

(I) 2022 ATS/ERS/JRS/ALAT guideline criteria with (1) worsening of respiratory symptoms; (2) absolute decline in FVC >5% or in DLCO >10% and (3) disease progression on HRCT over 12 months

(II) INBUILD criteria with (1) FVC decline ≥10%, (2) FVC decline >5-<10% and worsening of respiratory symptoms or an increased extent of fibrosis on HRCT, or (3) worsening of respiratory symptoms and an increased extent of fibrosis within any timeframe of 24 months.

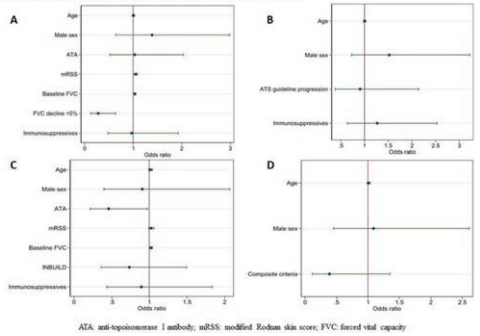
(III) Composite criteria with absolute decline in FVC ≥10%; or FVC >5%-9% and DLCO >15%.

Multivariable logistic regression was applied, adjusting for known risk factors of ILD progression, including treatment.

Results: Here, 231 SSc-ILD patients from Oslo and Zurich were included, with mean age at onset of 48 years, 55 (24%) being males, 94 (41%) with diffuse cutaneous SSc and 83 (35%) with anti-topoisomerase I antibodies (ATA). Mean FVC was 89%, mean DLCO 64%, 59 (19%) had NYHA functional class ≥3, 35 (27%) extent of ILD >20% and 40% extent >10%. At 12 months, 71 (30.7%) showed FVC decline >5% and were classified as progressors. In multivariable logistic regression, adjusted for age, male sex, ATA, mRSS and immunosuppressive treatment, ILD progression was significantly protective for further progression at the next annual follow-up (Odds ratio 0.28, 95%CI 0.12-0.63, p=0.002, Figure1a). When other definitions of progression were applied, similar results were obtained: 44 (19%) fulfilled the guideline criteria, 89 (39%) the INBUILD criteria and 33 (14%) the composite criteria. Multivariable regression analysis adjusted for age, sex and treatment (guideline), for age and sex (composite) and for age, sex, ATA, mRSS, baseline FVC and treatment (INBUILD) showed the same direction as the primary analysis (Figure 1b-d).

Conclusion: ILD progression does not predict further progression using any ILD progression definition in SSc. These results suggest changing current treatment practices, since waiting for progression to initiate or escalate treatment does not seem to be the adequate strategy to identify patients at risk of further progression. It also has important implications for clinical trial design, since selection of progressive SSc-ILD patients does not seem to enrich for a progressive SSc-ILD study population.

Figure 1: Multivariable logistic regression for ILD progression using definitions of ILD progression (A) FVC decline >5%, (B) Guideline criteria; (C) INBUILD criteria and (D) composite criteria



ATA: anti-topoisomerase I antibody; mRSS: modified Rodnan skin score; FVC: forced vital capacity

REFERENCES: NIL.

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POS1251 TREATMENT TAPERING IN SYSTEMIC SCLEROSIS: A 10-YEAR FOLLOW-UP STUDY

Keywords: Treat to target, Systemic sclerosis, Tapering

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Background: In systemic sclerosis (SSc), tailoring treatment to each patient's needs is challenging and it is unclear whether and how patients need to be treated in the long-term. The feasibility of tapering and even withdrawing immunosuppressive therapies in patients with stable disease is still an open question.

Objectives: Using data from the Leiden SSc cohort, our aim was to describe how often treatment is modified during a follow-up period of 10 years, with a special interest in the possibility of tapering immunosuppressors (i.e. either tapering the dosage or switching to a less immunosuppressive regimen).

Methods: We analyzed the use and changes of immunosuppressive therapies in the whole cohort and in patients stratified for sex and autoantibody status. We included 708 SSc patients with at least one visit performed between 2009 and 2021, accounting for 2968 visits.

Results: At the time of referral to the care pathway, 31% of patients were receiving immunosuppressors and tapering was possible in 8% of them (Table 1). During the follow-up, tapering was possible in a higher proportion of patients treated with immunosuppressive medications, up to the 20% at the third-year and 26% at the sixth-year visits. No significant differences emerged in the proportions of drug tapering between males and females or between patients with anticentromere and anti-topoisomerase I antibodies. Overall, immunosuppressive medications were tapered 137 times during the 2968 visits. Of the 107 patients who tapered medications at least once during the follow-up, in 64% of cases it happened during the first three years. In 24 patients, tapering occurred at the last available visit, whereas in 83 patients the management of medications could be evaluated after tapering (246 follow-up visits). In 31 cases, therapies were not changed further. In the other 52 patients, treatment regimen was modified again and in 31 cases we had to either increase the dosage of the current therapy or to initiate a new immunosuppressive drug. Analysing the type of immunosuppressive medication used (Figure 1), we observed that treatment with methotrexate tended to decrease, while mycophenolate mofetil gained favour over the years, especially in women and in patients with anti-topoisomerase I antibodies.

Conclusion: In conclusion, tapering of immunosuppressors could be considered in 15% of cases (107 of 708) in our large prospective cohort, and this was succesful in approximately two-thirds of cases in which follow-up was available (52 out of 83). If on the one hand early therapeutic intervention might be beneficial and a window of opportunity exists in SSc, on the other hand tapering immunosuppressive treatments might become feasible in a proportion of patients with stable disease.

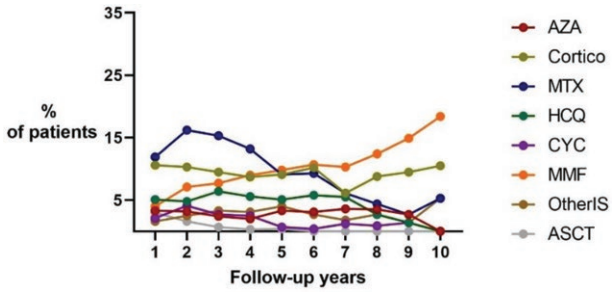


Figure 1. Medication use over time in 708 SSc patients from the Leiden SSc cohortASCT: autologous stem cell transplantation, AZA: azathioprine, Cortico: corticosteroids, MTX: methotrexate, HCQ: hydroxychloroquine, CYC: cyclophosphamide, MMF: mycophenolate mofetil, OtherIS: immunosuppressors including rituximab, tocilizumab, trial medications.

Table 1. Tapering of immunosuppressive (IS) therapies in patients from the Leiden SSc cohort

Visit year	All patients			Female patients	Male patients	ACA positive patients	ATA positive patients
	Whole group	Patients on IS therapy	Patients in which IS therapy is tapered	Patients in which IS therapy is tapered over total number of patients on IS therapy			
1	708	218/708 (31%)	17/218 (8%)	10/164 (6%)	7/54 (13%)	2/47 (4%)	6/67 (9%)
2	563	213/563 (38%)	24/213 (11%)	18/162 (11%)	6/51 (12%)	5/48 (10%)	4/58 (7%)
3	452	169/452 (37%)	34/169 (20%)	29/129 (22%)	5/40 (13%)	6/34 (18%)	8/54 (15%)
4	356	125/356 (35%)	19/125 (15%)	14/101 (14%)	5/24 (21%)	3/28 (11%)	5/36 (14%)
5	275	91/275 (33%)	11/91 (12%)	8/76 (11%)	3/15 (20%)	4/24 (17%)	3/27 (11%)
6	225	74/225 (33%)	19/74 (26%)	17/63 (27%)	2/11 (18%)	8/19 (42%)	6/26 (23%)
7	165	44/165 (27%)	7/44 (16%)	6/40 (15%)	1/4 (25%)	1/11 (9%)	3/18 (17%)
8	113	40/113 (35%)	2/40 (5%)	1/28 (4%)	1/2 (50%)	0/7	1/11 (9%)
9	74	21/74 (28%)	3/21 (14%)	3/19 (16%)	0/2	0/3	2/11 (18%)
10	38	13/38 (34%)	1/13 (8%)	1/10 (10%)	0/3	0/2	1/8 (13%)

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POS1252

CALIPER PARAMETERS AS PREDICTORS OF MORTALITY IN SYSTEMIC SCLEROSIS: A LONGITUDINAL STUDY

Keywords: Lungs, Systemic sclerosis, Artificial intelligence

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Background: Interstitial lung disease (ILD) is the leading cause of death in systemic sclerosis (SSc). High-Resolution Computed Tomography (HRCT) and pulmonary function tests (PFTs) are useful for the diagnosis and follow-up of ILD, but have limitations for assessing disease severity and progression, including poor reproducibility of the extent analysis by HRCT and low sensitivity of PFTs. Quantitative CT (QCT) methods, including Computed Aided Lung Informatics for Pathology Evaluation and Rating (CALIPER), are new tools that objectively measures parenchymal abnormalities and vascular features on CT images in a fully automated analysis.[1] This may bring benefits in detecting early disease and in the assessment of prognosis of patients with SSc-ILD.

Objectives: We investigated whether changes in parenchymal abnormalities measured by CALIPER are associated with mortality and their correlation with PFTs.

Methods: Seventy-one patients diagnosed with SSc (ACR/EULAR 2013 criteria) consecutively evaluated from January 2011 to October 2022 at the Scleroderma outpatients clinic at Federal University of São Paulo were retrospectively selected. To be included, patients should have volumetric HRCTs and PFTs performed at baseline and at 24 months of follow-up. All causes of death and clinical variables were collected from clinical records. HRCTs were analyzed using CALIPER. The following parameters were evaluated: ground glass opacities, reticular pattern, honeycombing, and pulmonary vascular volume (PVV), quantified and normalized to total lung volume (LV) and expressed as a percentage. The extent of ILD (ILD-extent), given by the sum of ground glass, reticular pattern and honeycombing and the fibrosis score given by the sum of the reticular pattern and honeycombing were also evaluated. The best thresholds for CALIPER measurements were calculated using ROC analysis. Factors associated with death were evaluated by Kaplan-Meier survival curves.

Results: Of the 71 SSc patients included the mean age was of 54.2 ± 11.6 years, (mean disease duration of 10 years) and 90.1% were females. Eleven patients (15.49%) died during follow-up and all had ILD. Most of the CAPILER variables remained stable over time (Table 1). All CALIPER parameters (except honeycombing), had a significant correlation with forced vital capacity (FVC) at baseline and follow-up (p<0.001). As shown by Kaplan-Meier survival curves, survival was worse among patients with ILD-extent% ≥ 6.32, fibrosis score% ≥ 1.42 and reticular pattern% ≥ 1.41 at baseline, and an ILD-extent% ≥ 4.75, a fibrosis score% ≥ 0.77, a reticular pattern% ≥ 4.34 and a PVV/LV% ≥ 2,8 at 24 months follow-up (Figure 1).

Table 1. PFTs and Caliper parameters at baseline and at 24 months of follow-up

	BASELINE (n= 71)	FOLLOW-UP (n=71)	Δ change from baseline to follow-up	p
FVC, % pred (Mean ± SD)	73.6 ± 19.1	69.6 ± 18.9	-3.93 ± 8.92	0.001
DLCO, % pred (Mean ± SD)	54.3 ± 13.7 (n=8)	51.8 ± 13.9 (n=9)	2.33 ± 8.96	0.696
CALIPER (Median [quartile range])				
Total normal volume (cm^3)	2986.5 [2236 – 3730]	2817.6 [2181 – 3503]	-81.6 [-295-112]	0.032
Reticular pattern, %	1.58 [0.671 – 2.85]	1.43 [0.666 – 3.19]	0.016 [-0.61 – 0.37]	0.720
Groundglass, %	6.06 [1.87 – 15.8]	5.96 [1.61 – 13.7]	0.239 [-2.22 – 2.75]	0.408
Honeycombing, %	0.015 [0.007-0.05]	0.017 [0.005-0.04]	0.000[-0.009– 0.01]	0.149
Fibrosis score, %	1.65 [0.68 – 3.25]	1.51 [0.67 – 3.19]	0.03 [-0.62 – 0.49]	0.920
ILD-extent, %	7.82 [3.27 – 19.1]	7.96 [2.58 – 19.7]	0.150 [-2.05 – 2.84]	0.565
PVV/LV, %	2.81 [2.09 – 4.20]	2.92 [2.00 – 4.45]	0.07 [-0.236– 0.52]	0.143

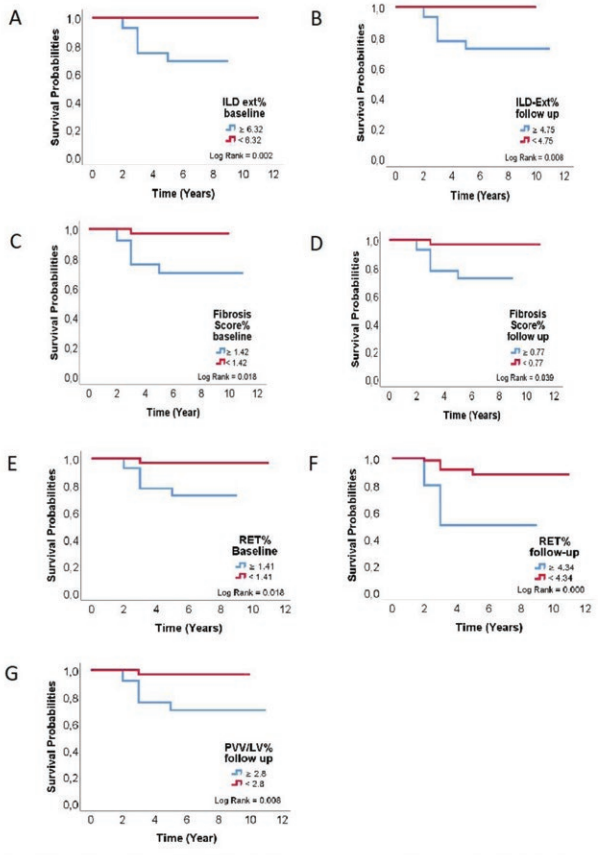


Figure 1. Kaplan-Meier survival curves according to CALIPER analysis at baseline (A, C, and E), and at follow-up (B, D, F, and G).

Conclusion: CAPILER is a useful tool for assessing lung damage and predict mortality in patients with SSc. Future studies are needed to confirm these data.

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POS1253 TIMP-1 AS WELL AS IL-6 IN PULMONARY CAPILLARIES REFLECT THE COMPLICATIONS AND SEVERITY OF PH IN SYSTEMIC SCLERODERMA

Keywords: Cytokines and chemokines, Biomarkers

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Background: Abnormal production of various cytokines is involved in the pathogenesis of CTD, and the cytokine abnormalities vary according to the type of organ lesion. Recent reports indicate that various cytokine production abnormalities are also involved in the pathogenesis of iPAH.1) The differences between PH associated with CTD and other PH-associated cytokines, including iPAH, are not well defined. The relationship between the severity of each PH and cytokines is also not clear.

Objectives: The purpose of this study was to determine the relationship between the cytokine profile in pulmonary capillaries in CTD-PH and hemodynamic indicators of PH, and to confirm the differences in cytokine profiles between CTD-PH and other PH, including iPAH.

Methods: Patients who underwent RHC for PH diagnosis at our hospital from 2015 to 2021 years were included in the study. Serum was collected before and after pulmonary capillaries during right and left heart catheterization performed for hemodynamic analysis of PH, and cytokines were measured. TIMP-1, IL-21 MCP-1, IL-17, IL-12p70 and IL-6, which have been previously reported to be associated with the pathogenesis of CTD and PH, were included in the measurements in this study. TIMP-1, IL-21 were measured by ELISA (ABCAM UK). MCP-1, IL-17, IL-12p70 and IL-6 were measured by ELISA (Ella simple plex USA). The relationship between the measured cytokine profiles and hemodynamic parameters was compared. Statistical analyses were performed using the Spearman's rank correlation coefficient and the Wilcoxon signed-rank test in JMP software v16.1.0 (SAS, USA).

Results: Eighty-one studies were performed on 56 patients who underwent right and left heart catheterization. Forty-seven were female and nine were male, with a mean age of 64.2 years. 33 were CTD patients, including 19 SSc, 10 MCTD, 2 SLE, and 2 SS, and 23 non-CTD patients, of which 5 were iPAH. All 23 non-CTD patients were able to diagnose PH, while 11 CTD patients (8 SSc, 3 MCTD) were unable to diagnose PH. The CTD duration was 7.5 years in the PH group and 10.8 years in the nonPH group. Three of the CTDs in which PH could not be diagnosed were using pulmonary vasodilators for treatment of DU.Ten cases in the CTD-PH group were receiving immunosuppressive therapy. WHOFC found no difference in CTD-PH and non CTD-PH. Mean mPAP was 29 +/- 9.3 mmHg in CTD-PH and 32 +/- 10 mmHg in non-CTD-PH, with no significant difference. In an analysis of all patients who were able to diagnose pulmonary hypertension, IL-6 and IL-12 levels in pulmonary capillary were significantly associated with mPAP ($p < 0.05$). Furthermore, an association between IL-6 and WHOFC was found in all patients with CTD-PH, SSc-PH, and non-CTD-PH ($p<0.05$). In an analysis focused on SSc, TIMP-1 and IL-6 were markedly higher in SSc patients diagnosed with PH (TIMP-1; 134+/-42.8 vs 243+/-135, $p <0.05$, IL-6; 2.04+/-0.82 vs 21.2+/-80, $p <0.05$).In all groups examined this time, IL-17, IL-21, and MCP-1 were not significantly associated with severity of PH or with any of the hemodynamic parameter.

Conclusion: In the analysis of cytokines in pulmonary capillaries, IL-6 was found to be associated with hemodynamics in all PH patients, but TIMP-1 was found to be associated only with the PH pathogenesis of systemic scleroderma.

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POS1254 REDUCED HEALTH-RELATED QUALITY OF LIFE USING PROMIS IN PATIENTS WITH SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL ANALYSIS FROM THE INTERNATIONAL COVAD-2 E-SURVEY

Keywords: Patient reported outcomes, Quality of life, Systemic sclerosis

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Background: The second COVID-19 vaccination in autoimmune disease (COVAD-2) study [1] is an international, multicentre, self-reported e-survey designed to evaluate several facets covering COVID-19 infection and vaccination as well as validated patient-reported outcome measures (PROMs) in a variety of autoimmune diseases (AIDs), including systemic sclerosis (SSc). Detailed assessment of the health-related quality of life (HRQOL) and its drivers in patients with SSc is lacking.

Objectives: To assess physical and mental health in a global cohort of SSc patients in comparison with non-SSc autoimmune inflammatory rheumatic diseases (AIRDs), non-rheumatic AIDs (NRAIDs), and those without AIDs (controls) using Patient-Reported Outcome Measurement Information System (PROMIS) global health data from the COVAD-2 survey.

Methods: The COVAD-2 database was used to extract demographics, AID diagnosis, comorbidities, disease activity, current therapies, and PROMs. PROMIS global physical health (GPH), global mental health (GMH) scores, PROMIS physical function short form-10a (PROMIS PF-10a), pain visual analogue scale (VAS), and PROMIS Fatigue-4a scores were compared between SSc, non-SSc AIRDs, NRAIDs, and controls. Outcomes were also compared between diffuse cutaneous SSc (dcSSc) vs limited cutaneous SSc (lcSSc). Multivariable regression analysis was performed to identify factors influencing GPH and GMH scores in SSc.

Results: A total of 10,502 complete responses from 276 SSc, 6006 non-SSc AIRDs, 545 NRAIDs, and 3675 controls as of May 2022 were included in the analysis. Respondents with SSc were older [SSc *vs.* non-SSc AIRDs *vs*. NRAIDs *vs*. controls: 55 (14) *vs.* 51 (15) *vs*. 45 (14) *vs*. 40 (14) years old, mean (SD), $p < 0.001$]. Among patients with SSc, 129 (47%) had dcSSc and 147 (53%) had lcSSc. SSc patients reported a significantly higher prevalence of ILD [SSc *vs.* non-SSc AIRDs *vs*. NRAIDs *vs*. controls: 30.4% *vs.* 5.5% *vs*. 1.5% *vs*. 0.2%, $p < 0.001$], and treatment with MMF [SSc *vs.* non-SSc AIRDs *vs*. NRAIDs *vs*. controls: 26.4% *vs.* 9.5% *vs*. 1.1% *vs*. 0%, $p < 0.001$].

Patients with SSc had lower GPH and PROMIS PF-10a scores [SSc *vs.* non-SSc AIRDs *vs*. NRAIDs *vs*. controls: 13 (11–15) *vs.* 13 (11–15) *vs*. 15 (13–17) *vs*. 17 (15–18), median (IQR), p < 0.001; 39 (33–46) *vs.* 39 (32–45) *vs*. 47 (40–50) *vs*. 49 (45–50), p < 0.001, respectively] and higher Pain VAS and PROMIS Fatigue-4a scores compared to those with NRAIDs or controls [SSc *vs.* non-SSc AIRDs *vs*. NRAIDs *vs*. controls: 3 (2–5) *vs.* 3 (1–6) *vs*. 2 (0–4) *vs*. 0 (0–2), p < 0.001; 11 (8–14) *vs.* 11 (8–14) *vs*. 9 (7–13) *vs*. 7 (4–10), p < 0.001, respectively]. Patients with AIDs including SSc had lower GMH scores compared to controls [SSc *vs.* non-SSc AIRDs *vs*. NRAIDs *vs*. controls: 12.5 (10–15) *vs.* 13 (10–15) *vs*. 13 (11–16) *vs*. 15 (13–17), p < 0.001]. Among SSc patients, GPH, GMH, and PROMIS PF-10a scores were lower in dcSSc compared to lcSSc [dcSSc *vs.* lcSSc: 12 (10–14) *vs.* 14 (11–15), p < 0.001; 12 (10-14) vs. 13 (10-15), p<0.001; 38 (30–43) *vs*. 41 (34–47), p < 0.001, respectively]. Pain VAS and PROMIS Fatigue-4a scores were higher in dcSSc compared to lcSSc [4 (2–6) *vs.* 3 (1–5), p < 0.001; 12 (8–15) *vs.* 9 (8–13), p < 0.001, respectively]. The independent factors for lower GPH scores in SSc were older age, Asian ethnicity, glucocorticoid use, and higher pain and fatigue scales, while mental health disorders and higher pain and fatigue scales were independently associated with lower GMH scores.

Conclusion: In a global cohort, patient-reported physical and mental health were significantly worse in patients with SSc in comparison to those with non-SSc AIDs and without AIDs. Our findings support the critical need for more attention to patient's subjective experiences including pain and fatigue to improve the HRQOL in patients with SSc.

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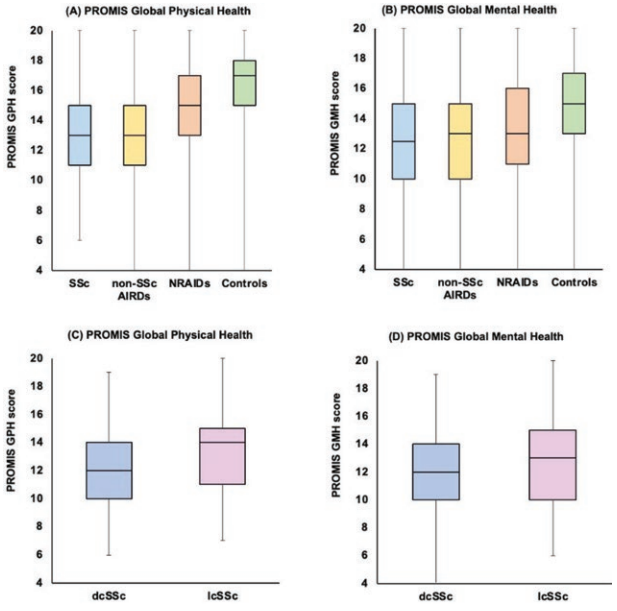


Figure: Global physical health scores and Global mental health scores in each disease category and SSc subgroup
AIRDs, autoimmune inflammatory rheumatic diseases;
dcSSc, diffuse cutaneous systemic sclerosis;
GMH, global mental health; GPH, global physical health;
lcSSc, limited cutaneous systemic sclerosis;
NARIDs, non-rheumatic autoimmune rheumatic diseases;
PROMIS, Patient-Reported Outcome Measurement Information System;
SSc, systemic sclerosis;

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POS1255

CLINICAL SIGNIFICANCE OF THE ANTI-NUCLEOLAR ORGANIZER REGION 90 ANTIBODIES (NOR90) IN SYSTEMIC SCLEROSIS: A EUROPEAN SCLERODERMA TRIALS AND RESEARCH (EUSTAR) ANALYSIS

Keywords: Systemic sclerosis, Autoantibodies

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Background: The anti-Nucleolar Organizer Region 90 antibodies (NOR90) are rare antinuclear antibodies (ANA) identified in up to 6% of patients with systemic sclerosis (SSc). However, due to the small number of available studies, the clinical relevance of NOR90 in SSc remains uncertain.

Objectives: To analyze clinical associations of NOR90 in patients with SSc in a multicentric cohort.

Methods: Post-hoc, cross-sectional study of prospectively collected data from the European Scleroderma Trials and Research (EUSTAR) group database, with additional information on NOR90 provided by participating centers (EUSTAR project CP105). NOR90 was tested using immunoassays. Differences between patients with and without NOR90 were assessed using the U Mann-Whitney and the Chi-square test, and clinical associations were tested using regression models.

Results: Overall, 1318 patients with SSc were included (mean age 58.3±13.7 years, 81.3% female), of whom 44 (3.3%) were positive for NOR90, that were also positive for other SSc-specific antibodies: anti-topoisomerase I (20.5%), anti-centromere (42.9%), and anti-RNA polymerase III (12.5%). The demographic and clinical data of NOR90-positive and -negative patients are displayed in Table 1. There was no difference in the presence of severe organ manifestations including interstitial lung disease, pulmonary hypertension, and renal crisis, but NOR90-positive patients were more frequently female, had lower modified Rodnan skin score (mRSS), and lower prevalence of upper and lower gastrointestinal symptoms compared to NOR90-negative patients. In multivariable regression models adjusted for the presence of the most frequent SSc-specific antibodies, NOR90 remained significantly associated with lower mRSS and with less frequent gastrointestinal symptoms (Figure 1).

Conclusion: To the best of our knowledge, this is the largest SSc cohort tested for NOR90 so far. Apart from negative associations with skin fibrosis and GI symptoms, which should be analyzed in further studies, we did not find any significant association of NOR90 with SSc-associated organ/ system involvement.

However, these patients had a considerable prevalence of severe organ manifestations and should therefore be carefully evaluated.

Table 1. Demographic and clinical SSc-related data of NOR90-positive and -negative patients.

Parameter	NOR90 (+)	NOR90 (-)	p-value
Age, years	61.5 (48.0; 68.0)	59.0 (50.0; 68.0)	0.663
Female, yes/total (%)	**43/44 (97.7%)**	**1029/1274 (80.8%)**	**0.005**
Disease duration, years	15.5 (9.7; 21.2)	12.0 (6.0; 21.5)	0.061
Anti-topoisomerase I, n/N (%)	9/42 (20.5%)	343/1241 (27.6%)	0.375
Anti-centromere positive, n/N (%)	18/42 (42.9%)	472/1252 (37.7%)	0.498
RNA Polymerase III positive, n/N (%)	5/40 (12.5%)	99/1186 (8.3%)	0.354
Diffuse cutaneous SSc, yes/ total (%)	6/29 (20.7%)	334/1089 (30.7%)	0.249
Digital ulcers, yes/ total (%)	4/9 (44.4%)	252/630 (40.0%)	0.101
mRSS	**2.0 (0.0; 7.0)**	**5.0 (1.2; 11.0)**	**0.001**
Pulmonary hypertension, yes/ total (%)	6/26 (23.1%)	118/850 (13.9%)	0.185
Lung fibrosis, yes/ total (%)	11/26 (42.3%)	427/897 (52.4%)	0.594
DLCO, % predicted	73.0 (44.7; 84.0)	69.5 (55.0; 83.0)	0.756
Upper gastrointestinal tract symptoms, yes/ total (%)	**17/40 (42.5%)**	**592/930 (63.7%)**	**0.007**
Lower gastrointestinal tract symptoms, yes/ total (%)	**5/40 (12.5%)**	**360/937 (38.4%)**	**0.001**
Renal crisis, yes/ total (%)	1/42 (2.4%)	34/1237 (2.7%)	0.886
Joint synovitis, yes/ total (%)	1/31 (2.3%)	138/914 (15.1%)	0.066

Data are presented as median (interquartile range) for the continuous variables and as number (percent) for the nominal ones. n = number of patients with positive results for the antibodies tested. N = total number of patients tested for the respective antibody. Significant p-values ($p < 0.05$) are marked in bold.

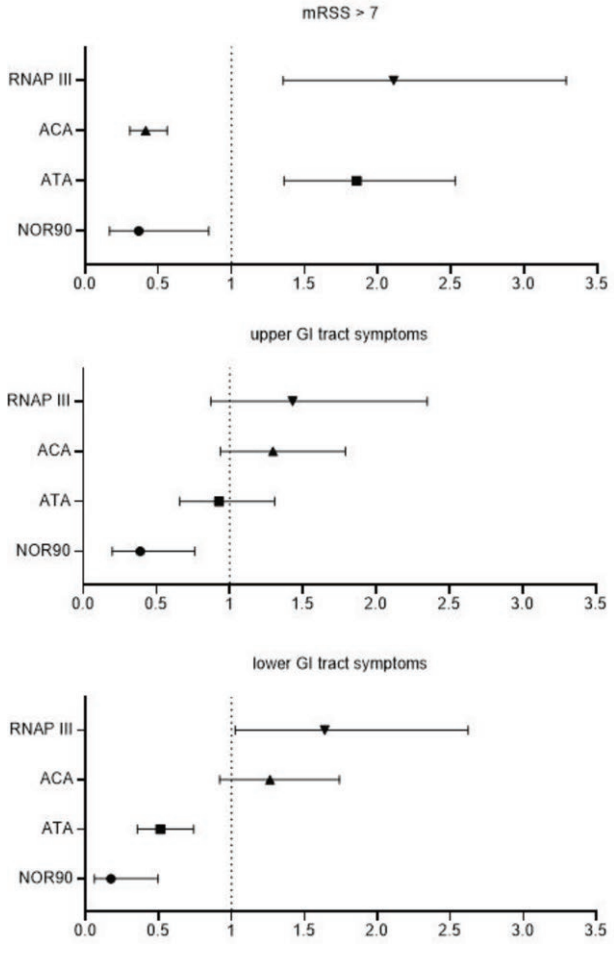


Figure 1. Association of NOR90 and SSc-criteria antibodies (ATA; ACA; RNAP III) with the mRSS and gastrointestinal (GI) manifestations.

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POS1256

MACROVASCULAR INVOLVEMENT IN SYSTEMIC SCLEROSIS AND ASSOCIATIONS WITH PULMONAL ARTERIAL HYPERTENSION: CAN AORTIC STIFFNESS AND CAROTID SONOGRAPHY PLAY A PREDICTIVE ROLE?

Keywords: Biomarkers, Cardiovascular disease, Systemic sclerosis

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Background: The vast majority of studies regarding vascular involvement in the context of systemic sclerosis (SSc), focus on microangiopatic manifestations, such as digital ulcers, capillaroscopic abnormalities and pulmonary arterial hypertension (PAH). On the other hand, SSc-associated macroangiopathy has not been sufficiently examined, even though a high cardiovascular (CV) and cerebrovascular (CVB) risk have been demonstrated [1,2]. Stiffness of the aortic vasculature and carotid sonography are well established markers of CV and CVB risk and their application has been shown to improve risk stratification in the general population [3].

Objectives: Thus, aim of this three-center prospective study was to investigate the presence of high aortic stiffness, subclinical carotid artery arteriosclerosis (SCAA) and carotid rigidity in a large SSc cohort and to examine their associations with clinical, laboratory and patient associated characteristics.

Methods: Carotid-femoral pulse wave velocity (cfPWV; gold standard of aortic stiffness), was examined in patients with SSc (ACR/EULAR classification) and healthy controls. Moreover, B-mode and Doppler sonography examinations of the common carotid arteries (CCA) were performed to assess plaque presence and/or possible abnormalities of carotid intima media thickness (cIMT), as well as resistance- and pulsatility-indices (RI, PI). Differences of these markers between patients and controls were statistically evaluated and subsequently controlled for the effects of possible confounding factors. Moreover, associations of the included CV and CVB surrogate parameters with clinical, laboratory and traditional CV risk factors were evaluated.

Results: *150* SSc-patients [84%♀, age 56.5 (50–65.3, IQR)] and *80* control subjects [86.3%♀, age 50.5 (35.2–57.8, IQR)] were recruited. cfPWV-values were statistically significantly higher in the patient group, compared to controls [8 m/s (6.86–9.44, IQR) vs. 6.85m/s (5.93–7.7, IQR); $p<0.001$], even after adjustment for the effect of confounding factors ($p_{adj}<0.001$). Similarly, cIMT [0.9 mm (0.65–1,

IQR) vs. 0.83 mm (0.65–0.89); p=0.001] and CCA-RI [0.76 (0.7–0.81, IQR) vs. 0.72 (0.68–0.76, IQR); p=0.02] were found to be significantly higher in the patient group. Interestingly, cfPWV was significantly higher in patients with PAH (p=0.029) and correlated moderately/poorly with erythrocyte sedimentation rate (rho=0.254; p=0.004). Moreover, cfPWV and cIMT associated among SSc-Patients significantly with several traditional CV risk factors, such as arterial pressure (p<0.001; cIMT and cfPWV) and type II diabetes (rho=0.193; p=0.018) (cfPWV).

Conclusion: This is one of the largest CV surrogate marker studies in the field of SSc and the first report of a potential diagnostic role of cfPWV in the PAH screening of SSc-patients. We were moreover able to show that patients with SSc had significantly higher aortic stiffness and more pronounced carotid atherosclerosis and resistance compared to healthy controls and thus could be under higher CV/CVB risk. In summary, cfPWV and carotid sonography may prove to be useful tools for the early identification of SSc patients under high risk for CV-events and PAH.

Table 1. Descriptive characteristics by groups (selection)

	SSc-patients *(n=150)*	Controls *(n=80)*	Significance *(p)*
Gender *(f)* %	84	86.3	0.652
Age *(y)*	56.5 (50-65.3, IQR)	50.5 (35.2-57.8, IQR)	**<0.001***
Smoking %	15.3	17.5	0.801
Hypertension %	56.7	18.8	**<0.001***
Cholesterol *(mg/dl)*	198 (170-221, IQR)	208.2 (178-239, IQR)	**0.041****
BMI *(kg/m^2)*	25.5 (22.8-28.9,IQR)	23,9 (21.3-27.2, IQR)	**0.018****
cfPWV *(m/s)*	8 (6.86-9.44, IQR)	6,85 (5.93-7.7, IQR)	**<0.001***
cIMT *(mm)*	0,9 (0.65-1, IQR)	0.83 (0.65-0.89, IQR)	**<0.001***
CCA-PI	1.7 (1.43-2.09, IQR)	1.56 (1.28-1.81, IQR)	0.080
CCA-RI	0.76 (0.7-0.81, IQR)	0.72 (0.68-0.76, IQR)	**0.020****

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POS1257 CCL24 SERUM CONCENTRATION PREDICTS BOTH VASCULAR AND FIBROTIC COMPLICATIONS IN SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Clinical trials, Cytokines and chemokines

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Background: CCL24 is a novel target that was found to play a dual role in advancing pro-inflammatory and pro-fibrotic processes in systemic sclerosis (SSc). Previous studies reported that skin and serum CCL24 levels are elevated in SSc and that blocking of CCL24 was effective in preventing and attenuating experimental-induced fibrosis in murine models as well as interfering with endothelial cell activation.

Objectives: Here we tested the concentration of CCL24 in an observational cohort of patients with SSc and available clinical follow-up to determine its clinical value in predicting fibrotic and vascular complications of the disease.

Methods: Consecutive patients from a single-centre observational cohort were enrolled in this analysis. Clinical data were collected according to the EUSTAR minimal essential data set. Serum Concentration of CCL24 was measured by Luminex assay (Myriad RBM) and defined as "High" for patients over the upper quartile of the Healthy control population (110 ng/ml). Interstitial Lung Disease (ILD) was defined by at least 10% parenchymal involvement at a High-Resolution CT scan of the chest while Digital Ulcer (DU) disease by the presence of current or history of DU in the previous 6 months. Progressive Fibrotic ILD was defined as previously described, according to Erice's criteria within 24 months. Clinical features were compared between CCL24 High vs Low by Chi-Square and T-student tests. R software was employed for statistical analysis.

Results: One-hundred-eighty-one SSc patients (13% males) fulfilling 2013 ACR/EULAR classification criteria were enrolled in this study. Median (IQR) disease duration was 4 (IQR 2-10) years. Thirty-seven (27%) had diffuse cutaneous SSc, 60 (32%) had ILD, and 90 (48%) had DU disease. Fifty-two patients (26%) were CCL24 High. These patients had a higher prevalence of DU (60%, p=0.042), a higher median (IQR) mRSS [4(2-7) vs 2(0-5), p=0.036) and showed a higher prevalence of ILD (42% vs 28%, p=0.055); this was more significant among patients with limited cutaneous SSc (7% vs 12%, p=0.037). Most importantly, among patients with PF-ILD (19/43 with available 24-month follow-up) 44% had significantly higher CCL24 serum concentration at baseline, compared to stable patients 1150 (817-1593) vs 725 (460-955); p=0.017. Consistent with these findings, in patients with ILD, having high CCL24 gave double the chances of progressing within 24 months (66% vs 32% of CCL24 Low; p=0.03).

Conclusion: We show here that within the context of an observational cohort of unselected patients, CCL24 serum concentration is associated with the presence of DU as well as worse skin and lung fibrotic involvement, suggesting that this molecule may be involved in both vascular and fibrotic manifestations of SSc. These results informed the rationale for a target-enriched basket randomized controlled trial to test the biological and clinical effect of CCL24 inhibition in SSc across cutaneous disease subsets.

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POS1258 RESULTS FROM A NOMINAL GROUP TECHNIQUE EXERCISE FOR THE CREATION OF A COMBINED RESPONSE INDEX FOR LIMITED CUTANEOUS SYSTEMIC SCLEROSIS: THE CRISTAL PROJECT

Keywords: Systemic sclerosis, Randomized control trial, Outcome measures

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Background: The lack of RCTs in limited cutaneous systemic sclerosis (lcSSc) is due, in part, to a paucity of relevant outcome measures to effectively evaluate this subset. This international project, supported by the World Scleroderma Foundation (WSF), Scleroderma &. Raynaud's UK (SRUK), the Scleroderma Clinical Trial Consortium (SCTC), and the US National Scleroderma Foundation, aims to create a combined response index for lcSSc for use in clinical trials; the CRISTAL index. The most bothersome symptoms from the patients' perspective were identified through lcSSc patient-centered focus groups [1] and already-identified domains and outcomes were identified through a scoping literature review [2].

Objectives: This phase of the overall CRISTAL project aimed to select candidate items for inclusion in a planned longitudinal prospective observational study assessing the psychometric properties of the selected items. We aimed to enrich the list of candidate outcomes from domains identified by the focus groups and scoping review: i) SSc-specific domains (gastro-intestinal involvement,

Raynaud's/microcirculation, musculoskeletal, digital ulcers, pulmonary involvement, cardiac involvement, hand functioning, calcinosis, skin involvement, Sicca syndrome; and ii) general domains (fatigue, pain, cognition, sleep disorder).

Methods: A two-round international online Delphi exercise was conducted to enrich the list of instruments. Experts in lcSSc were asked to suggest additional items/outcome measures for the domains. Candidate clinician-reported outcomes (ClinROs) and performance outcomes (PerfOs) were selected during a two-day meeting utilizing a nominal group technique (NGT) comprising 3 patient research partners and 8 international experts. Patient research partners received specific-training prior to the NGT meeting to become familiar with the domains, outcomes, and research processes.

Results: 100 experts were invited to the Delphi exercise and 71 provided answers for at least one round. Participants who provided answers in round 1 were invited to a second Delphi exercise, rating each item on scales (range: 1-9) for feasibility, face validity, content validity, and overall appropriateness for the CRISTAL Index. 59/71 participants provided answers to at least one survey. Items endorsed by more than 50% of the experts were included for discussion at the 2 day-NGT discussion. During the NGT meeting, for each lcSSc specific domain, the list of items selected during Delphi and their characteristics were presented and each voting member was asked to discuss the relevance of these items and to propose new items if important ones were considered missing. Voting members then ranked items from "most appropriate for the CRISTAL index" to "less appropriate". At the end of each ranking, voting members were asked if they agreed with the ranking; 80% agreement was required to move to the next domain. Across the 10 lcSSc specific domains discussed, a total of 19 items (17 ClinROs and 2 PerfOs) were identified and retained as draft items for testing in the planned observational longitudinal cohort study (Table 1).

Conclusion: These initial results from the CRISTAL initiative are essential first steps towards the development of a composite index for lcSSc. The next steps will include selection of patient-reported outcomes (PROs) from the PROMIS item bank, existing data in the reported literature, and cognitive debriefing with patients, followed by a prospective cohort study to assess and validate the draft CRISTAL index.

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POS1259 SYSTEMIC SCLEROSIS AND COVID-19 VACCINE-ASSOCIATED DELAYED ADVERSE EVENTS: INSIGHTS FROM THE COVAD-2 STUDY

Keywords: Vaccination/Immunization, Systemic sclerosis, Safety

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Background: We have previously reported short term safety of the COVID-19 vaccination in patients with Systemic sclerosis (SSc) but delayed adverse events (ADEs) (occurring >7 days post-vaccination) are poorly characterized in this rare yet vulnerable disease group.

Objectives: We analyzed delayed COVID-19 vaccine-related ADEs among patients with SSc, other systemic autoimmune and inflammatory disorders (SAIDs) and healthy controls (HC) using data from the ongoing 2nd global COVID-19 Vaccination in Autoimmune Diseases (COVAD-2) study [1].

Methods: The COVAD-2 study was a cross-sectional, patient self-reporting e-survey utilizing an extensively validated, pilot tested questionnaire, translated into 19 languages, circulated by a group of 157 physicians across 106 countries from February to June 2022.

We captured data on demographics, SSc/SAID disease characteristics (including skin subset, treatment history and self-reported disease activity), autoimmune and non-autoimmune comorbidities, COVID-19 infection history and course, and vaccination details including delayed ADEs as defined by the CDC.

Delayed ADEs were categorized into local injection site pain/soreness; minor and major systemic ADEs, and hospitalizations. We descriptively analyzed the risk factors for overall and specific ADEs in SSc and SAIDs, and further triangulated clinically significant variables in binominal logistic regression analysis with adjustment for age, gender, ethnicity, comorbidity, and immunosuppressive therapy to analyze the survey responses.

Results: From among 17 612 respondents, 10 041 patients (median age 51 (18-58) years, 73.4% females, 44.9% Caucasians) vaccinated against COVID-19 at least once (excluding incomplete responses and trial participants) were included for analysis. Of these, 2.6 % (n=258) had SSc, 63.7% other SAIDs, and 33.7% were HCs. BNT162b2 Pfizer (69.4%) was the most administered vaccine, followed by MRNA-1273 Moderna (32.25%) and ChadOx1 nCOV-19 Oxford/AstraZeneca (12.4%) vaccines. Among the patients with SSc, 18.9% reported minor

while 8.5% experienced major delayed ADEs, and 4.6% reported hospitalization. These values were comparable to those of the ADEs reported in other SAIDs and HCs. Patients with SSc reported higher frequency of difficulty in breathing than HCs [OR=2.3 (1.0-5.1), p=0.042]. Individuals receiving Oxford/AstraZeneca reported more minor ADEs [OR=2.5 (1.0-6.0), p=0.045]; whereas patients receiving Moderna were less likely to develop myalgia and body ache [OR=0.1 (0.02-1.0), p=0.047 and OR=0.2 (0.05-1.0), p=0.044 respectively]. Patients with diffuse cutaneous SSc experienced minor ADEs and specifically fatigue more frequently [OR=2.1 (1.1-4.4), p=0.036, and OR=3.9 (1.3-11.7), p=0.015] than those with limited cutaneous SSc. Self-reported active disease pre-vaccination did not confer any increased risk of vaccine ADEs in the adjusted analysis. Unlike our previous observations in myositis, autoimmune and non-autoimmune comorbidities did not affect the risk of delayed ADEs in SSc. SSc patients with concomitant myositis reported myalgia [OR=3.4 (1.1-10.7), p=0.035] more frequently, while those with thyroid disorders were more prone to report a higher frequency of joint pain [OR=5.5 (1.5-20.2), p=0.009] and dizziness [OR=5.9 (1.3-27.6), p=0.024] than patients with SSc alone. Patients with SSc-interstitial lung disease did not report increased frequency of ADEs.

Conclusion: A diagnosis of SSc did not confer a higher risk of delayed post COVID-19 vaccine-related ADEs than other SAIDs and HCs. Diffuse cutaneous phenotype and certain co-existing autoimmune conditions including myositis and thyroid disease can increase the risk of minor ADEs. These patients may benefit from pre-vaccination counselling, close monitoring, and early initiation of appropriate care in the post COVID-19 vaccination period.

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POS1260 SYSTEMATIC LITERATURE REVIEW FOR THE 2023 UPDATE OF EULAR RECOMMENDATIONS FOR THE TREATMENT OF SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Systematic review, Targeted synthetic drugs

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Background: EULAR recommendations for the treatment of Systemic Sclerosis (SSc) were updated in 2017, informed by a systematic literature review (SLR) completed in 2014. Given the high number of SSc-related clinical manifestations and therapy-related publications in the last decade, a new SLR providing the most up-to-date literature to underpin contemporary recommendations for the management of SSc was required.

Objectives: The aim of this SLR was to provide a critical review of the updated evidence to address the questions prioritized by an international task force.

Methods: 67 clinical questions addressing 30 interventions were explored. Three categories of questions were defined: Type I Questions that were unchanged as compared to the previous set of recommendations; Type II questions exploring the efficacy/effectiveness of an intervention already mentioned in the previous recommendations but with new outcome(s); Type III questions including interventions not mentioned in the previous recommendations. Each interventions was considered independently, with 30 SLRs for 30 interventions (including several outcomes/clinical questions), and 1 dedicated SLR (with several interventions) for calcinosis (31 searches in total). Search strategies were defined with a librarian and a methodologist. Questions were divided among 5 reviewers and three databases were screened (Embase, pubmed and Cochrane Library). Full texts eligible for data extraction were selected according to the PICOS strategy. Data extraction was performed using a pre-defined template. Quality appraisal was performed using the JADAD scale. 10% of all articles were assessed by a second reviewer ensuring consistency and reliability of data extraction. The level of evidence and grade of recommendations were defined according to the CEBM criteria.

Results: For the first round of SLR, search periods were defined as follows in all three databases: new abstracts released from October 1st 2014 to March 31st 2022 for type I & type II questions and from database inception to march 31st 2022 for type III questions. 14490 abstracts were retrieved from the databases on march 31st 2022 and 18 abstracts were selected manually from march 31st 2022 to October 11th 2022 (date of the nominal group technique (NGT) exercise). 483 new full-texts were evaluated and 172 new articles were included. 187 articles from the SLR for the 2017 recommendations were included as well. For each questions and sub-questions, the reviewers provided a summary of the current knowledge, specifying the level of evidence (1 to 5) and the level of recommendations (A to D). Each summary was reviewed by task force leaders and presented during the NGT meeting to inform discussion and voting on the new recommendations. The majority of the questions covered by this SLR explored new interventions that had not been explored in previous recommendations (40% of type III questions) or with new outcomes (26% of type II questions). New interventions included targeted therapies such as abatacept, JAK inhibitors or nintedanib, and updated questions incorporated the results from key game-changing RCTs including trials on tocilizumab, mycophenolate or rituximab in SSc-interstitial lung disease.

Conclusion: This SLR provides the highest level of evidence to address questions prioritized in the 2023 update of EULAR recommendations for the treatment of SSc, providing an unprecedented comprehensive overview of recent knowledge on SSc treatments and participating in defining the future research agenda for SSc management.

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POS1261

DIAGNOSTIC ACCURACY OF LUNG ULTRASOUND FOR DETECTING INTERSTITIAL LUNG DISEASE AMONG PATIENTS WITH SYSTEMIC SCLEROSIS: A COMPARATIVE STUDY OF TWO SCANNING PROTOCOLS

Keywords: Ultrasound, Lungs, Systemic sclerosis

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Background: Lung ultrasound (LUS) has proven useful to detect interstitial lung disease (ILD) among patients with systemic sclerosis (SSc) when compared to high-resolution computerized tomography (HRCT) as the gold standard; owing to its accessibility and innocuity it confers several advantages over the latter, which turns it into a potential valuable tool in clinical practice. Nevertheless, a key drawback is the lack of a standardized methodology to perform LUS.

Objectives: To evaluate diagnostic accuracy of LUS for ILD by comparing the systematic evaluation of 14 intercostal spaces (ICS) against 12 postero-basal ICS.

Methods: Patients with SSc were included according to the 2013 ACR/EULAR classification criteria of the Rheumatology clinic of the National Institute of Medical Sciences and Nutrition, reference hospital in Mexico City. Demographic, clinical, serological, and imaging variables were collected, followed by LUS assessment with the simultaneous scanning of 14 predetermined ICS and 12 postero-basal ICS. "B" lines (BL) and pleural abnormalities (PA) were documented for each ICS. HRCT was performed with a maximum 3 month-interval from the time of recruitment (before or after). Descriptive statistics for categorical and continuous variables was used. A bivariate analysis was undertaken to discriminate factors associated with the presence of ILD. A Pearson correlation test was carried out to compare findings between LUS and HRCT. Diagnostic accuracy was assessed through elaboration of ROC curves.

Results: We included 73 patients, with a median age of 54.5±15.1 years and 96.1% were women. Prevalence of ILD was 43.6%. Relevant baseline characteristics are shown in Table 1. Acknowledged risk factors for ILD were pulmonary hypertension (OR 6.27, CI 95% 1.75-22.4, p=0.005) and diffuse SSc (OR 6.17, CI 95% 1.92-19.76, p=0.002). The AUC were 0.87 (95% CI, 0.78-0.96), 0.94 (95% CI, 0.88-1.00) and 0.84 (95% CI, 0.74-0.94) for the evaluation of the number of BL in 14 ICS, in 12 ICS and the number of ICS with PA (22 EIC), respectively. ROC curves are represented in Image 1.

Conclusion: Our study confirms the robustness of LUS as a tool for the detection of ILD through the quantification of BL and PA when using any of two different scanning protocols (14 and 12 ICS). However, more studies are required to elucidate the added value of pleural abnormalities identification for the diagnosis of ILD by LUS.

Table 1. Characteristics of patients according to presence or absence of ILD

Variable	w/o ILD (*n*= 40)	ILD (*n*= 31)	*p*
Age	50.3 ± 13.05	56 ± 12.2	0.66
Gender (female)	40 (56.3)	28 (39.4)	0.079
Body Mass Index	23.3 ± 3.4	23.8 ± 4.7	0.601
SSc variant (n= 71):	33 (46.5)	14 (19.7)	**0.003**
Limited	7 (9.9)	17 (23.9)	
Diffuse			
Anti-Scl-70 (n= 64)	22 (34.3)	23 (35.9)	0.179
Anti-centromere (n= 68)	30 (44.1)	23 (33.8)	1.000
Time from RP (years) (n= 64)	12 (7-20)	12 (7-17)	0.849
Time from first non-RP symptom (years) (n= 67)	11 (6-20)	11 (6.3-13.7)	0.620
mRSS (n= 69)	3 (1-8)	9 (2-12.5)	**0.015**
Pulmonary Hypertension (n= 71)	5 (7.0)	14 (19.7)	**0.003**
Medsger global score (n= 69)	2 (1-2)	2 (1-3)	**0.048**
Warrick score	13.5 (9-20.8)	4 (0-9.5)	**<0.001**
Kazerooni score	1.1 (1-1.5)	0.5 (0-0.9)	**<0.001**
	1.2 (0.8-1.6)	0.3 (0-0.6)	**<0.001**
Immunosuppresants, no. (n= 71)	1 (0-1)	1 (0-2)	0.177
Methotrexate	6 (8.4)	6 (8.4)	0.753
Mycophenolate mophetil	7 (9.8)	13 (18.3)	**0.033**
Azathioprine	4 (5.6)	2 (2.8)	0.690
Prednisone	5 (7.0)	6 (8.4)	0.516

Continuous variables: Mean ± DE, Median (25-75), Categorical variables: Frequency (%)ILD: Interstitial Lung Disease, SSc: Systemic Sclerosis, RP: Raynaud's Phenomenon, mRSS: modified Rodnan Skin Score

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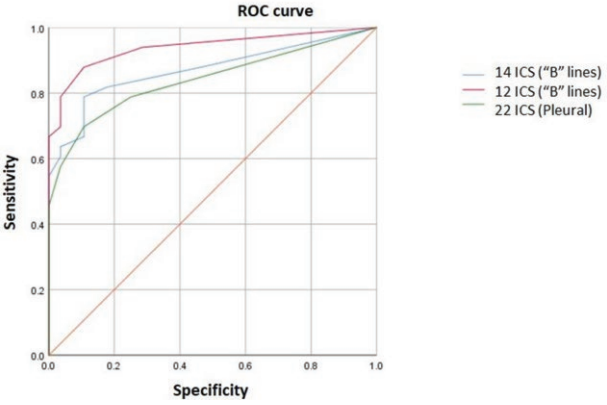


Image 1. ROC curves for the diagnosis of ILD by LUS

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POS1262

ULTRASONOGRPHIC EVALUATION OF SALIVARY GLANDS IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Imaging, Ultrasound

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Background: Although dry mouth is a common symptom in systemic sclerosis (SSc), there is a lack of studies evaluating the salivary glands in this heterogenous systemic disease.

Objectives: To study the ultrasonographic changes of salivary glands in patients with systemic sclerosis and to correlate these changes with disease activity markers, clinical data and autoantibodies.

Methods: Forty-seven SSc patients and forty-three healthy age and sex matched controls were studied. Duration of illness, sicca symptoms, Schirmer's test, joint symptoms, internal organ evaluation including interstial lung disease, pulmonary artery hypertension, Raynaud's phenomenon, digital pitting scars and the modified Rodnan total skin score. Laboratory investigations included acute phase reactants, antinuclear antibody, Anti-Ro-60/SSA, anti-La/SSB, anti-Topoisomerase 1 (anti–topo I) and anticentromere (ACA). Salivary glands were evaluated by ultrasound according to the most recent guidelines.

Results: The mean age of patients was 39.6±10.8 years with a mean disease duration of 5.1±4.3 years. Sicca symptoms were obvious among patients with SSc with significant difference compared to controls. pathological changes ≥2 was seen in 31 (66%) of the involved patients. The anti-topo 1 was seen to be significantly correlated with Doppler signals in the salivary glands (p=0.049) while the ACA and anti Ro were not found to be significant with any of the glandular pathology. Anti La was significantly correlated with pathological changes of the salivary glands (p=0.023). also, a significant correlation of anti-La and pathological changes in the submandibular and total gland score (p=0.03 and 0.045 respectively).

Conclusion: Ultrasonographic changes of the salivary glands are quite frequent in patients with SSc. The abnormalities are found correlating with the disease related autoantibodies especially anti La and anti topoisomerase antibodies.

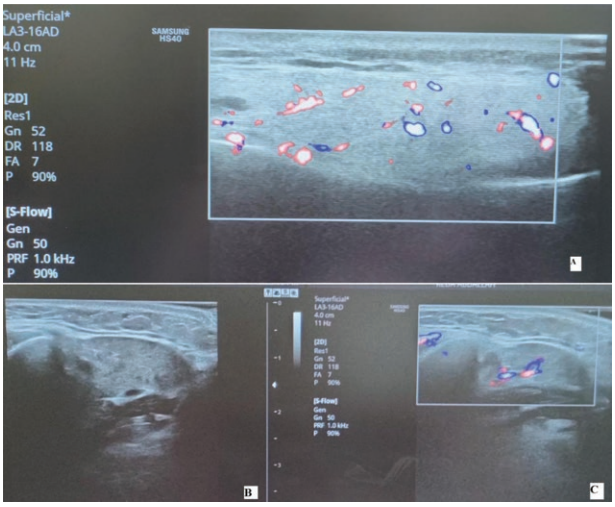


Figure 1. Gray scale and power Doppler abnormailites in a patient with diffuse systemic sclersosis (A; parotid gland longitudenal scan withPD, B and C; submandibular gland in GS and PD of the same patient.)

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POS1263

SMOKING INFLUENCE ON AUTOANTIBODY PROFILE AND DISEASE PROGRESSION IN SYSTEMIC SCLEROSIS: AN EUSTAR DATABASE ANALYSIS

Keywords: Prognostic factors, Registries, Systemic sclerosis

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Background: The available evidence suggests that there is no correlation between smoking and disease-specific cutaneous or pulmonary manifestations in systemic sclerosis (SSc) [1]. However, three studies showed that never-smokers had a higher prevalence of anti-topoisomerase I (ATA) positivity than ever-smokers [1-3], which might be important for risk stratification.
Objectives: This study has two objectives: (1) to determine whether patients exposed to cigarette smoking present a distinct autoantibody profile; (2) to determine whether smoking confers different risk of disease progression in men and women or in patients with different autoantibodies.
Methods: Adult patients registered in the EUSTAR database fulfilling the SSc classification criteria, whose information about smoking habit was available and consistent during follow-up, were included. Patients were categorised as "ever-smokers" or "never-smokers" at the first visit. Differences in autoantibody profile were analysed using Chi-square test. Kaplan-Meier curves and log-rank tests were performed to compare outcomes between ever-smokers and never-smokers for up to 20 years of follow-up. The association between smoking habit and progression in disease domains was estimated using Cox proportional hazards models adjusted for age, antibodies (anti-centromere – ACA, and ATA), sex and disease duration. Additionally, cox models including the interaction between smoking status and sex, and between smoking status and autoantibody positivity, were built to assess effect modification. The risk of death, newly diagnosed interstitial lung disease (ILD) and cardiac involvement were evauated. Furthermore, we investigated worsening of functional impairment in patients with ILD and progression of cutaneous involvement. The study protocol was reviewed and approved by the EUSTAR board (project number CP 126).
Results: At the time of data extraction (July 5, 2022), 12314 patients met the inclusion criteria. Of these, 84.4% were female and mean age was 55.5±13.8 years. ACA was positive in 38% of patients and ATA in 32%; 4271 individuals (35%) were ever-smokers. Among never-smokers, 35% of patients was ATA positive, compared to 27% among ever-smokers (p <0.001). When stratifying for sex, this difference was accounted for by female patients: 34% of never-smoking females was ATA positive compared to 21% of ever-smoking women (p <0.001). In men, no statistically significant difference in ATA positivity was observed. Survival was significantly lower in ever-smokers than in never-smokers (46% vs 55%; log-rank test p=0.0032; Figure 1). In multivariable Cox regression analysis, ever-smoking was associated with mortality (HR 1.24; 95% CI 1.07 to 1.43). Evidence for an interaction between smoking status and sex was found (HR of interaction term 1.44, 95% CI 1.03 to 2.03). Cox proportional hazards models did not show an increased risk of developing ILD (HR 1.03; 95% CI 0.92 to 1.16) or cardiac involvement (HR 1.10; 95% CI 0.99 to 1.21), neither of functional worsening in ILD (HR 1.01; 95% CI 0.93 to 1.10) or cutaneous progression (HR 1.11; 95% CI 0.97 to 1.26) for ever-smokers.
Conclusion: Our study in a large cohort of SSc patients from the EUSTAR registry confirms that ever-smoking is associated with lower prevalence of ATA positivity among female SSc patients. Our findings indicate that ever-smoking patients have a worse survival during follow-up, while no association between smoking and development of ILD, cardiac involvement or skin progression emerged.

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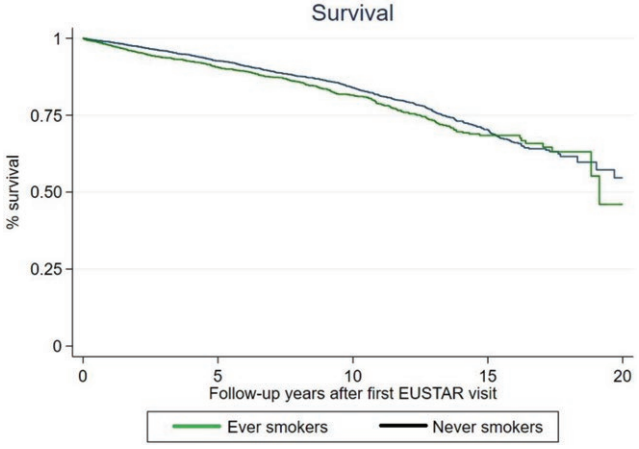


Figure 1. Kaplan-Meier curve according to smoking history in the EUSTAR cohort for survival

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POS1265

REAL-LIFE MULTICENTRIC NATIONAL OBSERVATIONAL STUDY OF THE USE OF NINTEDANIB IN SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

Keywords: Real-world evidence, Safety, Systemic sclerosis

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Background: Interstitial Lung Disease related to Systemic Sclerosis (ILD-SSc) is the first cause of mortality rate in this disease [1]. Significative functional decline in Forced vital capacity is one of the major pronostic factor in ILD-SSc and evaluation of the FCV is a key part of the follow-up of patient [2]. Nintedanib is a tyrosine kinase inhibitor that has been shown to be effective in ILD-SSc by significantly slowing decline in CVF [3]. To this day, no real-life data are available in ILD-SSc.

Objectives: Evaluation of efficacity and tolerance profile of Nintedanib in ILD-SSc patients in real life in France.

Methods: Multicentric data collection on call for observations through the GFRS, SNFMI and Orphalung. The data were obtained in an ambispective way with collection of epidemiological, clinical and paraclinical parameters including in particular CT scan, functional and cardiac data.

Results: 105 patients were included in 11 centers. 76 (74%) were female, mean age of patients was 58±11 years. 51 (48%) had diffuse SSc, 58 (60%) had anti-topoisomerase 1 antibodies. Median time from 1st non-Raynaud's sign to introduction of nintedanib was 6 years (1; 41). ILD-SSc was extensive (>20% of the lung) in 60% of cases, and CT pattern was PINS in 85% of cases. Mean FVC at nintedanib introduction was 1.96±0.47L (64±15%). Mean DLCO was 36 ±11%. Data were available at 6 months after introduction of nintedanib in 60 patients. Seven patients (12%) had discontinued treatment because of digestive intolerance (diarrhea in 5 cases, 1 significant weight loss) and including 1 death (cardiac decompensation). In the 53 remaining patients, the mean loss of FVC was 10 ± 120 mL at 6 months of nintedanib treatment versus 165 ± 225 mL in the year before the introduction of treatment. Two patients had severe infections (1 SARS CoV2 infection; 1 Clostridium difficile infection). 22 (40%) patients experienced adverse events, including 17 diarrhea, 6 abdominal pain, 4 nausea or vomiting, and 7 weight loss >5 kg.

Conclusion: ILD-SSc population in this real-life study of nintedanib has similar epidemiological characteristics to SENSCIS [3]. However, the FVC and DLCO of these patients are lower than those of the SENSCIS population (1.96± 0.47 L vs 2.46± 0.74 L and 36±11% vs 53±15%, respectively). At 6 months, there was a smaller decline in FVC in patients on nintedanib than the decline in the year before starting treatment. The current results at 6 months show a tolerance profile similar to that observed in idiopathic pulmonary fibrosis. These initial results in real-life study in a more severe ILD-SSc population than the pivotal trial suggest that nintedanib limits functional decline in FVC at 6 months. A significant number of side effects were observed, particularly related to the digestive tract, which reinforces need for better management of these side effects. Further data from this ongoing study will provide additional data at 6, 12 and 24 months.

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POS1266

A PHASE IA, RANDOMIZED STUDY TO EVALUATE SAFETY, TOLERABILITY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF SINGLE ASCENDING DOSES OF RO7303509, AN ANTI-TGFB3 MONOCLONAL ANTIBODY, IN HEALTHY VOLUNTEERS

Keywords: Systemic sclerosis, Randomized control trial, Biomarkers

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Background: Transforming growth factor beta (TGFβ) cytokines (TGFβ1, TGFβ2, and TGFβ3) play critical roles in tissue fibrosis.[1] However, treating fibrotic diseases with systemic pan-TGFβ inhibitors has demonstrated unacceptable toxicities.[2,3] In human lung and liver fibrotic tissue, and in the skin of patients with systemic sclerosis, elevated *TGFB3* gene expression suggests its use as a more specific therapeutic target.[2,4] RO7303509, a high-affinity, TGFβ3-specific, humanized immunoglobulin G1 (IgG1) monoclonal antibody, is being developed as a potential anti-fibrotic therapy.

Objectives: To evaluate RO7303509 safety, tolerability, pharmacokinetics, and pharmacodynamics.

Methods: This phase 1a, randomized, double-blind trial (ISRCTN13175485) in healthy adult volunteers (HVs) consisted of 6 cohorts that evaluated single doses of placebo or RO7303509, administered intravenously (IV; 50 mg, 150 mg, 240 mg) or subcutaneously (SC; 240 mg, 675 mg, 1200 mg). The follow-up period was 12 weeks. Throughout the study, we monitored frequency and severity of adverse events (AEs) and RO7303509 plasma concentrations. We also measured TGFβ pathway biomarkers, including serum periostin and cartilage oligomeric matrix protein (COMP), by immunoassay.

Results: The study enrolled 49 HVs, 18–73 years old, with a median baseline weight of 79 kg. Twenty-seven subjects (55%) were male; 8 (16%) were Black or African American, 1 (2%) was Asian, 1 (2%) was multiracial, and 39 (80%) were White; 1 (2%) was Hispanic or Latino. Ten (28%) RO7303509-treated subjects reported 24 AEs, and 6 (31%) placebo-treated subjects reported 6 AEs. All AEs were Grade 1 except for one Grade 2 AE of hyperamylasemia (unrelated) in the 1200-mg SC cohort. The most frequent AEs related to study drug were injection site reactions (1200 mg SC: 4 RO7303509, 1 placebo) and infusion-related reactions (240 mg IV: 1 RO7303509, 2 placebo). Median times to maximum plasma concentration (T_{max}) of RO7303509 after single IV and SC doses were 1–2 hours and 5–7 days, respectively. Geometric mean plasma half-lives ($t_{1/2}$) for IV and SC dosing were ~23 days. Maximum plasma concentrations (C_{max}) and area under the curve from time 0 to infinity ($AUC_{0\text{-}inf}$) values for RO7303509 appeared to increase proportionally across all doses tested after adjusting for the observed subcutaneous bioavailability of 73%. No subjects tested positive for anti-drug antibodies (ADAs) at baseline; 1 subject (2.8%; 50 mg IV) tested positive for ADAs at a single timepoint (Day 15). No clear pharmacodynamic effects were observed for the biomarkers periostin or COMP upon TGFβ3 inhibition.

Conclusion: RO7303509 was well tolerated at single IV and SC doses up to 1200 mg without any dose-limiting toxicities, Grade ≥3 AEs, serious AEs, deaths, or clinically significant vitals/ ECG changes. In addition to a favorable safety profile, the dose-proportional increase in RO7303509 exposure across the dose range after single dose administration supports further development using repeat-dosing regimens. The half-life supports SC administration every four weeks. The lack of an effect on TGFβ pathway biomarkers likely indicates that TGFβ3 is inactive during homeostasis, which suggests that targeting this pathway may have a favorable safety profile. These data support the further development of RO7303509 for the treatment of fibrotic diseases.

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POS1267 IGURATIMOD AS AN ALTERNATIVE THERAPY FOR SYSTEMIC SCLEROSIS AND PREVENTION OF ISCHEMIC DIGITAL ULCER OCCURRENCE

Keywords: Disease-modifying drugs (DMARDs), Systemic sclerosis, Descriptive studies

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Background: Systemic sclerosis (SSc) is not only one of the autoimmune diseases with the highest mortality but rises a severe disease burden through some not directly lethal but suffering complications such as digital ulcers (DU) [1].Iguratimod(IGU) is typically thought of as an anti-inflammatory and immunoregulatory drug [2]. On top of anti-inflammation, IGU has shown potential efficacy on fibrotic complications with autoimmune diseases[3].
Objectives: To assess the effectiveness of IGU as an alternative treatment for SSc, especially in the prevention of ischemic DU.

Table 1 Baseline Characteristics of the Study Participants with Digital Ulcers.

Characteristics	With IGU (N=11)	Without IGU (N=20)	P value
Age of Onset(years), median (IQR)	36.0(31.0-53.0)	43.0(34.0-54.0)	0.457
Sex(%)	2(18.2)	6(30.0)	0.676
Male	9(81.8)	14(70.0)	
Female			
Time since RP onset (years), median(IQR)	9.0(3.0-12.0)	7.5(3.0-14.8)	0.740
Time since first non-RP manifestation (years), median (IQR)	9.0(2.0-11.0)	5.5(2.3-12.8)	0.634
SSc subtype(%)	9(81.8)	10(50.0)	0.133
Diffuse	2(18.2)	8(40.0)	
Limited	0	2(10.0)	
Sine scleroderma			
ESR(mm/h), median (IQR)	29.0(15.5-53.8)	27.0(13.5-47)	0.880
Autoantibodies(%)	6(60.0)	12(75.0)	0.332
Anti-Scl70 antibody positive	1(10.0)	2(12.5)	
ACA positive	3(30.0)	1(6.3)	
Anti-U1RNP positive	0	1(6.3)	
Anti-Th/To positive			
Smoke(>25 pack-years)(%)	0	4(20.0)	0.269
Previous DU(s)	4(36.4)	8(40.0)	1.0
Vasodilator use (at least one agent) (%)	11(100)	20(100)	0.452
PDE5i	6(54.5)	14(70.0)	0.423
ERA	5(45.5)	5(25.0)	1
CCB	4(36.4)	6(30.0)	0.716
Beraprost	5(45.5)	11(55.0)	
Pulmonary hypertension(%)	3(27.3)	6(30.0)	1
ILD(%)	9(81.8)	13(65.0)	0.429
DU new occurrence during follow-up(%)	8(72.7)	5(25.0)	**0.021**
never	3(27.3)	15(75.0)	
new occurrence			

Methods: We constructed two cohorts from the Renji SSc registry. In the first cohort, SSc patients receiving IGU were observed prospectively with effectiveness and safety. In the second cohort, we picked up all the DU patients with at least a 3-month follow-up to investigate the prevention of IGU on ischemic DU.
Results: 1) IGU was a plausible alternative treatment for SSc with acceptable tolerance. 91.3% (21/23) of the SSc patients were disease worsening-free during IGU treatment (median follow-up: 61 weeks). 2) We unexpectedly discovered that IGU was protective against ischemic DU. Although with a limited patient number, 72.7% (8/11) of IGU-treated patients had no new DU occurrence in a median follow-up of 39 weeks; further in the second DU cohort (Table1), the protection of IGU was still true for new DU occurrence (adjusted RR = 0.25, 95% CI, 0.05-0.94, adjusted OR = 0.07, 95% CI, 0.01-0.49)(Figure 1).
Conclusion: Our study indicates IGU as a possible alternative treatment for SSc. Beyond expectation, this study for the first time describes IGU as preventative against ischemic DU occurrence and merits further investigation.
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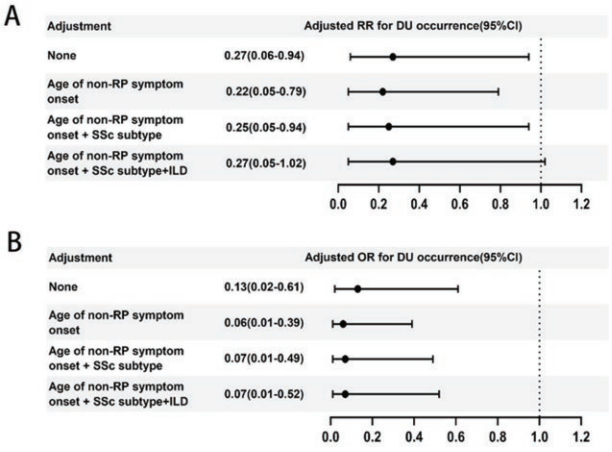


Figure 1. Forest plot displaying the association of the outcome (occurrence of ischemic DUs) with IGU treatment.

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POS1268 TYPE 2 (TH2) CYTOKINES AND SCLERODERMA INTERSTITIAL LUNG DISEASE (SSC-ILD)

Keywords: Systemic sclerosis, Cytokines and chemokines, Lungs

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by immune system dysregulation, endothelial dysfunction and fibrosis of skin and internal organs. Interstitial lung disease (ILD) is common in SSc and about 80% of patients will develop ILD during the disease course [1]. Although most patients have a stable or slowly progressive disease, showing a slow decline in lung function or a minimal increase in the extent of pulmonary fibrosis by high resolution computed tomography (HRCT), 25-30% of them will ultimately progress to respiratory failure or death [2]. Of the SSc-related deaths, 35% were attributed to ILD [3]. The underlying pathophysiologic mechanisms of SSc-ILD is still not completely understood [2]. The pathogenesis of SSc-ILD is initially characterized by an injury to alveolar epithelial and vascular endothelial cells which promotes the recruitment of inflammatory cells and the production of profibrotic mediators, in the attempt to repair the damage [4,5]. In this early inflammatory phase, profibrotic type 2 (Th2) cytokines, such as IL-4, IL-5, IL-13, play a key role [6,7].
Objectives: Aim of the study was to evaluate the Th2 cytokines serum levels in SSc-ILD.
Methods: Serum levels of IL-4, IL-5, IL-11, IL-13, IL-21, IL-31 and CXCL-13 were measured by Bio-Plex Multiplex Immunoassays in 60 SSc patients and 20 healthy controls (HC). Pulmonary function tests with diffusion lung capacity for carbon monoxide (DLco) and high resolution computed tomography (HRCT) were performed in SSc patients. ILD is defined as fibrotic changes (ground glass, reticular and honeycombing), assessed by Computer-Aided Lung Informatics for Pathology Evaluation and Ratings (CALIPER) software, affecting at least 10% of the lungs.
Results: Serum levels of Th2 cytokines were higher in SSc patients than HC. A linear correlation was observed between ground glass and IL-13 ($r=0.342$, $p<0.01$), IL-21 ($r=0.345$, $p<0.01$), IL-31 ($r=0.473$, $p<0.001$), IL-4 ($r=0.863$, $p<0.001$), IL-5 ($r=0.249$, $p<0.05$) and peripheral blood eosinophils ($r=0.463$, $p<0.001$). We found a negative correlation between DLco and IL-4 ($r=-0.511$, $p<0.001$) and peripheral blood eosinophils ($r=-0.446$, $p<0.001$). In the logistic regression analysis, IL-4 is associated with DLco≤ 60% of the predicted [OR 1.039 (CI 95%: 1.015-1.064), p<0.001], mRSS [OR 1.138 (CI 95%: 1.023-1.266), p<0.05] and IL-4 [OR 1.017 (CI 95%: 1-1.034), p<0.05] were associated with ILD.
Conclusion: Th2 cytokines might have a key role in early phase of ILD in SSc patients. Future large studies are needed to confirm these findings.

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POS1269

INVESTIGATING THE TRAJECTORY OF FUNCTIONAL DISABILITY IN SYSTEMIC SCLEROSIS: GROUP BASED TRAJECTORY MODELLING OF THE HEALTH ASSESSMENT QUESTIONNAIRE DISABILITY INDEX

Keywords: Patient reported outcomes, Systemic sclerosis

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Background: Up to 70% of people with systemic sclerosis (SSc) report impaired physical function[1,2], which can negatively impact quality of life[3]. The Health Assessment Questionnaire Disability Index (HAQ DI) is a self-administered measure of function, where higher scores (range 0-3) indicate worse function.
Objectives: To identify trajectories, clinical correlates and associations of functional disability in SSc.
Methods: Australian Scleroderma Cohort Study participants meeting ACR/EULAR criteria for SSc recruited within 5 years of SSc onset were included. Participants needed to have ≥2 HAQ DI scores available within 10 years of SSc onset. Group based trajectory modelling (GBTM) was used to identify the number and shape of HAQ DI score trajectories over 10 years. Between group comparisons were made using the chi-squared test for discrete variables and the two-sample t-test or Wilcoxon rank sum test for continuous variables. Generalised estimating equations were used to model longitudinal data involving repeated measures. Survival analyses were performed using Kaplan Meier and Cox proportional hazard modelling.
Results: 426 participants were included with incident SSc and ≥2 HAQ DI scores, with median time between HAQ DI scores of 1.1 (IQR 1.0-1.4) years. Median age at SSc onset was 53 years (IQR 44-61 years), 83% were female and 33% had dcSSc. We found two HAQ DI trajectory groups: low/stable disability (n=221, 52%), and high/increasing disability (n=205, 48%; Figure 1). Participants with high/increasing disability were older (p=0.01) and more likely to have dcSSc (p<0.01), PAH (p<0.01) and multiple cardiovascular risk factors (p<0.01; Table 1). High/increasing disability was associated with markers of poor hand function such as digital ulcers and synovitis (p<0.01), upper and lower GI involvement (both p<0.01) and proximal muscle weakness and atrophy (both p<0.001). Use of immunosuppression (p<0.001), including prednisolone (p<0.001), was more frequent in those with high/increasing disability. Those with high/increasing disability had worse survival after adjusting for age, sex, dcSSc, PAH and ischaemic heart disease (HR 1.9, 95% CI 1.0-3.8, p=0.05), as did those with increasing baseline HAQ DI scores (HR 1.8, 95%CI 1.2-2.7, p=0.01).
Conclusion: Two trajectories of functional disability in SSc were identified. Those with poorer function had a distinct clinical phenotype and survival compared to those with less functional disability. Further work is required to identify if amelioration of disease-specific features associated with higher HAQ DI scores results in a commensurate improvement in physical function.

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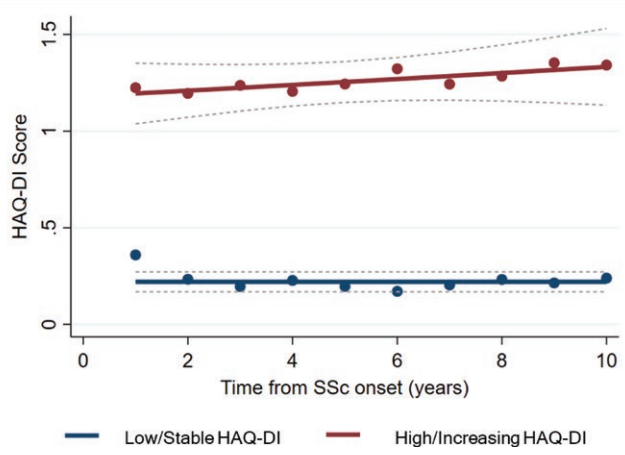


Figure 1 : Trajectory groups

Table 1 : Clinical features and treatments in trajectory groups

Variable	High/Increasing HAQ DI (N = 205)	Low/Stable HAQ DI (N= 221)	p-value
Age at SSc onset (y)	56 (44-63)	52 (41-59)	<0.01
DcSSc	97 (47%)	43 (20%)	<0.01
ANA Centromere	64 (32%)	104 (47%)	<0.01
Scl 70	42 (21%)	32 (15%)	0.09
IHD	32 (16%)	15 (7%)	<0.01
HTN	126 (62%)	85 (39%)	<0.01
PAH	22 (11%)	8 (4%)	<0.01
ILD	78 (63%)	54 (69%)	0.358
Digital ulcers	117 (57%)	90 (41%)	<0.01
Synovitis	118 (58%)	89 (40%)	<0.01
Proximal weakness	75 (37%)	31 (14%)	<0.01
Muscle atrophy	64 (31%)	24 (11%)	<0.01
Upper GI symptoms	196 (96%)	193 (87%)	<0.01
Lower GI symptoms	188 (92%)	175 (79%)	<0.01
Immunosuppression	165 (81%)	121 (55%)	<0.01
Prednisolone	126 (62%)	81 (37%)	<0.01

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POS1270

THE IMPACT OF OVERLAP SYNDROMES ON THE SCLERODERMA CLINICAL TRIAL CONSORTIUM DAMAGE INDEX (SCTC-DI) IN SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Organ damage

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease leading to tissue atrophy, vascular damage and organ failures, and therefore causing severe disability. Coexistent autoimmune diseases are called overlap syndromes. Due to the distinct clinical picture[1], the extent of damage in SSc-overlap may be affected compared to pure-SSc.

Objectives: To identify differences in the time course and characteristics of damage between pure-SSc and SSc-overlap patients by evaluating the Scleroderma Clinical Trials Consortium-Damage Index (SCTC-DI)[2].

Methods: Single tertiary care centre observational study with 160 enrolled SSc patients. Eighty-eight patients (55%) had diffuse cutaneous SSc (dcSSc), 86% were female and median disease duration was 9 years/4;16/. SSc-overlap was diagnosed based on the evaluation of the attending physicians. SCTC-DI was calculated. SCTC-DI score between 6-12 was considered as moderate and >12 points as severe damage. Damage profile of pure-SSc and SSc-overlap including subsets was compared.

Results: SSc-overlap was present in 24% of cases (n=39; 18 rheumatoid arthritis, 12 Sjögren, 12 myositis, 1 antiphospholipid syndrome). Age at enrolment and at disease onset, dcSSc/limited cutaneous (lcSSc) ratio, disease duration and gender distribution showed no difference between pure-SSc and SSc-overlap. Pure-SSc and SSc-overlap patients, including lcSSc/dcSSc subset comparison had the same damage burden (Kruskal-Wallis p>0.05). Median/IQR/ SCTC-DI was similar in pure-SSc and SSc-overlap (9/7;14/ and 9/6;13/ respectively). Moderate damage was found in around 53% and severe damage in 28% of patients in both pure-SSc and SSc-overlap. Gastrointestinal, cardiopulmonary, cardiac, vascular and renal domains of SCTC-DI did not differ between SSc-overlap and pure-SSc, whereas proximal muscle weakness was more prevalent in SSc-overlap compared to pure-SSc. ILD was scored similarly frequently in pure-dcSSc and dcSSc-overlap (82% vs 66.7%, χ^2 p>0.05), however, it was also present in 65% of pure-lcSSc and 60% of lcSSc-overlap patients. Severe damage was more prevalent in SSc-overlap patients at early stage of SSc (≤3 years duration, Fisher's p=0.029) compared to pure-SSc. Early severe damage was more frequent in dcSSc-overlap compared to pure-dcSSc (Fisher's p=0.042). Although in pure-SSc there were weak—to-moderate correlations between the SCTC-DI, age, and disease duration (Spearman's rho:.360-.498;p<0.001), no such associations were found in SSc-overlap patients. Differences in SCTC-DI items in pure-SSc and SSc-overlap are shown in Table 1.

Table 1. Differences in SCTC-DI items in SSc-overlap and pure-SSc

n (%)	**pure-SSc n=121**	**SSc-overlap n=39**	**pure-dcSSc n=67**	**pure-lcSSc n=54**	**dcSSc-overlap n=21**	**lcSSc-overlap n=18**
Small joint CC	59 (48.8)	**21 (53.8)**[d]	**41 (61.2)**[a]	18 (33.3)	14 (66.7)	7 (38.9)
Large joint CC	46 (38.0)	**19 (48.7)**[d]	**32 (47.8)** [a]	14 (25.9)	11 (52.4)	8 (44.4)
Proximal muscle weakness	12/118 (10.2)	**11/38 (28.9)**[b, c, d]	8 (11.9)	4/52 (7.7)	**7 (33.3)**[e,f]	4/17 (23.5)
Digital ulcers	45 (37.2)	13 (33.3)	**31 (46.3)**[a]	14 (25.9)	9 (42.9)	4 (22.2)
SSc-ILD	76/101 (75.2)	21/33 (63.6)	**50/61 (82)**[c]	26/40 (65)	12/18 (66.7)	9/15 (60)

CC: contracturesBold characters: p<0.05. [a] pure-dcSSc vs pure-lcSSc; [b] pure-SSc – SSc-overlap; [c] pure-dcSSc – SSc-overlap; [d] pure-lcSSc – SSc-overlap; [e] pure-SSc – dcSSc-overlap; [f] pure-dcSSc – dcSSc-overlap

Conclusion: SCTC-DI is a relevant tool to assess damage in SSc-overlap. In this cohort damage was not related to ageing and disease duration in SSc-overlap. Early dcSSc-overlap patients had higher risk to develop severe damage compared to early pure-dcSSc patients based on the SCTC-DI. Pulmonary damage was less frequent in SSc-overlap compared to pure-dcSSc, but similar in pure-dcSSc and dcSSc-overlap patients. As expected, musculoskeletal damage, especially proximal muscle weakness was present in a remarkable proportion of SSc-overlap patients.

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POS1271

LONGITUDINAL TRENDS IN MULTIMORBIDITY IN SYSTEMIC SCLEROSIS: RESULTS FROM AN INCIDENT POPULATION-BASED COHORT (1980-2018)

Keywords: Comorbidities, Systemic sclerosis, Epidemiology

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Background: Systemic sclerosis (SSc) is a chronic inflammatory autoimmune disease characterized by vascular dysfunction and widespread internal organ fibrosis. Multimorbidity (MM), defined as the co-occurrence of two or more chronic conditions, can impact life expectancy, increase risk of hospitalizations, healthcare resource utilization and reduce quality of life. The accrual of MM in SSc and its determinants are not well studied.

Objectives: To assess the longitudinal trends of MM (i.e., the presence of ≥2 morbidities) in an incident population-based cohort of patients with SSc vs. age- and sex-matched non-SSc comparators, and identify drivers of these trends.

Methods: A population-based cohort of incident physician diagnosed SSc patients between Jan 1, 1980, to Dec 31, 2018, was identified and compared to a 2:1 cohort of age- and sex-matched non-SSc comparators from the same population. Patients were followed until death, migration from the geographic area, or Dec 31, 2021. Data on 21 morbidities identified by the US Department of Health and Human Services (DHHS) and 13 morbidities included in the Charlson Comorbidity Index (CCI) was retrieved. Cumulative incidence of MM (MM2+) or substantial MM (MM5+; ≥ 5 morbidities) adjusting for the competing risk of death was estimated. Cox models adjusted for age, sex, index year and morbidity count at index date were used to compare cases and comparators. Patients who met criteria of event type before index date were excluded from respective analyses.

Results: 85 patients with SSc were compared to 170 age- and sex-matched non SSc comparators (mean age 55.4 y, 91% female, 90% white/non-Hispanic). At incidence/index date, a significantly higher prevalence of chronic obstructive pulmonary disease (COPD) (14% vs 4%, p=0.004), arthritis (33% vs 22%, p=0.054), peripheral vascular disease (40% vs 2%, p< 0.001) and liver disease (5% vs 1%, p=0.04) were noted in patients with SSc. During a mean length of follow-up of 12.4 y (SD 9.8) for SSc & 15.5 y (SD 9.8) for comparators, the development of DHHS morbidities of heart failure (HF) (HR 2.90; 95% confidence interval [CI] 1.46-5.74), cardiac arrhythmia (hazard ratio [HR] 1.60; 95% CI 1.03-2.49), stroke (HR 2.08; 95% CI 1.04-4.16), chronic kidney disease (HR 1.86; 95% CI 1.09-3.18), and COPD (HR 2.02; 95% CI 1.08-3.80) were higher in SSc vs. non-SSc comparators. While osteoporosis (HR 2.03; 95% CI 1.18-3.51) was also higher in SSc patients, it did not reach statistical significance when adjusted for baseline morbidity count at index date. Similarly, CCI morbidities of HF (HR 2.86; 95% CI 1.51-5.42), peripheral vascular disease (HR 11.32; 95% CI 6.59-19.44), cerebrovascular disease (HR 2.43; 95% CI 1.26-4.72), chronic pulmonary disease (HR 3.82; 95% CI 2.18-6.69), moderate/severe renal disease (HR 2.32; 95% CI 1.30-4.16), and any liver disease (HR 3.02; 95% CI 1.32-6.92) were also significantly higher in SSc when compared to non-SSc comparators. The cumulative incidence of DHHS MM2+ during follow-up did not differ, but the development of DHHS MM5+ was significantly higher in SSc patients vs. comparators at 10 (44% vs 32%), 15 (52% vs 45%) and 20 (64% vs 58%) years of follow up (HR 1.58; 95% CI 1.09-2.31). The development of CCI-MM2+ (HR 4.56; 95% CI 3.00-6.93) was significantly higher among SSc patients but CCI-MM5+ was not statistically significant after adjusting for morbidity count at index (HR 1.65; 95% CI 0.80-3.43).

Conclusion: Multimorbidity is significantly more prevalent in patients with SSc and adds a substantial healthcare burden on these patients. Patients with SSc have a 1.5-3 fold higher risk of developing multiple cardiopulmonary morbidities and >10 fold higher risk of developing peripheral vascular disease during longitudinal follow up than age- and sex-matched individuals without SSc. Multimorbidity assessment must be prioritized early in the disease course to reduce healthcare utilization and optimize long-term outcomes in this population.

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POS1272

INDUCTION OF REGULATORY T CELLS AND EFFICACY OF LOW DOSE INTERLEUKIN-2 IN SYSTEMIC SCLEROSIS: INTERVENTIONAL OPEN-LABEL PHASE 1–PHASE 2A STUDY

Keywords: Adaptive immunity, Investor initiated trial, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is a chronic autoimmune disease, with impaired immune response, increased fibrosis, and endothelial dysfunction. (1,2) Regulatory T cells (Tregs), which are essential to prevent autoimmunity, showed a decreased frequency and impaired function during SSc. (3,4) Low-dose interleukin-2 (ld-IL2) can expand and activate Tregs, but there are no data in SSc.

Objectives: We aimed to assess the in vivo biological efficacy of ld-IL2 on Tregs and its safety in patients with SSc.

Methods: We performed an interventional prospective, open-label phase I-IIa study in nine patients with SSc without severe organ involvement (eight patients with limited cutaneous subtype). This trial is a part of the TRANSREG study. All patients received 1 Million International Units (MIU)/day of IL-2 for five days, followed by fortnightly injections for 6 months. The primary endpoint was the change in the relative Tregs blood concentration identified as CD25hiCD127lo/–Foxp3+cells frequencies on day 8 among TCD4+ cells compared with baseline. Laboratory and clinical evaluations (modified Rodnan skin score (mRSS), Clinical Global Impression (CGI) activity and severity scale) were performed between day 8 and month 18.

Results: At day 8, the primary endpoint was reached with a 1.8(± 0.5) fold increase of Tregs levels among $TCD4^+$ lymphocytes (p= 0.008). Changes in concentration of effector T cells (Teffs) and $BCD19^+$ cells were not statistically significant at day 8 and during maintenance period until month 6. Patients' clinical assessments were stable throughout the follow-up with no modification on mRSS CGI activity and severity scale. Ld-IL2 was well tolerated, and no serious adverse events occurred.

Conclusion: Ld-IL2 at a dosage of 1 MIU/day for five consecutive days selectively activates and expands Tregs in SSc. Safety data were very encouraging. Phase II efficacy trials are needed to validate therapeutic potential of ld-IL2.

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Table: Lymphocyte subpopulations analysis

	Day 1	Day 8
Treg cells	46.1 ± 15.5	121 ± 7.4*
cells/mm^3	6.3 ± 1.4	10.7 ±.8*
% Among $CD4^+$		
Lymphocytes	1307 ± 458	1819 ± 14*
cells/mm3		
Treg cells/Teff cells	4.6 ± 1.2	8.1 ± 1.9*
% Among $CD4^+$		
$CD3^+$T cells	1039 ± 443	1463 ± 407*
cells/mm^3		
$CD4^+$ T cells	782 ± 353	1108 ± 369*
cells/mm^3		
$CD8^+$ T cells	281 ± 156	358 ± 150
cells/mm^3		
$CD19^+$ B cells	159 ± 89	140 ± 71
cells/mm^3		
$CD3^-CD56^\pm$ NK cells	84.8 ± 36.7	178 ± 66.5***
cells/mm^3		

Data are represented as mean ± sd. Changes between baseline and day 8 were analyzed using by ANOVA for ranked data considering factor time *p<0.05; **p<0.01; ***p<0.001.

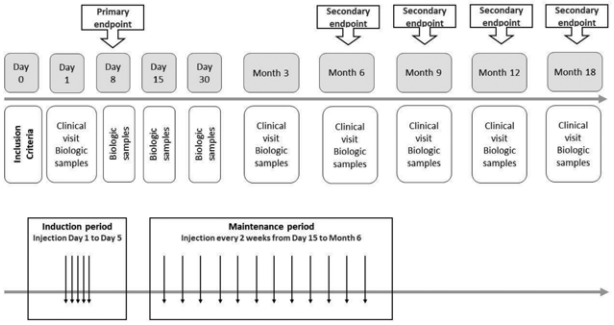


Figure 1. TRANSREG study design

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POS1273

CHARACTERISTICS AND DISEASE COURSE OF UNTREATED PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS IN A REAL-LIFE TWO-CENTER COHORT

Keywords: Systemic sclerosis, Lungs

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Background: Interstitial lung disease (ILD) is the leading cause of death in systemic sclerosis (SSc). Current guidelines consider that some patients may not require pharmacological treatment. To date, the characteristics and disease course of untreated SSc-ILD patients remain unknown.

Objectives: To describe disease characteristics and disease course in untreated SSc-ILD patients in two well characterized SSc-ILD cohorts.

Methods: We included SSc patients from Zurich and Oslo who had a diagnosis of ILD on high-resolution computed tomography (HRCT) and available data on pulmonary function tests and treatment. The longitudinal study included patients with at least one follow-up visit. Patients were classified as treated if they had received a potential ILD modifying drug (immunosuppressive therapy or nintedanib). Treated and untreated patients were compared at baseline. ILD progression in the untreated group was defined as (i) decline in forced vital capacity (FVC) from baseline of ≥10% or (ii) decline in FVC of 5-9% associated with a decline in diffusing capacity for carbon monoxide (DLCO) of ≥15%, or (iii) start of any ILD modifying treatment during follow-up. In the untreated group, patients with ILD progression at any time point were compared with patients with no ILD progression during follow-up. Multivariable logistic regression was performed to identify (i) factors associated with no treatment of ILD at baseline and (ii) factors associated with progression in untreated patients. Covariates were selected based on clinical experience and literature evidence.

Results: The cohort included 386 SSc-ILD patients, 301 (78%) had their first visit before 2016, 82 (21.5%) were males, mean age 57±14 years, mean disease duration 12±22 years, 120 (31%) had diffuse cutaneous SSc and 127/381 (33%) positive for anti-Scl70 antibodies. Of all, 290 (75%) were untreated at baseline. Untreated patients were more often women, had a longer disease duration, more frequently a limited cutaneous form, anticentromere antibodies and lower CRP levels. They had lower NYHA functional class, limited extent (<20%) of lung fibrosis, higher FVC (96±19 % vs. 81±22%), higher DLCO (69±20 % vs. 58±21) and better performances in the 6-minute walking test. In multivariable logistic regression, a less extensive disease on HRCT (OR: 3.71 [1.66-8.53], p=0.002) and anticentromere antibodies (OR: 5.18 [1.81-18.88], p=0.005) were independently associated with no treatment of ILD at baseline in our cohort. Over mean 56 months of follow-up, 135/233 (58%) untreated SSc-ILD patients showed progression. Among them, 116 progressed on lung function parameters. Half of the patients (68) progressed at the first follow-up visit (mean 14 months). Male sex, diffuse cutaneous subtype and extensive lung fibrosis were independently associated with lung progression during follow-up in untreated patients (Figure 1).

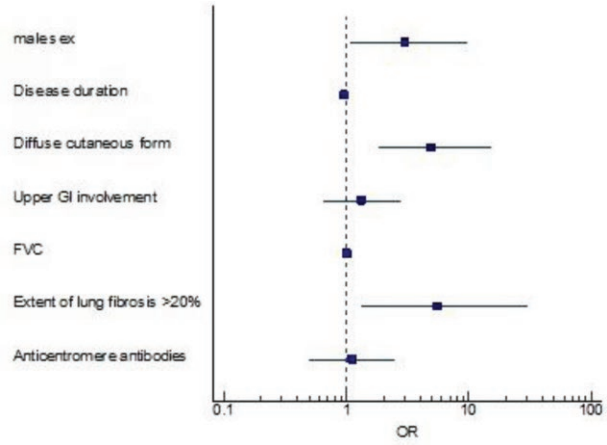


Figure 1.

Conclusion: In the past, a large number of SSc-ILD have been untreated, particularly patients with anti-centromere antibodies and overall less extensive ILD. However, during a follow-up of nearly 5 years, contrary to common belief, about 60% of untreated patients showed progression of ILD. With the development of effective and safe therapies for SSc-ILD, our results support a change in clinical practice in selecting patients for treatment.

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POS1274

FGF23 AND CARDIOVASCULAR STRUCTURE IN WOMEN WITH SYSTEMIC SCLEROSIS

Keywords: Cardiovascular disease, Biomarkers, Systemic sclerosis

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Background: Systemic sclerosis (SSc), an autoimmune disease characterized by fibrosis of the skin and various internal organs, is associated with cardiovascular abnormalities including pulmonary hypertension, atherosclerosis, right and left ventricular dysfunction, arrhythmias, conduction defects, pericardial disease, and valvular heart disease. Fibroblast growth factor-23 (FGF23) is a circulating regulator of phosphate and vitamin D metabolism and has been implicated as a putative pathogenic factor in cardiovascular disease. FGF23 has been associated with cardiac hypertrophy and reduced left ventricular ejection fraction among patients with chronic kidney disease and cardiovascular disorders.
Objectives: The aim of this study was to examine the possible association between serum FGF23 levels and echocardiographic abnormalities in women with SSc.
Methods: This cross-sectional study was performed in San Cecilio Hospital, Granada (Spain) from November 2017 to May 2019. Sixty-two women with SSc were enrolled in this study. All patients included in this study had normal serum creatinine (Cr) levels and met the 2013 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for SSc. Echocardiograms were performed at a single clinical site using Philips ie33 ultrasound machine with subjects in the left lateral decubitus position. Serum FGF23 was analyzed using ELISA.
Results: A total of 62 female patients were included in our study, with a mean (SD) age of 53 ± 10 years. The majority were Caucasian (90.5%). The mean disease duration was 8.8 ± 6.9 years. Forty-four (70.9%) patients had a limited form of the disease and 18 (29.1%) had a diffuse form. The mean left ventricular posterior wall thickness and left ventricular systolic diameter were 8.1±1.3 mm and 25.3±4.8 mm, respectively. We found a statistically significant inverse relationship between FGF23 and posterior wall thickness (r= -0.34; p= 0.03) and a statistically significant relationship between FGF23 and left ventricular systolic diameter (r= 0.5; p= 0.03) in women with SSc. Furthermore, in the linear regression model, lower FGF23 concentrations were associated with greater posterior wall thickness [β = -15.11 95% CI (-29.38, -0.848); $p < 0.05$].
Conclusion: We report an association between circulating FGF23 and left ventricular posterior wall thickness in SSc female patients, representing a novel pathway linking FGF23 to an increased cardiovascular risk.
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POS1275

THE HETEROGENEITY OF DEFINING SEVERITY, PROGRESSION AND OUTCOMES IN SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: RESULTS FROM A SYSTEMATIC LITERATURE REVIEW

Keywords: Outcome measures, Systemic sclerosis, Lungs

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Background: The course of systemic sclerosis associated interstitial lung disease (SSc-ILD) is highly variable. The SSc-ILD progression (SILPRO) project aims at developing a disease specific model to define SSc-ILD progression predicting long-term, severe SSc-ILD. The evaluation of currently used definitions of severity, progression and outcomes recorded in SSc-ILD represents the highly needed first step to achieve this aim.
Objectives: To identify definitions of progression, severity and outcomes related to SSc-ILD in the literature.
Methods: A systematic literature review was conducted according to PRISMA guidelines in Medline, EMBASE and the Cochrane Library up to 31/12/2021. Eligible papers included > 10 adult SSc patients, with ILD as primary target (at least one of population, exposure, outcome). Original papers in English were considered, while papers related to secondary lung involvement, ILD onset as an outcome or reviews were excluded. Two reviewers independently identified eligible studies and extracted data, including the abovementioned definitions used.
Results: We identified 299/8444 eligible papers, mostly reporting results of retrospective cohort studies (n=126, 42%), prospective cohort studies (n=120, 40%) and randomized clinical trials (n=24, 8%). A definition of SSc-ILD severity was included in 138 (46%) papers: it was based on high-resolution computed tomography (HRCT) data in 72 (52%) studies, on forced vital capacity (FVC) changes in 29 (21%), on combined FVC and carbon monoxide diffusing capacity (DLCO) changes in 14 (10%), on DLCO changes in 11 (8%). After combining some similar categories, 42 distinct definitions of SSc-ILD severity were identified (Figure 1 shows the most used).

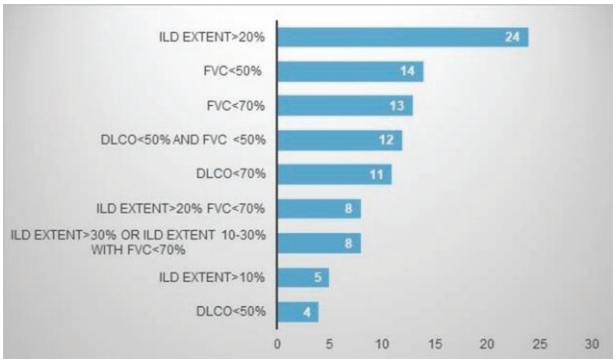


Figure 1. Most commonly used definitions of SSc-ILD severity (n papers).

Sixty-one of 169 studies (36%) provided a definition of SSc-ILD "progression" referred to combined DLCO and FVC changes, 49 (29%) to FVC changes, 23 (14%) to DLCO changes, 18 (11%) to ILD extent on HRCT, 6 (4%) to combination of pulmonary function test (PFT), clinical signs and HRCT data, 5 (3%) to vital capacity decline, 5 (3%) to combination of PFT and HRCT data and 2 (1%) to other aspects (Table 1).
Conclusion: The studies reporting a definition of SSc-ILD "progression", "severity" and "outcome" show a large heterogeneity. These results emphasize the need for developing a standardized, consensus definition of severe SSc-ILD, to link a disease specific definition of progression as a surrogate outcome for clinical trials and clinical practice.

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Table 1. Most frequently used definitions of SSc-ILD progression

	SSc mixed cohorts				SSc-ILD cohorts		
	Time, months (n papers)	n patients (n papers)	n ILD patients (n papers)	n progressors (n papers)	Time, months (n papers)	n patients (n papers)	n progressors (n papers)
decline FVC>10%	12 (8) 24 (3) 36 (3) >60 (2) Unk (3)	3347 (17)	1779 (16)	605 (17)	6 (3) 12 (3) 24 (4) >60 (4)	1544 (14)	263 (13)
decline FVC>5%	Unk (1)	138 (1)	100 (1)	49 (1)	12 (2) 24 (1) Unk (1)	836 (4)	179 (3)
decline FVC>3.3%	-	-	-	-	12 (2) Unk (1)	734 (2)	349 (2)
decline DLCO>15%	12 (2) 24 (1) 60 (2)	568 (5)	445 (5)	135 (5)	6 (2) 12 (2) 36 (1) 60 (2)	505 (7)	168 (7)
decline DLCO>10%	12 (2) 55 (1) >60 (1) Unk (2)	340 (5)	112 (2)	86 (5)	24 (1)	14 (1)	9 (1)
decline FVC>10% or DLCO>15%	6 (1) 12 (6) 24 (2) >36 (4) >60 (1) Unk (6)	6170 (17)	2327 (13)	1144 (14)	12 (8) 24 (4) 36 (1) >60 (3) Unk (8)	1516 (20)	449 (16)
decline FVC >10% or DLCO>10%	6 (1) 12 (2) >36 (4) 60 (1)	531	336	181 (8)	24 (1) 36 (2) >36 (2)	472 (5)	47 (4)
decline FVC≥10% or DLCO≥15% or ILD extent increase>20%	12 (1)	36 (1)	24 (1)	12 (1)	56 (1)	58 (1)	12 (1)
increased ILD extent>10%	12 (2)	347 (2)	213 (2)	6 (2)	24 (2)	145 (2)	5 (2)
increased ILD extent>20%		-	-	-	24 (1) Unk (1)	22 (2)	8 (2)
increased ILD extent	12 (1) 37 (1) 62 (1)	1024 (3)	440 (3)	99 (3)	12 (1)	75 (1)	34 (1)

Among all articles, 47 outcomes related to SSc-ILD were identified from 153 papers. The most frequent outcomes represented hard endpoints, such as mortality (131 papers), end stage lung disease (8 papers), hospitalization (6 papers) and malignancies (4 papers).

Scleroderma, myositis and related syndromes

POS1276

A SINGLE CELL TRANSCRIPTOMIC ANALYSIS REVEALS A PRO-INFLAMMATORY PROFILE IN PERIPHERAL BLOOD CD14+ MONOCYTES OF SYSTEMIC SCLEROSIS PATIENTS

Keywords: Biomarkers, Innate immunity, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is an immune-mediated disease, which affects mostly women over 50 years old. Recently, single cell mRNA sequencing techniques (scRNA-seq) have contributed to establish the relevance of different immune cell types in SSc. However, little is known about the diversity of the peripheral blood monocytes, which play a central role in the early inflammatory response and in the maintenance of inflammation in SSc.
Objectives: Our aim is to analyze the composition of the peripheral blood monocyte compartment of SSc patients and to establish disease and subtype specific transcriptomic profiles at the single cell level.
Methods: CD14+ monocytes were isolated from peripheral blood mononuclear cells (PBMC) of 8 SSc diagnosed women and 8 age matched unaffected females. All the patients were between 50 and 70 years old and classified as either limited cutaneous SSc (lcSSc) or diffuse cutaneous SSc (dcSSc). ScRNA-seq libraries were generated using the 10x Genomics Chromium platform and the Chromium Next GEM Single Cell 5' Reagent Kits. After QC a total of 98,543 cells remained, with an average of ~7,000 cells per sample and 36,601 detected genes. Dimensionality reduction and cell clustering were performed using Scanpy, establishing 5,000 high variable genes and 20 principal components to implement the Leiden clustering algorithm.
Results: We identified 11 different clusters in the SSc combined analysis of the single cell transcriptomes from both the SSc patients and the controls. Using known genes and cell markers, we identified classical monocytes, non-classical monocytes and intermediate monocytes, and a dendritic cell population (Figure 1.). Non-classical monocyte populations were under-represented in SSc patients. Overall, we observed a proinflammatory profile in SSc CD14+ monocytes, which overexpressed genes related to the interferon signaling pathways, such as *IFITM2*, *IFITM3* or *IRF1*, but also *S100* family genes. This proinflammatory profile is especially enriched in the activated monocyte clusters, i.e. those with high expression of *S100A8*/*S100A9* genes. Additionally, we identified the overexpression of *TMEM176A* and *TMEM176B in* lcSSc patients compared to dcSSc patients and controls.

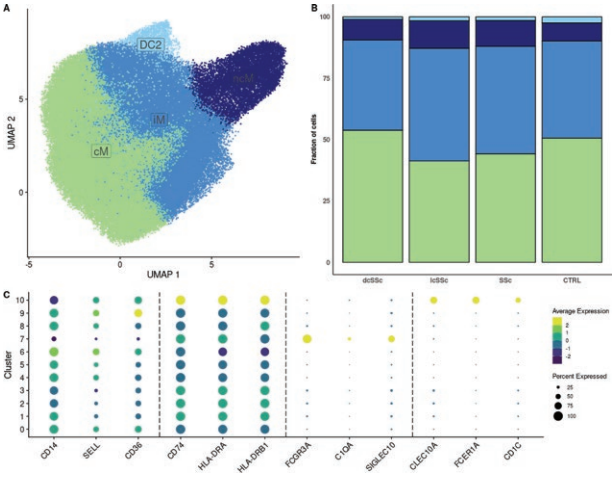


Figure 1. Monocyte subtype population in SSc. (A) UMAP visualization of monocyte CD14+ isolated from PBMCs sample of SSc and controls. (B) Proportion of cells of each monocyte subtype. (C) Dotplot of genetic and cell markers of monocyte subtype per cluster. The dot size indicates the number of cells expressing the gene in the cluster and the color the average of expression.

Conclusion: Our analysis of peripheral blood CD14+ monocytes in SSc patients showed an overrepresentation of non-classical monocytes and an increased interferon response compared to healthy controls. Moreover, we found subtype specific transcriptomic profiles, which suggested the possible use of monocyte subtypes as SSc biomarkers.

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POS1277 **WITHDRAWN**

POS1278

SAFETY AND PHARMACOKINETICS OF IGPRO20 (SUBCUTANEOUS IMMUNOGLOBULIN) AND IGPRO10 (INTRAVENOUS IMMUNOGLOBULIN) IN ADULTS WITH SYSTEMIC SCLEROSIS (SSC) – RESULTS FROM A PHASE 2 TRIAL

Keywords: Systemic sclerosis, Safety, Clinical trials

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Background: Systemic sclerosis (SSc) is a severe, progressive multisystem rheumatic disease with high mortality, but without approved disease-modifying treatment to stop or reverse course of disease. Intravenous immunoglobulin G (IgG) may have a positive impact on SSc based upon available literature reports. However, to date, there have been no clinical trials evaluating subcutaneous IgG (SCIG) in SSc. In particular, the impact of pathologically altered skin in SSc on local safety and pharmacokinetics (PK) of SCIG has not been explored yet.

Objectives: The primary and secondary objectives of this trial (NCT04137224) included safety, including local infusion safety, and bioavailability of subcutaneous IgG (IgPro20) in adults with diffuse cutaneous SSc (dcSSc).

Methods: This was a randomized, open-label, crossover study. Adult subjects with dcSSc diagnosis within 5 years from first non-Raynaud's phenomenon and modified Rodnan Skin Score of 15-45 at screening were randomized 1:1 to sequence A (IgPro20, 20% normal human subcutaneous immunoglobulin followed by IgPro10, 10% normal human intravenous immunoglobulin) or sequence B (IgPro10 followed by IgPro20). Each subject was to complete two treatment periods (16 weeks each), with up to 40 weeks (including screening) study duration for an individual subject. Doses received were 0.5g/kg/week split over two sessions for IgPro20, and 2g/kg/4 weeks split over 2-5 days for IgPro10. The primary endpoint was safety of IgPro20, described as treatment-emergent adverse events (TEAEs) and changes in clinical observations.

Results: 27 subjects were randomized, with 13 subjects to sequence A and 14 subjects to sequence B. In total, 25 subjects completed the study. Of 27 treated subjects, 107 TEAEs occurred in 22 subjects (81.5%) over the 36-week study period, the majority of which were mild or moderate. The most common TEAEs (>10% of subjects) by preferred term (PT) were headache (12 events occurring in 6 subjects [22.2%]), COVID-19 (3 events occurring in 3 subjects [11.1%]), diarrhoea (3 events occurring in 3 subjects [11.1%]), and vomiting (3 events occurring in 3 subjects [11.1%]). A total of 10 serious AEs (SAEs) were reported in 6 subjects (Viral infection, Chronic gastritis, Vomiting, Dehydration, Upper gastrointestinal haemorrhage, Chest pain, Myocardial infarction, Myocardial ischemia, Breast cancer, Interstitial lung disease). Among these, one subject experienced 2 SAEs (myocardial ischemia & myocardial infarction) and was discontinued from study treatment. None of the SAEs were considered related to study treatment by the investigator, and no deaths were reported. For IgPro20, 14 infusion site reactions (ISRs) occurred in 5 subjects (19.2%), all were mild or moderate in severity. The most common ISRs were infusion site pain and infusion site swelling (3 events in 2 subjects each, 7.7%). In total, 686 IgPro20 infusions were performed, resulting in an overall ISR rate per infusion of 0.02, ie 2 ISRs per 100 infusions. No ISRs were reported for IgPro10. No clinically relevant trends in vital signs, body weight, clinical laboratory tests, electrocardiograms, or pulmonary function tests were observed. PK profiles and bioavailability in dcSSc subjects were similar to those observed in other approved indications such as Primary Immunodeficiency. Population relative bioavailability of IgPro20, based on dose-normalized, baseline-corrected $AUC_{0\text{-}tau}$ was 0.761 (90% CI: 0.7033, 0.8232), ie 76.1% compared to IgPro10 (intravenous IgG).

Conclusion: The overall safety profiles of IgPro20 and IgPro10 in subjects with dcSSc were consistent with that in approved indications such as CIDP, including a relatively low ISR rate for IgPro20. PK profiles and bioavailability were also similar to other indications. This study indicates that subcutaneous administration of IgPro20 has acceptable safety, bioavailability and PK profiles in patients with dcSSc.

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POS1280

CIRCULATING EXTRACELLULAR VESICLES AS A POTENTIAL BIOMARKER OF INTERSTITIAL LUNG DISEASE AND ITS PROGRESSION IN SYSTEMIC SCLEROSIS –A PROSPECTIVE COHORT STUDY

Keywords: Biomarkers, Prognostic factors, Systemic sclerosis

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Background: Extracellular vesicles (EVs) are membrane-coated vesicles derived from virtually any cell type under different stimuli. Interstitial lung disease (ILD) is the leading cause of death in SSc. So far, only one study demonstrated elevated levels of EVs in patients with SSc-ILD (1), however the association between EVs and progressive ILD (pILD) was not previously investigated.
Objectives: To evaluate the concentration of different subpopulations of EVs in plasma from SSc patients in relation to the occurrence of pILD associated to SSc.
Methods: This was a prospective cohort study, including 59 SSc patients without any comorbidity (31 (52.5%) with ILD and 28 (47.5%) without).The median disease duration in ILD group was 3 years and 6 years in those without. ILD was defined either as X-ray positive findings or ground-glass opacification on HRCT. EVs were analyzed with flow cytometry after staining of platelet-poor plasma with fluorescent cell-specific monoclonal antibodies. The concentration of the following phosphatidylserine-positive EVs was analyzed at baseline: endothelial EVs (EEVs; $CD144^+$), platelet EVs (PEVs;$CD42b^+$), leucocyte EVs (LEVs; $CD45^+$), EVs expressing ICAM1 ($CD54^+$), TF ($CD142^+$) and HMGB1. The serum concentration of ICAM1,VEGF,and IL6 were measured by ELISA. Lung functional tests were done every 6-12 months over a 3-years period of follow-up (FU). pILD was defined by the decline of forced vital capacity (FVC) from baseline visit of ≥10%, or an FVC decline of 5-9% along with a DLCO decline of >15% [2].
Results: An inverse relation was noticed in SSc patients between EVs and FVC (EEVs r=-0.3, p<0.05; LEVs r=-0.4, p<0.01; EVsICAM1r=-0.4, p<0.01; EVsTF r=-0.4, p<0.01; EVS HMGB1r=-0.3, p<0.05). Significantly increased levels of VEGF, ICAM1, IL6, PEVs, and EVs expressing ICAM1, TF or HMGB1 were found in SSc ILD cohort compared to those without (p<0.05, respectively). There was a positive association between all explored EVs and VEGF in ILD group (p<0.05). Multivariable (Ml) logistic regression (R), adjusted for VEGF raveled that PEVs(OR 1.004, 95%CI 1.001-1.01) and EVs ICAM1 (OR 1.3, 95%CI 1.1-1.5) were independently associated with ILD. Over a FU period, 12/31ILD patients developed pILD, of which 58% had early diffuse subtype with < 1-year disease duration and were anti Scl 70 positive. Only 4/12 pILD patients have ever been treated with imunossupresive therapy. pILD occurred within 1st FU year in 50% of patients. All analyzed EVs (Figure 1), IL6 and VEGF, were found elevated in pILD (p<0.05, respectively). Moreover, the levels of PEVs, EVs expressing ICAM1 (AUC 0.9, p<0.001, respectively),TF, HMGB1, EEVs and LEVs (AUC 0.7, p<0.05, respectively) showed good validity in identifying pILD. There was only a positive correlation between VEGF and both EVs ICAM1 (r=0.8, p<0.01) and EVs HMGB1 (r=0.7, p<0.01) within pILD group. Applying Ml Cox R controlling for VEGF, EVs ICAM1 were confirmed independently significantly associated with pILD (OR 1.1, 95% CI 1.02-1.1).
Conclusion: Our results provide evidence that different circulating EV subpopulations might play a role not only in SSc ILD pathogenesis but also in the genesis of pILD. EVs expressing ICAM1 could be a novel predictive biomarker of SSc-related ILD progression, identifying patients who would potentially benefit from early aggressive treatment.
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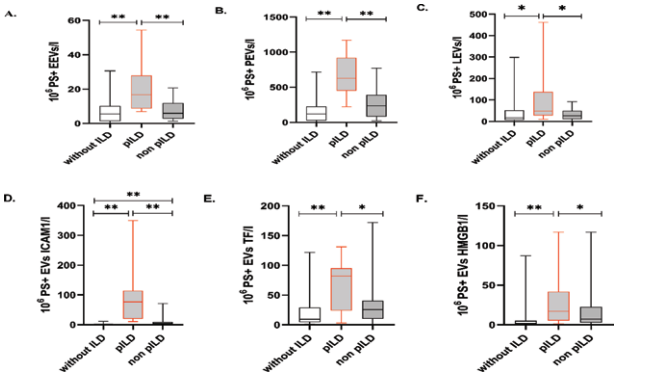


Figure 1. The levels of circulating (A) EEVs, (B) PEVs, (C) LEVs, (D) EVs ICAM1, (E) EVs TF,(F) EVs HMGB1 in patients without ILD, progressive ILD (pILD) and non-progressive ILD (non-pILD) over follow-up. *p < 0.05; **p < 0.01

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POS1281

INFLAMMATORY ACTIVITY IS ASSOCIATED WITH INCREASED RISK OF SARCOPENIA IN SYSTEMIC SCLEROSIS

Keywords: Sarcopenia, Systemic sclerosis

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Background: Sarcopenia is a muscular condition characterized by loss of skeletal muscle mass and function. It is a condition associated with chronic diseases and aging that predicts disability, hospitalization and death.
Objectives: To describe the prevalence of sarcopenia and its associated factors in a series of patients with Systemic Sclerosis (SSc).
Methods: Design: Cross-sectional descriptive study. Participants: consecutive recruitment of patients with SSc (ACR/EULAR 2013 criteria) followed up in our unit. Follow-up of these patients is carried out every 3 to 6 months in consultation and all patients were registered in a database. 90% of the patients accepted and signed the consent, the rest refused due to travel or work difficulties. Variables: The main variable was sarcopenia defined according to the European Working Group on Sarcopenia in Older People (EWGSOPII) criteria and severe sarcopenia, which according to EWGSOPII criteria also includes physical performance in the 4-meter walk test. Clinical and analytical data were collected, as well as Mini Nutritional Assessment (MNA) nutrition questionnaires (continuous: 0-14, considering 14 better nutritional status), physical activity assessed by GPAQ, polypharmacy (if they take >3 drugs) and functional grade of Steinbrocker. Statistical analysis: descriptive and two logistic regression models to identify factors associated with sarcopenia and severe sarcopenia.
Results: 52 patients were included, of whom 51 (98.1%) were women, with a mean (SD) age of 60.8 (11.0) years. A total of 12/52 patients (23.1%) had sarcopenia and 6/52 patients (11.5%) had severe sarcopenia (Table 1). Compared to the rest, patients with sarcopenia had anti-Scl70 antibodies more frequently (41.7% vs 12.5%; p=0.030) and were polymedicated (87.5% vs 60.0%; p=0.022). Likewise, patients with sarcopenia had worse mean (SD) values in the Steinbrocker functional class (2.58 [1.24] vs 1.75 [0.89]; p = 0.040). Patients with severe sarcopenia had lower mean (SD) values of prealbumin (19.2 [3.3] vs 21.6 [4.7]; p = 0.001) and were more frequently dependent at home than the rest (16.7% vs. 2.5%; p=0.03). In addition, a greater number (%) of patients with severe sarcopenia had an inability to perform the physical function tests of the chair and the balance test compared to the rest of the sample (50% vs 13.3%; p=0.05) and (66.7% vs. 8.9%; p=0.05), respectively. The multivariate analysis identified that the only variable associated with sarcopenia in patients with SSc was CRP (OR [95% CI], 1.125 [1.037-1.220]; p=0.004) (R2=0.282). Similarly, CRP was also independently associated with severe sarcopenia (OR [95% CI], 1.240 [1.081-1.423]; p=0.002) (R2=0.314).
Conclusion: Sarcopenia is linked to inflammatory activity in SSc. This comorbidity has serious consequences for functionality and independence, which is why prevention and early detection of sarcopenia and its associated factors is important.

Table 1. Clinical-epidemiological characteristics of the 52 patients in SSc

Variable	ES n=52
Woman n (%)	51 (98,1%)
Age mean (SD)	60,8 (11,0)
Limited skin patern n (%)	40 (76,9%)
Disseminated skin patern n (%)	12 (23,1%)
DILD n (%)	17 (32,7%)
HTAP n (%)	5 (9,6%)
Anti-Centrómere antibodies n(%)	28 (53,8%)
Anti-Sl70 antibodies n (%)	10 (19,2%)
Other antibodies n (%)	9 (17,3%)
Sarcopenia n(%)	12 (23,1%)
Severe sarcopenia n(%)	6(11,5%)
MNA Normal nutritional status n (%)	34 (64,5%)
MNA Risk of malnutrition n (%)	17 (32,7%)
MNA malnutrition n (%)	1 (1,9%)
Weight loss >1kg in the last 3 months n(%)	25 (48,1%)
Polypharmacy n(%)	12(23,1%)
Steinbrocker mean (SD)	1,94 (1,03)
GPAQ mean (SD)	669,5 (666,9)
Prealbúmina mean (SD)	21,41 (4,63)

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POS1282

CARDIAC MAGNETIC RESONANCE IN ANTI-SYNTHETASE SYNDROME: THE ADDITIONAL VALUE OF T2 MAPPING TO DETECT MYOCARDITIS

Keywords: Heart, Imaging, Cardiovascular disease

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Background: Myocarditis can be a subtle and underdiagnosed manifestation of anti-synthetase syndrome (ASS), and its occurrence is associated with a poor prognosis. Cardiac magnetic resonance (CMR) is the diagnostic modality of choice for the non-invasive diagnosis of myocarditis, which historically relies on the 2009 Lake Louise Criteria (LLC) [1]. LLC, however, have a low diagnostic accuracy in patients with coexisting myositis.
Objectives: To investigate the performance of the mapping techniques included in the revised LLC [2] for the identification of ASS myocarditis.
Methods: CMR data (right and left ventricular function and morphology, early and late gadolinium enhancement [LGE], T2 ratio, and T1 mapping, extracellular volume [ECV] and T2 mapping) of ASS patients diagnosed with myocarditis were reviewed. Myocarditis was clinically defined by the presence of signs and/or symptoms of ASS heart involvement with increased high-sensitive troponin T (hs-TnT) and/or NT-proBNP serum levels and at least an abnormality at 24 h ECG Holter and/or echocardiography and/or CMR.
Results: We identified 11 patients (mean age 58 ±13 years; females 45%; anti-Jo1 55%, antiPL-7 27%) with ASS myocarditis. Dyspnea was the most frequently reported symptoms (64%), 4 patients (36%) had echocardiographic abnormalities, while 24-hour-ECG Holter was normal in all patients. At baseline, troponin T levels were raised in all but 1 patient (mean value 461 ±351 ng/L), while NT-proBNP levels were raised in 45% of patients (mean value 1802 ±1484 pg/mL). All patients had at least one CMR abnormality: increased ECV in all patients, LGE in 10 (91%), and T2 mapping >50 ms in 10 (91%). Median T1 and T2 mapping were 1079 [range 906-1172] ms and 53.2 [range 48.8-57.4] ms, respectively. No statistical significant correlation emerged between CMR parameters (T1 mapping, T2 mapping and ECV) and disease parameters (troponin, NTproBNP, CPK levels and inflammatory markers). Six patients satisfied the 2009 LLC, 10 the 2018 LLC. With the new criteria including T2 mapping, the sensitivity improved from 54% to 91%.
Conclusion: The CMR mapping techniques improve the sensitivity to detect myocardial inflammation in patients with ASS-related heart involvement. The evaluation of T2 mapping increases diagnostic accuracy for the recognition of myocardial inflammation in ASS and should be always performed in ASS patients with suspected myocarditis.

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POS1283

HEART AND SYSTEMIC SCLEROSIS – FINDINGS FROM NATIONAL COHORT STUDY

Keywords: Epidemiology, Systemic sclerosis, Heart

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Background: Heart involvement is one of the leading causes of death in systemic sclerosis (SSc). Cardiac manifestations are heterogeneous. In particular, prevalence of SSc-related cardiopathy is poorly known due to a lack of consensus in its definition.
Objectives: Our objective was to investigate the prevalence and prognosis burden of the different heart diseases in a nationwide cohort of patients with SSc.
Methods: We used data from a national multicentric prospective study using the French SSc national database. We described the characteristics of 3 different types of heart involvement: SSc-related cardiopathy, pulmonary arterial hypertension and ischaemic heart disease. We analyzed overall survival and survival according to the heart disease. Focusing on SSc-related cardiopathy, we aimed to determine its incidence and risk factors.
Results: Over the 3528 patients with SSc available for baseline analyses 312 (10.9%) had SSc-related cardiopathy at baseline. They tended to have a diffuse SSc subtype more frequently, had more severe clinical features, and presented more cardiovascular risk factors. From the 1646 patients available for follow-up analysis, SSc-related cardiopathy was associated with an increased risk of death. No significant difference of overall survival was found between SSc-related cardiopathy, ischaemic heart disease or pulmonary arterial hypertension. Concerning survival analysis, 98 patients developed SSc-related cardiopathy at 5 years (5-year event-rate: 11.15% [9.01; 13.23]). Regarding reduced LVEF < 50% and left ventricular diastolic dysfunction, the 5-year event-rate were 2.49% [CI95%: 1.13; 3.83] and 5.84% [CI95%: 4.02; 7.62], respectively. The pericarditis cumulative incidence at 5 years was 3% [CI95%: 1.91; 4.08]). Diffuse SSc subtype was a risk factor of SSc-related cardiopathy and pericarditis (adjusted HR: 1.42 [CI95%: 1.02; 1.97], p = 0.04 and adjusted HR: 1.79 [CI95%: 1.06; 3.02], p = 0.03, respectively). Female sex was associated with less diastolic dysfunction incidence (adjusted HR: 0.39 [CI95%: 0.24; 0.63], p = 0.0001).
Conclusion: Our results further describe at a large scale the incidence and prognostic burden of SSc-related cardiopathy, with gender and diffuse SSc subtype as risk factors. Further analyses should assess the potential impact of treatment on these various cardiac outcomes.

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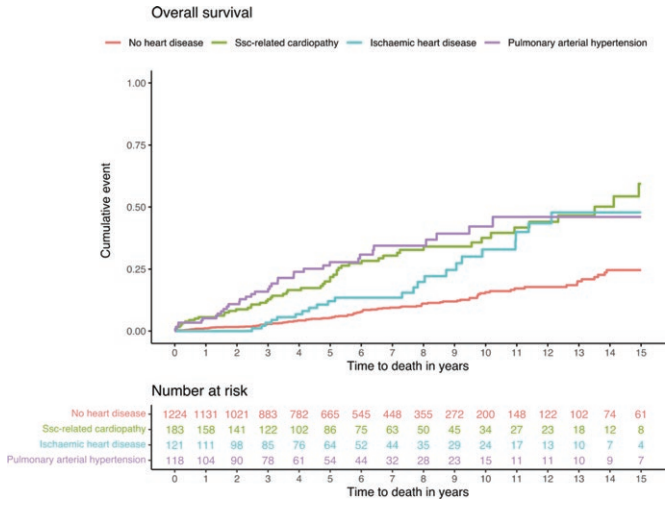


Figure 1.

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POS1284

MYOCARDIAL INVOLVEMENT CHARACTERIZES EARLY SYSTEMIC SCLEROSIS WITH ANTI-SCL70 ANTIBODIES AND LONGSTANDING DISEASE WITH ANTI-CENTROMERE ANTIBODIES

Keywords: Systemic sclerosis, Autoantibodies, Heart

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Background: Myocardial involvement is frequently asymptomatic at the early stages in systemic sclerosis (SSc) but accounts for one-third of SSc-related deaths [1]. First-line screening tools include cardiac enzymes, Holter ECG, and echocardiography [2,3], while the diagnosis relies largely on cardiac magnetic resonance [4], assessing myocardial inflammation and fibrosis [5]. The prevalence of SSc myocardiopathy and the associated factors are poorly defined [2].

Objectives: To evaluate the prevalence of myocardiopathy and the associated demographic, clinical, and instrumental features in a single center cohort of 317 SSc patients, including 49 (15%) early SSc, 66 (21%) anti-Scl70+, 178 (56%) anti-centromere (ACA)+, 45 (14%) diffuse, 99 (31%) ILD, 37 (12%) with pulmonary hypertension.

Methods: Retrospective analysis; myocardiopathy in SSc was defined as increased myocardial tissue to skeletal muscle T2 ratio, T2 TIRM or delayed enhancement areas, or increased T1 or T2 mapping native time at cardiac magnetic resonance [6].

Results: Forty-two SSc patients underwent cardiac magnetic resonance after developing symptoms (dyspnea, atypical angor, palpitations; 43%), elevated cardiac enzymes (55%), or Holter ECG alterations (38%). Myocardiopathy was detected in 29/42 patients (69%; 29/317, 9.2%). Early disease was significantly more frequent in patients with myocardiopathy (17/29, 59%; OR 7.8, 95% CI 1.45-41.7); 17/49, 35% considering early SSc in the whole cohort). Among patients with myocardiopathy, anti-Scl70 was more frequently observed in early compared to longstanding disease (9/17, 53% vs. 2/12, 17%; p = 0.05); the opposite was for ACA (4/17, 24% vs. 7/12, 58%; p = 0.06) (Figure 1). Clinical characteristics did not differ among patients with and without myocardiopathy, except digital ulcers (Table 1). Serum troponin I (TnI) was higher in patients with myocardiopathy (median 6 vs 1.6 ng/L; p = 0.049). Relevant alterations on Holter ECG, especially premature ventricular contractions (PVC) > 300/day, were observed more frequently in patients with myocardiopaty (p = 0.04 for both; Table 1).

Conclusion: We report a relevant overall prevalence of myocardiopathy in a cohort of SSc patients, similar pulmonary hypertension, affecting one third of patients with early SSc, especially with anti-Scl70. Conversely, a delayed onset of myocardiopathy was associated with ACA. Among other predictors, higher serum troponins and Holter ECG alterations, especially PVC, were significantly associated to myocardiopathy. As the early suspicion and diagnosis of myocardiopathy are crucial for promptly starting immunosuppressive treatment, we submit that the risk stratification should be performed in patients with SSc.

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Table 1

		CM (29)	No CM (13)	*p*
Serology	Scl-70 (%)	11 (38)	2 (15)	.15
	ACA (%)	11 (38)	9 (69)	.06
	RNA pol III (%)	3 (10)	2 (15)	.64
Clinical	dcSSc (%)	12 (41)	3 (23)	.26
	mRSS	4 (1-9)	2 (0-10)	.81
	Early SSc (%)	17 (59)	3 (23)	**.03**
	ILD (%)	16 (55)	5 (39)	.32
	Ulcers (%)	1 (3)	3 (23)	**.047**
	Calcinosis (%)	2 (7)	1 (8)	.93
	Gut (%)	7 (24)	4 (31)	.65
Holter	Holter any (%)	22/28 (79)	6/13 (46)	**.04**
	PSVC > 1.27/h (%)	21/28 (75)	6/12 (50)	.13
	PVC > 300/d (%)	11/28 (39)	1/13 (8)	**.04**
Cardiac magnetic resonance	Pericardial effusion (%)	11 (38)	3 (23)	.35
Lab	BNP	46.5 (34-138)	113.5 (52-190)	.20
	CK	88 (60-171)	91 (61-153)	.96
	CK-MB	3.2 (1.2-9.7)	1.4 (1.1-3.3)	.32
	TnI	6 (1.9-26)	1.6 (0-4.5)	**.049**

Legenda*: dcSSc: diffuse SSc; mRSS: modified Rodnan skin score; P(S)VC: premature (supra)ventricular contractions; Holter any: PSVC > 1.27/h or PVC > 300/d.* Continuous variables are reported as medians (interquartile range).

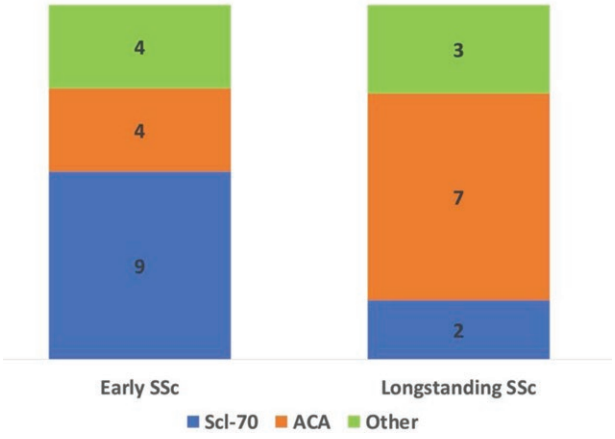


Figure Autoantibody distribution in patients with SSc-myocardiopathy

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POS1285 PERIPHERAL MICROVASCULAR FUNCTION IS LINKED TO CARDIAC INVOLVEMENT ON CMR IN SYSTEMIC SCLEROSIS-RELATED PULMONARY ARTERIAL HYPERTENSION PATIENTS

Keywords: Systemic sclerosis, Heart

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Background: Systemic sclerosis (SSc) is characterized by vasculopathy, inflammation and fibrosis, and carries one of the worst prognoses if patients also develop pulmonary arterial hypertension (PAH). Although PAH is a known prognostic factor, SSc-PAH patients demonstrate disproportionately high mortality, presumably due to cardiac involvement [1].
Objectives: To investigate the relation between cardiac involvement as revealed by Cardiovascular Magnetic Resonance (CMR) and systemic microvascular disease severity as measured with nailfold capillaromicroscopy (NCM) in SSc-PAH patients, compared to idiopathic PAH (IPAH) patients.
Methods: SSc-PAH and IPAH patients underwent CMR, transthoracic echocardiography (TTE), and NCM with post-occlusive reactivity hyperemia (PORH) testing on the same day [2-4]. CMR imaging included T2 mapping, native and postcontrast T1 mapping, to assess edema and fibrosis, and adenosine-stress perfusion imaging to measure the relative myocardial upslope (to determine microvascular coronary perfusion). Measures of peripheral microvascular function were related to CMR indices of edema, fibrosis and myocardial perfusion.
Results: SSc-PAH patients (n=20) had higher extracellular volume fraction (ECV) and T2 values than IPAH patients (n=5), and lower nailfold capillary density (NCD) and reduced capillary recruitment after PORH. NCD correlated with native T1, ECV, and T2 values (r=-0.431, -0.443, and -0.464, respectively, p<0.05 for all), and with markers of diastolic dysfunction on echocardiography. Furthermore, PORH-testing, but not NCD, correlated with the relative myocardial upslope by stress CMR (r=0.421, p<0.05) (Table 1).

Table 1. Nailfold capillaroscopy with post occlusive hyperemia reactivity testing

	SSc-PH (n=20)	IPAH (n=5)	p-value
Average capillary density (n/mm)	4 [3-6]	10 [10-11]	**<0.001**
Pattern (n)			
Normal	0	4 (80%)	
Non-specific	0	1 (20%)	
Systemic sclerosis: early pattern	1 (4%)	0	
Systemic sclerosis: active pattern	1 (4%)	0	
Systemic sclerosis: late pattern	18 (72%)	0	
Post-occlusive reactivity hyperemia testing			
Rest (n/mm^2)	55 [39-73]	93 [80-97]	**0.006**
Average capillaries after PORH (n/mm^2)	53 [46-77]	100 [81-120]	**0.006**
Total recruitment of capillaries (n/mm^2)	1 [-4-5)	23 [-3-27)	**<0.05**
Average capillaries at venous congestion (n/mm^2)	55 [50-78]	106 [81-126]	**0.006**
Total recruitment of capillaries (n/mm^2)	5 [1-11]	11 [-9-30]	0.613

Values are in medians [interquartile range] or number (%).*Abbreviations:* NT-proBNP, N-terminal pro-Brain Natriuretic Peptide; POHR, post-occlusive reactivity hyperemia test

Conclusion: SSc-PAH patients showed higher markers of cardiac fibrosis and inflammation, compared to IPAH patients. These markers correlated well with peripheral microvascular dysfunction, suggesting that SSc-driven inflammation and vasculopathy concurrently affect peripheral microcirculation and the heart. This may contribute to the disproportionately high mortality in SSc-PAH patients.
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POS1286 ARRHYTHMIA IN PATIENTS WITH SYSTEMIC SCLEROSIS: A SWEDISH REGISTER-BASED STUDY

Keywords: Heart, Epidemiology, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is a connective tissue disease with multiple organ manifestations including cardiac involvement. Several studies have reported arrhythmias and conduction defects to be frequent in patients with SSc, however with considerable limitations such as the lack of comparison group or of stratified analyses by arrhythmia subtypes in some studies in addition to some study populations being highly selected from tertiary care centres.
Objectives: To explore the incidence of cardiac arrhythmias and its different subtypes in an unselected national cohort of patients with SSc compared to a matched cohort from the general population in Sweden.
Methods: We used nationwide Swedish registers to identify patients with incident SSc diagnosed between 2004 and 2015 in addition to comparators from the general population (1:5), matched on sex, birth year and residential area. We excluded those with a history of arrhythmia prior to start of follow-up. The primary outcome was the first ICD-coded visit indicating arrhythmia. Follow-up started from the date of SSc diagnosis, the same date was assigned to the respective comparators, until the primary outcome, death, emigration, or the end of 2016. We estimated the incidence rate of arrhythmias overall and stratified by subtype of arrhythmia in both patients with SSc and their comparators. We estimated incidence rate ratios (IRRs) using poisson regression models and time-varying hazard ratios (HRs) using flexible parametric models.
Results: We identified 1049 patients with SSc and 5147 matched comparators with no prior history of arrhythmia. The median follow-up was 4.7 years in patients with SSc and 5.8 years for the comparators. The incidence rate of arrhythmias overall was 216.5 per 10,000 person-years (95% CI 179.8-258.5) in patients with SSc and 106.6 (95% CI 95.5-118.7) in the comparators corresponding to IRR of 2.0 (95% CI 1.7-2.5). Table 1 demonstrates the incidence rates and IRRs stratified by arrhythmia subtypes. The HR of arrhythmia overall in patients with SSc compared to the comparators decreased gradually during follow-up; 3.0 (95% CI 2.2-4.1) at the end of the first year of follow-up, 1.9 (95% CI 1.4-2.5) at the end of the fifth year of follow-up, and 1.3 (95% CI 0.8-2.3) at the end of the 10th year of follow-up.
Conclusion: Patients with SSc have higher incidence rate of arrhythmia overall compared with matched comparators from the general population.

Table 1. Incidence rates of arrhythmias in patients with SSc and in general population comparators, overall and stratified by arrhythmia subtypes. Incidence rate ratios are estimated using poisson regression models.

	Patients with SSc		General population comparators		
	Number of cases	Crude incidence rate* with 95% CI	Number of cases	Crude incidence rate* with 95% CI	Incidence rate ratio (IRR) with 95% CI
All arrhythmias	122	216.5 (179.8-258.5)	335	106.6 (95.5-118.7)	**2.0 (1.7-2.5)**
Conduction disorders	14	23.5 (12.9-39.5)	61	18.9 (14.5-24.3)	1.2 (0.7-2.2)
Atrial fibrillation and flutter	89	154.5 (124.1-190.2)	241	75.8 (66.5-86.0)	**2.0 (1.6-2.6)**
Cardiac arrest and ventricular arrhythmia	18	30.2 (17.9-47.7)	33	10.2 (7.0-14.3)	**3.0 (1.7-5.3)**
Paroxysmal supraventricular tachycardia	11	18.5 (9.2-33.0)	24	7.4 (4.7-11.0)	**2.5 (1.2-5.1)**
Other	20	33.7 (20.6-52.1)	40	12.4 (8.8-16.8)	**2.7 (1.6-4.7)**

* per 10,000 person-years

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POS1287

KL6 AND IL-18 LEVELS ARE NEGATIVELY CORRELATED WITH RESPIRATORY FUNCTION TESTS AND ILD EXTENT ASSESSED ON HRCT IN PATIENTS WITH SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE (SSC-ILD)

Keywords: Biomarkers, Lungs, Systemic sclerosis

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Background: Interstitial lung disease (ILD) is one of the leading causes of mortality in patients with systemic sclerosis (SSc). Serum biomarkers have been suggested as indicators for pulmonary damage with clinical value in the diagnosis and prognosis of SSc-ILD.
Objectives: To investigate the role of serum biomarkers (Krebs von den Lungen-6 KL-6, IL-18 and IL-18BP) as potential biomarkers reflecting the severity of SSc-ILD as assessed through high-resolution computed tomography (HRCT) and pulmonary function tests (PFT), including forced vital capacity (%FVC) and diffusing capacity of the lung for carbon monoxide (%DLCO).
Methods: A cross-sectional study including patients with SSc fulfilling the 2013 ACR/EULAR criteria was performed. Patients were classified according to disease duration and pulmonary involvement (presence of ILD). All SSc patients underwent chest HRCT scans and pulmonary function test at baseline. Serum concentration of KL-6, IL8 and IL18BP were determined using sandwich ELISA technique (solid phase sandwich Enzyme Linked-Immunosorbent Assay), with kits from MyBiosource for KL-6 and from Invitrogen for IL18 and IL18BP. A semiquantitative grade of ILD extent was evaluated through HRCT scan (grade 1, 0–20%; grade 2, >20%). Extensive lung disease was defined as >20% of lung involvement on HRCT, and FVC <70% predicted and limited lung involvement as ≤20% of ILD involvement on HRCT, and an FVC ≥70% predicted.
Results: 74 patients were included, 27% were male. The mean age at diagnosis was 57.5±15 years. The mean time since diagnosis was 7.67±8 years. 28 patients had ILD (38%). 64 % of patients had <20% of ILD extent classified through HRCT scan. SSc-ILD patients had elevated serum KL-6 and IL-18 levels compared to patients without ILD (p=0.003 and p=0.04), and those findings were preserved after adjusting for age and sex (Table 1). Mean erythrocyte sedimentation rate (ESR) was higher in patients with SSc-ILD. A negative correlation between KL-6 levels and %FVC (β=-0.25, p 0.037) and %DLCO (β=-0.28, p 0.02) and between IL-18 levels and %FVC (β=-0.20, p 0.03) and %DLCO (β=-0.14, p 0.04) were found. Linear regression models representing correlation between KL-6 and PFT are represented in the scatter plot in Figure 1. Serum KL-6 and IL-18 levels successfully differentiated grades 1 and 2 (p = 0.028 and p=0.021). Semiquantitative grades of ILD on the HRCT scan were significantly proportional to the KL-6 (p 0.01) and IL-18 (p=0.03). A positive correlation between extensive lung disease and KL-6 (β=0.61, p 0.007) but not with IL-18 was found.
Conclusion: Serum KL-6 levels and IL-18 were increased in patients with SSc-ILD and showed a positive correlation with ILD severity as measured using a semiquantitative HRCT grading scale and a negative correlation with PFT parameters. KL-6 is positively correlated with extensive lung disease. Serum KL-6 and IL-18 could be a clinically useful biomarker in screening and evaluating SSc-ILD.

Table 1 : Demographic and clinical characteristics of patients with SSc-ILD and non-SSc-ILD.

	ILD (28)	ILD (-) (46)	P value
Mean age, years	57.3±16	57.7±28	0.97
Sex, male	6 (21%)	13 (28%)	0.51
Mean ESR (mm/h)	23±16	9±8	**0.04**
Mean CRP (mg/dL)	7.1±4.3	5.03±3.25	0.36
Serum KL-6 (U/mL)	320±68	262.5±39	**0.003**
Serum IL-18BP (U/mL)	150.46±130	123.23±90	0.21
Serum IL-18 (U/mL)	300.63±167	209.65±180	**0.03**
Pulmonary function tests	96.2±34	111±22.3	**0.01**
Mean FVC %	65.7±18	77.5±19.7	**0.001**
Mean DLCO%			

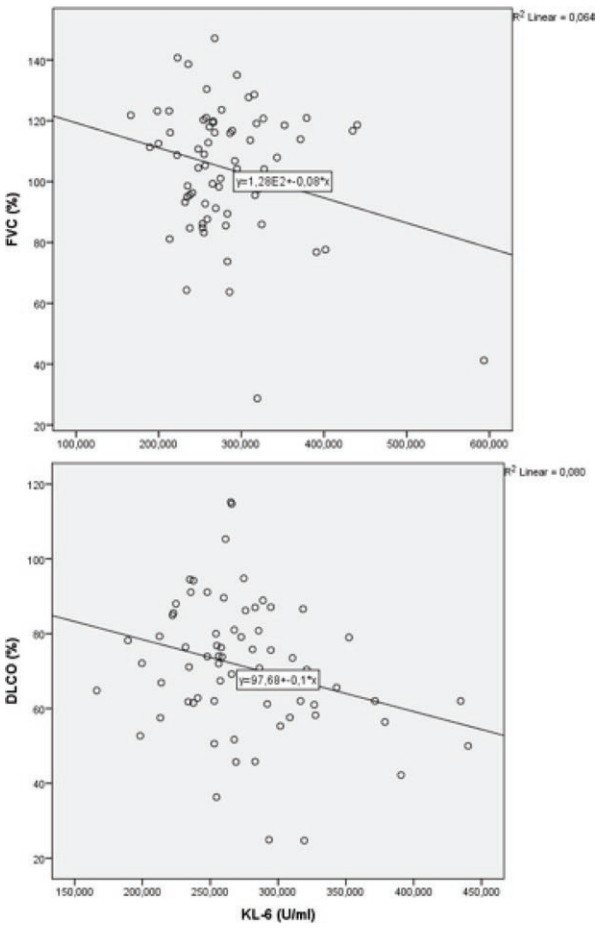


Figure 1 : Association between serum KL-6 level and FVC% and DLCO% of patients with ILD.DLCO%, diffusing capacity of carbon monoxide % predicted;FVC%, forced vital capacity % predicted;ILD, interstitial lung disease

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POS1288

PITFALLS WHEN ESTIMATING CAUSAL EFFECTS IN OBSERVATIONAL DATA: A SIMULATION STUDY BASED ON THE EUSTAR DATABASE

Keywords: Registries, Systemic sclerosis, Patient reported outcomes

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Background: To estimate the causal relationship between two variables it is important to first establish the potential causal pathways and to consider causes of bias. Omission of key confounders from the analysis, and biases introduced by selection processes and missing data, have the potential to yield coefficients that are smaller, larger, or even sign-reversed, compared to the true effect.

Objectives: To use simulation to illustrate the pitfalls of estimating causal effects in observational data, taking the relationship between forced vital capacity (FVC) and Health Assessment Questionnaire Disability Index (HAQ) in patients with Systemic Sclerosis (SSc) as an example.

Methods: We used a simplified directed acyclic graph (DAG) of the postulated causal pathways for simulation (Figure 1). The 8 nodes, some representing groups of variables, were: non-specific predisposing factors; SSc-specific predisposing factors; comorbidities; SSc; FVC; HAQ; selection; and non-missing data. Arcs (arrows) representing directed causal effects were drawn from earlier nodes in the pathway to each subsequent node. In statistical software [1] we drew the DAG and entered coefficients for each arc, informed in part by baseline descriptive data from ~17k patients in the EUSTAR registry (clinical project 96). We set a 'true' coefficient for the focal relationship between FVC and HAQ of -0.3; negative so that lower FVC would lead to higher HAQ. All variables were simulated to be continuous and all relationships were linear. We split the SSc variable at the 0.9997th and 0.9999th centiles to simulate three groups: no SSc, limited and diffuse SSc. We split the selection variable at the 1st or 3rd quartile to simulate weak selection (e.g. into the registry), or strong selection (e.g. into a clinical trial). We split the non-missing data variable at the 86th centile to simulate data missing not at random. We simulated 1000 datasets of N=76000000.

Results: Descriptive data from EUSTAR suggested that those with HAQ available were younger with shorter disease duration, higher rates of interstitial lung disease and lower rates of elevated systolic pulmonary pressure. In the simulated data, a regression model including all confounders (HAQ = FVC + SSc + Comorbidity + Specific + Non-specific) correctly estimated the coefficient for FVC in the population (median [95% simulation interval] -0.307 [-0.307 to -0.307]). Omitting confounders overestimated the coefficient by 5% to 28% depending which nodes were omitted. Including confounders, but sub-setting to include SSc only (-0.19 [-0.21 to -0.18]), to mimic weak (-0.18 [-0.20 to -0.17]) or strong selection (-0.17 [-0.20 to -0.15]) or to mimic both weak selection and missing data (-0.14 [-0.19 to -0.10]) underestimated the coefficient by 37% to 53%, although the model was correctly specified.

Conclusion: This simulation study illustrates the importance of considering the underlying causal pathways and potential biases when characterising relationships between key variables in observational datasets. Naïve analyses which do not account for confounding, selection bias and missing data can give misleading results. In this simplified example we might have concluded, in error, that the relationship between FVC and HAQ was weaker or stronger than it truly was. As we generated our own data, we knew the 'true' coefficient and the underlying data generating mechanisms. However, in practice we would know neither, but causal inference methods provide transparency as to the assumptions made during analysis and help identify any areas of concern. Careful consideration of the causal pathways to derive the appropriate model, and efforts to mitigate or remove sources of bias via study design and analysis, can improve accuracy and increase confidence in conclusions.

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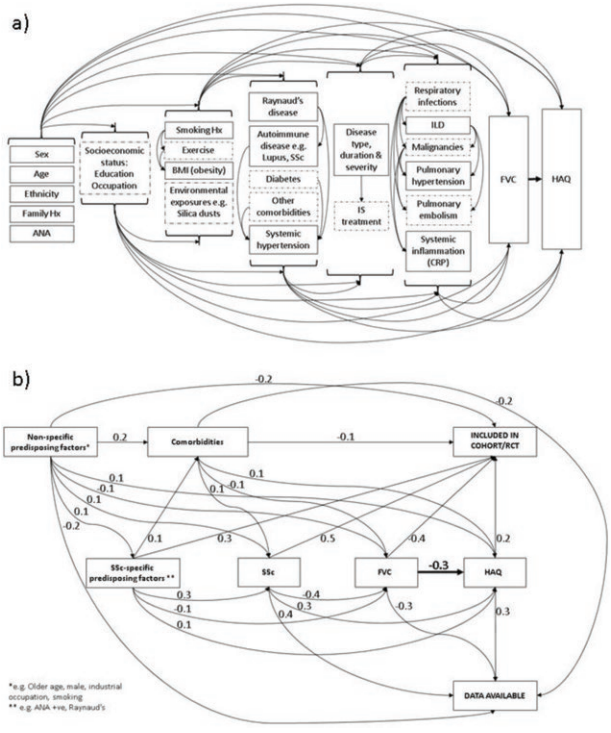


Figure 1 : Directed acyclic graphs a) full causal pathway b) simplified for simulation

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POS1289 MACHINE LEARNING ALGORITHM AS A USEFUL TOOL IN THE GREY AREA OF CARDIOPULMONARY MORTALITY IN SYSTEMIC SCLEROSIS

Keywords: Artificial intelligence, Cardiovascular disease, Systemic sclerosis

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Background: Prognosis of systemic sclerosis (SSc) patients is related to the presence of major internal organ involvement and specific autoantibody positivity. Cardiopulmonary complications are the leading cause of death in patients with SSc.
Objectives: The objective of the study is to evaluate the ability of an artificial intelligence algorithm based on laboratory and functional variables associated to SSc cardio-pulmonary involvement to predict the 5-year related mortality.
Methods: Laboratory and functional parameters of cardiopulmonary involvement of SSc patients symptomatic for dyspnoea, palpitations, or chest pain were recorded. Forced vital capacity (FVC), alveolar diffusion of CO (DLco), serum troponin, NT-pro-BNP, cardiac ejection fraction (EF) and pulmonary arterial systolic pressure (PAPs) were used for clustering by a partition around medoids (PAM) algorithm. The resulting clusters were compared for 5-year mortality due to SSc cardio-pulmonary causes.
Results: 216 patients were enrolled, aged 54.5±14.4 years, and with a disease duration of 7.4±7.0 years. The 12% of patients were male, 41% had a diffuse cutaneous disease, 45% were anti-Scl70 positive. With specific reference to cardiopulmonary involvement, 50% of patients had pulmonary fibrosis at HRCT, 15% pulmonary arterial hypertension, 16% a EF <55%, 11% increased levels of troponin, and 42% elevated NT-proBNP levels. During follow-up, 26 patients (12%) died because of causes related to cardiac-pulmonary involvement. The machine learning algorithm identified two different groups according to prognosis ($\chi 2(2) = 29.76$, $p<0.001$) with a 5-year mortality of 15% and 0.8%. Patients with higher mortality were characterized by lower FVC values and higher NT-proBNP and troponins compared to rest of the cohort ($p<0.001$). Furthermore, the prevalence of male gender, diffuse cutaneous disease, anti-Scl70 positivity and anti-centromere negativity were higher in the high-risk group compared with the alternative cluster ($p<0.05$ for all characteristics). Interstingly, in high mortality cluster a relevant percentage of patients apparently do not present classical risk factors for progressive SSc, in fact 40% were females, 30% of patients presented a limited cutaneous involvement, 36% were anti-Scl70 negative and 30% were anti-centromere positive, 26.4% did not presented pulmonary fibrosis, and 35% of patients did not have pulmonary hypertension.
Conclusion: An artificial intelligence algorithm based on laboratory-functional parameters of SSc cardio-pulmonary involvement was shown to be able to predict the prognosis of SSc patient more accurately than traditional predictors. Given the high mortality risk of patients with SSc, the application of dedicated prognostic algorithms could better support the clinician in the management of patients.
REFERENCES: NIL.
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Disclosure of Interests: None Declared.
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POS1290 INCREASED RISK OF MYOCARDIAL INFARCTION AND STROKE IN PATIENTS WITH SYSTEMIC SCLEROSIS: A NATIONWIDE COHORT STUDY

Keywords: Epidemiology, Systemic sclerosis, Cardiovascular disease

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Background: Previous studies have suggested a link between systemic sclerosis (SSc) and cardiovascular disease, but large-scale data are still lacking due to the nature of rare autoimmune diseases.
Objectives: We aimed to compare the incidence of myocardial infarction (MI) and stroke in patients with SSc and age- and sex-matched controls in a nationwide population-based cohort in Korea.
Methods: We included patients with SSc defined by the ICD-10 code (M34) and rare and intractable disease code (V138) and 1:5 age- and sex-matched controls using the Korean National Health Insurance Database. The outcomes of the study were MI and stroke. Cox proportional hazard analysis and Kaplan-Meier curve were used to compare the incidence of outcomes between patients with SSc and controls.
Results: A total of 4700 patients with SSc and 23500 controls were included in the study. The mean follow-up period was 5.6 ± 2.8 years. At baseline, patients with SSc had higher prevalent rates of comorbidities such as hypertension, hyperlipidemia, and congestive heart failure than controls. Patients with SSc had a 3-fold higher risk of MI (adjusted hazard ratio [aHR] 3.01, 95% confidence interval [CI] 2.41–3.76) and a 1.7-fold higher risk of stroke (aHR 1.65, 95% CI 1.28–2.14) compared to controls. There were no differences in the association between SSc and MI or stroke by age, sex, or comorbidities.
Conclusion: This nationwide population-based cohort study revealed an association between SSc and increased risk of MI and stroke. Therefore, careful monitoring and preventive measure for the cardiovascular diseases in patients with SSc are required.
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Disclosure of Interests: None Declared.
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POS1291 PREDICTION OF MORTALITY IN SSC-ILD DEPENDS ON DEFINITION OF ILD PROGRESSION

Keywords: Lungs, Systemic sclerosis, Prognostic factors

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Background: Progression of interstitial lung disease (ILD) is a candidate for long-term mortality in patients with systemic sclerosis (SSc). Different definitions of progression have been proposed. Declining lung function is often used, whereas others include composite definitions such as the 2022 ATS/ERS/JRS/ALAT guideline criteria for progressive pulmonary fibrosis (PPF) and the INBUILD criteria for progressive fibrosing ILD (PF-ILD). These different definitions have not been compared in SSc-ILD.
Objectives: To estimate the prevalence of ILD progression applying different definitions and test their performance of predicting mortality.
Methods: We included all SSc patients from the Oslo and Zurich cohorts who had ILD on HRCT and serial assessments of disease progression defined as:
(A) Absolute FVC decline >5% over 12 months
(B) PPF guideline criteria with 2/3 criteria present over 12 months of (1) worsening of respiratory symptoms; (2) absolute decline in FVC >5% or in DLCO >10% and (3) disease progression on HRCT
(C) INBUILD PF-ILD criteria within 24 months with (1) FVC decline ≥10%, (2) FVC decline >5-<10% and worsening of respiratory symptoms or increased lung fibrosis on HRCT, or (3) worsening of respiratory symptoms and increased lung fibrosis.
We assessed the prevalence of ILD progression using these competing definitions and applied multivariable cox regression models (with hazards ratios (HR) and 95%CI) adjusted for known risk factors for mortality and compared the performance using Harrels c-index.
Results: In total, 231 SSc-ILD patients from Oslo and Zurich were included, with 71 (31%) showing FVC decline >5%, 43 (19%) fulfilling the PPF guideline and 89 (39%) the INBUILD PF-ILD criteria. Most progressive patients fulfilled ≥1 definition of progression [60/107 (56%)] while 124 (54%) did not progress (Figure 1). Patient characteristics did not differ between the definitions, except for more extensive ILD and ground glass on HRCT and more frequent oxygen desaturation among those fulfilling the PPF criteria (Table 1). The number of deaths [44 (47%)] over mean 7.7 years (SD 3.9) follow up were comparable in the different groups. The progression definitions performed differently in multivariable cox models adjusted for age, sex, disease duration, SSc subtype, extent of lung fibrosis, baseline FVC and treatment using FVC decline>5% (HR1.87, 1.10-3.17

95%CI; p=0.020; c-index 0.7331), PPF guideline (HR1.42, 0.79-1.84 95%CI; p=0.231; c-index=0.7156) and INBUILD PF-ILD (HR 2.38, 1.40-4.04 95%CI: p<0.001; c-index=0.7338). The models discriminating ability was not significantly different (p=0.138).

Conclusion: The prevalence of ILD progression varies depending on which definition was applied. FVC decline alone and PF-ILD criteria predicted mortality significantly but not the 2022 PPF guideline criteria.

	FVC decline>5%	PPF	PF-ILD
Male sex, n (%)	20 (28)	12 (28)	25 (28)
Age at onset, y (SD)	49 (14.8)	50 (13.3)	49 (14.8)
Disease duration<3y, n (%)	43 (61)	24 (56)	33 (38)
dcSSc, n (%)	38 (54)	24 (56)	47 (53)
ATA, n (%)	33 (47)	20 (47)	35 (39)
CRP↑, n (%)	7 (14)	4 (15)	7 (14)
FVC, % (SD)	93 (19.6)	89 (19.5)	92 (20.7)
DLCO, % (SD)	66 (16.3)	61 (16.2)	64 (17.8)
Functional class 3&4, n (%)	9 (19)	6 (19)	12 (19)
ILD>10%, n (%)	20 (43)	18 (56)	26 (47)
Ground glass, n (%)	28 (42)	23 (56)	42 (48)
O_2 desaturation, n (%)	6 (14)	7 (30)	10 (18)
Immunosuppressives, n (%)	23 (32)	21 (49)	34 (38)
Death, n (%)	32 (45)	20 (47)	39 (44)

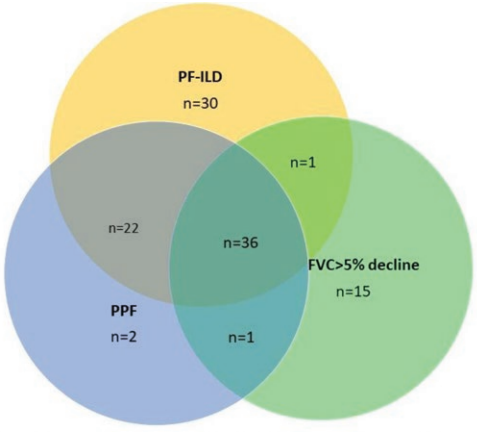


Figure 1: Venn diagram of patients fulfilling the different definitions of ILD progression

REFERENCES: NIL.

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POS1292 **WITHDRAWN**

POS1293 **STRAIN OF THE RIGHT VENTRICLE AS A TOOL OF EARLY DETECTION OF PULMONARY VASCULATURE ABNORMALITY IN SYSTEMIC SCLEROSIS**

Keywords: Cardiovascular disease, Systemic sclerosis, Lungs

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Background: Patients with systemic Sclerosis (SSc) are at risk of developing pulmonary hypertension (PH) of different etiologies. Two-dimensional and Doppler echocardiography is the reference screening tool and it is recommended yearly even in the absence of symptoms; however, elevated values of systolic pulmonary artery pressure (sPAP) are not detectable at rest in the early phases of the disease.
Objectives: The aim of the study was to determine whether early signs of right ventricular or right atrial dysfunction at speckle-tracking echocardiography might identify patients who are going to develop PH during follow-up.
Methods: We studied a consecutive cohort of 113 patients with a diagnosis of SSc according to the 2013 ACR/EULAR SSc classification criteria [1], undergoing screening for PH and who were followed-up regularly at a third-level centre of reference for SSc.
All patients underwent both the baseline echocardiographic examinations and at least one echocardiographic examination during follow-up in the referral center. Standard 2-D and Doppler echocardiography was performed with a Vivid 7 or Vivid E9 ultrasound system (GE Medical Systems, Norway); images and clips were saved for offline analysis on a GE workstation (EchoPAC PC SW). Clinical, laboratory and radiographical parameters, standard in the care of SSc, such as presence of Interstitial lung disease, left-heart disease (LHD), pulmonary function respiratory tests and biomarkers as BNP were concomitantly recorded for each patient. The DETECT step 1 and 2 values were calculated according to Coghlan JG et al [2]. When indicated according to guidelines, right heart catheterization to diagnose PH was performed. Statistical analysis was performed using SPSS by IBM for mac (v13).
Results: The study enrolled 93 females and 20 males, mean age was 58±13 yrs, median disease duration was 88 months (IQR 42-168); 86 (76%) patients had limited cutaneous involvement, 21 had a diffuse disease (18,6%) and 5 (4,4%) had no skin involvement at all. At baseline, anticentromere and antitopoisomerase antibodies were present in 38 (33,6%) and in 35 (31%) patients respectively. A clinically significant ILD was present in 17 (15%) of patients of the cohort at baseline. During follow-up (44±24 months), 10 patients were diagnosed with PH (overall incidence of 8.4%) which was classified as Group 1 PH in 4 cases (40%), Group 2 PH in 1 case (10%) in Group 3 PH in 5 cases (50%). Baseline standard echocardiographic parameters including the estimated sPAP and DETECT scores for step 1 and step 2 were similar in patients who developed PH and those who did not. However, peak longitudinal right ventricular (RV) strain (RVPLS) values were significantly lower in patients who subsequently developed PH (42,13 ± 12,21 vs 33,57 ± 11,52, p=0,019). In addition, PLS values tended to decrease over time and this decrease significantly predicted PH of any etiology (HR 0.94, 0,88-0,99; p=0,049).
Conclusion: In an SSc cohort of patients at risk of developing PH, adding the evaluation of 2D-Speckle-tracking echocardiography (STE) analysis, and in particular PLS of the RV, might intercept at an early stage an alteration of the right heart to aberrantly adapt to the pulmonary vasculature overload in different extrinsic pathological settings (ILD, LHD) and also in the presence of an intrinsic pulmonary vasculopathy.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1294 **PREVALENCE OF PULMONARY ARTERIAL HYPERTENSION IN PATIENTS WITH SYSTEMIC SCLEROSIS AND DIGITAL ULCERS TREATED WITH BOSENTAN AND SILDENAFIL: RESULTS FROM AN ITALIAN COHORT**

Keywords: Lungs, Systemic sclerosis, Cardiovascular disease

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Background: Systemic sclerosis (SSc) is a rare connective tissue disease where vascular damage, autoimmunity and fibrosis affect skin and organs. Among vascular manifestations, pulmonary arterial hypertension (PAH) is associated with poor prognosis accounting for about the 26% of SSc-related mortality rate [1]. Bosentan (an endothelin receptor antagonist) and Sildenafil (a selective inhibitor of phosphodiesterase 5) are approved for the treatment of SSc-related digital ulcers (DUs) and for PAH, both as mono and combination therapy.
Objectives: Evaluate the PAH prevalence in patients with SSc and DUs treated with Bosentan and Sildenafil combination therapy.
Methods: SSc patients with active or past DUs and in combination therapy for at least 3 months with Bosentan and Sildenafil were enrolled in a retrospective observational study. Demographical data, disease duration and antibody positivity were collected along with the most recent lung function test and echocardiographic esteem of pulmonary artery pressure (PAPs). Patients with a diagnosis of PAH preceding the introduction of the studied treatment were excluded. The prevalence of new onset PAH was then calculated and compared through Fisher Exact test with data from Morrisroe et al [1] whose studied population resulted homogenous to the one of the present study in term of age, sex and disease duration.
Results: Forty-seven patients were enrolled, of which 42 (89,4%) were female. Mean age was 57,87 (SD 14,87) and mean disease duration was 12,14 years (SD 5,87). Anti-Scl70 positivity was observed in 21 patients (44,7%) while anti-centromere positivity in 16 (34%). Pulmonary function tests and echocardiographic PAPs are resumed in Table 1. One out of 47 (2,1%) patients developed PAH. This was significatively lower in comparison to PAH prevalence (194 out of 1636, 11.8%) in Morrisroe et al (p 0.036)
Conclusion: The low prevalence of PAH recorded in this group of patients affected by SSc complicated by DUs suggests a protective role of the combination of Bosentan and Sildenafil against PAH, one of the most severe vascular manifestations of the disease. This data should be confirmed by prospective and controlled studies on larger populations.
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POS1295 **WITHDRAWN**

survival rates were calculated. The effect of age at disease onset, gender, clinical parameters, and autoantibodies were evaluated using Kaplan-Meier analysis.
Results: A total of 226 patients (85.8% female, mean age 61.9 years) were included. The mean ± SD duration of the disease was 12.24±8.9 years. The 5-year and 10-year survival were 95.59%, and 88.1%, respectively. In the majority of patients, the cause of death was related to SSc. The two main causes of death were interstitial lung disease (ILD) and heart disease (pulmonary arterial hypertension and/or arrythmias). Older age at disease onset was independently associated with worse survival (58.9± 11.9 years vs 47.3±14.6 years, p<0.05) and male patients had statistically worse OS compared to female patients (13.1 years vs 28.4 years, p=0,001). Patients with autoAbs against Th/To (12.1 years vs 28.2 years, p=0.013) or against NOR90 had worse OS compared to autoAb-negative patients (12.1 vs 28.2 years, p=0.013, and 12.7 vs 28.8 years p=0.007, respectively). There was a trend for a better survival in patients with anti-centromere autoAbs (29.4 vs 26.2 years, p=0.064).
Conclusion: Our results show that the overall survival rates of patients with SSc have improved over the years than those reported in the past. Cardiopulmonary diseases still remain the main causes of death, while male sex is associated with worse prognosis. Additional prognostic factors have emerged from autoAb profiles.
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POS1296 SURVIVAL RATES IN PATIENTS WITH SYSTEMIC SCLEROSIS ARE AFFECTED BY CONCURRENT CARDIOPULMONARY DISEASE, GENDER, AND AUTOANTIBODY PROFILE: A 15- YEAR SINGLE CENTER EXPIERENCE

Keywords: Autoantibodies, Epidemiology, Systemic sclerosis

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Background: Systemic Sclerosis (SSc) is a systemic autoimmune disease with a high mortality rate [1-3].
Objectives: The purpose of this study was to assess long-term survival rates of patients with SSc in a single rheumatology center and identify factors affecting the survival rates.
Methods: Retrospective analysis of unselected adult patients with SSc, diagnosed and followed up in the Rheumatology Clinic of the University Hospital of Larissa in Central Greece for 15 years (2007-2022). Demographics and clinical characteristics were retrieved from medical records. while autoantibodies (autoAbs) were assessed by indirect immunofluorescence and a SSc autoantibody line blot immunoassay (Euroimmun). Overall Survival (OS), 5-year and 10-year

POS1297 PULMONARY INVOLVEMENT IN VERY EARLY SYSTEMIC SCLEROSIS (VEDOSS): REPORT FROM A SINGLE CENTER

Keywords: Lungs, Systemic sclerosis

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Background: Previous work has described interstitial lung disease (ILD) in very early systemic sclerosis (VEDOSS) [1], but its progression over time is unknown. This can contribute decisively to the delineation of screening and monitoring strategies.
Objectives: To evaluate the prevalence of ILD and its course in a cohort of patients who persist in a VEDOSS state, followed in a tertiary systemic sclerosis unit, over 10 years.
Methods: Retrospective observational study of patients persistently fulfilling VEDOSS criteria [2], with sequential measurement of diffusing lung capacity for carbon monoxide (DLCO) and forced vital capacity (FVC), at 0, 1, 5 and 10 years. Chest CT at baseline was considered, when available. A DLCO or FVC <80% of predicted values was considered indicative of lung involvement [1]. A decline of

FVC or DLCO of ≥5% and ≥15% in any of the time intervals was considered clinically relevant [3]. Demographic, clinical, and immunological variables at baseline were taken as potential independent variables, including age, gender, disease duration, arthritis, capillaroscopy pattern, and autoantibody profile. Pearson $\chi 2$ test, Fisher's exact test or independent sample t-test were used for independent measures as appropriate. Repeated-measures ANOVA was used to compare variables over time.

Results: 30 patients (86,7% women, mean baseline age 46,9±12,87 yrs) were included; median time from first symptoms to diagnosis was 4,4 (IQR 7,6) yrs.

At baseline, 4 patients had mildly decreased DLCO values (60-79% of predicted), results being normal in all remaining persons (Table 1). During the first year of follow-up, a ≥5% decrease in FVC was observed in 6/30 patients (20%) and a DLCO decrease of ≥15% in 2/30 (6,7%). There was a non-significant trend for a higher probability of FVC and DLCO decrease in males vs females (M:50,0% vs F:15,3%F and M:25,0% vs F3,8%, respectively). None of the other variables was associated with FVC or DLCO decrease. Pulmonary tests were available for the 25 and 5 patients who reached 5 and 10 years of follow-up. No association was found between any of the clinical variables and significant change of FVC and DLCO at these time points. Mean values of FVC and DLCO consistently declined overtime, without reaching statistical significance (Table 1). The incidence of significant change in FVC and DLCO between contiguous evaluations is represented in Figure 1. There is a non-significant trend for a higher probability of decline as follow-up time increased.

Table 1 FVC and DLCO measurements at baseline and at 1, 5 and 10 years

	Baseline (n=30)	1 year (n=30)	5 years (n=25)	10 years (n=5)	p-value
FVC (% predicted), mean ± SD	112,7±15,9	111,5±15,5	109,6±18,4	110,8±26,1	NS
FVC <80% predicted, % (n)	0 (0)	0 (0)	4,0 (1)	20,0 (1)	NS
DLCO (% predicted), mean ± SD	96,6±14,1	97,8±16,1	90,7±13,9	85,7±10,6	NS
DLCO <80% predicted, % (n)	13,3 (4)	16,7 (5)	20,0 (5)	20,0 (1)	NS

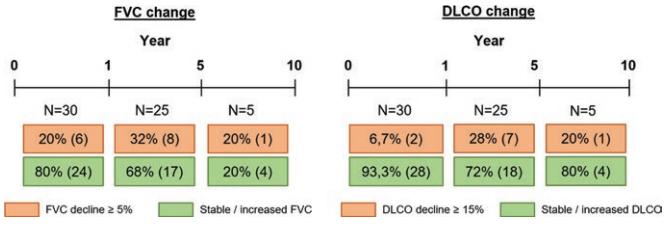


Figure 1 FVC and DLCO change at 1, 5 and 10 years

Conclusion: Our study provides data on the long-term assessment of FVC and DLCO in VEDOSS patients. There was a relevant decrease in FVC during the first year in 20% of the patients, and 20% had impaired DLCO (<80%) at 5 years, which suggests that a subset of patients who persist in VEDOSS state overtime still endure significant subclinical pulmonary involvement.

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POS1298

INTERSTITIAL LUNG DISEASE IN ANTI-CENTROMERE ANTIBODY POSITIVE SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Best practices, Lungs

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Background: Despite a lower risk of ILD and ILD progression in anti-centromere antibody (ACA) positive systemic sclerosis (SSc) patients, ILD may still occur and progress. Little is known regarding risk factors for ILD in ACA+ SSc patients to help guide screening with high-resolution computed tomography (HRCT), and risk of ILD progression in ACA+ SSc is understudied.

Objectives: To determine prevalence and risk factors for ILD in ACA+ SSc, to classify radiographic ILD patterns, and to evaluate rate of progression of ILD in ACA+ SSc.

Methods: A retrospective cohort of ACA+ SSc patients seen between 1/1/2007 and 12/31/2018, who met the 2013 ACR classification criteria or ≥3/5 CREST (calcinosis, Raynaud's, esophageal dysmotility, sclerodactyly, telangiectasias) criteria was identified. Subjects had to have ≥1 HRCT within 2 yrs. prior to or anytime following SSc diagnosis (dx). Two radiologists reviewed all HRCTs with interstitial abnormalities to classify by consensus into 9 radiographic patterns (1,2): confident usual interstitial pneumonitis (cUIP), probable UIP (pUIP), non-specific interstitial pneumonitis (NSIP), suggests hypersensitivity pneumonitis (sHP), lymphocytic interstitial pneumonia (LIP), organizing pneumonia (OP), not characteristic (NC) of a specific ILD pattern, too little fibrosis (LF) to characterize, and suggests sequelae of pulmonary arterial hypertension (PAH)/pulmonary venoocclusive disease (PVOD). Clinical and demographic characteristics were compared between ILD+ and no ILD (included PAH/PVOD sequelae) subjects using χ^2 tests of proportions for categorical data, and two-sample t-tests for continuous data. Kaplan-Meier curves estimated the risk of ILD progression, defined as a relative decline of 10% in forced vital capacity (FVC) from baseline PFT performed ±6 mo. of latter of SSc or ILD dx.

Results: 99/480 (21%) of subjects had interstitial changes on HRCT: 5 cUIP, 7 pUIP, 28 NSIP, 14 sHP, 6 LIP, 2 OP, 11 NC, 17 LF, and 9 PAH/PVOD sequelae. There were no differences in time between SSc dx and HRCT between ILD+ and no ILD groups (median 6 yrs. (IQR 2, 14) vs. 6 yrs. (IQR 1, 15), respectively, p=0.44) or Raynaud's phenomenon (RP) onset and HRCT (median 15 yrs. (8, 29) vs. 17 yrs. (9, 29), respectively, p=0.54). Older age at RP onset (median 55 yrs. (42, 62) vs. 44 yrs. (33, 55), ILD+ vs. no ILD, p<0.001) and at SSc dx (median 62 yrs. (55, 72) vs. 56 yrs. (45, 65), ILD+ vs. no ILD, p<0.001) were significantly associated with ILD. A positive SSA was more common in ILD+ vs. no ILD subjects (15/72 (21%) vs. 43/340 (13%), respectively, p<0.05). Sex, race/ethnicity, smoking status, cutaneous subtype, esophageal dysmotility, digital ischemia, abnormal nailfold capillaries, telangiectasias, calcinosis, and synovitis were not associated with ILD (p>0.05). In a subgroup analysis of UIP/NSIP (n=40) compared with no ILD (n=390), older age at RP onset was significantly associated with UIP/NSIP (median 55 yrs. (46, 61) vs. 44 yrs. (33, 55), p=0.042). There were no significant differences in baseline FVC% and DLCO% among ILD patterns (p>0.05). ILD progression was observed in 51% of patients with ILD by 72 mo. (Figure 1A). There was no significant difference in risk of ILD progression between the UIP/NSIP and sHP/LIP/OP/IP/LF subgroups (Figure 1B, p=0.67).

Conclusion: To our knowledge, this is the largest study characterizing radiographic ILD patterns and assessing risk factors for prevalent ILD in ACA+ SSc patients. Older age at onset of RP and SSc dx, and a positive SSA, identifies a higher risk population for HRCT screening. UIP/NSIP accounted for close to half of ILD cases. Other radiographic patterns including sHP and IP require further study to determine potential underlying factors (e.g. exposure history, aspiration). The rate of ILD progression was similar between UIP/NSIP vs. other interstitial patterns, with half of subjects experiencing progression by 6 yrs. This underscores the role of HRCT screening for ILD detection and periodic PFTs for monitoring even in lower risk SSc populations.

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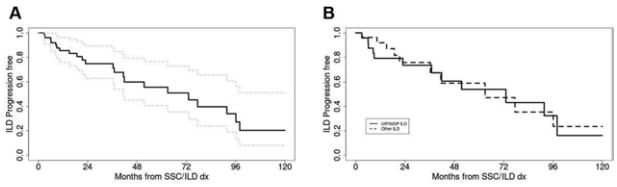


Figure 1. Kaplan-Meier Survival Curves Evaluating Time to ILD Progression in ACA+ SSc-ILD subjects. ILD progression is defined as a relative decline of 10% in FVC% predicted from baseline PFT. Baseline PFT was performed within 6 months of the latter of SSc or ILD diagnosis. The 2-year and 5-year progression free survival was 75% (95% CI 63% to 89%) and 56% (95% CI 41% to 76%), respectively (A). There were no significant differences in progression rates for the UIP/NSIP subgroup compared with the subgroup of all other ILD patterns (B, p=0.67, log-rank test).

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POS1299 LONG-TERM NEURODEVELOPMENTAL OUTCOME OF CHILDREN BORN TO SYSTEMIC SCLEROSIS WOMEN: PEDIATRIC NEUROPSYCHIATRIC ASSESSMENT THROUGH A SET OF VALIDATED TOOLS

Keywords: Pregnancy and reproduction, Quality of life, Systemic sclerosis

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Background: The neurodevelopmental (ND) outcome of children born to women with autoimmune disorders might be affected by factors related to maternal disease (*e.g.* the transplacental passage of maternal antibodies/drugs), as well as by mothers' coping with their disabilities during growth. These aspects have been studied in rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) [1]; no data are available for Systemic Sclerosis (SSc).

Objectives: To evaluate the long-term ND outcome of children born to SSc mothers.

Methods: A pediatric neuropsychiatric evaluation was proposed to SSc mothers with at least one child ≤18 years (August 2021-June 2022). Evaluations, performed by a child neuropsychiatrist, included the assessment of the following domains:

- Developmental/Cognitive skill (Griffiths Mental Development Scales III -GMDS-III- and Wechsler Scale for corrected age)
- Adaptive behavior (Vineland Adaptive Behavior Scales-II -VABS-II-)
- Social/Behavioral problems (Child Behavior CheckList and Youth Self Report -YSR- for children ≥11 years)
- Quality of life (Pediatric Quality of Life Inventory 4.0 -PedsQL-)

A set of questions to investigate the child's ND milestones were submitted to mothers. Data about maternal disease were retrieved from medical records.

Results: 20 children (median age 8 years; F/M 1:1) born to 12 SSc mothers were evaluated: 4 were born before and 16 after SSc onset. Four preterm births (<37 gestational weeks -GW-) (one twin pregnancy) and no small for gestational age babies were recorded. One child already had a diagnosis of autism spectrum disorder (ASD) at enrollment. All the children showed a normal score for developmental or intelligence quotient (IQ) and in all VABS-II domains, except for the child affected by ASD. YSR, administered to 6 children, highlighted an impairment in social abilities (*e.g.* extra-academic/social activities). In CBCL, externalizing problems (*e.g.* aggressive behavior, hyperactivity) were reported in 3 children (15%), while internalizing problems (*e.g.* anxiety, somatic complaints) in 2 (10%). The lowest scores at PedsQL were observed in the emotional domain. Different types of sleep disorders were reported in 45% of children. No significant differences were found in maternal characteristics upon the comparison between children with/without ND abnormalities. Children and mothers' features are shown in Table 1.

Conclusion: Children born to SSc mothers displayed normal intellectual functioning. The reported impairment in social abilities, suggesting an "adult profile", possibly reflect the effect of coping with maternal disabilities. Our data did not show a specific pattern of ND alterations in the offspring of SSc mothers; however the inclusion of a child neuropsychiatrist in the multidisciplinary team dedicated to SSc patients and their families seems to be important to detect and correct any possible ND problems at an early stage.

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Acknowledgements: he Authors would like to thank the Italian association of SSc patients 'GILS' (Gruppo Italiano Lotta Sclerodermia) for kindly supporting the project.

Disclosure of Interests: None Declared.

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POS1300 NAILFOLD CAPILLAROSCOPY FOR STANDARD CLINICAL PRACTICE: ARE TWO FINGERS AS ACCURATE AS EIGHT?

Keywords: Systemic sclerosis

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Background: Nail-fold capillaroscopy (NFC) is a non-invasive, in vivo diagnostic tool for the assessment of microvasculature of the proximal nail fold. The comprehensive approach based on assessment of four finger each hand excluding the thumbs (in total eight fingers are examined) is the gold standard for NFC evaluation and scoring. The patient is identified to have abnormal nailfold capillaries, if abnormality was present in any finger/nailbed. However, this process is time consuming and is not applicable in standard clinical practice. Therefore, a question was raised can a concise approach based on assessment of a smaller number of fingers be implemented in standard practice. The challenge to this hypothesis is that there may be marked variability in the nailfold morphology between different fingers, as abnormalities may only be seen in some but not all fingers.

Objectives: 1. To evaluate the comparability of the concise to the comprehensive approach (the gold standard) represented as the percentage of agreement of the NFC patterns recorded from each approach. 2. To assess the statistical difference on comparing the concise approach score to the gold standard score.

Methods: This was a prospective, cross sectional multicenter study. 164 Patients were recruited for this study. The patients' cohort included systemic sclerosis,

Table 1. Characteristics of SSc women and their offspring

Mother	Antibodies	Cutaneous involvement	Digital Ulcers	ILD	Child	GW at birth, pregnancy complications	Cognitive domain	Adaptive behavior	Social and behavioral domain	Sleep disorders
1	Scl-70	lcSSc	1	0	M, 12 yr	40	N	N	A	0
					M, 10 yr	40	N	N	N	0
2	ANA+	lcSSc	0	0	M, 7 yr*	40	A	A	A	1
					F, 5 yr	40	N	N	N	1
3	Th/To	lcSSc	1	0	M, 13 yr	39	N	N	A	0
					F, 9 yr	39	N	N	N	1
4	Scl-70	dcSSc	1	1	•F, 11 yr	39	N	N	A	1
					M, 5yr	39	N	N	N	0
5	Scl-70	dcSSc	0	1	•F, 11 yr	39	N	N	A	1
					M, 2 yr	35°	N	N	N	1
6	ACA	lcSSc	0	0	M, 3 yr	41	N	N	N	1
7	Scl-70	lcSSc	0	0	•F, 17 yr	32^	N	N	B	0
					•F, 13 yr	39	N	N	N	0
					M, 9 yr	39	N	N	N	0
8	ACA	lcSSc	0	0	F, 1 yr	39	N	N	N	0
9	Scl-70	dcSSC	1	1	F, 8yr$	31°	N	N	N	1
					M, 8yr$	31°	N	N	N	0
10	U1-RNP	lcSSc	0	0	F, 5 yr	38	N	N	N	0
11	Scl-70	dcSSc	0	0	M, 3yr	39	N	N	N	1
12	U1-RNP	lcSSc	1	0	F, 1 yr	40	N	N	N	0

ANA: anti-nuclear antibodies, ACA: anti-centromere antibodies, GW: gestational weeks; lcSSc: limited cutaneous SSc, dcSSc: diffuse cutaneous SSc, ILD: interstitial lung disease, 0: absent, 1: present, N: normal, B: borderline, A: abnormal*ASD diagnosis, •born before SSc onset $ Twins, °Gestational diabetes, ^Preeclampsia/IUGR

rheumatoid arthritis, psoriatic arthritis, systemic Lupus erythematosus, Behcet's disease, Sjogren's syndrome and mixed connective tissue diseases. Imaging sessions were carried following the national standard for NFC [1]. NFC with 200x magnification was used to capture panoramic nailfold videocapillaroscopy images. Images were recorded from 4-fingers each hand, excluding the thumbs. For each finger 5 parameters were assessed: density, architecture, hemorrhage, neoangiogenesis and dimension. Semiquantitative scoring system was implemented to score each parameter [2].

Results: Considering the correct diagnosis using the gold standard score was 100%, the concise approach based on mean of the scores recorded from the middle and ring fingers both hands gave the correct pattern in 155/164 (94.5%) of the cases. There was no statistical difference between the comprehensive approach total score (3.5+0.76 [CI 95% 1.918 - 5.082]), when compared to the concise total score from 2 fingers both hands which was (3.25+2.87 [1.873 - 4.626], p= 0.18. There was no significant difference on comparing the right to the left hand fingers.

Conclusion: Examining the NFC from middle and ring fingers in each hand, can be time saving and not inferior to the comprehensive NFC assessment. Concise approach can be used in the standard clinical practice and, in the meantime, are able to give an overall NFC picture reflecting the real state of the nailfold capillaries.

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POS1301 MORTALITY AND CAUSES OF DEATH AMONG FINNISH PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Epidemiology

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Background: Systemic sclerosis (SSc) is a rare rheumatic autoimmune disease, characterized by vasculopathy and fibrosis of the skin and internal organs [1]. Mortality and morbidity of systemic sclerosis is significant. The studies assessing changes in the mortality of SSc are controversial, only minor sign of improvement of prognosis is seen. Among SSc-related causes of death scleroderma renal crisis has become rare and cardiopulmonary causes have become more common. Most of the studies are conducted using either the ACR 1980-criteria or the LeRoy and Medsger -criteria.

Objectives: Aim of this study was to examine mortality and basic causes of death among Finnish patients with systemic sclerosis (SSc) during years 2000-2020 using the ACR/EULAR 2013 criteria for SSc diagnosis.

Methods: Patients with a diagnostic code of systemic sclerosis (ICD-10 codes beginning with M34) that appeared at least once in their medical records during the years 1996–2018 were identified from the hospital discharge registers of Turku and Oulu University hospitals. False diagnoses and typing errors were excluded. Using ACR/EULAR 2013 criteria and clinical findings, the diagnoses were reclassified and divided into different subsets of the disease. These subsets were diffuse cutaneous systemic sclerosis (dcSSc), limited cutaneous systemic sclerosis (lcSSc), over-lap SSc (diagnosis of other rheumatic disease fulfilled simultaneously) and sine scleroderma (SSc without skin affision). The clinical data was collected to the end of year 2020. The death certificates including the basic and imminent causes of death were obtained from Statistics Finland until August 2021. By examining patient records and death certificates the basic cause of death for each subject was re-evaluated. The study data were collected and managed using REDCap electronic data capture tools hosted at the University of Turku.

Results: Among 313 SSc patients, 91 deaths occurred between 4/2000- 9/2020. 35 deaths were caused by SSc, 20 by atherosclerosis, 18 by cancer and 18 by other causes. Majority of SSc-related deaths were due to interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH), 13 and 11 deaths respectively. Four deaths were due to scleroderma renal crisis (SRC), three deaths due to gastrointestinal tract involvement, two due to SSc-related myocardial involvement and two due to other SSc-related causes, those were vasculopathy complications. The mean age at dead of patients who died of a SSc-related cause was 65.6 years (SD 12.7, CI= 61.2-70.1) in contrast to patients who died due to other causes was 74.2 years (SD 9.6, CI= 71.5-76.9), the difference was statistically significant (p=0.0006). The median time from SSc diagnosis to death was 4.4 years [IQR 1.5, 11.8] in the SSc-related death group and 10.8 years [IQR 4.7, 17.1] for others, the difference was statistically significant (p=0.0061). Death due to renal crisis occurred fastest, in two months. An ILD related death occurred 11.8 years after and a PAH related death 3.7 years after the SSc diagnosis on average. In females, PAH and ILD were the most common causes of death, both nine of 25 subjects. In males, ILD was the most common cause of death, in four of ten subjects. In the group of dcSSc, the most common cause of death was ILD with five deaths out of twelve. In the group of lcSSc, PAH and ILD were the most common causes of death with both eight of 19 deaths. Four deaths due to SRC were all in the group of dcSSc. Twelve of 23 patients with dcSSc (52%) and nineteen of 60 patients with lcSSc (32%) died due to SSc.

Conclusion: The main finding in our study is the fact, that SSc disease itself is the major cause of death among Finnish SSc patients. Among the SSc related deaths, ILD and PAH were the leading causes of death. The patients who died due to SSc were significantly younger and the time from SSc diagnosis was significantly shorter compared to those who died due to other causes.

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Disclosure of Interests: Saara Kortelainen Speakers bureau: Boehringer-Ingelheim, UCB, Consultant of: Boehringer-Ingelheim, Markus Käyrä: None declared, Tiia Rissanen: None declared, Johanna Paltta Speakers bureau: UCB, Laura Pirilä Speakers bureau: Abbvie, Boehringer-Ingelheim, Jansen-Cilag, Novartis Finland, Sandoz, Eli Lilly and Swedish Orphan Biovirtum, Consultant of: Abbvie, Boehringer-Ingelheim, Jansen-Cilag, Novartis Finland, Sandoz, Eli Lilly and Swedish Orphan Biovirtum, Johanna Huhtakangas Speakers bureau: Boehringer Ingelheim, Abbvie, Amgen, Novartis, Consultant of: Boehringer Ingelheim, Abbvie, Amgen, Novartis.

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POS1302 SPECKLE-TRACKING GLOBAL LONGITUDINAL STRAIN AS A PREDICTOR OF CLINICAL OUTCOMES IN SYSTEMIC SCLEROSIS PATIENTS

Keywords: Prognostic factors, Systemic sclerosis

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Background: Primary cardiac involvement occurs in up to 40% of patients affected by systemic sclerosis (SSc), and although it may be asymptomatic is associated with negative outcomes. Speckle-tracking derived global longitudinal strain (GLS) has been proven to be a cost-effective tool in the detection of left ventricular (LV) and right ventricular (RV) dysfunction in patients with SSc and no overt cardiac disease [1].

Objectives: The aim of this study was to assess whether GLS can predict clinical outcomes in patients with SSc.

Methods: We conducted a prospective observational study enrolling all consecutive patients referred to our Scleroderma Unit between June 2016 and January 2022. All patients had a definite diagnosis of SSc according to ACR/EULAR criteria and no overt cardiac disease, pulmonary arterial hypertension, or atrial fibrillation at the time of enrollment. For each patient, echocardiogram and GLS calculations were performed at baseline and at each follow-up. We also collected all data regarding clinical history, hospitalizations or adverse events and ECGs.

Results: 164 patients (148 female, 58±14 years) were enrolled. Overall, 19 (11.6%) patients died during a median follow-up of 3.2 years for mainly non-cardiovascular deaths (7.3%) while cardiovascular deaths were lower (3% non-sudden, 1.3% sudden). Left GLS at first visit was associated with all-cause death, with a 1% left GLS worsening associated with a 19% increased risk of death after adjusting for age, gender, and LVEF (adjusted HR 1.19; 95% CI 1.05-1.35; p=0.007). Similarly, right GLS at first visit was associated with all-cause death, with a 1% right GLS worsening associated with a 12% increased risk of death after adjusting for age, gender, and TAPSE (adjusted HR 1.12; 95% CI 1.03-1.21; p=0.005). Patients with a left GLS worse (i.e. higher) than -20% had a 3.5-fold increased risk of death when compared to patients with better left GLS (HR 3.55; 95% CI 1.28-9.88; p=0.015; Figure 1a). Similarly, patients with a right GLS worse than -20% had a 4.5-fold increased risk of death when compared to patients with better left GLS (HR 4.47; 95% CI 1.4-13.74; p=0.009; Figure 1b).

Conclusion: We demonstrated that GLS is associated with clinical outcomes in patients with SSc. GLS is a reproducible and cost-effective echocardiographic

based method to assess SSc primary heart involvement and its progression, therefore allowing an earlier intervention in patients with worse prognosis.

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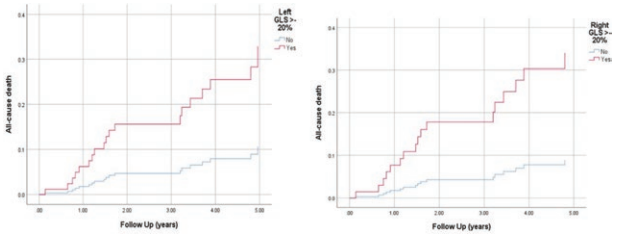


Figure 1.

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POS1303 ARTHRITIS AND RISK STRATIFICATION OF PATIENTS WITH VERY EARLY SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Inflammatory arthritides

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Background: Regular monitoring of patients with very early systemic sclerosis (veSSc) is essential for detecting disease progression. Whereas arthritis is associated with a worse prognosis in established disease [1], knowledge about its relevance in veSSc is scarce.

Objectives: Our objective is to assess the prevalence of arthritis in patients with veSSc, its association with other disease features and its impact on progression to established SSc.

Methods: We included patients with veSSc defined as presence of Raynaud's phenomenon and at least one of puffy fingers, antinuclear antibodies (ANA), abnormal capillaroscopy, not fulfilling the ACR/EULAR 2013 classification criteria for SSc at baseline. Data about arthritis were based on clinical diagnosis of synovitis by the treating physician, and verified in the electronic records in order to exclude arthritis due to other causes. *We investigated associations between arthritis and relevant clinical parameters cross-sectionally at baseline using Fishers' and Mann-Whitney-U tests. A longitudinal analysis* using Kaplan-Meier plots and multivariable Cox regression was performed to investigate arthritis as a potential predictor of progression towards established SSc (fulfilment of ACR/EULAR criteria at any follow-up visit).

Results: Of 161 patients included, 110 had at least one follow-up visit, with a median follow-up of 2.0 years. Baseline characteristics are shown in the Table 1. SSc-related arthritis was reported in 22/161 (13.7%) patients and was mostly seronegative (20/22, 90.9%), only one patient having an overlap syndrome with seropositive rheumatoid arthritis.

Table 1. Baseline characteristics

Variable	Frequency/Median
Age, median (years) (IQR, Q1-Q3)	48 (25, 35-60)
Female	144/161 (89.4%)
2013 EULAR/ACR classification criteria fulfilled at any time during follow-up	45/161 (28%)
Disease duration since first Raynaud symptom (years; median, IQR, Q1-Q3)	3.1 (9.33, 1.08-10.42)
SSc-related synovitis (n, %)	22/161 (13.7%)
CRP elevation (n, %)	18/153 (11.8%)
ESR elevation (>25mm/1h; n, %)	16/144 (11.1%)
Anti-centromere positive (n, %)	83/155 (53.5%)
Anti-Scl-70 positive (n, %)	13/153 (8.5%)
Anti-RNA Polymerase III positive (n, %)	12/135 (8.9%)
ILD on HRCT (n, %)	10/135 (7.4%)
SSc pattern on nailfold capillaroscopy (n, %)	82/161 (50.9%)
Digital ulcers (n, %)	5/135 (3.7%)
Pitting scars (n, %)	3/136 (2.2%)
Puffy fingers (n, %)	33/147 (22.4%)
Modified Rodnan skin score (median, IQR, min-max)	0 (0, 0-4)

Abbreviations: ILD-interstitial lung disease; HRCT-high resolution tomography; CRP C-reactive protein; ESR erythrocyte sedimentation rate

We found a statistically significant association between arthritis and presence of anti-centromere antibodies (p=0.008). Arthritis was neither associated with the other SSc-specific antibodies (anti-Scl70 and anti-RNA-Polymerase III), nor with inflammatory markers. Overall, 45/161 (28%) patients progressed to established SSc during follow-up. There was no statistically significant difference in fulfilling the classification criteria at follow-up between patients with- and without arthritis (Figure 1).

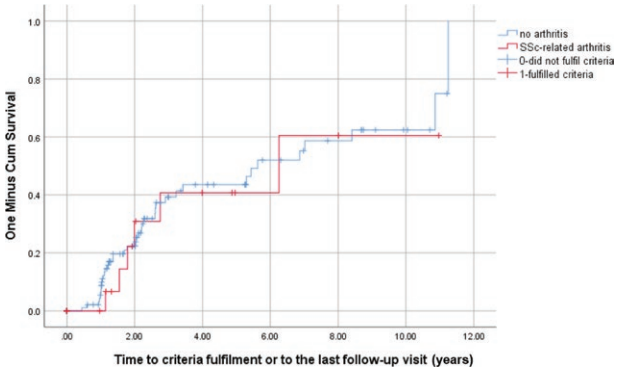


Figure 1. Kaplan Meier analysis for progression to SSc stratified by SSc-related arthritis.

Furthermore, arthritis was not a significant predictor for progression to established SSc in a multivariable Cox regression model adjusted for known predictors (specific antibodies, puffy fingers and SSc pattern on capillaroscopy [2]). In this model only the specific antibodies (p = 0.036) and puffy fingers (p = 0.045) reached significance.

Conclusion: In this first study analysing arthritis in veSSc, we found a relevant prevalence of arthritis in this mildly affected cohort. Presence of anti-centromere antibodies was significantly associated with arthritis at baseline. Arthritis was not a prognostic factor for progression towards established SSc in our cohort.

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POS1304 PREDICTORS OF DISEASE ACTIVITY PERSISTENCE AND DAMAGE IN A MONOCENTRIC SYSTEMIC SCLEROSIS COHORT

Keywords: Prognostic factors, Systemic sclerosis

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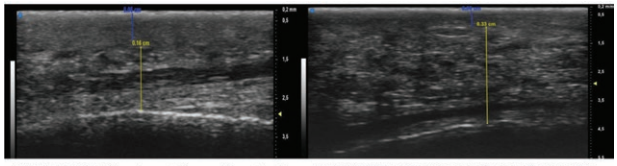
Background: Systemic sclerosis (SSc) carries a significant burden of disease-related morbidity and life-threatening complications. Unlike other rheumatic disorders (e.g., systemic lupus erythematosus and rheumatoid arthritis), the concepts of "disease activity" and "damage" have only recently been defined in SSc.
Objectives: We aimed to identify clinical and serological predictors of persistence of disease activity and remission in a monocentric prospective cohort of systemic sclerosis patients. Our second aim was to evaluate potential predictors of persistence or new onset of moderate-to-severe damage in our cohort.
Methods: Adult patients fulfilling the ACR/EULAR 2013 classification criteria for SSc and referring to our center from 2013 to 2021 were enrolled. Clinical findings, serological indices and internal organ involvement (pulmonary, cardiac, gastrointestinal, renal and musculo-skeletal) at baseline and at each visit during follow-up were retrospectively analyzed. At least one follow-up visit was required to be included in the study. EUSTAR-AI (European Scleroderma Trials and Research group Activity Index) [1], Medsger severity scale (MSS) [2] and SCTC (Scleroderma Clinical Trials Consortium) damage index [3] were calculated at each visit, at baseline and during follow-up. Follow-up period was defined as the time between baseline and the last available visit. Active disease was defined as an EUSTAR-AI ≥ 2,5, while remission as an EUSTAR-AI <2,5; activity persistence was defined as an EUSTAR-AI ≥ 2,5 in more than 50% of follow-up visits. According to the literature, damage was classified as mild (SCTC damage index < 6) and moderate-severe (SCTC damage index ≥ 6).
Results: 173 SSc patients (87,9% females) were enrolled in our study and followed up for a median time of 3,5 years. The median disease duration at baseline was 9 years while the median age at diagnosis was 45 years; 34,6% of patients had diffuse cutaneous SSc. Patients with persistently active disease during follow up (13,2%) had at baseline a significantly higher frequency of diffuse cutaneous subset (54% vs 17%, p<0,0001) and cardiac involvement (43,4% vs 20,7%, p=0,036) than persistently inactive patients; erythrocyte sedimentation rate (ESR) values were higher (p=0,002) and total lung capacity (TLC) values were lower (p=0,034) in persistently active patients. Positive anticentromere antibodies (ACA) were associated with persistent remission (p=0,042). Persistent disease activity was associated with higher disease severity [MSS 6,3 (±3) vs 3,5 (± 1,7)], p<0,0001] and more severe damage [SCTC-DI 3,7 (±4) vs 1,3 (±1,9), p<0,0001] at baseline. At the multivariate analysis, ESR values (OR 1,04 95% CI 1,01-1,07) and MSS values at baseline (OR 1,75, 95% CI 1,29-2,37) were independent predictors of activity persistence. Patients with persistent or new onset of moderate-severe SCTC at the end of the follow up (9%) had more frequently telangiectasia (81,3% vs. 38,6%, p=0,001) and ILD (62,5% vs. 31,6%, p=0,013) at baseline than patients with mild damage; they also showed lower DLCO values (p=0,047) and lower TLC values (p<0,0001), as well as higher systolic pulmonary arterial pressure (sPAP) on transthoracic echocardiography (p< 0,0001) at baseline. Multivariate analysis showed that TLC values (OR 0,95, 95% CI 0,92-0,98) and telangiectasia (OR 4,7, 95% CI 1,18-18,54) were independent predictors of moderate-severe damage. An association was found between persistence of disease activity and moderate-severe damage at the end of follow-up (p=0,003).
Conclusion: Identifying predictors of disease activity persistence and damage accrual at baseline may help to improve the risk stratification of SSc patients, through the identification of those patients who require prompt treatment and a more thorough clinical follow-up.
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POS1305 ULTRA-HIGH-FREQUENCY ULTRASOUND FOR THE EVALUATION OF SKIN INVOLVEMENT IN SYSTEMIC SCLEROSIS: PRELIMINARY RESULTS OF A MONOCENTRIC STUDY

Keywords: Ultrasound, Systemic sclerosis, Outcome measures

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Background: Cutaneous involvement is one of the most important clinical aspects of systemic sclerosis (SSc) and is characterized by three different phases in temporal sequence: oedematous, fibrotic and atrophic. The most widely used method to evaluate skin involvement is the modified Rodnan Skin Score (mRSS), which assigns a grade from 0 (normal) to 3 (severe) in 17 different areas of the body. However, the intra- and inter-operator variability of mRSS is considerably high. Thus, a more objective, sensitive and reproducible method for measuring skin involvement in SSc would be needed, both for clinical trials and for daily clinical practice.
Objectives: To evaluate the possible role of ultra-high-frequency skin ultrasound in patients with SSc.
Methods: Consecutive SSc patients fulfilling ACR/EULAR classification criteria were enrolled in this cross-sectional study. Patients with active immunosuppressive (IS) treatment were not excluded. Subjects with idiopathic Raynaud's phenomenon (RP) and healthy controls (HC) were also evaluated upon informed consent. All subjects underwent US evaluation, using a 70 MHz ultra-high frequency (UHF) probe, by an experienced radiologist, blinded to the clinical characteristics of the patients and controls, at six anatomical sites (forearm right and left, hand right and left, second finger right and left). The thickness of the dermis, epidermis and hypodermis was measured at each site, and the mean value between the right and the left side was used (Figure 1). Differences between groups were analysed using the ANOVA. The Pearson coefficient was used to evaluated correlations between variables.
Results: Sixty-two (62) SSc patients (43 limited cutaneous (lc) and 19 diffuse cutaneous (dc) SSc), 14 RP and 16 HC were enrolled. Patients with RP were significantly younger than SSc and controls. Mean disease duration of SSc was 9.74 years. 27% of patients were on active IS treatment, 30% were using bosentan and 48% intravenous prostanoids. UHF-US allowed a precise identification and measurement of the thickness of the dermis and hypodermis of all individuals. The mean dermal thickness in the fingers was significantly higher in dcSSc patients than in lcSSc, RP and HC (p<0.001), while in the hands it was significantly higher only compared to RP (p<0.001) and in the forearm there was no difference between groups. Dermal thickness at the finger level significantly correlated with age (r 0.28, p=0.0067) and mRSS (r 0.29, p=0.01). We found no differences in dermal thickness of SSc patients according to use of IS treatment. Hypodermal thickness of the hands and fingers was higher only in patients with lcSSc compared to all other groups but was also significantly correlated to age (r 0.31 and 0.22, p<0.05, respectively) and BMI (r 0.36 and 0.32, p<0.001, respectively). Hypodermal thickness of the fingers was lower in patients using bosentan treatment (p=0.01).
Conclusion: These data show that skin UHF-US allows to measure in detail the dermal thickness and that these measurements correlate with the skin score. UHF-US could be used as an objective, sensitive and reproducible method for measuring skin involvement in SSc.
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UHF-US (70 MHz) of dorsal aspect of second finger in a SSc patient with *sclerodactyly*.

UHF-US (70 MHz) of dorsal aspect of second finger in a SSc patient with *puffy finger*.

Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1306 HEALTH-RELATED QUALITY OF LIFE (HRQOL) ACROSS DIFFERENT CONNECTIVE TISSUE DISEASES (CTDS): ANALYSIS OF A MONOCENTRIC EXPERIENCE

Keywords: Systemic lupus erythematosus, Patient reported outcomes, Quality of life

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Background: patients with CTDs have a worse HRQoL compared with the general population and chronic non-rheumatic diseases. However, only few studies have compared HRQoL among CTDs that differ for age at diagnosis, type and severity of organ involvement, disease course.
Objectives: to analyze HRQoL and fatigue across different CTDs in a monocentric cohort.
Methods: a cross-sectional study that enrolls consecutive adult patients with a diagnosis of Systemic Lupus Erythematosus (SLE), Systemic Sclerosis (SSc) and Idiopathic Inflammatory Myopathies (IIM), regularly followed at the Rheumatology Unit of Pisa. For each patient, demographics, treatment, clinical and laboratory data were collected. At enrollment, each patient completed the SF-36 for HRQoL and the FACIT for fatigue.
Results: we enrolled 490 CTD patients: 255 (52%) SLE, 150 (30.6%) SSc, and 85 (17.3%) IIM. The majority were female (85.7%) and of Caucasian ethnicity (97.5%). At enrollment, patients with SLE were significantly younger (mean age: 44.6 ±12.7 years for SLE, 62.6 ±13.6 for SSc, 65.7 ±12.4 for IIM, p<0.001), with a significantly longer disease duration (14.1 ±10.1 years for SLE, 8.2 ±6.4 for SSc, 5.3 ±5.7 for IIM, p<0.001) compared to the other two groups. The rate of fibromyalgia was highest in SSc (24.7% in SSc, 15.3% in SLE, 11.8% in IIM). Among SLE patients, 79 (31%) presented a mild active disease at enrollment, with skin (35/255) and hematological (32/255) manifestations being the most frequent; only 11 patients (4.3%) presented an active renal disease. Among IIM patients, 67 (78.8%) presented an active disease according to the clinician evaluation: 31 had active myositis and 29 active skin lesions. 33 patients had an Interstitial Lung Disease (ILD). Among SSc patients, 62% presented limited skin involvement; 45 patients (30%) had an ILD and 41 (27.3%) presented a scleroderma heart involvement, while 18 patients had active digital ulcers at enrollment. As far as treatment is concerned, most patients were on Hydroxychloroquine (63.5%); almost half of patients enrolled (45.7%) were on a low dose of glucocorticoids (mean daily dose 2.12 ±2.78 mg of 6-methylprednisolone), and 43.9% were on immunosuppressants. The results of the SF-36 domains are represented in Figure 1. We compared the results of questionnaires across groups. At the univariate analysis, the domains of Physical Function (PF), Role Physical (RP) and Role Emotional (RE) resulted different between groups. In particular, the IIM patients presented the lowest scores compared with the other two groups (Table 1). However, at the multiple linear regression analysis, only the PF domain confirmed to be significantly different across the three groups, after adjusting for age at enrollment and disease duration (β-0.003, [95% CI-0.005, -0.001; p<0.01]).
Finally, the FACIT scores were not significantly different between groups.
Conclusion: in our monocentric cohort of patients with CTDs, there were no clear differences in HRQoL driven by diagnosis, except for the physical function domain which appeared more impaired in myositis patients. HRQoL appears as an independent domain of patients' health status, only marginally influenced by the clinical characteristics of the disease. This underlines the importance for clinicians managing patients with complex autoimmune diseases to develop common strategies to address and improve HRQoL, parallel to the clinical management of the disease.

Table 1. Results of SF-36 and FACIT across CTD patients

	IIM	SLE	SSc	p value
PF	55.3±32.1	75.8±24.5	67.39±28.4	**p<0.001** * **p<0.01** § **p<0.01** +
RP	40.3±44.2	64.4±29.3	50.7±41.9	**p<0.001** * p=0.12 § **p=0.001** +
BP	63±26.1	63.8±27.4	59.3±30.4	p=1 * p=1 § p=0.3 +
GH	43.3±22.1	49±18.6	45.4±19.4	p=0.07 * p=1 § p=0.25 +
VT	51.9±22.3	52.7±21.8	53.3±20.8	p=1 * p=1 § p=1 +
SF	69.5±24	68.3±24.4	70±24.7	p=1 * p=1 § p=0.87 +
RE	53.3±44.2	67.5±28.1	59.3±38.7	**p<0.01** * p=0.65 § p=0.06 +
MH	65.2±21.8	63.2±19.5	62.4±17.3	p=1 * p=0.85 § p=1 +
FACIT	35.5±10.8	37.7±10.3	37.9±9.5	p=0.42 * p=0.36 § p=1 +

*IIM vs SLE, §IIM vs SSc, +SLE vs SSc

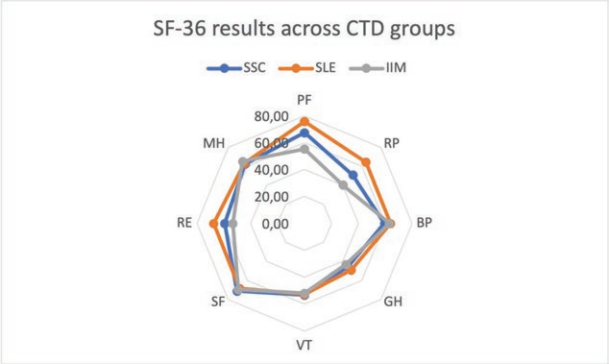


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1307

NINTEDANIB IN RHEUMATIC DISEASE-ASSOCIATED INTERSTITIAL LUNG DISEASE – A MULTICENTRE NATIONWIDE COHORT STUDY

Keywords: Lungs, Outcome measures, Imaging

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Background: Interstitial lung disease (ILD) is a severe manifestation of inflammatory rheumatic diseases (IRD). Conventional treatments have shown modest and short-lived success in the control of ILD [1]. Nintedanib (Nib) was recently approved for systemic sclerosis (SSc)-associated ILD and fibrosing ILD with a progressive phenotype [1]. However, its experience in other IRD-associated ILD is still scarce.
Objectives: To describe the clinical features and outcomes of patients with IRD-ILD treated with Nib across ten national rheumatology departments.
Methods: Retrospective cohort study, with chart review of the medical records for inclusion of patients with IRD-ILD treated with Nib. Data are presented as frequencies and mean±standard deviation (range) for categorical and continuous variables, respectively.
Results: A total of 64 patients (70% women) were identified (Table 1). The mean age at IRD and ILD diagnosis was 56.2±11.7 and 59.7±10.8 years (y), respectively, and the mean time for Nib initiation after ILD diagnosis was 5.1±3.9 y. The most frequently underlying IRD were SSc (55%) and rheumatoid arthritis (28%). ILD was diagnosed prior to the IRD in only 7 patients (11%). Computed tomography (CT) identified usual interstitial pneumonia (UIP) in 36 cases (56%), fibrotic nonspecific interstitial pneumonia (NSIP) in 27 (42%) and organizing pneumonia in one (2%). Patients with UIP took longer to start Nib (5.5±4.4 y) compared to patients with NSIP (4.7±2.4 y). Before Nib, respiratory function tests (RFTs) showed a low single-breath diffusing capacity of the lungs for CO (DLCO) in all patients, with a mean predicted value of 39±18%. All patients had previously received immunosuppressive therapy, most commonly glucocorticoids (70%) and mycophenolate mofetil (50%). Patients were exposed to Nib for a mean of 18.5±15.9 months (m), 17 were treated for more than 24m. After 6m, there was a statistical improvement in DLCOc SB (p=0.041) and DLCOc/VA (p=0.029) compared to baseline, which was not observed at 12 or 24m (p>0.05). No differences were found between patients with NSIP and UIP. Nevertheless, the latter showed a trend for an overall lower benefit on RFTs

Table 1 - Clinical features of patients

IRD	SSc	SSc+RA	DM	MCTD	MPA	PM	pSS	RA	SLE
Number of patients, n	35	1	1	1	1	1	5	18	1
Female, n (%)	29 (82.8%)	1 (100%)	1 (100%)	0 (0%)	1 (100%)	1 (100%)	4 (80%)	9 (50%)	1 (100%)
Age at IRD diagnosis, years (range)	54.7±12.2 (34-81)	64	54	49	73	33	63.8±3.8 (58-67)	55.7±11.7 (32-73)	70
Age at ILD diagnosis, years (range)	56.5±12.0 (33-79)	69	55	49	73	33	69.4±4.2 (65-75)	63.2±7.7 (43-75)	70
ILD pattern, n (%)	20 (57%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	0	2 (40%)	0	1 (100%)
NSIP	1 (3%)	0	0	0	0	0	0	0	0
OP	14 (40%)	0	0	0	0	1 (100%)	3 (60%)	18 (100%)	0
UIP									

ILD	UIP	NSIP	OP
Time for Nib initiation after diagnosis (years)	5.5±4.4 (0.5-19)	4.7±2.4 (0-13)	3
Nib treatment duration (months)	16.9±16.8 (2-67)	21.9±15.1 (1-52)	16

Abbreviations DM - dermatomiositis; MCTD - mixed connective tissue disease; MPA - microscopic polyangiitis; PM - polymyositis; pSS - Sjögren's Syndrome; RA - rheumatoid arthritis; SLE - systemic lupus erythematosus

(Figure 1), mainly in the first 12m of treatment (NSIP: forced vital capacity [FVC] p=0.173 and DLCOc SB p=0.199; UIP: FVC p=0.278 and DLCOc SB p=0.267). In patients with <3y of ILD duration (n=20 [8 NSIP; 12 UIP]) a significant improvement in DLCOc SB and DLCOc/VA was observed at 24m (p=0.003 and p=0.017). Regarding tolerance: 38 (59%) patients were able to maintain a daily dose of 150 mg bid, 24 (38%) required reduction to 100 mg bid due to gastrointestinal (GI) symptoms and 2 (3%) discontinued Nib.

Conclusion: An initial benefit was observed in the DLCO of patients treated with Nib at 6m. Only 1/3 of patients were started on Nib with less than 3y of ILD duration, possibly reflecting the recent approval of Nib for these diseases. In this subset of patients, a significant improvement in DLCO was observed at 24m, suggesting that early initiation of treatment may halt ILD progression.

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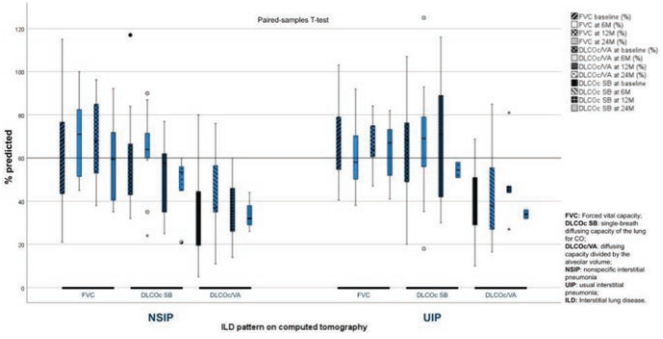


Figure 1. RFTs results over 24 months

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Disclosure of Interests: None Declared.
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POS1308 **WITHDRAWN**

POS1309

ASSOCIATION BETWEEN RED CELL DISTRIBUTION WIDTH AND INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS

Keywords: Descriptive studies, Biomarkers, Systemic sclerosis

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Background: Interstitial lung disease (ILD) and pulmonary arterial hypertension (PHT) account for 60% of deaths related to scleroderma (SSc) [1]. The Red Cell Distribution Width (RDW) is a biomarker that has been used as a marker of poor prognosis in various pathologies [2-9]. In SSc, the RDW has been found to be elevated in PHT and has been proposed as a predictor of cardiorespiratory compromise [10-11].

Objectives: To evaluate the association between the increase in RDW and the presence of ILD in patients with SSc.

Methods: Observational, retrospective, multicenter, cross-sectional study of patients with SSc (ACR/ EULAR 2013) between 1/1/2011 to 8/31/2021. Other concomitant autoimmune diseases, malignancy, active infections, anemia, recent transfusions, cardiovascular, renal, or hepatic disease were excluded. The diagnosis of ILD was made by high-resolution computed tomography (HRCT) and the extension evaluated by Goh criteria[12]. A review of medical records was performed, collecting relevant clinical and demographic characteristics.

Results: Seventy-five patients were included, with a mean age of 59.4 years (SD 14.1, 95% CI 56-63), 67 (89%) were women. A median of 8 years of disease evolution was observed (IQR 8). ILD was observed in 50 (66,6%) patients while 25 (33.3%) did not. According to Leroy's classification, limited SSc (lcSSc) was observed in 50 patients (66,6%) and diffuse SSc (dSSc) in 24 (33,3%); the last classification was significantly associated with the presence of ILD, as was as MRSS (Modified Rodnan Skin Thickness Score)> 14, digital ulcers, and positive ATA (DNA topoisomerase I), unlike ACA (anticentromere antibodies) (Table 1). The most frequent HRCT pattern was NSIP (Nonspecific interstitial pneumonia) in lcSSc (66.6%). An association was found between dSSc and fibrotic patterns (fNSIP and UIP). OR 6, 95% CI 1.6-21 (p 0.009). The extension of the disease was measured in 44 patients (6 missing data), being limited in 25 (57%) and extensive in 19 (43%). The extensive form was correlated with a higher RDW mean (p < 0.0001). The MRSS was measured in 70 patients, being less than 14 in 63 (90%). 100% of the patients with mRSS > 14 had a high RDW (p 0.01). Increased RDW was evidenced in the group with ILD, with a statistically significant difference (OR 6.06 95%CI 2-17 p 0.001).

Table 1. Clinical, demographic and laboratory characteristics

	ILD n=50	No ILD n=25	p value
Women n (%)	43 (86)	24 (96)	0,18
Age x (SD)	58,3 (12,9)	61,6 (16,4)	0,34
Disease duration (years) Me (IQR)	7,5 (6,2)	9 (9,5)	0,13
lcSSc n (%)	**27 (54)**	**23 (92)**	0,001
dSSc n (%)	**22 (44)**	**2 (8)**	
PHT n (%) MD 16	4 (8)	2 (8)	0,38
SRC n (%)	1 (2)	2 (8)	0,25
MRSS > 14 n (5)	**8 (16)**	**0**	0,034
Dysphagia / GERD n (%)	38 (76)	19 (76)	1
Calcinosis n (%)	5 (10)	2 (8)	0,59
Digital ulcers n (%)	**23 (46)**	**5 (20)**	0,024
Pigmentation disorders n (%)	11 (22)	3(12)	0,23
Telangiectasias n (%)	24 (48)	13 (52)	0,46
ESR Me (IQR)	20 (30)	18 (30)	0,25
CRP Me (IQR) MD 4	5 (11,8)	1,5 (5,6)	0,1
ACA n (%) MD 10	**9 (18)**	**18 (72)**	< 0,0001
ATA n (%) MD 4	**19 (38)**	**4 (16)**	0,037
RDW > 14 n(%)	**33 (66)**	**7 (28)**	0,01
HRCT pattern			
NSIP n (%)	**20 (66,6)**	**5 (25)**	0,009
fNSIP n (%)	7 (23,3)	8 (40)	0,22
UIP N (%)	3 (10)	7 (35)	0,067
	Increased RDW n (%)	**Normal RDW n (%)**	**p value**
Goh classification n (%)			
Limited	**20 (80)**	**5 (20)**	< 0,0001
Extensive	**15 (79)**	**4 (21)**	
MRSS n (%)			
< 14	**32 (50,8)**	**31 (49,4)**	0,01
> 14	**8 (100)**	**0**	

ACA: anticentromere antibodies; ATA: DNA topoisomerase I; CRP: C reactive protein; dSSc: diffuse SSc; ERS: erythrocyte sedimentation rate; fNSIP: fibrotic NSIP; GERD: gastroesophageal reflux disease; HRCT: high-resolution computed tomography; ILD: interstitial lung disease; IQR: interquartile range; lcSSc: limited SSc; Me: median; MD: missing date; MRSS: modified rodnan skin thickness score; NSIP: nonspecific interstitial pneumonia; PHT: arterial hypertension; RDW: red cell distribution width; SD: standard deviation; SRC: scleroderma kidney crisis; UIP: usual interstitial pneumonia.

The median RDW in the groups with isolated ILD and ILD plus PHT was significantly higher than in patients without lung disease (p < 0.001). We found no significant difference between the ILD and ILD plus PHT groups (p 0.350) (Figure 1).

Figure 1.

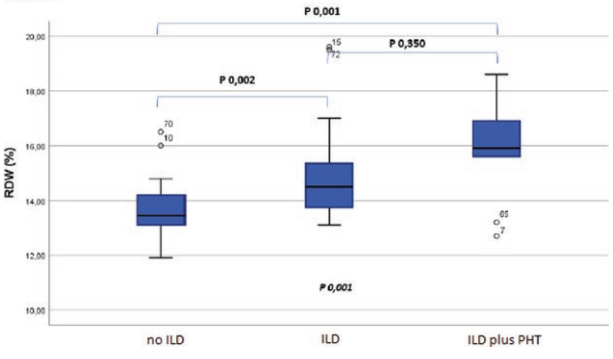


Figure 1.

Conclusion: We have been able to show that there is a significant relationship between the increase in RDW and the presence of ILD in patients with SSc; this association was more significant for the extensive forms of the disease as well as fibrotic patterns. These findings are relevant as the RDW is an easily accessible parameter that could be used in the follow-up of patients with SSc, and an elevation not explained by other causes of the RDW could be an alarming marker to search more exhaustively for the presence of cardiorespiratory compromise. The limitations of the study are those of any retrospective study, the presence of

missing data in addition to the limited number of patients. It is necessary to continue studies with a larger number of patients to grant robustness to the results.

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POS1310

FECAL MICROBIOTA TRANSPLANTATION IN PATIENTS WITH SYSTEMIC SCLEROSIS AND LOWER GASTROINTESTINAL TRACT SYMPTOMS: DATA FROM THE RESSCUE RANDOMIZED CLINICAL TRIAL

Keywords: Randomized control trial, Systemic sclerosis, Gastrointestinal tract

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Background: Lower gastrointestinal tract (GIT) complications are common in patients with systemic sclerosis (SSc), associate with a high disease burden, and current treatment alternatives are limited. Patients with SSc have also an altered intestinal microbiota composition. This provides a rational for the investigation of fecal microbiota transplantation (FMT) in SSc patients with lower GIT symptoms.

Objectives: To assess the safety and efficacy of a standardized intestinal microbiota infusion in SSc patients with lower GIT symptoms.

Methods: Patients with SSc and moderate to severe bloating and/or diarrhea assessed by the UCLA SCTC GIT score 2.0 were enrolled in a Norwegian multicenter, double-blind, randomized, placebo-controlled, phase 2 trial. Patients were randomized to receive an intestinal infusion of a standardized fecal microbiota culture (ACHIM) or placebo at weeks 0 and 2. At week 12, all patients received an ACHIM infusion and were followed in an open maintenance phase until week 20. The primary outcome was a change between baseline and week 12 in UCLA GIT score item diarrhea or bloating, depending on which was the worst symptom at the baseline evaluated separately for each patient, measured as the average marginal effect (AME). Secondary outcomes were safety and tolerability and total UCLA GIT score. Other outcome measures included the change in UCLA GIT score from week 12 to week 20.

Results: A total of 65 patients were randomized to receive ACHIM or placebo. Baseline characteristics in the placebo and ACHIM groups were comparable (Table 1). There was no significant difference in the change in lower GI symptoms from week 0 to week 12 between the ACHIM and placebo groups (AME=0.17 (-0.12, 0.47), p=0.25). Similarly, no significant difference was observed in the total GIT score between the two groups over the same time period (AME=0.09 (-0.04, 0.23), p=0.17). Furthermore, during the maintenance phase, there was no statistical difference in change between the ACHIM and the placebo group (AME= -0.04 (-0.32, 0.23), p=077). In ACHIM, 16 (37%) and in placebo 19 (42%) experienced any side effect. These were in general mild and short-lasting, with abdominal pain as the most frequent side effect present in 5 (15%) in ACHIM and 2 (6%) in placebo. Time to resolved pain was 2 days in both groups. One patient experienced an intramural perforation during gastroscopy and needed IV antibiotics but fully recovered.

Conclusion: We were unable to find indications that FMT improves lower GIT symptoms in SSc patients, but the treatment was found to be safe.

Table 1: Baseline characteristics

Parameter	ACHIM (N=33)	Placebo (N=34)
Age, y (SD)	58 (11.5)	60 (11.7)
Female, n (%)	33 (100)	29 (85)
Worst symptom Bloating, n (%)	22 (67)	22 (65)
Disease duration, y (SD)	9 (7)	10 (8)
Limited cutaneous SSc, n (%)	31 (94)	28 (85)
FVC% (SD)	95 (13.7)	90 (19.2)
Immunosuppressives, n (%)	3 (9)	5 (15)
PPI, n (%)	27 (82)	21 (62)
CCB, n (%)	18 (58)	20 (59)
Total GIT score	0.9 (0.5)	0.7 (0.3)
GIT scale Diarrhea	0.8 (0.7)	0.5 (0.5)
GIT scale Bloating	1.8 (0.8)	1.7 (0.7)

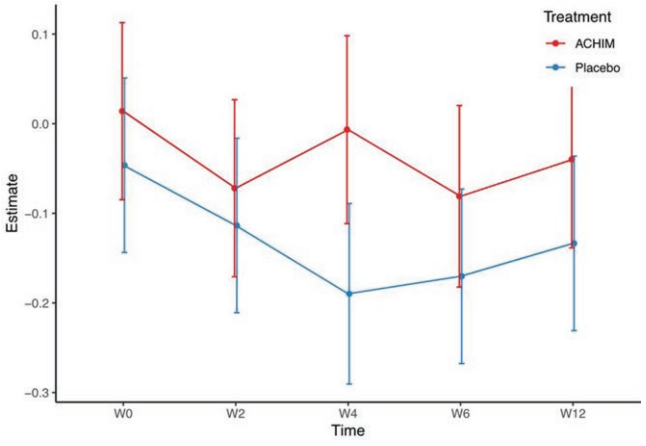


Figure: Change between baseline and week 12 in UCLA GIT score item diarrhea or bloating, depending on which was the worst symptom at the baseline in ACHIM (red) and placebo (blue), adjusted for baseline.

Acknowledgements: NOSVAR (Norwegian connective tissue disease and vasculitis registry)

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Scleroderma, myositis and related syndromes

POS1311 **A MULTINATIONAL SURVEY INVESTIGATING THE UNMET NEEDS AND PATIENT PERSPECTIVES CONCERNING PROTON PUMP INHIBITORS IN SYSTEMIC SCLEROSIS**

Keywords: Gastrointestinal tract, Systemic sclerosis

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Background: Gastrointestinal (GI) complications are a major cause of morbidity and mortality in systemic sclerosis (SSc) [1]. Proton pump inhibitors (PPIs) are widely used to treat gastroesophageal reflux disease in SSc. However, not all patients respond adequately to these drugs, and concerns about the safety of their long-term use of PPI's exist in the general population [2].
Objectives: To identify patients' unmet needs and perspectives concerning PPI therapy.
Methods: An online survey in the English language targeting patients with SSc treated with PPI was developed and distributed through international patient associations and social media. The survey was launched on 4th November 2022 and kept open for 4 weeks.
Results: Of 416 people starting the survey, responses from 301 subjects with self-reported SSc from 14 countries (US 70.4% and UK 19.3%) were evaluable. The majority of patients were between 30-70 years of age and were female (95%). The most frequent patient-reported symptoms were acid reflux (97%), dysphagia (60%), nausea, vomiting and the regurgitation of food or phlegm (>60%). 83% of patents had undergone at least 1 invasive test to diagnose gastroesophageal reflux disease (e.g., upper endoscopy). The most commonly prescribed PPIs were omeprazole (62%), esomeprazole (24%), and pantoprazole (10%). One third of patients (35%) had only taken one PPI, whereas the use of various PPI's (in series) was required by the majority (two PPIs: 30%, three PPIs: 21%). Daily PPI (46%) vs twice daily PPI regimens (47%) were divided equally among respondents. When on PPI, the majority of patients (89%) reported an improvement of GI symptoms when taking PPI, especially for symptoms of gastroesophageal reflux disease (94%). Only 19% experienced side effects from PPIs use, weak bones (osteoporosis) and calcium formation (calcinosis) being the most frequent. Half of patients (47%) experienced a return of symptoms despite initial improvement on PPI. Combination therapy (PPI plus other medication for reflux disease) was required for the optimal management of reflux disease in 41% of patients and was often deemed more beneficial than PPI monotherapy (72%). Many patients (83%) were worried that GI symptoms would return following PPI discontinuation. Furthermore, 79% of patients were worried about side effects from long-term use PPI, particularly the development of 'weak bones (i.e., osteoporosis)' (66%), kidney problems (55%), calcium formation (i.e., calcinosis) (39%), and cardiovascular disease (38%). PPIs were prescribed by a healthcare professional in 92% of respondents (8% bought over-the counter). Financial reimbursement for PPIs was only provided in around two-thirds of patients (64%). Only 58% of patients received information on lifestyle and diet to manage GI symptoms before starting PPI. Furthermore, the majority of patients (85%) obtained information about PPIs online. In only 12% of cases, a surgical approach to manage upper GI symptoms was discussed (rheumatologist or gastroenterologist). However, 46% of patients expressed their approval to undergo surgery (e.g., fundoplication) to resolve their reflux symptoms; however, many (80%) were worried about possible complications.
Conclusion: Our study benchmarks the importance of gastroesophageal symptoms in patients with SSc and the frequent use of PPIs. There is significant heterogeneity in the use of PPI in SSc and combination therapy is not uncommon. Patients live with great uncertainty including PPI side effects. Education about PPIs is often neglected, and patients rely on online information. A surgical approach is still not widely considered as a therapeutic option.

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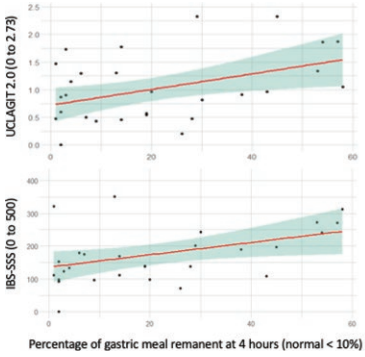
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POS1312 **PREVALENCE OF GASTROINTESTINAL SYMPTOMS AND OBJECTIVE GASTROINTESTINAL DYSMOTILITY IN PATIENTS WITH SYSTEMIC SCLEROSIS**

Keywords: Systemic sclerosis, Gastrointestinal tract, Quality of life

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Background: After the skin, the gastrointestinal tract is the most frequently affected system in systemic sclerosis (SSc). The pathophysiology of gastrointestinal symptoms is mostly secondary to gastrointestinal dysmotility. Due to the increase survival in patients with systemic sclerosis, digestive manifestations are becoming more relevant in the comprehensive management of the disease.
Objectives: To assess the prevalence of gastrointestinal symptoms, the presence of gastric and intestinal dysmotility in objective testing and to examine associations between gastrointestinal involvement and other systemic sclerosis features.
Methods: A cross-sectional study was conducted in the cohort of active SSc patients in a tertiary center. Patients who fulfilled LeRoy or ACR/EULAR 2013 classification criteria were contacted by telephone and asked to complete standardized questionnaires: UCLA-GIT 2.0, IBS-SSS (IBS symptom severity score), a gastrointestinal symptoms questionnaire and the SF-36 (quality of life). Questionnaire terminology was altered to replace references to 'IBS' with 'GI symptoms'. Demographic, clinical-immunological data and results of complementary motility tests were collected from the medical records. Gastrointestinal motility was assessed by gastric emptying scintigraphy, small intestinal manometry and/or abdominal CT scan.
Results: A total of 183 SSc patients participated in the study with a mean age ± standard deviation (SD) of 59±12 years, 103 (55%) patients had limited cutaneous SSc (lcSSc) subset, 43 (24%) diffuse cutaneous SSc (dcSSc), and 37 (21%) sine sclerosis SSc (ssSSc). 139 (77%) patients reported having at least one frequent digestive symptom (>1 day/week). The prevalence of digestive symptoms correlated negatively with overall quality of life measured by SF-36 (r= -0.503 p=<0.001). In univariate analysis, female gender (87 vs 73%; p=0.025), onset at an early age (44±7 vs 50±6 years; p=0.037) and a capillary loss pattern (23% vs 7%; p=0.023) were associated with the presence of digestive symptoms. Gastrointestinal motility assessment detected gastroparesis in 18/31 (total 58%; mild n=6, moderate n=5, severe n=7), small bowel abnormal motility patterns in 6/6 (total 100%, neuropathic n=1, myopathic n=5) and small bowel dilated loops in 6/65 patients (total 9%, CT scan). Among the patients studied by gastric emptying scintigraphy, gastric retention at 4 hours had a moderate positive correlation with IBS-SSS and UCLA GIT 2.0 scores (r=0.433 and r=407, p=<0,01 respectively).



Gastric meal retention at 4 hours measured by scintigraphy showed a moderate positive correlation with gastrointestinal symptom burden measured by UCLA GIT 2.0 (r= 0.407) and with the severity of gastrointestinal symptoms measured by the modified IBS severity symptom score (r=0.433).

Figure 1.

Moderate-severe gastrointestinal involvement (21 patients, 11%) was associated with older age at SSc onset (45 ± 9 vs 36 ± 14 years; p=0.012), dcSSc (57% vs 18%; p=0.001), myositis (24% vs 3%, p=0.011), tendon friction rubs (29% vs 3%, p=0.003) erosive esophagitis (10% vs 57%, p=0.001) despite proton bomb inhibitor treatment. Patients with moderate-severe gastrointestinal involvement had a worse (higher) UCLA GIT 2.0 score (1.05 ± 0.63 vs 0.62 ± 0.51; p=0.043) mainly due to reflux (1.07 ± 0.63 vs 0.58 ± 0.61; p=0.001) and bloating (1.85 ± 0.78 vs 1.23 ± 0.94; p=0.001) and greater severity of abdominal symptoms (IBS-SSS score, 185 ± 91 vs 146 ± 113; p=0.032). All patients (n=6) with chronic intestinal pseudo-obstruction presented dcSSc subset.

Conclusion: Patients with SSc have a high prevalence of digestive symptoms and objective gastrointestinal dysmotility that negatively impact their quality of life. Gastrointestinal dysmotility seems to worsen reflux disease. The dcSSc subset is associated with more severe gastrointestinal involvement.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1313 EFFICACY OF IMMUNOGLOBULIN TREATMENT ON GASTROINTESTINAL, CUTANEOUS AND VASCULAR INVOLVEMENT IN SYSTEMIC SCLEROSIS: DATA FROM AN ITALIAN COHORT OF 65 PATIENTS

Keywords: Skin, Gastrointestinal tract, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is a rare connective tissue disease characterized by autoimmunity, vasculopathy, and fibrosis involving many organs. To date, the gastrointestinal (GI) involvement accounts for few therapeutic options, while cutaneous and vascular manifestations are often refractory to standard treatments. Immunoglobulin (Ig) therapy is an interesting option as it exhibits both immunomodulatory and antifibrotic properties even though its efficacy on GI, skin and muscle involvement has been described only in case series with limited numbers of patients.

Objectives: To evaluate the efficacy of Ig therapy on GI, cutaneous, and vascular involvement in SSc.

Methods: a retrospective observational study was conducted evaluating SSc patients treated with Ig at a 2 gr/kg/month dosage either intravenously (IV) or subcutaneously (SC). Demographical data, antibodies positivity, associated therapies (vasoactive and immunosuppressants) and disease duration were collected. Moreover, the presence of diarrhea, gastroesophageal reflux (GER), dysphagia, digital edema, digital ulcers (DUs), as well as the modified Rodnan Skin Score (mRSS) and videocapillaroscopic pattern (VCP: normal, early, active, late) were assessed at baseline (BL) and after 6 (T6) and 12 (T12) months of Ig therapy. Variation of these items from BL to T6 and T12 was tested by Paired T Test, Mc Nemar test, Wilcoxon's signed rank test as appropriate. Regression analyses were than performed to assess influence of possible confounders variables (vasoactive and immunosuppressants drugs) on outcome variables (VCP, digital edema, DUs).

Results: Clinical records of 65 patients were analyzed. Mean age was 56.18 (± 12.32 SD) and median disease duration was 10.00 years (min-max 1.00-38.00). Sixty-three patients (96.9%) were ANA positive, with positivity for anti-centromeric antibodies in 23 (35.4%), SCL-70 in 27 (41.5%) and RNA polymerase III in 8 (12.3%) patients. Ig were administrated IV in 57 patients and SC in 8 patients. Table 1 summarized the trend of clinical items from BL to T12. At BL, 49.2% of patients complained diarrhea, 90.8% GER, 51.6% dysphagia, 76.9% digital edema; 38.5% presented DUs. VCP was normal in 3.1% of patients, early in 21.9%, active in 45.3%, and late in 29.7%. Also, median mRSS was 10 (min-max 0-50). At T6, median mRSS significatively improved [6 (min-max 0-34), p<0.0000001] together with VCP (normal in 15.6%, early in 15.6%, active in 35.6%, and late in 33.3%, p=0.00448). Moreover, a significative reduction of the prevalence of GER (49.2%, p<0.000001), diarrhea (19.4%, p<0.0001), dysphagia (22%, p<0.0001), digital edema (44.4%, p<0.0001), DUs (14.1%, p=0.0022) was noted. At T12, median MRSS improved even more [3 (min-max 0-23), p<0.00000001] along with VCP (normal in 19.0%, early in 23.8%, active in 28.6%, and late in 28.6%, p=0.00596). Also, the prevalence of GER was lower (25.9%, p<0.001). Regression analyses did not evidence any influence of other treatments on the tested outcome variables.

Conclusion: Our data confirms literature data on Ig therapy efficacy towards GI and skin manifestations [1]. To date, this is the first study presenting a possible positive effect on the vascular component shown by the improvement in VCP; these data should be confirmed with prospective randomized studies on bigger samples.

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Table 1.

	BL	T6	P value (BL-T6)	T12	P value (T6-T12)
GER, n (%)	59 (90.8)	31 (49.2)	p<0.000001	15 (25.9)	p<0.001
Dysphagia, n (%)	32 (51.6)	13 (22)	p<0.0001	6 (10.7)	0.0736
Diarrhea, n (%)	31 (49.2)	12 (19.4)	p<0.0001	4 (6.9)	0.0771
mRSS, median (min-max)	10 (0-50)	6 (0-34)	p<0.0000001	3 (0-23)	p<0.00000001
Digital edema, n (%)	50 (76.9)	28 (44.4)	p<0.0001	17 (30.9)	0.131
Digital ulcers, n (%)	25 (38.5)	9 (14.1)	0.0022	3 (5.3)	0.0736
VCP, n	64	45	0.00448	42	0.00596
- Aspecific, n (%)	- 2 (3.1)	- 7 (15.6)		- 8 (19.0)	
- Early, n (%)	- 14 (21.9)	- 7 (15.6)		- 10 (23.8)	
- Active, n (%)	- 29 (45.3)	- 16 (35.6)		- 12 (28.6)	
- Late, n (%)	- 19 (29.7)	- 15 (33.3)		- 12 (28.6)	

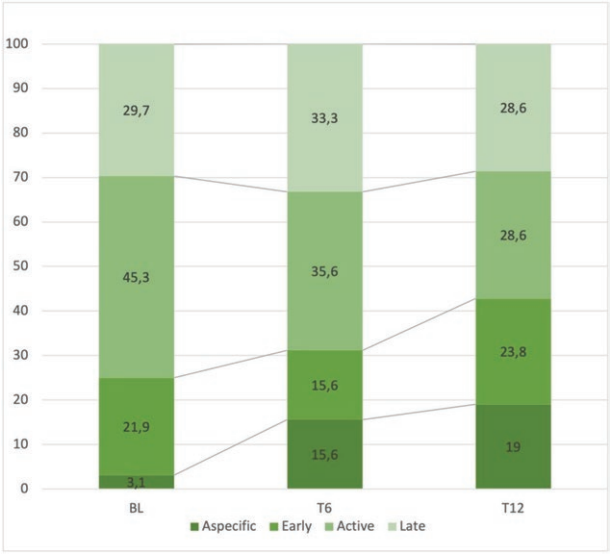


Figure 1.

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POS1314 AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION: LONG-TERM OUTCOMES IN A SINGLE-CENTER COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Disease-modifying drugs (DMARDs), Systemic sclerosis, Organ damage

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Background: Although various immunosuppressive drugs are used to treat Systemic Sclerosis (SSc), no therapy has proved to be actually effective in changing the natural history of the disease. Three randomized controlled trials have demonstrated the superiority of autologous hematopoietic stem cell transplantation (AHSCT) on conventional therapies for patients suffering from severe SSc. However, data on disease activity and progression after AHSCT are really scant.

Objectives: To retrospectively evaluate the long-term effectiveness of AHSCT in a monocentric cohort of SSc patients with a severe diffuse cutaneous disease at the baseline, and every 12 months up to 60 months after transplantation. In addition, we retrospectively compared the disease outcome of transplanted patients to an age-and sex-matched group of severe SSc patients selected from our historical cohort and treated with conventional therapies.

Methods: Clinical, instrumental and laboratory data of all SSc patients who underwent AHSCT between 2003 and 2020 in our center and with a regular follow up of 60 months after transplant, have been retrospectively analyzed. AHSCT was performed by mobilisation with CTX and G-CSF, selection of CD34+ cells and conditioning regimen with CTX and rabbit ATG. Survival, skin involvement assessed by modified Rodnan skin score (mRSS), cardiac and lung involvement assessed by echocardiography and lung functional parameters, and EUSTAR disease activity (EDA) scores were recorded. All transplanted patients had a rapidly progressive cutaneous disease characterized by a mRSS>14 and were unresponsive to conventional immunosuppressive therapies. Similar evaluations were made in the control group represented by age- and sex-comparable patients suffering from an exactly comparable disease-duration and clinical characteristics in term of skin involvement and disease activity, and treated with conventional therapies. For this group, the enrolment period was 1991-2020.

Results: 35 patients underwent AHSCT, 30 females and 5 males. Patients were eligible for AHSCT when they had mRSS>14 and an EDA score>2, in the absence of severe organ involvement (renal clearance<40mL/min, DLCO<40%, ejection fraction<45%). At the baseline mean, mRSS was 21.4 ± 5, mean FVC 90.1% ±17.9 and mean DLCO 66.5%±15. We observed a sustained improvement in skin thickening and a persistent reduction of EDA scores, with p-values<0.0001 for both parameters at any follow up time. Transplant-related mortality occurred in 2 patients, one at +65 days from interstitial pneumonia and one at +2 days from myocarditis (5.7%). Three patients died during the follow up from disease progression complications, one at +3 years due to fatal cardiac arrhythmia and two due to progressive lung failure at + 5 years and +7 years. In the control group (68 patients), 25 patients received 6 monthly pulses of intravenous cyclophosphamide (750mg/m^2), 10 received mycophenolate, 10 methotrexate, 12 rituximab, and 11 received steroids and vascular therapies, in the absence of real immunosuppressive therapies. AHSCT patients experienced a better overall survival compared with control patients (p=0.001). AHSCT was also more effective than other therapies for the outcomes of skin score (p<0.0001), lung function (p=0.0004) and disease activity (p<0.0001).

Conclusion: The results of this large historical cohort study of patients with severe SSc confirm efficacy of AHSCT in terms of survival, response to treatment and disease progression rate. The improvement of skin thickening and stabilization of organ function up to 5 years after transplantation, result in a global clinical improvement, as showed by the persistent reduction in the activity score. Probably as a consequence of an accurate patient selection, transplant related mortality results to be acceptable and similar to that reported in previous studies. Despite the limitation of a retrospective study, AHSCT is more effective than conventional therapies, including the latest immunosuppressive agents.

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POS1315 MYCOPHENOLATE USE AND SYSTEMIC SCLEROSIS-ASSOCIATED ESOPHAGEAL DISEASE

Keywords: Gastrointestinal tract, Disease-modifying drugs (DMARDs), Systemic sclerosis

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Background: Systemic Sclerosis (SSc) is an autoimmune disease characterized by fibrosis and vascular abnormalities in the skin and internal organs, which confers high morbidity and mortality [1]. Esophageal dysmotility (EsD) and gastrointestinal esophageal reflux disease (GERD) are among the most common manifestations of SSc, occurring in up to 80% of patients and decreasing quality of life [2]. To date, treatment of SSc-associated EsD/GERD consists of symptomatic management, including the use of pro-motility agents and anti-reflux medication [3]. Despite the elevated burden of SSc-EsD/GERD, no high-quality evidence to support the use of disease modifying immunomodulatory medications exists. This study explored mycophenolate (MMF), an inosine-5'-monophosphate dehydrogenase inhibitor, which has shown efficacy for suppressing other SSc manifestations including interstitial lung disease and skin thickening [4].

Objectives: To investigate the potential relationship of MMF with SSc-associated esophageal disease.

Methods: A retrospective chart review was completed for patients with SSc at the Mount Sinai Hospital between January 1, 2000 – January 6, 2022. Individuals with Ssc were identified using a validated ICD-10 M34 code. Data gathered included demographic factors, history of MMF use and cumulative dosing, GERD/EsD diagnosis, medication use, and other relevant clinical factors. Esophageal disease was considered to be present if a patient had any of the following: a formal diagnosis of GERD, absent/ineffective contractility on manometry, or Barrett's esophagus identified on endoscopy. Descriptive statistics were conducted, and X^2 tests/t-tests were computed to compare demographic and outcome variables between patients taking MMF and those not. Multivariable logistic regression analysis was conducted to identify the relationship between MMF use and GERD/EsD prevalence.

Results: 612 participants were included in the study. 167 (27.3%) patients were prescribed MMF, with an average dose of 28.1 g/kg. 141 (84.4%) of the patients prescribed MMF were diagnosed with esophageal disease, compared to 293 (65.9%) patients who were not prescribed MMF (p<0.01). Patients taking MMF were more likely to use a PPI (p<0.01). No differences were found in vascular risk factors (i.e. smoking, coronary artery disease, stroke, hypertension diabetes), head and neck or GI malignancy (thyroid, tongue, gastric, etc.) or presence of psychiatric comorbidities. Multivariable logistic regression revealed that total cumulative MMF dosage (OR=2.99, 95% CI=1.76-5.08, p=<0.0001) was significantly associated with increased likelihood of esophageal disease.

Conclusion: This study revealed that patients with SSc who were prescribed MMF were more likely to have GERD/EsD, and that total cumulative dose of MMF was significantly associated with an increased likelihood of esophageal disease. There are many potential explanations for this result, including possible MMF side effects and bias by indication (i.e. patients taking MMF may have more severe disease to warrant such therapy). Additional studies (notably prospective trials) are needed to examine other possible disease modifying treatments for SSc-associated GERD/EsD.

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POS1316 WITHDRAWN

transfusions and treatment-related mortality at 100 days. We report endoscopic and clinical results 12 months following AHSCT.

Results: Five dcSSc patients (mean age 49.2 ± 9.0 years, 4 [80%] females, 4 patients [80%] with RNA polymerase III antibodies and one [20%] with SCL-70 antibodies) were diagnosed endoscopically and histologically with GAVE 1-4 months prior to AHSCT. Two of them needed APC. The mean Hb level at baseline was 9.6±2.5 g/dl. At the AHSCT, three patients received conditioning with Cyclophosphamide 200mg/kg and 7.5 mg/Kg ATG, and two patients received "cardiac-safe" conditioning with rituximab 1000 mg, cyclophosphamide 60 mg/kg and fludarabine 120 mg/m². The mean nadir thrombocyte level was 41.2 × 10^9/L (±39.1 × 10^9/L). The mean duration of thrombocytopenia below 50× 10^9/L was 4.6±4.8 days. The mean number of blood transfusions during hospitalization for AHSCT was 4.4 ±4.0 units. Only one GI bleeding episode (melena) was noted in one patient during the transplantation. Treatment-related mortality was 0%. At the repeated upper gastrointestinal endoscopy following AHSCT (mean time after AHSCT 7.8 ± 4.4 months, range 4-12 months), all five patients (100%) had a complete resolution of the endoscopic as well as the histological findings of GAVE (**Figure 1**). The Hb level at the time of the second gastroscopy increased from baseline by 1.7 ± 1.8 g/dl, range 0-4.1 g/dl).

Conclusion: We describe the complete resolution of GAVE 12 months after AHSCT in five consecutive patients without treatment-related mortality.

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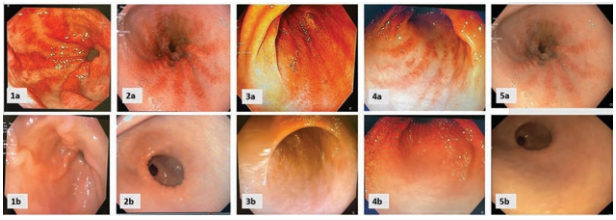


Figure 1 ***: Upper gastrointestinal endoscopy images before (a) and after (b) autologous hematopoietic stem cell transplant:***

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POS1317

COMPLETE RESOLUTION OF GASTRIC ANTRAL VASCULAR ECTASIA AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN SYSTEMIC SCLEROSIS

Keywords: Gastrointestinal tract, Systemic sclerosis

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Background: Gastric antral vascular ectasia (GAVE) is a known vascular gastrointestinal (GI) complication of systemic sclerosis (SSc), characterized by a distinctive endoscopic appearance of a "watermelon stomach" [1]. In patients screened for autologous hemopoietic stem cell transplantation (AHSCT) in the "Scleroderma: Cyclophosphamide or Transplantation" (SCOT) trial, the reported prevalence was up to 22%, and even higher, 45%, specifically in patients with RNA polymerase III antibodies [2]. GAVE carries significant morbidity due to frequent and recurrent GI bleeding, requiring blood transfusions and repeated endoscopic interventions with Argon plasma coagulation (APC). There is no well-established specific therapy for GAVE in the literature. AHSCT is grade A therapy for early diffuse progressive SSc, the population at risk for GAVE. During the conditioning period, thrombocytopenia may result in bleeding from active GAVE. In the SCOT trial, patients with active GAVE were excluded from the study [3]. The data regarding the safety and efficacy of AHSCT in SSC patients with GAVE is scarce.

Objectives: To evaluate the safety and efficacy of AHSCT in SSc patients with GAVE.

Methods: We selected from our cohort of twenty adult dcSSc patients who underwent AHSCT, patients who had GAVE according to gastroscopy prior to AHSCT. We recorded the number of APC procedures before AHSCT, The complications during AHSCT: the nadir thrombocytopenia level, the need for blood

POS1318

GASTRO-INTESTINAL INVOLVEMENT IN SYSTEMIC SCLEROSIS: IMPORTANCE OF AN EARLY DIAGNOSIS THROUGH POPULATION SCREENING AND THE "UCLA SCTC GIT 2.0" QUESTIONNAIRE

Keywords: Systemic sclerosis, Gastrointestinal tract

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Background: Gastrointestinal tract (GIT) involvement in Systemic Sclerosis (SSc), often identified late or sometimes unacknowledged, is estimated in nearly 90% of patients and can be severe in more than 10% of them. "UCLA SCTC GIT 2.0" is a validated questionnaire to assess GI symptoms, using a total score between 0 and 2.83.

Objectives: We aimed to study the role of "UCLA SCTC GIT 2.0" questionnaire in the outpatient practice, as a tool to optimize the diagnosis of GIT disorders and to characterize the specific manifestation for each patient. We also investigated the GIT prevalence in our population to identify predictors of more severe involvement.

Methods: We carried-out a prospective study in patients with SSc, according to the 2013 ACR/EULAR criteria, attending our "Scleroderma Clinic". GIT involvement was investigated through history and administration of "UCLA SCTC GIT 2.0" questionnaire. Patients were stratified according to the severity of 6 items (gastroesophageal reflux disease-GERD, distension/bloating-D/B, fecal

incontinence, bowel movements such as diarrhea or constipation, social activities, emotional well-being) into 3 subgroups: "none to mild", "moderate", "severe to very severe". GIT involvement and its severity have been compared with clinical-demographic and laboratory features.

Results: Study population consisted of 87 patients (M/F 7/80), median age [IQR] of 64 [54;70] years. 81(93%) cases presented GIT disorders where GERD symptoms showed the highest prevalence followed by the B/D ones. The descriptive analysis of the main characteristics is summarized in Table 1. The "UCLA SCTC GIT 2.0" questionnaire revealed a median Total score [IQR] of 0.41 [0.21;0.84]. Median scores and trend of each item are reported in Figure 1. The median D/B score 1 was the statistically highest among all the other reported GIT scores (p=0.0030; p=<0.0001; p=<0,0001 respectively). The analysis of the collected data showed a positive association between GERD and D/B (r=0.4144; p=<0.0001), while positive correlations were found for both total score and GERD with smoking habit (r= 0.2735; p= 0.0104) (r=0.2117; p= 0.0490) and with PPI therapy (r= 0.2270; p= 0.0345) (r= 0.2269; p= 0.0346) respectively. Diarrhea was positively associated with PPI treatment (r= 0.2765; p= 0.0095), while Total score (r= -0.2181; p= 0.0424), GERD (r= -0.2327; p= 0.0301), and diarrhea (r=-0.2386; p= 0.0261) were negatively associated with vascular therapy. D/B score was positively associated with the limited form of the disease (r= -0.2158; p=0.0447) but negatively with mRSS > 7(r=-0.3067; p=0.0039) and disease duration (r=-0.2602; p=0.0149). We didn't find any correlation between GIT involvement and specific autoantibody presence.

Conclusion: Although the results of the present study confirm the higher prevalence of GERD in SSc, they also highlight the highest median score of D/B, often underestimated, whereas its negative correlation with the disease duration, rather than with the extension of the cutaneous involvement, seems to point at an early phenomenon not to be disregarded at the beginning of the patient follow-up. Of interest is to investigate the effective role of vascular therapy for GIT involvement. These findings underline that timely diagnosis and early treatment could provide the opportunity to implement clinical action as well as improvement in the GIT prognosis in SSc, encouraging wider and longer studies.

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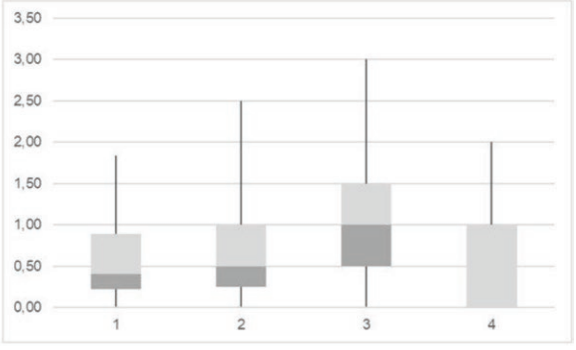


Fig 1. Median scores and trends.

1: Total score [IQR]0.41 [0.21;0.84];
2: GERD [IQR] 0.5 [0.25;1];
3: D/B [IQR]1 [0.5;1.5];
4: Diarrhea [IQR] 0 [0;1].

Features	Value
Age, Median Value [IQR]	64 [54;70]
M/F n° (%)	7 (8) /80 (92)
Disease Duration, Median Value [IQR]	8 [4;13]
Smoke n° (%)	16 (18)
Diffuse / Limited n° (%)	35 (40) / 52 (60)
Raynaud n° (%)	70 (80)
GIT Involvement n° (%)	81 (93)
GERD - total / severe	72 (83) / 29 (33)
D/B - total / severe	68 (78) / 5 (29)
Diarrhea - total /severe	40 (46) / 8 (10)
Constipation - total /severe	47 (54) / 3 (3)
PPI n° (%)	61 (70)
Vascular Therapy (Iloprost, PDE5i, CCB, ASA) n° (%)	78 (90)
SCL-70 / ACA / anti-RNAP3 n° (%)	29 (33) / 34 (39) / 3 (3)

Tab 1. Main features of population.

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POS1319

OUTCOMES IN SYSTEMIC SCLEROSIS PATIENTS TREATED WITH RITUXIMAB AND MYCOPHENOLATE MOFETIL COMBINATION THERAPY COMPARED TO HEMATOLOGICAL STEM CELL TRANSPLANTATION

Keywords: Safety, Systemic sclerosis, Lungs

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Background: Autologous hematological stem cell transplantation (AHSCT) is a grade A therapy for early diffuse progressive systemic sclerosis (SSc), that has been validated in three randomized controlled trials (RCT) compared to cyclophosphamide (CYC) [**1**]. CYC, however, is no longer considered the gold standard therapy for SSc and does not provide long-term benefit [**2**]. The efficacy of rituximab on skin and lung involvement in SSc has recently been demonstrated in an RCT, the DESIRES study. The combination of rituximab with mycophenolate mofetil (MMF) is a potential potent regimen for progressive SSc, that has not been evaluated compared to AHSCT.

Objectives: To retrospectively compare the outcomes of SSc patients in our cohort, fulfilling eligibility criteria for AHSCT studies, who received a combination therapy of MMF and rituximab, with patients who underwent AHSCT.

Methods: Repeated longitudinal assessments at baseline and every 6 months for 24 months, including modified Rodnan Skin Score (mRSS), forced vital capacity (FVC), and diffusing capacity of the lung for carbon monoxide (DLCO) values, were compared between groups using a linear mixed model regression. Clinical improvement (CI) was defined as a decrease in mRSS by more than 25% or an increase in FVC by more than 10%. Event-free survival (EFS) was defined as the occurrence of death or the development of persistent major organ failure (heart, lung, kidney). Hazard ratios (HRs) and 95% CIs were calculated by Cox regression.

Results: Twenty-one SSc patients in the combination group were compared to sixteen in the AHSCT group. There were no significant differences in the demographic or clinical variables, except for Nintedanib treatment (**Table 1**). CI at 12 months was seen in 86% of patients in the combination group, compared to 81% in the AHSCT group (p=0.7). The hazard ratio (HR) for EFS at 24 months favored the combination group (HR=0.09, 95% CI 0.009 to 0.9; P =0.04). In both groups, a statistically significant and similar increase in FVC values, but not in DLCO, was demonstrated at each time point during follow-up. The inclusion of Nintedanib usage in the mixed model did not influence these results. In both groups, there was a significant and similar reduction in mRSS at 12 and 24 months compared to baseline (**Figure 1).**

Conclusion: In our cohort, combination therapy of MMF and rituximab compared to AHSCT in SSc patients eligible for AHSCT, resulted in similar skin and lung clinical improvement with a better safety profile after 24 months.

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Table 1 . Baseline Characteristics of Study Patients

Variable	Transplantation, N = 16[1]	Combination therapy, N = 21[1]	p-value[2]
Age (years)	48 (9)	49 (15)	>0.9
Gender (female)	13 (81%)	15 (71%)	0.7
Autoantibodies			0.4
SCL70	8 (50%)	9 (45%)	
RNA POL3	7 (44%)	6 (30%)	
Negative/other	1 (6.2%)	5 (25%)	
Disease duration			>0.9
< 5 years	14 (88%)	19 (90%)	
Scleroderma subtype			0.050
Diffuse	15 (94%)	13 (62%)	
Lung fibrosis > 10% on lung CT	13 (81%)	16 (76%)	>0.9
Nintedanib (yes)	0 (0%)	9 (43%)	**0.005**
Smoking (yes)	3 (19%)	6 (29%)	0.7
Baseline FVC %	73 (16)	70 (15)	0.8
Baseline DLCO %	60 (13)	58 (16)	0.8
Baseline MRSS	23 (9)	16 (14)	0.072

[1]Mean (SD); n (%)
[2]Wilcoxon rank sum test; Fisher's exact test

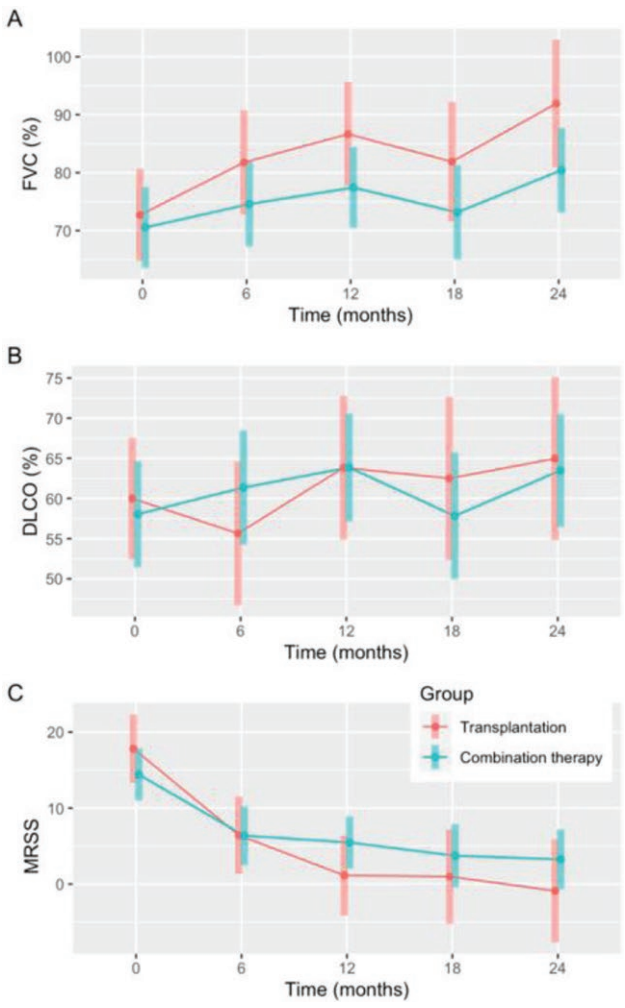


Figure 1 : A linear mixed model of the forced vital capacity (FVC) (**1A**), diffusing capacity of the lung for carbon monoxide (DLCO) (**1B**), and modified Rodnan Skin Score (mRSS) (**1C**) values at follow-up in the two groups.

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Disclosure of Interests: None Declared.
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POS1320

ANTI-RO/SSA - POSITIVE SYSTEMIC SCLEROSIS - COMMONLY ASSOCIATED CLINICAL AND SEROLOGICAL FEATURES INDEPENDENTLY FROM THE UNDERLYING DISEASE

Keywords: Systemic sclerosis, Organ damage, Autoantibodies

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Background: The significance of anti-Ro antibodies in systemic sclerosis (SSc) is still unclear as their presence could represent an epiphenomenon of the strong immune response in severe visceral involvement or directly participate in tissue damages in SSc patients. Recent data suggest that the presence of anti-SSA/Ro antibodies is an independent risk factor for worse pulmonary outcome and higher all-cause mortality in patients with SSc [1].
Objectives: To determine the frequency of anti-SSa/Ro antibodies in a cohort of SSc patients and its association with clinical, serological features and survival, in order to analyze the diagnostic utility of their separate detection.
Methods: This was a single-center retrospective study of a SSc cohort followed over a 10-year period in our rheumatology department. Duration of disease progression, symptoms and parameters related to a specific organ involvement according to MEDS evaluation sheets, were evaluated in all patients.
Results: 270 SSc patients were selected, from which we identified a final population of 28 (10%) anti-Ro-positive patients. The anti-SSA/Ro group included more women (26/28) with a mean age of 47.9 ± 13.7 years, most of them with diffuse subset (16/30). The presence of anti-SSA/Ro antibodies was positively correlated with presence of anti-Scl 70 antibodies (p=0.012), elevated modified Rodnan score (p=0.041), myositis (p=0.013), and lower DLCO (p=0.019). Moreover, associations were strongest for elevated CRP levels (p<0.001) and calcinosis cutis (p<0.001). Compared to non-anti-SSa/Ro patients, both groups were similar regarding demographic data, age at diagnosis, disease duration and type of skin involvement. As expected, the anti-SSa/Ro group had significantly more frequent erosive synovitis (p=0.002), myopathy (p=0.010), gastrointestinal involvement and interstitial lung disease (ILD) (p=0.001). No statistically significant differences were found regarding frequencies of Raynaud's phenomenon, pulmonary hypertension, renal, vascular and cardiac involvement, nor neoplasia. There was a greater proportion of digital ulcers and calcinosis in the anti-SSa/Ro group (42% vs 17% and 58% vs 14%), but without statistical significance. Again, among those patients, a much higher proportion (64% vs 42%) was treated with immunosuppressive agents. No differences in mortality were found between the groups.
Conclusion: Anti-SSA/Ro antibodies seem to characterize a distinct group of SSc patients who are almost exclusively female, express elevated CRP levels, have a high prevalence of ILD, myositis, joint involvement and calcinosis, and commonly receive immunosuppressants.

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Disclosure of Interests: None Declared.
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POS1321

ABSENCE OF NAILFOLD CAPILLAROSCOPIC FINDINGS DEFINES A CLINICALLY DISTINCT SYSTEMIC SCLEROSIS SUBSET

Keywords: Organ damage, Systemic sclerosis, Outcome measures

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Background: In systemic sclerosis (SSc), a specific nailfold videocapillaroscopy (NVC) pattern is observed in 90% of cases and seems to be associated with severity and progression of the disease. Data about SSc patients with normal/nonspecific NVC are scarce [1].
Objectives: This study aims to investigate the clinical and immunologic characteristics of SSc patients with normal or nonspecific NVC and to compare them to those with a scleroderma NVC pattern.
Methods: This was a single-center retrospective study which enrolled 270 SSc patients referred for NVC since January 2000, in our rheumatology department. Demographic and clinical features, symptoms and parameters related to a specific organ involvement according to MEDS evaluation sheets and survival were evaluated.
Results: 270 SSc patients were selected in the database, from which we identified a final population of 19 (7%) patients with normal/nonspecific NVC pattern. The group comprised 14 females and 5 males, with a mean age of 52.7 (±17.4) years, most of them with diffuse subset (12/19). Among the cases, 8 (42%) had normal NVC and 11 (58%) had nonspecific NVC changes, characterized by isolated ramified capillaries in 42%, curved capillary limbs in 33%, giant capillaries in 16% and focal microhemorrhages in 9 % of patients. The mean Raynaud phenomenon's (RP) duration was longer (18.4 ± 14.4 years) compared to the other cases (10.2 ± 1.5 years). The difference was not significant (p=0.107). Significantly higher percentages of cases had lower overall frequency of digital ulcers (28% vs 51%, p=0.04). Presence of synovitis (p=0.010) and myositis (p<0.001) was positively correlated with normal/nonspecific NVC changes. Regarding other organ involvement, the cases also had less severe pulmonary involvement, less frequent digestive involvement and/or pulmonary arterial hypertension than controls, but these differences did not reach significance. No differences in mortality were found between the groups.
Conclusion: SSc patients with normal/nonspecific NVC changes have less organ involvement and less overall disease severity than those with a typical SSc specific NVC pattern, with no between-group differences. Musculoskeletal involvement was the only factor independently associated with normal/nonspecific NVC. It is possible that SSc with normal NVC may be at lower risk of progression to severe visceral and skin involvements, but prospective studies are required.

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POS1322 LOW CD32 EXPRESSION ACCOUNTS FOR THE ASSOCIATION OF CD21LOW B CELLS WITH DIGITAL ULCERS IN SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis

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Background: Abberations of B cells have been implicated in the pathogenesis of systemic sclerosis(SSc) [1] and CD21^{low} B cells, which express high levels of activation markers, have recently been associated with vascular manifestations in SSc [2]. CD32 (FcγRII), comprised of three isoforms A, B and C, is involved in B cell regulation and antibody production. B cells do not express FcγRIIA and mainly express the inhibitory FcγRIIB isoform [3].

Objectives: The aim of our study was to assess the expression of CD32 in CD21^{low} B cells in SSc patients with digital ulcers (DUs).

Methods: Thirty patients, 23 women (median age 56 years. Interquartile range 32 -81) and 7 men (median age 60 years, Interquartile range 52-79) fulfilling the ACR/EULAR 2013 criteria for SSc were included in the study. Peripheral blood mononuclear cells from patients were analyzed with multicolor flow cytometry using anti-CD19 monoclonal antibody (moAb), anti-CD21 moAb, and anti-CD32 moAb, that recognizes both the FcγRIIA and FcγRIIB isoforms.

Results: The percentage of CD21^{low} B cells was significantly increased in patients with DUs compared to patients without DUs (difference between means: 24.6, 95% CI 5.37-43.8, p = 0.014). The percentage of CD21^{low}CD32^{low} B cells were significantly increased in patients with DUs compared to patients without DUs (difference between means: 23.24 ± 7.364, 95% CI 8.152-38.32, p = 0.0038) (Figure1A). The percentage of CD21^{low}CD32^{high} B cells was significantly decreased in the DUs group (difference between means: -26.61 ± 9.312, 95% CI -45.69 to -7.539, p = 0.0080) (Figure 1B).

Conclusion: Our study suggests that low expression of CD32 accounts for the association of CD21^{low} B cells with DUs in SSc and implies that CD32 may have an inhibitory effect on CD21^{low} B cells.

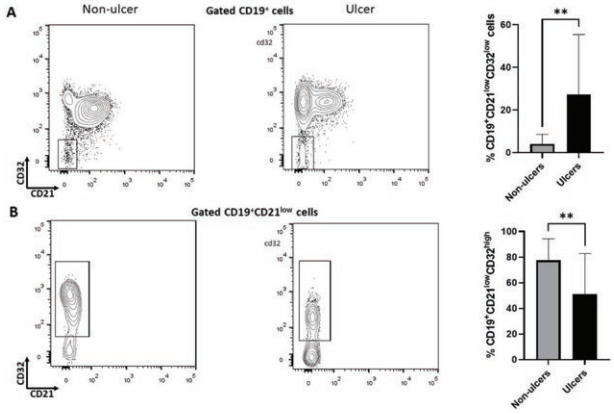


Figure 1

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POS1323 BODY COMPOSITION IN PATIENTS WITH SYSTEMIC SCLEROSIS: RESULTS OF A COMPUTED TOMOGRAPHY STUDY

Keywords: Imaging, Systemic sclerosis

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Background: Subclinical primary muscular involvement and malnutrition may occur in a significant percentage of patients with systemic sclerosis (SSc), and they are potential risk factors for the development of sarcopenia [1]. Sarcopenia is defined as age-associated loss of muscle mass, strength, and function, and unlike other chronic rheumatic inflammatory disorders, it has been poorly investigated in SSc patients. In recent years, some imaging methods have emerged for the identification of sarcopenic markers such as altered muscle composition and fat infiltration (myosteatosis).

Objectives: To evaluate the occurrence of myosteatosis and the prognostic role of body composition, assessed by computed tomography, in patients affected with SSc.

Methods: Patients affected with SSc (2013 EULAR/ACR criteria) referring to our tertiary center from 2015 to 2021 who underwent chest computed tomography to assess pulmonary involvement were included. A semi-automatic segmentation of the subcutaneous fat and paravertebral muscle was performed at the level of the 12th dorsal vertebra using a software and the following body composition variables (BCV) were collected: subcutaneous fat area, subcutaneous fat Hu, paravertebral muscle area, paravertebral muscle Hu. Myosteatosis was considered as Hu values <30. The Student's t-test was used to evaluate if any difference regarding BCV occurred between males and females. Logistic regression analysis was applied to assess the role of the BCV on the overall survival while the Spearman correlation coefficient was used to evaluate the relationship between the BCV and the skin score. For all the analyses the applied significance level was p<0.05.

Results: Sixty SSc patients were included (51 females; mean age 55.63±14 years). Most patients were positive for anti-nuclear antibodies (ANA, 90%), with anti-topoisomerase I specificity in 61.6% of them; twenty-nine patients (48.3%) were affected by the diffuse cutaneous form. At baseline, the mean modified Rodnan skin score (mRSS) was 10.22 (±8.8) and the mean revised EUSTAR activity index was 2.08 (±1.4). Signs of myosteatosis were detected in forty-seven (78.3%) SSc patients. Males showed significantly greater muscle areas (males 9732±3019 vs. females 6599±1328 mm^2; p<0.001) and less hypodense subcutaneous fat (males 76±18 vs. females 88±16 Hu; p=0.027). Overall, seven patients deceased at a 5-year follow-up. No correlation was found between BCV and the mRSS. None of the radiological variables emerged as a predictor of survival.

Conclusion: Most patients with SSc are affected by myosteatosis, even those without symptoms of muscle involvement, while overall body composition does not appear to predict survival. The results of our pilot study may open the door to evaluating the role of body composition in SSc patients: larger longitudinal studies looking at different time-points in the disease course may provide further insights.

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POS1324

MYCOPHENOLATE MOFETIL USE IN CLINICAL PRACTICE IN A MULTICENTRIC COHORT OF SCLERODERMA PATIENTS: PERSISTENCE ON THERAPY AND LONG-TERM ADVERSE EVENTS

Keywords: Disease-modifying drugs (DMARDs), Safety, Systemic sclerosis

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Background: Mycophenolate mofetil (MMF) is the most widely used immunosuppressant in Systemic Sclerosis (SSc) since the Scleroderma Lung Study II demonstrated the safety and efficacy of this drug. Real-life evidence about long early and long-term adverse events (AEs) associated to the use of MMF is lacking, and SSc predictors of drug's discontinuation are not identified yet.
Objectives: To evaluate the long-term persistence of MMF treatment and the adverse events (AEs) incidence in a multicentric cohort of SSc patients.
Methods: Medical records of SSc patients treated with MMF and followed up in 9 tertiary centers were retrospectively collected and evaluated. AEs occurrence (i.e. infections, gastrointestinal (GI) intolerance, laboratory abnormalities, new cancer diagnosis), and reasons for dosage reduction or discontinuation in the 5 five years after the MMF prescription were recorded. Infections were reported and classified according to the organ involved, the etiology, and the severity.
Results: Data from 494 SSc patients observed for 3.1 years (IQR 1.4-4.9) were analyzed. Combination therapy with steroids was reported in 37.0% of patients, while in 14.8% of cases MMF was associated with Rituximab or Tocilizumab treatment. Raw MMF therapy persistence at 12, 24 and 60 months was 91.37%, 88.37%, and 66.34%, respectively. MMF discontinuation incidence was 7.65 per 100 patient years due to any cause, 4.69 per 100 patient years due to drug-related AEs, 1.8 per 100 patient years due to GI intolerance, 1.01 per 100 patient years due to severe or recurrent infections, 0.79 per 100 patient years due to laboratory abnormalities, and 0.65 per 100 patient years due to new cancer diagnosis. Longer disease duration (p=0.003), low diffusing capacity for carbon monoxide (DLco) (p=0.003), late pattern at video-capillaroscopy (p=0.02), esophageal involvement (0.002), and intestinal involvement (p<0.001) were associated with MMF discontinuation. Of note, the most frequent recorded infections had a viral non-COVID19 and non-HZV etiology (21.7%), mostly affecting upper airways (7.1%), and were characterized as mildly severe (13.4%). During follow-up, 127 severe or moderately severe infections were reported, and they were associated with baseline low DLco (p=0.01), late capillaroscopy pattern (p=0.005), esophageal involvement (p=0.01), intestinal involvement (p=0.04), and smoking (p=0.005).

Table : Clinical characteristics of multicentric cohort

Clinical characteristics	N = 494
Age, years, mean±standard deviation	53±14
Female gender, n (%)	406 (82.3)
Diffuse cutaneous subset, n (%)	291 (58.9)
Disease duration, median (interquartile range)	2.0 (0.0, 6.0)
Anti-centromere antibody positive, n (%)	56 (17.6)
Anti-topoisomerase I antibody positive, n (%)	250 (50.6)
Late pattern on capillaroscopy, n (%)	125 (25.3)
Digital ulcers, n (%)	224 (45.3)
Severe gastroesophageal reflux n (%)	316 (64.0)
Chronic diarrhea, n (%)	57 (11.5)
Intestinal dysmotility (chronic constipation, incontinence), n (%)	54 (10.9)
Interstitial lung disease, n (%)	386 (78.1)

Conclusion: This real-life analysis of our multicenter cohort demonstrated that MMF is well tolerated with a high treatment persistence rate. The main reasons of MMF discontinuation were GI intolerance followed by infections and laboratory abnormalities. Advanced SSc microvascular damage on capillaroscopy and GI SSc involvement characterized the patients at higher risk of AEs during treatment.
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POS1325

TREATMENT WITH NINTEDANIB IN SYSTEMIC SCLEROSIS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE: SAFETY AND EFFECTIVENESS AFTER ONE YEAR IN A REAL-LIFE COHORT

Keywords: Safety, Systemic sclerosis, Lungs

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Background: Interstitial Lung Disease (ILD) is detected in 80% of the high resolution CT scans (HRCT) of patients with Systemic Sclerosis (SSc). ILD is responsible for 60% of the mortality related to SSc. Although classic treatment is based on immunosuppressant therapies, nintedanib has recently been approved for SSc-ILD as disease modifying antifibrotic drug.
Objectives: To describe the safety and effectiveness of nintedanib over one year follow-up in a cohort of SSc-ILD patients.
Methods: Basal characteristics of SSc patients, concomitant therapy, adverse events, and pulmonary function test after one year of nintedanib treatment were collected in a cohort with SSc-ILD from a tertiary hospital. SPSS 20.0 was used for descriptive statistics.
Results: Twenty-two patients were treated with nintedanib for SSc-ILD, 17 (77.3%) of the patients were women, with a median (interquartilic range, IQR) age at ILD diagnosis of 45.7 (39.4 – 56.8) years, and with a median extent of ILD features in the HRCT at the beginning of the treatment of 29.7% (20.0% - 39.9%). The median period from the ILD diagnosis to nintedanib initiation was 46.5 months. As concomitant therapies, 17 (77.3%) were under mycophenolate acid, 7 (31.8%) received previously intravenous cyclophosphamide, and 8 (36.4%) had taken rituximab previously or during nintedanib treatment. In terms of security profile, 17 out of 22 (81.4%) patients presented some infection –severe infections were described only in 3 cases-, taking into account that among them 14 (82.4%) patients were under concomitant immunosuppressant treatment. Nine (40.9%) patients suffered from diarrhea, and 5 (22.7%) presented elevation of liver enzymes, which required dose reduction in 2 (9.1%), temporary interruption of nintedanib in another 2 (9.1%), and permanent withdrawal in 1 (4.5%) patient. During a median period of follow-up of 29.5 months, 3 (13.6%) patients died, 13 (59.1%) required a nintedanib dose reduction, 4 (18.2%) temporary interruption, and 5 (22.7%) a permanent withdrawal. The absolute forced vital capacity (FVC) percentage after the first 12-month follow-up increased in 0.15 % (-3.8 – 5.5), which meant a relative increase in FVC of 2.3% (-4.7 – 7.9).
Conclusion: Nintedanib treatment for SSc-ILD showed a satisfactory safety profile, constituting diarrhea and elevated liver enzymes the most common adverse events related with the drug. An increase in infection rates cannot be established as the majority of the patients were under concomitant immunosuppressant therapies. FVC was stable during follow-up, which supports the effectiveness of nintedanib for SSc-ILD in real-life cohorts.
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Iñigo Ojanguren Consultant of: Consulting fees from Boehringer Ingelheim, Ana Villar Consultant of: Consulting fees from Boehringer Ingelheim, Carmen Pilar Simeon Aznar Speakers bureau: Received payment as speaker's bureau from Boehringer Ingelheim, Janssen and GSK., Paid instructor for: Received payment as speaker's bureau from Boehringer Ingelheim., Consultant of: Received consulting fees from Boehringer Ingelheim.
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POS1326 LONG TERM TREATMENT WITH RITUXIMAB IN PROGRESSIVE SYSTEMIC SCLEROSIS: A MONOCENTRIC RETROSPECTIVE STUDY

Keywords: Systemic sclerosis, Safety

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Background: Treatment of Systemic Sclerosis (SSc) remains challenging and some clinical studies reported the efficacy of Rituximab (RTX) in skin disease and in stabilizing lung involvement. Recently 2 randomized clinical trial demonstrated the efficacy of RTX in SSc and in lung involvement in connective tissue diseases (1,2), however current data are limited by the small number of samples examined and the short duration of follow-up.
Objectives: We aimed at retrospectively evaluate the efficacy, safety, and long-term persistence of RTX therapy in a monocentric SSc cohort.
Methods: All clinical records of SSc patients (pts) treated with RTX in our center were retrospectively analyzed. Demographic, clinical and disease characteristics, treatment approach, combination therapies, and adverse events during RTX were considered. Every 6 months, skin score, pulmonary function test and swollen joint count (SJC) modifications as well as digital ulcer occurrence were recorded.
Results: Fifty-two SSc pts (pts) have been treated with RTX in our center since 2005. The mean age of the pts was 55.3±24.3 years and 21.5% were male. The disease duration at the time of the first treatment with RTX was 4.4±2.8 years and the mean reached follow-up was 6.6±2.2 years (range 2-17 years). Forty pts (77.0%) had a diffuse cutaneous involvement, 33 pts (63.6%) had anti-topoisomerase positivity, 45 (88.2%) an interstitial lung disease on high resolution chest CT, 30 pts (59.2%) arthritis or tenosynovitis, and finally 38 pts (73.1%) presented any history of digital ulcers. Twenty-three (44.2%) pts had been previously treated with cyclophosphamide. During RTX treatment, 39 pts (75.0%) received an immunosuppressive combination therapy, most with mycophenolate mofetil (53.8%). Concomitant glucocorticoids treatment was assumed by the 53.8% of pts. Twenty-five pts (48.1%) were treated with Rituximab for only one clinical involvement, 27 pts (51.9%) received treatment for more than one organ involvement including skin, lung or joint. Overall, 82.7% were treated for progression of skin disease, 50.0% for lung involvement deterioration and 23.1% for active arthritis. Treatment showed improvement in the skin score, arthritis, and/or stabilization of the pulmonary functional status in 44 pts (84.6%), while in the remaining 8 pts, therapy was stopped because of worsening of the disease over the 6 months of follow-up. Among responders, skin score improved from 17.3±8.9 to 10.3±8.6 (p=0.04), while FVC and DLco remained stable (87.4±3.5% to 86.2±20.5% and 66.3±23.9% to 64.3±22.1%, respectively). As expected, there was an improvement in DAS28 (4.9±0.8 to 1.9±0.5, p<0.01). Finally, there was a reduction in the rate of ulcer occurrence (46.15% to 21.70%, p=0.04). Twenty-two pts (42.3%) were treated with one single cycle of therapy (1 gr two weeks apart), while the remaining 30 pts were treated with repeated cycles of RTX, with a mean number of cycles of 4.3±2.0. Among the re-treated pts, 50% were treated every year and 50.0% at the time of new clinical worsening, and retreatment was done every 60.5±31.4 months. All pts re-treated with RTX on demand responded to the therapy. Nineteen percent of pts developed adverse events (5.7% leukopenia, 7.7% infusion reactions, 1.9% sepsis, 3.8% pneumonia). Ten pts (19.2%) died during follow-up: 8 deaths were related to organ complication of SSc and 2 to cancer.
Conclusion: Our data suggest long-term efficacy and safety of RTX in pts SSc. Further real world studies will be necessary to evaluate the best therapeutic approach with RTX (regular cycles or retreatment when clinical worsening occurs) and/or the combination with other immunosuppressant drugs.
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POS1327 HORMONE REPLACEMENT THERAPY INCREASES THE RISK OF SYSTEMIC SCLEROSIS: RESULTS FROM LARGE POPULATION-BASED CASE-CONTROL STUDY

Keywords: Epidemiology

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Background: Systemic sclerosis (SSc) exhibits, similarly to other autoimmune diseases, a strong female preponderance. Estrogen has been found to activate signaling pathways involved in immune response and promote autoimmunity [1]. Several studies on cultured SSc skin fibroblasts have reported fibrinogenic role of female sex steroids, but the hormonal impact on the risk of SSc remains underexplored. In a recently published pharmacovigilance report, hormone replacement therapy (HRT) was highlighted as potentially implicated in SSc development [2].
Objectives: In this case-control study, we aimed to assess the relationship between HRT and risk of SSc in a population-based cohort of SSc patients and matched controls.
Methods: Participants with newly diagnosed SSc and their matched controls were identified from nationwide registers. Definition of SSc required a first-time diagnosis of SSc (ICD10 codes: M34.0, M34.1, M34.9, M34.8, as a primary diagnosis) in specialist care, with a second visit listing SSc within 12 months We included visits between Jan 1, 2009 and December 31, 2017 with the first visit representing the index date. Controls were sex, age and region-matched to SSc cases in 1:5 ratio. Study sample was restricted to women aged 40 or older at index date. Participants on progestogen in monotherapy and those with history of thromboembolism, stroke, ischemic heart disease, endometrial and breast cancer before index date, were excluded. Dispensations of HRT were extracted from Prescription register, using The Anatomical Therapeutic Chemical classification system codes. Study participants with a history of ever taking HRT (estrogen, estrogen and progestogen combination and tibolone) at least three years before the index date were considered exposed. The relationship between HRT and SSc was assessed using conditional logistic regression models adjusted for socioeconomic factors and polypharmacy. The impact of underlying comorbidities was evaluated by identifying the most common ICD-10 codes among the users of HRT and sequentially excluding cases and controls with a history of these comorbidities from the analyses.
Results: In total, 553 SSc cases and 2,696 controls were included. Twelve percent of cases and 9% of controls were taking HRT at any time ≥3 years before the index date was associated with a 42% increased risk of SSc (95% CI: 1.1,1.9; p=0.02, Figure 1 a). Combination of estrogen and progestogen showed statistically significant associations with SSc (OR=1.5; 95% CI: 1.0,2.05; p=0.03) (Figure 1 a). Subsequent sensitivity analyses indicated that underlying comorbidities did not influence the observed relationship between HRT and SSc (Figure 1 b).
Conclusion: The findings of this study implicate HRT in the development of SSc and add to a growing body of evidence pointing to the proinflammatory role of female sex steroids in the pathogenesis of immune-mediated disorders.
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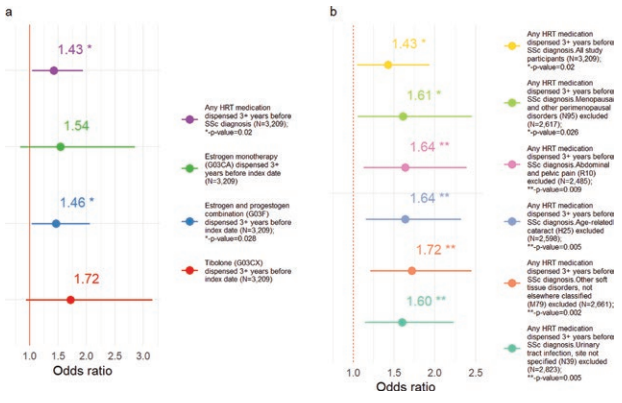


Figure 1 Associations between SSc and HRT. Panel a) and b) show associations with different HRT medications and results of sensitivity analyses, accordingly

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1328

DIFFERENTIATING "SCLERODERMA" WITH "NON-SCLERODERMA" PATTERNS IN NAILFOLD CAPILLARY MICROSCOPY USING A DEEP LEARNING MODEL

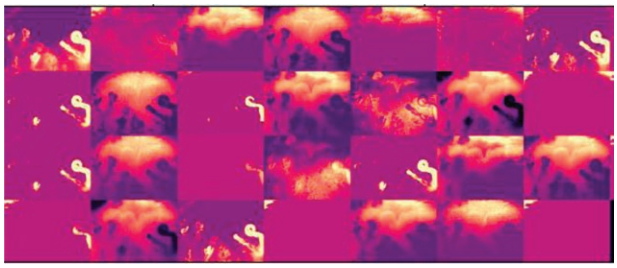
Keywords: Systemic sclerosis

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Background: Nailfold capillary microscopy is used for diagnostic purposes in rheumatology since many years. Abnormal nailfold capillaries are also listed in the 2013 ACR/EULAR classification criteria for systemic sclerosis (SSc) [1]. A fast-track algorithm to differentiate between "scleroderma" and "non-scleroderma" patterns of capillary microscopy was published in 2019, and is being applied in clinical routine as a useful decision algorithm [2]. Artificial intelligence is being increasingly implemented in many spheres of everyday life, including medicine. Keras is a publicly available deep learning framework, which is widely used for research purposes, in particular for constructing artificial neural networks [3].
Objectives: To estimate the ability of a deep learning model, to differentiate between scleroderma and non-scleroderma capillary microscopy patterns.
Methods: Capillary microscopy was performed using Optilia Digital Capillaroscope. We analyzed capillary microscopy images, which were equally subdivided into two groups, including scleroderma and non-scleroderma patterns. Subsequently the pictures were assigned to training, validation and test sets. Each set contained the same number of images with scleroderma- and non-scleroderma patterns. Then we trained a deep learning model using training and validation datasets to differentiate between the aforementioned capillaroscopy patterns. A test set was applied to estimate the model performance in an independent data set. The technical side of the study was performed using a 2D convolutional neural network, which was constructed based on Keras deep learning libraries (example Picture 1).
Results: A total of 1076 capillaroscopy images from 70 patients were analyzed the study: 780, 196 and 100 pictures in the training, validation and test sets accordingly. Each image dataset contained an equal amount of pictures from scleroderma- and non-scleroderma patterns. The trained model showed an accuracy of 87,8% with sensitivity of 94.9% (95% CI 0,905 to 0,99), specificity of 80,6% (95% CI 0,73 to 0,88) and an area under the curve (AUC) of 0.9326 in the validation set. In the test set, there was a slightly better model performance with an accuracy of 92%, a sensitivity of 96% (95% CI 0,91 to 1), a specificity of 88% (95% CI 0,79 to 0.97) and an AUC of 0,9742.
Conclusion: Despite the relatively small image dataset, the developed deep learning model could successfully discriminate scleroderma- vs. non-scleroderma capillaroscopy patterns, which may be applied in an automated assessment of capillaroscopy pictures in the future.

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Picture 1. Different deep learning filters, applied to a capillaroscopy image.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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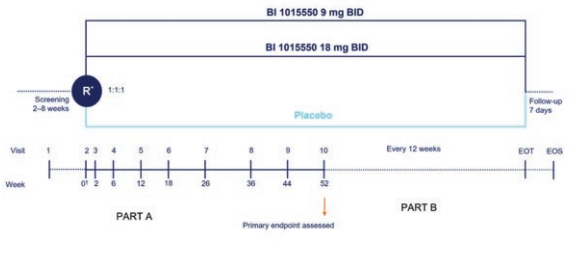
POS1329

DESIGN OF A PHASE III, RANDOMISED, PLACEBO-CONTROLLED TRIAL OF BI 1015550 IN PATIENTS WITH PROGRESSIVE FIBROSING INTERSTITIAL LUNG DISEASE

Keywords: Lungs, Systemic sclerosis, Clinical trials

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Background: Progressive pulmonary fibrosis (PPF) includes any diagnosis of progressive fibrotic interstitial lung disease (ILD) other than idiopathic pulmonary fibrosis (IPF), and occurs in a range of disorders such as connective tissue diseases or hypersensitivity pneumonitis. Patients with PPF have comparable disease progression, lung function decline and mortality as patients with IPF. It is therefore hypothesised that they share underlying pathobiology and may respond to the same treatments, as was also seen in the Phase III INBUILD trial of nintedanib. BI 1015550, a preferential phosphodiesterase 4B inhibitor, prevented lung function decline in a Phase II study in IPF and may provide an additional treatment option, alone or with nintedanib, in patients with PPF.
Objectives: This Phase III trial (FIBRONEER-ILD™) will investigate the efficacy and safety of BI 1015550 in patients with PPF.
Methods: This double-blind, randomised, placebo-controlled trial (NCT05321082) is underway at approximately 400 sites in 45 countries. It is planned that 1041 patients will be randomised in a 1:1:1 ratio to either 18 mg BI 1015550 twice daily (BID), 9 mg BI 1015550 BID or placebo, in addition to standard of care, over at least 52 weeks (Figure 1). Similar to the INBUILD trial, patients are stratified by high-resolution computed tomography pattern (usual interstitial pneumonia-like vs other fibrotic patterns), and by baseline use of nintedanib (yes/no). Patients are enrolled if they meet the predefined criteria for PPF and other criteria (Table 1).
Results: The trial initiated and began enrolment in October 2022. Enrolment is expected to complete by the end of 2023. The primary endpoint is absolute change from baseline in forced vital capacity (FVC) (mL) at Week 52. The key secondary endpoint is the time to first acute exacerbation, first hospitalisation for respiratory cause or death (whichever occurs first) over the duration of the trial.
Conclusion: The FIBRONEER-ILD™ trial is designed to investigate the potential use of BI 1015550 as a treatment option for patients with PPF, with and without background nintedanib treatment.



*Randomisation will be stratified by the presence of background nintedanib use (with or without nintedanib) and high-resolution computed tomography imaging pattern (usual interstitial pneumonia pattern vs other fibrotic patterns). In Part B, patients will continue treatment with blinded trial medication and have trial visits every 12 weeks, until the last randomised patient reaches 52 weeks of treatment. EOS is expected to be up to 130 weeks with an assumed recruitment period of 18 months. †Day 1. BID, twice daily; EOS, end of study; EOT, end of trial (i.e. last randomised patient reaches 52 weeks of treatment); R, randomisation.

Figure 1. Trial design

Table 1 . Main inclusion and exclusion criteria

Inclusion criteria
• ≥18 years old
• FVC ≥45% predicted
• DLco corrected for haemoglobin (Visit 1) ≥25% and <90% predicted
• Patients are on stable treatment with nintedanib for at least 12 weeks or not on treatment with nintedanib for at least 8 weeks
• Patients treated with permitted immunosuppressive agents for an underlying systemic disease (e.g. methotrexate, azathioprine) need to be on a stable treatment for at least 12 weeks prior to the initial screening period (Visit 1) and during the screening period
• Presence of fibrotic lung disease on HRCT, defined as reticular abnormality with traction bronchiectasis with or without honeycombing, with disease extent >10% on HRCT (confirmed by central review) within 12 months of Visit 1
• Patients must fulfil at least one of the following criteria within 24 months of Visit 1:
– Clinically significant decline in FVC% predicted based on a relative decline of ≥10%
– Marginal decline in FVC% predicted based on a relative decline of ≥5–<10% with worsening of respiratory symptoms
– Marginal decline in FVC% predicted based on a relative decline of ≥5–<10% with increasing extent of fibrotic changes on chest imaging
– Worsening of respiratory symptoms and increasing extent of fibrotic changes on chest imaging
Exclusion criteria
• Patients with airway obstruction (pre-bronchodilator FEV_1/FVC ratio <0.7) (Visit 1)
• Acute ILD exacerbation (investigator-determined) within 3 months prior to Visit 1 and/or during the screening period
• Treatment with oral corticosteroids >15 mg/day within 4 weeks; cyclophosphamide, tocilizumab, mycophenolate within 8 weeks; rituximab within 6 months
• Suicidal behaviour in the past 2 years

DLco, diffusing capacity of the lung for carbon monoxide; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease.

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Disclosure of Interests: Toby Maher Speakers bureau: Boehringer Ingelheim; Roche/Genentech, Paid instructor for: Boehringer Ingelheim; Roche/Genentech, Consultant of: Personal payment from: AstraZeneca, Bayer, Blade Therapeutics, Bristol-Myers Squibb, Galapagos, Galecto, GlaxoSmithKline, IQVIA, Pliant, Respivant, Theravance, Veracyte., Shervin Assassi Consultant of: Novartis; Boehringer Ingelheim; AstraZeneca; CSL Behring; Abbvie, Grant/research support from: Boehringer Ingelheim; Janssen, Arata Azuma Speakers bureau: Boehringer Ingelheim; Taiho Pharm. Co., Consultant of: Boehringer Ingelheim; Taiho Pharm. Co.; Toray Medical Co.; Kyorin Pharm. Co., Grant/research support from: Boehringer Ingelheim; Taiho Pharm. Co, Vincent Cottin Speakers bureau: Boehringer Ingelheim; Roche, Consultant of: Boehringer Ingelheim; Roche; Galapagos; Shionogi; RedX; Pure Tech; Celgene/BMS; AstraZeneca; CSL Behring; Sanofi, Grant/research support from: Boehringer Ingelheim, Anna-Maria Hoffmann-Vold Speakers bureau: Actelion; ARXX; Bayer; Boehringer-Ingelheim; Janssen; Lilly; Medscape; Merck Sharp & Dohme; Roche, Consultant of: Actelion; ARXX; Bayer; Boehringer Ingelheim; Janssen; Medscape; Roche, Grant/research support from: Boehringer Ingelheim; Janssen, Michael Kreuter Speakers bureau: Boehringer Ingelheim; Galapagos; Roche, Consultant of: Boehringer Ingelheim; Galapagos; Roche, Grant/research support from: Boehringer Ingelheim; Roche, Justin Oldham Consultant of: Boehringer Ingelheim; Roche/Genentech; Lupin Pharmaceuticals, Grant/research support from: Boehringer Ingelheim, Luca Richeldi Speakers bureau: Boehringer Ingelheim; Zambon; Cipla; Roche, Consultant of: Biogen; Celgene; Nitto; Pliant Therapeutics; Toray; BMS; RespiVant; CSL Behring; Roche; Boehringer Ingelheim; FibroGen; Promedior, Grant/research support from: Boehringer Ingelheim; Italian Drug Agency, CLAUDIA VALENZUELA Speakers bureau: Boehringer Ingelheim; Hoffmann-La Roche, Ltd; BMS, Consultant of: Boehringer Ingelheim; Hoffmann-La Roche, Ltd; BMS, Marlies Wijsenbeek Speakers bureau: Boehringer Ingelheim; Hoffman la Roche; Novartis; CLS Behring; Galapagos, Consultant of: Boehringer Ingelheim; Hoffman la Roche; Galapagos; Bristol Myers Squibb; Galecto; Respivant; Nerretherapeutics; Horizontherapeutics; PureTech health; Kinevant Sciences; Molecure; CLS Behring; Thyron; Vicore; Savara; Galapagos, Grant/research support from: Boehringer Ingelheim; Hoffman la Roche; The Netherlands Organisation for Health Research and Development; The Dutch Lung Foundation; The Dutch Pulmonary Fibrosis; AstraZeneca-Daiichi, Carl Coeck Employee of: Boehringer Ingelheim Pharmaceuticals, Inc, Florian Voss Employee of: Boehringer Ingelheim Pharmaceuticals, Inc., Daniel Wachtlin Employee of: Boehringer Ingelheim Pharmaceuticals, Inc., Fernando Martinez Consultant of: AbbVie; Boehringer Ingelheim; Bristol-Myers Squibb; Bridge Biotherapeutics; CSL Behring; DevPro; IQVIA; Roche/Genentech; Sanofi; Shionogi; twoXAR; United Therapeutics; Veracyte; Afferent/Merck; Bayer; Biogen; Nitto; Respivant; Roche.

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POS1330 LUNG ULTRASOUND FOR THE FOLLOW-UP OF SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE TREATED WITH NINTEDANIB: OUTCOMES AND COMPARISONS WITH OTHER ASSESSMENT TOOLS

Keywords: Systemic sclerosis, Ultrasound, Lungs

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Background: Nintedanib (NIN) is an antifibrotic drug used to slow the progression of systemic sclerosis-related interstitial lung disease (SSc-ILD), reducing the decline in forced vital capacity (FVC). High-resolution chest tomography (HRCT) is the gold standard imaging technique to assess SSc-ILD, whereas lung ultrasound (LUS) is a useful and repeatable non-invasive tool which is increasingly used in clinical practice.

Objectives: The aim of this work was to investigate the usefulness of LUS during the follow-up of SSc-ILD patients treated with NIN.

Methods: Adult SSc patients starting NIN for ILD were enrolled and followed for 12 months. LUS was performed at baseline and quarterly on 55 antero-posterior spaces, evaluating pleural line irregularities (PLI; semi-quantitative score 0-1-2) and the number of B-lines (BL), according to OMERACT definition. FVC was investigated every six months, whereas HRCT was performed at baseline and at 12 months. The following patient-reported outcomes were administered quarterly: Leicester cough questionnaire and St.George respiratory questionnaire. During follow-up, all of the aforementioned investigations were assessed for stability, improvement, or worsening from baseline, then evaluating the concordance with LUS variations.

Results: Ten SSc-ILD patients (70% female, mean age 62±10.9 years) starting NIN were enrolled. One patient had to prematurely discontinue NIN due to unbearable gastrointestinal adverse effects. The other 9 patients were followed for 12 months, achieving FVC stabilization in 87.5% of the cases. The mean PLI score and the mean BL number both showed a declining trend over time (Figure 1), with a 12-months significant overall reduction (p=0.02 for PLI; p<0.01 for BL). At the final evaluation, both PLI and BL were improved in 55.5% of the cases and stable in the rest, whereas HRCT resulted worsened in 62.5% of patients and stable in the rest. The concordance of these two imaging techniques was very low (12.5%). LUS concordance with FVC was quite good (61.5% for PLI and 46.1% for BL). Moreover, PLI variations showed a greater concordance for Leicester cough questionnaire and St.George respiratory questionnaire (69.2% and 42.3%, respectively) than BL variations (35.7% and 28.5%, respectively).

Conclusion: We performed LUS for the follow-up of SSc-ILD patients treated with NIN. Changes in PLI and BL fairly closely reflected the functional and subjective trend of the patients. PLI variations showed a good correlation with the outcomes of FVC and cough questionnaires. HRCT seems to progress regardless of the efficacy of NIN on lung function, therefore LUS could be used for monitoring SSc-ILD patients receiving NIN.

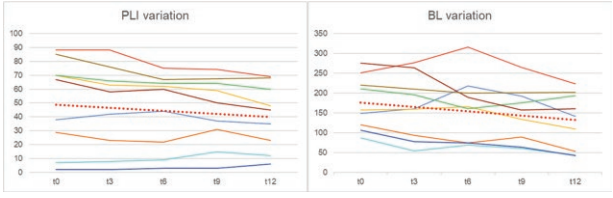


Figure 1.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1331 DEVELOPMENT AND VALIDATION OF A CLINICAL SCORE FOR MORTALITY PREDICTION IN SYSTEMIC SCLEROSIS: THE SSCORE STUDY

Keywords: Prognostic factors, Systemic sclerosis, Systematic review

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Alegre, Brazil; [3]*Hospital de Clínicas de Porto Alegre, Division of Internal Medicine, Porto Alegre, Brazil*; [4]*Nossa Senhora Conceição Hospital, Division of Rheumatology, Porto Alegre, Brazil*

Background: Systemic sclerosis (SSc) is one of the most lethal systemic autoimmune diseases. Considering recent advances in drug therapy and safety concerns, predicting mortality may contribute to a personalized treatment decision [1,2].
Objectives: Our goal was to develop and validate a clinical score for mortality prediction in SSc patients (SScore)
Methods: For SScore development, a systematic literature review (SLR) in PubMed and EMBASE (up to July 2022) was performed by two independent reviewers and hazard ratios (HR) from clinically relevant and statistically significant 5-year SSc mortality predictors were meta-analyzed. Considering heterogeneity (I2 test) and publication bias (Egger's test and funnel plots), we selected the most representative HR of each predictor. The weighted risk of death was estimated by Poisson's regression model, and the final SScore was the sum of each predictor score, varying from 0 to 1. For SScore validation, 91 SSc patients (ACR-EULAR 2013 or LeRoy and Medsger classification criteria) were consecutively included in a prospective cohort and followed-up between 2019 and 2022 in the outpatient clinics of two tertiary hospitals. Death was confirmed by medical records and phone calls.
Results: Out of 6,893 studies (2,539 in PubMed; 4,354 in EMBASE), 33 were included in the meta-analysis [3,449 deaths in 15,403 SSc patients over 8.6 years (mortality 22.4%)]. Six predictors were included in SScore: age, dyspnea, malignancy, renal impairment, anti-Scl70 and scleroderma renal crisis (Table 1). In the validation cohort, there were 13 deaths (mortality 14.3%) among the 91 SSc patients over 2.6 years [age 60.5 (±10.3) years-old; women 92.3%; 81.2% white; SSc duration 13.0 (±8.1) years; diffuse cutaneous SSc 22.0%]. The best SScore cut-off was 0.18 (sensitivity 61.5%, specificity 87.2%, positive and negative predictive values 44.4% and 93.2%, respectively, and accuracy 79.1%). The area under the receiver operating characteristic curve (Figure 1) was 0.78 (95%CI 0.64-0.92). SScore was higher among those who died (p<0.001).

Table 1 : Clinical score for mortality prediction in systemic sclerosis.

Predictor	Relative risk (95%CI)	Score
Age ≥ 60 anos	1.85 (0.61-5.56)	0.10
NYHA functional classes III and IV	2.18 (0.60-7.96)	0.15
Malignancy	5.33 (2.02-14.1)	0.30
Renal impairment	3.60 (1.28-10.1)	0.20
Anti-Scl70	1.89 (0.50-7.06)	0.10
Scleroderma renal crisis	2.44 (0.45-13.2)	0.15

NYHA (New York Heart Association) functional classes III and IV: dyspnea, palpitation or exhaustion with mild physical activity/at rest; renal impairment: creatinine elevation/proteinuria.

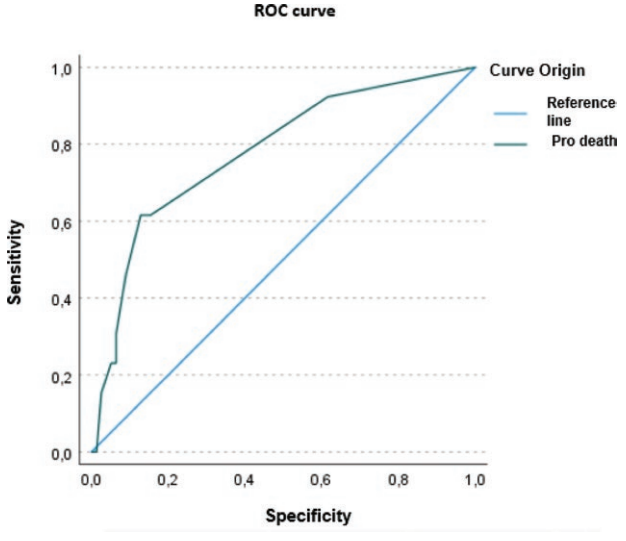


Figure 1 : Receiver operating characteristic curve for death prediction by SScore.

Conclusion: An accessible score for SSc mortality prediction (SScore) was developed from a SLR and validated in a real-life scenario with high specificity and negative predictive value and acceptable accuracy. Larger cohort studies are needed to clarify SScore usefulness in clinical practice, including treatment individualization.

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POS1332

ANTI-NUCLEAR VALOSIN-CONTAINING PROTEIN-LIKE AUTOANTIBODIES ARE ASSOCIATED WITH A NEW CLINICAL PHENOTYPE IN SYSTEMIC SCLEROSIS PATIENTS: LIMITED CUTANEOUS SUBSET WITH RECALCITRANT CALCINOSIS AND HIGHER RISK OF CANCER

Keywords: Systemic sclerosis, Autoantibodies, Malignancy

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Background: It has been reported that 80-85% of established systemic sclerosis (SSc) patients present anti-nuclear autoantibodies (ANAs) [1]. However, in a group of clinically heterogeneous patients with high-titer ANAs no SSc-specific autoantibodies are found. It is likely that these patients present autoantibodies that have not been previously described. Protein immunoprecipitation (IP) followed by mass spectrometry (MS) has the potential to identify these new autoantibodies.
Objectives: To identify novel autoantibodies through a new protein IP assay based on bioorthogonal non-canonical amino acid tagging (BONCAT) combined with MS and to describe the clinical associations of these novel autoantibodies.
Methods: Sera samples and clinical data of 307 SSc patients from Vall d'Hebron University Hospital were collected. All patients met the LeRoy and Medsger criteria and 84.0% fulfilled the 2013 ACR/EULAR classification criteria of SSc. ANAs were tested in all patients by indirect immunofluorescence (IIF) on HEp-2 cells and positive reactions were categorized according to the International Consensus on ANA Patterns (ICAP) classification. Specific autoantibodies (anti-Scl70, -centromere, -RNA-polymerase III, -fibrillarin, -NOR-90, -Th/To, -PM/Scl, -Ku, -U1-RNP, -U11/U12-RNP) were evaluated by a commercial immunoblot and chemiluminescence immunoassay and traditional RNA IP. Patients negative for all tested autoantibodies (n=51) were further studied by an IP assay based on BONCAT. Protein IP was performed by incubation of sera of these patients with protein A-sepharose beads in IP buffer, and subsequent incubation with labelled K562 cell extracts. Obtained immunoprecipitates were fractionated by 10% SDS-polyacrylamide gel electrophoresis (SDS-PAGE). Protein bands detected on SDS-PAGE were further analysed by Liquid Chromatography-MS.
Results: Five patients tested by protein IP showed a band with a molecular weight of 110-115kDa on SDS-PAGE and a homogeneous nucleolar pattern (AC-8) by IIF. These bands were identified as nuclear valosin-containing protein-like (NVL) by MS. All anti-NVL positive patients fulfilled the 2013 ACR/EULAR classification criteria of SSc and presented the limited cutaneous (lcSSc) subtype. Anti-NVL positive patients were characterised by higher age at SSc onset (51.7 vs. 39.9 years, p=0.041) and higher prevalence of calcinosis (100% vs 10.9%, p<0.001). More importantly, anti-NVL positive patients presented higher risk for malignancy (60.0% vs 4.3%, p=0.005; OR 33.0; 95% CI 3.4-323.4) and synchronous cancer (40.0% vs 2.2%, p=0.023; OR 30.0; 95% CI 2.1-433.1).
Conclusion: We have identified NVL as a novel autoantibody target on SSc patients by a new protein IP assay. Anti-NVL positive patients presented a lcSSc phenotype characterized by high prevalence of calcinosis and higher risk of cancer, including synchronous cancer. Further work is required to confirm the clinical associations that were found in this cohort of SSc patients and to evaluate the presence of anti-NVL in other autoimmune diseases and conditions.
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POS1333 ASSOCIATION BETWEEN SYSTEMIC SCLEROSIS AND CACNER: A NATIONWIDE COHORT STUDY

Keywords: Systemic sclerosis, Epidemiology, Malignancy

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Background: Previous studies have shown an association between systemic sclerosis and cancer. However, because the disease is rare, large-scale studies are lacking, especially in Asians.
Objectives: We aimed to compare the incidence of cancer in patients with SSc and age- and sex-matched controls in a nationwide population-based cohort in Korea.
Methods: We included patients with SSc defined by the ICD-10 code (M34) and rare and intractable disease code (V138) and 1:5 age- and sex-matched controls using the Korean National Health Insurance Database. The outcomes of the study were incidence of cancer. Cox proportional hazard analysis and Kaplan-Meier curve were used to compare the incidence of cancer between patients with SSc and controls.
Results: A total of 5,145 patients with systemic sclerosis and 25,725 controls were included in the study. During the study period, the overall cancer incidence rate was 11.07 per 1,000 person-years in patients with systemic sclerosis and 7.59 per 1,000 person-years in controls. Overall cancer risk was 1.5 times higher in patients with systemic sclerosis (adjusted hazard ratio 1.46, 95% confidence interval 1.28–1.67). Lung cancer and lymphoma had a high risk in both male and female patients with systemic sclerosis, and colorectal cancer had a high risk only in male patients with systemic sclerosis. The risk of biliary cancer, skin cancer, and cervical cancer was high in female systemic sclerosis patients.
Conclusion: This nationwide cohort study showed that patients with systemic sclerosis were associated with increased cancer risk. Clinicians should be aware of cancers that may increase the risk in patients with systemic sclerosis and apply appropriate screening measures.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1334 WORK PARTICIPATION AND WORK DISABILITY IN BELGIAN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis

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Background: Systemic sclerosis (SSc) is an immune-mediated connective tissue disease that potentially affects multiple organ systems. Besides health-related complications, patients often describe work-related difficulties (e.g. productivity loss, sick leave, work disability) that may result in a major individual burden and the rise of indirect costs for society.
Objectives: Despite the rheumatology community's growing interest, work participation and its influencing factors is still an underrecognized and underexplored field of research in SSc patients. This study therefore aims to provide up-to-date data about work status and its determinants in SSc patients.
Methods: Adult SSc patients were questioned on their socio-economic status at the occasion of an outpatient visit at the rheumatology clinic of Ghent University Hospital, a tertiary hospital in the Flemish region (February 2020 to March 2021). All patients were included in a SSc clinical care path (Belgian Systemic Sclerosis Cohort) and fulfilled the LeRoy and Medsger's classification criteria. Employment rate was compared with general Flemish population after adjustment for age and sex. Comparative data on the average duration of working life in Belgium were derived from Eurostat (reference year 2020).
Results: Among the 108 participants, 81 (75%) belonged to the working age category (18-65 y/o). The crude employment rate in SSc patients of work-productive age was 64%, resulting in a standardized employment ratio of 0.90 (95%CI 0.69-1.17). About half of these patients worked full time (53%), with a mean±SD of 41.7±8.7 weekly working hours. The median duration of labor force participation in SSc patients was 40.0 years, while the average career duration in the Belgian population amounted 33.4 years. Long term work disability was reported as the most common reason for leaving the labor market (20%). Patients on work disability were significantly older, less highly educated, more functionally disabled and reported a lower quality of life than patients having a paid job. Job characteristics did not differ significantly between patients with and without a paid job (Table 1).
Conclusion: Our data refute the common perception that SSc patients show a significantly lower work participation grade compared to the general population. Socio-demographic but not job-related characteristics are associated with work disability in this population. Quality of life is remarkably better in patients who perform a paid job, reinforcing the importance to support active labor force participation.

Table 1: Patients characteristics according to working status.

	SSc patients with a paid job N= 52	*SSc patients with work disability N=16*	*P-value*
Male	13 (26%)	3 (13%)	0.74
Age, y	46.8 ± 10.1	54.8 ± 8.2	**0.004**
Post-secondary education	25 (49%)	2 (13%)	**0.009**
Disease duration, years	3.0 (1.0-7.0)	4.0 (1.0-12.5)	0.49
Subtype			0.14
- DcSSc	6 (12%)	5 (31%)	
- LcSSc	31 (61%)	6 (38%)	
- LSSc	14 (27%)	5 (31%)	
Internal organ involvement	19 (37%)	7 (44%)	0.64
Cutaneous manifestations	42 (82%)	13 (69%)	0.29
Peripheral vasculopathy	51 (100%)	15 (93.8%)	0.23
SHAQ	0.4 (0.0-1.1)	1.1 (0.4-2.0)	**0.04**
EQ-5D-5L	0.8 (0.8-0.9)	0.5 (0.2-0.8)	**<0.001**
EQ-VAS	73 (65-81)	55 (40-70)	**<0.001**
Blue collar work	32 (65%)	11 (69%)	0.80
Full-time work	27 (54%)	9 (56%)	0.87
Laborer	17 (33%)	9 (56%)	0.10

SHAQ, Scleroderma specific Health Assessment Questionnaire; EQ-5D-5L, EuroQoL-5D; VAS, visual analogue scale.

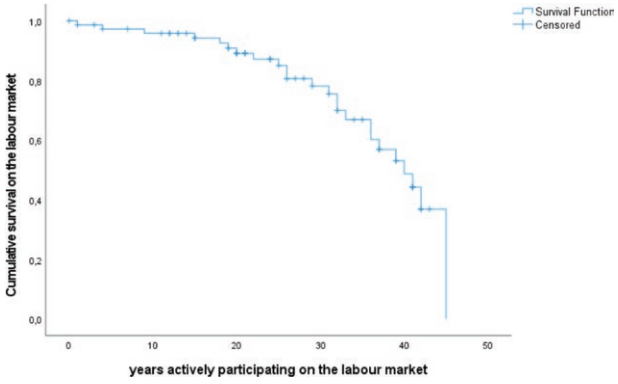


Figure 1 : Retention time on the labor market since start of patient's professional career.

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POS1335 ASSOCIATION BETWEEN LIPID PROFILE AND RISK OF INCIDENT SYSTEMIC SCLEROSIS: A NATIONWIDE POPULATION-BASED STUDY

Keywords: Epidemiology, Systemic sclerosis, Real-world evidence

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Background: Lipid metabolism is altered in patients with systemic sclerosis (SSc), mediating activation of immune cells and fibroblasts. However, it is unclear whether altered lipid profile in individuals without SSc is associated with a risk of future development of SSc.

Objectives: To assess the association between lipid profile and future development of SSc.

Methods: Individuals without SSc who underwent national health check-ups in 2009 were selected and followed up through 2019 from a nationwide database of the Korean National Health Insurance Service. Serum levels of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglyceride, measured on the date of health check-up in 2009, were each categorized into quartiles (Q1 [lowest], Q2, Q3, and Q4 [highest]). Individuals who developed SSc during follow-up were identified. Cox regression analyses adjusted for multiple covariates were performed to estimate the adjusted hazard ratios (aHRs), and 95% confidence intervals (CIs) according to the quartiles of levels of TC, HDL-C-, LDL-C, and triglyceride, respectively, using Q1 as the reference.

Results: Of the 9,894,996 individuals selected, 1,355 individuals developed SSc during a mean follow-up of 9.2 years, accounting for an incidence rate of 1.49 per 100,000 person-years. Compared with Q1 levels, Q4 levels of TC (aHR 0.691, 95% CI 0.592–0.806), HDL-C (aHR 0.611, 95% CI 0.521–0.716), and LDL-C (aHR 0.735, 95% CI 0.630–0.856) were associated with a lower risk of incident SSc, while Q4 levels of triglyceride (aHR 1.060, 95% CI 0.896–1.254) were not. Higher quartiles of TC (p for trend<0.001), HDL-C (p for trend<0.001), and LDL-C (p for trend=0.001) were associated with a larger effect size.

Conclusion: Serum levels of TC, HDL-C, and LDL-C were inversely associated with the risk of incident SSc. Our findings provide new insights that altered lipid profile could be considered a risk factor for incident SSc.

Reference: None.

Table 1. Risk of incident systemic sclerosis according to lipid profile

	Cut-off (mg/dL)	N	SScDuration (pyrs)	IR /100,000 pyrs	Model 1	Model 2
TC	Q1≤139	2,485,033	373 22,670,953.05	1.65	1 (Ref.)	1 (Ref.)
	Q2170–192	2,487,413	345 22,832,305.38	1.51	0.918 (0.793–1.063)	0.874 (0.754–1.012)
	Q3193–217	2,450,733	317 22,517,096.31	1.41	0.855 (0.736–0.993)	0.773 (0.664–0.900)
	Q4≥218	2,471,817	320 22,690,097.63	1.41	0.857 (0.738–0.995)	0.691 (0.592–0.806)
HDL -C	Q1≤45	2,599,835	367 23,703,987.10	1.55	1 (Ref.)	1 (Ref.)
	Q246–53	2,406,259	336 22,083,139.89	1.52	0.982 (0.847–1.139)	0.847 (0.730–0.983)
	Q354–63	2,507,100	352 23,041,299.39	1.53	0.986 (0.852–1.142)	0.760 (0.654–0.882)
	Q4≥64	2,381,802	300 21,882,025.99	1.37	0.885 (0.760–1.031)	0.611 (0.521–0.716)
LDL –C	Q1≤90	2,508,966	362 22,891,074.64	1.58	1 (Ref.)	1 (Ref.)
	Q291–111	2,485,047	322 22,808,239.53	1.41	0.892 (0.768–1.037)	0.829 (0.713–0.964)
	Q3112–134	2,467,601	336 22,667,147.88	1.48	0.937 (0.807–1.087)	0.826 (0.710–0.961)
	Q4≥135	2,433,382	335 22,343,990.32	1.50	0.947 (0.816–1.099)	0.735 (0.630–0.856)
Triglyceride	Q1≤74	2,446,904	381 22,542,116.72	1.69	1 (Ref.)	1 (Ref.)
	Q275–109	2,521,143	320 23,103,563.15	1.39	0.820 (0.706–0.951)	0.867 (0.745–1.009)
	Q3110–163	2,458,085	367 22,478,344.97	1.63	0.966 (0.837–1.115)	1.109 (0.953–1.292)
	Q4≥164	2,468,864	287 22,586,427.53	1.27	0.752 (0.645–0.876)	1.060 (0.896–1.254)

Model 1: Crude model.Model 2: Adjusted for age, sex, BMI, residence, income, smoking status, alcohol consumption, physical activity, hypertension, type 2 diabetes, CKD, and lipid-lowering agents.BMI, body mass index; CKD, chronic kidney disease; HDL-C, high-density lipoprotein cholesterol; IR, incidence rate; LDL-C, low-density lipoprotein cholesterol; pyrs, person-years; SSc, systemic sclerosis; TC, total cholesterol.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1336

MRI DIGITAL ARTERY VOLUME INDEX (DAVIX©) AS QUANTITATIVE, CONTINUOUS IMAGING OUTCOME MEASURE OF VASCULAR DISEASE IN SYSTEMIC SCLEROSIS

Keywords: Clinical trials, Outcome measures, Imaging

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Background: In Systemic Sclerosis, beyond the value of Nailfold capillaroscopy, there is still a deeply unmet need in quantitative imaging surrogate outcome measures to assess activity and/or severity of peripheral vascular disease. This has been halting the implementation of trials targeting vascular disease beyond crude endpoints such as number of digital ulcers (DU). Quantitative MRI based scores have boosted the implementation of new trials in inflammatory arthritis.

Objectives: To determine the value of MRI-based Digital Artery Volume Index (DAVIX©) score in predicting the burden of DU disease as well as other vascular endpoints including clinical manifestation and patient reported outcomes (PROs).

Methods: Consecutive patients with Raynaud's phenomenon were enrolled in two independent discovery and validation cohorts. Data collected included: pulmonary function tests, nailfold capillaroscopy, modified Rodnan Skin Score (mRSS), history/presence of DU (defined as DU Disease), sHAQ-DI, Cochin hand function and Borg scales. Discovery cohort had clinical follow up data at 12 months, Validation cohort had only baseline data. DAVIX© (dominant hand) was calculated by MRI time of flight based, digital artery volumetric assessment over the volume of each finger, as %mean of the 4 fingers [1, 2]. Mann-Whitney test was used to compare DAVIX© between patients' subgroups. Correlations between DAVIX© and clinical variables/PROs were performed using Pearson's and Spearman's tests, as appropriate. Data analysis was conducted using R software.

Results: 233 patients were recruited in discovery (D=91) and baseline validation (V=142) cohorts. 139 patients fulfilled 2013 SSc classification criteria (62 in discovery cohort and 77 in validation cohort), 94 were patients with VEDOSS (2013 ACR/EULAR SSc classification criteria <9) and not included in further analysis. Median (IQR) disease duration was 5.9 (7) and 4.7 (6) years in the two cohorts (P=0.618). DAVIX was significantly lower in patients with DUs disease in both cohorts (0.34% and 0.49% vs 0.65% and 0.75%) compared to patients with no DUs (D, P=0.0018; V, P=0.003). DAVIX© correlated with baseline DLCO% in both cohorts (r= 0.368 and 0.315; P=0.004 and 0.038, respectively). There was no correlation with mRSS or FVC% whereas, DAVIX© correlated with FVC/DLCO ratio (r=-0.337, P=0.009). The analysis of PROs showed that DAVIX correlated best with VAS DUs (r=-0.291 and -0.243, P<0.05 for both cohorts) and VAS Raynaud (r=-0.270, P=0.048 for the discovery cohort), whereas there was no significant correlation with the other PROs. Importantly, DAVIX© correlated inversely with disease duration in both cohorts (r=-0.415 and -0.441, P<0.001 for both). In the discovery cohort, 12 patients developed new (7) or their first (5) DUs during follow-up and their mean DAVIX© was 0.23% vs 0.66% of 73 patients who did not develop any new DUs (p=0.02). Standard Receiver Operating Curve indicated that DAVIX© <0.36% conferred a 4 times higher risk of new DUs, independently of any other clinical variable.

Conclusion: DAVIX© is a feasible, automated, contrast-free imaging outcome measure that reflects worse vascular disease as far as DU disease, DLCO% and patient reported burden of Raynaud's and DU disease. DAVIX© validation in Randomized Controlled Trials would offer a novel imaging based surrogate outcome measure of vascular disease in Systemic Sclerosis.

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Pain in rheumatic diseases, including fibromyalgia

POS1337 LONG-TERM OPIOID USE AMONG PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES: IMPACT OF VARYING DEFINITIONS

Keywords: Pain, Fibromyalgia, Inflammatory arthritides

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Background: People living with rheumatic and musculoskeletal diseases (RMD) are frequently prescribed opioids for non-cancer pain. A proportion of RMD patients newly prescribed an opioid will transition to long-term opioid use, and represent a high-risk subgroup for opioid dependence, abuse and harms. However, definitions of long-term opioid use in the literature vary considerably, making it difficult to characterise the scale of the issue and design future interventions to address it [1,2].
Objectives: (1) To evaluate the proportion of patients transitioning to long-term opioid use in new users across 6 RMD conditions using varying definitions used in the literature (2) To assess the proportion of long-term opioid users who transition to opioid dependence.
Methods: Patients aged ≥18 years with a diagnosis of rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthritis (AxSpA), systemic lupus erythematosus (SLE), osteoarthritis (OA) and fibromyalgia and without prior cancer, with a new episode of opioid use between 01/01/2006 and 31/10/2021 and at least a 1-year follow-up in the Clinical Practice Research Datalink (CPRD) were included. CPRD is a database of anonymised UK primary care electronic health records representative of the national population. Long-term opioid users were defined using 3 different definitions: 1) *Standard* (most commonly used): ≥3 opioid prescriptions issued within a 90-day period, or ≥90 days opioid supply, in the first year of follow-up (excluding the first 30 days). 2) *Stringent*: ≥10 opioid prescriptions filled over >90 days, or ≥120-day opioid supply in the first-year follow-up. 3) *Broad*: ≥3 monthly prescriptions (no need to be consecutive) in the first 12 months. Opioid dependence was defined as RMD patients who had relevant Read Codes within 5 years after a new episode of opioid use. The proportions of long-term opioid use and opioid dependence for RMDs were calculated.
Results: This study included 841,047 patients of whom 12,260 had a code for RA, 5,195 PsA, 3,046 AxSpA, 3,081 SLE, 796,276 OA, and 21,189 fibromyalgia. The highest proportion of long-term opioid users among the 6 RMDs was patients with fibromyalgia (27.4% for *Standard*, 20.9% for *Stringent*, and 33.7% for *Broad*), followed by RA (25.7%, 18.5%, and 32.3% respectively) and AxSpA (23.8%, 17.3%, and 29.6% respectively) (Figure 1-stacked bar chart). On average, using *Broad* definition showed 10-13% higher than *Stringent* definition for all RMDs. As the Venn diagram in Figure 1, 241,727 patients met any of the definitions of long-term use, of which half fulfilled all 3 definitions. The *Broad* definition was able to identify additional half of long-term users, with 24.0% overlapping with the *Standard* definition. In total, 685 (0.06%) RMD patients were diagnosed with opioid dependence within 5 years after starting opioids. Similar proportions of opioid dependence were observed in long-term opioid users across all definitions: 332 (0.18%) for *Standard*, 281 (0.23%) for *Stringent*, and 355 (0.15%) for *Broad* definitions. Moreover, 323 out of 685 RMD patients (47.2%) who had a diagnosis of opioid dependence were not classified as long-term opioid users by the 3 definitions.
Conclusion: Around 1 in 3 fibromyalgia patients and 1 in 4 RA/ AxSpA patients fulfilled definitions for long-term opioid use within 12 months after starting an opioid. The low prevalence of opioid dependence across all RMDs, defined using Read Codes alone is likely to be considerably underrepresented in clinical practice. This reflects both coding practises in primary care and under recognition of the issue in those on long-term opioids.

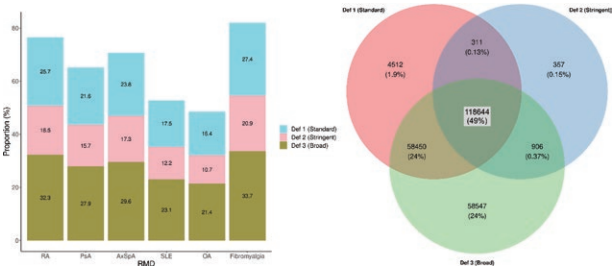


Figure 1 Long-term opioid users by definitions and overlap between them

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Disclosure of Interests: Joyce (Yun-Ting) Huang: None declared, David Jenkins: None declared, Belay Birlie Yimer: None declared, Carlos Ramirez Medina: None declared, Niels Peek: None declared, Mark Lunt: None declared, William Dixon Consultant of: WGD has received consultancy fees from Google unrelated to this work., Meghna Jani: None declared.
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POS1338 PHARMAKON OR THE ART THAT HEALS: TRANS-DISCIPLINARY ARTISTIC-TRANSFORMATIVE WORKSHOPS FOR FIBROMYALGIA SYNDROME

Keywords: Non-pharmacological interventions, Patient reported outcomes, Fibromyalgia

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Background: Fibromyalgia syndrome (FMS) is a widespread chronic pain syndrome with many associated symptoms. It is frequently related to a traumatic event (1), strong and of short duration, or slight but protracted over time. A multidisciplinary therapeutic approach is recommended by international guidelines. The transformative experience (TE) allows for a profound and immediate change that differs from linear and gradual psychological change; this helps create novel responses to the same initial thoughts and actions, thereby breaking the maladaptive emotional/behavioral loop elicited by chronic stress and trauma (2), creating a sort of "virtuous" cycle, adaptive rather than maladaptive and long-lasting. In this study, TE was specifically elicited through transformative art (TA), an intrinsically transdisciplinary tool, in different ways in the three arms of the study.
Objectives: Validation of the efficacy (in terms of quality of life and sleep, self-esteem, self-efficacy) of transdisciplinary TA workshops in patients with FMS.
Methods: Prospective observational study lasting 8 months (February-October, 2021), in which the effectiveness of three different TA workshops in patients with FMS was evaluated: in group 1 participants were encouraged to review their autobiography and illness in a humorous sense; in group 2 participants were guided to express their own realities of chronically ill patients in poetry; group 3 was based on the guided narration of works of art according to visual thinking strategies integrated with the principles of narrative medicine. Patients were divided into the three laboratories according to their preference. Tests were administered at baseline and post-workshop. The activities took place entirely online.
Results: 109 FM patients completed the study (n=3 males, mean age 52.9, mean years from diagnosis 11.2 [SD 8.6]). No differences were found among the three groups at baseline in terms of clinimetric variables. Data analysis made by a Wlicoxon non-parametric test (WNPT) of the three groups in conjunction showed a statistically significant improvement of the Pittsburgh Sleep Quality Index (PSQI) ($p<0.05$), Response to Stressful Experiences Scale (RSES) ($p<0.05$), World Health Organization- Five Well-Being Index (WHO-5) ($p<0.001$) and Global Health scale (GH) ($p<0.05$). No significant difference was found for The Mindful Attention Awareness Scale (MAAS) ($p=0.2663$). A WPNT was performed to compare baseline and final results of the three groups separately. The best performance was seen in Group 1, since patients ameliorated in almost all parameters: PSQI ($p<0.05$), GH ($p<0.05$), SAP dimension 1 ($p<0.05$), 2 ($p<0.05$) and 4 ($p<0.05$), WHO-5 ($p=0.0013$). MAAS ($p=0.895$), RSES ($p=0.0673$) and SAP dimension 3 ($p=0.0573$) resulted nonsignificant, although very close to significance. Sleep ($p<0.05$) and the 3rd dimension of SAP ($p<0.05$) improved in patients of Group 2; whilst self-esteem ($p<0.05$) and WHO-5 ($p<0.05$) did in Group 3.
Conclusion: Our research shows that art, experienced as TA, leads to significant improvements of the psychophysical condition of FMS patients. TA can be seen as a crucial mediator for overcoming the trauma/stressors, probably through the generation of "pivotal mental states" (PIMS), defined as a "hyper-plastic state aiding rapid and deep learning that can mediate psychological transformation" [3].

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Disclosure of Interests: None Declared.

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POS1339

EFFICACY OF VERY LOW-CALORIE KETOGENIC DIET IN OBESE PATIENTS WITH FIBROMYALGIA: PRELIMINARY RESULTS FROM A MONOCENTRIC INTERVENTIONAL STUDY

Keywords: Diet and nutrition, Pain, Fibromyalgia

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Background: Obesity can worsen fibromyalgia (FM) and very low-calorie ketogenic diet (VLCKD) is a potential therapeutic option in diseases that share clinical and pathophysiological features with FM [1].

Objectives: In this pilot interventional study, we investigate the effects of VLCKD in obese patients with FM.

Methods: Adult FM patients with a BMI ≥ 30 kg/m [2] and who had failed standard low-calorie diets, were eligible for VLCKD. The weight-loss program was preceded by 4 weeks of free-diet (W-4 to W0). During the first period of VLCKD (W1 to W4), patients could eat protein preparations and vegetables. In the next phase (W5 to W8), natural proteins were gradually integrated in the dietary regimen. Ketosis was assessed weekly with urine strips. Carbohydrates were then progressively reintroduced (W9 to W20). Changes in BMI, FM impact questionnaire (FIQ) and Hospital Anxiety and Depression Scale (HADS-A for anxiety and HADS-D for depression) were evaluated at established timepoints. As previously reported, a change of 14% in FIQ was considered clinically relevant [2]. This interim analysis evaluates patients who reached the final visit after 20 weeks from the beginning of VLCKD (W20).

Results: At data cut-off, 20 patients, all females, were enrolled in the study. Two patients discontinued the intervention while 4 are currently in the maintenance phase. Mean age of the 14 patients who reached W20 was 50.4 years and BMI was 36.9. Baseline characteristics are summarized in Table 1. No significant difference in BMI, FIQ, HADS-A and HADS-D was observed from W-4 to W0. All patients lost weight during the first period of VLCKD and this achievement was maintained through W20 (Figure 1, panel A). Mean BMI decreased from 36.9 at W0 to 34.5 at W4, 33.3 at W8 and 32.2 at W20 (all p <0.001 compared to W0). Compared to W0, a significant reduction of mean FIQ (Figure 1, panel B) from 64.3 to 35.2 was observed at the end of W4 (p <0.001) and was maintained also at W8 (mean FIQ of 38.8; p =0.004) and at W20 (mean FIQ of 39.1; p =0.007). Analysing the trend in each participant, at W4, all 14 patients showed a reduction in FIQ, which was clinically relevant in 13 (93%). Compared to W0, a meaningful improvement in FIQ was still observed at W20 in 12 cases (86%). However, change in BMI was not significantly correlated with change in FIQ at any timepoint. HADS-A and HADS-D improved significantly from W0 to W4, W8 and W20. (Figure 1, panels C, D). Mild constipation was reported by 8 patients (57%), fatigue by 4 (29%) and headache by 3 (21%). No major safety concern emerged.

Conclusion: These are the first data on the efficacy of VLCKD in FM. All patients achieved improvement in disease activity outcomes during the ketogenic phase, which was maintained also after carbohydrate reintroduction. Our data suggest that ketosis might exert beneficial effects in FM which extend beyond the promotion of rapid weight loss.

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Table 1. Characteristics of patients included in the study

Characteristics	Patients n=14
Age, mean (SD)	50.4 (9.6)
Body mass index, mean (SD)	36.9 (3.7)
Disease duration, years, median (IQR)	4.0 (1.6 - 6.4)
Comorbidities	
Diabetes, n (%)	0
Hyperlipidemia, n (%)	10 (71)
Hypertension, n (%)	7 (50)
Fatty liver disease, n (%)	5 (36)
Congestive heart failure, n (%)	0
Atherosclerosis, n (%)	0
Polycystic ovary syndrome, n (%)	2 (14)
Therapy	
Non-steroidal anti-inflammatory drugs, n (%)	6 (43)
Opioids, n (%)	1 (7)
Paracetamol, n (%)	6 (43)
Corticosteroids, n (%)	0
Muscle relaxants, n (%)	1 (7)
Antidepressants, n (%)	3 (21)
Gabapentinoids, n (%)	2 (14)
Benzodiazepines, n (%)	2 (14)

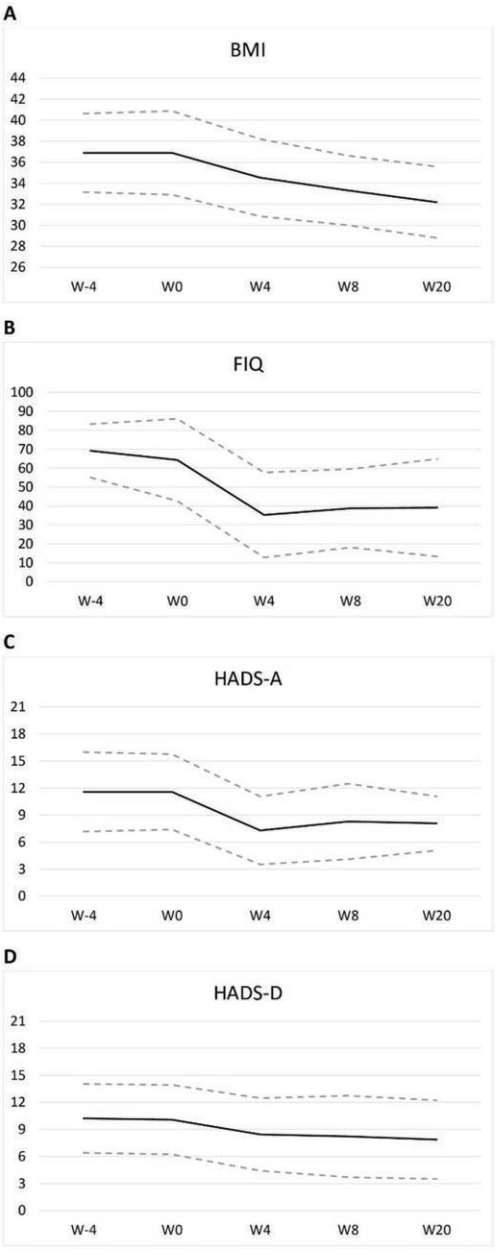


Figure 1. Changes in BMI, FIQ, HADS-A and HADS-D during the study period. Solid lines represent mean values, dashed lines represent standard deviations.

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Disclosure of Interests: None Declared.
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POS1340 VALIDATION OF QUALISEX QUESTIONNAIRE TO EVALUATE SEXUAL DYSFUNCTION IN WOMEN AFFECTED BY FIBROMYALGIA

Keywords: Quality of life, Lifestyles, Fibromyalgia

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Background: Fibromyalgia (FM) is a common chronic widespread pain condition, also characterized by fatigue, sleep and mood disorders, with higher prevalence in women. Sexual function is an important feature in people's well-being; its alterations include decreased sex drive, sexual satisfaction, orgasm, and arousal, as well as increased genital pain. Emerging but still too few studies observed a higher prevalence of sexual dysfunction in FM, especially related to depression.
Objectives: The aim of this study was to evaluate sexual dysfunctions in a large cohort of FM women through Qualisex questionnaire, used in other rheumatic diseases but not yet validated for FM.
Methods: We consecutively enrolled women affected by FM (ACR 2016) referring to our out-patient clinic. Demographic and clinical examination as well as evaluation of severity of FM symptoms (R-FIQ, SSS and WPI) were assessed for each patient. Moreover, Hospital Anxiety and Depression Scale (HADS) and questionnaire for sexual dysfunction-Qualisex were anonymously administered. Qualisex questionnaire is composed by 10 questions on different items of sexual life with higher scores suggestive of greater negative impact of FM on sexual life.
Results: The cohort was composed by 373 FM female patients, median age 49,1. Qualisex questionnaire was validated with Cronbach's alpha test (0,878), median value 5,3. Women with lower grade of education (p=0,002), married (p<0,001) and with lower sexual feeling with partner (p<0,001) showed higher values of Qualisex. Menopause status, drug assumption and comorbidity did not influence patients' sexual quality. High values of HADS-A and HADS-D showed a positive correlation with Qualisex Total (p<0,001 r=0,312; p<0,001 r=0,542 respectively) as well as high values of VAS pain, VAS fatigue and VAS dryness (p<0,001 r=0,438; p<0,001 r=0,375; p<0,001 r=0,70 respectively). Relationship duration also presented a positive correlation (p<0,001 r=0,202). Multivariate analysis observed a significantly influence of relationship duration, VAS pain, fatigue and dryness, HADS-A/D, R-FIQ and all specific items of Qualisex, on Qualisex Total correcting for patients' age (p<0,001).
Conclusion: Qualisex questionnaire represents a good test to evaluate sexual disorders in FM women. Different aspects contribute to sexual dysfunction both from a psychological (anxiety, depression, loss of self-esteem, decreased sexually attraction) and a physical (pain, fatigue etc..) point of view with an important impact of FM on sexual life and consequently a worsening of FM symptoms. Over a demotivation feeling, inability to live a "normal everyday life", the reduced sexual function contributes to a bad quality of life. Other studies are needed to analyze which interventions, pharmacological and non (physical activity, psychotherapy), could improve the sexual aspect in the global contest of FM and to investigate this important aspect in FM male patients.

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Table 1

	FM (n=373)
Age (yrs), media ± SD	49,1 ± 10,4
Menopause, n (%)	185 (49.6)
Age menopause (yrs), media ± SD	48,7 ± 7,3
Replacement therapy, n (%)	69 (18.3)
Sexual relationship duration (yrs), media ± SD	18,2 ± 11,7
Qualisex TOTAL	5,3 ± 2,7
HADS A, media ± SD	11,9 ± 4,3
HADS D, media ± SD	9,5 ± 4,1
VAS dryness (0-10), media ± SD	5,6 ± 3,4
VAS pain (0-10), media ± SD	6,8 ± 2,7
VAS fatigue (0-10), media ± SD	7,9 ± 1,9

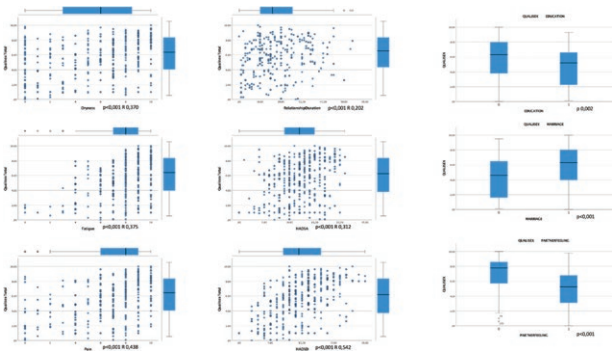


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1341 GENDER DIFFERENCES IN THE REVISED FIBROMYALGIA IMPACT QUESTIONNAIRE (FIQR) A PILOT STUDY

Keywords: Patient reported outcomes, Gender/diversity issues, Fibromyalgia

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Background: Fibromyalgia (FM) is a chronic syndrome clinically characterized by widespread musculoskeletal pain associated with symptoms like fatigue, sleep disturbances and cognitive impairment. Prevalence is higher in females but the 2010/2011 and 2016 revisions of the American College of Rheumatologist (ACR) criteria reduced prevalence differences and the actual female:male ratio is approximately 3:1. Even if in the last years some studies have been conducted regarding gender differences in FM, disease severity is still assessed using questionnaires, such as the Revised Fibromyalgia Impact Questionnaire (FIQR), designed for female patients and validated through a predominantly female sample.
Objectives: Aim of this pilot study was to compare the 21 items of the FIQ-R among male and female patients in order to evaluate the possible existence of a gender bias.
Methods: In this case control study, all the consecutive patients with a diagnosis of FM (2016 ACR criteria) referring to our out-patients *Fibromyalgia Clinic* between May 2020 and December 2022 were asked to answer an online survey, including demographic characteristics, disease variables and the Italian version of the FIQR. Among the 544 patients that compiled the questionnaire, 78 patients, 39 males and 39 females matched for age and disease duration, were consecutively enrolled in order to compare their total FIQR score and the different domains scores.
Results: The univariate analysis of the FIQR scores, taking account of the total score and of the different domains of FIQR, showed that total scores and physical function domain scores were significantly higher in females compared to males. No significant differences emerged between the two groups regarding overall impact domain score and symptoms domain score. Among the 21 items of the FIQR, the female group obtained significantly higher scores answering the questions FIQR1 (brush or comb your hair), FIQR4 (vacuum, scrub, or sweep floors), FIQR5 (lift and carry a bag full of groceries), FIQR7 (change bed sheets), FIQR9 (go shopping for groceries) and FIQR21 (sensitivity to loud noises, bright lights, odors, cold).
Conclusion: The results of our pilot study showed that female patients obtain significantly higher scores in the FIQR total score and in the physical function domain score, in particular in 5 out of the 9 sub-items of the FIQR physical function domain. These preliminary results indicate that the use of the FIQR as a severity index in male patients probably underestimates the disease impact in this group. In order to confirm these results the sample needs to be increased but it seems reasonable to conclude that the assessment of disease impact should be diversified, taking gender differences into account.

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Table 1. Significant differences in FIQR total, domains and single question scores based onsex

Score	M (39)	F (39)	p-value
FIQR Total	58.8 (23.5)	70.3 (14.7)	***.035***
FIQR Physicalfunction	14.8 (8.2)	20.1 (5.1)	***.003***
FIQR1 Brush or comb your hair	2.4 (3.3)	4.3 (2.9)	***.006***
FIQR4Vacuum, scrub, or sweep floors	5.2 (3.6)	7.5 (2.2)	***.005***
FIQR5Lift and carry a bag full of groceries	6.4 (3.1)	8.3 (1.6)	***.002***
FIQR7 Change bed sheets	4.7 (3.6)	7.1 (2.7)	***.001***
FIQR9 Go shopping for groceries	4.9 (3.3)	6.7 (2.4)	***.012***
FIQR21Sensitivity to loud noises, bright lights, odors, cold	6.2 (2.7)	7.9 (1.6)	***.005***

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Disclosure of Interests: None Declared.
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POS1342 COGNITIVE DYSFUNCTION IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RELATIONSHIP WITH BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF)

Keywords: Cognitive function, Spondyloarthritis, Fibromyalgia

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Background: Normal cognitive status is essential for daily activities, but many people with chronic autoimmune rheumatic diseases are impaired in this function. This is probably related to the age of the patients, the education level, the duration of the disease, the disease activity. Pronounced pain syndrome in ankylosing spondylitis (AS) patients is a risk factor of cognitive dysfunction [1, 2]. There are also literature data regarding the involvement neurotrophins, namely brain-derived neurotrophic factor (BDNF), in the mechanisms of pain regulation and psychoemotional disorders [3].
Objectives: Our study aimed to evaluate the cognitive status in patients with AS and the relationship with BDNF.
Methods: We examined 143 patients (81.8% male) with AS according to modified New York criteria. The mean age of the examined patients was 42.1±11.3 years. The Mini Mental State Examination MMSE (Folstein M.F. et al., 1975) was used to assess the psychological and cognitive status. The level of BDNF in plasma was determined twice a day (at 8:00 and 20:00) by the ELISA method, also we calculated the ratio between morning and evening BDNF level (BDNF index "8:00/20:00"). The study was conducted in compliance with bioethical standards. All data were analyzed using IBM Statistics SPSS 23 software.
Results: Cognitive dysfunction, according to MMSE, was diagnosed in 90 (62.9%) AS patients. The values of the MMSE scale in AS patients ranged from 25 to 30. It should be noted, that 57.4% had mild cognitive impairment (MMSE - 26-27 points) and only seven patients (4.9%) had moderate (MMSE - 24-25 points) cognitive impairment.
Plasma levels of BDNF (pg/ml) in AS patients shown in Table 1.

Table 1 Value of the plasma levels of BDNF (pg/ml) in AS patients

Group	BDNF			
	Morning level	Evening level	BDNF index "8:00/20:00"	Daily average level
AS with normal cognitive status	970.6±302.0	758.3±448.26	1.75±1.12	864.46±314.3
AS with cognitive dysfunction	957.8±387.2	879.7±357.2	1.59±1.25	918.7±416.1
P	0.836	0.077	0.444	0.413

We established the circadian rhythm of BDNF production during the day. It was revealed in patients with normal cognitive status, as well as in patients with cognitive dysfunction. The BDNF level in the morning was significantly higher than in the evening. We compare BDNF levels in patients with normal cognitive status and in patients with cognitive dysfunction. Patients with cognitive dysfunction showed a trend toward higher evening BDNF level compare patients with normal cognitive status (P=0.077). We established a negative correlation between cognitive status and the evening BDNF level - with an increase in evening BDNF level cognitive dysfunction deepens (P <0.05).
Conclusion: Cognitive dysfunction is a frequent condition in patients with AS. Our study results demonstrate circadian rhythm of BDNF production during the day and relationship between BDNF production and cognitive status – cognitive dysfunction in AS patients is associated with high evening BDNF levels.
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Disclosure of Interests: None Declared.
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POS1343 INFLUENCE OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION OF CNS ON FIBROMYALGIA PATIENTS - A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY (INTERIM ANALYSIS)

Keywords: Patient reported outcomes, Fibromyalgia, Non-pharmacological interventions

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Background: Fibromyalgia syndrome (FMS) is a chronic disorder characterized by diffuse pain, sensitivity to sensory stimuli, fatigue, cognitive impairment, mood and sleep disorder. The side effects of drugs used in treatment (i.e. antiepileptics) can mimic certain symptoms of fibromyalgia (i.e. impaired balance, dizziness), so there is a huge need for alternative treatment. Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive therapy utilizing a magnetic field to stimulate different brain structures. rTMS is registered as adjuvant therapy for major depressive disorder, migraine, and obsessive-compulsive disorder, and its efficacy is being investigated for other conditions.
Objectives: The main aim was to evaluate the influence of rTMS in alleviating the symptoms in patients with fibromyalgia.
Methods: Sixteen patients were randomized to rTMS (n=10) or sham treatment (n=6). rTMS was applied in 10-day sessions with a frequency of 10 Hz and an intensity of 130% of the predetermined motor threshold over the left dorsolateral prefrontal cortex (DLPFC). One session of rTMS consisted of 5 seconds of stimulation (frequency of 10 Hz, for a total of 50 stimuli) and a 10-second pause. Patients received 2000 stimuli per day (50 stimuli in 40 repeated sessions). The placebo was applied with an inactive "sham" coil which resembles active treatment. The intensity of symptoms was assessed with Tender Point Examination (TPE), Visual Analog Scale of Pain (VAS), Brief Pain Inventory (BPI), Beck Depression Inventory II (BDI II), Beck Anxiety Inventory (BAI), Montreal Cognitive Assesment (MoCa), Medical Outcome Studies Sleeping Scale (MOS SS), Functional Assesment of Chronic Illness Therapy – Fatigue (FACIT-F), 36-item Short Form Survey (SF-36), and Revised Fibromyalgia Impact Questionnaire (FIQR).
Results: There was no difference between groups in any of the characteristics at baseline. There was a decrease in BDI score after the treatment period, but the change was more prominent in the rTMS group compared to the placebo (p=0.064). rTMS was also superior in a decrease in FIQR score (p=0.054) (Table 2.) and an increase in vitality through SF-36 (p=0.003). Moreover, placebo treatment led to a significant reduction in sleep disturbances (p=0.035). There were no differences between groups in delta values before and after treatment regarding the rest of investigated characteristics (Table 1., p> 0.05).
Conclusion: Preliminary results suggest a reduction in the impact of the disease and depression, as well as an increase in the vitality of participants who have been treated with rTMS. The placebo effect on a reduction of sleep disturbance can be partly explained by the stimulating effect of rTMS. Because this was an interim analysis, the presented results should be taken with caution.

Table 1. Changes in patient-reported outcomes after the treatment period

	Placebo (6)		rTMS (10)		p value (t test)
	Mean	SD	Mean	SD	
BDI II	13.00	10.15	19.40	8.78	0.31
POST BDI II	12.33	13.65	15.33	6.91	0.62
Δ	-.67	4.51	-5.11	2.98	**0.064***
FIQR	48.05	29.35	51.65	20.23	0.81
POST FIQR	44.78	31.78	38.18	20.08	0.67
Δ	-3.27	15.49	-16.37	8.97	**0.054***
^MOS SS sleep disturbance	54.17	26.94	52.38	28.09	0.92
POST MOS	35.83	17.34	50.42	28.30	0.43
Δ	-18.33	11.55	-3.06	8.80	**0.035***
^SF-36 vitality	30.00	20.00	24.50	19.64	0.68
POST SF-36 vitality	31.67	22.55	33.89	19.00	0.87
Δ	1.67	2.89	12.22	4.41	**0.003***

Abb. Δ – delta changes after the treatment phase (POST – BASELINE); * - considered as statistically sifnificant; ^ - only one subscale within questionnaire was presented

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1344 CLINICAL AND HISTOLOGICAL FEATURES OF RESIDUAL PAIN IN RHEUMATOID ARTHRITIS REMISSION STATUS

Keywords: Pain, Synovium, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic disease characterized by a high degree of disability and pain. Remission is the optimal goal but, even when it is reached, the pain can persist as "residual pain".
Objectives: The aims of the study were (i) to characterize the size and perception of residual pain and (ii) to evaluate the possible impact of residual synovitis on pain perception in remission RA patients.
Methods: One hundred twenty-seven RA patients (defined by 2010 ACR/EULAR criteria), of which 68 in clinical and ultrasound remission (REM-RA) and 29 in high disease activity (HDA-RA) defined by DAS28-CRP were enrolled in the study. Thirty fibromyalgia patients (2016 ACR criteria) were enrolled as a control group (FIBRO). Upon enrolled, demographic, clinical and ultrasound features were collected for each patient and an assessment of pain symptom was performed for each patient according to the RAID, FACIT, GHQ and VAS-pain questionnaires. Patients with RA underwent minimally invasive ultrasound-guided biopsy of the synovial membrane of the knee in order to assess the degree of synovitis, according to the Krenn Score (KSS).
Results: Considering the RA group, the synovitis degree is directly correlated with the life quality and disability, as demonstrated by the inverse correlation between FACIT and DAS28-CRP (R2=-0.506, p<0.0001). Furthermore, considering the pain mental aspects, the total GHQ score (R2=0.407; p<0.0001) and the VAS-pain scale (R2=0.402, p<0.0001) are instead directly correlated to the DAS28-CRP in RA patients. Since GHQ value ≥24 identifies a subject requiring psychiatric attention, a higher score was found in 26% of REM-RA patients compared to 52% (p=0.004) and 77% (p<0.0001) in the HDA-RA and FIBRO groups respectively while, considering the VAS-pain, the REM-RA patients had lower values (20) compared to HDA-RA (50; p<0.0333) and FIBRO (70; p<0.0001), suggesting how the underlying pathology could affect psychological well-being and pain perception. Further confirmation was obtained with the RAID questionnaire: REM-RA patients presented lower scores (3.34) than HDA-RA (5.56; p = 0.0003) and FIBRO patients (7.63; p <0.0001). Finally, considering the synovitis degree, the presence of subclinical synovitis (KSS≥2) in REM-RA patients (50%) was not associated with a higher pain score, assessed by VAS-pain, suggesting the possible non-inflammatory nature of residual pain.
Conclusion: Remission status in RA is associated with a better psycho-physical state than in HDA patients but, despite that, there is the persistence of a certain degree of residual pain, regardless of the subclinical synovitis degree. It emerges that the features of pain in patients in remission is different from other conditions (high disease activity or fibromyalgia), suggesting different underlying biological mechanisms.
REFERENCES: NIL.
Acknowledgements: NIL.
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POS1345 PAIN OVER 5 YEARS IN OUR EARLY RHEUMATOID ARTHRITIS UCLOUVAIN BRUSSELS COHORT: RESULTS AND CORRELATION WITH CLINICAL RESPONSE, QUALITY OF LIFE

Keywords: Quality of life, Rheumatoid arthritis, Patient reported outcomes

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Background: Pain is a major patient reported outcome in early rheumatoid patients (ERA). Pain is associated with disease activity but could be also related to non-inflammatory conditions. Chronic pain has a negative impact on quality of life in ERA patients. The main treatment objective in ERA is remission or low disease control, but relief of pain is a priority of patient.
Objectives: To evaluate the pain course and the proportion of unacceptable pain (VASp >4) during a five-years follow-up in ERA patients and to investigate correlation with clinical response and quality of life.
Methods: 474 ERA patients fulfilling the 2010 EULAR/ACR criteria included in our ERA UCLouvain Brussels cohort were retrospectively analyzed. All were naïve to csDMARDs (MTX), b- or tsDMARDs with symptoms duration < 12 months. Pain was assessed using a visual analogue scale (0-100 mm) and unacceptable pain was defined as a VAS pain > 40mm (VASp>4) based on the patient acceptable symptom state. VASp, HAQ and DAS28-CRP scores were assessed at baseline (BL), 6, 12, 36 and 60 months in order to correlate the % of ERA with an unacceptable pain (VASp>4), non clinical response (DAS28-CRP> 3.2) and no restored quality of life (HAQ >0.5).
Results: Data from 474 eligible ERA patients were collected. The average age of the population is 48.5 years, and the BMI is 25.3. 70.5% of the patients are women. 27.1% are smokers and 68.8% are positive for anti-citrullinated protein antibody (ACPA). The evolution of VAS pain over 5 years of follow-up is shown in Figure 1:

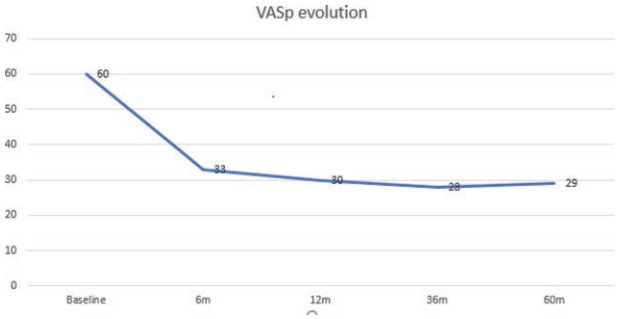


Figure 1.

At BL, the mean VAS pain at the baseline was at 60.2 +/- 26.5mm (range 0-100mm). VASp pain was reduced by 45% (mean 33.1+/- 28.5 mm) at 6 months and remained stable with 51,7% reduction (mean 29.0 +/-27.6mm) at 5 years. 78% of patients (n=308) reported an unacceptable pain at diagnosis which was reduced to 40.4% (n=163) at 6 months and 33% at year 5 (Figure 2):

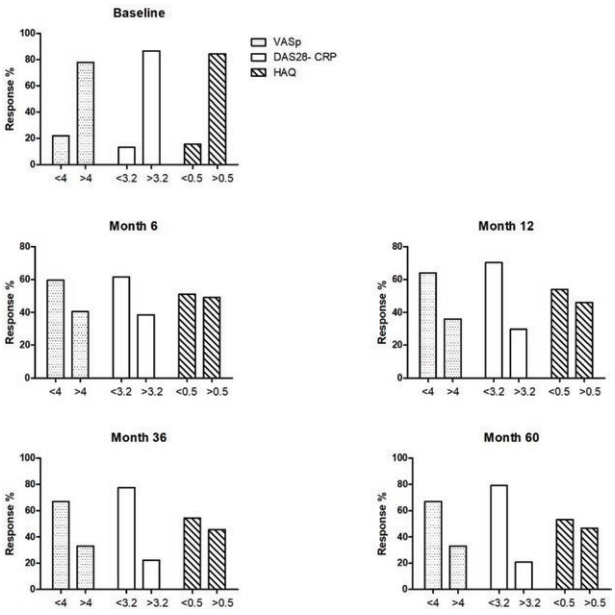


Figure 2. Clinical response: VASp, DAS28-CRP and HAQ throughout the follow-up

No statistical difference was observed for age, sex ratio, BMI, ACPA, or RF except for smokers (27.3% vs 15.6%) between patients with unacceptable pain or not.
A strong correlation was observed between the decrease of VAS pain, DAS28-CRP and HAQ at all-time points. Among the patients with an unacceptable pain at 6 months, HAQ BL score was statistically higher (1.30 +/- 0.69 vs 1.15 +/- 0.67), while the BL DAS28-CRP scores were similar (4.66 +/- 1.41 vs 4.67 +/-1.24). We identified also 20 patients with unacceptable pain throughout the 5 years follow-up, BL DAS28-CRP and HAQ values were statistically increased (5.4 +/- 1.1 vs 4.7 +/- 1.4 and 1.41 +/- 0.86 vs 1.21 +/- 0.62). By contrast, 31 patients reached a complete response defined by a VAS pain <4 + DAS28-CRP<3.2 + HAQ< 0.5 throughout the 5 years follow up). Baseline VAS pain, DAS28-CRP and the HAQ scores assessed at diagnosis were statistically lower in this group. (38.9 +/- 28.4 vs 61.9 +/- 25.7, 4.3 +/- 1.1 vs 4.8 +/- 1.4 and 0.86 +/- 0.60 vs 1.2 +/- 0.71). All patients were treated according the standard of care, mainly with Methotrexate.
Conclusion: We demonstrate that control of pain is achieved in a majority of ERA patient in our cohort. Decrease of pain was correlated with decrease of the disease activity score, meaning that the positive effect is mainly related to inflammation in ERA.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1346 CHASING PAIN: EXPLORING SOMATOSENSORY PROFILES IN PATIENTS WITH RHEUMATOLOGICAL DISEASES THROUGH QUANTITATIVE SENSORY TESTING

Keywords: Diagnostic tests, Pain, Clinical trials

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Background: Pain reflects a major symptom in many rheumatological diseases. To assess nociceptive and non-nociceptive submodalities of different afferent nerve fiber groups and central pathways, and to examine the presence of sensitive plus or minus signs such as hyperalgesia or hypesthesia, the "Quantitative Sensory Testing" (QST) approach was developed. QST, established by the German Neuropathic Pain Research Network (DFNS), is meant to be used for the generation of somatosensory profiles [1]. These can then be used as a guidance to improve a targeted pain medication.
Objectives: The goal of this study is to explore whether patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthritis (axSpA) and systemic sclerosis (SSc) show differences in somatosensory profiles between each other and in contrast to a healthy control group.
Methods: In this monocentric five-armed study (ethical approval under Institutional Review Board #065/20), four groups of each 20 patients with RA, PsA, axSpA or SSc, and one control group consisting of 20 healthy individuals were collected and a somatosensory profile using the standardized procedure of QST was created for each one of the 100 participants. QST included both small fiber mediated stimuli and large fiber mediated stimuli, via all categories shown in Figure 1. The vibration detection threshold where the detection of vibration is ranked on a scale from zero to eight, with '8' being normal perception of vibration, serves as an example for large fiber mediated stimuli. Additionally, standard questionnaires incorporating laboratory parameters, joint manifestations and pain condition were used to determine disease activities (BASDAI, PASDAS, CDAI and mRSS).
Results: A preliminary data analysis of all 100 study participants found occurrence of allodynia in 5% of patients with SSc, 15% of RA, 25% of PsA, and 15% of all axSpA patients, compared with 0% in the control group. Considering the vibration detection threshold, there was little difference between all disease groups, also in comparison to the control group: SSc (mean ± SD: 7,79 ± 0,34), RA (mean ± SD: 7, 66± 0,4), PsA (mean ± SD: 7,76 ± 0,34), AxSpA (mean ± SD: 7,69 ± 0,57) and control group (mean ± SD: 7,98 ± 0,16).
Conclusion: The analysis for allodynia occurrence indicates the presence of sensory gain towards small fiber mediated stimuli in all four disease groups studied. Until now, our vibration detection threshold studies do not suggest a loss or gain of sensory function for large fiber mediated stimuli. The full analysis completion is expected in March 2023.
REFERENCE:
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Figure :

Small fiber mediated stimuli		Large fiber mediated stimuli	
CDT[1]	A δ-Fibers	VDT[12]	Aβ-Fibers
WDT[2]	C-Fibers	MDT[13]	Aβ-Fibers
TSL[3], PHS[4]	A δ -Fibers, C-Fibers	ALL[11]	Aβ-Fibers
CPT[5], HPT[6]	A δ -Fibers, C-Fibers		
MPT[7]	A δ -Fibers, C-Fibers		
MPS[8]	A δ -Fibers, C-Fibers		
WUR[9]	A δ -Fibers, C-Fibers		
PPT[10]	A δ -Fibers, C-Fibers		
ALL[11]	A δ -Fibers, C-Fibers		

QST-Testing categories with their associated nerve fibers(1) Cold detection threshold, (2) Warm detection threshold, (3) Thermal sensory limen, (4) Paradoxical heat sensations, (5) Cold pain threshold, (6) Heat pain threshold, (7) Mechanical pain threshold, (8) Mechanical pain sensitivity, (9) Wind-up-Ratio, (10) Pain pressure threshold, (11) Allodynia, (12) Vibration detection threshold, (13) Mechanical detection threshold.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1347 EVALUATING THE EFFICACY OF LOCAL CORTICOSTEROID INJECTION, PLATELET-RICH PLASMA, AND EXTRACORPOREAL SHOCKWAVE THERAPY IN PATIENTS WITH PES ANSERINE BURSITIS: A PILOT RANDOMIZED, COMPARATIVE CLINICAL TRIAL

Keywords: Pain, Osteoarthritis

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Background: Pes anserine bursitis is one of the causes of painful knee syndromes. It limits physical activity and impairs the quality of life of a patient. Obesity and osteoarthritis (OA) of the knee are common predisposing factors for pes anserine bursitis. It is treated with non-steroidal anti-inflammatory drugs (NSAIDs), physiotherapy, injections of local anesthetics, and corticosteroids. This study examines the efficacy of local corticosteroid injection, Platelet-rich plasma (PRP) injection, and extracorporeal shock wave therapy (ESWT) as different modalities to alleviate pain and improve function in patients with pes anserine bursitis.
Objectives: This study examines the efficacy of local corticosteroid injection, Platelet-rich plasma (PRP) injection, and extracorporeal shock wave therapy (ESWT) as different modalities to alleviate pain and improve function in patients with pes anserine bursitis.
Methods: This randomized comparative clinical trial was performed between July 2021 and June 2022 in the rheumatology and rehabilitation department at Al-Azhar University hospitals in Egypt on 180 patients diagnosed with chronic pes anserine bursitis according to Larson and Baum criteria. The enrolled patients were divided into three groups, each including sixty patients. Group I received a local corticosteroid injection of 40 mg of methylprednisolone acetate/1 ml (n = 60); Group II received a PRP injection (n = 60); and in Group III, ESWT (n = 60) was used. The Visual Analog Scale (VAS), Western Ontario and McMaster Universities (WOMAC) pain score, WOMAC physical function score, and Ritchie score for tenderness were recorded at the baseline, after 1 week, and after 8 weeks.
Results: There are significant differences between the corticosteroid group compared to the PRP group (10.6± 2.5) and the ESWT group (9.7 ±2.6) regarding the WOMAC pain score and WOMAC physical function score one week after the application of procedures. There is a highly statistically significant (p= 0.001) decreased 8-week WOMAC pain score in the corticosteroid group (5.7 ± 2.7) when compared to the PRP group (9.4± 2.4) and ESWT group (7.1± 1.5) **Table [1].** As regards VAS, there isn't a statistically significant difference (p = 0.636) between the studied groups as regards baseline VAS or 8-week VAS after the procedure.
Conclusion: An examination of Pes anserine bursitis is essential and shouldn't be missed in knee OA patients complaining of pain. Our findings show that local corticosteroid injection is more effective than PRP injection and ESWT for pain relief.
Declarations: The authors declare that they have no competing interests.

Table (1): Post hoc analysis for multiple comparisons between studied groups as regard 1-week WOMAC score (pain & physical function) after the application of procedures.

1 week		Corticosteroid vs PRP	Corticosteroid vs ESWT	PRP vs ESWT
WOMAC pain score	**LSD**	**3.06**	**2.1**	0.93
	p-value	**< 0.001 HS**	**0.001 S**	0.126 NS
WOMAC physical function score	**LSD**	3.2	**9.1**	**6.0**
	p-value	0.120 NS	**< 0.001 HS**	**0.004 S**

S: p-value < 0.05 is considered significant.HS: p-value < 0.001 is considered highly significant.LSD: Least sig. difference. NS: p-value > 0.05 is considered non-significant.

Disclosure of Interests: None Declared.
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Osteoarthritis

POS1348

EFFECTS OF SPRIFERMIN ON A NOVEL OUTCOME OF OSTEOARTHRITIS SYMPTOM PROGRESSION: POST-HOC ANALYSIS OF THE FORWARD RANDOMIZED TRIAL

Keywords: Outcome measures, Clinical trials, Osteoarthritis

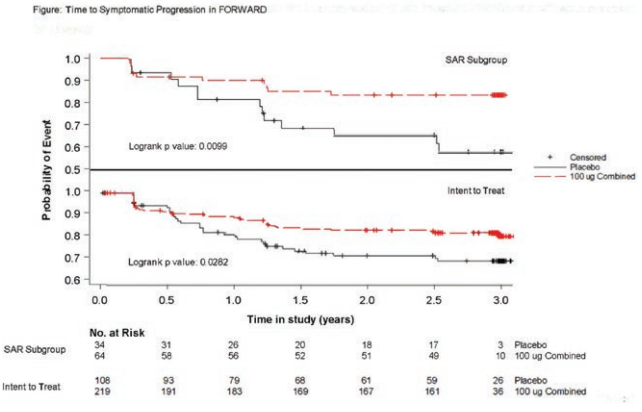
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Background: People with knee osteoarthritis (OA) (KOA) desire therapies which delay disease progression [1] supporting the need for disease-modifying OA drugs (DMOADs). Sprifermin, truncated recombinant human fibroblast growth factor-18, promotes chondrocyte proliferation and extracellular matrix production [2], improves cartilage biomechanical properties [3], and in the Phase 2 FORWARD study [4], dose-dependently increased knee cartilage thickness. In FORWARD, improvement from baseline in the Western Ontario and McMaster Universities OA Index (WOMAC) symptom subscales occurred in all study arms, but lack of differentiation from placebo (PBO) was thought to be due to inclusion of participants not at risk of KOA progression. A subsequent post-hoc analysis identified a subgroup at risk (SAR) enriched for disease progression [5]. Clinically meaningful change in WOMAC Pain and Function has been defined as ≥10 points (0-100 scale) [6,7], with this degree of worsening pain predictive of structural progression and knee replacement in KOA cohorts [8-10]; this endpoint has not been applied to evaluate symptomatic progression in DMOAD studies to date.
Objectives: Evaluate the effect of sprifermin on symptomatic progression of KOA.
Methods: In FORWARD, participants were randomized 1:1:1:1:1 to intra-articular PBO or sprifermin 30 µg or 100 µg every 6 or 12 months (Q6M or Q12M) for 18 months. WOMAC was collected Q3M and MRI performed Q6M. In the current Kaplan-Meier analysis, time to symptomatic progression (i.e., first occurrence of worsening [increase] of WOMAC Pain of ≥10 points with no improvement [≤9 point decrease] in WOMAC Function) was evaluated over 3 years. The individual treatment arms of the intent-to-treat population (ITT) and the SAR (i.e., baseline WOMAC Pain 40-90, mJSW of 1.5-3.5 mm) were analyzed, as well as the sprifermin 100 µg groups combined for additional power. Time to symptomatic progression was also analyzed by changes in cartilage thickness (decrease or no change/increase) for the populations with an evaluable MRI, i.e., the modified (m) ITT and SAR.
Results: The FORWARD ITT and SAR sprifermin individual treatment arms (Table 1) showed dose-dependent benefits in the time to symptomatic progression compared to PBO, with clinically meaningful and statistically significant separation from PBO for the sprifermin 100 µg groups combined (logrank p-value ITT=0.0282, SAR=0.0099) (Figure 1); separation from PBO was more pronounced in the SAR compared to the ITT. The sprifermin 100 µg groups combined also demonstrated less symptomatic progression than PBO regardless of an increase or no change/decrease in cartilage thickness in the mSAR and mITT.

Table 1: FORWARD Study Populations

Population (n)	Placebo	Sprifermin					Total (N)
		30 µg x 2	30 µg x 4	100 µg x 2	100 µg x 4	100 µg groups combined	
ITT	108	110	111	110	110	220	549
Modified ITT	96	99	99	99	101	200	494
SAR	34	36	27	31	33	64	161
Modified SAR	32	32	26	29	32	61	151

x 2=Q12M; x 4 = Q6M; ITT=intent-to-treat; SAR=subgroup at risk.



Conclusion: These post hoc results support the hypothesis that sprifermin may prevent symptomatic progression of KOA, with benefits seen in both ITT and SAR populations for the sprifermin 100 µg groups combined. As differences between the sprifermin- and PBO-treated groups were detectable in a 3-year time frame, time to symptomatic progression of KOA could be a meaningful endpoint for an

investigational DMOAD trial. Symptomatic and structural benefits of sprifermin need to be confirmed in the planned Phase 2b SPRING study.

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Disclosure of Interests: Philip G Conaghan Speakers bureau: AbbVie, Novartis, Consultant of: AbbVie, AstraZeneca, Biosplice, BMS, Eli Lilly, Galapagos, Genascence, GSK, Merck, Novartis, Pfizer, Regeneron, Stryker, and UCB, Nathaniel Katz Consultant of: TrialSpark, David Hunter Consultant of: Lilly, Novartis, Pfizer, TissueGene, TLCBio, Ali Guermazi Consultant of: AstraZeneca, Grunenthal, Levicept, Novartis, Organogenesis, Pfizer, Regeneron, TissueGene, TrialSpark, Employee of: Owner, Boston Imaging Core Lab (BICL), Marc Hochberg Paid instructor for: TrialSpark, Kenneth Somberg Shareholder of: TrialSpark, Consultant of: TrialSpark, Employee of: Former employee of TrialSpark, Julia Clive Consultant of: TrialSpark, Mary Johnson Consultant of: TrialSpark, Niti Goel Shareholder of: UCB, Employee of: TrialSpark.

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POS1349 A BIOMARKER APPROACH TO DATA-DRIVEN IDENTIFICATION OF ENDOTYPES IN KNEE OA PATIENTS

Keywords: Biomarkers, Osteoarthritis

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Background: Osteoarthritis (OA) is a heterogeneous and multifactorial disease. Despite its high prevalence, the underlying mechanisms of disease are not fully understood, and treatment options are limited. One of the challenges in understanding OA is the lack of clear subgroups or "endotypes" within the disease, which could help to identify specific causes and point to more targeted treatments. Recent research has suggested that molecular biomarkers may be able to help identify different endotypes of OA. For example, certain biomarkers may be elevated in OA patients with inflammation, while others may be elevated in patients with more severe cartilage degeneration.
Objectives: The objective of the study was to identify endotypes of OA using soluble biomarkers reflecting tissue turnover by applying unsupervised machine learning approaches.
Methods: Biomarkers of cartilage remodeling (CTX-II, C2M, T2CM, PRO-C2), bone remodeling (N-MID, UCTX-I, SCTX-I), and tissue inflammation (CRPM, VICM, C1M, C3M) were measured at baseline in the phase III clinical trials SMC01 (n=1176) and SMC02 studies (n=1030), testing efficacy and safety of oral salmon calcitonin in knee OA patients. Only patients from the placebo group with more than 5 biomarkers available were included (n=528). Approximately 4% of data was missing data and imputed using Random Forest. K-Means clustering was applied on UMAP dimensionality reduced data. The association of change in symptomatic and radiographic parameters over 2 years with the identified clusters was compared with Kruskal Wallis test for numerical variables and chi-square test for categorical variables.
Results: K-Means clustering identified three distinct clusters; 1) a low tissue turnover endotype, 2) a systemic inflammation endotype and 3) A structural damage endotype (Figure 1). The structural damage endotype was characterized by higher levels of bone remodeling markers CTX-I, N-MID and the cartilage degradation marker CTX-II. The systemic inflammation endotype presented with higher levels of C1M, C2M, C3M, CRPM and VICM related to tissue inflammation. Finally, the low tissue turnover endotype showed overall lower levels of both tissue-related and inflammatory markers. We observed a difference in JSW change over two years between the three groups (Cluster 1: -0.28 mm, Cluster 2: -0.16 mm, Cluster 3: -0.32 mm; p=0.049), but this difference was not significant in the corrected analysis. Overall, the three endotypes progressed similarly.
Conclusion: These findings suggest that distinct biomarker-based endotypes exist in OA and highlight that multiple mechanistic avenues may lead to joint deterioration. By identifying these endotypes we may enable the development of more targeted treatments that are tailored towards the underlying cause of OA in individual subgroups of patients.

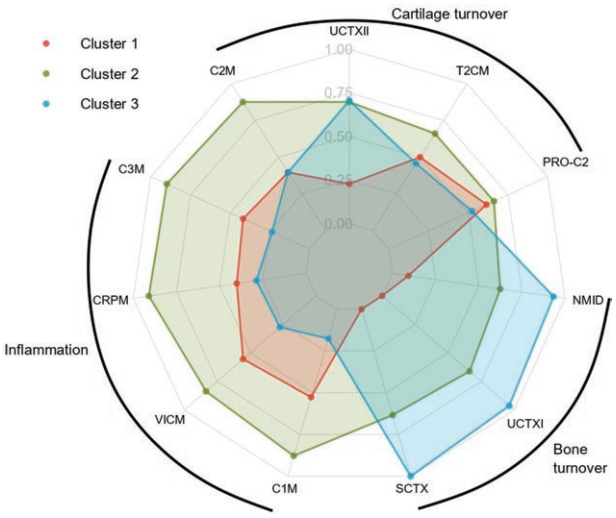


Figure 1.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Zofia Lisowska-Petersen: None declared, Monica Toft Hannani: None declared, Morten Karsdal Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, Cecilie Bager Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, Christian Thudium Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience.

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POS1350 FACTORS ASSOCIATED WITH SEDENTARY BEHAVIOR IN KNEE OSTEOARTHRITIS PATIENTS

Keywords: Lifestyles, Osteoarthritis, Physical therapy/Physiotherapy

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Background: Sedentary behavior is linked to poor physical and mental health outcomes. Despite of the known benefits of physical activity in patients with knee osteoarthritis, many individuals remain physically inactive.
Objectives: We aimed at investigating the socio-demographic and clinical factors associated with sedentary behavior (SB) in patients with knee osteoarthritis.
Methods: A cross-sectional study was performed among patients with knee osteoarthritis Aged between 40 and 75 years old who visited the outpatient clinic between April 2022 and October 2022. Patients with knee osteoarthritis were included then classified on the basis of the Kellgren and Lawrence radiograph scale. Socio-demographic and clinical findings were collected. Participants were assessed for pain and disability using visual analogic scale (VAS) and LEQUESNE scale. SB was assessed using the international physical activity questionnaire (IPAQ-SF). Furthermore the participants underwent screening for anxiety and depressive disorders using Patient health questionnaire (PHQ-9) and General anxiety disorder (GAD-7) respectively.
Results: The final study simple was made up of 178 patients with a mean (±SD) age of 58.48 ± 9.9 years, 88.2% of them were females, and 69.1% had comorbidities. Mean (±SD) of pain VAS score upon walking was 4.78 ± 2.21. According to the Kellgren and Lawrence classification, 64.4% of the patients had OA grade 2 and 25.6% had grade 3. Mean of Lequesne scale was 9.8 ± 3.8. The average daily duration of sedentary behavior was 151.02 ± 105.04 minutes.
The results of uni and multivariate analysis of associated factors with SB are showed in Table (1):

Table 1 : *Multiple regression with the duration of sedentary behavior as the dependent variable.*

	Univariate analysis OR (95%) P value	Multivariate analysis OR (95%) P value
Age	1.992 [0.354, 3.630] 0.017	1.445 [0.176, 3.066] 0.052
BMI (kg/m2)	-0.024 [-0.098, 0.049] 0.517	_____ _____
Educational level	-27.544 [-45.411, -9.676] 0.003	-27.544[-45.411, -9.676] 0.048
Socioeconomic status	-13.745 [-26.263, -1.227] 0.032	-13.108 [-25.417, -0.799] 0.037
Comorbidities	10.955 [-9.276, 31.185] 0.287	_____ _____
Disease duration (in Years)	-1.321 [-3.971, 1.971] 0.326	_____ _____
VAS Pain level	1.327 [-5.971, 8.626] 0.720	_____ _____
LEQUESNE Scale	-1.334 [-6.351, 3.684] 0.599	_____ _____
Kellgren and lawrence grading scale	-11.661 [-38.703, 15.381] 0.396	_____ _____
Anxiety scale (GAD-7)	-2.221 [-4.891, 0.449] 0.102	_____ _____
Depression scale(PHQ-9)	-1.181 [-1.965, -0.396] 0.002	-0.890 [-1.576, -0.205] 0.011

Conclusion: In the literature few studies discuss factors associated with sedentary behavior in patients with knee osteoarthritis. Our study shows that level of pain and disability are not associated with SB, on the contrary, educational level, socioeconomic status and depressive disorders are the principal factors associated with SB. Our study highlights the importance of therapeutic education and assessment of mental health to improve the management of patients with knee osteoarthritis.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1351 A PHASE 2, 104-WEEK STUDY OF REPEAT LORECIVIVINT INJECTIONS EVALUATING SAFETY, EFFICACY, AND BONE HEALTH UTILIZING QUANTITATIVE COMPUTED TOMOGRAPHY (QCT) IN KNEE OSTEOARTHRITIS (OA-06)

Keywords: Osteoarthritis, Imaging, Clinical trials

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Background: Knee osteoarthritis (OA) is a common joint disorder associated with pain, disability, and damage. There is unmet need for safe and efficacious treatments for symptoms and structural modification. Lorecivivint (LOR), an intra-articular (IA) CLK/DYRK inhibitor thought to modulate Wnt and inflammatory pathways, is in development as a potential knee OA treatment.

Objectives: To assess the safety and tolerability of repeated 6-month dosing of LOR in a 104-week trial (OA-06, NCT03727022). Additionally, to characterize juxta-articular bone health with quantitative computed tomography (qCT) and regional bone health via dual energy x-ray absorptiometry (DXA).

Methods: Participants with ACR-defined clinical and radiographic knee OA, aged 40-80, and Kellgren-Lawrence (KL) grades 2-3 were randomized 1:1 to receive IA injections of 2 mL 0.07 mg LOR or vehicle PBO at baseline, 24, 52, 72 weeks. The trial was conducted in two 52-week phases, part A (baseline to week 52) and part B (week 53 to week 104), with part A completers invited into part B. Safety was assessed by collection of adverse events (AEs), and serious AEs (SAEs). Bone safety assessments included qCT to assess target and non-target knee BMD, DXA to assess spine and hip BMD and bone/ cartilage biomarkers. Exploratory efficacy was assessed by patient-reported outcomes (PROs). For bone imaging endpoints, change from baseline was estimated using baseline-adjusted ANCOVA.

Results: 101 participants (mean age 60.9±9.1 years, BMI 28.6±3.7 kg/m^2, female 59.4%, KL2 52.5%) were enrolled. 77 participants completed part A and 53 completed part B. AE rates were similar between PBO and LOR, and no SAEs were deemed treatment related. There were no clinical bone health signals (no fractures, accelerated OA, osteoporosis) observed for LOR. Observed target knee qCT BMDs were similar between LOR and PBO (Figure 1). Change from baseline in BMD at Week 104 was -7.08 (12.34) mg/cm^3 in LOR and -2.95 (8.65) mg/cm^2 in PBO, (estimated difference -4.05 [95% CI -11.21, 3.11], not significant). Trends in target knee BMDs for those with higher risk of decreasing BMD, (female and age 65-80), showed no meaningful differences between LOR and PBO. There were no significant differences in total hip or spine BMD between LOR and PBO. Potential confounding factors included baseline imbalances in sex (PBO 68.0% vs. LOR 51.0% female), KL grade (PBO 62.0% vs LOR 42.1% KL 2), and site randomization. There were no meaningful differences in PRO changes between LOR and PBO groups. A trial conduct limitation was the small number of qCT-enabled sites available in the US.

Conclusion: The incidence of AEs was similar between treatment groups and not affected by repeated injections of LOR. Multiple injections of LOR over 2 years did not appear to lead to any bone health adverse effects locally around the knee or regionally at spine or hip.

Table 1A and 1B.

Phase A	#Events/#Subjects Reporting		Phase B	#Events/#Subjects Reporting	
	LOR (n=50)	PBO (n=50)		LOR (n=50)	PBO (n=50)
Adverse events	52/25	52/24	*Adverse events*	52/25	52/24
SAEs	5/2	3/2	*SAEs*	5/2	3/2
Target-knee AEs	7/6	4/3	*Target-knee AEs*	7/6	4/3

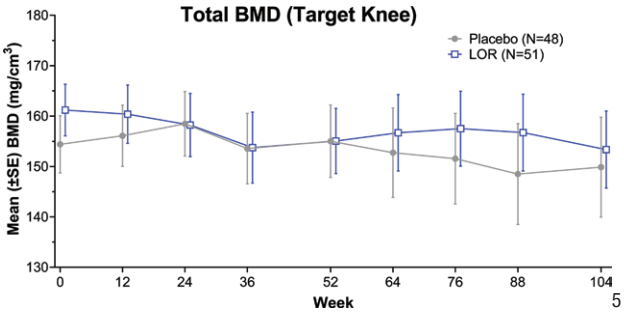


Figure 1. Total Target Knee BMD over 104 weeks

REFERENCES: NIL.

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Disclosure of Interests: Yusuf Yazici Shareholder of: Biosplice Therapeutics, Employee of: Biosplice Therapeutics, Christopher Swearingen Shareholder of: Biosplice Therapeutics, Employee of: Biosplice Therapeutics, Heli Ghandehari Shareholder of: Biosplice Therapeutics, Employee of: Biosplice Therapeutics, Jon Britt Shareholder of: Biosplice Therapeutics, Employee of: Biosplice Therapeutics, Sarah Kennedy Shareholder of: Biosplice Therapeutics, Employee of: Biosplice Therapeutics, Jeymi Tambiah Shareholder of: Biosplice Therapeutics, Employee of: Biosplice Therapeutics, Nancy Lane Consultant of: Biosplice Therapeutics.

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POS1352 COMPARISON OF VALIDATED QUESTIONNAIRES WITH CLINICAL ITEMS FOR THE MEASUREMENT OF CHANGE IN PAIN

Keywords: Osteoarthritis, Pain

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Background: Hand pain is a common symptom in hand osteoarthritis (OA). Questionnaires are used to measure and to monitor this pain over time. However, it is unknown whether these measurements reliably reflect patients' experience.

Objectives: This study aimed to compare pain development scored by a validated questionnaire with pain development scored by a direct question to the patient.

Methods: Data from the first four years of the ongoing HOSTAS (Hand OSTeoArthritis in Secondary care) cohort were used. HOSTAS consists of patients with primary hand OA diagnosed by a rheumatologist. Pain was measured with the Australian/Canadian hand Osteoarthritis index (AUSCAN) pain subscale (range 0-20) at baseline and annually afterwards. Partway through the study, an annual anchor question was added asking participants whether pain had worsened, improved, remained stable or if they had never had pain, compared with the year before. Patients were included in the current analysis when change in AUSCAN pain and the anchor question were available for at least one year. Change in pain measured with AUSCAN was categorized according to the minimal clinical important difference (MCID) of 1.49 between the yearly visits. Changes between annual visits on AUSCAN and the anchor questions were described and Cohen's kappa was calculated for each category (increase, stable and decrease). Annual results were comparable between years, and so the years were pooled.

Results: In 307 patients, the mean age was 61.0 (SD 8.2), with 82% women and a mean BMI of 27.3 (SD 4.8). The baseline AUSCAN pain was 9.1 (SD 4.2). Over 4 years, 708 annual intervals with both change in AUSCAN and anchor questions were available. Of the 309 patients, 95 provided one interval, 74 provided two intervals, 87 provided three and 51 provided four. Results are described in Table 1. In 203 intervals 172 patients reported an increase in AUSCAN pain (of which in 151

intervals patients (74%) indicated their pain had worsened on anchor questions), in 293 intervals 199 patients reported a stable level of pain (of which in 96 intervals (33%) indicated their pain had not changed) and in 212 intervals 176 patients reported a decrease in pain (of which 39 (19%) indicated their pain had improved) (Table 1). The most frequent answer was a worsening of pain, regardless of AUSCAN change. In total, in 286 out of 704 (40%) of the intervals, the anchor question was in accordance with the AUSCAN pain, with a Cohen's kappa of 0.12.

Conclusion: There are large differences between changes in AUSCAN pain and experienced changes in pain when reported by the patient. The patient experiences worsened pain more often than is reflected in the AUSCAN pain. Although recall bias may play a role in the answers to the anchor questions, they are close to the real-world clinical practice, in which patients are often asked how the symptoms compare to last visit. This indicates a difference between change in pain perceived in the clinical setting and in research setting, which should be addressed in order to improve research on pain development.

Table 1. ***Change in AUSCAN pain vs anchor questions.*** **Data presented as number (%), with the % calculated over the vertical columns. Change in AUSCAN pain horizontally, anchor questions vertically. The number and % of concordant answers in bold.**

		Change in AUSCAN pain			
		Worsening	Stable	Improvement	Total
Anchor question	Worse – more pain	**151 (74)**	173 (59)	98 (46)	422 (60)
	No change	41 (20)	**96 (33)**	74 (35)	211 (30)
	Better – less pain	11 (5)	20 (7)	**39 (19)**	70 (10)
	Never had this symptom	0 (0)	4 (1)	1 (0)	5 (1)
	Total	203 (100)	293 (100)	212 (100)	708 (100)

REFERENCES: NIL.

Acknowledgements: NIL.

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POS1353 SEMIQUANTITATIVE ASSESSMENT OF KNEE OSTEOARTHRITIS-RELATED SYNOVITIS COMPARED TO CHRONIC INFLAMMATORY ARTHRITIDES: RELATION TO AGE AND IMPACT ON BONE/ STRUCTURAL DAMAGE

Keywords: Descriptive studies, Synovium, Osteoarthritis

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Background: Knee Osteoarthritis (KOA) is one of the most frequent causes of pain and disability, representing a relevant clinical burden. Although it was largely considered a mostly mechanical-based pathology, low-grade synovial inflammation was found to contribute to radiographic progression and pain chronicity [1].

Objectives: To evaluate the histological characteristics of synovial membrane inflammation in KOA patients compared to chronic inflammatory diseases as Rheumatoid (RA) and Psoriatic Arthritis (PsA) across disease phases.

Methods: 170 patients with KOA, 240 patients with RA, 92 patients with PsA naive to pharmacological treatments and 200 patients with RA in sustained clinical and ultrasound remission (RA-r) underwent ultrasound-guided synovial biopsy of the knee and conventional X-rays. None of enrolled KOA patient had evidence of inflammatory condition (including chronic inflammatory diseases and crystal related arthritis). Synovial membrane samples were processed for histology (hematoxylin-eosin staining) for the semiquantitative assessment of synovitis degree (Krenn synovitis score [2] - KSS). Moreover, this analysis was implemented with the semiqualitative assessment of presence/absence of synovial lymphocytes, plasmacells, myxoid degeneration and inflammatory perivascular aggregates. X-rays were scored for Kellgren-Lawrence score [3] (KLs) assessment.

Results: RA and PsA patients naive to pharmacological treatment showed higher degree of synovial inflammation than patients with KOA as well as more likely presence of lymphocytes and plasmacells aggregates. Considering the whole KOA population, total KSS directly correlated with age (R^2=0.041; p=0.008), thickness of synovial membrane (R^2=0.115; p<0.001) and Power Doppler score (R^2=0.142; p<0.001) at ultrasound evaluation, VAS pain (R^2=0.025; p=0.039) and KLs (R^2=0.54; p<0.0001). Stratifying KOA patients based on age categories, KOA patients aged ≥70 years had higher KSS (mean ±SEM, 2.46 ±0.179) and KLs (2.14 ±0.17) than younger KOA patients (KSS 1.98 ±0.113, p=0.0182 and KLs 1.25 ±0.101, p<0.001). To distinguish residual inflammation from osteoarthritis-related synovitis, we compared KOA-derived synovial tissues with the ones of RA-r patients, showing that the degree of KOA-related synovitis is significantly higher (mean ±SEM, 2.10 ±0.09) than the subclinical residual synovitis detected in RA-r patients (1.77 ±0.08, p=0.0103).

Conclusion: KOA-related synovitis represents an unmet clinical need due to still uncovered pathogenetic mechanisms. The severity of KOA-related synovitis impacts on bone structural damage and is related to age, supporting the role of inflammageing in KOA pathogenesis.

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Disclosure of Interests: None Declared.

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POS1354 REGRESSION TO THE MEAN FOR PAIN OUTCOMES IN CLINICAL TRIALS FOR KNEE OSTEOARTHRITIS

Keywords: Epidemiology, Osteoarthritis, Pain

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Background: Improvements in pain in clinical trials for osteoarthritis (OA) are largely contextual.(1) Given known fluctuations of osteoarthritic pain, a substantial proportion of contextual response could be explained by the regression-to-the-mean (RTM) phenomenon.

Objectives: To estimate the size of RTM for a typical OA trial with pain as outcome.

Methods: We included participants of Osteoarthritis Initiative who fulfilled inclusion criteria typically required for enrolment in a clinical trial. These included: age 40-79 years, symptomatic knee OA, Kellgren-Lawrence grade 2-3, use of pain medication more than half the days of a month in past 12 months, numerical rating scale (NRS) pain of 4 to 9 in the target knee. We studied observed changes in the mean levels of pain with respect to conditioning on current knee pain.

Results: We identified 459 subjects who fulfilled inclusion criteria on at least one annual follow-up between year 1 and year 8. In these subjects, the mean NRS pain level at each follow-up time point was similar, ~4.6, but at the time of fulfilling the inclusion criteria, the mean level of pain in the same subjects was 6.2 (Figure 1). The difference in NRS pain between the theoretical point of inclusion in a trial and one year after was -0.8 (95% confidence interval -0.6, -0.9).

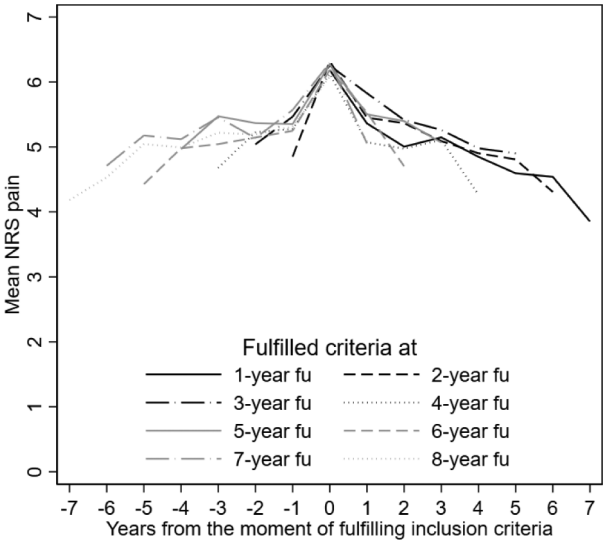


Figure 1. Mean levels of pain among 459 persons fulfilling criteria for inclusion in a hypothetical knee osteoarthritis trial. Time 0 means the moment when fulfilling the criteria. Each line represents a cohort of subjects fulfilling criteria at one follow-up occasion (between year 1 and year 8 post baseline). Each person can be included multiple times.

Conclusion: RTM in a typical osteoarthritis trial is likely to explain as much as about 0.8 NRS point improvement on a 0 to 10-point scale. RTM is a powerful phenomenon that may mislead interpretation of effectiveness as it neither represents improvement from the intervention nor placebo response.

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POS1355 COMBINED ASSESSMENT OF CARTILAGE AND SUBCHONDRAL BONE IN OSTEOARTHRITIC AND NON-OSTEOARTHRITIC KNEE COMPARTMENTS: A ULTRA-HIGH FIELD MRI STUDY

Keywords: Imaging

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Background: Knee osteoarthritis (OA) is one of the most common degenerative diseases causing disability in elderly people. Although X-ray radiography is widely used as a diagnostic tool, several limitations have been identified *[1]*. MRI is a non-invasive imaging method widely used in order to assess articular and periarticular structures of the knee joint *[2]*. However, the image resolution provided by conventional MRI is not high enough to assess subchondral bone so that ultra-high field MRI (7 Tesla) has been proposed as an alternative of interest to compute bone microarchitectural parameters *[3]*.

Objectives: We used ultra-high field MRI (UHF 7 Tesla MRI) to assess cartilage and subchondral bone microarchitecture in patients with mild and severe OA. For each patient, compartments classified as osteoarthritic were compared with non-osteoarthritic compartments.

Methods: Twenty-four patients were divided into 3 groups according to the Kellgren Lawrence staging and 12 volunteers were recruited as controls. UHF MRI was used to calculate cartilage thickness (Tc), volume (Vc), and T2*. MRI sequences used were T1 3D gradient recalled echo sequence (T1 3D GRE) and sagittal T2* mapping. Bone microarchitecture was assessed on the basis of trabecular thickness (TbTh), trabecular number (TbN), trabecular space (TbSp), and bone volume fraction (BVF).

Results: For the medial tibial plateau, while Tc was unchanged between the two OA groups, Vc was decreased in patients with severe OA (Δ= -49%, $p < 0.05$). For the patella, Vc was decreased in patients with mild OA (Δ = -36%, $p<0.05$), while Tc was unchanged. Similar results were found for the lateral femoral condyle. The study of T2* cartilage relaxation (T2* mapping) revealed no statistically significant changes in all knee joint compartments. Computed TbSp in the lateral tibial plateau and patella was significantly higher in the mild OA group (Δlateral tibial plateau = +25%; Δpatella = +31.5, $p<0.05$), whereas most subchondral bone parameters were unchanged. Medial femoral condyle cartilage volume was significantly correlated with patellar cartilage thickness r=0.46 ($p = 0.01$). Medial tibial plateau cartilage thickness and patellar cartilage thickness were linearly related r = 0.587 ($p < 0.05$). Medial tibial plateau cartilage volume was significantly correlated with patella TbTh, r = 0.41 ($p = 0.02$)

Conclusion: Cartilage volume seems to be more sensitive than thickness for the assessment of cartilage changes in OA. TbSp would be a sensitive marker of subchondral bone degradation. Cartilage degradation in a given OA compartment would be accompanied by changes in subchondral bone and cartilage in the opposite healthy compartments. UHF MRI can provide interesting information for the analysis of cartilage and subchondral bone and could be considered as a tool of interest for the subtle evaluation of changes associated to therapeutic strategies.#8232;#8232;

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POS1356 ASSESSMENT OF THE EFFICACY OF COMBINATION OF ORAL ACETAMINOPHEN AND TOPICAL DICLOFENAC IN OSTEOARTHRITIS PAIN: INSIGHTS FROM A MODEL-BASED META-ANALYSIS

Keywords: Osteoarthritis, Pain

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Background: Osteoarthritis (OA) is a major cause of chronic pain and disability in older adults and currently affects approximately 300 million people worldwide [1]. In the absence of curative therapy, symptomatic drugs comprise the backbone of pain management in OA. However, acetaminophen provides inadequate relief and oral non-steroidal anti-inflammatory drugs (NSAIDs) exhibit significant gastrointestinal and cardiovascular toxicity which prohibit their long-term use in the elderly [2,3]. Although opioids can be an effective alternative in patients experiencing insufficient pain relief with other analgesics, concerns have been raised about the risk of side effects, addiction, and overdose deaths [4]. Therefore, there is a significant unmet need for effective and well-tolerated treatments. Acetaminophen and topical diclofenac exhibit complementary mechanisms of action targeting pain and inflammation, respectively, and are therefore attractive candidates for use in combination analgesia in OA pain [5,6,7]. Although ample clinical evidence exists on the monotherapy of acetaminophen or topical diclofenac in OA, there is a data gap for evidence on their combination.

Objectives: The present study aims to assess the effect of the combination of acetaminophen and topical diclofenac in OA and compare its performance to acetaminophen and diclofenac monotherapy using a model-based meta-analysis (MBMA) leveraging published summary-level data on the combination from OA as well as other acute pain indications [8].

Methods: Randomized controlled trials (RCTs) investigating the combination of acetaminophen and diclofenac in OA and acute pain settings were identified through systematic literature searches. MBMA was implemented to infer the efficacy of the combination in the population of interest. Pain score reduction on numerical rating scale (NRS), visual analogue scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale along with opioid sparing effect (defined as reduced opioid dose without loss of analgesic efficacy) were selected as the clinical endpoints.

Results: In the absence of RCTs on the combination in OA, MBMA was implemented in conjunction with extrapolation principles on trials in acute pain setting (11 RCTs, n=1396 patients). The combination demonstrated greater reduction in pain scores versus acetaminophen monotherapy in 8 of the 11 RCTs. Moreover, a parsimonious MBMA was developed on 5 RCTs allowing PCA, which revealed a statistically significant 32% lesser opioid use with the combination than with acetaminophen monotherapy (Figure 1). However, the combination effect was less conclusive versus diclofenac monotherapy.

Conclusion: The current analysis demonstrates greater pain reduction and opioid sparing efficacy for the combination versus acetaminophen monotherapy in the treatment of acute pain. Considering the overlap in pain transmission pathways between acute and chronic OA pain, the combination may be anticipated to exhibit similar performance on extrapolation to chronic OA pain. Overall, our research tries to bridge the gap in pharmacological and clinical evidence supporting the use of combination of acetaminophen and topical diclofenac in mild-to-moderate OA pain.

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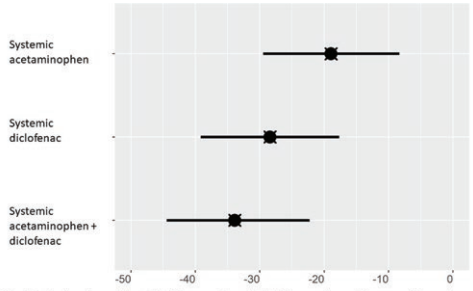


Figure 1. Simulated placebo-subtracted difference in opioid PCA use (in mg) for monotherapies and combination treatment assuming a typical placebo response (64.7 mg). Symbols indicate maximum likelihood model predictions and error bars present 95% CI of resampling parameter estimates from the final model variance-covariance matrix 1,000 times

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POS1358

BURDEN OF OSTEOARTHRITIS IN CHINA FROM 1990 TO 2019 AND PREDICTIONS OF THE BURDEN IN FUTURE 25 YEARS: FINDINGS FROM THE GLOBAL BURDEN OF DISEASE STUDY 2019

Keywords: Osteoarthritis, Epidemiology

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Background: China has the world's largest population and a high prevalence of osteoarthritis (OA), accompanying by a rapidly ageing and increasingly obese population [1-2]. However, the disease burden and secular trend of OA in China have not been well described nor predicted.
Objectives: To describe and predict the epidemiological features and secular trends attributable to OA in China from 1990 to 2044 in a comprehensive manner.
Methods: Data from the Global Burden of Disease (GBD) Study 2019 were used to estimate the incidence, prevalence, disability-adjusted life years (DALYs) and the related age-standardized rates (ASRs) of OA, as well as the burden of OA due to a high body mass index (BMI). The estimated annual percentage change (EAPC) in the ASRs was used to describe the temporal trend of OA changes and the Norpred age-period-cohort (APC) model was used to predict the disease burden over the next 25 years.
Results: The prevalence of OA in China increased from 51.76 (45.95-58.26) million in 1990 to 132.81 (118.00-149.08) million in 2019. The ASR of OA incidence increased from 472.53/100,000 in 1990 to 509.84/100,000 in 2019, with an EAPC of 0.36 (0.29-0.44); the ASR of OA prevalence increased from 5880.58/100,000 in 1990 to 6330.06/100,000 in 2019, with an EAPC of 0.35 (0.28-0.42), and the ASR of OA DALYs increased from 206.38/100,000 in 1990 to 224.78/100,000 in 2019, with an EAPC of 0.40 (0.32-0.48). The ASR of OA DALYs associated with high BMI increased rapidly from 1990 to 2019, especially in male and hip OA (Table 1). The projections suggested that there will be an increasing trend in the incidence (male 27.92%; female 15.51%), prevalence (male 71.08%; female 50.30%) and DALYs (male 71.93%; female 50.02%) of OA from 2020 to 2044, and the prevalence and DALYs of OA in China would increase by approximately 1.5 times in future 25 years. (Figure 1).
Conclusion: The disease burden of OA has increased in China in the past 30 years and will continue to rise over the next 25 years. Therefore, prevention and early intervention are pivotal to mitigating the growing burden of OA.
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Table 1. DALYs for all age and ASR due to a high BMI for OA in 1990 and 2019 and the percentage change as well as EAPC from 1990 to 2019 for China.

Site of OA	Sex	DALYs due to a high BMI						
		1990 (95% UI)		2019 (95% UI)		Percentage change		EAPC (95% CI)
		All age	ASR (per 100,000)	All age	ASR (per 100,000)	Count	ASR	
All OA	Both	99196.59 (16850.73, 280351.94)	10.94 (1.84, 30.78)	557902.37 (165070.11, 1343750.30)	25.99 (7.67, 62.55)	462.42	137.65	3.40 (3.26-3.54)
	Male	33196.90 (4882.35, 105084.82)	7.18 (1.05, 22.89)	193070.45 (51904.58, 471633.14)	18.18 (4.89, 44.53)	481.59	153.04	3.60 (3.42-3.78)
	Female	65999.69 (10513.94, 189125.01)	14.64 (2.32, 42.05)	364831.92 (94116.42, 879733.35)	33.52 (8.69, 80.82)	452.78	128.94	3.28 (3.14-3.41)
Knee OA	Both	98081.84 (16592.36, 275584.20)	10.81 (1.81, 30.43)	549963.53 (162522.40, 1325608.31)	25.61 (7.54, 61.65)	460.72	136.87	3.39 (3.24-3.53)
	Male	32655.59 (4805.87, 103252.26)	7.06 (1.03, 22.42)	189048.55 (50146.92, 463413.06)	17.79 (4.73, 43.87)	478.92	151.81	3.58 (3.4-3.76)
	Female	65426.25 (10373.35, 187931.73)	14.51 (2.29, 41.79)	360914.98 (93113.14, 869492.52)	33.15 (8.55, 79.85)	451.64	128.42	3.27 (3.14-3.4)
Hip OA	Both	1114.76 (179.91, 3521.08)	0.12 (0.02, 0.39)	7938.84 (2173.03, 21603.45)	0.38 (0.11, 1.03)	612.16	205.59	4.14 (4.02-4.26)
	Male	541.32 (78.08, 1832.14)	0.12 (0.02, 0.40)	4021.90 (996.68, 10699.58)	0.39 (0.10, 1.04)	642.98	224.98	4.32 (4.21-4.44)
	Female	573.44 (92.00, 1727.13)	0.13 (0.02, 0.39)	3916.94 (1045.57, 10410.57)	0.37 (0.10, 0.98)	583.06	187.39	3.95 (3.84-4.07)

95% UI, 95% uncertainty interval; 95% CI, 95% confidence interval.

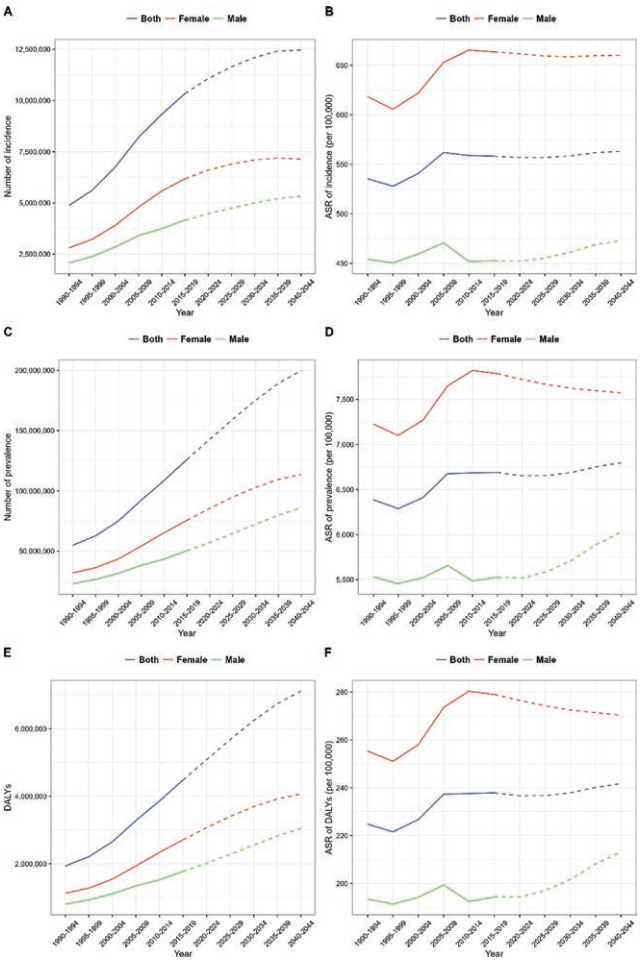


Figure 1. Prediction of number **(A)** and ASR **(B)** of incidence, number **(C)** and ASR **(D)** of prevalence, number **(E)** and ASR **(F)** of DALYs in OA by sex in China from 1990 to 2044. The solid lines indicate the observed values (1990 to 2019), and the dashed lines are the predicted values (2020 to 2044).

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1359 SURGICAL DENERVATION TO TREAT PAIN IN HAND OSTEOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

Keywords: Systematic review, Osteoarthritis, Pain

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Background: Surgical denervation has been proposed as a treatment for pain in hand osteoarthritis (OA).
Objectives: We performed a systematic literature review to summarize the available evidence and propose a research agenda.
Methods: A systematic literature search was performed up to September 2022. Two investigators identified studies that reported on denervation for OA of the proximal interphalangeal joint (PIPJ), distal interphalangeal joint (DIPJ), metacarpophalangeal joint (MCPJ) or first carpometacarpal joint (CMCJ). Reviews, comments, letters or editorials, studies in languages other than English and studies investigating other interventions, joints or conditions were excluded. Quality of studies was assessed with the Joanna Briggs Institute checklist for case series and the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I), where applicable. Study characteristics, patient characteristics, details of the surgical technique and outcomes of the surgery were extracted. Due to the nature of the data, no meta-analysis was performed. Data from the studies were pooled and minimal and maximal scores were estimated.
Results: The search yielded 212 articles from the Pubmed, OVID and Cochrane databases. From these, 17 articles (reporting on 384 denervation surgeries in 351 patients) were selected. Twelve studies described CMCJ denervation, three described PIPJ denervation, and the others described DIPJ (n=1), MCPJ (n=1) or a mixture of MPCJ, PIPJ and DIPJ denervation (n=1). The surgical techniques varied greatly, both in incisions and in the nerves severed, even between studies investigating denervation of the same joint. The innervation of the joints in the hand is still subject to debate. Most of the studies were case series (n=16), and one was a non-randomized clinical trial. Sample size ranged from 3 to 60 participants. All studies had significant risk of bias. The studies consisted of patient groups with average age ranging from 55 to 65 and 60-75% female participants. The sixteen case series reported positive outcomes with respect to pain, function and patient satisfaction. Average pain decrease ranged from 3 to 8.1 on a 10-point numeric rating scale (NRS) (n=8 studies), with a 56-92% patient satisfaction rate (n=5) and mean increase in range of motion of 3.5-27 degrees (n=3). The non-randomized clinical trial reported no differences in outcome when comparing denervation to trapeziectomy. Adverse event rates ranged from 0-75% of denervation procedures. Sensory abnormalities occurred most, followed by the need for revision surgery and infections of the area of the surgery.
Conclusion: Surgical denervation for pain in hand OA shows promise, but the available evidence does not allow conclusions, as for example regression to the mean can strongly influence the observations in case series. More and higher quality evidence is needed before it can be recommended as part of standard care. On the research agenda are 1) the innervation of the joints, 2) the best surgical technique to sever all relevant nerves, and 3) perform high-quality randomized clinical trials to investigate the efficacy of surgical denervation in comparison to sham, 4) to investigate other interventions targeted at the innervating nerves, and finally 5) the safety of the different surgical denervation techniques.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1360 PATIENTS ARE ALWAYS RIGHT! ASSOCIATION BETWEEN HUMIDITY LEVEL AND PAIN EXPERIENCE IN HAND OSTEOARTHRITIS

Keywords: Pain, Osteoarthritis

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Background: While many patients with joint disease report pain changes according to meteorological factors (1), this common belief has not been clearly demonstrated and never been documented in hand osteoarthritis (HOA).
Objectives: We aimed to investigate the cross-sectional association between meteorological factors that are ambient temperature and humidity on HOA symptoms.
Methods: We used the baseline data from the prospective DIGICOD HOA cohort including patients with established symptomatic HOA. The clinical outcomes were AUSCAN-pain, AUSCAN-stiffness and AUSCAN-function subscores, VAS-scale for pain during activity, number of spontaneous tender joints and tender joints at palpation. Meteorological data (from Météo France), ambient temperature and humidity, are defined as the mean value observed during the 3 days before inclusion (day of inclusion, D-1 and D-2). Considering non-normal distribution, each outcome was binarized by the median value, in order to define high and low symptoms intensity. Association between each outcome and meteorological data were studied using two logistic regression models (separate models for temperature and humidity), adjusted for age, sex, sum of Kellgren-Lawrence score of all hand joints and Hospital Anxiety Depression scale. Assumption of linearity between temperature or humidity and the logit of the outcomes being not verified, those two parameters were introduced in the models as categorical variables according to quartiles. Results are presented as odds ratio (OR) with 95% confidence intervals (CIs). The reference groups were respectively lower humidity and lower temperature quartile.
Results: We have studied 377 patients in whom all variables of interest were available (mean age ± standard deviation (SD) 66.5 ± 7.4 years, 85% women). Median AUSCAN-pain subscore was 20/100 (IQR [8; 38]), median AUSCAN-stiffness subscore was 22/100 (IQR [7; 53]), median AUSCAN-function subscore was 32/100 (IQR [13; 55]), median VAS-pain during activity was 42/100 (IQR [22; 66]), median number of spontaneous tender joints was 0/30 (IQR [0; 2]), median

number of tender joints at palpation was 3/30 (IQR [2; 6]). Results of models for humidity are presented in Table 1. There was an association between humidity percentage and AUSCAN pain ≥ 20 for third quartile vs. first quartile (OR [79-85%] vs. [43-68%] = 1.99 (1.08 to 3.68), p = 0.03) and between humidity and VAS pain during activity ≥ 42 for second quartile vs. first quartile (OR [68-79%] vs. [43-68%] = 1.97 (1.06 to 3.63) p = 0.03). Considering patients with at least 1 spontaneous hand joint pain, an association was found for all 3 higher quartiles of humidity ([68-79%], [79-85%] and [85-96%]) compared to the lower one ([43-68%]), but without dose-effect. There was no effect of humidity on AUSCAN stiffness or function, or number of tender joints at palpation. Temperature was not associated with any clinical outcomes (pain, function or stiffness).

Conclusion: This is the first study about impact of meteorological factors in HOA. While we did not find any association between temperature and symptoms, we found an association between humidity and pain. Although we cannot conclude on any causality between humidity and pain, our results support patient's belief about influence of humidity on joint pain.

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Table 1: Association between humidity and HOA symptoms: logistic regression models with systematic adjustment on sex, age, sum of Kellgren-Lawrence score for all hand joint and HAD score.

	OR (IC 95%)	p-value
AUSCAN-pain subscore ≥ 20		
Humidity (%)		0.14
1. [43 ; 68[	1	
2. [68 ; 79[	1.76 (0.96;3.25)	0.07
3. [79 ; 85[	1.99 (1.08;3.68)	0.03
4. [85 ; 96[	1.52 (0.83;2.79)	0.18
At least 1 spontaneous tender joint		
Humidity (%)		0.02
1. [43 ; 68[	1	
2. [68 ; 79[	1.74 (0.94;3.21)	0.08
3. [79 ; 85[	2.67 (1.44;4.94)	0.002
4. [85 ; 96[	1.95 (1.06;3.61)	0.03
VAS-scale for pain during activity ≥ 42		
Humidity (%)		0.1832
1. [43 ; 68[	1	
2. [68 ; 79[	1.97 (1.06;3.63)	0.03
3. [79 ; 85[	1.58 (0.86;2.91)	0.14
4. [85 ; 96[	1.56 (0.85;2.86)	0.15

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1361 THE INFLUENCE OF BASELINE DEMOGRAPHICS ON VARIABILITY OF OA PAIN ASSESSED BY WOMAC PAIN CHANGE FROM BASELINE IN INTERVENTIONAL TRIALS

Keywords: Biomarkers, Osteoarthritis, Randomized control trial

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Background: Development of new products for OA treatment is difficult, partly due to excessive placebo response and high variability in patient-reported pain outcomes, and exclusion of trial subjects with potentially confounding pain from non-target joints may increase the effect size. This may in part be due to reductions in variability, and hence in standard deviation (SD) of the mean changes in pain scores, which improves the statistical power to detect differences between study groups. The impact of refining the study population in terms of added benefit to the SD and statistical power vs. added screen failures is poorly described.

Objectives: To investigate the impact of common demographic and pain characteristics on the SD of mean pain change from baseline in a large interventional OA trial database.

Methods: Data from 2 randomized controlled trials of oral salmon calcitonin in OA (1) were analyzed post-hoc. The SD of the mean change from baseline (SD-CFB) to Year 2 in the WOMAC knee pain score (0-100) was calculated. The SD-CFB was also calculated for subgroups (e.g. demographics, pain of the target and non-target knee). The sample size required to identify a statistically significant difference of at least 8 out of 100 between groups (with 80% power) was calculated, and the additional proportion of eligible subjects to be screen-failed if the particular subgroup was excluded was calculated to quantify the potential impact on the study feasibility.

Results: A total of 1,487 subjects had WOMAC pain data throughout the trial period. Results are shown in Table 1. Few clinical characteristics influenced the SD and hence the required sample size, except for Asian race, associated with a lower SD compared to Caucasians (19.71 vs. 21.85), to detect a significant difference. Exclusion of those with high BMI (≥ 35 kg/m^2) led to a reduced sample size required of 113. Subjects with non-target knee pain above the median had higher pain variability and thus a larger sample sizes required to detect differences vs. those with pain scores below the median. However, exclusion of these groups required screen failing approx. extra 50 % of the eligible population to achieve this. A less exclusive method was excluding subjects with non-target knee pain not exceeding that of the target knee. Radiographic characteristics did not influence the SD, except for those with a KL grade 3 or 4 of the non-target knee (Table 1). This observation requires further scrutiny.

Table 1.

	SD of mean WOMAC pain change	n	Sample size per group to detect mean WOMAC pain difference of 8 out of 100 (n)	Proportion of eligible subjects screen failed if subgroup was excluded (%)
All study completers	21.58	1,487	115	0
Male	21.12	516	110	34.7
Female	21.82	971	117	65.3
Age < 64 yrs	21.49	799	114	53.7
Age ≥ 64 yrs	21.68	688	116	46.3
BMI < 35 kg/m^2	21.45	1,316	113	88.5
BMI ≥ 35 kg/m^2	22.53	171	125	11.5
Subgroups by **Non-Target knee characteristics** at Baseline				
KL grade 0	20.79	60	107	4.0
KL grade I	21.19	271	111	18.2
KL grade II	20.83	766	107	51.5
KL grade III	23.80	346	139	23.3
KL grade IV	17.55	42	76	2.8
WOMAC Pain ≤ 35 (0-100)	20.08	731	99	49.2
WOMAC Pain > 35 (0-100)	22.96	722	130	48.6
Low VAS (0-100, ≤ 37)	19.39	714	93	48.0
High VAS (0-100, > 37)	23.54	722	136	48.6
Nontarget knee WOMAC pain ≥ Target knee WOMAC pain	22.64	408	126	27.4
Nontarget knee WOMAC pain < Target knee WOMAC pain	20.84	1,024	107	68.9

Conclusion: High BMI and high baseline pain of the non-target knee may contribute negatively to the study power, however, the added study cost in terms of additional screened subjects required to replace those excluded based on these parameters should be carefully evaluated. The potential impact of these parameters on the magnitude of the difference between study groups was not evaluated and may also differ, with additional statistical implications.

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Acknowledgements: NIL.

Disclosure of Interests: Asger Reinstrup Bihlet Employee of: Full-time employee and shareholder of NBCD, Peter Alexandersen Employee of: Part-time employee at NBCD, Jeppe Ragnar Andersen Employee of: Full-time employee and shareholder of NBCD, Yanqi Li Employee of: Full-time employee and shareholder of NBCD, Morten Karsdal Employee of: Full-time employee and shareholder of NBCD, Claire Prener Miller Employee of: Full-time employee at NBCD.

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POS1362 THE OA TRIAL BANK: UPDATE OF INDIVIDUAL PATIENT DATA META-ANALYSIS OF INTRA-ARTICULAR GLUCOCORTICOIDS IN PERSONS WITH KNEE AND HIP OSTEOARTHRITIS

Keywords: Osteoarthritis

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Background: Intra-articular (IA) glucocorticoid injections are often employed in the management of osteoarthritis (OA) patients, but in whom to best target treatment is unclear. OA clinical guidelines have advocated for the identification of predictors of response to different treatments, but no reliable subgroups with treatment effect have been found.

Objectives: This study aims to conduct an individual patient data (IPD) meta-analysis to evaluate the efficacy of IA glucocorticoid for knee or hip OA in specific subgroups of patients according to the baseline pain severity and inflammatory signs. This is an update on an IPD meta-analysis on IA glucocorticoid by the OA Trial Bank [1].

Methods: Randomised trials evaluating one or more IA glucocorticoid preparations in hip and knee OA, published from 2012 to May 2018, were selected from the literature. IPD of participant and disease characteristics and outcome measures were acquired. The primary outcome was pain severity at short-term follow-up (around 4 weeks). A two-stage IPD analysis was performed. Potential interaction effect of baseline severe pain (≥70 points, 0-100 scale) and signs of inflammation were studied using linear mixed-effects models. Analysis of trend was conducted, assessing if a baseline pain cut-off was associated with the threshold for clinically important treatment effect of IA glucocorticoid compared to placebo.

Results: Four out of 16 eligible randomised clinical trials (n=641) were combined with the existing OA Trial Bank studies (n=620), yielding n=1261 from eleven studies. Participants with severe baseline pain compared to those with less severe pain had greater pain reduction at mid-term (around 12 weeks) (mean reduction: -6.90 (95%CI -10.91; -2.90)), but not at short- or long-term follow-up. No interaction effects were found between inflammatory signs and IA glucocorticoid injections compared to placebo at all follow-up time-points (Table 1). Analysis of trend showed treatment response to IA glucocorticoid injections from baseline pain levels >50 (0-100 scale) and above (Figure 1).

Conclusion: This IPD meta-analysis demonstrated that in participants with severe baseline pain, clinically relevant response is seen at mid-term follow-up, suggesting that sustained response to IA glucocorticoid injection may be seen in a subgroup of OA participants. As baseline pain score increases, treatment response is seen in participants from moderate pain levels onwards. No concrete conclusions can be made on baseline inflammatory signs. Ongoing IPD studies with an increased number of studies are required.

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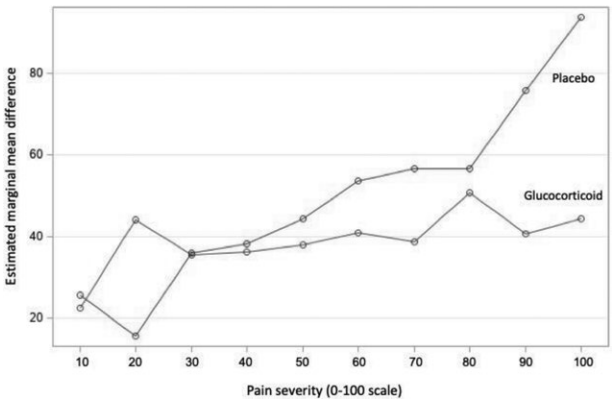
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Table 1: Interaction effects of severe pain (≥70 points) and inflammation with IA glucocorticoid for primary outcome of pain severity

	No. of studies	No. of participants	Adjusted mean reduction (β) (95%CI)	*P*	Cochran's Q	I^2 (%)	Tau^2
Interaction effect of severe pain with IA glucocorticoid[#]							
IA glucocorticoid versus placebo							
Short-term	6	345	-5.98 (-18.28; 6.31)	0.266	4.47	0	0
Mid-term	5	270	**-6.90 (-10.91; -2.90)**	**0.009**	0.17	0	0
Long term	3	160	-2.84 (-62.69; 57.01)	0.857	2.88	30.5	0
IA glucocorticoid versus hyaluronic acid							
Short-term	3	513	7.50 (-56.58; 71.57)	0.665	9.41	78.8	508.88
Mid-term	3	476	6.90 (-3.39; 17.20)	0.102	0.39	0	0
Long term	2	456	8.42 (-28.03; 44.86)	0.209	0.27	0	0
Interaction effect of inflammation with IA glucocorticoid*							
IA glucocorticoid versus placebo							
Short-term	5	296	-15.01 (-51.23; 21.21)	0.314	21.83	81.7	688.97
Mid-term	4	230	-5.96 (-35.81; 23.91)	0.571	5.95	49.6	172.64
Long term	2	126	-7.43 (-125.49; 110.63)	0.571	0.64	0	0
IA glucocorticoid versus hyaluronic acid							
Short-term	2	360	**-10.82 (-20.30; -1.33)**	**0.044**	0.02	0	0
Mid-term	2	334	-9.22 (-70.10; 51.662)	0.305	0.62	0	0

[#]Adjusted for age and sex, *Adjusted for age, sex and baseline pain

Figure 1: Comparison of marginal means of pain scores (grouped) of IA glucocorticoid compared to placebo at short-term follow-up



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POS1363

CIRCULATING GALECTIN-1 LEVELS IN INDIVIDUALS WITH KNEE AND/OR HAND OSTEOARTHRITIS – A HALLOA STUDY

Keywords: Biomarkers, Osteoarthritis

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Background: Circulating galectin-1 levels are associated with metabolic diseases including obesity, diabetes type II, and subclinical inflammation [1]. These medical conditions are often seen as comorbidities of osteoarthritis (OA) in the knees and hands.

Objectives: The aim was to study longitudinal associations between circulating galectin-1 levels and radiographic knee OA (RKOA), radiographic hand OA (RHOA), and general OA (GOA, RKOA and RHOA).

Methods: This longitudinal study included 232 individuals from the Halland osteoarthritis cohort (HALLOA) (2) with knee radiographs at inclusion and at a two-year follow-up. Of the included individuals, 211 had hand radiographs at the two-year follow-up. Body mass index (BMI), and waist circumference (WC) were measured. Visceral fat area (VFA) was assessed by bioimpedance (InBody 770). Serum/plasma levels of HbA1c, glucose, and C-reactive protein (CRP)≥1.0 mg/L were measured according to the current laboratory standards in Sweden. CRP below 1.0 mg/L, was further analysed with a sensitive CRP ELISA method (Abnova). Insulin resistance was assessed by the triglyceride glucose index (TyG). Galectin-1, IL-1 beta, IL-6, and TNF alfa using Quantikine, ELISA (biotechne, United Kingdom). RKOA was defined according to Ahlbäck, as grade 1 or more in at least one knee at two years follow-up; RHOA was defined according

to Kellgren and Lawrence as grade 2 or more in at least one joint at two years follow-up. GOA was defined as having RKOA and RHOA. Comparisons between groups at inclusion were performed using Mann-Whitney U test, chi-2, and univariate Logistic regression models for associations.

Results: At the two-year follow-up, 34% of the included individuals had RKOA, 42% had RHOA, and 50 individuals had GOA. Individuals with RKOA were older, more obese, and had higher median serum levels of HbA1c, CRP, and IL-6, but no increased serum level of galectin-1, Table 1. Age (OR 1.12; 95% CI 1.06-1.17) obesity (WC OR 1.04; 95% CI 1.01-1.06) and galectin-1 (OR 1.04; 95% CI 1.003-1.08) were associated with RKOA. Those with RHOA were older and had increased serum levels of HbA1c, galectin-1, TyG index, and IL-6, Table 1. Age (OR 1.21; 95% CI 1.14-1.28), HbA1c (OR 1.11; 95% CI 1.01-1.21), and galectin-1 (OR 1.05; 95% CI 1.01-1.10) were associated with RHOA. Individuals with GOA were older, more obese, had more inflammation, and increased levels of HbA1c and galectin-1, table 1. Age (OR 1.30; 95% CI 1.18-1.45) and galectin-1 (OR 1.06; 95% CI 1.01-1.12) were associated with GOA.

Conclusion: Circulating galectin-1 seems to associate with OA, especially RHOA. More studies are needed to assess a potential underlying pathophysiological mechanism of galectin-1 in OA.

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Table 1. Characteristics at inclusion of the groups with or without RKOA, RHOA, and GOA at two years follow-up, presented as median (IQR), respectively.

	No RKOA	RKOA	P-value	No RHOA	RHOA	P-value	No GOA	GOA	P-value
n	153	79		112	89		74	50	
Age, years	52 (13)	57 (5)	**<0.001**	49 (14)	58 (7)	**<0.001**	48 (14)	57 (5)	**<0.001**
Sex, female, %	70 (55)	69 (105)	0.87	63	66	0.64	66 (49)	68 (34)	0.84
BMI, kg/m^2	25.1 (5.8)	27.5 (5.6)	**<0.001**	25.5 (6.1)	25.6 (6.1)	0.36	24.9 (5.1)	26.2 (5.0)	0.05
WC, cm	93 (18)	100 (16)	**<0.001**	94 (18)	96 (18)	0.34	92 (19)	97 (18)	**0.04**
VFA, cm^2	86 (66)	124 (75)	**<0.001**	92 (68)	100 (67)	0.29	84 (66)	110 (68)	**0.03**
HbA1c, mmol/mol	36 (5)	38 (3)	**0.04**	36 (4)	38 (3)	**0.003**	36 (4)	38 (3)	**0.01**
Glucose, mmol/L	5.3 (0.7)	5.4 (0.5)	0.16	5.3 (0.8)	5.4 (0.6)	0.40	5.3 (0.7)	5.4 (0.4)	0.20
TyG	8.2 (0.6)	8.4 (0.6)	**0.03**	8.2 (0.6)	8.3 (0.5)	**0.04**	8.1 (0.6)	8.3 (0.7)	**0.03**
CRP, mmol/L	1.0 (1.1)	1.3 (1.6)	**0.03**	1.0 (1.0)	1.2 (1.6)	0.06	1.0 (1.0)	1.3 (2.0)	**0.01**
Galectin-1, ng/mL	28.0 (8.9)	29.0 (9.1)	0.20	26.6 (9.1)	28.5 (8.2)	**0.01**	26.0 (8.9)	28.5 (8.4)	**0.02**
IL-1 beta, pg/mL	0.06 (0.15)	0.08 (0.22)	0.15	0.05 (0.18)	0.06 (0.15)	0.70	0.05 (0.17)	0.06 (0.22)	0.39
IL-6, pg/mL	1.11 (0.89)	1.39 (1.31)	**0.02**	0.99 (1.14)	1.32 (0.93)	**0.01**	0.97 (1.14)	1.44 (1.33)	**0.005**
TNF alfa, pg/mL	1.10 (0.47)	1.23 (0.58)	0.06	1.05 (0.49)	1.13 (0.53)	0.20	1.04 (0.43)	1.11 (0.64)	0.18

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Disclosure of Interests: None Declared.

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POS1364

A COMPARISON OF SEMI-QUANTITATIVE AND QUANTITATIVE CARTILAGE LOSS ASSESSMENTS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

Keywords: Cartilage, Imaging, Osteoarthritis

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Background: In Disease Modifying Osteoarthritis Drug (DMOAD) trials, cartilage loss may be assessed semi-quantitatively or quantitatively, although the latter is higher cost and more technically challenging. The MRI Osteoarthritis Knee Score (MOAKS) is the most commonly used semi-quantitative knee OA scoring system that assesses thickness of MOAKS cartilage morphology loss (tMCM) and denudation (dMCM) on the articulating subregions of femur and tibia.

Objectives: This study aimed to compare the cross-sectional relationship and longitudinal responsiveness of MOAKS with the more accurate quantitative cartilage assessment.

Methods: Images and MOAKS scores from 297 participants with radiographic progression (groups 1 and 2) from the OAI FNIH sub-cohort were included. Quantitative cartilage thickness was measured using Active Appearance Models (AAMs). To facilitate direct comparison with MOAKS, novel quantitative measures of cartilage loss were matched to MOAKS regions (Q-MOAKS). Mean normative cartilage thickness was computed for each subregion (Figure 1) using FNIH controls (group 4). Q-MOAKS thickness loss score (tQCM) was based on the proportion of cartilage thickness over a subregion that was <95% normative thickness and denudation score (dQCM) was based on <5% normative thickness. Q-MOAKS area proportions were categorised into scores as for MOAKS (0: none, 1: 0-10%, 2: 10-75% and 3: >75%). Quantitative cartilage thickness (ThCtAB) was also measured in the central medial femur (cMF) and tibia (cMT). We compared MOAKS against Q-MOAKS and ThCtAB. Cross-sectional relationships between measures were assessed using Spearman's rank correlation. Responsiveness was assessed at 1 and 2 years using bootstrapped standardised response means (SRM).

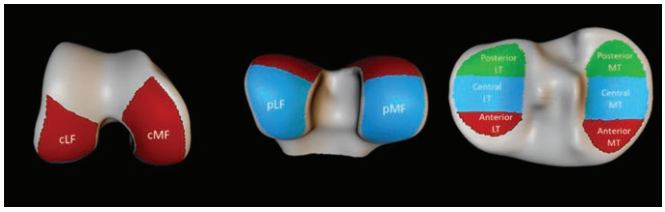


Figure 1: Cartilage regions definitions consisting of the medial and lateral central and posterior femur (cMF, cLF, pMF, pLF) subregions and the medial and lateral tibial anterior, central, posterior (aMT, cMT, pMT, aLT, cLT, pLT) subregions.

Results: Cross-sectionally, there was moderate correlation between MOAKS and Q-MOAKS denudation in the central medial femur (cMF r = 0.42, (95%CI: 0.32, 0.51)) and tibia (cMT r = 0.51, (0.42, 0.59)). There was a poor correlation between MOAKS and Q-MOAKS thickness loss and denudation scores in all other regions. In the tibia (cMT), 61% (96/159) of knees with thickness loss tMCM = 2 (the 10-75% score) were also tQMC = 2 and 66% of denudation dMCM = 2 were also dQCM = 2. In the femur (cMF), the figures were 56% and 23%. MOAKS tMCM and dMCM were less responsive than Q-MOAKS tQCM and dQCM in most subregions (selected SRMs presented in Table 1). Q-MOAKS tMCM in pMT demonstrated the most responsiveness for all the scores (SRM=+0.76 vs SRM = +0.20 for MOAKS tMCM). Quantitative cartilage thickness (ThCtAB) measures were most responsive. In the cMF region, the SRM= -0.46 (95% CI: -0.56, -0.33) at 1-year and 0.82 (-0.94, -0.72) at 2-years while the cMT SRM = -0.4 (-0.5, -0.28) at 1-year and -0.71 (-0.80, -0.60) at 2-years.

Table 1. Responsiveness of cartilage scores at follow up. Values are SRM (95% CI).

	YEAR ONE				YEAR TWO			
AREA	**tMCM**	**tQCM**	**dMCM**	**dQCM**	**tMCM**	**tQCM**	**dMCM**	**dQCM**
cMF	+0.28 (0.13,0.41)	+0.32 (0.20,0.43)	+0.07 (-0.05,0.18)	+0.20 (0.11,0.28)	+0.46 (0.32,0.57)	+0.53 (0.40,0.63)	+0.37 (0.26,0.48)	+0.44 (0.38,0.51)
cLF	+0.07 (-0.07.0.17)	+0.20 (0.09,0.33)	+0.02 (-0.09,0.14)	+0.14 (0.05,0.23)	+0.13 (0.02,0.20)	+0.24 (0.12,0.36)	+0.11 (-0.03,0.19)	+0.30 (0.24,0.36)
cMT	+0.32 (0.27,0.37)	+0.36 (0.24,0.47)	+0.23 (0.11,0.32)	+0.25 (0.13,0.33)	+0.45 (0.37,0.52)	+0.61 (0.49,0.72)	+0.42 (0.29,0.53)	+0.44 (0.36,0.51)
cLT	+0.18 (0.12,0.24)	0.22 (0.10,0.34)	+0.11 (-0.03,0.18)	+0.15 (0.04,0.24)	+0.23 (0.17,0.29)	+0.14 (0.02,0.26)	+0.17 (0.08,0.23)	+0.29 (0.20,0.37)

Conclusion: Quantitative measures or derived Q-MOAKS scores were more responsive than MOAKS. MOAKS appears to have better concordance with quantitative cartilage denudation than thickness loss, which might be explained by diagnostic accuracy for full thickness lesions being better than earlier grade lesions.

REFERENCES: NIL.

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POS1365 STRUCTURAL SEVERITY IN KNEE OSTEOARTHRITIS IMPACTS TREATMENT RESPONSE: A POST HOC POOLED ANALYSIS OF LORECIVIVINT CLINICAL TRIALS

Keywords: Imaging, Osteoarthritis, Clinical trials

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Background: Osteoarthritis (OA) is a leading cause of disability globally, with disease burden expected to rise [1]. Unmet needs remain for safe and efficacious treatments for symptoms and structural modification. Difficulties assessing pain and joint structure in clinical trials exist due to disease heterogeneity. This post hoc analysis of lorecivivint (LOR), an intra-articular (IA) CLK/DYRK inhibitor thought to modulate Wnt and inflammatory pathways, examined the structural heterogeneity of participants enrolled in Phase 2 and 3 LOR trials and associated treatment responses within KL grade subgroups.

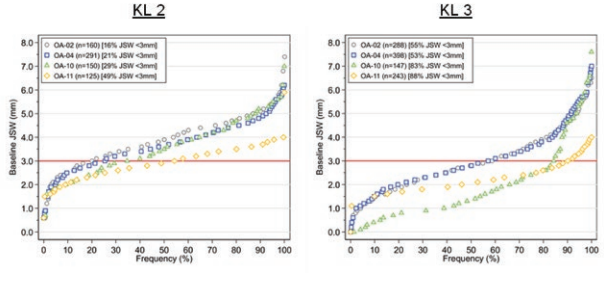
Objectives: To identify potential relationships between OA pain and knee joint structural damage which may aid future clinical trial design.

Methods: Data was analyzed from two Phase 2 (OA-02, NCT02536833; OA-04, NCT03122860), and two Phase 3 trials (OA-10, NCT04385303; OA-11, NCT03928184) trials. In all trials, participants had ACR-defined (clinical and radiographic) knee OA, Kellgren-Lawrence (KL) grades 2-3. For OA-04, OA-10 and OA-11, additional pain inclusion criteria included Pain Numeric Rating Scale (NRS) [0-10] ≥4 and ≤8 in the target knee and <4 in the contralateral knee. Baseline JSW for each study was compared using cumulative frequency distribution plots by KL grade; percentages of subjects with JSW < 3mm for each study was also summarized to provide a surrogate for loss of ~50% healthy JSW (Deep et al. *JBJS* 2003). For the trials which captured Pain NRS outcomes, treatment responses were assessed according to KL grade. For all treatment-related outcomes, change from baseline was estimated using baseline-adjusted ANCOVA at each timepoint.

Results: KL 2 participants with baseline mJSW < 3 mm comprised 16% (OA-02), 21% (OA-04), 30% (OA-10) and 49% (OA-11). KL 3 participants with baseline mJSW < 3 mm comprised 55% (OA-02), 53% (OA-04), 81% (OA-10) and 88% (OA-11) (Figure 1) Beneficial treatment effect of LOR vs. PBO was seen for KL 2 subgroup in OA-04 and OA-10, but not in OA-11. Beneficial treatment effect of LOR was seen only in OA-04 for KL 3 at week 12.

Conclusion: In this post hoc analysis, substantial heterogeneity in baseline mJSWs existed across LOR clinical trials within the KL grade 2-3 inclusion criteria. Participants with less structurally advanced knee OA showed greater pain treatment responses to 0.07 mg LOR compared to those with more advanced disease. These data support the hypothesis that the amount of OA structural damage is associated with the pain of knee OA and that earlier LOR intervention may improve outcomes.

Figure 1. Cumulative frequency of baseline mJSW by KL grade across LOR trials



REFERENCE:

[1] Wallace, IJ et al. *PNAS* 2017

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POS1366 EFFICACY OF DULOXETINE COMPARED TO NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN THE TREATMENT OF KNEE OSTEOARTHRITIS IN IRAQI KURDISTAN REGION

Keywords: Randomized control trial, Clinical trials, Osteoarthritis

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Background: Osteoarthritis (OA) is the most common degenerative joint disease [1]. Knee OA is an insidious disease related to structural changes in the joint over many years. Duloxetine, a selective serotonin, and norepinephrine reuptake inhibitor, seems to be effective in treating neuropathic and chronic pain conditions [6].

Objectives: The objective of this study was to assess the efficacy of duloxetine tablet compared to nonsteroidal anti-inflammatory (NSAID) for the reduction of pain in Osteoarthritis.

Methods: A Randomized open labelled clinical trial of a 13-weeks done in Rizgary Teaching and CMC (Consultant Medical City) hospitals in Iraqi Kurdistan Region. From 5th of September 2022 to 2nd of January 2023 with Trial Registration ID (NCT05486026). Those eligible to enter the study their ages were ≥ 40years, both Genders were included, who will meet the American College of Rheumatology clinical and radiographic criteria for the diagnosis of osteoarthritis of the knee [8]. Patients were divided into two groups, The first group received Duloxetine tablet 30 mg for two weeks then titrated up to 30 mg BID. were compared to control group that received NSAID (nonsteroidal anti-inflammatory drug). End points were recorded at baseline then 2nd visits at 13 weeks. Measurement of pain severity was done by the weekly mean of the 24-h average pain scores in patients with osteoarthritis knee pain by Brief pain inventory (BPI). Another tool is (WOMAC) WESTERN ONTARIO AND MCMASTER OSTEOARTHITIS INDEX used for evaluation of pain in knee Osteoarthritis which involve three categories. The Patient Global Impression of Improvement (PGI-I) scale measured patients' perceived change in overall well-being (in response to therapy/treatment) and even side effects.

Results: Out of two hundred patients, forty-six participants were excluded: one hundred fifty-four were enrolled in the study. Their mean ages ±SD (57.38 ±10.58, 58.47±12.03) in Duloxetine, NSAID group Respectively. BPI-Severity average pain improved significantly after treatment with Duloxetine were 4.64 (95%CI:4.25 to 5.02) and P value was 0.00. BPI during 24-hour pain interfere with (activity, Mood, walking ability, work, relations with other people, sleep, enjoyment of life) were lower in Duloxetine group after treatment in comparison to control group (NSAID) 4.45 (95% CI:4.01 to 4.87), 5.47 (95%CI:5.11 to 5.82) respectively p value was significant ‹ 0.001. The total WOMAC score after treatment in Duloxetine group decreased 31.74 (95%CI:27.05 to 36.42) while in NSAID groups were 42.46(95%CI:38.05 to 46.86). about (PGI-I) scale, the patients who treated with Duloxetine was generally better than those treated with NSAID group; as the response and cure rate were higher in the Duloxetine(34.2%,30.3%,7.9%) much improve, very much improved, minimally improved respectively so; total (72.4%) were improved in comparison to the control group(28.2%, 6.4%, 11.5%) much improved, much improved,minimally improved respectively so; total (46.1%) were improved, the p value were significant 0.002 and about adverse effect in Duloxetine group most common side effects were epigastric pain and headache(3,3), with one patient with nausea, one with tremor and one fatigability, the symptoms were mild they continue study with symptomatic treatment of side effects, and 4 in NSAID developed side effect.

Conclusion: Duloxetine reduced pain and improved function in patients with knee osteoarthritis, by reducing BPI inventory and WOMAC score, with much improvement on PGI scales in comparison to NSAID.

Table 1: primary outcomes by BPI and WOMAC scales

	scales	Duloxetine(case) 76(49.4%) N. 95%CI	NSAID(Control) 78(50.6%) N. 95%CI	P value
Mean average pain score BPI (Worst pain, least pain, average, right now) **at baseline**	0-10	6.58 (6.33 to 6.82)	6.46(6.67 to 0.90)	0.570
Mean average pain score BPI (Worst pain, least pain, average, right now) **after treatment**	0-10	4.64 (4.25 to 5.02)	5.78(5.47 to 6.09)	0.000
BPI during 24-hour pain interfere with (General activity, Mood, Walking Ability, Normal work, Relations with other people, Sleep, Enjoyment of life) **at baseline**	0-10	6.14 (5.75 to 6.5)	6.26 (5.92 to 6.60)	0.653
BPI during 24-hour pain interfere with (General activity, Mood, Walking Ability, Normal work, Relations with other people, Sleep, Enjoyment of life) **after treatment**	0-10	4.45 (4.01 to 4.87)	5.47(5.11 to 5.82)	0.000
WOMAC pain score **at baseline**	0-4	2.84(2.61 to 3.06)	2.88(2.68 to 3.06)	0.816
WOMAC pain score after treatment	0-4	1.97(1.65 to 2.28)	2.51(2.31 to 2.71)	0.004
WOMAC _morning & evening stiffness **at baseline**	0-4	2.901(2.62 to 3.18)	3.03(2.79 to 3.25)	0.496
WOMAC morning & evening stiffness **after treatment**	0-4	1.92(1.64 to 2.19)	2.54(2.25 to 2.82)	0.002
WOMAC Difficulty score (17) item **at baseline**	0-4	1.60(1.41 to 1.77)	1.65(1.46 to 1.82)	0.691
WOMAC Difficulty score (17) item **after treatment**	0-4	1.06(0.87 to 1.24)	1.46(0.87 to 1.24)	0.691
Total WOMAC 24 items **at baseline**	0-96	47.13 (42.97 to 51.28)	48.51(44.46 to 52.54)	0.638
Total WOMAC 24 items **after treatment**	0-96	31.74 (27.05 to 36.42)	42.46(38.05 to 46.86)	0.001

*BPI: Brief pain inventory, WOMAC;(WESTERN ONTARIO AND MCMASTER OSTEOARTHITIS INDEX)
NSAID (Nonsteroidal anti-inflammatory drug)

Table 2 secondary outcomes and adverse effect		**Case 76(49.4%)** N. %	**Control 78(50.6%)** N %	Total	P value
outcomes	**very much improved**	23(30.3%)	5(6.4%)	28(18.2%)	0.002
	Much improved	26(34.2%)	22(28.2%)	48(31.2%)	
	Minimally improved	6(7.9%)	9(11.5%)	15(9.7%)	
	No change	9(11.8%)	13(16.7%)	22(14.3%)	
	Minimally worse	11(14.5%)	26(33.3%)	37(24.0%)	
	Much worse	1(1.3%)	2(2.6%)	3(1.9%)	
	Very much worse	0(0.0%)	1(1.3%)	1(0.6%)	
Side effects	**nausea**	1(1.3%)	1(1.3%)	2(1.3%)	0.332
	Epigastric pain	3(3.9%)	3(3.8%)	6(3.9%)	
	Tremor	1(1.3%)	0(0.0%0)	1(0.6%)	
	headache	3(3.9%)	0(0.0%)	3(1.9%)	
	fatigability	1(1.3%)	0(0.0%)	1(0.6%)	

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POS1367 **WITHDRAWN**

POS1368 **THE LONGITUDINAL ASSOCIATION OF HAND OA WITH PAID AND UNPAID WORK IMPAIRMENT AND RELATED COSTS: THE HOSTAS COHORT**

Keywords: Patient reported outcomes, Epidemiology, Work-related issues

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Background: Hand osteoarthritis (OA) is associated with impairment in paid and unpaid work and contributes to societal burden and costs of OA. However, the longitudinal development of hand OA-related work impairment and related societal costs are unknown.
Objectives: To investigate the association of hand OA with paid and unpaid work productivity loss, hinder and societal costs longitudinally.
Methods: We used annual data of the Dutch Hand OSTeoArthritis in Secondary care (HOSTAS) cohort, consisting of patients with primary hand OA primary hand OA defined by the treating rheumatologist. Data from baseline to four years of follow-up was used. The Health and Labour Questionnaire (HLQ) was assessed over the last two weeks on (i) hand OA-related limitations and hours of productivity loss while at work, (ii) hours of sick leave, and (iii) limitations and hours of unpaid work replacement. Patients with HLQ data on >1 timepoint were included in this study. Societal costs of paid work productivity loss (=all hourly costs in order to employ a worker, such as salary and premiums) were estimated by multiplying the number of unproductive and sick leave hours due to hand OA by the estimated hourly costs of paid work in The Netherlands based on age and sex. Costs of unpaid work were estimated by multiplying the hours of unpaid work replaced by others by the Dutch gross average hourly salary of a household help (2021:€12.50). Costs were adjusted to 2021 values using conversion factors provided by the Dutch government, and to yearly values.
Results: 470 patients had data on more than one timepoint. Baseline data was available for 381 patients, of whom 256 patients (67%) completed four years of follow-up, and 215 (56%) completed all five follow-up moments. Of 256 patients

with baseline and four years follow-up, 113 (52%) had paid work at baseline and 104 (41%) at four years (**Table** 1 for patient characteristics). Unproductive hours at any timepoint were present for 85/470 patients (18%), for whom unproductive hours fluctuated over time (**Figure 1**). Median paid work hinder score (score range: 6-24) remained stable at 7 (interquartile range (IQR): 6;8) over the study period. Unproductive hours at any timepoint were present for 85/470 patients (18%). Regarding unpaid work, 105/256 (41%) required unpaid task replacement by others due to hand OA at baseline, which remained stable over time (108/256 at four years (42%)). Unpaid work hinder was reported by 100/256 patients (39%) at baseline and 97/256 (36%) at four years. Costs related to loss of paid and unpaid productivity were incurred at baseline by 136/256 patients, with a median of €63 per patient ((IQR) 38;125) per two weeks (€1630 per patient (978;3261 per year). At four years, these costs were present for 120/256 patients, with a median of €50 (38;100) per two weeks (€1304 (978;2609) per year).

Conclusion: Patients with hand OA experience significant impairment in paid and unpaid work participation over the years, which translates into substantial societal costs. Impairment and costs fluctuate on individual level but seem to remain stable over four years on group level.

Table 1. Demographics and hand OA characteristics of patients with at least baseline and four years of follow-up data.

	baseline, all patients (n=256)	baseline, paid work (133/255, 52%)	four years, all patients (n=256)	four years, paid work (104/255, 41%)
Age, years	61.3 (8.0)	60.2 (7.5)	64.6 (8.4)	62.0 (8.1)
Sex, women, *n (%)*	204 (80%)	108 (82%)	204 (80%)	87 (84%)
BMI, kg/m^2	27.3 (4.7)	27.2 (4.7)	27.4 (5.0)	27.1 (4.7)
AUSCAN hand pain (0-20)	9 (4.3)	9.1 (4.6)	9.3 (4.3)	7.9 (4.5)
AUSCAN hand function (0-36)	15.1 (8.4)	14.6 (8.5)	15.2 (8.4)	14.5 (7.7)
HADS anxiety score (range 0-21)^	4 (2;6)	4 (2;6)	4 (2;6)	3 (2;6)
HADS depression score (range 0-21)^	2 (1;5)	2 (1;4)	2 (1;5)	1 (1;4)
Retired, *n (%)*	83 (32%)	-	95 (37%)	-

Numbers represent (SD) mean unless otherwise specified. ^median (interquartile range). Abbreviations: SD = standard deviation, BMI = Body Mass Index, HADS = Hospital Anxiety and Depression Scale, AUSCAN = Australian Canadian Osteoarthritis Hand Index.

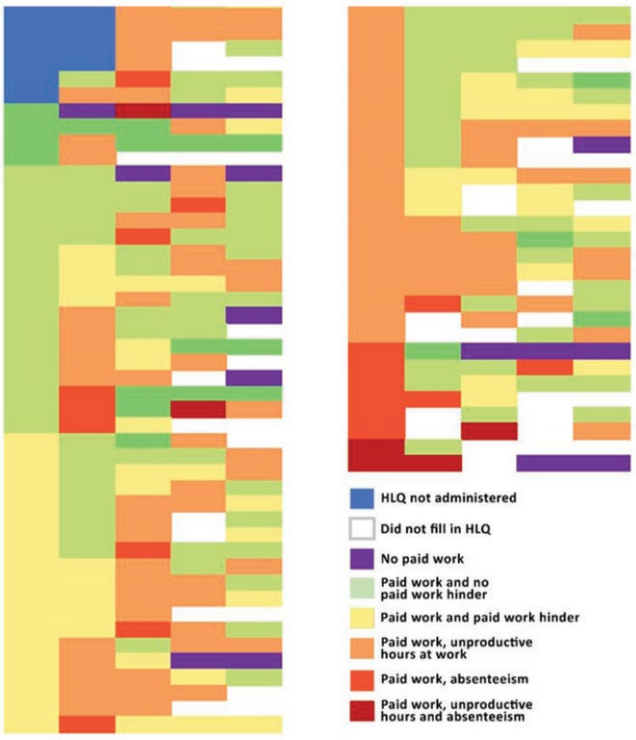


Figure 1. Heatmap of adverse paid work outcomes over time per patient per year, for all 85 patients having data for at least two timepoints and any production loss at any timepoint (baseline, 1, 2, 3 and 4 years of follow-up)

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Sietse Terpstra: None declared, Lotte A. van de Stadt: None declared, Annelies Boonen: None declared, Frits Rosendaal: None declared, Margreet Kloppenburg Grant/research support from: Received funding for the HOSTAS cohort, all paid to the institution.

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POS1369

CHANGES IN PAIN AND REACHING THE PATIENT ACCEPTABLE SYMPTOM STATE IN HAND OSTEOARTHRITIS OVER 4 YEARS

Keywords: Osteoarthritis, Pain

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Background: Hand pain is common in hand osteoarthritis (OA).

Objectives: This study aimed to characterize patients with an increase or decrease in pain, and to investigate which patients are likely to achieve a good clinical outcome after four years.

Methods: Four year data from the ongoing HOSTAS (Hand OSTeoArthritis in Secondary care) cohort were used, consisting of 538 consecutive patients with primary hand OA diagnosed by their rheumatologist. Hand pain was measured with the pain subscale of the Australian/Canadian hand osteoarthritis index (AUSCAN, range 0-20) annually. Demographics, disease characteristics and patient characteristics were collected, as were the Short Form (SF)-36 and Hospital Anxiety and Depression Scale (HADS). Change in pain was categorized as increase, stable or decrease according to the AUSCAN pain minimal clinical important difference (MCID, 1.6) between baseline and year 4. Good clinical outcome was defined as an AUSCAN pain score below the Patient Acceptable Symptom State (PASS) of 8.2 (Bellamy 2015). All patients with measurements at baseline and year 4 (MCID analysis) and at year 4 (PASS analysis) were included. Associations between determinants and change in pain or PASS were investigated using multinomial or binary logistic regression, respectively.

Results: Of 356 patients included in the MCID analysis, 83% were female, mean age was 60.6 years and mean AUSCAN pain score was 9.1. Over 4 years, pain decreased in 137, increased in 106, and 113 remained stable. In the decrease group, mean (SD) change in pain was -4.8 (2.8), in the stable group -0.1 (0.8), and in the increase 3.8 (1.9). Baseline BMI was positively associated with increase in pain. Health-related quality of life (HR-QoL) at baseline was positively associated with decrease in pain. Employment was positively associated with both increase and decrease in pain. HADS scores were negatively associated with decrease in pain (Table 1). Of 361 in the PASS analysis, 155 were below the PASS at baseline, and 177 were below the PASS after 4 years. Patient characteristics and disease characteristics at baseline were not associated with PASS after 4 years. Higher physical HR-QoL and lower pain level at baseline were associated with a higher chance of reaching PASS (data not shown).

Conclusion: Change in pain is associated with BMI, HR-QoL, mental wellbeing and employment status. Good clinical outcome is associated with physical health-related quality of life. These factors can help identify patients likely to achieve good clinical outcome and may aid stratified patient selection for trials.

Table 1. Associations with increase or decrease in pain

	Baseline characteristics	Adjusted Odds ratio (95% confidence interval)	
	N=356	Decrease (n=137)	Increase (n=106)
Patient characteristics			
Female sex; N(%)[1]	296 (83%)	0.80 (0.39-1.63)	1.02 (0.49-2.15)
Age, years; mean(SD)[2]	60.6 (8.2)	0.99 (0.96-1.02)	0.98 (0.94-1.01)
BMI, kg/m2; mean(SD)[3]	26.9 (4.5)	0.99 (0.93-1.05)	1.07 (1.01-1.14)
Currently working; N(%)*	163 (50%)	4.03 (1.94-8.4)	2.58 (1.21-5.47)
HADS	2 (1-5)	0.89	0.92 (0.82-1.03)
Depression (range 0-21); median (IQR)	4 (2-7)	(0.80-0.98) 0.91 (0.82-1.00)	0.92 (0.82-1.03)
Anxiety (range 0-21); median (IQR)			
Patient reported outcome measures			
AUSCAN function (range 0-36); mean(SD)	14.9 (8.4)	0.95 (0.91-1.00)	1.01 (0.95-1.06)
SF-36	51.8 (8.6)	1.06 (1.03-1.10)	1.03 (0.99-1.06)
MCS; mean(SD)	45.7 (7.7)	1.05 (1.01-1.10)	0.99 (0.95-1.04)
PCS; mean(SD)			

associations with changes in AUSCAN pain, defined by MCID, adjusted for baseline AUSCAN pain, age, sex and BMI. N=356. Stable group as index.. [1] Adjusted for baseline pain, age and BMI. [2] Adjusted for baseline pain, sex and BMI. [3] Adjusted for baseline pain, age and sex. *Compared to currently not working, excluding retirees (n=161). BMI = Body mass index. HADS = Hospital Anxiety and Depression scale. AUSCAN = Australian/Canadian osteoarthritis hand index. SF-36 = Short-form 36, with norm based scores with a mean of 50 and SD of 10 using age and sex-specific Dutch population-based norms. MCS = mental component scale. PCS = physical component scale.

REFERENCES: NIL.
Acknowledgements: NIL.
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POS1370 METABOLIC SYNDROME IS ASSOCIATED WITH MORE PAIN IN HAND OSTEOARTHRITIS: RESULTS FROM THE DIGICOD COHORT

Keywords: Comorbidities, Pain, Osteoarthritis

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Background: While association between metabolic syndrome (MetS) (combining central obesity, diabetes, dyslipidemia and/or hypertension) and the risk of osteoarthritis (OA) disease risk remains controversial at the structural level, MetS could be involved in OA-related pain. To analyze such an association, investigating hand OA is more relevant than knee OA to avoid the strong influence of weight on bearing joints.
Objectives: To determine whether the presence of MetS is associated or not with a higher pain level in hand OA.
Methods: This cross-sectional study involved patients included in the hospital-based hand OA DIGICOD cohort, for whom all baseline variables of interest were available (NCT01831570). The characteristics were described and compared according to the presence or absence of MetS (Adult Treatment Panel III criteria). We searched for an association between MetS and several outcomes measuring different aspects of OA-related pain (hand pain intensity using visual analog scale (VAS) on activity, VAS pain at rest, hand pain in various situations using the self-reported Australian Canadian Osteoarthritis Hand Index (AUSCAN) pain subscore, Arthritis Impact Measurement Scale (AIMS2) pain subscore assessing the OA pain nonspecifically related to hands, number of painful hand joints on pressure) using 2 logistic regression models: model 1: adjustment for age, sex, and the radiological Kellgren-Lawrence (KL) total sum score. model 2: model 1 + hospital anxiety and depression (HAD) scale. All pain outcomes were binarized by their median values defining thus high and low pain levels. Results are presented as odds ratios (OR) with 95% confidence intervals (CIs). The reference group was "no MetS" (MetS-).
Results: A total of 359 patients (85% women, 66.3±7.4 years) were analyzed out of 425 included, including 128 (36%) patients with MetS (MetS+). The 2 groups (MetS+ and MetS-) did not differ in their demographic characteristics except for BMI (27.1±4.5 and 24.0±3.8 kg/m^2, p<0.0001), age (67.9±7.1 and 65.5±7.5, p=0.003), KL sum score (48.9±17.7 and 44.5±17.5, p=0.03), and HAD (13.7±6.7 and 12.1±5.7, p=0.02) (Table 1). MetS was associated with a higher VAS pain at activity (median: 44/100) in model 1 (OR=1.63, 95%CI (1.04; 2.56), p=0.03) but this association was attenuated with further adjustment on HAD scale (OR=1.48, 95%CI (0.94; 2.35), p=0.09) (Table 1). MetS was also associated with a higher AUSCAN pain (median: 20/100) in non-adjusted analysis but this did not persist in adjusted model 2. No association was found with VAS pain at rest or the number of painful joints on pressure. MetS was associated with a higher AIMS2 pain subscore (median: 33/100) in both models (OR=1.70, 95%CI (1.06;2.74), p=0.03).

Table 1. Association between metabolic syndrome and pain in hand osteoarthritis according to various measurement tools*

	Unadjusted model	Adjusted for age, sex, KL total sum score	Adjusted for age, sex, KL total sum score and HAD
AUSCAN Pain subscore ≥ 20	1.59 (1.03; 2.46)°	1.51 (0.97; 2.37)	1.40 (0.89; 2.21)
AIMS 2 pain score ≥ 33	1.89 (1.21; 2.95)°	1.90 (1.20; 3.01)°	1.70 (1.06; 2.74)°
VAS at rest ≥ 15	1.39 (0.90; 2.15)	1.39 (0.89; 2.17)	1.30 (0.82; 2.04)
VAS at activity ≥ 44	1.64 (1.06; 2.54)°	1.63 (1.04; 2.56)°	1.48 (0.94; 2.35)
Number of painful joints ≥3	1.38 (0.88; 2.17)	1.38 (0.87; 2.20)	1.32 (0.83; 2.12)

° Statistically significant*Data are OR (95% CI) given for Mets+ versus Mets-.

Conclusion: MetS was associated with more hand pain in hand OA, partly mediated by anxiety-depression. MetS also increased the risk of OA pain nonspecifically related to hands suggesting a higher susceptibility to joint pain in general in patients with MetS.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1371 THE ASSOCIATION BETWEEN X-RAY PROGRESSION AND CLINICAL OUTCOMES IN PATIENTS WITH HAND OSTEOARTHRITIS WITH 5-YEAR FOLLOW-UP

Keywords: Pain, Quality of life, Imaging

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Background: Hand osteoarthritis (HOA) is a heterogeneous disorder with two main subtypes, non-erosive and erosive. The progression of HOA is assessed by various radiographic scoring methods, including the Kallmann scale, and the understanding of the association between radiographic changes and clinical symptoms might help improve the monitoring of disease progression.
Objectives: This study aimed to investigate the association of the Kallman scale with clinical assessment parameters and the erosive subtype in a Czech population of HOA patients over 5 years.
Methods: Consecutive patients with symptomatic HOA fulfilling the American College of Rheumatology (ACR) criteria were included in this study. All patients were evaluated at baseline and follow-up examinations over 2 and 5 years. Clinical examinations were performed by qualified rheumatologists. The number of clinically tender and swollen joints was recorded. Pain, stiffness, and function were assessed by the Australian/Canadian (AUSCAN) hand osteoarthritis index. Hand disability was evaluated based on the Algofunctional index. The visual analogue scale (VAS-pain) and the health assessment questionnaire (HAQ) was used for the assessment of pain and function/disability. Postero-anterior plain radiographs of both hands were examined, and radiographs were scored by two trained readers (rheumatologists) according to the Kallman scale. The inter-rater reliability was computed using weighted Cohen's Kappa for two ratters.
Results: Of 154 patients enrolled in this study, 129 subjects (89.3% females; mean age at baseline = 64.6±8.0 years) met the ACR classification criteria for HOA and were followed up over 5 years at the outpatient department of the Institute of Rheumatology in Prague. Out of these patients, 57 were diagnosed with the non-erosive form (87.7% females; mean age at baseline = 63.8±7.7 years) and 72 with the erosive form (90.3% females; mean age at baseline = 65.7±8.1 years), where erosive HOA was defined by at least one interphalangeal joint with radiographic signs of erosion. Firstly, we analysed each examination separately and found that the Kallman scale was both significantly increased in patients with the erosive subtype (2.95 – 3.12-fold, p<0.001 for all) and associated with age in all examinations (β = 1.27 – 1.57; p<0.001 for all). Next, we used generalized additive modelling (GAM) to analyse data collected over five years and discovered the association of the scale with HOA subtypes and age (p < 0.01 for both). GAM also revealed associations of the Kallman scale with HAQ (edf=2.5, p=0.016) in all patients and patients with non-erosive HOA (edf=1.7, p=0.027). Similarly, the scale was associated with the number of clinically swollen joints in all HOA patients (edf = 1, p = 0.041) and patients with non-erosive HOA (edf=4, p=0.046). Eventually, Algofunctional index (edf=1.9, p=0.02) was associated with the scale only in all patients with HOA. Other parameters (e.g., AUSCANs) were insignificant.
Conclusion: Our 5-year longitudinal study revealed the associations of structural progressions with both subtypes and age at each time point. In contrast, functional impairments were associated with the progression only in non-erosive subset and all HOA patients. Further studies in a larger cohort of patients are needed to validate these data.

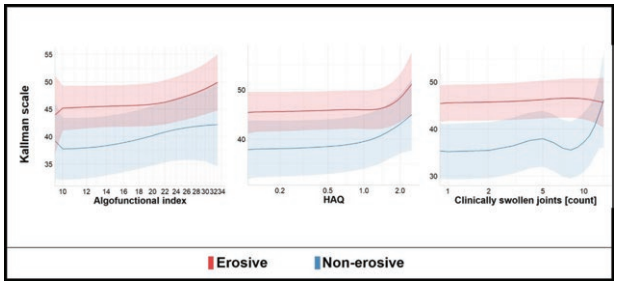


Figure 1. Associations of the Kallman scale with Algofunctional index, HAQ and the number of clinically swollen joints in patients with erosive and non-erosive HOA.

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Disclosure of Interests: None Declared.

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POS1372

INNOVATIVE PAIN MANAGEMENT DEVICE USING MILLIMETRE BAND RADIATION: ELECTRONIC-PAIN KILLER. ASSESSMENT IN PATIENTS WITH PERIPHERAL OSTEOARTHRITIS. MONOCENTRIC, PROSPECTIVE, RANDOMISED IN CROSS-OVER DESIGN AND CONTROLLED TRIAL

Keywords: Randomized control trial, Non-pharmacological interventions, Osteoarthritis

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Background: Osteoarthritis (OA) is one of the most common chronic health conditions. Painful and very disabling, it affects about 500 million people worldwide. For its management, the different guidelines recommend a combination of non-pharmacological and pharmacological treatments [1]. However, 90% of the patients in the stop osteoarthritis I and II survey feel that they are poorly managed in terms of their OA pain and we currently lack effective means to do so [2]. We propose to assess an innovative medical device (MD) for neuromodulation of pain in patients with peripheral OA. This MD is a wristband and consists of a very low-power millimetre wave transmitter. The application of these waves on the wrist, a highly innervated area, has neuromodulatory effects thanks to the synthesis and release of endorphins and the activation of the parasympathetic system.

Objectives: We conducted a clinical trial to evaluate if the regular use of this MD would reduce the pain felt by the patient as well as his consumption of analgesics and if it would improve quality of life (QoL).

Methods: This prospective study was performed between December 2020 and august 2022. Sixty patients with a peripheral OA and a pain score ≥4 on the visual analogic scale (VAS) was included and randomised in one of the two cross-over group. The randomization is stratified on the most painful OA localisation (upper/lower limbs). Patients of group A followed a 3-month period with their conventional treatment (CT) and after they get the device in add on for 3 months. Those of group B started by using for 3 months the MD added on CT and after they took only CT for 3 months. Between the 2 periods, there was a one-month wash-out with only CT. Patients were instructed to perform 1 to 3 sessions/day with the wristband. The duration of each session was 40 minutes. The intern memory of the MD allowed to measure this frequency of use. After 7 days of wristband use, a phone call was performed to ensure that patient had no difficulties with the wristband. A follow-up phone call was also made once a month to remind the patient to use wristband, to report data and to collect potential adverse events. The primary outcome was the difference of pain score between the period with and without the wristband use. The primary endpoint was collected on the VAS every day during the last two weeks of each month of follow-up (i.e. months 1 to 3 and 5 to 7). The other parameters, collected at the inclusion and follow-up visits are specific QoL of OA (WOMAC questionnaire/DREISER index), generic QoL with EuroQuol5D-5L, anxiety-depression questionnaire (HADS), antalgics and cares consumption, the sleep quality on VAS, usability questionnaire (meCUE), patient use of the MD and adverse events. In the aim of a personalized medicine a comparison is made for each patient between the real evolution of their pain score and the decreases in the pain score that they felt having a relevant impact.

Results: All analyses were performed in intention to treat. The mean age of patients was 65.78±7.2 years old. At baseline all parameters were similar between the two groups except the number of male (group A: 5M; group B: 1M) and the body max index (group A: 24.29±4.01 kg/m^2; group B: 27.80±4.7 kg/m^2). The mean pain score at baseline was 6.17±1.43. For this cross-over study, there were no carryover, no sequence, and no period effect. The two groups difference on the pain score was significative ($p<0.05$) with a VAS of 4.57±2.0 in the MD group and 5.32±1.77 in the conventional treatment group. The effect size of the MD, calculated with the Cohen's D formulae, was of 0.42. No serious adverse effect occurs.

Conclusion: We have demonstrated in this world first study the efficacy of this new medical device to reduce peripheral OA pain. Easy to use, discreet and safe, this free drug therapy opens a new field of OA pain treatment.

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POS1373

EROSIVE OR INFLAMMATORY HAND OA (HOA): A MORE SEVERE DISEASE? CROSS-SECTIONAL STUDY OF BASELINE ASSOCIATED RISK FACTORS IN PATIENTS FROM THE DIGICOD COHORT

Keywords: Osteoarthritis, Epidemiology, Descriptive studies

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Background: Erosive HOA (EHOA), defined by an erosive radiographic joint and inflammatory HOA (IHOA) defined by the presence of clinical synovitis are frequent in HOA. The association with specific risk factors and a more severe disease, remains still debated.

Objectives: To identify demographic, disease-related and clinical factors as risk factors for EHOA or IHAO.

Methods: Clinical and radiographic data were extracted from baseline data of the 6-years prospective longitudinal HOA French cohort DIGICOD [1]. Demographic and hand OA clinical and radiological data were compared at baseline between EHOA (≥1 erosive joint in E- or R-phase according to Verbruggen scoring) versus non EHOA, and IHOA (≥ 1 joint with clinical synovitis) vs non IHOA groups. A model of logistic regression analysis was performed for each demographic and clinical HOA-related studied parameter to identify factors associated with EHOA and/or IHOA. Analyses were adjusted for age, sex and body mass index. Results are expressed as Odd Ratios and their 95%Confidence Interval (OR (95%CI)).

Results: 425 patients were analyzed, 195 EHOA (46%), 185 IHOA (43%), with 113 both EHOA and IHOA (27%). The risk of EHOA was reduced by a half in case of current/past professional occupation involving hands (OR 0.6; 95%CI: 0,4; 0.9) and by at least 0.6 (0.3;1.0) if grip strength ≥ 19kg. It was increased by at least 2.0 (1.1; 3.5) if OA duration was ≥6 years, by 2.6 (1.7; 3.9) if aesthetic damage scored ≥40 on a 0-100 mm VAS, by 2.2 (1.4; 3.5) if ≥2 painful joints on pressure, by 2 (1.3; 3,1) if the AUSCAN stiffness subscale scored ≥20 (0-100 VAS), by 2.3 (1,5; 3,5) if the Functional Index for HOA (FIHOA) scored ≥20 (score normalized to 0-100). The risk of IHOA was increased by 2.4 (1.4; 4.0) if OA duration was ≥11 years versus < 6 years, by 1.8 (1.1; 3.0) if pain at rest VAS was ≥40 and by 2.1 (1.4; 3.2) if pain on activity was ≥40, by 2.5 (1.6; 3.8) if aesthetic damage scored ≥40, by 2.5 (1.5; 4.1) if ≥2 painful joints on pressure and by 1.9 (1.2; 2.9) if ≥2 spontaneous painful joints, by 1.9 (1.2; 3.0) if AUSCAN stiffness subscale ≥40, by 1.8 (1.2; 2.7) if the FIHOA was ≥20. Structural damage was higher in both EHOA and IHOA than in those without EHOA and IHOA, respectively: the mean ±standard deviation number of joints at a Kellgren-Lawrence grade ≥2 was 18±5 in erosive vs 13±6 in non-erosive patients and 18±6 vs 13±6 in IHOA vs non IHOA.

Conclusion: There was a high prevalence of EHOA and IHOA in our cohort, partly due to a tertiary-care recruitment. Structural damage was more severe in both phenotypes than in those without erosive or inflammatory signs.

There was an inverse correlation between hand use and EHOA, confirming that EHOA is rather linked to systemic factors. Risk factors for both EHOA and IHOA were a longer disease duration, a higher aesthetic damage (notably in IHOA), number of painful joints on pressure, stiffness, and functional impairment (FIHOA). IHOA was also associated with more pain. Prospective longitudinal studies are needed to confirm these risk factors.

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Disclosure of Interests: None Declared.

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POS1374 RELATIONSHIP BETWEEN POSSIBLE TIBIOFEMORAL OSTEOPHYTE AND CREPITUS AND EFFUSION IN PATIENTS WITH KNEE SYMPTOMS BUT WITHOUT JOINT SPACE NARROWING

Keywords: Pain, Osteoarthritis

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Background: Osteophytes are common structural sign identified to be associated with knee osteoarthritis (OA) and has been included as a criterion for presence and progression of knee OA.

Objectives: Our aim was to investigate the association of possible tibiofemoral osteophyte with knee-joint-related physical examination in symptomatic knees without radiographically detected joint space narrowing.

Methods: We used the Osteoarthritis Initiative (OAI) open access database (http://www.oai.ucs.edu), approved by the local institutional review boards. The OAI comprises data of 4796 men and women aged 45–79 years at baseline. We selected subjects, from the following two sub-cohorts: 1) progression cohort, individuals with symptomatic knee OA (n=1390); 2) incidence cohort, individuals at risk for knee OA (n=3284). Crepitus was examined at baseline by placing the palm of the hand over the patella to detect the presence of a continuous grinding sensation during passive knee flexion-extension movement in the supine position. A positive bulge sign was considered as presence of knee joint effusion. We included subjects with no joint space narrowing but no or doubtful osteophyte in either knee at baseline based on fixed-flexion posteroanterior knee radiographs. We further required subjects to have answered YES to the following question at baseline: "*Do you have knee pain, aching or stiffness for more than half the days of a month during the past 12 months?*" We used unconditional logistic regression to evaluate the association between the presence of knee crepitus and effusion possible tibiofemoral osteophyte. Only one knee per subject was randomly included if both knees were eligible. In the first model the outcome was structural OA development irrespective of knee symptoms at 4 years, and in the second model we required the presence of knee pain, aching or stiffness also at the 4-year follow-up (i.e., the subjects remained symptomatic).

Results: We included 726 subjects with no or little radiographic evidence of OA and a symptomatic knee (60% women, mean [SD] age 58.9 [8.5], BMI 29.6 [4.9]. Our results indicated that presence of crepitus and/or effusion on physical examination were (statistically) significantly associated with possible tibiofemoral osteophyte (**Table 1**).

Conclusion: Presence of both crepitus and effusion at examination in subjects with no or minimal radiographic OA of their symptomatic knee showed moderate association with possible osteophyte in the tibiofemoral joint. An important limitation is that radiographic changes in the patellofemoral joint was not systematically evaluated within the OAI.

Table 1. The association between crepitus and effusion and possible tibiofemoral osteophyte in 726 subjects with a symptomatic knee but without joint space narrowing

	Crude odds ratio (95% CI)	Adjusted* odds ratio (95% CI)
Crepitus	1.6 (1.2 – 2.1)	
Effusion	2.1 (1.5 – 3.2)	

CI: confidence interval. The number of subjects in each model are shown as presence of the sign/total number of subjects included.*Unconditional logistic regression adjusted for age, sex, and body mass index.

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Disclosure of Interests: None Declared.

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POS1375 RELIABILITY AND VALIDITY OF THE LIE-TO-SIT-TO-STAND-TO-WALK TRANSFER TEST IN HIP OSTEOARTHRITIS

Keywords: Safety, Outcome measures, Osteoarthritis

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Background: Falls represent a major health problem for older adults and often lead to disability and mortality. Each year 30% to 50% of community-dwelling older adults report a fall and almost 75% of falls occur in bedrooms or bathrooms, and 41% of all falls occur during transfers [1,2]. Patients with hip osteoarthritis (OA) have many hip and age-related dysfunctions including muscle weakness, sensory loss, gait and balance deficits, which all increase the risk of falls [3]. Task-specificity has been shown to be a critical factor in the effectiveness of fall-reducing interventions [4]. The Lie-to-Sit-to-Stand-to-Walk Transfer Test (LSSWT) was created to measure complicated transfer abilities in older people [5]. However, the LSSWT's reliability and validity are not known in patients with hip OA.

Objectives: The aim of this study was to investigate the reliability, validity, and minimal clinically important difference (MCID) of the LSSWT in patients with hip OA.

Methods: Twenty-seven patients with hip OA were included in this study. Patients performed trials for the LSSWT and the Timed up-and-go (TUG) test. Between the trials, patients rested for an hour to prevent fatigue.

Results: The relative (ICC coefficient) and absolute (SEM and SRD95) reliability of the LSSWT were 0.95, 0.49, and 1,35 respectively. The Pearson correlation coefficient between the LSSWT and the TUG was 0.69.

Conclusion: The analysis showed that the LSSWT has excellent reliability and high validity in hip OA. ($p<0.001$). The low MCID of the LSSWT (1.35) shows its sensitivity and can be used as a responsive outcome measure of interventions and fall risk. the LSSWT also can be valuable in determining independent transferring ability, admissions, or discharges from/to healthcare/residential facilities.

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POS1376 PARACETAMOL PRESCRIPTION PATTERNS IN LOW BACK PAIN AND OSTEOARTHRITIS IN REAL-WORLD GENERAL PRACTICE IN FRANCE

Keywords: Pain, Osteoarthritis, Real-world evidence

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Background: Lower back pain (LBP) and osteoarthritis (OA) are the most frequent musculoskeletal disorders in the general population significantly impacting patients' quality of life. An adequate pain management is key. General practitioners (GPs) are the front-line decision-makers in the French primary care system. In France, paracetamol remains a first-line analgesic in LBP and OA, according to the national guidelines. Few data on the real-world paracetamol prescriptions in LBP and OA are available.
Objectives: This observational retrospective cohort study aimed to identify the paracetamol prescription patterns in LBP- and OA-related pain in real-world GP practice.
Methods: Prescription data from IQVIA's French EMR database with a representative panel of approximately 1,200 GPs. Data collection was systematic, non-interventional, reflecting the daily clinical practice. Patients aged more than 18 years old presenting with LBP- and OA- related pain and receiving a paracetamol prescription during a GP consultation over a 10-month period were included in the analyses.
Results: A total of 18,677 LBP and 8,882 OA patients were included. In more than 90% of these patients, the paracetamol prescriptions were not preceded by any other analgesic for the same diagnosis within the previous month. Paracetamol was mainly prescribed alone (57% LBP, 78% OA). The most frequent associations were NSAIDs and grade II analgesics. Treatment discontinuation at Month 1 was the most frequent event (67% LBP and 52% OA). In case of treatment restart, paracetamol was prescribed again in 57% LBP and 81% OA patients. At Month 3, 78% LBP and 71% OA patients discontinued treatment.
Conclusion: Paracetamol remains a pivotal analgesic and is prescribed first line in the majority of the patients in both indications. Paracetamol is the treatment of the given painful episode, with more than a half of patients discontinuing treatment at Month 1.
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POS1377 HAND OSTEOARTHRITIS: CORRELATION BETWEEN HAND ULTRASOUND AND CONVENTIONAL RADIOGRAPHY

Keywords: Osteoarthritis, Diagnostic tests, Ultrasound

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Background: Hand osteoarthritis (OA) is among the most prevalent OA phenotypes. The simultaneous involvement of multiple hand joints makes hand OA a heterogeneous disorder that is complex to study [1]. It is widely accepted that radiography is the gold standard for the diagnosis of hand OA [2].
Objectives: We aimed to investigate the correlation between ultrasound (US) and X-ray findings in hand OA.
Methods: We conducted a cross-sectional study, including patients with hand OA, fulfilling American College of Rheumatology criteria. All patients underwent a physical examination followed by an US exam. US was performed in all metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints, and features were quantitatively scored (0/1). Recent (less than six months old) posterior-anterior view X-rays of the hands were analyzed. Pearson correlation coefficient was calculated.
Results: We examined 280 joints in a total of 10 patients with hand OA (9 women and one man). The mean age was 66±11 years [46–78]. The mean duration of hand OA symptoms was 4±3 years. The mean tender and swollen joints were 1.5 [0-5] and 0.1 [0-1], respectively. X-rays showed joint space narrowing and osteophytes in all patients. Sclerosis was found in 2,4 [0-8] joints. A significant correlation was found between the number of osteophytes in both US and X-rays ($p<0.001$). Joint space narrowing was correlated to calcifications ($p=0.003$) and enthesophytes ($p=0.039$). X-rays subchondral cysts correlated with osteophytes ($p=0.015$) and calcifications ($p=0.04$) in US. No significant association was noted between sclerosis and US findings.
Conclusion: Despite the small study population, our results showed a significant match between US and X-ray in hand OA. This finding is likely to have practical implications for facilitating the diagnosis and the monitoring of hand OA.
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POS1378 PERCEIVED BENEFITS AND BARRIERS TOWARDS EXERCISE AMONG PATIENTS WITH KNEE OSTEOARTHRITIS

Keywords: Mental health, Osteoarthritis, Rehabilitation

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Background: Physical activity (PA) is highly recommended in patient with osteoarthritis. Despite the major benefits of PA and exercise, patients with knee osteoarthritis report low level of PA and engage more in sedentary behavior (SB). Understanding the perception of these patients towards exercise is essential to help find better interventions.
Objectives: The Aim of this study is to assess the perception of benefits and barriers towards exercise among patients with knee osteoarthritis and analyze the associated factors.
Methods: This is a cross-sectional study that was conducted from April to September 2022. Patients with knee osteoarthritis were included then classified on the basis of the Kellgren and Lawrence radiograph scale. Socio-demographic and clinical characteristics were collected. Level of PA was assessed using (IPAQ-SF). Perceived benefits and barriers towards exercise was assessed using Perceived benefits and barriers to exercise scale (PBBS). Participants were also assessed for anxiety and depression (GAD-7) and (PHQ-9) scales respectively.
Results: A Total of 178 patients were enrolled in the study, with a mean (±SD) age of 58.48 ± 9.9 years, 88.2% of them were females, and 69.1% had comorbidities. Mean (±SD) VAS pain score upon walking was 4.78 ± 2.21. According to the Kellgren and Lawrence classification, 64.4% of the patients had OA grade 2 and 25.6% had grade 3. Mean of Lequesne scale was 9.8 ± 3.8. The mean of PBBS benefits scale was 94.35 ± 20.25. The Mean of PBBS barriers scale was 27.01 ± 8.23. Top three ranked perceived benefits to exercise were (Mean ± SD): «Exercise improve my mental health» 3.53± 0.62, «My disposition is improved with exercise » 3.48 ±0.63 and «Exercise decreases feelings of stress and tension for me » 3.43± 0.65. Top three ranked perceived barriers to exercise were

(Mean ± SD): «Exercise tires me» 2.42± 1.18, «I'm fatigued by exercise » 2.32 ± 1.17 and «Exercise is hard work for me» 2.27± 1.17.

Table 1: ***uni and multivariate analysis of associated factors with PBBS benefits/barriers scale.***

	Perceived benefits of exercise (PBBS)		Perceived barriers of exercise (PBBS)	
	Univariate analysis OR (IC=95%) P value	Multivariate analysis OR (IC=95%) P value	Univariate analysis	Multivariate analysis
habitat	-16.184 [-26.730, -5.639] p=0.003	-19.535 [-29.408, -9.663] p=0.000	1.298 [-3.096, 5.692] p=0.561	*
Socioeconomic status	2.397 [0.033, 4.762] p=0.047	1.891 [-0.347, 4.128] p=0.097	1.363 [0.412, 2.314] p=0.005	1.490[0.495,2.394] p=0.003
VAS Pain	-1.215 [-2.564, 0.134] p=0.07	*	0.412 [-0.138, 0.962] p=0.141	*
Lequesne scale	-0.317 [-1.303, 0.669] p=0.526	*	0.306 [-0.089, 0.702] p=0.128	*
SB: IPAQ-SF.	-0.041 [-0.069, -0.014] p=0.003	-0.035 [-0.061, -0.009] p=0.009	0.007 [-0.005, 0.018] p=0.264	*
PHQ-9:	-4.998 [-7.784, -2.211] p=0.001	-0.839 [-1.376, -0.302] p=0.002	0.967[0.366,1.665] p=0.002	0.979[0.212,1.508] p=0.015

Conclusion: In Our study, the most highly ranked perceived barriers to exercise reported were items related to physical exertion. Some studies have found similar findings in patients with multiple sclerosis (1) and HIV female patients [2]. Pain and handicap related to knee osteoarthritis were not associated with the perception of barriers to PA. The most highly rated perceived benefits to exercise were those related to improvements in mental health. Regular PA have shown to improve mood and fight depression, in addition depression often alter the perception of benefits and barriers to exercise as shown in our study. Screening and treating Depressive disorders is essential to help patient break the cycle.

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POS1379

A NOVEL MEASURE OF END-STAGE KNEE OSTEOARTHRITIS REDUCES THE DURATION AND SAMPLE SIZE REQUIRED FOR OBSERVATIONAL STUDIES AND TRIALS

Keywords: Outcome measures, Osteoarthritis, Clinical trials

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Background: Total knee replacement (TKR) has been used as an outcome measure in research into the causes and possible treatments for knee osteoarthritis (KOA). However, because KOA progresses slowly, and because TKR has a low incidence, research using TKR as an outcome measure necessitates long duration and/or large sample sizes. Moreover, TKR is influenced by multiple factors (such as education and income) besides the progression of KOA.

Objectives: We defined a novel outcome measure that signifies end-stage KOA (esKOA); and determined whether esKOA was sensitive enough to detect the effect of an exposure that is known to have a modest effect on reducing TKR, namely weight loss.

Methods: A knee was considered to have esKOA if any of the following two conditions were met: 1) moderate, intense, or severe KOA symptoms (i.e., the sum of the pain and disability scores on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) ≥ 12) and severe radiographic knee osteoarthritis (RKOA), defined as a Kellgren and Lawrence Grade (KLG) of 4); or 2) intense or severe KOA symptoms (i.e., the sum of the pain and disability scores on the WOMAC ≥ 23) and frequent knee pain (i.e., knee pain on most days of one or more months in the past 12 months) and mild or moderate RKOA (KLG = 2 or 3). We used data from two prospective cohort studies: the Osteoarthritis Initiative (OAI) and the Multicenter Osteoarthritis Study (MOST). We analyzed the data in two ways: as an observational study; and as an emulated trial. In the emulated trial, participants who lost ≥ 5% of their weight between baseline and 1 - 1.25 years (weight loss group) were matched with participants who gained ≥ 5% of their weight in that same period (weight gain group), using 1:1 nearest-neighbour matching on propensity scores. In both analyses, we used a multilevel mixed-effects generalized linear model. In the observational study, we investigated the association of weight loss between baseline and the following time points with esKOA and TKR at these time points: 1 - 1.25 years; 2 - 2.5 years; and 4 - 5 years. In the emulated trial, we compared the odds of incidence of esKOA and TKR between the weight loss and weight gain group at the following time points: 2 - 2.5 years; and 4 - 5 years.

Results: The observational study included 7107 participants (58.4% female, mean ± SD age and BMI 61.4 ± 8.8 years and 29.2 ± 5.1 kg/m^2 at baseline, and an incidence of esKOA of 2.9, 6.8, and 10.4% at 1 - 1.25 years, 2 - 2.5 years, and 4 - 5 years, respectively, and a corresponding incidence of TKR of 0.1, 0.5, and 1.6%. While weight loss was associated with a reduced adjusted odds ratio (aOR) for both esKOA and TKR at 4 - 5 years (for 5% weight loss: 0.85 [95% CI 0.79 - 0.92] for esKOA and 0.79 [0.67 - 0.93] for TKR), weight loss was only associated with a reduced aOR for esKOA - and not TKR - at the earlier time point of 2 - 2.5 years (for 5% weight loss: 0.80 [0.72 - 0.90] for esKOA and 1.05 [0.76 - 1.45] for TKR). At 1 - 1.25 years, there was no association between weight loss and esKOA or TKR. The sample size required to detect a 50% reduction in the odds of esKOA was 6% to 13% of the sample size required for that of TKR (236 versus 3990 at 2 - 2.5 years; 162 versus 1286 at 4 - 5 years). In the emulated trial, compared to the weight gain group (367 participants), the weight loss group (also 367 participants) had significantly lower odds of esKOA but not TKR at 4 - 5 years (0.43 [0.22 - 0.84] for esKOA and 0.39 [0.06 - 2.67] for TKR). There was no difference between groups in the odds of esKOA or TKR at the earlier time point of 2 - 2.5 years in the emulated trial.

Conclusion: Given that our novel measure of esKOA could detect an association with weight loss at a time point 1.5 - 3 years earlier than TKR in an observational study, and in a sample size that was too small to detect an association with TKR at 4 - 5 years in an emulated trial, esKOA is recommended as an outcome measure for observational studies and trials investigating causes and possible treatments for KOA. Our powerful novel measure of esKOA enables shorter and smaller – hence cheaper – studies, which can boost the research on effective treatment for KOA.

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POS1380

PLACE NOT RACE: COMMUNITY-LEVEL SOCIAL DETERMINANTS OF HEALTH MAY BE MORE IMPORTANT THAN PATIENT RACE IN TOTAL HIP ARTHROPLASTY OUTCOMES

Keywords: Osteoarthritis, Registries

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Background: With total hip arthroplasty (THA) utilization rising rapidly, [1] it is important to understand social determinants of health (SDOH) that contribute to disparities in THA outcomes.

Objectives: We sought to explore the relationship of multiple community-level SDOH with 90-day readmission, 90-day mortality, 1-year revision post-THA, and length of stay (LOS) using prediction modelling.

Methods: Our retrospective study using the Pennsylvania Health Care Cost Containment Council Database included 105,336 patients undergoing THA 2012-2018. Community-level variables include walkability index; median household income; and percent unpaid family workers, without health insurance and not in the labor force, above high school, above college, foreign-born, speaking languages other than English, with computer access, and with internet access. They were extracted from US census via geocoding. We trained explainable boosting machine using Generalized additive models to predict readmission, mortality, LOS, and revision. Resulting mean absolute scores (MAS) were aggregated to measure collective importance of the above "community-factors."

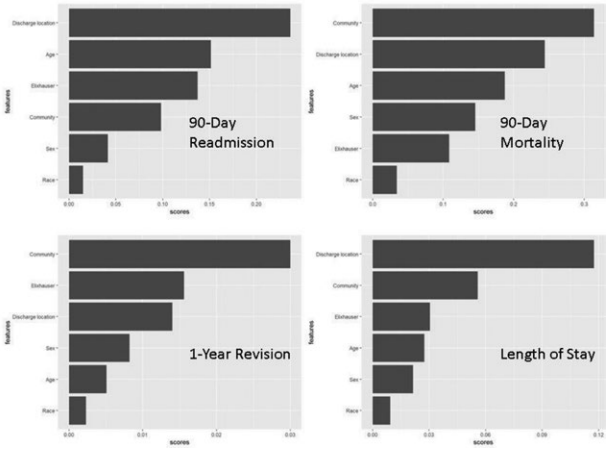
Results: Predictive performance was best for mortality (AUROC=0.76); it was moderate for readmission (AUROC=0.66), revision (AUROC=0.58), and LOS (RMSE=0.41, R^2=0.2). Community factors relatively contributed more to adverse outcomes than race in all models. The top 3 predictors of readmission were discharge location, age, and comorbidities (MAS =0.24, 0.15, 0.13, respectively). The top 3 predictors of mortality were community factors, discharge location, and age (MAS=0.31, 0.24, 0.19, respectively). The top 3 predictors of revision were community factors, discharge location, and comorbidities (MAS=0.03, 0.01, 0.005, respectively). Lastly, the top 3 predictors for LOS were discharge location, community factors, and comorbidities.

Conclusion: In all THA outcome models, aggregated community factors were more important than individual race in predicting 90-day readmission, 90-day mortality, 1-year revision, and length of stay.

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Figure 1. Variable importance scores predicting total hip arthroplasty outcomes



"Community" is the aggregate importance score for % householder living alone, % foreign born, % speaking language other than English, % with computer access, % with internet access, national walkability index, % not in labor force without insurance, % above high school, % above college, % with unpaid family workers, and median household income, extracted from American Community Survey or calculated by the National Walkability Index software from patient zip code.

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Table 1. Patient-level characteristics by outcome

	Outcome								
	90-day readmission			90-day mortality			Revision		
	No	Yes	p	No	Yes	p	No	Yes	p
	N = 96914	N = 8422		N = 105027	N=309		N = 103719	N = 1617	
Age	65.0 [58.0; 73.0]	69.0 [60.0; 77.0]	****	65.0 [58.0; 73.0]	77.0 [67.0; 84.0]	****	65.0 [58.0; 73.0]	65.0 [58.0;74.0]	NS
Sex			**			*			***
Female	52330 (54.0%)	4647 (55.2%)		56826 (54.1%)	151 (48.9%)		56046 (54.0%)	931 (57.6%)	
Male	44584 (46.0%)	3775 (44.8%)		48201 (45.9%)	158 (51.1%)		47673 (46.0%)	686 (42.4%)	
Race			****			NS			NS
Black	6262 (6.47%)	692 (8.22%)		6936 (6.60%)	18 (5.83%)		6835 (6.59%)	119 (7.36%)	
Other	2956 (3.05%)	186 (2.21%)		3135 (2.98%)	7 (2.27%)		3108 (3.00%)	34 (2.10%)	
White	87619 (90.5%)	7539 (89.5%)		94874 (90.4%)	284 (91.9%)		93695 (90.4%)	1463 (90.5%)	
Missing	77	5		82	0		81	1	
Length of stay	2.00 [1.00; 3.00]	3.00 [2.00; 3.00]	****	2.00 [1.00; 3.00]	3.00 [2.00; 4.00]	****	2.00 [1.00;3.00]	2.00 [2.00;3.00]	****
Elixhauser comorbidity index			****			****			****
>5	4797 (4.95%)	1078 (12.8%)		5792 (5.51%)	83 (26.9%)		5751 (5.54%)	124 (7.67%)	
0	16952 (17.5%)	714 (8.48%)		17647 (16.8%)	19 (6.15%)		17488 (16.9%)	178 (11.0%)	
1-4	75165 (77.6%)	6630 (78.7%)		81588 (77.7%)	207 (67.0%)		80480 (77.6%)	1315 (81.3%)	

Categorical variables N(%), continuous variables median[IQR].**** p < 0.001; *** p < 0.01; ** p < 0.05; * p < 0.1; NS = nonsignificant

Clinical cases

POS1381 TRANSIENT PERIVASCULAR INFLAMMATION OF THE CAROTID ARTERY (TIPIC) SYNDROME: A RARE CAUSE OF CAROTIDYNIE

Keywords: Vasculitis, Ultrasound, Rare/orphan diseases

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Background: Carotidynie defines localised, unilateral neck pain in the region of the carotid bifurcation and is a relatively frequent event with a myriad of causes. Differential diagnosis include mainly arterial dissection, large vessel vasculitis or local inflammation or surrounding structures (e.g. lymphadenitis). We herein describe a patient with carotidynie caused by a TIPIC syndrome under follow up by ultrasound imaging.
Methods: The logiq S8 from GE2 with 2 different linear probes was used.
GE L8-18i-D Hockey Stick probe. ML 6-15-D Matrix probe.
Case presentation: A 36 year old male patient was referred to our rheumatological outpatient department because of localized pain in the left lateral part of the neck, which persisted over two days. Swallowing of fluids or solid food was painful, but unimpaired. The patient mentioned no recent trauma, but he reported symptoms of an upper respiratory tract infection, without fever, two weeks before. Clinical investigation showed no signs of local swelling or palpable lymph nodes. ENT consultation ruled out inflammatory processes causing the symptoms including tonsillitis, pharyngitis or laryngitis. Analgesic treatment with tramadol was not effective. Laboratory investigations revealed slightly increased CRP and Erythrocyte Sedimentation Rate (ESR) values. ANA and subsets, as well as ANCA were negative. An ultrasound of the region showed a localized swelling of the media and adventitia of the left common carotid artery, involving half of the circumference over a length of 4 mm. Multiple lymph nodes with signs of inflammation were present on both sides of the vessel. No dissection or stenosis was detectable. Due to a typical clinical presentation and ultrasound appearance without carotid stenosis, typical lokalisation at the distal part of the carotid communis artery the diagnosis of carotidynie or TIPIC was made. Treatment with nonsteroidal antirheumatic drugs was initiated without any effect. Therefore, we initiated a treatment with steroids (0,3mg/kg body weight). 3 days after the beginning of the therapy the before unbearable pain nearly resolved. A MRI angiography of the vessel performed 5 days after the inition of the steroid treatment showed an eccentric wall thickening with diameter of 5 mm near the bifurcation of the common carotid artery, with a slightly increased enhancement of the carotid wall, but no further inflammatory structures. Awareness of this syndrome and its excellent visualization for diagnosis, exclusion of other pathologies and follow up by high resolution ultrasound could be useful to reassure patients about the benign nature of this syndrome and help the clinician to avoid more invasive imaging modalities.
Conclusion: The disease is first reported by Fay in 1927. Despite only a few case reports are available in the last 20 years and mostly one case only is reported. Usually an inflammatory process is suspected. Although a rare event sonography is capable to diagnose such vessel abnormality with high precision. Treatment with NSAIDs and, if not sufficient, eventually steroids are required.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4353

POS1382 DON'T TURN A BLIND EYE - ANTERIOR CIRCULATION STROKE IN GIANT CELL ARTERITIS

Keywords: Remission, bDMARD, Vasculitis

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Background: Giant cell arteritis (GCA) is a form of systemic vasculitis involving large and medium sized vessels. It is more common in women and affects adults greater than 50 years old. Typical presentations include insidious onset of headache, scalp tenderness, jaw claudication, visual changes, and constitutional symptoms. Stroke is an uncommon complication of GCA with an incidence rate of 3% - 7% and usually occurs between the onset of arteritis symptoms and one month after initiating steroid therapy. GCA related strokes usually involve the vertebrobasilar artery and less commonly the carotid artery.
Objectives: To discuss a patient with GCA progression to strokes despite steroid therapy.
Methods: A 77 year old female with a history of hypertension, diabetes, uterine and breast cancer in remission presented to the hospital with right eye vision loss. She reported two weeks of blurry vision in her right eye, bilateral temporal headache, jaw claudication, weight loss, and loss of appetite. She denied prior similar episodes. Exam revealed scalp and right temporal artery tenderness, right eye vision loss. She had equal radial and brachial pulses, and 5/5 strength in bilateral upper and lower extremities. Labs showed sedimentation rate >120 (ESR 0-38mm/hr) and C-reactive protein 62 (CRP 0-5 mg/L). Patient was started on intravenous (IV) methylprednisolone 1g daily for presumed GCA, then tapered and discharged on oral methylprednisolone 48mg (1mg/kg) daily. Temporal artery biopsy confirmed GCA showing patchy moderate chronic inflammation in the intima and media with small lymphocytes, macrophages, and rare giant cells. On follow up, she continued to have right eye vision loss but improvement of other GCA symptoms. Within one month of her initial presentation, she returns to the hospital for left sided weakness, facial droop, and dysarthria.
Results: She endorsed compliance with methylprednisolone, aspirin, and atorvastatin. Computerized tomography angiography (CTA) showed interval worsening of the severe stenosis of the clinoid segment of the right internal carotid artery (ICA) now with near occlusion. Labs with ESR 33, CRP <0.2. Exam with 4/5 strength in the left upper extremity (LUE) and left lower extremity (LLE). On hospital day 3, she had fluctuating weakness in the LUE and methylprednisolone was increased to 1g daily. Repeat CTA with stable severe focal stenosis of the right clinoid ICA. Cerebral angiogram showed multiple vessels in the anterior and posterior circulation with evidence of irregularity in the lumen suggestive of diffuse vasculitis but no evidence of atherosclerosis in the right ICA. On hospital day 6, weakness worsened in the proximal and distal LUE to 1/5 strength and LLE to 3/5 strength. Given concern for GCA progression she was started on IV tocilizumab 6mg/kg and had emergent angiography with right ICA angioplasty. Patient completed 5 days of IV methylprednisolone 1g and was tapered and discharged on methylprednisolone 48mg daily and tocilizumab 162mg subcutaneous weekly. On follow up she continues to improve; exam without facial droop, 5/5 upper extremity strength, and 3/5 lower extremity strength.
Conclusion: This highlights a rare case of GCA related stroke within the ICA territory despite being on high dose steroids. There was a diagnostic dilemma and the initial suspicion for GCA related stroke was low because the patient had been on high dose steroids for 3 weeks with normal inflammatory markers, but cerebral angiography confirmed the evidence of vasculitis. Progression of symptoms despite high dose steroids called for aggressive therapy with angioplasty until therapeutic effect of tocilizumab was achieved. Patient's response to therapy suggests that tocilizumab is effective for GCA related stroke.
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Disclosure of Interests: None Declared.
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POS1383 ANTI-TIF-1-Y DERMATOMYOSITIS IN OVERLAP WITH GREAT VESSEL VASCULITIS: A CASE REPORT

Keywords: Vasculitis, Myositis

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Background: Dermatomyositis (DM) are systemic autoimmune diseases that are part of Idiopathic inflammatory myopathies. The peak incidence is at the age of 50–60 years. The DM-related autoantibodies Anti-TIF-1γ are found in DM associated with aggressive skin lesions. However, in adults above the age of 40, anti-TIF-1γ antibodies are strongly associated with malignancy [1].
Objectives: The aim of the work is to illustrate a difficult management of anti-TIF1-y dermatomyositis in overlap with great vessel vasculitis.
Methods: In January 2022 a 79-year-old woman suffering only from arterial hypertension was beginning to develop heliotropic and occipital rash, initially interpreted as an allergic reaction to an antihypertensive drug and treated with antihistamines without clinical benefit. Over the following weeks rhinolalia, mixed dysphagia, and Gottron's papules developed simultaneously. She performed a laryngoscopy excluding a deficit of the vocal cords. In the suspicion of esophageal diverticulosis performed X-ray with gastrografin, showing no alterations of the esophageal tract. The picture was related to a major depressive episode and antidepressant therapy was initiated. In May 2022 worsening of muscle symptoms led the patient to go to the hospital again, with subsequent transfer to our rheumatological department. She was cachectic, dysphagic, with hypostenia (MMT8 35/80) and skin rash typical for DM. Therefore, some investigations were ordered, showing:

- High titer positivity for anti-TIF1y, PL-12, SSA-Ro52
- Significant retention in the oro-pharyngeal region at swallowing study

- Edema of the pelvic girdle muscles, compatible with a picture of myositis in the phase of activity on magnetic resonance
- Increase CPK and inflammation indices in blood chemistry tests

Hence, a diagnosis of DM was performed. Because the recent onset of the disease, and for the association described in the literature between Anti-TIF1y and neoplastic disease, further investigations were required to exclude the paraneoplastic nature of the clinical picture. While waiting to conclude the investigations, therapy with intravenous pulse of glucocorticoids has been started (1.5mg/kg) with progressive decalage. Despite a predominantly cutaneous improvement, the symptoms progressively worsened by reducing the steroid below the threshold dose of 1mg/kg, with the appearance of a new cutaneous flare. During hospitalization, the patient showed a gradual increase in inflammation indices, associated with pancytopenia. After excluding an underlying hematological cause, FDG-PET was performed. It showed uptake of the drug in the ascending and arch of the thoracic aorta, and both subclavian arteries. In order to exclude infectious causes of aortitis, in-depth examinations were performed, with negative results (HIV, syphilis).

Results: The finding of vascular uptake despite therapy with intravenous pulse of glucocorticoids, the absence of infections and the clinical symptoms led us to diagnose dermatomyositis overlapping with vasculitis of the great vessels.

Conclusion: Our case represents the first description of overlap between these two diseases within 5 months of clinical onset. Therefore, we decided to initiate therapy with intravenous pulse of glucocorticoids (2mg/kg) with progressive tapering, associating it with IntraVenous ImmunoGlobulin (IVIG) and periodic intravenous immunosuppressive therapy with Cyclophosphamide (CFX), since the efficacy of these drugs was demonstrated both on systemic vasculitis and on DM. After the first days of combination therapy, the patient showed marked improvement in the muscles and skin, regaining the ability to eat and being able to resume daily activities (MMT8 70/80).

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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HPR Professional education, training and competencies

POS1384-HPR THE FUTURE OF PATIENT EDUCATION: DESIGN FOR A WEB PLATFORM FOR EDUCATION IN RHEUMATOID ARTHRITIS

Keywords: Education, Patient information and education, Patient reported outcomes

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Background: In 2018, a multi-component educational program called UniversitAR was launched. This program was aimed at patients diagnosed with Rheumatoid Arthritis. In the process of training the patients, topics such as clinimetry, comprehensive treatment of the disease, healthy lifestyles, and the enhancement of personal and interaction skills were included. After 3 years of implementation of this program, the certification of 91 expert patients in rheumatoid arthritis was achieved. However, there is a major challenge for health education to have a greater reach for the entire population.

Objectives: The objective of this study is to design a digital education platform, with reach for patients in any country in Latin America and the Caribbean and with a thematic content that is effective for the care of their disease and the improvement of their quality of life.

Methods: A review and digital adaptation of the 3 educational levels of UniversitAR was made. It was considered feasible to maintain the 3 levels of education to respect the criteria of social inclusion, which is a fundamental principle of the multicomponent educational program (Level 1: Basic Knowledge of the Disease Program, Level 2: Patient Empowerment Program for Effective Self-Management of the Disease and Level 3: Expert Patient Program). Contents were updated, the total training time was reduced and evaluation and measurement criteria were added for each educational level. A total of 104 educational sessions were reviewed, as well as the measurements included in the training process in aspects such as: the level of disease activity, autonomy and independence, quality of life and satisfaction with the educational program.

Results: The multicomponent educational program was reconstructed, reducing the educational program from 104 to 84 educational sessions and minimizing the academic intervention times in each session. The total estimated training time for the patient went from 22 months to be carried out in a period between 8 months and 1 year, considering that it will be the patient who will decide the number of sessions they want to see per day. In December 2022, an event for patients with Rheumatoid Arthritis was held and a demo of the platform was presented. The official launch of this digital educational program will be in the third quarter of 2023 and the training of 600 patients is expected this year.



Figure 1. Description of the multi-component educational program web platform

Conclusion: The creation of alternatives that facilitate the education of patients, such as digital platforms, are very important strategies that allow reaching the population, since this breaks down access barriers such as: the geographical location of the patient with respect to their place of training, mobility limitations and out-of-pocket expenses incurred to attend your training sessions.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Gabriel-Santiago Rodríguez-Vargas: None declared, Fernando Rodriguez: None declared, NORALMA PINTO-FLOREZ: None declared, Liliana Realpe: None declared, Adriana Rojas-Villarraga: None declared, Pedro Santos-Moreno Speakers bureau: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi, Grant/research support from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi.

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POS1385-HPR ARTIFICIAL INTELLIGENCE APPROACHES FOR RHEUMATOLOGY PRACTICE: RESULTS FROM AN INTERNATIONAL E-SURVEY OF THE DIGITAL RHEUMATOLOGY NETWORK

Keywords: Artificial intelligence

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Background: Artificial Intelligence (AI) is emerging as a promising tool to improve clinical decision-making and enhancing patient care. In rheumatology, AI may enable precision medicine, allowing patient profiling, prediction and treatment personalization [1]. Healthcare professionals' (HPs') perceptions regarding implementation of AI in rheumatology have been not investigated sufficiently so far.

Objectives: This international e-survey aimed to evaluate healthcare professionals' attitudes towards AI's potential benefits in managing patients with rheumatic diseases.

Methods: An online self-reported questionnaire (August 2022-December 2022) promoted using social media platforms was used to capture data on the knowledge of state-of-the-art AI methods. We evaluated attitudes, perceptions and expectations related to AI-powered clinical prediction modelling, computer vision and natural language processing (NLP) on e-health records (EHR). Univariate logistic regression was used to explore associations between demographic

characteristcs of participants and their trust in machine learning and AI (Figure 1, panel A, expressed as a boolean.variable).

Results: Fifty-nine HPs (male n.36/58 respondents, 37.93%, 1 skipped) of mean age (±SD) 37.55 ± 10.12 years at a mean of 12.33 ± 10.54 years since graduation were considered for the analysis. Fifty-two out of 59 were specialists (88.14%), the largest part working in University Hospitals (45/58, 77.59%, 1 skipped). Thirty-seven out of 59 (62.71%) declared an open attitude in adopting machine learning tools for clinical prediction modelling for rheumatoid arthritis patients (Figure 1, Panel B). More than half of the respondents were interested in a prediction horizon of ≥1 year (33/59, 55.93%, Figure 1 Panel C). The vast majority (51/59, 86.44%) liked having an AI-powered clinical prediction embedded in EHRs, preferring disease activity scores as the target outcome (54/59, 91.53%). Consistently, most of the participants considered that clustering algorithms assigning patients to phenotypes have room in clinical practice, (45/59, 76.27%) especially in treatments selection (46/58, 79.31%, 1 skipped) and early arthritis management (37/59, 63.79%). Computer vision algorithms were considered of particular interest for the detection of erosions (39/59, 66.1%). Most of the participants agreed that machine learning could be beneficial to extract information from EHR (52/58, 89.66%). In particular, NLP was seen as a tool for capturing longitudinal changes among critical patient outcomes (36/54, 66.67%, 4 skipped) and for Reducing diagnostic delay by promptly identifying symptoms in primary care EHRs 36/58, 62.07%, 1 skipped). In general about an half of respondents (33/58, 56.90%), considered machine learning-based prediction as more powerful than conventional statistics in terms of clinical predictive modelling, especially for the potential of providing more sensitive analysis and identify smaller contributing variables (39/57, 68.42%). Neither age, gender, and time from degree were associated with trust in machine learning.

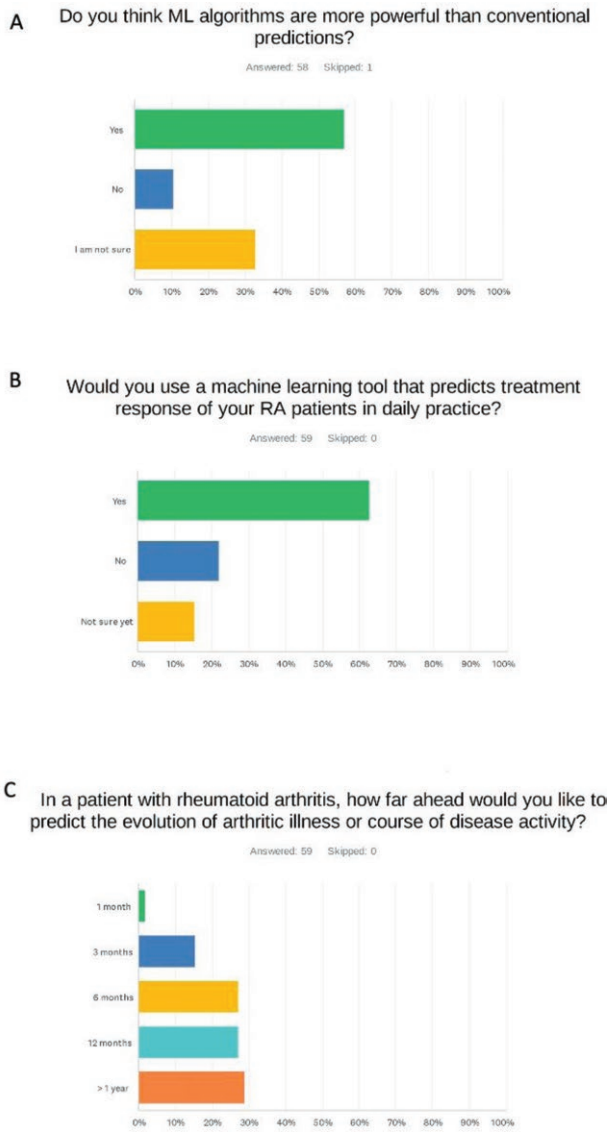


Figure 1. Participants answers to relevant questions.

Conclusion: The participants of this international survey showed an open and optimistic attitude regarding AI implementation in clinical rheumatology. Expectations were mainly centered on improving patient management by allowing for accurate mid-to-long term prognosis.

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Disclosure of Interests: None Declared.

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HPR Interdisciplinary research

POS1386-HPR

EFFECTIVENESS OF SUBCUTANEOUS METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ITS PERSISTENCE IN THE LONG TERM

Keywords: Rheumatoid arthritis, Disease-modifying drugs (DMARDs)

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Background: Methotrexate (MTX) has been established as the headstone of treatment for rheumatoid arthritis (RA). However, many patients treated with oral MTX experience adverse events. For this reason, new forms have been developed, such as the subcutaneous presentation in a prefilled syringe, which improve tolerance, adherence and response to treatment.

Objectives: The aim of this study is to describe the effectiveness of treatment with subcutaneous MTX (SC MTX) in a prefilled syringe in a reference center for the management of patients with RA and the persistence of treatment during 5 years of follow-up.

Methods: Retrospective observational cohort study (1-Jan-2018 and 31-Dec-2022) in patients with RA, with more than one year of treatment with MTX SC; Patients <12 months with MTX SC and those who had concomitant biological therapies were excluded. Response to treatment was analyzed by DAS28.

Results: 1062 patients treated with MTX SC were analyzed. At the time of analysis, 877 patients persisted in treatment and 185 abandoned due to adverse events (17.4%). 190 received it as monotherapy, 285 in combination with other conventional DMARDs, 184 with a corticosteroid, and 218 with cDMARDs and a corticosteroid. 368 (42%) started therapy due to intolerance to the oral formulation, 20 (2.3%) received the 7.5 mg dose, 114 (13%) 10 mg and 234 (26.7%) 15 mg, while 509 patients (58%) did so to optimize the dose, 259 (29.5%) with 20mg and 250 (28.5%) with 25mg. At one year of follow-up, there was an increase in the number of patients who achieved low disease activity [573 (65.3%) remission and 139 (15.85%) low activity] and there was a decrease in patients with moderate activity and high (Figure 1). Of the 877 patients, 27.6% have remained in treatment between 12 and 24 months, 18.8% between 25 and 36, 19% between 37 and 48, and 34.5% for more than 48 months. Over the 5 years, a gradual increase in the percentage of patients achieving low disease activity is observed (Figure 2).

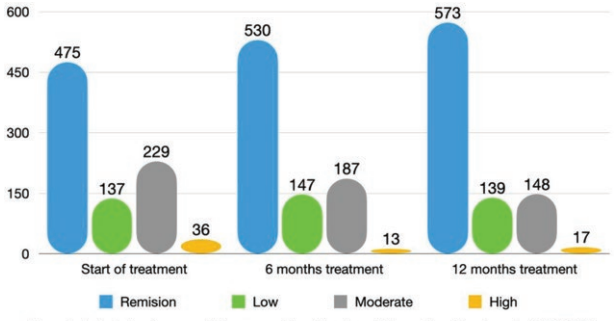


Figure 1. Patients by disease activity group at baseline, 6, and 12 months of treatment with MTX SC

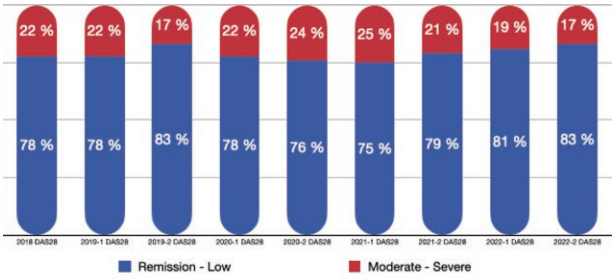


Figure 2. Persistence of the effectiveness of subcutaneous methotrexate over 5 years

Conclusion: This study shows high effectiveness of treatment with MTX SC in patients with RA; an increase in the percentage of patients who achieved remission was observed, with low treatment abandonment rates. After 5 years of follow-up, high persistence rates are observed. This makes MTX SC an excellent alternative for patients with intolerance or insufficient response to oral MTX.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Laura Villarreal: None declared, Nicolás Gutiérrez: None declared, Pedro Rodríguez-Linares: None declared, Manuel Cardozo: None declared, Adriana Rojas-Villarraga: None declared, Pedro Santos-Moreno Speakers bureau: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi, Grant/research support from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi.

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HPR Measuring health (development and measurement properties of PROs, tests, devices)

POS1387-HPR THE IMPACT OF PSYCHOEMOTIONAL MOOD DISORDERS ON MUSCULOSKELETAL PAIN IN PATIENTS WITH INFLAMMATORY JOINT DISEASES

Keywords: Pain, Prognostic factors, Quality of life

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Background: Chronic inflammatory joint diseases such as rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) are most common rheumatic diseases that may cause musculoskeletal pain [1]. The genesis of pain is very complex and many different mechanisms are involved. It is the result of multiple biochemical reactions and is influenced to varying degrees by biological, physiological and social factors. (2) The presence of pain is largely determined by the inflammatory activity of the underlying disease, but subjective factors that depend on the psycho-emotional state of the patient are involved in the assessment of the severity of pain symptoms [3].

Objectives: The aim of the study is to assess the intensity of musculoskeletal pain - arthralgia and myalgia and its correlation with anxiety and depressive mood disorders among a Bulgarian cohort of patients with chronic inflammatory diseases.

Methods: A single-center, observational study including patients with RA, AS and PsA, dispensary in the Rheumatology clinic, "St. Marina" UMBAL - Varna. All the patients were diagnosed according to the criteria for the specific inflammatory joint disease and were treated with a biological medication. Visual analogue scales (VAS) to assess pain intensity (muscular and joint) and Zung self-report scales for depression (SDS) and anxiety (SAS) were used. Laboratory acute phase indicators were investigated in all patients. Descriptive statistics, one-Sample T test, correlation and linear regression analyses were used. A significance level of p<0.01 was accepted.

Results: 130 patients with inflammatory joint disease (RA, AS, PsA), were included in the study. The average age of the study population was 56.37 years (from 21-76 years). 41.5% (n=54) of them were women, 58.5% (n=76) were men. No significant differences were found in evaluating the visual-analog scales for assessing joint and muscle pain between men and women (p=0.177 for joint pain and p=0.717 for muscular pain). On the other hand women scored higher on the anxiety and depression scales, and the difference was again significant (p<0.001 for the depression scale and p=0.001 for the anxiety scale). The self-assessment on the depression scale (SDS) shows a significant correlation with the self-assessment of muscle and joint pain, but the self-reported anxiety scale (SAS) showed a significant correlation only with the self-reported joint pain (SDS and VASm, p=0.008; SDS and VASa, p<0.001; SAS and VASm, p=0.031, SAS and VASa, p=0.004 respectively). Inflammatory indicators (predictors) determine about 8% of the variation of the two pain indicators - for joint pain - R square 7.8%, for muscle pain - R square 8.1%

Conclusion: Musculoskeletal pain is one of the most common clinical presentations of inflammatory join diseases. Chronic pain can lead to mood disorder. The intensity of the pain correlates with anxiety and depressive symptoms in these patients.

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POS1388-HPR RELATIONSHIP BETWEEN CENTRAL SENSITIZATION AND PSYCHOLOGICAL FACTORS IN RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL, MULTICENTER STUDY

Keywords: Rheumatoid arthritis, Quality of life, Patient reported outcomes

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Background: Affective distress (clinically significant depression, anxiety and stress) and central sensitization (CS) are consistently associated with the reported sensitivity and severity of pain, physical disability, poor treatment outcomes, and inflammatory disease activity, and potentially with early mortality in rheumatoid arthritis (RA).

Objectives: We aimed to explore affective distress in patients with RA and determine how they connected to CS.

Methods: Used the CSI to measure CS and the Depression, Anxiety and Stress Scale - 21 Items (DASS-21) to evaluate the negative emotional states of depression, anxiety and stress. The total CSI score ranges from 0 to 100, and a score of 40 or greater has been established to indicate CS. Each of the three DASS-21 scales contains 7 items, divided into subscales with similar content. Multiple regression analysis was used to find out which factors were most likely to be linked to CS.

Results: Overall we included 192 RA patients (age ranging from 22 to 86 years) with a mean disease duration of 5.95 (SD 13.75) years. The CSI score was ≥ 40 in 70/192 patients (36.5%). In our RA cohort, the DASS-21 total score was 32.3 (SD29.8). The mean Anxiety score (Mean=10.68 and SD=8.92 was in the moderate range (10-14), whereas the mean Depression (Mean = 10.11 and SD = 11.66) and Stress (Mean = 15.8 and SD=12.05) scores were in the mild range (10-13 and 15-18, respectively). In the 70 patients with CSI score > 40, the mean Anxiety score (Mean=12.20 and SD=10.01) and the mean Depression (Mean = 14.01 and SD = 13.83) and Stress (Mean = 19.51 and SD=12.77) scores were all in the moderate range (10-14, 14-20 and 19-25, respectively).

Conclusion: Affective distress symptoms (clinically significant depression, anxiety and stress) and CS are common in RA patients. Screening and recognition of such psychosocial disorders may help patients achieve optimal disease control and a good outcome. Overall, our findings have implications for health policy and emphasize the significance of identifying high-risk fibromyalgia (FM) patients by monitoring CS as an indicator of severe disease.

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HPR Epidemiology and public health (including prevention)

POS1389-HPR AGE-SUBSET INCIDENCE AND PREVALENCE ANALYSIS OF JUVENILE SYSTEMIC SCLEROSIS IN THE UNITED STATES

Keywords: Real-world evidence, Systemic sclerosis, Epidemiology

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Background: Juvenile systemic sclerosis (jSSc) is an extremely rare orphan disease. To date, there is very limited published data regarding incidence and prevalence of jSSc. Specifically, there are no published data on jSSc incidence rates by age group and only one Columbian report of jSSc prevalence rates by age group. These data are important given the significant developmental differences between age subsets.
Objectives: To evaluate jSSc age-subset incidence and prevalence using U.S. administrative claims data.
Methods: Children <18 years old with medical claims for SSc and who received methotrexate, mycophenolate mofetil, or cyclophosphamide at a pediatric age (<18 years old) were identified from the OPTUM Clinformatics claims database 2007-2021. jSSc patients were identified using ≥2 medical claims (710.1, 517.2 for ICD-9-CM codes and M34, M34.x for ICD-10-CM codes) for SSc on different dates within a 1-year period. Incidence and prevalence were estimated overall, by age group, and were age and sex adjusted using 2020 US census data.
Results: Adjusted incidence and prevalence estimates are presented in the table below. Overall, jSSc incidence and prevalence rates among children in the US were 1.4 per million person-years (PY) and 7.3 per million, respectively. Both incidence and prevalence rates increased with age.

Table 1.

Age	Adjusted incidence per 1,000,000PY	Adjusted prevalence per 1,000,000
Overall (0-≤18)	1.4 (0.9, 1.9)	7.3 (5.5, 9.1)
0-<6	0.6 (<0.01, 1.4)	0.6 (<0.01, 1.4)
6-<10	0.5 (<0.01, 1.1)	3.1 (0.6, 5.6)
10-<12	1.7 (0.03, 3.3)	5.2 (0.6, 9.7)
12-<18	2.7 (1.5, 3.8)	16.6 (12, 21.3)

Conclusion: jSSc is an extremely rare disease with incidence and prevalence rates increasing with age. Specifically, incidence and prevalence rates vary dramatically for different age subsets, with increasing rates at 10 years and older. To our knowledge, this is the first study to estimate jSSc incidence and prevalence rates by age group.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: John Mattson Employee of: Boehringer Ingelheim Pharmaceuticals Inc, Haikun Bao Employee of: Boehringer Ingelheim Pharmaceuticals Inc, Mary Flack Employee of: Boehringer Ingelheim Pharmaceuticals Inc, Karen Coeytaux Employee of: Boehringer Ingelheim Pharmaceuticals Inc.
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POS1390-HPR LUPUS NEPHRITIS PROFILE IN TUNISIAN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

Keywords: Systemic lupus erythematosus, Autoantibodies, Clinical trials

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Background: Lupus Nephritis(LN) is associated with morbidity and worse survival and its clinical, the immunological and the follow-up profile varies between studies due to race and ethnicities differences. Previous studies have evaluated clinical and immunological factors associated with LN. only few studies were done in the north African region.
Objectives: To define clinical, immunological and treatment differences according to the presence of lupus nephritis (LN) in tunisian Systemic Lupus Erythematosus (SLE) patients.
Methods: We studied SLE 141 patients. A clinical examination and a laboratory evaluation were performed in all SLE patients at the onset of the disease.
Results: Of all patients, 26.24% presented LN. The mean age of patients with LN was lower than patients without LN (34.3 ±14.61 years vs 40.46 ±14.94 years). LN was associated with pleural effusion, pericarditis, higher SLEDAI score, higher levels of creatinine and proteinuria, lower rate of glomerular filtration, anemia, leukopenia, thrombocytopenia, necessity of immunosuppressive drugs, antibodies such as anti-dsDNA, anti-Sm, anti-Sm/RNP and anti-SSA/La. In terms of renal histopathological findings, when we combined class IV and V (profilerative nephritis), we found that this form was more prevalent (56.8%) and associated with higher rate of proteinuria, C-reactive protein and necessity of immunosuprissive drugs.
Conclusion: The north African studies in the term of Lupus Nephritis are scarce. Nonetheless, severe forms seem to be frequent with a high prevalence of proliferative nephritis in our study. Pleural effusion, anti-dsDNA positivity, leukopenia and thrombocytopenia are the predective factors to develop LN.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1391-HPR HEALTH PROFILE AND QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A BRAZILIAN CITIZENS SURVEY

Keywords: Epidemiology, Systemic lupus erythematosus, Quality of life

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Background: Systemic Lupus Erythematosus (SLE) is a chronic inflammatory disease, multisystemic, of unknown cause, autoimmune, with periods of exacerbations and remissions, which may generate limitations in functional and occupational capacity. Brazil has high prevalence rates of SLE (20 to 150 cases per 100,000 inhabitants). The survival rate of these patients has increased in the last century (from 50% to 95%). This context raises questions about the social, health, and quality of life profile of the patient.
Objectives: To profile and evaluate the quality of life of patients with SLE residing in Brazil.
Methods: This is a cross-sectional study, in subjects aged ≥18 years, diagnosed with SLE and residing in Brazil. We applied online form through Google Forms and collected sociodemographic (age, sex, marital status, years of study, occupational activity, and self-reported race), clinical (Body Mass Index (BMI), duration of disease, presence of comorbidities and use of corticosteroids) and quality of life data through the Systemic Lupus Erythematosus Quality of Life (SLEQOL). Data analysis was descriptive (mean, sample standard deviation, and percentage).
Results: 642 volunteers were female (98.29%), aged between 18 and 73 years, and BMI of 27.3 ± 45.8. Greater representation from the Southeast region (60.12%); self-reported white race (54.98%); married marital status (39.88%), education with ≥12 years of schooling (64.64%), have already withdrawn from occupational activity (74.92%) and changed profession after SLE diagnosis (37.85%). The duration of SLE was ≥ 5 years (45.64%) and they have other diagnosed comorbidities (63.24%), and they use corticoid (62.62%). Quality of life had a score of 137.72 ± 51.89, closer to the minimum score (minimum score = 40 and maximum = 280; whereby, higher values correspond to worse quality of life).
Conclusion: Most of the sample are female as already pointed out in other studies; the most recurrent self-reported race was white, unlike studies that the Afro-descendant race was more frequent. Throughout their illness, patients encounter physical, psychological, and social challenges, reflecting on their functional capacity, interfering with occupational activity (leaves of absence and sometimes changing professions) even with education ≥12 years of study. These changes can interfere with health-related quality of life. Care strategies aimed at decreasing the impact of the disease for the patient and his family are needed; as

well as, future studies to explore non-drug therapeutic resources for an integral care of the patient.

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HPR Interventions (educational, physical, social and psychological)

POS1392-HPR EFFECTS OF DIGITAL-BASED HIGH-INTENSITY TRAINING INTERVENTION IN INDIVIDUALS WITH AXIAL SPONDYLOARTHRITIS – A RANDOMIZED CONTROLLED PILOT STUDY (RCT)

Keywords: Spondyloarthritis, Non-pharmacological interventions

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Background: Physical exercise is an important treatment for individuals with axial spondyloarthritis (axSpA). Although high-intensity training (HIT) has been shown to reduce disease symptoms and risk of comorbidity without exacerbating disease activity (1), compliance tends to decrease over time. Increased knowledge is needed on how to optimize and tailor individual exercise programs for continued regular exercising and improved health.

Objectives: To study the effects of HIT on aerobic capacity, body composition, disease activity, physical function, health status and fatigue in individuals with axSpA after a 12-week intervention supported by digital coaching.

Methods: Twenty-two individuals (women, n=12), recruited from two rheumatology clinics in southern Sweden, were randomized to a HIT intervention group (HG; n=11) or a control group (CG; n=11). The HG completed three HIT sessions/week, including two interval training sessions (4x4 min), in self-selected activities for 12 weeks. The individuals in the HG were individually coached and had regular support from a physical therapist primarily by digital coaching. The CG continued exercising as usual. Assessment of aerobic capacity (VO2max), body composition (BMI and visceral fat area [cm2]), disease activity (CRP [µg/ml], BASDAI, 0-10 best-worst), physical function (BASFI, 0-10 best-worst), health status (EQ5D, 0-1 worst-best, ASAS health index [ASAS-HI], 0-17 best-worst), and fatigue (fatigue severity scale [FFS], 0-7 best-worst) were sampled at baseline and after 12 weeks. Mean and standard deviation (SD) were used for descriptive statistics. Repeated measures analysis of variance (ANOVA) was used to investigate effect of group (HG*CG) and time (PRE*POST), with a post-hoc analysis using t-tests when ANOVA indicated a significant difference in main effects or interactions. A significance level of $p \leq 0.05$ was used. Fisher´s exact test was used to study the effects over time for CRP (as dichotomized variable, > or < 4 µg/ml).

Results: Results presented are part of an ongoing RCT based on 19 individuals (women n=11) that have completed the 12-week follow-up analyses. The participants mean (SD) age was 48 (10) years, BMI 25 (4), VO2max 37 (6) mlO2/kg/min, and BASDAI 2.6 (0.3). No differences were present between the HG (n=9) and the CG group (n=10) at baseline for the studied variables. After 12 weeks of HIT an ANOVA interaction ($p<0.05$ showed that HG increased their VO2max (6.4 [3.6] mlO2/kg/min; $p<0.001$) but CG did not. For BMI, visceral fat area, disease activity (BASDAI), physical function (BASFI), fatigue (FFS) no differences in main effects or interactions were found ($p>0.05$). Health status (EQ5D) showed an ANOVA time main effect ($p=0.007$) where the HG increased their health status (0.10 [0.06] units; $p=0.02$) after 12-weeks, but CG did not. For health status measured with ASAS-HI no differences between groups were found. For dichotomized CRP-values no differences were found in either of the group's pre-post.

Conclusion: This pilot RCT shows that after 12 weeks of digital-based HIT intervention, the HG increased their aerobic capacity and EQ5D health status compared to CG, while body composition, disease activity, physical function, and fatigue did not show any significant differences between the groups.

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POS1393-HPR THE INTERVENTION OF AN EXPERT PATIENTS GROUP IN RHEUMATOID ARTHRITIS IN AN INTEGRAL HEALTH MANAGEMENT MODEL

Keywords: Rheumatoid arthritis, Self-management, Patient information and education

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Background: Education for patients is a powerful tool that allows them to participate more efficiently in the relationship with their medical teams and to generate high adherence to their therapy. However, there is a high possibility of establishing lasting relationships between medical teams and patients thanks to the intermediation of expert patients. An expert patient is a person who has received education for the care of their health condition, the improvement of the relationship with their medical team and has been trained to educate, guide and support other patients who have the same health condition.

Objectives: The objective of this study is to implement a participation model that integrates expert patients into healthcare teams so that they can help other patients to learn about the benefits of a correct relationship between doctor and patient and to be more adherent to their treatment, becoming thus in a support axis in the medical care model.

Methods: After the training and certification of 50 expert patients in Rheumatoid Arthritis, a review of the literature was carried out to demonstrate intervention strategies in which expert patients have leadership roles and are integrated into comprehensive medical care models. Then, the patients received training dedicated to: knowledge of the health care model, the algorithm used for the intervention of the interdisciplinary team, the importance of therapeutic adherence in the treatment of a chronic disease, clinimetry and the characterization of patients. to determine a treatment by objectives (Treat to Target Strategy). Finally, expert patients were trained so that they can establish effective communication strategies with other patients in real time.

Results: The intervention will be carried out in groups between 2 and 3 patients and they will be able to interact with other patients in the medical center in a group or individual way. Expert patients will exchange experiences, resolve concerns, conduct literacy, and provide feedback to the medical team and other relevant information (see Figure 1). Likewise, a data collection will be carried out in each interaction to determine through a qualitative study the impact of the support of the expert patients. The duration of each day of intervention will be 6 hours, which denotes a reach of 72 patients per day and an impact on nearly 1,400 patients who come to the medical center per month.

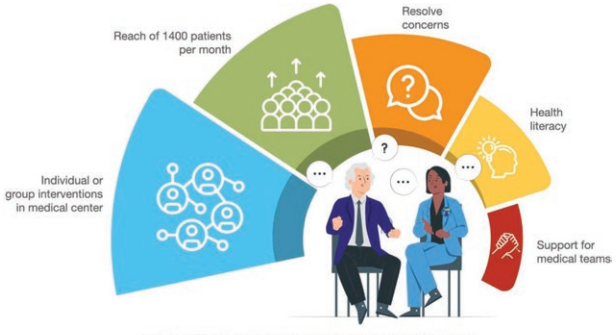


Figure 1: Intervention method of expert patients in care model

Conclusion: It is important to create strategies that allow the education of patients towards therapeutic adherence and integrate them into healthcare teams, since the inclusion of expert patients in medical care models can generate high impacts on the doctor-patient relationship and improve the degrees of adherence in the population, thanks to the relationship between peers that will lead to a better understanding of the role of patients in their treatment.

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POS1394-HPR **WITHDRAWN**

POS1395-HPR **EMOTIONAL INTELLIGENCE: A NOVEL OUTCOME ASSOCIATED WITH QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC SCLEROSIS**

Keywords: Systemic sclerosis, Quality of life

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Background: Health related quality of life (HrQoL) in patients with systemic sclerosis (SSc), a systemic autoimmune disease, is severely impaired. Patients suffer from Raynaud's phenomenon, stiff hands, tight skin, pruritus, difficulty in swallowing, gastrointestinal disturbances, dyspnoea on exertion, and depression, significantly affecting their HrQoL. While several studies have addressed HrQoL in patients with SSc, no studies so far have investigated the trait emotional intelligence (TEI) of these patients.

Objectives: To investigate for the first time whether HrQoL of SSc patients is influenced by TEI in a cross-sectional study.

Methods: Sixty patients with SSc (Female: 86.67%) completed three questionnaires: TEI Questionnaire Short-Form (TEIQue-SF); Short-Form Health Survey (SF-36); and demographic characteristics. A series of multiple linear regression models were used to analyze the data with dependent variables (DV) every dimension of SF-36 (Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, Mental Health) and independent variables TEI total and every TEI factor (Well-being, Self-control, Emotionality, Sociability).

Results: The average age of participants was 56.4±13.4 years and the mean disease duration was 7.7±7.5 years. TEI total was found to affect both physical and mental component summaries ($p<0.001$) and all 8 dimensions of the HrQoL ($p<0.001$). Well-being appeared to have a positive effect on Role-Physical, General Health, Vitality, Social Functioning and Mental Health. Self-control appeared to influence Physical Functioning and Pain, and Emotionality appeared to influence Role-Emotional. Sociability was not an important factor for any dimension of HrQoL (Table 1).

Conclusion: Understanding the relationship between TEI and HrQoL dimensions is important for the support and empowerment of SSc patients, as well as the establishment and implementation of appropriate psychotherapeutic interventions.

Table1. Multiple linear regression analyses results for elements of the TEI and HrQoL dimensions

Dependent Variables	Independent Variables	B	SE B	Standardized β
Physical Functioning (PF)	Self-control	15.27	2.09	.69*
Role-Physical (RP)	Well-being	15.31	2.1	.69*
Bodily Pain (BP)	Self-control	7.81	3.43	.34***
General Health (GH)	Well-being	5.96	1.6	.44*
Vitality (VT)	Well-being	9.82	1.62	.62*
Social-Functioning (SF)	Well-being	14.87	2.51	.61*
Role Emotional (RE)	Emotionality	11.68	2.61	.51*
Mental Health (MH)	Well-being	9.51	1.5	.64*
PCS	Well-being	7.13	2.52	.44**
MCS	Well-being	11.26	1.6	.68*

*P <.001 **P <. 01 ***P <.05

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

POS1396-HPR **DOES FIBROMYALGIA WORSEN CATASTROPHIZING IN PATIENTS WITH RHEUMATOID ARTHRITIS?**

Keywords: Fibromyalgia, Rheumatoid arthritis

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Background: Pain is a cardinal symptom of several rheumatic conditions such as rheumatoid arthritis (RA) and fibromyalgia. Catastrophizing incorporates an amplification of symptoms associated with pain, and therefore contributes to its sustainability.

Objectives: We aimed to assess the impact of RA-associated fibromyalgia on catastrophizing.

Methods: We conducted a cross-sectional study including RA patients meeting the 2010 ACR/EULAR criteria. Patients were divided into two groups: group 1 (G1) including patients with fibromyalgia associated to RA, and group 2 (G2) including patients with RA. Fibromyalgia screening was based on the Fibromyalgia Rapid Screening Tool (FIRST). RA activity was assessed using the Disease Activity Score (DAS_{28} ESR). Quality of life was assessed using the Health Assessment Questionnaire (HAQ). Catastrophizing was assessed using the Pain Catastrophizing Scale (PCS), which is composed of 13 items. The PCS total score varies between 0 (absence of catastrophizing) to 52 (significant tendency to catastrophizing). The cognitive and emotional representation of pain was assessed by the Brief

Perception Illness Score (BPIS). It consists of 9 items: 8 quantitative questions on a numerical scale ranging from 0 to 10, and one last item in the form of a qualitative question. The total score varies from 0 to 90, without predefined thresholds. The higher the score, the more threatening the patient's perception of the disease is. The significance threshold was set at a p value of 0.05.

Results: Our study included 80 patients (G1: N= 40 and G2: N=40), 76 women and 4 men, with an average age of 59±9 years [42-77] in G1 and 53±10 years in G2 [37-74]. The mean disease duration was 11.29±6.24 years. RA was erosive in 90% of cases. Rheumatoid factor and/or ACPA were positive in 85% of cases. The mean delay between fibromyalgia and RA diagnosis was 49±7 months. Seventy five percent of patients were on corticosteroids with an average dose of 10 mg per day of Prednisone equivalent. All patients were receiving a DMARD: methotrexate 85%, leflunomide 11.2%, and biologics 37.5%. The mean VAS pain was 6.3±1.8 cm in G1, and 5±1.1 cm in G2. The mean VAS fatigue was 6±2.3 cm in G1, and 4 ±0.9 cm in G2. The mean global patient assessment was 5.9±2 in G1, and 3±0.5 in G2. The mean morning stiffness duration was 30 minutes in G1, and 55 minutes in G2. The mean DAS_{28} ESR was 5±0.7 in G1, and 3.97±0.5 in G2. The mean HAQ was 1±0.3 in G1, and 0.7±0.1 in G2. Catastrophizing was greater in patients with RA-associated fibromyalgia with a mean PCS of 41± 8.2 in G1 vs 32±4.4 in G2 (p=0.01). Cognitive and emotional impact was also greater in G1 compared to G2: the mean BPIS was 71±9 in G1 vs 55±7.5 in G2 (p=0.05).

Conclusion: Our study showed that fibromyalgia aggravates catastrophizing and illness perception in patients with RA. It is important to remind the place of cognitive therapy in the management of these chronic conditions.

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Disclosure of Interests: None Declared.

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POS1397-HPR

SHARED DECISION MAKING ON SUBCUTANEOUS METHOTREXATE OPTIONS FOR RHEUMATOID ARTHRITIS PATIENTS, WHAT DOES THIS LOOK LIKE FOR PATIENTS AND HEALTHCARE PROFESSIONALS?

Keywords: Disease-modifying drugs (DMARDs), Rheumatoid arthritis, Best practices

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Background: Methotrexate (MTX) is the most commonly used rheumatoid arthritis (RA) drug and will often be the first drug prescribed to treat RA [1]. Enhanced bioavailability of subcutaneous (SC) administration of MTX and improved tolerability compared to oral MTX may make this route of administration preferable to the oral route in certain patients [2]. RA patients with 'dexterity' issues have physical challenges impacting their ability to use their SC MTX device, therefore making the need to offer choice of device to the individual patient to suit their needs are important. Single device policy within hospitals is a major issue as it results in an inability for health care professionals (HCP) to offer a choice, deliver shared decision making and limits the ability to provide optimal disease management [3].

Objectives: The aims of this study were to quantify the cohort of UK RA patients with impairments affecting their ability to self-administer SC MTX, to explore whether such patients are treated any differently or experience inequity of care due to restrictions in device choice, and to identify the challenges facing prescribers and patients of only having one device available for RA patients.

Methods: A 30-minute computer-assisted telephone interview (CATI) was performed during 16 May-24 June 2022. Twenty-nine UK HCPs (22 rheumatology nurses and 7 consultant rheumatologists) were included. CATI included questions categorised in 4 sections including how to choose a device and importance of patient choice (8 questions), impairments (7 questions), impairment management (5 questions), and challenges and progression (4 questions). Data was further validated using a virtual expert panel meeting with another group of HCPs working within rheumatology on 11 June 2022.

Results: 31% of HCPs feel there are significant challenges for some patients using a SC device specifically, those with reduced hand function or with active or significant disease, which results in being unable to self-inject leading to non-adherence to treatment. It was estimated that 23% of RA patients have impairment (mostly reduced manual dexterity) impacting their ability to self-administer. HCPs feel patients with impairments have different needs which are mostly identified during the patient assessment or device observation. 90% of HCPs stated they rely on patients telling them of any issues, however patients do not always raise their challenges with their device to their HCP. 90% of HCPs defined patient choice in terms of facilitating patients to make an informed decision. 83% of HCPs mentioned ability to use a device as the most important factor for choosing a device. ~70% of hospitals only have one SC MTX device available (Figure 1), and this is due to formulary restraints. To be able to offer patient choice, HCPs believed that >1 device should be available (76%), and patients should be informed on benefits of different devices (55%). HCPs consider single device policy is a big issue in the ability to offer a choice (59%) and to manage the disease (50%). Main challenges are difficulties physically using the device and accurately administering drug. 31% of HCPs feels that the impaired patients have poorer compliance and progress to biologics more quickly (8.5 vs. 11.5 months) and 52% of HCPs feel these patients require more frequent visits. The subsequent expert panel meeting essentially confirmed the results.

Conclusion: A significant number of patients (23%) have challenges using SC MTX devices impacting both clinical and non-clinical outcomes. These patients have different needs, thus different devices may offer different benefits. Most rheumatology units in hospitals (69%) have only one SC MTX device on their formulary. Current perception of 'one device fits all' is inconsistent with the Royal College of Nursing guidelines on SC MTX and the NHS Long Term plan (regarding patient choice) [3].

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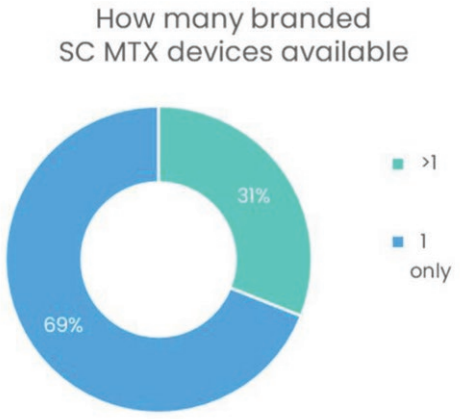


Figure 1. Distribution of the number of branded SC MTX devices available (>1, only one) for RA patients within the hospital/clinic

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POS1398-HPR

SUPPORT NEEDED BY PEOPLE WITH SYSTEMIC SCLEROSIS TO REMAIN IN THE WORKFORCE

Keywords: Work-related issues, Systemic sclerosis

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Background: Systemic sclerosis (SSc) severely limits one's ability to participate in paid employment, which may threaten an individual's economic, social, physical, or mental well-being. No programs and very little resources exist to help people with SSc remain in the work force despite the high prevalence of work disability. The few programs that do exist were developed for persons with other rheumatic conditions. One evidence-based program, Making it Work™ (MIW), has the potential to be adapted to meet the specific work related problems faced by people with SSc.
Objectives: This study identified challenges in the work environment and supports received or desired by persons with SSc as a preliminary step to identify adaptations that could make the MIW™ more relevant to people with SSc.
Methods: Participants were recruited through virtual communication from the National Scleroderma Foundation and word of mouth to participate in one 2-hour virtual focus group. Participants were >18 years of age, currently employed or stopped work in the past 5 years, United States residents, English-speaking, and self-reported a diagnosis of SSc and that SSc affected their work ability. Participants were first asked about difficulties working with SSc. The facilitator created a list of challenges based on initial discussion, then participants identified the top five most important challenges according to their experience. Participants were then asked about supports received or desired to help maintain employment. Focus group notes and transcripts were analyzed to determine challenges and supports that must be addressed in an employment intervention for people with SSc.
Results: The sample included 14 participants (85.7% women, mean age 48.8±10.1 years, mean disease duration 7.7±7.4 years; 78.6% had diffuse SSc). 71.4% had college degrees and 71.4% were employed full time. 42.9% described their jobs as having mostly mental demands while 35.7% had both physical and mental demands. Important challenges prioritized by the most participants were: 1) challenges with physical tasks, particularly related to hand use [11, 78.6%] –"*My hands are pretty messed up; typing is a challenge*"; 2) fatigue [9, 64.3%]-"W*hen you say fatigue, people are like, "Well, go take a power nap," but that's not what it is. I could sleep 12-hours and still be exhausted";* 3) mental and emotional health, related to coping with how the unpredictability of SSc affects the body, identity, and employment [8, 57.1%]-"*This disease does not just knock us down one time or challenge us on one level. It's like one body system after another.*""*You have to deal with the issues of your self-esteem, feeling like you're different than everybody else, mourning that loss of ability or career or work ethic that you had prior to your diagnosis"* Participants identified a variety of individualized strategies that enabled them to overcome challenges with SSc at work, including ways to plan ahead, adaptive equipment, and strategies to adapt job tasks. However, participants emphasized that in order to use these tools, it is most helpful to: 1) have the knowledge and advocacy skills to know what to ask for; 2) feel confident that asking for support or accommodations in the workplace will lead to a beneficial change; and 3) be able to problem solve with others (e.g., clinicians, work-related program, therapists, support group).
Conclusion: This study identified the prominent barriers and supports to employment from the perspectives of patients with SSc. While there is some overlap with issues reported by persons with other rheumatic conditions, there are also SSc-specific concerns. This information will be used to adapt the MIW™ intervention, and warrants further consideration for how to incorporate better supports in healthcare, workplaces, and vocational counseling for people with SSc.
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POS1399-HPR ONLINE SCHOOL AS A METHOD OF INCREASING THE MEDICAL LITERACY OF PATIENTS WITH RHEUMATIC DISEASES

Keywords: Patient information and education

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Background: Today, most of the population of Kazakhstan have access to the Internet. Due to this fact, the use of online schools for patients with rheumatic diseases seems to be a promising direction [1,2].
Objectives: The purpose of the study is to analyze whether online rheumatology schools can be used as one of the methods to improve the medical literacy of patients.
Methods: A survey was conducted with 90 patients IN the city of Astana attending an online school on RH from September 2021 to September 2022 after graduation. The online questionnaire included 20 questions (part A and part B). The questions in Part A concerned the age of patients, gender, bad habits, heredity, sources of information about the school, and the desire to study at an online school. In part B, the questions concerned the novelty and quality of the information received. Patients had to choose one/several of the presented answer options. In some questions, a differentiated assessment was used on a 5-point scale, where 0 points is the minimum, and 5 is the maximum positive assessment. The lecture course consisted of 36 lectures and 6 practical exercises on rheumatic diseases. The questionnaire data were processed in Statistical Analysis Software15.0. Statistical significance was handled using Analysis of variance.
Results: Part A. The number of patients under the age of 30 was 9 (10%) respondents, 31-40 years old - 41 (45.6%) respondents, 41-50 years old - 12 (13.3%) respondents, 51-60 years old - 17 (18.9%) respondents, over 60 years old - 11 (12.2%) respondents. 75 (83.3%) patients were women. 26 (28.8%) patients had bad habits. 17 patients (18.8%) knew about rheumatic diseases FROM relatives. Most of the participants received information about the online school from the clinic staff - 42 (46.7%) or FROM the clinic website - 27 (30.0%), from other sources - 21 (23.3%) respondents. 72 (80%) respondents noted their desire to attend such classes in the future. These data indicates on the interest of respondents of different age groups in improving the level of medical literacy in rheumatic diseases. Part B. 77 (85.5%) and 82 (91.1%) respondents learned about new risk factors for RD (the role of infection and stress), respectively. 39 (43.3%) patients understood the need to correct their lifestyle. A total of 26 (28.8%) respondents realized that they could independently control treatment. 92% of respondents rated the quality of the information received by the maximum score.
Conclusion: The online school can be used as one of the methods to improve the medical literacy of patients with rheumatic diseases.
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POS1400-HPR COMPARISON OF BODY AWARENESS, PHYSICAL ACTIVITY, KINESIOPHOBIA, PAIN CATASTROPHIZING, AND PSYCHOSOCIAL STATUS IN INDIVIDUALS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS

Keywords: Rheumatoid arthritis, Spondyloarthritis, Patient reported outcomes

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Background: Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) are among the most common rheumatic (joint) conditions. RA and AS are different types of arthritis. Living with RA or AS can significantly affect your quality of life, mental health, and emotional well-being.
Objectives: We report the preliminary results of an ongoing prospective observational study that compare the body awareness, physical activity, kinesiophobia, pain catastrophizing and psychosocial status in individuals with RA and AS.
Methods: A total of 78 individuals (RA=48; AS=30; women/men=48/30) recruited from two university hospitals in Turkey. All individuals were assessed regarding physical characteristics (age, BMI, duration of disease, BASDAI, DAS-28); body awareness by Body Awareness Questionnaire, physical activity level by International Physical Activity Questionnaire Short Form, fear of movement by Tampa Scale of Kinesiophobia, pain catastrophizing by Pain Catastrophizing Scale and psychosocial status by Beck Depression Inventory.
Results: Individuals' characteristics and outcome measures are presented in Table 1. As expected, there were statistical differences between age and gender in study groups ($p<0.001$). However, disease duration and disease activity, mild depression level were similar between groups. Individuals with AS were

significantly more physically active compared to individuals with RA (p<0.005). Body awareness, kinesiophobia, pain catastrophizing and psychosocial status were similar between groups (p>0.05). In addition, disease activity was moderately correlated with body awareness, pain catastrophizing and kinesiophobia individuals with AS (r=-0.529; r=0.613; r=0.427, p<0.05).

Conclusion: Treatment of RA and AS is similar, but there are key differences. According to our results, individuals with AS is more physically active than individuals with RA regardless of disease duration and disease activity. Health professionals can also focus on correlation between disease activity and higher body awareness, pain catastrophizing and kinesiophobia in individuals with AS.

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Table 1. Characteristics of patients and outcome measures

Patients' characteristics		RA n=48	AS n=30	p*
Age (year): mean ± SD		51.34 ± 11.0	40.27 ± 10.38	**0.000***
BMI (kg/m^2): mean ± SD		28.21 ± 4.47	26.66 ± 5.78	0.101
Gender (n, %)	Female	41 (85.4%)	7 (23.3%)	**0.000***
	Male	7 (14.6%)	23 (76.7%)	
Duration of disease (year): mean ± SD		7.20 ± 9.39	5.91 ± 7.28	0.488
ESR (mm/h)		13 (2-58)	9 (3-54)	0.115
CRP (mg/dl)		3.65 (0.18-37.70)	5.2 (0.60-49.06)	0.300
BASDAI (0-10) n (%)	Active disease		18 (60)	
	Inactive disease		12 (40)	
DAS-28 n (%)	Remission	24 (50)		
	Low activity	12 (25)		
	Moderate activity	12 (25)		
Outcome measures				
BDI (0-29)		14.5 (0-45)	14 (0-42)	0.991
IPAQ-SF		594 (0-4380)	1188 (66-5805)	**0.005***
PCS (0-52)		29 (4-51)	27 (7-50)	0.610
TSK (0-68)		39 (23-56)	42.5 (25-57)	0.102
BAQ (18-126)		94 (50-126)	91.5 (49-1200)	0.463

RA= Rheumatoid arthritis; AS= Ankylosing spondylitis; SD= Standard deviation; BMI= Body mass index; ESR= Erythrocyte sedimentation rate; CRP= C reactive protein; Bath Ankylosing Spondylitis Disease Activity Index, BDI= Beck Depression Inventory. IPAQ-SF= International Physical Activity Questionnaire-Short Form; PCS= Pain Catastrophizing Scale; TSK= Tampa Scale for Kinesiophobia; BAQ: Body Awareness Questionnaire. * Mann-Whitney U test.

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Disclosure of Interests: None Declared.

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POS1401-HPR LIVED EDUCATIONAL EXPERIENCE OF YOUNG ADULTS WITH CHILDHOOD- AND ADULT-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: A MULTI-CENTER CANADIAN QUALITATIVE STUDY

Keywords: Qualitative research methods, Systemic lupus erythematosus, Work-related issues

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Background: Education and employment established in young adulthood predict future lifetime socioeconomic achievements. Young adults with Systemic Lupus Erythematosus (SLE) have physical, cognitive and mental health issues and other comorbidities that may impact employment.

Objectives: To understand the lived experiences of young adults with SLE (YASLE), as students, and to assess their perceived barriers from SLE.

Methods: YASLE were recruited from two Lupus clinics in Toronto and Winnipeg. Semi-structured qualitative interviews were conducted individually via secure video conferencing. As this study was conducted during the coronavirus pandemic, participants were also asked about the pandemic impacts on their education experiences. All interviews were transcribed verbatim, double-coded and analysed using a reflexive thematic approach.

Results: Twelve participants (2 males), 9 of childhood- and 3 adult-onset SLE (cSLE, aSLE) were interviewed. Nine participants (82%) were <25 years old. Five also worked while studying. Five were Asians, 5 were White, 2 of other ethnicities. Half have severe disease (central nervous system or renal involvement). Median duration of disease was 4.0 (25th-75th percentile, 1.8- 5.3) years. The impacts of SLE on their education experience emerged in 5 themes:

1) *Challenges imposed by SLE:* Difficulties adjusting to the diagnosis, physical and cognitive symptoms of SLE. While most participants disclosed their diagnosis to their schools, some expressed hesitation.
2) *Changes in aspirations:* Education/career goals were modified by reducing course load or shifting to more sedentary or less cognitively demanding careers.
3) *Coping and acceptance*: More adaptive than maladaptive coping strategies were used to manage their SLE, including self-acceptance, pacing, planning and avoidance. All strived to do well in their studies despite SLE and were hopeful for their futures.
4) *Facilitating factors for education success:* Family and friends' social support, individualized accommodations from school and parental financial support were identified.
5) *Pandemic impacts*: Virtual learning and flexible schedules enabled participants to adapt their schedules according to their physical conditions (e.g. pain, fatigue). However, fewer opportunities to interact in-person were viewed as challenges. Participants want hybrid options to continue even after the pandemic.

Conclusion: SLE affected students' performance through physical symptoms, fatigue and cognitive dysfunction. Ongoing social and school supports help to support them. Maintaining the remote learning options may increase accessibility for them. These results identified opportunities for developing future supportive interventions for YASLE patients in their schooling which then better prepare them for future employment.

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POS1402-HPR BODY MASS INDEX MAY HAVE A ROLE IN THE PROGRESSION OF STRUCTURAL DAMAGE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Lifestyles, Spondyloarthritis

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Objectives: To examine the association between basline body mass index (BMI) and progression of radiographic damage in axial spondyloarthritis (ax-SpA) patients. We also assessed the correlation between baseline BMI and baseline radiographic damage in terms of mSASSS score and the presence of syndesmophytes.

Methods: In total 657 (431[65.6%] r-axSpA and 226 nr-axSpa; 243 [37%] female and mean age of 39.9 ± 11.7 years) patients classified as axSpA according to the "Assessment of Spondyloarthritis International Society [ASAS]" criteria were

included in the study. mSASSS progression was defined as at least 2 units mSASSS score increase on radiographs taken at least two years apart. An increase in mSASSS score and/or the development of new syndesmophyte was considered as radiolographic progression.

Results: Age, age at diagnosis, symptoms duration and education level were significantly different between the patients with BMI<30 and BMI≥30. BASDAI, C-reactive protein and erythrocyte sedimentation rates were similar between groups. BASFI, BASMI, fasting blood glucose, triglyceride, total cholesterol, low-density lipoprotein levels and aspartate aminotransferase values measured in the same period were significantly higher in axSpA patients with BMI≥30. While baseline total and lumbar vertebrae mSASSS scores were similar between the groups, cervical mSASSS scores were significantly high in the BMI≥30 group. In our study group baseline BMI was positively correlated with radiographic progression (r=0.201; P=<0.005) and the development of new syndesmophyte (r=0.134; P=<0.05).

Conclusion: The results of this study showed that BMI was associated with both basline and the progression of structural damage in axSpA patients. The effect of high BMI on structural damege may be related to mechanical factors. However, BMI was found to be associated with cervical, but not lumbar syndesmophyte at baseline. Thse findings might be the results of increase in proinflammatory cytokines such as TNF-alfa and IL-6 and the reduction of anti-inflammatory cytokines such as IL-10 and adiponectin secreted from dysfunctional adipose tissue.

Table 1. Demographic and clinical characteristics of patients with axial spondyloarthritis categorized according to body mass index.

	BMI<30* N=453(%80.7)	BMI≥ 30* N=109(%19.3)	P**
Age (year)	37(15.5)	44(12)	**<0.001**
Education Duration (year)	11(8)	8(7)	**<0.005**
Age at diagnosis (year)	32.5(15)	38(62)	**<0.001**
Diagnosis duration (year)	1(7)	3(10)	**<0.05**
Symptom duration (year)	10(11)	14(16)	**<0.001**
BASDAI	3.7(3.6)	3(3.8)	0.942
BASFI	2.8(4.7)	4.1(4.4)	**<0.05**
BASMI	3(2.8)	2.8(2.7)	**<0.001**
Sedimentation rate	19(28)	15(7)	0.215
C-Reactive protein	6.6(16.7)	7.8(8.2)	0.097
Fasting blood sugar	93(13)	99(17.25)	**<0.001**
Triglyceride	101(64)	135(80.5)	**<0.001**
Total cholesterol	184(52.25)	201(43.25)	**<0.005**
LDL	116(46)	127.5(43.75)	**<0.05**
HDL	43(13)	44(18)	0.364
Creatinine	0.75(0.15)	0.77(0.18)	**<0.05**
AST	16(6)	19(8)	**<0.005**
mSASS score basal	0(8)	2(9)	0.123
mSASS score cervical	0(2)	0(4)	**<0.05**
mSASS score lumbar	0(0)	0(4)	0.301

*Values are presented as median (IQR), **P value is given according to Mann Whitney U test results.

REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3311

POS1403-HPR

LONGITUDINAL PILOT-STUDY EXPLORING CHANGES IN EDUCATIONAL NEED AMONG PATIENTS WITH NEWLY DIAGNOSED AAV USING ENAT

Keywords: Vasculitis, Patient information and education

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Background: Previous studies have shown that disease duration associate with an increased need of educational support in ANCA associated vasculitis (AAV) [1]. Shorter disease duration showed to significantly increase educational needs although not yet investigated whether the disease duration or time itself is the deciding factor. Longitudinal studies using the Educational Needs Assessment Tools (ENAT) are in general scarce.

Objectives: The aim of this pilot study was to explore how educational needs changes over two years among newly diagnosed patients with AAV using ENAT.

Methods: This pilot study included longitudinal data from the Rheumatology and Nephrology clinics at the Karolinska University Hospital in Sweden during 2009-2022. Inclusion criteria were being diagnosed with AAV (GPA, MPA and EGPA), minimum age of 18 years and literate in Swedish. Exclusion criterion was cognitive impairment interfering with literate capabilities. Disease activity was estimated using Birmingham Vasculitis Activity Score version 3 (BVAS). Educational needs were captured by patients' answers to the ENAT questionnaire at baseline and after 24 months. The ENAT consists of 39 questions, presented as total ENAT and seven domains (managing pain, movement, feelings, disease process, treatment, self-management and, support) each containing 4-7 items (item answers ranging from 'not at all important' = 0, to 'extremely important' = 3). Paired samples t-test was used to compare means between the two timepoints.

Results: 17 individuals (47% men) with GPA (n=15) and MPA (n=2) completed the questionnaire. At baseline mean age was 51 years, ranging from 20-66, and mean years of education 14.6. Mean disease duration at baseline was 0.2 years. All but three were newly diagnosed at baseline and 3 was diagnosed the year before inclusion. All individuals had an active disease, with a mean BVAS of 15.2, range 1-25. The mean total ENAT score decreased from 83.5 at baseline to 72.6 at 24 months (p=0.04) (Table 1). Change in individuals total ENAT scores ranged from +10 to -73. Educational needs decreased within two of the seven domains, 'Self-help measures' 15.4-12.9 (p=0.03) with individual score change ranging from +5 to -13 and 'Treatment' 16.8-12.1 (p=0.005) with individual score change ranging from +7 to -21 (Graph 1). Domains indicating lower educational needs at baseline were still low after 2 years. Over time the domain with highest educational needs shifted from 'Self-help measures' at baseline to 'Disease process' at follow-up.

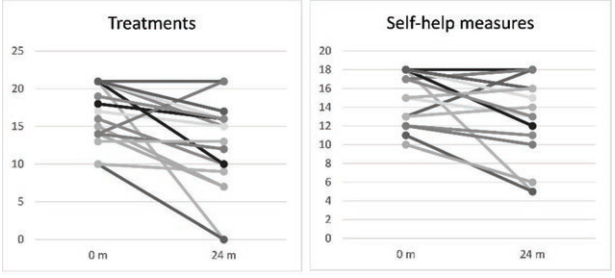
Conclusion: This pilot study demonstrates that patients newly diagnosed with AAV expressed high educational needs at baseline compared to previous studies on both patients with established and newly diagnosed AAV [1]. The educational need decreased over time in total and within two of the domains but was still high after 24 months. Our findings point to the fact that patients need continuous educational support during the first years of diagnosis. To further explore patterns and clusters of changes in educational needs more data is needed, including data on what and how information and patient education is received.

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	0 months n=17	*24 months n=17*	*dif.*	*p*
Managing pain (0–18)	10.1 (56.1%)	10.3 (57.2%)	+0.2	0.89
Movement (0–15)	8.5 (56.6%)	7.5 (50%)	-1	0.35
Feelings (0–12)	8.4 (70%)	7.3 (60.3%)	-1.1	0.31
Disease process (0–21)	17.8 (84.7%)	16.5 (78.6%)	-1.3	0.25
Treatments (0–21)	16.8 (80%)	12.1 (57.6%)	-4.7	**0.005**
Self-help measures (0–18)	15.4 (85.5%)	12.9 (71.7%)	-2.5	**0.03**
Support systems (0–12)	6.9 (57.5%)	6.3 (52.5%)	-0.6	0.43
Total ENAT (0–117)	83.5 (71.3%)	72.6 (62%)	-10.9	**0.04**

Table 1. ENAT raw scores, mean (percentage of domains maximum score).



Graph 1. Domain "Treatments" range 0-21 and "Self-help measures" range 0-18 at baseline and after 24 months.

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Disclosure of Interests: None Declared.
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SLE, Sjön's and APS - aetiology, pathogenesis and animal models

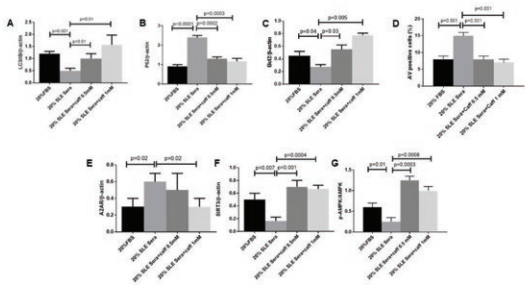
POS1404 **CAFFEINE IMPROVES SYSTEMIC LUPUS ERYTHEMATOSUS ENDOTHELIAL DYSFUNCTION BY PROMOTING ENDOTHELIAL PROGENITOR CELLS SURVIVAL**

Keywords: Systemic lupus erythematosus, Diet and nutrition, Cardiovascular disease

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Background: Circulating endothelial progenitor cells (EPCs) are widely demonstrated biomarkers of endothelial function. Their frequency and function varied in systemic lupus erythematosus (SLE) patients, with a significant association with subclinical atherosclerosis [1]. Caffeine, one of the most widely consumed products in the world, seems to improve endothelial cells number and EPCs migration in coronary artery disease both in mouse models and in patients [2]. We recently demonstrated the impact of caffeine on SLE disease activity status, in terms of SLE Disease Activity Index 2000 (SLEDAI-2K) values and serum cytokine levels [3].
Objectives: The aim of this study was to evaluate the possible role of caffeine intake on endothelial function in SLE patients, by assessing its effect on number and function of EPCs both *ex vivo* in SLE patients and *in vitro* in healthy donors (HD) treated with SLE sera.
Methods: We performed a cross-sectional study enrolling SLE patients, excluding patients with history of traditional cardiovascular risks factors. Caffeine intake was evaluated using a 7-day food frequency questionnaire. At the end of questionnaire filling blood samples were collected from each patient to assess circulating EPC percentage. EPCs were detected by using a flow cytometry analysis defined as KDR CD34 double positive cells. Subsequently, EPCs pooled from 6 HD were co-cultured with caffeine at 0.5 mM and 1 mM with and without SLE sera. After 7 days, we evaluated the cells morphology and the ability to form colonies; moreover, we analyzed for the percentage of annexin V-positive (AV) apoptotic cells by flow cytometry analysis and for levels of autophagy and apoptotic markers LC3-II, p62 and Bcl2 by western blot, alone or in the presence of protease lysosomal inhibitors E64d and Pepstatin A. Finally, we performed a WB analysis to assess the A2AR/SIRT3/AMPK pathway.
Results: We enrolled 31 SLE patients (F:M 30:1, median age 43 years, IQR 18; median disease duration 144 months, IQR 180). We found a EPCs median percentage of 0.03% (IQR 0.04) observing a positive correlation between caffeine intake and circulating EPCs percentage (p=0.03, r=0.4). Moving on *in vitro* experiments, HD EPCs treated with SLE sera and caffeine showed an improvement in morphology and in number of EPCs-CFU in comparison with those incubated without caffeine (p=0.0003). The colonies treated with SLE sera were poorly organized in comparison with HD; the addition of caffeine restored the colony structure. After treating HD-EPCs with SLE sera we observed an increase in AV positive cells and p62 values and a reduction of LC3-II and Bcl2 values; the addition of caffeine was able to significantly reduce AV positive cells and p62 values and to significantly increased LC3-II and Bcl2 values, without any significant differences between caffeine 0.5 mM and 1 mM (Figure 1 A-D). After E64d and pepstatin A treatment, both LC3IIB and p62 trend didn't change, compared to untreated cells. Finally, we observed after caffeine treatment, in comparison with SLE sera alone, a significantly reduction in A2AR levels leading to an increase in protein levels of SIRT3 and subsequently AMPK phosphorylation (Figure 1 E-G).

Figure 1. A-D. Percentage of LC3IIB, p62, Bcl2, AV positive cells in HD-EPC co-coltured with caffeine 0.5 mM and 1 mM with and without SLE sera
E-G. A2AR, SIRT3, p-AMPK/AMPK levels in HD-EPCs co-coltured with caffeine 0.5 mM and 1 mM with and without SLE sera



Conclusion: We demonstrated, for the first time, a protective role of caffeine on endothelial function in SLE patients. Caffeine intake positively correlated with the percentage of circulating EPCs in SLE patients; moreover, caffeine in vitro treatment was able to improve EPCs survival and vitality through the inhibition of apoptosis and the promotion of autophagy via A2AR/SIRT3/AMPK pathway.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4619

POS1405 **FERROPTOSIS OF CD163+ TISSUE INFILTRATING MACROPHAGES IN LUPUS NEPHRITIS**

Keywords: Systemic lupus erythematosus, Kidneys, Cell biology

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Background: Lupus nephritis (LN) is one of the most common complications of systemic lupus erythematosus (SLE), with high morbidity and mortality. Despite a better understanding of the pathogenesis of LN, treatment progress is still insufficient. Dysregulation of cell death and deficient clearance of dying cells lead to the production of autoantigens, induction of autoantibodies, deposition of circulating immune complexes, and other abnormal immune responses in SLE and LN patients [1]. Ferroptosis, a recently discovered PCD, has hardly been reported in detail in LN [2]. Thus, the purpose of this study was to investigate the role of ferroptosis and its associated metabolic pathways in the pathogenesis of LN.
Objectives: The purpose of this study was to investigate the role of ferroptosis and its associated metabolic pathways in the pathogenesis of LN.
Methods: Transcriptome datasets containing LN and Living donors was obtained from GEO database, and gene sets associated with different PCD modes and different metabolic pathways was extracted from the signaling pathway database or literature search. Composite gene expression scores were calculated by averaging z-scored transformed log2 expressed genes within the pathway. Immunohistochemistry and immunofluorescence were used to detect the expression of 4-HNE and CD163 in LN.
Results: We found that ferroptosis was significantly increased in LN, especially in the glomeruli, while ferroptosis of tubulointerstitial compartment was different in two datasets (Figure 1A, B, C). By immunohistochemistry, we found that the expression of 4-HNE (key medium for ferroptosis) was significantly increased in both glomerulus and tubules (Figure 1D). Next, we explored changes in LN of eight metabolic pathways associated with ferroptosis. In the glomerular compartment, iron metabolism and oxidative phosphorylation pathways were significantly enhanced, while fatty acid synthesis pathway was significantly reduced. In the tubulointerstitial compartment, fatty acid synthesis and oxidative phosphorylation pathways were significantly reduced (Figure 1E). Only iron metabolism and ferroptosis were positively correlated in glomerulus and tubules (Figure 1F). By intersecting differentially expressed genes and metabolism-related genes, we finally obtained one up-regulated gene (CD163) and two down-regulated genes (PC and ATP6V0A4) in glomerulus (Figure 1G, H). The expression of CD163 in glomerulus was positively correlated with ferroptosis (Figure 1I). Meanwhile, immunofluorescence showed that CD163 and 4-HNE co-located in the glomerulus (Figure 1J).
Conclusion: In conclusion, this study reveals that different PCD modes, especially ferroptosis, markedly elevated in LN. In addition, we provided the first in-depth analysis of the changes of different ferroptosis-related metabolic pathways in LN and found that enhanced iron metabolism pathway may be the most important factor in ferroptosis of glomerular. Finally, we identified an upregulated iron metabolism gene, CD163, that was significantly associated with ferroptosis. Due to the lack of studies on the mechanism of CD163+ tissue infiltrating macrophages in LN, we believe that ferroptosis is a very novel and promising option and direction.

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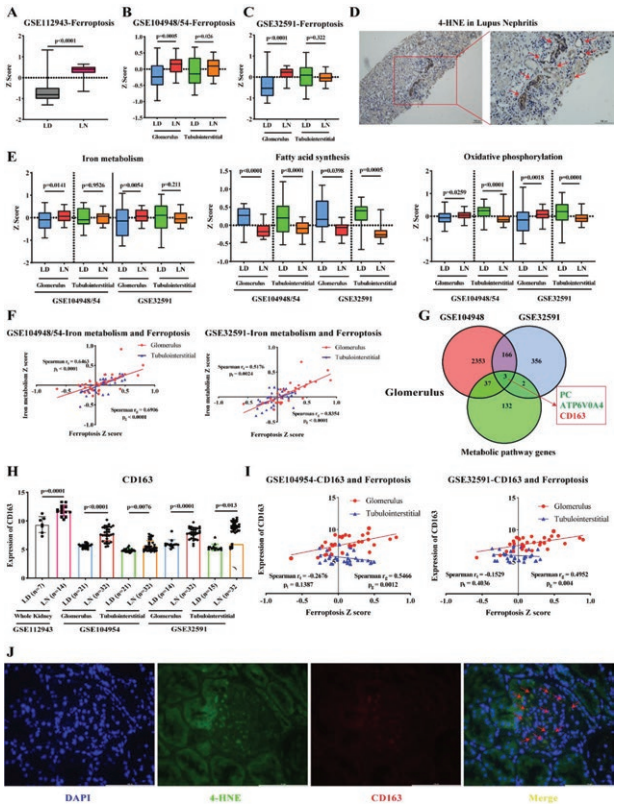


Figure 1. Ferroptosis of CD163+ tissue infiltrating macrophages in lupus nephritis.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1406 **WITHDRAWN**

POS1407

UNBALANCED LEVELS OF CIRCULATING NEUROACTIVE STEROIDS IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS: A PILOT STUDY FOR AN UNEXPLORED SCENARIO

Keywords: Gender/diversity issues, Systemic lupus erythematosus, Mental health

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Background: Sex hormones have effects on the development, progression and severity of SLE, prevalently affecting women (F:M=9:1). The neuroprotective, neurotrophic and anti-inflammatory properties of a class of progesterone-derived NeuroActive Steroids (NASs), prompted numerous investigations about the potential of these GABAA receptor allosteric modulators. However, no data about NASs on neuropsychiatric SLE (NPSLE) are available.
Objectives: This exploratory pilot study aims to delve into a new unexplored landscape by assessing circulating NASs levels in NPSLE patients.
Methods: A cohort of 16 SLE patients without NP manifestations and 16 with new onset NP diffuse symptoms was enrolled. Mood disorders and cognitive dysfunction were defined according to the Center for Epidemiologic Studies Depression Scale (CES-D) and a battery of neuropsychological tests, respectively, interpreted by a neuropsychologist. A group of 8 healthy controls (HCs) matched for mean age and gender ratio was also recruited. Exclusion criteria: ongoing contraceptive or hormonal treatment; glucocorticoid pulse or treatment variations 6-month before blood collection; anxiolitic, anticonvulsivant, antiepilettic drug intake; gonadal-adrenal surgical intervention or pathologies. Data regarding demographics, SLEDAI andSLICC organ damage index (SDI) were collected. NASs serum levels and their precursor were measured by ELISA assay, as listed: Progesterone, Diidroepiandrosterone (DHEA), Diidroepiandrosterone-Sulphate (DHEA-S), Allopregnanolone. To appreciate differences between groups, women's fertile or menopausal subgroups were formed and p-value <0.05 has been set.
Results: Table 1 reports on data from the whole cohort. Progesterone levels in fertile women were significantly higher in the NPSLE versus HCs group (p=0.011). The Progesterone-direct metabolite, Allopregnanolone, was significantly increased in NPSLE compared to both groups of fertile SLE (p=0.026) and HCs females (p=0.027). Inversely, low levels of DHEA and DHEA-S in SLE patients versus HCs (p=0.025 and p=0.005) were found. Looking for NP symptoms, DHEA titer inversely correlates with cognitive deficit diagnosis (p=0.04), while depression diagnosis (62.5% of NPSLE cohort) correlates with Allopregnanolone levels (p=0.042). Moreover, depression severity measured by the CES-D score correlates with Progesterone (r=0.550, p=0.041) and Allopregnanolone (r=0.712, p=0.004; Figure 1). At multivariate analysis after correction for age, disease duration, SLEDAI and SDI, Allopregnanolone confirmed its independent correlation (β=0.712, p=0.004) with depression severity.
Conclusion: In this pilot study, we describe for the first time the unbalanced levels of the most potent neuroactive steroid Allopregnanolone in SLE fertile patients with new onset neuropsychiatric diffuse manifestations. Moreover, in NPSLE patients, the diagnosis of cognitive deficit associates with circulating DHEA low levels and that of depression associates with Allopregnanolone high levels, significantly correlated also with the severity of this manifestation. Since the appropriate NASs balance is needed for optimal brain and neuroimmune function, our preliminary observations – that needs to be validated in an extended cohort - open a new perspective in the field, where the circulating NASs assessment in NPSLE patient could be a new promising diagnostic and preclinical research strategy.

Table 1. Demographic and clinical characteristics of the participants

	NPSLE (16)	SLE (16)	HC (8)
Age mean (DS)	48.2 (15.9)	42.1 (10.8)	49 (16)
Gender (F, %)	100	100	100
Fertile (%)	50	50	50
Menopausal (%)	50	50	50
Disease duration, yrs median (IQR)	6(2.3-9.3)	6.7(3.0-10.4)	-
SLEDAI median (IQR)	5 (1.8-11)	2 (0-4)	-
Dose PDN mg/daily median (IQR)	9.5 (5.1-14.6)	3.8 (3.2-7)	-
Cognitive disorder (%)	50	-	-
Major depression (%)	62.5	-	-

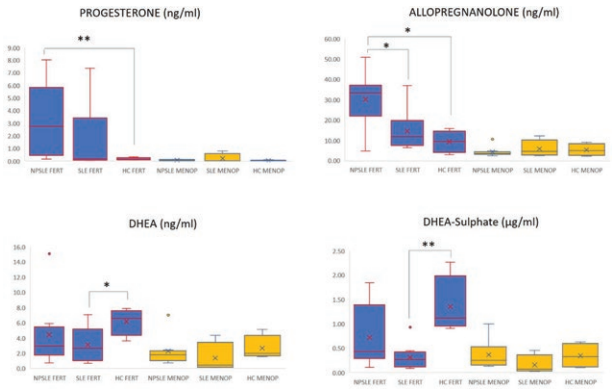


Figure 1. Median value of NASs circulating levels on NPSLE/SLE/HCs fertile and menopausal female. **pvalue* ≤ 0,05; *** pvalue* ≤ 0,01

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Disclosure of Interests: Maria Maddalena Angioni: None declared, Elisabetta Chessa: None declared, alessandra perra: None declared, elisa pintus: None declared, Alberto Floris: None declared, MATTIA CONGIA: None declared, Mauro Giovanni Carta: None declared, Alberto Cauli: None declared, Matteo Piga Speakers bureau: GSK, Consultant of: GSK, GALAPAGOS, ASTRAZENECA.
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POS1408

INTEGRATED METABOLOMICS AND PROTEOMICS NETWORK ANALYSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS HIGHLIGHTS METABOLIC AND IMMUNITY PATHWAYS ASSOCIATED WITH DISTINCTIVE CLINICAL PROFILES

Keywords: Biomarkers, -Omics, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a severe multisystem disease, notably heterogeneous in terms of clinical course and therapeutic response, which converts it into a significant challenge at the diagnostic and treatment levels.
Objectives: This study investigated the serum proteomic and metabolomic profiles of SLE, in order to identify new mechanisms underlying relevant clinical patterns.
Methods: Proteomic and metabolomic approaches were used to assess the serum levels of 184 inflammation and organ damage-related proteins [by proximity extension immunoassay (PEA, Olink)] and 250 metabolic markers [by nuclear magnetic resonance (NMR) covering glycolysis metabolites, amino acids and 130 lipid measures (NMR, Nightingale)] in consecutive SLE patients (n = 133) and age-matched healthy donors (HD) (n = 27). In parallel, an extensive clinical and analytical profile of recruited subjects was performed. To evaluate the contribution of molecular profiles to the disease severity, unsupervised clustering analyses were developed.
Results: Thirty-six proteins related to inflammation and organ damage, and 17 metabolites were coordinately altered in the serum of SLE patients in relation to HD. Unsupervised clustering analyses differentiated 2 patient clusters (C1 and C2) presenting different proteomic profiles. Clinically, although no differences were found in terms of age or disease duration, patients belonging to C1 were characterized by a significantly higher status of disease activity (SLEDAI > 6) and prevalence of positivity for anti-ENA and anti-dsDNA antibodies than patients belonging to C2, along with a preponderance of patients with biopsy diagnosed lupus nephritis (LN), abnormal creatinine and proteinuria. Besides, this cluster comprised SLE patients with higher CV risk, revealed by an elevated incidence of atheroma plaques, dyslipidemia, and hypertension. Statistical analysis between clusters revealed 67 serum proteins deregulated, among which C1

displayed elevated well-recognized inflammatory cytokines and regulatory proteins of leukocyte activity [(IFN, IL, CSF-1, LIF-R, MCP-1, MCP-4, CCL, CXCL, MMP, PDL, 4E-BP1), accompanied by proteins involved in renal damage (KIM1, LAT2, NPPC, ERBB2IP). Regarding metabolomic profile, comparative analysis between proteome clusters characterized increased levels of proatherogenic VLDL and LDL lipoprotein subsets in C1, and reduced levels of anti-atherogenic HDL lipoproteins subsets, total cholesterol, ketone bodies (acetate) and glycolysis related metabolites (lactate). Interestingly, statistical analyses showed that proteins and metabolites markers correlated significantly, suggesting potential interconnections related to different aspects of lupus pathology.

Conclusion: The present study showed a multi-omics landscape identifying molecular patterns that distinguished patients with high disease activity and lupus nephropathy, including several novel candidate proteins and metabolites markers. The study of the specific role and suitability of these mediators as SLE biomarkers would provide insights for the management of this complex autoimmune disorder.

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Disclosure of Interests: None Declared.

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POS1409 NEW INSIGHTS INTO THE ANTIPHOSPHOLIPID SYNDROME SPECTRUM: FROM ANTIPHOSPHOLIPID ANTIBODIES POSITIVE SUBJECTS PROFILING TO IDENTIFICATION OF SYSTEMIC APS SUBSET THROUGH TYPE I INTERFERON PATHWAY ACTIVATION

Keywords: Autoantibodies, Anti-phospholipid syndrome

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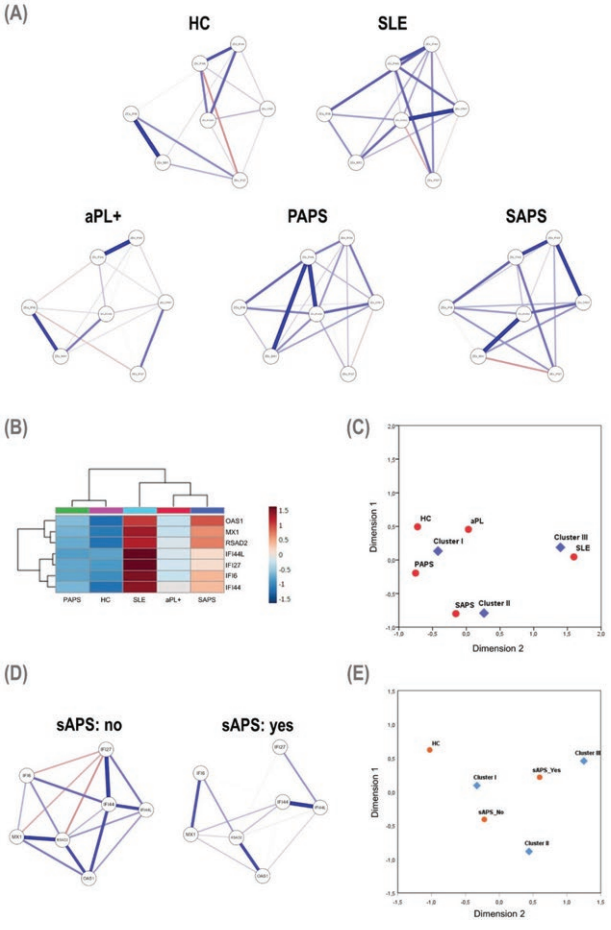


Figure 1.

Background: Type I Interferon (IFN) pathway activation plays a central role in the pathogenesis of several autoimmune conditions. However, limited evidence is available on the IFN pathway activation in antiphospholipid antibody (aPL) positive subjects, including aPL carriers and antiphospholipid syndrome (APS) patients. In addition, recent evidences have highlighted the existence of a bridging condition between pure primary APS (PAPS) and defined systemic lupus erythematosus (SLE) with higher general features, such as cytopenia and arthritis, which is known as *systemic APS* [1] and needs further clarification.

Objectives: The aim of this study was to evaluate the differential expression of IFN stimulated genes (ISG) among different subsets of aPL positive subjects.

Methods: For the purpose of this study, 31 primary APS, 25 secondary APS (SAPS), 27 SLE patients without aPL, 29 aPL carriers [2,3] and 19 healthy controls (HCs) were recruited. Complete demographic, clinical, and laboratory data were collected at the time of the inclusion. *Systemic APS* was defined as in previous papers [1]. IFI6, IFI44, IFI44L, MX1, IFI27, OAS1 and RSAD2 gene expression was evaluated by RT-PCR in whole blood. Normalized gene expression levels (Z-scores) were averaged into a global IFN signature (IFN score). Differences were measured by Kruskal-Wallis tests, and associations among genes were studied by cluster, correspondence and network analyses.

Results: An overall IFN pathway activation was noted across APS subsets, but certain differences were noted among genes. Some genes were already upregulated in the aPL-positive group compared to HC (IFI44, IFI44L, MX1, IFI27, OAS1 and RSAD2, all $p<0.050$), while others were only increased in SLE (IFI6). MX1 differed between SLE and SAPS, whereas IFI27 and OAS1 showed differences between PAPS and SAPS. The composite IFN score revealed quantitative differences across APS subsets, being elevated in aPL carriers/PAPS groups compared to HCs (both $p<0.050$) and increasing in SAPS ($p<0.010$) and SLE ($p<0.001$). Network analyses (Figure 1A) revealed qualitative differences in the gene-gene correlation networks: (i) weaker structures were found in HCs and aPL carriers, compared to stronger and higher-degree networks in SAPS and SLE; and (ii) the influence of each node was different across groups. Unsupervised cluster analysis revealed 3 clusters (Figure 1B), whose usage differed across APS subsets, thus correlating clinical status (Figure 1C). *Systemic APS* (n=51) was hallmarked by a higher IFN pathway activation ($p=0.032$) which was attributed to the expression of certain genes (IFI6, IFI44, IFI44L and IFI27; all $p<0.050$), compared to those without *systemic APS*. Gene-gene interactions also showed differences between subsets (Figure 1D). Individuals with *systemic APS* were more likely to use cluster III ($p=0.042$) (Figure 1E).

Conclusion: IFN pathway activation is a common hallmark among aPL-positive individuals as well as in *systemic APS*, in which a differential and unique expression of ISG has been observed. Qualitative and quantitative differences across the APS spectrum can be identified, leading to the identification of distinct IFN signatures with different clinical value beyond traditional categorization.

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Disclosure of Interests: None Declared.

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POS1410 PROTEOMIC ANALYSIS OF CUTANEOUS LUPUS ERYTHEMATOSUS AND DERMATOMYOSITIS DERMAL INFILTRATE REVEALS DIFFERENTIALLY EXPRESSED CANONICAL PATHWAYS

Keywords: Skin, Systemic lupus erythematosus, Myositis

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Background: Cutaneous lupus erythematosus (CLE) and dermatomyositis (DM) are autoimmune diseases with characteristic cutaneous rashes. Both are histopathologically characterized by interface dermatitis and they are difficult and sometimes impossible to differentiate based on skin biopsies. The specific pathogenesis of both conditions remains enigmatic.

Objectives: To systematically identify patterns of protein expression in CLE and DM dermal infiltrate that differentiate the two conditions from each other.

Methods: Punch biopsies were obtained from lesional skin from 6 patients with CLE and 5 patients with DM. Healthy or unaffected skin from 6 individuals was used as control material. Laser capture microdissection was used to isolate 1,000,000µm2 of tissue within the LE and DM dermal inflammatory infiltrates or control dermis. The samples were analyzed by nano-LC tandem mass spectrometry. Qiagen Ingenuity pathway analysis was performed based on the obtained proteomic database, and identified canonical pathways were compared between CLE, DM, and controls.

Results: Comparing CLE vs controls we identified 246 pathways, while 51 of them were enriched (threshold $p<0.05$). Comparing DM vs controls 200 pathways were identified, while 72 were enriched. Canonical pathways enriched in both CLE and DM were those involved in antigen presentation, protein ubiquitination, acute phase response, interferon signaling, GP6 signaling, tRNA charging, and B cell development. Analysis of CLE vs DM showed 237 pathways, 70 of which were enriched ($p<0.05$). The top differentially enriched canonical pathways in CLE compared to DM included EIF2 signaling, complement system, LXR/RXR and FXR/RXR activation, acute phase response signaling, mTOR and granzyme A signaling, clathrin mediated endocytosis signaling, and coagulation system.

Conclusion: Canonical pathways enriched in both CLE and DM skin are associated with activation of innate and adaptive immune systems, including the interferon system. A major difference between CLE and DM was that the EIF2 pathway, involved in cellular stress and induction of cell death, was enriched in CLE. Enriched granzyme A signaling indicates cytotoxic T lymphocyte activity in CLE, which is in line with that the top differentially upregulated cytokine in CLE in the proteomics was IL-16 (1), as CD8 T lymphocytes are well-described expressors of IL-16. Further, results indicate differentially activated metabolic pathways and deposition of complement and coagulation components in CLE dermal infiltrate.

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POS1411 **WITHDRAWN**

POS1412 **MULTIPARAMETRIC COMPARISON OF THE ADULT-ONSET AND CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IMMUNOMES REVEALS MULTIPLE DERANGEMENTS**

Keywords: Artificial intelligence, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a complex, systemic autoimmune disease. Disease presentation is heterogeneous and characterized by alternating flares and remissions. Recent treatment developments have been made with FDA approval of anifrolumab for adult SLE in 2021 [1] but there are many patients with inadequate therapeutic response. Furthermore, with lack of specific molecular therapeutic targets, current therapy relies mainly on general immunosuppression. This can adversely affect bone health and impede growth of childhood-onset SLE patients. Treatment for paediatric patients is extrapolated from adult studies with the assumption that underlying immunopathogenic mechanisms are similar. However, children are not little adults and a better

understanding of underlying disease mechanisms using a holistic and multiparametric approach is needed to improve current theragnostics.

Objectives: We aim to use a high-dimensional approach to characterise and compare immune signatures of adult-onset and childhood-onset SLE patients, as well as compare their immunological profiles with age-matched healthy controls. In the process, we hope to study the roles of B and T cells in SLE to better understand the adaptive immune response.

Methods: Peripheral blood mononuclear cells from adult-onset and childhood-onset SLE patients underwent mass cytometry. The adult-onset SLE group consists of 26 SLE (timepoints: 40, median age: 40 years) and 23 age-matched healthy subjects. The childhood-onset SLE group consists of 30 SLE (53, 14 years) and 17 age-matched healthy subjects. Data was analysed and visualized using the Extended Polydimensional Immunome Characterisation (EPIC) machine learning platform [2]. Normalization and FlowSOM clustering were performed with 43 functionally and phenotypically important immune markers. Mann Whitney U test identified significantly different cluster frequencies.

Results: Unsupervised analysis revealed multiple significant differences ($p<0.05$) between the adult-onset and childhood-onset SLE immunomes. Of note, an activated $CD11c^+Tbet^+CD21^-$ B cell subset was significantly enriched in childhood-onset SLE (median: 0.42%, interquartile range 0.16-0.72% of $CD45^+$ PBMCs) versus adult-onset SLE (0.15%; 0.09-0.31%; $p<0.001$). These age-associated B cells (ABCs) increase in prevalence with age and presence of autoimmune disease. A significant increase in childhood-onset SLE may offer us insights into the differences with adult-onset SLE; the former group tends to have more active disease over time. Transitional B cells ($CD24^+CD38^+$) were also significantly increased in childhood-onset SLE (0.91%; 0.41-1.84%) compared to their adult counterparts (0.3%; 0.043-0.65%; $p<0.001$). In the T cell compartment, an activated $CD4^+IL21^+$ subset was expanded in childhood-onset SLE (0.41%; 0.23-0.68%) compared to adult-onset SLE (0.19%; 0.1-0.38%; $p<0.001$). IL21 plays a key role in B cell activation and this cell subset is therefore of mechanistic interest. Another $CD8^+CD45RA^+BAFF^+$ T cell subset was enriched in adult-onset (1.95%; 1.24-2.86%) versus childhood-onset SLE (0.88%; 0.45-1.37%; $p<0.001$). B-cell activating factor (BAFF) supports autoreactive B cell survival in autoimmune disease and an anti-BAFF drug (belimumab) is FDA-approved for SLE. Despite increasing use of belimumab, not all patients respond equally, so BAFF inhibition alone may not adequately alter disease activity.

Conclusion: With a multiparametric unbiased approach comparing adult and paediatric SLE patients, we identified cell subsets that may be of immunopathogenic importance. Studying these cell interactions in further detail may identify pathological pathways to facilitate improvements in SLE theragnostics.

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POS1413

PRECLINICAL EVIDENCE FOR THE GLUCOCORTICOID-SPARING POTENTIAL OF A DUAL TLR7/8 INHIBITOR IN AUTOIMMUNE DISEASES

Keywords: Tapering, Cytokines and chemokines, Systemic lupus erythematosus

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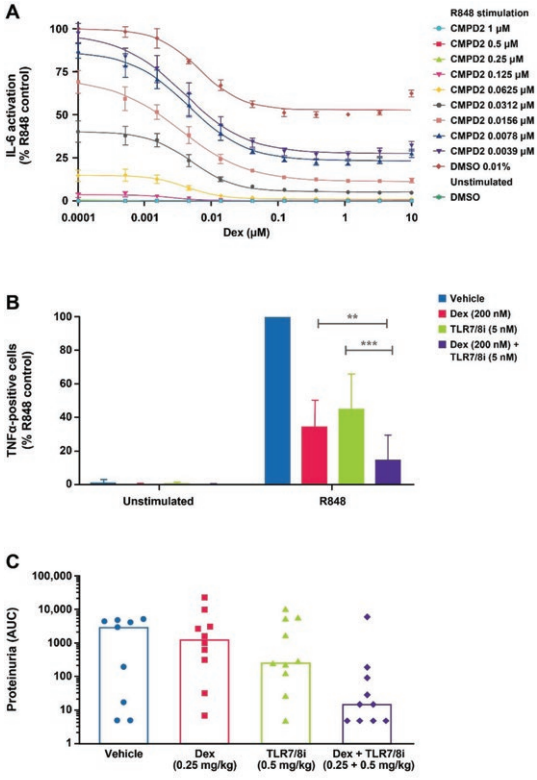
Background: Toll-like receptor 7 (TLR7) and TLR8 are single-stranded RNA-sensing endosomal pattern recognition receptors that evolved to defend against viral infections, however their dysregulation and activation by endogenous ligands has been implicated in autoimmune diseases including lupus. While glucocorticoids (GC) are effective, they have many undesirable effects that limit their use. In addition, resistance to GC, which was recently shown to be imparted by TLR activation and Type I interferon (IFN), is a major challenge for the treatment of patients with autoimmune diseases including lupus. New treatment approaches that allow for the use of lower doses of GC would be highly beneficial.

Objectives: To evaluate the GC-sparing effects of a dual TLR7 and TLR8 inhibitor (TLR7/8i).

Methods: Human peripheral blood mononuclear cells (PBMC) from healthy donors were treated with TLR7/8i, dexamethasone, or both. Cytokine production was measured using an AlphaLISA immunoassay, gene expression was analyzed by NanoString and single-cell RNA sequencing, and effects on protein markers were evaluated by flow cytometry. In addition, the efficacy of combined TLR7/8i and dexamethasone treatment was evaluated in the MRL/*lpr* mouse model of lupus.

Results: Studies in human PBMCs revealed synergistic effects of TLR7/8i and GC on inflammatory cytokine production resulting in increased GC potency in the presence of TLR7/8i (Figure 1A), an effect that was most pronounced in myeloid cells, especially monocytes (Figure 1B). Gene expression analysis revealed that the combination of TLR7/8i plus GC substantially impacted myeloid cell clusters, particularly modules for IFN and GC response genes, as well as nuclear factor-kappa B-regulated cytokines. Treatment with TLR7/8i and GC *in vivo* was more efficacious then either agent alone, as evidenced by reduced proteinuria (Figure 1C) and improved survival.

Conclusion: These results demonstrate that TLR7/8 inhibition increases the potency of GC by alleviating TLR activation-dependent GC resistance in a cell type-specific manner. Our findings suggest a GC-sparing potential for TLR7/8i compounds and indicate that TLR7/8 inhibition may offer a new therapeutic strategy for the treatment of autoimmune diseases. The safety, efficacy and GC-sparing effect of the TLR7/8i enpatoran is being evaluated in patients with systemic and/or cutaneous lupus erythematosus in the randomized, double-blind, placebo-controlled Phase II WILLOW study (NCT05162586), which has a mandatory GC tapering schedule.



**p<0.005; ***p<0.0005. AUC, area under the curve; Dex, dexamethasone; CMPD2, compound 2; DMSO, dimethylsulfoxide; HC, healthy controls; IL-6, interleukin-6; PBMCs, peripheral blood mononuclear cells; TLR7/8i, toll-like receptor 7/8 inhibitor; TNFα, tumor necrosis factor alpha.

Figure 1. Dexamethasone and TLR7/8i have synergistic effects on (A) IL-6 production in R848-stimulated PBMCs, (B) TNFα production in monocytes, and (C) proteinuria in a mouse model of lupus.

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Disclosure of Interests: Ankita Deshmukh Employee of: EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Albertina Pereira Employee of: EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Nicholas Geraci Employee of: EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Evgeni Tzvetkov Employee of: EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Melinda Przetak Employee of: EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Michelle Catalina Employee of: EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Eric F. Morand Consultant of: EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Grant/research support from: EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Andrew Bender Shareholder of: Merck KGaA, Darmstadt, Germany, Employee of: EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Bharat Vaidyanathan Employee of: EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA.
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POS1414 TYPE I INTERFERONS INDUCE TIE2-MEDIATED ENDOTHELIAL CELL DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Cytokines and chemokines, Cardiovascular disease

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Background: Endothelial cell (EC) dysfunction is a hallmark of Systemic Lupus Erythematosus (SLE) and has been generally accepted to be one of the important factors contributing to the higher risk of thrombosis and atherosclerotic events observed in SLE patients. Although the presence of traditional factors (smoking, diabetes, increased age, obesity) and the presence of autoantibodies are associated with atherosclerosis and thrombotic events, they do not completely explain the higher risk of these events in SLE, suggesting the existence of other mechanism/factors. Tie2 is a tyrosine kinase receptor essential for vascular development and blood vessel remodeling through interaction with its ligands angiopoietin-1 (Ang-1) and Ang-2. In homeostatic conditions, both Ang-1 and Ang-2 activate Tie2 signaling and induce vascular stabilization in a Tie1-dependent manner. However, inflammatory processes induce Tie1 cleavage, leading to the inhibition of Ang-1-induced Tie2 activation, and to the increase of Ang-2 now acting as a Tie2 antagonist, culminating in vascular dysfunction and EC activation [1,2]. Importantly, this process has been implicated in both atherosclerosis and thrombosis.
Objectives: As type I Interferons (IFN-α and IFN-β) are key cytokines in the pathogenesis of SLE, the aim of this study is to determine whether these cytokines induce Tie2 signaling-mediated endothelial cell dysfunction.
Methods: Serum levels of Ang-1, Ang-2 and sTie1 in SLE patients (n=48) and healthy control (HC, n=29) were measured by ELISA. Human Umbilical Vein EC (HUVEC) were stimulated with SLE serum (20%), IFN-α and IFN-β (1000 IU) for 5, 15, 30 min and 1, 2, 4, 6, 8, 12, 24, 48 and 72 hours and mRNA and protein expression of Ang-1, Ang-2, Tie1 and Tie2 were determined by quantitative PCR (qPCR) and ELISA, respectively. The phosphorylation of Tie2 was determined by *Western Blot* and HUVEC viability by calcein assay. The angiogenic capacity was measured by tube formation assay. Silencing assays were performed with siRNAs addressed to IFNAR1 and Tie1 receptors.
Results: Type I IFNs, mainly IFN-β, significantly reduced *TIE1* and *TIE2* levels. IFN-β stimulation significantly increased the secretion of the Tie1 ectodomain (sTie1). Both IFNs significantly reduced protein secretion of Ang-1 after 24h of stimulation. Also, IFN-β induced Ang-2 secretion at early time points (<4h). Furthermore, IFN-α and IFN-β stimulation reduced Tie2 activation (Figure 1). Both type I IFNs significantly reduced the viability of HUVEC. SLE serum increased Ang-2 and sTie1 secretion levels in HUVEC at early time points (<1h). We found reduced levels of Ang-1 and elevated Ang-2 and sTie1 in SLE patients compared to HC. Also, IFN-β induced tube formation at short times (4h) and decreased at 24h. Remarkably, this effect was reversed by silencing the receptors Tie1 and IFNAR1.

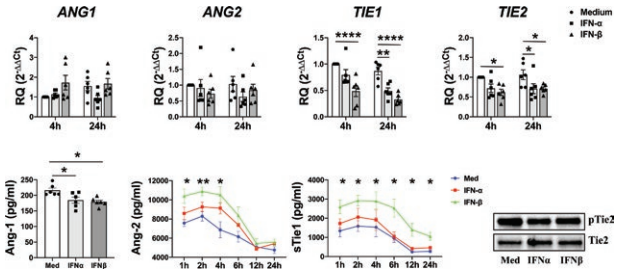


Figure 1. Ang-1, Ang-2, Tie1 and Tie2 mRNA expression and protein secretion in HUVEC stimulated with IFN-α or IFN-β (1000 IU/ml) for the indicated time points. Means and SEM are shown. * p<0.05, ** p<0.01 and **** p<0.0001. Also, representative immunoblot of Tie2 phosphorilation in HUVEC stimulated with IFN-α or IFN-β (1000 IU/ml) for 24 h is shown.

Conclusion: Our results demonstrate that type I IFNs play a relevant role in the stability of endothelial cells by inhibiting Tie2 signaling, suggesting that these processes may be implicated in the cardiovascular events observed in SLE patients.

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POS1415 ENDOTHELIAL INFLAMMAGING AND MITOCHONDRIAL DYSFUNCTION IN THE ANTIPHOSPHOLIPID SYNDROME

Keywords: Anti-phospholipid syndrome, Cardiovascular disease

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Background: Inflammageing, vascular ageing and mitochondrial dysfunction are important contributors to cardiovascular risk in the rheumatic diseases. In antiphospholipid syndrome (APS), endothelial dysfunction is underpinned by a thrombo-inflammatory state mediated by antiphospholipid antibodies (aPL). The contribution of endothelial senescence and metabolic disturbances is not known.
Objectives: To assess senescence, inflammation and metabolic function in *ex vivo* blood derived endothelial colony forming cells (ECFC), a novel source of patient endothelium.
Methods: ECFC were isolated from PBMC of 17 thrombotic APS and 11 healthy control (HC) donors, cultured in endothelial growth media containing 20% FBS. ECFC frequency, days from PBMC seeding to first colony appearance and days to initial passage (from P0 to P1) were similar between APS and HC. ECFC were phenotyped at P4 by flow cytometry (CD31+/CD144+/CD146+/CD14-/CD45-) and assayed at P4-P5. Proliferation was measured by fluorescent EdU incorporation. Senescence was determined by staining for senescence-associated β-galactosidase activity (SA-βgal) and nuclear DAPI, expressed as % senescent cells against total cell number. Mitochondrial function and glycolysis were assessed in live cells using extracellular flux assays (Seahorse). Molecular analysis was informed by RNA-seq (5 APS, 5 HC) and targets validated in the extended cohort at the mRNA and protein level. Data was analysed by non-parametric Mann-Whitney, ANOVA and Spearman's correlation tests.
Results: Impaired proliferative capacity and a greater proportion of senescent cells were observed in APS *vs* HC ECFC (median % senescent, 13.1% *vs* 7.9%) (p=0.02). RNA-seq analysis revealed 266 differentially expressed genes in APS ECFC (188 up, 78 down) primarily representing elevated inflammatory cytokines, chemokines, cell adhesion and fibrosis-remodelling molecules. Target validation at the mRNA level confirmed a hypoproliferative inflammatory phenotype in APS; elevated genes included *CDKN2A*/p16 (late senescence), *GADD45B* (growth arrest, DNA damage); *IFNA1* (cytokine), *CXCL10* (chemokine), *CD274*/PDL1 (exhaustion), *PTX3* (fibrosis-remodelling), *SERPINE1* (fibrinolysis-remodelling), *EDN1* (vasoconstrictor), all p<0.05. A positive correlation was noted between senescent and inflammatory gene expression (e.g. *p16 vs CXCL10*, r=0.4,

p=0.03). Upregulation of selected targets was confirmed at the protein level (e.g. p16 and PDL1 by flow cytometry, APS *vs* HC p=0.002 and p=0.03 respectively). Diminished mitochondrial respiration and ATP production (p<0.01) coupled with elevated glycolysis (p=0.02) was seen in APS *vs* HC ECFC. Mitochondrial parameters positively correlated with proliferative capacity (r≥0.5, p<0.01) and negatively correlated with senescence and inflammation (r≤-0.4, p<0.05), indicating a relationship between endothelial health and mitochondrial function. Glycolysis negatively correlated with proliferation (r=-0.6, p<0.01). Comparing ECFC from patients with previous cardiovascular events (CVE, n=9) *vs* those without (no-CVE, n=8) revealed more pronounced senescence and mitochondrial dysfunction in CVE, while greater loss of proliferative capacity was observed in no-CVE. Inflammatory markers varied between the two patient groups e.g. PTX3 was higher in CVE and CXCL10 in no-CVE. Collectively, these observations suggest different underlying biological processes in patients with severe thrombotic complications compared to those without.

Conclusion: We propose APS as a paradigm disease for immune-mediated endothelial ageing, defined by a hypoproliferative-senescent, inflamed and metabolically perturbed phenotype. Evidence for a more severe dysfunctional phenotype in ECFC from patients with CVE compared to no-CVE, agrees with published studies associating vascular ageing and mitochondrial damage with cardiovascular risk. Ongoing work is assessing the impact of *ex vivo* treatment with IgG aPL, cytokines and relevant drugs capable of modulating senescence and immunometabolic processes.

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POS1416 IL-6, IL-8, TNF-A ARE SIGNIFICANTLY INCREASED IN CEREBROSPINAL FLUID AND ASSOCIATED WITH ALTERATIONS OF EYE SIGN IN PATIENTS WITH NEUROPSYCHIATRIC LUPUS ERYTHEMATOSUS

Keywords: Biomarkers, Systemic lupus erythematosus, Cytokines and chemokines

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Background: Several pro-inflammatory cytokines such as interleukin (IL)-6, IL-8 have been implicated in the pathogenesis of in patients with neuropsychiatric systemic lupus erythematosus (NPSLE) [1]. The alterations of eye sign has been reported and correlated with disease activity in NPSLE [2].

Objectives: To ascertain whether the intrathecal levels of cytokines/chemokines relative to serum levels is associated with microvacular changes of eye sign in the patients with neuropsychiatric systemic lupus erythematosus (NPSLE).

Methods: SLE Patients (>18 years) were consecutively enrolled, for whom the cerebrospinal fluid (CSF) and serum samples were collected at the same time, 6 kinds of cytokine/chemokine concentrations in the CSF and serum samples were measured by Chemiluminescent Immunoassey. The diagnosis of NPSLE was evaluated and based on the consensus from rheumatologist, neurologist, radiologist and psychiatrist. Bulbar conjunctival microvascular changes in eye sign were performed and scored for all SLE patients by rheumatologist using our criteria. NP assessments were evaluating in all SLE patients by psychiatrist, including the mini-mental state examination (MMSE), self-rating anxiety scale (SAS), self-rating depression scale (SDS). Demographic and clinical data were compared between two groups and to identify potential predictors for NPSLE by using multivariable logistic regression analysis.

Results: 120 SLE patients were recruited (30 [24-41] years) including 30 NPSLE and 90 non-NPSLE. In multivariable logistic analysis, total score of eye sign in model 1 and ramified loops, microangloma and wound spot of eye sign in model 2 were predictors for NPSLE after adjusting SLEDAI (Table 1). A significant positive correlation between IL-6, IL-8, TNF-α in CSF and total score microangioma in eye sign and between TNF-α in CSF and ramified loops, wound spot in eye sign were found (Figure 1), moreover, significant positive correlation between IL-6, IL-8, TNF-α in CSF and SLEDAI were also observed (r=0.35, p<0.001, r=0.43, p<0.001, r=0.22, p=0.027, respectively), while no significant positive correlation was observed between CSF levels and serum levels of each cytokine/chemokine in these 120 SLE patients.

Conclusion: In NPSLE the production of IL-6, IL-8, TNF-α in CSF might take place in the nervous system, especially in active disease state. These increased CSF cytokines/chemokines along with ramified loops, microangioma and wound spot in eye sign might have an interaction and prerequisite role in the pathogenesis of NPSLE.

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Table 1. Multivariable logistic regression analysis of predictors for developing NPSLE.

	Model 1		Model 2	
	OR 95%CI	P value	OR 95%CI	P value
ACCI	3.94 (0.82-18.89)	0.087	8.43 (0.96-74.22)	0.055
aPL	10.43 (0.65-166.61)	0.097	7.50 (0.18-319.42)	0.292
Rp	3.83 (0.47-31.41)	0.211	40.93 (0.36-4607.34)	0.124
SLEDAI	1.53 (0.98-2.38)	0.061	1.59 (1.01-2.50)	0.044*
ESR	0.97 (0.88-1.08)	0.616	0.99 (0.87-1.08)	0.992
MMSE	1.27 (0.79-2.03)	0.321	1.26 (0.62-2.57)	0.525
SAS	0.95 (0.87-1.04)	0.239	0.97 (0.87-1.08)	0.645
SDS	1.01 (0.92-1.10)	0.902	0.97 (1.03-1.11)	0.547
Ramified loops			39.54 (1.06-1472.48)	0.046*
Vascular tone			0.74 (2.63-157.60)	0.945
Microangloma			5.85 (1.23-27.92)	0.027*
Wound spot			6.95 (1.04-46.25)	0.045*
Total score	3.68 (1.62-8.36)	0.002*		

*Statistically significant at p <0.05.ACCI: age adjusted Charlson Comorbidity Index; aPL: Antiphospholipid antibody; Rp: Raynauds' phenomenon; SLEDAI: Systemic lupus erythematosus disease activity index; ESR: Erythrocyte sedimentation rate.

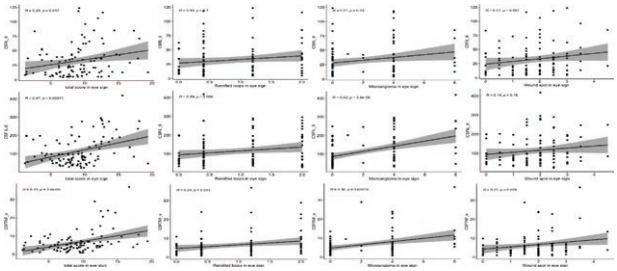


Figure 1. The association between IL-6, IL-8, TNF-α in CSF and predictors of eye sign for NPSLE.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1417 CATEGORIZATION OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS USING DISEASE ACTIVITY, PATIENT-REPORTED OUTCOMES AND TRANSCRIPTOMIC SIGNATURES

Keywords: Systemic lupus erythematosus

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Background: Patients with systemic lupus erythematosus (SLE) display symptoms that are not always related to disease activity and may distort clinical trial results. Recently, a clinical categorization based on the presence of type 1 (inflammatory manifestations) and/or type 2 (widespread pain, fatigue, depression) symptoms has been proposed in SLE (1) and tested in a cohort of 212 patients [2]. This allowed the categorization of patients at the time of clinical assessment into four distinct groups: “type 1”: patients displaying only type 1 symptoms; “type 2”: patients displaying only type 2 symptoms; “mixed”: patients displaying both type 1 and type 2 symptoms; “minimal”: patients with no symptoms. This classification was built upon the SLEDAI score (type 1 symptoms), which is widely available in SLE studies, and on American College of Rheumatology fibromyalgia criteria (type 2 symptoms), which are less commonly used in SLE and are rarely available.

Objectives: Our aim was to develop a type 2 score derived from the Short-Form health survey (SF-36) to categorize SLE patients and to compare immunological and transcriptomic profiles between groups.

Methods: Seventeen items from the SF-36 were selected to build a type 2 score for 50 SLE patients (100 visits; LUPUCE cohort) and the SLEDAI was used to define type 1 symptoms. Patients were categorized in four groups: minimal (no symptoms), type 1, type 2 and mixed (both type 1 and type 2 symptoms).

Clinical, immunological and transcriptomic profiles (3) were compared between the groups. The PSY-LUP cohort (from a study evaluating the psycho-social consequences of SLE) (4) was an independent cohort used to confirm the results found in the LUPUCE cohort.

Results: Type 2 scores ranged from 0 to 31, with a cut-off value of 14 (75th percentile) that was the chosen threshold to define the type 2 symptoms. The sample categorization was: minimal in 39%, type 1 in 37%, type 2 in 9% and mixed in 15%. The type 2 score was calculated in an independent cohort of 100 SLE patients (PSY-LUP cohort). This showed a similar pattern of values to the LUPUCE cohort: the score ranged from 0 to 33, and 23% of patients were above the threshold of 14. Type 2 patients were older than minimal patients (52 vs. 31 years, p=0.016) and had a longer disease duration than type 1 and mixed patients (10 vs. 5 years and 10 vs. 2 years, p=0.011, respectively). Immunological data (elevated anti-dsDNA antibodies, anti-dsDNA level, low C3 and/or C4) and modular interferon (IFN) signatures (modular IFN score, number of activated IFN modules and level of regulation of each IFN module) did not differ between the groups.

Conclusion: Patients with SLE can be categorized into four clinical groups using the SLEDAI score and our SF-36-derived type 2 score. This categorization is non-redundant with immunological or transcriptomic profiles and could prove useful to stratify patients in clinical trials.

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POS1418 ANTIGEN-SPECIFIC T-CELL DYNAMICS AND MULTIDIRECTIONAL IMMUNE DYSREGULATION IN SLE

Keywords: Biomarkers, Systemic lupus erythematosus, Adaptive immunity

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Background: Systemic lupus erythematosus (SLE) is associated with autoimmune and allergic events along with impaired defensive responses. Dysregulated T-cell responses might account for this evidence but antigen-specific T-cell behaviour in SLE has not been characterised.

Objectives: To test for clinical/pathophysiological correlates of SLE immune dysfunction by characterising CD4+ T-cells selectively recognising key SLE-related, major histocompatibility complex (MHC)-restricted epitopes.

Methods: Human leukocyte antigen (HLA) DRB1*03:01 or 11:01-positive subjects were selected from a cohort of 222 patients with SLE and compared with patients with Takayasu's arteritis (TAK) and healthy controls (HC). *In silico* analyses through the Immune Epitope Database identified suitable HLA-peptide epitope pairs from a shortlist of autoantigens (histone H3 and H4), allergens (penicilloylated albumin) and pathogen-derived antigens (Epstein-Barr virus, EBV, nuclear antigens) based on the cohort clinical/serological profile. Fluorochrome-conjugated epitope-bound MHC tetramers were eventually built and used to detect antigen-specific CD4+ T-cells through flow cytometry. T-cell differentiation was assessed by CD45RA, CD62L and CD95 and polarisation by CD25, CD127, CD183, CD196 and CD194 staining. Epitope-specific reactivity was validated by multi-cytokine release assays and measurement of CD40L, CD137, OX40 and CD69 expression upon T-cell stimulation with the study peptides. SLE disease activity index 2000 (SLEDAI-2K) and lupus low disease activity state (LLDAS) were used to assess activity and remission.

Results: Total stem-cell memory T-cells (T_{SCM}) were expanded in SLE compared to control groups. Histone-specific CD4+ T-cells were selectively found in SLE and clustered with anti-DNA antibodies. Only patients with beta-lactam allergy had anti-penicilloylated albumin T-cells. Anti-EBV-specific T cells were found in patients and controls (**Figure 1A-C**). Antigen-specific T-cell counts were reciprocally correlated. Histone-specific regulatory T-cells (Treg) were inversely correlated with SLEDAI-2K. Circulating histone- and EBV-specific effector memory T-cells (T_{EM}) and Treg were lower in active SLE (**Figure 1D-F**). EBV-specific T_{SCM} decreased in patients transitioning from remission to active SLE. Immunosuppressive treatment was associated with expanded CD4+ histone-specific T-cells. *In vitro* T-cell reactivity assays to study epitopes were consistent with *ex vivo* evidence. Higher IL17F and IL5 were released in response to histones and higher IL5 and IL22 in response to penicilloylated albumin-peptides in SLE. Defective anti-EBV IFNγ, TNF and IL22 release was observed in active SLE compared to HC.

Conclusion: Histone-specific T-cell responses constitute a hallmark of SLE and might defectively be regulated during active disease, promoting autoreactive effector peripheralisation into target tissues. Dysfunctional T-cell reactivity to EBV might also subtend a constitutional defect in the control of endogenous or exogenous viral stimuli and possibly contribute to autoreactivity through misdifferentiation of precursors. Aberrant responses to beta-lactam might also synergise with autoreactive responses and can accurately be detected through penicilloylated-albumin peptide T-cell reactivity. Antigen-specific (rather than total) T-cell dynamics might faithfully reflect the occurrence of key pathogenic events accounting for SLE immune dysfunction in response to multiple types of antigens and efficiently be used to track SLE phenotype heterogeneity.

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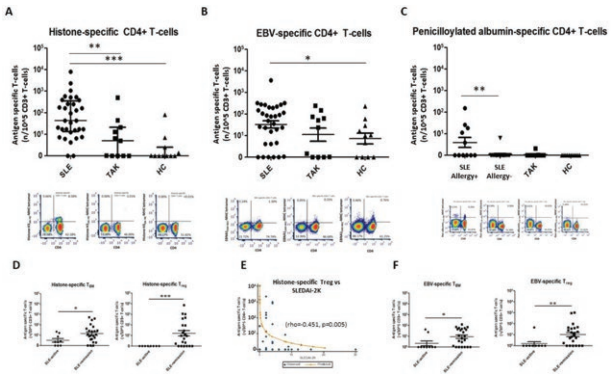


Figure 1.

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POS1419

SINGLE CELL ANALYSIS REVEALING THE LECTIN BINDING PATTERN OF T-CELLS, NKT-CELLS, NK CELLS, B-CELLS AND MONOCYTE SUBSETS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus

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Background: Cell surface glycosylation serves as a binding platform for endogenous lectin families such as galectins (Gals) or sialic acid immunoglobulin-like lectins (Siglecs) with well-known immunoregulatory functions. Several studies, including our own work [1], have shown that Gals play an important role in pathogenesis of systemic lupus erythematosus (SLE) in animal models but their contribution to human SLE must be better elucidated. For these lectins to act, the appropriate glycan structures should be available on the target cells and should not be masked by alpha-2,6-sialylation which prevents binding of Gal-1, but not Gal-3. Although cancerous diseases are well-characterized by an altered glycome, limited information regarding cell surface glycosylation is gathered for autoimmune diseases like SLE.
Objectives: In the current study, we aim to analyse the ability of certain immune subsets to bind Gal-1, Gal-3, sialic acid binding C-type lectin (Siglec-1), the fucose binding *Aleuria aurantia* lectin (AAL), the sialic acid binding *Sambucus nigra* Agglutinin (SNA) lectin in SLE patients versus healthy controls.
Methods: We collected peripheral blood mononuclear cells (PBMCs) from 19 new or relapsing SLE patients with active disease (mean age: 47.5, SLEDAI-2K:15.8, anti-dsDNA level: 76.4 IU/ml) with no or minimal immunosuppressive therapy and 19 healthy age-matched controls. Multicolor antibody panel was designed to identify the main peripheral immune subsets: CD4+T-cells, CD8+ T-cells, CD4-/CD8- T-cells, CD4+/CD8+ T-cells; CD4+NKT-cells, CD8+NKT-cells, CD4-/CD8-NKT-cells, CD4+/CD8+NKT-cells; CD56+ NK cells; naive B-cells, memory B-cells, plasmablasts; classical monocytes, non-classical monocytes and intermediate monocytes. The five lectins (Gal-1, Gal-3, Siglec-1, AAL, SNA) were conjugated with different fluorophores for FACS. The binding of fluorochrome labelled lectins to each of these populations was assessed simultaneously by flow cytometry directly after thawing (resting state) and following activation. In case of T-cells, activation was achieved by a polyclonal activator (CytoStim), while B-cells and monocytes were activated by LPS.
Results: In our experiments with control PBMCs, titration and compensation of both antibodies and lectins were carried out and gating strategies were built to identify the above-mentioned immune subsets and their lectin binding characteristics. There were remarkable differences in lectin binding among different immune populations, e.g. classical and intermediate monocytes outperformed non-classical monocytes and lymphocytes in all lectin binding. Interestingly, naive B-cells were more sialylated (Median Fluorescence Intensity(MFI_{SNA}:2737) and bound less Gal-1 (MFI_{Gal-1}:5730) than both memory B-cells (MFI_{SNA}:2368; MFI_{Gal-1}:16189) or plasmablasts (MFI_{SNA}:1263; MFI_{Gal-1}:16515). Similarly, highest SNA (MFI_{SNA}:144) and lowest Gal-1 (MFI_{Gal-1}:3658) binding was observed for CD4+ T-cells among the analysed T-cell subsets (MFI_{SNA} range:12-120; MFI_{Gal-1} range: 4201-5460) or NK cells (MFI_{SNA} not detectable; MFI_{Gal-1}:14288) or NKT-cells (MFI_{SNA} range: not detectable-108; MFI_{Gal-1} range:3580-6327).
Conclusion: The focus of this study is to identify relevant changes in the cell surface glycosylation of SLE immune subsets which is a unique approach and could contribute to a better understanding of the glycobiology of lupus.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1420

INCREASED INTERLEUKIN-6 (IL-6) RECEPTOR SHEDDING UNDER INTERFERON-α AND IL-6 EXPLAINS LOW C-REACTIVE PROTEIN (CRP) LEVELS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Keywords: Cytokines and chemokines, Systemic lupus erythematosus, Biomarkers

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Background: In active SLE, CRP levels are disproportionally low for increased IL-6 levels. While a molecular explanation is lacking, these low CRP levels have been found associated with increased type I interferon signature in SLE. IL-6 signalling requires gp130 and IL-6 receptor-α (IL-6R). Leukocytes and hepatocytes carry surface IL-6R (CD126). Other cells express only gp130 and require soluble IL-6R receptor (sIL-6R) for IL-6 signalling. This sIL-6R derives from membrane-bound CD126 shedded by metalloproteinases.
Objectives: To comprehensively analyze IL-6 and its signal transduction via signal transducer and activator of transcription (Stat) 3 in patients with SLE and in healthy individuals (HC).
Methods: We analyzed peripheral blood mononuclear cells (PBMC) and sera of 41 SLE patients and 71 HC. IL-6 and soluble IL-6 receptor (sIL-6R) were measures by ELISA. CD126 was stained with phycoerythrin (PE)-labelled antibodies. PBMC were stimulated with recombinant human IL-6, fixed, permeabilized and stained with PE-labelled antibodies to phosphorylated Stat3 (pStat3) or control antibodies. Healthy PBMC were incubated for 24 hours with or without the addition of IL-6, IL-10, tumor necrosis factor (TNF), interferon-α (IFNα), or combinations of these cytokines. Flow cytometry was performed on a Becton Dickinson FACSCalibur fluorocytometer, determining percentages of CD126+ lymphocytes or the increase in pStat3 mean fluorescence intensity (Δmfi). sIL-6R in supernatants was detected by immunoprecipitation (IP) and immunoblotting.
Results: IL-6 was increased in SLE (median 3.64 vs 0.89 pg/ml in HC, p<0.0001). Significant correlations with SLE disease activity by ECLAM were found for serum IL-6 (Spearman r=0.40, p<0.01), but not CRP (r=0.29). CD126+ lymphocytes were decreased in SLE (median 46% vs. 61% for HC, Mann Whitney p<0.0001), in line with reduced IL-6 induced phosphorylation of Stat3 in SLE (median Δmfi 14.2 vs. 18.8 in HC, p=0.0044). In a mirror image of CD126, sIL-6R serum levels were increased in SLE (median 42.2 ng/mL vs. 38.6 ng/mL in HC, p=0.02). Stimulation of healthy PBMC with the combination of IL-6 and IFNα led to a reduction in CD126+ cells by 39±13% (p<0.0001)(A) and to an increase in sIL-6R (normalized for IgG) (p=0.0055)(B) detected by IP and Western blotting, mimicking the in vivo situation.

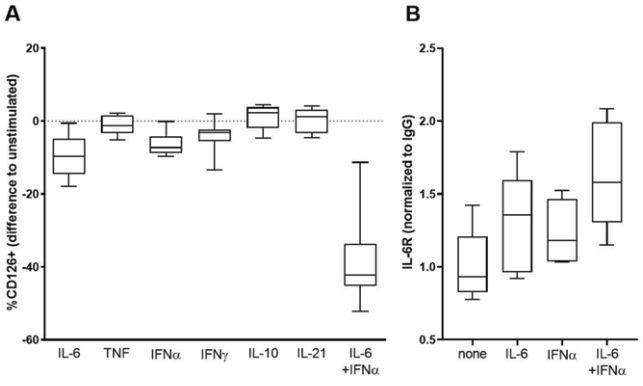


Figure 1.

Conclusion: The combination of type I interferon and IL-6, both of which are well known to be increased in SLE, leads to shedding of membrane bound CD126 to sIL-6R. This moves IL-6 effects from the liver, which produces CRP, to other cells, effectively increasing IL-6 inflammatory effects while limiting CRP levels.
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POS1422

SINGLE-CELL RNA SEQUENCING OF HAEMATOPOIETIC STEM/PROGENITOR CELLS IN HUMAN SLE: EVIDENCE FOR A CHRONIC IFN EXPOSURE AFFECTING EARLY HAEMATOPOIETIC PROGENITORS IN SLE, AND DRIVING THEIR PROLIFERATION AND MYELOID SKEWING

Keywords: Descriptive studies, Systemic lupus erythematosus, -Omics

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Background: All immune cells that contribute to the pathogenesis of systemic lupus erythematosus (SLE) derive from adult haematopoietic stem and progenitor cells (HSPCs) within the bone marrow (BM). We reasoned that the fundamental abnormalities in the disease can be traced back to HSPCs.
Objectives: I) To delineate human haematopoietic CD34+ progenitor subpopulations that may be involved in the pathogenesis of the disease and II) to identify deregulated pathways in each subpopulation in SLE as compared to healthy controls.
Methods: BM samples from 6 SLE patients and 5 healthy controls and 2 umbilical cord blood (CB) samples were used. CD34+ cells were isolated from BM and CB samples and single cell capture and RNA extraction were performed on Fludigm C1 IFC. Libraries were prepared and 75bp or 150bp paired-end sequencing was performed. Cells were excluded if total reads were <25,000, alignment rate was <50%, the number of detected genes (at least 1 count) was <200 and >6,000 and the percentage of reads mapping to mitochondrial genes was >20%. The Seurat and harmony R packages were used for normalization, marker identification and graph-based clustering. Pseudobulk differential expression (DE) analysis was performed using edgeR R package. Enrichment analysis was performed using EnrichR.
Results: A total of 426 out of 836 cells and 24,473 genes were used in the analysis. There was a statistically significant difference in the total number of detected genes between the three sample types (Kruskal-Wallis chi-squared=14.9, p<0.001) with CB samples expressing more genes compared to the other two sample types. The top 3,000 highly variable genes across cells were identified and loaded into a PCA and the top 10 principal components were provided as the input for the UMAP visualization which resulted in seven distinct clusters of cell types (Figure 1). Mutually exclusive markers, which were characteristic of each cell type were identified. Cluster 0 cells (T-like progenitors) uniquely expressed IL32 and CD3E, whereas cluster 1 (Myeloid-1 progenitors) uniquely expressed MMP8. Of note, there was a significantly lower proportion of SLE BM B-like progenitor cells (3.5% of total SLE BM cells) and SLE BM HSCs-3, characterized by primitive progenitors with low expression of the cell cycle gene MKI67 (4% of total SLE BM cells) compared to 10% B-like progenitors and 21% HSCs-3 of total healthy BM cells respectively. Following DE analysis between SLE and healthy BM there were statistically significant differences (FDR<0.1) in Myeloid-2 progenitors, with differentially expressed genes (DEGs) enriched for TNF signaling and DNA repair pathways, and in HSCs-1, with DEGs enriched for IFN alpha-beta signaling and heme metabolism. Interestingly, we observed an upregulation in the expression of IFN inducible genes, such as IFI44, IFI44L, in SLE compared to healthy in all three HSC subpopulations.
Conclusion: Single-cell RNA sequencing analysis from CD34+ progenitor cells from patients with SLE revealed both quantitative- as evidenced by decreased numbers of non-proliferating early progenitors, and qualitative differences- characterized by an IFN signature, which is known to drive loss of function and attrition of HSPCs. Chronic IFN exposure affects early hematopoietic progenitors in SLE, driving their proliferation and myeloid skewing and may account for the immune abberancies and the cytopenias in SLE.

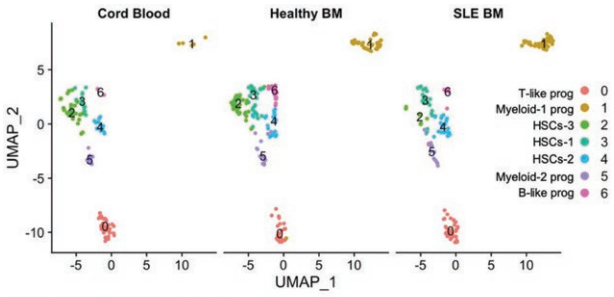


Figure 1. UMAP clustering per sample type.

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POS1423 **WITHDRAWN**

POS1424 **AQUAPORIN EXPRESSION IN LUPUS NEPHRITIS: INSIGHTS INTO TUBULAR PATHOLOGY**

Keywords: Systemic lupus erythematosus, Kidneys

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Background: Lupus nephritis is a severe and life-threatening manifestation of systemic lupus erythematosus. Tubulointerstitial hypoxia is a key factor in the progression to end-stage renal disease. Numerous aquaporins are expressed by renal tubules and are essential for their proper functioning. Several mouse models have shown their involvement in the regulation of renal inflammation during acute stress episodes. However, the expression of aquaporins (AQP) in human lupus nephritis has been poorly studied.
Objectives: The aim of this study is to characterise the tubular expression of AQP1, AQP2 and AQP3 which could provide a better understanding of tubulointerstitial stress during lupus nephritis.
Methods: This retrospective monocentric study was conducted at Erasme-HUB Hospital, Brussels with the approval of the ULB-Erasme Ethical Committee (P2020/710). A total of 37 lupus nephritis samples and 9 healthy samples collected between 2000 and 2020 were obtained from the biobank of the pathology department. Kidney biopsy sections were reviewed according to the ISN/RPS 2018 classification. Immunohistochemistry was performed to detect AQP1, AQP2 and AQP3 and followed by digital image analysis. Digital image quantification analysis was performed using ImageJ software.
Results: We observed weak expression of AQP1 in glomeruli and strong expression on the apical side of proximal convoluted tubules in the cortex. In the medulla, it was confined to the descending loop of Henle and the vasa recta. AQP2 was exclusively expressed on the apical side of collecting tubules in both the cortex and the medulla. AQP3 was not detected in glomeruli, weakly expressed on the basolateral side of proximal convoluted tubules, and strongly expressed on the basolateral side of distal convoluted tubules and collecting tubules. No difference in staining location was found between healthy and lupus nephritis kidney biopsies. By digital quantitative analysis, we observed a significant decrease in AQP1 expression in the renal cortex ($p<0.0001$), a non-significant trend towards a decrease in AQP2 expression and a significant cortical and medullary decrease in AQP3 expression ($p<0.001$). This decrease was more pronounced in the subgroup of membranoproliferative glomerulonephritis (class III/IV), particularly for AQP3 ($p<0.05$). Within the subgroup of membranoproliferative glomerulonephritis, there was a strong negative correlation between both cortical and medullary AQP2 expression and interstitial inflammation ($r=-0.5238$; $p<0.01$). Decreased cortical AQP3 expression was strongly negatively correlated with interstitial fibrosis ($r=-0.6651$; $p<0.001$) and tubular atrophy ($r=--0.6651$; $p<0.001$).
Conclusion: We found a significant decrease in the expression of several AQPs in the parenchyma of lupus nephritis. We believe that this decrease is a feature of tubulointerstitial damage. Immunohistochemical analyses of AQPs on lupus nephritis samples could help to assess the tubulointerstitial hypoxia and cell damage and therefore renal prognosis.
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Disclosure of Interests: None Declared.
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POS1425 **ANTIB2GLYCOPROTEIN I ANTIBODIES CAN INDUCE NETOSIS**

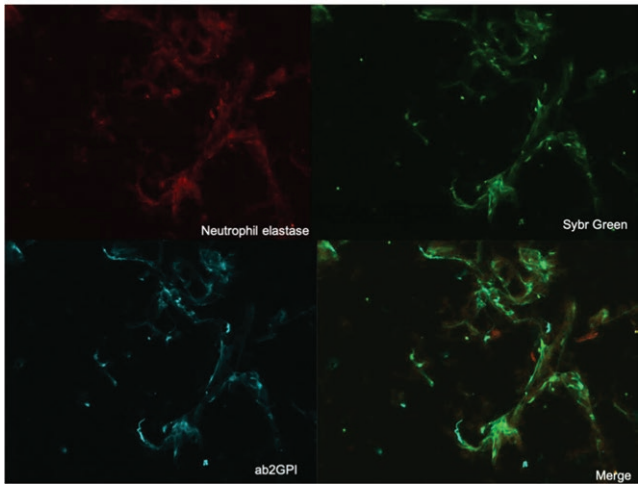
Keywords: Anti-phospholipid syndrome, Cell biology, Autoantibodies

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Background: NETosis has been described to play a role in the pathogenesis of APS. IgG and sera of APS patients are known to induce NETosis [1], however the direct role of aβ2GPI on NETosis is not fully known.
Objectives: The aim of this study is to evaluate the interplay between NETosis and aβ2GPI antibodies.
Methods: HD neutrophils were stimulated either with polyclonal aβ2GPI isolated from a serum pool of primary APS, with immunoglobulin isolated from HD (IgHD) or PMA. NETs were stained with anti-neutrophils elastase, SYBR green and DAPI. NET quantification was performed with NETQUANT, an automated approach. To evaluate the ability of aβ2GPI to bind to NET, HD neutrophils were stimulated with PMA and stained with anti-neutrophil elastase, SYBR green and with aβ2GPI and, as a control, with IgHD instead of aβ2GPI. Colocalization of aβ2GPI and NET signal was performed with Just Another Co-localization Plugin (JACoP). In order to evaluate the ability of aβ2GPI to bind to NETs and prevent DNA degradation, incubation with DNase I was also performed.
Results: Stimulation of HD neutrophils with aβ2GPI was able to induce a significantly higher number of NETs compared to stimulation with IgHD (77.6% vs 20%, $p<0.0001$). The prevalence of NETs in stimulated IgHD and unstimulated neutrophils was similar (20% vs 16%, p=ns). Two different shapes of NET were identified in neutrophils stimulated with aβ2GPI: "cloudy-like" and "spiky-like". Unlike IgHD, aβ2GPI binds to NETs (Figure 1), and the aβ2GPI signal colocalized with the anti-neutrophil elastase signal at 93.6%. In addition, we showed that aβ2GPI binding to NETs did not prevent NETs degradation by DNase.
Conclusion: Aβ2GPI antibodies are able to induce NETosis and to bind to NETs.
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Fig. 1 Aβ2GPI antibodies bind to NETs



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POS1426 **UNRAVELING THE MYSTERIES OF THE CONNECTION BETWEEN GUT AND THE CHRONIC ACTIVATION OF THE IMMUNE SYSTEM IN SYSTEMIC LUPUS ERYTHEMATOSUS**

Keywords: Systemic lupus erythematosus, Diet and nutrition, -Omics

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Background: In a systemic lupus erythematosus (SLE) murine model, the translocation of a gut pathobiont induced an autoimmune response and death, which were prevented by antibiotics and a vaccine [1]. These findings suggest that the gut microbiota modulates SLE phenotype. Previously, we found increased circulating lipopolysaccharide (LPS) in SLE patients, which could be associated with decreased gut barrier integrity and translocation from the gut to the bloodstream [2]. We hypothesize that dysbiosis, impaired intestinal barrier integrity, and endotoxemia are crucial to the chronic activation of the immune system seen in SLE.
Objectives: To study diet, physical activity, body composition, gut microbiota, and gut permeability in SLE patients in comparison with healthy controls (HC).
Methods: Evaluation of HC and SLE patients (children and adults) who fulfill the 2019 EULAR/ACR SLE classification criteria. Individuals with inflammatory bowel disease, celiac disease, irritable bowel syndrome, diabetes, malignancy, or other immune-mediated diseases were excluded. The SLEDAI-2K score was used to evaluate disease activity. Diet and physical activity were assessed by three-day diet recall, PREDIMED, KIDMED, and the International Physical Activity questionnaires. Body composition was analysed by whole-body air-displacement plethysmography. Gut microbiota was studied by Next Generation Sequencing, with amplicon sequencing-based 16S rRNA analysis. The lactulose/mannitol test, which directly assesses intestinal permeability, was quantified by mass spectrometry (LC-MS/MS). Serum markers of gut permeability and inflammation (zonulin, sCD14, IFABP) were measured by ELISA. The biological activity of LPS was assessed through serum-induced toll-like receptor 4 (TLR4) stimulation in a reporter cell line.
Results: We studied 16 HC (median age 35.5Y **[**14-50Y**]**; 88% females) and 45 SLE patients (11 children and 34 adults; median age 32Y **[**11-57Y**]**; 87% females; median age at diagnosis 19Y **[**8-43Y**]**; median disease duration 7Y **[**3M-29Y**]**; 64% had lupus nephritis; median SLEDAI-2K at sample collection 4].
SLE patients had lower physical activity and higher sitting time, lower adherence to the Mediterranean diet, and higher fat mass than HC ($p<0.05$). In addition, SLE patients had a lower intake of α-linolenic acid and manganese ($p<0.05$). A decreased α-diversity of gut microbiota ($p<0.05$) was identified in SLE patients, reflecting dysbiosis. Lower adherence to the Mediterranean diet, higher zonulin levels, and longer SLE disease duration were significantly associated with decreased gut diversity in this cohort ($p<0.05$). The lactulose/mannitol ratio was significantly higher in SLE patients compared to HC ($p<0.05$), reflecting greater gut permeability. Patients with lupus nephritis had a higher lactulose/mannitol ratio than SLE patients without renal involvement ($p<0.05$). Interestingly, we found that zonulin was significantly increased in SLE patients ($p<0.05$). We also found significantly increased levels of sCD14 in SLE patients ($p<0.05$) and increased levels of IFABP, but only in adult patients ($p<0.05$). No significant correlation was observed between any evaluated biomarker and SLEDAI-2K.
The serum of SLE patients induced a significantly higher TLR4 response compared to HC ($p<0.05$), which may reflect endotoxemia.
Conclusion: Our data support the hypothesis that gut dysbiosis and higher intestinal permeability contribute to SLE pathogenesis, being two promising therapeutic targets in this disease.

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[2] PMID: **24796678**

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5741

POS1427 **WITHDRAWN**

POS1428 AMLEXANOX INHIBITS PRODUCTION OF TYPE I INTERFERON AND SUPPRESSES B CELL DIFFERENTIATION AND IMMUNOGLOBULIN PRODUCTION IN VITRO: A POTENTIAL NOVEL THERAPEUTIC OPTION FOR SLE

Keywords: Systemic lupus erythematosus

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Background: The immunopathology of systemic lupus erythematosus (SLE) is characterized by production of autoantibodies and aberrant activation of the type I interferon (IFN) system. In SLE, type I IFNs directly and indirectly affect differentiation and survival of autoreactive B cells, partly by IFN induced release of B cell activating factor (BAFF). TANK-binding kinase 1 (TBK-1) is an important upstream mediator of type I IFN production, which has been implicated in several systemic autoimmune diseases [1]. Additionally, B cell intrinsic TBK-1 was recently shown to be essential for germinal center (GC) formation and proper B cell development in mice [2]. Amlexanox (AMX), a small molecule TBK-1 inhibitor, has been used to treat aphthous ulcers and asthma. Systemic administration of AMX has indicated that the drug is well tolerated with little evidence of safety concerns [3]. Therefore, we hypothesize that AMX, by inhibition of TBK-1, could be a novel therapeutic option in SLE.
Objectives: To determine whether AMX can inhibit type I IFN and IFN induced BAFF production, and to unravel its potential direct effects on B cells in human in vitro culture systems.
Methods: Cultured PBMC from healthy donors were stimulated with Imiquimod, CpG-A, Poly:IC, G3-YsD or 3p-hpRNA to induce type I IFN production through various routes, with or without presence of AMX. Production of type I IFN was assessed by a HEK IFN-α/β reporter cell line and the ability of supernatants to induce transcription of the BAFF and MX1 genes was measured by real-time quantitative PCR. Sorted CD19+ B cells were cultured for 6 or 9 days under GC-like conditions with CD40L and IL-21 (4), as well as IFN, BAFF, and AMX at various concentrations. Viability and differentiation into CD38highCD27highCD138+/- cells was assessed by spectral flow cytometry. Immunoglobulin M and IgG were measured in supernatants by ELISA.
Results: Amlexanox significantly inhibited production of type I IFN through all investigated endosomal and cytosolic routes (p=0.03 to p=0.001). Likewise, supernatants from cells treated with AMX were unable to induce expression of BAFF and MX1. The inhibiting capacity of AMX in this setting was comparable to blocking of the interferon alpha/beta receptor (IFNAR) with a monoclonal antibody. As could be expected, AMX did not affect expression of BAFF and MX1 upon IFNAR ligation, indicating no effect on signaling downstream of the receptor. To mimic an autoimmune setting, IFN and BAFF was added to the CD40L/IL-21 B cell culture system, resulting in increased B cell differentiation. Addition of AMX resulted in significantly decreased differentiation into CD38highCD27highCD138+/- cells (p<0.0001) without affecting cell viability. Correspondingly, production of IgM and IgG was lower in the AMX condition.
Conclusion: Our data demonstrate *in vitro* inhibitory effects of AMX on type I IFN production and B cell differentiation in primary human cells. Inhibition of TBK-1 is a promising therapeutic target for treatment of SLE warranting further investigations.
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POS1429 AN ANALYSIS OF THE GUT MICROBIOTA IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS REVEALS THE RELATIONSHIPS BETWEEN GUT BACTERIA AND DISEASE SEROLOGY

Keywords: Autoantibodies, Systemic lupus erythematosus, Kidneys

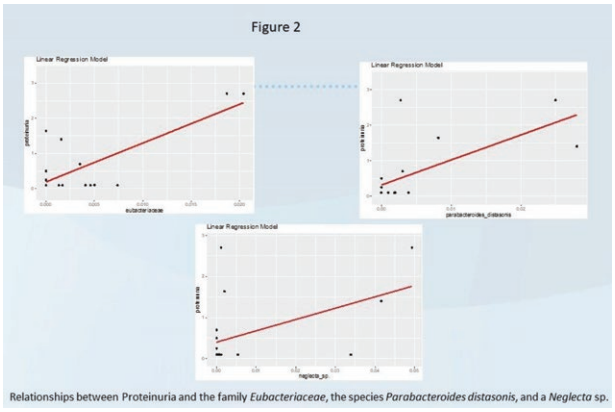
A. Bankole[1], X. Cabana-Puig[2], J. Michaelis[2], M. Pop[3], Z. Lin[4], S. Church[4], X. Luo[2]. *[1]Virginia Tech Carilion School of Medicine, IM, Roanoke, United States of America*; *[2]Virginia tech, Biomedical Sciences and Pathobiology, Blacksburg, United States of America*; *[3]The University of Maryland Center for Bioinformatics and Computational Biology, Bioinformatics and Computational Biology, College Park, United States of America*; *[4]Virginia Tech, Department of Statistics, Blacksburg, United States of America*

Background: Systemic lupus erythematosus (SLE) is the prototypical systemic autoimmune rheumatic disease and is characterized by hyperactive B cells leading to autoantibody production. Changes in gut microbiota are associated with autoimmune disease including SLE. We theorize that changes in the gut microbiota seen in patients with SLE relate to both serological, clinical manifestations as well as disease activity in SLE. A better understanding of the gut microbiota may lead to its use as a biomarker, part of disease activity scoring in SLE, or a potential future therapeutic target.
Objectives: The objective was to determine the relationship between changes in the gut microbiota and the patient reported outcomes using patient global health assessment (PG) and overall disease assessment using Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDI). Secondary objective including the relationship between serological markers of SLE, and proteinuria was also investigated.
Methods: A total of 36 patients were enrolled, and 20 patients who met the Systemic Lupus Collaborating Clinics (SLICC) criteria for SLE each provided a stool sample. Table 1 demonstrates some of the patient and disease related information collected. The stool samples were homogenized, and the DNA was extracted. The V4 region of 16S rRNA gene was amplified using PCR. The purified amplicons were sequenced bi-directionally. Samples were analyzed using the R package phyloseq. Reads were processed and amplicon sequence variants (ASVs) were generated using DADA2 in R. Taxonomy was assigned using the SILVA 138 rRNA database training set using the DADA2 functions, assignTaxonomy and addSpecies. Two samples with fewer than 1000 reads were removed from the dataset, resulting in 18 samples and 1311 ASVs used for downstream microbiota and statistical analyses.
Results: There was also no statistical relationship between the gut microbiota and patient global health assessment or SLEDI. We found no statistical correlation between the gut microbiota and lymphopenia, complement C3/C4, ANA titers, SSA/SSB results or the presence of lupus nephritis. There was an inverse relationship between the family of Ruminococcaceae and dsDNA antibody levels (Figure 2). We also noted significant positive correlation between the level of proteinuria and the genus Eubacterium (family Eubacteriaceae) and the species Parabacteroides distasonis and a Neglecta sp. (Figure 2).
Conclusion: There were significant changes in gut microbiota in SLE that correlated with the levels of dsDNA antibodies and proteinuria. The findings are suggestive that there may be a direct relationship between lupus nephritis serology, clinical symptoms, and the gut microbiota.

Table 1. Patient Demographics

Age	Race	Sex	dsDNA	C3/C4	Proteinuria	SLEDAI-2K	PGA	LN
18	W	F	No	No	<0.1	0	50	No
41	W	M	Elevated	No	<0.1	2	0	Yes
21	A	F	Elevated	Low	1.64	8	0	Yes
66	W	F	Elevated	No	<0.1	0	0	No
39	AA	F	No	Low	0.25	0	0	No
29	AA	F	Elevated	Low	<0.1	2	15	No
65	W	F	Elevated	Low	0.7	13	50	Yes
27	AA	M	Elevated	Low	0.5	6	10	Yes
36	W	M	No	No	<0.1	0	5	No
25	W	F	Elevated	Low	1.4	8	15	Yes
64	AA	F	No	Low	<0.1	6	10	No
23	W	M	Elevated	No	<0.1	2	0	Yes
56	W	F	No	No	<0.1	1	0	No
40	AA	F	No	No	2.7	4	20	Yes
35	AA	F	No	No	<0.1	0	0	No
37	AA	F	Elevated	No	<0.1	0	0	No
39	AA	F	No	No	2.7	5	50	Yes
47	W	F	No	No	<0.1	0	0	No
53	W	F	Elevated	Low	0.1	0	0	Yes

dsDNA = Double Stranded DNA antibody, C3 = Complement, C4 = Complement 4, SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000, PGA = Physician Global assessment, LN = Lupus nephritis, Race: W=White, A= Asia, AA, African American, Sex: F= Female, M= Male



Relationships between Proteinuria and the family *Eubacteriaceae*, the species *Parabacteroides distasonis*, and a *Neglecta* sp.

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POS1430 ROLE OF IL-10 -SECRETING CELLS IN THE PATHOGENESIS OF SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Cell biology, Adaptive immunity, Systemic lupus erythematosus

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Background: Systemic Lupus Erythematosus (SLE) is characterized by great clinical heterogeneity. Its complex pathogenesis has not been fully understood and factors influencing the development of different clinical phenotypes are still to unveil. A better understanding of these aspects could help in identifying new potential biomarkers and possible therapeutic targets to manage different disease subsets. Interleukin-10 (IL-10) has two opposite effects: it inhibits pro-inflammatory cytokine production but can also exert stimulatory effects by promoting B cell growth and differentiation [1-3]. Consequently, follicular and extrafollicular IL-10 producing B Helper T cells could play a pathogenic role. In SLE patients an increased frequency of circulating extrafollicular CCR6+ B Helper T cells have been reported especially in patients with active disease [1,4]. CRR6+ B helper T cells produce IL-10 and spontaneously induce IgG in SLE patients, including the pathogenic anti-dsDNA autoantibody [4].

Objectives: Our aim was to evaluate the role of IL-10 -secreting cells in the pathogenesis of SLE and to highlight differences in the expression of these cells in different disease stages and clinical phenotypes.

Methods: We analyzed the percentages of IL-10-producing lymphocytes either ex vivo (a standard negative control) or after brief stimulation with PMA and ionomycin, which activates all T-cells to produce cytokines. Surprisingly, 4 patients had very high levels of IL-10 production ex vivo, while the remaining patients produced some IL-10 only upon stimulation, similarly to healthy controls. We then divided our population into 2 groups according to disease activity: patients with SLEDAI ≥ 4 displayed significantly higher IL-10 production than inactive patients. To assess which cells were responsible for spontaneous IL-10 production, we analyzed the phenotype of IL-10+ cells. Spontaneously IL-10 secreting lymphocytes were mainly CD4+ helper T-cells that expressed high levels of CCR6, CXCR5 and IL-7R.

Results: We looked at the percentage frequency of IL-10 -producing cells out of total lymphocytes under two conditions: ex vivo and after stimulation with PMA and ionomycin. Surprisingly, 4 patients had high levels of IL-10 production ex vivo, while the remaining patients produced IL-10 only following stimulation as expected. We then divided the test population into two groups according to disease activity: patients with SLEDAI ≥ 4 displayed significantly higher IL-10 levels than inactive patients. To assess which cells were responsible for IL-10 production, we analyzed the percentage of CD4 and CD8 cells in two populations of lymphocytes, those that expressed IL-10 and those that did not (Figure 1). Spontaneosly IL-10 secreting cells were mainly CD4+ helper T-cells that expressed high levels of CCR6, CXCR5 and IL-7R.

Conclusion: IL-10 was reported to be spontaneously produced by B-cells and monocytes, but this is to our knowledge the first evidence that also T-cells spontaneously produce Il.-10 in SLE. IL-10 levels were higher in active disease and produced mainly by B helper T-cells, suggesting that it stimulates autoreactive B cells to produce pathogenic autoantibodies: the ex vivo production of IL-10 by B helper T cells in selected patients suggest that they are continuously activated by autoantigens and contribute to the aberrant production of autoantibodies. However, further analysis are needed to better characterize the spontaneously IL-10 producing lymphocytes in these patients.

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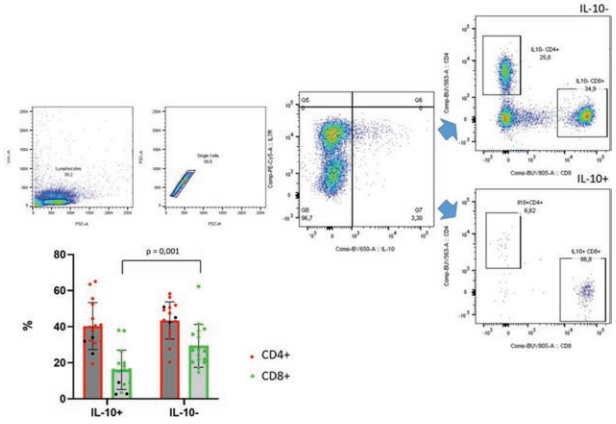


Figure 1. CD4 and CD8 cells in IL10+ and IL10- T cells

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1431 IMMUNE CELLS AND THEIR EFFECTOR FUNCTIONS IN NEONATES BORN TO ANTI-RO/LA POSITIVE WOMEN

Keywords: Autoantibodies, Sjögren syndrome, Pregnancy and reproduction

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Background: Neonatal lupus, including autoimmune congenital heart block, is a passively acquired autoimmune condition dependent on placental transfer of maternal Ro/La autoantibodies to the fetus. The mothers are commonly diagnosed with Sjögren's syndrome or systemic lupus erythematosus, and present with elevated plasma interferon (IFN) levels and signs of immune activation. Recent studies demonstrate both a correlation between the maternal and neonatal IFN-scores, as well as elevated plasma IFNα levels in the neonates. Whether IFNα can be produced by the fetus or whether it originates from the mother is not known.

Objectives: To characterize immune cells in Ro/La autoantibody-exposed neonates with regard to phenotypes, effector functions and cytokine production.

Methods: We used full spectrum multi-color flow cytometry staining for an array of cell phenotype, activation and proliferation markers combined with intracellular cytokine staining to cover the most important innate and adaptive immune cell populations in cord blood cells of anti-Ro/La-exposed (n=12) and non-exposed (n=6) newborns.

Results: We confirmed an increased surface expression of Sialic acid-binding Ig-like lectin-1 (Siglec-1) on CD14+ monocytes and further show increased Siglec-1 expression also on CD14-CD16+ non-classical monocytes and conventional dendritic cells in anti-Ro/La-exposed compared to healthy control neonates. We did not observe any major differences in general populations such as CD4+, CD8+ or gamma delta T cells. However, we found a decreased frequency of regulatory CD4+ FoxP3+ T cells in the autoantibody-exposed newborns. In line with this, we observed an increase in conventional CD4+ FoxP3- T cells and that these cells have less of a naïve phenotype with significantly lower frequency of CD62L+ and more CD69-expressing cells in the CD4+ FoxP3- population. Interestingly, Ro/La-exposed newborns also had less CD5-expressing CD19+ B cells compared to healthy newborns, while the frequency of CD19+ CD5- B cells was not affected. Further, we noted a decreased surface expression of CD19 and CD11b on both these CD19+ subpopulations. Interestingly, for neonates born to mothers with high levels of all three of Ro52, Ro60 and La autoantibodies, we also found intracellular cytokine IFNα and TNFα production in B cell, dendritic cell, and monocyte populations.
Conclusion: Together, our data provide valuable insight into the effects of Ro/La autoantibody exposure *in utero* on immune activation of both innate and adaptive immune cell populations in exposed fetuses, enhancing our understanding of the immunological basis of neonatal lupus.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3507

POS1432 CAR-TREGS FOR SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Adaptive immunity, Animal models

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by an abnormal inflammatory response against nuclear antigens with consequent tissue damage. Autoreactive B cells and auto-antibodies have a fundamental role in SLE pathogenesis. Regulatory T cells (Tregs) physiologically maintain the immune tolerance and are impaired in SLE. Polyclonal Treg trnasfer obtained unsatisfactory results due to the low number of disease-relevant antigen-specific cells. Chimeric Antigen Receptors (CARs) are molecules capable of redirecting T cell specificity. CAR-Tregs proved effective in pre-clinical mouse models of autoimmunity.
Objectives: We aimed at developing a CAR-Treg based product to be employed in SLE.
Methods: We isolated Tregs from Healthy Donors Peripheral Blood Mononuclear Cells (PBMCs) and expanded them with IL-2 and rapamycin. We transduced Tregs with a Lentiviral Vector encoding for a second-generation anti-CD19 CAR, considering the relevant role of autoreactive B cells and autoantibodies in SLE.
Results: Engineered cells retained their immune suppressive capabilities upon polyclonal stimulation. Noticeably, they acquired new antigen-specific suppressive capacities, being able to block autologous B cell proliferation. We set up a humanized mouse model of SLE. In vivo, CAR-Tregs delayed the occurrence of B cell lymphopenia, producing immunomodulatory cytokines and without showing toxicity or reprogramming towards Th17 pro-inflammatory cells. In inflamed organs, CAR-Tregs restored the normal composition of the immune system.
Conclusion: In conclusion, we efficiently generated anti-CD19 CAR-Tregs and proved their efficacy both in vitro and in an in vivo humanized mouse model of lupus.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1433 RELATIONSHIP BETWEEN THE EFFECT OF BELIMUMAB ON IMMUNOPHENOTYPE AND THE DISCONTINUATION OF GLUCOCORTICOIDS IN PATIENTS WITH SLE: LOOPS REGISTRY, FLOW STUDY

Keywords: Systemic lupus erythematosus, Real-world evidence

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Background: The efficacy of belimumab (BEL) for maintenance therapy in patients with systemic lupus erythematosus (SLE) remains unclear. Furthermore, the effects of BLM on the peripheral blood immunophenotype in patients with SLE are unknown.
Objectives: Patients with SLE in the maintenance phase were analyzed to determine the relationship between the efficacy of BEL and peripheral immunophenotypes. This study aimed to identify patients with SLE for whom belimumab was optimal by clinical findings and peripheral immunophenotypes.
Methods: In this retrospective observational study, patients with SLE (n=110) in the maintenance phase (SELENA-SLEDAI < 10, glucocorticoid [GC] dose ≤ 0.2 mg/kg/day) were assessed. Based on the standard human immune cell subset classification protocol by NIH/FOCIS, peripheral immunophenotypes were analyzed in SLE patients and age/gender-matched healthy controls (n=76), and were compared. The efficacy of BEL combined with standard-of-care (BEL+SoC group, n=64) was compared with SoC alone (SoC group, patients using either mycophenolate mofetil or hydroxychloroquine, n=46). Selection bias was adjusted by propensity score-based inverse probability of treatment weighting (PS-IPTW). Peripheral immunophenotypes were also compared between the baseline and after six months for the SoC group and BEL+SoC group.
Results: The proportion of naïve-CD4 T-, -CD8 T-, and -B cells were lower, and that of the memory CD4 T-, memory CD8 T-, class-switched memory B-, and IgD^-CD27^-B cells, and plasmocytes was higher in the SLE patients than in controls. No significant difference was observed in the patient background between the two groups after adjustment by PS-IPTW. Compared with the SoC group, the GC dose after one year was significantly lower (BEL+SoC, 1.7±2.3 vs. SoC, 5.4±4.8 mg/day, p<0.0001) in the BEL+SoC group. In the BEL+SoC group, 31.3% (20/64) of patients discontinued GC, significantly more than the SoC group (BEL+SoC, 31.3% vs. SoC, 5.0%, p=0.0012). The relapse rate (BEL+SoC, 6.1% vs. S oC, 22.4%, p=0.0128) was significantly lower in the BEL+SoC group than in the SoC group. The incidence of infections was significantly lower in the BEL+SoC group compared to the SoC group before and after PS-IPTW. No significant difference between the two groups was observed in peripheral immunophenotypes at baseline. The proportion of activated Tfh cells (p=0.0323), IgD^-CD27^-B cells (p<0.0001), and plasmocytes (p=0.0370) was significantly decreased six months after BLM introduction. In the BEL+SoC group, 18 (28.1%) who discontinued GC had no relapse for one year and showed a significantly lower proportion of IgD^-CD27^-B cells six months after BLM introduction (p=0.0387). These changes were not observed in the SoC group.
Conclusion: In maintenance-phase SLE, administration of BLM was able to achieve a reduction or discontinuation of GC dose while suppressing flare-ups. A reduction in IgD-CD27-B cells due to BLM may help to control disease activity and enable the reduction/discontinuation of GC in SLE patients in the maintenance phase.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Vasculitis - aetiology, pathogenesis and animal models

POS1434 ABERRANT PHENOTYPE OF CIRCULATING ANTIGEN PRESENTING CELLS IN GIANT CELL ARTERITIS AND POLYMYLAGIA RHEUMATICA

Keywords: Innate immunity, Vasculitis

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Background: Giant Cell Arteritis (GCA) and Polymyalgia Rheumatica (PMR) are overlapping diseases occurring exclusively in people older than 50 years. Antigen-presenting cells (APCs), including monocytes and dendritic cells (DCs), are main contributors to the immunopathology of GCA and PMR. In GCA tissues, DCs may be prone to activation, leading to chemokine production and recruitment of CD4+ T-cells and monocytes to the arterial wall. However, little is known about APC phenotypes in the peripheral blood at the time of GCA/PMR diagnosis.
Objectives: We aimed to investigate the phenotype of the circulating monocytes and DCs in GCA and PMR patients.
Methods: APCs among peripheral blood mononuclear cells (PBMCs) of treatment-naive GCA and PMR patients were compared to those in age- and sex-matched healthy controls (HCs) using flow cytometry (n=15 in each group). Using a 13-colour panel, we identified three monocyte subsets: classical (CD14+CD16-), intermediate (CD14+CD16+), and non-classical (CD14lowCD16+) monocytes. DC subsets were subdivided in CD303+CD11c- plasmacytoid DCs (pDCs), CD11c+CD141+ conventional DCs (cDC1) and CD11c+CD1c+ conventional DCs (cDC2). Each of these subsets was analysed for expression of pattern recognition receptors (Toll-like receptor 4 (TLR4), TLR2) and activation markers (CD86, Programmed Death- Ligand 1 (PD-L1), CD40, HLA-DR, CD11c) by assessing the mean-fluorescence intensity of these markers. Data were analysed by conventional gating strategies and by unsupervised tSNE.
Results: GCA and PMR patients displayed a monocytosis, which was due to increases in classical and intermediate monocyte counts, whereas the proportion of non-classical monocytes was reduced. Intermediate monocytes of GCA patients had significantly higher TLR2 expression, a similar trend was observed in non-classical monocytes of GCA and PMR patients. A divergent pattern was observed in the expression of activation markers on classical versus non-classical monocytes: classical monocytes of GCA/PMR patients appeared to be less activated, whereas non-classical monocytes showed an increased marker expression compared to HCs (Figure 1). Even though no differences were observed in DC counts in the peripheral blood, cDC2 counts correlated negatively with CRP levels (r=-0.60 for GCA, r=-0.55 for PMR).
Conclusion: Circulating non-classical monocytes, but not DCs, display an activated phenotype in GCA and PMR patients at diagnosis. These cells are thought to be pro-inflammatory, representing the end stage of monocyte maturation in the blood. In contrast, classical monocytes show reduced expression of activation markers in GCA and PMR patients, potentially signalling either an immature or exhausted phenotype.

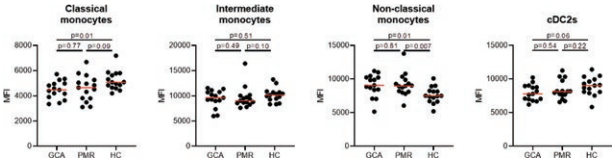


Figure 1. CD11c expression on monocyte subsets and cDC2 for GCA patients, PMR patients and HCs

Shown is the mean fluorescence intensity (MFI) of CD11c on the surface of monocyte subsets and CD1c+ conventional dendritic cells (cDC2). Data are shown for patients with giant cell arteritis (GCA) or polymyalgia rheumatica (PMR) and age-matched healthy controls (HCs), n=15 for each group. Statistics by Mann Whitney U. CD11c expression data for pDCs (no CD11c expression) and cDC1 (too small population) are not shown.

REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: Rosanne Reitsema: None declared, Bernd-Cornèl Hesselink: None declared, Kornelis van der Geest Speakers bureau: Roche, Grant/research support from: Abbvie, Wayel Abdulahad: None declared, Annemieke Boots: None declared, Elisabeth Brouwer: None declared, Peter Heeringa: None declared, Yannick van Sleen: None declared.
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POS1435 A GM-CSF AND IFN-γ-DRIVEN PRO-INFLAMMATORY MACROPHAGE SIGNATURE IN POLYMYALGIA RHEUMATICA

Keywords: Cytokines and chemokines, Innate immunity, Biomarkers

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Background: Polymyalgia rheumatica (PMR) is a common, rheumatic inflammatory disease. Synovial inflammation of the shoulder bursae and tendon sheaths is a hallmark feature of PMR. Data on the immune pathology of PMR are scarce, with glucocorticoid treatment remaining the mainstay treatment for this condition. An earlier study reported that macrophages dominate the inflammatory infiltrates in the synovium of PMR patients [1]. Recently, macrophages were identified as potent producers of IL-6 and GM-CSF in PMR bursa tissue [2,3], while a strong IFN-γ signature was observed among bursa T cells [4]. GM-CSF and IFN-γ might potentially skew macrophages towards a pro-inflammatory phenotype. To what extent bursa macrophages in PMR also produce other pro-inflammatory cytokines remains unknown.
OBJECTIVES:
1) To investigate the pro-inflammatory cytokine signature of bursa tissue macrophages in PMR.
2) To determine whether GM-CSF and IFN-γ stimulated monocytes adopt a pro-inflammatory macrophage phenotype.

Methods: Ultrasound-guided bursa tissue biopsies were obtained from 12 PMR patients with active disease. Immunohistochemistry staining for proinflammatory cytokines (IL-6, IFN-γ, IL-1β, TNF-α, IL-12, IL-23 and GM-CSF) and homeostatic cytokines M-CSF was scored quantitatively. Double immunofluorescence staining was performed linking cytokine expression to CD68+ macrophages. *In vitro* studies were performed with monocytes isolated from peripheral blood mononuclear cells of 8 patients with active PMR and 8 healthy donors. Monocytes were differentiated into macrophages during a 7-day culture in the presence of GM-CSF, with or without 24 hours co-incubation with IFN-γ on day 7 for additional polarization. Real-time qPCR was performed to determine expression of IL-6 in the cultured cells.
Results: CD68+ macrophages were the predominant immune cells in PMR bursa biopsies. IHC staining showed high expression (>60% of positive cells) of proinflammatory cytokines (IL-6, IL-12, IL-23, TNF-α and GM-CSF) and the homeostatic cytokine M-CSF throughout the bursal tissue, while IFN-γ and IL-1β were moderately expressed (>35% of positive cells). Double immunofluorescence staining confirmed the expression of these cytokines by the bursa tissue macrophages. *In vitro* experiments showed a slight upregulation of IL-6 expression when monocytes were differentiated into macrophages by GM-CSF. In the presence of IFN-γ, a substantially stronger upregulation of IL-6 was observed. In essence, similar *in vitro* findings were observed for monocytes/macrophages obtained from PMR patients and healthy controls.
Conclusion: Macrophages are the predominant immune cells in PMR bursa tissue and produce a wide array of pro-inflammatory cytokines. GM-CSF and IFN-γ may contribute to the pro-inflammatory phenotype of macrophages in PMR, as indicated by their strong ability to promote IL-6 expression *in vitro*. This study provides the first glance on the complex cytokine network present in key tissues affected by PMR.

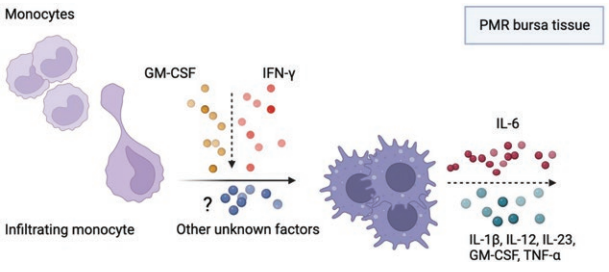


Figure 1. Hypothetic pathogenesis of PMR in bursa tissue. GM-CSF and IFN-γ, together with other factors in the bursa tissue steer monocytes to differentiate into macrophages that produce pro-inflammatory cytokines such as IL-6.

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Disclosure of Interests: William Febry Jiemy: None declared, Anqi Zhang: None declared, Maria Sandovici: None declared, Peter Heeringa: None declared, Arjan Diepstra: None declared, Elisabeth Brouwer Speakers bureau: E. Brouwer reports speaker and consulting fees from Roche in 2017-2018, outside the submitted work, Consultant of: E. Brouwer reports speaker and consulting fees from Roche in 2017-2018, outside the submitted work, Kornelis van der Geest Consultant of: K. van der Geest reports personal fees from Roche and AbbVie, outside the submitted work.
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POS1436 IMMUNE CELLS ARE HIGHLY DISTURBED IN POLYMYALGIA RHEUMATICA PATIENTS

Keywords: Adaptive immunity, bDMARD

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Background: Polymyalgia rheumatica (PMR) is an inflammatory disease. But it's pathophysiology and the impact of the treatments on immune cells are poorly known.
Objectives: Our objectives were to describe the immune cells of patients with PMR dependent from glucocorticoids and to analyze their evolution under tocilizumab.
Methods: The SEMAPHORE trial (NCT02908217, (1)) was a randomized control trial including patients with PMR dependent from glucocorticoids. Between inclusion and week 12, patients were blindly treated with either tocilizumab infusion or placebo infusion every 4 weeks associated to a tapering of glucocorticoids. Age and sex-matched healthy controls (HC) were recruited in the rheumatology department of the Brest University Hospital. HC did not have any history or presence of cancer, auto-immune disease or active infection and did not received treatment with a known impact on the immune system. We analyzed immune cells on whole fresh blood after red cell lysis on flow cytometry (Navios, Cytoflex, Beckmann Coulter) after staining for CD16, CD56, CD19, CD14, CD4, CD8, CD3, CD45, IgD, IgM, CD21, CD27, CD24, CD38, CD5 CD126, CD62L, CD45RA, CD127, CD25, in four different panels.
Results: Samples were obtained for 40 PMR patients and 34 HC. At inclusion, in PMR patients, compared to HC, CD14+CD16- classical monocytes were increased (82±1% vs 77±2%, p=0.01), CD14-CD16+ non-classical monocytes were decreased (4±0.3% vs 7±0.6%, p<0.0001), granulocytes were increased (63±2% vs 52±2%, p<0.0001), natural killer cells were decreased (8±1% vs 13±1%, p=0.007). B cells were decreased (8±0.6% vs 10±0.8%, p=0.03), but with an enrichment in CD27-IgD- senescent B cells (p<0.0001) and in $CD21^{low}$ B cells (p=0.04). T cells were increased (70±2% vs 64±2%, p=0.02) with an enrichment in CD4+ T cells (p=0.02) and in $CD4+CD25^{high}CD127-$ regulatory T cells (p<0.0001). At week 12, in PMR patients receiving tocilizumab therapy, compared to PMR patients receiving placebo, granulocytes were lower (58±5% vs 73±2%, p=0.006) and monocytes were higher (8±1% vs 5±0.5%, p=0.02).
Conclusion: In patients with a PMR dependent from glucocorticoids, immune cells homeostasis is disturbed. Tocilizumab has an impact more pronounced on granulocytes and monocytes. Knowledge about immune disturbance in PMR might help to choose to use a targeted therapy when glucocorticoids are not sufficient.
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POS1437 INTERSTITIAL ANCA-ASSOCIATED VASCULITIS ASSOCIATES WITH SEVERE KIDNEY INJURY INDEPENDENT OF GLOMERULONEPHRITIS

Keywords: Kidneys, Vasculitis

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Background: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a small vessel vasculitis affecting multiple organ systems, including the kidney. Small vessels in the kidney include small-sized arteries (interlobular artery, afferent and efferent arteriole), capillaries (glomerular and peritubular capillary) and venules.
Objectives: Although crescentic ANCA glomerulonephritis (GN) is a common histological finding reflecting glomerular small vessel vasculitis, it is reasonable that manifestation of AAV could also contribute to interstitial small vessel vasculitis. Therefore, we here aimed to expand our current knowledge focusing on interstitial vasculitis in ANCA GN by systematic histological scoring of vascular lesions analogous to Banff.
Methods: A total number of 49 kidney biopsies with confirmed renal involvement of AAV at the University Medical Center Göttingen were retrospectively included between 2015 till 2020. A renal pathologist evaluated all biopsies and was blinded to clinical data collection and analysis.
Results: Since previous studies established that crescentic ANCA GN associates with severe kidney injury and acute deterioration of kidney function in AAV, we first systematically scored interstitial vasculitis in association with requirement of renal replacement therapy (RRT). Among all active and chronic tubulointerstitial lesions analogous to the Banff scoring system, the only association between severe kidney injury requiring RRT was observed for interstitial vasculitis in AAV reflected by peritubular capillaritis (ptc, p=0.0002) and arteritis (v, p=0.0069), affecting 5/49 (10.2%) and 11/49 (22.4%) of renal biopsies, respectively. Since it is known that severe deterioration of kidney function also correlates with crescentic ANCA GN, we next directly compared glomerular and tubulointerstitial lesions. The fraction of normal glomeruli was inversely associated with interstitial fibrosis (ci), total (ti) and inflammation in IFTA (i-IFTA), whereas glomerular crescents were associated with interstitial inflammation (i), tubulitis (t) and total inflammation (ti). In contrast, global glomerular sclerosis associated with less interstitial inflammation (i) but correlated with interstitial fibrosis (ci) and tubular atrophy (ct), confirming established mechansim that chronic glomerular injury leads to tubular atrophy and interstitial fibrosis. Interestingly, no association between interstitial vasculitis (ptc and v correlating with severe kidney injury) and any glomerular lesion in ANCA GN (also correlating with severe kidney injury) was observed, thereby confirming that interstitial vasculitis contributes to severe kidney injury independent of ANCA GN. By contrast, short-term renal recovery from RRT was equal in both groups, suggesting a distinct association with acute decline of kidney function at disease onset.
Conclusion: Taken together, by using the Banff scoring system we here expand our current knowledge of renal interstitial lesions in AAV revealing peritubular capillaritis and arteritis as important histological alterations associated with severe kidney injury in a considerable subset of AAV. Furthermore, our findings that interstitial vasculitis did not correlate with crescentic ANCA GN implicate that the characteristics of each vasculitis manifestation are independent and could further improve our understanding of mechanisms contributing to renal injury. These observations suggest that interstitial vasculitis in AAV may also affect long-term prognosis requiring further investigation.
REFERENCES: NIL.

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Disclosure of Interests: Björn Tampe Grant/research support from: Support from Evotec and Vifor.
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POS1438

ANALYSIS OF THE PLASMA PROTEOME PROVIDES MECHANISTIC INSIGHTS INTO THE PATHOPHYSIOLOGY OF ANCA-ASSOCIATED VASCULITIS

Keywords: -Omics, Vasculitis

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Background: The pathogenesis of ANCA-associated vasculitis (AAV) remains largely unknown. Proteinase 3 (PR3)- and myeloperoxidase (MPO)-AAV are two cateogories of AAV with distinct genetic background, but mechanistic differences between the two are poorly characterized. We hypothesized that in-depth studies of the plasma proteome in patients with active AAV would provide clues to the molecular and cellular mechanisms behind these disorders.
Objectives: To improve our understanding of the disease mechanisms behind AAV and pathophysiological differences between PR3- and MPO-AAV.
Methods: Plasma samples were collected at six Swedish rheumatological and/or nephrological centers from 42 PR3-AAV- and 25 MPO-AAV patients with active disease prior to commencement of therapy and from 138 healthy matched controls. All patients were classified into granulomatosis with polyangiitis or microscopic polyangiitis according to the European Medicines Agency algorithm. Samples were analysed for the relative levels of 181 proteins associated with inflammation or cardiovascular disease, using proximity extension assay (OLINK Proteomics). Differentially expressed proteins (DEPs) between groups were analyzed using ANOVA, where proteins with a fold change ≥ 1.5 and adjusted P value < 0.05 were considered as significant DEPs. Partial least square discriminant analysis (PLS-DA) was used to identify proteins contributing most to PR3-AAV/MPO-AAV separation from healthy controls. The STRING database was used to analyse protein–protein interaction networks. Gene ontology, KEGG and Reactome databases were used for pathway enrichment analyses using ClueGO.
Results: In comparison with healthy controls, 63 DEPs were identified for PR3-AAV and 62 for MPO-AAV; of these, 49 DEPs were common to both AAV groups. Pathway enrichment analysis of the 49 common DEPs identified IL-17-, IL-10-, TNF-α- and NF-kappa B signaling and neutrophil chemotaxis among the significantly enriched processes. The 14 DEPs unique for PR3-AAV formed a functional and physical protein-protein interaction network in STRING analysis, with significant enrichment for regulation of B cell proliferation, activation of matrix metalloproteinases, collagen degradation and IL-17- and TNF-α signaling pathways. The 13 DEPs unique for MPO-AAV did not show any significant functional enrichment. Of the top 15 proteins contributing most to group separation in the PLS-DA analysis, 11 proteins where common to both PR3- and MPO-AAV and 4 proteins were unique for PR3-AAV and MPO-AAV, respectively (Table 1).
Conclusion: Combining quantitative proteomics and bioinformatics analyses, we have identified a large group of DEPs characterizing both active PR3- and MPO-AAV and have determined their associated biological mechanisms. DEPs unique for PR3-AAV formed an interconnected protein network associated with biological processes of high relevance for AAV-pathogenesis. In conclusion, these findings may provide new insights into similarities and differences in the pathogenesis of MPO- and PR3-AAV.

Table 1. PLS-DA results showing the top 15 proteins contributing most to separation of PR3-AAV and MPO-AAV patients, respectively, from healthy controls.

Common for MPO-AAV and PR3-AAV vs healthy controls	Unique for MPO-AAV vs healthy controls	Unique for PR3-AAV vs healthy controls
CCL23	EPHB4	EN-RAGE
CD40	LTBR	MCP-3
IL2-RA	PLC	PRTN3
OPN	RETN	ST2
TGF-alpha		
TIMP-1		
TNF-R1		
TNF-R2		
TNFRSF14		
U-PAR		
VEGFA		

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POS1439

DEREGULATION IN ADULT IGA VASCULITIS SKIN AS THE BASIS FOR THE DISCOVERY OF NOVEL SERUM BIOMARKERS

Keywords: -Omics, Vasculitis, Biomarkers

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Background: Immunoglobulin A vasculitis (IgAV) is a small vessel leukocytoclastic vasculitis, characterized by vascular IgA deposits, and a variable clinical presentation. While IgAV might be self-limiting with a complete recovery, the severe acute form of the disease with gastrointestinal tract (GIT) and renal involvement may lead to significant morbidity, especially in adults. A skin or renal biopsy is still the golden standard for diagnosis. Currently, clinically used markers for IgAV cannot predict patients at risk for severe renal involvement and GIT complications with long-term consequences and which patients will exhibit a mild and self-resolving course limited to skin.
Objectives: This study aimed to use deregulated biological processes in patients' skin to identify potential serum biomarkers in adult IgAV, enabling stratification of patients with different clinical presentation.
Methods: Skin biopsy samples were collected from treatment-naïve adult IgAV patients at the time of diagnostic procedure: 1) skin-limited disease (n=3), 2), IgAV with renal involvement (n=3), and age-/sex-matched HC (n=3). RNA was isolated and 100 bp paired-end sequenced using the Illumina HiSeq 4000 platform (25.9 to 30.8 million reads were obtained per sample). Reads were mapped with Salmon tool against the human transcriptome (Ensemble Release 104). Differentially-expressed genes (log2 fold change ≥ $\left|1\right|$, padj < 0.05) were computed using the R package DESeq2. Potential serum biomarkers were measured in sera of 59 IgAV patients and 22 healthy controls by magnetic bead-based multiplex assay using the Luminex platform. Statistically significant differences between groups were determined by the Mann-Whitney U test (for 2 groups) and the Kruskal-Wallis test followed by Dunn's post-test for multiple comparisons (≥ 3 groups). Spearman's rank correlation was calculated to measure the correlation between parameters.
Results: Based on differentially-expressed genes and deregulated biological pathways in IgAV patients' skin, we identified adipokines (fatty acid binding protein 4 (FABP-4), adiponectin, leptin, serpin A12 and angiopoietin-like protein 4 (ANGPTL4)), extracellular matrix associated proteins (osteopontin and matrix metalloproteinase-1 (MMP1)) and acute phase protein lipopolysaccharide binding protein (LBP) that were measured in patients' sera. We detected significantly higher serum levels of FABP-4 ($p < 0.001$), leptin ($p = 0.002$), ANGPTL4 ($p < 0.001$), osteopontin ($p < 0.001$), MMP1 ($p = 0.007$) and LBP ($p < 0.001$) in adult IgAV patients, as compared with healthy controls. Most highly enriched biological pathways identified only in skin of IgAV patients with renal involvement were the Regulation of lipolysis in adipocytes (padj 9.066×10^{-4}) and ECM-receptor interaction (padj = 4.2882×10^{-3}). Among the top 30 most differentially-expressed genes identified specifically in the skin of IgAV patients with renal involvement were LBP, LEP, SPP1, ADIPOQ, HP and RBP4. Serum levels of adiponectin ($p=0.0043$) and FABP-4 ($p=0.049$) were significantly higher in patients with renal involvement as compared to those with gastrointestinal involvement. The level of adiponectin ($p=0.018$) was significantly higher in patients with skin-limited IgAV compared to patients with gastrointestinal involvement. LBP positively correlated with the levels of two already routinely measured acute-phase proteins, C-reactive protein (CRP) (correlation coefficient = 0.550, $p < 0.001$) and serum amyloid A (SAA) (correlation coefficient = 0.545, $p < 0.001$), established markers of inflammation. Among adipokines, the level of ANGPTL4 positively correlated with CRP (correlation coefficient = 0.514, $p < 0.001$) and SAA (correlation coefficient = 0.528, $p < 0.001$).
Conclusion: We identified novel biomarkers of deregulated lipid metabolism and inflammation in adult patients with IgAV that are associated with internal organ involvement. Further analysis of their involvement in disease pathogenesis is warranted.
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POS1440 EVIDENCE FOR INCREASED RESPONSIVENESS TO INTERFERON TYPE I IN CD8+ T CELLS IN PATIENTS WITH GIANT CELL ARTERITIS

Keywords: Innate immunity, Cytokines and chemokines, Vasculitis

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Background: Giant cell arteritis (GCA) is a vasculitis which can lead to severe complications when not timely recognized and treated. There is a need for the discovery of biomarkers to expedite the diagnostic process. Interferon type I (IFN-I) is increasingly recognized as a key player in a range of autoimmune diseases and might play a role in GCA pathogenesis [1]. However, evidence for IFN-I potentially linking innate and adaptive immune responses in GCA is limited. IFN-I activates the Janus kinase/signal transducers and activators of transcription (JAK-STAT) pathway, leading to an increased expression of interferon stimulated genes (ISGs).
Objectives: In this study, IFN-I involvement in GCA pathogenesis is explored.
Methods: Phopho-STAT1 (pSTAT1) expression was investigated in IFN-α-stimulated peripheral mononuclear cells (PBMCs) gated separately for CD8+ T-cells of patients with GCA (n=18), healthy controls (HC, n=15) and infection controls (n=11) by fluorescent cell barcoding and flow cytometry. Also, in 3 GCA patients and 3 HCs, single cell RNA sequencing was performed on PBMCs focusing on ISG expression. Furthermore, IFN-I induced myxovirus-resistance protein A (MxA) and CD8+ expression was investigated in temporal artery biopsies (TAB) of GCA patients (n=20) and GCA mimics (n=20) by immunohistochemistry.
Results: pSTAT1 expression was increased in IFN-α stimulated CD8+ T-cells from patients with GCA compared to both HC ($p<0.05$) and infection controls. Furthermore, Interferon Induced Transmembrane Protein 1 (IFITM1) mRNA expression was upregulated in peripheral blood CD8+ T cells ($p<0.001$). MxA was present in TABs of 13/20 GCA patients compared to 2/20 mimics and MxA location co-localized with CD8+ expression in the tissue.
Conclusion: Our results provide evidence for IFN-I involvement in GCA pathogenesis, with CD8+ T cells as IFN-I responding effector cells. Increased pSTAT1, IFITM1 and MxA expression may reflect increased IFN-I responsiveness in CD8+ T-cells of GCA patients, both locally and systemically. These findings warrant further investigation regarding IFN-I induced biomarkers and IFN-I related novel therapeutic options.
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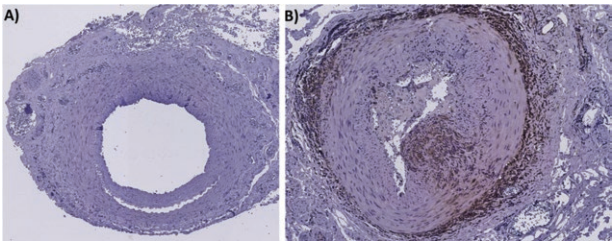


Figure 1 MxA expression (brown staining) in temporal artery biopsy of A) a non-GCA patient and B) a biopsy-proven GCA patient.

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POS1441 OCULAR AND PERIPHERAL BLOOD IMMUNE PHENOTYPES SUGGEST TRANSMIGRATION OF CD16+ MONOCYTES TO AN IMPORTANT EFFECTOR SITE IN BEHÇET'S DISEASE

Keywords: Cell biology, Behcet's disease, -Omics

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Background: Cellular immunity of Behçet's Disease (BD) remains poorly understood. Previous work has provided clues pointing to most innate and adaptive immune cell types in BD, but strong signals from non-immunogenetic studies are rare and often inconclusive.
Objectives: Here we aimed to identify BD/HD discriminant single immune cell profiles in semi-biased and targeted approaches and determine their significance at a BD relevant effector site.
Methods: We utilized multi-parametric flow cytometry to dissect cellular phenotypes in PBMC of untreated BD patients (n=27) and HD (n=22) consisting predominantly of active ocular and major vascular BD subjects. Data were subjected to supervised machine learning (CITRUS) and results verified with targeted gating. We also analyzed anterior chamber (AC) fluid cells and autologous PBMC from BD uveitis subjects with scRNA seq.
Results: CITRUS identified CD16+, CD14low, CD4low, CD3-, CD19- cells as a BD/HD distinguishing cellular expression pattern at an FDR of >0.05. Targeted gating confirmed highly significant differences with large effect sizes in PBMC of BD vs HD for "non-classical" (CD14lowCD16hi) and "intermediate" (CD14+CD16+) monocytes at decreased frequencies compared to peripheral blood. "Classical" (CD14++CD16-) monocytes were more abundant in BD PBMC than in HD. CD16+ dendritic cells (DC) were significantly decreased in BD PBMC. CD14+ cells showed high abundance in the AC during BD uveitis and co-expressed CD16 far more frequently than CD14+ cells in autologous peripheral blood.
Conclusion: Significantly lower frequencies of CD16+ monocyte and DC subsets in PBMC of untreated active BD vs HD strongly point to their importance in BD. The high abundance of CD14+ cells with CD16 co-expression in the eye during uveitis relative to their frequency in autologous peripheral blood, suggests their transmigration or post-migrational interconversion within the eye during BD uveitis rather than a stochastic process.
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POS1442 AMELIORATION OF IGA VASCULITIS BY SUPPRESSION OF THE PATHOLOGICAL EXPANSION OF TFH17 CELLS

Keywords: Vasculitis, Animal models, Treat to target

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Background: Immunoglobulin A vasculitis (IgAV), also named Henoch–Schönlein purpura, is a systemic vasculitis characterized by the deposition of IgA1-dominant immune complexes in small vessels that often involves the skin, joints, gastrointestinal tract, and kidney [1-3]. Research indicated increased frequencies of circulating activated B cells and plasmablasts in IgAV, which may serve as the source of the rising IgA levels [4]. T follicular helper (Tfh) 17 cells are considered to support the activation of B cells and help germinal center (GC) B cells switch to high-affinity IgA production. In human, Tfh17 cells prompt naive B cells to produce higher concentrations of IgA [5]. T cell-deficient mice that receive an adoptive transfer of Th17-Tfh cells show induced development of IgA-expressing GC B cells and an increase in the concentration of IgA. Transfer of non-Tfh17 phenotype $CD4^+$ T cells leads to higher amounts of IgG in serum but fails to increase the serum IgA level [6]. Therefore, targeted therapy against Tfh17 cells may specifically inhibit the secretion of IgA and thereby ameliorate IgAV condition.
Objectives: Our previous study has confirmed that Tfh17 cells increase in the peripheral blood of IgAV patients [7]. However, there is no further study on the pathogenesis of IgAV. To evaluate the pathological role of Tfh17 cells in IgAV, we investigated the mechanism responsible for the differentiation of Tfh17 and the production of IgA in IgAV patients and IgAV rats respectively, and explored how to ameliorate IgAV by modulating Tfh17 generation.
Methods: Peripheral blood mononuclear cells from IgAV patients were analyzed by flow cytometry. In vitro culture was performed to assess the modulation of

cytokine-induced phenotypes. IgAV rat model was established by intragastric administration of mixed solution, intraperitoneal injection of ovalbumin and Freund's adjuvant. IgAV rats were used to explore the therapeutic effects of IL-6 blockade and the regulatory functions of IL-6 and TGF-β-producing dendritic cells in Tfh17 cells. Serum cytokine and IgA levels were measured by ELISA while histopathological changes were evaluated by H&E and PAS staining. Flow cytometry and immunofluorescence staining were used to detect T cell and GC B cell phenotypes in circulation and tissues of IgAV rats.

Results: Frequency of $CD4^+CXCR5^+CCR6^+$ Tfh17 cells were increased in IgAV patients and associated with disease severity. IL-6 promoted the dendritic cell production of TGF-β and Tfh17 differentiation. Blockade of IL-6 signaling using tocilizumab inhibited Tfh17 differentiation, resulting in reduction of the germinal center and IgA production. Suppression of Tfh17 cells using IL-6 blockade greatly ameliorated clinical symptoms such as hemorrhagic rash and bloody stool and decreased IgA deposition and mesangial proliferation in the kidney in IgAV rats.

Conclusion: Our findings suggest that suppression of Tfh17 differentiation can alleviate IgA-mediated vasculitis and may permit the development of tailored medicines for treating IgAV.

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SLE, Sjön's and APS - clinical aspects (other than treatment)

POS1443 CORRELATION BETWEEN SAXON TEST AND UNSTIMULATED SALIVARY FLOW RATE IN PATIENTS WITH SUSPECTED SJÖGREN´S SYNDROME

Keywords: Sjögren syndrome, Diagnostic tests

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Background: Sjögren syndrome (SS) is a chronic systemic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands, which alters their function producing dryness of the mouth, eyes and other mucous membranes. The method used to quantify glandular hypofunction is by whole saliva flow stimulated and unstimulated (UWSF) [1], which takes between 5 and 15 minutes (min).The Saxon test (St) [2], is another tool with the same objective but requires less time: 2 minutes. In the literature, we only have found one study that compared the Saxon test with other diagnostic methods although it is developed in patients without SS [3].

Objectives: To compare the Saxon test and UWSF in a cohort of patients with suspected SS.

Methods: In a consecutive cohort of patients who attended the rheumatology department for suspected SS, UWSF was measured (mL/5 min) and the Saxon test (gr/2 min) was performed. The Index Reported by Patients with SS of the EULAR (ESSPRI) was collected too. This is a patient-reported index designed to assess the severity of patients' symptoms (dryness, pain, somatic and mental fatigue) in SS through an average of single 0–10 numerical scale for each domain. To measure the UWSF, patients were asked to swallow their saliva before the start of the test and then to spit into a container for 5 min. The St was performed by calculating the difference in the weight of two pieces of sterile gauze that the patient chews for two minutes. A UWSF >0.25 mL/min and a St >2.75 g/2min were considered normal, as well as and ESSPRI<5. Spearman's rank correlation coefficient (rs) was used to determine the correlation between both quantitative variables. The Chisquare test and the Gamma test were used in the comparisons between the groups (altered and normal) and the Mann-Whitney U in the comparisons of the quantitative variables based on the groups (altered and normal) previously defined. *P* values <0.05 were considered statistically significant.

Results: We enrolled 199 patients (166 women), with a mean age ± standard deviation of 55,1±13,7 years. The medians (Me) and interquartile ranges (IQR) obtained were 1,50 (0.70 – 2.50) mL/5min for the UWSF, 2,31 (1,60-3,10) g/2min for the St, 6,33 (3.67- 7.67) for ESSPRI and 7,00 (5,00-8,00) for ESSPRI-dryness score. A direct and significant correlation between the St and the UWSF (rs=0,391; $P=2{,}236x10^{-7}$) was observed; 76 patients (38,2 %) presented an altered UWSF and 107 patients (65,2 %) had an altered St. When we analysed the intensity of the association between the different groups (altered/normal) of both variables, we observed a direct and significant association (Gamma value=0,4, *P*=0,019) between both tools. We also detected differences in the St between patients with altered UWSF (Me: 1,72gr/2min; IQR: 1,04-2,50) and those with normal UWSF (Me: 2,62 gr/2 min.; IQR: 1,95-3, 54) ($P=3{,}9x10^{-6}$). Similarly, we observed significant differences in UWSF values between patients with altered St (Me: 1,50 mL/5min IQR: 0,60-2,50) and those with a normal St (Me: 2,00 mL/5min IQR: 1,00-3,00) (*P*=0,014). Regarding the ESSPRI, 129 (65,8 %) patients presented an altered ESSPRI and 153 (78,1%) had an altered ESSPRI-dryness score. The group patients with ESSPRI-dryness score≥5 obtained significantly lower scores on the St (Me: 2,10 g/2min IQR: 1,39-3.01), on the UWSF (Me: 1,5 ml/5min IQR: 0,6-2,0), and on the ESSPRI (Me:7,00 IQR:5,33-8,00) than the normal ESSPRI-dryness score group: Me:2,98 g/2min, IQR:2,22-3,75, on St (*P*=0,001); Me:2,45 ml/5min, IQR:1,50-3,50, on UWSF ($P=6{,}547x10^{-5}$); Me: 3,17 IQR:1, 00-4.08, on the ESSPRI ($P=1{,}17x10^{-15}$).

Conclusion: In patients with suspected SS, there is a direct and significant correlation between the St and the UWSF. Therefore, the St could be useful in the initial assessment of oral gland dysfunction, to save time and/or to select patients who require performing the UWSF.

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POS1444 EXTRAGLANDULAR INVOLVEMENT AND AUTOANTIBODY STATUS AS RISK FACTORS FOR CARDIOVASCULAR DISEASE IN PRIMARY SJÖGREN'S SYNDROME (PSS): A 20-YEAR FOLLOW-UP STUDY

Keywords: Autoantibodies, Sjögren syndrome, Cardiovascular disease

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Background: Primary Sjögren's syndrome (pSS) is an autoimmune disorder characterized by chronic multisystem inflammation with shared pathophysiology with SLE and RA. Cardiovascular events have emerged as major causes of morbidity and mortality in patients with autoimmune diseases however, the clinical significance of cardiovascular disease in patients with pSS remains unclear.

Objectives: To study the association between cardiovascular disease and primary Sjögren's syndrome (pSS) and analyze the risk of cardiovascular disease accordingly to glandular/extraglandular involvement and anti-Ro/SSA and/or Anti-La/SSB autoantibody status.

Methods: pSS patients fulfilling the 2016 ACR/EULAR classification criteria for pSS was consecutively evaluated and followed in our department between 2000 and 2022. We evaluated the prevalence and clinical significance of cardiovascular risk factors with primary Sjögren's syndrome (SS), focusing on the possible association with clinical and immunological features, the therapies administered, and the impact on cardiovascular disease. A two-tailed value of p<0.05 was taken to indicate statistical significance. Potential risk factors associated with cardiovascular involvement were determined by multivariate regression analyses.

Results: A total of 102 pSS patients were included. 90% were female, with a mean age of 65±24 years and a disease duration of 9.9 ±7 years. The baseline prevalence of comorbidities was 59% for hypertension, 29% for cardiovascular diseases, 34% for dyslipidemia, 15% of diabetes, 29% for obesity, 12% had history of stroke and 17% had arterial/venous thrombosis. 39% of patients had a history of smoking. Patients with extraglandular involvement had a higher

prevalence of cardiovascular risk factors, including arterial hypertension (OR 2.28 95% CI (1.01-5.09), p 0.04), dyslipidemia (OR 4.4 95% CI (1.67-11.6), p 0.003), LDL mean values (116±48 vs 99±44, p 0.038), uric acid (6.58±1.7 vs 4.3±1.03, p 0.04) and higher risk for myocardial ischemia (OR 4.09 95% CI (1.46-11.4), p 0.01) after adjustment for age, sex, disease duration, and the significant variables in the univariate analysis. Patients positive for both Ro/SSA and La/SSB autoantibodies had a substantially higher risk of arrythmia (OR 3.4 95% CI (1.01-10.6), p 0.04), arterial and venous thrombosis (OR 5.5 95% (1.18-25.7), p 0.03) and stroke (OR 3 95% (1.02-8.8), p 0.04). In the multivariate logistic regression analysis, extraglandular organ involvement (p=0.008), beta2microglobulin levels (p=0.001), the use of glucorticoids (p=0.02), hypergammaglobulinemia (p=0.02), ESR levels (p=0.007) and an ESSDAI (Sjögren's syndrome disease activity index)>13 (p=0.02) were found to be risk factors associated with cardiovascular events in pSS patients, meanwhile C3 levels (p=0.01) and treatment with HCQ (p=0.03) were protective factors. Anti-Ro/SSA and anti-La/SSB were significant predictors in univariate but not in multivariate analysis.

Conclusion: pSS patients are more vulnerable to cardiovascular diseases (CVDs). In addition to traditional CVD risk factors, we identified risk factors independently associated with cardiovascular involvement in pSS patients, which suggests the need for early detection and prevention measures to improve the prognosis in those patients.

Table 4. Significant logistic regressions for predictors for CV risk

	OR 95% IC	P value
Extraglandular involvement	16.5 (4.51-28.5)	0.008
Beta2microglobulin (mg/dL)	7.83 (3.16-12.5)	0.001
C3 (mg/dl)	0.92 (0.24-0.98)	0.01
Glucocorticoids	7.2 (2.34-15.7)	0.02
Hypergammaglobulinemia	10.2 (4.5-21.2)	0.02
ESSDAI >13	1.2 (0.23-4.52)	0.02
ESR (mm/h)	1.1 (0.42-3.45)	0.007
HCQ	0.82 (0.26-0.92)	0.03

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POS1445 INCLUSION BODY MYOSITIS ASSOCIATED WITH SJÖGREN SYNDROME HAS DIFFERENT IMMUNE CELLS INFILTRATE FROM SPORADIC INCLUSION BODY MYOSITIS

Keywords: Myositis, Sjögren syndrome, Biomarkers

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Background: Within the group of inflammatory myopathies, Inclusion-Body Myositis (IBM) is a distinct pathology with clinical and histological features very different from other entities. In the literature, an association between primary Sjögren's syndrome (pSS) and IBM has been previously reported.

Objectives: The aim of our study was to compare the inflammatory infiltrates between IBM associated or not with pSS and, among patients with pSS, between muscle and salivary gland.

Methods: We conducted a translational research project, from formalin-fixed and paraffin-embedded muscle biopsies of patients with IBM, associated with Sjögren's syndrome (IBM-pSS) and sporadic (sIBM) forms, from 6 French expert centers, and salivary glands were collected when available. Imaging mass cytometry (IMC) multiplex immunostaining (37 markers) was used to quantify and decipher the composition of the inflammatory infiltrates within samples (Figure 1). Supervised and unsupervised statistical analyses were performed to compare IMC data between IBM-pSS and sIBM patients and muscle and salivary glands among patients with pSS.

Results: No statistically significant difference was encountered in our comparisons between IBM-pSS and sIBM muscle biopsies. Nevertheless, some trends were pointed and could merit further work in larger case series. Indeed, IBM-pSS samples (14 patients) tended to have more widespread inflammatory infiltrate than sIBM samples (7 patients) involving on average 4.8% versus 1.6% of muscle biopsy surface respectively (p=0.12). Macrophages and T cells were the predominant populations in both IBM-pSS and sIBM patients' groups. Among T cells, CD8+ cells predominated compared to CD4+ cells in both groups. The proportion of plasma cells (CD138+ CD38+ CD27+) was higher in IBM-pSS than in IBMs patients (medians of 14.7% and 8.5%, respectively, p=022), as was the proportion of B cells (median of 3.1% and 0.5%, respectively, p=0.14). Comparing salivary gland and muscle biopsies in patients with pSS, the plasma cells were predominant in the salivary gland with more numerous plasma cells and B cells and less numerous macrophages and T cells in salivary glands than in muscle samples. Nodular inflammatory infiltrate pattern containing B cells appeared to be restricted to pSS patients both in muscle and salivary gland biopsies.

Conclusion: Using for the first time IMC on muscle biopsy and salivary gland has allowed us 1) to point difference between IBM-pSS and sIMB and 2) similarities between salivary and muscle inflammatory infiltrates in patients with pSS samples. These differences suggest that IBM associated with pSS has a distinct pSS-related pathophysiology compared to sIBM, which could raise potential diagnostic and therapeutic applications.

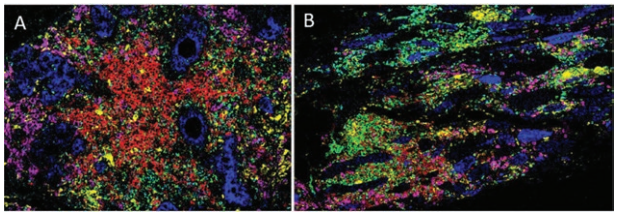


Figure 1. Example of markers of multiplex immunostaining in salivary glands (A) and in muscle (B)

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3249

POS1446 VARIATION IN SYSTEMIC DISEASE ACTIVITY MEASURED WITH ESSDAI IN A PROSPECTIVE LONGITUDINAL COHORT OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME WITHOUT IMMUNOSUPPRESSIVE TREATMENT

Keywords: Outcome measures, Sjögren syndrome

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Background: The EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) has been used as primary endpoint in many recent randomised clinical trials (RCTs) in patients with primary Sjögren's syndrome (pSS). In multiple RCTs, a large placebo effect (>50%) was observed with the ESSDAI. Since patients are often included with a moderate or high disease activity (ESSDAI ≥5), this placebo effect may partly be due to regression to the mean [1]. Little data is available on the natural course of the ESSDAI in patients who are not treated with immunosuppressives in daily clinical practice.

Objectives: To assess the variation in ESSDAI up to five years of follow-up in a cohort of pSS patients without immunosuppressive treatment.

Methods: This prospective longitudinal study included consecutive outpatients with pSS from the ongoing Registry of Sjögren Syndrome LongiTudinal (RESULT) cohort who fulfilled the ACR/EULAR classification criteria for pSS and who reached at least two years of follow-up with available ESSDAI until December 2022. Patients who received immunosuppressive treatment (biological DMARDs, conventional synthetic DMARDs, including hydroxychloroquine, or prednisone) were excluded. Patients visited the outpatient clinic once a year, or on clinical indication more often, and at each visit the ESSDAI was recorded. All

available visits from baseline up to five years of follow-up were used for analyses. For the analysis at group level, yearly visits were used, defined as the nearest available ESSDAI within a time frame of ±6 months from the yearly visit. For analyses at individual patient level, all available ESSDAI scores were used. The largest change (Δ) in ESSDAI was calculated for each patient by subtracting the lowest ESSDAI from the highest ESSDAI score during follow-up.

Results: In total, 247 pSS patients fulfilled ACR/EULAR classification criteria and reached at least two years of follow-up with available ESSDAI. Of these, 142 patients did not receive immunosuppressive treatment and were included. 126 (89%) of these patients were female, median age was 53 years (IQR 43-65), median disease duration was 6 years (IQR 2-10) and 122 (87%) were anti-SSA positive. Median ESSDAI at baseline was 3 (IQR 1-6) and 93 (67%) patients had a low disease activity according to ESSDAI (score<5). At group level, ESSDAI remained stable during five-year follow-up (Figure 1A). At individual patient level, the ESSDAI varied in the majority of patients (Figure 1B). The median largest Δ (worsening or improvement) in ESSDAI was 4 (IQR 2-8, range 0-22). In total, 93 (65%) patients had a Δ of ≥3 points in ESSDAI, and 65 (46%) patients a Δ of ≥5 points at some point during follow-up. Of the 93 patients with an ESSDAI<5 at baseline, 50 (54%) patients remained in a low disease activity state during follow-up (median follow-up 40 months). Of the 46 (89%) patients who had a moderate or high disease activity (ESSDAI≥5) at baseline, 41 (89%) improved to a low disease activity for at least one visit (Figure 1B) and 37 (80%) patients reached the previously defined minimal clinically important improvement of ≥3 points improvement at some point during follow-up compared to baseline.

Conclusion: In this prospective longitudinal cohort of pSS patients without immunosuppressive treatment, a large variation in ESSDAI was observed during follow-up in individual patients, despite the median ESSDAI scores remaining stable at group level. This study underlines that natural variation in systemic disease activity measured with ESSDAI should be taken into account when using ESSDAI as study endpoint.

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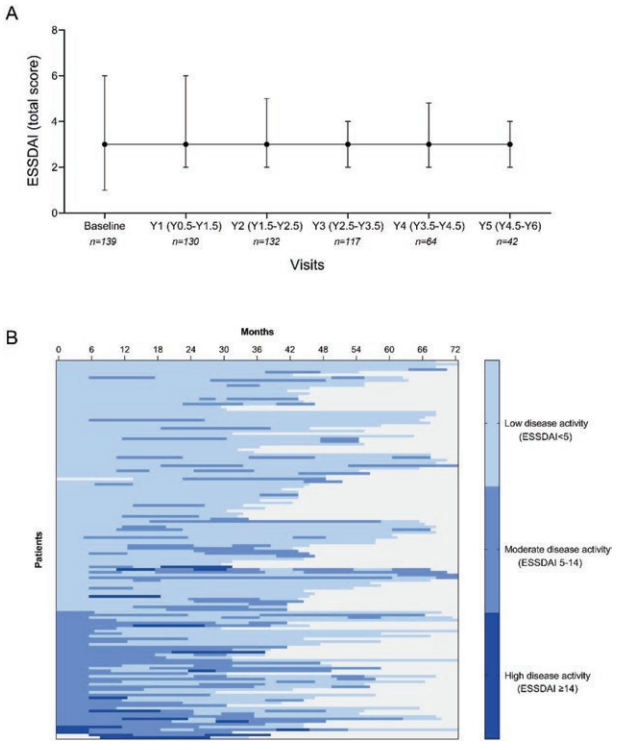


Figure 1. ESSDAI scores up to five years of follow-up in pSS patients without immunosuppressive treatment. A) Median ESSDAI scores (with IQR) at group level B) ESSDAI scores in categories (low, moderate and high disease activity) at individual patient level, with last observation carried forward until next available ESSDAI assessment, sorted by baseline ESSDAI.

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Disclosure of Interests: Liseth de Wolff: None declared, Gwenny M. Verstappen Consultant of: ArgenX, Alja J. Stel: None declared, Greetje S. van Zuiden: None declared, Jolien F. van Nimwegen Speakers bureau: Bristol-Myers Squibb, Consultant of: Bristol-Myers Squibb, Arjan Vissink Grant/research support from: Unrestricted research grants from Bristol-Myers Squibb and Roche, Frans G.M. Kroese Speakers bureau: Bristol-Myers Squibb, Roche, Janssen-Cilag, Consultant of: Unrestricted research grants of Bristol-Myers Squibb, Grant/research support from: Bristol-Myers Squibb, Suzanne Arends Consultant of: ArgenX and Novartis, Hendrika Bootsma Speakers bureau: Bristol-Myers Squibb and Novartis, Consultant of: Bristol-Myers Squibb, Roche, Novartis and Union Chimique Belge, Grant/research support from: Unrestricted research grants from Bristol-Myers Squibb, Roche and AstraZeneca.

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POS1447

"IF I HAVE SJÖGREN'S SYNDROME, I WANT TO KNOW IT AS EARLY AS POSSIBLE": PERSPECTIVES OF FIRST-DEGREE RELATIVES OF PEOPLE WITH SJÖGREN'S SYNDROME FROM AN INTERNATIONAL SURVEY

Keywords: Sjögren syndrome

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Background: In recent years, rheumatology research focused on first-degree relatives of people with rheumatic diseases, mainly rheumatoid arthritis, since they have a higher risk of developing the disease compared with the general population and offer a potential source of insight into the preclinical phase of the disease. However, evidence on preclinical Sjögren's syndrome is still lacking.

Objectives: To explore the perspective of first-degree relatives of people with SS and inform the Pre-Sjögren's Syndrome Targeted Immunology Evaluation (PreSStige) study, conducted under the auspices of the EULAR Study Group on Sjögren's Syndrome (eSSential).

Methods: An online survey targeting first-degree relatives of people with SS was developed in English and translated into 11 languages (Italian, German, French, Spanish, Portuguese, Greek, Swedish, Finnish, Romanian, Norwegian and Maltese). The survey was launched on social media on December 15, 2022 and distributed via patient associations, forums, support groups, and in 3 Rheumatology participating centres (Austria, Italy and Portugal). Respondents without a diagnosis of SS were confronted with a scenario where they were offered a free rheumatology examination to assess whether they had symptoms suggestive of pSS. If so, they are advised to undergo additional exams (within a variable range of costs) to ascertain whether they have pSS. Surveys were accepted until January 10, 2023.

Results: Of 1064 people starting the survey, 677 respondents from 32 countries fulfilled the entry criteria (age >18 years, being a first-degree relative of a person living with pSS). 90% of respondents were siblings, 7% were offspring, and 3% were parents of pSS patients. Respondents were mainly females (80%), aged 30-49 years (31%) and 50-70 years (38%). 155 (23%) of respondents already had a diagnosis of SS, while 119 (17%) had a diagnosis of other autoimmune diseases (AD) (23/119, 19% had more than one AD). When asked about their perceived risk of developing SS or another AD, several respondents did not feel to be at higher risk being first-degree relatives of affected people (Figure 1). When confronted with an hypothetical scenario, over half of the respondents without a diagnosis of pSS (N=522) mentioned feeling either worried, sad or scared about the possibility of being diagnosed with pSS. Nonetheless, the majority of them (86% of 522) were keen on accepting a preclinical rheumatology consultation, with the main reason for that being, "If I have pSS/other autoimmune diseases, I want to know it as early as possible" (82%). Conversely, those that would decline a free rheumatology examination mainly justified their decision based on the absence of symptoms suggestive of pSS (56%). Among respondents that would accept a free rheumatology consultation, 84% would proceed further and perform additional exams if advised by the rheumatologist based on the detection of symptoms/signs suggestive of pSS. As above, the main reason was the possibility of achieving an early diagnosis. The respondents that accepted the free rheumatology consultation but would not proceed further even if the rheumatologist would identify red flags for pSS mentioned the economic aspect as the main barrier (specifying they would accept performing additional exams if free of charge).

Conclusion: Our study explored, for the first time, the perspective of first-degree relatives of people with SS highlighting an overall willingness to undergo preclinical examinations for an early SS diagnosis. Economic challenges (namely,

paying for diagnostic exams) have been identified as a barrier. The survey is still open and is being translated into additional languages to increase its reach.. The results of the survey will inform the next steps of the Pre-Sjögren's Syndrome Targeted Immunology Evaluation (PreSStige) study.

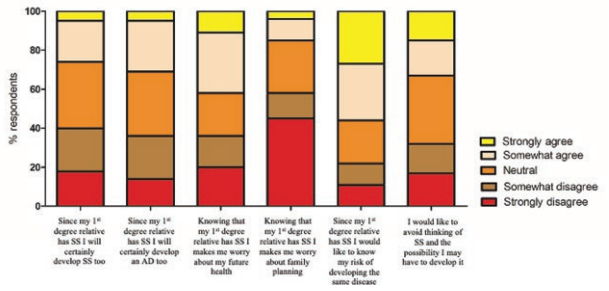


Figure 1. Respondents' level of agreement with statements related to their perceived risk and attitude towards the development Sjögren's Syndrome or other autoimmune diseases

Acknowledgements: The authors are grateful to the individuals and patient associations who supported this project and helped with the translation and distribution of the survey.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3851

POS1448 INDIVIDUALS AT RISK FOR SJÖGREN'S SYNDROME – TWO-YEAR DATA OF THE PRESSTIGE (THE PRE-SJÖGREN SYNDROME TARGETED IMMUNOLOGY EVALUATION) STUDY

Keywords: Sjögren syndrome, Autoantibodies

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Background: Primary Sjögren's syndrome (pSS) is a chronic autoimmune disease often diagnosed years after appearance of the first symptoms. Therefore, little is known about initial development of the disease. Anti-Ro antibodies can be found years before the first symptoms appear.
Objectives: To identify individuals at risk for pSS and follow up over 10 years to examine symptoms and immunopathology before and during the development of pSS.
Methods: This ongoing longitudinal study enrolled individuals at risk for developing pSS but have not met the ACR-EULAR classification criteria. We recruited three groups: A.) Anti-Ro positive individuals without any symptoms for an underlying systemic autoimmune disease; B.) First degree relatives of patients with a diagnosis of pSS AND an abnormal immunologic laboratory value (ANA ≥ 1:160 and/or anti-Ro$^+$ and/or rheumatoid factor$^+$) C.) Individuals with at least one feature of the ACR-EULAR classification criteria for pSS, but not fulfilling the criteria. At screening and at annual follow-up visits, demographic data, blood, urine and saliva samples were obtained. Salivary flow, Schirmer's test, and salivary gland ultrasonography (SGUS) using Hocevar-Score were performed. A lip salivary gland biopsy (LSB) was obtained at the screening visit and repeated once when typical symptoms appeared within the follow-up visits. The primary endpoint was the development of definite pSS according to the ACR-EULAR classification criteria or a diagnosis of another systemic autoimmune disease.
Results: After two years, 53 subjects were recruited from all three groups, of whom 31 were enrolled in the study (Anti-SSA$^+$ n=25, relatives n=4, incomplete n=2). Most of the 22 screening failures were relatives who did not have an abnormal immunologic laboratory value. 28 individuals were female, they had a mean age of 49.6 ± 12.7 years (SD; standard deviation) and a mean body weight of 71.4 ± 15 kg. 11 individuals reported having a relative with an underlying autoimmune disease. The median ESSDAI was 0 (0-5; min-max). individuals had a pathological stimulated whole saliva flow (mean 3.7 ± 1.4 g) and eight had pathological Schirmer's test (left eye: mean 13.6 ± 13.1 mm; right eye: 13.2 ±12.2 mm). Three of 14 individuals had a pathological SGUS score. All three individuals were recruited in the Anti-Ro$^+$ group. At screening visit, 11 LSB were performed (mean focus score of 0.53 ± 1.2) and one individual reached a focus score ≥ 1. So far, 18 individuals have completed the two-year visit. Two of them had pathological stimulated whole saliva flow (mean 3.85 ± 1.4 g) and five of them a pathological Schirmer's test (left eye: mean 15.4 ± 13 mm; right eye: 14.5 ± 13). The median ESSDAI was 0 [0-4]. Eight SGUS were performed with a mean Hocevar-Score of 5.6 ± 8. Within two years, four patients (13%) were diagnosed with pSS, one (3%) with systemic lupus erythematosus and one (3%) with rheumatoid arthritis.
Conclusion: This longitudinal study for the first time provides us with data on the evolution of pSS. Future recruitment at multiple centers and longer follow-ups will shed light on the earliest phase of pSS.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3724

POS1449 CARDIOVASCULAR DISEASE IN PRIMARY SJÖGREN SYNDROME

Keywords: Sjögren syndrome, Cardiovascular disease

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Background: Primary Sjögren's syndrome (pSS) is associated with an increased prevalence of traditional risk factors and cardiovascular diseases (CVDs).
Objectives: The study aimed to identify specific risk factors for CVD in pSS patients.
Methods: PSS patients with and without CVD were compared. All patients fulfilled the EULAR/ACR classification criteria. Patients with CVD presented at least one of the following manifestations: myocardial infarction, transient ischemic attacks, ischemic or hemorrhagic stroke, peripheral artery disease, coronary artery disease and carotid plaques. Data were collected by a standardized protocol and review of medical records.
Results: 61/312 (19.6%) pSS patients presented with CVD. Traditional risk factors such as hypertension, hypercholesterinemia and diabetes (p<0.05), pSS manifestations, in particular vasculitis (p=0.033) and Raynaud's phenomenon (p=0.018) were associated with CVD. Among patients with ischemic events (28/312, 9%), particularly cerebrovascular disease (n=12/28, 42.9%), correlations with increased EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) (p=0.039) and EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) (p=0.048) were observed. Age at first cerebrovascular event was 55.2 [48.9 – 69.6] years. Multivariate analysis confirmed hypertension (odds ratio (OR) 3.7, 95% confidence interval (CI) 1.87–7.18, p<0.001), hypercholesterinemia (OR 31 3.1, 95% CI 1.63–5.72, p<0.001), male gender (OR 0.4, 95% CI 0.17–0.78, p=0.009), Raynaud's phenomenon (OR 2.5, 95% CI 1.28–4.82, p=0.007) and CNS involvement (OR 2.7, 95% CI 1.00–33 7.15, p=0.048) as independent CVD predictors.
Conclusion: Raynaud´s phenomenon as well as vasculitis and high ESSDAI have shown a significant association to CVD. PSS patients with cerebrovascular events were younger than expected. Knowledge about risk factors may help clinicians to identify pSS patients at risk for CVD. After diagnosis of pSS, patients should be screened for risk factors such as hypertension and receive appropriate therapy to prevent or at least reduce sequelae such as infarction. However, further investigations are necessary in order to achieve a reliable risk stratification for these patients.
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Disclosure of Interests: None Declared.
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POS1450 3-YEAR ANALYSES OF AT-RISK ANA-POSITIVE COHORT: PROGNOSTIC VALUE OF CLINICAL AND INTERFERON BIOMARKERS TOWARDS AUTOIMMUNITY

Keywords: Biomarkers, Sjögren syndrome, Systemic lupus erythematosus

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Background: Autoimmune connective tissue disease (AI-CTD) arise from a common "At-Risk" ANA-positive population in which clinical phenotype does not reliably predict progression. We previously showed that higher IFN-Score-B and family history were predictive of progression to meeting classification criteria at 12-months[1]. However, classification criteria may undergo revision and not capture all significant outcomes. There is limited data on longer-term outcomes since some may progress at later time-points.

Objectives: To describe the 3-year outcomes of At-Risk individuals; to assess discriminative ability of baseline clinical and IFN-Score-B in predicting various progression endpoints at 1 and 3 years.

Methods: We conducted a prospective cohort study in At-Risk individuals (ANA-positive, non-specific symptoms of ≤1 year and treatment naïve). Patients were assessed at baseline, then annually for 3 years. We used multiple RMD classification criteria, including the revised 2019 EULAR/ACR for SLE, and need for therapy, to group patients as below:

1. Absolute non-progressors (ANP) (no clinical criteria)
2. Undifferentiated CTD (U-CTD) (≥1 clinical criteria but not fulfilling RMD criteria). This group was subdivided into those requiring an immunosuppressant (IS) excluding antimalarials only and those who did not)
3. Year 1 progressors (meeting criteria for RMD by 1 year)
4. Late progressors (meeting criteria for RMD in Years 2-3)
5. Clinically significant disease (CSD) (progressors OR U-CTD on IS)

Bloods were analysed for two IFN-stimulated gene expression scores previously described[2]. Discrimination of single or combined clinical and IFN-Score-B markers were assessed using ROC curve analyses.

Results: Of 148 patients, 132 (89%) were female, 107 (72%) were Caucasians, 48 (32%) had a family history of RMD, 56 (38%) were anti-dsDNA+ and 8 (6%) had low C3 and/or C4 level. Number of established clinical criteria at baseline were 0 (30%), 1 (64%) and 2 (6%). Outcomes were: Year 1 progressors: 21 (14%) [SLE=14; pSS=6; AS=1]; Late progressors: 12 (8%) [SLE=10; pSS=1; AS=1]; U-CTD on IS: 8 (5%); U-CTD on antimalarials only: 20 (14%); U-CTD not on therapy: 52 (35%) and ANP: 35 (24%). Thus, 41 (28%) patients were classified as CSD. Only 2/148 (1%) patients progressed after the first 2 years. For the prediction of Year 1 progressor, in addition to baseline IFN-Score-B and family history, multivariable logistic regression showed total number of any established clinical criteria was associated with increased risk, OR 6.8 (95% CI 1.8-25.4). Table 1 showed that the combined baseline markers (IFN-Score-B, family history and number of clinical criteria) had good accuracy in predicting various definitions of progression at Years 1 and 3 as per AUROC.

Conclusion: Just over a quarter of At-Risk individuals developed into CSD (progressors and patients who did not meet criteria but needed IS therapy) by 3-year follow-up. Combined baseline clinical and IFN biomarkers could be used to risk stratify ANA-positive referrals to rheumatology at the first visit to exclude imminent or future disease/requirement of immunosuppressant. A validation study with cost-effectiveness analysis of these markers is in progress and would help translate their use in clinical practice and inform early therapy trials in the "High Risk" individuals.

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

Table 1

Progression Criteria	No. of Progressors (n/N)	AUC (95% CI) for Family History of RMD Only	AUC (95% CI) for No. of criteria Only	No. of Progressors with samples available (n/N)	AUC (95% CI) for IFN-Score-B Only	AUC (95% CI) for Combined 3 Markers
Year 1 Classification	21/148	0.67 (0.54, 0.80)	0.70 (0.56, 0.81)	20/122	0.81 (0.72, 0.91)	0.89 (0.83, 0.96)
Year 1 CSD	26/148	0.65 (0.53, 0.77)	0.70 (0.59, 0.80)	24/122	0.76 (0.66, 0.87)	0.86 (0.77, 0.95)
Year 3 Classification	33/148	0.60 (0.49, 0.72)	0.71 (0.61, 0.80)	31/122	0.64 (0.52, 0.76)	0.77 (0.67, 0.87)
Year 3 CSD	42/148	0.59 (0.49, 0.69)	0.71 (0.63, 0.80)	40/122	0.59 (0.48, 0.70)	0.74 (0.64, 0.83)

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POS1451

THE PROGNOSTIC VALUE OF THE IMMUNOHISTOCHEMICAL STAINING OF THE MINOR SALIVARY GLAND BIOPSY IN SJOGREN'S SYNDROME: 3 YEARS FOLLOW UP

Keywords: Prognostic factors, Organ damage, Sjögren syndrome

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Background: The most important diagnostic test in Sjogren's syndrome is the minor salivary gland test (MSGB). Immunohistochemical staining of the MSGB may provide prognostic value for organ affection.

Objectives: To compare the lymphocytic composition of the MSGB and major organ affection in patients with Sjogren's syndrome during 3 years of follow-up. To compare the lymphocytic composition of the MSGB and worsening of SSDDI index more than 2 points.

Methods: A retrospective cohort study was conducted. Inclusion criteria was patients ≥18 years that met 2016 ACR/EULAR criteria for Sjogren's Syndrome with focal lymphocytic sialadenitis (≥1 infiltration of ≥50 lymphocytes) by MSGB. CD45, CD4, CD8, CD20 staining was carried out for all samples. Infection, amyloidosis, IgG4 related diseases or head radiation therapy were excluded. Finally, 78 patients from the systemic autoimmune diseases division between September 2017 – October 2018 were included. Patients were followed up for 3 years. The outcomes evaluated were: 1. Severe organ affection (defined as lymphoma, interstitial lung disease, central or peripheral nerve system, renal involvement or arthritis) that required steroids or disease modifying drugs; 2. Worsening of SSDDI index ≥ 2 points.

Results: The mean age was 60.6 (SD 12.7) and 8 (10.3%) of the patients were men. There was overlap with other SAD in 13 (16.7%) patients. Severe organ damage was present in 16 (20.5%) and moderate or high ESSDAI in 6 (7.7%) at baseline. Ro52/60 was present in 15 (19.3%). Steroid treatment was used in 6 (7.8%). The baseline characteristics of patients with severe organ affection was compared with patients that did not present severe organ affection. Patients with severe organ affection had a significantly higher proportion of male sex (56.3% vs 35.7%), higher median baseline ESSDAI (3.81 vs 1.06, p=0.00) and SSDDI (1.88 vs 1.02, p=0.04). Higher proportion of lymphoma (18.8% vs 3.2%, p=0.024), higher proportion of steroids (37.5% vs 0, p=0.00) and higher proportion of disease modifying drugs (37.5% vs 3.2%, p=0.00) were observed as well. The comparison of lymphocytic composition of the BGSM according to outome 1 and outcome 2 are summarized in Table 1.

Table 1.

Variable, mean (SD)	Stable disease	Severe organ affection	p-value	SSDDI ≤ 2	SSDDI > 2	p-value
Number of infiltrates	1.44 (0.88)	1.88 (1.15)	**0.049**	1.46 (0.87)	1.68 (1.13)	0.18
Total lymphocytes	121.05 (112.52)	191.56 (256.17)	**0.051**	124.91 (117.56)	162.5 (222.27)	0.17
T cells	58.95 (38.77)	115 (157.06)	**0.0062**	60.27 (38.98)	96.36 (137.57)	**0.038**
CD4+ cells	41.4 (3.39)	82.11 (27.58)	**0.046**	42.39 (25.21)	70.25 (93.61)	**0.027**
CD8+ cells	24.69 (2.38)	49.32 (17.94)	**0.0084**	23.59 (17.10)	46.97 (59.56)	**0.007**
B cells	62.10 (84.06)	76.56 (132.71)	0.30	64.64 (88.66)	66.14 (112.45)	0.48
Limfos aïllats	0.18 (0.39)	0.19 (0.40)	0.46	0.19 (0.40)	0.13 (0.35)	0.27

Conclusion: There were significantly increased number of total lymphocytes and number of infiltrates in the MSGB of patients that presented severe organ affection within 3 years of follow up. Also a significantly increased number of T cells, both CD4+ and CD8 cells, were observed in patients with severe organ affection.

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POS1452

PERIODONTITIS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: A NORWEGIAN NATION-WIDE REGISTER STUDY OF 10 086 PATIENTS

Keywords: Sjögren syndrome, Registries, Epidemiology

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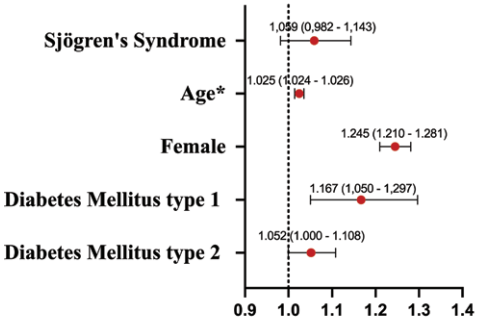
Background: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disorder characterized by focal lymphocytic infiltration of the exocrine glands causing dry eyes and dry mouth. Immunological mechanisms in pSS have similarities with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), which have increased risk for periodontitis [1]. Patients with pSS already have inferior oral health and information regarding a possible connection between periodontitis and pSS is sparce. There is a need to explore this further in a large-scale study.
Objectives: To investigate the association between periodontitis and primary Sjögren's syndrome in a large national cohort.
Methods: We conducted a population-based study, where the cohorts were identified based on International Classification of Disease (ICD)-10-codes registered in the Norwegian Patient registry (NPR) during the period January 2011 – December 2017. The outcome was the manifestation of periodontitis defined by either at least one registration of periodontal surgery or 6 or more registrations of systematic treatment of periodontitis in the Norwegian Control and Payment of Health Reimbursement (KUHR). To be included in the pSS cohort (n=10 086) patients had to have 4 or more registrations with M35.0 as the main diagnosis in NPR. This limit was set to minimize the risk of miscoding. The comparative cohort (n=310 573) entailed patients treated for assumed non-osteoporotic fracture or having undergone hip- or knee replacement due to osteoarthritis during the study period. Only patients between 20 – 80 years of age were included, and patients with RA or SLE was excluded from the study population. Odds Ratio (OR) for periodontitis was calculated using logistic regression analyses adjusting for sex, age, diabetes mellitus (DM) 1 and 2, myocardial infarction (MI) and death. Lastly, similar regression analyses were performed for 6 age categories.
Results: A total of 760 (7.5%) patients in the pSS cohort had periodontitis, compared to 22 178 (7.1%) in the control cohort (p = 0.13), **Table 1**. When adjusting for age, sex, DM1 and DM2, the presence of pSS had no significant association to periodontitis (OR: 1.06, 95% CI: 0.98 – 1.14), **Figure 1**. In the age group 50 – 60 years the presence of pSS was statistically significantly associated periodontitis (OR: 1.22, 95% CI: 1.06 – 1.40). The same association could not be seen in any other age group. Furthermore, increasing age was associated with increased risk of periodontitis (OR: 1.025, 95% CI: 1.024 – 1.026.)
Conclusion: These results indicate that patients with pSS age 50-60 years have a significant increased risk of periodontitis compared to a control population. However, we observed no association between periodontitis and pSS in any of the other age groups in this large nationwide study.
REFERENCE:
[1] Bolstad et al., J Periodontol 2022

Table 1. Characteristics of the study population

	Sjögren's syndrome cohort n=10 086	Control cohort n=310 573	*p*-value*
Female sex, n (%)	8090 (80.2%)	176 122 (56.7%)	**<0.001**
Age, years, median (IQR)	59 (20.0)	62 (18.0)	**<0.001**
Age in years			
20 – 29, n (%)	525 (5.2%)	9125 (2.9%)	-
30 – 39, n (%)	817 (8.1%)	14 517 (4.7%)	-
40 – 49, n (%)	1439 (14.3%)	39 217 (12.6%)	-
50 – 59, n (%)	2386 (23.7%)	72 709 (23.4%)	-
60 – 69, n (%)	2852 (28.3%)	94 506 (30.4%)	-
70 – 80, n (%)	2067 (20.5%)	80 499 (25.9%)	-
Periodontitis, n (%)	760 (7.5%)	22 178 (7.1%)	0.131
DM1, n (%)	150 (1.5%)	5127 (1.7%)	0.204
DM2, n (%)	687 (6.8%)	23 556 (7.6%)	**0.004**
MI, n (%)	327 (3.2%)	10 382 (3.3%)	0.579
Death during study period, n (%)	296 (2.9%)	16 464 (5.3%)	**<0.001**

*p-values derived from chi-square analyses for categorical variables and t-test for continues variables. IQR: interquartile range

Figure 1: OR (95% CI) for periodontits in patients with primary Sjögren's Syndrome versus controls



*Age was included as a continuous variable and the OR refers to each increasing year of age

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POS1453

PROGRESSIVE PULMONARY FIBROSIS ACCORDING TO THE NEW ATS DEFINITION IS NOT UNCOMMON IN THE CONTEXT OF SJÖGREN'S SYNDROME-ASSOCIATED INTERSTITIAL LUNG DISEASE

Keywords: Sjögren syndrome, Lungs

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Background: Interstitial Lung Disease is relatively frequent in Primary Sjögren's Syndrome patients (SS-ILD), however, data on its prognosis are heterogenous. The American Thoracic Society (ATS) recently provided clinical-instrumental criteria for the definition of Progressive Pulmonary Fibrosis (PPF) (1), based on the assumption that this clinical phenotype is associated with worse prognosis and may benefit from treatment with the novel antifibrotic agents. Frequency and characteristics of PPF, defined according to ATS, have not been investigated in the context of SS-ILD.
Objectives: 1. To describe the outcome of SS-ILD in terms of ILD progression according to the recent definition of PPF in our cohort. 2. To identify specific factors associated to PPF in well characterized SS-ILD patients.
Methods: Demographic, clinical, biological and imaging data of SS patients attending our center were retrospectively analyzed. SS-ILD was defined based on clinical history, pulmonary function tests (PFT) and HRCT assessed by an expert thoracic radiologist for all patients. She also defined ILD pattern, extension (by Warrick score) and progression on HRCT. The new ATS definition of PPF was applied to all SS-ILD patients in follow-up in the last 4 years, who presented at least 2 clinical-instrumental evaluations at 1 year of distance. PPF was defined in the presence of 2/3 among: worsening symptoms, significant functional decline (FVC ≥5% or DLCO ≥10%) and radiological progression, within 1 year. PPF and non-PPF SS-ILD patients, with complete imaging and functional follow-up data available, were then compared in terms of clinical, biological, functional and imaging features. For statistical analysis, we used the Fisher test for categorical data and the ANOVA t-test or Mann-Whitney test for continuous data.
Results: Out of 620 primary SS patients attending our center, 52 (8.4%) were diagnosed with SS-ILD (F:M=46:6). Mean age at diagnosis was 61 (±13) years, positive SSA were present in 44/52 (84.6%), and the mean follow-up time was 8 (±7) years. ILD was the first manifestation of SS in 32/52 (61.5%) and followed SS diagnosis in 20/52 (38.5%) cases, with a mean latency of 8.5 (±6) years. The distribution of ILD patterns was in line with recent literature, with 24/52 (46.2%) patients presenting NSIP, 9/52 (17.3%) UIP, 7/52 (13.5%) LIP, 8/52 (15.4%) NSIP+OP, 2/52 (3.8%) OP, and 2/52 (3.8%) an unclassifiable pattern. Out of 46 SS-ILD patients with available follow-up data: 13/46 (28.3%) presented worsening clinical symptoms; 13/42 (31%) experimented significant decline of FVC (≥5%) and/or DLCO (≥10%), while 4 patients were unable to perform PFT due

to desaturation; 3/46 (6.5%) patients died because of ILD progression. Complete seriate evaluations including HRCT at 1-year distance were available for 17 patients: 8/17 (47.1%) were defined as PPF and 10/17 (58.8%) as non-PPF according to the ATS definition. The former group exhibited older age at diagnosis (p=.001) and a UIP pattern in 5/8 vs 0/9 cases (p=.06). Standard of care immunosuppressive treatment did not differ significantly between the two groups, while no patients were treated with antifibrotics.

Conclusion: The clinical phenotype of PPF is relatively common among SS-ILD patients and is associated with older age at diagnosis and a UIP pattern on HRCT. These characteristics may aid in the selection of patients eligible for antifibrotic therapy.

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POS1454 ARE ULTRASOUND SALIVARY PARENCHYMAL ABNORMALITIES MORE SEVERE IN PRIMARY SJÖGREN PATIENTS WITH A HIGHER DISEASE DURATION? A TRANSVERSAL INTERNATIONAL STUDY

Keywords: Ultrasound, Sjögren syndrome

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Background: Salivary gland ultrasonography (SGUS) is commonly used in primary Sjögren Disease (pSD) as a diagnostic tool [1]. It could also be used to monitor disease activity, but severity of SGUS parenchymal abnormalities in relation to disease duration is not well characterized.

Objectives: To assess transversally the severity of ultrasound salivary parenchymal abnormalities in relation to pSD duration.

Methods: In this prospective cross-sectional international multicentric study, patients with pSD according to 2002 or 2016 ACR/EULAR classification criteria were included. Parenchymal abnormalities assessed by ultrasound within both parotid and sub-mandibular glands were reported on a standardized form and classified according to the semi-quantitative score of the OMERACT (global score and each item evaluated separately) [2]. Reliability between experts was measured after online training. Demographic, clinical and paraclinical data were also collected and patients were separated into 4 groups according to disease duration from the first buccal dryness symptoms (group A: < 5 years, group B: between 5 and 10 years, group C: between 10 and 20 years, group D: > 20 years of evolution).The association between disease duration groups and SGUS parenchymal abnormalities was quantified in terms of odds ratio and its 95% confidence interval.

Results: 247 patients were consecutively included between May 2019 and February 2022 in 12 international centers. They were 47, 69, 78 and 53 in groups A, B, C and D, respectively. Women represented 94.7% of patients, with a median age of 58 [range 19-89] years old. Oral and ocular dryness were reported by 99.6% and 95.1% of patients, respectively. Salivary flow was abnormal in 74.7% of patients and Schirmer's test in 82.1%. The focus score was ≥1/4mm2 in 89% of patients. 85% of patients had positive anti-SSA and 59.6% had rheumatoid factor. The median ESSDAI score was 3 [0-48]. Considering for each patient the gland with the highest US OMERACT score, there was a global significant association between disease duration and OMERACT score (OR for 5 years duration: 1.23 [IC95% 1.04; 1.47], p=0.02). When comparing groups A+B versus C+D on the OMERACT score, the OR was 1.95 [IC95% 1.10; 3.46], p=0.02, while no significant difference was found when comparing group A versus B+C+D. Considering each item of the OMERACT score, there was not any statistical difference between the 4 groups in relation to the proportion of an/hypoechoic areas in the gland nor homogeneity or posterior border visibility. The only statistical difference between groups was found regarding the proportion of hyperechoic bands (p = 0.0009). When comparing group A versus B+C+D on this item, the OR was 2.55 [95%CI 1.30-5.01], p=0.006).

Conclusion: This large international transversal study in patients with pSD found a positive association between global SGUS lesions evaluated by the OMERACT score and disease duration, with a significant difference only observed in the proportion of hyperechoic bands, when considering separately each item of the score. This may suggest a progressive fibro-adipous evolution of the gland across disease duration. The presence of diffuse hyperechoic bands (grade 3 in the OMERACT scoring system), corresponding to a higher disease duration group, could be useful in the future to stratify patients in clinical trials and to interpret SGUS modifications after treatment.

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POS1455 INTERSTITIAL LUNG DISEASE IN SJOGREN'S SYNDROME: PREVALENCE, PATTERNS, TREATMENT, AND PROGNOSIS

Keywords: Real-world evidence, Sjögren syndrome, Comorbidities

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Background: Interstitial lung disease (ILD) is a potentially serious yet underdiagnosed manifestation of primary Sjogren's syndrome (pSS).

Objectives: This observational study aimed to investigate the clinical, functional, and imaging characteristics of ILD in pSS, together with treatment and prognosis.

Methods: Longitudinal clinical and laboratory data of patients with pSS were extracted from three hospitals of the Catholic Medical Center through a clinical data warehouse, between March 1, 2012, and February 28, 2022. Predisposing factors for the development of ILD and acute exacerbation were identified using a logistic regression model.

Results: A total of 1,402 patients with pSS were included in this study (Female, 98%; median age, 55 years). Among them, 92 patients with pSS (7%) were comorbid with ILD (21 biopsy-proven cases). Fibrosing nonspecific interstitial pneumonia (NSIP) was the most prevalent CT pattern in pSS-ILD (58%), followed by usual interstitial pneumonia (20%), and organizing pneumonia (16%). At the diagnosis with pSS-ILD, 64% of patients showed reduced diffusion capacity, and 54.3% of patients with pSS-ILD showed a restrictive functional pattern. The median follow-up period was 3.2 years. During follow-up, six patients died (6.5%) and 26 patients (28.3%) experienced acute exacerbation (AE). However, 64% of patients showed no AE without treatment. Lower baseline forced vital capacity (FVC) (Odds ratio (OR), 0.962, P = 0.026) and high neutrophil-to-lymphocyte ratio (OR, 3.59, P = 0.046) were significant predisposing factors for AE.

Conclusion: ILD accounted for 7% of the comorbidity of SS, and 64% showed stable lung function without treatment. AE was associated with NLR and baseline FVC.

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POS1456 DIAGNOSTIC ACCURACY OF THE LABIAL SALIVARY GLAND BIOPSY INCREASES WHEN OTHER HISTOPATHOLOGICAL PARAMETERS BESIDES FOCUS SCORE ARE TAKEN INTO ACCOUNT IN PRIMARY SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Diagnostic tests

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Background: Salivary gland biopsies play an important role in the classification and diagnosis of primary Sjögren's syndrome (pSS). Currently, salivary gland biopsies are considered positive for pSS if the focus score (FS), calculated by the number of characteristic lymphocytic periductal infiltrates per 4 mm2, is ≥1. However, the FS has several limitations, and other histopathological parameters, such as (pre-)lymphoepithelial lesions, IgA/IgG plasma cell shift and germinal centers can also be present in salivary glands of pSS patients. Although the diagnostic value of these histopathological features in pSS was already shown separately, no study explored the added diagnostic value of these histopathological parameters together.

Objectives: To evaluate the diagnostic accuracy of the labial salivary gland biopsy based on multiple histopathological parameters (FS, (pre-)lymphoepithelial lesions, IgA/IgG plasma cell shift and germinal centers) in patients suspected for pSS.

Methods: Consecutive sicca patients who were clinically suspected for pSS and underwent a labial gland biopsy were included. Classification of patients as pSS or non-SS was based on clinical vignettes scored by an expert panel of three experienced rheumatologists. Labial gland biopsies were analyzed for the four histopathological parameters: focus score (FS) and presence of (pre-)lymphoepithelial lesions, IgA/IgG plasma cell shift and germinal centers. Sensitivity and specificity of these histological parameters were calculated, and ROC analysis was used to determine the optimal cut-off value for the number of histopathological parameters needed to diagnose pSS.

Results: Of the 103 included patients, 38 patients were classified as pSS and 65 as non-SS sicca by the expert panel. In pSS patients, the prevalence of FS≥1 was 82%, followed by 68% for presence of (pre-)lymphoepithelial lesions, 63% for plasma cell shift and 24% for germinal centers. FS≥1 showed the highest sensitivity for pSS (82%), but specificity was higher for the other three parameters (98-100%, Table 1). Although the sensitivity of presence of ≥2 (out of 4) histopathological parameters was comparable to the sensitivity to FS alone, the specificity of presence of ≥2 (out of 4) histopathological parameters increased with 12% to 100%. Regarding the biopsy item in the ACR-EULAR criteria, specificity increased from 84% to 95% when FS≥1 was replaced by the presence of ≥2 histopathological parameters.

Conclusion: The diagnostic accuracy of the labial gland biopsy increases when other histopathological parameters besides FS are taken into account. Also, the performance of the ACR-EULAR criteria increases when the biopsy item is replaced by the presence of ≥2 histopathological parameters. This will lead to a lower number of false positive biopsies and a lower number of patients misclassified as pSS.

Table 1. Sensitivity, specificity, positive and negative predictive value of histopathological parameters for the diagnosis of primary Sjögren's syndrome (pSS), within the total diagnostic sicca cohort of patients suspected for pSS.

		Sensitivity	Specificity	PPV	NPV
Focus score≥1	N=103	82% (31/38)	88% (57/65)	80% (31/39)	89% (57/64)
(pre-)lymphoepithelial lesions	N=101	68% (26/38)	98% (62/63)	96% (26/27)	84% (62/74)
IgA/IgG plasma cell shift	N=103	63% (24/38)	100% (65/65)	100% (24/24)	82% (65/79)
Germinal centers	N=102	24% (9/38)	100% (64/64)	100% (9/9)	69% (64/93)
≥2 histological parameters	N=102	79% (30/38)	100% (64/64)	100% (30/30)	89% (64/72)

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POS1457 CLINICAL COURSE AND RISK FACTORS FOR DEVELOPMENT AND PROGRESSION OF INTERSTITIAL LUNG DISEASE IN PRIMARY SJÖGREN'S SYNDROME: A SINGLE-CENTERED, RETROSPECTIVE, OBSERVATIONAL STUDY

Keywords: Sjögren syndrome, Imaging, Lungs

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Background: Interstitial lung disease (ILD) is the most frequent pulmonary manifestation in patients with Primary Sjögren's syndrome (pSS). Data on the clinical and radiographic course based on high resolution computed tomography (HRCT) findings are limited.

Objectives: We aimed to investigate the long-term course and prognostic factors of patients with primary Sjögren syndrome-associated interstitial lung disease (pSS-ILD).

Methods: This single-center, retrospective study included 120 pSS patients who underwent at least two high-resolution computed tomography (HRCT) scans between March 2013 and February 2021. Clinical symptoms, laboratory data, HRCT findings, and pulmonary function test results were collected. Two thoracic radiologists reviewed the HRCT findings.

Results: In patients with pSS without ILD at baseline (n=81), no development of ILD was found on follow-up (median, 2.8 years). In patients with pSS-ILD (n=39), total disease extent, extent of coarse reticulation, and traction bronchiectasis increased on HRCT, whereas the extent of ground glass opacity (GGO) decreased at follow-up (median, 3.2 years) (each $p<0.001$). In progressive group of pSS-ILD (n=19/39, 48.7%), the extent of coarse reticulation and coarseness score of fibrosis were increased at follow-up ($p<0.05$). Multivariate logistic regression analysis showed that LDH (OR, 1.012) and diffusing capacity for carbon monoxide (OR, 0.922) were independent risk factors for pSS-ILD at baseline. Usual interstitial pneumonia pattern on CT (OR, 15.237) and follow-up duration (OR, 1.403) were independent risk factors for disease progression in patients with pSS-ILD. In response to glucocorticoid and/or immunosuppressants, GGO decreased, whereas the extent of fibrosis increased even after treatment.

Conclusion: In pSS patients with no ILD during baseline evaluation, no newly developed ILD was identified during follow-up over two years. Progression occurred in approximately half of the pSS-ILD patients with slow gradual deterioration. The extent of fibrosis increased, even after anti-inflammatory treatment.

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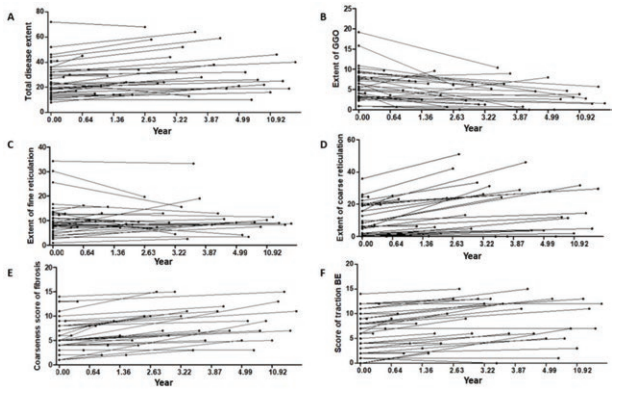


Figure 1. Changes in HRCT variables in patients with pSS-ILD during the follow-up period.

Plots are shown for the total extent (A) ground-glass opacities (GGO) (B), fine reticulation (C), coarse reticulations (D), coarseness score of fibrosis (E), and score of traction bronchiectasis (BE).

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POS1458 PREVALENCE OF SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

Keywords: Cardiovascular disease, Sjögren syndrome

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Background: It is well established that patients with inflammatory rheumatic diseases have an increased cardiovascular risk [1]. Most data exists for rheumatoid arthritis, but there are also a few studies for primary Sjoegren's syndrome (pSS)[2].

Objectives: Aim of our study was to investigate the extent of subclinical atherosclerosis in a large group of patients with pSS compared to control subjects without pSS. Secondary, correlations with clinical factors, such as organ involvement or antibody positivity, and disease activity were investigated.

Methods: From September 2021 to April 2022, pSS patients from the outpatient clinic of our hospital were consecutively included after informed consent. In addition, age- and sex-matched control subjects were recruited in a 2:1 ratio via multimedia call for participation. All pSS patients fulfilled current EULAR classification criteria for pSS and had a disease duration of at least 5 years. Participants with additional rheumatic or inflammatory diseases, tumor disease in the past 5 years, or end-organ manifestations of atherosclerotic disease were excluded. Data collection was performed by standardized questionnaire and Doppler ultrasonography for evaluation of plaque extent and intima-media thickness measurements (cIMT).

Results: Analysis included data from 199 pSS patients and 100 control subjects. 38 (19.4%) subjects of the pSS cohort were male and the median age was 58.92 years [50.50-65.21]. The median disease duration (since initial manifestation) of pSS patients was 136 months. The cohorts were analyzed for differences regarding to the cardiovascular risk profile: There were no significant differences in age, gender distribution, tobacco consumption, body mass index (BMI), pre-existing arterial hypertension, hypercholesterolemia, or diabetes mellitus. Similarly, there were no differences in LDL cholesterol, HDL cholesterol, or HbA1c in laboratory tests at enrollment. Only a positive family history for cardiovascular disease was significantly more frequent in the pSS cohort (p=0.003). After adjustment via propensity score matching, the pSS cohort was found to have a significantly greater intima-media thickness (p= <0.001). When age was added as a covariate, there was an earlier onset of intima-media thickening recognizable in the pSS patients (p=0.014). Furthermore, there was a significantly more frequent occurrence of plaque in the pSS cohort (p=0.031). pSS-patients had a 1.82times increased odds of having plaque in comparison to the control cohort. Organ involvement in the pSS-cohort was associated with a thicker cIMT (p=0.025) and pSS-patients with organ involvement also showed a 1.74times increased odds of having plaque compared to pSS-patients without organ involvement.

Conclusion: PSS appears to accelerate the development and progression of atherosclerosis as an independent risk factor. It seems to promote not only an increased incidence of atherosclerotic changes, but also an earlier onset of wall thickening in the sense of vascular aging. An increased risk for patients with organ involvement was observed. Further longitudinal studies are required to answer the question if this subgroup of pSS patients in particular or all pSS patients could benefit of screening with Doppler ultrasonography and preventive medication with HMG-CoA reductase inhibitors or acetyl salicylic acid.

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POS1459 THE WEIGHT OF ANTI-LA/SSB ANTIBODIES IN RO/SSA-POSITIVE PATIENTS WITH A NEWLY DIAGNOSED SJÖGREN'S SYNDROME: A PHENOTYPE CHARACTERIZED BY A MORE SEVERE MAJOR AND MINOR GLANDULAR INVOLVEMENT AND A HIGHER BIOLOGICAL ACTIVITY

Keywords: Biomarkers, Autoantibodies, Sjögren syndrome

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Background: Recently, a growing interest has arisen in investigating the association between patients' serological profiles and the different clinical phenotypes in primary Sjögren's syndrome (pSS). The double positivity for anti-Ro52/anti-Ro60 has been associated with B-cell hyperactivity and a more prominent INF-a signature. Whether the positivity of anti-La/SSB antibodies influences the clinical features of triple positive pSS patients at the time of diagnosis remains controversial.

Objectives: 1.To compare the clinical, biological, histological and ultrasonographic distinctive features of pSS patients presenting a triple positivity for anti-La/SSB and anti-Ro52/anti-Ro60 with those of patients with different serological profiles at the time of pSS diagnosis. 2. To specifically describe the presenting features of pSS patients with a triple positivity in comparison with the features of patients with a double positivity for anti- Ro52/anti-Ro60.

Methods: This is a cross-sectional study including newly diagnosed pSS patients (ACR/EULAR 2016 criteria) enrolled prospectively from 2018 to 2022. Patients were stratified in five groups according to the serological profile (i.e seronegative, isolated anti-Ro52, isolated anti-Ro60, double positive and triple positive). Demographic, clinical, biological and histological data were compared among the groups. Ultrasonographic features of major and minor salivary glands were also analyzed. Data were presented as mean±SD or as percentage frequency, as appropriate. Intergroup comparisons were made using the t-test/Mann–Whitney test for continuous variables and Fisher's exact test for categorical variables.

Results: We included 199 pSS patients (M:F= 19:180, mean age 56±13.7 years). 33/199 (16.58%) were seronegative, 50/199 (25.12%) presented isolated anti-Ro52, 49/199 (24.62%) had double positivity, 55/199 (27.64%) had triple

positivity and 12/199 (6.03%) presented isolated Ro60 antibodies. Triple positives were younger than seronegatives. No further differences in demographic features were detected among the groups. Triple positives were found to have a more complex infiltrate in the minor salivary gland biopsies than double positives with a higher mean Focus Score (2.34±2.05 vs 1.32±0.84, p=0.005) and a higher mean number of ectopic lymphoid structures (2.40±2.88 vs 1.21±1.25, p=0.004). Regarding major salivary glands ultrasound (SGUS), double positives and triple positives were found to have a score ≥2, according the OMERACT system, more frequently than the other groups (p = 0.001, Figure 1). Particularly, triple positives presented SGUS abnormalities more frequently than double positives (68.9 vs 43.6%, p=0.03). The same findings were observed for Ultra-high frequency ultrasonography (UHFUS) of minor salivary glands (Figure 1). Indeed, triple positives had the highest UHFUS scores (p= 0.01). Furthermore, triple positives presented a higher mean ESSDAI score than the other groups including the double positives (p= 0.001) due to a higher disease activity in the ESSDAI glandular and biological domains.

Conclusion: Triple-positive patients were characterized by a more severe glandular involvement documented by ultrasound and histology and by a higher disease activity. These results support the amount of data suggesting that the separate detection of anti-Ro52, anti-Ro60 and anti-La/ SSB may significantly contribute to patients' stratification at the time of the diagnosis, thus paving new avenues for tailored approaches in pSS.

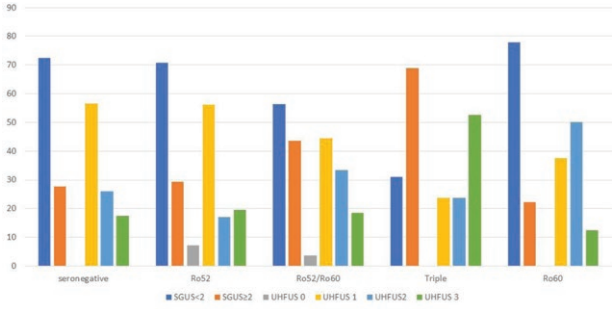


Fig. 1 Histogram showing SGUS and UHFUS scores in the five subgroups of patients

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1460

MAJOR SALIVARY GLAND ULTRASOUND AND ELASTOGRAPHY FOR ASSESSMENT OF DISEASE ACTIVITY IN PATIENTS OF PRIMARY SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Ultrasound

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Background:
Objectives: To assess major salivary gland involvement by ultrasonography and elastography in patients with Primary Sjögren's syndrome (pSS), correlate the severity of ultrasonographic and elastographic involvement of major salivary gland with disease activity.
Methods: In 54 pSS patients, disease activity was assessed by the European League Against Rheumatism (EULAR) Sjögren's Syndrome Disease Activity Index (ESSDAI) and the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI). The Salivary gland were assessed using the Hocevar and OMERACT score and Real time Elastography was performed for the salivary glands and were scored semiquantitatively.
Results: 54 patients of primary Sjögren's Syndrome and 55 controls were included in the study. The patients were younger with a mean age of 37.61±11.56 years (Refer to Figure 1 for demographic and clinical data of pSS patients in the study). Mean USG/Elastography scores were significantly higher (p < 0.001) in cases than controls. ESSDAI correlated strongly with Hocevar Score and OMERACT and Moderately with Elastography. ESSPRI correlated well with Hocevar Score and OMERACT score but poorly with Elastography. All the scores differentiated sufficiently between high and activity efficiently (p<0.001), however, for the OMERACT(p-0.13) and Elastography score(p-0.083) the difference between moderate and low disease activity was not statistically significant. A multivariate linear regression analysis found an association with USG Scores with ESSDAI and ESSPRI, Elastography with ESSDAI and Disease duration.
Conclusion: The Hocevar score had a robust correlation with disease activity. The Elastography scores moderately correlated with disease activity and duration of disease. There was a near-complete correlation of USG scores with Unilateral, Parotid, and submandibular scores.

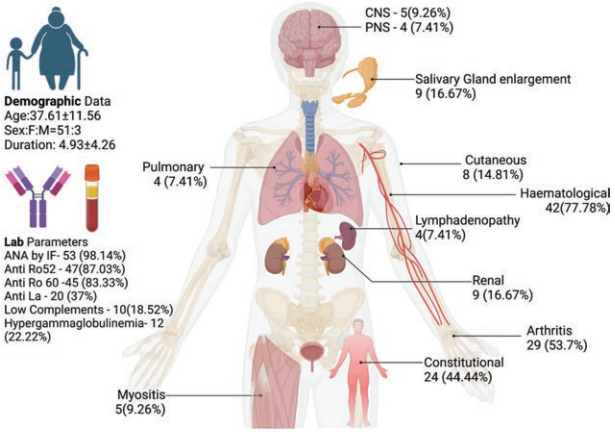


Figure 1. Demographic data, Clinical and Serologic Features of patients with pSS in the study (Created using Biorender.com)

Table 1a. Correlation between ESSDAI & ESSPRI with USG and Elastography scores

ESSDAI		Hocevar Score	OMERACT score	Elastography score	hyper-echoic reflections	Hypoechoic lesions
Correlation	Correlation Coefficient	0.824	0.797	0.421	0.724	.821
	p value	0	0	0.002	0	.000
Multivariable linear regression analysis	β	0.559	0.508	0.457	0.531	0.506
	p value	<0.001	<0.001	0.003	0	0.000
logistic regression	Odds Ratio	4.63	4.63	1.8	NA	NA
ESSPRI		**Hocevar Score**	**OMERACT score**	**Elastography score**	**hypere-choic reflec-tions**	**Hypoechoic lesions**
Correlation	Correlation Coefficient	.711**	.677**	.270*	.543**	.692**
	p value	0	0	0.048	0	.000
Multivariable linear regression analysis	β	0.337	0.355	-0.105	0.232	0.358
	p value	0.003	0.005	0.478	0.102	0.004

Table 1b. Comparison of Cases and different control groups for USG and elastography score

	Case		Disease Controls With Sicca Symptoms		Disease Controls without Sicca Symptoms		Healthy Controls		Mann Whitney Test		
	N=54		N=16		N=18		N=21				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	p1*	p2*	P3*
Hocevar Score	17.31	14.202	2.15	2.68	0.33	con	0.19	0.873	<0.001	<0.001	<0.001
OMERACT score	4.59	3.955	1.125	1.31	0.22	0.647	0.14	0.655	0.003	<0.001	<0.001
Elastography Score	6.04	2.719	0.69	0.793	0.22	0.428	0.19	0.402	<0.001	<0.001	<0.001

*-p1-Cases vs Disease Controls With Sicca Symptoms, p2- cases vs Disease Controls without Sicca Symptoms, p3- cases vs Healthy Controls

Table 1c. Comparison of patients with high, moderate and low disease activity and their Ultrasound and Elastography scores

	Case		High Disease activity		Moderate Disease activity		Low disease Activity		Mann Whitney Test		
	N=54		N=19		N=13		N=22				
	Mean	Mean	Mean	SD	Mean	SD	Mean	SD	P1#	P2#	P3#
Hocevar Score	17.31	14.202	30.84	7.9	19.77	10.87	4.18	6.17	0.003	0.0002	<0.001
OMERACT Score	4.59	3.955	7.89	2.47	5.85	3.29	1	1.93	0.13	<0.001	<0.001
Elastography Score	6.04	2.719	7.58	2.83	5.85	2.34	4.82	2.22	0.083	0.193	0.002

#-P1- High vs moderate, P2 – Moderate vs Low, P3 – High vs low

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1461

ADVANTAGES OF DOPPLER IN LABIAL SALIVARY GLAND ULTRA-HIGH FREQUENCY ULTRASOUND: CORRELATIONS WITH HISTOLOGICAL INFLAMMATION, PSS DIAGNOSIS, DISEASE ACTIVITY, AND PROGNOSIS

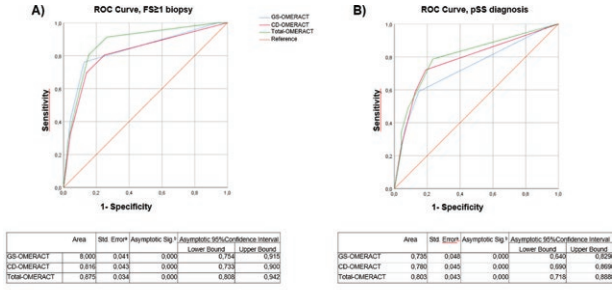
Keywords: Sjögren syndrome, Ultrasound, Prognostic factors

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Background: Musculoskeletal Doppler US is currently used to estimate the level of inflammation and to differentiate between arthritis and degenerative disease. In addition, Doppler is associated with disease activity and damage, namely prognosis. Recently, a novel colour Doppler Score has been proposed for major salivary glands. However, clinical associations of salivary glands Doppler US are unclear, both in major salivary glands (MSG) and in labial salivary glands (LSG).
Objectives: To investigate potential associations between colour Doppler of LSG Ultra-High Frequency Ultrasound and histology, pSS diagnosis, clinical manifestations and prognosis.
Methods: From January 2021 to October 2022 consecutive patients, undergoing LSG biopsy, were enrolled in our cross-sectional study. LSG Ultra-High Frequency ultrasound (UHFUS) was performed with a 70 MHz probe, evaluating parenchymal inhomogeneity (score 0-3, as MSG four-grade OMERACT grey scale scoring system, GS-OMERACT) and vascularization (score 0-3, as MSG four-grade OMERACT colour Doppler scoring system, CD-OMERACT) and their sum (score 0-6, Total-OMERACT). Patients' histological, biological and clinical features were collected. ACR/EULAR 2016 criteria fulfilment was the gold standard for diagnosis. LSG biopsy with a Focus Score (FS) >1 was considered positive. For statistical analysis, following tests were applied: Student's t test, Mann- Whitney U test, contingency table analysis, Spearman's correlation. Receiver operating characteristic analysis was calculated to assess the accuracy of UHFUS to predict histology inflammation and pSS diagnosis.
Results: 127 patients were enrolled: 61 pSS patients, 47 sicca controls and 20 sicca patients with other connective tissue diseases. GS-OMERACT predicted a positive biopsy with an area under the curve (AUC) =0.835. UHFUS inflammation prediction was increased considering both grey scale and colour Doppler (Total-OMERACT), with a sensitivity=80.4%, a Specificity=84.7% and an AUC raised to 0.875 (Figure 1A). In addition, CD-OMERACT revealed a higher accuracy for pSS diagnosis than GS-OMERACT (AUC 0.780 vs 0.735). Total-OMERACT score was characterised by a sensitivity of 78.7% and a specificity of 76.6% for pSS diagnosis (AUC 0.803, Figure 1B). Both GS-OMERACT and CD-OMERACT, in pSS patients, were correlated with serological activity: autoantibodies (SSA/Ro52, SSA/Ro60, SSB) IgG levels and Rheumatoid Factor. However, CD-OMERACT presented a stronger correlation than GS-OMERACT, and significantly correlated with low C3 and C4 (Table 1). Similarly, both GS and CD also correlated with total ESSDAI and separate lymph nodes, glandular and biological domains. The correlation observed was higher with Doppler signal than inhomogeneity. The latter also exhibited a significant correlation with renal activity. All 5 patients with LSG severe/atypical inflammatory infiltrate had GS-OMERACT score 3 and CD-OMERACT score 3 with a typical pattern: multiple very hypoechoic areas and high perilesional CD signal.
Conclusion: UHFUS Colour Doppler, combined with grey scale, allows a better detection of labial salivary glands inflammation. Compared to grey scale, CD offers a unique opportunity in patient's phenotyping, due to its higher correlation with disease activity and pSS serological hallmarks. Eventually, a high doppler signal could be a key feature to identify more severe/atypical inflammatory infiltrate thus allowing the early recognition of lymphoproliferative complications.

Table 1. – Spearman's correlations of UHFUS. * p<0.05

	GS-OMERACT	CD-OMERACT	GS+CD OMERACT
SSA/Ro52	0.384*	0.452*	0.440*
SSA/Ro60	0.418*	0.464*	0.487*
SSB	0.390*	0.424*	0.435*
Rheumatoid factor	0,352*	0,424*	0,404*
IgG Level	0,316*	0,491*	0,465*
Low C3	0,065	0,247*	0,203
Low C4	0,239	0.410*	0.367*
Lymphadenopathy	0,354*	0,479*	0,434*
Glandular domain	0,258*	0,326*	0,301*
Renal domain	0,396*	0,243	0,327*
Biological domain	0,337*	0,428*	0,408*
Total ESSDAI	0,497*	0,513*	0,524*



	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
GS-OMERACT	0.835	0.041	0.000	0.754	0.915
CD-OMERACT	0.816	0.043	0.000	0.733	0.900
Total-OMERACT	0.875	0.034	0.000	0.808	0.942

	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
GS-OMERACT	0.735	0.048	0.000	0.640	0.829
CD-OMERACT	0.780	0.045	0.000	0.690	0.869
Total-OMERACT	0.803	0.043	0.000	0.718	0.888

Figure 2

Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1462

IMMUNOEMATHOLOGIC FEATURES IN A COHORT OF PEDIATRIC PATIENTS WITH SJÖGREN'S SYNDROME: AN OVERLAP WITH AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME (ALPS)-LIKE DISORDERS

Keywords: Cytokines and chemokines, Sjögren syndrome

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Background: Childhood Sjögren's syndrome (cSS) is a chronic autoimmune disease characterized by lymphocytic infiltration of salivary and lacrimal glands leading to their dysfunction [1]. Even though recurrent parotitis and sicca symptoms seems to be the most frequently reported features, cSS could have a wide range of clinical and laboratory manifestations such as autoimmune cytopenia, hypergammaglobulinemia, lymphadenopathy, fever and arthralgia [2]. These manifestations can also be seen in patients with autoimmune lymphoproliferative syndrome (ALPS). ALPS is a rare hematologic disorder characterized by an altered lymphocyte homeostasis due to a defective apoptotic mechanism [3]. In addition, cSS and ALPS are significantly associated with increased risk of lymphoid malignancy, most commonly non-Hodgkin lymphoma.
Objectives: To examine the prevalence of clinical and laboratory characteristics of ALPS in a cohort of pediatric patients with cSS in order to better characterize this autoimmune disorder and discover potential novel therapeutic targets.
Methods: Patients with cSS were recruited from the Paediatric Rheumatology Department at the Gaslini Children's Hospital of Genoa, Italy. All consecutive cSS

patients underwent clinical and ultrasound assessment to evaluate the presence of signs of lymphoproliferation, such as splenomegaly or lymphadenopathy. The following laboratory examination were performed: complete blood count (CBC), total immunoglobulins and immunoglobulins G (IgG) subclasses, vitamin B12 levels, peripheral blood lymphocyte subsets including double negative T cells (DNTs), interleukin 10 (IL-10), interleukin 18 (IL-18) and soluble FAS ligand (sFASL) levels, a lymphocyte apoptosis test and a Next Generation Sequencing (NGS) panel.

Results: Twenty patients were included in the present study. All but one patient were female (95%) with a median age at disease onset of 9,5 years. 4/20 (20%) had persistent lymphadenopathy and 1/20 (5%) had a splenomegaly. Four patients (20%) had persistent cytopenias and 12/20 (60%) had a hypergammaglobulinemia. Three patients (15%) had a deficit of IgG4 and another one (5%) had a deficit of IgG1 and IgG2. Three patients (15%) fulfilled the Oliveira's criteria for ALPS-like disorders [3] and of these, two had mutations in ALPS-like involved genes (PI3KCD and TNFRSF13B). Two other patients (10%) were diagnosed as ALPS-like disorders based on the presence of at least three out of four screening markers in cytofluorimetric panels (DNTs > 1,5%, TCR$\alpha\beta$ B220$^+$ > 60%, CD3$^+$CD25$^+$/CD3$^+$HLA DR$^+$ ratio < 1, CD27$^+$ B cells < 15%) [4]. Overall, 5 out of 20 (25%) cSS patients had an ALPS-like phenotype and started treatment with sirolimus with a good clinical and biochemical response.

Conclusion: This is the first description of an overlapping syndrome between cSS and ALPS. A substantial proportion of cSS patients followed at our Centre fulfilled diagnostic criteria for ALPS-like disorders and were treated successfully with sirolimus, a mammalian target of rapamycin (mTOR) inhibitor. Our results emphasize the need for a broader understanding of the immune dysregulation underlining cSS to identify novel therapeutic targets.

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POS1463

FACTORS ASSOCIATED WITH DISEASE DAMAGE AT 20 YEAR FOLLOW-UP IN AN ITALIAN MULTICENTER SJÖGREN'S SYNDROME COHORT

Keywords: Organ damage, Sjögren syndrome

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Background: Sjögren's syndrome (SS) represents a chronic autoimmune disorder characterized by a relatively benign course. However, up to 40% of SS patients develop systemic extra-glandular involvement which, in turn, may lead to long-term damage accrual. Few studies assessed damage accrual in SS with a follow-up ranging from 5 to 10 years. Knowledge of long-term risk of damage and awareness of factors contributing to damage accrual in SS represent important issues to identify patients requiring a closer follow-up and to better stratify therapy.

Objectives: To examine disease damage progression every 5 years until 20 years of follow-up and disease related features associated with higher damage score at 20 years in a multicenter SS cohort.

Methods: A cohort of 252 SS patients fulfilling the 2002 AECG and/or 2016 ACR-EULAR classification criteria was retrospectively analysed. The following variables were collected at diagnosis and every 5-year timepoints until 20 years: demographic, clinical and serologic parameters; disease activity by ESSDAI; Charlson Comorbidity Index (CCI); disease damage by SSDDI and treatments. Patients were grouped according to damage degree at 20 years: "low/no damage", LND (SSDDI ≤ 1) and "moderate/high damage", MHD (SSDDI ≥ 2). Continuous variables were compared by Mann-Whitney U test and categorical variables by Chi-squared test of Fisher's exact test, as appropriate. Significant variables at univariate analysis were include in a multivariable logistic regression analysis model with wild bootstrapping to account for collinearity and heteroscedasticity.

Results: A total of 50 patients (mean age at diagnosis 44±12 years, mean disease duration 24±5 years) had 20 year follow-up. Mean SSDDI increased from 1.2 (±1.5) at 5 to 1.5 (±1.7) at 10 years and from 1.54 (±1.7) at 15 to 2.04 (±2.2) at 20 years. Oral/ocular damage, peripheral nervous (PN) involvement and lymphoproliferative disease mainly contributed to damage accrual. Mean ESSDAI reduced from 6.4 (±3.7) at baseline to 4.9 (±5.4) and mean CCI increased from 1.6 (±0.8) to 3.5 (±1.6) at 20 years. At univariate analysis, MHD patients had significant higher median ESSDAI at all timepoints and CCI at 5 and 20 years, higher frequency of parotid swelling at 5 years (35% vs 7%, p=0.021), low C4 (30% vs 3%, p=0.012) at 15 years and monoclonal component at 20 years (30% vs 7%, p=0.047) and lower of arthritis at 10 years (0% vs 23%, p=0.033) in comparison to LND. Patients with MHD had higher prevalence of glucocorticoid (GC) use at 20 years in comparison to LND (75% vs 27%, p=0.001). Multivariable logistic regression analysis model was able to correctly classify 87.5% of patients. None of the included parameters was independent predictor of outcome variable, likely due to a non-linear relationship among variables and the low subject number included.

Conclusion: This is the first study exploring disease damage at 20 year follow-up in SS patients. Notably, damage occurs early, increases already in the first 5-10 years and is mainly driven by oral and ocular damage, PN involvement and lymphoma. Higher disease activity at baseline and during follow-up and higher GC use, also reflecting a more active disease, represent two important variables contributing to damage. Thus, controlling disease activity since diagnosis and minimizing steroid prescription may reduce long-term damage accrual. Among disease-related features, appearance of parotid swelling in the first 5 years requires awareness. Surely, further studies are needed to identify, at diagnosis, patient phenotype at higher risk of long-term damage.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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SLE, Sjön's and APS - clinical aspects (other than treatment)

POS1464

DYSPHAGIA AND RELATED SYMPTOMS ARE FREQUENT, SEVERE AND HEAVILY AFFECT THE QUALITY OF LIFE OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

Keywords: Gastrointestinal tract, Sjögren syndrome, Quality of life

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Background: Dysphagia is the most frequent symptom reported by pSS patients with gastrointestinal involvement and may be related to a combination of hyposalivation and oropharyngeal/oesophageal dysmotility.
Objectives: To explore the burden of dysphagia and related symptoms and the access to specialist care in patients with pSS.
Methods: Consecutive patients with pSS fulfilling the 2016 ACR-EULAR classification criteria and referring to our institution were interviewed. Patients reporting swallowing problems filled the Swallowing Quality of Life (SWAL-QOL) questionnaire. The SWAL-QOL includes 10 domains: food selection, burden, mental health, social functioning, fear, eating duration, eating desire, communication, sleep, and fatigue. It also explores presence and frequency of various symptoms such as cough, choke on food or liquids). Patients having sought for specialist care for dysphagia filled the SWAL Quality of Care (SWAL-CARE) questionnaire. The SWAL-CARE includes 2 domains to report on the clinical and general advice received (e.g. on food/drinks to avoid) and on the patient satisfaction. The scores of each domain (Likert scales) are transformed to a 0–100 metric with 100 indicating the most favorable state and 0 the least favorable state. Disease activity (ESSDAI) and patient reported symptoms (VAS scales, ESSPRI, xerostomia inventory (XI) and Oral Health Impact Profile (OHIP)-14) were calculated at the time of enrollment.
Results: An interim analysis on 108 recruited patients as of December 4, 2022 was performed. Twenty-five patients (23%) reported swallowing problems. All SWAL-QOL domain scores and the total SWAL-QOL score were very low while symptom presence and frequency were very high. The most affected domains (mean value <30) were fear, mental health, fatigue and sleep (Table 1). The "mental health" and "social functioning" domains were more affected in people with shorter disease duration regardless of age (p<0.01). Conversely, the "burden" domain, reflecting the capability to cope with dysphagia, was more affected in younger people (p=0.03). A proportion of patients ranging between 48 to 84% reported having symptoms often or almost always and none of the patients responded "never" for any of the symptoms (Figure 1). When exploring how the extent of dryness relates to dysphagia, the VAS scales for xerostomia and xerotrachea did not differ between patients with or without dysphagia. However, patients with dysphagia had significantly higher scores of the XI and the OHIP-14 compared to those without (both p<0.01). No differences in terms of age, disease duration, autoantibody profile and disease activity emerged between pSS patients with or without dysphagia. Focusing on ESSDAI domains, we observed that all patients with dysphagia also had articular manifestations (p<0.01) while haematological manifestations were more frequent in patients without dysphagia (p=0.03). Of the 25 patients with dysphagia only 10 (40%) sought specialist care. Most of the patients judged the advice received poor (mean =10.4) and overall patient satisfaction was very low (mean= 28.5).
Conclusion: Our study demonstrated that dysphagia and related symptoms are frequent and severe in pSS, heavily impact on the patient quality of life and satisfactory specialist care remains an unmet need. Younger people and those with a shorter disease duration seem those whose QoL is more affected. We are currently increasing the patient cohort and planning further investigations in patients with dysphagia (e.g. oesophageal manometry) to better characterise the mechanisms underlying this problem in pSS.

Table 1. Domains and total SWAL-QoL score in pSS patients with dysphagia

SWAL-QoL domains	Mean	SD
Burden	48.3	26.1
Eating desire	31.1	24.4
Eating duration	39.6	28.2
Food selection	42.9	30.0
Communication	38.3	29.6
Fear	28.5	29.5
Mental health	29.2	27.0
Social functioning	35.0	29.5
Fatigue	29.2	25.5
Sleep	25.0	24.1
TOTAL SWAL-QOL	36.4	17.6

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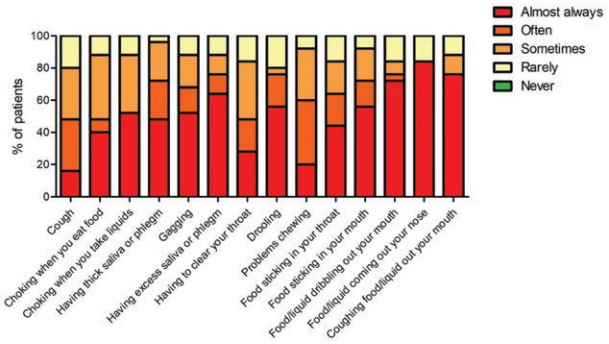


Figure 1. Frequency of dysphagia-related symptoms

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POS1465

ASSOCIATION OF COMPLEMENT ACTIVATION AND TNFA WITH PREGNANCY PROGNOSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

Keywords: Systemic lupus erythematosus, Anti-phospholipid syndrome, Biomarkers

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Background: Complement activation is associated with adverse pregnancy outcomes in in patients with systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS). TNFα is accused in the etiology of impaired placenta development and preeclampsia.
Objectives: We aimed to investigate the association of complement(c) activation and TNFα with poor pregnancy outcomes in patients with SLE/APS.
Methods: Four groups were examined: pregnant SLE/APS (n=37), non-pregnant SLE/APS(n=15), healthy pregnant (n=20) and healthy women (n=14). C3b, C5a and TNFα were tested by ELISA in the serum (s) samples taken at the last trimester of each pregnancy. Collected placental tissues were examined histopathologically and were stained for TNFα and C4d.
Results: sC3b levels and positivity rates were higher in pregnant SLE/APS compared to all other groups (p<0.05 for all). Pregnancy loss (18,9%) and preeclempsia (16,2%) were the most common pregnancy morbidities. Renal (30,5%) followed by hematologic (thrombocytopenia) (19,4%) were the most common flares in pregnant patients with SLE/APS and compared to patients without, they had significantly higher sTNFα levels (p<0,05). The frequency of sTNFα positivity were significantly higher in SLE/APS patients with preeclampsia (p<0.05). Sixty-six % of SLE/APS placentas had C4d deposition whilst none of the healthies were stained (p <0,001). Frequency of strong staning with TNFα in SLE/APS (75,8%) was significantly higher compared to healthy placentas (27,8%) (p<0,001). Decidual vasculopathy, decidual inflammation and villous infarction were significantly more frequent in SLE/APS (Table 1). Significant associations were found between these findings and preeclampsia, intrauterine growth retardation and the need for neonatal intensive care (p<0,001).
Conclusion: Results of our study shows TNFα and complement activation both at tissue level and serum, and supports their association with adverse pregnancy outcome in SLE/APS.Further work is necessary to test whether these biomarkers can be used for follow up and to explore whether TNFα and complement directed therapies may improve maternal/fetal prognosis in patients with SLE/APS.

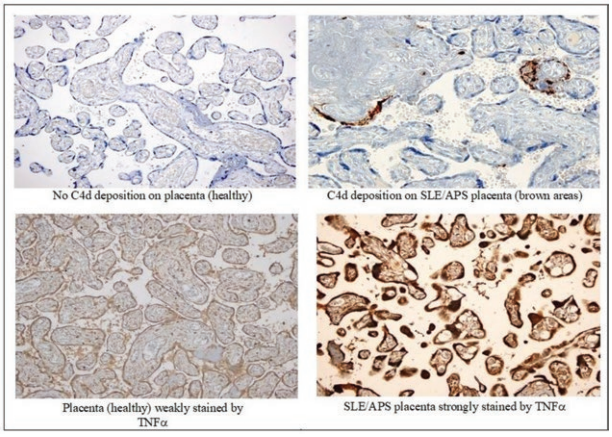


Image 1 . Immunohistochemistry findings of placenta tissue: healthy vs SLE/APS

Table 1. ***Comparison of immunohistochemistry and histopathologic findings of placental tissues between SLE/APS and healthy groups***

Immunohistochemistry	Pregnant SLE/APS n=33	Healthy pregnant n=20	p
Staining with C4d n (%)	22 (66,7)	0 (0)	**<0,001**
Strongly staining with TNF-alpha n(%)	25 (75,8)	5(27,8)	**<0,001**
Histopathologic findings	Pregnant SLE/APS n=27*	Healthy pregnant n=20	p
Desidual inflamation n (%)	11 (40,7)	2 (10)	**0,025**
Decidual vasculopathy n (%)	23(85,2)	3 (15)	**< 0,01**
Villous vasculopathy n (%)	4 (14,8)	0	0,12
Villous infarction n (%)	11 (40,7)	2 (10)	**0,02**
Percentage of villous infarction (%)	22,7 ± 20,9	7,5 ± 3,5	0,3
Accelerated villous maturation n (%)	7 (26,9)	0	**0,01**

* number of placentas available for histopathologic examination

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Acknowledgements: NIL.
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POS1467

PREDICTORS OF NEUROPSYCHIATRIC FLARES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM FIVE PHASE III CLINICAL TRIALS OF BELIMUMAB

Keywords: Outcome measures, Systemic lupus erythematosus, Clinical trials

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Background: Neuropsychiatric (NP) flares in systemic lupus erythematosus (SLE) constitute a challenging issue for the clinician on many levels as they are rather unpredictable and include severe and potentially life-threatening manifestations [1]. The identification of clinical and serological profiles predictive of NP flares would be instrumental for early detection of NP involvement, thus allowing early treatment, and hopefully resulting in improved outcomes. The B-cell depleting agent belimumab has widely shown ability to reduce rates of flare in SLE (2), but little is known on its potential benefits in the treatment of NPSLE.
Objectives: To evaluate predictors of NP flares in patients with SLE under standard therapy (ST) with or without add-on belimumab, given for active disease yet not ongoing severe NP involvement.
Methods: Data from five clinical trials of belimumab in SLE (BLISS-52 (NCT00424476), BLISS-76 (NCT00410384), BLISS-NEA (NCT01345253), BLISS-SC (NCT01484496), and EMBRACE (NCT01632241)) were used (N=3638). Flares were defined using the British Isles Lupus Assessment Group (BILAG) activity index as development of any new NP BILAG score A in patients with baseline NP BILAG score B, and development of any new NP BILAG score A or B in patients with baseline NP BILAG score C–E during a 52-week follow-up. Predictors of NP flare were investigated using univariable and multivariable Cox regression analysis. A subgroup analysis was performed to determine predictors of *de novo* NP flare in patients with no NP history (baseline NP BILAG E). Organ damage was assessed using the SLICC/ACR Damage Index (SDI). *p* values <0.05 were considered statistically significant.
Results: In total, 105 (2.9%) NP flares were documented. Of these, NP flare occurred in 52 (1.6%) patients with baseline NP BILAG E. In multivariable analysis adjusting for age, sex, ethnicity, and variables that were significant in univariable analysis, male sex (HR: 2.37; 95% CI: 1.31–4.28; *p*=0.004) and NP BILAG score B–D at baseline (HR: 5.91; 95% CI: 3.86–9.06; *p*<0.001) were highly associated with NP flare development in the pooled study population. Belimumab use displayed no clear protection at any dose or administration form. In the subgroup analysis of the baseline NP BILAG E population, male sex (HR: 3.26; 95% CI: 1.51–7.04; *p*=0.003) was the strongest predictor of *de novo* NP flare. In a separate analysis of SDI domains, the NP domain (HR: 3.25; 95% CI: 2.72–3.88; *p*<0.001) was the strongest predictor of NP flare, with cognitive impairment (HR: 14.29; 95% CI: 9.22–22.14; *p*<0.001), transverse myelitis (HR: 21.89; 95% CI: 5.40–88.72; *p*<0.001), and neuropathy (HR: 8.87; 95% CI: 5.59–14.09; *p*<0.001) mainly driving this association.
Conclusion: Current or past NP activity and established organ damage in the NP domain at baseline were the strongest predictors of NP flare in SLE patients treated for active disease yet not ongoing severe NP involvement. Whether belimumab treatment protects against NP events remains unclear and warrants future investigation.
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POS1468

A HIGH GENETIC RISK OF SLE IS ASSOCIATED WITH AN INCREASED RISK OF MYOCARDIAL INFARCTION AND IMPAIRED KIDNEY FUNCTION; A COMBINED OBSERVATIONAL AND MENDELIAN RANDOMIZATION STUDY

Keywords: Prognostic factors, Cardiovascular disease, Genetics/epigenetics

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Background: Cardiovascular morbidity, severe infection and renal damage are amongst the most serious complications of SLE.
Objectives: To combine a mendelian randomization (MR) approach and investigation of a clinical SLE cohort to evaluate the contribution of SLE-genetic risk to the development of myocardial infarction (MI), end-stage renal disease (ESRD) and death from bacterial infections (BI).

Methods: 1487 patients with SLE from Norway and Sweden who fulfilled ≥4 ACR-82 (97%), ACR-97 (98%) or SLICC2012 (94%) classification criteria were included in the study. Clinical data was collected from medical charts and causes of death were retrieved from death certificates. Patients were genotyped using the Global Screening Array or the Immunochip (Illumina). Established, independent SLE risk SNPs (p<5e-8, n=67) were selected and summary statistics for coronary artery disease (CAD) and MI were identified for each SNPs using the MRBase catalog. MR was conducted using the inverse variance weighted method as well as three additional MR methods, on the largest available dataset using a strict definition of MI (ncases=11,622, ncontrols=187,840). The same method was used for analysis of the largest available datasets for dialysis (ncases= 648, ncontrols= 212,841) and BI (ncases= 21,132, ncontrols= 197,660). SNP-manifestation associations from the datasets were used to construct weighted MI/CAD, BI and dialysis PRSs for each patient in the clinical cohort.
Results: The MR analysis revealed a significant association between the genetic risk of SLE and MI (p<0.01). The association was robust to outliers and pleiotropy and consistent across the investigated MR methods. No influence by confounding factors such as hypertension, smoking, alcohol consumption or hyperlipidemia was identified. Individually, 14 SLE SNPs displayed association with MI/CAD and were included in the CAD/MI PRS. In addition, we found an association between the SLE genetic risk and dialysis (p<0.05), whereas the association between SLE genetic risk and BI was not statistically significant (p=0.051). SLE SNPs displaying association with dialysis and BI were included in two separate PRSs. In the clinical cohort, 7.7% of patients had experienced at least one MI, with a mean age at the first event of 60 years. Patients with a CAD/MI PRS in the top quartile displayed a three-fold higher risk of MI (OR 3.04 (1.43–6.49), p<0.01) and a higher risk of ischemic heart disease (MI and/or angina pectoris) (OR 2.64 (1.37–5.11), p<0.01) compared with patients with a CAD/MI PRS in the lowest quartile. In total, 35 % of patients fulfilled the ACR-82 nephritis criterion, and 5.8% had developed ESRD. Patients with a high dialysis PRS displayed a higher risk of nephritis (OR 1.72 (1.15-2.58), p=0.0079), however, a significant association with ESRD could not be demonstrated (OR 1.84 (0.67-5.03), p=0.23). Of the 94 patients in our cohort who were deceased at the time of follow-up, 71 had available death certificates, of which 15 (21%) mentioned infection as a contributing factor. In this data we could not find evidence of an association between a high BI PRS and death from infection (p=0.35).
Conclusion: A high genetic risk of SLE displayed a clear association with MI in the general population, and may also be associated with renal morbidity. Our findings show that combining analysis of large biobank datasets and well-characterized clinical cohorts, may be a useful method for understanding the role of individual SLE risk SNPs in the development of severe SLE sub-phenotypes.
REFERENCES: NIL.
Acknowledgements: NIL.
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POS1469

LONGITUDINAL CHARACTERIZATION OF DISEASE COMPLEXITY AND FLARES IN SYSTEMIC LUPUS ERYTHEMATOSUS: DEVELOPMENT OF AN ELECTRONIC HEALTH RECORDS ALGORITHM

Keywords: Artificial intelligence, Best practices

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Background: Systemic Lupus Erythematous(SLE) is a heterogeneous disease, with a relapsing-remitting pattern that contributes to create difficulties for diagnosis and management. Besides, disease activity indices are not always able to capture the complexity of the disease over time and to guide therapy modification. Data mining and machine learning algorithms developed based on Electronic Health Records(EHR) could help in characterizing the disease complexity and electronic trajectory of evolution.
Objectives: to develop a machine-learning methodology to identify SLE phenotypes and flare trajectories in a large longitudinal database.
Methods: an observational retrospective monocenter study was performed using the EHR of our Tertiary Care University Hospital. Adult SLE patients (pts), with at least one hospital contact between January 2012 and December 2020, were included. For each patient, clinical reports including demographics characteristics, symptoms and clinical history retrieved from text notes recorded during the hospitalization and the out-patient visits, laboratory values, medication and laboratory prescriptions as well as therapy, were extracted from EHR (ICD9 710.0 and 695.4 to identify the pts). A predefined combination of Natural Language Processing techniques (NLP) and abnormal laboratory parameters at each visit was used to identify: 1)presence of 8 different SLE clinical phenotypes (hematological, muco-cutaneous, articular, renal, systemic, neurologic, vascular involvement and serositis); 2)disease complexity based on the combination of the presence of single or multiple organ domains involved and therapy escalation (defined as low, medium, high complexity); 3)disease flares in each of the above clinical phenotypes. Data extraction, from unstructured data of EHR, was performed using topic models and rule-based techniques to build a usable data mart. A p-value<0.05 was considered as significant. Typical explorative analyses were also used to identify SLE phenotypes, together with longitudinal analyses, for the observation of evolution of complexity trajectories.
Results: A total of 1000 SLE pts with at least one contact were identified in our EHR; of them 477 presented at least one hospitalization and 255 pts presented at least one year of follow-up with a median of years of observation of 5.0(3.0, 8.0). In the longitudinal cohort of 255 pts, the median number of outpatient clinic contacts was 14(8-20) and of hospitalizations: 1 [0-2]. The median number of clinical phenotypes identified at baseline was 4(2.25-5), with 50.3% of pts having more than 3; and their distribution was: hematological(71.4%), muco-cutaneous(68.2%), articular(64.3%), renal (62.4%), vascular(34.9%), serositis(24.3%), systemic(16.5%), neurological(16.1%). At baseline, SLE complexity was categorized as low, medium and high in 13.7%, 34.5% and 51.8% of cases respectively. During follow up the complexity of pts changed as reported in *Figure 1*, and 93% of pts had a flare. During longitudinal evaluation, 65.9% pts presented hematologic flare, 60% muco-cutaneous, 47.8% renal, 18.8% articular, 12.9% vascular, 7.8% systemic, 5.1% serositis and 3.9% neurological. The median number of flares significantly increased with disease complexity [(3.5(2.0-6.0), 4.0(2.0-8.0), 6(3.0-9.2) in pts with low, medium and high complexity respectively,p<0.05]. Moreover, the severity of flares for each clinical phenotypes also increased according to the patient's complexity(p<0.05). Overall, 279 therapy escalations were made over the follow up time, 62% due to disease flares, and 38% due to other situations (e.g. intolerance, contraindications).
Conclusion: Machine learning algorithms can help to describe SLE heterogeneity and to characterize clinical phenotypes and trajectories of pts. Next step will be the evaluation of the present procedure on external cohorts to develop a tool able to identify situations needing more intensive and personalized care.

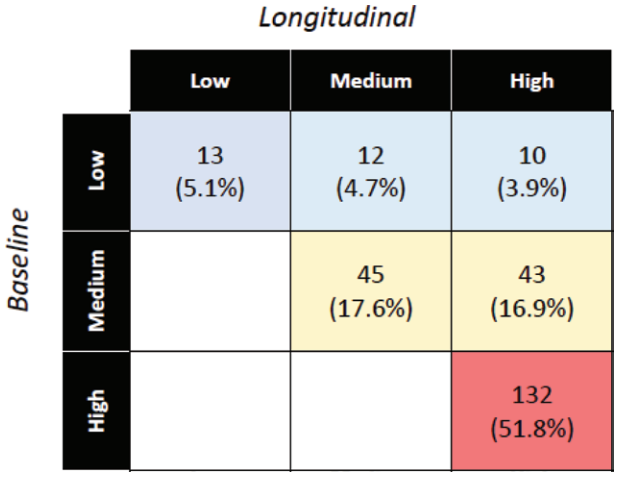


Figure 1.

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Disclosure of Interests: None Declared.
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POS1470

POOR LONG-TERM OUTCOMES AND SUBSTANTIAL UNMET NEEDS IN EUROPEAN PATIENTS WITH LUPUS NEPHRITIS

Keywords: Real-world evidence, Comorbidities, Systemic lupus erythematosus

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Background: Lupus nephritis (LN) is a serious complication of systemic lupus erythematosus (SLE), associated with considerable morbidity and an increased risk of end-stage kidney disease (ESKD). Despite various therapies used in clinical practice, a notable proportion of patients may not achieve sustained remission, leading to adverse disease outcomes.
Objectives: To review and summarize evidence on natural history of LN, burden of comorbidities, and real-world (RW) effectiveness of therapy in European patients with LN.
Methods: A targeted literature review was conducted using MEDLINE/Pubmed and Embase to identify studies in patients with LN. Search strategies were developed for the two databases to identify relevant peer-reviewed articles published in English from March 2012 - March 2022, and conference abstracts from 2019. All records were screened according to pre-specified inclusion/exclusion criteria. Studies conducted in a European setting were summarized.
Results: Of 4,216 identified records, 55 studies reported long-term outcomes of disease and RW effectiveness of treatment in European adults with LN. Up to 36% of patients with SLE developed LN, and nearly all LN cases occurred within 5 years of SLE diagnosis. Patients with LN often suffered from serious infection (19-35%), chronic kidney disease (CKD)/ESKD (6-22%), and cardiovascular disease (CVD) (26%), and were more likely to experience cardio- and cerebrovascular events than patients with SLE only (p=0.001). Immunosuppressive therapies contributed to increased infections and patients treated with high-dose steroids (≥0.5mg/kg/day) had 5-times increased risk of infections compared to those on low-dose regimens. Patients with LN had a higher risk of mortality compared to patients with SLE or other lupus manifestations (p<0.001). The main causes of death among patients with LN were infections (8-32%), CVD (22-58%), or malignancies (5-27%). The majority of RW studies evaluated effectiveness of standard of care (SOC) induction and/or maintenance therapy, mostly with mycophenolate mofetil and cyclophosphamide. Treatment response rates varied across the studies likely due to heterogeneity in study design, drug dosing, and patient population; comparative studies did not find significant differences in response rates between the regimens. Overall, 30-86% of patients with LN achieved complete renal response/remission (CRR) within 1 year of starting SOC therapy, and 25-63% achieved CRR within 2 years. Patients who were non-responders after 1 year had a significantly increased risk of mortality and CKD compared to responders (p<0.005), highlighting the need to reach any degree of response. Over a 5-year period, one study reported that only 38% of patients maintained CRR while on SOC, further suggesting inadequate maintenance on existing therapies. Limited studies focused on treatment-experienced/refractory patients, with the majority evaluating rituximab (RTX)-based regimens. After 1 year of treatment, 29-64% of patients with refractory LN treated with RTX achieved CRR and 35% of patients with active LN despite SOC treated with belimumab (BEL) achieved CRR. Despite initial response to current therapies, 20-35% of patients experienced a renal relapse/flare while on maintenance therapy, with one study noting significantly increased risk of proteinuric flares with azathioprine compared to other maintenance therapies (p=0.01). Very limited evidence was identified on the impact of therapy on extra-renal manifestations in patients with refractory LN, with few studies reporting improvements in SLEDAI scores with RTX after 1 year and with BEL over 2 years of treatment.
Conclusion: European patients with LN have substantial burden from comorbidities that contribute to poor long-term outcomes. Treatment with SOC also contributes to increased morbidity and mortality, particularly due to infections. Furthermore, despite initial response to treatment, a notable proportion of patients experience renal relapse, indicating a need for effective therapies that provide sustained remission.
REFERENCES: NIL.
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Disclosure of Interests: Laurent Arnaud Consultant of: Abbvie, Alexion, Alpine, Amgen, Astra-Zeneca, Biogen, BMS, Boehringer-Ingelheim, GSK, Grifols, Janssen, LFB, Lilly, Kezar, Medac, Novartis, Oséus, Pfizer, Roche-Chugaï, Sêmeia, UCB, Janice Ma Consultant of: Kezar Life Sciences, Inc., Konrad Pisarczyk Consultant of: Kezar Life Sciences, Inc., Eunmi Park Shareholder of: Kezar Life Sciences, Inc., Employee of: Kezar Life Sciences, Inc., Kiruthi Palaniswamy Shareholder of: Kezar Life Sciences, Inc., Employee of: Kezar Life Sciences, Inc., Richard Leff Shareholder of: Kezar Life Sciences, Inc., Consultant of: Kezar Life Sciences, Inc.
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POS1472

ACCURACY OF DISEASE-SPECIFIC ICD-10 CODE FOR INCIDENT SYSTEMIC LUPUS ERYTHEMATOSUS; RESULTS FROM A POPULATION-BASED COHORT STUDY SET IN NORWAY

Keywords: Systemic lupus erythematosus, Validation, Epidemiology

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Background: Accurate estimations of incidence rates are important in all epidemiological studies. Register derived International Classification of Disease (ICD) codes appear near ideal case defining items being seemingly specific and easy to access in large populations, but their applicability in complex clinical syndromes like SLE is still unclear.
Objectives: We aimed to clarify accuracy of ICD-10 coding in incident SLE by directly comparing incidence rates from code-based case-definitions and verified SLE diagnosis by expert clinical assessment in a defined population.
Methods: From administrative data, we identified all individual cases who were registered at least once with the SLE-specific ICD-10 code M32 (i.e M32.1, M32.8 or M32.9) during 1999-2017 in three Southeast Norway counties (including Oslo), with total population 2.1 million. We manually reviewed the chart of every M32 coded case to confirm or reject SLE diagnosis. In cases found not to have SLE, most likely cause of inaccurate ICD-code was recorded. For the analyses of incidence rates by ICD-code, we applied a five-year washout period (1999-2003) and included only cases with first time M32 code from 2004 and onwards. Incidence rates were estimated from five case-definition; (a-c) first occurrence of one or more, two or more and three or more M32 codes from 2004-2017, respectively, (d) SLE diagnosis confirmed by chart review and (e) SLE classified by 1997 American College of Rheumatology classification criteria of SLE. To define accuracy, we applied incidence rate ratios obtained from dividing M32-derived incidence rate to those from SLE diagnosis.
Results: We identified 1975 unique cases registered with a M32 code from 1999-2017. Chart review confirmed SLE diagnosis in 936 of the 1975 cases (45 %), while 1033 (52%) were found to have conditions other than SLE (most frequently another systemic connective tissue disease or cutaneous lupus).
Of the 936 cases with confirmed SLE diagnosis, 323 (34%) were incident in the years 2004-2017 (Table 1). Figure 1a-c shows the incidence curves by different SLE case-definitions. Overall, the incidence rate ratio from two or more M32 code divided by SLE diagnosis was 2.1 (95 % confidence interval 1.8-2.4). Accuracy of ICD-coding was low for incident SLE across all ages, except in those under 25 years were the incidence rate ratio was 1.0 (95 % confidence interval 0.8-1.4) (Figure 1d). When reducing washout period to two instead of five years, the incidence rate ratio from two or more M32 codes divided by SLE diagnosis increased to 4.4 (95% confidence interval 3.8-4.7).
Conclusion: Case definitions based solely on ICD-10 code gave incidence rates of SLE twice as high as when cases were defined by expert clinical assessment, with a maximum discrepancy of seven times more in elderly (70-79 years of age) to a minimum of no discrepancy before 25 years of age.

Table 1. Number of incident cases 2004-2017 in study area by different case definition of SLE

	Total, n	Women, n	Men, n
First occurrence of ICD code 2004-2017[1]			
ICD code of SLE≥ 1 in time period	1035	867	168
ICD code of SLE≥ 2 in time period	670	582	88
ICD code of SLE≥ 3 in time period	543	478	65
Verified SLE diagnosis by chart review	323	279	44
SLE by 1997 ACR criteria[2]	289	249	40

[1]No ICD code of SLE 1999-2003 [2]American College of Rheumatology classification criteria SLE

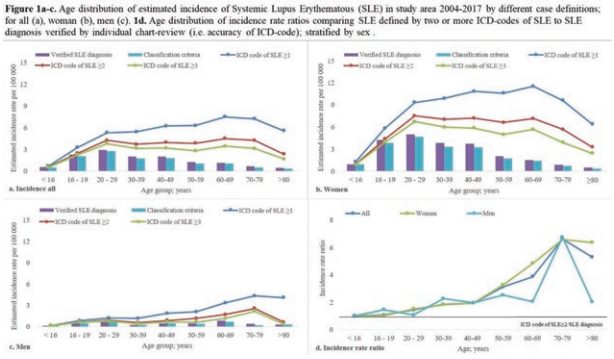


Figure 1a-c. Age distribution of estimated incidence of Systemic Lupus Erythematous (SLE) in study area 2004-2017 by different case definitions; for all (a), woman (b), men (c). **1d.** Age distribution of incidence rate ratios comparing SLE defined by two or more ICD-codes of SLE to SLE diagnosis verified by individual chart-review (i.e. accuracy of ICD-code); stratified by sex .

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POS1473 ASSESSLE- A NEW TOOL TO ASSESS SLE DISEASE ACTIVITY- THE PATIENTS' PERSPECTIVE

Keywords: Systemic lupus erythematosus, Quality of life

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous, waxing, waning, multisystem autoimmune disease. The complexity and clinical unpredictability of SLE challenge the assessment of disease activity over time, especially in everyday clinical practice. Multiple clinical disease- monitoring instruments have been developed, however, they are limited in ability to detect the change in disease activity over time, too cumbersome to be utilized in daily practice, and do not include patient-reported outcomes (PROs).

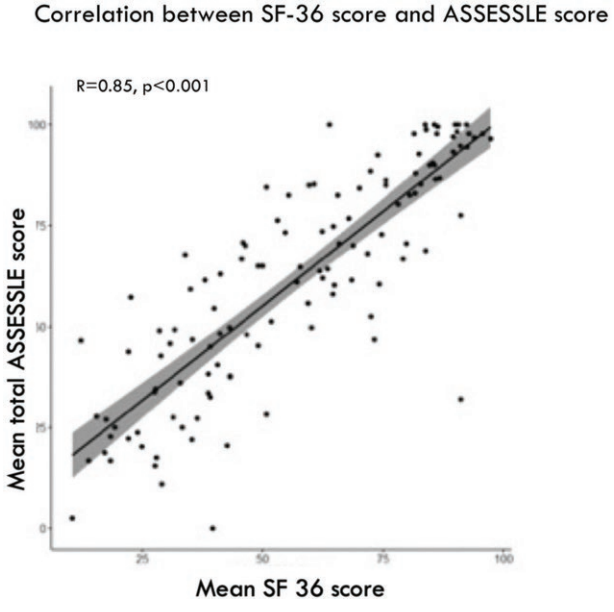


Figure 1.

Objectives: To construct a new disease activity score that will simplify and improve disease activity assessment in daily practice, and include PROs. Here we present the PRO component.

Methods: The new instrument for the assessment of SLE activity is comprised of 7 visual analog scales (VAS), which separately address the physician's global assessment and 6 organ systems. The PRO consists of 5 VAS questions that address general well-being, global disease activity, activities of daily living, medication compliance, and mood. The ASSESSLE PRO is compared to the Short Form Health Survey (SF-36), a 36-item, patient-reported survey of patient health. We applied the ASSESSLE PRO to 46 consecutive patients with SLE attending the rheumatology clinic in 2 tertiary medical centers in Israel.

Results: Psychometric evaluation of the reliability of all 5 PRO questions indicated that question 4, regarding compliance, correlated poorly with the other items and lowered the reliability (Cronbach's α=0.80 95% CI (0.74,0.85). Following the omission of question 4, Cronbach's α was recalculated, leading to increased internal reliability (Cronbach's α = 0.86, 95% CI [0.82, 0.90]). All other remaining items had a satisfactory correlation with the other items ("item-other" correlation between 0.58-0.70). Therefore, the score was computed as the mean of the 4 remaining questions. Aiming to compare the ASSESSLE PRO to the SF-36 survey, the Spearman correlation coefficient between absolute scores was computed and a strong and significant effect was found (R=0.85, p<0.0001). (Figure 1).

Conclusion: The ASSESSLE PRO is a short PRO that allows a reliable, reproducible and simple PRO form showing excellent correlation with the SF-36. Following the omission of question 4, regarding patient compliance, the ASSESSLE PRO consists of only 4 questions, as compared to the SF-36 which requires a response to 36 items. The ASSESSLE PRO seems to have significant advantages due to its intuitive VAS questions and brevity which allows use of this PRO in everyday practice and may increase the validity of disease activity evaluation of SLE when combined with the physician's assessment.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1474 TEMPORAL TRENDS IN JOINT SURGERY FOR LUPUS PATIENTS – A POPULATION BASED LONGITUDINAL STUDY

Keywords: Real-world evidence, Registries, Systemic lupus erythematosus

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Background: Joint damage in SLE results from (peri-) articular inflammation and can present as erosive arthropathy (considered to represent the overlap syndrome Rhupus), deforming Jaccoud's arthropathy or osteonecrosis [1,2] in addition to common causes as trauma and degenerative joint disease.

Objectives: We investigated the burden of joint disease requiring orthopaedic procedures (OP) in lupus patients in Western Australia (WA).

Methods: Patients registered in the state-wide Hospital Morbidity Data Collection with a diagnostic code for SLE in the period 1985-2015 (n=2010; 84.7% females, age 42 years (IQR 30-59) were age/gender/index year matched with controls (n=12840, 86% female, age 41 yrs) and procedure codes for arthroplasty, arthrodesis, synovectomy and arthroscopy were extracted. Figures represent median (IQR), frequency (%) and incidence rate (IR) per 100 person years with incidence rate ratios (IRR) to compare IR across groups and over three study decades.

Results: A total of 298 lupus patients (16.1%) underwent 676 OP during 12.3 years follow-up. The IRR for any OP in lupus vs controls was 7.18 (CI 2.5-20.7, p<0.001). In lupus patients, the IR for arthroplasties (1.44, CI 1.26-.56; n=330, 65% hip and knee) and arthrodesis (0.27,CI 0.21-0.34, n= 68) did not change, but IR for synovectomy (n= 58) decreased (0.58 to 0.15) and for arthroscopy (n= 225) increased significantly (0.05 to 1.16). Osteonecrosis affected 32 (1.7%) patients necessitating arthroplasty in 24/32 (75%) while IR for osteonecrosis reduced from 0.19 to 0.11 over time (p=0.12). The proportion of Rhupus patients (with both SLE+RA diagnosis) (11.8%) was stable over time, while OA was a

co-diagnosis in 49.1 % of patients undergoing OP vs 2.6 % in patients not requiring OP. Undergoing an OP (with or without arthroscopy) did not impact on long term survival (logrank p =0.16).

Conclusion: There is a high burden of joint damage in lupus patients as one in six patients required an OP at a rate seven times that of controls. These data illustrate that joint symptoms in lupus patients need careful evaluation, including imaging studies [3] and comprehensive strategies to reduce long term joint damage.

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Disclosure of Interests: None Declared.

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POS1475 EMPLOYMENT TRAJECTORY OF CANADIAN YOUNG ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Work-related issues, Systemic lupus erythematosus, Registries

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Background: Young adulthood, 18-30 years, is a time when many individuals start working. Failing to establish employment during young adulthood could predict lifetime financial hardships. Lack or limited employment could limit access to healthcare benefits, adversely affecting treatment access and health outcomes.

Objectives: To determine the average employment trajectory of childhood- and adult-onset systemic lupus erythematosus patients in young adulthood (YASLE).

Methods: Patients (with ≥ 2 visits) were from two longitudinal cohorts: the Canadian national lupus cohort (via the Canadian Network for Improved Outcomes in SLE, CaNIOS) and the University of Toronto (UT) lupus cohort from Toronto Western Hospital. The CaNIOS cohort (2002-2020) included participants from multiple provinces, the UT cohort only Ontario patients (1983-2020). Participants report employment states annually. The employment states were: employed, unemployed, homemaker, student, work disabled. This was reduced to: employed, unemployed or not in labour force (NLF, student, homemaker, work disabled) for modelling. The Markov multistate model (msm) was used to model employment trajectory. Transition probabilities at 1, 6, 12 years from age 18 years were calculated.

Results: 841 participants (85.4% females): 253 (CaNIOS) and 588 (UT). Mean age (standard deviation, SD) at baseline (cohort entry) was 23.1 (SD 3.7) years. Participants' age: 38.2% (18-20 years), 19.3% (21-23 years), 21.9% (24-26 years), 20.7% (27-30 years). 403 (47.9%) were cSLE. 89.5% completed high school. Median disease duration was 3.3 (0.7-6.6, 25th-75th percentile, P) years. Median follow-up was 2.8 (0.9- 6.5, 25th-75th P) years. At baseline, 16.6% were employed, 5.6% were unemployed and 77.8% were NLF (42 work disabled, 226 homemakers, 386 students). 374/6615 (6%) visits showed state changes. 58% occurred in the NLF group. YASLE patients have the highest probabilities of remaining in the same employment state as baseline (Table 1). With increasing age, there was a reduced rate of staying employed (0.69 to 0.64). Those unemployed showed low probability to become employed (0.28 to 0.38). The NLF group has static rate of transition to employment (0.65), without expected increase with age.

Conclusion: YASLE patients showed minimal or no increase in transitions into employment from non-employed states, and no increase in employment with age as expected in the general young adult population. This could suggest a lowered labour force attachment in YASLE patients, suggesting difficulties in establishing employment during young adulthood. Future work should focus on YASLE patients' perceived barriers and facilitators for employment, to target interventions for supporting patients' employment.

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Table 1. Probability of Transitions in Unadjusted Markov Multistate Model by Age From 18 Years Old.

	Employed	Unemployed	Not in Labour Force*
	Age= 19 years		
Employed	0.69	0.14	0.17
Unemployed	0.28	0.61	0.10
Not in Labour Force	0.65	0.14	0.21
	Age=24 years		
Employed	0.67	0.17	0.17
Unemployed	0.33	0.55	0.11
Not in Labour Force	0.65	0.17	0.18
	Age=30 years		
Employed	0.65	0.19	0.17
Unemployed	0.38	0.49	0.12
Not in Labour Force	0.64	0.19	0.17

Acknowledgements: NIL.

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POS1476 AUTOANTIBODY TRAJECTORIES ASSOCIATE WITH CLASSIFICATION AND TREATMENT RESPONSE IN LUPUS NEPHRITIS

Keywords: Biomarkers, Systemic lupus erythematosus, Autoantibodies

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Background: Autoantibodies are a hallmark of lupus nephritis (LN). While there is known heterogeneity in autoantibody expression among LN patients, the association of autoantibodies with LN subtypes and the implications of longitudinal changes in LN are not entirely understood.

Objectives: In this study, we quantified circulating autoantibodies in the Accelerating Medicines Partnership (AMP) LN longitudinal cohort to identify novel serum biomarkers of LN classification and treatment response and to provide insights into the pathogenesis of LN.

Methods: SLE patients meeting ACR or SLICC criteria (n=268) indicated for kidney biopsy by a urine protein/creatinine (UPCR) >0.5 were recruited for this study as part of the AMP. Kidney biopsies were evaluated by a renal pathologist according to ISN/RPS classification, and serum samples were collected at the time of diagnostic kidney biopsy and 3-, 6-, and 12-months post-biopsy. Serum autoantibodies against dsDNA, chromatin, ribosomal-P, Ro, La, Sm, SmRNP, RNP, Jo-1, Scl-70, and centromere-B were measured using the BioPlex 2200 ANA kit (Bio-Rad Technologies, Hercules, CA), while anti-C1q positivity was determined by ELISA (QUANTA Lite, Werfen, Bedford, MA). Clinical response was determined at 12 months using the Abatacept and Cyclophosphamide Combination Efficacy and Safety Study definitions for patients with ISN/RPS class III, IV, V, or a combination thereof and a baseline UPCR ratio >1.0.

Results: Most LN patients exhibited autoantibodies against chromatin (78%) dsDNA (70%), SmRNP (63%), C1q (56%), RNP (54%), and Sm (52%) (Figure 1A). Patients with proliferative LN (class III, IV, III+V, or IV+V) had higher positivity rates of several autoantibodies, including those against dsDNA, chromatin, and C1q, compared to patients with membranous LN (class V) (Figure 1A). Similarly, patients with pure proliferative (class III or IV) and mixed (class III+V or IV+V) LN had significantly higher titers of these autoantibodies compared to those with mesangial (class I or II), membranous, and advanced sclerosis (class VI) LN (Figure 1B-D). Furthermore, increased titers of these autoantibodies were associated with higher odds of having proliferative LN. Proliferative LN patients with a complete treatment response exhibited a significant decline in several autoantibodies including anti-dsDNA, C1q, chromatin, Smith, and ribosomal P (Figure 1F). Autoantibody levels remained relatively stable in partial- and non-responder proliferative LN patients, as well as in patients with membranous LN.

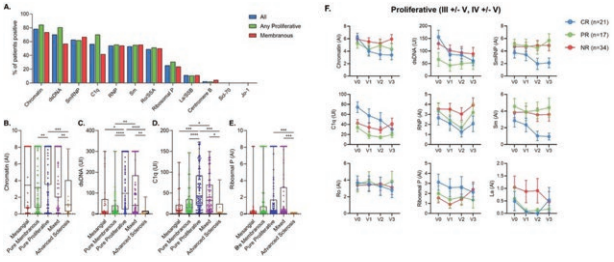


Figure 1.

Conclusion: LN patients exhibit heterogeneous autoantibody profiles associated with ISN/RPS classification. Specifically, levels of autoantibodies against dsDNA, C1q, chromatin, and ribosomal P may serve as noninvasive biomarkers of proliferative LN. In patients with proliferative but not membranous LN, a decline in the titers of several autoantibodies, including many not routinely measured over time, such as anti-Sm, was associated with treatment response, suggesting a possible role in LN pathogenesis. In addition, these autoantibodies may serve as early biomarkers of treatment response.

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POS1477 DISEASE FLARES AFTER SARS-COV-2 MRNA VACCINATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ARE ASSOCIATED WITH DISEASE ACTIVITY BEFORE VACCINATION

Keywords: COVID, Vaccination/immunization, Systemic lupus erythematosus

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Background: While some reports suggest the development and flare of autoimmune inflammatory rheumatic diseases after vaccination, the frequency of disease flare after vaccination in patients with systemic lupus erythematosus (SLE) has been reported to be low. When we assess risk-benefit balance of vaccine administration, it is crucial to understand the effect of vaccines in patients with SLE. However, SARS-CoV-2 mRNA vaccines are new types of vaccines, and little is known about the effectiveness and safety of the vaccines and factors associated with disease flare in patients with SLE after SARS-CoV-2 mRNA vaccination.

Objectives: To elucidate the effect of SARS-CoV-2 mRNA vaccinations including adverse reactions to vaccines, neutralising antibody titres and disease flare rates after their vaccination and the associated factors in patients with SLE.

Methods: We enrolled the uninfected patients receiving two doses of vaccine (BNT162b2 or mRNA-1273) between June and October 2021. The neutralizing antibodies in peripheral blood, adverse reactions, and disease flares defined by the SELENA-SLEDAI Flare Index were evaluated four weeks after the second dose of vaccine. The neutralizing antibodies were measured using the STACIA SARS-CoV-2 Neutralization Antibody Test (MBL Corporation, Nagoya, Japan), and the cut-off level of seroconversion was defined as an antibody concentration of more than 1.67 U/mL.

Results: Ninety SLE patients were enrolled. The median age was 46.5 years, and the disease duration was 9.0 years. The median SLEDAI before vaccine administration was 2. Four weeks after the second dose of vaccination, 19 (21.1%) were still negative for neutralising antibodies. Adverse reactions were observed in 88.9%, including fever above 37.5° C in 20.8%. Factors associated with negative neutralising antibodies were older age, anemia (Hb ≤ 11 g/dL), mycophenolate mofetil (MMF) use (p=0.030 [55 years vs 44 years], p=0.014 [36.8 % vs 11.3%], and p=0.029 [42.1% vs 16.9%], respectively). Regarding disease activity, SLEDAI modestly but significantly increased significantly vaccination (p=0.016, median change 0 [IQR: 0–1]). Thirteen (14.4%) and 4 (4.4%) patients experienced flares and severe flares (nephritis in 3 and vasculitis in 1), respectively. High titres of SLEDAI, anti-dsDNA antibodies, rash, and azathioprine use were associated with flares in univariate analysis (p=0.046, p=0.034, p=0.037 and p=0.038, respectively, Table 1). Multivariable logistic regression analysis showed that high levels of SLEDAI and anti-dsDNA antibodies were associated with flares. Types of vaccines, neutralising antibody titres, and frequency of adverse reactions were not relevant for flares.

Conclusion: Older age, anemia, and MMF use are associated with negative seroconversion of neutralising antibodies. Residual disease activity before vaccination is a risk factor for flares.

Table 1. Factors associated with flares after second vaccination.

	Flare, N=14	Non-flare, N=76	Univariable, P-value	Multivariable model 1, P-value	Multivariable model 2, P-value	Multivariable model 3, P-value
Age, years	51 (32.5–61.5)	46 (36–56)	0.622	-	-	-
SLEDAI before first vaccination	2 (0.5–5)	2 (0–2)	0.046	0.031	-	-
Anti-dsDNA antibodies before first vaccination, U/mL	23.1	3.9	0.037	-	0.031	-
Rash before first vaccination, %	7.4 (4.0–54.7)	4.8 (2.7–7.0)	0.033	-	-	0.063
Use of azathioprine before first vaccination, %	38.5	13.0	0.038	0.044	0.122	0.088
Positive neutralizing antibodies, %	76.9	79.2	1.000	0.706	0.357	0.483

Multivariable analysis was performed on three models with separate variables, which are components of SLEDAI.

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POS1478 THE QRISK3 CLASSIFIED MORE JAPANESE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS AS HIGH RISK OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD) WHEN COMPARED TO THE HISAYAMA STUDY SCORE

Keywords: Systemic lupus erythematosus, Comorbidities, Cardiovascular disease

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Background: The QRISK3, an atherosclerotic cardiovascular disease (ASCVD) risk tool including SLE as a risk factor, has been reported to demonstrate better performance in predicting risk of ASCVD in SLE patients compared with

Table 1. Comparison between patients classified as high risk and low to moderate risk by QRISK3

	Low-moderate risk (n=59)	High risk (n=46)	P-value
The Hisayama study score	2.28 (1.77-2.80)	4.71 (3.99-5.43)	**< 0.0001***
Female (%)	58 (98.3)	42 (91.3)	0.16
Age, years	48.1 (46.8-49.4)	59.8 (57.6-62.1)	**< 0.0001***
Disease duration, years	19.0 (16.6-21.5)	20.2 (16.8-23.6)	0.56
SLEDAI-2K	5.18 (4.02-6.35)	5.76 (3.92-7.59)	0.59
Prednisolone (PSL) (%)	51 (86.4)	40 (86.9)	0.93
Daily intake of PSL (mg)	4.79 (3.77-5.82)	4.8 (2.97-6.62)	0.99
Body mass index, kg/m^2	20.9 (20.16-21.74)	21.4 (20.4-22.4)	0.43
Current smokers (%)	3 (5.0)	9 (19.5)	**0.02****
Family history of early CVD (%)	4 (6.7)	6 (13.0)	0.32
Systolic blood pressure (mmHg)	119 (115-123)	135 (130-139)	**< 0.0001***
Antihypertensive therapy (%)	7 (11.8)	22 (47.8)	**< 0.0001*****
Glucose intolerance (%)	26 (44.0)	29 (63.0)	0.05
Serum LDL-C (mg/dL)	111 (105-117)	115 (104-126)	0.52
Serum HDL-C (mg/dL)	75 (69-80)	70 (63-76)	0.21

* student t-test ** Fisher exact test *** Pearson's chi-square test

Framingham risk score (FRS) [1]. However, it is unknown how the QRISK3, the risk score established in the United Kingdom (UK), can estimate the ASCVD risk of Japanese SLE patients in comparison to the risk score validated for the Japanese population.

Objectives: To compare two algorithms for ASCVD risk estimation, QRISK3 and Hisayama study score [2], a general risk calculator used in Japan Atherosclerosis Society (JAS) guideline for Prevention of Atherosclerotic Cardiovascular Diseases 2022, in our cohort of Japanese SLE patients.

Methods: We performed a cross-sectional study in SLE patients attending Kyoto University Hospital by using questionnaires and laboratory tests. In primary prevention subjects without high-risk comorbidities (peripheral artery disease, chronic kidney disease, diabetes) and aged 40 to 79, both the Hisayama study score based on traditional risks (sex, systolic blood pressure, glucose intolerance, serum lipid and smoking) and QRISK3 (ethnicity was selected as "Other Asians") were calculated to estimate the ASCVD risk over the next 10 years.

Results: Among 335 patients enrolled, 105 were eligible for both ASCVD risk calculators. QRISK3 estimated 46 patients as high risk (score >10 %), while the Hisayama study score classified no patients as high risk. The patients classified as high risk by QRISK3 had significantly higher Hisayama study score (4.71 [3.99-5.43] vs 2.28 [1.77-2.80], p<0.0001) and more traditional risks, such as old age (59.8 [57.6-62.1] vs 48.1 [46.8-49.4], p<0.0001), current smoking (9 [19.5%] vs 3 [5%], p=0.02) and hypertension on treatment (22 [47.8%] vs 7 [11.8%], p<0.0001) than the patients with low-moderate risk (Table1). QRISK3 score was positively correlated with the Hisayama study score (r=0.4945, p<0.0001). As a reference for each risk stratification score, the proportions to achieve target values for serum low-density lipoprotein cholesterol (LDL-C) recommended by the JAS guideline were 94.3 % and 69.5 % respectively.

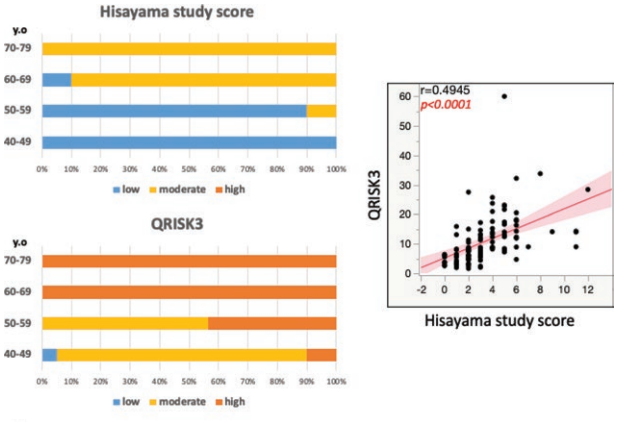


Figure 1.

Conclusion: QRISK3 classified more Japanese SLE patients as high risk of ASCVD when compared to the Hisayama study score. Lipid management might be insufficient according to QRISK3. The validation of QRISK3 by longitudinal studies should be warranted in Japanese SLE patients.

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POS1479

MORTALITY OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS: A STUDY OF THE BATH LUPUS COHORT

Keywords: Autoantibodies, Systemic lupus erythematosus, Descriptive studies

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Background: The Bath CTD cohort study contains a mixed prevalent and inception cohort of 281 SLE patients recruited between 2001 and 2018 from outpatient Rheumatology clinics at the Royal United Hospital for Rheumatic Diseases, Bath,UK. Work from other lupus cohorts in the UK (1) has demonstrated residual poor mortality outcomes for SLE patients. We set out to describe mortality outcomes for our local cohort of SLE patients, with reference to expected trends and autoantibody profiles.

Objectives:

1) Describe mortality outcomes (proportion of cohort, age of death and cause of death) from a longitudinal cohort of SLE patients.
2) Calculate prematurity of death (years of life lost) for deceased patients with reference to estimated mortality reference figures for the UK population.
3) Compare autoantibody profiles between deceased and non-deceased patients to assess for associations between mortality and patient serology.

Methods: Data was extracted from secure research databases. Copies of death certificates where obtained. Estimated life expectancy (for year of birth and gender) was calculated using Office of National Statistics (ONS) data. Years of life lost (or gained) was calculated. A paired samples t-test was performed to compare the difference between age at death and predicted age at death for the deceased cohort. Autoantibody profiles between deceased and non-deceased patients were compared using Chi squared (Fisher's exact test if n <5) and relative risks, confidence intervals and p values calculated.

Results: The cohort comprised 251 female and 30 male patients. Average age at diagnosis was 37.9 (18 to 62). 97% were ANA positive. 21% (61/281) of the cohort had died. Proportionally more male (13/30) than female (48/251) patients died. Cause of death data was available for 60 patients. The most common causes of death were malignancy (23.3%, 14/60), cardiovascular (21.6%, 13/60) and infection (18.3%,11/60). 8 patients (13.3%) died of SLE. 21 patients died earlier than their predicted life expectancy (-1.5 to – 32.6 years less). Mean of the difference (between actual and predicted life expectancy) for the cohort was + 4.64 (95% CI 0.4281 to 8.854, p value 0.0314). Patients that died early were more likely to die of SLE (20%, 4/20 vs 10%, 4/40), infection (15%,3/20 vs 20%, 8/40) and malignancy (40%,8/20 vs 15%, 6/40) vs than those who died late. Those who died later more likely to die of cardiovascular disease (28%,11/40 vs 10%, 2/20). Numerically those who died early were more likely to be male, older at diagnosis and be dsDNA+ve, but these numbers did not reach statistical significance. No

significant differences in autoantibody profiles were detected between deceased and non-deceased patients.

Conclusion: We observed a bimodal distribution of causes of death, with SLE, malignancy and infection more likely to cause early deaths, and cardiovascular disease more likely to cause later deaths. Across the whole cohort, patients lived longer than was expected. However, a third of patients still died early, suggesting future work should focus on addressing these highest risk patients. Across the cohort proportionally more male than female patients died. This may reflect known differences in life expectancy between genders, but highlights male patients as a group with persisting poorer mortality outcomes. No significant differences in autoantibody profiles were observed between patients that died versus those that survived. This may be because the entire cohort is enriched for positive serology, perhaps making it less likely that differences will be identified.

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Disclosure of Interests: None Declared.

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POS1480 DESCRIBING RENAL FUNCTION TEST USE IN REAL-WORLD DIAGNOSIS AND MONITORING OF LUPUS NEPHRITIS PATIENTS IN EUROPE

Keywords: Systemic lupus erythematosus, Real-world evidence

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Background: Lupus nephritis (LN) is a severe renal manifestation of the autoimmune disease lupus. Tests for renal function, such as estimated glomerular filtration rate (eGFR), should be standard in the diagnosis and monitoring of patients with renal disease as recommended by the Kidney Disease Improving Global Outcomes (KDIGO) Chronic Kidney Disease (CKD) Working Group [1]. These tests are important to identify renal function decline and prompt interventions to prevent further disease progression. It has been found that use of eGFR is low in Italy for CKD patients [2] but data on real-world testing in other countries is limited.

Objectives: To understand renal function test use by nephrologists in the diagnosis and monitoring of LN patients in Europe in a real-world clinical setting.

Methods: Data were sourced from the Adelphi Lupus IV Disease Specific Programme™, a point-in-time survey of nephrologists and their LN patients conducted in France, Germany, Italy, Spain and the United Kingdom in April – October 2021. Nephrologists completed patient record forms covering each patient's management, including tests and assessments used for diagnosis and monitoring. The data was analysed descriptively.

Results: 72 nephrologists provided data for 376 LN patients. Overall, 20% of LN patients in the sample did not have a Glomerular Filtration Rate (GFR) or eGFR test documented to diagnose their condition. The use of these tests at diagnosis was lower in Germany and Italy (≤72%) compared to the other countries where use was over 80%. Of all the patients without GFR/eGFR at diagnosis, only 43% had an alternative renal test completed (e.g. urine protein, creatinine clearance (CrCl), albumin-to-creatinine ratio (ACR) or 'other urinalysis test' (including urine protein creatinine ratio)). Across Europe, the use of GFR/eGFR to monitor patients with LN was 85% or above, apart from Italy where 31% of patients did not have either test. In patients without GFR/eGFR for monitoring, the use of alternative renal tests was higher than at diagnosis (60% vs. 43%). However, 40% of those patients received no other renal test (e.g. urine protein, CrCl or ACR) to monitor their condition.

Conclusion: GFR/eGFR are key markers of renal function as discussed in the KDIGO recommendations [1], but this analysis observed lower-than-expected use of GFR/eGFR among nephrologists. This was especially apparent in Germany and Italy. There may be even less use of these tests among non-nephrology specialities. Lower-than-expected use of these recommended tests indicates a need for improvement in the diagnosis and monitoring of LN patients in Europe. This suboptimal management may be affecting patient outcomes, but further research is needed to assess this. Results are subject to recall bias which was minimised by asking survey respondents to use patient medical records for the completion of forms.

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POS1481 INFORMING TRIAL MEASUREMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS: FREQUENCY OF DOMAIN-SPECIFIC DISEASE ACTIVITY IN A MULTI-NATIONAL OBSERVATIONAL COHORT

Keywords: Systemic lupus erythematosus, Outcome measures, Real-world evidence

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Table 1. Renal test use in Europe

		Overall	France	Germany	Italy	Spain	UK
Renal tests used at LN diagnosis, n (%)	**Sample**	**n=376**	**n=63**	**n=75**	**n=75**	**n=81**	**n=82**
	GFR	133 (35)	31 (49)	27 (36)	31 (41)	35 (43)	9 (11)
	eGFR	220 (59)	25 (40)	37 (49)	33 (44)	59 (73)	66 (80)
	GFR and/or eGFR	302 (80)	56 (89)	54 (72)	53 (71)	71 (88)	68 (83)
	Neither GFR nor eGFR	74 (20)	7 (11)	21 (28)	22 (29)	10 (12)	14 (17)
Of patients without GFR/eGFR at diagnosis – Other renal tests to diagnose, n (%)	**Sample**	**n=74**					
	At least one renal test other than eGFR/GFR	32 (43)					
Renal tests used in monitoring of LN*, n (%)	**Sample**	**n=368**	**n=62**	**n=73**	**n=74**	**n=78**	**n=81**
	GFR	129 (35)	28 (45)	29 (40)	29 (39)	32 (41)	11 (14)
	eGFR	225 (61)	25 (40)	43 (59)	34 (46)	53 (68)	70 (86)
	GFR and/or eGFR	311 (85)	53 (85)	62 (85)	51 (69)	70 (90)	75 (93)
	Neither GFR nor eGFR	57 (15)	9 (15)	11 (15)	23 (31)	8 (10)	6 (7)
Of patients without GFR/eGFR for monitoring – Other renal tests to monitor, n (%)	**Sample**	**n=57**					
	At least one renal test other than eGFR/GFR	34 (60)					

*Patients with available data,Abbreviations: eGFR, Estimated Glomerular Filtration Rate; GFR, Glomerular Filtration Rate; LN, Lupus Nephritis; UK, United Kingdom

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Background: Systemic lupus erythematosus (SLE) has heterogeneous organ manifestations that occur in different combinations at an individual patient level. Current SLE clinical trial eligibility criteria and efficacy endpoints, based on legacy disease activity measures, have multiple weaknesses. Understanding the frequency with which different organ manifestations are represented in contemporary SLE cohorts is required, to allow focus on the most frequent and impactful manifestations of disease in both eligibility criteria and endpoints.

Objectives: To report the prevalence of disease activity in individual organ domains in SLE patients, both overall and in patients meeting the most common disease activity cut-off for clinical trial eligibility (SLEDAI2K ≥6).

Methods: We used data from a multinational SLE cohort, prospectively collected between 2013 and 2020. We analysed data from 4,102 patients with criteria-defined SLE, who contributed 42,345 visits with complete SLEDAI-2K assessments. Disease activity assessed using SLEDAI-2K was categorised according to activity in 9 organ systems: central nervous system (CNS), vasculitis, musculoskeletal, renal, cutaneous, serositis, serological, haematological, and fever. Proportions of organ-specific disease activity in the overall cohort, and stratified by total SLEDAI-2K ≥6 or <6, were calculated.

Results: In the overall cohort, 3,659 patients (89.2%) had SLEDAI-2K >0 on at least one visit (31,290 visits, 73.9%). Serological disease activity was the most prevalent in the cohort overall, affecting 75.5% of patients at least once, followed by renal (41.6%), cutaneous (36.5%), musculoskeletal (20%) and haematological (19%) activity. Infrequent active manifestations affecting <5% of patients were serositis (3.4%), vasculitis (3.4%), CNS (3.0%) and fever (3%). We further examined the prevalence of domain-specific disease activity in patient visits stratified by a SLEDAI-2K cut-off of 6 (Table 1). In patient visits with a SLEDAI-2K >6 (n = 10,031 visits, 24% of total) the most common manifestations were serological (90%) and renal (73%), followed by cutaneous (26%) and musculoskeletal (14%). Conversely, 7.3% of visits with renal, 6.7% with cutaneous, 5.8% with haematological and 1.3% with musculoskeletal activity did not have a SLEDAI-2K ≥6 (Table 1).

Table 1. Frequencies and percentages of patient visits with specific organ system disease activity, stratified by total SLEDAI score cut-off of ≥6 vs <6.

	All visits	SLEDAI<6	SLEDAI≥6	
	n = 42,345	*n = 32,314*	*n =10,031*	*p-value**
Serological	25,745 (60.8%)	16,740 (51.8%)	9,005 (89.8%)	<0.001
Renal	9,684 (22.9%)	2,367 (7.3%)	7,317 (72.9%)	<0.001
Cutaneous	4,806 (11.3%)	2,158 (6.7%)	2,648 (26.4%)	<0.001
Haematological	2,615 (6.2%)	1,862 (5.8%)	753 (7.5%)	<0.001
Musculoskeletal	1,856 (4.4%)	422 (1.3%)	1,434 (14.3%)	<0.001
Serositis	255 (0.6%)	81 (0.3%)	174 (1.7%)	<0.001
Vasculitis	250 (0.6%)	0	250 (2.5%)	<0.001
CNS	200 (0.5%)	0	200 (2.0%)	<0.001
Fever	149 (0.4%)	59 (0.2%)	90 (0.9%)	<0.001

*P-values derived from Pearson's Chi-Squared tests.

Conclusion: Serological, renal, cutaneous, musculoskeletal and haematological manifestations predominate in patients with active SLE in our cohort, with other organs only rarely affected. Measures of improvement in SLE trial endpoints could focus on measuring change in these systems, and omit detailed analysis of rare events. Conversely, a notable proportion of patients with active disease in commonly affected organ domains had SLEDAI-2K <6, meaning they would be excluded from clinical trials. Incorporation of organ-specific activity measures and inclusion criteria for SLE clinical trials may overcome this limitation and improve recruitment to and results of trials.

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POS1482 **PREDICTORS AND CLINICAL SIGNIFICANCE OF LUPUS LOW DISEASE ACTIVITY STATE 12 MONTHS AFTER LUPUS NEPHRITIS**

Keywords: Systemic lupus erythematosus, Kidneys, Treat to target

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Background: Lupus nephritis (LN) is a significant comorbidity that affects around 50% of patients with systemic lupus erythematosus (SLE). Complete or partial renal response 12 months after LN is a recommended treatment target. Low disease activity in extra-renal domains by achieving LLDAS may also contribute to one of the critical treatment goals in LN patients [1]. However, the predictors of LLDAS in LN patients and the renal-specific benefits of LLDAS were also not fully understood.

Objectives: To investigate the predictors of LLDAS at 12 months post-LN and the clinical usefulness of achieving this state in LN patients.

Methods: Patients with biopsy-proven LN during 2010-2020 were included. Baseline demographics, blood parameters and urinalysis results were recorded. Patients were then followed up every 4 months to repeat blood tests and urinalysis. Renal response and LLDAS were assessed at 12 months post-LN, and any future relapses were recorded. Complete renal response (CRR) was defined as proteinuria ≤0.5g/day with normal estimate glomerular filtration rate (eGFR); partial renal response (PRR) was defined as a reduction in proteinuria by ≥50% with near normal eGFR. LLDAS was attained by meeting: (1) SLE Disease Activity Index ≤4 with no major organ activity; (2) no new lupus disease; (3) physician global assessment ≤1; (4) prednisolone dose ≤7.5mg; (5) standard maintenance immunosuppressants [1]. Relapse was a biopsy-proven LN after an initial treatment response of proteinuria reduction of ≥50% or to subnephrotic range. We assessed the predictors of LLDAS at 12 months post-LN and performed time-to-relapse survival analysis.

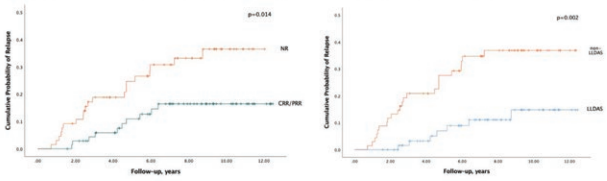
Results: 143 LN patients were included with a median follow-up duration of 10.4 years. At 12 months, 57 (40%), 14 (10%) and 69 (48%) patients achieved CRR, PRR and LLDAS, respectively. Among 136 patients who achieved treatment response, 30 (22%) patients developed LN relapse after a median of 2.98 years. LN at age greater than 30 or the presence anti-smith autoantibodies had significantly lower odds of reaching LLDAS at 12 months after LN, with odds ratio of 0.35 (p = 0.047) and 0.30 (p = 0.043) respectively (Table 1). Patients reaching CRR/PRR and LLDAS both had a significantly lower chance of relapse with p = 0.014 and p = 0.002 respectively (Figure 1).

Table 1. Predictors of LLDAS 12 months post-LN.

	Predictors	Number (row%) in LLDAS 12 months post-LN	Univariate Logistic Regression		Multivariate Logistic Regression	
			OR (95% CI)	*p* value	OR (95% CI)	*p* value
LN age	≤30	15/24 (63%)	ref			
	>30	54/119 (45%)	0.50 (0.20-1.23)	0.130	0.35 (0.13-0.99)	**0.047**
Time from SLE to LN	≤1Y	3/10 (30%)	ref			
	>1Y	66/133 (50%)	2.30 (0.57-9.27)	0.242	2.30 (0.46-11.36)	0.309
	Serum albumin (g/L)		1.04 (0.98-1.11)	0.197	1.02 (0.95-1.10)	0.548
	Serum creatinine (μmol/L)		1.00 (0.99-1.00)	0.248	0.99 (0.99-1.00)	0.189
Anti-Sm	Never	55/106 (52%)	ref			
	Ever	7/23 (30%)	0.41 (0.15-1.07)	0.067	0.30 (0.09-0.97)	**0.043**
Anti-RNP	Never	46/88 (52%)	ref			
	Ever	16/41 (39%)	0.58 (0.28-1.24)	0.163	1.04 (0.40-2.66)	0.941
Anti-dsDNA	Normal	16/27 (59%)	ref			
	High	53/116 (46%)	0.58 (0.25-1.35)	0.207	0.38 (0.13-1.16)	0.089
C3	Normal	14/21 (67%)	ref			
	Low	55/122 (45%)	0.41 (0.16-1.09)	0.073	0.52 (0.16-1.73)	0.287
CNI as induction	No	64/137 (47%)	ref			
	Yes	5/6 (83%)	5.70 (0.65-50.11)	0.116	7.50 (0.80-70.72)	0.078

C3=Complement 3; CNI=Calcineurin inhibitors; LLDAS=Lupus low disease activity state; LN=Lupus nephritis; RNP=Ribonucleoprotein; SLE=Systemic lupus erythematosus; Sm=Smith. Significant *p* values are in bold.

Figure 1. Kaplan-Meier Curve of LN relapse risk by CRR/PRR (left) and LLDAS (right)



CRR=Complete renal response; LLDAS=Lupus low disease activity state; NR=No response; PRR=Partial renal response.

Figure 1. Kaplan-Meier Curve of LN relapse risk by CRR/PRR (left) and LLDAS (right)CR-R=Complete renal response; LLDAS=Lupus low disease activity state; NR=No response; PRR=Partial renal response.

Conclusion: Age of LN and anti-smith autoantibodies are predictors of LLDAS 12 months post-LN. We advocate LLDAS as a target for LN patients as LLDAS attainment lowers the risk of future relapse.

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Disclosure of Interests: None Declared.

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POS1483 IS EARLY REMISSION A PREDICTIVE FACTOR FOR STEROID-FREE REMISSION IN SYSTEMIC LUPUS ERITHEMATOSUS? A REAL-LIFE EXPERIENCE FROM A MONOCENTRIC COHORT

Keywords: Remission, Real-world evidence, Systemic lupus erythematosus

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Background: Glucocorticoid (GC) dose minimization and, if possible, complete withdrawal is one of the main targets in the daily management of Systemic Lupus Erythematosus (SLE).

Objectives: to describe frequency and clinical characteristics of SLE patients in GC-free remission in a real-life setting and to identify predictive factors for achieving GC-free remission.

Methods: this is a retrospective analysis of prospectively collected data from a monocentric SLE cohort. The following variables were retrieved: demographic data, cumulative organ involvement; at last observation: disease activity (SLEDAI-2K score), ongoing therapy, disease state (remission defined according to the 2021 DORIS criteria) and organ damage (SDI score). Disease state at 1 year from disease onset was also recorded.

Results: from our cohort, a total of 390 SLE patients had at least 1 year of follow-up and complete clinical data to be included in the analysis; of these, 142 (36.4%) were in GC-free remission at the last evaluation, and 44 (11.3%) were GC-free for 5 years (Table 1). The mean follow-up duration was 10.5 years (min 1-max 41). No significant differences were found with regard to age at disease onset, disease duration and organ involvement between the GC-free remission group (GC-) and the other SLE patients under GC treatment (GC+). Patients GC- were less frequently taking immunosuppressants (IS) (28.9%, vs 43.5% p<0.01) or biological drugs (6.3% vs 20.2% p<0.01) and were more frequently under HCQ treatment (85.2% vs 75.8%, p=0.03) at last observation. Being GC- at last observation was associated with a significantly lower organ damage with respect to GC+ (mean SDI 0.7 vs 1.5, p<0.01); significant differences regarded cardiovascular (CV) events (4.9% vs 12.1%, p=0.01) and osteoporosis (OP) (12.7% vs 27.0%, p<0.01) were also found. Overall, 212 patients were in remission after 1 year from disease onset (78.2% in GC- and 57.2% in the GC+) and this condition resulted significantly associated with GC-free remission at last evaluation (p<0.01). At multivariate analysis, being in remission at 1 year resulted an independent predictor of GC-free remission (OR=2.06, p=0.02); the multivariate analysis also confirmed that GC- patients were less likely on IS or biological treatment at last evaluation (OR 0.46 p<0,01 and OR 0.20 p<0.01, respectively).

Conclusion: these data suggest that GC-free remission is an achievable goal in SLE patients with today's drugs, and in our cohort GC-free remission is also a IS-free remission in most of patients. Our study also confirms that GC withdrawal has important advantages in term of organ-damage sparing. Of note, the early achievement of remission during the disease history is associated with a good probability of GC withdrawal over time.

Table 1. characteristics of the cohort

	GC- N=142 (40.4%)	GC+ N=248 (59.6%)	P value
Female (%)	123 (86.6)	218 (87.9)	0.71
Age at disease onset, years[1]	28.7±11.8	29.8±12.2	0.44
Cumulative dose of GC, grams[1]	14.7±13.3	23.8±24.7	**<0.01**
Disease duration, years[1]	16.9±8.6	16.6±10.3	0.72
Remission after 1 year from disease onset (%)*	97 (78.2)	115 (57.2)	**<0.01**
Renal involvement (%)	61 (42.9)	114 (45.7)	0.55
Joint involvement (%)	100 (70.4)	190 (76.6)	0.06
Skin involvement (%)	82 (57.7)	162 (65.3)	0.11
Haematological involvement (%)	84 (59.1)	157 (63.3)	0.23
Serositis (%)	24 (16.9)	61 (24.5)	0.05
Neuropsychiatric involvement (%)	10 (7.0)	29 (11.7)	0.12
HCQ (%)	121 (85.2)	188 (75.8)	**0.03**
IS (%)	41 (28.9)	108 (43.5)	**<0.01**
Biologicals (%)	9 (6.3)	50 (20.2)	**<0.01**
SLICC-Damage Index[1]	0.7±1.1	1.5±2.0	**<0.01**
CV event (%)	7 (4.9)	30 (12.1)	**0.01**
OP (%)	18 (12.7)	67 (27.0)	**<0.01**

[1] Mean±standard deviation; *Data on 325 patients

REFERENCES: NIL.

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POS1484 SELF-ESTEEM AS A DETERMINANT OF SEXUAL FUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

Keywords: Gender/diversity issues, Pregnancy and reproduction, Systemic lupus erythematosus

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Background: Patients with rheumatic diseases, particularly systemic lupus erythematosus (SLE), present with greater sexual dysfunction (SxD) than patients with other chronic diseases. SxD is multifactorial and may be linked to both disease-related and psychological factors, as well as hormonal imbalance and drug treatment. Self-image and self-esteem, which have not been thoroughly studied in SLE patients, may be related to sexual interest and thereby may also affect sexual function.
Objectives: We addressed the association between body self-esteem, global self-worth and sexual functioning in SLE patients.
Methods: We performed a transversal study in a tertiary care center in Mexico City. Patients ≥18 years old who fulfilled EULAR/ACR criteria for SLE were included. Body self-esteem was assessed by the Body Self-esteem Scale (BSES) and global self-esteem by the Rosenberg´s Self-Esteem Scale (RSES). Sexual function was evaluated by the CSFQ-14 questionnaire. Disease activity and damage was assessed by the SLEDAI and SLICC scores, respectively. Relevant demographic, clinical and serological characteristics were recorded. We used univariate and multivariate analysis to determine association between variables. Statistical analysis was performed using SPSS (V.25).
Results: We included a total of 343 patients, in whom self-esteem was analyzed. SxD was assessed in 280 patients, since 62 did not complete the CSFQ-14 questionnaire. Most patients were female (87%), the mean age was 41 years (±12) and mean BMI was 25.65 kg/m^2 (±4.9). The mean SLEDAI and SLICC scores were 2.45 (±2.72) and 0.8 points (±1.04), respectively. The mean score for the RSES was 32.09 (± 5.84) in females and 33.57 (± 4.97) in males. The BSES was 189.5 (±47.3) in females and 207.1 (±36.6) in males. There was no association between these scores and prednisone dosage, BMI, or SLEDAI and SLICC scores. We found that SxD is associated with lower global self-esteem (*p<0.0001*) and lower body self-esteem (*p<0.0001*), according to their respective scores (see Table 1). Also, a correlation between both self-esteem questionnaires (BSES and RSES) and CSFQ-14 scores was found. Interestingly, the correlation was higher in the male population (r=0.45, *p=0.008* and r=0.47 p=*0.006* for BSES and RSES, respectively) than in women (r=0.25, *p=0.0001* and r=0.18 *p=0.004*) in both scores. The multivariate analysis showed that age (*p=0.003*, 0.96 [0.94-0.98 95% CI]) and lower global self-esteem (*p=0.013*, 1.080 [1-1.14 95% CI]) were independent risk factors for SxD. We observed a trend related to lower body self-esteem scores (p=0.055, 1.007 [1-1.15 95% CI]) as a risk factor. Other variables, such as prednisone, major depressive disorder and BMI did not show an association with SxD (see Table 1).
Conclusion: To our knowledge, this is the first study to demonstrate a reliable association between self-esteem and SxD in SLE patients, particularly in male patients. Considering the high impact of both self-esteem and sexual function on quality of life, our findings reinforce the importance of routinely acknowledging the biopsychosocial aspects (and not only the disease-related ones) in the medical care of these patients.

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Table 1. Differences between patients with and without sexual dysfunction

Variables	SxD Mean ± SD	No SxD Mean ± SD	Comparison (*p* value)
BMI (kg/m^2)	25.2 ± 4.6	26.1 ± 5.5	0.16
SLEDAI score (points)	2.4 ± 2.7	2.3 ± 2.5	0.71
SLICC-DI score (points)	0.8 ± 1.0	0.6 ± 0.9	0.09
C3 levels (mg/dL)	111.6 ± 30.3	117.1 ± 32.8	0.19
C4 levels (mg/dL)	22.1 ± 10.3	20.7 ± 10.9	0.34
anti-dsDNA antibodies (IU/mL)	151.1 ± 732.4	36.1 ± 63.5	0.16
Prednisone dose (mg)	4.6 ± 8.7	3.8 ± 6.1	0.42
Body Attractive (points)	37.2 ± 13.8	46.8 ± 8.6	**<0.0001**
Body Satisfaction (points)	151.2 ± 35.7	162.7 ± 29.1	**<0.006**
BSES (points)	188.4 ± 44.9	207.9 ± 40.1	**<0.0001**
RSES (points)	31.6 ±5.0	34.4±6.4	**<0.0001**

*Values shown in bold represent statistically significant *p* values.

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POS1485 SEMIQUANTITATIVE ASSESSMENT OF SYNOVIAL INFLAMMATION ON US-GUIDED SYNOVIAL TISSUE BIOPSIES OF SYSTEMIC LUPUS ERYTHEMATOSUS COMPARED TO OTHER CONNECTIVE TISSUE DISEASES AND RHEUMATOID ARTHRITIS

Keywords: Systemic lupus erythematosus, Synovium

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Background: Systemic Lupus Erythematosus patients might experience the development of arthritis clinically resembling other forms of chronic joint inflammation. However, to date, no systematic analysis of the histological composition of synovitis was performed in SLE patients.
Objectives: To dissect the inflammation degree and the histological composition of synovial tissue of SLE patients compared with other Connective Tissue Disorders (CTD) and naive to treatment Rheumatoid Arthritis (RA).
Methods: Seventy-five patients with connective tissue diseases [n=30 SLE, n=13 Sjogren Syndrome (SS), n=19 Undifferentiated Connective Tissue Disease (UCTD), n=13 other CTD] were included in the study. Thirty-four naive to treatment RA patients were included as comparison. Each patient underwent ultrasound-guided minimally invasive synovial tissue biopsy at the study entry. Each synovial tissue sample was processed for H&E staining for the Krenn Synovitis Score (KSS) assessment by a pathologist blinded to clinical characteristics [1]. This evaluation was implemented with the additional assessment of lymphocytes and plasmacells presence, and with the assessment of the microanatomical organization in terms of inflammatory aggregates presence.
Results: Considering the whole cohort, SLE patients showed comparable synovial inflammation in terms of KSS compared to SS and other CTD (p>0.05 for both). However, synovial tissue of SLE patients showed significantly milder inflammation when compared to naive to treatment RA (p=0.002) and more severe compared to UCTD (p=0.009), mainly in terms of inflammatory infiltrate (p=0.015). Moreover, among SLE cohort, patients with Rhupus showed higher KSS compared to SS (p=0.03), mainly for synovial hyperplasia (p=0.016) and comparable synovial inflammation than naive to treatment RA (p>0.05). Considering the composition of the inflammatory infiltrate, synovial tissue of SLE patients was enriched of lymphocytes compared to synovial tissue of SS (p=0.0028), UCTD (p=0.014) and other CTD (p=0.018), similarly than synovial tissue of naive to treatment RA (p>0.05). Moreover, SLE patients showed, at synovial tissue level, higher rate of plasmacells compared to SS (p=0.038) despite significantly lower than naive to treatment RA (p=0.007). Interestingly, among the whole SLE cohort, synovial tissue of Rhupus patients was enriched of plasmacells compared to synovial tissue of SLE patients (p=0.04). Finally, considering the microanatomical organization of synovial inflammation, SLE patients showed lower rate of synovial aggregates compared to naive to treatment RA (p=0.03), the latter having similar aggregate rate compared to Rhupus patients (p=0.23).
Conclusion: Synovitis in SLE patients, despite milder than in naive to treatment RA, is characterized by more severe features compared to other CTD. In particular, Rhupus patients show a degree of synovial inflammation in terms of KSS and microanatomical organization comparable to naive to treatment RA, supporting the need to dissect pathogenetic pathways driving this clinical phenotype.
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[1] Alivernini S, et al. Arthritis & Rheumatology 2021
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POS1486 RELATIONSHIP BETWEEN THE EULAR/ACR CLASSIFICATION CRITERIA AND ORGAN DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Organ damage, Systemic lupus erythematosus

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Background:
Objectives: To study the relationship between the 2019 EULAR/ACR classification criteria and organ damage in patients with systemic lupus erythematosus (SLE)
Methods: Patients involved in a cross-sectional validation study of the EULAR/ACR criteria and judged by a panel of rheumatologists to be clinical SLE were studied. Those who fulfilled the EULAR/ACR criteria at their last clinic visit were stratified into 2 groups based on a cut-off score of 20. The last SLE international collaborating clinic (SLICC) organ damage index (SDI) was compared between these two groups. Relationship among the domains of the EULAR/ACR criteria and SDI in all patients was studied by Spearman's rank correlation.
Results: 562 SLE patients were studied (93.6% women; age 36.5±14.1 years; follow-up duration 11.6±6.6 years). The mean and median EULAR/ACR criteria scores in those who fulfilled the EULAR/ACR criteria (N=542) was 24.6±7.3 and 24 (interquartile range 19-30), respectively. A total of 392 patients had EULAR/ACR scores of ≥20 (group 1) and 150 patients had scores of 10-19 (group 2). Group 1 patients had significantly higher prevalence of fever, alopecia, oral ulcers, acute lupus skin lesions, arthritis, serositis, seizure, hemolytic anemia, leukopenia and renal disease, and so were the anti-dsDNA, anti-Sm, antiphospholipid antibodies and low complement state. Organ damage (SDI score of ≥1) occurred in 232 (42.8%) patients. Patients in group 1 had significantly higher SDI scores in the renal, cardiovascular, dermatological and gonadal domains than group 2. The renal, neuropsychiatric and antiphospholipid antibodies domain scores of the EULAR/ACR criteria correlated positively with the total SDI. The renal domain of the EULAR/ACR criteria had the strongest correlation with renal damage (Rho 0.30; p<0.001). Patients who scored 10 points in the renal domain had significantly higher renal damage score than those scored 8 points or 4 points. Gonadal damage score was also significantly more common in the 10-point than 8-point group.
Conclusion: In addition to disease classification, the EULAR/ACR SLE criteria may have a role in predicting organ damage and disease prognosis.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1487 CLINICAL SIGNIFICANCE OF DIFFERENT PROFILES OF ANTI-RO ANTIBODIES IN CONNECTIVE TISSUE DISEASES

Keywords: Autoantibodies, Clinical trials, Organ damage

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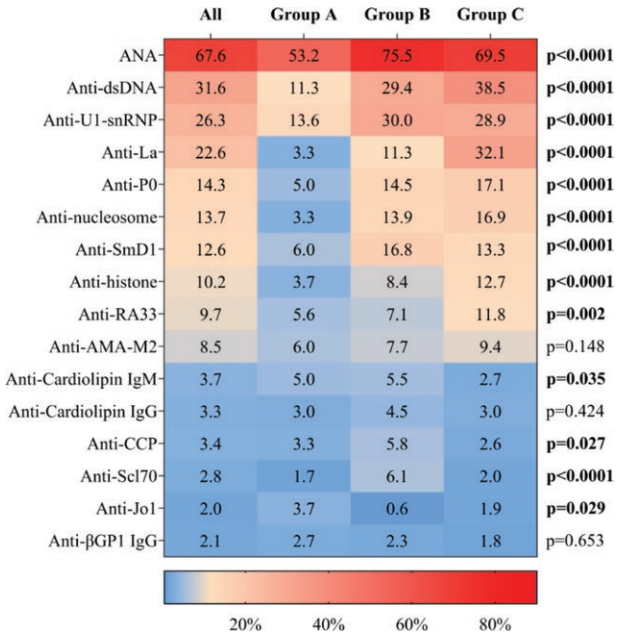


Figure 1 Comparison of autoantibody profiles in patients with positive anti-Ro antibodies

Background: Anti-Ro60 and anti-Ro52 antibodies are associated with different connective tissue diseases (CTDs) [1]. However, the clinical significance of anti-Ro antibodies is not always consistent among different global regions.
Objectives: To investigate the clinical characteristics of patients with anti-Ro antibodies.
Methods: A total of 1596 inpatients with anti-Ro antibodies were included in the study. Demographic, clinical, and serological data were compared between individuals with different profiles of anti-Ro antibodies: patients with anti-Ro52 antibodies alone, patients with anti-Ro60 antibodies alone, and patients with combined anti-Ro52 and anti-Ro60 antibodies.
Results: Of the 1596 patients, 1362 (85.3%) were female, the mean age was 45.5 years, and systemic lupus erythematosus (SLE) (46.0%) and Sjogren's syndrome (SS) (19.0%) were the most common CTD diagnoses. Among the patients with anti-Ro52 antibodies alone, idiopathic inflammatory myopathy (18.8%) and SLE (17.6%) were the most common CTD diagnoses. The coexistent autoantibodies of this group were significantly lower compared with those of the other two groups, while the presence of anti-Jo1 antibodies were significantly higher compared with those of the other two groups (3.7% vs. 0.6% vs. 1.9%, p=0.029) (**Figure 1**). In addition, the patients with isolated anti-Ro52 antibodies were more likely to suffer from interstitial lung disease (35.5% vs.11.3% vs.13.7%, p<0.0001) and pulmonary arterial hypertension (10.1% vs. 5.3% vs. 3.6%, p=0.001) compared with the other two groups of patients (**Table 1**). Compared with patients with isolated anti-Ro52 or anti-Ro60 antibodies, the patients with combined anti-Ro52 and anti-Ro60 antibodies were more likely to suffer from xerophthalmia and xerostomia. Furthermore, hypocomplementemia, hyperglobulinemia, and proteinuria were particularly prevalent in patients with anti-Ro60 antibodies.
Conclusion: Different profiles of anti-Ro antibodies were significantly associated with clinical phenotypic features in CTDs, indicating the potential diagnostic and prognostic value of these antibodies in clinical practice.
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TABLE 1 Comparison of clinical features in patients with connective tissue diseases

Parameters (n, %)	Groups				p values			
	All: n=1319	Group A: Ro52 alone n=169	Group B: Ro60 alone n=283	Group C: Ro60 and Ro52 n=867	Group A vs. group B	Group A vs. group C	Group B vs. group C	Overall
Skin rash	349(26.5)	40(23.7)	101(35.7)	208(24.0)	**0.008**	0.928	**< 0.0001**	**< 0.0001**
Arthralgia	512(38.8)	72(42.6)	164(58.0)	276(31.8)	**0.002**	**0.007**	**< 0.0001**	**< 0.0001**
Myalgia	80(6.1)	16(9.5)	26(9.2)	38(4.4)	0.921	**0.007**	**0.002**	**0.002**
Xerophthalmia	277(21.0)	31(18.3)	39(13.8)	207(23.9)	0.160	0.118	**< 0.0001**	**0.001**
Xerostomia	310(23.5)	34(20.1)	47(16.6)	229(26.4)	0.346	0.085	**0.001**	**0.002**
Anemia	375(28.4)	39(23.1)	78(27.6)	258(29.8)	0.292	**0.079**	0.481	0.198
Leukocytopenia	295(22.4)	28(16.6)	61(21.6)	206(23.8)	0.197	**0.041**	0.446	0.114
Thrombocytopenia	128(9.7)	11(6.5)	27(9.5)	90(10.4)	0.261	0.121	0.685	0.297
Proteinuria	208(15.8)	10(5.9)	53(18.7)	145(16.7)	**< 0.0001**	**< 0.0001**	0.438	**0.001**
Hematuria	99(7.5)	3(1.8)	29(10.2)	67(7.7)	**0.001**	**0.005**	0.183	**0.004**
ILD	211(16.0)	60(35.5)	32(11.3)	119(13.7)	**< 0.0001**	**< 0.0001**	0.296	**< 0.0001**
PAH	63(4.8)	17(10.1)	15(5.3)	31(3.6)	0.056	**< 0.0001**	0.199	**0.001**
RP	88(6.7)	18(10.7)	22(7.8)	48(5.5)	0.297	**0.013**	0.172	**0.036**

ILD: interstitial lung disease; PAH: pulmonary arterial hypertension; RP: Raynaud's phenomenon

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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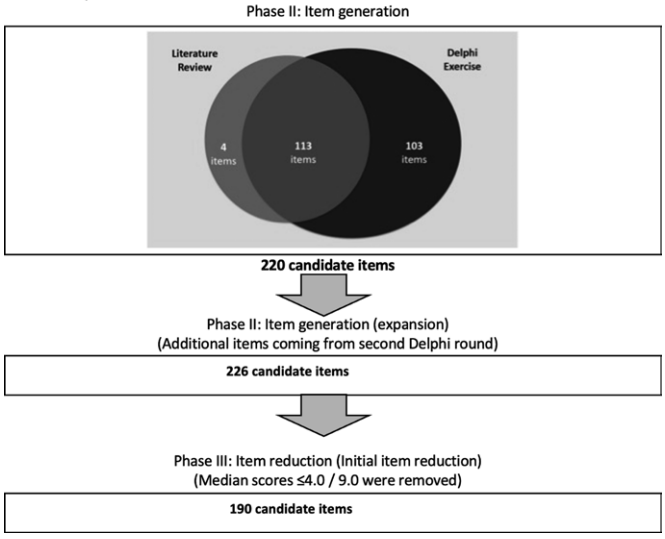
POS1488 **LUPUS DAMAGE INDEX REVISION – INITIAL ITEM REDUCTION PHASE**

Keywords: Organ damage, Systemic lupus erythematosus

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Background: An international initiative is underway to develop a revised systemic lupus erythematosus (SLE) organ damage index (SDI) using a multi-phase process that is supported by the SLE International Collaborating Clinics (SLICC), American College of Rheumatology (ACR) and Lupus Foundation of America (LFA). The first two phases (evaluating the construct of damage and item generation through literature review and an international Delphi exercise) were previously reported [1,2], and 220 candidate items were generated.
Objectives: To report the initial reduction phase results of a five-phase process for developing a revised SDI.
Methods: An international two-part Delphi exercise asked SLE experts and patients to rate 220 items for how appropriate they were for inclusion in a revised SDI on a 9-point Likert scale (where 1 = not at all appropriate and 9 = completely appropriate) considering the new construct of damage in SLE [1]. The definitions of items in plain English were provided for the patient representatives. In the first part of the item reduction Delphi round, participants were asked to suggest any additional items. In the subsequent Delphi round, participants were presented their own rating, median scores and 25th-75th percentiles for each item. They were given the opportunity to revise their rating. Items with ratings less than or equal to 4.0/ 9.0 were considered for removal.
Results: A total of 143 out of 146 participants who completed the first round Delphi for the item generation were invited for the item reduction rounds. Completion rates for the second and third Delphi rounds for the item reduction were 95% and 91.7% respectively. Appropriateness rating scores included the full range of scoring possibilities from 1 to 9. Participants suggested 53 potentially new items, however only 6 were retained, as others were duplicates or invalid.
226 items were presented to re-rate for appropriateness. There was stability in terms of summary median scores and 25th-75th percentiles for each item. Thirty-six items had a median score of less than or equal to 4. Figure 1 shows the number of candidate items identified at different stages of the project. All original SDI items were retained with group median appropriateness scores of 7, 8 and 9; the exceptions were upper gastrointestinal tract surgery (median appropriateness score 5) and osteomyelitis (median appropriateness score 5).

Figure 1. Number of candidate items identified at different stages of Phase II/III during revised SDI development



Conclusion: The item reduction phase using Delphi methods reduced the candidate items for consideration. All original 1996 SDI [3] items were retained in this step. Further steps are now underway to refine and rationalize this candidate list.

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POS1489 **WITHDRAWN**

POS1490 **ANTI-RO/SSA-ANTIBODIES AND ELECTROCARDIOGRAPHIC ABNORMALITIES IN PATIENTS WITH SYSTEMIC LUPUS ERYHEMATOSUS (SLE): DATA OF A MULTIDISCIPLINARY STUDY IN A MONOCENTRIC COHORT**

Keywords: Cardiovascular disease, Biomarkers, Systemic lupus erythematosus

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Background: Cardiovascular involvement is common in patients with SLE and heart rhythm disorders are frequent in addition to the manifestations included in the classification criteria ACR/EULAR 2019. Previous studies provided evidence that anti-Ro/SSA-positivity is an independent risk factor for marked QTc prolongation; suggesting that subjects who are anti-Ro/SSA-positive may represent a subgroup with an increased predisposition to ventricular arrhythmias, particularly when other QT-prolonging risk factors are concomitantly present [1].

Objectives: The aim of this study is to estimate the prevalence of QTc-prolongation in a monocentric cohort and to evaluate possible correlation with the presence of anti-Ro/SSA-antibodies and other QT-prolonging risk factors.

Methods: An electrocardiographic study (ECG) was proposed to patients affected by SLE consecutively attending our Lupus Clinic from November 2021 to March 2022. All subjects were tested for anti-Ro/SSA-antibodies. Exclusion criteria included: severe valvulopathies, hypertrophic or dilated cardiomyopathy, previous implantation of pacemaker or implantable cardioverter-defibrillator.
QTc measurement was calculated using the Bazett's formula and QTc-prolongation was defined according to American College of Cardiology (ACC)/American Heart Association (AHA) recommendations (QTc>470 ms for males, QTc>480 ms for females) [2]. Data on 24-hour ECG holter were available in 26 patients.
Results: One hundred and forty-one patients with SLE, consecutively attending our clinic, accepted to undergo an ECG, 128 (91%) females, 13 (9%) males; 124 (88%) Caucasians (median age 53.2 [IQR 42.3-58.7], median disease duration 20.0 years [12.0-28.2]). Median QTc was 415ms [IQR 394-436]; only 4/141 (2.8%), all Caucasian and female, had a prolonged QTc (Table 1).

Table 1 Features of patients with prolonged QTc

	age	Anti-Ro/SSA	QTc	Cardiological history	HCQ therapy
1	56	Positive	492 ms	none	yes
2	57	Negative	488 ms	HT, D	no
3	60	Positive	480 ms	HT	yes
4	63	Positive	508 ms	D	no

HT: hypertension, D: dyslipidaemia

Sixty-eight (48%) patients were positive for anti-Ro/SSA-antibodies. No significant differences were observed between anti-Ro/SSA-positive vs. negative patients in term of QTc intervals (416.0 [395-437] ms vs 413.0 [392-432] ms; p=0.545) using Mann-Withney Test. Other electrocardiographic alterations were found: 4 first-degree atrioventricular blocks, 25 bundle branch blocks (BBB), 31 repolarization anomalies, 1 Wolff-Parkinson-White. Patients were grouped according to hydroxychloroquine (HCQ) therapy and antibody profile into 4 groups: HCQ+/Ro/SSA+(56, 39.7%), HCQ+/Ro/SSA-(58, 41.1%), HCQ-/Ro/SSA+ (12, 8.5%) and HCQ-/Ro/SSA- (15,106%); no statistical differences (p=0.178) were observed in QTc length comparing the 4 groups using ANOVA test. Twenty-six (18.4%) underwent a 24-hour ECG holter evaluation. None of these patients had a QTc prolongation, and no major elettrocardiographic anomalies were found. These patients were divided in 4 groups (as previously done for all patients). No statistical differences were found comparing the QTc of groups of patients (p=0.783).
Conclusion: These preliminary data show a lower prevalence of QTc prolongation compared to previous studies, with no differences between anti-Ro/SSA-positive and anti-Ro/SSA-negative patients. Otherwise, considering previous studies which observed a role of anti-Ro/SSA antibodies as an independent risk factor for QTc prolongation, further analysis will be performed in order to identify standardized markers for cardiovascular risk stratification. The evaluation of 24-hour ECG Holter in a larger number of patients and the characterization of anti-Ro/SSA (anti-Ro/SSA-52kD and anti-Ro/SSA-60kD) are ongoing.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1492

FIBROMYALGIA AND GLUCOCORTICOIDS USE DRIVES SELF-PERCEIVED DEPRESSION IN SYSTEMIC LUPUS ERYTHEMATOSUS: INSIGHTS FROM A LARGE PROSPECTIVE AND MULTICENTER STUDY USING RELESSER-PROS REGISTER'S DATABASE

Keywords: Systemic lupus erythematosus

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Background: The prevalence of depression and associated factors in systemic lupus erythematosus (SLE) are not well known and there are no longitudinal studies addressing this relevant subject in SLE.
Objectives: We aimed to evaluate the prevalence of self-perceived depression in patients with SLE and associated factors in a large, multicenter cohort (RELESSER-PROS).
Methods: Prospective longitudinal study of patients with SLE (1997 ACR criteria) answering positively to the depression question of the Lupus Impact Tracker (LIT) questionary (namely: "I was depressed" question number 7) (LITQ7), over 4 years of follow-up (5 annual visits, V1 to V5). Self-perceived depression was addressed as "depression any time" or "depression most of time", according to the kind of answer to the LITQ7 (answers 1,2,3 or 4 and answers 3 or 4 respectively). Only patients with no missing values in the covariates, making possible run longitudinal models, were included in the multivariable analysis. The following covariates, with potential impact in depression, were considered: SLEDAI, age,

duration of the disease, SLICC/AR DI (SDI), fibromyalgia, Charlson index, smoking, BMI, menopause, sedentary lifestyle, marital status, unemployment and glucocorticoid use. Friedman test was used to test if the change in repeated measures was significative. Generalized estimating equation (GEE) models with binomial response, were built exploring the associations of individual longitudinal determinants with longitudinal assessment of depression. The best model was selected using quasi-likelihood under the independence model information criterion (QIC)

Results: A total of 1463 were included. Mean age: 55 (DS±13.59) years, 90% were female. Mean duration of the disease: 14 (±8.59) years. Fibromyalgia was present in 5.7% (76/1343). Corticosteroids use ranged from 49.4% to 57%, depending on the visit. Median SLEDAI ranged from 0 to 2 and SDI ranged from 1 to 2. Prevalence of "depression any time" was 89.9% (1104/1228) and 34.6% (200/578) were in depression "most of time". Up to 26.5% (153/578) answered to LITQ7 "depression most of time" in the five visits; 89.7% of the patients which perceived themselves as depressed at least in 2 out of 5 visits. Only 6.9% of the patients with previous diagnosis of depression answered "0" to the Q7 of LIT ("none of the time"). Only following covariates showed changes, statistically significative, during the follow up: SLEDAI, SDI, Charlson and glucocorticoids use (Friedman test). Patients with "depression any time" develop more damage at V5 than patients without depression (answer to LITQ7=0) (p = 0.00931, T-test). In the GEE binomial analysis considering all the predefined covariates, that included only patients with no missing values for any of them (namely, 155 patients), fibromyalgia (OR 2.79; 95%CI: 1.28-6.05), unemployment (OR 1.95; 95%CI 1.02 -3.73), and glucocorticoids use (OR 1.88; 95%CI 1.18-2.99) were significant associated with "depression any time". The best model (according QIC) displayed a statistically significant association only with fibromyalgia (OR 2.90; 95%CI: 1.58-5.33) and glucocorticoids use (OR 1.85; 95%CI 1.17-2.93). Neither SDI nor unemployment reached significance here (Table 1). Without entering glucocorticoids, SLEDAI turns significant in the model, suggesting collinearity.

Conclusion: The prevalence of self-perceived depression is high in SLE. Longitudinal data analysis suggests a causal relationship between glucocorticoids use, fibromyalgia and self-perceived depression.

Table 1. best multivariable GEE model

	OR	Lower limit	Upper limit
(Intercept)	0,121	0,028	0,529
SLEDAI	1,066	0,991	1,147
SLICC/ACR DI	1,138	0,962	1,346
Age	1,022	0,994	1,051
Fibromyalgia	2,898	1,576	5,328
BMI	1,485	0,685	3,219
Unemployment	1,86	0,972	3,56
Low incomes	1,726	0,89	3,347
Glucocorticoids use	1,853	1,173	2,928
Single marital status	1,292	0,766	2,179

QICC: 1006.75SLICC/ACR DI: SLICC/ACR damage index; BMI: body mass index

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POS1493 GLOMERULAR INVOLVEMENT IN ANTIPHOSPHOLIPID SYNDROME

Keywords: Anti-phospholipid syndrome, Vasculitis, Kidneys

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Background: Antiphospholipid syndrome (APS) is a complex autoimmune systemic disease, characterized by the presence of circulating antibodies directed against anionic phospholipids and the protein bound to them (aPL), leading to recurrent thrombosis and/or obstetrical complications. Renal manifestation of antiphospholipid syndrome conform a wide spectrum of disease renal syndrome [1, 2]. APS nephropathy (APSN) is considered a renal small-vessels vasculopathy, that can present acutely or chronically.

Objectives: The aim of the study is to identify glomerular lesions in patients with APSN.

Methods: We studied retrospectively 114 patients (51 male, 63 female; age between 19 and 58 years; duration of follow-up was between 2 and 16 years) fulfilling classification criteria for APS. Renal and extra-renal symptoms were analyzed. None of the patients developed SLE in follow up. 18 patients with evidence of renal involvement underwent renal biopsy. All cases had proteinuria and five of them presented nephrotic syndrome.

Results: Of 18 patients with kidney biopsy, 8 (44,44 %) were male and 10 (55,56 %) - female. Four of patients with renal biopsy had membranous glomerulonephritis, two had diffuse proliferative glomerulonephritis, 2 - mesangial C3 nephropathy, 2 - minimal change disease, 1- focal segmental glomerulosclerosis, the other seven had classic pathologic findings consistent with APSN. Chronic lesions with fibrous intimal hyperplasia being the most common. Thrombotic microangiopathy (TMA) in glomeruli was characterized by fibrin thrombi without inflammatory cells or immune complexes. Double contour of the glomerular basement membrane was associated with mesangiolysis and endothelial cell swelling in 5 patients with APSN. Electron microscopy confirmed subendothelial edema. Segmental glomerulosclerosis was observed in 4 patients. Tubulointerstitium was injured with interstitial fibrosis and tubular atrophy. Patients with APS and renal involvement were older (p<0,05), had LA positive test (p<0,005) and low complement levels (p<0,05). Hypertension is present in all cases with APSN, reduced glomerular filtration rate – in 4. All cases had proteinuria and five of them presented with nephrotic syndrome. Microscopic hematuria is observed in 4 patients. The treatment of APSN includes standard anticoagulant treatment for APS, inhibitors of the angiotensin system in patients with hypertension and proteinuria, steroids, intravenous immunoglobulin, cyclophosphamide and azathioprine.

Conclusion: The occurrence of kidney abnormalities including hypertension, proteinuria, or increased serum creatinine levels in patients with APS should lead to a kidney biopsy. Renal pathology revealed that some findings including arterioles obstructed by thrombi and organized components, diffuse collapsed glomeruli and no tubulitis suggested that the extensive tubulointerstitial damage was caused by chronic ischemic changes due to vascular occlusion upstream to the glomeruli. Other findings including mesangiolysis with endothelial cell swelling and arterioles obstructed by non-organized fibrin thrombi indicated that acute TMA was superimposed by chronic TMA.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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SLE, Sjön's and APS - clinical aspects (other than treatment)

POS1494 HOSPITALIZATIONS DUE TO INFECTIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS: CAUSES AND ASSOCIATED FACTORS

Keywords: Systemic lupus erythematosus, Infection-related RMDs

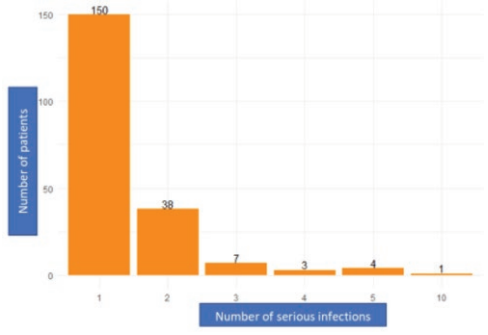
L. Garcia[1], R. Quintana[1], C. Gobbi[1], P. Alba[1], S. Roverano[1], A. Alvarez[1], C. Graf[1], C. Pisoni[1], A. Spindler[1], C. Gomez[1], H. M. Figueredo[1], S. Papasidero[1], R. H. Paniego[1], M. De la Vega[1], E. E. Civit De Garignani[1], L. Gonzalez Lucero[1], V. Martire[1], R. Águila Maldonado[1], S. A. Gordon Dolimpio[1], M. L. Micelli[1], R. Nieto[1], G. Rausch[1], V. Góngora[1], M. A. D'amico[1], D. Dubinsky[1], A. O. Orden[1], J. Zacariaz[1], J. Romero[1], M. A. Pera[1], M. A. Goñi[1], O. Rillo[1], R. Baez[1], V. Arturi[1], A. Gonzalez[1], F. Vivero[1], M. E. Bedoya[1], M. Schmid[1], V. Caputo[1], M. S. Larroude[1], N. Dominguez[1], B. Pons-Estel[1], G. Pons-Estel[1], V. I. Bellomio[1], M. García[1]. [1]*GESAR LES, Rheumatology, Buenos Aires, Argentina*

Background: The pathophysiology of Systemic Lupus Erythematosus (SLE) involves genetic and acquired immune dysregulation, both of which predispose patients to infection. Infections are a leading cause of hospital admission, intensive care unit admission and death.

Objectives: To evaluate the frequency and associated factors of hospitalizations due to infections in patients with SLE.

Methods: Cross-sectional study carried out with the RELESSAR trans registry. Patients with SLE (ACR 1997 criteria) were included. Sociodemographic variables, autoantibodies, manifestations of the disease, comorbidities and activity and chronicity index were analyzed. A serious infection was defined as one that required hospitalization. We evaluated number and localization of the infections, microorganisms and treatments received during the admissions and these variables were compared between patients hospitalized versus not hospitalized.

Results: A total of 1515 patients participated in the registry and 815 patients had been admitted: 41 cases were hospitalized due to infection exclusively and 162 patients of both infection and flare of the disease (total=203). The mean time of admissions was 1.42 (SD 0.99). Graphic 1 shows the number of serious infections per patient. The most frequent localization was the respiratory tract and bacterial were the most frequently microorganism isolated. We compared 203 patients and 646 patients not hospitalized (Table 1). In multivariate analysis, age at SLE diagnosis (OR 0.96 95%CI 0.94-0.98, p< 0.001), level of education (OR 0.89 95%CI 0.83-0.94, p< 0.001), pericarditis (OR 3.25 95%CI 1.89-5.60, p< 0.001), low complement (OR 3.16 95%CI 1.33-8.10, p=0.010), SLICC index (OR 1.95 95%CI 1.61-2.37, p< 0.001) and 10-30 mg/d of prednisone (OR 3.70 95%CI 1.66-9.00, p=0.002), 30-60 mg/day of prednisone (OR 8.40 95%CI 3.58-21.5, p< 0.001), azathioprine (OR 1.67 95%CI 1.02-2.73, p= 0.042), mycophenolate (OR 2.15 95%CI 1.27-3.67, p=0.005) and Igiv (OR 8.25 95%CI 2.33-39.3, p=0.003) were variables independently associated to hospitalization due to infection.



Graphic 1. Number of serious infections per patient.

Conclusion: Almost 25% of patients presented at least one hospitalization due to infection, being the respiratory infections the most frequent. Lower age al diagnosis, lower educational level, higher damage score, low complement, pericarditis, high esteroids doses and immunosuppressant increased the chance of having an admission due to serious infection. As well as the treatment with Igiv, an association that we can only explain by the reason that we only indicate it in severely active and infected patients.

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Table 1. Comparation between hospitalizated due to infections and non hospitalizated patients of RELESSAR-T registry.

	Hospitalization due to infection (N=203)	Non hospitalization (N=646)	Total (N=849)	P-value
Age at SLE diagnosis Median [Q1, Q3]	25.4 [18.9, 34.6]	30.6 [23.0, 40.7]	29.1 [21.9, 39.2]	<0.001
Years of education Mean (SD)	10.9 (3.76)	12.7 (3.95)	12.3 (3.98)	<0.001
Pericarditis	76 (37.6%)	68 (10.6%)	144 (17.1%)	<0.001
Lupus Nephritis	121 (59.6%)	160 (25.0%)	281 (33.3%)	<0.001
Convulsion	23 (11.3%)	22 (3.45%)	45 (5.36%)	<0.001
Anti-DNA	160 (78.8%)	370 (58.4%)	530 (63.3%)	<0.001
Low complement	136 (68.0%)	333 (53.7%)	469 (57.2%)	<0.001
Charlson index Median [Q1, Q3]	2.00 [1.00, 3.00]	1.00 [1.00, 3.00]	1.00 [1.00, 3.00]	<0.001
SLICC index Median [Q1, Q3]	1.00 [1.00, 3.00]	0 [0, 1.00]	1.00 [0, 1.00]	<0.001
SLEDAI Median [Q1, Q3]	2.00 [0, 5.00]	2.00 [0, 4.00]	2.00 [0, 4.00]	0.073
10-30 mg/day	89 (47.8%)	131 (25.0%)	220 (30.9%)	<0.001
>30-60 mg/day	67 (36.0%)	50 (9.52%)	117 (16.5%)	<0.001
Azathioprine	100 (51.8%)	149 (25.1%)	249 (31.7%)	<0.001
Cyclophosphamide	105 (54.4%)	90 (15.2%)	195 (24.8%)	<0.001
Mofetil Mycophenolate	79 (41.6%)	83 (14.0%)	162 (20.7%)	<0.001
Igiv	17 (8.90%)	3 (0.514%)	20 (2.58%)	<0.001

Acknowledgements: To Karen Roberts who did the statical analysis and the UNISAR for the support.

Disclosure of Interests: None Declared.

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POS1495 LOW INTENSITY OF C1Q DEPOSITION WITH RENAL IMMUNOFLUORESCENCE PREDICTS LONG-TERM POOR RENAL PROGNOSIS IN LUPUS NEPHRITIS

Keywords: Systemic lupus erythematosus, Prognostic factors, Kidneys

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Background: Although the prognosis of lupus nephritis (LN) has been improved due to recent advances in diagnosis and treatment, its long-term renal outcome is still poor. In spite of previous studies that investigated a number of prognostic factors, association of long-term renal outcome with renal histological findings focusing on immunofluorescence has been little elucidated.

Objectives: To clarify renal histological and immunofluorescent findings associated with deterioration of renal function in LN.

Methods: Consecutive patients with biopsy-proven LN class III/IV/V from 2008 to 2017 in our hospital were included in the study. They were classified into two groups: patients with deterioration of renal function and those without. The deterioration of renal function was defined as more than 30% decline in estimated glomerular filtration rate (eGFR) from baseline. Clinical characteristics and renal histological findings with immunofluorescence at the time of LN diagnosis were compared between the two groups.

Results: Sixty-nine patients (class III/IV 34; class III/IV+V 21; class V 14) were included in the analysis. Renal function was deteriorated during 5 years observation in 12 patient (17.4%). There was no significant difference in age (48 vs 42 years, p=0.16), disease duration (11.4 vs 9.8 years, p=0.65), and urinary protein-to-creatinine ratio (2.3 vs 2.2 g/gCr, p=0.56) between the deterioration and non-deterioration groups. The treatment regimens including maximum prednisolone dose (41 vs 47 mg/day, p=0.14), cyclophosphamide use (42 vs 54%, p=0.53) and mycophenolate mofetil use (0 vs 24%, p=0.11) were also not different. Regarding renal histopathological findings, while proportion of III/IV class (83 vs 79%, p=1.00), activity index (1 vs 4, p=0.14), and chronicity index (4 vs 3, p=0.19) were not different between the two groups, intensity of C1q deposition in renal immunofluorescence was significantly weaker in the deterioration group than the non-deterioration group; proportion of C1q deposition in renal immunofluorescence ≤ 1+ was 100% in the deterioration group compared to 47% in the non-deterioration group (p=0.006). When we divided the patients according to the intensity of C1q deposition, the cumulative deterioration rates of renal function were significantly different (p=0.01, Figure 1). The patients with low intensity of C1q deposition (≤ 1) had a lower positivity of serum anti-dsDNA antibody (75 vs 96%, p=0.04) and a higher serum C3 levels (54 vs 40 mg/dl, p=0.03) at LN diagnosis. Anti-SSA antibodies tended to be higher in the deterioration group than the non-deterioration group (80 vs 64%, p=0.43).

Figure

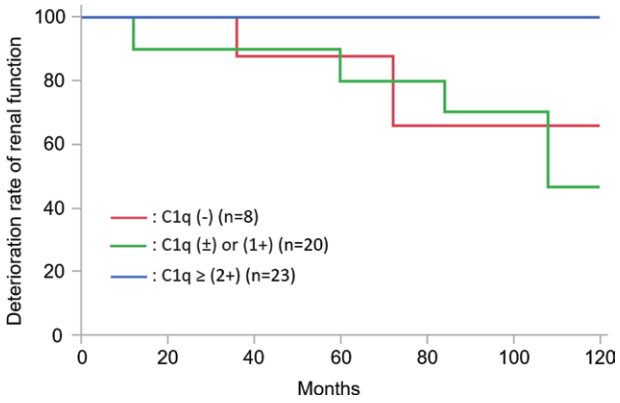


Figure 1.

Conclusion: Low C1q deposition in renal immunofluorescence at LN diagnosis is associated with poor renal prognosis in LN.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1496

THE AUTOANTIBODY FOR BETA-2-GLYCOPROTEIN I COMPLEXED WITH HLA-DR LINKED TO ARTERIAL THROMBOSIS IN FEMALE PATIENTS WITH SYSTEMIC RHEUMATIC DISEASES

Keywords: Autoantibodies, Cardiovascular disease, Anti-phospholipid syndrome

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Background: Beta-2-glycoprotein I complexed with HLA-DR molecules (β2GPI/HLA-DR) was found to be a major autoantibody target in APS.

Objectives: We aim to reveal the association between anti-β2GPI/HLA-DR antibodies and vascular thrombosis or obstetric morbidities in females with various systemic rheumatic diseases.

Methods: This was a single-center, retrospective longitudinal study of female patients in our center from 2020 to 2021. Clinical and laboratory data were retrieved from medical records and questionnaires. Anti-β2GPI/HLA-DR antibody was compared with the risk score reported as an adjusted global APS score (aGAPSS). The optimal cutoff value was calculated using receiver operating characteristic (ROC) analysis to detect arterial thrombosis. Finally, we assessed the impact of anti-β2GPI/HLA-DR antibodies on arterial thrombosis in addition to the conventional risk model with multivariable logistic regression analysis.

Results: We evaluated 704 patients, including 66 (obstetric or thrombotic) APS, 13 primary APS, and 78 asymptomatic aPL carriers, that comorbid 260 Systemic Lupus Erythematosus (SLE) or Mixed Connective tissue diseases (MCTD). Seventy-seven patients had one or more histories of arterial thrombosis, and 14 patients of them had a history of both arterial and venous thrombosis. The titers were significantly higher in patients with arterial and venous thrombosis than in those without thrombosis. In cases with aGAPSS>10 or triple positive aPL, the titers tended to be higher. The ROC showed that the sensitivity, specificity, and area under the curve (AUC) for arterial thrombosis were 33.8%, 91.4%, and 0.60 with a cutoff value of 172.359 U/ml. By the multivariable logistic regression analysis with multiple imputation, the odds ratio of anti-β2GPI/HLA-DR antibody ≧172.359 was 5.11(95% confidence interval: 2.84-9.19; P<0.001) (Table 1). When adding the cutoff value to conventional cardiovascular risk factors improved the AUC from 0.677 to 0.730 (p = 0.088). Determined net reclassification improvement and integrated discrimination improvement were statistically significant (Figure 1).

Conclusion: Anti-β2GPI/HLA-DR antibody is associated with arterial thrombosis in females with various systemic rheumatic diseases.

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Table 1. Univariable and Multivariable logistic regression analysis

	Univariate		Multivariate					
			Complete-cases (*n* = 409)				Multiple imputation (*n* = 704)	
			Conventional cardiovascular risk factors alone (model 1)		the addition of anti-β2GPI/HLA-DR antibody status (model 2)			
Variables	OR(95%CI)	p-value	OR(95%CI)	p-value	OR(95%CI)	p-value	OR(95%CI)	p-value
Age	1.02 (1.00-1.03)	0.050	1.02 (1.00-1.04)	0.043	1.03 (1.00-1.05)	0.027	1.01 (0.99-1.03)	0.059
Disease duration	1.01 (0.99-1.03)	0.341	1.00 (0.98-1.03)	0.790	1.00 (0.98-1.03)	0.850	1.00 (0.98-1.02)	0.610
Body mass index	1.04 (0.97-1.10)	0.270	1.02 (0.95-1.09)	0.651	1.01 (0.94-1.09)	0.730	1.01 (0.94-1.08)	0.750
Pack-year smoking	1.04 (1.02-1.07)	0.002	1.03 (1.00-1.07)	0.063	1.03 (1.00-1.07)	0.073	1.04 (1.01-1.07)	0.007
Current doses of prednisolone	1.07 (1.01-1.13)	0.014	1.11 (1.02-1.20)	0.012	1.11 (1.03-1.20)	0.009	1.07 (1.01-1.13)	0.018
Dyslipidemia	1.13 (0.68-1.89)	0.632	0.73 (0.35-1.49)	0.387	0.78 (0.37-1.61)	0.500	0.77 (0.42-1.40)	0.401
Arterial hypertension	2.54 (1.56-4.16)	<0.001	1.82 (0.93-3.58)	0.081	1.81 (0.91-3.61)	0.092	2.37 (1.33-4.23)	0.003
Diabetes	1.62 (0.83-3.17)	0.155	1.04 (0.42-2.56)	0.932	1.26 (0.51-3.12)	0.620	1.15 (0.52-2.52)	0.723
Anti-β2GPI/HLA-DR antibody status (cutoff = 172.359 U/ml)	5.10 (2.94-8.87)	<0.001	—	—	4.39 (2.14-9.03)	<0.001	5.13 (2.85-9.24)	<0.001

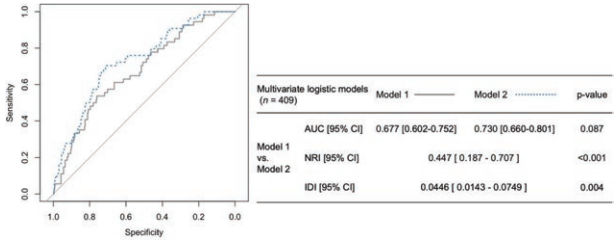


Figure 1. Comparison of ROC curves between multivariate models and reclassification analysis

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Disclosure of Interests: Katsuhiko Yoneda: None declared, Yo Ueda: None declared, Hirotaka Yamada: None declared, Keisuke Nishimura: None declared, Sho Sendo Speakers bureau: Abbvie, Chugai, Kenji Tanimura: None declared, Hisashi Arase: None declared, Hideto Yamada: None declared, Jun Saegusa: None declared.

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POS1497

PREVALENCE OF SARCOPENIA IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Sarcopenia, Motor function, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disease with multisystem involvement [1]. Organs and systems may be affected, such as the musculoskeletal system [1,2]. This inflammatory condition may lead to a decrease in strength and muscle mass [3]. Sarcopenia is considered a muscle disease that leads to decreased physical functionality, increased risk of falls, fractures, hospitalization and mortality [4,5]. The sarcopenia still needs to be better understood in SLE. Therefore, more studies are necessary to assess the sarcopenia prevalence and the impact on SLE patients.

Objectives: To assess the prevalence of sarcopenia in SLE patients and its associations with clinical parameters.

Methods: In this cross-sectional study, women with SLE (18 to 50 years old) were included. The following data were collected: disease duration, disease chronicity (SLICC/ACR-DI), disease activity (SLEDAI-2k), treatment regimen, quality of life (SLEQoL), physical activity level (IPAQ,min/week), muscle strength by handgrip test (kg) and chair stand tests (seconds), Appendicular skeletal muscle mass (ASM;kg) was evaluated Dual energy X-ray absorptiometry (DXA). Sarcopenia diagnosis (handgrip <16kg or chair stand tests >15s + ASM <15 kg) was based on the values indicated by the European Working Group on Sarcopenia in Older People-2 (EWGSOP2). Severity of sarcopenia was assessed by the Short Physical Performance Battery (SPPB ≤8 points) test. The descriptive analysis, Pearson's or Spearman's correlation coefficients, and Chi-squared test were performed. The significance was considered $p<0.05$.

Results: Forty-nine patients were included [median age: 35.0 (28.0–43.5) years; median disease duration: 8.0 (4.0–14.5)] years. Chronicity and disease activity were low, being 0.0 (0.0-1.0) and 2.0 (0.0-4.0), respectively. The median of physical activity level by IPAQ was 583.60 (0.00–409.50) min/week. The majority of patients (83.7%) showed low physical activity level (IPAQ). The patients presented muscle strength by the handgrip test of 24.71±9.01 kg and 14.32±3.68s using the chair stand test. Eight patients (16.3%) showed low muscle strength by the handgrip test and twenty-four patients (49%) showed low muscle strength by the chair stand test. The mean of ASM was 17.03±2.32 kg. Ten patients (20.4%) had low muscle mass. The prevalence of sarcopenia was 16.3% following the EWGSOP2 criteria. On the other hand, we did not find severe sarcopenia. In addition, we did not find a relationship among sarcopenia and age, disease duration, disease chronicity, disease activity, cumulative corticosteroid dose, quality of life, and physical activity level ($p>0.05$).

Conclusion: The prevalence of sarcopenia was 16.3% in patients with SLE. Almost half of our patients had low muscle strength in the chair stand test (49%) and only 16.3% had low muscle strength by handgrip test. Furthermore, sarcopenia is not associated with clinical parameters. Therefore, further studies should be developed to assess risk factors for sarcopenia in patients with SLE.

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Disclosure of Interests: None Declared.

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POS1498 COMORBIDITIES AND SAFETY EVENTS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Real-world evidence, Systemic lupus erythematosus, Epidemiology

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Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disease with multiorgan involvement. High disease activity may drive the development of comorbidities and safety events in SLE.

Objectives: To assess the prevalence of comorbidities and history of safety events at the time of Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) assessment and the incidence of newly diagnosed comorbidities and safety events post-SLEDAI assessment among a prevalent cohort of adult SLE patients ≥18 years old.

Methods: This was a retrospective observational cohort study using the OM1 SLE Registry data from January 2013 to February 2022 (OM1, Inc., Boston, MA). The index date was defined as the first observed or estimated SLEDAI score with ≥12 months of prior data occurring after the first observed SLE diagnosis. The baseline period included all observed time prior to and including the index date. The follow-up period for identifying incident comorbidities and safety events included all available data after the index date. Incidence rates were stratified by disease activity.

Results: Among 10,837 patients, mean age was 52 years and 92% were female. The most common existing comorbidities were hypertension (44%), fibromyalgia (32%), anemia (29%), dyslipidemia (29%), thyroid disease (26%), obesity (25%), depression (22%), rheumatoid arthritis (22%), anxiety (19%), and Sjögren's syndrome (18%). History of safety events at baseline most commonly included any infection (11%), abnormal liver function tests, hepatitis, or acute liver injury (ALI) (8%), elevated creatinine or acute kidney injury (AKI) (6%), and any malignancy (5%). Most patients were treated with first-line therapy for SLE (glucocorticoids and/or antimalarials) during follow-up (89%). Use of second-line (methotrexate, azathioprine, leflunomide) and third-line (belimumab, anifrolumab, mycophenolate mofetil, mycophenolic acid, tacrolimus, cyclosporine, voclosporin, rituximab) SLE therapies were less common (29% and 30%, respectively). During follow-up, 36% of patients had no disease activity, 28% had mild activity, 22% had moderate activity, and 14% had severe activity. Greater disease activity was associated with higher rates of incident hypertension, dyslipidemia, anxiety, thyroid disease, end-stage renal disease or dialysis, chronic liver disease/cirrhosis, avascular necrosis, seizures or epilepsy, and Sjögren's syndrome. The most common incident safety events regardless of disease activity were any infection (30.7 per 1000 person-years [PY]), abnormal liver function tests, hepatitis, or ALI (20.3 per 1000 PY), and elevated creatinine or AKI (17.9 per 1000 PY). Correlation between incident safety events and disease activity varied by outcome.

Conclusion: Many common comorbidities occur more frequently among patients with higher SLE disease activity. The association between disease activity and the incidence of safety events was less clear. SLE-related systemic inflammation, comorbidities, and effects of SLE treatment (both positive and negative) likely contribute to patients' risk profiles.

Table 1. Incidence Rates per 1000 person-years Stratified by Index SLEDAI Score

Comorbidity or Safety Event	No Activity N=3,919	Mild N=3,022	Moderate N=2,413	Severe N=1,483
Hypertension	38.0	38.7	42.7	43.3
Dyslipidemia	31.8	32.0	34.3	35.7
Anxiety	26.9	30.9	32.3	38.5
Thyroid disease	23.6	24.3	27.2	29.0
End-stage renal disease or dialysis	3.2	3.6	3.6	5.3
Chronic liver disease	3.6	4.0	5.0	5.2
Avascular necrosis	2.5	2.9	3.4	4.4
Seizures or epilepsy	5.3	6.3	7.1	8.4
Sjögren's syndrome	7.2	7.8	8.2	12.7
Abnormal liver function	16.3	22.4	25.4	19.2
Abnormal kidney function	14.4	20.9	20.3	18.0
Any infection	24.7	23	36.4	30.6
Major adverse cardiovascular events	8.1	9.2	6.3	6.6
Venous thromboembolism	2.3	4.4	4.0	4.6
Any malignancy	7.0	4.6	5.6	5.2

Disease activity cutoffs: No activity (SLEDAI=0), low (SLEDAI=1-5), moderate (SLEDAI=6-10), severe (SLEDAI=11+)

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POS1499 FACTORS ASSOCIATED WITH CARDIOVASCULAR EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS IN A MONOCENTRIC COHORT WITH UP TO 40 YEARS OF FOLLOW-UP

Keywords: Systemic lupus erythematosus, Cardiovascular disease, Antiphospholipid syndrome

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Background: Systemic lupus erythematosus (SLE) is associated with an increased cardiovascular risk. Several traditional and disease-specific risk factors have been shown to correlate with the occurrence of cardiovascular events (CVE) in patients with SLE. However, results of previous studies are diverse.

Objectives: The objectives of this study were to report number, type and those factors associated with CVE in patients with SLE in a large, single-centre, ethnically diverse cohort with a long follow-up duration.
Methods: Medical records of patients treated at the Lupus Clinic at University College London Hospital (UCLH) between 1979 and 2020 were retrospectively reviewed. Data about CVE, traditional cardiovascular risk factors, demographic and disease features, and treatment history were collected. Only patients with complete available information were included in the study. Regression analyses were performed to identify factors associated with CVE.
Results: Four hundred and nineteen patients were included in the study. Maximum follow-up length was 40 years. Seventy-one (17%) patients had at least one CVE. Forty (50%) events were VTE, 26 (32.5%) were CVA, and 14 (17.5%) were CAD. Mean age at CVE was 44 (SD 12) years. Median time from diagnosis to CVE was 8 (IQR 4-15) years. Descriptive comparative analysis showed an increased prevalence of hypercholesterolemia (41% vs 28%, p-value=0.035), diabetes (10% vs 4%, p-value=0.027), and antiphospholipid antibodies (aPL) positivity (58% vs 27%, p-value<0.001) among patients with CVE. Furthermore, these patients were treated less frequently with hydroxychloroquine (80% vs 89%, p-value=0.049). However, univariable analysis (**Table 1**) showed that only aPL positivity was significantly associated with CVE. This association was confirmed at multivariable analysis (p<0.001). Survival curve for CVE according to the presence of aPL is shown in **Figure 1**. When analysing different types of CVE, aPL were specifically associated with both venous thromboembolic events (p-value<0.001) and cerebrovascular events (p-value=0.007). Dedicated subanalyses revealed that cumulative glucocorticoid dose (p-value=0.010) and a diagnosis of SLE before 2000 (p-value<0.001) were also significantly associated with CVE.
Conclusion: Cardiovascular disease is highly prevalent among patients with SLE and is associated with aPL, glucocorticoid therapy, and diagnosis before 2000.

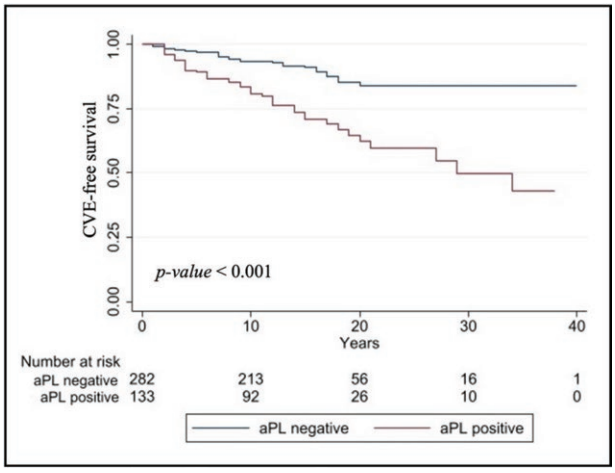


Figure 1. Survival curves for cardiovascular events according to the presence of antiphospholipid antibodies. aPL, antiphospholipid antibodies.

Table 1. Univariable Cox regression analysis to evaluate the association between independent variables and cardiovascular events in the whole study population.

Covariate	Hazard Ratio	95% Confidence Interval	*p-value*
Age at diagnosis	1.012	0.994 – 1.031	0.178
Female sex	0.619	0.307 – 1.250	0.182
Caucasian ethnicity	1.379	0.834 – 2.281	0.210
Raised BMI (>25kg/m^2)	0.948	0.579 – 1.553	0.834
Ever smoker	1.177	0.713 – 1.942	0.522
Hypertension	1.098	0.670 – 1.801	0.708
Hypercholesterolemia	1.496	0.921 – 2.429	0.103
Diabetes	2.165	0.988 – 4.746	0.054
Lupus nephritis	1.132	0.693 – 1.847	0.619
adsDNA positivity	1.208	0.724 – 2.014	0.468
Decreased C3	1.217	0.755 – 1.960	0.419
aPL positivity	3.205	1.975 – 5.201	**< 0.001**
Use of hydroxychloroquine	0.632	0.350 – 1.143	0.129
SDI	0.986	0.788 – 1.235	0.907

aPL, antiphospholipid antibodies; BMI, body mass index; SDI, Systemic Lupus International Collaborating Clinics Damage Index score.

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Acknowledgements: NIL.
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POS1500

ALL-CAUSE MORTALITY IN A SYSTEMIC LUPUS ERYTHEMATOSUS COHORT

Keywords: Gender/diversity issues, Real-world evidence, Systemic lupus erythematosus

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Background: Multiple studies have documented that patients with SLE have a higher all-cause mortality. Active disease contributes to early deaths with later deaths more likely due to cardiovascular disease and malignancy.
Objectives: In this study we present the pattern of mortality in a single long-term, prospective cohort using death certificates to document cause of death.
Methods: The cohort consists of 2,238 patients (92% female, 52% Caucasian, 39% African American) with 92% from Maryland and surrounding states (MD 71%, VA 9%, PA 7%, DE 3%, WV 1%, DC 1%). Death records for 1,288 patients lost to follow up prior to 2020 were obtained from the National Death Index (NDI) at the Center for Disease Control (Atlanta, GA). The NDI identified 11,369 death records from 1985 to 2019 as possible matches based on name, gender, race, and date of birth. Primary and secondary causes of death were provided for the best match for each patient. The causes of death were based on CDC classifications of ICD10 and ICD9 codes. Lupus was identified as a cause of death if ICD10 code M32.X or L93.0, or ICD9 code 695.X or 710.0 was listed on the death record. There were 207 death records identified by matching the NDI data elements and the date of death on the certificate to the date of death reported by the family. Analysis of these 207 records provided the following set of criteria that identified additional death records from the remaining 1,079 patients lost to follow up: 1) date of death occurred after the patient was lost to follow up; 2) at least six out of seven data elements sent to NDI matched those on the death record; and 3) EITHER lupus was listed as a cause of death on the death record OR the state of residence matched the state listed on the death record. Using these criteria, an additional 297 death records were found (Table 1).
Results: The leading primary causes of death listed on the death certificate were: lupus (n=116, 23%), cardiovascular (n=114, 23%), cancer (n=74, 15%), infection (n=66, 13%), other (n=55, 11%), respiratory (n=28, 6%), accidental (n=17, 3%), renal (n=9, 2%) and gastrointestinal (n=8, 2%). Lupus deaths and accidental deaths occurred at a significantly younger age (p-values less than 0.05 for paired t-tests; Figure 1). African Americans died at a younger age compared to Caucasians (50 ± 15 years vs 58 ± 16 years, p<0.001). African Americans had a higher proportion of deaths from infections and renal causes compared to Caucasians (p=0.0017 Likelihood ratio test).
Conclusion: SLE patients died at an average of 55 years of age for all causes of death (compared to life expectancies of >80 years for females in the US), with lupus and cardiovascular disease identified as the leading causes of death on death certificates. Cancer and infection were the third and fourth causes of death. African Americans died younger than Caucasians and had more infection and renal causes of death. Only respiratory deaths were significantly more common in Caucasians.

Table 1 – Matching Criteria for Death Records

Date of Death after Lost to Follow Up	NDI Criteria Match	Lupus = Cause of Death	State Match	Family Reported Deaths	Additional Death Records	Total Death Records
Y	7	Y	Y	115	99	214
Y	7	N	Y	70	143	213
Y	7	Y	N	3	12	15
Y	6	Y	Y	9	3	12
Y	6	N	Y	10	39	49
Y	6	Y	N	0	1	1
Totals				207	297	504

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Michelle A Petri Consultant of: MP is a consultant to Alexion, Amgen, AnaptysBio, Argenx, AstraZeneca, Aurinia, Biogen, Caribou Biosciences, CVS Health, EMD Serono, Eli Lilly, Emergent Biosolutions, GSK, IQVIA, Janssen, Kira Pharmaceuticals, MedShr, Sanofi and SinoMab, Grant/research support from: MP received grant support from GSK, Lilly, Exagen, Thermofisher, AstraZeneca and Aurinia, Joseph Levy: None declared, Urbano Sbarigia Shareholder of: US is an employee of Janssen Pharmaceutica NV,

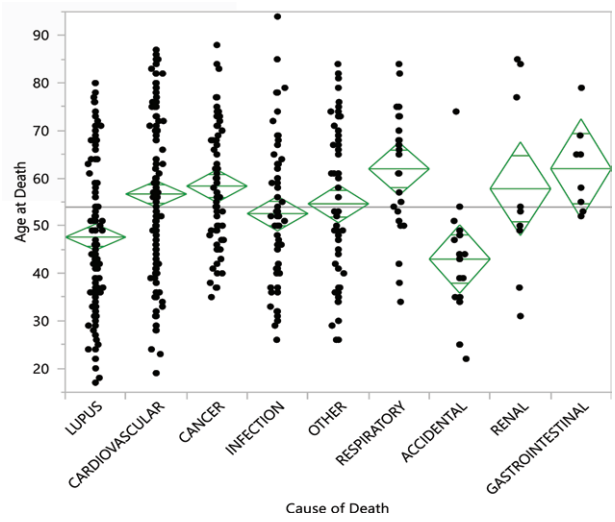


Figure 1 : Age at Death versus Cause of Death

which is a wholly owned subsidiary of Johnson & Johnson, and owns Johnson & Johnson stock and stock options, Employee of: US is an employee of Janssen Pharmaceutica NV, which is a wholly owned subsidiary of Johnson & Johnson, Daniel Goldman: None declared.

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POS1501

LUPUSNET – A FEDERATED MODEL/NETWORK TO SUPPORT REAL-WORLD DATA RESEARCH IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Real-world evidence, Registries

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with a broad range of clinical manifestations and a high unmet need. Real-world data on SLE are available and currently scattered across more than 50 registries worldwide. The Lupus Federated Data Network (LupusNet) is an interdisciplinary initiative that aims to standardize data and harmonize methodology to create a large, global SLE database from existing registries.

Objectives: This initiative will allow the analysis of real-world data across lupus registries worldwide.

Methods: The central paradigm of LupusNet is a federated model whereby the data reside with the respective registries/data owners and analyses are executed at the local center. As data from different sources have different infrastructures, the Observational Medical Outcomes Partnership (OMOP) common data model (CDM) will be used to standardize data into a common format. Standardization will reduce the heterogeneity in data structure and semantics, allowing for uniform data analysis, collaborative research, large-scale analytics, and sharing of sophisticated tools and methodologies. LupusNet will include prospective, observational registries designed to capture real-world data on demographics, treatments, and outcomes in patients with SLE. Other data, including data originating from randomized clinical trials, will also be part of this initiative.

Results: Currently, 6 registries representing 4 regions of the globe and ~30,000 lupus patients are engaged at the start of this initiative. Examples of the types of data from each registry that are available for standardization and harmonization in LupusNet are shown in **Figure 1**. Other lupus registries that may be interested in participating in this initiative should contact the authors. Participating registries are not required to collect all types of data to be included in the initiative. Contact the LupusNet team at www.lupusnet.org.

Conclusion: Through the standardization of global registry data, LupusNet hopes to demonstrate the potential of real-world evidence to answer important questions related to SLE with the ultimate goal of improving patient outcomes.

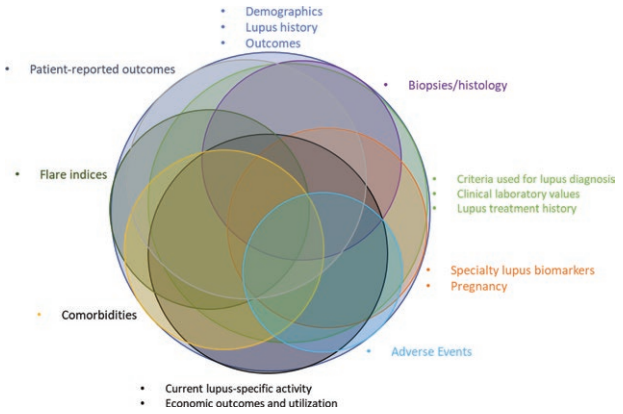


Figure 1. Example of Data Collected from Lupus Registries and Clinical Trials

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Joerg Schreiber Shareholder of: Johnson & Johnson, Employee of: Janssen-Cilag, Neuss, Germany, Michel van Speybroeck Shareholder of: Johnson & Johnson, Employee of: Janssen Pharmaceutica, Beerse, Belgium, Federico Zazzetti Shareholder of: Johnson & Johnson, Employee of: Janssen Medical Affairs Global Services, LLC, Wim Noel Shareholder of: Johnson & Johnson, Employee of: Janssen Pharmaceutica, Beerse, Belgium, Teresa A. Simon: None declared, Frederic Lavie Shareholder of: Johnson & Johnson, Employee of: The Janssen Pharmaceutical Companies of Johnson & Johnson, Paris, France.

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POS1502

HERPES ZOSTER INCIDENCE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE COHORT STUDY

Keywords: Real-world evidence, Systemic lupus erythematosus

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Background: Herpes zoster (HZ) results from reactivation of the varicella-zoster virus and is characterized by a painful dermatomal rash. HZ is associated with increased healthcare costs and reduced patient quality of life.

Objectives: To estimate HZ incidence in patients with systemic lupus erythematosus (SLE) and in a general immunocompetent adult population in the United States.

Methods: This retrospective cohort study used administrative claims data (Optum Research Database) to identify adults (≥18 years) between October 2015 and May 2022 who were assigned to one of two cohorts based on ICD-10-CM diagnosis codes: SLE cohort and immunocompetent cohort. Patients with diagnosis codes for other immunocompromising conditions (ICC) were excluded from the immunocompetent cohort and from the main SLE cohort to create a sub-cohort (SLE without other ICC). The immunocompetent cohort represented a random sample of 1 million individuals meeting the cohort criteria. Indexing occurred at the later of 12 months of continuous enrollment (CE) or the first SLE diagnosis for the SLE cohorts, and after 12 months of CE for the immunocompetent cohort. Patients with HZ vaccination prior to index or a HZ diagnosis in the 12-month baseline period were excluded. Patients were followed for a variable period from index until the earlier of an incident HZ diagnosis or censoring event (HZ vaccination, disenrollment, death, or the end of the study period). Overall incidence rates of HZ were estimated in each cohort and stratified by age at index, and by baseline disease severity for the SLE cohorts using a published algorithm [1].

Results: The SLE cohort included 60,430 patients, among which 21,206 comprised the SLE without other ICC cohort. The immunocompetent cohort included 1,000,000 patients. Mean (standard deviation) age and percent female for the SLE (55 [15] years; 89% female) and for the SLE without other ICC (53 [16] years; 89% female) cohorts were higher compared to the immunocompetent (46 [18] years; 50% female) cohort ($p < 0.001$). For the SLE cohort, HZ incidence (95% confidence interval [CI]) per 1,000 person-years was 19.72 (18.93-20.55) overall and 16.27 (15.04-17.58) and 21.50 (20.48-22.56) per 1,000 person-years for patients aged 18-49 and ≥ 50 years, respectively. HZ incidence (95% CI) for the SLE without other ICC cohort was 14.03 (12.83-15.32) per 1,000 person-years

overall (18-49 years: 11.24 [9.61-13.07]; ≥50 years: 16.08 [14.39-17.91]). HZ incidence (95% CI) for the immunocompetent cohort was 5.64 (5.53-5.74) per 1,000 person-years (18-49 years: 3.46 [3.35-3.57]; ≥50 years: 8.57 [8.37-8.77]). HZ incidence rates in the SLE cohorts increased with baseline disease severity (Table 1).
Conclusion: HZ incidence was high among patients with SLE. HZ prevention strategies in this population may be warranted.
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Table 1 . Herpes Zoster Incidence Rates (per 1,000 person-years) for Patients with SLE, Patients with SLE without Other Immunocompromising Conditions, and Immunocompetent Patients

	SLE		SLE without Other ICC		Immunocompetent	
	N	*Incidence rate (95% CI)*	*N*	*Incidence rate (95% CI)*	*N*	*Incidence rate (95% CI)*
Overall	60,430	19.72 (18.93-20.55)	21,206	14.03 (12.83-15.32)	1,000,000	5.64 (5.53-5.74)
Age (years)						
18-49	21,167	16.27 (15.04-17.58)	9,118	11.24 (9.61-13.07)	578,585	3.46 (3.35-3.57)
≥50	39,263	21.50 (20.48-22.56)	12,088	16.08 (14.39-17.91)	421,415	8.57 (8.37-8.77)
Baseline SLE disease severity						
Mild	16,795	14.95 (13.69-16.29)	7,893	13.17 (11.36-15.18)		
Moderate	31,201	21.25 (20.11-22.45)	10,025	14.49 (12.70-16.46)		
Severe	12,434	23.06 (21.10-25.15)	3,288	15.04 (11.81-18.88)		

SLE, systemic lupus erythematosus; ICC, immunocompromising conditions; CI, confidence interval; N, number of patients.

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Disclosure of Interests: Nikita Stempniewicz Shareholder of: GSK, Employee of: GSK, Andrea Steffens Consultant of: GSK, Kimvi Kim Employee of: GSK, Anamaria Jorga Shareholder of: GSK, Employee of: GSK, Christopher Bell Shareholder of: GSK, Employee of: GSK, Mary DuCharme Consultant of: GSK, Helen Trenz Consultant of: GSK, David Singer Shareholder of: GSK, Employee of: GSK.
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POS1503 LONGITUDINAL STUDY OF PREGNANCY OUTCOMES IN INDIGENOUS VERSUS NON-INDIGENOUS LUPUS PATIENTS IN WESTERN AUSTRALIA

Keywords: Systemic lupus erythematosus

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Background: Ethnicity remains a key determinant of outcome in SLE and Indigenous Australian patients (IA) are disproportionately affected in term of renal failure and mortality [1,2]. Pregnancy in SLE patients associates with maternal and foetal morbidity, but there is no data on pregnancy in IA SLE patients.
Objectives: To compare pregnancy outcomes and complications between IA and non-IA (NI) patients with SLE over three decades between 1985-2015.
Methods: Using state-wide hospital morbidity data, we compared rates for live birth (LB), abortive outcome (AO), preterm birth and gestational complications across pregnancies in IA (n = 31) and non-Indigenous (NI) SLE patients (n = 357) in Western Australia over a thirty-year period. Results presented are medians compared by Kruskal-Wallis test and proportions with odds ratios (ORs) (95% CI) compared by $\chi 2$ testing across groups and study decades.
Results: A total of 702 SLE pregnancies were recorded (62 in IA and 640 in NI). Median age at first pregnancy was significantly lower in IA (27 years, IQR 20-32) than NI patients (30 years, IQR 26-34) (p<0.001), with no difference in median number of pregnancies (2 vs 2, OR 1.1 CI 0.56-2.4). Over the whole study period, LB rate was similar for IA and NI patients (74.2 % vs 72.8, OR p=0.45); however, LB rate increased from 65.5 to 79.6% in NI patients over time (p=0.01) and decreased from 88.9 to 75.9 in IA patients (p=0.34). In NI patients, the proportion of caesarean births was stable over time (35.5 to 37.7%, p= 0.56) but decreased in IA patients (44.4 to 20.7%, p=0.24). Preterm birth occurred in 10.3 % of live births in NI and 9.7 % of IA patients (OR 1.14, CI 0.49-3.10, p = 0.82) with the proportion of preterm deliveries increasing over time in both groups (from 0 to 10.3% in IA and from 4.9 to 7.9% in NA). A single case of congenital heart block occurred (prevalence 0.15%). Gestational diabetes (16.1 vs 2.4 %), infections 12.4 vs 4.1%) and renal disease (22.6 vs 4%) complicated more pregnancies in IA patients (all p<0.001) and showed increasing rates over the three study decades, while these rates remained stable in NI patients except for an increase in diabetes (1.3 to 5.1%).
Conclusion: While LB rates have increased in NI lupus patients over time, they decreased in IA patients in association with an increase in comorbid complications. This suggest that stricter monitoring of pregnancy in IA lupus patients is required to achieve the level of improvement observed in NI lupus patients, that is in line with current literature data [3].
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Disclosure of Interests: None Declared.
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POS1504 PREVALENCE AND CHARACTERISTICS OF PATIENTS WITH LUPUS NEPHROPATHY IN A MULTICENTER REGISTRY IN ARGENTINA (RELESSAR)

Keywords: Systemic lupus erythematosus

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Background: Lupus nephritis (LN) is one of the most frequent serious Lupus manifestations and it is an important risk factor for overall morbidity and mortality in patients with SLE. Despite potent anti-inflammatory and immunosuppressive therapies, it persists with a significant number of patients who progress to chronic renal failure.
Objectives: To evaluate the prevalence of LN and the characteristics of patients with this complication in search of a potential higher risk profile for the development of kidney disease.
Methods: It was a retrospective, observational and analytical study, based on the database of the national registry of SLE of the Argentine Society of Rheumatology (RELESSAR). Adult patients who met the ACR 1997 Classification Criteria were included. Sociodemographic data, time of disease evolution, and delay in diagnosis were collected. The antibody profile, activity indices (SLEDAI), comorbidities (Charlson), treatments and damage (SDI) were determined. Patients with current or past LN were compared with those without LN.
Results: 1502 patients were analyzed, of which 643 (42.8%) had LN. The predominant histological classes were class IV in 253 cases, class III in 81, class II in 78, and class V in 33 patients. In the univariate analysis, patients with LN were characterized by belonging more frequently to the mestizo ethnic group (p=0.017), having a younger age at entry into the registry (p<0.001), less delay in diagnosis in months (p<0.001) and longer disease duration (<0.001). They also presented higher SLEDAI in the last evaluation (p<0.001) as well as low complement levels (p<0.001) and a higher frequency of positive anti-SM antibodies (p<0.007). Within the comorbidities they had significantly more dyslipidemia (p<0.001) and arterial hypertension (p <0.001). They had more episodes of hospitalization (p<0.001), more serious infections (p<0.001) and a higher SLICC damage index (p=0.001). The treatments received any time were Azathioprine (44.3% vs 27.9%, p<0.001), Cyclophosphamide (66.2% vs. 8.72%, p<0.001), mycophenolate mofetil (47.0% vs 7.37%, p< 0.001), mycophenolic Acid (5.59% vs. 0.39%, p<0.001) and Belimumab (3.7% vs. 8.03%, p<0.001). The multivariate analysis is described in Table 1.
Conclusion: In the RELESSAR registry, the prevalence of LN was 42.8%. These patients were characterized by being more frequently of mestizo origin, younger at last evaluation, and of lower socioeconomic level. There was also a correlation with the global activity of the disease as well as with low complement levels and anti-SM antibodies positive. Within the comorbidities there was a strong association with arterial hypertension. We also highlight the negative association with acute cutaneous lupus and with the presence of antiphospholipid antibodies.

Table 1. - Result of the multivariate model.

Characteristics	OR	CI	p
Age at last visit	0.96	0.94-0.97	<0.001
SLE duration	1.01	1.00-1.01	<0.001
SES Media/low/very low	1.65	1.02-2.71	0.044
SLEDAI	1.09	1.06-1.13	<0.001
Acute Cutaneous Lupus	0.57	0.42-0.78	<0.001
Positive Anti SM antibodies	1.43	1.06-1.92	= 0.019
Low Complement (> than 10 days or persist during the last 10 days	4.52	2.78-7.65	<0.001
Negative Anti phospholipid antibodies	1.74	1.27-2.39	<0.001
Arterial Hypertension	3.00	2.10-4.31	<0.001
Gastroduodenal ulcer	0.36	0.17-0.73	0.006

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1505 THE IMPACT OF HIGH-RISK ANTIPHOSPHOLIPID ANTIBODIES PROFILE ON MAJOR ORGAN DAMAGE PROGRESSION IN SYSTEMIC LUPUS ERYTHEMATOSUS: CSTAR MULTIPLE PROSPECTIVE COHORT STUDY

Keywords: Organ damage, Autoantibodies, Systemic lupus erythematosus

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Background: With the improvement in survival, the prevention of cumulative organ damage has become a major goal in the management of systemic lupus erythematosus (SLE). Patients with autoimmune disease suffered from an increasing risk of cardiovascular disease (23·3 events per 1000 patient-years [1]). Although antiphospholipid (aPLs) antibodies, including anticardiolipin antibodies, anti-β2 glycoprotein I, and lupus anticoagulant, were associated with vascular events in antiphospholipid syndrome, the role of APLs in SLE patients was not yet determined.
Objectives: Based on the Chinese SLE treatment and research (CSTAR) multi-center prospective study, we aimed to identify the predictive value of high-risk aPLs on cumulative organ damage progression in SLE.
Methods: Demographic characteristics, autoantibody profiles, clinical manifestations, disease activity status, and organ damage were collected at baseline. High-risk aPLs profile was defined according to 2019 EULAR recommendations for APS [2] (the presence of lupus anticoagulant, or double or triple aPL positivity, or the presence of persistently high aPLs titers).
Results: A total of 2132 SLE patients with full follow-up data were recruited and 424 (19.9%) showed high-risk aPLs profiles. 453 (21.2%) patients developed new organ damage during a mean follow-up of 4.40±2.64 years, and 143(31.6%) are cardio-cerebral vascular damage. At baseline, patients with high-risk aPLs profile have a higher rate of neurological involvement (12.5% vs 7.6%, p=0.001). As shown in Figure 1, cox regression analysis showed that high-risk aPLs profile can predict new-onset organ damage (HR=1.99, 95% CI, 1.63-2.43, p<0.001) and cardio-cerebral vascular damage (HR=7.83, 95% CI, 5.56-11.03, p<0.001). After adjusted of gender(male), age, smoking history, diabetes mellitus, hypertension, and other SLE related potential confounders, high-risk aPLs profile was still found to be an independent predictor which can predict cardio-cerebral vascular events (HR=7.12, 95% CI, 5.03-10.14, p<0.001) (Figure 1).

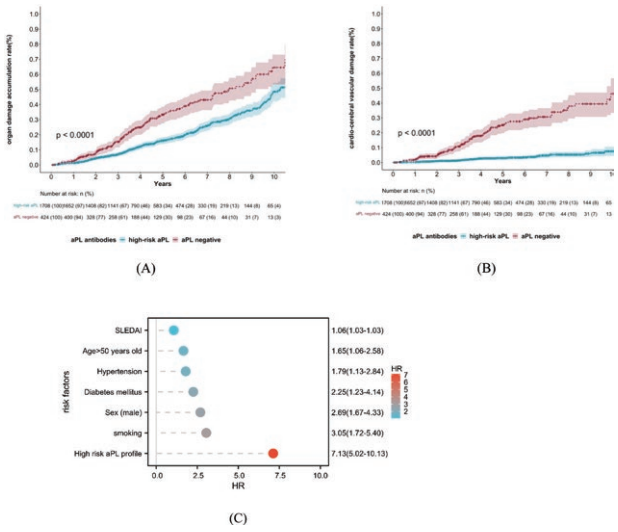


Figure 1. (A). Cumulative probability of new-onset organ damage in patients with or without high-risk aPLs profile. (B). Cumulative probability of cardio-cerebral vascular damage in patients with or without high-risk aPLs profile. (C). Risk factors of cardio-cerebral vascular damage in SLE patients.

Conclusion: SLE patients with high-risk aPLs profile warrant more care and surveillance of cardio-cerebral vascular events during follow-up.
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POS1506 IDENTIFYING DETERMINANTS OF FAVOURABLE AND POOR PHYSICAL FUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM AN INTERNATIONAL COLLABORATIVE STUDY

Keywords: Systemic lupus erythematosus, Comorbidities

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Background: Systemic lupus erythematosus (SLE) can result in impaired daily physical function through various mechanisms including active disease, chronic damage, and mental health symptoms that are common in the disease. However, the key drivers of reduced physical function are poorly understood, and no large-scale global studies investigating this have been conducted to date.

Objectives: To investigate key factors that contribute to impaired physical function in SLE globally.

Methods: SLE patients were identified from the COVAD 2 database, a global register of more than 20,000 respondents. Healthy controls (HC) were included to compare differences in physical function using the Patient Reported Outcome Measurement Information System (PROMIS) questionnaire. Demographics, medication, comorbidities, disease activity, Global Physical Health (GPH) and Global Mental Health (GMH) were collected. Multivariable regression analysis was used to identify contributing factors to favourable or poor physical function (measured by PROMIS Physical Function shortform PF-10a score).

Results: 979 SLE patients and 3358 HCs were included in analysis. Patients with SLE had significantly lower PF-10a score as compared to HCs (median 42, IQR 36-47 vs median 49, IQR 45-50, p<0.0001). Determinants of physical function status in patients with SLE are summarised in Table 1. Briefly, factors associated with poor physical function included increasing age (-0.042, 95% CI -0.069 to -0.015, p=0.002) and methotrexate use (-0.928, 95% CI -1.844 to -0.012, p=0.047). Diabetes (-1.862, 95% CI -3.481 to -0.243, p=0.024) and interstitial lung disease (ILD) (-2.441, 95% CI -4.366 to -0.517, p=0.013), but not asthma or COPD, also contributed to lower PF-10a score. From a mental health perspective, anxiety (-0.970, 95% CI -1.853 to -0.087, p=0.031) but not depression contributed to a lower physical function score. Higher Pain Visual Analogue Scales (VAS) (-2.889, 95% CI -3.107 to -2.671, p<0.001) and Fatigue VAS (-1.459, 95% CI -1.974 to -0.945, p<0.001) also contributed to lower PF-10 scores. Hydroxychloroquine use (0.844, 95% CI 0.190 to 1.498, p=0.012) and higher GPH score (2.287, 95% CI 2.079 to 2.494, p<0.001) were associated with favourable physical function.

Conclusion: Patients with SLE show significantly reduced physical function compared with HCs. Key contributors to poor physical function include intercurrent diabetes and ILD. Screening for, and aggressive early treatment of these conditions may confer improved long-term function. As expected, higher levels of pain and fatigue were associated with poor physical function. Methotrexate use was also identified as a contributing factor to reduced function, which could represent its use in articular manifestations that limit physical function. Importantly, use of hydroxychloroquine was associated with favourable physical function, adding to the well-recognised benefits of this drug in SLE.

Table 1

	Unstandardised B	Beta	95% Confidence Interval for B		Significance
			Lower Bound	Upper Bound	
Age	**-0.042**	**-0.074**	**-0.069**	**-0.015**	**0.002****
Disease Duration (years)	-0.004	-0.005	-0.037	0.029	0.814
Methotrexate	**-0.928**	**-0.040**	**-1.844**	**-0.012**	**0.047***
Mycophenolate mofetil	0.507	0.027	-0.265	1.278	0.198
Azathioprine	0.409	0.022	-0.346	1.164	0.288
Hydroxychloroquine	**0.844**	**0.050**	**0.190**	**1.498**	**0.012***
Steroid Dose	-4.34	-0.044	-.845	-0.023	0.038
Lupus flare within last 6 months	-0.819	-0.039	-1.644	0.007	0.052
Chronic Kidney Disease	-0.430	-0.017	-1.434	0.575	0.401
Interstitial Lung Disease	**-2.441**	**-0.049**	**-4.366**	**-0.517**	**0.013***
Ischaemic Heart Disease	-0.925	-0.020	-2.798	0.947	0.332
Diabetes	**-1.862**	**-0.045**	**-3.481**	**-0.243**	**0.024***
Stroke	-0.663	-0.011	-3.049	1.723	0.586
Anxiety	**-0.970**	**-0.047**	**-1.853**	**-0.087**	**0.031***
Depression	0.594	0.029	-0.290	1.477	0.188
Pain VAS	**-2.889**	**-0.945**	**-3.107**	**-2.671**	**<0.001*****
Fatigue VAS	**-1.459**	**-0.171**	**-1.974**	**-0.945**	**<0.001*****
PROMIS Global Physical Health	**2.287**	**0.634**	**2.079**	**2.494**	**<0.001*****

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POS1507 IC3B/C3 RATIOS MORE STRONGLY CORRELATE WITH SLE DISEASE ACTIVITY IN AFRICAN-AMERICANS COMPARED WITH WHITES

Keywords: Biomarkers, Systemic lupus erythematosus

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Background: Complement activation is a hallmark of SLE pathophysiology. We previously found that iC3b/C3 ratios associated with active disease and clinically meaningful changes in SLE disease activity. Since SLE is more severe in non-white populations, we hypothesized that iC3b/C3 ratios would be a more sensitive marker of disease activity in nonwhite populations.

Objectives: We examined the relationship of iC3b/C3 ratios between African-American (AA) and White subjects with classified SLE.

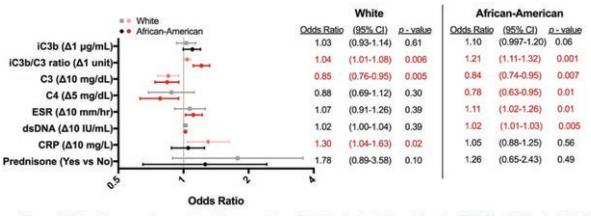
Methods: 159 adult SLE patients treated at the Washington University Lupus Center were enrolled in this observational study. 83 patients with 3-7 study visits were used for this longitudinal analysis. C3 and C4 were measured by nephelometry; iC3b by a lateral flow assay using an investigational medical device. SLE disease activity was measured using the SLEDAI 2K Responder Index-50 instrument. Statistical analyses were performed using SAS v9.4. Multilevel regression models examined associations for SLE disease activity. Ordinal logistic regression models with generalized estimating equation modeling (GEE) examined associations for clinically meaningful changes since the outcome variable is ordinal. Odds ratios and 95% confidence intervals were estimated using Proc GLIMMIX and Proc GENMOD.

Results: iC3b/C3 ratios and C3 associated with active disease in AA and White SLE subjects, with the association of the iC3b/C3 ratio in AA was stronger (Figure 1). In addition, AA with SLE associated C4, ESR, and dsDNA with active disease, while Whites associated with CRP. In multiple regression analysis, iC3b/C3 ratios independently associated with active disease in both groups, although the effect was more pronounced in AA (AA: OR=1.48, 95% CI=1.21-1.82; Whites: OR=1.17, 95% CI=1.02-1.34). Furthermore, in univariate regression analysis, only the iC3b/C3 ratio in AA associated with clinically meaningful changes in disease activity.

Conclusion: iC3/C3 ratios better correlated with active disease in AA compared to Whites. Furthermore, iC3b/C3 ratios correlated with clinically meaningful changes in disease activity only in AA. These data suggest that complement activation in SLE is dependent on race.

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	White			African-American		
	Odds Ratio	(95% CI)	p - value	Odds Ratio	(95% CI)	p - value
iC3b (Δ1 µg/mL)	1.03	(0.93-1.14)	0.61	1.10	(0.997-1.20)	0.06
iC3b/C3 ratio (Δ1 unit)	1.04	(1.01-1.08)	0.006	1.21	(1.11-1.32)	0.001
C3 (Δ10 mg/dL)	0.85	(0.76-0.95)	0.005	0.84	(0.74-0.95)	0.007
C4 (Δ5 mg/dL)	0.88	(0.69-1.12)	0.30	0.78	(0.63-0.95)	0.01
ESR (Δ10 mm/hr)	1.07	(0.91-1.26)	0.39	1.11	(1.02-1.26)	0.01
dsDNA (Δ10 IU/mL)	1.02	(1.00-1.04)	0.39	1.02	(1.01-1.03)	0.005
CRP (Δ10 mg/L)	1.30	(1.04-1.63)	0.02	1.05	(0.88-1.25)	0.56
Prednisone (Yes vs No)	1.78	(0.89-3.58)	0.10	1.26	(0.65-2.43)	0.49

Figure 1. Univariate regression analysis of the association of biochemical variables with active SLE. Red (AA) and pink (whites) whiskers represent statistically significant variables, while grey (white) and black (AA) represent non-significant variables.

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POS1508 PREVALENCE OF REMISSION ACCORDING TO PHYSICIAN AND PATIENT AND LEVEL OF AGREEMENT IN A REAL-WORLD MULTICENTER LUPUS REGISTRY

Keywords: Patient reported outcomes, Systemic lupus erythematosus, Remission

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Background: Improvement on health-related quality of life (HRQoL) in patients with Systemic Lupus Erythematosus (SLE) remains a challenge. There is limited data on the level of agreement on remission according to physician and patient and remission impact on HRQoL and long-term outcomes.

Objectives: To investigate the prevalence and level of agreement between remission according to physician and patient criteria and to evaluate the impact of remission on HRQoL in patients with SLE.

Methods: Prospective study of patients included in RELESSER-PROS, a multicenter register of SLE patients. Protocol of the register has been previously described [1]. Remission according to physician was defined in agreement with DORIS 2021 criteria: clinical SLEDAI 0, physician global assessment ≤2 on a 0-10 Likert scale (equivalent to ≤0.5 on a 0-3 scale), stable low-dose prednisone (≤5mg) and stable immunosuppressive/ biologic agents if remission on therapy. Remission according to patient was defined as SLAQ (Systemic Lupus Activity Questionnaire) question 1 with no flare in the last 3 months (score 0). Patients were classified in three groups according to remission status by DORIS, SLAQ or both. Level of agreement was assessed using kappa statistics. Acceptable level of agreement was considered if kappa >0.60.

Results: 1102 patients, with a follow-up of at least 2 years (data from 3 visits available) were included in this analysis. Patient characteristics according remission status at baseline are presented in the Table 1. At baseline, remission by DORIS was present in 16.1%, by SLAQ 16.7% and 2.45% by both. Remission by DORIS was more frequent among patients with higher education, on immunosuppressant and biological therapy and patients with history of hospitalization; remission by SLAQ was more frequent among women, obese patients, and those on antimalarials ($p<0.05$). Symptoms reported in patients who considered themselves in remission were mainly cutaneous and articular (53.3%). Mean SLEDAI in patients on remission by SLAQ was 3.28 (3.78). Patients in remission by DORIS had significantly better results in patient reported outcomes (PRO) measured by EQ-5D and LIT ($p<0.05$). Level of agreement in remission according to physician and patient was 78.04% (k=0.061) at baseline, 63.39% (k=0.039), and 62.73% (k=0.099) in year 2 and 5 respectively. Kappa level of agreement was low.

Conclusion: Our results reflect low level of agreement between physician and patients in terms of remission status with increasing disagreement in the follow-up. Patients in remission by DORIS shows better results in EQ-5D and LIT.

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Table 1. Patient characteristics according remission status at baseline

	Remission by DORIS (n=177)	Remission by SLAQ (n=184)	Remission by both criteria (n=27)	*p-value*
Age at diagnosis (years), mean (SD)	34.6 (14.87)	36.64 (13.74)	33.77 (13.12)	0.181
Female sex, n (%)	160/176 (90.9%)	166/182 (91.2%)	27/27 (100%)	0.004
Disease duration (yrs), mean (SD)	15.26 (8.18)	13.71 (7.7)	19.8 (7.66)	0.069
Highest education	57/172 (33.1%)	40/180 (22.2%)	13/26 (50%)	<0.001
Medication, n (%)	0/177 (0%)	36/182	0/27 (0%)	1
Off-therapy	79/176	(19.8%)	14/27 (51.9%)	<0.001
Antimalarials	(44.9%)	100/182	12/27 (44.4%)	<0.001
Immunosuppressants (AZA, MTX, MMF)	63/175 (36%) 14/176 (8%)	(54.9%) 36/180 (20%)	4/27 (14.8%)	<0.001
Biological therapy (rituximab, belimumab)		8/178 (4.5%)		
Obesity (BMI>30), n (%)	18/162 (11.1%)	44/176 (25%)	3/24 (12.5%)	0.003
Hospital admission, n (%)	57/176 (32.4%)	40/182 (22%)	7/26 (26.9%)	<0.001
SLEDAI, mean (SD)	1.66 (1.66)	3.28 (3.78)	1.78 (1.5)	<0.001
SLAQ, mean (SD)	26.15 (2.55)	27.98 (1.81)	27.63 (1.96)	<0.001
EQ-5D	67.53 (19.31)	63.22 (20.12)	64.54 (17.7)	0.041
LIT	26.68 (21.76)	34.37 (20.34)	31.3 (18.34)	0.0007
SLICC/ACR Damage Index	1.57 (1.74)	1.42 (1.84)	1.37 (1.9)	0.437
Mortality	0/177 (0%)	0/184 (0%)	0/27 (0%)	1

AZA azathioprine, MTX methotrexate, MMF mycophenolate, BMI body mass index, EQ-5D EuroQol-5D, LIT lupus impact tracker

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Disclosure of Interests: None Declared.

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POS1509 **WITHDRAWN**

POS1510

IDENTIFICATION OF THE MINIMAL REQUIRED DURATION OF RENAL-EXTRARENAL REMISSION ASSOCIATED WITH REDUCED RISK OF CHRONIC KIDNEY DISEASE AND OF DAMAGE ACCRUAL IN LUPUS NEPHRITIS

Keywords: Remission, Treat to target, Systemic lupus erythematosus

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Background: There is an increasing need for data exploring the effect of remission on kidney-oriented outcomes and terminal organ damage in patients with lupus nephritis (LN).
Objectives: To investigate the effects of renal-extrarenal clinical remission on chronic kidney disease (CKD) development and organ damage accrual in patients with LN.
Methods: We performed a multicentric retrospective cohort study on biopsy-proven LN patients with at least five years follow-up, in whom we assessed i) the minimum duration of remission able to prevent CKD (serum creatinine >1.0mg/dl with eGFR <60ml/min/1.73 m2 and inactive urinary sediment, confirmed by at least three determinations for at least 3 months); ii) the impact of remission on organ damage increase, evaluated by the SLICC Damage Index (SDI). Renal-extrarenal clinical remission was defined as serum creatinine <1mg/dl, eGFR>60 ml/min/1.73m2, proteinuria <0.5g/24h and cSLEDAI=0, lasting for at least one year. Cox regression was used to test the effect of different durations of remission on CKD and SDI accrual. The minimum duration of remission needed to prevent CKD was estimated through Kaplan-Meier curves. The potential relationship between renal-extrarenal clinical remission and SDI was assessed by Spearman correlation between percentage of follow-up spent in remission and annual increase in SDI.
Results: 303 LN patients were included (females 86.5%, mean follow-up 14.8 (9.8-22.0) years). 84.8% achieved renal-extrarenal clinical remission that persisted for 8.70 (5.40-13.30) years. Overall, 17.6% patients developed CKD after a median of 14.1 (8.9-20.9) years. Patients achieving remission developed CKD significantly less frequently than patients never achieving remission (12.1% vs. 56.6%, p<0.001). Among patients with at least 10-year follow-up (n=224), a remission duration of at least 2 years protected from CKD development (p<0.001), yet the best CKD-free survival was obtained in patients reaching at least 3 years of remission (HR95%CI 2.34 (1.38-3.98) p<0.001) (**Figure 1**). Considering the whole population, the increase in SDI from baseline to the last observation was significantly higher in patients who had never achieved remission (median: 2[1-3] vs. 1[0-1]; p= 0.047). We observed that the higher the percentage of follow-up spent in remission, the lower the yearly SDI accrual (r=-0.324, p<0.001). Among patients achieving remission, the risk of any SDI increase was significantly lower in patients maintaining at least 3 years on remission vs. shorter durations (HR95% CI 0.54 (0.31-0.54), p=0.03).
Conclusion: Renal-extrarenal clinical remission is an achievable treatment target which protects against CKD development and SDI increase in patients with LN. At least 3 years of renal-extrarenal clinical remission confers significant protection against renal function deterioration and chronic damage, hence emerging as a desirable therapeutic target for LN.

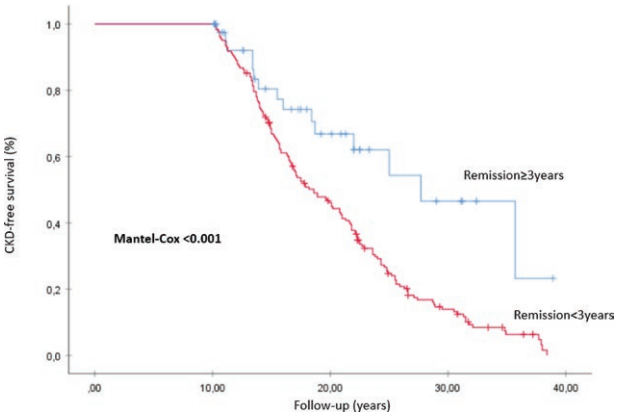


Figure 1. CKD-free survival according to years spent in remission (Kaplan-Meier method; Mantel-Cox for comparison)

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POS1511

PERSISTENCE OF RENAL-EXTRARENAL REMISSION AND EFFECT ON RISK OF SLE FLARES AND OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH LUPUS NEPHRITIS

Keywords: Systemic lupus erythematosus, Kidneys, Remission

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Background: How renal and extrarenal remission affects risk of flares and of chronic kidney damage (CKD) development in systemic lupus erythematosus (SLE) patients with active lupus nephritis (LN) was not clearly disentangled.
Objectives: To investigate the effect of maintained or interrupted renal-extrarenal clinical remission on the risk of SLE flares and CKD development in LN.
Methods: We conducted a retrospective cohort study on biopsy-proven LN patients in whom we evaluated i) the probability of achieving and maintaining renal-extrarenal clinical remission; ii) the impact of renal-extrarenal clinical remission on the risk of SLE flares and CKD development (defined as serum creatinine >1.0mg/dl with eGFR <60ml/min/1.73 m2 and inactive urinary sediment, confirmed by at least three determinations for at least 3 months); iii) the predictors of renal-extrarenal clinical remission. Renal-extrarenal clinical remission was defined as serum creatinine <1mg/dl, eGFR>60ml/min/1.73m2, proteinuria <0.5g/24h and cSLEDAI=0 lasting for at least one year. Time to renal-extrarenal clinical remission, the likelihood of its maintenance and the risk of SLE flares were estimated through Cox regression.
Results: 303 patients were included in the study. Over a 14.8-year-follow-up, 46 patients never achieved while 257 achieved remission after a median of 1.44 (0.69-3.58) years from initial therapy for LN. In 142 out of 257 patients, remission ended after a median of 3.6 (2.30-5.90) years due to SLE flares. 115 patients maintained an uninterrupted remission for 9.5 (5.8-14.5) years. At multivariate analysis, age >40 years (OR95%CI: 1.017 (1.005-1.028); p=0.004), hydroxychloroquine use (OR95%CI:1.384 (1.109-1.661); p=0.021) and absence of arterial hypertension (OR95%CI: 0.699 (0.425-0.975); p= 0.011) were independent predictors of renal-extrarenal clinical remission. CKD occurred in 56% of patients who had never reached renal-extrarenal clinical remission, in 21.8% of those who lost remission due to SLE flares and in none of those who maintained remission permanently (p<0.0001). Five, 10 and 15 years after the beginning of

renal-extrarenal clinical remission 63%, 47% and 38% of patients respectively were still in remission. After the 15th year from the start of renal-extrarenal clinical remission, no patient developed SLE flare and remission persisted without interruption until the end of the observational period. The risk of SLE flares decreased to 10%, 5% and dropped to 2% on remission lasting<5, 5-10 and 10-15 years respectively. No achievement or loss of renal-extrarenal clinical remission due to SLE flares were associated with CKD development.

Conclusion: Older age, hydroxychloroquine use, absence of arterial hypertension predict remission among LN patients upon initial therapy. The longer the remission, the higher the chance of it persisting uninterrupted, and the lower the risk of SLE flares and of CKD.

REFERENCES: NIL.

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Disclosure of Interests: Gabriella Moroni Speakers bureau: GSK, Mariele Gatto Speakers bureau: GSK, Giulia Frontini: None declared, Marta Calatroni: None declared, Silvana Quaglini: None declared, Francesco Reggiani: None declared, Barbara Trezzi: None declared, Luca Iaccarino Speakers bureau: GSK, Renato Alberto Sinico: None declared, Andrea Doria Speakers bureau: GSK, Pfizer, AZ, Celgene, EliLilly, BMS, Roche.

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POS1512 THROMBOCYTOPENIA AND IMPAIRED KIDNEY FUNCTION ARE MAJOR RISK FACTORS FOR RECURRENT THROMBOSIS IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

Keywords: Epidemiology, Anti-phospholipid syndrome

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Background: Recurrent thrombosis in patients with antiphospholipid syndrome (APS) is a major clinical concern and treatment challenge. Data regarding risk factors and markers of recurrent thrombosis in APS patients, particularly during long-term follow-up, is limited.

Objectives: We aimed to study the effect of cardiovascular (CV) risk factors and antiphospholipid antibody (aPL) profiles on recurrent thrombosis in APS. We continued to explore if the occurrence of thrombocytopenia and decline in kidney function over time could be considered risk factors.

Methods: This retrospective cohort study comprises all patients identified with APS in the electronic medical records at Karolinska University Hospital, Sweden 2014-2020. The patients were followed until death, last medical visit, and thrombotic event. Cox proportional-hazard model was used to estimate hazard ratios (HR) and 95% confidence intervals (95% CI) between groups. A time-varying model was applied when the effect of the occurrence of thrombocytopenia and decline in renal function and time to recurrent thrombosis were assessed. Ethical approval was obtained from the Swedish Ethical Review Authority.

Results: 263 patients were included in the cohort and 52.1% of patients had primary APS. The median age at inclusion was 45 years (35–60) and 66% were women. During follow-up, 47 re-thrombotic events occurred; 29 arterial and 18 venous events, with an incidence of 4.1 per 100 person-years (95% CI: 3 – 5.3). A significant CV risk factor for re-thrombosis was current smoking; hazard ratio 3.62 (95% CI: 1.4 – 9.2). Twenty-two patients (64.7%) with re-thrombosis were triple positive for aPL compared to 99 (43.2 %) without any event at follow-up (p <0.01). There was no difference in the number of patients with re-thrombosis between the primary and secondary APS. The time-varying Cox regression analyses revealed chronic kidney disease (eGFR<60) and thrombocytopenia (platelet count $<100x10^9$) hazard ratios 2.41, (95% CI: 1.2 – 5.0) and 7.60 (95% CI: 1.9 – 30.1), respectively, as the major risk factors for re-thrombosis in this cohort of APS patients. The cumulative mortality incidence was 4.5% (n=12). The most common cause of death was sepsis due to bacterial infection at a median age of 63 (IQR 51-71).

Conclusion: Our results demonstrate that the decline of kidney function and the occurrence of thrombocytopenia in APS patients over time are major risk factors for recurrent thrombosis. Adequate surveillance and treatment options are necessary to improve kidney function and thrombocytopenia and thereby prevent further morbidity in APS patients.

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POS1513 IDENTIFYING HIGH-RISK PROFILE IN PRIMARY ANTIPHOSPHOLIPID SYNDROME THROUGH CLUSTER ANALYSIS: FRENCH MULTICENTRIC COHORT STUDY

Keywords: Epidemiology, Cardiovascular disease, Anti-phospholipid syndrome

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Background: Antiphospholipid syndrome (APS) is an autoimmune disease characterized by thrombosis (arterial, venous or small vessel) or obstetrical events and persistent antiphospholipid antibodies (aPL), according to the Sydney classification criteria. Many studies have performed cluster analyses among patients with primary APS and associated autoimmune disease, but none has focused solely on primary APS.

Objectives: We aimed to perform a cluster analysis among patients with primary APS and asymptomatic aPL carriers without any autoimmune disease, to assess prognostic value.

Methods: In this multicenter French cohort study we included all patients with persistent APS antibodies (Sydney criteria) measured between January 2012 and January 2019. We excluded all patients with systemic lupus erythematosus or other systemic autoimmune diseases. We performed hierarchical cluster analysis on the factor analysis of mixed data coordinates results with baseline patient characteristics to generate clusters.

Results: We identified four clusters: cluster 1, comprising "asymptomatic aPL carriers", with low risk of events during follow-up; cluster 2, the "male thrombotic phenotype", with older patients and more venous thromboembolic events; cluster 3, the "female obstetrical phenotype", with obstetrical and thrombotic events; and cluster 4, "high-risk APS", which included younger patients with more frequent triple positivity, antinuclear antibodies, non-criteria manifestations, and arterial events. Regarding survival analyses, asymptomatic aPL carriers relapsed less frequently than the others, but no other differences in terms of relapse rates or deaths were found between clusters.

Conclusion: We identified four clusters among patients with primary APS, one of which was "high-risk APS". Clustering-based treatment strategies should be explored in future prospective studies.

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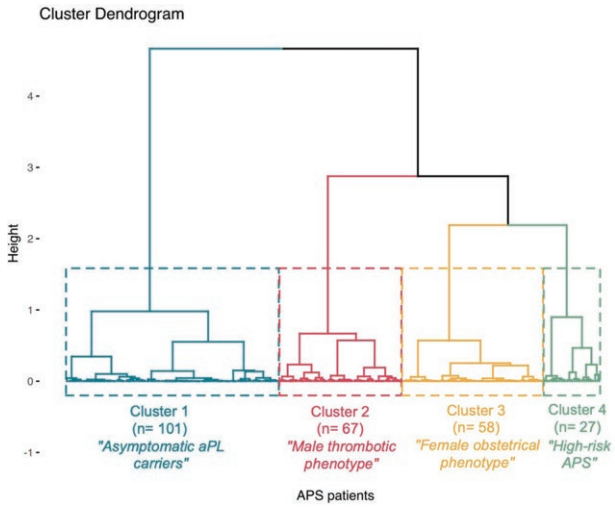


Figure 1.

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POS1514 DIFFERENTIALLY EXPRESSED GENES OF PATIENTS WITH LUPUS NEPHRITIS THROUGH INTEGRATIVE BIOINFORMATICS

Keywords: Biomarkers, -Omics, Systemic lupus erythematosus

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune chronic disease characterized clinically by periods of flares and remission. Although its pathophysiology has not yet been well understood, it is well documented that SLE courses with systemic inflammation, as well as affection to specific organs [1]. Lupus nephritis (LN) is the most common complication and cause of death appearing in SLE patients, often leading to end-stage renal disease [2]. A type I interferon (IFN) signature is present in SLE, however, there is no consensus on which genes are expressed in LN. We performed a metanalysis through integrative bioinformatics to identify differentially expressed genes (DEGs) in patients with LN.
Objectives: We aimed to identify and assess overlapped DEGs of patients with LN through integrative bioinformatics and functional enrichment analysis.
Methods: We designed a search strategy in the Gene Expression Omnibus platform to identify datasets of expression profiling by array of kidney samples of patients with LN. The inclusion criteria were: 1) Presence of healthy controls in the datasets, and 2) Analysis of data with GEO2R. The exclusion criteria were: 1) Incomplete information in the datasets, 2) Failure to identify cases and controls, or 3) Gene expression through RNAseq. DEGs were filtered when $p < 0.05$ and logfold change > 2 or < -2. We assessed the DEGs with David database and performed a prediction analysis with GeneMania. Protein-protein interactions analysis was realized with String through Cytoscape platform, and iRegulon was used to predict a possible regulatory target of the cluster.
Results: 3 datasets fulfilled the inclusion criteria and 9 DEGs were identified. Prediction analysis yielded 23 co-expressed genes. David database recognized the principal biological processes involving those genes (Table 1). PPI analysis recognized the top 10 genes with the strongest interactions, and proposed STAT1 as the regulatory target (Figure 1).

Table 1. ***Top 3 biological processes involving overlapped DEGs among the datasets, in which the IFN signature is present.***

Biological Processes		
Term	**Gene Count**	***p*-value**
Defense Response to Virus	21	1,6E-33
Response to Virus	15	3,4E-25
Negative Regulation of the Viral Genome	11	1,7E-20

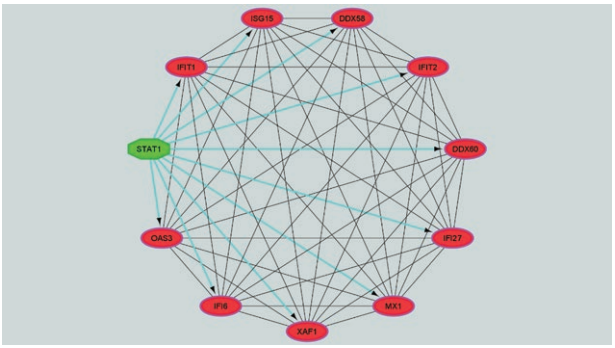


Figure 1. *DEGs with the strongest interactions in patients with LN, in which the IFN signature is present.*

Conclusion: We aimed to identify and assess DEGs of patients with LN and recognize the ones with the strongest interactions. Our results suggest that type I IFN is crucial on the pathophysiology of LN, and STAT1 can serve as a possible therapeutic target for treating LN. We propose further *in vivo* studies to validate these results, given that they can serve as diagnostic biomarkers and even possible therapeutic targets for LN treatment.

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POS1515 PREVALENCE AND CLINICAL FEATURES OF LATE AND VERY LATE ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Outcome measures

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Background: Whether late-onset (LO) SLE is associated with a different, more benign disease course and better prognosis than early-onset SLE is still contradictory.[1-3]
Objectives: To describe the prevalence and clinical features of LO-SLE and very late onset (VLO) SLE and to compare their outcomes with those of non-LO SLE.
Methods: We performed a retrospective study using prospectively collected data from our cohort involving 516 patients with SLE (ACR criteria) followed between 2008 and 2022. Patients older than 50 or older than 60 years at SLE onset were defined as LO-SLE and VLO-SLE, respectively. Demographic data, and clinical and treatment history were retrieved from clinical charts. SLEDAI-2K, daily prednisone dose, SLICC Damage Index (SDI), and low disease activity (according to LLDAS definition) [1] at last follow-up in 2022 were assessed. Early mortality, within 10 years after diagnosis, was assessed in patients diagnosed in the last 15 years.
Results: Among 516 SLE patients regularly followed, 38 (7.4%) were LO-SLE: mean±SD age at diagnosis 56.5 ±5.7 years (range 50-72), females 78%. Of them, 10 (2% of the overall cohort) were VLO-SLE: mean±SD age at diagnosis 65 ±4.0 years (range 60-72), females 60%. Compared to early-SLE patients, LO-SLE patients had more frequently skin involvement and positive antiSSA/SSB antibodies (Table 1). Compared to non-LO-SLE, no difference in life-threatening manifestations was observed, including renal and neuropsychiatric involvement. The same trend was found in VLO-SLE. Accordingly, the use of immunosuppressants (including types of drugs) and biologics was similar (Table 1). At last follow-up, SLEDAI-2K was lower in LO-SLE patients (1±2 vs. 2±3, p=0.01), whereas the proportion of patients on glucocorticoids (21% vs 37%) and in LLDAS (84% vs 74%) was similar to that observed in non-LO-SLE. Despite that, SDI was higher in LO-SLE (2, range 0-8) than in non-LO-SLE patients (1, range 0-10, p=0.004) but after excluding items possibly related to aging (cataract, osteoporosis, low GFR, malignancy) the difference was not significant anymore. Among 165 patients diagnosed in the last 15 years, mortality was similar in LO and early-onset SLE, although deaths within 10 years after diagnosis (2 cases) all occurred in early-SLE patients.

Conclusion: According to our data, LO- and VLO-SLE are uncommon and seem not to be associated with more benign disease outcomes. Since life-threatening manifestations can occur in LO-SLE, these patients deserve regular follow-up.

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Table 1. Clinical and therapeutic features of late-onset and early-onset SLE

	Late onset SLE (N=38)	Early onset SLE (N=478)	P value
Skin rash	13 (34.2)	262 (54.8)	0.027
Alopecia	3 (7.8)	60 (12-.5)	n.s.
Cutaneous vascu-litis	1 (2.6)	45 (9.4)	n.s.
Arthritis	23 (61)	353 (73.8)	n.s.
Leukopenia	17 (44.7)	191 (40)	n.s.
Thrombocitopenia	11 (29.9)	86 (18)	n.s.
Serositis	8 (21)	91 (19)	n.s.
Lupus nephritis	16 (42.1)	258 (54)	n.s.
Neuro-SLE	8 (21)	81 (16.9)	n.s.
Anti-dsDNA Abs	25 (66)	335 (70)	n.s.
Anti-SSA/SSB Abs	23 (61)	201 (42)	0.044
Anti-U1RNP Abs	9 (23.6)	129 (27)	n.s.
Antiphospholipid Abs	13 (34.2)	138 (28.9)	n.s.
Immunosuppressants ever	23 (61)	339 (71-)	n.s.
MMF	13 (34.2)	210 (44)	
CYC	4 (10.5)	103 (21.5)	
AZA	6 (15.7)	143 (29.9)	
MTX	8 (15.7)	87 (18.1)	
Belimumab	6 (16)	75 (15.7)	
Rituximab	3 (7.6)	39 (8.2)	
HCQ ever	35 (92)	454 (95)	n.s.

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POS1516 CHARACTERISATION OF AN ANA-ARTHRITIS BASKET POPULATION FOR CLINICAL TRIALS

Keywords: Undifferentiated connective tissue disease, Systemic lupus erythematosus, Sjögren syndrome

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Background: Musculoskeletal (MSK) manifestations are common in systemic lupus erythematosus (SLE) and other ANA-associated rheumatic musculoskeletal diseases (ARMDs). Presently clinical trials recruit patients from individual diagnoses; consequently, recruitment is often difficult, effect sizes using multi-organ outcome measures are small and licensed therapies are only available to patients with SLE. Basket trials that pool patients with similar clinical or immunological features from many conventional legacy diagnoses may improve trial outcomes and access to therapy.

OBJECTIVES:

1. To characterise a pooled population of patients with MSK manifestations associated with any of multiple ANA-RMDs
2. To assess the homogeneity of this population in terms of disease activity, patient reported outcomes, quality of life, therapeutics, and immune biomarkers
3. To explore the validity of MSK-BILAG across ANA-RMDs

Methods: Participants were ANA+, met criteria for an ARMD (SLE, pSS, IIM, SSc, MCTD), or had a consultant diagnosis of undifferentiated CTD. Patients with MSK manifestations were identified by MSK items of validated instruments and medical history terms. We collected patient and physician-reported outcomes, SLE gene expression signatures, and flow cytometry for major cell subsets. The pooled ARMD population was compared to healthy controls using t-tests. Variables were compared across ARMDs using ANOVA and χ^2 tests. Physician VAS was compared between MSK-BILAG grades for all diseases.

Results: Of 294 ANA-RMD patients 215 with MSK manifestations were analysed. Key clinical variables are shown in Table 1. We found no difference between ARMDs for IFN, plasmablast, neutrophil, myeloid, inflammation and erythropoiesis scores, nor for naïve, memory B cells, plasmablasts, T cells, monocytes, NK or NKT cells in flow cytometry. Physician VAS was strongly associated with BILAG grade across all ARMDs.

Table 1.

Mean (SD)*	Total	HC	p value	SLE	UCTD	pSS	MCTD	IM	SSc	p value
N total	294	7	-	104	111	31	13	19	16	-
N with MSK	215	-	-	90	77	22	11	6	9	NA
FACIT-F total	29.18 (13.26)	8.57 (4.86)	<0.001	30.35 (13.07)	27.98 (13.06)	25.29 (14.00)	40.43 (12.11)	17.80 (7.66)	32.40 (12.12)	0.045
EQ5D-5L index	0.64 (0.22)	0.97 (0.03)	<0.001	0.61 (0.22)	0.67 (0.23)	0.72 (0.14)	0.44 (0.21)	0.72 (0.10)	0.62 (0.25)	0.016
SF36 MCS	36.26 (5.57)	40.79 (4.31)	0.036	36.10 (6.14)	36.65 (5.09)	34.98 (5.32)	33.11 (3.90)	36.54 (6.77)	39.72 (3.87)	0.417
SF36 PCS	45.29 (6.68)	52.28 (6.97)	0.008	45.82 (7.91)	45.15 (5.44)	46.63 (6.45)	44.64 (6.06)	43.08 (4.22)	41.78 (6.42)	0.704
Patient arthritis VAS (0-10)	5.89 (2.90)	0.50 (1.20)	<0.001	5.97 (2.81)	5.94 (2.81)	4.76 (3.51)	7.08 (2.94)	4.22 (3.08)	8.25 (2.01)	0.232
Patient early morning stiffness VAS (0-10)	5.76 (2.86)	0.84 (1.69)	<0.001	5.42 (2.94)	6.01 (2.76)	5.82 (3.49)	6.61 (2.28)	3.87 (1.86)	7.11 (2.56)	0.281
Patient pain VAS (0-10)	5.12 (2.85)	0.87 (1.53)	<0.001	5.06 (3.01)	5.54 (2.51)	4.05 (3.20)	5.36 (2.78)	3.80 (2.91)	5.34 (3.17)	0.414
Current HCQ*	116 (54.0)	-	-	53 (58.9)	41 (53.2)	9 (40.9)	7 (63.6)	4 (66.7)	2 (22.2)	0.231
Current MTX*	43 (20.0)	-	-	13 (14.4)	20 (26.0)	2 (9.1)	4 (36.4)	2 (33.3)	2 (22.2)	0.178
Current AZA*	23 (10.7)	-	-	9 (10.0)	8 (10.4)	2 (9.1)	2 (18.2)	1 (16.7)	1 (11.1)	0.964
Current prednisolone*	55 (25.6)	-	-	33 (36.7)	9 (11.7)	3 (13.6)	4 (36.4)	4 (66.7)	2 (22.2)	0.001
Nodal OA*	17 (7.9)	-	-	6 (6.7)	4 (5.2)	3 (13.6)	1 (9.1)	1 (16.7)	2 (22.2)	0.398
X-ray OA*	33 (15.3)	-	-	11 (12.2)	12 (15.6)	4 (18.2)	2 (18.2)	2 (33.3)	2 (22.2)	0.745

*Or n(%) where indicated

Conclusion: MSK manifestations have similar clinical impact and immune profile across ARMDs. Current therapies used are similar. ANA-arthritis is therefore a homogenous and impactful population for basket trials.

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POS1517 MICROANGIOPATHY, INDEPENDENT RISK FACTOR FOR DAMAGE ACCRUAL IN ANTIPHOSPHOLIPID SYNDROME: A RETROSPECTIVE MULTI-CENTER STUDY

Keywords: Organ damage, Anti-phospholipid syndrome

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Background: Antiphospholipid syndrome is characterized from venous, arterial and small vessels thromboembolic events leading to significant morbidity and mortality despite current treatments. Albeit, the acute diseases manifestations of antiphospholipid syndrome are well known, data on damage accrual are still lacking.

Objectives: To assess the frequency of accrual damage in antiphospholipid syndrome (APS) and to evaluate the association with different laboratory and clinical APS subsets.
Methods: Medical records of 274 patients, 231 (84.3%) female and 43 (15.7%) males with a mean (±SD) age at diagnosis of 37.8 (±11.5) years, followed prospectively from 1990 to 2021, were reviewed.
Results: Ninety-six (35%) presented pregnancy morbidity alone, 140 (51.1%) thrombosis alone and 38 (13.9%) both thrombosis and pregnancy morbidity. A single, double or triple antiphospholipid antibodies (aPL) positivity was registered, respectively in, 82 (29.9%), 78 (28.5%) and 114 (41.6%) of the patients. Following a mean (±SD) follow up of 208.4 (±91.7) months, a total of 58 (21.2%) organ damage accrual was recorded. This included neurological damage in 19 (32.8%) patients, hemiparesis in 9, epilepsy in 7 and cognitive dysfunction/dementia in three cases, cardiac valvopathy in 4 (6.9 %) patients of which 3/4 (75%) require valve replacement with mechanical valve in two cases and bioprosthetic in one. Chronic heart failure was found in 4 (6.9%) patients, chronic renal failure in 15 (25.9%), amputation due to peripheral arterial thrombosis in 5 (8.6%), visual loss in 2 (3.4%), post thrombotic syndrome in 6 (10.3%), adrenal insufficiency in one (1.7%). Some of the patients present more than one organ disfunction. Both thrombotic and thrombotic and pregnancy morbidity subsets were significantly associated with a higher rate of damage accrual compared with pregnancy morbidity alone, respectively p<0.0001 (OD 40.7; 95% CI: 6.9-418.8) and p<0.0001 (OD 61.9; 95% CI 10.5-659.7). Moreover, the presence of microangiopathy as well as the presence of both venous and arterial thrombosis were significantly associated with damage accrual, respectively (p<0.0001, OD 10.99; 95% CI 5.7-21-36) and (p=0.001). Regarding laboratory subsets, triple aPL positivity was significantly associated with a higher rate of damage accrual compared to single and double aPL, respectively, p<0.0001 (OD 9.6; 95% CI: 3.7-23.5) and p<0.0001 (OD 4.8; 95% CI: 2.2-10.81). At the multivariate analysis only microangiopathy was an independent risk factor for damage accrual (p=0.001).
Conclusion: Overall, our data show a higher frequency of damage accrual in APS patients. Microangiopathy was independent risk factor for damage accrual. These findings should be in mind when counselling APS patients and might help guide clinicians in therapeutic decision.
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POS1518 PULMONARY INVOLVEMENT IN LUPUS IS ASSOCIATED WITH ENHANCED MORBIDITY: A MULTICENTRE STUDY

Keywords: Lungs, Systemic lupus erythematosus, Autoantibodies

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Background: Although several studies report a high incidence of pulmonary manifestations in SLE, lung involvement is often underestimated in SLE clinical assessment [1]. This is also mirrored by the absence of pulmonary manifestations other than pleurisy in the old and new classification criteria for SLE [2]. Moreover, limited evidence on the management of SLE-related pulmonary manifestations is available.
Objectives: To assess prevalence and clinical impact of the spectrum of SLE-related pulmonary manifestations and their association with patient autoantibody profiles in a large SLE cohort and to describe the effectiveness of different therapeutic approaches in distinct clinical settings.
Methods: Patients followed at the Lupus Clinics of ASST G. Pini-CTO and San Raffaele Hospital (Milan, Italy) were enrolled. Data regarding demographics, disease characteristics, autoantibody profile, pulmonary manifestations, damage accrual and treatment were collected. The following types of lung involvement were recorded: pleurisy, acute lupus pneumonitis, interstitial lung disease (ILD), alveolar haemorrhage, pulmonary embolism, arterial pulmonary hypertension and shrinking lung syndrome.
Results: Of the 471 SLE patients enrolled, we identified 78 patients (16.5%) displaying at least one pulmonary manifestation. Epidemiological data on each manifestation are reported in Table 1. Pleurisy was the most common pulmonary manifestations and manifested at disease onset in most cases (56%). Patient home environment (urban vs countryside) did not seem to impact the risk of developing lung disease. Damage accrual was relevant, as 2/3 of patients displayed at least 1 point increase in SLICC Damage Index (SDI) after the onset of lung involvement in comparison to baseline. All patients received at least one steroid course. Immunosuppressive treatment choices and efficacy differed among distinct manifestations: only half of the patients with pleurisy received immunosuppression, mainly azathioprine, with 100% of improvement, while 80% of cases of ILD received immunosuppression, predominantly mycophenolate, with a 50% risk of non-response. By comparing demographics and clinical characteristics among cases and controls, we found a significantly lower median age at disease onset (p=0.002) and a higher frequency of male sex (18% vs 9%; p=0.07), joint involvement (p=0.02) and constitutional symptoms (p=0.02) in patients with lung involvement, while no differences were observed in the autoantibody profile, including anti-dsDNA and anti-ENA autoantibodies.
Conclusion: Our study confirms that, in addition to the known epidemiological burden of pleurisy, other types of pulmonary involvement can complicate the disease course and contribute to damage accrual. In particular, ILD can frequently occur and respond to immunosuppressants in only half cases. Consistent with the association of lung involvement with increased morbidity, higher-risk categories for severe disease such as males and subjects with early-onset SLE were more represented among patients with pulmonary manifestations.
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Table 1. Demographic and disease characteristics of SLE patients with lung involvement

Demographics and clinical characteristics		
Females, n (%)	65 (83)	
Age at diagnosis (years): median (IQR)	29 (22 – 39)	
Disease duration (years): mean ±DS	19 ± 12	
Subjects with >0 and >1 point SDI increase from baseline: n (%)	48 (61.5); 26 (33)	
Lung involvement		
	N (%)	**immunosuppressive therapy, %**
Pleurisy	61 (78)	49
Acute pneumonitis	4 (5)	100
ILD	15 (19)	80
PAH	6 (8)	50
Pulmonary embolism	4 (5)	50
Shrinking lung	1 (1)	100
Alveolar hemorrage	4 (5)	100

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POS1519 BASELINE CHARACTERISTICS OF A LONGITUDINAL, MULTINATIONAL, MULTIETHNIC STUDY OF LUPUS PATIENTS, WITH OR WITHOUT LUPUS NEPHRITIS

Keywords: Registries, Autoantibodies, Systemic lupus erythematosus

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Background: Clinically evident kidney disease eventually occurs in up to one-half of SLE patients.

Objectives: To describe sociodemographic, clinical, serological and treatment characteristics of a multicenter and multiethnic Latin American SLE cohort of patients with or without lupus nephritis (LN)

Methods: GLADEL2.0 is an ongoing observational cohort. Patients were categorized according to renal involvement: Group I (LN never); II (prevalent renal involvement currently inactive); III (prevalent renal involvement, currently active) and IV (incident renal involvement). Demographic, clinical manifestations, treatments, disease activity were examined at baseline. A descriptive cross-sectional analysis was performed.

Results: A total of 991 SLE patients were included, 884 (89.2%) female and 656 (68.3%) Mestizos (Amerindian and European ancestry). Median (IQR) age at cohort entry was 35 (28-45) years and disease duration were 67 months (18-139). Patients with incident LN had a higher proportion of males, were younger, had shorter disease duration and were more frequently Mestizos. Pericarditis and anti-dsDNA were less frequent in group I and MMF in groups I and IV (Table 1). A predominance of class IV (49%) was evidenced in 510 patients in which a kidney biopsy was performed.

Conclusion: Baseline characteristics of GLADEL2.0 well characterized lupus patients' cohort with or without LN are described with distinct demographic, clinical and laboratory patterns that will allow both centralized laboratory evaluation of urinary biomarkers and exploratory biomarker analyses including transcriptome and their impact on the outcome of these patients.

Table 1. Sociodemographic and clinical characteristics and treatment at cohort entry

Variable	Group I (n=393)	Group II (n=213)	Group III (n=224)	Group IV (n=161)	p-value	Variable	Group I (n=393)	Group II (n=213)	Group III (n=224)	Group IV (n=161)	p-value
Female n%	361/393 91.9	193/213 90.6	200/224 89.3	130/161 80.7	0.002[a]	**Ethnic group n%**					<0.001[b]
Age (years)[d]	39 (30-48)	38 (30-48)	30 (25-37)	33 (25-40)	<0.001[c]	*Caucasian*	106/372 28.5	54/208 26.0	37/222 16.7	28/159 17.6	
Disease duration (months)[d]	77.1 (32-146)	106 (52-187)	64.4 (25-130)	3.0 (0.7-26)	<0.001	*Mestizo*	236/372 63.4	138/208 66.3	167/222 75.2	115/159 72.3	
Education (years)[d]	12.5 (11-16)	14 (11-16)	13 (11-16)	12 (11-16)	<0.001[c]	*Indigenous*	4/372 1.1	2/208 1.0	0/222 0	2/159 1.3	
Fever n%	132/375 (35.2)	105/210 (50.0)	82/224 (36.6)	75/153 (49.0)	<0.001	*Afro-LAtin American*	26/372 7.0	14/208 6.7	18/222 8.1	14/159 8.8	
Discoid rash n%	40/376 (10.6)	11/210 (5.2)	20/224 (8.9)	6/151 (4.0)	0.025	*Methylprednisolone bolus* n%	107/349 (30.7)	145/199 (72.9)	161/205 (78.5)	102/142 (71.8)	<0.001
Pleuritis n%	73/373 (19.6)	49/208 (23.6)	67/224 (29.9)	50/153 (32.7)	0.003	*Hydroxychloroquine* n%	321/365 (87.9)	182/205 (88.8)	194/220 (88.2)	121/136 (89)	0.985
Pericarditis n%	40/375 (10.7)	49/209 (23.4)	41/224 (18.3)	40/152 (26.3)	<0.001	*Azathioprine* n%	197/291 (67.7)	101/205 (49.3)	108/216 (50.0)	23/89 (25.8)	<0.001
Anti-dsDNA n%	231/361 (64.0)	167/204 (81.9)	194/216 (89.8)	134/150 (89.3)	<0.001	*Cyclophosphamide-IV* n%	47/289 (16.3)	129/202 (63.9)	139/214 (65.0)	38/89 (42.7)	<0.001
Anti-Sm n%	88/324 (27.2)	47/167 (28.1)	73/187 (39.0)	60/128 (46.9)	<0.001	*Mycophenolate* n%	75/291 (25.8)	151/206 (73.3)	183/218 (83.9)	35/89 (39.3)	<0.001
Positive Anti-Cardiolipin n%	79/320 (24.7)	41/184 (22.3)	38/187 (20.3)	12/126 (9.5)	0.005	*Tacrolimus* n%	1/291 (0.3)	6/206 (2.9)	28/216 (13.0)	3/87 (3.4)	<0.001
Positive Anti-B2GP1 n%	41/254 (16.1)	15/148 (10.1)	19/149 (12.8)	6/106 (5.7)	0.037	*Belimumab* n%	23/290 (7.9)	8/205 (3.9)	7/216 (3.2)	3/88 (3.4)	0.083
Low C3 n%	228/367 (62.1)	158/205 (77.1)	193/218 (88.5)	137/150 (91.3)	<0.001	*Rituximab* n%	25/291 (8.6)	21/205 (10.2)	37/215 (17.2)	6/87 (6.9)	0.009
Low C4 n%	244/367 (66.5)	155/203 (76.4)	193/217 (88.9)	134/150 (89.3)	<0.001	**SLEDAI[c]**	2 (0-6)	2 (0-4)	10 (6-16)	16 (11-21.2)	<0.001

[a] Chi-squared test was used. [b] Fisher exact test was used. [c] Kruskal-Wallis test was used. [d] Median and IQR

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POS1520

RELIABILITY STUDY OF THE SLE-DAS, SLEDAI-2K AND PGA INSTRUMENTS FOR MEASURING SLE DISEASE ACTIVITY

Keywords: Systemic lupus erythematosus

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Background: The Systemic Lupus Erythematosus Disease Activity Score (SLE-DAS) has been recently developed and validated, providing improved accuracy and sensitivity for changes in SLE disease activity in comparison to SLE Disease Activity Index 2000 (SLEDAI-2K) [1]. New recommendations to standardize the Physician Global Assessment (PGA) scoring may improve its reliability [2].

Objectives: To assess the intra- and interrater reliability of SLE-DAS, SLE-DAI-2K and PGA for measuring SLE disease activity.

Methods: A set of 24 clinical vignettes were abstracted, each from a real clinical visit of patients followed at an academic lupus clinic. These vignettes were selected to include a wide spectrum of SLE manifestations, organ-system involvements, and global severity of disease activity. Abstracted data were presented in a standardized format, including demographic, past medical history, current clinical picture and treatment, laboratory, and other workup assessments. A group of 19 raters were recruited as a random multicenter sample of Rheumatologists. All raters completed a preliminary training session on scoring rules for SLE-DAS, SLEDAI-2K and PGA. Each rater scored each clinical vignette with SLE-DAS, SLEDAI-2K, and PGA through an online survey. The scoring was repeated in a second round 7-14 days after the first one. The clinical vignettes were randomly ordered for each round. Inter and intra-rater reliability of each instrument was estimated using the intraclass correlation coefficient (ICC) with 95% confidence intervals (95%CI), based on single-measurement, absolute agreement, with a two-way random effect or two-way mixed-effects model, respectively.

Results: The 19 raters included 8 rheumatologists and 11 rheumatology trainees from 11 hospitals, with a mean of 12.1±7.1 and 3.6±0.5 years of rheumatology practice, respectively, and 78.9% of the participants assess ≤5 SLE patients per week in their regular clinical practice. The 24 clinical vignettes included 83.3% female patients, with a mean of 36.5±17.9 years of age. Active SLE organ involvement included: skin rashes (20.8%); arthritis (12.5%); nephritis (12.5%); thrombocytopenia (12.5%); cardiac/pulmonary involvement (12.5%); mucocutaneous vasculitis (8.3%); serositis (8.3%); neuropsychiatric lupus (8.3%). Systemic vasculitis, myositis, alopecia, hemolytic anemia, and leukopenia were each present in 4.2% of the vignettes. Hypocomplementemia and/or high anti-dsDNA were present in 75.0%. Twenty-one percent of the cases were in remission. All raters completed the survey, totaling 912 case assessments. Scores attributed by the raters ranged from 0.37 to 49.53 in SLE-DAS, 0 to 24 in SLEDAI-2K, and 0.0 to 3.0 in PGA. The interrater reliability was good for SLE-DAS and SLEDAI-2K, and moderate for PGA. The intra-rater reliability was excellent for SLE-DAS, and good for SLEDAI-2K and PGA (Table 1).

Table 1: Interrater and intra-rater reliability of SLE-DAS, SLEDAI-2K and PGA.

	ICC (95%CI)	
	Interrater reliability	**Intra-rater reliability**
SLE-DAS	0.877 (0.807-0.934)	0.908 (0.891-0.923)
SLEDAI-2K	0.812 (0.717-0.896)	0.892 (0.871-0.909)
PGA	0.704 (0.578-0.828)	0.900 (0.881-0.916)

CI: confidence interval; ICC: intraclass correlation coefficient.

Conclusion: SLE-DAS presents high intra- and interrater reliability for measuring SLE disease activity. The high reliability of SLE-DAS is an important quality both in clinical practice and research, allowing consistent scoring among different clinicians including those who are not SLE experts.

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Psoriatic arthritis - treatment

POS1521 CHARACTERISTICS OF DIFFICULT TO TREAT PSORIATIC ARTHRITIS: A COMPARATIVE ANALYSIS

Keywords: Psoriatic arthritis, bDMARD

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Background: The concept of difficult-to-treat rheumatoid arthritis (D2T RA) has recently emerged. It is defined by the persistence of disease activity and the failure of at least 2 b/tsDMARDs of 2 different mechanisms of action (MoA) [1]. In this definition, the period of time during which the treatments have failed is not included. The D2T concept has not yet been applied with consensus in psoriatic arthritis (PsA).
Objectives: To study the characteristics of patients with D2T PsA to better identify the potential causes of treatment failure. The 2nd objective was to study a sub-group of D2T PsA patients with a predefined time criteria.
Methods: A monocentric retrospective longitudinal study was performed in a tertiary center. PsA diagnosis was based on CASPAR criteria. Patients were followed up from February 2004 to August 2022. Patients starting a b/tsDMARDs with a minimum of 2-year follow-up were included. D2T PsA patients were defined as patients who received more than 2 b/tsDMARDs with different MoA among b/tsDMARD available. These patients were compared to non-D2T PsA patients (nD2T PsA) using statistical tests. Very D2T PsA patients were defined as patients who received at least 2 b/tsDMARDs in less than 2 years during the time of follow-up.
Results: 150 patients were included, 49 were D2T PsA and 101 nD2T PsA. Baseline characteristics are presented in the Table 1. No statistical difference was found between the 2 groups regarding main comorbidities, including fibromyalgia and depression. In the D2T PsA group, 91.7% and 69.1% of patients received an anti-TNF alpha as the 1st and 2nd lines of treatment; anti-IL17 drugs represented 0% and 12.2% of 1st and 2nd lines; anti-IL12-23 represented 8% and 18.4% of prescriptions in 1st and 2nd lines. After 3 lines, 38.8% of patients had received 3 bDMARDs with different MoA, 30.6 % received 2 bDMARDs with different MoA. 17 patients were categorized as very D2T PsA. When compared to the rest of the D2T PsA group, no significant difference was observed. Proportion of men was 64.7% (p=0.39). Mean age was 55.0 ± 8.3 yo (p=0.67) and mean BMI was 30.4 ± 6.5 kg/m^2 (p=0.65).

Table 1. Baseline characteristics of patients

Parameters	N	D2T PsA n = 49	N	nD2T PsA n = 101	p value
Men	49	29 (59.2)	101	52 (51.5)	0.37
Age (years), mean ± SD	49	54.2 ± 11.9	101	53.7 ± 14.2	0.82
BMI, mean ± SD	46	29.6 ± 7.2	96	27.7 ± 5.7	0.093
PsA duration (years), median (IQR)	49	17.0 (8.0 to 20.0)	99	11.0 (6.0 to 21.0)	0.22
Current smoker status	49	16 (32.7)	101	33 (32.7)	1.00
Clinical PsA characteristics at baseline					
Axial involvement	48	21 (43.8)	100	26 (26.0)	**0.030**
Peripheral involvement	49	49 (100)	101	99 (98)	NA
Monoarthritic	48	3 (6.3)	101	11 (10.9)	-
Oligoarthritic	48	22 (45.8)	101	51 (50.5)	-
Polyarthritic	48	23 (47.9)	101	37 (36.6)	-
Dactylitis	45	10 (22.2)	101	32 (31.7)	0.24
Psoriasis at baseline	49	6 (12.2)	101	12 (11.9)	0.95
Structural damage at baseline (axial and peripheral)	42	32 (76.2)	96	49 (51.0)	**0.006**
IBD	49	0 (0.0)	101	3 (3.0)	NA
Baseline CRP (mg/L), median (IQR)	40	13.6 (6.0 to 31.5)	86	8.1 (3.0 to 20.0)	0.11
BASDAI Baseline, mean ± SD	8	65.1 ± 16.6	22	58.5 ± 11.7	0.23
bDMARD discontinuation due to poor dermatological control	47	19 (40.4)	101	19 (18.8)	**0.005**

Values are expressed as number (%) unless otherwise stated. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; bDMARD: biological disease modifying antirheumatic drug; BMI: body mass index; CRP: C-reactive protein; (n)D2T: (non) difficult-to-treat; HLA: human leukocyte antigen IBD: inflammatory bowel disease; IQR: interquartile range; N: number of available observations; NA: not applicable; PsA: psoriatic arthritis; SD: standard deviation.

Conclusion: Significant differences were found between the characteristics of patients D2T PsA and nD2T PsA, which were the presence of axial manifestation, structural damage at baseline and discontinuation due to poor dermatological control. Limitations exist about applying the EULAR D2T RA definition to PsA. The inclusion of a time period should also be considered.

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POS1522 CHANGES IN SERUM CYTOKINES BY WEEK 24 CORRELATE WITH LONG-TERM EFFICACY OF GUSELKUMAB THROUGH 2-YEARS IN BIO-NAÏVE ADULTS WITH PSA

Keywords: Psoriatic arthritis, Randomized control trial, Biomarkers

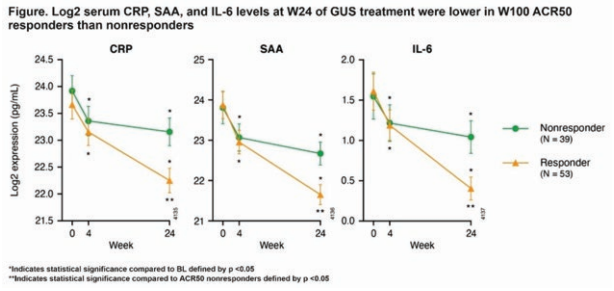
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Background: The IL-23p19 inhibitor guselkumab (GUS) has shown robust efficacy vs placebo (PBO) in phase 3 DISCOVER-1 and -2 studies of adults with active psoriatic arthritis (PsA) [1,2], with continuous overall clinical improvement observed through 2 years of DISCOVER-2 [3]. GUS has previously been shown to significantly reduce levels of inflammatory biomarkers associated with PsA over 24 weeks [4].
Objectives: To assess whether earlier changes (by Week [W] 24) in serum biomarker levels associate with long-term (W100) clinical response to GUS.
Methods: DISCOVER-2 enrolled biologic-naïve adults with active PsA ≥6 months defined by the CASPAR criteria, swollen and tender joint counts ≥5, and C-reactive protein (CRP) ≥0.6 mg/dL. Patients (pts) were randomized 1:1:1 to GUS 100mg at W0, W4, then every 4 weeks (Q4W); GUS at W0, W4, then Q8W; or PBO [2]. Using Spearman linear regression and General linear model, serum cytokine levels determined in GUS-treated pts (pooled Q4W/Q8W) were assessed for: 1) correlations between reductions in cytokine levels, including selected Th17 cytokines (IL-17A, IL-17F, IL-22), acute phase cytokines (CRP, serum amyloid protein A [SAA], IL-6), and β-defensin 2 (BD-2), from baseline (BL) at W24 and in PsA disease severity from BL at W100, measured by changes in Disease Activity in PSoriatic Arthritis (DAPSA) scores, Psoriatic Arthritis Disease Activity Score (PASDAS), and Psoriasis Area and Severity Index (PASI) scores (significant correlation=r>0.25 and p<0.05); and 2) associations between changes in selected cytokine levels from BL through W24 and achievement of ACR50 response at W100.
Results: BL demographics, disease severity, and medication use of GUS-treated DISCOVER-2 pts with available biomarker data (N=100) were consistent with the overall GUS-treated DISCOVER-2 population (N=493). With GUS treatment, PASI score change from BL at W100 correlated with changes from BL at W24 in serum BD-2, IL-17A, IL-17F, and IL-22 levels (all r>0.25, p<0.05; **Table 1**), though PASDAS and DAPSA score change at W100 did not correlate with changes in these biomarkers at W24. DAPSA score change at W100 correlated with changes at W24 in serum IL-6. W100 ACR50 responders (N=53) to GUS also demonstrated significantly lower serum CRP, SAA, and IL-6 levels at W24 than nonresponders (N=39) (p<0.05; **Figure 1**).
Conclusion: This analysis reported correlations between earlier changes in Th17 cytokine levels and long-term reductions in PASI scores, and associations between earlier changes in acute phase cytokine levels and long-term ACR50 response with GUS. The substantial reductions in these cytokines from BL at W24 may portend durable improvements in skin and joint symptoms of PsA.
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Table 1. Rho values indicating correlations between changes from BL at W24 in serum cytokine levels and changes from BL at W100 in PsA disease severity among D2 GUS-treated pts with available biomarker data.

Cytokine	DAPSA score change	PASDAS change	PASI score change
BD-2	0.096	0.128	**0.599**
IL-17A	0.035	0.056	**0.412**
IL-17F	0.016	0.068	**0.412**
IL-22	-0.027	0.044	**0.382**
CRP	0.222	0.217	-0.051
SAA	0.175	0.215	0.061
IL-6	**0.316**	0.193	-0.033

Shaded cells represent significant correlation between cytokine levels and clinical activity (r>0.25 and p<0.05). *BD-2=β-defensin 2, BL=baseline, DAPSA=Disease Activity Index for Psoriatic Arthritis, PASDAS=Psoriatic Arthritis Disease Activity Score, PASI=Psoriasis Area and Severity Index, W=week*



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POS1523

EFFICACY OF SECUKINUMAB ON INDIVIDUAL DOMAINS OF PSORIATIC ARTHRITIS: EXPERIENCE FROM ROUTINE CLINICAL PRACTICE IN THE CZECH NATIONAL REGISTRY ATTRA

Keywords: Registries, bDMARD, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a heterogeneous disease with a number of skeletal and extraskeletal manifestations. It is desirable that DMARDs affect the maximum number of domains of PsA manifestations. Only limited data regarding the impact of bDMARD treatment on individual domains in routine clinical practice is available.

Objectives: The aim of the study is to assess how the IL-17A inhibitor secukinumab affects the individual domains of PsA in the routine clinical practice using data from the ATTRA national registry in the Czech Republic.

Methods: ATTRA is a prospective registry of patients receiving bDMARD therapy for rheumatic diseases collecting data on efficacy, safety and quality of life of all patients treated in the Czech Republic. Adult patients with psoriatic arthritis treated with secukinumab were included in the analysis. The monitored indicators were survival on therapy, DAS 28 ESR, response to treatment according to EULAR, HAQ, EuroQol, physician-assessed psoriasis, dactylitis, enthesitis, nail involvement, physical function and ability to work. Patients were described at the beginning of secukinumab treatment and after 3, 6, 12, 18, and 24 months through absolute and relative frequencies in categorical variables and means with standard deviations (SD) and medians with 5th and 95th percentiles when describing continuous variables. Survival on therapy was computed through the Kaplan-Meier method. Statistical analyses were conducted using IBM SPSS Statistics (version 25.0).

Results: A total of 426 patients were included in the study, of which 237 were women and 189 were men. The average age at the start of treatment was 51 ± 12 years, duration of the disease 10 ± 8 years. About 40% of patients were bDMARD naïve, 60% had failed 1 or more bDMARDs. At the start of secukinumab treatment, 66.4% were on concomitant csDMARD therapy, with 47% receiving methotrexate (MTX) in monotherapy or in combination with other csDMARDs. Survival on therapy was 79.1% (95% CI: 75.0; 83.3) at 1 year, 69.6% (95% CI: 64.6; 74.6) at 2 years, and 53.6% (95% CI: 44.8; 62.5) at 5 years of treatment. The reason for treatment discontinuation was primary non-response (30.6%), secondary non-response (47.6%) and adverse effects (6.5%). Mean DAS 28 had decreased from initial 5.0 ± 1.3 to 2.5 ± 1.1 after 2 years of treatment. Remission (DAS 28 < 2.6) was achieved by 54.1% and low disease activity (DAS 28 ≤ 3.2) was achieved by 74.8% of patients still on secukinumab (Figure 1). There was also a significant improvement in the assessment of physical function and quality of life (HAQ, SF 36, EuroQol). The prevalence of heel enthesitis decreased from 12.2% to 1.5%, prevalence of dactylitis from 22% to 4.7%, and prevalence of moderate to severe nail involvement from 33.2% to 3.8% during the first 2 years of treatment. 43.8% (95% CI: 32.2; 55.4) were able to resume work and 13.9% (95% CI: 8.7; 19.0) of PsA patients lost their jobs during the first two years of treatment. The overall safety of the treatment was good with no unexpected serious side effects.

Figure: Achieving remission and a state of low disease activity with secukinumab in the treatment of PsA in the Czech national registry ATTRA

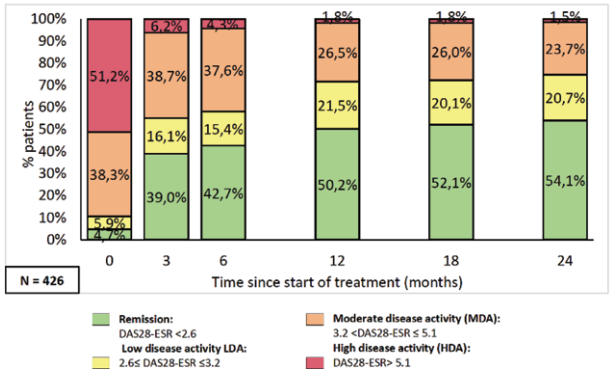


Figure 1. Achieving remission and a state of low disease activity with secukinumab in the treatment of PsA in the Czech national registry ATTRA

Conclusion: This analysis of patients in a national registry demonstrated a robust and long-term effect of secukinumab in the treatment of individual PsA domains: arthritis, dactylitis, enthesitis, nail involvement, psoriasis, quality of life and in increasing work capacity in patients with PsA.

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POS1524

DURABLE CLINICALLY-MEANINGFUL IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE, FATIGUE, PAIN, AND WORK PRODUCTIVITY AMONG PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS TREATED WITH RISANKIZUMAB AT WEEK 100

Keywords: Psoriatic arthritis, Patient reported outcomes

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Background: Risankizumab (RZB) demonstrated efficacy and safety in the treatment of psoriatic arthritis (PsA) in phase 3 trials KEEPsAKE-1 (NCT03675308), patients with an inadequate response to disease-modifying antirheumatic drugs (DMARD-IR), and KEEPsAKE-2 (NCT03671148), DMARD-IR and inadequate responders to biologics.

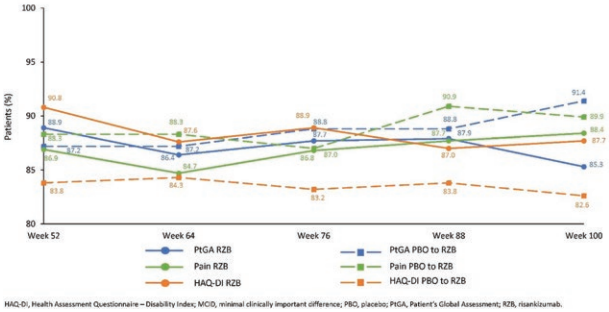
Objectives: This analysis aims to assess the durability of the RZB treatment response on health-related quality of life (HRQoL) and patient-reported outcomes (PROs) in patients with PsA at Week 100.

Methods: In the KEEPsAKE 1 and 2 trials, patients were randomised 1:1 to receive RZB 150 mg or PBO in the 24-week double-blind period. During the open-label maintenance period, all patients received RZB 150 mg. This analysis evaluated observed cases of RZB-treated patients who achieved minimal clinically important differences (MCIDs) in PROs at Week 24. Results are presented as the percentage of patients, of those who achieved MCIDs at Week 24, who maintained MCIDs in PROs from Week 52 to Week 100. MCIDs included a ≥10-point decrease in Patient's Global Assessment (PtGA), ≥10-point decrease in Pain, ≥0.35-point decrease in Health Assessment Questionnaire – Disability Index (HAQ-DI), ≥4-point decrease in Functional Assessment of Chronic Illness Therapy (FACIT) – Fatigue, ≥2.5-point increase in 36-Item Short Form Survey (SF-36) physical component summary (PCS), ≥1.1-point decrease in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), ≥1-point decrease in morning stiffness, and ≥20% reduction in Work Productivity and Activity Impairment Questionnaire (WPAI) Presenteeism, ≥15% in Work Productivity Loss, and ≥20% in Activity Impairment.

Results: In KEEPsAKE 1, 54–68% and 31–52% of RZB-treated patients and PBO to RZB patients achieved MCIDs across PROs at Week 24, respectively. In KEEPsAKE 2, 44–67% and 33–47% of RZB-treated patients and PBO to RZB patients achieved MCIDs across PROs at Week 24, respectively. Among the patients who achieved MCIDs at Week 24 in KEEPsAKE 1, a high percentage of RZB and PBO to RZB-treated patients maintained MCIDs from Week 52 to 100 in PtGA (RZB: 85.3–88.9%; PBO to RZB: 87.2–91.4%), Pain (RZB: 84.7–88.4%; PBO to RZB: 87.0–90.9%), and HAQ-DI (RZB: 87.0–90.8%; PBO to RZB: 82.6–84.3%) (**Figure 1**). In KEEPsAKE 2, similarly high percentages of RZB and PBO to RZB-treated patients maintained MCIDs in PtGA (RZB: 77.0–80.5%; PBO to RZB: 78.4–84.0%), Pain (RZB: 77.2–85.6%; PBO to RZB: 84.3–94.2%), and HAQ-DI (RZB: 74.0–83.8%; PBO to RZB: 89.6–95.8%). At Week 100, 77.6–88.9% and 73.5–95.5% of RZB and PBO to RZB-treated patients, respectively, in KEEPsAKE 1 maintained MCIDs in FACIT-Fatigue, SF-36 PCS, BASDAI, morning stiffness, and WPAI; similar results were demonstrated in KEEPsAKE 2 (RZB: 73.1–96.4%; PBO to RZB: 76.2–100.0%) (**Table 1**).

Conclusion: In KEEPsAKE 1 and 2 trials, the majority of RZB-treated patients with PsA who achieved MCID in PROs at Week 24 maintained responses through Week 100. Achieving MCIDs at Week 24 is associated with sustained and clinically meaningful changes in HRQoL.

Figure 1. Percentage of patients who maintained MCIDs through Week 100 in patients who achieved MCIDs at Week 24 in PtGA, Pain, and HAQ-DI in KEEPsAKE 1



HAQ-DI, Health Assessment Questionnaire – Disability Index; MCID, minimal clinically important difference; PBO, placebo; PtGA, Patient's Global Assessment; RZB, risankizumab.

Table 1. Percentage of patients who achieved MCIDs at Week 24 and maintained MCIDs at Weeks 52 and 100

n (%)	KEEPsAKE 1				KEEPsAKE 2			
	Week 52		Week 100		Week 52		Week 100	
	RZB	PBO to RZB	RZB	PBO to RZB	RZB	PBO to RZB	RZB	PBO to RZB
FACIT-Fatigue	220 (84.6)	155 (79.9)	197 (82.4)	151 (83.0)	82 (81.2)	67 (90.5)	75 (77.3)	63 (91.3)
SF-36 PCS	275 (91.1)	205 (90.7)	241 (87.6)	183 (87.6)	102 (79.7)	77 (87.5)	95 (77.2)	74 (89.2)
BASDAI[a]	46 (90.2)	36 (90.0)	38 (86.4)	31 (88.6)	18 (69.2)	11 (91.7)	22 (91.7)	12 (100.0)
Morning stiffness	50 (94.3)	47 (92.2)	40 (88.9)	42 (95.5)	22 (77.4)	19 (95.0)	27 (96.4)	18 (94.7)
WPAI	73 (85.9)	36 (73.5)	60 (80.0)	36 (73.5)	19 (73.1)	23 (92.0)	21 (80.8)	17
Presenteeism[b]	78 (89.7)	39 (72.2)	66 (77.6)	58 (81.7)	18 (64.3)	21 (87.5)	19 (73.1)	(81.0)
Work Productivity Loss[b]	180 (80.0)	133 (84.2)	163 (80.3)	116 (80.6)	60 (70.6)	53 (85.5)	62 (77.5)	16 (76.2)
Activity Impairment								48 (84.2)

[a]Patients with Spondylitis only; [b]Reported for employed patients.

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POS1525

BIOLOGICS THERAPIES FOR PSORIASIS AND PSORIASIS ARTHRITIS AFFECT ON FUTURE RISK FOR DEVELOPING MAJOR ADVERSE CARDIOVASCULAR EVENTS

Keywords: Cardiovascular disease, bDMARD, Psoriatic arthritis

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Background: Major adverse cardiovascular events (MACE) are some of the numerous comorbidities associated with psoriasis (PsO) and psoriasis arthritis (PsA). Previous studies addressed the contribution of sufficient anti-inflammatory therapy for PsO and PsA in decreasing MACE incidence [1,2].
Objectives: Assessing the risk of developing MACE in patients with pre-existing PsO treated with different treatment regimens; topical treatment, conventional disease-modifying anti-rheumatic drugs (cDMARDs), and biologic disease-modifying anti-rheumatic drugs (bDMARDs) which had not previously studies sufficiently on real-world data.
Methods: We conducted a retrospective exploratory study with real-world data using the databases of the third largest Israeli health maintenance organization, 'Meuhedet' which covers approximately 1,300,000 subjects. All patients of 'Muehedat' diagnosed with PsO from January 2000 until January 2020 were included in the analysis. Overall, 61,003 patients with PsO were detected. In addition, each PsO patient was paired with four control subjects by gender, age, and ethnicity (general, Arabic, or Orthodox). We defined PsO and PsA according to physicians' diagnoses. MACE included patients with either cerebral vascular accident (CVA), ischemic heart disease (IHD), or peripheral artery disease (PVD). The date of the MACE incident was defined by the first occurrence of one of the diagnoses. We classified the patients diagnosed with PsA into a separate group; thus, patients were categorized according to their diagnosis (control, PsO or PsA). Furthermore, we analyzed the patients by the most advanced treatment prescribed to the patient; sub-grouped 1- topical therapy, sub-grouped 2 - cDMARDs (methotrexate or sulfasalazine), sub-grouped 3 - bDMARDs (anti-TNF, anti-IL17, or anti-IL12/23 agents) (**Table 1**). The Incident cases of MACE were analyzed according to the different lines of therapy mentioned above. In addition, Time-dependent Cox proportional hazard models were used to evaluate the adjusted risk of developing MACE by treatment group.
Results: 287,392 patients were included after exclusion by the defined criteria, contributing a total of 2,997,001 patient-years. Adjusted Cox proportional hazards regression analysis showed that the risk of developing MACE in PsO patients treated with topical treatment and those treated with cDMARDs was significantly higher in comparison to controls (Topical, HR: 1.1, CI: 1.02 - 1.1, p-value: <0.001; cDMARDs, HR: 1.2, CI: 1.0 - 1.5, p-value: 0.05). Yet, the risk of developing MACE in PsO patients treated with bDMARDs was not significantly different compared to controls (HR: 1.1, CI: 0.82 - 1.5, p-value: 0.55). On the contrary, the risk of developing MACE in all treatment groups of PsA patients was found to be significantly higher in comparison to controls (Topical, HR: 1.6, CI: 1.45 - 1.7, p-value: <0.001; cDMARDs, HR: 1.4, CI: 1.2 - 1.6, p-value: <0.001, bDMARDs, HR: 1.6, CI: 1.35 - 1.8, p-value: <0.001) (**Figure 1**). This analysis was adjusted to gender, body mass index (BMI), age of PsO diagnosis, lifetime diagnosis of diabetes mellitus type 2 (DM2), dyslipidemia, hypertension (HTN), and chronic heart failure (CHF); notably, male gender, higher BMI, older age, DM2, dyslipidemia, HTN, and CHF were all associated with a greater risk of developing MACE.
Conclusion: Despite that the psoriasis and arthritis severity is higher in patients treated with bDMARDs treatment compared to those treated with cDMARDs and topical treatment alone, bDMARDs have a protective effect on the risk of developing PsA.

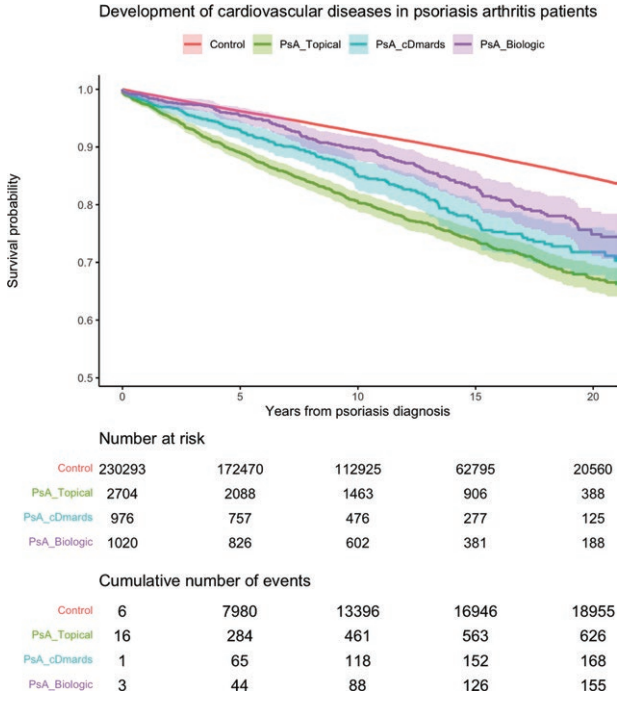


Figure 1.

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POS1526

TREATMENT EFFECTS OF IXEKIZUMAB AND ADALIMUMAB AT THE INDIVIDUAL DIGIT LEVEL WITH NAIL AND DISTAL INTERPHALANGEAL JOINT INVOLVEMENT IN PATIENTS WITH PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Clinical trials, bDMARD

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Background: The prevalence of nail disease in patients with psoriatic arthritis (PsA) ranges between 41% and 93% [1]. Psoriatic nail disease is intimately linked to adjacent distal interphalangeal joint (DIP) disease, and it is important to ascertain whether DIP-nail complex behaves differently under different biological therapies.
Objectives: The aim of this analysis was to comparatively assess the effect of ixekizumab (IXE) and adalimumab (ADA) at the individual digit level in improving nail and joint disease, in patients with PsA and concomitant nail involvement.
Methods: This post hoc analysis included patients from SPIRIT-H2H (NCT03151551) treated with either IXE or ADA who had baseline nail disease (NAPSI total score >0) and DIP involvement in at least one simultaneous digit, with either tenderness, swelling or both, at the individual digit level for each hand. Proportions of patients having a NAPSI total score >0 and proportions of patients having DIP involvement (tenderness or swelling) were evaluated at baseline and Week 24; post-baseline assessments were compared between treatment arms using Fisher's exact test.
Results: Of the intent-to-treat population of SPIRIT-H2H (N=566), 354 patients had a NAPSI total score >0 and DIP involvement (swelling or tenderness) in at least 1 digit simultaneously at baseline (IXE, N=186 and ADA, N=168). Of these patients, significantly fewer IXE- vs. ADA-treated patients had a NAPSI total score of > 0 at Week 24 (p<0.05 for 9/10 digits; Table 1) and numerically fewer IXE- vs. ADA treated patients had DIP involvement at Week 24 across all 10 digits (p<0.05 for 4/10 digits; Table 1). Numerically fewer IXE- vs. ADA-treated patients had joint tenderness at Week 24. A similar pattern of improvement was seen out to Week 52 (Table 1).
Conclusion: In this analysis, in patients from SPIRIT-H2H with psoriatic arthritis who had nail involvement and DIP involvement at baseline, patients treated with IXE had less nail involvement, less DIP involvement and less tenderness compared to those treated with ADA at Week 24.

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Table 1. The proportion (%) of patients with (A) NAPSI >0 and (B) DIP involvement (tenderness or swelling) at Week 24 at the individual digit level among patients treated with either IXE (N=186) or ADA (N=168) who had NAPSI >0 and distal interphalangeal joint involvement at baseline. *p<0.05, †p<0.1, ‡p<0.001 vs ADA, Fisher's Exact test p-value.

	Left Hand				Right Hand					
	Little	Ring	Middle	Fore	Thumb	Thumb Fore	Middle	Ring	Little	
NAPSI >0 (%)										
Week 24										
IXE Q4W	17.0*	17.6*	14.2†	15.3†	11.4†	15.3†	13.6†	15.3*	15.9†	13.1
ADA Q2W	27.9	27.9	25.5	27.3	23.6	27.3	25.5	26.7	26.7	21.2
p-value*	**0.0191**	**0.0276**	**0.0097**	**0.0079**	**0.0039**	**0.0079**	**0.0062**	**0.0113**	**0.0169**	0.0602
Week 52	10.9	10.3	10.9	10.3	9.1	12.1	9.7	10.9	7.3	10.9
IXE Q4W	21.4	16.6	15.9	17.2	14.5	19.3	17.2	19.3	12.4	14.5
ADA Q2W										
p-value*	**0.0128**	0.1304	0.2400	0.0958	0.1547	0.0859	0.0641	0.0538	0.1770	0.3924
DIP involvement (%) Week 24										
IXE Q4W	10.7	11.3	15.8	19.8	17.5	15.8	20.9	21.5	11.9	10.7
ADA Q2W	15.2	20.0	25.5	27.3	24.8	22.4	28.5	30.9	17.0	18.8
p-value*	0.2590	**0.0357**	**0.0319**	0.1249	0.1115	0.1307	0.1312	**0.0495**	0.2168	**0.0459**
Week 52	1.2	2.4	7.2	5.4	1.2	1.8	4.2	4.2	4.8	1.2
IXE Q4W	2.8	4.8	8.3	5.5	6.2	4.1	7.6	9.7	4.1	4.1
ADA Q2W										
p-value*	0.4228	0.3578	0.8322	1.0000	**0.0273**	0.3128	0.2305	0.0703	1.0000	0.1521

Data are presented as proportion of patients (%). *Fisher's Exact test p-value. Abbreviations: ADA, adalimumab; IXE, ixekizumab.

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POS1527

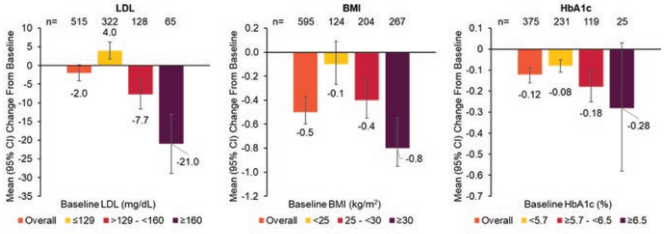
EFFECTS OF APREMILAST ON CHANGES IN CARDIOMETABOLIC PARAMETERS BY DIABETES AND OBESITY STATUS IN PATIENTS WITH PSORIATIC ARTHRITIS

Keywords: Cardiovascular disease, Comorbidities, Psoriatic arthritis

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Background: The prevalence of cardiometabolic diseases including obesity and diabetes are higher in patients with psoriatic arthritis (PsA) than those without PsA. Apremilast (APR) is associated with weight loss and a reduction in HbA1c.
Objectives: To evaluate the effects of APR on cardiometabolic parameters over 52 weeks in patients with active PsA from 5 pooled phase 3 trials.
Methods: Data from 5 randomized, placebo-controlled, phase 3 studies (PALACE 1–4 and ACTIVE) in patients with active PsA receiving APR 30 mg BID were pooled. Included in this analysis were patients who were treated with APR for 52 weeks. Changes from baseline to Week 52 in low and high density lipoprotein (LDL, HDL), body mass index (BMI), and HbA1c were assessed and stratified by baseline level of these parameters and Week 52 disease activity (Clinical Disease Activity Index for Psoriatic Arthritis [cDAPSA] remission/low disease activity [REM/LDA] vs moderate/high disease activity [ModDA/HDA]).
Results: Data from 781 patients with PsA who received APR were pooled (mean age: 50 years, 55% female). Mean LDL was 119.6 mg/dL in the overall population at baseline and decreased by 2.0 mg/dL on average at Week 52 (**Figure 1**). The greatest decreases in LDL were seen in patients with the highest LDL levels at baseline (**Figure 1**). Similar favorable changes in HDL were observed. A total of 34/65 (52.3%) moved from the high LDL category (≥160 mg/dL) at baseline to borderline (>129 – <160 mg/dL) or normal (≤129 mg/dL) at Week 52 and 49/128 (38.3%) changed from borderline high to normal LDL levels (**Table 1**). Mean BMI was 30.3 kg/m^2 in the overall population at baseline and decreased by 0.5 kg/m^2 at Week 52 (**Figure 1**). A trend was again seen where patients with higher BMI at baseline saw greater decreases in BMI at Week 52 (**Figure 1**). Additionally, 24/267 (9.0%) patients changed from the obese category (≥30 kg/m^2) to the overweight category (25 – <30 kg/m^2) and 25/204 (12.3%) patients changed from the overweight category to the normal category (<25 kg/m^2) (**Table 1**). Mean HbA1c was 5.6% in the overall population at baseline and decreased by 0.1% at Week 52 (**Figure 1**). Greater changes in HbA1c were seen in patients who were pre-diabetic (HbA1c 5.7% – <6.5%) and diabetic (HbA1c ≥6.5%) at baseline vs those who had normal HbA1c (HbA1c <5.7%) (**Figure 1**). Furthermore, 60/119 (50.4%) patients who had prediabetes changed to normal HbA1c levels and 10/25 (40.0%) moved from diabetes to pre-diabetes (**Table 1**). Results were consistent across Week 52 cDAPSA psoriatic disease activity subgroups; greater changes in cardiometabolic parameters were seen in patients with higher baseline LDL, BMI, or HbA1c regardless of whether REM/LDA was achieved at Week 52.
Conclusion: APR treatment was associated with improvement in cardiometabolic parameters observed across psoriatic disease activity groups. The most favorable changes were seen in patients with high LDL, low HDL, obesity, or diabetes at baseline. These findings suggest that those with a high burden of comorbid cardiometabolic diseases and active PsA treatment may gain benefit beyond joint disease with APR. However, these findings require larger, prospective studies.
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Disclosure of Interests: Philip J Mease Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, and UCB – speakers bureau, Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Inmagene, Janssen, Novartis, Pfizer, Sun, and UCB – grant/research support and consultant; Acelyrin, Aclaris, Boehringer Ingelheim, GlaxoSmithKline, and Moonlake – consultant, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Eli

Figure. Changes in Cardiometabolic Parameters from Baseline to Week 52 by Baseline Subgroup



Includes patients who were treated with APR for 52 weeks and had both baseline and Week 52 values.

Table. LDL, BMI, and HbA1c Shift from Baseline to Week 52

	Week 52 LDL (mg/dL), n/N (%)		
Baseline LDL (mg/dL)	Normal (≤129)	Borderline (>129 – <160)	High (≥160)
Normal (≤129)	274/322 (85.1)	41/322 (12.7)	7/322 (2.2)
Borderline (>129 – <160)	49/128 (38.3)	63/128 (49.2)	16/128 (12.5)
High (≥160)	13/65 (20.0)	21/65 (32.3)	31/65 (47.7)
	Week 52 BMI (kg/m²), n/N (%)		
Baseline BMI (kg/m²)	Normal (<25)	Overweight (25 – <30)	Obese (≥30)
Normal (<25)	111/124 (89.5)	13/124 (10.5)	0/124 (0.0)
Overweight (25 – <30)	25/204 (12.3)	163/204 (79.9)	16/204 (7.8)
Obese (≥30)	0/267 (0.0)	24/267 (9.0)	243/267 (91.0)
	Week 52 HbA1c (%), n/N (%)		
Baseline HbA1c (%)	Normal (<5.7)	Pre-diabetes (5.7 – <6.5)	Diabetes (≥6.5)
Normal (<5.7)	224/231 (97.0)	6/231 (2.6)	1/231 (0.4)
Pre-diabetes (5.7 – <6.5)	60/119 (50.4)	53/119 (44.5)	6/119 (5.0)
Diabetes (≥6.5)	1/25 (4.0)	10/25 (40.0)	14/25 (56.0)

Includes patients who were treated with APR for 52 weeks.

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POS1528

PREDICTION OF LOW DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH SECUKINUMAB IN REAL WORLD – DATA FROM THE GERMAN AQUILA STUDY

Keywords: Artificial Intelligence, Real-world evidence, Psoriatic arthritis

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Background: Secukinumab (SEC) proved to be an effective treatment for patients with psoriatic arthritis (PsA) in previous randomized clinical trials [1]. There is only limited knowledge on prediction of low disease activity (LDA) and treatment strategy in PsA patients under SEC treatment in routine clinical care.
Objectives: Using real-world data from the German non-interventional study AQUILA [2], the main objectives were (1) to predict LDA in individual PsA patients treated with SEC through machine learning methods and (2) to identify the most important predictors and their influence on the prediction using explainable artificial intelligence (XAI).
Methods: Data of 1041 PsA patients from the AQUILA study were used. Thirty-three demographic, clinical and treatment parameters at baseline (BL) served as input data to develop prediction models. LDA was defined as physician global assessment (PhGA) ≤ 2 at week (w) 16 (+/- 6 w). Samples were divided into training (70%) and validation (30%) cohorts. Ten different prediction models were applied and compared. Model performance was measured using area under the receiver operating characteristic curve (AUROC) which represents the probability that a randomly selected patient with LDA will have higher prediction to achieve LDA than a patient with moderate/high disease activity. Additionally, sensitivity and specificity of the prediction model were computed and express the proportion of correctly identified patients who reach or don't reach LDA at w16, respectively. Shapley XAI estimated importance and impact of each predictor based on how it affected the change in individual prediction [3].
Results: The most influencing predictor was patient global assessment (PGA) at BL, followed by PhGA, number of pretreatments with biologics, tender joint count and age (Figure 1 A). AUROC of the best prediction model was 0.68 in validation cohort. Sensitivity and specificity were 0.62 and 0.64, respectively. Applied XAI approach showed that lower BL values of all main predictors have higher probability of reaching LDA at w16. The highest probability was evident in biologic-naive patients (Figure 1 A). The approach also provided visual explanations of patient-individual predictions: Variables with values shown in green color increased probability of reaching LDA at w16, whereas red ones showed the opposite effect (Figure 1 B).
Conclusion: A promising prediction model accuracy of LDA in PsA patients treated with SEC could be reached and validated. Identified main predictors at BL, such as PGA and number of pretreatments with biologics, and their direction of influence on the prediction mostly match the existing clinical knowledge [4]. The analysis showed that XAI can provide useful clinical insights in patient-individual predictions, potentially guiding PsA treatment decisions in future.

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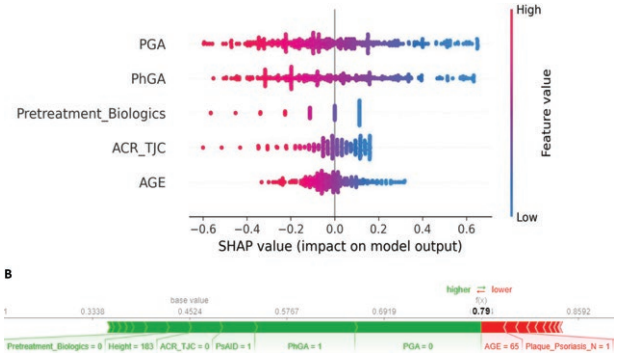


Figure 1: Main resultsA: Main predictors at baseline and their direction of influence based on Shapley values [3]**B**: Explanation of patient-individual prediction of 79% using baseline data-American College of Rheumatology (ACR), TJC (tender joint count), patient global assessment (PGA), physician global assessment (PhGA), Psoriatic Arthritis Impact of Disease (PsAID), Shapley Additive exPlanations (SHAP)

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POS1529

DOMAINS IMPACTING MINIMAL DISEASE ACTIVITY NON-ACHIEVEMENT IN PATIENTS WITH PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO TNFI RECEIVING GUSELKUMAB (COSMOS)

Keywords: Clinical trials, Psoriatic arthritis, Outcome measures

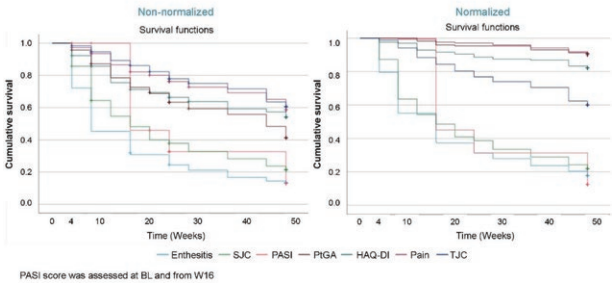
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Background: Sustained minimal disease activity (MDA) is achieved by a minority of patients (pts) receiving biologics for psoriatic arthritis (PsA) [1]. Pt-reported MDA domains are less frequently achieved than physician-reported domains [2,3]. Here, we assessed MDA achievement in pts with PsA and inadequate response to 1–2 tumour necrosis factor inhibitors (TNFi-IR).
Objectives: Identify PsA disease domains and factors contributing to the lack of MDA achievement at Week (W)48 for TNFi-IR PsA pts treated with guselkumab (GUS) using data from the Phase 3b COSMOS trial.
Methods: In COSMOS, adults with active PsA (swollen/tender joint counts [SJC/TJC] each ≥3) and TNFi-IR were randomized 2:1 to subcutaneous GUS 100 mg or placebo (PBO) at W0, W4, then every 8 weeks. PBO pts crossed over to GUS at W16 (early escape) or W24 (planned). MDA was defined as fulfilment of ≥5/7 domains: tender entheses (Leeds Enthesitis Index [LEI]; 0–6) ≤1; Health Assessment Questionnaire – Disability Index (HAQ-DI; 0–3) ≤0.5; pt pain (0–100) ≤15; Psoriasis Area and Severity Index. (PASI; 0–72) ≤1; Pt Global Assessment (PtGA; 0–100) ≤20; SJC (0–66) ≤1; and. TJC (0–68) ≤1. Fibromyalgia (pFM) was defined at baseline (BL) using TJC minus SJC ≥7 as a proxy [3]. A longitudinal trajectory of achieving each MDA domain through W48 was derived (non-responder imputation). Time to achieving each domain was assessed with. Kaplan–Meier analyses; to account for differences in scales and domain strictness, scores were also normalized to SJC (0–66) scale. Response predictors (for pts not meeting each MDA domain criteria at BL) were identified using multivariate regression for time to achievement (Cox proportional hazards) and W48 achievement (logistic) of MDA.
Results: GUS pts (n=189) showed improvement from BL in all MDA domains, with overall W24/48 response rates (%) of: LEI (74.5/79.8), HAQ-DI (26.1/37.0), pt pain (14.7/30.6), PASI (66.8/81.5), PtGA (24.5/39.9), SJC (46.2/63.0) and TJC (14.7/28.3) respectively. Times to achievement of minimal scores for LEI, SJC and PASI were faster than for PtGA, HAQ-DI, pt pain and TJC for native-scale scores; when normalized, PtGA, HAQ-DI and pt pain showed a slower response (**Figure 1**). Higher BL HAQ-DI and worse fatigue (lower functional assessment of chronic illness therapy [FACIT]-fatigue score) were significantly associated with longer time to HAQ-DI ≤0.5; these factors plus older age predicted W48 non-achievement of HAQ-DI ≤0.5 (**Table 1**). Worse BL pt pain and fatigue were significant predictors of longer time to pt pain ≤15; these factors plus pFM predicted W48 non-achievement of pt pain ≤15. Worse BL fatigue was also significantly associated with longer time to PtGA ≤20 and W48 non-achievement of PtGA ≤20. Higher TJC, methotrexate (MTX) use and no pFM at BL were significantly associated with longer time to TJC ≤1; higher BL TJC, MTX and older age predicted W48 non-achievement of. TJC ≤1.
Conclusion: GUS provided sustainable improvement in all MDA domains through W48. Physician-reported domains (LEI, PASI and SJC) were achieved faster than pt-driven domains (PtGA, HAQ-DI, pt pain and TJC). BL domain scores, worse fatigue and MTX use (for TJC only) were inversely correlated with MDA in the refractory domains.

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Figure 1. Time to achieve MDA for each domain with GUS treatment



PASI score was assessed at BL and from W16

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Table 1. Predictors of time to achievement and achievement of pt-reported MDA domains at W48 in GUS pts

	BL variable	HAQ-DI ≤0.5	Pt pain ≤15	PtGA ≤20	TJC ≤1
Time to achievement HR (95% CI)	FACIT-fatigue	1.0 (1.0–1.1)†	1.0 (1.0–1.1)†	1.0 (1.0–1.1)‡	
	HAQ-DI	0.3 (0.2–0.6)‡			
	Pt pain		1.0 (1.0–1.0)‡		
	MTX use				0.6 (0.4–0.9)*
	pFM presence				1.8 (1.0–3.2)*
	TJC				0.9 (0.9–1.0)‡
Achievement at W48 OR (95% CI)	Age	1.0 (0.9–1.0)*			1.0 (1.0–1.0)*
	FACIT-fatigue	1.1 (1.0–1.1)†	1.1 (1.0–1.1)†	1.1 (1.0–1.1)‡	
	HAQ-DI	0.2 (0.1–0.5)†			
	Pt pain		1.0 (1.0–1.0)†		
	MTX use				0.4 (0.2–0.8)†
	pFM presence		0.5 (0.3–1.0)*		
	TJC				0.9 (0.9–1.0)‡

CI, confidence interval; HR, hazard ratio; OR, odds ratio*P<0.05; †P<0.01; ‡P<0.001

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POS1530

FACTORS ASSOCIATED WITH THE RETENTION OF SECUKINUMAB (SEC) IN PATIENTS WITH PSORIATIC ARTHRITIS (PSA) IN REAL WORLD PRACTICE: RESULTS FROM THE RETROSPECTIVE FORSYA STUDY

Keywords: Psoriatic arthritis, Real-world evidence, Prognostic factors

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Background: While data on real-life retention of SEC in patients (pts) with PsA is accumulating, there are few data on predictive factors of this retention.
Objectives: To assess if objective signs of inflammation (OSI) were predictive of SEC retention at 1 year.
Methods: French retrospective study collecting between Oct 2019 and May 2022 data from PsA pts a) having initiated and received at least one dose of SEC between Aug 2016 and Aug 2018 (cohort 1) and Sept 2018 and Nov 2020 (cohort 2) (b) with at least a 1 year follow-up period. Retention rate of SEC at 1 year was estimated by the Kaplan Meier (KM) method. OSI were defined by at least one of the following within the 3 months before initiation of SEC: CRP> N, confirmed

clinical dactylitis, confirmed clinical synovitis or ultrasonography power-Doppler positive synovitis. The following a priori baseline preselected factors of SEC retention at 1 year (cohort, ≥1 OSI, age, sex, BMI, smoking, axial feature, history of arthritis or synovitis/ psoriasis/ uveitis/ IBD, diagnostic delay, disease duration, SEC line (L) of biologic/targeted synthetic (b/ts)DMARD, SEC dose, csDMARD/ corticosteroids at initiation, history of fibromyalgia/ depression) were analyzed by cox model regression. Only variables with <20% missing data were included in the model after multiple imputation and stepwise selection (significance level for entering variables = 20%; for removing variables = 10%). OSI and cohort variables were forced into the model whatever their significance level or rate of missing data.

Results: 842 pts (male: 38.6%, mean age: 52.5 ± 12.3 years, mean disease duration: 8.7 ± 8.5 years) from 50 centers were included in the analysis. At initiation of SEC, 63.0% of pts had ≥ 1 OSI and respectively 15.8%, 24.2% and 60.0% were in 1st, 2nd and ≥ 3rd (L) of b/ts DMARD. The 1 year retention rate for SEC was 64% [95%CI: 61%-68%] and was numerically greater in 1st L vs 2nd and ≥3rd L (77% [69%-84%], 65% [59-72%], 61% [57%-66%] respectively). The 1 year retention rates of SEC were 65% [61%-69%] and 69% [62%-75%] respectively for OSI+ and OSI- at SEC initiation. In multivariate analysis after adjustment, OSI was not identified as predictive of SEC discontinuation at 1 year (HR=1.19 l0.93;1.52], p=0.169). The others predictive factors identified are listed in Table 1.

Table 1. Predictive factors of SEC discontinuation at 1 year identified by multivariate cox regression analysis

Predictive factors (* reference)		SEC retention at 1 Year$	HR*adjusted*# [95% CI]	p vs ref	p type III
Secukinumab treatment line	1st L (N=129)*	77%			0.011
	2nd L (N=199)	65%	1.61 [1.05; 2.48]	0.030	
	≥ 3rd L (N=499)	61%	1.82 [1.23; 2.69]	0.003	
Age	<= 40 (N=132) (ref)	60%			0.085
	]40;60] (N=474)	66%	0.71 [0.52; 0.98]	0.040	
	> 60 (N=221)	66%	0.69 [0.48; 0.99]	0.045	
csDMARD at SEC initiation	No (N=501)*	63%			0.034
	Yes (N=326)	69%	0.77 [0.60; 0.98]	0.034	
Corticosteroids at SEC initiation	No (N=708)*	68%			<.001
	Yes (N=119)	54%	1.71 [1.26; 2.31]	<.001	
History or suspicion of fibromyalgia	No (N=753)*	66%			0.016
	Yes (N=74)	56%	1.57 [1.09; 2.26]	0.016	

Interpretation for predictor: HR> 1: the hazard of discontinuation at 1 year is X times higher in category vs reference.$ without imputation for missing data# adjusted on cohort and OSI

Conclusion: In this large cohort of PsA patients, the overall retention rate of SEC was 64% at 1 year in daily practice. Previous exposure to b/tsDMARD, concomitant corticosteroids at initiation of SEC and history of fibromyalgia were associated with an increased risk of SEC discontinuation at 1 year while concomitant csDMARD at initiation of SEC and age > 40 year with a decreased risk.

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POS1531

GUSELKUMAB, AN IL-23P19 SUBUNIT–SPECIFIC MONOCLONAL ANTIBODY, BINDS CD64+ MYELOID CELLS AND POTENTLY NEUTRALISES IL-23 PRODUCED FROM THE SAME CELLS

Keywords: Cell biology, Psoriatic arthritis, Cytokines and chemokines

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Background: Monoclonal antibodies targeting the interleukin (IL)-23p19 subunit are effective in the treatment of psoriatic disease but have different molecular attributes that may translate to differences in clinical efficacy. Within this class, guselkumab (GUS) is a fully human IgG1 monoclonal antibody with a native Fc region, while risankizumab (RIS) is a humanised IgG1 antibody with a mutated Fc region. Binding of these therapeutic antibodies to Fcγ receptor (FcγR) I, also known as CD64, is of interest, as $CD64^+$ IL-23-producing myeloid cells are increased within inflamed tissue of patients with psoriatic disease [1]. Furthermore, the incidence and prevalence of psoriatic arthritis increases with the severity of psoriasis [2], and joint disease activity is positively correlated with frequency of peripheral $CD64^+$ monocytes [3].

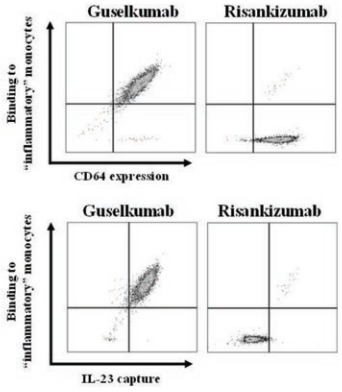
Objectives: Functional characteristics of the antigen-binding and Fc regions of GUS and RIS were compared.

Methods: IL-23 binding affinity was evaluated *in vitro* using a kinetic exclusion assay (KinExA) and surface plasmon resonance. *In vitro* cellular potency was measured by impact on IL-23-induced signal transducer and activator of transcription 3 (STAT3) phosphorylation in human peripheral blood mononuclear cells. Binding of GUS and RIS to FcγRs was assessed in cells transfected with individual FcγRs. Primary human "inflammatory" monocytes differentiated with granulocyte-macrophage colony-stimulating factor and interferon-γ (IFN-γ) were induced to produce IL-23 via toll-like receptor stimulation and used to assess binding of GUS and RIS to CD64 and potential capture of endogenously secreted IL-23 by flow cytometry. The potential for GUS binding to CD64 on IFN-γ primed monocytes to trigger activation was assessed using a 41-plex cytokine bead assay.

Results: GUS and RIS displayed comparable picomolar binding affinity for IL-23 and equivalent high potency for inhibiting IL-23-induced STAT3 phosphorylation. GUS showed strongest binding to CD64 compared with other FcγRs, whereas RIS had negligible binding to any FcγR. GUS, but not RIS, showed dose-dependent Fc-mediated binding to CD64 on primary human "inflammatory" monocytes. Moreover, CD64-bound GUS was able to simultaneously capture IL-23 endogenously secreted from the same cells (**Figure 1**). GUS binding to CD64 on monocytes did not induce cytokine production.

Conclusion: GUS, but not RIS, simultaneously binds $CD64^+$ myeloid cells via its Fc region and neutralises IL-23 with high affinity and potency. Our *in vitro* data suggest a mechanistic benefit through enrichment of GUS within inflamed tissue of patients with psoriatic disease, where $CD64^+$ IL-23-producing myeloid cells are increased, such that GUS potently neutralises IL-23 at its source of production. These findings may contribute to differences in clinical-therapeutic profiles between antibodies.

Figure. Guselkumab binds to the surface of CD64⁺ "inflammatory" monocytes and captures IL-23 at its source of production. Representative flow cytometry dot plots showing that guselkumab, but not risankizumab, binds to the surface of "inflammatory" monocytes, correlating with CD64 expression (*top panels*), and simultaneously captures IL-23 endogenously secreted from the same cells (*bottom panels*).



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POS1532 WHAT IS THE REAL IMPACT OF DEPRESSION ON CLINICAL RESPONSE TO THERAPY IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS?

Keywords: Psoriatic arthritis, bDMARD

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Background: The estimated prevalence of depression in patients with psoriatic arthritis (PsA) ranges from 20 to 30% and is higher than in the general population. The relationship between depression, systemic inflammation, disease activity and response to therapy in PsA patients remains unclear and under investigation. Patients with depression seems to have overexpression of pro-inflammatory cytokines involved in the pathogenesis of PsA, such as interleukin (IL)-6, IL-17 and tumor necrosis factor-alpha (TNF-α). On the other hand, depression leads to pain sensitization and plays a pivotal role in the shaping of pain responses and patient reported outcome measures (PROMs).

Objectives: To compare the response to therapy in PsA patients with or without depression, treated with biologic disease-modifying antirheumatic drug (bDMARD) for the first time.

Methods: An observational monocentric retrospective cohort study of patients with PsA (according to CASPAR criteria) registered in the national database (Reuma.pt), who started their first bDMARD between June 2010 and December 2021, was conducted. Demographic data, disease activity data, functional parameters and response to therapy 12 months after the start of bDMARD were collected. Depression was defined according to Hospital Anxiety and Depression scale (HADS). In patients who didn't fill out the questionnaire, depression was identified by consulting medical records. For patients with peripheral involvement, DAS28 (4V), CDAI and SDAI were collected at baseline. For patients with axial involvement, Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-reactive protein (CRP) was also collected. American College of Rheumatology (ACR) response criteria, change in Ankylosing Spondylitis Disease Activity Score (ΔASDAS), BASDAI50 response, change in HAQ (ΔHAQ) and EULAR response (good, moderate or no response) were calculated at month 12. Chi-square test and t-test were conducted (for categorical and normally distributed continuous variables, respectively). A p-value <0.05 was considered statistically significant.

Results: 129 PsA patients were included (66 females, 51.2%). The mean age was 52.2±10.9 years and the disease duration was 13.9±7.2 years. All patients were treated with bDMARD, 122 (94.6%) with anti-TNFα agents and 7 (5.4%) with anti-IL-17 agents. Thirty-two (24.8%) patients had depression and the mean value of HADS was 10.0±3.8. The majority of these patients were treated with antidepressants (n=25, 78.1%). Patients with and without depression had similar sociodemographic characteristics, except for gender, since there were significantly more females in the depression group (p<0.001). These 2 groups had similar disease activity scores at baseline. Patients with depression and peripheral involvement had a significantly lower ACR20/50/70 responses (p=0.001, p=0.002 and p=0.001 respectively) after 12 months of therapy. Also, these patients had a significantly poorer EULAR response (p=0.002). Furthermore, patients with depression and axial involvement had a lower Δ-ASDAS (p=0.03) and a lower BASDAI50 response (p=0.06), after 12 months of therapy. Switch due to ineffectiveness in the first 12 months was higher in patients with depression (p=0.002).

Conclusion: In our study, depression was associated with poorer response to therapy and higher bDMARD discontinuation rates. Depression might be associated with a pro-inflammatory state but also has a close relationship with chronic widespread pain which can influence some composite disease activity measures. Clinical judgement of the degree of disease activity, using objective measures of disease activity, is important in patients with depression, in order to avoid inappropriate escalation of therapy. Furthermore, recognition and treatment of depression in patients with PsA are crucial, as this might improve their quality of life and also their ability to manage their rheumatic disease.

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POS1533

BIMEKIZUMAB TREATMENT RESULTED IN CLINICALLY MEANINGFUL IMPROVEMENTS IN THE PSORIATIC ARTHRITIS IMPACT OF DISEASE-12 (PSAID-12) SCORES USING POOLED RESULTS FROM TWO PHASE 3 TRIALS IN PATIENTS WITH PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Patient reported outcomes, Clinical trials

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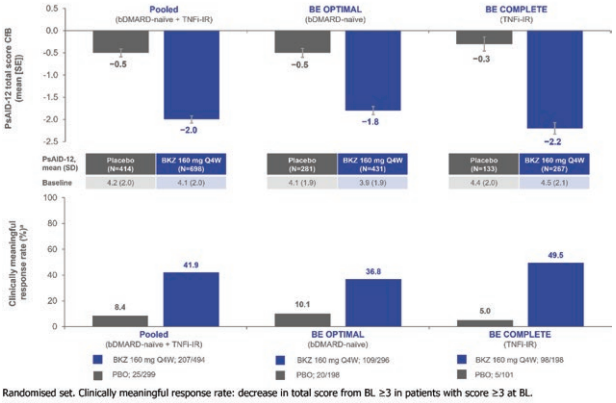
Background: The Psoriatic Arthritis (PsA) Impact of Disease-12 (PsAID-12) questionnaire assesses PsA impact from the patient (pt) perspective [1]. Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17A and IL-17F, has shown superior efficacy vs placebo (PBO) and tolerability to 16 weeks (wks) in pts with PsA [2,3].
Objectives: To assess the efficacy of BKZ from the pt perspective, over 16 wks of treatment, using data from two phase 3 trials.
Methods: Analysis of pts with PsA randomised to subcutaneous BKZ 160 mg every 4 wks vs PBO in BE OPTIMAL (NCT03895203, N=712, biologic DMARD-naïve pts) and BE COMPLETE (NCT03896581, N=400, tumour necrosis factor alpha inhibitor-inadequate responders). PsAID-12 total and single-item domain scores range from 0 to 10; higher scores indicate worse status. Change from baseline (CfB) data and clinically meaningful within pt improvement response (threshold: decrease of ≥3 from baseline [BL] when respective PsAID-12 score ≥3 at BL) for total and single-item domain scores were calculated. Missing data imputed using multiple imputation (continuous) and non-responder imputation (binary).
Results: Of 1,112 pts randomised to BKZ or PBO, 96.5% completed Wk 16. BL characteristics were generally similar between treatment groups within trials; mean age: 49.3 years, BMI: 29.5 kg/m^2, years since diagnosis: 7.2; 46.6% male. At BL, mean (SD) PsAID-12 total score: 4.1 (2.0) BKZ, 4.2 (2.0) PBO. Mean (SE) Wk 16 PsAID-12 total CfB: –2.0 (0.1) BKZ, –0.5 (0.1) PBO (**Table 1**). Clinically meaningful response rate for Wk 16 PsAID-12 total score: 41.9% BKZ, 8.4% PBO with results similar in both pt populations (**Figure 1**). Similar differences between BKZ and PBO results were found for single-item domain responders, for example Wk 16 PsAID-12 pain score response rate: 46.5% BKZ, 18.7% PBO; skin problem score response rate: 68.5% BKZ, 21.4% PBO (**Table 1**).
Conclusion: By Wk 16, over half of BKZ-treated pts reported clinically meaningful improvements in most PsAID-12 single-item domain scores assessing PsA-specific symptoms and impact. Results may support shared treatment decisions.

Table 1. Pooled BL scores, Wk 16 CfB and clinically meaningful response rate for PsAID-12 total and single-item domain scores

	Pooled Analysis (bDMARD-naïve + TNFi-IR)					
	PBO (N=414)			BKZ 160 mg Q4W (N=698)		
	BL mean (SD) [OC]	Wk 16 CfB mean (SE) [MI]	Response rate[a] % (n/N) [NRI]	BL mean (SD)[b] [OC]	Wk 16 CfB mean (SE) [MI]	Response rate[a] % (n/N) [NRI]
Total Score	4.2 (2.0)	–0.5 (0.1)	8.4 (25/299)	4.1 (2.0)	–2.0 (0.1)	41.9 (207/494)
Pain	5.6 (2.3)	–0.6 (0.1)	18.7 (69/369)	5.5 (2.3)	–2.3 (0.1)	46.5 (282/606)
Fatigue	4.8 (2.5)	–0.6 (0.1)	20.7 (68/328)	4.8 (2.6)	–1.8 (0.1)	44.7 (241/539)
Skin Problems	4.7 (2.8)	–0.4 (0.1)	21.4 (65/304)	4.7 (2.8)	–2.9 (0.1)	68.5 (348/508)
Work and/or Leisure Activities	4.6 (2.6)	–0.6 (0.1)	25.2 (79/314)	4.5 (2.6)	–2.2 (0.1)	53.6 (281/524)
Functional Capacity	4.8 (2.5)	–0.6 (0.1)	23.2 (76/328)	4.8 (2.5)	–2.3 (0.1)	53.0 (289/545)
Discomfort	4.5 (2.7)	–0.6 (0.1)	25.4 (75/295)	4.5 (2.6)	–2.3 (0.1)	58.1 (297/511)
Sleep Disturbance	3.8 (3.0)	–0.5 (0.1)	28.5 (70/246)	3.7 (2.8)	–1.6 (0.1)	54.7 (222/406)
Coping	4.0 (2.4)	–0.6 (0.1)	24.4 (70/287)	3.8 (2.4)	–1.7 (0.1)	53.6 (245/457)
Anxiety, Fear and Uncertainty	2.3 (2.5)	–0.2 (0.1)	33.3 (50/150)	2.2 (2.4)	–0.9 (0.1)	57.5 (134/233)
Embarrassment and/or Shame	2.6 (2.7)	–0.2 (0.1)	35.9 (60/167)	2.5 (2.7)	–1.6 (0.1)	70.6 (187/265)
Social Participation	2.9 (2.7)	–0.4 (0.1)	36.3 (70/193)	2.7 (2.6)	–1.5 (0.1)	61.0 (191/313)
Depression	1.4 (2.2)	0.0 (0.1)	28.7 (25/87)	1.3 (2.1)	–0.6 (0.1)	68.6 (96/140)

Randomised set. PsAID-12 scores range from 0–10; higher scores indicate a worse status. [a]Clinically meaningful response rate: decrease in score from BL ≥3 in patients with score ≥3 at BL. [b]N=697.

Figure. PsAID-12 total score CfB [MI] and clinically meaningful response rate [NRI] at Wk 16



Randomised set. Clinically meaningful response rate: decrease in total score from BL ≥3 in patients with score ≥3 at BL.

Abbreviations: bDMARD: biologic disease-modifying anti-rheumatic drug; BKZ: bimekizumab; BL: baseline; CfB: change from baseline; MI: multiple imputation; NRI: non-responder imputation; OC: observed case; PBO: placebo; PsAID-12: Psoriatic Arthritis Impact of Disease Questionnaire-12; Q4W: every 4 weeks; TNFi-IR: tumour necrosis factor alpha inhibitor-inadequate responder; SD: standard deviation; SE: standard error, Wk: week.

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POS1534

BIMEKIZUMAB MAINTAINED EFFICACY RESPONSES THROUGH 52 WEEKS IN BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG-NAÏVE PATIENTS WITH PSORIATIC ARTHRITIS WHO WERE RESPONDERS AT WEEK 16: RESULTS FROM BE OPTIMAL, A PHASE 3, ACTIVE-REFERENCE STUDY

Keywords: Psoriatic arthritis, Clinical trials

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Background: Given the chronic, long-term nature of psoriatic arthritis (PsA), sustaining high levels of disease control with treatment is important. Assessing the maintenance of response in patients (pts) that achieve treatment targets is of interest, particularly as pts can experience loss of response with long-term therapy [1]. Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated rapid, statistically significant and clinically meaningful joint and skin efficacy responses at Week (Wk) 16 versus placebo (PBO), in pts with PsA [2,3]. Responses were sustained to Wk 52 [4].

Objectives: To report the maintenance of response in joint and skin efficacy outcomes to 52 wks in BKZ-treated pts with PsA who were responders at Wk 16.

Methods: BE OPTIMAL (NCT03895203) included a 16-wk double-blind, PBO-controlled period, and a 36-wk active treatment-blind period. Biologic disease-modifying antirheumatic drug (bDMARD)-naïve pts were eligible if they had adult-onset, active PsA with ≥3 tender and ≥3 swollen joints, and ≥1 active psoriatic lesion and/or history of psoriasis. Pts were randomised 3:2:1 to subcutaneous BKZ 160 mg every 4 wks (Q4W), PBO or reference arm (adalimumab 40 mg every 2 wks). At Wk 16, PBO pts switched to subcutaneous BKZ 160 mg Q4W (PBO/BKZ). Maintenance of response is reported as the percentage of BKZ-treated pts who achieved a response at Wk 16, who maintained that response at Wk 52. Data are reported for pts randomised to subcutaneous BKZ 160 mg Q4W at baseline. Endpoints include American College of Rheumatology (ACR)20/50/70, Psoriasis Area and Severity Index (PASI)75/90/100, minimal and very low disease activity (MDA, VLDA), and Disease Activity Index for PSoriatic Arthritis (DAPSA) remission or low disease activity (REM+LDA; ≤14) and remission (REM; ≤4) responses. Wk 16 responders are reported using non-responder imputation (NRI); maintenance of response to Wk 52 is reported using NRI and observed case (OC) data. The number of treatment-emergent adverse events (TEAEs) to Wk 52 are reported for pts who received ≥1 dose of BKZ, including pts who switched from PBO to BKZ at Wk 16.

Results: At baseline, 431 pts were randomised to BKZ 160 mg Q4W; 217/431 (50.3%) had psoriasis affecting ≥3% body surface area (BSA). 414/431 (96.1%) pts completed Wk 16 and 383 (88.9%) completed Wk 52. The majority of pts who achieved responses at Wk 16 maintained their response at Wk 52, across a range of joint and skin outcomes (**Figure 1**). At Wk 16, 268 (62.2%), 189 (43.9%) and 105 (24.4%) pts achieved ACR20/50/70, respectively. Of those responders, ACR20/50/70 responses were maintained at Wk 52 by over 80% of pts: 88.4%, 86.8%, 82.9% (NRI); 92.9%, 91.1% and 87.9% (OC). Of 217 pts with psoriasis affecting ≥3% BSA at baseline, 133 (61.3%) and 103 (47.5%) achieved PASI90/100 at Wk 16. The majority of pts maintained the response at Wk 52: 82.7%, 79.6% (NRI); 94.0%, 89.1% (OC). The same pattern was observed for the composite measures of efficacy. 194 (45.0%) pts achieved MDA at Wk 16; of those, 85.6% (NRI) and 90.7% (OC) maintained their response at Wk 52. A high proportion of Wk 16 responders also maintained their response at Wk 52 for VLDA, DAPSA REM+LDA and DAPSA REM (**Figure 1**). To Wk 52, 555/702 (79.1%) pts reported ≥1 TEAE whilst receiving BKZ; 46 (6.6%) reported serious TEAEs.

Conclusion: With BKZ treatment, a high proportion of Wk 16 responders maintained robust efficacy responses to Wk 52, including across joint, skin and composite efficacy outcomes. The safety profile of BKZ was consistent with previous reports [2,3].

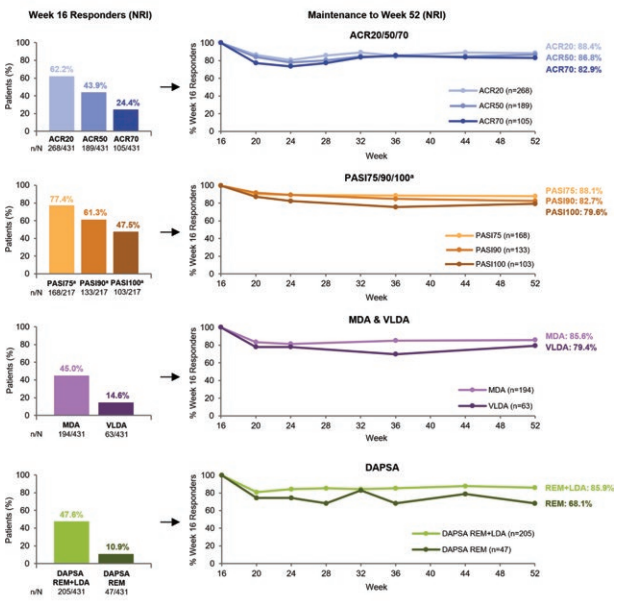
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Figure 1: Maintenance efficacy responses to Week 52, in Week 16 responders (NRI)



Randomised set. Wk 16 responders reported as NRI; maintenance of response to Wk 52 reported as NRI. ªIn pts with psoriasis affecting ≥3% BSA at baseline. Pts are considered to achieve MDA and VLDA when they meet 5/7 and 7/7 of the following criteria, respectively: TJC ≤1, SJC ≤1, PASI ≤1 or BSA ≤3%, pt pain (VAS ≤15 mm), pt global assessment (VAS ≤20), HAQ-DI ≤0.5 and tender entheseal points (LEI) ≤1. DAPSA score is the sum of SJC, TJC, pt pain (VAS 0–10), pt global assessment (VAS 0–10) and C-reactive protein (mg/L). DAPSA REM+LDA is defined as DAPSA total score ≤14; DAPSA REM is defined as DAPSA total score ≤4.

Abbreviations: ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology criteria; BSA: body surface area; DAPSA: Disease Activity Index for PSoriatic Arthritis; HAQ-DI: Health Assessment Questionnaire–Disease Index; LDA: low disease activity; LEI: Leeds Enthesitis Index; MDA: minimal disease activity; NRI: non-responder imputation; PASI: Psoriasis Area and Severity Index; PASI75/90/100: ≥75/90/100% improvement in PASI; Pt: patient; REM: remission; SJC: swollen joint count; TJC: tender joint count; VAS: visual analogue scale; VLDA: very low disease activity; Wk: week.

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POS1535

EARLY IMPROVEMENT IN 3VAS/4VAS PREDICTS REDUCED RATES OF RADIOGRAPHIC CHANGE IN BIO-NAIVE ACTIVE PSORIATIC ARTHRITIS PATIENTS RECEIVING GUSELKUMAB TREATMENT

Keywords: Psoriatic arthritis, bDMARD, Outcome measures

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Background: Guselkumab (GUS), a fully human IL-23p19 subunit inhibitor, was shown to reduce mean changes in radiographic progression vs placebo (PBO) by week (W)24 [1] and to be associated with low rates of radiographic progression through W100 among GUS-treated patients (pts) with PsA, irrespective of dosing regimen (every [Q] 4W or Q8W) [2] Furthermore, earlier clinical response predicted improved long-term radiographic outcome in GUS-treated pts with active PsA [3]. The recently developed 3 Visual Analogue Scale (VAS) and 4 VAS scores are the first short multidimensional composite measures specifically for use in PsA routine clinical care [4].

Objectives: Determine whether early improvement in 3VAS/4VAS predicts radiographic change through W100.

Methods: DISCOVER-2 included biologic-naïve pts with active PsA (≥5 swollen and ≥5 tender joint counts [SJC/TJC]; CRP ≥0.6 mg/dL) randomized (1:1:1) to GUS 100 mg Q4W; GUS 100 mg at W0, W4, then Q8W; or PBO with crossover to GUS 100 mg Q4W at W24. In the current analysis, only pts randomized to GUS were included (N=493), pooling Q4W and Q8W. Response at W8 was defined as achievement of low disease activity (LDA) in 3VAS (≤3.4), 4VAS (≤3.5), RAPID3 (≤6), DAPSA (≤14), and PASDAS (≤3.2). Association of W8 response with change from baseline (BL) to W100 in total PsA-modified van der Heijde-Sharp [vdH-S] score was assessed with the independent samples t-test and generalized linear models adjusting for known BL determinants of radiographic progression (vdH-S score, age, gender, and CRP). Pairwise correlations and agreement in LDA classification between the endpoints assessed were assessed with Pearson's correlation coefficient and the kappa statistic, respectively.

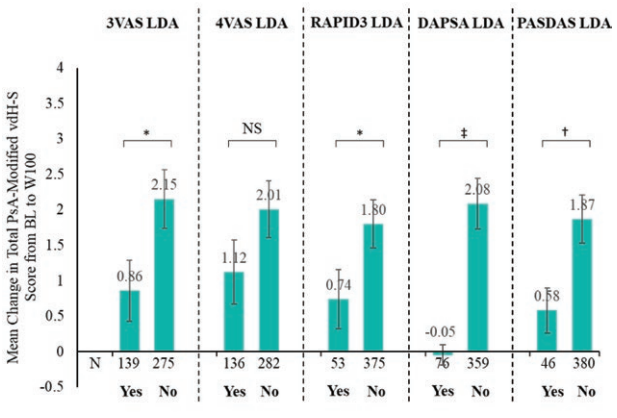
Results: Among GUS-treated pts not meeting the respective endpoints at BL, 32.9%, 31.6%, 12.4%, 17.8%, and 10.8% achieved LDA in 3VAS, 4VAS, RAPID3, DAPSA, and PASDAS, respectively, at W8. LDA achievement in 3VAS (0.86 vs. 2.15, p=0.03), RAPID3 LDA (0.74 vs. 1.80, p=0.049), DAPSA LDA (-0.05 vs. 2.08, p<0.001), and PASDAS LDA (0.58 vs. 1.87, p=0.006) at W8 were associated with significantly less radiographic progression through W100 **(Figure 1)**. For 4VAS, achievement of remission (≤2.1; 0.71 vs. 1.84, p=0.045), but not LDA (1.12 vs. 2.01, p=0.142), was also associated with improved radiographic outcome. In multivariate analyses, improved response to GUS treatment at W8 in all endpoints assessed was associated with numerically less radiographic progression through W100. 3VAS and 4VAS at W8 showed strong correlations with RAPID3 (r_{3VAS}=0.787; r_{4VAS}=0.877) and PASDAS (r_{3VAS}=0.795; r_{4VAS}=0.790) and moderate correlations with DAPSA (r_{3VAS}=0.466; r_{4VAS}=0.524), whereas fair to moderate agreement (kappa range: 0.325-0.545) in LDA classification was noted.

Conclusion: Approximately one-third of GUS-treated patients achieved early response (W8 LDA) in 3VAS/4VAS, which was associated with reduced rates of radiographic change, as was early response in the other outcomes assessed. These results suggest that, in addition to their usefulness in assessing disease activity in routine clinical care, 3VAS and 4VAS, the former being more sensitive, may predict long-term radiographic changes.

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Figure. Mean Change in Total PsA-Modified vdH-S Score from BL to W100 by Achievement of LDA in Outcomes of Interest



*p<0.05; †p<0.01; ‡p<0.001; LDA: low disease activity; NS: not significant; REM: remission

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POS1536 ASSESSMENT OF PAIN OUTCOMES IN A PHASE 2 TRIAL OF DEUCRAVACITINIB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

Keywords: Targeted synthetic drugs, Pain, Psoriatic arthritis

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Background: Pain is commonly cited by patients with psoriatic arthritis (PsA) as affecting their daily activities and quality of life. Pain signaling involves a variety of cytokines, such as interleukin (IL)-17, interferon (IFN)-γ, and IL-6. TYK2 mediates signaling of key cytokines, such as IL-23, which is upstream of IL-17, involved in PsA pathogenesis. Deucravacitinib (DEUC) is a first-in-class, oral, selective, allosteric inhibitor of TYK2, approved in multiple countries for the treatment of adults with plaque psoriasis [1,2]. DEUC was efficacious vs placebo (PBO) in a phase 2 trial in patients with active PsA, and cytokine levels were reduced with DEUC treatment vs PBO, including IL-17A and other cytokines reflecting

downstream anti-inflammatory effects of TYK2 inhibition, including IL-6 and tumor necrosis factor alpha [3,4].

Objectives: To characterize the effect of DEUC on pain across different instruments, and alignment across pain instruments, in patients in the phase 2 PsA trial.

Methods: Patients with PsA (N=203) were randomized 1:1:1 to PBO, DEUC 6 mg once daily (QD), or DEUC 12 mg QD. Three instruments were used to assess pain up to week 16: (1) Patient Global Assessment of Pain visual analog scale (Pain VAS), scored from 0-100; (2) Psoriatic Arthritis Impact of Disease (PsAID) Pain instrument, scored from 0-10; and (3) 36-Item Short-Form Health Survey (SF-36) Bodily Pain question, which asks patients to rate their pain on scale of 1-6 ranging from "none" to "very severe." Mean change from baseline (BL) in pain scale scores, the proportion of patients who reported meaningful improvements in pain, and Pearson's correlation between pain scales (Pain VAS and PsAID Pain) and disease efficacy measures were evaluated.

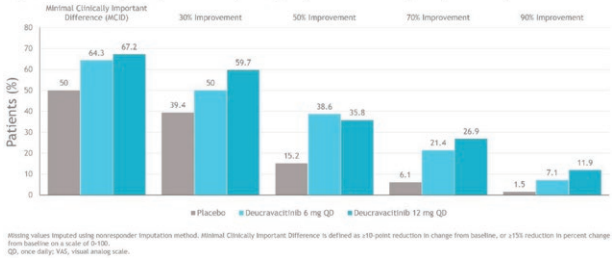
Results: BL mean Pain VAS score was 64.1 and BL mean PsAID Pain score was 6.4, and scores were generally similar across treatment groups. Percentages of patients who reported improvements in Pain VAS (**Figure 1**) and PsAID Pain were consistently greater with DEUC treatment compared with PBO, with improvements in pain being similar between males and females across instruments. The pain assessments correlated with one another both at baseline (**Table 1**) and over time through week 16, with some divergent responses to pain questions also being observed. At baseline, both assessments of pain strongly correlated with Psoriatic Arthritis Disease Activity Score (PASDAS) and with Patient Global Assessment of Disease Activity (PtGA) (**Table 1**).

Conclusion: A higher proportion of patients with PsA treated with DEUC reported clinically meaningful improvements in pain compared with PBO. Patient-reported pain was overall well-correlated across instruments; however, some divergence was also observed.

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Figure. Percentage of patients reporting improvements in pain (Pain VAS) at week 16



Missing values imputed using nonresponder imputation method. Minimal Clinically Important Difference is defined as ≥10-point reduction in change from baseline, or ≥15% reduction in percent change from baseline on a scale of 0-100.
QD, once daily; VAS, visual analog scale.

Table 1. Pearson's correlation between pain assessments at baseline and other baseline disease activity measures

	Pain VAS	PsAID Pain
Pain VAS	–	0.751
PsAID Pain	0.751	–
PASDAS	0.618	0.578
PtGA	0.653	0.583
DAPSA	0.495	0.483
DAS28	0.466	0.475
HAQ-DI	0.423	0.498
TJC	0.351	0.386
PGA	0.367	0.286
SJC	0.305	0.291
CRP	0.190	0.220

The strength of the Pearson's correlation coefficient is coded by color, with green being a strong correlation (0.5-1.0), yellow is medium (0.3-0.5), and blue is weak (0.1-0.3). CRP, C-reactive protein; DAPSA, Disease Activity in Psoriatic Arthritis; DAS28, Disease Activity Score – 28 joint; HAQ-DI, Health Assessment Questionnaire – Disability Index; PASDAS, Psoriatic Arthritis Disease Activity Score; PGA, Physician Global Assessment of Disease Activity; PsAID, Psoriatic Arthritis Impact of Disease; PtGA, Patient Global Assessment of Disease Activity; SJC, swollen joint count; TJC, tender joint count; VAS, visual analog scale.

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POS1537

BIMEKIZUMAB EFFICACY AND SAFETY IN BIOLOGIC DMARD-NAÏVE PATIENTS WITH PSORIATIC ARTHRITIS WAS CONSISTENT WITH OR WITHOUT METHOTREXATE: 52-WEEK RESULTS FROM THE PHASE 3 ACTIVE-REFERENCE STUDY BE OPTIMAL

Keywords: Clinical trials, Psoriatic arthritis

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Background: Given the chronic nature of psoriatic arthritis (PsA), understanding long-term efficacy and safety of biologic monotherapy or therapy in combination with ongoing methotrexate (MTX) is of interest. Studies have shown reduced efficacy of tumour necrosis factor inhibitors without MTX than with MTX [1]. Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, has shown efficacy and tolerability to 52 weeks (wks) in patients (pts) with PsA [2].

Objectives: To report BKZ efficacy and safety to Wk 52 from the phase 3 study BE OPTIMAL in bDMARD-naïve pts with PsA, with or without ongoing concomitant MTX.

Methods: BE OPTIMAL (NCT03895203) comprised a 16-wk double-blind placebo (PBO)-controlled period and a 36-wk active treatment-blind period. Pts were randomised 3:2:1 subcutaneous BKZ 160 mg every 4 wks (Q4W):PBO:reference arm (adalimumab [ADA] 40 mg Q2W). From Wk 16, PBO pts received BKZ 160 mg Q4W. Pts could not adjust their background medication during the 16-wk PBO-controlled period. Efficacy and safety were evaluated by concomitant MTX use at baseline (BL). Missing data were imputed using non-responder (discrete) or multiple (continuous) imputation.

Results: 761/852 (89.3%) pts completed Wk 52 (+ MTX: 454/497 [91.3%], – MTX: 307/355 [86.5%]). BL characteristics were generally similar +/– MTX: mean age 48.1 vs 49.4 years, BMI 29.1 vs 29.4 kg/m^2, 5.7 vs 6.2 years since diagnosis, 47.3% vs 46.2% male, 49.5% vs 50.4% with psoriasis affecting ≥3% body surface area. To Wk 52, the proportion of BKZ-randomised pts who achieved American College of Rheumatology (ACR)50, complete skin clearance (Psoriasis Area and Severity Index [PASI]100) and minimal disease activity (MDA) were similar regardless of BL MTX use. Fewer pts receiving ADA – MTX achieved ACR50 or MDA at Wk 52 compared to ADA + MTX (**Figure 1**). Other Wk 52 efficacy

responses on BKZ were generally of a similar magnitude +/– MTX (**Table 1**). To Wk 52, pts with ≥1 treatment-emergent adverse event +/– MTX: PBO/BKZ 124/158 (78.5%) vs 89/113 (78.8%), BKZ 214/252 (84.9%) vs 150/179 (83.8%), ADA 63/82 (76.8%) vs 50/58 (86.2%).

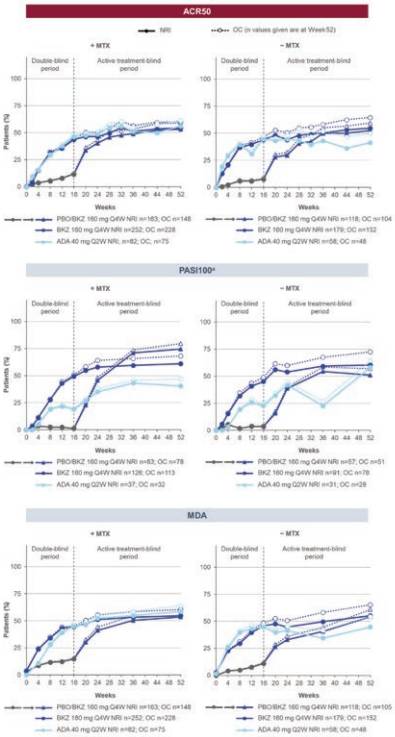
Conclusion: BKZ treatment demonstrated consistent sustained clinical efficacy across disease manifestations to Wk 52 in bDMARD-naïve pts with PsA, irrespective of concomitant MTX. BKZ was well tolerated in pts with PsA with or without MTX.

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Figure. Pts achieving ACR50, PASI100 and MDA to Wk 52 [NRI and OC]



Randomised set. ACR50 at Wk 16 was the primary endpoint for BE OPTIMAL. [a]In pts with BL psoriasis ≥3% BSA.

Abbreviations: ACR: American College of Rheumatology; ADA: adalimumab; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; BL: baseline; BSA: body surface area; CfB: change from baseline; HAQ-DI: Health Assessment Questionnaire-Disability Index; LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; MDA: minimal disease activity; MI: multiple imputation; mNAPSI: modified Nail Psoriasis Severity Index; MTX: methotrexate; NRI: non-responder imputation; OC: observed case; PASI: Psoriasis Area and Severity Index; PBO: placebo; Pt: patient; Q2W: every 2 weeks; Q4W: every 4 weeks; SE: standard error; VLDA: very low disease activity; Wk: week.

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Table 1. Wk 52 efficacy endpoints for pts +/– MTX

Endpoint	PBO/BKZ 160 mg Q4W N=281		BKZ 160 mg Q4W N=431		Reference Arm (ADA 40 mg Q2W) N=140	
	+ MTX n=163	– MTX n=118	+ MTX n=252	– MTX n=179	+ MTX n=82	– MTX n=58
ACR20 [NRI], n (%)	113 (69.3)	78 (66.1)	184 (73.0)	123 (68.7)	65 (79.3)	37 (63.8)
ACR70 [NRI], n (%)	60 (36.8)	41 (34.7)	96 (38.1)	73 (40.8)	36 (43.9)	17 (29.3)
PASI75[a] [NRI], n (%)	71 (85.5)	48 (84.2)	105 (83.3)	72 (79.1)	23 (62.2)	22 (71.0)
PASI90[a] [NRI], n (%)	67 (80.7)	39 (68.4)	89 (70.6)	66 (72.5)	20 (54.1)	21 (67.7)
VLDA [NRI], n (%)	35 (21.5)	27 (22.9)	72 (28.6)	53 (29.6)	25 (30.5)	14 (24.1)
ACR50+PASI100[a] [NRI], n (%)	43 (51.8)	22 (38.6)	61 (48.4)	41 (45.1)	12 (32.4)	12 (38.7)
HAQ-DI CfB [MI], mean (SE)	–0.37 (0.04)	–0.37 (0.05)	–0.30 (0.03)	–0.38 (0.04)	–0.49 (0.06)	–0.30 (0.08)
Enthesitis resolution[b] [NRI], n (%)	24 (66.7)	20 (58.8)	53 (64.6)	34 (55.7)	11 (61.1)	10 (55.6)
Dactylitis resolution[c] [NRI], n (%)	18 (81.8)	11 (100.0)	21 (75.0)	24 (85.7)	4 (80.0)	4 (66.7)
Nail psoriasis resolution[d] [NRI], n (%)	68 (73.9)	43 (67.2)	100 (68.5)	60 (61.2)	24 (57.1)	21 (63.6)

Randomised set. [a]In pts with BL psoriasis ≥3% BSA; + MTX: PBO/BKZ n=83; BKZ n=126; ADA n=37; – MTX: PBO/BKZ n=57; BKZ n=91; ADA n=31. [b]In pts with BL enthesitis (LEI >0); + MTX: PBO/BKZ n=36; BKZ n=82; ADA n=18; – MTX: PBO/BKZ n=34; BKZ n=61; ADA n=18. [c]In pts with BL dactylitis (LDI >0); + MTX: PBO/BKZ n=22; BKZ n=28; ADA n=5; – MTX: PBO/BKZ n=11; BKZ n=28; ADA n=6. [d]In pts with BL nail psoriasis (mNAPSI >0); + MTX: PBO/BKZ n=92; BKZ n=146; ADA n=42; – MTX: PBO/BKZ n=64; BKZ n=98; ADA n=33.

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POS1538

SAFETY OF GUSELKUMAB ACROSS DIVERSE PATIENT SUBGROUPS WITH PSORIATIC DISEASE: AN INTEGRATED ANALYSIS OF 11 PHASE 2/3 CLINICAL STUDIES IN PSORIASIS AND PSORIATIC ARTHRITIS

Keywords: Safety, Psoriatic arthritis

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Pharmaceutical Companies of Johnson & Johnson, Immunology Global Medical Affairs, Horsham, PA, United States of America; [8]*Icahn School of Medicine at Mount Sinai, Department of Dermatology, New York, NY, United States of America*; [9]*Memorial University of Newfoundland, Craig L Dobbin Genetics Research Centre, St. John's, Newfoundland, Canada*

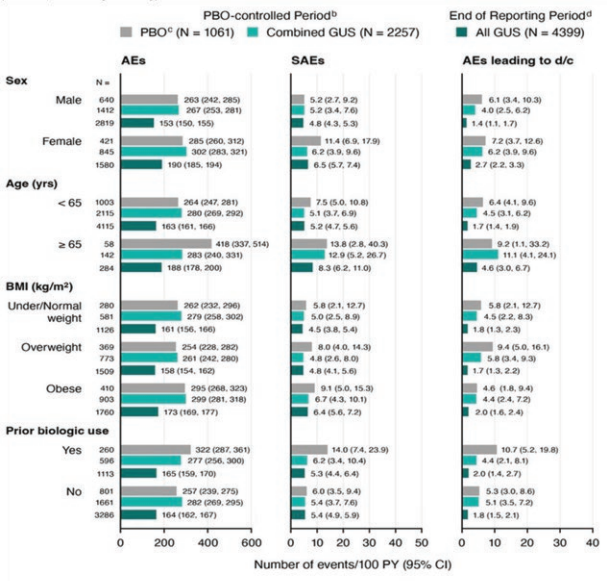
Background: A higher prevalence of comorbidities, such as obesity, prior treatments, and certain demographics (e.g., age and sex) in patients (pts) with psoriatic disease (PsD) may lead to an increased risk of adverse events (AEs), sometimes serious [1]. Guselkumab (GUS), a fully human, selective IL-23p19-subunit inhibitor approved to treat (tx) adults with active psoriatic arthritis (PsA) and moderate to severe plaque psoriasis (PsO), has shown a favorable safety profile consistent between PsA and PsO pts through up to 2 and 5 years (yrs) of follow-up in the pooled PsA and PsO trials, respectively [2].

Objectives: An integrated post hoc analysis evaluated GUS safety in subgroups of pts with PsD, stratified by baseline (BL) characteristics of interest, using pooled safety data from 11 Phase 2/3 trials of GUS, including four in PsA (Phase 2, DISCOVER-1, DISCOVER-2, COSMOS) and seven in PsO (X-PLORE, VOYAGE-1, VOYAGE-2, NAVIGATE, ORION, ECLIPSE, Japanese registration).

Methods: GUS 100 mg subcutaneous (SC) was administered at Week (W) 0, W4, then every 4 W (Q4W) or Q8W in PsA trials and at W0, W4, then Q8W in PsO trials (additional doses were investigated in X-PLORE). Pts randomized to placebo (PBO) crossed over to GUS Q4W or Q8W at W24 in PsA trials and to GUS Q8W at W16 in 5 of the PsO trials. Pooled safety data were summarized for the PBO-controlled period (PsA: W0-24; PsO: W0-16) and through the end of the reporting period (PsA: up to 2 yrs; PsO: up to 5 yrs). Incidence rates of key safety events were adjusted for duration of follow-up and reported per 100 pt-yrs (PY), along with 95% CI. BL characteristics of interest in pts randomized to GUS or PBO (N=3318), were prior biologic use (26% yes; 74% no), age (94% <65; 6% ≥65 yrs), sex (62% male; 38% female), and BMI (26% under/normal weight; 34% overweight; 40% obese).

Results: During the PBO-controlled periods, 1061 pts received PBO (395 PY) and 2257 received GUS (856 PY). Through the end of the reporting periods, 4399 GUS-tx pts (PsA: 1508; PsO: 2891) contributed 10,787 PY of follow-up (PsA: 2125 PY; PsO: 8662 PY). BL characteristics were similar across 4 PsA trials and generally similar across 7 PsO trials. The PsO trials included more males and pts with extensive skin disease than the PsA trials. Distribution of PsD pts across BL subgroups generally provided sufficient sample size, although pts ≥65 yrs accounted for only 6% of all PsD pts. Throughout the PBO-controlled period, pooled incidence rates of overall AEs were generally similar between GUS- and PBO-tx pts and rates of serious AEs (SAEs), AEs leading to study agent discontinuation, infections, and serious infections were low and comparable between GUS- and PBO-tx pts, regardless of the BL characteristics assessed. The rates of safety events evaluated were stable or reduced through the end of the reporting period for GUS-tx pts within each BL subgroup (Figure 1).

Figure. Rates of AEs, SAEs, and AEs Leading to Discontinuation Stratified by BL Characteristics (events/100 PY [95% CI])[a]



[a] Confidence intervals based on an exact method assuming that the observed number of events follows a Poisson distribution. Events are counted only once if events were started from same date with same derived term.
[b] Includes pts who discontinued study treatment early with the last study treatment (PBO or GUS) administered prior to W16/24 and who did not receive any study agent (PBO or GUS) at or after W16/24; all data including the final safety follow-up visit collected through up to 2 years were included in this period.
[c] Only includes data prior to administration of GUS in PBO pts who switched from PBO to GUS.
[d] Only includes data after administration of GUS in PBO pts who switched from PBO to GUS.
BMI=body mass index, under/normal weight: <18.5-24.9; overweight: 25.0-29.9; obese: 30.0-34.9; d/c=discontinuation.

Conclusion: This comprehensive integrated analysis of GUS safety demonstrated a favorable safety profile across a broad population of pts irrespective of the BL characteristics assessed. Overall, safety event rates in GUS-tx pts were comparable to or lower than PBO during short-term follow-up. Rates of SAEs and serious infections remained low and stable through long-term follow-up.

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POS1539

SAFETY AND EFFICACY OF UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO BIOLOGICS: 3-YEAR RESULTS FROM THE PHASE 3 SELECT-PSA 2 STUDY

Keywords: Psoriatic arthritis, Targeted synthetic drugs, Safety

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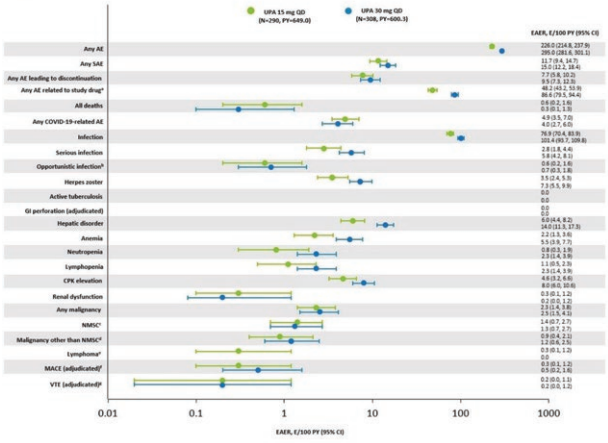
Background: The efficacy and safety of upadacitinib (UPA) in patients (pts) with psoriatic arthritis (PsA) and inadequate response to ≥1 biologic disease-modifying antirheumatic drug (bDMARD-IR) have been demonstrated up to 56 and 104 weeks of treatment [1,2].
Objectives: To assess the long-term safety and efficacy of UPA in bDMARD-IR pts with PsA through 152 weeks of treatment in the SELECT-PsA 2 study.
Methods: Pts were randomized to receive UPA 15 or 30 mg once daily (QD), or placebo (PBO) for 24 weeks, followed by blinded switch to UPA 15 or 30 mg QD for pts initially randomized to PBO. After 56 weeks, pts continued their assigned dose up to 152 weeks in an open-label extension (OLE). Following approval of the 15 mg QD dose, the protocol was amended and all pts on UPA 30 mg QD were switched to the approved dose (earliest switch at week 116). Endpoints assessed at 152 weeks included: % of pts achieving 20/50/70% improvement in American College of Rheumatology (ACR) criteria, minimal disease activity (MDA), and 75/90/100% improvement in Psoriasis Area and Severity Index, as well as patient-reported outcomes. Efficacy data were evaluated using non-responder imputation (NRI) and as-observed (AO) data (binary endpoints), and mixed effect model for repeated measures (continuous endpoints). Treatment-emergent adverse events (TEAEs) through 3 years (cut-off date, 05 May 2022) are also reported.
Results: Of the 641 pts randomized to receive UPA 15 or 30 mg QD, or PBO followed by UPA 15 or 30 mg QD (n=211, 218, 106, and 106, respectively), 478 entered the OLE. Improvements in efficacy outcomes with UPA observed at 56[1] and 104[2] weeks were maintained through the OLE, with ACR20 achieved by 43–51% (NRI) and 79–87% (AO) of pts across treatment arms at week 152. The highest % of MDA responders at week 152 (31% [NRI] and 44% [AO]) were in the continuous UPA 15 mg arm (**Table 1**). UPA was well tolerated through 152 weeks, with no new safety signals identified. The overall exposure-adjusted event rates for any TEAE were higher for UPA 30 vs 15 mg (295 vs 226 events/100 PY, respectively [**Figure**]).
Conclusion: Observed improvements in the signs and symptoms of PsA with UPA were maintained through 3 years of treatment in bDMARD-IR pts. The long-term safety profile of UPA in this treatment-refractory population was consistent with its known safety profile across indications.

Table 1. Efficacy endpoints at week 152

Endpoint	UPA 15 mg QD (n=211)		UPA 30 mg QD[a] (n=218)		PBO/UPA 15 mg QD (n=106)		PBO/UPA 30 mg QD[a] (n=106)	
Proportion of patients (%)	**NRI**	**AO**	**NRI**	**AO**	**NRI**	**AO**	**NRI**	**AO**
ACR20/50/70	51/39/24	81/60/36	49/35/22	79/56/34	43/29/20	87/60/40	43/28/18	79/53/36
MDA	31	44	25	41	16	41	19	37
PASI75/90/100	43/31/20	66/46/30	41/36/29	72/61/48	45/34/23	79/61/42	41/35/30	75/63/55
Resolution of enthesitis (LEI=0)[b]	38	69	36	68	24	76	25	62
Resolution of dactylitis (LDI=0)[c]	49	94	50	100	34	100	28	100
Change from BL	**Mixed effect model for repeated measures** mean (95% confidence interval)							
Health Assessment Questionnaire – Disability Index	-0.4 (-0.5, -0.3)		-0.5 (-0.5, -0.4)		-0.5 (-0.6, -0.3)		-0.3 (-0.4, -0.2)	
Bath Ankylosing Spondylitis Disease Activity Index[d]	-2.6 (-3.1, -2.1)		-2.0 (-2.5, -1.5)		-2.3 (-3.1, -1.5)		-2.5 (-3.2, -1.7)	
Ankylosing Spondylitis Disease Activity Score[d]	-1.4 (-1.6, -1.1)		-1.1 (-1.4, -0.9)		-1.0 (-1.4, -0.7)		-1.2 (-1.5, -0.8)	

[a]Following a protocol amendment, all pts on UPA 30 mg QD switched to UPA 15 mg QD (earliest switch at week 116).[b]BL LEI >0.[c]BL LDI >0.[d]Among pts with psoriatic spondylitis at BL, as determined by the investigator.ACR20/50/70, 20/50/70% improvement in American College of Rheumatology Criteria; AO, as observed; BL, baseline; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; NRI, non-responder imputation; PASI75/90/100, 75/90/100% improvement in Psoriasis Area and Severity Index; PBO, placebo; pt, patient; QD, once daily; UPA, upadacitinib.

Figure. Treatment-emergent exposure-adjusted AE rates through 3 years*



*Cut-off date, 05 May 2022

[a]Reasonable possibility of being related to the study drug, as per the investigator.

[b]Excluding tuberculosis and herpes zoster.

[c]Six cases of BCC and three cases of SCC in the UPA 15 mg QD group (including one pt who had one event of BCC and two events of SCC); four cases of BCC and four cases of SCC in the UPA 30 mg QD group (including one pt with two events of BCC and three events of SCC).

[d]Two cases of prostate cancer and one case each of malignant melanoma (Stage III), malignant neoplasm (not specified), ovarian cancer, and rectal cancer in the UPA 15 mg QD group; one case each of basosquamous carcinoma, endometrial cancer, intraductal papillary breast neoplasm, malignant melanoma, oropharyngeal SCC, ovarian cancer, and rectal adenocarcinoma in the UPA 30 mg group (including one pt with both ovarian and endometrial cancer).

[e]Two cases of abnormal lymphocyte morphology in the UPA 15 mg QD group are shown, as this preferred term is included in the Malignant Lymphoma Standardised MedDRA Queries. These non-SAEs were based on single laboratory results and were not confirmed to be lymphomas.

[f]Defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

[g]Includes deep vein thrombosis and pulmonary embolism.

AE, adverse event; BCC, basal cell carcinoma; CI, confidence interval; CPK, creatine phosphokinase; E, event; EAER, exposure-adjusted AE rate; GI, gastrointestinal; MACE, major adverse cardiovascular event; MedDRA, Medical Dictionary for Regulatory Activities; NMSC, non-melanoma skin cancer; SAE, serious adverse event; SCC, squamous cell carcinoma; pt, patient; PY, patient-years; QD, once daily; UPA, upadacitinib; VTE, venous thromboembolic event.

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POS1540

EARLY SKIN AND EARLY ENTHESITIS RESPONSES IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH GUSELKUMAB ASSOCIATE WITH LONG-TERM RESPONSE: POST HOC ANALYSIS THROUGH 2 YEARS OF A PHASE 3 STUDY

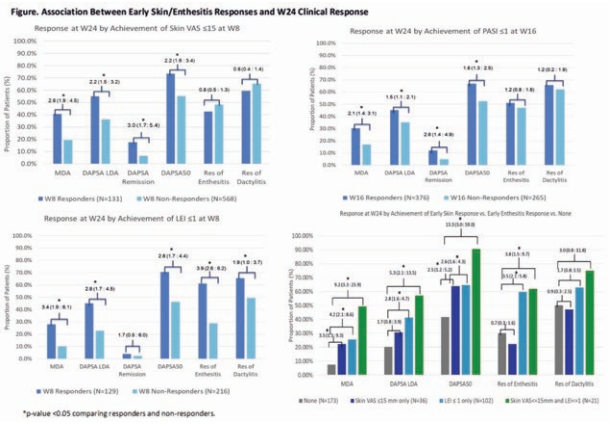
Keywords: Enthesitis, Psoriatic arthritis, Skin

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Background: Guselkumab (GUS), an IL-23p19 inhibitor, has demonstrated efficacy in psoriatic arthritis (PsA) across key Group for Research and Assessment of Psoriasis (PsO) and Psoriatic Arthritis (GRAPPA)-recommended domains [1,2]. Skin disease and enthesitis have been identified as disease manifestations with earlier response times than others [3].
Objectives: In this analysis we: (a) Determined whether early skin and/or entheseal response predicts future response in other PsA domains; (b) Evaluated the trajectory for achieving skin/entheseal responses by 52 weeks (W) in patients (pts) without early responses.
Methods: Pts in the DISCOVER-1 and DISCOVER-2 (D1/2) studies were adults with active PsA despite standard therapies. D1 pts had ≥3 swollen and ≥3 tender joints (SJC/TJC) and C-reactive protein (CRP) ≥0.3 mg/dL; D2 pts had SJC ≥5, TJC ≥5, and CRP ≥0.6 mg/dL. 31% of D1 pts received 1-2 prior TNF inhibitors; D2 pts were biologic-naïve. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then every 8 weeks (Q8W); or placebo. These post hoc analyses included only pooled GUS Q4W and Q8W pts (N=748). Early skin response was defined as PsO Area and Severity Index (PASI) score ≤1 at W16 or skin visual analogue scale (VAS) ≤15mm at W8 among pts with a baseline (BL) PASI score >1 and skin VAS >15mm (first assessment time for both); early entheseal response was defined as Leeds Enthesitis Index (LEI) score ≤1 at W8; and categories of early response were defined as skin VAS ≤15mm only vs LEI score ≤1 only vs combined skin VAS ≤15mm & LEI score ≤1 vs none at W8. Potential responses at W24 & W52 included achievement of minimal disease activity (MDA), Disease Activity in PsA (DAPSA) low disease activity (LDA) or remission, DAPSA50, and enthesitis/dactylitis resolution. Associations between early skin/entheseal response and W24/W52 response were assessed with crosstabulations and logistic regression.
Results: Early skin response associated with greater odds of achieving W24 MDA, DAPSA LDA, DAPSA remission, and DAPSA50, but not enthesitis or dactylitis resolution (Figure 1). Early entheseal response associated with greater odds of achieving all W24 outcomes, including resolution of enthesitis or dactylitis, with the exception of DAPSA remission; DAPSA remission was achieved by a greater proportion of early responders, though the association was significant only at W52. In pts with both BL PsO and enthesitis, early responders in both domains were even more likely to subsequently demonstrate MDA, DAPSA LDA, DAPSA50, DAPSA remission only at W52, and dactylitis resolution than pts with individual responses. Among pts who did not achieve early responses, approximately half did so by W52.
Conclusion: Early skin and entheseal responses predicted long-term clinical response, including disease remission. A synergistic effect was observed, in which pts with BL PsO and enthesitis exhibiting early response in both domains were more likely to achieve later clinical response. These results highlight the importance of early response in these two domains on the trajectory of long-term pt outcome.

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POS1541

LONG-TERM EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS: 3-YEAR RESULTS FROM THE PHASE 3 SELECT-PSA 1 STUDY

Keywords: Psoriatic arthritis, Safety

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Background: Upadacitinib (UPA) improved symptoms in patients (pts) with psoriatic arthritis (PsA) with prior inadequate response or intolerance to ≥1 non-biologic disease-modifying antirheumatic drug (nbDMARD-IR) through week (wk) 104 or 2 years of treatment in SELECT-PsA 1 [1].
Objectives: To evaluate efficacy and safety of UPA vs adalimumab (ADA) through wk 152 or 3 years from the ongoing long-term open-label extension of SELECT-PsA 1.
Methods: Pts were randomized to receive UPA 15 mg (UPA15) or UPA 30 mg (UPA30) once daily, ADA 40 mg (ADA) every other wk, or placebo (PBO). At wk 24, PBO pts switched to UPA15 or UPA30. Following approval of UPA15, the

protocol was amended so pts on UPA30 switched to UPA15 (earliest at wk 104). Efficacy was assessed through wk 152, and safety through June 13, 2022.

Results: Of 1704 pts randomized, 911 completed 152 wks of treatment. The proportions of pts achieving. ≥20%/50%/70% improvement in American College of Rheumatology criteria (ACR20/50/70), minimal disease activity (MDA), and ≥75%/90%/100% improvement in Psoriasis Area and Severity Index at wk 152 were generally consistent with those at wk 104[1]. UPA had greater ACR20/50/70 and MDA responses vs ADA, and a greater mean change from baseline (BL) in Health Assessment Questionnaire-Disability Index, pt's assessment of pain, and Bath Ankylosing Spondylitis Disease Activity Index vs ADA. Change from BL in modified total Sharp/van der Heijde score were similar between UPA30 and ADA, and numerically higher with UPA15 **(Table 1)**. The overall UPA safety profile remained unchanged (**Figure 1**) [1,2]. UPA had numerically higher rates of serious infection (SI), herpes zoster (HZ), anemia, lymphopenia, creatine phosphokinase (CPK) elevation, and non-melanoma skin cancer (NMSC) vs ADA. Increases for SI, HZ, anemia, and CPK elevation with UPA were dose dependent. Rates of major adverse cardiovascular events, venous thromboembolism, and malignancy excluding NMSC were low and generally similar across groups. The most common cause of death was COVID-19.

Conclusion: Efficacy of UPA in nbDMARD-IR pts with PsA was maintained through 3 years of treatment. No new safety signals were identified.

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Table 1. Efficacy endpoints at wk 152

	UPA15 (n=429)		UPA30[a] (n=423)		ADA (n=429)	
Proportion of pts (%)	**NRI**	**AO**	**NRI**	**AO**	**NRI**	**AO**
ACR20/50/70	64.6/52.0/35.9*	89.8/71.6/48.2	63.1/54.1*/35.7	87.9/74.4/47.8	61.1/46.6/28.7	86.2/65.2/39.8
Minimal disease activity	37.5	55.1	43.5*	60.3	35.9	50.2
PASI75/90/100[b]	50.5/42.5/32.2	69.2/58.5/43.4	58.1/46.7/7.6	78.6/63.5/50.9	54.0/40.8/30.3	79.6/59.9/44.6
Resolution of enthesitis by Leeds Enthesitis Index[c]	50.4	75.2	48.9	73.8	46.0	77.0
Resolution of dactylitis by Leeds Dactylitis Index[d]	65.4	95.2	66.1	97.9	65.4	97.1
Change from BL[e]	**MMRM**	**AO**	**MMRM**	**AO**	**MMRM**	**AO**
Health Assessment Questionnaire-Disability Index	-0.51	-0.55	-0.53*	-0.58	-0.45	-0.49
Pt's assessment of pain (numeric rating scale)	-3.3*	-3.5	-3.3*	-3.6	-2.8	-3.0
Bath Ankylosing Spondylitis Disease Activity Index[f]	-3.09	-3.27	-3.16	-3.54	-2.81	-2.71
Modified total Sharp/van der Heijde score	0.21	0.19	0.05	0.04	0.09	0.09

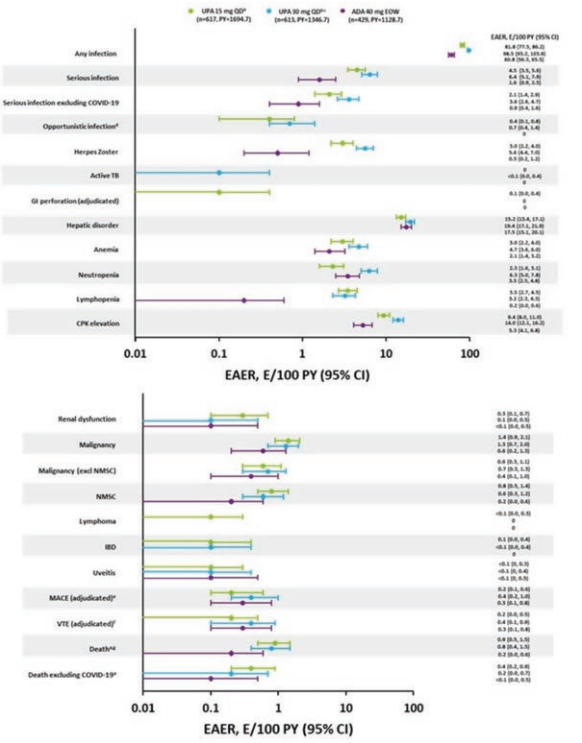
[a]Following a protocol amendment, all pts on UPA30 switched to UPA15 (earliest switch at wk 104); data are presented by originally randomized group. [b]Pts with psoriasis affecting ≥3% of body surface area at BL. [c]Pts with LEI >0 at BL; resolution LEI=0. [d]Pts with LDI >0 at BL; resolution LDI=0. [e]Data shown as MMRM (least squares mean) and AO (mean). [f]Pts with psoriatic spondylitis at BL. n value ranges: UPA15 (99–429), UPA30 (95–423), ADA (89–429). Nominal *p<0.05 UPA vs ADA.ACR20/50/70, ≥20%/50%/70% improvement in American College of Rheumatology criteria; ADA, adalimumab; AO, as observed; BL, baseline; MMRM, mixed effect model repeated measurement; NRI, non-responder imputation; PASI75/90/100, ≥75%/90%/100% improvement in Psoriasis Area and Severity Index; pt, patient; UPA15/30, upadacitinib 15/30 mg once daily; wk, week

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Figure. EAERs of Treatment-Emergent Adverse Events[a] through June 13, 2022



[a]Both treatment-emergent and non-treatment-emergent deaths are included. [b]Includes PBO pts who switched to UPA. [c]Following a protocol amendment, all pts on UPA30 were switched to UPA15, with the earliest switch at wk 104. For pts who switched from UPA30 to UPA15, adverse events and exposure to UPA30 were censored at the time of dose switch. [d]Opportunistic infections excluding herpes zoster and TB. [e]Defined as cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke. [f]Includes deep vein thrombosis and pulmonary embolism [fatal and non-fatal]. [g]Deaths: UPA15: 4 COVID-19, 3 COVID-19 pneumonia; 1 septic shock, 1 metastatic lung cancer, 1 pulmonary embolism, 1 sudden cardiovascular death, 1 lower respiratory tract infection, 2 sudden death, 1 road traffic accident, and 1 multiple organ dysfunction syndrome; UPA30: 1 arteriosclerosis of coronary artery, 1 cardiac arrest, 1 interstitial lung disease, 1 COVID-19, 5 COVID-19 pneumonia, 1 myocardial infarction, and 1 circulatory collapse; ADA: 1 COVID-19 pneumonia and 1 road traffic accident.

ADA, adalimumab; CI, confidence interval; CPK, creatine phosphokinase, EAER, exposure-adjusted event rate; EOW, every other week; GI, gastrointestinal; IBD, inflammatory bowel disease; MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer; PBO, placebo; PY, patient-years; QD, once daily; TB, tuberculosis; UPA, upadacitinib; VTE, venous thromboembolism; wk, week.

POS1542

THE PSORIATIC ARTHRITIS IMPACT OF DISEASE (PSAID-12) QUESTIONNAIRE IS VALID IN ARABIC AND STRONGLY LINKED TO DISEASE ACTIVITY AND PATIENT-REPORTED OUTCOMES IN ARAB-SPEAKING COUNTRIES: AN ARLAR INITIATIVE

Keywords: Psoriatic arthritis, Patient reported outcomes

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Background: The Psoriatic Arthritis Impact of Disease (PsAID) is a patient-reported questionnaire assessing multiple domains in patients with psoriatic arthritis (PsA), developed under the aegis of EULAR, and recommended by OMERACT and GRAPPA. To be usable in different contexts, translations and cross-cultural validations are necessary. Arabic is the sixth most-spoken language in the world; however, many patient-reported outcomes are not available in Arabic.

Objectives: To translate, culturally adapt and validate the PsAID-12 questionnaire in Arabic, to study its psychometric properties, and to evaluate its association with the demographic and disease characteristics of PsA patients.

Methods: This multicentric multinational study was conducted by the Arab League of Associations of Rheumatology (ArLAR) research group (ARCH). Validated methodologies were applied. (A) Phase 1: Translation of PsAID-12 into Arabic, including a double translation, synthesis by a steering committee, back-translation, and cognitive debriefing with feasibility and timing assessment with a sample of patients with PsA in four countries. (B) Validation phase: Cross-sectional study, with a longitudinal part for reliability testing, conducted in thirteen Arab countries. Patients were consecutive adult patients, diagnosed with PsA (rheumatologist opinion + CASPAR criteria), literate, and agreeing to participate. Data collected: (1) From the patient: PsAID-12 in Arabic, demographic and disease information, Health Assessment Questionnaire (HAQ), Patient Global Assessment for pain and disease activity (PGA), Fibromyalgia Rapid Screening Tool (FiRST) and Patient Health Questionnaire (PHQ4). (2) From the rheumatologist: Disease Activity in Psoriatic Arthritis (DAPSA) score. Psychometric properties of the PsAID-12 were investigated: internal consistency (Cronbach α), construct validity (Spearman correlation with DAPSA, HAQ, PGA, FiRST, PHQ4), and test-retest reliability (intraclass correlation coefficients (ICCs) and Cohen kappa at one week). (C) Factors associated with high PsAID-12 total score (defined as >= 4) were explored using multivariable binary logistic regression.

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[1] Translation phase: a culturally adapted questionnaire was obtained, with minor rephrasing and addition of examples for better clarity. Feasibility was scored at 2/10 (SD 1.7) (10 being the most difficult) and the time needed to complete the questionnaire was 4.16 minutes.

[2] Validation phase: in 554 patients from 13 countries, mean age was 45 years [SD 13], 57% were females. The mean PsAID score was 3.86 (SD 2.33). Internal consistency was excellent (Cronbach $\alpha = 0.95$). The correlation coefficients with other measures were moderate to strong (range, 0.63 to 0.78 (Figure 1). Test-retest reliability (N=138 patients) was excellent (ICC 0.95 (95%CI 0.86;0.93) and agreement between the first and second measurements was substantial (Cohen kappa 0.797).

[3] In the multivariable analysis, factors associated with a higher PsAID were DAPSA, FiRST, and PHQ4 (after adjustment for axial involvement, education, gender, and CRP).

Conclusion: The Arabic PsAID is a consistent, reliable, and feasible measure in patients with PsA. The correlation with other PsA-related measures appears similar to the correlation noted in other cultures and languages. The PsAID appears to be a stable measure of impact across cultures. These results comfort the recommendation to use the PsAID for clinical practice and research purposes.

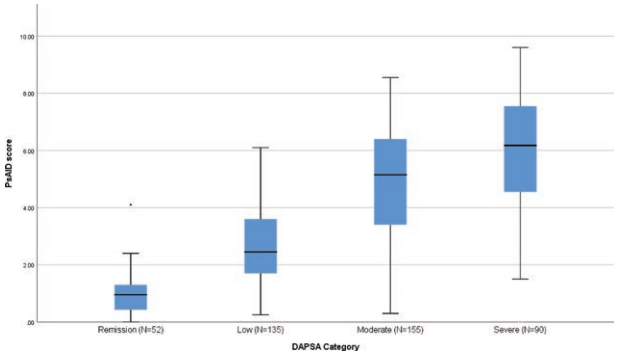


Figure 1. Correlation between the PsAID-12 total score and DAPSA categories, in 432 Arabic-speaking patients

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POS1543 EFFICACY OF RISANKIZUMAB IN THE TREATMENT OF PSA PATIENTS WITH LIMITED AND EXTENSIVE JOINT INVOLVEMENT

Keywords: Psoriatic arthritis, Enthesitis, Remission

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Background: PsA is a systemic disease involving multiple domains. Peripheral joints are frequently affected, and patients often initially present with asymmetrical oligoarthritis (2-4 swollen joints). KEEPsAKE 1 and KEEPsAKE 2 are double-blind, phase 3 clinical trials that evaluated the efficacy of risankizumab (RZB) versus placebo (PBO) for the treatment of adults with active PsA and at least 5 tender and swollen joints. RZB is a humanized monoclonal antibody that binds specifically to the p19 subunit of interleukin 23 and is approved to treat PsA.

Objectives: Here we assess response rates in PsA patients with limited (5 to ≤ 8) and extensive (≥ 9) swollen joint count (SJC) after treatment with RZB to examine whether its efficacy differed according to the extent of joint involvement.

Methods: In KEEPsAKE 1 and KEEPsAKE 2, patients were originally randomized 1:1 to receive RZB 150 mg or PBO at weeks 0, 4, 16 and every 12 weeks thereafter with an open label extension beginning for all patients at week 24 and is currently ongoing. Integrated efficacy results are reported for continuous endpoints by mixed-effect model repeated measure for week 24 and by as observed for week 52. Categorical endpoints are reported by non-responder imputation.

Results: Of the 707 patients initially randomized to RZB across both trials, 303 had a limited (5 to ≤ 8) SJC and 404 had extensive SJC (≥ 9) at baseline. Baseline characteristics for each group are presented in **Table 1**. At baseline, both groups of patients had high disease activity with a mean Disease Activity in PsA (DAPSA) score of 31.47 in the limited joint involvement population and 57.31 in the extensive joint involvement population (**Table 1**). In both groups, patients achieved minimal disease activity (MDA), Disease Activity in PsA (DAPSA) remission or low disease activity and resolution of enthesitis and dactylitis at weeks 24 and 52 (**Figure 1**). A higher proportion of patients in the limited joint involvement population achieved these stringent end points than did patients with extensive joint involvement (**Figure 1**). Both patient groups also had a decreased total number of swollen or tender joints at weeks 24 and 52 compared to baseline and showed improved scores for PsA disease activity (PASDAS), Psoriasis Area and Severity Index (PASI), Physician and Patient's Global Assessment of Disease Activity, pain, and HAQ-Disability Index (**Figure 1**). As expected, a greater reduction in swollen and tender joints was seen in patients in the extensive joint involvement population, due to a higher baseline joint involvement. Efficacy

results were maintained or further improved from week 24 to 52 for both limited and extensive SJC patients (**Figure 1**)

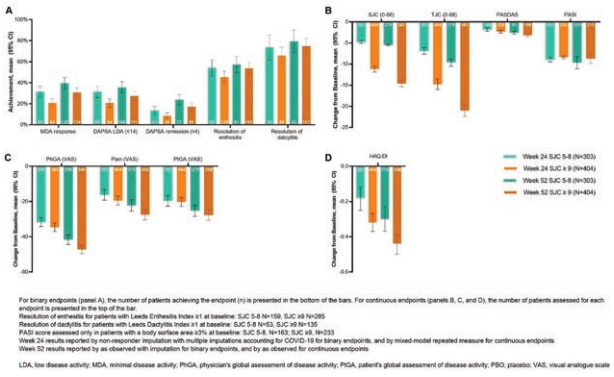
Conclusion: RZB is efficacious in reducing signs and symptoms of PsA in patients, regardless of patterns of joint involvement. More patients in the limited joint involvement group achieved stringent treatment targets such as MDA and DAPSA remission at both weeks 24 and 52.

Table 1. Baseline Disease Characteristics

	SJC 5-8 (N=303)	SJC ≥9 (N=404)
SJC66	6.5 (1.1)	16.8 (8.3)
TJC68	13.4 (9.4)	27.5 (14.5)
DAPSA	31.5 (11.3)[a]	57.3 (21.4)
PASDAS[b]	5.8 (0.9)	6.8 (1.1)
LEI[c]	2.3 (1.3)	3.1 (1.5)
LDI[d]	54.1 (60.8)	110.3 (128.3)
PASI[e]	10.5 (9.6)	9.5 (9.0)
HAQ-DI	1.0 (0.6)[a]	1.3 (0.6)
PhGA (VAS)[f]	58.3 (18.0)	64.5 (16.6)
PtGA (VAS)	54.1 (22.2)[a]	59.8 (21.2)
Pain (VAS)	51.6 (23.0)	60.0 (22.1)

All parameters are mean (SD)[a]N = 302[b]SJC 5-8, N=148; SJC ≥9, N=220[c]For pts with LEI >0 at BL; SJC 5-8, N=159; SJC ≥9, N=285[d]For pts with LDI >0 at BL; SJC 5-8, N=53; SJC ≥9, N=135[e]For pts with BSA ≥3% at BL; SJC 5-8, N=163; SJC ≥9, N=233[f]SJC 5-8, N=290; SJC ≥9, N=395LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; PASDAS, PsA Disease Activity Score; VAS, visual analogue scale.

Figure. Efficacy Endpoints at Weeks 24 and 52 in Patients With Limited and Extensive Joint Involvement



For binary endpoints (panel A), the number of patients achieving the endpoint (n) is presented in the bottom of the bars. For continuous endpoints (panels B, C, and D), the number of patients assessed for each endpoint is presented in the top of the bar.
Resolution of enthesitis for patients with Leeds Enthesitis Index ≥1 at baseline: SJC 5-8 N=159, SJC ≥9 N=285
Resolution of dactylitis for patients with Leeds Dactylitis Index ≥1 at baseline: SJC 5-8 N=53, SJC ≥9 N=135
PASI score assessed only in patients with a body surface area ≥3% at baseline: SJC 5-8, N=163; SJC ≥9, N=233
Week 24 results reported by non-responder imputation with multiple imputations accounting for COVID-19 for binary endpoints, and by mixed-model repeated measure for continuous endpoints
Week 52 results reported by as observed with imputation for binary endpoints, and by as observed for continuous endpoints

LDA, low disease activity; MDA, minimal disease activity; PhGA, physician's global assessment of disease activity; PtGA, patient's global assessment of disease activity; PBO, placebo; VAS, visual analogue scale

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POS1544

LONG-TERM SAFETY AND EFFICACY OF TOFACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS BY PRIOR BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG EXPOSURE

Keywords: Targeted synthetic drugs, Psoriatic arthritis, bDMARD

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Background: Patients (pts) with psoriatic arthritis (PsA) exposed to tumour necrosis factor inhibitors (TNFi) may have attenuated response or higher adverse event (AE) risk with subsequent treatment. Tofacitinib efficacy/safety in PsA pts was shown in 3 Phase (P)3 trials and 1 long-term extension (LTE) trial.

Objectives: Assess long-term safety/efficacy of tofacitinib in TNFi-inadequate responder (IR) and biologic disease-modifying antirheumatic drug (bDMARD)-naïve PsA pts.

Methods: Pooled data from P3 trials (NCT01877668/NCT01882439/NCT03486457) of PsA pts receiving ≥1 tofacitinib dose and 1 LTE trial (NCT01976364) of PsA pts receiving tofacitinib 5 mg BID (dose switching allowed after 1 month) were stratified by TNFi-IR or bDMARD-naïve status at P3 trial baseline (BL). Safety assessed in P3/LTE trials. Efficacy assessed in LTE trial only to Month (M)36 (longitudinal models, data as observed): MDA and HAQ-DI (≥0.35 improvement) response rates and change from BL (Δ) in PASDAS. Data reported as all tofacitinib (pts receiving ≥1 tofacitinib dose) or constant tofacitinib 5 mg BID (pts assigned to tofacitinib 5 mg BID in P3/LTE trials or placebo→tofacitinib 5 mg BID in P3 trials and maintained this dose).

Results: 408 TNFi-IR (incl. 29 TNFi-exposed with unknown IR status) and 562 bDMARD-naïve pts from P3/LTE trials were assessed. Differences in P3 trial BL characteristics in TNFi-IR vs bDMARD-naïve pts included longer disease duration (all tofacitinib, mean: 8.9 vs 5.6 years), higher HAQ-DI scores (mean: 1.2 vs 0.9) and a higher proportion (%) of pts aged ≥65 years (9.6 vs 7.7) and from North America (27.5 vs 8.0). Treatment-emergent AE (TEAE) incidence rates were higher in TNFi-IR vs bDMARD-naïve pts; serious AE (SAE), serious infection (SI) and herpes zoster (HZ; all tofacitinib) incidence rates were numerically higher in TNFi-IR vs bDMARD-naïve pts (confidence intervals [CIs] overlapped; Table 1). Deaths, malignancies excl. non-melanoma skin cancer (NMSC), NMSC, major adverse cardiovascular events (MACE) and venous thromboembolism (VTE) events were observed (Table 1). Tofacitinib response/improvements were sustained to M36 in pts remaining in LTE trial, regardless of prior treatment. At all time points, TNFi-IR vs bDMARD-naïve pts had lower MDA response rates and slightly lower HAQ-DI response rates (Figure 1) and ΔPASDAS (all tofacitinib/constant tofacitinib 5 mg BID: M1 -2.3/-2.5 vs -2.9/-3.0; M6 -2.5/-2.8 vs -3.0/-3.1; M12 -2.7/-2.9 vs -3.0/-3.2; M24 -2.9/-3.1 vs -3.2/-3.4; M36 -3.0/-3.2 vs -3.1/-3.4).

Table 1. Safety in P3/LTE trials[a]

	All tofacitinib		Constant tofacitinib 5 mg BID	
	TNFi-IR[b] N=408 899 PY	bDMARD-naïve[c] N=562 1255 PY	TNFi-IR N=217 282 PY	bDMARD-naïve N=325 422 PY
n Incidence rate (95% CI)				
TEAE	373 181.8 (163.8, 201.2)	457 117.8 (107.3, 129.1)	180 219.6 (188.7, 254.2)	240 161.2 (141.5, 183.0)
SAE	67 8.2 (6.4, 10.5)	71 6.0 (4.7, 7.6)	25 9.5 (6.1, 14.0)	23 5.6 (3.6, 8.4)
Death	1 0.1 (0.0, 0.6)	1 0.1 (0.0, 0.4)	1 0.4 (0.0, 2.0)	1 0.2 (0.0, 1.3)
SI	13 1.5 (0.8, 2.5)	11 0.9 (0.4, 1.6)	5 1.8 (0.6, 4.1)	5 1.2 (0.4, 2.8)
HZ	19 2.2 (1.3, 3.4)	19 1.6 (0.9, 2.4)	4 1.5 (0.4, 3.7)	6 1.4 (0.5, 3.1)
Malignancies excl. NMSC[d]	3 0.3 (0.1, 1.0)	12 1.0 (0.5, 1.7)	2 0.7 (0.1, 2.5)	5 1.2 (0.4, 2.8)
NMSC[d]	7 0.8 (0.3, 1.6)	9 0.7 (0.3, 1.4)	4 1.4 (0.4, 3.6)	2 0.5 (0.1, 1.7)
MACE[d]	2 0.2 (0.0, 0.8)	4 0.3 (0.1, 0.8)	0 0.0 (0.0, 1.3)	3 0.7 (0.2, 2.1)
VTE	0 0.0 (0.0, 0.4)	2 0.2 (0.0, 0.6)	0 0.0 (0.0, 1.3)	0 0.0 (0.0, 0.9)

[a]Concomitant csDMARD required at start of P3 trials; allowed but not required in LTE trialMedian exposure (range), days: [b]988 (1, 1544); [c]744 (1, 1715)[d]Adjudicatedn, number of pts with events; PY, pt-years

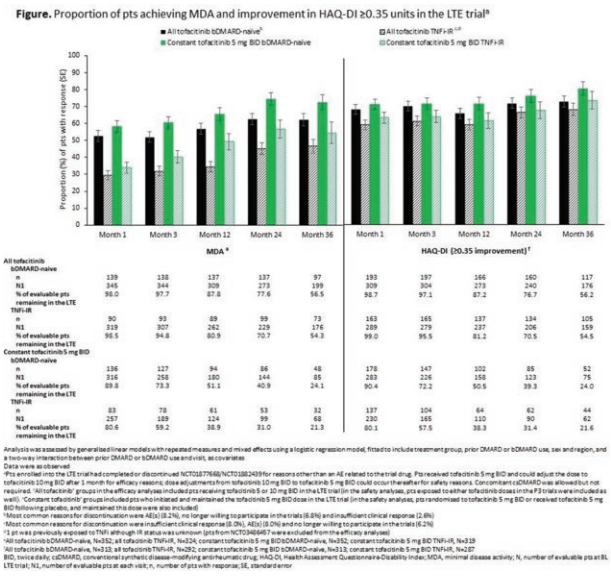


Figure. Proportion of pts achieving MDA and improvement in HAQ-DI ≥0.35 units in the LTE trial[a]

Conclusion: For pts remaining in LTE trial, tofacitinib efficacy was greater in bDMARD-naïve vs TNFi-IR pts; response was maintained over time in both groups. Incidence rates were higher for TEAEs and numerically higher for SAE, SI and HZ (all tofacitinib) in TNFi-IR vs bDMARD-naïve pts. Results consistent with other advanced PsA treatments. Limitations included small event numbers, as observed data and BL characteristic differences.

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POS1545

MODULATION OF SERUM BIOMARKERS IN PATIENTS WITH PSA TREATED WITH RISANKIZUMAB IN THE PHASE 3 KEEPSAKE 2 STUDY

Keywords: Psoriatic arthritis, Biomarkers, Clinical trials

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Background: Risankizumab (RZB) is a selective interleukin (IL) 23 p19 subunit monoclonal antibody that inhibits IL-23. RZB 150 mg has shown greater improvements in key clinical domains such as skin, joints, enthesitis, and dactylitis compared with placebo (PBO) in patients with active psoriatic arthritis (PsA) in the global phase 3 trials KEEPsAKE 1 (NCT03675308) and KEEPsAKE 2 (NCT03671148) [1,2].

Objectives: To elucidate the mode of action of RZB in patients with PsA by assessing the dynamics of circulating protein biomarkers in the KEEPsAKE 2 study.

Methods: Serum samples from patients who participated in the optional biomarker exploratory analysis in the KEEPsAKE 2 study (PBO, n=189; RZB 150 mg, n=183) were used for this analysis. A commercially available multiplexed Proximity Extension Assay platform was used to assess the levels of 92 inflammation-related protein biomarkers (BMs) and a validated immunoassay was used to evaluate beta-defensin 2 (BD-2) in serum samples collected at baseline, week 4, and week 24. Changes from baseline in protein levels were expressed as log2 fold change. A repeated measure mixed linear model was used to determine BMs modulated by RZB. Correlations between relative BM levels and disease activity measures were derived using Pearson's correlation; Psoriasis Area and Severity Index (PASI) was transformed as log10 (x+1) before the analysis.

Results: Key demographics and baseline characteristics for the subset of patients included in the biomarker evaluation were comparable between PBO and RZB and were consistent with those reported in the total population for the clinical study. At baseline, the relative levels of 10 BMs (chemokine ligand 20 [CCL20], IL-17A, IL-17C, IL-24, IL-6, S100 calcium-binding protein A12 [S100A12], oncostatin M [OSM], vascular endothelial growth factor A [VEGF-A], C-X-C motif chemokine ligand 1 [CXCL1] and colony stimulating factor 1 [CSF-1]) positively correlated with at least 1 baseline disease activity measure. IL-6 was significantly and positively correlated with the inflammation marker high sensitivity C-reactive protein [hsCRP]) and musculoskeletal endpoint (Psoriatic Arthritis Disease Activity Score [PASDAS]). CCL20, IL-17A, IL-17C, and BD-2 (BMs known to contribute to psoriasis) were correlated with baseline PASI. RZB treatment significantly decreased IL-17A, IL-17C, IL-6, and BD-2 compared with PBO treatment at week 4 (the earliest time-point when samples were available), with further decreases continuing through week 24 (**Figure 1**). In patients with PsA treated with RZB the decrease in IL-6 correlated with PASDAS improvement, while the decrease in BD-2 correlated with PASI improvement.

Conclusion: IL-23, a cytokine that is important in the generation, maintenance, and proliferation of Th17 cells, serves as a major contributor to the pathophysiology of PsA [3]. Treatment with the IL-23 inhibitor RZB downregulated biomarkers associated with musculoskeletal and skin-related disease activity, and resulted in a favorable clinical response for patients with active PsA. Further investigation is needed to assess the possible relationship between changes in IL-23–related biomarkers at week 4 and long-term clinical response.

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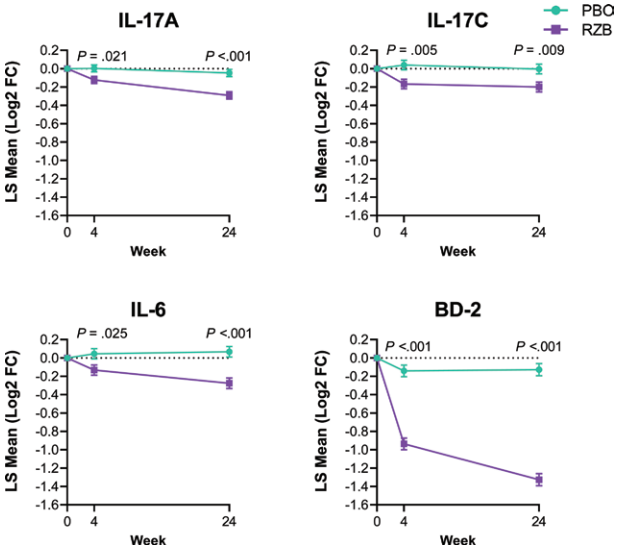


Figure 1. Biomarkers decreased following treatment with RZB compared with PBO. Nominal *P* values compare RZB and PBO at weeks 4 and 24. FC, fold change; IL, interleukin; LS, least squares; PBO, placebo; RZB, risankizumab.

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POS1546 PATIENTS WITH PSORIATIC ARTHRITIS AT BIOLOGIC THERAPY SWITCH: THE COREVITAS PSORIASIS REGISTRY

Keywords: Registries, Psoriatic arthritis

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Background: Up to 40% of patients with psoriasis (PsO) develop psoriatic arthritis (PsA), which can have a significant impact on health-related quality of life (HRQoL) [1]. Among patients with both PsO and PsA (PsO/PsA) who are treated with a biologic agent, individual symptom profiles and response to treatment can vary, with many patients switching biologic agents over their disease course. Whether patient-centred factors, beyond skin clearance, influence biologic switching remains a critical gap in the medical literature.

Objectives: To evaluate the association of psoriatic disease burden with biologic agent switch among patients with PsO/PsA in a real-world setting.

Methods: This study included data from the CorEvitas PsO Registry, a prospective, multicentre, non-interventional registry that collects data at ~6-month intervals. Biologic therapy initiations by patients with plaque PsO and dermatologist-diagnosed PsA or history of ≥3 PsO Epidemiology Screening Test (PEST) score who initiated a biologic agent at a registry visit and had ≥1 visit in the subsequent 30 months between April 2015 and August 2021 were included in this study. Disease burden at each follow-up visit after biologic initiation was defined by combinations of Psoriasis Area and Severity Index (PASI) level (≤10 vs >10) with Dermatology Life Quality Index (DLQI) level (≤5 vs >5) or patient-reported joint pain (VAS-100) level (<40 vs ≥40) [2]. The outcome of biologic switch, defined as a start of a different biologic agent within 45 days of discontinuing the initial biologic, was assessed at each follow-up visit. Proportional hazards regression was used to calculate hazard ratios (HR) and 95% confidence intervals (CIs) to evaluate associations between disease burden categories and biologic switch, adjusted for age, sex, race, ethnicity, duration of PsO, baseline disease burden category, body mass index (BMI), employment status, number of comorbidities, and treatment history.

Results: There were 2,580 patient-initiations included in this study. The mean age at patient-initiation was 52 years (Standard Deviation=13) and 52% occurred in females. Over 56% of patient-initiations were obese (BMI≥30), and 27% had at least one comorbidity. Twenty percent of patient-initiations switched biologic agents over 30 months of follow-up after a median (Interquartile Range) of 6.5 (4.6, 12.4) months of treatment. Patients with combined highest skin involvement and impact on HRQoL (PASI>10 & DLQI>5) were 14 times more likely to switch biologic (HR=14.2; 95% CI: 10.7, 18.9) than those with the lowest combined skin involvement and impact on HRQoL (PASI≤10 & DLQI≤5). Patients with DLQI>5 were over five times more likely to switch biologic vs the DLQI≤5 group among patients with PASI≤10 (HR=5.25; 95% CI: 4.23, 6.51) and nearly twice as likely to switch biologic among those with PASI>10 (HR=1.70; 95% CI: 1.06, 2.71). Similarly, patients with joint pain ≥40 had nearly a four times higher likelihood of switching vs the pain <40 group among those with PASI≤10 (HR=3.78; 95% CI: 2.91, 4.92) and tended to be more likely to switch biologic in patients with PASI>10 (HR=1.35; 95% CI: 0.79, 2.33).

Conclusion: Patients with PsO/PsA treated in a real-world clinical setting with more significant disease burden due to impaired HRQoL (DLQI and joint pain) after initiation were more likely to switch biologic agents, regardless of PASI level. These findings suggest that patient-centred factors, as well as skin clearance, have an important impact on the occurrence of biologic agent switch and the management of patients with PsO/PsA.

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POS1547 EFFICACY OF UST IN ACTIVE PSA MONITORED BY MUSCULOSKELETAL ULTRASOUND IS INDEPENDENT FROM CONCOMITANT MTX USE: SUBGROUP ANALYSIS FROM A RANDOMIZED PLACEBO-CONTROLLED INVESTIGATOR INITIATED CLINICAL TRIAL

Keywords: Psoriatic arthritis, Treat to target, Ultrasound

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Background: BDMARD treatments in patients with psoriatic arthritis (PsA) are initiated after insufficient response to csDMARD either in monotherapy or by in parallel continuing csDMARDs. Here, the value of MTX in combination with bDMARDs in PsA is still unclear. We designed an investigator-initiated, randomized, placebo-controlled trial (IIT) in active PsA to examine the potential impact of MTX-continuation or -initiation parallel to newly started UST on different outcomes beyond clinical examination (MSUS; PsASon22 score [1]).

Objectives: To compare sensitive imaging efficacy outcomes measured by MSUS changes [PsASon22] from week 4 and 24 to baseline in UST+PBO vs UST+MTX (stratified to ongoing or new onset of MTX treatment).

Methods: A total of 186 patients with active PsA (defined as TJC≥4, SJC≥4 [68/66 joint count] and DAS28≥3.2) were screened for eligibility. 173 patients were randomized to UST+MTX (new or ongoing) or UST+PBO. 84 patients were included in the subgroup analysis with MSUS scoring of PsASon22 at BL, weeks 4 and 24. Results were compared between the groups with prior MTX treatment (UST+ ongoing MTX or UST+PBO) and with new initiation of MTX to UST (UST+ new MTX or UST+PBO) according to the study design.

Results: BL data were well-balanced between treatment groups (UST+MTX, n=44; UST+PBO, n=40) and subgroups with exception of slightly higher age (mean age 53.3 years) and more (45%) female patients in the UST with ongoing MTX group. All baseline data are shown in Table 1. After UST initiation, improvement of inflammatory activity measured by MSUS using PsASon22 score was seen early at week 4 in all treatment groups. The improvement was delayed in patients with previous MTX failure ("prior MTX") and, in overall less pronounced compared to the patients without previous MTX treatment (Figure 1). At week 24,

clinical meaningful changes in PsASon22 score were seen in all treatment groups but with most prominent differences in both treatment groups with UST+PBO.
Conclusion: IL12/23 inhibition with UST is an effective treatment for active PsA independent of MTX use. Data from this IIT indicate that additional MTX has no positive impact on UST efficacy for musculoskeletal manifestations such as arthritis and enthesitis measured sensitively by PsASon22 ultrasound score validated for PsA monitoring. Moreover, by monitoring in MSUS, patients on UST monotherapy seem to benefit best from the treatment.
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Table 1. Baseline Characteristics: Subgroup analysis on MSUS

Parameters	with prior MTX, UST + MTX	with prior MTX, UST + Placebo	without MTX, UST + MTX	without MTX, UST + Placebo
	N=20	N=17	N=24	N=23
Age [years]	53.3 (SD 10.0)	46.8 (SD 15.8)	45.5 (SD 14.6)	45.2 (SD 15.6)
Sex [Female]	9 (45.0%)	6 (35.3%)	9 (37.5%)	8 (34.8%)
BMI [kg/m²]	28.0 (SD 6.1)	28.5 (SD 5.5)	30.4 (SD 4.7)	28.1 (SD 4.8)
Age at PsA diagnosis [years]	47.8 (SD 12.2)	42.5 (SD 15.0)	42.0 (SD 14.0)	40.6 (SD 16.2)
PsASon22	5.0 (1.5 to 13.0)	2.0 (1.0 to 8.0)	3.0 (1.0 to 7.0)	6.0 (3.0 to 10.0)
Presence of Enthesitis [LEI > 0]	9 (45.0%)	7 (41.2%)	16 (66.7%)	11 (47.8%)
Presence of Dactylitis [LOCF]	1 (5.0%)	1 (5.9%)	13 (54.2%)	9 (39.1%)
TJC68 [LOCF]	14.5 (9.0 to 23.5)	13.0 (9.0 to 16.0)	10.5 (8.0 to 15.0)	13.0 (9.0 to 18.0)
SJC66 [LOCF]	8.5 (6.5 to 20.5)	8.0 (6.0 to 10.0)	8.0 (7.0 to 12.0)	8.0 (5.0 to 10.0)
Nail involvement [mtNAPSI > 0]	7 (35.0%)	9 (52.9%)	17 (70.8%)	14 (60.9%)
BSA [%]	2.0 (1.0 to 6.0)	1.0 (1.0 to 3.0)	5.5 (1.0 to 12.1)	2.0 (1.0 to 5.0)
PASI	2.5 (0.7 to 5.8)	1.8 (0.6 to 3.8)	7.1 (2.5 to 10.4)	4.2 (0.8 to 8.2)
HAQ-DI [LOCF]	0.8 (0.4 to 1.4)	0.9 (0.3 to 1.5)	1.1 (0.4 to 1.6)	1.0 (0.4 to 1.3)
DLQI [LOCF]	5.5 (3.0 to 12.5)	6.0 (1.0 to 9.0)	11.5 (3.0 to 15.5)	6.0 (3.0 to 11.0)
EQ5D Health Scale VAS100 [LOCF]	47.7 (SD 24.1)	50.2 (SD 20.2)	54.2 (SD 22.9)	59.1 (SD 16.0)

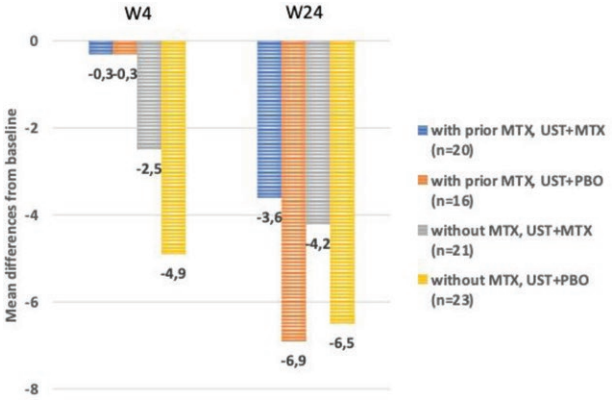


Figure 1. Improvement in PsASon22 score from baseline to week 4 and 24 (mITT population)

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POS1548

ENTHESITIS OUTCOMES IN PATIENTS WITH PSORIATIC ARTHRITIS INITIATING A TUMOUR NECROSIS FACTOR INHIBITOR IN A REAL-WORLD SETTING: DATA FROM THE EUROSPA COLLABORATION NETWORK

Keywords: Psoriatic arthritis, Enthesitis, Disease-modifying drugs (DMARDs)

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Background: Enthesitis in patients with psoriatic arthritis (PsA) can be a therapeutic challenge.
Objectives: To explore the impact of tumor necrosis factor inhibitors (TNFi) on enthesitis in patients with PsA in the EuroSpA collaboration network [1].
Methods: Prospectively collected data from biologic-naïve PsA patients ≥18 years at diagnosis, who initiated a TNFi between 2010-2020 and had available baseline data on enthesitis (defined as tenderness at any enthesis included in the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES, mainly axial entheses) and/or Spondyloarthritis Research Consortium of Canada score (SPARCC, peripheral entheses) were pooled from European countries in the EuroSpA collaboration. Changes from baseline to follow-up (6-24 months) in enthesitis scores were calculated both for the first (TNFi-1) and second TNFi (TNFi-2), as were the percentage of sites with complete resolution of enthesitis.
Results: Demographics and clinical variables of the 723 patients who had a baseline evaluation by MASES (N=549) and/or SPARCC (N=358) are detailed in Table 1. Of these, 192 (35%) and 239 (66.8%) had enthesitis by MASES (3.1±2.4, mean±standard deviation) and SPARCC (3.9±3.4) scores, respectively. The patterns of involvement are shown in Figure 1. MASES/SPARCC baseline and follow-up scores for TNFi-1 were available for 93/85 patients, respectively. Corresponding values were 27/38 patients for TNFi-2. Following TNFi-1, 58 (62.4%) patients (MASES) and 43 (50.9%) patients (SPARCC) achieved complete resolution of enthesitis. These proportions were lower following TNFi-2. SPARCC sites observed an overall lower site-specific enthesitis resolution as compared to MASES sites (61.1% vs 76.2% for TNFi-1).
Conclusion: Real-life registry data on enthesitis from several European countries are presented. Enthesitis resolution was observed in a substantial proportion of patients with PsA following TNFi-1.
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Disclosure of Interests: Ashish Jacob Mathew Speakers bureau: Novartis, IPCA Laboratories, CIPLA, Grant/research support from: Novartis, IPCA Laboratories, Lykke Midtbøll Ørnbjerg Speakers bureau: Abbvie, Eli-Lilly, Sandoz, Novartis, Egis, UCB, Consultant of: Abbvie, Eli-Lilly, Sandoz, Novartis, Egis, UCB, Grant/research support from: Novartis, Jakub Zavada, Mads Pedersen: None declared, Stylianos Georgiadis: None declared, Bente Glintborg Grant/research support from: Pfizer, Abbvie, BMS, Anne Gitte Loft Speakers bureau: Abbvie, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Grant/research support from: Novartis, Michael J. Nissen Speakers bureau: AbbVie, Eli Lilly, Janssens, Novartis, Pfizer, Burkhard Moeller Speakers bureau: Eli-Lilly, Janssen, Novartis, Pfizer, Grant/research support from: Amgen, Ana Maria Rodrigues Speakers bureau: Abbvie and Amgen, Grant/research support from: Novartis, Pfizer and Amgen, Fernando M Pimentel-Santos Speakers bureau: Abbvie, UCB, Janssen, Novartis, MSD, Tecnimed, Eli Lilly, Pfizer, Grant/research support from: Abbvie, Novartis and Janssen, Ziga Rotar Speakers bureau: Abbvie, Novartis, MSD, Medis, Biogen, Eli Lilly, Pfizer, Sanofi, Lek, Janssen, Consultant of: Abbvie, Novartis, MSD, Medis, Biogen, Eli Lilly, Pfizer, Sanofi, Lek, Janssen, Matija Tomšič Speakers bureau: Abbvie, Amgen, Biogen, Eli Lilly, Janssen, Medis, MSD, Novartis, Pfizer, Sanofi, Sandoz, Lek, Heikki Relas Speakers bureau: Abbvie, Celgene, Pfizer, UCB and Viatris, Ritva Peltomaa Speakers bureau: UCB, Lilly, Celtrion, Boehringer

Table 1. Demographics, disease activity variables and patient reported outcomes at the initiation of TNFi-1, and effectiveness of TNFi-1 and TNFi-2 regarding change and resolution of enthesitis at follow-up

	MASES		SPARCC	
Enthesitis	**Present n = 192**	**Absent n = 357**	**Present n = 239**	**Absent n = 119**
Demographics				
Age*	47.2±12	50.6±13	46.7±11	48.5±11
Sex** (Male)	84 (44)	188 (53)	98 (41)	70 (59)
BMI*	27.3±5	27.3±5	27.7±4	26.9±5
Infliximab**	7 (3.6)	37 (10.4)	43 (18)	10 (8.4)
Etanercept**	39 (20.3)	87 (24.4)	41 (17)	36 (30.3)
Adalimumab**	76 (39.6)	140 (39.2)	116 (49.4)	45 (37.8)
Golimumab**	55 (28.6)	81 (22.7)	21 (8.8)	22 (18.5)
Certolizumab**	15 (7.8)	12 (3.4)	16 (6.7)	6 (5)
Disease activity variables (Baseline)				
SJC66***	3 (0-4.5)	3 (1-6)	3 (1-5)	3 (1-7)
TJC68***	6 (3-13)	4 (2-8)	8 (4-14)	5 (2-9)
CRP*	11±18.1	10.6±14.4	8.5±15.1	12.5±15.6
DAPSA-28*	30.8±15.8	29.7±18.3	28.7±13.5	25.4±15.5
Phys Global*	48.9±20	47±22	36.3±18	45.8±23
Patient reported outcomes (Baseline)				
Pain*	67.1±21	57.6±25	67.1±21	55.6±26
PGA*	66.8±2	59.2±25	73.5±20	55.7±26
HAQ*	1±1	0.9±1	1.1±1	0.8±1
Effectiveness of TNFi in change and resolution of enthesitis at follow-up				

Timeline	**TNFi-1 MASES (N=254)**		**TNFi-2 MASES (N=70)**		**TNFi-1 SPARCC (N=167)**		**TNFi-2 SPARCC (N=59)**	
	Baseline	**Follow up**	**Baseline**	**Follow up**	**Baseline**	**Follow up**	**Baseline**	**Follow up**
Enthesitis +	**n = 93**	**n = 93**	**n=27**	**n=27**	**n=85**	**n=85**	**n=38**	**n=38**
Score, Mean±SD	3.1±2.2	1.1±2	3.6±2.7	2.3±2.5	4.4±3.5	3±3.5	5.5±4.1	3.8±3.6
Score, Median (IQR)	2 (2-4)	0 (0-1)	2 (2-4.5)	1 (1-3)	3 (2-5)	2 (1-4)	4.5 (2-8)	2 (1.2-5)
Change in Score from baseline to Follow up								
Mean±SD	0.6±1.9		0.2±2.2		0.6±2.8		0.9±3.5	
Median (IQR)	0 (0-1)		0 (0-0)		0 (0-1)		0 (0-2)	
Complete resolution at follow-up								
Number (%)	58 (62)		7 (26)		43 (51)		5 (13)	

* Mean±standard deviation; ** Frequency (Percentage); *** Median (Range)

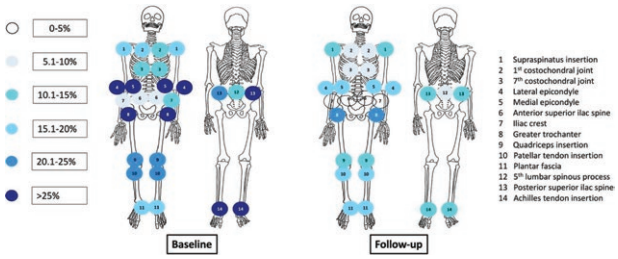


Figure 1. Distribution of enthesitis at baseline and follow-up after TNFi-1

Ingelheim, Abbvie, Janssen, Consultant of: Janssen, UCB, Boehringer Ingelheim, Lilly, Sanofi, Björn Gudbjornsson Speakers bureau: Novartis and Nordic Pharma, Thorvardur Jon Löve Speakers bureau: Abbvie, Celgene, Sinem Burcu Kocaer: None declared, Aydan Köken Avşar: None declared, Merete Lund Hetland Speakers bureau: Pfizer, Medac, Sandoz, Grant/research support from: AbbVie, Biogen, BMS, Celltrion, Eli Lilly, Janssen Biologics B.V, Lundbeck Fonden, MSD, Medac, Pfizer, Roche, Samsung Biopies, Sandoz, Novartis, Mikkel Østergaard Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, UCB, Consultant of: Abbvie, Amgen, Biogen, Eli Lilly, Janssen, Medis, MSD, Novartis, Pfizer, Sanofi, Sandoz, Lek.

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POS1549

BETTER DRUG SURVIVAL ON MONOCLONAL ANTIBODIES COMPARED TO ETANERCEPT IN FIRST LINE ANTI-TNF THERAPY IN PATIENTS WITH PSORIATIC ARTHRITIS MAY BE DUE TO DIFFERENTIAL THERAPEUTIC RESPONSE IN SKIN INVOLVEMENT: A PROPENSITY SCORE-MATCHED ANALYSIS FROM THE NATIONWIDE CZECH ATTRA REGISTRY

Keywords: Psoriatic arthritis, Skin, bDMARD

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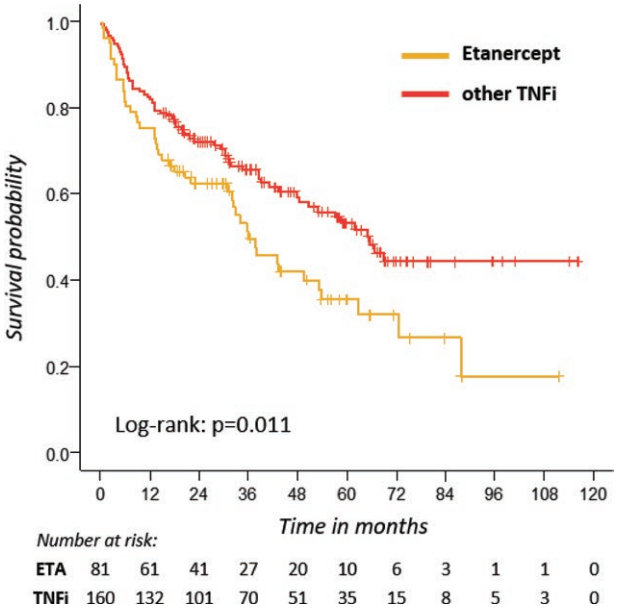


Figure 1. Drug survival of etanercept vs. other TNF inhibitors in patients with PsA.

Background: Etanercept is an agent of specific molecular structure and its efficacy in extraarticular disease differs from monoclonal antibodies. This could affect drug survival in some rheumatic diseases with a larger presence of extraarticular involvement.
Objectives: To compare the drug survival of etanercept to monoclonal anti-TNF antibodies in psoriatic arthritis and describe the response of skin disease to treatment in the two groups.
Methods: Patients with PsA starting first-line biological treatment from 01/01/2012 to 30/06/2020 were enrolled from the Czech ATTRA registry and split into two groups as either being treated with etanercept (ETA) or any other anti-TNF. Propensity scores were calculated using covariates based on statistically significant differences in the baseline characteristics and clinical relevance (Table 1). PS was then used to match 81 etanercept to 160 other TNFi patients. We performed a Kaplan-Meier survival analysis and checked for statistical significance using the log-rank test. We calculated survival rates at set time points, median survival time in each group and the hazard ratio of etanercept for drug discontinuation. The Physician global assessment of psoriasis variable (measured on a numerical rating scale 0-5) was sorted in categories of mild (0-1), intermediate (2-3) and severe (4-5) and respective percentages were calculated in the propensity-matched groups at 3, 6, 12 and 24 months. Pearson's chi-squared test or Fisher's exact test were used to check the differences for statistical significance.
Results: We found significantly worse drug survival on ETA compared to other TNFi at each time point (Figure 1). The median survival time on ETA was 35.8 (95% CI 25.1 – 46.6) months compared to 65.7 (95% CI 51.9 – 79.6) months on other TNFi. The HR of ETA for treatment termination was 1.61 (95% CI 1.11 - 2.34), p=0.011. At baseline, there were no differences in skin disease severity. The percentages of mild, intermediate and severe skin disease were 22.2%, 59.3% and 18.5% on etanercept and 25.0%, 55.6% and 19.4% on other TNFi, p=0.853. At 3 months, skin disease was significantly more severe in ETA with 50.0%, 44.8% and 5.2% compared to 76.2%, 23.8% and 0% on other TNFi, p<0.001. At 12 months, the respective percentages were 66.6%, 31.9% and 2.1% on ETA and 84.7%, 15.3% and 0% on other TNFi, p=0.015; at 24 months 62.9%, 37.1% and 0% compared to 84.9%, 15.1% and 0%, p=0.010.
Conclusion: Etanercept had worse drug retention than monoclonal antibodies in PsA. Patients treated with ETA had more severe skin disease during follow-up compared to those treated with other TNFi, which could lead to earlier switching to another drug.

Table 1. Selected baseline characteristics after propensity score matching.

	Etanercept (n=81)	Other TNFi (n=160)	p
Females	42 (51.9%)	78 (48.8%)	0.649
Age at diagnosis	40.0 (34.0–50.0)	42.0 (34.0–49.0)	0.847
Age at 1st line treatment	51.0 (42.0–59.0)	52.0 (44.0–59.0)	0.835
Disease duration (yrs)	7.1 (2.3–14.4)	7.8 (2.9–15.2)	0.587
DAPSA	36.3 (28.1–43.6)	36.2 (26.7–45.8)	0.946
CRP (mg/dl)	12.0 (4.8–25.0)	15.4 (6.3–28.0)	0.227
ESR (mm/h)	26.0 (16.0–37.0)	30.0 (15.0–40.0)	0.728
Tender joint count (68)	12.0 (9.0–19.0)	12.0 (7.0–19.0)	0.602
Swollen joint count (66)	8.0 (5.0–11.0)	8.0 (4.0–12.0)	0.759
Patient global assess. (0-100)	68.0 (50.0–80.0)	70.0 (50.0–80.0)	0.832
Physician global assess. (0-100)	60.0 (45.0–70.0)	60.0 (38.5–72.5)	0.942
Yr of administration 2012-2013	7 (8.6%)	15 (9.4%)	0.973
2014-2015	16 (19.8%)	35 (21.9%)	
2016-2017	21 (25.9%)	41 (25.6%)	
2018-2020	37 (45.7%)	69 (43.1%)	
Concomitant csDMARD	66 (81.5%)	126 (78.8%)	0.619
Concomitant MTX	53 (65.4%)	97 (60.6%)	0.467
Concomitant glucocorticoids	25 (30.9%)	54 (33.8%)	0.652

Median (IQR) in continuous variables, n (percentage) in categorical variables.

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POS1550

IMPACT OF ORAL, SELECTIVE, ALLOSTERIC TYROSINE KINASE 2 (TYK2) INHIBITOR, DEUCRAVACITINIB, ON PSORIASIS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM A PHASE 2 TRIAL

Keywords: Skin, Targeted synthetic drugs, Psoriatic arthritis

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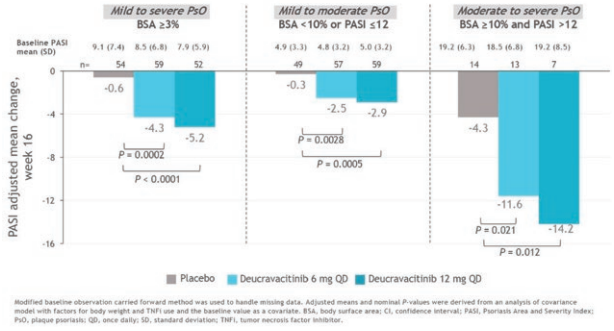
Background: TYK2 mediates signaling of key cytokines (eg, IL-23) involved in plaque psoriasis (PsO) and psoriatic arthritis (PsA) pathogenesis. Deucravacitinib (DEUC) is a first-in-class, oral, selective, allosteric TYK2 inhibitor approved in multiple countries for the treatment of adults with PsO. This was based on superiority of DEUC to apremilast and placebo (PBO) in a variety of PsO disease activity measures in 2 phase 3 trials in patients with moderate to severe PsO [1,2]. In addition, DEUC was efficacious on multiple measures of arthritis severity compared with PBO in a phase 2 trial in patients with active PsA who had ≥1 PsO lesion (≥2 cm) [3]. In patients with body surface area (BSA) ≥3% at baseline (mild to severe; 80% of patients in this trial), a greater proportion of patients achieved a ≥75% reduction in Psoriasis Area and Severity Index (PASI 75) with DEUC treatment (6 mg QD: 42.4%, *P*=0.01; 12 mg QD: 59.6%, *P*<0.0001) vs PBO (20.4%) at week (wk) 16.
Objectives: This analysis further evaluated the impact of DEUC on PsO in patients with PsA in the phase 2 trial.
Methods: The phase 2 double-blind PsA trial randomized patients (N=203) 1:1:1 to PBO, DEUC 6 mg once daily (QD), or 12 mg QD. After wk 16 (Part A), patients could enroll in an optional, double-blind period until wk 52 (Part B). In Part B, patients receiving DEUC who achieved minimal disease activity (MDA) at wk 16 continued DEUC treatment to wk 52. Measurements of PsO disease activity, including mean BSA, mean PASI score, and achievement of PASI and BSA thresholds, were assessed.
Results: At baseline (BL), PsO characteristics were generally comparable across treatment groups, with most patients (≥74%) having mild to moderate PsO (BSA <10% and PASI ≤12; **Table 1**). At wk 16, significant decreases from BL in mean PASI score were observed with DEUC treatment vs PBO both in patients with mild to moderate PsO as well as in those with moderate to severe PsO (BSA ≥10%; PASI >12) (**Figure 1**). These significant changes in PASI were observed in the mild to moderate PsO population even with very low BL PASI scores. Significant decreases in PASI from BL were observed with DEUC treatment vs PBO in both patients with background csDMARD use (DEUC 6 mg, -4.0 and 12 mg, -4.9 vs PBO, -2.3; *P*<0.05 for both) and those without csDMARD use (-3.7 and -4.0 vs -2.5, respectively; *P*<0.001, for both). At wk 16, a greater proportion of patients treated with DEUC vs PBO achieved PASI ≤1 in patients with mild to severe PsO (DEUC 6 mg, 32.2% and 12 mg, 44.2% vs PBO, 18.5%) and in patients with moderate to severe PsO (23.1% and 28.6% vs 0.0%, respectively). In mild to severe PsO, decreases in mean PASI score at wk 16 were maintained through wk 52 in patients who continued treatment with DEUC 6 mg (absolute PASI score, wk 16: 2.39, wk 52: 1.22) and 12 mg (wk 16: 0.64, wk 52: 0.24).
Conclusion: Treatment with DEUC significantly improved PsO in patients with PsA, regardless of BL PsO severity and background csDMARD use. Of note, improvement in the subgroup of patients with moderate to severe PsO in this trial was comparable to that observed in the phase 3 POETYK PSO-1 trial in patients with moderate to severe PsO [1].
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Table 1. Baseline psoriasis characteristics

		Placebo n=66	Deucravacitinib 6 mg QD n=70	Deucravacitinib 12 mg QD n=67
BSA Severity	**BSA <3%, n (%)**	9 (14)	11 (16)	14 (21)
	BSA ≥3% – <10%, n (%)	32 (49)	37 (53)	29 (43)
	BSA ≥10%, n (%)	22 (33)	22 (31)	23 (34)
PASI Severity	**PASI ≤5, n (%)**	30 (46)	33 (47)	29 (43)
	PASI >5 – ≤12, n (%)	18 (27)	23 (33)	30 (45)
	PASI >12, n (%)	15 (23)	14 (20)	7 (10)
	NR, n (%)	3 (5)	0	1 (2)
BSA ≥3% *(mild to severe)*	**n (%)**	54 (82)	59 (84)	52 (78)
BSA <10%, PASI ≤12 *(mild to moderate)*	**n (%)**	49 (74)	57 (81)	59 (88)
BSA ≥10%, PASI >12 *(moderate to severe)*	**n (%)**	14 (21)	13 (19)	7 (10)

BSA, body surface area; NR, not reported; PASI, Psoriasis Area and Severity Index; QD, once daily; SD, standard deviati

Figure. PASI mean change from baseline at week 16 by psoriasis severity at baseline



Modified baseline observation carried forward method was used to handle missing data. Adjusted means and nominal *P*-values were derived from an analysis of covariance model with factors for body weight and TNFi use and the baseline value as a covariate. BSA, body surface area; CI, confidence interval; PASI, Psoriasis Area and Severity Index; PsO, plaque psoriasis; QD, once daily; SD, standard deviation; TNFi, tumor necrosis factor inhibitor.

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POS1551 DRUG SWITCHING DUE TO INEFFICACY IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH BIOLOGICAL AGENTS. DAILY CLINICAL EXPERIENCE

Keywords: Psoriatic arthritis, bDMARD, Epidemiology

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Background: Psoriatic arthritis (PsA) is a chronic and heterogeneous inflammatory disorder that requires targeted treatment. Biological agents are often one of the first therapy regiment; however, PsA patients can experience a first line biological drug lack of efficacy. Although there are currently a variety of therapies, there is a gap of knowledge to identify the correct treatment algorithms that can be followed when PsA patients need to switch their therapy due to inefficacy.
Objectives: To evaluate the switching therapy regimens due to inefficacy in PsA patients on treatment with biological agents.
Methods: Retrospective longitudinal observational study. Subjects: Cohort of patients who assisted the outpatient rheumatology clinic from January 2006 to December 2021, and followed up to June 2022, diagnosed with PsA according to ICD-10 code and on treatment with biological agents. Main outcome: Switching of a first line of biological treatment due to inefficacy. Covariables: Sociodemographic, clinics and treatment. Statistical analysis: To estimate biological agent switching inefficacy rates, survival techniques were used, expressing the incidence rate (IR) per 100 patients*year with their respective CI at 95% [CI 95%].
Results: 141 patients with a diagnosis of PsA and on treatment with biological agents were included, with an 893.09 Patients*year follow-up. 52.48% were female, the mean age was 48.06 ± 13.22 years and 94 (80.34%) were actively working. 105 patients (74.47%) presented peripheral arthritis and 22 (15.60%) inflammatory low back pain as principal clinical domain. 108 (76.60%) patients had a history of psoriasis at baseline. 262 courses of treatment were recorded. Throughout the follow-up, Tumor necrosis factor inhibitor (TNFi) was the most used biological agent with 192 courses (73.28%) flowed by interleukin-17 inhibitors with 43 (16.41%) courses of treatment. 243 courses were on combination therapy, 185 (76.13) with methotrexate. Describing the switching due to inefficacy, 109 were recorded with a 12.20 IR [10.11-14.72], similar IR occurred according to age range, 79 occurred in female sex (IR 18.28 [14.66-22.79]), 27 (IR 18.12 [12.43-26.42]) presented inflammatory low back pain, 7 (IR 49.54 [23.61-103.91]) had dactylitis and 16 (IR 30.80 [18.87-50.28]) enthesitis. 67 (IR 11.04 [8.67-14.02]) switching had previous history of psoriasis and 65 (IR 10.73 [8.41-13.68]) were on combination therapy with methotrexate. Table 1, shows the therapy regimens switching inefficacy rates for each type of drug.
Conclusion: The biological drug switching rate due to inefficacy in our study was 12.20 per 100 patients*year. In this description study, we have identified some clinical disease manifestations and therapy regimen factors that might affect the drug switching due to inefficacy on PsA. TNFi seems to be the drug with the lowest rate of switching due to inefficacy in our study.

Table 1. Incidence rates of drug switching due to inefficacy per 100 *patient year in PsA patients treated with biological agents.

	Patients*year	Events (n)	IR	95% CI
Total, discontinuation	893.09	109	12.20	10.11 – 14.72
Abatacept	5.90	2	33.88	8.47 – 135.50
Interleukin-17 inhibitors	70.84	18	25.40	16.01 - 40.33
Ustekinumab y Guselkumab	10.29	5	48.59	20.23 - 116.75
JAK inhibitors	14.06	5	35.56	14.80 - 85.45
Tumor necrosis factor inhibitors	792.00	79	9.97	8.00 – 12.43

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1604 IL-13 INHIBITION USED FOR ATOPIC DISEASES IS ASSOCIATED WITH RISK OF PSORIATIC ARTHRITIS

Keywords: Spondyloarthritis, Psoriatic arthritis, Genetics/epigenetics

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Background: Inhibitors of the IL-13 pathway, such as dupilumab and tralokinumab, are licensed to treat atopic diseases such as eczema and asthma. Musculoskeletal adverse events that resemble enthesitis and psoriatic arthritis (PsA) after dupilumab initiation have been reported, but evidence is limited to case reports and spontaneous pharmacovigilance with uncertain causal inference. Naturally occurring genetic variation in drug targets can provide insight into their potential adverse effects.
Objectives: To investigate whether genetically proxied IL-13 inhibition (IL-13i) increases risk of PsA and other spondyloarthritis-related diseases.
Methods: Dupilumab is recognised to reduce eosinophil count in clinical studies; we therefore used it as the biomarker of IL-13i. We instrumented IL-13i using missense (protein coding) variants within the *IL13* gene that are associated with circulating eosinophil count at genome-wide significance ($p<5x10^{-8}$) in a study of 563,946 individuals. Outcome genetic associations were taken from studies of PsA, psoriasis, Crohn's disease, ulcerative colitis, ankylosing spondylitis and iritis. To examine instrument validity, we used atopic eczema and asthma as positive control outcomes, and rheumatoid arthritis as a negative control. We used the ratio method, with estimates scaled to per standard deviation (SD ~$0.14x10^9$/L) reduction in eosinophil count.
Results: One missense variant, rs20541, was selected to proxy IL-13i. Genetically proxied IL-13i was associated with increased risk of PsA (OR 37.39; 95%CI 11.52, 121.34), psoriasis (OR 20.08; 4.38, 92.01), Crohn's disease (OR 3.49; 1.38, 8.81), but not ulcerative colitis, ankylosing spondylitis or iritis. IL-13i was associated with reduced risk of positive control outcomes, but not with the negative control (Table 1).
Conclusion: Genetically proxied IL-13 inhibition is associated with increased risk of PsA, psoriasis and Crohn's disease, which may be a class effect relevant to

other IL-13i that are not yet reported to have Th17-type adverse events. These findings are compatible with the hypothesis that Th2 cytokines IL-4/-13 may act as a restraint toward Th17-type disease activation in some organs. Clinicians assessing adverse events after dupilumab initiation should be aware of incident PsA and related features. This study demonstrates the value of genetic instrumental variable analyses in evaluating rare adverse events in the study of drug safety.

Table 1. Effect of genetically proxied interleukin-13 inhibition on psoriatic arthritis and related diseases.

Outcome	Number of cases/ controls	Odds ratio	95% confidence interval	p
Psoriatic arthritis	3,609/ 9,192	37.39	11.52, 121.34	$1.64x10^{-9}$
Psoriasis	10,588/22,806	20.08	4.38, 92.01	$1.12x10^{-4}$
Crohn's disease	5,956/14,927	3.49	1.38, 8.81	0.01
Ulcerative colitis	6,968/20,464	0.92	0.40, 2.13	0.85
Ankylosing spondylitis	9,069/13,578	0.94	0.80, 1.10	0.45
Acute and subacute iritis	3,126/209,287	1.12	0.47, 2.64	0.80
Atopic eczema (positive control)	10,788/30,047	0.12	0.06, 0.23	$8.49x10^{-11}$
Asthma (positive control)	56,167/352,255	0.21	0.16, 0.28	$9.25x10^{-30}$
Rheumatoid arthritis (negative control)	14,361/43,923	0.85	0.37, 1.98	0.71

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1605 A PROOF-OF-CONCEPT STUDY EVALUATING THE USE OF FUNCTIONAL BRAIN MAGNETIC RESONANCE IMAGING IN ASSESSING TREATMENT RESPONSE IN PSORIATIC ARTHRITIS PATIENTS

Keywords: Psoriatic arthritis, Pain, Imaging

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Background: Inflammatory cytokines can alter the way the central nervous system processes pain as shown in patients with rheumatoid arthritis [Rech et al., 2013]. However, the relationship between TNFα inhibition and pain processing in individuals with psoriatic arthritis (PsA) has not been investigated.

Objectives: To assess the feasibility of functional magnetic resonance imaging (fMRI) paradigm to estimate the respone to pain and the effect of treatment in PsA patients (pts).

Methods: 6 pts with active PsA eligible to start a TNFi were included: 3 were naïve to biological disease modifying anti-rheumatic drugs and 3 were experienced. Four healthy subjects (HS) were also included. Subjects were scanned in a 3.0T scanner at baseline (BL) and week 1 (W1) after starting treatment. Each acquisition included 2 fMRI runs. The physician selected a swollen and tender joint (affected joint) and a control joint in the contralateral hand (non-affected joint). First, the brain pain response was investigated pressing the non-affected joint followed by the affected joint. The fMRI effect of pressure was represented for each subject individually, for each time point ($p<0.0001$ uncorrected level, minimum extension 10 voxels). We provided a descriptive analysis of the differences in PsA pts brain response between BL and W1 and the clinical response evaluated by the percentage of improvement of Disease Activity in Psoriatic Arthritis (DAPSA) score and visual analogue scale pain (VASp) change.

Results: All subject's demographic characteristic and PsA patients' clinical response are shown in Table 1. Brain response to pressure in HS produced activation in the sensory motor cortex, with more or less involvement of additional areas in the prefrontal, parietal and temporal cortex. In PsA pts with a higher treatment response (PsA 1, 2, 5), the brain response to pressure did not show any activation at BL whilst sensory motor cortex activation was seen at W1, with amygdala and insula activation in pts PsA 2 and 5 and prefrontal and frontal activity in pts PsA 1 and 2. In those with less response (PsA 3, 4, 6), the sensory motor cortex was activated at BL with little changes when evaluated at W1 (Figure 1). No evident differences in brain response activation were observed between naïve and TNFi experienced patients.

Conclusion: The proposed fMRI paradigm seems to be a promising candidate to predict response to treatment with TNF inhibitors in PsA patients. Studies with more patients are needed to confirm our preliminary results.

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Table 1. All subject's demographic characteristic and PsA patients' clinical response

Variables	HS1	HS2	HS3	HS4	PsA1	PsA2	PsA3	PsA4	PsA5	PsA6
Age (year)	48	30	26	59	61	52	47	66	23	63
Sex (F/M)	F	F	F	F	M	F	F	M	F	F
BMI	20	17	20	22	34	24	29	30	19	19
TJC BL					6	15	13	22	7	8
SJC BL					5	12	3	11	6	5
CRP BL (mg/dL)					0.27	0.35	0.80	0.60	0.33	0.45
CRP W1 (mg/dL)					0.04	0.05	0.44	0.16	0.14	0.20
TNFi naive					Yes	Yes	Yes	No	No	No
DAPSA improvement (%)					57	46.4	22.6	12.8	70.4	16.6
VASp change (Δmm)					-14	-21	-5	0	-51	-7

HS: healthy subject; PsA: psoriatic arthritis patient; BMI: body mass index; TJC: tender joint count; SJC: swollen joint count; CRP: C-reactive protein; TNFi: TNF inhibitor; VASp: visual analogue scale pain; BL: baseline; W1: week 1.

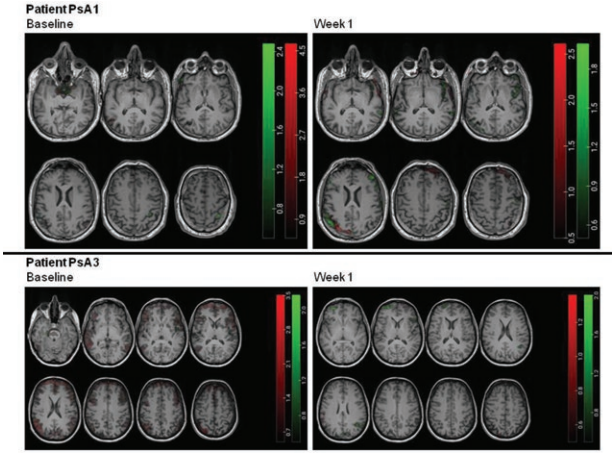


Figure 1 : Brain fMRI response to pressure of the non-affected joint (green) and the affected joint (red) overlaid on top of the structural image. Upper panel corresponds to a patient with clinical improvement (PsA1) and lower panel to a patient that did not respond (PsA3) at baseline (left column) and week 1 (right column). Differences are observed in the sensorimotor cortex activation between patients: there is an increase in the activation after week 1 in PsA1 while PsA3 showed activation at baseline but not in week 1.

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POS1606 DIFFERENTIAL AND COMBINATORIAL MECHANISM OF ACTION OF GOLIMUMAB AND GUSELKUMAB IN ULCERATIVE COLITIS INDUCTION THERAPY: IL-23 BLOCKADE DRIVES RESTORATION OF NORMAL EPITHELIUM AND MUCOSAL HEALING

Keywords: Clinical trials, Organ damage, Remission

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Background: The combination treatment of golimumab (GOL), a tumor necrosis factor-alpha (TNFα) antagonist, and guselkumab (GUS), an interleukin (IL)-23 inhibitor was shown to induce higher rates of clinical remission, endoscopic improvement, and histologic remission than each monotherapy in a randomized phase 2 induction study in TNFα-naïve patients with moderate-to-severely active ulcerative colitis (UC) (VEGA; NCT03662542).
Objectives: To investigate the underlying mechanism of action of GOL, GUS, and the combination (GUS+GOL).
Methods: Colon biopsies were obtained at screening and at Week 12 in patients who received GOL (n=48), GUS (n=52), or GUS+GOL (n=50). Tissue transcriptional profiles were determined with RNA-seq. Differentially expressed genes were analyzed in the context of cell-type specific transcriptional modules by first defining a gene correlation network and unsupervised network clustering. We then developed a method to create a single-cell-derived co-expression network using published UC single-cell data to provide high-resolution gene modules associated with specific cell types and pathways. Gene set variation analysis (GSVA) was used to quantitatively assess changes in specific biologic modules in the context of responder and non-responder analyses.
Results: By Week 12, combination therapy induced a greater magnitude of transcriptional changes in the colon compared with each monotherapy (Table 1). These genes were associated with IL-23/Th17/myeloid-related processes, inflammation, and epithelial homeostasis. Significant changes were observed in Th17 cells and inflammatory epithelial cell modules in patients that achieved endoscopic improvement (subscore 0 or 1) at Week 12 compared with non-responders (Table 1). The magnitude of change relative to baseline was greater in the GUS monotherapy and GUS+GOL arms compared with GOL alone. These changes were consistent with a decrease in crypt destruction in responders at Week 12, as observed by histologic changes in the Geboes score. Genes modulated by GUS+GOL were indicative of greater suppression of inflammation, particularly myeloid cell activation and inflammatory fibroblast development. In contrast, genes modulated by either GUS or GUS+GOL were associated with increased epithelial normalization and decreased Th17 activity compared to GOL alone.
Conclusion: Combination induction with GOL+GUS for 12 weeks drove a greater reduction in inflammation and improvement in epithelial homeostasis compared to each monotherapy, demonstrating the differential and complementary mechanisms of action of TNFα and IL-23 blockade. Combination therapy drives a significant increase in the overall magnitude of response with marked improvement in the restoration of normal epithelium.

Table 1. Differentially expressed genes at Week 12 compared with baseline pre-treatment

	Golimumab	Guselkumab	Combination
Number of genes up at Week 12	633	495	4,776
Number of genes down at Week 12	709	613	4,867
Th17 module: Responder vs Non-Responder Week 12 (p-value)	<0.001	<0.001	<0.001
Th17 module: Responder Week 12 vs Baseline (p-value)	<0.05	<0.001	<0.001
Th17 module: Non-Responder Week 12 vs Baseline (p-value)	NS	0.01	<0.001
Epithelial module: Responder vs Non-Responder Week 12 (p-value)	<0.01	<0.001	<0.001
Epithelial module: Responder Week 12 vs Baseline (p-value)	<0.05	<0.001	<0.001
Epithelial module: Non-Responder Week 12 vs Baseline (p-value)	NS	<0.01	<0.001

P-values associated with GSVA enrichment of biologic modules associated with endoscopic response and at Week 12.

REFERENCES: NIL.
Acknowledgements: NIL.
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POS1607 BIOLOGICS THERAPIES FOR PSORIASIS DECREASE FUTURE RISK FOR DEVELOPING PSORIATIC ARTHRITIS

Keywords: bDMARD, Disease-modifying drugs (DMARDs), Psoriatic arthritis

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Background: Psoriasis (PsO) is an inflammatory skin disorder with an estimated worldwide prevalence of 2–4% [1]. Psoriatic arthritis (PsA) is highly associated with higher severity of PsO, present in up to 30% of patients and 0.3–1.0% of the global population and PsA typically develops after PsO [1,2]. There are some contradictory studies in relationship to the impact of biological therapies for PsO in relationship to the prevention of PsA.
Objectives: To ascertain whether biological therapies for pre-existing psoriasis (PsO) may reduce the incidence of psoriatic arthritis (PsA) according to different treatment regimens for PsO ranging from topical therapy to biological therapy.
Methods: We conducted a retrospective exploratory study with real-world data from the third largest Israeli health maintenance organization, 'Meuhedet' which covers approximately 1,300,000 subjects. All patients of 'Muehedat' diagnosed with PsO from January 2000 until January 2020 were included in the analysis. Overall, 61,003 patients with PsO were detected. In addition, each PsO patient was paired with four control subjects by gender, age, and ethnicity. Patients diagnosed with PsA before the diagnosis of PsO or less than six months after were excluded from the analysis. We defined PsO according to physicians' diagnoses. PsA included patients with either peripheral or axial arthritis. Patients were classified according to their treatment; Group 1-topical therapy, phototherapy or no therapy, Group 2 - conventional DMARDs (cDMARDs; methotrexate or sulfasalazine), Group 3 -biologics DMARDs (bDMARD) The incident cases of PsA were analyzed according to the aforementioned different lines of therapy. Patients in the bDMARDs group were further sub-grouped according to the first-line prescribed treatment. Time-dependent Cox proportional hazard models were used to evaluate the adjusted risk of developing PsA by treatment group. Data analysis was conducted with Python Software Foundation, Python Language Reference, version 3.9.12, R version 4.2.0, RStudio (RStudio Team, 2020), and the 'Survival' package (v3.2; Therneau, 2020).
Results: 58,671 patients were included contributing a total of 628,228 patient-years. This analysis was adjusted to gender, body mass index (BMI), age of PsO diagnosis, time from psoriasis diagnosis to the group treatment, and number of biological treatments lines. Adjusted Cox proportional hazards regression analysis showed that the risk of developing PsA in PsO patients treated with cDMARDs was significantly higher in comparison to those treated with topical therapy (HR: 2.76, CI: 2.19 – 3.48, p-value: <0.001). On the contrary, the analysis also showed that the risk of developing PsA in PsO patients was significantly decreased in those treated with biological agents in comparison to topical therapy (HR: 0.62, CI: 0.42 – 0.90, p-value: <0.014).
Conclusion: PsO patients treated with cDMARDs are at higher risk of developing PsA in comparison to those treated with topical therapy alone which may reflect the severity of extent of psoriasis in the c DMARD group been linked to PsA. Biological therapy decreased risk of developing PsA in comparison to topical therapy.
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Disclosure of Interests: None Declared.
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POS1608 **MIRNA BIOMARKERS FOR ARTICULAR AND CUTANEOUS RESPONSE TO METHOTREXATE IN PSORIATIC ARTHRITIS**

Keywords: Genetics/epigenetics, Disease-modifying drugs (DMARDs), Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a chronic, progressive disease associated with psoriasis that can lead to joint damage, disability, and increased mortality. Early diagnosis and management of inflammation is essential for improving clinical outcomes. Methotrexate (MTX) is the recommended first-line treatment for early PsA patients with polyarthritis and relevant skin involvement, however many patients are unresponsive to therapy. MicroRNA (miRNA) modulate gene expression at a post-transcriptional level and constitute a promising source of biomarkers that could enable the future personalization of treatment plans.
Objectives: To identify a set of miRNAs that serve as biomarkers for MTX treatment response by comparing miRNA expression between responders and non-responders before initiation of therapy.
Methods: From our prospective PsA database we identified biologic-naive PsA patients satisfying the CASPAR criteria before the initiation and 6 months after MTX treatment. Articular response to MTX was defined as achieving a treatment target of low disease activity (4 ≤ DAPSA < 14) or remission (DAPSA < 4). Cutaneous response to MTX was defined as a reduction of at least 50% in PASI score. miRNA expression was evaluated in biobanked serum samples through next-generation sequencing. Differential expression was assessed by linear modelling with empirical Bayes moderation (using the Limma R package). Linear models were corrected for sequencing batch, age, sex, ethnicity, BMI, smoking, use of NSAIDs, MTX treatment duration and dose. Enrichment of biologic pathways corresponding to gene targets of the identified miRNAs was examined using the integrative tool pathDIP by restricting the analysis to literature curated pathways and experimentally detected protein-protein interactions with a prediction confidence of 0.99.
Results: 70 biologic-naive, PsA patients were included in the study. Articular and cutaneous response to MTX was observed in 28.57% and 34.28% of patients, respectively. Pretreatment expression of miR-127-3p was significantly lower in patients showing an articular response to MTX ($p<0.001$). Of note, miRNA 127 expression has been associated with a protective effect in inflammatory lung fibrosis and osteoarthritis[1]. A set of 7 miRNAs (miR-155-5p, miR-140-3p, miR-432-5p, miR-382-5p, miR-532-5p, miR-139-3p, and miR-379-5p) were significantly associated ($p<0.01$) with cutaneous response to MTX. The most commonly enriched signaling pathway targeted by these miRNAs is the PI3K/AKT/mTOR which is a key regulator of keratinocyte proliferation[2].

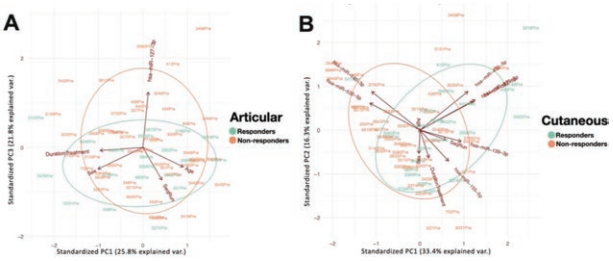


Figure 1. Principal component analysis of samples before methotrexate (MTX) treatment. A. Patients showing articular response to MTX (reaching treatment target of low disease activity or remission: DAPSA score below 14) present lower expression of miR-127-3p. B. Patients showing cutaneous response to MTX treatment (reaching a reduction of 50% in PASI) present lower expression of miR-140-3p and miR-532-5p and higher expression of miR-155-5p, miR-432-5p, miR-382-5p, miR-139-3p and miR-379-5p.

Conclusion: We identified miR-127-3p as a biomarker of articular response, and 7 other miRNAs as biomarkers of cutaneous response to MTX treatment in PsA patients.

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Disclosure of Interests: None Declared.
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Other orphan diseases

POS1552

NO BURN-OUT IN PEDIATRIC-ONSET BEHÇET'S DISEASE PATIENTS DURING ADULTHOOD FOLLOW-UP

Keywords: Behcet's disease

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Background: Although onset of Behçet's Disease (BD) is common in the second or third decade, initial symptoms occur under the age of 16 years in 4–26% of the patients [1].
Objectives: In this study we aimed to assess the clinical course of pediatric onset BD in adulthood period.
Methods: The files of 1114 BD patients were reviewed retrospectively. 51 (4.6%) (F/M:21/30) pediatric-onset BD patients were included in the analysis. Demographic and clinical characteristics, follow-up and treatment data of the patients were recorded from files.
Results: The median age at diagnosis was 16 (14-17) years, and the median follow-up duration was 51 (26-96) months. Of all patients, 33.3% (n=17) had ocular involvement, 27.5% (n=14) had vascular involvement, 17.6% (n=9) had central nervous system involvement, and 3.9% (n=2) had gastrointestinal system involvement. Erythema nodosum was more common in females (p=0.008) and vascular involvement was more common in males (p=0.025). At the end of follow-up, 32 (62.8%) patients had major organ involvement, half of them had at the time of diagnosis. Forty-seven (M:27/F:20) patients had a follow-up with median of 50 (20-82) months in adulthood period. Thirty-one (65.6%) patients had major organ involvement. While 20 (64.5%) patients had major organ involvement in the pediatric period, 11 (35.5%) patients developed major organ involvement in adulthood. Overall, 19 (40.4%) patients had active disease manifestations (relapse and/or new major organ involvement) in adulthood follow-up. Of these patients, 11 (57.9%) had new major organ involvement, 7 (36.8%) had a relapse of the same organ, and one (5.3%) had both new major organ involvement and a relapse. The disease course of patients is seen in Table 1.
Conclusion: Our results show that, about half of the pediatric-onset BD patients still have active disease manifestations (mainly new major organ involvement) in adulthood period.

Table 1. Disease course of patients followed in adulthood period.

Patients followed in adulthood	**n=47 (%)**
Major organ involvement in childhood	20 (42.6%)
Relapse or/and new major organ involvement	*8 (17%)*
No relapse or major organ involvement	*12 (25.5%)*
Mucocutaneous disease in childhood	27 (57.4%)
New major organ involvement	*11 (23.4%)*
No major organ involvement	*16 (34%)*

REFERENCE:
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1553

THE SIGNIFICANT ASSOCIATION OF HLA-A26 WITH UVEITIS AND GASTROINTESTINAL INVOLVEMENT IN PATIENTS WITH BEHÇET'S DISEASE IN A MULTICENTER STUDY

Keywords: Behcet's disease

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Background: Specific haplotypes of human leukocyte antigen (HLA) are associated with susceptibility and disease activity of Behçet's disease (BD). However, the clinical importance of HLA-A26 in BD is not well recognized compared to that of HLA-B51.
Objectives: This study aimed to examine the association between HLA-A26, HLA-B51, clinical manifestations, and disease severity in BD, especially focusing on HLA-A26 possession.
Methods: This study was a multicenter cross-sectional observational study and patients with BD were enrolled from 2006 to 2021. All patients met the International Criteria for BD [1] or the diagnostic criteria of the Behçet's Disease Research Committee of Japan [2]. Disease severity was evaluated using Krause score reflecting the entire spectrum of disease manifestations [3]. Both serotypes and genotypes were accepted for HLA typing.
Results: In total, 200 patients were enrolled in this study. Uveitis was observed in 95/196 patients (48.5%) and gastrointestinal involvement in 57/167 patients (34.1%). HLA haplotypes were identified for HLA-B51 (n = 52/106, 49.1%), HLA-A26 (n = 25/88, 28.4%), and both HLA-B51 and HLA-A26 (n = 6/88, 6.8%). While HLA-A26 showed no significant association with clinical manifestations without adjustment for HLA-B51, HLA-A26 possession showed a higher frequency of uveitis (HLA-A26 positive vs. negative: n = 6/6, 100% vs. n = 16/32, 50.0%, respectively, p = 0.03) and higher Krause scores (median: 7 vs. 5, respectively, p = 0.02) under conditions with HLA-B51. Furthermore, the association between uveitis and gastrointestinal involvement was influenced by HLA-A26: HLA-A26 possession was associated with a higher frequency of uveitis in patients with gastrointestinal involvement (HLA-A26 positive vs. negative: n = 5/9, 55.6% vs. n = 0/21, 0%, respectively, p = 0.001), as well as for gastrointestinal involvement in patients with uveitis (HLA-A26 positive vs. negative: n = 5/11, 45.5% vs. n = 0/24, 0%, respectively, p = 0.001). All 5 patients with both uveitis and gastrointestinal involvement had HLA-A26 (HLA-A26 positive vs. negative: n = 5/21, 23.8% vs. n = 0/58, 0%, respectively, p = 0.001).
Conclusion: HLA-A26 was associated with severity of BD and uveitis in patients with HLA-B51, and was associated with coexistence of uveitis and gastrointestinal involvement. This study suggested the importance of confirming HLA-A haplotype in patients with BD.
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Table 1. Comparison of clinical characteristics of BD patients with and without HLA-A26

	Total (n = 88)	HLA-B51 (+) (n = 38)	Uveitis (+) (n = 40)	Gastrointestinal involvement (+) (n = 30)
Uveitis†, %	56.0 vs. 41.3, p = 0.24	**100 vs. 50.0, p = 0.03**	-	**55.6 vs. 0, p = 0.001**
Gastrointestinal involvement†, %	42.9 vs. 36.2, p = 0.61	60.0 vs. 24.1, p = 0.14	**45.5 vs. 0, p = 0.001**	-
Uveitis + Gastrointestinal involvement†, %	**23.8 vs. 0, p = 0.001**	**60.0 vs. 0, p = 0.002**	-	-
Krause score¶, mean	6 vs. 5, p = 0.43	**7 vs. 5, p = 0.02**	7 vs. 6, p = 0.27	**6.5 vs. 5, p = 0.04**

†: HLA-A26 positive (%) vs. negative (%); Fisher's exact test ¶: HLA-A26 positive vs. negative; Mann-Whitney U test

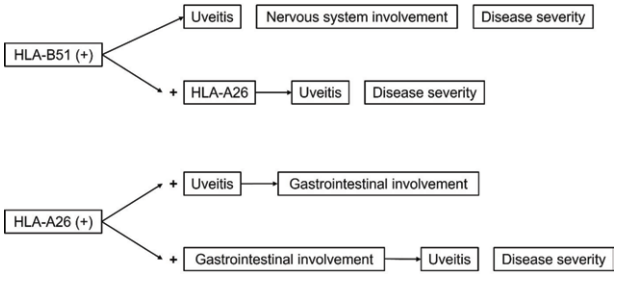


Figure 1. Association between haplotypes and clinical manifestations

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1554

AN OBSERVATIONAL MULTICENTER STUDY COMPARING THE EFFECTIVENESS BETWEEN TNF INHIBITORS AND APREMILAST ON ORAL ULCERS OF BEHCET'S DISEASE

Keywords: Behcet's disease

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Background: Recurrent oral and genital ulcers are the most nagging clinical manifestations of Behcet's disease (BD) and colchicine should be used first for the treatment and prevention of ulcers relapse. In contrast, TNF-α inhibitors (TNFi) are helpful in resistant cases, leading to a rapid improvement of mucosal lesions [1]. More recently, the phosphodiesterase-4 inhibitor apremilast was evaluated in two RCTs showing a significant improvement of oral ulcers compared to placebo [2, 3]. Moreover, several observational studies also investigated the effectiveness of apremilast in BD patients with mucosal ulcers [4].

Objectives: To date, there are no comparative data about the effectiveness between TNFi and apremilast in mucocutaneous involvement of BD. The present study aims to compare the effectiveness between TNFi and apremilast on oral ulcers of BD.

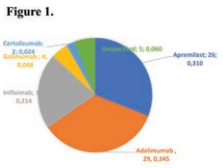
Methods: Data on patients classified as BD (according to International Criteria for BD and International Study Group criteria) who underwent apremilast or TNFi for refractory oral ulcers from March 2017 to January 2022 in 7 tertiary rheumatology centers (6 Italian and 1 Spanish) were retrospectively analyzed. Retrieved data including demographics and clinical characteristics were collected. We also recorded the presence of active oral aphtosis at either baseline, 3-month and 6-month follow-up as well as the occurrence of oral ulcers during the intervals between visits. Patients on TNFi were considered controls for nearest-neighbour propensity score (PS-)-matching (neighbours for replacement matching, minimum 1, maximum 4). PS is an epidemiological tool used for the adjustment of non-randomized longitudinal studies. It is a conditional probability of being exposed to a disease given an asset of covariates. In brief, this was carried out using the patients' age, disease duration and gender, with a selected calliper of 0.2. Chi-square test was used to test difference between proportions of patients with active aphtosis in both groups at different follow-up times.

Results: Among 159 patients with BD on TNFi or apremilast, the matching algorithm retrieved 84 patients. More in detail, 26 patients in the apremilast group and 58 patients in TNFi group. All had active aphtosis at treatment start. Clinical ad demographic characteristics of patients at baseline are reported in Table 1 and Figure 1 and 2. Concerning proportion of patients with active oral aphtosis, no difference was observed either at 3-month (p=0.60) and 6-month (p=0.66) follow-up visits (Figure 2). Consistently, the rate of flares in the time intervals between visits was not different between groups (46.15% vs 37.93% from month 0 to 3, p=0.47; 34.62% vs 34.48% from month 3 to 6, p=0.99).

Conclusion: The main limitations of our study are the small sample size and the short-term follow-up. Nevertheless, we provide evidence that apremilast and TNFi show similar effectiveness, inducing a meaningful and early benefit in BD patients with refractory oral ulcers.

Table 1.

	Apremilast		TNF-α inhibitors	
	Av.Obs.		Av.Obs	
Female, n(%)	26	17(65.38)	58	30 (51.72)
Age at diagnosis, mean (SD)	26	31.15(14.05)	58	26.60(12.39)
Age at baseline, mean (SD)	26	28.34(14.57)	58	40.84 (12.73)
Disease Duration, mean (SD)	26	7.19 (8.24)	58	4.24(5.35)
csDMARDs combotherapy, n(%)	26	7(26.92)	58	37(63.79)
Current bDMARD/tsDMARD treatment line, median (IQR)	26	1 (1-2)	58	1(1-2)



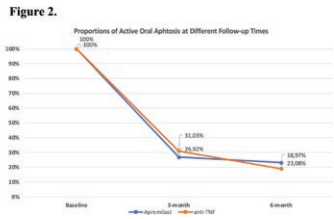


Figure 1.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1555

MEASUREMENT OF COMMON FEMORAL VEIN WALL THICKNESS IS A USEFUL DIAGNOSTIC TOOL TO DIFFERENTIATE OCULAR BEHÇET'S DISEASE FROM OTHER INFLAMMATORY UVEITIS

Keywords: Ultrasound, Behcet's disease

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Background: Diagnosis of Behçet's Disease (BD) can be challenging, especially in patients presenting with single major organ involvement. Our group showed that common femoral vein (CFV) wall thickness measured by Doppler ultrasonography (US) can be a non-invasive diagnostic method [1] and can also be used to diagnose incomplete BD [2]. Since ocular involvement of BD may result in irreversible vision loss if untreated, it is important to diagnose without delay and initiate immunosuppressive therapy promptly.

Objectives: In this study, we aimed to assess the discriminative role of CFV wall thickness measurement in uveitis associated with BD compared to other inflammatory uveitis.

Methods: Patients with BD uveitis (n=41) and age-gender matched 58 non-BD uveitis patients were included in the study. Demographics, clinical characteristics, and treatment data were recorded during routine visits. CFV wall thickness was measured by an experienced and blinded radiologist on the same day.

Results: Twenty-four (58.5%) of BD patients and 23 (39.7%) of non-BD patients were male. All BD patients had panuveitis. 3 (3.0%), 8 (8.1%), 8 (8.1%) of non-BD patients have anterior uveitis due to sarcoidosis, HLA-B27 positivity, ankylosing spondylitis, respectively, and 7 (7.1%) had idiopathic anterior uveitis. 12 non-BD patients had panuveitis caused by sarcoidosis. The most common complaint was decreased visual acuity in both groups. Right CFV (0.73 mm± 0.08) and left CFV (0.73 mm± 0.07) wall thickness of BD patients was significantly higher than right and left CFV (0.57 mm± 0.1 for both) wall thickness of non-BD patients (p < 001).

Conclusion: Diagnosis of ocular BD can be challenging, especially when there is no other clinical finding or organ involvement specific to BD. Our results suggest that measurement of CFV wall thickness by Doppler US can be helpful for the differentiation of ocular BD from other causes of inflammatory uveitis in daily practice.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5935

POS1556 EFFICACY OF APREMILAST TREATMENT FOR ARTHRITIS IN BEHÇET'S DISEASE

Keywords: Behcet's disease, Disease-modifying drugs (DMARDs)

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Background: The arthritis that occurs in Behcet's disease (BD) is considered to be an oligoarthritis but one of the intractable symptoms related to quality of life [1]. Apremilast is effective for oral ulcers in BD, but its efficacy against arthritis has not been well established.
Objectives: This study aims to determine the effect of apremilast treatment on arthritis in BD.
Methods: Patients diagnosed with BD disease between January 2011 and June 2022 who had a history of arthritis within the past five years were included in this study. Patients with Behçet's disease treated with apremilast were compared with those not treated (control group). Frequency of oral and genital ulcers, skin lesions, arthritis, and other typical domains of Behcet's disease, evaluated every 3 months for 12 months. The number of tender and swollen joints and DAS28 as indicators of arthritis activity and Behçet's disease activity form (BDCAF) as an indicator of disease activity were investigated retrospectively.
Results: There were 55 patients with Behçet's disease available for analysis in this study, 16 of whom were treated with apremilast. There was no clear difference between the two groups for pre-existing BD disease domains. Active lesions at the beginning of the analysis included significantly more oral ulcers and skin pustules in the apremilast group than in the control group, but there was no significant difference in the incidence of arthritis (Table 1). Similarly, there were no significant differences in the number of swollen joints, tender joints, or serum CRP levels between the two groups. The frequency of having arthritis was present in 56.3% of the apremilast group at baseline and decreased in the apremilast group at 3 and 6 months, but remained unchanged in the control group (Figure 1). In the apremilast group, not only did oral ulcers, genital ulcers, and skin pustular lesions improve after 3 and 6 months, but DAS28 and BDCAF also significantly decreased after 3 months (DAS28: p = 0.0010, BDCAF: p = 0.0019).
Conclusion: Apremilast is effective against arthritis as well as skin mucosal lesions in BD and could be one of the treatment strategies for arthritis in BD.
REFERENCE:

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Table 1. Characteristics of BD patients.

	Apremilast Treatment N=16	Control N=39	P value
Age, mean (SD), years	46.2 (13.6)	40.3 (10.9)	0.128
Sex, female, number (%)	12 (75)	28 (71.8)	0.807
Disease duration, mean (SD), years	11.0 (5.7)	15.1 (10.7)	0.272
Active organ involvement, number (%)			
Oral ulcer	16 (100)	23 (59.0)	0.0002
Genital ulcer	5 (31.3)	4 (10.3)	0.067
Skin lesion	11 (68.8)	6 (15.4)	0.0001
Erythema nodosum	1 (6.3)	5 (13.2)	0.439
Thrombophlebitis	1 (6.3)	0 (0)	0.115
Skin pustules	10 (62.5)	3 (7.9)	<0.0001
Ocular involvement	0 (0)	1 (2.6)	0.404
Epididymis	0 (0)	1 (2.6)	0.172
Gastrointestinal involvement	1 (6.3)	0 (0)	0.113
Arthritis	9 (56.3)	24 (61.5)	0.717
Tender joints (28 joints)	1 [0-2.8]	1 [0-1]	0.523
Tender joints (68 jouints)	2 [0-3.8]	1 [0-2]	0.410
Swollen joints (28 jouints)	0 [0-0]	0 [0-1]	0.117
Swollen joints (66 jouints)	0 [0-0]	0 [0-1]	0.268
CRP, mg/dl	0.09 [0.04-0.31]	0.09 [0.02-0.21]	0.551

The statistical analyses were conducted using the chi-squared test or Mann-Whitney U test.[#]Nonparametric distributions are represented as medians (interquartile range).

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5262

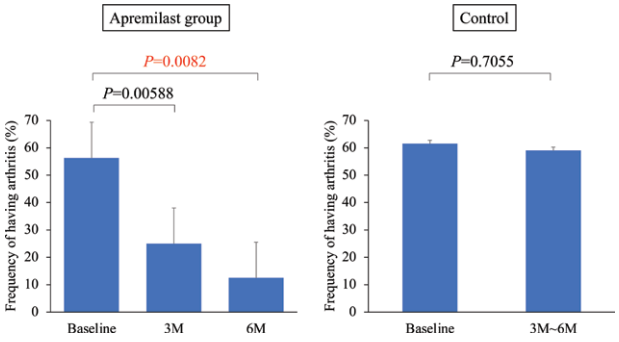


Figure 1. Effect of apremilast treatment on the rate of specific organ lesionsThe graph summarizes changes in the rate of oral ulcers, genital ulcers, skin lesions, and arthritis in the control group and at baseline (0M), 3 (3M), and 6 (6M) after apremilast treatment. P-values were determined using McNemar test. M, months.

POS1557 MUSCULOSKELETAL ULTRASOUND IN PATIENTS WITH HEREDITARY ANGIOEDEMA DUE TO C1-INHIBITOR DEFICIENCY: PROBING DISEASE ACTIVITY AND DAMAGE

Keywords: Descriptive studies, Rare/orphan diseases, Ultrasound

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Background: Hereditary angioedema (HAE) due to C1 esterase inhibitor protein (C1INH) deficiency is a rare disorder (1:50000) that is characterized by widely variable and potentially fatal attacks of subcutaneous and submucosal swelling which are generally self-limiting. The defect of C1INH allows for a dysregulated kallikrein–kinin pathway, and thus for the overproduction of bradykinin with, in turn, the consequent activation of the bradykinin B2 receptors. The resulting increased vascular permeability induces painful angioedema attacks most often involving the hands. Musculoskeletal ultrasound (MSUS) enables evaluation of the soft tissues, providing additional and more accurate assessment of inflammation and visualization of structural damage.
Objectives: To explore the potential damage at the site of angioedema attack, we performed an US-study of hands and wrists in consecutive C1INH-HAE patients referring to the HAE Reference Centre at "Tor Vergata" University Hospital in Rome (Italy).
Methods: Consecutive C1INH-HAE patients underwent biochemical analyses and, in the same day, MSUS evaluation that has been performed by an expert rheumatologist at wrists and hands. The US (Esaote MyLab™X75, 4-15 MHz) semi-quantitatively graded subcutaneous tissue edema, synovitis/tenosynovitis-like lesions, erosions, osteophytes, and bone edema according to the 2021 Outcome Measures in Rheumatology (OMERACT). HAE Quality of Life Questionnaire (HAE-QoL) and HAE Activity Score (HAE-AS) were registered.
Results: 94 C1INH-HAE patients from 50 independent families (aged 43.2 ± 17 yrs) has been included, with 60% females and 20.6% smokers. All patients experienced recurrent acute attacks at the hands: a third of the cohort (31.3%) was on long-term-prophylaxis at the time of the study and 20% of subjects had the last acute attack more than 12 months before. In 75% of the cohort, the HAE-QoL described a mild-moderate QoL and HAE-AS showed a mild disease activity. Smokers were prevalent among patients in high disease activity than in patients in low disease activity (P<0.05). High level of C-reactive protein (≥5 mg/dl) has been documented in 13.8% of patients while rheumatoid factor and anti-cyclic-citrullinated-peptide-antibody (ACPA) resulted in rare cases (2.1% for both). A vitamin D deficiency (< 7 ng/dl) has been registered in 3.6% of patients although insufficient vitamin D (7-30 ng/dl) resulted in 50% and hyperuricemia (>7 mg/dl) in 4% of cases. ANA titer≥1:160 occurred in 25.5%. The joint pain at the hands/wrists have been reported by 70% of patients: patients with joint pain showed a lower mean C1INH antigen level and a higher number of attacks in the last 3 months than patients without (P<0.05). Patients with at least 1 US lesion (62.8%) were significantly older and affected by a greater number of angioedema attacks than patients without lesions (37.2%, P<0.05 for both). US lesions were mainly represented by osteophytes (63.5%) and cartilage damage (35.3%). Synovitis/tenosynovitis involving at least 1 joint has been documented in 44.7% of the cohort but a positive Power Doppler signal was revealed in rare cases (2.1%). The subcutaneous tissue edema resulted in a third of the cohort (29.8%). Cartilage damage and subcutaneous edema was similarly distributed among hands and wrists. The distal radioulnar joints were the most affected (25.5%) while metacarpophalangeal were affected in 17.6% of cases. Synovitis/tenosynovitis was mild-moderate in 98% of cases. In patients showing subcutaneous tissue edema, it was documented in 78.7% of cases at the hands and in 21.3% at the wrists.

Conclusion: C1-INH-HAE patients reported pain at joint level in an elevated frequency. Our findings support the role of MSUS in C1-INH-HAE patients by highlighting that US lesions at the specific sites of attacks, although mild, occur in more than a half of patients and appear to be linked with the age and/or disease duration and the number of attacks.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1558

LONG-TERM SAFETY OF CANAKINUMAB IN AUTOINFLAMMATORY PERIODIC FEVER SYNDROMES – 48-MONTH DATA FROM THE RELIANCE REGISTRY

Keywords: Innate immunity, Real-world evidence, Rare/orphan diseases

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Background: Autoinflammatory periodic diseases (AID) can be treated with the interleukin-1β inhibitor canakinumab (CAN). CAN has been shown to be safe and effective in controlled trials and routine clinical practice.

Objectives: In this study general safety parameters in patients with canakinumab in cryopyrin-associated periodic syndromes (CAPS), familial Mediterranean fever (FMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) and tumor necrosis factor receptor-associated periodic syndrome (TRAPS) on CAN therapy were investigated in routine clinical practice.

Methods: RELIANCE is a prospective, non-interventional, observational study in Germany enrolling pediatric (age ≥2 years) and adult patients with a clinically confirmed diagnosis of AID who routinely receive CAN. Efficacy and safety parameters are recorded at baseline and assessed at 6-month intervals.

Results: Data from N=232 patients (N=229 with baseline visit yet documented) diagnosed with autoinflammatory diseases enrolled in the RELIANCE registry between October 2017 and December 2022 were included in the present interim analysis. Median age of the total study cohort was 20.0 years (2–80 years), 52% were female and median duration of CAN treatment before study entry was 2 years (0–15 years). During the study, 898 adverse events (AE) occurred in N=164 patients (71%). Among the most common AE classified as suspected adverse drug reactions (ADR) were decreased neutrophil count (8 events, IR 1.46), increased inflammatory markers (12 events, IR 2.19), nasopharyngitis (14 events, IR 2.55), and pyrexia (17 events, IR 3.10). In N=35 patients (15%), a total of 98 serious adverse events (SAE) were reported. Of these events, 31 SAE were classified as suspected adverse drug reactions (SADR; Table 1). During the last 3 years of observation within the study, incidence rates (IR) decreased from 76.21 to 51.44 (ADR) and 7.44 to 5.66 (SADR). Patients receiving greater than standard dose CAN experienced higher levels of ADR/SADR compared to patients under less than standard and standard dosing. How much high dosage or severeness of disease contribute to this phenomenon remains unclear. AE related dose reductions have not been reported. **Conclusion:** The 48-month interim data of the RELIANCE study confirm sustained safety of long-term treatment with CAN in the entire study population.

Table 1. Overview of adverse events in the RELIANCE study across all study indications (N=232 patients).

AE	Number of events		IR‡ per 100 patient-years	
All types of AE	898		163.82	
ADR	282		51.44	
SAE	**Number of events**		**Incidence rate‡ per 100 patient-years**	
All types of SAE	98		17.88	
SADR	31#		5.66	
Patients with adverse drug reactions by dose category, n (%)	**Less than standard dose (N=58)**	**Standard dose (N=60)**	**Greater than standard dose (N=85)**	**Dose missing (N=29)**
ADR	13 (22.4)	15 (25.0)	37 (43.5)	10 (34.5)
SADR	2 (3.4)	2 (3.3)	7 (8.2)	1 (3.4)

#Abdominal pain, Alport's syndrome, appendicitis, arthralgia, blister, cardiovascular disorder, chest pain, circulatory collapse, dehydration, diplopia, dyspnoea, erythema, febrile convulsion, gastroenteritis, glomerulonephritis, Haemophilus test positive, myalgia, oedema, pneumonia, premature delivery, skin discoloration, tachycardia, tonsillitis bacterial, tonsillitis streptococcal, vision blurred (1 event each, IR 0.18‡), tonsillectomy (2 events, IR 0.36‡), pyrexia (3 events, IR 0.55‡), not yet coded (1 event, IR 0.18‡)‡ IR = number of events * 36525/ sum of observation days (=200218)ADR, suspected adverse drug reaction; AE, adverse event; SADR, suspected serious adverse drug reaction; SAE, serious adverse event

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POS1559

THE CHARACTERISTICS OF THE PATIENTS UNDER NINTEDANIB TREATMENT DUE TO INTERSTITIAL LUNG DISEASES ASSOCIATED WITH CONNECTIVE TISSUE DISEASES

Keywords: Sjögren syndrome, Lungs, Systemic sclerosis

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Background: Nintedanib provides a decline in the reduction of forced vital capacity (FVC) in patients with progressing lung fibrosis.
Objectives: To assess demographical, clinical, and radiological characteristics of the patients with connective tissue diseases (CTDs) associated interstitial lung disease (ILD), who were under nintedanib treatment.
Methods: This retrospective observational study was conducted with the patients who received nintedanib for progressing lung fibrosis associated with CTDs. The patients who had followed up between January 2020 and December 2022 included in the study. The demographical, clinical, and radiological data were obtained from patients' files.
Results: Twenty-two (14.8%) patients (11 male/11 female) with CTD related ILD who had a mean age of 65.9 ±7.6 had received nintedanib. The median disease duration was 49.5 (35.8-101.8) months for CTD and 43 (26.3-95) months for ILD. Eighteen (81.8%) patients had a CTD diagnosis prior to an ILD diagnosis. The median duration for nintedanib treatment was 10.5 (7-14.8) months. Eight (36.4%) patients had Sjogren's syndrome, 7 (31.8%) patients had systemic sclerosis, 5 (22.7%) patients had rheumatoid arthritis, and 2 (9.1%) patients had undifferentiated CTD. Ten (45.5%) patients had a history of smoking. Only one patient was using nintedanib 150 mg/day due to gastrointestinal intolerance. Hypertension was the most frequent comorbidity in 5 (22.2%) patients, and the second most frequent one was pulmonary hypertension in 3 (13.6%) patients. During 6 minutes walking test, 12 (55.5%) patients had desaturation. According to high-resolution computed tomography (HRCT) findings, 18 (81.8%) patients had usual interstitial pneumonia (UIP) pattern, and 4 (18.2%) patients had nonspecific interstitial pneumonia (NSIP) pattern. The most frequent parenchymal pattern was UIP (p<0.005). There was no mortality in the study group. Twelve (55.5%) patients had received at least one immunosuppressive treatment. Nintedanib was initiated due to the progression of fibrosis in HRCT in half of the patients or declined pulmonary function test results in the other half. All patients had worsening pulmonary symptoms. The mean FVC value of the patients at the beginning was 87±12.2 ml, and it was 89.3±14.8 ml at the 6th-month follow-up visit with no statistically significant difference (p=0.51). Four (66.7%) patients had stable findings, 2 (33.3%) patients had progression on HRCT, of whom had control HRCT under nintedanib treatment. Combined with nintedanib, cyclophosphamide (1 patient), rituximab (1 patient), azathioprine (3 patients), and mycophenolate mofetil (4 patients) were used. The most common side effect of nintedanib was diarrhea.

Table 1. Demografic and clinical characteristics of the study group

		Nintedanib (n = 22)
Gender, n (%)	Female	11 (50)
	Male	11 (50)
Age, [a] year		65.9±7.6
Disease duration for CTD, [b] month		49.5 (35.8-101.8)
Disease duration for ILD, [b] month		43 (26.3-95)
Duration of nintedanib treatment, [b] month		10.5 (7-14.8)
Sjogren's syndrome, n (%)		8 (36.4)
Systemic sclerosis, n (%)		7 (31.8)
Rheumatoid arthritis, n (%)		5 (22.7)
Undifferentiated CTD, n (%)		2 (9.1)
Desaturation with 6 minutes walking test		12 (55.5)
Interstitial lung disease, n (%)	UIP	18 (81.8)
	NSIP	4 (18.2)
FVC ml, [a] initiation		87±12.2
FVC ml, [a] 6th month		89.3±14.8
CT findings, 6th month*	Stabil, n (%)	4 (66.7)
	Progression, n (%)	2 (33.3)

CTD= Connective tissue disease, ILD= Interstitial lung disease. NSIP= Nonspecific interstitial pneumonia, UIP= Usual interstitial pneumonia, FVC= Forced vital capacity, CT= Computerize tomography[a]Mean (SD). [b]median (Q1-Q3).

Conclusion: Nintedanib is a promising agent for progressive lung fibrosis in patients with CTD-related ILD. Since physicians can safely combine it with immunosuppressive agents, more patients will benefit in the course of time. Prospective studies with longer follow-up, and larger samples are necessary to examine the role of nintedanib on lung fibrosis.

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POS1560

USING SURVIVAL CLASSIFICATION AND REGRESSION TREES AND SURVIVAL RANDOM FOREST TO INVESTIGATE ASSOCIATIONS AMONG FACTORS FOR CANCER PROGRESSION AND ARTHRITIS CONTROL IN A MULTI-CENTER RETROSPECTIVE COHORT OF PATIENTS WITH IMMUNE CHECKPOINT INHIBITOR ASSOCIATED INFLAMMATORY ARTHRITIS

Keywords: Prognostic factors, Inflammatory arthritides, Malignancy

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Background: It is unknown whether particular presentations of immune checkpoint inhibitor-associated inflammatory arthritis (ICI-IA) are associated with better cancer responses or faster time to arthritis control. Machine learning methods have the ability to determine important factors in datasets where there are often many variables.
Objectives: To identify variables associated with arthritis control and cancer progression among persons with ICI-IA.
Methods: This study is ancillary to a retrospective observational study of 147 DMARD-treated (TNFi, IL-6Ri, or methotrexate) patients with ICI-IA seen at 6 U.S sites. Variables from the medical record included demographics, patterns of swollen joints, medications, lab values, and concomitant irAEs. Arthritis control and cancer progression were the two outcomes analyzed. survival Classification and Regression trees (sCART) were created using the rpart and partykit R packages [1]. Random Survival Forest (RSF) was performed using the R package randomForestSRC [2]. Variable importance (VI) for sCART and Relative Importance Score (RIS) were computed to assess influential variables..
Results: We analyzed 147 people with ICI-IA. 69% received PD-1/PD-L1 monotherapy, and 43% had melanoma. ICI-A treatment was a TNFi in 17%, IL6Ri in 26%, methotrexate in 33%, and 24% received >1 DMARD. Median time to cancer progression was 333 (IQR 110, 811) days for the 26% that progressed. Median time to arthritis control was 109 days (IQR 32, 287) for the 93% that achieved control. For cancer progression the following were identified by both sCART and

Table 1. Demographics, Variable Importance (VIMP) from survival Classification and Regression Trees (sCART) and Relative Importance Score (RIS) from Random Survival Forest (RSF).

		Arthritis Control		Cancer Progression	
Characteristic	(%) Or median(IQR)	sCART VIMP [1]	RSF RIS [2]	sCART VIMP [1]	RSF RIS [2]
Steroid duration, days	318 (181, 658)	12	1.0	23	1
Cancer type		6	0.49	14	
First DMARD class		3	0.37	2	
>1 DMARD	36 (24.5)	11	0.33	4	0.37
ICI type*		1	0.05	5	0.22
Study site		19	0.02	8	0.36
Age (years)	62.3 (52.2, 69.0)	7	0.42	10	0.04
Maximum prednisone dose (mg)	40 (20,60)	4		6	0.10
Arthritis affected Joints					
Knee	106 (72.1)	1	0.75		
Shoulder	54 (36.7)	11		2	0.49
Wrist	82 (55.8)		0.46		0.41
Hand	111 (75.5)		0.23		0.35
Elbow	44 (29.9)	10	0.25	1	
Ankle	64 (43.5)	4	0.10		
Total Joint Count	3 (2, 4)	5	0.23	15	0.26
Characteristics ≤3 for sCART VIMP and ≤0.3 RIS from RSF		Sex, cancer stage, number of IRAEs, Sicca, thyroiditis, colitis, RF+, RF+ or CCP+, arthritis affecting hip, feet			

[1]sCART VIMP the higher the number the more influential the variable[2]sRF RIS A value of 1 indicates an influential variable; values that are negative or close to 0 are "noise" variables.*ICI combination vs monotherapy

RSF as important: steroid duration, total joint count (TJC), study site, maximum steroid dose, ICI type, shoulder arthritis, >1 DMARD and number of IRAEs. For classifying arthritis control, the following variables were found to be important in both sCART and RSF: steroid duration, >1 DMARD, elbow arthritis, age, cancer type, TJC and first DMARD (Table 1). The Figure 1 shows the sCART for arthritis control.

Conclusion: Both methods, SCART and RSF, demonstrated the important influence of steroid duration on arthritis control and cancer progression. Machine learning methods demonstrated the potential prognostic importance of specific joint involvement for each outcome- knee for time to arthritis control and shoulder and wrist for cancer progression.

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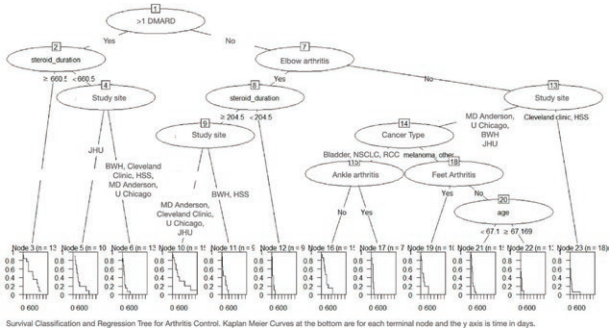


Figure 1. Survival Classification and Regression Tree for Arthritis Control. Kaplan-Meier curves are displayed at the bottom for each terminal node (or group) with time on the x axis measured in days.

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POS1561

MIXED CONNECTIVE TISSUE DISEASE AND COURSE OF PREGNANCY - RESULTS FROM THE NATIONWIDE PREGNANCY REGISTER REVNATUS

Keywords: Registries, Pregnancy and reproduction, Mixed connective tissue disease

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Background: Mixed connective tissue disease (MCTD) is a complex and multisystemic disorder of unknown etiology. MCTD is classified by the presence of antibodies to U1-RNP and associated with clinical symptoms like "puffy hands", Raynaud's phenomenon, arthritis, synovitis, sclerodactyly/acrosclerosis and/or myositis. It is commonly diagnosed in women of reproductive age. Pregnancy outcomes are reported in previous studies with discrepancies in the rate of pregnancy-related complications [1].

Objectives: To describe the course of pregnancy in patients with MCTD.

Methods: We prospectively collected data on pregnancy outcome in women with MCTD through the nationwide Norwegian quality registry on pregnancy and rheumatic diseases (RevNatus) from 2016-2022. All women were diagnosed with ICD-10 code M35.1. 48 pregnancies in 38 women were recorded. One woman had twin birth.

Results: Mean maternal age at first trimester was 31 years, (SD= 4,3). Mean disease duration was seven years (SD= 4,2). One patient had BMI > 30 at first trimester, and one patient had diabetes. Median gestational age at delivery was 37 weeks (range 25-41). No stillbirths were recorded. Two pregnancies were not planned. 69% of the women were in clinical remission at inclusion.

	At enrollment (N=48)	1. trimester (N=37)	2.trimester (N=35)	3.trimester (N=39)	delivery (N=48)	6 weeks post partum (N=48)
CRP in mg/l mean (SD)	5 (8)	4 (10)	7 (9)	3 (2)		3 (4)
CRP >5mg/l n (%)	8 (17)	4 (11)	12 (35)	3 (8)		2 (5)
patient global (VAS 0-100) mean (SD)	30 (28)	32 (32)	29 (27)	40 (28)		22 (22)
patient pain (VAS 0-100) mean (SD)	21 (21)	19 (22)	22 (23)	25 (22)		19 (22)
patient fatigue (VAS 0-100) mean (SD)	46 (28)	53 (31)	49 (31)	45 (27)		34 (24)
Use of Hydroxykloroquin n (%)	32 (67)	30 (79)	26 (74)	30 (77)		31 (65)
Miscarriages < week 12 N					4	
Birth weight (gram) of singleton mean					2995	
Birth weight (gram) of singleton born at term mean					3265	
Preeclampsia n (%)					8 (17)	
HELLP n (%)					4 (8)	
Vaginal delivery n (%)					22 (46)	
Caesarean section planned n (%)					8 (17)	
Caesarean section acute n (%)					12 (26)	

Conclusion: Most patients with MCTD in this cohort had a favourable course and outcome of pregnancy and most pregnancies were planned. Four patients were diagnosed with HELLP syndrome and we observed an increased rate of preeclampsia compared to the frequency reported in the Norwegian birth registry (NFR) (17% vs 4%) and we found lower mean birth weight in gram compared to NFR (2995 vs 3480). Hydroxykloroquin was used by a majority (>70%), of the women throughout pregnancy and might have contributed to the favorable course and outcome. Analysis on the association to specific risk factors predicting adverse pregnancy outcomes should be done in the future.

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POS1562

FACTORS ASSOCIATED WITH HANDGRIP STRENGTH IN YOUNG ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Rare/orphan diseases, Inflammatory arthritides, Sarcopenia

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Background: Decreased handgrip strength is associated with many adverse outcomes, including increased all-cause mortality, and is considered a key criterion for sarcopenia [1, 2].
Objectives: The study aims to determine handgrip strength in young adults with juvenile idiopathic arthritis (JIA) and to detect factors associated with low handgrip strength.
Methods: The single-center, cross-sectional study included 46 young adults with JIA. Anthropometric and clinical characteristics were collected, including assessment of disease activity by DAS28 and JADAS27 indices and calculation of articular and extra-articular damage by JADI-A and JADI-E indices. To determine hand grip strength, dynamometry with Jamar hand dynamometer, three times for both hands with the time of rest and fixed the highest value, was used. Thresholds for reduced muscle strength were as follows: <27 kg for males; <16 kg for females. To determine the bone mineral density (BMD) and bone mineral content (BMC) dual photon X-ray absorptiometry (DXA) was done. Calculation of skeletal mass index (SMI=appendicular lean mass divided by height^2) was counted. Logistic regression analyses estimated the associations of the following independent variables: age, sex, BMI, disease activity, articular and extra articular damage, BMD, BMC, on the dependent variable handgrip strength. Statistical significance was defined as a p-value <0.05.
Results: The study involved 26 female and 20 male patients. The average age of the patients was 24.4±5 years; the average age at the onset of the disease was 10.1±4.4 years. Thirty-two patients had reduced muscle strength (70%). Factors associated with handgrip strength are presented in Table 1.

Table 1. Univariate logistic regression analyses: factors associated with reduced handgrip strength in young patients with JIA

Variable		Coefficient, b±m	P-value	Odds ratio, OR (95% CI)	AUC (95% CI)
Age, years		0.073 ± 0.066	0.262	-	-
Sex	f				0.75 (0.58
	m	-2.15 ± 0.80	0.00	0.12 (0.02 - 0.56)	- 0.87)
BMI, kg/m^2		-0.25 ± 0.12	0.043	0.78 (0.61 - 0.99)	0.74 (0.57 - 0.86)
Disease duration, years		0.17 ± 0.07	0.020	1.18 (1.03 – 1.37)	0.76 (0.60 – 0.89)
ESR, mm/hour		0.062 ± 0.032	0.055	-	-
C-reactive protein, mg/l		0.007 ± 0.010	0.521	-	-
Disease activity by DAS28		0.49 ± 0.27	0.072	-	-
Disease activity by JADAS27		0.16 ± 0.07	0.022	1.18 (1.02 – 1.35)	0.77 (0.60 – 0.89)
Current glucocorticoid use		1.39 ± 0.87	0.109	-	-
Glucocorticoid cumulative dose, mg		0.00026 ± 0.00015	0.081	-	-
Articular damage index JADI-A		0.79 ± 0.39	0.045	2.20 (1.02 – 4.75)	0.78 (0.62 – 0.90)
Extra-articular damage index JADI-E		0.91 ± 0.48	0.059	-	-
Health Assessment Questionnaire, HAQ		1.28 ± 0.76	0.092	-	-
BMD total, g/cm^2		-9.29 ± 3.64	0.011	0.001 (0.000 - 0.12)	0.77 (0.60 – 0.89)
Fat arms, %		0.086 ± 0.043	0.010	1.09 (1.02 - 1.16)	0.78 (0.62 -0.90)
Lean mass arms, g		-1.14 ±0.34	0.001	0.32 (0.16 – 0.63)	0.94 (0.81 – 0.99)
Fat legs, %		0.093 ± 0.035	0.007	1.10 (1.03 - 1.17)	0.77 (0.60 – 0.89)
Lean mass legs, g		-0.73 ± 0.22	0.001	0.48 (0.31 – 0.74)	0.96 (0.84 – 0.99)
Appendicular lean mass, g		-0.49 ± 0.14	0.001	0.61 (0.46 -0.81)	0.96 (0.84 -0.99)
Lean mass total, g		-0.00025 ± 0.00008	0.001	0.9997 (0.9996-0.9999)	0.94 (0.82 – 0.99)
Skeletal mass index, kg/m^2		-2.29 ± 0.73	0.002	0.10 (0.02 – 0.42)	0.97 (0.86 – 0.99)

Conclusion: The results of our study demonstrate a high prevalence of low handgrip strength, up to 70 % among young patients with JIA. In these participants, lower BMI, lower total BMD and arms, legs, total lean mass and SMI, longer disease duration, higher disease activity by JADAS27 and articular index damage JADI-A, and higher percentage fat were linked to reduced handgrip strength.

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POS1563

ARTHRITIS PHENOTYPE FOLLOWING CHECK POINT INHIBITION IS UNSPECIFIC AND SERONEGATIVE IN MOST PATIENTS – RESULTS FROM THE PROSPECTIVE OBSERVATIONAL RIMRA STUDY

Keywords: Inflammatory arthritides, Disease-modifying drugs (DMARDs), Malignancy

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Background: Patients with rheumatic immune related adverse events (irAEs) after cancer therapy with immune check point inhibitors represent a new challenge for rheumatologists. The incidence of irAEs is expected to increase and more knowledge about pathogenesis, disease course and treatment response is needed. The ongoing RIMRA (Rheumatic Immune Related Adverse events in patients treated with check point inhibitors) study aims to describe clinical presentation, disease course and outcome of rheumatic irAEs in patients treated with immune check point inhibitors.
Objectives: To describe baseline characteristics and treatment of arthritis patients included in the RIMRA cohort.
Methods: RIMRA is an ongoing prospective, observational study including adult patients with de novo symptoms of rheumatic disease or flare of established rheumatic disease after > 1 dose of treatment with immune check point inhibitor. Eligible patients who are referred to Rheumatology departments at Diakonhjemmet Hospital, (DH), Oslo University Hospital Rikshospitalet (RH), University Hospital of North Norway (UNN), Ålesund Hospital (ÅH) and Hospital of Southern Norway (HSN) are asked to participate in the study. Clinical and biochemical data

Table 1. Demographics/baseline characteristics

N=56		
Age (y)		65 (12)
Women n (%)		33 (59)
Cancer diagnosis n (%)	Melanoma	30 (56)
	Lung cancer	11 (21)
	Urothelial/renal cancer	6 (11)
	Hodgkin lymphoma	2 (3,5)
	Laryngeal cancer	1 (,1,8)
	MPNST	1 (1,8)
	Colon cancer	1 (1,8)
Check point inhibitor n (%)	Anti-CTLA-4	0 (0)
	Anti-PD1/PDL-1	35 (67)
	CTLA-4 and PD1/PD-L1	15 (29)
	PD1+LAG-3	1 (1,9)
	CTLA-4 and PD-1 and PD1+LAG-3	1 (1,9)
Preexisting rheumatic disease n (%)	Psoriatic arthritis	2 (3,5)
	Seronegative RA	1 (1,8)
	Seropositive RA	4 (7)
CTCAE grade n (%)	G1	15 (28)
	G2	24 (44)
	G3-4	15 (28)
Anti-CCP/RF positive n (%)		7 (13)
ESR mm/h		35 (29)
CRP mg/L		30 (40)
SJC (66 joints)		5 (7)
TJC (68 joints)		5 (8)
Physician global VAS mm (0-100)		36 (26)
Patient global VAS mm (0-100)		53 (24)
CDAI		18 (15)

Values are mean (SD), if not otherwise indicated.

as well as blood samples for biobanking, are collected at study visits at baseline and after 3,6 and 12 months. Patients are treated at the discretion of the treating rheumatologist in collaboration with the oncologist.

Results: Between August 2018 and January 2023 56 patients have been included at 4 centers (DH, UNN, ÅH, HSN). 49 patients had de novo disease and 7 patients had flare of preexisting rheumatic disease (RA n=5, PsA n=2). Polyarthritis was the dominant phenotype in 45% of the patients followed by oligoarthritis and monoarthritis (Figure 1). Joint distribution was heterogenic. 7 patients were positive for RF/anti-CCP, of whom 5 had preexisting RA. Disease characteristics at baseline are presented in Table 1. The mean Clinical Disease Activity Index (CDAI) score was 18, corresponding to a level of moderate disease activity. Throughout the study period anti-rheumatic treatment has been given to the following proportions of patients: i.a steroid injection:45%, prednisolone: 71%, methotrexate: 30%, anti-TNF: 21%, tocilizumab: 1,7%, sekukinumab: 1,7 %, ustekinumab: 1,7%, leflunomide: 1,7%, apremilast: 1,7%. Death has been registered in 13 (23%) patients, of whom 10 patients had received prednisolone, 3 patients had received methotrexate and 1 patient had received anti-TNF treatment.

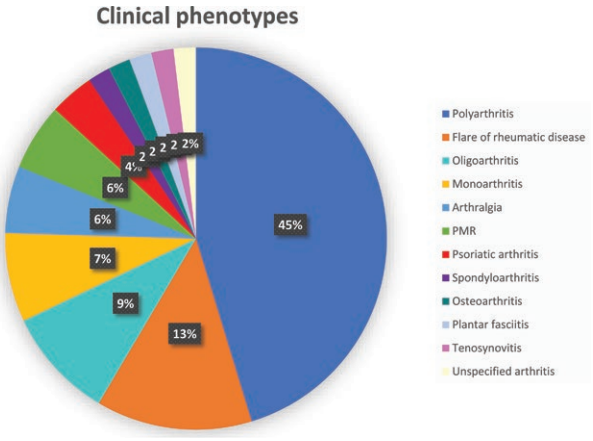


Figure 1.

Conclusion: Most patients with rheumatic immune related adverse events in the RIMRA study have seronegative inflammatory arthritis with no specific arthritis pattern/phenotype. The disease activity varies, but is on average moderately high upon referral to rheumatologist, as reflected in both CDAI and CTCAE grading at baseline. Most patients need anti-rheumatic treatment.

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POS1564 AUTOIMMUNE INNER EAR DISEASE WITH A RHEUMATOLOGIC APPROACH

Keywords: Descriptive studies, Tapering, Best practices

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Background: Autoimmune inner ear disease (AIED) is a rare entity that presents with sensorineural hearing loss. In the US, the incidence rate is less than 5 per 100,000 people [1]. The pathophysiology behind the disease is thought to be a humoral and cell-mediated process that damages the cochlea [2]. Clinical presentation is characterized by fluctuating, asymmetric hearing loss that tends to progress over time. Half of patients with AIED present with vestibular (eg, dizziness, vertigo, imbalance) and other ear symptoms (eg, tinnitus, ear pressure and aural fullness) [2,3]. Diagnosis of AIED remains challenging as no diagnostic test has demonstrated high sensitivity or specificity [1]. Diagnosis remains clinical and based on response to corticosteroids, which suggests the disease's autoimmune nature. Corticosteroid-sparing agents have been used with various degrees of success [1-4].

Objectives: The aim of our study was to describe our experience treating patients with AIED with immunosuppressive therapy.

Methods: We performed a retrospective chart review of patients diagnosed with AIED at all Mayo Clinic locations for the past 10 years. AIED was diagnosed based on 3 main characteristics: progressive fluctuating hearing loss, response to high-dose corticosteroids, and audiometric evidence supporting sensorineural hearing loss. We recorded audiography results at the time of diagnosis and 1 and 3 months after treatment. We divided treatment efficacy into 2 categories: subjective (patient-reported) and objective (audiometric) improvement.

Results: Thirty-one patients met the inclusion criteria; the mean age was 48.5 years and 17 were women. Patients were initially evaluated by the Department of Otorhinolaryngology and 29 patients were subsequently referred to the Department of Rheumatology with a mean of 12.2 weeks after the first evaluation. While initial hearing loss was more commonly unilateral (21 [67.7%]), it remained unilateral in only 8 (25.8%) patients. Tinnitus, aural fulness, and ear pressure were the 3 most common ear symptoms, followed by imbalance, vertigo, dizziness, and discharge. Treatment with corticosteroids showed improvement of hearing and vestibular symptoms during the first month, but no further improvement by the end of the third month. Other immunosuppressive medications were used with various degrees of response (Table 1). Methotrexate was the second most used therapy with 11 of 17 patients reporting an improvement in symptoms.

Conclusion: Prompt treatment of these patients is vital to prevent irreversible hearing loss. Corticosteroids remain the criterion standard initial treatment; however, our study supports potential use of corticosteroid-sparing agents such as methotrexate for long-term therapy. Our study has some limitations including small patient population and a retrospective design.

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Table 1. Treatments and Outcomes Based on Subjective Responses

Treatment	Improvement, No. (%)	No improvement, No. (%)
Prednisone (n=31)	27 (87.1)	4 (12.9)
Intratympanic corticosteroid injection (n=9)	9 (100.0)	0 (0.0)
Methotrexate (n=17)	11 (64.7)	6 (35.3)
Azathioprine (n=3)	3 (100.0)	0 (0.0)
Adalimumab (n=3)	2 (66.7)	1 (33.3)
Rituximab (n=2)	1 (50.0)	1 (50.0)
Mycophenolic acid (n=1)	1 (100.0)	0 (0.0)
Etanercept (n=1)	0 (0.0)	1 (100.0)

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Disclosure of Interests: None Declared.

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POS1565 ACUTE PERICARDITIS WITH PLEUROPULMONARY INVOLVEMENT, FEVER AND ELEVATED C-REACTIVE PROTEIN: A SYSTEMIC AUTOINFLAMMATORY DISEASE? A COHORT STUDY

Keywords: Innate immunity, Lungs, Cardiovascular disease

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Background: Pericardial diseases may involve only the pericardium, or may be part of a systemic condition, with an inflammatory phenotype sharing similarities with autoinflammatory diseases.

Objectives: This cohort study aims to describe the prevalence and features of systemic phenotype of pericarditis characterized by pleuropulmonary involvement, fever, and elevation of C-reactive protein (CRP), comparing this phenotype with other forms of pericarditis.
Methods: All patients in our center were enrolled in a prospectively maintained registry from 2019 to 2022. 412 patients with idiopathic recurrent pericarditis were analyzed. "Systemic" subset was defined as the presence of all of the following criteria: fever > 38 C°, CRP higher than 2 times normal values, pleural effusion detected with any imaging techniques. The absence of any of the 3 criteria was defined as "isolated" subset.
Results: We found that 211 (51.2%) of 412 patients presented the systemic subset and the variables significantly associated with this subset in univariate analysis (p<0.001) were: higher mean age of onset 45.5 (±SD 17.2) vs 39.9 (±SD 16.4) years, higher mean CRP values 128.8 (95% CI 117.8-139.8) vs 49.9 (95% CI 41.5-58.3) mg/L, higher proportion of pericardiocentesis 40 (19%) vs 3 (1.5%), higher mean leukocyte count 13143.3 (95% CI 12790.4-13496.2) vs 9910.3 (95% CI 9556.2-10264.4)/mm^3, higher mean neutrophils number 10402.5 (95% CI 10082.1-10723) vs 6779.8 (95% CI 6505.2-7054.4)/mm^3 and lower mean lymphocyte count 1693.9 (95% CI 1621.9-1765.8) vs 2079.3 (95% CI 1979-2179.6)/mm^3. As results the neutrophil-to-lymphocyte ratio was higher in systemic phenotype: 6.6 (95% CI 6.2-6.9) vs 3.4 (95% CI 3.3-3.6). Anti-IL1 therapy was started more frequently in the systemic subgroup (55/211, 26%) than in the isolated subset (15/201, 7.5%) (p < 0.001). On multivariate analysis neutrophil count and lymphopenia, were statistically associated with the systemic subset (p < 0.001).
Conclusion: These results demonstrate the clinical relevance of the systemic phenotype in a referral center and confirm its analogy with the autoinflammatory diseases, suggesting a pivotal role of IL1 in the genesis of this subset.
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POS1566

SOLVING SARCOIDOSIS: A TRANSCRIPTOME-BASED META-ANALYSIS OF CLINICAL SARCOIDOSIS STUDIES ILLUSTRATES SHARED PATHOPHYSIOLOGY, EXAMINES MEDIATORS OF FIBROSIS, IDENTIFIES CANDIDATE BIOMARKERS AND SUGGESTS A THERAPEUTIC MECHANISM OF JAK INHIBITION

Keywords: -Omics, Biomarkers, Rare/orphan diseases

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Background: Sarcoidosis is a systemic, non-caseating granulomatous disease driven by a dysregulated immune response to environmental antigens. Disease manifestations are driven by both active inflammation and resultant fibrosis in a wide variety of tissues, but the dynamics and mediators of these two states are not well understood. Diagnosis relies on imaging and biopsy and treatment typically includes steroids. JAK inhibitors have been utilized as steroid-sparing therapies for cutaneous and pulmonary sarcoidosis, however the mechanism is unclear.
Objectives: We performed a meta-analysis of 20 transcriptome studies on clinical sarcoidosis to explore perturbed pathways, examine mediators of fibrosis, prioritize candidate biomarkers, and study the JAK/STAT pathway.
Methods: We searched publicly available data repositories for clinical sarcoid datasets with healthy controls and at least 3 biological replicates evaluated with transcriptome analysis and found 20 studies (14 microarray and 6 RNAseq), comprising 316 sarcoid patients and 383 healthy controls. The majority of samples came from peripheral blood; tissue-based samples included lung, skin, anterior orbit, lacrimal gland and lymph nodes. We performed differential gene expression on each of the 20 studies independently with Limma (microarray) and DESeq2 (RNAseq). Results were merged for the 17,705 genes that were evaluated by at least 9 of the studies. For microarray studies, data from the probe with lowest adjusted p-value and largest absolute fold change (FC) was selected. Genes were selected for pathway enrichment analysis if at least 10 studies identified them as differentially expressed. Candidate biomarkers were genes that were consistently differentially expressed in both tissue and peripheral samples with a fold change magnitude of at least 1.5x. Pathway enrichment analysis was performed with Reactome. We mined our dataset with 232 fibrosis related genes identified by the FibROAD project and the 11 central genes of the JAK/STAT pathway.
Results: We prioritized 2,349 genes that were differentially expressed in the majority of the datasets. Unsupervised clustering of these studies showed a distinct difference between peripheral and tissue sample types. Of the 15 biomarker candidates, some have been associated with sarcoidosis (ie STAT1, ITGA6, LEF1) and others have been reported in tuberculosis (ie GBP5, ANKRD22), however the majority have not been associated with either (ie RHOH, SPTBN1, UBASH3A). Pathway enrichment identified significant perturbation of interferon signaling and antigen presentation which supports two established mechanisms of sarcoid pathophysiology: an abnormal TH1 response and existence of MHC risk alleles. Qualitative exploration of the JAK/STAT pathway (Figure 1) shows a predominant upregulation of the pathway, most strongly in STAT1 and JAK2. We prioritized 25 fibrosis related genes that were significantly differentially expressed in at least 10 of our studies and included STAT1, HBEGF, FOXP1 and JAK2.
Conclusion: This meta-analysis summarizes the current transcriptional landscape of sarcoidosis, including pathophysiology, mediators of fibrosis, biomarkers and therapeutics targeting the JAK/STAT pathway. We hypothesize that JAK2 may be an important therapeutic target for sarcoid by disrupting the JAK/STAT component of an abnormal TH1 response as well as a possible JAK2/STAT1 associated fibrosis mechanism.
Reference: Cited inline.

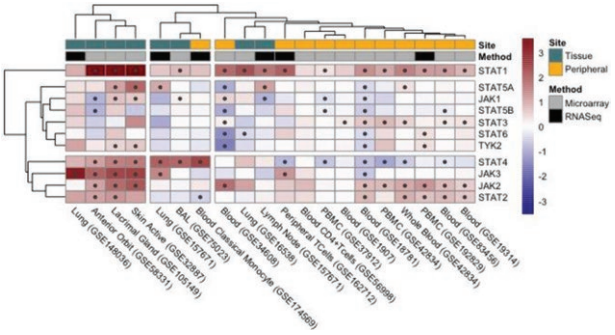


Figure 1. Meta-analysis of 11 JAK/STAT pathway genes show significant differential expression(•) which is most notable in STAT1, JAK2 and STAT2. Red indicates higher expression (log2fold change) in sarcoid compared to control.

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POS1567

OUTCOMES AND PREDICTORS OF CHRONIC IMMUNE CHECKPOINT INHIBITOR INDUCED INFLAMMATORY ARTHRITIS: DATA FROM THE CANADIAN RESEARCH GROUP OF RHEUMATOLOGY IN IMMUNO-ONCOLOGY (CANRIO) RETROSPECTIVE COHORT

Keywords: Inflammatory arthritides, Malignancy, Prognostic factors

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Background: Immune checkpoint inhibitors (ICI) improve overall survival and progression-free survival in many types of malignancies and are the new pillar of cancer treatment [1]. ICIs harness a patient's own immune system to fight their cancer. However, this activation of the immune system can result in off-target immune-related adverse events (irAEs). One of the most disabling irAE is inflammatory arthritis (ir-IA) [2] affecting up to 7.5% of those treated with ICI [3]. Unlike most irAE which usually resolve within a few months, ir-IA can become chronic and persist even after ICI cessation, requiring long term immunosuppression [4]. The factors associated with chronic ir-IA and its significance regarding tumor outcomes remain largely unknown. With the increasing use of ICI in the adjuvant therapy, it is important to understand predictors and outcomes of chronic ir-IA in order to best counsel patients.

Objectives: To determine predictors and outcomes of chronic ir-IA in cancer patients exposed to ICI.

Methods: The CanRIO group, established since 2018, includes 9 academic sites in Canada and aims to describe the clinical presentation, management and outcomes of patients who developed rheumatic irAE (Rh-irAE) or those with pre-existing autoimmune diseases exposed to ICI using standardized data collection. The sites pooled data to develop a retrospective cohort of patients identified as having a Rh-irAE. We identified patients who developed ir-IA defined by new onset joint tenderness or synovitis in the absence of pre-existing rheumatic disease and who had at least 3 months of follow-up following ICI cessation. Chronic ir-IA was defined as having either persistent symptoms of ir-IA or the continued use of prednisone or DMARDs 3 months after ICI cessation.

Results: The CanRIO Retrospective Cohort included 193 ir-IA individuals of which 54 met our inclusion criteria. Forty-five of 54 (83%) had chronic ir-IA. Fifteen (33%) were female. Nineteen (42%) patients with chronic ir-IA had melanoma, 14 (31%) lung cancer and 8 (18%) genito-urinary cancer. Thirty-three (73%) were treated with anti PD-1/PD-L1, 14 (31%) with combination and none with anti-CTLA-4 only. Thirty-five (78%) were treated with conventional DMARDs and 1 (2%) with biologic DMARDs. Univariable logistic regression showed that ir-IA was more likely to become chronic in those with peripheral synovitis compared with those who did not have peripheral synovitis at presentation, (Table 1). Patients with chronic ir-IA had greater overall survival and progression-free survival compared to those with acute ir-IA (log rank tests, p<0.01), (Figure 1).

Conclusion: A large proportion of ir-IA becomes chronic. The presence of synovitis at presentation is associated with arthritis persistence. Ir-IA is associated with improved overall survival and progression-free survival.

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Table 1. Logistic regression model: univariable analysis to assess factors associated with chronic ir-IA compared with acute ir-IA

	Chronic ir-IA		
Characteristic	OR	95% CI	p value
Male	1.00	0.22-4.56	1.00
Age	0.98	0.93-1.04	0.54
Past or current smoking history	0.61	0.11-3.38	0.58
Family history of rheumatic autoimmune disease	1.83	0.20-16.77	0.59
One or more other irAE	2.33	0.43-12.53	0.323
Combination ICI	1.57	0.29-8.61	0.29
Duration of ICI therapy	1.04	0.98-1.15	0.95
Polyarthritis	1.55	0.32-7.51	0.31
Peripheral synovitis	12	1.95-73.97	0.007
CDAI	1.07	0.95-1.20	0.95
C-reactive protein	1.02	0.99-1.05	0.17
Time from ir-IA onsets to treatment	0.99	0.85-1.15	0.89

irAE: immune-related adverse event; ICI: immune checkpoint inhibitors; CDAI: clinical disease activity index

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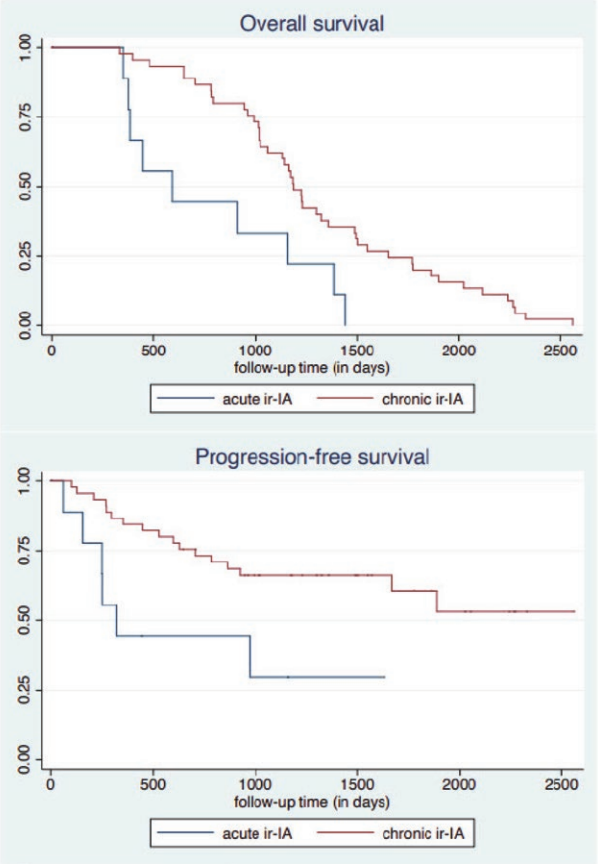


Figure 1. Kaplan-Meier curves for overall survival and progression-free survival based on acute and chronic ir-IA

POS1568

ANAKINRA TREATMENT IN COLCHICINE RESISTANT PERICARDITIS: A SINGLE CENTER EXPERIENCE

Keywords: Rare/orphan diseases, Heart, bDMARD

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Background: Recurrent pericarditis (RP) may be encountered in autoinflammatory diseases, such as familial Mediterranean fever (FMF), however, the etiology stands principally unknown [1]. Alternative treatments have been suggested for the treatment of colchicine-resistant cases whether idiopathic or related to FMF [2].

Objectives: This study describes our experience of anakinra treatment for colchicine-resistant pericarditis cases.

Methods: All patients with pericarditis followed in our center who received anakinra since 2014 were evaluated retrospectively. Relevant data were retrieved from archives and verified with telephone interviews. Therapeutic efficacy, as well as the side effect profile, of anakinra was assessed.

Results: Our series consists of 15 patients (10 males, 5 females) with colchicine-resistant pericarditis whose demographic, clinical, and treatment features are given in Table 1. The mean age was 38.9±15.9. 6 cases were secondary to FMF and the remaining were idiopathic other than one perimyocarditis and one multisystem inflammatory syndrome in adults. Two of all patients whose autoinflammatory genetic panels were screened were detected to carry FMF mutations K695R het. and E148Q. The median follow-up duration was 53 months (range 10-174); the median number of recurrences before anakinra was 4 (range: 1-14). Ten patients (66.7 %) experienced no episode of pericarditis (mean episode count: 0.86) during anakinra treatment. Corticosteroids were discontinued in all patients except one transplant recipient. The anakinra dose of those who progressed attack-free was tapered without relapse in 5 cases, whereas 7 cases relapsed after tapering. Currently, 11 patients carry on anakinra treatment, while 3 patients stopped anakinra since remission was achieved. No side effect of anakinra was observed, with the exception of skin reaction in two patients.

Table 1. Demographic features of patients and response to anakinra therapy

Patient #	Age/ Sex	Diagnosis/ Etiology	Duration of pericarditis before anakinra treatment (mo)	Prior medication(s)	Number of recurrences before anakinra	Anakinra treatment duration (mo)	Time to corticosteroid discontinuation (mo)	Recurrences during regular anakinra treatment	Current treatment dose
1	56/F	FMF	88	CLC, CS	2	13	NA	0	100 mg/day
2	14/F	FMF	24	CLC, CS, NSAIDs	5	2	1	3	Switched to canakinumab
3	21/M	RPM	36	CLC, CS, NSAIDs	2	3	4	2	100 mg/day
4	77/M	IRP	11	CLC, CS	3	42	0	0	100 mg/3-days-in-a-week
5	49/M	MIS-A	3	CLC, NSAIDs	4	3	NA	0	Withdrawn-Remission
6	55/M	IRP	120	CLC, CS	6	29	0	1	100 mg/day
7	18/M	IRP	1	CLC, CS, NSAIDs	1	18	1	0	Remission
8	44/F	FMF	14	CLC, NSAIDs	14	23	NA	3	Withdrawn-Remission
9	47/M	FMF	3	CLC, CS	3	27	0	4	100 mg/day
10	42/F	IRP	10	CLC	6	35	NA	0	100 mg/3-days-in-a-week
11	26/M	IRP	77	CLC, CS, Hydroxychloroquine	6	101	1	0	100 mg/day
12	35/F	IRP	124	CLC, NSAIDs	4		9	0	Withdrawn-Remission
13	23/M	IRP	3	CLC, CS	3	86	2	0	100 mg/2days
14	27/M	FMF	15	CLC, CS	5	49	1	0	100 mg/3days
15	23/M	FMF	8	CLC, CS	5	29	1	0	*On demand full dose

F: Female, M: Male, IRP: Idiopathic recurrent pericarditis, FMF: Familial Mediterranean fever, RPM: Recurrent Perimyocarditis, MIS-A: Multisystem Inflammatory Syndrome in Adults, CLC: colchicine, NSAIDs: Nonsteroidal anti-inflammatory drugs, CS: Corticosteroid, NA: Not applicable*Patient -under colchicine treatment- uses anakinra only in the event of a FMF attack because of injection site skin reactions.

Conclusion: Anakinra was found to be a safe and effective agent against colchicine-resistant pericarditis, notably recurrent pericarditis. Long-term treatment should be anticipated when initiating treatment and dose tapering should be kept in mind for patients in remission. Relapses should be watched for attentively in tapering and anakinra should be resumed promptly in case of a recurrence. Furthermore, anakinra is important in sparing cortisol treatment.

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POS1569 CONTRIBUTION OF GENETIC ANALYSIS TO THE DIAGNOSIS OF FAMILIAL MEDITERRANEAN FEVER

Keywords: Genetics/epigenetics

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Background: Familial Mediterranean fever (FMF) affecting mainly Mediterranean and Middle Eastern populations.is an autosomal recessive inherited inflammatory disease caused by mutations in the Mediterranean fever (MEFV) gene. It is characterized by periodic attacks of fever and inflammation affecting serosal membranes. The most common symptoms of the disease are fever, abdominal pain, arthritis, erysipelas-like erythema, pleuritis, and pericarditis. Patients are usually treated by life-long colchicine, which has been shown to be effective in preventing the attacks of FMF as well as the development of amyloidosis. FMF diagnosis remains often difficult due to the lack of pathognomonic laboratory findings. The definitive clinical classification of FMF is made by Tel Hashomer criteria [1]. Genetic analyzes may support the clinical diagnosis of patients for mutation complications.

Objectives: This study aimed to not only investigate the contribution of MEFV mutations to FMF diagnosis but also to show whether there is a phenotype–genotype correlation in the same patient population.

Methods: We evaluated 12 MEFV gene mutations screened with a commercial kit based on real-time polymerase chain reaction technique in 1064 adults between January 2016 and November 2021. We were able to interview 208 of 484 people with AAA mutations by telephone. We investigated whether they were diagnosed with FMF according to Tel Hashomer criteria or clinician opinion, and compared their clinical and genetic characteristics. In addition, it was investigated whether there was a colchicine or interleukin-1 inhibitor drugs use report issued for drug fee exemption from the medical records of everyone who underwent genetic analysis, since it assumed the diagnosis of FMF in our country.

Results: According to the results of 1064 genetic analysis (484 with MEFV mutation), 228 patients (21.4%) were either still using colchicine with the diagnosis of FMF or had previously used colchicine before IL-1 inhibitor treatment. The rate of giving colchicine with the diagnosis of FMF in patients with MEFV mutation (39.7%) was found to be significantly higher than those without mutation (p<0.001). Of the 208 patients with genetic mutations which we interviewed by telephone, 89 (42.8%) met the Tel Hashomer criteria. The most detected mutations in patients meeting Tel Hashomer criteria were M694V (46,1%), M680I (24,7%), V726A (8,9%), and E148Q (8,9%) respectively. The positive significant associations were found between M694V and M680I homozygous mutations and definite/probable diagnosis according to Tel Hashomer criteria (p=0,001, p=0,021, respectively). A negative correlation was found between E148 heterozygous mutation and diagnosis (p=0,002). When the relation between genetic mutations and clinical findings was examined, it was shown that there was a positive correlation between fever and M694V, and between abdominal pain and M680I (p=0,000, p=0,007, respectively). Patients with the E148Q mutation had significantly less fever and abdominal pain (p=0,028, p=0,017, respectively).

Conclusion: Considering that approximately one-fifth of those undergoing genetic analysis are diagnosed with FMF, it can be concluded that unnecessary genetic testing is performed in our hospital. In clinical practice, the precence of MEFV gene mutations M694V and M680I is helpful for FMF diagnosis. E148Q mutation were not been found to be associated with both the diagnosis and the clinical findings. Genetics plays a critical role in confirming the diagnosis, but it should never take the place of a clinical diagnosis. The clinicians should be aware of the indications and limitations of genetic testing and know how to interpret the results.

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POS1570 LONG-TERM SAFETY AND EFFECTIVENESS OF CANAKINUMAB IN FAMILIAL MEDITERRANEAN FEVER (FMF) – 36-MONTH DATA FROM THE RELIANCE REGISTRY

Keywords: Real-world evidence, Rare/orphan diseases, Innate immunity

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Background: Familial Mediterranean Fever (FMF) is characterized by recurrent attacks of fever, serositis, and elevated laboratory parameters (CRP, SAA). According to EULAR recommendations, treatment goals are the control of acute attacks and subclinical inflammation as well as the improvement of patient´s quality of life. In a phase 3 pivotal study (CLUSTER study), FMF patients have been successfully treated with the interleukin-1β inhibitor canakinumab (CAN).
Objectives: The RELIANCE registry explores the long-term efficacy and safety of CAN under routine clinical practice conditions in pediatric (age ≥2 years) and adult patients with FMF and other recurrent hereditary fever conditions.
Methods: RELIANCE is a prospective, non-interventional, observational study that enrolls patients with clinically confirmed diagnoses of FMF routinely receiving CAN. Clinical data, physician assessments and patient-reported outcomes are assessed at baseline and 6-monthly intervals.
Results: This interim analysis includes baseline as well as 18- and 36-month data from N=96 FMF patients (CAN-pretreated: N=71, CAN-naïve: N=20) enrolled by December 2022. Median age in this cohort was 21.5 years (2–61 years) and the proportion of female patients was 46%. At baseline, median duration of prior CAN treatment was 1.0 years (0–6 years). The MEFV genotype has been documented in 67 patients. Among 53 (79%) carriers of pathologic MEFV variants, 17 were homozygous, 6 heterozygous plus a second pathologic variant, 8 heterozygous plus a non-pathologic variant, and 22 heterozygous plus wild type. At month 36, disease activity was mild (3 and 2 out of 10) according to patients rating and lab parameters. Physician assessment indicated disease remission in 60% of the patients (53% at baseline) and 57%/14% of the patients having no/mild-moderate disease activity. The majority of patients reported no impairment of social life (100%, 75%) nor negative impact on mood (88%, 100%) due to the disease. Disease activity parameters decreased in the observation period, particularly in patients without prior CAN therapy (Table 1). In total, 22 serious adverse events (SAE) were reported, of which 3 were classified as drug related.
Conclusion: Interim data from the RELIANCE study, the longest running real-life CAN registry confirm efficacy and safety of long-term CAN treatment in FMF patients.

Table 1. Assessment of clinical disease activity and laboratory markers in CAN pretreated and CAN naïve FMF patients.

	Baseline		18 months		36 months	
CAN pretreated patients vs. patients CAN naïve at baseline	**CAN pre-treated**	**CAN naïve**	**CAN pre-treated**	**CAN naïve**	**CAN pre-treated**	**CAN naïve**
Number* of patients, N	71	20	34	11	19	5
Number (%**) of patients with days off work/school during the last 6 months	8 (11)	2 (10)	9 (27)	1 (9)	5 (26)	0 (0)
Number (%**) of patients in disease remission (physician assessment)	32 (59)	2 (20.0)	16 (64)	3 (60.0)	10 (63)	2 (50.0)
Patient's assessment of current disease activity; 0–10, median (min; max)	2.0 (0; 10)	7.0 (0; 10)	2.0 (0; 6)	0.0 (0; 7)	3.0 (1; 8)	2.0 (0; 4)
Patient's assessment of current fatigue; 0–10, median (min; max)	4.0 (0; 10)	5.5 (0; 9)	3.0 (0; 9)	2.0 (0; 7)	3.5 (0; 9)	2.0 (0; 6)
Number (%**) of patients without impairment of social life by the disease	28 (56)	9 (60)	17 (85)	7 (88)	8 (100)	3 (75)
Current influence of the disease on mood; %** of patients with negative | positive | no influence	18 | 10 | 71	19 | 0 | 81	5 | 14 | 81	13 | 0 | 88	13 | 13 | 75	0 | 25 | 75
CRP, median (mg/dl)	0.1	0.5	0.1	0.2	0.2	0.0
SAA, median (mg/dl)	0.6	3.3	0.6	1.0	0.7	0.6
ESR, median (mm/h)	5.0	9.0	7.0	5.0	5.0	7.0

SAE	**Number of events**	**Incidence rate‡ per 100 patient-years**
All types of SAE	22	11.64
SADR	3#	1.59
CAN-pretreated patients	3	2.19
CAN-naïve patients	0	0.00

Tachycardia, tonsillitis, and one further SAE (not yet coded), each N=1*CAN status not reported for all patients*not reported for all patients‡ Incidence rate = number of events * 36525/ sum of observation days (=69050)CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; n. a., not annotated; SAA, serum amyloid A; SADR, serious adverse drug reaction

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POS1571

CARDIOVASCULAR DISEASES IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER OVER 50 YEARS OF AGE

Keywords: Cardiovascular disease, Rare/orphan diseases, Epidemiology

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Background: Familial Mediterranean Fever (FMF) is one of the most common monogenic autoinflammatory diseases inherited in an autosomal recessive manner. FMF attacks are characterized by episodes of fever and serositis lasting up to 3 days. The most important long-term complication is renal amyloidosis (Alghamdi, 2017). Furthermore, FMF can lead to cardiovascular complications (Malik et al., 2021; Vampertzi et al., 2020; Erken & Erken, 2018).
Objectives: Cardiovascular diseases (CVD) in patients with FMF are not elucidated. CVD includes hypertension, coronary artery disease, heart failure, heart valve diseases, arrhythmias, and hyperlipidemia.
Methods: This study surveyed patients with FMF over 50 years of age.
Results: 343 patients with FMF over 50 years of age were enrolled. Our results demonstrated that 173 of 343 (50.3%; male n=126, female n=47) patients have CVD whereas 170 patients (49.7%; male n=98, female=72) do not have CVD. The means of age were 59.1±7.37 in patients with CVD and 56.1±5.07 in patients without CVD. The means of symptom onset ages were 24.1±15.4 in patients with CVD and 23.9±13.3 in patients without CVD. The median diagnostic delay was 17.9±15.6 in patients with CVD and 18.6±16.3 in patients without CVD. Illness duration was 17.1±9.95 in patients with CVD and 16.4±9.63 in patients without CVD. Among CVD, hypertension (n=148, 43.14%) is the most frequent concomitant comorbidity, followed by coronary artery disease (n=44, 12.82%), hyperlipidemia (n=32, 9.32%) heart valve insufficiency (n=11, 3.20%), heart failure (n=5, 1.45%), and arrhythmias (n=5, 1.45%) (Figure 1). A statistically significant increase in colchicine resistance is observed in patients with CVD (n=30, p<0.031) compared to patients without CVD. Patients with CVD are significantly more adherent to colchicine treatment (n=117, p<0.025). Patients with CVD use significantly more antidepressant drugs (n=27, p<0.002) and bisphosphonates (n=7, p<0.008). Multiple drug usage is significantly more encountered in patients with CVD (n=21, p<0.001). A statistically significant rise in active biologic agent receipt is present in patients with CVD (n=17, p<0.009).
Conclusion: In patients with FMF over 50 years of age, the presence of CVD might be an independent risk factor for the development of colchicine resistance, reflecting the requirement of active biological agents. Patients with CVD could have an increased risk for major depressive disorder and osteoporosis.

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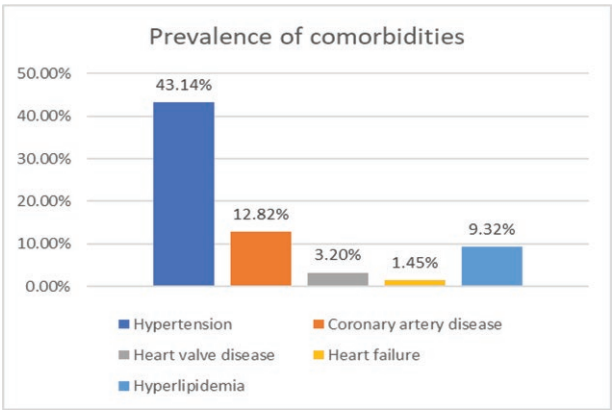


Figure 1. Prevalence of cardiovascular diseases in patients with FMF over 50 years of age.

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Disclosure of Interests: None Declared.
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POS1572

AN OVERVIEW TO THE INTERSTITIAL LUNG DISEASES RELATED TO CONNECTIVE TISSUE DISEASES: A RETROSPECTIVE ANALYSIS

Keywords: Descriptive studies, Lungs

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Background: Interstitial lung disease (ILD) is a critical manifestation of connective tissue diseases (CTDs) that may cause morbidity and mortality.
Objectives: This study aimed to evaluate the clinical and demographic characteristics and treatment of the patients who had CTD-related ILD.
Methods: This retrospective observational study includes patients who followed up with CTD-related ILD in a tertiary rheumatology outpatient clinic between January 2020 and December 2022. Patients' files were assessed retrospectively for demographic, clinical, and radiologic data.
Results: There were 149 patients (96 Female/53 Male) with a mean age of 62.6±11.8. The CTD types of the patients were Sjogren's syndrome (SS) in 49 (32.7%) patients, rheumatoid arthritis (RA) in 47 (31.3%) patients, systemic sclerosis (SSc) in 40 (26.7%) patients, undifferentiated CTD in 9 (6%) patients, inflammatory myositis in 3 (2%) patients, and systemic lupus erythematosus (SLE) in one (0.7%) patient. The median disease duration was 58 (24-134.5) months for CTDs. According to computed tomography findings, 86 (57.7%) patients had nonspecific interstitial pneumonia (NSIP), 48 (32.2%) patients had usual interstitial pneumonia (UIP), 9 (6%) patients had lymphocytic interstitial pneumonia (LIP), 6 (4%) patients had organizing pneumonia (OP). The median disease duration was 35.5 (12-65.8) months for ILD. Patients with NSIP were more frequent in the SSc and SS groups, with 29 (33.7%) patients for each. Both UIP and OP were most frequent in the RA group (45.8% and 66.6%, respectively). LIP was common in the SS group (77.8%). Seventy-five (50%) patients were diagnosed with CTD prior to ILD, 20 (13.3%) patients were diagnosed with ILD prior to CTD, and 54 (36%) patients had CTD and ILD diagnoses concurrently. NSIP was more frequent among female patients (p=0.001), but no significant difference was found in terms of gender among patients with UIP. Immunosuppressive (IS) treatment for ILD was more frequently initiated for patients with NSIP than for UIP. The mainly preferred drug for initiation ILD therapy was rituximab for RA patients, mycophenolate mofetil for myositis, and azathioprine for other disease groups. In addition to IS treatment, usually, 7.5-30 mg/day prednisolone was administered for both NSIP and UIP. Prednisolone up to 100mg/day was used for OP treatment. Only two patients with OP used azathioprine as IS treatment added to prednisolone. RA patients with LIP did not receive an IS treatment for pulmonary involvement. Besides, mycophenolate mofetil and azathioprine were given to two patients with LIP associated with SS. Six patients (4 NSIP/2UIP) died that of whom were using IS agents.

Table 1. Demografic and clinical characteristics of the study group

Characteristics of the patients				Interstitial lung disease (n = 149)
Gender, n (%)	Female			96 (64.4)
	Male			53 (35.6)
Age, [a] year				62.6±11.8
Disease duration for CTD, [b]month				58 (24-134.5)
Disease duration for ILD, [b]month				35.5 (12-65.8)
	NSIP (n=86)	UIP (n=48)	OP (n=6)	LIP (n=9)
Sjogren's syndrome, n (%)	29 (33.7)	12 (25)	1 (16.7)	7 (77.8)
Rheumatoid arthritis, n (%)	19 (22.1)	22 (45.8)	4 (66.6)	2 (22.2)
Systemic sclerosis, n (%)	29 (33.7)	11 (22.9)	0 (0)	0 (0)
Undifferentiated CTD, n (%)	6 (7)	2 (4.2)	1 (16.7)	0 (0)
Inflammatory myositis, n (%)	2 (2.3)	1 (2.1)	0 (0)	0 (0)
Systemic lupus erythematosus, n (%)	1 (1.2)	0 (0)	0 (0)	0 (0)

CTD= Connective tissue disease, ILD= Interstitial lung disease, NSIP= Nonspecific interstitial pneumonia, UIP= Usual interstitial pneumonia, OP= Organizing pneumonia, LIP= Lymphocytic interstitial pneumonia[a]mean±standard deviation), [b]median (Q1-Q3)

Conclusion: ILD is a critical manifestation of CTDs. IS biologic treatment options may be required during the management of CTD-related ILD.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1573

LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH TRAPS (TUMOR NECROSIS FACTOR RECEPTOR-ASSOCIATED PERIODIC SYNDROME) - INTERIM ANALYSIS OF THE RELIANCE REGISTRY

Keywords: Real-world evidence, Rare/orphan diseases, Innate immunity

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Background: Autoinflammatory periodic fever syndromes are characterized by severe systemic and organ inflammation as well as high burden for the patients and their families. Successful treatment was achieved in clinical trials and in real life with the interleukin-1β inhibitor canakinumab (CAN) leading to rapid remission of symptoms and normalization of laboratory parameters in most patients.
Objectives: The present study explores the long-term efficacy and safety of CAN under routine clinical practice conditions in pediatric (age ≥2 years) and adult patients with autoinflammatory periodic fever syndromes including TRAPS (tumor necrosis factor receptor-associated periodic syndrome).

Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany. Patients with clinically confirmed diagnoses of TRAPS who routinely receive CAN are enrolled to evaluate efficacy and safety of CAN under standard clinical practice conditions. Disease remission by physicians´ assessment, disease activity and fatigue by patients' assessment, days absent from school/work due to study indication, and inflammatory markers were assessed at baseline and at 6-monthly intervals.
Results: The interim analysis of TRAPS patients enrolled by December 2022 includes data from baseline (N=21), 18- (N=12) and 30-month visits (N=10). At baseline, median age was 15 years (3–43 years) and median duration of prior CAN treatment was 1 year (0–4 years). The proportion of female patients was 67%. At month 30, 3 patients received standard dose CAN, 4 patients greater than standard dose CAN and 2 patients lower than standard dose CAN. Preliminary results indicate stable remission by physicians´ assessment (in 62.5 % of patients), low disease activity by patient´s assessment (1.5 out of 10) and inflammatory markers within normal limits (**Table 1**). However, a fatigue score of 4 out of 10 might contribute to the impairment of social life reported by patients. One patient was affected by N=9 serious adverse events, none of which was classified as drug related.
Conclusion: The present interim data from TRAPS patients indicate that long-term CAN treatment is safe and effective. Patient reported fatigue and impairment of social life leave room for further improvement. Further RELIANCE interim and end-of-study data will be analyzed to assess efficacy and safety of long-term CAN treatment in patients with TRAPS.

Table 1. Baseline characteristics and interim analysis data of patients with TRAPS.

	Baseline	18 months	30 months
Number of patients, N	21	12	10
Number (%*) of patients in disease remission (physician assessment)	11 (58)	7 (78)	5 (62.5)
Patient´s assessment of current disease activity; 0–10, median (min; max)	1.5 (0; 8)	0.0 (0; 5)	1.5 (0; 6)
Patient´s assessment of current fatigue; 0–10, median (min; max)	1.5 (0; 8)	4.0 (0; 7)	4.0 (0; 8)
Number (%*) of patients without impairment of social life by the disease	64 (60)	3 (43)	3 (50)
Number (%*) of patients with days absent from work/ school during last 6 months	8 (40)	3 (25)	3 (33)
Current influence of the disease on mood; % of patients* with negative I positive I no influence	20 I 40 I 40	20 I 20 I 60	0 I 25 I 75
CRP, median (mg/dl)	0.2	0.0	0.1
SAA, median (mg/dl)	0.5	0.3	0.4
ESR, median (mm/h)	7.0	5.0	7.5
SAE	**Number of events**	**Incidence rate‡ per 100 patient-years**	
All types of SAE	9#	17.21	
SADR	0	0.00	

CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; SAA, serum amyloid A; SADR, serious adverse drug reaction; SAE, serious adverse event*not reported for all patients‡ Incidence rate = number of events * 36525/ sum of observation days (=19104)#SAE: arthropod bite, circulatory collapse, dizziness, dyspnea, headache, peripheral swelling, pruritus, urticaria, poisoning (each N=1, incidence rate per 100 patient-years: 1.91)

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POS1574

SAPHO SYNDROME, CLINIC CHARACTERISTICS FROM THE SAPHO-SORCOM COHORT

Keywords: Spondyloarthritis, Rare/orphan diseases, Inflammatory arthritides

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Background: The SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, and osteitis) is a rare disease (<1/10,000) with multiple cutaneous and musculoskeletal manifestations [1]. The most common dermatological manifestations are palmoplantar pustulosis (PPP) and severe acne (SA). Musculoskeletal manifestations are diverse, including the thoracic wall, spine, temporomandibular joint, and peripheral joints [2]. It is considered as part of spondyloarthropathies, however, no significant relationship with HLA-B27 has been found [3]. For treatment, non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying drugs (DMARDs) and bisphosphonates have been traditionally used. More recently, new therapies such as apremilast and biological DMARDs (4) are being used more frequently.
Objectives: To examine the characteristics of individuals diagnosed with SAPHO syndrome during follow-up at multiple Rheumatology Services in Spain.
Methods: This is a descriptive, cross-sectional, multi-center study, carried out in the Rheumatology Services of several hospitals in Spain. A convenience sampling was carried out, including all patients with SAPHO under active follow-up.
Results: 50 patients were included (76% women), with a mean age of 48.56 (±12,28) years. The mean BMI was 24.84 (±4.31). Regarding cardiovascular risk factors, 36.2% and 23.4% were smokers and ex-smokers, respectively. 18% had hypertension, 28% had dyslipidaemia and 8% were diabetic. Regarding of the musculoskeletal involvement, the most affected region was the anterior chest wall (74%), followed by peripheral arthritis (56%) and the spine (34%). 24% presented enthesitis and only 6% dactylitis. The most frecuent skin involvement was palmpplantar pustulosis in 54% (27), the distribution of dermatological manifestations is shown in Figure 1.

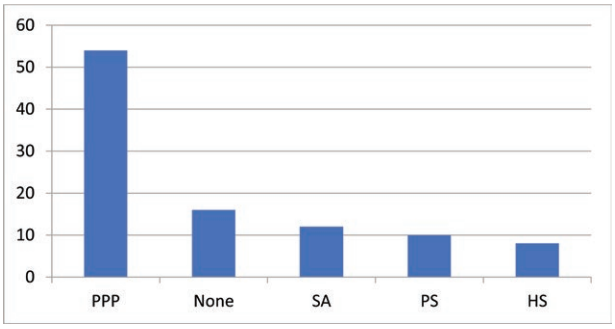


Figure 1. Skin manifestations in SAPHO syndrome.

In laboratory tests at diagnosis, acute phase reactants were slightly elevated, with a mean of CRP of 11.13 (±17.34) and ESR of 21.21 (±24.56). HLA-B27 and CW6 were positive in 12% (6) and 6% (3) of patients, respectively. The most commonly used imaging tests in the diagnosis and follow-up were plain x-rays (90%), MRI (76%), bone scintigraphy (72%), and CT scan (52%). The least used test was ultrasound, used in 17 patients (34%). The treatment was mostly based in NSAIDs, 94% of patients received it at some point. 60% used DMARDsc (mostly methotrexate). 50% of patients received bDMARDs, and 9 patients received more than two bDMARDs throughout the follow-up. The distribution of the first bDMARD used is shown in Table 1.

Table 1. First bDMARD used in the treatment of SAPHO syndrome in our cohort.

bDMARD	N	% patients (25/50)	% FAMEb/other molec's (25/25)
Adalimumab	12	24	48
Infliximab	4	8	16
Etanercept	3	6	12
Ustekinumab	2	4	8
Secukinumab	1	2	4
Anakinra	1	2	4
Apremilast	1	2	4
Cartolizumab-pegol	1	2	4
Total	25	50	100

The course of the disease was mostly recurrent (54%) with asymptomatic periods between flare-ups. About half of the patients (44%) in follow-up currently have active disease.

Conclusion: Our cohort presented axial involvement like other series and significant peripheral involvement. The most frequent skin condition was PPP. Half of the patients in our cohort required bDMARD, with ADL being the most widely used.

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Clinical cases

POS1575 ASSOCIATION OF IGG4-RELATED DISEASE AND SYSTEMIC RHEUMATIC DISORDERS

Keywords: Rare/orphan diseases

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Background: Autoimmune disorders can occur together especially in genetically predisposed individuals.

Objectives: We here aimed to assess the occurrence of IgG4-related disease (IgG4-RD) in association with other systemic immune-mediated conditions.

Methods: We retrospectively analyzed the clinical records of our routinely followed patients with IgG4-RD for pre-existing or concomitant immune-mediated disorders. IgG4-RD was diagnosed based on histological findings and on the 2011 Comprehensive Diagnostic criteria. Associated immune-mediated disorders were diagnosed based on available classification and/or diagnostic criteria.

Results: Two-hundred and thirty-four patients with a definitive diagnosis of IgG4-RD were included in this study. A pre-existing immune-mediated connective tissue disease was reported in 6/234 patients (3%): one case each of sarcoidosis, Takayasu arteritis (TA), eosinophilic granulomatosis with polyangitis (EGPA), and rheumatoid arthritis; and two cases of granulomatosis with polyangitis (GPA). Organs involved by IgG4-RD included the lungs, the pancreas, the peritoneum, lacrimal glands, meninges and orbits. Sarcoidosis, EGPA, and TA preceded the onset of IgG4-RD. GPA preceded IgG4-RD onset in one case and occurred simultaneously in the other case. Rheumatoid arthritis occurred together with IgG4-RD in one case.

Conclusion: IgG4-RD can present in the context of pre-existing systemic immune-mediated disorders. Our observation suggests that "secondary" IgG4-RD may preferentially complicate chronic granulomatous conditions including large- and small-vessels vasculitis as well as sarcoidosis.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1576 AN UNUSUAL INITIAL PRESENTATION OF VEXAS SYNDROME

Keywords: Rare/orphan diseases

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Background: VEXAS (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) syndrome is an adult-onset multisystem autoinflammatory disease caused by a somatic mutation in the ubiquitin-activating enzyme (UBA1) gene in myeloid or erythroid precursor cells, causing a variety of symptoms including fever, cytopenia, vacuoles in myeloid and erythroid progenitors, dysplastic bone marrow, neutrophilic dermatosis, pulmonary infiltrates, chondritis and/or vasculitis.

Table 1 Characteristics of IgG4RD and other immunological diseases

Patient		#1	#2	#3	#4	#5	#6
Sex (age)	M (69)	F (16)	M (67)	F (34)	F (51)	M (65)	
IgG4-related disease	**Organs involved**	Salivary glands, pancreas, biliary tract, lung	Peritoneum	Pancreas	Eyelid	Periorbital region, lacrimal gland	Meninges, abdominal aorta
	ACR/EULAR CC	36	26	26	20	21	24
	2011 CDC [13]	definite	definite	definite	probable	definite	definite
	Organ biopsy	Lung	Peritoneal lesion	Pancreas	Periorbital tissue	Periorbital tissue, lacrimal gland	Meninges
	Therapy	PDN + RTX	Surgery + PDN + MTX	Surgery	PDN	MPDN + RTX	PDN + MTX
	Response	Y	Y	Y	Y	Y	Y
Systemic Rheumatic Disease	**Diagnosis**	**Sarcoidosis**	**Takayasu**	**RA**	**GPA**	**GPA**	**EGPA**
	Clinical manifestations	Lymph nodes	Subclavian, common carotid, anonymous, and right pulmonary arteries + artery, thoracic and suprarenal abdominal aorta	Wrists	subglottic stenosis	Lung nodules, scleritis	Respiratory tract (asthma), skin, peripheral nervous system, blood eosinophilia
	Fulfillment of disease specific CC	NA	Y[#]	Y^	Y*	Y*	Y[§]
	Autoantibody	none	none	FR, ACPA	c-ANCA	c-ANCA	p-ANCA
	Definite histological diagnosis	Lymph nodes	NA	NA	NA	Lung nodule	Skin
	Onset vs IgG4-RD	Prior	Prior	Concomitant	Prior	Concomitant	Prior
	Years before IgG4-RD	1	14	-	13	0	3
	Therapya	PDN + MTX	IFX → TCZ	PDN + MTX	PDN + AZA	MPDN + RTX	PDN + CYC
	Response	Y	Y	Y	Y	Y	Y

[#]Modified diagnostic criteria for Takayasu arteritis. Shanna et al. 1995; *ACR/ EULAR 2017 provisional classification criteria for GPA; ^ACR/EULAR 2010 Classification criteria for Rheumatoid Arthritis; [§]ACR 1990 Classification criteria for EGPA **Abbreviations**: ACPA: Anti-citrullinated protein antibodies; ANCA: Anti-neutrophil cytoplasmic antibodies; RA: Rheumatoid Arthritis; AZA: Azathioprine; CYC: Cyclophosphamide; EGPA: Eosinophilic Granulomatosis with Polyangiitis; ENG: electroneurography; GPA: Granulomatosis with Polyangiitis; IgG4-RD: IgG4-Related Disease; IFX: Infliximab; TCZ: tocilizumab; F: female; M: male; MPDN: Methylprednisolone; MTX: Methotrexate; N: No; PDN: Prednisone; RTX: Rituximab

Objectives: This report describes an atypical initial presentation of peri-orbital inflammation and neurological manifestations associated with this newly recognized syndrome.
Methods: This is a case report.
Results: An 82-year-old male with insulin-treated diabetes mellitus type II, prostate hyperplasia and chronic atrial fibrillation, presented with persistent unilateral peri-orbital swelling and pain for 6 months. An initial evaluation in the ophthalmology department with biopsy showed no evidence of malignancy, myositis, vasculitis or IgG4-related disease. Due to significantly elevated inflammatory markers (CRP 250-300 mg/L, ESR around 100 mm/h), the patient received high-dose glucocorticoids (60mg Prednisolone) with a good clinical response. During the tapering of Prednisolone, the patient developed a maculopapular skin rash in the lower extremities. Skin biopsy showed signs of urticaria-like dermatitis, while immunofluorescence examination was negative. In the following months, he was hospitalized three times due to recurrent fever, generalized weakness, fatigue and general asthenia. Extensive evaluation regarding infectious and neoplastic causes was negative. An extensive autoimmune panel (including ANA and ANCA) was tested and came out negative. CT scan of the thorax and abdomen was unremarkable. During the last hospitalization, he developed expressive aphasia and fascial paresis. MRI of the brain showed signs of leptomeningeal enhancement. Examination of the cerebral fluid showed pleocytosis (leucocyte count 124, with monocytosis), while all cultures were negative. He came to the rheumatology department in November 2022 for further evaluation. He had generalized myalgias and arthralgias but no arthritis. The skin rash had disappeared. The inflammatory markers were still highly elevated and he had a mild anemia, normocytic and normochromic, but no thrombocytopenia or leukopenia. PET-CT scan showed hyperactive bone marrow, while subsequent biopsy showed normal hematopoiesis without signs of dysplasia and no vacuoles. Endoscopic evaluations revealed no pathological findings. Prednisolone was re-introduced after PET-CT with good regress of the symptoms. Repeated MRI of the brain showed regression of the area with enhancement while all neurological symptoms had subsided. A few weeks later, we received the result of the genetic testing showing a mutation of the UBA1 gene, confirming the diagnosis of VEXAS. Our patient had already started methotrexate as a cortisone-sparing agent and started tapering off Prednisolone, so far with reasonable clinical response.
Conclusion: VEXAS syndrome should be suspected in elderly patients (especially males) with systemic inflammation when other common conditions are excluded. Orbital/peri-orbital inflammation and neurological manifestations can occur and should raise the suspicion of VEXAS.
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POS1577 VENOUS INFLAMMATION MIGHT BE ONE OF THE FEATURES OF VEXAS SYNDROME AND ASSOCIATED THROMBOSIS

Keywords: Rare/orphan diseases, Imaging

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Background: VEXAS syndrome is an often fatal, X-linked disease characterized by hematological dysplasia overlapping with severe autoinflammatory manifestations. Thrombosis, predominantly as unprovoked venous thrombosis, has been reported in up to 56% of VEXAS patients. Although chronic inflammation, vasculitis, endothelial dysfunction, disrupted anticoagulant mechanisms, or prothrombotic antibodies are suggested mechanisms, the exact pathogenesis of thrombosis is yet to be elucidated. VEXAS has clinical similarities with Behçet's syndrome (BS), a systemic vasculitis involving arterial and venous vessels of all sizes. Recently, venous wall thickening (VWT) on Doppler ultrasound has been shown to be a highly sensitive and specific (>80%) finding for the diagnosis of BS. Given the clinical and pathogenetic similarities with BS, we thought venulitis might be the underlying cause of thrombosis in VEXAS syndrome.
Objectives: Herein, we report venulitis in two consecutive VEXAS patients with the demonstration of severe thickening of the walls of large veins.
Methods: Bilateral lower extremity common femoral veins (CFV) were examined with Doppler ultrasound in craniocaudal direction for the presence of thrombi, occlusion, venous insufficiency, and arterial occlusive disease. VWT was measured using the methodology described by Alibaz-Oner F et al. **[1].** All measurements were performed thrice, and the arithmetic mean of them was given as the result. We also assessed the internal jugular vein (IJV) in one patient but not in the other due to the jugular venous catheter. VEXAS patients had thickened walls on ultrasound in all examined large veins.
Results: Demographic and clinical features of our VEXAS patients are presented in Table 1. VWT in BS seemed significantly greater than non-inflammatory DVT (0.34±0.1 mm) but not significant with the anti-phospholipid syndrome (APS, 0.49 ±0.1 mm) **[2].** Our VEXAS patients had VWT greater than BS and APS suggesting remarkable vein inflammation. Patients with extensive thrombosis (Case#1) had the most severe VWT of CFV on the affected side, while the latter case (Case#2) had equivalent VWT in both CFVs.
Conclusion: Consequently, our findings suggest that venulitis might be one of the features of VEXAS syndrome and the underlying mechanism for thrombosis. Further studies are needed to clarify the role of inflammation in venous thrombotic diseases.
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Table 1. Demographic, clinical, laboratory and ultrasonographic findings of patients

	Case# 1	Case # 2
Sex	Male	Male
Age (years)	73 y	77 y
Smoking	Former (30 pc/y)	Never
UBA1 variant	M41L	M41V
Duration of symptoms	2 years	1 year
Age at diagnosis	72	77
Co-morbidities	COPD	CAD
Clinical features	Fever, weight loss, arthritis, neutrophilic dermatitis, periorbital edema, pericardial effusion, lung infiltrates, pulmonary embolism, left femoral vein thrombosis, and occlusion of left femoral artery	Fever, weight loss, arthritis, neutrophilic dermatitis, periorbital edema, right lower extremity superficial thrombophlebitis, MDS
Hemoglobin (g/dL)	8.8	6.8
MCV (fL)	>110	99.3
ESR, (mm/h)	117	135
CRP, (mg/L)	88	235
Right CFV thickness*, mm	0.91	1.43
Left CFV thickness, mm	1.21	1.02
Right IJV thickness**, mm	0.57	0.46
Left IJV thickness, mm	0.70	0.65

*Typical CFV thicknesses for healthy adult and child populations are less than 0.5 mm **(2),** and typical IJV thickness is <0.5 mm for adults

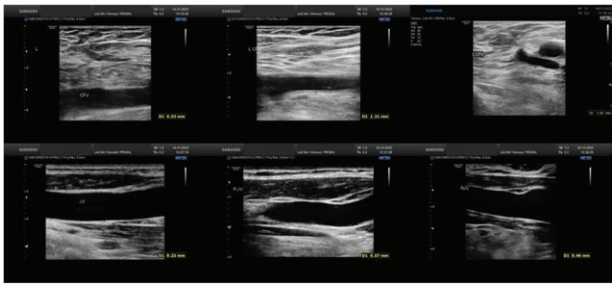


Figure 1. B-mode USG image of the common femoral vein,juguler vein and vena safena magna. **A.** A healthy individual's femoral vein ultrasonography, **B.**Vexas patient's femoral vein (case #1), **C.**Vexas patient's femoral vein (case# 2), **D.** A healthy individual's juguler vein ultrasonography, **E.**Vexas patient's juguler vein (case #1), **F.** Vexas patient's juguler vein (case# 2)

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POS1578 JAK INHIBITORS AND VEXAS SYNDROME: A SUCCESSFULLY CASE TREATED WITH FILGOTINIB

Keywords: Targeted synthetic drugs, Treat to target, Rare/orphan diseases

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Background: VEXAS syndrome is a novel described autoinflammatory entity for which the diagnosis is defined by somatic mutations in the *UBA1* X-linked gene in hematopoietic progenitor cells. The clinical manifestations are heterogeneous, ranging from autoinflammatory symptoms to the presence of underlying hematologic disorders. Response to treatment in VEXAS is very poor and to date the therapeutical strategies adopted are only partially effective. However, recently described cohorts of VEXAS patients treated with Janus-Kinases Inhibitors (JAK-I) demonstrated that these drugs can be effective for the treatment of several manifestations related to the disease.
Objectives: To describe the case of a 65-year-old man affected by VEXAS who was successfully treated with the selective JAK-1 inhibitor filgotinib.
Methods: We present the case of a 65-year-old man, diagnosed with a myelodysplastic syndrome (MDS grade 3, sec WHO, 2016) one year earlier, presenting with a recent history of leukocytoclastic vasculitis, deep vein thrombosis, tenosynovitis, and ear chondritis. He was admitted to the hospital for hyperpyrexia (39° TC), increased inflammatory markers, macrocytic anemia with Hb 7,7 g/l and MCV 104 fL and requiring multiple blood transfusions, and shortness of breath caused by a pleural effusion; after excluding neoplastic conditions, infections, and other potential mimickers (such as vasculitis), a genetic analysis was performed, revealing the somatic mutation Met41Leu (c.121A>C) in the *UBA1* gene. Methylprednisolone was started from 16 mg/day (not reducible for recurrent flares). A peripheral blood smear was stained with May Grunwald-Giemsa staining to perform a cytogenic evaluation of leucocytes. Oil immersion microscopy with 1000× magnification was applied for the analysis.
Results: Following the diagnosis of VEXAS, the patient started filgotinib 200 mg/day, with a subsequent clinical and biological improvement that allowed for a slow reduction of glucocorticoids. After 1.5 month his laboratory exams showed: Hb 9,4 g/L, MCV 106 fL, C-reactive protein (CRP) 2,24 mg/dL. At peripheral blood smear, the patient had granulocytes with morphological changes, including cytoplasmic vacuoles (2%), immature neutrophils (29.8%) such as band neutrophils, hyposegmented neutrophils, and pseudo Pelger Huët-like morphology. Vacuolated/activated monocytes (4.5%) and nuclear abnormality (binucleated cells, buds) were also observed.
Conclusion: VEXAS syndrome is a new genetically-determined rare disease that requires a prompt treatment to avoid a rapid worsening. Glucocorticoids often represent the first line therapy and blood transfusion support is usually required; however, given the promising results derived from recently published cohorts, JAK-inhibitors, in particular selective JAK-1 (filgotinib, upadacitinib), or JAK1/2 blockers (ruxolitinib), may represent a suitable therapeutic approach.
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POS1579 VEXAS SYNDROME IN A PATIENT WITH BIOPSY POSITIVE GCA AND IMAGING PROVEN LARGE VESSEL VASCULITIS TREATED WITH TOCILIZUMAB

Keywords: Comorbidities, Vasculitis, Rare/orphan diseases

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Background: VEXAS syndrome (Vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) was first reported in late 2020 in 25 men, mostly in their fifth decade of life or after, with adult-onset concomitant autoinflammatory disease and myeloid dysplasia (Beck et al., 2020). It is the first for a proposed new subset of 'haemato-inflammatory diseases and its underlying pathophysiology is thought to be governed by monogenic, somatic missense mutations affecting Met-41 of in the myeloid-restricted UBA1 gene. This results in deranged cellular ubiquitination and a broad range of clinical manifestations (Beck et al., 2020).
Objectives: We describe the case of a patient with the ultimate unifying diagnosis of VEXAS syndrome with an initial presentation of cranial GCA and PET-CT proven large vessel vasculitis. Immunosuppressive regime was challenging due to patient co-morbidities including brittle diabetes and myelodysplastic syndrome.
Methods: Case report.
Results: A 73-year-old gentleman with a history of type 2 diabetes mellitus was admitted with persistent fever, recurrent orbital swelling, thrombophlebitis and severe weight loss of 30kg over 24 months. A wide infectious screen revealed no source with ongoing symptoms despite antibiotic therapy.

Table 1. Blood Results.

Components	Result
HB 125-172g/L	70
MCV 80-101.0 FL	96.2
WBC 3.6-10.5 10*9	19.4
NEUT 1.50-7.70 10*9	18.68
LYMP 1.10-4.00 10*9	0.33
PLAT 160-370 10*9	109
UREA 2.5-7.8mmol/L	9.3
CREAT 62-115umol/L	86
Na 133-146mmol/L	125
CRP 0-9mg/L	292
Procalcitonin 0.00-0.50	0.78
Albumin 35-50g/L	16
Adj Ca 2.20-2.60mmol/L	2.40

Prior review at the bone marrow failure clinics had revealed a macrocytic anaemia with a Heamoglobin of 96g/L, MCV of 105.1FL and thrombocytopenia of 117 X10*9. Bone marrow biopsy revealed hypercellularity with trilineage dysplasia however genetic screening did not detect the UBA1 missense mutation. CT scan revealed perivascular stranding and thickening around the origin of the right carotid and subclavian artery. PET CT scan showed high tracer uptake in the wall of the ascending aorta, subclavian, carotid arteries and bone marrow. New onset headache, jaw pain,scalp tenderness and shoulder stiffness prompted a temporal artery biopsy which revealed lymphohistiocytic inflammatory infiltrates in the intima with focal loss of internal elastic lamina. 60mg of prednisolone led to dramatic resolution of symptoms and inflammatoryb markers. A diagnosis of VEXAS was revisited due to the unique combination of inflammatory and haematological features.Repeat bone marrow biopsy using a newer version of haem oncology gene panel was positive for UBA1 missense variant in exon 3 (c. 122T>C, p.Met41Thr.). Vacuoles were found to be present on erythroid precursor cells. He developed fatigue, rashes and CRP>100 on tapering down prednisolone to 20mg OD. SC Tocilizumab was introduced rather than Methotrexate and Leflunomide due to bone marrow failure. SC Tocilizumab was switched to Intravenous form to optimise bioavailability. He is clinically stable on IV tocilizumab with slower wean of steroid. He suffers with heavy burden of steroid toxicity, including weight gain, erratic blood sugars, steroid induced acne, hypertension and recurrent infection.
Conclusion: VEXAS, should be explored as a potential unifying diagnosis in conditions of overlap between autoinflammatory and haematological condition. Treatment paradigm is still evolving with no current standardised regime hence fraught with uncertainty between high risk of morbidity/mortality from uncontrolled and poorly treated inflammation versus iatrogenic complications from steroid therapy. There is a research gap pertaining to patient cohorts with specific patterns of systemic disease.
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POS1580 A CASE SERIES OF VEXAS SYNDROME IDENTIFIED IN THE WEST MIDLANDS, UNITED KINGDOM

Keywords: Rare/orphan diseases

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Background: VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome was first described in 2020 when a mutation in ubiquitin activating enzyme 1 (UBA1) was identified in three patients [1]. This adult-onset autoinflammatory and haematological disease primarily affects males over the age of 50 years. The clinical features are diverse but commonly include skin lesions, non-infectious fever, weight loss, lung involvement, arthralgia/arthritis, relapsing chondritis, ocular symptoms, venous thrombosis, and lymphadenopathy [2]. Whilst corticosteroids are effective, high doses are often required to control the disease and the ideal standard of care, including the choice and efficacy of steroid-sparing agents, is yet to be defined.

Objectives: After identifying three cases of VEXAS in our region within a 6-month period, our objective was to present each case alongside the current knowledge of the condition in order to increase the awareness amongst clinicians.
Methods: We examined each case, comparing the clinical features, investigations, management, and events leading to the diagnosis.
Results: The cases are presented in the table below.

Table 1.

	Case 1	Case 2	Case 3
Demographics	Male, White-British, 59 years old	Male, White-British, 73 years old	Male, White-British, 76 years old
Clinical Features	Fatigue, Fever, Weight loss, Arthralgia, Diarrhoea, Subcutaneous nodules, Lymphadenopathy, Salivary gland swelling, Epididymo-orchitis	Fatigue, Fever, Weight loss, Erythematous papules, Cough, Lymphadenopathy, Ocular involvement, Nasal crusting and discharge	Fatigue, Fever, Weight loss, Arthritis, Diarrhoea, Lymphadenopathy, Headache, Sinusitis, Uveitis, Lung involvement
Investigations (present in all patients)	Macrocytic anaemia, significantly raised inflammatory markers, diffuse marrow activity on PET Scan, reactive features on bone marrow and lymph node biopsy, multiple negative microbiology and immunology investigations, UBA1 mutation		
Management, including outcome	Excellent response to corticosteroid (normalisation of CRP). Clinical deterioration at 15mg daily prednisolone. Azathioprine (minimal benefit).	Multiple blood transfusions. Excellent response to corticosteroid (normalisation of CRP). Methotrexate (awaiting response)	Moderate response to corticosteroid (CRP improvement). Clinical deterioration at 15mg daily prednisolone.
Working diagnosis prior to VEXAS diagnosis	Polyarteritis Nodosa/ vasculitis	Unspecified vasculitis	Giant cell arteritis
Time from presentation to diagnosis	13 months	12 months	41 months
Specialties involved	Rheumatology, Acute Medicine, Haematology, Dermatology, Infectious diseases, Ophthalmology, Respiratory, Immunology, Gastroenterology, Urology	Rheumatology, Acute Medicine, Haematology, Dermatology, Infectious Diseases, Ear Nose and Throat.	Rheumatology, Acute Medicine, Haematology, Infectious diseases, Ear Nose and Throat, Orthopaedics, Respiratory, Ophthalmology, Geriatric Medicine, Immunology, Gastroenterology

Conclusion: The true prevalence of VEXAS is unknown however after we diagnosed three cases of the condition in a short period of time, it is perhaps more prevalent than initially thought. Clinicians should remain vigilant and consider genetic testing in patients presenting with the common inflammatory and haematological manifestations.

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POS1582 **VEXAS SYNDROME: TWO CASES PRESENTING WITH PERIORBITAL EDEMA**

Keywords: Rare/orphan diseases

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Background: VEXAS syndrome (vacuoles, E1enzyme, X-linked, autoinflammatory, somatic) is a X-linked autoinflammatory condition. The 3 most frequent somatic missense mutations affect methionine 41 of exon 3 (p.Met41Thr, p.Met41Val, p.Met41Leu) of ubiquitin-activating protein (UBA)1 gene, which encodes the E1 protein. Patients are usually men in their fifth-to-seventh decade of life and present with inflammatory symptoms, as well as hematologic manifestations with progressive bone marrow failure.
Objectives: We describe 2 patients with some key features that allow us to diagnose this syndrome.
Results: Case 1. AM, 78-year-old man, with chronic kidney disease. In August 2021 onset of left orbital inflammation, treated with antibiotics. A month later admission to our hospital for normocytic anemia, inflammation, oligoarthritis, moderate thrombocytopenia, superficial vein thrombosis and severe respiratory failure due to cryptogenic organizing pneumonia, which required ICU admission: no response to antibiotic therapy but to high dose iv steroid. He was discharged with oral prednisone (PDN), discontinued in three months. New hospitalization for headache, periorbital inflammation, diplopia, and right lateral gaze. No CNS involvement at brain CT-scan. Lab: Hb 9 g/dL, MCV 104 fl CRP 28 mg/dL, ESR 126 mm/h, ferritin 2710 ng/mL, fibrinogen 1142 mg/dL, creatinine 1.5 mg/dL. Normal levels of vitamin B12, folate, haptoglobin, LDH. Autoimmunity and microbiological work-up negative. MRI: bilateral orbital cellulitis, submandibular and parotid gland inflammation. PET-CT with ^{18}F-FDG: diffuse uptake in skeleton, spleen and in pulmonary left superior lobe. Bone marrow aspirate: no signs of myelodysplastic syndrome (MDS): vacuoles in the myeloid and erythroid series. UBA1 gene point mutation p.Met41* Val on bone marrow blood. PDN (0.75 mg/kg/day) was started with benefit on symptoms, anemia and inflammation. Mycophenolate mofetil was introduced as steroid sparing agent and PDN was tapered to 10 mg/day. Macrocytosis has not improved although Hb levels increased with normal reticulocyte count. CRP and ESR are normal and serum ferritin decreased. Case 2. SR, 70 years old man, in October 2021 he had superficial venous thrombosis of right leg, treated with LMWH. Two months later left leg deep venous thrombosis (DVT) and pulmonary thromboembolism, fever, arthritis, weight loss, elevation of CRP (23 mg/dL), Hb 13.3 g/dL with normal MCV. Apixaban and antibiotic were started. After the discharge, onset of periorbital edema with maxillary and ethmoid sinusitis and right arm DVT were diagnosed, and apixaban was changed into warfarin. Genetic and acquired thrombophilia were excluded. At ^{18}F-FDG PET scan diffuse increased uptake in bone marrow. Again periorbital edema and dysphagia. MRI: edema and solid tissue with contrast enhancement of left pyriform sinus without evidence of lymphadenopathy. ER admission for urticarial rash, fever, and severe chest pain due to pericarditis: elevated CRP, and macrocytic anemia (Hb 9.5 g/dl, MCV 107 fl) with normal folic acid and B12 vitamin. Infections and CTD were ruled out. Bone marrow biopsy findings were coherent with MDS. Though vacuoles absence, UBA1 pMet41Val missense mutation was found. PDN 1 mg/kg/day with subsequent tapering was started with clinical improvement, normalization of acute phase reactants and Hb concentration (13.8 g/dl), but persistent macrocytosis. The subsequent needed dose of PDN was > 25 mg/day and the patient is a candidate for 5-Azacytidine therapy.
Conclusion: The VEXAS syndrome increased the awareness of complex associations between MDS and adult-onset inflammatory conditions. In our experience recurrent periorbital edema could be a clinical clue for this syndrome. Macrocytic anemia appeared with persisting inflammation after some months and supports the link between inflammation and MDS development; nevertheless macrocytosis remain stable irrespective of clinical and acute phase reactants improvement. Finally,the lack of vacuolization on bone marrow biopsy should not preclude a search of UBA1 gene mutation.

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HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

POS1583-HPR **THE EFFECT OF VITAMIN D DEFICIENCY ON EXERCISE CAPACITY, RESPIRATORY MUSCLE STRENGTH, AND PERIPHERAL MUSCLE STRENGTH IN PATIENTS WITH CONNECTIVE TISSUE DISEASES**

Keywords: Vitamin D, Systemic sclerosis, Systemic lupus erythematosus

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Background: Vitamin D is one of the fat-soluble vitamins and is also a group of sterols that are hormone and hormone precursors. Vitamin D deficiency and/or insufficiency have been found to be associated with many chronic diseases, including cancers, metabolic syndrome, and autoimmune diseases. Vitamin D is involved in modulation of immune responses in autoimmune disorders including multiple sclerosis, asthma, diabetes mellitus, connective tissue disorders such as rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE). In addition; Previous studies conducted in other patient populations indicate that higher vitamin D levels are related to higher exercise capacity, muscle strength, and better lung function.
Objectives: The purpose was to investigate the effects of vitamin D deficiency on exercise capacity, respiratory muscle strength, and peripheral muscle strength in patients with connective tissue disease (CTD).
Methods: This cross-sectional observational study included CDT (SLE and systemic sclerosis (SSc)) patients and healthy participants. Serum 25(OH)D, calcium, and phosphorus levels were measured and Vitamin D levels 10.0-20.0 ng/mL defined insufficiency and levels <10.0 ng/mL defined deficiency. The exercise capacity, respiratory muscle strength, and peripheral muscle strengths were set as the primary outcomes of the study. Secondary outcomes included evaluation of physical activity, dyspnea, pain, emotional status, fatigue, and quality of life.
Results: There were 23 SLE (36.82±10.06), 21 SSc (44.38±14.63), and 24 healthy controls (37.62±11.74). Compared to healthy controls, CTD groups with vitamin D deficiency had significantly lower respiratory muscle strength ($p<0.001$), peripheral muscle strength (knee extension and shoulder flexion) ($p<0.05$), exercise capacity ($p<0.05$), physical activity ($p<0.05$), and quality of life ($p<0.05$) while having significantly more dyspnea ($p<0.001$), pain ($p<0.001$), fatigue ($p<0.001$), anxiety, and depression ($p<0.05$).
Conclusion: The results of our study indicate that vitamin D deficiency is associated with reduced muscle strenghts and related symptoms and complaints in CTD patients, hence, in order to increase the efficacy of rehabilitation and treatment programs, attention should be paid to vitamin D levels and should be corrected appropriately.

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POS1584-HPR **IMPACT OF TELEMEDICINE ON DISEASE ACTIVITY ASSESSMENT: A CASE-CROSS OVER NESTED WITHIN A COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS**

Keywords: Systemic lupus erythematosus, Outcome measures, COVID

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Background: The utilization of telemedicine has been rapidly growing among patients with rheumatic disease especially following COVID-19 pandemic. The ease and convenience seems to dominate the reasons of such growth. Yet the effect of this approach on patients with systemic lupus erythematosus (SLE) is yet to be revealed.
Objectives: In this study, we aimed to examine the effect of telemedicine in SLE patients on the outcome of disease activity.
Methods: This is a case-cross over study nested within the national prospective cohort of SLE, Saudi Arabia. SLE patients who fulfils the SLICC classification criteria within the period between March 2020 to March 2021 and have been assessed at three-time point with three months' time difference between assessments according to standardized protocol were included. Telemedicine was conducted at first point while in person assessment were used for second and third points. Primary outcome was difference in SLEDAI-2K score. Primary analysis was conducted using GEE model and adjusted for potential confounders including demographics, medications and changes in steroid doses. Several sensitivity analyses were conducted to mitigate selection and time varying confounders.
Results: A total of 92 participants were included. Majority of them were females (88%), with a mean (±SD) age of 36 (±13). mean (±SD) disease activity scores at baseline as follows: SLEDI 5 (±5); SRI 3.8 (±3.5); SDI 1 (±1). Mean difference of SLEDI score of -1.641 (95% CI -2.773 — -0.510), p=0.005* between telemedicine and follow up visits. Adjusted value and mean with mean diffrence in Figure 1. Results were consistent in all sensitivity analyses.
Conclusion: We found that the Telemedicine assessment was associated with much higher disease activity score compared to in person in subsequent assessments which may suggest potentially overestimation of disease activity and later assessment accuracy. Cautious adoption is suggested in SLE patients with active disease.

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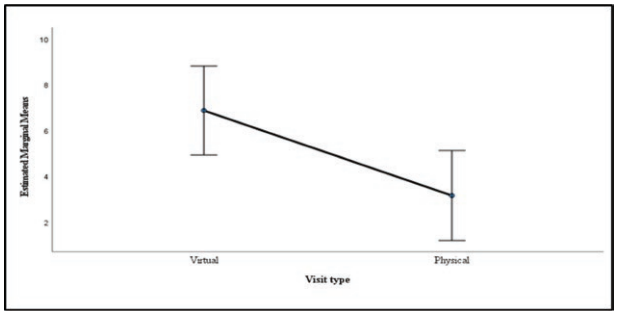


Figure 1 Repeated measure analysis of difference in SLEDAI between the virtual visit and the physical visit taking factors affecting SLEDAI on univariate analysis into consideration (abnormal urine test, fibromyalgia, haemolytic anaemia and mycophenolate use).

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Disclosure of Interests: None Declared.
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POS1585-HPR **"SO, MEN WILL BE ABLE TO RECEIVE #METHOTREXATE FOR LUPUS AND RHEUMATOID ARTHRITIS BUT NOT WOMEN" THE OVERTURN OF ROE V. WADE BEYOND ABORTION**

Keywords: Qualitative research methods, Pregnancy and reproduction, Quality of life

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Background: On June 24, 2022; the Supreme Court of the United States (US) overturned the right established in Roe v. Wade to terminate a pregnancy. Roe v. Wade, 410 U.S. 113 (1973), was a landmark decision of the US Supreme Court in which the Court ruled that the Constitution conferred the right to have an abortion. This decision returns to the states the power to set abortion laws. Pregnant people considering abortion already had been dealing with a near complete ban in Oklahoma and a prohibition after six weeks in Texas. Other states immediately passed abortion ban laws prohibiting the use of abortive methods, which include the medication used for this procedure such as prostaglandins, mifepristone, and methotrexate (MTX). In the case of MTX, despite its use as an abortive agent, it has been a cornerstone drug in the treatment of rheumatic and musculoskeletal diseases (RMDs). Consequently, the medication ban laws has triggered a deep fear among people with RMDs and the health professionals who treat them which have voiced concerns about potential restrictions. Some of these concerns were expressed in social media (SoMe) platforms specially on Twitter.
Objectives: To explore and analyze SoMe data on Twitter to better comprehend the short-term implications of the overturn of Roe v. Wade for those treating RMDs as well as for those living with RMDs.
Methods: This study is a secondary source convergent parallel mixed methods study using SoMe public data. All the tweets publicly posted using "#Methotrexate or Methotrexate" were tracked with Keyhole (http://www.keyhole.co). The tweets were monitored from June 24 to July 1. A combination of SoMe performance data with a qualitative analysis of tweets was conducted. In addition, usage metrics and location were collected. Regarding the qualitative analysis we performed a hashtag co-occurrence analysis and a content analysis.
Results: A total of 5,180 posts using #Methotrexate or Methotrexate were generated. Retweets were more frequent than original posts and replies. In addition, female users posted more than 50% of all publications. Users from 88 countries tweeted using the tracked hashtag or keyword. However more than half of all publications came from the US (73%). Focusing the analysis at the national level, users from the 50 states tweeted using the tracked hashtag or keyword. However, five states made up 38% of all publications: California (10%), New York (10%), Texas (9%), Florida (5%), and Pennsylvania (4%). From the hashtag co-ocurrence analysis the three pairs of hashtags with higher co-ocurrence with #Methotrexate were: #roevswade, #abortionishealthcare, and #rheumatoidarthritis. These relations provided context to the MTX restrictions and revealed more details about the complexities of the judicial decision. Finally, from the content analysis three main themes were generated: (i) Violence against women, (ii) Health policy without public health intelligence, and (iii) Call for strategic alliances in favor of public health.
Conclusion: Biological sex differences will condition the usage of MTX. Men will be able to continue their treatment without hesitation. However, women treated with MTX could lose the continuity of their treatment and may be switched to another medication. Moreover, women in childbearing age with a recent RA diagnosis could be denied MTX as the standard of care for the initial management of the disease. Inequity in access to treatment is a political decision, just as it is to reproduce inequities and vulnerabilities through the actions taken. Not having access to MTX for RMDs is a critical issue. Limiting the access to MTX endangers the physical and mental health of people with RMDs. MTX is an affordable drug and the options to replace it are very expensive for poor people with minimal or no health insurance. Our study is a snapshot of the immediate effects of the overturn of Roe v. Wade in the treatment and management of RMDs. Future research should focus on the mid-term and long-term effects of this decision in the states level and its impact in health outcomes in people with RMDs.
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POS1586-HPR DOES DEVELOPING SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) MAKE A DIFFERENCE IN PATIENTS WITH UNDERLYING IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP)?

Keywords: Geographical differences, Systemic lupus erythematosus

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Background: An estimate of 30–40% of patients with thrombocytopenia have idiopathic thrombocytopenic purpura (ITP) and thrombocytopenia is a common manifestation of systemic lupus erythematosus (SLE). Previous studies have shown the incidence of SLE in patients with ITP to be between 7% and 30% [1,2]. However, there are limited data on this especially in an Asian population.
Objectives: This study aims to investigate the incidence of SLE among Asian patients with underlying ITP and assess the differences between ITP patients who develop SLE and ITP patients who do not.
Methods: A retrospective review of electronic medical records of ITP patients from University of Malaya Medical Centre in Kuala Lumpur was conducted from January 2000 to June 2022. All adult patients with a diagnosis of ITP, verified by treating physicians, who fulfilled inclusion criteria within the time period were included into the study. Patients who subsequently developed SLE were identified. Patients with known SLE who developed secondary ITP after SLE diagnosis were excluded from the study. Data collected included age, sex, race/ethnicity, basic demographics, initial symptom presentation, comorbidities, and blood tests including hemoglobin and platelet levels upon initial presentation of ITP.
Results: Total of 181 ITP patients who fulfilled the inclusion criteria were recruited; 25 (13.8%) were males, 84 (46.4%) patients were of Chinese race and 30 (17.6%) were of Indian race. Eleven (6%) patients developed SLE with a mean age of ITP presentation at 35 years. There were no Indian race ITP patients who developed SLE in comparison to other races (p=0.01). Patients who developed SLE had lower haemoglobin at ITP diagnosis (8.0 [4.08] vs 11.8 [2.83] g/dL, p=0.005) and also lower levels of platelets upon diagnosis of ITP (3.0 [2.00-10.75] vs 24.0 [6.00-53.25] x109/L, p=0.025) in comparison to ITP patients who do not develop SLE. There were no differences in initial symptom presentation or comorbidities between the 2 groups.
Conclusion: Our study found that there are racial differences and differences in hematological presentation upon diagnosis of ITP in patients with ITP who subsequently develop SLE. However, further larger studies are required to further explore the differences, especially in the Asian population.
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Disclosure of Interests: siti fadillah skh ali: None declared, Fariz Yahya Speakers bureau: Pfizer, Novartis, Zuellig Pharma, Janssen, Abbvie and Gilead, Grant/research support from: Abbvie, Janssen, Gilead and Novartis, nurul aini mohd zin: None declared, anis elly suraya mohamed ridza: None declared, ping chong bee Speakers bureau: J&J, Consultant of: BMS, ASTRA ZENECA and J&J.
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POS1587-HPR DISABILITY IN AN ITALIAN COHORT OF RHEUMATIC DISEASES: A MIXED METHOD STUDY FOR THE ANALYSIS OF THE PHENOMENON AND PROPOSALS FOR NURSING APPROACH

Keywords: Descriptive studies, Nursing, Quality of life

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Background: Rheumatic diseases are heterogeneous clinical conditions that often lead to functional disability with consequent impairment of Quality of Life (QoL). Assessing the risk factors of disability is required to find improvement strategies geared toward patient empowerment and implementation of current health services.
Objectives: The aim of the present observational-descriptive study was to analyse the impact of disability in an Italian cohort of rheumatic patients and suggest nursing intervention hypotheses to approach disability-related problems and improve QoL in rheumatology patients.
Methods: Data collection was carried out through in-person or remote interviews with rheumatic patients of a Rheumatology Unit in Florence, Italy. The interviews aimed at observing the phenomenon of disability and the following questionnaires were administered: Short Form-12 (SF-12) for QoL, Health Assessment Questionnaire (HAQ-DI) for disability, Visual Analogue Scale (VAS) for pain, Work Productivity and Activity Impairment Questionnaire: General Health (WPAI:GH) for workability. Afterwards, the nursing group met to discuss the results and, based on recent literature, propose strategies for approaching the patient with disabilities in daily clinical practice.
Results: 21 rheumatic patients were interviewed. For mental and physical health SF-12 showed scores of 47.6 and 46.1, respectively. Pain level averaged 2.2 score, while disability index as assessed with HAQ-DI was 0.3 score. As for the workability, 50% of the sample interviewed work on average for 33.6 hours with a mean of 2.6 hours of absence from work due to the disease. Lastly, 6.25% report work suspension with disability pension due to illness. Nursing intervention hypotheses to curb disability-related problems and improve QoL in rheumatology patients are summarized as follows in Figure 1.

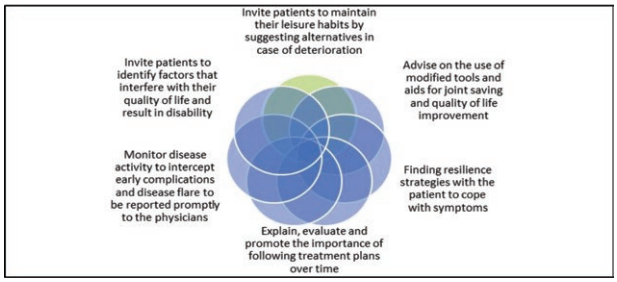


Figure 1. Proposals for nursing approach in disability

Conclusion: Psychological well-being falls within the determinants of QoL, jointly with other factors such as occupational and relational well-being and control of disease progression, in line with the reviewed studies. Understanding and investigating the determinants of QoL for each patient is the starting point for holistic care geared toward his or her well-being: this attitude cannot be separated from a multidisciplinary approach by healthcare professionals.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1589-HPR HIGH DISEASE ACTIVITY HAS A NEGATIVE EFFECT ON PAIN CATASTROPHIZING, FEAR AVOIDANCE AND BODY AWARENESS LEVELS IN PATIENTS WITH ANKYLOSING SPONDYLITIS- A PRELIMINARY STUDY

Keywords: Pain, Spondyloarthritis, Patient reported outcomes

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Background: Ankylosing spondylitis (AS) is a rheumatic disease that affects patients in a biopsychosocial framework due to its chronic inflammatory nature. It is known that patients with AS experience negative body judgment and insecurity and anxiety about their bodies [1], high levels of fear of movement, depression [2], low level of physical activity [3].

Objectives: The aim of this study was to investigate the effects of disease activity (DA) on depression, physical activity, pain catastrophizing, fear avoidance, and body awareness in patients with ankylosing spondylitis.

Methods: Thirty AS patients were included in the study. Socio-demographic informations of patients were collected. The mean age of the patients was 40.27 ± 10.38 years. Beck Depression Inventory (BDI), International Physical Activity Questionnaire-Short Form (IPAQ-SF), Pain Catastrophizing Scale (PCS), Tampa Scale for Kinesiophobia (TSK), and Body Awareness Questionnaire (BAQ) were used for depression, physical activity, pain catastrophizing, kinesiophobia and body awareness levels of the patients, respectively. DA was measured with Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and a score of four and higher than four was considered active.

Results: Patients characteristics were similar between the groups (p>0.05). A statistically significant difference was observed in PCS (p= 0.004), TSK (p=0.007), and BAQ scores (p=0.015) when the groups were compared (Table 1). The patients in the low DA group had mild depression, and the group with high DA had moderate depression. Catastrophizing pain and fear of movement were higher in the group with higher DA; body awareness level was lower (p<0.05). A high kinesiophobia level was detected in both groups.

Conclusion: It was observed that high disease activity negatively affected catastrophic thoughts, body awareness, and kinesiophobia in patients with AS. These parameters should be considered in the management of disease activity in AS patients for optimum results.

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Table 1. Patients characteristics and outcome measures

Patients Characteristics	Total n=30	High Disease Activity n= 18	Low Disease Activity n= 12	p-value*
Age (year): mean ± SD	40.27 ± 10.38	39.39 ± 9.41	41.58 ± 12.0	0.518
BMI (kg/m^2): mean ± SD	26.66 ± 5.78	27.00 ± 6.92	26.16 ± 3.81	0.790
Gender (n, %) Female	7 (23.3%)	5	2	0.632
Male	23 (76.7%)	13	10	
Duration of disease (year): mean ± SD	5.91 ± 7.28	4.77 ± 6.54	7.56 ± 8.36	0.556
CRP (mg/dl)	5.2 (0.60-49.06)	5 (0.70-49.06)	5.6 (0.60-23.40)	0.884
ESR (mm/h)	9 (3-54)	10 (3-54)	7.5 (3-21)	0.811
BASDAI (0-10)	5.2 (1.40-8.90)	6.75 (4.0-8.90)	3.05 (1.40-3.85)	**0.000**
Outcome Measures				
BDI (0-63)	14 (0-42)	18 (6-42)	13.5 (0-24)	0.107
IPAQ-SF	1188 (66-5805)	1287 (198-5805)	1089 (66-4158)	0.450
PCS (0-52)	27 (7-50)	35.5 (7-50)	17 (10-30)	**0.004**
TSK (0-68)	42.5 (25-57)	44.5 (34-57)	39 (25-47)	**0.007**
BAQ (18-126)	91.5 (49-120)	80 (49-118)	108 (83-120)	**0.015**

Values are medians (minimum-maximum) unless otherwise stated. AS= Ankylosing spondylitis; SD= Standard deviation; BMI= Body mass index; m= meter; kg= kilogram; CRP= C reactive protein; ESR= Erythrocyte sedimentation rate; BDI= Beck Depression Inventory; IPAQ-SF= International Physical Activity Questionnaire-Short Form; PCS= Pain Catastrophizing Scale; TSK= Tampa Scale for Kinesiophobia; BAQ= Body Awareness Questionnaire. * = Mann-Whitney U test.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1590-HPR ASSOCIATION OF SELF-PERCEIVED ORAL HEALTH STATUS WITH ESSPRI REPORTED BY PATIENTS WITH SJÖGREN'S SYNDROME

Keywords: Descriptive Studies, Patient reported outcomes, Sjögren syndrome

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Background: Salivary gland hypofunction, manifested as xerostomia in Sjögren's syndrome (SS), causes dental, language, and nutritional problems, leading to a detriment in oral health [1]. The Geriatric/General Oral Health Assessment Index Spanish Version (GOHAI-SP) is a useful tool that has been used to assess the self-perception of oral status in SS patients [2].

Objectives: To describe oral health status using the GOHAI-SP in patients with primary (pSS) and secondary (sSS) Sjögren's syndrome and correlate it with EULAR SS Patient Reported Index (ESSPRI), Schirmer's test for both eyes and unstimulated salivary flow (USF).

Methods: A cross-sectional and observational study was conducted from October to December 2022 in the rheumatology service of the Hospital Universitario "Dr. José Eleuterio González", Mexico. Patients meeting ACR/EULAR criteria for pSS and sSS were included and assessed with ESSPRI and GOHAI-SP during their follow-up appointment or contacted by telephone. The latter index consists of 12 questions on a 1 to 5 Likert-type scale. The lowest obtainable score is 12 and the maximum 60. Scores ≤ 44 were classified as poor oral health, moderate from 45 to 50, and good ≥ 51. Questions 1-4 assesses oral functionality, 6, 7, 9-11 psychosocial status; 8 and 12 for pain. Objective data such as Schirmer's test and USF/15 minutes were obtained from patients' charts.

Results: A total of 41 patients were included: 31 (75.6%) with pSS and 10 (24.4%) with sSS most of whom were woman (n=40, 97.6%) with a mean age of 53.41 (SD: 12.58). The median score of GOHAI-SP was 50 [IQR 43.5-52], medians for dryness, fatigue, and pain reported in ESSPRI domains were: 3 [0-7], 2 [0-6.5] and 1 [0-5]; for Schirmer test 5 [1-16] and 10 [3-17.5] in right and left eyes respectively and USF 1.5 [0.5-2.25]. The self-perceived health status was classified as good in 19 (46.3%), moderate and poor both in 11 (26.8%). We found that the worse the self-perceived oral condition, the higher ESSPRI medians for dryness (p <0.001), fatigue (p 0.003) and pain (p 0.002) were reported. No significant differences were found when compared to Schirmer and USF tests. Results for Spearman's correlation model are shown in Table 1. No significant differences were found between pSS and sSS groups.

Conclusion: The greater the severity of dryness, fatigue and muscular or joint pain, the greater the functional impairment of mouth and oral pain; as well as the worse the psychosocial aspect manifested as concern, nervousness, discomfort and limitation of interaction with people due to the dental appearance.

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Table 1. ***Correlation between GOHAI-SP, ESSPRI, Schirmer's test and USF***

		GOHAI-SP domains							
	Median [IQR]	*Oral functionality 4 [3.5-4.37]*		*Psychosocial 4.2 [4-4.5]*		*Pain 4 [3-4.75]*		*Total 50 [43.5-52]*	
		r =	*p* =	*r* =	*p* =	*r* =	*p* =	*r* =	*p* =
ESSPRI dryness	3 [0-7]	-0.37	**0.016**	-0.42*	**0.006**	-0.51*	**<0.001**	-0.581	**<0.001**
ESSPRI fatigue	2 [0-6.5]	-0.29	**0.066**	-0.14	0.355	-0.58*	**<0.001**	-0.460	**0.002**
ESSPRI pain	1 [0-5]	-0.36	**0.018**	-0.13	**0.038**	-0.54*	**<0.001**	-0.445	**0.004**
USF/15min	1.5 [0.5-2.25]	0.183	0.252	0.101	0.529	-0.085	0.596	0.659	0.071
Schirmer for right eye	5 [1-16]	-0.137	0.393	0.027	0.869	-0.026	0.874	0.014	0.929
Schirmer for left eye	10 [3-17.5]	0.124	0.440	0.139	0.386	0.175	0.274	0.211	0.185

GOHAI-SP: Geriatric/General Oral Health Assessment Index Spanish Version, ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index, USF: Unstimulated salivary flow

Disclosure of Interests: None Declared.

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POS1591-HPR BREASTFEEDING IN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES

Keywords: Pregnancy and reproduction

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Background: The World Health Organization recommends exclusive breastfeeding for the first 6 months of life and then starting complementary feeding while continuing breastfeeding until 2 years of age or older [1]. However, women with autoimmune rheumatic diseases (ARDs) face barriers of ignorance regarding medications that are compatible with breastfeeding and the control of their disease activity. It has been reported that some women did not follow through with their desire to breastfeed due to concerns about their ARDs medications, the baby's health, and low milk supply. Nowadays, international guidelines agree that most drugs used in rheumatology are compatible with breastfeeding [2].

Objectives: To describe the frequency of breastfeeding in women with ARDs.

Methods: An observational, cross-sectional and descriptive study. A survey on breastfeeding was carried out on patients with ARDs who had ever been pregnant, belonging to the Pregnancy and Reproductive Health Clinic for Rheumatic Diseases (CEER) of the University Hospital "Dr. José Eleuterio González", in Mexico.

Results: A total of 63 patients were included, with a mean age of 38.84 (±7.49). The diagnosis most frequently reported was rheumatoid arthritis with 35 (55.6%), followed by systemic lupus erythematosus with 9 (14.3%). Other diagnoses were antiphospholipid syndrome, juvenile idiopathic arthritis and undifferentiated connective tissue disease each one with 1 (1.6%) respectively, primary Sjögren's syndrome, scleroderma and spondylarthritis each one with 2 (3.2%) respectively and others with 10 (15.9%). The urban area was the most common place of residence with 61 (96.8%), while only 2 (3.2%) patients habited in the rural area. College education was the most predominant education level with 33 (52.4%). The sociodemographic and breastfeeding characteristics are found in **Table 1.** 49 (77.8%) of the patients referred that they had breastfed their last child. Regarding the duration, 3 (6.1%) reported having continued to breastfeed for less than 1 month and 24 (49%) for less than 6 months, being the cessation of milk production being the main cause of abandonment with 10 (37.1%) in those who breastfed for less than 6 months. Of the 14 (22.2%) patients who did not offer to breastfeed, the most frequent reason they reported was low milk production with 4 (28.6%), followed by their illness with 3 (21.4%). The other reasons can be observed in **Figure 1**.

Conclusion: Most of the surveyed patients with ARDs provided breastfeeding, however, more than half of them discontinued it before 6 months, with cessation of milk production being the most frequent reason.

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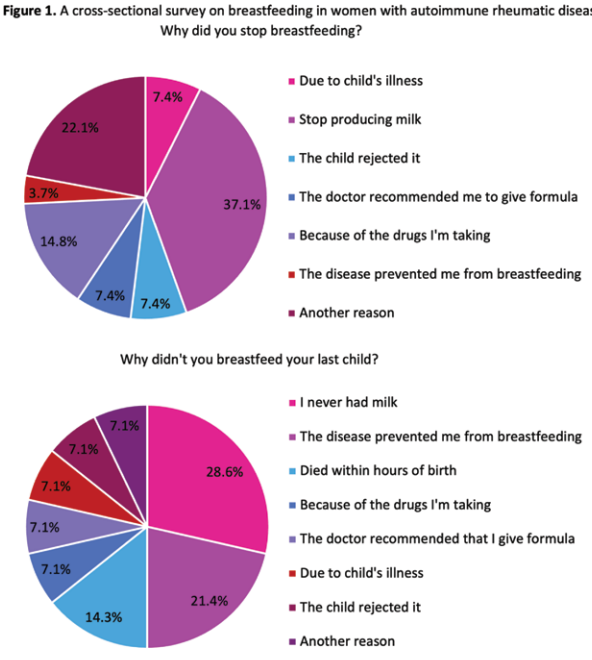
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Table 1. Sociodemographic characteristics and breastfeeding.

		n (%) n= 67
Age, mean ± SD		38.84 ± 7.49
Education, n (%)		
Elementary school		3 (4.8)
Middle school		11 (17.5)
High school		16 (25.4)
College or more		33 (52.4)
Breastfeeding, n (%)		
Skin to skin contact	Yes	23 (36.5)
	No	40 (63.5)
Explanation on how to breastfeed	Yes	52 (82.5)
	No	11 (17.5)
Contraceptive method recommendation	Yes	45 (71.4)
	No	18 (28.6)
Provided breastfeeding	Yes	49 (77.8)
	No	14 (22.2)
Breastfeeding duration	Less than 1 month	3 (6.1)
n=49	Less than 6 months	24 (49)
	More than 6 months	22 (44.9)

SD: Standard deviation

Figure 1. A cross-sectional survey on breastfeeding in women with autoimmune rheumatic diseases.



Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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POS1592-HPR UTILISING THE PERSPECTIVES OF PATIENTS WITH FIBROMYALGIA ON PHYSICAL ACTIVITY PROMOTION: A QUALITATIVE STUDY

Keywords: Fibromyalgia, Physical therapy/physiotherapy, Qualitative research methods

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Background: Physical activity (PA) promotion remains a significant clinical challenge in patients with fibromyalgia (FM) despite its evidenced beneficial impact on health outcomes [1]. Integrating behavior change theory into PA interventions ensures efficient interventions through the understanding of PA behaviors [2].
Objectives: The aim of this study was to determine the behaviours, needs and beliefs of patients with FM regarding PA interventions with the use of Social Cognitive Theory (SCT) constructs.
Methods: A Qualitative study was designed using semi-structured interviews according to 5 SCT constructs (ie, Behavioral Capability, Outcome Expectations, Self-efficacy, Self-regulation, Social Support). Female patients with FM, aged between 18-65 years (n=10) were interviewed for 30-60 minutes. Data were audio recorded, transcribed verbatim and analyzed using the content analysis technique. Besides two researchers independently conducted the thematic analysis.
Results: Totally nine main themes were determined. Key themes comprising the behavioural capability were [1]lack of knowledge on PA and [2]person-centered approach. Outcome expectations are associated with [1]health benefits. It emerged that self-efficiency is affected by four themes as follows; [1]past negative experiences, [2]environmental barriers, [3]personal barriers and [4]follow up. Besides, [1]incorporating the PA into daily life were categorized as self-regulation and [1]constructive social dialogs categorized as social support parameters of the theory. The themes, subthemes and supporting quotations related to the SCT structures are summarized in Table 1.
Conclusion: This study revealed the factors, needs, and beliefs related to PA behaviour in FM patients based on SCT and provided suggestions for how SCT constructs could be used to develop the optimal PA intervention. Future research should design PA interventions for FM patients based on behaviour change theories and evaluate the efficacy of these interventions.
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Table 1.

SCT Construct	Key Themes	Subthemes	Supporting Quotations
Behavioral Capability	Lack of knowledge	-FITT (frequency, intensity, time, type of exercise) recommendations	"…every day 1 hour.." "… 3 times a week …" "… 5000 steps…"
		-Definition and differences of the terms PA and exercise	"I guess both are the same things."
	Person-centered approach	-Desire to take tailored advice	"I would like to know how much exercise I should do, how I should do it"
Outcome Expectations	Health benefits	-Lose weight -Reduce the symptoms	"Of course, exercise is beneficial for health, but my priority is to lose weight."
Self-efficacy	Past negative experiences	-Inappropriate exercise programs -Unrealistic expectations	"I started Pilates class. But I quitted because it was too much. I had incredible pain."
	Environmental barriers	-Location/accessibility -Safety issues	"Dogs scare me when I go for a walk, and it scares me when it's dark"
	Personal barriers	-Lack of money -Lack of time -Lack of motivation	"Without motivation, you don't feel as though you have the ability to take action."
	Follow-up	-Feeling responsible to someone (HCP) -Self monitoring	"I need a driving force. If you give homework it can be helpful for me."
Self-regulation	Incorporate PA into daily life	-Set a spesfic time -Break up into short session	"Sometimes I can get some exercise before dinner or at lunch break"
Social Support	Constructive social dialogs	-Positive mindset -Peer support -Family support	"I want to be with patients who are open to communication and healing."

Abbreviations: HCP:Healthcare Professional

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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POS1593-HPR

GASTROINTESTINAL INVOLVEMENT IS ALREADY REPORTED IN AN ITALIAN VEDOSS COHORT: RESULTS FROM A RHEUMATOLOGICAL NURSE ASSESSMENT

Keywords: Systemic sclerosis, Gastrointestinal tract, Nursing

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Background: Gastrointestinal tract (GIT) is often involved in Systemic Sclerosis (SSc), even in the very early diagnosis of SSc (VEDOSS). In SSc, the oesophagus is mainly involved, followed by the anorectum: therefore, the GIT is the second most affected organ system in SSc patients. Patient education performed by rheumatology nurses on GIT symptoms prevention and management can be of help in the disease management, starting from a meticulous data collection.
Objectives: The aim of our study was to investigate the differences, in VEDOSS and SSc patients of GIT involvement assessed by the UCLA GIT questionnaire administered by rheumatology nurses.
Methods: 50 patients (22 VEDOSS and 28 SSc) from the Scleroderma Unit of Careggi University Hospital were enrolled. Demographic data, Raynaud's phenomenon, autoantibodies, videocapillaroscopy patterns, puffy fingers and digital ulcers were recorded for VEDOSS and SSc patients. GIT symptoms, disability and quality of life were respectively assessed by the administration UCLA GIT 2.0, HAQ and SF36 questionnaires guided by the rheumatology nurse.
Results: Demographic data, Raynaud's phenomenon, autoantibodies, videocapillaroscopy patterns, puffy fingers and digital ulcers manifestations are reported in Table 1 for both groups of patients. Disability and quality of life, respectively assessed by HAQ and SF36 are shown to be more significantly modified in the SSc group than in the VEDOSS ($p < 0.05$), especially the impact of the disease on physical health ($p<0.005$) (table2). Moreover, VEDOSS patients presented GIT symptoms and pain, assessed by UCLA GIT 2.0 and VAS pain, not different from the SSc group ($p > 0.05$) (Table 2). GIT symptoms and complications such as gastroesophageal reflux disease (GERD), malnutrition, diarrhea, constipation, and small intestinal bacterial overgrowth, occurred in both SSc and VEDOSS groups impairing significantly patients' quality of life.
Conclusion: our data suggest that it is important to consider GIT involvement also in VEDOSS patients. Therefore, a specific assessment of GIT involvement should be always performed in clinical practice. This work also shows that the role of Rheumatology nurses is important as their help in patients' assessment of patients reported outcomes and symptoms becomes pivotal to prepare the patient for the physician's analysis. Thus, recognising the early GIT involvement with a standard screening may lead to shape an early treatment to improve patients' quality of life.
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Table 1. Differences between groups for disease characteristics and manifestations

	VEDOSS n=22 44%)	SSc n=28 (66%)	p-Value
Age	50.6±3.4 (M±DS)	63.7±2.1(M±DS)	<0.005
Body Mass Index	22.6±0.7(M±DS)	24.7±0.9(M±DS)	NS
Smoke	4.8%	17.9%	NS
Smoke in the past	33.3%	34.8%	<0.5
Raynaud P	95.5%	100%	NS
NVC aspecific	66.7%	7.1%	<0.0001
NVC early	28.6%	25%	
NVC active	4.8%	35.7%	
NVC late	0%	32.1%	
mRSS	0 (M±DS)	3.6±4 (M±DS)	<0.0001
Digital Ulcers	0%	53.9%	<0.0001
Puffy fingers	9.5%	66.7%	<0.001
Teleangectasie	22.7%	77.8%	<0.001
Pulmonar involvement	0%	61.5%	<0.0001
Arthritis	0%	55.6%	<0.0001
Use of PPIs	9.5%	53.6%	-
ANA	95.2%	100%	NS
Anti scl70	9.52%	51.9%	
ACA	42.9%	42.9%	
Anti RNA pol III	4.8%	7.1%	

Table 2. Differences of disability, QoL and GIT symptoms in the sample of VEDOSS and SSc patients

	VEDOSS (M±DS)	SSc (M±DS)	p-Value
HAQ	0.2±0.3	0.4±0.5	<0.05
VAS pain	2.3±2.4	3.6±3.3	NS
SPI-SF36	48.2±1.8	40.1±1.5	<0.005
SMI-SF36	46.7±2.0	39.8±2.3	<0.05
UCLA GIT	0.1±0.4	0.4±0.4	NS

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DOI: 10.1136/annrheumdis-2023-eular.6362

HPR Service developments, innovation and economics in healthcare

POS1594-HPR A REGIONAL MULTICENTRE REVIEW OF THE DELAY TO DIAGNOSIS IN PATIENTS WITH AXIAL SPONDYLOARTHRITS- HOW WELL ARE WE DOING? RESULTS FROM THE SCAN GROUP (UK)

Keywords: Health services research, Spondyloarthritis, Best practices

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Background: Due to the insidious onset and non-specific nature of axial spondyloarthritis (AxSpA), there is often a significant delay to diagnosis. The average delay to diagnosis in the UK is 8.5 years [1]. This is associated with several adverse sequalae including poor disease-related quality of life and worse overall health outomes [2,3]. In addition, there are substantial health-economic costs associated with this. Recent modelling data in the UK, commissioned by the National Axial Spondylarthritis Society (NASS), demonstrated the average financial cost of this delay to be £196,000 (221,000 Euros) per person affected [1]. There is a focus on reducing diagnostic delay for patients with AxSpA. The SCAN (South Central Axial Spondylarthritis Network) is a network of NHS (National Health Service) Rheumatology departments in hospitals across south-central UK. The group comprises of; doctors, nurses and physiotherapists. SCAN has a working interest in service development.
Objectives: The SCAN group carried out a service evaluation to establish the average delay to diagnosis for patients with AxSpA across our region. Data was gathered from a total of 7 hospitals within the SCAN region. We also aimed to assess the degree of variability across the 7 different hospitals. The baseline data will be used to support potential implementation of service development initiatives, which in turn, will aim to ultimately reduce the delay to diagnosis for patients with AxSpA across the SCAN region.
Methods: Retrospective patient data was collected from 7 different hospitals within the SCAN network area. Data was gathered on 5-10 sequential cases of newly diagnosed AxSpA at each hospital. A total of 65 cases were included in our dataset. Data was collected on; date of symptom onset, date of diagnosis, age and gender.
Results: Chart 1 summarises our main findings across the 7 different hospitals.

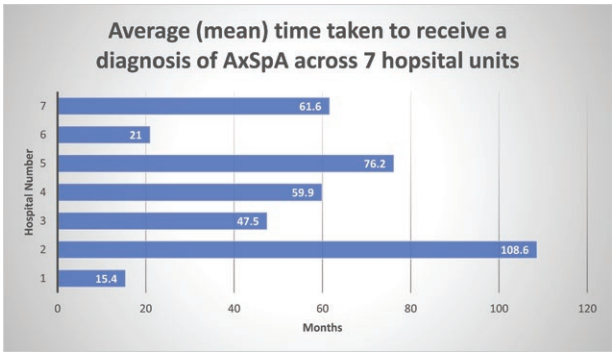


Chart 1.

Based on our representative sample from our region, the overall average (mean) delay to diagnosis in the SCAN area hospitals is 4.6 years. This is new data. The average age of the patients was 37 years old and 70% of the patients were male. The range for delay to diagnosis across the 65 cases was from 1 month to 30 years. The observed variability between the hospitals may be related to sample size, differences within local referral systems or reflective of areas where primary care education has been undertaken. Whilst acknowledging the relatively modest size of the sample, this regional multicentre dataset has allowed us to importantly establish what our average delay to diagnosis is for patients within the SCAN region. This valuable information will provide support for planning and implementation of further regional service improvements.
Conclusion: Our data suggests the delay to diagnosis within our region is significantly shorter than the national average (4.6 years versus national average 8.5 years). However, this delay remains unacceptably long and is likely to be associated with worse disease-related quality of life and a wider detrimental socio-economic impact. The SCAN group will consider introducing changes to the referral processes (*e.g.,* an agreed single referral proforma with local education). We may also aim to replicate any successful local arrangements in place at those hospitals with the shortest delay to diagnosis. We aim to re-evaluate the delay to diagnosis across the SCAN region in 12-36 months where we are optimistic of demonstrating further progress with reducing diagnostic delay for our patients with AxSpA.
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POS1595-HPR INTEGRATION OF TELEMEDICINE AND MEDICAL STUDENTS INTO A NEW DIAGNOSTIC PATHWAY FOR PATIENTS WITH SUSPECTED AXSPA: A QUALITATIVE EXPLORATION OF THE PATIENTS' EXPERIENCE

Keywords: Health services research, Qualitative research methods, Patient reported outcomes

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Background: Increasing demand and shortage of specialists lead to long waiting times for initial appointments in rheumatology care [1]. These result in diagnostic delays in several rheumatic diseases, with the longest total delay reported for patients with axial spondyloarthritis (axSpA) [1]. Telemedicine, including symptom checkers (SC), capillary self-sampling, and electronic patient-reported outcomes (ePRO) could enable patients to prepare a standardized pre-visit assessment at home. Additionally, fast-track appointments supported by medical students could complement this standardized assessment to enable fast diagnostic assessments and ultimately accelerate start of therapy.
Objectives: This qualitative study was embedded in a clinical trial that investigated a new diagnostic pathway for patients with suspected axSpA, including telehealth tools and fast-track visits supported by medical students. The aim of this qualitative study was to explore patient experiences with this new care model.
Methods: Patients, purposively selected to reflect a heterogeneous sample in terms of age, gender, education and occupation, participated in an explorative, qualitative study using semi-structured phone interviews. Interview data was analyzed using structured qualitative content analysis.
Results: Qualitative interviews were conducted with twenty patients with suspected axSpA (Table 1). Patients perceived the initial consultation supported by students to be equivalent to standard rheumatology care. Patients considered the student consultation to be a valuable option to relieve workforce shortage in rheumatology care. The overall experience with the students was described as holistic and thorough by patients. Some participants pointed out that rheumatic patients often have long medical histories and, thus, may find it difficult to engage with initial care provided lead by students. Patients reported that using SC and performing capillary blood collection helped to better assess their disease status and promote mindfulness in this regard. Some patients described that the SC-questions were unspecific, which led to difficulties answering them. Furthermore, several patients requested a free-text note section to specify their standardized ePRO data. Patients considered the capillary blood collection to be helpful, especially in regard of travel and time savings. Reported disadvantages of self-administered blood collection were uncertainties about the amount of material and the unsustainable packaging material.

Table 1. Patient characteristics

Patient characteristics	Unit	Value (n=20)
Median Age (IQR)	Years	45.6 (18.2)
Mean Age (SD)	Years	43.3 (12.4)
Sex	patient number male/female	12/8
Final diagnosis	patient number axSpA/no axSpA	12/8

Conclusion: Patients perceived the new diagnostic pathway as an efficient and high-quality alternative to standard axSpA-care. Particularly, savings in time and travel were considered favourable by the interviewed patients. Personal comments or chat options could provide an even more individual patient experience.
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POS1596-HPR

IMPACT OF THE HEALTH STATUS ON THE WILL TO USE TELEMEDICINE AMONG RHEUMATIC PATIENTS: SECONDARY ANALYSIS OF DATA FROM A GERMAN NATIONWIDE SURVEY

Keywords: Health services research, Telemedicine

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Background: Telemedicine (TM) is an effective tool to supplement rheumatology care and address staff shortages [1]. A previous study revealed that patients' willingness to try TM is closely connected to their perceived health status [2]. Yet, it is still unclear which factors are associated with patients' motivation to use TM according to the perceived health status.
Objectives: The study aimed to identify factors that determine patients' willingness to try TM (TM-try) and their wish that their rheumatologists offer TM services (TM-wish) according to their perceived health status.
Methods: We conducted a secondary analysis of data from a German nationwide cross-sectional survey among patients with rheumatic and musculoskeletal diseases (RMDs) [3]. Bayesian univariate logistic regression analysis was applied to the data in order to determine which factors were associated with TM-try and TM-wish, respectively. Predictor variables (covariates) studied individually included sociodemographic factors (e.g., age, sex) and health characteristics (e.g., health status). All the variables positively and negatively associated with TM-try and TM-wish in the univariate analyses were then considered for Bayesian model averaging analysis (BMA) after a selection based on the variance inflation factor (≤ 2.5) to identify determinants of TM-try and TM-wish, respectively.
Results: Regarding TM-try, a total of 26 (30.6%) and 45 (27.1%) variables/factors (answers to the 25 questions), out of 85, were found to be positively or negatively associated (ROPE% ≤ 5%) with a perceived okay and bad/very bad health statuses, respectively. Regarding TM-wish, a total of 14 (16.5%) variables/factors (answers to the 25 questions), out of 85, were found to be positively or negatively associated for both a perceived okay and bad/very bad health statuses, respectively. A total of 19 and 13 determinant factors (Figure 1) were identified for TM-try and TM-wish, respectively. Patients with a perceived bad/very bad health status that did not want to try TM were more frequently 60-69 years old, living 10-15 km from the GP's office, being diagnosed with rheumatoid arthritis and had more often less TM knowledge than patients wanting to try TM. Patients with a perceived bad/very bad health status that did wish that TM services were offered by rheumatologist were more frequently older, not documenting their health status and more being diagnosed with osteoporosis than patients wishing that TM services were offered by RM.
Conclusion: Our results indicate that RMD knowledge, age, RMD type, health status documentation and access to technical equipment and infrastructure influence RMD patients' motivation to use telehealth.
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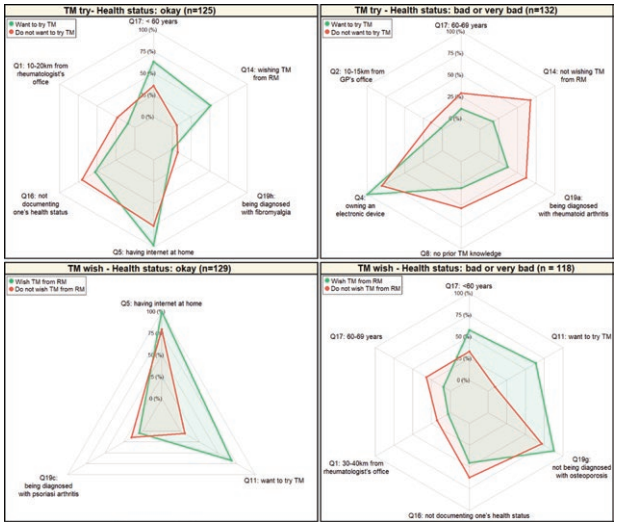


Figure 1. Profile of RMD patients motivated to try TM vs. RMD patients not motivated to try TM

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POS1597-HPR **ASSESSING THE USE OF VOICE COMMANDS IN THE CLINICAL SETTING**

Keywords: Artificial intelligence, Health services research

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Background: Artificial intelligence (AI) could reduce the administrative workload of clinicians, thus allowing them to focus more on clinical work. AI-powered voice-recognition programs can record appointments and request additional diagnostic tests through automatic flows generated by specific voice commands, reducing the administrative burden. Although some clinicians consider these programs helpful in the clinical setting, others consider them challenging to learn and not to save time.

Objectives: To investigate the impact of voice commands in clinical practice: i) on time spent on different tasks (clinical and administrative) during the appointment, ii) on the accuracy of records, iii) on patients' and clinicians' satisfaction.

Methods: We undertook a single-centre prospective quality improvement project between 26/10/22 and 20/12/22 in the rheumatology department of Nuffield Orthopaedic Centre - Oxford University Hospitals. We included patients attending general rheumatology (GR), complex musculoskeletal (CMSK) and vasculitis clinics, performed by clinicians using voice commands (group 1, N=1) and clinicians not using voice commands (group 2, N=4). The voice command program used was Dragon Medical One. We defined "using voice commands" when this tool was used to insert a pre-prepared text template or order diagnostic exams. One investigator attended the clinics and timed the tasks performed during the appointment. Clinicians and patients answered questionnaires attributing satisfaction scores from 0 (very unsatisfied) to 10 (very satisfied). Univariate analysis was performed, as appropriate, using SPSSV25.

Results: Data regarding 80 appointments were collected: 40 from group 1 and 40 from group 2. The proportion of the clinic types in groups 1 and 2 was: GR 52.5% vs. 0%; CMSK 0% vs. 40%; and vasculitis 47.5% vs. 60%, respectively. There were no differences between the groups regarding new and follow-up patients or face-to-face and phone clinics. Group 1 finished recording the consult in a shorter time than group 2 (mean±SD: 5.6±1.8min vs. 8.9±3.7min, p<0.001). The time spent with the patient (mean±SD: 16.9±7.0 vs. 17.7±7.6, p=0.637) and ordering diagnostic tests (mean±SD: 2.9±1.7 vs. 2.7±1.2, p=0.803), did not differ between the groups. To compare the groups performing the same type of clinic, we conducted a subanalysis including only the vasculitis clinics (group 1 N=19 and group 2 N=24). In this setting, group 1 also finished recording the vasculitis consultations in a shorter time than group 2 (mean±SD: 5.2±1.6min vs. 8.9±4.5min, p<0.001). Moreover, group 1 had more final records with spelling mistakes than group 2 (26 vs. 13, p=0.004) but no more clinically significant errors (8 vs. 3, p=0.105). The latter consisted of one drug dose error, seven nonsense sentences from group 1, and 3 nonsense sentences from group 2. Regarding the clinicians' satisfaction levels, 5 out of 7 items evaluated showed significant differences between both groups. Group 1 had higher median scores of satisfaction regarding how the consultation went (9 [1] vs. 8 [1], p<0.001); the time they had to address the patient's concerns (9 [1] vs. 8 [2], p<0.001); and the way the dictation worked (8 [1] vs. 6 [1.75], p<0.001), compared to group 2. Moreover, group 1 felt that they spent more time listening and talking to the patient as opposed to doing administrative work (8 [1] vs. 7 [3], p<0.001), and also considered they had to do less writing (2 [1] vs. 5 [2], p<0.001), than group 2. There was no difference between the groups concerning patient satisfaction levels.

Conclusion: We report that voice commands: (i) were useful in reducing the time spent recording the consultation but did not influence the time spent with the patient or the time spent ordering diagnostic tests; (ii) resulted in a higher number of spelling mistakes but not clinically significant errors; and (iii) improved the clinicians' satisfaction at most levels and did not influence patients' satisfaction. Medical staff should be trained to adopt this technology, and developers should focus on improving accuracy and misspelling minimization.

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HPR Professional education, training and competencies

POS1598-HPR **TEACHING AND CLINICAL OUTCOMES OF A NOVEL FELLOWS' INJECTION CLINIC**

Keywords: Education, Patient reported outcomes

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Background: The skills of performing joint/periarticular injections by rheumatology fellows are learned during training but achieving the necessary level of expertise can be challenging if the rotations lack dedicated skills teaching. There is also a paucity of literature reporting how injection proficiency evolves and how the type and number of procedures can affect performance.

Objectives: To combat these issues and enhance fellow training and patient outcomes, we started an exclusive fellows' monthly injection clinic and assessed the learners' progress by analyzing their proficiency scores (PS) over time, and asking if these differ between size of joints and number of procedures done. We selected 10 or more procedures as the number needed to achieve higher expertise and determined the patient response (efficacy) and side effects as secondary outcomes.

Methods: The clinic is led by a single attending rheumatologist who demonstrates the proper technique prior to the encounter, supervises the procedure and provides feedback. Outcome measures include the procedure type classified as small/medium or large joint/periarticular structures. The PS was measured by the same teacher throughout and used a numerical scale of 1-3 defined as 1 – early, 2 – progressing, or 3 - advanced. Factors affecting proficiency score included preparation, technique, and cleanup. Efficacy was measured by successful aspiration and for steroid injections, by patient report of >50% improvement in joint pain at the next follow-up visit. Patients were advised to call the clinic to report any adverse events.

Results: Thirteen clinics took place between December 2020-August 2022. Fellows performed an average of 4 procedures per clinic for a total of 52 procedures. PS were compared at initial (n=15) and last clinic encounter (n=17), and between large (n= 32) and small/medium joints/periarticular procedures (n=20). PS steadily increased over time with higher proficiency achieved by the 3rd or 4th clinic compared to the initial clinic [2(1-3) vs 1(1-2), p=0.018]. Fellows tended to achieve higher PS for large joint/periarticular procedures (hip and knee) compared to the more technically difficult small/medium joint/periarticular procedures (shoulder, feet and hands) [2[1-3) vs 1(1-2), p < 0.0001]. We arbitrarily selected 10 or more procedures as the number needed to achieve higher expertise but found no difference in PS between performing <10 versus > 10 injections [2(1-3) vs 2(1-3), p= 0.35]. The procedures were highly effective and safe with favorable responses seen in 94.0% (49/52 procedures) with no reported side effects.

Conclusion: The longitudinal injection clinic demonstrated a steady improvement in proficiency among fellows while minimum number of procedures needed to attain expertise needs further studies. Our data can provide a useful template for designing a skills-based curriculum for rheumatology training programs.

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HPR Interdisciplinary research

POS1599-HPR ANTI-CCP+ AT-RISK INDIVIDUALS HAVE A MILD PHENOTYPE OF PERIODONTAL DISEASE, WHICH IS TREATABLE WITH A COURSE OF NON-SURGICAL PERIODONTAL THERAPY

Keywords: Autoantibodies, Biomarkers

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Background: Rheumatoid autoimmunity may be initiated at mucosal sites such as the periodontium. Patients with RA and anti-CCP+ at-risk individuals have an increased prevalence of periodontal disease (PD) [1]. PD is often asymptomatic and diagnosed by clinical examination. We hypothesised that comprehensive periodontal assessment of CCP+ at-risk individuals would identify PD, which would be amenable to treatment with a single course of non-surgical periodontal therapy (NSPT).

Objectives: To determine the periodontal disease phenotype in anti-CCP+ at-risk individuals and to investigate the feasibility/efficacy of a course of NSPT.

Methods: Anti-CCP+ at-risk individuals with musculoskeletal symptoms but no clinical synovitis ('CCP+ at risk') were recruited from the Leeds CCP cohort. All participants had a high anti-CCP level (>3 X ULN) and had periodontal screening by a dentist, including radiographs. Clinically significant PD was defined as clinical attachment loss ≥4mm on at least two non-adjacent teeth, ≥40mm of cumulative probing pocket depth (minimum 4mm per site). Those with PD were offered NSPT. Periodontal indices were recorded before and after NSPT. Treatment completion occurred when PD had stabilised, as determined by clinically significant reduction in bleeding/probing indices.

Results: Seventy-two CCP+ at-risk were offered screening; 51 (71.8%) accepted. The main reason cited for declining was time pressures. 31/51 (59%) subjects had clinically significant PD and were offered NSPT. Of these, 15 have completed treatment over a median of three treatment sessions (median timeframe 17 weeks). The remaining participants are receiving ongoing treatment. The mean age for patients with PD was 51.22 and 64.5% were female. Seven (22.6%) patients were current smokers, 16 (51.6%) ex-smokers and 8 (25.8%) never smokers. Mean baseline scores were; 49.41% plaque free, 15.14% bleeding, 21.46% mild pocketing, and 4.42% deep pocketing. Radiographic assessment revealed a predominantly mild (stage I/II) disease phenotype; 8 (25.8%) stage I, 11 (35.4%) stage II, 9 (29%) stage III, and 3 (9.7%) stage IV PD. Plaque free scores improved by 27.89% (p<0.05), demonstrating high patient motivation. Bleeding indices, (indicating gingival inflammation) reduced to 8.49%, within the accepted level for PD stabilisation [2]. There was significant probing depth reduction at both mild (10.02%) and deep (3.1%) sites (Table 1).

Table 1. Demographic and clinical data of anti-CCP positive at-risk individuals who underwent periodontal assessment and treatment.

	Variable			
Participants with PD (n=31)	Age (mean/SE)		51.22 (11.09)	
	Females (n/%)		20 (64.5%)	
	Baseline anti-CCP level (n/%)			
	>300u/ml		11 (35.5%)	
	100-300		9 (29%)	
	10-99		11 (35.5%)	
	Baseline radiographic data (n/%)			
	Stage I		8 (25.8%)	
	Stage II		11 (35.4%)	
	Stage III		9 (29%)	
	Stage IV		3 (9.7%)	
Treated patients (n=15)		**Before treatment**	**After treatment**	**P value**
	Mean plaque free scores (%)*	51.23% (SE 21.88)	79.12% (SE 25.23)	<0.05
	Mean bleeding on probing (%)*	16.32% (SE 9.91)	8.49% (SE 4.13)	<0.05
	Mean mild (4-6mm) pocketing* (%)	17.22% (SE 11.1)	7.2% (SE 4.33)	<0.05
	Mean deep (>6mm) pocketing* (%)	3.7% (SE 1.1%)	0.69% (SE 1.7%)	<0.05

Conclusion: Routine periodontal assessment of anti-CCP+ at risk individuals identifies a mild and treatable phenotype of periodontal disease. Periodontal screening and treatment with a course of NSPT is acceptable to at-risk individuals and results in effective treatment of periodontal disease. This approach may form part of future personalised strategies for RA prevention.

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POS1600-HPR MATERIALS FOR HEALTH PROMOTION ON LIFESTYLE FACTORS FOR PEOPLE WITH RMDS ACROSS EUROPE: ASSESSMENT OF CURRENT MATERIALS AND IMPLEMENTATION NEEDS

Keywords: Patient information and education, Non-pharmacological interventions, Education

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Background: healthy lifestyle is known to prevent the progression of rheumatic and musculoskeletal diseases (RMDs). Despite contemporary improvements in RMD clinical care, the management of lifestyle factors has received less attention. Underlying causes may be the lack of awareness and insufficient evidence, but patient and physician education may also play a role.

Objectives: to collect and review currently available materials for health promotion on lifestyle factors for people with RMDs across Europe and to assess their implementation needs.

Methods: materials on lifestyle factors (diet, weight control, physical activity, work participation, alcohol consumption and smoking) were collected from health professionals in rheumatology and patient associations through EULAR and EMEUNET channels.

Results: 38 materials from 11 countries were retrieved (Table 1), including North, South, and Central European regions. Documents (22) or leaflets (12) were the most frequent materials. The most reported factor was diet (23) followed by physical activity (17), whereas information on work participation was scarce [2]. The materials were more commonly focused on rheumatoid arthritis (8), although documents for people with RMDs in general were also frequent (12). Only eight materials included scientific references. Although 23 materials contained some kinds of recommendations, only two were evidence-based, whereas the rest contained general statements. Materials were mostly available in the official national language, and 16 were accessible on the internet, whereas no information on accessibility or

Table 1

Country	Materials (n)	Factors covered (n)	RMDs covered (n)	Supportive references	Recommendations (n)	Extension	Language	Access
Austria	Paper Leaflet	Diet	Gout (and hiperuricemia)	Yes	Yes (evidence-based)	6 pages 2 pages + figure	10 languages	Online
Croatia	Documents (3)	Diet	SSc (1) OA (1) RA and gout (1)	No	No	20-40 pages	Croatian	Unclear
Italy	Leaflet	Diet	RMDs	No	No	12 pages	Italian	Unclear
Lithuania	Documents (2) Leaflet (1)	Diet, smoking, alcohol, physical activity (various combinations)	Gout (1) SLE (1) RMDs (1)	No	No (2) Yes (general) (1)	2-28 pages	Lithuanian	Online (1) Unclear (2)
Moldova	Documents (6)	Lifestyle (general)	Gout (1) PsA (1) RA (1) SSc (1) SLE (1) SpA (1)	Yes	Yes (general) (5) No (1)	2-33 pages	Moldovan	Online
Norway	Document	Lifestyle (general)	RMDs	No	No	2 pages	Norwegian	Unclear
Portugal	Documents (7)	Diet, smoking, alcohol, physical activity (various combinations)	PsA (1) SpA (1) AIJ (1) RA (1) SSc (1) SLE (1) SS (1)	No	No	19-28 pages	Portuguese	Unclear
Slovenia	Leaflets (6)	Diet, weight, smoking, alcohol, physical activity (various combinations)	RMDs (3) SpA (1) PsA (1) RA (1)	No	Yes (general) (6)	2-27 pages	Slovenian	Unclear
Spain	Video (1) Document (1) Website (1)	Weight, diet, physical activity, smoking and work adaptations (various combinations) Lifestyle (general) (1)	RA (2) RMDs (1)	No	Yes (general)	2 minutes (1) 62 pages (1) Website (1)	Spanish	Online (2) Unclear (1)
Sweden	Leaflets (4) Videos (4)	Diet (1) Smoking (1) Physical activity (1) Diet (1)	RMDs (4)	No	Yes (general) (4)	4 pages (4) 10 minutes (4)	Swedish	Online
Turkey	Documents (2)	Physical activity (1) Diet (1)	RMDs (1) RA (1)	No	Yes (general) (2)	20-288 pages	Turkish	Unclear

reach was obtained for the remainder. Significant limitations across implementation domains (process model, determinant frameworks, and evaluation) were observed, mostly due to flawed knowledge generation, poor identification of barriers and facilitators, and lack of evaluation frameworks. **Conclusion:** although materials on lifestyle factors were common, they were not always available at the national level across Europe. Current materials are hallmarked by a lack of consistency in formats, layouts, content, focus, lack of scientific evidence and patient involvement. Major impediments for implementation were found. These findings will inform the implementation of EULAR-endorsed recommendations on lifestyle factors for people with RMDs.

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POS1601-HPR

ADVERSE EVENTS AND ADVERSE REACTIONS WITH THE USE OF ANTITNF'S DETECTED BY THE PHARMACOVIGILANCE PROGRAM OF A SPECIALIZED RHEUMATOLOGY CENTER

Keywords: Disease-modifying drugs (DMARDs), bDMARD

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Background: Pharmacovigilance is the science that is responsible for the detection, notification, and monitoring of possible drug adverse events (DAE) that occur with the administration of medications. In the pharmaceutical service process, the information generated through its programs constitutes evidence that provides a solution to the management of drug-related problems, especially those obtained by biotechnology.

Objectives: The aim of this study is to show the main DAEs and drug adverse reactions (DARs) with the use of anti-TNF (Anti-Tumor Necrosis Factor) drugs detected by the Pharmacovigilance program of an IPS specialized in rheumatology during the period 2018-2022.

Methods: The current method carried out in the institution is the so-called S*pontaneous Notification*. A retrospective review of the DAE and DAR detected by an institutional Pharmacovigilance program with the use of Anti-TNF drugs, in patients with autoimmune diseases, during the period 2018-2022, was carried out. Indicators were established through descriptive statistics to measure the frequency of DAE and DAR.

Results: 408,914 medical records were reviewed, the Table 1 shows the comparative percentages of DAE and DAR detected by the program between conventional disease-modifying antirheumatic drugs (csDMARDs) and biologics during the follow-up period. The Pharmacovigilance program had growth in the detection of DARs with the use of anti-TNF drugs, strengthening knowledge in the information for these. The causality with the anti-TNF was established, being the DAE classified as probable and the DAR as possible. Of the total subgroup of patients treated at the institution for medication application (46,832), notifications were received as follows: (Infliximab 17, Etanercept 17, Adalimumab 22, Golimumab 15, Certolizumab 51). Additionally, dermatological reactions are the most recurrent types of reactions. Herpes is found as the main DAR with Certolizumab

in the last year. According to the results obtained, Certolizumab is the drug that has presented the most adverse reactions during the follow-up period (Figure 1).
Conclusion: Dermatological reactions are the most frequent with anti-TNF drugs. Infliximab and Certolizumab stand out for this type of commitment. Studies are needed in populations from the same country to compare these results and generate more knowledge.
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Disclosure of Interests: Wilberto Rivero: None declared, Pedro Rodríguez-Linares: None declared, Fernando Rodriguez: None declared, Gabriel-Santiago Rodríguez-Vargas: None declared, Adriana Rojas-Villarraga: None declared, Pedro Santos-Moreno Speakers bureau: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi, Grant/research support from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi.
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POS1602-HPR

PAIN AND CATASTROPHIZING IN RHEUMATIC DISEASES: IMPACT ON PSYCHOLOGICAL DATA AND QUALITY OF LIFE

Keywords: Pain, Quality of life

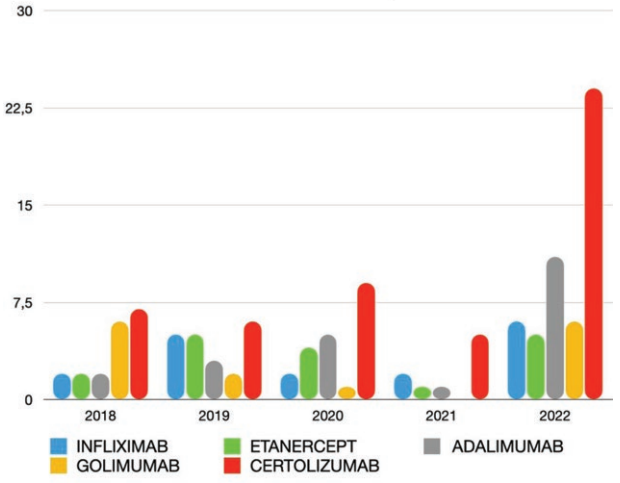
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Background: Catastrophizing is a common behavior in patients with chronic pain.It is a negative cognitive-affective response to pain. It is thought to be associated with the persistence and exacerbation of chronic pain.
Objectives: To determine the prevalence and the associated factors of catastrophizing in rheumatic diseases(RD).
Methods: A cross-sectional study on patients with RD followed in the rheumatology department of hached hospital. Biological and clinical data were collected from medical records. Depression and anxiety were evaluated by the HAD scale (Hospital Anxiety and Depression scale). Quality of life was assessed by the SF-12, which is a self-assessment scale of quality of life that is a shortened version of the SF-36. Catastrophizing was assessed by the Pain catastrophizing scale (PCS). A PCS score of 30 or more represents a high level of catastrophizing.
Results: Our study included 60 patients with RD: 44 patients with rheumatoid arthritis(RA),12 patients with ankylosing spondylitis(SpA) and 4 patients with psoriatic arthritis (PsA). The mean age was 48.83 years (73.33% female). The mean PCS score was 31± 10.34. The prevalence of high catastrophizing(PCS ≥ 30) was 73.3% in all patients: 72.7% of patients with RA,66.7% with SpA and 100% with PsA. A high catastrophizing score was found in 91.7% of anxious patients and 95% of depressed patients.No statistically significant association of catastrophizing with age nor gender was noted. Catastrophism was significantly associated with depression, anxiety ($p < 10^{-4}$) and pain VAS (p=0.001). The decrease in quality of life assessed by the physical (PCS12) and mental (MCS12) components of the SF12 was significantly associated with catastrophizing ($p < 0.01$).
Conclusion: In our study more than two-thirds of the population had high PCS scores with a significant correlation with pain VAS, anxiety and depression and a low quality of life score.

Table 1. COMPARISON OF ADVERSE REACTIONS BETWEEN CONVENTIONAL AND BIOLOGICAL DMARDs

AÑO	DAR	DAE	csDMARD	BIOLOGICO
2018	52,5%	46%	62,9%	28,7%
2019	39,3%	52,3%	26,1%	61,4%
2020	40,2%	40%	31,3%	65,5%
2021	25,0%	51%	45,8%	52,1%
2022	35,5%	36%	32,0%	68,9%

Figure. Rate of reports of adverse reactions to anti-TNF biologics



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Publication Only

Genomics, genetic basis of disease and functional genomics

AB0001 GUT MICROBIOTA IMBALANCE IN INFLAMMATORY ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Inflammatory arthritides

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Background: Inflammatory arthritis (IA) is a group of autoimmune arthritis characterized by a pro-inflammatory/anti-inflammatory disbalance of local mediators[1] [2]. Research on the influence of gut microbiota(GM) on systemic IA has exploded in the past decade. GM changes may be a crucial regulatory component in systemic IA[3]. However, the link between them has yet to be fully elucidated.
Objectives: This study aims to study the GM composition of IA to provide evidence for its potential role in the pathogenesis, progress, and treatment of IA.
Methods: We systematically searched the trials for PubMed, EMBASE, Web of Science, Medline, Wanfang database, VIP, CNKI, and CBM database from the establishment of the database to January 1, 2023. Standardized mean difference (SMD) and 95% confidence interval (CI) were calculated to assess alterations in α-diversity and the abundance of certain microbiota families in IA. Literature quality was evaluated according to the requirements of systematic review, and meta-analysis was performed using STATA v.12.0.
Results: A total of 70 studies, including 3,322 patients and 4,412 healthy controls, were identified. Compared with HCs, the GM of patients with IA has a lower Simpson index(SMD=-0.307, 95%CI -0.509, -0.106) and Shannon index(SMD=-0.184, 95%CI -0.344, -0.024). When specific IA was examined, significant decreases were observed in rheumatoid arthritis(Simpson index: SMD=-0.558, 95%CI -0.891, -0.225; Shannon index: SMD=-0.608, 95%CI -0.935, -0.281; ACE: SMD=-0.414, 95%CI -0.697, -0.132; Chao1: SMD= -1.373, 95%CI -1.980, -0.766; eveness index: SMD=-1.863, 95%CI -3.181, -0.544), psoriatic arthritis(Simpson index: SMD=-0.733, 95%CI -1.367, -0.099), osteoarthritis(Chao1: SMD=-0.793, 95%CI -1.096, -0.491) and gout(Simpson index: SMD=-1.037, 95%CI -1.959, -0.115). In other diseases, we found that the α-diversity index was higher than that of the HCs group[reactive arthritis(Shannon index: SMD=0.697, 95%CI 0.265, 1.130; ACE: SMD=1.878, 95%CI 1.375, 2.380; Chao1:SMD=0.835, 95%CI 0.398, 1.273; InvSimpson: SMD=0.823, 95%CI 0.386, 1.260; Observed species: SMD= 2.004, 95%CI 1.491, 2.517); osteoporosis(eveness index: SMD=0.488, 95%CI 0.047, 0.928); ankylosing spondylitis(InvSimpson: SMD=0.525, 95%CI 0.272, 0.777); Juvenile idiopathic arthritis(Observed species: SMD=1.672, 95%CI 1.100, 2.243)]. Furthermore, to exclude sequencing methods' influence on species abundance detection, we conducted a subgroup analysis of Observed species. The results showed that the observed species abundance through high-throughput sequencing was higher(SMD=1.376, 95%CI 0.394, 2.358) and 16S rRNA gene sequencing was lower(SMD=-0.842, 95%CI -1.575, -0.108) than that of HC. At the phylum level, there was a significant reduction in *Firmicutes*(SMD=-0.455, 95%CI -0.796, -0.114) and *Fusobacteria*(SMD=-0.422, 95%CI -0.692, -0.152). At the genus level, the abundance of *Bacteroides*(SMD=0.898, 95%CI 0.003, 0.003) was higher and *Faecalibacterium*(SMD=-0.380, 95%CI -0.713, -0.047) was lower. The two groups had no significant differences in *Bifidobacterium* and *Butyricicoccus*(P >0.05).
Conclusion: Our research showed a definite relationship between IA and GM. Further diet and drug therapy research are needed to explore the relationship between human GM and IA.

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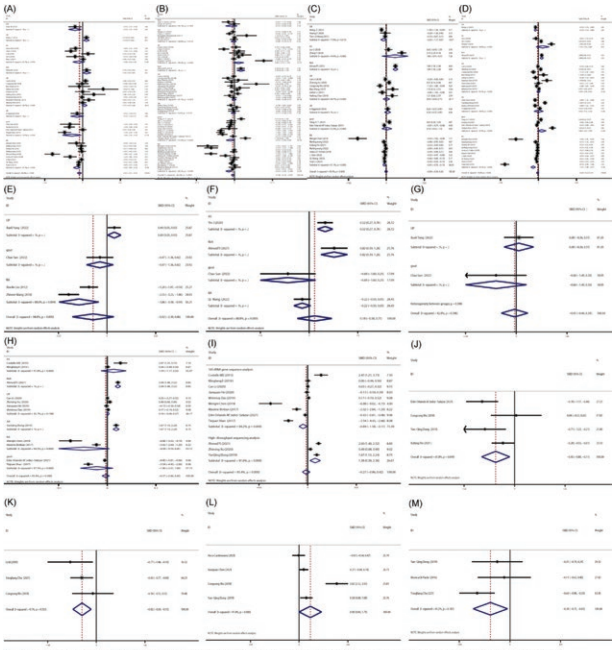


Figure 1: Forest plots of alterations in the gut microbiota of patients with inflammatory arthritis versus healthy controls. (A)Simpson index; (B)Shannon index; (C)ACE; (D)Chao1; (E)eveness index; (F)InvSimpson; (G)Richness; (H)Observed specifications grouped by type of disease; (I)Observed specifications grouped by type of sequencing type; (J)Firmicutes; (K)Fusobacteria; (L)Bacteroides; (M)Faecalibacterium.

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Disclosure of Interests: None Declared.
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AB0002 THE GENETIC BACKGROUND OF ANKYLOSING SPONDYLITIS INDICATES A STRONG CORRELATION WITH OTHER AUTOIMMUNE DISEASES

Keywords: Inflammatory arthritides, Genetics/Epigenetics, Spondyloarthritis

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Background: Ankylosing Spondylitis (AS) is considered to be a rare autoimmune disease that has been studied in genetic level the last decades [1]. The cases reported suggest that there might be an improvement in disease diagnosis with an overlap by other autoimmune diseases [2]. Patients can be diagnosed and the clinical symptoms are in alignment with a diagnosis of the disease. Meanwhile, novel studies propose various genetic factors that may be related to the disease has emerged. Most of the patients carrying various subtypes of the *HLA-B27* gene, such as B*2702, B*2703 and B*2710, are at an increased risk of developing AS [3]. Importantly, the relationship between the genetic factors and the development of the disease is still remains unclear.
Objectives: To create the disease genomic grammar (DGG) with the most credible genetic and epigenetic variants as well as and single nucleotide polymorphisms (SNPs) causing the basis for the development of AS and identify the correlation with other candidate autoimmune diseases [4].
Methods: AS related publications have been analyzed with the use of data mining and semantic techniques for the extraction of information regarding SNPs associated with the disease and the estimation of a candidate DGG. The extracted SNPs have been filtered, evaluated, annotated, and classified in the DGG, using several layers of information from well-known biological databases including dbSNP, LitVar, ClinVar, OMIM and KEGG. Moreover, the AS DGG has been further analyzed towards identifying the hidden connections with other autoimmune diseases.
Results: A holistic genetic map of the AS DGG with 658 related SNPs has been estimated and the specific sub-clusters with crucial SNPs have been correlated with several other autoimmune disease including RA, PS, CD and SEL (Figure 1). This indicates that AS has a common genetic background as many other autoimmune diseases [5]. The candidate DGG of the AS has been estimated using the SNPs annotated information and 3 major clusters of SNPs have been estimated. The DGG of the AS, 85% responds to non-coding regions and 15%

responds to coding regions of which 684 related with promoter and coding gene regions as well as pseudogenes, 74 with LNC, miR and LOC regions and 54 with uncharacterized regions (Figure 1). Moreover, they have been identified the most highly correlated genes with AS using the DGG and the frequency-corresponding SNPs (Table 1).

Conclusion: Despite the several studies performed in AS, is still difficult to identify and categorize the representative variants that may contribute to its. Therefore, crucial genes and specific epigenetic locations must be recognized towards understanding the biological mechanisms of the disease [6, 7]. In the framework of the present study, the DGG of AS was created, using novel bioinformatic techniques. The identification of the DGG in AS may assist in the deeper understanding of this rare disease and the hidden connections with other autoimmune diseases, and will also provide beneficial knowledge regarding common biological pathways leading to autoimmunity regardless of the clinical phenotype of each disease.

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Table 1. List of crucial genes and characterized genetic loci in AS based on the DGG.

A/A	Gene	Cor. SNPs	A/A	Gene	Cor. SNPs
1	*BLOC1S5-TXNDC5*	26	**9**	*TNFRSF1A*	8
2	*ERAP1*	25	**10**	*AP4B1-AS1*	8
3	*TXNDC5*	22	**11**	*PTPN22*	8
4	*IL23R*	15	**12**	*IL1R1*	7
5	*KIF21B*	14	**13**	*ERAP2*	7
6	*ANTXR2*	10	**14**	*RUNX3*	7
7	*IL33*	9	**15**	*LOC107987046*	7
8	*IL1A*	9	**16**	*IL1B*	7

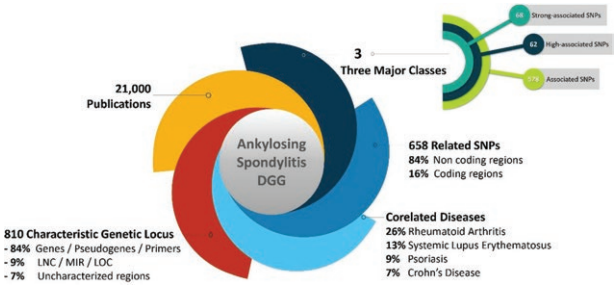


Figure 1. The disease genomic grammar of Ankylosing Spondylitis.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2310

AB0003 INTERLEUKIN 17A RS2275913 GENE POLYMORPHISM IS RELATED TO SEVERITY AND DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS AND INCREASED SERUM IL17A LEVELS IN EGYPTIAN PATIENTS.

Keywords: Cytokines and chemokines, Rheumatoid arthritis, Genetics/ Epigenetics

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Background: Interleukin 17A (IL17A), one of the IL-17 family, performs a critical role in the inflamed synovial tissue of Rheumatoid Arthritis (RA) patients. Several studies have been performed to investigate the role of IL 17A rs2275913 polymorphism in RA pathogenesis, however, data about its role in RA severity and activity is inconsistent.
Objectives: We aimed to investigate the influence of IL17A rs2275913 polymorphism on IL17A serum levels in Egyptian RA patients and disease severity and activity.
Methods: The study included 100 healthy subjects and 100 RA patients. Gene polymorphism rs2275913 was measured by Taqman genotyping assay in both patients and healthy control groups. IL17A serum levels and clinical and laboratory parameters were measured using the enzyme-linked immune sorbent assay (ELISA) technique.
Results: RA patients showed higher IL 17A serum levels than the control group (121.9 ± 24.3 ng/dl vs 20.4 ± 2.6 ng/dl, P < 0.001). RA patients showed a higher frequency of rs2275913 G allele than healthy subjects (P = 0.01). Patients carrying GG genotype showed higher values of all disease severity parameters including Rheumatoid Factor (52.79 ± 16.65 IU/ml, P<0.001) and Anti-Cyclic Citrullinated Peptide Antibody (36.6 ± 14.86 U/ml, P < 0.001). The high-risk GG genotype carriers had higher IL17A serum levels than the GA and AA genotypes carriers (129.74 ± 23.03 ng/dl vs 107.49 ± 19.85 ng/dl, P <0.001).
Conclusion: The major allele of IL17A rs2275913 polymorphism was associated with higher IL17A serum levels, and greater RA severity. It is thus very likely that the rs2275913 polymorphism of IL17A gene is associated with an increased risk of RA, as well as with higher severity in Egyptian RA patients.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0004 THE DISEASE GENOMIC GRAMMAR OF MYASTHENIA GRAVIS INDICATES A COMMON GENETIC BACKGROUND WITH RHEUMATOID ARTHRITIS

Keywords: Genetics/Epigenetics, Rheumatoid arthritis, Inflammatory arthritides

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Background: Myasthenia Gravis (MG) is a rare, multifactorial autoimmune disease. It is caused by the presence of autoantibodies to the postsynaptic membrane of the neuromuscular junction causing impairment to neuromuscular transmission [1]. Various SNPs have been associated with MG with a number of genes possibly contributing to the disease pathogenesis [2]. Through the Disease's Genomic Grammar (DGG), as formulated by Bioinformatics tools, common genetic associated components have been established with RA, thus suggesting a genetic overlap in the manifestation of both diseases and possible concurrency in patients [3].
Objectives: To create an ensemble of the genetic factors contributing to MG, to evaluate the most credible SNPs associated with disease manifestation, to establish a relationship with RA and to potentially assist in prognosis, prevention and personalized treatment of both diseases.
Methods: PubMed publications containing the term "myasthenia gravis" were analyzed with data mining and semantic techniques. Data Annotation enhanced the data collected, including SNPs obtained through GWAS, with information including variation type, alleles, relevance with phenotypes and additional clinical, genomic and functional information from databases including dbSNP, LitVar, ClinVar and Genes. Strong-Associated SNPs were further analyzed and validated. Genes related with both MG and RA were used to estimate a gene network with the use of the GeneMANIA tool and genetic and protein interactions, pathways and co-expression was studied.
Results: A candidate DGG was established containing a total 77 SNPs associated with MG and further categorized into three major classes. Within this database, different types of SNPs were identified with 27 SNPs representing Intron Variants (32.5%), 17 were 2KB Upstream/500B Downstream Variants (20.5%), 12 concerned Missense Variants (14.5%) and 7 SNPs were identified as 3' or 5' UTR Variants (8.4%). Class A included 40 Strong-Associated SNPs, related with 24 genes. MG and RA share 10 common Strong-Associated (Class A) SNPs (25%) related with 10 genes, based on the retrieved data. In a second level of analysis, these common genes create a functional network of a total of 29 genes and 855 total links, with 90.1% co-expression as generated by the GeneMANIA tool (Figure 1).
Conclusion: A higher frequency of concurrent autoimmune diseases is observed than the background prevalence and it has been demonstrated that MG coexists with other ADs in population studies [4,5]. Patients with concomitant MG and RA encounter more challenges in the therapeutic aspects of their health, considering that known disease-associated polymorphisms can be utilized in early diagnosis, prognosis and specialized treatment. Identifying the optimal genomic grammar in MG with the use of

novel Bioinformatic tools may assist in the better understanding of this polygenic disease, while its association with RA and other ADs is a helpful step towards comprehending the shared biological pathways leading to autoimmunity. The data resulting from our study can be utilized towards the development of an application designed to assist clinical diagnosis by using the patients' genomic data, like the integrated bioinformatics tools Demetra for endometriosis [6] and Epione for SLE [7].

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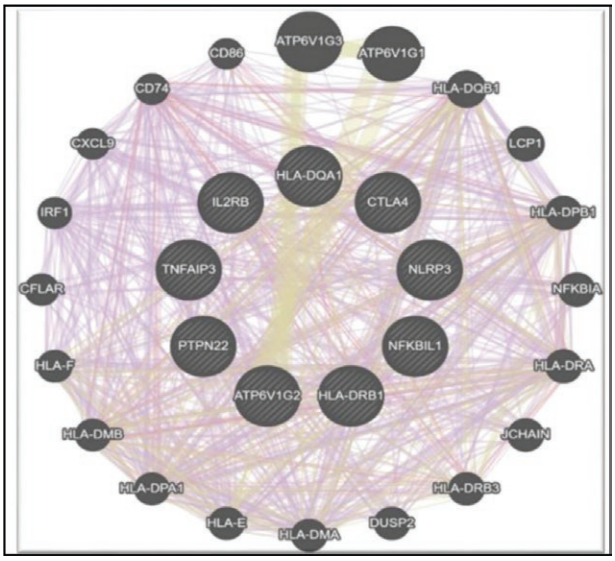


Figure 1. Functional network of the 9 common genes between RA and MG as generated by GeneMANIA.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0005

CHANGES OF SALIVARY MICROBIAL COMMUNITY IN PATIENTS WITH PERIODONTITIS

Keywords: Prognostic factors, Adaptive immunity, Biomarkers

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Background: Periodontitis (PD) is a chronic, progressive polymicrobial disease[1]. In the context of the microbiome in the pathogenesis of rheumatic disease, microorganisms located in the periodontal tissues play an important role as potential initiators of immune-mediated inflammatory conditions at distant sites[2]. Studies have shown that the microbiota associated with PD is different from that in health, and the chronic inflammatory response induced by salivary microbiota plays an important role in the development of PD.
Objectives: Study to evaluate and quantify the differences in the composition of salivary microbiota in patients with PD, and investigate the correlation between salivary microbiota in patients with PD and clinical variables.
Methods: In the same race, 34 salivary samples of patients with PD and 28 salivary samples of periodontal health controls(HC) were collected for 16S rRNA gene sequencing. Compare salivary microbiota alpha-diversity,beta-diversity and microbial composition (at the phylum and genus levels) were used to determine differences in salivary microbiota characteristics between periodontitis patients and periodontal health controls. LefSe analysis was carried out to identify differentially abundant genera.The correlation between different taxa and clinical variables was calculated by the Spearman rank test.
Results: Consistent with the observed diversity trend, compared with periodontal health, the richness of patients with periodontitis is relatively high ($P<0.05$, Figure 1a), which indicates that the diversity of salivary microbiome in patients with periodontitis is significantly higher. The Beta diversity based on Bray Curtis distance at the species level demonstrated a significant differences in microbial communities between periodontitis patients and periodontal health (analysis of variance, r2=0.094, p=0.001,Figure 1b). At different phylogenetic levels, the 10 selected taxonomic biomarkers showed strong discrimination ability, with log10 LDA score >4.0 (Figure 1e-g). Specifically, at the phylum level, the Firmicutes phylum frequency of periodontitis patients is lower, while the Spirochaetota frequency is higher. Patients with periodontitis have more genus Treponema at the genus level (Figure 1c-d). PICRUSt analysis found that in the KEGG pathway, the function of microbial genes related to amino acid metabolism in the salivary microbiota of periodontitis patients was higher (Figure. 1h). Treponema was positively correlated with periodontal probing depth (PPD). Total, plaque index (PI) and periodontitis extent Calc. Spirochaetota was positively correlated with PPD Total, PI ($p<0.05$, Figure 1i).
Conclusion: Specific salivary microbiota played an important role in the pathogenesis of periodontitis, which may help to diagnose or determine individual susceptibility to periodontitis by detecting salivary microbiota.

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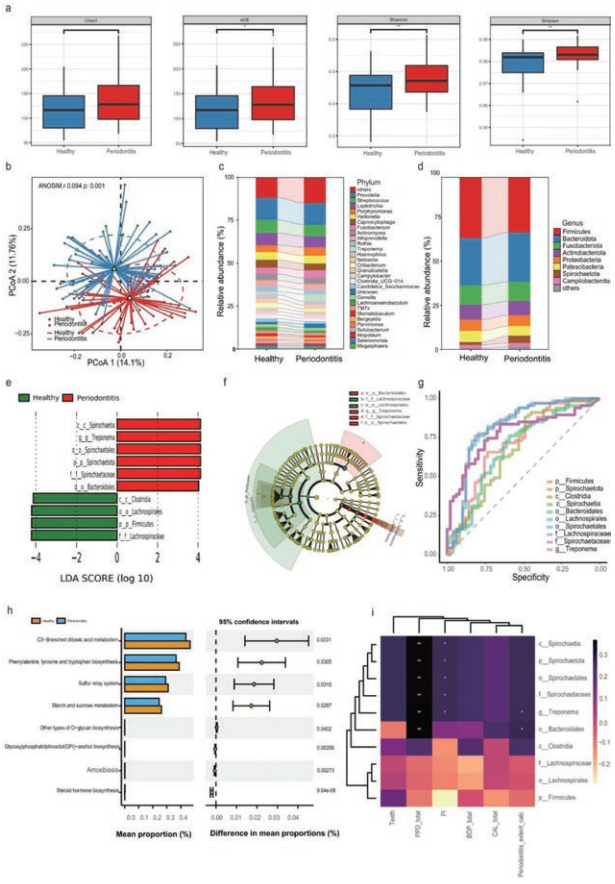


Fig1. (a) Alpha-diversity assessed by richness (Chao1, ACE) and diversity (Shannon, Simpson), Median estimates compared across cohorts. (b) Principal component analysis (PCoA) plot produced by the Bray-Curtis distances. (c-d) Salivary microbiota composition of periodontitis patients and HCs based on relative abundance at the phylum and genus levels. (e-f) LEfSe was utilized to analyze the differences of bacterial taxa between periodontitis patients and HCs.(g) ROC was conducted on all samples using 10 separate classified biomarkers. (h) Picrust analysis in KEGG pathway. Functional prediction of salivary microbiota in patients with periodontitis and HCs. Stamp software defines the important KEGG pathway of salivary microbiome Level 3 in patients with periodontitis and HCs. (i) Spearman correlation heat maps the relationship between bacterial taxa and periodontitis and clinical variables *p<0.05, **p<0.01.

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Disclosure of Interests: None Declared.
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AB0006

CLINICAL, BIOLOGICAL AND GENETIC BIOMARKERS ASSOCIATED WITH DIFFERENT PHENOTYPES OF SYSTEMIC LUPUS ERYTHREMATOSUS IN PARAGUAYAN PATIENTS

Keywords: Systemic lupus erythematosus, Biomarkers, Genetics/Epigenetics

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Background: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease characterized by a very heterogeneous clinical picture that makes diagnosis and follow-up of these patients difficult.
Objectives: Identify correlations between clinical, immunological and genetic biomarkers with clinical manifestations in SLE in Paraguayan patients.
Methods: Retrospective study of data from medical records and immunological and genetic studies of patients with SLE from Paraguay. A descriptive analysis was performed based on the type of variable. HLA allele frequency (DPA1, DPB1, DQA1, DQB1, and DRB1) was calculated and univariate logistic regression analysis was performed between each of the explanatory variables and the presence/absence of each of the phenotypes. The odds ratio. (OR), the 95% confidence interval (95%CI), and the p-value were recorded. Associations with a p-value less than 0.05 were considered statistically significant associations.
Results: 104 patients with SLE were included, 86% female with a mean age value of 32.80 ±10.36 years. An association was identified between anti-dsDNA and the presence of the renal phenotype and anti-dsDNA with the absence of the joint and hematological phenotype. The IgM isotype RF was associated with the absence of the renal phenotype. HLA DQB1* 02:02 and HLA DRB1* 07:01 associated with cutaneous phenotype were identified. An association was identified between the age of onset of the disease and the presence of the joint phenotype. No other associations were identified with the other variables studied.
Conclusion: Possible clinical, immunological and genetic biomarkers of phenotypes have been identified in patients with SLE of Paraguayan origin.

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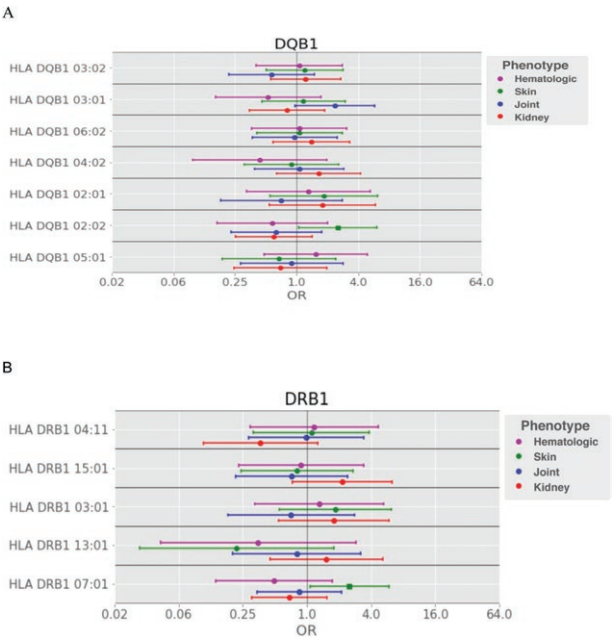
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Table 1. Analysis of association and Odds Ratio (OR) of the presence of autoantibodies and the phenotypic manifestations of those with SLE.

Auto antibodies	Articular OR(IC95%);p	Skin OR(IC95%);p	Hematologic OR(IC95%);p	Kidney OR(IC95%);p
Anti-dsDNA	0.17 (0.06-0.46) p=0.001	0.91 (0.38-2.17) p=0.838	0.28 (0.09-0.86) p=0.027	49 (15-157) p=0.0001
Anti-Sm	0.99 (0.28-3.44) p=0.99	0.64 (0.16-2.48) p=0.52	0.25 (0.03-2.06) p=0.2	1.57 (0.51-4.82) p=0.42
Anti-Ro	0.99 (0.28-3.44) p=0.98	0.64 (0.16-2.48) p=0.52	0.25 (0.03-2.06) p=0.19	1.57 (0.51-4.82) p=0.42
Anti-RNP	1.76 (0.43-3,15) p=0.747	0.54 (0.18-1.65) p=0.287	0.38 (0.10-1.43) p=0.15	1.59 (0.64-3.90) p=0.30
RF total	1.06 (0.36-3,11) p=0.906	0.58 (0.17-1.94) p=0.38	1.96 (0.64-6.02) p=0.235	0.41 (0.15-1.14) p=0.09
RF IgG	1.06 (0.36-3,11) p=0.906	0.58 (0.17-1.94) p=0.38	1.96 (0.64-6.02) p=0.235	0.41 (0.15-1.14) p=0.09
RF IgM	1.96 (0.62-6,18) p=0.247	0.65 (0.16-2.52) p=0.53	2.46 (0.72-8.32) p=0.14	0.20 (0.05-0.76) p=0.019

anti-dsDNA: anti-double-stranded DNA antibodies, Anti-Sm: Anti-Smith, anti RNP: anti nuclear ribonucleoprotein U1, RF: rheumatoid factor.

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Disclosure of Interests: None Declared.
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Graph 3. Odds Ratio (OR) of the presence of alleles of HLA DQB1 and HLA DRB1 gene and the development of the different phenotypes analyzed.

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

AB0007

DYNAMIC INTERPLAY OF FUNCTIONALLY DISCORDANT CD4+HLA-DR+ SUBSETS WITH A COMMON PATHOLOGICAL ONTOGENIC ORIGIN IN HUMAN ARTHRITIS

Keywords: Rheumatoid arthritis, Synovium, Adaptive immunity

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Background: We have previously described the presence of pathogenic-like lymphocyte (CPLs; $CD4^+HLA\text{-}DR^+$) subset within the circulation, that is phenotypically similar to their synovial counterparts. CPLs are inflammatory T effectors that correlate with disease activity and possess a TCR repertoire with strong synovial overlap. We also discovered a similar inflammation-associated T-regulatory (iaTreg; $CD4^+HLA\text{-}DR^+$) circulatory subset, that is activated, suppressive, poised to migrate to inflamed site and sharing TCR between the peripheral and synovial compartments. iaTreg and CPL were found to be phenotypcally quite similar. Their striking similarity, inspired the hypotheses of a common ontogeny driven by the synovial micro-environment, and whether their functionally discordant roles, pointed to an undetermined dynamic interplay.
Objectives: In this study, we seek to establish if a common disease ontogeny exists between synovial CPLs/iaTregs in human arthritis and why CPLs continue to perpetuate synovial inflammation.
Methods: We performed mass cytometry analysis of PBMCs from RA patients and healthy adults. CD4 subsets from active JIA PBMCs, paired JIA SFMCs and healthy paediatric controls were sorted for bulk RNA sequencing. CpG profiling of FoxP3 TSDR site was performed for synovial iaTregs. Treg suppression assays were performed in iaTregs for healthy paediatric controls, paired JIA PBMCs and SFMCs.
Results: Mass cytometry analysis of RA patients revealed memory induction of CPLs and iaTreg as compared with healthy adults. Importantly, CPLs/iaTregs from RA patients demonstrated reactivity to the dnaJP1 peptide, which is a pro-inflammatory epitope in RA patients, thus underscoring disease relevance. Circulatory JIA CPLs/iaTreg subsets displayed transcriptomic convergence, exhibiting (a) common pathway dysregulations, (b) restriction in TCR repertoire and (c) common transcription factor drivers, suggesting a common pathogenic

ontogeny. This phenomenon is further reinforced across the spatial/disease continuum, with synovium CPLs/iaTregs presenting common dysregulated pathways including IFNg signalling. In particular, TCR clonatype sharing in CPLs/iaTregs is higher in the synovium, suggesting a common antigenic origin. To understand the dynamic interplay between CPLs and iaTregs, we assess the regulatory capacity of iaTregs. Epigenetic profiling of CpG sites on the FoxP3 TSDR promoter, revealed typical Treg demethylation status within iaTregs, indicating a stable lineage. Suppression assays reveal that iaTreg rather than non-iaTregs were poised to suppress disease T effectors from JIA PBMC/SFMC, with higher rates of suppression. This is in contrast with healthy controls, where iaTregs were inferior in suppression, mirroring their disease ontogeny. Despite superior suppression from iaTreg in SFMC T effectors, synovial CPLs were resistant to suppression from iaTreg as compared with synovial Non-CPLs. Destabilisation assays in iaTregs, reveal a drop in FoxP3 levels in the presence of IFNg, suggesting a role for IFNg in CPL evasion of suppression.

Conclusion: Our study highlights the disease relevance of CPLs/iaTregs in human arthritis, whilst revealing evidence of a common pathological ontogeny for CPLs/iaTregs, that is antigenically driven by the inflammatory synovium environment. The dynamic interplay between CPLs/iaTregs, could be titled towards suppression evasion through IFNg, allowing for continual synovium inflammation.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.3435

AB0008 ROLE OF IL-23/TH17 AXIS CYTOKINES IN RHEUMATOID ARTHRITIS

Keywords: Cytokines and chemokines, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is an autoimmune inflammatory arthritis driven by an inflammatory cascade of different cytokine families. IL-23/Th17 axis cytokine (IL-23, IL-17) has been studied as a key pathway for disease development and its association with disease severity, joint erosion and functional outcome [1], but the data supplementing to support the hypothesis is lacking and conflicting. Also, there is a paucity of data on the role of IL-23/Th17/IL-17 axis cytokines in an Indian subset of patients.

Objectives: The objective was to find the correlation between serum cytokines (IL-17, IL-23) and clinical parameters of Rheumatoid arthritis patients, e.g., disease activity (DAS28) and functional status.

Methods: This cross-sectional observational study was conducted in General Medicine OPD from 2021 to 2022. ACR/EULAR 2010 classification criteria was used to diagnose RA. Eighty-four consecutive RA patients were recruited after taking consent. Serum IL-17 and IL-23 levels were measured by the ELISA method. Clinical and laboratory parameters, DAS28-ESR, and HAQII were recorded. Data were analyzed to find the correlation between cytokine and disease parameters, and compare cytokine levels in different subgroups.

Results: The study showed a higher proportion of females than males (n=76,90.5% vs n=8,9.5%). 14.28%(n=12) cases were elderly RA. 90.5% were taking cDMARDs, whereas 48.8% (n=41) were steroid users. Majority of cases, 57.14% (n=48) had high disease activity, whereas 25% (n=21) had moderate disease activity. Cases achieved remission was 5.95%. The median value of serum IL-17 and IL-23 were 103.72 pg/ml (IQR=39.91-524.13) and 981.87 pg/ml (IQR=793.25-1205.0), respectively. Swollen joint count, but not tender joint count, correlated positively with both IL-17 and IL-23 levels (r_s=0.229, p=0.036; r_s=0.098, p=0.016, respectively). Among the inflammatory marker, only CRP correlated positively with IL-23 (r_s=0.269, p=0.014). Both IL-17 and IL-23 levels showed an insignificant, weak positive correlation with the disease activity DAS28 (r_s=0.183, p=0.097 & r_s=0.125, p=0.259), respectively. There was no difference in IL-17 and IL-23 levels among the disease severity group (p=0.130 & p=0.215). It was also noted that IL-17 was positively correlated with IL-23 (r_s=0.221, p=0.044). Among the cytokines, only IL-23 had shown a statistically positive correlation with functional status (HAQII) (r_s=0.284, p=0.009). IL-23 level differed significantly between males and females (p=0.013). Also, advanced RA had higher IL-17 level than early RA (p=0.028). Neither IL-17 nor IL-23 level showed any difference between the subgroup e.g., age (younger RA vs elderly RA), obesity (obese vs nonobese), DMARDs or steroid (user vs naïve), serology status (RF+ vs RF- & CCP+ vs CCP-).

Conclusion: Serum IL-17 levels were high in advanced RA as compared to early RA. Both IL-17 and IL-23 correlated positively with the swollen joint count. Only IL-23 was directly correlating with CRP and functional status. Both IL-17 and IL-23 had a weak, insignificant positive correlation with disease activity, and there was no difference in cytokines level among severity classes. Even cDMARD/steroid use did not affect the cytokines level. IL-17 receptor activation triggers transformations of acute synovitis to chronic persistent arthritis [2]. IL-23/IL-17 may be a factor for advanced/erosive disease develoment, which need further research. Hence, blocking IL-23 and IL-17 at an early stage may diminish IL-17 activity, retard the progression to chronic inflammatory arthritis and advanced disease.

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Disclosure of Interests: None Declared.

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AB0009 UNTREATED EARLY RHEUMATOID ARTHRITIS PATIENTS HAVE AN ABNORMAL DISTRIBUTION OF B AND FOLLICULAR T HELPER CELL SUBSETS IN PERIPHERAL BLOOD

Keywords: Adaptive immunity, Rheumatoid arthritis

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Background: Disturbances in B cell immune responses have been implicated in rheumatoid arthritis (RA) pathogenesis since the first weeks of RA development. However, the mechanisms responsible for these immune alterations remain unclear. Follicular helper T (Tfh) cells are crucial for B cell maturation, activation and class-switching as well as for germinal center (GC) formation, whereas follicular regulatory T (Tfr) cells can modulate the GC reaction by suppressing Tfh and B cells.

Objectives: The main goal of this study was to analyze the frequency and phenotype of B, Tfh and Tfr cells in peripheral blood of untreated early RA patients when compared to patients with early non-RA polyarthritis, established RA and healthy controls.

Methods: Blood samples were collected from 35 untreated early polyarthritis patients (<1 year of disease duration), who later evolved into RA (early RA, ERA) (n=23) or other diagnoses (early non-RA, ENRA) (n=12); established seropositive RA patients (n=62) treated with methotrexate and a group of age- and sex-matched healthy controls (n=20). Peripheral blood mononuclear cells were isolated and the frequency and phenotype of B, Tfh and Tfr cells were evaluated by flow cytometry.

Results: ERA patients had similar frequencies of B, Tfh and Tfr cells in circulation when compared to ENRA, established RA and controls. Nevertheless, ERA patients had significantly lower frequencies of pre-switch memory B cells (IgD+CD27+) and higher levels of double negative B cells (IgD-CD27-), CD21low-CD38low B cells and plasmablasts (IgD-CD38++) in peripheral blood when compared to controls. Furthermore, the frequencies of PD-1+ICOS+ Tfh cells and Th2-like Tfh cells were significantly increased in ERA patients when compared to controls. Changes in B, Tfh and Tfr cells phenotype were also observed in ERA patients when compared to controls, particularly an increase of the expression levels of activation markers (CD28, CD69, CD86 and HLA-DR).

Conclusion: ERA patients have alterations in B and Tfh cell subpopulations, but not in Tfr cells, in circulation when compared to healthy controls. Our results suggest a pre-activation state of B and Tfh cells since early RA development, which supports a role of these cells in disease physiopathology.

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AB0010 FERROPTOSIS PROMOTES DYSFUNCTION OF NTREG BUT NOT ITREG IN RHEUMATOID ARTHRITIS

Keywords: Adaptive immunity, Cell biology, Rheumatoid arthritis

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Background: Magnetic resonance imaging and histological studies have shown that iron levels are dysregulated in rheumatoid arthritis (RA) patients, with iron accumulation in gray matter and a considerable loss in healthy white matter. Iron accumulation in RA environment is closely related to immune disorders. Deferoxamine (DFO) is an iron complexing agent that has been shown to attenuate RA development. It has previously been reported that the suppression funtction of natural regulatory T cells (nTreg) is impaired in RA patients. It is still unclear how iron disrupts immune cells dysfunction in the RA milieu, and whether regulating iron is beneficial for Treg cell expansion and function maintenance.
Objectives: The purpose of this work is to identiy the underlying gene expression profile of ferroptotic-induced dysregulatory RA-Treg, and to investigate the possible application of TGF-induced Treg (iTreg) in the treatment of RA.
Methods: We established a collagen-induced arthritis (CIA) mouse model, a typical animal model of autoimmune arthritis, and performed single cell RNA-sequencing (scRNA-seq) to discover different Treg populations in the joints of CIA mouse models. We also analyzed RNA-seq data from imidazole ketone erastin (IKE), a ferroptosis inducer treated nTreg and iTreg.
Results: Data from single-cell RNA sequencing further identify two groups of Treg cells that have distinct susceptibility to RA challenges, with the ferroptosis-susceptibility Treg associated with an increased insulin-like growth factor 1 (IGF1)-related transcriptome. Mechanistically, IGF1 receptor (IGF1R) activates the AKT-mTOR pathway, increases aerobic glycolysis, promotes Treg conversion toward Th17 differentiation, and increases pro-inflammatory cytokines production. Moreover, RNA-sequencing analysis indicated that imidazole ketone erastin (IKE), a ferroptosis inducer, increases the expression of ferroptosis-associated genes in nTreg but not iTreg, and iTreg attenuated arthritis progression in the IKE-aggravated CIA model.
Conclusion: Our findings suggest that increasing IGF1 and glycolysis account for Treg dysfunction and inflammation in RA, and the novel iTreg may serve as a potential candidate for RA therapy.
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Disclosure of Interests: None Declared.
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AB0011 **CYTOMETRIC ANALYSIS OF ACTIVATED ENTHESEAL TISSUE RESIDENT T-CELLS REVEALS IL-17F AS THE DOMINANT IL-17 ISOFORM EXPRESSED BY INNATE AND ADAPTIVE LYMPHOCYTES**

Keywords: Spondyloarthritis, Adaptive immunity, Enthesitis

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Background: The IL-17/IL-23 pathway has been implicated in many inflammatory diseases such as ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease and psoriasis, and has led to the development of several IL-17 inhibitors. The enthesis is connective tissue where the tendon or ligament attaches to the bone. Enthesitis is the cardinal pathological process in spondyloarthritis (SpA) related diseases and T-cell derived cytokines including IL-17A, IL-17F and TNFα and are thought to be central to SpA immunopathology [1-3]. Clinical advances from the inhibition of both IL-17A and IL-17F has shown great success in treating psoriasis. However, our understanding of IL-17F biology at the human enthesis is rudimentary.
Objectives: Investigate the expression of IL-17A and IL-17F at the enthesis and identify innate and adaptive subsets capable of IL-23-independent production of IL-17.
Methods: Peripheral blood and spinal enthesis samples collected from patients undergoing spinal decompression or surgery for scoliosis correction. Immune cell populations were isolated, for peripheral blood, the lymphocyte population was isolated using red cell lysis and mechanical isolation was used for the enthesis samples. T-cells were stimulated with anti-CD3 (100ng/ml) and soluble CD28 (100ng/ml) for 72hrs in RPMI media. 3-4hrs before the end of the stimulation GolgiPlug was added and the cells harvested for analysis of intracellular IL-17A & IL-17F via flow cytometry or were fixed and frozen for further CyTOF analysis. The same setup was used for IL-23 stimulations with IL-23 (50ng/ml) with or without anti-IL-23p19 (20ng/ml) added to the cells and downstream inflammatory cytokine production was assessed using a multiplex bead immunoassay.
Results: IL-17F was preferentially expressed over IL-17A by CD4+ T-cells in peripheral blood and enthesis after 72hrs of inflammatory activation. Only a small percentage of cells were found to express IL-17A or co-express IL-17A and IL-17F. IL-17 expression by CD8+ T-cells was lower than their CD4+ counterpart, with IL-17F again being the predominant isoform expressed by this cell type. Analysis of IL-17 expression by cell types within the peri-entheseal bone revealed a similar trend to PBMC, albeit, lower expression of IL-17 was observed. CyTOF analysis revealed IL-17A and IL-17F expression from rare $\gamma\delta$ T-cells in the enthesis. The additional IL-23 stimulation enhanced IL-17F production from CD4 T-cells; yet IL-23 alone could not induce IL-17F production. Addition of an IL-23p19 neutralising antibody reduced IL-17F levels equivalent to those seen with TCR activation showing that IL-17 production was not solely dependent on the presence of IL-23.
Conclusion: This is the first study looking at IL-17A and IL17F induction from normal entheses where biological differences between these IL-17A and IL-17F family members has emerged.
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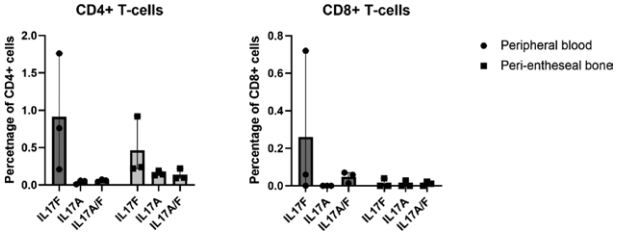


Figure 1. Summary of the percentage of IL17F, IL17A and IL17A/F co-expression via flow cytometry. N=3. IL-17 expression by CD4 & CD8 T-cells in peripheral blood & peri-entheseal bone was measured following 72hrs stimulation with anti-CD3 & CD28 (100ng/ml). Error bars representative of the mean with range.

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AB0012 ANALYSIS OF THE EXPRESSION OF T-BET IN B LYMPHOCYTES OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Biomarkers, Cell biology

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease causing significant morbidity and mortality. B cells play a central role in SLE pathogenesis. T-bet, is a transcription factor promoting T helper-1 development. B cells expressing T-bet are expanded in aging, chronically infected individuals, and murine models of autoimmunity [1, 2].
Objectives: The aim of our work is to analyze the expression and regulatory mechanisms of the transcription factor T-bet in B cells of patients with systemic lupus erythematosus (SLE).
Methods: The intracellular expression of T-bet was evaluated by flow cytometry in the different subsets of B lymphocytes of SLE patients and controls (HD). Peripheral blood mononuclear cells (PBMCs) were stimulated in vitro with IFNγ and IFNα and the expression of T-bet was evaluated by flow cytometry. The clinical characteristics of patients were analyzed by Multiple Factor Analysis (MFA). The analysis was carried out with the software R.
Results: We performed B cell staining and assessed the expression of T-bet in B cell subsets in patients with SLE and HD. We observed a significant expansion of naïve B cells and double negative (DN) B cells expressing T-bet in patients with SLE compared to HD (Figure 1A-B). An expansion of T-bet+ naïve B cells above the 99th percentile of HD (>1% of total naïve B cells) was evident in 68% of patients; 47% of patients showed an expansion of T-bet+ DN B cells above the 99th percentile of HD (>22% of total DN B cells). We assessed if patients with expanded T-bet+ naïve or DN B cells showed significant clinical differences from patients without the expanded subpopulations. To this end we collected clinical and laboratory parameters (SLEDAI, organ involvement as classified in the BILAG, damage with SDI, autoantibody profile, treatment and disease duration) and performed a multiple factor analysis (MFA). The aim of this analysis was to reduce the dimensionality of the complex data to few variables without losing information. The first 4 dimensions of MFA explained 58% of the total variance. The first dimension accounted for 23.6% of variance, and it was mostly driven by therapy and BILAG scores; the second dimension accounted for 17.7% of the variance and it was mostly driven by SLEDAI, SDI and serology. Patients with expanded T-bet+ naïve B cells, distributed differently from patients with no expansion of T-bet+ naïve B cells (Figure 1C). The first dimension was the most informative in separating the two groups of patients: significantly higher values were reported for patients with expanded T-bet+ naïve B cells. No differences were observed for patients with and without expanded T-bet+ DN B cells (Figure 1C). We investigated in vitro if the expression of T-bet in B cells was driven by interferons. We stimulated PBMCs of HD with IFNγ or IFNα and assessed the frequency of T-bet+ B cells: both interferons induced the expression of T-bet in naïve (CD19+CD27-) and memory (CD19+CD27+) B cells (Figure 1D). Interestingly, when cells were stimulated with IFNα in the presence of IFNγ-blocking antibodies the expression of T-bet was not induced.
Conclusion: Altogether, T-bet+ naïve B cells are expanded in patients with SLE and define a group of patients with clinically different disease from patients without expanded T-bet+ Naïve B cells. The expression of T-bet is induced specifically by IFNγ and not by IFNα.

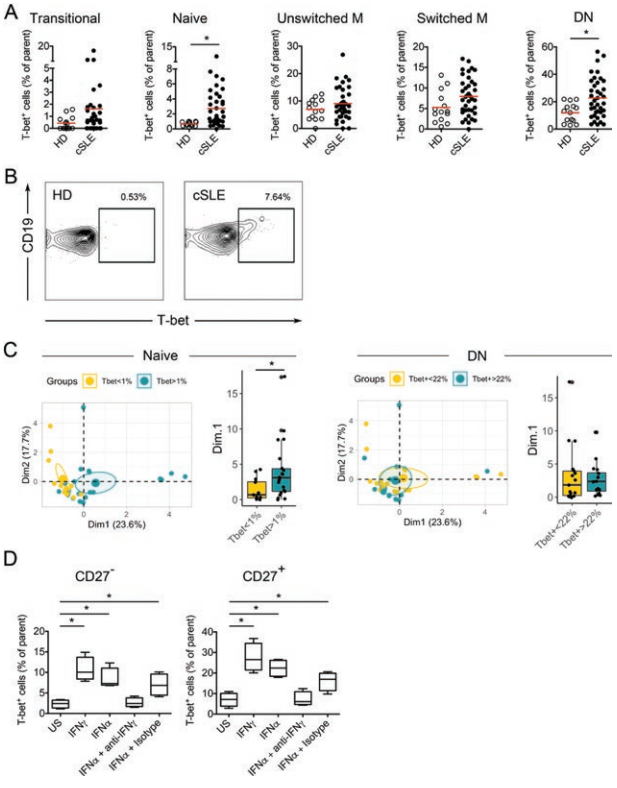


Figure 1.

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AB0013 LONGITUDINAL CHANGES IN VARICELLA ZOSTER VIRUS (VZV)-SPECIFIC T CELL IMMUNITY IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH DIFFERENT JAK INHIBITORS

Keywords: Adaptive immunity, Rheumatoid arthritis, Targeted synthetic drugs

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Background: Targeted synthetic agents such as the JAK inhibitors (JAKi) used for the treatment of various inflammatory diseases, including rheumatoid arthritis (RA), have been associated with increased risk for VZV reactivation and herpes zoster (HZ). Although this has been attributed to decreased T cell surveillance of latent VZV, detailed data on the effect of the different JAKi on VZV-specific T cell immunity are limited.
Objectives: To study longitudinally the kinetics of VZV-specific T cells in RA patients treated with different JAKi (baricitinib-BARI, tofacitinib-TOFA, upadacitinib-UPA) or methotrexate (MTX, control group).
Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from RA patients before and after 4 and 12 weeks of treatment with JAKi or MTX. PBMCs were stimulated *in vitro* for 18 hours either specifically with VZV antigen (VZV lysate) or non-specifically with a polyclonal stimulus (Staphylococcus aureus enterotoxin B, SEB) and anti-CD28/49d. The percentage of $CD4^+CD69^+$ effector T cells as well as of VZV specific $CD4^+CD69^+$ T cells expressing IFNγ were measured by flow cytometry.
Results: 22 patients with active RA were included; 16 were treated with JAKi (BARI n=7, TOFA n=4, UPA n=5) and 6 with MTX. For the JAKi group, 88% were females with median age and disease duration of 62 and 8 years, respectively, and mean baseline DAS28-ESR of 5.6, while in the MTX group, 100% were females with median age and disease duration of 57 and 0.5 years and mean DAS28-ESR of 5, respectively. Treatment with JAKi for 12 weeks did not change significantly the % of the overall population of $CD4^+CD69^+$ T cells stimulated *in vitro* with VZV or SEB (p=0.3). Similarly, there was no significant change in the % of SEB-stimulated $CD4^+CD69^+IFN\gamma^+$ T cells between pre-treatment and after 12 weeks of JAKi treatment (median, from 0.1% to 0.075%, p=0.370, Figure 1a). In contrast, there was a significant decrease in VZV-specific $CD4^+CD69^+IFN\gamma^+$ T cells between these 2 time points (median, from 0.049% to 0.01%, p<0.001, Figure 1b). The decrease in VZV-specific T cells was similar between the 3 different JAKi (Figure 1c). Patients treated with MTX (n=6) had a slight decrease in VZV specific T cells, but this did not reach the statistical significance (p=0.5).
Conclusion: Treatment of RA patients for 12 weeks with JAKi significantly reduced VZV-specific T cells without affecting the overall effector T cell population. The effect on VZV specific T cell immunity was similar with the 3 different JAKi. These preliminary findings provide novel information regarding the effect of JAKi on VZV-specific T cell immunity.

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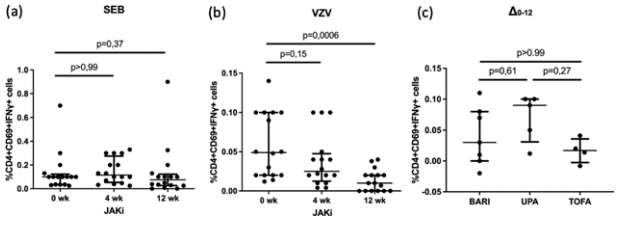


Figure 1 (a) Percentage of SEB-stimulated CD4+CD69+IFNγ+ T cells during 12 weeks of JAKi treatment (Friedman test, n=16, p=0,37), **(b)** Percentage of VZV-specific CD4+CD69+IFNγ+ T cells during the same period (p=0.0006) **(c)** Decrease of the % of VZV-specific CD4+CD69+IFNγ+ T cells (Δ0-12) during the same period of treatment with BARI (n=7), UPA (n=5) or TOFA (n=4).

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Disclosure of Interests: None Declared.

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AB0014 IMMUNE RESPONSES TO VACCINATION AGAINST HERPES ZOSTER (HZ) IN PATIENTS WITH RHEUMATIC DISEASES UNDER TREATMENT WITH JAK-INHIBITORS: OUR PRELIMINARY RESULTS

Keywords: Adaptive immunity, Vaccination/Immunization, Real-world evidence

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Background: Shingrix is a recombinant inactive vaccine available for prevention of herpes zoster (HZ) infection, recently approved for patients with rheumatic diseases under treatment with JAK-inhibitors. Because of its novelty, scant information is available on Shingrix vaccine responses in patients with immune mediated rheumatic diseases (IMRD).

Objectives: To investigate the antibody responses to the HZ vaccine in selected rheumatic diseases treated with JAK-inhibitors (JAKi) pre- and post-Shingrix vaccination (weeks 4–6) and to identify factors associated with reduced immunogenicity.

Methods: Patients with selected rheumatic diseases under treatment with JAKi underwent two series of IM Shingrix vaccine (0.5mL each) administered 2 months apart. Bloodwork was performed 4-8 weeks following 2nd dose of vaccine to assess post- vaccination antibody response. Pre and post vaccination response was then compared using Anti Varicella Zoster Virus IgG Multiplex Flow Immunoassay (MFI). Blood lymphocyte distributions (CD3+, CD4+, CD8+, CD19+) and NK cells, total serum IgG and IgM levels, and VZV-IgG and IgM, were investigated pre- and post-Shingrix vaccination (weeks 4–6).

Results: 38 patients were included, 79% were female with a median age at inclusion of 57±10.5 years. 21% of patients had rheumatoid arthritis, 8% had systemic lupus erythematosus, 16% had psoriatic arthritis, 16% had ankylosing spondylitis and 5% had dermatomyositis. VHZ IgG antibody levels and distributions of lymphocyte subpopulations in peripheral blood pre- and post-immunization are represented in Table 1. Positive humoral responses were observed in 86% of patients. Mean changes VHZ-IgG antibody between post- and pre-vaccination sera were 4.6±0.33 and 1.8±1.98 (p<0.0001), respectively. After immunization, the number of T cells (CD3+, CD4+, CD8+) and NK cells remained relatively unchanged however, the number of B cells (CD19+) increased significantly from 147.4±156 to 780.62±475.5 significantly (p<0.0001). There was a 2.5-fold increase in antibody titers after immunization in RA patients, a 2.4-fold increase in SLE patients, a 2-fold increase in AP patients, a 2.5-fold increase in AS patients and a 3.5-fold increase in DM, with no significant difference between the different patients' subgroups. Results from multivariate regression analysis adjusted by age, gender, disease duration, treatments and glucocorticoid and MTX cumulative dose, showed a negative correlation between VHZ-IgG and age >65 years (β=-0.34, p 0.03), disease duration (β=-0.58, p 0.04) and glucocorticoid cumulative dose (β=-0.42, p 0.02).

Conclusion: Our preliminary results show preserved seroconversion rates and VHZ-IgG antibodies and concurrently increase the number of CD19+ B-cells and total serum IgG in patients with rheumatic diseases on treatment with JAKi. Age>65 years, disease duration and glucocorticoid cumulative dose are negatively correlated with humoral response.

Table 1. Varicella zoster virus IgG Ab levels and distributions of lymphocyte subpopulations in peripheral blood pre- and post-immunization

	Pre-vaccination	Post-vaccination	P value
Total serum IgG (mg/dL)	958±300	1328.5±308	**0.04**
Total serum IgM (mg/dL)	126±98	118.5±156	0.84
VZV IgG Ab (Ab Index)	1.8±1.98	4.6±0.33	**0.0001**
VZV IgM Ab (Ab Index)	0.32±2.1	1.3±3.4	0.72
CD3 (cells/mm3)	1065.5±716.5	1128±721	0.63
CD19 (cells/mm3)	147.4±156	780.62±475.5	**0.0001**
CD4 (cells/mm3)	653±584	783±475.5	0.34
CD8 (cells/mm3)	386.2±260	392.7±297.5	0.42
NK (cells/mm3)	281.05±189	284.52±145.5	0.42

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Disclosure of Interests: None Declared.

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AB0015 ANTINUCLEAR ANTIBODIES PATTERN CLASSIFIER WITH CONVOLUTIONAL NEURAL NETWORKS

Keywords: Diagnostic tests, Biomarkers, Artificial intelligence

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Background: To detect antinuclear antibodies (ANA) on the blood's patients is a mostly used technique to diagnose immunologic diseases. The Indirect Immunofluorescence method (IIF) generates images with ANA patterns on them and is commonly used by immunology laboratories around the world. Those patterns are documented in the International Consensus of ANA Patterns (ICAP) and there are 29 of them at present, split into three main groups: Nuclear, Cytoplasmic and Mitotic. Classifying these patterns is a subjective task that has a strong dependence on the physician's experience and training, thus the professionals need a second reader to reach a successful classification of images with these patterns. To support the professionals, we developed a Machine Learning model (ML), based on Convolutional Neural Networks (CNN) able to classify ANA patterns between positive and negative and then classifying only positive samples between the three main groups mentione.

Objectives: Developing a machine learning model to help physicians reach a successful ANA pattern classification without a second reader and to train entry-level professionals to classify different ANA images by themselves.

Methods: Using a public database with 2079 samples of ANA pattern images we defined the limitations of our model; we preprocessed the dataset and made a data augmentation process to avoid overfitting issues. To reach our objectives we define a model with two parts, the first one was a CNN classifying each sample between positive and negative, the second one was another CNN classifying the positive samples from the last step into the main three groups before mentioned. Following this idea, we proved 17 pre-trained CNN and compared their results based on commonly used metrics in machine learning: accuracy, precision, recall and F1. To prove our final model we train it with the mentioned augmented public dataset and test it with a private dataset with 445 samples from Inmuno21 Laboratory in Caracas, Venezuela.

Results: Finally, our model reached acc: 93%, pre: 93%, recall: 93% and F1: 93% classifying between positives and negatives, improving the state of the art models presented before as a solution for this problem1. On the other hand, our model shows an acc: 75%, pre: 85%, recall: 92% and F1: 87% for the second stage, classifying positives samples in Nuclear, Mitotic and Cytoplasmic, becoming the first model documented that be able to classify ANA patterns images in this three groups with multilabel capability and positives-negatives previous discrimination.

Conclusion: It's necessary to make efforts to create a bigger datasets of ANA patterns images, better documented and with more samples for each label, since the major problem we found when we've developed the project was there was poor data and there was only one public dataset that had not samples for each label, the other public datasets were not available, had lower samples amount than the ones used or had no samples in the three main groups. Thus it was necessary to augment data to front the overfitting issues. Despite this, we made

a model that shows high performance compared with state of the art works, and it can be used as a second reader or training partner for new professionals.

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Disclosure of Interests: None Declared.

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AB0016 HEPATITIS B SEROPREVALENCE AND REACTIVATION FREQUENCY IN PATIENTS USING BIOLOGICAL DRUGS OTHER THAN RITUXIMAB; SINGLE CENTER RESULTS

Keywords: bDMARD, Safety

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Background: Biological drugs target immune or genetic mediators and are important treatment alternatives in rheumatology, especially in patients with inadequate response to the conventional treatment. Hepatitis B reactivation may emerge during the use of these agents. There is a higher risk of reactivation with rituximab (RTX) therapy. The frequency of hepatitis B reactivation with non-RTX biologics is unclear.

Objectives: Hepatitis B seroprevalence and reactivation frequency were evaluated in patients followed in Kocaeli University Faculty of Medicine rheumatology outpatient clinic and treated with non-RTX biological drugs.

Methods: The HBsAg, anti-HBs, and anti-HBcIgG data of 170 patients who received non-RTX biological drug therapy for different indications between 2010 and 2022 were analyzed retrospectively. HBV DNA PCR, liver enzyme elevation and HBeAg reversion were evaluated for reactivation, especially in HBsAg and anti-HBcIgG positive patients. The patients were divided into 5 groups as HBsAg (+) patients (Group 1), HBsAg (-), anti-HBs (+) and anti-HBcIgG (+) patients (Group 2), anti-HBc IgG (+) patients (Group 3), whole serology negative patients (Group 4) and vaccine-immunized anti-HBs (+) patients (Group 5).

Results: The mean age of the study population was 47.4±10.6 years. 57.6% of the patients were ankylosing spondylitis (AS), 24.1% were rheumatoid arthritis, and 8.8% were psoriatic arthritis. Behçet's disease and Takayasu arteritis were observed in 3.5% and 2.4% of patients, respectively. 3.5% of patients were consisting of a various of rheumatological diseases including Familial Mediterranean fever, giant cell arteritis, adult Still's disease. In these patients, anti-tumor necrosis factor (TNF) and non-TNF biological drug (tocilizumab, abatacept, secukinumab) treatment use were 80% and 20%, respectively. Most of patients were in group 4 (n=114, 67.1%). The distribution of patients based on serology is shown in Table 1. The patients in group 1 were receiving antiviral treatment. Other groups did not receive any antiviral therapy. In group 3, reactivation was observed in a patient who was followed up with the diagnosis of AS and on infliximab treatment. After reactivation, this patient started to take the antiviral treatment. In a patient of which was classified in group 1, a non-significant increase in viral load (<1 log10 IU/mL) revealed. However, we did not consider this patient had reactivation due to the normal level of liver enzymes and the absence of HBeAg reversion.

Conclusion: Patients using non-RTX biological treatments have a medium risk in terms of HBV reactivation. However, the usage of antiviral prophylaxis is quite low. In our study, HBV reactivation was observed less. On the other hand, patients should be carefully screened in terms of hepatitis serology in order to prevent the reactivation.

Table 1. Data of Patients Receiving Non-Rituximab Biological Treatment

	N(%)
Gender	
Female	79(46,5)
Male	91(53,5)
Diagnosis	
Rheumatoid Arthritis	41(24,1)
Ankylosing spondylitis	98(57,6)
Psoriatic Arthritis	15(8,8)
Behcet 's disease	6(3,5)
Takayasu Arthritis	4(2,4)
Other	6(3,5)
Groups by Viral Markers	
Group 1 - HBsAg (+)	5(2,9)
Group 2 - HBsAg (-), anti-HBs (+), anti-HBcIgG (+)	13(7,6)
Group 3 - HBsAg (-), anti-HBs (-), anti-HBcIgG (+)	14(8,2)
Group 4 - HBsAg (-), anti-HBs (-), anti-HBcIgG (-)	114(67,1)
Group 5 - HBsAg (-), anti-HBs (+), anti-HBcIgG (-)	24(14,1)
Hepatitis B Reactivation Rate	
Group 1	-
Group 2	-
Group 3	1(7,1)

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0017 HOW DO B CELLS EVADE RITUXIMAB THERAPY IN AUTOIMMUNITY; IS IT TIME TO TARGET THE CD19+CD20- B CELLS?

Keywords: Biomarkers, Adaptive immunity, Cell biology

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Background: Following treatment of autoimmune disease with anti-CD20 monoclonal antibody, Rituximab, insufficient B cell depletion relates to poor clinical response, in particular an expansion of memory B cells [1].

Objectives: We investigated whether the relative expression of the target antigen CD20 on B cell subpopulations underlies drug resistance.

Methods: Peripheral blood samples from 6 rituximab naïve (RTX-N) patients with autoimmune rheumatic diseases (active systemic lupus erythematosus) and rheumatoid arthritis), 6 patients previously treated with rituximab (RTX-T); and 6 healthy controls (HC) were obtained. B cell subpopulations were defined using the relative expression of IgD and CD27 using flow cytometry.

Results: Patients in the RTX-N group had significantly higher frequency of CD19+CD20-B cells (median=25.9% of total B cell, compared to 1.26% in HC), p =0.0022. CD19+CD20-B cells were predominantly swMBC and DN cells. All patients in the RTX-T group (median 22 months post rituximab) had detectable CD19+CD20-B cells (median=52.25 % of total B cells), of which the majority were swMBC (median=4.54%, range 0.23-74%) and DN B cells (median=53.5%, range 11.6-98.1%). Collectively, we noted that the median frequency of CD19+CD20-B cells in peripheral circulation was higher in RTX-T > RTX-N > HC.

Conclusion: Our preliminary results have identified greater frequency of CD19+CD20- population of B cells in peripheral blood of patients with autoimmune disease, particularly after treatment with rituximab suggesting that they evade rituximab. These are predominantly of the switched MBC and DN B cell subpopulations. Given, the potential of these cells to contribute to disease activity in autoimmune disease, is it now time to seek alternative strategies targeting CD19 in order to overcome rituximab resistance?

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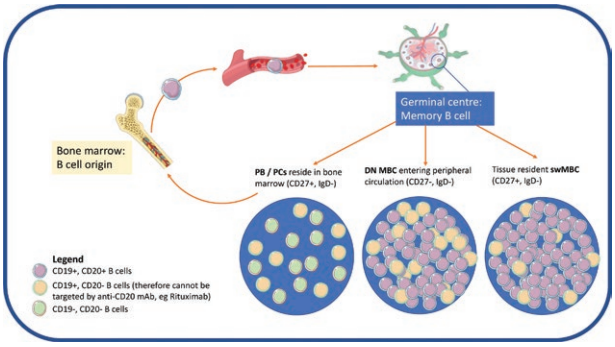


Figure 1.

Figure above demonstrates the cycle of B lineage cells which originate in the bone marrow and migrate into the peripheral circulation and into lymphoid tissues such as lymph nodes and the spleen. In germinal centres the naïve B cells mature into memory B cells which then differentiate into tissue resident switched memory B cells (CD27+, IgD-), or double negative memory B cells entering the peripheral circulation (CD27-, IgD-) or plasma blasts and plasma cells of which the long-lived ones reside in the bone marrow. Proportions of CD19+CD20+ v CD19+CD20- B cells are demonstrated pictorially within each subpopulation. The CD19+CD20- B cells cannot be targeted by anti-CD20 monoclonal antibodies such as rituximab, and therefore alternative strategies to target CD19 may help to overcome rituximab resistance in autoimmunity.

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Disclosure of Interests: Kavina Shah Grant/research support from: Roche Glycart, Christian Klein Shareholder of: Roche, Employee of: Roche Glycart, Geraldine Cambridge: None declared, Debajit Sen: None declared, Madhura Castelino: None declared, Arne Akbar: None declared, David Isenberg: None declared, Maria José Leandro: None declared, Venkat Reddy: None declared.

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AB0018

IMPACT OF AN EX-NOVO INDUCED ADAPTIVE IMMUNE RESPONSE ON CXCL13 SERUM LEVELS IN ESTABLISHED AUTOANTIBODY-POSITIVE RHEUMATOID ARTHRITIS

Keywords: Biomarkers, Inflammatory arthritides, Cytokines and chemokines

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Background: C-X-C motif chemokine ligand 13 (CXCL13) is a chemokine involved in the recruitment of B cells in secondary lymphoid organs and ectopic inflamed sites. Recent studies in animals models and in healthy individuals have shown that serum levels of CXCL13 correlate with GC activity after immunization, pointing at their role as an early biomarker of the adaptive immune response. In rheumatoid arthritis (RA) CXCL13 systemic expression has been shown to be upregulated. However, the factors involved in CXCL13 systemic upregulation and its significance as putative biomarker in patients with autoimmune diseases are currently unclear.
Objectives: To analyze the dynamics of CXCL13 systemic expression over time in RA after controlled induction of an adaptive immune response.
Methods: Fifty-five autoantibody-positive RA patients with established disease under stable treatment with b/tsDMARDs and with no evidence of previous SARS-CoV-2 infection were included in the study. All patients received two doses of the BNT162b2 vaccine at a three weeks interval. Serum samples were collected at the time of the first BNT162b2 dose (baseline - BL), after three weeks at the time of the second dose (post dose 1 – PD1) and after two further weeks (post dose 2 – PD2). At each time point CXCL13 (pg/mL) and SARS-CoV-2 anti-spike protein antibody titres were measured.
Results: The majority of patients were female (n=42, 76%) and both ACPA and RF positive (n=42, 76%). All patients were receiving stable b/tsDMARD treatment (anti-CTLA4: 23 patients [41.8%], JAKi: 16 [29%], anti-IL6: 8 [14.5%] and anti-TNF alpha: 8 [14.5%]). At baseline the median (IQR) CXCL13 values were 81.1 (58.6-125) and all patients were negative for SARS-CoV-2 anti-spike protein antibody. Effective immunization was confirmed in all patients, in particular in 22/55 (40%) after the first dose and in 55/55 (100%) after the second dose, with a significant increase in SARS-CoV-2 anti-spike protein IgG antibody titer at PD2 (median [IQR], 142 [95.4-224]). Despite the effective induction of an adaptive immune response, no significant changes in the median (IQR) values of CXCL13 were observed at PD1 (three weeks after induction: 92.2 [61.8-141]) and PD2 (two weeks after booster: 74.2 [56-126]) with respect to each other and compared to baseline (Friedman p-value=0,947). Sub-analyses based on patients' stratification according to the b/tsDMARD treatment, confirmed a non-significant variation in CXCL13 titers between baseline, PD1 and PD2 in all groups (Friedman p-value= 0,911). Further sub-analyses limited to patients with baseline-PD1 value of CXCL13<100 pg/ml (to exclude potential biases derived from high starting value of CXCL13 titers on the delta of response) confirmed the absence of significant changes (Friedman p-value= 0.237).
Conclusion: At the time-point analysed, the induction of an adaptive immune response *per se* does not appear sufficient to impact on of the expression dynamics of serum CXCL13 in established autoantibody-positive RA.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0019

AUTOANTIBODY BIOMARKERS OF IMMUNE-RELATED ADVERSE EVENTS AND SURVIVAL IN MELANOMA PATIENTS RECEIVING IMMUNE CHECKPOINT INHIBITOR THERAPY

Keywords: Malignancy, Autoantibodies, Biomarkers

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Background: Immune checkpoint inhibitor (ICI) therapy has greatly improved the prognosis of advanced cancers but is often complicated by immune-related adverse events (irAEs). Biomarkers of ICI safety and efficacy are needed.
Objectives: To identify autoantibodies (AAbs) associated with irAEs and cancer outcomes in ICI-treated patients.
Methods: This analysis used clinical data and biospecimens from a prospective trial of 60 patients with advanced melanoma who received 2-4 doses of combination ICI (anti-PD1 + anti-CTLA4) followed by anti-PD1 monotherapy. [1] Patients were followed for three years for irAE development, cancer progression, and death. Plasma was collected at baseline and six weeks after ICI initiation and assayed for AAbs using PhIP-Seq with a human peptide library spanning the entire human proteome. Baseline levels of AAbs with a ≥2 fold-change in ≥10 patients at follow-up (n = 833 AAbs) were concurrently included in a bootstrapped LASSO Cox proportional hazards model (1000 replications; $\alpha = 0.5$; λ chosen by cross-validation for each replication) that was separately run for each outcome: ≥1 severe irAE (CTCAE grade ≥ 3), progression-free survival (PFS), and overall survival (OS). The proportion of times each AAb was replicated was reported as its "validation frequency."[2] Hazard ratio confidence intervals were reported after individually calculating bias-corrected and accelerated (BCa) bootstrap intervals (1000 replications) for each AAb. The AAbs with the highest validation frequencies were used for Partial Least Squares Discriminant Analysis (PLS-DA) clustering.
Results: Among the 60 patients, 47% developed a severe irAE, 25% progressed, and 23% died. **Table 1** shows the six AAbs with the highest validation frequencies for severe irAE, PFS, and OS. PLS-DA was able to cluster patients by the development of severe irAEs using only six AAbs with a 10-fold cross-validated AUROC of 0.86 ± 0.01 (p <.001) (**Figure 1**). PLS-DA performed similarly well for PFS and OS. **Table 1** reflects that higher levels of the identified AAbs at baseline were associated with worse PFS and OS (HR > 1); this pattern remained true across the 25 AAbs with the highest validation frequencies for PFS (21/25, 84%) and OS (23/25, 92%). Conversely, amongst the top AAbs linked to severe irAEs, lower levels in the majority (15/25, 60%) of the identified AAbs were associated with this outcome (HR < 1). Most of the identified top AAbs were unique to each outcome, but there was some overlap: PFS and OS shared seven AAbs (28%), PFS and severe irAEs shared two AAbs (8%), and OS and severe irAEs shared one AAb (4%). No AAbs overlapped between more than two outcomes.
Conclusion: These results suggest that specific autoantibodies may be useful biomarkers for predicting outcomes in melanoma patients receiving ICI therapy. However, these results require validation.
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Table 1. Hazard ratios and 95% confidence intervals for the top six autoantibodies for each outcome

≥1 Severe irAE (n = 60, events = 28)				Progression-Free Survival (PFS) (n = 60, events = 15)				Overall Survival (OS) (n = 60, events = 14)			
AAb	**Hazard Ratio (95% CI)**	**VF***	**sVF****	**AAb**	**Hazard Ratio (95% CI)**	**VF**	**sVF**	**AAb**	**Hazard Ratio (95% CI)**	**VF**	**sVF**
AKAP9	1.25 (1.08-1.42)	76.4%	100	*ACAN*	1.72 (1.21-2.35)	66.3%	100	*KHSRP*	1.34 (1.13-1.65)	52.8%	100
KTN1	1.26 (1.02-1.50)	60.0%	79	*POLR2A*	1.29 (1.04-1.57)	62.7%	95	*EN2*	1.31 (1.05-1.61)	51.8%	98
GCN1	0.66 (0.45-0.95)	54.4%	78	*ZGRF1*	1.47 (1.03-1.81)	50.9%	77	*SBNO2*	1.33 (1.04-1.65)	50.0%	95
FCHO2	1.21 (0.98-1.48)	49.5%	71	*DYNC2H1*	1.39 (0.97-1.85)	45.2%	68	*PAK4*	1.46 (1.16-1.87)	43.5%	82
NRXN2	0.72 (0.44-0.95)	44.2%	58	*TRIOBP*	1.26 (1.05-1.43)	41.3%	62	*DYNC2H1*	1.35 (0.95-1.78)	39.0%	74
EPC1	1.28 (1.09-1.53)	43.2%	57	*SDCCAG8*	1.40 (1.08-1.74)	39.4%	59	*ACAN*	1.43 (0.71-2.11)	34.0%	64

*VF = Validation Frequency (proportion of times each AAb was replicated by the LASSO model) **sVF = Scaled Validation Frequency (validation frequency scaled to highest value for each outcome)

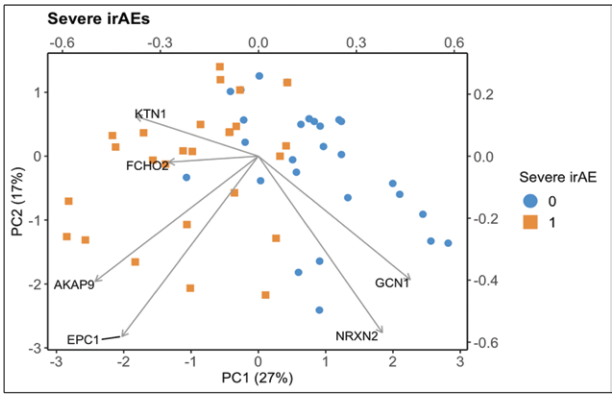


Figure 1. Partial Least Squares–Discriminant Analysis (PLS-DA) clustering of patients using the top six AAbs associated with Severe irAEs with a cross-validated **AUROC of 0.86 ± 0.01 (p < .001)**. Predictor AAbs are represented as vectors on the plot, and patients are represented as points; the length and direction of the AAb vectors indicate the relative importance of the corresponding AAb in the model, while the position of the patient roughly indicates the predicted group or class to which they belong.

*Legend: 0 = no severe irAEs, 1 = ≥1 severe irAE occurred

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Disclosure of Interests: Carlos Aude: None declared, Nilasha Ghosh Grant/research support from: Hospital for Special Surgery, Deanna Jannat-Khah Shareholder of: Walgreens Boots Alliance, AstraZeneca, and Cytodyn, Grant/research support from: Hospital for Special Surgery, Karmela Kim Chan: None declared, Michael Postow Consultant of: BMS, Merck, Novartis, Eisai, Pfizer, and Chugai, Grant/research support from: RGenix, Infinity, BMS, Merck, and Novartis, H Larman Consultant of: Scientific Advisory Board member for TScan Therapeutics, Employee of: Founder of ImmuneID, Portal Bioscience, and Alchemab, Anne Bass Grant/research support from: Hospital for Special Surgery, Memorial Sloan Kettering Cancer Center, and the Rheumatology Research Foundation.
DOI: 10.1136/annrheumdis-2023-eular.772

AB0020 CYTOCHEMICAL ASSESSMENT IN TREG CELLS OF PSORIASIC ARTHROPATHY BY INHIBITION OF IL23 (IN REAL LIFE) AND ITS CORRELATION WITH CLINICAL REMISSION

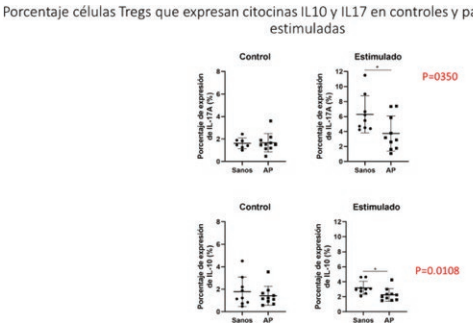
Keywords: Psoriatic arthritis, Cytokines and chemokines

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Background: Psoriatic arthropathy (PsA) is a heterogeneous chronic entity with multiple clinical domains that evolves to irreversible damage both organic and psychological. Therapeutic recommendation guidelines advise differentiated therapies according to the dominant clinical domain (e.g., peripheral arthritis, dactylitis, enthesitis, spondylitis, cutaneous or nail psoriasis). Moderate-severe involvement requires the use of targeted biological or synthetic medication. Primary and secondary failures or intolerances often force the change of therapeutic target in order to achieve greater efficiency. The interrelation of cytokines (mainly IL23, IL17, and IL10) in their pathogenesis at the "in vitro" level seem proven, but their modification "in vivo" and correlation with the clinic are little studied.
Objectives: To identify the cytokine profile of IL -10 and IL -17 in CD4+FoxP3+ cells of patients with PsA, (ii) to identify the degree of expression of CD152 in CD4+FoxP3+ cells of patients with PsA and (iii) to correlate the expression of these molecules and the state of Minimal Activity of the disease (MDA).
Methods: The present study involved 9 healthy volunteers and 10 patients with Psoriatic Arthritis (CASPAR criteria) in treatment for at least 6 months with anti-IL23 and in clinical remission (MDA). To analyze the production of IL-17A and IL-10 by regulatory T cells under basal culture and stimulated conditions (1 µg/ml Ionomycin (Fisher Scientific, EU) and 25 ng/ml forbol-12-myristate-13-acetate (PMA) (MP Biomedicals, EU)., monoclonal antibodies were used: anti-CD4-FITC, anti-CD25-PECy5, anti-FoxP3-PE, anti-IL-10-PECy7 and anti-IL-17A-APC (eBioscience, EU), were processed by flow cytometry (FACS Canto, BD Bioscience, EU).
Results: Percentage of Tregs expressing IL-10 in control condition Healthy: 1.787% BP: 1.418% P value = 0.7354. Percentage of Tregs expressing IL-10 in Healthy stimulated condition: 3.178% PA: 2.256% P value = 0.0108. Percentage of Tregs expressing IL-17A in control condition Healthy: 1.617% AP: 1.665% P value = 0.8923. Percentage of Tregs expressing IL-17A in Healthy stimulated condition: 6.298% PA: 3.742% P value = 0.0350
Conclusion: Although the controls and PsA patients in remission expressed a similar percentage of Tregs cells of both IL10 and IL17 at baseline, the same does not occur after stimulation in culture, showing an increase in both populations of Tregs (IL10-IL17) of the controls that did not occur in ArP patients in remission. This differs from RA patients in remission in which Tregs expressing IL10 is increased, as an expression of the different immunological mechanisms in both pathologies. Likewise, the Treg phenotype has been described with double marker RORγt/ FOXP3 and IL17 production. The plasticity of the T-cell compartment allows the immune response to adapt to the local environment. This is further emphasized by the recent recognition that Tregs themselves can differentiate into IL-17-producing cells, particularly when exogenous IL-1β, IL-23, or IL-21. In patients with psoriatic arthritis, IL-10 levels are increased. The inhibition of IL23 would be suppressing this production hence the double lack of response (Il10-IL17) of ArP patients in remission.

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Disclosure of Interests: None Declared.
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Innate immunity in rheumatic diseases

AB0021 REAL LIFE DATA ON TAPERING AND DISCONTINUATION OF ANAKINRA TREATMENT IN RECURRENT PERICARDITIS: AN INTERNATIONAL REGISTRY

Keywords: Cardiovascular disease, Tapering, Real-world evidence

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Background: Recurrent pericarditis (RP) affects up to 30% of patients after a first episode of acute pericarditis. The effectiveness of anakinra, an IL-1 recombinant receptor antagonist (IL-1r), has been established in recent clinical trials and multicenter studies[1,2] Currently the treatment with anakinra is usually prescribed as a third-line option in patients with RP and corticosteroid dependence not responsive to colchicine[3]. However, guidance for addressing optimal tapering strategies and discontinuation of biological treatment in RP is limited.
Objectives: To explore key factors for successful anakinra tapering and discontinuation and to investigate potential predictors of disease relapse after complete biologic treatment suspension.
Methods: An international, multicenter, retrospective registry including 18 recruiting centers from five countries (Italy, Greece, Slovenia, Canada, United States) was designed to investigate the disease characteristics of patients with recurrent pericarditis undergoing complete discontinuation of the anti-IL1r therapy anakinra.
Results: A total of 149 patients who had fully discontinued anakinra (59.6% female, median age 51.7 years) were included in the present registry. Most patients had idiopathic aetiology (109; 73.2%) while a first episode of pericarditis after post-cardiac injury syndrome (PCIS) or related to systemic inflammatory diseases was established in 30 and 10 cases (20.1% and 6.7%), respectively, with a median of 3 prior recurrences (interquartile range 2-4). Patients started anakinra treatment after a median time of 12 months (IQR 5-24) after a first episode of acute pericarditis, followed by a period at anakinra full-dosage with a median duration of 6 months (IQR 3–12). Among patients who experienced a recurrence (54 cases; 36.2%), 39 were female (72.2%, $p = 0.019$). Moreover, we observed a significant reduction in the recurrence of flares after an early introduction of anti-IL-1r treatment from first pericarditis episode (mean median time 10 months; IQR 4-18 vs 14 months; IQR 14-29; $p = 0.004$).
Conclusion: The main preliminary findings of this global registry suggest that an early introduction of anakinra in patients with RP, corticosteroid-dependent and not responding to colchicine, significantly reduces the recurrence of flares after discontinuation.
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Disclosure of Interests: None Declared.
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AB0022 IL-23 POSITIVE NEUTROPHIL IS THE MAIN CELL SUBTYPE IDENTIFIED FROM SYNOVIAL FLUID OF PSORIATIC ARTHRITIS WITH THE POTENTIATION OF NEUTROPHIL EXTRACELLULAR TRAPS FORMATION

Keywords: Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a systemic autoimmune disease. Interleukin-23 (IL-23) and IL-17 are two main cytokines involving in the pathogenesis of psoriasis (PsO) and PsA. The origin and maintenance of IL-23 is the stakeholder of disease progression in PsA and should be carefully evaluated.
Objectives: To validate the role of neutrophils in maintaining the inflammation in PsA joint.
Methods: Synovial fluid from PsA was obtained from swelling knee joints, and the immune cells were classified by flowcytometry. The IL-23 positive cells were evaluated with marker of CD66b, CD14, and CD16. Neutrophils from healthy donor were collected and treated with interferon-α (IFN-α) and proteoglycan (PGN) for mimicking the neutrophils activation in PsO/PsA patients. Subsequent evaluation neutrophil extracellular traps (NETs) formation was conducted.
Results: 10 PsA joints fluid was collected. Among active and chronic PsA synovial fluid, neutrophil is the most abundant cell type identified among IL-23 positive cells (ranging from 65-90%). The t-SNE plot for mapping the repertoire of IL-23 containing cells confirmed the majority cell subtype with CD66b+ positive neutrophils. After stimulating neutrophils from healthy donor with IFN-α and PGN revealed increasing IL-23p19 expression after 16 hours stimulation. The NETs formation is profound and IL-23p19 containing NETs material could be identified.
Conclusion: IL-23 containing CD66b+ neutrophil is the main cell type in synovial fluid of PsA, which might be activated by inflammatory factors and release IL-23 with NETs material to promote type 17 T cell differentiation in joints.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0023 GLUCOCORTICOIDS AND TNF INHIBITOR EXERT NOVEL REGULATORY MECHANISM THROUGH LAG-3 MODULATION IN SYNOVIAL CELLS

Keywords: Disease-modifying drugs (DMARDs), bDMARD, Synovium

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Background: Intra-articular (IA) injections of glucocorticoids (GCs) are clinically effective for the treatment of synovial inflammation in patients with persistent arthritis. TNF inhibitors (TNFi) utilization for IA injections was also reported with a varying efficacy [1, 2]. The mechanism of action of GCs and TNFi on regulatory mediators in the synovium is not fully understood. LAG-3 is a regulatory molecule that promotes suppressive immune response. LAG-3 expression could be regulated through multiple mechanisms, including modulation by different drugs.
Objectives: To investigate whether the regulatory mechanism of GCs and other anti-rheumatic drugs is mediated through change in LAG-3 expression in synovial cells derived from psoriatic arthritis (PsA) patients ex-vivo.
Methods: Synovial fluid mononuclear cells (SFMCs) derived from nine PsA patients were cultured ex-vivo with GCs ((betamethasone (BET) and methylprednisolone acetate (MPA)), Methotrexate (MTX), TNF, IL-17A, IL-12/23, and IL-1 receptor inhibitors namely: (Infliximab (IFX), Secukinumab, (SEC), Ustekinumab, (UST), and Anakinra (ANK), respectively) or with medium alone. After 5 incubation days, %$CD45^+LAG\text{-}3^+$ expressing cells was analyzed. We further assessed if the drugs' effect on SFMCs cell numbers in culture was accompanied with LAG-3 modulation. LAG-3 distribution on CD45, CD3, and CD14 cells was analyzed by flow cytometry (FACS).
Results: SFMCs treated with GCs showed a significant increase in %$CD45^+LAG\text{-}3^+$ cells (BET 1µg/ml, 6.8±1.3; BET 10µg/ml, 7.1±1.4; MPA 1µg/

ml, 6.7±1.3; and MPA 10µg/ml, 9.4±2.0, $p< 0.002$, respectively), while IFX showed only a small increase of these cells' population (2.0±0.3, $p= 0.08$) compared to the medium (1.0±0.3). Other treatments, including SEC, UST, ANK and MTX had no effect on %CD45$^+$LAG-3$^+$ cells compared to the medium, (1.0±0.2, 0.8±0.2, 0.8±0.2 and 0.9±0.2, respectively) (Figure 1A). After 5 days in culture, GCs (MPA) and IFX reduced SFMCs cell counts but this change was statistically significant only for GCs (21±5.1X10^5/well, $p< 0.01$ and 41±5.1X10^5/well, respectively), while MTX had no effect compared to the medium (49±4.8X10^5/well and 51±5.1X10^5/well, respectively) (Figure 1B). In this culture setting, GCs significantly increased the %LAG-3$^+$CD14$^+$ cells (12.8±2.1, $p< 0.001$) compared to the medium (0.9±0.4) but not the %LAG-3$^+$CD3$^+$ cells (Figure 1C and D).

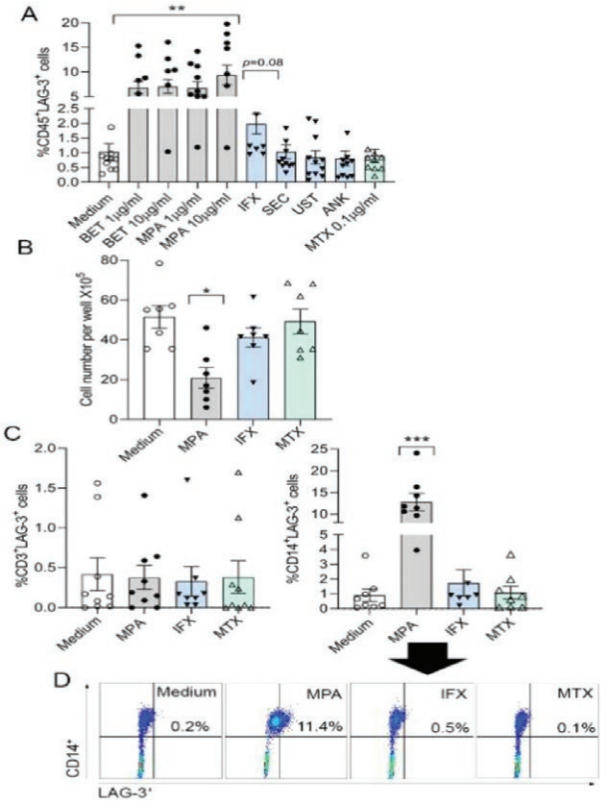


Figure 1. GCs and to a lesser extent infliximab up-regulate LAG-3 in SFMCs (A) PsA patients (n=9) SFMCs were cultured with BET, MPA, IFX, SEC, UST, ANK and MTX and analyzed by FACS for %CD45$^+$LAG-3$^+$ cells (B) SFMCs cell count analysis was performed after 5 days in culture with: MPA, IFX, MTX or medium (C) Cultures were then analysed for %CD3$^+$LAG-3$^+$ and %CD14$^+$LAG-3$^+$ cells by FACS (D) Representative PsA patient SFMCs FACS plots showing CD14 and LAG-3 expression after 5 days in culture with medium or the drugs indicated. Positive staining is presented in each plot right upper quadrant with the % indicated, *$p < 0.01$, **$p < 0.002$, ***$p < 0.0001$.

Conclusion: Our data shows that GCs immunosuppressive activity is mediated through LAG-3 up-regulation in SFMCs. Within the drugs tested, this activity was exclusively mediated by GCs and to a lesser extent by a TNF inhibitor. GCs reduced the SFMCs cell numbers and concomitantly up-regulated LAG-3 expressing cells, mainly in monocytes. This emphasizes that monocytes seem to be the main mediators of the GCs immunosuppressive effect.

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Disclosure of Interests: None Declared.

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AB0024

GENE EXPRESSION OF ABCG2, ALPK1, SLC22A12 AND IL-1B IN PERIPHERAL BLOOD LEUKOCYTES OF GOUT PATIENTS WERE CORRELATED WITH THEIR COMORBIDITIES AND HYPERURICEMIA

Keywords: Innate immunity, Gout, Crystal arthritis

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Background: Genes ABCG2, SLC22A12 (URAT1), and ALPK1 have been strongly associated with dysfunction of urate metabolism in patients with gout [1], but it is unknown how these transporters are expressed in patients with acute or chronic gout. Studies in murine and in vitro models have suggested that the enzyme ALPK1 kinase and the urate transporters ABCG2 and URAT1 may be involved in urate dysregulation and inflammation due to the presence of monosodium urate crystals [2-3]. It is important to know if the patient with acute or chronic gout can differentially express these genes in different tissues. Likewise, it is necessary to know if the patient's comorbidities may be associated with the expression of these transporters or pro-inflammatory molecules such as ALPK1 or IL-1β.

Objectives: To analyze the expression of urate transporters ABCG2, SLC22A12 and inflammation molecules ALPK1 and IL-1β in peripheral blood leukocytes from gout patients and to compare them with their metabolic profile and with the gene expression of people without gout and without hyperuricemia.

Methods: A total of 36 chronic and acute patients and 52 controls were recruited, ABCG2, SLC22A12, IL-1β and ALPK1 gene expression was evaluated by quantitative real-time PCR. Correlations of gene expression with clinical and laboratory parameters of patients were also analyzed.

Results: IL-1β was significantly increased in Peripheric blood monocytes cells (PBMCs) of patients when compared with their polymorphnuclear leukocytes

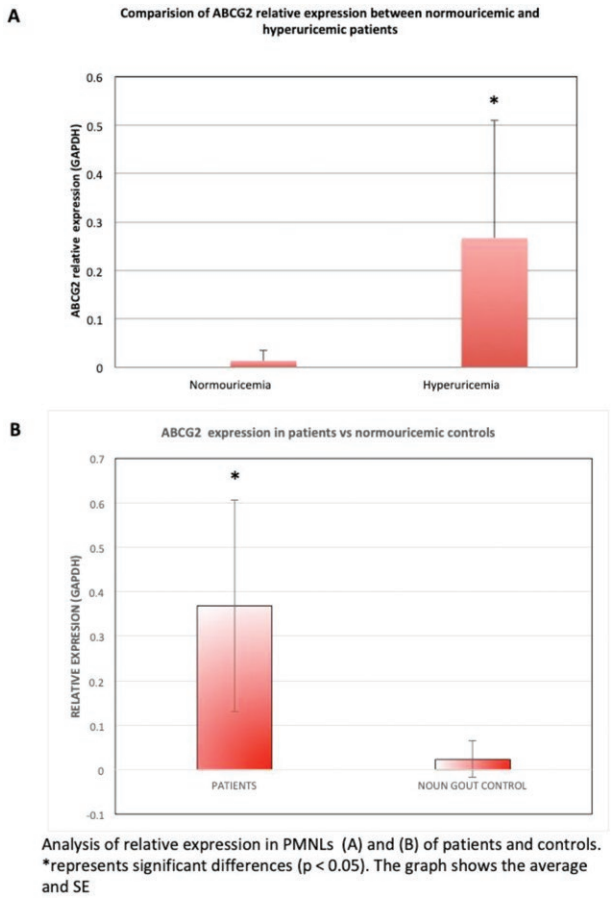


Figure 1.

(PMNLs) ($p<0.05$). A significant increase in ABCG2 were found in PMNLs from patients compared to controls ($p<0.05$) and in hyperuricemic patients compared to normouricemic patients ($p<0.05$) (see Figure 1). Correlations of gene expression in patients were related to levels of serum uric acid (sUA), serum creatinine, CRP, triglycerides, BMI, kidney disease, hypertension, and metabolic syndrome.
Conclusion: Our data suggest that the leukocyte cells of the patients respond to the presence hyperuricemia and comorbidities expressing ABCG2 gene differentially compared to normouricemic and non disease state. Hyperuricemia, dyslipidemias and obesity should stimulate the differential gene expression of peripheral blood leukocytes (neutrophils and monocytes) even in an asymptomatic stat.e.

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AB0025 LOW-DENSITY GRANULOCYTES AND NEUTROPHIL EXTRACELLULAR TRAPS IN INCOMPLETE SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Innate immunity, Systemic lupus erythematosus, Biomarkers

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with a complex and only partly understood pathophysiology, while incomplete SLE (iSLE) defines a group of patients with symptoms typical of SLE but not meeting sufficient criteria required for the classification of SLE. Up to 55% of patients with iSLE will eventually develop SLE, but it is unclear which patients are at risk of progression. [1] Neutrophil dysfunction, among which aberrant neutrophil extracellular trap (NET) formation driven by low density granulocytes (LDGs), has been implicated in SLE pathogenesis. [2] However, the role of neutrophil dysfunction in early forms of SLE is still unclear.
Objectives: The aim of this study was to investigate whether LDGs are elevated in the peripheral blood mononuclear cell (PBMC) fraction of iSLE patients, compared to healthy controls (HCs) and SLE patients with quiescent disease (SLEDAI<4). Next to that, we investigated presence of circulating NETs in plasma of iSLE as well as SLE patients and HCs.
Methods: Circulating plasma NETs were measured cross sectionally in 38 iSLE patients, 30 SLE patients with quiescent disease and 12 HCs while LDGs were measured in 18 iSLE patients, 13 SLE patients and 14 HCs. SLE patients were classified according to the Systemic Lupus International Collaborating Clinics (SLICC) criteria. Patients with iSLE had to meet at least one clinical and one immunological criterion but less than four SLICC criteria in total. LDGs ($CD14^{low}CD15^{+}$) were measured in freshly isolated PBMCs with flow cytometry as previously described [3] and were expressed as percentage of total PBMCs. Circulating plasma NETs were measured by using a previously validated sandwich enzyme linked immunosorbent assay [4] using a plate coated with an anti-myeloperoxidase antibody. Kruskal-Wallis tests were used to compare LDGs and NETs between groups. In case of significance, Mann-Whitney tests were used for pairwise comparison. A two tailed p-value of ≤ 0.05 was considered statistically significant.
Results: Proportions of LDGs and NET-levels were significantly increased in iSLE patients compared to HCs, as shown in Figure 1. The proportion of LDGs and circulating plasma NETs was similar between SLE and iSLE patients.
Conclusion: Our data shows significantly higher amounts of LDGs and circulating NETs in the iSLE and SLE cohort compared to healthy controls, suggesting that aberrant NET formation and clearance is present in early stages of the disease. In future studies, we aim to investigate the correlation between LDGs, circulating NETs and other immunological parameters, such as complement C3 and C4, and anti-dsDNA levels.

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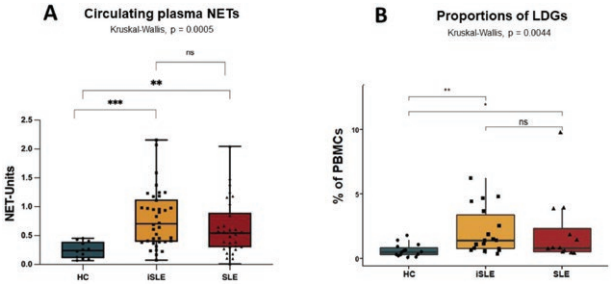


Figure 1. A: Circulating plasma NETs (neutrophil extracellular trap) per group measured with enzyme linked immunosorbent assay. **B**: Low density granulocytes (LDGs) measured with flow cytometry; Single data points represent individual cases. Median and interquartile range are depicted per group. Stars represent p-values for pairwise comparison calculated with Mann Whitney tests. *p <0.05, ** p<0.01, *** p<0.0001. HCs: healthy controls; iSLE: incomplete systemic lupus erythematosus, SLE: systemic lupus erythematosus.

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AB0026 mtDNA OXIDATIVE DAMAGE IS PROINTERFEROGENIC AND PRONETOTIC, AND RELATES TO ANTIPHOSPHOLIPID ANTIBODY POSITIVITY IN SLE

Keywords: Systemic lupus erythematosus, Innate immunity, Autoantibodies

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Background: Mitochondria are essential eucaryotic cell organelles with several bacterial features such as a circular genome with hypomethylated CpG areas, and a double cardiolipin membrane [1]. A fundamental role of mitochondria in systemic lupus erythematosus (SLE) was recently shown; mitochondrial ROS participate in neutrophil extracellular traps (NETs) formation [2], while extrusion of cell-free mitochondria and highly oxidised interferogenic mitochondrial DNA (ox-mtDNA) causes disease in an SLE animal model [3, 4]. Moreover, plasma mtDNA is a sensitive biomarker for SLE diagnosis and the clinical monitoring of SLE activity [5].
Objectives: The present study aimed to explore the cellular mechanisms controlling the inflammatory responses triggered by mtDNA in SLE.
Methods: Total DNA was isolated from healthy individuals' (HC) and SLE patients' plasma. Copy numbers were analysed by qPCR for mtDNA (ATP-6) and nuclear DNA (GAPDH). mtDNA was isolated from HC and SLE patients' platelets. Neutrophils were isolated from EDTA blood by negative selection; cells were incubated with SLE patients' plasma, and NET formation was assessed by Sytox-Green staining. Tofacitinib, a JAK1-JAK3 inhibitor, was utilised to assess the JAK-STAT pathway activation. DNA oxidation was assessed by MitoSOX Red staining *in vitro* and 8-hydroxy-diguanosine (8-OHdG) ELISA of plasma. Plasma IFN type 1 was measured by ELISA. Anti-phospholipid antibodies (aPL Abs) comprising of anti-cardiolipin (aCL) and anti-β2GPI, were analysed by ELISA and the lupus anticoagulant (LAC) test was performed.

Results: Neutrophils from healthy donors exhibit enhanced NET formation when incubated with from SLE patients' plasma (P=0.001), compared to HC plasma. Their NETs are decorated with ox-mtDNA (P=0.01). SLE patients' mtDNA elicits increased NETs (P=0.001) decorated with ox-mtDNA (P=0.001), which are both not entirely abolished after DNase1 treatment. Formation of NETs and ox-mtDNA extrusion seems to be partially regulated through the type I IFN pathway; JAK inhibition with tofacitinib diminishes, however not entirely, NET formation and ox-mtDNA release (56% and 60% decrease, respectively). mtDNA amounts correlate with 8-OHdG (R^2=0.87; P<0.0001) and type I IFN levels (R^2=0.60; P=0.001) in SLE patients' plasma. aPL Ab-positive SLE patients were characterised by higher plasma levels of mtDNA (P=0.004), but not nDNA, compared to aPL Ab-negative SLE patients. Interestingly, aPL Ab-positive and aCL Ab-positive SLE patients' plasma demonstrated a higher proNETotic capacity.
Conclusion: Oxidative damage of mtDNA promotes the formation of NETs, is particularly interferogenic, and NETs relate to the antiphospholipid antibody positivity in SLE patients' circulation. Circulatory ox-mtDNA might promote endothelial damage and vasculitis in SLE. A significant link between aPL, namely aCL IgG, and circulating mtDNA in SLE patients was evident, potentially aggravating the inflammatory state linked to disease severity and promoting thrombotic events.
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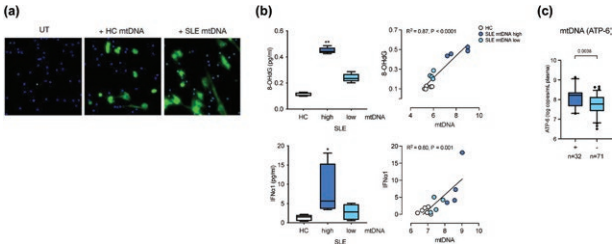


Figure 1. (a) SLE patients' mtDNA elicits increased NETs from HC neutrophils as assessed with SytoxGreen. **(b)** 8-OHdG levels are elevated in SLE plasma and correlate with mtDNA copy numbers and IFNa1 concentrations. **(c)** aPL Ab-positive SLE patients' plasma contains higher levels of mtDNA compared to aPL Ab-negative patients, as assessed by qPCR.

Disclosure of Interests: UW is coinventor of patents owned by Freiburg University; NV is coinventor of patents owned by Freiburg University.
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AB0027

ANTI-INFLAMMATORY EFFECTS OF TNF INHIBITOR AND METHOTREXATE ON IMMUNE CELLS FROM PERIPHERY AND SYNOVIAL FLUID: EX-VIVO STUDY

Keywords: Disease-modifying drugs (DMARDs), bDMARD

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Background: Methotrexate (MTX) and TNF inhibitors (TNFi) are pivotal treatments for inflammatory arthropathies. Even to date, the mode of action of these drugs on diverse inflammatory cell populations is not well characterized.
Objectives: To study the impact of MTX and TNFi on the proliferation of peripheral blood mononuclear cells (PBMCs) and the intermediate monocytes ($CD14^+CD16^+$) frequency in synovial fluid mononuclear cells (SFMCs). The study focused on monocytes expressing the $CD16^+$ as these cells promote synovial inflammation producing pro-inflammatory cytokines, including: TNF, IL-1β, and IL-6.
Methods: In this pilot exploratory study, we analyzed ex-vivo healthy donors PBMCs (n=19) proliferation without or with phytohemagglutinin (PHA) and PHA in presence of MTX and/or TNFi. Next, the effect of these drugs on $\%CD14^+CD16^+$ cells derived from psoriatic arthritis (PsA) patients SFMCs (n=11) was determined. Both assays were analysed by flow cytometry.
Results: Healthy donors PBMCs proliferation was inhibited by MTX (0.01 µg/ml and 0.1 µg/ml; 41.9±2.3 and 86.3±1.8, respectively) and to a lower extent by TNFi (infliximab, IFX) (1 µg/ml and 10 µg/ml; 43.1±2.5 and 49.4±2.5, respectively), whereas the combination of IFX 10 µg/ml and MTX 0.1 µg/ml led to the highest inhibition (91.0±2.0) (Figure 1 A and B). In PsA patients derived SFMCs, IFX 10 µg/ml significantly reduced ($p < 0.01$) the $\%CD14^+CD16^+$ cells (5.5±1.3) as compared to medium control (10.9±12.4), whereas MTX 0.1 µg/ml had only modest effect on this cell population (10.2±1.4). The combination of IFX 10 µg/ml and MTX 0.1 µg/ml resulted in the greatest reduction of $\%CD14^+CD16^+$ cells (5.1±1.1) (Figure 1 C and D).

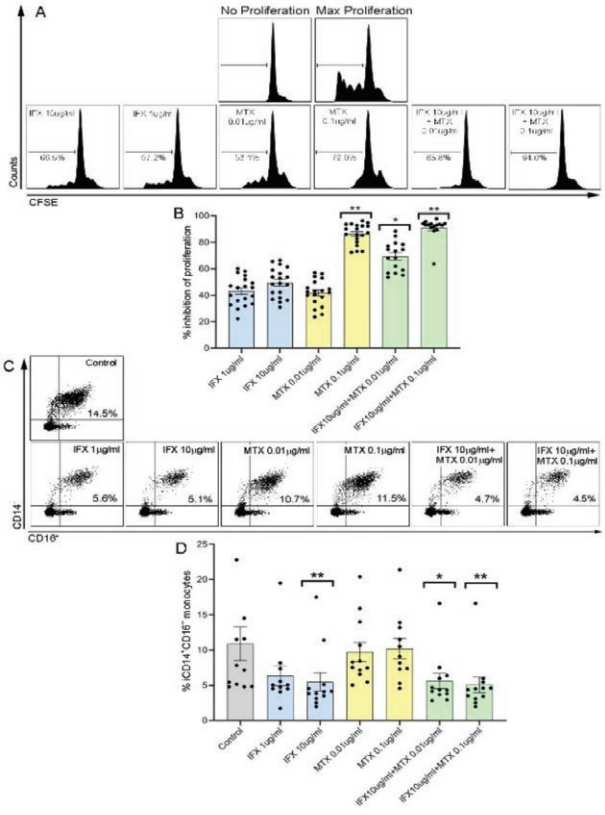


Figure 1. Ex-vivo effects of TNFi and MTX on proliferation inhibition and synovial $CD14^+CD16^+$ monocytes. CFSE-labeled healthy donors PBMCs (n=19) were incubated 5 days without PHA or with PHA alone (5µg/ml), or PHA in the presence of the drugs. (A) Representative plots showing CFSE-labeled healthy subject PBMCs. In the **upper panel**: Proliferation was measured either without PHA (no proliferation) or with PHA alone (maximal proliferation). Proliferation extent is shown in the left side of each plot. **Lower panel**: PHA with different drugs. Each image indicates %proliferation inhibition exerted by each drug. (B) Graph shows mean %proliferation inhibition, $*p < 0.05$, $**p < 0.01$.

SFMCs from PsA patients (n=11) were co-cultured for 7 days with the drugs or with medium alone. (C) Representative PsA patient SFMCs image gated for CD14 and CD16. Positive staining is presented in the right upper quadrant of each plot with $\%CD14^+CD16^+$ monocytes indicated. (D) Graph shows comparison between the groups. Statistical analysis was performed by the non-parametric one-way ANOVA Kruskal-Wallis test followed by Dunn's multiple comparison test, data are shown as mean ± SEM, $*p < 0.05$, $**p < 0.01$.
Conclusion: The immunomodulatory effects induced by TNFi and MTX provide indications for their anti-proliferative activity on PBMCs and on reduction of intermediate synovial monocytes, both involved in perpetuation of arthritis. While both TNFi and MTX inhibited PBMCs proliferation, only TNFi reduced the intermediate synovial monocytes, suggesting that different immune reactions could be controlled by specific drugs targeting distinct immune populations.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0028

LEUCOCYTE ABNORMALITIES IN SYNOVIAL FLUID OF DEGENERATIVE AND INFLAMMATORY ARTHROPATHIES

Keywords: Inflammatory arthritides, Cytokines and chemokines

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Background: Genome damage has been related to the induction of autoimmune processes, chronic inflammation, and apoptosis. Recent studies suggest that some rheumatological disease are associated with overall genomic instability in the T cell compartment [1,2]. However, no data regarding leucocytes abnormalities in synovial fluid (SF) and their relationship with inflammation are available.
Objectives: The aim of this study was to investigate cellular phenotypes in SF collected from patients with different inflammatory arthropathies, including rheumatoid arthritis (RA), psoriatic arthritis (PsA), crystal-induced arthritis (CIA) and non-inflammatory arthropathies such as osteoarthritis (OA).
Methods: SFs were collected by arthrocentesis from swollen knees of untreated adult patients with RA (n = 6), PsA (n = 12), CIA (n = 10), and OA (n = 7). Total white blood cell (WBC) count was performed using a Bürker counting chamber. Differential leucocyte count was performed by microscopic examination of 300 cells on May Grunwald Giemsa-stained preparations (MGG). Crystal search was performed using compensated polarized light microscopy. MGG staining was used for studying cellular morphology and to perform a cytogenic evaluation of leucocytes. All slides were examined for micronuclei (MN) and nuclear abnormality (NA) included binucleated cells, and karyolitic, karyorrhectic, and pyknotic cells. The following cytokines, chemokines and growth factors were measured in SFs using commercially available ELISA kits: interleukin (IL)-1β, IL-6, IL-8, IL-10, TGFβ, and TNFα. The expression levels of factors involved in apoptosis such as BCL-2, BAK, BID, BAD and BAX were measured by real-time quantitative PCR (qPCR). Caspase-3 activity was determined using commercially available colorimetric assay kit.
Results: We found high percentage of MN in SF from CIA and RA compared to the OA group ($p<0.05$) and a high frequency of pyknotic cell in RA ($p<0.05$) and CIA patients ($p<0.01$). The percentage of karyorrhectic and karyolitic cells were higher in RA patients with respect to OA and PsA patients ($p<0.05$). A correlation between pyknosis and immature polymorphonuclear cells with local inflammatory indices was observed. A strong positive correlation between local inflammatory cellular indices including WBC and PMN and the cytokines IL-1β, IL-6, IL-8, IL-10 was found. The study of apoptosis process revealed an increased BAX expression in CIA ($p<0.05$) and RA ($p<0.08$) compared to OA and PsA, while Bcl-2 was higher in CIA ($p<0.05$). Caspase-3 activity was increased in SF from RA patients compared to OA and PsA ($p<0.05$) and correlates with inflammatory and anti-inflammatory cytokines (IL-1β, IL-8, IL-10).
Conclusion: Our results showed that inflammatory SF are associated with genomic instability and abnormal cell subsets. A deeper knowledge of different abnormal cell subsets and their function could lead to a better understanding of the mechanisms underlying in the resolution of inflammation in these diseases.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0029 DISBALANCE OF SYNOVIAL FLUID CYTOKINES IN CHRONIC KNEE SYNOVITIS

Keywords: Synovium, Cytokines and chemokines

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Background: One of the most important issues of orthopedics remain long-standing synovitis despite the treatment after traumas and arthroscopy even after removal of mechanical irritating factor (meniscal resection, chondroplasty). In the long term prolonged treatment of arthritis may lead to irreversible joint damage progression. Current generally accepted strategy is to start the treatment as early as possible which affects the following disease course. Due to this, the study of pathogenetic features of posttraumatic synovitis is of interest as based on them, the choice of the most specific and effective treatment may be made.
Objectives: To study the features of cytokine level changes in synovial fluid in knee synovitis.
Methods: The prospective study of patients with long-standing knee synovitis included knee arthroscopy and outcome registration, measurement of cytokines in aspirated prior to surgery synovial fluid using flow fluorometry.
Results: The study included 41 patients (31.7% males and 68.3% females) with an average age 51.3±12.5 years. Trauma was present in 48.8% of patients. The duration of synovitis below 1 years was observed in 68.3% of patients, 56.1% of them had it for less than 6 months. Osteoarthritis stage 1 was observed in 24.4% of patients, stage 2 – in 22%, stage 3 – in 39%, stage 4 – in 14.6% of patients. The average VAS score on inclusion prior to arthroscopy was 3.56±0.72. Improvement immediately after the surgery was observed in 28 patients (68.3%). Other patients (31.7%) had long-standing synovitis (for over 2 weeks after the intervention), and 7 of them (17%) – for over 2 months. In the synovial fluid the level of IL-10 and TNFα decreased with increasing age (rs=-0,637, p=0,014 и rs=-0,481, p=0,044, respectively). The level of IL-10 positively correlated with synovitis duration (rs=0,830, p=0,011). Besides, in patients with synovitis duration more than a year, the level of IL-4 (r=0,578, p=0,024) and IL-10 (r=0,769, p=0,022) was higher. IL-4 was also higher with higher intensity of pain according to VAS score (rs=0,799, p=0,041). Also, there was a correlation of IL-6 level and presence of trauma in past medical history (p=0.05).
Conclusion: Proinflammatory TNFα and anti-inflammatory IL-10 positively correlated with the age. If synovitis was present for over a year, patients had higher levels of IL-4 and IL-10, which could be explained by proliferation processes in osteoarthritis. High pain intensity was associated with higher levels of IL-4. Trauma was associated with increased levels of IL-6 in synovial fluid, which may probably be the trigger factor of inflammation.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Osteo arthritis, aetiology, pathology and animal models

AB0030 OSTEOMODULIN DOWN-REGULATION IS ASSOCIATED WITH OSTEOARTHRITIS DEVELOPMENT

Keywords: Animal models, Osteoarthritis, Cartilage

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Background: Osteoarthritis (OA) is associated with metabolic and structural changes in all joint tissues. Subchondral bone sclerosis, cartilage degradation, and synovial inflammation are the main hallmarks of OA [1–3]. OMD is a keratan sulfate proteoglycan, a member of the small leucine-rich proteoglycan (SLRP) family. OMD was first identified in bone where it is involved in the mineralization process [4,5]. Our previous work demonstrated that in the secretome of osteoblasts, OMD was one of the most differentiating factors between osteoblasts originating from the sclerotic and non-sclerotic zone of OA subchondral bone [3]. OMD levels were lower in the supernatant of osteoblasts coming from the sclerotic area.
Objectives: The present work examined if OMD is involved in bone and cartilage changes occurring during skeletal development and in OA.
Methods: We used *Omd* knock-out (KO) or overexpressing male mice and mutant zebrafish to study *in vivo* the impact of OMD on skeletal development and aging. We investigated the influence of OMD on the severity of cartilage and bone damage induced by destabilization of the medial meniscus in these mice. We also analyzed the animals' gait using the CatWalk XT system. The effect of OMD on gene expression by human trabecular osteoblasts in monolayer culture was analyzed by RNA sequencing method. Finally, OMD binding to RANKL was assessed using a solid phase binding assay.
Results: In wild-type mice, we identified OMD mainly in bone and calcified cartilage. Tibial growth plate significantly decreased in all genotypes with age but to a lesser extent in the KO mice than in other genotypes. In KO mice, the calcified cartilage layer was thinner in the medial tibial plateau and thicker in the tibial lateral plateau than in the wild-type, while total cartilage thickness was not different between genotypes. We also demonstrated that *Omd* deficiency led to thicker and less porous bone and subchondral bone sclerosis. *Omd* knock-out mice spontaneously developed more severe OA cartilage lesions in the medial

tibial plateau than the wild-type during aging. In contrast, OMD production did not influence cartilage and bone changes induced by median meniscus destabilization. The gait pattern of mice was abnormal in KO compared to the wild-type genotype with a shorter swing and a smaller paw contact intensity. *omd*$^{-/-}$ zebrafish developed more severe cartilage lesions than wild-type. In osteoblasts culture, OMD down-regulated some genes involved in the extracellular matrix organization and up-regulated other genes responsible for the collagen network degradation. Finally, OMD bound to RANKL and inhibited osteoclastogenesis.

Conclusion: Alterations of the OMD expression modify bone and cartilage metabolism and structure. OMD helps to preserve bone and cartilage integrity and a local decrease in its production leads to the development of OA mainly by increasing subchondral bone sclerosis and thinning the calcified cartilage.

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Disclosure of Interests: None Declared.

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AB0031 ASSOCIATION BETWEEN OMEGA-3/6 FATTY ACIDS AND OSTEOARTHRITIS: A TWO-SAMPLE MENDELIAN RANDOMIZATION STUDY

Keywords: Osteoarthritis, Validation, Biomarkers

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Background: Osteoarthritis (OA) is the most common degenerative joint disorder worldwide. Accumulating evidence has demonstrated the associations of omega-3 and omega-6 PUFAs with the disease activity and inflammatory mediators of OA, omega-3 polyunsaturated fatty acids (PUFAs) are recognized for their anti-inflammatory properties[1], while omega-6 FAs are inflammatory mediators that are increased in joints with OA[2]. However, the evidence of causal links of omega-3 and omega-6 PUFAs on the risk for OA remains inconclusive.

Objectives: This study was conducted to evaluate the causal relationships between omega-3/6 and OA by performing the two-sample Mendelian randomization (MR) analysis.

Methods: The data set of this study was from the publicly available genome-wide association study (GWAS). The genetic instrumental variables for omega-3/6 were derived from the UK Biobank (UKB) and included 114,999 participants. Summary statistic data for OA originated from a meta-analysis of GWAS with an overall 50 508 subjects of European ancestry. In the MR Approach, the IV analysis is based on three strict assumptions, namely that IV should be strongly correlated with exposure, independent of confounding factors associated with direction and outcome, and influence outcome solely through exposure. We screened SNPs with genome-wide significance ($P < 5 \times 10^{-8}$). To ensuring that the SNPs were valid and independent, we removed the linkage disequilibrium (LD) between the SNPs at $r^2 < 0.001$, and <10,000 kb in size. Furthermore, the secondary phenotype of each SNP was retrieved to ensure that it was not associated with OA. The F statistic > 10 indicated a relatively strong estimated effect of IVs. Subsequently, two-sample Mendelian randomization analyses were conducted with inverse variance weighted (IVW), MR-Egger regression and weighted median methods. Sensitivity analyses were then conducted to assess the robustness of our results.

Results: The inverse-variance weighted (IVW) method revealed that higher omega-6 levels were correlated inversely with the risk of OA (β = -0.08, 95% CI [-0.16 to -0.02], P = 0.01), but no causal effect of omega-3 on the risk OA was observed (β = -0.04, 95% CI [-0.10 to -0.02], P = 0.15). The causal estimates from MR-Egger and weighted median methods revealed completely concurring effect directions ($\beta < 0$, $p < 0.05$). Cochran's Q of IVW analysis showed that there was heterogeneity among SNPs ($P < 0.05$), it does not affect the results of IVW, which shown the reliability of our results. MR-Egger regression analysis demonstrated that SNPs could have no-horizontal pleiotropy between omega-6 fatty acids and risk of OA ($P > 0.05$). Moreover, Results of the leave-one-out method suggested that MR results were not influenced by individual SNPs.

Conclusion: This study revealed that the high level of omega-6 predicted by genes can reduce the risk of OA. This implies that supplementing omega-6 fatty acids in our diet may be a potential nutritional modality for the prevention of OA.

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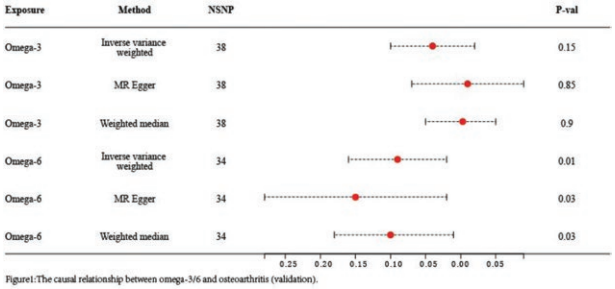


Figure 1. The causal relationship between omega-3/6 and osteoarthritis (validation).

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Disclosure of Interests: None Declared.

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AB0032 LOCAL EXPRESSION OF miRNAS IN OSTEOARTHRITIS PATIENTS

Keywords: Osteoarthritis, Biomarkers

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Background: Microribonucleic acids (miRNAs) comprise a class of small non-coding RNAs that negatively regulate the gene expression on posttranscriptional level. Altered expression of miRNAs has been described systemically as well as locally in the inflamed joints of patients with osteoarthritis (OA) [1-3].

Objectives: The aim of our study was to evaluate the synovial fluid (SF) expression of miRNA-146a (miR-146a), miR-155, miR-193 in OA patients and to determine their role as potential diagnostic biomarkers for this disease.

Methods: 16 OA patients were included in the analysis. Expression levels of miR-146a, miR-155 and miR-193b in SF samples were determined by qPCR (SybrGreen technology) and compared to healthy controls (HCs). Relative changes of gene expression levels of the studied miRNAs were calculated by $2^{-\Delta\Delta Ct}$ method. SPSS v20 was used for statistical analysis.

Results: OA SF showed statistically significant overexpression of miR-146a (in 75.00%), of miR-155 (in 68.75%) and of miR-193b (in 75.00%) when compared to HCs and these miRNAs could be used to differentiate OA from HCs ($p=5.9x10^{-3}$, p=0.043 and $p=5.5x10^{-3}$, respectively). Receiver operating characteristic (ROC) curve analysis was constructed in order to evaluate the diagnostic accuracy of the studied miRNAs in SF to distinguish OA from HCs by using relative expression (RQ) values. Area under the curve (AUC) for miR-146a was 0.830 (95%CI=0.674÷0.985, with 75.00% sensitivity and 72.70% specificity, p=0.004), AUC for miR-155 was 0.767 (95% CI=0.582÷0.952, with 75.00% sensitivity and 54.50% specificity, p=0.020) and AUC for miR-193b was 0.801 (95% CI =0.622÷0.981, with 87.50% sensitivity and 63.60% specificity, p=0.009). There was a correlation between the SF expression levels of miR-146a and miR-193b and the radiographic stage of the disease (p=0.0071 and p=0.0105, respectively). SF levels of miR-146a and miR-155 correlated with the SF cell count ($p=5.16x10^{-3}$ and p=0.0188, respectively).

Conclusion: We found an altered SF expression of miR-146a, miR-155 and miR-193b in OA patients when compared to HCs and these miRNAs could serve as potential diagnostic biomarker for inflammatory OA. Larger sets are needed to confirm the diagnostic accuracy of the studied miRNAs in OA.

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AB0033 JANUS KINASE INHIBITOR CAN SUPPRESS STAT3 ACTIVATION IN THE SYNOVIAL TISSUES FROM THE HIP JOINT IN THE EARLY STAGE OF RAPIDLY PROGRESSIVE OSTEOARTHRITIS OF THE HIP

Keywords: Osteoarthritis, Synovium, Targeted synthetic drugs

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Background: Rapidly progressive osteoarthritis of the hip (RPOH) is an unusual subset of hip osteoarthritis (OA). RPOH with femoral head destruction within 12 months after the onset is associated with increased serum levels of matrix metalloproteinase-3 (MMP-3). Interleukin-6 (IL-6) signaling activates STAT3, resulting in MMP-3 production in OA synovial fibroblasts in culture. The IL-6/gp130-associated Janus kinases/STAT3 axis plays a critical role in mediating inflammatory signals. No information is currently available on STAT3 activation in the synovial tissues in the early stage of RPOH. Recently, tofacitinib and meloxicam have been shown to inhibit STAT3 activation.
Objectives: This study aimed to investigate suppression of phosphorylated STAT3 in the synovial tissues from the hip joint with RPOH after incubation with the potential STAT3 inhibitors.
Methods: Synovial tissues near the acetabular notch of the hip joint were obtained from four RPOH patients with femoral head destruction at the time of total hip replacement. Whereas the initial radiograph showed no typical feature of OA such as joint space narrowing, formation of osteophytes or bone cysts, each patient developed chondrolysis with bone destruction. Duration between the disease onset and operation were 5-7 months. The serum concentration of MMP-3 was determined within two weeks before operation. The tissue samples were incubated for 1 hour with or without tofacitinib or meloxicam. Immunohistochemical examination was performed using anti-human CD3 antibody, anti-human CD68 antibody and anti-human phospho-STAT3 antibody. The number of phospho-STAT3-positive cells was counted in the three different areas of the synovium at a magnification of X 400. A mean percentage was calculated as phospho-STAT3-positive cells in all cell counts out of the three high-power fields in each of the four patients.
Results: The serum concentration of MMP-3 in each RPOH patient were above the reference intervals. RPOH synovial tissues demonstrated the synovial lining hyperplasia with an increase of CD68-positive macrophages and CD3-positive T lymphocytes. STAT3 activation was found in the synovial tissues by immunohistochemistry. The majority of phospho-STAT3-positive cells were the synovial lining cells and showed negative expression of CD68 or CD3. Treatment with tofacitinib resulted in a decrease in phospho-STAT3-positive cells. Immunohistochemical intensity of phospho-STAT3 staining in the nucleus were further classified as high or low, and phospho-STAT3-positive cell numbers were counted separately as high and low intensities. Tofacitinib decreased the percentage of phospho-STAT3-positive cells with high intensity with no alteration in the percentage of low intensity. In contrast, meloxicam showed no inhibition of STAT3 activation.
Conclusion: This study is the first report to show that Janus kinase inhibitor tofacitinib can suppress STAT3 activation in the synovial tissues in the hip joint with RPOH, mainly in synovial fibroblasts. STAT3 may be a potential therapeutic target for prevention of joint structural damage in RPOH. Currently, no non-operative treatment modality is available for RPOH. Based on the present results, tofacitinib may be an effective intervention before the occurrence of significant joint destruction by RPOH.
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Disclosure of Interests: None Declared.
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AB0034 NEXT GENERATION SEQUENCING AND SHIKONIN EFFECTS ON HUMAN PRIMARY ARTICULAR OSTEOARTHRITIS CHONDROCYTES

Keywords: Osteoarthritis

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Background: Osteoarthritis (OA) is one of the most common joint disorders, leading to functional disability, especially in people aged over 50 years, causing loss to the economy and affecting social development [1]. Drugs addressing the underlying biological causes of OA are not currently available [2].
Objectives: Naturally occurring naphthoquinone derivatives, such as shikonin and derivatives thereof, were shown to inhibit inflammatory processes and chondrocyte apoptosis by regulating the PI3K/AKT pathway in a rat model of OA [3]. The corresponding regulatory mechanisms in human OA chondrocytes and their influence by shikonin have not yet been investigated. To develop new therapeutic approaches, we investigated the effect of shikonin derivatives on inflammation, MMP expression, the regulation of MAPK signalling, and the gene expression patterns of DNA repair metabolism and the cell cycle in human healthy (HC) and OA chondrocytes (pCH-OA).
Methods: Viability was analyzed using the CellTiter-Glo® Assay. Inflammatory processes were investigated using a proteome profiler™ assay. Furthermore, we analyzed the effects of the shikonin derivatives by protein expression analysis of the phosphorylation pattern and the corresponding downstream gene regulation using RT-qPCR. Using next generation sequencing (NGS), we have analysed more than 70 key genes of the DNA damage metabolism and cell cycle.
Results: Both HC and pCH-OA showed a dose-dependent decrease in viability after treatment. The strongest effects were found for shikonin with IC50 values of 1.2 ± 0.1 µM. Shikonin counteracts the inflammatory response by massively reducing the expression of the pro-inflammatory mediators. The phosphorylation level of ERK changed slightly. pJNK and pp38 showed a significant increase, and the downstream targets c/EBPs and MEF2c may play a role in the cartilage homeostasis. STAT3 phosphorylation decreased significantly and has a chondroprotective function through the regulation of cyclin D1 and Sox9. NGS data showed a highly significant difference in gene expression under the influence of shikonin.
Conclusion: Our results demonstrate for the first time that shikonin derivatives have extensive effects on the inflammatory processes, MAPKs, the IL6/STAT3 downstream regulation and the DNA repair gene expression pattern in healthy and OA chondrocytes.
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AB0035 CHEMOKINES (IL-8 & GRO-A) AND CXCR1/2 PATHWAY INDUCES SENESCENCE INDUCTION IN CHONDROCYTES

Keywords: Cytokines and chemokines, Cartilage, Osteoarthritis

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Background: Tumor Necrosis Factor-α(TNF- α) and Interleukin(IL-1) are well-known in the induction of senescence in chondrocytes and play an important role in the pathogenesis of Osteoarthritis (OA). However, targeting these pathways has not yielded promising results. The chemokines IL-8(CXCL8) and Gro-α(CXCL1), as well as the CXCR1/2 pathways, are known to mediate inflammation and apoptosis. However, the precise role of these chemokines in the

pathogenesis of OA is unknown. We hypothesize that the CXCR1/2 signaling pathway is involved in the induction of senescence in chondrocytes.

Objectives: To evaluate the role of chemokines and CXCR1/2 pathway in induction of senescence in chondrocytes derived from patients with OA and healthy chondrocytes cell.

Methods: Healthy primary chondrocytes(HPC) cell lines and human primary chondrocyte cells derived from patients diagnosed with OA cultured and expanded up to passage 5. Cells were induced with IL-8 and GRO–a followed by determining the senescence marker via β -galactosidase(β-GAL, histochemical staining) and UPAR and P16NKa using qRT-PCR. Apoptosis in both HPCs and OPCs were done via Annexin V and Proprium iodide (PI) using Flow-cytometry. Statistical analysis was performed using un-paired t test and One-way-Anova.

Results: This study showed that the % of β-GAL in the HPC were almost negligible. However, showed significantly higher % in OPC(*p<0.001*). Moreover, when stimulated with IL-8, exhibited markedly increase in the positive blue cells in both HPCs and OPCs in a time dependent manner (p<*0.001*)(at 24 hrs., 48 hrs., 72 hrs. & 96 hrs.). In line with results of HPC and OPC stimulated with IL-8, OPC also showed higher % of senescence when induced with Gro- α (p<*0.001*)(at 24 hrs., 48 hrs.,72 hrs. & 96 hrs **{Figure 1(A)(B)(C)}.** Since TNF-α and IL1-β reported to have role in induction of senescence in chondrocytes, we have examined the β-GAL in HPC and OPC treated with TNF-α and IL1-β and found significant higher no. of blue stained in the OPC**(Table 1)**. These results were further validated by fold change expression of senescence induced genes *P16NKa* and *UPAR* at time dependent manner. We observed higher fold change expression of *P16NKa* in IL-8 induced OPC at 24 hrs. (*p=0.01*); at 48 hrs. (*p<0.001*); at 72 hrs. (*p=0.03*) and at 96 hrs. (*p<0.001*) with that of IL-8 induced HPC. However, stimulation with Gro-α showed increase in the expression of *P16NKa* in a time dependent manner(at 24 hrs., 48hrs., 72hrs. and 96 hrs.) in both OPCs and HPCs. Similarly, the expression of *UPAR in* IL-8 induced OPCs at 24 hrs.(*p=0.69*); at 48 hrs.(*p=0.05*); at 72 hrs. (*p<0.0001*) and at 96 hrs. (*p=0.01*) with that of Gro–α induced HPC. While the expression of *UPAR* in Gro–α induced OPCs and HPCs showed increase in a time dependent manner(at 24 hrs., 48 hrs., 72 hrs. and 96 hrs.). Flow-cytometric analysis revealed that induced cells were negative expression for apoptotic markers viz., Annexin V and PI.

Conclusion: Overall, this study highlights that IL-8 and Gro- α induce senescence in chondrocytes, a key event in the pathogenesis of OA. However, CXCR2 pathway may be explored further for therapeutic potential.

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Table 1. The % of β-GAL positive chondrocytes, mean ± SD

Time (Hrs.)	24	48	72	96
		HPCs		
C	2.959±2.131	3.563±1.627	2.402±2.110	2.817±2.279
IL-8	14.602±12.411	17.7893±6.808	36.808±5.314	46.956±16.709
Gro-α	10.112±4.420	19.328±5.840	34.544±9.813	47.852±13.321
TNF-α	14.496±16.698	20.731±8.859	38.899±11.321	50.712±13.865
IL1-β	11.283±3.926	18.944±5.945	34.279±5.812	32.445±11.695
		OPCs		
C	12.890 ± 3.2101	14 ± 6.309	13.094± 4.909	15.098± 3.980
IL-8	19.614 ± 3.3804	43.614 ± 10.301	66.234± 9.026	77.162± 10.936
Gro-α	18.021 ± 4.092	67.814 ± 11.3041	76.414± 5.024	83.112 ± 4.936
TNF-α	18.978±4.098	54.627 ± 8.337	79.902± 8.673	88.782±10.352
IL1-β	14.141±9.018	56.982 ± 9.378	77.834±6.342	89.342±7.892

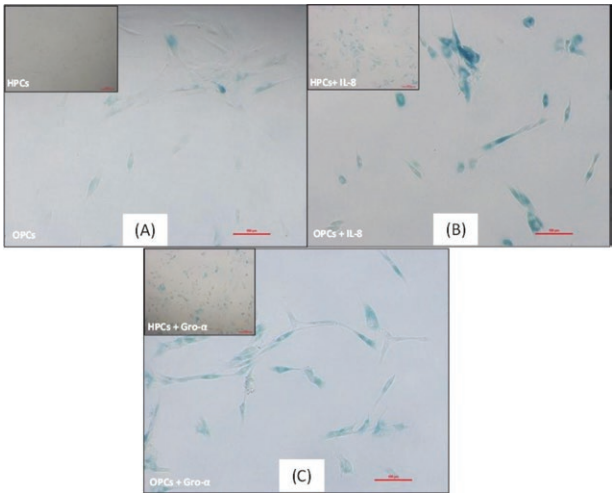


Figure 1.

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Disclosure of Interests: None Declared.

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AB0036 HIGH THROUGHPUT SIRNA EFFICACY SCREENING USING FLUORESCENCE SYSTEM

Keywords: Cartilage, Osteoarthritis, Genetics/Epigenetics

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Background: Osteoarthritis (OA) is characterized by loss of articular cartilage, bone remodelling and pain. It is a leading cause of disability in the elderly population. Currently, there are no disease modifying drugs to stop progression of OA. One bottleneck in clinical translation is that the cartilage extracellular matrix is avascular and impenetrable for large macromolecules. siRNA induces highly specific gene silencing and can be used for targets that are "undruggable". A novel therapeutic target that has been identified for treatment of OA include using siRNA to silence receptor tyrosine kinase–like orphan receptor 2 (ROR2) which offers great potential in improving pain outcomes and structural integrity in OA mice (Thorup et al., 2020). However, efficacy of "naked" siRNA is limited as it is instantly targeted for degradation by nucleases. To improve utility of siRNA as a therapeutic modality, chemical modifications can be introduced to the siRNA backbone, and it can be coupled with carrier molecules.

Objectives: To identify RNA backbone modifications to achieve long-term silencing in joint tissues following intra-articular injection.

Methods: Cos7 cells transduced with a lentivirus encoding EGFP and one specific clone was selected and expanded for downstream experiments (Eldridge *et al.*, 2016). Transfections were performed using JetPrime. Modified siRNA was generated by Integrated DNA Technologies.

Results: As a screening system, we optimized a microtitre plate system coupled with live fluorescent detection to measure GFP expression in cell monolayers. The fluorescence system uses a 96-well plate and allows for repeat measurements over time, without the need to harvest samples at each timepoint. Using this system, we compared 5 different modifications were compared. The best modification allowed to silence GFP in GFP-expressing cells for at least 10 days. The best modification was coupled with atelocollagen and administered via intra-articular injections into mice expressing GFP ubiquitously. After 3 weeks, GFP was efficiently silenced in the full thickness of the cartilage.

Conclusion: Chemical modifications of the RNA backbone and coupling with atelocollagen affords stable gene silencing in cartilage for at least 3 weeks. This technology enables fast, dose-dependent loss of function experiments in animal models of osteoarthritis. This methodology could be developed in the future to therapeutically target pathogenic molecules that are out of reach of traditional biologics such as transcription factors.

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Disclosure of Interests: None Declared.

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AB0037 GENETIC EVIDENCE REVEALS A CAUSAL ROLE OF WHITE BLOOD CELL COUNT IN OSTEOARTHRITIS

Keywords: Genetics/Epigenetics, Osteoarthritis

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Background: Osteoarthritis (OA) is increasingly recognized as a disease with a significant inflammatory component[1]. Signs of inflammation such as synovitis can be identified in OA patients using magnetic resonance imaging (MRI) and ultrasonographic imaging. The white blood cell count in synovial tissue has been considered useful in the assessment and diagnosis of arthritis. However, the causal relationship between the white blood cell count and OA has yet to be well.

Objectives: To investigate associations between white blood cell count and OA.
Methods: Mendelian randomized analysis (MR) was performed using white blood cell count as exposure data and OA as outcome data. This study included 173,480 individuals of European ancestry for exposure traits from three extensive UK studies[2]. The random effects inverse variance weighting (IVW) method was used for the primary analysis, and the weighted median and MR-Egger methods were supplemented for analysis. Then, we performed Cochran's Q test, MR pleiotropy residual sum and outlier (MR-PRESSO), to test for heterogeneity and horizontal multiplicity. The sensitivity analysis was also performed to verify the robustness of the primary results of the MR analysis.
Results: IVW method showed that knee or hip (OR=0.942, 95% CI:0.895-0.990, P =0.019), knee (OR=0.944, 95% CI:0.886-1.007, P=0.041) and hip (OR=0.929, 95% CI:0.868-0.995, P=0.035)had a protective effect on white blood cell count. After removing the confounding factors, we identified a significant causal association between white blood cell count and OA by IVW using residual single nucleotide polymorphisms (157 remaining in knee, 159 remaining in hip, and 159 remaining in knee or hip). P values of IVW were less than 0.05, indicating a significant causal relationship. Further sensitivity analyses validated the robustness of the MR results.(Figure 1)
Conclusion: There was a significant causal relationship between white blood cell count and OA. This is meaningful for the prevention and treatment of OA in the future.
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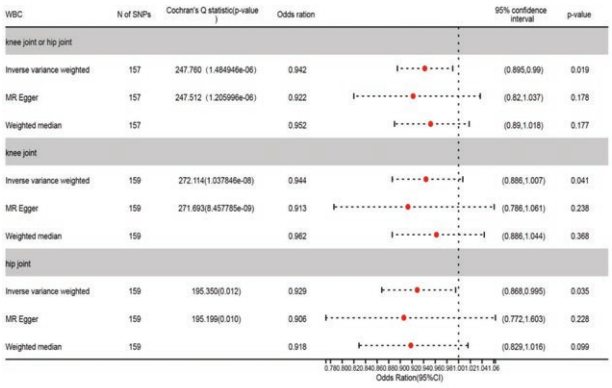


Figure1:Mendelian randomization estimates for association between WBC and osteoarthritis. WBC: white blood cell count.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0038 HINDLIMB SUSPENSION INDUCES KNEE MALALIGNMENTS WITH PATELLOFEMORAL OSTEOARTHRITIS IN GROWING RATS

Keywords: Cartilage, Physical therapy/Physiotherapy

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Background: Patellofemoral instability is a common disease in pediatrics and patients with Down's syndrome. Reduced weight bearing during growth in the rat hindlimb suspension (HS) model leads to abnormal morphologies of distal femur, which are associated with patellofemoral instability[1]. However, no study has examined whether reduced weight bearing can induce knee joint instability.
Objectives: The aim of this study was to test whether hindlimb suspension in skeletally immature rats affects knee joint alignments and patellofemoral joint pathology. We hypothesized that reduced weight bearing results in knee malalignments such as externally translocation of patella and lateral tibial rotation. Furthermore, lateral patellar dislocation occurs with arthritic changes in the patellofemoral joint.
Methods: Four-week-old female rats were used in this study. In HS groups, rats were applied hindlimb suspension for up to 8 weeks using a tail suspension method. Age-matched untreated rats were used as controls. Knee joints (tibia-femur complex) were isolated and three-dimensional reconstructed images were obtained using X-ray computed tomography. Tibial tubercle-trochlear groove (TT-TG), patellar tilt angle, and bisect offset were measured as indexes of femorotibial or patellofemoral joint malalignment. Histological analysis was also performed to evaluate the osteoarthritic changes in the patellofemoral joints. In addition, gene expression profiles of medial patellofemoral ligament (MPFL), which plays as a stabilizer of the medial aspect of the patella, were analyzed with microarrays in both groups at week 4.
Results: Knee alignment data are shown in Table 1. At week 8, TT-TG, patella tilt angle, and bisect offset in HS group were larger than those in age-matched control, respectively (all $P < 0.05$). These results indicated that tibial external rotation, patellar tilt outward, and external displacement of patella, respectively. In addition, lateral patellar dislocation appeared frequently after 8 weeks of HS (5/8 knee joint, Fisher's exact test, $P < 0.05$). Articular cartilage in the trochlear grooves decreased or disappeared at 8 weeks of HS, especially in the dislocated patellofemoral joint. Modified Mankin's histological score supported these osteoarthritic changes. Synovial hypertrophy was observed at 4 weeks and progressed at 8 weeks of HS. The findings were supported by OARSI synovitis score. Microarray analysis of MPFL revealed that the gene expression of matrix metalloproteinase (MMP)-2, -3, enzymes of collagen degradation, were higher in HS than control (log2 ratio: 1.24 and 3.09, respectively), and tissue inhibitor of metalloproteinase (TIMP)-3, -4, MMPs inhibitor, were lower in HS than control (log2 ratio: -1.79 and -2.84, respectively).
Conclusion: Reduced joint loading during growth resulted in knee malalignments such as external rotation of tibia, lateral tilt, and translocation of patella. In addition, high incidence of lateral patellar dislocation with concomitant patellofemoral OA was found after HS for 8 weeks. Patellofemoral instability may be involved in dysfunction of MPFL via degradation of collagens.

Table 1. Measurements of knee alignment

	Period (Age)	2 w (6 w old)	4w (8 w old)	8 w (12 w old)	Two-way ANOVA (*P*-values)		
					Interaction	Period	Intervention
Knee alignment index							
TT-TG (mm)	Cont	- 0.11 ± 0.51	- 0.07 ± 0.21	- 0.00 ± 0.42	0.565	0.184	**0.004**
	HS	0.17 ± 0.30	0.11 ± 0.26	0.44 ± 0.23*			
Patellar tilt angle (°)	Cont	9.2 ± 2.3[a]	7.9 ± 2.4[a]	4.6 ± 2.4[a]	**0.002**	0.704	**< 0.001**
	HS	9.7 ± 1.1[a]	10.5 ± 1.6[a]	16.2 ± 9.7[b]*			
Bisect offset (%)	Cont	54.3 ± 3.8[a]	53.1 ± 3.5[a]	52.0 ± 2.4[a]	**0.002**	**0.004**	**0.003**
	HS	56.3 ± 1.0[a]	56.0 ± 3.7[a]	104.7 ± 51.7[b]*			

Values are mean ± standard deviation. Different letters indicate statistically differences among same groups. *: significant difference between two groups at the same time point. Note: Statistically significant values for two-way ANOVA are indicated in bold. Cont: age-matched control. HS: hindlimb suspension.

Values are mean ± standard deviation. Different letters indicate statistically differences among same groups. *: significant difference between two groups at the same time point. Note: Statistically significant values for two-way ANOVA are indicated in bold. Cont: age-matched control. HS: hindlimb suspension.
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Disclosure of Interests: None Declared.
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AB0039 EXPRESSION OF INFLAMMATORY MARKERS IN PATIENTS WITH PAINFUL KNEE OSTEOARTHRITIS: A MULTIVARIATE ANALYSIS OF PRESURGICAL SERUM SAMPLES

Keywords: Pain, Biomarkers, -omics

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Background: Knee osteoarthritis (KOA) is a pathological condition prevalent in the general population. Exercise and pharmaceutical approaches are first-line treatments and the end-stage treatment is total knee replacement (TKR).

Interestingly, around 20% of patients experience chronic postoperative pain and the reason for this is not fully understood. Pain in OA is multifactorial and low-grade chronic inflammation has been indicated as a potential cause. Pre-clinical evidence suggests that pro-inflammatory mediators, such as interleukin 6, can sensitize the peripheral and central nerves and these molecules might be associated to clinical pain. Clinical evidence has demonstrated differences in pro-inflammatory mediators when comparing patients with OA and healthy individuals. A recent study has linked these profiles to chronic postoperative pain after TKR but an in-depth analysis, as seen for neuropathic and widespread pain is needed to advance the field. Currently, no specific biomarkers have been identified, despite initiatives on focused molecular inflammatory mediators. In an attempt to advance the field, a comprehensive analysis of an extensive network of cytokines, chemokines, and growth factors could identify the role of low-grade inflammation in patients with OA and potentially stratify patients more prone to experiencing pain.

Objectives: This study aimed 1) to evaluate preoperative serum levels of 92 inflammatory biomarkers in KOA patients compared to healthy controls, 2) to investigate preoperative differences of inflammatory biomarkers within different subgroups of patients with KOA and link these subgroups to clinical pain before and after TKR surgery.

Methods: Blood samples from preoperative patients with KOA scheduled for TKR (n=200) and healthy participants (n=39) were collected. After centrifugation of the serum was frozen at -80C until analysis. Serum samples were analyzed for inflammatory markers using the OLINK inflammation panel, which included 92 protein markers. Clinical pain was assessed using a Visual Analog Scale (VAS). Moreover, patients completed the Knee injury and Osteoarthritis Outcome Score (KOOS) questionnaire before and 12 months after TKR. Multivariate data analysis was performed to identify differences between patients and controls. Hierarchical cluster analysis (HCA) and Orthogonal Partial least squares discriminant analysis (OPLS-DA) was used for comparing groups (patients vs controls) and to identify subgroups within patients. T-tests were used to evaluate difference within the KOA cohort in terms of VAS and KOOS scores before and 12 months after TKR.

Results: Multivariate analysis showed that 12 proteins were differentially expressed between patients and controls (P<0.05). Hierarchical cluster and OPLS-DA analysis identified two patient subgroups (pat-1, n = 46; pat-2, n= 72) and 23 proteins were dysregulated comparing these two groups (p<0.01). Post-operative VAS and KOOS assessments were significantly different between the two subgroups (p-<0.05).

Conclusion: The present study suggest a low-grade inflammation in patients with KOA when compared to healthy pain free subjects. Additionally, this study suggests that a high inflammatory subgroup for patients with KOA exist and this group is likely to have more clinical and worst function 12-months after TKR.

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Disclosure of Interests: None Declared.

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AB0040 DIFFERENCIALLY EXPRESSED GENES IN PATIENTS WITH OSTEOARTHRITIS

Keywords: Biomarkers, -omics, Osteoarthritis

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Background: Osteoarthritis (OA) is a chronic degenerative disease that affects the joints, causing symptoms of arthralgias, swelling, loss of flexibility, etc. It is the most common rheumatic disease with an estimate of 27 million patients in the US [2]. Its pathophysiology is not yet well understood, as it is thought to be a result of multiple factors that induce metalloproteases, synovial angiogenesis and inflammatory cytokines that leads to inflammation and cartilage destruction [3]. To better understand the molecular mechanisms underlying this disease, we performed a meta-analysis with integrative bioinformatics.

Objectives: We aimed to obtain and assess overlapped differentially expressed genes (DEGs) in datasets of patients with OA through functional enrichment and protein-protein interactions (PPI).

Methods: We designed a search strategy in the Gene Expression Omnibus platform to identify datasets of gene expression profiling by array of patients with osteoarthritis. The inclusion criteria were: 1) Presence of healthy controls in the datasets, and 2) Analysis of data with GEO2R. The exclusion criteria were: 1) Incomplete information in the datasets, 2) Failure to identify case and controls, and 3) Gene expression by RNAseq. DEGs were selected when $p < 0.05$ and Logfold change > 2. We assessed the genes with DAVID database, and PPI through String and Cytoscape; and performed a prediction analysis of possible therapeutic targets.

Results: 6 datasets fulfilled the inclusion criteria, and 128 overlapped DEGs were identified. DAVID database yielded the top 3 Biological Processes involving those genes (Table 1). Cytoscape detected 3 clusters in which those genes interact, and iRegulon proposed CHD1 gene as a possible therapeutic target to regulate the entire cluster (Figure 1).

Table 1. Top 3 biological processes involving overlapped DEGs among the datasets.

Biological Processes		
Term	**Gene Count**	***p*-value**
Positive Regulation of B-cell activation	9	3,7E-7
Complement activation, classical pathway	9	2,0E-6
Phagocytosis, recognition	8	5,3E-6

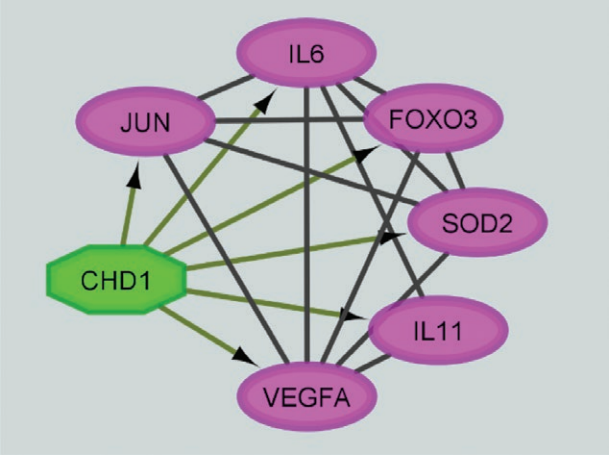


Figure 1. This cluster shows the genes with the strongest interactions. Cytoscape yielded other 2 clusters with a lower punctuation.

Conclusion: We aimed to identify and assess DEGs involved Osteoarthritis pathophysiology, as well as predict a possible therapeutic target. Our results suggest that immune processes involving B-cell activation and phagocytosis, as well as complement activation underlie OA pathophysiology. Validation of these results in patients with OA is needed since they can serve as possible diagnostic biomarkers. Further research is necessary to analyze the other clusters, and CHD1 characterization as a possible therapeutic target.

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Disclosure of Interests: None Declared.

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AB0041 IDENTIFICATION AND PROPERTIES OF EXOSOMES (EX) OF SYNOVIAL FLUID (SF) WITH GONARTROSIS (GA)

Keywords: Osteoarthritis, Synovium

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Background: EX - poorly studied extracellular vesicles, 30-150 nm in diameter, found in various biological fluids and have high functional activity, including immunomodulatory effects.
Objectives: The participation of EX in the development of complex connective tissue immunopathology requires further study. The aim of the work was to study EX of SF in GA.
Methods: SF of knee joints of 12 patients with GA with active synovitis and 7 conditional donors postmortem (D) were researched. EX was isolated by ultrafiltration and double ultracentrifugation (105 g).EX was identified by transmission electron microscopy and flow cytometry. Electrokinetic mobility (EM) determined by the automatic microscope. Registration of the active forms of oxygen (AFO2) was carried out by EPR. The activity of Cu-Zn superoxidismutase (Cu-Zn SOD), as well as DNA and RNA levels, was estimated by employing classical biochemistry methods.
Results: The EX population undergoes significant morphofunctional changes in GA: EX become smaller, their diameter decreases by an average of 2.5 times, and the value of the negative surface charge changes to 45.5%. EM EX at GA increases by 2.4 times. Against the background of the intensification of free radical processes in EX with GA, a decrease in the activity (on average by 1.7 times) of the pathogenic protein Cu-Zn-SOD is observed. The pronounced secretion of EX in GA is accompanied by an enhanced synthesis of information molecules, especially DNA, the amount of which increases by an average of 2 orders of magnitude (Table 1). At the same time, the floating density of EX in the sucrose gradient (g/ml) is normally 1.24 ± 0.09, and at GA 2.52 ± 0.14*.

Table 1. Some Characteristics of Synovial Fluid EX Populations in Normal (D) and in GA

EX	Diameter range, nm	Range charge, mV	DNA, µg/ml	RNA, µg/ml	Cu-Zn SOD, units/mg of protein	AFO2, units/mg of protein	EM, m/v sec
D	80 -120 (100)	-15,3; -13,4 (-14,4)	0,014 ± 0,003	0,085 ± 0,017	17,8 – 23,6 (20,7)	21,7 ± 3,7	0,84 ◆ 10-8
GA	30 – 50 (40)**	-10,2; -7,1 (-8,7)*	1,43 ± 0,32***	1,31 ± 0,2***	9,4 - 14,7 (12,1)*	48,4 ± 3,5 **	1,97 ◆ 10-8 **

* - p <0.05; ** - p <0.01; *** - p <0.001

Conclusion: The molecular mechanisms of GA progression are associated with the ability of EX to influence intercellular communication, epigenetically reprogram various target cells, activate protein biosynthesis, and be carriers of a number of mediators. Violation of exosomal immune intercellular communications, apparently, underlies the development of a variety of pathologies, including systemic connective tissue diseases.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4142

Bone diseases, aetiology, pathology and animal models

AB0042 AUTOPHAGY IS DECREASED IN BONE FROM OSTEOPOROTIC PATIENTS

Keywords: Osteoporosis, Bone diseases, Cell biology

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Background: Osteoporosis (OP) is a diffuse skeletal pathology characterized by major bone fragility that affects one out of 3 women after menopause. In addition to estrogen loss, an increase in oxidative stress is now recognized as a central mechanism in this pathology. Autophagy is an intracellular process allowing the removal and recycling of damaged proteins and organelles. Thanks to the elimination of damaged mitochondria, which are the main sources of reactive oxygen species, autophagy plays a major role in reducing oxidative stress. An age-related autophagy decline, associated with various experimental arguments in animal models, suggests autophagy implication in OP. However, a definitive proof in humans remains to be obtained.
Objectives: Our objective was to show for the first time that there is a defect in autophagy in the bone of osteoporotic patients.
Methods: We have analyzed autophagy by Western Blot in bone samples from 14 postmenopausal women with OP fracture compared to 30 controls undergoing total hip replacement for osteoarthritis.
Results: Our results indicate that the expression level of the autophagosome marker LC3-II is significantly decreased in OP patients compared to the age-matched controls. We also observed a tendency for the accumulation of the SQSTM1/p62 protein, which is an autophagy substrate, thus supporting the previous results. Finally, we also demonstrate a significant decrease in the hormonally up-regulated neu-associated kinase (HUNK) in bone samples from OP patients compared to the control group. This kinase, whose expression is upregulated by female hormones, promotes autophagy by inhibiting the autophagy inhibitor Rubicon through phosphorylation.
Conclusion: Taken together, these data demonstrate for the first time that OP patients have a deficit in osteocytes autophagy and suggest the involvement of the HUNK kinase in OP pathogenesis. This study should contribute to better understand the role of autophagy in OP pathophysiology and could lead to the design of new therapeutics targeting autophagy for the management of pathological aging.
Acknowledgements: We thank the French Society of Rheumatology for their funding.
Disclosure of Interests: None Declared.
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AB0043 SERIAL ADMINISTRATION OF RECOMBINANT HUMAN BONE MORPHOGENETIC PROTEIN-2 AND OSTEOPROTEGERIN-FC ENHANCES THE DIFFERENTIATION OF OSTEOBLASTS

Keywords: Bone diseases, Osteoporosis

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Background: Osteoprotegerin (OPG) is an intrinsic antagonist of the RANKL. A recent study reported that RANKL reverse signaling in osteoblasts may prepare osteoblasts for further maturation and that vesicular RANK stimulates osteoblast differentiation. Hence, OPG is expected to accelerate osteoblastogenesis by affecting RANKL reverse signaling.
Objectives: We compared the level of differentiation from preosteoblasts to osteoblasts by serially administrating recombinant human bone morphogenetic protein-2 (rhBMP-2), involved in bone formation and regeneration, and osteoprotegerin-immunoglobulin Fc segment complex (OPG-Fc), an osteoclast inhibitor.
Methods: The MC3T3-E1 preosteoblast cell line was differentiated for one, three, and seven days with a treatment of OPG-Fc in 10–200 ng/mL concentration and the cell viability was evaluated by Cell Counting Kit-8 analysis. The level of differentiation from MC3T3-E1 cells to osteoblasts was determined by alkaline phosphatase activity. The level of runt domain-containing transcription factor 2 (Runx2) and osteopontin (OPN) manifestation, involved in osteoblast differentiation, was examined by real-time polymerase chain reaction and western blotting.
Results: During MC3T3-E1 cell differentiation, the differentiation level was high with one-day treatment using 100 ng/mL OPG-Fc. The treatment with 50 ng/mL rhBMP-2 for seven days, followed by one-day treatment with 100 ng/mL OPG-Fc produced the highest differentiation level, which was approximately 5.3 times that of the control group ($P < 0.05$). The expression of Runx2 mRNA significantly increased, reaching 2.5 times the level of the control group under the condition of seven-day treatment with rhBMP-2 and one-day treatment with OPG-Fc ($P < 0.001$). The expression of Runx2 protein significantly increased to approximately 5.7 times that of the control group under the condition of seven-day treatment with rhBMP-2, followed by one-day treatment with OPG-Fc ($P < 0.01$). The expression of OPN protein showed no change from that of the control group under various conditions of rhBMP-2 and OPG-Fc combinations.
Conclusion: Differentiation ability of preosteoblasts to osteoblasts was strong with serial treatment and rhBMP-2, followed by OPG-Fc. Runx2 and OPN mRNA levels and Runx2 protein levels increased. These results imply that the combination of OPG-Fc and rhBMP-2 increased osteoblast differentiation efficacy.
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Rheumatoid arthritis - aetiology, pathogenesis and animal models

AB0044 **INTERLEUKIN-18 BINDING PROTEIN REGULATES THE APOPTOSIS AND NECROPTOSIS OF FIBROBLAST-LIKE SYNOVIOCYTES AND CHONDROCYTES IN RHEUMATOID ARTHRITIS**

Keywords: Adaptive immunity, Rheumatoid arthritis, Cartilage

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Background: Interleukin (IL)-18 plays a pro-inflammatory role in rheumatoid arthritis (RA), and its decoy receptor IL-18 binding protein (IL-18BP) has a potential therapeutic role.
Objectives: We investigated the role of IL-18BP on the joint destruction process of RA by accessing the effects of IL-18BP on fibroblast-like synoviocytes (FLSs) and chondrocytes.
Methods: Peripheral blood mononuclear cells (PBMCs) from patients with RA and healthy controls were cultured under T cell proliferative conditions with 10, 50, or 100 ng/mL of IL-18BP. After three days of culture, flow cytometry for CD4+ T cells was performed using various IL-18BP concentrations. The apoptosis and necroptosis of FLSs and chondrocytes were measured by flow cytometry using annexin V and propidium iodide (PI) and western blot under TNF-α stimulation with IL-18BP (10, 50, and 100 ng/mL).
Results: Differentiation of CD4+ IL-17A+ and CD4+ IL-4+ cells decreased and that of CD4+ CD25high Foxp3+ and CD4+ interferon (IFN)-γ+ cells increased on addition of IL-18BP to cultured RA patient-driven PBMCs. RA-FLS migration ability was not suppressed by IL-18BP after 12 or 24 h. IL-18BP increased annexin V+ FLS level and reduced annexin V+ chondrocyte level in a dose-dependent manner, whereas PI+ annexin V- FLS and chondrocyte levels were suppressed by 50, 100 ng/mL IL-18BP in culture.
Conclusion: The administration of IL-18BP regulated the type 17 helper T cell/ regulatory T cell imbalance and attenuated the production of pro-inflammatory cytokines. IL-18BP further increased FLS apoptosis and decreased the necroptosis of FLS/chondrocytes and apoptosis of chondrocytes suggesting the joint preservative potential of IL-18BP.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1067

AB0045 **CXCL14 IN EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS**

Keywords: Cytokines and chemokines, Biomarkers, Rheumatoid arthritis

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Background: Single cell sequencings studies have identified a CXCL14+ synovial fibroblast cluster in synovial tissue. This CXCL14+ cluster express CD34 and correlate to lower DAS28 and swollen joint count, while being similar between genders, age or sero status [1]. The biological role of CXCL14 in rheumatoid arthritis (RA) is unknown, but CXCL14+ synovial fibroblasts have been shown to express abundant GAS6, which regulate remission functions in MerTK+CD206+ synovial tissue macrophages [2]. This may suggest an anti-inflammatory or pro-remission role of the CXCL14+ synovial fibroblast cluster in specific RA pathotypes [1].
Objectives: Our study aimed to investigate soluble CXCL14 in plasma and synovial fluid and its potential connection to long term joint deterioration and disease activity in RA.
Methods: We used optimized commercial CXCL14 ELISA kits to investigate CXCL14 levels in 3 cohorts. 1) Plasma samples from patients with early RA (eRA) from the methotrexate arm of the CIMESTRA trial (N=80) [3]. 2) Plasma and synovial fluid from patients with established RA included at time of therapeutic arthrocentesis (the INART cohort) (N=41). 3) Plasma from matched healthy controls (HC) (N=44).
Results: Plasma CXCL14 was significantly higher compared to synovial fluid, median 2.3 ng/ml. CXCL14 levels in the two compartments corelate. Plasma and synovial fluid CXCL14 were not influenced by gender, ACPA, smoking status, disease duration or time since sampling. Age and rheumatoid factor status may affect plasma CXCL14 levels, but this was not consistent in both RA cohorts. Analysis showed a significant higher amount of plasma CXCL14 in patients with RA from the INART cohort, median 6.9 ng/ml, compared to eRA, median 4.8 ng/ml and HC, median 4.3 ng/ml. Plasma CXCL14 did not change significantly in patients with eRA after 1 year of treatment. Baseline plasma CXCL14 in patients with eRA significantly correlated to baseline tender joint count, but not DSA28, swollen joint count or total sharp score. Baseline plasma CXCL14 correlated to DAS28 after 5 years of treatment. Evaluating DAS28 after 11 years of treatment we observed a difference between patients in remission (DAS<2.6) and patients with active disease (DAS28 ≥ 2.6). For patients in remission, baseline CXCL14 correlated inversely with DAS28, whereas this correlation was positive in patients with active disease (Figure1). No associations were present between CXCL14 and change in total sharp score over a 11-year period.
Conclusion: Soluble CXCL14 can be measured in both plasma and synovial fluid from patients with RA. Plasma CXCL14 levels are higher compared to synovial fluid but a significant correlation is present between to two compartments. This suggests plasma CXCL14 as a potential proxy for CXCL14 activity in the joint and joint fluid. CXCL14 was not affected by gender, disease duration, smoking or 1 year of cDMARD treatment. Baseline CXCL14 correlated to higher DAS28 in the CIMESTRA cohort after 5 years and in patients with active disease after 11 years. Interestingly, we noticed that baseline CXCL14 may associate to lower DAS28 in patients in remission after 11 years. Together, this may support previous studies associating CXCL14 to an active anti-inflammatory (positive CXCL14/DAS28 correlation in active disease group) and pro-remission (negative CXCL14/DAS28 in remission group) role in RA.
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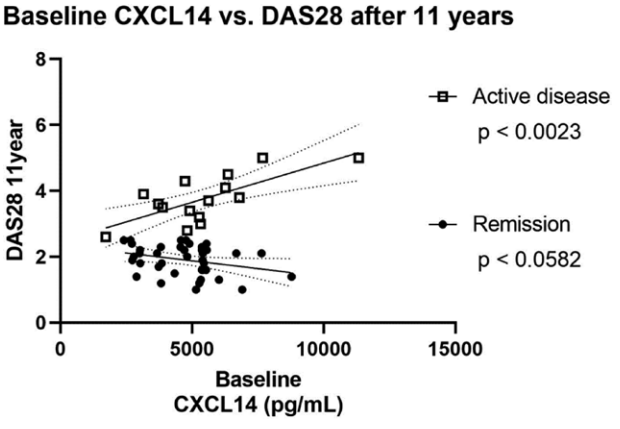


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: Søren Lomholt: None declared, Louisa Hunskjær: None declared, Stinne Ravn Greisen: None declared, Tue Wenzel Kragstrup Shareholder of: Co-founder and clinical developer in Aptol Pharma., Speakers bureau: Speaking fees from Pfizer, Bristol-Myers Squibb, Eli Lilly, Novartis, UCB, and Abbvie., Consultant of: Consultancy fees from Bristol-Myers Squibb, UCB, Gilead, and Eli-Lilly., Grant/research support from: Research grants from Gilead.
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AB0046 **OMEGA-3 EPOXIDES AMELIORATE MURINE INFLAMMATORY ARTHRITIS**

Keywords: Diet and nutrition, Animal models, Inflammatory arthritides

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Background: Epoxy fatty acids (EpFA), cytochrome P450(CYP)-mediated metabolites of polyunsaturated fatty acids (PUFA), have anti-inflammatory effects[1]. However, EpFA is quickly converted to an inactive form by the soluble epoxide hydrolase(sEH). In recent years, the efficacy of sEH inhibitors (sEHi) has been reported in a variety of diseases[2-4]. However, compared to ω-6 epoxides, such as epoxyeicosatirienioic acids (EET) derived from arachidonic acid (AA), there are few reports on ω-3 epoxides, epoxyeicosapentaenoic acid (EEQ) from eicosapentaenoic acid (EPA) and epoxydocosapentaenoic acids (EDP) from docosapentaenoic acid (DHA)5), and their effects on arthritis are not well understood.

Objectives: To investigate and compare the effects of ω-6 and ω-3 epoxides on inflammatory arthritis.

Methods: Collagen induced arthritis (CIA) were treated with three different diets (ω-6 PUFA rich, ω-3 PUFA rich, and Control) and two types of drinking solution, one containing sEHi and the other containing only polyethylene glycol as solvent control (total 6 groups, 8 mice each). Arthritis and pathological scores were evaluated, and feces were collected before the onset of arthritis (day 25) for intergroup comparative analysis of bacterial flora.

Results: In all the dietary groups, there was a tendency for arthritis scores to decrease with sEHi administration, but the incidence of arthritis, arthritis scores, and pathological scores decreased dramatically in the group fed with the ω-3 rich diet and sEHi combination. The groups fed the ω-6 rich diet and Control diet showed almost similar results. In the ω-3 rich diet and sEHi combination group, showed an increase in a certain specific bacterial strain.

Conclusion: ω-3 epoxides were found to be more effective in reducing arthritis, and changes in intestinal bacteria may have influenced this pathological change.

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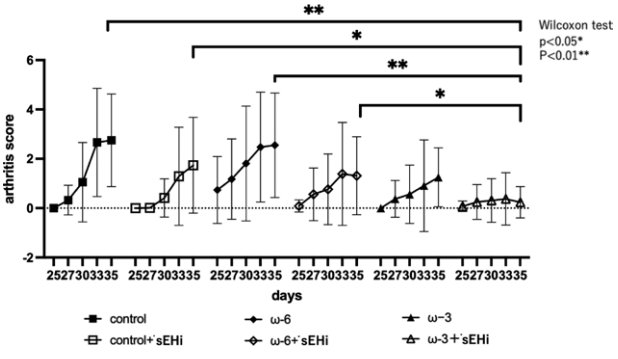


Figure 1.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0047 **THERAPEUTIC POTENTIAL OF COLLAGEN-DERIVED PEPTIDE P90578 IN THE TREATMENT OF RHEUMATOID ARTHRITIS**

Keywords: Autoantibodies, Rheumatoid arthritis, Vaccination/Immunization

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Background: Antigen-specific peptide immunotherapy is a booming treatment strategy for autoimmune diseases and designs to restore immune tolerance against self-antigens. Published research findings and our previous study using peptides derived from type II collagen with chemical modification such as glycosylation and fructosylation as therapeutics showed promising outcomes in the reduction of arthritis progression[1,2]. However, the optimal choice of peptide doses in the rheumatoid arthritis (RA) murine model and its therapeutic effect on human samples still awaits to be investigated.

Objectives: The present study further investigated the optimal dose and therapeutic potential of our novel collagen-derived peptide P90578 in the arthritis murine model and RA patient serum samples.

Methods: Male 8-week-old DBA/1 mice were immunized s.c. at the base of the tail with 0.1 mg bovine collagen II and s.c. at the left flank with 0.2 mg human fibrinogen, each of which was separately emulsified in a 1:1 ratio with complete Freund´s adjuvant. On day 21 after the immunization, mice were boosted with 0.2 mg human fibrinogen in incomplete Freund´s Adjuvant s.c. at the left flank. Peptide P90578 or NaCl was intraperitoneally administered three times weekly at 3-day intervals starting on days 7, 24, and 42. Hind paws of the mice were examined for macro-anatomical pathology. Right hind paws of the mice were prepared post mortem and fixed in 4% paraformaldehyde, and embedded in OCT compound. Sagittal sections of 7 µm were cut with an interval of 500 µm and stained with H&E using standard protocols. A histological score was determined based on microscopically pathologic changes of the ankle and tarsal joints. Antibody level against assayed peptides was measured in the serum collected on days 0, 14, 35 and 56 by ELISA assay. Competitive ELISA assays were done by pre-incubation of 10 mg peptide P90578 with sera from RA diseased mice (day 56) and RA patients. Then, the mixture of peptide P90578 and sera was cultured in the plates coated with each of the assayed peptides.

Results: We administered peptide P90578 at a concentration of 1mg/kg, 3mg/kg or 5mg/kg to the arthritic mice. Among the three test groups, the dose of 5mg/kg P90578 revealed the most optimal outcome on arthritis treatment with a reduced severity of tarsal and carpal joint swelling and a lower mean arthritis score compared to the NaCl control (Figure 1A). Hence, we applied the dose of 5mg/kg P90578 in our following experiments. In order to confirm the observation of our findings, we then performed a detailed microscopic examination on the right hind paws. The NaCl-treated mice showed signs of inflammatory cell infiltration, cartilage & bone erosion and typical pannus formation. In contrast, the mice receiving peptide P90578 had structural intact cartilage and minimal infiltration of lymphocytes in the subchondral bone. P90578-treated mice also showed a lower histological score of the joint sections (Figure 1B). Autoantibody levels in all three measurements represented a consistent trend toward decreased antibody titers in the serum of mice treated with peptide P90578 (Figure 1C). Considering the diversity of autoantigens in RA, the cross-reactivity of peptide P90578 binding to each epitope-specific autoantibodies was determined by competitive ELISA. The recognition of autoantibodies against the measured peptide epitopes was reduced by the peptide P90578 about an average of 20% in the RA diseased mice and by approximately 10% in the sera of RA patients, in some cases even exceeding 30% (Figure 1D).

Conclusion: Our study provides evidence showing this novel therapeutic peptide P90578 (5mg/kg) alleviated arthritic burden in the arthritis murine model. Also, autoantibody levels against CCP and peptides derived from collagen and fibrinogen were also reduced after peptide P90578 treatment. Moreover, peptide P90578 can effectively block the binding of autoantibodies in the serum from RA diseased mice and RA patients to the autoantigens.

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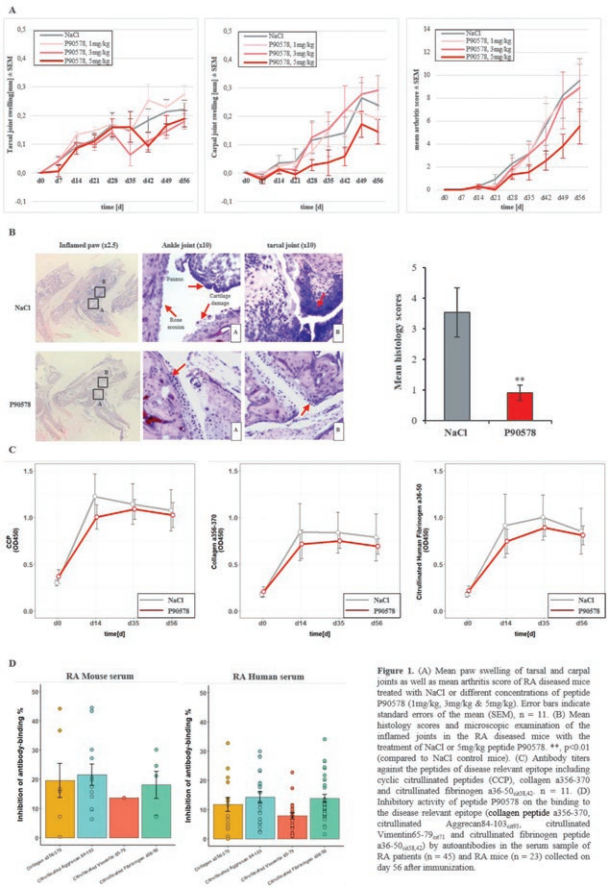


Figure 1. (A) Mean paw swelling of tarsal and carpal joints as well as mean arthritis score of RA diseased mice treated with NaCl or different concentrations of peptide P90578 (1mg/kg, 3mg/kg & 5mg/kg). Error bars indicate standard errors of the mean (SEM), n = 11. (B) Mean histology scores and microscopic examination of the inflamed joints in the RA diseased mice with the treatment of NaCl or 5mg/kg peptide P90578. **, p<0.01 (compared to NaCl control mice). (C) Antibody titers against the peptides of disease relevant epitope including cyclic citrullinated peptides (CCP), collagen a356-370 and citrullinated fibrinogen a36-50$_{cit36,cit}$. n = 11. (D) Inhibitory activity of peptide P90578 on the binding to the disease relevant epitope (**collagen peptide** a356-370, citrullinated Aggrecan84-103$_{cit93}$, citrullinated Vimentin65-79$_{cit71}$ and citrullinated fibrinogen peptide a36-50$_{cit36,cit}$) by autoantibodies in the serum sample of RA patients (n = 45) and RA mice (n = 23) collected on day 56 after immunization.

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Disclosure of Interests: None Declared.
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AB0048

IL-37 ALLEVIATES TNF-Α-INDUCED PYROPTOSIS OF RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES BY INHIBITING THE NF-ΚB/GSDMD SIGNALING PATHWAY

Keywords: Rheumatoid arthritis, Cytokines and chemokines, Animal models

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Background: Pyroptosis is crucial to rheumatoid arthritis (RA) by inducing and aggravating inflammation. TNF-α is abundant in fibroblast-like synoviocytes of RA (RA-FLSs) and plays a key role in pyroptosis by inducing nuclear factor (NF)-κB activation. Additionally, interleukin (IL)-37 is involved in autoimmune diseases as an anti-inflammatory cytokine and innate and acquired immune response inhibitor. However, the effect of IL-37 on pyroptosis in RA-FLSs remains unclear.
Objectives: To investigate the effects and mechanism of IL-37 on RA-FLS pyroptosis induced by TNF-α and the effect in collagen-induced arthritis (CIA)+TNF model.
Methods: In this study, the serum cytokines in patients with RA and healthy controls were detected using ELISA. The RA-FLSs were then cultured with TNF-α, with or without various IL-37 concentrations, to test the cytokine levels in the cell supernatant. 5-Ethynyl-2′-Deoxyuridine (EdU) assay assessed the effects of IL-37 on RA FLS proliferation. RA-FLS apoptosis was assessed using flow cytometry and mitochondrial membrane potential (MMP) measurement. In addition, transmission electron microscopy (TEM) was used to examine cell pyroptosis. We selected the optimal concentration for the following experiments and detected the signal pathway of IL-37 on pyroptosis of RA FLSs by quantitative reverse-transcription polymerase chain reaction (qRT-PCR) and Western blotting. Finally, we validated the therapeutic effects of IL-37 on CIA rat model in vivo.
Results: IL-37 inhibited inflammation in vitro and in vivo and reduced pyroptosis-related protein expression in RA FLSs. Furthermore, we determined that nuclear factor κB (NF-κB) signaling is required for GSDMD-mediated pyroptosis in RA FLSs.
Conclusion: IL-37 alleviates TNF-α-induced pyroptosis of RA FLSs by inhibiting NF-κB/GSDMD signaling. Additionally, our data revealed a novel mechanism for IL-37 in RA FLSs, suggesting a new potential therapy for IL-37 to treat RA.

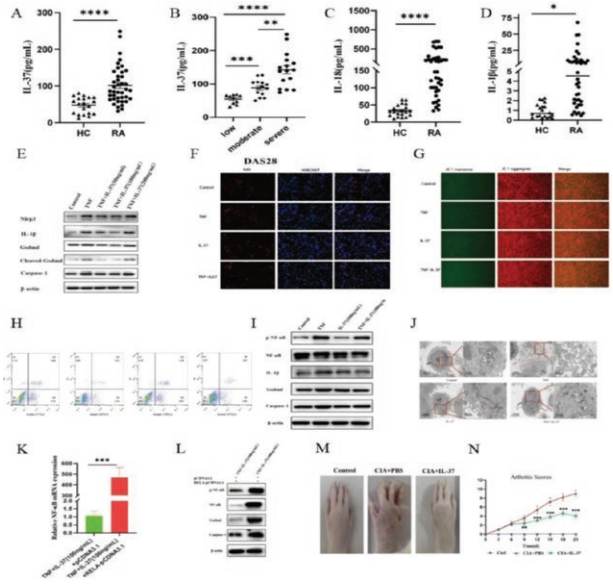


Figure 1. Serum levels of IL-37,IL-1β,IL-18, the mechanism of IL-37 on RA-FLSs and the therapetic effects in CIA-TNF model. (A)IL-37,(C)IL-1β,(D) IL-18 in RA patients and healthy controls. (B) Levels of IL-37 in RA patients with low,moderate and severe DAS28.(E)The expression of pyroptosis-related proteins analyzed by Western blot.(F) Cell proliferation activity in TNF-α and/or IL-37 stimulated groups..(G) Detection of mitochondrial membrane potential by JC-1 (H) Flow cytometry analysis of each group.(I) Representative Western blots of the NF-κB signaling pathway and the protein of pyroptosis(J)Pyroptosis of RA-FLSs colltected by transmission electron microscopy in each group.(K)The expression of p65 in each group of cells was determined by qRT-PCR. (L) Representative Western blots of p-p65,p65,Gsdmd,Caspase-1. (M) Representative images of arthritis in rat paws. (N) The arthritis score of different groups.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0049

A RAPID HEMAGGLUTINATION ASSAY FOR ACPA DETECTION IN PATIENT BLOOD

Keywords: Rheumatoid arthritis, Autoantibodies, Diagnostic tests

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Background: Anti-citrullinated protein antibodies (ACPA) are the most specific serological marker of rheumatoid arthritis (RA) and are produced by about 75% of RA patients. The presence of ACPA early in the disease, even before onset of clinical symptoms, facilitates early diagnosis and ACPA is among the most prominent classification criteria for RA.[1] Importantly, early diagnosis and immediate start of treatment is strongly correlated with improved outcomes. Several ACPA-detection assays are available for clinical use, which nearly all are based on the same principle: ELISA or related assays with cyclic citrullinated peptides or citrullinated proteins.[2] While these methods can be automated in modern diagnostic laboratories, they are ill-suited for low volume laboratories or resource-poor environments.
Objectives: The aim of this study was to develop a rapid and easy to perform assay for ACPA detection. The assay is based on ACPA-dependent agglutination of erythrocytes and can be executed with whole blood.
Methods: An agglutination mediator was developed by protein engineering. Addition of this mediator to (diluted) blood samples results in hemagglutination when ACPA are present. After optimization of the assay with RA serum-spiked blood samples, the applicability was assessed by the analysis of fresh blood samples from 100 RA patients and from 100 psoriatic arthritis (PsA) patients as a control group. Anti-CCP2 and RF levels in these patient samples were determined by standardized ELISAs.

Results: The agglutination mediator that was generated is based on a single-chain antibody fragment that binds to glycophorin A,[3] one of the major surface proteins of erythrocytes. It is conjugated to a citrullinated peptide that is efficiently recognized by ACPA. In the presence of erythrocytes and ACPA the mediator induces agglutination of the erythrocytes, which can be detected by the naked eye. The addition of the mediator resulted in detectable agglutination in 64% percent of the RA patient samples. Agglutination correlated well with the results obtained with a commercial anti-CCP2 ELISA for ACPA detection. Efficient agglutination was observed with only 7% of the PsA samples. No correlation with rheumatoid factor levels was observed.

Conclusion: An ACPA-dependent hemagglutination mediator was generated. This agglutination mediator allows the rapid and efficient detection of ACPA by hemagglutination in human blood samples.

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Disclosure of Interests: Ilmar Kruis: None declared, Annemarie Van der Heijden: None declared, Martin Salden Employee of: CEO/ R&D director Novio Catalpa BV, Ger Pruijn Grant/research support from: Research grant from Novio Catalpa B.V.

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AB0050 EVALUATION OF THE ASSOCIATION BETWEEN CIRCULATING NON-CODING RNA CIRC_0005567 AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ITS BIOLOGICAL FUNCTION IN THE CELL LINE MODEL

Keywords: Genetics/Epigenetics, Biomarkers, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic, autoimmune disease that leads to chronic inflammation of synovial tissue, ultimately causing joint damage, disability and premature mortality. Disease affects about 1% of the global population. Circular RNAs (circRNAs) are non-coding molecules and are generated through back splicing, during which the 5 ‘ and 3′ ends are covalently joined. Consequently, the lack of free ends makes them stable and resistant to exonucleases, and they become more suitable biomarkers compared with linear RNAs such as microRNAs (miRs) or long non-coding RNAs. CircRNAs are still poorly understood molecules in relation to RA pathogenesis.

Objectives: The aim of the study was to find an association between circ_0005567 plasma levels and disease activity in RA patients and to evaluate its molecular function.

Methods: A total of 66 individuals, 39 RA patients, and 27 healthy controls. RA patients were selected based on disease activity and RA patients with high disease activity (DAS28 >5,1) and remission (≤2,6) were included. RNA was extracted from plasma and quantitative real-time PCR was used to analyze concentration of circ_0005567. The SW982 cell line was cultured in Dulbecco’s Modified Eagle’s Medium and supplemented with 10% fetal bovine serum. The cell line was grown at 37 °C, in a humidified atmosphere, with 5% CO2. The circ_0005567 silencing was performed by designed small interfered RNAs (siRNAs). Bioinformatic analysis was applied to select the miRs and mRNAs that may interact with circ_0005567. The expression levels of microRNAs were evaluated, subsequently the expression levels of selected mRNAs were performed. The expression levels of miRs and mRNA were evaluated at three time points: after 24h, 48h, and 72h.

Results: The expression level for circ_0005567 in RA patients was elevated compared to the control group (mean±SD; 173.6±123.8 vs 108.9±81.03, p=0.017). The molecule also showed significant differences in disease activity. Patients with high disease activity had about 70% higher concentration of circ_0005567 than the control group (186.99 vs 108.9, p=0.015). In the cell line model we found an association between silencing circ_0005567 and elevated miR-194 concentration and elevated concentration of three mRNAs: *KPNA1, HBEGF, TLN2.*

Conclusion: The expression of circ_0005567 was related to genes that are significant for the pathogenesis of RA. For example, *HBEGF* gene expression in fibroblasts plays a role in the remission of rheumatoid arthritis, and *KPNA1* was reported as seed gene related to RA. Due to the fact that circRNAs are stable and resistant to degradation, plasma concentration of circRNAs may be a new potential epigenetic markers of RA and disease activity.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0051 DESCRIPTION OF PULMONARY INVOLVEMENT IN THE RAT ADJUVANT-INDUCED ARTHRITIS MODEL

Keywords: Rheumatoid arthritis, Animal models, Lungs

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Background: Interstitial lung disease (ILD) is detected until 60% of patients with rheumatoid arthritis (RA), but is clinically significant in around 10% of cases. It is one of the leading causes of disease and death in RA patients. High levels of anti-cyclic citrullinated peptide (CCP) autoantibodies are associated with co-occurrence of pulmonary disease and RA [1]. Moreover, the pulmonary fibrosis marker mucine (MUC-1) was described to be a predictive indicator for ILD [2]. The adjuvant-induced arthritis (AIA) model is commonly used to investigate arthritic diseases due to some pathophysiological similarities to human arthritis [3].

Objectives: The first objective of this study was to investigate the pulmonary involvement occurring in the rat AIA model. The second objective was to investigate the presence of potential biomarkers such as CCP and MUC-1.

Methods: This study was performed from lungs from 64 AIA rats and 6 control rats without arthritis. Lungs were collected to perform histological and immunological analyses. Pulmonary disease was measured with a score based on the percentage of lung damage and the thickness of the alveolar walls (0: absent, 1: mild, 2: moderate, or 3: severe). CCP and MUC-1 immunostaining was also performed.

Results: A nonspecific interstitial lung disease was detected in the lungs of 80% of AIA rats, whereas only half control rats developed it. A heterogeneous percentage of lung damage was observed, which correlated with the thickness of the alveolar walls but not with arthritis severity. Granulomas were observed in the most affected lung tissues, with a slight fibrosis at their periphery. The number of CCP markings correlated positively with the percentage of lung damage in AIA rats. MUC-1 was found homogeneously in the lung tissue of control and AIA rats, but more prominently in the periphery of granulomas in AIA rats.

Conclusion: We have described the pulmonary involvement in the AIA rat model, which developed the extra-articular complication similar to RA-ILD. We identified CCP and MUC-1 as potential biomarkers of this pulmonary involvement. Thus, the lung may be a site of initiation of CCP immunity. The AIA model will then allow a better understanding of RA-ILD, which may lead to earlier diagnosis and the potential development of new targeted therapies.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0052 GENETIC EVIDENCE REVEALS CAUSAL LINK BETWEEN RHEUMATOID ARTHRITIS AND MTOR PROTEINS : A MENDELIAN RANDOMIZATION STUDY

Keywords: Genetics/Epigenetics, Rheumatoid arthritis

Z. J. Yuan[1,2], R. Zhao[1,2,3], J. Y. Li[1,2], M. K. Yao[1,2], S. Y. Liu Yue[1,2], S. X. Zhang[1,2,3], X. Li[1,2,3], C. Wang[1,2,3]. [1]*Shanxi Medical University, Shanxi Provincial Key Laboratory of Rheumatism Immune Microecology, Taiyuan, China*; [2]*Shanxi Medical University, Key Laboratory of Cellular Physiology, Taiyuan, China*; [3]*The Second Hospital of Shanxi Medical University, Rheumatology, Taiyuan, China*

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease with hyperplasia of joint tissue and synovial inflammation1. And the mammalian target of rapamycin (mTOR) is a serine/threonine protein kinase, which relates with cellular metabolism, promotes cell growth and inflammatory process2. Some studies show that some downstream proteins of mTOR are associated with RA, but having no directly genetic evidence.
Objectives: We conducted Mendelian randomization (MR) study to discover the genetically and statistically casual association between mTOR and RA.
Methods: A two-sample MR study was applied to investigate the association. Firstly, the GWAS data of 14 downstream proteins of mTOR, including plasma RP-S6K, EIF-4EBP2 and so on was obtain from the 3,301 European samples. And a summary statistic involved 14,361 cases and 43,923 controls was also acquired from the IEU OpenGWAS database. Meanwhile, we extracted Single-nucleotide polymorphisms (SNPs) which were related with mTOR ($P < 1.0\times10\text{-}5$) and satisfied the three assumptions for MR analysis as instrumental variables (IVs). Then, Inverse variance weighting (IVW), weighted median (WM), and MR-Egger regression were performed for MR statistical analysis by R Studio with packages "TwoSampleMR." Additionally, MR Pleiotropy RESidual Sum and Outlier (MR-PRESSO) analysis was conducted to detect outlier instrument and remove pleiotropy. A leave-one-out analysis was conducted to avoid bias caused by a single SNP.
Results: Our study showed that no indication supporting the fact that the 14 downstream proteins of mTOR were causally associated with RA risk. The 15 SNPs of RP-S6K, 12 SNPs of EIF-4EBP2 and so on were selected as IVs for each 14 proteins. MR results showed that there was no causal relationship between RP-S6K and RA (OR = 1.03, CI: 0.89 - 1.20, P = 0.68). The results were same for EIF-4EBP2 (OR = 0.89, CI: 0.74 - 1.06, P = 0.18) and the other 12 proteins. No single SNP significantly biased the causal effect of mTOR and RA. No significant directional horizontal pleiotropy between each 14 downstream proteins and RA was presented.
Conclusion: Our study showed that a cause–effect connection did not appear to exist between mTOR proteins and RA, the findings of this study increased our understanding of the genetic associations, and may provide novel insights into the functional mechanism underlying the associations between SNPs and mTOR and RA.

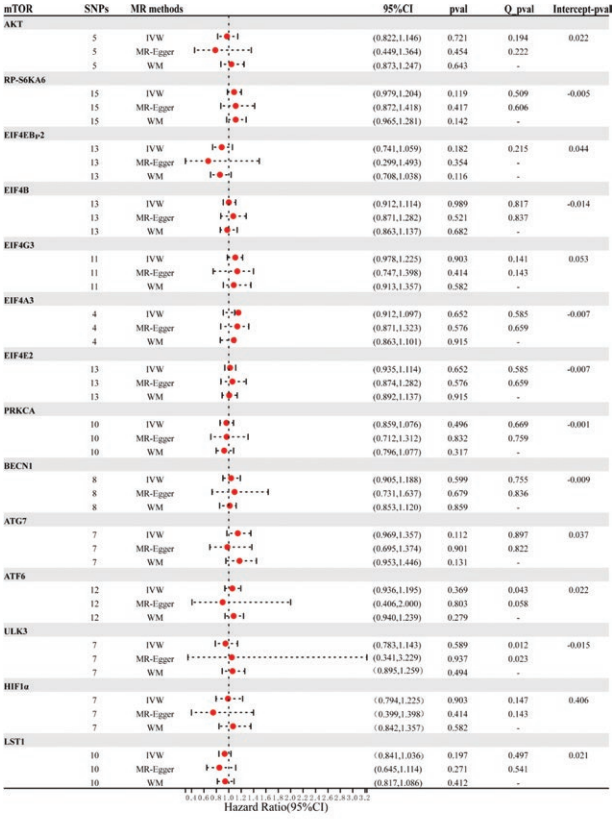


Figure1: Forest plot of MR results by IVW, MR-Egger and WM methods.Odds ratio (OR) and 95% confidence interval (CI) represent the change in the odds ratio of RA 's disease per 1-SD increase in the protein level.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3751

AB0053 ANGIOPOIETIN-2, VEGFA, VEGFC, VEGFD, EGF, PLGF AND HB-EGF ARE GROWTH FACTORS ASSOCIATED WITH SUBCLINICAL ARTERIOSCLEROSIS IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS.

Keywords: Biomarkers, Cardiovascular disease, Rheumatoid arthritis

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Background: Patients with rheumatoid arthritis (RA) present increased risk of cardiovascular (CV) disease compared to the general population. Moreover, CV risk factors that have causal relationship with atherosclerosis do not seem to fully explain the accelerated process that they exhibit[1]. Over the years, several serum growth factors have been associated with atherosclerosis and some of them have been targeted as potential immunotherapy targets for the treatment of CV disease[2,3]. However, very few studies have studied these associations in RA patients.
Objectives: We evaluated the association of 8 plasmatic growth factors (angiopoietin-2, EGF, HB-EGF, PLGF, TGF-α, VEGFa, VEGFc, VEGFd) with surrogate markers of subclinical arteriosclerosis (carotid intima media thickness (cIMT), carotid plaque presence (cPP) and pulse wave velocity (PWV)) in a cohort of RA patients.
Methods: A total of 199 patients with RA were included. Subclinical markers of arteriosclerosis, (cIMT, cPP and PWV) were measured with the My Lab 50 X-Vision sonogram. The different plasmatic growth factors were measured with Bio-Plex Pro Human Cancer Biomarker Panel 2, from BIO-RAD. Multivariate models and Partial Least Square Discriminant Analysis (PLS-DA) were used for analysis. Analyses were performed in the overall cohort and stratified by sex.
Results: The multivariate models showed that angiopoietin-2 was significantly associated with cPP and PWV in the overall cohort. Moreover, VEGFc was also associated with PWV. Stratified analyses showed that VEGFa, VEGFd, EGF, PLGF, HB-EGF were associated with cPP in men patients. In this direction, PLS-DA analysis showed that the mentioned growth factors properly classified patients with and without cPP (Figure 1). Furthermore, angiopoietin-2, EGF, VEGFc, VEGFa, HB-EGF were associated with PWV. Regarding women, angiopoietin-2 was associated with PWV. Result from the lineal and logistic regressions are summarized in Table 1.
Conclusion: Plasmatic growth factors, especially in men, are highly associated with subclinical arteriosclerosis surrogate markers and could be potential predictors of CV disease in patients with RA.

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Table 1. Summaries of the multivariate lineal and logistic regression models to estimate the associations between growth factors (GF) and cPP and PWV in the overall cohort and stratified by sex. Basal models are adjusted for age, sex, body mass index, disease onset, disease-modifying antirheumatic drugs, non-steroidal anti-inflammatory drugs, corticosteroids, biological drugs and DAS28. GF = growth factor, β = beta coefficient, OR = odds ratio, p = p-value

GF associations with subclinical arteriosclerosis

	OR	p	R^2 (%)
cPP			
OVERALL COHORT			
Basal Model			24
+ angiopoietin-2	1.0005	0.02	26
MEN			
Basal Model			33
+ VEGFa	1.002	0.04	39
+ VEGFd	1.002	0.04	38
+ EGF	1.02	0.02	40
+ PLGF	1.01	0.03	39
+ HB-EGF	1.02	0.04	38
	B	**p**	**R^2 (%)**
PWV			
OVERALL COHORT			
Basal Model			32
+ angiopoietin-2	0.0006	0.001	36
+ VEGFc	0.0005	0.04	34
MEN			
Basal Model			33
+ angiopoietin-2	0.0007	0.02	40
+ VEGFa	0.002	0.02	39
+ VEGFc	0.001	0.008	41
+ HB-EGF	0.01	0.04	38
WOMEN			
Basal Model			36
+ angiopoietin-2	0.0005	0.01	39

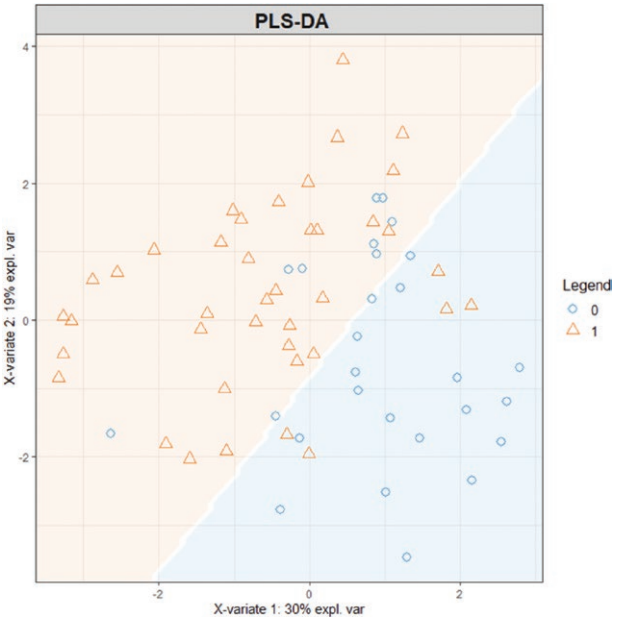


Figure 1. PLS-DA of men with cPP and without cPP, adjusted for the significant growth factors and age, body mass index, disease onset, disease-modifying antirheumatic drugs, non-steroidal anti-inflammatory drugs, corticosteroids, biological drugs and DAS. 28 0 = no cPP, 1 = cPP

Acknowledgements: We would like to thank all patients for their essential collaboration.

Disclosure of Interests: ANNA PAMIES CORTS Speakers bureau: Novartis, Galapagos, Didac Llop: None declared, Daiana Ibarretxe Speakers bureau: Sanofi, Sobi, Genzyme, Rubio, Delia Taverner Speakers bureau: Galapagos, Amgen, Roser Rosales: None declared, Nuria Plana Speakers bureau: Amgen, Sanofi, Servier, Consultant of: Servier, Luis Masana Speakers bureau: Amgen, Sanofi, Servier, Consultant of: Servier, Amgen, Joan Carles Vallve: None declared, Silvia Paredes Speakers bureau: Lilly, Bristol, Amgen, Consultant of: Galapagos, Sanofi, Bristol.

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AB0054 BIOMARKERS OF BONE ACTIVITY IN RHEUMATOID ARTHRITIS SYNOVIAL TISSUE AND THEIR RELATIONSHIP WITH CLINICAL OUTCOME

Keywords: Bone diseases, Rheumatoid arthritis, Biomarkers

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease which can involve bone joint degradation. The Wnt-β/catenin signalling pathway is a major promoter of bone formation. Following triple-DMARD treatment of rheumatoid arthritis patients, systemic levels of sclerostin are increased, correlating with improved patient response. This lies in contrast with the established role of sclerostin as a Wnt-antagonist, which would inhibit bone formation and suggests a protective role for sclerostin against bone loss. However, it is not known if this change is reflected in synovial tissues, the site of inflammation in RA.
Objectives: This study characterised the expression of sclerostin and other biomarkers associated with bone metabolism in synovial tissue biopsy samples in relation to patient erosive status (Sharpe/van der Heijde method), the presence of TNF (as judged by immunohistochemistry (IHC)) and response to treatment (European League Against Rheumatism (EULAR) scores).
Methods: Arthroscopic synovial tissue biopsies from patients with early rheumatoid arthritis, before and after treatment with adalimumab or abatacept were examined for sclerostin and LRP5/6, by immunohistochemistry (IHC), immunofluorescence staining, flow cytometry and bulk RNA sequencing, in addition to other biomarkers associated with bone metabolism. Total RNA libraries were produced using the Tecan Universal Plus Total RNA library preparation kit. Samples were sequenced on 3 x S4 lanes of the NovaSeq using paired end 100 bp reads (Illumina).
Results: No significant changes were observed for both sclerostin and LRP5/6 between erosive and non-erosive patients and at 6-month post-treatment. However, the expression of sclerostin in IHC stains of synovial tissues was significantly increased in TNF-non-dominant patients compared to those who were TNF-dominant. Sclerostin and LRP5/6 expression was localised to different cell populations in synovial tissue.
Conclusion: Bulk assessment of sclerostin and other bone biomarkers within synovial tissue does not currently demonstrate a relationship with clinical outcome. However, further assessment of sclerostin and other biomarkers of bone activity in specific cell types, within synovial tissue, can provide further insights into the role of sclerostin and Wnt pathway molecules in bone homeostasis in the context of RA and may provide biomarkers of erosive disease progression.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5123

AB0055 THE ROLES OF OX40L AND TNF BISPECIFIC ANTIBODY IN OSTEOCLASTOGENESIS

Keywords: Osteoarthritis, Rheumatoid arthritis, Adaptive immunity

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Background: Rheumatoid arthritis (RA) is a chronic, inflammatory disease that leads to progressive cartilage and bone destruction. OX40 ligand (OX40L) is expressed predominantly on antigen-presenting cells and highly associated with joint inflammation in RA[1]. Yet, the role of OX40L in osteoclastogenesis is unclear.
Objectives: In this study, we investigated the effects of dual blocking of TNF and OX40L by bispecific antibody (IMB-101) on RANKL-induced osteoclastogenesis.
Methods: CD14+ monocytes were isolated from peripheral blood mononuclear cells (PBMCs) of healthy donors (n=6). CD14+ monocytes were cultured with M-CSF (20ng/ml) and RANKL (40ng/ml) for 6 to 7 days in the presence of TNF antibody, OX40L antibody, or bispecific antibody. TRAP-positive multinucleated giant cells (>3 nuclei/cell) were counted as osteoclast. PU.1, RANK and NFATc1, markers of osteoclast differentiation were assessed by the quantitative reverse

transcription PCR (RT-qPCR). The expression of OX40L was analyzed in the presence of RANKL or TNF at the early and late stage of osteoclast differentiation.
Results: The expression of OX40L was increased by RANKL and TNF at the early stage of osteoclast differentiation (day 3) in a TNF dose-dependent manner. IMB-101 decreased RANKL-induced osteoclastogenesis via downregulating NFATc1 expression (Figure 1). IMB-101 further reduced PU.1, RANK and NFATc1 expression during early stage of osteoclast differentiation (day 3) compared to TNF inhibitor or TNF inhibitor and OX40L inhibitor (n=3).
Conclusion: Our data suggested that IMB-101 might have a beneficial effect on imbalance of the bone resorption in RA especially by suppressing osteoclast differentiation.

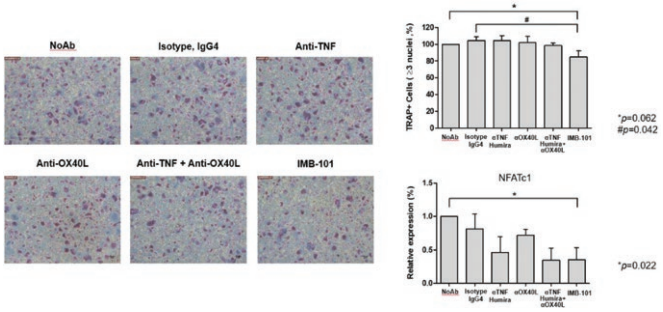


Figure 1.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0056 CYTOKINE-DIRECTED CELLULAR CROSSTALK IMPRINTS SYNOVIAL PATHOTYPES IN RHEUMATOID ARTHRITIS

Keywords: Synovium, Cytokines and chemokines, Rheumatoid arthritis

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Background: The chronic inflammatory disease Rheumatoid Arthritis (RA) is characterized by synovial inflammation promoting cartilage and bone degradation when left untreated. Interaction between infiltrating immune cells, such as CD4+ T cells and activated fibroblast-like synoviocytes (FLS) might contribute to joint inflammation ultimately amplifying progressive joint destruction.
Objectives: To elucidate the interaction of stimulated FLS and CD4+ T cells within an inflammatory environment and to define its impact on synovial inflammation.
Methods: To define the effect of inflammatory mediators, FLS were stimulated with different pro- and anti-inflammatory cytokines. Transcriptomic changes were measured using RNA sequencing (RNA-seq). Co-cultures of cytokine pre-treated FLS and fluorescence activated cell sorting (FACS)-purified naïve CD4+ T cells were established. Using high-content fluorescence microscopy combined with bioinformatic image analysis, cell-cell interactions were visualized and quantified. The consequence of FLS co-culturing on CD4+ T-cell development was addressed by flow cytometry of re-isolated CD4+ T-cells.
Results: RNA-seq on cytokine-stimulated FLS revealed cytokine-specific gene expression profiles. In line, we observed cytokine-specific patterns of interaction with CD4+ T-cells which could be further observed in flow cytometry data of T cell activation, proliferation and differentiation. Cytokine-stimulated FLS signatures could be detected in transcriptomic data of RA patient synovial tissue samples.
Conclusion: In this study, we highlight the role of FLS in orchestrating inflammation-associated synovial tissue remodeling and how cytokine induced CD4+ T cells – FLS interactions impact on T-cell development.

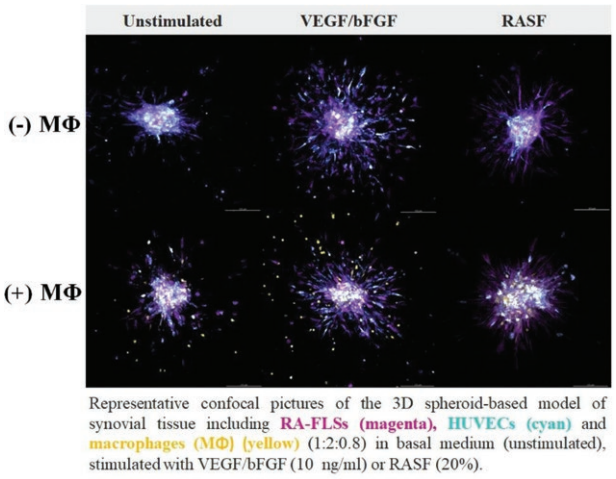
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AB0057 ESTABLISHMENT OF NOVEL 3D SPHEROID-BASED MODEL OF RHEUMATOID ARTHRITIS SYNOVIAL TISSUE TO INVESTIGATE THE INTERACTION BETWEEN DIFFERENT CELL TYPES

Keywords: Rheumatoid arthritis, Synovium

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Background: Rheumatoid Arthritis (RA) is a progressive and systemic autoimmune disorder associated with chronic and destructive inflammation of the joints. The hallmarks of RA are synovial cell proliferation, extensive neoangiogenesis and infiltration of numerous immune cells into the synovial tissue. *In vitro* approaches simulating RA synovial tissue are crucial in preclinical and translational research to expand our knowledge on RA human pathophysiology and to test new diagnostic and therapeutic applications.
Objectives: Here, we present the engineering of a spheroid-based model of RA synovial tissue which mimics the close interaction between cells and key pro-inflammatory mediators present in the inflamed synovium.
Methods: Following differentiation in 20 ng/ml GM-CSF for 6-7 days, monocyte-derived macrophages were cultured with RA fibroblast-like-synoviocytes (RA-FLSs) and endothelial cells (ECs) for 24 hours to allow for spheroid formation. Three RA-FLS/EC/macrophage ratios were tested: (1:2:0.4), (1:2:0.8) and (1:2:1.6). Then, the spheroids were placed in a collagen-based matrix for 40 hours to study spheroid outgrowth in 3 dimensions. The spheroids were left unstimulated, or cultured in the presence of growth factors VEGF/bFGF or RA synovial fluid. Sprout formation and cell migration were quantified for all conditions using confocal microscopy and digital image analysis.
Results: Addition of macrophages to the previously established 3D model of RA angiogenesis consisting of ECs and RA-FLSs resulted in close interaction of macrophages with RA-FLSs and ECs within the spheroid structure. The optimal ratio between RA-FLSs, ECs and macrophages in our system was established as 1:2:0.8, based on the proportions of macrophages that remained within the core and migrated throughout the matrix as well as the effect of stimuli on sprout formation. Addition of growth factors (VEGF/bFGF) significantly promoted spheroid outgrowth compared to the unstimulated condition in the new model *($p<0.01$)*.



Representative confocal pictures of the 3D spheroid-based model of synovial tissue including **RA-FLSs (magenta), HUVECs (cyan)** and **macrophages (MΦ) (yellow)** (1:2:0.8) in basal medium (unstimulated), stimulated with VEGF/bFGF (10 ng/ml) or RASF (20%).

Figure 1.

Conclusion: We present a novel 3D-spheroid based model consisting of RA-FLSs, ECs and macrophages that mimics the RA synovial tissue microenvironment. This model is useful to dissect the role of specific cell types in inflammatory responses in RA, to study specific signaling pathways involved in the disease pathogenesis and examine the potential of novel diagnostic (molecular imaging) and therapeutic compounds, including small molecule inhibitors and biologics.

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AB0058

NOVEL BIOMARKERS FROM THE S100 PROTEIN FAMILY OF RHEUMATOID ARTHRITIS PROGRESSION WHICH CAN BE REGULATED BY EPIGENETIC DRUGS

Keywords: Genetics/Epigenetics, Rheumatoid arthritis, Biomarkers

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Background: Monocytes are key players in initiating and maintaining inflammation by producing proinflammatory cytokines and S100 proteins in rheumatoid arthritis (RA). Several studies demonstrated that epigenetic drugs affecting DNA methylation can modulate the production of proinflammatory mediators.

Objectives: This study aimed to test specific DNA methylation inhibitor (RG108) and activator (budesonide) in the regulation of proinflammatory cytokines and S100 proteins in RA monocytes. Our study also looked for new and better biomarkers of high disease activity in RA patients.

Methods: RNA sequencing (RNA-seq) analysis of healthy controls (HC) and RA monocytes was performed. Cell viability was determined in THP-1 monocytic cell line following RG108 and budesonide treatment. Pro- and anti-inflammatory genes such as the S100 family, TNF, IL-8 were validated by qRT-PCR following DNA methylation-targeted drug treatment. The concentrations of proteins from the S100 family in serum and synovial fluid were tested with ELISA assays and their correlation with clinical parameters was carried out.

Results: Based on the RNA-seq analysis, RA monocytes had significantly increased levels of S100A8 (2,2-fold, p=0,024), S100A9 (1,9-fold, p=0,017), S100A11 (1,2-fold, p=0,007), S100A12 (1,6-fold, p=0,007), MYD88 (1,2-fold, p=0,008), JAK3 (1,8-fold, p=0,009), IQGAP1 (1,4-fold, p=0,02), and decreased level of IL10RA (0,7-fold, p=0,011), TGIF1 (0,3-fold, p=0,046) transcripts. In addition, stimulation of THP-1 cells with budesonide (DNA methylation activator) statistically reduced expression of S100A8 (3,0-fold, p= 0,0390), S100A9 (4,4-fold, p= 0,0317), S100A12 (3,3-fold, p= 0,0260), IL-8 (6,8-fold, p= 0,0286) and TNF (7,5-fold, p= 0,0260) genes. In contrast, THP-1 monocytic cell line treated with RG108 (DNA methylation inhibitor) had an increased level of S100 family (S100A8, -A9, -A11, -A12) and TNF genes. ELISAs analysis also revealed significant increased levels of S100A8 (p = 0.0116), S100A11 (p = 0.0138), and S100A12 (p = 0.0296) proteins in RA patients compared to HC sera, similar in early RA sera compared to HC S100A8 (p = 0.0024), S100A11 (p = 0.0020) and S100A12 (p = 0.0059). Moreover, protein levels of S100A8 (p=0.0005), S100A11 (p=0.0007) and S100A12 (p=0.0005) in the synovial fluid of advanced RA patients compared to HC serum were significantly elevated. All these data suggest that a protein of the S100 family may be a promising biomarker of RA progression. In ROC analyses, serum levels of S100A8 and S100A12 proteins were more specific {area under the curve (AUC)=0.78, p=0.006 and AUC=0.87, p=0.0006} respectively in RA patients than CRP levels. In addition, results indicate that S100A8 and S100A12 can serve as a better biomarker of high disease activity than CRP levels.

Conclusion: We have demonstrated that S100 family proteins are increased in RA monocytes (transcriptomics) similar to enhanced S100 production in sera and synovial fluids (ELISA) in RA patients. Our data suggest that the proteins S100A8 and S100A12 in particular are strongly increased during ongoing inflammation, so they could be used as a better biomarker of disease activity than CRP. Interestingly, S100 proteins can be regulated by epigenetic drugs, suggesting their potential use in the targeting of RA inflammation.

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AB0059

THE POTENTIAL ROLE OF THE T2 FAMILY OF EXTRACELLULAR RIBONUCLEASES (RNASET2) AS CIRCULATING BIOMARKER IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Biomarkers

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Background: Circulating biomarkers with diagnostic and prognostic value in early Rheumatoid Arthritis (RA) are still an unmet need, especially for the subgroup of seronegative RA [e.g., negative for anti-citrullinated peptides autoantibodies (ACPA) and/or rheumatoid factors (RF)]. In a recent gene-based genome-wide association analysis (GWAS) study, RNASET2 was identified as a potential susceptibility gene [1-3]. Furthermore, the extracellular ribonuclease RNASET2 was demonstrated to be involved in the regulation of several immune processes [4].

Objectives: The aim of this study was to analyse RNASET2 serum levels in a cohort of RA patients upon their disease activity, in comparison with healthy controls (HC).

Methods: Forty consecutive patients with RA (75% female, 55% seropositive) with a median age (25^{th}-75^{th} percentile) of 55 years (45-68) and a CRP-DAS28 index of 3.09 (2.50-3.70), and 25 sex and age-matched HC were enrolled in the study. RNASET2 serum levels were assessed through a commercial hELISA test (WuHan Fine Biotech Co., China).

Results: Serum levels of RNASET2 were higher in RA patients than in HC [29.42 (17.73 – 69.82) vs 18.15 (12.15 – 28.35) ng/mL; p= 0.001]. Among patients with RA, there were no differences between RNASET2 levels in seropositive or seronegative ones [33.14 (16.79 – 74.89) vs 29.01 (17.83 – 39.85) ng/mL; p=0.308]. Furthermore, there were no differences in RNASET2 serum levels between patients in treatment with corticosteroids or not [42.09 (18.11 – 78.78) vs 23.42 (18.29 – 43.87) ng/mL; p=0.239]. RNASET2 serum levels were significantly different across 3 groups of RA patients identified upon the CRP-DAS28 score (high plus moderate disease activity –group A-; low disease activity –group B-; remission –group C-) (p= 0.024). RNaseT2 levels were higher in both group A and B as compared to group C [56.73 (30.22 – 79.67) - 83.72 (52.68 – 113.89) vs 25.43 (20.15 – 39.85) ng/mL; p= 0.005 & p= 0.007]. No difference was found between group A & B. When combining groups A & B, RNASET2 levels were significantly higher than in group C [67.14 (36.07 – 86.68) vs 25.43 (20.15 – 39.85) ng/mL; p= 0.013]. No significant correlation was found between RNASET2 serum levels and CRP-DAS28 (r= 0.36; p= 0.055).

Conclusion: This is the first description of circulating serum levels of RNASET2 as a potential diagnostic biomarker in RA. Higher levels of RNASET2 clustered in RA patients as compared to HC. Low levels of RNASET2 seem to characterize the remission phase of RA. These preliminary results deserve to be expanded in larger cohorts of RA patients, patients with other form of chronic arthritis and other pathological and healthy controls.

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AB0060 ANALYSIS OF THE HUMAN GUT MICROBIOME AND NUTRITION PATTERNS IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Diet and nutrition, Gastrointestinal tract

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Background: The association of the gut microbiome with obesity and metabolic diseases as type 2 diabetes (T2D) as well as the influence of environmental factors like nutrition on its composition is well established. In addition, recent studies[1] described the composition of gut microbiota to be altered in inflammatory rheumatic diseases highlighting a pathogenetic link between the microbiome and autoimmune joint diseases.
Objectives: The aim of this study was to analyze food intake and the composition of the gut microbiota in rheumatoid arthritis (RA) in comparison to healthy controls (adjusted for metabolic conditions known to influence the gut microbiota composition).
Methods: A subset of the FoCus (Food chain plus) cohort (a cross-sectional survey of the general population in northern Germany) with RA and matched controls without RA (matched for age, gender, body mass index and diagnosis of Type 2 Diabetes mellitus [T2D]) was investigated regarding their nutrition patterns and gut microbiome in a case-control analysis. Nutrition patterns were derived from Food Frequency Questionaires (FFQ) and analyzed by hierarchical cluster analysis. The gut microbiota composition was analyzed by 16S rRNA gene sequence data clustered into operational taxonomic units (OTUs). Microbiome composition was analyzed by alpha- (phylodiversity, Shannon index, Chao index) and beta-diversity measures (Bray-Curtis distance, Jaccard index) and by hurdle-models.
Results: We identified n = 94 individuals with RA and n = 94 matched controls (mean age 57 years, SD 12.9; mean BMI 31.1, SD 8.9). Interleukin 6 was significantly higher in the RA group compared with controls (p=0.012), while no differences were observed between groups for HOMA-Index, CRP, lipoprotein (a) or triglycerides. Nutrition data from FFQs was used in a hierarchical cluster analysis, resulting in two main clusters (the second one defined by a significantly higher intake of vegetables, fruit and dairy products). Nutrition clusters did not differ significantly between RA cases and controls (p=0.228). When comparing the composition of the intestinal microbiota between RA patients and controls (adjusted for nutrition cluster and IL-6), significant differences in the beta-diversity were detected using Bray-Curtis distance (p=1.82e-9) and Jaccard index (p=1.82e-9). Hurdle model analysis of the core measurable microbiome identified three candidate species OTUs (Flavonifractor and 2x Blautia). No significant differences in alpha diversity was observed when analyzed by species richness (p=0.9), Shannon (p=0.3) and Chao index (p=0.6).
Conclusion: Participants suffering from RA had significant differences in the composition of the gut microbiome compared to controls matched for age, BMI, gender and T2D after adjusting for nutrition patterns and IL-6. Investigating differences in the functional capacity of the altered gut microbiome in RA may better characterize a possible link of gut microbes to the development of RA.
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AB0061 ENDOTHELIN-1 AS A POTENTIAL CANDIDATE TO SHED LIGHT ON THE CHALLENGE OF INTERSTITIAL LUNG DISEASE DIAGNOSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Lungs, Biomarkers, Rheumatoid arthritis

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Background: Interstitial lung disease (ILD) is one of the main causes of death in patients with rheumatoid arthritis (RA), constituting its **e**arly diagnosis in these patients a challenge for the clinicians [1]. In this sense, pulmonary endothelial activation is one of the essential steps to the development of lung lesions [2,3]. In this regard, endothelin-1 (ET-1), the most potent endogenous vasoconstrictor, has been described as a profibrotic molecule [3]. Accordingly, it is plausible to think that ET-1 is involved in the pathophysiology of RA-ILD$^+$.
Objectives: To explore the role of ET-1 as a biomarker of pulmonary fibrosis in RA-ILD$^+$.
Methods: Peripheral venous blood was collected from 21 RA-ILD$^+$ patients and two comparative groups: 25 RA-ILD$^-$ patients and 21 idiopathic pulmonary fibrosis (IPF) patients. All the subjects were recruited from the Rheumatology and Pneumology departments of Hospital Universitario Marqués de Valdecilla, Santander, Spain. Serum levels of ET-1 were determined by ELISA.
Results: RA-ILD$^+$ patients showed increased levels of ET-1 compared to those with RA-ILD$^-$ ($p<0.01$, **Figure 1A**). Interestingly, the ability of serum ET-1 levels to discriminate patients with RA-ILD$^+$ from those with RA-ILD$^-$ was further confirmed by receiver operating characteristic curves (area under the curve: 0.77, $p<0.01$, **Figure 1B**). The optimal cutoff value for ET-1 showing the best sensitivity and specificity was 1.02 pg/mL. Moreover, patients with RA-ILD$^+$ presented similar levels of ET-1 than those with IPF (p=0.50, **Figure 1A**). Additionally, a negative correlation between ET-1 serum levels and both forced vital capacity and forced expiratory volumen at first second was disclosed in patients with RA-ILD$^+$ (r=-0.56, p=0.04 and r=-0.65, p=0.01, respectively).
Conclusion: Our study suggests that ET-1 levels are linked to lung injury and worse lung function, supporting its role as a potential blood biomarker of ILD in RA patients.
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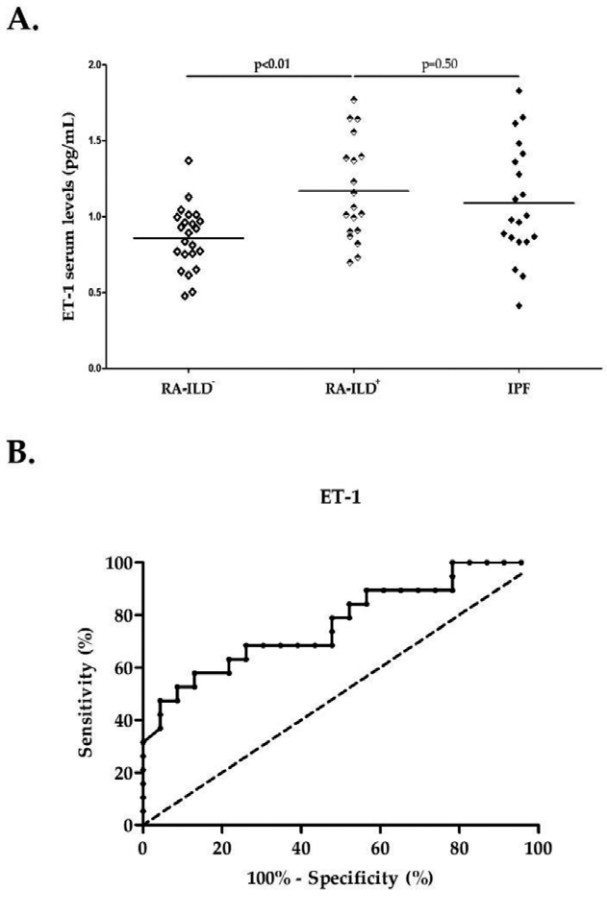


Figure 1. ET-1 for the diagnosis of RA-ILD$^+$. Differences in serum levels of ET-1 between patients with RA-ILD$^+$ and those with RA-ILD$^-$ and IPF (A), as well as ROC curves analysis of ET-1 for the discrimination of RA-ILD$^+$ from RA-ILD$^-$ (B). ET-1: endothelin 1; RA: rheumatoid arthritis; ILD: interstitial lung disease; IPF: idiopathic pulmonary fibrosis;. Significant results are highlighted in **bold**.

AB0062

ABUNDANCE AND ACTIVATION OF MEMORY B-CELLS CHARACTERIZE SYNOVITIS IN RHEUMATOID ARTHRITIS PATIENTS WITH EARLY TREATMENT RESPONSE

Keywords: Rheumatoid arthritis, Synovium, Biomarkers

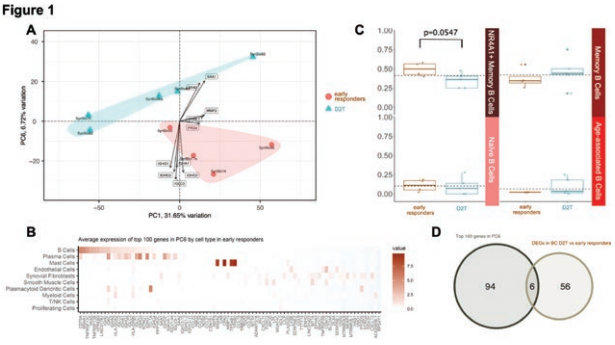
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Background: A relevant percentage of patients with rheumatoid arthritis (RA) do not respond to individual (40%) or all available disease modifying anti-rheumatic drugs DMARDs (5-20%). A recent study using synovial bulk RNAseq from a phase 4 trial has shown that humoral immune response gene signatures are associated with response to rituximab and tocilizumab [1]. Other biomarkers that can predict early response to alternative DMARDs are still lacking.
Objectives: This study, performed in a real-life clinical care setting, aimed at characterizing synovitis of RA patients with an early drug response on a single-cell level to identify potential biomarkers and molecular signatures.
Methods: Synovial tissue was obtained by ultrasound-guided synovial biopsy from inflamed joints. Four patients were defined as early responders not meeting the D2T EULAR definition criteria (median (IQR) number of treatments 1.5 (1.25)) [2], but meeting 2022 ACR/EULAR remission within 3 months on the DMARD started after the synovial biopsy. Five patients met the D2T EULAR definition criteria (median (IQR) number of treatments 7 (1)). Two out of five from the D2T group went into ACR/EULAR remission 3 months after the biopsy following DMARD initiation (abatacept (n=1) and upadacitinib (n=1)). Both groups fulfilled the ACR/EULAR classification criteria for RA. 6000 cells were targeted for single-cell encapsulation (10X Genomics workflow v3.1). Libraries were sequenced on NovaSeq6000. The following R packages were used: Cell Ranger, Seurat, Harmony, PCAtools.
Results: Clinical characteristics (sex, age, swollen joint count, C-reactive protein, body mass index, smoking status) were comparable between the two groups, except for the presence of autoantibodies (all D2T compared to only one early responder patient were seropositive). The patients in the early responder group received the following drugs after the biopsy: methotrexate plus certolizumab (n=1), methotrexate alone (n=1) or abatacept (n=2). Patients in the D2T group had received a median of seven treatments before the biopsy. 29,408 cells were integrated for scRNA-seq analysis (mean of 3,267 cells after quality control filtering per patient). Unsupervised dimensionality reduction analysis showed 8 principal components (PCs) explaining all variations in gene expression between samples. PC6 was significantly associated with the early responder/D2T categorization, accounting for 6.72% of the sample variation. Immunoglobulin genes (IgH-, IgL-), Prostaglandin D2 Synthase (PTGDS) and B-cell antigen receptor complex-associated protein alpha chain (CD79A) were among the top 100 genes associated with early response to treatment (PC6) (Figure 1A). Analysis of the average expression of these genes in the early responder and D2T group revealed expression mostly in B cells and plasma cells (Figure 1B). Comparing the proportions of cell populations using graph-based clustering showed no significant differences between early responder and D2T patients. Further clustering of the primary cell populations also did not show changes in proportions except for B cells: the proportions of NR4A1+ memory B cells (B cells recently receiving antigen stimulation) were higher in early responder compared to D2T patients (mean 48%±10 vs 36%±10, p-value = 0.0547) (Figure 1C). Analysis of differentially expressed genes in B cells between early responder and D2T patients revealed 62 genes differentially expressed (p-value<0.05, average fold change > or < 0.3). Still, only six of these genes were among the top 100 genes associated with PC6 (Figure 1D).
Conclusion: Synovitis in rheumatoid arthritis patients with early treatment response was associated with activation of B cells and an abundance of NR4A1+ memory B cells. This finding in a real-life cohort is in concordance with previous results showing an association of humoral immune activation and response [1] and sets the path for future biomarkers predicting early response in RA.

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Figure 1



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AB0063

OSTEOCLASTS DIFFERENTIATED FROM DENDRITIC CELLS POSSESS THE INFLAMMATORY OSTEOCLAST PHENOTYPE

Keywords: Synovium, Rheumatoid arthritis

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Background: Osteoclasts (OCs) can differentiate from monocytes (MoOC) and dendritic cells (DCOC) in in vitro. On the other hand, there are two OC subsets in in vivo. One is involved in normal bone remodeling, and the other originating

from arthirits-associated osteoclastogenic macrophages (AtoM), characterized by CX3CR1 and FOXM1 expression. However, the relationship between MoOC and DCOC with AtoM is unknown[1].

Objectives: To investigate the phenotype of oteoclasts differentiated from dendritic cells.

Methods: Bone marrow cells or bone marrow derived dendritic cells were cultured with RANKL+M-CSF for 6 days to generate MoOC or DCOC.(2) Osteoclast differentiation was assessed by TRAP staining. NFATc1, CX3CR1 and FOXM1 mRNA expression was evaluated with whole cultured cells, OC or undifferentiated cells residing by OC collected by laser microdissection. Fluorescent immunostaining of cultured cells was used to analyze protein expression, and IL-6 or TNFα was added during OC differentiation to assess effects on OC differentiation, CX3CR1 and FOXM1 expression.

Results: MoOCs and DCOCs differentiation was confirmed by TRAP staining and NFATc1 mRNA expression in whole cultured cells on day 6 of RANKL+M-CSF culture. The expression of CX3CR1 mRNA was significantly higher in DCOC than in MoOC. In DCOCs recovered by microdissection on day 4, confirmed significantly higher expression of CX3CR1 mRNA compared to MoOCs. Comparison of CX3CR1 mRNA expression with residing undifferentiated cells resulted in significantly higher expression in DCOCs, but not in MoOCs. Immunostaining on day 6 showed nuclear translocation of FOXM1 in both DCOCs and MoOCs. IL-6 or TNFα stimulation decreased viable cells in a concentration-dependent manner, with TNFα promoting MoOC differentiation and IL-6 promoting DCOC differentiation.

Conclusion: Compared to MoOCs, DCOCs expressed significantly higher CX3CR1 and FOXM1 from early stage of development specific to progenitor of inflammatory osteoclasts in in vivo. In addition nuclear translocation of FOXM1 suggested its role in gene regulation during OC differentiation. In addition, enhancement of DCOC differentiation by IL-6 is suggesting the usefulness of IL-6 inhibition for the pathophysiology of joint destruction in rheumatoid arthritis.

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AB0064 DISCOVERY OF NOVEL LONG-NONCODING RNAS IMPLICATED IN RHEUMATOID ARTHRITIS

Keywords: Genetics/Epigenetics, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a representative systemic autoimmune disease characterized by synovial inflammation and proliferation accompanied by joint destruction. Fibroblast-like synoviocytes (FLS) are a key constituent of the synovium and paly an important role in the pathogenesis of RA. Although accumulating evidence has implicated the role of long non-coding RNAs (lncRNAs) in autoimmune diseases, the role of lncRNAs in the pathogenesis of RA remains unknown.

Objectives: In this study, we aim to investigate the expression profile of lncRNAs in the FLS from the patients with RA (RA FLS) and discover promising candidates involved in the pathogenesis of RA.

Methods: The next-generation sequencing (NGS) data were analyzed to identify differential expressed lncRNAs in RA FLS compared with FLS from the patients with osteoarthritis (OA FLS). NGS data were also analyzed to reveal differentially expressed lncRNAs between unstimulated RA FLS and IL-1-stimulated RA FLS. And then, the intersection of two analysis results was obtained. Data obtained by intersection was validated by RT-qPCR using RA FLS and OA FLS. Changes in lncRNA expression induced by pro-inflammatory cytokines were investigated by RT-qPCR.

Results: According to NGS analysis, among the lncRNAs whose expression was increased in RA FLS compared to OA FLS, there were 4 lncRNAs whose expression was also increased by IL-1 stimulation in RA FLS. On the other hand, among the lncRNAs whose expression was decreased in RA FLS compared to OA FLS, there were 6 lncRNAs whose expression was also decreased by IL-1 stimulation. Of the 4 upregulated and 6 downregulated lncRNAs, we validated the top 3 of each when listed in order of fold change. As a result, it was confirmed that the expression of only one (NR_030732) was increased in RA FLS. The expression level of NR_030732 was more enhanced after treating with IL-1, IL-6, or TNF-α in RA FLS. Although not confirmed in validation, the expression of the top 3 downregulated lncRNAs (NR_034107, NR_046240, NR_121608) derived from NGS analysis was also decreased after the treatment with IL-1, IL-6, or TNF-α in RA FLS.

Conclusion: Our study found that NR_030732 was prominently expressed in RA FLS, and confirmed that the expression of NR_030732 was also increased by pro-inflammatory cytokines. Thus, our data suggest that the lncRNA NR_030732 might be a candidate lncRNA involved in the pathogenesis of RA.

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AB0065 COMPARISON OF HISTOLOGICAL AND MOLECULAR FEATURES IN PATIENTS WITH AN ACTIVE RHEUMATOID ARTHRITIS AND PATIENTS IN REMISSION

Keywords: Rheumatoid arthritis, Synovium, Remission

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease. The disease is manifested by inflamed synovium and destruction of cartilage and bone. So far, the disease cannot be cured, which is why remission is considered as the therapeutic goal. Although the number of patients in remission is increasing, patients still have different prognostic outcomes, which is why a better understanding of remission is needed.

Objectives: Characterization of remission in RA by comparison of histological and molecular features in the synovium of active RA patients compared to patients in remission.

Methods: After joint replacement surgery, RA patients between 43 and 81 years were clinically classified into either remission or active RA. Clinical classification was based on laboratory (e.g. ESR, CRP, leucocytes) and clinical parameters (e.g. painful joint, pain degree, medication). Subsequently, the Krenn Score was applied to characterize synovitis in the synovial tissue. To investigate remission on RNA level, RA synovial fibroblasts (RASF) from both patient groups were either stimulated with IL-1 or left unstimulated for 24h. RNA was isolated and analysed by RNA sequencing. Evaluation included analysis of differentially expressed genes (DEG) based on a combination of absolute expression, divergence and significance as well as gene set enrichment analysis of DEGs to identify the enriched gene sets or pathways.

Results: A total of 39 patients were included in the Krenn Score, of whom 20 were active and 19 in remission. Patients in remission showed a generally lower synovitis score for all parameters. In particular, a reduced synovial hyperplasia of the lining layer (P=0.021) and the total Krenn score (P=0.022) was observed. Sub-analyses regarding medication (biologics, DMARDs, NSAIDs, glucocorticoids) also showed a decreased hyperplasia for patients in remission, especially for patients who received biologics (4.2 fold decrease). Regarding the RASF, RNA sequencing showed a general homogeneity of the expressed genes and the underlying pathways between patients in remission and active RA patients. This observation was evident in both, the unstimulated approach and the stimulated RASF. However, RNAseq identified several DEGs including IL-36B (-7.14 fold) and the IL-36 receptor antagonist (-11.49 fold), cathepsin K (-1.66 fold) and folliculin (-1.54 fold), which were downregulated in patients in remission.

Conclusion: The histological analysis illustrates that patients in remission, especially patients receiving biologics, show a lower degree of inflammation and hyperplasia. RNAseq identified several genes showing altered gene expressions related to the diminished pro-inflammatory and destructive processes during RA. Of note, pro-inflammatory IL-36 family members were predominantly downregulated, which could be used as biomarker for remission.

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AB0066 ACCELERATED MONOCYTE DIFFERENTIATION AND HIGH EXPRESSION OF MACROPHAGE COLONY-STIMULATING FACTOR RECEPTOR IN THE MONOCYTES MAY BE INVOLVED IN ACCELERATED OSTEOCLASTOGENESIS IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic proliferation of synovial cells and destructive polyarthritis. Various kinds of cells are involved in the pathogenesis of RA, including myeloid cells, lymphocytes, and synovial fibroblasts. It has been reported that there are abnormal myeloid cells in bone marrow of RA patients (Ochi, *et al.*, Arthritis Res. Ther., 2007). In addition, myeloid cells differentiate into monocytes/macrophages, which can thereafter differentiate into osteoclasts that mediate bone destruction in RA. In fact, we have previously reported CD14+ monocytes differentiated from induced pluripotent stem cells (iPSCs) derived from RA patients expressed more mRNA of receptor activator of nuclear factor-kappa B (RANK) than those from a healthy donor, non-onset family member (NOF), resulting in the accelerated osteoclastogenesis (Ito, *et al.*, The 36th annual meeting of the Japanese society of inflammation and regeneration, 2015). However, the question remains if distinct monocyte differentiation besides high RANK expression may also be involved in the accelerated osteoclastogenesis in RA.
Objectives: To investigate whether there is distinct monocyte differentiation between a RA patient and NOF.
Methods: iPSCs have been established from skin fibroblasts from a RA patient. For the controls, NOF of the patient are recruited as a donor in order to adjust hereditary background as much as possible. Monocytes were induced from each iPS clone culture on feeder-free conditions using a previously reported method (Cui, *et al.*, Front. Cell Dev. Biol., 2021). Floating cells were sequentially collected on days 10, 14, 18 and 22 during induction of monocytes from iPSCs. Surface phenotypes and the expression of differentiation markers of monocytes were analyzed with flow cytometry using the corresponding antibodies.
Results: RA-iPSCs differentiated into CD43+ (hematopoietic marker) cells earlier than NOF-iPSCs did (the data shown in Table 1). In addition, the proportion of CD45+ in CD43+cells (myeloid progenitors) was achieved in 93.0±4.8% (RA) and 51.0±21.3% (NOF) on day 18 (*p=0.029*) (the data shown in Table 1). The proportion of CD11b+CD45+ cells (monocytes and granulocytes) derived from RA-iPSCs was not significantly different from that from NOF-iPSCs. However, the proportion of $CD45^{high}$ in CD11b+CD45+ cells (monocytes) derived from RA-iPSCs was significantly higher than that from NOF-iPSCs on day 18 and 22 (the data shown in Table 1). $CD45^{high}$ in CD11b+CD45+ cells were mostly CD14+ cells. The proportion of CD115+, macrophage colony-stimulating factor receptor (MCSF-R), in CD14+ cells induced from RA-iPSCs tended to increase compared with NOF-iPSCs as the days of differentiation progressed (the data shown in Table 1).
Conclusion: Hematopoietic stem cells differentiate into myeloid progenitors in monocyte differentiation in RA earlier than those in NOF. Moreover, they differentiate into more CD14+CD11b+$CD45^{high}$ monocytes which are likely to express more MCSF-R as compared with those in NOF. We speculate that these distinct monocyte differentiation may play in accelerated osteoclastogenesis in RA.

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AB0067 MODE OF ACTION AND TARGET INVESTIGATION OF THE NEW ANTI-RHEUMATIC DRUG RABEXIMOD.

Keywords: Innate immunity, Rheumatoid arthritis, Cell biology

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Background: Rheumatoid arthritis (RA) is a chronic systemic inflammatory autoimmune disease which primarily affects the joints [1]. Numerous agents are currently used to modify the natural course of the disease, however, several RA patients still do not reach clinical remission[2]. A recently developed quinoxaline analogue named Rabeximod (RBM) showed clinical benefits comparable to TNF-α blockers in a mouse model of collagen antibody-induced arthritis[3]. Moreover, in a phase IIa clinical trial a significantly higher clinical efficacy of RBM + Methotrexate versus Methotrexate alone has also been confirmed.
Objectives: Since RBM's exact biologic target has not been entirely established yet, our objective is to investigate its mode of action at the cellular and molecular level.
Methods: Two *in vitro* models were developed: i) Toll-like receptor (TLR)-4 and TLR-2–stimulated peripheral blood mononuclear cells (PBMCs) cultured for 24-hours and ii) Monocytes derived-macrophages (MDMs), cultured for 96-hours in persisting inflammation conditions mimicking the different phases of ACPA-positive rheumatoid synovial inflammation: recruitment, initiation, development, and persistence of the inflammatory process. PBMCs-transcriptomic analysis was performed using a NanoString nCounter SPRING Profiler (customised panel). Cytokine production was measured by ELISA.
Results: RBM induced dose-dependent cell mortality. Among PBMCs, monocyte viability was preferentially affected compared to lymphocytes. RBM treatment reduced IL-6 and TNF-α production both in TLR4/TLR2-stimulated PBMCs and MDMs supernatants at 24h (PBMCs) and 10-, 24-, 48- and 72-hour time-points (MDMs). RBM-induced down-regulation of IL-6 and TNF-α in PBMCs was also obtained when PBMCs were pre-incubated for 7 hours prior to TLR activation (without additional RBM), suggesting an internalisation process. After 24h, RBM induced the downregulation of several pro-inflammatory genes in TLR-4 and-2 stimulated PBMCs, including IL-6, TNF-α, CSF1, FCN1, and SPP1. Finally, after 24 hours, MDMs treated with RBM developed an altered morphology independently of the frequency of treatment exposure and the stage of inflammation.
Conclusion: Overall, our data suggest that RBM acts predominantly on monocytes/macrophages and can inhibit the production of pro-inflammatory molecules playing a crucial role in RA.
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Table 1. Proportion of cells differentiated from RA-iPSCs and NOF-iPSCs

	CD43+ cells			CD45+ in CD43+ cells			$CD45^{high}$ in CD11b+CD45+ cells			CD115+ in CD14+ cells		
D	RA-iPSCs (% ± SD)	NOF-iPSCs (% ± SD)	p value	RA-iPSCs (% ± SD)	NOF-iPSCs (% ± SD)	p value	RA-iPSCs (% ± SD)	NOF-iPSCs (% ± SD)	p value	RA-iPSCs (% ± SD)	NOF-iPSCs (% ± SD)	p value
10	52.0± 6.5	23.4± 2.8	*0.002	36.3± 18.8	35.4± 14.5	0.953	27.3± 3.2	30.9± 9.8	0.584	28.0± 4.1	30.9± 8.9	0.638
14	49.8± 8.1	43.7± 20.8	0.662	78.4± 11.4	59.2± 25.5	0.298	36.9± 14.3	33.8± 8.9	0.769	44.4± 16.6	31.4± 9.9	0.309
18	44.4± 11.0	47.7± 10.9	0.735	93.0± 4.8	51.0± 21.3	*0.029	52.9± 7.2	28.6± 2.6	*0.005	75.5± 28.4	40.8± 8.8	0.113
22	32.3± 4.1	47.6± 12.6	0.116	87.0± 18.6	80.7± 6.6	0.611	53.3± 7.8	18.3± 2.7	*0.001	82.7± 7.5	45.7± 22.1	0.051

D = Day, * = significant

Sally Abdelmoaty Employee of: Cyxone AB, Carl Högerkorp Employee of: Cyxone AB, Costantino Pitzalis: None declared.
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AB0068 LOW-DOSE RADIOTHERAPY ATTENUATES EXPERIMENTAL AUTOIMMUNE ARTHRITIS BY INDUCING LYMPHOCYTE APOPTOSIS

Keywords: Animal models, Adaptive immunity, Rheumatoid arthritis

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Background: Disease-Modifying Anti-Rheumatic Drugs (DMARDs) have therapeutic effects on rheumatoid arthritis (RA) through the modulating immune responses of systemic and synoviums. However, DMARDs be used for an extended period, drug-related adverse effects can be a severe problem. Therefore, it is necessary to develop a treatment strategy to minimize the adverse effects of DMARDs, such as infection, abnormal liver function tests, and hematological abnormalities.
Objectives: Radiation therapy is one of the crucial therapeutic strategies for cancers. Low-Dose Radiotherapy (LDRT), the total dose may be given in fewer treatments or over a shorter period, has been tried to treat various inflammatory diseases, but its theoretical basis is poor. Therefore, this research aims to elucidate the mechanism and standardization of LDRT for RA.
Methods: The CIA (collagen-induced arthritis) and K/BxN mice used an experimental arthritic model representing RA. At the point of the highest arthritis symptoms, CIA and K/BxN mice were treated with LDRT. Then, the clinical score of the fore or hind paws was measured twice a week for 30 days. After 30 days of LDRT, the mice were sacrificed. Splenocytes, popliteal and inguinal lymphoid cells were analyzed by flow cytometry to measure the level of activation, proliferation, inflammatory-cytokines, and apoptosis of immune cells. To evaluate whether LDRT is effective on human immune cells, RA patients' PBMC were treated with LDRT and analyzed by flow cytometry.
Results: LDRT did not affect the lymphocyte activation, proliferation, differentiation, and inflammatory cytokine secretion. However, LDRT enhanced lymphocyte apoptosis and decreased immune cell numbers and clinical scores in CIA and K/BxN mice. In addition, the degree of cartilage destruction was reduced by treating with LDRT in K/BxN mice. Likewise, the proportion of apoptotic lymphocytes was increased by LDRT in PBMC of a patient with RA, not fibroblast-like synoviocytes (FLS).
Conclusion: We uncovered that LDRT diminished experimental arthritis such as CIA and K/Bx models via augmented lymphocyte apoptosis in draining lymph nodes. Thus, these findings suggest that LDRT can be a new therapeutic strategy with minimal adverse effects for RA.
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AB0069 MEASUREMENT OF IL-33/ST2 AXIS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND ITS ASSOCIATION WITH OTHER CYTOKINES IN SW982 AND U937 CELL LINES

Keywords: Cytokines and chemokines, Rheumatoid arthritis, Cell biology

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Background: An inflammatory maelstrom is a characteristic feature of autoimmune diseases including Rheumatoid Arthritis (RA). IL-33, a member of IL-1 cytokine family has been studied in animal models with induced RA and a few studies in RA patients. These studies have shown the exacerbation of IL-33, however little is known about its pathogenesis and association with other cytokines in vivo and in vitro.
Objectives: This study evaluated the expression of IL33 and ST2 in serum and Peripheral blood mononuclear cells (PBMC's) of active RA patients, in addition to other cytokines (IL-13, IL-5, IL-17) and biochemical parameters. TNF-alpha stimulated and synovial fluid (SF) conditioned growth medias were used to grow cell lines (SW982, U937) so as to have ambient physio-pathological microenvironment during experiments, typically of RA and then the levels of IL-33 were evaluated. Association of IL-33 with expression of LTB4 was also studied.
Methods: PBMC's and sera from 50 active RA patients and 50 healthy individuals were obtained. IL-33 and ST2 were measured using Real Time PCR with specific primers including internal controls. Sandwich ELISA was done for studying protein expressions. Cell lines were grown RPMI-1649 + 10%FBS for U937 and DMEM + Glutamine + 10% FBS for SW982 cells at 5% CO_2.
Results: IL-33 and ST2 mRNA expression was significantly higher in patients with active RA, with estimated fold change of 3.533($\Delta\Delta$Ct = -1.82121) and 4.172 ($\Delta\Delta$Ct = -2.15229) respectively, as compared to controls. ELISA results revealed mean value of IL-33 to be significantly higher in RA patients than in controls (119.32±63.49 and 22.835±12.24 respectively). An increase in serum protein of ST2 was also observed in RA patients as compared to healthy controls (2434.328±834.60 and 705.22±310.05). Out of the total (n^{RA} =50), 35 RA patients showed a hike in serum and mRNA expression of IL-33 which also showed correlation with other disease biomarkers like anti-CCP, CRP, DAS-28 CRP and HAQ-DI. Significant increase in serum protein of IL-17 (1542.112±120.21) and IL-5 (624.21±78.09) were observed. SF stimulated SW982 cells showed a 1.8 fold increase in levels of IL-33 as compared to cells which were stimulated with TNF alpha alone. Further monocytic cell line was treated with recombinantanti human IL-33 antibody and showed direct association with levels of Leukotriene B4 (LTB4) expression.
Conclusion: Elevated IL-33 and ST2 in both serum and PBMC's of RA patients showed correlation with the disease activity. Therefore, IL-33/ST2L signalling represents to be involved in the pathogenesis of RA and also indicates it to be a promising biomarker. Synovial fluid gives a natural microenvironment to cells in in-vitro studies showing increased expression of cytokines. This is the first study that shows a direct relation with IL-33 and LTB4 expression, thus proving the chemoattractive role of LTB4.
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AB0070 PIM KYNASES AS POSSIBLE THERAPEUTIC TARGETS IN INFLAMMARORY ARTHRITIDES

Keywords: Biomarkers, Cell biology, Inflammatory arthritides

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Background: Proviral integration site for Moloney murine leukemia virus (PIM) 1 kinase and its family members (PIM2 and PIM3) regulate several cellular functions including survival, proliferation and apoptosis. These proteins have been extensively studied in tumorigenesis, whereas their role in autoimmune and chronic inflammatory diseases remain unclear. PIM kinases are involved in T-cell amplification and differentiation in inflammatory Th1 and Th17 effector T cells subsets. Recent studies suggest that the expression of PIM1 is upregulated in fibroblast-like synoviocytes and CD4+ T cells from patients with rheumatoid arthritis (RA). However, data are

lacking regarding the potential role of PIM kinases in spondyloarthritis (SpA) such as psoriatic arthritis (PsA) and axial spondyloarthritis (AxSpA).
Objectives: To explore the potential role of PIM kinases in inflammatory arthritides, we evaluated PIM kinases expression at gene and protein level in patients with RA, PsA, and AxSpA compared to healthy controls (CTR).
Methods: PIMs expression was analysed in 26 (11 RA, 7 AxSpA, and 8 PsA) biologic DMARDs (bDMARDs)-naive arthritis patients and 13 controls. PIMs mRNA levels were determined in total RNA extracted from freshly isolated peripheral blood mononuclear cells (PBMC) by real-time semi-quantitative PCR. Protein levels were quantified in serum by ELISA test. Data were analysed by Kruskal Wallis test followed by Dunn's correction for multiple comparisons.
Results: All the samples showed expression of PIM1, 2, and 3 kinases both at gene and protein level, with PIM 3 being the less expressed protein. A trend towards lower expression of PIM1 was appreciated in AxSpA samples compared to other groups, reaching statistical significance only for serum protein levels compared to controls ($p < 0.05$). No significant differences were found in PIM2 and PIM3 expression, although all arthritis patients showed a trend towards higher serum levels compared to controls, not mirrored at gene expression levels.
Conclusion: PIM 1 mRNA expression in PBMCs seems to mirror PIM1 protein expression in the serum in all groups, supporting this molecule as a candidate biomarker. Controls, RA and PsA patients displayed similar levels, whereas AxSpA patients showed a trend towards reduced PIM1 levels deserving further investigation. Conversely, serum PIM2 and PIM3 levels did not mirror PIM2 and PIM3 gene expression in resting PBMC. Unlike PIM1, the expression of PIM2 and PIM3 have never been studied in PsA and AS, and additional data are required to explore the potential relevance of PIM2 and PIM3 in SpA pathophysiology. Further studies are also required to evaluate PIM kinases modulation after in vitro cell stimulation, the differential expression in PBMC subpopulations, and the impact of disease activity and concurrent disease-modifying medications.
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Table 1. PIM1, 2, and 3 expression in rheumatoid arthritis, axial spondyloarthritis, psoriatic arthritis and healthy controls. Data are expressed as medians with interquartile ranges [25th-75th percentiles].

PIM 1	RA	AxSpA	PsA	CTR
Gene expression in PBMC (in respect to GAPDH)	0.17 [0.11-0.22]	0.12 [0.06-0.67]	0.3 [0.25-0.42]	0.22 [0.14-0.30]
Serum protein concentration (ng/ml)	21.1 [0.19-37.18]	4.05 [2.44-19.74] p<0.05 vs CTR	23.43 [9.4-38.13]	27.35 [15.73-29.36]
PIM 2	**RA**	**AxSpA**	**PsA**	**CTR**
Gene expression in PBMC (in respect to GAPDH)	0.28 [0.2-0.32]	0.19 [0.14-0.32]	0.38 [0.35-0.43]	0.3 [0.23-0.37]
Serum protein concentration (ng/ml)	8.09 [4.28-10.01]	6.22 [5.08-9.24]	6.2 [2.69-11.38]	4.57 [4.57-8.64]
PIM 3	**RA**	**AxSpA**	**PsA**	**CTR**
Gene expression in PBMC (in respect to GAPDH)	0.012 [0.007-0.018]	0.014 [0.009-0.022]	0.013 [0.012-0.034]	0.015 [0.01-0.02]
Serum protein concentration (ng/ml)	1.57 [0.83-2.07]	1.25 [0.53-2.22]	0.91 [0.55-1.51]	0.79 [0.29-1.54]

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Disclosure of Interests: None Declared.
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AB0071 PRE-CLINICAL EVALUATION OF ANTI-ANGIOGENIC EFFECTS OF CANDIDATE AGENTS FOR MOLECULAR DIAGNOSTIC IMAGING AND THERAPY IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Synovium, Imaging

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Background: The role of pathological angiogenesis is widely recognized in cancer and various inflammatory diseases, including rheumatoid arthritis (RA). In RA, angiogenesis and inflammation are mutually dependent and play a cooperative role in the disease progression. Angiogenesis mainly relies on the interaction of vascular endothelial cells (ECs), fibroblasts, macrophages, and the extracellular matrix. This phenomenon promotes the infiltration of inflammatory cells into the joints, resulting in more synovial inflammation and structural damage. In this process, a number of soluble and cell surface-bound angiogenic mediators are involved providing candidate targets for diagnosis and therapy [1, 2]. Anti-angiogenesis strategy has been widely used in tumor treatment and its potential value in RA as a single or in combination therapy need to be further explored.
Objectives: To assess potential anti-angiogenic effects of selected compounds with different mechanisms of action in preclinical models of angiogenesis for exploitation as candidate agents for molecular imaging and/or therapeutics purposes.
Methods: Two *in vitro* models of angiogenesis were employed in this study: (i) a scratch assay assessing the closure rate of scratches made in human microvascular endothelial cells (HMEC-1) [3] in the presence of drugs for 24 hr, and (ii) 3D-spheroid model of angiogenesis composed of ECs and fibroblasts, assessing the impact of drugs on EC sprout formation after 40 hr of incubation. Sprout quantification was performed via confocal microscopy and digital image analysis [2]. Candidate anti-angiogenic compounds examined in this study included: sunitinib (pan-kinase inhibitor), a small molecule NF-κB-inducing kinase inhibitor (NIKi), tofacitinib (selective JAK1/3 inhibitor) and fluciclatide (RGD-peptide targeting $\alpha_V\beta_3$ and $\alpha_V\beta_5$ integrins) and tested in concentration range of 0-10 μM. An MTT-proliferation inhibition assay was used to monitor any drug-induced cytotoxicity.
Results: In scratch assays, sunitinib exhibited irreversible inhibition (max 75% at 10 μM after 24 hr incubation) compared to NIKi which had a transient inhibitory effect (max 59% at 10 μM after 8 hr incubation). No apparent effects were observed for tofacitinib up to concentrations of 10 μM. Interestingly, fluciclatide, induced morphological changes at concentration of 0.1 μM, impairing scratch closures. Next, the anti-angiogenic effects of the compounds were verified in the 3D-spheroid model that more closely mimics the *in vivo* situation. Here, marked blockade of sprout formation was noted at 0.1 μM for sunitinib, and 1-2.5 μM for NIKi, tofacitinib and fluciclatide. MTT assays indicated that none of the observed drug-effects were due to induction of cytotoxicity at the indicated concentrations.
Conclusion: This study identified various compounds (sunitinib, NIKi, tofacitinib and fluciclatide) exhibiting potential anti-angiogenic properties *in vitro,* encouraging their further evaluation as radionuclide imaging and therapeutic agents for diagnosis and therapeutics in vivo.
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Disclosure of Interests: None Declared.
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AB0072 THE METABOLITES WERE ALTERED IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Biomarkers, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is characterized by persistent synovitis and abnormal antibodies production[1].The discovery of follicular helper T cells (Tfh) and follicular regulatory T cells (Tfr) has added a new understanding of the mechanisms of antibody production in RA such as anti-cyclic peptide containing citrulline (anti-CCP) [2]. The gut microbiota-derived metabolites are also important in regulating immune system to balance disease and health. And the altered gut microbiota-derived metabolites had been found in RA patients[3]. However, the relationship between gut microbiota-derived metabolites and Tfr/Tfh cells has not been comprehensively evaluated in RA patients to date, which is the focus of our study.
Objectives: We detected the gut microbiota-derived metabolites and the expression of Tfr and Tfh cells in new-onset RA patients, and then analyzed the relationship between gut microbiota-derived metabolites and Tfr/Tfh cells.
Methods: 17 patients with new-onset RA from the Second Hospital of Shanxi Medical University were recruited. And 13 sex- and age-match healthy controls

(HCs) were enrolled. Fecal samples were collected to determine the gut microbiota-derived metabolites by LC-MS/MS-based nontargeted metabolomic. And blood samples were collected to detect the expression of circulating Tfr and Tfh cells by flow cytometry.

Results: The fecal metabolite profiles between RA and HC groups were different (Figure 1A, B). There were 61 differential annotated metabolites in RA including 34 metabolites upregulated and 27 metabolites downregulated compared to HCs (Figure 1C, D). The KEGG pathway enrichment analysis of the differentially abundant metabolites showed that there were only four pathways were the main pathways related to RA including biosynthesis of unsaturated fatty acids, arginine biosynthesis, tryptophan metabolism as well as alanine, aspartate and glutamate metabolism (Figure 1E). And eleven differentially abundant metabolites were involved in the four mainly altered pathways. The correlation heatmap of the association of the eleven differentially abundant metabolites with indicators of RA was shown in Figure 2A. It showed that the increased arachidonic acid was positively correlated with DAS28, ESR and anti-CCP. We identified the potential biomarker value of RA by performing receiver operating characteristic (ROC) curve analysis, which showed that arachidonic acid yielded the area under curve (AUC) of 0.724 [95% CI = 0.539-0.909, *P*=0.038]. It suggested that arachidonic acid was the potential biomarker of RA (Figure 2B). And arachidonic acid was negatively associated with the number of Tfr cells (r=-0.645, *P*=0.006) and the c-Tfr/c-Tfh ratio (r=-0.623, *P*=0.009).

Conclusion: There was an obvious difference in the fecal metabolite profiles between RA and HCs. Arachidonic acid was identified as the potential biomarker of RA, and the increased arachidonic acid was negatively associated with Tfr cells to affect the disease activity and the production of anti-CCP in RA.

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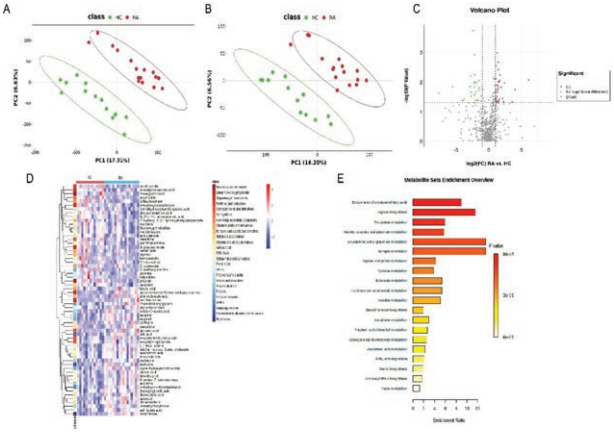


Figure 1. (A) The fecal metabolite profiles between RA and HC groups in the positive ion mode were different. (B) The fecal metabolite profiles between RA and HC groups in the negative ion mode were different. (C) The volcano plot showed the differentially altered metabolites. (D) The heatmap of differentially abundant metabolites. (E)The KEGG pathway enrichment analysis of the differentially abundant metabolites.

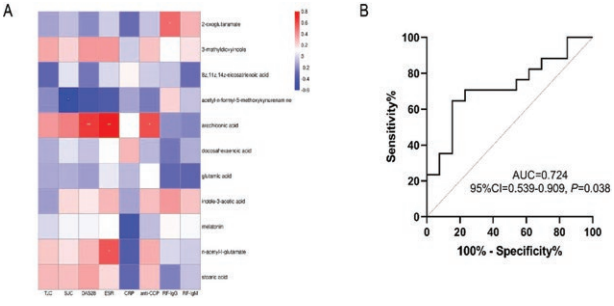


Figure 2: (A) The correlation heatmap of differentially abundant metabolites with indicators of RA. (B)The ROC curve analysis of arachidonic acid.

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AB0073

ANTI-ARTHRITIC ACTIVITIES OF THE ELEUTHEROCOCCUS SENTICOSUS, ACHYRANTHES JAPONICA, AND ATRACTYLODES JAPONICA MIXED EXTRACT FERMENTED WITH NURUK IN A TYPE II COLLAGEN-INDUCED ARTHRITIS MOUSE MODEL

Keywords: Rheumatoid arthritis, Animal models, Inflammatory arthritides

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Background: Rheumatoid arthritis (RA) is an autoimmune disease that is accompanied by chronic synovitis, progressive cartilage, and bone destruction and is affected by inflammatory-associated factors. Vigeo is a mixture of fermented extracts of *Eleutherococcus senticosus* Maxim (ESM), *Achyranthes japonica* (Miq.) Nakai (AJN), and *Atractylodes japonica* Koidzumi (AJK) manufactured using the traditional Korean nuruk fermentation method. Although the bioactive effects of ESM, AJN, and AJK have already been reported, the pharmacological effects of Vigeo have not been proven.

Objectives: In this study, we investigated whether Vigeo had inhibitory effects on RA and its intracellular mechanisms using a type II collagen-induced arthritis (CIA) mouse model.

Methods: CIA was induced in DBA/1 mice by immunization with bovine type II collagen. The mice were administered orally with Vigeo (200 and 500 mg/kg/day, i.g.) from days 21 to 42 after immunization. The clinical scores, hind paw swelling, and histopathological finding were evaluated in the paw of CIA mice. The levels of tumor necrosis factor α (TNF-α), interleukin (IL)-6, and IL-1β in the serum were measured by enzyme-linked immunosorbent assay.

Results: The results showed that Vigeo 500 mg/kg treatment significantly alleviated the severity of the disease, based on the reduced hind paw swelling and clinical scores, compared with untreated CIA mice. Comparing with untreated CIA mice, Vigeo 500 mg/kg treatment inhibited the levels of TNF-α, IL-6, and IL-1β in the serum.

Conclusion: Our results suggest that anti-inflammatory effects of Vigeo against collagen-induced arthritis in mice may be due to its ability to inhibit pro-inflammatory mediators. Vigeo may be a promising potential therapeutic reagent for arthritis treatment.

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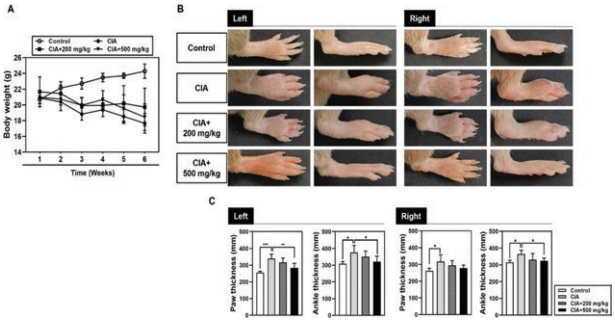


Figure 1. Effect of Vigeo on the progression of collagen-induced arthritis (CIA). Eight-week-old male DBA/1 mice were first immunized with Col 2 and CFA on day 0 and then immunized intraperitoneally with Col 2 on day 21. Next, booster injection with LPS was given on day 28. CIA mice were orally administrated with Vigeo (200 mg/kg or 500 mg/kg) every day from day 22 to 42. The body weight change was determined on the indicated days (A). Representative photographs of control, PBS-, and Vigeo-treated CIA mice (B). The paw thickness and ankle thickness were determined as described. #p < 0.05, ##p < 0.01 and ###p < 0.001.

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Disclosure of Interests: None Declared.
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AB0074 PROTEOMIC ANALYSIS OF CARDIOMETABOLIC AND CARDIOVASCULAR BIOMARKERS FOR THE DIAGNOSIS OF RHEUMATOID ARTHRITIS. REGULATION BY METHOTREXATE AND JAK INHIBITORS

Keywords: Biomarkers, Cardiovascular disease, Rheumatoid arthritis

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Background: Patients with rheumatoid arthritis (RA) have a high risk of suffering cardiovascular disease. The cardiovascular and cardiometabolic proteome analysis in RA patients may provide disease biomarkers and insights into the biological pathways that contribute to cardiovascular risk.
Objectives: 1) To evaluate the changes in the cardiometabolic and cardiovascular serum proteome in two cohorts of active RA patients: newly diagnosed (naïve-treated) and well-established disease and its relationship with the clinical characteristics and 2) to analyze the modulation of the levels of these proteins by methotrexate and tofacitinib.
Methods: 1) Cross-sectional study in two cohorts of RA: patients at diagnosis (n=25) and patients with established disease (evolution time>25 years, n=25), age and sex-matched with healthy donors (n=25). 2) Longitudinal study was performed on 25 RA patients treated with methotrexate and 25 RA patients treated with Tofacitinib combined with DMARDs for 6 months. Clinical and analytical variables were recorded. Proteomic profiling of 184 proteins (cardiometabolic and cardiovascular II panels) was performed in the serum using Olink Proteomics technology.
Results: There were no statistical differences between the RA at diagnosis and RA-established disease groups in age and DAS28. The evolution time average in the RA-established disease group was 37.48±11.79 years. One hundred and seven proteins were significantly increased in the serum of RA patients at diagnosis, among these 47 proteins were elevated in RA patients with established disease. The PCA analysis showed that the alteration of these proteins could discriminate between RA patients and healthy donors. The molecules that more significantly increased in the RA at diagnosis group were SAA4, ST6GAL1, CCL18, TNC, IGLC2, IL6, SORT1, TNFRSF10A, AGRP, and CD4. In addition, the top ten molecules significantly elevated in RA patients with the established disease were SAA4, CCL18, ST6GAL1, CRTAC1, ANGPTL3, TNFRSF10A, LEP, Gal-9, SORT1, and TRAIL-R2. The increase of these proteins was associated with the inflammation shown by the correlation with C reactive protein (CRP) levels and DAS28. The elevated levels of SAA4 (serum amyloid A protein-4) discriminated between RA patients and healthy donors with high sensitivity and specificity (AUC=0.95). Treatment with methotrexate in RA patients at diagnosis reduced the levels of 64 proteins (50% of the altered proteins) while tofacitinib modulated the expression of 30 proteins (50% of the altered proteins) in RA patients with established disease after 6 months. These reductions were associated with a decrease in CRP and DAS28 levels.
Conclusion: 1)The cardiovascular and cardiometabolic serum proteome is altered in RA patients at diagnosis and after a long time of the disease evolution and chronic treatments, 2) SAA4 may represent a biomarker for the diagnosis of RA with high sensitivity and specificity, 3) Methotrexate and tofacitinib specifically modulate the alteration on the serum proteome after six months of treatment alongside the reduction of clinical inflammatory and disease activity markers.
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AB0075 PRESENCE AND EFFECT OF MUSCLE GDF-8 AND GDF-11 IN THE SYNOVIUM OF PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Synovium

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Background: Myokines, such as the growth differentiation factor (GDF) 8 and 11, have the function of regulating autocrine and paracrine activities on muscle tissue metabolism. In Rheumatoid Arthritis (RA), there is increased expression of GDF-8 in the synovial membrane compared to osteoarthritis (OA) patients, more specifically by fibroblast-like synoviocytes (FLS). On the other hand, the GDF-11 treatment appears to have a protective effect against the development of experimental arthritis. Therefore, more studies evaluating the serum and synovial membrane levels of the GDF-8 and GDF-11 in RA patients are needed to better define their possible roles in this disease.
Objectives: To evaluate the GDF-8 and GDF-11 in serum and synovial membrane levels in RA patients and to assess their *in vitro* effect on FLS.
Methods: Patients diagnosed with RA and patients with knee OA with the indication of knee arthrocentesis were included in the study. Disease activity was assessed by Clinical Disease Activity Index (CDAI). The evaluation of serum and synovial fluid levels of GDF-8 and GDF-11 was performed by ELISA. FLS were isolated from the synovial fluid of RA patients, and cell viability was determined in the presence and absence of GDF-8 and GDF-11 (10nM; 20nM and 50nM) for 24h and 48h by the MTT assay. Kolmogorov–Smirnov, Mann-Whitney U and Spearman's correlation tests were performed using SPSS version 20.0 (accepted at $p \leq 0.05$).
Results: As preliminary data, samples from 11 patients with RA and 5 patients with knee OA were evaluated. GDF-8 synovial fluid levels were lower than serum levels in RA patients (p=0.007) and were negatively correlated with disease duration (r=-0.684, p=0.02). GDF-11 levels in synovial fluid were also lower than in serum in RA (p=0.018) and were higher in RA patients than in the OA group (p= 0.052). Furthermore, treatment with different concentrations of GDF-8 and GDF-11 did not affect FLS viability.

Table 1. Clinical features of study population

Characteristics	RA (n=11)	OA (n=5)
Age in years (mean ± SD)	65.3 ± 9.26	66.6 ± 5.22
Women, n (%)	10 (90.9)	3 (60)
Disease duration in years (mean ± SD)	16 ± 12.41	
CDAI (mean ± SD)	12.8± 5.68	
Synovial fluid		
GDF-8 (pg/ml) (median (IQR))	31.30 (31.30-181.80)	232.10 (106.15- 855.50)
GDF-11 (pg/ml) (median (IQR))	31.30 (31.30- 88.13)	31.30 (31.30- 31.30)
Serum		
GDF-8 (pg/ml) (median (IQR))	817.20 (334.30- 994.70)	761.70 (440.55- 1312.05)
GDF-11 (pg/ml) (median (IQR))	347.50 (31.30- 1818.00)	31.30 (31.30- 31.30)

RA, rheumatoid arthritis; OA, osteoarthritis; SD, standard deviation; CDAI, clinical disease activity index; IQR, interquartile range.

Conclusion: In this preliminary research, we found lower GDF-8 and GDF-11 synovial fluid levels than in serum in RA patients and higher GDF-11 serum levels in the RA group compared to the OA group. This result could be related to local compensatory mechanisms against the inflammatory state. *In vitro*, both GDF-8 and GDF-11 did not induce proliferation or death of FLS, and more studies are undergoing to analyze their impact on the FLS phenotype. Our results contribute to the knowledge about the participation of myokines in the pathogenesis of RA.
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AB0076

THE THERAPEUTIC POTENTIAL OF CIRCULATING AUTOLOGOUS TISSUE HOMING EXTRACELLULAR VESICLES FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS PATIENTS

Keywords: Animal models, Rheumatoid arthritis, bDMARD

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Background: Progress has been achieved with the introduction of biologics for the management of inflammatory/autoimmune diseases such as rheumatoid arthritis (RA), however such medications induce immune suppression, which is nonselective to the pathogenesis of the disease, resulting in higher rates of infections. Therefore, there are unmet medical needs in the treatment of such diseases, which should be addressed by novel approaches. Accumulating evidence suggests that extracellular vesicles (EVs) play a role in the establishment, maintenance and modulation of autoimmune processes.
Objectives: In the current study, we hypothesized that isolation of circulating autologous tissue-specific homing EVs from RA patients - may improve the delivery of current FDA-approved anti-inflammatory drugs, which will be encapsulated into these EVs. The drug-loaded EVs will be injected back to the diseased subjects and will naturally find their way to the inflamed tissue.
Results: Indeed, we found that autologous labeled EVs, expressing joint/synovia-specific homing receptors (e.g. αVβ3 integrin), derived from blood of diseased arthritic mice (Collagen antibody-induced arthritis model), can migrate toward the inflamed synovia, using *in vivo* imaging system (IVIS). Moreover, we show that these EVs strongly expresses glucose transporter 1 (mGLUT1) which in turn, improve their therapeutic potential to be loaded with anti-inflammatory drugs using glucose-coated gold nanoparticles (GNPs). Finally, we show that EVs derived from plasma of RA patients overexpresses αVβ3 integrin and taken up by LPS/TNFα-induced activated human synovial cell line *in vitro*.
Conclusion: Overall, we show the potential of autologous circulating EVs of RA patients to serves as natural nano-carrier for current FDA-approved drugs. We believe that this strategy will increase the specificity and efficiency of current treatment, therefore it will reduce side effects and will improve the quality of life of RA patients and potentially other autoimmune disease patients.
REFERENCES: NIL.
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Disclosure of Interests: None Declared.
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AB0077

SEMAPHORIN4B IS UPREGULATED IN RHEUMATOID ARTHRITIS PATIENTS AND INDUCES EXPRESSION OF INFLAMMATORY MEDIATORS BY MACROPHAGES AND FIBROBLAST-LIKE SYNOVIOCYTES

Keywords: Rheumatoid arthritis, Cytokines and chemokines, Synovium

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Background: Several studies have shown that different semaphorin family members are involved in the pathogenesis of rheumatoid arthritis (RA). On one hand, our group has demonstrated that (Sema)phorin 3B and Sema3F are reduced in RA patients and play a protective role. On the other hand, Sema4A and Sema4D are increased in RA patients and are associated with inflammatory processes (Garcia, 2019; Igea, 2022).
Objectives: The aim of this study is to determine the role of Sema4B in the pathogenesis of RA.
Methods: Gene expression of Sema4B was obtained from the gene expression array available in Gene Expression Omnibus-NCBI (GSE77298). Fibroblasts-like synoviocytes from RA patients (RA-FLS) (n=8) were stimulated 4 and 24 h with Sema4B (200ng/mL), TNF (10 ng/mL) or the combination of both. Peripheral blood monocytes from RA patients (n=12) were differentiated into M1 macrophages by culturing in the presence of IFN-γ (10 ng/mL) for 6 days. Afterwards, macrophages were stimulated 24 h with Sema4B (200ng/mL), LPS (10 ng/mL) or the combination of both. The expression of inflammatory mediators was determined by quantitative PCR (qPCR) and ELISA. Viability and migration of FLS were determined using calcein assays and wound closure assays, respectively.
Results: Sema4B expression was significantly higher in the synovial tissue and FLS of RA patients compared to healthy controls (HC) and osteoarthritis patients (OA), respectively. A significantly higher expression of *SEMA4B* in the synovium and FLS of RA patients compared to, respectively, was found. Interestingly, TNF stimulation induced the expression of *SEMA4B* by RA-FLS. Functional studies showed that Sema4B did not affect the viability of FLS but increased their migratory capacity. Moreover, Sema4B alone did not induce the expression of inflammatory mediators (data non shown), but significantly enhanced the TNF-induced expression of *IL6, IL8, TNF, CCL2* and *MMP3* (Figure 1A) and the secretion of TNF. Finally, Sema4B alone did not modulate the expression of inflammatory mediators in macrophages, but significantly enhanced the LPS-mediated expression of *TNF*, *CCL2*, and *MMP1* (Figure 1B), as well as the TNF protein secretion.

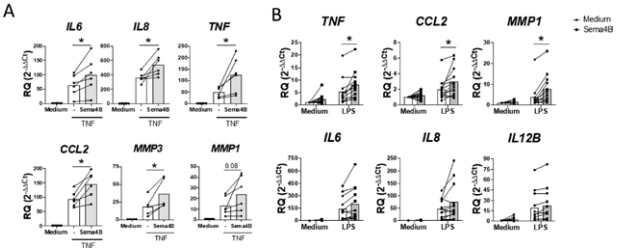


Figure 1. Sema4B enhances pro-inflammatory activity in FLS (n=6) and macrophages (n=10) of RA patients. (A) Significative increment of the genetic expression of pro-inflammatory mediators in RA-FLS stimulated with Sema4B (200 ng/ml), TNF (10 ng/mL) and their combination for 24 hours. (B) Significative increase of the genetic expression of pro-inflammatory mediators in M1 macrophages. Macrophages differentiated from monocytes of RA patients during 6 days (IFN-γ 10 ng/mL) and stimulated with Sema4B (200 ng/ml), LPS (10 ng/mL) and their combination for 24 hours. Symbols represent individual patients; bars show the mean ± SEM. *P < 0.05.

Conclusion: Our data demonstrate that, in an inflammatory context, Sema4B induces FLS migration and the production of inflammatory mediators by FLS and macrophages. These results suggest that Sema4B is involved in inflammatory processes observed in the RA synovium and might be a potential therapeutic target in the treatment of RA.
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AB0078

EARLY ARTHRITIS: IS JAK-STAT SIGNALING KEY TO DISEASE PROGRESSION?

Keywords: Innate immunity, Targeted synthetic drugs, Inflammatory arthritides

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Background: Janus kinase inhibitors (JAKi) are a new therapeutic class approved for the treatment of chronic arthritis. JAKi suppress the activity of STAT tyrosine kinases, interfering with the signaling pathway which is critical for immune cell proliferation, survival and differentiation. Our group has demonstrated that early treatment with a JAKi, in animal models, abrogates disease and prevent bone damage. We hypothesize that JAK-STAT pathway is key to chronic arthritis onset and its early inhibition might have a major effect on disease control.

Objectives: The main goal of this study is to characterize the JAK-STAT signaling pathway activation in untreated early arthritis patients.
Methods: Peripheral blood mononuclear cells were isolated from blood samples collected from untreated early arthritis patients (<12 months of disease duration). Frequency, phenotype and STAT phosphorylation (by mean fluorescence intensity, MFI) levels were evaluated on T and B cells, monocytes and dendritic cells (DC) by flow cytometry. A group of age and sex-matched healthy individuals was included for comparison.
Results: The frequency of total CD19+ B cells was similar between patients and controls, although patients presented a significantly decreased level of pre-switch memory B cells when compared to controls. No significant differences were observed in naïve, post-switch memory, double negative B cells, transitional B cells and plasmablasts. The frequency of total CD3+ T cells, CD14+ monocytes and DCs was similar, however patients had significantly decreased levels of plasmacytoid DCs. In addition, we found that STAT3 phosphorylation levels were significantly increased in B cells and DCs in early arthritis patients. The STAT1, STAT5 and STAT6 phosphorylation levels were similar in T and B cells, monocytes and DCs, when compared with the control group.
Conclusion: Alterations in the frequencies of circulating memory B cell subsets and pDCs, but not in T cells and monocytes, are found in untreated early arthritis patients when compared to healthy controls. Changes in STAT3 phosphorylation MFI levels observed in B cells and DCs from early arthritis patients in comparison to controls support an early activation of JAK-STAT pathway in the initial phase of arthritis and a role of these cells in disease pathogenesis.
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AB0079 THEAFLAVIN ALLEVIATES COLLAGEN-INDUCED ARTHRITIS IN MICE BY DECREASING REACTIVE OXYGEN SPECIES AND PRO-INFLAMMATORY CYTOKINES

Keywords: Rheumatoid arthritis

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Background: An autoimmune disease that causes inflammation and bone and cartilage deterioration is rheumatoid arthritis (RA). In the pathogenesis of RA, oxidative stress and pro-inflammatory cytokines are important factors. The main polyphenol in black tea, theaflavins (TFs), has been used medically to treat a variety of inflammatory illnesses by reducing inflammation and reactive oxygen species (ROS)
Objectives: The medications available to treat RA have a variety of side effects. The current study was designed to assess the anti-arthritic properties of theaflavin in a mouse collagen-induced arthritis model.
Methods: In order to induce arthritis in DBA/1 mice, type II collagen was administered intradermally. From days 21 through days 42, different doses of theaflavin (50 and 100 mg/kg/day) were orally administered. To determine the effect of theaflavin on collagen-induced arthritis, histological analyses were conducted. In addition, the generation of reactive oxygen species (ROS), nitric oxide, and the activities of enzymatic antioxidants (superoxide dismutase, glutathione peroxidase, catalase, and glutathione reductase) in the joint homogenate of mice were examined. The levels of TNF-, IL-6, and IL-1β were also measured by ELISA to detect inflammation.
Results: Our results showed anti-oxidant and anti-inflammatory effects of theaflavin in arthritic mice. Histopathological studies corroborated the anti-arthritic properties of theaflavin. The compound was found to be effective in lowering ROS and nitric oxide levels while increasing enzymatic antioxidant levels. Theaflavin therapy also reduced TNF-, IL-6, and IL-1β levels.
Conclusion: In mice with arthritis, theaflavin was successful in reducing inflammation and oxidative stress. These results suggest that theaflavin may be used in conjunction with other treatments to manage RA.

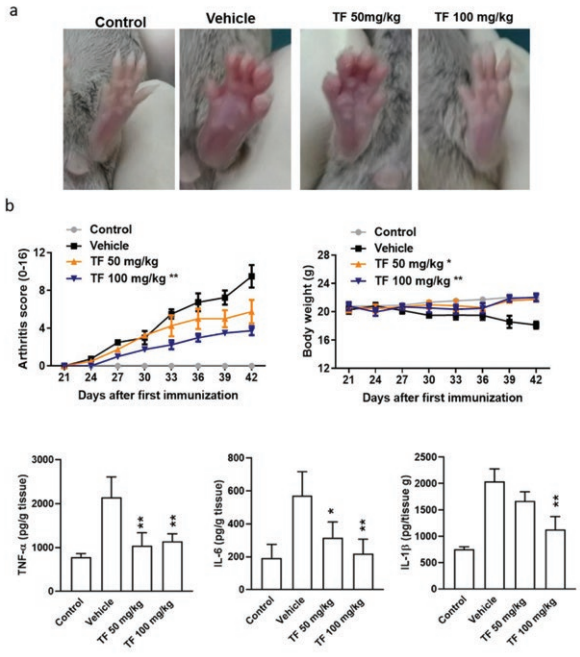


Figure 1. TF ameliorated the severity of arthritis in CIA mouse models. (a) Representative photographs depicted the swollen and reddened rear paws of four animal groups 42 days following the initial vaccination. (b) Accumulated clinical arthritis scores in each leg ranged from 0 to 4 and were evaluated every three days using a visual scoring system. The changes in body weight of normal control or CIA mice treated with or without TF or vehicle were recorded every three days till day 42. (c) TNF-, IL-6, and IL-1 inflammatory cytokine protein levels in arthritic mouse hind paw tissues. On day 42, CIA in DBA/1 mice hind paw homogenates were taken from the normal control, vehicle-treated, or TF-treated (50 or 100 mg/kg) groups of mice. The cytokine profiles were measured using ELISA according to the techniques given. ** $p < 0.01$ and * $p < 0.05$ showed statistically significant differences in two-way ANOVA compared with the vehicle-treated CIA group

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Acknowledgements: NIL.
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AB0080 IMBALANCE OF MONOCYTE/MACROPHAGE POLARIZATION IN PERIPHERAL BLOOD AND SYNOVIAL FLUID OF RHEUMATOID ARTHRITIS PATIENTS

Keywords: Innate immunity, Rheumatoid arthritis

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Background: Macrophages strongly contribute to the pathogenesis of rheumatoid arthritis (RA), initiating the inflammatory response, the join damage, but also may promote the resolution of inflammation and the restoration of tissue immune-homeostasis [1,2]. This seems to be related to an unbalanced immunological response mediated by macrophages through their polarization into "classically" and "alternatively" activated phenotypes (M1 or M2) [3,4]. However, little is known about the M1 and M2 phenotype of their circulating precursors (monocytes) in the peripheral blood (PB) and the synovial fluid (SF) of RA patients.
Objectives: To characterise the polarization status (M1 and M2) of PB and SF monocytes of RA patients together with their distribution in the monocyte subsets by flow cytometry (FC).
Methods: Nineteen RA patients not yet treated with biological DMARDs (mean age 62±14 years), who fulfilled the 2010 ACR/EULAR classification criteria for RA and treated in accordance with EULAR recommendation, as well as 19 age-matched healthy subjects (HSs) were enrolled after signed informed consent.

PB and SF cells were collected from each RA patient, whereas only PB cells were collected from HSs. The expression of CD14 and CD16 surface markers allowed to identify the monocyte population and the monocyte subsets: "classical"(CD14++CD16-), "intermediate"(CD14++CD16+), and "non-classical"(CD14-CD16+). The M1 phenotype (M1 monocytes) was identified by the evaluation of CD80, CD86, TLR2 and TLR4, whereas the M2 phenotype (M2 monocytes) was identified evaluating CD204, CD163 and CD206 surface markers. Results were expressed as percentage of positive cells over total leukocytes from PB and SF. Statistical analysis was carried out by Mann-Whitney non-parametric test.

Results: In RA patients, the percentage of CD14++CD16+monocytes was significantly higher in PB compared to that in HS ($p<0.001$), and it was higher in SF compared to PB ($p<0.05$). The percentage of CD14-CD16+monocytes was significantly increased in RA-PB compared to HS-PB and RA-SF ($p<0.01$; $p<0.05$). RA patients were characterized by an increased percentage of M1 monocytes ($CD80^+CD86^+TLR2^+TLR4^+CD204^-CD163^-CD206^-$cells) in PB compared to HSs and compared to RA-SF. The percentage of M2 monocytes ($CD204^+CD163^+CD206^+CD80^-CD86^-TLR2^-TLR4^-$cells) was also increased in RA-PB compared to HS-PB and to RA-SF, but this increase was lower and not significant than that observed for M1 monocytes. Moreover, the M1-M2 monocyte ratio was 8:1in RA-PB. Therefore, in RA patients, circulating M1 monocytes belonged to the "non-classical" subset, whereas M2 monocytes belonged to the "classical" subset. The percentage of circulating mixed M1/M2 monocytes ($CD80^+CD86^+TLR2^+TLR4^+CD204^+CD163^+CD206^+$cells) was higher in RA patients compared to HSs. Moreover, in RA patients, the percentage of these cells was higher in SF than in PB and they primarily belonged to the "intermediate" monocyte subset. Interestingly, the highest percentage of M2 and mixed M1/M2 monocytes was observed in PB and SF of RA patients receiving a higher daily (25mg) and cumulative glucocorticoid dosages.

Conclusion: The results confirm that RA is an immune-inflammatory disease mainly mediated by both M1 monocytes and macrophages, as demonstrated by the increase in the percentage of circulating M1 monocytes. Glucocorticoids might contribute to the M1 to M2 transition, which characterizes RA patients under remission by increasing mixed M1/M2 and M2 monocyte percentage.

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Disclosure of Interests: Stefano Soldano: None declared, Emanuele Gotelli: None declared, Paola Montagna: None declared, Rosanna Campitiello: None declared, Alberto Sulli: None declared, Vanessa Smith: None declared, Maurizio Cutolo Grant/research support from: BMS, Boehringer, Amgen.
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AB0081 GLUTATHIONE PEROXIDASE 3 IS A NOVEL CLINICAL DIAGNOSTIC BIOMARKER AND POTENTIAL THERAPEUTIC TARGET FOR NEUTROPHILS IN RHEUMATOID ARTHRITIS

Keywords: Biomarkers, Rheumatoid arthritis

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Background: Neutrophils have a critical role in the pathogenesis of rheumatoid arthritis (RA) with immune system dysfunction. However, the molecular mechanisms of this process mediated by neutrophils still remain elusive.

Objectives: The purpose of the present study is to identify hub genes in neutrophils for diagnosis and treatment of RA utilizing publicly available datasets.

Methods: Gene expression profiles were downloaded from the Gene Expression Omnibus and batch-corrected and normalized expression data were obtained using the ComBat package. Gene Ontology and Kyoto Encyclopedia of Genes and Genomes enrichment analysis were used to conduct significantly functional analysis and crucial pathways. The resulting co-expression genes modules and hub genes were generated based on the weighted gene co-expression network analysis and visualization by Cytoscape. Flow cytometry was conducted to detect reactive oxygen species (ROS) levels in neutrophils.

Results: Neutrophils underwent transcriptional changes in synovial fluid (SF) of RA patients, different from peripheral blood of healthy controls or patients with RA. Especially, glycolysis, HIF-1 signaling, NADH metabolism, and oxidative stress were affected. These hub genes were strongly linked with classical glycolysis-related genes (ENO1, GAPDH, and PKM) responsible for ROS production. The antioxidant enzyme glutathione peroxidase 3 (GPX3), a ROS scavenger, was first identified as a hub gene in RA neutrophils. Neutrophils from patients with autoimmune diseases had markedly enhanced ROS levels, most notably in RA SF.

Conclusion: This research recognized hub genes and explored the characteristics of neutrophils in RA. Our findings suggest that the novel hub gene GPX3 is involved in the neutrophil-driven oxidative stress-mediated pathogenesis of RA. It has the potency to be a target for neutrophil-directed RA therapy.

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Disclosure of Interests: None Declared.
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AB0082 AGE-RELATED GENES USP2 AND ARG2 ARE INVOLVED IN THE REDUCTION OF IMMUNE CELL INFILTRATION IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Biomarkers, Rheumatoid arthritis, -omics

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Background: As the prevalence of rheumatoid arthritis (RA) in the elderly is increasing, rheumatologists are increasingly concerned about this group of patients. There is a large gap between the clinical manifestations and biological markers of elderly patients with RA (EPRA, age > 60) and younger patients with RA (YPRA, age ≤ 60), in part from the differences in the immune system in different age groups. The current understanding of EPRA remains insufficient.

Objectives: For better understanding of the mechanism of RA disease progression and subsequent treatment options, here we focused on the changes of immune cell infiltration in YPRA and EPRA.

Methods: R package "ssGSEA" and "GSEA" were used to identify the changes in immune cell infiltration and immune-related pathways. R package "WGCNA" and "DEseq2" were used to screening and verifying age-related differentially expressed genes (DEGs). Hub genes were identified by Cytoscape and cytoHubba. ROC (receiver operator characteristic) analysis was performed to determine the prediction and value of biomarkers. Spearman correlation analysis was conducted to evaluate the correlation between hub age-related genes and immune cells.

Results: In early RA patients (defined as within 12 months of onset of symptoms), there were no differences in the infiltration of 28 types of immune cells between younger and older patients. However, in established RA patients, several immune cells were markedly decreased in older patients, including activated B cells, immature B cells, natural killer cells, CD56dim natural killer cells, MDSCs, monocytes, effector memory CD8+T cells, regulatory T cells, type 1 T helper cells, type 17 T helper cells and T follicular helper cells. Moreover, 78 age-related DEGs related to amino acid and glycosphingolipid synthesis and metabolism were identified by WGCNA analysis and DEG screening. AGMAT, ARG2, OMG, USP2, IL4I1, and ISG15 were obtained by construction of molecular interaction regulatory networks. After verification by GEO validation set and our own RA synovial samples, only two genes, USP2 and ARG2, were still upregulated in EPRA after verification (Figure 1) and ARG2 and USP2 could effectively distinguish YPRA and EPRA and had potential as biomarkers.

Conclusion: In conclusion, this study is the first to systematically analyze changes in immune cell infiltration between younger and older RA patients and obtain hub age-related genes, which may provide the basis for illuminating the pathogenesis of RA and informing treatment strategies.

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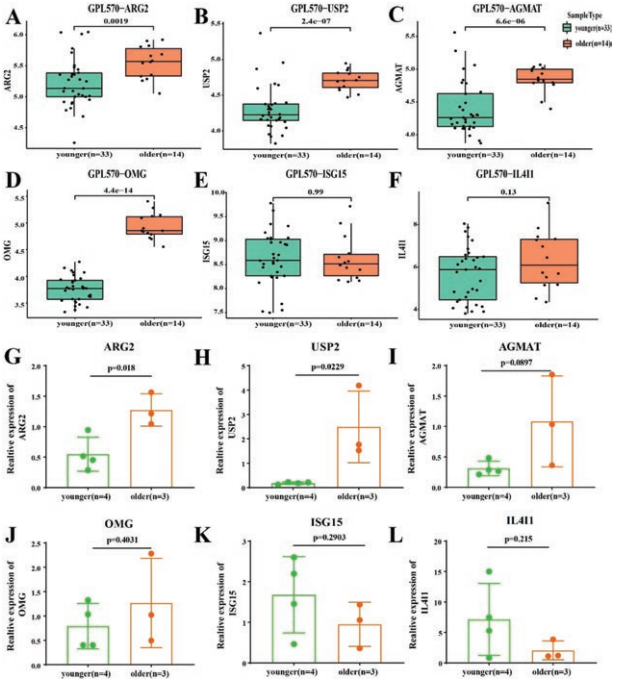


Figure 1. Verification of six hub age-related DEGs by GEO validation set and our own samples.

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Disclosure of Interests: None Declared.
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AB0083 CD14+CD90+ CELLS IN PERIVASCULAR AREAS OF RHEUMATOID ARTHRITIS SYNOVIAL TISSUES HAVE POTENTIAL TO DIFFERENTIATE INTO DENDRITIC CELLS

Keywords: Rheumatoid arthritis, Synovium

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Background: We have previously reported that CD14+ dendritic-shaped cells show a dendritic morphology under the electron microscopy and engage in a pseudoemperipolesis phenomenon with lymphocytes. CD14+ dendritic-shaped cells express CD90 in the perivascular areas of RA synovial tissues.
Objectives: To examine the differentiation potential of CD14+CD90+ cells into dendritic cells and their relationship to chronic inflammation in RA.
Methods: RA synovial tissues harvested at the time of joint surgeries were used after obtaining informed consent. The harvested tissues were cultured in vitro, and CD14+CD90+ cells were sorted using flow cytometry. Subsequently, the cells were divided into CD14+CD90+ and non-CD14+CD90+ cell groups and cultured in dendritic cell differentiation medium. The populations of cells expressing CD83 and HLA-DR were examined by flow cytometry to determine their differentiation potential into dendritic cells.
Results: At day 7 after dendritic cell differentiation culture, the group of CD14+CD90+ cells had a higher percentage of cells expressing CD83 and HLA-DR than the group of non-CD14+CD90+ cells.
Conclusion: CD14+ dendritic-shaped cells detected in RA synovial tissues are considered to be derived from CD14+CD90+ cells in the perivascular areas, which may be involved in RA inflammation as dendritic cells.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1045

AB0084 EVALUATING THE IMPACT OF METFORMIN TARGETS ON THE RISK OF RHEUMATOID ARTHRITIS: A MENDELIAN RANDOMIZATION STUDY

Keywords: Rheumatoid arthritis

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Background: Metformin is a first-line therapeutic agent for the treatment of type 2 diabetes, and despite its widespread long-term use in type 2 diabetes, the A variety of specific mechanisms of action of metformin are still being elucidated. Metformin is able to regulate cellular metabolism, proliferation, growth and autophagy, so it may have disease-modifying effects under a variety of other conditions. Metformin has been reported to improve a number of autoimmune diseases. Metformin has anti-inflammatory effects through a variety of mechanisms, including inhibition of tumour necrosis α (TNF-α)- induced synovial cell inflammation and angiogenesis[1]. Previously, observational studies have demonstrated the ability of metformin to ameliorate the pathogenesis of rheumatoid arthritis (RA). However, the causality from metformin related targets on the risk of RA remains unknown.
Objectives: The aim of this study was to assess the causal effect of metformin related targets (AMPK, MCI, MG3, GDF15 and GLP1/GCG) on the risk of RA using a two-sample Mendelian randomization (MR) study.
Methods: Genetic proxies for the effects of metformin drug targets were identified as variants in the gene for the corresponding target that associated with HbA1c level. we selected genetic variants within 1 megabase pairs downstream and upstream of the genes encoding the five targets, and low-linkage disequilibrium ($r^2 < 0.3$) variants associated with HbA1c at a nominal level of statistical significance ($p \leq 0.05$) in the Meta-Analyses of Glucose and Insulin-related traits Consortium (MAGIC) , restricted to people of European ancestry to minimise population stratification (n = 88355). Data on RA have been obtained from the NHGRI-EBI Catalog of human genome-wide association studies (14361 cases and 42923 healthy controls)[2]. Two-sample Mendelian randomization (MR) study was conducted to examine the association of metformin related targets and the risk of RA, including the inverse-variance weighted (IVW) method, MR-Egger, and Weighted median (WM), which was followed by sensitivity analyses. In addition, we also performed Cochran's Q test, MR pleiotropy residual sum and outlier (MR-PRESSO), leave-one-out sensitivity test to test for heterogeneity, horizontal multiplicity and stability of results.
Results: Genetically predicted 5 targets were not associated with RA with odds ratio (AMPK [OR=1.21, 95% CI=0.61, 2.39, p = 0.58], MCI [OR=1.16, 95% CI=0.92,1.48, p = 0.20], MG3[OR=1.76, 95% CI=0.49, 6.31, p = 0.14], GDF15 [OR=0.63, 95% CI=0.19, 2.05, p = 0.31], GLP1/GCG [OR=0.97, 95% CI=0.80, 1.16, p = 0.78])(Figure1). In addition, no apparent heterogeneity and no horizontal pleiotropy were observed in the sensitivity analysis.
Conclusion: Our study using MR herein indicated that the metformin related targets is not causally associated with the risk of RA. Future studies shall further systematically explore other potential pathways that metformin may affect to explore the association.

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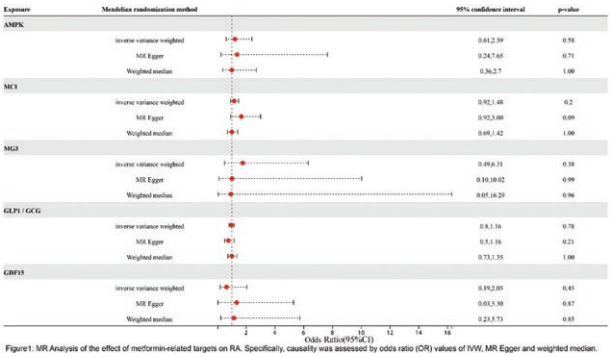


Figure1: MR Analysis of the effect of metformin-related targets on RA. Specifically, causality was assessed by odds ratio (OR) values of IVW, MR Egger and weighted median.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1670

AB0085 CYTOKINE DRIVEN ECM PRODUCTION IS HIGHLY DEPENDENT ON DISEASE DRIVERS IN FIBROBLAST-LIKE SYNOVIOCYTES

Keywords: Biomarkers, Synovium, Cell biology

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Background: Fibrosis is a significant component in arthritis diseases that involves the joint. It can lead to joint swelling, stiffness and ultimately to pain. It is the synovial fibroblasts which secrete the extracellular matrix (ECM) components, and upon activation the production increases. The healthy synovial membrane consists of multiple ECM components, including type I, III and VI collagen[1]. The ECM composition of the fibrotic and fibro-inflamed membrane is unclear. We have previously shown that TGF-β increases the formation of type I, III and VI collagens in osteoarthritis (OA) fibroblasts-like synoviocytes (FLS)[2]. Both IL-1 and TNFα receptors have been found in the synovium of rheumatoid arthritis (RA) patients[1]. We hypothesize that both fibrosis and inflammation are likely to be present in arthritis diseases at the same time. And that the interplay between different disease drivers is crucial for the structural manifestation. Therefore, the combination of both growth factors and cytokines may be directing the composition of the synovial ECM in the joint.
Objectives: The objective of this study was to characterize the effect of inflammation on the fibrotic response of OA FLS using biomarkers of collagen formation.
Methods: Primary human FLS were isolated from synovial membranes, from OA patients undergoing total knee replacement (n=4) and cultured in the Scar-in-a-Jar model. Briefly, the fibroblasts were cultured in 0.4% fetal bovine serum DMEM, ficoll (to create a crowded environment) and ascorbic acid for 12 days. The fibroblasts were stimulated with TGF-β1 [1 nM], IL-1β [0.5 nM] or TNF-α [0.5 nM], either alone or in combination from day 0 and the treatments changed twice a week. Non-stimulated fibroblasts were used as control. Biomarkers of type I, III, and VI collagen formation (PRO-C1, PRO-C3 and PRO-C6, respectively), were measured in the culture supernatants at days 0, 4, 8 and 12 using validated ELISAs.
Results: Treatment with IL-1β or TNF-α alone did not affect PRO-C1, PRO-C3 or PRO-C6, compared control (Figure 1.A). TGF-β1 increased the total release of PRO-C1 and PRO-C6, compared to control ($p<0.001$, Figure 1.A). The total release of PRO-C3 did not increase, while at day 12 the PRO-C3 level was higher compared to control ($p<0.05$; data not shown). Both IL-1β and TNF-α in combination with TGF-β1 decreased PRO-C1 ($p<0.01$, Figure 1.A; decrease of 32-53%, Figure 1.B) and PRO-C6 compared to of TGF-β1 alone ($p<0.001$, Figure 1.A; decrease of 56-78%, Figure 1.B). TNF-α in combination with TGF-β1, increased the release of PRO-C3 ($p<0.01$, Figure 1.A; increase of 172-264%, Figure 1.B), while the combination with IL-1β did not seem to affect the PRO-C3 response compared to TGF-β1 alone (Figure 1.A; increase of 48% to decrease of 39%, Figure 1.B).
Conclusion: The combination of inflammatory cytokines and TGF-β1 leads to a differential effect on formation of ECM components such as type III collagen. These findings suggest that the presence of an inflammatory component, may be important for the development of a fibrotic component in joint diseases. Consequently, this also underlines the need for a better understanding of the molecular mechanisms driving the joints diseases.

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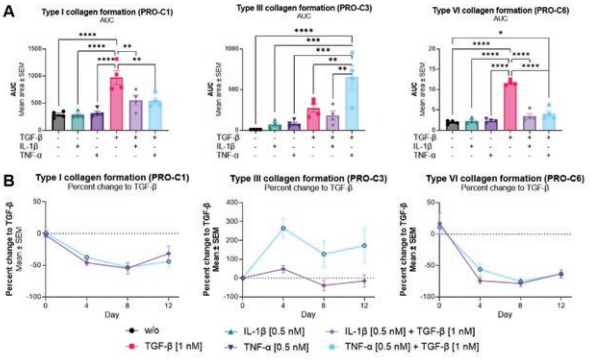


Figure 1. The type I, III and VI collagen formation after stimulation with TGF-β1, IL-1β and TNF-α. (A) The area under the curve (AUC) of the type I, III and VI collagen formation (PRO-C1, PRO-C3 and PRO-C6, respectively) after 12 days of stimulation. (B) The percent change of the collagen formation of TGF-β1 in combination with either IL-1β or TNF-α, compared to the formation of TGF-β1 alone on the 4 different days.

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Disclosure of Interests: Sofie Falkenløve Madsen: None declared, Dovile Sinkeviciute Employee of: Nordic Bioscience, Morten Karsdal Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, Christian Thudium Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience.
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AB0086 PLASMA EXPRESSION OF CAROTID PLAQUE PRESENCE-RELATED MIRNA-24, MIRNA-146 AND MIRNA-LET7A IS ASSOCIATED WITH INFLAMMATORY VARIABLES (DAS28 AND ESR) IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Cardiovascular disease, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) causes problems beyond the joints such as cardiovascular (CV) disease. It is estimated that the risk of developing CV disease in RA patients is approximately 50% higher than that in the general population[1]. The formation of atherosclerotic plaques is the main mechanism of the development of CV disease in RA patients[2]. The pathogenesis of atherosclerotic plaques is multifactorial and includes vascular, metabolic and inflammatory components[3]. In this regard, miRNA-24, 146 and Let7a have previously been associated with the presence of carotid plaques in RA patients[4].
Objectives: Given that there is a strong relationship between the chronic inflammatory state of RA and arteriosclerosis, we evaluated, individually and globally, whether miRNA-24, 146 and Let7a were involved in the inflammatory state of RA and could link inflammation and arteriosclerosis.
Methods: A total of 199 patients with RA were included. Inflammatory variables such as disease activity score 28 (DAS28) and erythrocyte sedimentation rate (ESR) were quantified. MicroRNAs were extracted from plasma and quantified with qPCR. Multivariate models were used for analysis. An expression score was created to evaluate all the miRNAs conjunctively.
Results: The multivariate models showed that miRNA-146 was significantly associated with DAS28 ($\beta = -0.15$), and miRNAs 24, 146 and Let7a were significantly associated with ESR ($\beta = -5.17$, $\beta = -5.29$ and $\beta = -6.47$, respectively) in the overall cohort. When miRNAs were evaluated globally, they were also significantly associated with DAS28 and ESR in the overall cohort ($\beta = 0.41$ and $\beta = 14.23$, respectively). Sex-stratified analyses also showed different associations of these miRNAs with the inflammatory variables (Table 1).
Conclusion: Plasmatic expressions of miRNA-24, 146 and Let7a were associated with inflammatory markers of RA. These miRNAs are associated with both

inflammation and atherosclerosis, which could link these processes, and are potential therapeutic targets for RA.

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Table 1. Summaries of the multivariate lineal regression models to estimate the associations between miRNAs and DAS28 and ESR in the overall cohort and stratified by sex. Basal models are adjusted for age, sex, body mass index, disease onset, disease-modifying antirheumatic drugs, non-steroidal anti-inflammatory drugs, corticosteroids and biological drugs. β = beta coefficient, p = p-value.

MiRNAs association with DAS28 and ESR			
	β	p	R^2 (%)
DAS28			
OVERALL COHORT			
Basal Model			12.75
+ miRNA – 146	-0.15	0.04	14.16
+ Expression Score	0.41	0.049	15.30
MEN			
Basal Model			13.91
+ miRNA – 146	-0.23	0.02	22.06
+ Expression Score	0.78	0.01	26.34
ESR			
OVERALL COHORT			
Basal Model			10.57
+ miRNA – 24	-5.17	0.002	15.25
+ miRNA – 146	-5.29	0.0003	16.41
+ miRNA – Let7a	-6.47	0.0005	16.15
+ Expression Score	14.23	<0.0001	18.63
MEN			
Basal Model			15.73
+ miRNA – 24	-5.18	0.03	23.16
+ miRNA – 146	-5.01	0.01	24.84
+ miRNA – Let7a	-6.54	0.02	24.03
+ Expression Score	14.79	0.01	26.37
WOMEN			
Basal Model			9.95
+ miRNA – 24	-5.29	0.02	13.97
+ miRNA – 146	-5.55	0.008	14.82
+ miRNA – Let7a	-6.37	0.01	14.48
+ Expression Score	15.26	0.008	17.29

Acknowledgements: We would like to thank all the patients for their essential collaboration.

Disclosure of Interests: SILVIA PAREDES Speakers bureau: Lilly, Bristol, Amgen, Consultant of: Galapagos, Sanofi, Bristol, Didac Llop: None declared, Daiana Ibarretxe Speakers bureau: Sanofi, Sobi, Genzyme, Rubio, Delia Taverner Speakers bureau: Galapagos, Amgen, Roser Rosales: None declared, Nuria Plana Speakers bureau: Amgen, Sanofi, Servier, Consultant of: Servier, Luis Masana Speakers bureau: Amgen, Sanofi, Servier, Consultant of: Servier, Amgen, Joan Carles Vallve: None declared.

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AB0087

THE SYNOVIAL EXPRESSION OF PSTAT1-3-5 IN PATIENTS WITH KNEE TREATMENT-RESISTANT MONOARTHRITIS IN THE COURSE OF RHEUMATOID AND PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Synovium, Rheumatoid arthritis

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Background: Rheumatoid and Psoriatic Arthritis are both chronic inflammatory diseases of the joints characterized by synovial proliferation [1]. The JAK/STAT signalling pathway is critical in the pathogenesis of both diseases, and among them STAT3 is activated by numerous cytokines, growth factors, and interferons [1]. Hypoxia is also an important stimulus for STAT3 activation and the consequent production and accumulation of HIF-1α, leading to neovascularization [2].

Objectives: The aim of the present study was to analyse the phosphorylation pattern of pSTAT1, pSTAT3 and pSTAT5 and the inflammatory score of synovial tissue from RA and PsA patients with knee treatment resistant monoarthritis.

Methods: The diagnosis of RA and PsA was based on the 2010 American College of Rheumatology/European League Against Rheumatism [3] and Classification Criteria for Psoriatic Arthritis [4], respectively. All patients presented knee treatment-resistant monoarthritis and underwent In Office Needle Arthroscopy (IONA) of the knee with a maximum of 3 samples of synovial tissue taken during each procedure. Synovial tissue specimens were examined histologically using the Krenn scoring system [5]; immunohistochemistry (IHC) was used to assess the phosphorylation of STAT1, STAT3 and STAT5 and the expression of activated STATs was assessed semi-quantitatively with a score ranging from 0 to 3.

Results: The present study evaluated 12 patients with RA (n = 6) or PsA (n = 6). Patients demographic and clinical characteristics are reported in Table 1. According to the pathologic analysis, Krenn median score was 2 (IQR 4). Seven patients showed a synovitis score≤3, the other 5 cases showed a median Krenn score of 6. The IHC analysis did not demonstrate a clear association between the synovitis score and pSTAT expression. The phosphorylated form of STAT1 showed a weak expression in all samples. Conversely, pSTAT3 showed a more intense expression in synovial fibroblasts in those samples with higher synovitis score; moreover, pSTAT3 was expressed in endothelial cells in those patients presenting higher cellularity and stronger stromal infiltration. Finally, pSTAT5 was scarcely expressed in the synovial tissue from RA and PsA patients.

Conclusion: Inflammatory synovial infiltration in course of RA and PsA is associated with the production of VEGF and endothelial proliferation. The phosphorylation of STAT3 – which is associated to the signalling of IL-6 and other gp130 ligands as well as other pro-inflammatory cytokines - could be a marker of hypercellularity and hypoxic metabolism in the synovial tissue, in the context of treatment-resistant monoarthritis.

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Table 1. Patients demographic and clinical characteristics

Demographic and clinical characteristics		N= 12
Age, years	Median (IQR)	57 (8)
Gender	Male:Female	9:3
BMI	Median (IQR)	24.6 (6.9)
Ethnicity		
- Caucasian	N (%)	11(91.7)
- Asian	N (%)	1 (8.3)
RA	N (%)	6 (50)
PsA	N (%)	6 (50)
Disease duration, months	Median (I(IQR)	126 (120)
Number of previous bDMARDs	Median (IQR)	1 (2)
Ongoing treatment:		
- TNF-inhibitors	N (%)	5 (41.7)
- JAK-inhibitors	N (%)	1 (8.3)
- Anti-IL17	N (%)	1 (8.3)
- csDMARDs	N (%)	5 (41.7)

csDMARDS= conventional synthetic disease-modifying anti-rheumatic drugsbDMARDs= biological disease-modifying anti-rheumatic drugs

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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Spondyloarthritis - aetiology, pathogenesis and animal models

AB0088 GENETICALLY DETERMINED GUT MICROBIOME AND THE RISK OF ANKYLOSING SPONDYLOARTHRITIS

Keywords: Genetics/Epigenetics, Bone diseases

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Background: Ankylosing spondyloarthritis (AS) is a common chronic inflammatory autoimmune disease affecting the sacroiliac joint and spine, with or without systemic symptoms such as peripheral arthritis[1]. The etiology of AS is still unclear, which is affected by genetic risk factors and the environment, especially microorganisms. In addition, growing evidence suggests that the influence of the microbiota extends beyond the gut and affects the systemic immune system[2]. The observational association between the gut microbiome and AS has been well documented. However, the causal relationship between the gut microbiome and AS has yet to be well studied.

Objectives: This study aimed to evaluate the causal relationship between the gut microbiome and AS using a two-sample Mendelian randomization (MR) study.

Methods: Gut microbiome genome-wide association study (GWAS) data were extracted by the MR-base platform. Data on AS have been obtained from genome-wide association data collected by the UK Biobank (968 cases and 336,191 healthy controls). First, we identified SNPs associated with the gut microbiome by genome-wide significance level ($p < 1 \times 10^{-5}$), and Removal of linkage disequilibrium (LD) by conducting a clumping process (R^2<0.001, window size=10,000 kb). Then, a two-sample MR study was conducted to examine the association of gut microbiome and AS, including the inverse-variance weighted (IVW) method, MR-Egger, and Weighted median (WM). In addition, we also performed Cochran's Q test, MR pleiotropy residual sum and outlier (MR-PRESSO), and leave-one-out sensitivity test to test for heterogeneity, horizontal multiplicity, and stability of results.

Results: *Ruminococcaceae* was positively associated with the risk of AS(OR=0.998, 95%CI =0.997, 0.999, p =0.037). *Butyricicoccus*(OR=1.001, 95%CI =1.000, 1.003, p = 0.042, *Coprococcus3*(OR=1.001, 95%CI =1.000, 1.003, P = 0.042), and *Defluviitaleaceae* (OR=1.001, 95%CI =1.000, 1.002, p = 0.004 were negatively correlated with the risk of AS. (Figure 1) In addition, no apparent heterogeneity or horizontal pleiotropy were observed in the sensitivity analysis.

Conclusion: This study supports a causal relationship between gut microbial composition and risk for AS, thus providing novel insights into the gut microbiota-mediated development mechanism of AS.

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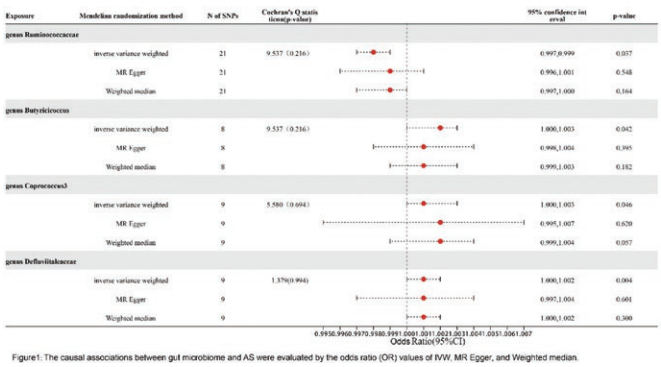


Figure1: The causal associations between gut microbiome and AS were evaluated by the odds ratio (OR) values of IVW, MR Egger, and Weighted median.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0089 MENDELIAN RANDOMIZATION REVEALS CAUSATIVE GUT BACTERIA FOR ANKYLOSING SPONDYLITIS

Keywords: Spondyloarthritis

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Background: Genetic, clinical and experimental evidence has mounted to suggest the implication of gut dysbiosis in the pathogenesis of ankylosing spondylitis (AS) through the gut-joint axis of inflammation[1]. A series of cross-sectional studies have unraveled the alterations of gut microbiome composition in patients with AS using metagenome sequencing. However, such observational associations might be limited to the small sample sizes and the influences from confounders. Furthermore, whether gut dysbiosis is a cause or a consequence of AS remains elusive. Mendelian randomization (MR) is an epidemiologic approach for causal inference using genetic variants as instrument variables.

Objectives: To assess the causal relationship between gut bacteria taxa and risk of AS using two-sample MR.

Methods: To select instrument variables for gut bacteria taxa, we filtered genome-wide significant (p ≤ 5 x 10-8) and independent (r 2 < 0.01 within the window size of 500kb) variants for 211 taxa from a large-scale genome-wide association study (GWAS) on gut microbiota which included 18,340 individuals from 24 cohorts[2]. The summary statistics on AS from the UK Biobank (UKB) and the FinnGen consortium were utilized for the discovery and replication analyses, respectively[3]. Under the framework of two-sample MR, the inverse variance weighted method or the Wald ratio method was used to assess the causal effect of gut microbial taxa on risk of AS. In addition, multiple sensitivity analyses and reverse MR analyses were conducted to validate the robustness of results and evaluate reverse causation, respectively.

Results: Despite no taxa passing the multiple-testing correction, six known taxa were identified to have causal effects on the onset of AS in the UKB cohort at the nominal significance level ($p < 0.05$). In the FinnGen cohort, only one bacterial genus, *Anaerotruncus* was replicated (UKB: β_{IVW} = -0.0016, p = 0.04; FinnGen: β_{IVW} = -0.3990, p = 0.04). Sensitivity analyses led no support to the presence of heterogeneity ($Q_p > 0.05$) and pleiotropy (Intercept_$p > 0.05$). Reverse MR analysis found no reverse causality from AS to *Anaerotruncus*.

Conclusion: Despite no current evidence supporting the association between *Anaerotruncus* and AS, this study provides the first genetic evidence for the protective effect of this short-chain fatty acid (SCFA)-producer against AS. Intriguingly, several studies have suggested a relationship between *Anaerotruncus* and immune-mediated diseases including rheumatoid arthritis and inflammatory bowel diseases[4]. These MR findings shed light on the causative microbiota and microbiome-modulating strategies for AS.

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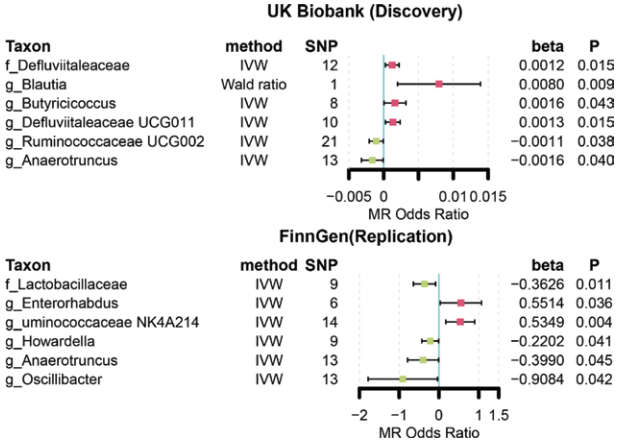


Figure 1. Forestplots showing nominally significant ($p < 0.05$) Mendelian randomization estimates of gut bacterial taxa in the UK Biobank (discovery) and the FinnGen (replication) cohort.

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Disclosure of Interests: None Declared.
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AB0090 IN VITRO EFFECTS OF METHOTREXATE, ANTI-PDE-4, AND ANTI-JAK TREATMENTS ON HEPATOCYTES STIMULATED BY PSORIATIC ARTHRITIS SERUM

Keywords: Biomarkers, Psoriatic arthritis

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Background: In recent years, the increased prevalence of liver abnormalities in Psoriatic Arthritis (PsA) has acquired relevance. The liver dysfunction in PsA might be induced by inflammatory components in parallel with the presence of metabolic complications or due to the potential hepatotoxicity of the treatments administered.
Objectives: 1) to analyze the impact of PsA serum on hepatocytes and 2) to investigate the effect of methotrexate, anti-PDE-4, and tofacitinib on hepatocytes treated with PsA serum.
Methods: serum from 12 healthy donors (HDs) and 20 age and sex-matched PsA patients were collected to perform *in vitro* experiments with the hepatocyte cell line (HEPG2). Cells were treated with HDs serum or PsA serum alone or combined with methotrexate (50μM), roflumilast (1nM), or tofacitinib (250nM) for 24 hours. The expression of genes related to inflammation, immune response, apoptosis, and liver dysfunction was analyzed by RT-PCR. Cell stress protein array was performed. The levels of 92 inflammatory proteins were determined on the treated hepatocytes using PEA technology (Olink Target 96 Inflammation panel, Cobiomic Biosciences). STRING platform (version 11.5) was used to determine the functional protein association networks.
Results: PsA patients showed a mean disease activity in PsA (DAPSA) of 27.10 ±12.52 (moderate-high disease activity) and significantly elevated levels of c-reactive protein and erythrocyte sedimentation rate with respect to HDs. In hepatocytes, the treatment with PsA serum induced the mRNA expression of ADAM-17, CHUK, CTSD, FAF-1, GDF-15, IFGR-1, IL-6, IL-8, MMP-1, STAT-3, TGF-β and TFPI compared to HDs serum, genes directly associated with biological processes which might impact liver function, such as inflammatory response, immune system, apoptotic process and even directly associated with non-alcoholic fatty liver disease. In addition, PsA serum promoted the expression of 22 proteins mainly involved in cell stress in hepatocytes compared to HDs serum treatment. These proteins are also associated with lipids and atherosclerosis, apoptosis, regulation of inflammatory response, hepatic diseases, and regulation of the extracellular matrix. Surprisingly, 33 out of 92 inflammatory-related proteins were significantly increased in hepatocytes treated with PsA serum compared to HDs serum (36% of proteins). On the other hand, the treatment with anti-PDE-4 promoted the reduction of 11 out of 33 proteins altered by the treatment with PsA serum, proteins mainly involved in leukocyte migration and the immune system. The treatment with anti-JAK reduced levels of 20 out of 33 proteins altered by the treatment with PsA serum. However, the treatment with methotrexate significantly increased the expression of 5 out of 33 proteins altered by the treatment with PsA serum.
Conclusion: 1) PsA serum characterized by the presence of inflammatory components profoundly impacts the hepatocyte function promoting the alteration in proteins and genes involved in the inflammatory response, immune system, and the apoptotic and fibrotic process; 2) the treatment with anti-PDE-4 or anti-JAK is able to partially reverse the deleterious inflammatory effect of PsA serum produced in the hepatocytes. Funded by ISCIII (PI20/00079 and RICOR-RD21/0002/0033), the Andalusian government (1381035-F) co-financed by ERDF.
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AB0091 IMPACT OF COMORBIDITY BURDEN AS SCORED USING THE RHEUMATIC DISEASE COMORBIDITY INDEX (RDCI) ON RESPONSE TO TREATMENT WITH THE FIRST BDMARD AMONG PSORIATIC ARTHRITIS PATIENTS

Keywords: Comorbidities, bDMARD, Psoriatic arthritis

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Background: In addition to the impact of Psoriatic Arthritis (PsA) on risk of death and increased morbidity, other factors, such as comorbidity burden (CB), have also an important role[1]. Identifying comorbidities and estimating their impact on the disease course are critical to safely and effectively treating a patient with PsA, as these comorbidities have often implications on therapy selection.
Objectives: To measure the impact of CB on PsA patients treated with a first-line Biologic Disease Modifying AntiRheumatic Drug (bDMARD) using the Rheumatic Disease Comorbidity Index (RDCI).
Methods: Retrospective observational cohort-study of patients with diagnosis of PsA, fulfilling the CASPAR criteria and treated with a first bDMARD, using data from the Reuma.pt database. Patients were divided in 2 groups according the RDCI (RDCI=0 and RDCI≥1) for evaluating its role in clinical response and disease activity at baseline and follow up (6 and 12 months). An univariate analysis was performed followed by a multivariate analysis.
Results: A total of 115 patients were included. 53% (n=61) were females, mean age was 47(±10.7) years old and the median disease duration 10.5 years [1.4-44.1]. At baseline, most of patients exhibited a very high or high disease activity (median DAS284V 4.44, ASDAS-CRP 3.98, BASDAI 6.69) and 68% were concomitantly treated with other DMARD and/or corticosteroids. 43% of patients had at least one comorbidity and the median RDCI score was 1.1 [0.0-6.0]. The most frequently reported comorbidities were cardiovascular disorders (37.7%), depression (13.2%) and pulmonary disease (6.1%). When comparing baseline demographic and clinical characteristics of the 2 subgroups, stratified according RDCI score, we found statistically significant differences in age, age at diagnosis, disease duration, BMI and smoking status. RDCI was poorly correlated with CRP (r=0.162, p<0.01), DAS284V (r=0.263, p=0.008), ASDAS CRP (r=0.284, p<0.001) at 12 months. We also found moderate correlations in RDCI with BASFI (r=0.370, p<0.001) and HAQ-DI (r=0.351, p<0.01). Patients with higher RDCI had lower chance to obtain low disease activity (OR 0.69 (95%CI, 0.61–0.79); $p < 0.001$). EULAR response rate at 12 months was lower in PsA patients with comorbidities (69.7%vs90.5%, p=0.02).
Conclusion: To conclude, our study demonstrates that baseline CB is an independent predictor for insufficient 12 months response to the first bDMARD. This confirmed the hypothesis that comorbidity should be treated to improve the long-term prognosis in PsA patients.
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Table 1.

	RDCI=0 (n=70)	RDCI≥1 (n=45)	*p*
Current age,years	48.7±9.8	58.8±7.7	**<0.001**
Sex (M/F)	34/70	20/45	0.665
Age of diagnosis,years*	37.8±7.9	58.7±6.5	**<0.001**
Disease duration,years*	6.6±4.1	10.1±4.4	**0.02**
Smoking status,n(%)	26(10.7)	41(13.6)	**0.013**
Psoriasis,n(%)	55(78.5)	33(73.3)	0.706
Nail involvement,n(%)	29(41.4)	12(26.6)	0.107
Axial involvement,n(%)	37(53)	27(0.6)	0.452
Dactylitis,n(%)	27(38.5)	15(33)	**<0.001**
Enthesitis,n(%)	27(38.5)	7(15.5)	0.873
BMI(*)	25.4±4.7	31.2±4.9	**<0.001**
DAS28 4VCRP baseline*	3.6±1.4	3.6±1.1	0.736
ASDAS CRP baseline*	3.9±1.1	4.0±0.9	0.295
BASDAI baseline*	6.8±2.1	7.1±1.5	0.978
BASFI baseline*	5.8±2.7	6.2±1.9	0.378
ESR baseline*	29.1±23.5	39.1±22.8	**0.02**
CRP baseline*	2.1±3.5	2.3±2.6	0.275
HAQ baseline*	0.6±0.7	0.7±0.6	**0.006**
DAS28 4VCRP 12M*	2.0±0.7	2.9±1.1	**0.022**
ASDAS CRP 12M*	2.0±0.9	2.8±1.9	**0.04**
BASDAI 12M*	3.2 ±2.6	4.4±2.1	**0.106**
BASFI 12M*	2.6 ±2.7	5.3±2.7	**<0.001**
HAQ 12M*	0.6±0.7	1.1±0.6	**0.006**
EULAR response 12M,n(%)	57/63(90.5)	30/43(69.7)	**0.02**
ASDAS response 12M,n(%)	47/70(67.1)	24/45(53.3)	0.137
PSARC response 12M,n(%)	45/60(75)	23/37(62)	0.180
Therapeutic,n(%)			
cDMARDs	48(68.5)	29(64.4)	0.862
Glucocorticoids	40(57.1)	23(51.1)	0.526
Antidepressants	4(5.8)	9(20)	**0.01**

*(mean±SD)

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Disclosure of Interests: None Declared.
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AB0092

ANTIBODIES OF THE IMMUNOGLOBULIN G AND A ISOTYPE TO NOVEL PEPTIDES IN EARLY AXIAL SPONDYLOARTHRITIS PATIENTS

Keywords: Biomarkers, Spondyloarthritis, Autoantibodies

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Background: There is an unmet need for biomarkers to identify patients with axial spondyloarthritis (axSpA), as clinical manifestations often overlap with other disorders. Previously, we identified immunoglobulin G (IgG) antibodies to 3 Hasselt University (UH)-axSpA peptides which could provide a novel tool for diagnosis of a subset of axSpA patients [1].
Objectives: The aim of this study was to identify novel IgA antibodies in early axSpA patients and to determine their diagnostic potential in combination with previously determined IgG antibodies against UH-axSpA-IgG antigens.
Methods: An axSpA cDNA phage display library constructed from axSpA hip synovium, was used to screen for novel IgA antibodies in plasma from early axSpA patients. The diagnostic value of these antibodies against novel UH-axSpA-IgA and previously identified UH-axSpA-IgG antigens was determined in two independent axSpA cohorts [UH cohort and the Leuven spondyloarthritis biologics cohort (BIOSPAR)], in healthy controls and in patients with chronic low back pain (CLBP) using ELISA.
Results: We identified antibodies to 7 novel UH-axSpA-IgA antigens, of which 6 correspond to non-physiological peptides and 1 to the human histone deacetylase 3 (HDAC3) protein. IgA antibodies against 2 of these 7 novel UH-axSpA-IgA antigens and IgG antibodies against 2 of 3 the previously identified antigens were significantly more present in axSpA patients from the UH cohort (18/70, 25.7%) and the (Bio)SPAR cohort (26/164, 15.9%), compared to controls with CLBP (2/66, 3%). Antibodies to this panel of 4 antigens were present in 21.1 % (30/142) of patients with early axSpA from the UH and (Bio)SPAR cohorts. The positive likelihood ratio for confirming early axSpA using antibodies to these 4 UH-axSpA antigens was 7.0. So far, no clinical correlation between the novel identified IgA antibodies and inflammatory bowel disease could be identified.
Conclusion: Screening an axSpA cDNA phage display library for IgA reactivity resulted in the identification of 7 novel UH-axSpA-IgA antigens, of which 2 show promising biomarker potential for the diagnosis of a subset of axSpA patients, in combination with previously identified UH-axSpA-IgG antigens.

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3092

AB0093

COMPLEMENT IN THE DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS (AXSPA). INVESTIGATIONS IN A CROSS-SECTIONAL COHORT (OPTIREF) OF PATIENTS SUSPECTED OF AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Innate immunity

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease without specific diagnostic biomarkers. However, recent evidence suggests an involvement of the innate immune system in the pathogenesis of axSpA [1]. The lectin pathway of complement activation serves essential functions in the innate immune system, regulates homeostasis and development. We have previously shown the lectin pathway proteins (LPPs) L-ficolin and M-ficolin to be elevated in axSpA-patients compared with clinically relevant controls with unspecific low back pain (uLBP).
Objectives: To investigate the diagnostic potential of LPP levels in patients recruited from a well-defined cross-sectional prospective cohort (OptiRef), including newly diagnosed axSpA-patients and uLBP-patients.
Methods: Serum samples were obtained from 515 individuals from the OptiRef cohort; 151 newly diagnosed axSpA-patients and 364 uLBP-patients [2]. All patients were assessed according to a standardized protocol, incl. clinical information as demographics, SpA features, symptom duration, and disease activity. Routine lab tests (HLA-B27 and CRP) were performed. Imaging (x-ray and MRI) was performed if deemed clinically relevant. Serum levels of all 10 LPPs (MBL, CL-L1, M-ficolin, H-ficolin, L-ficolin, MASP-1, MASP-2, MASP-3, MAp19, and MAp44) and the complement activation product C3dg were measured by immunoassays.
Results: Patient characteristics are shown in Table 1. L-ficolin, MASP-2, and C3dg serum levels were increased in axSpA-patients compared with uLBP-patients, whereas CL-L1 and MASP-3 serum levels were decreased (Figure 1). After adjustments for CRP, C3dg serum levels remained significantly increased in axSpA-patients, whereas M-ficolin and MASP-3 serum levels were decreased in axSpA-patients. The diagnostic potential of combining either L-ficolin, MASP-3, and C3dg with HLA-B27 increased specificity to 93-95% compared with HLA-B27 alone (77%) but decreased sensitivity to 29-33% compared with HLA-B27 alone (83%). In a univariate logistic regression analysis, CL-L1, MASP-2, MASP-3, and C3dg were associated with an axSpA-diagnosis, and C3dg and MASP-3 remained significant in a multivariate logistic regression analysis.
Conclusion: In this study, serum levels of C3dg, MASP-3, and CL-L1 differed significantly between axSpA-patients and uLBP-patients after adjustment for CRP. Although combining HLA-B27 with measurements of L-ficolin, MASP-3, and C3dg increased diagnostic specificity for axSpA, it seems unjustified due to the concomitant loss of sensitivity. However, both C3dg and MASP-3 were associated with the axSpA-diagnosis in multivariate logistic regression, indicating the complement system's involvement in axSpA-pathogenesis. This should be further investigated.

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Table 1. Patient characteristics of the included patients from the OptiRef cohort

	Total cohort *n* = 515	axSpA *n* = 151	uLBP *n* = 364	*p*-value*
Median age, years (IQR)	36 (29-45)	33 (26-40)	38 (30-46)	**<0.001**[a]
Males, n (%)	240 (47)	83 (55)	157 (43)	0.008[b]
HLA-B27 positive, n (%)	203 (41)	121 (83)θ	82 (23)θθ	**<0.001**[b]
Smoking, n (%)	138 (30)	47 (31)	91 (25)	0.154[b]
BMI, median (IQR)	24 (22-27)	24 (22-26)ϵ	24 (22-28)ϵϵ	0.464[a]
Symptom duration, years median (IQR)	6 (2-12)	5 (2-10)	7 (2-14)	**0.027**[a]
Inflammatory back pain, n (%)	210 (41)	130 (86)	175 (48)	**<0.001**[b]
Good response of back pain to NSAID, n (%)	274 (73)	102 (84)σ	172 (68)σσ	**0.002**[b]
Elevated CRP (> 5 mg/L), n (%)	91 (18)	53 (35)Δ	38 (10)ΔΔ	**<0.001**[b]
Radiographic axSpA, n (%)		77 (59)		
ASDAS-CRP, median (IQR)		2.7 (1.8-3.3)[§]		
BASDAI, median (IQR)		4.6 (2.9-5.7)ω		

* axSpA vs. uLBP. [a] Mann Whitney U test. [b] Chi2 test. Notations in the table indicate available data. If no marks, data were available on all patients. θ *n*=146. θθ *n*=353 ϵ *n*=141. ϵϵ *n*=340. σ *n*=122. σσ *n*=252. Δ *n*=150.ΔΔ *n*=358. [§] *n*=142. ω *n*=148.

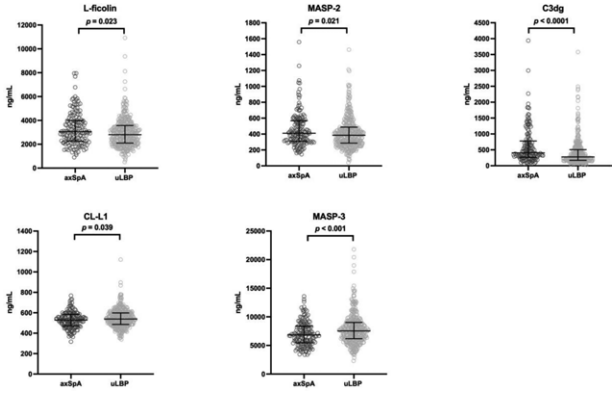


Figure 1. Serum levels of significantly altered complement LPPs in the two patient groups.

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AB0094 ANALYSIS OF CUMULATIVE DOSES OF METHOTREXATE IN THE HEPATIC DISEASE RISKTHROUGH IN VIVO AND IN VITRO APPROACHES IN PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Disease-modifying drugs (DMARDs)

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Background: Liver abnormalities, particularly non-alcoholic fatty liver disease (NAFLD) are strongly associated with psoriatic arthritis (PsA). In the last decades, the possible hepatotoxic effects of methotrexate in PsA have been studied, however, up to date, the results are controversial.
Objectives: 1) to evaluate the liver damage risk in PsA patients and its relationship with clinical features of the disease; 2) to determine the influence of cumulative doses of methotrexate by *in vivo* and *in vitro* approaches.
Methods: a cross-sectional study was performed on 326 subjects: 155 PsA patients, 87 NAFLD non-PsA patients, and 84 healthy donors (HDs). Clinical and laboratory parameters, liver disease biomarkers, and several indexes to evaluate the risk of suffering hepatic steatosis or fibrosis were evaluated. Cumulative doses of methotrexate were calculated retrospectively. Mechanistic studies were carried out on hepatocytes (HEPG2 cell line) treated with cumulative doses of methotrexate for up to 72 hours and 150μM. The changes in the levels of 92 inflammatory proteins on the hepatocytes were analyzed using PEA technology (Olink Target 96 Inflammation panel, Cobiomic Biosciences).
Results: using a NAFLD non-PsA BMI, age and sex-matched cohort, a cut-off value of hepatic steatosis index (HSI) (35.68; AUC=0.865 $p<0.0001$) was calculated to distinguish NAFLD patients from HDs. Taking this value into account, PsA patients showed a significantly high risk of suffering NAFLD *vs* HDs, 65% respect to 22%. In addition, PsA patients with a high risk for steatosis displayed a significant prevalence of insulin resistance, obesity, type 2 diabetes mellitus, and arterial hypertension compared to PsA patients without that risk. Interestingly, these PsA patients also showed significantly elevated levels of triglycerides, complement component 3, DAPSA, c-reactive protein, and erythrocyte sedimentation rate. Next, PsA patients were divided into two groups depending on mean cumulative doses of methotrexate (<1.5 gr for no hepatotoxic risk group and >1.5 gr for the hepatotoxic risk group). Patients with more than 1.5gr of methotrexate cumulative dose showed significantly lower levels of acute phase reactants and no significant differences in metabolic profile or liver disease biomarkers. However, fibrosis-4 score (FIB-4) was significantly elevated in the group of hepatotoxic risk and positively correlated with cumulative doses. Although, this association was influenced by the age variable and not due to the levels of transaminases or platelets. On the other hand, *in vitro* treatment of hepatocytes with methotrexate for 24 h induced the expression of 19 inflammatory proteins out of 92. These changes were not significantly altered after 72 hours of treatment with methotrexate added each 24h.
Conclusion: 1) PsA patients with a high risk of liver disease show elevated rates of cardiometabolic comorbidities, inflammatory clinical markers and disease activity suggesting the link between metabolic alterations and the clinical features of PsA with the development of NAFLD, 2) PsA patients with high cumulative doses of methotrexate had no alteration of hepatic enzymes and indexes and 3) High cumulative doses of methotrexate *in vitro* did not show a significant impact on hepatocyte cells compared to low doses. Funded by ISCIII (PI20/00079 and RICOR-RD21/0002/0033), the Andalusian government (1381035-F) co-financed by ERDF.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0095 EARLY INCREASED SYNOVIAL IMMUNOHISTOCHEMISTRY REACTIVITY OF IL17A AND TGF-B1 IN PSORIATIC ARTHRITIS AND RHEUMATOID ARTHRITIS PATIENTS PREDICTING USE OF BIOLOGICS

Keywords: bDMARD, Biomarkers, Psoriatic arthritis

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Background: PsA diagnosis and treatment delayed is commonly leading to progressive articular damage, and research has aimed to improve PsA diagnosis and prognosis by identifying novel disease biomarkers.
Objectives: The present research aimed to analyze cytokines regarding inflammation and bone destruction/regeneration in patients with psoriatic arthritis (PsA), rheumatoid arthritis (RA), osteoarthritis (OA), and ankylosing spondylitis (AS) as possible biomarkers.
Methods: The patients underwent knee arthroscopy between 2009 and 2013 because they clinically presented with knee joint swelling and tenderness that did not improve with the medical treatment indicated for their diagnosed disease. So, samples were obtained from the swollen knee of patients who had been referred for undergoing arthroscopies and the synovial membrane was processed for pathological description, and protein IHC quantification (% Expressed in Ratio_Area-Intensity) for TGF-β1, IL-23, IL-6, IL-17A, IL-22, Dkk1, Sclerostin, BMP2, BMP4, Wnt1, and Wnt5a was done. All these data were analyzed and compared with the demographic, clinical, analytical, and radiological characteristics of the patients, and their predictive abilities using receiver operating characteristic (ROC) curves.
Results: Synovial membrane samples were obtained from 44 patients (PsA n=13, RA n=9, OA n=18, AS=4) for IHC quantification analysis. At baseline, 9 patients were being treated with csDMARDs, and no one of them was previosly treated with biologics. After 5 years, 4 of 13 with PsA and 2 of 9 the RA patients were treated with biologics. In general, early IHC reactivity for TGF-β1 in the synovial tissue was higher in patients with psoriatic arthritis (p=0.024) and was positively correlated with IL-17A (r = 0.355, p = 0.024), and Dkk1 (r = 0.444, p = 0.004). Early IHC reactivity for TGF-β1 in the synovial tissue was higher in PsA patients treated after with biologics (p = 0.015). Patients with PsA and RA treated with biologics had higher IHC reactivity for IL-17A in the synovial tissue (p = 0.004), for Dkk1 (p = 0.02), and for BMP2 (p = 0.045). There were no differences found regarding gender (p = 0.944), age (p = 0.947), or the Kellgren-Lawrence scale in the knee target (p = 0.608) for TGF-β1 but IL-17A IHC expression was higher in men (p = 0.02). In the logistic regression analysis, these differences seem to be independent of age, gender, or csDMARD use at the basal moment, for TGF-β1 (p=0.014), IL-17A (p=0.009), and Dkk1 (p=0.015). ROC curve analysis of IHC reactivity for TGF-β1 and IL-17A in the synovial seems to predict future treatment with biologics in the next 10 years with the areas under the curve (AUC) of 0.835 (95% CI: 0.695-0.976; p < 0.006), and 0.853 (95% CI: 0.725-0.980; p < 0.004), respectively.

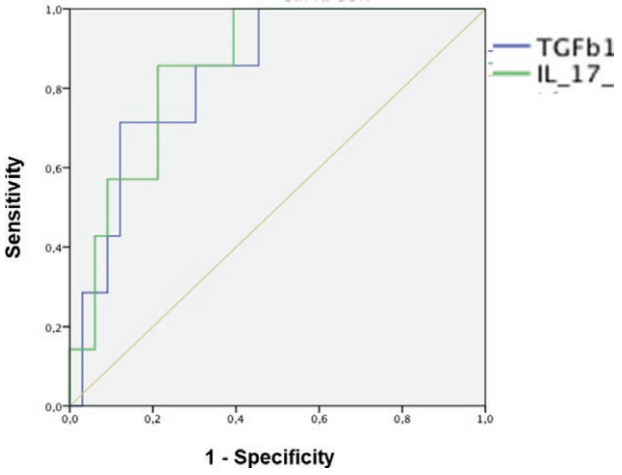


Figure 1.

Conclusion: It was observed that IHC reactivity for TGF-β1 and IL17A was higher in patients who needed biologics after 5 years of following. Early increased synovial immunohistochemistry reactivity of IL17A and TGF-β1 in psoriatic arthritis and rheumatoid arthritis patients could predict the need to use biologics.
Funding sources: Grant (PI11/00390) from Plan Nacional de Investigación Científica, Desarrollo e Innovación Tecnológica 2008-2011 and co-financed by the ISCIII-Subdirección General de Evaluación y Fomento de la Investigación - Fondo Europeo de Desarrollo Regional (FEDER).
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3956

AB0096 INVESTIGATION OF THE EFFECTS OF KYNURENIC ACID ANALOG IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS

Keywords: Spondyloarthritis, Cytokines and chemokines

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Background: The anti-inflammatory and immunosuppressive functions of kynurenic acid (KYNA) is in the center of attention. Previously, we demonstrated the effects of KYNA analog on the blood samples of rheumatoid arthritis patients *in vitro*. The results showed the suppression of tumor necrosis factor-α (TNF-α), S100A12 (EN-RAGE), S100A8/9 (calprotectin) and α-defensin production, with the increase of tumor necrosis factor-stimulated gene-6 protein (TSG-6) levels.
Objectives: In the present study, we compared the effects of the previously used newly synthetized KYNA analog on the TNF-α, S100A8/9, S100A12 alarmins, α-defensin and interleukin-17 (IL-17) production, correlation with the effects on the TSG-6 expression in ankylosing spondylitis (AS) and psoriatic arthritis (PsA).
Methods: 38 PsA and 54 AS patients were involved and divided in subgroups based on disease activity. Heat inactivated *Staphylococcus aureus* (SA1) were used as cytokine inducers on peripheral blood mononuclear cells (PBMC) isolated from blood samples of healthy controls, and patients. In parallel *in vitro* experiments, the SA1 induced PBMCs were pretreated with the KYNA analog. The concentrations of the above mentioned inflammatory mediators in the supernatants were quantified by ELISA.
Results: The SA1 induced the TNF-α, TSG-6, calprotectin and α-defensin production while only a modest increase could be seen in the concentration of EN-RAGE, and had no effect on the IL-17 levels. KYNA analog attenuated the SA1 induced TNF-α, calprotectin and α-defensin production, and increased the TSG-6 production. Addition of KYNA analog had no effect on the EN-RAGE and IL-17-levels. The cytokine inducer effect of SA-1 was the mildest in the blood samples of patients with csDMARD or NSAID therapy. The TNF-α inhibitory effect of the KYNA analog correlated inversely with the TSG-6 stimulatory effect.
Conclusion: TSG-6 expression could participate in the suppression of inflammatory cytokines, such as TNF-α, calprotectin and α-defensin in spondylarthropathies. The elevation of the TSG-6 production by KYNA analog is a possible mechanism behind the antiinflammatory effect of KYNA, marking it a potential target for therapeutic application in the treatment of immune mediated diseases such as AS, PsA or RA.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5149

AB0097 DISSOCIATION OF SERUM IL-23 AND IL-17 LEVELS IN PATIENTS WITH SPONDYLOARTHRITIS ACCORDING TO RADIOGRAPHIC STAGE

Keywords: Spondyloarthritis, Cytokines and chemokines

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Background: Spondyloarthritis (SpA) is a chronic inflammatory disease with a pathogenesis which has not been fully understood. In recent years, interleukin (IL)-23/IL-17 axis has been widely proposed, but clinical trials of IL-23 inhibitors have failed in the treatment of SpA.
Objectives: This study aimed to evaluate serum IL-23 and IL-17 levels in SpA patients compared with control subjects according to radiographically different stage and disease activity scores.
Methods: The analysis were included 61 subjects with SpA, fulfilling the Assessment of SpondyloArthritis International Society (ASAS) classification criteria for SpA and 10 controls (8 with osteoarthritis and 2 with healthy controls). IL-17 (pg/ml) and IL-23 (pg/ml) in serum from all subjects and in synovial fluid from additional 9 subjects (4 with SpA and 5 with osteoarthritis) were measured by enzyme-linked immunosorbent assay. At the same time, all SpA patients were examined with the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS) using clinical and laboratory data.
Results: Among 61 SpA subjects, 83.6% were men, mean [SD] age was 43.2 [12.3] years and mean disease duration was 13.8 [9.1] years. Mean BASDAI was 2.6 [2.0] and mean ASDAS-CRP was 1.6 [1.1]. While median [IQR] serum IL-17 was similar in both SpA and control groups (1.3 [0.6-5.5] pg/ml in SpA vs 1.1 [0.6-5.2] pg/ml in controls, p=ns), serum IL-23 level was significantly higher in controls compared with SpA patients (9.7 [8.0-16.9] pg/ml in SpA vs 20.9 [10.5-66.8] pg/ml in control, p=0.016). Higher level of synovial IL-17 and IL-23 were observed in additional 4 SpA patients (12.3 [0.9-30.6] pg/ml for IL-17 and 82.6 [33.5-112.1] pg/ml for IL-23) than 5 controls (0.4 [0.3-6.4] pg/ml for IL-17 and 57.7 [50.5-108.6] pg/ml for IL-23), albeit not significant (p=ns). Interestingly, significantly higher serum IL-23 was observed in patients with non-radiographic axial SpA (nrAxSpA) (n=20, 13.1 [8.7-49.4] pg/ml) than advanced ankylosing spondylitis (AS) (n=41, 9.1 [7.9-12.6] pg/ml) (p=0.039), but not with IL-17 (1.3 [0.8-3.7] pg/ml in nrAxSpA vs. 1.3 [0.5-6.8] pg/ml in AS, p=ns). Nevertheless, no significant difference regarding serum IL-17 and IL-23 levels was found between patients with less active SpA (ASDAS-CRP ≤2.1, n=44) and more active SpA (ASDAS-CRP >2.1, n=13). No associations of serum IL-17 and IL-23 levels with other clinical parameters including disease duration, syndesmophyte, tumor necrosis factor inhibitors uses were found.
Conclusion: Peripheral blood IL-23/IL-17 concentrations did not show the association with inflammatory burden of the disease. However, the level of serum IL-23 was higher in patients with nrAxSpA than in those with advanced AS. IL-23 might dissociate from IL-17 in advanced AS and play an important role only at early stage of axSpA.
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Acknowledgements: This research was supported by a grant awarded to JY from Gachon University Gil Medical Center (Grant number: FRD2021-08).
Disclosure of Interests: None Declared.
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AB0098 THE CAUSAL RELATIONSHIP BETWEEN MULTIPLE SCLEROSIS AND PSORIASIS: A TWO-SAMPLE MENDELIAN RANDOMIZED STUDY

Keywords: Psoriatic arthritis, Randomized control trial

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Background: Psoriasis is an immune-related, chronic inflammatory skin disease.The disease often presents with clearly delineated areas of erythematous patches on the skin covered with silvery scales[1].As the research progresses, more and more evidence suggests that multiple sclerosis may help reduce the occurrence of psoriasis.
Objectives: To explore whether there is a causal relationship between having multiple sclerosis and obtaining psoriasis.
Methods: We used a 2-sample Mendelian randomization (MR) method to evaluate the causal effect of multiple sclerosis on psoriasis. Multiple sclerosis (MS) and psoriasis (Ps) Ps summary data from IEU database (http://gwas.mrcieu.ac.uk/).The multiple sclerosis cohort consisted of 9,722 samples and 17,376 controls.The psoriasis cohort consisted of 4510 samples and 212242 controls. To reduce bias due to race-related confounding factors, the genetic background of the study population was limited to European ancestry.In the MR Approach, the IV analysis is based on three strict assumptions, namely that IV should be strongly correlated with exposure, independent of confounding factors associated with direction and outcome, and influence outcome solely through exposure[2]. We screened for significant (p<5× 10-06) and approximately independent (r 2 < 0.01) genome-wide single nucleotide polymorphisms (SNPS) and retained only SNPS with scores over 10 that were considered sufficiently strongly associated. To estimate the causal relationship between exposure and outcome, inverse variance weighting (IVW), MR-Egger regression, and weighted median methods were used. Mendelian random multivariate residuals and outliers, Cochran Q test and MR-Egger regression were used for sensitivity analysis.
Results: MR Statistics showed that genetic prediction of multiple sclerosis was associated with a reduced risk of psoriasis (IVW: OR=0.698,95%CI= 0.5788-0.843 P= 2.098-e-2), which we found to be statistically significant as the weighted

median method (OR=0.827; 95%CI= 0.760- 0.898p =4.476e-06), MR-Egger also showed a similar effect (OR=0.668; 95%CI= 0.482-0.926 P = 2.184e-02). Cochran's s Q test (Q=322.585; p=9.057e-51) found potential heterogeneity. MR-egger regression (P=0.164, intercept=0.043) was used to test the nonexistent horizontal multi-directivity. Similarly, we examined the level of pleiotropy again with MR-PRESSO's global test, and the results showed no evidence of horizontal pleiotropy. In addition, no SNP was found to be a significant factor affecting the association in the residual analysis.

Conclusion: Our results provide causal evidence for the effect of multiple sclerosis on psoriasis risk. This Mendelian randomization study showed a causal relationship between multiple sclerosis and the risk of psoriasis. Multiple sclerosis may help reduce the burden of psoriasis.

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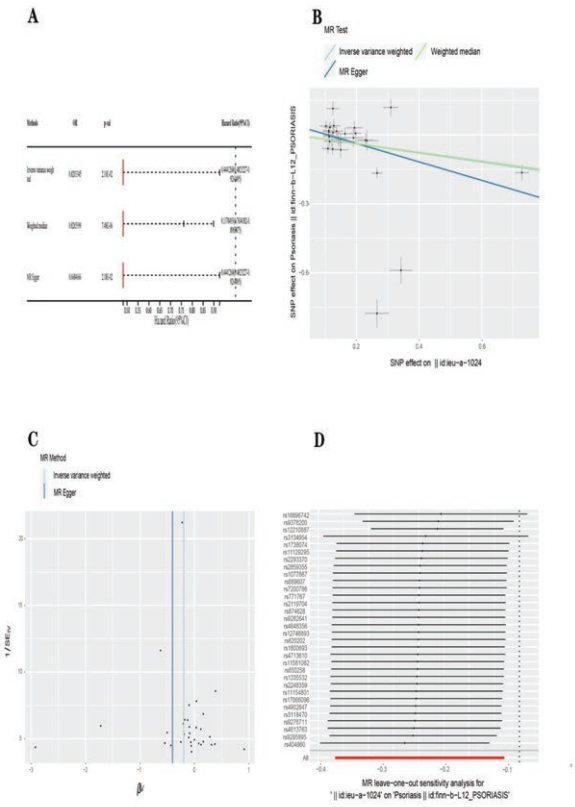


Figure A The MR Assessment assessed the causal relationship between multiple sclerosis and psoriasis.
Figure B Scatter plots of the causal relationship between multiple sclerosis and psoriasis using different MR Methods. The slope of each line corresponds to the causal estimate of each method. The effect of the individual snp effect on the result (dots and vertical lines) is plotted against its effect on exposure (dots and horizontal lines) in the background.
Figure C Funnel plot visualised Mendelian randomization (MR) estimated the overall heterogeneity of the effects of multiple sclerosis on psoriatic arthritis. Each black dot represents the IVW MR Method used to estimate the causal effect of multiple sclerosis on psoriasis, excluding the specific variation in the analysis. The red dots describe the IVW estimates using all SNPS. The horizontal line indicates 95% CI.
Figure D The image shown an analysis of psoriasis retention sensitivity in multiple sclerosis. Leave-one-out plots of the estimate of multiple sclerosis on the risk for psoriasis for each or all single nucleotide polymorphisms.

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Disclosure of Interests: None Declared.
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AB0099 CLONORCHIS SINENSIS-EXCRETORY/SECRETORY PROTEIN AMELIORATES INFLAMMATION IN ANKYLOSING SPONDYLITIS

Keywords: Spondyloarthritis, Animal models

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Background: Ankylosing spondylitis (AS) is a sort of inflammatory arthritis that affects axial skeleton, peripheral joints, and certain extra-articular organs, including the eyes, skin, and gut. Recently, many attempts have been made to use parasite administration (e.g., ingestion of eggs of the nematode Trichuris suis) as a new modality for treating inflammatory disorders. Our group published that Clonorchis sinensis protein attenuated inflammation in AS.

Objectives: Thus, this study aimed to assess the therapeutic potential of Clonorchis sinensis-Excretory/Secretory protein (Cs-ESP) for AS.

Methods: Cytotoxicity of Cs-ESP at different doses was assessed by MTS and flow cytometry before performing experiments. Peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs) were obtained from AS patients. Inflammatory cytokine-producing cells were analyzed using flow cytometry. The levels of INF-g, IL-17A, TNF-a, and IL-6 were measured by enzyme-linked immunosorbent assay (ELISA). SKG mice were treated with Cs-ESP or vehicles. Inflammation was evaluated using immunohistochemistry.

Results: Treatment with Cs-ESP resulted in no reduced cell viability of PBMCs or SFMCs. In experiments culturing PBMCs and SFMCs, the frequencies of IFN-g and IL-17A producing cells were significantly reduced after Cs-ESP treatment. In the SKG mouse model, Cs-ESP treatment significantly suppressed arthritis and enthesitis.

Conclusion: We provide the evidence demonstrating that Cs-ESP can ameliorate clinical signs and cytokine derangements in AS.

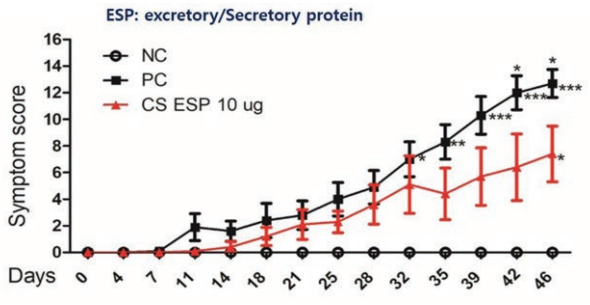


Figure 1. Clonorchis sinensis-Excretory/Secretory protein (Cs-ESP) ameliorates clinical symptoms in SKG mice

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0100 TO STUDY THE T CELL AND CYTOKINE PROFILE IN ANKYLOSING SPONDYLITIS WITH EFFECTS OF TACROLIMUS AND TADALAFIL ON THE CYTOKINES IN-VITRO

Keywords: Adaptive immunity, Spondyloarthritis

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Background: Most studies have shown mixed results of Interleukin (IL)17 and IL-23 levels in patients with Ankylosing Spondylitis (AS) compared to controls; with animal studies showing a good correlation between activation of IL 23-IL

27 pathway and radiologic progression. Targeting this pathway in humans has yielded benefits with reduced inflammation and radiologic progression in AS. Controlling inflammation and fibrosis is the key to prevent osteoproliferation. Tacrolimus and tadalafil have shown to inhibit the Th17 pathway and profibrotic pathways respectively.

Objectives: To study the T cell (Th17, PD1, CD25+ CD4 T cells) and cytokine profile (IL-17, IL-23, TGF- β) in AS with influence of disease duration and activity on the above profile. To also study the effect of tacrolimus and tadalafil in ex-vivo peripheral blood monocyte (PBMC) cultures to study their anti-inflammatory and anti-fibrotic potential.

Methods: Patients with AS (ASAS classification criteria) without peripheral disease and not on biologic therapy were recruited and their demographic, clinical profile, disease activity and radiologic indices were recorded. Age and sex matched healthy controls (HC, n=21) were also recruited. Peripheral blood was drawn and sera stored; PBMCs were isolated and cultured. Serum and PBMC culture supernatant (CS) were measured for IL-17, IL-23 and TGF-β. These cytokines were measured at baseline, after stimulation with anti-CD3CD28 antibodies, and after treatment with tacrolimus(10mM/ml), tadalafil(10mM/ml) and both the drugs combined by ELISA(R&D systems, USA). The T cell profile was characterized by flow cytometry (CD4 Th17, CD4 PD1, CD4 Th17 PD1 and CD4 CD25). Statistical analysis was done using GraphPad prism v9.

Results: Twenty-five patients [28(24-36),M:F, 7.3:1] were enrolled with 90% HLA-B27 positivity. The majority had moderate-high disease activity as per ASDAS CRP and were on NSAIDs(24), complementary medications (7) and two each on methotrexate and sulfasalazine. Serum IL-17 and TGF-β, CS TGF- β were significantly elevated in AS compared to controls. All the measures cell populations were significantly elevated in AS compared to HC. When stratified by duration of disease, clinical parameters, disease activity indices, cytokine and T-cell profile was similar across the two groups. ASDAS CRP showed a significant correlation with CD4Th17+ cells (r=0.7, p=0.009) and CD4 PD1/T reg (r=-0.6, p=0.03). A positive association as observed with some cells but not with the cytokines on generalized linear modeling (Table 1). No significant correlation was observed between cytokines or T cell profiling with Modified Stokes Ankylosing Spondylitis Score. There was a significant decline in TGF- β levels in the culture supernatant with tacrolimus and tadalafil combined, however, no such difference was observed with IL-17 or IL-23. (Figure 1)

Conclusion: Serum IL-17 and TGF- β were elevated in the peripheral blood in AS. There was no difference in the cytokine and T-cell profile across early and late disease. A significant decline in TGF- β levels was seen with combined tacrolimus and tadalafil. This needs further exploration in a larger sample size with subgroup characterization as well as testing on synovial fluid and joint tissue samples.

Table 1. Association of disease activity and T cell/cytokine profile

Multivariate GLM	OR (95%CI)	
Model 1		
CD4+Th17	1.4(0.6-2.2)	0.003**
CD4+PD1+	-0.3(-0.7-0.1)	0.07
PD1+Th17	-0.1(-0.12-0.01)	0.1
Model 2		
CD4+Th17/CD25+	3.5(0.7-6.3)	0.02*
CD4+PD1+/CD25+	-0.2(0.4- -0.02)	0.03*
PD1+Th17/CD25+	-0.6(-2.3-1.1)	0.5
Model 3		
Serum IL-17	-0.01(-0.05-0.03)	0.5
Serum IL-23	-0.01(-0.1-0.08)	0.8
Serum TGF-β	-0.00(-0.001-6.7)	0.1

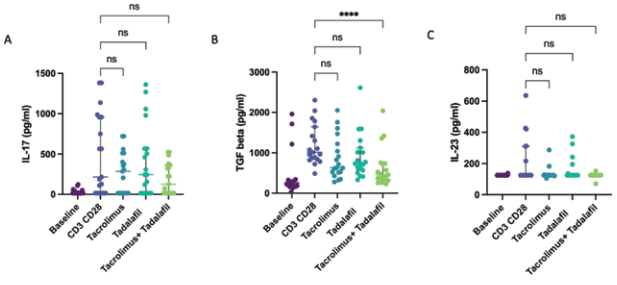


Figure 1. In vitro effect of drugs on culture supernatant cytokine levels at baseline, CD3 CD28 stimulation, and after addition of tacrolimus, tadalafil and its combination.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0101 ABNORMAL KYNURENINE LEVEL CONTRIBUTES TO THE PATHOLOGICAL BONE FEATURES OF ANKYLOSING SPONDYLITIS

Keywords: Spondyloarthritis

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Background: Ankylosing spondylitis (AS) exhibits paradoxical bone features typically characterized by new bone formation and systemic bone loss.

Objectives: Although abnormal kynurenine (Kyn), a tryptophan metabolite, has been closely linked to the disease activity of AS, the distinct role of its pathological bone features remains unknown.

Methods: Kynurenine sera level was collected from healthy control (n = 22) and AS (n = 87) patients and measured by ELISA. In the AS group, we analyzed and compared the Kyn level based on mSASSS scores, MMP13, and OCN. Under osteoblast differentiation, the effect of Kyn in AS-osteoprogenitors resulted in cell proliferation, alkaline phosphatase activity, bone mineralization-related alizarin red s (ARS), von kossa (VON), hydroxyapatite (HA) staining, and mRNA expression markers (ALP, RUNX2, OCN, and OPG) for bone formation. TRAP staining was used for osteoclast formation in RANKL-mediated RAW264.7 cells.

Results: Kyn sera level was significantly elevated in the AS group compared to the healthy control group. In addition, Kyn sera level was correlated with mSASSS score (r = 0.03888, p = 0.067), MMP13 (r = 0.0327, p = 0.093), and OCN (r = 0.0436, p = 0.052). During osteoblast differentiation, treatment with Kyn exhibited no difference in cell proliferation and alkaline phosphate (ALP) activity for bone matrix maturation but promoted ARS, VON, and HA staining for bone mineralization. Interestingly, osteoprotegerin (OPG) and OCN expression was augmented in the presence of Kyn treatment during differentiation. In growth medium, Kyn treatment of osteoprogenitors resulted in induction of OPG mRNA, protein expression, and AhR response genes (AhRR, CYP1b1, and TIPARP). Secreted OPG proteins were observed in the supernatant of osteoprogenitors treated with Kyn. Notably, the supernatant addition to osteoclastogenesis interrupted the TRAP-positive osteoclast formation of RANKL-mediated RAW264.7 cells and reduced osteoclast differentiation markers.

Conclusion: Our results revealed that elevated Kyn level increased the bone mineralization of osteoblast differentiation in AS and decreased RANKL-mediated osteoclast differentiation by inducing OPG expression, suggesting a potential therapeutic target where abnormal Kyn level could be involved in pathological bone features of AS.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3439

AB0102 POTENTIAL BIOMARKERS TO PREDICT TNF INHIBITORS OUTCOME IN PSORIATIC ARTHRITIS

Keywords: bDMARD, Psoriatic arthritis, Biomarkers

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Background: Psoriatic Arthritis (PsA) is a chronic immune-mediated inflammatory disease characterized by axial and peripheral arthritis, dactylitis, nail changes and most of the time, is associated with psoriasis. Patients are initially treated with conventional synthetic Disease-Modifying Anti-Rheumatic Drugs (csDMARDs), but if they do not respond to these, they are treated with biologics, particularly TNF inhibitors (TNFi) which are common first-line biologics. However, about 40% of patients do not or only partially respond to TNFi. Blood biomarkers predicting response to TNFi would allow patients to be treated earlier with a more appropriate drug [1].

Objectives: We studied pro- and anti-inflammatory cytokines and adaptive immune cells that could be used as biomarkers for TNFi outcome. Predicting responses to TNFi will help clinicians to choose a more appropriate treatment for patients.

Methods: Blood from patients with PsA (n = 8) was analysed before starting TNFi and compared with blood from patients with rheumatoid arthritis (RA) (n = 8). PsA patients were characterised as 'psoriasis positive' and 'psoriasis negative'. Patients were followed at 3 and 6 months after treatment (n = 6). Leukocytes were isolated with Lymphoprep and their phenotype was characterised by

CD45, CD3, CD4, CXCR3, CCR6, HLA-DR, CD38, CD25 and CD127. Levels of 12 cytokines in plasma were measured using a cytokine kit (MACSPlex Cytokine 12 Kit, human, Miltenyi Biotec Ltd, UK). Clinical data from patients were collected to determine treatment outcome.

Results: Mean level of TNFα was higher in our RA patients (6.2 pg/ml) compared to our PsA patients (4.6 pg/ml). Initial analysis of clinical data suggested that our PsA patients without psoriasis (n = 2) responded better to TNFi than those with active psoriasis (n = 4) at 3 months and 6 months after treatment, with a clear reduction in the number of tender joints ('psoriasis positive': 6.65 vs 1.67; 'psoriasis negative': 11.5 vs 0.67) and swollen joints ('psoriasis positive': 2 vs 0.67; 'psoriasis negative': 3.50 vs 0). The mean proportion of activated Th17 cells was higher in our patients with active psoriasis (5.1% of Th17 cells) than those without psoriasis (3.6% of Th17 cells). The mean level of IL-12 and INFγ was higher in the 'psoriasis positive' group (respectively 129.2 pg/ml and 266.1 pg/ml) than the 'psoriasis negative' group (respectively 52.7 pg/ml and 115 pg/ml).

Conclusion: We hypothesize that PsA patients have a lower level of TNFα because of other pro-inflammatory cytokines potentially involved in the inflammatory process. IL-12 can induce IFNγ production by Th1 cells and is involved in the IL12/IL23 axis in psoriasis pathogenesis. IFNγ can induce Th1 and Th17 cells expansion through myeloid dendritic cells activation. In PsA, the high levels of IL-12 and IFNγ involved in psoriasis pathogenesis might be one of the reasons for a poor response to treatment, but larger sample sizes are needed to find a biomarker that could be used routinely by clinicians, and to determine if the same biomarker can also be used for other types of arthritis such as rheumatoid arthritis.

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Acknowledgements: We would like to acknowledge the Rheumatology clinical team and research nurses at the RAJH Orthopaedic Hospital, and PsA and RA patients for participating in the study.

Disclosure of Interests: None Declared.

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AB0103 THE CAUSAL ASSOCIATION BETWEEN MTOR-DEPENDENT CIRCULATING PROTEINS AND PSORIATIC ARTHRITIS: A MENDELIAN RANDOMIZATION STUDY

Keywords: Spondyloarthritis, Enthesitis, Inflammatory arthritides

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Background: Psoriatic arthritis (PsA) is a chronic, immune-mediated arthropathy mainly affecting the peripheral joints, spine, and sacroiliac joints[1] The key pathologic outcomes of PsA are 'uncontrolled proliferation' of synovial fibroblasts (FLS), along with the proliferation of endothelial cells (EC) and T cells. Growing evidence found that the proliferation of these cells of psoriatic arthritis are dependent on the PI3K-AKT-mTOR kinase system.[2]

Objectives: This study aimed to investigate the causality between key mTOR kinase cascade proteins and psoriatic arthritis.

Methods: We used a 2-sample Mendelian randomization (MR) method to evaluate the causal effect of five mTOR-dependent circulating proteins on psoriatic arthritis. Data about mTOR-related gene exposure (eIF4A3, eIF4E2, eIF4E-BP2, eIF4G3, RP-S6KA) in plasma were obtained from the publicly available proteomics-GWAS INTEVAL study (https://www.phpc.cam.ac.uk/ceu/proteins/), which included 3,622 plasma protein assays from 3,301 participants. PsA relative single nucleotide polymorphisms (SNPs) were obtained from the FinnGen study(https://r5.finngen.fi/). 1637 cases and 212242 controls of European descent were included in our study. Effect estimates were evaluated using inverse-variance weighted method. There are also other MR analyses, including MR-Egger regression, and the weighted median methods. Mendelian Randomization Pleiotropy RESidual Sum and Outlier (MR-PRESSO) test, Cochran's Q test, and MR-Egger regression were performed in sensitivity analyses. All statistical analyses were performed in R (version 4.0.3).

Results: Five proteins were extracted from the downstream target of mTOR, which were eIF4A3 eIF4E2, eIF4E-BP2, eIF4G3 and RP-S6KA. Subsequently, 15, 9, 10, 16, and 18 IVs with mTOR significantly associated with psoriatic arthritis were extracted from genome-wide association studies ($P<5x10^{-6}$). F statistics of all the selected IVs are greater than 10, indicating that all IVs were strongly correlated with exposure. After the removal of SNPs with high linkage disequilibrium and palindrome, the final 8,13,10,7, and 13 SNPs were used as final instrument variables for them, respectively. Evidence for an effect of eIF4E2 on PsA risk was found in inverse-variance weighted method (OR=0.844; 95%CI,0.735,0.969; p=0.016) and weighted median (OR=0.819; 95%CI,0.687,0.977 P=0.026) using 13 single nucleotide polymorphisms (SNPs) as the instruments. For the other four common mTOR related targets, we have not found a causal relationship between them and PsA including eIF4A3 (IVW: OR = 0.912;95% CI,0.749,1.111; p = 0.359), eIF4E-BP2 (IVW: OR = 0.842; 95% CI,0.788,1.031; p = 0.075), eIF4G3 (IVW: OR = 0.768;95% CI,0.709,1.135; p = 0.366) and RP-S6KA (IVW: OR = 0.893; 95% CI, 0.767,1.040; p = 0.146). To verify the robustness of our model, we performed sensitivity analysis. No potential heterogeneity was found by Cochran's Q test (Q=6.311; p=0.852). MR-Egger regression (P=0.425, intercept=0.038) found no horizontal pleiotropy. Similarly, the result of MR-PRESSO test found no evidence of horizontal pleiotropy. In addition, no SNP was identified as an obvious factor affecting the association in the leave-one-out analysis. (Figure 1)

Conclusion: In summary, this 2-sample mendelian randomization study found a causal protective association of eIF4E2 with psoriatic arthritis. This novel result provides the scope to develop new therapeutics targeting PI3K/Akt/mTOR signaling pathway in psoriatic arthritis.

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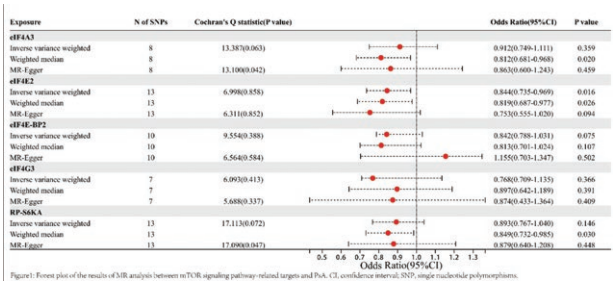


Figure1: Forest plot of the results of MR analysis between mTOR signaling pathway-related targets and PsA. CI, confidence interval; SNP, single nucleotide polymorphisms.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0104 THE CAUSAL EFFECT OF LIPID METABOLISM ON THE RISK OF PSORIATIC ARTHRITIS: A MENDELIAN RANDOMIZATION STUDY

Keywords: Genetics/Epigenetics, Psoriatic arthritis

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Background: Psoriatic disease, including psoriatic arthritis (PsA) and psoriasis, is driven by a combination of genetic, biomechanical, metabolic, and microbial factors which promote an aberrant immune response and the consequent development of chronic disease.(1) Genetic evidence has indicated that body mass index and glycemic control are associated with an increased risk of psoriasis and PsA, and also with an increased risk of cardiovascular disease.(2) However, the causal relationship between serum lipids and risk of incident PsA remains unclear.

Objectives: To investigate whether lipid metabolites are causally associated with incident psoriatic arthritis (PsA), in comparison with rheumatoid arthritis (RA) and ankylosing spondylitis (AS).

Methods: The publicly available summary-level findings from two genome-wide association studies (GWAS) were used to identify loci influencing circulating metabolites as exposure and a GWAS for PsA (n=1,637, control=212,242), RA (n=6,236, control=147,221), AS (n=1,462, control=164,682) as the outcome. Bi-directional Mendelian randomization (MR) analysis and multivariable MR analysis were used in main and validation analysis.

Results: In the main analysis, pooled data suggested a causal association of PsA risk with total cholesterol (P=0.005), cholesterol esters (P=0.003), free cholesterol (P=0.009), total lipids (P=0.004), phospholipids (P=0.010), and concentration of particles (P=0.005) in large low-density lipoprotein (LDL); total cholesterol (P=0.009), cholesterol esters (P=0.006), total lipids (P=0.009), phospholipids (P=0.002), and concentration of particles (P=0.009) in medium LDL; total cholesterol (P=0.001), total lipids (P=0.001), concentration of particles (P<0.001) in small LDL (Figure 1). Multivariable MR analysis identified cholesterol esters in large LDL as the strongest causal risk factor for PsA (P=0.017) (Table 1). In validation analysis, genetically predicted cholesterol (P=0.004), cholesteryl esters (P=0.001), and total lipids (P=0.003) in LDL; cholesteryl esters in large LDL (P=0.006); phospholipids (P=0.007) and concentration of particles

(P=0.006) in medium LDL; and total lipids in small LDL (P=0.008) were also causally associated with PsA. However, there is no causal association of lipid metabolites with RA and AS.
Conclusion: The present findings supported causal relationships between LDLs and an increased risk of PsA, especially for cholesterol esters in large LDL.
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Table 1. Multivariable Mendelian randomization analyses estimating the direct effects of low-density lipoprotein cholesterol (LDL-C) traits on psoriatic arthritis

Exposure	Outcome	No. of SNPs	β	SE	p-value
Multivariate MR analysis of univariate significant all LDL composition and apolipoprotein					
Apolipoprotein B	Psoriatic arthritis	19	0.142	0.347	0.682
Cholesterol esters in large LDL		22	3.722	1.565	**0.017**
Total cholesterol in LDL		24	-1.365	1.297	0.293
Cholesterol esters in medium LDL		22	-2.269	1.529	0.138

SNP, single-nucleotide polymorphism; Significant results are in bold.

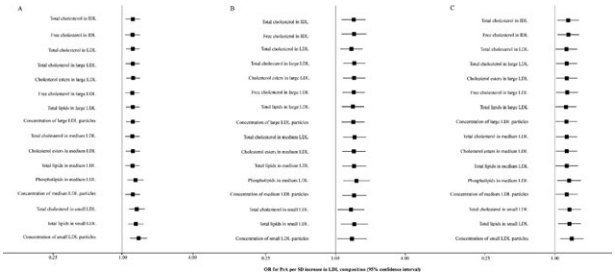


Figure 1. Mendelian randomization results for associations between low-density lipoprotein cholesterol (LDL-C) traits and psoriatic arthritis. PsA: psoriatic arthritis; OR: odds ratio; SD: standard deviation.

Acknowledgements: We are immensely grateful to the study participants from the circulating metabolites GWAS study.
Disclosure of Interests: None Declared.
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AB0105

CAUSAL ASSOCIATION BETWEEN IL-7 LEVELS AND ANKYLOSING SPONDYLITIS: A TWO-SAMPLE MENDELIAN RANDOMIZATION STUDY

Keywords: Biomarkers, Genetics/Epigenetics, Inflammatory arthritides

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Background: Ankylosing spondylitis (AS) is an immune-mediated inflammatory arthritis that affects the axial skeleton. Currently, the cause of AS is still not known, so there is no way to prevent AS. Interleukin-7 (IL-7) is a restrictive and non repetitive cytokine, mainly produced by epithelial and stromal cells. The relationship between IL-7 and some inflammatory cytokines such as AS has been discussed in recent advances in the pathogenesis of AS, but a direct effect of IL-7 on AS has not been demonstrated[1].
Objectives: Study to investigate the casual association between IL-7 and AS.
Methods: We evaluated the causal relationship between IL-7 levels and AS using a Mendelian randomization approach. The GWAS summary statistics of IL-7 (N = 3409) and AS (Ncase = 968, Ncontrol = 336,191) were downloaded from the IEU GWAS database in the study. Instrumental variables (IVs) were constructed using single nucleotide polymorphisms (SNPs). To assess the causal relation of IL-7 and AS, we used three analytical methods: MR-Egger mode, Weighted median mode, and Inverse variance weighted (IVW). In addition, we also conducted sensitivity tests, including the heterogeneity test, the pleiotropy test, the funnel plot, leave-one-out approach and MR-PRESSO.
Results: When selecting SNPs associated with IL-7, in the situation of the genome-wide significant threshold of P < 5×10-6 and LD r2 = 0.001, we finally obtained 9 IVs that could be used in the subsequent steps. Based on the IVW mode with high statistical power, a prudent and credible causal relationship was demonstrated between IL-7 and AS [IVW: P=0.025, OR(95%CI)=0.999(0.999, 1.000)]. As the level of IL-7 increased, the risk of developing AS also decreased, proving that IL-7 was a protective factor for this disease (Figure 1a). The Cochrane Q test (Q test p = 0.99) showed a good homogeneity among studies. The results of a leave-one-out sensitivity analysis suggested that causal associations were not strongly influenced by any of the selected IVs (Figure 1b). Funnel plot results (Figure 1c) and the intercept of the MR-Egger regression (Figure 1d) further showed that pleiotropy did not bias the causal effect in this study.
Conclusion: Our research results show that IL-7 is causally associated with the pathogenesis of AS. which enables the early detection of AS, this findings have great clinical value.
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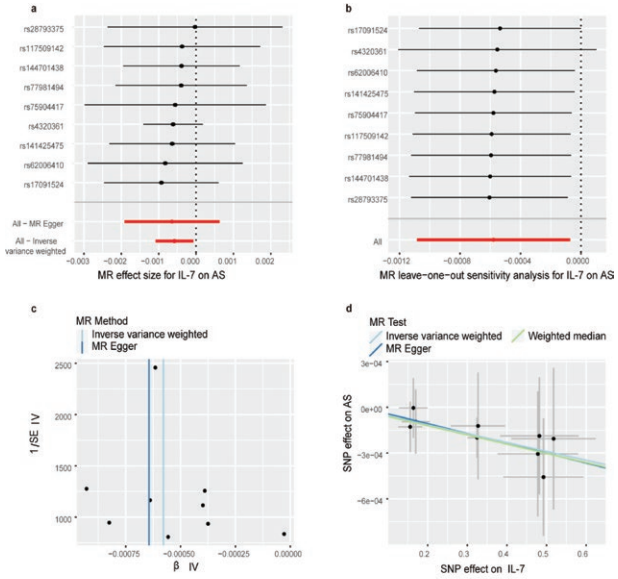


Fig 1. (a) The forest plot for MR analyses of the causal effect between IL-7 and AS using the MR-Egger and IVW. **(b)** The leave-one-out sensitivity analysis for MR analyses of the causal effect between IL-7 and AS. **(c)** The funnel plot was used to visualize pleiotropy of effect estimates through the symmetry of the points. **(d)** The scatter plot for MR analyses of the causal effect between IL-7 and AS using the IVW, MR-Egger and Weighted median.

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5327

AB0106

CAUSAL RELATIONSHIP BETWEEN IL-17 FAMILY MEMBERS AND THEIR RECEPTORS AND ANKYLOSING SPONDYLITIS: A TWO-SAMPLE MENDELIAN RANDOMIZATION STUDY

Keywords: Spondyloarthritis, Cytokines and chemokines, -omics

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Background: Ankylosing spondylitis (AS) is an axial rheumatic and spinal disease based on autoimmune and genetic susceptibility that affects the sacroiliac joints and the spine[1]. Interleukin 17 (IL-17) as an inflammatory cytokine positively correlated with disease activity in AS patients[2]. However, the causal relationship between the IL-17 family and its receptors and AS is inconclusive.
Objectives: The aim of this study was to discover the casual association between the IL-17 family members with their receptors and AS.
Methods: To clarify the causal relationship between the IL-17 family members (and their receptors) and AS, we used two-sample Mendelian randomization (MR).

We selected single-nucleotide polymorphisms (SNPs) from genome-wide association studies (GWAS) which included IL-17 family members and their receptors (N = 3301) and AS (Ncase = 968, Ncontrol = 336,191). Confounding factors were excluded, heterozygosity and lateral polymorphisms were examined and corrected.
Results: We found that IL-17RB level was significantly causally associated with AS (IVW OR=1.0007, 95%CI 1.0002~1.0011, P= 0.0020, Figure 1a). Sensitivity analysis also confirmed the absence of horizontal polymorphism (MR-Egger intercept = 6.5989×10^{-5}, P = 0.5158, Figure 1b) and heterogeneity (IVW Q = 10.7388, Q_pval = 0.5514) that biased the causality. The leave-one-out sensitivity test showed that no single SNP strongly affected the causal relationship between IL-17RB and AS (Figure 1c). Furthermore, funnel plot symmetry suggests that our study fits the IV hypothesis(Figure 1d). However, our results show no significant causal relationship between AS and other IL-17 family members and their receptors.
Conclusion: Our results show that IL-17RB is a protective factor for AS. We offer a new insight into the drug targets of AS.
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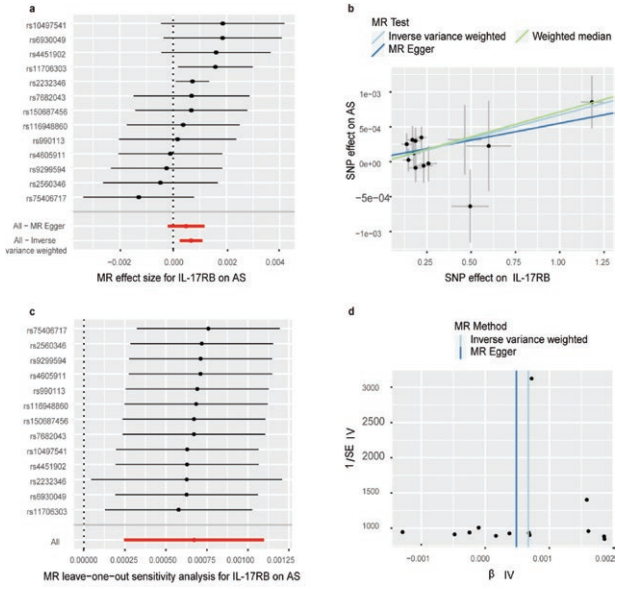


Fig 1. (a) Forest plot. Each horizontal solid line reflects the results estimated by a single SNP using the Wald ratio method: some are complete to the left of 0, indicating that the result calculated by this SNP is that increased exposure reduces the risk of outcome; some are complete to the right of 0, indicating that the result estimated by this SNP is that increased exposure increases the risk of the outcome, and those over 0 are not significant. Looking at the effects of a particular SNP alone may be problematic; only when the results are put together can we see that good results can be obtained. The solid red line reflects that the elevated IL-17RB under IVW and MR-Egger methods will increase the risk of AS. IL17RB is a risk factor for AS. **(b)** Scatter diagram. Each point on the graph represents an IV, the line on each point reflects the 95% confidence interval, the abscissa is the effect of SNP on exposure (IL-17RB level), and the ordinate is the effect of SNP on the outcome (AS), the colored lines represent the MR fit result. As the level of IL-17RB increases, the risk of developing AS also increases. **(c)** Leave-one-out sensitivity test. All the lines are on the right side of 0, indicating that either SNP was removed would not fundamentally affect the results, indicating that the MR was robust in our study. **(d)** Funnel plot. Dashed lines perpendicular to the horizontal axis indicate the combined effect sizes. The studies should be evenly distributed on both sides in a symmetric inverted funnel shape in an ideal state. Our analysis of the individual SNP in the funnel plot is roughly symmetric, suggesting almost no bias in the study.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0107 A CAUSAL EFFECT OF IL-10 LEVELS ON THE RISK OF ANKYLOSING SPONDYLITIS: A MENDELIAN RANDOMIZATION STUDY

Keywords: Spondyloarthritis, Cytokines and chemokines

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory immune response disease mainly presenting with fibrosis of the sacroiliac joint and calcification [1]. Interleukin-10 (IL-10) is a factor that suppresses Th17 cell activity and induced Treg cells to achieve immunosuppression. Observational studies show that IL-10 may be one of the important contributing sources of important inflammatory cytokines for AS [2], but the causal relationship between them is not clear.
Objectives: The objective was to investigate the casual association between AS and IL-10.
Methods: The GWAS summary statistics of IL-10 and AS (Ncase = 968, Ncontrol = 336,191) were downloaded from the IEU GWAS database in the study. After a series of screens, SNPs strongly associated with exposure were included as instrumental variables(IVs). The results are from using robust analyses with three two-sample different assumptions (Inverse variance weighting (IVW), Weighted median (WM) and MR-Egger). Meanwhile, we used MR-Egger intercept test, Cochran'sQ test and leave-one-out sensitivity analysis for assessment to avoid the biasing effects of potential genetic variation, horizontal pleiotropy and heterogeneity. MR-PRESSO outlier test was used to identify and eliminate horizontal pleiotropy.
Results: Our result showed that the level of IL-10 has a causal relationship with the risk of developing AS (IVW: OR=0.9992, 95% confidence interval (CI) 0.9985-0.9999, P = 0.03, Figure 1a, 1b). Increasing the IL-10 level can reduce the risk of AS disease. MR-Egger intercept test (MR-Egger intercept = -1.5705×10^{-5}, P = 0.5158, Figure 1b), Cochran's Q test (IVW Q = 4.3071, Q_pval = 0.8284), leave-one-out sensitivity analysis (Figure 1c) and the funnel plot (Figure 1d) suggest almost no bias in the study, indicating that the MR was robust.
Conclusion: Our results indicate a protective role for IL-10 in AS, suggesting that elevated IL-10 levels may be able to alleviate the inflammatory response in AS, providing new insights into AS treatment.
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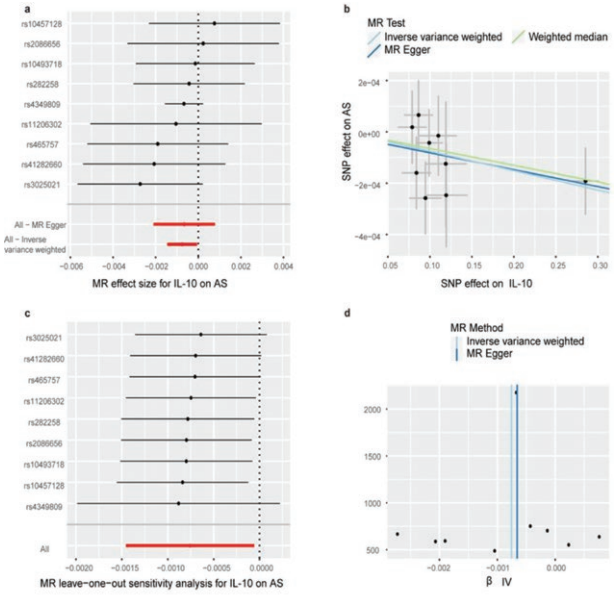


Fig 1. (a) Forest plot. The solid red line reflects that the elevated IL-10 under IVW will decrease the risk of AS. IL-10 is a protective factor for AS. (b) Scatter diagram. Each point on the graph represents an IV, the line on each point reflects the 95% confidence interval, the abscissa is the effect of SNP on exposure (IL-10 level), and the ordinate is the effect of SNP on the outcome (AS), the colored lines represent the MR fit result. As the level of IL-10 increases, the risk of developing AS decreases. (c) Leave-one-out sensitivity test. All the points are on the right side of 0, indicating that either SNP was removed would not fundamentally affect the results, indicating that the MR was robust in our study. (d) Funnel plot. The studies should be evenly distributed on both sides in a symmetric inverted funnel shape in an ideal state. Our analysis of the individual SNP in the funnel plot is roughly symmetric, suggesting almost no bias in the study.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3430

AB0108 THE ASSOCIATION BETWEEN ELEVATED SERUM IL22 AND THE CLINICAL DIAGNOSIS OF AXIAL SPA.

Keywords: Biomarkers, Inflammatory arthritides, Spondyloarthritis

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Background: Interleukin-22 (IL-22) is produced by T helper type 1, type 17, type 22 cells, and type 3 ILC, being probably a marker of osteogenic differentiation and new bone formation. Diagnosis and treatment are commonly delayed due to different clinical presentations that lead the patient to progressive articular damage. In recent studies, it seems that the serum levels of IL-22 are elevated in axial spondyloarthritis (AxSpA) and do not allow differentiation between AxSpA and other joint inflammatory disorders.
Objectives: The present research aimed to analyze serum cytokines as possible biomarkers regarding inflammation and bone destruction/regeneration in four rheumatic diseases.
Methods: Serum samples were acquired from patients with psoriatic arthritis (PsA), rheumatoid arthritis (RA), osteoarthritis (OA), and AxSpA. Serum levels of TGF-β1, IL-23, IL-6, IL-17A, IL-22, Dkk1, Sclerostin, BMP2, BMP4, Wnt1, and Wnt5a were measured by enzyme-linked immunosorbent assay (ELISA). All these data were analyzed and compared with the demographic, clinical, analytical, and radiological characteristics of the patients. Statistical analysis was performed using the SPSS version 23 program (IBM SPSS Statistics). Values of $p < 0.05$ were considered statistically significant.
Results: The serum samples were obtained from 35 patients (PsA n=11, RA n=7, OA n=13, AxSpA=4). All these patients were previously treated with NSAIDs and corticosteroids (oral/intraarticular); 4 were treated with csDMARDs, but no none of them was previously treated with biologics. IL-22 levels were higher in AxSpA patients ($p = 0.046$), although serum IL-22 levels did not correlate with modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) ($p = 0.154$) or C-reactive protein ($p = 0.208$). The sensitivity and specificity of the serum IL-22 for the AxSpA diagnosis were 75% and 81% respectively, for the cut-off value of 58 ng/mL, with AUC 0.798 (95% CI 0.634-0.962

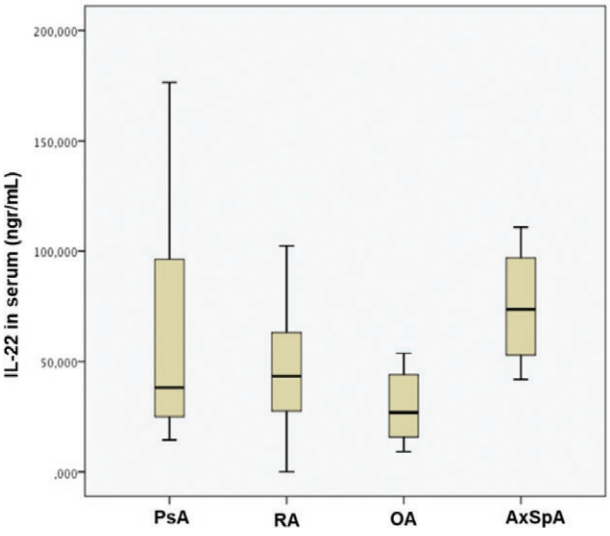


Figure 1.

Conclusion: Serum levels of IL-22 are elevated in patients with clinical diagnoses of AxSpA and could be an independent serum biomarker of this disease.
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Funding sources: Grant (PI11/00390) from Plan Nacional de Investigación Científica, Desarrollo eInnovación Tecnológica 2008-2011 and co-financed by the ISCIII-Subdirección General de Evaluación y Fomento de la Investigación - Fondo Europeo de Desarrollo Regional (FEDER).
Disclosure of Interests: None Declared.
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AB0109

ASSESSING PREVALENCE OF SPONDYLOARTHRITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: AN ANALYSIS OF RETROSPECTIVE DATA FROM A NOVEL COMBINED RHEUMATOLOGY AND GASTROENTEROLOGY CLINIC

Keywords: Spondyloarthritis, Disease-modifying Drugs (DMARDs), Gastrointestinal tract

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Background: Spondyloarthritis (SpA) associated with inflammatory bowel diseases (IBD) is a subtype of SpA affecting the axial spine (AxSpA) and peripheral musculoskeletal system causing arthritis, enthesitis and dactylitis (peripheral SpA) in patients with Crohn's Disease (CD) or Ulcerative Colitis (UC). The prevalence of SpA in IBD is variable but reported to range from 5-15% for axial SpA and 30-45% for peripheral SpA. Detection of SpA in IBD patients requires a multidisciplinary approach to ensure early diagnosis and tailored treatment. This highlights the need for combined assessment by rheumatology and gastroenterology to prevent disability and loss of function.
Objectives: We aimed to assess the prevalence of SpA in IBD patients evaluated for arthralgia in a combined gastroenterology and rheumatology clinic (IB-DART), in a large tertiary care center in New York City.
Methods: We conducted a retrospective chart review of patients with IBD and arthralgia who were evaluated by physicians of both specialties in the IB-DART clinic. Patients over the age of 21 with a diagnosis of IBD and symptoms of joint pain were included. A multidisciplinary approach was taken for both diagnosis and treatment. Prevalence of axial SpA, peripheral SpA, HLA B27 positivity were calculated. Descriptive statistics were used.
Results: 63 patients (61.9% females) were seen in the IB-DART clinic, the average age was 48.5. There were 10 (15.8%) patients with non-inflammatory arthritis and 53 (84.1%) patients with axial or peripheral SpA. Of the 53 patients, 7 (13.2%) had AxSpA, 32 (60.3%) had peripheral SpA, and 14 (26.4%) had both axial and peripheral SpA. SpA was seen in 90.9% of the 44 CD patients, 68.7% of the 16 UC patients, 66.6% of the 3 undifferentiated IBD patients. 9 (42.8%) patients with AxSpA were found to have x-ray and MRI evidence of sacroiliitis. 1 had MRI findings of enthesitis. HLA B27 was only positive in 3 of the 39 tested patients and did not correlate with axial or peripheral involvement. In patients with SpA, 23 were on TNF inhibitor therapy, 10 on JAK inhibitors, 13 on interleukin-12/23 inhibition, and 6 on conventional DMARDs (ie Methotrexate, 6MP, hydroxychloroquine) and prednisone. (Table 1)

Table 1. Patient characteristics

SpA	53 patients
Axial	7/53 (13.2%)
Crohn's DIsease	6/7
Ulcerative Colitis	1/7
Peripheral	32/53 (60.3%)
Crohn's DIsease	21/32
Ulcerative Colitis	9/32
Undifferentiated IBD	2/32
Both axial and peripheral	14/53 (26.4%)
Crohn's DIsease	13/14
Ulcerative Colitis	1/14
Radiographic evidence of sacroiliitis in AxSpA	9/21 (42.8%)
HLA B27	
Positive	3/39 (7.69%)
Negative	36/39 (92.3%)

Conclusion: We report a high prevalence of IBD associated SpA in patients presenting for evaluation of arthralgia to a multidisciplinary clinic. Diagnosis and management of SpA in the context of IBD can be challenging and warrants a multidisciplinary approach to timely diagnosis and management. Combined efforts to make treatment changes to induce and maintain disease remission can lead to improvement in morbidity in these patients. This study highlights the characteristics of patients with IBD associated SpA and demonstrates the value of integrated management in clinical practice.
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Acknowledgements: I have no Acknowledgements to declare.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4006

AB0110 FEASIBILITY OF AN IL-17A ASSAY IN PATIENTS WITH ACTIVE AXIAL SPONDYLOARTHRITIS

Keywords: Prognostic factors, Spondyloarthritis, bDMARD

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Background: In Spondyloarthritis (SpA), the method of determination of IL-17 is questionable. Indeed, studies measuring plasma levels of IL-17A without stimulation have shown discordant results.
Objectives: The objective of our study is to show the validity of an IL17 assay method using both innate and acquired immunity stimulation.
Methods: We included volunteer SpAs presenting for consultation between February 2021 and March 2022 in the study. They were axial SpA meeting the ASAS criteria, naïve to any biological treatment, having failed at least two NSAIDs and in need of biological treatment. The control population was issued from a previews cohort of healthy subjects recruited between January 2020 and February 2021. Serum levels of 11 cytokines (IL-17A, IL-6, IL-1β, IFN-γ, IL-12p70, TNF-α, IL-10, IL-5, IL-4, IL-13, and GM-CSF) were measured with and without stimulation by immune ligands (anti-CD3 as a T-cell stimulant, R848 as TLR 7/8 agonist). Clinical evaluation was performed at 3 months after initiation of biological treatment at the discretion of the investigator (anti-TNFα (TNFi) or anti-IL17). The primary outcome was a BASDAI50 response.
Results: A total of 45 patients with SpA (25 males and 20 females; median age, 41 ± 11 years) were included in the study, along with 27 controls (11 males and 16 females; median age 50.5 ± 28 years). Without stimulation levels of the pro-inflammatory cytokines TNF-α, IL-8, IL-6, and IL-1β were significantly increased in the patients with SpA group in comparison to controls and IL-4, IL-5, IL-12p70, and IL-17A levels in all patients with SpA were below the detection threshold (<2,1 pg/mL for IL-17A). After stimulation, Th17 cytokine IL-17A was significantly increased in the patient group with SpA in comparison to controls (IL-17A 317 pg/mL IQR [59–441] versus 59,9 pg/mL IQR [21,2–127], p = 0,0002). On the other hand, the concentration of Th1 cytokines (IFN-γ, IL-12p70 and TNF-α, IL-1β) were lower in the patient group with SpA than in the controls and the cytokines of the Th2 pathway (IL-4, IL-5) were higher in patients with SpA than in controls. Twenty-eight patients were treated with TNFi, and 14 patients with IL-17i. At three months, 55% of the treated patients had a BASDAI decrease of at least 50% (57.1% of the patients treated with TNFi and 64.3% treated with IL17). In SpA, patients, responders had higher baseline IL17A concentration (383 pg/mL IQR [109–887,2] vs. 30 pg/mL IQR [9–133] p = 0.049). A 145 np/mL threshold was defined to distinguish the patients (responders and non-responders). Positive IL-17A activity was determined using receiver operating characteristic analysis, with a sensitivity of 75% and specificity of 88% (Area Under the receiver operating characteristic Curve = 0,88 p = 0,0415). There was no difference in TNF-α levels without or after stimulation between patients who responded to TNFi treatment and those who did not.
Conclusion: Our study shows the feasibility of a cytokine stimulation method that allows the determination of IL-17A in current practice in axial SpA. The potential interest in guiding the practitioner in their therapeutic choice (IL-17i or TNFi) should be confirmed in future studies.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Christian Roux Speakers bureau: Novartis, MSD, Lilly, Abbvie, Galapagos, Pfizer, Elodie Delannoy: None declared, mathilde Cremoni: None declared, marie-charlotte trojani: None declared, lea Evenor: None declared, delphine Graca: None declared, Jeremy Genovese: None declared, Véronique Breuil: None declared, Barbara Seitz-Polski: None declared.
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AB0111 CHARACTERIZING THE PRE-DISEASE STATE OF PSORIATIC ARTHRITIS: CXCL10 LEVELS ARE ASSOCIATED WITH SUBCLINICAL SYNOVITIS IN PATIENTS WITH PSORIASIS

Keywords: Psoriatic arthritis, Ultrasound, Cytokines and chemokines

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Background: The chemokine C-X-C Motif Chemokine Ligand 10 (CXCL10) has been found to be elevated in those patients with psoriasis (PsO) who will develop psoriatic arthritis (PsA), thus being proposed as a predictor of joint involvement [1]. CXC10 progressively declines in these PsO patients until the diagnosis of PsA and further, in parallel with the duration of the disease [2]. In contrast, CXCL10 remains invariable on time in the rest of PsO patients. Subclinical ultrasound synovitis may be considered a pre-disease state of PsA [3]. CXCL10 serum levels in patients with preclinical PsA are still unknown.
Objectives: To better characterize the preclinical phase of PsA and to assess the relationship of CXCL10 levels with subclinical joint involvement in PsO patients.
Methods: 62 patients with PsO without PsA were included, all of them naïve to biological therapy. Ultrasonography (US) was performed on the wrist and metacarpophalangeal 1–5 joints (MCP), proximal interphalangeal 1–5 joints (PIP), and distal interphalangeal 2–5 joints (DIP) bilaterally, and grey scale (GS) synovitis were scored semiquantitatively (0–3) using the OMERACT scoring system. Serum CXCL10 levels were also determined by ELISA in all the patients.
Results: 31 men and 31 women were recruited. GS synovitis ≥1 was present in 30 patients, 10 men and 20 women, while only 7 patients exhibited GS synovitis ≥2, 4 men and 3 women. The mean logCXCL10 was inferior in patients showing any grade of GS, both in the whole group and after stratifying by sex (Table 1), although the difference was only statistically significant for grade 1 of GS in men (p=0.02) and grade 2 of GS in women (p=0.02).
Conclusion: PsO patients with subclinical synovitis show lower serum levels of CXCL-10 than patients without it, as occurs in patients with established PsA. This finding confirms a close relationship between this biomarker and joint involvement in PsO and supports its potential use as a predictor marker in the preclinical phase of PsA.
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Group	Variable	Category	LogCXCL10 Mean ± SD	p	p*
PsO	Presence of GS synovitis ≥1 in hands	**Yes** (n=30)	3.3 ± 1.1	0.07	0.13
		No (n=32)	3.8 ± 1.1		
	Presence of GS synovitis ≥2 in hands	**Yes** (n=7)	2.9 ± 0.9	0.15	0.22
		No (n=55)	3.6 ± 1.1		
Male PsO	Presence of GS synovitis ≥1 in hands	**Yes** (n=10)	2.9 ± 0.9	**0.02**	**0.02**
		No (n=21)	3.9 ± 1.2		
	Presence of GS synovitis ≥2 in hands	**Yes** (n=4)	3.4 ± 0.5	1.00	0.96
		No (n=27)	3.6 ± 1.3		
Female PsO	Presence of GS synovitis ≥1 in hands	**Yes** (n=20)	3.5 ± 1.1	0.76	0.98
		No (n=11)	3.6 ± 1.0		
	Presence of GS synovitis ≥2 in hands	**Yes** (n=3)	2.2 ± 0.8	**0.02**	**0.03**
		No (n=28)	3.7 ± 1.0		

*Adjusted by sex and age at the study in the PsO group and by age at the study in the male and female PsO groups.

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Disclosure of Interests: Verónica Pulito-Cueto: None declared, Susana Armesto: None declared, Sara Remuzgo-Martínez: None declared, Raquel López-Mejías: None declared, María Sebastián Mora-Gil: None declared, J. Gonzalo Ocejo-Vinyals: None declared, Alfonso Corrales: None declared, Vanesa Calvo-Río: None declared, Ana María Salas Martínez: None declared, Marcos González López: None declared, Cristina López-Obregón: None declared, Elena Aurrecoechea: None declared, Luis Rodriguez Rodriguez: None declared, Carolina Aguirre Portilla: None declared, Miguel A González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi, Lilly, Celgene, MSD and GSK, Grant/research support from: Abbvie, MSD, Jansen and Roche, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Consultant of: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD and Roche, Fernanda Genre Romero: None declared, Javier Rueda-Gotor: None declared.
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SLE, Sjön's and APS - aetiology, pathogenesis and animal models

AB0112 IT IS SAFE AND EFFECTIVE TO USE HUMAN CXCL5 TO TREAT MURINE LUPUS

Keywords: Systemic lupus erythematosus, Cytokines and chemokines, Animal models

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Background: As a novel myeloid/neutrophil-targeting therapy for systemic lupus erythematosus (SLE), the therapeutic efficacy of administering mouse (*m*) CXCL5 to lupus-prone mice have been demonstrated by our group recently[1,2].
Objectives: The aim of this study is to examine the pre-clinical safety and establish the pharmacokinetic (PK) response of human (*h*)CXCL5 to ease the commercialization and bring our discovery from bench to bedside.
Methods: Immediate and accumulative liver and kidney toxicity were determined by alanine transaminase and aspartate transaminase activity and urinary albumin-to-creatinine ratio (ACR). *m*CXCL5 expression in major internal organs (e.g., kidneys, lungs, liver, heart, brain and spleen) was determined by immunofluorescent staining on snap-frozen sections. Whether administering *h*CXCL5 promoted cancer cell growth was examined in both *in vitro* and *in vivo* renal cell carcinoma models. Haematological toxicity and circulating immunity, cell counts for white blood cells, red blood cells, monocytes, neutrophils, T cells and B cells, were evaluated in both Institute of Cancer Research (ICR) healthy and MRL/lpr (Fas^{lpr}) lupus-prone mice. PK study of *h*CXCL5 was performed in both ICR healthy and Fas^{lpr} lupus-prone mice intravenously.
Results: Our study showed that it was safe to administer CXCL5. There was no liver or kidney toxicity or cancer inducing effects. There was no further inflammation caused by *h*CXCL5 administration. Major components of the immune system were also not compromised. PK study showed that blood endogenous *m*CXCL5 levels were not altered by exogenous *h*CXCL5 administration in ICR healthy mice, but increased in Fas^{lpr} lupus-prone mice. Blood exogenous *h*CXCL5 was only detectable within 24 hours post-administration and the peak levels were positively correlated with the administration dosage. Mice survival was improved and reversely correlated with administration dosage.
Conclusion: It is safe and effective to use *h*CXCL5 to treat murine lupus.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.577

AB0113 CHRONIC STIMULATION WITH SARS-COV-2 SPIKE PROTEIN DOES NOT TRIGGER AUTOIMMUNITY

Keywords: COVID, Autoantibodies, Animal models

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Background: Systemic autoimmunity is a complex and multifactorial process for which underlying mechanism are unclear. Several theories have been formulated to explain the development of autoimmunity, including excessive self-immunosurveillance, danger, and antigen discontinuity. The antigen discontinuity and the self-criticality theories presume that repetitive antigen exposure leads to a dysregulated immune response. Supporting these theories, Tsumiyama and Shiozawa have shown that repetitive immunization of BALB/c mice with ovalbumin induces auto-antibodies production and a glomerulonephritis with immune deposit resembling lupus nephritis [1]. These data prompted us to consider the potential impact of repetitive SARS-CoV-2 infection in the onset of autoimmune diseases in human. Indeed, since 2020, a large majority of the population has encountered SARS-CoV-2 antigens multiples times, either through vaccination or through infection/reinfection. Hence, we hypothesized that repetitive exposure to the SARS-CoV-2 spike antigen may induce autoimmunity in healthy individuals.
Objectives: Evaluate whether repetitive exposure to SARS-CoV-2 spike protein induces autoimmunity in mice.
Methods: We immunized intraperitoneally C57Bl/6 mice (n = 5/group) with recombinant SARS-CoV-2 spike protein (1µg per injection) or vehicle (phosphate buffered saline [PBS]); **Figure 1A**). The first injection was mixed with Alum as an adjuvant, and the other injections were diluted in PBS, administered intraperitoneally every 5 days, 16 times in total. Five days after the final injection, the mice were sacrificed to retrieve serum. We measured anti-spike and anti-dsDNA IgG using ELISA. The serum from 5 34-week-old C57Bl/6.lpr autoimmune mice were used as positive control. Briefly, 96-well plate were coated overnight with either spike protein (0.2µg/mL) or calf thymus DNA (0.1mg/mL; after precoating with poly-L-lysin 0.05mg/mL). After blocking with PBS-BSA, the diluted serum samples were incubated on the plate for 2 hours at room temperature. Plate-bound IgG were revealed using an alkaline phosphatase-conjugated anti-mouse IgG (1:5000). For anti-dsDNA IgG measurement, the serum of an autoimmune mice was used as a reference standard and the result expressed in unit per mL.
Results: After immunization, the phenotype of control and spike-immunized mice was clinically similar. All the immunized mice were exempt of proteinuria (**Figure 1B**). Only the mice which were injected with spike protein developed measurable amounts of anti-spike IgG as determined by ELISA, while those injected with PBS and the C57Bl/6.*lpr* mice did not (**Figure 1C**). None of the mice in the immunization group developed measurable anti-dsDNA IgG (**Figure 1D**).
Conclusion: In our study, the repetitive exposure of C57Bl/6 mice to the SARS-CoV-2 spike antigen did not lead to autoimmunity. Although these results are reassuring, large scale epidemiological studies are needed to evaluate the incidence of autoimmune diseases in individuals with multiple exposure to SARS-CoV-2 antigens.
REFERENCE:
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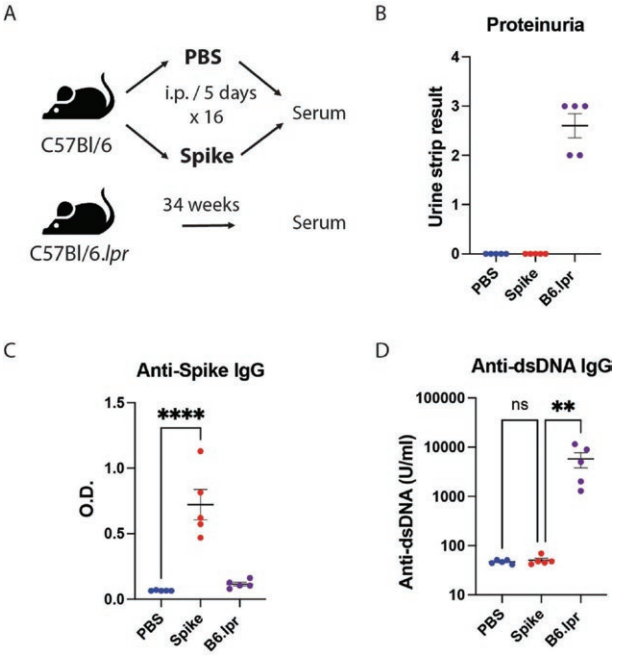


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: Marc SCHERLINGER Speakers bureau: Amgen, Sandoz, Nordic Pharma, Jean Sibilia Speakers bureau: Roche, Chugai, Bristol-Myers Squibb, UCB, GSK, LFB, Actelion, Pfizer, MSD, Novartis, Amgen, Abbvie, Sandoz, Gilead, Lilly, Sanofi Genzyme, Janssen, Mylan, Galapagos, Sobi., Grant/research support from: Pfizer, BMS, Roche, MSD, George Tsokos: None declared, Jacques-Eric Gottenberg Speakers bureau: AbbVie, BMS, CSL Behring, Galapagos, Gilead, Lilly, Roche-Chugai, Pfizer, Sanofi, and UCB., Grant/research support from: BMS.
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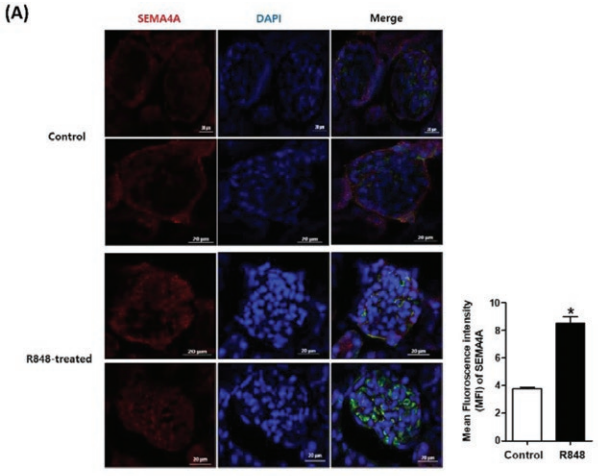
AB0114 INCREASED EXPRESSION OF SEMAPHORIN 4A IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS ASSOCIATION WITH THE ACTIVITY OF LUPUS NEPHRITIS

Keywords: Systemic lupus erythematosus, Biomarkers, Animal models

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Background: Semaphorin (SEMA), initially identified as a neural guidance molecule, has been recently highlighted for its role in regulating the immune response.

Among seven categories of SEMA, Class 4A SEMA (SEMA4A) involves the T cell-mediated immune responses through the expression of itself in dendritic cells.
Objectives: This study aimed to investigate the expression of SEMA4A in systemic lupus erythematosus (SLE) and the association between the expression of SEMA4A and the activity of lupus in the lupus mouse model and patients with SLE.
Methods: The expression of SEMA4A was measured from peripheral blood mononuclear cells (PBMCs) in healthy controls and patients with SLE by polymerase chain reaction. Bone marrow-derived dendritic cells (BMDCs) and renal tissues from control mice and Toll-like receptor (TLR)-7 agonist (R848)-induced lupus mice were investigated for the expression of SEMA4A using western blotting and immunofluorescence assay. Immunohistochemistry was performed to examine the expression of SEMA4A in the kidney of the patients with SLE and they were analyzed according to the activity index of lupus nephritis.
Results: The expression of SEMA4A of PBMCs was elevated in the patients with SLE (n=20, 3.86±0.80) compared to those of healthy control (n=20, 1.0±0.37). SEMA4A is constitutively expressed by dendritic cells, so we analyzed the expression of SEMA4A in BMDCs of TLR-7 agonist (R848)-induced lupus murine group and control group. The SEMA4A was highly expressed in the BMDCs of the lupus group (2.06±1.67) compared to the control group (1.0±0.29). The immunocytochemistry also showed enhanced fluorescence intensity of SEMA4A in BMDCs of the lupus mouse group (19.57±1.37) compared to the control group (10.43±1.87). The kidneys, one of the main target organs of SLE, were analyzed for the protein level of SEMA4A in the murine lupus group and control group. The western blotting of the whole kidney and isolated glomeruli showed a marked expression of SEMA4A in the lupus group compared to the control group. The mean fluorescence intensity of SEMA4A in the kidneys of lupus mice was significantly enhanced compared to the control group (8.51±0.47 Vs. 3.75 ±0.13). In the analysis of immunohistochemistry of SEMA4A in the kidneys of the patients with SLE, the positivity of SEMA4A staining was markedly higher in lupus nephritis with higher activity score (≥10) (80%) compared to those of lupus nephritis with lower activity score (<10) (0%).
Conclusion: The expression of SEMA4A is significantly increased in the dendritic cells and kidneys of the lupus murine group and the patients with SLE compared to the control group. The expression of SEMA4A in the kidneys in the patients with SLE correlates with the severity of lupus nephritis. These results indicate the possible contribution of SEMA4A in the pathogenesis of SLE and the potential of targeting SEMA4A for the treatment of SLE.
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Characteristics		Total	SEMA4A IHC		p
			Positive	Negative	
Lupus nephritis, activity score					
	<10	4	0 (0%)	4 (100%)	
	≥10	5	4 (80%)	1 (20%)	0.016

Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0115 CD14+ MYELOID CELLS EXPRESS THE PDC MARKERS BDCA-2, BDCA-4, CD123 UPON DIFFERENTIATION IN BOTH HEALTHY INDIVIDUALS AND SLE PATIENTS

Keywords: Systemic lupus erythematosus, Innate immunity, Cell biology

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Background: Plasmacytoid dendritic cells (pDCs) are crucial mediators of the immune system linking innate and adaptive immune responses [1]. pDCs exhibit high expression of the IL-3 receptor (CD123) as well as other receptors such as BDCA-2 (CD303) and BDCA-4 (CD304). These molecules are used to identify pDCs in mechanistic studies and for therapeutic targeting. A recent clinical trial showed a reduction in interferon-stimulated gene expression and improvement in skin and joint inflammation in lupus patients who received treatment targeting BDCA-2 [2,3]. However, extensive functional and single-cell transcriptomic data have previously shown that pDCs are immunologically inert, not contributing to the type I IFN production seen in patients with systemic lupus erythematosus (SLE) [4,5].
Objectives: To investigate whether the markers BDCA-2, BDCA-4, CD123 are expressed by myeloid cells other than pDCs.
Methods: Peripheral blood mononuclear cells (PBMCs) were obtained from healthy individuals and patients with SLE. PBMCs were analysed fresh or after 24-hour in vitro culture using flow cytometry for the pDC markers. $CD14^+$ monocytes were purified from freshly isolated PBMCs by negative selection. For M1 differentiation, monocytes were cultured for 6 days in the presence of GM-CSF; IFN-γ and LPS were added on day 6 and the cells were incubated for additional 24 hours. For M2 differentiation, monocytes were cultured for 6 days in the presence of M-CSF; IL-4 and IL-13 were added on day 6 and the cells were incubated for an additional 24 hours. After a 7-day culture, M1 and M2 cells were collected, stained for flow cytometry, and analysed using CytExpert (Beckman Coulter) software.
Results: On freshly analysed PBMCs, the expression of BDCA-2 and BDCA-4 was unique to pDCs in healthy controls. CD123 expression was also seen in a subset of $CD14^+$ monocytes as well as in $CD3^-CD19^-CD14^-CD11c^-HLA\text{-}DR^-$ cells. In some SLE patients, $CD14^+$ cells presented positive expression of BDCA-2, although at a lower level compared to pDCs ($CD3^-CD19^-CD14^-CD11c^-HLA\text{-}DR^+CD123^{high}$). After 24-hour in vitro culture, $CD14^+$ cells from both healthy and SLE patients presented strong expression of BDCA-2, BDCA-4, and CD123. After purification of $CD14^+$ cells and differentiation to either M1 ($CD14^+CD16^+CD206^+CD80^{high}CD163^{low}$) or M2 ($CD14^+CD16^+CD206^+CD80^{low}CD163^{high}$) phenotype, positive expression of these markers was seen. M1 macrophages showed high expression of BDCA-2 and BDCA-4 and almost universal expression of CD123. In contrast, M2 macrophages showed a meagre expression of BDCA-2 but universal expression of BDCA-4 and CD123.
Conclusion: We show that the BDCA-2, BDCA-4, CD123 markers -previously thought to be expressed exclusively by pDCs- are also expressed by differentiated $CD14^+$ myeloid cells in both healthy controls and patients with SLE. These findings can limit the significance of those markers to identify pDCs in tissue samples by simple immunohistochemistry. Finally, as monocytes have been shown to be the primary contributor to the interferon signature in blood, these data may explain how therapeutic targeting of BDCA-2 and related markers can impact disease activity and interferon activity in SLE patients.
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Acknowledgements: NIL.
Disclosure of Interests: Antonios Psarras: None declared, Zoe Wigston: None declared, Edward Vital Speakers bureau: AstraZeneca, Novartis, Paid instructor for: AstraZeneca, Novartis, Consultant of: UCB, Pfiser, Aurinia, Lilly, Roche, Genentech, Otsuka, GSK, Capella.
DOI: 10.1136/annrheumdis-2023-eular.2330

AB0116 EVALUATING THE IMPACT OF METFORMIN TARGETS ON THE RISK OF SYSTEMIC LUPUS ERYTHEMATOSUS: A MENDELIAN RANDOMIZATION STUDY

Keywords: Systemic lupus erythematosus, Genetics/Epigenetics

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Background: Metformin is a biguanide oral hypoglycemic agent that is widely used as a first-line drug treatment for type II diabetes. In addition, metformin is also used in the treatment of certain autoimmune diseases, such as systemic lupus erythematosus (SLE). It plays a key role in the pathogenesis of SLE through pathways such as inhibiting type 1 IFN, regulating T effector cells and proinflammatory cytokines[1]. However, the causal relationship of the metformin-related targets on the risk of SLE is still unclear.
Objectives: The purpose of this study was to assess the causal effect of metformin targets (AMPK, MCI, MG3, GDF 15 and GLP 1/ GCG) on the risk of SLE using Mendelian randomization (MR).
Methods: Genetic variants including downstream and 100 kb upstream of encoding five genes were selected as candidate tool variants. The SNP was further screened as in low linkage disequilibrium ($r2 < 0.3$) and associated with HbA 1 c ($P \leq 0.05$). The Genome-wide association study (GWAS) of HbA 1 c comes from the Meta-Analyses of Glucose and Insulin-related traits Consortium (MAGIC) (n = 88,355)[2]. The SLE data (ncase = 5,201, ncontrol = 9,066) are pooled from publicly available GWAS. Two-sample MR was performed using inverse variance weighted (IVW), MR-Egger, and weighted median (WM) to obtain causal estimates of metformin-related targets and risk of SLE. In addition, sensitivity analysis, outlier (MR-PRESSO) and leave-one-out analysis were conducted to test the heterogeneity and level pleiotropy of the results.
Results: Genetically predicted increase in HbA1c instrumented by GDF 15 variants was associated with increased risk of SLE (GDF 15[p = 0.028]). However, genetically predicted AMPK, MG3, MCI, and GLP 1/ GCG were not associated with SLE risk (AMPK [p = 0.122], MG3 [p = 0.105], MCI [p = 0.762], GLP 1/ GCG [p = 0.361]) (Figure 1). No outlier between GDF 15 and the risk of SLE was identified via the MR-PRESSO test. The leave-one-out analysis verified the robustness of the outcomes.
Conclusion: This study suggests that the GDF 15 gene may be a plausible mechanism of action to reduce the risk of SLE and provides critical evidence to guide future clinical trials of metformin.

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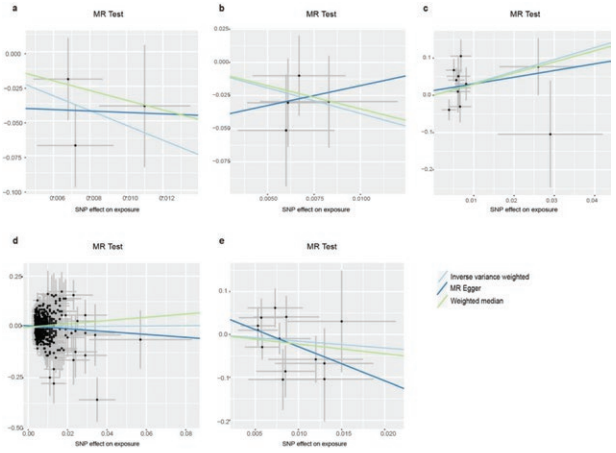


Fig 1. Scatter diagram. Each point on the graph represents an IV, the line on each point reflects the 95% confidence interval, the abscissa is the effect of SNP on exposure ([a] GDF 15, [b] AMPK, [c] MG3, [d] MCI, [e] GLP 1/GCG), and the ordinate is the effect of SNP on the outcome (SLE), the colored lines represent the MR fit result.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2355

AB0117 **ASSOCIATION OF AUTOANTIBODIES WITH THE IFN SIGNATURE AND NETOSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

Keywords: Autoantibodies, Systemic lupus erythematosus, Innate immunity

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by a variety of disease symptoms and an unpredictable clinical course. SLE can lead to premature death as the result of disease activity or because of treatment side effects. This underlines the urgency to identify patients at risk for a complicated disease course, and the need to tailor therapy. Stratification based on immunological manifestations such as autoantibodies, upregulation of type I interferon (IFN) regulated genes (IFN signature) and neutrophil extracellular trap (NET) formation via NETosis can help to improve treatment outcome in SLE.
Objectives: Here we study the association between SLE-related autoantibodies, the IFN signature and NET formation in patients with SLE, which could lead to improved tools for patient stratification and more targeted treatment options.
Methods: We studied the association between the IFN signature and plasma induced NET formation with 57 autoantibodies in 25 patients with SLE. The presence of an IFN signature was determined using the sum of standardized mRNA expression of IFI44L, IFITM1, SERPING1, and LY6E in monocytes from SLE patients. Plasma induced NET formation was studied with quantitative live imaging. The threshold for the presence of an IFN signature or NET formation were both set at 2 SD above the mean of a group of healthy controls. With principal component analysis (PCA) and hierarchical clustering we associated autoantibody concentrations with the IFN signature and NET formation. This study was a separate analysis from larger cohorts, of which results have been previously published.[1,2]
Results: We observed two distinct clusters with the PCA: one cluster contained mostly patients with an IFN signature, and another cluster contained a mix of patients with (IFN) and without (noIFN) an IFN signature. Patients with (NET) and without (noNET) plasma induced NET formation were equally distributed between the clusters. PC1 explains 22.7% of total variability, and is mainly driven by antibodies against histones, RibP2, RibP0, EphB2, RibP1, PCNA, dsDNA, and nucleosome. Hierarchical cluster analysis confirmed the two clusters (Figure 1). In addition, we found a trend towards increased concentrations of autoantibodies against EphB2, RibP1, and RNP70 in patients with an IFN signature. We found a negative correlation of NET formation with anti-FcER and anti-PmScl100.
Conclusion: We identified a subgroup of patients with an IFN signature who express increased concentrations of antibodies against DNA and RNA-associated proteins. We did not find positive associations between autoantibodies and plasma induced NET formation. Our study further strengthens the evidence of a correlation between RNA-binding autoantibodies and the IFN signature. As the IFN signature currently is not part of the standard follow-up for patients, partially due to its associated costs, a profile of DNA and RNA-binding autoantibodies might be used for patient stratification, especially related to anti-IFN treatment.

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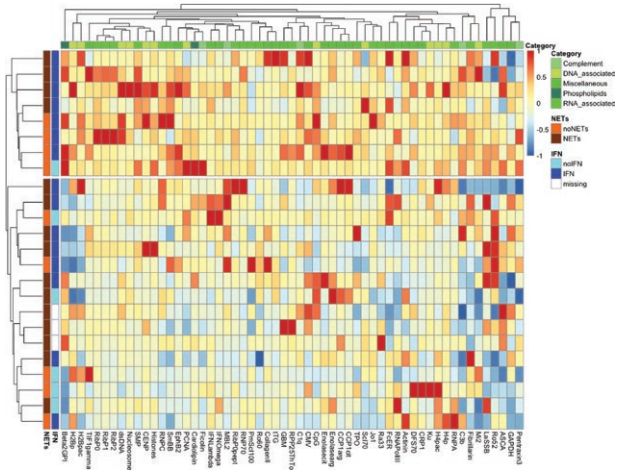


Figure 1. A distinct autoantibody pattern is present in a subgroup of patients with an IFN signature. Footnote: Heatmap of Z-scores for 57 autoantibodies in 25 SLE patients. Vertical axis shows clustering of patients based on IFN signature (blue) or NET formation (orange/brown). Horizontal axis represents clustering based on autoantibody profiles.

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Disclosure of Interests: None Declared.
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AB0118

DIAGNOSTIC PREDICTIVE VALUE OF SOLUBLE PSGL-1 AND THEIR LIGANDS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Keywords: Biomarkers, Autoantibodies, Systemic lupus erythematosus

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Background: Rheumatic diseases are generally diagnosed in advanced stages. Systemic lupus erythematosus (SLE) are systemic inflammatory autoimmune disease characterized by presence of autoantibodies against DNA and nuclear proteins and a wide variety of clinical symptoms **(Fava 2019, Wang 2019)**. Actually, it has not curative treatment **(Mathias 2020)**. Therefore, the search for biomarkers for SLE diagnosis in earlier stages and its derived complications is mandatory **(Thanou 2021, Wan 2018)**. Adhesion molecules are crucial to leukocytes infiltration to inflammation sites **(Ponthieux 2004, Ivetic 2019, Tinoco 2017)**, thus they play an important role in autoimmune diseases and have been suggested as a useful markers of diagnosis and prognosis in rheumatic disease **(Gonzalez-Tajuelo 2017, Skeoch 2014, da Rosa Franchi 2018)**.
Objectives: To study the possible involvement of adhesion molecules in the development of disease, we have analysed the pattern of PSGL-1 serum levels together with its main ligands P- E- and L-selectins and ADAM8 in SLE patients.
Methods: Serum samples from 52 SLE patients, 36 inactive (iSLE) and 16 active (aSLE) and 55 healthy donors (HD) sex and age matched per group were collected and proteins levels were measured by available ELISA kits: Human PSGL-1/CD162 kit (Novus Biologicals, Colorado, USA), Human Selectins/CD62 kits CD62E, CD62L and CD62P (Diaclone, France), and Human ADAM8 (A Disintegrin And Metalloprotease 8) Kit (Elabscience, Texas, USA).
Results: SLE patients showed a statistically significant increase of PSGL-1, E-Selectin and ADAM8 and decrease of L-Selectin serum levels with respect to HD. No difference were observed between inactive and active SLE patients. Patients with anti-dsDNA and/or anti-SSA autoantibodies showed lower serum level of PSGL-1 and higher level of L-Selectin and ADAM8 compared to patients with absence of these autoantibodies. Importantly, the expression profile study of these proteins revealed that L-Selectin/ADAM8 ratio in SLE patients is a good predicted marker in a multivariable binary logistic regression model (OR=1,701, CI:1,188-2,450, p<0.005). Receiver operating characteristic (ROC) curve presented an area under curve (AUC) of 0.80 and the optimal cut off value maximizing sensitivity (98%) and specificity (48%) jointly corresponded to ratio<2,06. In this model the 97% of patients were correctly grouped.
Conclusion: SLE patients show significantly different serum levels of PSGL-1, E-Selectin, L-Selectin and ADAM8 with respect to healthy controls. This specific profile of serum protein levels could be a potentially valuable tool for the early diagnosis of SLE.
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AB0119

EVALUATION OF P-GP AND MRP-1 EXPRESSION ON PLASMA CELLS AND TH17 LYMPHOCYTES IN PERIPHERAL BLOOD AND BONE MARROW OF LUPUS NEPHRITIS

Keywords: Adaptive immunity, Systemic lupus erythematosus, Kidneys

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Background: P-glycoprotein (p-gp) and multidrug resistance protein 1 (MRP-1) contribute towards resistance to glucocorticoids and/or immunosuppressive drugs in lupus nephritis (LN). Long-lived plasma cells (PCs) persistently produce antibodies and are resistant to most immunosuppressive therapies including B-cell depletion. Elevated T helper 17 lymphocytes (Th17) are associated with resistant LN phenotypes. We hypothesize the overexpression of p-gp and MRP-1 on these two cell types which might eventually contribute towards drug-resistant phenotype in LN.
OBJECTIVES:
1.To evaluate the frequency of peripheral blood PCs and Th17 cells expressing p-gp and MRP-1 in LN compared with healthy controls (HCs).
2.To evaluate the frequency of PCs expressing p-gp in bone marrow of LN.
Methods: Patients with LN fulfilling the 2019 ACR/EULAR classification criteria and HCs were recruited after written informed consent. p-gp and MRP-1 expression on peripheral PCs (CD45+ CD138+), p-gp expression on Th17 (CD4+ IL-17+ p-gp), Th1 (CD4+IFN-γ), Th2 (CD4+ IL-4) and regulatory T lymphocytes (Tregs, CD4+ CD25+ FoxP3+) were determined using flowcytometry (BD FACS Canto II). Proportions of T lymphocytes were normalized to Tregs. Frequencies of P-gp+ PCs were enumerated in bone marrow aspirate of two patients and one control. Results were expressed as median (interquartile range, IQR). Intergroup comparisons were performed with Mann-Whitney U test. p-value were corrected for multiple testing using Bonferroni-Sidak method. Statistical significance was set at p<0.05.
Results: Twenty-one LN [17 females, median (interquartile range – IQR) age 26 (23.25-35) years] and 10 controls [7 females, median (IQR) age 28 (27–31) years] were recruited. Of 21 LN, 13 had active disease (66% had low complements, 59% had elevated anti-dsDNA). Median SLEDAI-2K score of LN patients was 12 (2-21). In peripheral blood, overall PCs as well as PCs expressing P-gp or MRP-1 were increased in LN than in HC. Th17/Tregs ratio, p-gp-expressing Th17 lymphocytes and MRP-1-expressing Th17 lymphocytes were significantly increased in LN compared to HC (Table 1). p-gp expressing Th17 lymphocytes and PCs were significantly increased in active LN than in inactive LN (Table 1). As an exploratory analysis, p-gp-expressing PCs were more prevalent in bone marrow aspirate of LN than non-lupus controls (Figure 1).
Conclusion: We observed for the first time an increased frequency of P-gp and MRP-1-expressing PCs and Th17 lymphocytes in the peripheral blood of LN, which were also associated with disease activity. Whether these cell populations contribute to refractory LN requires evaluation.

Table 1. Peripheral blood cell populations in LN and HC

Cell Population	Lupus Nephritis [median(Q1-Q3)]		Healthy Control [median(Q1-Q3)] (n=10)	p- value*	
	Active (n=13)	Inactive (n=8)		LN vs HC	Active vs Inactive
Th1	35.9(35.1-38.7)%	35.13 (33.73-39.55) %	10.5(9.16-13.08) %	**0.001**	0.998
Th1/Treg	10.64(7.98-12.16)	10.51(9.71-12.21)	4.24(3.83-4.92)	**0.001**	0.998
Th2	46.3(41.02-50.1) %	44.85(39.93-48.79) %	10.45(8.37-13.3) %	**0.001**	0.997
Th2/Treg	13.78(11.72-15.18)	12.58 (11.27-15.16)	4.30(4.07-5.28)	**0.001**	0.997
Th17	2.9(2.2-3.5)%	1.79(1.59-2.28) %	0.27(0.2-0.44) %	**0.001**	0.876
Th17/Treg	0.73(0.64-0.98)	0.53 (0.40-0.82)	0.11(0.05-0.23)	**0.001**	0.641
Th17+P-gp+	2.6(1.97-3.34) %	1.32(0.89-1.73) %	0.07(0.06-0.1) %	**0.001**	**0.016**
Th17+ P-gp+/ Treg	0.78(0.55-1.06)	0.37 (0.33- 0.49)	0.03(0.018-0.04)	**0.001**	**0.053**
Th17+ MRP1+	2.06(1.7-2.5) %	1.56 (1.10-2.00) %	0.15(0.09-0.23) %	**0.001**	0.815
Th17+ MRP1+/ Treg	0.66(0.47-0.82)	0.42 (0.31-0.70)	0.05(0.03-0.11)	**0.001**	0.806
Treg	3.3(2.7-3.5) %	3.45(3.00-3.9) %	2.55(1.95-3.18) %	**0.040**	0.998
PCs	3.2(2.59-4.8) %	2.36(2.25-3.22) %	0.53(0.35-0.98) %	**0.001**	0.791
p-gp+PCs	3.23(2.88-3.9) %	1.61(1.21-2.21) %	0.11(0.09-0.21) %	**0.001**	**0.010**
MRP1+PCs	4.2(3.01-7.1) %	3.40(2.69-5.93) %	0.885(0.63-1) %	**0.001**	0.998

*corrected for multiple testing

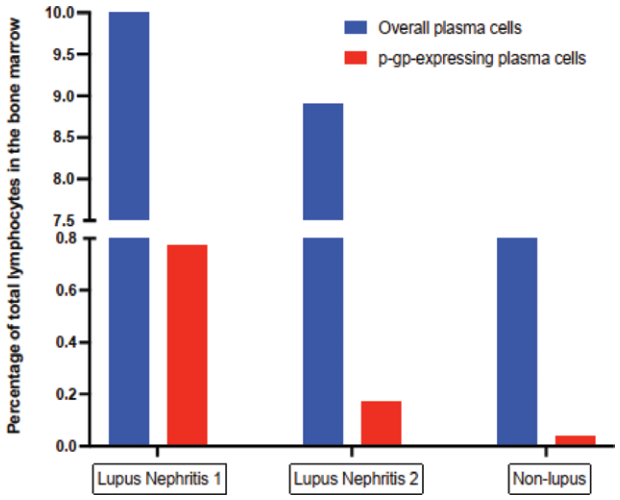


Figure 1. Plasma cells and p-gp expressing plasma cells in bone marrow of lupus nephritis and control subjects.

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AB0120

DIFFERENT PATTERNS OF LONGITUDINAL CHANGES IN ANTINUCLEAR ANTIBODIES TITRES IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Autoantibodies

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the presence of antinuclear antibodies (ANA). Monitoring of anti-DNA antibody levels may reflect disease activity, by contrast a single anti-RBP antibody determination is thought to suffice for clinical purposes. Recent data suggests that ANA levels may decrease over time secondary to the natural history or to treatments.
Objectives: To investigate the trend of ANA and anti-dsDNA titers over time in children with a diagnosis of SLE.
Methods: We enrolled 15 children with SLE. ANA and anti-dsDNA testing were carried out in all patients from diagnosis every 3-4 months for 2 years. ANA were defined as negative for titers < 1:80. Laboratory parameters, clinical and demographic data was retrieved and analyzed. Interferon Gene Signature (IGS was assessed by the expression of 6 interferon-induced genes (IFI27, IFI44L, IFIT1, ISG15, RSAD2, SIGLEC1) in whole blood RNA. Statistical analysis was performed with SW R_v. 4.0.3.
Results: Following 2 years of follow-up, all patients had ANA titers significantly lower than at time of the onset (MWW, p=0.0002) (Figure 1A). After two years of follow-up, 11 patients (73%) remained ANA positive (group 1), while 4 patients (26%) became negative (group 0). At time of diagnosis no significant differences in ANA titers (MWW, p=0.74) nor in disease activity, measured by SLEDAI, (MWW, p=0.88) were observed (table 1; Figure 1E). No significant differences in organ involvement were observed (Table 1). Assessing the change over time in ANA titers, the 2 groups of patients showed 2 different patterns: in group 0, ANA titers quickly declined and disappeared in the first 6 months after diagnosis; in group 1, ANA titers declined more slowly, remaining positive at 2 years (Figure 1C). ANA pattern (by IFA) was also evaluated, changes from homogenous pattern to speckled was observed during follow up (Figure 1B). Both C3 and C4 increased, with no different patterns between the 2 groups (Figure 1D). Similarly, anti-dsDNA antibodies titers declined over time with no clear different patterns between the groups (Figure 1C). We also analyzed the levels of IGS at last of follow-up, observing significant differences between the groups (MWW, p=0.018) with higher levels of IGS in ANA+ patients (Figure 1F).
Conclusion: Our analysis showed 2 different patterns in the reduction of ANA titers over time in children with SLE, with 26% of them becoming ANA negative after 6 months from diagnosis and remaining persistently negative during follow-up. Our data have important implications, specifically for the recruitment of patients into clinical trials, where the latest classification criteria of SLE require ANA positivity as entry criterion. A seronegative state may represent a different subcategory of patients with SLE with specific pathogenetic pathways, possibly independently from autoantibodies. Therefore, further studies are needed to confirm our data.

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Table 1.

	ANA- at 2y	ANA+ at 2y
Patients, n	4	11
Female, n (%)	3 (25)	10 (9)
Age, mean ± SD (years)	13.80 ± 1.91	13.45 ± 2.72
Disease duration, mean ± SD (years)	6.47 ± 4.22	6.17 ± 2.71
EULAR/ACR 2019 criteria		
Fever, n (%)	3 (75)	8 (73)
Acute cutaneous, n (%)	4 (100)	6 (55)
Chronic cutaneous, n (%)	0 (0)	0 (0)
Non-scarring alopecia, n (%)	0 (0)	1 (9)
Oral/nasal ulcers, n (%)	2 (50)	7 (64)
Joint involvement, n, (%)	3 (75)	4 (36)
Serositis, n (%)	0 (0)	2 (18)
Renal, n (%)	1 (25)	2 (18)
Neurological, n (%)	0 (0)	0 (0)
Hemolytic anemia, n (%)	1 (25)	4 (36)
Leukopenia, n (%)	4 (100)	9 (82)
Thrombocytopenia, n (%)	3 (75)	5 (45)
Anti-dsDNA, n (%)	4 (100)	11 (100)
Anti-Sm, n (%)	1 (25)	2 (18)
LA, n (%)	0 (0)	1 (9.1)
aCL, n (%)	2 (50)	2 (18)
aB2GPI, n (%)	2(50)	2 (18)
Low complement, n (%)	4 (100)	11 (100)
C3, mean ± SD (mg/dl)	40.25 ± 5.51	52.73 ± 20.81
C4, mean ± SD (mg/dl)	3.67 ± 2.89	4.60 ± 2.72
SLEDAI at diagnosis, mean ± SD	12.75 ± 4.50	12.18 ± 7.14
SLEDAI at last follow-up, mean ± SD	0.00 ± 0.00	1.36 ± 1.43
Damage (SDI at last follow-up >0), n (%)	0 (100)	0 (100)
Treatment		
PDN, n (%)	3 (75)	11 (100)
HCQ, n (%)	4 (100)	11 (100)
MMF, n (%)	4 (100)	11 (100)
RTX, n (%)	0 (0)	2 (18)

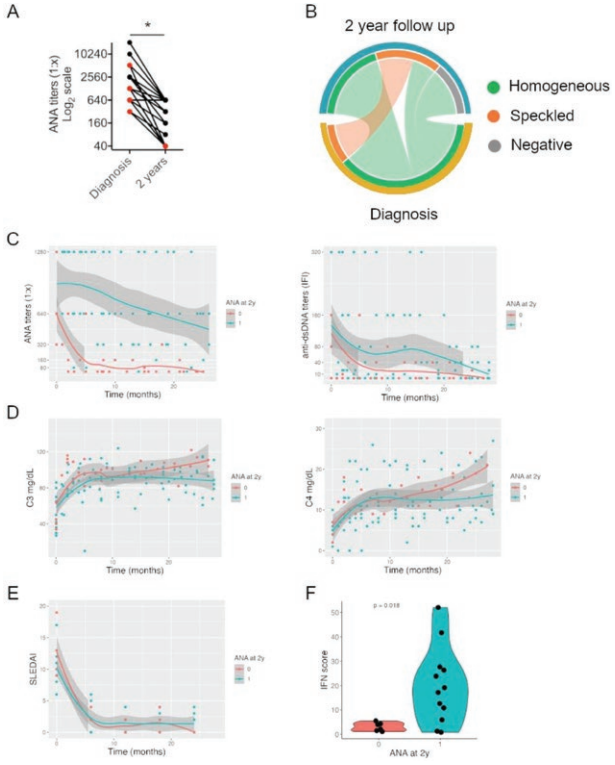


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0121

MULTI-OMICS ANALYSIS REVEALS COX5A AS A BIOMARKER OF DISEASE ACTIVITY AND ORGAN DAMAGE OF LUPUS

Keywords: Systemic lupus erythematosus, Biomarkers

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Background: Systemic Lupus Erythematosus (SLE) is a heterogeneous systemic autoimmune disease with protean clinical manifestations[1]. Although the long-term outcome of patients with SLE has been greatly improved, increased organ damage is associated with poor prognosis in a number of patients. The type I interferon signature, a hallmark of SLE, is not an ideal treatment target or outcome predictor[2, 3], suggesting other critical immunological pathways might contribute to disease pathogenesis.
Objectives: To explore key immunological pathways and gene markers in SLE more precisely, we performed a systematic analysis of transcriptional data from 27 immune cells in the blood and from single cells in the skin and kidney.
Methods: We included a large RNA-seq data from a total of 64 SLE and 62 control with 27 immune cells. Integrated analyses were conducted to find key pathways and driver genes in SLE pathogenesis. The expression of COX5A between SLE phenotypes was compared in two independent cohorts. Single-cell RNA sequencing(scRNA-seq) data from skin and kidney were used to further determine the association of COX5A expression with organ damage.
Results: We found that lymphocytes in SLE showed an overall active immuno-metabolic state when compared to healthy controls, and oxidative phosphorylation (OXPHOS) is the most significant metabolic pathway that differs between SLE and HC, especially for effector T cells. Besides, the OXPHOS enrichment score was significantly correlated with IFN response molecular signature across various T cell subtypes. Particularly, we identified an OXPHOS hub gene, COX5A, as a key driver in SLE T cells. COX5A expression was significantly higher in effector T cells than those in naïve T cells and showed associations with SLE clinical phenotypes including disease activity index, flare, and organ damage. Furthermore, we revealed that high expression of COX5A in T cells contributes to skin and kidney involvement of SLE through scRNA-seq analysis.
Conclusion: Our results identified OXPHOS signature is a prominent feature in SLE T cells. The key gene of OXPHOS, COX5A, showed associations with IFN response molecular signature, severity, skin, and kidney involvement of SLE, which supported that COX5A as a potential candidate biomarker of severity and organ damage of SLE.
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AB0122

ANTI-HISTONE AND ANTI-NUCLEOSOME ANTIBODIES, RATHER THAN ANTI-DSDNA ANTIBODIES ARE ASSOCIATED WITH INTERFERON-INDUCED BIOMARKERS IN SUDANESE AND SWEDISH SLE PATIENTS

Keywords: Cytokines and chemokines, Autoantibodies, Systemic lupus erythematosus

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Background: Antibodies against double stranded DNA (anti-dsDNA) can induce production of interferon-alpha and other cytokines after forming immune complexes. In SLE, anti-dsDNA often exists together with autoantibodies against other chromatin components, like histones and nucleosomes. These antibodies are known to characterize a SLE subgroup with early disease onset and increased occurrence of nephritis.
Objectives: We investigated how anti-nuclear autoantibody (ANA) specificities associate with pro-inflammatory cytokines in two ethnically different cohorts of SLE patients, from Sudan and Sweden.
Methods: We included 93 Sudanese and 480 Swedish SLE patients. Serum levels of autoantibodies against dsDNA, Sm, the Sm/U1RNP complex, U1RNP, SSA/Ro52, SSA/Ro60, SSB/La, ribosomal P, PCNA and histones were quantified with a bead-based multiplex immunoassay; with positive reactions determined as above the 98th percentile among respective national controls. In the Swedish cohort another bead-based multiplexed immunoassay including anti-nucleosome antibodies was also used. Relative levels of 73 plasma biomarkers were determined with Proximity Extension Assay technique except for Interferon gamma-induced protein (IP-10) in the Swedish cohort that was quantified by ELISA. Adjusted p values were considered significant when <0.05.
Results: Among Sudanese patients, levels of 5/73 biomarkers showed significant associations to ANA-associated antibodies. Anti-histone antibodies showed the strongest positive correlations with interferon-inducible factors (monocyte chemoattractant protein [MCP-1] and IP-10), monocyte chemoattractant protein-3 (MCP-3) and S100 calcium-binding protein A12 (S100A12), and negative correlation with stem cell factor (SCF); R^2(P values) were 0.15(0.04), 0.18(0.008), 25(0.0001), 0.13(0.04) and 0.31(<0.0001) respectively. Biomarker associations remained significant for anti-histone antibody after adjustment for age and sex. Also, anti-dsDNA antibodies associated with MCP-3 (0.13(0.04)), IP-10 (0.13(0.03)) and S100A12 (0.13(0.04)), but when combining with anti-histone in the same regression model, anti-dsDNA associations were lost while anti-histone antibodies remained. Positive associations with lower R^2 values were found also for anti-ribosomal P antibodies with MCP-1, MCP-2 and C-C motif ligand 19 (CCL-19), and for anti-Sm with IP-10. Validation analysis among Swedish patients for MCP-1, IP-10, SA100A12 also demonstrated significantly stronger associations to anti-histone and anti-nucleosome antibodies compared to anti-dsDNA and other ANA specificities, and in combined regression models, anti-dsDNA either became non-significant or considerably less significant than anti-histone/nucleosome antibodies. When excluding anti-histone or anti-nucleosome positive patients, the associations between interferon-inducible factors MCP-1/IP-10 and anti-dsDNA were lost. In contrary, when excluding anti-dsDNA positive patients, associations with anti-histone and anti-nucleosome remained significant. SA100A12 associations with anti-dsDNA antibodies remained significant after exclusion of anti-histone positive patients, but were lost when excluding anti-nucleosome positive patients.
Conclusion: Using uni- and multi-variate analyses as well as patient stratification, levels of mainly IFN-induced inflammatory biomarkers correlate strongest with anti-histone and anti-nucleosome antibodies compared to other ANA specificities including anti-dsDNA. Our results, from two lupus cohorts with different ethnicities, suggest that autoantibodies against DNA-complexes or DNA-associated proteins rather than anti-dsDNA antibodies per se may drive the induction of the interferon signature in SLE.
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AB0123

ENTEROCOCCUS GALLINARUM IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

Keywords: Descriptive studies, Outcome measures, Systemic lupus erythematosus

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Background: Systemic Lupus Erythematosus (SLE) is associated with epithelial defects and disrupted intestinal barrier, risking bacterial translocation and promoting systemic inflammation, known as dysbiosis, which is associated with increased disease activity [1]. *Enterococcus gallinarum* has been previously linked to gastrointestinal autoimmune diseases, like autoimmune hepatitis and primary sclerosing cholangitis. [2] However, little is known about *E. gallinarum* prevalence in SLE.
Objectives: To describe the prevalence of *E. gallinarum* in SLE stool samples, as well as clinical and laboratory characteristics.
Methods: A cross-sectional, descriptive study was conducted at the University Hospital ¨Dr. José Eleuterio González¨, in northern Mexico. We included adult patients who met current criteria for SLE and had recent (<3 months) paraclinical routine tests, including acute phase reactants. Patients with other autoimmune

diseases, chronic infections, pregnancy, cancer, abdominal surgery or gastrointestinal bleeding were excluded. Demographic, clinical data, as well as Anti-nuclear antibodies and complement were obtained from records. No participant received antibiotics, probiotics or synbiotics 3 months prior to the study. DNA was extracted with the DNeasy PowerLyzer PowerSoil DNeasy kit, Qiagen (Hilden, Germany) according to the manufacturer's specifications. *E. gallinarum* was detected by endpoint polymerase chain reaction essay.

Results: Sixty patients were included, where most subjects were women (51, 85%). Mean age was 41.79 (± 16.6) and time of diagnosis 107.03 months (± 95.46). *E. gallinarum* and *Enterococcus spp* were found in 7 (11.6%) cases. The most frequent MEX-SLEDAI parameter was arthritis in 34 (56.6%) cases, followed by acute cutaneous lupus in 23 (38.3%). Clinical manifestations and paraclinical findings are shown in Table 1. We found a significant difference in *E. gallinarum* positive patients in creatinine levels (0.98 vs 0.72, *p* 0.032), ESR (11.14 vs 19.49, *p* 0.031) and frequency of serositis (57.14% vs 7.54%, *p* 0.001). When analyzing ESR by age-adjusted upper limit, significance was lost (*p* 0.4)

Conclusion: Prevalence of *E. gallinarum* in SLE stool samples was 11.7%. Serositis, higher mean creatinine and lower mean ESR was more common in *E. gallinarum* positive subjects. Further research is needed to better understand *E. gallinarum* dysbiosis in SLE.

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Table 1. Sociodemographics, clinical and paraclinical features.

	E. gallinarum Positive n= 7	E. gallinarum Negative n= 53	p
Sociodemographic, mean ± SD			
Age, years	37.14 ± 20.6	42.3 ± 13.8	0.10
Months since diagnosis	75.85 ± 59.3	112.72 ± 99.5	0.23
Weight, kg	58.88 ± 9.16	68.19 ± 15.98	0.06
Size, m	1.61 ± 0.08	1.59 ± 0.06	0.20
BMI, Kg/m2	23.02 ± 4.02	26.65 ± 5.89	0.22
Clinical features, n (%)			
Oral ulcers	0 (0.0)	5 (9.43)	0.42
Alopecia	2 (28.57)	11 (20.75)	0.51
Arthritis	3 (42.85)	31 (58.49)	0.61
Serositis	4 (57.14)	4 (7.54)	**0.001**
Nephritis	1 (14.28)	8 (15.09)	0.95
CNS	0 (0.0)	2 (3.77)	0.62
Hemolytic anemia	0 (0.0)	6 (11.32)	0.37
CKD	0 (0.0)	1 (1.88)	0.72
Chronic liver disease	0 (0.0)	2 (3.77)	0.62
MEX-SLEDAI, mean ± SD	1.71 ± 2.92	1.83 ± 2.12	0.89
Laboratories, mean ± SD			
Hemoglobin	13.87 ± 1.46	13.29 ± 1.04	0.19
Leukocytes	6.46 ± 1.73	6.23 ± 2.49	0.81
Lynphocytes	5.98 ± 10.16	5.69 ± 11.24	0.94
Platelets	217.71 ± 31.7	250.47 ± 79.1	0.28
BUN	16.38 ± 8.8	13.15 ± 5.4	0.23
Creatinine	0.98 ± 0.29	0.72 ± 0.29	**0.03**
Albumin	4.24 ± 0.47	4.16 ± 0.34	0.62
TGO	21.42 ± 6.5	25.21 ± 10.8	0.37
TGP	23.71 ± 22.2	23.14 ± 15.4	0.93
CRP	0.78 ± 1.35	2.81 ± 7.56	0.55
ESR	11.14 ± 7.6	19.49 ± 13.18	**0.03**
ANAS	2248 ± 2653	730 ± 1499	0.27
Anti-Sm	13.93 ± 24.13	29.11 ± 122.47	0.83
C3	42.62 ± 36.19	54 ± 52.85	0.48
C4	9.12 ± 9.32	10.4 ± 10.95	0.77

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Disclosure of Interests: None Declared.

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AB0124

DIMETHYL FUMARATE MODULATES T CELL METABOLISM AND FUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENT SAMPLES

Keywords: Systemic lupus erythematosus

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Background: Activated T cells make a significant contribution to inflammation in systemic lupus erythematosus (SLE). Their ability to secrete proinflammatory cytokines and express activating NK receptors allows them to mediate inflammation. We know that cellular metabolism regulates the activation of T cells. A phase II study has reported on efficacy of DMF in cutaneous lupus [1]. Evidence from patients with multiple sclerosis indicates that dimethyl fumarate (DMF), an electrophile, targets cellular metabolism to modulate T cell activation and function [2]. However, the potential of DMF to modulate T cell metabolism and activation in SLE is not known.

Objectives: We investigated whether DMF modulates T cell metabolism, activation and function in samples from patients with SLE in a series of in vitro experiments.

Methods: All experiments were performed using isolated T cells from freshly drawn whole blood samples from patients with SLE. T cells were isolated using negative selection using Stem cell or Miltenyei magnetic bead separation kit. Isolated T cells were activated with anti-CD3 and IL-2 and incubated with either DMF at 25μM concentration or DMSO alone for three or seven days at 37°C and 5% CO2 before harvesting and analysing on BD FACS flow cytometer. Analysis of cytokines in supernatants was performed using cytometric bead arrays. Flow jo software was used to analyse flow cytometry files. Graph Pad Prism software was used to perform statistical analysis.

Results: In Seahorse experiments, after three days of incubation dimethyl fumarate (DMF) inhibited the oxygen consumption rate (OCR) and extra cellular acidification rate (ECAR) in isolated T cells when compared with samples incubated with vehicle, dimethyl sulfoxide (DMSO). Our results revealed that DMF significantly inhibited: 1) aerobic glycolysis and oxidative phosphorylation in activated CD4+T cells from patients with SLE (n=4), in vitro; 2) T cell activation and proliferation as assessed by a reduction in the frequency of CD69 (n=4) and Ki67 (n=2) positivity, respectively. Collectively, these results suggest that DMF inhibits T cell activation and proliferation in samples from patients with SLE. After 7 days of incubation, DMF significantly inhibited the expression of activating NK receptors CD158a and NKG2D on CD4+T cells whereas DMF seemed to have a trend toward enhancing the expression of inhibitory NK receptors NKG2A and CD158b (n=6). After 7 days of incubation, DMF significantly reduced CD4+T cell intracellular expression of IFN-γ, TNF-α, IL-17 and secretion of pro-inflammatory cytokines IFN-γ and TNF-α in supernatants (n=6).

Conclusion: Our data indicated that DMF modulates metabolic programming, both glycolysis and oxidative phosphorylation, to inhibit activation, proliferation, and secretion of proinflammatory cytokines from CD4+T cells from patients with SLE. These results provide strong mechanistic rationale for considering dimethyl fumarate as a novel therapeutic agent to treat systemic lupus erythematosus.

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AB0125

SPECIFIC AUTOANTIBODY CONTENT OF CIRCULATING IMMUNE COMPLEXES IN SLE – PHENOTYPIC CHARACTERIZATION AND CLINICAL ASSOCIATIONS

Keywords: Biomarkers, Autoantibodies, Systemic lupus erythematosus

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Background: Systemic Lupus Erythematosus (SLE) is characterised by autoantibody production and immune complex (IC) formation. The relative abundance of different autoantibodies within circulating ICs as compared to serum in SLE is hitherto unclear; moreover, the clinical relevance of the IC-carried fraction of SLE-specific and associated autoantibodies is mostly unknown.

Table 1.

	Anti-Ro52 IC + %	Anti-Ro60 IC + %	Anti-SSB IC + %	Anti-Sm IC + %	Anti-U1RNP IC + %	Anti-dsDNA IC + %	Anti-Histone IC + %
Anti-Ro52+ sera n= 139	**84.9%**	90.6%	56.8%	17.9%	23.7%	12.2%	16.5%
Anti-Ro60+ sera n= 192	62%	**94.3%**	49.5%	17.2%	22.4%	13%	17.7%
Anti-SSB+ sera n= 95	74.7%	90.5%	**91.6%**	13.7%	16.8%	15.8%	17.9%
Anti-Sm+ sera n= 88	39.7%	47.7%	26.1%	**45.5%**	54.5%	31.8%	32.9%
Anti-U1RNP+ sera n=99	29.3%	35.4%	17.2%	32.3%	**66.7%**	17.2%	23.2%
Anti-dsDNA+ sera n= 196	27.6%	38.8%	21.9%	16.8%	28%	**20.9%**	30.1%
Anti-Histone+ sera n=160	32.5%	42.5%	23.8%	19.4%	30.6%	21.9%	**38.1%**

Objectives: To investigate cross-sectionally the IC-derived fraction of SLE specific and associated antibodies, together with the total circulating C1q-binding immune complex (CIC) levels, in a large well-characterized SLE cohort.
Methods: We studied n=530 consecutive SLE patients (≥ 4 ACR 1982 revised criteria for SLE) who received care at a tertiary referral center for SLE. All participants gave written informed consent for inclusion. The control population consisted of region of residence, age and sex-matched controls (n=192) and n=200 local experimental controls. ACR criteria (at study inclusion), SLEDAI scores, clinical and laboratory variables were obtained at inclusion and through medical file review. At inclusion, fasting blood was drawn from an antecubital vein and was processed to serum, which was stored at -80°C. To obtain IC-derived antibodies, a novel validated method, described in detail elsewhere[1], was employed. Briefly, sera were incubated with C1q-coated beads; the C1q-bound ICs were then eluted through two sequential washes with an acidic and alkaline solution respectively, yielding disassembled IC eluates with conserved antibody specificity. Antibody levels of Anti-dsDNA, Anti-Histone, Anti-Sm, Anti-U1RNP, Anti-Ro52, Anti-Ro60, Anti-SSB were measured in IC eluates and in serum with a bead-based multiplex assay. CIC levels were measured with a commercial ELISA according to the manufacturer's instructions. Parallel analyses of autoantibody levels in serum and in IC eluates were performed on the same day. The results were reported on a standard curve; the 98th percentile of the standard curve values of control sera were set as the threshold for positivity for binary analyses.
Results: CIC levels were higher and more widely dispersed in SLE patients than controls (p<0.0001). A higher CIC load was associated with nephritis, arthritis and SLEDAI > 6 (p<0.0001). Among autoantibody specificities, Anti-dsDNA in serum was independently associated with a high CIC load (OR 4.8, 95% CI 2.5-9.5, p<0.0001, see also Figure 1). Concordance between serum and IC-eluate positivity varied strongly among autoantibody specificities, being highest for Anti-SSA/SSB, and lowest for Anti-dsDNA (Table 1). Among serum Anti-dsDNA+ patients, carriers of Anti-dsDNA from ICs displayed higher Anti-dsDNA titers, lower complement levels, and higher SLEDAI scores (p<0.01 for all).
Conclusion: Different autoantibodies are differentially represented in circulating ICs in SLE. Anti-dsDNA in serum is an independent marker of a higher CIC load, carrying facets of a more IC-mediated disease. Patients with elevated Anti-dsDNA in IC eluates, compared to anti-dsDNA only in serum, are a more clinically and biologically active subset, showing promise of IC-derived Anti-dsDNA as a potential SLE biomarker.
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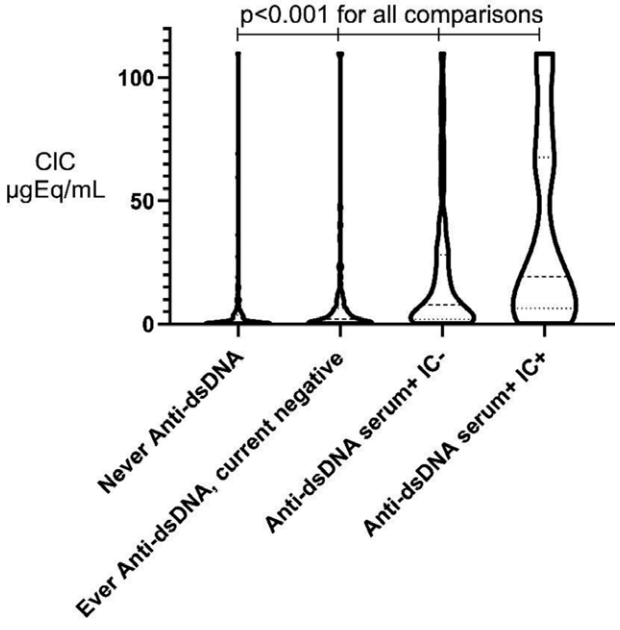


Figure 1

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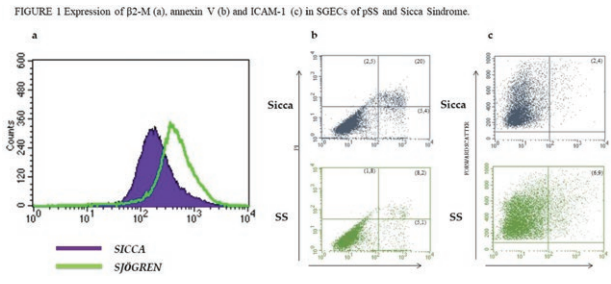
AB0126

EXPRESSION OF B2 MICROGLOBULIN IN SALIVARY GLAND EPITHELIAL CELLS OF PATIENTS WITH SJOGREN SYNDROME

Keywords: Sjögren syndrome, Biomarkers

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Background: Salivary glands epithelial cells (SGECs) activation and loss of homeostasis play a key role in primary Sjogren Syndrome (pSS) [1]. High serum and saliva levels of β2-mycroglobulin (β2-M) have been described [2] in pSS, however, the exact origin of this molecule is still unclear. Our preliminary data from single cell analysis on pSS salivary glands treated with immunosuppressors show a downregulation of this protein in SGECs following treatment.
Objectives: Aim of this study is to evaluate the expression of β2-M in pSS SGECs and to dissect its modulation in inflammatory conditions.
Methods: To mimic the inflammatory microenvironment of pSS, a human salivary gland (HSG) cell line was treated (48h) with 1) Poly-I:C (40 µg/ml), 2) LPS (50 µg/ml), 3) culture medium (untreated). The HSG expression of β2-M (Ab anti-β2-M) was evaluated by flow cytometry along with the expression of apoptotic [(annexin V (MBL)] and activation [ICAM-1 (Ab anti-CD54)] molecules. Ex vivo expression of β2-M was then assessed in SGECs deriving from both pSS patients (n=3) and sicca (controls) (n=3).
Results: In the HSG cell line treated with both Poly I:C and LPS a significant increase in β2-M was documented [mean fluorescence index (MFI): untreated=1 (1-1), Poly-I:C=2.46 (1.5-3.9), LPS=1.3 (1-1.3); p=0.003]. The increased expression of β2-M was paralleled by an increase in ICAM-1 (MFI: untreated=1 (1-1), Poly-I:C=1.61 (1-2.5), LPS=1.26 (1-1.2); p=0.06) and annexin V (mean%: untreated=7.6% (5-9), Poly-I:C=14.3% (9-18), LPS=8% (6-11); p=0.003). In SGECs from pSS a higher expression of β2-M was detected as compared to controls (MFI: pSS=2.5 (2-3) vs sicca=1 (0.5–1.5) (Figure 1).
Conclusion: Our preliminary data suggest that β2-M is actively expressed by SGECs in pSS and that its exposure is driven by the local inflammatory milieu. Such expression is particularly interesting in view of the already demonstrated capacity of β2-M to activate pro-inflammatory pathways and to influence cellular viability and autoantigens exposure [3]. Functional studies are currently ongoing to dissect the potential pathogenic role of β2-M in pSS.



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Acknowledgements: NIL.
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AB0127

ANTIGENIC ASSESSMENT FOR THE B2GPIOX-PF4 COMPLEX IN A MONOCENTRIC COHORT OF PATIENTS WITH APS, THROMBOSIS DURING SARS-COV-2 INFECTION AND VITT

Keywords: Autoantibodies, Vaccination/Immunization, Anti-phospholipid syndrome

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Background: Platelet factor 4 (PF4) is a protein with a pro-clotting function expressed by activated platelets with a high affinity for anionic glycosaminoglycans present on the platelet surface. It has been shown that the positively charged surface of PF4 tetramer interacts with the negatively charged regions of β2glycoprotein I (β2GPI) domains, stabilising the link between the antigen and the phospholipid surface, thus increasing the possibility of binding with the respective antibodies. In particular, a tetramer of PF4 selectively binds two molecules of β2GPI, favouring the dimerization of the same, which is crucial in platelet activation and therefore in thrombotic manifestations of antiphospholipid syndrome (aPS). PF4 may be a common denominator in syndromes such as aPS and heparin-induced thrombocytopenia (HIT), which share similar clinical manifestations as thrombocytopenia and thrombosis. Other syndromes, which share the same clinical and laboratory features of HIT despite not having previously received heparin, appear to be associated with the presence of anti-PF4 antibodies. Such pathologies could only be explained by HIT antibodies with heparin-independent platelet-activating properties. One of these could be vaccine-induced Immune thrombotic thrombocytopenia (VITT) post-somministration of ChAdOx1 nCoV-19 vaccine. Recent studies have shown structural similarities between heparin and β2GPI, which may be responsible for thrombotic events in those infected with SARS-Cov-2 and VITT, who never had heparin. In particular, oxidised-β2GPI (β2GPIox) may mimic heparin by structural analogy and link to PF4. Considering the structural similarities between heparin and β2GPIox, and demonstrating the immunogenicity of the hypothesised complex in APS, the alternative molecule could be represented by β2GPIox itself, thus explaining the thrombotic events following vaccination in subjects who have never received heparin.
Objectives: The aim of the study is to test the potential immunogenicity of the β2GPIox-PF4 complex and the presence of antibodies against this complex in patients with aPS, thrombosis during infection with SARS-CoV-2 or VITT.
Methods: 34 patients with proven diagnosis of APS, 17 patients with thrombosis related to infection SARS CoV-2 and 3 patients with VITT were enrolled. Only one aPS patient received heparin prior to testing. Antibodies to the β2GPIox-PF4 complex were evaluated by home made ELISA immunoenzyme testing. Competitive inhibition (homologous) experiments of the bond of PF4 with β2GPIox in the fluid phase were conducted in order to verify the binding specificity.
Results: Anti-β2GPIox-PF4 antibodies were detected in 11 of 34 aPS patients (32%) and all VITT patients (100%), while none of covid-19 patients tested positive. In addition, Anti-β2GPIox-PF4 antibodies positivity significantly correlated with the presence of anti-β2GPI antibodies (p=0.0259) and with a triple positive antibody profile (p=0.0017) (Figure 1). There was no significant association between anti-β2GPIox-PF4 antibodies' title and clinical features of aPS patients.
Conclusion: The results of this study show a new antibody positivity in aPS and VITT. In particular we have identified a high prevalence of anti-β2GPIox-PF4 antibodies which may be involved in the pathophysiology of both aPS and VITT. In addition the absence of anti-β2GPIox-PF4 antibodies in covid-19 patients suggest that the thrombotic mechanism that underlies VITT is different from covid-19 and, on the contrary, could resemble aPS.

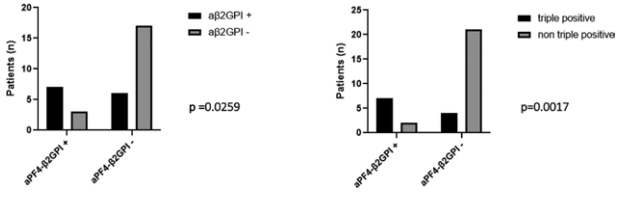


Figure 1.

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AB0128

DIFFERENTIAL EXPRESSION OF PROTEINS IN PATIENTS WITH SUSPECTED SJÖGREN'S SYNDROME

Keywords: Biomarkers, Cytokines and chemokines, Sjögren syndrome

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Background: Sjögren's Syndrome (SS) is a chronic systemic autoimmune disease characterized by involvement of the exocrine glands in addition to a wide spectrum of systemic manifestations. At present, conventional biomarkers do not respond to unresolved needs regarding diagnosis, stratification of phenotypes and appropriate effective therapies[1]. SS is an orphan disease and new biomarkers could constitute potential future therapeutic targets[2].
Objectives: The purpose of this study was to carry out an exploratory analysis in six serum and saliva samples from suspected SS patients to identify protein biomarkers to distinguish SS patients who were diagnosed with SS from those who were not.
Methods: We selected six patients from a cohort of 199 consecutive patients attended the rheumatology department for suspected SS: 3 patients who met SS classification criteria from 2002 and/or 2016 who were diagnosed with SS by a rheumatologist and 3 patients who did not meet SS classification criteria who were not finally diagnosed. Serum samples were collected and centrifuged at 1800g, divided into aliquots and stored at -80ºC. Saliva samples were cold collected to prevent degradation of proteins, centrifuged at 1800g at 4ºC and stored at -80ºC. A semiquantitative analysis of protein expression was performed using the "Proteome Profiler Human XL Cytokine Array Kit" arrays from R&D system that detects 105 proteins containing interleukins, chemokines, inflammatory factors and other soluble proteins. Analytes optical densities were quantified using Image J software. The content of the analytes was compared between SS patients and non-SS patients using an unpaired Student´s t test and a measure of the odds of an analyte happening in one group compared to the odds of the same analyte happening in another group (OR: odds ratio) is shown. Statistical analysis were performed using Microsoft Excel software. *P* values ≤0.05 were defined as significant and values of 0.1<*P*> 0.05 were considered as borderline.
Results: We found increased serum levels of CD14 (OR:1.21; *P*=0.033), EGF (OR:1.18; *P*=0.050), IP-10 (OR: 1.23; *P*=0.090) Pentraxin 3 (OR:1.32; *P*=0.095) and VEGF (OR:1.41; *P*=0.091) in patients diagnosed with SS who met SS classification criteria, compared with patients who did not meet SS classification criteria who were not diagnosed, although only in the case of CD14 and EGF, statistical significance was reached. In saliva samples, we found significantly increased values of ICAM1 (OR: 1.67; *P*=0.019), IL-6 (OR:1.20; *P*=0.042) and IL-19 (OR:1.51; *P*=0.039) in patient who did not meet SS classification criteria. compared with patients who did.
Conclusion: Sjögren's syndrome patients presented significantly higher levels of CD14 and EGF in serum, as well as significantly decreased levels of ICAM1, IL-6, and IL-19 in saliva, when compared to patients who did not meet SS classification criteria. It is necessary to confirm these results in a larger cohort of patients.
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Disclosure of Interests: None Declared.
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AB0129

EXPLORING LONG NON-CODING RNA GAS5 IN SLE PATIENTS AND ITS RELATION TO INTERFERON SIGNATURE

Keywords: Genetics/Epigenetics, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease with diverse pathogenesis. Excessive apoptosis and impaired clearance of apoptotic cells are the primary drivers of Interferon I (IFN) signaling pathways. Upregulation of the long noncoding RNA Growth arrest-specific 5 (GAS5) was found to be associated with apoptosis [1]. Oncological studies discovered that GAS5 is regulated by IFN signaling pathways and acts as a positive feedback loop on IFN response [2,3]. In a mouse model, GAS5 was linked to SLE susceptibility [4]. However, the exact mechanism is still unknown. Furthermore, GAS5 has been proposed to act by interfering with glucocorticoid action, with a key role in regulating glucocorticoid resistance and sensitivity [5].
Objectives: To evaluate the expression levels of GAS5 in serum of SLE patients in comparison with healthy controls, assess their relation to SLE Disease Activity Index 2000 (SLEDAI-2K) and Systemic Lupus International Collaborating Clinics/ American College of Rheumatology Damage Index (SDI), and explore their association with each of the 3 IFN stimulatory genes (MX1, IFI44L, IFIT1) as well as IFN signature to elucidate how GAS5 shares in the pathogenesis of SLE.
Methods: 30 adult SLE patients and 20 age and sex-matched healthy controls were enrolled. SLE disease activity and damage were assessed by SLEDAI-2K and SDI respectively. The expression levels of GAS5 as well as 3 IFN stimulatory genes (MX1, IFI44L, IFIT1) were measured by quantitative real-time PCR. IFN signature score was calculated as described in a previous study [6].
Results: GAS5 expression levels were insignificantly upregulated in SLE patients compared to control (p-value 0.11). At cut-off value 1.3-fold change, GAS5 could discriminate SLE from control (AUC 0.63) with high specificity 100 % and modest sensitivity 63%. Their expression levels were not associated with SLEDAI-2K or SDI scores. GAS5 levels were positively correlated with the cumulative dose of steroids in the last 6 months. However, it was not statistically significant. GAS5 was significantly correlated with IFIT1 gene expression (p-value <0.001) and IFN signature score (p-value 0.005) in SLE patients (Figure1), these findings were not previously reported.
Conclusion: GAS5 may be considered a diagnostic biomarker for SLE, but it is not a reliable biomarker for disease activity or damage. GAS5 is suggested to be incorporated into the IFN signaling pathway in SLE raising possible contribution in SLE pathogenesis.

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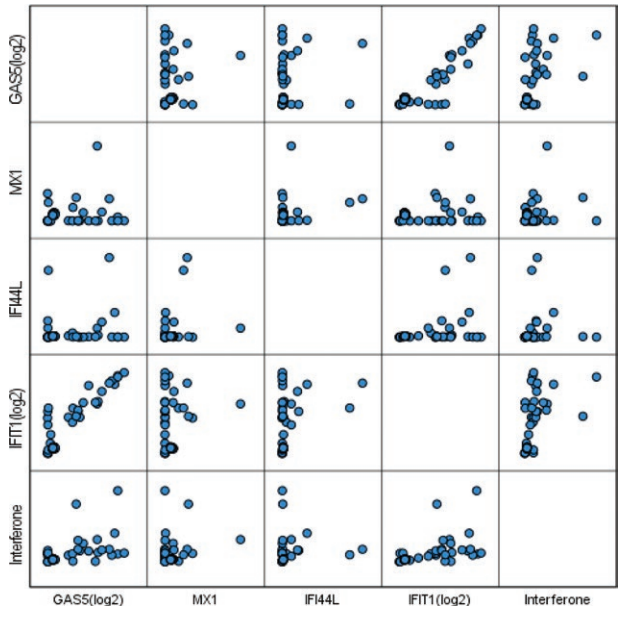


Figure 1. Scatterplot shows the relation between gene expression levels with each other and with interferon signature score in cases.

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Disclosure of Interests: None Declared.
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AB0130 KYNURENINE PATHWAY CAN BE A POTENTIAL BIOMARKER OF FATIGUE IN PRIMARY SJOGREN'S SYNDROME

Keywords: Biomarkers, Sjögren syndrome

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Background: Primary Sjogren's syndrome (pSS) is a chronic autoimmune disease with low quality of life caused by various constitutional symptoms and glandular dysfunction. Although fatigue is one of the most frequent symptoms in pSS, its etiology or biomarkers are poorly elucidated.
Objectives: We investigated potential relationship between severity of fatigue and the kynurenine pathway in pSS.
Methods: Clinical data and blood samples of 81 patients were obtained from a prospective cohort for pSS and compared with age- and sex-matched healthy controls (HC). Severity of fatigue was defined according to the fatigue domain scores in the ESSPRI. Potential biomarkers related to the kynurenine pathway were determined using ELISA.
Results: Of the total, 44 patients were defined as the "severe fatigue (ESSPRI fatigue ≥ 5)" group, whereas 37 as the "less fatigue (ESSPRI fatigue < 5)". Serum tryptophan levels in the severe fatigue group were significantly lower while those of kynurenine were higher. Serum interferon gamma, IDO1, and quinolinic acid levels were mostly higher in the less fatigue group. Kynurenine/tryptophan ratios were distinctly higher in the severe fatigue group than both HC and the less fatigue group ($p < 0.001$). This ratio showed a strong degree of positive correlation ($r = 0.624$, $p < 0.001$) with severity of fatigue in pSS while the other markers showed fair degrees of correlation.
Conclusion: Serum markers related to the kynurenine pathway, especially the kynurenine/tryptophan ratio, may be associated with severity of fatigue in pSS. These results can provide guidance for further investigations on fatigue in pSS.

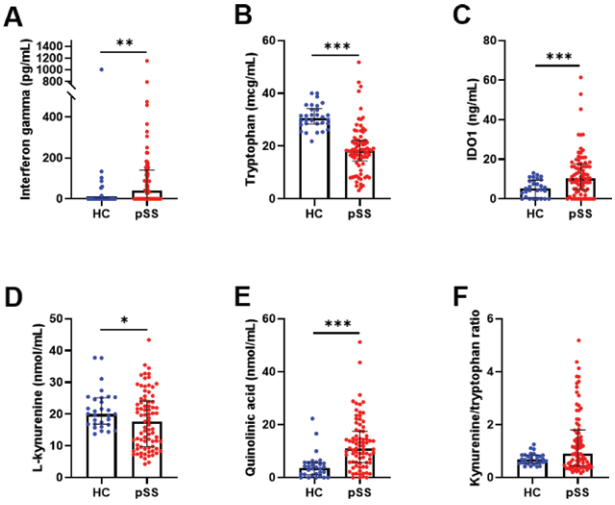


Figure 1. Serum levels of tryptophan, its metabolites, and related enzymatic activities in patients with primary Sjogren's syndrome (pSS) and healthy controls (HC). (A) Interferon gamma; (B) tryptophan; (C) indoleamine-2,3-dioxygenase 1 (IDO1); (D) L-kynurenine; (E) quinolinic acid; (F) ratio of L-kynurenine to tryptophan. All data were measured using enzyme-linked immunosorbent assay. The bars indicate the median and interquartile range. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1130

AB0131

ASSOCIATION OF CYTOKINE AND CLINICAL EVALUATION BASED ON ULTRASOUND OF SALIVARY GLAND GRADE CLASSIFICATION IN PATIENTS WITH EARLY PRIMARY SJÖGREN'S SYNDROME

Keywords: Imaging, Sjögren syndrome, Cytokines and chemokines

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Background: Primary Sjögren's syndrome (pSS) is a chronic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands, the presence of anti-SSA/Ro, anti-SSB/La antibody and hypergammaglobulinemia.
Objectives: To investigate the clinical manifestations in patients with early primary Sjögren's syndrome (pSS), and cytokine difference based on the severity score under salivary gland ultrasonography.
Methods: Forty-six newly diagnosed patients with early pSS were enrolled and divided into mild (score 0-1) and severe (score 2-3) groups according to the salivary gland ultrasonography grade (SGUS) scores at baseline. Clinical evaluation, ESSPRI and ESSDAI index values, sicca symptoms of mouth, salivary capacity, and serum autoantibody and cytokines were investigated.
Results: Mean age of pSS patients at diagnosis were 50.02 ± 12.4 years and the mean duration of sicca symptoms were 1.4 years. ESSPRI (EULAR Sjögren's syndrome patient report index) and ESSDAI (EULAR Sjögren's syndrome disease index) scores were 5.71 and 5.37, respectively. The higher prevalence of rheumatoid factor (p=0.04), antinuclear antibody (p=0.009) and elevation of total IgG (p=0.08) were found in severe group than in mild group. In addition, elevated titer of IL-18, IL-31 and IL-33 were detected in patients with pSS than in healthy subjects, but there were shown no statistical significance between mild and severe groups.
Conclusion: Salivary gland ultrasonography grade (SGUS) scans may help physician diagnose pSS. Clinical manifestation including the low production of saliva and autoantibody production such antinuclear antibodies, rheumatoid factor, and anti-SSA antibody were found. The elevated titer of IL-18, IL-31 and IL-33 in patients may be implicated in the pathogenesis of pSS.
REFERENCES: NIL.

Characteristics	SS Patients (n=46)	Mild (n=24)	Severe (n=22)	P-value
Mean Age, y (SD)	50.8 (12.4)	50.7(13.1)	50.8 (11.8)	0.9785 [a]
Female, n (%)	45 (97.8%)	23 (95.8%)	22 (100%)	1.0000 [b]
Disease duration, y (SD)	1.4 (2.0)	0.9 (1.0)	1.9 (2.7)	0.0974 [a]
ESSDAI, mean (SD)	**5.37 (4.80)**	**4.04 (2.99)**	**6.82 (5.95)**	**0.0486 [a]**
Salivary gland ultrasonography scores (SD)	**1.26 (0.85)**	**0.54 (0.51)**	**2.05 (0.21)**	**<.0001 [a]**
Parotid gland, degrade scoring (SD)	**1.22 (0.84)**	**0.54 (0.51)**	**1.95 (0.38)**	**<.0001 [a]**
Submandibular gland, degrade scoring (SD)	**1.24 (0.85)**	**0.54 (0.51)**	**2.0 (0.31)**	**<.0001 [a]**
ESSPRI, mean (SD)	**5.71 (2.3)**	**5.6 (2.5)**	**5.8 (2.1)**	**0.8052 [a]**
Sicca syndrome, level score (SD)	6.6 (2.4)	6.4 (2.6)	6.9 (2.2)	0.4871 [a]
Fatigue, level score (SD)	5.9 (2.9)	5.3 (3.3)	6.5 (2.2)	0.1577 [a]
Arthralgia, level score (SD)	4.6 (3.8)	5.2 (3.4)	4.0 (4.1)	0.2843 [a]
RF, n (%)	**18 (39.1)**	**6 (25.0)**	**12 (54.5)**	**0.0403 [c]**
Anti-SSA, n (%)	46 (100)	24 (100)	22 (100)	1.0000 [b]
Anti-SSB, n (%)	15 (32.6)	6 (25.0)	9 (40.9)	0.2502 [c]
Anti-RNP, n (%)	0 (0)	0 (0)	0 (0)	-
Anti-Sm n (%)	0 (0)	0 (0)	0 (0)	-
Antinuclear, n (%)	**31 (67.4)**	**12 (50.0)**	**19 (86.4)**	**0.0086 [c]**
Low C3, n (%)	6 (13)	2 (8.3)	4 (18.2)	0.4052 [c]
Low C4, n (%)	2 (4.3)	0 (0)	2 (9.1)	0.2232 [b]
Anti-dsDNA, n (%)	1 (2.2)	0 (0)	1 (4.5)	0.4783 [b]
High IgG, n (%)	21 (45.7)	8 (33.3)	13 (59.1)	0.0798 [c]
High IgG4, n (%)	4 (8.7)	3 (12.5)	1 (4.5)	0.6093 [c]
Low saliva production, n (%)	**17 (37.0)**	**4 (16.7)**	**13 (59.1)**	**0.0029 [c]**

[a] Independent t test [b] Fisher's exact test [c] Chisq-square test.

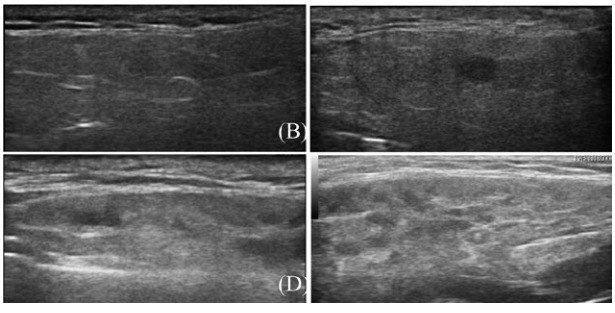


Figure 1. Ultrasonographic images of four parotid glands illustrating varying grades of non-specific to pathological changes. Score 0-3 were determined by evaluation of US examination of each patient's parotid and submandibular glands. (A) Score 0, (B) grade 1, (C) score 2, and (D) score 3. score 0-1 were considered as normal morphology, and score 2-3 were diagnosed as pathological changes, which were related to primary SS.

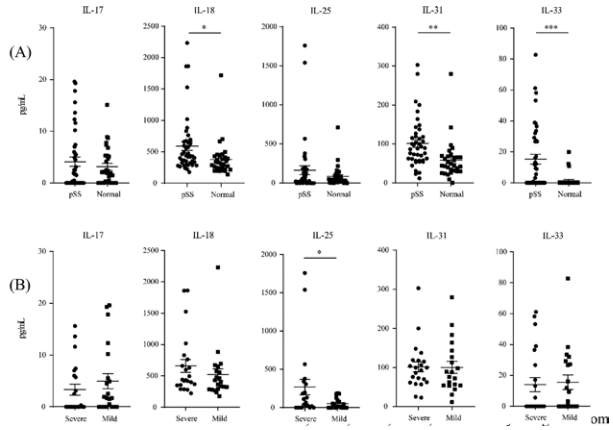


Figure 2. The measurement of serum level of IL-17, IL-18, IL-25, IL-31, and IL-33 by using sera from patients with pSS and normal healthy controls. (A) pSS patient vs normal healthy controls. (B) Severe group vs mild group.

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Disclosure of Interests: None Declared.
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AB0132

AFIMETORAN (BMS-986256), AN EQUIPOTENT TLR7/8 ANTAGONIST, DEMONSTRATES STEROID-SPARING EFFECTS IN A LUPUS MOUSE MODEL

Keywords: Systemic lupus erythematosus, Animal models

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with extensive heterogeneity in disease presentation due to an underlying molecular diversity of dysregulated pathways. Glucocorticoids, like prednisolone, are part of the standard-of-care treatment for SLE. However, over time, patients develop resistance to glucocorticoid therapies, and steroid resistance is an important unmet need for patients with SLE. Furthermore, patients can experience side effects, which make long-term use undesirable. Toll-like receptors (TLR) 7 and 8 are endosomal receptors that play a key role in innate immunity. TLR7 and 8 are expressed in various immune cells where they recognize single-stranded RNA and initiate downstream signaling via the Nuclear Factor kappa B (NFkB) and interferon regulatory factor pathways. Activation of the NFkB pathway contributes to the resistance to steroids, and its activation via TLR7 and 8 pathways, along with inhibition of plasmacytoid dendritic cell (pDC) apoptosis via TLR7, could be a driving factor leading to steroid resistance.
Objectives: To evaluate the steroid-sparing potential of afimetoran, an equipotent, dual antagonist of TLR7 and TLR8, currently in clinical development for SLE and cutaneous lupus erythematosus.
Methods: NZB/W mice with moderate disease (proteinuria of 60–100 mg/dL) were treated therapeutically once daily with vehicle or selected doses of afimetoran and/or prednisolone. Survival, kidney injury, splenomegaly, age-associated B-cells (ABCs, measured by CD19, T-bet, and CD11c positivity), serum auto-antibody titers (anti-double stranded DNA antibodies, anti-nuclear antibodies [anti-Smith, anti-ribonucleoprotein, anti–Sjögren's-syndrome-related antigen A autoantibodies]), and plasma interleukin-12p40 (IL-12p40) were assessed in all treatment groups. To assess the impact of afimetoran on the effect of steroids on TLR7 activation in vitro, C57 wild-type mouse bone marrow cells (BMCs) were challenged with the TLR7 agonist gardiquimod and treated with prednisolone alone, or in combination with afimetoran. Both for C57 wild-type BMCs treated in vitro and NZB/W BMCs from mice dosed orally, B-cell and pDC apoptosis was evaluated by annexin V staining using flow cytometry.
Results: In the NZB/W mouse model, afimetoran improved survival when used alone or in combination with prednisolone. It also significantly and dose-dependently suppressed kidney injury markers such as proteinuria, neutrophil gelatinase-associated lipocalin (NGAL), and tissue inhibitor of metalloproteinases 1 (TIMP1). Splenomegaly and suppression of ABCs were improved, particularly when afimetoran was combined with prednisolone. Significant and dose-dependent suppression of plasma IL-12p40 and serum auto-antibody titers was also observed in all active treatment groups, demonstrating the potential of afimetoran in this mouse model of SLE. An improved steroid response was

seen in gardiquimod-stimulated mouse BMCs collected from C57BL/6 mice and exposed in vitro to afimetoran, which showed a significant increase in prednisolone-induced apoptosis of pDCs and B cells compared to baseline control or prednisolone alone. A similar trend was seen in vivo for BMCs collected from NZB/W mice dosed with combinations of afimetoran and prednisolone.

Conclusion: Afimetoran, either alone or in combination with prednisolone, showed efficacy in NZB/W mice with moderate disease. It also reversed the resistance of bone marrow pDCs and B cells to prednisolone-induced apoptosis. These data confirm that afimetoran, an equipotent TLR7/8 antagonist, has the clinical potential to be steroid-sparing.

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Disclosure of Interests: Shailesh Dudhgaonkar Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Puneet Chopra Employee of: Syngene, Anjuman Rudra Employee of: Syngene, Siva Subramani Employee of: Syngene, Sourabha Palachandra Employee of: Syngene, Nikita Bhatt Employee of: Syngene, Veeresh Pabbala Employee of: Syngene, Sourabh Ranade Employee of: Syngene, Durga Shiva Prasad Ega Employee of: Syngene, Alaric Dyckman Employee of: Bristol Myers Squibb, Qihong Zhao Employee of: Bristol Myers Squibb.

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AB0133 DYSAUTONOMIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CROSS-SECTIONAL STUDY

Keywords: Cardiovascular disease, Systemic lupus erythematosus, Diagnostic tests

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Background: Systemic lupus erythematosus (SLE) is a chronic, inflammatory, autoimmune disease associated with increased cardiovascular risk. Impaired autonomic nervous system (ANS) function (dysautonomia) is one of the causes and a marker of increased cardiovascular risk. Heart rate variability (HRV) is an accepted method of ANS evaluation. Pupillary light reflex (PLR) test is indicative of ANS dysfunction in healthy adults. The efficiency of PLR test for ANS evaluation among SLE patients has yet to be reported.

Objectives: To evaluate ANS function among SLE patients using PLR and HRV testing. The secondary objective was to assess the correlation between PLR and HRV tests among patients with SLE and to evaluate whether they are correlated.

Methods: A cross-sectional study was conducted. Forty-nine SLE patients and a matched group of 87 healthy volunteers were recruited. The participants were questioned about risk factors and other conditions that affect the ANS. Autonomic functions was evaluated by HRV and PLR testing. Strength of correlations were also evaluated.

Results: Maximum pupil diameters (PDmax) and maximal constriction velocity (MCV) was significantly lower in the SLE group (4.80±0.13 mm vs. 5.59±0.15 mm, p<0.01 and 4.01±0.44 mm/s vs. 5.94±0.51 mm/s, p<0.01, respectively). Compared with controls, the SLE patients had significantly lower values of NN50 (number of successive RR intervals that differ by more than 50ms, 12.78±3.78 vs. 25.08±2.84, p = 0.031), pNN50 (percentage of pNN50, 4.03±1.30 % vs. 8.84±0.98 %, p<0.01), SDNN (standard deviation of interbeat intervals, 38.44±3.19 ms vs. 50.19±2.39 ms, p<0.01) and HRV triangular index after 5 minutes standing (11.19±0.63 vs. 14.27±0.47, p<0.01).

Conclusion: Patients with SLE have excessive parasympathetic activity, manifested as decreased HRV parameters and indices reflective of heart rate response to autonomic maneuvers. Similar results demonstrated by pupillary autonomic function. PLR test may be used as an alternative to HRV testing due to its simplicity and reproducibility.

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AB0134 RESTORATION OF ABERRANT GENE EXPRESSION OF MONOCYTES IN SYSTEMIC LUPUS ERYTHEMATOSUS VIA A COMBINED TRANSCRIPTOME-REVERSAL AND NETWORK-BASED DRUG REPURPOSING STRATEGY

Keywords: Biomarkers, Genetics/Epigenetics, Systemic lupus erythematosus

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Background: Monocytes -key regulators of the innate immune response- are actively involved in the pathogenesis of systemic lupus erythematosus (SLE). Monocytes and macrophages constitute a major cellular compartment derived from hematopoietic myeloid precursors. Monocyte-macrophage lineage cells exhibit versatile immunoregulatory, inflammatory and tissue repairing capabilities and play an instrumental role in the development of systemic lupus erythematosus (SLE). Abnormal activation of autoreactive T and B cells in SLE could also be caused by dysregulated cytokine production by monocytes. Monocytes in SLE display excess production of the B-lymphocyte stimulator (BLyS) which promotes the survival and proliferation of B cells.

Objectives: We sought to identify novel compounds that might serve as monocyte-directed targeted therapies in SLE.

Methods: We performed mRNA sequencing in monocytes from 15 patients with active SLE and 10 healthy individuals. Disease activity was assessed with the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). Leveraging the drug repurposing platforms iLINCS, CLUE and L1000CDS[2], we identified perturbagens capable of reversing the SLE monocyte signature. We identified transcription factors and microRNAs (miRNAs) that regulate the transcriptome of SLE monocytes, using the TRRUST and miRWalk databases, respectively. A gene regulatory network, integrating implicated transcription factors and miRNAs was constructed, and drugs targeting central components of the network were retrieved from the DGIDb database, in order to build a final drug-protein interaction network.

Results: Inhibitors of the NF-κB pathway, compounds targeting the heat shock protein 90 (HSP90), as well as a small molecule disrupting the Pim-1/NFATc1/NLRP3 signaling axis were predicted to efficiently counteract the aberrant monocyte gene signature in SLE. Based on our network-based drug repurposing approach, an IL-12/23 inhibitor, an EGFR inhibitor and the proteasome inhibitor bortezomib may represent potential drug candidates in SLE.

Conclusion: Application of two independent - a transcriptome-reversal and a network-based -drug repurposing strategies uncovered novel agents that might remedy transcriptional disturbances of monocytes in SLE.

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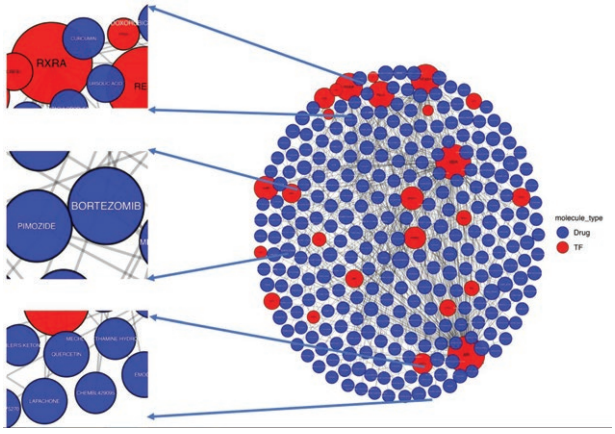


Figure 1. Drug-protein Interaction Network

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AB0135 ASSOCIATION OF STAT1, STAT4 AND JAK2 IMMUNOEXPRESSION WITH THE GRADE OF MONONUCLEAR CELL INFILTRATION IN MINOR SALIVARY GLAND BIOPSIES IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

Keywords: Sjögren syndrome, Prognostic factors

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Background: Signal transducer and activator of transcription 4 (STAT4) is an important for Interferon-γ induction (type 2 IFN signaling). Whereas type 1 IFN signaling pathway depends on signal transducer and activator of transcription 1 (STAT1) and Janus kinase 2 (JAK2). JAK2 is a non-receptor tyrosine kinase that plays a role in signal transduction via others type II receptors including IFN-α, IFN-ß, IFN-γ. The IFN signature in Sjogren's syndrome and overexpression of IFN-1 and IFN-2 in minor salivary glands biopsies (MSGBs) were described.
Objectives: The aim of the study was to analyze the immunoexpression of STAT4, STAT1 and JAK2 in biopsies of MSG depending on the severity of mononuclear cell infiltration (focus score, FS) in patients with primary Sjogren's syndrome(pSS).
Methods: The study group consisted of 64 patients with pSS aged 48.25±16.47. 89% of the subjects were women. MSGBs were routinely stained with HE for conventional histopathological examination with determination of FS. Monoclonal antibodies were used to determine the immunoexpression of the STAT1, STAT4, and JAK2,Quantitative Computer Image Analysis of Immunoexpression (ScanScope AT2 scanner) has been conducted. The percentage of positive immunostaining for each protein was determined in 20 HPF in each group of patients according to FS. Results were analyzed using TIBCO Statistica v. 13.3 Obtained values failed normal distribution assumption, therefore the non-parametric Kruskal–Wallis test with Dunn's multiple comparison test for post hoc analysis was used to assess the differences between the groups. $p < 0.05$ were considered to be statistically significant.
Results: 33% pSS patients were characterized by FS=1; 30%-FS= 3; FS=0 - 9%; 3% and 2% of patients revealed FS=5 and FS=6, respectively. In MSGBs JAK2-, STAT1-, and STAT4-immunopositive cells were observed. The various nuclear and cytoplasmic immunoexpression of JAK2, STAT1 and STAT4 in acinar and ductal cells and also in lesions displaying immune-cell infiltration were observed. However the immunoexpression of STAT4 in the nucleus was relatively rarely found. The percentage of JAK2-, STAT1- and STAT4-positive cells in FS = 0 was significantly lower in comparison with FS equal or greater than 3. However for STAT4, already in FS=2 there was a stronger signal compared to FS=0. The percentage of JAK2- and STAT1-positive cells in MSG in FS = 0 was statistically insignificant in comparison with FS = 1 and 2. There was no statistical significance in the percentage of STAT4- positive cells in patients with FS = 0 in comparison with FS = 1 (Figure 1). mRNA level of *STAT4* in whole blood in patients with pSS revealed the opposite trend. The increase of FS was correlated with the decreased mRNA level of *STAT4*.

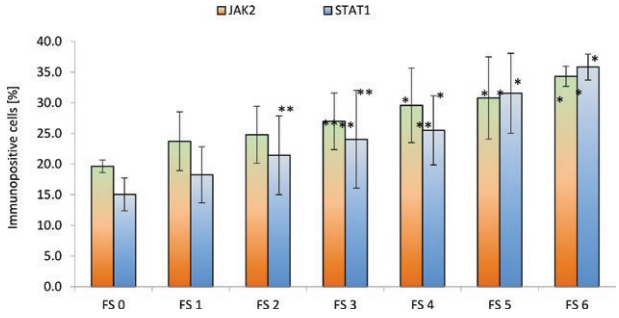


Figure 1. The percentage of JAK2-, STAT1- and STAT4-immunopositive cells in the human labial salivary glands according to the focus score (FS 0, FS 1, FS2, FS 3, FS 4, FS 5, FS 6) in the patients with pSS ** $p < 0.05$ vs. F0 group; * $p < 0.001$ vs. F0 group

Conclusion: Notably, in the case of STAT4 immunoexpression increased with increasing FS. Interestingly, mRNA level of *STAT4* determined in the whole blood decreased with increasing FS (data not shown).
The question remains why the immunoexpression of STAT4 in nucleus was relatively rarely found, and what is the impact of the dynamics of STAT4-dependent gene expression on the pathogenesis of pSS. In studied patients STAT4 activity dominates in MSG infiltrates which confirms the role of this factor in the pathogenesis of pSS.
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AB0136 INTERFERON STIMULATED GENES IN CD4 T CELLS ARE ASSOCIATED WITH PYROPTOSIS PATHWAYS IN PATIENTS WITH LUPUS

Keywords: Systemic lupus erythematosus, -omics

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Background: Single cell RNA sequencing (scRNA-seq) of kidney tissues in patients with lupus has led to landscape of complete cellular composition and states for immune and non-immune cells. These studies suggested type I interferon (IFN) signatures prime inflammatory responses. However, there is a lack of knowledge regarding the characteristics of subsets of IFN stimulating genes (ISG) high expressed cells.
Objectives: Here we investigated immune cell compositions between peripheral blood mononuclear cells (PBMCs), skin and kidney tissues in patients with lupus using scRNA-seq. We characterized a subset of ISG high CD4 T cells, which are commonly expressed across PBMCs, skins and kidneys of lupus but not skins of healthy.
Methods: scRNA-seq dataset of PBMCs, skin and kidney tissues in patients with lupus were collected. We integrated and analyzed immune cell compositions from this scRNA-seq dataset. We focused on subset of ISG high expressed CD4 T cells and characterized top 200 genes of this subset.

Results: There is one subset of ISG high expressed CD4 T cells in the lupus PBMCs, kidneys, and skins but not in the healthy skins. This ISG high expressed CD4 T cells have the greatest number of type I interferon signatures and gasdermin D gene, which is related to pyroptosis of cells, among top 200 genes. We further investigated pyroptosis pathway genes in the subsets of CD3 T cells. Interestingly, the subset of ISG high expressed CD4 T cells have most increased pyroptosis related upstream regulating genes including IRF1, GBP1, CASP4 and CASP1. Furthermore, this subset highly expressed inflammasome gene such as NLRC5 not NLRP3

Conclusion: There are ISG high expressed CD4 T cells across tissues of lupus. Those cells highly expressed pyroptosis pathway related genes. Further investigation is needed to characterize association between ISG and pyroptosis.

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AB0137 FIRST-IN-HUMAN INVESTIGATION OF HYDROGEN VOLTAGE-GATED CHANNEL 1 (HVCN1) EXPRESSION AND LEVELS OF MYELOPEROXIDASE AND OXIDIZED DNA (8-OHDG) IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLEOX STUDY) – AN INTERIM ANALYSIS

Keywords: Systemic lupus erythematosus, Cell biology

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Background: Within the still poorly understood pathogenesis of systemic lupus erythematosus (SLE) granulocyte neutrophils have been shown to play a key role. In our research on mouse models, we found that important functions of neutrophils are regulated by the hydrogen voltage-gated channel 1 (HVCN1), whose deficiency causes an SLE-like autoimmune disorder in old mice [1]. Among other effects, HVCN1 regulates the secretion of myeloperoxidase (MPO) and the release of neutrophil extracellular traps (NETs) in mice, thereby controlling inflammation. Based on this knowledge and a previous gene array analysis of CD16+ peripheral blood cells from SLE patients that showed reduced HVCN1 mRNA expression in neutrophils [2], we hypothesize that reduced HVCN1 expression leading to increased MPO and NET release might be a pathomechanism observable in humans that could contribute significantly to the pathogenesis and disease activity in SLE.

Objectives: This first-in-human trial prospectively assesses HVCN1 protein expression of leukocytes and plasma levels of MPO and 8-OHdG in correlation with clinical disease activity in SLE patients and matched healthy controls, in order to gain deeper understanding of SLE pathogenesis.

Methods: In this prospective study (ethical approval obtained under Institutional Review Board #112/22), 50 patients with SLE and 50 healthy controls are investigated for HVCN1 expression in peripheral blood leukocytes and plasma levels of myeloperoxidase (MPO) and oxidized DNA (8-OHdG), accompanied by application of the SLEDAI-2K assessment for clinical disease activity and recording of further clinical (demographics, patient and treatment history) and laboratory data (autoimmune, urine and routine serum diagnostics). HVCN1 protein expression is quantified by flow cytometry (BD FACS Symphony A5) via targeted HVCN1 staining (Alomone labs anti-HVCN1 rabbit IgG and Invitrogen anti-rabbit IgG Alexa Fluor 488). Previous processing steps include leukocyte staining (CD45, CD14, CD15 and CD16), cell fixation and permeabilization. Reference quantification of HVCN1 protein expression via Western Blot and further mRNA and DNA measurements are planned. MPO and 8-OHdG levels will be quantified by ELISA and mass spectrometry.

Results: The preliminary analysis of 18 SLE patients revealed a statistically significant positive correlation between SLEDAI-2k scores and HVCN1 protein expression (Pearson correlation coefficient: 0.563; p=0.015). Also, within the typical SLEDAI-2k disease activity categories, there was a clear tendency towards ascending HVCN1 protein quantities expressed with every severity category step-up [see Figure 1]. Further analysis is ongoing.

Conclusion: Unlike previous studies, our preliminary SLEOx trial data suggests a positive correlation of HVCN1 protein expression and SLE activity. General HVCN1 upregulation following leukocyte activation in response to disease activity (among other factors) could be one explanation. Validation in a larger study cohort is currently underway.

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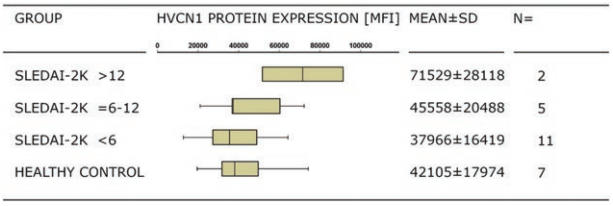


Figure 1. Graphic display of HVCN1 expression across disease activity groups and healthy individuals.
MFI= median fluorescence intensity
SLEDAI-2K= Systemic Lupus Erythematosus Disease Activity Index 2000

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0138 CHARACTERIZATION OF SERUM CYTOKINE PROFILE IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS

Keywords: Cytokines and chemokines, Systemic lupus erythematosus

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Background: Cytokines (CKs) are known to play a role in the pathogenesis of lupus nephritis (LN), yet their role as biomarkers is still debated.

Objectives: To describe the CKs picture in patients with active LN and to assess possible clinical correlates in LN course.

Methods: A prospective cohort study including patients with active biopsy-proven LN was performed. Serum CKs were assessed at the time of diagnosis and at 3 subsequent time points (3, 6 and 12 months) during follow-up. Clinical and serological data were collected for further analysis. BLyS (B Lymphocyte stimulator) and interleukin (IL)-37 were measured by ELISA assays (Quantikine BAFF, R&D, USA, detection limit DL 0.02 ng/mL; IL37 ELISA kit, Adipogen, Swizerland, DL 0.001 ng/mL), IL-2, IL-10, IL-17A and IL-18 (pg/mL) by Luminex multiplex assay (Millipore, USA, DL 0.6 pg/mL for all), according to the manufacturers' instructions. Measurements for IL-37 and BLyS were matched with sera of sex- and age-matched healthy subjects (HC). Mann-Whitney test was used for comparisons between two independent groups, Wilcoxon log-rank test for paired comparisons at different time points, Spearman's correlation coefficient for associations between CK and between CK and clinical features.

Results: Twenty-seven patients with active LN (mean±SD age 41.75±14.74, 78.8% women) were included for initial CK analysis at the time of LN activity. At baseline (T0), BLyS levels were significantly increased in LN compared with HC (median [range], 1.107 [0.326-4.00] vs. 0.563 [0.265-1.409]; p<0.0001); IL-37 was significantly reduced in LN compared with HC (median [range] 0.016 [0.001-0.251] vs. 0.056 [0.001-1.147]; p = 0.0185). At T0, median (range) levels of IL-2, IL-10, IL-17A and IL-18 were: IL-2 0.640 (0-37.82), IL-10 2.60 (0-106.86), IL-17A 2.10 (0-138.20), IL-18 243.10 (28.20-950.30). The longitudinal association study between CK levels of the entire cohort revealed a trend of inverse correlation between IL-37 and BLyS (r=-0.281, p=0.06) and a direct correlation between BLyS and IL-18 (r=0.330, p=0.04) and between IL-2 and IL-17A (r=0.470, p<0.001) (Figure 1). A subset of 17 patients (70.6% F, mean age at renal flare 34.3±18.6y, mean duration of disease at the time of renal flare 4.99±8.94y, caucasian ethnicity n=14, 82.3%), was followed-up prospectively: 7 (41.18%) had biopsy-proven (III-IV class) proliferative glomerulonephritis. Proteinuria at T0 was 2.19±1.35 g/24h. All patients were treated with pulsed glucocorticoids (GCS, 750-2500 mg) followed by oral GCS (0.3-0.5mg/kg/day prednisone equivalent) and immunosuppression1. Higher titres of IL-18 were present in the sera

of patients with proliferative forms of LN (p=0.053) and with a higher SLEDAI-2K score at T0 (p=0.0759). A significant correlation was found between IL-2, and to a lesser extent of IL-17, with anti-dsDNA antibodies (IL2: r=0.6098, p=0.0094; IL17: r=0.4591, p=0.0638). High levels of IL-17 correlated with lower C3 at T0 (r=-0.5085, p=0.0372). No significant longitudinal changes in CKs levels nor correlation with clinical features were observed.

Conclusion: Patients with proliferative LN and higher SLEDAI-2K scores displayed higher levels of IL-18, thus supporting IL-18 likely role in the pathogenesis of LN. We documented a correlation between IL2 and higher titres of anti-dsDNA antibodies and an inverse correlation between IL-17 and C3 at baseline, suggesting a contribution of CKs to LN onset. Our study was limited by the small sample size, limiting retrieval of significant data on CK levels and clinical-laboratoristic changes at different time points, demanding further studies.

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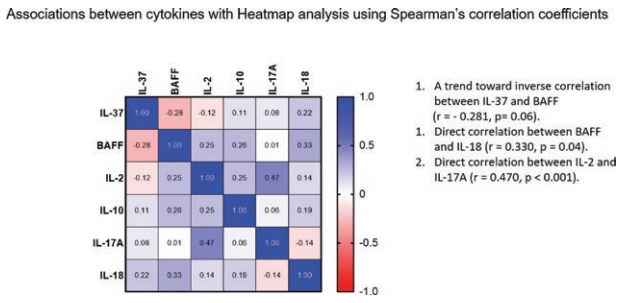


Figure 1

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.5076

AB0139

VALIDATION AND THE CLINICAL UTILITY OF POLYGENIC RISK SCORING IN ASIAN SLE

Keywords: Descriptive studies, Systemic lupus erythematosus, Epidemiology

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune rheumatic disease with a complex pathogenesis. The etiology of SLE is multifactorial, and includes contributions from genetic, epigenetic, environmental, hormonal, and immune regulatory factors. The hereditary pattern of the disease is polygenic in most patients. A polygenic risk scoring (PRS) model has been used to estimate the genetic risk of SLE in individuals. This approach assumes independent and additive contribution of genetic variants to disease development. The Taiwan Precision Medicine Project (TPMI) in our hospital invited patients with various diseases to participate in the research project. We had collected and analyzed clinical data from electric medical records. We had also established SLE-PRS risk analysis for our TPMI cohort.

Objectives: To validate the clinical utility of PRS in Asian SLE.

Methods: To understand the clinical characteristics of individuals with high SLE-PRS, we recruited female individuals, aged 20-50, from the top 5% subjects with the highest SLE-PRS from TPMI cohort. Pre-existing diagnosis of SLE was excluded (Figure 1). Questionnaire was assessed with self-reported symptom. Autoantibodies and serum complement levels were also assessed.

Results: Among 442 patients had high SLE-PRS, we included 131 patients in our study. Antinuclear antibody detection rate was 37.3%. 16.8% of recruited individuals had either low serum complements level or defected complement function (Table 1). Overall, 20.37% of individuals with high SLE-PRS had two immunological abnormalities by SLICC criteria, while 5.56% of individuals had more than three immunological abnormalities.

Conclusion: High SLE-PRS may be helpful for early lupus detection.

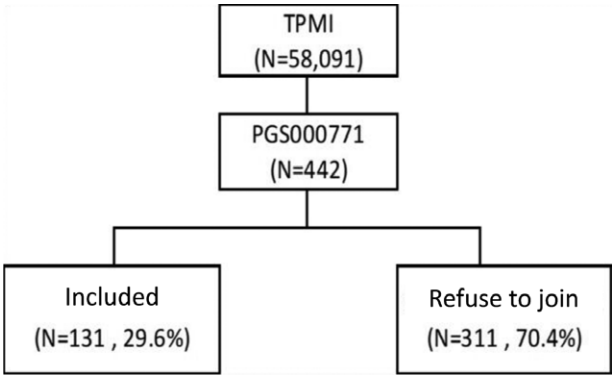


Figure 1. Study flow of SLE-PRS

Table 1. Proportion of SLE related immunologic abnormality in high SLE-PRS individuals

	SLE immunologic criteria	Positive	
		N	%
1	ANA	41	37.3
2	dsDNA Ab	6	5.3
3	C3 +C4+ CH50	19	16.8
4	Sm Ab	1	0.9
5	ACA, IgM+ACA, IgG+Aβ2GPI Ab, IgM +Aβ2GPI Ab, IgMG+LA	5	4.4
6	WBC + ALC	14	12.4
7	PLT	0	0.0
8	DAT POLYSPECIFIC TEST	5	4.5
9	UPCR (mg/g)+Microscopic Examination-RBC	15	13.3

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0140

UTILITY OF MONOCYTES, THEIR SUBSET ANALYSIS, CIRCULATING IMMUNE COMPLEXES AND CYTOKINES IN ASSESSMENT OF SLE DISEASE ACTIVITY

Keywords: Innate immunity, Biomarkers, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous disease with interaction of innate and adaptive immunity in pathogenesis and clinical activity. Monocyte and its subset role in SLE disease activity is not well defined. Complement levels and dsDNA levels are used for monitoring but are less than perfect and there is a need for newer prognostic markers in SLE management.

Objectives: To assess the prognostic utility of monocyte subsets,circulating immune complex (CIC) against C1q, cytokines like Tumour necrosis factor-alpha (TNF-a), Transforming growth factor-beta (TGF-b), interleukin-6 (IL-6) in lupus.

Methods: We conducted a prospective observational study in patients with SLE and no flare (as per SELENA-SLEDAI score =>4). A single visit interview of patients along with routine laboratory reports was used to select samples. A voluntary written consent was obtained and a blood sample (10ml) was collected to separate peripheral blood mononuclear cells (PBMC) and Serum. Cell analysis for monocyte subtypes was done using antibodies against cell surface markers using Fluorescence-activated cell sorting (FACS). Monocyte was sorted as classical and non-classical by CD14 and CD16 expression. Serum cytokines levels of IL-6, TNF-α, TGF-β and circulating immune complexes (CIC) were measured using ELISA kits.

Results: Among the 42 patients of SLE, 22 had active disease and 15 were newly diagnosed cases. The median age was 31 years (IQR 22.75 to 39.25) and the disease duration was 22 months (IQR 0-70.5). Musculoskeletal (76.2%), mucocutaneous (69%), renal (52.4%) and neuropsychiatric involvements (26.2%) were the common organ system involvements. Total monocytes were significantly reduced in active disease and Intermediate monocyte subset was numerically increased but not statistically different in active group(p=0.09). Mean fluorescence intensity (MFI) of CD 163 was significantly elevated in active disease(p=0.006).TNF alpha levels was elevated in active disease(p=0.042) but

other cytokines didn't correlate with disease status. CIC levels significantly differentiated active from inactive disease ($p<0.001$).

Conclusion: CIC along with TNF alpha levels might be a novel valuable predictors of disease activity whereas other serum cytokine levels did not correlate with SLEDAI-based activity. Intermediate subset of monocytes was increased numerically. CD 163 MFI was significantly increased in active SLE and should be evaluated in further studies.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0141 GUT MICROBIOTA DYSBIOSIS IN KOREAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus

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Background: In the development of various illnesses including autoimmune diseases, many studies proving the crucial role of gut microbes are gradually being reported. Alterations of gut microbiota can lead to abnormalities in the host immune system, causing autoimmune, which can ac as pathogenesis of systemic lupus erythematosus (SLE).

Objectives: The purpose of this study was to analyze the diversity and taxonomic composition of the gut microbiotas affecting SLE and to investigate their association with disease activities.

Methods: Fecal samples of 38 patients with SLE in Ajou Lupus Cohort and 52 age and sex-matched healthy volunteers were provided by the same protocol. We analysed the components of the gut microbiota in feces via 16S rRNA next-generation sequencing, and evaluated alpha and beta diversities. Demographic, laboratory, and medication data of SLE patients were obtained through medical records, and Pearson correlation analysis was performed to analyse the association between disease activity and gut microbiota.

Results: We observed a significant decrease in species richness in the beta diversity analysis by NMDS plots compared to controls in the SLE group. Compared with SLE and healthy controls (HCs), significant differences were found at phylum, genus, species levels in the taxonomic composition. At the species level, there were 7 species with a significantly higher relative abundance and 7 species with a lower relative abundance in the SLE group compared to the HCs, of which the reduction of *Faecalibacterium prausnitzii* and *Prevotella copri* ($p = 0.001$ and $p = 0.001$, respectively) played an important role in SLE. Pearson correlation analysis suggested that *Faecalibacterium prausnitzii was* positively correlated with complement 3 and complement 4 ($r = 0.44$ and $r = 0.49$, respectively), and *Prevotella copri* was positively correlated with total lymphocytes ($r = 0.45$).

Conclusion: There was a significant difference in the composition and diversity of gut microbiota between SLE patients and healthy controls in Korean population. In particular, *Faecalibacterium prausnitzii* and *Prevotella copri,* which are greatly reduced in patients with SLE, are expected to provide potential targets for new treatment.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0142 AVAILABLE EVIDENCE ON RENAL FIBROSIS SERUM BIOMARKERS

Keywords: Organ damage, Biomarkers, Kidneys

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Background: Renal fibrosis is the main biological mechanism underlying chronic kidney disease (CKD), representing a point of no return of tissue damage and dysfunction. The best tool clinicians can use to address the extent of renal fibrosis at any level (glomeruli, tubule-interstitium, vasculature) is kidney biopsy that, despite its overall safety, remains an invasive procedure showing some shortcomings. The identification of novel non-invasive biomarkers would be of fundamental importance to improve patients' diagnosis, management and responsiveness to therapy.

Objectives: To investigate the recent evidence supporting the use of available serologic biomarkers to evaluate the degree of kidney fibrosis.

Methods: We systematically reviewed the available evidence on serological biomarkers associated with renal fibrosis evaluated in patients suffering from CKD. Inclusion criteria were as follow: a) studies including at least 25 patients; b) published in the last five years; c) presenting clinical related data (not just *in vitro* analysis).

Results: The literature search identified 29 eligible studies according to the inclusion criteria. A total of 65 different biomarkers were evaluated in patients' serum and a statistically significant association has been found between 42 of them and/or other fibrotic biomarkers/histopathological findings. Among these, the most frequently tested were: MCP-1 (4/29=13.8%), KIM-1 (3/29=10.3%), MMP-7 (3/29=10.3%), Pro-C3 (3/29=10.3%), Pro-C6 (3/29=10.3%), TNFR-1 (3/29=10.3%), and TNFR-2 (3/29=10.3%). 14 studies out of 29 (48.3%) compared the circulating biomarkers of interest to findings from kidney biopsy (Table 1), while 15/29 (51.7%) compared them to other biomarkers presumed to have a role in CKD and fibrosis according to the literature. When focusing on the first group, the following biomarkers were associated with fibrosis: MMP-7, C3M, Pro-C6, Klotho, HE4, miR-181, PTX-2, LOX, CDH11, SMOC2, PEDF, RelB, ETP, NGAL, cystatin C, TGF-β1, TGF-β2, TGF-β3, BMP-7, uromodulin, and DKK-3. Interestingly, among those biomarkers associated with fibrosis in the overall cohort of patients included, only MMP-7 and Pro-C6 maintained this association with biopsy-proven renal fibrosis.

Conclusion: The current evidence on potential novel biomarkers to assess kidney fibrosis is still very scattered. Probably, the idea of a panel combining different biomarkers, rather than the employment of a single one, could be the best path to follow in order to capture the high complexity characterizing renal fibrotic process, deeply impacting on clinical practice by improving prevention, diagnosis, and management.

Biomarkers Tested	Significant Biomarkers	Fibrosis grade assessment
MMP-7	MMP-7	MEST-C (Oxford classification)
C3M, Pro-C3, C4M, C5M, Pro-C6, C6M	C3M, Pro-C6	Not specified
Klotho	Klotho	% of glomeruli affected by segmental or global glomerulosclerosis • Degree of foot process effacement assessed based on the % of evaluated areas • IFTA evaluated semi-quantitatively according to the proportion of the cortical area involved • Intimal thickening assessed as the % of narrowing lumen of most severely affected blood vessel
HE4	HE4	Banff classification
miR-181	miR-181	Not specified
PTX-2	PTX-2	Not specified
LOX	LOX	Not specified
CDH11, SMOC2, PEDF, MGP, TSP2	CDH11, SMOC2, PEDF	IFTA was graded as involvement of <10%, 11%–25%, 26%–50% or>50% of total cortical volume.
RelB, HE4	RelB, HE4	Not specified
ETP	ETP	MEST-C (Oxford classification)[66], Banff classification
Pro-C3, Pro-C6	Pro-C6	• % of interstitial fibrosis • % of tubular atrophy • Interstitial mononuclear cell infiltration
NGAL, cystatin C, TGF-β1, TGF-β2, TGF-β3, BMP-7	NGAL, cystatin C, TGF-β1, TGF-β2, TGF-β3, BMP-7	Not specified
Uromodulin	Uromodulin	Areas with fibrosis were determined at 5% level for each visual field and 1% level for averaged values.
DKK-3	DKK-3	ISN/RPS

Acknowledgements: None.

Disclosure of Interests: None Declared.

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AB0143 **VORINOSTAT IMPROVES THE PATHOGENESIS OF SLE MODEL MICE BY SUPPRESSING IFN-I AND TLR7/8 SIGNALS**

Keywords: Systemic lupus erythematosus

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Background: SLE is a systemic autoimmune disease caused by impaired innate and acquired immune tolerance, resulting in increased Type I IFN (IFN-I) and aberrant B cell development, in which cGAS and TLR 7/8 signaling play critical roles. TLR7/8 and cGAS signal is activated due to the overresponse to nucleic acid derived from impaired clearance of apoptotic cells, which leads to increased IFN-I production. Activation of TLR7/8 signaling also leads to the development of abnormal B cell populations, including short-lived plasma blasts, double negative B cells (DNB), and active native B (NAB). It suggests that signaling pathway via TLR7/8 and cGAS would be a good therapeutic target for SLE. Therefore, we screened agents that inhibit the induction of interferon-stimulated genes (ISGs) by LPS, R848 or cGAMP stimulation using an approved drug library and found that vorinostat inhibits ISG induction upon cGAMP and LPS stimulation.
Objectives: The purpose of this study is to elucidate the mechanism by which vorinostat suppresses IFN-I production and to demonstrate that vorinostat improves the severity of the disease phenotype in SLE-prone mice.
Methods: We investigated the effect of vorinostat on the expression and phosphorylation of TBK1, IRF3, IRF5, and IRF7, upon LPS or cGAMP stimulation, as well as on the in vitro differentiation of human B cells into plasma cells by a culture medium containing R848. Additionally, the effect of Vorinostat on the severity of SLE-prone mice, such as NZB/W F1 mice and SAVI mice with point mutations in STING, was also investigated.
Results: Vorinostat inhibited TBK1 phosphorylation and subsequent nuclear translocation of IRF3 and expression of IRF5 and IRF7. Consequently, the expression of IFN-β and ISGs were suppressed. Additionally, differentiation of human B cells cultured in R848-containing medium into plasma cells was inhibited in the presence of vorinostat. Furthermore, vorinostat improved the disease severity of NZB/W F1 mice, including survival, proteinuria, and glomerulonephritis, and decreased autoantibody titer and TLR7 expression. Vorinostat also ameliorated the lung inflammation and fibrosis, and interstitial nephritis in SAVI mice by inhibiting the ISG expression.
Conclusion: We found vorinostat ameliorates the disease severity of SLE prone mice by inhibiting IFN-I production and pathogenic B cell development via suppressing the downstream signal of TLR7/8 and cGAS. This finding represents a new therapeutic candidate for SLE.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2874

AB0144 **PHARMACOLOGICAL CHARACTERIZATION OF GLPG3667, A SELECTIVE TYK2 INHIBITOR, SUPPORTS DEVELOPMENT IN DERMATOMYOSITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS**

Keywords: Myositis, Targeted synthetic drugs, Systemic lupus erythematosus

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Background: Tyrosine kinase 2 (TYK2) is an intracellular kinase that transduces signalling from type 1 interferons (IFN), interleukin (IL)-12/ IL-23 and the IL-10 family of cytokines. Genetic analyses show an association of TYK2 variants with risk of inflammatory and autoimmune diseases. In addition, clinical data obtained with deucravacitinib (a TYK2 selective inhibitor) in SLE patients suggest that inhibition of TYK2 could be beneficial to patients with diseases driven by type I IFN such as systemic lupus erythematosus (SLE) and dermatomyositis (DM).
Objectives: We describe here GLPG3667, a TYK2 inhibitor in development for treatment of DM and SLE.
Methods: Potency and selectivity of GLPG3667 on TYK2 was assessed using radioactive, luminescent and fluorescent biochemical assays. Peripheral blood mononuclear cells (PBMC) and human whole blood assays for various Janus kinases (JAK)-dependent pathways were performed to assess GLPG3667 potency and selectivity, using flow cytometry or ELISA. GLPG3667 pharmacological activity was investigated in a psoriasis mouse model driven by IL-23. In healthy human volunteers (NCT04097938), pharmacodynamic activity of GLPG3667 was evaluated by measuring signal transducer and activator of transcription (STAT) phosphorylation using flow cytometry. Selectivity was assessed by analysing the impact of GLPG3667 on IFNα, IL-2 and granulocyte-macrophage colony-stimulating factor (GM-CSF) pathways. Biological effects of orally administered GLPG3667 in humans were assessed using transcriptomic analysis of blood cells after in vivo IFNα (1 million IU of Intron-A) challenge in healthy volunteers.
Results: Biochemical assays showed that GLPG3667 displayed a nanomolar potency on TYK2 with a >3-fold selectivity over the other JAK kinases. In human PBMC activated with phorbol m12-myristate 13-acetate and ionomycin calcium salt, GLPG3667 showed comparable potency (around 50 nM) on the IFNα and IL-23 pathways. Potency of GLPG3667 was >14-fold and >19-fold higher in the IFNα pathway vs the IL-2 and GMCSF pathways in human PBMC and whole blood, respectively. In mice, dermal ear inflammation driven by IL-23 was prevented by GLPG3667 with a minimal effective dose of 3 mg/kg given orally once daily. This effect was associated with a decrease in neutrophil infiltration and STAT3 phosphorylation at sites of inflammation. In human healthy volunteers, GLPG3667 completely inhibited IFNα-induced STAT1 and STAT3 phosphorylation but did not impact IL-2- or GM-CSF-induced STAT5 phosphorylation. GLPG3667 strongly inhibited the expression of IFN-response genes induced by in vivo IFNα challenge in healthy human subjects.
Conclusion: GLPG3667 demonstrated selectivity for TYK2 relative to the three other JAK family members in biochemical and cellular assays, and in human whole blood assays ex vivo and in vivo during a phase 1 study in healthy human volunteers. Pharmacological effects of GLPG3667 were demonstrated in a mouse model of psoriasis driven by IL-23 and in human healthy volunteers challenged with IFNα. These data support the development of GLPG3667 in autoimmune diseases driven by type I IFN such as DM and SLE.
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Disclosure of Interests: Rohit Aggarwal Consultant of: Mallinckrodt, Octapharma, CSL Behring, Bristol Myers-Squibb, EMD Serono, Kezar, Pfizer, AstraZeneca, Alexion, Argenx, Boehringer Ingelheim, Corbus, Janssen, Kyverna, Roivant, Merck, Galapagos, Actigraph, Abbvie, Scipher, Horizontal Therapeutics, Teva, Biogen, Beigene, ANI Pharmaceutical, Nuvig, Capella, CabalettaBio, Grant/research support from: Mallinckrodt, Pfizer, Bristol Myers-Squibb, Q32, EMD Serono, Janssen, Boehringer Ingelheim, Eric F. Morand Speakers bureau: AstraZeneca, Consultant of: AbbVie, Bristol Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen, Merck Serono, UCB, Amgen, Biogen, CSL, Neovacs and Wolf Biotherapeutics, Grant/research support from: AstraZeneca, AbbVie, Bristol Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen, Merck Serono, UCB, Roland Blanque Employee of: Galapagos SASU, Kenji Shoji Employee of: Galapagos SASU, Mia Jans Employee of: Galapagos NV, Florence Marsais Employee of: Galapagos SASU, Laetitia Furio Employee of: Galapagos SASU, Maikel Colli Employee of: Galapagos NV, Stephanie Lavazais Employee of: Galapagos SASU, Celine Cottereaux Employee of: Galapagos SASU, Christelle David Employee of: Galapagos SASU, Nicolas Houvenaghel Employee of: Galapagos NV, Isabelle

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AB0145 GENETIC EVIDENCE REVEALS A CAUSAL ROLE OF BLOOD LEUKOCYTE COUNTS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus

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Background: Blood leukocyte counts are important biomarkers for the onset of systemic lupus erythematosus (SLE)[1-3]. However, the causal relationship is unclear.
Objectives: We implement a two-sample Mendelian Randomization (MR) analysis to investigate the potential association.
Methods: The summary statistics of blood leukocyte counts were available from public databases (n=172435)[4]. The SNPs related to SLE risk were extracted from a large SLE GWAS with 5201 cases and 9066 controls of European ancestry[5]. All genetic variants significantly associated with blood leukocyte counts ($p<5\times10^{-8}$) were used as instrumental variables (IVs). Then, the linkage disequilibrium (LD) was excluded (distance threshold = 10,000 kb, r^2 = 0.001). In this study, the inverse variance weighted (IVW) method, the MR-Egger method, and the weighted median (WM) were used to estimate the causal effect of the blood leukocyte counts and SLE. In addition, Cochran's Q test, MR pleiotropy residual sum and outlier (MR-PRESSO), and leave-one-out analysis were implemented as sensitivity tests.
Results: We selected 119 independent SNPs as IVs in the MR analysis of total WBC. Higher blood leukocyte counts were associated with a lower risk of SLE (OR:0.629, 95% CI: 0.436-0.907, P: 0.013) by IVW method (Figure 1). However, the results of Cochrane Q statistics showed heterogeneity ($p<0.05$). Therefore, we used the random-effects model[6].
Conclusion: Our study predicted genetically that individuals with lower blood leukocyte counts face a higher risk of SLE, which was consistent with the previous observational studies.
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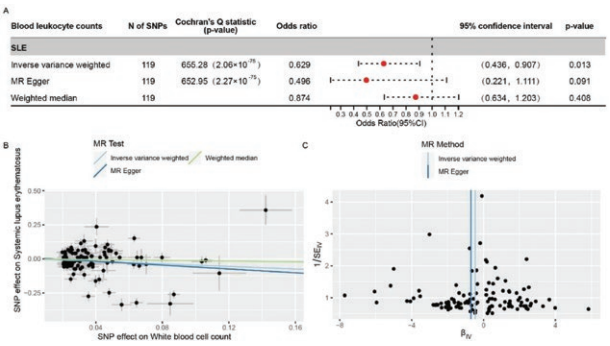


Figure 1: (A) Forest plot for MR estimates for causal effect of blood leukocyte counts on SLE from different methods. (B) Scatter plots for MR analyses. (C) Funnel plot for MR analyses. SLE, systemic lupus erythematosus.

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AB0146 A SINGLE-CELL AND SPATIALLY RESOLVED ATLAS OF LUPUS NEPHRITIS

Keywords: Systemic lupus erythematosus, Kidneys, -omics

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Background: Systemic lupus erythematosus is a typical autoimmune disease with multiple clinical complications. Lupus nephritis (LN) affects half of the patients and is the leading cause of both death and morbidity[1]. Although previous studies have reported that a variety of cell types are locally present in the kidneys of patients with lupus nephritis[2,3], the specific mechanism of pathogenesis, especially considering the spatial content in LN, remains unknown.
Objectives: To investigate the pathways and gene expression changes in the kidneys of patients with lupus nephritis in a spatial context, we conducted an in-depth study of kidney tissues using multi-omics and spatial transcriptomics.
Methods: We included multi-omics and spatial transcriptome samples from ten patients and five controls. The integrative analysis identifies key pathways and potential disease-associated driver genes in the pathogenesis of lupus nephritis. Finally, heritability enrichment identifies genetic associations of endothelial and fibroblast alterations.
Results: Multimodal data integration enabled us to assess the composition of renal cell types at higher resolution and gain insight into changes in the nephritis transcriptome and epigenome by identifying injury, inflammation, and fibrotic changes in different histoarchitectural disease states. We identified and validated disease-specific fibroblast and endothelial cell states of major cell types and analyzed the disease-associated alterations in their spatial context. Finally, genetic association analysis identified heritability enrichment and specific transcription factor alterations in fibroblasts, endothelial cells, and immune cells.
Conclusion: Our data elucidate key pathways and genetic alterations in human kidney tissue following the onset of lupus nephritis and correlate such alterations with genetics, provide a comprehensive molecular map of lupus nephritis, and present guidance for advanced mechanistic and therapeutic studies.
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Disclosure of Interests: None Declared.
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Systemic sclerosis, myositis and related syndromes - aetiology, pathogenesis and animal models

AB0147 ANTI-FIBROTIC EFFECTS OF MT-5562, A NOVEL POTENT SELECTIVE AUTOTAXIN INHIBITOR, IN PRECLINICAL STUDIES: CLUES TO TREAT SKIN AND LUNG FIBROSIS IN SYSTEMIC SCLEROSIS

Keywords: Animal models, Systemic sclerosis

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Background: Autotaxin (ATX) is the lysophosphatidic acid (LPA)-producing enzyme. Targeted small-molecule therapies to ATX have been shown to be potentially effective in systemic sclerosis (SSc) treatment, but the clinical benefit and safety of selective inhibition remains unclear.

Objectives: To explore the potential of MT-5562, a novel oral selective inhibitor of ATX, as a therapeutic agent for SSc by evaluating its efficacy and toxicity in preclinical models.

Methods: MT-5562 and a free form of MT-5562 (MT-5562F) were evaluated, and other ATX inhibitors (ziritaxestat and cudetaxestat) were used as comparators in the present study. In vitro ATX activity was measured by choline assay using fluorescent substrate Amplex UltraRed. The effects of MT-5562F on IL-6 and connective tissue growth factor (CTGF) production in TGF-beta stimulated dermal fibroblasts from healthy donors and lung fibroblasts from idiopathic pulmonary fibrosis patients were evaluated in vitro. Cell toxicity was evaluated in human pulmonary alveolar epithelial cells (HPAEpiC), human lung fibroblasts from idiopathic pulmonary fibrosis patients (DHLF-IPF) and lung microvascular endothelial cells (HMVEC-L) by live cell counting. The plasma concentration of MT-5562F and LPA production were evaluated in C57BL/6 mice. The effects of MT-5562F on skin and lung fibrosis were evaluated in murine SSc models induced by bleomycin (BLM).

Results: MT-5562F, ziritaxestat, and cudetaxestat inhibited the enzyme activity of human ATX with IC50s of 0.45, 49.3, and 2.77 nmol/L, respectively. MT-5562F and ziritaxestat inhibited the enzyme activity of mouse ATX with IC50s of 0.15 and 10.9 nmol/L, respectively. MT-5562F concentration-dependently inhibited TGF-beta-induced IL-6 and CTGF production in human dermal fibroblasts from healthy donors and lung fibroblasts from IPF patients. MT-5562 showed minimal effects on cell viability using lung structural cells such as alveolar epithelial cells (HPAEpiC), pulmonary fibroblasts (DHLF-IPF) and endothelial cells (HMVEC-L) even at the maximum dissolved concentration (60 µmol/L). On the other hand, ziritaxestat showed more cytotoxic effects than MT-5562 on cell viability in vitro. MT-5562 didn't show any specific off-target inhibition on receptor binding and kinase profiling assays. In vivo, MT-5562F and ziritaxestat (10, 30 mg/kg) dose-dependently reduced plasma LPA concentration in mice according to the plasma drug exposure and mouse ATX inhibitory activity, and MT-5562F showed more sustained effects compared with ziritaxestat. Therapeutic treatment with MT-5562F (30, 60 mg/kg, once daily) significantly suppressed skin thickening and the numbers of myofibroblasts in pre-established subcutaneous BLM-induced skin fibrosis model. Therapeutic treatment with MT-5562F (30, 60 mg/kg, twice daily) and ziritaxestat (30 mg/kg, twice daily) showed significant reduction of the average Ashcroft score and collagen severity score in the BLM-induced lung fibrosis model together with the reduction of the biomarker LPA. All doses of MT-5562F significantly reduced the expression of inflammatory and fibrotic mediators such as C-reactive protein, IL-6R-alpha, epidermal growth factor receptor (EGFR) and periostin in bronchoalveolar lavage fluid.

Conclusion: Our results suggest that MT-5562 is a selective and potent ATX inhibitor. It is expected to be a safer compound comparing other ATX inhibitors under development, and it may offer a good option to treat lung and skin fibrosis in SSc.

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AB0148 IDENTIFICATION OF CANDIDATE MIRNA MOLECULES AS BIOMARKERS IN INTERSTITIAL PNEUMONIA WITH AN UNDERLYING AUTOIMMUNE DISEASE. A DISCOVERY COHORT FROM THE NEREA PROJECT

Keywords: Biomarkers, Lungs, -omics

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Background: A group of patients with chronic interstitial pneumonia (IP) have an underlying autoimmune disease -typically a connective tissue disorder (CTD)-. In turn, autoimmune-related IP (AIP) processes are highly heterogenous as regards to their clinical presentation, extra-pulmonary features and risk of fibrotic progression. A better understanding of clinically-relevant disease phenotypes is needed in order to tailor therapeutics.

Objectives: MicroRNA are short non-coding RNAs which orchestrate multiple biological processes by regulating mRNAs via cleavage or translational repression. Circulating levels of miRNA molecules provide excellent information about pathogenic processes in complex diseases, help identify specific disease subgroups and therapeutic targets.

Methods: We have conducted NGS of small-noncoding RNA in patients with AIP enrolled in the NEREA register of AIP and being followed at any of the Special Multidisciplinary Clinics from the participating Centers. The study population comprised 29 subjects (24 cases, 5 controls; 93% women, 87% newly diagnosed patients). Sixty seven % of the patients were diagnosed with interstitial pneumonia with autoimmune features (IPAF) and all patients had a pulmonary dominant disease at the time of blood sampling. QIAGEN genomic services and a NextSeq (Illumina Inc.) instrument were used. For statistical comparisons, the sample was further segregated according to clinical diagnosis, radiographic pattern, evidence of fibrosis in HRCT, relative levels of Krebs von den Lungen (KL-)6 and type of autoantibodies (classified into those potentially-associated to vasculopathy, the ones typically associated to rheumatoid arthritis, and non-specific ANA). The association was considered true for a p level < 0.02 and a low false discovery

rate (FDR), p < 0.1. DIANA tools including the Tarbase v8.0 were used to assess functional pathways with GO and KEGG analysis.
Results: As compared to the healthy controls, patients with IP showed higher levels of let-7i-5p (1.9-fold, p <0.01), miR-483-5p (3.5-fold, p <0.0005) and the miR-320 family. Fibrotic disease was associated to an up-regulation of the let-7 cluster, miR-151a-5p (2.04-fold, p < 0.01), miR-185-5p (2.4-fold, p 0.011), miR-320a-3p (2-fold, p 0.016), miR-320e (2-fold, p 0.016) and miR-423-5p (1.9-fold, p < 0.01). Besides, there was an up-regulation of both of let-7e-5pb levels (3.55-fold, <p 0.005) and miR-483-5p (4.78-fold, p <0.005) in patients with high KL6. On the other hand, patients with vasculopathy-related autoantibodies had a characteristic microRNA signature, with an up-regulation of the miR-10 and miR-30 families as well as levels of miR-320b (2.77-fold, p <0.005), miR-320c (3.71-fold, p < 0.005) and miR-320d (3.84-fold, p <0.005), in addition to miR-483-5p (4.2-fold, p < 0.005), miR-675-5p (7.74-fold, p < 0.005) and miR-1283 (7.40-fold, p < 0.005). The cluster dendogram showed association between miR-10a, miR-10b, miR320c and miR320d regulated processes, with an enrichment in the Hippo signalling, the TFGβ pathway and the fatty acid biosynthesis.
Conclusion: Or data suggests a common miRNA signature in patients with AIP, which includes 2 miRNA molecules, miR-483-5p and miR-320a, which have already been identified in in patients with CTD and IP. In addition, a specific microRNA pattern was found in those patients with a "SSc-like" autoantibodies, pointing to the existence of particular driving processes in this subtype of disease. Confirmation of these findings and validation of targets in a larger sample is warranted in order to advance to a pathophysiologic classification of AIP.
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Disclosure of Interests: None Declared.
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AB0149 THE EXPRESSION AND REGULATION OF NOX4 IN DAMAGED MYOBLASTS IN INFLAMMATORY MYOPATHY

Keywords: Myositis, Adaptive immunity

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Background: Idiopathic inflammatory myopathy (IIM) is a rare autoimmune disease characterized by proximal muscle weakness, elevated muscle enzymes, inflammation in the muscle. If the muscle is already damaged in IIM, it may not regain full strength even after treatment. Also the mechanisms that contribute to muscle weakness in myositis are currently unknown. Nox is the main source of ROS production in various cells types, and is also the source of mitochondria ROS. Excessive expression of Nox4 is characteristic of sclerosis, fibrosis, and cardiac related diseases, and it had been reported that knock down of Nox4 lowers the production of superoxide and hydrogen peroxide. However, the effect of Nox4 in myositis has not been reported.
Objectives: We investigated the expression and role of Nox4 in damaged myoblasts of myositis.
Methods: Myoblasts were isolated from IIM patients who underwent muscle biopsy in Seoul National University Hospital between February 2019 and February 2021. Skeletal muscle cell(SMC) was purchased. Myoblasts and SMCs were treated with cytokine mixture {interferon gamma(IFN-γ), interleukin(IL)-6, IL-15} or PBS for 30 minutes. The expression of Nox4, MyoD and myosin heavy chain(MYH) in myoblast and myotube was analysed by Western blot. For inhibition of Nox4, GKT137831(inhibitor of Nox4) was treated before the cytokine stimulation.
Results: Myoblasts from IIM patients did not differentiate into myotubes like healthy myoblasts suggesting impaired muscle regeneration. Myoblasts from IIM patients express higher level of Nox4 compared to healthy myoblasts. When treated with cytokine mixture(IFN-r, IL-6, IL-15), healthy myoblasts or SMC mimicked inflammatory myositis and showed increased expression of Nox4 and decreased expression of MYH similar to myositis phenotype. Nox4 inhibitor suppressed Nox4 expression and MyoD overexpression in inflammatory myoblasts.
Conclusion: We showed that Nox4 expression is increased in myoblasts from IIM patients and is associated with impaired muscle regeneration. Nox4 inhibition attenuated Nox4 and MyoD overexpression in inflamed myoblasts.
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AB0150 ISOLATION AND PHENOTYPIC CHARACTERIZATION OF CIRCULATING EXTRACELLULAR VESICLES IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Keywords: Myositis, Cell biology

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Background: Idiopathic Inflammatory myopathies (IIM) encompass a group of heterogeneous systemic autoimmune diseases for which biomarkers are needed. Extracellular vesicles (EVs) are cell-derived nanoparticles regulating several biological functions[1] and likely involved in the pathogenesis of autoimmune diseases[2], yet their role in IIM was not investigated thoroughly.
Objectives: 1) to develop an effective and reproducible laboratory method to isolate EVs from venous blood; 2) to trace any prominent EVs cellular origin; 3) to perform a quantitative and comparative evaluation of EVs between IIM patients and healthy donors (HD) and across distinct IIM subsets.
Methods: We enrolled adult (≥18 years) consecutive IIM patients (EULAR 2017 criteria) and sex- and age-matched HD. Clinical evaluation of IIM patients was performed by an expert rheumatologist. A venous blood sample (5 mL) was collected from each participant and processed through size exclusion chromatography (SEC) and subsequent ultra-filtration (UF). Particles morphology was observed via transmission electron microscopy (TEM). Nanoparticle tracking analysis (NTA) was performed to evaluate the concentration of EV. The characterization of EV surface markers was conducted through imaging flow cytometry (IFC). Comparisons were carried out using Student's t-test or one-way ANOVA with multiple comparisons.
Results: Sixty-five consecutive IIM patients (dermatomyositis (DM) n=19; polymyositis (PM) n=8; inclusion body myositis (IBM) n=2; anti-synthetase syndrome (ASyS) n=17; cancer-associated myositis (CAM) n=16; unspecified n=3) and 65 HDs were included. Isolated EVs concentration values reached 10^{10}EV/mL. IFC showed surface expression of EVs tetraspanins CD63, CD81, CD9, and integrin CD11c and highlighted a predominance of CD19+ EVs vs. CD3+ EVs in both IIM and HDs (p<0.0001 for both). TEM images showed intact small particles with the typical EVs-"cup-shape" morphology. NTA showed a significantly higher mean concentration of circulating EVs in IIM vs. HD (mean [EVs/mL] ± SD $1.71x10^{10}$ ± $1.29x10^{10}$ vs. $1.31x10^{10}$ ± $7.17x10^{9}$, p=0.031). Across IIM subsets, the highest EVs levels were found in CAM vs. HD ($2.35x10^{10}$ ± $2.20x10^{10}$ vs. $1.31x10^{10}$ ± $7.17x10^{9}$, p=0.0026) and vs. no-CAM patients ($2.35x10^{10}$ ± $2.20x10^{10}$ vs. $1.51x10^{10}$ ± $7.51x10^{9}$, p=0.0206). Patients in clinical remission (n=26, 40%) displayed higher EVs levels than active patients ($2.13x10^{10}$ ± $1.60x10^{10}$ vs. $1.46x10^{10}$ ± $1.02x10^{10}$, p=0.0452) (**Figure 1)**. Concerning treatment, patients on glucocorticoids (GC) alone (n=20, 30.7%) displayed higher EVs levels than patients receiving GC plus immunosuppressants (IS) ($2.23x10^{10}$ ± $1.99x10^{10}$ vs. $1.49x10^{10}$ ± $7.25x10^{9}$, p=0.0341). EVs concentration was significantly decreased in patients receiving rituximab (RTX) vs. other IS ($9.63x10^{9}$ ± $3.26x10^{9}$ vs. $1.96x10^{10}$ ± $1.46x10^{10}$, p<0.001).
Conclusion: The combination of SEC and UF is a reliable approach to obtain intact EVs with preserved morphology and good purity from blood, as confirmed by diverse characterization techniques. The prevalence of CD19+ circulating EVs might indicate B cells as their main origin. Different EVs concentrations discriminate IIM from HD and may provide distinction among specific IIM subsets and treatment response.
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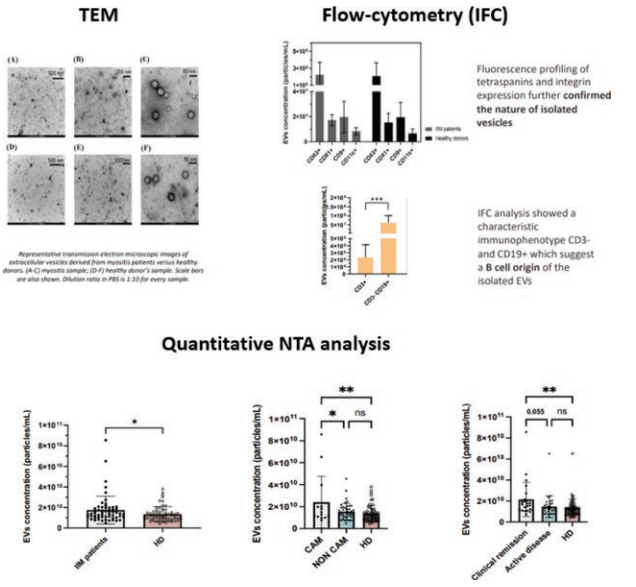


Figure 1. Representation of EVs shape (TEM), surface markers (IFC) and quantitative analysis (NTA) across IIM susbets

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AB0151

DYSFERLIN AS A POTENTIAL ANTI-FIBROTIC PROTEIN INVOLVED IN TGF-B/FOSL-2/AUTOPHAGY CROSSTALKING IN CARDIAC FIBROBLASTS UNDER IMMUNOFIBROTIC CONDITIONS

Keywords: Heart, Cell biology, Cardiovascular disease

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Background: Myocardial fibrosis, ultimately leading to heart failure (HF), represents a point of convergence for most cardiac disorders. Heart involvement is a common finding in autoimmune rheumatic patients. The TGF-β-FOSL-2-autophagy axis controls cardiac fibroblast differentiation, driving the progression of profibrotic changes [1]. Limited evidence suggests the pro-regenerative potential of adult cardiac fibroblasts directed to restrain the excessive profibrotic response and support tissue regeneration following myocardial injury.
Objectives: To identify the molecular basis of fibroblast-mediated compensatory response to myocardial fibrosis in adult heart.
Methods: Adult cardiac fibroblasts were isolated from the left atria of patients undergoing heart transplantation due to end-stage HF caused by inflammatory dilated cardiomyopathy (n=5) and from unaffected myocardium of brain-dead donors (Ctrl, n=5). Protein quantification was performed using liquid chromatography tandem-mass spectrometry (LC–MS/MS), and the data analysis was conducted with MaxQuant v1.6.2.3 software. The Enrichr tool was used for pathway enrichment analysis [2]. Selected gene knockdown was achieved through Lipofectamine 2000-mediated siRNA transfection of human foetal cardiac fibroblasts (HCFs, Sigma), untreated or stimulated with TGF-β (10 ng/mL, 48-72h). Chosen gene and protein expression was evaluated by RT-qPCR and Western Blot, respectively. Cell viability was determined with PrestoBlue HS reagent, and ATP levels were measured with CellTiter-Glo assay 48h after transfection.
Results: Quantitative proteomic analysis of adult cardiac fibroblasts revealed 14 differentially expressed proteins (adj. p<0.05) in HF compared to Ctrl. The identified proteins belong to biological pathways mainly involved in ECM remodeling and associated with several pathologies, such as atherosclerosis, muscular dystrophy and myocardial ischemia. The most upregulated protein in HF fibroblasts was dysferlin (DYSF, log2FC=5.78, adj. p<0.005), which is known to promote sarcolemma repair in skeletal muscle fibres and cardiomyocytes. Further *in vitro* study showed that TGF-β stimulation significantly upregulates DYSF gene (n=4, p<0.001) and protein (n=3, p<0.001) expression in cultured HCFs. *DYSF* silencing upregulated *COL1A1* expression in untreated (n=4, p<0.05) and TGF-β-stimulated (48h, n=4, p<0.05) HCFs. On the protein level, *DYSF* knockdown upregulated the profibrotic transcription factor FOSL-2 in untreated HCFs (n=9, p=0.004) and following 72h of TGF-β stimulation (n=9, p<0.001). In turn, *FOSL-2* silencing in HCFs significantly upregulated DYSF protein level (n=5, p<0.0001) after 72h of TGF-β stimulation, suggesting a mutual regulation between DYSF and FOSL-2. Further analysis of autophagy-related proteins revealed that *DYSF* silencing increases LC3BII expression (n=6, p<0.05) and downregulates P62 (n=6, p=0.01) in TGF-β-stimulated HCFs. Finally, we observed reduced viability of cells subjected to *DYSF* knockdown in both untreated (n=4, p<0.01) and TGF-β-stimulated (n=4, p<0.05) conditions. *DYSF* silencing was also associated with decreased ATP production in TGF-β-treated HCFs (n=6, p=0.05).
Conclusion: Proteomic profiling of human cardiac fibroblasts supported by *in vitro* analysis identified DYSF as an anti-fibrotic protein compensatory upregulated under immunofibrotic conditions and involved in TGF-β-FOSL-2-autophagy axis regulation. This newly proposed candidate may serve as a potential therapeutic target for stimulating fibroblast-induced myocardial regeneration.

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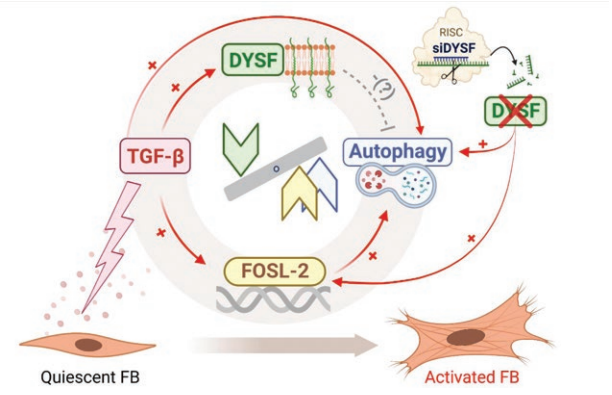


Figure 1. Graphical abstract.

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Disclosure of Interests: Ievgeniia Kocherova: None declared, Elena Pachera: None declared, Daria Nurzynska: None declared, Franca Di Meglio: None declared, Oliver Distler Speakers bureau: Bayer, Boehringer Ingelheim, Janssen, Medscape, Consultant of: 4P-Pharma, Abbvie, Acceleron, Alcimed, Altavant Siences, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos, Glenmark, Horizon, Inventiva, Kymera, Lupin, Miltenyi Biotec, Mitsubishi Tanabe, MSD, Novartis, Prometheus, Redxpharna, Roivant, Sanofi and Topadur, Grant/research support from: Kymera, Mitsubishi Tanabe, Boehringer Ingelheim, Przemyslaw Blyszczuk: None declared, Gabriela Kania: None declared.
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AB0152

URIC ACID IN SYSTEMIC SCLEROSIS-RELATED PULMONARY ARTERIAL HYPERTENSION:INNOCENT BYSTANDER OR COVERT ACCOMPLICE?

Keywords: Systemic sclerosis, Cardiovascular disease, Cytokines and chemokines

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Background: When uric acid levels increase to reach the supersaturation level (>70 μg/ml), it transforms into its crystalline form and binds to surface lipids on immune cells. Phagocytes ingest this cellular debris and thereby receive a 'danger signal' from uric acid and are stimulated to mature and become immunostimulatory [1,2].
Objectives: Considering uric acid helps to predict the development of pulmonary arterial hypertension (PAH) in systemic sclerosis (SSc) (3), we aim to establish whether uric acid induces a pro-inflammatory response in SSc in general and in SSc-PAH in particular.
Methods: Peripheral blood mononuclear cells (PBMCs) were harvested from 16 SSc-PAH patients. PMBCs were isolated from 32 age- and sex-matched SSc-nonPAH patients with similar skin distribution and autoantibodies. Finally, PMBCs from 5 idiopathic PAH (iPAH) patients and 16 age- and sex- matched healthy controls were collected. Cells were treated with or without uric acid in

soluble form for 24 hours, and subsequently cytokine production was measured by Luminex, and mRNA levels were assessed using qPCR.

Results: Baseline expression of interleukin (IL)-1β and IL-6 was similar in SSc-PAH, SSc-nonPAH, iPAH and healthy controls. On mRNA level, urid acid stimulated IL-1 and IL-6 expression in all PBMCs but IL-1 and IL-6 expression was most potently upregulated in SSc patients compared to healthy controls (a 2-fold versus an 8-fold increase respectively). However, induction of IL-1 and IL-6 expression by urid acid-stimulated PBMCs was similar in SSc-PAH and SSc-nonPAH patients. Similarly, on protein level, production of IL-1β, IL-6 and TNF-α was increased in PBMCs from SSc patients compared to iPAH patients and healthy controls. Interestingly, we observed that urid-acid stimulated PBMCs from SSc-PAH patients produced significantly more IL-1β, IL-6 and TNF-α compared to SSc-nonPAH patients.

Conclusion: In this study we demonstrate that soluble uric orchestrates an excessive inflammatory response by facilitating more enhanced IL-1β, IL-6 and TNF-α production in SSc-PAH compared to SSc-nonPAH, iPAH and healthy controls. These findings suggest that uric acid not only has a role in prediction of SSc-PAH but also contributes to the development of SSc-PAH.

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Table 1. Baseline characteristics. Values in medians (SD) or number (%). LcSSc denotes limited cutaneous SSc, DcSSc diffuse cutaneous SSc, mRSS modified Rodnan skin score, NYHA New York Heart Association, NT-proBNP N-terminal pro-Brain Natriuretic Peptide, 6MWD 6 minutes walk distance.

	SSc-PAH (n=16)	SSc-nonPAH (n=32)	Idiopathic PAH (n=5)	Healthy controls (n=16)
Age in years, mean	67.7 (10.5)	66.9 (8.9)	63 (15.8)	61.4 (9.4)
Female, n (%)	13 (81.3)	26 (81.3)	5 (100)	13 (8.3)
SSc subtype LcSSc	13 (81.3)	26 (81.3)		
DcSSc	3 (18.7)	6 (18.7)		
mRSS	4.8 (4.2)	4.7 (4.2)		
Anticentromere positive (%)	5 (31.3)	13 (40.6)		
Telangiectasias, n (%)	9 (56.3)	13 (40.6)	0	
NYHA class, n (%)				
I	0	26 (81.3)	0	
II	4 (25)	5 (15.6)	5 (100)	
III	8 (50)	1 (3.1)	0	
IV	4 (25)	0	0	
Creatinine (μmol/L)	91.4 (27.4)	76.4 (18.3)	78.2 (23.5)	
Urate (μmol/L)	0.4 (0.2)	0.3 (0.1)	0.4 (0.1)	
NT-proBNP (pg/ml)	1455 (2228.2)	129.4 (152.7)	96.6 (42.0)	
6MWD (m)	362.1 (103.5)	593 (127.8)	447.6 (42.3)	
Immunosuppression, n (%)	9 (56.3)	22 (68.8)	0	
Urate lowering treatment, n (%)	1 (6.3)	1 (3.1)	0	
Diuretics, n (%)	11 (68.8)	3 (9.4)	3 (60)	

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AB0153 GENETIC EVIDENCE SUPPORTS CAUSAL EFFECT OF GUT MICROBIOTA AND DERMATOMYOSITIS

Keywords: Genetics/epigenetics, Myositis

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Background: Recent observational research has documented that dermatomyositis (DM) has lower gut microbial diversity and a distinct taxonomic composition[1]. However, the underlying causality remains unclear.

Objectives: To explore the potential causal associations between gut microbial genera and DM, a two-sample Mendelian randomization (MR) analysis was conducted.

Methods: We selected genetic variants associated with gut microbiota traits (n = 14,306) [2]and DM (n=213,353) from genome-wide association studies (GWAS). Two-sample MR analysis was conducted to identify potential causal gut microbial genera for DM using the inverse-variance weighted (IVW) method, weighted-median, and MR-Egger regression. The sensitivity analysis was also performed to verify the robustness of the primary results of the MR analysis. Cochran's Q statistics were used to quantify the heterogeneity of instrumental variables[3].

Results: Three bacterial genera were associated with the risk of DM in the IVW method. *Ruminococcaceae* genus(id.11360) was positively associated with DM [odds ratio(OR):2.44, 95%CI:1.17-5.07], as well as for *Sutterella* genus (id.2896, OR:3.39, 95%CI:1.30-8.84). In addition, results indicated a negative association for the *Anaerotruncus* genus (id.2054, OR:0.31, 95%CI:0.11-0.88) with DM (Table 1). Moreover, the sensitive analysis excluded the influence of heterogeneity and horizontal pleiotropy. Leave-one-out analysis also suggested the results were robust.

Conclusion: This study demonstrates that the *Ruminococcaceae*, *Sutterella*, and *Anaerotruncus* are causally related to DM, providing novel insights into the gut microbiota-mediated development mechanism of DM to access more therapeutic methods.

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Table 1. Mendelian Randomization results for association between gut microbiota and DM. DM, dermatomyositis.

DM	N of SNPs	Cochran's Q statistic(p-value)	Odds ration	95% confidence interval	p-value
Anaerotruncus genus					
inverse variance weighted	13	8.083(0.697)	0.314	(0.112,0.881)	0.027
MR-Egger	13	9.067(0.705)	0.075	(0.003,1.526)	0.120
weighted median	13		0.278	(0.069,1.118)	0.075
Ruminococcaceae genus					
inverse variance weighted	22	13.54(0.809)	2.439	(1.173,5.070)	0.025
MR-Egger	22	11.34(0.879)	8.456	(1.222,58.477)	0.038
weighted median	22		2.801	(1.056,7.428)	0.1122
Sutterella genus					
inverse variance weighted	12	6.922(0.805)	3.392	(1.301,8.838)	0.012
MR-Egger	12	6.427(0.778)	14.542	(0.225,936.652)	0.236
weighted median	12		3.244	(0.851,12.363)	0.071

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0154 MENDELIAN RANDOMIZATION STUDY IMPLIES CAUSAL LINKAGE BETWEEN POLYMYOSITIS AND PHYSICAL ACTIVITY

Keywords: Myositis, Genetics/epigenetics, Self-management

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Background: Polymyositis (PM) is autoimmune myopathy characterized clinically by proximal muscle weakness, muscle inflammation, extra-muscular manifestations, and frequently, the presence of autoantibodies[1].The causal relationship between physical activity (PA) and PM remains uncertain.

Objectives: This study aimed to determine the effect of physical activity on PM.

Methods: The instrumental variables proposed SNP at the genome-wide significance threshold ($p < 5\times10^{-8}$).To mitigate collinearity between the contained SNPs, we excluded SNPs in the linkage disequilibrium (LD) (pairwise $r^2 > 0.01$). F-Statistics, above the threshold of 10, showed the result's sensitivity. Summary statistics of PM were obtained from a genome-wide association study (GWAS) meta-analysis

of the descent, including 16,380,451 cases and 213,145 controls[2].The data of PA, including accelerometer-based physical activity(APA), vigorous physical activity(VPA),moderate to vigorous physical activity (MVPA),moderate physical activity 10+ minutes(MPA10+), vigorous physical activity 10+ minutes(VPA10+) and sedentary behavior (Time spent watching television (TV), Time spent using computer and Time spent driving) were available from UK Biobank dataset. To evaluate the causal association between PA and PM, the inverse variance weighted (IVW) was conducted as the primary method. In sensitivity analyses, we used the MR-Egger method to evaluate the potential pleiotropy effects. Moreover, we also applied weighted median and MR-PRESSO to assess the presence of pleiotropy. Meanwhile, leave-one-out analysis was performed to test the influence of outlying values.
Results: We selected 313 SNPs (10 SNPs for APA,2 SNPs for VPA, 23 SNPs for MVPA, 19 SNPs for MPA10+, 13 SNPs for VPA10+, and 246 SNPs for sedentary). APA was positively associated with the risk of PM (OR 1.53 95%CI 0.03-0.82 P=0.036). MR-Egger, MR-PRESSO, and leave-one-out analysis did not indicate horizontal pleiotropy. Based on the result of IVW method, there was little evidence of causal associations of the remaining seven exposures with the risk of PM. (p > 0.05)(Figure1).

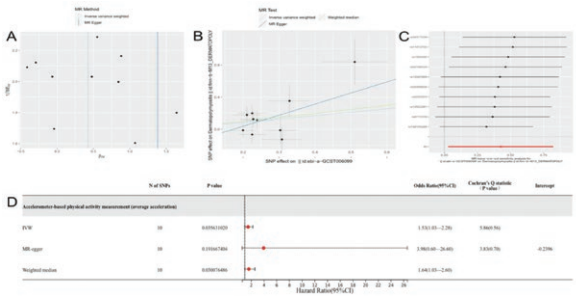


Figure 1. Mendelian randomization analysis for gene-level causality between PA, sedentary behaviors, and PM were evaluated by the odds ratio (OR) values of IVW, MR Egger, and Weighted median. Funnel plot (A), scatter plot (B), leave-one-out analysis (C), and forest plot (D) assessed that APA increases the risk of PM. MR, mendelian randomization; IVW, inverse-variance weighted method; MR-Egger, Mendelian randomization-Egger; SNP, single nucleotide polymorphisms; CI, confidence interval.

Conclusion: APA was causally associated with the risk of PM.
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Disclosure of Interests: None Declared.
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AB0155 POTENTIAL DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF ANTI-CARBAMYLATED PROTEIN ANTIBODIES IN THE SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Biomarkers, Autoantibodies

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Background: Spondyloarthritis (SpA) include a group of inflammatory rheumatic diseases with different clinical manifestations. The diagnosis of SpA is still a challenge in clinical practice, in that specific serological markers are still missing. Recently, anti-carbamylated protein antibodies (anti-CarP Ab) have been detected in patients with psoriatic arthritis (PsA) and their levels appear to be associated to disease activity [1].
Objectives: The aim of this esplorative study was to evaluate the potential role of anti-CarP Ab in the diagnosis and prognosis of peripheral enthesitis or arthritis (E/A).
Methods: Serum samples and clinical data from 91 patients with peripheral E/A, of which 43 with PsA, 8 patients with uSpa and 40 with E/A responding to disease-modifying antirheumatic drugs (DMARDs) not fulfilling ASAS classification criteria ($ASAS^-$), were collected. Anti-CarP Ab were detected by indirect ELISA. Serum anti-CarP were also determined in 35 healthy donors (HD).
Results: Anti-CarP were detected in both PsA (14%) and E/A $ASAS^-$ (5.2%) patients, being their prevalence significantly higher in PsA patients than in HD (*chi-square* p=0.019). No anti-CarP Ab were detected in uSpA. Kendall's correlation analysis showed that in the whole E/A population, anti-CarP Ab levels directly correlated with disease activity (p=0.047), plantar fasciitis (p=0.037) and family history of psoriasis (p=0.012). Anti-CarP Ab levels were also directly correlated with the presence of autoimmune thyroiditis in PsA subgroup (p=0.02), and with family history of psoriasis in E/A $ASAS^-$ subgroup (p=0.016).
Conclusion: This study suggests an association of anti-CarP Ab levels and disease activity in peripheral E/A. Whether the presence of anti-CarP Ab in E/A $ASAS^-$ may predict evolution in PsA remains to be assessed.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0156 MECHANOTRANSDUCTION VIA MYOSIN II ISOFORMS IN DEVELOPMENT OF SKIN FIBROSIS WITHIN SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Cytokines and chemokines, Skin

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Background: Skin fibrosis, the hallmark of systemic sclerosis (SSc), is a complex inflammatory process leading to excessive extracellular matrix (ECM) deposition and increased stiffness in the dermis [1]. The mechanical properties of the extracellular environment can be sensed by the cells and transformed into intracellular signalling and gene expression regulation in the process of mechanotransduction. The upregulation of mechanotransduction has been linked to the progression of fibrosis in SSc, particularly through the Rho-ROCK-dependent myosin II pathway, which activates intracellular contractility [2]. Nonmuscle myosin II itself is expressed as three isoforms (NMIIA, NMIIB, NMIIC) with common and unique functions. However, the specific role of Rho activation and distinct NMII isoforms in SSc pathogenesis is unknown.
Objectives: To investigate the role of NMII isoform regulation in the development of skin fibrosis in SSc.
Methods: The expression of NMIIA and NMIIB, as well as their activation through phosphorylation of Myosin Light Chain (MLC) were evaluated by immunofluorescence in primary fibroblasts from four SSc and four healthy donor (HD), which were stimulated with rhTGFβ. The NMII contractility was inhibited with Y-27632, a small molecule inhibitor of ROCK that phosphorylate MLC, or blebbistatin, a small molecule that inhibit NMII. The production of IL-6 and type-I collagen by fibroblasts was assessed by ELISA.
Results: We have observed a re-distribution of NMII isoforms within the intracellular contractile system and increased MLC phosphorylation in cultured SSc fibroblasts compared to HD. A similar phenotype was observed in HD fibroblasts primed with TGFβ. Treatment of TGFβ-primed HD fibroblasts with Y-27632 or blebbistatin substantially reduced IL-6 and collagen I production.
Conclusion: Our data point to an altered actomyosin cytoskeleton dynamics and force distribution in SSc fibroblasts and indicate that NMII isoforms are required for the TGFβ-dependent secretion of inflammatory cytokines and collagen deposition by fibroblasts.
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Acknowledgements: NIL.
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AB0157 SYNERGISTIC EFFECT OF AT1R-AUTOANTIBODIES AND EXTRACELLULAR VESICLES IN SSC PATHOGENESIS

Keywords: Systemic sclerosis, Innate immunity, Autoantibodies

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Background: Systemic sclerosis, a rare chronic inflammatory disease, are characterized by immune system activation, vasculopathy, and fibrosis of the body organs. Emerging evidence have so far indicated that autoantibodies (abs) directed against G protein-coupled receptors (GPCRs) particularly contribute to the SSc pathogenesis and inducethe release of inflammatory and profibrotic proteins by immune cells such as monocytes [1-3]. Increased levels of autoantibodies against the angiotensin II type 1 receptor (AT1R abs) have been found in SSc patients [4-5], which are associated with increased secretion of extracellular vesicles (EVs) [6]. Interestingly, upregulated CCL18 levels could be associated with AT1R-EVs in SSc patients [8]. EVs play an important role in the pathogenesis of diseases by packing and transfer of AT1R to different tissues and immune cells, exemplary shown by activated cardiomyocytes leading to higher responsiveness to angiotensin II of recipient cells and vessels [9]. Taken together, the importance of studying anti-GPCR-abs together with GPCR-EVs in the pathogenesis of SSc becomes evident [10].
Objectives: Here we decipher the immune response of peripheral blood monocytes mediated by anti-AT1R-abs and EVs, in the pathogenesis of SSc.
Methods: Monoclonal AT1R ab (AT1R mab) has been generated by hybridoma technique, sequenced and recombinantly expressed in HEK cells. Human peripheral blood monocytes and monocytic cell lines were stimulated by the recombinant monoclonal anti-human AT1R ab and, in comparison, in the presence or absence of EVs precipitated from sera of SSc patients versus sera of HD. The response of the monocytes was measured via CCL18 secretion by ELISA.
Results: We compared CCL18 release, a profibrotic cytokine, of monocytic cells upon stimulation for 24 h with the AT1R mab in presence or absence of sera EVs (SSc vs. HD). The recombinant monoclonal anti-human AT1R antibody induced secretion of CCL18 by monocytes. Our data indicate that EVs together with AT1R mab have an effect on monocyte activation and CCL18 secretion. Remarkably, combination of SSc-EVs, but not of HD-EVs, with the recombinant AT1R mab showed an additive effect on monocyte activation and CCL18 response (Figure 1).

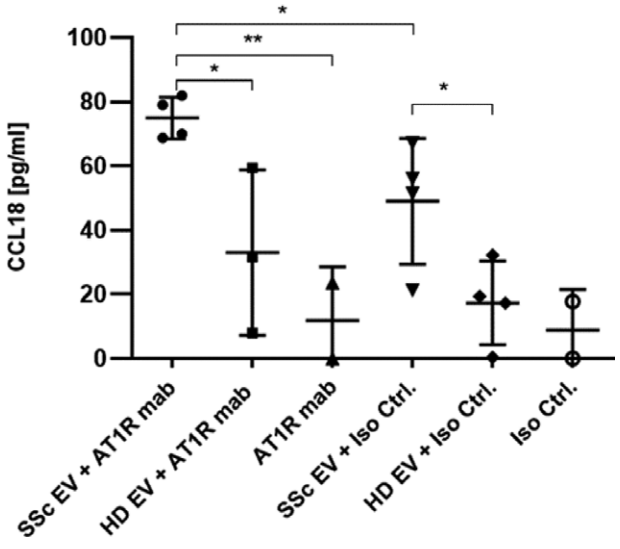


Figure 1. CCL18 levels released by monocytic cells after stimulation with EVs and AT1R mab or isotype.

Stimulation with SSc EV + AT1R mab (n=4), HD EV + AT1R mab (n=3), AT1R mab control, SSc EV + isotype (n=4), HD EV + isotype (n=3) and isotype control. One-way ANOVA was used to test for statistical significance (*p<0.05, **p<0.01, ***p<0.001).
Conclusion: The secretion of pro-fibrotic CCL18 by human monocytes in response to a monoclonal AT1R antibody as well as to SSc IgG indicates that anti-AT1R abs are involved in the SSc pathogenesis. Further, this effect could also be due to SSc-EVs potentially presenting anti-GPCR abs to their receptors on immune cells.
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AB0158

GENETIC EVIDENCE OF CASUAL ASSOCIATION BETWEEN POLYMYOSITIS AND RISK OF INTERSTITIAL LUNG DISEASE: A MENDELIAN RANDOMIZATION STUDY

Keywords: Lungs, Myositis

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Background: Polymyositis (PM) is an immunologically abnormal inflammatory myopathy, which is one of the common types of idiopathic inflammatory myopathy[1]. A global prevalence of approximately 41% of Interstitial lung disease (ILD) in PM patients has been estimated, which causes significant morbidity and mortality[2]. There have been a number of studies shown that PM and ILD may have similar pathogenesis, which focus on PM may induce ILD cellular immune system components[3]. While the two diseases may occur at the same time, but there is no directly evidence that the two diseases are causally related.
Objectives: Our study aimed to discover the casual association between PM and ILD, and determine the impact of PM on ILD.
Methods: We retrieved two large European genome-wide association study (GWAS) summary data of PM and ILD from MRC IEU OpenGWAS, which included 213,264 and 218,072 individuals, respectively. Single-nucleotide polymorphisms (SNPs) linked with disease were selected as instrumental variables (IVs) using genome-wide significance levels ($P < 1.0 \times 10^{-5}$). And the interference of confounding factors, including smoking, drinking and BMI were eliminated. The two-sample Mendelian randomization (MR) method was applied to estimate the casual relationship of PM on ILD. The random-effects inverse variance weighted method (IVW) was mainly used to the MR analysis. Additionally, the horizontal pleiotropy effect was analyzed by MR-Egger and weighted median method sensitivity test. A leave-one-out analysis was conducted to avoid bias caused by a single SNP.
Results: Our study discovered that PM was considered as a risk factor of ILD. 15 SNPs strongly associated with PM were extracted from GWAS. The existence of PM may increase the risk of ILD by 1% (OR = 1.008, 95% CI: 1.001 - 1.016, p = 0.002) No single SNP significantly biased the causal effect of PM on ILD (Q = 0.18). No significant directional horizontal pleiotropy between PM and ILD was presented in the MR-Egger regression analysis.
Conclusion: This study provides evidence of an adverse effect of PM on ILD. And these may be meaningful for the prevention and intervention of PM and ILD. Meanwhile, our work also provides genetic statistical evidence for the study of the causal relationship of PM and ILD.
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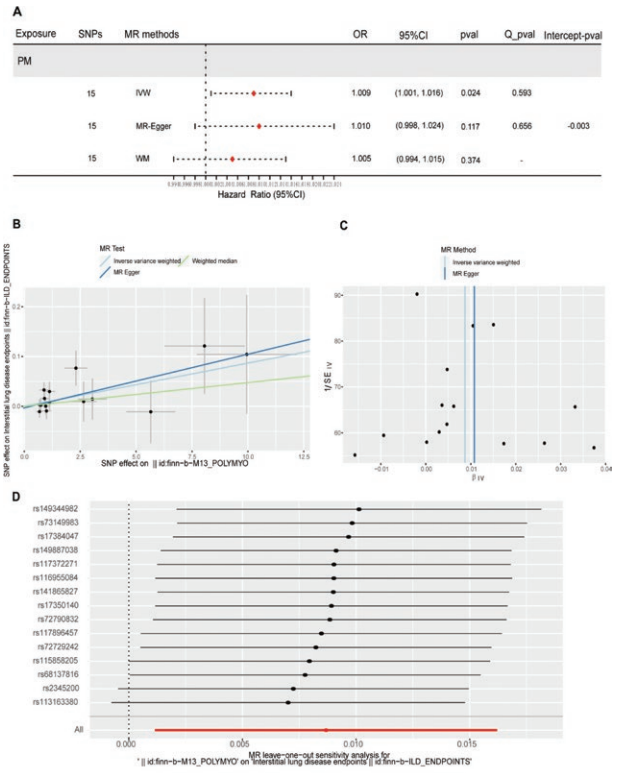


Figure1: (A) Forest plot of MR results by IVW, MR-Egger and WM. (B) The scatter plot of MR analyses the casual effect between PM and ILD using the conventional IVW, MR-Egger and WM methods. (C) Funnel plot shows the estimation using the inverse of the standard error of the causal estimate using each individual SNP as a tool. The vertical line shows the results of the IVW method using all SNPs. (D) Results of the leave-one-out method in MR sensitivity which evaluating the stability of effect sizes.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0159 THE POSITIVE EFFECT OF VITAMIN D3 AND Α-TOCOPHEROL ACETATE ON PULMONARY ARCHITECTONICS IN AN EXPERIMENTAL MODEL OF SYSTEMIC SCLEROSIS

Keywords: Animal models, Lungs, Systemic sclerosis

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Background: Systemic scleroderma (SSc) is an autoimmune disease characterized by a wide range of clinical manifestations. One of the main targets of this pathology is the pulmonary system. In turn, SSc-associated damage of lung structures is characterized by a significant negative impact on the survival and quality of life of patients.
Objectives: Therefore, we aimed to assess the possible favorable influence of vitamin D3 (VD3) and α-tocopherol acetate (ATA) on the morphological structure of lungs' parenchyma in the experimentally induced SSc.
Methods: We assembled our experimental animals into three groups: a control group (CG) (20 animals), an experimental group (EG) #1 (25 animals), and #2 (25 animals). Experimental animals were mature laboratory rats, belonged to the Wistar line, and were 180-220 g of weight. Animals in EG #1 were injected with sodium hypochlorite (NaClO) according to the reported previously schedule [1] for SSc modeling purposes. Laboratory animals of the CG were receiving isotonic solution according to the same scheme. In EG #2, rats were subjected to intramuscular injections of ATA solution 10 mg/ 100 g of body weight, and of a VD3 solution 1000 IU/ 100 g of body weight for 3 weeks (second half of the experiment performance). All three groups of animals were removed from the experiment 8 weeks after its beginning. The lung tissue specimens were examined using light (Leica DM750, x200 magnification) microscopy. Data distribution was evaluated with descriptive statistics, and a $p<0.05$ was considered statistically significant. Statistical analysis was carried out using IBM SPSS version 26.
Results: The lung parenchyma samples obtained from CG did not show significant deviations from the normal histological picture. (Figure 1A). The histological analyses of lung specimens of experimental animals reviled non-specific interstitial pneumonia (NSIP) which is the most common type of SSc-associated interstitial lung disease (ILD) (Figure 1B). There were productive and sclerotic modifications of the interalveolar septum, their infiltration by the lymphoid and plasma cells with significant disfigurement of alveolar structure. (White arrow – alveolar wall thickening; black arrow – thickening of basal membrane of microvessels). After using VD3 and ATA animals demonstrated a distinct decrease in the intensity of lymphoid and plasma cells infiltration of interalveolar spaces (Figure 1C). Furthermore, the sclerotic alteration of the alveolar-capillary barrier was less prominent compared to EG #1 specimens. The Ashcroft score was significantly higher in EG#1 (3.7±0.6) compared to EG#2 (1.8±0.3) ($p<0,05$) and CG (0.6±0.1) ($p<0,05$).
Conclusion: This study confirms positive effect of vitamins D3 and α-tocopherol acetate on morphological structure of pulmonary parenchyma in the preclinical model of SSc.
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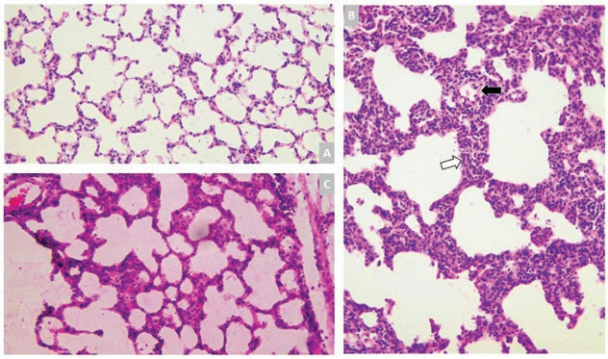


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0160 GUT MICROBES AND SYSTEMIC SCLEROSIS: CAUSE OR CONSEQUENCE?

Keywords: Systemic sclerosis, Gout, Genetics/epigenetics

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Background: There is growing evidence supporting an association between gut microbiota and the risk of systemic sclerosis (SSc)[1]. However, the causal relationship between gut microbiota and SSc remains ambiguous.
Objectives: A two-sample Mendelian randomization (MR) analysis was performed to reveal the causal relationship between gut microbiota and SSc.
Methods: We obtained data on intestinal flora from the MR-base website [2] and 218,499 samples for systemic sclerosis from the IEU database for a two-sample MR analysis. Inverse variance weighting, MR-Egger, and weighted median were used to examine the causal relationship between gut flora and SSc. Then a series of sensitivity analyses were performed to verify the robustness of the results. Finally, the bacteria which appeared causality with SSc were subjected to reverse MR analysis to assess the possibility of reverse causality.
Results: Inverse variance-weighted estimates indicated that genus *Collinsella* (odds ratio(OR) = 8.982, 95% confidence interval(CI): 1.571-51.366 , P = 0.014), phylum *Actinobacteria* (OR = 5.746, 95% CI: 1.247-26.491 , P = 0.025), genus *Ruminococcaceae* (OR = 5.500, 95% CI: 1.477-20.477 , P = 0.011) had a risk effect on SSc (**Table 1**). According to the results of the reverse MR analysis, SSc had no significant causal effect on intestinal flora. No significant heterogeneity or horizontal pleiotropy of instrumental variables was found.
Conclusion: The present study revealed a causal relationship between three gut microflora genera and SSc, providing new insights into the mechanisms of gut microbiota-mediated scleroderma development.
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Table 1. Mendelian randomization analysis for the association between gut microbiota and SSc

SSc	N of SNPs	Cochran's Q statistic(p-value)	Odds ratio	95% CI	p-value
Genus *Collinsella*					
Inverse variance weighted	9	3.853 (0.870)	8.982	(1.571 , 51.366)	0.014
MR Egger	9	3.545 (0.8301)	1.515	(0.002 , 1029.541)	0.904
Weighted median	9		14.103	(1.466 , 135.692)	0.022
Phylum *Actinobacteria*					
Inverse variance weighted	15	17.720 (0.220)	5.746	(1.247,26.491)	0.025
MR Egger	15	16.880 (0.205)	79.147	(0.110, 57116.960)	0.216
Weighted median	15		2.109	(0.275,16.168)	0.448
Genus *Ruminococcaceae*					
Inverse variance weighted	12	6.317 (0.851)	5.500	(1.477,20.477)	0.011
MR Egger	12	6.183 (0.800)	2.552	(0.034,191.160)	0.680
Weighted median	12		5.698	(1.009,32.173)	0.052

SSc, systemic sclerosis; MR, Mendelian randomization; CI, confidence interval

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3079

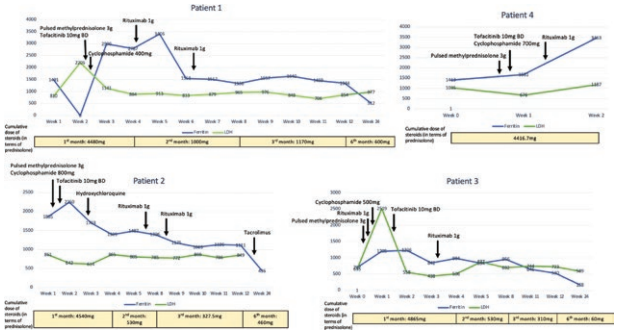
AB0161

EARLY INITIATION OF QUADRUPLE THERAPY IN PATIENTS WITH ANTI-MELANOMA DIFFERENTIATION-ASSOCIATED 5 GENE ANTIBODY-POSITIVE (MDA5) DERMATOMYOSITIS (DM) WITH RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE (RP-ILD) – A RETROSPECTIVE CASE SERIES

Keywords: Disease-modifying drugs (DMARDs), Lungs, Myositis

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Background: MDA5 autoantibodies have been associated with an amyopathic form of dermatomyositis, with a subset developing RP-ILD with high mortality of 50%, despite intensive immunosuppressive therapies like high dose prednisolone, cyclophosphamide and calcineurin inhibitors.[1] Tofacitinib and rituximab have also been used as single agents, mainly as salvage therapy. [2]
Objectives: We aimed to investigate the role of early use of quadruple therapy (high dose steroids, one dose of cyclophosphamide, tofacitinib, rituximab) in patients with anti-MDA5 Ab-positive DM with RP-ILD.
Methods: This is a retrospective case series involving 4 patients with anti-MDA5 Ab-positive DM with RP-ILD from 2019 to 2021. They were treated with quadruple therapy. Their clinical outcomes including survival and adverse events were evaluated.
Results: At initial diagnosis of RP-ILD, all patients were given pulsed methylprednisolone and 1 dose of cyclophosphamide. Tofacitinib was started within 2 weeks, followed by rituximab. 3 patients achieved clinical and biochemical improvement over time, with reduction of glucocorticoids by 6 months. Of the 4 patients, 1 required ICU stay and died. Severe adverse events were observed, most of which were infective complications.



Graph 1. Trend of ferritin and LDH during clinical course over 6 months

Conclusion: We report a general improvement of survival in anti-MDA5 Ab-positive DM with RP-ILD when treated early with quadruple therapy.

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Table 1. Characteristics of patients with anti-MDA5 Ab-positive DM with RP-ILD

	Case 1	Case 2	Case 3	Case 4
Age/Gender	60 F	72 F	48 M	61 F
Clinical Presentation				
1st symptom onset to RP-ILD	4 weeks	5 weeks	4 weeks	8 weeks
Systemic	Fever, LOA, LOW	Fever, LOA, LOW	Fever, LOW	Fever
Respiratory	Cough, hoarse voice	Cough, SOB, ↓ ET	Cough, SOBOE, ↓ ET	Cough, SOBOE
Musculoskeletal	Arthralgia, proximal UL weakness	Arthralgia	Arthralgia, proximal UL weakness	
Mucocutaneous	- V sign - Mechanic's hands - Ragged cuticles - Gottron's papules - Holster's sign - Ulcerated skin lesions	- Alopecia - Heliotrope rash - Shawl sign - Mechanic's hands - Nailfold infarcts - Gottron's papules - Ulcerated skin lesions	- Alopecia - Shawl sign - Mechanic's hands - Ragged cuticles	- Gottron's papules - Ragged cuticles - Ulcerated skin lesions
Investigations				
HRCT	OP pattern	NSIP/OP pattern	Diffuse infiltrative OP	NA
Baseline FVC (% predicted)/DLCO (% predicted)	65/70 (lowest 45/30)	56/61 (lowest 50/34)	50/74	NA
Treatment	GC + CYC + TOF + RTX + IVIG	GC + CYC + TOF + RTX + HCQ + tac	GC + CYC + TOF + RTX	GC + CYC + TOF + RTX
Cumulative dose of steroids (mg): Month 1/2/3/4/5/6	4480/1000/1170/735/725/600	4540/530/327.5/265/385/460	4865/530/310/107.5/80/60	4416.7
Required ICU stay	No	No	No	Yes
Outcome (week from presentation)	Alive (week 40)	Alive (week 72)	Alive (week 35), then lost to follow up	Death (week 2)
Complications	- Invasive pulmonary aspergillosis - Pneumomediastinum, subcutaneous emphysema - Esophageal candidiasis	Leukopenia that resolved with cessation of Tofa		

OP = organizing pneumonia, NSIP = nonspecific interstitial pneumonia, GC = glucocorticoids, CYC = cyclophosphamide, TOF = tofacitinib, RTX = rituximab, HCQ = hydroxychloroquine, tac = tacrolimus

with high-dose glucocorticoid, tacrolimus, and cyclophosphamide in interstitial lung diseases accompanied by anti-melanoma differentiation-associated gene 5-positive dermatomyositis. Arthritis Rheum 2020; 72(3): 488-98.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Vasculitis - aetiology, pathogenesis and animal models

AB0162 RELATIONSHIPS BETWEEN THE SIGNALING PATHWAY OF BAFF/APRIL AND CIRCULATING B CELLS IN ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

Keywords: Vasculitis, Cytokines and chemokines

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Background: Increased production of B-cell activation factor of the TNF family (BAFF) and a proliferation-inducing ligand (APRIL) have been identified in antineutrophil cytoplasmic antibody-associated vasculitis (AAV). BAFF and APRIL exhibit biological activities by binding to three different types of receptors; BAFF receptor (BAFF-R), transmembrane activator and calcium modulator and cyclophilin ligand interactor (TACI), and B-cell maturation antigen (BCMA). Meanwhile, it is uncertain how these three receptors could express or be altered depending on disease activity in AAV.
Objectives: We investigated the characteristics of circulating B cells, serum levels of BAFF, and APRIL, as well as the expression of their binding receptors on B cells, and analyzed the relationships among them in patients with AAV.
Methods: This study used peripheral blood samples from 24 patients with active AAV (a-AAV), 13 with inactive AAV (i-AAV), and 19 healthy controls (HC). The proportion of B-cell subsets, including CD19+ cells, CD19+CD27-CD38+ (immature B) cells, CD19+CD27+CD38- (memory B) cells, and CD19+CD27+CD38+ cells (plasmablasts/plasma cells: PB/PC), and their expressing BAFF-R, TACI, and BCMA were analyzed using flow cytometry. Serum levels of BAFF, APRIL, and interleukin (IL)-6 were also evaluated using an enzyme-linked immunosorbent assay. The relationships among these experimental results were statistically analyzed using univariate regression analyses.
Results: The proportion of PB/PC was significantly higher in a-AAV than in HC ($p < 0.0001$). Higher serum levels of BAFF, APRIL, and IL-6 were significantly observed in a-AAV than in HC ($p < 0.0001$), while serum levels of BAFF and APRIL were significantly higher in i-AAV than in HC ($p = 0.0003$ and $p = 0.005$, respectively). BAFF-R expression on memory B cells was significantly lower in the patients with a-AAV and i-AAV than in the HC ($p = 0.017$ and $p = 0.016$) but not significantly different between patients with a-AAV and i-AAV. Expression of TACI was significantly higher in a-AAV and i-AAV than in HC on CD19+ cells ($p = 0.011$ and $p = 0.028$, respectively), immature B cells ($p = 0.014$ and $p = 0.002$, respectively), and PB/PC ($p = 0.013$ and $p = 0.011$, respectively), despite not being significantly different between the patients with a-AAV and i-AAV. The regression analyses demonstrated that the population of memory B cells was positively associated with serum APRIL levels (coefficient 0.071, 95% confidence interval [CI] 0.035 to 0.106, $p = 0.0004$) and BAFF-R expression (coefficient 0.0001, 95% CI 0.00006 to 0.0002, $p = 0.002$).
Conclusion: Decreased expression of BAFF-R on memory B cells and increased expression of TACI on CD19+ cells, immature B cells, and PB/PC, as well as increased serum levels of BAFF and APRIL, were significantly demonstrated even in patients with remission AAV. Our results suggested that the signaling of BAFF/APRIL and their receptors was pivotally implicated in the generation of B cells. Furthermore, persistently activated signaling of BAFF/APRIL may lead to disease relapse.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0163 FUNCTIONAL ANNOTATION OF DIFFERENTIALLY-EXPRESSED GENES BETWEEN TAKAYASU ARTERITIS AND HEALTHY CONTROLS USING WHOLE-BLOOD TRANSCRIPTOME ANALYSIS REVEALS DIFFERENCES RELATED TO PROTEIN BINDING AND INTRACELLULAR SIGNALING PROCESSES

Keywords: Vasculitis, -omics, Adaptive immunity

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Background: The pathophysiology of Takayasu arteritis (TAK) is incompletely understood. Gene expression profile of peripheral blood mononuclear cells (PBMCs) in TAK has been scarcely studied and may provide new insights into its pathogenesis.
Objectives: To identify and functionally annotate differentially expressed genes (DEGs) in immunosuppressive-naïve TAK compared with healthy controls (HCs).
Methods: Fifteen immunosuppressive-naïve TAK [10 Females, mean (SD) age 34.13(13.28) years] and 10 healthy controls (HC) [8 females, mean (SD) age 31.8(4.57) years] were recruited after obtaining written informed consent. After isolating PBMCs, RNA was extracted using Trizol method. RNA quality was checked using Nanodrop™ (260/280~2, 260/230≥2). Whole gene transcriptome signature was assessed using Affymetrix Clariom™ D human microarray. Using Transcriptome analysis console (version 4.0.3.1.4), signal output from raw CEL files was normalized (group-averages with standard deviations and gene-level limma) to generate CHP files which were analysed for DEGs (up- & down-regulated), filtered on fold-change in TAK versus HC (≥2 or ≤-2) and p value < 0.05.Thereafter, functional annotation of up- and down-regulated genes was performed using Database for Annotation, Visualization, and Integrated Discovery (DAVID) to evaluate Gene Ontology (GO) clusters and processes.
Results: Of 135750 genes, 558 genes passed filter criteria [up-regulated 185 - Coding 33 (17.84%), micro RNA 1 (0.54%), multiple complexes 93 (50.27%), non-coding 23 (12.43%); down-regulated 373 - Coding 53 (14.21%), micro RNA 61 (16.35%), multiple complexes 35 (9.38%), non-coding 190 (50.94%)] (Volcano plot in Figure 1). After functional annotation for 111 up-regulated genes identified on DAVID, two clusters were generated. Cluster 1 (enrichment score 2.20) comprised hemoglobin complex, oxygen transport activity, heme binding, and oxygen binding pathways. Cluster 2 (enrichment score 0.70) comprised JNK cascade, protein kinase activity, and protein phosphorylation. Sixty-seven up-regulated processes were identified (Table 1). Functional annotation for 14 down-regulated genes identified on DAVID identified one cluster (enrichment score 0.76) comprising extracellular exosomes, cytoplasm, nucleoplasm, cytosol and protein binding pathways. Four down-regulated processes were identified (Table 1).
Conclusion: We identified an up-regulation of processes related to protein-specific domain binding, serine/threonine kinase activity, magnesium ion binding, oxygen transporter activity, and various cellular components in TAK than in HC.

Down-regulated processes in TAK than in controls related to protein translation and generation of exosomes. A detailed pathway analysis of these processes may provide novel pathophysiological insights into TAK.

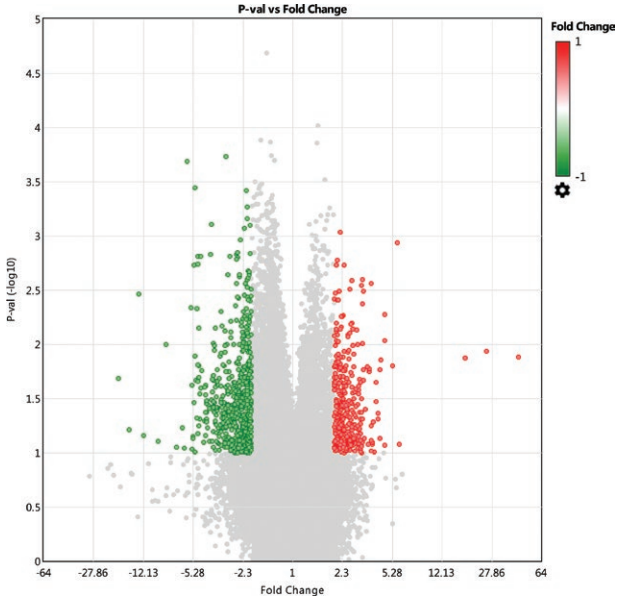


Figure 1. Volcano plot of DEGs for TAK vs HCs

Table 1. Functional annotation of top DEGs in TAK compared with HCs using DAVID

Functional annotation of up-regulated genes		% of total up-regulated DAVID IDs (n= 67)	Functional annotation of down-regulated genes		% of total down-regulated DAVID IDs (n=4)
GO annotation	Process		GO annotation	Process	
CC	Cytosol	45.05%	BP	Cytoplasmic translation	14.99%
CC	Membrane	34.23%	CC	Extracellular exosome	28.67%
CC	Specific granule membrane	5.41%	MF	Structural constituent of ribosome	14.36%
BP	Erythrocyte development	3.60%	BP	Translation	14.36%
CC	Tertiary granule membrane	4.50%			
MF	Protein domain specific binding	7.21%			
MF	Magnesium ion binding	6.31%			
CC	Hemoglobin complex	2.70%			
BP	Oxygen transport	2.70%			
MF	Oxygen transporter activity	2.70%			
CC	Ficolin-1-rich granule membrane	3.60%			
CC	Extracellular exosome	19.82%			
CC	Cortical cytoskeleton	2.70%			
CC	Integral component of membrane	36.94%			
BP	Positive regulation of protein serine/threonine kinase activity	3.60%			

BP= Biological processes; CC=Cellular functions; MF= Molecular functions

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AB0164

SERUM LEVELS OF INTERLEUKIN-36 A TO DISTINGUISH BEHÇET'S SYNDROME AND PSORIATIC ARTHRITIS

Keywords: Biomarkers, Vasculitis, Cytokines and chemokines

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Background: Behçet's syndrome (BS) is a rare systemic vasculitis hallmarked by oral, genital and ocular involvement, often accompanied by articular, cutaneous, vascular, neurological, and gastrointestinal manifestations [1, 2]. Articular involvement is present in up to 80% of BS patients [3], and, from a clinical point of view, it may resemble seronegative arthritis, particularly psoriatic arthritis (PsA), with which an overlap has also been described [4-6]. To this date, no specific instrumental or laboratory biomarker is available to help the differential diagnosis between BS and PsA, which currently relies only on clinical assessment and might be particularly challenging. On these bases, there is a growing interest on the identification of new laboratory biomarkers which might assist in the diagnostic process. Among them, interleukin (IL)-36 belongs to the IL-1 family and is involved in skin and joint-related inflammatory conditions [7, 8]. Increased serum levels of IL-36, especially IL-36α, have been described in PsA at synovial level [9], while no study investigated its levels in BS.
Objectives: This study aimed to assess the ability of serum IL-36α to differentiate BS from PsA patients.
Methods: A cross-sectional study was performed on a cohort of 90 adult patients with BS followed at two referral centres for BS (Behçet Center of the Careggi University Hospital of Florence, and University Hospital of Siena, Italy), 80 patients with PsA from the University Hospital Erlangen (Germany), and 80 healthy controls (HCs). Serum IL-36α concentrations were measured in blood samples using human IL-36α enzyme-linked immunosorbent assay (ELISA) kits (MyBioSource, San Diego, Ca), and compared in the three groups.
Results: Serum IL-36α concentrations were significantly higher among BS patients [median level of 201.7 (112.7 – 320.2) pg/mL] as compared to HC [16.9 (13.7-22.2); p<0.001]. Conversely, BS patients displayed significantly lower IL-36α levels as compared to the PsA group (544 (296-759); p<0.001) (**Figure 1**). When we investigated the ability of IL-36α to discriminate BS patients from PsA patients, an empirical optimal cut-off of 420.6 pg/ml displayed a specificity of 0.93, with a sensitivity of 0.70 (AUC 0.82) in discriminating PsA from BS. This cut-off displayed a good diagnostic performance also in BS patients with mucosal and ocular manifestations, i.e., the two BS involvement associated with the highest IL-36α levels, as well as in those lacking major organ involvement, who represent a challenging group from a diagnostic point of view.
Conclusion: Serum IL-36α is remarkably increased in patients with PsA as well as in BS, although to a lesser extent. Serum IL-36α could be a candidate biomarker for the differential diagnosis between these two conditions.

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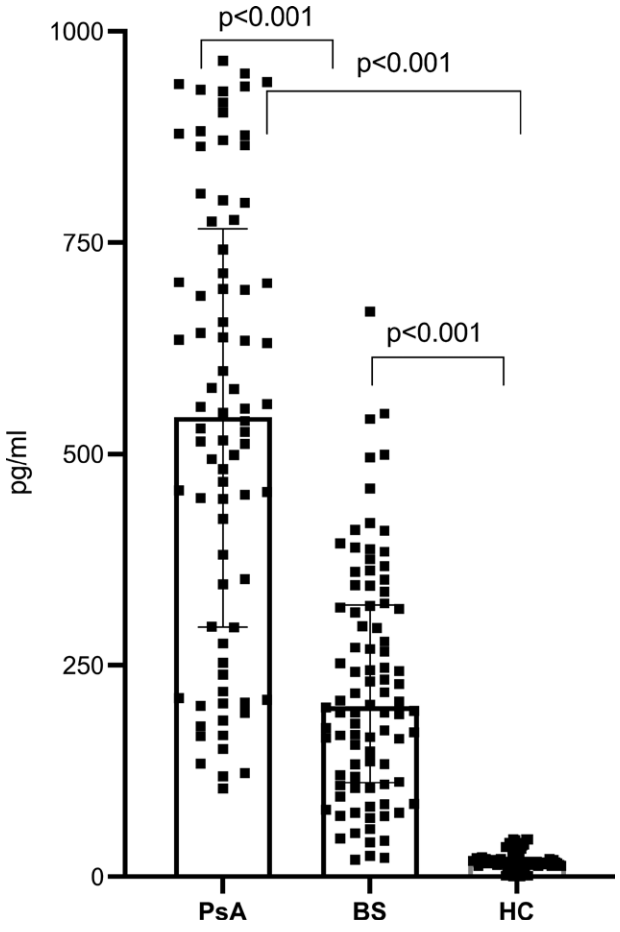


Figure 1. IL-36α levels in patients with Behçet's syndrome (BS), with psoriatic arthritis (PsA), and in healthy controls (HC).

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AB0165 **BIOMARKERS ASSOCIATED WITH GIANT CELL ARTERITIS IN PATIENTS WITH POLYMYALGIA RHEUMATICA FEATURES**

Keywords: Vasculitis, Biomarkers

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Background: Polymyalgia Rheumatica (PMR) is a frequent inflammatory rheumatism associated with giant cell arteritis (GCA) in 16-21% of cases. GCA is characterised by large vessel vasculitis which is absent in isolated PMR [1]. The identification of serum biomarkers reflecting vascular involvement could allow the selection of PMR patients in whom further investigations are indicated to confirm or rule out GCA.
Objectives: This study aimed to identify serum biomarkers associated with GCA in a population of patients with PMR features.
Methods: Patients were prospectively enrolled in Dijon University Hospital, France. At inclusion, no patient had yet received glucocorticoids or immunosuppressive treatment. All PMR patients fulfilled 2012 ACR/EULAR classification criteria [2] and GCA was ruled out by at least an exam evaluating temporal arteries (biopsy and/or color doppler ultrasound) and another evaluating large vessels (angio-CT or FDG-PET/CT). All GCA patients fulfilled the 2022 ACR/EULAR classification criteria [3]. Usual clinical, biological, and therapeutic data were recorded at diagnosis. Several serum biomarkers were measured by Luminex assays: CD141, CD146, CD31, ICAM-1, VCAM-1, ANGPTL-4, ANGPTL-6, and C3L1. Student t test or Mann-Whitney test were performed to compare data, as appropriate. The significance threshold was set at P<0.05 (two-tailed). Analyses were performed with Graphpad PRISM software.
Results: Fifty patients with PMR without GCA (isolated PMR) and 33 patients with PMR and GCA overlap were included. In PMR/GCA overlap patients, 14 (42.4%) had aortitis. Serum level of CD141 was significantly higher in the PMR/GCA overlap group in comparison to isolated PMR group (mean = 6854 pg/mL *vs.* 5558 pg/mL, p = 0.003). The area under cover (AUC) was 0.68 (CI95%: 0.56; 0.80). No differences were found regarding serum levels of ANGPTL-4 (p = 0.39), ANGPTL-6 (p = 0.22), CD31 (p = 0.74), CD146 (p = 0.35), C3L1 (p = 0.75), ICAM-1 (p = 0.94) and VCAM-1 (p = 0.52) between PMR without GCA and PMR/GCA overlap. Likewise, no significant differences were found for the usual markers of inflammation between both groups: ESR (p = 0.22), CRP (p = 0.39) or fibrinogen (p = 0.92). Comparison between PMR without GCA and PMR/GCA overlap with aortitis found higher level of ANGPTL-4 and ANGPTL-6 in isolated PMR patients (median = 160.7 ng/mL *vs.* 128.9 ng/mL [p = 0.04] and 4.3 ng/mL *vs.* 3.1 ng/mL [p = 0.02], respectively). CD141 was positively correlated with CD146 (r =0.48; p < 0.001) and VCAM-1 (r = 0.34; p = 0.001). VCAM-1 was positively correlated with CD141 (r = 0.34; p = 0.001), C3L1 (r = 0.35; p = 0.001) and ANGPTL-4 (r = 0.47; p < 0.001)
Conclusion: This study found lower serum concentrations of CD141 in PMR patients without GCA *versus* those having PMR and GCA overlap. However, the diagnostic performance of CD141 does not appear to be sufficiently discriminative to rule out GCA in PMR patients. ANGPTL-4 and ANGPTL-6 could be interesting serum biomarkers to detect aortitis in patients with PMR features. The study of other biomarkers reflecting endothelial aggression during GCA is needed with larger patients' cohorts.

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AB0166 **IGAV AND IGAN: A SINGLE ENTITY REGARDING CD40, BLK AND BANK1 POLYMORPHISMS**

Keywords: Adaptive immunity, Vasculitis

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Background: IgA vasculitis (IgAV) and IgA nephropathy (IgAN) are inflammatory conditions that share pathophysiological mechanisms, being B-cells crucial players in both diseases [1]. In this regard, some authors have suggested that IgAV and IgAN may represent different outcomes of a continuous spectrum of a disease [2]. In addition, *CD40, BLK* and *BANK1* are relevant genes involved in the development and signalling of B-cells and are also identified as susceptibility *loci* for several immune-mediated diseases [3-6].
Objectives: To determine whether IgAV and IgAN may be different outcomes of a single disease, by assessing the *CD40, BLK* and *BANK1* genetic pattern.
Methods: Three genetic variants within *CD40* (rs1883832, rs1535045, rs4813003), three genetic polymorphisms within *BLK* (rs2254546, rs2736340, rs2618476) as well as two *BANK1* genetic variants (rs10516487, rs3733197) were genotyped in 380 Caucasian patients diagnosed with IgAV, 90 patients diagnosed with IgAN and 1,012 ethnically matched healthy controls. The eight polymorphisms selected were previously associated with several inflammatory diseases [3-6].
Results: Similar genotype and allele frequencies were observed in IgAV patients when compared to those with IgAN, when *CD40, BLK* and *BANK1* variants were analyzed independently (**Table 1**). In addition, no statistically significant differences were observed between patients with IgAV and healthy controls as well as between patients with IgAN and healthy controls, when *CD40, BLK* and *BANK1* genetic variants were analyzed independently (**Table 1**). Similar results were disclosed when haplotype frequencies of *CD40, BLK* and *BANK1* were compared between patients with IgAV and those with IgAN, as well as between patients with IgAV and healthy controls and between IgAN and healthy controls.
Conclusion: Our results reveal a similar *CD40, BLK* and *BANK1* genetic distribution in IgAV and IgAN, supporting that IgAV and IgAN may represent different outcomes of a single disease.
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AB0167

SINGLE-CELL SPATIAL TRANSCRIPTOME ANALYSIS IDENTIFIES DISEASE-SPECIFIC FIBROBLASTS IN RHEUMATOID VASCULITIS

Keywords: Vasculitis, Rheumatoid arthritis, Biomarkers

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Background: Spatial transcriptome analysis is an advanced technique that adds spatial information to gene expression analyses to identify differences in gene expression based on the location in specimen tissues. It can also provide disease-specific gene expression data in individual cells. This method has the potential to identify important gene expression related to disease pathogenesis, which cannot be obtained through conventional bulk analysis. CosMx™ Spatial Molecular Imaging (SMI) is a platform for spatial transcriptome analysis of formalin-fixed paraffin-embedded tissue samples at subcellular resolution (NanoString® Technologies, Seattle, WA, USA). The use of high-plex in situ hybridization followed by cyclic hybridization of immunofluorescent detection reagents and imaging enables the localization and identification of approximately 1,000 RNA targets in situ, and antibody-based, machine learning-augmented cell segmentation with nuclear and membrane markers localizes these targets to individual cells[1]. Cutaneous vasculitis is characterized by vasculitis of small-sized vessels of the skin and causes skin lesions, such as purpura or ulcers, resulting in a low quality of life. A variety of autoimmune diseases can cause cutaneous vasculitis, but its pathogenesis is unknown. In particular, cutaneous vasculitis associated with rheumatoid arthritis (RA) (referred to as rheumatoid vasculitis) is often difficult to treat and is associated with high rates of premature mortality[2]. Histologically, cutaneous vasculitis associated with autoimmune diseases is characterized by fibrinoid degeneration or neutrophilic

Table 1. Genotype and allele frequencies of *CD40, BLK* and *BANK1* in patients with IgAV, patients with IgAN and healthy controls.

	Change		Genotypes, % (n)			Alleles, % (n)	
Polymorphism	1/2	Data set	1/1	1/2	2/2	1	2
CD40 rs1883832	C/T	IgAV	54.0 (204)	37.0 (140)	9.0 (34)	72.5 (548)	27.5 (208)
		IgAN	56.5 (48)	36.5 (31)	7.0 (6)	74.7 (127)	25.3 (43)
		Healthy controls	52.9 (532)	40.4 (409)	6.7 (68)	73.1 (1,479)	26.9 (545)
CD40 rs1535045	C/T	IgAV	53.6 (200)	39.4 (147)	7.0 (26)	73.3 (547)	26.7 (199)
		IgAN	51.8 (44)	41.2 (35)	7.1 (6)	72.4 (123)	27.6 (47)
		Healthy controls	56.7 (574)	36.2 (366)	7.1 (72)	74.8 (1,514)	25.2 (510)
CD40 rs4813003	C/T	IgAV	78.0 (291)	20.1 (75)	1.9 (7)	88.1 (657)	11.9 (89)
		IgAN	76.6 (59)	20.8 (16)	2.6 (2)	87.0 (134)	13.0 (20)
		Healthy controls	74.9 (758)	22.7 (230)	2.4 (24)	86.3 (1,746)	13.7 (278)
BLK rs2254546	G/A	IgAV	74.5 (278)	22.3 (83)	3.2 (12)	85.7 (639)	14.3 (107)
		IgAN	64.7 (55)	31.8 (27)	3.5 (3)	80.6 (137)	19.4 (33)
		Healthy controls	71.3 (722)	26.8 (271)	1.9 (19)	84.7 (1,715)	15.3 (309)
BLK rs2736340	C/T	IgAV	62.8 (236)	31.9 (120)	5.3 (20)	78.7 (592)	21.3 (160)
		IgAN	67.5 (52)	31.2 (24)	1.3 (1)	83.1 (128)	16.9 (26)
		Healthy controls	59.9 (606)	35.8 (362)	4.3 (44)	77.8 (1,574)	22.2 (450)
BLK rs2618476	T/C	IgAV	60.2 (227)	34.2 (129)	5.6 (21)	77.3 (583)	22.7 (171)
		IgAN	68.2 (58)	24.7 (21)	7.1 (6)	80.6 (137)	19.4 (33)
		Healthy controls	57.9 (586)	37.3 (377)	4.8 (49)	76.5 (1,549)	23.5 (475)
BANK1 rs10516487	G/A	IgAV	52.8 (200)	39.8 (151)	7.4 (28)	72.7 (551)	27.3 (207)
		IgAN	50.6 (42)	38.6 (32)	10.8 (9)	69.9 (116)	30.1 (50)
		Healthy controls	50.8 (514)	41.8 (423)	7.4 (75)	71.7 (1,451)	28.3 (573)
BANK1 rs3733197	G/A	IgAV	50.0 (187)	39.0 (146)	11.0 (41)	69.5 (520)	30.5 (228)
		IgAN	47.1 (40)	37.6 (32)	15.3 (13)	65.9 (112)	34.1 (58)
		Healthy controls	49.5 (501)	41.6 (421)	8.9 (90)	70.3 (1,423)	29.7 (601)

vasculitis; however, these findings are nonspecific and do not lead to a precise diagnosis.

Objectives: In the present study, we aimed to identify disease-specific cell types and gene expression via single-cell spatial transcriptome analysis of skin tissues from patients with autoimmune disease-associated cutaneous vasculitis. This can lead to improved diagnosis, pathogenesis understanding, and treatment.

Methods: Single-cell spatial transcriptome analysis was performed using NanoString's CosMx™ SMI on tissues from vasculitis associated with five autoimmune diseases, including rheumatoid vasculitis, and a case with toxic rashes as controls. Following data collection, NanoString's data processing pipeline[1] was used to identify transcripts, define cell locations and boundaries, and count the number of transcripts per cell to determine the expression profiles for each cell. Cell types were inferred from these expression data using InSituType[3] and a reference Human Cell Atlas skin dataset. Immunostaining was performed to validate the identified gene markers.

Results: A total of 35,503 cells and 4,530,981 transcripts were analyzed. Clustering of cells based on gene expression levels revealed cells with a high expression of several specific genes, including MMP1, in rheumatoid vasculitis. CosMx™ SMI analysis revealed that these cells were primarily located in the perivascular area (Figure 1A). Immunostaining with anti-MMP1 antibody (1:100; ab52631, Abcam) revealed that the cells were histologically fibroblasts (Figure 1B). These findings revealed that fibroblasts expressing MMP1 are specific to rheumatoid vasculitis. MMP1 is highly expressed in synovial fibroblasts in RA and plays a substantial role in disease pathogenesis[4]. Our results suggest that disease-specific fibroblasts expressing MMP-1 are involved in the pathogenesis of rheumatoid vasculitis. The pathological roles of MMP1 and other markers merit further investigation.

Conclusion: Single-cell spatial transcriptome analysis revealed fibroblasts specific to rheumatoid vasculitis. The result of this study might contribute to understanding of etiology and treatment of rheumatoid vasculitis.

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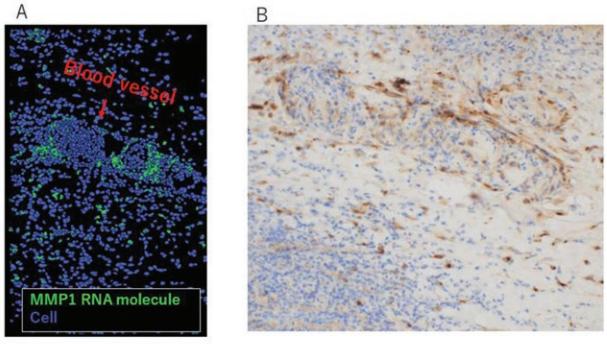


Fig 1A. Spatial map for expression of MMP1 from rheumatoid vasculitis, generated from CosMx™ SMI
Fig 1B. A picture of anti-MMP1 antibody immunostaining of the skin tissue from rheumatoid vasculitis

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AB0168 **IMBALANCE IN THE TAXONOMIC COMPOSITION OF GUT MICROBIOTA IN TAKAYASU ARTERITIS**

Keywords: Gastrointestinal tract, Vasculitis

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Background: Takayasu arteritis (TAK) is one form of the large vessel vasculitis and predominantly affects young female. TAK sometimes coexists with other inflammatory diseases which include ulcerative colitis (UC) and spondyloarthropathy. Recent evidences revealed close genetic background between TAK and these diseases, and we found the common autoantibodies against endothelial protein C receptor among TAK and UC. These evidences suggest the common underlying pathophysiology among these diseases. UC and spondyloarthropathy are known to be associated with dysbiosis. Therefore, the involvement of dysbiosis in the pathogenicity of TAK is possible. However, little is known regarding the composition of gut microbiota in TAK.

Objectives: This study aimed to investigate whether there existed the imbalance in the taxonomic composition of gut microbiota in TAK.

Methods: 31 patients with TAK who satisfied the classification criteria of American College of Rheumatology 1990 and 31 background-matched healthy controls (HC) were included in this study. Feces were collected from each individual, and fecal microbial DNA was isolated. 16S rRNA gene amplicon sequencing was performed to analyze the microbiota. Microbial richness and β-diversity were compared among HC and TAK, and the differences in the abundant taxa were analyzed by the LEfSe algorithm.

Results: The clinical background of each group was as follows; the mean age, 41 years; female, 87%. The disease activity of TAK was assessed using the Indian Takayasu arteritis score (ITAS)-A, and 17% were in an active disease status when they collected feces. Then, 16S rRNA gene amplicon sequencing was successfully performed using microbial DNA extracted from the collected feces. Microbial richness was compared between HC and TAK using the Shannon index, which revealed significant decrease of microbial richness in TAK patients (P=0.02). β-diversity between HC and TAK was next investigated, and approximately half of the patients with TAK were clearly separated from the clusters of HC. Therefore, the presence of dysbiosis in TAK was confirmed even in the condition in which most of patients with TAK were in inactive status. Analysis of composition of microbiomes (ANCOM) showed abundance of eight and 10 genera in TAK and HC, respectively with the cut-off of centered log ratio as 1. Cladograms showed changes in the microbiota, in which each level of phylum, class, order, family, and genus were related. Differential microbiota at the genus level were observed at a linear discriminant analysis threshold of >2.0. Altered microbial genera in our study included enrichment of Streptococcus, Lactobacillus, Veillonella, Enterococcus, Dialister, Actinomyces, Sardovia, Sellimonas, Rothia, and Campylobacter. More numbers of genera were depleted in TAK, which included Bacteroides, Phascolarctobacterium, Dorea, Parasutterella, Barnesiella, and Acidaminococcus. Importantly, enrichment of oral bacteria species was documented in most of the patients with TAK. Among them, two cases were complicated with infectious endocarditis during the treatments with tocilizumab, suggesting the contribution of dysbiosis for such complication in TAK.

Conclusion: Significant imbalance of gut microbiota was observed in TAK. The diversity of fecal microbiota was reduced in TAK, and altered genera were relevant for the exacerbation of inflammation. Dysbiosis could be related to the exacerbation of inflammation and the complications in TAK.

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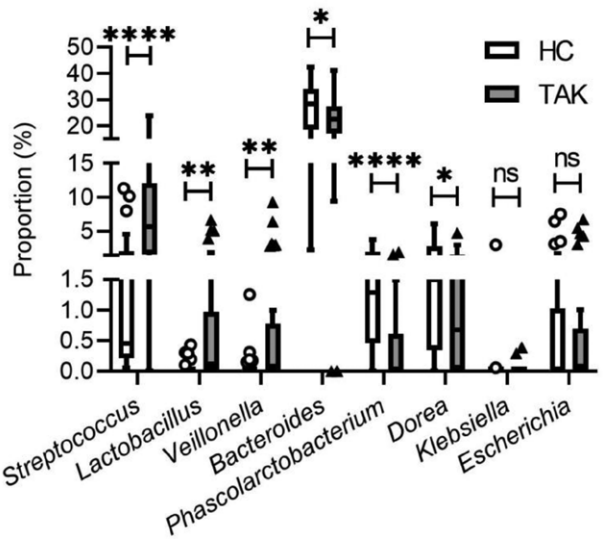


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.845

AB0169 PROTEINASE 3 EXPRESSION IS ASSOCIATED WITH DISTURBED ROS PRODUCTION AND INCREASED INTERLEUKIN-1-RELATED CYTOKINES IN GRANULOMATOSIS WITH POLYANGIITIS

Keywords: Vasculitis, Cell biology, Kidneys

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Background: Neutrophils play a key role in ANCA-associated vasculitis, where they are both targets of autoimmunity and facilitators of vascular damage.
Objectives: This study analyzed the production of reactive oxygen species (ROS) in neutrophils from patients with granulomatosis with polyangiitis (GPA) and investigated its associations with IL-1–related cytokines and proteinase 3 (PR3).
Methods: Thirty-eight GPA patients with a disease flare were included in the NEUTROVASC prospective clinical study. ROS production was evaluated in peripheral blood neutrophils of patients with active GPA and compared to the same patients after 12 months of immunosuppressive treatment in remission as well as to healthy controls. Associations between ROS production, membrane expression of PR3 on neutrophils and serum levels of IL-1–related cytokines were analyzed.
Results: Under basal conditions, neutrophils from patients with active GPA produced less ROS compared to neutrophils from healthy controls. While there was no intrinsic defect in ROS production when using a pharmacological trigger, there was a robust defect in ROS production in response to physiologic mediators combined with TNF in GPA neutrophils compared with healthy control neutrophils. Serum levels of IL-1-related cytokines were significantly increased in GPA patients, particularly in those with kidney involvement, and levels of these cytokines returned to normal in remission. There was a positive correlation between membrane PR3 expression and ROS production in GPA patients, but not in healthy controls. Similarly, there was a positive correlation between PR3 expression and the serum levels of IL-1-related cytokines in GPA patients.
Conclusion: Our data suggest that membrane expression of PR3 links ROS production and regulation of inflammation in patients with GPA and may be a potential therapeutic target.

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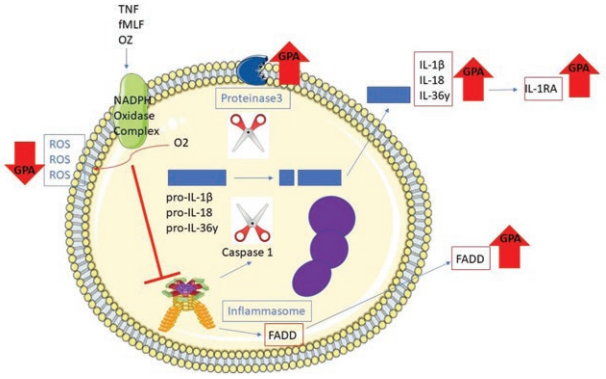


Figure 1.

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Disclosure of Interests: None Declared.
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AB0170 ACTIVATED SENESCENCE PATHWAYS IN THE TEMPORAL ARTERIES OF PATIENTS WITH GIANT CELL ARTERITIS

Keywords: Vasculitis

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Background: Giant cell arteritis (GCA) is an inflammatory disease marked by granulomatous inflammation of the large- and medium-vessels. GCA exclusively affects older patients above 50 years old, suggesting a role of senescence in the pathobiology of GCA. IL-6 receptor blocking therapy has been shown to be effective treatment for GCA.(1) More recently, a phase two randomized control trial has shown the efficacy of GM-CSF receptor blocking therapy for the treatment of GCA.(2) Both IL-6 and GM-CSF are senescence-associated secretory phenotype (SASP) cytokines,(3) implicating the roles of cellular senescence and SASP in the immunopathology of GCA.
Objectives: We seek to find clues of senescent and SASP in the inflamed arteries of GCA patients.
Methods: Immunohistochemical stainings of the senescence markers p21 WAF1/CIP1 and p16/INK4A as well as SAPS cytokines IL-6 and GM-CSF were performed on temporal artery biopsies (TABs; n=8) from patients with giant cell arteritis. Non-inflamed arteries from age-matched controls were included (n=14). Stainings were scored quantitatively by using QuPath software. Opal based multiplex fluorescent stainings were performed to confirm the colocalization of p21 WAF1/CIP1 and p16/INK4A with IL-6 and GM-CSF.
Results: All four markers were detected in the inflamed GCA temporal arteries, most notably by giant cells surrounding the intimal lamina elastica although expression by other cells was also detected throughout the vessels. The expression of all four markers were significantly lower in control arteries. Cells positive for p21 WAF1/CIP1 and p16/INK4A that co-express IL-6 and GM-CSF were detected throughout the vessels.
Conclusion: Our data suggest the presence of activated senescence pathways at the site of vascular inflammation in GCA and support further research into the role of senescence in GCA.

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Disclosure of Interests: William Febry Jiemy: None declared, Yannick van Sleen: None declared, Jacoba Carolien Graver: None declared, Sarah A. Pringle: None declared, Elisabeth Brouwer Speakers bureau: EB reports personal fees from Roche, outside the submitted work., Consultant of: EB reports personal fees from Roche, outside the submitted work., Kornelis van der Geest Speakers bureau: KSMvdG reports personal fees from Roche, outside the submitted work., Consultant of: KSMvdG reports personal fees from Roche, outside the submitted work., Divi Cornec: None declared, Annemieke Boots: None declared, Maria Sandovici: None declared.
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AB0171 MENDELIAN RANDOMIZATION ANALYSIS REVEALS CAUSAL EFFECTS OF GUT MICROBIOTA ABUNDANCE ON GIANT CELL ARTERITIS RISK

Keywords: Vasculitis, Gout, Genetics/epigenetics

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Education,Taiyuan, China; [3]*Shanxi Medical University, Shanxi Key Laboratory of Big Data for Clinical Decision Research,Taiyuan, China*; [4]*Second Hospital of Shanxi Medical University, Department of Rheumatology,Taiyuan, China*

Background: Gut microbiota (GM) abundance is associated with giant cell arteritis, but their causality remains unclear[1].
Objectives: In order to comprehensively investigate the causal relationship between gut microbiota abundance and giant cell arteritis risk and to identify specific beneficial or pathogenic microbe taxa, we performed a two-sample Mendelian randomized (MR) analysis.
Methods: MR analysis was conducted on genome-wide association study (GWAS) summary statistics of gut microbiota abundance and giant cell arteritis. Specifically, the microbiome GWAS in 14,306 individuals from the MiBioGen consortium was used as exposure[2], while the GWAS (n = 213,604) for giant cell arteritis was used as the outcome. At the suggestive significance level ($p = 1\times10^{-5}$), SNPs associated with bacteria abundance were utilized as instrumental variables. Inverse variance weighted (IVW) was the primary method for analyzing causality, and Cochran's Q statistic was used to quantify the heterogeneity of instrumental variables.
Results: Inverse variance weighted estimates suggested that genus Eubacterium rectale group (odds ratio = 0.38, 95% confidence interval: 0.16-0.93, P = 0.03), class bacteroidia (odds ratio = 0.44, 95% confidence interval: 0.21-0.93, P = 0.03), order Bacteroidales (odds ratio = 0.44, 95% confidence interval: 0.21-0.93, P = 0.03), family Lachnospiraceae (odds ratio = 0.32, 95% confidence interval: 0.16-0.63, P = 0.001) and genus Lactobacillus (odds ratio = 0.6, 95% confidence interval: 0.37-0.97, P = 0.04) had a protective effect on Giant cell arteritis. In addition, the relative abundance of class Betaproteobacteria (odds ratio = 2.53, 95% confidence interval: 1.03-6.19, P = 0.04) and relative abundance of genus Ruminococcaceae (odds ratio = 1.7, 95% confidence interval: 1.04-2.8, P = 0.04) were negative significant correlated with Giant cell arteritis risk (Figure 1). Further sensitivity analyses validated the robustness of the MR results.
Conclusion: The study suggested that gut microbiota abundance was causally associated with the risk of giant cell arteritis, which may provide novel insights into the prevention and diagnosis of giant cell arteritis.
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GCA	N of SNPs	Cochran's Q statistic (p-value)	Odds ratio	95% confidence interval	p-value
genus Eubacterium rectale group					
Inverse variance weighted	8	5.699(0.575)	0.383	(0.157,0.931)	0.034
MR Egger	8	5.514(0.480)	0.758	(0.030,19.398)	0.873
Weighted median	8		0.559	(0.158,1.975)	0.366
class bacteroidia					
Inverse variance weighted	14	16.540(0.221)	0.442	(0.210,0.929)	0.031
MR Egger	14	8.338(0.758)	0.080	(0.021,0.306)	0.003
Weighted median	14		0.401	(0.152,1.058)	0.065
class Betaproteobacteria					
Inverse variance weighted	11	14.130(0.167)	2.528	(1.032,6.194)	0.043
MR Egger	11	12.440(0.190)	12.454	(0.648,239.403)	0.129
Weighted median	11		2.129	(0.742,6.104)	0.160
genus Ruminococcaceae					
Inverse variance weighted	22	7.577(0.997)	1.704	(1.036,2.802)	0.036
MR Egger	22	7.091(0.996)	2.627	(0.705,9.784)	0.165
Weighted median	22		2.082	(1.057,4.099)	0.034
order Bacteroidales					
Inverse variance weighted	14	16.540(0.221)	0.442	(0.210,0.929)	0.031
MR Egger	14	8.338(0.758)	0.080	(0.021,0.306)	0.003
Weighted median	14		0.401	(0.151,1.067)	0.067
family Lachnospiraceae					
Inverse variance weighted	16	14.270(0.505)	0.316	(0.159,0.628)	0.001
MR Egger	16	13.420(0.494)	0.924	(0.085,10.056)	0.949
Weighted median	16		0.344	(0.127,0.930)	0.035
genus Lactobacillus					
Inverse variance weighted	9	6.633(0.577)	0.600	(0.369,0.974)	0.039
MR Egger	9	6.176(0.519)	0.396	(0.110,1.423)	0.199
Weighted median	9		0.552	(0.284,1.073)	0.080

Figure 1 Mendelian randomization estimates for the associations between GCA and genus Eubacterium rectale group, class Betaproteobacteria, class bacteroidia, genus Ruminococcaceae, order Bacteroidales, family Lachnospiraceae, genus Lactobacillus. GCA, Giant cell arteritis.

Figure 1. Mendelian randomization estimates for the associations between GCA and genus Eubacterium rectale group, class Betaproteobacteria, class bacteroidia, genus Ruminococcaceae, order Bacteroidales, family Lachnospiraceae, genus Lactobacillus. GCA, giant cell arteritis.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0172 ANTI-MITOFUSIN-1 AND THROMBOSPONDIN-1 AS POTENTIAL MARKERS FOR POLYMYALGIA RHEUMATICA

Keywords: Vasculitis, Biomarkers

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Background: Polymyalgia rheumatica (PMR) is a chronic, inflammatory disorder characterized by aching and stiffness in the proximal regions of the extremities and elevated markers of inflammation. PMR and giant cell arteritis (GCA) are two conditions frequently coexisting [1,2], with increased incidence of large vessel vasculitis and aneurysm development found at long term follow-up. Furthermore, PMR can be one of the manifestations of GCA in 20-40% of cases [3]. The etiology of the diseases are still largely unknown, and specific serological markers, including to monitor arterial disease, are lacking. Recent studies have shown that mitochondrial dysfunction may play a central role in immune activation and could act as a potential source of antigens, including mitofusin-1 (MFN1), in autoimmune diseases [4,5,6].
Objectives: To determine whether patients with PMR, with or without overlapping GCA, have elevated levels of markers of platelet activation (e.g. thrombospondin-1; TSP-1), and mitochondrial autoantibodies (e.g. anti-MFN1).
Methods: Plasma levels of anti-MFN-1 IgG and TSP-1 were measured in healthy controls (HC) (n=30) and patients with PMR (n=60), before and after treatment with glucocorticoids using in-house and commercial ELISAs, respectively.
Results: Plasma levels of anti-MFN-1 IgG and TSP-1 were elevated in patients with PMR, compared with HC, both before and after treatment with corticosteroids ($p<0.001$). The highest levels of anti-MFN-1 and TSP-1 were found before treatment of corticosteroids ($p<0.001$). Co-existence of GCA did not affect levels of either anti-MFN1 or TSP-1, nor treatment response to corticosteroids. Elevated levels of TSP-1 were found to be significantly elevated in patients with symptoms from hips/glutes (n=39) as compared to patients without these symptoms (n=13), median (P25-P75) 27.11 ug/mL (22.5-35.0) vs 19.6 ug/mL (14.1-27.9), p=0.046. Lower concentration of anti-MFN1 IgG was found in patients with symptoms from the spine (n=31) in comparison with those without symptoms from the spine (n=21), median (P25-P75) 0.37 U/mL (0.27-0.57) vs 0.54 U/mL (0.47-0.96), p=0.043.
Conclusion: Increased levels of anti-MFN-1 IgG and TSP-1 were found in PMR patients and decreased significantly after treatment with corticosteroids, although still significantly higher than HC. The highest concentration of TSP-1 was found in individuals with symptoms from hips/glutes. Increased concentrations of anti-MFN-1 and TSP-1 are suggested as novel biomarkers for PMR and further, could serve as potential biomarkers for treatment response.
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AB0173 MUCOSAL IMMUNE DEFENCE POLYMORPHISMS: RELEVANT PLAYERS IN IGA VASCULITIS?

Keywords: Vasculitis, Innate immunity

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Background: Several mucosal immune defence polymorphisms have an impact on IgA production by plasma cells in the mucosa [1]. In this regard, these genetic variants have been previously reported as susceptibility *loci* for IgA nephropathy [1]. Given the pathophysiological similarities described between IgA nephropathy and Immunoglobulin-A vasculitis (IgAV) [2, 3], mucosal immune defence polymorphisms may also be implicated in the pathogenesis of IgAV.

Objectives: To determine whether mucosal immune defence polymorphisms represent novel genetic risk factors for the pathogenesis of IgAV.

Methods: 6 mucosal immune defence polymorphisms previously described as susceptibility *loci* for IgA nephropathy (*ITGAM-ITGAX* rs11150612, *VAV3* rs17019602, *CARD9* rs4077515, *CFHR3.1-del* rs6677604, *DEFA* rs2738048 and *HORMAD2* rs2412971) were selected. These 6 genetic variants were genotyped in 300 unrelated Caucasian patients with IgAV (the largest series of Caucasian IgAV patients assessed for genetic studies) and 1,012 matched healthy controls. 36.1% of the IgAV patients developed renal manifestations.

Results: No statistically significant differences were observed in the genotype and allele frequencies of mucosal immune defence polymorphisms when IgAV patients and healthy controls were compared (**Table 1**). Moreover, no statistically significant differences were disclosed in the genotype and allele frequencies of the 6 polymorphisms selected when patients with IgAV were stratified according to the presence/absence of renal manifestations (**Table 1**). Likewise, similar genotype and allele frequencies of these polymorphisms were disclosed in patients with IgAV stratified according to the age at disease onset and to the presence/absence of gastrointestinal manifestations.

Conclusion: Our results reveal that mucosal immune defence polymorphisms do not contribute to the genetic background of IgAV.

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AB0174 EXPLORING A POTENTIAL ANTI-TUMOR IMMUNE MICROENVIRONMENT IN GIANT CELL ARTERITIS

Keywords: Cytokines and chemokines, Vasculitis

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Background: The diagnosis of giant cell arteritis (GCA) is confirmed by temporal artery (TA) biopsy findings of internal elastic lamina disruption, activated macrophages and T-lymphocytes infiltrating the arterial layers. The immune microenvironment in GCA becomes T helper-1 polarized after steroid therapy and consists of potential anti-tumor cytokines including interferon-gamma (IFG) and interleukin-12 (IL-12) which can be protective against the development of cancer. We have previously identified folate receptor beta positive macrophages in GCA, which can serve as a target for hacking this immune microenvironment.

Table 1. Genotype and allele frequencies of mucosal immune defence polymorphisms in controls, patients with IgAV as well as patients with IgAV stratified according to the presence/absence of renal manifestations.

	Change		Genotypes, % (n)			Alleles, % (n)		
Polymorphism	**1/2**	**Data set**	**1/1**	**1/2**	**2/2**	**1**	**2**	*ITGAM-ITGAX* rs11150612
G/A	Controls	40.2 (407)	46.3 (468)	13.5 (137)	63.3 (1,282)	36.7 (742)		
IgAV	39.6 (113)	43.2 (123)	17.2 (49)	61.2 (349)	38.8 (221)			IgAV with nephritis
								IgAV without nephritis
33.0 (36)	44.0 (48)	22.9 (25)	55.0 (120)	45.0 (98)	*VAV3*	A/G	Controls	59.8 (605)
43.8 (77)	42.6 (75)	13.6 (24)	65.0 (229)	35.0 (123)	rs17019602			
35.4 (358)	4.8 (49)	77.5 (1,568)	22.5 (456)			IgAV	62.1 (177)	34.0 (97)
3.9 (11)	79.1 (451)	20.9 (119)			IgAV with nephritis	62.4 (68)	35.8 (39)	1.8 (2)
					IgAV without nephritis	61.9 (109)	33.0 (58)	5.1 (9)
80.3 (175)	19.7 (43)	*CARD9*	C/T	Controls	38.4 (389)	46.1 (466)	15.5 (157)	61.5 (1,244)
78.4 (276)	21.6 (76)	rs4077515						
38.5 (780)			IgAV	35.4 (101)	49.5 (141)	15.1 (43)	60.2 (343)	39.8 (227)
		IgAV with nephritis	35.8 (39)	45.9 (50)	18.3 (20)	58.7 (128)	41.3 (90)	*CFHR3.1-del*
		IgAV without nephritis	35.2 (62)	51.7 (91)	13.1 (23)	61.1 (215)	38.9 (137)	rs6677604
G/A	Controls	63.5 (642)	31.1 (315)	5.4 (55)	79.0 (1,599)	21.0 (425)		
IgAV	63.9 (182)	30.9 (88)	5.2 (15)	79.3 (452)	20.7 (118)			IgAV with nephritis
								IgAV without nephritis
67.0 (73)	28.4 (31)	4.6 (5)	81.2 (177)	18.8 (41)	*DEFA*	A/G	Controls	51.8 (524)
61.9 (109)	32.4 (57)	5.7 (10)	78.1 (275)	21.9 (77)	rs2738048			
39.8 (403)	8.4 (85)	71.7 (1,451)	28.3 (573)			IgAV	46.7 (133)	42.8 (122)
10.5 (30)	68.1 (388)	31.9 (182)			IgAV with nephritis	50.5 (55)	40.4 (44)	9.1 (10)
					IgAV without nephritis	44.3 (78)	44.3 (78)	11.4 (20)
70.6 (154)	29.4 (64)	*HORMAD2*	G/A	Controls	27.4 (277)	51.2 (518)	21.4 (217)	53.0 (1,072)
66.5 (234)	33.5 (118)	rs2412971						
47.0 (952)			IgAV	29.1 (83)	52.3 (149)	18.6 (53)	55.3 (315)	44.7 (255)
		IgAV with nephritis	30.3 (33)	47.7 (52)	22.0 (24)	54.1 (118)	45.9 (100)	
		IgAV without nephritis	28.4 (50)	55.1 (97)	16.5 (29)	56.0 (197)	44.0 (155)	

Objectives: To compare the tumor outcomes in our cohort of GCA vs controls who had TA biopsies. To select a line-up of CD3, IFG, IL12 and FRB as potential anti-tumor proteins and compare their expression in GCA+ TA tissue that did not develop tumors versus GCA -negative tissues that developed tumors. To assess the persistence of this line-up over time.
Methods: We performed a retrospective chart review of GCA subjects and controls to assess development of tumors over long-term follow up. Formalin-fixed paraffin embedded tissue sections were obtained from both groups and immunohistochemical stains were performed using CD3, IFG, IL12 and FRB antibodies.
Results: 40 GCA and 40 controls demonstrated similar follow-up durations (76.9 vs 70.1 years; NS), time-to-incident cancer (21 vs 62 mos; NS) and deaths from cancer (5% vs 17.5%;NS). GCA subjects were older than controls (77.2 vs 69.7 years; p= 0.004). Cancer incidence is lower in GCA than controls (25% vs.47.5%; p=0.036). The incident cancers in GCA include 8 basal or squamous cell skin cancer(BCC/SCC) and 1 each of chronic lymphocytic leukemia, thyroid, esophageal and angiosarcoma. The controls had 6 BCC/SCC, 2 each of breast, skin melanoma and lymphoma, and 1 each of tonsil, parotid, colon, lung, renal, prostate, myelodysplastic syndrome and metastatic disease of unknown primary. Histopathology/IHC Findings: FRB was selectively expressed in macrophages and correlated with IFG, IL12 and CD3 expression. FRB, IFG, IL12 and CD3 expression were higher in GCA without incident cancer compared to controls with cancer: FRB (14 vs 2.3;p=0.006), IFG (3 vs 1;p=0.005), IL12 (1.5 vs 0;p=0.003), CD3 (79 vs 0;p=0.004). This multi- protein expression persisted for years in 3 repeat biopsies.
Conclusion: GCA has a lower risk of cancer which was associated with a chronic FRB+-macrophage and Th1-polarized anti-tumor autoimmunity.

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AB0175 EVALUATION OF THE STATE OF ACTIVATION OF PERIPHERAL BLOOD MONONUCLEAR CELLS IN PATIENTS WITH POLYMYALGIA RHEUMATICA

Keywords: Cytokines and chemokines, Innate immunity

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Background: Polymyalgia rheumatica (PMR) is a chronic inflammatory disease that affects individuals of 50 or more years of age. It is characterised by shoulder and pelvic girdle pain, morning stiffness, functional limitation, and an increase in inflammatory indexes. Glucocorticoids (GC) represent the cornerstone of treatment. The pathogenesis is still not completely understood, although many shreds of evidence show the role of innate immunity.
Objectives: To evaluate whether peripheral blood mononuclear cells (PBMCs) of patients with newly diagnosed PMR and not yet treated with GC show a baseline activation that is affected by treatment with GC.
Methods: We carried out an observational study, enrolling patients with PMR (2012 EULAR/ACR criteria) not yet treated with GC and controls. Blood samples were obtained from patients at baseline (T0) and after 4 months since the beginning of GC (T4), and from controls. An ultrasound (US) of shoulder and pelvic girdles was performed in PMR patients at T0 and T4. Demographic, clinical and US results were recorded in an electronic database. Patients with a personal history of rheumatic, inflammatory or oncologic diseases or subjects that received such a diagnosis during the study were excluded. PBMCs were isolated by density gradient centrifugation and analyzed in triplicates, among which one was stimulated with lipopolysaccharide (LPS). Then, the supernatant was collected and ELISA was performed for the determination of IL-1β, TNF, and IL-6 levels. The same cytokines were searched in the sera of PMR patients at T0 and at T4 and in the controls.
Results: We consecutively enrolled 8 patients with a new diagnosis of PMR (F/M 6/2; median age/IQR 73/9.75 years; median disease duration 2/2.75 months) and 8 individuals without PMR matched for gender, age, and comorbidities with PMR patients (F/M 6/2; median age/IQR 69/10.5 years). We found higher concentrations of IL-1β and IL-6 in the unstimulated supernatant of PMR patients at T0 compared to T4 (p=0.0313 for both) (Figure 1A-B). Higher TNF levels were found in the unstimulated supernatant of PMR patients at baseline compared to controls (p=0.0127). Surprisingly, IL-6 levels in the stimulated supernatant of PMR patients at T0 were lower than those of controls (p=0.0426). No significant differences were found in the serum levels of IL-1β and TNF, while IL-6 levels in the sera of PMR patients at baseline were higher compared to those of the control group (p=0.0123).
Conclusion: PBMCs of PMR patients seem to be activated at baseline compared to controls. Our data indicate a possible role of immunosenescence or an "exhaustion" of PMBCs, that could be constitutively activated and not prone to responding to further stimuli, such as LPS. Moreover, we observed higher serum levels of IL-6 in PMR patients. More studies are needed to confirm the role of PBMCs and inflammatory cytokines in the pathogenesis of PMR.

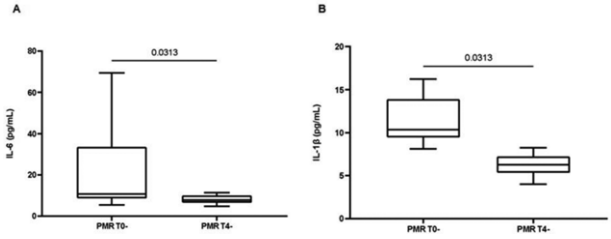


Figure 1. - IL-6 (A) and IL-β (B) levels in the unstimulated supernatant of PMR patients at baseline (PMR T0-) and after 4 months of GC therapy (PMR T4-)Data are shown as Tukey boxplots; lines represent the median level with the 25th-75th percentile.

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AB0176 GENETIC EVIDENCE REVEALED A CAUSAL ROLE OF GUT MICROBIOTA IN POLYMYALGIA RHEUMATICA

Keywords: Genetics/epigenetics, Fibromyalgia

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Background: Polymyalgia rheumatica (PMR) is an inflammatory disease characterized by bilateral pain involving and less commonly the neck and the pelvic girdle[1]. However, no definitive evidence supports that gut microbiota is associated with PMR.
Objectives: In this study, we conducted Mendelian randomization (MR) to assess the associations of genera of gut microbiota with PMR.
Methods: The data of gut microbiota were derived from the Integrated Epidemiology Unit (IEU) GWAS database, which included 1523 PMR cases and 213145 healthy controls[2]. A series of results were calculated to analyze the causal effects between gut microbiota and PMR. Inverse variance weighted is the primary and we did several analyses to prove MR result, weighted-median, MR Egger regression, and MR-presso. Cochran's Q statistics were used to quantify the heterogeneity of instrumental variables[3].
Results: The MR results for the causal effect of gut microbiota on PMR showed that genus Erysipelatoclostridium(odds ratio (OR)=0.910, 95% confidence interval (CI) =0.307-2.39, p =0.867) and genus Ruminococcaceae(OR=0.394, 95% CI =0.124-1.250, p =0.145) are protective factors for PMR. And genus Butyricimonas(OR=2.837, 95% CI=0.861-9.346, p=0.114), genus Eisenbergiella(OR=1.5818551, 95% CI =0.251-9.945,p=0.631), genus Coprobacter(OR=1.359, 95% CI =0.470-3.925, p =0.586)were correlated with the risk of PMR. In the meantime, heterogeneity(P>0.05) and pleiotropy (P>0.05) analysis confirmed the reliability of MR results.(Figure 1)

Conclusion: These findings provided that partial gut microbiota have an obvious causal relationship with PMR. Further trials are needed to clarify the protective effect of gut microbiota.

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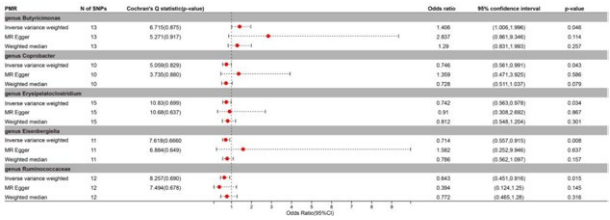


Figure 1. Forest plot of our main mendelian randomization analysis. PMR, Polymyalgia rheumatica.

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AB0177

ESTIMATING CAUSALITY FOR POLYARTERITIS NODOSA WITH IL-1, AND IL-10: MENDELIAN RANDOMISATION ANALYSES

Keywords: Cytokines and chemokines, Vasculitis

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Background: Polyarteritis nodosa (PAN) is a primary form of vasculitis characterized by inflammation of primarily medium-sized arteries[1]. Although the etiology of vasculitis is not fully understood, it has been suggested that cytokines(including interleukin-1 (IL-1) and interleukin-10(IL-10)) are significantly associated with a high susceptibility to vasculitis[2, 3]. However, there is no relevant research to explore the causality and direction of this association between interleukin and PAN.

Objectives: In this study, we intended to detect the casual association between PAN and interleukin using two-sample Mendelian randomization (MR) analysis.

Methods: The summary statistics of PAN were obtained from the FinnGen consortium release data (82 cases and 213145 controls). We also selected genetic instruments associated with il-1 and il-10 from the study of Sun et al. (3301 sample size). Initially, SNPs associated with interleukin at the genome-wide significance threshold ($p<1\times10^{-5}$) were extracted. Afterwards, We used a two-sample mendelian randomization analysis to explore the causal associations between PAN with IL-1, and IL-10. The inverse variance weighted (IVW) was the primary approach to calculating the effect estimates. To increase the IVW estimates, we also used other MR methods, such as MR-Egger and weighted median. Additionally, Sensitivity analyses of evaluating the influence of outliers and pleiotropy effects were performed by a variety of MR methods. All Statistical analyses were performed using R (version 4.2.1).

Results: Using single-nucleotide polymorphisms (SNPs) of genome-wide significance as instrumental variables, we did not find a significant association of IL-1α(odds ratio[OR] = 1.044, 95% confidence interval [CI]: 0.551 to 1.981, p = 0.895), IL-1β (odds ratio[OR] = 0.986, 95% confidence interval [CI]: 0.557 to 1.745, p = 0.962), and IL-10 (odds ratio[OR] = 1.066, 95% confidence interval [CI]: 0.621 to 1.832, p = 0.815) on PAN. Likewise, Comparable results were obtained using MR-Egger regression, and weighted median. We did not find evidence to support a causal association between IL-1α, IL-1β, IL-10, and PAN.

Conclusion: The results of this study based on genetic data did not support a causal relationship between PAN and Il-1, IL-10.

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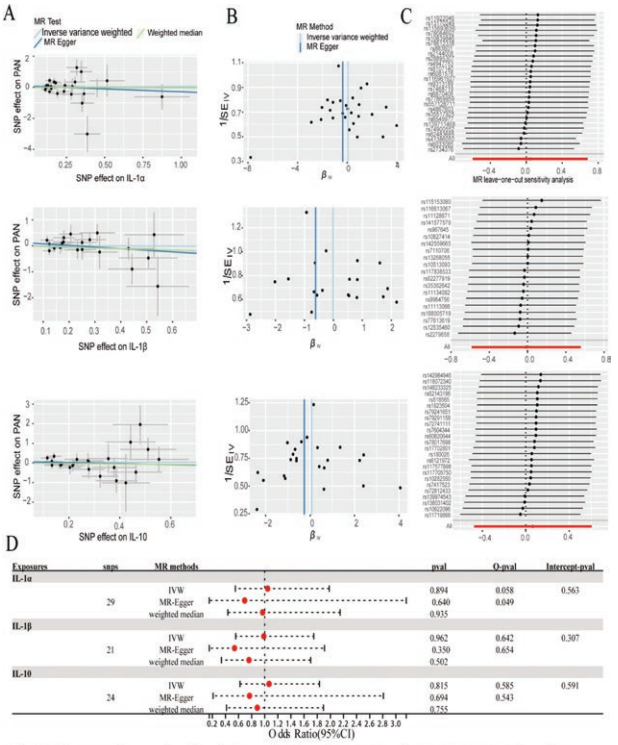


Fig.1(A)Scatter plots to visualize the causal effect of IL-1α, IL-1β, IL-10 on PAN using the conventional IVW, MR-Egger, Weighted median. (B)Funnel plots to visualize the overall heterogeneity of MR estimates for the effect of IL-1α, IL-1β, IL-10 on PAN. (C)Results of the leave-one-out method in MR sensitivity analysis. (D)Forest plot of the causal effect of IL-1α, IL-1β, IL-10 on PAN risk.

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Basic and translational science in paediatric rheumatology

AB0178

POSTURAL DEFECTS IN CHILDREN AT EARLY SCHOOL AGE - CROSS-SECTIONAL STUDY

Keywords: Physical therapy/physiotherapy, Lifestyles

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Background: The physical posture of a person is a movement habit which is formed on a morphological and functional basis, associated with everyday activity. During a person's life, body posture changes, especially during growth. The first critical period for physical posture is the age of 7-10 years. It is associated with a change in the current lifestyle, with the transition from a large freedom of movement to staying in a sitting position at school for several hours [1-3].

Due to the prevalence of the problem and the possibility of effective prevention, it is important to detect posture defects early and identify risk factors in order to identify a group of children potentially at risk of posture defects.

OBJECTIVES:

1.Assessment of the occurrence of posture defects viewed from the back and side in the study group of school-aged children.
2.Identification of factors related to the formation of posture abnormalities in the study group.

Methods: The study was covered among 141 children aged 7-10 attending grades 1-3 of the primary school in Bialystok, north-eastern Poland. The criterion for inclusion in the study was the child's age and parental consent.

The study consisted of:

1.Measuring the child's height using a standard centimeter measure and the child's weight using an electronic scale.
2.Evaluation of body posture using the Kasperczyk scoring method.
3.Interview with the parents of the examined children using a self-designed questionnaire.

Results: Among the examined children (n=141), only one had not been diagnosed with any postural abnormalities, both from the back and from the side. Irregularities most often concerned: shoulders 73% (projected forward), feet 71% (lowered longitudinal), arch 49%, valgus heels 22%, flat feet 19%, shape of the spine (hyperlordosis 24%, flat back 18%), scoliotic posture 28% and pelvis (anterior tilt 43%). Gender differentiated only the occurrence of abnormalities in the waist triangles (p=0.0489) and knees (p=0.038) in boys. On the other hand, age differentiated the incidence of defects in the position of the shoulder blades (p=0.0037) and shoulders (p=0.0129) with a negative tendency with age. In 67% of the examined children, the BMI index was normal and did not differentiate the occurrence of posture defects. There was also no statistically significant correlation between the weight of the school bag and the number of posture defects. Looking for factors further, the parents of the surveyed children were asked about their lifestyle. Almost half of the children (47%) were transported to school by car. Most had a separate room (67%), their own desk (81%) and an adjustable chair (70%). Most children participated in physical education classes (96%), they also participated in extracurricular activities (77%) up to 2-3 times a week (43%). The eating habits of the majority of children were also correct, and the majority (92%) spend their free time in the yard.

Conclusion: Factors related to BMI, children's physical activity and nutrition were not related to the occurrence of posture defects. Despite this, almost all of the examined children had postural defects of varying severity, and mostly several defects. The posture that is revealed on the basis of research is a closed posture with the head pushed forward, with extended, retracted shoulders, hyperlordosis and anteversion. It seems that the research should be deepened and the causes of such a large number of posture defects among children should be found, for the purpose of early prevention.

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Basic and translational pain science

AB0180

PAIN SENSITISATION IN FIBROMYALGIA. THE CROSS-SECTIONAL ASSOCIATIONS BETWEEN MEASURES OF QUANTITATIVE SENSORY TESTING AND FIBROMYALGIA SEVERITY

Keywords: Fibromyalgia, Patient reported outcomes, Biomarkers

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Background: Whether patient's experience of fibromyalgia severity is related to measures of pain sensitisation assessed by quantitative sensory testing is not clear. How disease duration effects the relationship between disease severity and pain sensitisation changes is also unknown.

Objectives: To examine the associations between pain sensitisation and fibromyalgia disease severity, as measured by the Polysymptomatic Distress scale (PDS) and Fibromyalgia Impact Questionnaire (FIQ). Secondly, to examine the impact of disease duration on the associations.

Methods: Participants were recruited from referrals to a hospital clinic and the diagnosis verified by a specialist rheumatologist. Patients self-reported PDS and FIQ. Quantitative sensory testing included assessments of pressure pain threshold (PPT), temporal summation (TS) and conditioned pain modulation (CPM) were performed. PPT was tested 3 times at 5 predefined sites (a non-painful interphalangeal joint, dorsal radio-ulnar joint, lateral epicondyle of the elbow, middle surface of the trapezius muscle, and tibialis anterior muscle) using an algometer (FPIX 25). The pressure at which the patient first reported a slight pain was recorded, and the mean PPT values at each site and for all measurements (aggregated mean) were calculated. Lower PPTs indicate more pain sensitization. TS was estimated using probes of increasing weight that were tapped against the radioulnar joint. Pain was recorded on a numeric rating scale for the 1st, 5th, and 10th tap of the probe that elicited a pain ≥ 4 on a 0-10 scale. The maximum difference in pain between the 1st and either 5th or 10th tap was calculated, and an increase in pain during repetitive stimuli indicate TS. PPT was also tested before and after a conditioning stimulus with a blood pressure cuff around the contra-lateral arm, and the ratio of the PPTs (post:pre) was calculated. A positive ratio indicates adequate CPM. Cut-offs of pain sensitization were defined as PPT < median, TS ≥ 2 and CPM <1. Disease duration was dichotomized at ≤ 5 vs. > 5 years. The associations between quantitative sensory testing and disease severity were explored in linear regression models adjusted for age, sex and body mass index and interactions with disease duration were explored.

Results: A total of 78 patients (90% women, mean age 40.9 years (SD 7.3)) were recruited. In linear regression models, aggregated mean PPT was weakly associated with the PDS score, the FIQ total score and the pain, fatigue and depression components (Table 1). The mean PPTs from the trapezius and tibialis anterior muscles were also weakly but significantly associated with several components of the PDS and FIQ. TS was weakly associated with the anxiety and depression components of FIQ while there was no association between CPM and PDS or FIQ (Table 1). We found no evidence of disease duration being an effect modifier for the associations.

Conclusion: In this cohort of patients with clinically verified fibromyalgia, pain sensitisation was weakly associated with self- reported disease severity. Disease duration did not impact on the relationship. Our results point to the multifactorial nature of the fibromyalgia symptom burden.

Table The cross-sectional associations between measures of quantitative sensory testing and fibromyalgia severity

	Measures of quantitative sensory testing (Independent variables) (β (95% CI))		
(Dependent variables)	PPT<vs.>=median	TS ≥ 2 vs. <2	CPM < 1vs. ≥ 1
PDS	3.5 (1.1, 5.8)*	1.1 (-1.3, 3.6)	-0.6 (-3.2, 2.1)
-SSS	1.2 (0.4, 2.1)* $^{\alpha}$	0.4 (-1.6, 2.4)	0.0 (-1.0, 1.0)
-WSP	2.2 (0.3, 4.1)*	0.7 (-0.2, 1.6)	-0.6 (-2.7, 1.6)
FIQ total	8.7 (1.2, 16.2)*	5.6 (-2.2, 13.3)	2.3 (-6.2, 10.8)
-pain	1.1 (0.1, 2.1)*	0.3 (-0.8, 1.3)	-0.3 (-1.4, 0.8)
-fatigue	0.9 (0.2, 1.7)*	0.6 (-0.2, 1.4)	-0.1 (-0.9, 0.8)
-depression	1.5 (-0.0, 2.9)*	1.9 (0.4, 3.3)*	0.2 (-1.5, 1.8)

*=p<0.05, α=R^2 adj >=0.1 & <0.2, all other R^2adj <0.1

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AB0181 **PAIN SENSITIZATION IN ADOLESCENCE: MUSCULOSKELETAL PAIN HISTORY AND EXPERIMENTAL PAIN RESPONSES IN A POPULATION-BASED COHORT STUDY**

Keywords: Pain, Patient reported outcomes, Epidemiology

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Background: Prolonged exposure to pain may induce sensitisation through neuroplastic processes, resulting in gain/loss of function and alteration of signal processing, and probably playing an important role in the experience and chronification of pain. Quantitative sensory testing (QST) assesses responses to standardised stimuli, allowing for an estimation of the effects of health conditions on somatosensory function [1]. Sensitized pain mechanisms are often reported in adults with musculoskeletal pain conditions, but population-based pediatric studies are lacking.

Objectives: To investigate the association between reported musculoskeletal pain history (based on complementary criteria) and pain sensitisation measures at age 13 years in a population-based cohort. We hypothesised that adolescents reporting more adverse musculoskeletal pain experiences would have higher pain sensitivity, impaired anti-nociceptive and/or facilitated pro-nociceptive mechanisms.

Methods: We analyzed data from 1496 adolescents of the population-based Generation XXI birth cohort study in Porto, Portugal. Pain history was collected using the Luebeck Pain Questionnaire (self-reported at 13 years, parent-reported at 7 and 10 years). Musculoskeletal pain was considered present if reported in the back, neck, shoulders, upper/lower limbs, hips, or widespread musculoskeletal. Three case definitions for adverse musculoskeletal pain history were used: 1) chronic (3+ months) musculoskeletal pain at age 13; 2) musculoskeletal pain with an impact on daily living (school and/or hobbies) at age 13; and 3) musculoskeletal pain at age 13 together with previous musculoskeletal pain reports at ages 7 and/or 10 (reported in previous data collection waves). Lower limb cuff pressure algometry was conducted at age 13 using a computerized system coupled with a visual analogue scale for pain intensity rating. We extracted pain sensitivity (pain detection and tolerance thresholds), conditioned pain modulation (CPM, changes in thresholds in the presence of a distant painful conditioning) and temporal pain summation (TSP, changes in pain intensity to ten phasic painful cuff stimulations). Non-parametric tests were used to compare QST parameter distributions.

Results: Adolescents with musculoskeletal pain at age 13 who had a history of musculoskeletal pain at ages 7 and/or 10 had lower pain tolerance threshold compared to the remaining sample (mean 40.2 vs. 49.0 kPa, p=0.020) and lower pain detection threshold point estimate (14.5 vs. 18.2, p=0.072). Slightly lowered pain tolerance was also found in adolescents with musculoskeletal pain with an impact on daily living at age 13 (42.4 vs. 49.0, p=0.091). No differences were found for pain sensitivity measures according to the presence of pain lasting 3+ months at age 13. No differences were found for CPM-effects and TSP-effects according to pain history regardless of the case definition used.

Conclusion: Repeated musculoskeletal pain up to age 13 years may contribute to lower pain tolerance in the general adolescent population. This does not seem to be the case when reported pain experiences are recent or when the outcomes are temporal pain summation or conditioned pain modulation. In this community-based sample the vast majority showed no sign of altered central pain processing but a small fraction with longer pain experiences may reveal some pain sensitization at 13 years of age.

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AB0182 **CONDITIONED MEDIA FROM PRIMARY OA CHONDROCYTES AFFECT THE BEHAVIOUR OF PHEOCHROMOCYTOMA PC 12 CELLS**

Keywords: Pain, Cartilage, Osteoarthritis

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Background: Osteoarthritis (OA) is the most common joint disease characterized by progressive degradation of articular cartilage, synovial hyperplasia, bone remodeling and angiogenesis [1]. Symptomatic painful OA leads to psychological distress and significant restrictions in daily living. Shortening of work life accompanied by an exponential rise in healthcare costs causes OA to become a major socio-economic burden [2]. Although, OA induced pain represents the most frequent cause of chronic pain, its mechanisms are poorly understood and treatments are not satisfactory [3].

Objectives: It is of great interest to investigate whether OA-induced changes in chondrocyte metabolism can affect neurons. Neurons with increased expression of neurogenic markers could contribute to enhanced pain perception. An investigation of the influence of conditioned media from primary OA chondrocytes on PC12 cells may serve to elucidate interactions.

Methods: PC12 cells, have been treated with conditioned media from primary OA chondrocytes (pCH-OA) and tested for changes in expression by RNA sequencing. Expression of neurogenic markers nestin, microtubule-associated protein 2 (Map2) and tyrosine hydroxylase (TH) from PC12 cells after treatment were analyzed by qPCR. Screening of the conditioned media for relevant factors was performed by using a cytokine proteome profiler array. Electrophysiological measurements were performed by the patch clamp method on rat dorsal root ganglia neurons (DRGs) treated with specific cytokines.

Results: RNA sequencing of treated PC12 cells showed changes in expression profile when cells were treated with conditioned media from pCH-OA and HC control chondrocytes compared with standard differentiation and growth media, respectively. Specific qPCR for the neuronal differentiation markers nestin, Map2, and Th showed an increase in expression in PC12 cells induced by most of the conditioned media from pCH-OA cells tested. In particular, Map2 and TH were increased by treatment in almost all conditioned media (n=14). Results of a cytokine proteome profiler array showed high levels of IL6, IL8, and MCP1 in conditioned media from pCH-OA cells of different patients. Treatment of DRGs with an interleukin cocktail altered the electrophysiological behavior tested by the patch-clamp technique and provided the first evidence that chondrocytes might secrete neuromodulatory substances.

Conclusion: Changes in the electrophysiological behavior of neurons caused by OA and the identification of the responsible metabolites should help to shed more light on the process of neuronal sensitization and pain generation in the development of OA in more detail and at the molecular level. In addition, the results also suggest that there are individual responses in individual patients. This information lays the groundwork for explaining why differences in pain perception may vary among OA patients and why there are different pain phenotypes in OA.

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AB0183

DEVELOPMENT AND VALIDATION OF THE PLACEBO SENSITIVITY QUESTIONNAIRE (PSQ): CAN THE PSQ PREDICT PLACEBO ANALGESIA RESPONSIVENESS?

Keywords: Treat to target, Pain, Prognostic factors

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Background: People respond to placebo to different degrees, and some do not respond at all (Frisaldi et al., 2018). Several studies investigated whether there are psychological aspects that predict these differences, but the results remain heterogeneous (Horing et al., 2014; Kern et al., 2020)
Objectives: Here, we develop and validate the Placebo Sensitivity Questionnaire (PSQ), an instrument that measures behaviors potentially related to placebo responsiveness. The idea is to treat placebo as a personality trait, with its own dimensions and its set of marker behaviours, instead of a phenomenon determined by multiple personality traits as it has been done up to now.
Methods: 330 individuals completed the initial version of the PSQ along with 9 additional scales measuring psychological traits associated with placebo responsiveness. These data were used to reduce the dimension of the PSQ, identifying a shorter set of predictive items, and to bring evidence of construct validity. A second experiment, currently ongoing, tests the predictive validity of the PSQ using a classic placebo analgesia experimental paradigm. Here, healthy volunteers are administered a placebo cream, presented as a potent analgesic, and receive noxious stimulations by means of thermal stimulation.
Results: Principal component analysis revealed a 3-factor structure – Symptoms Exaggeration, Seek for Support, Alternative Medicine Beliefs - and the number of items was reduced from 40 to 19. Construct validity indicated that the PSQ correlates with most of the scales previously associated with placebo responsiveness. For the predictive validity study, which is in due course at the time of this abstract submission, we hypothesise that the PSQ will be successful in discriminating a priori placebo sensitivity and non-responders.
Conclusion: The PSQ has the potential to become an important tool for researchers and clinicians working with pain, moving us a step forward toward personalised pain management.
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AB0184

SENSORY PROFILING IN CLASSICAL EHLERS-DANLOS SYNDROME: EVIDENCE FROM A CASE-CONTROL STUDY REVEALS PAIN CHARACTERISTICS, SENSORY CHANGES AND IMPAIRED PAIN MODULATION

Keywords: Pain, Genetics/epigenetics

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Background: The Ehlers-Danlos syndromes (EDS) are a paradigm group of rare heritable connective tissue disorders caused by pathogenic defects in genes involved in biosynthesis, fibrillogenesis, and/or supramolecular organization of collagen fibrils in the extracellular matrix (ECM). Joint hypermobility, skin hyperextensibility, abnormal wound healing and easy bruising are among the cardinal clinical features. The classical EDS type, caused by caused by defects in type V or rarely type I collagen, is the most prevalent genetically elucidated EDS type [1]. (Chronic) pain is highly prevalent in individuals with EDS and is one of the foremost reasons these individuals seek medical attention. There is a high use of analgesics, surgery, and physical therapy but these treatment modalities often bring only modest relief at best, and some are associated with unwanted side effects. Few studies, almost exclusively conducted in the molecularly unexplained hypermobile EDS type, have brought limited evidence for neuropathic pain and decreased intra-epidermal nerve fiber density. Interestingly, functional and structural abnormalities of the nervous system and associated pain-related behaviors have also been described in mouse models of EDS [2]. Comprehensive human studies on pain prevalence and pain mechanisms in molecularly solved EDS types are however currently not available, thereby representing a major gap in the study of pain in EDS.
Objectives: The primary aim of this cross-sectional study was to identify the sensory profile of individuals with cEDS. Secondly, we aimed to identify the pain characteristics and the emotional-cognitive burden in cEDS.
Methods: Nineteen individuals with molecularly confirmed cEDS and 19 healthy matched control were recruited. Sensory profiling included sensitivity to innocuous and noxious stimuli of multiple modalities (electrical, thermal, vibration, touch, pressure) and a parallel and sequential conditioned pain modulation protocol. Moreover, pain characteristics and emotional-cognitive factors that are known to influence pain processing were studied using a set of validated questionnaires (PD-Q, DN4, HADS, HAQ, SF-36, CSI, PVAQ, TAMPA scale).
RESULTS:

Table 1.

cEDS cohort compared to control group	
Pain	+
Emotional burden	(+)
Detection thresholds	
Electrical	=
Thermal	=
Vibration	+
Touch	=
Paradoxical thermal sensations	+
Pain thresholds	
Electrical	=
Cold	-
Heat	=
Pressure	-
Conditioned pain modulation	-

+/-: statistically significant differences; = non-significant

The cEDS cohort showed an altered sensory profile. Higher (p=0.04) detection thresholds for vibration stimuli at the lower limb were found indicating the presence of hypoesthesia. Reduced/altered thermal sensitivity was found with significantly more (p<0.001) paradoxical thermal sensations at the lower limb (usually to heat). Lower pain thresholds were found to mechanical (p<0.001) stimuli at both the upper and lower limbs and to cold (p=0.005) stimulation at the lower limb indicating hyperalgesia. Using a parallel conditioned pain paradigm, significantly (p=0.005 and p=0.046) smaller antinociceptive responses were shown in cEDS suggestive of impaired central pain inhibition.
Conclusion: This study represents the first systematic investigation of pain in a genetically defined EDS type. With evidence for sensory changes and impaired pain modulation in cEDS, we provide new insights on the possible role of the ECM in the development and persistence of pain.
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AB0185

INVESTIGATION OF THE RELATIONSHIP BETWEEN PATIENTS WITH ARTHROPLASTY AND PATIENTS WITHOUT ARTHROPLASTY FOR LOWER EXTREMITY OSTEOARTHRITIS IN TERMS OF PAIN COPING STRATEGIES, FUNCTIONAL STATUS AND QUALITY OF LIFE.

Keywords: Quality of life, Osteoarthritis, Pain

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Background: Osteoarthritis (OA) is the most common joint disease worldwide and a major source of pain, disability, and socioeconomic cost [1]. Most of the pain or functional disability induced by these diseases can be improved by the surgery. Arthroplasty currently is considered the international gold standard of treatment the knee and hip joints osteoarthritis [2]. In the literature it was defined that pain can be exacerbated and inhibited by the psychological variable. Except the surgical trauma and social factors, the psychological factors have huge influence on the occurrence of the pain [3]. Pain coping strategies are the person's responses to manage pain and they are generally classified as active and passive strategies. While active strategies identify as controlling the pain or functioning despite the pain, passive strategies identify as withdrawing and surrendering control over the pain [4]. Pain is very effective factor on the patients' outcomes after arthroplasty. Some psychological coping strategies have been introduced to minimize the effects of pain, but there are no guidelines to follow to reduce pain, because the psychological interventions are different based on the surgery types, technique mechanism and pain specific information [5].
Objectives: This study aims to investigate the relationship between patients with arthroplasty and patients without arthroplasty for lower extremity osteoarthritis in terms of coping with pain, functional status and quality of life.
Methods: Twenty patients with bilateral arthroplasty (mean age 62,75±12,22) and thirty-two patients with OA (mean age 58,87±9,22) were included in the study. The Pain Coping Inventory (PCI), Timed Up and Go Test (TUG), 5 Times Sit to Stand Test (FTSST), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Short Form (SF)-12 Quality Life Questionnaire administered to the patients.
Results: Demographics were statistically similar in both the lower extremity arthroplasty group (LEAG) and osteoarthritis group (OAG). PCI passive total score, PCI passive worrying, PCI passive retreating, PCI passive resting, PCI active total, PCI active distraction and PCI active reducing demands scores were similar in the groups. PCI active pain transformation score was significantly lower in the OAG. TUG and FTSST were similar in groups. WOMAC pain, WOMAC stiffness, WOMAC physical function and WOMAC total scores were significantly higher in the OAG. SF12 PCS and SF12 total scores were significantly higher in the LEAG than in the OAG. SF12 MCS score was similar between the groups.
Conclusion: This study demonstrated that LEAG have better pain transformation, pain intensity, stiffness, patient reported function and physical component of quality of life compared to OAG. Surgery has been effective in improving function and reducing pain according to the results. The difference in active pain transformation in PCI between groups is thought to be related to this. However, it was determined that psychosocial approaches should be included in pain management in the rehabilitation program of patients with OA and arthroplasty.
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AB0186

THE EFFECT OF KNEE JOINT LOSS ON PROSTHESIS AWARENESS IN LOWER LIMB AMPUTEES

Keywords: Patient reported outcomes, Physical therapy/physiotherapy, Quality of life

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Background: In knee disarticulation, transfemoral and hip disarticulation amputations, unlike transtibial amputations, the anatomical knee joint is replaced by a prosthetic knee joint. In amputations where the natural knee joint is not preserved, compared to transtibial amputations; It has been stated that it is difficult to reach the normal functional level and more energy is spent [1]. The closer the amputation level is to the proximal, the more restrictions the amputee has in activities of daily living [2].
Objectives: In this study, we compared the ability of forgetting the prosthesis, which is an indicator of adaptation with the prosthesis, of amputees with and without an anatomical knee joint in daily life activities. The aim of this study is to examine the effect of loss of the knee joint on the ability to forget the prosthesis in daily life in amputees.
Methods: Lower limb amputees aged 18-65 years, who used prosthesis for at least 6 months were included in this study. Prosthesis awareness was evaluated with the Forgotten Joint Score-12 (FJS-12) amputee version [3]. The FJS-12 amputee version consists of 12 questions about awareness of the artificial limb during daily living activities. The raw scores are transformed to range from 0 to 100 points, with high scores indicating as a percentage (%) the extent to which the patient can forget the artificial limb, that is, adapt them to their lives. Amputees were divided into two groups as with and without knee joint loss. The prosthetic awareness scores of the two groups were compared. Independent sample t-test was used to compare the data.
Results: 29 transtibial amputees (mean age: 37.17 ± 11.05 years; Body Mass Index: 25.21 ± 3.02 kg/m2) were included in the knee joint group. A total of 26 amputees (mean age: 35.07 ± 10.29 years; Body Mass Index: 23.77 ± 3.59 kg/m2) were included in the group without knee joint, including 5 knee disarticulations, 18 transfemoral and 3 hip disarticulations. The groups were similar in terms of mean age, body mass index, and years of prosthesis use (respectively p=0.470;p= 0.143; p=0.980) When the FJS-12 total score means of the groups with and without knee joint were compared, there was a statistically significant difference between the two groups (p=0.017; Z=-2.337).
Conclusion: This study showed that loss of the knee joint affects the way amputees perceive their prosthesis. In the absence of a anatomical knee joint, amputees' attention to their prosthesis is increasing. Amputees with a knee joints focus less on their prostheses in daily life activities. Our study revealed that the knee joint, which is frequently used in activities of daily living, is also a determining factor in the adaptation of amputees to the prosthesis.
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Rheumatoid arthritis - prognosis, predictors and outcome

AB0187 **CONSIDERATIONS OF REALISTIC TREATMENT GOALS BASED ON PREDICTORS OF FRAILTY PROGRESSION IN PRE-FRAIL PATIENTS WITH RHEUMATOID ARTHRITIS: A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY.**

Keywords: Real-world evidence, Prognostic factors, Rheumatoid arthritis

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Background: Frailty is a common geriatric syndrome that involves an elevated risk of catastrophic declines in health and function [1]. Rheumatoid arthritis (RA) is an autoimmune disease that causes synovitis in the joints, resulting in a high prevalence of joint deformity (0.5–1.0% in Japan) [2]. Japan is one of the world's most rapidly aging societies [3]. Many older adults in Japan are in the pre-frailty category (4), and older RA patients are generally at a greater risk of frailty than the general population. Against this backdrop, the present study aimed to examine predictors of frailty progression in RA patients. Pre-frailty patients with RA were focused on because, in the short term, they are more prone to frailty than robust patients.

Objectives: To examines the predictors of frailty progression in pre-frail patients with RA.

Methods: A total of 287 RA patients who were pre-frailty in 2020 were evaluated on the basis of our observational study data. Of the patients, 55 were robust, 186 were pre-frailty, and 46 were frailty in 2021 and were assigned to the Better, Stable, and Worse groups, respectively. After comparing the characteristics of the patients in the three groups at baseline, the two-year change was assessed with respect to the use of DAS28-ESR, HAQ-DI, and methotrexate (MTX); biological and targeted synthetic disease-modifying antirheumatic drugs (b/ts-DMARDs); and steroids. The Better and Stable groups were compared to clarify the difference between the two groups. The Stable and Worse groups were compared by univariate analysis. The predictors of transitioning to the Worse group were assessed by logistic regression analysis.

Results: At baseline, mean DAS28-ESR for all groups exhibited low disease activity levels, but only the Worse group deteriorated, eventually reaching moderate disease activity levels. The Better and Stable groups maintained sub-low disease activity over two years (Figure 1A). HAQ-DI in the Worse group was significantly higher than in the other two groups. However, comparing HAQ-DI in the Stable and Better groups, the Stable group was substantially worse (Figure 1B), although there were no differences in the other factors, suggesting an irreversible gap between the two groups. There were no differences in MTX and steroid use among the groups, although the rate of steroid use in the Worse group was slightly higher than in the other two groups over two years (Figure 1C, 1D). On the other hand, b/ts-DMARDs in the Stable group were higher than in the other two groups (Figure 1E). This suggested that most patients in the Stable group required a combination of MTX and b/ts-DMARDs to maintain treat-to-target strategy, unlike the Better group. In comparing the Stable and Worse groups, age, DAS28-ESR, and non-use of b/ts-DMARDs were predictors of frailty progression (Table 1).

Conclusion: DAS28-ESR and non-use of b/ts-DMARDs were predictors of frailty progression over two years in pre-frail patients with RA. The ideal treatment goal is to improve from pre-frailty to robust, but a realistic goal is not to worsen from pre-frailty to frailty by using a combination of MTX and b/ts-DMARDs.

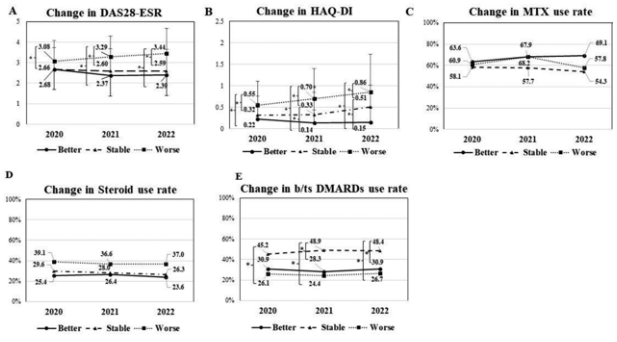


Figure 1: Two-year change in patient background.
A *p*-value <.05 was considered statistically significant and was represented as an asterisk (*)

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Table 1. Predictors of Frailty progression for RA patients with pre-frailty.

Factor	Odds ratio	P value
Age	1.04 (1.01-1.07)	0.024
Sex, female	0.82 (0.34-1.96)	0.660
Duration of disease	1.04 (1.00-1.07)	0.031
BMI	0.96 (0.87-1.06)	0.410
DAS28-ESR	1.48 (1.04-2.10)	0.028
b/ts-DMARDs use	0.40 (0.19-0.86)	0.019

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0188 **A BIOINFORMATIC APPROACH TO IDENTIFYING SENSITIZING THERAPEUTICS FOR RHEUMATOID ARTHRITIS**

Keywords: Rheumatoid arthritis, -omics

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Background: Rheumatoid Arthritis (RA) is a systemic and chronic autoimmune disorder that has significant impact on quality of life and work capacity for the patient. Treatment and management of RA is aimed at gaining control of inflammation and alleviating pain, however, achieving remission and low disease activity with minimal toxicity is frequently not possible with the current suite of drugs. Additionally with escalating de novo drug development costs, alternate bioinformatic approaches which scope the potential to repurpose already licenced compounds and their ability to work synergistically have become attractive.

OBJECTIVES:

1)Develop, test and refine a bespoke connectivity mapping based bioinformatic pipeline, DrugExpress, with capability of mining treatment response gene signatures using public RNAseq and microarray datasets.

2)Verify treatment response signatures and prioritise novel drugs to generate a list of robust sensitising drugs.

Methods: Public RNAseq (GSE198529) and microarray datasets (GSE93777 and GSE24742) were mined based on the presence of DAS score, clinical features, sample size and technological platform. R/Bioconductor packages and Perseus software were used to pre-process and carry out differential expression (DE) analysis to obtain a list of differentially expressed genes (DEGs), based on the cut off criteria of padj < 0.05 and a minimal 2-fold change of expression, and derive gene signatures characteristic of treatment response. DEGs from multiple datasets were combined to create a master gene list consisting of 21 DEGs. Gene Ontology (GO) enrichment analysis was performed on the genes in the master list to identify the top biological pathways. A list of inferred genes involved in each of these pathways was compiled to determine the overall direction of expression with response to treatment. DEGs in the master list were extracted and mapped to Affymetrix probeset IDs to create treatment response gene signatures to be entered into a sscMap search for candidate drugs. Connectivity mapping (CMap) analysis was used to establish networks between DEGs in the gene signature and FDA approved drugs. P-value and connection score of each reference drug in the CMap was obtained and used to determine statistical significance and perturbation stability.

Results: GO enrichment analysis performed on the master gene list identified the top 3 pathways: transport of connexons to the plasma membrane, oligomerization of connexins into connexons, and gap junction assembly. CMap analysis identified a total of 36 statistically significant compounds with a perturbation stability score of 1. Candidate compounds were selected based on whether they enhanced a theoretical response phenotype. The top 3 ranked compounds (by p value) which would induce theoretical reduction in disease activity were: ciclosporin (p-value = 0.0001), demecarium bromide (p-value = 0.0002) and 2-aminobenzenesulfonamide (p-value = 0.0002).

Conclusion: The analysis using the DrugExpress pipeline illustrates the process of treatment response DEG extraction from public expression datasets.

These response signatures can be used for CMap analysis to predict new compounds for treatment refractive patients and can potentially simulate the effective changes observed in responders. Next step in the pipeline would be to implement *in silico* toxicity screening methods to identify any contraindications with existing treatments.

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Disclosure of Interests: None Declared.

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AB0189 THE BEST CARDIOVASCULAR RISK ALGORITHM FOR PREDICTING THE PRESENCE OF CAROTID PLAQUE IN WOMEN WITH RHEUMATOID ARTHRITIS

Keywords: Gender/diversity issues, Rheumatoid arthritis, Cardiovascular disease

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Background: Atherosclerotic cardiovascular disease is the leading cause of death in patients with rheumatoid arthritis (RA). Chronic inflammation increases cardiovascular risk (CVR) in these patients [1]. Heart disease remains the most likely cause of death for women, and a higher risk is established than for men [2].

Objectives: To compare six CVR algorithms with carotid ultrasound findings in women with RA and to identify the algorithm with the cutoff point with the best sensitivity for carotid plaque (CP) detection.

Methods: Cross-sectional, and descriptive study. Patients aged 40 to 75 years who met the ACR/EULAR 2010 classification criteria for the diagnosis of RA. Patients with a history of cardiovascular disease were excluded. CVR was calculated using 6 algorithms: ACC/AHA 2013, FRS-Lipids, FRS-BMI, RRS, QRISK3 and SCORE2. Carotid ultrasound was performed on all study participants, and the presence of CP, defined as diffuse carotid intima-media thickness (cIMT) ≥1.2 mm or focal thickness ≥0.5 mm, was assessed. Subclinical atherosclerosis was defined as the presence of CP or a cIMT ≥0.8mm. An ROC curve analysis was performed and the cutoff points for each algorithm were determined using the Youden index. Area under the curve (AUC) sensitivity, specificity, and likelihood ratios (LR) were calculated. A value of $p \leq 0.05$ was considered statistically significant.

Results: A total of 158 women with a diagnosis of RA were included. The prevalence of CP was 32.3%. Results are shown in Figure 1.

Conclusion: The FRS-Lipids algorithm was one of the best algorithms for the detection of CP in women, with the best sensitivity compared to the other algorithms, however, in the low-risk group none of the algorithms proved to be sufficiently effective in predicting CVR. Therefore, we suggest to consider carotid ultrasound as part of the evaluation in women with RA.

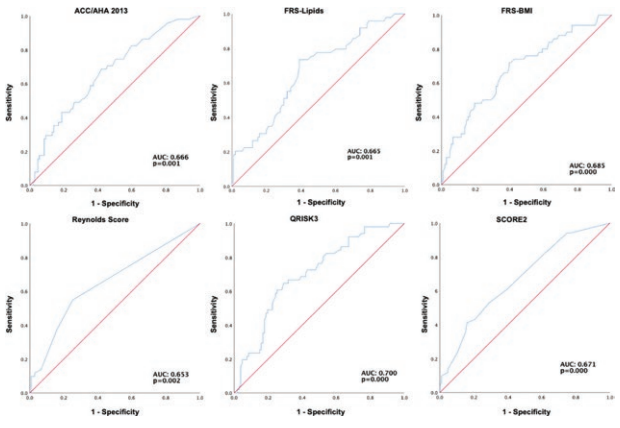


Figure 1. ROC curves of the cardiovascular risk algorithms.

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Disclosure of Interests: None Declared.

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AB0190 GENDER DIFFERENCES IN OSTEOPOROSIS RISK FACTORS IN PATIENTS WITH RHEUMATOID ARTHRITIS REFERRED FOR BONE DENSITY ESTIMATION – AN OBSERVATIONAL STUDY

Keywords: Osteoporosis, Epidemiology, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is associated with a loss of bone density and fragility fractures [1]. There are few studies that compare bone loss by gender.

Objectives: This study aims to explore the bone loss by gender in a large RA cohort referred for bone mineral density (BMD) estimation.

Methods: RA patients referred to a district BMD scanner in the northwest of England between 2004 and 2019 were included. The cohort was divided by gender and the prevalence of fracture, and risk factors for fractures modelled. Initially, traditional risk factors as defined by FRAX(tm) were compared between men and women and subsequently the ability of those risks to predict fractures were modelled. For the characteristic of secondary osteoporosis, only coeliac disease was included. Comparison was made using Chi-squared test for categorical variables and T-test for continuous variables. Predictors of fracture were modelled using logistic regression.

Results: 2072 patients, mean age 66.97 years (s.d. 11.34) were included, of whom 1628 (78.6%) were females. The mean age was significantly higher in Males at 68.02yrs compared to Females at 66.69yrs (p=0.0284). Height (171.62cm) and Weight (80.97) was higher in males and History of fractures was higher in females (33.11% vs 23.42% - p<0.001). Excess alcohol (6.08% vs 2.58% - p<0.001) and Steroid therapy (46.4% vs 28.62% - p<0.001) were higher in men. All other characteristics had no significant difference except lumbar spine BMD which was higher in men (-0.24 vs -0.82 - p<0.001). A summary of the differences is shown in Table 1.

Table 1. Results of logistic regression on fracture risk in men and women in the cohort

	Male OR	Male 95% CI	Female OR	Female 95% CI
Age	0.997	0.976-1.018	1.028	1.019-1.038
Height	1.017	0.986-1.049	0.969	0.955-0.984
Weight	1.005	0.991-1.018	0.992	0.986-0.999
FHx of fracture	1.101	0.479-2.530	1.371	1.038-1.810
Smoker current	1.801	1.011-3.210	0.969	0.722-1.300
Steroid therapy	0.761	0.488-1.186	0.785	0.622-0.991
Excess Alcohol	1.158	0.476-2.821	0.904	0.466-1.754
R NOF BMD	0.640	0.511-0.803	0.719	0.652-0.793
L NOF BMD	0.646	0.512-0.814	0.735	0.667-0.810
Lumbar spine BMD	0.957	0.922-0.992	0.956	0.940-0.973
Malabsorption – Secondary osteoporosis	2.410	0.748-7.748	2.235	1.321-3.781

Yellow – Statistically significant with P<0.05

Conclusion: The study identifies gender differences in the risk factors for fractures in rheumatoid arthritis patients. This will have implications when assessing fracture risk using FRAX(tm) underestimating fracture risk in this population. FHx of fractures was only significant in fractured RA females. Steroid therapy had an idiosyncratic effect and was seen as protective; this was previously described in this cohort [3]. Being a current smoker was only a significant risk factor in males. Finally, Left and Right NOF and lumbar spine BMD were significantly smaller in both fractured genders making a reduced BMD on these sites an important risk factor to consider in any patient with RA. The strength of this study was the large cohort of rheumatoid arthritis patients included while it was limited by lack of detail on disease activity, treatment and duration. A variety of significant data was found, but further work is required

to find accurate differences between the risk factors associated with fractures in both genders with RA.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0191 SAFETY OUTCOMES IN PATIENTS (PTS) WITH RHEUMATOID ARTHRITIS (RA) TREATED WITH FILGOTINIB (FIL) IN FILOSOPHY: INTERIM RESULTS FROM A PROSPECTIVE OBSERVATIONAL STUDY

Keywords: Real-world evidence, Safety, Rheumatoid arthritis

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Background: Consideration is needed when using Janus kinase (JAK) inhibitors to treat RA in pts aged ≥65 years or those with cardiovascular (CV) risk factors. The JAK1 preferential inhibitor FIL was generally well tolerated in clinical trials[1]; safety has not been determined in a real-world setting.

Objectives: To report baseline characteristics and up to 6-month safety data from the first 480 pts treated with FIL in the FILOSOPHY study (NCT04871919), and in two mutually exclusive subgroups based on age and CV risk.

Methods: FILOSOPHY is an ongoing, phase 4, non-interventional, European study of pts with RA who have been prescribed FIL for the first time and in accordance with the product label in daily practice. Baseline characteristics and the incidence of select adverse events (AEs) are assessed in pts aged ≥65 years and/or with ≥1 CV risk factor (**Table 1**), and in those aged <65 years with no CV risk factors.

Results: As of the end of June 2022, 480 pts had been treated: 441 received FIL 200 mg and 39 received FIL 100 mg. Of the 480 pts, 148 (30.8%) were aged ≥65 years; 332 (69.2%) were aged <65 years. In total, 86 (17.9%) were former smokers, 81 (16.9%) were current smokers and 203 (42.3%) were non-smokers (data were missing for 110 pts [22.9%]). In addition to smoking, the most frequent CV risk factors included a history of hypertension (32.3%), a history of dyslipidemia (10.2%) and a family history of myocardial infarction (8.5%; **Table 1**). 23 pts (4.8%) discontinued treatment due to AEs. Of the 354 pts aged ≥65 years or with ≥1 CV risk factor, infections affected 64 pts (18.1%), 34 (9.6%) had COVID-19, 2 (0.6%) had herpes zoster, and cardiac disorders (angina pectoris, atrial fibrillation, palpitations and tachycardia) affected 5 pts (1.4%); no cases of malignancies were observed. In the subgroup aged <65 years and with no CV risk factors (n=126), infections occurred in 18 pts (14.3%) (9 [7.1%] had COVID-19; 3 [2.4%] had herpes zoster) and malignancies (myeloproliferative neoplasm) affected 1 pt (0.8%); no pts had cardiac disorders. There were no cases of deep vein thrombosis or pulmonary embolism in either subgroup.

Conclusion: In this interim analysis of FILOSOPHY, no unexpected safety signals emerged at up to 6 months. Although infections and cardiac disorders affected a numerically greater proportion of pts aged ≥65 years or with ≥1 CV risk vs those aged <65 years with no CV risk, longer follow-up on a broader cohort is necessary to further characterize the safety of FIL in different groups of pts with RA.

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Table 1. Baseline characteristics and CV risk factors

Baseline demographics/CV risk factors	All FIL-treated pts (N=480)	≥65 years or with ≥1 CV risk factor (n=354)	<65 years and no CV risk factor (n=126)*
Female sex, n (%)	351 (73.1)	252 (71.2)	99 (78.6)
Age, years, mean (SD)	57.6 (11.5)	60.4 (10.8)	49.6 (9.6)
Rheumatoid factor positive, n (%)†	228 (47.5)	167 (47.2)	61 (48.4)
Anti-citrullinated protein antibody positive, n (%)‡	243 (50.6)	176 (49.7)	67 (53. 2)
Body mass index, kg/m^2, mean (SD)	27.6 (5.7) n=437	28.0 (5.4) n=331	26.3 (6.4) n=106
RA disease duration, years, mean (SD)	10.4 (9.4) n=478	10.5 (9.5) n=353	10.0 (8.8) n=125
Tender joint count 28, mean (SD)	8.6 (6.9) n=457	8.7 (7.1) n=340	8.3 (6.3) n=117
Swollen joint count 28, mean (SD)	5.6 (5.2) n=452	5.7 (5.4) n=336	5.4 (4.4) n=116
Former smoker, n (%)§	86 (17.9)	86 (24.3)	0
Current smoker, n (%)§	81 (16.9)	81 (22.9)	0
Non-smoker, n (%)§	203 (42.3)	130 (36.7)	73 (57.9)
Family history of myocardial infarction, n (%)	41 (8.5)	41 (11.6)	0
Medical history of: n (%)			
CV disease	33 (6.9)	33 (9.3)	0
Diabetes	35 (7.3)	35 (9.9)	0
Dyslipidemia	49 (10.2)	49 (13.8)	0
Hypertension	155 (32.3)	155 (43.8)	0
Ischemic CNS vascular disorders	11 (2.3)	11 (3.1)	0
Peripheral vascular disease	17 (3.5)	17 (4.8)	0

*Includes 53 pts with missing smoking status data who were aged <65 years with no other CV risk factors. †Missing/unknown in 154 pts; ‡Missing in 153 pts; §Smoking status data missing in 110 pts (22.9%).

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AB0192 ANALYSIS OF ULTRASOUND FINDINGS IN PATIENTS WITH DIFFICULT TO TREAT RHEUMATOID ARTHRITIS

Keywords: Ultrasound, bDMARD, Rheumatoid arthritis

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Background: In recent years, the concept of D2TRA (difficult-to-treat rheumatoid arthritis) has become widespread, and D2TRA patients are defined as a state in which activity cannot be controlled even with the use of various molecular-targeted drugs. In this study, we investigated the ultrasound synovial findings in D2TRA patients. However, ultrasound findings in D2TRA patients are unknown.

Objectives: In this study, we investigated the ultrasound findings of D2TRA patients.

Methods: A total of 750 RA patients who underwent ultrasound examination were included. Ultrasond examination was performed at the of bilateral first to fifth metacarpophalangeal (MCP) joints, first interphalangeal (IP) and second to fifth proximal interphalangeal (PIP) joints, wrist joints (three part of radial, medial and

ulnar) and first to fifth metatarsophalangeal (MTP) joints. Of all 750 RA patients, 517 RA patients (68.9%) who treated bDMARDs/JAKi were included and devided in D2TRA patients and non-D2TRA patients. The patients' characteristics, total gray scale (GS) and power Doppler (PD) score (GSUS/ PDUS) were compared between D2TRA patients and non-D2TRA patients.

Results: There were 40 D2TRA patients and 477 non-D2TRA patients. Mean age was 61.2 vs. 65.0 years (p=0.133), mean disease duration of RA was 17.6 vs. 14.9 years (p=0.199), CDAI was 12.6 vs. 9.8 (0.166), and CRP level was 0.79 vs. 0.28 mg/dL (p=0.233), MMP-3 level was 295.6 vs 10.8ng/mL (p=0.057), respectively. In the D2TRA group, concomitant use ratio of MTX was low (50.0 vs 70.9 %, p=0.011), but there was no difference in the average dose of MTX (8.9 vs 9.2 mg/w, p=0.581). The concomitant use ratio of glucocorticoid (32.5 vs 12.6 %, p=0.002) and the average dose of glucocorticoid (7.7 vs 3.1 mg/d, p=0.003) were higher in D2TRA group. Regarding ultrasound findings, GSUS score (16.2 vs 9.5, p=0.011) and PDUS score (11.0 vs 6.4, p=0.034) were significantly higher in the D2TRA group.

Table 1.

	D2TRA (n=40)	non D2TRA (n=477)	p value
Age (years)	61.2±17.3	65.0±14.1	0.113
Female, %	77.5	82.1	0.390
BMI (kg/m^2)	22.5±4.9	22.3±3.4	0.750
Disease duration (years)	17.6±9.6	14.9±12.7	0.199
RF+, %	95.0	89.9	0.410
RF titer (mg/dL)	754.3±1284.7	301.2±423.4	0.032
CCP+, %	94.8	85.2	0.144
CCP titer (U/mL)	227.0±183.2	134.0±165.6	0.001
MTX use, %	50.0	70.9	0.011
MTX dose (mg/week)	8.9±2.6	9.2±3.6	0.581
Glucocorticoid use, %	32.5	12.6	0.002
Glucocorticoid dose (mg/day)	7.7±4.4	3.1±1.8	0.003
DAS28 ESR	3.2±1.9	3.0±1.4	0.668
DAS28 CRP	2.8±1.4	2.7±1.2	0.438
SDAI	13.4±12.6	10.1±9.5	0.120
CDAI	12.6±12.0	9.8±9.3	0.166
HAQ	0.90±0.98	0.66±0.74	0.137
ESR (mm/h)	26.2±30.2	17.6±20.6	0.085
CRP (mg/dL)	0.79±2.67	0.28±0.77	0.233
MMP-3 (ng/mL)	295.6±611.9	105.8±157.2	0.057
GSUS	16.2±15.7	9.5±9.5	0.011
PDUS	11.0±13.0	6.4±7.7	0.034

Conclusion: The definition of D2TRA is resistant to multiple mode of bDMARDs/ JAKi. Although, disease activity and inflammatory markers tended to be worse in the D2TRA group, there was no statistically significant difference in this study. However, ultrasound findings were significantly worse in D2TRA. Suppression of synovitis might be important to prevent D2TRA.

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AB0193 PATIENT-PHYSICIAN DISCORDANCE IN GLOBAL ASSESSMENTS AMONGST SOUTH AFRICANS WITH RA

Keywords: Patient reported outcomes, Rheumatoid arthritis, Outcome measures

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Background: Discordance between the patient global assessment (PGA) and physician global assessment (PhGA) is well reported in rheumatoid arthritis (RA) and can lead to suboptimal care[1]. There are no published studies on discordance in South African (SA) patients.

Objectives: To measure and explore patient-physician discordance amongst RA patients attending a tertiary SA hospital.

Methods: Consenting adults (≥18 years) with RA completed demographic, clinical and patient-reported outcome measures including Health Assessment Questionnaire-Disability Index (HAQ-DI),FACIT fatigue scale, Hospital Anxiety and Depression Scale (HADs), Brief Pain Questionnaire-short form (BPI-SF), and EuroQOL five dimensions questionnaire (EQ5D). Poor socio-economic status (SES) was defined using a pooled index. The Clinical Disease Activity Index (CDAI) was calculated based on the swollen and tender joint counts (SJC and TJC), PGA and PhGA visual analogue scale. Patients were categorized into high, moderate or low disease activity (HDA, MDA and LDA) states. Discordance was calculated by subtracting the PhGA score from the PGA and positive discordance was defined as a difference of > 2.5 points. Determinants of PGA and PhGA were also analyzed.

Results: Of 550 patients (467 females), the mean (SD) age and disease duration were 55.8 (12.9) and 10.5 (9.7) years, most were in LDA (47.8%), and 371 (67.4%) had poor SES. Positive discordance was seen in 136 patients (24.7%). Fifteen patients with negative discordance (PGA- PhGA < - 2.5) were excluded from this analysis. Comparing concordant and positive discordant patients, there were no significant differences in age, sex, disease duration, SES, RA therapy or number of comorbidities, nor in fatigue, HAD-DI, or HADs. The discordant group had significantly lower SJC, TJC and PhGA. More patients in the discordant group were in LDA (58.1% vs. 45.4%), with fewer in MDA (32.4 % vs. 29.1 %) and HDA (9.6% vs. 25.6%), p = 0.001. In addition, the discordant group included more fibromyalgia (FMS) patients, reported higher pain severity score and a higher EQ5D level sum score, with problems with usual activities being the only statistically significant domain (p<0.001). In logistic regression analysis, pain severity score and problems with usual activities on EQ5D were predictors of positive discordance. Pain was the main determinant of PGA (R^2 0.24, p<0.001) and SJC was the main determinant of PhGA (R^2 0.44, p<0.001).

Table 1. Factors influencing Discordance

Variables	No discordance n=399	Positive discordance n= 136	p-value
Age (years)	55.7(13.3)	55.8(11.6)	ns
Poor SES	260(65.2%)	96(70.6%)	ns
Duration of RA (years)	10 (5-16)	9 (5-15)	ns
Comorbidities ≥3	67 (16.8 %)	29 (21.3%)	ns
Fibromyalgia	22 (5.5%)	17(12.5%)	0.007
HAQ-DI	1.49(0.72)	1.54 (0.71)	ns
EQ5D-3L- Level Sum Score	9(8-11)	10(9-11)	0.04
Pain severity score	4.6(2.1)	5.2(1.8)	0.005
Pain interference score	4.4(2.5)	4.8(2.2)	0.06
HADS-Anxiety Score	8.2(4.7)	8.9(4.8)	ns
HADS-Depression Score	8.9(6.0)	9.7(6.2)	ns
FACIT-F scale	28.6(13.5)	27.9(12.5)	ns
Tender joint count	2(0-5)	1(1-3)	0.005
Swollen joint count	2(1-5)	0(0-1.75)	<0.001
Physician Global Assessment	3.8(2.8)	1.7(1.7)	0.001
Patient global assessment	4.4 (2.7)	6.6 (1.9)	<0.001

ns not significant; categorical data reported as n (%); continuous data reported as mean (standard deviation (SD), median (Interquartile rang, IQR)

Conclusion: In this cohort of indigent SA RA patients, patient-physician discordance was found in a quarter of participants, and was noted in the LDA states, FMS and in patients with high pain scores and those who have problems with usual activities. We have shown, similar to studies elsewhere, that patients and clinicians focus on different aspects of disease when making their global assessments. Studies to understand the impact of discordance and the role of interventions, including pain management and occupational therapy are planned.

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AB0194 PROGRESSION OF RHEUMATOID PULMONARY NODULES: WHAT ARE THE PREDICTIVE FACTORS?

Keywords: Prognostic factors, Rheumatoid arthritis, Lungs

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Background: Pulmonary rheumatoid nodule(RPN) is an serious extraarticular manifestation of rheumatoid arthritis (RA). The clinical features and activity of the RA, used DMARDs and the characteristics of the nodule may affect the progression of the RPN. [1]

Objectives: To identify the characteristics of the PRN and factors affecting its progression.
Methods: In this study, 4117 patients with RA according to the ICD-10 code from the hospital database and who had at least one computed tomography (CT) were identified. The RA diagnosis of the patients were confirmed by examining the medical files (history, physical examination, radiography and laboratory evaluations). Then, chest CTs of the patients with confirmed RA diagnosis were examined by an experienced radiologist. To classify pulmonary nodules as ''pulmonary rheumatoid nodule'', following inclusion and exclusion criteria were used; For inclusion: 1) nodules with changing dimension on follow-up, 2) At least two nodules with different dimensions, 3) Cavitary nodule at any chest CT. For exclusion: 1) Solitary nodules OR all nodules ≤ 5mm and without follow-up OR no change on follow-up. Biggest nodule was named as dominant nodule. Then, patients were grouped according to status of progression. Progression was defined as growth or new nodule formation.
Results: Of 680 RA patients who had pulmonary nodule in chest CT, 208 (30.6%) patients were classified as having PRN. Of these patients, 135 had at least one control chest CT for PRN follow-up and were included in the study. The median disease duration from diagnosis of RA to baseline CT with PRN was 6.74(0.1-33.9) years. Before the baseline CT, 59 (43.7%) patients were recieving methotrexate and it was discontinued in 22 (37.2%) patients after RPN detection. 39 (28.9%) patients had PRN progression on their final chest CT compared to baseline. The median duration between baseline and final CT was 1.58(0.04-33.81) years. Anti-CCP positivitiy(OR 3.39, %95 CI 1.15-9.94), usage of bDMARDs between baseline and last CT (OR 2.48, %95 CI 1.1-5.5), cavitation (OR 3.31, %95 CI 1.5-7.4) and diameter of dominant nodules at baseline CT (OR 1.03, CI %95 1.00-1.07) were significantly assosiated factors with progression in RPN.

Table 1.

	PRN Progressed (n=39)	PRN Non-progressed, n=96	p
Female, n(%)	26/39(66.7)	63(65.6)	0.5
Age at the time of CT, med(min-max)	58.3(37.6-79.9)	60(19.5-83.1)	0.4
Time between the diagnoses of RA and RPN, years, med(min-max)	8.92(0.4-24.4)	6.61(0.1-33.9)	0.7
Disease duration, years, med(min-max)	13.1(3.8-32.8)	14.6(0.6-41.2)	0.9
Follow up duration between baseline and last CT,months, med(min-max)	20.1(0.4-124.8)	18.6(0.95-405)	0.2
RF	24/38(63.1)	58/91(63.7)	0.5
CCP	**24/29(82.7)**	**41/70(58.5)**	**0.017**
Positivite RF or CCP	31/38(81.5)	68/94(72.3)	0.18
Smoking	10/18(55.5)	22/36(61.1)	0.48
Presence of ILD	14/37(37.8)	30/92(32.6)	0.3
Pleural effusion	8/37(21.6)	10/85(11.8)	0.1
Pleural thickening	3/38(7.9)	8/87(9.2)	0.7
Treatments between baseline and last CT, n(%)			**0.02**
csDMARDs	16(41)	75(78.1)	
bDMARDs+csDMARDs	26(66.6)	21(21.8)	
Anti-TNF drugs	9(23)	5(5.2)	
Non-antiTNF drugs	22(56.4)	23(25.5)	
Diameter of dominant nodule, med(min-max)	**6.29(2.7-26.1)**	**5.27(3-16)**	**0.03**
Number of nodules at baseline, med(min-max)	**8.5(3-82)**	**7(3-40)**	**0.028**
Cavitation,	**19(48.7)**	**21(21.8)**	**0.002**
Calcification,	13(33.3)	26(27)	0.3

Anti-CCP: Anti- Cyclic citrullinated peptide, RF: Rheumatoid Factor, ILD: interstitial lung disease, csDMARDs: conventional synthetic Disease Modifying Anti-Rheumatic Drugs)

Conclusion: Our study shows that there are multiple factors that predict RPN progression. Especially the presence of cavitary nodules and seropositivity is important.Although clinicians tend to discontinue MTX when RPN is detected, MTX is not associated with RA nodule progression.
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AB0195 **GENETIC ASSOCIATION BETWEEN INTERLEUKIN-17 AND SUSCEPTIBILITY TO RHEUMATOID ARTHRITIS**

Keywords: Cytokines and chemokines, Rheumatoid arthritis, Genetics/epigenetics

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Background: The pathogenesis of rheumatoid arthritis (RA) is immune imbalance, in which various inflammatory immune cells and pro-inflammatory factors are involved[1]. In particular, interleukin-17 (IL-17) is a potent pro-inflammatory cytokine[2], but the causal relationship between the expression level of IL-17 or IL-17 receptor (IL-17R) and rheumatoid arthritis remained unknown at genetic.
Objectives: In this study, two-sample Mendelian randomization (MR) was used to investigate the causal relationship between IL-17 and RA.
Methods: Summary statistics for RA (14,361 RA cases and 43,923 healthy controls (HCs)) and IL-17 (3,301 samples) were obtained from an available meta-analysis of published genome-wide association studies (GWAS). Relevant single nucleotide polymorphisms (SNPs) were selected by executing quality control steps ($p < 1.0 \times 10^{-5}$) from the GWAS summary results. Mendelian randomization (MR) analyses progressed mainly using inverse variance weighted (IVW), weighted median (WM), and MR-Egger regression methods. For assessing the robustness of the results, we also carried out sensitivity analysis to assess heterogeneity and pleiotropy, such as MR-Egger, leave-one-out and MR pleiotropy residual sum and outlier (MR-PRESSO).
Results: MR Methods were applied to the genetic instrumental variables (IVs) of IL-17A/IL-17 RA, IL-17C/IL-17 RC and IL-17D/IL-17RD and RA. The result of MR analysis indicated that the higher level of IL-17RA (95%CI = 1.006-1.231, p = 0.038) was associated with a significantly higher risk of RA, while remaining exposure IVs did not show a causal relationship with RA, including IL-17A(95%CI = 0.990-1.210, p = 0.078), IL-17C(95%CI = 0.890-1.139, p = 0.910), IL-17RC(95%CI = 0.904-1.119, p = 0.913), IL-17D(95%CI = 0.843-1.137, p = 0.778), IL-17RD(95%CI = 0.876-1.104, p = 0.773). More importantly, sensitivity analysis showed no heterogeneity or pleiotropy in any of the above results.
Conclusion: MR analysis supported a potential causal relationship between IL-17RA and the risk of RA, prompting that doctors should pay close attention to the level of IL-17RA during the examination of RA patients. Furthermore, it will promote future studies on reducing the risk of RA by developing drugs that limitation IL-17A.
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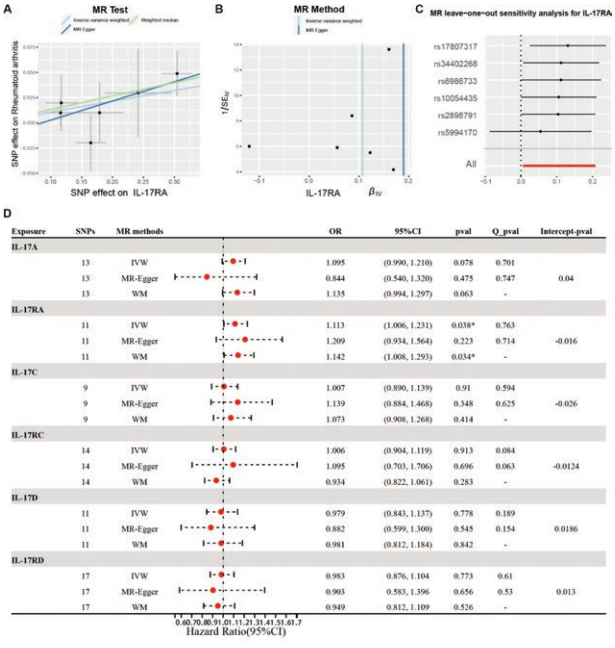


Fig1.(A) The scatter plots for MR analyses the causal effect between IL-17RA and RA using the conventional IVW, MR-Egger, and Weighted median. **(B)** Funnel plot of Inverse variance weighted, MR Egger's multiple validity test for IVs, with the vertical line in the middle indicating the sum of different effect sizes. **(C)** Results of the leave-one-out method in MR sensitivity analysis. It was performed by removing one SNP at a time to explore whether any single SNP drove causal association. After each SNP was removed, the IVW method was conducted to estimate the effect of the remaining SNPs on the outcome, thus evaluating the stability of effect sizes. **(D)** Forest plot of MR results by IVW, MR Egger and weighted median.

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AB0196

IMPACT OF ANTIRHEUMATIC TREATMENTS ON THE INDIVIDUAL COMPONENTS OF THE ACR COMPOSITE SCORE IN PATIENTS WITH RA: REAL-WORLD DATA FROM TWO REGISTRIES

Keywords: Rheumatoid arthritis, Outcome measures, bDMARD

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Background: Standard criteria for measuring treatment efficacy in patients with RA include ACR response rates, which require meeting a threshold of ≥ 20/50/70% improvement in several physician- and patient-reported measures, including tender and swollen joint counts (TJC and SJC, respectively; primary criteria) and at least 3 of 5 secondary criteria (Physician (Ph) global assessment (GA), Patient (Pt) GA, Pain, HAQ-DI, and CRP).
Objectives: The purpose of the analysis was to evaluate the impact of csDMARDs, TNF inhibitors (TNFi), and tofacitinib (TOFA) on each ACR score component in real-life practice.
Methods: Clinical data of RA patients with a CDAI >10 at the time they started a csDMARDs (all biologic naïve), TNFi or TOFA were pooled from two registries: Ontario Best Practices Research Initiative (OBRI) and RHUMADATA. Endpoints summarized descriptively included proportions of pts achieving: ACR20/50/70 responses, ≥ 20/50/70% improvements and mean percent improvement in individual ACR components (TJC, SJC, PhGA, PtGA, Pain, HAQ-DI, and CRP) at Month (M6).
Results: A total of 669 pts were included (csDMARD, n=157, TNFi, n=252; TOFA, n=260). At baseline, patients starting TOFA had longer disease duration, failed more bDMARDs and used more corticosteroids than csDMARDs and TNFi. The CDAI was similar between the 3 groups. ACR50 response rates were numerically lower for the TOFA group (Table 1). The ACR70 response was similar in the 3 groups. An overall higher proportion of patients in all three-medication groups achieved ≥20/50/70% improvement in primary ACR components vs secondary components. Among secondary components, ≥20/50/70% improvement rates were numerically highest for PhGA and lowest for HAQ-DI and pain. The improvement in the SJC and TJC were numerically similar between all groups (Table 1). Among ACR20/50/70 responders for all medications, mean percent improvement was more than 80% for primary components, and ranged from 30% to 80% for secondary components (Figure 1).
Conclusion: In this real-world practice analysis, physician-reported measures (TJC, SJC, and PhGA) contribute slightly more to overall ACR20/50/70 responses, compared with Pt-reported outcomes (PROs; PtGA, Pain and HAQ-DI). In the ACR20 response group, a lower-level outcome, the improvement of the SJC and TJC, exceeded 80%. Pain was the most important factor in achieving an ACR50 for pts treated with TOFA, possibly reflecting the different effects of JAKi on pain.

Table 1. Percentage of patients treated with csDMARD, TNFi, and TOFA who reported an ACR50 response and ≥ 50% improvement at month 6

	csDMARD (N=157)	TNFi (N=252)	TOFA (N=260)
ACR50 response and ≥ 50% improvement in each component of the ACR50 score, n (%)			
ACR50 response	27.4%	25.3%	19.4%
TJC	62.1%	63.8%	68.5%
SJC	64.9%	67.8%	67.2%
PhGA	58.3%	51.7%	50.3%
PtGA	44.9%	38.8%	32.7%
Pain	27.6%	23.7%	26.7%
HAQ-DI	23.6%	17.3%	17.7%
CRP	40.9%	41.4%	35.6%

The analysis is based on observed case data (without imputation) of patients with all 7 components assessed ACR50/70: American College of Rheumatology ≥ 50/70% response rates; CRP: C-reactive protein; csDMARD: conventional synthetic disease-modifying antirheumatic drug; HAQ-DI: Health Assessment Questionnaire–Disability Index; Pain: patient-reported pain (visual analog scale); PhGA: physician global assessment; PtGA: patient global assessment of disease activity; SJC: swollen joint count; TJC: tender joint count; TNFi: tumour necrosis factor inhibitors; TOFA: tofacitinib.

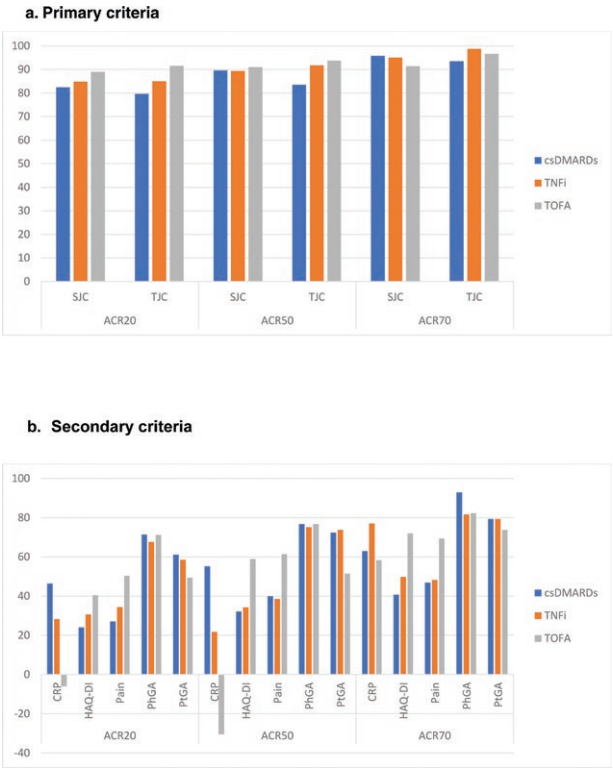


Figure 1. Mean percent improvement in ACR components in those patients who achieved an ACR20/50/70 at month 6
Analysis is based on observed case data (without imputation) of patients with all 7 components assessedACR20/50/70: American College of Rheumatology ≥ 20/50/70% response rates.

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AB0197

PARASYMPATHETIC ACTIVITY IS NEGATIVELY ASSOCIATED WITH DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS – RESULTS OF AN EXPLORATORY PROSPECTIVE STUDY

Keywords: Comorbidities, Rheumatoid arthritis

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Background: Rheumatoid Arthritis (RA) is often associated with autonomic dysfunction, which is presumably playing a role in the pathogenesis of the disease and may contribute to disease activity [1,2]. Accordingly, patients with RA show reduced heart rate variability (HRV) [3].
Objectives: The aim of this prospective pilot study was to examine a possible connection between disease activity and activity of the autonomic nerve system in patients with RA.
Methods: In the non-randomized prospective exploratory study, patients with active RA and an upcoming change in treatment were included. Assessments were performed at baseline before treatment initiation (T0) and after 3 months (T1), including the Disease Activity Score 28 (DAS28-CRP), HRV measurement, and the physician and patient global assessment (PGA, PtGA). HRV was measured through a 5-minute ECG with finger electrodes, using Kardia App®. Total variability was measured by the variance of RR intervals over the temporal segment (Total Power) as well as by standard deviation of the average RR intervals (SDRR). Root Mean Square of successive differences (RMSSD) and percentage of number of pairs of adjacent RR intervals differing by more than 50 milliseconds (pRR50) were used for estimating parasympathetic activity. In addition, blood concentrations of Neuropeptide Y (NPY), vasoactive intestinal peptide (VIP) were measured as surrogate parameters for activity of the sympathetic (NPY) and parasympathetic (VIP) nervous system. Statistical analysis was performed using linear regression analysis.
Results: A total of 40 patients was included. Our results showed an overall improvement in both disease activity measured by DAS28-CRP (p= <0,001; SMD= 1.393) and HRV (Total Power p= 0.014; SDRR p= 0.0023) between visits (Table 1). DAS28-CRP was inversely associated with parasympathetic activity (pRR50, p= 0.0494). PtGA also correlated inversely with pRR50 (p= 0.0049). RMSSD as another parasympathetic indicator was negatively predictive for percentage change of PGA (p= 0.0109). Patients with lower parasympathetic activity at baseline had a higher change in disease activity than patients with higher parasympathetic activity at baseline.

Table 1. HRV parameters and disease activity at T0 and T1 (*all parameters at T0 and T1as mean values*)

Parameter	T0	T1	p-Wert	SMD
SDRR (ms)	36,23	64,06	0,007	0,621
RMSSD	37,61	76,64	0,013	0,565
PtGA	6,55	4,47	0,001	0,780
PGA	5,42	3,02	< 0,001	1,064
DAS28	4,25	2,76	< 0,001	1,393
SDAI	26,95	13,70	< 0,001	1,216
Remission (n)	0	16	< 0,001	1,376

DAS28 disease activity score 28, HRV heart rate variability, ms milliseconds, PGA physician global assessment, PtGA patient global assessment, RMSSD Mean Square of successive differences, SDAI Simple Disease Activity Index, SDRR standard deviation of the average RR intervals, SMD standardized mean difference

Conclusion: The results of our prospective study underline the importance of the autonomic nerve system regarding disease activity and prognosis in RA. Higher parasympathetic activity was associated with lower disease activity. Patients with initially lower parasympathetic profile and higher disease activity benefited to a greater extend from initiation or change of therapy. In our study, the specific blood parameters NPY and VIP showed no relevant association with disease activity and treatment response.
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AB0198

THRESHOLDS OF PRESENTEEISM MEASUREMENT INSTRUMENTS FOR UNACCEPTABLE WORK PARTICIPATION AND FUTURE ADVERSE WORK OUTCOMES IN RA

Keywords: Rheumatoid arthritis, Patient reported outcomes, Work-related issues

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Background: Presenteeism is associated with lower work satisfaction and increased risk of future sick leave in rheumatic diseases. Presenteeism is generally measured on a continuous scale; however, despite a lower precision, identifying persons with a meaningful level of presenteeism can improve interpretation in clinical studies and might be useful in routine practice. Recently, thresholds of meaning for presenteeism instruments were established for axial spondyloarthritis (axSpA).
OBJECTIVES:
1)To identify thresholds for presenteeism instruments that reflect unacceptable work status in patients with RA and whether those thresholds could predict future adverse work outcomes (AWO);
2)To assess in patients with RA the performance of presenteeism thresholds previously established in axSpA for the same instruments.
Methods: We used data from the 1-year multinational prospective study on Patient-Reported Outcomes in Employment Study in Rheumatoid Arthritis (RA-PROSE). Thresholds to determine when patients consider themselves in 'unacceptable work status' were calculated at baseline for 4 presenteeism instruments (Work Productivity and Activity Impairment questionnaire -WPAI-, Quality and Quantity method -QQ-, Workplace Activity Limitations Scale -WALS- and Work Limitations Questionnaire -WLQ 25-) and for a patient global assessment of pain. We created receiver operating characteristic (ROC) using as external criterion a Patient Acceptable Work State question, addressing one's ability to perform their current job satisfactorily. We used different approaches (75th percentile, Youden index, Liu method, nearest to 0.1) to determine the optimal cut-off, while balancing over-under diagnosis. Accuracy of thresholds to predict "future adverse work outcome" throughout 12 months (defined as sick leave or long-term disability) was assessed. The recently developed presenteeism thresholds for axSpA were also tested.
Results: A total of 105 employed patients were included: 77% females, mean age 48 (SD 9), with a mean symptom duration of 9.8 (8.7) years. 15% of the patients considered themselves in an unacceptable work status and 7 (8%) had at least one AWO during 12 months. All instruments (presenteeism and pain) showed good performance vs the external criterion (AUC >0.75) except for the QQ method (AUC 0.62). The Table 1 shows the optimal thresholds for each instrument and their performance to correctly identify an unacceptable work status and AWO during 12 months for the RA-specific threshold (1st row) and the available axSpA threshold (2nd row). Interestingly, the axSpA thresholds performed better to classify work status as 'unacceptable' and to predict AWO. For adverse work outcome over 12 months, pain and WPAI performed better specially in predicting AWO.
Conclusion: Thresholds for presenteeism and pain representing unacceptable work status have been established for RA. Previously developed thresholds for axSpA showed an even better performance and are therefore the preferred to be used. WPAI performed the best and can be used to identify patients requiring more tailored care in order to avoid future AWO.

Table 1. Optimal thresholds for presenteeism measures and patients correctly classified for unacceptable work status and adverse work outcome during 12 months.

	Optimal threshold (SE/SP)	Correctly classified for unacceptable work status n (%)	Correctly classified for AWO during 12 months n (%)
WPAI presenteeism (0-100)	**≥30 (89/70)**	66 (73)	57 (69)
	≥40 (78/82)	77 (82)	62 (75)
QQ method (0-10)	**≥2 (67/55)**	53 (56)	49 (59)
	≥3 (56/64)	59 (63)	57 (69)
WALS (0-3)	**≥0.61 (89/59)**	51 (62)	44 (61)
	≥0.75 (67/68)	56 (68)	49 (68)
WLQ 25 (0-100)	**≥27 (89/77)**	53 (57)	45 (55)
	≥29 (77/80)	57 (61)	46 (56)
Pain (0-10)	**≥4 (67/68)**	64 (68)	61 (73)

The final thresholds are colored in green and correspond to the one's derived from axSpA. For pain measurement there was no axSpA derived threshold.

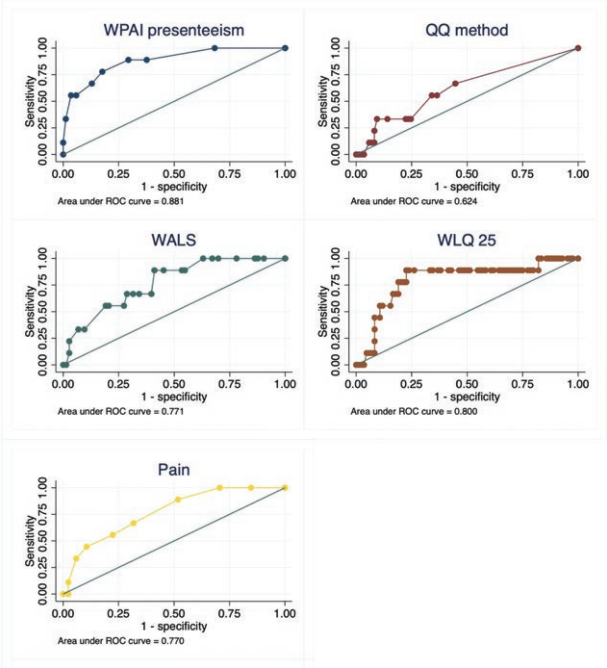


Figure 1. ROC curves for presenteeism (4 different measurement instruments) and for pain according to unacceptable work status

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AB0199

THE PROGNOSTIC VALUE OF IGA ANTI-CITRULLINATED PROTEIN ANTIBODY AND RHEUMATOID FACTOR IN AN EARLY ARTHRITIS COHORT WITH A TREAT-TO-TARGET APPROACH

Keywords: Prognostic factors, Rheumatoid arthritis, Autoantibodies

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Background: The EULAR research agenda states that new biomarkers are needed to stratify patients and to predict therapeutic response or lack of response in rheumatoid arthritis. Currently, IgG anti-citrullinated protein antibody (ACPA) and IgM rheumatoid factor (RF) are used as poor prognostic factors for treatment decisions in RA. The mucosal origin hypothesis of RA renewed the interest in the role of IgA isotype autoantibodies for disease pathogenesis. However, the value of IgA ACPA and RF for prognostication of treatment response under a treat-to-target approach is not clear to date.

Objectives: To evaluate the prognostic value of IgA ACPA and RF by considering 'quick-attained and persistent remission', DMARD-free remission (DFR) and biological use in an early (rheumatoid) arthritis population.

Methods: All patients from the treatment in the Rotterdam Early Arthritis Cohort (tREACH) trial with available baseline sera were included. The tREACH trial is a multicentre, stratified, single-blinded trial with a treat-to-target approach. IgA ACPA and RF isotypes were measured by automated fluorescence enzyme-immuno assay (FEIA) in baseline sera. The prognostic value of positivity for IgA ACPA and RF was evaluated for three outcome measures: (1) quick-attained (at 6 months) and persistent (to 2 years) remission, analysed with logistic regression analysis; (2) achievement of DFR for at least 6 months over a 2 year follow-up period, analysed with survival analysis; and (3) incident biological use over 2 years, analysed with mixed effects logistic regression analysis. Results were stratified for IgG ACPA, since it is known that IgG ACPA is related to lower (DMARD-free) remission rates and more biological use.

Results: IgA isotypes of ACPA and RF were measured in baseline sera of 480 tREACH patients. 66% was female, mean age was 53 years, median symptom duration 21 weeks, and median swollen joint count 5. A positive IgA ACPA titre was present in 109 (23%) patients and most of them also had a IgG ACPA result above the cut-off value for positivity (n=102, overlap of 94%). Positive IgA RF on the other hand was present in 172 (36%) of patients, which overlapped with IgM RF for 90% (n=154). Double positivity for IgA and IgG ACPA (n=102) revealed lower DFR rates after 2 years compared to IgG ACPA positivity alone (6% and 11%, respectively, Figure 1A), although this finding was not significant (p=0.09). No differences were observed in 'quick-attained and persistent remission' and biological use for both IgA ACPA and RF, after stratification for IgG ACPA.

Conclusion: IgA isotypes of ACPA and RF almost completely overlap with the commonly measured isotypes (IgG ACPA and IgM RF, respectively). In addition, both an IgA ACPA and IgA RF response do not predict persistent remission, DFR and biological use in this treat-to-target population. Based on these results, there is no rationale for measuring these isotypes in newly diagnosed (rheumatoid) arthritis patients in daily clinical practice.

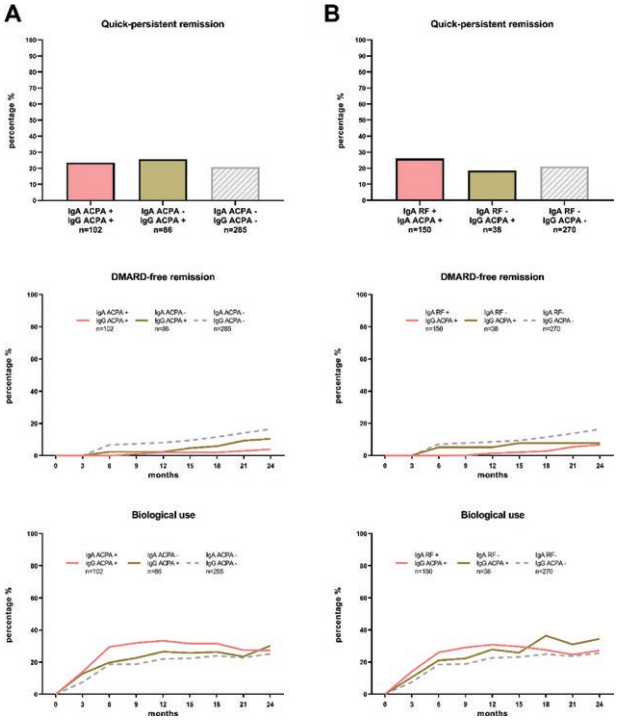


Figure 1. Quick-persistent (6-24 months) remission, DMARD-free remission and biological use over 2 years in (A) IgA/IgG ACPA positive patients vs. IgG ACPA positive patients, with IgA/IgG ACPA negative patients as a reference group; and in (B) IgA RF/IgG ACPA positive

patients vs. IgA RF negative/IgG ACPA positive patients, with IgA RF/IgG ACPA negative patients as a reference group.

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AB0200

IMPROVEMENT OF SLEEP IMPAIRMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS ACHIEVING REMISSION OR PAIN RELIEVE WITH UPADACITINIB: RESULTS FROM THE POST-MARKETING OBSERVATIONAL SLEERA STUDY

Keywords: Rheumatoid arthritis, Quality of life, Real-world evidence

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Background: Sleep impairment is a common clinical condition in the rheumatoid arthritis (RA) population, which has been reported in over 60% of patients[1]. Although few longitudinal studies demonstrated change from baseline on sleep quality with advanced therapies[2,3], none of them described the clinical meaningfulness of these changes by subjective and objective measures.

Objectives: The SLEERA study aims to investigate the impact of upadacitinib (UPA), a selective and reversible JAK inhibitor, on sleep quality in a real-world RA population in Switzerland, by using a validated patient-reported measure, the Pittsburgh Sleep Quality Index (PSQI)[4], and an actigraphy-based objective measure with the GT9x wearable.

Methods: SLEERA is a sub-study of UPHOLD, an international, multicenter, prospective, non-interventional, open-label, observational cohort study (NCT04497597) that assesses sleep quality in a real-world population of adult Swiss patients with moderate-to-severe active RA, initiating treatment with UPA 15 mg once daily according to the product label and with the treatment decision made prior to study participation. This primary interim analysis reports data for all enrolled patients up to 3 months after treatment start. Results are presented for the total sample using descriptive measures reflecting sample size (N), average values (standard deviation) for each visit and average change scores (standard deviation) for follow-up visit at month 3. All data were analyzed as observed, with no imputation of missing data.

Results: Of the 39 patients (87% female) included in this study, 35 completed the follow-up visit at month 3. The mean age and disease duration were 59.5 (13.9) years and 7.0 (8.3) years, respectively. The mean initial DAS28-CRP was 4.1 (1.0). At baseline, 76% of patients showed subjective sleep impairment (defined by PSQI >5) and 51% had objective poor sleep efficiency (defined by actigraphy sleep efficiency <85%) (Table 1). At month 3, upadacitinib showed significant improvement in the PSQI total score with a decrease of 2.26 (2.92, p value <0.001), as well as other subjective outcomes. The proportion of objective poor sleepers decreased to 38%, while sleep efficiency and physical activity outcomes in total remained unchanged. However, patients achieving DAS28-CRP remission or absence of pain after 3 months of treatment showed higher improvements in both subjective and objective measures compared to those who did not achieve DAS28-CRP remission or have residual pain (Figure 1).

Table 1.

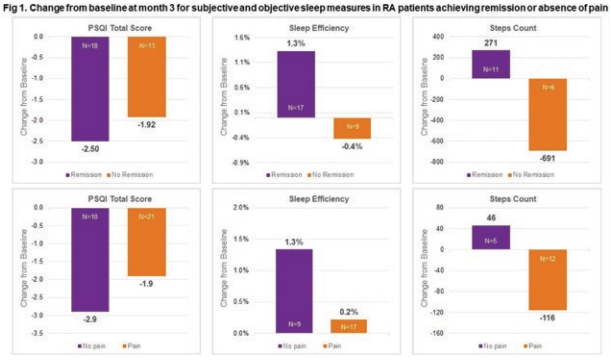
PSQI	BL Visit N = 37	Visit at Month 3 N = 33	Change from BL N = 31
Sleep impairment (PSQI >5), n (%)	28 (76%)	18 (55%)	
PSQI total score	7.84 (3.12)	6.06 (4.26)	-2.26 (2.92)
PSQI sleep efficiency (%)	78.5% (18.5%)	84.2% (16.0%)	5.0% (17.7%)
PSQI sleep duration (hours)	6.8 (1.0)	6.9 (1.2)	0.2 (0.9)
Actigraphy	**N = 39**	**N = 26**	**N = 26**
Poor sleep efficiency (SE <85%), n (%)	20 (51%)	10 (38%)	
Sleep efficiency (%)	84.2% (6.8%)	84.5% (7.9%)	0.5% (3.9%)
Total sleep time (hours)	6.7 (0.9)	6.8 (1.0)	-0.1 (1.4)
Total awake time (minutes)	74 (37)	73 (49)	-7 (36)
Physical Activity	**N = 32**	**N = 17**	**N = 17**
Steps count	4,272 (2,270)	4,509 (2721)	-68 (1157)
MVPA (minutes)	177 (98)	181 (95)	-2 (37)

Conclusion: In this Swiss cohort, a high proportion of RA patients exhibited sleep impairment as shown by subjective and objective measures. Patients treated with upadacitinib significantly improved their subjective sleep quality after 3 months. Higher improvements for both subjective and objective sleep measures were observed in patients achieving remission or absence of pain. This research provides evidence of sleep impairment in RA patients which can be improved following a treatment, and further supports the importance of remission when assessing disease treatment goals.

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Fig 1. Change from baseline at month 3 for subjective and objective sleep measures in RA patients achieving remission or absence of pain



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AB0201

"IT SURPRISED ME A LOT THAT THERE IS A LINK": A QUALITATIVE STUDY OF THE ACCEPTABILITY OF PREVENTIVE PERIODONTAL TREATMENT FOR INDIVIDUALS AT-RISK OF RHEUMATOID ARTHRITIS

Keywords: Qualitative research methods, Rheumatoid arthritis, Patient information and education

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Background: Current evidence suggests that periodontitis could be a causal risk factor for rheumatoid arthritis (RA) onset and progression, and periodontal treatment may improve disease activity in patients with established RA [1, 2]. Earlier periodontal intervention in individuals at-risk of RA could provide a unique opportunity to delay progression or prevent RA entirely.

Objectives: To explore the acceptability of preventive periodontal treatment among individuals at-risk of RA and healthcare professionals from dental and medical backgrounds.

Methods: This was a qualitative study using a phenomenological approach. Anti-CCP positive at-risk individuals with musculoskeletal symptoms but no synovitis were recruited from the Leeds CCP cohort, and healthcare professionals were recruited through dental and rheumatology professional networks. Individual semi-structured interviews were conducted via video or telephone. Interviews were audio-recorded and transcribed verbatim. Data were analysed thematically.
Results: Nineteen at-risk participants (ten women; age range 35-70) and 11 healthcare professionals (rheumatology clinicians, dentists, general practitioners, commissioners) participated. Three themes (six subthemes) were identified as important to understand factors that may influence participants' acceptance of preventative periodontal treatment to reduce the risk of RA: i) understanding risk (knowledge of shared risk factors; information and communication); ii) oral health perceptions and experiences (personal challenges for dental intervention and oral health maintenance; external barriers); iii) oral health treatment and maintenance (making oral health changes to prevent RA; acceptability of participation in periodontal research to prevent RA). The majority of at-risk participants lacked awareness of the association between oral health and the risk of developing RA, and perceived a lack of knowledge of this link among dentists. Healthcare professionals highlighted disjoin between dentistry and medicine due to commissioning and financial barriers, and inadequate training. Preference for information provision relating to oral health as a risk factor varied extensively among all participants. At-risk participants discussed oral health issues, but oral health was less of a priority when compared to comorbidities that had a bigger impact on daily life, e.g. irritable bowel syndrome. Both groups of participants perceived that dental anxiety, the cost of dental treatment, and difficulty in accessing NHS dentists were barriers to seeking dental care. Participation in a clinical trial involving preventive periodontal treatment was perceived to be acceptable for most at-risk participants. Comparatively, taking medication to prevent RA was perceived to be less acceptable. Facilitators to trial participation included reducing risk, access to a dentist, and not having to pay for treatment. At-risk participants with dental anxiety indicated that seeing the same dentist at every visit was important.
Conclusion: The impact of poor oral health may not be well understood by individuals at-risk of RA. Information relating to this risk factor should be tailored to the individual and is a key first step before clinical trial involvement. Whilst periodontal disease is common in individuals at-risk of RA, both at-risk participants and healthcare professionals identified that seeking dental treatment can be hindered by dental anxiety, treatment costs and a shortage of dentists. Future trials involving preventive periodontal treatment should take into account what has been identified as important by this group of individuals at-risk of RA.

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AB0202 CHARACTERISTICS OF PATIENTS WITH DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS IN REAL LIFE: DATA FROM THE BIOBADASER REGISTRY

Keywords: Registries, Disease-modifying drugs (DMARDs), Rheumatoid arthritis

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Background: In the last decade there have been multiple attempts to characterize patients with refractory rheumatoid arthritis (RA). In 2020, EULAR proposed a definition for difficult-to-treat RA (D2T-RA) to standardize this population. The mechanisms leading to D2T RA are varied and not fully understood. A better understanding of clinical profile of this specific population may be helpful to support rheumatologists in their clinical decisions.
Objectives: To determine the prevalence of D2T-RA in a multicenter national registry (BIOBADASER) and to investigate the influence of the initial successive lines of treatment (LoT) in the development of D2TRA.
Methods: Longitudinal and prospective cohort study of patients with RA from BIOBADASER (a multicenter national registry of adverse events of biologics and targeted therapies in rheumatic diseases). Patients were classified as refractory if failure to at least 2 biologics or targeted synthetic disease modifying antirheumatic drugs (b/tsDMARDs) with different mechanisms of action (MoA) and as D2TRA if refractory RA who presented moderate to high disease activity according to DAS 28-ESR at their last visit. The comparator group included patients with refractory RA but low disease activity/remission. The therapeutics groups were stablished as TNF inhibitors (TNFi), JAK-inhibitors (JAKi) and other biological therapies non-TNFi bDMARD. Demographic, clinical and therapeutical data on the 1st and 2nd LoT were compared between groups.
Results: A total of 3852 patients with RA with at least one year follow up were included in the analysis, 1612 (42%) had refractory RA and 348 (9%) D2TRA. Patient and therapeutic characteristics are shown in Table 1. No differences were found between D2TRA and non-D2TRA in clinical variables except for age, being patients with D2TRA significantly older. The use of JAKi as their first or second LoT was more frequent in patients with non-D2TRA, although no statistical significance was reached.
Conclusion: Around 40% of patients were classified as refractory RA in our registry but only 9% as D2T-RA. Earlier treatment with JAKi was more frequent in the non-D2TRA group. Further research should analyse the influence of LoT on the development of D2TRA.

Table 1. Demographic, clinical and therapeutic characteristics in the refractory RA, D2TRA and non-D2TRA population

	Refractory RA (n= 892)	D2TRA (n=348)	Non-D2TRA (n=544)	p-value
Age (years), mean ± SD	63.1 (12.8)	64.2 (12.8)	62.5 (12.8)	0.047
Sex (female), n (%)	712 (79.8)	286 (82.18)	426 (78.31)	0.160
FR positivity, n (%)	159 (22.3)	51 (18.3)	108 (24.8)	0.104
aCCP positivity, n (%)	523 (73.6)	207 (74.29	316 (73.29	0.108
Smoking habit, n (%)				0.88
Smoker	565 (63.3)	219 (62.93)	346 (63.6)	
Non-smoker	159 (17.8)	68 (19.54)	91 (16.73)	
Former smoker	129 (14.5)	47 (13.51)	82 (15.07)	
Charlson Index, mean ± SD	0.3 ± 0.8	0.4 ± 0.8	0.3 ± 0.8	0.215
DAS28-ESR, mean ± SD	2.1 ± 0.7	4.3 ± 0.9	3.0 ± 0.8	<0.001
Concomitant csDMARD, n (%)	470 (52.7)	194 (55.8)	276 (50.7)	0.144
Time to first b/tsDMARD (years)	6.6 (7.1)	6.9 (7.3)	6.5 (7.0)	0.374
Lines of treatment				0.145
TNFi -> other bDMARD	583 (65.4)	233 (67.0)	350 (64.3)	
TNFi -> JAKi	138 (15.5)	46 (13.2)	92 (16.9)	
Other bDMARD -> TNFi	75 (8.4)	34 (9.8)	41 (7.5)	
Other bDMARD -> JAKi	23 (2.6)	8 (2.3)	15 (2.8)	
JAKi -> TNFi	15 (1.7)	2 (0.6)	13 (2.4)	
JAKi -> other bDMARD	8 (0.9)	5 (1.4)	3 (0.69	
other bDMARD-> other bDMARD	50 (5.6)	20 (5.8)	30 (5.5)	

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AB0203 REAL WORLD EXPERIENCE OF MODERATE DISEASE ACTIVITY STATE (MDAS) RA PATIENTS OVER 4-YEAR FOLLOW-UP

Keywords: Inflammatory arthritides, Pain, Fibromyalgia

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Background: In recent years despite improved therapies for RA, there is an increased awareness of persistent pain in people with RA. Before the pandemic we assessed a large group of patients with RA with comprehensive joint ultrasound (US) and for presence of fibromyalgia (FM) meeting 2010 ACR diagnostic criteria. When combinations of synovitis and/or FM were made we noted 4 groups

Table 1.

	FM-PD- (n=12)	FM-PD+ (n=18)	FM+PD- (n=29)	FM+PD+ (n=13)	ANOVA p-value
Female (n, %)	10 (83%)	13 (72%)	24 (83%)	13 (92%)	
CCP+ve (n, %)	4 (33%)	12 (67%)	14 (48%)	6 (46%)	
Disease duration (years) (mean, SEM)	11.04 (2.676)	16.19 (2.889)	12.29 (1.709)	16.23 (3.340)	
On csDMARD (n, %)	11 (92%)	15 (83%)	24 (83%)	10 (77%)	
On bDMARD (n, %)	4 (33%)	5 (28%)	7 (24%)	8 (61.5%)	
Baseline DAS28 (mean, SEM)	4.412 (0.1641)	4.344 (0.1177)	4.192 (0.08910)	4.366 (0.1461)	
Total visits (mean, SEM)	11.67 (2.647)	10.50 (2.031)	8.724 (1.039)	8.308 (1.407)	0.533
F2F visits (mean, SEM)	7.909 (2.164)	7.944 (1.924)	5.793 (1.033)	5.769 (1.311)	0.5959
Telephone visits (mean, SEM)	4.417 (1.474)	2.556 (0.3154)	2.931 (0.3327)	2.538 (0.6162)	0.2268
Tender joint count (mean, SEM)	3.604 (1.101)	3.506 (0.6177)	5.376 (0.6899)	4.603 (1.246)	0.3179
Treatment escalations (mean, SEM)	2.917 (1.062)	3.722 (1.028)	2.000 (0.5526)	1.615 (0.6257)	0.2671
Steroid prescriptions (mean, SEM)	1.833 (0.7160)	1.611 (0.5310)	1.000 (0.3908)	0.7692 (0.5329)	0.503
csDMARD prescriptions (mean, SEM)	0.7500 (0.3046)	0.7778 (0.2070)	0.5185 (0.1634)	0.3636 (0.2787)	0.5789
Biologic prescriptions (mean, SEM)	0.3333 (0.2247)	1.778 (0.6291)	0.3793 (0.1257)	0.3077 (0.2371)	0.009
Progress score (mean, SEM)	-1.167 (1.461)	0.6111 (0.3889)	-0.1379 (0.2366)	0.4615 (0.6265)	0.2579

of patients. As well as some with only FM, we also noted a group we believe had peripheral non-inflammatory pain, a new concept in RA. Here we investigate if these different groups change over time in our T2T routine care pathway.

Objectives: To assess the progress and outcomes patients with RA with different well defined pain states during 4 years of follow up including the COVID19 pandemic.

Methods: The TITRATE-ULTRASOUND patient cohort categorised patients with RA into 4 groups depending on the presence or absence FM and the presence or absence of power doppler synovitis (PD, defined as positive PD signal in ≥2 joints in a 44 joint US). We identified 72 patients with active RA (DAS28 3.2 – 5.1) from this cohort with sufficient clinical data during the study period and collected the following data on each follow up encounter: visit type, treatment changes and disease activity measures. In the COVID19 pandemic follow up visits were largely virtual without the ability to collect physician assessed disease activity scores. Progress assessment was performed as to whether the patient had improved, no change or worse with a numerical value of +1, 0 and -1 at each visit to calculate a score tracking patient progress during the pandemic. Statistical analysis was performed using 1-way ANOVA to assess for difference between the 4 groups.

Results: 72 patients with were assigned into the following categories: FM-PD-, 12 (peripheral pain group); FM-PD+,18; FM+PD-, 29; FM+PD+, 13. Table 1 shows baseline characteristics of the 4 groups and reveals no significant difference by ANOVA between the 4 groups in total visits, face to face visits, telephone visits, tender joint count, treatment escalations, steroid prescriptions, csDMARD prescriptions, and progress score. Biologic prescriptions did vary significantly between the groups (p = 0.009).

Conclusion: Over the follow-up period we show the management of RA patients without active power doppler synovitis or fibromyalgia did not differ significantly from other categories of patients. Similar numbers of visits, treatment escalations, csDMARDs and corticosteroid prescriptions were observed. This illustrates how it can be difficult to define the specific causes of disease activity without access to US. Despite similar management strategies, FM-PD- patients tended towards worse progress scores, suggesting a potential unmet need in such patients.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Mark Gibson: None declared, Nadia Ladha Hassan: None declared, L Bruce Kirkham Speakers bureau: Abbvie, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer, UCB, Consultant of: Abbvie, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer, UCB, Grant/research support from: Eli Lilly.

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AB0204

GENETICALLY PREDICTED EOSINOPHIL COUNT IS ASSOCIATED WITH INCREASED RHEUMATOID ARTHRITIS SUSCEPTIBILITY

Keywords: -omics, Rheumatoid arthritis

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Background: Increasing evidence shows that eosinophils – white blood cells typically linked to atopic and parasitic diseases – are involved in regulating adaptive immune responses. Baseline eosinophilia has been associated with poor prognosis in early arthritis patients, while synovial regulatory eosinophils are associated with rheumatoid arthritis (RA) remission [1,2]. However, the role of eosinophils for RA susceptibility is unclear. Traditional observational designs are limited by reverse causation, that is, RA onset or prodrome may influence eosinophil count and/or function. Using genetic variants in instrumental variable analysis can reduces such biases.

Objectives: To investigate the association between genetically predicted circulating eosinophil count and RA risk using genetic instrumental variable analysis.

Methods: We selected uncorrelated (r^2<0.001) and significant (p-value <$5x10^{-8}$) single nucleotide polymorphisms (SNP) as genetic instruments for circulating eosinophil count from a genome wide association study of 563,085 individuals. Genetic association data for RA was obtained from 22,350 cases and 74,823 controls. We included psoriatic arthritis (PsA; 3,609 cases, 9,192 controls) and osteoarthritis (OA; 177,517 cases, 649,173 controls) as negative control outcomes, and asthma (56,167 cases, 352,255 controls) and atopic eczema (10,788 cases, 30,047 controls) as positive controls. We used the ratio method and meta-analysed estimates from each SNP using the inverse-variance weighted method. We used weighted median, mode and the Egger method to test for horizontal pleiotropy (i.e., violation of the model assumption that genetic instruments only affect the outcome through the exposure).

Results: Circulating eosinophil count was instrumented using 448 SNPs that explained 11% of variance, with a mean F statistic of 157 suggesting adequate instrument strength. For each standard deviation increase in eosinophil count, risk of RA was increased (OR 1.60; 95% CI 1.35, 1.89; p-value=$6.9x10^{-8}$). Genetically predicted eosinophil count was not associated with risk of PsA and OA negative controls, but were associated with increased risk of asthma and eczema positive controls (Figure 1). Pleiotropy robust sensitivity analyses showed consistent estimates.

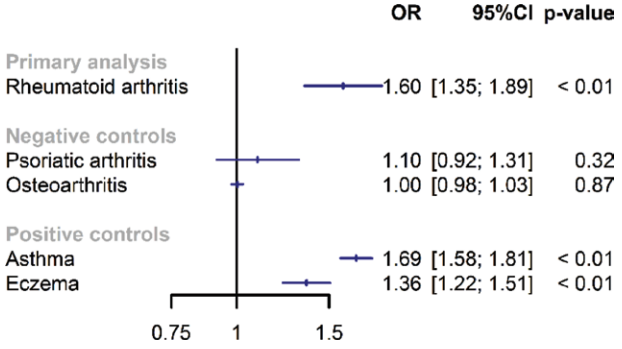


Figure 1. Association between genetically predicted circulating eosinophil count and risk of rheumatoid arthritis and control outcomes.

Conclusion: This study provides genetic data to support a causal relationship between circulating eosinophil count and RA susceptibility. Eosinophils may play a causal role in RA aetiology and, if these results are replicated in future studies, may represent a novel predictor of RA onset and potential modifiable factor for RA prevention.

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AB0205

RA TREATMENT EFFECTS IN WRIST MRIS, DETERMINED BY DEEP LEARNING

Keywords: Artificial intelligence, Rheumatoid arthritis, Imaging

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Background: Determining the response to early treatment of Rheumatoid Arthritis (RA) or the at-risk stages for RA from MRI scans requires sensitive and specific measurements of imaging biomarkers of inflammation. Employing artificial intelligence (AI), especially deep learning, can be an option to measure RA treatment effects.
Objectives: We aimed to assess the ability of deep learning to determine treatment response by distinguishing MRIs of the wrist between treatment and placebo arms (as proxy for treatment effects) from the TREAT-EARLIER trial.
Methods: Wrist MRIs (contrast enhanced T1-weighted TSE fat suppressed sequences) were collected from 236 patients with clinically suspect arthralgia at four time points (baseline, with 4, 12 and 24 months follow-up) to determine the response to treatment by intramuscular methylprednisolone followed by methotrexate during one year [1]. 3D wrist MRI data were reconstructed in super-resolution from axial and coronal images. Since a statistically significant treatment effect was determined previously y RAMRIS [1], we used these 3D wrist MRI data from baseline and after 4 months to classify patients into treatment arms by a 3D convolutional neural network. Five different inputs were explored for training the model: 1) a difference image (baseline image simply subtracted from follow-up); 2) the combination of baseline and follow-up image; 3) the combination of baseline and difference image; 4) change maps (AI-based maps containing changes between two time points); and 5) the combination of baseline and change maps (see bottom panel in Figure 1). To evaluate the proposed model, 10-fold cross-validation was repeated five times with five different splits, and the area under the receiver operator curve (AUC) was reported.
Results: The mean (±SD) AUCs are presented in Table 1. As shown, the combination of different MRIs obtained promising results. Specifically, the combination of baseline images and AI-based extracted change maps could improve the accuracy. Compared to a setting where follow-up and baseline scans were simply 'subtracted', this improved the prediction of treatment from 0.72 to 0.76.

Table 1. Obtained AUC using Wrist MRI. (BL: baseline MRI; FU: Follow-up MRI; Diff: Difference image; and CM: Change Map)

Input	AUC (mean ± SD)
Diff (= BL-FU)	0.71 ± 0.027
BL and FU	0.70 ± 0.032
BL and Diff	0.72 ± 0.017
CM	0.73 ± 0.009
BL and CM	**0.76 ± 0.008**

Conclusion: The results show that deep learning models using baseline and follow-up MRI specifically AI-extracted change maps can accurately determine treatment response in CSA patients.
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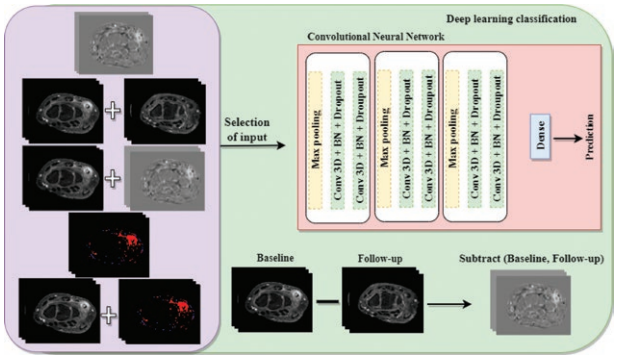


Figure 1. Overview of the proposed model.

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AB0206

DIFFICULT TO TREAT RHEUMATOID ARTHRITIS (D2T-RA) IN THE REAL LIFE SETTING IS INDEPENDENT OF AUTOANTIBODY STATUS OR GENDER BUT IS ASSOCIATED WITH OBESITY, FIBROMYALGIA, AND EROSIONS AT DIAGNOSIS.

Keywords: Rheumatoid arthritis, Prognostic factors, Comorbidities

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Background: Despite the growing number of available drugs for Rheumatoid Arthritis (RA) and the significant improvement in disease management, numerous patients continue to fail multiple lines of DMARDs. The EULAR definition of Difficult to Treat Rheumatoid Arthritis (D2T-RA) is based on 3 criteria: the failure of 2 or more b/tsDMARDs with different mechanism of action, the persistence of signs of active/progressive disease despite treatments, and the clinician or patients' perception of a "problematic" management. There is limited evidence on the prevalence of D2T-RA in real life and the factors associated with this entity.
Objectives: To characterize D2R-RA cases in a real-life cohort of patients.
Methods: We retrospectively collected data of patients with RA fulfilling the ACR/EULAR 2010 classification criteria who attended our outpatient clinics between January 2019 and November 2022. The comparison between D2T-RA and other patients was performed using T-, Mann-Whitney and Chi-Square tests while logistic regression models analyzed the impact of principal clinical features and comorbidities on outcome variable, adjusted for confounders.
Results: Eighty-seven/400 (21%) patients enrolled met the DT2-RA criteria. No significant differences were found in median age (no-D2T 62±12 vs. D2T 64±15, p= 0.6), median disease duration (no-D2T 8±9 vs. D2T 12±10 years, p=0.9) and gender (female 77%, p=0.9). D2T-RA had similar autoantibody profile, prevalence of interstitial lung disease, C-reactive protein levels at diagnosis, number of tender and swollen joints at diagnosis) and major comorbidities (hypertension, dyslipidemia, COPD, depression, autoimmune thyroiditis). At univariate D2T-RA correlated, without reaching statistical significance, with diabetes (p=0.055), a previous history of major cardiovascular events (p=0.071), previous or current history of smoking (p=0.081) and GERD (p=0.079). Of note, D2T-RA significantly correlated with fibromyalgia (p=0.004), previous surgical intervention to treat RA (p=0.01), peripheral arteriopathy (p=0.035), obesity (p=0.023) and evidence of erosions at diagnosis (p=0.045). The multivariate analysis confirmed the correlations between D2T-RA and baseline erosions (p=0.034, OR 2.23 IC 1.06-4.69), obesity (p=0.041, OR 2.05 IC 1.03-4.09) and fibromyalgia (p=0.004, OR 3.28 IC 1.47-7.32) regardless of age and gender or, in the case of fibromyalgia, obesity.
Conclusion: Our data support the importance of comorbidities to determine D2T-RA which is not influenced by the autoantibody profile. In particular, fibromyalgia and obesity likely increase the probability of a DMARDs multi-failure. Data on baseline erosions and a previous history of surgery possibly suggest that a better timing of intervention with earlier treatments may reduce the risk of D2T-RA.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Nicoletta Luciano Speakers bureau: Abbvie, BMS, Eli-Lilly, Janssen, Consultant of: Galapagos, Elisa Barone: None declared, Enrico Brunetta: None declared, Maria De Santis: None declared, Angela Ceribelli: None declared, Marta Caprioli: None declared, Giacomo Maria Guidelli Speakers bureau: Janssen, Lilly, Novartis, Abbvie, Galapagos, Consultant of: Janssen, Arianna Sonaglia: None declared, Daniela Renna Speakers bureau: Janssen, Natasa Isailovic: None declared, Carlo Selmi Speakers bureau: AbbVie, Amgen, Alfa-Wassermann, Biogen, Eli-Lilly, Galapagos, Janssen, Novartis, Pfizer, SOBI, Consultant of: AbbVie,

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AB0207

VOLATILITY OF WORK PARTICIPATION DOMAINS AFTER A FLARE OF RHEUMATOID ARTHRITIS UNDER TREAT-TO-TARGET THERAPY

Keywords: Rheumatoid arthritis, Work-related issues, Treat to target

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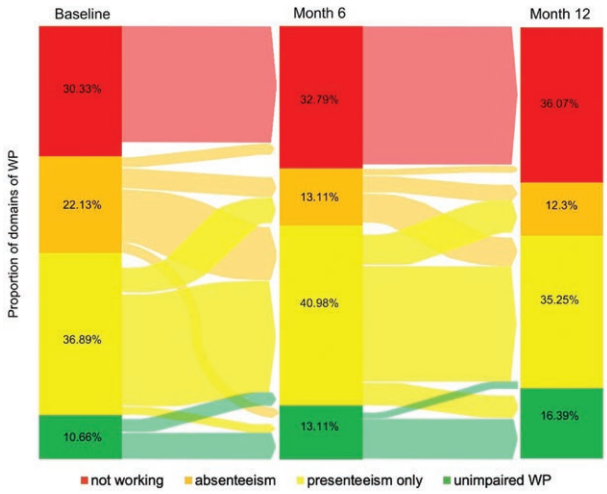
Background: Rheumatoid arthritis (RA) is one of the most common diseases worldwide with a need for rehabilitation despite recent advantages in pharmacological treatment options. Furthermore, data show a numerical increase in years of life with disability in RA patients in Germany from 1990 to 2017. Limitations in work participation (WP) also remain highly prevalent.
Objectives: We investigate the development of different domains of WP (unimpaired WP, presenteeism, absenteeism, and no employment) at the patient level under drug therapy over 12 months to understand the impact of pharmacological treatment.
Methods: The multicenter ERFASS study prospectively enrolled seropositive RA patients with an active flare of disease initiating treat-to-target (T2T) drug therapy over 12 months [1]. Patients were enrolled between 01/2018 and 12/2019. We examine the different domains of WP in working-age patients (18-65 years) excluding students and old-age pensioners using the WPAI of patients with a complete dataset at all three measurement time points (month 0, 6 and 12). Disease activity was measured using the DAS28.
Results: A total of 122 patients (73.0% female) with a mean age of 52.8 years (SD: 8.5) were included. Disease activity according to DAS28-CRP decreased significantly over the course of the study from 4.2 at baseline to 2.5 at month 12 (p<.001). The proportion of non-working patients increased numerically over the course of the study from 30.3% to 36.1% (p=0.085). The proportion of patients with absenteeism decreased significantly from 22.1% at baseline to 12.3% at month 12 (p=0.033). There were small changes in presenteeism (month 12: 35.2%; p=0.086). The proportion of patients with unrestricted WP increased significantly from 10.7% at baseline to 16.4% at month 12 (p<0.001) (Table 1). Graph 1 shows the quantitatively relevant changes in WP over the course of the study in a sankey diagram. The group of not working patients mainly gains growth from the group of patients with absenteeism. Patients with unimpaired WP proportionally become more because patients with presenteeism or absenteeism at baseline improve their WP to unimpaired WP. However, we detected a substantial proportion of patients with initially unimpaired WP facing impairments as most likely presenteeism during T2T. At all measure points we see the most substantial fluctuations in patients with presenteeism and absenteeism.
Conclusion: Besides good therapy response in terms of disease activity, we demonstrate that the majority of unemployed patients during an acute disease flare does not find their way back into the work force within twelve months of T2T pharmaceutical treatment. The greatest improvements in WP were observed in patients with absenteeism at baseline. Although the proportion of patients without limitations in WP increased significantly, it remained at a low level at the end of the study. Our data provide an understanding of the development of the different domains of WP in patients after a flare of RA which helps to tailor occupational rehabilitation concepts.

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Table 1. Demographics, disease activity and domains of WP during study course.

	Baseline	Month 6	Month 12	p-value
Age years (SD)	52.8 (8.5)			
Gender (female) n (%)	89 (73.0)			
DAS28-CRP (mean)	4.2	2.8	2.5	<.001
Not working n (%)	37 (30.3)	40 (32.8)	44 (36.1)	.085
Absenteeism n (%)	27 (22.1)	16 (13.1)	15 (12.3)	.033
Presenteeism only n (%)	45 (36.9)	50 (41.0)	43 (35.3)	.086
Unimpaired WP n (%)	13 (10.7)	16 (13.1)	20 (16.4)	<.001



Graph 1. Development of domains of WP in a Sankey diagram. The width of the arrows equivalents the proportion of patients changing between groups.

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AB0208

COMPARISON OF PERFORMANCE OF ACR EULAR 2022 REMISSION CRITERIA IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM INDIA

Keywords: Remission, Disease-modifying drugs (DMARDs), Rheumatoid arthritis

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Background: Remission is a state, not change or transition with absence of disease activity in rheumatoid arthritis (RA) [1]. Remission at 6 months has been shown to predict future good outcomes such as arresting radiographic progression and better functional status at 12 and 24 months [2]. ACR EULAR have endorsed Boolean2.0 in the revised remission criteria in 2022 [3]. None of these participants were recruited from India. In this ongoing study, we compare the various remission criteria in patients with RA in our setting.
Objectives: To compare the performance of various remission criteria (Disease Activity Score 28 (DAS28 ESR), Disease activity Score 28 CRP (DAS28 CRP), Simple Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Boolean, Boolean2.0, and BooleanX) in patients with RA presenting to our rheumatology clinic, at Jodhpur, India.
Methods: A longitudinal study was initiated in July 2021 after Ethics Committee approval. Demographic and treatment details were collected after written informed consent. Remission criteria were calculated at 6 months follow up. We analysed agreement between the Boolean- and index-based criteria SDAI, CDAI, DAS28 ESR and DAS28 CRP. The study is an ongoing study, with a calculated sample size of 165.
Results: Follow-up data of 85 participants of which 85.9% female with median age of 47 (12) years with RA diagnosed by ACR EULAR 2010 were collected. At enrolment, 10.6% (n = 9) were on biologicals, 35.3% (n = 30) on methotrexate alone and 54.1% (n = 46) on combination Disease-modifying Antirheumatic Drugs (DMARDs) therapy and at 6 months, 5.9% (n = 5) were on biologicals, 61.17% (n = 52) on methotrexate alone and 32.9% (n = 28) on combination DMARDs therapy. The proportion of patients in remission at 6 months using DAS28 ESR was 65.9% (n = 56), DAS28 CRP was 54.1% (n = 46), SDAI was 38.8% (n = 33), CDAI was 32.9% (n = 28), Boolean was 10.6% (n = 9), Boolean2.0 was 40% (n = 34) and BooleanX was 47.1% (n = 40) (Figure 1). DAS28 CRP showed substantial agreement with Boolean2.0 (kappa 0.63) at enrolment and moderate

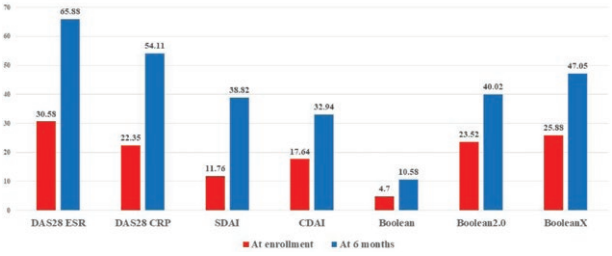
agreement (kappa 0.49) at 6 months, however, SDAI had only slight agreement with modified Boolean based indices (Table 1).

Table 1. Agreement between modified Boolean indices and disease activity

Kappa	SDAI at enrolment (CI)	SDAI at 6 months (CI)	DAS28 CRP at enrolment (CI)	DAS28 CRP at 6 months (CI)
Boolean	0.23 (0.00-0.08)	0.09 (0.20-0.38)	0.10 (0.09-0.23)	0.15 (0.00-0.03)
Boolean2.0	0.13 (0.13-0.29)	0.08 (0.27-0.45)	0.63 (0.00-0.03)	0.49 (0.00-0.03)
BooleanX	0.03 (0.97-1.00)	0.06 (0.39-0.59)	0.71(0.00-0.03)	0.39 (0.00-0.03)

Conclusion: This study provides evidence of external validation of the newly proposed modification of the Boolean ACR/EULAR remission criteria; however, we found that the Boolean2.0 criteria did not exhibit agreement with index-based remission definitions in the Indian population from our centre. Our results replicate the findings that a Boolean definition using 2 cm as threshold for patient global assessment of disease activity (Boolean2.0) yields better agreement than Boolean [2]. With the validation Boolean2.0 in our settings, our data support the revised ACR/EULAR remission criteria as a target in clinical practice.

Fig 1: Comparison of different ACR/EULAR remission criteria and Boolean indices at enrollment and at 6 months after treatment initiation



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Disclosure of Interests: None Declared.

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AB0209

VALIDATION OF REVISED 2022 ACR/EULAR REMISSION CRITERIA FOR RHEUMATOID ARTHRITIS IN ASIAN INDIAN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Outcome measures, Rheumatoid arthritis

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Background: Remission has become a key target in the management of rheumatoid arthritis (RA) patients[1]. In 2022, American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) has revised the Boolean based remission criteria in RA by increasing the patient global assessment of disease activity (PtGA) threshold to ≤2cm (range 0–10 cm). This has not been validated in an Asian Indian cohort of RA patients[2,3].

Objectives: To validate ACR/EULAR remission criteria for RA: 2022 revision in Asian Indian RA patients by using data of an ongoing clinical trial.

Methods: For the purpose of validating the remission criteria, data generated at our center from an ongoing clinical trial (SMART study) which enrolled patients with active seropositive RA, who were 18-60 years old with disease duration ≤5 years was used. This is a 24-week multicenter, open-label RCT to compare efficacy of split versus non-split doses of methotrexate (MTX). For this analysis, data from both groups was analyzed together. Patients are started on oral MTX 15 mg/week which was escalated every two weeks by 5 mg, to reach a maximum dose of 25 mg/week by 4 weeks. At the end of 16 weeks, if Disease Activity Score 28 (DAS28) >3.2 another DMARD can be added. Disease activity was measured using the DAS28, Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI) at 24 weeks. Proportion of patients achieving remission with index-based (SDAI≤3.3 & CDAI≤2.8) and ACR/EULAR Boolean-based criteria was compared. The proposed PtGA threshold of 2 cm (Boolean2.0) (range 0–10 cm) was compared with the original threshold of 1 cm (Boolean1.0) as well as with 1.5 cm, 2.5 cm and no PtGA (Boolean X) for remission. Agreement (Cohen's kappa) was assessed between Boolean-based and index-based criteria. #Trial registration number: **CTRI/2021/02/031361**.

Results: This study included 125 patients, majority being females (105 (84%)), with mean (±SD) age of 42.8 (±10.8) years and mean (±SD) disease duration of 2 (±1.5) years. At 24-weeks, using the index based (SDAI and CDAI) criteria, remission was achieved in 24.8% and 24% of patients respectively. Among the various Boolean criteria, remission occurred in only 21.6% using the original Boolean1.0. This increased with Boolean2.0 to 23.2%, and further increased with Boolean2.5 and Boolean X [Figure 1]. The highest agreement between SDAI or CDAI-defined remission was found to occur with Boolean2.0-defined remission rather than Boolean1.0 (or 1.5, 2.5 or X) defined remission [Table 1]. Also, there was strong agreement (0.89 (95% CI 0.79-0.99)) between SDAI and CDAI-defined remission criteria.

Conclusion: We validated the performance of revised 2022 ACR/EULAR remission criteria for RA in Asian Indian RA patients and found the higher agreement of Boolean2.0 (rather than Boolean1.0) with index-based remission cutoffs.

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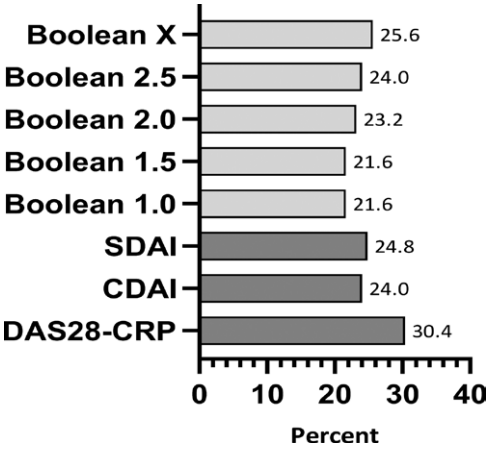


Figure 1. Rate of RA remission at 24-weeks according to Boolean definitions; using a PtGA threshold of 1.0, 1.5, 2.0, 2.5 0r X (omitting PtGA completely) and index-based SDAI, CDAI and DAS28-CRP definitions.

Table 1. Kappa values with 95% CIs representing agreement between modified Boolean remission definition and SDAI/CDAI defined remission for RA patients at 24-weeks.

Kappa Value (95% CI)	All patients (n=125)	
	SDAI	CDAI
Boolean 1.0	0.82 (0.70 – 0.94)	0.84 (0.72 – 0.96)
Boolean 1.5	0.82 (0.70 – 0.94)	0.84 (0.72 – 0.96)
Boolean 2.0	**0.83 (0.71 – 0.95)**	**0.85 (0.73 – 0.97)**
Boolean 2.5	0.81 (0.69 – 0.93)	0.83 (0.71 – 0.95)
Boolean X	0.81 (0.69 – 0.93)	0.79 (0.65 – 0.93)

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Disclosure of Interests: None Declared.
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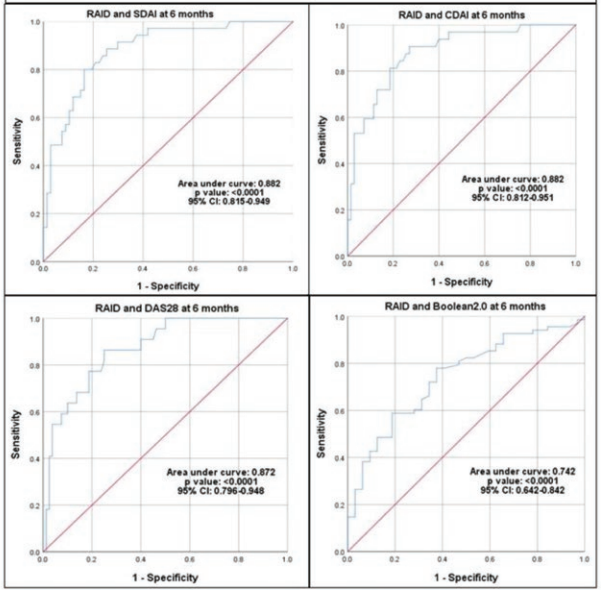
AB0210 CAN RHEUMATOID ARTHRITIS IMPACT OF DISEASE (RAID) SCORE BE USED AS A PATIENT REPORTED OUTCOME BASED TARGET IN A TREAT-TO-TARGET APPROACH: A PROSPECTIVE STUDY FROM INDIA

Keywords: Patient reported outcomes, Rheumatoid arthritis, Treat to target

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Background: Rheumatoid arthritis impact of disease (RAID) is a well validated patient reported outcome (PRO) in patients with Rheumatoid Arthritis (RA) [1]. RAID score involves the active participation of patients and can be easily calculated at the comfort of home with minimal training and assistance or while the patient is waiting to see the doctor in the outpatient department. It is helpful in giving an idea of the overall well-being of the patient and takes into account sleep and depression which are the unmet needs in RA treatment. However, the effectiveness of RAID as a patient reported outcome and the optimal RAID score which can be used as a target for treat-to-target approach has not been studied in the Indian population.
Objectives: To determine if the RAID score can be used as a PRO target along with a clinician reported disease activity score for managing patients with RA under a treat-to-target approach. To establish an acceptable cut-off for the RAID score which can be used as a target in patients with RA and validate it against disease activity indices.
Methods: We prospectively enrolled patients with RA diagnosed using ACR/EULAR 2010 criteria in our tertiary care institute, at Jodhpur, India from March 2021 to May 2022 and followed them over 6 months after their written informed consent and Ethics Committee approval (AIIMS/IEC/2021/3370). DAS28, patient assessment of global disease activity (PtGA), Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), RAID score and modified Boolean indices (2) were calculated at enrolment and 6 months. Binary logistic regression analysis was used to determine if RAID could reliably predict DAS28 <3.2 and Boolean remission indices at enrolment and 6 months. DAS28 <3.2, CDAI ≤10 and SDAI ≤11 were considered as the target as per EULAR recommendations, with remission and low disease activity as acceptable goals to achieve while treating patients with RA.
Results: We included 156 patients with a mean age of 47.0±12.3 years, 86.5% were females. Among them, 23.4% patients had DAS28 <3.2, 11.7% had SDAI ≤11, 13.6% had CDAI ≤10 while only 0.6% were in Boolean and Boolean2.0 remission. At 6 months, 110 patients were followed up and among them, 78.6% had achieved DAS28 <3.2, 66.0% had achieved SDAI ≤11, 68.9% had achieved CDAI ≤10 while only 1.9% had achieved remission according to Boolean remission criteria. However, Boolean2.0 criteria showed that 20.9% were in remission. RAID score could reliably and independently predict DAS28, SDAI, CDAI, PtGA and Boolean2.0 criteria. We constructed multiple Receiver Operating Characteristic (ROC) curves to determine the optimal cut-off of RAID for defining low disease activity and remission using SDAI, CDAI, DAS28 and Boolean2.0 remission criteria (Figure 1). We noted that the RAID score of 2.32 had 85.7% sensitivity and 76.1% specificity in predicting SDAI ≤11 and 87.5% sensitivity and 74.3% specificity in predicting CDAI ≤10. Further, RAID score of 2.32 had a sensitivity of 86.4% and specificity of 72.5% in predicting DAS28 <3.2 and a sensitivity of 55.9% and specificity of 81.2% in predicting remission as per Boolean2.0 criteria.
Conclusion: RAID score can be used as a reliable and validated PRO in patients with RA. We also propose a cut-off of a composite RAID score of 2.32 as an additional target to achieve while treating patients with RA in the Indian population.

Fig 1: ROC curves of RAID with SDAI, CDAI, DAS28, and Boolean2.0 to predict remission and low disease activity



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Disclosure of Interests: None Declared.
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AB0211 ASSESSMENT OF STIGMATIZATION IN RHEUMATOID ARTHRITIS USING THE STIGMA SCALE FOR CHRONIC ILLNESSES-SHORT FORM (SSCI-8)

Keywords: Rheumatoid arthritis, Cognitive function, Mental health

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease that occurs among productive patients. It often causes functional disability that can be permanent, with both physical and mental impact.
Objectives: We aimed to assess the degree of stigmatization and associated factors in patients with RA.
Methods: This was a cross-sectional study including patients with RA. Sociodemographic, clinical, paraclinical, and therapeutic data were collected. Stigma was assessed using the Stigma Scale for Chronic Illnesses-Short Form (SSCI-8) [1]. This scale is composed of 8 items. Responses for each item are made as follows: 1 = never, 2 = rarely, 3 = sometimes, 4 = often, and 5 = always. The range of raw scores assigned for the SSCI-8 was 8 to 40. The closer the score was to the upper value, the greater the degree of stigma.
Results: These were 100 RA patients: 81 women (81%) and 19 men (19%). The mean age was 55.33±10.08 years [25-76]. The mean disease duration was 14.21±10.10 years [1-46]. RA was immunopositive in 50% of patients. It was erosive in 75% of cases. Coxitis was present in 6 patients. The mean disease activity measured by DAS28-CRP was 3.81±1.56 [0.12-6.90]. The mean value of functional impairment assessed by HAQ was 0.91±0.64 [0-2.4]. Regarding the SSCI-8 score, the mean value was 17.85±6.02 [8-32]. The stigma score was not correlated with patient age (r=-0.184, p=0.075), nor with age at diagnosis (r=-0.001, p=0.993). It was not statistically different by gender (p=0.648). This score was positively correlated with DAS28 (CRP) (r=0.244, p=0.034). It was not correlated with HAQ (r=0.037, p=0.754). The presence of coxitis and the erosive nature of RA had no influence on stigma (p=0.923, p= 0.895 respectively).
Conclusion: According to our study, stigma was associated with disease activity during RA. The degree of stigma was not very high in our population, which can be explained by a moderately active disease.

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Disclosure of Interests: None Declared.
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AB0212 FUNCTION AND PAIN IN KNEE JOINTS IN PATIENTS WITH RHEUMATOID ARTHRITIS AFTER TOTAL KNEE ARTHROPLASTY

Keywords: Osteoarthritis, Rheumatoid arthritis

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Background: Total knee arthroplasty (TKA) in patients with rheumatoid arthritis (RA) is considered the most effective intervention reducing knee pain and improving physical function. However, higher risk of late complication and worse surgery outcomes may be observed in patients with active disease.[1]
Objectives: To study the knee joint function and pain before and after the TKA in patient with rheumatoid arthritis.
Methods: 69 RA patients (10 (14,5%) males and 59 (85,5%) females) with an average age of 59 [52; 64] years were included into the study group. 81 osteoarthritis (OA) patients (38 males (46,9%) and 43(53,1%) females) aged 66 [61; 73] years, were included into the control group. 23,2% of RA patients had a highly active disease at the moment of intervention. All patients underwent cemented TKA and completed Oxford Knee score (OKS) before the surgery, after discharge and 3 and 12 months after the surgery. Knee pain was assessed using VAS score also before intervention, straight after and 3 and 12 months after the surgery. All analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). A p value of less than 0.05 was considered statistically significant.
Results: Patients in RA group had significantly lower preoperative OKS results, than OA patients (25.0 [23.5; 27.0] versus 29.0 [26.5: 30.0], p=0.00, Mann-Whitney) as well as lower postoperative OKS results before the discharge (34.0 [34; 38] versus 40.0 [35; 40] p=0.00, Mann-Whitney). 3 months after the intervention OKS scores were comparable within the two groups (43.0 [42; 44] versus 43.0 [42; 44], p=0.557; Mann-Whitney). The same was found for OKS scores 12 months after the surgery (44.0 [44; 47] versus 44.0 [44; 47], p=0.328, Mann-Whitney). Pain intensity in RA patients varied from 60 to 90 mm according to VAS prior to surgery and was lower than among OA patients (80.0 [80; 90] versus 90.0 [80; 100], p=0.00, Mann-Whitney) which can be explained by patients' higher pain tolerance due to "usual" pain in RA. The same tendency was observed immediately after the intervention (55.0 [50; 60] versus 65.0 [50; 65], p=0.00, Mann-Whitney). 3 months after the surgery pain intensity was similar in both groups (30.0 [30; 35], p=0.349, Mann-Whitney). 1 year after the intervention RA patients reported higher VAS scores probably due to RA activity (20.0 [20; 20] versus 10.0 [10; 15], p=0.00, Mann-Whitney).
Conclusion: The effectiveness of TKA for pain reduction and improvement of knee function in patients with RA was comparable to that among patients with OA. OKS scores were lower in RA group prior to surgery, however, 3 and 12 months after the intervention they did not differ between the patients with RA and OA.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6309

AB0213 EQ5D SCORES ARE NOT AFFECTED BY AGING

Keywords: Outcome measures, Rheumatoid arthritis, Patient reported outcomes

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Background: Estimating cost-effectiveness in the treatment of rheumatoid arthritis (RA) has received increasing attention in recent years as a large number of new drugs have been developed and generated through huge development costs and soaring drug costs.
Objectives: EuroQol-5th dimension score (EQ5D) is a most popular index for measuring the quality of life in patients with rheumatoid arthritis (RA). In this study, an association between EQ5D and aging using retrospective cohort data.
Methods: RA patients who had been followed up for more than 3 years were picked up. Patients' simplified disease activity index score (SDAI), HAQ, pain score using a visual analog scale (PS), Sharp/van der Heijde score (SHS), and EQ5D were monitored since the start of treatment (baseline: BL). Patients were divided into 3 groups; G-YY who began treatment before age 65 and continued until age 65; G-YY who began treatment before age 65 and continued until age 65 or older; G-OO who began treatment at age 65 or older. The crude model and SHS or HAQ matched models were used to compare the mean EQ5D during treatment of G-YY and G-OO statistically using Mann-Whitney U test. We also statistically compared the EQ5D of each subject under age and over age 65 in the G-YO group using repeated T-test measurements.
Results: There were 143 G-YY, 88 G-YO and 307 G-OO, for a total of 538. The means for each group were 49.9, 61.2 and 76.9 for ages G-YY, G-YO and G-OO, 12.5, 12.1 and 13.0 for SDAI, 0.281, 0.353 and 0.627 for HAQ, 29.7, 55.4 and 56.3 for SHS, 35.5, 31.1 and 36.6 for PS and 0.807, 0.761 and 0.724 for EQ5D, respectively. The mean EQ5D score of G-YY was significantly higher than that of G-OO using crude data, but there was no significant difference between the two groups after adjusting for SHS or HAQ. Comparing the mean EQ5D scores of G-YO before age 65 and after age 65 also showed no difference between the two periods. Using data from all patients, HAQ scores were significantly correlated with age.
Conclusion: HAQ scores were significantly correlated with aging, and EQ5D scores were significantly correlated with HAQ scores, but EQ5D scores were not correlated with aging. This explains why EQ5D scores are independent of aging. This may be useful in calculating cost-benefit assessments for older RA patients.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0214 VALIDATION OF JOINT INDEX VECTOR FOR PATIENT WITH RHEUMATOID ARTHRITIS

Keywords: Validation, Outcome measures, Rheumatoid arthritis

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Background: There are only few indices that can estimate joint involvement in both of upper and lower extremities in patients with rheumatoid arthritis (RA).
Objectives: One indicator can measure involvement on both upper and lower joint and large and small joint. The index developed by Nishiyama is called "Joint Index Vector," which can represent the affected state of upper and lower joints as well as large and small joints by using three-dimensional coordinates. The aim of this study is to validate the efficacy and availability in clinical practice using monitoring data from RA patients.
Methods: Patients who started treatment for RA after January 2016 and whose Simplified Disease Activity Index (SDAI), Health Assessment Questionnaire Disability Index (HAQ-DI), Pain Score with Visual Analog Scale (PS-VAS), and EuroQol 5th dimension (EQ5D) were monitored at each visit and Sharp/van der Heijde score (SHS) was monitored annually were included in the study. The JIV represents the joint prevalence of the upper limb in X coordinates (Vx), the joint prevalence of the lower limb in Y coordinates (Vy), and the difference in joint prevalence between large and small joints in Z coordinates (Vz) [1]. The relationship between each clinical parameter and three elements of the JIV was evaluated statistically. Each parameter was defined as the dependent factor, and the three elements of the JIV were defined as the independent factor, and correlation was examined using linear regression analysis. These procedures were performed at the first visit (BL), 1 year after the first visit (1Y), and at te last visit (LT). Additionally, the change in the HAQ score and SHS at 1Y (dHAQ and dSHS) were defined as the dependent variant, and the other parameters including the three coordinates of JIV were defined as the independent variant. Then, correlation between these parameters were statistically examined also using linear regression analysis.
Results: A total of 419 patients in whom 113 were male and 306 were female, were recruited in the study. Mean age at baseline was 68.1 and mean follow-up period was 65.3 months. Vx, Vy, and Vz significantly correlated with SDAI at all periods of BL,1Y, and LT. Vy significantly correlated with HAQ-DI at all periods, whereas Vx and Vy significantly correlated with PS-VAS at all periods. Vy significantly correlated with SHS at 1Y and LT. Vz significantly correlated with EQ5D at 1Y and LT. Mean dHAQ significantly correlated with age, SHS, PS-VAS, and Vz. Mean dSHS significantly correlated with Vx, Vy and annual change of Vx.
Conclusion: These results demonstrated that Vx, Vy, and Vz suggested significant correlation with other clinical parameters, especially Vy which represents affected joints in the lower extremities significantly correlates with important patient related outcomes.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0215 MAGNITUDE OF THE INFLUENCE BY JOINT INVOLVEMENT ON HEALTH ASSESSMENT QUESTIONNAIRE DISABILITY INDEX SCORE

Keywords: Rheumatoid arthritis, Outcome measures, Validation

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Background: The Health Assessment Questionnaire Disability Index (HAQ-DI) is the best-known index for measuring functional capacity in patients with rheumatoid arthritis (RA). This index is well known to be influenced by disease activity, aging, joint deformities and pain. However, these parameters are related to each other and it remains unclear how joint involvement affects HAQ-DI in RA patients.

Objectives: The aim of this study is to determine how joint involvement affects HAQ-DI in RA patients using a retrospective cohort study.

Methods: Patients with RA who have been monitored since the first visit for tenderness and swelling of the whole body and limb joints, patient's global assessment (PGA), evaluator's global assessment (EGA), pain score using a visual analog scale (PS), and HAQ-DI at every visit were included in the study. The patient's mean age, HAQ score, PGA, EGA, C-reactive protein (CRP), and Sharp/van der Heijde score (SHS) were collected. Joint Index Vector (JIV) was used as an index of joint lesions. JIV represents the joint prevalence of the upper limb in X coordinates (Vx), the joint prevalence of the lower limb in Y coordinates (Vy), and the difference in joint prevalence between large and small joints in Z coordinates (Vz) [1]. The average value of the triaxial coordinates of the JIV was also collected. As a preliminary study, the correlation between the mean HAQ score of all cases collected and other parameters such as patient gender and serum albumin level (ALB) was evaluated using multivariate linear regression analysis. Statistical significance was set as less than $1.0*10^{-10}$. Next, the association of the HAQ score with other parameters at baseline, the association of the HAQ score after 1 year at baseline with other parameters at baseline and the change from baseline to 1 year, and the annual change in the HAQ score and other parameters at baseline and the annual change in these parameters were statistically evaluated using multivariate linear regression analysis. Statistical significance was set as less than 5.0%.

Results: A total of 601 patients in these 166 males and 435 females data were used in the study. The HAQ score positively correlated with male gender, older age, higher SHS, higher PGA, lower EGA, higher PS, higher Vy, and higher Vz with beta values of 0.09, 0.22, 0.17, 0.19, -0.12, 0.17, 0.07, and 0.11, respectively. The HAQ score at baseline positively correlated with older age, higher PGA, higher CRP, higher PS, higher SHS, and higher Vy at baseline with beta values of 0.26, 0.13, 0.21, 0.14, 0.14, and 0.10, respectively. The HAQ score at one year after the baseline positively correlated with older age, higher PS, and higher SHS at the baseline, and higher annual change of the PS with beta values of 0.26, 0.25, 0.22, and 0.15, respectively. The annual change of the HAQ score positively correlated with higher SHS and higher Vy at the baseline, and higher annual change of PS, Vx, Vy, and Vz with beta values of 0.04, 0.11, 0.04, 0.67, 0.43, and 0.09, respectively.

Conclusion: These results indicate that there is a close association between HAQ scores and aging, degree of pain, and joint deformities, and in addition, joint involvement also influences HAQ scores. In particular, changes in HAQ scores are governed by joint involvement. The effect of disease activity on HAQ scores will be largely governed by joint involvement.

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Disclosure of Interests: None Declared.

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AB0216 INHIBITION OF RADIOGRAPHIC JOINT DAMAGE BY JAK INHIBITORS IN PATIENTS WITH DESTRUCTIVE RHEUMATOID ARTHRITIS WITH EXTENSIVE BONE MARROW EDEMA IN HAND

Keywords: Prognostic factors, Imaging, Rheumatoid arthritis

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Background: Rapid radiographic progression (RRP) is considered to be one of the factors in difficult to treat rheumatoid arthritis (RA). MRI bone marrow edema has been reported to be a risk factor for RRP. We reported that extensive bone marrow edema (BE) determined by hand MRI is a prognostic indicator for rapid radiographic progression in MTX inadequate response to early RA treated with MTX+ Adalimumab combination therapy (1) and we reported biologics were more effective for radiological damage compared with MTX +csDMARDs enhanced therapy for RA inadequate response to MTX accompanying with extensive BE in hand[2].

Objectives: To investigate the radiographic joint damage by usage of JAK inhibitors (JAKi) in RA patients inadequate response to MTX/ Biologics/ other JAKi with or without BE in clinical practice.

Methods: Twenty-four RA patients (pts) with extensive BE by hand MRI (BE group) and 30 pts without BE (non-BE group) despite treatment with MTX/biologics/JAKi were retrospectively recruited from JAK inhibitor treated pts (total:130 pts; two JAK1,3 selective inhibitor-Toficitinib(TOF):34 pts; Peficitinib(PEF):33 pts and two JAK1 selective inhibitor- Upadacitinib(UPA):35 pts; Filgotinib(FIL):28 pts). Baseline demography of patients in BE and non-BE group were shown in Table 1. Significant difference of baseline factors between BE(+) group and BE(-) group were only observed in mTSS/y (6.76 vs 3.21,P = 0.0000582, t test). Bone destruction expressed as yearly progression of mTSS (ΔmTSS/y) was determined before and after treatment by modified total Sharp scoring (mTSS) using conventional radiography. BE score measured by RAMRIS method using T1 or STIR image of hand MRI (CANON, 1.5T). Based on our previous data, extensive BE in hand was defined designated as BE score≥15[1].

Results: DAS28-ESR values from baseline to 1 year was significantly reduced from 4.82 to 3.39(P<0.01) in the BE group and from 4.83 to 3.45(P<0.01) in the non-BE groups. After 1 year treatment by JAKi, RRP(ΔmTSS/y≥5) was more observed in 5 pts in the BE group, however RRP were not observed in the non-BE group (Figure 1). Significant differences betwwen JAK1 inhibitors and JAK1/3 inhibitors were not observed. Yearly radiographic progression observed from 6.39 to 1.59 (P=0.000003)in the BE group and from 3.21 to 0.16 (P= 0.000545) in the non-BE group.

Conclusion: Results of this study in the baseline and 1 year treatment indicated that BE may be a predictor of RRP not only in the MTX, biologics treatment, but in the JAKi treatment. A further prospective, randomized study may be required to clarify this.

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Table 1.

	BE group(n = 24)	non-BE group(n =30)	P
Age(yrs)	66.9(+-11.88)	65.8(+-11.51)	0.72
Sex(M:F)	2:22	8:22	0.157
duration(Months)	174.(+-120.7)	180.0(+-124.3)	0.863
RF IU/ml	154.9(+-175.7)	193.5(+-495.1)	0.718
RF positive%	91.7	75.9	0.16
ACPA	78.25(11.43-290.7)	63.75(6.58-286.0)	0.614
ACPA positve%	83.3	76.7	0.736
mTSS	84.5(+-83.4)	57.4(+-57.5)	0.163
mTSS/y	6.76(+-3.69)	3.21(+-2.24)	0.0000582
mean number of pre BIO	0.88	0.8	0.775
mean number of pre JAKi	0.29	0.16	0.401
MTX dose mg/w	8	8.29	0.799
MTX use(%)	54.2	46.7	0.7846
CRP(mg/dl)	1.69(+-2.18)	1.15(+-2.30)	0.387
DAS28-ESR 0M	4.82(+-1.02)	4.83(+-0.91)	0.982
Patient VAS	50.75(+-22.35)	48.67(+-20.34)	0.722
MMP3(ng/ml)	170.9	135.6	0.233
anti-JAK 1/3 : anti-JAK1(total)	11 pts : 13 pts	16 pts :11 pts	0.785
No of pts with RRP（ΔmTSS≥５）(%)	5 (20.8%)	0(0%)	0.0134

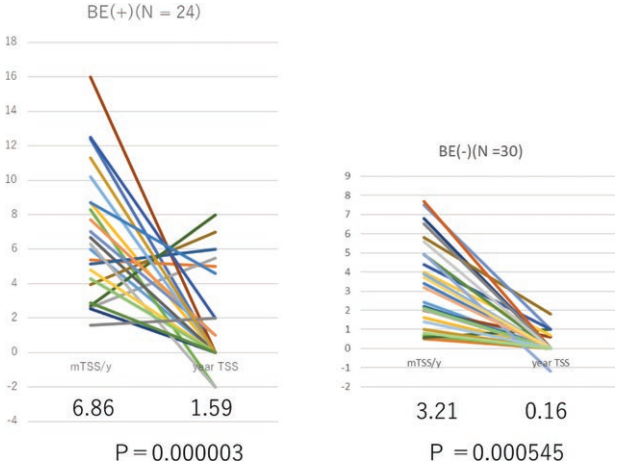


Figure 1.

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Rheumatoid arthritis - prognosis, predictors and outcome

AB0217 MANAGEMENT OF RHEUMATOID ARTHRITIS THERAPIES IN TELECONSULTATION

Keywords: Rheumatoid arthritis, Telemedicine

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Background: Therapeutic adjustment is of major importance in the treat to target strategy proposed for rheumatoid arthritis (RA). This aspect can be challenged in teleconsultation given the multiplicity of treatments, efficacy/ safety issues of RA therapies and the absence of clinical examination. These could lead the physician to prefer modifying the treatment in face-to-face visit rather than in teleconsultation.
Objectives: To evaluate how clinicians adapted RA therapies in teleconsultation.
Methods: Retrospective monocentric routine care cross-sectional study conducted in the Rheumatology department of Cochin Hospital. We reviewed electronic medical report (EMR) to identify all teleconsultations performed by telephone or video consultation in a 2-year period and extract data of interest. We compared treatment adaptation performed in teleconsultation to treatment adaptation that requested a face-to-face visit following teleconsultation. Treatment adaptation was defined by the introduction of a new treatment, modification of treatment dose and/or route or discontinuation of the treatment. This treatment adaptation may be motivated by efficacy or safety issues. Different treatment classes were considered: corticosteroids, methotrexate and targeted biologic/ synthetic therapies (b/tsDMARDs).
Results: We included 187 patients (150 females, 80%) who had a teleconsultation performed, with a mean age of 56±16 years and a disease duration of 13±11 years. Positive rheumatoid factor and positive anti-CCP pantibodies were detected in 125 (67%) and 139 (74%) patients respectively. 96 patients (51%) had erosive disease. A total of 56 therapeutic adaptations were collected: 34 were performed in teleconsultation and 22 requested face-to-face visits (**Table 1**). Demographics and RA disease characteristics did not differ between patients who had therapeutic adaptations performed during teleconsultation or during face-to-face visits. Corticosteroid and methotrexate were more likely to be adapted in teleconsultation compared to face-to-face visits (16/34, 47% vs 2/22, 9%, p=0.003 and 15/34, 44% vs 1/22, 5% p=0.002, repectively). Interestingly, methotrexate was adapted in teleconsultation for both efficacy and safety issues, leading do dose increase/reduction, switch from oral to subcutanous route, or drug discontinuation. In the other hand, targeted therapies were preferentially initiated or modified during face-to-face visits which all included clinical examination, lab tests and power doppler ultrasounds (19/22, 86% vs. 3/34, 9%, p<0.001).
Conclusion: Corticosteroids and methotrexate were mainly adaptated in teleconsultation without requesting a face-to-face visit, supporting their flexibility in teleconsultation and clinician's confidence in their use, even at a distance from the patient. In the other hand, b/tsDMARDs were preferentialy adapted in face to face consultation, highlighting the need of a careful evaluation of disease activity by clinical examination before modifying this class.

Table 1. Therapeutic adaptations performed in teleconsultation or in face-to-face visits

	Adapted therapy	Adaptation	Cause
Teleconsultation (n=34)	Corticosteroids (n=16)	Introduction (n=3)	Disease flare
		Dose increase (n=7)	Disease flare
		Dose reduction (n=6)	Low disease activity or remission
	Methotrexate (n=15)	Introduction (n=3)	Active disease
		Dose increase (n=2)	Active disease
		Swith from oral to SC (n=3)	Active disease (n=2), nausea (n=1)
		Dose reduction (n=2)	Increased liver enzymes
		Discontinuation (n=5)	(n=1) and asthenia (n=1) Asthenia (n=3), nausea (n=2)
	b/tsDMARDs (n=3)	Introduction of JAKi (n=1)	Active disease
		JAKi dose reduction (n=2)	Age (n=1) and CV risk factors (n=1)
Face-to-face visits (n=22)	Corticosteroids (n=2)	Corticosteroid infusion (n=2)	Active disease
	Methotrexate (n=1)	Swith from oral to SC (n=1)	Active disease
	b/tsDMARDs (n=19)	Introduction (n=3)	Active disease
		Swith to a new b/tsDMARD (n=16)	Active disease

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0218 RHEUMATOID ARTHRITIS OUTCOMES: A MULTICENTRE CROSS-SECTIONAL STUDY OF PATIENTS IN IRELAND (CONTEXT-RA)

Keywords: Remission, Patient reported outcomes, Quality of life

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Background: Despite increasing treatment options for RA, many patients still do not appear to achieve remission, especially in more established disease.[1]
Objectives: To evaluate disease outcomes and quality of life (QoL) of DMARD treated patients with RA in clinical remission (CR) in routine Irish rheumatology clinics vs those with residual disease activity.
Methods: A multicentre, cross-sectional study with a 9-month recruitment period (Mar-Nov 2021). Demographics, disease activity, patient reported outcomes, comorbidities, workability & healthcare resource utilisation (HRU) data were collected. Patients on a stable dose of any DMARD (> 3 months) were classified according to disease activity state as follows:

- Responder group 1 (RG1) CR (CDAI≤2.8)
- Responder group 2 (RG2) CR/ Low Disease Activity (LDA) (CDAI>2.8 -10) &
- Non-responders (NR) moderate/high disease activity (CDAI>10)

Results: 130 RA patients were recruited (Table 1). 69% were female, mean age of 60.1 yrs and disease duration of 11.5 yrs. There was no significant difference in seropositivity between responder and non-responder groups (~75% RF+, ~69% ACPA+), 69% were treated with advanced therapy (biologic/targeted synthetic DMARDs), primarily TNFi's.

- 26% of patients were in CR, 32% in LDA & 42% NR. Significant differences in QoL-primary endpoint were noted between CR/LDA patients vs NR group. The difference in QoL index score (EQ5D-5L) for patients in CR and LDA vs those in remission alone, suggest QoL is considerably higher in patients in CR compared even to those in LDA.
- Joint pain (VAS), fatigue (FACIT-F) and function (HAQ-DI) scores all yielded strong negative correlations, indicating that CR/LDA patients had significantly better outcomes than those with MDA/HDA (Figure 1). A similar pattern was seen amongst patients in CR vs LDA, although significance was not achieved.
- In addition, more impaired productivity was noted in NR vs CR/LDA regarding ability to work and perform regular 'non-work' activities.
- Comorbidities were common, affecting over 90% of the non-responder group and 74% of patients in CR. The NR group had higher proportions of patients with cardiac, gastrointestinal, psychiatric and vascular disorders vs patients in CR/LDA.
- With respect to HRU, more patients in the NR group required medical visits for both RA and non-RA reasons vs patients in CR/LDA.
- Of the 54 patients in MDA/HDA, the study found there was a plan to add or switch DMARD, for only 32% of patients.

Table 1. Patient Characteristics

	RG1 1 N=34	RG 2 N=76	NR N=54
Age Mean (SD), yrs	57.1 (12.91)	57.6 (13.13)	63.7 (13.00)
Female, mean N (%)	23 (67.6)	51 (67.1)	38 (70.4)
Duration of disease, yrs, mean (SD)	12.1 (10.5)	11.2 (11.4)	11.3 (11.02)
Comorbidities, n (%)	25 (73.5)	36 (85.7)	49 (90.7)
Employed^, n (%)	19 (55.8)	37 (48.6)	11 (20.3)
Employment sick leaves due to RA^*, mean (SD)	0.3 (0.58)	0.3 (0.57)	0.6 (1.21)
Smoking status: Never smoked, n (%)	17 (50.0)	35 (46.1)	18 (33.3)
Alcohol Units, mean (SD)	4.0 (5.98)	3.3 (6.31)	3.8 (6.05)
Disease Activity (CDAI score)	1.21 (0.883)	4.06 (3.088)	19.46 (11.162)

^ Patients in either full or part time employment *Sick leave in the past 6 months

Figure 1. Patient reported outcomes across pain, fatigue and function

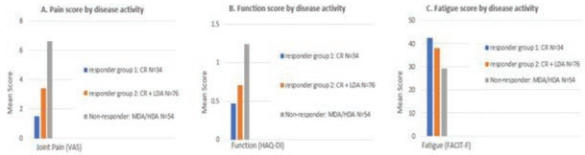


Figure 1a-c. Patient reported outcomes per disease activity state. **A.** Patients assessment of worst joint pain measured by VAS. 0 means no joint pain and 10 means worst possible joint pain. **B.** Function scores as measured by HAQ-DI. HAQ-DI is the sum of scores in the 8 categories divided by 8. Scores are adjusted for the use of aids/devices and/or help. The higher the score, the worse the patients functioning. **C.** Fatigue scores (FACIT-F). FACIT F score is the sum of individual item scores multiplied by 13 & divided by number of items answered. The higher the score the lower the level of reported fatigue.
Responder group 1 CDAIs≤2.8. Responder group 2 CDAI <10. Non responder group CDAI>10.

CDAI: clinical disease activity; CR: clinical remission, HDA: high disease activity, LDA low disease activity; MDA moderate disease activity

Conclusion: Overall, these data support the treat-to-target approach of striving for remission in RA, with important differences reported between non-responder & responder groups 1 & 2 but additionally between patients achieving CR vs LDA. The relatively low % of non-responder patients with a documented 'action plan', suggests improved approaches to shared decision making are warranted for patients not yet at the agreed target.

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AB0219

LONG-TERM OUTCOMES OF METHOTREXATE IN ELDERLY-ONSET RA IMPLEMENTING THE TREAT-TO-TARGET STRATEGY

Keywords: Outcome measures, Rheumatoid arthritis, Disease-modifying drugs (DMARDs)

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Background: Continuation of methotrexate (MTX) treatment is recommended in both MTX responder and non-responder elderly-onset RA (EORA) patients. However, there are insufficient data on its effectiveness and long-term safety, although we have previously reported that a treat-to-target (T2T) strategy targeting low disease activity (LDA) is safe and effective in the prospective CRANE cohort study of MTX-naïve EORA patients [1, 2].

Objectives: To identify factors predicting failure to achieve LDA by month 6 in EORA patients starting MTX, and effectiveness and safety of MTX over 5 years in MTX responders and non-responders.

Methods: MTX-naïve patients (mean age 73.8 years, n=163) from the CRANE cohort [2] had started MTX with moderate-to-high disease activity. Maximum dose of MTX was 0.19±0.06 mg/week/kg with folate supplementation. Treatment was adjusted to target LDA. Treatment intensification using biological disease-modifying antirheumatic drugs (bDMARDs) for EULAR-unresponsive patients by month 3 and moderate-high disease activity at month 6 was applied. MTX non-responsiveness was defined as no LDA and/or initiation of bDMARDs by month 6. Primary outcomes were achievement of Simplified disease activity index (SDAI) LDA and discontinuation of MTX due to adverse events (AEs). Secondly outcomes were achievement of remission and Health Assessment Questionnaire Disability Index (HAQ-DI) ≤0.5, and incidence of serious AEs.

Results: At week 24, 77 (47.2%) patients achieved LDA without bDMARDs (MTX responders), and of the remaining 86 (MTX non-responders), 35 (21.5%) had started bDMARDs by month 6 and 51 (31.3%) had moderate-to-high disease activity on MTX at week 24. At baseline, MTX non-responders had longer disease duration, higher SDAI and HAQ-DI, higher prevalence of erosion score ≥2 (modified total sharp score) and chronic lung disease (CLD), but baseline glucocorticoid use was similar. Multivariable analysis identified CLD as a predictor of MTX non-responsiveness. Regarding long-term outcomes, 14 (18.2%) of the 77 MTX responders and 55 (64%) of the 86 MTX non-responders received intensified treatment with bDMARDs within 5 years. MTX was continued in 65 (94.2%) of the 69 patients at the start of bDMARDs. The Cumulative rate of MTX discontinuation due to AEs was similar in MTX responders and non-responders (34.0% and 33.1%) as was the time to discontinuation of MTX due to AEs. The time to discontinuation of MTX for any reason was also similar. SDAI LDA and HAQ-DI ≤0.5 achievement by year 5 applying the last observation carried forward (LOCF) method was 92.2% and 74.0% respectively for MTX responders and 77.9% and 53.5% for MTX non-responders, respectively (p=0.011 for SDAI LDA and 0.007 for HAQ-DI). SDAI remission at year 5 by LOCF was similar (62.6% and 52.3% in MTX responders-vs-non responders). The time to serious AEs was also similar, as was the cumulative incidence of serious AEs over the 5 years was 32.6% and 44.3% in MTX responders-vs-non-responders.

Conclusion: CLD was a predictive factor of non-achievement of LDA by month 6 in EORA patients starting MTX, and early application of bDMARDs may be adequate for treating EORA with CLD at baseline. The 5-year long-term outcome for MTX responders was excellent, and continuation of MTX was tolerable even in MTX non-responders. Treatment intensification on MTX could be an optimal T2T strategy for EORA.

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AB0220 THE ASSOCIATION BETWEEN LAUGHTER AND FRAILTY IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM THE FAIRY STUDY

Keywords: Rheumatoid arthritis, Patient reported outcomes

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Background: In the treatment of rheumatoid arthritis (RA), advances in drug therapy have led to better control of disease activity. However, RA is a systemic chronic inflammatory disease that causes frailty, a fragile state of mind and body. It is important for RA patients, who are prone to physical anxiety due to poor disease control and frailty, to be able to smile and live their lives. While there is anxiety about the disease, daily laughter may be helpful in resolving anxiety and preventing frailty. Although there have been reports on laughter and health, there are no reports on RA and laughter, so we decided to conduct a new study on laughter.

Objectives: The purpose of this study was to investigate the association between disease activity, laughter, and frailty in RA patients.

Methods: Data were obtained from participants in the Fairy study (The prospective cohort study of frailty in patients with rheumatoid arthritis to extend healthy life expectancy), a prospective cohort study of frailty in RA patients at Nagoya University Hospital. A frailty questionnaire was administered to 243 RA patients from February 2021 to January 2022. Patients' subjective assessments of Kihon checklist for frailty (KCL), the 25-question Geriatric Locomotive Function Scale (GLFS-25), Health Assessment Questionnaire Disability Index (HAQ-DI), Beck Depression Inventory-II (BDI-II), and frequency of laughter were investigated using a self-administered questionnaire. The frequency of laughter was divided into four levels: " "Almost every day", "1-5 days per week", "1-3 days per month" and "Never or almost never" [2], and the association with each item was analyzed by analysis of variance. The frequency of laughter was divided into two groups: "Almost every day, 1-5 days per week" and "1-3 days per month, never or almost never", and multivariate logistic analysis was conducted to examine factors affecting laughter.

Results: Mean age (± standard deviation) was 64.5±10.4 years at baseline, 85.6% were female, duration of disease was 13.1±9.9 years, disease activity score (DAS28)-CRP was 1.92±0.84, KCL was 4.7±3.7, GLFS-25 was 15.1±13.6, HAQ-DI was 0.37±0.51, and BDI-II was 10.7±8.0. Regarding drug therapy, 67.9% of the patients used Methotrexate and 23.0% used glucocorticoid. The frequency of laughter was "Almost every day" (43%), "1-5 days per week" (40%), "1-3 days per month" (11%), and "Never or almost never" (6%). The DAS28-CRP was 1.89/1.87/2.15/1.81 (P=0.487), KCL score was 3.5/4.6/7.3/8.1 (P<0.001), GLFS-25 was 13/15/22/21 (P=0.003), HAQ-DI 0.30/0.38/0.55/0.48 (P=0.105), and BDI-II 8.4/10.9/15.1/16.5 (P<0.001) for "Almost every day", "1-5 days per week", "1-3 days per month", and "Never or almost never", respectively. Multivariate analysis showed that KCL score (Odds Ratio [OR]: 0.81, 95% confidence interval [CI]: 0.73-0.90), GLFS-25 (OR: 0.97, 95% CI: 0.94-0.99) and BDI-II (OR: 0.91, 95% CI: 0.86-0.95) were independently associated with laughter frequency (Table 1).

Conclusion: We found that frailty was associated with laughter in RA patients with controlled disease activity. Evaluation of laughter as a patient-reported outcome (PRO) may be novel as a positive indicator for patients themselves. Interventions not only for disease activity but also for frailty may lead to a life with laughter.

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Table 1 Factors associated with the frequency of laughter in patients with rheumatoid arthritis

	Model 1	Model 2	Model 3	Model 4
Age	0.98 (0.94–1.02)	0.97 (0.93–1.01)	0.96 (0.93–1.01)	0.96 (0.92–1.01)
Female	1.90 (0.67–5.40)	1.69 (0.62–4.60)	1.43 (0.53–3.85)	2.01 (0.71–5.71)
Disease duration	1.01 (0.97–1.05)	1.01 (0.97–1.05)	1.02 (0.98–1.06)	1.01 (0.96–1.05)
BMI	0.99 (0.90–1.10)	0.99 (0.90–1.10)	0.99 (0.90–1.10)	0.99 (0.89–1.11)
DAS28–CRP	0.93 (0.58–1.47)	0.95 (0.60–1.50)	0.86 (0.55–1.32)	0.83 (0.53–1.31)
KCL	**0.81 (0.73–0.90)**			
GLFS–25		**0.97 (0.94–0.99)**		
HAQ–DI			0.63 (0.30–1.32)	
BDI–Ⅱ				**0.91 (0.86–0.95)**

BMI: Body mass index; DAS28: disease activity score with 28 joint counts; CRP: C-reactive protein; KCL: Kihon checklist for frailty; GLFS-25: the 25-question Geriatric Locomotive Function Scale; HAQ-DI: Health Assessment Questionnaire-Disability Index; BDI-II: Beck Depression Inventory-II.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0221 A STUDY OF REVERSIBILITY OF FRAILTY IN RHEUMATOID ARTHRITIS FROM THE T-FLAG STUDY

Keywords: Patient reported outcomes, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a systemic chronic inflammatory disease that causes joint symptoms due to inflammation in bones and joints, leading to physical dysfunction such as loss of activities of daily living. With advances in the treatment of RA, it has become possible to achieve the goal of treatment to a state in which joint destruction causes little deformity and no physical disability. However, RA is a disease that causes not only physical dysfunction but also generalized fatigue due to chronic inflammation. Therefore, there is a decrease in patient satisfaction due to pain and physical fatigue, which may lead to a decline in daily life. Frailty, a state of physical and mental frailty due to decreased physical and mental function and social connectedness, is a condition that can easily lead to functional disability in daily living and the outcome of requiring long-term care [1]. RA is known to cause pain and limited range of motion of joints as the disease activity worsens, which may contribute to frailty. Since frailty is reversible and patients can return to a healthy state with appropriate interventions [2], it is expected that appropriate interventions will help maintain and improve the functions of daily living.

Objectives: The purpose of this study was to investigate factors associated with improvement from frailty in RA patients.

Methods: Of 460 RA patients (a observational study, T-FLAG study) who completed a questionnaire on frailty including the Kihon Checklist (KCL) from June 2020 to August 2022, 321 patients who were Frailty/Pre-frailty at baseline were included. After 2 years, patients who had improved from frailty to pre-frailty/robust or pre-frailty to robust were included in the improvement group, and the other patients were included in the non-improvement group. Multivariate analysis was used to examine the factors associated with improvement at 2 years. The cutoff values of the factors related to improvement were calculated by ROC analysis.

Results: Mean age (± standard deviation) was 67±13 years at baseline, 76% were female, duration of disease was 12±10 years, and BMI was 22.1±4.0. There were 83 patients (25.9%) in the improvement group. There were significant differences in age at baseline (63 vs. 68 years), DAS28-ESR (2.57 vs. 3.06), HAQ-DI (0.19 vs. 0.65), and KCL score (7.0 vs. 8.7) in the improvement group vs. the non-improvement group. There was no significant difference in gender (76% vs. 77%), disease duration (10 vs. 12 years) and BMI (21.8 vs. 22.3 years). Multivariate analysis revealed that age (OR: 0.97, 95% CI: 0.95-0.99) and HAQ-DI (OR: 0.19, 95% CI: 0.08-0.42) were independent factors associated with improvement (Table 1). The age and HAQ-DI cutoff values related to improvement were 72 years (sensitivity 73.5%, specificity 44.1%) and 0.25 points (sensitivity 78.3%,

specificity 58.9%). The cutoff value of HAQ-DI was used to examine the rate of improvement group in the two groups. In the HAQ-DI≤0.25 group, 40.1% of patients were in the improvement group, while only 11.5% were in the improvement group in the HAQ-DI>0.25 group, indicating a significant difference between the two groups (P<0.001).

Conclusion: Age and HAQ-DI were found to be indices for improvement in RA patients. Since frailty is a state in which physical and mental vitality declines with age, it is important to know age, which is a reversible state of frailty. In addition, among the multifactorial components of frailty, a low HAQ-DI, an assessment of physical function, may indicate the possibility of improving from a frailty state with appropriate intervention.

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Table 1. Factors associated with improvement from frailty/pre-frailty.

	OR	95% CI	P values
Age	0.97	0.95–0.99	0.014
Female	0.90	0.45–1.79	0.760
BMI	0.96	0.89–1.04	0.318
Disease duration	0.99	0.97–1.04	0.975
DAS28-ESR	0.92	0.69–1.22	0.556
MTX use	1.40	0.74–2.63	0.301
tDMARDs use	0.90	0.50–1.64	0.734
Glucocorticoid use	0.51	0.26–1.01	0.053
HAQ-DI	0.19	0.08–0.42	<0.001

BMI: Body mass index; DAS28: disease activity score with 28 joint counts; ESR: erythrocyte sedimentation rate; MTX: methotrexate; tDMARDs; targeted disease-modifying antirheumatic drugs; HAQ-DI: Health Assessment Questionnaire-Disability Index.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0222 PICTORIAL REPRESENTATION OF ILLNESS AND SELF-MEASURE (PRISM): A VISUAL TOOL TO ASSESS THE BURDEN OF RHEUMATOID ARTHRITIS

Keywords: Patient reported outcomes, Rheumatoid arthritis, Quality of life

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Background: Rheumatoid arthritis (RA) has a negative impact on patients' quality of life, with both physical and psychosocial impact. Treatment recommendations advocate a treat-to-target (T2T) approach with the ideal goal of remission. Composite clinimetric scores are available to assess and monitor disease activity; however, although now widely recognized as an important aspect, the patients' perceived burden of disease still remains not regularly checked during medical consultation in daily practice. Pictorial Representation of Illness and Self Measure (PRISM) was developed to measure this global suffering but, to our knowledge, not yet used in RA patients.

Objectives: To understand the relationships and correspondences between common clinimetric indexes and patients' perception of RA impact on daily life measured by PRISM.

Methods: The present single-center explorative study included 86 RA patients, consecutively evaluated between July and December 2022 at our Rheumatoid Arthritis Clinic. During routinely scheduled follow up visits, disease activity, organ damage, treatment changes, and a number of clinimetric indices were regularly recorded. Patients were also asked to complete the basic PRISM. The physician showed patients a blank sheet with a yellow circle in a corner and they were asked to imagine the sheet as their "life" at the moment, while the yellow circle as "themselves." Next, patients were asked to imagine another smaller as RA and were asked the question: "Where would you place the RA-red circle in your life now?" The distance between both circles (SIS) reflects the patient's burden of suffering. A higher SIS indicates a lower burden. A blue circle has been used as an example before testing. Statistical tests produced regression R2 values and Pearson correlation coefficients.

Results: PRISM proved to correlate very well particularly with the Rheumatoid Arthritis Impact of Disease (RAID) score (p = -0,6), patient's global assessment (PtGA) (p = -0,59), patient's pain (p = -0,52) and global health (p = -0,52) but no correlation was observed with swollen joint count or tender joint count. PRISM also correlates to composite clinimetric indexes exploring disease activity but to a lesser extent, while it revealed no correlation with inflammatory indexes such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).

Conclusion: Our investigation showed significant correlation with subjective patient reported outcome (PRO) tool, not counting inflammatory indexes nor joint count. To a lesser extent, it correlates also with physician's global assessment (PhGA). PRISM strongly correlates with RAID questionnaire, which is one of the most valid tool to measure the impact of RA in different domains (pain, function, fatigue, sleep disturbance, emotional well-being, physical well-being and coping). PRISM may therefore represent a reliable new, easy, more intuitive and friendly approach to quantify each individual perceived burden of disease. It may serve as complementary to common disease activity measures in setting agreed personalized therapeutic targets. Patients who were asked for a degree of approval with the test showed satisfaction with the possibility of visually showing the degree of suffering caused by their disease. To the best of our knowledge, this is the larger cohort of RA patients described in literature tested with PRISM. A prospective validation study in RA is now ongoing.

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VARIABLES	Pearson
DAS28 - PRISM	-0,43
RAID - PRISM	-0,61
SDAI - PRISM	-0,43
CDAI - PRISM	-0,46
PhGA - PRISM	-0,40
PtGA - PRISM	-0,59
CRP - PRISM	0,03
ESR - PRISM	0,03
PAIN - PRISM	-0,52
GH - PRISM	-0,52
HAQ - PRISM	-0,48
RF/ACPA+ - PRISM	0,10
Female - PRISM	-0,32
Disability - PRISM	-0,09
SJC - PRISM	-0,13
TJC - PRISM	-0,26

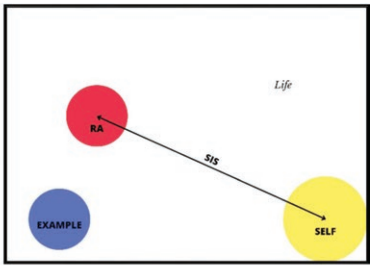


Figure 1.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0223 ADHERENCE TO TREAT-TO-TARGET APPROACH IN A RHEUMATOID ARTHRITIS COHORT: RETROSPECTIVE ANALYSIS FROM 3 YEARS OF REAL-LIFE EXPERIENCE IN A REFRACTORY CLINIC

Keywords: Treat to target, Rheumatoid arthritis, bDMARD

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Background: The European Alliance of Associations for Rheumatology (EULAR) advocates a "treat-to-target" (T2T) strategy for rheumatoid arthritis (RA) management, consisting in adjusting therapy if target is not achieved at 6 months. However, patients with moderate disease activity (MDA) currently constitute the most

common RA patient subset in clinical practice, possibly leading to refractory RA, defined as resistance to multiple drugs with different mechanisms of action and persistence of physical symptoms and/or high disease activity (HDA). Real-life studies examining the impact of switching/swapping versus not switching/swapping therapies in RA active patients are still limited.

Objectives: To evaluate predictors of therapy switch/swap in a population of patients with refractory RA who already failed ≥ 1 biological/targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD), not reaching predefined target at 6-months after starting subsequent lines of DMARDs.

Methods: This single-center study retrospectively included 117 patients evaluated at our Clinic from 2019 to 2022. During subsequent 3- and 6-months T2T visits, disease activity through 28-joint disease activity score (DAS28), organ damage, treatment changes and composite disease activity indices were recorded. Chi square and Fisher's exact test was used for comparison of dichotomous variables and oneway analysis of variance (ANOVA) for continuous variables. Threshold of statistical significance was defined as a p-value < 0.05.

Results: 66 patients (56.4%) did not achieve remission or low-disease activity target 6 months after starting b/tsDMARD; among them, 47/66 (71.2%) were in MDA, 11/66 (16.6%) in HDA and 8/66 (12.1%) were lost at follow up. 24/66 patients (36.4%) switched/swapped therapy at 6-months follow up. Longer disease duration correlated with treatment continuation (p=0.04). HDA at 6-months was a strong predictor of treatment change (p=0.009), as well as drug suspension for all reasons (e.g., safety issues, lack of therapeutic efficacy reported in medical records; p < 0.001). Major results from ANOVA are summarized in Figure 1: Evaluator's Global Assessment (EGA) at 6-months significantly correlated with treatment switch (p=0.007), while patients taking drugs from more time tend to be switched less frequently (p=0.01). Remarkably, we did not find any correlation between the variations of DAS28, Global Health (GH), swollen joint count (SJC), tender joint count (TJC), Health Assessment Questionnaire (HAQ), Visual Analogue Scale (VAS) for Pain, steroid dependence. Similarly, baseline erosions, seropositivity, or number of prior DMARDs did not influence the outcome.

Conclusion: In our retrospective cohort study, drug switching seems not linked to a more severe disease. Examining disease activity indexes, neither baseline data nor PROs, but only 6-months EGA, appears statistically significant. While a number of explanations might be offered, including limitations of the current RA measurement tools, such as DAS28, and the limited sample size, our findings are concerning, suggesting that probably, in real-practice, a sort of physician "general impression" rather than objective findings of disease activity still guide therapeutic switching.

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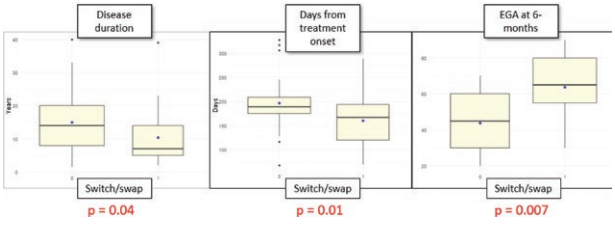


Figure 1. Boxplots proportional to class variability and averages (blue dots) between RA patients not at target at 6-months who switched/swapped therapy, and those not switching/swapping. In the x-axis, 0 means no therapy switch/swap, and 1 stands for therapy switch/swap.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0224

CORONARY CALCIUM, CAROTID SUBCLINICAL ATHEROSCLEROSIS AND CAROTID STIFFNESS AS PREDICTORS OF ALL-CAUSE MORTALITY AND CARDIOVASCULAR EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A 10-YEAR PROSPECTIVE FOLLOW-UP STUDY.

Keywords: Cardiovascular disease, Rheumatoid arthritis, Prognostic factors

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Background: The risk of mortality is increased in patients with RA compared to the general population. Different non-invasive surrogate markers of atherosclerosis have been implemented to identify RA patients who are at high risk of cardiovascular (CV) disease.

Objectives: In the present study, we aimed to establish the predictive capacity of the following surrogate markers: Coronary calcium (CAC), carotid ultrasonography (US), and pulse wave velocity (PWV) to predict CV events and all-cause mortality in a cohort of RA patients prospectively followed.

Methods: We conducted a prospective longitudinal study that included 126 patients with RA. The patients were recruited in 2011 and followed-up for 10 years. All patients had undergone baseline CAC score, evaluation of subclinical carotid atherosclerosis by US, and PWV. Multivariate Cox regression analysis was performed to identify the predictive ability of these surrogate markers for CV events and all-cause mortality.

Results: After a follow-up of 14.479 person (p)/months (m), 15 deaths (incidence rate -IR- 0.001 p/m) and 24 CV events (IR 0.001 p/m) in 18 RA patients were recorded. The causes of mortality in decreasing order of frequency were infections 7 (47%, IR 0.012 p/m), malignancies 5 (33%, IR 0.011 p/m) and others 3 (20%). To our surprise, none of the recorded deaths was from CV causes. The main results of the study are summarized in **Table 1**. After multivariate analysis, CAC score was associated with a significantly increased risk of CV events. When the CAC score was stratified into different categories, CAC>400 showed an increased risk of CV events on univariate analysis. However, this association was lost after adjustment. Carotid plaque and intima media thickness and PWV did not show a significant association with CV events. Regarding any-cause of death, CAC score, carotid plaque and PWV showed an association with higher risk of mortality. However, they were lost after adjustment for traditional CV risk factors.

Conclusion: Infections and malignancies were the most common cause of mortality in RA after a 10-year prospective follow-up study. CAC score, but neither carotid plaque nor PW, was significantly associated with increased risk of CV events at 10 years.

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Table 1. Cox regression analysis hazard ratios for death of any cause and cardiovascular events of non-invasive surrogate markers of atherosclerosis.

	Death of any cause					Cardiovascular event				
	Hazard ratio, (95% confidence interval), p									
	Univariate			Multivariate		Univariate			Multivariate	
CAC										
CAC, Agatson units	1.00	0.99-1.00	0.25			**1.002**	**1.0008-1.003**	**0.001**	**1.002 (1.0004-1.003)**	**0.011**
log CAC, Agatson units	1.10	0.78-1.55	0.59			**1.81**	**1.20-2.75**	**0.005**	**1.91 (1.15-3.17)**	**0.012**
CAC Categ										
0	ref.			ref.		ref.			ref.	
1-100	2.47	0.64-0.58	0.19	0.78 (0.16-3.75)	0.76	1.31	0.40-4.28	0.66	0.77 (0.21-2.84)	0.69
101-400	2.21	0.37-13.22	0.39	0.83 (0.12-5.66)	0.85	1.34	0.26-6.93	0.72	0.72 (0.13-4.13)	0.71
>400	**5.13**	**1.03-25.41**	**0.045**	1.55 (0.23-10.45)	0.65	**5.71**	**1.64-19.82**	**0.006**	2.23 (0.45-11.03)	0.32
Carotid ultrasond										
IMT, mm	**15.40**	**1.09-218.12**	**0.043**	3.81 (0.14-102.69)	0.43	4.54	0.34-61.53	0.26		
IMT > 0.9 mm.	2.77	0.95-8.11	0.063	1.51 (0.47-4.83)	0.48	1.67	0.55-5.06	0.37		
Carotid plaque	2.83	0.64-12.53	0.17	1.18 (0.24-5.71)	0.84	2.34	0.68-8.09	0.18	1.16 (0.31-4.44)	0.82
Carotid stiffness										
PWV, m/s	**1.29**	**1.08-1.52**	**0.004**	1.18 (0.96-1.44)	0.12	1.14	0.99-1.31	0.078	1.04 (0.85-1.26)	0.73
PWV > 10 m/s	**3.19**	**1.11-9.20**	**0.032**	2.29 (0.69-7.63)	0.18	1.90	0.67-5.40	0.23		

CAC: coronary calcium, IMT: intima media thickness, PWV: pulse wave velocity. Multivariate analysis is adjusted for age, smoking, hypertension, diabetes mellitus, dyslipidemia and body mass index.

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Disclosure of Interests: Cristina Corrales-Selaya: None declared, Nuria Vegas-Revenga: None declared, Jose Antonio Parra Blanco: None declared, Virginia Portilla: None declared, Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Lilly, Bristol-Myers, Janssen, Galapagos and MSD, Consultant of: Abbvie, Pfizer, Roche, Lilly, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD, Novartis and Roche, Miguel A González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi, Lilly, Amgen, and MSD., Grant/research support from: Abbvie, MSD, Jansen, and Roche, Iván Ferraz-Amaro Speakers bureau: Abbott, Pfizer, Roche, Sanofi, Celgene and MSD, Grant/research support from: Abbott, MSD, Jansen and Roche, Alfonso Corrales: None declared.
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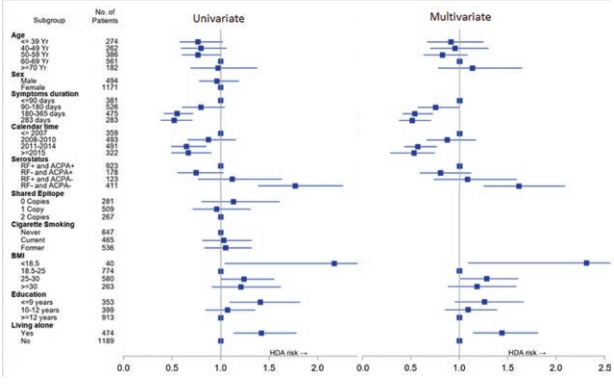
AB0225 WHAT FACTORS INFLUENCE RA PRESENTATION AT DIAGNOSIS?

Keywords: Rheumatoid arthritis, Prognostic factors, Epidemiology

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Background: Researchers have mostly focused in understanding which factors influence the risk of rheumatoid arthritis (RA) and its progression. However, little is known on the determinants of disease presentation at diagnosis. This is a fundamental prerequisite for studies focusing in understanding disease progression.
Objectives: To estimate the association between demographic and disease related factors and high disease activity (HDA) of RA at diagnosis by a rheumatologist.
Methods: Data from newly diagnosed RA patients between October 2004 and May 2018 from the Epidemiological Investigation of RA study (EIRA) will be included in these analyses. The outcome of interest is high disease activity, defined as having either DAS28 ESR >5.1 or DAS28 CRP>4.6. Patients without an HDA evaluation at baseline (defined as recorded in a visit between 40 days before and 75 days after EIRA inclusion) have been excluded from the analyses. Odds ratios (ORs) and their 95% confidence intervals (CIs) of HDA were estimated through a mixed model with region as random intercept, to account for between regions variations. The association between each of the factors and HDA was first evaluated with a univariate model. Then, only factors with a significant association were included in the multivariable model. Missing values were excluded in the univariate analyses, but included as separated category in the multivariable analysis.
Results: A total of 1665 patients were included in this study, of which 995 (60%) had HDA at diagnosis. In the univariate analyses, young age at diagnosis (50-59 years: OR=0.76 (0.59-1.00)), longer symptoms duration (>365 days: OR= 0.51 (0.37-0.7)), and diagnosis in more recent years (≥2015: OR= 0.66 (0.48-0.9)) were inversely associated with HDA, while being underweight (BMI <18.5: OR= 2.17 (1.04-4.51)), low education (≤9 years: OR= 1.41 (1.09-1.82)), living alone (OR= 1.42 (1.13-1.78)) and being seronegative (OR=1.78 (1.39-2.28)) had higher odds of HDA. Sex, shared epitope, and cigarette smoking were not associated with HDA at diagnosis. In the multivariable analyses, age and education were no longer associated with HDA.
Conclusion: In this study we observed that sex, symptoms duration, calendar time, living alone, serostatus were associated with high disease activity at diagnosis, while age, sex, education, shared epitope, and cigarette smoking were not.

Figure 1. Univariate (on the left) and multivariable (on the right) odds ratio of high disease activity. Abbreviations: BMI=body mass index, RF=rheumatoid factor, ACPA= anti-citrullinated protein antibody



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Disclosure of Interests: Daniela Di Giuseppe: None declared, Johan Askling Grant/research support from: Agreements between Karolinska Institutet (with JA as PI) and Abbvie, BMS, Eli Lilly, Galapagos, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, mainly for the national safety monitoring of rheumatology immunomodulators in Sweden (ARTIS), Helga Westerlind: None declared.
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AB0226 PREDICTORS OF RESPONSE AFTER CESSATION OF JAKI THERAPY IN PATIENTS WITH RA

Keywords: bDMARD, Rheumatoid arthritis, Remission

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Background: In a previous study based on data from the Belgian register "Tool for Administrative Reimbursement Drug Information Sharing" (TARDIS)[1], IL6 inhibitors showed a better clinical response after JAKi cessation compared to other b/tsDMARDs. However, considerable baseline differences in demographic and clinical variables, and previous exposure to advanced therapies were found between treatment groups, which could have influenced our results.
Objectives: We aimed to find predictors of short-term response after cessation of JAKi therapy in patients with RA.
Methods: Patients were selected from TARDIS for this analysis if they had stopped JAKi therapy and initiated a subsequent therapy between register inception and December 2021. Patients were grouped per subsequent therapy: TNFi, Abatacept, IL6 inhibition or JAKi. Rituximab was excluded as patients are reimbursed on RA flare in Belgium. Linear and logistic regression models were constructed to establish predictors of clinical response. DAS28 change between baseline and first follow-up, DAS28 remission (DAS28<2.6) and DAS28 low disease activity (LDA, DAS28≤3.2) at first follow-up were taken as dependent variables. Following variables were inserted in the models: age, disease duration, b/tsDMARD naive, treatment group and baseline values for HAQ, swollen/tender joint count, PGA, ESR, and CRP. Final models included only variables reaching statistical significance of 0.05 (by backwards elimination).
Results: In total, 193 RA patients, who had stopped JAKi therapy and had complete baseline and follow-up data, could be included. Table 1 shows baseline demographic and clinical characteristics. TNFi, Abatacept, IL6 inhibition or JAKi therapy was initiated in 33% (63/193), 11% (20/193), 18% (34/193) and 39% (76/193) of patients respectively. Remission and LDA were reached in 42% (81/193) and 63% (122/193) of patients respectively. Common predictors for achieving remission and LDA were baseline HAQ and not receiving abatacept (Figure 1). Variables positively associated with a higher DAS28 change were baseline PGA (Relative Risk (RR) 0.02 (0.01, 0.03)), TJC (0.06 (0.01, 0.12), SJC (RR 0.10 (0.03, 0.16)) and CRP (RR 0.02(0.01, 0.03)), while baseline HAQ (RR -0.60 (-0.88, -0.31) and not receiving abatacept (RR -0.70 (-1.25, -0.15)) were negatively correlated with DAS28 change in the adjusted multivariate linear regression model.

Table 1. Patient characteristics at the start of next treatment after failing the first JAKi therapy

	Total population
Number	193
Age (mean ±SD, years)	57 ±13
Disease duration (mean ±SD, years)	10 ±8
ESR (mean ±SD, mm/hour)	24 ±18
CRP (mean ±SD, mg/L)	11 ±18
SJC28 (mean ±SD)	6 ±5
TJC28 (mean ±SD)	8 ±5
DAS28 (mean ±SD, years)	4.6 ±1.1
HAQ-DI (mean ±SD, 0-3)*	1.3 ±0.7
PGA (mean ±SD, 0-100)	64 ±20
Used JAKi as first line advanced therapy	76/193 (39%)

Legend: Number given are mean ± SD or number, proportion. TNFi = tumour necrosis factor inhibitor, JAKi = Janus Kinase inhibitor, HAQ= health assessment questionnaire, PGA= Patient Global assessment; CRP= C-reactive protein; ESR= erythrocyte sedimentation rate; TJC= tender joint count; SJC= Swollen joint Count; DAS28 = disease activity score based on the 28joints. *Missing HAQ(0-3) scores were imputed by regression using age and HAQ(0-60) scores, the sum of the scores (0-3) on all (20) individual HAQ questions.

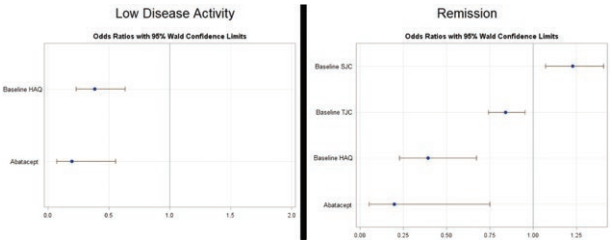


Figure 1. Predictors of remission or LDA

Conclusion: This explorative analysis reveals that after adjustment, patients who have worse functionality and receive abatacept compared to other b/ts DMARD show worse clinical outcomes in the short-term. This treatment effect should be further explored, but caution is warranted as the sample size was relatively small and indication bias cannot be excluded.

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Acknowledgements: on behalf of the Royal Belgian Society for Rheumatology.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.3713

AB0227 EARLY RHEUMATOID ARTHRITIS DIAGNOSIS: PRIMARY CARE PHYSICIAN'S PERSPECTIVE AND NEEDS

Keywords: Education, Rheumatoid arthritis

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Background: Primary care physicians (PCPs) play a crucial role in early recognition and rapid referral of patients with inflammatory arthritis to improve early management and patient outcomes. However, there is limited information on perceived barriers for referral and areas of improvement [1]. The purpose of this study is to explore the perspective and needs of PCPs to guide a specialist's referral program.

Objectives: To explore the perspective and needs of primary care physicians (PCPs) to guide a specialist's referral program at an academic rheumatology center in Madrid and to identify areas of improvement to facilitate early referral for early rheumatoid arthritis.

Methods: A PCPs-rheumatology early referral program (REUCARE) has been initiated at our area in January 2022 with 257 PCPs participating. Up to May 2022, 88 patients have been referred, however only 24 (27%) fulfil inclusion criteria. In order to improve the referral strategy, a survey has been developed in collaboration with primary care investigators to explore areas of improvement. The survey included 5 domains covering: PCPs demographics, previous knowledge about RA, level of confidence, factors and potential barriers influencing referral and interest on rheumatological training. Data were captured using four-point Likert scales, yes/no question or free text, and were analyzed descriptively.

Results: E-mail invitations were sent to 257 PCPs through their primary care center coordinator and completed by 26 (10% response rate). More respondents were women (76%) in practice for over more than 20 years who reported having 30-40 patients per day and only 1-5 patients diagnosed of RA in the last year. The majority (83%) reported additional rheumatological training besides medical school, however they were no familiar with the incidence and prevalence of the disease. Around 67% were aware of the importance of early diagnosis and treatment, however they felt not very confident making the initial diagnostic (61% "somehow confident" and 35% "not confident"). Main reasons for referral were clinical presentation (65%), positive rheumatoid factor (46%) and elevation of acute phase reactants (46%). Most PCPs considered the waiting time for rheumatology prolonged (65%) and very prolonged (22%) and reported insufficient feedback information from rheumatologists (60%). Main reasons for delay from PCPs perspective were nonspecific initial symptoms of the disease (48%) followed by rheumatology long waiting list (39%) (Figure 1).

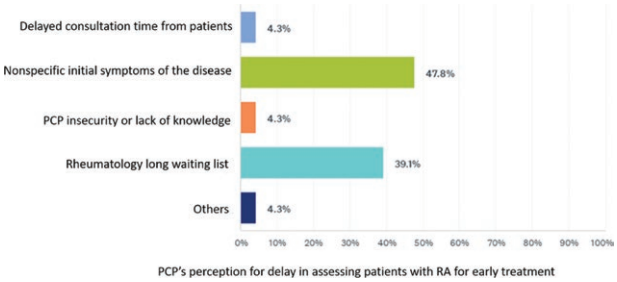


Figure 1.

Although 77% indicated using additional resources to improve their knowledge in RA, all participants stated that they would be interested in receiving more information on early diagnosis, being the preferred resources a specific e-consult (87%), updated mini guidelines (78%) and face-to face meetings with rheumatologists.

Conclusion: Most PCPs are aware of the importance of early diagnosis and management of RA but feel uncomfortable making the initial diagnosis. Non-specific initial symptoms and long waiting lists for rheumatology are the main reasons for delay from PCPs perspective. Resources to improve referral, including e-consult and specific guidelines, are in need as part of the actual referral program.

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Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.4013

AB0228 UTILITY OF SERUM KL-6 IN PATIENTS WITH STABLE OR SLOWLY DECLINING LUNG FUNCTION IN RA-ILD

Keywords: Rheumatoid arthritis, Lungs, Biomarkers

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Background: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). Previously, we stratified the patients with rheumatoid arthritis-associated interstitial lung disease (RA-ILD) into four distinctive groups according to their change of percent predicted forced vital capacity using trajectory analysis: persistently improving, stable, slowly declining, and rapidly declining.[1] Till October 2020, a total of twelve patients died, of which eight patients died even though they belonged to either stable or slowly declining groups. Therefore, it advantages additional biomarkers benefits to anticipate poor prognosis.

Objectives: To analyze whether serum Kreb von den Lungen 6 (KL-6) predicts mortality among patients with stable or slowly declining % FVC pred. trajectory group.

Methods: The Korean RA-ILD (KORAIL) cohort is the prospective observational cohort. Patients diagnosed with RA based on either 1987 or 2020 ACR criteria and with ILD based on CT scans had been recruited from six tertiary medical hospitals in Korea from January 2015 to July 2018 and followed for 3 years. Pulmonary function tests and chest CT scans were conducted annually. Serum KL-6 level at enrollment was measured by Nanopia KL-6 assay (SEKISUI, Japan). The cut-off value of KL-6 was referenced in the previous report.[2] Kaplan-Meier Log-rank tests and Cox proportional hazard analysis were conducted using SPSS statistics 21.0.

Results: Among patients with stable (n=68) and slowly declining (n=54) lung function groups, three and five patients died, respectively. The mean age of the stable disease group was statistically significantly higher than that of the slowly declining group (64.9±7.7 vs 67.9±6.8-year-old, p=0.03). There was no significant difference between groups in the proportion of males (n=21 vs 19, p=0.70) or ever-smokers (76.1% vs 66.7%, p=0.31), and the mean duration of RA or ILD (RA duration 8.6±8.8 vs 6.7±7.1 years, p=0.21; ILD duration 3.2±3.6 years vs 2.5±2.9 years, p=0.25). Serum KL-6 levels at baseline were comparable between groups (636.3±454.6 U/mL vs 590.6±547.3 U/mL, p=0.62). The hazard ratio for death in the KL-6>1000 U/mL compared with the KL-6 group≤1000U/mL was 3.77 (95% confidence interval, 0.90-15.8, p=0.07) in an unadjusted model and 4.05 (95% CI, 0.68-24.2, p=0.13) in a model adjusted for age, sex, history of smoking (Figure 1).

Conclusion: In RA-ILD, patients with serum KL-6 levels>1000U/mL at baseline tend to have 3.8 times as high mortality as those with serum KL-6 levels≤1000U/mL, although not statistically significant. The current study result implies that serum KL-6 level can be a useful tool to predict poor prognosis even in the case when the lung function of patients is stable or slowly declining.

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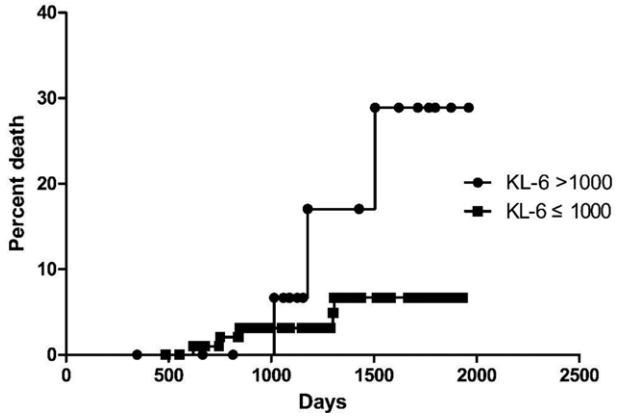


Figure 1. Kaplan-Meier estimates of death stratified by serum KL-6 levels.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4624

AB0229

TREAT TO TARGET IN RHEUMATOID ARTHRITIS DID NOT SHOW RACIAL DIFFERENCES: COHORT REAL STUDY

Keywords: Rheumatoid arthritis, Real-world evidence, Treat to target

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Background: Rheumatoid arthritis (RA) is defined as a systemic autoimmune pathology associated with a chronic inflammatory process, which can damage joints and extra-articular organs. The target of therapy is to obtain remission and to reduce side effects [1].

Objectives: Analyze racial differences in the context of RA, from an epidemiological, disease activity, diagnosis and treatment standpoint.

Methods: This work is part of a Brazilian multicentric study called REAL-Rheumatoid Arthritis in Real Life in Brazil, which is a prospective observational cohort study of patients with RA from 11 public healthcare centers in different geographic regions of Brazil that are specialized in RA management. For the present article, a cross-sectional cohort was analyzed (2), which included 754 patients who classified themselves as caucasian or Afro-Latin Americans. Others ethnicities were excluded.

Results: We enrolled 754 patients, 83.8% were caucasians and 16.2% were Afro-Latin Americans. In the caucasians group 88.4% were female and in the Afro-Latin Americans group 92.6% were female. The mean age was 63.4 years in the caucasians group versus 61.7 years in the Afro-Latin Americans (p = 0.137). The mean years of schooling was 8.28 among caucasians and 7.87 among Afro-Latin Americans (p = 0.341). There was no statistically significative difference in relation to social class between the groups (p = 0.266). 55.5% among the caucasians and 56.7% among the Afro-Latin Americans had erosive disease (p = 0.822). The average time between beginning of symptoms and diagnosis in the caucasians group were 28.1 months and in the Afro-Latin Americans were 33.3 months (p = 0.123), the average time between beginning of symptoms and beginning of treatment were 33.1 months among the caucasians and 42.2 months among the Afro-Latin Americans (p = 0.115). The CDAI mean in the caucasians group was 11.8 and in the Afro-Latin Americans group was 13.7 (p = 0.179). The following tests were applied: SF-12 (Medical Outcomes Study Short Form 12), presenting an average in the physical component of 36.7 among the caucasians and of 36 among the Afro-Latin Americans (p=0.253) and in the mental component of 44.4 and 48.4 respectively (p< 0.001); SF-6D (Short-Form 6 Dimensions – Brazil), that verified a mean of 0.373 between the caucasians and 0.357 between the Afro-Latin Americans (p=0.292). Current medications in use were described in Table 1.

Conclusion: Health disparity has multiple consequences and represent differences in health outcomes between different ethnicities, for example. Working toward health equity in society is fundamental to provide excelente care for all groups, as demonstrated in our study, which did not evidenced statisticallt significant diferences in most of the characteristics of RA between caucasians and Afro-Latin Americans, this may demonstrate that there is no difference between diagnosis, indications and disease control betwee races. It is important to highlight that Brazil is a country with a racial multiplicity that can be a limiting factor for this type of analysis and the lack of undestanding of the epidemiology of RA by race and ethinicity limits our understanding about the disease.

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Table 1. Disease Modifying Anti-rheumatic Drugs (DMARDS)

DMARDS	Caucasians	Afro-Latin Americans	p
Corticosteroids	44.7%	51.6%	0.159
Methotrexate	68.6%	58.2	0.026
Leflunomide	34.1%	27.9%	0.179
Hydroxychloroquine	10.1%	12.3%	0.470
Cyclosporine	0.6%	0	1.000
Azathioprine	0.9%	1.6%	0.622
Sulfasalazine	4.3%	7.4%	0,140
Tofacitinib	1.1%	0	0.606
Infliximab	3.9%	4.1%	0.939
Etanercept	5.5%	8.2%	0.254
Certolizumab	1.4%	0.8%	1.000
Adalimumab	5.2%	5.7%	0.813
Golimumab	2.7%	4.1%	0.396
Tocilizumab	5.5%	4.1%	0.518
Abatacept	6%	7.4%	0.565
Rituximab	5.7%	4.9%	0.734

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5184

AB0230 **IS IT POSSIBLE TO STOP TAKING GLUCOCORTICOIDS IN RHEUMATOID ARTHRITIS WHILE USING THE SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS?**

Keywords: Rheumatoid arthritis

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Objectives: to investigate the possibility of withdrawing glucocorticoids (GC) or reducing their dose to the target (<7.5 mg/d in terms of prednisone) when using traditional synthetic disease-modifying antirheumatic drugs (DMARD) in patients (pts) with rheumatoid arthritis (RA); to study independent prognostic factors that affect the continuation of taking GC.
Methods: 270 patients with RA (women - 86.6%) aged 51.2 ± 0.71 years, with a disease duration of 50.2 ± 3.82 months were examined. Rheumatoid factor (RF) was found in 64.8% of individuals, antibodies to cyclic citrullinated peptide (ACCP) - in 66.6%. DMARD therapy included methotrexate (n = 91), leflunomide (n = 95), sulfasalazine (n = 51), hydroxychloroquine (n = 3) or its combination (n = 126). Statistical analysis was performed using program SPSS 22.0. Certainty disagreements average values were estimated using non-parametric of the Mann-Whitney criterion for quantitative signs and criteria χ^2 for frequency indicators. To identify prognostic markers that affect the possibility of canceling GC, the method of logistic regression analysis was used with the calculation of the risk ratio (RR) and 95% confidence interval (95%CI). In order to identify the decisive factor affecting the possibility of achieving the target dose of GC, a stepwise logistic regression analysis of multivariate models was performed. The difference was considered probable at p<0.05.
Results: During 3 years of study, GC was canceled in 33% of pts in the period from 3 to 30 months (mostly in the first 6 mth). Among those who continued to take GC, the target dose (<7.5 mg/d) was achieved only in 32.6% of pts. Among pts continuously receiving GC, compared with pts who discontinued GC, there were probably more women (89.5% vs. 80.8%, p<0.05), ACCP-positive pts (88.4% vs. 55.0%, p<0.01), with higher DAS (ESR) values (5.29 ± 0.1 vs 4.84 ± 0.15, p<0.05) and more pronounced structural changes on the SHS scale (43.4 ± 2.42 vs 32.4 ± 2.71, p<0.05). According to the logistic regression analysis, the risk of continuing GC treatment was probably associated with female gender (RR 2.39 (1,09–4,97)), elderly pts (RR 1.02 (1,001–1,04)), ACCP-positivity (RR 3.73 (1,26–11,0)), disease activity by DAS (ESR) (RR 1,19 (1,0–1,43)) and structural joint changes (RR 1,01 (1,005–1,02)). Only the initial dose of GC ≥ 7.5 mg/d was associated with the inability to reach the target dose of GC during the entire follow-up period (RR 6.32 (2,0–19,5)).
Conclusion: Despite of the treatment with traditional synthetic DMARD, only a third of RA pts can cancel GC, mainly in the first 6 months. For the pts who continue taking GC, the target dose can be achieved in 33% of them. Independent predictors of the impossibility of GC discontinuation are female gender, old age, ACCP-positivity, higher RA activity according to DAS (ESR) and more pronounced joint destruction at the initial stage. A negative prognostic factor in achieving the target dose of GC is their initial dose ≥ 7.5 mg/d.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5999

AB0231 **COMPARISON OF THE CLINICAL IMPLICATIONS AMONG SIX DIFFERENT NUTRITIONAL AND INFLAMMATORY INDICES IN PATIENTS WITH RHEUMATOID ARTHRITIS**

Keywords: Rheumatoid arthritis

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Background: The most commonly used disease activity index in rheumatoid arthritis (RA) is Disease Activity Score 28 (DAS28). However, the need for objective disease activity indices retains. The nutritional and inflammatory indices were recently evaluated in many rheumatologic and non-rheumatic conditions as predictors of disease activity.
Objectives: We aimed to evaluate the association of six different nutritional and inflammatory indices with disease activity and patient reported outcomes (PROs) in patients with RA.
Methods: In this cross-sectional study, we recruited RA patients who fulfilled the 2010 ACR/EULAR classification criteria. Participants' demographic features, disease duration, current medication, disease activity indices [DAS28 with erythrocyte sedimentation rate (DAS28-ESR), simplified disease activity index (SDAI), clinical disease activity index (CDAI)], PROs [Health Assessment Questionnaire-Disability Index (HAQ-DI), Rheumatoid arthritis Impact of Disease (RAID)], Multimorbidity Index (MMI), hand and foot erosions, deformities, extra-articular manifestations of RA, nutritional and inflammatory status [prognostic nutritional index (PNI), controlling nutritional status (CONUT) score, neutrophil/lymphocyte ratio (NLR), monocyte/lymphocyte ratio (MLR), platelet/lymphocyte ratio (PLR), systemic inflammation response index (SIRI), Mini Nutritional Assessment-Short Form (MNA-SF), body mass index (BMI), waist and hip circumference] were noted. Patients were divided into 2 groups (remission and low disease activity vs. moderate and high disease activity) according to their DAS28-ESR scores.
Results: A total of 183 RA patients were analyzed. The mean age was 29.5±5.7 years, the median time of disease duration was 120 (60-238) months, 83.1% (n=152) were female, 69.9% were RF positive (n=128), 59% (n=108) were anti-CCP positive, 79.1% (n=145) were on conventional synthetic disease-modifying antirheumatic drugs (csDMARD), 5.5% (n=10) used targeted synthetic DMARD (tsDMARD), 16.4% (n=30) were used biologic DMARD (bDMARD). Median PNI values were lower in patients with extra-articular involvement (p<0.001). Mean PNI values were lower in patients with hematologic involvement, anemia, and thrombocytopenia (p<0.001, p=0.026, p=0.033), those with erosion on the foot X-ray (p=0.005), and CCP positive ones (p=0.028). NLR and SIRI were positively correlated with physician's global assessment (PGA) score (r=0.270, p<0.001; r=0.227, p=0.002), SDAI (r=0.219, p=0.003; r=0.199, p=0.007), CDAI (r=0.192, p=0.009; r=0.154, p=0.037), DAS28-ESH (r=0.232, p=0.002; r=0.186, p=0.012), ESR (r=0.233, p=0.001; r=0.218, p=0.003) and c-reactive protein (r=0.324, p<0.001; r=0.380, p<0.001). MNA-SF was negatively correlated with HAQ-DI (r=-0.199, p=0.007), RAID (r=-0.179, p=0.015), PGA score (r=-0.280, p<0.001), SDAI (r=-0.205, p=0.005), CDAI (r=-0.224, p=0.002), and DAS28-ESH (r=-0.186, p=0.012). PNI was not correlated with disease activity scores and PROs.
Conclusion: In this study where we aimed to determine the role of a variety of nutritional inflammatory indices in disease activity ascertainment of RA patients, while NLR, MNA-SF, and SIRI had significant associations with other composite disease activity indices, PNI failed to establish such a relationship. However, PNI was significantly higher in CCP-positive RA patients and ones with extraarticular involvement. Prospective longitudinal studies on larger samples are needed to elucidate the role of nutritional inflammatory indices in determining RA disease activity.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6070

AB0232 **COMPARATIVE FUNCTIONAL ABILITY OF PATIENTS WITH RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS AFTER TOTAL KNEE ARTHROPLASTY**

Keywords: Osteoarthritis, Rheumatoid arthritis

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Background: Patients with rheumatoid arthritis (RA) often require adequate disease control prior to total knee arthroplasty (TKA). At the same time, they may have worse outcomes and late complications compared to osteoarthritis (OA) patients.
Objectives: To study the functional abilities of RA patients undergoing TKA compared to OA patients using the KSS scoring system.
Methods: The study included 150 patients: 69 patients (46%) with RA and 81 patients (54%) with OA. 32% of them were males and 68% were females. Th average age of patients with RA was 59.0 [52; 64] years, while in OA group – 66.0 [61; 73] years. Among patients with RA, 60.9% had moderately active diseases and 23.2% had highly active disease prior to intervention. All patients underwent cemented TKA. All of them also completed KSS score prior to surgery, immediately after that and 3 and 12 months after the discharge. Statistical analysis was performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). A p value of less than 0.05 was considered statistically significant.
Results: Prior to intervention patients with RA had significantly lower KSS scores compared to OA patients (45.0 [40; 55] versus 60.0 [50; 60], p=0.00, Mann-Whitney). After the surgery KSS became comparable between the two groups (83.0 [74; 84] versus 82.0 [80.5; 85], p=0.754, Mann-Whitney). 3 months

after the intervention RA patients had significantly higher KSS scores than prior to surgery (Mdn=88.0, n=69 versus Mdn=40.0, n=69, z=-7.23, p=0.00) or at discharge (Mdn=88.0, n=69 versus Mdn=83.0, n=69, z=-7.25, p=0.00, Wilcoxon test). The same trend was observed for KSS completed 12 months after the surgery (Mdn=93.0, n=69 versus Mdn=88.0 in KSS 3 months after the surgery, n=69, z=-7.26, p=0.00). At the same time, the results of KSS were comparable between RA and OA groups 3 and 12 months after the intervention (88.0 [88; 88] in RA group versus 88.0 [87; 89] in OA group, p=0.772, Mann-Whitney; 94.0 [93; 95] in RA group versus 94.0 [93;95] in OA group, p=0.702, Mann-Whitney, respectively).

Conclusion: The functional abilities of patient with RA after TKA did not differ from those among OA patients regardless of diseases activity despite, despite the fact that among RA patients KSS scores were significantly lower prior to surgery. KSS scores of RA patients improved 3 and 12 months after the intervention and were comparable to OA group.

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AB0233 ONE YEAR RESPONSE AND ASSOCIATED FACTORS FOR REMISSION AND LOW ACTIVITY DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE MEXICAN BIOLOGICS REGISTRY

Keywords: Registries, bDMARD, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is the most common autoimmune disease. Clinical remission is the main therapeutic target for patients with RA, with low disease activity (LDA) as a best possible alternative[1].

Objectives: Evaluate clinical response of patients with RA treated with biologic (bDMARDs) and the associated factors for remission and low activity disease at the first year of treatment.

Methods: BIOBADAMEX is a Mexican ongoing cohort of patients using bDMARDs since 2016. In this analysis we included all patients with diagnosis of RA with at least two assessments, baseline and at one year of follow up. Clinical response was measured by DAS-28 score and factors associated with having a remission or low disease activity vs moderate/high activity were estimated using univariable and multivariable logistic regression analysis adjusting by potential confounders, such as age, gender, disease duration.

Results: A total of 336 RA patients were included in this analysis. At baseline 68 (20%) and after one year of follow 171 (50.1%) were in remission or low activity disease. Mean baseline disease duration was 8.8 years. Table 1 shows baseline characteristics by groups. Baseline steroid treatment and previous biologic treatment were the only factors associated with less probability of being in remission/low disease activity at one year in our cohort. In multivariable analysis adjusted by age, gender, disease duration, these two factors were no longer associated with remission/low disease activity (p=0.055 and p=0.14, respectively).

Conclusion: In our registry baseline steroid treatment and previous biologic treatment were the only factors associated with less probability of being in remission/low disease activity at one year on biologic treatment, however these factors did not remain significant associated after adjusted analysis. Follow up and inclusion of more participants is going on and will allow us to perform further analyses.

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Table 1. Baseline characteristics

Baseline characteristics of patients with RA by groups

	Remission/low disease activity at one year n =171 (51)	Moderate/high activity at one year n =165 (49)	**Univariable Analysis OR(95%CI)**
Age, median(IQR)	51.8 (44.4-58.4)	54.5 (45.7-60.4)	0.9 (0.9-1.0)
Female, n(%)	156 (91.2)	151 (91.5)	0.9 (0.4-2.0)
Body Mass Index, median (IQR)	27.1 (23.9-30.8)	27.3 (24.0-29.9)	0.9 (0.9-1.0)
Obesity, n(%)	52 (30.4)	41 (24.9)	1.3 (0.8-2.1)
Disease duration (years), median (RIC)	8.5 (4.8-15.0)	10.1 (4.5-16.5)	0.9 (0.9-1.0)
Rheumatoid factor, n(%)	131 (76.6)	111 (67.3)	1.6 (0.9-2.6)
ACPA, n(%)	26 (15.2)	24 (14.5)	1.0 (0.6-1.9)
DAS-28, median (IQR)	4.5 (3.1-5.4)	5.2 (4.1-6)	0.7 (0.6-0.9)
Comorbidities, n(%)	84 (49.1)	87 (52.7)	0.8 (0.5-1.3)
Number of comorbidities, median (IQR)	2 (1-3)	2 (1-3)	0.9 (0.7-1.1)
cDMARD use, n(%)	143 (83.6)	131 (79.4)	1.3 (0.8-2.3)
Steroids, n(%):	47 (27.5)	62 (37.6)	**0.6 (0.3-0.9)**
Steroids dose, median (RIC)	5 (5-6)	5 (5-10)	0.9 (0.9-1.0)
bDMARD previous use, n(%)	77 (45.0)	92 (55.8)	**0.6 (0.4-0.9)**
Abatacept	29 (16.9)	42 (25.4)	1.0 (0.9-1.1)
Tocilizumab	39 (22.8)	43 (26.1)	
Adalimumab	30 (17.5)	23 (13.9)	
Certolizumab	28 (16.4)	16 (9.7)	
Etanercept (originator)	10 (5.8)	4 (2.4)	
Etanercept (biosimilar)	10 (5.8)	6 (3.6)	
Golimumab	7 (4.1)	5 (3.0)	
Infliximab (originator)	6 (3.6)	1 (0.6)	
Rituximab (originator)	11 (6.4)	17 (10.3)	
Tofacitinib	5 (2.9)	3 (1.8)	
Baricitinib	1 (0.6)	0	

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AB0234 PROGNOSTIC POTENTIAL OF EXOSOMES (EX) AS IMMUNOMODULATORS IN SYNOVIAL FLUID (SF) IN RHEUMATOID ARTHRITIS (RA)

Keywords: Synovium, Rheumatoid arthritis

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Background: Secretory EX various biological fluids, including synovial, – key mediators of intercellular communication, regulating the body's immune responses, information transfer, vesicular transport, etc. Penetrating into cells, EX can cause a cascade of changes in them at the genomic and epigenomic levels.

Table 1. The level of some endonucleases, tetraspanins and chaperones in normal (D) and in RA SF

EX	DNA-ase (acid)	DNA-ase (alk.)	RNA-ase (acid)	RNA-ase (alk.)	CD9	CD81	Hsp70	Hsp90
D	0,08± 0,01	0,45±0,03	0,18 ±0,04	0,89±0,21	935±97	697±68	9,8±2,3	6,4±1,5
RA	4,4± 0,7***	0,17± 0,02*	5,4 ±0,3***	0,47 ±0,08*	2987 ± 237**	893±76*	21,3± 3,7**	8,9±2,3*

* - p <0.05; ** - p <0.01; *** - p <0.001

Objectives: The aim of the study was to assess the degree of expression of exosomal membrane proteins and endonucleases from SF in RA.
Methods: SF of knee joints of 10 patients with RA with active synovitis and 7 conditional donors postmortem (D) were researched. EX was isolated by ultrafiltration and double ultracentrifugation (105 g).EX was identified by transmission electron microscopy and flow cytometry. The expression level of tetraspanins (CD9, CD81) and chaperones (Hsp70, Hsp90) was determined (conv. units) by flow cytofluorimetry and by immunoblotting, respectively. The activity of endonucleases of EX (units/ml) was carried out spectrophotometrically.
Results: In RA, there is a pronounced expression of transmembrane markers of exosomes: tetraspanins CD9 and CD81 (on the surface of exosomes) and chaperones Hsp70 and Hsp90 (obligate internal components). The levels of major tetraspanins CD9 and Hsp70 were significantly increased (by 3.2 and 2.2 times, respectively). Functional groups of proteins such as acidic and alkaline endonucleases show multidirectional changes in EX with RA: a sharp increase in the activity of acidic DNA-as and RNA-as (by 55-30 times) and a 2-3-fold decrease in the activity of alkaline analogues (Table 1). It is obvious that the shift of the pH of SF at RA (on average, from 7.75 units in normal to 7.21 – at RA) noted by many authors, affects the implementation of exosomal secretion of proteins and nucleic acids, which disrupts the immunomodulatory intercellular signaling.
Conclusion: EX-secretion of proteins and nucleic acids in RA can be not only a fundamental way of intercellular communication, but also an immunomodulatory factor of etiopathogenetic significance. EX obtained from SF have potential prognostic value in the study of immunocomplex pathologies.
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Disclosure of Interests: None Declared.
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AB0235 ANALYSIS OF FACTORS AFFECTING FATIGUE IN PATIENTS WITH RHEUMATOID ARTHRITIS - TOMORROW STUDY-

Keywords: Patient reported outcomes, Rheumatoid arthritis, Quality of life

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Background: Great advances have been made in the treatment of rheumatoid arthritis (RA), and remission has become a viable target. However, some patients complain of fatigue even in remission.
Objectives: The purpose of this study was to investigate whether RA patients are more likely to experience fatigue than the general population, and to clarify the factors involved in the formation of fatigue.
Methods: We analyzed data from the TOMORROW study (UMIN000003876) study, which is a 10-years prospective cohort consisting of age and sex matched RA patients (n=208) and volunteers (Vo) (n=205). We conducted a QOL survey using SF-36 in 2019. Fatigue was assessed using the vitality component (VT) of the SF-36. First, each scale of SF-36 was compared between RA patients and Vo, and the effects of RA on fatigue and QOL were evaluated by multiple liner regression analysis. Next, we limited the target to RA patients and tried to identify the factors involved in fatigue. We included anthropometric measurements parameters, disease activity score 28-erythrocyte sedimentation rate (DAS28-ESR), RA medication (methotrexate (MTX) dose, prednisolone dose, use of biologic disease modifying anti-rheumatic-drugs (bDMARDs)), tender joint count, swelling joint count, VAS and modified Health Assessment Questionnaire (mHAQ) as candidate factors.
Results: Subjects were 186 Vo and 167 RA patients in 2019. In RA, average age was 65.8 ± 12.7 year, 143 patients (85.6%) were female, average disease duration was 13.8 ± 11.8 year and DAS28-ESR was 3.10 ± 1.45. Compared with Vo, Physical Component Summary (PCS) (Vo 46.9 ± 12.2, RA 34.1 ± 18.0: p<0.01), Mental Component Summary (MCS) (Vo 52.2 ± 9.5, RA 49.4 ± 9.5: p<0.01) and VT (Vo 50.5 ± 10.1, RA 44.0 ± 10.8: p<0.01) were significantly lower in RA patients. In multiple liner regression analysis, RA was a significant decreasing factor of PCS (β -12.8, 95%CI -15.7 - -9.89: p<0.01), MCS (β -2.75, 95%CI -4.68 - -0.82: p<0.01) and VT (β -3.01, 95%CI -4.57- -1.45: p<0.01). In RA patients, multiple liner regression analysis shows that VAS (β -0.06, 95%CI -0.12 - -0.00: p=0.03), ESR (β -0.09, 95%CI -0.16 - -0.02: p=0.02), and mental health component of the SF-36(MH) (β 0.55, 95%CI 0.42 – 0.68: p<0.01), were significant affecting factor for VT. (Table 1)
Conclusion: In this study, RA was a significant QOL declining factor. High VAS score, high ESR values and low mental health score were associated with fatigue in patients with RA.

Table 1. Summary of multiple liner regression analysis for fatigue (vitality score of SF-36) in patients with rheumatoid arthritis.

	β	95% Confidence interval	P value
Age	0.19	0.07-0.30	<0.01
BMI	-0.19	-0.54-0.16	0.28
Female	-0.05	-3.67-3.57	0.98
Tender joint count	-0.06	-0.32-0.19	0.63
Swelling joint count	0.12	-0.40-0.65	0.65
VAS	-0.06	-0.12-0.00	0.03
mHAQ	-0.56	-3.05-1.92	0.65
ACPA positive	-0.92	-4.66-2.82	0.63
CRP	0.21	-0.42-0.85	0.51
ESR	-0.09	-0.16--0.02	0.02
Dose of MTX (mg/week)	-0.03	-0.30-0.23	0.8
Dose of PSL (mg/day)	-0.54	-1.22-0.14	0.12
bDMARDs use			
non	ref	-	-
anti-TNF	-0.9	-3.74-1.94	0.53
non anti-TNF	-2.56	-6.44-1.32	0.19
MH score	0.55	0.42-0.68	<0.01

BMI, body mass index; ACPA, Anti-cyclic citrullinated peptide antibody; MTX, methotrexate; PSL, prednisolone; bDMARDs, biologic disease modified anti-rheumatic-drugs; prednisolone; MS, mental health component of the SF-36.

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AB0236 THE HAPTOGLOBIN 2-2 GENOTYPE IS ASSOCIATED WITH INCREASED RISK OF CARDIOVASCULAR DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A CASE-CONTROL STUDY

Keywords: Rheumatoid arthritis, Cardiovascular disease

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Background: Traditional risk factors do not fully explain the increased risk of cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA). [1] The Hp2-2 genotype is known to confer a lower anti-oxidant and higher inflammation effect when compared to the non Hp2-2 genotype. [2]
Objectives: This study aims to investigate the association of Hp genotype with CVD in patients with RA.
Methods: Sixty-nine with CVD cases and 207 gender and ethnicity matched control (without CVD) with allocation of 1:3, were retrieved from the Tan Tock Seng Hospital RA registry from 1 Jan 2000 to 31 Dec 2020. Hp genotype was determined using TaqMan-based real-time polymerase chain reaction (PCR). CVD was examined against demographics, clinical and laboratory variables in univariate models. Associations between Hp genotypes and CVD were analyzed using conditional logistic regression. All analysis was done using Stata version 16.1.
Results: The prevalence of Hp2-2 genotype was: Group 1 (CVD group): Chinese: 29/57, 50.9%, Indian: 5/5, 100%, and Malay 2/7, 28.6%; Group 2 (Control group): Chinese 80/171, 46.8%, Indian: 10/15, 66.7%, and Malay 11/21, 52.4%). CVD was significantly associated with age, disease duration, disease activity score 28 (DAS28), diabetes, hypertension, hyperlipidemia, Hp 2-2 allele, rheumatoid factor, cyclic citrullinated peptide (CCP), cumulative dose of prednisolone and methotrexate. Hp 2-2 genotype significantly associated with CVD outcomes in the logistic regression model adjusting for age, smoking status, DAS28, diabetes, hypertension, hyperlipidemia, and CCP (adjusted matched odds ratio: 1.13 (95% CI: 1.01 – 1.27); p = 0.033).
Conclusion: The Hp 2-2 genotype is associated with an increased risk of CVD in patients with RA in the Singapore multi-ethnic Asian cohort. Further epidemiological and mechanistic studies are warranted to understand the role of the Hp-genotype in rheumatoid arthritis.
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AB0237 EFFECTS OF ONE-YEAR TOFACITINIB THERAPY ON ANGIOGENIC BIOMARKERS IN RHEUMATOID ARTHRITIS

Keywords: Biomarkers, Rheumatoid arthritis, Targeted synthetic drugs

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Background: Rheumatoid arthritis (RA) has been associated with increased angiogenesis and the production of angiogenic factors. Targeted therapies may attenuate angiogenic molecule production.
Objectives: We wished to determine how the Janus kinase (JAK) inhibitor tofacitinib influences the production of various angiogenic mediators including growth factors, cytokines, chemokines, adhesion molecules and others. We correlated these biomarkers with ultrasound-based vascular pathophysiology and ^{18}F-FDG-PET-CT.
Methods: Thirty RA patients with active disease were treated with either 5 mg bid or 10 mg bid tofacitinib and evaluated at baseline and after 6 and 12 months. We assessed numerous angiogenic mediators including VEGF, bFGF, EGF, PIGF, TNF-α, IL-6, cathepsin K (cathK), angiopoetins (Ang1, Ang2), PECAM-1 (CD31), CXCL8/IL-8, galectin 3 and NT-proBNP. For comparisons, we determined DAS28, CRP, IgM rheumatoid factor (RF) and anti-cyclic citrullinated peptide (aCCP) levels. We assessed brachial artery flow-mediated vasodilation (FMD), carotid intima-media thickness (IMT) and pulse-wave velocity (PWV) by ultrasound. We also performed simultaneous PET-CT assessment of joints and vessels.
Results: Twenty-six patients completed the study. Tofacitinib treatment significantly decreased VEGF (p=0.019), PIGF (p=0.019), IL-6 (p=0.001), cathK (p=0.04) and galectin 3 levels (p=0.013) after 12 months of treatment. Seropositive patients had increased bFGF, PIGF and NT-proBNP levels (p<0.05). Uni- and multivariable regression analysis indicated variable correlations of baseline and 12-month TNF-α, IL-6, bFGF, PIGF, NT-proBNP and PECAM-1 with IMT, as well as synovial and vascular inflammation as determined by PET-CT (p<0.005).
Conclusion: Tofacitinib suppressed the production of multiple angiogenic biomarkers. Number of these biomarkers are involved in carotid atherosclerosis, as well as synovial and vascular inflammation.
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AB0238 USEFULNESS OF RAPID3 IN ASSESSING UNMET NEEDS OF RHEUMATOID ARTHRITIS PATIENTS FROM THE T-FLAG STUDY

Keywords: Patient reported outcomes, Rheumatoid arthritis

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Background: Routine Assessment of Patient Index Data 3 (RAPID3) is a patient-reported outcome (PRO) that can be used to assess the condition of rheumatoid arthritis (RA) patients using only a questionnaire that can be completed in a short time. It is useful as a simple method for assessing disease activity. In previous reports, RAPID3 could be used as an assessment similar to Disease Activity Score 28 (DAS28), a common disease activity assessment [1]. However, in the treatment of RA, there are unmet needs in which patients have low satisfaction with treatment, even though they are in remission according to disease activity assessments such as DAS28. To investigate the cause of this discrepancy, we decided to conduct a study using RAPID3 as a subjective patient assessment and DAS28 as a general disease activity measure.
Objectives: The purpose of this study was to investigate the association between disease activity and RAPID3 in RA patients.
Methods: The data for this study were obtained from the Tsurumai-Frailty and Locomotive Syndrome of Rheumatoid Arthritis for Globalization (T-FLAG), a observational study involving three centers. A PRO questionnaire was administered to 467 RA patients between June 1 and August 31, 2020. Disease activity was assessed using the RAPID3, DAS28-CRP, DAS28-ESR, Clinical Disease Activity Index (CDAI), and Simplified disease activity index (SDAI). the RAPID3 (30 points total) consists of three domains: physical function (0-10), pain (Visual Analogue Scale 0-10), and Patient global assessment (PtGA) of disease activity (0-10). It consists of three domains, divided into disease activity categories (remission: ≤3, low disease activity: 3.1-6, moderate disease activity: 6.1-12, high disease activity: >12). PRO assessment was performed using PtGA, Health Assessment Questionnaire Disability Index (HAQ-DI), Kihon checklist (KCL),

and the 25-question Geriatric Locomotive Function Scale (GLFS-25). We compared the disease activity categories using DAS28-CRP and RAPID3.

Results: The mean age (± standard deviation) was 66±13, female was 73%, disease duration was 11±10, RAPID3 was 5.6±5.7, DAS28-CRP was 2.19±1.03, HAQ-DI was 0.46±0.66, and KCL was 6.6±4.4. RAPID3 and DAS28-CRP showed a strong correlation with a correlation coefficient of 0.743, and CDAI and SDAI as other disease activity assessment methods also showed a strong correlation (CDAI: r=0.883, SDAI: r=0.880). On the other hand, the HAQ-DI and GLFS-25, which are PRO assessments of physical function, showed strong correlations, but the KCL, which includes psycho-social assessments along with physical function assessments, showed a slightly weaker correlation (r=0.507). Morning stiffness was not correlated with RAPID3 (r=0.206). In the disease activity category, 59.5% of patients had RAPID3 and DAS28-CRP in the same category (RAPID3 = DAS28-CRP). In addition, RAPID3 belonged to the worse category than DAS28 in 31.3% of cases (RAPID3 > DAS28-CRP). The group with RAPID3 > DAS28-CRP (31.3%) vs. the group with RAPID3 = DAS28-CRP (59.5%) showed no significant differences in age, gender, and tender/swollen joint count (Table 1). On the other hand, there were significant differences between the two groups in disease duration (14 vs. 11 years), PtGA (36 vs. 14mm), HAQ-DI (0.84 vs. 0.29), KCL (8.5 vs. 5.8), and GLFS-25 (28 vs. 13).

Conclusion: In this study, we showed that the correlation between RAPID3 and disease activity assessment was quite strong. In the disease activity category, approximately 60% of all patients had similar DAS28-CRP and RAPID3. However, the discrepancy between DAS28-CRP and RAPID3 may be caused by physical dysfunction and frailty. Therefore, it is important to achieve clinical remission and improve PRO in RA treatment as an intervention to address unmet needs.

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Table1. Baseline characteristics of patients

	DAS28-CRP < RAPID3	DAS28-CRP = RAPID3	P value
N, %	146 (31.3)	278 (59.5)	
Age, year *	68 ± 14	66 ± 14	0.169
Female, % †	74	75	0.031
Disease duration, year *	14 ± 11	11 ± 9	< 0.01
RAPID3 *	9.6 ± 5.0	3.8 ± 5.2	< 0.01
DAS28-CRP *	2.27 ± 0.77	2.01 ± 1.11	0.014
CRP *	0.26 ± 0.50	0.36 ± 0.91	0.251
TJC *	1.5 ± 2.7	1.9 ± 4.1	0.304
SJC *	0.4 ± 1.4	0.6 ± 1.7	0.322
PtGA, mm *	36 ± 23	14 ± 21	< 0.01
PhGA, mm *	30 ± 21	12 ± 18	< 0.01
Pain VAS, mm *	37 ± 23	14 ± 22	< 0.01
HAQ-DI *	0.84 ± 0.79	0.29 ± 0.52	< 0.01
KCL *	8.5 ± 4.5	5.8 ± 4.1	< 0.01

RAPID3: Routine Assessment of Patient Index Data 3; DAS28: disease activity score with 28 joint counts; CRP: C-reactive protein; TJC: tenderness joint count; SJC: swollen joint count; PtGA: Patient global assessment; PhGA: Physician global assessment; VAS: Visual Analogue Scale; HAQ-DI: Health Assessment Questionnaire-Disability Index; KCL: Kihon checklist. * Student's t-test † Chi-squared test

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Disclosure of Interests: None Declared.

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AB0239 THE REDUCTION OF CIRCULATING LEVELS OF SERUM CALPROTECTIN IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ABATACEPT

Keywords: Biomarkers, bDMARD, Rheumatoid arthritis

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Background: The research of new biomarkers is still an unmet need in the field of rheumatoid arthritis (RA), especially for patients (pts) without rheumatoid factor and/or anti-citrullinated peptides positivity (seronegative RA), and for those without the elevation of inflammatory markers, such as the C-reactive protein (CRP) [1]. Calprotectin (CLP) is a heterodimeric complex of two calcium binding proteins which is expressed in granulocytes and monocytes. It mediates cell differentiation, activation, migration, apoptosis and the production of pro-inflammatory factors [2]. Recent studies showed that CLP synovial fluid levels are higher in RA pts and that its serum levels might directly reflect the synovitis severity [3]. Abatacept (ABA) was demonstrated to interfere with the migration of monocytes to the joint, reducing the expression of adhesion molecules via hampering actin dynamics [4]. No studies are available on the potential value of CLP as a biomarker of ABA treatment response in pts with RA.

Objectives: To analyse CLP levels in ABA treated RA pts.

Methods: Forty-three consecutive ABA treated RA pts [84% female, median age (1^{st}-3^{rd} quartile)=61 (52-68) years, 81% seropositive, DAS28-CRP=4.57 (3.95-5.27)] were enrolled. EULAR criteria were used to evaluate the response to the treatment after 6 months (T6). CLP serum levels (μg/ml) were measured at baseline (T0) and at T6, by a commercial kit (Quanta Flash Calprotectin assay, Werfen; cut-off value=4).

Results: At T0, RA pts showed increased CLP serum levels (65%) irrespective of their seropositivity (p=0.50) or the presence of elevated CRP (p=0.23). T0 CLP was not different comparing pts according to their response [good+moderate, 67% vs non-responders, 33%: 4.44 (2.68-7.64) vs 6.66 (4.80-8.71); p=0.33], even in pts with T0 normal CRP levels [5.8 (3.27-6.36) vs 4.54 (3.61-7.47); p=0.86]. CLP decreased after treatment with ABA (T0 vs T6) (4.98 (3.04-7.88) vs 3.24 (2.20-5.72); p=0.0049), both in responders [4.44 (2.68-7.64) vs 3.24 (1.90-5.64); p=0.034], and in non-responders (6.66 (4.80-8.71) vs 2.95 (2.18-4.30); p=0.039). CLP was not significantly correlated with CRP at T0 or at T6, nor with DAS28-CRP at T0, whereas a significant correlation was observed with DAS28-CRP at T6 (r=0.34; p=0.034). The T6-T0 variations of CLP and DAS28-CRP were not correlated (r=0.06; p=0.6919), even evaluating separately pts according to their response.

Conclusion: CLP serum levels are increased in RA pts, without differences in groups separated on the basis of their seropositive status or their CRP levels, confirming the potential role of CLP as a biomarker of RA [3, 5]. The correlation between CLP levels and the composite index at T6, but not with CRP levels, suggests a possible clinical value, independent from CRP [6]. Circulating levels of CLP, a myeloid-related protein, did not have a predictive value for the response to ABA, an agent mainly targeting lymphocytes [4].

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AB0240 RHEUMATOID ARTHRITIS CLINICAL ACTIVITY IS NOT ASSOCIATED TO CARDIOVASCULAR RISK AS MEASURED BY TRADITIONAL RISK SCALES

Keywords: Cardiovascular disease, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) patients have a higher cardiovascular risk (CVR) than the general population, being atherosclerotic cardiovascular disease the main cause of mortality [1]. Such increased could be explained by traditional CVR factors and chronic inflammatory state of disease. Clinical activity of disease, which is evaluated by DAS-28, is a parameter that denotes the current inflammatory status. [2]

Objectives: To compare CVR, by six scales: ACC/AHA ASCVD 2013, Framingham lipids and BMI, SCORE2, QRISK3 and Reynolds risk score, according to clinical activity of RA patients using DAS-28 CRP.

Methods: Descriptive, comparative and cross-sectional study. We enrolled RA patients between 40 and 75 years old who fulfilled ACR/EULAR 2010 classification criteria and recruited in the Rheumatology service from a tertiary care hospital, in Monterrey, Mexico. Patients were divided by time of disease evolution

Table 1. Demographic characteristics (n= 377)

Variable	Remisión (n= 121)	Low activity (n=51)	Moderate activity (n=156)	High activity (n=49)	p
Duration of disease, years. median (p25-p75)	7.0 (3.0-14.0)	7.9 (2.7-14.9)	7.0 (3.0-15.4)	5.1 (1.6-12.9)	NS
Women, (n)%	103 (85)	47 (92)	149 (95)	49 (100)	0.002
Age, years. median (p25-p75)	57 (49-62)	53 (48-63)	54 (48-59)	55 (45-58)	NS
BMI, kg/m2. median (p25-p75)	27.2 (25.0-30.4)	26.7 (24.7-30.8)	28.0 (24.6-31.8)	28.4 (24.7-32.3)	NS
Laboratory tests, median (p25-p75)					
CPR, mg/dL.	0.5 (0.2-0.9)	0.7 (0.3-1.4)	0.9 (0.4-1.6)	1.2 (0.6-2.9)	0.000
ESR, mm/H.	22.0 (15.0-32.5)	23.0 (16.0-41.0)	28.0 (18.0-42.0)	30.0 (18.0-56.0)	0.003
ACPA, U/mL.	99.8 (2.6-199.1)	23.2 (1.4-195.5)	44.9 (1.1-198.7)	7.6 (1.2-191.3)	NS
RF IgG, U/mL.	4.3 (2.0-12.2)	4.6 (2.0-11.5)	4.8 (2.0-16.0)	3.2 (2.0-9.9)	NS
RF IgM, U/mL.	200.0 (38.0-200.0)	200.0 (35.4-200.0)	200.0 (56.7-200.0)	160.1 (20.4-200.0)	NS
RF IgA, U/mL.	75.6 (11.3-200.0)	68.8 (7.0-200.0)	47.4 (6.6-197.1)	68.1 (2.8-200.0)	NS
Cardiovascular risk scores, %. median					
ASCVD	4.8	2.8	2.6	3.1	NS
FRS-Lipids	8.8	7.6	7.3	7.8	NS
FRS-BMI	12.5	11.1	9.3	11.1	NS
SCORE 2	6	4.5	4.5	4.5	NS
Q-RISK III	6.1	5.3	4.5	5.7	NS
RRS	1.5	1.5	1.5	1.5	NS

This table shows demographic and clinical characteristics. BMI Body Mass Index; CRP C Reactive Protein; ESR Erythrocyte Sedimentation Rate; ACPA Anti–Citrullinated Protein Antibody; RF Rheumatoid Factor; ASCVD Atheroesclerotic Cardiovascular Disease; FRS Framingham Risk Score; RRS Reynolds Risk Score; SCORE 2 Systematic Coronary Risk Evaluation 2.

into quartiles. CVR results from scales were multiplied by 1.5 factor according to EULAR 2016 recommendation. Normality was assesed by Kolmogorov-Smirnov test. Variables with a non-normal distribution were described by median and interquartile range (p25-p75). Differences between groups was analyzed by Kruskal-Wallis test or Chi-squared, accordingly.

Results: A total of 377 RA patients were included. Demographic characteristic are shown in Table 1. An increased in acute phase reactants, CRP (p= 0.000) and ESR (p= 0.003) was found, as severity of clinical activity increased, meanwhile CVR did not show significative changes, regardless of which of scales it was measured by.

Conclusion: CVR did not increase according to clinical activity of RA, which suggests that such severity can not explain by itself the increased in risk showed in this population.

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AB0241

PATIENTS WITH RHEUMATOID ARTHRITIS AND RHEUMATOLOGISTS AGED ≤ 40 YEARS HAVE DIFFERENT PRIORITIES AND PERSPECTIVES ON DISEASE MANAGEMENT: THE ITALIAN SOCIETY FOR RHEUMATOLOGY YOUNG (SIRYOUNG) COMMISSION SURVEY

Keywords: Remission, Rheumatoid arthritis, Health services research

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Background: Rheumatoid Arthritis (RA) represents a huge burden for patients' quality of life and there are still relevant unmet needs in its management due to uncovered patients' needs even once sustained remission is achieved.

Objectives: This study aimed to investigate disease burden, treatment priorities and preferences across disease phases comparing patients' and physicians' perspectives.

Methods: Consultants or residents in rheumatology (across Academic and non-academic hospitals) and patients with RA both aged ≤40 years were reached by an anonymous online survey between November 2021 and November 2022, designed by the SIRyoung commission. For each included RA patient, demographic and clinical parameters (RA diagnosis timing, current and previous treatments) were collected. For each included physician demographic, education and professional profile details were collected.

Results: Two-hundred seventy-four consultants or residents in rheumatology and 90 RA patients, both aged ≤40 years, completed the online survey. All Italian regions were equally represented for both physicians' and patients' subgroups. Considering the patients' disease referral status, 26(28.9%) received RA diagnosis at the very early stage (≤3 months), 33(36.7%) at early stage (3-12 months) and 31(34.4%) after 12 months from symptoms' onset. When asked for the priority in RA treatment objectives, the survey revealed a different priority among the subgroups with a higher importance given to fatigue resolution (p<0.0001) and morning stiffness reduction (p<0.0001) by patients and to radiological damage prevention (p=0.01) and disability reduction (p=0.0108) by physicians, while comparable priority was given by the 2 groups to pain relief, physical function restoration and work-ability recover (p>0.05 for all). When asked about the factors that could improve RA management, the survey revealed higher agreement scores for patients compared to physicians in educational need (p<0.0001), increase of outpatient visits and access to treatment (both p<0.0001) and use of digital apps (p<0.0001). Stratifying patients based on self-perceived disease control, 30(33.3%) were well controlled, 52(57.8%) moderately controlled and 8(8.9%) very poorly controlled. When questioned about their will to treatment modification once sustained remission status is achieved, patients showed a higher agreement of maintaining the treatment unchanged (p=0.0002) and a higher fear of modification consequences (p<0.0001) compared to physicians, mostly if not guided by the treating rheumatologist or out of established decisional algorithms.

Conclusion: Young patients with RA and young rheumatologists have variable agreements on treatment aims and priority. In particular, when dealing with the sustained remission status, a shared decisional algorithm between physicians and patients is needed to reduce patients fear and improve their empowerment.

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AB0242

IMPACT OF DISEASE ACTIVITY ON SLEEP DISORDERS IN RHEUMATHOID ARTHRITIS: A CROSS SECTIONAL STUDY ABOUT 100 PATIENTS

Keywords: Rheumatoid arthritis, Lifestyles

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Background: Rheumatoid arthritis (RA) is an inflammatory autoimmune disease, characterized by joint pain, joint swelling in period of active disease and poor sleep.
Objectives: The present study aims to evaluate the sleep disorders in RA patients and to determine their relationship with disease activity.
Methods: This is a cross sectional study including RA patients followed in the rheumatology department at TAHER SFAR university hospital in Mahdia. All patients were diagnosed with RA based on 2010ACR/EULAR criteria. For each patient, we evaluated the Epworth sleepiness scale (ESS) [0-24] and Pitsburg sleep score [0-21] with its 7components.
Results: We included 100 participants with a mean age of 53,2 ±11,2 years [21-76 years] in which most of them (89%) were female. The average duration of diseases was 11,1±8,9 years [1- 40 years]. The assessment of the RA activity showed a mean DAS28(ESR) and DAS28(CRP) of 3.88±1.19 [1-6.15] and 4.6 ±1.19 [1-6.15] respectively. Highly active RA (DAS 28 ≥ 5.1) was found in 34 patients. The mean Epworth score was 7,9±5,6 [0-24], 28 patients (28% of cases) had signs of daytime sleepiness (ESS ≥ 11 points). The mean Pittsburgh global score was 6.9± 5.1 [0-19]. 51 patients (51% of cases) had disturbed sleep (PSQI >5.5 points). Over half of participants (65.7%) rated the quality of sleep as very good or fairly good. 47.5 % of them were scored 0 for sleep duration; however, 17,2 % were sleeping fewer than five hours a night. 26 participants had long sleep latency (>1 hour). The average sleep efficiency score was 0.92 ±1.25 [0-3]; only 21 reported such complaints. The mean score for sleep disturbance was 1.19±0.86 [0-3] and for daytime dysfunction was 0.79 ± 1.05 [0-3]; however, half of them (55%) presented this complaint. 86,9% of patients have not used a sleeping medication. Statistical analysis showed that the Pittsburg score was associated with a severe activity stage(p=0.045). Furthermore, we did not found any relationship between ESS and the disease activity.
Conclusion: Sleep disorders are common among RA patients and were frequently associated with severe disease activity.
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AB0243 ASSOCIATION BETWEEN THE GERIATRIC NUTRITIONAL RISK INDEX (GNRI) AND THE DISEASE ACTIVITY IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Diet and nutrition, Rheumatoid arthritis, Prognostic factors

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Background: The Geriatric Nutritional Risk Index (GNRI) is a tool that assesses the risk of malnutrition-related complications in elderly patients. Some recent publications have suggested that the GNRI could predict disease activity in people followed for rheumatoid arthritis (RA) [1].
Objectives: Our aim was to evaluate the correlation between the GNRI and the disease activity in elderly RA patient.s.
Methods: This is a cross-sectional study including patients followed for RA and aged at least 65 years. The GNRI was calculated for all patients: *GNRI = [1.489*albumin (g/L)] + [41.7 *(weight/WLo)]*, where WLo means ideal weight and was calculated from the **Lorentz** equations: for men: H-100-[(H-150)/4]; for women: H-100-[(H-150)/2.5](H: height).
Results: We included 63 patients (52 women and 11 men). The mean age was 68.17±4.35 years. The median duration of disease progression was 11 years with an IQR of [4-16]. The mean DAS28 was 3.72±1.48. The mean HAQ was 1.6±0.58. The median value of GNRI was 116.47 with an IQR of [106.6-125.12] and extremes ranging from 70.06 to 145.02. According to the GNRI, 58 patients (92.1%) had a GNRI > 98 indicating no nutritional risk, 2 patients (3.2%) were low risk with GNRI between 92 and 98, no patient had a GNRI between 82 and 92 indicating moderate risk and 3 patients (4.8%) had a GNRI < 82 indicating a high risk of malnutrition-related complications. After statistical analysis, we found significant association between GNRI and DAS28 score (p=0.05). We also found a significant association between GNRI and higher ESR (p=0.03), CRP (p<0.001) and higher daily doses of corticosteroids (p=0.024). However, we did not found significant association between the GNRI and advanced age (0.11), duration of RA progression (p=0.07), VAS of pain (p=0.2) or with HAQ score (p=0.06).
Conclusion: Our results showed that the GNRI is associated with DAS28, inflammatory biomarkers and higher corticosteroid doses. The GNRI could be used as a simple and reliable tool to assess both nutritional status and disease activity in RA elderly patients.
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AB0244 ROLE OF FATIGUE IN DIFFICULT TO TREAT RHEUMATOID ARTHRITIS PATIENTS OUTCOME

Keywords: Rheumatoid arthritis, Quality of life, Mental health

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Background: In difficult to treat rheumatoid arthritis patients (D2T RA), a wide spectrum of factors may contribute to the persistence of signs and/or symptoms, although these are not always directly related to inflammation (eg, functional disability, pain and fatigue). Of these, fatigue is still the least evaluated and taken into account.
Objectives: To identify the role of fatigue in D2T RA.
Methods: Cross-sectional study. 143 patients patients followed up in the rheumatology outpatient clinic of Hospital Clínico San Carlos, Madrid, Spain were included. Data were collected between July 2018 and November 2022. All patients met the ACR/EULAR 2010 criteria and they were in treatment with Biological agents (anti-TNF and Non anti-TNF) or Targeted Synthetic DMARDs (jakinibs). D2T RA was defined based on EULAR criteria (treatment failure, signs suggestive of currently active/progressive disease, and management being perceived as problematic by the rheumatologist and/or patient). Main variable: Fatigue was assessed by the Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire (BRAF-MDQ). Covariables: Sociodemographic and disease-related variables. Statistical analysis. A descriptive and comparative analysis was carried out for the different variables. To identify factors independently associated to D2T RA a multivariable logistic regression was applied. Results were expressed as OR with their corresponding 95% CI. A value of $p < 0.05$ was consider as statistically significant.
Results: The study population comprised 143 patients and 22 (15.38%%) developed D2T RA. The D2T RA group were older, with a higher DAS28 and disability. Sociodemographic, clinical, disease-related variables, and the fatigue scores used in the study are shown in Table 1. In our final logistic regression model, age (OR: 1.05; p=0.017) and fatigue were independently associated with D2T RA (OR: 1.04; p=0.011).
Conclusion: Despite the absence of an explicit mention of fatigue in the definition of AR D2T, it appear to be a main factor explaining the D2T RA outcome. The evaluation and management of fatigue should be one of the objectives in the treatment of patients with RA.

Table 1. Characteristics of the sample

Variable	D2T RA (n=22)	Non D2T RA (n=121)	p
Age (years), mean (SD)	62.82 (13.45)	56.19 (11.89)	0.019
Women, n (%)	11 (50)	73 (60.83)	0.34
Disease duration, mean (SD), years	17.76 (8.47)	13.41(8.74)	0.03
Positive RF at baseline, n (%)	14 (63.60)	75 (63.02)	0.95
Positive ACPA at baseline, n (%)	14 (63.60)	77 (64.70)	0.90
DAS28, mean (SD)	4.10 (0.67)	2.46 (0.99)	0.00
CRP, mean (SD)	0.46 (0.36)	0.46 (0.67)	0.99
ESR, mean (SD)	15.86 (12.11)	9.87 (9.91)	0.01
PGHA (mm), mean (SD)	56.22 (24.91)	32.19 (23.88)	0.001
PhGHA (mm), mean (SD)	27.5 (13.34)	14.22 (11.37)	0.001
Pain VAS (mm), mean (SD)	54.45 (25.27)	32.38 (24.21)	0.001
HAQ (0-3) mean ± SD	1.45 (0.64)	0.76 (0.59)	0.001
BRAF-MDQ (0-70), mean (SD)	29.59 (13.67)	21.05 (14.73)	0.01
Physical (0-22)	13.45 (5.36)	10.49 (5.86)	0.02
Living (0-21)	7.22 (4.29)	4.63 (4.71)	0.02
Cognitive (0-15)	4.68 (3.88)	3.27 (3.23)	0.07
Emotional (0-12)	4.22 (2.54)	2.65 (2.66)	0.01
BRAF-NRS, mean (SD)			
Fatigue severity (0-10)	6.59 (2.32)	4.90 (2.57)	0.005
Effect of fatigue (0-10)	5 (2.54)	4.09 (2.60)	0.13
Poor coping of fatigue (0-10)	4.13 (2.29)	3.28 (2.49)	0.13

D2T RA: difficult-to-treat rheumatoid arthritis; SD: standard deviation; RF: rheumatoid factor; ACPA: anti-citrullinated-protein antibody; DAS28: 28-joint disease activity score; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; PGHA: patient global health assessment, PhGHA: physician global health assessment; VAS: visual analog score; HAQ: Health Assessment Questionnaire; BRAF-MDQ Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire; BRAF-NRS Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scales.

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AB0245 IMPACT OF EXTRA-ARTICULAR RHEUMATOID ARTHRITIS MANIFESTATIONS ON ATLANTOAXIAL SUBLUXATION

Keywords: Prognostic factors, Osteoporosis, Rheumatoid arthritis

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Background: The cervical spine is frequently affected during RA. It's the third joint location after the hands and feet [1].

Objectives: The objective of our work was to investigate the association between atlanto-axial subluxation (AAS) and the presence of extra-articular manifestations (EAM).

Methods: This is a cross-sectional comparative, single-center and hospital-based study of 102 RA patients (ACR/ EULAR 2010). Population was divided into two groups: Group 1 (study group) including 51 patients with AAS and Group 0 (control group) including 51 RA patients without AAS. AAS was defined as: the presence of an anterior C1C2 diastasis on the cervical spine radiograph in hyperflexion and/or by the presence of anterior, posterior, lateral or rotational C1C2 dislocation on MRI with/or without inflammatory signal.

Results: The study group (G1) consisted of 37 women and 14 men (M/F sex ratio = 0.37). The control group (G0) consisted of 40 women and 11 men (M/F sex ratio =0.28). The mean age was 60.3 ± 14.1 and 59 ± 11.3 years in G1 and G0, respectively. Median disease duration was 144 [6-480] and [5-216] months in G1 and G0 respectively. In G1, the median time to onset of AAS was 48 months [0-492]. At AAS diagnosis, EAM were present in 49% of G1 patients: dry ocular and/or mouth syndrome (60%), pulmonary involvement (16%) (3 cases of usual interstitial pneumonia and one case of constrictive bronchitis) and rheumatoid subcutaneous nodules (24%). Furthermore, 30 patients of G1 had bone densitometry. Osteoporosis and osteopenia were found respectively in 66% and 26% of cases. In the control group, only 3.9% of G0 patients had EAM. It was dry ocular syndrome in 2 patients. Bone densitometry, performed in 34 patients, was normal in 26.5% of cases. Osteoporosis and osteopenia were found respectively in 35.3% and 38.2% of patients. In analytical study, patients of G1 had higher prevalence of EAM (p<0.001) and osteoporosis (p=0.012). Though, no association was found between the presence of AAS and osteopenia (p=0.79).

Conclusion: In this work, patients with AAS had significantly more EAM and osteoporosis. A regular monitoring of cervical spine radiographic assessment in these patients is highly recommended to prevent such complication.

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Disclosure of Interests: None Declared.

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AB0246 IMPACT OF RHEUMATOID ARTHRITIS DISEASE ACTIVITY ON PATIENT'S NUTRITIONAL STATUS

Keywords: Quality of life, Diet and nutrition, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a potentially destructive chronic inflammatory disease that can be responsible for a deterioration of quality of life. Deformities, loss of autonomy and depression can lead to malnutrition in these patients.

Objectives: The aim of this study was to evaluate the impact of RA disease activity on the patient's nutritional status.

Methods: We conducted a cross-sectional study including RA patients according to the ACR/EULAR 2010 criteria. Sociodemographic data and disease parameters were collected. RA activity was assessed using the Disease Activity Score (DAS28), Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Nutritional status was assessed by the Mini-Nutritional Assessment (MNA). Then, the patients were divided into two groups: Group 1: no risk of malnutrition if the MNA score was >23.5 and Group 2: risk of malnutrition (if the MNA score was between 17 and 23.5) or poor nutritional status (if the MNA score was <17). The significance value "p" was set at 0.05.

Results: A total of 30 patients were included. The gender ratio was 0.43 with a female predominance. The mean age was 57.8±13.8 years [25-79]. The most frequent comorbidities were arterial hypertension (43.3%), diabetes (20%) and gastritis (16.7%). RA was immunopositive and erosive in 80% of cases. The mean duration of the disease was 14.4 years [13-23]. More than half of the patients (55.2%) were on corticosteroids, 48.3% were on methotrexate, 27.6% were on biotherapy, 13.8% were on sulphasalazine and 6.9% were on hydroxychloroquine. The mean value of the visual analogue pain scale was 4.7 [0-9] and the mean value of the patient's global assessment was 5 [2-9]. The mean ESR and CRP values were 50.6mm [3.9-131] and 22.2mg/l [0.9-77], respectively. The mean DAS-28ESR was 4.2± 1.3[1.1-6.9] reflecting moderate activity. The mean body mass index was 25.1±4.45kg/m² [16.8-39] and the mean brachial muscle circumference was estimated at 26.1±3.6cm [20-31]. The mean DAS28 ESR score was higher in G2, but the difference was not statistically significant. A significant association was noted between RA activity level and patient nutritional status (p=0.017). In patients with high activity, 71.3% were at risk of malnutrition and one patient was in poor nutritional status. Among patients with moderate activity, 42.9% were at risk of malnutrition and 50% had normal nutritional status. Among patients with low activity, the majority (60%) had normal nutritional status.

Conclusion: Our study shows an impact of RA disease activity on the patient's nutritional status. The higher the disease activity, the higher the patient's risk of malnutrition.

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Rheumatoid arthritis - prognosis, predictors and outcome

AB0247 WHICH PARAMETERS INFLUENCE DOMESTIC AND OCCUPATIONAL PRODUCTIVITY IN RHEUMATOID ARTHRITIS

Keywords: Quality of life, Work-related issues, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic rheumatism that mainly affects young adults. It has an impact on the patient's quality of life and professional abilities.
Objectives: The aim of this study was to evaluate the influence of RA activity, its impact, and its functional impact on patients' domestic and professional productivity.
Methods: We conducted a cross-sectional study over an 8-month period. Seventy adult patients diagnosed with RA for more than a year and receiving an antirheumatic therapy were interviewed. We assessed disease activity by the Disease Activity Score (DAS28), the impact of RA by the Rheumatoid Arthritis Impact of Disease (RAID) and functional impairment by the Health Assessment Questionnaire (HAQ). The impact of RA on domestic and professional productivity over the last month was assessed by the Rheumatoid Arthritis Specific Work Productivity Survey (WPS-RA).
Results: We noted a female predominance (63 women and 7 men) with an average age of 57.8 ±10.6 years [29-81]. At the time of the study, 13 (19%) patients were employed, 4 (6%) were unable to work because of RA while the rest were either unemployed or retired. The mean DAS28 was 3.31 ±1.13 [1.14-5.92]. The DAS28 was positively correlated with the degree of interference of RA on domestic work (p=0.001), professional work (p=0.005), and the decrease of domestic productivity (p=0.012) and professional productivity (p=0.021). Absenteeism was not influenced by RA activity (p=0.109). The average RAID score was 4.72 ±2.11 [0.6-9.48]. The RAID score was positively correlated with the degree of interference of RA on domestic work ($p < 0.001$) and professional work ($p = 0.013$). No correlation was noted between the impact of RA and the decrease of domestic productivity (p=0.511), professional productivity ($p = 0.109$) or the absenteeism ($p = 0.248$). The mean value of HAQ score was 1.04 ±0.61 [0-2.60]. We noted a positive correlation between the HAQ score and the degree of interference of RA at domestic work ($p < 0.001$) as well as the interference of RA at professional work ($p = 0.012$). The decrease of domestic productivity (p=0.133) and professional productivity (p=0.128) as well as the absenteeism (0.125) were not correlated with the functional impairment of RA.
Conclusion: According to these results, RA activity, impact, and functional impairment influenced mainly the degree of RA interference at work and domestic work. Productivity was essentially correlated with RA activity. Absenteeism was not influenced by any of the parameters studied previously.
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AB0248 USEFULNESS OF THE C-REACTIVE PROTEIN TO ALBUMIN RATIO IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Biomarkers

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Background: C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are commonly used to assess rheumatoid arthritis (RA) activity. New biomarkers have been developed, such as the CRP to albumin ratio (CAR), which has been proposed as a new inflammatory marker for monitoring disease activity in RA [1].
Objectives: The aim of our study was to evaluate the relationship between the CAR and RA parameters in a population of elderly patients.
Methods: We conducted a cross-sectional study including patients followed up for RA and aged 65 years or older. CRP, albumin, ESR, orosomucoid and haptoglobin levels were dosed. We calculated the CAR for each patient.
Results: Sixty-three patients (11 men and 52 women) were included. The mean age was 68.17±4.35 years. The median duration of disease progression was 11 years with an IQR of [4-16]. The median CRP was 8.33 mg/L. Mean albumin level was 41.43±4.58 g/L. The median ESR was 47 mm at 1 hour. The mean orosomucoid level was 1.29±0.46 g/L. The mean haptoglobin value was 2.07±0.97 g/L. The mean CAR value was 0.51±0.81 [0.01-3.72]. After statistic analysis, we found a significant association between the CAR and the DAS28 (p=0.03). In addition, CAR was positively correlated with ESR, CRP and Orosomucoid (p<0.001, p=0.01 and p=0.002, respectively). In addition, this ratio was significantly associated with HAQ score (p=0.01), and was higher in patients with major functional impairment (HAQ>2) (p=0.002). However, we did not found significant association between CAR and age, duration of evolution, VAS of pain, seropositivity, structural damage or with the use of corticosteroids.
Conclusion: Our study showed the association of the CAR with DAS28, inflammatory biomarkers and functional impairment among elderly RA patients. This suggests that this ratio could be a reliable tool as a prognostic index to assess disease activity and inflammation in this population.
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AB0249 RHEUMETRIC QUANTITATIVE 0-10 PHYSICIAN ESTIMATES OF INFLAMMATION, DAMAGE, AND DISTRESS IN RHEUMATOID ARTHRITIS: VALIDATION AGAINST REFERENCE MEASURES

Keywords: Rheumatoid arthritis, Fibromyalgia, Outcome measures

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Background: A physician global assessment (DOCGL) distinguishes active from control treatments in rheumatoid arthritis (RA) effectively in clinical trials. However, RA trials select for patients who have high inflammatory activity, generally only 5-30% of all RA patients. In routine care, DOCGL, and all clinical RA measures and indices, may be elevated not only by inflammatory activity but also by joint damage and/or patient distress, complicating interpretation of RA indices and clinical decisions. A RheuMetric checklist provides feasible physician 0-10 subscale estimates of inflammation (DOCINF), damage (DOCDAM), and distress (DOCSTR), in addition to DOCGL.
Objectives: To analyze criterion validity and specificity of 0-10 RheuMetric physician estimates for inflammation, damage, and distress, by comparing these estimates to reference RA core data set measures, as well as joint deformity/limited motion (DJC), radiographic scores and indices for FM and DEP.
Methods: A cross-sectional assessment was performed at one routine care visit in Liverpool, Australia. Rheumatologists recorded RheuMetric, with 4 0-10 scales for DOCGL, DOCINF, DOCDAM, DOCSTR, and 28 joint counts for swelling (SJC), tenderness (TJC), and limited motion/deformity (DJC), laboratory tests, and radiographic scores. Patients completed a multi-dimensional health assessment questionnaire (MDHAQ), which includes RAPID3 (routine assessment of patient index data), FAST4 (fibromyalgia assessment screening tool) and MDS2 (MDHAQ depression screen). RheuMetric estimates of inflammation, damage and distress were compared to reference and other measures using correlations and linear regressions.
Results: In 173 RA patients, variation in RheuMetric DOCINF was explained significantly by SJC and inversely by disease duration, DOCDAM by DJC, radiographic scores, and physical function, and DOCSTR by fibromyalgia and depression.
Conclusion: RheuMetric DOCINF, DOCDAM, and DOCSTR estimates were correlated significantly and specifically with reference measures of inflammation, damage, and distress, documenting criterion validity.

Table 1.

Significant Variables	Multivariable analyses		
DOCINF r square=0.56	B (95% CI)	Standardised *B*	P-value
Swollen joint count (SJC)	**0.428 (0.342; 0.515)**	**0.641**	**<0.001**
Disease duration	**-0.030 (-0.054; -0.005)**	**-0.137**	**0.018**
DOCDAM r square=0.51	B (95% CI)	Standardised *B*	P-value
Deformity/limited motion joint count (DJC)	**0.153 (0.087; 0.220)**	**0.400**	**0.000**
Radiographic Sharp van der Heijde score	**0.023 (0.007; 0.039)**	**0.248**	**0.006**
MDHAQ Physical function (FN) DOCSTR	**0.265 (0.039; 0.492)**	**0.229**	**0.022**
DOCSTR rsquare=0.42	B (95% CI)	Standardised *B*	P-value
MDHAQ FAST4 fibromyalgia assessment screening tool	**1.858 (0.530; 3.187)**	**0.302**	**0.006**
MDHAQ MDS2 (MDHAQ depression screen)	**1.164 (0.228; 2.103)**	**0.204**	**0.015**

REFERENCES: NIL.
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AB0250 PATIENT BELIEFS AND FEARS IN RHEUMATOID ARTHRITIS ASSESSED BY QUESTIONNAIRE FOR ARTHRITIS DIALOGUE

Keywords: Rheumatoid arthritis, Quality of care

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Background: Misinterpretation of patient beliefs can complicate shared decision making in rheumatoid arthritis (RA) leading to inadequate treatment adherence.
Objectives: The aim of this study was to determine patients' beliefs and fears about their disease and its treatment.
Methods: This is a cross sectional study conducted among patients diagnosed with RA based on ACR/EULAR criteria. All patients completed the Arthritis Dialogue Questionnaire (QuAD) which included 21 opinion statements that they scored from 0 (totally disagree) to 10 (totally agree). A score of more than 7 was interpreted to mean that the person significantly agreed with the opinion. The beliefs in this questionnaire include those that are supported by scientific evidence and those that are inconsistent with current medical opinion.
Results: A total of 56 RA patients were included in this study. There were 53 females (94.6% of cases) and 3 males (5.4%). The mean age of participants was 51.5 ± 11.7 years [21-74 years]. The average duration of disease was 11.5 ± 8.6 years [1-40 years]. The mean of DAS 28 ESR and DAS 28 CRP were respectively 4 ± 1.5 and 3.4 ± 1.5. The socio-economic status was low in 14 patients (25% of cases). 19.6% of patients were illiterate and 50% of patients had no education beyond primary level. Twenty-four patients (42.8%) believed that the onset of RA and its flare-ups were due to physical overload. As a result of these false beliefs, these same patients did not believe that doing sport or a physical activity can reduce flare-ups. Sixteen patients (28.5%) believed that RA was triggered by an emotional shock and 10 (17.8%) patients considered that flare-ups of the disease are triggered by psychological factors. The belief that the disease has a genetic cause was reported by 11 patients (19.6%). Uncertainty about disease progression was reported by 31 patients (55.3%) and 19 patients (33.9%) thought that all treatments have negative effects in the long term. The relationship between change in the weather and disease flare-ups was reported by 10 patients (17.8%).
Conclusion: The most widely held beliefs were related in our study to uncertainty about disease progression, physical and psychological factors that may trigger the disease, and fears about side effects of treatments. It is important to understand patients' beliefs about RA in order to optimize the adherence to treatment and to encourage patients to take up healthy lifestyles and habits that are beneficial for their disease management.
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AB0251 RELATIONSHIP BETWEEN ANXIETY, DEPRESSION AND FUNCTIONAL DISABILITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Quality of life, Rheumatoid arthritis

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Background: The management of rheumatoid arthritis (RA) must be multidisciplinary in order to relieve pain, prevent functional disability and improve quality of life.
Objectives: The objective of this study was to evaluate the impact of functional status on the psychological state in patients with RA.
Methods: This is a cross sectional study conducted among patients diagnosed with RA based on ACR/EULAR criteria. We assessed them for anxiety and depression symptoms using the Hospital Anxiety and Depression scale (HADS). The functional status was assessed by the Health Assessment Questionnaire (HAQ).
Results: A total of 100 RA patients were included in this study. There were 89 females (89% of cases) and 11 males (11%). The mean age of participants was 53.2 years [21-76 years]. The average duration of disease was 11.1 years [1-40 years]. Very active RA disease (DAS 28 greater than 5.1) was observed in 34 patients. The mean HAQ value was 1.28 [0-2.87]. 25% of our patients had high functional disability (HAQ >2). Nearly half of the study population (54% of cases) suffered from depression and/or anxiety symptoms. The mean HADS-D score was 8.39 [0-16] and thirty patients (30% of cases) had certain depressive symptoms (HADS-D ≥11). The mean HADS-A score was 7.79 [0-15] and 24 of our patients (24% of cases) presented certain symptoms of anxiety (HADS-A≥11). In statistical analysis, the HAD-A scale was associated with higher HAQ level (p<0,01). In addition, depressive patients (HADS-D ≥11) had higher HAQ level than patients without signs of depression with significant difference (p<0.01).
Conclusion: Our study showed that more than quart of RA patients suffers from anxiety and/or depression, and these troubles were related to functional disability. This suggests that treatment should focus also on improving physical function, detection and management of depression or anxiety.
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AB0252 IMPACT OF ADHERENCE TO THE MEDITERRANEAN DIET ON DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Disease-modifying drugs (DMARDs), Diet and nutrition

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Background: The Mediterranean diet (MD), mainly consists of olive oil, cereal products, fresh or dried fruit and vegetables, nuts, a moderate amount of dairy and meat, and many condiments and spices, has been suggested to have a beneficial effect on mortality and cardiovascular diseases. However, there is limited evidence regarding its impact on rheumatoid arthritis (RA) disease activity.
Objectives: The aim of this study was to assess association between adherence to MD and disease activity in RA patients.
Methods: In this cross-sectional study, we included patients with RA in remission or low disease activity. Patients with intestinal disease and smorkers were not included. Socio demographic data (age, sexe, educational level and living area) were recorded. Tender and Swollen Joint Count (T/SJC), Disease Activty Score (DAS28), Clinical Disease Activity Index (CDAI) and Score Disease Activity Index (SDAI) were used to access disease activity. Levels of C-reactive protein (CRP) and hemoglobine (Hb) were determined. Medication (paracetamol, Non Steroidal Anti-inflammatory Arugs (NSAIDs) and Disease-modifying antirheumatic drugs (DMARDs)) were recorded. We assessed MD adherence through a 14-item questionnaire in RA patient. The MD adherence score was classified as follows: good adherence (≥ 10 points) and low and medium adherence (≤ 9 points). We divided patients into two groups: G1: good adherence and G2: low and medium adherence to MD. We compared parameters of G1 and G2 using the Mann-Whitney U test.
Results: We enrolled 39 patients (34 female) with mean age of 52.74 ± 11.31 [20-74] years. Most of patients lived in rural area (61.5%). Half of patients (53.8%) had primary school level. The mean disease duration was 8.68 ± 6.6 years. The mean CRP and Hb levels were respectively 2.9 ± 9.67 [0-21] and 11.72 ± 1.4 [10-14]. The mean DAS28, CDAI and SDAI were respectively: 2.06 ± 0.71 [1-3.1], 5.46 ± 3.4 [1-10] and 8.26 ± 5.62 [2-28]. The most of patients were on paracetamol (53.9%) and conventional synthetic DMARDs (82.1%). NSAID were used by 35.9% of patients. The mean MD score was 9.1 ± 2.67 [4-12]. G1 enrolled 20 patients and G2 19. No significant differences emerged in the distribution of sexe, age, living area and educational level between two groups. G1 had significant lower disease activity in comparison to G2: (median [extrema]) TJC (0 [0-1] vs 1 [0-2], p=0.02), DAS28 (1.7 [1 - 3.1] vs 2.2 [1.7-3.1], p=0.001), CDAI (2 [1-7] vs 9 [3 - 11] p<0.001) and SDAI (4 [2 - 9] vs 11 [5 - 30], p<0.001). No significant differences was observed in SJC and CRP level, p=0.11 and p=0.22 respectively. However, Hb levels were higher in G1 (13 [13-14]) than in G2 (10 [10-13]), p<0.001. G2 had higher paracetamol and NSAID consumption with 84.3% and 57.9% vs 57.9% and 84.3 % respectively. Less use of biological DMARD were observed in G1 since all patients were on conventional synthetic DMARDs.

Conclusion: In our study, higher adherence to a MD was associated with reduced RA activity, symptomatic treatement consumption and more remission and low disease activity with conventional synthetic DMARD. Therefore, nutritional therapy could be a promising adjunct to pharmacological therapy in RA. Further studies are needed to confirm these findings.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0253 IDENTIFICATION OF FACTORS ASSOCIATED WITH A WORSE OUTCOME -EXITUS- IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SEVERE INFECTION

Keywords: Prognostic factors, Rheumatoid arthritis

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Background: Infections constitute an important and frequent cause of morbidity and mortality in patients with chronic inflammatory and systemic autoimmune rheumatic diseases. In rheumatoid arthritis (RA), this increased risk has been related to the immune system alterations inherent to the disease, the drugs used to control it (corticosteroids, DMARDs and immunosuppressants) and associated comorbidities. Most studies focus on the search for factors associated with the development of infections but do not explore the worst outcome: patient failure.

Objectives: To identify factors that help to predict an unfavorable outcome (exitus) after a severe infection in patients with rheumatoid arthritis.

Methods: This study was a retrospective case-control study at a single institution over a 10-year period. Patients with a diagnosis of rheumatoid arthritis with hospital admission for infection from January 1, 2010, to December 31, 2019 (pre-pandemic SARS-COV-2) were selected. The main variable was exitus due to the infectious episode. We collected: age, sex, time of evolution of RA, previous treatment and at the time of admission, number of admissions for infection, location of the infection, comorbidities, and other associated serious diseases. The statistics included a descriptive analysis of the different variables (expressed as median and interquartile range -IR- for quantitative variables and percentages for qualitative variables), and the association study using the $\chi 2$ test or Fisher's exact test for qualitative variables, and t-student or Mann-Whitney U and Kruskal Wallis for quantitative variables.

Results: We obtained 152 patients (71.7% female, 28.3% male), with a total of 214 episodes of admission for infection (115 patients with 1 episode (75.7%), 25 (16.4%) with 2 episodes, 6 being the maximum number of episodes recorded). The median age at admission was 77 years, and the median time of RA evolution was 8 years (IR 4-16). The location of the infection responsible for admission was mainly respiratory and urinary. Forty-eight patients died in the episode (31.6% of the sample, 15 males and 33 females, median age 81.5 years (IR 69.5-86.5)). Comparing the patients with unfavorable outcomes (exitus) with the rest, we only found a statistically significant difference in the number of previous admissions (p=0.011), and in the coexistence of some other serious disease (exitus 85.4%, rest 61.5% p=0.003). There were no differences by sex, age, time of RA evolution, drugs, location of the infection, or comorbidities.

Conclusion: A history of hospital admission due to infection, and having another serious disease, are factors associated with an unfavorable outcome (exitus) in patients with RA admitted for an infectious process.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0254 ACCEPTABILITY OF A SMARTPHONE APPLICATION AMONG TUNISIAN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Rheumatoid arthritis, Self-management, Quality of care

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Background: Nowadays, the utility of smartphone application for patients with rheumatic diseases, especially rheumatoid arthritis (RA) is well established and codified [1]. Indeed, patient-centered smartphone applications have the potential to assist with the adoption and maintenance of self-management behaviors [2].

Objectives: The purpose of our study was to investigate the willingness of RA patients to use smartphone applications for managing their disease.

Methods: This was a cross-sectional survey conducted in our rheumatology department including patients with RA, fulfilling the ACR/EULAR 2010 criteria. Sociodemographic data were initially collected. Patients were invited to answer a questionnaire regarding their willingness to accept smartphone application as part of their management strategies. We evaluated their points of view and suitability by inquiring about their experience with smartphones, as well as the previous applications used. Moreover, additional questions probed the patients' willingness to pay for this monitoring app.

Results: The study included 40 RA patients. There was a female predominance with a sex ratio of 0.11. The mean age was of 52.25±14.4 years [21-78]. The mean disease duration was of 11.97±6.69 years [1-29]. Regarding the educational level, 10 patients (25%) were illiterate, 14 (35%) had primary education, 11 (27%) had secondary education, and 5 patients (13%) were university graduates. Most of them (60%) were unemployed, and 13% were retired. As for marital status, 37 patients (92%) were married, and 1 was divorced. According to the patients, the two main reported mobile phone utility concerned the ability to communication with other individuals (48%) and internet navigation (52%). None of them had uploaded a healthcare application before and only 4 patients had previously contacted their doctor via text messages or e-mail. Overall, 67% of the respondents agreed on the usefulness of a patient-centered smartphone app and 65% were willing to accept this alternative as a model of care. Similarly, most of the patients refused to pay for the app (63%). The adherence to the smart app was significantly higher among females compared to males (p=0.011). Moreover, willingness to accept these applications was associated with a higher level of education without reaching a statistically significant correlation (p=0.07). There was no association between the marital, profession, age or disease duration and the acceptability of the smartphone app (p=0.418, p=0.246, p=0.382 and p=0.527 respectively).

Conclusion: Findings from this study showed that RA patients were not as reluctant to accept a health-related smart phone application. The willingness to adopt these applications was higher among female patients. Further steps are needed for a better implementation of this utility in clinical practice.

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Disclosure of Interests: None Declared.

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AB0255 CORRELATION BETWEEN PATIENT GLOBAL ASSESSMENT AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: ANY CHANGE OVER TIME?

Keywords: Outcome measures, Patient reported outcomes, Rheumatoid arthritis

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Background: Patient-reported outcomes (PROs) such as the Patient Global Assessment (PGA) are included in the definition of disease activity in rheumatoid arthritis (RA). Major determinants of the PGA are pain severity, functional limitations and fatigue. In contrast, the correlation with more objective measures of inflammation is weaker. In the early stages of the disease, the PGA might in theory more strictly reflect the patient's perception of inflammation.

Objectives: The aim of this study was to investigate the correlations between the PGA and disease parameters in patients with RA over time.

Methods: We conducted a prospective study including patients with RA (ACR/EULAR 2010). Demographic data and the following disease parameters were collected at inclusion and at 12 months follow-up: PGA, pain Visual Analog Scale (VAS), tender joint count (TJC), swollen joint count (SJC), Erythrocyte Sedimentation Rate (ESR), C Protein Reactive (CRP), Disease Activity Score 28 (DAS28), and Health

Assessment Questionnaire (HAQ). Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) which is a short 13-item questionnaire validated in RA. The score FACIT-F ranges between 0 and 52. Fatigue was considered mild if the FACIT-F score was ≥40, moderate if 20≤FACIT-F<40 and severe if 0≤FACIT-F<20. A *p* value inferior to 0.05 was considered significant.

Results: We included 100 RA patients (84 women and 16 men) with a mean age of 49.5±10 years old [18-65]. The mean disease duration was 87.3 months [1-360]. Rheumatoid Factor (RF) and Anti-Citrullinated Protein Antibodies (ACPA) were positive in 75% and 72.6%, respectively. At inclusion, the mean PGA was 47.8 cm [0-100] and the mean pain VAS was 49 cm [0-100]. The mean TJC and SJC were 5.3 [0-36] and 1 [0-9], respectively. The mean levels of ESR and CRP were 38.1 mm [10-120] and 10.8 mg/l [2-61], respectively. The mean DAS28 ESR was 3.68 [1.90-8.33] and the mean HAQ score was 0.9 [0-2.75]. The mean FACIT-F score was 27.1 [0-51] in RA patients versus 46.2 [0-52] in healthy controls (p<0.001). Among RA patients, 57% had moderate fatigue and 26% had severe fatigue. A significant positive correlation was noted between PGA and, TJC (r=0.508, p<0.001), SJC (r=0.331, p=0.001), pain VAS (r=0.763, p<0.001), ESR (r=0.364, p<0.001), DAS28 ESR (p=0.743, p<0.001) and HAQ (r=0.660, p<0.001). A significant negative correlation was noted between GPA and FACIT-F score (r=-0.658, p<0.001). At 12 months follow-up, the correlations became stronger between PGA and, TJC (r=0.664, p<0.001), SJC (r=0.673, p<0.001), pain VAS (r=0.893, p<0.001), ESR (r=0.536, p<0.001), DAS28 ESR (p=0.867, p<0.001), HAQ (r=0.686, p<0.001), and FACIT-F score (r=-0,792, p<0.001). A positive correlation was also noted between PGA and disease duration (r=0.205, p=0.045).

Conclusion: Disease activity, functional limitation, pain and fatigue directly correlate with PGA. This relation seems to strengthen over time as RA patients gain the ability to better understand and assess their illness.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0256 ARE CRP/ALBUMINE, PLATELET/LYMPHOCYTE, NEUTROPHIL/LYMPHOCYTE RATIO INDICATORS OF SPONDYLARTHRITIS ACTIVITY?

Keywords: Biomarkers, Cell biology, Spondyloarthritis

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Background: Spondylitis is a chronic inflammatory rheumatism that most often affects young adult males. In recent studies it has been reported that the platelet ratio (PLR) and neutrophil lymphocyte ratio (NLR) are important in demonstrating systemic systemic inflammation, the CRP albumin ratio (CAR) has been reported as a marker of of inflammation.

Objectives: Our objective is to study the relationship between the value of CAR, PLR, NLR, and the BASDAI score.

Methods: A cross-sectional study including patients with spondyloarthritis according to ASAS 2009 criteria. For each patient CAR, PLR, NLR and BASDAI score were calculated.

Results: 112 patients were included in this study. The average age was 46.9 (+/- 12.7) years, the sex ratio M/F is 1.29, the mean duration of the disease is 7.8 years, 68.8% of the axial spondyloarthritis are severe, 70.5% of spondyloarthritis are radiographic, the average EVA pain is 61.6, 54.5% of patients have a BASDAI >=4, the average CRP is 30.16, the average SR(sedimentation rate) is 32.77, 41.7% of patientsnhave stage III sacroiliitis, 93.9% have bilateral sacroiliitis. The average CAR is 0.88 (+/-1.84), the mean PLR is 157.6, the mean NLR is 3.32, the mean CAR is of 0.88. In the bivariate analysis, the CAR ratio was significantly associated with BASDAI (p=0.038), CRP is also significantly associated with BASDAI score (p= 0.028).

Conclusion: The CAR can be a practical measurement method in the follow-up of patients with axial spondyloarthritis axial spondyloarthritis because it can be used quickly under routine ambulatory conditions,in correlation with the BASDAI.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0257 GENETIC EVIDENCE REVEALS A CAUSAL ROLE BETWEEN LEUKOCYTE COUNTS AND THE RISK OF RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis

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Background: Accumulating inflammatory leukocytes in articular tissues is the hallmark feature of rheumatoid arthritis (RA). However, no relevant study indicates whether there is insidious causation between leukocyte count (LC) and the risk of RA. Traditional observational studies were susceptible to bias from confounding and reverse causation. It was necessary to estimate an exact correlation between LC and the risk of RA.

Objectives: This study aimed at evaluating the correlation between LC and the risk of RA by performing two-sample Mendelian Randomization(MR).

Methods: This study selected single nucleotide polymorphism (SNPs) associated($p<5e^{-8}$) with exposure (LC) from a genome-wide association study (GWAS), which included 171846 European ancestry participants and wiped off confounding factors. The association estimates of these SNPs with the risk of RA were obtained from another GWAS, including 14361 RA cases and 42923 controls. Upon SNPs were compared with SNPs related to the risk of RA and performed harmonization analysis to wipe off the irrelevant or inconsistent site SNPs. Ultimately, the remaining SNPs were selected as instrument variables(IVs). Then, we utilized two-sample Mendelian randomization (MR) to evaluate whether LC was causally associated with the risk of RA. Furthermore, Cochran's Q test, MR pleiotropy residual sum and outlier (MR-presso), and leave-one-out analysis were performed as a sensitivity test.

Results: A total of 70 independent SNPs were selected as IVs in the MR analysis of total WBC. Higher leukocyte counts were associated with a higher risk of RA (OR=1.025,95% CI: 0.998-1.053,p-value=0.038) by the IVW method (**Figure 1**). The MR-Egger regression test did not reveal any evidence of directional pleiotropy (intercept = -0.0002, stand error (SE) = 0.008, p = 0.981). In addition, leave-one-out sensitivity analysis showed similar findings, which further emphasized the effectiveness and stability of the causation. However, in the Cochrane's Q test, it turned out [Cochrane's Q statistic= 69, p-value=$3.472e^{-20}$], suggesting heterogeneity exists. For this reason, the processed steps were rechecked, and finally got, the conclusion that heterogeneity is produced from sysmaticness.

Conclusion: This study indicated the insidious causation between LC and the risk of RA. Further studies are warranted to determine how related pathways may contribute to the unnormal LC to promote the comprehension of the pathology of the happening of RA and access more therapeutic methods.

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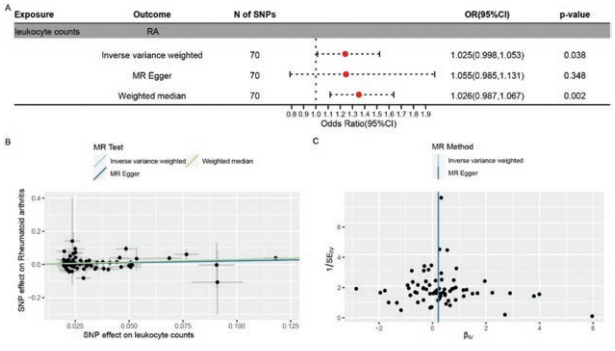


Figure 1. (A) Forest plot derived from the analyses of different Mendelian Randomization methods. **(B)** Scatter plot showing causal effect estimates. **(C)** Funnel plot for Mendelian Randomization analyses.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0258 PREPULSE INHIBITION OF THE BLINK REFLEX -A PUTATIVE MARKER OF "FIBROMYALGIANESS" - IS ALTERED IN PTS WITH RHEUMATOID ARTHRITIS COMPARED TO HEALTHY CONTROLS, BUT NOT PREDICTIVE FOR PAIN LEVEL OR THERAPEUTIC RESPONSE TO BDMARDS

Keywords: bDMARD, Fibromyalgia, Rheumatoid arthritis

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Background: Concomitant fibromyalgia (FM) is highly prevalent in pts with RA. In FM patients, altered abnormalities in processing of sensory stimuli including abnormal subcortical sensorimotor integration measured using prepulse inhibition (PPI) have been described [1]. PPI is a robust neurophysiological phenomenon in which a weak sensory event leads to reduction in magnitude of the reflex response that would be otherwise elicited by a reflex-eliciting stimulus presented 30-500 ms later. Its physiological purpose is to protect salient from irrelevant information at the subcortical level, thereby preventing undesired motor reactions. In RA patients, abnormal processing of sensory information may affect subjective aspects of disease activity indices, and thus influence treatment decisions.
Objectives: We aimed to investigate, whether PPI may serve as a predictive marker of FM in pts with RA starting their first targeted therapy.
Methods: PPI was measured in 15 patients with RA before initiation of treatment with bDMARDs, and 50 healthy controls (HC). We examined the effect of a weak electrical stimulus to the index finger (prepulse) on the blink reflex magnitude induced by electrical stimuli delivered to the supraorbital nerve at interstimulus interval 100 ms. To analyze the degree to which PPI affects baseline actual pain (VAS-NRS), patient global assessment PGA, discordance between PGA and EGA (expert global assessment) calculated as PGA minus EGA we performed univariate linear regression analyses using VAS-NRS, PGA, and PGA minus EGA as dependent variables. We selected the following predictive variables: age; sex; BMI; disease duration; erosive disease; SJC; TJC; pain VAS, ESR; mHAQ; ACPA. We used standardised β to compare the strengths of the relationships. We also analyzed the contribution of PPI to therapeutic response in month 3 and 6.
Results: As compared to HC, patients with RA were older, reported higher pain levels, and their mean PPI scores were significantly lower (Table 1). In RA pts PPI was neither predictive for baseline VAS-NRS, PGA, PGA-EGA, nor for ΔDAS28, ΔHAQ or ΔVAS in month 3 or 6. The trajectory of mean DAS28 according to ordinal level of PPI is shown in Figure 1.
Conclusion: Lower PPI in RA patients may reflect abnormal filtering of afferent information flow to the brain. Together with previous findings in FM, our results suggest abnormal subcortical sensory information may be involved in nociplastic pain in RA patients. However, PPI was neither predictive for baseline level of pain, PGA, or EGA-PGA, nor for therapeutic response in pts with RA.
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Table 1. Comparison of PPI, age and gender between RA patients (*n*=15) and controls (*n*=50)

Predictor	**RA patients** (n=15)	**Controls** (n=50)	**p-value**
Age, median (IQR)	47 (43–69)	44 (35–49)	**0.023**
Women, n (%)	11 (73.3%)	34 (68.0%)	0.761
PPI, mean (SD)	0.53 (0.12)	0.65 (0.17)	**0.020**
Actual pain (0–10), median (IQR)	6.0 (4.0–7.0)	1.6 (0.3–2.3)	<**0.001**

IQR – inter-quartile range; SD – standard deviation

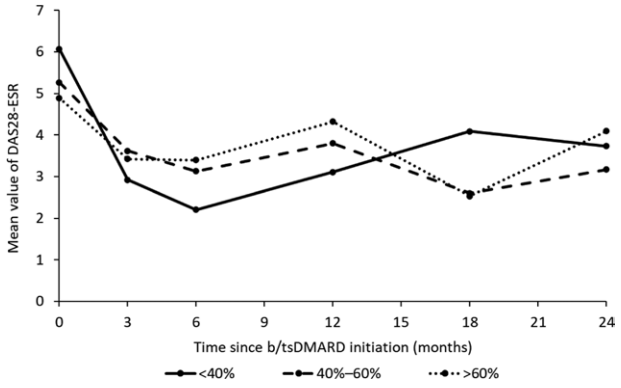


Figure 1. The average trajectory of disease activity after start of targeted therapy in pts with RA according to their baseline PPI. PPI results are stratified as follows: normal, borderline and abnormal inhibition >60%, 40-60%, and <40% resp.

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Disclosure of Interests: Jakub Zavada Speakers bureau: Abbvie, Elli-Lilly, Sandoz, Novartis, Egis, UCB, Sanofi, Astra Zeneca, Sobi, Zuzana Forejtová: None declared, Lucia Nováková: None declared, Tereza Serranová: None declared.
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AB0259

PREDICTIVE VALUE OF C-REACTIVE PROTEIN/ ALBUMIN RATIO(CAR) FOR THE DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A PROSPECTIVE COHORT STUDY

Keywords: Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic, systemic and disabling autoimmune disease with inflammatory synovitis. Many biochemical factors are used as diagnostic, activation and prognostic markers in certain diseases. The C-reactive protein/albumin ratio(CAR) is an inflammatory marker that is considered to have prognostic value in many disease. The CAR has shown high value in colorectal cancer, inflammatory bowel disease and ANCA-associated vasculitis activity.
Objectives: In this study, we aimed to evaluate the predictive value of CAR for disease activity in RA patients.
Methods: This prospective study included 144 RA patients who fulfilled the 2010 revised criteria of the American College of Rheumatology (ACR) for RA. The demographic characteristics of the patients, duration of the disease and clinic characteristics of the patients such as the 28-joint Disease Activity Score based on the erythrocyte sedimentation rate (DAS28-ESR), Visual Analogue Scale, Health Assessment Questionnaire-Disability Index were collected. Labotaruvary finding such as erythrocyte sedimentation rate, CRP, albumin were noted. The CAR ratio was obtained by dividing the CRP level with albumin level. Based on the DAS28-ESR level, the included patients were categorized into two groups, namely, inactive to mild active RA (n=69; DAS28-ESR level <3.2) and moderate to highly active RA (n=75; DAS28-ESR level ≥3.2). These group were compared with the parameters described above.
Results: One hundred ten patients (76.4% female) with mean age 52.3 SD 11.8 years were recruited into the study. Age and disease therapy duration of the patients were similar in both groups. Female gender was significantly higher in the DAS28-ESR ≥3.2 group. Patients who DAS28-ESR ≥3.2 had a significantly higher CAR compared to those who did not (0,11 SD 0,09 *vs*. 0,20 SD 0,16, *p*<0.001) (Table 1). Multivariate logistic regression analyses revealed that CAR was an independent predictor of moderate to highly active RA (OR: 2.180, 95%CI: 1.307–3.637; *p*=0.003). A receiver operating characteristic curves analysis yielded that the optimal cut-off value of CAR for moderate to highly active RA was 0.126 with sensitivity 64.0% and specificity 66.2% (AUC: 0.683, 95%CI: 0.597-0.769, p<0.001) (Figure 1).
Conclusion: Based on the study findings, we were able to show that simple and easily obtained CAR could be an independent predictor of disease activity in rheumatoid arthritis patients.
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Table 1. Demographic, clinical features and laboratory findings of the patients with rheumatoid arthritis based on disease activity measured by DAS28-ESR

	DAS28-ESR <3.2 n=(69)	**DAS28-ESR ≥3.2 n=(75)**	**P value**
Age (years; mean SD)	53,46 SD 11,57	51,30 SD 12,00	0.275
Female, gender, n (%)	46 (%66,7)	64 (%85,3)	0.008
Disease symptoms duration (month; mean SD)	117,1 SD 116,3	98,6 SD 75,0	0.265
Disease therapy duration (month; mean SD)	97,7 SD 105,2	90,9 SD 73,0	0.663
DAS28-ESR (mean SD)	2,41 SD 0,55	4,27 SD 0,80	<0.001
Visual Analogue Scale (mm, mean SD)	30,14 SD 19,66	61,60 SD 17,55	<0,001
Health Assessment Questionnaire-Disability Index (mean SD)	0,61 SD 0,64	0.82 SD 0,99	0,151
ESR (mm/h, mean SD)	19,72 SD 15,80	27,20 SD 16,37	0.006
CRP (mg/L, mean SD)	4,88 SD 3,94	8,54 SD 6,44	<0.001
Albumin (g/L, mean SD)	44,10 SD 2,69	42,72 SD 3,59	0.011
C-reactive Protein/Albumin Ratio (mean SD)	0,11 SD 0,09	0,20 SD 0,16	<0,001

Abbreviations: DAS28-ESR, the 28-joint Disease Activity Score based on the erythrocyte sedimentation rate; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0260 **DISABILITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: RELATIONSHIP WITH ALEXITHYMIA.**

Keywords: Quality of life, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is the chronic, destructive, immune-mediated inflammatory process that has a gradient course and causes disability of approximately 50% over the next 5 years of the disease. Acute pain syndrome, which is accompanied by RA, often leads to a violation of the psycho-emotional sphere with manifestations in the form of depression, anxiety and alexithymia. Alexithymia defined as a personal emotional disorder that characterized by difficulty in identifying and describing subjective feelings. As there are insufficient data on disability in patients with RA in combination with alexithymia, we screened patients with RA, investigated the level of disability and found a connection with alexithymia.
Objectives: To investigate the level of disability in patients with rheumatoid arthritis and clarify a probable connection with alexithymia.
Methods: RA patients diagnosed according to the ACR/EULAR 2010 classification criteria (Daniel Aletaha et al., 2010). The presence of alexithymia was determined by TAS-20 – «Toronto Alexithymia Scale» questionnaire (Graeme J. Taylor, D. Ryan, R. Michael Bagby, 1994). Disability was determined by a questionnaire DRI - «The Disability Rating Index» (Bo A. Salen, Erik V. Spangfort, Ake L. Nygren and Rolf Nordemar, 1994).[1] RA activity was assessed with the Disease Activity Score (DAS28), Simplified disease activity index (SDAI), Clinical disease activity index (CDAI), functional status with the Health Assessment Questionnaire (HAQ), pain intensity was determined by the Visual Analogue Scale (VAS). Statistical analyses were performed using IBM Statistics SPSS 20. Results are presented as mean with standard deviation (M ± SD).
Results: The study included 146 patients with RA (90.7% of women). The average age of the patients was 50.1 ± 12 years, and the duration of the disease ranged from 1 to 21 years (7.4 ± 4.7). Among 146 examined, alexithymia (TAS-20 ≥ 61) was detected in 36 people (24.7%). All patients had different level of disability detected by the DRI questionnaire, with scores ranging from 5.4 to 79.8; and the average value was - 31.1 ± 17.1. In patients without alexithymia, the disability was 26.8 ± 14.8, in patients with alexithymia – 44.5 ± 16.8. Functional ability in individuals with RA without alexithymia according to the HAQ was 0.9 ± 0.6, in contrast to the group of patients with RA and alexithymia - 1.7 ± 0.6. The significance of the differences between groups depending on the presence of alexithymia according to functional ability and intensity of pain was at the level of $p < 0.05$; and disability - at the level of $p < 0.01$. A direct strong correlation was established between alexithymia and disability, functional ability and VAS: DRI ($r = 0.514$; $p < 0.01$); HAQ ($r = 0.450$; $p < 0.01$); VAS ($r = 0.457$; $p < 0.01$). We found that the presence of alexithymia in patients with RA was associated with an increased risk of functional disability. Odds ratios are used to identify the risk of functional disorders in patients with alexithymia. RA patients with TAS-20 score ≥ 61 had an odds ratio of 7.57 [95% CI: 2.13 – 26.98] ($p < 0.002$) for moderate functional disability and 21.47 [95% CI: 4.82 – 95.61] ($p < 0.0001$) for severe functional disability by HAQ, and 14.98 [95% CI: 4.48 – 50.13] ($p < 0.0001$) by DRI.
Conclusion: The alexithymia in patients with rheumatoid arthritis is associated with a bigger disability, as well as with impaired functional ability and severity of pain syndrome. We concluded that alexithymia may be consider as a risk factor of the disability in patients with RA.
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AB0261 **PREVALENCE OF HEART VALVULAR REGURGITATION ACCORDING TO THE TIME OF DISEASE EVOLUTION IN RHEUMATOID ARTHRITIS PATIENTS**

Keywords: Heart, Rheumatoid arthritis, Imaging

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Background: Rheumatoid arthritis (RA) patients are at higher risk of developing cardiovascular (CV) diseases, both ischemic and non-ischemic, than the general population [1]. Inflammatory status and fibrotic changes at cardiac valves in these patients predispose them to a higher risk of valve diseases, which could be detected by echocardiography [2].
Objectives: To determine the prevalence of valvular regurgitation, according to the time of disease evolution in RA patients.
Methods: Descriptive, comparative, and cross-sectional study. We enrolled RA patients between 40 and 75 years old who fulfilled ACR/EULAR 2010 classification criteria and recruited in the Rheumatology service from tertiary care hospital. Patients were divided by time of disease evolution into quartiles. A transthoracic echocardiogram performed by a certified cardiologist blinded to clinical data. Normality was assesed by Kolmogorov-Smirnov test. Variables with normal and non-normal distribution were described by media and standard deviation, such as median and interquartile range (p25-p75), respectively. Differences between groups was analyzed by ANOVA, Kruskal-Wallis test or Chi-squared, accordingly.
Results: We included 151 RA patients. Demographic characteristics are in Table 1. Overweight/obesity was found between 62-87% of patients, hypertension between 26-34%, and Type 2 Diabetes mellitus between 8-26%. The tricuspid valve was the most affected (73-84%). There was no differences in prevalence of valvular regurgitation.
Conclusion: RA patients have a high prevalence of valvular regurgitation, which could predispose them to develop heart failure, therefore it is important to consider echocardiography in the approach of this population, despite not showing an increase.
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Table 1. Demographic characteristics (n= 151)

Variable	1st Quartile (n= 38)	2nd Quartile (n=38)	3rd Quartile (n=38)	4th Quartile (n=37)	p
Duration of disease, years. median (p25-p75)	1.5 (1.0-2.0)	5.0 (3.9-6.0)	10.6 (9.4-12.6)	20.5 (16.5-25.2)	
Women, (n)%	37 (97)	34 (89)	36 (94)	35 (94)	NS
Age, years. mean (±SD)	54 (9.6)	56 (8.5)	55 (8.8)	56 (8.0)	NS
Comorbidities, n (%)					
Overweight/Obesity	28 (73.7)	33 (86.8)	31 (81.6)	23 (62.2)	NS
Hypertension	13 (34.2)	13 (34.2)	10 (26.3)	12 (32.4)	NS
T2DM	6 (15.8)	10 (26.3)	8 (21.1)	3 (8.1)	NS
Valvular regurgitation, n (%)					
Aortic valve	3 (7.9)	7 (18.4)	2 (5.3)	8 (21.6)	NS
Mitral valve	26 (68.4)	21 (55.3)	17 (44.7)	20 (54.1)	NS
Pulmonary valve	9 (23.7)	7 (18.4)	9 (23.7)	8 (21.6)	NS
Tricuspid valve	28 (73.7)	31 (81.6)	31 (81.6)	31 (83.8)	NS
Any of valves	32 (84.2)	33 (86.8)	33 (86.8)	31 (83.8)	NS

This table shows demographic and clinical characteristics. Quartiles were divided according to rheumatoid arthritis duration, meanwhile, each variable was described individually. T2DM Type 2 Diabetes Mellitus.

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AB0262 **FATIGUE PATTERNS IN DIFFICULT TO TREAT RHEUMATOID ARTHRITIS PATIENTS**

Keywords: Quality of life, Rheumatoid arthritis, Mental health

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Background: Fatigue study is scarce in D2T RA. The experience of fatigue is multidimensional, implying complex, multicausal pathways.
Objectives: to identify the factors associated with fatigue on its different subscales (Physical, Living, Cognitive and Emotional).
Methods: Cross-sectional study. 22 patients with D2T RA were included; patients were being followed up in the rheumatology outpatient clinic of Hospital Clínico San Carlos, Madrid, Spain. Data were collected between July 2018 and November 2022. All patients met the ACR/EULAR 2010 criteria and they were in

treatment with Biological agents (anti-TNF and Non anti-TNF) or Targeted Synthetic DMARDs (jakinibs). Outcome: Difficult to treat Rheumatoid Arthritis Patients (fulfillment of EULAR criteria). Main variable: Fatigue was assessed by the Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire (BRAF-MDQ) and the Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scale (BRAF-NRS). Covariables: Sociodemographic and disease-related variables. Statistical analysis: A descriptive analysis was carried out for the different variables. To identify factors independently associated to BRAF-MDQ and its subscales, multivariable linear regression was applied. Results were expressed as coef with their corresponding 95% CI. A value of $p < 0.05$ was consider as statistically significant.

Results: A total of 22 (15.38%) patients were found D2T RA, comprising of 11 females (50%) with a mean age of 62.82±13.45 years and mean disease duration of 17.76±8.47 years. RF was positive in 59% of patients. Regarding comorbidities, 32% had dyslipidemia, 28% hypertension, 10% vascular disease, 27% hypothyroidism and 23% depression. The DAS28-ESR mean score of the patients were 4.10 ± 0.67. The factors affecting the global fatigue and its different subscales was evaluated in multivariate analyze **Table 1.** Our results shows a different correlation structure between disease and treatment factors and the different dimensions of the BRAF-MDQ. Patients who reported high disability scores had more global fatigue, while those with a poor patient global health assessment perceived more physical fatigue. In addition, an association was observed between depression and cognitive fatigue. Male sex and positive RF was associated with less living fatigue.

Conclusion: It is important to evaluate fatigue in a multidimensional perspective, each of the different subscales could be modulated by different factors. The results of our study indicated that disability predicts global fatigue, however, other factors can configure different patterns of fatigue in D2T RA patients, and identify them is key to the approach of this complex symptom.

Table 1. Multivariate analyses of BRAF-MDQ and its subscales

	Total BRAF-MDQ	Physical	Living	Cognitive	Emotional
Age	1.014 (0.881)	-0.027 (0.151)	-0.011 (0.126)	-0.063 (0.090)	0.006(0.073)
Sex	0.794 (0.585)	2.292 (0.610)	**-4.334 (1.871)***	3.525(1.752)	0.163(3.905)
RF positive	1.264 (0.809)	-2.266 (3.749)	**-4.919 (1.951)***	-0.769(1.845)	-0.070(1.303)
HAQ	**6.200 (3.11)****	2.199(1.881)	1.207 (1.664)	2.077(1.14)	0.035(1.905)
PGHA: patient global health assessment	0.154 (0.117)	**0.127(0.038)***	-0.030(0.046)	-0.069(0.027)	-0.295(0.045)
VAS Pain	0.170(0.244)	-0.006(0.094)	-0.020(0.158)	-0.038(0.083)	0.014(0.020)
Depression	9.2(6.783)	-1.137(2.956)	-0.676(3.163)	**4.566(2.048)***	0.963(1.256)
Other biological (vs TNFi)	-0.717(6.490)	-1.853(2.164)	0.006(1.924)	1.486(1.368)	0.003(2.007)
JAKi (vs TNFi)	-12.221(10.965)	-2.455(3.657)	-4.949(3.447)	-1.866(2.433)	-0.99(2.072)

BRAF-MDQ Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire,*$p < 0.05$,**$p < 0.001$. Cells represent beta coefficients with standard error

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AB0263 FAT AND LEAN MASS DISTRIBUTION USING DUAL ENERGY X-RAY ABSORPTIOMETRY (DEXA) IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ITS RELATIONSHIP TO DISEASE SEVERITY

Keywords: Sarcopenia, Rheumatoid arthritis, Quality of life

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Background: Obesity and sarcopenia have been associated with higher disease activity, poor response to disease modifying agents and lower remission achievement in rheumatoid arthritis (RA) patients [1, 2]. Weight loss has been associated with increased chances of remission [1]. The prevalence of obesity in the Asian population is 64% but the relationship between fat distribution and disease activity is not explored in the Indian population [3].

Objectives: To describe fat mass, lean mass, fat mass index, lean mass index, fat mass percentage, fat-to-lean mass ratio, android-gynoid ratio and trunk-leg fat ratio measured using dual energy x-ray absorptiometry (DEXA) in patients with rheumatoid arthritis and assess their relationship with DAS28, patient global assessment of disease activity (PtGA), and Indian health assessment questionnaire (IHAQ) disability index.

Methods: A hospital based cross-sectional study was initiated after Ethics Committee approval in patients with RA at our rheumatology clinic from March 2022 onwards, at Jodhpur, India. Demographic, clinical, anthropometric and treatment details of the patients were collected after informed written consent. Whole body DEXA was done using a DEXA scanner Hologic Corp, model no - Horizon A S/N 303237M). Correlation of fat mass, lean mass, fat mass index, lean mass index, fat mass percentage, fat-to-lean mass ratio, android-gynoid ratio and trunk-leg fat ratio with DAS28, PtGA, and IHAQ was determined using Spearman correlation. Multivariable logistic regression was done to see if fat distribution indices could predict disease activity and IHAQ disability index. This is an ongoing study, with a calculated sample size of 104.

Results: Sixty patients have been enrolled so far with a mean age of 46 ± 11 years, 78.3% were females. Mean body mass index was 23.7 ± 5.1 kg/m^2 and 51.7% (n = 31) patients were overweight. Mean waist-hip ratio was 0.88 ± 0.07 among females and 0.98 ± 0.08 among males. The mean fat mass percentage, lean mass index, fat lean mass index, android-gynoid ratio and fat trunk-leg ratio were 39.87 ± 6.13%, 14.46 ± 2.31 kg/m^2, 67.19 ± 19.26, 0.92 ± 0.14 and 0.81 ± 0.12 respectively. The median fat mass, lean mass and fat mass index in the study population were 22.98 ± 10.42 kg, 33.53 ± 10.42 kg and 10.05 ± 4.19 kg/m^2 respectively (Table 1). The fat mass percentage had significant correlation with previous history of steroid use for more than 21 days ($r = 0.347$, $p = 0.008$). None of the fat distribution indices evaluated could reliably predict DAS28, PtGA, and IHAQ disability index using multivariable logistic regression models.

Conclusion: The proportion of patients who were overweight was less in our patients with RA compared to the general population [3]. In this ongoing study, body fat composition and distribution did not exhibit any relationship with disease severity, or disability. However, prolonged steroid use increased fat mass percentage. Further studies are needed to evaluate the changes in fat and lean mass distribution and their relationship to disease activity.

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Table 1. Fat distribution indices in patients with rheumatoid arthritis.

Fat distribution indices	Mean ± SD or Median ± IQR
Fat mass (kg)	22.98 ± 10.42
Lean mass (kg)	33.53 ± 10.42
Fat mass %	39.87 ± 6.13
Fat mass index (kg/m^2)	10.05 ± 4.19
Lean mass index (kg/m2)	14.46 ± 2.31
Fat to lean mass ratio	67.18 ± 19.26
Android - gynoid ratio	0.92 ± 0.14
Trunk - leg fat ratio	0.81 ± 0.12

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Disclosure of Interests: None Declared.

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AB0264 PREDICTION OF FLARE FOLLOWING GLUCOCORTICOIDS WITHDRAWAL IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING CSDMARDS: A REAL-LIFE STUDY

Keywords: Outcome measures, Rheumatoid arthritis, Real-world evidence

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Background: In patients with rheumatoid arthritis (RA), glucocorticoids (GC) should be firstly discontinued before considering tapering conventional synthetic disease-modifying anti-rheumatic drugs (csDMARD) or other biological agents.

Objectives: We aim to determine risk factors for flare after GC withdrawal in RA patients undergoing csDMARDs.

Methods: Electronic database searches of PubMed, EMBASE and Cochrane Library were performed. Observational studies that assessed the association of dementia with DMARDs in RA were included. Pooled risk ratios (RRs) with 95% confidence intervals (CIs) were used as summary statistic, with either fixed-effects or random-effects model. The certainty of evidence using the GRADE system.

Results: In total, 115 RA patients discounted GC in the context of csDMARDs (methotrexate: 80%; hydroxychloroquine: 61%; csDMARDs combination: 79%). Of these, twenty-four patients experienced flare after GC discontinuation. Compared with relapse-free patients, flare patients were more likely to have established RA (75% vs. 49%, p=0.025), higher median cumulative prednisolone dosages (3.3g vs. 2.2g, p=0.004), and higher proportion of dissatisfied RA control during GC usage (66% vs. 33%, p=0.038). In multivariate analysis,

significantly increased flare risk was predicted by established RA (OR 2.93 [1.02-8.43]), cumulative prednisolone doses>2.5g (OR 3.69 [1.34-10.19]) and dissatisfied RA control (OR 3.00 [1.09-8.30]).
Conclusion: Flare following GC withdrawal is not common in RA patient undergoing csDMARDs therapy. Established RA, higher cumulative GC doses and dissatisfied RA control before GC discontinuation are important factors associated with flare after GC withdrawal.

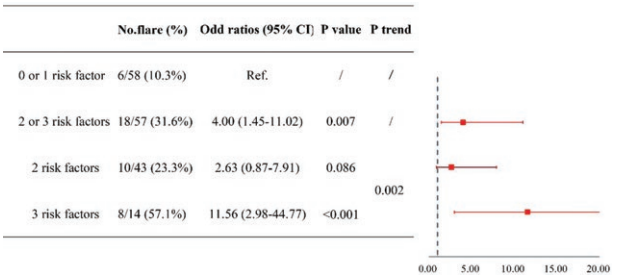


Figure 1. Flare risk following GC withdrawal in RA patients with different number of risk factors.

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Acknowledgements: NIL.
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AB0265

SLEEP QUALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SINGLE CENTER EXPERIENCE FROM JODHPUR, INDIA

Keywords: Patient reported outcomes, Mental health, Quality of life

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Background: Sleep disorders are prevalent in rheumatoid arthritis (RA). Sleep is closely related to disease activity, depression, stress, fatigue and pain [1]. Community prevalence of sleep disorders in India varies from 6.2% to 36.3% [2,3]. Studies assessing sleep quality in the Indian population with RA are limited.
Objectives: To assess the prevalence of impaired sleep quality using Pittsburgh Sleep Quality Index (PSQI) and determine factors predicting impaired sleep quality in patients with RA.
Methods: A cross-sectional study was conducted in patients with RA presenting to our rheumatology clinic after informed consent and Ethics Committee approval from January 2021. Sleep quality was assessed by PSQI, depression by Patient Health Questionnaire (PHQ-9) and Quality of life by Indian Health Assessment Questionnaire (IHAQ). Disease activity was assessed using Disease Activity Index (DAS28 CRP) and Clinical Disease Activity Index (CDAI). Serum samples for interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α) were collected and stored at -80^0 C. Relationship of fatigue was examined with age, serum TNF-α, IL-1, IL-6, CDAI, DAS28 CRP and patient global assessment (PtGA) using Spearman correlation coefficient. Linear regression analysis was performed to determine the predictors of impaired sleep quality in patients with RA.
Results: One hundred and fifty-four patients were enrolled, 133 were females (86.3%). Median pain VAS score was 6[2]. Mean DAS was 4.35 ± 1.31, mean CDAI: 19.75 ± 7.91 and median IHAQ was 9.5[8]. The prevalence of depression (PHQ-9 >10) was 5.8% (n = 9) with a median PHQ-9 of 2[3]. One patient was on tofacitinib, 20 were on methotrexate monotherapy and others were on combination of conventional DMARDs. The prevalence of impaired sleep (PSQI >5) was 8.4% (n = 13) with a median PSQI of 2[2]. PSQI had significant correlation with PHQ-9 (r = 0.471, p<0.0001), IHAQ (r = 0.288, p<0.0001), DAS28 (r = 0.197, p = 0.015) and CDAI (r = 0.235 p = 0.003). Age, pain VAS, serum TNF-α, IL-1 and IL-6 had no correlation with PSQI. Among individual components of DAS, PtGA (r = 0.296 p <0.0001) alone correlated with PSQI. PHQ-9, IHAQ and PtGA were significant predictors of impaired sleep quality (Table 1).
Conclusion: Compared to other studies within India, our patients had very low prevalence of impaired sleep quality. Sleep quality significantly influences disease activity likely by affecting PtGA. Risk factors for poor sleep quality are presence of depression, poor quality of life and patient global assessment of disease activity. Hence a holistic management of RA must involve addressing these risk factors.

Table 1. Predictors of impaired sleep quality

Predictors	β (95% CI)	P value
PtGA	0.176(0.023 - 0.412)	0.004
Depression (PHQ-9)	0.282 (0.101 - 0.342)	<0.0001
IHAQ	0.230 (0.025 -.129)	0.004

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AB0266

THE INFLUENCE OF HEREDITY ON RHEUMATOID ARTHRITIS: EXAMINING THE DISTINCT CHARACTERISTICS IN PATIENTS WITH A FAMILY HISTORY

Keywords: Prognostic factors, Rheumatoid arthritis

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BACKGROUND: NIL.
Objectives: The aim of this study was to describe the particularities of patients diagnosed with rheumatoid arthritis (RA) who have a family history of the disease.
Methods: In this retrospective study, a total of patients diagnosed with RA between the years 2011 and 2022 were included. The primary aim of the study was to investigate the relationship between different parameters such as age of disease onset, Disease Activity Score using C-reactive protein(DAS CRP), serological profile, erosive character,extra-articular manifestations, and use of biotherapy. Data were collected from the medical records of the patients, and analyzed using statistical test such chi-squared, Fisher's exact test and t-test.the level of significance was set at p=0.05.the study design included a thorough data cleaning process.
RESULTS:

Table 1.

	RA with Family History (n=21)	RA without Family History (n=386)	(p)
Sex-Ratio	6	6.12	1.00
Young onset RA (%)	66.7	55.3	0.30
Extra-articular manifestations (%)	66.7	46.3	**0.05**
Serological profile (%)	85.7	87.5	0.73
C-reactive protein (mg/L)	22.25 ± 37.23	27.87 ± 25.11	0.487
DAS CRP*	5.3 ± 1.63	5.4± 2.5	0.90
Erosions (%)	81	87	0.50
The use of biological treatment (%)	38.1	39.2	0.91

DAS CRP: Disease Activity Score using C-reactive protein*

The study included 407 patients with a mean age of 58.86 years ± 12.441, and a sex ratio of 6 (F/M). The median duration of the disease was 14 ± 7.523 years. Erosions were found in 87.2% of patients. Rheumatoid factor (RF) was positive in 85% of patients and anti-citrullinated protein antibodies (ACPA) were positive in 64.9% of patients. The mean DAS 28 score was 5.409± 2.52, the mean CRP was 33.84±35.19, and extra-articular manifestations were found in 46.4% of patients and 39.1% of patients were receiving biological treatment. 21 patients (5.17%) reported a family history of RA. In bivariate analysis, RA patients with a family history had more extra-articular manifestations compared to patients without a family history of the disease (66.7%) versus (46.3%) (p =0.05). No association was found for the other parameters.
Conclusion: The results of this study suggest that a family history of RA may be a predictive factor for extra-articular manifestations in patients with the disease. These findings highlight the importance of considering family history when

evaluating and treating patients with RA. Further research is needed to confirm these results and to better understand the underlying mechanisms.
REFERENCES: NIL.
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AB0267 DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS STRATIFIED BY HEMOGLOBIN LEVELS: A MULTI-CENTER STUDY

Keywords: Descriptive studies, Rheumatoid arthritis, Clinical trials

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Background: Anaemia is a multifactorial, pervasive, extra-articular manifestation that is a significant burden in RA. The most common types of anaemia in RA are chronic anaemia and iron-deficiency anaemia. A number of existing studies observed anaemia in 24.0%–70.6% of RA patients.
Objectives: The primary objective of this study was to examine the association between haemoglobin (Hb) levels and disease activity in patients with rheumatoid arthritis (RA).
Methods: This retrospective study obtained data from adult RA patients with Hb reports from the Kuwait Registry for Rheumatic Diseases (KRRD). Patients were recruited from four public hospitals in Kuwait between February 2013 and February 2022. The cohort was stratified into two groups: low Hb (anaemic, ≤ 110 g/L) and high Hb (non-anaemic, > 110 g/L). Demographic, treatment, clinical, and laboratory characteristics were used to compare the two Hb cohorts. Multivariate and univariate statistical analyses were used to analyse the data.
Results: The total number of patients visited (N_v) was 11393 and consecutive patients with RA diagnoses and Hb data (N_p) was 1584. Both N_v and N_p were included in the study. Of these, 72.5% (n = 8260) had high Hb levels and 27.5% had low Hb levels (n = 3133). The average age of the cohort was 55.9±12.5 years. Logistic regression analysis revealed that a greater number of non-Kuwaiti patients had anaemia than Kuwaiti patients [adjusted odds ratio (aOR), 1.34; 95% confidence interval (CI):1.16-1.56; *P* <0.001). Patients who received biologic treatment were more likely to be non-anaemic [aOR, 1.33; 95% CI:1.23-1.45; *P* <0.001). Additionally, the study demonstrated that patients with anaemia had greater odds of acquiring Disease Activity Score 28-joint count (DAS-28) ≥ 3.2 as opposed to DAS-28 < 3.2 [aOR, 0.74; 95% CI:0.61-0.90; *P* =0.002].
Conclusion: Lower haemoglobin levels in RA are independent predictors of disease activity.
Acknowledgements: I would like to acknowledge Kuwait Registry for Rheumatic Diseases (KRRD), for providing us the needed data.
Disclosure of Interests: None Declared.
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AB0268 IS THERE A CORRELATION BETWEEN PLATELET/ LYMPHOCYTE RATIO AND NEUTROPHIL/ LYMPHOCYTE RATIO AND RHEUMATOID ARTHRITIS ACTIVITY?

Keywords: Biomarkers, Rheumatoid arthritis, Prognostic factors

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease, the evaluation of its activity is based on several scores, including the DAS28, which is the most frequently used. In recent years, platelet to lymphocyte ratio (PLR) and neutrophil to lymphocyte ratio (NLR) have become markers of systemic inflammation.
Objectives: Evaluate the correlation of RPL and RNL with disease activity in patients followed for RA.
Methods: Retrospective study conducted in the rheumatology department between 2007-2021, including patients followed for RA. Demographic, clinical, biological data and RA activity indices were collected from patient records. The RNL and the RPL were obtained by dividing the neutrophil and platelet levels respectively by the lymphocyte level.
Results: Were included 260 patients followed for RA, the average age was 49.91 ± 12.96 years, with a female predominance of 86.9%. Structural damage was noted in 84.8% of patients. RA was seropositive for ACPA in 82.9% of cases and 77.5% for rheumatoid factor. The mean RPL and RNL were 163.32 and 2.88 respectively. The mean DAS28-CRP was 5.26 ±1.42. A highly significant correlation was found between RPL and CRP and sedimentation rate (p<0.0001, P<0.001 respectively). RNL was also correlated with ESR (P: 0.005) and CRP (p=0.0001). RPL was significantly correlated with DAS28-CRP (p=0.032), unlike RNL (p=0.36). No correlation was noted between these two ratios and age, sex, BMI and comorbidities.
Conclusion: In recent years, RNL and RPL have emerged as markers of systemic inflammation. Our results are consistent with data from the literature.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0269 RHUMATOID FACTORS ISOTYPES DIAGNOSTIC SENSITIVITY AND SPECIFICITY IN RHUMATOID ARTHRITIS PATIENTS IN TUNISIA

Keywords: Rheumatoid arthritis, Biomarkers, Diagnostic tests

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Background: Rheumatoid factor (RF) is a well-established marker for the diagnosis and classification of rheumatoid arthritis (RA). Most studies have evaluated IgM RF or isotype-nonspecific total RF tests.
Objectives: We evaluated the importance of rheumatoid factor isotype in this study.
Methods: An international cohort consisting of samples from 52 RA patients and 57 patients suffer from other rheumatologic deseases were tested for IgA, IgM and IgG RF. Clinical and biological data were collected.
Results: IgM, IgA, and IgG were positive in RA patients 96,15%, 88,46% and 17,3% respectively. The sensitivity of IgG RF for the diagnosis of RA was the lowest 16,7%, IgA RF sensitivity was lower than IgM RF (87,8% vs 95,9%). The specificity of IgM, IgA and IgG RF for the diagnosis of RA were (29,8 %vs 61,4 %vs 89,4% respectively). Double positivity for RF IgM and RF IgA had a higher specificity for RA than RF IgM or RF IgA (92.6% vs. 29,8% vs 89,4%). However, combined positivity for IgA RF, IgM RF, and IgG ACPA had higher specificity and lower sensitivity for RA classification than positivity for either antibody.
Conclusion: IgA RF showed lower sensitivity than IgM RF. The combination of IgA RF with IgM RF and ACPA did not improve the sensitivity of RA classification. Combined positivity (IgA-RF/IgM-RF/ACPA) increased specificity.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0270 DESIGN OF A PROSPECTIVE MULTI-NATIONAL CROSS-SECTIONAL STUDY ON SCREENING FOR INTERSTITIAL LUNG DISEASE (ILD) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) GUIDED BY RISK FACTORS

Keywords: Real-world evidence, Rheumatoid arthritis, Lungs

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Background: ILD is a significant complication of RA, but diagnosis of RA-ILD is often delayed as respiratory symptoms do not develop until the disease is advanced. Several risk factors for the development of ILD in patients with RA have been identified. Screening tools are required to facilitate earlier detection of RA-ILD in clinical practice.
Objectives: The aim of this prospective cross-sectional study is to develop and validate a multivariable prediction model for RA-ILD screening based on risk factors.
Methods: Investigators will enrol consecutive patients diagnosed with RA who have ≥2 of the following risk factors for ILD: male; current or previous smoker; age ≥60 years at RA onset; high-positive rheumatoid factor and/or anti-cyclic citrullinated peptide (titre >3 x upper limit of normal); high RA disease activity score (based on DAS-28, SDAI, CDAI, RAPID-3, PAS, or PAS-II) ≤12 months prior to screening; presence or history of extra-articular manifestations of RA (vasculitis, Felty's syndrome, secondary Sjögren's syndrome, cutaneous rheumatoid nodules, serositis, and/or scleritis/uveitis). Patients previously identified as having ILD, or who have had a high-resolution computed tomography (HRCT) scan in the prior 2 years, will not be eligible. Patients will undergo an HRCT scan, which will be assessed centrally by two thoracic radiologists. Data will be collected on demographic and RA-related characteristics, patient-reported outcomes, comorbidities and pulmonary function. It is planned that up to 1200 patients will be enrolled at approximately 30 sites in the USA, UK, Germany, France, Italy, Spain.
Results: The results of this study will elucidate the prevalence of RA-ILD, and of features of RA-ILD on HRCT, in the study population and enable development of a probability score for RA-ILD based on a multivariable model incorporating risk factors. The performance, area under the receiver operating characteristic (ROC) curve, sensitivity, specificity and predictive value of the model for predicting the presence of RA-ILD on HRCT (yes/no) will be reported.
Conclusion: The results of this prospective multi-national cross-sectional study will enable development of a screening tool for RA-ILD, guided by risk factors, to identify patients with RA who should be screened for ILD using HRCT.
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AB0271 PREDICTIVE FACTORS OF CARDIAC IMPAIRMENT IN RHEUMATOID ARTHRITIS

Keywords: Imaging, Heart, Comorbidities

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Background: In view of the insidious and serious nature of cardiac involvement in rheumatoid arthritis (RA), systematic screening for these diseases and the identification of risk factors is of paramount importance in order to preserve and improve patients' quality of life and life expectancy.
Objectives: The objective of our study is to determine the predictors of cardiac involvement.
Methods: We performed a cross-sectional study conducted in Taher Sfar Hospital, Mahdia, Tunisia. Each patient underwent a transthoracic echocardiography (TTE) coupled with Strain technique. The comparison between a quantitative variable and a qualitative variable was made by the "Student's t" test if the quantitative variable follows the normal law, if not, the "Mann-Whitney" test was used. The multivariate study was done by binary logistic regression. A p value <0.05 was considered statistically significant.
Results: Seventy-two patients with RA were included in our study. There was a clear female predominance with a sex ratio of 0.07. The mean age of RA patients was 52.9 ± 11.72 years [21-75 years]. The mean duration of disease progression was 12.4 ± 9.9 years [6 months-40 years]. The means of DAS 28 (CRP), DAS 28 (ESR) and HAQ score were respectively 3.4 ± 1.4 [1.2-6.7]; 3.9 ± 1.4 [1.4-7.4] and 0.9 ± 0.7 [0-2.5]. 51.4% of patients had an increased ESR and 37.5% of cases had an increased CRP (CRP>6). Corticosteroid therapy was used in 94.4% of patients with a mean duration of 5.9 ± 5.2 years [1-20 years], methotrexate (MTX) in 98.6% of patients with a mean duration of 8.1 ± 6.9 years [1-40 years] and biotherapy in 19.4% of cases. Rheumatoid factor was positive in 51.7% of cases and ACPAs were positive in 73.3% of cases. TTE revealed abnormalities in 58 patients (80.6% of cases). Echocardiographic impairments were dominated by valvular involvement (45.8%), followed by subclinical left ventricular myocardial damage assessed by the Global Longitudinal Strain (GLS) method (37.5%), Left ventricular diastolic dysfunction (36.1%), Left ventricular hypertrophy (22.2%), pericardial effusion and pulmonary arterial hypertension (2,8%). The bivariate analysis found a statistically significant relationship between echocardiographic damage and disease activity ($p<0.01$), the number of painful joints ($p<0.01$), the functional impact of the disease (HAQ) ($p=0.01$), the importance of the CRP level ($p<0.01$) and the use and dose of corticosteroid therapy ($p=0.02$; $p=0.01$). The multivariate study showed only one significant association between echocardiographic involvement and disease activity ($p = 0.03$; OR = 1.8; CI [1.04-3.3]).
Conclusion: Our study proved an association between cardiac involvement and disease activity. Therefore, early and appropriate management of RA may decrease the risk of cardiac impairment.
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AB0272 INSUFFICIENCY OF VITAMIN D AS A PREDICTOR OF RHEUMATOID ARTHRITIS SEVERITY

Keywords: Prognostic factors, Vitamin D, Rheumatoid arthritis

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Background: The main function of VitD was historically linked with Ca/P03 metabolism and bone homeostasis, but recent research data have shown its major role in modulating the immune system. Taking into consideration the expression of the vitamin D receptor (VDR) and 1a-hydroxy- lase on dendritic cells, monocytes, macrophages, neutrophils, natural killer cells and B and T cells, VitD regulates both innate and adaptive immunity. It has been proposed, that VitD suppresses autoimmunity by different mechanisms and there is a growing interest in the role of VitD deficiency in the etiopathogenesis of RA and worst prognosis. With all this mentioned above in mind, it is clear that deficit of VitD has the potential to contribute to severity and progression of RA.
Objectives: The aim of this study is to evaluate VitD levels among patients with RA, investigate corelations between VitD levels and RA activity.
Methods: 47 patients with mean age of 52±9,8 were included in this study. All patients fulfilled EULAR/ACR 2010 classification criteria for rheumatoid arthritis.

Disease activity was measured with help of DAS28. All patients were examined using the same protocol, ESR, CRP and VitD level were assessed. 51 healthy patients with the same statistical data were included in the control group.

Results: 68,085% of examined patient were female and 31,91%- male. Duration of the RA at the moment of the study was 5,2±8,1 years and mean DAS28 score was 4,8±1,02. According to our study significant negative correlation between levels of VitD and DAS28 score was found (p=0,02), correlations between CRP, ESR were also found, but the results were not significant. The mean VitD level in patient group was 13,3± 8,5 ng/mL and in control group 38,4±2,6 ng/mL. The difference of VitD levels between groups was significant (p<0,05).

Conclusion: According to our data, levels of VitD are lower among patients with RA, especially among patients with high activity. Taking that into consideration, the levels of VitD should be assessed in patients with RA and insufficiency of VitD should be corrected in the course of Ra treatment.

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AB0273 INTERSTITIAL MATRIX DESTRUCTION IS A CENTRAL PATHOLOGICAL FEATURE OF RHEUMATOID ARTHRITIS

Keywords: Disease-modifying drugs (DMARDs), Rheumatoid arthritis, Biomarkers

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Background: The interstitial matrix is the ground substance of all connective tissues, such as bone, skin, tendons, internal organs, and ligaments[1]. Type I collagen (COL1) is not only the most abundant protein, but also crucial for tissue integrity and stability as it act as the skeletal network of most organs. COL1 is organized in fibrils and connecting other extracellular matrix proteins to form a dynamic tissue. In bone, COL1 is 80% of the total protein amount and 95% of the total collagen amount, and thereby bone is by far the most COL1 rich tissue[1]. Matrix metalloproteinase (MMP) driven COL1 degradation is a central feature of in the pathogenesis of rheumatoid arthritis (RA) resulting in the release of C1M into the circulation. The common soluble biomarkers in RA are measures of inflammatory factors such as CRP, thus there is room for blood-based biomarkers reflecting tissue destruction.

Objectives: MMP-mediated tissue destruction may be a central part of inflammatory disorders, albeit overlooked. The biomarker C1M was developed more than a decade ago[2]. C1M originates from soft tissue turnover (from the action of MMP-2, -9, and -13[2]), not bone, thus very different from the bone degradation biomarker CTX-I. The aim was to review the literature to provide an overview on the potential context of use of assessing MMP-mediate COL1 degradation in RA, according to the FDA BEST guidelines[3].

Methods: PubMed and google scholar were searched for full-text original articles in English using the keywords C1M, biomarker, and rheumatoid arthritis. The search period was set to 2011 to 2022, included. Also, we limited the included articles to those assessing blood levels of C1M in clinical RA samples and animal models, thus excluding articles assessing the biomarker assessed in cell cultures or in silico models.

Results: 396 titles were identified of which 14 were full text, English written articles. The figure provides the main conclusions of the 14 articles. C1M was 2-4 times elevated in patients with RA compared to healthy donors or to patients with undifferentiated arthritis (UA) and is increased in a rat model of RA (orange box). C1M release is inhibited by biologics, such as anti-IL6 receptor, anti-TNFs, and Jak inhibitors, and was shown to be associated with disease activity (blue box). C1M was predictive of treatment response (purple box) and associated with disease progression (green box).

Conclusion: MMP-mediated COL1 degradation was more than 100% elevated in RA, suggesting that tissue destruction is actively ongoing in these patients. Tissue destruction was prognostic for further joint damage. Only those treatments that strongly inhibited this tissue destruction was efficacious. In alignment, changes in tissue destruction were predictive for efficacy.

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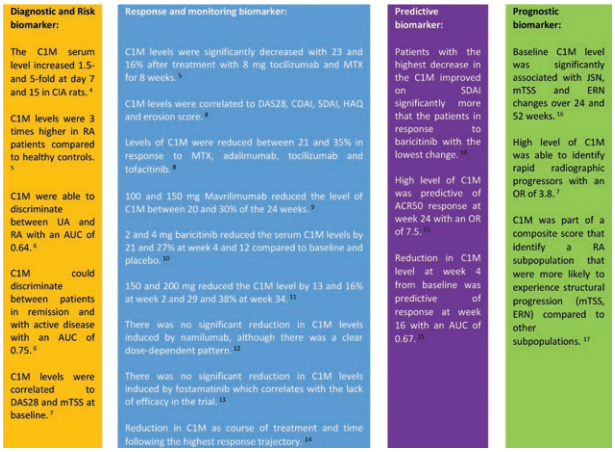


Figure 1.

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AB0274 EFFECT OF RHEUMATOID ARTHRITIS ON BONE MINERAL DENSITY AND ITS RELATIONSHIP WITH INFLAMMATORY MILIEU IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Osteoporosis, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is an inflammatory disorder, associated with significant systemic and local bone loss. Factors determining bone mineral (BM) loss in rheumatoid arthritis (RA) are important. This study aimed to determine the occurrence and predictors of low bone mineral density (BMD) in patients with RA.

Objectives: To estimate Bone Mineral Density in patients with Rheumatoid arthritis. To determine the frequency and risk factors for osteopenia/osteoporosis in patients with Rheumatoid arthritis.

Methods: We studied 102 RA patients diagnosed using ACR/EULAR 2010 at our Rheumatology clinic in Jodhpur, India from January 2021 to August 2021 after written informed consent and Ethical Committee approval. We collected the clinical, demographic, treatment history and calculated disease severity with Disease Activity Score (DAS28 CRP) and Clinical Disease Activity Index (CDAI). BMD was assessed (Dual-energy X-ray absorptiometry scanner-Hologic Corp, model no-Horizon A S/N 303237M). Serum samples for Interleukin-1 (IL-1) and Interleukin 6 (IL-6) were collected and stored at -80^{0}C and analysed by ELISA.
Results: In the study population, with mean age of 46.7±12.3 years, median disease duration of 48±36 months, mean DAS28 CRP score of 4.5±1.2, mean CDAI value of 18.6±8.58 prevalence of osteopenia and osteoporosis calculated using T score were found to be 43.1% and 15.7% at left hip, 42.2% and 16.7% at lumbar spine, 18.6% and 17.6% at left forearm respectively(Table 1, Figure 1). There was significant variation in BMD across various age categories at lumbar spine (P value-0.031) and left forearm (P value < 0.0001). There was statistically significant reduction in BMD with higher disease activity at hip (p value-0.019), however significance was not observed at lumbar spine and forearm. There was no significant association between BMD and CDAI. There was statistically significant difference in the lumbar spine BMD across the DAS 28 CRP <3.2 and DAS 28 CRP >3.2 subgroup. Lower values of BMD were observed in female patients, RF positive patients and established RA patients but these were not statistically significant. There was no association between Serum vitamin D3 levels, cumulative steroid dose, Interleukin-1 levels, Interleukin-6 levels, IL-17 levels, TNF α levels, Serum Osteoprotegerin (OPG) levels, Serum Receptor activator of nuclear factor kappa-B ligand (RANKL) levels and BMD.
Conclusion: Prevalence of osteopenia and osteoporosis and magnitude of bone mineral loss is significantly higher in our population compared to previous Indian studies including Sharma et al [1]. This lower BMD may be partially attributed to lower remission rates and low BMI in our study population. Hip joint appears to be particularly vulnerable to bone loss in those with higher disease activity suggesting that local effects maybe more important in bone loss. This observation is also supported by the finding that serum inflammatory markers or bone loss markers did not have a significant relationship to bone mineral density in our population.
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Table 1. Prevalence of osteopenia/osteoporosis at different sites in RA patients

BMD category (Based on T score)	Left Hip (N=100)	Lumbar spine (N=99)	Left forearm (N=98)
Normal	40 (40%)	39 (39.4%)	61 (62.2%)
Osteopenia	44 (44%)	43 (43.4%)	19 (19.4%)
Osteoporosis	16 (16%)	17 (17.2%)	18 (18.4%)

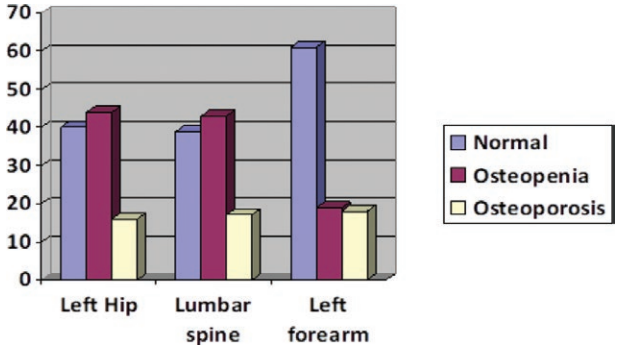


Figure 1. Prevalence of osteopenia/osteoporosis at different sites in RA patients

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AB0275

SERUM LEVELS OF HOMOCYSTEINE, LEPTIN AND NEOPTERIN AS MARKERS OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

Keywords: Biomarkers, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic, systemic disorder characterized by the presence of many proinflammatory cytokines that have been involved in the pathogenesis, comorbidity, and premature mortality, due to increased atherosclerotic heart disease[1]. homocysteinemia is an independent risk factor for coronary heart disease, stroke, and an independent predictor for cardiovascular mortality in atherosclerotic patients.[2] leptin is a component of cytokines that mediates immune response and plays an important role in the T-cell related inflammatory process.[3] Neopterin is a pteridine derivative produced by monocytes and macrophages primarily as a response to interferon-gamma stimulation induced by the activation of the cellular immune system.(4)
Objectives: To investig the relationship between serum levels of homocysteine, leptin and neopterin and clinical & laboratory parameters of disease activity in patientes with rheumatoid arthritis.
Methods: This study included 80 RA patients and age& sex-matched 80 healthy controls. RA patients were divided into two groups (A&B) depending on the presence or absence of Extra-articular manifestations. There was 40 with Extra-articular manifestations (9 patients with Cutaneous vasculitis, 7 with Nodules, 6 with Neuropathy, 5 with Reynaud's phenomenon,7 with secondary sjogren, 2 with Fealty's syndrome, 2 with Interstitial nephritis, 2 with Interstitial lung disease).
Results: In the RA group (A+B), mean serum homocysteine, leptin and neopterin levels were (11.79 + 8.72 µmol/L), (22.43 ± 7.37 ng/ml) & (3.83±1.84 nmol/L) respectively with No statistically significant difference was found between RA and control groups regarding serum Leptin (p=0.674). While a significant difference was found between RA and control groups regarding serum Neopetrin (< 0.001) & homocysteine. (< 0.001). Also, In RA groups (A, B) there was a statistically significant difference regarding serum Neopterin (p< 0.03) and DAS 28 ESR (p< 0.05). there was a Positive significant correlation between serum (neopterin - Hcy) and ESR, TNF-α, IL-6, and DAS-28 (p < 0.05) while no significant correlation was found between serum (neopterin- homocysteine) and CRP (p > 0.05).
Conclusion: Serum leptin cannot be considered of value as an marker of disease activity in RA patients. Serum neopterin can be used as a sensitive marker for assaying inflammation and disease activity in RA patients while serum homocysteine can be used as a predictor of RA extra articular complications.
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AB0276

NAILFOLD VIDEO CAPILLAROSCOPY SUPPORT THE DIAGNOSIS OF OVERLAP CONNECTIVE TISSUE DISEASE: A PILOT STUDY IN A SAMPLE OF RHEUMATOID ARTHRITIS PATIENTS

Keywords: Diagnostic tests, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease characterized by arthritis and a range of extra-articular organ involvement. Altered microcirculation is an important contributor to the inflammatory reaction characterizing RA and is involved in synovitis and systemic organ manifestations[1]. Nailfold video capillaroscopy (NVC) is a reliable, safe and highly sensitive method for evaluating the morphology of microcirculation and detailed alterations[2].

Objectives: The objective of the study was to evaluate the microcirculation in adult RA patients by using NVC and to identify morphological and quantifiable NVC parameters with possible correlations with clinical and laboratory findings.

Methods: NVC was performed at baseline on 8 fingers of both hands of 25 RA patients (EULAR/ACR 2010 criteria) (mean age 68.57±13.47 years, mean disease duration 14.6±8.6 years)[3]. Different NVC parameters indicating microvascular damage were detected and analyzed, such as microvascular architecture, capillary morphology and loss of capillaries (linear/mm). The results were categorized into "non-scleroderma" pattern, such as "normal" and "non-specific alterations", as well as "scleroderma" and "scleroderma-like" pattern. The RA patients were treated (at the time of the analysis) with low dose glucocorticoids, NSAIDs and cDMARDs (see Table 1). Statistical analysis was performed by non-parametric tests.

Results: The patient's mean age at the time of NVC was 62.68±12.68 years and they consisted mostly of women (84%). The caucasian cohort was composed of 56% seropositive RA patients, all of which were RF positive (100%) and 71.43% also presented anti-CCP positivity. Nine patients (36%) were affected by Raynaud phenomenon. Eighty-four percent of RA patients (84%) presented together with normal capillaries a varying degree of microvascular nonspecific findings, like tortuosity, capillary crossing as well as some abnormal shapes (ramified capillaries). Interestingly, "Early" scleroderma NVC pattern was observed in 1 patient (4%), showing giant capillaries and microhaemorrhages. "Scleroderma-like" capillaroscopic pattern was found in 2 patients (8%) with the following features: dilatations, giant capillaries, microhaemorrhages, abnormal capillary shape with ramifications and reduced mean capillary number per linear mm. NVC observation of "Early" scleroderma pattern and "Scleroderma-like" pattern in 3 patients (12%), suggested the coexistence of an overlap syndrome (most likely MCTD), also supported by clinical and autoantibodies specificities. No specific RA NVC pattern was detectable. No statistically significant correlations were found between different NVC parameters and autoantibodies or specific RA clinical features.

Conclusion: The results of present study confirm in sample size that a specific NVC pattern is not detectable in RA, even in early RA patients. The presence of specific patterns, like "Early" scleroderma NCV pattern and "scleroderma-like" pattern, suggest in those "RA patients" the presence of an overlap syndrome. The inclusion of the NVC analysis in patients affected by autoimmune connective tissue diseases (like RA) may contribute to a better definition of the diagnosis, especially in presence of complex clinical symptomatology (overlap syndromes).

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Table 1. Demographic and clinical characteristics of RA patients

	n. 25
female/male	21/4 (5.25:1)
current age (years, mean±SD)	68.56 (13.47)
age at diagnosis (years, mean±SD)	53.96 (14.48)
seropositive RA	14 (56%)
FR+	14/14 (100%)
ACPA+	10/14 (71.43%)
ANA+	7 (28%)
ENA+	2 (8%)
Raynaud phenomenon	9 (12%)
NVC performed at diagnosis	5 (20%)
Therapy at NVC baseline	
NSAIDs	2 (8%)
glucocorticoids	19 (76%)
cDMARDs	19 (76%)

NSAIDs: non-steroidal anti-inflammatory drugs;cDMARDs: conventional disease-modifying antirheumatic drugs.

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AB0277 WHAT IS THE LINK BETWEEN LUNG INVOLVEMENT AND ANTI-CCP ANTIBODIES IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE STUDY

Keywords: Rheumatoid arthritis, Lungs

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Background: Rheumatoid arthritis (RA) is chronic inflammatory rheumatism responsible for joint destruction and also a systemic disease. Pulmonary involvement is one of the most common extra-articular manifestations of RA and it is associated with a poor prognosis. Several studies have demonstrated an association between the occurrence of RA and the positivity of anti-cyclic citrullinated peptide antibodies (anti-CCP), an immunological biomarker that is used to evaluate the disease activity in RA patients.

Objectives: The objective of this study was to investigate the link between anti-CCP and lung damage in patients with RA.

Methods: The study was a retrospective analysis that included 407 patients who were followed for RA between January 2011 and March 2022. Data were collected from the medical records of the patients, and analyzed using statistical test such chi-squared, Fisher's exact test and t-test. The level of significance was set at p=0.05.The study design included a thorough data cleaning process.

Results: The mean age of patients (n=407) was 58.86 years ± 12.441 with a sex ratio of 6 (F/M). The median duration of evolution was 14 ± 7.523 years, 16% of patients were hypertensive and 19.5% were diabetic RA was erosive in 87.2% of patients, rheumatoid factor (RF) was positive in 85% of patients, and anti-CCP was positive in 64.9% of patients. The mean RF level was 165.8982 ± 278.49, and the mean anti-CCP level was 224.26 ± 440.18. Pulmonary involvement was present in 14.5% of patients, with a restrictive pattern seen on pulmonary function tests in 40.4% of cases, and rheumatoid nodules, diffuse interstitial lung disease lesions, and bronchiectasis seen on thorax CT scan in 67.2%, 31.6%, and 25.9% of cases respectively. The study found that anti-CCP was positive in 96.6% of patients with lung involvement, compared to those without lung involvement, with a statistically significant difference (p<0.001). This suggests that a high anti-CCP level may be a risk factor for pulmonary involvement in RA patients.

Conclusion: The study demonstrated the positive association between anti-CCP and the existence of pulmonary involvement in RA, which is consistent with data from the literature. It's important to note that this study is a retrospective one and further studies with larger population and different design are needed to validate the findings.

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Disclosure of Interests: None Declared.
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AB0278 PERIPHERAL MICROANGIOPATHY ASSESSED WITH VIDEO-CAPILLAROSCOPY IS ASSOCIATED WITH SURROGATE MARKERS OF ACCELERATED ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis

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Background: Rheumatoid Arthritis (RA) is characterized by increased risk for cardiovascular disease [1]. Microvascular dysfunction often coexists with or even precedes macrovascular disease, possibly due to common mechanisms of vascular damage, such as inflammatory processes and oxidative stress [1, 2].

Objectives: To investigate the correlation between microcirculatory changes and markers of atherosclerosis in patients with RA.

Methods: The study evaluated the structural capillaroscopic parameters using video-capillaroscopy (NVC). Applying the tonometry method, the augmentation index (Aix) was calculated, as well as its adjustment to a heart rate of 75 (Aix75). Additionally, pulse wave velocity (PWV), and mean intima-media thickness (cIMT) of the two common carotids, as well as central systolic and diastolic blood pressure (cSBP, cDBP), were calculated in each patient.
Results: A total of 32 patients with a mean age of 63.06±11.05 years were studied. At the same time, the existence of ramified capillaries was significantly correlated with PWV (r=0.38, p=0.032), while the existence of crossed capillaries was inversely correlated with cSBP (r=-0.43, p=0.014). Based on the measurements performed in each capillary, a significant correlation was found between the internal capillary diameter and cSBP (r=0.36, p=0.043). In 16 patients the subpapillary venous plexus was visible and this finding was significantly correlated with the mean value of left cIMT (p=0.005).
Conclusion: The findings of this small study indicate an association between NVC alterations and markers of atherosclerosis in patients with RA.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0279 FACTORS AFFECTING QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Quality of life

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Background: Rheumatoid Arthritis (RA) has an important impact on patients 'quality of life (QoL), affecting both physical and mental domains of well-being.
Objectives: This study aims to assess the QoL of RA patients based on the Short Form Health Survey-36 (SF-36) questionnaire and to evaluate the associated factors.
Methods: This is a cross-sectional study including patients with RA disease. Each patient answered to the SF-36 Questionnaire assessing quality of life, which evaluates 8 domains: physical functioning (PF), bodily pain (BP), role limitations due to physical health problems (RP), role limitations due to personal or emotional problems (RE), mental health (MH), social functioning (SF), energy/fatigue or vitality (VT), and general health perceptions (GH).
Results: We included 78 patients with a mean age of 52.9±11.3 years and a female preponderance (88.5%). The mean duration of disease progression was 11.1±9.5 years. The average of patient global health, numbers of swollen and tender joints were respectively 51.4 ± 2.2, 3.7± 3.2 and 8.6 ± 7.6. Two thirds of patients had moderate to severe disease activity (DAS 28 >3.2). The mean Health Assessment Questionnaire (HAQ) was 1.3 ± 0.8. Hospital Anxiety and Depression Scale (HADS) showed that 16.7% of patients had anxiety and 18% had depression. The SF-36 global score was 52.3 ± 24.8 [15.5-92.8] with an impaired QoL (SF-36 <66.7) in 51 (65.4%) patients. Among the eight domains, the most affected domain was the "role limitations due to physical health problems" (RP) with a mean of 45.4±20.3. Impaired QoL was associated with disease activity parameters: number of swollen joints (p<0.01), number of tender joints (p<0.01), patient global health (p=0.02) and DAS 28 score (p<0.01). Patients with high functional disability (HAQ ≥ 1), high scores of depression and anxiety had poor quality of life (p<0.01). No significant associations were found between QoL and age, gender or duration of disease activity.
Conclusion: RA has a significant physical, psychological and social impact on affected patients. This impairment of QoL was associated with disease activity, functional impact and psychological disorders. Therefore, it is necessary to improve these parameters for a better management of the disease.
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AB0280 PREGNANCY, BIRTH OUTCOMES, AND BREASTFEEDING IN CHRONIC RHEUMATIC DISEASES WOMEN

Keywords: Pregnancy and reproduction

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Background: Parenthood is usually challenging in chronic rheumatic diseases, such as rheumatoid arthritis (RA) and spondyloarthritis (SpA). It seems to be affected by the disease state and pharmacological therapies [1,2].
Objectives: We aimed to assess pregnancy, birth, and breastfeeding outcomes in patients with RA and SpA.
Methods: We conducted a cross-sectional study including patients followed for RA or SpA. We collected the following data: age, disease duration, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels, disease activity was assessed using DAS28 score for patients with RA and ASDAS-CRP scores for patients with SpA. We asked patients about their pregnancies, birth outcomes, and breastfeeding. Statistical analysis was performed using SPSS software.
Results: Forty-six women were included. They were 23 RA patients and 23 SpA patients. The mean age was 50.2 ± 13.1 years. The mean disease duration was 9.64 ± 8.27 years. The mean ESR and CRP levels were 40.45 ± 33.12mm and 15.22 ± 24.21 mg/L. The mean DAS28-ESR and ASDAS-CRP were 5.25 + 1.21 and 2.7 + 0.6, respectively. Forty-one women were married, 3 were divorced and 2 were widows. The mean age at the marriage was 24.9 + 6.66 years. Half of the patients had suffered from infertility (n=23). Eight of them never had kids (17%). The mean numbers of gestation and parity were 3 + 2 [0-7] and 2+ 1 [0-6], respectively. Seven patients discontinued their treatment to get pregnant without discussing it with their rheumatologists (15%). Only 6 patients had complications during their pregnancies (16%). Complications were abortion in 5 cases and preeclampsia with premature birth in one case. Twenty-five patients gave natural vaginal birth (66%), 7 patients gave birth by C-section (18%), and 6 patients needed obstetrical forceps to give birth (16%). Two patients had a post-partum hemorrhage. The mean term birth was 39.18 ± 1.44 weeks of amenorrhea. Thirty-four patients had breastfed the children (74%). The mean breastfeeding duration was 13.76 ± 8.8 months. Eight patients reported impairment of breastfeeding due to their diseases (21%). Birth with cesarean section was associated with a younger age at the onset of the disease (32.75 ± 5.73 vs 43.16 ± 10.3 years, p=0.031). DAS28-ESR and ASDAS-CRP were higher in patients who had cesarean section but the difference was not significant (DAS28: 5.12 ± 0.45 vs 4.34 ± 0.79, p=0.08; ASDAS: 3.04 ± 0.9 vs 2.59 ± 0.6, p=0.3). Furthermore, younger age was associated with impaired breastfeeding (39.4 ± 9.23 vs 56.11 ± 11.27 years, p=0.01). Discontinuing the treatment was associated with infertility (p=0.003), a younger age of the patient (40.8 ± 7.82 vs 51.33 ± 14.47 years, p=0.002), older age at the marriage (34 ± 6 vs 23.21 ± 5.02 years, p=0.042), and higher CRP (22.08 ± 27.58 vs 8.18 ± 8.36 mg/L, p=0.04).
Conclusion: Our results are consistent with other studies [2], caesarean section rates seem to be high in RA and SpA patients [3]. Strikingly, our youngest patients were the ones that discontinued their treatment to get pregnant. This highlights the importance of informing and discussing pregnancy with patients with chronic inflammatory diseases.
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AB0281 THE ALBUMIN LEVEL AND THE ACTIVITY OF RHEUMATOID ARTHRITIS, WHAT CORRELATION?

Keywords: Rheumatoid arthritis, Descriptive studies

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Background: Inflammation during rheumatoid arthritis (RA) can cause changes in the serum levels of certain proteins, including albumin. Our study aims to find a link between albumin level and disease activity.
Objectives: The objective of our study was to study the correlation between the albumin level and the indices of RA activity.
Methods: Descriptive and comparative study including patients with RA between 2007 and 2021.
Statistical data analysis was performed using SPSS version 20 software.
The correlation between albumin level and RA activity indices was assessed using Pearson's correlation coefficients (p-values).
Results: 260 patients were included. The average age was 49.91 years, with a female predominance in 86.9% of cases. The average duration of evolution was 4.64 years. Chronic polyarthritis was the most frequent mode of revelation (74.2%), it was deforming in 64.1% of cases. Structural damage was present in 84.8% of patients, RA was seropositive for ACPA in 82.9% and seropositive for RF in 77.5% of cases. The mean ESR and CRP levels were 44.08 mm/h and 32.68 mg/l respectively. Hypoalbuminemia was found in 41.1% of patients with an average albuminemia of 36.5 ± 6.78 g/l. The mean DAS28-CRP was 5.26 and the mean CDAI was 35.75. Patients with severe activity had more frequent hypoalbuminemia than those with moderate and low activity (67% vs 22% and 7%). A significant negative correlation was found between the albumin level and the DAS28 - CRP (r= -0.24, p=0.003), on the other hand the CDAI score was not correlated with the albumin level (r= -0.22, p=0.16). There is a significant correlation between albumin level, CRP level and ESR (r=-0.27,p=0.001, r=-0.27, p=0.001).
Conclusion: These results suggest that the albumin level could provide additional information on the intensity of inflammation in RA.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0282 NEW INFLAMMATORY MARKER IN RHEUMATOID ARTHRITIS: NEUTROPHIL/LYMPHOCYTE RATIO (NLR)

Keywords: Rheumatoid arthritis, Biomarkers

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Background: Although neutrophils and lymphocytes play well-established roles in the pathogenesis of Rheumatoid arthritis (RA), their count is most often ignored by clinicians. However, the neutrophil/lymphocyte ratio (NLR) seems to be of great value in the evaluation of disease activity.
Objectives: Our objective is to determine the interest of this ratio and to study its relationship with the other parameters of RA activity.
Methods: Cross-sectional study of 70 patients followed for RA. We performed a biological check-up including a complete blood count (CBC), an ESR and CRP level. A NLR was calculated for each patient.
Results: There were 58 women (82.9%) and 12 men (17.1%) with a mean age of 54.7 ± 13.6 years [19-82]. The mean duration of the disease was 10.1± 9.9 years. Sixteen patients (22.8%) had recent RA (<2 years). The mean DAS 28 ESR was 5.38± 1.48. Thirty-nine patients (55.7%) had high disease activity. The average of ESR and CRP were 59 mmH1± 35 [12-150] and 30.3 mg/l ± 28.6 [0-159], respectively. Anemia of inflammation was observed in 43.3% of cases. Lymphopenia was found in 28.6% of cases, neutropenia in 1.4% and neutrophilic polynucleosis in 17% of cases. The mean of neutrophil/lymphocyte ratio was 3.62±2.68 [0.48-13.26]. It was 3.7 in patients with severe activity and 3.5 in those with low to moderate activity. Statistical analysis found a significant association between this ratio (NLR) and anemia (p=0.003), ESR (p=0.005), CRP (p=0.038) and disease activity assessed by DAS 28 ESR (p=0.04).
Conclusion: Despite the fact that in RA there are few studies evaluating the interest of the NLR, our study concludes that this ratio is considered as an alternative inflammatory biomarker that could be used to assess the disease activity.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0283 THE IMPACT OF POLLUTION ON DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS: A 112 PATIENT GROUP STUDY

Keywords: Rheumatoid arthritis, Prognostic factors, Geographical differences

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Background: Air pollution is incriminated in a large number of respiratory and cardiovascular pathologies. More recently, the role of particulate matter from pollution has been studied in autoimmune diseases and in particular in rheumatoid arthritis (RA).
Objectives: The objective of our study is to evaluate the impact of air pollution measured by the air quality index (AQI) on different disease parameters during rheumatoid arthritis.
Methods: We included in this study 112 patients with seropositive rheumatoid arthritis, residing in different regions of southern Morocco. Inclusion criteria were: established rheumatoid arthritis, duration of residence exceeding one year in the same region. Exclusion criteria were: specific professional exposure to industrial pollutants and passive and active smoking. The air quality was evaluated by the new ATMO index which classifies the air quality in five levels: Good, average, degraded, bad, very bad and extremely bad according to the concentration of the four air pollutants. The following parameters were collected: duration of disease progression, age, number of exacerbations per year, the mean DAS 28 CRP during the last year, the mean CRP during the last year, the use of analgesics, the number of hospitalizations, an univariate and multivariate analysis evaluating the association and the correlation with the different parameters was carried out by the SPSS 2021.
Results: 112 patients were included. The female sex represents 66%. The different regions included in the study were: Marrakech in 68 cases with an AQI of 47, Safi in 9 cases with an AQI of 21, Beni Mellal in 6 cases with an AQI of 29, Sidi Rehal in 1 case with an AQI of 1, Demnate in 2 cases with an AQI of 29, Ouarzazate in 4 cases with an AQI of 25, Azilal in 10 cases with an AQI of 34, Zagora in 4 cases with an AQI of 21, Youssoufia in 1 case with an AQI of 9, Guelmim in 7 cases with an AQI of 17, Semara in 1 case with an AQI of 46. The average DAS 28 was 3.11. The mean CRP was 23.1 mg/l. The average number of hospitalizations during the last year was 2.5. The average number of exacerbations in the last year was 5.6. The use of level 1 analgesic was noted in 22%, level 2 in 13%. A positive correlation was found between the number of exacerbations and AQI (p 0.001, rs 0.67), CRP and AQI (p 0.013, rs 0.71).
Conclusion: The associations between rheumatoid arthritis and air pollution seem complex, it can be considered as a risk factor aggravating rheumatoid arthritis, and these hypotheses have to be demonstrated on a larger sample.
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AB0284 EVALUATION OF THE RELATIONSHIP BETWEEN SERUM NETRIN-1 LEVEL AND PATIENT CHARACTERISTICS IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis

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Background: Although many predictors have been proposed to predict rheumatoid arthritis (RA) disease activity, most of these markers are not specific to RA and their levels can be affected by many other factors. The need for ideal markers to predict disease activity in RA continues. The association of netrin-1 with RA disease activity has not been evaluated before.

Objectives: This study aimed to investigate the plasma levels of the netrin-1 molecule in RA patients and its relationship with RA disease activity.

Methods: Sixty RA patients and 41 age and sex-matched healthy volunteers were included in this study. An ELISA kit (Elabscience, Texas, USA; catalog number: E-EL-H2328; lot number: GZWTKZ5SWK) analyzed by quantitative sandwich enzyme immunoassay method was used to calculate netrin-1 values. Disease Activity Score-28 (DAS-28) and Clinical Disease Activity Index (CDAI) were calculated to measure disease activity, and Rheumatoid Arthritis Disease Impact (RAID) score was calculated to measure disease-related deterioration in the quality of life.

Results: Netrin-1 serum levels were similar in RA and healthy controls (respectively, 64.4 [35.8-551.4] and 65 [35.8-436.6], p:786). No significant correlation was found between levels of Netrin-1 and DAS-28-CRP, DAS-28-ESR, CDAI, and RAID scores (p>0.05).

Conclusion: Netrin-1 is not elevated in RA patient serum and its levels are not correlated with RA disease activation scores.

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Table 1. The relationship between disease activity, treatment status, and serum Netrin-1 levels

Netrin-1 level, pg/mL, median (min-max)	DAS28 disease activity				p
Control (n=41)	Remission (n=35)	Low (n=11)	Moderate (n=11)	High (n=3)	
65 (35.8-436.6)	67.7 (38.1 – 551.4)	61.2 (35.9 – 305.6)	60.8 (36.2 – 133.5)	70.6 (52.3 – 187.1)	0.809
	CDAI disease activity				**p**
Control (n=41)	Remission (n=17)	Low (n=24)	Moderate (n=14)	High (n=5)	
65 (35.8-436.6)	54.1 (38.1 – 501.9)	87.5 (35.9 – 551.4)	58.4 (41.6 – 133.5)	73.1 (41.8 – 187.1)	0.240
	Treatment status				**p**
Treatment naïve (n=5)	cDMARD alone (n=43)		bDMARD with or without cDMARD (n=12)		
70.6 (46.9 – 501.9)	57.3 (35.9 – 551.4)		71.3 (41.8 – 273.4)		0.735

DAS28: Disease Activity Score 28, CDAI: Clinical Disease Activity Index, cDMARD: conventional disease-modifying rheumatic drug, bDMARD: biologic disease-modifying rheumatic drug, tsDMARD: target specific disease- modifying rheumatic drug

Table 2. Netrin-1 levels in RA patients according to clinical characteristics

		n	Netrin-1, pg/mL, median (min-max)	p
Gender	Female	42	71.8 (35.9-501.9)	0.302
	Male	18	55.0 (36.3-551.4)	
Seropositivity	Seropositive	44	64.4 (35.9-551.4)	0.757
	Seronegative	16	65.5 (38.1-273.4)	
RF positivity	Absent	31	61.1 (35.8-551.4)	0.819
	Present	29	67.6 (32.3-501.9)	
Anti-CCP positivity, n	Absent	45	70.5 (35.8-551.4)	0.453
	Present	15	57.3 (36.3-305.6)	
Interstitial lung disease, n	Absent	56	61.0 (35.9-501.9)	0.083
	Present	4	284.4 (41.8-551.4)	
Lung nodules	Absent	55	61.2 (35.9-551.4)	0.402
	Present	5	75.3 (41.8-295.4)	
Hand deformity	Absent	21	60.1 (35.8-305.6)	0.361
	Present	37	70.5 (38.5-551.3)	

RA: rheumatoid disease, RF: rheumatoid factor; anti-CCP: anti-citrullinated peptide

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Disclosure of Interests: None Declared.

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AB0285 MANAGEMENT OF ATLANTO-AXIAL SUBLUXATION IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Rheumatoid arthritis, Prognostic factors, Disease-modifying drugs (DMARDs)

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Background: Recent studies have shown that around 86% of Rheumatoid Arthritis (RA) have cervical spine involvement [1]. The synovial inflammation in the upper cervical spine causes instability. Atlanto-axial subluxation (AAS) is the most frequent injury of the cervical spine in RA.

Objectives: Our study aimed to assess the medical management of AAS in our RA patients.

Methods: We conducted a retrospective, monocentric study, including patients fulfilling the ACR/EULAR 2010 criteria for RA. All patients had a confirmed AAS on MRI of the cervical spine findings. Disease activity was assessed using the disease activity score 28 (DAS-28). Treatment received by each patient, before and after the occurrence of AAS, was noted.

Results: We included 19 patients with a confirmed AAS. The mean age was 62±14.91 years. Male to female ratio was 0.5. The mean disease duration was 19.27±8.04 years. RA was erosive in all patients and immunopositive in 87% (n=13). When AAS occurred, twelve patients were on csDMARDS. The mean DAS28 ESR was 5.25±1.1. According to DAS28ESR, high disease activity was noted in 10 patients (66.7%). Methotrexate was the most frequent treatment used (n=9, 60%). An association of Methotrexate and sulfasalazine was prescribed in 5 cases (33%). Two patients were using leflunomide. Three patients were on bDMARDS. Nine patients (60%) received bolus steroid therapy. These patients had a vascularized synovial pannus on MRI findings. Four patients remained on the same DMARDs. An association of sulfasalazine to methotrexate was performed in 6 patients. A change from csDMARDs to bDAMRDs was undergone in only two patients (from sulfasalazine to rituximab, and from leflunomide to etanercept). A switch of bDMARDs was performed in three patients: from infliximab to rituximab in one case, and from rituximab to tocilizumab in two others. Surgical treatment was indicated in three patients for neurological complications, but the patients did not agree to proceed with the surgery.

Conclusion: AAS is a potentially lethal complication of RA. The use of bolus steroid therapy can be handy to reduce acute inflammation. However, adjustment of DMARDs is needed to better control RA activity and to slow its progression.

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Disclosure of Interests: None Declared.

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Rheumatoid arthritis - comorbidity and clinical aspects

AB0286 **RETENTION RATE OF BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH DECREASED KIDNEY FUNCTION: RESULTS FROM THE IORRA COHORT**

Keywords: Disease-modifying drugs (DMARDs), Safety, Rheumatoid arthritis

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Background: We previously reported that rheumatoid arthritis (RA) patients with chronic kidney disease (CKD) were at increased risk of failure to achieve remission and of occurrence of hospitalized infections [1]. Although biologic disease-modifying anti-rheumatic drugs (bDMARDs) are a promising treatment option, their effectiveness and safety for this population have not been fully evaluated to date.

Objectives: To determine the optimal bDMARD selection for treatment of RA patients with decreased kidney function, we compared the retention rates of patients receiving tumor necrosis factor inhibitor (TNFi), interleukin-6 inhibitor (IL-6i), and abatacept (ABT) in RA patients using data from the IORRA cohort, the real-world data registry of Japanese RA patients.

Methods: Renal function was calculated using the Japanese versions of the equations for estimated glomerular filtration ratio (eGFRcr). Deceased renal function was defined as $eGFR_{Cr}$ <60 mL/min/1.73m^2. Among RA patients enrolled in the IORRA cohort between 2003 and 2020, data from patients with decreased kidney function who started bDMARDs were extracted. Renal function and use of bDMARDs by the extracted patients were identified in their medical records. Reasons for discontinuation were classified as ineffectiveness, adverse events caused by bDMARDs, or other reasons. Retention rates due to ineffectiveness or adverse events caused by TNFi (adalimumab or adalimumab biosimilar [ADA], certolizumab pegol [CZP], etanercept or etanercept biosimilar [ETN], golimumab [GLM], infliximab or infliximab biosimilar [IFX]), IL-6i (tocilizumab [TCZ], sarilumab [SAR]) and ABT spanning 36 months were calculated using the Kaplan-Meier method, and adjusted hazard ratio [aHR] of discontinuation of each bDMARD was calculated using the Cox proportional hazard model, with adjustments for age, sex, disease duration, clinical disease activity index (CDAI), methotrexate (MTX)/ prednisolone (PSL) use, and previous bDMARD use at baseline.

Results: A total of 238 treatment courses administered to 191 patients with decreased renal function were included. Median $eGFR_{Cr}$ was 52.5 mL/min/1.73m^2 (interquartile range: 43.3–57.4). The numbers of bDMARD users were as follows: TNFi, 143 (ADA, 15; CZP, 5; ETN, 67; GLM, 30; IFX, 26); IL-6i, 59 (all were TCZ); and ABT, 36, respectively. ABT users were older than IL-6i users, and TNFi users had higher $eGFR_{Cr}$ and a higher proportion of MTX and previous DMARD use than the other groups. Sex, seropositivity, CDAI, health assessment questionnaire, and the proportion of PSL use were similar between groups. The retention rates at 36 months were 59.9%, 72.9%, and 61.7% for TNFi, IL-6i, and ABT, respectively. aHR of discontinuation when TNFi served as reference was 0.60 (95% confidence interval: 0.32–1.10) for IL-6i, and 0.85 (95% confidence interval: 0.44–1.64) for ABT.

Conclusion: Because the retention rate of IL-6i was numerically high compared with TNFi and ABT in this study, IL-6i may offer a treatment advantage in RA patients with decreased renal function.

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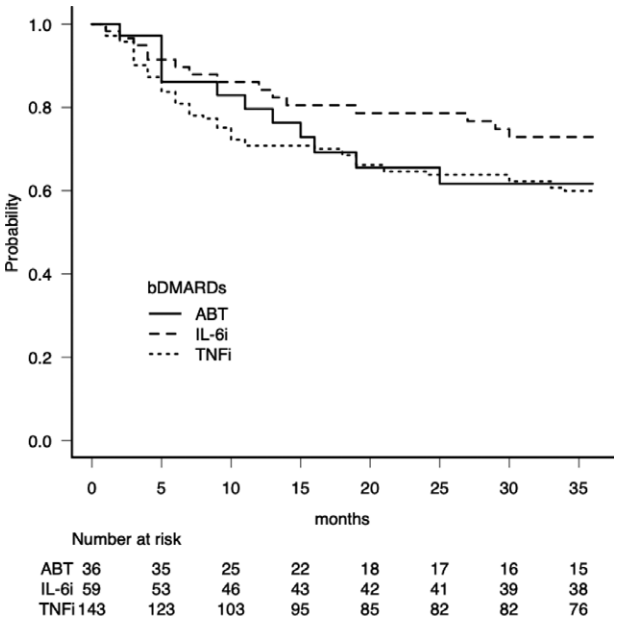


Figure 1. The Kaplan-Meier curve of the retention rates of bDMARDs in patients with RA with decreased renal function.

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AB0287

RHEUMATOID ARTHRITIS PATIENTS WITH INTERSTITIAL PNEUMONIA NEED APPROPRIATE TREATMENT ENHANCEMENT TO RECOVER FROM FRAILTY: A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY

Keywords: Rheumatoid arthritis, Comorbidities, Lungs

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Background: Frailty is a common geriatric syndrome that embodies an elevated risk of catastrophic health and physical function declines among older adults [1]. Rheumatoid arthritis (RA) is an autoimmune disease that causes synovitis in the joints, resulting in joint deformity with a high prevalence (0.5-1.0% in Japan) [2]. Japan is one of the world's most rapidly aging societies [3], and older RA patients are generally at a greater risk of frailty than the general population. Most patients with comorbidities such as pulmonary, renal, and liver dysfunction are more prone to become frailty in the short term than healthy people [4], as well as poor control of disease activity in RA patients [5]. Against this background, the present study aimed to investigate factors associated with frailty in RA patients, including their comorbidities.

Objectives: This study investigates factors associated with frailty in RA patients.

Methods: 656 RA patients were evaluated from our observational study data in 2022. Of the patients, 152 were frailty, and 504 were not frailty assigned to the frailty group and the non-frailty group, respectively. Both patient characteristics were compared in univariate analysis. The factors associated with frailty were assessed by logistic regression analysis. As a sub-analysis, patients who have Interstitial pneumonia (IP) history and patients who do not were assigned to the IP (n =102) and non-IP (n =554) groups, respectively, to clarify differences between both groups.

Results: The frailty group was older (mean: 73.6 vs. 66.8 years) and had a higher DAS28-ESR (mean: 3.67 vs. 2.66) than the non-frailty group. DAS28-ESR (OR: 1.85, P<0.001) and IP history (1.74, P =0.043) were associated with frailty (Table 1). The IP group was older (mean: 73.3 vs. 67.5 years), had a higher DAS28-ESR (mean: 3.30 vs. 2.80) (Figure 1 A), a higher HAQ-DI (mean: 0.32 vs. 1.19) (Figure 1 B), lower use of methotrexate (MTX) (26,5 vs. 62.9%), and higher use of steroid (44.1 vs. 26.8%) than the non-IP group. There was no difference in the use of biological and targeted synthetic disease-modifying antirheumatic drugs (b/ts-DMARDs) between both groups (38.3 vs. 37.3%) (Figure 1 C). The IP group had a higher frailty proportion than the non-IP group (20.6 vs. 37.3%) (Figure 1 D).

Conclusion: DAS28-ESR and IP history were associated with frailty in RA patients. Most RA patients with IP had frailty with insufficient treatments, i.e., low use of MTX, high use of steroid, and low use of b/ts-DMARDs. They might recover from frailty through appropriate control of disease activity using b/ts-DMARDs, which are easy to use for patients with comorbidities.

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Table 1. Predictors of Frailty progression for in RA patients with pre-frailty.

Factor	Odds ratio	P value
Age (years)	1.03 (1.01-1.06)	< 0.001
Sex, female	0.90 (0.54-1.48)	0.666
Duration of disease (years)	1.03 (1.00-1.05)	0.034
BMI (kg/m2)	1.00 (0.95-1.06)	0.933
Steinbrocker stage	1.03 (0.83-1.28)	0.818
Steroide use	1.33 (0.85-2.08)	0.206
Methotrexate use	0.95 (0.61-1.48)	0.815
Interstitial pneumonia	1.74 (1.02-2.99)	0.043
DAS28-ESR	1.85 (1.55-2.21)	< 0.001

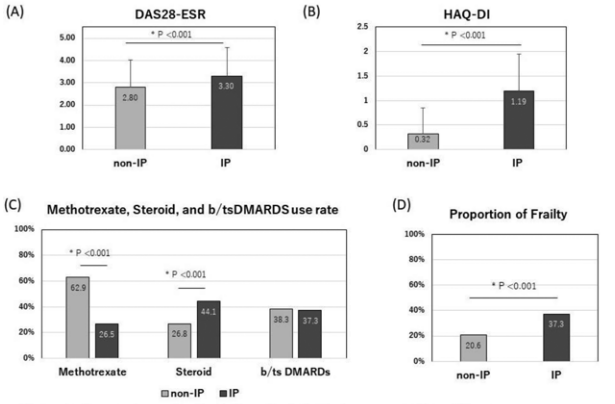


Figure 1: Comparison of patient characteristics between non-IP and IP groups. A p-value <.05 was considered statistically significant and was represented as an asterisk (*)

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AB0288

COMORBIDITY CLUSTERS IN PATIENTS WITH RHEUMATOID ARTHRITIS ARE ASSOCIATED WITH DISEASE ACTIVITY AND PREDICT SURVIVAL PROGNOSIS

Keywords: Prognostic factors, Rheumatoid arthritis, Comorbidities

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Background: Comorbidities are common in patients with rheumatoid arthritis (RA), but there is little information regarding distinct comorbidity patterns in patients with RA and how these patterns impact disease activity and mortality.

Objectives: To examine clusters of patients with RA based on comorbidities, the association between these clusters and RA disease activity, and their impact on mortality.

Methods: In this retrospective, population-based study, residents of a geographically well-defined area with prevalent RA on 1-1-2015 were identified. Patients were followed for vital status until death, last contact or 12-31-2021. Clinical Disease Activity Index (CDAI) was obtained from the medical visit closest to the prevalence date (±1 year). Diagnostic codes were retrieved for 5 years prior to the prevalence date. Using 2 codes ≥30 days apart, 55 comorbidities were defined. Latent class analysis (LCA) was used to cluster patients based on comorbidity patterns with the optimal number of clusters determined by Bayesian Information Criteria. Standardized mortality ratios (SMR) were used to assess differences in mortality across the clusters.

Results: A total of 1643 patients with prevalent RA (72% female; 94% white; median age 64 years, median RA duration 7 years) were studied. Comorbidities were present in 1548 (94%) of the subjects with 5+ comorbidities present in 980 (59%) subjects. LCA identified 4 clusters of patients. Although only comorbidities were used in the LCA, the clusters differed by age, sex, number of comorbidities, smoking status, body mass index (BMI) and RF/ anti-CCP positivity (Table 1). Cluster 1 (n=686) included younger patients who were less likely to smoke and had fewer comorbidities compared to other clusters. In contrast, cluster 4 (n=134) included older patients with 6+ comorbidities who were more likely to have smoked. Cluster 2 (n=200) included younger patients with 6+ comorbidities and high prevalences of depression and obesity, while cluster 3 (n=623) included the remaining patients with 3+ comorbidities consisting mainly of hypertension, hyperlipidemia and back pain). Cluster 1 had no increased mortality based on US lifetables (SMR 0.8; 95% confidence interval [CI: 0.55-1.1). Cluster 4 had the worst survival (SMR 3.5; 95% CI 2.8-4.4). Cluster 2 also had poor survival (SMR 1.6; 95% CI 1.03-2.2), while the poor survival in cluster 3 was less pronounced (SMR 1.2; 95% CI 0.99-1.4). Data on CDAI were available on 725 patients who were mostly like those without CDAI except they were slightly younger (mean age 62 vs 64 years), fewer ever smoked (51% vs 58%) and more were seropositive (71% vs 63%) compared to those without CDAI. CDAI differed across the clusters (p<0.001) with the highest proportion of remission in Cluster 1 and the lowest proportion of remission and the largest proportion of high disease activity in Cluster 2.

Conclusion: Clustering of patients with RA based on comorbidity profiles identified distinct groups exhibiting different prognosis. This demonstrates comorbidities congregate in some patients, leading to poor prognosis, while others

experience fewer comorbidities and better survival than people without RA. The cluster with both better survival and more remission despite a high proportion of seropositivity is intriguing.

Table 1. Characteristics of four clusters of patients with RA

Characteristic	C1 (N=686)	C2 (N=200)	C3 (N=623)	C4 (N=134)	p value
Age, years	55 (46, 63)	60 (51, 68)	72 (63, 78)	77 (71, 82)	< 0.001
Female sex	75%	86%	64%	66%	< 0.001
RF/anti-CCP positive	70%	62%	64%	65%	0.073
RA duration, years	6 (3, 12)	5 (3, 11)	8 (3, 17)	9 (4, 21)	< 0.001
BMI, kg/m^2	27 (24, 33)	31 (27, 35)	29 (25, 34)	28 (25, 34)	< 0.001
Ever smoker	50%	60%	57%	62%	0.005
Number of comorbidities					< 0.001
0-2	43%	0%	0%	0%	
3-5	43%	0%	29%	0%	
6+	4%	100%	71%	100%	
Disease activity	N=327	N=94	N=260	N=44	
CDAI	4 (1, 13)	11 (6, 20)	8 (3,13)	7 (4, 13)	<0.001
Remission (≤2.8)	40%	11%	26%	25%	
Low (>2.8 to 10.0)	29%	36%	38%	39%	
Moderate (>10.0 to 22.0)	19%	31%	23%	20%	
High (>22.0)	12%	22%	13%	16%	

Values in the table are median (25th, 75th %ile) or %

REFERENCES: NIL.

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AB0289 FACTORS ASSOCIATED WITH DEVELOPMENT OF MENTAL ILLNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING BIOLOGICAL AND TARGETED SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS: A POPULATION-BASED STUDY

Keywords: Targeted synthetic drugs, bDMARD, Mental health

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Background: Rheumatoid arthritis (RA) is a leading chronic inflammatory systemic disease worldwide, and increasing evidence have shown under-recognised impacts on mental health. However, the assessment and management of mental health is somehow not included in the T2T despite increasing evidence have shown that mental illnesses, particularly depression and anxiety, were not only highly prevalent in patients with RA but also associated with control of disease activity. In the present study, we used a population-based database with 10,852 patients with RA who had initiated biollogical or targeted synthetic disease modifying antirheumatic drugs (b/tsDMARDs) thereapy to address the incidence of mental illness and to investigate risk factors for mental illness.

Objectives: This population-based study aim to address the incidence and risk factors of mental illness among patients with RA starting b/tsDMARDs therapy.

Methods: We used the 2001–2020 Taiwanese National Health Insurance Research Database to identify patients with RA receiving b/tsDMARDs. The primary outcome was newly developed mental illness, including anxiety and mood disorders, among spouses. We performed a Cox regression analysis to determine factors associated with mental illness. The results were presented as hazard ratios (HR) with 95% confidence interval (CI).

Results: We enrolled 10,852 patients with RA and had received b/tsDMARDs. Of them, 7,854 patients received tumor necrosis factors inhibitors (etanercept n=3,322; adalimumab n=2,689; golimumab n=1,346; certolizumab n=490; infliximab n=7), 1,693 patients received non-TNFi bDMARDs (tocilizumab n=856; abatacept n=837), and 1,305 patients were treated with tsDMARD (tofacitinib n=1,192; barticitinib n=113). We found that 13.62% of enrolled patients developed mental illness, with the incidence was 4,054 per 100,000 person-year. Those receiving tocilizumab (aHR 0.65, 95%CI 0.51–0.82), Abatacept (aHR 0.69, 95%CI 0.55–0.87) and tsDMARDs (aHR 0.59, 95%CI 0.47–0.73) had a lower risk of mental illness compared with receiving TNFi. We also found that old age (aHR 1.02, 95%CI 1.01–1.02), low income (aHR: 1.16, 95% CI: 1.04–1.29), use of cyclosporine (aHR: 1.20, 95% CI: 1.05–1.38), and use of steroid higher than 5 mg/day (aHR: 1.23, 95% CI: 1.02–1.48) correlated with incident mental illness.

Conclusion: This population-based study investigated the incidence and risk factors of mental illness among the patients with RA receiving b/tsDMARDs. Our findings highlight the need for vigilance of mental illness in patients with RA.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0290 EFFECT OF FILGOTINIB ON PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS IN THE PHASE 3 FINCH 1, 2 AND 3 STUDIES

Keywords: Clinical trials, Rheumatoid arthritis, Pain

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Background: Patients (pts) with rheumatoid arthritis (RA) often experience substantial pain despite treatment, and pain control is considered an important treatment outcome. The FINCH 1–3 studies demonstrated the efficacy and acceptable safety of the preferential Janus kinase (JAK) 1 inhibitor filgotinib (FIL) in pts living with RA.

Objectives: This *post-hoc* analysis of the FINCH studies assessed specific effects of FIL on pain.

Methods: FINCH 1–3 (NCT02889796, NCT02873936, NCT02886728) were Phase 3, randomized, double-blind trials of FIL 100 mg and 200 mg (FIL100/200). In FINCH 1, pts with an inadequate response (IR) to methotrexate (MTX) received FIL, adalimumab (ADA) or placebo (PBO) + MTX for 52 weeks. In FINCH 2, pts with an IR to biologic disease-modifying anti-rheumatic drugs (DMARDs) received FIL or PBO + conventional synthetic DMARDs for 24 weeks. In FINCH 3, MTX-naïve pts received FIL ± MTX or MTX for 52 weeks. For each treatment group, pts reported pain on a 100-mm visual analog scale (VAS). Scores of ≤10 mm reflected limited to no pain; scores of ≤20 mm indicated health status was not negatively affected by pain.[1] Time to first VAS score of ≤10 mm was assessed. The proportion of pts who achieved remission (as per Disease Activity Score 28 with C-reactive protein [DAS28-CRP] <2.6 or Clinical Disease Activity Index [CDAI] ≤2.8) at Week 24 was evaluated. Of pts who achieved DAS28-CRP or CDAI remission, the proportion who also reported VAS pain scores of ≤10 mm or ≤20 mm was determined.

Results: In FINCH 1, there was a higher probability of achieving a VAS pain score of ≤10 mm with FIL200, vs ADA + MTX or PBO + MTX; responses were better or comparable with FIL100 vs other treatment arms (**Figure 1**). Similar findings were observed in FINCH 2 and 3 for FIL vs PBO and MTX, respectively. In FINCH 1, the proportion of pts achieving DAS28-CRP remission was greater with FIL200 + MTX (48.4%) and comparable for the FIL100 + MTX (35.2%) vs ADA + MTX arms (35.7%; **Table 1**). Further, the proportion of pts who achieved VAS pain scores of ≤10 mm and ≤20 mm in addition to DAS28-CRP remission was 26.3% and 35.8%, respectively, in the FIL200 + MTX group, compared with 17.2% and 24.6% in the ADA + MTX group (**Table 1**). In FINCH 2 and 3, a

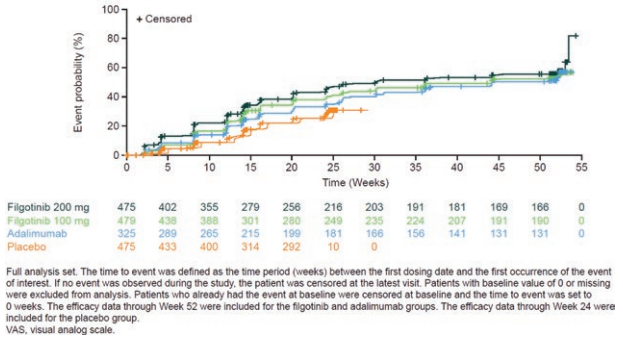
greater proportion of pts in the FIL groups achieved remission vs the PBO or MTX arms, respectively. A greater proportion of pts achieved pain responses in addition to DAS28-CRP remission in the FIL groups of FINCH 2 and FINCH 3 compared with PBO or MTX, respectively. Findings were similar when CDAI remission was assessed.

Conclusion: FIL positively affected pain parameters across the FINCH studies as early as Week 2, with responses sustained over time (up to Week 52 [FINCH 1 and 3] and Week 24 [FINCH 2]). In FINCH 1, FIL200 had a particularly favorable impact when pain response and remission were assessed together. Similar findings were seen with FIL compared with PBO and MTX in FINCH 2 and 3, respectively. These findings suggest that JAK inhibition may offer potential added value with respect to patient-reported pain outcomes when treat-to-target goals are met.

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Figure. Cumulative incidence of time to first VAS pain score ≤10 mm in FINCH 1



Full analysis set. The time to event was defined as the time period (weeks) between the first dosing date and the first occurrence of the event of interest. If no event was observed during the study, the patient was censored at the latest visit. Patients with baseline value of 0 or missing were excluded from analysis. Patients who already had the event at baseline were censored at baseline and the time to event was set to 0 weeks. The efficacy data through Week 52 were included for the filgotinib and adalimumab groups. The efficacy data through Week 24 were included for the placebo group.
VAS, visual analog scale.

Table 1. Disease response and improvement in VAS pain score (up to Week 24)

	FINCH 1			
	FIL200 + MTX (n=475)	**FIL100 + MTX (n=480)**	**ADA + MTX (n=325)**	**PBO + MTX (n=475)**
DAS28-CRP remission	230 (48.4)	169 (35.2)	116 (35.7)	77 (16.2)
With VAS ≤10 mm	125 (26.3)	86 (17.9)	56 (17.2)	36 (7.6)
With VAS ≤20 mm	170 (35.8)	120 (25.0)	80 (24.6)	55 (11.6)
	FINCH 2			
	FIL200 + MTX (n=147)	**FIL100 + MTX (n=153)**	**PBO (n=148)**	
DAS28-CRP remission	45 (30.6)	40 (26.1)	18 (12.2)	
With VAS ≤10 mm	23 (15.6)	19 (12.4)	8 (5.4)	
With VAS ≤20 mm	32 (21.8)	27 (17.6)	10 (6.8)	
	FINCH 3			
	FIL200 + MTX (n=416)	**FIL100 + MTX (n=207)**	**FIL200 (n=210)**	**MTX (n=416)**
DAS28-CRP remission	225 (54.1)	88 (42.5)	89 (42.4)	121 (29.1)
With VAS ≤10 mm	138 (33.2)	57 (27.5)	49 (23.3)	62 (14.9)
With VAS ≤20 mm	169 (40.6)	64 (30.9)	68 (32.4)	79 (19.0)

ADA, adalimumab; DAS28-CRP, Disease Activity Score-28 with C-reactive protein; FIL(100/200), filgotinib (100/200 mg); MTX, methotrexate; PBO, placebo; VAS, visual analog scale.

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AB0291

QUICK ATTAINMENT OF LOW DISEASE ACTIVITY LESSENS THE DISEASE BURDEN OF RHEUMATOID ARTHRITIS IN THE LONG TERM, EVEN WHEN A TREAT-TO-TARGET APPROACH IS APPLIED

Keywords: Patient reported outcomes, Rheumatoid arthritis, Treat to target

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Background: Treat-to-target (T2T) strategies in early rheumatoid arthritis (RA) are aimed at achieving sustained remission or low disease activity. Remission and low disease activity are both associated with improved clinical outcomes and patient-reported outcomes (PROs). However, it is currently unknown if achieving sustained remission in the first year improves long-term PROs in RA.

Objectives: To examine associations between functional ability, health-related quality of life, pain and depression over 1-3 years in RA patients who have (1) sustained remission, (2) low disease activity or (3) active disease in the first year after the diagnosis is made.

Methods: We included all RA patients, according to 2010 or 1987 criteria, from the tREACH trial. The tREACH is a multicenter, stratified single blinded trial with a T2T approach, aiming for low disease activity (DAS44 <2.4). Included patients were categorized in 3 groups depending on their DAS44/ESR-3 items (DAS), thus not including general health, in the first year:

- **Sustained remission**, includes patients who were in remission (DAS <1.6) at the 6, 9 and 12 month visit;
- **Low disease activity**, includes patients who had low disease activity (DAS ≤2.4) at 6, 9 and 12 months and did not fit in the sustained remission group;
- **Active disease**, includes patients who had an active disease (DAS >2.4) at least at 6 and 9 months, 6 and 12 months or 9 and 12 months.

Functional ability was measured with the Health-Assessment Questionnaire – Disability Index (HAQ-DI). Health-related quality of life (HRQoL) was measured with the Short form-36 (SF-36). Pain was measured with a 10-point Likert scale and depression was measured with the Hospital Anxiety and Depression Scale (HADS). Linear mixed models from 1-3 years, with gender, initial treatment, DAS and baseline PRO score as covariates, were used to compare PROs over time.

Results: We included 304 RA patients (61% female) of whom 90 (30%) had sustained remission, 148 (49%) low disease activity and 66 (22%) active disease. RA patients with active disease were, compared to the low disease activity and remission groups, more often female (79% vs 65% vs 42%) and had more tender joints (median 14 (IQR 9-21) vs 8 (IQR 5-14) vs 5 (IQR 2-10)) and a higher baseline DAS (mean 3.6 (sd 0.8) vs 3.1 (sd 0.8) vs 2.8 (sd 0.9)). After 15 months all 3 groups had a mean DAS <2.4 (Figure 1A). Nevertheless, RA patients in the active disease group continued to have more functional limitations and pain during 1-3 years of follow-up compared to the other groups, respectively low disease activity (β -0.35 (95% CI -0.47, -0.23), p<0.001 for HAQ-DI and β -0.91 (95% CI -1.42, -0.39), p=0.001) for pain) and remission (β -0.42 (95%CI -0.57, -0.28), p<0.001 for HAQ-DI and β -1.26 (95% CI -1.86, -0.66), p<0.001) for pain) (Figure 1B-C). No differences were seen in depression scores and mental health items over time. However, at baseline, a higher proportion of RA patients in the active disease group (26%) had a score suggestive of the presence of depression (HADS >7) compared to the low disease activity (18%) and sustained remission (13%) groups (Figure 1D). HRQoL was comparable to the general Dutch population after 1 and 3 years of follow-up, except for patients with an active disease (Figure 1E-F).

Conclusion: Failure to achieve remission or low disease activity in the first year after RA diagnosis is associated with persistent functional impairment and pain, despite the T2T approach that aims for low disease activity.

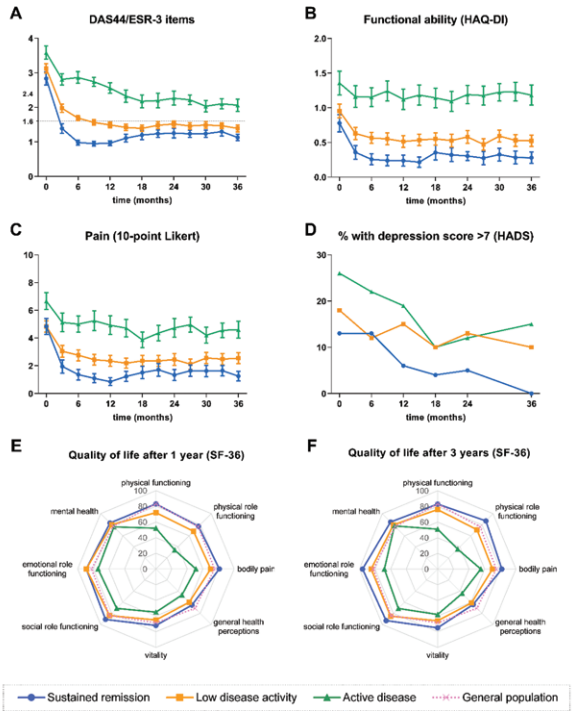


Figure 1. (A) DAS-44 3-items, **(B)** Functional ability and **(C)** Pain scores over 3 years per group, **(D)** Percentage of patients who have depression scores >7 per group, **(E)** 1 year and **(F)** 3 year HRQoL scores, measured with the SF-36 domains, for disease activity groups and compared with the general Dutch population norms

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0292 A CROSS-SECTIONAL STUDY OF THE CENTRAL SENSITIVITY SYNDROME USING THE CENTRAL SENSITIZATION INVENTORY IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Pain

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Background: Despite having low levels of inflammation, 47.3% of patients with rheumatoid arthritis (RA) continued to report moderate-to-high pain and fatigue [1], indicating that chronic pain can interfere with disease activity assessment. And chronic pain have linked to central sensitization syndromes (CSSs) of pain [2]. The central sensitization inventory (CSI) is a valid and reliable tool for detecting CSS, its severity, and associated syndromes [3]. However, there have been few reports of CSS in patients with RA being analysed with CSI.
Objectives: This study aims to conduct a cross-sectional analysis of CSS in RA patients using the CSI and investigate the relationship with disease activity.
Methods: We performed a retrospective, cross-sectional study on 269 consecutive RA patients (70 males and 196 females; mean ± SD = 69.9 ± 12.2 years, range: 27–92 years; mean ± SD, disease duration: 12.9 ± 10.4 years, range: 0–55 years; mean ± SD DAS28CRP: 1.89 ± 0.78; range: 0.99–4.88). Patients were evaluated by the CSI; clinical and laboratory examinations were performed on all patients on the same day. SJC, TJC, CRP, ESR, PtVAS, pain VAS, DAS28CRP, DAS28ESR, HAQ-DI, and CDAI were compared in the "CSS group (CSI ≧ 40)" and the "non-CSS group (CSI < 40)" [4]. Furthermore, the relationship between each parameter and the CSI was also investigated.
Results: CSI had a mean ± SD of 18.4 ± 14.6. CSI ≥ 40 was found in 9.6% (26 patients). The number of PtGA, pain VAS, CDAI, and HAQ-DI were all significantly higher in the "CSS group" than in the "non-CSS group" (Table 1). PtGA ($r = 0.352$, $p < 0.001$), pain VAS ($r = 0.369$, $p < 0.001$), CDAI ($r = 0.253$, $p < 0.001$), and HAQ-DI ($r = 0.477$, $p < 0.001$) were all found to have significant correlations with CSI.

Table 1. Compared with CSS group and non-CSS group

	CSS group(n=26) Mean±SD, %	non-CSS group (n=243) Mean±SD, %	*p* value
Disease duration (years)	15.4±11.3	12.6±10.3	0.202
Steinbrocker stage 1 2/3 4(%)	26.9/73.1	45.9/54.1	0.064
Tender joint count (0-28)	0.7±0.9	0.4±0.9	0.054
Swollen joint count (0-28)	0.2±0.5	0.4±1.0	0.389
CRP (mg/dl)	0.38±0.67	0.47±1.02	0.874
ESR (mm)	15.4±16.9	18.0±18.3	0.636
PtGA (VAS/100mm)	37.3±24.2	20.2±23.7	<0.001*
DAS28CRP	2.14±0.80	1.85±0.77	0.068
CDAI	5.23±28.4	3.46±3.82	<0.01*
Pain VAS/100mm	42.1±28.4	19.4±23.2	<0.001*
HAQ-DI	1.41±0.97	0.40±0.64	<0.001*

*significant

Conclusion: In RA patients, CSI was not associated with inflammation (CRP or ESR) but was related to subjective assessment (PtGA or pain VAS), functional impairment, and disease activity (CDAI). CSS may influence disease activity assessment, and CSS treatment may improve functional impairment.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0293 RISK FACTORS ASSOCIATED WITH VENOUS THROMBOEMBOLISM IN RHEUMATOID ARTHRITIS IN CLINICAL PRACTICE

Keywords: Comorbidities, Rheumatoid arthritis

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Background: Increased risk of venous thromboembolism (VTE) has been reported in rheumatoid arthritis (RA) compared to the general population [1]. However, factors associated with the risk of VTE have been barely studied in RA.
Objectives: To identify classical or disease-related risk factors of VTE in RA patients in clinical practice.
Methods: Retrospective observational study performed on all RA patients fulfilling the 2010 ACR/EULAR clarification criteria attending the one-day hospitalization program of the Rheumatology department, Cochin hospital, in 2021. We used the electronic medical report to identify the occurrence of VTE in 2021 and collect RA disease characteristics and risk factors for VTE. Multivariate analysis by logistic regression was performed to determine the factors independently associated with VTE.
Results: We included 317 RA patients (263 females, 83%), with a mean age of 59±14 years and a mean disease duration of 16±14 years. Positive rheumatoid factor and positive anti-CCP antibodies were detected in 255 (80%) and 271 (85%) patients respectively. 190 patients (60%) had erosive disease. The mean DAS28 was 3.5±1.4 and the mean CRP level was 6.8±15.9 mg/L; 161 patients (51%) received corticosteroids (mean dose 3.0±3.5 mg/L), 195 (62%) methotrexate, and 151 (48%) targeted biologic or synthetic DMARDs (b/tsDMARDs), including 60 on TNF-α inhibitors, 34 on rituximab and 27 on JAK inhibitors (10 baricitinib, 7 tofacitinib and 10 upadacitinib). We identified 12 (4%) venous thromboembolic events that occurred in 2021, including 9 PVT and 6 PE (incidence of 3.8 for 100 patient/year). The mean duration between the occurrence and VTE and the visit was 3.6±4.8 months. Among these 12 VTE patients, 9 were women (75%, vs. 97% in patient without VTE, p<0.001), with a mean age of 65±12 years (vs. 59±15, p=0.14). Age >65 years was more frequent in patient with VTE (58%

vs. 33%, p=0.064); 7 (58%) patients with VTE had a history of previous VTE (vs. 3%, p<0.001), 6 (50%) were hospitalized up to 6 months before the event (vs. 6%, p<0.001), 3 (25%) experienced surgery up to 3 months bfore the event (vs. 2%, p<0.001) and 4 (33%) had a history of fracture (vs. 3%, p<0.001). No difference was oberved regarding body mass index, the frequency of smoking, neoplasia, recent travel (up to 3 months) and estrogen/antidepressant therapies. No patient had thrombophilia. Regarding RA characteristics, patients with VTE were more likely to present extra-articular manifestations (67% vs. 33%, p=0.015) and higher CRP levels (20±40 mg/L vs. 6.4±14.5 mg/L, p=0.006). They also received more frequently corticosteroids (83% vs. 50%, p=0.025) and JAKi (25% vs. 8%, p=0.041). Disease duration, autoantibody status, frequency of erosions, DA28 and treatment with methotrexate or bDMARDs did not differ between these 2 groups. Logitic regression analysis identified the following risk factors independently associated with the occurrence of VTE: history of previous VTE, hospitalization up to 3 months before the occurrence of VTE, surgery up to 6 months before the occurrence of VTE and treatment with JAKi (**Table 1**).

Conclusion: History of VTE was identified as the strongest risk factor of the occurrence of VTE. Our results suggest a specific warning on recent hospitalization and surgery as precipitating events to VTE. As recommended by the PRAC JAKi should be used with caution in patients with risk factors for VTE.

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Table 1. results of the logistic regression analysis including VTE as the dependent variable

Variable	Odd ratio (95% CI)	p-value
Age >65 years	0.97 (0.11-8.39)	0.98
Male sex	0.36 (0.02-6.13)	0.48
Extra-articular manifestation	5.86 (0.70-49.16)	0.10
CRP levels	4.41 (0.51-31.28)	0.39
Corticosteroids	3.28 (0.25-42.92)	0.36
JAK inhibitors	7.99, (1.21-81.15)	0.047
History of previous VTE	33.06 (3.57-306.56)	0.002
Hospitalization up to 3 months	15.29 (1.47-159.59)	0.022
Surgery up to 6 months	19.12 (1.23-297.35)	0.035
History of fracture	0.56 (0.07-4.34)	0.58

Acknowledgements: NIL.

Disclosure of Interests: Fiona Oudart: None declared, Marion Thomas: None declared, Alice Combier: None declared, Anna Moltó: None declared, Yannick Allanore: None declared, Jérôme Avouac Speakers bureau: Pfizer, Bristol Myers Squibb, Nordic pharma, Sanofis, Boehringer, Abbvie, Galapagos, Biogen, Fresenius Kabi, Sandoz, AstraZeneca, Lilly, Consultant of: Pfizer, Galapagos, Abbvie, Fresenius Kabi, Bristol Myers Squibb, Grant/research support from: Pfizer, Bristol Myers Squibb, Fresenius Kabi, Novartis, Nordic Pharma, Galapagos.

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AB0294

INFLAMMATION AND IMMUNOMODULATORY THERAPIES INFLUENCE THE RELATIONSHIP BETWEEN ATP-BINDING CASSETTE TRANSPORTER A1 (ABCA1)-MEDIATED CHOLESTEROL EFFLUX AND CORONARY ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Imaging, Cardiovascular disease

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Background: Cholesterol efflux capacity (CEC) measures the ability of high-density lipoprotein (HDL) to remove cholesterol from atherosclerotic plaques. It is mediated by various membrane transporters exporting cholesterol to HDL particles based on their maturation. It is unclear whether CEC associates with coronary atherosclerosis independently of HDL-C levels in RA or whether CEC itself or its impact on atherogenesis are influenced by inflammation or RA-specific therapies. Conventional and biologic DMARDs are atheroprotective while corticosteroids are proatherogenic. ATP-binding-cassette membrane transporter A1 (ABCA1) exports cholesterol to apo A1 or lipid-poor HDL particles.

Objectives: We here explored associations between ABCA1 CEC and coronary atherosclerosis and whether inflammation and disease-specific therapies influence this relationship.

Methods: Coronary atherosclerosis (noncalcified, partially or fully calcified plaque and coronary artery calcium [CAC] score) was evaluated with computed tomography angiography in 140 patients without cardiovascular disease and reassessed in 99 after 6.9±0.4 years. ABCA1 CEC was measured in J774 macrophages as previously described. Multivariable negative binomial regression evaluated associations of ABCA1 CEC with plaque numbers at baseline and follow-up. Robust logistic regression tested the association of ABCA1 CEC with CAC progression (>2.5 U difference in square root CAC scores).

Results: ABCA1 CEC was not associated with baseline atherosclerosis. Inflammation, prednisone, methotrexate or bDMARD use did not influence the relationship between ABCA1 CEC and baseline plaque. However, both baseline and cumulative inflammation modulated the relationship between ABCA1 CEC and plaque progression. Each standard deviation (SD) increase in ABCA1-CEC associated with 41% fewer new plaques in patients with low (<median) baseline ESR but 67% more new plaques in those with high (>median) ESR (p for interaction = 0.015, Figure 1). Likewise, each SD increase in ABCA1 CEC associated with 53% fewer new calcified plaques in patients with low (<median) but not high (>median) time-averaged CRP (p for interaction = 0.028). Higher ABCA1 CEC (per SD) associated with 37% fewer new calcified plaques in baseline prednisone nonusers but not users (p for interaction = 0.021). For time-weighted mean daily prednisone dose, each SD increase in ABCA1 associated with 31% fewer new plaques in unexposed patients (p for interaction vs. high exposure group = 0.034), as well as 53% fewer and 2.4 times more new calcified plaques in the unexposed and high exposure groups respectively (p for interaction unexposed vs. high exposure = 0.004). Higher ABCA1 CEC (per SD) was linked to 2.2 times higher adjusted likelihood of CAC progression in methotrexate nonusers but not in users (p for interaction = 0.018). Likewise, each SD increase in ABCA1 CEC associated with 2.7 times more new plaques in baseline bDMARD nonusers and 35% fewer new plaques in users (p for interaction ≤ 0.001).

Conclusion: ABCA1 CEC attenuated plaque progression exclusively in patients with low baseline and cumulative inflammation as well as in baseline methotrexate and bDMARD recipients. In contrast, ABCA1 CEC associated with plaque progression in baseline corticosteroid recipients and those receiving high time-weighted daily average prednisone dose during follow-up. In uncontrolled or inadequately treated disease ABCA1 CEC fails to counteract and may in fact contribute to the proatherogenic state promoted by inflammation and oxidation. The latter also occurs during treatment with prednisone, known to promote intracellular cholesterol accumulation. When RA is sufficiently treated and controlled, ABCA CEC effectively performs its atheroprotective function.

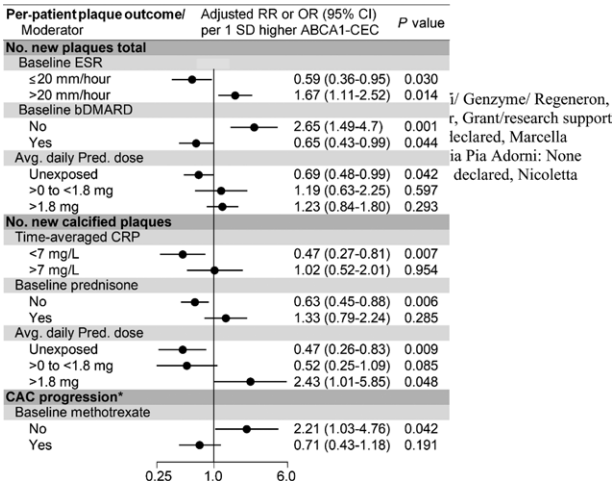


Figure 1. Influence of inflammation and RA therapies on associations of ABCA1 CEC with coronary atherosclerosis progression

REFERENCES: NIL.

Acknowledgements: NIL.

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AB0295

PREVALENCE OF CARDIOVASCULAR DISEASES AND TRADITIONAL CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH RHEUMATOID ARTHRITIS:A REAL-LIFE EVIDENCE FROM BIOSTAR NATIONWIDE REGISTRY

Keywords: Cardiovascular disease, Rheumatoid arthritis

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Background: Patients with rheumatoid arthritis (RA) have increased morbidity and mortality due to cardiovascular (CV) comorbidities.
Objectives: The association of CV diseases (CVD) and traditional CV risk factors have been debated, depending on patient and RA characteristics. This study aimed to find the prevalence of CVD and CV risk factors in patients with RA.
Methods: A multi-center cross-sectional study was performed on RA patients using the BioSTAR (Biological and Targeted Synthetic Disease-Modifying Antirheumatic Drugs Registry). Socio-demographic, clinical, and follow-up data were collected. Patients with and without major adverse cardiovascular events (MACE) were grouped as Group 1 and Group 2. Prevalence rates of CVD and traditional CV risk factors were the primary outcomes. Secondary outcomes were the differences in the clinical characteristics between patients with and without CVD.
Results: We analyzed 724 RA patients with a mean age of 55.1 ±12.8 years. There was a female preponderance (79.6%). The prevalence rate of CVD was 4.6% (n=33). The frequencies of the diseases in the MACE category were ischemic heart disease in 27, congestive heart failure in 5, peripheral vascular disorders in 3, and cerebrovascular events in 3 patients. The patients with CVD (Group 1) were significantly male, older, and had higher BMI (p=0.027, p<0.001, and p=0.041). Obesity (33.4%) and hypertension (27.2%) were the two CV risk factors most frequently. Male sex (HR=0.085, 95% CI:0.028-0.257, p<0.001) and hypertension (HR=4.63, 95% CI:1.251-17.134, p=0.022) were the independent risk factors for CVD.
Conclusion: The prevalence of CVD in RA patients was 4.6%. Some common risk factors for CVD in the general population, including male sex, older age, and hypertension, were evident in RA patients. sex and hypertension were the independent risk factors for developing CVD in patients with RA.

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[2] Charles-Schoeman C, Buch MH, Dougados M, et al. Risk of major adverse cardiovascular events with tofacitinib versus tumour necrosis factor inhibitors in patients with rheumatoid arthritis with or without a history of atherosclerotic cardiovascular disease: a post hoc analysis from ORAL Surveillance. Ann Rheum Dis. 2023;82(1):119-129.

Table 1. Socio-demographic and clinical characteristics of the study groups.

		Overall (n=724)	Group 1 (n=33)	Group 2 (n=691)	p
Age group ‡	<40 years	92 (12.7)	0 (0)	92 (13.3)	0.015
	≥40 years	632 (87.3)	33 (100)	599 (86.7)	
Sex ‡	Male	148 (20.4)	12 (36.4)	136 (19.7)	0.027
	Female	576 (79.6)	21 (63.6)	555 (80.3)	
BMI group ‡	<30 kg/m^2	482 (66.6)	17 (51.5)	465 (67.3)	0.087
	≥30 kg/m^2	242 (33.4)	16 (48.5)	226 (32.7)	
Smoking ‡	Current smoker	101 (14.1)	1 (3.0)	100 (14.7)	0.071
Alcohol ‡	Current consumer	21 (3.0)	2 (6.3)	19 (2.8)	0.248
Educational status ‡	Illiterate/primary	448 (61.9)	22 (66.7)	426 (61.6)	0.865
	High school	202 (27.9)	9 (27.3)	193 (27.9)	
	University or higher	73 (10.1)	2 (6.1)	71 (10.3)	
Comorbidities ‡	Hypertension	197 (27.2)	22 (66.7)	175 (26.6)	<0.001
	Diabetes mellitus	100 (13.8)	12 (36.4)	88 (13.7)	0.001
	Chronic renal failure	23 (3.2)	5 (15.2)	18 (2.9)	0.004
	Dyslipidemia	61 (8.4)	11 (44.0)	50 (11.9)	<0.001
	COPD	39 (5.4)	6 (18.2)	33 (4.8)	0.007
	Coagulopathy	6 (0.8)	3 (10.3)	3 (0.5)	0.002
	Malignancy	12 (1.7)	2 (6.3)	10 (1.6)	0.113
	Valvular heart disease	11 (1.5)	2 (6.1)	9 (1.3)	0.256

†: median (min-max), ‡: n (%)Group 1 and 2: Patients with and without major adverse cardiovascular event (cardiovascular disease).BMI: body mass index, COPD: chronic obstructive pulmonary disease.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0296

THE REAL IMPACT OF DEPRESSION AND ANXIETY ON RHEUMATOID ARTHRITIS PATIENTS: A COHORT STUDY

Keywords: Patient reported outcomes, Quality of care, Health services research

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Background: Rheumatoid Arthritis (RA) patients are more prone to have depression and anxiety compared to the general healthy population. Although it's been increasingly recognised that mental health conditions are associated with higher disease activity and worse disease outcomes, depression and anxiety are not widely considered in routine care of arthritis patients.
Objectives: This study aims to estimate, in a large cohort of Portuguese patients with RA, the prevalence of depression and anxiety and to explore associations with demographic characteristics and disease-related measures.
Methods: We performed a retrospective analysis including patients diagnosed with RA, according to the 2010 ACR/EULAR criteria, who started their first biological Disease Modifying Antirheumatic Drug (bDMARD). Demographic, clinical and laboratory data were obtained by consulting Rheumatic Diseases Portuguese Register (Reuma.pt). Associations with demographic characteristics and disease-related measures were examined at baseline, 6, 12, 18 and 24 months. Statistical analyses were performed using SPSS statistical software, version 23.0.
Results: A total of 357 patients with RA were included. Eighty-two per cent were females (82%). The mean age was 54 ± 11.01 years and the median disease duration was 10 years [min 0.5, max 45]. Rheumatoid Factor (RF) was positive in 75% of patients and Antibodies to Citrullinated Peptides (anti-CCP) in 82%. The prevalence of depression and anxiety were 34.7% and 23.5%, respectively. Both groups (RA depressed/anxiety) had statistically significant differences concerning gender. Patients with RA and depression/anxiety were significantly more likely to be women and had a lower disease duration. Depressed patients showed a younger RA onset. Unemployed patients were more likely to be depressed. Other factors such as education, smoking or alcohol consumption were not significantly associated. Baseline depression/anxiety was associated with increased patient's global assessment and number of painful joints but not with levels of acute phase reactants. Treatment with conventional synthetic DMARD and/or glucocorticoids did not have any significant association with either depression or anxiety. The proportion of patients achieving disease

remission and good/moderate EULAR response was overall lower in patients with depression/anxiety during the follow-up.
Conclusion: The presence of depression and anxiety among patients with RA was associated with worse response to the first bDMARD. Screening and recognition of such psychosocial disorders may help patients achieve optimal disease control and a good outcome.
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Table 1. Patient and disease characteristics at baseline and comparison between therapeutic groups

	All patients N=357	Depression N=124	Anxiety* N=84	*p*-value
Sociodemographic characteristics				
Age (years)	54.1 ± 11.4	52.7 ±11.4	53.6 ± 11.2	NS
Gender (Female)	293 (82.1%)	115 (92.7%)	75 (89.3%)	< 0.001 0.049
Unemployed	214(60%)	124(74.2%)	63 (75%)	0.002 0,05*
Disease characteristics				
Age at diagnosis	42.3 ± 11.7	41.7 ± 11.9	43.2 ± 12.1	0.005 NS*
RF	268 (75%)	93 (75%)	71 (85%)	NS
Anti-CCP	291 (82%)	102 (82%)	69 (82%)	NS
Erosive	200 (56%)	78 (63%)	46 (55%)	NS
Baseline disease activity				
Tender joints 28	9 ± 6.9	9.9 ± 7.3	9.4 ± 7.4	0.05 NS*
Swollen joints 28	7.6 ± 5.7	7.68 ± 5.6	7.21 ± 5.6	NS
ESR (mm/1st hour)	36.9 ± 22.1	39.8 ± 23.9	38.2 ± 21.8	NS
CRP (mg/L)	18.5 ± 25.6	19.5 ± 2.3	19.4 ± 36.1	NS
Patients VAS	67.3 ± 22.6	74.6 ± 21.7	72.8± 24.4	0.01 NS*
DAS 28	5.6 ± 1.1	5.9 ± 1.21	5.8 ± 1.3	0.03 NS*
DAS 3V	5.0 ± 13.8	5.4 ± 1.2	5.3 ± 1.3	0.048 NS*
HAQ	1.6 ± 0.6	1.8 ± 0.6	1.7 ± 0.7	0.002 0.032*
EULAR response (24 months) N=174				
Non responders	22/174 (12%)	11/72 (15.3%)	7/40 (17.5%)	0.05 NS*

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0297 FOOT AND ANKLE INVOLVEMENT IN RHEUMATOID ARTHRITIS IS ASSOCIATED WITH DISEASE ACTIVITY AND LESS INTENSIVE TREATMENT

Keywords: Outcome measures, Pain, bDMARD

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Background: Foot and ankle involvement is not encompassed in joint counts routinely used for the management of rheumatoid arthritis (RA). For this reason, RA patients with foot and ankle involvement are at risk of undertreatment.
Objectives: To assess the prevalence of foot and ankle involvement in people with RA, and disease severity and RA-related comorbidities in this group.
Methods: This cross-sectional cohort study included all patients with established RA treated with biological and targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs) at our Unit between 11/2014 and 12/2021. The following variables were recorded systematically: demographics, RA characteristics and joints involved, glucocorticoid therapy and dose, DMARDs, disease activity score in 28 joints with C-reactive protein (DAS28), and extra-articular manifestations (RA-related lung diseases, rheumatoid vasculitis, rheumatoid nodules, neuropathy, skin diseases, systemic symptoms including Felty's syndrome, and secondary Sjogren's syndrome). We also assessed comorbidities as recommended by EULAR (cardiovascular disease, gastrointestinal disease, depression, osteoporosis, malignancy and infections). We performed crude comparisons between patients with and without foot and ankle involvement by chi-squared test of association and independent T-tests. We used logistic regression to determine the odds ratio (OR) of the association between foot and ankle involvement and b/tsDMARDs, adjusting for DAS28, use of hydroxychloroquine (HCQ), and cardiovascular and lung disease.
Results: Among 1192 RA patients included in this study, foot or ankle involvement was reported in 469 (39%), equally distributed for age (mean±SD 61±13 years) and sex (females 82%). Age at onset, disease duration, erosions, seropositivity, use and dose of glucocorticoid therapy and methotrexate were similar between groups. DAS28 was significantly higher (4.3±1.2 vs 3.7±1.4, p<0.0001) in RA patients with foot and ankle involvement, consistently with a significantly higher patient global assessment (55±22 vs 47±25 mm, p<0.001), and number of tender joints (7±5 vs 5±5, p<0.001) and swollen joints (4±4 vs 3±9, p<0.001); the distribution of RA patients according to categories of disease activity was also significantly different between groups (p<0.001; **Figure 1**). Nevertheless, the use of b/tsDMARDs was less intense in this group, as significantly fewer patients had received ≥2 b/tsDMARDs (28 vs 47%, p<0.0001) despite similar disease duration. They also received more frequently hydroxychloroquine (55.2 vs 46.5%, p=0.003). These patients had significantly more cardiovascular (20.3 vs 15.8%, p=0.046) and lung disease (6.0 vs 2.9%, p=0.008). The body mass index was also significantly higher (25.6±6.5 vs 24.7±8.2 kg/m^2, p=0.048), yet the proportion of patients with obesity was similar between groups (11.3% and 9.3%, respectively). Logistic regression confirmed the significant associations of foot and ankle involvement with a less intensive b/tsDMARDs use and higher disease activity (**Table 1**).

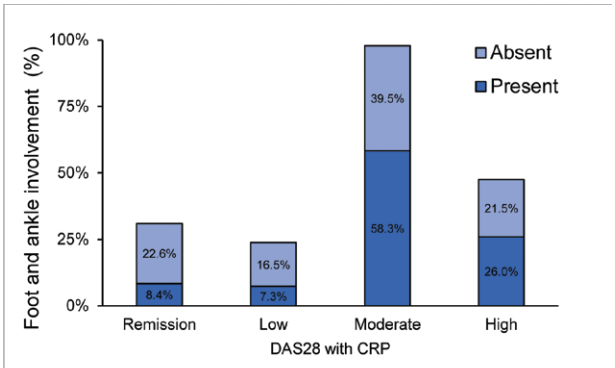


Figure 1. Foot and ankle involvement in 1192 RA patients according to disease activity

Table 1. Factors associated with foot and ankle involvement

	P-value	Odds ratio	95% C.I. Lower	95% C.I. Upper
b/tsDMARDs (vs none)				
1 b/tsDMARDs	0.784	1.05	0.73	1.51
≥2 b/tsDMARDs	0.009	0.59	0.39	0.88
Hydroxychloroquine	0.002	1.46	1.15	1.86
Cardiovascular disease	0.619	1.08	0.79	1.49
Lung disease	0.091	1.69	0.92	3.11
DAS28	<0.0001	1.25	1.13	1.38

Conclusion: Nearly 40% of RA patients have foot and ankle involvement that associates with higher disease activity in other joints. However, we noticed low use of b/tsDMARDs in this group, a finding only partially explained by a substantially increased burden of RA-related cardiovascular and lung comorbidities.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Alessandro Giollo Speakers bureau: Galapagos, Lilly, Consultant of: Galapagos, Novartis, Sandoz, Francesca Frizzera: None declared, Mariangela Salvato: None declared, Federico Arru: None declared, Filippo Vesentini: None declared, Margherita Zen: None declared, Andrea Doria: None declared.
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AB0298 SAFETY OF THE JAK INHIBITORS IN COMPARISON WITH THE TNF INHIBITORS IN RHEUMATOID ARTHRITIS: REAL WORLD DATA FROM THE HONG KONG BIOLOGICS REGISTRY

Keywords: Targeted synthetic drugs, bDMARD, Rheumatoid arthritis

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Background: The recent Oral Surveillance study has raised concerns about major cardiovascular events and malignancies related to tofacitinib in older rheumatoid arthritis (RA) patients with cardiovascular risk factors.
Objectives: To compare the incidence of major adverse cardiovascular events (MACEs), cancer and infective complications in RA patients using the JAK (JAKis) and TNF inhibitors (TNFis).

Methods: A retrospective analyses of data retrieved from the Hong Kong Biologics Registry from 2008 to 2021 were performed. Patients with RA (fulfilling the EULAR/ACR criteria) who had ever been treated with the JAK or TNF inhibitors were included. Withdrawal rates due to inefficacy or serious adverse events (SAEs) were compared between the two groups, along with the incidence of MACEs, cancer, infective complications and all-cause mortality. The hazard ratios (HRs) of these outcomes were calculated for the JAKis with reference to the TNFis and adjusted for confounding factors in regression models.
Results: A total of 2471 courses of JAKis (n=551) and TNFis (N=1920) were used in 1732 RA patients (83.7% women, age 53.8±12.5 years; follow-up 6431 patient-years). The most frequent JAKi and TNFi prescribed were tofacitinib (81%) and etanercept (37%). Users of the JAKis, compared to the TNFis, had significantly longer RA duration, older age and were more likely to have atherosclerotic risk factors (diabetes mellitus, hypertension, hyperlipidemia, previous coronary heart disease) and a past history of malignancy. The withdrawal rate of the JAKis was significantly lower than the TNFis due to clinical inefficacy or occurrence of SAEs (p<0.001 by survival analyses). A total of 15 and 40 MACEs developed in the JAKi and TNFi group of patients, respectively (incidence 1.34 vs 0.75 per 100 patient-years; p=0.22, adjusted for age, sex and follow-up duration). Moreover, there was no significant difference in the incidence of new cancers between the two groups (0.81 [JAKi] vs 0.85 [TNFi] per 100 patient-years; p=0.25). The adjusted HRs of MACE and cancer in the JAKi users were 1.36[0.62-2.96] (p=0.44) and 0.87[0.39-1.95] (p=0.74), respectively. Rates of infections were significantly higher in the JAKi than TNFi users (16.3 vs 9.9 per 100 patient-years; p=0.02), particularly herpes zoster (3.49 vs 0.94 per 100 patient-years; p<0.001) reactivation. The incidence of tuberculosis infection was similar between the two groups (0.45 [JAKi] vs 0.60 [TNFi]; p=0.21). All-cause mortality occurred in 8 patients in the JAKi group and 25 in the TNFi group and the difference was not statistically significant (0.72 vs 0.47 per 100 patient-years; p=0.54).
Conclusion: In a real-life setting, the JAKis have a better retention rate than the TNFis in patients with RA. There is no increase in the incidence of MACEs, cancers and all-cause mortality observed with the JAKis in comparison to the TNFis, adjusted for age, sex and other confounding factors. However, infective complications, particularly herpes zoster, are more common in the JAKi users.
Acknowledgements: Drs. Cheuk Wan Yim, Chi Hung To, Weng Nga Lao, Stella Pui Yan Wong, Hoi Yan Ng, Jolly Man Yee Lee, Patrick Man Leung Lee, Shirley King Yee Ying, Moon Ho Leung (who contributed to data collection)
Disclosure of Interests: chi chiu mok Speakers bureau: one-off speaker honorarium from Pfizer during the APLAR 2022 meeting, Ho So: None declared, Carmen Ho: None declared.
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AB0299 THE RISK OF ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS IS COMPARABLE TO THE GENERAL POPULATION IN THE TREAT-TO-TARGET ERA

Keywords: Treat to target, Rheumatoid arthritis, Comorbidities

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Background: Patients with rheumatoid arthritis (RA) suffer form an increased cardiovascular disease (CVD) risk compared with the general population. This is due to the fact that systemic inflammation not only accelerates the progress of RA but also promotes the development of atherosclerotic plaque.[1] Intima-media thickness of the carotid artery (cIMT) is considered as a reliable marker of the presence and the burden of atherosclerosis.[2] Since the treat-to-target (T2T) strategy was first introduced into RA management in 2010, it has been widely proved that patients treated with an underlying T2T strategy could obtain clinical remission more rapidly and achieve higher clinical remission rates[3]. However, what's the effect of a better controlled disease on the development of atherosclerosis?
Objectives: To compare the prevalence and incidence of carotid atherosclerosis monitored by ultrasound between patients with RA treated guided by a T2T strategy and age, gender-matched healthy controls, as well as identify risk factors of atherosclerosis aggravation among RA patients.
Methods: We used data from a longitudinal prospective cohort of RA patients and a community-based atherosclerosis cohort in the general population. Age and gender-matched participants were picked up by propensity score matching to be compared in their clinical characteristics and the process of atherosclerosis. And then a comparison was made according to the traditional CVD risk factors and RA-related factors between RA patients with carotid atherosclerosis progress (CAP) and without. A Cox proportional hazards regression model was operated to find out the risk factors of carotid atherosclerosis progress in the patients with RA.
Results: A total of 182 patients with RA were included. After a median 28 months of follow-up, 91.76% of patients reached remission or low disease activity target. The mean (or median) cIMT in RA patients was increased significantly after the follow-up, and 39 participants were recognized as CAP. Age at entry (HR 1.095, 95% CI 1.043, 1.149, P<0.001) and time adjusted body mass index (HR 1.127, 95% CI 1.011, 1.257, P=0.030) were identified by the multivariate Cox regression hazard model as the independent risk factor of carotid atherosclerosis progress for this group of RA patients. The prevalence of carotid atherosclerosis between 80 RA patients and 400 age, gender-matched controls, was compared, and no significant difference was found, no matter at the baseline (52.50% vs 49.67%, P=0.652)(Figure 1A) or the endpoint of the follow-up (53.75% vs 54.75%, P=0.870)(Figure 1B). The incidence of carotid atherosclerosis during the follow-up between 50 RA patients and 50 age, gender, and BMI- matched controls was also comparableb(28.00% vs 28.00%, P=1.0)(Figure 1C).
Conclusion: Compared with the general population, the patients with RA treated adhering to a T2T strategy presented with a similar incidence and prevalence of atherosclerosis. Among disease well-controlled RA patients, RA-related factors have little impact on the carotid atherosclerosis progress.
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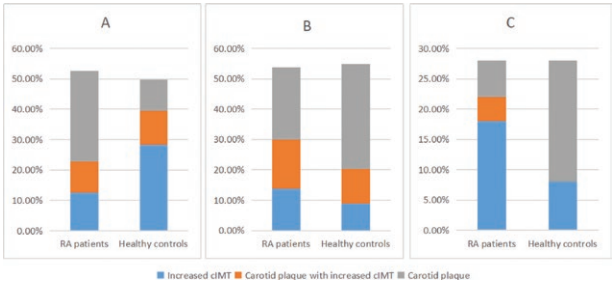


Figure 1. Comparisons in percentage of carotid atherosclerosis between RA patients and healthy controls
A. Comparisons in the prevalence of carotid atherosclerosis at the baseline
B. Comparisons in the prevalence of carotid atherosclerosis after follow-up
C. Comparisons in the incidence of carotid atherosclerosis after follow-up

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3478

AB0300 GENETIC EVIDENCE REVEALS A CAUSAL RELATIONSHIP BETWEEN RHEUMATOID ARTHRITIS AND INTERSTITIAL LUNG DISEASE

Keywords: Comorbidities, Rheumatoid arthritis, Genetics/Epigenetics

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Background: The most common extra-articular manifestation of rheumatoid arthritis (RA) is interstitial lung disease (ILD)[1] which in severe cases can lead to a range of complications and is one of the leading causes of death in patients with RA[2]. Many genetic studies found that patients with RA demonstrated an excess of mutations in genes that have been previously linked to ILD like TERT and RTEL1 et al. However, there is no directly evidence that the two diseases are causally related.

Objectives: In this paper, bidirectional two-sample Mendelian method was used to focus on the genetic factors related to ILD and RA, and to explore the causal relationship between ILD and RA in the pathogenesis.
Methods: A two-sample bi-directional Mendelian randomization (MR) approach was conducted to investigate the causal relationships between RA and ILD. Summary statistics for RA (14,361 RA cases and 43,923 healthy controls (HCs)) and ILD (1,969 cases and 196,986 HCs) were obtained from an available meta-analysis of published genome-wide association studies (GWAS). Relevant single nucleotide polymorphisms (SNPs) were selected by executing quality control steps ($p < 1.0 \times 10^{-5}$) from the GWAS summary results. MR analyses progressed mainly using inverse variance weighted (IVW), weighted median (WM), and MR-Egger regression methods. For assessing the robustness of the results, we also carried out sensitivity analysis to assess heterogeneity and pleiotropy, such as MR-Egger, leave-one-out and MR pleiotropy residual sum and outlier (MR-PRESSO).
Results: Our study discovered a bidirectional causal effect between RA and ILD. The presence of ILD may increase the risk of RA by 12.8% (OR: 1.128, 95%CI: 1.013-1.256, P = 0.029). Similarly, the existence of RA may increase the risk of ILD by 9.4% In addition, reverse MR analysis found that RA also influenced the risk of ILD significantly (OR: 1.094, 95%CI: 1.023-1.171, P = 0.009). Sensitivity analysis showed no pleiotropy but have heterogeneity (Q = 0.030) in reverse MR analysis.
Conclusion: MR analysis supported a potential causal relationship between RA and ILD. In RA and ILD, no matter which disease the patient has, it will greatly increase the risk of another disease. This study increases the emphasis on therapeutic or defensive interventions for patients with RA or ILD in the future to reduce severe complication and mortality.
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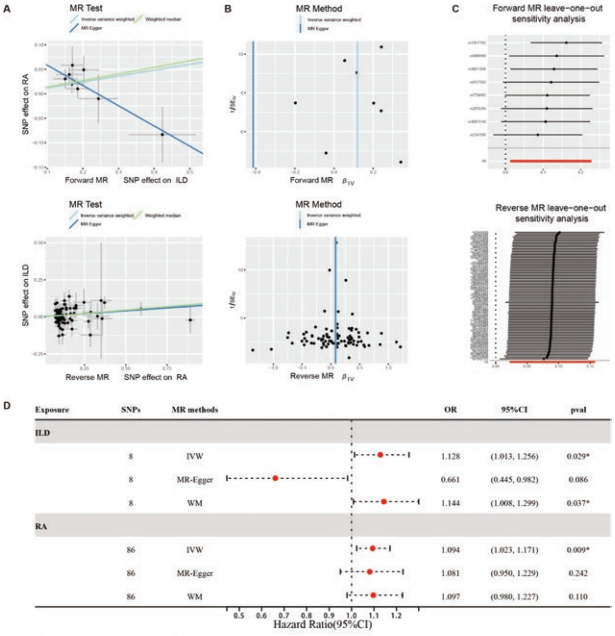


Fig1.(A) The scatter plots for MR analyses the causal effect between ILD and RA using the conventional IVW, MR-Egger, and Weighted median. **(B)** Funnel plot of Inverse variance weighted, MR Egger's multiple validity test for IVs, with the vertical line in the middle indicating the sum of different effect sizes. **(C)** Results of the leave-one-out method in MR sensitivity analysis. It was performed by removing one SNP at a time to explore whether any single SNP drove causal association. After each SNP was removed, the IVW method was conducted to estimate the effect of the remaining SNPs on the outcome, thus evaluating the stability of effect sizes. **(D)** Forest plot of MR results by IVW, MR Egger and weighted median.

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Disclosure of Interests: None Declared.
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AB0301

AUTOIMMUNE POLYENDOCRINOPATHY SYNDROMES IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SINGLE-CENTER STUDY ON 2166 PATIENTS

Keywords: Epidemiology, Comorbidities, Rheumatoid arthritis

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Background: Autoimmune polyendocrinopathy syndromes (APS) include heterogeneous clinical conditions characterized by functional alterations of at least one endocrine gland associated with other autoimmune diseases. APS-1 is a rare disease due to gene AIRE mutation and characterized by at least two of the following manifestations: chronic mucocutaneous candidiasis, hypoparathyroidism and Addison's Disease (AD). APS-2 is characterized by the presence of AD associated with at least one between Diabetes Mellitus Type 1 (DM1) and autoimmune thyroid disease (Hashimoto's Thyroiditis (TH) or Graves-Basedow Disease (GD)). APS-3 includes the association of autoimmune thyroiditis and other autoimmune manifestations, excluding hypoparathyroidism and AD. APS-4 is characterized by autoimmune activity against an endocrine organ in combination with at least one more autoimmune disease not included in previous definitions. As of today, there is very little data in literature about the prevalence of APS. Scarce data are available on the association between rheumatologic diseases and endocrine disorders.
Objectives: This paper aims to describe the prevalence of APS in our cohort of rheumatoid arthritis (RA) patients and to assess the possible association between autoimmune endocrine diseases, RA and gender.
Methods: This retrospective observational study collected medical history, biochemical and immunological data and risk factors about 2166 RA patients older than 18 years of age examined by our Department of Rheumatology from January 1, 2020 to August 1, 2022. Patients included presented at least one additional non-rheumatologic organic autoimmune disease. The prevalence of autoimmune diseases in our cohort were compared with those reported in the literature.
Results: This study included 2166 RA patients (534 men, 1632 women, M/F ratio 1:3). We found 352 patients (16%) having at least one autoimmune disease other than RA. The cohort consisted of 307 (87%) women, 45 (13%) men, M/F ratio 1:7, with mean age 63 ± 17 years at the time of examination. Among our patients, 300 (85%) presented with one additional non-rheumatologic autoimmune disease, 43 (12%) two non-rheumatologic autoimmune diseases, and 9 (3%) three non-rheumatologic autoimmune diseases. Figure 1 shows the autoimmune disorders collected. No cases of AD, chronic mucocutaneous candidiasis, hypoparathyroidism, myasthenia and AIRE mutation were found. In our cohort, no patient satisfied diagnostic criteria for APS 1 and 2; 212 (61%) patients presented with APS-3, 7 (2%) patients had APS-4 (all with RA and DM1 association). The diagnosis of APS occurred more frequently in female than in male patients, 199/1632 (12%) vs 20/534 (4%) (p< 0,001, OR 3,56, CI 2,29-5,71). Moreover differences related to gender were also evaluated for all the non-rheumatologic autoimmune disease, and a significant association between RA female patients and HT was found: 179/1632 (11%) vs 18/534 (3%) (p<0,001, OR 2,30, CI 1,22-4,33). Finally, comparing the prevalence of these autoimmune diseases in our cohort with those of the general population, we found higher prevalence for HT (9% vs 5%), autoimmune urticaria (0,7% vs 0,1%), DM1 (0,5% vs 0,3%), inflammatory bowel disease (0,5 vs 0,3%), alopecia (0,5% vs 0,1%), primary biliary cirrhosis (0,1% vs 0,03%), autoimmune hepatitis (0,09% vs 0,01%), autoimmune thrombocytopenia (0,05% vs 0,01%) and pemphigoid (0,05% vs 0,025%). Concerning risk factors, 78 (22%) patients had family history of autoimmune disease, 93 (26%) smoked, 23 (7%) had BMI>30.
Conclusion: The presence of at least one non-rheumatologic autoimmune disease was a nor rare event in our cohort of RA patients, with HT as the most frequent endocrine disease in our cohort. Among these cases, the diagnosis of APS was present in 62% of cases, mostly APS-3 and is more frequently found in female RA patients. Finally, we observed how the frequency of non-rheumatologic autoimmune diseases seems to be higher in RA patients than in general population.

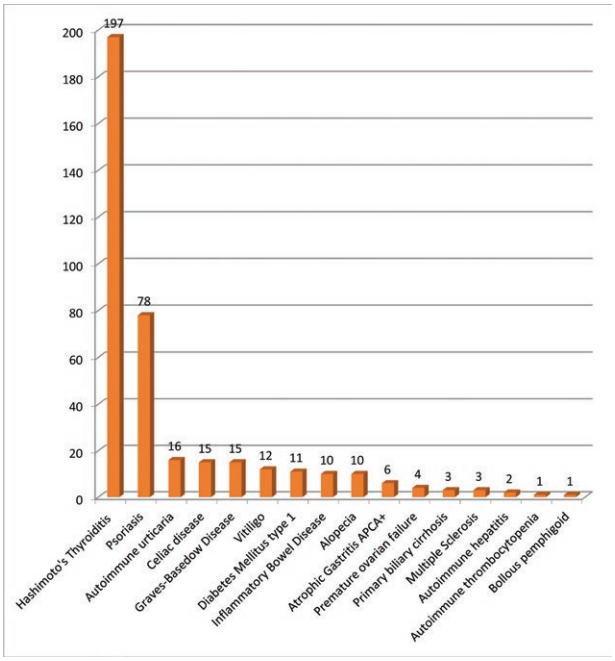


Figure 1 Autoimmune disorders associated to RA collected

REFERENCES: NIL.
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Disclosure of Interests: None Declared.
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AB0302

DISCONTINUATION RATE AND PREDICTORS OF JAKI DISCONTINUATION IN A REAL LIFE COHORT: RESULTS FROM A MULTICENTRIC ITALIAN STUDY ON 864 PATIENTS WITH RA

Keywords: Disease-modifying Drugs (DMARDs), Epidemiology, Rheumatoid arthritis

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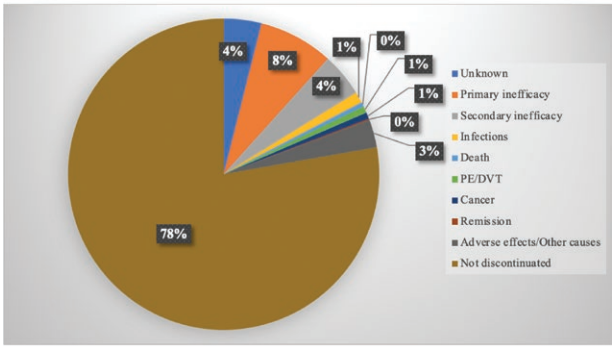
Background: The recent EULAR recommendations [1,2] suggest using JAK-inhibitors (JAKis) for treating RA patients. These drugs include both selective (upadactinib and filgotinib) and unselective (tofacitinib and baricitinib) JAKis.
Objectives: To describe JAKis' discontinuation rate and to determine predictors of JAKIs' discontinuation in a real life setting.
Methods: All patients with RA treated with JAKis were prospectively followed up for at least 12 months in this multicentric study carried out on 23 Italian centres. For each patient, the following variables were collected: sex, age, disease duration, smoking, BMI, comorbidities (diabetes, hypertension, hypercholesterolemia, cancer, major cardiovascular events), positive RF/ACPA, cDMARDs at baseline, prednisone at baseline, previous use of JAKis, discontinuation, time to discontinuation, JAKis line of treatment, DAS28-ESR at baseline, 6 and 12 months. Statistical analyses were performed using R (2022.12.0).
Results: 864 patients were included (**Table 1**). 487 (55.2%) received baricitinib, 213 (24.6%) tofacitinib, 111 (12.8%) upadacitinib and 62 (7.2%) filgotinib. 192 (22.2%) patients discontinued JAKis after a median time of 334 days (IQR 154.5-879.5). Among them, a statistical difference was found between selective-JAKis and other JAKis (p=0.03, 14.6% of selective JAKis vs 85.4% of other JAKis); finally unselective JAKis were discontinued later than selective JAKis (p<0.001, median 401.5 days, IQR 197.5-976 for unselective JAKis vs median 74 days, IQR 129-212 for selective JAKis). Discontinuation's causes are reported in **Figure 1**. Notably, VZV infection determined JAKis withdrawal in 4 patients and pulmonary embolism/deep venous thrombosis in 6 patients (both with baricitinib). Regarding discontinuations' causes, no differences between selective JAKis and other JAKis were found with factor logistic regression model. At multivariate analysis, predictors of discontinuation were prednisone at baseline (OR 1.48, p=0.03), treatment with unselective JAKis (OR 1.79, p=0.01), and line of treatment (OR 1.29 p<0.001).
Conclusion: Our study showed that only a minority of patients discontinued JAKis. Among discontinuation's causes, no differences between selective JAKis and other JAKis were found. Predictors of JAKis discontinuation were prednisone at baseline, treatment with unselective JAKis and line of treatment (with more advanced lines of treatment associated with a higher risk of discontinuation).
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[2] Smolen JS, et al. Ann Rheum Dis 2023.

Table 1. General features of 864 RA patients

Variable	N (%)
Mean age at baseline (SD) (N=863)	58.79 (12.84)
Females	678 (78.47)
Mean BMI (Kg/cm^2) at baseline (SD) (N=626)	25.19 (3.79)
Smoking (N=799)	
Yes	151 (18.89)
No	504 (63.01)
Former	144 (18.02)
Positive RF (N=809)	533 (65.88)
Positive ACPA (N=796)	498 (61.56)
Diabetes (N=770)	70 (9.09)
Hypertension (N=771)	302 (39.17)
Hypercholesterolemia (N=769)	196 (25.49)
Previous MACE (N=768)	47 (6.12)
Previous cancer (N=770)	42 (5.45)
Disease duration (months), (median, IQR) (N=855)	77 (30-157)
Mean DAS28-ESR at baseline (SD) (N=746)	5.29 (1.06)
cDMARDs at baseline (N=781)	287 (36.75)
PDN at baseline (N=780)	444 (56.92)
Median dosage (IQR) of PDN (mg/day)	5.00 (4.00-5.00)
JAKis naïve (N=853)	731 (85.70)
Line of JAKis treatment	
1^	247 (26.59)
2^	211 (24.42)
3^	181 (20.64)
4^	111 (12.84)
5^	65 (7.52)
6^	29 (3.35)
7^	12 (1.39)
8^	3 (0.35)
9^	2 (0.23)
10^	3 (0.35)
Patients who discontinued JAKis	192 (22.2)
Time to discontinuation (days), (median, IQR) (N=863)	334 (154.5-879.5)

Legends to Table 1: RA: rheumatoid arthritis; SD: standard deviation; BMI: Body Mass Index; RF: Rheumatoid Factor; ACPA: Autoantibodies against citrullinated peptides/proteins; MACE: Major cardiovascular events; PDN: prednisone; IQR: interquartile range; DAS28-ESR: Disease Activity Score-28 for Rheumatoid Arthritis with ESR; cDMARDs: conventional Disease-modifying antirheumatic agents; JAKis: JAK inhibitors.

Figure 1. Causes of JAKis' discontinuation among 864 patients



Legend to Figure 1. PE/DVT: Pulmonary Embolism/Deep Vein Thrombosis.

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Disclosure of Interests: Maddalena Larosa: None declared, Alarico Ariani: None declared, Dario Camellino Speakers bureau: Abiogen, GSK, Paid instructor for: Mylan, Andrea Becciolini: None declared, Gerolamo Bianchi: None declared, Eleonora Di Donato: None declared, Giuditta Adorni: None declared, Daniele Santilli: None declared, Gianluca Lucchini: None declared, Massimo Reta: None declared, Olga Addimanda: None declared, Alberto Lo Gullo: None declared, elisa visalli: None declared, Rosario Foti: None declared, Giorgio Amato: None declared, Francesco De Lucia: None declared, antonella farina: None declared, Francesco Girelli: None declared, Simone Bernardi: None declared, Giulio Ferrero: None declared, Romina Andracco: None declared, Marino Paroli: None declared, Natalia Mansueto: None declared, rosalba caccavale: None declared, Patrizia Del Medico: None declared, Aldo Molica Colella: None declared, Veronica Franchina: None declared, Francesco Molica Colella: None declared, Federica Lumetti: None declared, Gilda Sandri: None declared, Carlo Salvarani: None declared, Marta Priora: None declared, Aurora Ianniello: None declared, Valeria Nucera: None declared, Francesca Ometto: None declared, Ilaria Platé: None declared, eugenio arrigoni: None declared, Alessandra Bezzi: None declared, Maria Cristina Focherini: None declared, Fabio Mascella: None declared, Vincenzo Bruzzese: None declared, Palma Scolieri: None declared, Simone Parisi: None declared, Maria Chiara Ditto: None declared, Enrico Fusaro: None declared, Viviana Ravagnani: None declared, Rosetta Vitetta: None declared, Alessia Fiorenza: None declared, Guido Rovera: None declared, Alessandro Volpe: None declared, Antonio Marchetta: None declared, Matteo Colina: None declared, Elena Bravi: None declared.

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AB0303 ASSESSMENT OF SEXUAL DISORDERS IN TUNISIAN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Quality of life

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Background: Sexual dysfunction is common in patients with rheumatoid arthritis (RA), but is often under-estimated.
Objectives: The aim of this study was to assess the sexual function and to identify the associated factors of sexual disorders in Tunisian RA patients.
Methods: This is a cross-sectional study conducted in the Rheumatology department of Monastir in Tunisia including patients followed for RA. Functional impact was assessed by the Health Assessment Questionnaire (HAQ) and Rheumatoid Arthritis Quality of Life (RAQoL). Disease activity was evaluated using the DAS28 score. Sexual function was assessed for women by a self-assessment questionnaire: the Female Sexual Function Index (FSFI) including several parameters: desire, arousal, lubrication, orgasm, satisfaction and pain. For men, it was evaluated by the Sexual Health Inventory (SHIM) assessing erectile dysfunction.
Results: One hundred patients were included. There were 85 women and 15 men. The mean age was 55.88 ± 10.5 years. Sixty out of 85 women were sexually active. Thirty-five women (58.3%) had sexual dysfunction (FSFI ≤ 26.55). Lack of arousal and loss of desire were the most reported disorders with mean scores of 2.33 and 2.58 respectively. Among the 15 men, nine were sexually active. Only one men had normal sexual activity. Erectile dysfunction was the most common disorder with a mean score of 11. After statistical anlysis, significant association was found between sexual dysfunction assessed by FSFI and SHIM total scores and increased age (p=0.01 and p=0.005, respectively). More intense pain (visual analog scale) was significantly associated with sexual disability in women and men (p=0.01 and p=0.05, respectively). A significant correlation was found between lower FSFI score and higher disease activity by the DAS28 (p=0.001). Concerning the relationship with RA functional impact: we noted that among women, the alteration of arousal and satisfaction domains of the FSFI were correlated with higher HAQ (p=0.05 and p=0.004, respectively). In men, there was a significant association of lower SHIM score with HAQ and RAQoL (p=0.015 and p=0.001, respectively). However, there was no significant association between sexual dysfunction and the duration of RA progression, biological inflammatory syndrome, joint deformities, sturtural damage or the used treatments.
Conclusion: Our study showed that sexual dysfunction is frequent in women and men with RA, and that these disorders can affect their quality of life. Therefore, the sexual life of RA patients should be considered as one of the important therapeutic targets in the global management of this disease.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0304 PATIENTS WITH RHEUMATOID ARTHRITIS PRESENTING WITH MONO- OR OLIGO-ARTHRITIS AND HIGH PATIENT GLOBAL ASSESSMENT REMAIN MOST FATIGUED DURING 5-YEARS FOLLOW-UP

Keywords: Rheumatoid arthritis, Patient reported outcomes

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Background: The severity of fatigue in rheumatoid arthritis (RA) has hardly improved in recent decades, leaving a large unmet need. Fortunately, not all RA-patients suffer from persistent fatigue, but the subgroup of patients who suffer the most is insufficiently recognizable at diagnosis. As disease activity is partly coupled to fatigue, Disease-Activity-Score (DAS)-components may associate with the course of fatigue.
Objectives: We aimed to identify the RA-patients who remain fatigued by studying DAS-components at diagnosis in relation to the course of fatigue over a 5-year follow-up period in two independent early RA-cohorts.
Methods: 1560 consecutive RA-patients included in the Leiden Early-Arthritis Cohort and 415 RA-patients included in the tREACH-Cohort were studied. Swollen Joint Count (SJC), Tender Joint Count (TJC), Erytrocyte Sedimentation Rate (ESR) and Patient Global Assessment (PGA) (Visual Analogue Scale(VAS),0-100mm) were studied in relation to fatigue (VAS, 0-100mm) during 5-years using linear mixed models.
Results: Higher TJC and PGA at diagnosis were associated with a more severe course of fatigue. The SJC, in contrast, showed an inverse association; patients with mono- or oligo-arthritis at diagnosis remained more fatigued. The combination of aforementioned characteristics revealed that patients presenting with a mono- or oligo-arthritis and PGA≥50 remained the most fatigued over time(+20mm versus polyarthritis with PGA<50), whilst the DAS-course over time was not different. This subgroup comprised 14% of the early RA-population. Data from the tREACH-cohort showed similar findings.
Conclusion: RA-patients who remain the most fatigued are characterized by mono- or oligo-arthritis and high PGA(VAS≥50) at diagnosis. This understanding may enable early-intervention with non-pharmacological approaches in dedicated patient groups.

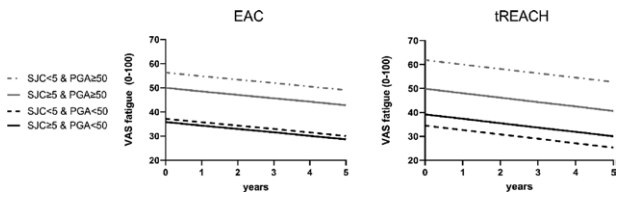


Figure 1. Fatigue trajectories stratified for combined DAS-characteristics at diagnosisLegend: Depicted are mean effect sizes from linear mixed models of fatigue scores stratified for different subgroups. The subgroups are based on two combined DAS-characteristics, SJC and PGA, at diagnosis.

Abbreviations: EAC, Early Arthritis Cohort; DAS, Disease Activity Score; SJC, Swollen Joint Count; PGA, Patient Global Assessment, tREACH; treatment Rotterdam Early Arthritis Cohort.

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Disclosure of Interests: None Declared.

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AB0305 HOW DOES PSYCHOLOGICAL TRAUMA AFFECT THE COURSE OF RHEUMATOID ARTHRITIS?

Keywords: Rheumatoid arthritis

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Background: Psychological trauma is a short-term or long-term stressful event associated with a sense of extreme threat or catastrophe. Psychological trauma predisposes to the development of a systemic inflammatory process. Dysregulation of the immune response occurs, which leads to an increase in the rate of aging of immune cells and changes in gene expression in immune cells, contributing to the development of autoimmune aggression [1]. The effect of psychic trauma on the decrease in IL-6 promoter methylation in patients with rheumatoid arthritis was revealed [2].

Objectives: The purpose of the study: to evaluate the impact of psychological mental trauma on the course of rheumatoid arthritis.

Methods: The study was conducted from September 2021 to September 2022. 80 patients with RA of varying severity were examined. Inclusion criterion was a European Antirheumatic League diagnosis of RA (EULAR/ACR 2010). The age of the patients ranged from 20 to 69 years. (Mean age of patients was 48 +/- 6.24). Most of the examined women - 85%. The study was carried out in two stages. The first stage is (screening). All patients admitted to the hospital were determined the level of situational and personal anxiety according to the Spielberger questionnaire modified by Yu.L. Khanina. The results obtained were interpreted: up to 30 points - a low level of anxiety, 31-45 points corresponded to the average level, over 45 points - a high level of anxiety. At the second stage (39 patients with medium and high levels of situational and/or personal anxiety), a survey was conducted, consisting of two blocks. The first block revealed the psychotraumatic factor by groups. 1. Shock injuries (a situation that threatens a person's life, various types of violence). 2. Injuries of loss (loss of a loved one, job, property). 3. Relationship trauma (betrayal, family relationship discomfort). 4. Others. The second set of questions assessed the relationship between the course of RA and psychic trauma, especially the onset of the disease. Statistical processing of the results was carried out in MS Office Excel programs.

Results: Almost half of 39 (48.7%) patients entered the second stage of the study, i.e. they had an average or high level of situational and/or personal anxiety. Shock injury was observed in 3 (3.75%) patients, loss trauma in 5 (6.72%) patients, relationship trauma in 29 (36.25%) patients, other causes indicated in 2 (2.5%) patients Acute trauma was detected in 5 (6.25%) patients, chronic trauma in 32 (40%) patients, 2 (2.5%) patients found it difficult to answer. In the analysis of the second block of questions of the questionnaire, 31 (38.75%) patients note the relationship between PT and worsening of the course of RA. Deterioration in the form of increased pain syndrome was noted by 37 (46.25%) patients, an increase in edema of the affected joints was noted by 30 (37.5%) patients, a decrease in mobility in the joints was noted by 26 (32.5%) patients. Most of the 36 patients note that about 2 months passed from the moment of PT to the worsening of the course of RA. In 2.5% of patients, the onset of RA disease with a history of acute PT was observed.

Conclusion: Psychological trauma worsens the course of RA. This deterioration manifests itself in the form of an increase in pain, an increase in swelling of the affected joints, and a decrease in joint mobility. In the treatment of patients with RA, it is necessary to use a multidisciplinary approach involving psychologists and psychotherapists in order to timely identify and treat psychological trauma.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0306 IMPACT OF TOFACITINIB ON LIPID METABOLISM IN PATIENTS WITH RHEUMATOID ARTHRITIS: A REAL-WORLD STUDY

Keywords: Real-world evidence, Rheumatoid arthritis

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Background: Tofacitinib is the first Janus Kinase (JAK) inhibitor available in China, and it has significantly improved the efficacy of treatment of rheumatoid arthritis (RA). Previous clinical trials found that tofacitinib can affect lipid metabolism in patients.

Objectives: Whether lipid and lipoprotein concentrations can recover by themselves and whether lipid-lowering drugs intervention is required, are currently inconclusive, and there is a lack of real-world experience.

Methods: Patients from the CENTRA (Collaboratively intENsive Treat-to-target in RA) cohort, a prospective follow-up cohort for RA in the Department of Rheumatology and Clinical Immunology, Peking University First Hospital were enrolled, and those who used lipid-lowering drugs were excluded. Patients were divided into tofacitinib exposure group and non-exposure group according to whether patients were prescribed with or without tofacitinib. Disease activity scores, TG, TCHO, HDL and LDL at baseline and during follow-up were calculated, and the ratios of TCHO/HDL to HDL/LDL was also calculated. Changes in lipid and lipoprotein concentrations after use of tofacitinib during follow-up were analyzed. Age, gender, disease duration, and the Simplified Disease Activity Index (SDAI) at baseline as covariates for propensity score matching was performed on patients with and without tofacitinib, and the lipid and lipoprotein profiles of the two groups were compared.

Results: A total of 304 patients were included, with 88 prescribed with tofacitinib and 216 without tofacitinib. (1) In patients with tofacitinib, the median TG and TCHO were 0.95 mmol/L and 4.45 mmol/L, respectively, the mean HDL and LDL were 1.32 mmol/L and 2.63 mmol/L at baseline, and the median TCHO/HDL and HDL/LDL ratios were 3.62 and 2.24, respectively. After 4 weeks of use of tofacitinib, the levels of TCHO, HDL and LDL increased compared with baseline by 16.6%, 12.9% and 14.4%, respectively. At week 12, LDL increased by 12.9% compared with baseline, indicating the returning to baseline levels, while the levels of TCHO and HDL were still significantly elevated. At week 48, TCHO also returned to baseline levels (increased by 2.9%). HDL levels remained elevated during follow-up. There were no significant increases in TG, TCHO/HDL and LDL/HDL ratios throughout the follow-up. In addition, there was no significant difference in lipid and lipoprotein changes between tofacitinib monotherapy (43 patients) and tofacitinib combined with csDMARDs (45 patients) during follow-up. (2) After 1:1 matched by propensity score matching, there were 83 patients prescribed with tofacitinib exposure and 83 without. In the 4 weeks of follow-up, there was no significant difference in the increase of lipid and lipoprotein between the two groups. At week 12, week 24, and week 48, the increase of TCHO in patients with tofacitinib was significantly higher than those without (0.47 vs. -0.1, $p<0.001$; 0.33 vs.-0.06, $p=0.001$; 0.22 vs.-0.1, $p=0.017$). The LDL elevation in patient with tofacitinib was higher than that in patients without at week 12 and continued to week 24 (0.17 vs.-0.07, $p=0.002$; 0.18 vs.-0.09, $p=0.001$), but at week 48, there was no significant difference between the two groups compared with baseline. At week 12, patients in the tofacitinib-exposure group had higher HDL elevations (0.22 vs. 0.02, $p < 0.001$), but there was no significant difference between the two groups form week 24 to week 48. Elevation in TG, THCO/HDL or LDL/HDL was not significantly different between the two groups throughout the follow-up.

Conclusion: After 4 weeks of using tofacitinib, TCHO, HDL and LDL levels increased in RA patients. LDL and TCHO returned to the baseline level at the week 12 and week 48, respectively, while HDL continued to increase. There was no significant change in TG, THCO/HDL or LDL/HDL throughout the follow-up. The elevation in lipid and lipoprotein profiles in RA patients prescribed with tofacitinib was significantly higher than those without.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0307

JAK INHIBITORS DO NOT WORSEN RA-ILD; COMPARISON OF CHANGES IN CT IMAGES AND KL-6/SP-D LEVELS BETWEEN PERIODS WITH BIOLOGICS AND WITH JAK INHIBITORS IN THE SAME INDIVIDUALS

Keywords: Rheumatoid arthritis, Targeted synthetic drugs, Lungs

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Background: Interstitial lung disease (ILD) is a serious organ involvement that influences the prognosis of RA patients and limits RA therapy. The association between RA activity and ILD progression has been suggested. However, the effects of biologics (Bio) on ILD are controversial; several studies showed that Bio increased ILD-related death, whereas others reported that Bio stabled the progression of ILD. Moreover, the effects of JAK inhibitors (Jaki) on ILD are largely unknown.
Objectives: To clarify the effects of Jaki on RA-ILD by comparing the changes in CT images and KL-6/SP-D levels between periods with biologics and with JAK inhibitors in the same individuals.
Methods: Participants were consecutive RA patients who received Jaki from June 2014 to April 2022. Among them, patients who received Bio prior to Jaki therapy underwent analysis of changes in CT images and serum KL-6/ SP-D levels in the same individuals. Change in CT images of pulmonary abnormalities, such as reticular pattern, was assessed by CT score: the extent of lesions of 6 lung fields was scored as follows; score 0 (absent), 1 (-25 %), 2 (25–50 %), and 3 (50 %-). The CT scan score for each patient was obtained by adding the score for each field (max 18).
Results: Patients included in the analysis were 79 RA patients, M/F; 34/45. When they started Bio, their mean age was 59.3 years old, disease duration was 7.7 years, positive for anti-CCP antibody in 82.9%, and positive for RF in 83.5%. They received 3.7 (average) different Bios for 4.6 years (average) prior to JAKi therapy for 2.8 years. Serum KL-6 levels increased by 91.2±416.0 U/ml (average+sd) during Bio treatment but decreased by 82.1±383.3 mg/dl during JAKi therapy. Similarly, serum SP-D levels increased by 10.1±60.3ng/ml during Bio but decreased by 23.7±83.1 ng/dl during JAKi therapy. However, no differences were found in KL-6/SP-D levels between periods with Bio and JAKi in the same individuals. ILD was found in 22 out of 79 RA patients. GGO was found in 2 cases. Reticular opacities were found in 18 cases, and 3 of them developed during Bio. Honey-combing occurred in 9 cases; 3 and 1 developed during Bio and JAKi, respectively. CT score of reticular opacities was increased in 9 cases (50%) during Bio but in 3 cases (16%) in JAKi (Figure 1) (p=0.04). The CT score change was significantly greater in the period with Bio than with JAKi in between-group comparisons and the same individuals (Figure 1).
Conclusion: The frequencies and severities of worsening in the CT imaging, particularly reticular opacities, were less in patients with JAKi than in Bio. JAKi did not worsen ILD but rather may stable it.

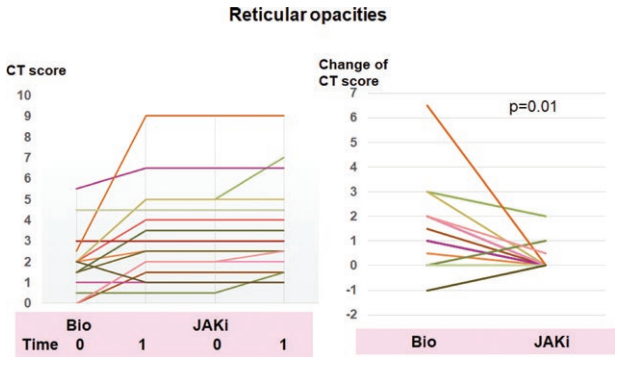


Figure 1. Changes in CT scores under therapy with biologics and JAK inhibitors in the same individuals

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0308

QUANTIFICATION OF SARCOPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS BY MEASURING THE CROSS-SECTIONAL AREA OF THE THIGH MUSCLES WITH MAGNETIC RESONANCE IMAGING

Keywords: Comorbidities, Imaging, Rheumatoid arthritis

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Background: Sarcopenia is a prevalent condition in patients suffering from rheumatoid arthritis (RA), estimated to affect 31% of them. Magnetic resonance imaging (MRI) allows the measurement of cross-sectional area (CSA) and volume of a muscle and the visualization of its morphological features and their distribution. Quality deterioration of the muscle, characterised by the presence of adipose tissue (defined as myosteatosis) and of fibrous connective tissue (defined as myofibrosis), is best diagnosed with MRI.
Objectives: To determine the utility of CSA measurements on MRI, at the level of the thigh muscles, to estimate muscle mass in discriminating RA patients with sarcopenia from those without.
Methods: Consecutive female RA patients were enrolled for this cross-sectional study. Patients were assessed for disease activity, radiological damage, handgrip strength, physical performance and for the presence of sarcopenia, identified in accordance with the EWGSOP2 criteria. A 1.5T MRI machine was used to scan the thigh muscles. A dimensional region growth algorithm (Horos™) was used to semiautomatically segment the muscles cross-sectional areas (CSAs, in cm^2) on MR images located 25 cm above the knee joint (MRI-CSA-25) (Figure 1). The MRI-CSA-25 was obtained by summing the areas of the individual muscles. MRI-CSA-25 was correlated (Pearson's r) with the other variables, and its optimal cut-off point (Youden index) for sarcopenia diagnosis was identified in relation to the EWGSOP2 criteria.
Results: 32 RA female patients were studied, 34.4% diagnosed as sarcopenic. The mean MRI-CSA-25 was 151.00 cm^2 for patient with sarcopenia, 275.57 cm^2 for patient without sarcopenia ($p < 0.001$). MRI-CSA-25 correlated significantly with measures of physical performance, and disease activity, but not with radiological damage or age. The MRI-CSA-25 optimal cut-off point in discriminating sarcopenic patients was identified at 182 cm^2 (AUC-ROC = 0.894).
Conclusion: MRI-CSA-25 can differentiate sarcopenic versus non-sarcopenic RA patients, representing an imaging biomarker of this condition.
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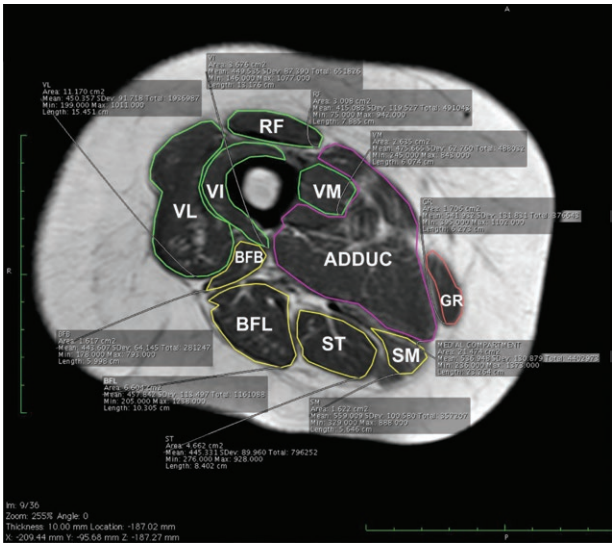


Figure. 1 Illustrative magnetic resonance image of a segmented muscle region of the thigh at a 25 cm above the knee joint (MRI-CSA-25) of a 50-year-old female patient, acquired as axial T1-weighted gradient-echo. Group muscles are color-coded: rectus femoris (RF), vastus lateralis (VL), vastus intermedius (VI), and vastus medialis (VM), the four muscles composing the hamstrings muscles (HAMST) [biceps femoris short head (BFB), biceps femoris long head (BFL), semitendinosus (ST) and semimembranosus (SM), and adductors (ADDUC) [adductor longus, brevis, magnus, pectineus, sartorius and gracilis (GR)]. Because the delineations between adductors muscles were not so obvious at proximal part, all adductors' muscles were segmented together, except for the gracilis which was easily recognizable. Note the exclusion of non-muscular elements (blood vessels, nerves) in the manual segmentation.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3016

AB0309 **CLINICAL EFFICACY AND SAFETY OF TOFACITINIB COMBINED WITH IGURATIMOD FOR RHEUMATOID ARTHRITIS-ASSOCIATED USUAL INTERSTITIAL PNEUMONIA**

Keywords: Rheumatoid arthritis, Comorbidities

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Background: Research has found that iguratimod(IGU) could be an effective therapeutic strategy for pulmonary fibrosis[1-3].The results of the Vitro and in vivo studies indicated that tofacitinib(TOF),slowing the progression of ILD associated with connective tissue diseases,is a potential therapeutic option for rheumatoid arthritis with usual interstitial pneumonia(RA-UIP)[4-7]
Objectives: This study aimed to investigate the efficacy and safety of TOF plus IGU in RA-UIP.
Methods: This was a prospective observational cohort,single-center study. Data were analyzed from 52 RA-UIP patients.24 were treated with TOF(5mg twice daily) plus IGU.28 were treated with Methotrexate(MTX)/Leflunomide(LEF) plus conventional synthetic disease-modifying anti-rheumatic drugs(csDMARDs).A clinically relevant response was defined as a decrease in disease activity score 28-joint count CRP(DAS28-CRP) score and high-resolution computed tomography(HRCT) scores from baseline.Deterioration and regression were respectively defined by an increase or decrease of at least 10% of the overall disease extent according to HRCT,whereas changes of less than 10% defined stability.Clinical indicators were compared between the two groups to evaluate the efficacy.
Results: A total of 24 RA-UIP patients treated with TOF plus IGU and 28 treated with MTX/LEF plus csDMARDs were enrolled and followed up for 6 months.The DAS28-CRP of the TOF plus IGU group was significantly lower than baseline(4.8±1.6vs.3.8±1.9),but there was no significant difference compared with the MTX/LEF plus csDMARD group(P=0.762). The FVC% was significantly improved after 6 months of TOF plus IGU treatment;the change from baseline was more significant than the MTX/LEF plus csDMARD group(-1.89±2.33,P=0.031).TOF plus IGU group had a significantly HRCT fibrosis scores improvement(-0.17±2.52)than the MTX/LEF plus csDMARD group(1.36±2.42,P=0.038)(**Table 1**).In the TOF plus IGU group,8 patients(8/24,33.3%) showed RA-UIP deterioration,6 patients(6/24,25.0%) were considered stable,and 10 patients(10/24,41.7%) demonstrated regression.In the MTX/LEF plus csDMARD group,18 patients(18/28,64.3%) showed deterioration,6 patients(6/28,21.4%) were stable,and 4 patients(4/28,14.3%) demonstrated RA-UIP regression.TOF plus IGU-treated group had a significantly higher response(regression + stability) than MTX/LEF plus csDMARD-treated group,66.7%(16/24) vs.33.5%(10/28)(P=0.008),respectively.
Conclusion: Our results indicated that TOF plus IGU could simultaneously relieve RA and RA-UIP,and be better than the MTX/LEF plus csDMARDs with a higher response rate in RA-UIP,which may be a potential choice for dual treat-to-target.

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Table 1. Clinical,lung functional and HRCT score data,and signifcance level at base line and follow-up,expressed in means and standard deviations or number(percentage,%)

Variables	TOF+IGU n=24		MTX/LEF+csDMARD n=28		*P-value
	Baseline	Follow-up	Baseline	Follow-up	
RF(<20IU/ml)	63.2±60.5	57.6±53.9	76.9±58.6	69.5±46.2	0.756
CCP(<5RU/ml)	141.5±64.6	136.5±74.5	140.0±80.4	130.5±77.2	0.642
CRP(<10mg/L)	28.2±56.7	20.7±24.8	28.3±31.1	23.7±16.6	0.563
ESR(<15mm/h)	41.2±21.7	30.3±18.2	28.6±14.5	29.3±23.1	0.486
DAS28-CRP	4.8±1.6	3.8±1.9	4.3±2.2	3.5±1.8	0.762
FVC(%,predicted)	84.7±14.7	90.7±15.4	81.6±11.2	75.9±6.8	**0.031**
DLCO SB(%,predicted)	69.4±16.1	61.6±14.6	54.5±11.3	49.4±24.0	0.753
GGO score	2.1±0.9	3.4±6.9	2.3±1.3	2.1±1.4	0.359
Fibrosis score	7.3±3.4	7.0±5.6	6.4±3.9	7.9±5.2	**0.038**
R	-	10(41.7)	-	4(14.3)	**0.009**
S	-	6(25.0)	-	6(21.4)	0.657
R+S	-	16(66.7)	-	10(35.7)	**0.008**

CCP:anti-cyclic citrullinated peptide;RF:rheumatoid factor;CRP:C-reactive protein;ESR:erythrocyte sedimentation rate;DAS:Disease Activity Score;PGA:physician global access;TLC:total lung capacity;FVC:forced vital capacity;DLCO SB:carbon monoxidediffusion capacity single-breath method;GGO:ground glass opacity;R:regression,S:stability;*P＜0.05:The difference in change from baseline between the two groups after 6 months of treatment was statistically significant.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3346

AB0310 **CARDIOVASCULAR RISK STRATIFICATION IN PATIENTS WITH RHEUMATOID ARTHRITIS**

Keywords: Cardiovascular disease, Rheumatoid arthritis

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Background: Patients with Rheumatoid Arthritis show an increased mortality population due predominantly to cardiovascular complications, which represent up to 50% of deaths. There are CVR scales that include RA as an independent risk factor. Even with constantly revised and updated assessment tools such as Qrisk III and SCOREm, there is still a tendency to underestimate the cardiovascular risk evidenced by asymptomatic atherosclerosis on ultrasound of the carotid vessels in patients previously classified in intermediate or low risk strata.
Objectives: To determine the cardiovascular risk stratum in adult patients with rheumatoid arthritis to stratify them according to the 2008 Framingham Risk Score, ScoreM and Qrisk III scales and to identify those high-risk patients who developed carotid lesions in ultrasonographic studies.
Methods: Descriptive, prospective, cross-sectional study, in a Paraguayan cohort of patients with RA meeting ACR/EULAR2010 criteria. A standardized questionnaire according to the variables included in the Cardiovascular Risk project (PINV15-0346), from the National Sciences and Technology Council (CONACYT), physical examination was made, and carotid ultrasound evaluation

by a trained specialist, to evaluate subclinical atherosclerosis. Subclinical atherosclerosis was defined as carotid intima-media thickness (CIMT) >0,9mm and/or presence of carotid plaques. The 2008 Framingham score, QRisk III and modified mSCORE were used for CV risk stratification. Quantitative variables were presented as means and qualitative as frequencies. Chi square test was performed for comparisons between dichotomous variables and t Student for continuous, and $p \leq 0.05$ for statistical significance. Kappa coefficient was performed between scales, interpreted as: ≤ 0 as no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement. All patients signed informed consent.

Results: 100 were included, 87% were women, with a mean age of 51±11.3 years and mean disease duration 130.9±102.64 month. 9 (9%), 13 (13%) and 5 (5%) were classified as high risk according to the QriskIII, Framingham 2008 and ScoreM scales respectively. 27.14% of patients had subclinical atherosclerosis, exceeding by 14% the high-risk patients according to the Framingham classification, while mSCORE and QriskIII underestimated cardiovascular risk in 22 and 18 individuals, respectively. The kappa coefficient for agreement of high-risk patients according to QRiskIII was 0.593 (moderate concordance) relative to Framingham 2008 while ScoreM had a Kappa coefficient of 0.401 (fair concordance) relative to Framingham 2008.

Conclusion: In contrast to the estimation scales frequently used in clinical practice, which have a tendency to underestimate the risk in patients with rheumatoid arthritis, these results show that the cardiovascular risk demonstrated through ultrasonography of the carotid vessels more effectively characterizes high-risk patients.

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AB0311

ANALYSIS OF THE MALIGNANCY-RELATED SAFETY OF ABATACEPT FOR RHEUMATOID ARTHRITIS IN CLINICAL PRACTICE

Keywords: Malignancy, bDMARD, Rheumatoid arthritis

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Background: In 2019, a study based on post-marketing surveillance data in Japan reported that ABT was as effective and safe in elderly patients with rheumatoid arthritis (RA) as non-elderly[1]. However, there were inconsistent reports on the impact of ABT on malignancies which are more common in the elderly and strongly related to prognosis[2-4], and there are still unanswered questions.

Objectives: To evaluate the incidence of malignancy and the efficacy and safety of previous malignancy in RA patients using ABT in our clinical practice. In addition, to explore the predictive risk factors of developing or relapsing malignancy during ABT use.

Methods: Patients who received ABT for RA at our department from October 2010 to May 2022 were included in the study. Patient background, prior malignancy at starting ABT, disease activity from starting ABT up to 60 months, continuation rates of ABT, and safety, including onset or recurrence of malignancy during ABT use, were retrospectively collected from electronic medical records. The patients were divided into two groups according to the absence or presence of previous malignancy (No previous malignancy: NP group, previous malignancy: PM group), and the collected parameters were compared between the groups.

Results: A total of 276 patients were included, of which 61 had previous malignancies when starting ABT. The age of starting ABT was significantly higher in the PM group (72.5 ± 10.6 vs. 68.5 ± 13.0years-old, $p = 0.025$), and the rate of methotrexate use was significantly lower in the PM group (29.5 vs. 51.2%, $p = 0.0028$), although there were no significant differences in other patient backgrounds between the groups (Table 1). The disease activity improved significantly at three months after starting ABT in both groups, and DAS28-CRP remission was maintained after that. There was no significant difference in disease activity between the groups from starting ABT to 60 months after. There were no significant differences in the continuation rates for 1-year and 5-year of ABT between the groups (86.3 vs. 86.6%, and 70.5 vs. 65.7%, respectively, Figure 1). There were 14 cases of occurrence and recurrence or progression of malignancy during the observation period. The incidence of malignancy was 1324.6 per 100,000 person-years, and there were no differences in the risk of malignancy in a Japanese national survey of similar age. Despite the significantly older patient population in the PM group, the 5-years incidence rate of malignancy was no significant difference between the groups. Binomial logistic analysis was performed using factors such as age, disease duration, history of previous malignancy, concomitant disease and medications, and disease activity at starting ABT. However, no predictive risk factors were found to be associated with the development or relapse of malignancy during ABT use in this study.

Conclusion: In our clinical practice, ABT was effective and safe in both patients with and without previous malignancy.

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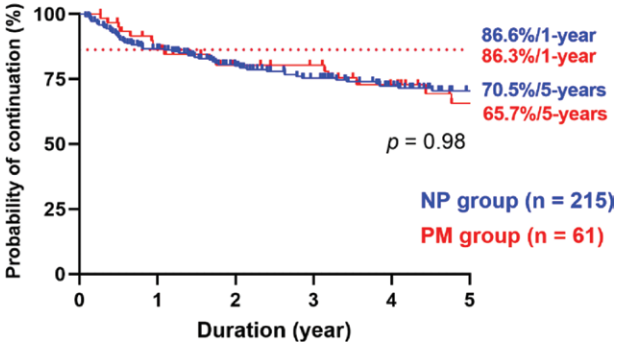
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Table 1. Patient background at the start of ABT in the groups.

	NP group (n = 215)	PM group (n=61)	*p*
Female (n, %)	182/215 (84.7)	49/61 (80.3)	0.42
Age (y.o.)	68.5 ± 13.0	72.6 ± 10.6	0.025
Disease duration (year)	9.7 ± 9.5	11.8 ± 10.3	0.13
Body weight (kg)	53.4 ± 12.0	52.2 ± 9.6	0.49
RF seropositivity (n, %)	181/214 (84.6)	52/61 (85.2)	0.94
Anti-CCP Ab seropositivity (n, %)	152/184 (82.6)	47/52 (90.4)	0.25
Complications of CTD (n, %)	31/214 (14.5)	12/61 (19.7)	0.33
Interstitial pneumoniae (n, %)	47/215 (21.9)	9/61 (14.8)	0.30
b/tsDMARDs naïve (n, %)	152/214 (71.0)	45/61 (73.8)	0.68
Concomitant drug			
MTX (n, %)	110/215 (51.2)	18/61 (29.5)	0.0028
MTX dose (mg/week)	10.4 ± 2.7	9.9 ± 2.2	0.43
PSL (n, %)	60/213 (28.2)	20/61 (32.8)	0.48
PSL dose (mg/day)	5.8 ± 5.1	5.2 ± 4.1	0.65
MMP-3 (ng/ml)	262.1 ± 278.3	294.1 ± 303.8	0.46
DAS28-CRP	3.8 ± 1.0	3.9 ± 1.2	0.91
DAS28-ESR	5.3 ± 1.1	5.3 ± 1.4	0.86
CDAI	20.2 ± 11.8	21.2 ± 12.3	0.62
SDAI	22.4 ± 12.9	23.6 ± 13.2	0.61

Figure 1. Continuation rates of ABT



Acknowledgements: NIL.

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AB0312

ASSOCIATION BETWEEN DISEASE ACTIVITY AND CHANGES IN FIBROSIS-4 INDEX LEVEL IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH METHOTREXATE FOR A SHORT PERIOD

Keywords: Rheumatoid arthritis, Descriptive Studies, Comorbidities

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Background: Liver fibrosis and liver damage are major concerns associated with long-term side effects in patients with rheumatoid arthritis (RA) treated with methotrexate (MTX). Recently, fibrosis-4 index (FIB-4) has often been used as an indicator of liver fibrosis. However, most studies examining the association between MTX and liver fibrosis, including FIB-4, have involved patients with RA treated with MTX for an extended period. To the best of our knowledge, no study has reported associations between FIB-4 and disease activity in patients with RA after using MTX for a short period.
Objectives: We focused on FIB-4 as an indicator of liver fibrosis in patients with RA treated with MTX in phase I and aimed to evaluate the changes in FIB-4 level in these patients for a short period.
Methods: Patients diagnosed with RA at our hospital and who had not received MTX before diagnosis (using the 2010 ACR/EULAR criteria) were included. Patients with hepatitis virus infection, alcoholism, or severe obesity were excluded from the study. Patients unable to continue using MTX for more than 12 months and those who used a maximum dose of MTX of 10 mg/week or less during the observation period were excluded. Patients' clinical and functional data were recorded at baseline and at all subsequent visits (6 and 12 months). We used the Mann–Whitney U test to compare aspartate transaminase (AST), alanine aminotransferase (ALT), and FIB-4 levels between the baseline and each observation period. Multiple regression analysis was performed to examine the effect of the cumulative MTX dose on the changes in FIB-4 levels from baseline to 6 and 12 months, after adjusting for factors involved in RA.
Results: A total of 144 patients were examined. The median FIB-4 levels increased from baseline to 6 and 12 months ($p < .001$). Multiple regression analysis revealed that the cumulative MTX dose was not a factor independently influencing the changes in FIB-4 levels. Therefore, to identify predictors other than the cumulative MTX dose for changes in FIB-4 levels from baseline, we performed multiple linear regression analysis, after adjusting for sex, body mass index (BMI), CRP, MMP-3, mHAQ, RF, ACPA, DAS28ESR, and FIB-4 level at baseline, defining the changes in FIB-4 level from baseline as the dependent variable. The factors independently influencing the changes in FIB-4 level were DAS28ESR ($\beta = 0.107$) at 6 months and DAS28ESR ($\beta = 0.086$) at 12 months. DAS28ESR at baseline affected the changes in FIB-4 level from baseline to both observation periods. There was also a significant correlation between the change in FIB-4 from baseline to each period and the DAS28ESR ($p < .001$). Further, a mediation analysis was performed for the association between DAS28ESR and the changes in FIB-4 level, considering the cumulative MTX dose as a mediator. The results indicated that the cumulative MTX dose did not mediate the relationship between DAS28ESR at baseline and the changes in FIB-4 level at either observation period.
Conclusion: The cumulative MTX dose did not affect the changes in FIB-4 level over a short period. In contrast, disease activity in patients with RA before MTX administration showed an effect on the changes in FIB-4 level. Clinicians should be more careful regarding liver fibrosis after MTX administration when treating patients with higher disease activity before treatment.
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AB0313

UNDERSTANDING DISEASE PREVALENCE AND COMORBIDITY PROFILES AMONG SEROPOSITIVE AND SERONEGATIVE RHEUMATOID ARTHRITIS PATIENTS IN PUERTO RICO

Keywords: Rheumatoid arthritis, Comorbidities, Autoantibodies

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Background: Prevalence of rheumatoid factor (RF) and/or anti-cyclic citrullinated peptide antibody (ACPA) positivity in US patients with rheumatoid arthritis (RA) is around 70% [1]. Seropositive RA status, defined by positivity for RF and/or ACPA, is associated with poor disease prognosis [2]. Little is known about the prevalence of RA, percentages of seropositive RA versus seronegative RA, and the comorbidity profile and infections of these patients in Puerto Rico (PR).
Objectives: To estimate the prevalence of seropositive and seronegative RA in PR and to understand the demographic and clinical characteristics among Puerto Ricans with seropositive versus seronegative RA.
Methods: This was a descriptive retrospective observational cohort study using Merative™ MarketScan® claims database. To examine RA prevalence, eligible Puerto Rican adults were required to have ≥6 months of continuous enrolment (CE) from October 1, 2016, through April 30, 2021 (index period), have ≥3 visits with RA diagnose codes (ICD-10-CM M05 or M06, ignoring M06.1 and M06.4, with ≥2 claims with RA diagnoses occurring between 7 and 365 days of one another). Those patients with ≥1 M05 diagnosis code during the index period were categorized into the seropositive cohort (SP), the index date is the date of the first M05 diagnosis during the index period; otherwise, they were classified into the seronegative cohort (SN), the index date was the date of first an M06 (excluding M06.1 and M06.4), Patients with RA diagnosis in the baseline period were excluded. To assess comorbidity profile and infections, the eligible patients were also required to have ≥12 months CE prior to index date. The demographics, clinical characteristics, and infections were assessed during 12 months prior to the index date (baseline period), and standardized differences were estimated. The crude incidence rate (total new cases/100 person-year) of comorbid conditions and infections were estimated during the follow-up period.
Results: The prevalence of RA among Puerto Ricans was 1.03%. Of 141 patients with RA, 56.7% of them were seropositive. Within eligible seropositive (n=53) and seronegative (n=42) RA patients for the evaluation of comorbidities and infections, the mean (SD) of age were 50.75±12.93 and 49.36±11.22 years (d = 0.11), respectively. Most patients were females (79.25% for SP vs 71.43% for SN, d=0.18) and had commercial insurance (92.45% for SP vs 97.62% for SN, d=0.24). The mean (SD) of Charlson Comorbidity Index scores were 0.79±1.17 vs 0.64±1.01(d=0.14) for seropositive and seronegative respectively. For both seropositive and seronegative cohorts, the most prevalent comorbidities were hyperlipidemia (37.74% vs 30.95%, d=0.14), hypertension (33.96% vs 66.67%, d=0.69) and Type II diabetes (24.53% vs 21.43%, d=0.07) respectively. The most frequent infections were those happening in the urinary tract (18.87% for SP vs 14.29% for SN, d=0.12). In the follow-up period, the crude IR/100-person year were 79.34 and 33.45 for hyperlipidemia; 42.74 and 32.46 for T2DM; 27.47 vs 29.46 for hypertension, and 19.53 vs 25.00 for urinary tract infection for seropositive and seronegative RA cohorts, respectively.
Conclusion: This study found that the prevalence of RA among Puerto Ricans was similar to that reported in US mainland, with most (56.7%) presenting seropositive RA. We also observed a substantial burden of comorbidities among both seropositive and seronegative RA patients. Future studies with a large sample size are warranted.
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Disclosure of Interests: Fernando Arenal-Cruz Shareholder of: Hold stock or stock options at Bristol Myers Squibb, Employee of: During the conduct of the study, I was an employee of Bristol Myers Squibb, Greeta Jobson Consultant of: Bristol Myers Squibb, Eneida Villanueva Shareholder of: Hold stock or stock options at Bristol Myers Squibb, Employee of: During the conduct of the study, I was an employee of Bristol Myers Squibb, Julia Zhu Shareholder of: Hold stock or stock options at Bristol Myers Squibb, Employee of: During the conduct of the study, I was an employee of Bristol Myers Squibb.
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AB0314

DMARD INITIATION IN OLDER ADULTS WITH NEW DIAGNOSIS OF LATE-ONSET RHEUMATOID ARTHRITIS

Keywords: Real-world evidence, Rheumatoid arthritis, Disease-modifying Drugs (DMARDs)

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Background: The number of older adults living with rheumatoid arthritis (RA) is growing as the world population is aging. Older adults with RA are less likely to receive disease modifying anti-rheumatic drug (DMARD) despite these medications being effective and generally well tolerated in older adults. Up to one-third of the older RA population are diagnosed after the age of 65 and have late-onset RA (LORA). Older adults with LORA experience more symptomatic and progressive disease, and yet, their treatment in usual care is not well understood.
Objectives: To evaluate initiation of DMARDs in older adults with new diagnosis of LORA.
Methods: In this retrospective observational study, using 20% Medicare data from 2009-2017, we identified adults 66 years of age or older with new diagnosis of LORA without any DMARD use during the 12 months prior to cohort entry. Information on baseline patient characteristics and DMARD initiation during the first 12 months after LORA diagnosis were collected. We also assessed concomitant use of glucocorticoids (GCs) and opioids that are not disease modifying but can improve symptoms of RA.
Results: We identified 25,139 older adults with new diagnosis of LORA in continuous fee-for-service Medicare. Average age at LORA diagnosis was 76.9 (SD 7.6), 76.4% were female, 76.7% were non-Hispanic white, 37.2% had low-income subsidy, and 63.1% had three or more comorbid conditions. Less than one third were initiated on some form of DMARD (28.8%) during the first 12 months after LORA diagnosis. Among those on any DMARDs (N=7252), 87.7% were initiated conventional synthetic DMARD only, 2.2% on biologic DMARD only, and 10.1% on both classes of DMARDs. Concomitant long-term (≥3 months) GC use was greater among those on any DMARD (44.7%) compared to those without DMARD (15.0%). Opioid use was common and observed in 50.4% and 46.9% of those on any DMARD and those without DMARD, respectively. In multivariable analyses, DMARD initiation was associated with younger age, fewer comorbidities, and absence of low-income subsidy status (Table 1).
Conclusion: DMARD use in older adults with new diagnosis of LORA is low despite current clinical practice guidelines recommending early aggressive initiation of treatment. Long-term GC use is common among those on any DMARDs, raising concern for suboptimal DMARD use. Further studies are needed to understand drivers of DMARD use in older adults with LORA.
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Table 1. Patient characteristics associated with initiation of any DMARD after new diagnosis of LORA among Medicare beneficiaries ≥66 years of age

Variables	OR (95% CI)	
	Unadjusted	Adjusted
Age at diagnosis	0.941 (0.937, 0.944)	0.944 (0.940, 0.948)
Female	0.853 (0.801, 0.909)	0.985 (0.922, 1.051)
Race		
White (Ref)	1	1
Black	0.715 (0.650, 0.787)	0.928 (0.837, 1.028)
Hispanic	0.730 (0.659, 0.810)	0.985 (0.881, 1.102)
Other	0.899 (0.785, 1.030)	1.042 (0.903, 1.203)
Low Income Subsidy	0.519 (0.489, 0.551)	0.567 (0.530, 0.606)
Comorbidity		
<3 (ref)	1	1
3-5	0.716 (0.675, 0.760)	0.848 (0.797, 0.902)
≥6	0.431 (0.396, 0.468)	0.566 (0.519, 0.617)

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AB0315

ESTABLISHED RHEUMATOID ARTHRITIS PATIENTS APPEAR TO HAVE IMPAIRED QUADRICEPS MUSCLE MORPHOLOGY ASSESSED BY ULTRASOUND AND MUSCLE STRENGTH IMPAIRED OVER TIME: A COHORT STUDY

Keywords: Rheumatoid arthritis, Ultrasound

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Background: Rheumatoid arthritis (RA) patients usually present extra-articular manifestations [1], which affect muscle strength, muscle mass and physical functional [2]. There are several methods to assess muscle mass and, among these methods, muscle ultrasound (MU) has been suggested as an alternative to assess muscle morphology [3].
Objectives: [1] To assess the MU of the quadriceps muscle and verify changes over time (1-year) in muscle thickness and pennation angle in RA patients; and [2] to verify the of changes in clinical features, muscle strength, physical functional in over time in RA patients.
Methods: RA patients, age ≥18years and who met 2010 American College of Rheumatology criteria were included. Morphological parameters in quadriceps muscle consisted of the muscle thickness and pennation angle of rectus femoris (RF), vastus intermedius (VI) and vastus lateralis (VL). RA activity was measured by 28-joint disease activity score (DAS28) assessed by C-reactive protein (CRP), muscle strength by handgrip, and physical functional by health assessment questionnaire (HAQ) and timed-up-and-go (TUG) test. The paired samples Wilcoxon test was used to compare variables between the baseline and 1-year assessments. The significance level was set at $p \leq 0.05$ for all analyzes.
Results: At baseline, 155 patients with median of age 60.00 (52.00-65.00) years old, disease duration 11.00 (6.00-20.00) years and DAS28-CRP 2.77 (2.02-3.76) were included. Until moment, twenty-two patients completed the 1-year follow-up. Among these re-evaluated patients, there was a decrease in the VL (-11%) and VI (-13%) pennation angles of quadriceps muscle, and decrease in muscle strength assessed by handgrip test (-36%) after 1-year. On the other hand, no changes were observed in muscle thickness, RF pennation angle, DAS28-CRP, HAQ, and TUG test in over time ($p>0.05$; table 1).
Conclusion: These preliminary observations indicate that established RA patients have impaired muscle quality (pennation angles) and impaired muscle strength over time. However, it is necessary to complete the remainder of the reassessments to confirm these findings, besides verifying the associations with clinical parameters.
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Table 1. Changes after 1-year in quadriceps morphological parameters, clinical features, muscle strength, and physical functional in RA patients.

	At baseline, [n]	At 1-year,[n]	Δ,[n]	*p* value
Muscle thickness (cm)				
Rectus femoris	1.01 (0.81–1.31), [154]	0.89 (0.59–1.34), [22]	-0.07 (-0.22–0.13), [22]	0.485
Vastus intermedius	1.06 (0.88–1.32), [154]	0.95 (0.76–1.07), [22]	-0.02 (-0.06–0.01), [22]	0.115
Vastus lateralis	1.47 (1.24–1.78), [155]	1.36 (1.15–1.51), [22]	-0.02 (-0.23–0.08), [22]	0.230
Pennation angle (º)				
Rectus femoris	9.67 (7.80–11.48), [154]	8.51 (7.57–9.50), [22]	0.03 (-1.79–0.51), [22]	0.338
Vastus intermedius	9.08 (7.17–10.63), [154]	7.56 (6.86–9.80), [22]	-0.59 (-1.22–0.07), [22]	0.013*
Vastus lateralis	13.09 (11.10–14.58), [155]	11.89 (11.26–13.64), [22]	-1.23 (-2.37– -0.03), [22]	0.003*
Handgrip test (kg)	18.00 (10.00–24.00), [154]	9.00 (3.75–14.25), [22]	-2.50 (-11.25–2.25), [22]	0.049*
DAS28-CRP	2.77 (2.02–3.76), [154]	2.43 (2.03–3.39), [22]	-0.31 (-1,76–0.31), [22]	0.088
HAQ (score)	1.00 (0.50–1.63), [138]	1.13 (0.60–1.47), [22]	0.12 (-0.44–0.44), [13]	0.944
TUG (s)	9.45 (7.33–10.34), [137]	8.00 (7.22-8.80), [22]	-0.49 (-1.15–0.92), [18]	0.514

Abbreviation: Δ, Delta (1year - at baseline); DAS28-CRP, 28-joint disease activity score assessed by C-reactive protein CRP; HAQ, Health assessment questionnaire; TUG, Timed-up-and-go; cm, centimeters; º, degrees; kg, kilograms; s, seconds. *p<0.05. The data are shown in median (interquartile range, IQR).

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Rheumatoid arthritis - comorbidity and clinical aspects

AB0316 CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS AND THE PRESENCE OF PORPHYROMONAS GINGIVALIS IN THE ORAL FLORA

Keywords: Rheumatoid arthritis, Descriptive Studies, Comorbidities

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Background: It has been shown that periodontal disease, together with the presence of other germs, may play an important role in the development and maintenance of rheumatoid arthritis (RA). In particular, Porphyromonas gingivalis (Pg), a large anaerobic gram-negative bacteria, produces the extracellular proteases arginine-gingipain and petidyl-arginine deiminase, which contribute to oral periodontal destruction but also promote peptide citrullination, inducing the synthesis of anti-citrullinated peptide antibodies that have been linked to the onset of rheumatoid disease, its severity and its perpetuation[1,2].
Objectives: The purpose of the present work is to characterize patients with RA who are carriers of Pg in the oral cavity.
Methods: Oral flora has been analyzed by semiquantitative PCR for 5 germs involved in periodontal disease, which includes Pg (Peiropoc-Genspeed biotect) in 236 RA patients and 84 healthy controls, obtained from an outpatient clinic of non-inflammatory conditions: 172 women and 63 men, mean age 57.69 years. Correspondence analyses were performed with Pearson's test for different non-parametric variables and Mann-Whitney test for continuous variables.
Results: Presence of Pg was detected in 80 patients with RA(34%) and in 28 controls (33.7%). The mean age of the carriers was slightly higher (62.04; p>0.05) and the majority were women (72.5%). 22.5% of the smokers were carriers of Pg, while 10.8% were in the control group (p= 0.16). The mean activity, measured by DAS28 was 2.05 in carriers and 2.66 in non-carriers, with no significant differences (p=0.84). The mean CRP in carriers was 0.47 and in the overall RA of 1.08 (p=0.61) and the mean ESR was 13.37 in carriers and 16.83 in noncarriers (p=0.11). Anti-CCP were found in 55% of Pg carriers and in 72% of noncarriers (p=0.009). The functional capacity measured by HAQ was 0.245 in carriers vs 0.442 in non-carriers (p>0,05). Interestingly, in all the cases where Pg was identified, other bacteria capable of causing periodontal disease were also detected, especially Tanerella forsythia.
Conclusion: The presence of Prophyromonas gingivalis is more frequent in older and smoker patients with RA. Pg in the oral flora of patients with RA does not seem to contribute to a greater severity of the disease, in terms of functional capacity or activity, as well as in its measurement parameters. It should be noted that whenever Pg has been detected there is co-infection with other germs involved in periodontal disease.
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AB0317 PLASMA NETS LEVELS IN ESTABLISHED RHEUMATOID ARTHRITIS PATIENTS RECEIVING BIOLOGICAL OR JAK INHIBITOR THERAPY AND ASSOCIATION WITH DISEASE ACTIVITY

Keywords: bDMARD, Outcome measures, Rheumatoid arthritis

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Background: Neutrophil extracellular traps (NETs) may play a pathogenic role in rheumatoid arthritis (RA)[1]. Elevated circulating NETs have been found in RA plasma, but their relationship with synovial inflammation and antirheumatic therapy including biologics and JAK inhibitors (JAKi) is unclear.
Objectives: To evaluate whether plasma levels of NETs remnants in patients with established RA are associated with disease activity or type of antirheumatic therapy (biologics or JAKi).
Methods: Observational cross-sectional study. RA patients (ACR/EULAR 2010) receiving treatment with IL6 inhibitors (IL6i), JAKi, or TNF inhibitors (antiTNF) were consecutively included regardless of disease activity and previous therapy. Controls were RA patients with high disease activity (≥ 4 swollen joints), regardless of treatment, as was a second control group of healthy blood donors. Clinical disease activity indexes (DAS28, SDAI, CDAI) and laboratory parameters of inflammation, including high-sensitive CRP (hsCRP) and calprotectin were evaluated. Plasma levels of elastase-DNA (EN-DNA) and histone-DNA complex (H_3-DNA) (NETs remnants) were examined by ELISA. We analysed NETs remnant levels and clinical variables using Spearman's correlation test.
Results: 111 patients (90.1% female, 85.6% seropositive (RF and/or ACPA), mean age 56.45 years and mean RA duration 15.9 years) were included: 83 received biologics (53 IL6i and 30 antiTNF) and 28 JAKi (19 baricitinib and 9 tofacitinib). Mean DAS28 and CDAI were 3.00 and 10.5, respectively. Controls were 18 active RA patients (mean DAS28 5.72 and CDAI of 34.9), 11 without biological or JAKi treatment [Table 1]. 30 healthy blood donors were also analysed. NETs levels of patients under biologic or JAKi therapy showed no significant differences with healthy controls. No significant differences were observed in NETs values according to the type of therapy. In the control group of patients with high disease activity, plasma NETs were higher than in the main group (treated with JAKi or biologics), but only with statistically significant in H3-DNA levels (EN-DNA 2.96 (sd 5.42) vs 1.25 (sd 1.03) p=0.03; H3-DNA 2.67 (sd 4.52) vs 1.36 (sd 1.15) p >0.05). The two NETs were strongly correlated (ρ=0.97; p<0.001). A weak correlation between NETs and clinical disease activity (DAS28, CDAI, SDAI) was found, but not with laboratory parameters of inflammation including calprotectin.
Conclusion: NETs are elevated in active RA patients but weakly correlated with clinical disease activity. Patients with established RA under biologic or JAKi

TABLE 1. Results shown as mean (standard deviation) or number of patients (%)

	IL6i N 53	JAKi N 28	antiTNF N 30	p	ACTIVE N 18	p	TOTAL N 129	Healthy controls N 30
Age	58.1 (11.3)	54.5 (11.4)	55.4 (13.2)	NS	52.6 (11.8)	NS	55.92 (11.86)	
Female	48 (90.6)	25 (89.3)	27 (90.0)	NS	17 (94.4)	NS	117 (90.7)	
Disease evolution (years)	16.8 (9.3)	13.7 (9.7)	16.5 (11.7)	NS	10.0 (8.5)	NS	15.1 (10.0)	
Disease activity								
28TJC	3.3 (4.9)	4.0 (5.7)	2.4 (3.7)	NS	12.1 (7.5)	<0.001	4.43 (6.1)	
28SJC	0.96 (1.3)	2 (2.5)	1.4 (2.3)	NS	7.61 (2.6)	<0.001	2.2 (3.0)	
PGA	3.24 (2.1)	4.1 (2.5)	3.9 (2.9)	NS	7.3 (2.4)	<0.001	4.1 (2.7)	
PhGA	2.2 (1.6)	2.9 (2.07)	2.4 (2.3)	NS	7.9 (1.3)	<0.001	3.2 (2.7)	
CDAI	9.57 (7.8)	13.0 (10.2)	9.9 (9.5)	NS	34.9 (12.1)	<0.001	13.9 (12.1)	
SDAI	9.5 (7.9)	13.6 (10.4)	10.7 (10.8)	NS	37.1 (12.5)	<0.001	14.6 (13.5)	
DAS28	2.53 (1.11)	3.81 (1.38)	3.08 (1.17)	<0.001	5.72 (1.27)	<0.001	3.38 (1.60)	
Laboratory								
hsPCR mg/dL	0.10 (0.24)	0.38 (43)	0.77 (2.5)	<0.001	1.83 (1.94)	<0.001	0.55 (1.51)	
ESR mm/h	6.28 (3.97)	29 (29.5)	15.7 (11.50)	<0.001	29.67 (23.46)	<0.001	16.52 (19.88)	
Plasma calprotectin (µg/ml)	0.61 (0.56)	1.21 (1.40)	1.25 (2.24)	NS	3.27 (2.93)	<0.001	1.25 (1.88)	
NETs remnant levels								
EN-DNA	1.15 (0.32)	1.05 (0.22)	1.13 (0.61)	NS	2.30 (4.29)	NS	1.29 (1.67)	1.16 (0.91)
H_3-DNA	1.12 (0.33) *	1.05 (0.21)*	1.13 (0.21)	NS	2.16 (3.60) *	0.03	1.26 (1.39)	1.27 (1.40)

therapy have low levels of plasma NETs. NETs levels may be influenced by biologic or JAKi treatment.

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AB0318 DAS28 WITH THREE VARIABLES PERFORMANCE IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT CONCOMITANT FIBROMYALGIA

Keywords: Rheumatoid arthritis, Fibromyalgia

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Background: Several studies have shown that rheumatoid arthritis (RA) patients with concomitant fibromyalgia (FM) can cause an overestimation of the disease. activity assessed by the 28 disease activity score (DAS28) by inflating the patient reported components. DAS28 V3 is calculated based on only three variables: swollen and tender joint counts and CRP.

Objectives: The aim of this study was to evaluate the performance of the DAS28 V3 in a cohort of RA patients with and without concomitant FM.

Methods: Cross-sectional observational study that included consecutive patients with diagnosis of RA (ACR/EULAR 2010 criteria) with and without concomitant FM (ACR 2016). Demographic and RA characteristics were collected. All patients underwent a clinico-biological and an ultrasound (US) assessment of RA activity. US examination included the assessment of synovial/tenosynovial hypertrophy in grey scale and in Power Doppler (PD). P<0.5 was accepted for significance.

Results: Eighty patients distributed into 40 patients in each group were recruited. Epidemiological and RA characteristics were comparable between groups. Subjective. activity parameters were higher in RA with FM group (p ≤0.05). No significant difference was observed between the groups in regards to mean DAS28, DAS28 V3, SDAI and CDAI (p=0.12, p=0.14, p=0.2 and p=0.5 respectively). DAS28 was significantly greater than DAS28 V3 in RA with FM group (p=0.000). However, no difference between DAS28 and DAS28 V3 was not significant in the PR without FM group. Multivariate analysis in RA with FM group showed that DAS28 V3 was significantly positively associated with the presence of US synovial hypertrophy (r=0.494, p=0.001) and the presence of US PD synovitis (r=0.155, p=0.032), while Patient Global Activity expressed a significant negative association (r=-0.392, p=0.049 and r=-0.642, p=0.005 respectively).

Conclusion: Our study confirms that DAS28 V3 score would represent a better alternative for the clinical assessment of disease activity in RA patients with concomitant FM.

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Disclosure of Interests: None Declared.

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AB0319 HIGH PREVALENCE OF HYPOALBUMINEMIA IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Diet and Nutrition

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Background: Hypoalbuminemia is associated with worse medical conditions in chronic diseases and surgery outcomes. The concentration of serum albumin in patients with rheumatoid arthritis (RA) has been reported to decline. However, less is known about the prevalence and severity of hypoalbuminemia in RA patients and its association with RA disease.

Objectives: To investigate the association of hypoalbuminemia with RA disease characteristics and its potential mechanism in RA.

Methods: This cross-sectional study collected clinical data from a Chinese RA cohort, including disease activity, physical function, and radiographic assessment. Serum levels of albumin and inflammatory cytokines including soluble interleukin 2 receptor (sIL-2R), IL-6, IL-10, TNF-α, IL-8, and IL-1β were detected. According to the level of serum albumin, RA patients were divided into four groups as normal albumin (≥ 35.0 g/L), mild hypoalbuminemia (30.0 - 34.9 g/L), moderate hypoalbuminemia (25.0 - 29.9 g/L) and severe hypoalbuminemia (< 25 g/L).

Results: ①Among 1510 RA patients recruited in the cohort, 890 RA patients were eligible for analysis. Their mean age was 53.5 years old and 77.2% were female. There were 87.9% patients with active RA (CDAI > 2.8). ② The prevalence of hypoalbuminemia was 48.2% (429/890) in all RA patients and 50.9% (398/782) in active RA. The prevalence of hypoalbuminemia increased with age, disease activity, but decreased with BMI (all *P* trend < 0.05, Figure 1). ③ Compared with those with normal albumin, RA patients with hypoalbuminemia were older, had lower BMI, higher levels of ESR and CRP, higher disease activity, and higher HAQ-DI. ④ RA patients with hypoalbuminemia had higher levels of serum inflammatory cytokines, including sIL-2R, IL-6, TNF-α and IL-10 than those without, regardless the severity of hypoalbuminemia. Moreover, the level of albumin was negatively correlated with all six inflammatory cytokines (*r* range from -0.124 to -0.334, all *P* < 0.001). ⑤ Multivariate ordinal logistic regression analysis showed that BMI [adjusted odd ratio (AOR) = 0.889) and IL-10 (AOR = 0.971) were negatively, age, ESR, CRP, previous treatment with glucocorticoids, sIL-2R, IL-6, and IL-8 were positively associated with hypoalbuminemia in RA patients (AOR range from 1.001 to 1.671, all *P* < 0.05).

Conclusion: Our data show high prevalence of hypoalbuminemia in patients with active RA which is associated with high inflammation. These data imply the importance of the control of inflammation and nutrition supply. Further prospective study is needed in future.

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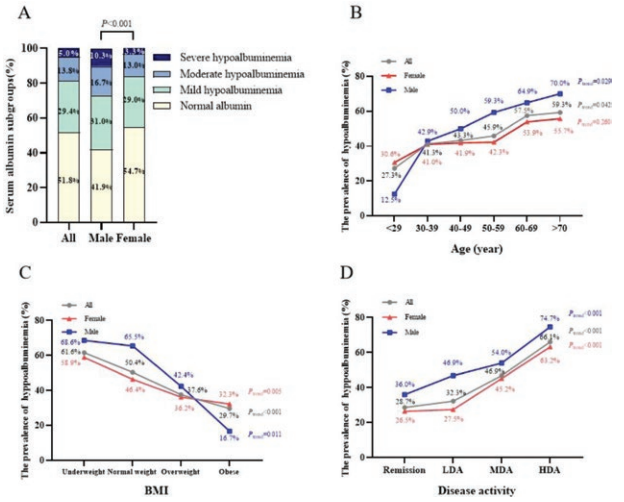


Figure 1. The prevalence of hypoalbuminemia in RA patients with different stratification

The prevalence of hypoalbuminemia in different sex **(A)**, age **(B)**, BMI **(C)**, and disease activity groups **(D)**. RA, rheumatoid arthritis; **Remission** (CDAI ≤ 2.8), **LDA** low disease activity (2.8 < CDAI ≤ 10), **MDA** moderate disease activity (10 < CDAI ≤ 22), **HAD** high disease activity (CDAI > 22)

Disclosure of Interests: None Declared.

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AB0320 SACROILIITIS AND ACPA POSITIVE: IS THIS AN ASSOCIATION OF RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS? ABOUT 16 CASES

Keywords: Psoriatic arthritis, Spondyloarthritis, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) and spondyloarthritis (SpA) in particular psoriatic arthritis (RP) are two distinct inflammatory rheumatisms having in common destructive peripheral involvement.

Objectives: We report a series of chronic inflammatory rheumatism with features of RA and SpA.

Methods: Descriptive retrospective study including patients with chronic inflammatory rheumatism, collected in the rheumatology department over a period of 10 years (2009-2019).

Results: 16 patients were included. The average age was 45.94 ± 12.10 years [28-71], with a female predominance of 87.5%. The mean age at onset of symptoms was 34.69 ± 12.71 years [14-57]. The disease duration was 11.25 ± 10.44 years. History was dominated by hepatic steatosis in 25%, diabetes in 18.8%, hypertension and smoking in 12.5%. A history of familial rheumatism and cutaneous psoriasis was found in only one patient. The revealing symptomatology was dominated by chronic polyarthritis in 75%, polyarthralgia in 18.8%

and mono-arthritis in one case. Deformities were described in 43.8%. On the immunological assessment, the mean ACPA was 191.25 ± 155.68 [36-500]. Rheumatoid factor and Anti-nuclear antibodies were positive in 50% and 37.5% respectively. HLA B27 was done in 2 patients, 1 of whom was positive. Sjögren's syndrome was present in 37.5% of patients. A biological inflammatory syndrome was found in the majority of patients with an average ESR and CRP of 37.38 and 20.41 respectively. Radiographic sacroiliitis was noted in 56.3%, and the rest were non-radiographic. Syndesmophytes were noted in 3 patients (18.8%). Coxitis was present in 12.6%. Structural damage in 81.3% made of erosions, geodes and pinching with reconstruction images in 4 patients. Patients were treated with corticosteroid therapy in 87.5%, methotrexate in 62.5%, sulfasalazine in 43.8%, and biotherapy in 25% of cases with anti-TNF alpha type.

Conclusion: These associations pose difficulties in diagnosis and management. A more in-depth study of these patients can help with an accurate diagnosis and therefore with optimal management.

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AB0321 APPLICATION OF NOVEL REFERENCE VALUES FOR 24-HOUR PROFILE OF CENTRAL SYSTOLIC BLOOD PRESSURE IN RHEUMATOID ARTHRITIS: CORRESPONDENCE WITH PERIPHERAL BLOOD PRESSURE AND CLINICAL ASSOCIATIONS OF HYPERTENSIVE PHENOTYPES

Keywords: Comorbidities, Heart, Cardiovascular disease

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Background: Prognostic significance of 24-h profile of peripheral BP is well-known. The growing insights in the role of arterial stiffening in cardiovascular disease led to the viewpoint that vascular risk must be more closely associated with central than brachial BP. While the upper limits for clinic and ambulatory peripheral BP have been routinely used for a long time and the reference values for clinical central BP have been developed some years ago, the hypertensive threshold for 24-h central BP hasn`t been investigated until 2022.

Objectives: To apply novel reference values of 24-h central SBP (cSBP) in the patients with rheumatoid arthritis and to characterize the hypertensive profile.

Methods: The study group included 85 patients with RA (females 77.6%, age 59.7±14.3 (M±SD) years, HTN 65%, median HTN duration 6.6 years, RA duration – 7 years seropositive RA 65%, mean DAS-28(CRP) 3.7±1.1) and control group (40 patients matched by gender, age and risk factors). All patients with HTN received antihypertensive therapy. Office peripheral BP was measured with a validated oscillometric device, 24-hour ABPM was performed with BPLab Vasotens, arterial stiffness – by applanation tonometry. CV risk was calculated by mSCORE (EULAR recommended modified version). The upper limits for normal central SBP were 125 mmHg for daytime, 115 mmHg for nighttime and 120 mmHg for 24-h BP. P<0.05 was considered significan.t.

Results: Mean central SBP in patients with RA was 123±21 mmHg (108±13 mmHg in normotensive and 132±20 in hypertensive patients, p<0.05). Hypertensive patients with RA vs controls were characterized by significantly higher frequency of elevation of daytime cSBP (44.1% vs 12.5%, p=0.01) and a trend to higher frequency of elevation of nighttime cSBP (58.8% vs 37.5%, p=0,09) and 24-h SBP (47.1% vs 25%, p=0.05). In normotensive RA patients compared to controls cSBP was elevated in 7.1% vs 0% for daytime, 14.3% vs 0% for nighttime and 7.1% vs 0% for 24H BP respectively (p>0.05 or the trend). All patients with normal peripheral ambulatory SBP (daytime, nighttime and 24-h) had normal central ambulatory SBP. 2 patients with elevated 24-h pSBP and 5 patients with elevated nighttime pSBP had normal cSBP while 2 patients with normal daytime pSBP had elevated cSBP. Patterns of diurnal index were similar for peripheral and central SBP (the discordance was observed only in 4 patients who were dippers by peripheral BP and non-dippers by central). Patients with RA and central 24-h BP elevation compared to patients with normal profile had higher ESR, longer RA duration, higher BMI, higher frequency of obesity, HTN, longer duration of HTN, higher cfPWV, central pulse pressure, stiffness gradient (cfPWV/crPWV), CAVI and higher CV risk. There were significant correlations between central 24-h BP elevation and ESR, hypertension-related parameters (PWV, pulse pressure, stiffness gradient, CAVI) and SCORE index.

Conclusion: The first application of novel reference values of ambulatory cSBP in RA showed that cSBP elevation is highly prevalent and in hypertensive individuals the frequency of daytime cSBP elevation is higher than in controls. Not only hypertension related parameters but also high ESR may be the markers of 24-h cSBP elevation.

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AB0322 RELATIONSHIP BETWEEN PHYSICAL BALANCE ABILITY AND PHASE ANGLE OBTAINED BY BIOELECTRICAL IMPEDANCE ANALYSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Quality of life, Rheumatoid arthritis, Sarcopenia

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Background: We have reported that a decrease in phase angle (PhA), an index of cell membrane fragility, nutritional status, and muscle strength, measured by bioelectrical impedance analysis (BIA), is associated with falls in patients with rheumatoid arthritis (RA) [1]. Since a decline in physical balance ability is thought to be related to falls, assessing physical balance ability is important, and in recent years, assessment of physical balance ability has been included in the diagnostic criteria for sarcopenia. The PhA reflects muscle status and may be related to physical balance ability, but the relationship between physical balance ability and the PhA in RA patients is unclear.

Objectives: To examine the relationship between physical balance ability and the PhA in RA patients.

Methods: A cross-sectional analysis of 89 RA patients (78% female, mean age: 66.7±14.3 years) was performed. The PhA was evaluated at 50 kHz on a BIA device (MC-780A; TANITA, Japan). Assessment of physical balance ability was performed with a muscle function analyzer (BM-220; TANITA), which can assess physical balance ability based on changes in load during standing up from a chair. Of the indices obtained by the muscle function analyzer, lateral balance was evaluated by dividing the lateral directional variation value (Vx mm/sec) by the load variation value (Vw kg/sec) (Vx/Vw). The balance score, which is the score of the stability time (stable time) from the point after the maximum load value and Vx/Vw compared to the reference value, was also assessed. The associations of PhA with Vx/Vw being above the median and the z-score of Vx/Vw and of the balance score being above -0.5 were tested by logistic regression analysis, and the association between Vx/Vw and the PhA as continuous variables was tested by multiple regression analysis. The cutoff value of PhA for the balance score z-score of -0.5 was calculated by receiver-operating characteristic (ROC) curve analysis.

Results: Even after adjusting for covariates (sex, age, BMI, ADL, disease activity, and medication status), the PhA was significantly associated with Vx/Vw greater than the median [odds ratio (OR): 0.44, 95% confidence interval (CI): 0.19-0.995)] and z-score > -0.5 (OR: 0.42, 95%CI: 0.19-0.93). Multiple regression analysis adjusted for covariates also showed that the PhA was significantly associated with Vx/Vw (β=-0.22, p=0.023). A balance score z-score ≥ -0.5 was significantly associated with a PhA above the 75th percentile (OR: 9.34, 95%CI: 1.45-60.1). The cutoff value of the PhA for a balance score z-score of -0.5 was 4.87° (AUC = 0.64, p = 0.32) for men and 4.30° (AUC = 0.78, p < 0.001) for women.

Conclusion: The PhA may be associated with physical balance ability.

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Disclosure of Interests: None Declared.

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AB0323 DOES FRAILTY PREDICT METHOTREXATE DISCONTINUATION DUE TO ADVERSE EVENTS IN RHEUMATOID ARTHRITIS PATIENTS?

Keywords: Disease-modifying Drugs (DMARDs)

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Background: Rheumatoid arthritis (RA) patients are more likely to develop frailty than general population [1]. Frailty is defined as the intermediate stages of health and disability in physical and cognitive function, and can lead to various negative health outcomes. On the other hand, Methotrexate (MTX) is an anchor disease-modifying antirheumatic drug. RA treatment has advanced significantly with the introduction of MTX. However, it was reported that 94.3% of MTX-naïve RA patients had adverse events (AEs) (C-OPERA study) [2]. Thus, RA patients on MTX should always be aware of complications and AEs.
Objectives: Since RA patients with frailty have more comorbidities than those with non-frailty, complications of RA or RA drugs are also expected to increase. The purpose of this study was to clarify whether frailty in RA patients influences the occurrence of AEs related to MTX.
Methods: Of 538 RA patients (an observational study, T-FLAG study) who visited us in 2020, 320 used MTX. After 2 years of follow-up, we investigated final follow-up date and AEs leading to MTX discontinuation. Frailty was defined as a score of 8 or more on the Kihon Checklist (KCL). Logistic regression analysis was performed to determine factors associated with MTX discontinuation due to AEs. MTX retention rates were calculated by Kaplan–Meier analysis, and crude retention rates were compared using the log-rank test.
Results: Of the 320 patients (249 females) in this study, 23 patients (7.2%) discontinued MTX due to AEs. AEs included liver disorder (26.1%), MTX pneumonia (21.7%), decreased renal function (13.0%). There were no patients with MTX discontinuation due to inefficacy. Mean age at baseline (standard deviation [SD]) was 68.2 (11.9)/ 64.5 (13.9) years (MTX discontinuation/ MTX continuation), MTX dose was 8.1 (2.8)/ 8.1 (2.9) mg, Clinical Disease Activity Index (CDAI) was 6.1 (6.1)/ 5.6 (7.3), KCL was 9.0 (5.0)/ 5.8 (4.0) point ($p<0.05$), and the proportion of frailty was 56.5%/ 31.3% ($p<0.05$). Logistic regression analysis revealed significant associations of MTX discontinuation with KCL (OR: 1.16, 95%CI: 1.06–1.28), and frailty (OR: 2.77, 95%CI: 1.16–6.61), adjusting for age and sex. The rate of MTX retention (at 1 year, and 2 years) was significantly lower in subjects with frailty (91.2%, and 86.6%) than in those with non-frailty (96.2%, and 95.1%) respectively. Comparing the patient characteristics at baseline in subjects with frailty and non-frailty, mean age, CDAI, KCL, and the proportion of MTX discontinuation due to AEs were significantly higher in subjects with frailty.
Conclusion: Our finding suggest that frailty was the significant factor of MTX discontinuation due to AEs, and the rate of MTX retention was significantly lower in the subjects with frailty compared to non-frailty. Moreover, the subjects with frailty had significantly higher mean age and disease activity, suggesting that frailty comprehensively reflects a bad condition. Frailty is significantly associated with poor physical function, and poorer physical function is reportedly associated with a poorer response to treatment [3]. Poor physical function (physical frailty) may make patients more prone to MTX discontinuation due to AEs. These findings suggest that frailty is a comprehensive index with high predictive power for MTX discontinuation due to AEs. Therefore, the occurrence of MTX AEs should be carefully monitored when using MTX in RA patients with frailty.

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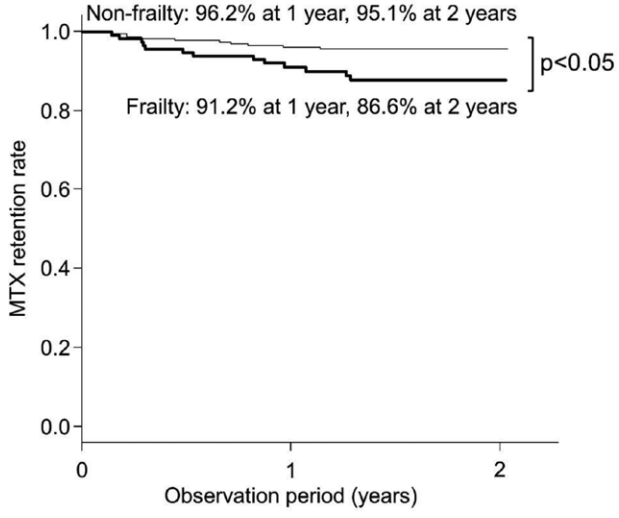


Figure 1.

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AB0324

DEVELOPMENT OF A MOBILE APP TO SUPPORT SELF-MANAGEMENT IN INDIVIDUALS WITH INFLAMMATORY ARTHRITIS

Keywords: Self-management, Rheumatoid arthritis, Artificial Intelligence

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Background: EULAR has recently highlighted the vital role of digital health in standard practice and the possibility to enhance the self-management abilities of the patients. Self-management strategies play an important role in improving clinical outcomes in patients with inflammatory arthritis. Smartphone technology has the potential to engage the patients with their treating health care professionals through suitable self-monitoring and easy access to information. In addition, having a more accurate summary of self-reported fluctuations in symptoms, psychosocial problems and behaviors can help both the patients and the treating health care professionals better understand the patient's condition, identify barriers to self-management, and assess treatment effectiveness and additional health care needs. However, evidence regarding these supporting digital tools, including smartphone apps, is currently very limited. So far there is no comprehensive mobile app developed to facilitate the collaboration between the patients and their treating physicians.
Objectives: 1.To provide basic data on system requirement specifications for a mobile app to self-manage inflammatory arthritis. 2. Identify the target audience, characteristics of the app, and correlations between the system requirements and the established behavior change techniques.
Methods: A participatory action research design was adopted to inform the app developer of the major themes recognized as the main pillars for the app development, implementing artificial intelligence. Qualitative data were collected using multiple methods in several workshops. Participants were 2 Rheumatologists, 1 rheumatology nurse specialist, 1 rheumatoid arthritis patient, 1 psoriatic arthritis patient, 1 patient Ankylosing spondylitis, and an App/ machine learning engineer. A taxonomy was used to determine the degree of correlation between the system requirements and established behavior change techniques.
Results: The app targets the optimization of self-management and provide non-medical management approach. The major themes identified were: 1. collect self-reported patient reported outcomes (disease functional ability, quality of life, motivation), 2. Collect information on patient demographics, comorbidity(ies), disease activity status (self-reported disease activity score), past and current medications, 3. Identify the individual patient's target to be achieved, 4. Develop a patient profile that focuses on the patient's disease activity status, well-being, targets and attitude, 5. Using artificial intelligence, construction of a personalized, evidence-based disease self-management program based on recommendations from medical guidelines, medical standards, and state-of-the-art clinical research; 6. implementation of personalized recommendations into the patient's daily life by providing short daily tasks that accelerate positive behavior change. 7. a calendar feature for goal setting, planning, and recording of (HRQoL) performance and progress, 8. a small community feature for positive feedback, support from peers and support the patient in coping with stress, sadness, depression, fatigue, and further disease-related symptoms, 9. Implementation of cognitive behavioral techniques, meditation and relaxation methods, 10. adapt a reward system to motivate end users for using the app, and, 11. Format the app interface.
Conclusion: These findings highlight the potential of implementing digital therapy to encourage self-management and engagement with health care professional for the management of patients with inflammatory arthritis. The results of this work suggest that using an app-based personalized disease management program may reflect significantly on several measures of patient-reported outcomes and disease activity in patients with RA/PsA/SpA. Future feasibility testing in a prospective study will firmly establish the reliability, efficacy, and cost-effectiveness of such an app intervention for this cohort of patients.

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AB0325

DEVELOPMENT OF A MOBILE APP FOR DISEASE-SPECIFIC COGNITIVE BEHAVIOR THERAPY MANAGEMENT IN INDIVIDUALS WITH RHEUMATOID ARTHRITIS

Keywords: Cognitive Function, Self-management, Rheumatoid arthritis

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Background: EULAR has recently highlighted the vital role of digital health in standard practice and the possibility to enhance the patient's quality of life. Cognitive Behavior Therapy (CBT) plays an important role in improving clinical outcomes in inflammatory arthritis patients. The aim of CBT is to boost patients' self-efficacy for pain management, or their confidence in their ability to control their pain, and lessen the interference that pain causes in their everyday lives. CBT does this by educating patients on how to develop more efficient coping mechanisms to deal with everyday pain sensations and enhance functionality and quality of life. So far, no comprehensive mobile app has been developed to facilitate the collaboration between patients and their CBT therapist, especially with those having monetary and physical constraints related to their disease.
Objectives: 1-To provide basic data on system requirement specifications for a mobile app to provide constructed CBT program for RA patients 2. Identify the target audience, characteristics of the app, and correlations between the system requirements and the established CBT.
Methods: To identify the major themes recognised as the main pillars for app development and inform the app developer/machine learning engineer, a participatory action research design was implemented. Qualitative data were collected using multiple methods in four workshops. Participants were 2 Rheumatologists, 1 rheumatology nurse specialist, 1 Psychiatrist4 rheumatoid arthritis patient, and an App developer. A taxonomy was used to determine the degree of correlation between the system requirements and established cognitive behavioral therapy techniques.
Results: The app targets the optimization of patient-reported outcomes and quality of life to provide a non-medical management approach via modifying Disease-specific dysfunctional beliefs and behaviors using cognitive and/or behavioral exercises in a structured manner. The major themes identified were: 1. collect self-completed patient-reported outcomes (disease functional ability, quality of life, motivation), 2. Collect information on patient demographics, comorbidity(ies), disease activity status (self-reported disease activity score), plus past and current medications, 3. Identify the individual patient's target to be achieved, 4. Develop a patient profile that focuses on the patient's perpetuating factors, 5. construction of a personalized, evidence-based disease management program based on recommendations from medical guidelines, medical standards, and state-of-the-art clinical research; 6. implementation of a personalized CBT program for Effective Coping, Life Goals, Pain Management, Emotional Responses, Managing Change, Self-Esteem, Relationships 7. a calendar feature for goal setting, planning, and recording of physical activity performance and progress, 8. a small community feature for positive feedback, support from peers and support the patient in coping with stress, sadness, depression, pain, fatigue, and further disease-related symptoms, 9. Implementation of relaxation exercises, 10. adapt a reward system to motivate end users for using the app,11. to help the patients learn ways to cope with increased resilience to disease-related episodes.12. Format the app interface.
Conclusion: These findings highlight the potential of implementing digital CBT to encourage RA patients to be able to cope with their disease, change wrong beliefs, allow them to retain jobs, socialize normally, and engage with healthcare professionals. The results of this work suggest that using an app-based personalized disease management program may reflect significantly on several measures of patient-reported outcomes and disease quality of life in RA considering alleviating conventional physical CBT barriers. Future feasibility testing in a prospective study will firmly establish the reliability, efficacy, and cost-effectiveness of such an app intervention for this cohort of RA patients.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0326

IMPACT OF ANTI-CITRULLINATED PROTEIN ANTIBODIES AND RHEUMATOID FACTOR ON BONE MINERAL DENSITY CHANGE IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH DENOSUMAB

Keywords: Autoantibodies, Osteoporosis, Rheumatoid arthritis

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Background: Osteoporosis is one of the major comorbidity in patients with rheumatoid arthritis (RA). A low bone mineral density (BMD), especially in the femoral neck, was associated with the presence of anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF). However, there are few reports investigated the influence of autoantibody on BMD change in patients with RA after osteoporosis treatment.
Objectives: There are a lot of evidence that denosumab increased BMD in patients with osteoporosis, and improved bone eroison in patients with RA. We evaluated the BMD change in patients with RA treated denosumab, and assessed the effect of autoantibody, such as ACPA and RF.
Methods: This study included 196 RA patients (187 female; mean age, 71.0 ± 9.0 years; mean disease duration, 17.8 ± 15.3 years; mean DAS28-CRP, 2.9 ± 1.2) who fullfilled the criteria of osteoporosis and treated with denosumab. Disease activity of RA was treated according to EULAR recommendation 2022. BMD at the lumbar spine, proximal femoral and femoral neck were evaluated by dual energy X-ray absorptiometry at baseline and 12 months after denosumab treatment. We evaluated the influence of ACPA and RF for BMD change.
Results: Improvement ratio of BMD at the lumbar spine, proximal femoral and femoral neck were 6.4% (p<0.01), 3.4% (p<0.01) and 1.6% (p=0.10) after 12 months treatment. There were no differences in BMD at the lumbar spine, proximal femoral and femoral neck before denosumab treatment between 101 ACPA-positive patients and 30 ACPA-negative patients (0.77 vs 0.77g/cm^2, p=0.68; 0.58 vs 0.61 g/cm^2, p=0.13; 0.48 vs 0.47 g/cm^2, p=0.7), between 128 RF-positive patients and 42 RF-negative patients (0.75 vs 0.76 g/cm^2, p=0.47; 0.59 vs 0.59 g/cm^2, p=0.68; 0.47 vs 0.46 g/cm^2, p=0.12). Improvement ratio of BMD at the lumbar spine, proximal femoral and femoral neck were 6.1% (p<0.01), 3.6% (p<0.01) and -0.18% (p=0.49) in ACPA-positive patients, 5.8% (p<0.01), 2.3% (p=0.01) and 3.7% (p<0.01) in ACPA-negative patients after 12 months treatment. Although there were no differences between ACPA-positive patients and ACPA-negative patients in BMD change at the lumbar spine (p=0.86) and proximal femoral (p=0.72), BMD change at femoral neck in ACPA-positive patients were lower than ACPA-negative patients (p=0.03). Improvement ratio of BMD at the lumbar spine, proximal femoral and femoral neck were 6.6% (p<0.01), 3.5% (p<0.01) and 1.1% (p=0.47) in RF-positive patients, 6.5% (p=0.04), 2.5% (p<0.01) and 2.0% (p=0.06) in RF-negative patients after 12 months treatment. There were no differences between RF-positive patients and RF-negative patients in BMD change at the lumbar spine (p=0.08), proximal femoral (p=0.66) and femoral neck (p=0.45). Multivariate linear regression analysis revealed that low BMD at baseline (β=-0.35, p<0.01) and ACPA positive (β=-0.2, p=0.04) inhibited the improvement of BMD at femoral neck (table 1).

Table 1. Multivariate linear regression analysis of risk factors to inhibit the improvement of BMD at femoral neck in patients with RA.

	β	95% CI	p
Age (years)	-0.054	-0.193, 0.103	0.551
Male (0, male; 1, female)	-0.007	-5.815, 5.367	0.937
ACPA (0, negative; 1, positive)	-0.199	-6.814, -0.233	0.036
RF (0, negative; 1, positive)	0.011	-2.995, 3.364	0.909
BMD of femoral neck at baseline (g/cm^2)	-0.355	-44.361, -14.521	<0.01
Glucocorticoid dose (mg/day)	-0.032	-0.741, 0.500	0.701
b/tsDMARDs use (0, no; 1, yes)	-0.110	-4.219, 0.908	0.204
Preosteoporosis treatment (0, no; 1, yes)	0.029	-2.078, 2.945	0.733

RA, rheumatoid arthritis; BMD, bone mineral density; ACPA, anti-citrullinated protein antibodies; RF, rheumatoid factor; b/tsDMARDs, biological and targeted synthetic disease-modifying antirheumatic drugs.

Conclusion: Denosumab improved BMD at the lumbar spine and proximal femoral in patients with RA independently regardless of ACPA and RF. ACPA-positive patients were difficult to improve BMD at femoral neck despite denosumab treatment.
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AB0327

DEVELOPING A CLINICAL ASSESSMENT TOOL FOR DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: RESULTS FROM A SYSTEMATIC LITERATURE REVIEW AND FEASIBILITY ASSESSMENT

Keywords: Rheumatoid arthritis, Inflammatory arthritides

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Background: Management of difficult-to-treat rheumatoid arthritis (D2T-RA) is challenging since poor treatment response also incorporates non-inflammatory symptoms that can mimic or amplify pain and scores on composite disease activity measures. Identification of modifiable non-inflammatory factors is vital to improve health outcomes and minimise harm from inappropriate escalation of drug therapy.
Objectives: To develop and assess feasibility of a systematic, evidence-based clinical assessment tool for the identification of modifiable non-inflammatory factors in D2T-RA.
Methods: A systematic literature search of PubMed, Embase and Web of Science databases for studies pertaining to D2T-/treatment refractory RA was undertaken from database inception to October 2021. Studies were screened against inclusion/exclusion criteria, and further excluded if deemed to have a high risk of bias. Data pertaining to factors associated with treatment non-response were extracted from eligible papers and categorised to inform composition of the clinical assessment tool. Through patient involvement, the proposed tool's components were assessed for their feasibility and ease of capture in an outpatient setting. Eight patients fulfilling EULAR definition of D2T-RA were recruited from a single centre. Clinical data and responses to relevant questionnaires mapped to the clinical tool, including: Patient Health Questionnaire-9 (PHQ-9), Brief Illness Perception Questionnaire (B-IPQ), Beliefs about Medicines Questionnaire-Specific (BMQ-S), Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) and Medication Adherence Report Scale-5 (MARS-5) were collected.
Results: 1154 records were screened, of which eight studies informed the development of a clinical assessment tool. Modifiable factors including raised BMI, smoking status, non-adherence, and co-morbidities, such as fibromyalgia and worse mental health were identified and incorporated into an initial tool. These factors were apparent and readily assessed within a local cohort of D2T-RA patients (Table 1). In summary, data from this cohort revealed a low burden of classified fibromyalgia, mild depression severity, and responses in keeping with a high illness concern. Despite general acceptance of pharmacological treatments, 'ever' non-adherence, classified as a response other than 'never' within the MARS-5 questionnaire was noted in two, five, and three patients regarding steroids, csDMARDs and b/tsDMARDs respectively.

Table 1. Clinical demographics and disease characteristics (n=8)

	Age (years)	59.5 (56.5-64.8)
	Female*	8 (100)
	Disease duration (years)	17 (11-23)
	Anti-CCP positive*	7 (87.5)
	RF positive*	6 (75)
	DAS28-ESR	4.6 (4.0-5.9)
	No. of comorbidities	4 (2-4)
	No. of previous csDMARDs	3 (2-4)
	No. of previous b/tsDMARDs	5 (5-6)
	Ever Smoker*	2 (25)
	BMI	26 (25.5-33.4)
Fatigue	FACIT-F score (0-52)	31 (23-36)
Fibromyalgia	Fulfils Fibromyalgia 2016 Revised Criteria*	1 (12.5)
Depression	PHQ-9	6 (3-9)
'Ever' non-adherence	Steroids*^	2 (33.3)
	csDMARds*	5 (62.5)
	b/tsDMARDs*	3 (37.5)
B-IPQ	B-IPQ (0-80)	42 (30-55)
BMQ-Specific	Necessity-Concerns Differential (-4 to +4)	1.2 (1-1.7)

Results presented as median (IQR); *n (%); ^n=6

Conclusion: Following a systematic review of the literature, we identified several modifiable factors that inform the development of a clinical assessment tool in D2T-RA and can be readily evaluated in an outpatient setting. A holistic approach is required to address both inflammatory and non-inflammatory aspects of D2T-RA. The development of an evidence-based clinical assessment tool is the first step in providing this, by identifying and targeting patient-specific non-inflammatory modifiable factors, in conjunction with pharmacological escalation.
REFERENCES: NIL.
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AB0328 EFFECTS OF BIOLOGICAL-DMARDS ON THE SERUM URIC ACID LEVEL IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis

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Background: Hyperuricemia associated with rheumatoid arthritis (RA) has been reported to be a risk factor for cardiovascular disease. It has been reported that uric acid (UA) levels decrease with the use of leflunomide and increase with tumor necrosis factor (TNF) inhibitor therapy. However, the effects of long-term biological disease-modifying antirheumatic drugs (bDMARDs) therapy and non-TNF inhibitor biologic therapy on UA levels have not been reported.
Objectives: We aimed to investigate the changes in UA levels during TNF and non-TNF inhibitor therapy.
Methods: Patients with RA treated with bDMARDs from 2008 to 2018 were studied based on the All Showa University of RA (ASHURA) database. The association between uric acid level reduction and treatment was evaluated in 629 patients treated with the bDMARDs, and the medical records of 256 patients with available uric acid levels were included. The following background factors were investigated: age; sex; type of bDMARDs; dosage of methotrexate and prednisolone; usage of conventional synthetic DMARDs, dyslipidemia drugs, hyper uremia drugs, and nonsteroidal anti-inflammatory drugs; body mass index; smoking history; HbA1c; presence or absence of hypertension and dyslipidemia; and serum creatinine, C-reactive protein, and matrix metalloproteinase-3 levels. We also used the simplified disease activity index (SDAI) to evaluate RA disease activity. The analysis was performed in two groups, TNF inhibitor-treated group (148 patients) and the non-TNF inhibitor-treated group (108 patients, tocilizumab and abatacept). The primary endpoint was UA levels before and after six months and one year, which was determined using the repeated-measures analysis of variance (ANOVA), and the secondary endpoint was the proportion of patients with hyperuricemia (uric acid level of 7.0 or higher was defined), determined using spearman's correlation coefficient by rank test.
Results: In TNF inhibitor-treated group, the UA levels were not increased from 4.9 ± 1.4 (mg/dl) to 4.9 ± 1.4 and 5.1 ± 1.7 before treatment and after six months and one year, respectively (p=0.50). The number of patients with hyperuricemia increased from 7 to 12 and 16 (p=0.026). The UA levels were not raised in non—TNF inhibitor-treated group from 5.2 ± 1.4 (mg/dl) to 5.2 ± 1.4 and 5.3 ± 1.4 (p=0.78). The number of patients with hyperuricemia increased from 8 to 16 and 12 (p=0.193). There was a difference in the type of drug but no difference in the duration of administration by repeated-measures ANOVA.
Conclusion: Our study suggests that TNF inhibitor therapy may affect an increased percentage of patients with hyperuricemia. On the other hand, non-TNF inhibitor therapy may not affect the increased rate of patients with hyperuricemia, and bDMARD treatment has a mild effect on UA levels in patients with RA.
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AB0329 THE IMPACT OF WEIGHT ON FOOT INVOLVEMENT DURING RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis

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Background: Overweight and obesity are highly common in patients with Rheumatoid Arthritis (RA), with probable impact on bearing foot joints.
Objectives: The aim of the present study was to explore the associations between Body Mass Index (BMI) and measures of foot health (foot pain, foot-related activity limitation, foot synovitis and deformities) in patients with RA.

Methods: A cross sectional study was conducted on 50 patients with RA consulting a rheumatology departement with different complains. Domains of foot health studied comprised: foot pain (Numeric Rating Scale), foot-related activity limitations (Foot Function Index), foot synovitis (Metatarsophalangeal Joint Count), and foot deformity (Platto Score).
Results: The mean age was 45.68 +/-10.3 years [20-76], most were female (82%), and most patients had moderately long disease duration (12.12 ± 7.67 years). RA was often moderately active (mean DAS28: 3.25 ± 0.98). Sixty six percent of our population were overweight or obese with a mean BMI 29 Kg/m2±5.74. The average foot pain intensity while walking was 6 ± 1.75, the mean FFI pain subscale was 40 ± 15.7 and the mean WOMAC pain subscale was 30 ± 13.2. Seventy percent of our patients had chronic foot pain (> 6 months). The heel was the most symptomatic location (62%). Podoscopic examination showed flat feet in 46% of cases, hollow feet in 20%, a valgus heel and varus heel were noted in 34 % and 12 % of cases respectively. The mean tender foot joint count was 5.5 ± 1.79and of swollen foot joint was 2.2 ± 1.55. The average of the foot structure index (Platto score) was 7.8 ± 2.73. Hallux valgus was the most common deformity (74 %) followed by claw toe in 43.5 % of cases and then subluxation of MTP joints in 26 %. Concerning foot-related activity limitation, the mean FFI score of Disability subscale was 32 ± 14.2 and the mean WOMAC score of physical functioning subscale was 33.8 ± 13.98. Half of our patients suffered from problems fitting their shoes because of claw toe, heel pain and Hallux valgus in 40 %, 36% and 32 % of cases respectively. Our study showed that higher BMI was associated with lower foot health in many of the studied measures. Patients with higher BMI reported significantly more foot pain (p = 0.001), more foot-related activity limitations: for both scales: FFI (p = 0.01; B=21.71) and WOMAC (p<0.001; B=20.64), more foot deformities assessed with Platto score (p= 0.02; B=4.78), more foot synovitis (p<0.001; OR=4.66) and more problems with footwear (p=0.05).However, in our population, higher BMI was significantly associated with less radiological joint damage (p=0.01) and lower feet sharp score (B= -13,9; *P* = 0.06).
Conclusion: Despite our findings of a possible protective effect of obesity on structural damage, obesity is still, as seen in this and many other studies, an important cause of increased pain, increased functional disability and impaired quality of life in patients with RA that requires special interventions.
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AB0330 EVALUATION OF THE ASSOCIATION BETWEEN MOOD DISORDERS AND THE REGION OF THE AFFECTED JOINTS IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY

Keywords: Rheumatoid arthritis

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Background: The prevalence of mood disorders, such as anxiety and depression, is higher in patients with rheumatoid arthritis (RA) than the general population. Even in the absence of a formal mood disorder, a significant number of RA patients are reported to have anxiety or depression. Although there have been reports of several factors associated with anxiety and depression in RA patients, few have evaluated associations with specific region of the affected joints.
Objectives: We aimed to evaluate the association between mood disorders and specific regions of the affected joints and compare them with previously reported associated factors.
Methods: We performed an analysis of data from 15,553 RA patients registered in a large database (NinJa: National Database of Rheumatic Diseases in Japan) in 2020. Patients for whom hospital anxiety and depression scale (HADS) data were acquired were included in this study. Presence of anxiety and depression were defined by a HADS score ≥11. We analyzed the data using multivariable logistic regression analyses. The affected joints from 68 joint counts were divided into four regions: upper/large, upper/small, lower/large, and lower/small. We performed the logistic regression analyses with anxiety or depression as dependent variables respect to age, sex, body mass index (BMI), disease duration, smoking history, the Steinbrocker's stage, CRP, regions of affected joints, and use of PSL, MTX, biologics, and JAK inhibitors as independent variables.
Results: In total, 8,982 patients were included in this study; of which; 7,154 were women (79.6 %) with a mean age 67.1 years (standard deviation [SD] = 12.8). The mean disease duration was 14.2 (SD = 11.6) years. In total, 489 (5.5 %) patients had anxiety, and 992 (11.2 %) had depression. The mean HADS-anxiety (A) in the non-anxiety, and anxiety groups, were 3.61 (SD = 2.70) and 13.24 (SD = 2.29), respectively. Moreover, mean HADS-depression (D) in the non-anxiety, and anxiety groups were 5.74 (SD = 3.30) and 10.45 (SD = 3.87), respectively. The mean HADS-A in the non-depression and depression groups were 3.67 (SD = 3.03) and 7.75 (SD = 4.40), respectively. Lastly, mean HADS-D scores in the non-depression and depression groups were 5.15 (SD = 2.62) and 12.73 (SD = 1.90), respectively. In logistic regression analysis, anxiety was associated with lower/large, and small joints, along with female sex, smoking history, and use of PSL. Moreover, depression was associated with upper/small and lower/large joints, along with female sex, lower BMI, disease duration, smoking history, use of PSL, non-use of MTX, and CRP.
Conclusion: Anxiety and depression were associated with the region of the affected joints, but in different patterns. When assessing the patient's mood in RA, the distribution of affected joints should also be noted.
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		anxiety			depression		
Variable		OR (95 % CI)	p value	VIF	OR (95 % CI)	p value	VIF
sex (women)		2.37 (1.70-3.29)	<0.05	1.21	1.26 (1.02-1.55)	<0.05	1.33
BMI		1.00 (0.97-1.02)	0.8	1.06	0.98 (0.96-1.00)	<0.05	1.06
disease duration (per years)		1.01 (1.00-1.02)	0.06	1.77	1.01 (1.00-1.02)	<0.05	1.83
smoking history	non	1.00 (reference)		1.27	1.00 (reference)		1.36
	past	1.48 (1.15-1.90)	<0.05		1.39 (1.16-1.67)	<0.05	
	current	2.09 (1.49-2.93)	<0.05		1.90 (1.48-2.44)	<0.05	
use of PSL		1.59 (1.28-1.96)	<0.05	1.11	1.51 (1.30-1.76)	<0.05	1.10
use of MTX		0.84 (0.68-1.04)	0.11	1.14	0.80 (0.69-0.93)	<0.05	1.14
CRP (mg/dL)		1.00 (0.91-1.09)	0.92	1.10	1.10 (1.04-1.16)	<0.05	1.11
region of affected joints	upper/large	0.93 (0.74-1.16)	0.5	1.18	1.01 (0.86-1.19)	0.86	1.19
	upper/small	1.12 (0.90-1.40)	0.3	1.14	1.22 (1.04-1.43)	<0.05	1.14
	lower/large	1.72 (1.38-2.15)	<0.05	1.16	1.43 (1.21-1.70)	<0.05	1.15
	lower/small	1.44 (1.03-2.01)	<0.05	1.11	1.10 (0.84-1.44)	0.49	1.09

Table. Logistic regression analysis model for anxiety (left) and depression (right)
BMI: body mass index; CI: confidence interval; OR: odds ratio; MTX: methotrexate; PSL: prednisolone; VIF: variance inflation factor

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Disclosure of Interests: Kenichiro Tokunaga: None declared, Hideto Oshikawa: None declared, Takahiro Nishino: None declared, Toshihiro Matsui Speakers bureau: AbbVie, Asahikasei Pharma Corp., Astellas, Chugai Pharmaceutical Co, Ltd., Eisai Co., Ltd. Eli Lilly Japan, Ono Pharmaceutical Co., Ltd., Pfizer Japan Inc., Grant/research support from: Asahikasei Pharma Corp., Chugai Pharmaceutical Co, Ltd., Shigeto Tohma Speakers bureau: Pfizer Japan inc., Abbie Japan Co., Ltd., Eisai Co., LTD., Janssen Pharmaceutical K. K., Celltrion healthcare Japan Co., Ltd., Consultant of: Mitsubishi-Tanabe Pharma Co., Grant/research support from: Chugai Pharmaceutical Co., LTD., Mitsubishi-Tanabe Pharma Co., Abbie Japan Co., Ltd.
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AB0331 CHEST HIGH-RESOLUTION COMPUTED TOMOGRAPHY IN PATIENTS WITH LONG STANDING RHEUMATOID ARTHRITIS: IS THERE ANY BENEFIT?

Keywords: Rheumatoid arthritis, Imaging, Lungs

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Background: Pulmonary involvement is a frequent and severe extraarticular manifestations of rheumatoid arthritis (RA). Chest high resolution computed tomography (HRCT) have been shown to be of interest in the detection and characterization of morphological changes in the lungs of RA patients.
Objectives: The aim of our study was to investigate the prevalence and types of pulmonary involvement in patients with longstanding RA using chest HRCT.
Methods: A retrospective study was conducted in a single rheumatology hospital in Morocco, including patients diagnosed as having RA according to the ACR/EULAR 2010 criteria from Avril 2018 to Avril 2022. Longstanding RA was defined as disease duration > 2 years. All patients underwent chest X-ray and chest HRCT.
Results: Our study included 148 patients with longstanding RA. The cohort was predominantly female (87,2%) with a mean age of 60,56 ± 11,79 years. 8 patients (5.4%) had a history of smoking. Mean age at RA onset was 44,77 ± 12,82 years and disease duration was 14,75 ±7,55 years. The mean BMI was of 28,19 ± 6.47 Kg/m2. RA was seropositive in 95,3 %, erosive in 91,2% and deforming in 66,2 % of our subjects.

Methotrexate was used in 142 patients (95,9%). 41 patients (27.7%) were complaining of respiratory symptoms: dyspnea (n=20, 13.5%), cough (n=11, 7.4%), and both (n=10, 6.8%). The chest X-ray abnormalities were present in 41 patients (27,7%). Abnormal spirometry was found among 49.4% of subjects. Pulmonary HRCT abnormalities were found in 60,8% of patients and the most common were: subpleural micronodules (25 %), bronchiectasis (23,6%), non-septal linear opacities (16,9 %), pulmonary nodules (11,5%), ground glass opacity (10,8%), reticulation (8.8%) and honeycombing (8,8%). The presence of HRCT pulmonary lesions was associated with smoking history (p=0,020), seropositivity (p=0,010), respiratory symptoms (0,002) and chest X-ray changes (< 0,0001). However, there were no significant association with the other clinical, biological, radiological and therapeutic criteria.

Conclusion: Our study confirms that a large proportion of patients with long-standing RA has abnormal findings in chest HRCT even in those with no chest X-ray findings or respiratory symptoms. RA patients should undergo chest HRCT to detect pulmonary abnormalities as early as possible.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0332 APPLICATION IN CLINICAL PRACTICE OF THE SCREENING CRITERIA FOR INTERSTITIAL LUNG DISEASE IN RHEUMATOID ARTHRITIS PROPOSED BY SER-SEPAR IN A COHORT OF RHEUMATOID ARTHRITIS. PRELIMINARY STUDY

Keywords: Rheumatoid arthritis, Diagnostic Tests, Lungs

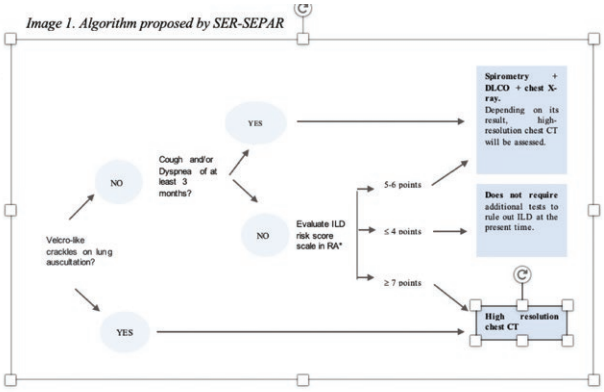
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Background: A screening tool has recently been proposed by two scientific societies (Spanish Society of Rheumatology and Pneumology), combining clinical and serological data to improve the detection of interstitial lung disease (ILD) in rheumatoid arthritis(RA) [1].

Objectives: To apply a new ILD screening tool in a cohort of patients with RA in order to determine its prevalence, and evaluate the burden of complementary exams generated for this purpose derived from its thorough application.

Methods: Observational and single-center cross-sectional study of a cohort of RA patients under active follow-up at the Rheumatology Service of the Vall d'Hebron Hospital. The sample will be all the patients who attend the clinic routinely for 1 year (July 2022- 23) and who have not been previously diagnosed with ILD. To assess the presence of pulmonary involvement, a detailed history and pulmonary auscultation will be performed. Subsequently, the screening tool will be applied to decide the use of complementary exams if necessary (image 1). The orders of High Resolution Chest CT (HRCTs), lung function tests (LFTs) and chest X-rays are carried out routinely in the regular circuit with the radiology and pulmonology services.

Image 1. Algorithm proposed by SER-SEPAR



*Set of variables and score proposal for each of the variables for the global calculation.	Punctuation
Age ≥ 60 years old	2
Male	1
Tobacco use (current or ex-smoker)	
≤ 20 pack-year	2
> 20 pack-year	3
Disease duration > 5 years	1
Moderate-high disease activity (average DAS28-ESR >3.2) from diagnosis of the disease in early RA (<12 months) or for a minimum of 6 months in established RA.	1
Serology (only the criterion with the highest weight is counted for the total score)	
- Positive rheumatoid factor > 3 times the ULN	1
- ACPA positive < 3 times the ULN	2
- ACPA positive > 3 times the ULN	3
ILD family history	1

Results: In 6 months (July-December 2023), 349 patients have been screened. Of these, in 22.3% (78) a HRCT request has been recommended, in 31.2% (109) chest X-rays and LFT and in 46.5% (162) regular follow-up. Of the 78 patients to whom HRCT has been recommended, this has already been carried out in 19 patients (the characteristics of these patients are described in Table 1), in two of whom the diagnosis of ILD has been made (1 Non-Specific Interstitial Pneumonia -NSIP- and 1 Usual Interstitial Pneumonia -UIP-), both in mild degree. Neither of the two patients had symptoms or auscultation abnormalities, and both are awaiting LFTs.

Table 1. Characteristics of patients who have already undergone HRCT according to the recommendation of the algorithm proposed

Female, n(%)	11 (57.9%)
Age, mean±SD, years	65.52±10.95
RA disease duration, median(IQR), years	11(5-21.5)
FR +, n (%)	
<3 ULN	5 (26.3%)
≥ 3 ULN	14(73.7%)
ACPA +, n (%)	
<3ULN	0
≥ 3ULN	17 (89.5%)
ANA	
Positive (>1/160), n (%)	3(15.8%)
Erosive, n (%)	11(57.9%)
Tobacco use, n (%)	
< 20 pack-year	4 (21.1%)
≥ 20 pack-year	13 (68.4%)
≥ 1 cardiovascular risk factors, n (%)	8 (42.1)
Moderate-high disease activity from diagnosis of the disease in early RA or for a minimum of 6 months in established RA.	0
Dry cough and/or dyspnea for more than 3 months, n (%)	2 (10.5%)
Velcro-like crackles, n (%)	1 (5.3%)
ILD family history, n (%)	2 (10.5%)
Chest X-rays, n (%)	
- Made during evolution	16 (84.2%)
- Not available	3 (15.8%)
HRCT compatible with ILD, n (%)	2 (10.5%)
Other HRCT findings, n (%)	
- Emphysema	10 (52.3%)
- Bronchiectasis	13 (68.4%)

Of the 109 patients for whom chest X-rays and LFTs were recommended, in 26 (24%) have been performed, due to usual delay in the pneumology service for LFTs. A restrictive pattern was detected in 4 patients (15.4%), half of whom also presented a decrease in DLCO. HRCT in those patients is still pending. 50% of the LFTs performed were normal and in the rest of the cases alterations compatible with other respiratory pathologies have been observed.

Conclusion: The application of this screening algorithm is allowing to diagnose patients with asymptomatic ILD. However, the costs of performing the various complementary exams and its effect in treatment decisions in this profile of patients must continue to be studied.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0333 PERIODONTITIS AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS: A CASE CONTROL STUDY

Keywords: Rheumatoid arthritis

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Background: Different studies have estimated a higher risk of dental and periodontal abnormalities in patients with rheumatoid arthritis (RA), but it is often under-diagnosed.

Objectives: In this context, we conducted this study, whose objectives were to evaluate the frequency and the type of oral and periodontal abnormalities in patients with RA compared to control subjects and to determinate the predictive factors of the periodontal disease.

Methods: This is a case control study conducted during the period between July 2020 and June 2022. The oral and osteoarticular examination was performed for each patient. The different dental and periodontal indices were calculated: CAO index, plaque index (PI) and gingival index (GI).

Results: Sixty patients diagnosed with RA according to the ACR/EULAR 2010 classification and 71 control patients were included. The mean age of patients with RA was 51.5 ± 12.4 years [21-78 years] and that of the control group was 47.2 ±12.8 years [22-74 years]. The oral examination showed poor oral hygiene based on the plaque index (PI). The frequency of moderate to abundant plaque

accumulation (PI≥ score 2) was comparable between the two groups with non-significant difference (91.7% versus 94.4%; p=0.5). Regarding dental caries, the median CAO was greater in the RA group than in the control group with a significant difference (5 [1-10] versus 2 [0-5]; p<0.01). The mean numbers of missing and decayed teeth in RA patients were higher than those found in controls (3.3±4.6 versus 2±3.06; 1.9±2.3 versus 1.39±2.2 respectively). Analysis of the superficial periodontal status showed that 88.3% of RA patients had gingivitis compared with 90.1% of controls. The mean gingival index was 1.72±0.8 in RA group versus 1.76±0.7 in control group without a significant difference. As for the alteration of the deep periodontium, 53.3% had periodontal pockets and/or gingival recessions compared to 19.8% of controls with a statistically significant difference (p=0.01). This involvement in RA patients was significantly correlated with disease activity DAS 28 and the importance of the CRP level (p=0.02, p=0.03 respectively). Tooth mobility was experienced by 28.4% of RA patients versus 11.2% of controls with a significant difference between the two groups (p=0.01).

Conclusion: Our study confirmed the frequency of periodontitis and dental caries in RA patients compared to controls and their association with disease activity. Hence the importance of early detection and management of these abnormalities in order to improve the disease activity and the quality of life of our patients.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0334 PREVALENCE AND ASSOCIATED FACTORS OF MULTIMORBIDITY IN PATIENTS WITH STABLISHED RHEUMATOID ARTHRITIS. DATA FROM THE CRHREAR REGISTRY

Keywords: Comorbidities, Real-world evidence, Rheumatoid arthritis

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Background: Patients with Rheumatoid Arthritis have an increased risk of developing comorbidities that contribute to increased worsened quality, disability and mortality. Knowledge of comorbidity is important when attempting to identify the conditions most associated with the greatest morbidity and mortality. However, comorbidities in RA are often underrecognized despite their impact on disease activity and treatment outcomes.

Objectives: To evaluate the prevalence of multimorbidity in a cohort of patients with stablished Rheumatoid Arthritis (RA) and the factors associated with such condition.

Methods: Cross-sectional observational study of a cohort of patients with RA according to the ACR/EULAR 2010 criteria of the CRhreAR registry of the Reina Sofia University Hospital of Córdoba. Multimorbidity was defined, according to the WHO, as the presence of two or more chronic diseases, in addition to RA. Comorbidities included in the Charlson index were collected, in addition to others such as arterial hypertension (HT), dyslipidemia (DL), diabetes mellitus, depression, osteoporosis, interstitial lung disease, and thyroid pathology. Other sociodemographic and disease-related variables were collected. Statistical analysis: descriptive, bivariate analysis and multivariate logistic regression to evaluate variables independently associated with multimorbidity.

Results: A total of 233 patients were included (mean age 63.6 (13.4) years and 70.4% women). More than 70% were ACPA and RF positive. 99.1% had used any csDMARD and 42.1% any bDMARD. The disease duration was 13.7 years (11.6). 192 patients had at least one comorbidity. 151 (64.8%) had multimorbidity, and the mean age-adjusted Charlson index was 2.9 (2.4). The most frequent morbidity was HT (45.1%) and DL (47.6%), followed by osteoporosis (27.5%) and ILD (16.7%). The most frequent comorbidities included in the Charlson index were cardiovascular disease (14.2%) and cancer (11.2%). Table 1 shows the differences between patients with and without multimorbidity. The multivariate analysis showed that the diagnosis delay of RA [OR 1.31; IC95 (1.1-1.7)], age [OR: 1.2; IC95 (1.1-1.23)] and the number of bDMARDs used since the diagnosis [OR: 2.7; IC95 (1.7-4.3)] were independently associated with multimorbidity, adjusted by sex.

Table 1. Differences between patients with multimorbidity and those without multimorbidity.

Variable	Multimorbidity (n= 151)	No multimorbidity (n= 82)	p-value
Age (years), mean (SD)	68.8 (11.5)	53.8 (10.9)	**<0.001**
Sex (female), n (%)	96 (63.6)	68 (82.9)	**0.002**
Ever smoked, n (%)	70 (46.3)	29 (35.4)	0.123
Disease duration (years), mean (SD)	14.5 (9.5)	12.1 (14.6)	0.196
Diagnosis delay (years), mean (SD)	3.4 (11.1)	0.9 (1.4)	**0.013**
Positive Rheumatoid factor, n (%)	112 (74.2)	61 (74.4)	0.971
Rheumatoid factor, mean (SD)	145 (205)	156 (313)	0.805
Positive ACPA, n (%)	110 (72.8)	63 (76.8)	0.558
ACPA, mean (SD)	240 (260)	260 (309)	0.674
Erosions, n (%)	58 (38.4)	32 (39.02)	0.926
Nodules, n (%)	13 (8.6)	11 (13.4)	0.249
DAS28-VSG, mean (SD)	2.7 (1.1)	2.6 (1.1)	0.648
SDAI, mean (SD)	10.5 (10.3)	8.4 (6.9)	0.086
CDAI, mean (SD)	8.7 (7.2)	7.5 (6.3)	0.226
Current csDMARDs, n (%)	99 (65.6)	70 (85.4)	**0.002**
csDMARDs ever, n (%)	147 (98)	82 (100)	0.292
Current bDMARDs, n (%)	66 (97.3)	26 (31.7)	0.006
bDMARDs ever, n (%)	71 (47.01)	27 (32.9)	**0.024**
Charlson index, mean (SD)	1.5 (1.7)	0.3 (0.6)	**<0.001**
Age-adjusted Charlson index, mean (SD)	3.9 (2.3)	1.2 (1.3)	**<0.001**

Conclusion: These results suggest that the presence of multimorbidity in stablished RA was high (64.8%). The most frequent comorbidities were arterial hypertension, dyslipidemia, interstitial lung disease, and osteoporosis. The diagnosis delay of RA, age and the number of bDMARDs used were independently associated with the presence of multimorbidity.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0335 INCIDENT CHRONIC KIDNEY DISEASE IN PATIENTS WITH RHEUMATOID AND PSORIATIC ARTHRITIS – A COMPARATIVE ANALYSIS

Keywords: Psoriatic arthritis, Kidneys, Rheumatoid arthritis

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Background: Patients with inflammatory joint conditions have a high prevalence of comorbidities including chronic kidney disease (CKD) [1]. The data pertaining to CKD in rheumatoid arthritis (RA) is limited [2], however and its association with psoriatic arthritis (PsA) remains unclear. Renal disease in RA and PsA is clinically important as it can lead to restrictions in the management of the primary disease, and is also associated with increased all-cause morbidity and mortality [3].

Objectives: To determine and compare the rate of incident CKD in patients with rheumatoid and psoriatic arthritis and to determine the rate of estimated glomerular filtration rate (eGFR) change over time.

Methods: Patients with RA and PsA who were first diagnosed between 1st January 2005 and 31st December 2010 were included in this retrospective, longitudinal analysis. All eGFR values, calculated using the Modification of Diet in Renal Disease equation, for each patient were collected from time of diagnosis until 31st December 2020. Demographic details, disease-specific characteristics, the presence of cardiovascular disease at baseline and anti-rheumatic drug use at each appointment were recorded. Generalized additive models (GAMs) were used to smooth the eGFR trajectories for each patient, and mixed-effects models were then used to estimate crude linear trends in eGFR across the period of observation. The primary outcome measure was diagnosis of CKD, defined as patient's eGFR falling below 60ml/min/m 2 for a period of at least 90 days in their smoothed eGFR trajectory.

Results: The patient sample (n = 159) included 114 RA and 45 PSA patients. RA patients were less likely to be male (39 vs 51%, p = 0.2) and older (mean age at baseline 52 vs 46 years, p < 0.001) than PsA patients. They also tended to have moderately lower eGFR upon initial observation (78 vs 83 ml/min/m2, p = 0.07). Baseline comorbidity profiles were broadly similar between the two groups. Treatment profiles were also similar, but with RA patients prescribed DMARDs at 69% of their appointments on average vs 56% in PSA patients (p = 0.003). There were 22 incident cases of CKD in the RA patients (19%), vs 7 in the PSA patients (16%, p = 0.6), and 17 RA patients died during the observation period (15%) vs 2 PSA patients (4.4%, p = 0.07). Results from a sex- and age-adjusted

mixed effects models suggested that eGFR trajectories tended to slowly decline on average in PSA patients (-0.22 ml/min/m2 per year, p vs no trend = 0.14), but increased on average (0.79 ml/min/m2 per year) among RA patients (p for interaction < 0.001).

Conclusion: Incident CKD diagnosis was high in both patient populations. While rate of eGFR decline was greater in patients with PsA, overall rates of CKD diagnosis did not differ significantly. Monitoring of kidney function should be an important part of management of inflammatory joint conditions, as the majority of these patients non-steroidal inflammatory drugs and immunosuppressive therapies which may be contraindicated or require dose adjustment if renal impairment is present.

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AB0336 RHEUMATOID ARTHRITIS AND UPPER DIGESTIVE TRACT BLEEDING: ASSOCIATED FACTORS BEYOND THE USE OF NSAIDS AND CORTICOSTEROIDS

Keywords: Safety, Rheumatoid arthritis, Gastrointestinal tract

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Background: Rheumatoid arthritis (RA), with a prevalence of 0.52% in Colombia, is an autoimmune disease with erosive joint involvement associated with significant manifestations in other organs and systems. RA has been associated with a greater risk of upper gastrointestinal bleeding (UGIB), highlighting the greater exposure to non-steroidal anti-inflammatory (NSAID) and corticosteroids [1].

Objectives: Describe the safety profile with emphasis on UGIB associated with the use of NSAIDs and corticosteroids in patients with RA treated at the Central Military Hospital.

Methods: Analytical cross-sectional study of patients diagnosed with RA according to EULAR/ACR 2010 classification criteria between 2015-2021, describing the clinical and demographic variables and evaluating the association with UGIB. Patients with variceal UGIB were excluded. A bivariate and multivariate statistical analysis was performed by binary logistic regression. Approved by the institutional ethics committee.

Results: 405 individuals were evaluated, 80.5% were female, UGIB was present in 16 patients (4%). ESR was elevated in 60.9% and CRP in 67.9%. Rheumatoid factor (RF) >20U/mL was positive in 68.6% and anti-CCP in 62.30% of the total population; 100% of the UGIB group were RF+ (p=0.006) and anti-CCP+ (p=0.002). DAS28 presented a median of 3.46 (IQR=2.2-4.9), with higher levels in patients with UGIB -median of 5.1 (IQR=3.7-6.0) p=0.009-. In UGIB group, 6.25% used NSAIDs (p=0.97), while 62.5% used corticosteroids (p=0.44). NSAIDs doses and time of use did not present statistical differences between both groups (p=0.640 and p= 0.80). Neither does the type of NSAIDs (p=0.480). There were no significant differences regarding the type of corticosteroid (p=0.441) or the time of use (p=0.847); however, there were differences in doses used (p=0.036). As a result of logistic regression, the presence of anemia was identified with ORA 12.3 (95%CI 1.4-110.3), HAQ moderate or severe disability with ORA 7.6 (95%CI 1.4-39.9) and DAS28-CRP ORA 0.52 (95% CI 0.29-0.94) as factors associated with UGIB.

Conclusion: Our RA population shows an adequate control of disease activity. Lower use of NSAIDs is reported compared to other populations and the use of corticosteroids and DMARDs was used in a similar proportion to the literature. In patients with RA and UGIB, there were no statistically significant differences regarding NSAIDs and corticosteroid use. The presence of anemia, greater disability, and high levels of activity were associated. The study group presented a lower proportion of UGIB compared to the evidence published to date.

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AB0337 MENTAL HEALTH AND RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis

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Background: Rheumatoid arthritis(RA) is a chronic systemic inflammatory disorder characterised by symmetrical involvement of small and large joints of the body. It has a prevalence of 0.5 – 1% in the world, affecting more commonly women [1].Due to the inflammatory burden of the disease, RA patients develop articular damage of various joints causing disability, reduced quality of life, and reduced life expectancy.[2,3] Patients with long standing or severe disease can also manifest with extraarticular symptoms. These in addition to chronic pain and disability can affect mental status of the patients [4]. Poor quality of sleep, anxiety and depression have been thought to contribute to the disease flare.[5] DMARDs are the best treatment offered to control disease activity in patients with rheumatoid arthritis.However it is important to emphasize that sleep, depression and stress have also an important role to play in the disease management. Treatment of depression, improvement of sleep quality in addition to DMARDS should always be kept in mind.Through this study we attempt to find there is any correlation of mental health with disease activity in RA.

Objectives: To find the prevalence of depression, anxiety, and disturbed sleep in RA patients. To find the correlation of depression, anxiety and quality of sleep with disease activity in RA.

Methods: A cross sectional study was done on RA patients in a tertiary care centre from western India. A questionnaire-based study was conducted among adult RA patients attending Rheumatology clinic at P D Hinduja Hospital Mumbai between March 2020 to July 2021. Depression was assessed using Becks depression scale, anxiety using Becks anxiety scale and sleep quality using sleep quality scale.

Results: A total of 200 RA patients within 5 years of disease were included in the study. Out of 200 patients, majority (84 %) were females.The prevalence of depression, anxiety and disturbed sleep in our RA population was 23.5%, 27.5% and 44.5 % respectively. Using Spearman correlation, we found a positive correlation of depression(Figure1), anxiety and disturbed sleep with disease activity using DAS 28 score. We also found a positive correlation of number of joints involved with pain (PAS) scores, depression with anxiety, anxiety with both depression and disturbed sleep and poor sleep quality with anxiety.

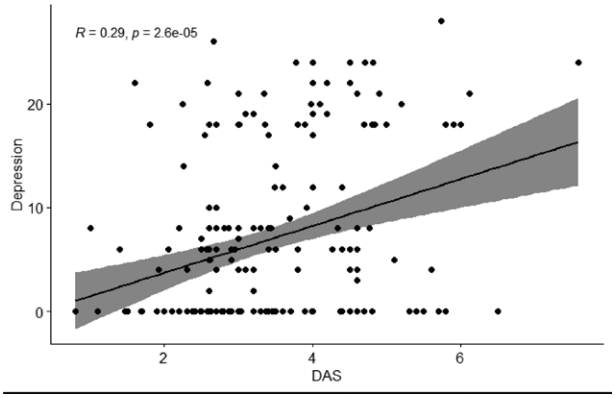


Figure 1: Correlation between Disease activity using DAS Score and Depression Score:- Interpretation: - The p-value of the test is <0.0001.DAS Score and Depression Score are significantly correlated with correlation coefficient 0.29 and P-value <0.0001

Conclusion: Depression, anxiety, and sleep disturbance is significantly higher in patients with early RA. Rheumatologists in addition to assessing disease activity in RA should also include assessment of the mental health. Early evaluation and intervention might result in better outcomes, reduce disease burden and avoid unnecessary immunosuppressive drug escalation.

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Disclosure of Interests: None Declared.

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AB0338 METABOLIC SYNDROME AND ITS COMPONENTS HAVE A DIFFERENT PRESENTATION AND IMPACT ON THE CARDIOVASCULAR RISK PROFILE OF PATIENTS WITH PSORIATIC AND RHEUMATOID ARTHRITIS

Keywords: Comorbidities, Cardiovascular disease, Inflammatory arthritides

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Background: Patients with inflammatory arthritidies have a higher cardiovascular (CV) risk than the general population. Traditional CV risk factors are involved, while the impact of the metabolic syndrome (MetS) is less defined. Whether MetS clinical presentation and its components are comparable across conditions is unclear.

Objectives: To compare the prevalence of MetS and their components, and the impact on the CV risk profile, in psoriatic arthritis (PsA) versus rheumatoid arthritis (RA).

Methods: a retrospective analysis with follow-up of real-world PsA (CASPAR criteria) and RA (2010 EULAR/ACR classification criteria) patients referred to a rheumatology clinic was performed. Demographical, clinical data and presence of CV risk factors were evaluated from patient charts using national guidelines, both at baseline and after 12-months of follow-up. MetS was defined according to the American Heart Association (AHA)/National Heart, Lung, and Blood Institute (NHLBI) criteria. Univariate and multivariate models were used to compare the impact of the MetS and its components in patients with PsA versus RA.

Results: PsA patients (n=78) were younger (45.23 (16.99) vs 60.81 (13.19) years, p<0.001), exhibited lower disease duration (18.86 (48.43) vs 176 (169.77) months, p<0.001) and prevalence of autoantibodies (RF: 7.7 vs 58.7%, ACPA: 7.9 vs 57.6%; both p<0.001) than their RA counterparts (n=92). PsA patients were more likely to present with MetS (40(51.3%) vs 25(27.2%), p=0.003) and dyslipidemia (56(71.8%) vs 26(28.3%), p<0.001) compared to RA. No differences were observed for smoking (22(28.2%) vs 26(28.3%), p=0.836), diabetes (26(38.3%) vs 33(35.9%), p=0.823 and hypertension (44(56.4%) vs 51(55.4%), p=0.749). These differences were maintained after adjusting for age. Multivariate analyses revealed that hypertension (OR 11.818 [95% CI: 2.046–58.053, p=0.002) and dyslipidemia (OR 5.190 [95% CI: 1.118–24.092], p=0.035) were predictors of MetS in PsA, and no effect was observed for diabetes (p=0.066) smoking (p=0.367), age (p=0.445) or sex (p=0.445); whereas diabetes (OR 15.58, [95% CI: 2.41–100.45], p=0.004), hypertension (OR 20.44, [95% CI: 2.58–161.05], p=0.004) and dyslipemia (OR 43.29 [95% CI: 6.82–274.75], p<0.001) predicted MetS in RA, and no effect of age (p=0.473), sex (p=0.615) or smoking (p=0.317) was noted. No effect was observed for autoantibodies or treatments received. Despite the history of CV events was similar between disorders (PsA: 22(28.2%) vs RA 24(26.1%), p=0.602), differences in predictors were found. Multivariate analyses revealed that hypertension and MetS predicted CV history in PsA, whereas dyslipidemia was the only factor predicting CV history in RA (Table 1). Associations were stronger in PsA, and total variance explained in each model differed across groups.

Table 1. Multivariate analysis of predictors of history of CV events in RA PsA and RA

	OR	95% CI	p-value
PsA (R^2 = 0.693)			
Smoking	3.88	0.60–25.05	0.154
MetS	22.61	1.32–58.65	**0.031**
Diabetes mellitus	0.27	0.03–2.46	0.250
Hypertension	50.30	2.58–97.66	**0.010**
Sex	0.50	0.08–2.92	0.445
Dyslipidemia	3.22	0.45–22.87	0.241
CRP	0.95	0.79–1.12	0.560
Age	0.98	0.91–1.06	0.740
Disease duration	0.96	0.92–1.01	0.134
RA (R^2 = 0.296)			
Smoking	1.89	0.56–6.23	0.298
MetS	1.35	0.28–6.53	0.702
Diabetes mellitus	1.89	0.56–6.32	0.413
Hypertension	3.00	0.72–12.43	0.129
Sex	0.58	0.17–2.68	0.586
Dyslipidemia	4.50	1.11–16.12	**0.011**
CRP	1.02	0.96–1.08	0.518
Age	1.01	0.96–1.06	0.669
Disease duration	0.99	0.99–1.00	0.329

Finally, follow-up analyses revealed that progression of MetS and its components in PsA and RA were negligible after 12 months of follow-up (Figure 1).

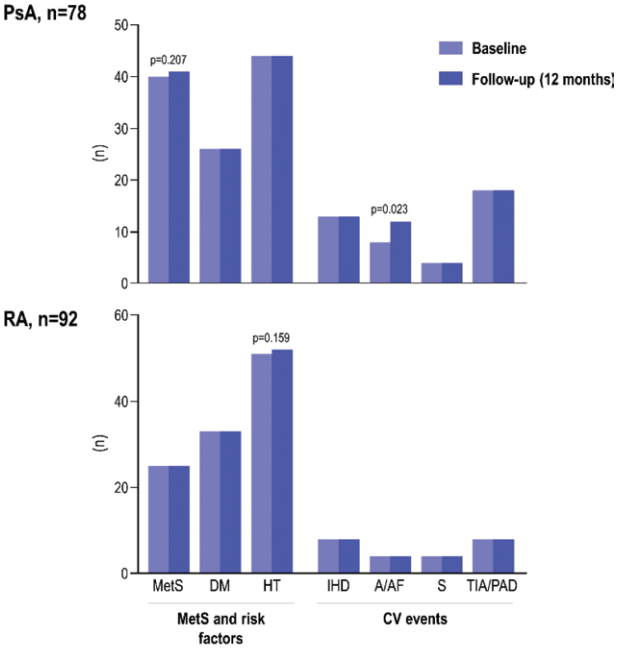


Figure 1

Conclusion: Occurrence and presentation of MetS differed between inflammatory arthritidies. The impact of these risk factors on CV risk profile was stronger in PsA compared to RA, and showed no progression in one year. This suggests the implication of different mechanisms, which may require distinct CV preventive strategies in PsA and RA.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0339 DYNAMIC RESPONSE TO INTRAVENOUS IRON, MEASURED BY NOVEL RETICULOCYTE INDICES, AS A PREDICTOR OF COEXISTING IRON DEFICIENCY IN ANAEMIA OF INFLAMMATION

Keywords: Comorbidities, Diagnostic Tests, Biomarkers

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Background: Anemia of inflammation (AI) can be referred to as the proverbial “Starvation amidst plenty” as body iron stores are unavailable for

the erythron[1]. Anemia of iron deficiency(AID) is prevalent in developing countries and often coexists with AI [2]. There is no simple, single static iron or red blood cell parameter, which reliably predicts iron deficiency in patients with AI. The erythron is in a state of flux; modulated by physiological demands (e.g., hemoglobin(Hb) levels, tissue hypoxia), metabolic substrates (e.g., iron, Vitamin B12, Folic acid, etc), and pathologic states (e.g., inflammation, malignancies, etc). Therefore, even at the risk of oversimplification, it may be hypothesized that dynamic tests are needed to determine limiting factors for erythron responsiveness.

Objectives: This study aimed to evaluate the performance of novel reticulocyte (Ret) indices Reticulocyte Hemoglobin (RetHb) and Immature Reticulocyte Fraction (IRF) in identifying coexistent iron-deficient states in AI. We correlated the change in RetHb & IRF with an increase in Hb after intravenous iron in AI.

Methods: In this study, we have used intravenous iron in patients with AI (hemoglobin<10gm/dL and serum ferritin <500ng/ml) and employed changes in Ret parameters - RetHb/IRF to predict coexisting iron deficiency "Iron challenge test". All participants received intravenous Iron sucrose after sensitivity testing (100 mg day 1 and 400mg Day 3). An increase in Hb of at least 1gm/dL at one month was considered a positive iron response & diagnostic of coexistent iron deficiency with AI. Change in RetHb/IRF on 3rd day from baseline was compared in Iron responders(AID with AI) vs non-responders (AI only).

Results: Out of 62 patients who were enrolled, 46 patients completed the study protocol & were finally analyzed for the study. The majority of the participants had chronic autoimmune inflammatory disorders (Rheumatoid arthritis-30 Ankylosing Spondylitis-5, Systemic Lupus Erythematosus-4, Sjogren -1, Psoriatic arthritis-1) while the rest were Chronic liver disease/ Chronic heart disease. About 63% of participants were iron responders and therefore, considered to have AID with AI; while the rest were iron non-responders and considered to have predominant AI. There was no significant difference between the change in RetHb/IRF amongst responders and non-responders at 72 hrs (Table 1). Baseline serum iron parameters (Serum iron, Total Iron Binding Capacity, % Saturation, Serum ferritin) and Red blood cell (RBC) indices (Mean corpuscular volume, Mean Corpuscular Hb) were also not statistically different in iron responders vs non-responders.

Conclusion: Diagnosing and treating coexisting iron deficiency in AI is a clinical conundrum. In this study, a significant proportion of AI (37%) didn't respond to intravenous iron at 1 month. Baseline iron parameters like serum ferritin/ % saturation and RBC Mean corpuscular volume didn't predict response to iron in this study. Change in novel automated Ret indices (RetHb and IRF) failed to predict response to iron and therefore, failed to diagnose co-existent iron deficiency in AI. Dynamic studies demonstrating erythron responsiveness to iron therapy using "point of care" automated hematologic parameters may provide a template for further studies.

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Table 1. Comparing change in hematological parameters-baseline to 72hrs-between responders and non-responders.

Characteristic	No Response, N= 17	Response, N = 29	p-value[1]
Change in Ret-Hb			0.8
Median, (IQR)	1.10, (-0.70, 3.70)	1.60, (0.70, 3.10)	
Mean ± SD	1.52 ± 2.84	1.78 ± 2.47	
Change in IRF			0.3
Median, (IQR)	2.30, (-0.20, 6.20)	1.50, (-2.10, 4.00)	
Mean ± SD	3.49 ± 5.65	1.36 ± 7.31	

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Disclosure of Interests: None Declared.

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AB0340

MULTI-DRUG RESISTANT RA IS ASSOCIATED WITH HIGHER BASELINE DISEASE ACTIVITY, MULTI-MORBIDITY, AND LOWER QUALITY OF LIFE: ANALYSES FROM THE R4RA BIOPSY-DRIVEN CLINICAL TRIAL

Keywords: Comorbidities, Clinical Trials, Rheumatoid arthritis

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Background: We have recently described a fibroblast/stromal signature in patients with multi-drug resistant Rheumatoid Arthritis (MDR-RA). However, MDR-RA is known to be extremely heterogeneous, with multiple clinical and pathogenetic factors potentially contributing to multi-drug resistance.

Objectives: Define the association of MDR-RA with clinical and demographic factors.

Methods: Patients with multi-drug resistant RA (MDR-RA), defined as failure of 3x bDMARDs with a different mechanism of action (TNF-inhibitor, tocilizumab and rituximab) were identified from the R4RA clinical trial (n=40) and compared with first-line responders to either rituximab or tocilizumab (n=72) for: disease activity scores, including composite indexes and individual components; baseline demographics, including co-morbidities, and quality of life scores (HAQ and SF-36 domains); synovitis, assessed by ultrasound and immunohistochemistry.

Results: MDR-RA patients did not differ significantly from first-line responders in terms of age, disease duration and ethnicity, as shown in Table 1. MDR-RA patients were treated more often with a csDMARDs combination, while the number of previous anti-TNF did not differ. Baseline disease activity was significantly higher in MDR-RA compared to first-line responders. This difference was mainly driven by tender joints, while there were no significant differences for 28 swollen joints count, pain, and patient/physician global health scores (Table 1). Ultrasound scores and synovial pathotype distribution were not significantly different between MDR-RA and responders, but responders had a numerically higher power doppler score and significantly higher sub-lining macrophages, in line with the known association of synovial macrophages with treatment response. The incidence of individual comorbidities such as diabetes, hypercholesterolemia, hypertension, anxiety/depression, and obesity was non significantly different between MDR-RA and responders; however, the prevalence of multi-morbidities was significantly higher in MDR-RA patients, as 50% had more than 2 comorbidities compared to 22.8% of responders (p=0.0343). Finally, MDR-RA patients had significantly lower FACIT fatigue scores and worse scores for multiple SF-36 domains (physical functioning, emotional well-being, social functioning, and general health). Although the difference in baseline disease activity was mainly driven by tender joints, the longitudinal assessment of disease activity across 48 weeks showed persistently elevated tender and swollen joint counts, pain, and global health scores in MDR-RA patients compared with responders (Figure 1).

Conclusion: MDR-RA, defined as lack of response to 3x biologics with different mechanisms of action, is associated with worse disease activity baseline and multi-morbidity. There were no specific associations with pain scores, but MDR-RA had a huge impact on multiple quality-of-life domains. At follow-up, MDR-RA was associated with persistently elevated disease activity scores, including both higher tender and swollen joints, in keeping with persistently active inflammatory disease.

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Table 1.

	MDR-RA (N=40)	Responder (N=72)	p value
Age,	53.6 (14.1)	56.4 (11.9)	0.291
RA duration	14.9 (12.0)	12.3 (10.2)	0.254
Gender, F	35 (87.5%)	51 (70.8%)	0.077
csDMARDs			<0.001
0	11 (27.5%)	50 (69.4%)	
1	13 (32.5%)	6 (8.3%)	
2	11 (27.5%)	12 (16.7%)	
>3	5 (12.5%)	4 (5.6%)	
Steroids	24 (60.0%)	36 (50.0%)	0.413
Previous anti-TNF			0.153
1	33 (82.5%)	47 (65.3%)	
2	6 (15.0%)	22 (30.6%)	
>3	1 (2.5%)	3 (4.2%)	
CDAI	36.9 (14.0)	31.0 (13.0)	0.0305
DAS28 ESR	6.12 (1.05)	5.60 (1.21)	0.0191
ESR	33.5 (21.2)	32.6 (26.3)	0.839
CRP	21.5 (30.6)	21.9 (34.0)	0.946
TJC 28	15.5 (8.30)	11.2 (7.01)	0.00641
SJC 28	7.68 (4.81)	7.04 (5.64)	0.532
Pain (VAS)	66.1 (21.8)	68.0 (23.4)	0.671
GH (VAS)	70.0 (20.5)	66.5 (25.5)	0.437

Data shown as mean (SD) or n (%).

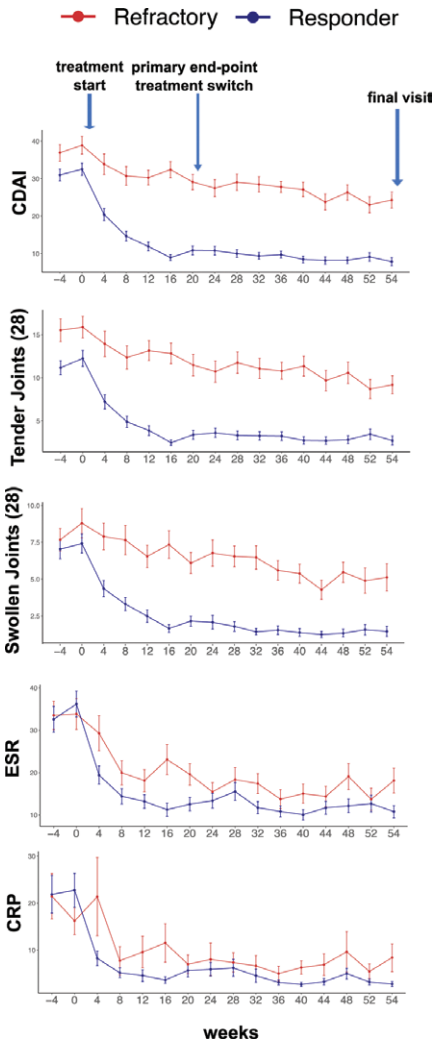


Figure 1.

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Disclosure of Interests: None Declared.

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AB0341 COMPARISON OF CANDIDATE KEY FACTORS FOR INCIDENT FRAGILITY FRACTURE IN POSTMENOPAUSAL FEMALE PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Biomarkers, Osteoporosis

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Background: Bone fragility fracture (BFF) in patients with rheumatoid arthritis (RA) is still a significant comorbidity that deteriorates the quality of life after that. Some reports clarified risk factors and the keys to preventing them.
Objectives: The aim of this study is to evaluate the factors statistically and advocate a novel key to preventing the incidence of BFF.
Methods: A retrospective cohort study data was used. Postmenopausal RA patients were picked up. They have been treating RA and measured bone mineral density (BMD) with dual-energy X-ray absorptiometry. The initial target of therapy is the attainment of remission with SDAI within 6 months of initiation. The primary outcome was incident BFF (inc-BFF). Follow-up started at BMD measurement (baseline) and continued until the development of the first fracture or censoring at death, loss to follow-up or end of the study. In these subjects, T-scores and pr-BFF were combined, and T-score < -2.5 in the lumbar spine (LS) or femoral neck (FN), or presence of pr-BFF was evaluated as primary osteoporosis criteria matched (pr-OP). Potential key factors for incident BFF, such as age, disease duration of RA, anti-citrullinated polypeptide antibodies (ACPA), rheumatoid factor (RF), remission rate using clinical disease activity index (CDAIRR), C-reactive protein, Health Assessment Questionnaire Disability Index, pain score using a visual analog scale (PS-VAS), vector value of coordinate on X-axis and Y-axis (Vxy) using Joint Index Vector (JIV), body mass index (BMI), presence of comorbidities such as hyper-fallability (Fall), lifestyle-related diseases (LSD), cognitive impairment (CI), estimated glomerular filtration rate calculated with cystatin C (eGFR_CysC), anti-osteoporotic drug administration and glucocorticoid administration, and serum albumin level (ALB) were chosen as variants. Receptor operation characteristics (ROC) curve was examined for each variant in regard to inc-BFF and the Cut-off index (COI) for each variant was determined. A Cox regression analysis with a multivariate mode in the variants that had statistical significance with the ROC. Kaplan-Meier survival curve (K-M) was examined for each variant in regard to COI. Finally, the K-M study examined the chi-square test by dividing it into positive pr-OP, positive all single significant variants, and positive combined conditions, and simultaneously calculated inc-BFF rates for each subgroup. Differences in BFF rates were compared for each matching pair. Statistical significance was set at less than 5% for all statistical methods.
Results: A total of 239 patients were recruited. The mean age was 73.6 years and the mean follow-up period was 52.4 months. In the ROC study, pr-OP, ACPA, CDAIRR, PS-VAS, Vxy, Fall, LSD, CI, eGFR_CysC, and ALB demonstrated statistical significance with the COI of presence, 0.9 (U/mL), 0.52, 25.0 (mm), 0.012, presence, presence, presence, 50.7 (ml/min/1.41m2), and 4.0 (g/dL), respectively. In these, PS-VAS, Vxy, and ALB had significant risk ratios with values of 1.04, 0.07, and 0.20, respectively. Hazard ratios of each variant in the K-M study were 3.51, 4.56, and 1.81, however, p-values were <0.001, <0.01, and 0.07 for PS-VAS, Vxy, and ALB, respectively. The BFF rate in the pr-OP and PS-VAS ≥ 25.0 subgroups were 4.5%, 12.9%, 14.7%, and 37.9% in the negative/negative, negative/positive, positive/negative, and positive/positive groups, respectively, whereas the BFF rate in the pr-OP and Vxy ≥ 0.012 subgroups were 4.3%, 8.3%, 6.3%, and 32.4% in the negative/negative, negative/positive, positive/negative, and positive/positive group, respectively, When PS-VAS and Vxy were combined to matching either of these, the BFF rate in the subgroups were 5.6%, 12.5%, 12.8%, and 49.0% in the negative/negative, negative/positive, positive/negative, and positive/positive group, respectively.
Conclusion: These results suggest that Vxy > 0.012 and PS-VAS > 25 mm are available risk indicators for inc-BFF. The composite indicator should be more predictable.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0342 ASSOCIATION OF GLUCOCORTICOID USE WITH HEALTHCARE UTILIZATION AMONG PERSONS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus

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Background: Glucocorticoids (GCs) have long been a mainstay of treatment for systemic lupus erythematosus (SLE). While GCs do provide benefit, there are potential side effects which increase with dose and duration. GC-associated adverse events have been linked to significant increased health care costs, although excess healthcare utilization due to GC events has not been examined in SLE.
Objectives: To examine the association of GC use and healthcare utilization.
Methods: Data are from FORWARD, The National Data Bank for Rheumatic Diseases, questionnaires collected from participants with physician-diagnosed SLE and no concomitant RA at 6-month intervals during July 2015 – July 2020. Respondents provided comprehensive health information including GC use and dosage and healthcare use during the prior 6 months. Analyses examined 6-month utilization according to GC use/non-use, as well as by GC dose (0, 1- <5 mg, 5- <10 mg, ≥10 mg). For GC users, data were drawn from the questionnaire in which GCs were first reported during the analysis period. Data for non-users were drawn from the first questionnaire completed during the observation period. Adjusted analyses used double selection LASSO to form the best fitting model considering the

following co-variates: age, sex, race, BMI, comorbidities, education level, smoking, SLE duration, self-reported lupus disease activity, SLE organ damage measured by BILD (Brief Index of Lupus Damage), and other medications. Results of LASSO analyses are reported as incidence rate ratios (IRRs).

Results: 512 participants qualified for the analysis; 46.3% reported GC use in at least one 6-month period. Over 90% of the cohort was male, mean age 58 ±13 years, SLE duration 24 ±12 years. GC users were significantly less likely to be male or white, had more comorbidities, had lupus of greater duration, were more likely to also be taking immunosuppressive medications, and reported more active SLE and greater disease damage (BILD). In bivariate analyses (Table 1), GC users reported significantly more rheumatology and other doctor visits, and more PT/OT visits. They also reported more lung function, blood, and urine tests. There was no difference between GC users and non-users in the occurrence of a hospitalization, but users had significantly longer hospitalizations. The multivariable LASSO regression analyses[1] revealed similar results, with significantly IRRs for GC users for rheumatology and other visits, blood and urine tests, and hospitalizations. In analyses based on GC dosage, IRRs for rheumatology visits, other medical visits and blood tests were significantly elevated for each dosage group compared to the no-GC group; the highest GC dosage group also had significantly elevated IRRs for lung and urine tests and hospitalizations.

Conclusion: GC use is associated with greater healthcare utilization among this cohort with SLE, even after adjusting for a wide range of sociodemographic and disease-related factors. Additional analyses are needed to explore whether greater GC use reflects more severe disease, and/or whether GC use itself leads to increased healthcare utilization.

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Table. Healthcare utilization for GC users and non-users and by GC dose

	Non-GC user N =275 (53.7%)	GC user N = 237 (46.3%)	p	Adjusted analyses, GC non-users vs. users IRR (95% CI)	p	Adjusted analyses, by GC dose (mg/day), compared to non-users >0 - <5 (n = 51)	5 - <10 (n = 112)	≥10 (n = 74)
Rheumatology visits*	1.5 (1.4)*	2.1 (1.7)*	0.000	**1.2 (1.1, 1.3)**	**<0.0001**	**1.2 (1.1, 1.4)**	**1.1 (1.04, 1.3)**	**1.4 (1.2, 1.6)**
Other doctors	1.6 (1.9)	1.6 (1.9)	0.000	**1.3 (1.8, 1.5)**	**<0.0001**	**1.3 (1.1, 1.5)**	**1.2 (1.1, 1.4)**	**1.5 (1.3, 1.8)**
PT/OT visits	0.8 (2.3)	1.3 (2.9)	0.05	1.2 (0.95, 1.5)	0.13	**1.7 (1.2, 2.3)**	1.0 (0.7, 1.3)	1.2 (0.9, 1.8)
Non-traditional therapy visits	0.4 (1.4)	1.1 (3.4)	0.79	1.2 (0.9, 1.6)	0.17	1.1 (0.7, 1.7)	0.8 (0.5, 1.1)	**2.4 (1.6, 3.5)**
Lung tests	0.2 (0.5)	0.3 (0.9)	0.04	1.3 (0.96, 1.8)	0.9	**1.5 (1.0, 2.3)**	1.0 (0.7, 1.5)	**1.9 (1.3, 2.9)**
Bone density tests	0.3 (0.5)	0.4 (0.5)	0.40	1.04 (0.8, 1.3)	0.74	1.0 (0.8, 1.4)	1.0, 0.7, 1.3)	1.2 (0.8, 1.6)
Blood tests	2.0 (1.6)	2.9 (1.8)	0.000	**1.1 (1.07, 1.2)**	**<0.0001**	**1.1 (1.0, 1.2)**	**1.1 (1.1, 1.2)**	**1.2 (1.1, 1.3)**
Urine tests	1.2 (1.4)	2.0 (1.7)	0.000	**1.1 (1.02, 1.2)**	**0.02**	1.0 (0.9, 1.1)	**1.2 (1.0, 1.3)**	**1.2 (1.1, 1.4)**
Any hospitalization†	10.4 (28)	15.1 (35)	0.11	**1.6 (1.1, 2.2)**	**0.01**	1.1 (0.7, 1.9)	1.3 (0.9, 2.0)	**2.7 (1.6, 4.3)**
Number of days hospitalized	0.7 (6.5) (n=28)	7.9 (8.0) (n=35)	0.04					

* Values are mean (SD) unless otherwise noted
† % (n)
IRR: Incidence rate ratio from multiple regression analyses using double section LASSO methods
Bolded values are statistically significant, p<0.05.

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Disclosure of Interests: Patti Katz Grant/research support from: Contractor with FORWARD, The National Databank for Rheumatic Diseases, Wichita, KS, a health care research organization contracted to support this research, Sofia Pedro Grant/research support from: Employee of FORWARD, The National Databank for Rheumatic Diseases, Wichita, KS, a health care research organization contracted to support this research, Jiyoon Choi Employee of: Employee of and may own stock options in Bristol Myers Squibb, Kaleb Michaud Grant/research support from: Employee of FORWARD, The National Databank for Rheumatic Diseases, Wichita, KS, a health care research organization contracted to support this research.

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AB0343

DEVELOPMENT OF PERSONALISED CARE PACKAGES FOR PEOPLE WITH EARLY RHEUMATOID ARTHRITIS: A MIXED-METHODS STUDY

Keywords: Inflammatory arthritides, Qualitative research methods, Rheumatoid arthritis

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Background: Disease management in early rheumatoid arthritis (RA) needs careful assessment of various aspects of the patient and their condition. We previously showed a need to address socioeconomic (SE) factors to improve clinical and patient-reported outcomes in RA, and benefits of a syndemics approach to care. We aimed to design a tailored care package which is acceptable, beneficial and relevant to the care of people with early RA.

Objectives: i) Determine aspects of care that people with early RA find beneficial to be included in potential care packages, based on individual needs and disease characteristics; ii) determine factors considered important by patients and healthcare professionals caring for people with RA to be included in care packages.

Methods: This work comprised two stages: i) three workshops involving healthcare professionals caring for people with RA, and patients with RA, using a modified-Delphi approach; ii) online survey informed by outcomes from the workshops, featuring responses from an expanded cohort of participants from the above two groups (Figure 1). Purposive sampling was used to identify potential UK-based participants including patients, rheumatology healthcare professionals, members of national rheumatology charities, and academics with an interest in RA. The online survey was based upon: i) key themes identified by the thematic analysis from the workshops; ii) results from previous findings from quantitative datasets conducted prior to this study, e.g. SE circumstances, clinical factors, and disease outcomes. Views were sought on future 'care packages' for people with early RA relevant to disease progression/ stages.

Results: Thematic analysis from the workshops identified two conceptual care pathways, with distinct MDT care packages, allowing for expansion of the core MDT as needed. The first pathway related to the time prior to RA diagnosis. Attendees considered this an early opportunity to potentially change the disease course, highlighting the importance of exploring risk factors e.g. obesity, smoking, social deprivation and isolation. The second pathway related to individuals with existing RA, with participants emphasising the importance of 'the right MDT member at the right time'. Core care packages were suggested, containing three distinctive components: 1) **early care package** (up to 6 weeks post-diagnosis) with introduction to MDT; 2) **personalised holistic care package** in collaboration with AHPs; 3) **continuity of care package** between primary and secondary providers. Thematic analysis results also informed the survey. We received 41 responses: 17 (43%) rheumatology consultants, 7 (18%) specialist nurses, 6 (15%) rheumatology trainees, 5 (13%) occupational therapists, 3 (8%) physiotherapists, 1 (3%) patient and 1 (3%) dietician. 34 (82.9%) of respondents agreed people with RA need access to the same 'early care package', (a core MDT) at diagnosis. A further 35 (85.4%) approved that the care package for people with early RA can be tailored to individual's clinical, psychological and social needs at subsequent reviews. There was strong consensus for the following two statements: 'A care package with core members of the multidisciplinary rheumatology team need to be available to people newly diagnosed with RA' (mean 9.05, using scale 0-10) and 'Personalised comprehensive care packages, comprising a core plus various additional members of the multidisciplinary team, need to be offered and adapted according to a person's individual disease characteristics and socio-economic circumstances' (mean 9.49). Fleiss' Kappa calculations demonstrated fair level of agreement amongst respondents in the quantitative survey questions.

Conclusion: We identified two care pathways with tailored care packages to optimise management in people with RA. Our results reiterate the benefits of holistic care in early and established disease. This can be further explored using syndemics to focus and better understand the relationships between bio-psycho-social factors influencing RA disease outcomes.

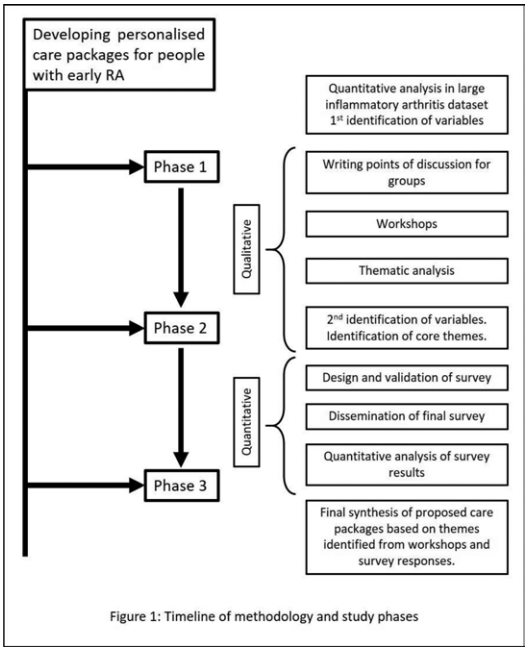


Figure 1: Timeline of methodology and study phases

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.
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AB0344 **EFFICACY AND SAFETY OF NINTEDANIB IN INTERSTITIAL LUNG DISEASE ASSOCIATED WITH RHEUMATOID ARTHRITIS: A SINGLE CENTER 6 MONTHS OBSERVATIONAL STUDY**

Keywords: Lungs, Rheumatoid arthritis

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Background: Nintedanib, an intracellular inhibitor of tyrosine kinases, inhibits processes involved in the progression of lung fibrosis [1]. Although the efficacy and safety of nintedanib have been demonstrated for interstitial lung disease (ILD) associated with systemic scleroderma (SSc) [2-4], information of the efficacy and safety of nintedanib in patients with rheumatoid arthritis (RA) is limited [5].
Objectives: The aim of this study was to compare the efficacy and safety of nintedanib in patients with RA-ILD with those in patients with ILD associated with collagen tissue diseases, including SSc-ILD.
Methods: We extracted patients who visited our department and were received nintedanib and had pulmonary function tests performed 6 months after. Then, they were divided into two groups, which were RA group and non-RA group. Clinical and epidemiological parameters, fibrosis pattern on HRCT, pulmonary function at the time of nintedanib administration and 6 months after nintedanib administration and adverse events were compared between the two groups. Those data were collected from medical records and statistically analyzed.
Results: Ten patients were enrolled. RA group had 6 patients and non-RA group had 5 patients. Among the RA and non-RA group, 50% and 60% were women, respectively (*P*=0.74). Age at the time of nintedanib administration was 70.8±5.5 years and 59.0±9.1 years, respectively (*P*=0.035). At the time of nintedanib administration, oral glucocorticoids (GC) were used in 83.3% and 100%, oral GC dose was 8.5±10.9 mg/day and 9.4±1.7 mg/day, and immunosuppressants were used in 83.3% and 100% (*P*=0.27, 0.17, and 0.27, respectively). Usual interstitial pneumonia (UIP) pattern on HRCT was 100% and 40%, and nonspecific interstitial pneumonia pattern on HRCT was 0% and 60%, respectively (*P*=0.013). At the time of nintedanib administration, FVC was -1977±867.2 ml and 1654±507.3 ml, %FVC was 66.9±20.7% and 53.2%±10.9%, and %DLco was 54.8±8.9% and 46.2%±15.9% (*P*=0.58, 0.36, and 0.51, respectively). After 6 months of nintedanib treatment, ΔFVC was -18.3±103.5 ml and -24.0±101.5ml (Figure 1.), Δ%FVC was 0.75±5.03% and -2.4%±1.91%, and Δ%DLco was 0.375±4.02% and -7.27%±6.54% (*P*=0.52, 0.20, and 0.28, respectively). The incidence of adverse events was 50% and 40%, respectively. In the both groups, there was no patients with severe adverse events and acute exacerbations of ILD, and the continuation rate was 100%, respectively.
Conclusion: This observational cohort study revealed that there was no statistically significant difference in the reduction of respiratory function in both FVC, %FVC, and %DLco in the RA group compared to the non-RA group, and the safety was also comparable between the two groups. Although RA-ILD have more UIP pattern on HRCT than SSc-ILD, nintedanib may effective for RA-ILD as same as SSc-ILD.

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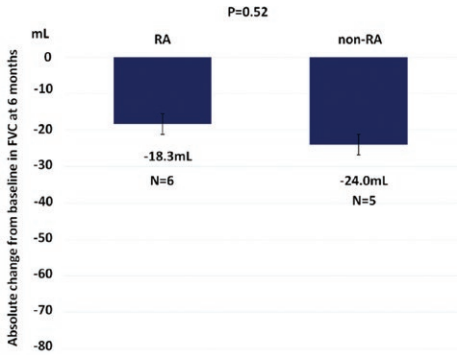


Figure 1. Absolute change from baseline in FVC at 6 months of rheumatoid arthritis (RA) (n=6) and non-RA (n=5).

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0345 **ACPA TITER IS AN INDEPENDENT DETERMINANT OF SERUM CTX IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS**

Keywords: Prognostic factors, Rheumatoid arthritis, Bone diseases

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Background: Serum C-terminal telopeptide of type I collagen (CTX - a marker of bone resorption) and ACPA titer have been associated to higher erosive score in rheumatoid arthritis (RA) and lower bone mineral density (BMD), even in patients with pre-arthritis. Prominent inflammatory status cannot totally explain such association. The interplay between ACPA, disease activity, BMD and CTX is still unclear.
Objectives: To investigate the determinants of CTX serum levels in RA patients.
Methods: We conducted a cross-sectional analysis on RA patients with active disease activity failure to first-line cDMARDs candidate to bDMARDs. Clinical, laboratoristic and densitometric and BMD parameters were collected. ACPA, CTX, Procollagen I Intact N-Terminal Peptide (P1NP), Dkk1, Sclerostin (SOST), 25-OH-Vitamin D (VitD), PTH, RANKL, OPG, B-ALP were dosed. Potential predictors of serum were analyzed using hierarchical regressions. Potential predictors were selected based screened via simple regression analyses which included CTX and a single candidate baseline predictor in each model. Any baseline predictor with $p < 0.10$ entered the multivariable model (model 1). We also conducted a multivariable linear regression forcing variables associated with CTX serum levels from the literature (model 2). Results were analyzed using GraphPad Prism version 9.5.0 for Windows, GraphPad Software, San Diego, California USA.
Results: We enrolled 62 RA patients in the study. DAS28-CRP at baseline was 4.17 (SD 1.28). 80.6% of patients were ACPA positive. The factors associated with CTX serum levels in the univariate analysis were: ACPA titer, DAS28-CRP, B-ALP, P1nP and BMD levels (**table 1**). ACPA titer was the only independent factor significantly associated with CTX serum levels in both model 1 and model 2 (**table 1**).
Conclusion: We found that ACPA titer is an independent determinant of serum CTX levels in RA patients with active disease activity.

REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: Giovanni Adami Speakers bureau: Eli-Lilly, Theramex, Galapagos, UCB, Amgen, BMS, Fresenius Kabi, Giovanni Orsolini: None declared, Angelo Fassio: None declared, Davide Bertelle: None declared, Camilla Benini: None declared, Ombretta Viapiana: None declared, Davide Gatti: None declared, Maurizio Rossini: None declared.
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	Univariate			Model 1			Model 2 (fully adjusted)		
Variable	**Estimate**	**SD**	**P value**	**Estimate**	**SD**	**P value**	**Estimate**	**SD**	**P value**
ACPA	**4,815e-005**	**1,299e-005**	**0,0005**	**3,602e-005**	**1,344e-005**	**0,01**	**4,730e-005**	**1,497e-005**	**0,003**
Age	0,001	0,001	0,34				-0,0004	0,001	0,69
GC daily dose	0,002	0,003	0,46						
DAS28-CRP	0,01	0,009	*0,09*	0,01	0,009	0,18	0,02	0,01	0,11
RF	0,0001	0,0002	0,51						
B-ALP	**0,006**	**0,002**	**0,005**	0,001	0,002	0,37	0,004	0,002	0,11
P1nP	**0,001**	**0,0005**	**0,002**	0,0005	0,0006	0,40	-0,0001	0,0006	0,87
Dkk1	9,143e-005	0,0008	0,91				-0,0009	0,0007	0,20
SOST	-0,0003	0,001	0,73						
RANKL/OPG ratio	-0,30	0,47	0,53						
PTH	0,0001	0,001	0,86				0,0005	0,001	0,61
VitD	-0,0009	0,001	0,44				-0,0008	0,001	0,53
BMD Neck (g/cm2)	**-0,24**	**0,11**	**0,03**	-0,1531	0,1001	0,13	-0,23	0,11	0,06

Rheumatoid arthritis - comorbidity and clinical aspects

AB0346 INTESTINAL MICROECOLOGICAL DISORDERS IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease characterized by a persistent immune response leading to arthritis and destruction. Mounting evidence has suggested that dysbiosis of the intestinal microbiome is a vital environmental element that triggers the onset of RA[1]. Unraveling the interactions between the gut microbiome and metabolome could provide new insights to discover novel targets for treating various inflammatory diseases. However, the current understanding of the potential association between intestinal microbiota and RA still needs to be improved.

Objectives: Recent studies have reported that the change in the interaction between the microbiome and the immune system is one of the characteristics of RA. Therefore, we conducted a meta-analysis and Mendelian randomization(MR) to explore the association and causality between RA and intestinal flora.

Methods: The PubMed, Embase, Medline, Web of Science, CNKI, Wanfang, VIP, and CBM databases were searched from the establishment of the databases to January 1, 2023, to retrieve trials about RA and intestinal flora. We performed a meta-analysis to calculate the odds ratio(OR) and 95% confidence intervals (95%CI). In addition, we conducted a bi-directional MR study to explore the causal relationship between RA and intestinal microbial composition. Single nucleotide polymorphisms (SNPs) associated with RA from 22 genome-wide association studies (14,361 cases and 43,923 controls) were selected as instrumental variables (IVs) at a genome-wide significance level. The aggregated statistical data of intestinal microbiota were obtained from a large-scale multiracial GWAS meta-analysis, including 18,340 people from 24 cohorts. The random-effects inverse variance weighted method (IVW) was used to combine the causal effect of IVs. Sensitivity analyses were performed to test the robustness of our findings. All analyses were conducted in R 4.2.1 and STATA 12.0.

Results: We included 17 case-control studies that examined 1,062 RA patients and 921 healthy controls(HCs). Compared with HCs, decreases in α-diversity indices were consistently found in RA[Shannon-Wiener diversity index (SMD=-0.608, 95% CI -0.935 to -0.281, p<0.001); Simpson index-(SMD=-0.558, 95% CI -0.891 to -0.225, p<0.001); ACE index(SMD=-0.414, 95% CI -0.697 to -0.132, p<0.001); Chao1 index(SMD=-1.373, 95% CI -1.980 to -0.766, p<0.001); Eveness index(SMD=-1.863, 95% CI -3.181 to -0.544, p=0.004)]. There was no significant difference in Observed_species between the two groups(SMD=-4.342, 95% CI -9.098 to 0.415, p<0.001). Further, we conducted a bi-directional MR analysis to test the causal relationship between RA and intestinal microorganisms, which included three phyla(*Firmicutes, Proteobacteria, Actinobacteria*), six families(*Bacteroidaceae, Actinomycetaceae, Clostridiales, Lactobacillaceae, Bifidobacteriaceae, Lachnospiraceae*) and seven genera(*Bifidobacterium, Butyricicoccus, Escherichia Shigella, Lachnospiraceae, Lactobacillus, Actinomyces, Bacteroides*). However, no genetic prediction causal relationship was found between them (all p>0.05). These results were robust in a wide range of sensitivity analyses.

Conclusion: This study suggested a significant correlation between RA and lower intestinal microflora abundance. This may provide new insight into the development mechanism of RA mediated by intestinal microbiota and may provide a evidence for regulating intestinal microecology to target the treatment of RA.

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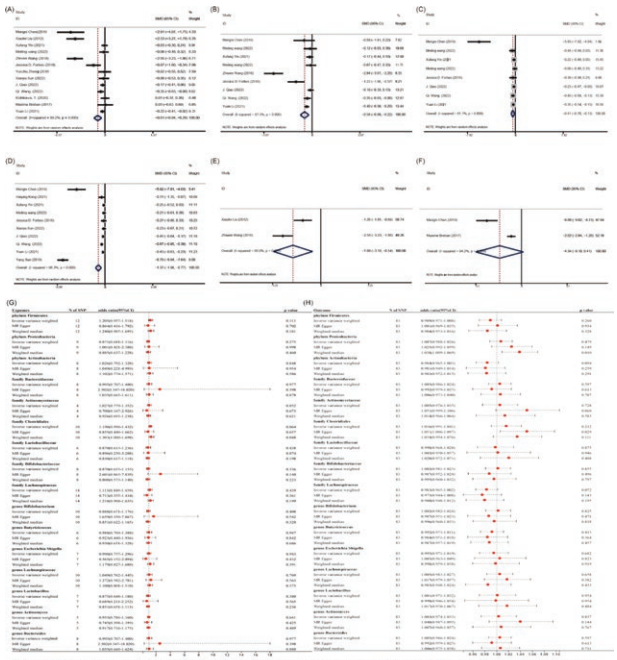


Figure 1: Forest plots of α-diversity richness estimators in the gut microbiota of patients with rheumatoid arthritis compared with healthy controls. (A) Shannon-Wiener diversity index. (B) Simpson index. (C)ACE index. (D)Chao1 index. (E)Eveness index. (F)Observed_species. (G-H)Mendelian randomization of RA and gut microbiota abundance.

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Disclosure of Interests: None Declared.

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AB0347 PREDICTIVE FACTORS OF SLEEP DISORDERS IN RHEUMATOID ARTHRITIS PATIENTS: A CROSS-SECTIONAL STUDY

Keywords: Rheumatoid arthritis, Quality of life

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Background: Rheumatoid Arthritis (RA) is a chronic inflammatory disease that causes chronic inflammatory joint pain that disturbs the quality of life of patients including sleep disorders.

Objectives: The aim of our study was to evaluate the quality of sleep of RA patients and to determine the predictive factors of sleep disturbance.

Methods: This is a cross-sectional study conducted among patients followed in the rheumatology department for RA. All patients were diagnosed with RA based on ACR/EULAR criteria. We assessed them for sleep disorders using the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS) after clear consent.

Results: One hundred patients (11 men (11%) and 89 women (89%)) were included. The average age was 53.2 ±11.21 years. The mean duration of the disease was 11.1 years [1 - 40 years]. 70% of the participants had joint deformities,35% had extra-articular manifestations and 17% were obese. 81% of patients were treated with Methotrexate and 10% received biological treatment. The mean visual analogic scale (VAS) was 5.19/10 [1-9] and the average Swollen joints count (SJC) and Tender joints count (TJC) were consecutively 8.5 et 3,95 [0-24]. The average DAS28(CRP) score was 4.6±1,19 and DAS28(ESR) was 3,8±1,19. The mean ESR and CRP values were 46 mm at the first hour and 14.7 mg/L respectively. The disease was very active (DAS 28 ≥ 5.1) in 34% of patients. The average HAQ (Health Assessment Questionnaire) was 1.28±0.7. The mean Epworth score was 7.9 with extremes ranging from 0 to 24. The majority of our population (72%) had normal daytime sleepiness (ESS≤10) and 28% had excessive daytime sleepiness (ESS ≥11). The mean PSQI score was 6,9 [0-19]. Almost half of our RA patients had sleep disorders with an index of PSQI≥5.5. Statistical analysis found a positive significant correlation between the ESS score and the VAS, TJC, SJC, DAS28, HAQ scales, and female gender. Also, we proved a significant relationship between sleep disorders based on the PSQI scale and higher DAS28 (p<0.01), TJC (<0.01), SJC (<0.01), CRP (p<0.01), VAS (p<0.05), and HAQ (p<0.01).

Based on the multivariate study, a high CRP and SJC were found to be predictive factors to sleep disorders according to the PSQI score. on the other hand, the presence of extra-articular manifestations, female gender, and higher VAS were considered as predictive factors of this disorder in conformity with the Epworth score.
Conclusion: Sleep disorders are common among RA patients and they were essentially related to disease activity and functional disability, so it is important to guarantee the remission or low disease activity to improve sleep quality in these patients.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0348 DEPRESSION IN RHEUMATOID ARTHRITIS: PREVALENCE AND PHENOTYPIC CHARACTERISTICS - A SINGLE CENTER EXPERIENCE

Keywords: Rheumatoid arthritis, Mental health

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Background: Psychiatric comorbidities are frequent extra-articular manifestations in rheumatoid arthritis (RA) and depression is the most common [1]. A 2013 study estimated that 16.8 % of RA patients suffer from major depressive disorder, being more prevalent than diabetes, Parkinson's disease or cancer [2-3]. Patients with RA have constitutional symptoms, frequently encountered in depression, like fatigue, weight loss, insomnia and lack of appetite. The overlap of depression in inflammatory immune mediated diseases is recognized for some time [4]. Studies show that immune mediated inflammation affects and modulates neurogenesis, neurotransmission, neuroendocrine activity and neuroplasticity [5]. Depression has important effects on RA patients: worse prognosis, pain, fatigue, functional deficit, more comorbidities, higher rate of mortality, increased healthcare resource utilization and lowered quality of life [6].
Objectives: The scope of this article is to highlight the importance of managing depression in RA. The primary objective was to estimate the prevalence of depression in a cohort of RA patients. The secondary objective was to describe the phenotypic characteristics of RA patients with depression.
Methods: RA patients from the Center of Rheumatic Diseases in Bucharest were included in the study if they were at least 18 years-old and if they had two or three follow-ups, after 2019. The protocol included collection of demographical, clinical and biological data. Prevalence of depression is derived from patients' medical history, known depression. Demographical characteristics and RA phenotype were compared between the two groups. Disease activity was estimated with DAS28 and its components, tender joint count, swollen joint count, CRP and were followed over time to compare disease activity between patients with known depression and patients without depression.
Results: We collected data from 203 patients with RA, among whom 37 were known with depression, generating a prevalence of 18.2%. A meta-analysis from 2013 reported that 16.8 % patients with RA suffer from a major depression disorder [1]. Most of the patients with depression were women (87.2%). Female sex is a potential risk factor for depression [7]. The prevalence of active smoking among the depression subgroup was higher (8.1%, 1.8%, p = 0.041). Depression is a known risk factor for negative behaviors like smoking [8]. Patients had a longer disease duration (in median, 13 years compared to 10 years, p = 0.059) and also the seropositivity prevalence was lower. In 2022 a correlation between depression and seronegative RA was found [9]. DAS28 and the components of DAS28 were higher in the depression RA subgroup; DAS28 was higher at all time points (p < 0.001). Higher tender joint count was expected (p < 0.001), but swollen joint count was also higher among depressive RA patients (p < 0.001), as well as CRP (p = 0.009, Figure 1).

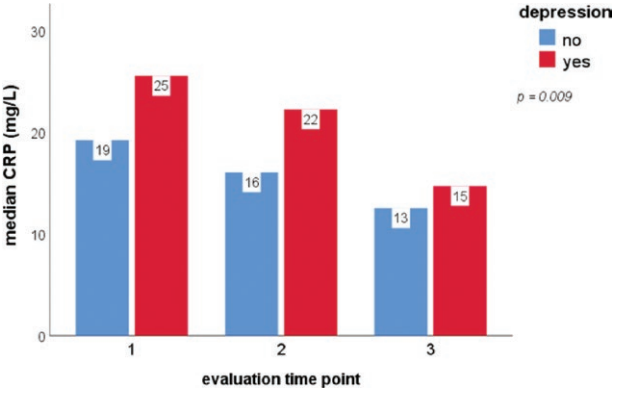


Figure 1. Median CRP levels as three time points among depressive and non-depressive RA patients (ANCOVA)

Conclusion: Depression is prevalent among RA patients and it has an important impact on the quality of life; so depressive symptoms should be addressed in clinical practice. The correlation between the prognosis of rheumatic disease and depression is strong, regardless of the direction of causality. The assessment of depression could be a psychomarker for assessing RA prognosis. DAS28 is used to make therapeutic decisions, so given that depression scores increase DAS28, it follows that they also influence therapeutic decisions.
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AB0349 ENDOCRINE DYSFUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS AND THEIR RELATIONSHIP TO DISEASE SEVERITY

Keywords: Comorbidities, Rheumatoid arthritis, Descriptive Studies

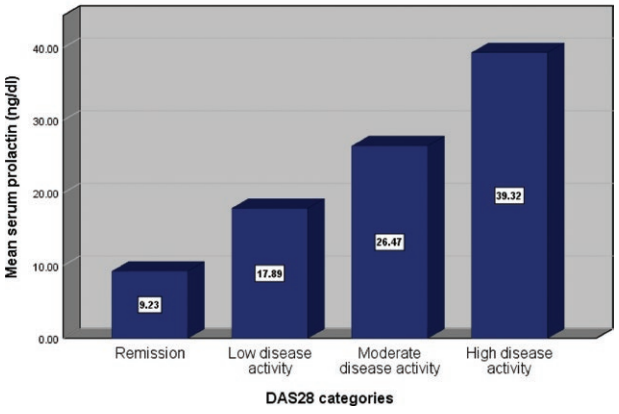
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Background: Rheumatoid arthritis (RA) is known to be associated with multiple endocrine dysfunctions including hypothyroidism, adrenal insufficiency, hyperprolactinemia, and hypoandrogenism. The link between endocrine system and synovitis in RA is attributed to the presence of functional receptors for glucocorticoids, androgens and estrogen in the synoviocytes which function as an intracrine system [1,2].
Objectives: To describe endocrine dysfunction in patients with RA and to determine its relationship with disease severity and disease duration.
Methods: We studied RA patients diagnosed using ACR/EULAR 2010 at our clinic in Jodhpur, India from January 2021 to August 2021 after written informed consent and Ethical Committee approval. We collected the clinical, demographic, treatment history and calculated disease severity with Disease Activity Score (DAS28) and Simplified Disease Activity Index (SDAI). Serum samples for thyroid profile, prolactin, dehydroepiandrosterone sulphate (DHEAS), testosterone, cortisol, Tumor Necrosis Factor alpha (TNF-α) and Interleukin 6 (IL-6) were collected and stored at -80^{0}C and analysed by chemiluminescent immunoassay (Siemens Advia Centaur© immunoassay system, USA) as per the standard hospital protocol. Spearman's correlation was used to determine the relationship between endocrine dysfunction with disease severity scores and total disease duration.
Results: Among the 160 patients included in the study, 4 were on levothyroxine supplementation for hypothyroidism. Thirteen patients (8.8%) had primary hypothyroidism, 2 patients (1.3%) had subclinical hypothyroidism with no cases of central hypothyroidism and 31 patients (20.9%) had sick euthyroid syndrome (Table 1). Hyperprolactinemia was seen in 24.3% patients and the mean level of serum prolactin increased as the disease severity increased but it was not statistically significant (Figure 1). DHEAS levels were below the accepted age and gender cut-offs in 56.4% patients while 56.6% had low testosterone. Among the 99 patients who had random cortisol values, 36 patients (36.4%) had adrenal insufficiency (random cortisol range<3 µg/dl). Serum cortisol was negatively correlated with serum TNF-α but had no relationship with serum IL-6. None of the endocrine parameters were correlated with disease severity scores (SDAI/DAS) or their individual components.
Conclusion: Considerable percentage of patients with RA have endocrine dysfunction compared to the general population, likely secondary to raised inflammatory cytokines produced at synovial tissues. However, they do not correlate to disease activity or disease duration in RA.
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Table 1. Endocrine dysfunction in patients with Rheumatoid arthritis.

Endocrine Abnormality	No of Patients/Total patients (%)
Primary hypothyroidism	13/148 (8.8%)
Subclinical hypothyroidism	2/148 (1.3%)
Sick Euthyroid cases	31/148 (20.9%)
a. low fT3 and low fT4	13/148 (8.7%)
b. low fT3 and normal fT4	14/148 (9.5%)
c. low fT3 with increased fT4	4/148 (2.7%)
Hyperprolactinemia	37/152 (24.3%)
Low DHEAS	88/156 (56.4%)
In males	15/21 (71.4%)
In females	73/135 (54.1%)
Low Testosterone	86/152 (56.6%)
In males	13/21 (61.9%)
In females	73/131 (55.7%)
Primary Adrenal insufficiency	36/99 (36.4%)

Fig 1: Bar graph showing mean serum prolactin levels in various DAS28 categories



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AB0350

DRUG SAFETY AND PREGNANCY OUTCOME IN INDIAN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

Keywords: Safety, Rheumatoid arthritis, Pregnancy and reproduction

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Background: Due to ethical issues conducting controlled trials to assess safety, teratogenicity of medicines to treat Rheumatoid Arthritis (RA) is not feasible and pregnant women are excluded from drug trials. Hence data concerning safety of arthritis medicines in RA is limited. To our knowledge no study is available from India regarding pregnancy outcome and drug safety in RA patients.
Objectives: Analyze safety of arthritis medicines and pregnancy outcome in Indian women suffering from RA.
Methods: Retrospective analysis of RA women with pregnancy treated at Punjab Rheumatology Immunology Centre, Ludhiana and DMC, Ludhiana between 2012 to 2022. Patients were classified as RA based on ACR/EULAR 2010 criteria. Compliance to treatment and additional medication usage was self-reported by the patients. Delivery of healthy baby was counted as successful while spontaneous abortion, MTP due to fetal abnormality were counted as adverse pregnancy outcome.
Results: 77 patients (Mean age 31.3 years) and 82 pregnancies were evaluated. 68 were successful. 10 patients had 11 spontaneous abortions out of whom 4 subsequently had successful pregnancy. Anticardiolipin antibodies were negative in 7, not available in 3. Patient with 2 spontaneous abortions had a successful pregnancy following low molecular weight heparin treatment throughout pregnancy despite negative anticardiolipin antibodies. 3 patients underwent MTP due to antenatal fetal defects (Table 1). Most commonly used medicines during pregnancy were Sulfasalazine(SSZ), Hydroxychloroquine(HCQ), Low dose Prednisolone, Azathioprine(AZA) (Table 1). No specific teratogenicity pattern was identified. 3 patients without Methotrexate(MTX) and 1 patient without MTX+Leflunomide washout had successful pregnancy.

Table 1.

Pregnancy Outcome	Successful	Adverse
Number	68	14
Hydroxychloroquine (HCQ) Monotherapy	9	
Sulfasalazine (SSZ) Monotherapy	10	2 (1 spontaneous abortion, 1 MTP due to hydrocephalus)
SSZ + HCQ	28	4 (spontaneous abortions)
SSZ+Prednisolone	1	2 (spontaneous abortions)
HCQ+Prednisolone	1	
SSZ+HCQ+Prednisolone	13	5 (4 spontaneous abortions, 1 MTP due to fetal spine limb developmental defect)
Azathioprine (AZA) +HCQ+Prednisolone	1	1 (MTP due to fetal spine abdominal defect)
Prednisolone	2	
Treatment default	3	

Conclusion: To our knowledge this is the first study evaluating drug safety and pregnancy outcome in Indian RA patients. Most RA patients can have successful pregnancy. SSZ, HCQ, Azathioprine and low dose prednisolone are safe during pregnancy. Limited data indicates patients can have successful pregnancy without observing MTX washout but more data is required.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Parshant Aggarwal Speakers bureau: Novartis, not related to abstract submitted, Bharti Aggarwal: None declared, Vikas Gupta Speakers bureau: Janssen; not related to submitted abstract, Palak Gupta: None declared.
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AB0351

RELATIONSHIP BETWEEN NUTRITIONAL STATUS AND OSTEOPOROSIS IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Osteoporosis, Diet and Nutrition, Rheumatoid arthritis

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Background: Malnutrition is a recognised risk factor for osteoporosis. These two conditions are frequent comorbidities in rheumatoid arthritis (RA), especially in elderly patients.
Objectives: The aim of our study was to evaluate the association between malnutrition and osteoporosis among elderly patients followed for RA.
Methods: This is a cross-sectional study including patients followed for RA aged 65 years or older. Nutritional status was assessed by body mass index (BMI) and the Mini-Nutritional Assessment (MNA) questionnaire. Patients were divided into 2 groups according to the MNA: an "impaired nutritional status" group with an MNA score ≤ 23.5 and a "normal nutritional status" group with an MNA ≥ 24. Bone mineral density was assessed by two-photon X-ray absorptiometry.
Results: There were 63 patients (52 women and 11 men). The mean age was 68.17±4.35 years. The median duration of RA was 11 years with a IQR of [4-16]. The mean DAS28-VS was 3.72±1.48. The mean total MNA score was 20.19±4.71 [8-27.5]. According to the MNA, 76.2% of the patients had an «altered nutritional status» and 23.8% of the patients had a «normal nutritional status». The mean BMI was 27.97±5.44 kg/m². Osteoporosis was found in 25 patients (39.7%). In the «impaired nutritional status» group according to the MNA, there were significantly more osteoporotic patients (p=0.05). The mean T-score at the lumbar spine site was significantly lower in patients with MNA indicating «impaired nutritional status» (-2.36±1.17 SD vs -1.53±0.81; p=0.04), as was the mean T-score at the femoral site (-1.89±1.18 SD vs -1.03±0.76; p=0.001). A lower BMI was significantly associated with the T-score at the femoral site (p=0.04) but not at the lumbar spine site (p=0.18).
Conclusion: Our study showed that in elderly patients followed for RA, malnutrition diagnosed with the MNA score was significantly associated with osteoporosis and lumbar and femoral T-scores, and low BMI was associated with the femoral site T-score.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0352

FREQUENCY, CLINICAL AND FUNCTIONAL IMPACT OF FOOT INVOLVEMENT IN RHEUMATOID ARTHRITIS

Keywords: Descriptive Studies, Inflammatory arthritides, Rheumatoid arthritis

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Background: Rheumatoid Arthritis (RA) is a chronic inflammatory disorder affecting the joint synovium. Foot involvement is frequent throughout the disease course[1]. However, definition of foot involvement differs, with some scientific works using patient reported outcomes, especially pain, rather than arthritis detected by clinical examination or ultrasound[2,3].
Objectives: Primary – to study the frequency and pattern of foot involvement in RA's patients. Secondary – to compare patients with or without foot involvement concerning sociodemographic, clinical, radiographic and laboratorial characteristics.
Methods: Single center, retrospective study including patients evaluated in our center with a diagnosis of RA, between June-December, 2022. All patients fulfilled the 2010 ACR/EULAR classification criteria for RA. Patient records were searched for sociodemographic, clinical, laboratorial, and radiographic data. Multimorbidity was defined as the coexistence of 2 or more comorbidities. Patients were divided into two groups, according to the presence/absence of cumulative foot involvement, defined as the presence of clinical arthritis or synovitis in ultrasound. Descriptive analysis used mean, median, standard deviation, and interquartile range for continuous data, as well as frequency counts and percentages for categorical variables. A statistical analysis was performed, with a statistically significant p-value ≤ 0.05. The two groups of patients (with/without foot involvement) were compared using parametric and non-parametric tests for continuous variables, and Chi-squared test for categorical variables.
Results: 110 patients were enrolled, with a mean age of 62.97 ± 13.81 years. 84 patients were women (76.36%). Cumulative foot involvement was found in 71 patients (64.55%). The forefoot was the most frequently affected area (69.01% of the patients with foot involvement, n=49), followed by the tibiotarsal joint (53.52%; n=38), the mid foot (12.68%; n=9) and the hindfoot (11.27%; n=8). Patients with foot involvement were more likely to receive a biologic disease modifying anti-rheumatic drug (p <0.05). We found no statistically significant differences between patients with or without foot involvement regarding gender, age at diagnosis, disease duration, rheumatoid factor or anti-citrullinated protein antibodies positivity, bone erosions, multimorbidity, inflammatory markers levels, number of tender or swollen joints at last evaluation, mean Disease Activity Score (DAS)28-C-reactive protein (CRP) and DAS28-erythrocyte sedimentation rate (ESR) or Health Assessment Questionnaire Disability Index Score (HAQ-DI).
Conclusion: In our study, objective foot involvement in RA was frequent and associated with higher probability of biological therapy. However, it did not correlate with poor prognosis factors[4] such as seropositivity, bone erosions or high disease activity measured by DAS28-CRP and DAS28-ESR. We found no higher levels of disability (as measured by the HAQ-DI) in patients with RA involving the foot. Studies with greater sample sizes are paramount to better comprehend the clinical and functional impact of foot involvement in RA, using clearer definitions of the former.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0353 ASSESSMENT OF KIDNEY INVOLVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Kidneys, Rheumatoid arthritis, Comorbidities

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Background: In rheumatoid arthritis (RA) kidney is commonly affected organ with clinical presentation characterized by proteinuria and microalbuminuria, followed by chronic renal failure. RA is associated with reduced kidney function, possibly due to chronic inflammation or the use of nephrotoxic therapies. Renal diseases occurring in patients with RA may have a variable clinicopathological picture. Little is known about the effects of using the novel biological agents on the risk of kidney diseases.
Objectives: The aim of this study was to determine the relationship between effect of therapy and kidney involvement in patients with RA and evaluated the histopathological findings and associated clinical manifestation.
Methods: In this retrospective study 275 patients with diagnosis of RA were included. In 48 patients renal biopsy was performed. The patients were divided in three groups according to changes in management of RA: 1991-2001, 2002-2011 and 2012-2022 year. Data of demographic characteristics, clinical symptoms and pathological diagnosis were extracted from medical records and pathological reports [1,2,3].
Results: In our study amyloidosis was the most common histologic pattern, followed by chronic glomerulonephritis (GN) and tubulointerstitial nephritis. Renal amyloidosis was diagnosed in 13 patients, membranous GN – in 9, mesangioproliferative GN - in 7 patients, focal segmental necrotizing GN – in 5, focal segmental sclerosis – in 4, minimal change disease – in 3, tubulointerstitial nephritis – in 7 patients. Between 1991 and 2001 year the most common clinical manifestation was nephrotic syndrome and the most common histopathological findings - renal amyloidosis, followed by membranous GN and focal segmental necrotizing GN. The membranous GN was related to the use of gold and its frequency decreased after 2001. The mesangioproliferative GN was the leading cause of kidney disease between 2002 - 2011 years and focal segmental sclerosis – between 2012-2022. In our study 68 patients had a decrease of glomerular filtration rate (GFR) < 60 mL/min/ m2. No kidney biopsies were performed in these cases because no urine abnormalities were detected. We found that age, duration of the disease, arterial hypertension, C-reactive protein were significant risk factors for GFR decline in patients with RA. Patients with RA who are treated with biologic agents are less likely to experience progressive decline in kidney function than those not receiving biologic treatment (hazard ratios {HRs] [95% CI], 0,84 [0,68-1,02]}.
Conclusion: In all patients with RA, renal function should be monitored and in the case of pathologic results, renal biopsy should be performed. In RA patients with renal disorder, suspected causal drug should be removed from the treatment and specific immunosuppressive therapy initiated. Improved pain management associated with biologic treatment may help to reduce the need for potentially nephrotoxic anti-inflammatory agents such as NSAIDs and certain types of non-biologic DMARDs, which could consequently reduce the risk of drug-induced nephrotoxicity and thereby contribute to the lower risk of renal diseases.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0354 ORBITAL MYOSITIS ASSOCIATED WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW OF CLINICAL FEATURES AND PARACLINICAL DATA

Keywords: Rheumatoid arthritis, Myositis, Systematic review

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Background: Orbital myositis (OM) is an inflammatory condition that mainly involves extraocular muscles. The exact etiology of this disease is not known [1]. However, rheumatoid arthritis (RA) has been reported as a possible cause of OM in some cases.
Objectives: The aim of this study was to assess the clinical features and paraclinical data of patients with OM associated with RA.
Methods: This study is a systematic review that followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The search was performed in PubMed, Web of Science, Scopus, and ScienceDirect for English articles published between 1990 and 2022. Google Scholar was also utilized to find more studies. The keywords used were: "orbital myositis", "ocular myositis", and "rheumatoid arthritis". There was no limitation in age, gender, nationality, and severity of disease.
Results: A total of 6 studies, describing 5 females and 1 male with age ranging from 38 to 61 years, were included [2-7]. The time between the diagnosis of RA and OM was different, with a maximum of 34 years. The most common sign/symptom found in the patients was diplopia (5 cases) followed by proptosis (3 cases), headache (2 cases), drooping eyelid, periorbital swelling, pain on eye movement, conjunctival

chemosis, and eye movement limitation (each 1 case). In physical examination, decreased vision and weakness/paralysis of the orbital muscles including medial, lateral, and superior rectus were found. Laboratory data revealed increased thyroxine and mildly raised inflammatory markers including ESR and CRP in 1 case. MRI/CT showed thickening of the involved orbital muscles in all cases and tendon enlargement in 2 cases. Although most of the patients being treated with corticosteroids had good outcomes, paresis of the orbital muscles and mild restriction of horizontal movements due to fibrosis remained as sequels in 2 cases.

Conclusion: Although more research is needed on the relationship between RA and OM, RA should be considered as a rare possible cause of OM, which can lead to nonspecific findings such as headache and elevated inflammatory markers to ocular manifestations like diplopia, proptosis, and drooping eyelid. In addition, in patients with RA and ophthalmological diseases, it is recommended that OM be evaluated as a differential diagnosis to avoid irreversible complications with timely treatment.

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Disclosure of Interests: None Declared.
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AB0355 CURRENT CARDIOVASCULAR RISK (MANAGEMENT) IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS

Keywords: Cardiovascular disease, Rheumatoid arthritis

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Background: Patients with rheumatoid arthritis (RA) are at an increased risk for developing cardiovascular diseases. While advice regarding cardiovascular risk screening and management in RA patients has been incorporated in several guidelines in recent years, its implementation and adherence is still poor (1, 2).

Objectives: To assess the cardiovascular disease risk in patients with newly diagnosed RA, and evaluate whether advice to initiate preventive medical treatment of high risk patients was followed.

Methods: All patients with RA, aged 40-70 years, are screened for cardiovascular diseases and risk factors within the first year after diagnosis at the outpatient rheumatology clinic of Reade, as part of standard care. Screening included a physical examination with blood pressure measurement, and laboratory tests with lipid profile tests. All patients and their general practitioner (GP) received an overview with their cardiovascular risk profile and calculated 10-year cardiovascular mortality risk. Risk was defined as low (<1%), intermediate (1-5%), high (5-10%) and very high (>10%).The national pharmacy network was consulted to check whether or not patients started preventive medication after screening.

Results: A total of 125 RA patients were included in this study. The mean age was 56 years and 78% was female. Median RA disease duration at screening was 6 months. 6 patients (5%) indicated to have been screened before, and used antihypertensive medication. During screening, hypertension was found in 46% of patients, with 57% occurring in men and 43% in women. Dyslipidemia was found in 33% of patients, with 36% in male patients and 32% in female patients. 21% of female patients and 46% of male patients currently smoked. Hypertension and dyslipidemia are shown in Table 1. A low 10-year cardiovascular mortality risk was found in 36% of patients, an intermediate risk in 49%, a high risk in 11% and a very high risk in 4% of patients (Figure 1). Only 26% of high and very high risk patients started antihypertensive or statin medication after screening.

Conclusion: An increased cardiovascular disease risk in RA patients, especially male patients, is often present soon after diagnosis, with a large proportion having undiagnosed and untreated hypertension and hypercholesterolemia. Even with structural screening and informing the GP, treatment of cardiovascular risk factors in high risk patients remains insufficient. Obviously, a better collaboration between GPs and rheumatologists is urgently needed to lower the cardiovascular burden of our patients.

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Table 1. Prevalence of hypertension and dyslipidemia components

	All (n = 125)	Women (n = 97)	Men (n = 28)
Systolic BP > 140	39 (31%)	25 (26%)	14 (50%)
Diastolic BP > 90	41 (33%)	36 (37%)	5 (18%)
TC > 6.3	20 (16%)	16 (16%)	4 (14%)
LDL-c > 4.2	21 (17%)	15 (15%)	6 (21%)
HDL-c < 1.3 (women)/ 1.0 (men)	16 (13%)	12 (12%)	4 (14%)
TC/HDL-c ratio > 6	2 (2%)	0 (0%)	2 (7%)
Triglycerides > 2.3	9 (7)	4 (4%)	5 (18%)

BP = blood pressure, TC = total cholesterol, LDL-c = low-density lipoprotein-cholesterol, HDL-c = high-density lipoprotein-cholesterol.

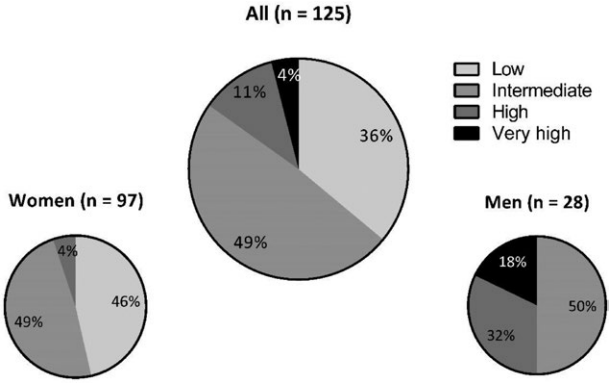


Figure 1. 10-year cardiovascular mortality risk-distribution calculated using SCORE1. Risk distribution is defined as low (<1%), intermediate (1-5%), high (5-10%) and very high (>10%).

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AB0356 EVALUATION OF CARDIOVASCULAR RISK AND OSTEOMETABOLIC ALTERATIONS IN A POPULATION OF PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS: PRELIMINARY RESULTS OF A MULTIDISCIPLINARY PROSPECTIVE STUDY

Keywords: Comorbidities, Rheumatoid arthritis, Real-world evidence

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Background: Rheumatoid Arthritis (RA) is associated with increased cardiovascular (CV) morbidity and mortality and osteometabolic alterations risk, associated with chronic inflammation, the use of glucocorticoids (GC) and the reduced physical exercise.[1]

Objectives: The objective of the study is to cross-sectionally estimate cardiovascular risk and osteometabolic status in patients (pts) with RA and to evaluate the association with some disease parameters such as positivity of autoantibodies, disease activity and steroid therapy.
Methods: At the current time, 61 consecutive pts with diagnosis of RA, admitted to the Rheumatology Unit of the University Hospital of Turin, were prospectively recruited and assessed for cardiometabolic risk by the Endocrinology Unit, by undergoing laboratory and instrumental tests.
Results: The following prevalences were observed: arterial hypertension (52%), type 2 diabetes mellitus (7%), dyslipidemia (56%), osteoporosis (42%), and vertebral fracture (30%). At the univariate analysis, the enrolled pts were divided according to serodiagnosis, GC therapy and disease remission. No statistically significant results were highlighted stratifying population by serodiagnosis. Pts with high disease activity showed lower bone mineral density (BMD) values [BMD femoral trochanter: 0.53± 0.08 vs 0.60 ± 0.08 (g/m^2), p=0.031] and T-score value on bone densitometry [T-score Femoral total: -1.88 ± 0.53 vs -1.07 ± 0.83, p=0.005], higher percentage of osteoporosis [67% vs 27%, p=0.047] and vertebral fractures [60% vs 12%, p=0.001], and higher sarcopenia score [SARC-F: 5 (3-7) vs 2 (2-4), p=0.020], in comparison with pts with remission disease. These differences were not confirmed when the population was divided according to the use of GC therapy. For CV risk factors, disease activity group showed a trend of higher prevalence compared to remission group, but without reaching statistical significance. At the multivariate analysis, advanced age (p=0.001), GC therapy (p=0.021) and copeptin (p=0.002) showed an inverse association and lumbar T-score (p=0.002) a direct one with lumbar trabecular bone score (TBS). Moreover, male gender (p=0.001) revealed a direct and significant association, while copeptin (p=0.086) an inverse and not significant one with percentage of lean mass on total densitometry, correcting for advanced age, duration of disease, GC therapy, and disease activity. In the last model, advanced age (p<0.001) and copeptin (p<0.001) showed a direct and significant association with HeartSCORE, correcting for parameters of disease while serodiagnosis, duration of disease, GC therapy, and disease activity.

Table 1. Multivariate linear regression analysis

Covariates associated with lumbar TBS	B-coefficient	CI 95%	p-value
Age	-0.005	(-0.007- -0.002)	0.001
GC	-0.068	(-0.125- -0.011)	0.021
T-Score	0.049	(0.020-0.079)	0.002
Copeptin	-0.014	(-0.023- -0.006)	0.002
Covariates associated with HeartSCORE cardiovascular risk score	**B-coefficient**	**CI 95%**	**p-value**
Age	0.242	(0.180-0.304)	<0.001
Duration of disease	-0.045	(-0.099-0.008)	0.096
RF and/or ACPA +	-0.224	(-1.855-1.407)	0.782
GC	0.840	(-0.454-2.135)	0.195
Copeptin	0.345	(0.172-0.518)	<0.001
Remission	0.502	(-0.848-1.853)	0.454

Conclusion: At univariate analysis osteometabolic alterations were associated with disease activity, but not with GC therapy and serodiagnosis. At the multivariate analysis, the association of disease activity and TBS values, did not reach the statistical significance, probably for the loss of statistical power. However, GC therapy, as well as advanced age, low lumbar T-score and high value of copeptin, remained independently associated with lower TBS value. Disease parameters were not associated with lower percentage of lean mass at total body densitometry and higher HeartSCORE values, while advanced age and copeptin were associated with bone health and cardiovascular risk.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0357 INCREASED SOLUBLE INTERLEUKIN 2 RECEPTOR IS ASSOCIATED WITH UNDERWEIGHT IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis

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Background: It have been reported that adipose tissue with proinflammatory properties and obese body mass index (BMI) are involved in rheumatoid arthritis (RA) disease severity. However, less attention was focused on underweight BMI in RA, especially in the early stage.
Objectives: This study aims to investigate the association of underweight with RA disease characteristics and its potential mechanism in early RA.
Methods: This cross-sectional study was carried out retrospectively based on our Chinese RA cohort and controls of general population. Clinical data in RA patients as well as BMI in both RA patients and controls were collected. Early RA patients (disease duration ≤ 12 months) and age- and sex- matched controls were included in this study. Serum levels of inflammatory cytokines including soluble interleukin 2 receptor (sIL-2R), TNF-α, IL-6, IL-1β, IL-8, and IL-10 were detected by chemiluminescent immunoassay.
Results: ① Among 1511 RA patients recruited in the cohort, there were 293 (19.4%) patients with early RA, and 221 early RA patients (mean age 49.4±13.1 years with 69.7% female) and 442 age- and sex- matched (1:2 ratio) controls were eligible for analysis. ② Compared with matched controls, early RA patients had a lower BMI (21.9 ± 3.2 kg/m^2 *vs.* 23.3 ± 2.9 kg/m^2) together with a higher proportion of underweight (16.3% *vs.* 2.0%, both $P < 0.05$). Further compared with matched male controls, male patients with early RA also had a higher proportion of underweight (22.4% *vs.* 0%, $P < 0.001$). Surprisingly, compared with female patients, male patients with early RA had a lower BMI (21.1 ± 2.9 kg/m^2 *vs.* 22.3 ± 3.3 kg/m^2) together with a higher proportion of underweight (22.4% *vs.* 13.6%, both $P < 0.05$). On the contrary to patients, matched male controls had a higher BMI (25.0 ± 2.6 kg/m^2 *vs.* 22.6 ± 2.7 kg/m^2) and less proportion of underweight (0% *vs.* 2.9%, both $P < 0.05$) than female controls. ③ Compared with those without underweight, early RA patients with underweight were younger, more male, more active smoking and lower rate of positive ACPA (all $P < 0.05$). ④ Early RA patients with underweight had a higher level of sIL-2R than those without (median 7.83×10^2 U/ml *vs.* 4.97×10^2 U/ml, $P < 0.001$). Spearman correlation analysis showed that BMI was negatively correlated with sIL-2R (r = -0.393, $P < 0.001$). ⑤ Multivariate logistic regression analysis showed that sIL-2R (OR = 1.127, 95% CI 1.058-1.401) was positively associated with underweight in patients with early RA.
Conclusion: Increased serum sIL-2R was associated with underweight in patients with early RA. The underling mechanism of sIL-2R and underweight in RA need further exploration.
Funding: This study was supported by the National Natural Science Foundation of China (82171780, 81971527, and 82101892), Guangzhou Municipal Science and Technology Project (202102010188), Basic and Applied Basic Research Foundation of Guangdong Province (2019A1515011928, 2020A1515110061, and 2022A1515010524).

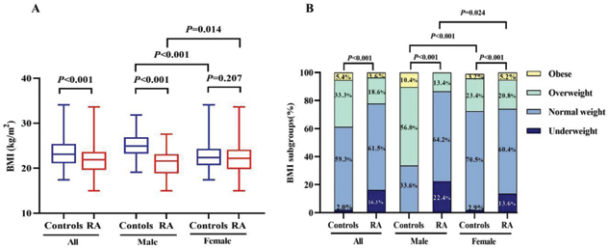


Figure 1. Comparisons of BMI between patients with early RA and matched controls RA, rheumatoid arthritis; BMI, body mass index

Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1834

AB0358 PLAIN HAND X-RAY-BASED MACHINE LEARNING MODEL THAT PREDICTS BONE MINERAL DENSITY IN RA PATIENTS

Keywords: Osteoporosis, Rheumatoid arthritis

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Background: Rheumatoid arthritis(RA) is known as a risk factor for osteoporosis. However, few patients with osteoporotic fractures have measured bone mineral density (BMD) before fracture[1]. Therefore, there is still a need for the development of a simple screening method.
Objectives: The previous studies showed that BMD correlates with the second metacarpal cortical index (2MCI)[2,3,4]. This study aims to build a machine learning model that effectively predicts BMD from plain X-rays to identify high-risk patients for osteoporosis.
Methods: Among the RA patients enrolled in KURAMA cohort between 2012 and 2020, 302 patients received a set of tests, including Dual-energy X-ray absorptiometry(DXA) and bilateral hand X-rays multiple times with a minimal interval of two years. 2MCI was defined as the ratio between the thickness of the cortex and the width of the bone of the second metacarpal(Figure1). We examined the correlation between changes in 2MCI and BMD of the hip and the forearm. Then, we built a machine learning model that predicts BMD using 2MCI and clinical variables. In addition, we evaluated the robustness of the model using an external validation dataset.
Results: The mean age was 62.6 years, and the mean disease duration was 14.1 years. Baseline cross-sectional analysis showed a significant correlation between 2MCI and BMD of the hip and forearm ($p<0.01$). Longitudinal analysis showed a significant correlation between changes in BMD and 2MCI ($p<0.01$). For exploring the best machine learning model, we used Pycaret and found that Bayesian Ridge showed the best performance for predicting BMD of the hip using 2MCI and clinical parameters (MAPE; Mean Absolute Percentage Error = 0.109). Furthermore, model validation using an external dataset revealed good generalized performance (MAPE= 0.145).
Conclusion: Establishing a simple and efficient screening method for osteoporosis is a social issue in an aging society. This study showed that 2MCI significantly correlates not only with BMD at a single time point but also with changes in BMD. Furthermore, a machine learning model built from KURAMA cohort dataset showed good predictive performance when testing on external data. In this study, we proposed a robust model for predicting BMD using a plain hand X-ray in RA patients.
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Figure 1.

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Disclosure of Interests: Ryohei Saito: None declared, Takayuki Fujii Speakers bureau: Abbie, Asahi Kasei, Jansen, Tanabe Mitsubishi, and Eisai., Tamami Yoshida: None declared, Koichi Murata Speakers bureau: AbbVie GK, Eisai Co., Ltd., Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Corporation, Pfizer Inc., Bristol-Myers Squibb, Asahi Kasei Pharma Corp., Hideo Onizawa Speakers bureau: AbbVie, Asahi Kasei, Astellas Pharma Inc., Eisai Co. Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Corporation, and Daiichi Sankyo Co. Ltd., Akira Onishi Speakers bureau: Pfizer Inc., Bristol-Myers Squibb., Advantest, Asahi Kasei Pharma Corp., Chugai Pharmaceutical Co. Ltd., Eli Lilly Japan K.K, Ono Pharmaceutical Co., UCB Japan Co., Mitsubishi Tanabe Pharma Co., Eisai Co. Ltd., Abbvie Inc., Takeda Pharmaceutical Co. Ltd., and Daiichi Sankyo Co. Ltd., Kosaku Murakami Speakers bureau: Eisai Co. Ltd, Chugai Pharmaceutical Co. Ltd., Pfizer Inc., Bristol-Myers Squibb, Mitsubishi Tanabe Pharma Corporation, UCB Japan Co. Ltd, Daiichi Sankyo Co. Ltd., and Astellas Pharma Inc., Masao Tanaka Speakers bureau: AbbVie GK, Asahi Kasei Pharma Corporation, Astellas Pharma Inc., Chugai Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Eli Lilly and Company, Pfizer Inc., UCB Japan Co., Ltd., Janssen Pharmaceutical K.K., Kyowa Kirin Co., Ltd., Mitsubishi Tanabe Pharma Corporation, Taisho Pharma Co., Ltd, and Teijin Pharma, Ltd., Koichiro Omura: None declared, Akio Morinobu Speakers bureau: AbbVie G.K., Chugai Pharmaceutical Co. Ltd., Eli Lilly Japan K.K., Eisai Co. Ltd., Pfizer Inc., Bristol-Myers Squibb., Mitsubishi Tanabe Pharma Co., Astellas Pharma Inc., and Gilead Sciences Japan., and has received research grants from AbbVie G.K., Asahi Kasei Pharma Corp., Chugai Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Co. and Eisai Co. Ltd. outside the work., Shuichi Matsuda Speakers bureau: Astellas Pharma Inc., Daiichi Sankyo Co. Ltd., Mitsubishi Tanabe Pharma Corporation, Eisai Co., Ltd., Takeda Pharmaceutical Company Limited, Chugai Pharmaceutical Co. Ltd, Pfizer Inc., and Asahi Kasei Corporation.
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AB0359 SALIVARY ULTRASONOGRAPHY AND HISTOPATHOLOGIC EVALUATION OF SECONDARY SJÖGREN'S SYNDROME IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Ultrasound, Sjögren syndrome, Diagnostic Tests

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Background: Novel modalities, such as salivary ultrasonography (SGUS) and shear wave elastography (SWE), have previously been introduced to evaluate Sjögren's syndrome (SS). However, in secondary SS (sSS), the diagnostic performance of SGUS and its relationship with clinicopathological characteristics have not yet been clearly defined.
Objectives: In this study, we aimed to investigate sSS in RA patients using SGUS and SWE and sought to determine its pathological correlations.
Methods: Thirty-one RA patients who presented with sicca symptoms were included to be evaluated on SS, and were compared with 18 primary SS (pSS) patients. All subjects were assessed through SGUS and SWE, as well as conventional diagnostic approaches for SS, including minor salivary gland biopsy (MSGB). In SGUS evaluation, two separate scoring systems, suggested by Hocevar and OMERACT, were used.
Results: Among 31 RA patients with sicca symptoms, 19 (61.2%) were diagnosed as sSS. RA patients with sSS showed significantly lower positivity for anti-Ro/La antibody than did pSS patients. Similar to pSS, SGUS showed good diagnostic performance in differentiating sSS from RA patients with simple sicca symptoms. The sSS and pSS patients exhibited significantly higher lymphoid infiltration areas in MSGB than RA patients without SS. Focus score and lymphoid infiltration areas correlated well with sonographic severity. The severity of fibrosis in MSGB showed better positive correlation with SWE than with SGUS.
Conclusion: sSS is frequent in RA patients and presents with less positivity for anti-Ro/La antibodies than does pSS. Similar to pSS, SGUS and SWE show good diagnostic performance for sSS, reflecting histopathologic severity well in MSGB.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1984

AB0360 IMPACT OF PSYCHOLOGICAL STATUS ON COPING STRATEGIES IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Rheumatoid arthritis, Patient reported outcomes

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Objectives: The aim of our study was to determine whether psychological status has an impact on coping strategies in patients with rheumatoid arthritis (RA).
Methods: We conducted a single-centre cross-sectional study for 6 months from 28 March to 28 September 2021 in which we included patients with RA fulfilling the ACR/EULAR 2010 criteria. Characteristics of RA including disease duration and disease activity by the DAS 28 CRP were recorded. The Brief Cope score was used to assess coping strategies. Five grouped coping strategies were evaluated: problem-focused strategies, cognitive restructuring-based strategies, support-based strategies, avoidance-based strategies, and distraction-based strategies. We assessed anxiety and depression using the Hospital Anxiety and Depression Scale (HAD).
Results: Sixty-five patients were included (89.2% women). Mean age was 58.6 ± 9.9 [24-73 years]. Mean duration of RA was 15 ± 10.6 years. Median DAS28 (CRP) was 3.4 (IQR 25-75: 2.8- 4.6) [1.54-6.67]. Median anxiety score was 6 (IQR 25-75: 1-10). Twelve patients (18.5%) had anxiety. Median depression score was 7 (IQR 25-75: 1-13). Eighteen patients had depression (27.7%). Problem-focused and support-based strategies were the most used among all patients, with respective means of 5.6 and 5.5. The association of grouped coping strategies with anxiety and depression was shown in table I.

Table I: Association of grouped coping strategies with depression and anxiety

	Depression		Anxiety	
	p	β	**p**	β
Problem-focused strategies	0,107	0,202	**0,004**	0,357
Cognitive restructuring-based strategies	**0,000**	-0,434	**0,000**	-0,447
support-based strategies	0,100	-0,206	0,142	-0,184
avoidance-based strategies	**0,001**	0,412	**0,000**	0,470
distraction-based strategies	0,202	-0,160	0,212	0,157

Conclusion: Among our patients, depression and anxiety decreased the use of cognitive restructuring strategies. However, they were associated with an increase in avoidance-based strategies and problem-focused strategies.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0361

BONN PULSA: PULMONARY SCREENING IN ARTHRITIS - PREVALENCE OF PULMONARY MANIFESTATIONS IN PATIENTS WITH NEWLY DIAGNOSED RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, AND PERIPHERAL SPONDYLOARTHRITIS

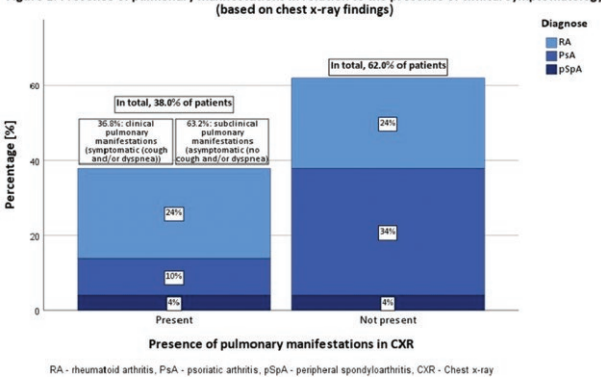
Keywords: Diagnostic Tests, Psoriatic arthritis, Rheumatoid arthritis

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Background: Pulmonary impairment in rheumatic diseases is a common, but poorly understood and deficient screened and managed extraarticular manifestation, which causes a huge increase in morbidity and mortality[1]. As previous studies focused on rheumatoid arthritis (RA) and in some intent on psoriatic arthritis (PsA), data for patients with peripheral spondyloarthritis (pSpA) is lacking.
Objectives: To investigate the prevalence of clinical and subclinical pulmonary manifestations in newly diagnosed patients with RA, PsA, and pSpA and to compare different baseline examination results to develop a screening proposal for detecting patients at risk.
Methods: This clinical-prospective, longitudinal cohort study included a diagnostic workup consisting of a questionnaire for patient history, a physical examination, a body plethysmography with CO diffusion capacity (DLCO), a 6-minute walk test, laboratory parameters, and a chest x-ray (CXR) at the time of the initial diagnosis of arthritis disease, and at four additional time points in three-month intervals. This paper focuses on the baseline characteristics.

Results: 54 outpatients (26 RA, 24 PsA, 4 pSpA) and 26 age- and gender-matched controls were examined. Pulmonary impairment, in the sense of a morphologically abnormal CXR, was diagnosed in 19 arthritis patients (38.0%). 36.8% of these suffered from clinical symptoms, such as cough and/or dyspnea. However, 63.2% presented subclinical, asymptomatic pulmonary abnormalities (see Figure 1). The baseline results of several examinations are illustrated in Table 1. An elevation of rheumatoid factor (> 14 IU/ml) showed an association with the manifestation of RA (p=0.002) as well as with the presence of pulmonary affection (p=0.008). In addition, the mean age of patients with pulmonary abnormalities (57.0 ± 12.8 yrs.) was different from that of patients without such abnormalities (43.9 ± 14.3 yrs.), with a p-value of 0.002. The association between the activity of arthritis disease, assessed by Disease Activity Score in 28 joints using CRP (DAS-28CRP), and CXR findings proved to be significant (p=0.011). A DAS28CRP less than 3.2 (remission or low disease activity) indicated non-pathological findings in CXR.
Conclusion: The prevalence of pulmonary manifestations was more than one-third, of which more than two-thirds presented asymptomatic. The large proportion of asymptomatic subjects highlights the need for the implementation of a pulmonary screening at the initial diagnosis of arthritis disease. By alerting physicians, especially in the observed age cohort of 57 years with elevated RF levels, morbidity and mortality could be reduced.
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Figure 1: Presence of pulmonary manifestations in relation to the presence of clinical symptomatology (based on chest x-ray findings)



RA - rheumatoid arthritis, PsA - psoriatic arthritis, pSpA - peripheral spondyloarthritis, CXR - Chest x-ray

Table 1. Findings in bodyplethysmography with CO diffusion capacity and laboratory parameters

		Presence of rheumatic disease		Presence of pulmonary disorders in chest x-ray	
		RA[a]/PsA[b]/ pSpA[c] (n=54)	**Control proband (n=26)**	**Present (n=19)**	**Not present (n=31)**
Restrictive lung disease	Not present	39 84.8%	16 64.0%	15 88.2%	21 84.0%
	Present (FVC < 70%; TLC < 80%)	7 15.2%	9 36.0%	2 11.8%	4 16.0%
Obstructive lung disease	Not present	46 100.0%	25 100.0%	17 100.0%	25 100.0%
	Present (FEV1/FVC < 70%)	0 0.0%	0 0.0%	0 0.0%	0 0.0%
Emphysema	Not present	39 86.7%	19 76.0%	14 82.4%	23 95.8%
	Present (RV > 140%)	6 13.3%	6 24.0%	3 17.6%	1 4.2%
Diffusion disturbance	Not present	37 86.0%	21 91.3%	13 81.3%	21 91.3%
	Present (DLCO < 60%)	6 14.0%	2 8.7%	3 18.8%	2 8.7%
C-reactive protein	Non-pathological (≤ 3 mg/l)	19 35.2%	19 86.4%	4 21.1%	13 41.9%
	Pathological (> 3 mg/l)	35 64.8%	3 13.6%	15 78.9%	18 58.1%
Rheumatoid factor	Non-pathological (≤ 14 IU/ml)	31 66.0%	19 95.0%	6 37.5%	21 77.8%
	Pathological (> 14 IU/ml)	16 34.0%	1 5.0%	10 62.5%	6 22.2%

PsA – psoriatic arthritis, RA – rheumatoid arthritis, pSpA – peripheral spondyloarthritis

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Disclosure of Interests: None Declared.
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AB0362 PROFESSIONAL COUNTRY-WIDE SURVEY ON CLINICAL DECISION-MAKING IN THE TREATMENT OF RHEUMATOID ARTHRITIS

Keywords: Work-related issues, Disease-modifying Drugs (DMARDs), Best practices

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Background: Incorporation of conventional synthetic (cs), biologic (b) and targeted synthetic (ts) disease-modifying drugs (DMARDs) has enriched the therapeutic arsenal, but at the same time has complicated the decision-making process, since it requires considering not only the profile of each patient and the characteristics of each drug, but also the high cost of many of them and diverse administrative limitations.
Objectives: To analyze the way of acting of Spanish rheumatologists in different clinical situations in order to understand the decision-making process in the treatment of rheumatoid arthritis (RA).
Methods: A questionnaire that consisted of 15 questions was sent to several groups of rheumatologists country wide between October 19 and 26, 2022. Descriptive statistical analysis and Pearson's Chi2 test were performed to compare responses to the items by the different groups, significance level 0.05 (p>0.05 N.S.)
Results: A total of 108 questionnaires were collected. Work experience of the respondents is reflected in Table 1. In patients with recent-onset RA associated with poor prognostic factors, in addition to corticosteroids half of the respondents (50%) opt to start treatment with csDMARD + rapid escalation to d/tsDMARD if clinical response is insufficient. The most important factor when choosing the drug is the patient´s profile (47.2%), followed by clinical practice guidelines (34.3%). The most relevant factors when choosing each DMARD were: anti-TNF - cost-effectiveness (47.2%); anti-IL6 - efficacy (72.2%); abatacept - efficacy and safety in patients with RA-associated interstitial lung disease (53.7%); rituximab - its safety in patients that didn´t respond to other treatments (76.9%); and JAK inhibitor - its possibility of use in monotherapy (40.7%). The most important factors that lead to change treatment are the disease activity measures (57.4%) and personal perception of the clinician based on anamnesis and physical examination (31.5%). If there is a good therapeutic response, the majority of respondents first taper the b/tsDMARD (50%). If bDMARD-csDMARD combination therapy is used, 59.3% of respondents try to maintain csDMARD in addition to b/tsDAMRD. Regarding the use of corticosteroids, the vast majority of colleagues (79.6%) prefer to try to discontinue them as soon as possible. In case of pregnancy, more than half of the respondents (59.3%) switch to a safer drug. Incidentally diagnosed cancer is a reason for discontinuation of all b/tsDMARD for 47.2% of respondents, while 29.6% additionally discontinue csDMARD and use corticosteroids for disease control; in this clinical situation, respondents with <30 years of work experience discontinue all DMARDs in higher proportion than those with >30 years of work experience (p<0.05). The majority of respondents (80.6%) consider biosimilar drugs to be equally effective and safe as the origininator.

Table 1. Years of work experience in rheumatology.

Resident	9,3%
0-10 years	43,4%
11-20 years	17,6%
21-30 years	9,3%
>30 years	20,4%

Conclusion: The study revealed a striking heterogeneity in the way of acting in complex clinical situations, which confirms that the decision-making process depends on many factors but also that there is still room for homogenizing clinical practice guidelines in rheumatology. However, there seems to be agreement on the need to minimize systemic exposure to corticosteroids, on the use of disease activity measures to evaluate therapeutic response and on the wide acceptance of biosimilar drugs.
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Disclosure of Interests: None Declared.
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AB0363 UTILITY OF EPITHELIAL CELL BIOMARKERS TO ASSESS SEVERITY AND DISCRIMINATE BETWEEN DIFFERENT PATTERNS OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Biomarkers, Lungs

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Background: Several biomarkers have been studied in rheumatoid arthritis (RA) interstitial lung disease (ILD), but their clinical application has not been well established yet [1]. Given that usual interstitial pneumonia (UIP) is the most common pattern of ILD in patients with RA, the utilization of biomarkers that give information about the epithelial cell activation could be an interesting approach to assess the severity of lung disease in these patients [2].
Objectives: To know the ability of CA19-9, CA125 and CEA to discriminate different patterns on HRCT and assess the severity of ILD in patients with RA.
Methods: We conducted a cross sectional study. Patients with a diagnosis of RA-ILD who were evaluated in three different rheumatic diseases clinics between December 2021 and January 2023 were consecutively included. The diagnosis of RA was defined according to ACR/EULAR 2010 classification criteria. The diagnosis of ILD was confirmed by an experienced radiologist. We performed HRCT, lung function tests, joint disease evaluation, and blood extraction to determine the values of CA 19-9, CA 125, CEA, rheumatoid factor (RF) and ACPAs. The pattern found on HRCT was classified in UIP pattern, probable UIP, indeterminate for UIP, and suggestive of another diagnosis, as proposed the inter society consensus of 2022 [4]. The score proposed by Goh was calculated to determine the extension of lung opacities (inflammatory, fibrotic, and total extension scores) [5]. The joint disease activity was assessed using the DAS28 score. The values of the biomarkers in serum were measured by electrochemiluminescence. T-test, Mann Whitney test, and Chi square were used for comparisons. The Spearman test was used for correlation analysis.
Results: We included 38 patients, 29 were women (76.3%). The mean (SD) age was of 62.1 (11.5) years. The median (IQR) of DAS28 was 3.3 (2.6-4). Regarding serologic tests, 35/36 (97.2%) and 36/37 (97.3) were positive for ACPAs and RF respectively. In relation to lung disease, the mean (SD) of FVC% was 83.8 (23.4) and the median (IQR) DLCO was 59 (52-81). Eighteen patients (47.3%) showed UIP or probable UIP pattern in the HRCT, while 20 (52.7%) had another pattern. The median (IQR) of Goh score for total lung disease extension was 20 (8-25). Patients with UIP pattern showed significantly higher values of CA19-9 [11.5 (7-35.7) vs 6.5 (2-12.5), p=0.017] and a trend to higher values of CA125 [22 (15-52) vs 14 (11.4-20.7), p=0.06] than those with other patterns. The values of CA19-9 showed a good correlation with total Goh score (r=0.52, p=0.02) and fibrosis Goh score (r=0.65, p=0.03) in patients with UIP pattern. Also, the values of CEA showed an acceptable correlation with total Goh score (r=0.46, p=0.05) and fibrosis Goh score (r=0.43, p=0.07) in patients with UIP pattern.
Conclusion: Patients with RA ILD and UIP pattern showed higher plasmatic values of biomarkers that reflect epithelial cell activation. Also, the values of some of these biomarkers showed good correlation with the extension of the disease on HRCT. Therefore, these biomarkers could be a useful tool to identify a more aggressive clinical behavior in patients with RA ILD.

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AB0364 CIGARETTE SMOKING AMONGST RHEUMATOID ARTHRITIS PATIENTS IN A TERTIARY CENTER IN SOUTH AFRICA

Keywords: Patient reported outcomes, Descriptive Studies, Rheumatoid arthritis

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Background: Cigarette smoking is associated with poorer outcomes amongst rheumatoid arthritis (RA) sufferers, with poorer disease control, increased extra-articular complications and more comorbidities[1]. There are currently no data from sub-Saharan Africa.

Objectives: To describe the prevalence of cigarette smoking, and explore disease control, comorbidities, extra-articular disease and attitudes of smokers to their habit amongst RA patients in an outpatient clinic at tertiary level public hospital in South Africa. Further, we asked patients about the impact of prohibition during the COVID pandemic.

Methods: A cross-sectional study of consenting adult outpatients with RA meeting the EULAR/ACR 2010 Classification Criteria. Demographic, clinical and patient-reported outcome measures (PROMs) including the Health Assessment Questionnaire-Disability Index (HAQ-DI), FACIT-fatigue scale, Brief Pain Inventory-short form and Hospital Anxiety and Depression Scale (HADs) together with a questionnaire about smoking and Fagerström test for nicotine dependence were collated.

Results: Of 632 patients (536 females), the mean (SD) age and disease duration were 55.4 (13.0) and 10.1 (9.3) years. A poor socio-economic setting (SES) (defined using a pooled index) was noted in 67.0%. The mean (SD) Clinical Disease Activity Index (CDAI) and HAQ-DI were 14.3 (11.8) and 1.5 (0.7). The cohort included 218 (34,5%) smokers, and 89 (14.1%) ex-smokers, and more males smoked (49/218 vs 47/414, p=0,0002). Compared to non- or ex-smokers, smokers had lower BMI (29.7 vs 32.7 (p= 0.01), higher anxiety scores (8.8 vs 8.0, p=0,048) and incidence of COPD (7.8 % vs 1.0%, p< 0.005). The vast majority (74.1%) had two or more comorbidities, and the commonest comorbidities were hypertension, dyslipidaemia and diabetes. There were no significant differences in age of RA onset, disease duration, SES, number of comorbidities, CDAI nor its individual components, extra-articular diseases nor in HAQ-DI, FACIT, depression or pain scores. Of 160 patients who completed the smoking questionnaire, 83 (51.9%) believed smoking worsened their arthritis, and 119 (74.4%) reported receiving smoking cessation advice at the RA clinic. Participants' most common reasons for smoking were emotional support (32.2%), nicotine craving (21.7%) and pain control (27.3%). Although 50.1% felt that living with RA made quitting difficult, 86.9% had considered quitting, and almost half (45.6%) had previously quit for more than 3 months. The Fagerström score revealed mild, moderate and severe nicotine dependence in 67.5%, 24.4%, and 7.5% respectively. The Fageström score was significantly associated with anxiety (r=0.2, p=0.02) and depression (r=0.28, p<0.005). Smoking prohibition during COVID pandemic resulted in 60.0% (96) patients quitting or reducing cigarette consumption. Patients felt that helpful services from their RA team might include referral to a smoking cessation clinic (48.1%) and availability of more reading material (36.1%).

Conclusion: In this cohort of indigent RA patients, a third of RA patients are smokers, with higher prevalence in males, and associated with lower BMI and higher anxiety scores but with no differences in disease parameters or other PROM's. Smoking is a modifiable risk factor, of great importance given the high prevalence of comorbidities in the cohort. Only half the cohort were aware that smoking worsened their RA disease control. The mild to moderate nicotine dependence in this cohort, together with patients' willingness to quit should encourage both patient and health care providers to positively engage in smoking cessation.

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AB0365 PATIENTS WITH RHEUMATOID ARTHRITIS CLASSIFIED AS "HIGH ACTIVITY" ACCORDING TO DAS28 OR CDAI INCLUDE 55% AND 70% WHO SCREEN POSITIVE FOR DEPRESSION AND 67% AND 80% WHO SCREEN POSITIVE FOR FIBROMYALGIA, RESPECTIVELY

Keywords: Rheumatoid arthritis

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Background: No single measure can serve to assess all patients with rheumatoid arthritis (RA), and indices based on a core data set of 7 measures are used in clinical trials and clinical care. Two prominent RA indices are DAS28 (disease activity score 28) and CDAI (clinical disease activity index), which are classified into 4 categories of high, moderate, low disease activity and remission. It has been reported that comorbid fibromyalgia (FM) and depression (DEP) may elevate DAS28 and CDAI values, but systematic comparison of the proportions of patients in different activity categories who screen positive for these comorbidities has not been reported. Feasible screening for FM and DEP is available using MDHAQ (multiple dimensional health assessment questionnaire) FM and DEP indices, which agree more than 80% with reference standards.

Objectives: To analyze the proportion of routine care RA patients who screen positive for FM and DEP according to the 4 DAS28 and CDAI activity categories.

Methods: The 7 RA core data set measures - SJC, TJC, PaGA, PhGA, ESR, CRP, physical function and pain - were collected in unselected RA patients in a cross-sectional study at a routine care visit to an academic site. The patient measures were all collected on an MDHAQ which is completed by all patients and includes physical function, pain, PaGA, fatigue visual numeric scales (VNS), 0-3.3 DEP query, self-report 0-54 patient RADAI painful joint count, 60-symptom checklist including DEP, medical history queries, and FAST4 and MDS2 indices. FAST4 FM screen is positive if 3/4 of: pain VNS ≥6/10, fatigue VNS ≥6/10, self-reported painful joint count ≥16/54, and/or symptom checklist ≥16/60. MDS2 DEP screen is positive if 0-3.3 DEP response is ≥2.2 OR positive DEP on the symptom checklist. DAS28-ESR and CDAI were computed according to standard methods, and patients were classified into 4 activity categories: high (>5.1/28 and >22/76), moderate (3.2-5.1 and 10.1-22), low (2.6-3.2 and 2.9-10), and remission (≤2.6 and 2.8), for DAS28-ESR and CDAI, respectively. The median SJC, TJC, and proportions of FAST4 and MDS2 patients in each category were compared using chi-square analyses.

Results: Among 122 patients, categories of remission, low, moderate, and high activity, respectively, included 44%, 15% 34%, and 7% by DAS28-ESR, and 13%, 31%, 39% and 16% by CDAI. Median SJC was 0, 0, 2 and 4 for DAS28-ESR and 0, 0, 0 and 4 for CDAI categories. Median TJC was 0, 2, 5 and 5 in DAS28-ESR and 0, 1, 3 and 14 in 4 CDAI categories (Table 1). Positive FM FAST4 FM screen was seen in 13%, 22%, 44% and 67% in 4 DAS28-ESR categories and 0%, 2.6%, 38%, and 80% in 4 CDAI categories. Positive DEP MDS2 was seen in 20%, 44%, 46% and 56% in 4 DAS28-ESR categories, and 6%, 24%, 40% and 70% in 4 CDAI categories.

Conclusion: Among RA patients classified as high DAS28-ESR or CDAI "activity", respectively, 55% and 70% screened positive for DEP, 67% and 80% for FM respectively. These phenomena may affect treat-to-target and other aspects of RA management.

Measure (Range or units)	Median (IQR)	Remission Median IQR	Low Median IQR	Moderate Median IQR	High Median IQR
DAS28-ESR	2.9 (2.2-3.7)	≤2.6	2.6-3.2	3.2-5.1	>5.1
Number of pts (%)	122	54 (44.3)	18 (14.7)	41 (33.6)	9 (7.4)
SJC (0-28)	0 (0-2)	0 (0-1)	0 (0-1)	2 (0-4)	6 (3-10)
TJC (0-28)	2 (0-5)	0 (0-1)	2 (0-4)	5 (2-8)	5 (2-8)
FAST4 (%pos) Fibromyalgia	35 (28.7)	7 (13.0)	4 (22.2)	18 (43.9)	6 (66.7)
MDS2 (% pos) Depression	43 (35.2)	11 (20.4)	8 (44.4)	19 (46.3)	5 (55.6)
CDAI	11.5 (5-18.5)	≤ 2.8	2.9-10	10.1-22	>22
Number of pts (%)	122	16 (13.1)	38 (31.1)	48 (39.3)	20 (16.4)
SJC (0-28)	0 (0-2)	0 (0-0)	0 (0-1)	0 (0-3)	4 (1-8)
TJC (0-28)	2 (0-5)	0 (0-0)	1 (0-2)	3 (1-5)	14 (10-18)
FAST4 (% pos) Fibromyalgia	35 (28.7)	0	1 (2.6)	18 (37.5)	16 (80.0)
MDS2 (% pos) Depression	43 (35.2)	1 (6.25)	9 (23.7)	19 (39.6)	14 (70.0)

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Disclosure of Interests: None Declared.

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AB0366 RHEUMATOID ARTHRITIS PATIENTS WITH ≥6/28 TENDER JOINTS AND PATIENT AND PHYSICIAN GLOBAL ASSESSMENTS ≥3/10 HAVE SIGNIFICANTLY HIGHER LEVELS OF COMORBIDITIES WHICH MAY NOT BE RELATED TO INFLAMMATORY ACTIVITY, INCLUDING FIBROMYALGIA, DEPRESSION, FATIGUE, NECK PAIN, BACK PAIN, AND DEFORMED JOINTS

Keywords: Rheumatoid arthritis

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Background: Patients with rheumatoid arthritis (RA) are assessed in clinical trials and clinical care according to a core dataset and derived indices, which include tender (TJC) and swollen (SJC) joint counts, erythrocyte sedimentation rate (ESR), and patient (PaGA) and/or physician global assessments (PhGA). Many clinical trials require TJC and/or SJC ≥6 for enrollment, and improvement criteria require that SJC and TJC are 20%, 50%, or 70% better. It has been reported that TJC, PaGA, and PhGA may be elevated by comorbidities in the presence of little or no (or high) inflammatory activity, associated with high levels of fibromyalgia (FM), depression (DEP), fatigue (FT), back pain (Bpain), neck pain (Npain), and/or joints with deformity/limited motion (DJC). The likelihood and extent of elevations of RA measures associated with these comorbidities has not been extensively analyzed. FM, DEP, BPain, Npain, and FAT can be screened for on a multidimensional health assessment questionnaire (MDHAQ), and DJC can be included on a 28 joint count.

Objectives: To analyze RA patients seen in a routine care academic setting for possible elevations of SJC, TJC, ESR, PaGA and PhGA associated with positive screening for FM, DEP, FT, Bpain, Npain, and DJC.

Methods: A cross-sectional study was conducted at a routine care visit of RA patients to an academic rheumatology setting. All 7 RA core dataset measures were collected, including SJC, TJC, ESR, PaGL, and PhGL. The patient self-report measures were collected on an MDHAQ, completed by all patients in 5-10 minutes at this setting, which includes queries for FT, Npain, Bpain, and indices to screen for FM - FAST4 (fibromyalgia assessment screening tool), and DEP - MDS2 (MDHAQ depression screen). FAST4 and MDS2 agree more than 80% with reference standards but can be feasibly collected in routine care on a single questionnaire. Patients were classified into 2 groups according to clinically relevant cut-points for each possibly non-inflammatory variable, and the number of patients above and below these cut points compared by chi square analyses.

Results: In 125 RA patients with complete data, significant differences (p<0.01) were seen for TJC <6 vs ≥6, PaGA <3 vs ≥3, and PhGA <3 vs ≥3, according to positive FAST4 FM, DEP MDS2, Bpain and Npain, FAT ≥3/10, and DJC ≥6. No significant differences were seen according to ESR <30 vs ≥30 or SJC <6 vs ≥6, other than a difference in SJC <6 vs ≥6 for patients with DJC <6 vs ≥6, (Table 1).

Conclusion: TJC, PaGA, and PhGA, but not ESR or SJC, are associated with positive screening for FM, depression, back pain, neck pain, fatigue, and joints with deformity/limited motion, that may not result from inflammatory activity. These elevations may affect DAS28 and CDAI scores, interpretation for treat-to-target, and general management. It is feasible to screen for these comorbidities in routine care, which may enhance clinical decisions and outcomes.

Number of patients in different categories

a. Measure	No of Pts(%)	c.FM+ (FAST4+)	d.DEP+ (MDS2+)	e.Fatigue VNS ≥3	f. Back pain+	g. Neck pain+	h. DJC≥6
SJC <6/28	113 (91%)	30	37	74	71	62	21
SJC≥6/28	12 (10%)	5	7	8	7	6	10
P		0.44	0.15	1	1	0.99	<0.0001
TJC <6/28	94 (75%)	16	24	55	52	44	0
TJC≥6/28	31 (25%)	19	20	27	26	24	31
p		<0.0001	0.0002	0.0072	0.0085	0.0058	<0.0001
ESR<30/150	97 (78%)	27	38	63	63	54	27
ESR≥30/150	28 (22%)	8	6	19	15	14	4
P		1	0.13	0.95	0.38	0.75	0.22
PaGL<3/10	46 (37%)	0	5	12	20	17	5
PaGL≥3/10	79 (63%)	35	39	70	58	51	26
P		<0.0001	<0.0001	<0.0001	0.0017	0.0051	0.01
PhGA<3/10	52 (42%)	3	9	21	25	19	5
PhGA≥3/10	73 (58%)	32	35	61	53	49	26
p		<0.0001	0.0008	<0.0001	0.0092	0.0014	0.0019

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Disclosure of Interests: None Declared.

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AB0367 ANXIETY AND DEPRESSION IN RHEUMATOID ARTHRITIS DISEASE: A CROSS SECTIONAL STUDY AMONG 100 TUNISIAN PATIENTS

Keywords: Quality of life, Rheumatoid arthritis, Mental health

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Background: Rheumatoid Arthritis (RA) is a common chronic inflammatory disease, which can lead to structural joint damage and important handicap. RA is associated with pain, fatigue, functional disability and deterioration of emotional state that influence people's lives and may cause psychiatric signs and symptoms, particularly anxiety and depression.

Objectives: The present study aims to Assess the frequency of anxiety and depression in patients with RA and to determine their associated factors.

Methods: This is a cross sectional study conducted among patients followed in the rheumatology department at TAHER SFAR University Hospital in Mahdia. All patients were diagnosed with rheumatoid arthritis based on ACR/EULAR criteria. We included only patients without any previous psychiatric history and assessed them for anxiety and depression symptoms using the Hospital Anxiety and Depression scale (HADS) after a clear consent.

Results: We included in our study 100 patients with a mean age of 53.2 years (±11.21). The average duration of disease was 11.1 ± 8.9 years. The assessment of the RA activity showed a severe activity RA in 34% of participants. After analyzing the questionnaire results, according to HADS, the mean HAD-D score was 8.39 ±3.84 with 30% of definite depressed patients while the mean HAD-A score was 7.79± 3.6 with 24 patients presenting definite anxiety disorder. A significant association was found between the presence of depressive disorder and high disease activity (p<0.01), higher HAQ level (p=0.02), higher NTJ (Number of Tender Joints) (p<0.01), NSJ (Number of Swollen Joints) (p<0.01) and higher VAS (Visual Analogue Scale) (p=0.04). Anxiety was also associated with severe activity stage (p<0.01), higher HAQ level (p<0.01), higher NSJ (p=0.01) and NTJ (p<0.01).

Conclusion: Our study showed that more than quart of RA patients suffers from anxiety and/or depression, and these troubles were related essentially to active disease and functional disability. Screening for these disorders and the management of the RA activity will be necessary during follow up of our patients to ameliorate their quality of life.

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AB0368

DIFFERENCES IN THE ASSESSMENT OF COMORBIDITIES (FATIGUE AND DEPRESSION) BETWEEN RA PATIENTS AND PHYSICIANS. DO WE MEASURE THE SAME?

Keywords: Patient reported outcomes, Rheumatoid arthritis, Outcome measures

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Background: Differences in physicians' assessment of disease activity and patients' perception of disease activity have been described [1]. Two of the most important disease-related symptoms experienced by patients are fatigue and depression, which are not routinely assessed by physicians [2].
Objectives: To study the differences between patient and physician perspectives on fatigue and depression, as well as on other biological, clinical and self-reported disease variables in a group of patients with established rheumatoid arthritis (RA).
Methods: Patients with RA (ACR/EULAR,2010) followed up by the Arthritis Unit who agreed to participate in this study were included consecutively in the Arthritis Unit for 3 months. They fulfilled 3 questionnaires to evaluate fatigue and depression: 1. MDHAQ, that includes: 0-10 physical function (FN) according to modified HAQ (0-10), visual analogue scale (VAS) 0-10 for pain (PN), VAS 0-10 for fatigue (VAS-Fatigue) (in the question 9, considering high fatigue with >5 cut off) and patient global assessment (PGA) to calculate RAPID3, a review of 60 symptoms (ROS60) and self-assessment 48 joint count (RADAI48). 2. FACIT-(FS)=FACIT-Fatigue, 13 questions (0-4 score) with a global score of 0-52 (lower scores indicate worse fatigue). 3. Patient Health Questionnaire 9= PHQ9, 10 questions with PHQ9>10 screened for depression. Physical articular examination (28TJC, 28SJC), laboratory test (CRP, ESR), composite EULAR disease activity indices (DAS28, DAS28 CRP, CDAI and SDAI), demographic (sex, age, BMI), patient´s disease characteristics and the Physician Global Assessment (PhGA) for the disease were collected. A descriptive analysis of the variables was done, and Pearson´s correlation between PhGA and PGA, and the rest of variables studied was performed.
Results: A total of 75 patients (84% females) with RA were recruited, with a mean age of 62±11.6 years, a mean disease duration of 14.6± 5 years and a mean BMI of 22.8 ± 8.0. 64% were under with bDMARD and 45.3% with glucocorticoids treatment. Depression (PHQ9>10) was observed in 12 patients (16%) and in 31 (41.2%) of patients we observed high fatigue (VAS-fatigue>5/10). Correlation results between PGA and Fatigue (FS) were almost good for VAS-Fatigue (r=0.604, p<0.001) and for PHQ9>10(r=0.616, p<0.001), and almost good for FACIT(FS)(r=-0.517, p<0.001). On the other hand, correlations between PhGA were smaller with fatigue (Fatigue (FS): r=-0.428, p<0.001; VAS-Fatigue: r=0.451 p<0.001) and with depression (PHQ9: r= 0,477 p<0.001). Correlation of the rest of studied variables (DAS28, CDAI, SDAI, 28TJC, 28SJC, CRP, ESR and ROS) were smaller for PhGA than for PGA, except for 28SJC, where the assessment of physician is closer to that the patient (Table 1).
Conclusion: The patient's perception of disease status is better than the physician's perception of these two important comorbidities associated with RA, as well as disease activity indices. Clinicians have to take into account scores on fatigue and depression questionnaires or scales when assessing patients with RA.

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Acknowledgements: NIL.

Disclosure of Interests: Rosa Morlà: None declared, Beatriz Frade-Sosa: None declared, Nuria Sapena: None declared, José A Gómez-Puerta Speakers bureau: Abbvie, Astra Zeneca, Lilly, Galápagos, Pfizer, Roche, Consultant of: Abbvie, Astra Zeneca, Lilly, Galápagos, Pfizer, Roche, Raimón Sanmartí Speakers bureau: Abbvie, Lilly, Pfizer, Roche, Consultant of: Abbvie, Lilly, Pfizer, Roche.
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AB0369

EVOLUTION AND PROGNOSIS OF A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS AND SUBCLINICAL INTERSTITIAL LUNG DISEASE.

Keywords: Rheumatoid arthritis, Comorbidities, Lungs

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Background: Clinical RA-associated ILD (RA-ILD) presents in almost 10% of RA patients but subclinical RA-associated ILD is detected in 20-60%. The course of subclinical RA-ILD is not fully known. Some patients have disease progression to pulmonary symptoms, decreased respiratory function and high levels of morbidity and mortality. It is necessary to improve ways to determinate risk of progression in patients with subclinical RA-ILD.
Objectives: To describe a cohort of patients with clinical and subclinical Rheumatoid Arthritis-associated Interstitial Lung Disease (RA-ILD) and to compare the evolution and progression of both.
Methods: Ambispective observational study of a cohort of patients with RA-ILD confirmed by respiratory function tests (RFT) or high-resolution computed tomography (HRCT). From January 2019 to December 2021, all patients with these diagnoses from RA monographic clinic were included consecutively. Data on the onset of ILD were included retrospectively and data at the end of follow-up prospectively (last review). The % of patients who had subclinical ILD was evaluated, defined as pulmonary involvement due to a requested HRCT without any previous respiratory symptoms. Outcome: evolution of the final ILD: (1) improvement (improvement in FVC ≥10% or DLCO ≥15% and no radiological progression); 2) no progression (stabilization or improvement in FVC ≤10% or DLCO <15% and no radiological progression); 3) progression (>10% worsening of FVC or >15% DLCO and radiological progression); or 4) death. Demographic variables, activity data (DAS28VSG accumulated 24 months prior to the diagnosis of ILD), RF and ACPA levels, RA severity data and treatments. Descriptive analysis, χ^2 or t-Student, and multivariate logistic regression analysis were performed to find predictive variables for the evolution of ILD.
Results: 50 patients with RA-ILD were included, 18 (36%) had subclinical ILD. The reason for requesting HRCT when they were diagnosed was abnormal chest X-ray in 11 patients (61.1%) and crackles in 7 patients (38.8%). The baseline characteristics of both groups at the time of ILD diagnosis and the evolution are shown in Table 1. The disease duration of the clinical ILD was longer than that of the subclinical ILD 5.6 (5.2) vs. 3.5 (2.4) years, p=0.053). At the moment of ILD diagnosis, the treatments were modified in 10 patients with clinical ILD and in 7 with subclinical ILD (p= 0.593): 8 abatacept, 7 rituximab and one antifibrotic drug were started. A total of 13 patients (26%) progressed and 25 (48%) showed a stabilization or improvement. Four patients died because of non-pulmonary causes. The only variable independently associated with the progression of ILD in the complete sample, adjusted for ACPA titres and age at diagnosis of ILD, was UIP pattern [OR = 5.3 (95%CI 1.1-26.2), p = 0.037]

Table 1. Heatmap of correlation between Patient Global Assesment.

	FACIT-F(FS)	Patient Health Questionnaire 9 (PHQ9)	ROS60	VAS Fatigue (0-10)	DAS28 ESR	DAS28 CRP	SDAI	CDAI	28TJC	28SJC	PGA	PhGA	CRP	ESR
PGA	0,517	0,616**	0,423**	0,604**	0,672**	0,798**	0,834**	0,842**	0,627**	0,390**	1,000	0,732**	0,269**	0,112**
PhGA	-0,428	0,477**	0,317**	0,451**	0,668**	0,794**	0,875**	0,900**	0,641**	0,656**	0,732**	1,000	0,249**	0,163**

(PGA); Physician Global Assessment (PhGA) and fatigue, depression, clinical evaluation and disease activity indices. Pearson`s correlations.Data shonw are Rho value. ** p value<0.001.

Table 1.- Characteristics of patients at diagnosis of RA-ILD and evolution of ILD.

Variables	Clinical RA-ILD (n=32)	Subclinical RA-ILD (n=18)	*p-value*
Age at RA diagnosis (years), mean (SD)	48.8 (13.7)	56.5 (11.4)	**0.042**
Age at ILD diagnosis (years), mean (SD)	61.7 (11.2)	65.2 (11.7)	0.311
Sex (male), n (%)	13 (40.6))	11 (61.1)	0.164
Tobacco, n (%)	18 (60)	13 (81.2)	0.143
RA disease duration (years), mean (SD)	19.7 (11)	12.2 (7.5)	**<0.001**
Time from RA diagnosis to ILD (years), mean (SD)	16.3 (9.6)	8.7 (7.4)	**<0.001**
RA diagnosis delay (years), mean (SD)	1.3 (2.5)	1.4 (2.5)	0.952
Positive RF, n (%)	29 (90.6)	17 (94.4)	0.632
RF titers, mean (SD)	247.3 (244)	339.2 (390)	0.338
Positive ACPA, n (%)	32 (100)	16 (88.9)	0.054
ACPA titers, mean (SD)	395.6 (643)	468 (698)	0.740
Erosions, n (%)	10 (31.2)	5 (27.8)	0.797
Rheumatoid nodules, n (%)	6 (18.8)	3 (16.7)	0.854
Secondary S. Sjogren, n (%)	2 (6.2)	0	0.279
Osteoporosis, n (%)	10 (31.2)	3 (16.7)	0.259
Cumulative DAS28-VSG, mean (SD)	3.4 (1.1)	3.3 (1.2)	0.949
Cumulative ESR, n (%)	26.6 (14.7)	19.1 (13.4)	0.097
Cumulative CRP, n (%)	10.4 (8.9)	13.5 (9.8)	0.299
DMARDs, n (%)	23 (71.9)	16 (88.9)	0.163
Methotrexate, n (%)	13 (40.6)	12 (66.7)	0.077
Leflunomide, n (%)	9 (28.1)	5 (27.8)	0.979
Hydroxichloroquine, n (%)	4 (12.5)	6 (33.3)	0.077
Sulfasalazine, n (%)	1 (3.1)	0	0.448
bDMARD, n (%)	9 (28.1)	3 (16.7)	0.362
Rituximab, n (%)	1 (3.1)	0	0.448
Abatacept, n (%)	2 (6.2)	1 (5.6)	0.920
Anti-TNFα, n (%)	6 (18.8)	2 (11.1)	0.478
Glucocorticoids, n (%)	20 (69)	12 (66.7)	0.869
Glucocorticoids dose, mean (SD)	4.6 (2.2)	6.6 (4.3)	0.153
HRCT pattern			0.407
UIP, n (%)	9 (28.1)	4 (22.2)	
UIP Probable, n (%)	8 (25)	1 (5.6)	
Indeterminate UIP, n (%)	9 (28.1)	9 (50)	
NSIP, n (%)	4 (12.5)	3 (16.7)	
Others, n (%)	2 (6.2)	1 (5.6)	
DLCO-SB, mean (SD)	66.1 (17.9)	80.3 (12.7)	**0.013**
FVC, mean (SD)	86.4 (19.3)	90.6 (15.6)	0.461
FVC<80%, n (%)	10 (40)	5 (38.5)	0.926
ILD evolution at the end of the follow-up (total)			
Improvement, n (%)	8 (25)	4 (22.2)	0.896
Stabilization, n (%)	11 (34.4)	8 (44.4)	
Progression, n (%)	10 (31.2)	5 (27.8)	
Death, n (%)	3 (9.4)	1 (5.5)	

Conclusion: In our cohort, the prevalence of subclinical ILD was high (36%). Although RFT at diagnosis of ILD, specifically DLCO levels, were higher in subclinical ILD than in clinical ILD, progression at the end of follow-up was the same in both groups. The UIP pattern was independently associated with progression. Therefore, taking into account that ILD is one of the main causes of mortality in our patients, we must actively search for this condition in order to treat it early and improve the prognosis.

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Disclosure of Interests: None Declared.

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AB0370

DISORDERS OF PERIPHERAL LYMPHOCYTE SUBSETS IN RHEUMATOID ARTHRITIS PATIENTS COMPLICATED WITH HASHIMOTO'S THYROIDITIS

Keywords: Comorbidities, Rheumatoid arthritis, Descriptive Studies

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Background: Hashimoto's thyroiditis (HT) is an organ-specific autoimmune disease that is not rare in RA. Hypothyroidism caused by HT can affect the prognosis and quality of life in patients with RA [1]. Many studies showed that immune cells play a critical role in HT [2-3]. However, the alterations of lymphocyte subsets in RA patients with HT are unclear.

Objectives: This study aimed to assess the absolute numbers and proportions of peripheral lymphocyte subsets in RA with HT and investigate the clinical significance.

Methods: A total of 1636 RA patients and 54 gender- and age-matched healthy controls (HCs) were enrolled in this study. Patients were divided into RA-non-HT and RA-HT groups according to the thyroid peroxidase antibody (TPOAb) and thyroid globulin antibody (TgAb). Peripheral lymphocyte subsets of all participants were assessed by flow cytometry. All clinical and laboratory data were analyzed by SPSS 23.0.

Results: Among 30 (1.83%) RA-HT patients, there were more female (P=0.005), suggesting female was more susceptible to developing HT (Figure 1A). In addition, there were higher levels of erythrocyte sedimentation rate (ESR) (P=0.045) and C-reactive protein (CRP) (P=0.042) than those in RA-non-HT (Figure 1B-C). Compared with those of HCs and RA-non-HT, the level of circulating Th17 in RA-HT patients was significantly increased (P<0.05), while those of Tregs decreased (P<0.05), leading to a higher ratio of Th17/Treg (P<0.01). Notably, the level of B cells and Th1 cells, as well as the Th1/Th2 ratio, increased in the RA-HT compared with those of the RA-non-HT (P<0.05) (Figure 1D-F).

Conclusion: The occurrence of RA-HT is closely related to female patients with high disease activity. Disorders of lymphocyte subsets, especially Th17/Treg imbalance, may contribute to HT in RA, which deserves more clinical attention.

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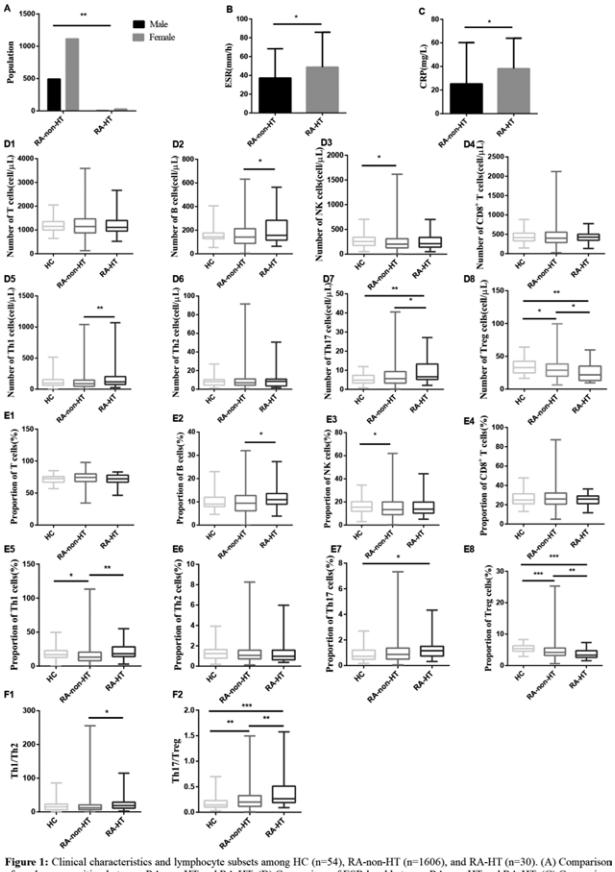


Figure 1: Clinical characteristics and lymphocyte subsets among HC (n=54), RA-non-HT (n=1606), and RA-HT (n=30). (A) Comparison of gender composition between RA-non-HT and RA-HT. (B) Comparison of ESR level between RA-non-HT and RA-HT. (C) Comparison of CRP level between RA-non-HT and RA-HT. (D) Comparison of absolute numbers of peripheral lymphocyte subsets (T、B、NK、CD8+T、Th1、Th2、Th17、Treg) among HC, RA-non-HT and RA-HT. (E) Comparison of proportion of peripheral lymphocyte subsets (T、B、NK、CD8+T、Th1、Th2、Th17、Treg) among HC, RA-non-HT, and RA-HT. (F) Comparison of the ratio of Th1/Th2 and Th17/Treg in peripheral blood among HC, RA-non-HT, and RA-HT. *P<0.05，**P<0.01，***P<0.001.

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Disclosure of Interests: None Declared.

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Rheumatoid arthritis - comorbidity and clinical aspects

AB0371 PREVALENCE OF CACHEXIA IN A POPULATION OF MOROCCAN WOMEN WITH RHEUMATOID ARTHRITIS

Keywords: Diet and Nutrition, Descriptive Studies

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Background: Prevalence of cachexia in a population of Moroccan women with rheumatoid arthritis.
Objectives: The objective of our study is to assess body composition in women with rheumatoid arthritis (RA) compared to healthy controls.
Methods: We conducted a case-control study of 112 female patients with rheumatoid arthritis according to ACR/EULAR 2010 Rheumatoid Arthritis Classification Criteria; and 224 healthy women of the same age. Body composition and bone mineral density (BMD) results were obtained by Dual-Energy X-Ray Absorptiometry (DXA). Rheumatoid cachexia (RC) was defined as a Lean mass index (LMI) below the 10th percentile and a Fat mass index (FMI) above the 25th percentile compared with the control group. We performed a comparison between RA patients and healthy controls and then performed multiple regression looking for factors associated with rheumatoid cachexia.
Results: The prevalence of rheumatoid cachexia was 42.85% while the mean body mass index (BMI) was the same in both groups. RA patients had higher fat mass and lower lean mass compared with healthy controls. In our population, 78.60% of patients were on methotrexate and 12.50% on TNF inhibitor. Comparison between patients with and without CR showed that patients with CR have high disease activity, with the presence of more bone erosions. Regression showed that CR was significantly associated with bone erosions and disease activity (OR at 33.31 (8.42- 131.70) and 8.98 (1.64 - 49.20) respectively) This was independent of age, erythrocyte sedimentation rate, C-reactive protein, duration of disease, cumulative steroid dose, and use of conventional or biologic background therapies.
Conclusion: Our study showed that nearly half of our RA patients have CR even with high BMI. CR in our work is associated with the presence of high disease activity, and the presence of bone erosions.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0372 THE IMPACT OF BODY MASS INDEX ON BONE MINERAL DENSITY IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis

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Background: It has long been thought that a higher body mass index is protective against osteoporosis. However, recent studies showed an increase in fracture risk in obese individuals.
Objectives: To study the impact of body mass index (BMI) on bone mineral density (BMD) during rheumatoid arthritis (RA).
Methods: Retrospective study including 260 RA patients meeting the ACR/EULAR 2010 criteria. We collected demographic, clinical, biological, and bone densitometric data from patients.
Results: The mean age was 49.91 ± 12.97 years. The sex ratio F/H was 6.6. The mean DAS28-VS was 5.32 ± 1.35. According to the DAS28-VS, 60.7% of the patients were high activity. The mean BMI was 26.26 ± 4.83 Kg/m². 21.9% of patients were obese, 31.5% were overweight and 2.3% were underweight. The mean BMD was 0.856 ± 0.200 g/cm² at the femoral neck and 0.950 ± 0.218 g/cm² at the lumbar spine. The mean T-SCORE was -1.41 ± 1.48 at the femoral neck and -1.90 ± 1.58 at the lumbar spine. Osteoporosis at one of the two sites was found in 38.4% of patients. Eleven patients (4.8%) had a severe fracture and 6 patients (2.6%) a non-severe fracture. A negative correlation was found between BMI and the presence of osteoporosis at one of the two sites (r=-0.138; p=0.04). BMI was also correlated with T-Score and BMD at the lumbar spine (r=0.196; p=0.007 and r=0.278; p=0.001 respectively). No correlation was found between BMI and T-Score and BMD at the femoral neck level as well as fracture occurrence.
Conclusion: In our study, BMI correlated with BMD and T-SCORE at the lumbar spine, and negatively correlated with the presence of osteoporosis.
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AB0373 DEPRESSION IN RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY FROM A TERTIARY CARE HOSPITAL IN NORTH INDIA.

Keywords: Rheumatoid arthritis, Descriptive Studies, Mental health

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Background: Rheumatoid arthritis(RA) is a chronic inflammatory polyarthritis, with deformities associated with poor functional outcome. Psychiatric comorbidities are common among them, contributing to poor outcome.
Objectives: This study was aimed at determining prevalence of depression in RA and its association with disease severity.
Methods: This is a cross-sectional study carried out in the OPD/IPD of Rheumatology in a tertiary care hospital in India. This study recruited 272 patients classified as RA, fulfilling 2010 ACR/EULAR criteria, with minimum duration of illness of at least 1 year. Patients with prior psychiatric illness were excluded. Informed consent was taken from all participating patients, after institute ethical clearance. RA disease activity was measured using DAS28 ESR, and these patients were screened for depression with PHQ-2 questionnaire.**[1]** Patients with depression were further assessed with Depression, Anxiety and Stress Scale (DASS) for depression severity.**[2]** The functional status was assessed with Health Assessment Questionnaire –Disability Index(HAQ-DI). Data were interpreted by descriptive statistics, and correlation assessed using Spearman correlation coefficient. Regression analysis was used to find odds of significant variables associated with depression.
Results: Twenty-three percent of these patients had depression according to PHQ-2 screen. Forty-four (69.8%) of these had depression on further assessment using DASS questionnaire. The median DAS-28 in mild, moderate, severe and extremely severe depression groups were 4.6, 4.9, 6.4 and 5.3, respectively. There was a significant difference between the 5 groups in terms of DAS-28 ($X^2 = 42.209$, $p = <0.001$), with the median DAS-28 being highest in severe depression group. It had a strong association with DASS depression score and with significant p value of <0.001. There was a weak positive correlation between DAS-28 and DASS depression score, though this correlation was not statistically significant (rho = 0.18, p = 0.167). With further regression analysis, it was clear that, TJC, SJC, and ESR, were significantly associated with depression. All of these parameters had an odds ratio of >1, indicating that if each of them increased, odds of having depression would significantly increase.
Conclusion: Depression, though very common, is yet an underestimated co-morbidity in RA and contributes to their functional impairment/ morbidity. RA patients with high TJC, SJC, ESR and disease activity were found to have depression of more severity, which favors the inflammatory hypothesis of depression.**[3]** Depression, is indeed an under-estimated yet significant comorbidity in patients with RA. This is often missed or over looked by rheumatologists/ clinicians. Early identification with subsequent referral to concerned specialty will definitely improve functional outcomes.
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Box and whisker plot shows mean DAS28 score in different groups according to DASS category.

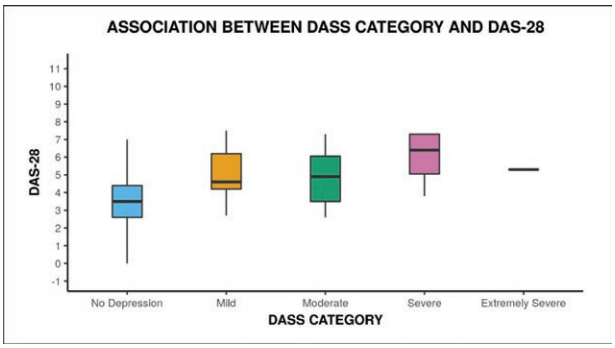


Figure 1.

Table showing characteristics of RA patients in this study

n=272	Mean (SD)
Age (yrs)	47.77 (11.55)
Gender	
Male	50 (18.3%)
Female	223 (81.7%)
Duration of illness (mon)	60 (84)
RF (+)	208 (76.2%)
ACPA (+)	219 (80.6%)
DAS28 ESR	3.87 (1.42)
HAQ-DI (max score of 3)	0.58 (0.70)
Depression by PHQ-2	63(23.1%)
DASS (on n=63)	
Depression	44(16.1%)
Mild	16 (5.9%)
Moderate	15 (5.5%)
Severe	12 (4.4%)
Extremely severe	1 (0.4%)

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0374

A STUDY OF MYOSTATIN LEVELS IN A GREEK COHORT OF POST-MENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS

Keywords: Osteoporosis, Rheumatoid arthritis

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Background: Myostatin is expressed in skeletal muscles and exerts a negative feedback in myogenesis. Chronic inflammation has been associated with increased serum myostatin levels (Baig MH, Front Physiol. 2022).
Objectives: The calculation of serum myostatin levels in patients with rheumatoid arthritis (RA) and association with disease parameters.
Methods: A cross-sectional study of 30 post-menopausal women with RA, classified according to the 1987 ACR criteria. Blood samples were collected and inflammatory markers (erythrocyte sedimentation rate, ESR, and C-reactive protein, CRP) were calculated. Serum myostatin levels were assessed using the ELISA method. Seropositive disease was defined according to a positive history of antibodies against rheumatoid factor (RF) or against citrullinated proteins (ACPA). Disease activity and patient functionality were expressed by using the DAS28 (ESR) and the HAQ-DI scores respectively.
Results: In our cohort, 47% (n=14) had seropositive disease. Mean values for ESR, CRP, DAS28 (ESR) and HAQ-DI were 29 ± 20 mm, 1.6 ± 2.6 mg/dl, 3.9 ± 1.7 and 0.9 ± 0.6 respectively. The mean serum myostatin levels were 5.9 ± 1.3 μg/ml. According to the DAS28 (ESR) score, 17% (n=5) patients were in disease remission, 20% (n=6) had low disease activity, 40% (n=12) had medium disease activity and 23% (n=8) had high disease activity. Serum myostatin was not associated with disease activity (p=0.32), patient functionality (p=0.08) or the inflammatory burden attributed to active disease (p=0.67 for ESR and p=0.83 for CRP). Seropositive disease did not correlate with serum myostatin levels (p=0.08).
Conclusion: In post-menopausal women with rheumatoid arthritis, serum myostatin levels are independent of disease activity, patient functionality, inflammatory burden, RF or ACPA seropositivity. Except for inflammation per se, other disease parameters associated with RA influence the regulation of myostatin.
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Table 1. Association of serum myostatin with disease parameters in RA patients (statistical significance: p<0.05)

Parameter	Coefficient	p
Age	0.084	0.658
BMI	-0.156	0.412
Disease duration	0.131	0.492
Seropositive disease	-0.809	0.084
ESR	-0.081	0.672
CRP	0.041	0.830
DAS28 (ESR)	-0.190	0.315
HAQ-DI	-0.322	0.083

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0375

DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS (D2T-RA): CLINICAL ISSUES AT EARLY STAGES OF DISEASE

Keywords: Rheumatoid arthritis, Disease-modifying Drugs (DMARDs), Epidemiology

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Background: Most studies on difficult-to-treat rheumatoid arthritis (D2T RA) have focused on established RA.
Objectives: To analyze whether disease activity in the early stages of RA could influence progression to a D2T RA under real-life conditions. Other clinical and treatment-related factors were also analyzed.
Methods: A longitudinal multicenter study of RA patients was conducted from 2009 to 2018. Patients were followed up until January 2021. D2T RA was defined based on EULAR criteria (treatment failure, signs suggestive of currently active/progressive disease, and management being perceived as problematic by the rheumatologist and/or patient). The main variable was disease activity in the early stages. The covariates were sociodemographic, clinical, and treatment-related factors. We ran a multivariable logistic regression analysis to investigate risk factors associated with progression to D2T RA.
Results: The study population comprised 631 patients and 35 (5.87%) developed D2T RA. At the time of diagnosis, the D2T RA group were younger, with a higher disability, DAS28 score, tender joint count and pain scores. In our final model, DAS28 was not statistically significantly associated with D2T RA. No differences were found between groups for therapy. Disability was independently associated with D2T RA (OR: 1.89; p=0.01).
Conclusion: In this cohort of patients newly diagnosed with RA, our results do not allow us to prove the influence of active disease according to DAS28. However, we did find that younger patients and those with elevated initial disability scores are more likely to develop D2T RA regardless of other factors.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1529

AB0376

CARDIOVASCULAR RISK STRATIFICATION ACCORDING TO SERUM NON-HDL CHOLESTEROL LEVELS IN PATIENTS WITH RECENTLY DIAGNOSED RHEUMATOID ARTHRITIS.

Keywords: Biomarkers, Comorbidities, Rheumatoid arthritis

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Background: It is estimated that rheumatoid arthritis (RA) increases the risk of cardiovascular disease (CVD) by 50% compared to the general population [1,2]. Non-HDL cholesterol (non-HDL CT) has become an innovative marker of cardiovascular risk (CVR). According to the recommendations of the ESC of 2022 [2], patients with RA start from an intermediate CVR and recommend non-HDL TC levels <130mg/dL.
Objectives: To evaluate long-term risk of CVD according to nonHDL CT levels in a cohort of patients with recently diagnosed RA who started biological therapy and describe its characteristics.
Methods: 71 patients with RA under biological treatment were reviewed. Demographic, clinical, and analytical data were obtained at the time of diagnosis. To estimate the risk of CVD in the long term, we applied the model developed by Brunner F. J. et al. [3] -Figure 1-. Based on this, the patients were stratified into 5 CVR groups according to the non-HDL CT and grouped into three age ranges. Statistical analysis was carried out using IBM-SPSS Statistics version 26.
Results: The demographic, clinical, laboratory characteristics and CVR groups are indicated in Table 1. Regarding the mean age according to the CVR group: in the 8 patients of group 1 it was 38.13 ± 15.28 years - 7 with age < 45 years and one > 60 years -, in group 2 it was 42.93 ± 11.76 years - 17 patients < 45 years, 10 between 45 and 59 years and 2 ≥ 60 years -, in the 31 patients of group 3 it was 51.45 ± 11.49 years - 8 < 45 years, 15 between 45-59 years and 8 ≥ 60 years -. In the 2 patients in group 4 it was 52.5 years (45-59) and the patient in group 5 was 36 years old at diagnosis. No significant correlations were found between CRP, ESR, RF, ACPAs levels and presence of radiographic erosions with nonHDL CT values. Significant differences (p value < 0.01) were observed between the youngest individuals (age < 45 years) in groups 1 and 2 with respect to individuals older than 60 years in risk groups 3 or 4. The application of the current model -Figure 1- estimated a mean probability of CVD of 9.7% at 75 years with a reduction to 3.54% after a 50% decrease in non-HDL TC. A single fatal cardiovascular event was recorded in an obese, hypertensive, and diabetic man, classified in risk group 3.
Conclusion: In our cohort of patients with new-onset RA, the majority (46%) were classified as CVR group 3 (nonHDL CT 145-184 mg/dL), despite approximately 50% being <45 years of age. Exposure from an early age to a moderate increase in non-HDL CT induces an increase in long-term CVR, not captured by the 10-year CVR estimate. For all this, emphasis should be placed on the establishment of measures to reduce CVR guided by non-HDL CT levels in patients diagnosed with RA.

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[2] https://doi.org/10.1016/j.rec.2022.04.003
[3] https://doi.org/10.1016/s0140-6736(19)32519-x

Table 1.

			N	%
DEMOGRAPHIC	**Total number of patients**		71	
	Sex	M	11	15.5%
		W	60	84.5%
	Median age at diagnosis		46,28 ± 12,73	
CLINICAL	**Radiographic erosions**		24	33.8%
	Corticosteroid therapy		45	63.38%
LABORATORY	**RF (+)**		47	66.19%
	ACPA (+)		46	64.78%
			Mean	**Median**
	CRP		13.35 ± 19.06	6.74 IQR 15.90
	ESR		25.06 35 ± 16.56	20 IQR 17.00
	Total CT		203	
	Non-HDL CT		144	
	Colesterol LDL		121.5	
			N	**%**
CVR	**Previous CVD**		0	
	Statins		2	2.81%
	Active smoking		21	29.57%
	Hypertension		13	18.30%
	IMC > 30		15	21.12%
	Diabetes		2	2.81%
CVR group according to nonHDL CT	**1 (<100 mg/dL)**		8	11.3%
	2 (100-144 mg/dL)		29	40.8%
	3 (145-184 mg/dL)		31	43.7%
	4 (185-219 mg/dL)		2	2.8%
	5 (≥ 220 mg/dL)		1	1.4%

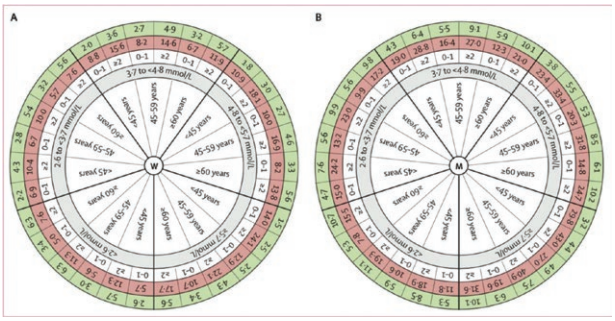


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1705

AB0377

CHARACTERISTICS OF BLOOD TEST RESULTS IN D2T RA BEFORE INITIATING DMARDS TREATMENT: HIGHER IFN AND LESS IL-6 INVOLVEMENT WERE PRESUMED BY PROPENSITY SCORE MATCHING ANALYSIS

Keywords: Rheumatoid arthritis, Biomarkers

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Background: Difficult-to-treat rheumatoid arthritis (D2T RA) is a new concept of RA patients who do not achieve remission despite several types of treatment. It remains to be elucidated what makes the clinical differences between D2T RA and non-D2T RA.
Objectives: To analyze blood test results of D2T RA patients and non-D2T RA patients before initiating treatment to see if there are differences in their trends and characteristics.
Methods: We conducted a retrospective, observational cohort study using blood tests, including patients diagnosed with RA who attended our institute. The patients were divided into two groups; those who satisfied EULAR definition of D2T were included as D2T-RA, and the others who did not meet the definition after at least 2 years of treatment were included as non-D2T RA patients. To eliminate the influence of treatment on blood test data and disease activity, only patients whose blood test data existed prior to starting treatment with disease modifying antirheumatic drugs (DMARDs) were picked from both groups. The two groups were then matched 1:1 using propensity scores adjusted for gender, age, duration of RA disease, BMI, smoking habits, and DAS28-ESR. Comparisons were made between these two adjusted groups for each blood test item using an independent-samples t-test. SPSS statistical software was used.
Results: Ninety-four RA patients (mean age 60.3±12.6 years, 74% female) were included, 23 (mean age 55.4±13.2 years, 83% female) belonged to D2T RA and 71 (mean age 61.8±12.1 years, 72% female) to non-D2T RA. Of these, 13 cases of D2T RA and 2 cases of non-D2T RA were excluded due to lack of blood test data before starting DMARDs therapy. D2T RA patients were 57.6 ± 11.1 years old (86% female) and non-D2T RA patients were 57.0 ± 10.1 years old (100% female). In D2T RA, mean corpuscular volume (MCV: D2T vs non-D2T = 95.6±3.8 vs 85.6±3.9, p<0.001), mean corpuscular hemoglobin (MCH: 32.0±1.7 vs 28.7±1.7, p=0.003), serum transferrin saturation (TSAT) ratio (Fe*100/TIBC: 32.3±7.2 vs 19.3±9.6, p=0.020) and lactate dehydrogenase (LDH: 203±33U/L vs 164±16U/L, p=0.026) were significantly higher. On the other hand, unbound iron binding capacity (UIBC: 184±42 vs 253±35, p=0.007) was significantly lower in D2T RA. Although it was not reaching statistical significance, lower lymphocyte count (1068±304/μ vs 1816±867/μ, p=0.052), fewer red blood cell (RBC: 4.03±0.34*10^6/μ vs 4.45±0.51*10^6/μL, p=0.096) and higher neutrophil ratio (76.9±8.2% vs 66.5±10.7%, p=0.065) were observed in D2T RA.
Conclusion: In a comparison of blood test results before initiating treatment, the differences between D2T and non-D2T cases were mainly related to iron metabolism and white blood cell differential. Patients with non-D2T RA had significantly lower

TSAT than patients with D2T RA, with a trend toward having a microcytic hypochromic anemia. This reminds us of the involvement of hepcidin and may suggest that Interleukin 6 (IL-6) is involved in the pathogenesis of non-D2T RA but it is less involved in that of D2T RA 1). The hypothesis explains the clinical features of resistance to treatment with IL-6 inhibitors in patients with D2T-RA. Furthermore, a clear lymphocyte count decrease was observed in D2T RA cases, suggesting a strong IFN signature 2). Interestingly, D2T RA cases showed a greater tendency toward anemia than non-D2T RA cases, with a tendency toward macrocytic rather than microcytic anemia. A trend of increased neutrophil ratio was also observed in D2T RA cases. On the other hand, there were no significant differences in immunological background, such as rheumatoid factor (RF) nor anti-citrullinated protein antibodies (ACPA).

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AB0378 RELATIONSHIP BETWEEN EGO STATE, DISEASE ACTIVITY, AND ACTIVITY OF DAILY LIVING IN RHEUMATOID ARTHRITIS PATIENTS: USING EGOGRAMS

Keywords: Rheumatoid arthritis

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Background: Although there have been several previous reports on the personality patterns of rheumatoid arthritis (RA) patients and their habits and tendencies in thinking, feeling, and behaving when interacting with others (ego state), there have been no new research reports in the last ten years. During this period, the treatment outcome of RA has improved, and changes in ego states are expected.
Objectives: This study investigated the relationship between ego state, disease activity, and activity of daily living (ADL) in RA patients.
Methods: A total of 133 RA patients attending outpatient clinics at Showa University Hospital and Showa University Northern Yokohama Hospital who agreed to participate in this study were included. The patient background had age, gender, type of DMARDs, and prednisolone use; the simplified disease activity index (SDAI) was used to assess RA disease activity, and the health assessment questionnaire (HAQ) was to sed determine ADL. The University of Tokyo Egogram (TEG-II) was to sed determine ego status; the TEG-II consists of pattern categories and types from critical parental ego (CP), nurturing parental ego (NP), adult ego (A), free child ego (FC), and submissive child ego (AC). The scores for each item were evaluated, and associations with SDAI, HAQ, and gender were examined.
Results: The AC was the highest (15.0 points), and the CP and A were the lowest (6.0 points each) on the TEG-II for all the subject patients. The pattern classification showed that the AC-dominant type was the most common (45 patients, 33.8%), with no significant difference in HAQ remission (<0.5) and non-remission, low disease activity (SDAI≤11) and SDAI>11, nor in gender.
Conclusion: In previous reports, TEG-II in RA patients was predominantly NP, but in the present study, AC was predominant. The behavioral pattern was inferred to be cooperative, honest, able to listen to other's opinions, and patient, but loose, lax, lack discipline, inconsistent in thought and action, and poor planning. The results may be influenced by the improvement of rheumatoid arthritis performance and the decrease in disease activity.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0379 EVALUATION OF BODY COMPOSITION IN RHEUMATOID ARTHRITIS PATIENTS WITH HIGH CUMULATIVE INFLAMMATORY ACTIVITY.

Keywords: Sarcopenia, Comorbidities, Rheumatoid arthritis

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Background: Previous studies have reported a higher prevalence of sarcopenia in patients with systemic diseases. Thus, it is believed that the inflammation may contribute to the onset of sarcopenia.
Objectives: To study whether there is an association between high sustained inflammatory activity and with a major frequency of sarcopenia and others alterations in body composition in rheumatoid arthritis (RA) patients.
Methods: We conducted a controlled cross-sectional observational study of a prospective cohort of RA patients. The cases were RA patients with mean moderate-high inflammatory activity during the disease course who were selected to start first biologic treatment. The controls were subjects without inflammatory disease, matched for sex and age with cases. All patients were recruited consecutively from a rheumatology clinic. Body composition was measured using dual-energy x-ray absorptiometry. The main variables were sarcopenia (RSMI <5.5 kg/m^2 for women and <7.26 kg/m^2 for men), fat mass (Kg) and body mass index (BMI). Other variables included average inflammatory activity by DAS28-ESR since diagnosis, epidemiological characteristics, lifestyles (physical activity and adherence to the Mediterranean diet), comorbidities and treatment. Statistical analysis included descriptive analysis, bivariate and two models of multivariate analysis.
Results: A total of 62 subjects were included, 32 with RA and 32 healthy controls. Most of them were female (84.4%) with a mean (DS) age of 57.1 (10.8) years. The main baseline characteristics of subjects are shown in Table 1. Compared with controls, RA patients had higher prevalence of sarcopenia (7 [21.9%] vs 2 [6.3%]; p=0.074), a higher mean (DS) of fat mass (31.8 [7.4] vs 27.1 [13.8]; p=0.129) and BMI (28.0 [5.2] vs 26.6 [4.4]; p = 0.278). The RA patients with sarcopenia, compared with the other RA patients, had a higher frequency of erosions (85.7% vs 32.0%; p=0.011), dyslipidemia (71.4% vs 16%; p =0.100), higher mean (DS) of age (64.8 [10.2] vs 55.9 [10.3]; p = 0.021), DAS28-ESR (4.5 [0.7] vs 3.7 [0.8]; p = 0.031), average of DAS28-ESR (1.6 [0.3] vs 1.0 [0.5]; p = 0.024) and ESR (33.0 [18.1] vs 15.8 [10.7]; p = 0.003). The multivariate analysis showed the factors associated independently with sarcopenia in RA patients were age (OR [CI 95%], 1.125 [1.002-1.262]; p=0.045), and the average of DAS28-ESR (OR [CI 95%], 2.761 [1.843-10.430]; p=0.048) (R2= 0.173).
Conclusion: Our preliminary data show a significant trend to a higher prevalence of sarcopenia in RA patients with moderate to high inflammatory activity. In addition, RA patients with sarcopenia have higher mean of age and inflammatory activity, compared to the rest of the patients.

Table 1. Baseline characteristics of 32 RA patients and 32 controls.

VARIABLE	RA N= 32	CONTROL N = 32	P-value
Sex, female, n (%)	27 (84.4)	27 (84.4)	1.000
Age in years, mean (SD)	57.9 (10.7)	56.4 (10.8)	0.577
Smokers, n (%)	17 (53.1)	9 (28.1)	0.042
Obesity, n (%)	11 (34.4)	8 (25.0)	0.412
Dislipidemia, n (%)	23 (71.9)	10 (31.1)	0.784
Arterial Hypertension, n (%)	9 (28.1)	10 (31.1)	0.492
Diabetes mellitus, n (%)	4 (12.5)	3 (9.4)	0.689
Time since diagnosis of RA, months, median (IQR)	83.6 (34.1-191.0)		
Diagnostic delay, median (IQR), months	8.1 (4.7-12.6)		
Erosions, n (%)	14 (43,8)		
Rheumatoid factor >10 U/ml, n (%)	28 (87.5)	0 (0.0)	<0.001
ACPA > 20 U//ml, n (%)	27 (84.4)	0 (0.0)	<0.001
DAS28-ESR, mean (SD)	3.9 (0.8)		
HAQ, mean (SD)	1.1 (0.5)		
Methotrexate, n (%)	22 (68.8)		
Hydroxychloroquine, n (%)	5 (15.6)		
Leflunomide, n (%)	2 (6.3)		
Sulfasalazine, n (%)	2 (6.3)		

Abbreviation; SD: standard deviation; IQR interquartile range; ACPA: anti-citrullinated C-peptide antibodies; DAS28-VSG: 28-joint Disease Activity Score; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire.

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Disclosure of Interests: None Declared.

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AB0380 PREVALENCE OF SLEEP-RELATED BREATHING DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, AND PERIPHERAL SPONDYLOARTHRITIS

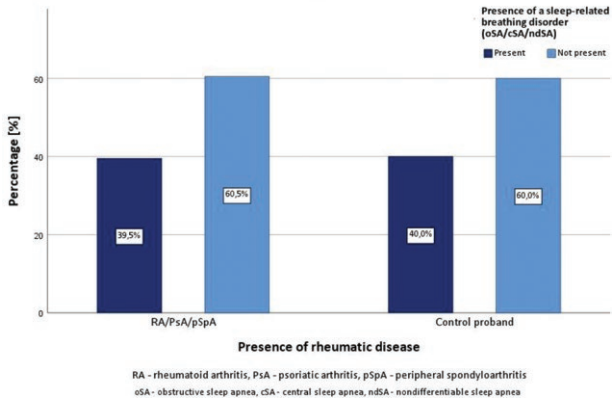
Keywords: Spondyloarthritis, Rheumatoid arthritis, Psoriatic arthritis

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Background: Quality of life in patients suffering from rheumatological diseases is negatively affected by sleep disturbances, a frequently observed phenomenon. In rheumatoid arthritis, the prevalence of sleep disturbances ranges from about 50% to 70% [1]. The non-restorative sleep patterns result in excessive daytime sleepiness, reduced physical and mental performance, depression, and concentration disorders, as well as increased cardiovascular morbidity and risk of accidents [2].
Objectives: To investigate the prevalence of sleep-related breathing disorders (SRBD), including obstructive and central sleep apnea (oSA, cSA), in patients with rheumatoid arthritis, psoriatic arthritis, and peripheral spondyloarthritis and to examine the relation between deterioration in sleep quality and selected clinical parameters.
Methods: This cross-sectional assessment consisted of a diagnostic workup, encompassing a questionnaire regarding sociodemographic characteristics, the assessment of arthritis disease activity using the Disease Activity Score (DAS-28CRP), and the evaluation of daytime sleepiness using the Epworth Sleepiness Scale (ESS). Cardiorespiratory polygraphy (RPG) was performed to detect SRBD.
Results: A total of 54 patients (26 RA, 24 PsA, 4 pSpA) and 28 age- and gender-matched controls were recruited. The prevalence of sleep apnea in this study accounted for 39.7%, with a more than twofold higher presence of oSA than cSA. However, sleep apnea was diagnosed in approximately equal proportions of arthritis patients (39.5%) and controls (40.0%) (Figure 1). Male gender (p=0.013) and an increased age of approximately 55 years (p<0.001) were found to be significant risk factors for the presence of sleep apnea. Furthermore, differences, but without statistical significance, were found between subjects with sleep apnea and subjects without sleep apnea with respect to body mass index (p=0.085), positive smoking status (p=0.191), and arthritis disease activity as assessed by DAS28CRP (p=0.275). 42.3% of subjects affected by oSA or cSA showed excessive daytime sleepiness rated by ESS (p=0.024).
Conclusion: Despite the fact that the prevalence of SRBD in arthritis patients and controls is the same, physicians should be especially cautious of male patients over the age of 55. ESS score assessment helps to estimate the clinical risk. An early diagnosis of sleep apnea in arthritis patients may improve physical and psychological quality of life.
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Figure 1: Presence of sleep-related breathing disorders in arthritis patients and controls



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Disclosure of Interests: None Declared.
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AB0381 **TREATMENT EXPECTATIONS OF PATIENTS WITH RHEUMATOID ARTHRITIS BEFORE STARTING METHOTREXATE**

Keywords: Rheumatoid arthritis

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Background: Although the long-term efficacy, tolerability, and safety of methotrexate (MTX) in patients with rheumatoid arthritis (RA) are well documented, the clinical response and incidence of adverse events (AE) vary. Data on adherence to MTX in RA patients vary between retention rate of 35% to 80% in 5 years. In addition to aspects of safety, important determinants for continuing MTX therapy are patient-associated factors including individual treatment preferences and expectations.
Objectives: This study investigated treatment expectations in RA patients who were about to start therapy with MTX, and aim to identify variables associated with discontinuation of MTX.
Methods: Consecutive patients with RA who were about to start MTX were prospectively included after informed consent. Treatment expectations, medication-related beliefs and AE, treatment satisfaction and health–related quality of life were assessed using the generic rating scale for previous experiences, expectations and effects of treatment (G-EEE), the general assessment of side effects (GASE), the beliefs about medicines questionnaire (BMQ), the treatment satisfaction questionnaire for medication (TSQM) and the EuroQol-5 dimensions (EQ-5D) before treatment initiation (T0), and after 3 months (T1). Treatment adherence to MTX was checked at month 6 (T2). Associations treatment expectations and adherence to MTX were explored by regression analyses.
Results: A total of n=100 consecutive RA patients before starting MTX treatment were included (table 1). A history of inadequate response to sulfasalazine was determined in n=6 (6%) and to hydroxychloroquine in n=1 patient, respectively. At T0, patients perceived the need for treatment with MTX as high, and they were only moderately concerned regarding potential adverse events of this therapy. Treatment expectations regarding the decrease of pain levels and development of adverse events did not differ much between T0 and T1, when disease activity had significantly decreased and physical function increased. MTX was withdrawn in 3 out of 59 patients (5.0%) and in 13 out of 64 patients (20.3%) assessed at T1 and T2, respectively, with a mean of 16.0 (5.9) weeks after treatment initiation. The most frequent reason for discontinuation of MTX was the occurrence of adverse events (n=12) followed by infections or malignancies (both n=2). There was no significant relationship between patients' treatment expectations reported at T0 and their adherence to MTX at T2.
Conclusion: In this study, we found no evidence for the assumption that patients' expectations before the start of MTX did substantially influence adherence to treatment.

Table 1. Patients and disease characteristics

Variables*	T0 Treatment initiation (n=100)	T1 (n=59)
Age, in years	59.1 (11.5)	
Gender female, n (%)	55 (55%)	
Education, university level, n (%)	17 (17%)	
Employment, n (%)	59 (59%)	
Time (months) since RA symptoms	11.9 (25.3)	
BMI, kg/m^2,	25.6 (4.2)	
No. of patients using GC n (%)	56 (56.6%)	
Prednisolone dosage, mg/d	8.8 (10.1)	
ACPA positive (%)	42	
CRP, mg/dl	1.9 (2.2)	0.5 (0.7)
Pain, 0-10	6.4 (2.2)	3.0 (2.1)
Patient global assessment (PtGA), 0-10	6.3 (2.3)	3.7 (2.3)
DAS-28-CRP	4.7 (0.8)	3.0 (0.8)
RADAI-5	5.6 (1.9)	3.9 (1.9)
FFbH, 0-100	65.2 (21.1)	83.5 (16.8)
G-EEE, improvement	8.6 (1.9)	8.2 (2.1)
G-EEE, adverse events	2.1 (1.9)	2.9 (2.7)
GASE-P total	0.5 (4.4)	12.2 (10.2)
BMQ necessity score, 5-25	18.4 (3.6)	19.1 (3.2)
BMQ concern score, 5-25	14.3 (3.8)	15.8 (3.9)
RAID	6.1 (2.1)	3.2 (1.8)

given as mean (SD), otherwise indicated

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AB0382

COMPARISON OF CARDIOVASCULAR RISK SCALES ACCORDING TO TIME OF EVOLUTION IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Cardiovascular disease, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic, multisystemic and multifactorial disease. RA patients are at increased risk of cardiovascular (CV) morbimortality, with atherosclerotic CV disease being the leading cause of death. The traditional risk factors cannot explain such an increase by themselves. (1) There are many algorithms for CV risk (CVR) prediction, and results obtained by these must be multiplied by 1.5 factor, since the EULAR recommendation from 2016. (2)
Objectives: To compare CVR by six scales: Framingham lipids and BMI, ACC/AHA ASCVD 2013, Reynolds (RRS), SCORE 2 and QRISK III, according to the time of disease evolution in RA patients.
Methods: Descriptive, comparative, and cross-sectional study. We enrolled RA patients between 40 and 75 years old who fulfilled ACR/EULAR 2010 classification criteria and recruited in the Rheumatology service from a tertiary care hospital. Patients were divided by time of disease evolution into quartiles. CVR results from scales were multiplied by 1.5 factor according to EULAR 2016 recommendation. Normality was assessed by Kolmogorov-Smirnov test. Variables with a non-normal distribution were described by median and interquartile range (p25-p75). Differences between groups was analyzed by Kruskal-Wallis test or Chi-squared, accordingly.
Results: Total of 406 RA patients were included. Demographic characteristics are shown in table 1. For longer disease evolution, CV scales showed an increased (except for RRS; p= 0.123), just like anti-citrullinated peptide antibody (p=0.001), rheumatoid factor IgG (p=0.003), IgM (p=0.00) and IgA (p=0.00).
Conclusion: CVR increased according to disease duration. Despite that most of the scales showed such increased, CVR varies between them, which may be attributable to the variables evaluated in each one. More studies are required to define which scale is the best to predict in RA patients.

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Table 1. Demographic characteristics (n= 406)

Variable	1st Quartile (n= 102)	2nd Quartile (n=101)	3rd Quartile (n=102)	4th Quartile (n=101)	p
Duration of disease, years. median (p25-p75)	1.12 (0.93-2.00)	4.84 (3.62-5.70)	10.62 (9.03-12.80)	19.69 (15.94-24.43)	
Women, (n)%	94 (92)	89 (88)	98 (96)	93 (92)	NS
Age, years. median (p25-p75)	56 (49-62)	55 (48-62)	56 (48-60)	57 (49-62)	0.002
BMI, kg/m2. median (p25-p75)	27.2 (24.6-31.1)	28.6 (26.1-32.1)	28.1 (24.5-32.5)	26.9 (23.1-29.4)	0.012
Laboratory tests, median (p25-p75)					
CPR, mg/dL.	0.6 (0.2-1.0)	0.8 (0.3-1.4)	0.8 (0.4-1.7)	0.7 (0.4-1.2)	0.047
ESR, mm/H.	20.0 (15.0-36.2)	25.0 (14.5-34.0)	29.5 (17.0-44.2)	24.0 (15.0-36.0)	0.045
ACPA, U/mL.	2.7 (1.0-192.8)	20.3 (1.5-197.7)	99.1 (4.0-199.5)	114.1 (5.98-199.2)	0.001
RF IgG, U/mL.	3.7 (2.0-8.4)	4.0 (2.0-11.6)	5.5 (2.0-14.5)	7.0 (3.0-20.5)	0.003
RF IgM, U/mL.	81.4 (22.0-200.0)	200.0 (38.5-200.0)	200.0 (96.6-200.0)	200.0 (71.7-200.0)	0.000
RF IgA, U/mL.	16.4 (2.2-138.0)	43.6 (7.6-188.3)	66.5 (13.8-200.0)	128.2 (17.6-200.0)	0.000
Cardiovascular risk scales, %. median					
ASCVD	2.1	3.3	2.92	4.65	0.008
FRS-Lipids	6.3	8.1	7.95	9.3	0.028
FRS-BMI	8.55	10.95	11.85	12.6	0.023
SCORE 2	3	4.5	6	6	0.006
Q-RISK III	5.55	8.7	7.8	10.8	0.001
RRS	1.5	1.5	1.5	4.5	NS

This table shows demographic and clinical characteristics. Quartiles were divided according to rheumatoid arthritis duration, meanwhile, each variable was described individually. BMI Body Mass Index; CRP C Reactive Protein; ESR Erythrocyte Sedimentation Rate; ACPA Anti–Citrullinated Protein Antibody; RF Rheumatoid Factor; ASCVD Atheroesclerotic Cardiovascular Disease; FRS Framingham Risk Score; RRS Reynolds Risk Score; SCORE 2 Systematic Coronary Risk Evaluation 2.

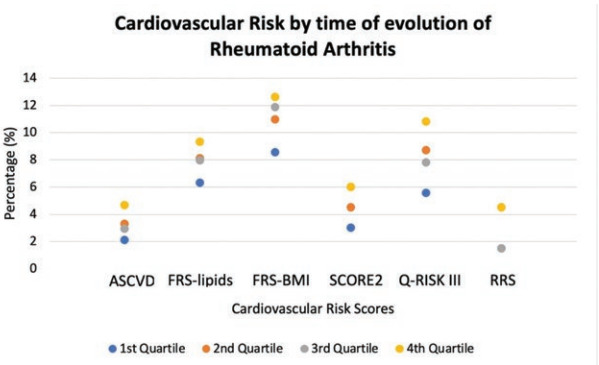


Image 1: Cardiovascular Risk according to the time of evolution of Rheumatoid Arthritis. The graphic shows risk percentages for each quartile, measured by 6 calculators. ASCVD Atherosclerotic Cardiovascular Disease; FRS Framingham Risk Score; BMI Body Mass Index; SCORE2 Systematic Coronary Risk Evaluation 2; RRS Reynolds Risk Score.

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AB0383

CARDIAC INVOLVEMENT IN RHEUMATOID ARTHRITIS: A COMPARATIVE TRANSTHORACIC ECHOCARDIOGRAPHY STUDY

Keywords: Comorbidities, Rheumatoid arthritis, Heart

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Background: Cardiac involvement in rheumatoid arthritis (RA) is one of the most frequent and severe extra-articular manifestations, but it is often under-diagnosed.
Objectives: In this context, we conducted this study, whose objective is to determine the prevalence and types of cardiac abnormalities in patients with RA using the transthoracic echocardiography (TTE) and to compare them with control subjects.
Methods: We performed a comparative cross-sectional study conducted in Taher Sfar Hospital, Mahdia, Tunisia. Each patient underwent a TTE coupled with Strain technique.
Results: Seventy-two patients with RA according to the ACR/EULAR 2010 criteria and 72 control subjects (control group) were included. In our study, there was a clear female predominance in both groups with a sex ratio of 0.07 in the RA group and a sex ratio of 0.05 in the control group (p=1). The mean age of RA patients was 52.9 ± 11.72 years [21-75 years] and that of the control group was 49.26 ± 10.74 years [19-76 years] (p=0,06). Abnormalities detected by TTE were more frequent in subjects with RA compared with the control group (80.6% vs 36.1%; p < 0.01) and they were asymptomatic in 65.5% of cases of RA group. Pericardial effusion was more frequent in the RA group compared with the control group but without significant difference. Valvular involvement was significantly more frequent in patients with RA compared to the control group (45.8% vs 1.4%; p<0.01) with predominance of tricuspid involvement (31.9%). Left ventricular diastolic dysfunction was more frequent in RA patients compared with the control group with a significant difference (36.1% vs 13.9%; p<0.01). Regarding the left ventricular systolic dysfunction, left ventricular ejection fraction impairment was absent in both groups, but subclinical left ventricular myocardial damage assessed by the Global Longitudinal Strain (GLS) method was detected in 37.5% of RA patients and 16.6% of control subjects (p<0.01). The mean of GLS in RA patients was -17.8% ± 2.9 [-22 to -10.7%], while it was -19.4% ± 1.9 [-24.7 to -15.7%] in control subjects. Left ventricular hypertrophy was detected on TTE in 22.2% of RA patients and in 6.9% of control group (p<0.01). Pulmonary arterial hypertension was present only in the RA group (2.8% of cases).
Conclusion: Our study showed that cardiac involvement is more frequent in RA than the general population, hence the interest of systematic screening, in order to improve the quality of life and the vital prognosis of patients.

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Table 1. Demographic characteristics and Echocardiographic findings. (N=186)

	Rheumatic patients (N=146)	P value	RA (N=75)	SLE (N=48)	PsA (N=23)	Control (N=40)	P value
Women, n (%)	126 (86.3%)	-	73 (97.3%)	43 (89.6%)	10 (43.3%)	20 (50%)	-
Age, years (iSD)	48.6 (±13.7)	**0.018**	54.1 (±9)	35.7 (±12.2)	55.4 (±10.4)	42.8 (±14)	**<0.001**
Dyslipidemia, n (%)	41 (28%)	**0.046**	26 (34.7%)	3 (6.4%)	12 (52.2%)	7 (17.5%)	**<0.001**
Diabetes Mellitus, n (%)	31 (21.2%)	**0.003**	12 (16%)	2 (4.2)	17 (73.9%)	1 (2.5%)	**<0.001**
Hypertension, n (%)	48 (32.8%)	**0.012**	27 (36%)	10 (20.8%)	11 (52.2%)	7 (17.5%)	**<0.001**
LV Mass index, g/m^2 (iQR)	64.9 g/m^2 (52-82.3)	NS	67.6 g/m^2 (58.3-80)	54.5* g/m^2 (45.3-77.1)	68.7 g/m^2 (58.3-88.4)	61.9 g/m^2 (51- 76)	**0.014**
LV ejection fraction, % (iQR)	60% (56-65)	**0.007**	60 % (57-64)	58† % (52-64)	65† % (57-67)	62 % (57 - 68)	**<0.001**
LV end-diastolic volume, ml (iQR)	72 ml (61-93)	NS	66†† ml (59-80)	83* ml (69-101)	74 ml (64- 101)	73 ml (61- 89)	**<0.001**
LV end-systolic volume, ml (iQR)	29 ml (23-38)	NS	27† ml (22-32)	34† ml (26-45)	25 ml (23-38)	28 ml (20- 34)	**0.001**
Left Atrial volume index, ml/m^2 (iQR)	25.6 ml/m^2 (20-32)	**0.004**	24.3 ml/m^2 (19.2-32)	27† ml/m^2 (26.2-45.2)	25.3 ml/m^2 (21.1- 29)	20.7 ml/m^2 (16.8- 28)	**0.016**
MV peak E velocity, m/s (iQR)	0.84 m/s (0.7-0.94)	NS	0.85 m/s (0.73-0.97)	0.83 m/s (0.65-0.93)	0.8 m/s (0.7-0.94)	0.81 m/s (0.67- 0.93)	NS
MV peak A velocity, m/s (iQR)	0.71 m/s (0.56-0.89)	**0.002**	0.78†† m/s (0.64-0.93)	0.56 m/s (0.52-0.75)	0.81†† m/s (0.58-0.91)	0.61 m/s (0.46- 0.71)	**<0.001**
MV E/A Ratio (±SD)	1.17 (±0.36)	**0.001**	1.11†† (±0.3)	1.33 (±0.43)	1.03†† (±0.28)	1.43 (±0.45)	**<0.001**
E, m/s (iQR)	0.1 m/s (0.08-0.11)	**0.002**	0.1 m/s (0.08-0.11)	0.1 m/s (0.08- 0.12)	0.08† m/s (0.07- 0.1)	0.11 m/s (0.9-0.13)	**0.001**
E/E (iQR)	8.07 (6.24-10)	**0.04**	8.88 (7.08-10.97)	6.38*†† (5.69- 8.24)	9.12 (7.72-11.5)	6.86*†† (5.43- 9.15)	**<0.001**

LV, left ventricle; MV, Mitral valve; SD, Standard deviation; iQR, Interquartile range; NS, Non-significant.[1] p<0.05 compared to control* p<0.05 compared to RA† p<0.05 compared to SLE[1]† p<0.05 compared to SLE and control†† p<0.05 compared to PsA*†† p<0.05 compared to RA and PsA

AB0384

CHANGES IN LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC FUNCTION IN PATIENTS WITH AUTOIMMUNE INFLAMMATORY DISEASES

Keywords: Systemic lupus erythematosus, Rheumatoid arthritis, Heart

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Background: Rheumatological diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and psoriatic arthritis (PsA) increase the cardiovascular (CV) risk by the development of a pro-inflammatory state that can affect the ventricular function of the heart. (1)
Objectives: To compare left ventricular (LV) systolic and diastolic function in patients with RA, SLE, and PsA as compared with healthy controls.
Methods: A cross-sectional and comparative study. Patients included in the cohort were between 30–75 years old, who fulfilled 2006 Classification Criteria for PsA; patients between 40-75 years old who fulfilled 2010 ACR/EULAR criteria for RA; Patients older than 18 years old who fulfilled 2019 ACR/EULAR Criteria for SLE, and Controls. A transthoracic echocardiogram was performed by a certified cardiologist blinded to clinical data. Normality was assessed by the Kolmogorov-Smirnov test and the Kruskal-Wallis test for comparison among groups. P value <0.05 was considered significant.
Results: 186 patients were included in the study, divided into groups as its shown in Table 1. Most of them were women (146); the most common comorbidities were hypertension (36%, 20.8%, and 17.5% in the RA, SLE, and Control groups, respectively), and dyslipidemia (73.9% in the PsA group). Echocardiographic findings are shown in Table 1.
Conclusion: LV systolic and diastolic function changes in the rheumatic population, especially RA, SLE, and PsA, are higher in comparison with healthy people and affect the prognosis in these patients, those changes can be detected by echocardiogram, which is a safe tool that may prevent complications and improve the prognosis with early detection and management of this CV involvement.
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AB0385

RISK FACTORS AND CARDIOVASCULAR DISEASES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN A TERTIARY GOVERNMENT HOSPITAL IN THE PHILIPPINES

Keywords: Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammatory arthritis and extra-articular involvement [1] Comorbidities are highly prevalent in patients with RA, [2] in particular cardiovascular disease (CVD), which is responsible for over 50% of premature deaths among these patients.[3] It causes lower life expectancy in 3 to 10 years and higher mortality rate compared to the general population. [4]
Objectives: To describe cardiovascular (CV) diseases and their risk factors among patients with rheumatoid arthritis.
Methods: This is a review of the medical records of patients with rheumatoid arthritis, ambulatory and hospitalized, at the Philippine General Hospital from January 2019-December 2022.
Results: There were 123 patients included in the study, 95.1% were females with a mean age and disease duration of 51.31 and 9.78 years, respectively. Only a few (6.5%) were hospitalized. Disease activity was low in 41.5% and moderate in 35% based on disease activity score (DAS 28) and/or clinical disease activity index (CDAI) scores. Methotrexate (54%) was the most commonly used conventional synthetic disease modifying antirheumatic drug (csDMARD). The use of glucocorticoids was observed in 51.2% while no patients were on biologic (DMARD) at the time of data collection. There were 12 (9.7%) patients with CV diseases, namely myocardial infarction, heart failure, and stroke. There were 87 (70%) patients with at least one CV risk factor and 60 (48%) with multiple risk factors. The risk factors identified were: dyslipidemia (43.1%), hypertension (40.7%), elevated body mass index (35.7%), and diabetes mellitus, (15.4%). However, there were 18 (14.6%) patients without a lipid determination. Five hospitalized patients (4%) died, three from infectious causes, one from malignancy, and one from myocardial infarction.
Conclusion: The majority (70%) in our cohort had at least one CV risk factor and 10% had an identified CV disease. Dyslipidemia was the most common CV risk factor. The high proportion of patients with CV disease and risk factors highlights the need to add the screening and management of CV diseases as a priority among patients with rheumatoid arthritis.

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AB0386

DIFFERENCES BETWEEN JAKIS-NAIVE AND JAKIS-NOT NAIVE PATIENTS IN A REAL LIFE CLINICAL SETTING: DATA FROM AN PROSPECTIVE MULTICENTRIC ITALIAN STUDY.

Keywords: Descriptive Studies, Rheumatoid arthritis, Disease-modifying Drugs (DMARDs)

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Background: Current and previous EULAR recommendations (1,2) suggest using JAK-inhibitors (JAKis) for treating Rheumatoid Arthritis (RA). However, little is known about differences of patients who are JAK-inhibitors (JAKis) naïve and patients who have already experienced at least one JAKi.

Objectives: To analyse differences between JAK-naïve and JAKis not naive patients in a real life setting.

Methods: All patients with RA on JAKis were prospectively followed up for 12 months in this multicentric study conducted in 23 centres. For each patient, the following variables were recorded: sex, age, disease duration at JAKi prescription, smoking, BMI, comorbidities, positive RF/ACPA, DAS28-ESR at baseline, 6 and 12 months, cDMARDs and prednisone at baseline, JAKis discontinuation, JAK-naïve. Statistics were performed by R (2022.12.0).

Results: 864 patients were included (**Table 1)**. Among them, 731 (84.60%) were JAKis naïve, whereas 122 (14.12%) were not naïve (missing data in 11-1.27%-patients). 473 (55.22%) patients were treated with baricitinib (JAK-naïve were 412, 87.3%), 213 (24.6%) with tofacitinib (JAKis-naïve 187, 87.79%), 111 (12.84%) with upadacitinib (JAKis-naïve 78.37%) and 62 (7.17%) with filgotinib (JAKis-naïve 72.58%). Significant differences between JAKis-naïve and not naïve were found for hypercholesterolemia (p=0.04), hypertension (p=0.02), previous cancer (p<0.001), disease duration (p<0.001), line of treatment (p<0.001). No difference was found for JAKis discontinuation (p=0.13) **(Table 1).**

Conclusion: Our data suggest that line of treatment and disease duration result higher in JAKis not naive compared to naïve ones. Notably, JAKis naïve and not naïve did not differ regarding drug discontinuation, suggesting a similar retention rate irrespective of previous JAKis.

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Table 1. Differences between JAKis naïve and not naïve patients

Total	Total (N=864)	JAKis naive (N=731)	JAKis not naïve (N=122)	P value
	N (%)	N (%)	N(%)	
Mean age at baseline (SD) (N=852)	58.83 (12.87)	58.54 (12.92)	60.61 (12.45)	0.10
Females (N=853)	668 (78.31)	564 (77.15)	104 (85.25)	0.05
Mean BMI (Kg/cm^2) (SD) (N=616)	25.15 (3.77)	25.18 (3.62)	25.02 (4.46)	0.68
Smoking (N=788)				0.13
Yes	150 (19.03)	135 (19.97)	15 (13.39)	
No	496 (62.94)	425 (62.87)	71 (63.39)	
Former	142 (18.02)	116 (17.16)	26 (23.31)	
Positive RF (N=800)	527 (65.89)	444 (64.91)	83 (71.55)	0.16
Positive ACPA (N=787)	491 (62.39)	411 (61.43)	80 (67.80)	0.19
Diabetes (N=760)	68 (8.95)	56 (8.78)	12 (9.84)	0.71
Hypertension (N=761)	297 (39.03)	238 (37.25)	59 (48.36)	**0.02**
Hypercholesterolemia (N=759)	195 (25.36)	155 (24.29)	40 (33.06)	**0.04**
Previous MACE (N=758)	47 (6.20)	39 (6.13)	8 (6.56)	0.86
Previous cancer (N=760)	42 (5.52)	39 (6.10)	3 (2.48)	**<0.001**
Disease duration (months), (median, IQR) (N=844)	76 (29-155)	71 (24-142.50)	142 (69-226)	**<0.001**
Mean DAS28-ESR at baseline (SD) (N=736)	5.29 (1.06)	5.27 (1.09)	5.40 (0.89)	0.22
cDMARDs at baseline (N=771)	280 (36.31)	235 (36.21)	45 (36.89)	0.88
PDN at baseline (N=438)	438 (50.69)	368 (57.38)	70 (56.79)	0.90
Median dosage (IQR) of PDN (mg/day) (N= 438)	5 (4.00-5.00)	2.50 (0.00-5.00)	4.00 (0.00-5-00)	0.08
Line of JAKis treatment (N=853)				**<0.001**
1^	244 (28.60)	244 (33.38)	0 (0.00)	
2^	211 (24.74)	207 (28.32)	4 (3.28)	
3^	175 (20.63)	172 (23.53)	(3.28)	
4^	109 (12.78)	56 (7.66)	53 (3.44)	
5^	65 (7.62)	32 (4.38)	33 (27.05)	
6^	28 (3.28)	12 (1.64)	6 (13.11)	
7^	12 (1.41)	6 (0.82)	6 (4.92)	
8^	3 (0.35)	1 (0.14)	2 (1.64)	
9^	2 0.23)	1 (0.14)	1 (0.82)	
10^	3 (0.35)	0 (0.00)	(2.46)	
Patients who discontinued JAKis (N=853)	192 (22.51)	158 (21.61)	34 (27.87)	0.13

SD: standard deviation; BMI: Body Mass Index; RF: Rheumatoid Factor; ACPA: Autoantibodies against citrullinated proteins; MACE: Major cardiovascular events; PDN: prednisone; IQR: interquartile range; DAS28-ESR: Disease Activity Score-28 for Rheumatoid Arthritis with ESR; cDMARDs: conventional Disease-modifying antirheumatic agents; JAKis: JAK inhibitors.

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AB0387 PREDICTIVE FACTORS OF DETECTION OF ULTRASOUND SYNOVITIS IN RHEUMATOID ARTHRITIS PATIENTS WITH CONCOMITANT FIBROMYALGIA

Keywords: Rheumatoid arthritis, Fibromyalgia, Ultrasound

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Background: Recent studies have shown that ultrasound (US) assessment of disease activity in rheumatoid arthritis (RA) with associated fibromyalgia (FM) before disease-modifying antirheumatic drug (DMARD) escalation is primordial.
Objectives: The purpose of this study was to identify predictive factors of detection of US synovitis and Doppler activity in RA patients with and without concomitant FM.
Methods: Cross-sectional study that included patients with diagnosis of RA (ACR/EULAR. 2010 criteria) with concomitant FM (ACR 2016) and to compare it to RA patients without FM. Demographic and RA characteristics were collected. US examination of 22 joints was blindly. performed by a single physician. US-detected synovitis was defined and scored 0-3 using. the OMERACT scoring system at the joint level for both grey-scale (GS) and Doppler power. (DP). The number of joints with ≥ grade 1 GS synovitis and those with ≥ grade 1 DP were. calculated. Multiple linear regression analysis performed, adjusting for clinical and. demographic variables.
Results: Eighty patients distributed into 40 patients in each group were recruited. Epidemiological and RA characteristics were comparable between groups. No significant. difference was observed between the groups in regards to mean DAS28 and the three- variables (DAS28 V3). Multiple linear regression showed that in RA-FM group US synovitis detection was positively. associated with male gender (B=0.135, p=0.045) and with DAS28 V3 (B=0.454,p=0.004), and negatively associated with the Patient global assessment (PGA) (B=-1.092,p=0.007). In. RA group (witout FM), US synovitis was positively associated with Swollen joints count. (SJC) (B=0.837, p=0.001). In RA-FM group, Doppler activity was positively associated with. the DAS28 V3 (B=0.637,p=0.04) and with Physician global assessment (B=0.873,p=0.023), negatively associated with the PGA (B=-0.642, p=0.005) while it was positively associated. with the DAS28 (β=3.08, p=0.047) in RA group.
Conclusion: Our study shows that a high DAS28 V3 seems to be significantly associated. with active synovitis in US assessment in RA patients with comorbid FM.
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Disclosure of Interests: None Declared.
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AB0388 RHEUMATOID ARTHRITIS WITH CONCOMITANT FIBROMYALGIA: THE ROLE OF ULTRASOUND IN ASSESSING DISEASE ACTIVITY

Keywords: Fibromyalgia, Rheumatoid arthritis, Ultrasound

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Background: Fibromyalgia (FM) is a chronic painful condition frequently associated with rheumatoid. arthritis (RA) which may falsely increase RA activity by modifying the subjective components. of disease activity scores.
Objectives: The aim of our study was to compare clinical scoring and ultrasound (US) assessment in RA patients with concomitant FM to RA patients without FM.
Methods: Cross-sectional study that included patients with diagnosis of RA (ACR/EULAR 2010 criteria) with concomitant FM (ACR 2016) and to compare it to RA patients without FM. Demographic and RA characteristics were collected. US examination of 22 joints was blindly performed by a single physician. US-detected synovitis was defined and scored 0-3 using the OMERACT scoring system at the joint level for both grey-scale (GS) and Doppler power (DP). The number of joints with ≥ grade 1 GS synovitis and those with ≥ grade 1 DP were calculated. Multiple linear regression analysis performed, adjusting for clinical and demographic variables.
Results: Eighty patients distributed into 40 patients in each group were recruited. Epidemiological characteristics and RA characteristics were comparable between groups. Biologic DMARDs prescription was more frequent in RA with FM patients than control group (p=0.04). Subjective activity parameters were higher in RA with FM group (p<0.05). DAS28 was significantly greater than DAS28 V3 in RA with FM group (p=0,000). FM group had significantly less US synovitis (p=0.035) and less Power Doppler (PD) activity (p=0.035). Grey scale (GS) US score (p=0.87) and DP US score (p=0.162) were similar in the two groups. Multivariate analysis in RA with FM group showed that DAS28 V3 and male gender were positively associated with the presence of US synovitis, while Patient Global Activity expressed a negative association.
Conclusion: Our study confirms the overestimation of disease activity by the clinical scores in RA with concomitant FM. DAS28 V3 score and US assessment would represent a better alternative.
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AB0389 EXTRA-ARTICULAR MANIFESTATIONS ARE FREQUENT IN SOUTH INDIAN PATIENTS WITH RHEUMATOID ARTHRITIS AND ARE INDEPENDENT OF THE DISEASE ACTIVITY OR SEROPOSITIVE STATUS.

Keywords: Rheumatoid arthritis, Comorbidities, Inflammatory arthritides

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Background: Extra-articular manifestations are seen in around 40% of patients with Rheumatoid arthritis (RA) in western studies and increase the mortality in patients with RA [1]. There is a paucity of data from India, especially from South India on the prevalence and associations of extra-articular manifestations in RA.
Objectives: To estimate the frequency of extra-articular manifestations (EAM) and their associations with disease characteristics in patients with Rheumatoid arthritis attending the Rheumatology clinic of a tertiary care teaching hospital in South India.
Methods: A cross-sectional study of 316 consecutive patients fulfilling the 2010 ACR EULAR classification criteria of RA was done at a Rheumatology clinic in South India between October 2020 and December 2022. The various EAM studied were keratoconjunctivitis SICCA, Interstitial lung disease (ILD), pleuritis/ pleural effusion, bronchiectasis, small airway disease, pericarditis/ pericardial effusion, myocarditis, subcutaneous nodules, peripheral neuropathy, anaemia and Rheumatoid vasculitis. The comorbidities studied were diabetes mellitus, systemic hypertension, coronary artery disease, chronic obstructive pulmonary

disease, hypothyroidism, and stroke. Various parameters like age, gender, disease duration, comorbidities, seropositivity, erythrocyte sedimentation rate (ESR), smoking, disease activity score (DAS28 ESR), and methotrexate use were compared between patients with EAM and those without EAM. Comparisons between groups were made with the chi-squared test when testing categorical variables and the Mann-Whitney *U* test or Independent samples' t test for continuous data. A binomial logistic regression analysis was also carried out to find the independent factors associated with EAM.

Results: Among the 316 patients, 272 were female (86.1%). The mean age of the study population was 51.6 ± 11.38 years and the median disease duration was 36 months (84). 141 patients (44.6%) had at least one comorbidity and 23 patients (7.3%) were current or former smokers. 264 patients (84.1%) were Rheumatoid factor (RF) positive and 298 patients (94.6%) were cases of seropositive RA (RF and/or Anti CCP positive) The median ESR was 50 mm/ hour and the median DAS 28 ESR was 4.65. 164 patients (51.9%) were methotrexate naïve. At least one EAM was seen in 134 patients (42.4%) and the most frequently seen EAM was anaemia (48 patients, 15.2%). Keratoconjunctivitis SICCA was seen in 32 patients (10.1%) and symptomatic ILD was seen in 30 patients (9.5%). Rheumatoid vasculitis was seen in 20 patients (6.3%). Age, disease duration, and ESR (table 1) were found to have significant association with extra-articular manifestations by univariate analysis. On binomial logistic regression, disease duration (p=0.002) and ESR (p=0.047) were found to have a significant association with the presence of extra-articular manifestations.

Conclusion: Extra- articular manifestations were seen in a significant proportion of our RA patients irrespective of the seropositivity status, disease activity, or methotrexate use and had a positive association with disease duration and ESR.

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TABLE 1. Comparison of parameters between patients with extra articular manifestations and patients without extra articular manifestations

PARAMETER	PATIENTS WITH EXTRA ARTICULAR MANIFESTATION (n= 134)	PATIENTS WITHOUT EXTRA ARTICULAR MANIFESTATION (n = 182)	*p* value
Mean Age (years)	53.1 ± 10.3	50.5 ± 11.5	**0.039**[a]
Gender			0.229
Female -	119	153	
Male -	15	29	
Median disease duration in months	60 (108)	36 (60)	**0.003**
Smoker	8	15	0.442
Comorbidities	57	84	0.523
Median ESR (mm/hr)	58 (52)	49 (44.8)	**0.026**
Median DAS28 ESR	4.81 (2.24)	4.58 (1.61)	0.479
Seropositive RA	298	18	0.678
RF positive	114	150	0.497
Methotrexate naive	69	92	0.868

[a] Significant ($p< 0.05$)

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AB0390 OVERACTIVATION OF THE RENIN ANGIOTENSIN SYSTEM AS A POSSIBLE CONTRIBUTOR TO THE INCREASED CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS (RA); EVALUATION OF LEUKOCYTE EXPRESSION OF ANGIOTENSIN II RECEPTOR TYPE 1 AND TYPE 2 IN A POPULATION OF RA PATIENTS.

Keywords: Rheumatoid arthritis, Cardiovascular disease

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Background: rheumatoid arthritis (RA) is a chronic systemic autoinflammatory disease of unknown aetiology characterized by joint inflammation and multiple comorbidities, with a prevalence of approximately 1% of the adult population. It is considered an independent cardiovascular (CV) risk factor, in fact it is associated with significantly increased CV morbidity and mortality. The renin angiotensin system (RAS) is a hormonal cascade with pleiotropic effects. Not only is it crucial in blood pressure regulation but it also plays an important role, among many other effects, in inflammation. High circulating levels of proinflammatory cytokines such as TNF-α and IL-6 are critical in the pathogenesis of RA as well as in determining increased CV morbidity and mortality among these patients. TNF-α and IL-6 activate the systemic and local RAS; in turn, Angiotensin II (Ang II) increases several proinflammatory cytokines among which TNF-α and IL-6. Therefore, a self-perpetuating vicious circle between RAS and cytokines is triggered. Activation of the classical RAS leads to Angiotensin II (Ang II) formation which binds to Ang II receptors type 1 (AT1R) and 2 (AT2R). RAS overactivation is essential in determining vascular inflammation and endothelial dysfunction through its proinflammatory and profibrotic effects.

Objectives: to determine whether RAS activity is higher among RA patients.

Methods: leukocyte AT1R and AT2R mRNA was extracted and measured by real-time polymerase chain reaction analysis (RT-PCR) from 18 RA patients with stable disease and no traditional CV risk factors (mean age 52.17±11.4) and 10 healthy controls (mean age 43.8±8.61). Intergroup comparisons were made using the Mann-Whitney U test.

Results: A significantly higher expression of AT1R was found in RA patients compared to healthy controls (p<0.01). Even though the finding did not reach statistical significance, AT2R expression was also higher in RA patients (p =0.072).

Conclusion: the results suggest AT1R and possibly AT2R upregulation in RA patients, indicating that RAS overactivation could contribute to the increased CV risk observed in RA patients. If such findings are confirmed by further research, they could have important implications in terms of prevention and treatment strategies for RA patients as RA is associated with an elevated CV risk that is often overlooked and underdiagnosed in these populations.

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AB0391 THE IMPACT OF OBESITY ON LIPID PROFILE AND ATHEROGENIC INDEXES AMONG RHEUMATOID ARTHRITIS ELDERLY PATIENTS

Keywords: Rheumatoid arthritis, Comorbidities

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Background: Obesity and dyslipidemia are two common comorbidities in rheumatoid arthritis (RA). They are considered as important cardiovascular and atherosclerosis risk factors in RA.

Objectives: The aim of our study was to evaluate the impact of obesity on lipid parameters as well as on atherogenic indexes among RA elderly patients.

Methods: A cross-sectional study was conducted including patients followed for RA and aged ≥ 65 years. All patients had lipid measurements of standard (total cholesterol (TC), high-density lipoproteins (HDL), low-density lipoproteins (LDL), and triglycerides (TG)) and specific (Apolipoproteins (Apo) A1 and B) parameters. We calculated the atherogenic indexes TC/HDL and LDL/HDL and apoB/apoA1. Patients were divided according to body mass index (BMI), into 2 groups: G1=obese patients with BMI ≥ 30 Kg/m² and G2 of non obese patients with BMI <30.

Results: We included 63 patients (52 women and 11 men). The mean age was 68.17±4.35 years [65-83]. The median duration of disease was 11 years. The mean BMI was 27.97±5.44 kg/m2 [14.85-43.2]. Twenty-two patients (34.9%) were obese (G1) and 41 patients (65.1%) had a BMI < 30 (G2). Mean levels of Apo A1, Apo B, TC, HDL, LDL and TG were 1.53±0.34 g/L, 1.1±0.29 g/L, 4.91±1.03 mmol/L, 1.09±0.29 mmol/L, 2.96±0.86 mmol/L and 2.02±1.47 mmol/L, respectively. Mean values of the atherogenic indexes TC/HDL, LDL/HDL and ApoB/ApoA1 were 4.77±1.59, 2.96±1.39 and 0.74±0.2 respectively. Comparing the G1 of obese patients with the G2, we found that obese patients had changes in lipid profile with significantly higher levels of Apo B (1.22±0.29 g/L vs. 1.04±0.27; p=0.018), TC (5.6±0.82 mmol/L vs 4.2±1.07; p=0.008) and LDL (3.5±0.84 mmol/L vs 2.54±0.84; p=0.03). A significantly lower ApoA1 level was noted in G1 (1.47±0.3 g/L vs 1.66±0.24; p=0.019). A lower level of HDL was noted in the

G1 (1.06±0.33 mmol/L vs 1.15±0.2), but without significant association (p=0.5). However, there was no significant difference in TG levels (p=0.9) and atherogenic indexes including TC/HDL (p=0.07), LDL/HDL (p=0.1) and ApoB/ApoA1 (p=0.2).
Conclusion: We demonstrated that obesity is associated with alterations in many lipid parameters among RA elderly patients. Obesity actually acts in synergy with the various conventional factors, including dyslipidemia, to increase the cardiovascular risk in this population.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0392 RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: RISK FACTORS

Keywords: Rheumatoid arthritis, Organ damage, Lungs

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Background: Interstitial lung disease (ILD), a severe extra-articular manifestation of rheumatoid arthritis (RA), contributes to significantly increased morbidity and mortality [1].
Objectives: Our study aimed to determine the risk factors of RA-associated ILD.
Methods: We conducted a retrospective, monocentric study over 4 years (2018-2022). Patients with RA, fulfilling the ACR/EULAR 2010, were included. ILD was defined as the presence of a radiologist-defined pattern consistent with ILD on chest computed tomography. Potential risk factors included age, sex, smoking, obesity, immunopositivity, extra-articular manifestations, disease activity, and medications. A statistical study was carried out using SPSS software.
Results: We included 128 patients with RA. The mean age was 53,03±12,87 years, with a male-to-female ratio of 0,31. The mean disease duration was 8,88±7,33 years. Nineteen patients had a confirmed ILD. Usual interstitial pneumonia was the most frequent subtype of ILD (63%, n=12). Using logistic regression analysis, the significant risk factors of ILD were: age (>60 years) (OR=29,516, IC95% [1,416-615,176], **p=0,029**), the erosive nature of RA (OR=24,302, IC95% [1,185-498,175], **p=0,038**), the presence of cutaneous rheumatoid nodules (OR=52,558, IC95% [1,696-1628,890], **p=0,024**) and ocular involvement (OR=45,377, IC95% [1,825-1128,183], **p=0,020**).
Conclusion: Our study showed that older patients (age>60 years), with an erosive RA, cutaneous rheumatoid nodules, and ocular manifestations are at higher risk of developing ILD. These findings suggest that an early screening of ILD in these patients can be advised.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0393 SLEEP DISORDERS IN PATIENTS AFFECTED WITH RHEUMATOID ARTHRITIS: ASSESSMENT AND CORRELATION WITH FLARE-UPS

Keywords: Rheumatoid arthritis, Quality of life, Inflammatory arthritides

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Background: Patients with rheumatoid arthritis (RA) suffer from augmented inflammatory pain during flare-ups. Their quality of sleep (QOS) is altered, but to the best of our knowledge no local data has been published on the matter.
Objectives: We aim to assess the quality of sleep in Patients with RA and to study its correlation with the disease flare-ups. QOS was altered among patients with RA. Poor sleep quality has been linked to pain, mood, fatigability, stress, and disease activity in the rheumatic disease population [1]. This study established the link between flare-ups and the presence of sleep disorders. We found greater frequence of sleep disturbance in this population [1] which may be explained by the presence of more patients with higher DAS28.
Methods: We conducted a cross sectional study using a self-administered questionnaire. Patients with RA consulting in physical medicine and rehabilitations outpatient clinics were included. Data was collected during the period from September 1, 2020 until the end of Mai 2022. We collected sociodemographic and clinical data. Disease Activity Scale (DAS28) greater than 5.1 was used to define a flare-up. QOS was assessed using the Pittsburg Sleep quality index (PSQI) in its validated Arabic version. Sleep disorder was defined by PSQI greater than 5.
Results: We included 54 patients. Their mean age was 38.6. Mean duration of progression of the disease was 6.9 years. Almost half of the patients were having a flare-up (42.6%). Mean score of PSQI was 9.6. 82.5% of the patients had a sleep disorder. The most common sleep disorder was multiple nocturnal wake ups (94.4%). We found a significant correlation between sleep disorder and a rheumatoid flare. Odds Ratio was 11.8 (p= 0,012).
Conclusion: QOS was altered among patients with RA. Poor sleep quality has been linked to pain, mood, fatigability, stress, and disease activity in the rheumatic disease population [1]. This study established the link between flare-ups and the presence of sleep disorders. Clinicians dealing with patients with patients with RA should have more attention to the QOS especially on flare-ups.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0394 DYSLIPIDEMIA IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Comorbidities, Rheumatoid arthritis

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Background: Patients with rheumatic diseases characterized by a pronounced inflammatory process. Systemic chronic inflammation, which is characteristic of patients with rheumatoid arthritis (RA), determines the high risk of developing metabolic disorders. Most often, patients with RA have disorders of lipid metabolism.
Objectives: To investigate the dystipidemia frequency in RA patients and in the control group without autoimmune and inflammatory diseases.
Methods: Were investigated 126 RA patients (102 women and 24 men, average age 43,82±2,8 years) and 30 subjects (control group) without autoimmune and inflammatory diseases (25 women and 5 men, average age 42,4±2,6 years). RA was diagnosed according to ARA criteria (1987); patients with hepatitis, alcohol abuse, >55 years old were not included. Statistical analysis was performed using program Statistica. The reliability of differences was defined at p <0.05.
Results: The evaluated of lipid metabolism in RA patients and control group are presented in Table 1.

Table 1. Characteristics of lipid metabolism in RA patients and in the control group. (M - the average value, m - the standard deviation).

The investigated indicator	RA patients (n=126) M±m	The control group (n=30) M±m	p
Total cholesterol, mmol/ L	5,21±0,84	4,51±0,31	p<0,001
HDL cholesterol, mmol/ L	1,41±0,25	1,52±0,28	p<0,05
LDL cholesterol, mmol/ L	3,10±0,90	2,51±0,42	p<0,001
VLDL cholesterol, mmol/ L	0,70±0,22	0,49±0,14	p<0,001
TG, mmol/ L	1,55±0,48	1,08±0,30	p<0,001
Atherogenicity index	4,21±0,84	2,09±0,74	p<0,001

***** - the difference between groups is significant, p<0.05.

In conduct an analysis of lipid metabolism in RA patients and in the control group, a high level of statistical significance p<0.001 was found in the indicators of lipid metabolism in patients with RA compared with those of the examined control group.
Conclusion: Disorders metabolism of lipids have a high prevalence among patients with RA. For the purpose of timely diagnosis of metabolic disorders of lipid metabolism in patients with RA, it is recommended to carry out a laboratory blood test with the determination of lipidogram indicators at least once a year.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Rheumatoid arthritis - biological DMARDs

AB0395 **IMMUNE-MEDIATED SKIN LESIONS RELATED TO BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS: A 22-YEAR EXPERIENCE OF A TERTIARY CENTER**

Keywords: bDMARD, Skin

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Background: Biological disease-modifying antirheumatic drugs (bDMARDs) have revolutionized the treatment of chronic inflammatory rheumatic diseases. However, the physician and the patient should be aware of possible adverse reactions. Skin is one of the most frequent organs involved in bDMARD adverse reactions and immune-mediated skin lesions (IMSL) have rarely been described before in cohort studies and their incidence is unknown.
Objectives: To explore the cumulative incidence, type of lesions, management and outcomes of IMSL related to bDMARD in a large cohort of patients with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA).
Methods: We conducted a retrospective single-center study including patients with RA, axSpA and PsA followed at a Rheumatology Department from a University Hospital Center between April 2000 and December 2021, treated with at least one bDMARD for at least 6 months. Sociodemographic characteristics, disease duration, age at diagnosis, concomitant immunosuppressive medications, type and duration of the treatment with bDMARD and number of previous bDMARD were collected. For all patients with IMSL, age at onset, disease duration at the time of the IMSL, culprit bDMARD and duration of the treatment, specific management and outcomes were collected. Descriptive statistics for continuous variables were presented with mean and standard deviation and categorical variables were presented with absolute and relative frequencies.
Results: A total of 441 patients with RA, 386 with axSpA and 162 with PsA were included. The majority were female (63.4%), with a mean age of 54.3 ± 12.8 years. An important proportion of patients (47.6%, n=471) were taking csDMARDs and the most prescribed bDMARD was adalimumab (21.8 %), followed by etanercept (16.5%). Twenty-seven (2.7%) patients presented IMSL potentially related to the bDMARD. Regarding the patients with IMSL, 55.6% were females, mean age at the onset of IMSL was 48.4 ± 12.0 years, mean duration of the treatment with bDMARDs was 4.3 ± 4.5 years and mean duration of the treatment with the culprit bDMARD was 2.3 ± 2.1 years. The majority of patients had SpA (n= 14), followed by RA (n=10) and PsA (n=3). Adalimumab was the culprit agent in half of the patients (n=14), followed by etanercept (n=4), golimumab (n=3), infliximab (n=3), rituximab (n=2) and tocilizumab (n=1). Four patients (14.8%) needed hospitalization with the purpose of performing a clinical, laboratorial and histological investigation. In most patients, skin lesions resolved completely with topical (n=12) or systemic (n=6) treatment. IMSL led to withdrawal of bDMARD in 18 patients (66.7%). More information about the type of IMSL was described in table 1.

Table 1. Description of number of cases, age at IMSL onset, disease duration and duration of treatment with the culprit bDMARD for each type of IMSL.

Type of immune-mediated skin lesion	Number of patients, n(%)	Age at skin lesion onset, mean±SD, years	Female, n(%)	Disease duration, mean±SD, years	Duration of treatment with culprit bDMARD, mean±SD, years
Psoriasis	**12**	49.3 ± 14.5	6 (50.0)	19.5 ± 15.3	1.9 ± 1.7
Plaque psoriasis	5 (41.7)				
Palmoplantar pustulosis	4 (33.3)				
Guttate psoriasis	1 (8.3)				
Inverse psoriasis	1 (8.3)				
Undefined	1 (8.3)				
Drug-induced lupus erythematosus	**6**	40.8 ± 2.9	4 (66.7)	15.2 ± 7.8	2.4 ± 1.4
Malar Rash	1 (16.7)				
Alopecia	2 (33.3)				
Chilblains	2 (33.3)				
Subacute cutaneous LE	1 (16.7)				
LE tumidus	1 (16.7)				
Alopecia areata	3	4.4 ± 6.7	1 (33.3)	12.2 ± 627	1.2 ± 0.6
Leukocytoclastic vasculitis	2	60.9 ± 2.8	0 (0)	31.9	2.9 ± 3.6
Urticaria	2	57.3 ± 15.9	2 (100)	27.8 ± 22.1	0.9 ± 1.2
Rosacea	1	48	1 (100)	18.5	9.7
Erythema nodosum	1	60	1 (100)	40.7	2.9

Conclusion: IMSL related to bDMARDs are unusual events with an estimated cumulative incidence of 2.9%, in our sample. The most frequent IMSL were psoriasis and cutaneous manifestations of DILE and the most frequent culprit bDMARD was adalimumab. The majority of patients didn't need hospitalization and presented complete resolution of IMSL. IMSL led to withdrawal of the bDMARD in 2/3 of patients.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0396 **DISCONTINUATION AND EFFECTIVENESS OF ORIGINATOR AND BIOSIMILAR TNFI IN PATIENTS WITH RHEUMATOID ARTHRITIS: REAL WORLD DATA FROM A RHEUMATOID ARTHRITIS REGISTRY IN CANADA**

Keywords: Rheumatoid arthritis, Outcome measures, bDMARD

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Background: In recent years, biosimilars, highly similar copies of originator biologics, have been available in clinical practice to patients with Rheumatoid Arthritis (RA) in Canada. The Ontario government is expected to implement a policy mandating a switch from originator biologics to biosimilars. We may be able to anticipate the outcomes of implementing such a policy by analyzing the existing data for patients already using biosimilars in Ontario.
Objectives: We aimed to describe discontinuation and disease activity in patients starting an originator or biosimilar TNFi, using real-world data from the Ontario Best Practices Research Initiative (OBRI), Canada.
Methods: Patients with active RA enrolled in the OBRI and initiating an originator or biosimilar TNFi between 1st Jan 2015 and 30st March 2022 were included. We investigated time to discontinuation by using Kaplan-Meier (KM) survival curves in the two groups. Due to a small number of biosimilar users, curves were not statistically compared. Using clinical disease activity index (CDAI), disease status was also described for patients with available data at 12 months after treatment.
Results: A total of 494 patients started an originator TNFi (n=401) or biosimilar TNFi (n=93) with mean (SD) disease duration of 12.0 (9.4) and 9.7 (9.3) years, respectively. In the originator group, 81.5% were female and mean age (SD) was 57.2 (11.9) years. In the biosimilar group, 82.8% were female and mean (SD) age was 59.2 (11.5) years. The originator group was less likely to have prior biologic use (31.9%) compared to the biosimilar group (58.1%). The mean (SD) baseline CDAI was lower in the originator group [17.2 (11.6)] compared to the biosimilar group [22.6 (13.7)]. Over a mean follow-up of 25.9 months, discontinuation was reported in 154 (38.4%) and 21 (22.6%) originator and biosimilar groups, respectively. The mean survival (standard error) in originator group was 49.5 (1.85) months and 56.1 (4.70) months in biosimilar group. The retention rate (95% Confidence Interval) at 12 months was 74.8% (70.1%-78.9%) in the originator group and 84.6% (74.4%-91.0%) in the biosimilar group (Table 1). At 12 months after treatment initiation, disease activity was similar in the two groups (mean of CDAI: 14.0 vs.13.0).
Conclusion: In this real-world data descriptive study, we found that the proprtion of patients who remained on their medication in the biosimilar group was numerically higher than the originator TNFi. We also found that disease activity after 12 months after initiation was numerically similar in both groups. Next steps include, comparing discontinuation and disease activity between the two groups using a statistical regression analysis adjusting for potential confounders.

Table 1. Survival rate over 2 years of follow-up by treatment group

	TNFi Biosimilar N=93	Originator TNFi N=401
Number of discontinuation	21	154
Probability of survival		
6 month (%, (95%CI))	92.9 (84.9-96.8)	88.4 (84.7-91.2)
12 months (%, (95%CI))	84.6 (74.4-91.0)	74.8 (70.1-78.9)
18 months (%, (95%CI))	77.8 (65.9-85.9)	69.8 (64.7-74.2)
24 months (%, (95%CI))	70.9 (57.5-80.8)	65.9 (60.7-70.6)

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AB0397 NO CLINICALLY RELEVANT CHANGES IN COAGULATION ACTIVATION BETWEEN PATIENTS INITIATING TNF-BLOCKERS VERSUS JAK-INHIBITORS

Keywords: bDMARD, Cardiovascular disease, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is associated with a 2-fold higher risk of venous thromboembolism (VTE) compared with the general population [1]. The immune system and hemostatic system are closely linked by a shared origin. Inflammation affects thrombotic responses by upregulating procoagulants and downregulating anticoagulants and fibrinolysis [1]. Tumor necrosis factor (TNF), an important mediator in the inflammatory pathway, induces a disbalance between the coagulation system and fibrinolytic system, resulting in a hypercoagulable state. In addition, several studies have suggested that some Janus kinase-inhibitors (JAKi) might be associated with an increased risk for VTE [2]. However, the underlying pathogenic mechanisms have yet to be elucidated.
Objectives: To compare changes in hemostatic parameters during treatment with TNF-blockers (aTNF) and JAKi in RA.
Methods: Biomarkers for the coagulation system, including D-dimer, fibrinogen, PT, aPTT, F1+2, TAT, F IX and vWF, were prospectively measured in 121 consecutive RA patients: 83 patients treated with aTNF and 38 patients with JAKi. Data were collected at baseline, after 1, 3, and 6 months.
Results: Mean age for all patients was 57 (±14) years, 76% were female. Mean DAS28-CRP at baseline for TNF-inhibitor group was 3.6 (±1.3) and 4.1 (±1.4) for JAKi group, steadily declining in aTNF users, while decreasing in JAKi users with an intermittent peak at 3 months. Baseline coagulation markers levels were comparable between the groups. D-dimer and vWF levels were slightly higher in the JAKi group (p = 0.30 and p = 0.08, respectively), while F IXa levels were lower (p = 0.17). D-dimer and fibrinogen levels steadily declined in the aTNF group, while fluctuating in the JAKi group, with a peak at 3 months with a subsequent decline thereafter (Figure 1). In aTNF users, TAT increased slightly during follow-up. VWF, PT and aPTT remained relatively stable, while F IXa and F 1+2 showed an increase after 3 months of follow-up, after which they returned to baseline. In JAKi users, D-dimer, fibrinogen, VWF and F 1+2 fluctuated, with a peak after 3 months and then a subsequent decline. F IX and PT initially decreased slightly but increased steadily after 6 months, while TAT and aPTT remained stable during follow-up.
Conclusion: The pro-thrombotic tendency in active RA declined during effective treatment with both aTNF as well as JAKi. A gradually decrease in D-dimer and fibrinogen was seen after 6 months of treatment. The transient increase of coagulation activation in JAKi users at three months coincided with increased disease activity. Altogether, our data suggests that an increased VTE risk in the first six months due to either treatment aTNF or JAKi seems unlikely. Whether or not the risk increases beyond this time period remains to be investigated.

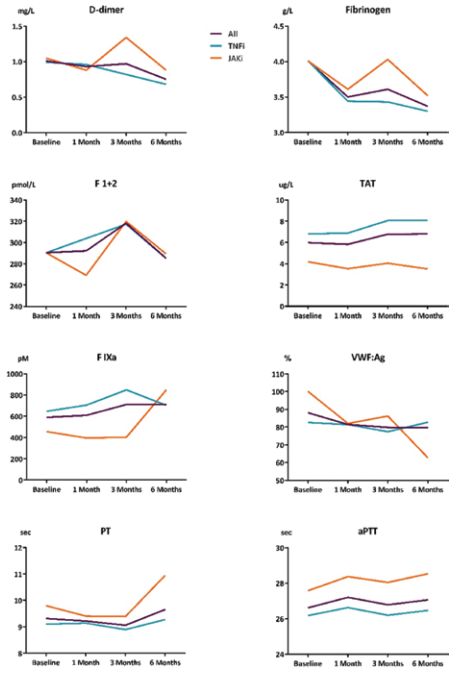


Figure 1. Progression of coagulation markers.

Table 1. Progression of mean coagulation markers.

	Baseline	1 Month	3 Months	6 Months
D-dimer				
TNF	0,99	0,96	0,82	0,68*
JAK	1,05	0,88	1,34	0,88
Fibrinogen				
TNF	4,01	3,44*	3,43*	3,3*
JAK	4,01	3,61	4,03	3,52
F1+2				
TNF	290,46	303,88	317,27	285,21
JAK	290,39	269,24	319,87	289,37
VWF				
TNF	82,56	81,45	77,42	82,74
JAK	100,13	82,00	86,23	62,72
TAT				
TNF	6,81	6,89	8,06	8,06
JAK	4,19	3,54	4,05	3,51
FIX				
TNF	646,86	705,61	848,85	703,32
JAK	456,53	395,40	403,36	848,85
PT				
TNF	9,10	9,14	8,90	9,28
JAK	9,80	9,41	9,39	10,95
aPTT				
TNF	26,17	26,63	16,19	26,47
JAK	27,58	28,37	28,04	28,53

* Significantly different from baseline, p < 0,05. TNF = tumor necrosis factor, JAK = Janus kinase, F1+2= prothrombin fragment 1+2, VWF= von Willebrand factor, TAT= thrombin-antithrombin complex, FIX= Factor 9, PT = prothrombin time, aPTT = activated partial thromboplastin time.

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AB0398 COMPARATIVE SAFETY OF BIOLOGIC AND TARGETED SYNTHETIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS FOR CARDIOVASCULAR AND CANCER OUTCOMES IN RHEUMATOID ARTHRITIS

Keywords: Cardiovascular disease, Rheumatoid arthritis, Disease-modifying Drugs (DMARDs)

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Background: The ORAL-surveillance trial showed a higher risk of major adverse cardiovascular events (MACE) and cancer in patients with rheumatoid arthritis (RA) taking tofacitinib, a Janus kinase inhibitor (JAKi), compared to those taking tumor necrosis factor alpha inhibitors (TNFi's). However, little is known regarding the comparative safety of these two drug classes relative to non-TNFi biologics.
Objectives: To assess the comparative safety of TNFi's, non-TNFi's, and JAKi's in RA patients for the risk of MACE (e.g., myocardial infarction, cardiac arrest, sudden death, stroke, percutaneous coronary intervention, and coronary artery bypass graft), cancer, deep vein thrombosis (DVT), and pulmonary embolism (PE).

Methods: We performed a retrospective cohort study using IBM Watson MarketScan databases (2012-2019) of RA patients 18-64 years of age who initiated treatment with TNFi's, non-TNFi's, or JAKi's on or after January 2012. We used Cox Proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for developing MACE, cancer, DVT, and PE within 2 years of initiation in patients on non-TNFi's or JAKi's relative to TNFi's, adjusting for multiple confounders, including age, gender, geographic region, year of initiating a biologic, Charlson Comorbidity Index, frailty status, healthcare utilization within 12 months prior to starting treatment (i.e., major infection requiring hospital admissions, general hospital admissions, outpatient visits, and emergency department visits), and RA severity (i.e. disease-modifying antirheumatic drug, nonsteroidal anti-inflammatory drug, glucocorticoid, and opioid fills 3 months prior to starting treatment).

Results: A total of 39,032 drug initiation events met eligibility criteria for our study (73.6% initiation of TNFi's, 18.6% non-TNFi's, and 7.80% JAKi's). The mean age of the patients in each of the groups ranged from 47-49 years old; the majority were female. The mean follow-up time was 349 days for TNFi's, 272 days for non-TNFi's, and 266 days for JAKi's. Non-TNFi's were associated with an increased risk of MACE, cancer, and DVT, though the incidence of adverse health outcomes overall was still quite low (Table 1). In multivariable models, patients who started non-TNFi's had a significantly higher risk of MACE (HR 1.75; 1.34-2.28), incident cancer (HR 2.06; 1.70-2.50), and DVT (HR 1.84; 1.45-2.32) compared to those who initiated TNFi's. Patients who filled JAKi's had a significantly higher risk of developing cancer compared to those who filled TNFi's (HR 1.48; 1.09-2.03).

Conclusion: TNFi's may be safer for RA treatment than non-TNFi's and JAKi's for RA in this generally younger and predominantly female population. However, since most RA patients initiate treatment with TNFi's, results could be confounded by the possibility of more severe or prolonged disease in patients on non-TNFi's and JAKi's. These findings need to be replicated in other study populations. Future steps include looking at the risk conferred by individual non-TNFi's towards these risks. Studies with longer follow-up are needed for better assessment of cancer risk among these drug classes.

Table 1. Incidence per 10,000 person-years of each adverse health outcome* stratified by drug class in RA patients 18-64 years of age.

Adverse Health Outcome	TNFi n = 28,716 (73.6%)**	Non-TNFi n = 7,290 (18.6%)**	JAKi n = 3,026 (7.80%)**
MACE	72.9	162.6	94.8
Cancer	132.9	296.4	192.3
DVT	90.9	216.5	107.7
PE	22.1	43.9	24.6

*Outcomes are not mutually exclusive; each patient could have experienced multiple outcomes.**Number and percentage of drug class initiation events.

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AB0399 EFFICACY AND SAFETY OF ABATACEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, bDMARD

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Background: Rheumatoid arthritis(RA) is a systemic inflammatory disorder that mainly affects the diarthrodial joint. Abatacept was approved by the US Food and Drug Administration (FDA) in December 2005 for use in RA[1,2].

Objectives: This study aimed to systematically evaluate the efficacy and safety of abatacept therapy in RA.

Methods: Eight databases (PubMed, Web of Science, Embase, Cochrane Library, Web of Knowledge, MEDLINE, Clinical Trials.gov, and FDA.gov) were searched for studies on abatacept treatment of RA published from the date of establishment of the database to January 1, 2022. A random effect model was used to conduct a meta-analysis of the efficacy and safety of abatacept in patients with RA using (Stata 12.0).

Results: The DAS28-CPR of RA receiving abatacept therapy at 24 weeks was significantly decreased compared with the baseline[SMD= -1.624, 95%CI -1.903 - -1.345, P<0.01]. After receiving abatacept therapy for 24 weeks, patients with RA had a significantly decreased in DAS28-ESR [SMD= -1.067 (95% CI: -1.399 - -0.735), P<0.01], SDAI [SMD= -1.484 (95% CI: -2.167 - -0.802) P<0.01], and CDAI [SMD=-1.726 (95% CI: -2.671 - -0.781), P<0.01] compared with the baseline. The incidence of adverse events was 58.7%. The incidence of serious adverse events was 8.7%. General infection is a typical effect of abatacept, occurring in 25.2% of RA. Most of these adverse events were mild and recovered

Table 1. Available evidence including patients with RA treated with abatacept.

Study.Year.	Patients (include in analysis)	Age (year)	Gender (female %)	DAS-28CRP	DAS-28ESR	SDAI	CDAI
Andrea Rubbert-Roth 2022	309(309)	55.8±11.9	81.88	NA	NA	NA	NA
William Rigby 2021	40(39)	47.2±12.2	72.50	before:5.2±1.1 after:2.6±0.938	NA	before:34.5±16.1 after:6.3±7.0952	before:33.3±15.2 after:6±8.1
Hiroto Tsuboi 2015	32(31)	55.3±14.4	100.00	NA	NA	before:19.8±11.0 after:9.9±9.9	NA
Yoshiya Tanaka 2014	137(137)	60.9±13.4	81.02	NA	before:5.2±1.4 after:3.9±1.4	before:24.6±12.5 after:12.9±11.6	NA
Masayoshi Harigai 2016	3016(3016)	61.1±12.8	82.40	before:4.47±1.23 after:3.25±1.33	before:5.07±1.30 after:3.93±1.40	NA	NA
Shuzo Sato 2021	15(15)	75.1±7.93	86.70	before:3.27 ± 1.33 after:2.26±0.92	NA	NA	NA
Yoshifumi Tada 2016	10(10)	59.8±15.4	80.00	before:3.91 ± 1.00 after:2.74 ± 1.00	NA	NA	NA
Paul Emery 2019	55(55)	46.1±11.5	NA	before:5.47±1.15 after:2.45±0.98	NA	NA	NA
Koichi Amano 2015	56(56)	55.4±12.2	66.07	before:5.65±0.85 after:2.74±0.9709	NA	NA	NA
Sei Muraoka 2021	67(67)	74.7±5.7	79.10	before:4.6±1.2 after:2.705±1.252	before:5.2±1.2 after:3.3±1.205	before:24.9±11.8 after:9.323±12.24	before:22.7±10.9 after:8.652±11.256
Masayoshi Harigai 2019	3882(2544)	72.2 ± 5.0	79.70	before:4.6±1.2 after:3.25±1.28	NA	NA	NA
Nobunori Takahashi 2014	128(128)	64.9 ± 10.9	80.50	before:5.35±0.86 after:3.87±1.33	NA	NA	NA
M Schiff 2009	597(468)	53.2±12.3	82.10	before:6.2±0.7 after:4.2±2.613	NA	NA	NA

quickly after discontinuation. Besides, severe infection occurred in 2.3 % of RA (Figure 1).

Conclusion: Abatacept was effective and well-tolerated in RA patients. The incidence of adverse events was high, but most were mild and recovered quickly after discontinuation.

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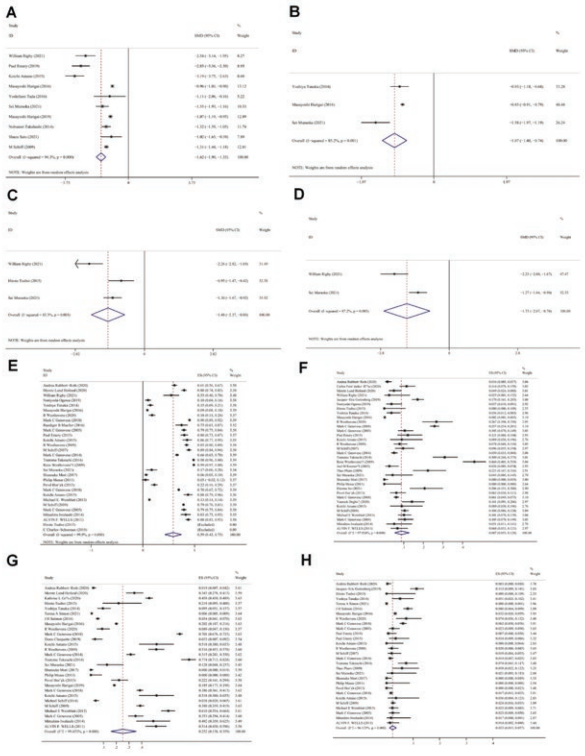


Figure 1. Efficacy and safety of abatacept in patients with RA. (A) The DAS28-CPR of RA patients at 24 weeks. (B) The DAS28-ESR of RA patients at 24 weeks. (C) The SDAI of RA patients at 24 weeks. (D) The CDAI of RA patients at 24 weeks. (E)Forest plot of the incidence of adverse events. (F) Forest plot of the incidence of serious adverse events. (G) Forest plot of the incidence of general infection. (H) Forest plot of the incidence of serious infection.

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Disclosure of Interests: None Declared.

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AB0400

THE PATTERN OF INTERLEUKIN-6 INHIBITORS VERSUS OTHER BIOLOGIC DRUG USE IN PATIENTS WITH RHEUMATOID ARTHRITIS IN WALES, UK: A REAL-WORLD STUDY USING ELECTRONIC HEALTH RECORDS

Keywords: bDMARD, Rheumatoid arthritis, Real-world evidence

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Background: Rheumatoid arthritis (RA) guidelines highlight the importance of early treatment to reduce disease activity and prevent long term damage [1-4]. Infection risk must be considered when starting biologic therapy as infections account for significant morbidity and mortality in RA [5]. Tocilizumab and sarilumab are anti-interleukin-6 (IL-6) receptor antibodies also effective in treating RA symptoms and preventing progression of structural damage [6-9]. Risk of infections in RA patients treated with IL-6 inhibitors have also been reported [10]. However, IL-6 inhibitor monotherapy has a superior efficacy than adalimumab [11]. More information is required to assess real-life burden and predict infection risk in RA patients using biologics [12].

Objectives: Examine the treatment pathway, factors associated with drug initiation and treatment discontinuation in patients with RA treated with either IL-6 inhibitors versus non-IL-6 biologic disease modifying anti-rheumatic drugs (bDMARDs).

Methods: A retrospective cohort study of RA patients in the Secure Anonymised Information Linkage databank, including primary care, secondary care and rheumatology clinic records of over 90% of the population in Wales, UK. Patients initiated on first treatment initiation, discontinuation and clinical outcomes including infection and hospitalisation were analysed using cox regression analysis.

Results: Data from 4922 patients with RA were analysed. The majority of patients had taken at least one conventional synthetic disease modifying anti-rheumatic drug (csDMARD) 95.7%, (4,691/4,922) while 29.6% (1,457) went on to take bDMARDs. Of these, 2% (97) biologic-naïve patients were treated with IL-6 inhibitors. Earlier treatment with bDMARDs was associated with increasing disease duration (HR: 1.11, 95% CI: 1.07 to 1.15) while younger age at diagnosis, orthopaedic surgery pre-treatment and kidney disease reduced the likelihood of being treated with biologics. Previous history of infection was associated with increased likelihood of treatment with IL-6 inhibitors rather than non-IL-6 bDMARDs (HR: 1.73, 95% CI: 1.15 to 2.59). The rate of treatment discontinuation was significantly higher in the non-IL-6 bDMARDs-treated patients compared to the IL-6 inhibitor treated individuals (difference: 9.4, 95% CI: 1.1 to 15.7). Treatment failure, orthopaedic surgery pre-treatment and steroid use was associated with non-IL-6 bDMARDs treatment failure (HR: 1.64, 95% CI: 1.00 to 2.68; HR: 1.62, 95% CI: 1.26 to 2.08, respectively). No factors were associated with treatment failure in the IL-6 inhibitor treated patients.

Conclusion: Patients treated with IL-6 inhibitors and other biologics were similar in demographics but had a different comorbidities pre- treatment; there was more orthopaedic surgery in those who went on to be treated with non-IL-6 biologics and more prior history of infections and kidney disease in those treated with IL-6 inhibitors. Treatment failure was higher in the non-IL-6 bDMARDs-treated patients.

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AB0401

EFFICACY OF ABATACEPT FOR SUPPRESSING RADIOGRAPHIC PROGRESSION OF CERVICAL LESIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARISON WITH METHOTREXATE TREATMENT; THREE YEARS OF FOLLOW-UP ~A MULTICENTER REGISTRY STUDY ~

Keywords: Rheumatoid arthritis, bDMARD

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Background: Cervical lesions are known to occur at high frequency as a complication of rheumatoid arthritis (RA). Treatment with biological agents are more clinically effective than the DMARDs that were in use previously, in particular, with their efficacy in suppressing joint destruction having been emphasized. We reported the efficacy of infliximab, anti-tumor necrosis factor antibodies for suppressing the radiographic progression of RA cervical lesions at ACR2009, EULAR2010, 11, 12, 13, 14, 16, 18, 19 and 20. However there is still few studies of efficacy of against RA cervical lesions of Abatacept (ABT) that inhibits T cell activation by binding to CD80/86.
Objectives: To evaluate the efficacy of ABT for suppressing the radiographic progression of RA cervical lesions comparison with MTX for 3 years.
Methods: We used ABT or MTX for treating Japanese patients with active RA who fulfilled the ACR criteria in 1987. The final study cohort of each 49 and 75 patients received continuous ABT and MTX treatment for at least 3 years. For evaluation of cervical lesions, the atlanto-dental interval (ADI), the space available for the spinal cord (SAC), and the Ranawat value were measured by plain lateral radiographs in the flexion position, at initiation and Year 1, 2, 3.
Results: In the patients receiving ABT (n=49) and MTX (n =75), the number of female were each 39(80%) and 52(69%) cases(p=0.206). The mean age was 67.1 ± 13.1 and 63.6 ± 11.0 years old (p=0.010); disease duration was 17.3 ± 14.0 and 8.0 ± 9.5 years (p<0.001) and the mean dose of MTX was 8.1 ± 3.5 and 8.2 ± 2.9 mg/w (p=0.970). Clinical findings related to RA were as follows; CRP 2.2± 2.1 and 1.7± 2.3 mg/dl(p=0.010); ESR 44.1 ± 21.1 and 31.9 ± 21.8mm/h(p=0.001); MMP3 273 ± 303 and 223 ± 350ng/ml(p=0.002); the number of RF-positive 48(98%) and 60(80%) cases(p=0.004); DAS28-ESR 5.12 ± 1.03 and 4.30 ± 1.38 (p<0.001); ADI 3.7 ± 2.1 and 2.6 ± 1.6mm(p<0.001); SAC 18.6 ± 2.9 and 20.8 ± 2.5mm(p<0.001) and Ranawat value 14.4 ± 2.0 and 16.0 ± 1.5mm (p<0.001). The respective changes in cervical lesion parameters after 1 year were as follows: ADI: 0.20 ± 0.41 and 0.25 ± 0.45 mm (p = 0.528); SAC: −0.14 ± 0.35 and −0.17 ± 0.38 mm (p = 0.653); and Ranawat value: −0.18 ± 0.39 and −0.13 ± 0.34 mm (p = 0.449). The respective changes in cervical lesion parameters after 2 years were as follows: ADI: 0.35 ± 0.56 and 0.55 ± 0.70 mm (p = 0.126); SAC: −0.27 ± 0.49 and −0.45 ± 0.62 mm (p = 0.087); and Ranawat value: −0.27 ± 0.49 and −0.33 ± 0.55 mm (p = 0.528). The respective changes in cervical lesion parameters after 3 years were as follows: ADI: 0.47 ± 0.77 and 0.71 ± 0.80 mm (p = 0.063); SAC: −0.39 ± 0.73 and −0.63 ± 0.82 mm (p = 0.040); and Ranawat value: −0.41 ± 0.71 and −0.44 ± 0.66 mm (p = 0.606) in the patients receiving ABT and MTX (Figure 1). The numbers of patients who did not showed progression in ADI, SAC and Ranawat value were each 33(67%) and 37(49%) cases(p=0.048); 37(76%) and 40(53%) cases(p=0.013) and 35(71%) and 49(65%) cases(p=0.478) after 3 years. Also the number who was able to suppress progression in all three parameters were each 32 cases (65%) receiving ABT and 37 cases (49%) receiving MTX (p=0.128) after 3 years (Figure 2).
Conclusion: This study suggested that ABT treatment can be used to suppress the progression of RA upper cervical lesions more than MTX treatment.

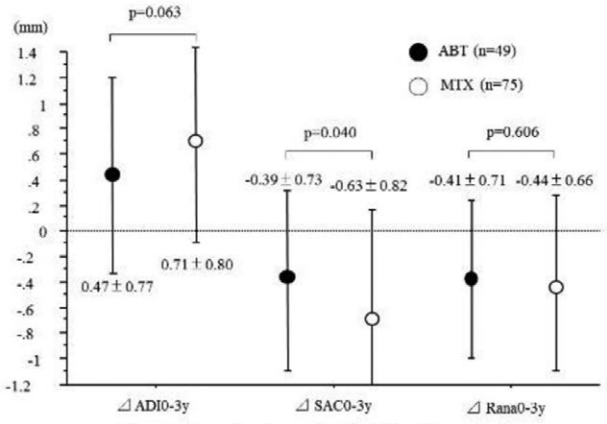


Figure 1 : Respective changes in ADI, SAC and Ranawat value from Year 0 to Year 3 between ABT and MTX patients

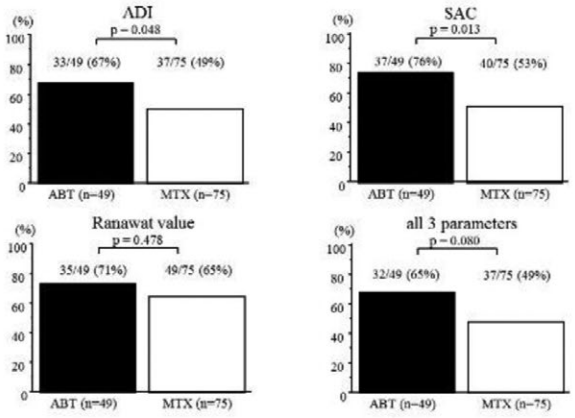


Figure 2 : The rate of patients who did not showed progression in ADI, SAC, Ranawat value and all three parameters after 3 years

REFERENCES: NIL.
Acknowledgements: NIL.
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AB0402

PHARMACOKINETICS AND SAFETY OF CT-P47, A PROPOSED TOCILIZUMAB BIOSIMILAR, IN COMPARISON WITH EU-APPROVED TOCILIZUMAB; A PHASE 1, RANDOMIZED, DOUBLE-BLIND, TWO-ARM, SINGLE-DOSE STUDY IN HEALTHY SUBJECTS

Keywords: Rheumatoid arthritis, Clinical Trials, bDMARD

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Background: CT-P47 is a recombinant humanized monoclonal antibody that was developed as a proposed biosimilar of tocilizumab.
Objectives: The purpose of this study was to compare the pharmacokinetics (PK), safety, and immunogenicity of CT-P47 and EU-approved tocilizumab (EU-tocilizumab) up to 42 days after a single subcutaneous injection of 162 mg of each product in healthy subjects.
Methods: 289 healthy subjects aged 19 to 55 years were randomly assigned 1:1 to receive either CT-P47 or EU-tocilizumab. The primary PK endpoints included area under the serum concentration-time curve (AUC) from time zero to infinity ($AUC_{0\text{-}inf}$), AUC from time zero to the last quantifiable concentration ($AUC_{0\text{-}last}$), and maximum serum concentration (C_{max}). Secondary endpoints were additional PK, safety, and immunogenicity.
Results: Demographics and baseline characteristics were well balanced between groups. The 90% confidence intervals for the geometric least squares mean ratios of each of the primary PK parameters ($AUC_{0\text{-}inf}$, $AUC_{0\text{-}last}$, C_{max}) were within the predefined equivalence margin of 80% to 125% (Table 1). Secondary PK variables (T_{max}, $t_{1/2}$, λ_z, CL/F, V_z/F, $\%AUC_{ext}$) were also comparable between groups. Mean serum concentrations of tocilizumab observed through 42 days post-dose were comparable between groups (Figure 1). Overall, 55 (38.2%) and 72 (51.4%) subjects reported ≥1 treatment-emergent adverse event (TEAE) in the CT-P47 and EU-tocilizumab groups, respectively. Most of TEAEs were grade 1 or 2 in intensity and TEAEs considered to be related to study drug were reported by 47 (32.6%) and 61 (43.6%) subjects, respectively. Neutrophil count decreased was the most commonly reported TEAE overall (14 [9.7%] and 15 [10.7%] subjects, respectively). There were 3 treatment-emergent serious adverse events (2 [1.4%] and 1 [0.7%] subjects, respectively). Of these, only 1 case was considered to be related to study drug (EU-tocilizumab: headache). Overall, 20 (13.9%) and 29 (20.7%) subjects in the CT-P47 and EU-tocilizumab groups, respectively, had ≥1 post-treatment positive result for anti-drug antibodies (ADA) and 17 (11.8%) and 20 (14.3%) subjects, respectively, had ≥1 positive result post-treatment for neutralizing antibody. Primary PK parameters of $AUC_{0\text{-}inf}$, $AUC_{0\text{-}last}$, and C_{max} were slightly lower in subjects with at least 1 ADA positive compared with those subjects with all ADA negative, at post-dose, among groups in the PK set.
Conclusion: This study demonstrated PK equivalence of CT-P47 to EU-approved tocilizumab in healthy subjects. Safety profiles, including immunogenicity, were comparable between groups.
REFERENCES: NIL.

Table 1. Statistical Analysis of the Primary PK Endpoints (PK Set)

Parameter (units)	Treatment	gLSM (n)	Ratio of gLSMs (90% CI)[a]
$AUC_{0\text{-}inf}$ (day·µg/mL)	CT-P47	79.37 (138)	107.92 (98.04, 118.80)
	EU-tocilizumab	73.54 (136)	
$AUC_{0\text{-}last}$ (day·µg/mL)	CT-P47	77.55 (144)	106.93 (97.36, 117.43)
	EU-tocilizumab	72.52 (139)	
C_{max} (µg/mL)	CT-P47	8.89 (144)	103.00 (94.67, 112.06)
	EU-tocilizumab	8.63 (140)	

Abbreviations: ANCOVA, analysis of covariance; $AUC_{0\text{-}inf}$, area under the concentration–time curve from time zero to infinity; $AUC_{0\text{-}last}$, area under the concentration-time curve from time zero to the last quantifiable concentration; CI, confidence interval; C_{max}, maximum serum concentration; EU-tocilizumab, European Union-approved tocilizumab; gLSM, geometric least squares mean; PK, pharmacokinetic.[a]Determined by ANCOVA performed with the natural log-transformed PK parameters as the dependent variable, treatment as a fixed effect and stratification factors (body weight at Day -1, gender [male versus female], and study center) as covariates.

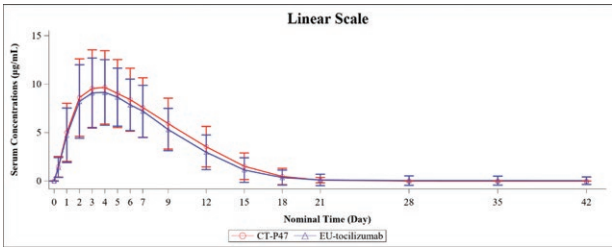


Figure 1. Mean (± SD) Serum Concentrations of Tocilizumab (PK Set)

Abbreviations: EU-tocilizumab, European Union-approved tocilizumab; PK, pharmacokinetic; SD, standard deviation.
Acknowledgements: NIL.
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AB0403 LONGITUDINAL ANALYSIS OF CHANGES IN THE FINE ARTICULAR STRUCTURE BY CTLA4-IG USING HR-PQCT IN RHEUMATOID ARTHRITIS

Keywords: Imaging, Rheumatoid arthritis, Real-world evidence

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Background: Although the clinical effect of CTLA4-Ig (abatacept: ABT) on rheumatoid arthritis (RA) has been shown by a several kinds of large scale clinical trials and postmarketing surveillances, detail of its effect at a local joint has not been sufficiently analyzed. Recently, it has been shown that CTLA4-Ig has not only inhibition effect on T-cell activation but also has inhibition effect on osteoclast differentiation by directly affecting osteoclast precursors,[1] therefore analysis of the effect on changes in the bone structural at an actual clinical site has been expected. A novel imaging test method of High Resolution peripheral Quantitative CT (HR-pQCT) can detect fine structure of bones that could not have been detected in the past and it can evaluate not only conditions of joint destruction but also periarticular osteoporosis.
Objectives: To compare the changes in fine articular structure including bone erosion and micro-architecture by ABT and csDMARD in patients with RA using HR-pQCT.
Methods: In this open-label, parallel-group study, twenty patients who started newly csDMARD and 15 patients who started ABT were enrolled. Fine articular structure in 2,3 metacarpal head were assessed by HR-pQCT every 6 month for 12 months. Synovitis was assessed by musculoskeletal ultrasound (MSUS) and magnetic resonance imaging (MRI) of wrist and fingers. We also measured

the bone mineral density (BMD) of lumber spine. The estimated difference in adjusted mean and mean (ABT–csDMARD group) and 95% CIs and P-values were calculated using a linear mixed model with treatment group, allocation factor, baseline disease activity, observation time-point, and treatment group × observation time-point as fixed effect, patients as random effect, and baseline value as covariates.

Results: Baseline characteristics including disease activity were similar between the ABT and csDMARD groups. The mean Δdisease activity scores (DAS)28-ESR from baseline to 12 months were −1.61 (ABT) and −1.71 (csDMARDs). The estimated difference of mean changes in erosion volume, depth and width of 2,3 metacarpal head between ABT and cs DMARDs group were -1.86mm^3, -0.02mm and -0.09mm, respectively (Table 1). During observational period (12 months), only one new erosion detected by HR-pQCT appeared, and 14 erosions were repaired in ABT group, whereas, in csDMARD group, 5 new erosions appeared, and 5 erosions were repaired. Regarding synovitis, changes in synovitis score defined by MSUS and the RA-MRI score (RAMLIS) were similar between these two groups. Compared with patients in the csDMARD group, those in ABT group had better bone micro-architectures improvement (Table 1). In the other hand, % change of BMD of lumbar at 12 months were less improved in ABT group as compared csDMARDs group (0.17%, 1.82%, respectively).

Conclusion: Our results indicated that the ABT could repair bone erosions and had better inhibitory effect of bone erosion, improvement periarticular osteoporosis as compared with csDMARD treatment regardless of improvement of disease activity, synovitis and progress of systemic osteoporosis. Thus, CTLA4-Ig treatment might be beneficial not only in terms of inhibition of bone erosion but also improvement of bone micro-architecture.

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		Estimate difference (ABT group - cs DMRAD group)	95%CI	P value
Bone erosion volume, mm^3	Month 6	-0.97	-3.07-1.13	0.337
	12	-1.86	-4.28-0.56	0.122
Bone erosion depth, mm	Month 6	0.02	-0.20-0.25	0.860
	12	-0.02	-0.30-0.27	0.890
Bone erosion width, mm	Month 6	-0.11	-0.34-0.11	0.293
	12	-0.09	-0.35-0.17	0.476
vBMD of the 2–3 MCP bones, %	Month 6	3.46	-3.97-10.88	0.355
	12	1.22	-7.37-9.81	0.778
BV/TV of the 2–3 MCP bones, %	Month 6	0.62	-0.46-1.71	0.254
	12	0.38	-0.87-1.63	0.548
Tb.Th of the 2–3 MCP bones, %	Month 6	0.88	-2.94-4.70	0.645
	12	-0.45	-4.77-3.88	0.837

BV/TV, trabecular bone volume fraction; Tb.Th, trabecular thickness

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AB0404 DE-ESCALATION OF ANTI-TNFS IN OLDER ADULTS WITH RHEUMATOID ARTHRITIS

Keywords: bDMARD, Tapering, Rheumatoid arthritis

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Background: Biologic disease modifying anti-rheumatic drugs (bDMARDs) such as anti-TNFs improve clinical and radiographic outcomes in rheumatoid arthritis (RA). However, their use is associated with dose- and age-dependent adverse effects including increased risk of serious infections. In recent years, de-escalation (or deprescribing) has been proposed as an approach to reduce polypharmacy and optimize medication use in older adults more prone to the negative, often additive, adverse effects of medications. Current clinical practice guidelines recommend de-escalating bDMARDs in RA patients with low disease activity or in remission. Whether and how bDMARDs are de-escalated in usual care in older adults with RA is poorly understood.

Objectives: To evaluate prevalence and factors associated with anti-TNF de-escalation in older adults with RA.

Methods: In this retrospective observational study using 20% Medicare data from 2009-2017, we identified adults 66 years of age or older with RA, on anti-TNF therapy within 6 months of cohort entry date with at least 6-7 months duration (proxy for stable use). We evaluated the use of five anti-TNFs: Adalimumab, Etanercept, Certolizumab, Golimumab, and Infliximab. Baseline patient characteristics including comorbidity and concomitant use of glucocorticoid (GC) and other DMARDs were collected. Anti-TNF use was categorized as either continuation or de-escalation, identified by dose reduction, dosing interval increase or cessation of use.

Results: We identified 5720 Medicare beneficiaries who met study inclusion criteria. Average age was 74.0 (SD 5.8), 77.9% were female, 83.3% were non-Hispanic white, 26.4% had low-income subsidy, and average Elixhauser comorbidity count was 2.2 (SD 2.0). At baseline, 65.7% had concomitant conventional synthetic DMARD (csDMARD) use and 30.9% were on long-term (≥90 days) GCs. During the study period, one in five de-escalated anti-TNFs (20.1%), of whom 61.3% either reduced dose or increased dosing interval and 38.7% ceased use. Compared to those with continuation of use, de-escalators had more concomitant csDMARD use (60.0% versus 56.5%) and less long-term GC use (26.6% vs 30.9%). In multivariable analyses, de-escalation was less likely in those with low-income subsidy (HR 0.70, 95% CI 0.60-0.82, p<0.0001), adjusting for patient age, sex, race/ethnicity, and comorbidity as a time-varying variable (Table 1).

Conclusion: Anti-TNFs are de-escalated in one in five older adults with RA in usual care. Further study is needed to evaluate impact of de-escalation on RA outcomes.

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Table 1. Factors associated with de-escalation of anti-TNFs in older adults with RA enrolled in fee-for-service Medicare

Variables	HR (95% CI) N=5720			
	Unadjusted	P-value	Adjusted	P-value
Age at index	0.99 (0.98, 1.00)	0.26	0.99 (0.98, 1.00)	0.23
Female	1.00 (0.87, 1.15)	0.98	1.05 (0.92, 1.21)	0.46
Race				
White (ref)	-		-	
Black	0.89 (0.69, 1.16)	0.39	1.01 (0.77, 1.32)	0.95
Hispanic	0.99 (0.80, 1.24)	0.98	1.22 (0.96, 1.55)	0.098
Other	0.64 (0.46, 0.90)	0.010	0.74 (0.52, 1.04)	0.079
Low Income Subsidy	0.72 (0.63, 0.83)	<0.0001	0.70 (0.60, 0.82)	<0.0001
Comorbidities (time-varying)	1.00 (0.98, 1.02)	0.87	1.01 (0.99, 1.04)	0.31

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Disclosure of Interests: None Declared.

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AB0405 NO DIFFERENCE IN RISK OF MYOCARDIAL INFARCTION AMONG PATIENTS RECEIVING EITHER IL6 OR TNF INHIBITORS FOR RHEUMATOID ARTHRITIS

Keywords: Cardiovascular disease, bDMARD, Rheumatoid arthritis

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Table MI in RA patients treated with IL-6i or TNFi

	n	Person-years	Events	IR per 1000 person year (95% CI)	Crude HR (95% CI)	PS Adjusted HR (95% CI)
All lines of therapy						
TNFi	26,744	110,981	379	3.41 (3.09, 3.78)	Ref	Ref
IL-6i	3,278	8,816	30	3.40 (2.38, 4.87)	0.93 (0.64, 1.35)	0.87 (0.56, 1.37)
First line						
TNFi	16,383	71,654	244	3.41 (3.00, 3.86)	Ref	Ref
IL-6i	352	1,057	4	3.78 (1.42, 10.08)	1.04 (0.39, 2.80)	1.26 (0.46, 3.41)
Second line						
TNFi	7666	31,473	102	3.24 (2.67, 3.94)	Ref	Ref
IL-6i	749	1,899	4	2.11 (0.79, 5.61)	0.59 (0.22, 1.61)	0.64 (0.23, 1.76)
Third line						
TNFi	1,718	5,652	26	4.60 (3.13, 6.76)	Ref	Ref
IL-6i	1,059	2,838	11	3.88 (2.15, 7.00)	0.79 (0.38, 1.60)	0.80 (0.37, 1.70)
Fourth line and above						
TNFi	977	2,203	7	3.18 (1.51, 6.67)	Ref	Ref
IL-6i	1,118	3,023	11	3.64 (2.92, 6.57)	1.16 (0.45, 3.01)	0.90 (0.33, 2.47)

*Baseline variables used for propensity score adjustment: age, gender, time between BSRBR-RA registration and drug start, DAS28, disease duration, RF status, smoking history, BMI, current methotrexate, total number of prior csDMARDs, line of therapy (only in analyses of all LoTs), prior use of TNFi (not in analyses of first LoT only), prior use of IL6i (not in analyses of first or second LoT only), current use of steroids, ever use of antiplatelet or anticoagulant drugs; history of: hypertension, dyslipidaemia, diabetes, lung disease, renal disease, depression, cancer, venous thromboembolism, ischemic heart disease (myocardial infarction and angina), stroke

Background: Interleukin 6 inhibitors (IL-6i) can increase LDL cholesterol levels, which raises concerns about the risk of myocardial infarction (MI) in patients with rheumatoid arthritis (RA) receiving this therapy.
Objectives: This study aims to compare the risk of MI between people with RA in the UK clinical setting receiving IL-6i or tumour necrosis factor inhibitors (TNFi) overall or by line of therapy (LoT).
Methods: Patients with RA registered between 01/10/2001 and 30/05/2022 with BSRBR-RA starting IL-6i or TNFi treatments were included. Occurrence of MI was identified from clinical follow-up forms and through cause of death reported by the national UK death register. Only those MIs occurring whilst patient was actively receiving drug were included. The risk of MI in patients receiving IL6i compared to TNFi was compared using Cox regression, adjusted for baseline co-variates using propensity scores (PS, see Table 1). Follow-up commenced at the start of the drug of interest and patients were censored at occurrence of MI, death, discontinuation of therapy or last follow-up visit, whichever came first. Multiple imputation was used for missing data. To account for known differences in LoT use of TNFi and IL6i (with IL6i more likely as a later line bDMARD), overall analyses adjusted for LoT in PS and secondary analyses by LoT were conducted. Direct switches between originator to biosimilars were considered the same treatment.
Results: A total of 30,022 IL6i or TNFi LoTs in 20,898 patients were included (3,278 IL-6i; 26,744 TNFi), representing 119,797 person-years of exposure. Compared to patients receiving TNFi, patients starting IL-6i treatment were older, had longer disease duration, less likely to use methotrexate and steroids, and had more comorbidities. During follow-up, 409 MIs occurred, 30 on IL-6i and 379 on TNFi. After PS adjustment, the risk of MI was not significantly different between the two treatment overall (HR 0.87, 95% CI 0.56-1.37) or when stratified by LoT (Table 1).
Conclusion: This study could not identify any difference in risk of MI between IL-6i and TNFi treatment after patient characteristics and LoT were considered.
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AB0406

EFFICACY OF TNF-ALPHA INHIBITORS IN MANAGEMENT OF IMMUNE CHECKPOINT INHIBITOR RELATED ARTHRITIS

Keywords: Malignancy, Inflammatory arthritides, bDMARD

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Background: Use of immune checkpoint inhibitors (ICI) has revolutionised management of multiple malignancies but may be complicated by development of immune-related adverse events including inflammatory arthritis. Once triggered, arthritis may persist, with 50% patients having ongoing symptoms even 1 year after stopping ICI treatment. EULAR guidance, based on small retrospective and prospective studies and case reports, recommends treatment with corticosteroids, with escalation to DMARDs particularly where arthritis remains active at doses of prednisolone >10mgs [1]. There is some evidence to support use of biologic DMARDs in management, but a lack of studies using validated rheumatology scoring tools to objectively assess ICI arthritis response to biologic agents [2-4].
Objectives: The aim of this study was to assess efficacy of TNF-alpha inhibitors in ICI arthritis, using change in Clinical Disease Activity Index (CDAI) as an outcome measure. The CDAI was chosen as it is independent of ESR and CRP which may be influenced by other complications of malignancy and its treatment.
Methods: This was a single centre retrospective study of 65 patients referred with musculoskeletal symptoms following use of an ICI. Patients with ICI arthritis treated with a TNF-alpha inhibitor were identified and their notes systematically reviewed for information about malignancy diagnosis, use of ICI, presentation with inflammatory arthritis and its response to treatment, with arthritis activity monitored using the CDAI.
Results: 40 of the 65 patients referred presented with an inflammatory arthritis and 9 were treated with a TNF-alpha inhibitor to manage arthritis. These included 4 male and 5 female patients, with mean age 65 years. 5 patients had melanoma, 2 renal cell cancer, 1 mesothelioma and 1 gall bladder adenocarcinoma. All 9 patients had received treatment with a PD-1/PDL-1 inhibitor, with 5 patients also receiving a CTLA-4 inhibitor. 1 patient had a prior diagnosis of psoriatic arthritis and 1 had a prior diagnosis of rheumatoid arthritis. Both experienced increased arthritis activity following ICI treatment. The remaining 7 patients developed new onset polyarthritis following ICI treatment, with 1 of 7 being anti-CCP and RF positive. Prior to use of a TNF-alpha inhibitor, all 9 patients had received treatment with prednisolone. 4 patients had been treated with methotrexate, of whom 3 had also had sulfasalazine. 6 of 9 patients received adalimumab as a first biologic, with the other 3 receiving infliximab. CDAI prior to use of a TNF-alpha inhibitor ranged from 20 to 62, with a mean of 32.8. 2 patients had moderate disease activity (CDAI>10 and ≤22) and 7 patients had high disease activity (CDAI>22). The CDAI at follow up ranged from 4 to 31 with a mean of 13.2. 5 patients had low disease activity (CDAI≤10), 4 patients had moderate disease activity and 2 patients had high disease activity at this time. Use of a TNF-alpha inhibitor was associated with a clinically meaningful improvement in CDAI in 8 of 9 patients at follow up after a mean of 11 weeks of treatment, including 1 patient who continued with ICI treatment.
Conclusion: This single centre retrospective study suggests efficacy of TNF-alpha inhibitors in management of ICI arthritis. Similar to previous work, this study is small and limited by lack of a control cohort but has the advantage of using a validated rheumatology scoring tool to confirm changes in arthritis activity. TNF-alpha inhibitors have a shorter time to onset of action than csDMARDs and so offer an opportunity for early control of ICI arthritis, with potential for use in parallel with continued ICI treatment if needed for management of the underlying malignancy.
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AB0407

IMPACT OF SEROPOSITIVITY ON DRUG RETENTION OF BIOLOGICS AND JAK INHIBITORS -THE ANSWER COHORT STUDY

Keywords: bDMARD, Rheumatoid arthritis, Biomarkers

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Background: 2022 EULAR recommendation announced that biological disease-modifying antirheumatic drugs (bDMARDs) and janus kinase inhibitors (JAKi) are considered in the phase IItreatment of rheumatoid arthritis (RA). On the other hand, serum rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (ACPA) titer are reported to affect bDMARDs and JAKi efficacy. However, we still lack reliable evidence of the impact of RF and ACPA titer on these agents' retention, which may reflect both effectiveness and safety.

Objectives: The aim of this multicenter (7 university-related hospitals)[1,2], retrospective study was to clarify the impact of RF or ACPA titer on treatment retention of bDMARDs and JAKi in patients with RA, which may be useful for adequate treatment selection in a real-world setting.

Methods: This study assessed 5,343 treatment courses of bDMARDs and JAKi introduced from 2001 to 2022 (TNF inhibitors [TNFi]=2,724, anti-IL-6 receptor antibody [aIL-6R]=1,227, cytotoxic T lymphocyte-associated antigen-4-Ig [CTLA4-Ig]=906, JAKi=486; bDMARDs/JAKi naive cases 50.6%, baseline age 60.0 years, female 83.5%, disease duration 10.3 years, DAS28-ESR 4.3, RF positivity 78.3%, ACAP positivity 82.8%, combined methotrexate [MTX] dose 8.4mg/week [47.8%], and prednisolone [PSL] dose 5.9mg/day [28.2%]). Patients were classified into three groups according to their serum RF (IU/mL) and ACPA (U/mL) titer: negative (RF<15 or ACPA<4.5), low positive (15≦RF<100 or 4.5≦ACPA<100), or high positive (100≦RF or 100≦ACPA), respectively. Reasons for discontinuation were classified into four categories by each attending physician: 1) lack of effectiveness (primary and secondary), 2) toxic adverse events (infection, malignancies, and cardiovascular events, et al.), 3) non-toxic reasons (patient preference and pregnancy, et al.), and 4) remission. Retention rates of each discontinuation reason were estimated at 24 months using the Kaplan-Meier method and adjusted for potential clinical confounders (age, sex, concomitant PSL and MTX, switched number of bDMARDs or JAKi, and prior use of TNFi, aIL-6R, CTLA4-Ig, or JAKi) using Cox proportional hazards modeling.

Results: Adjusted discontinuation rates for each reason were as follows: due to lack of effectiveness was aIL-6R=21.4%, JAKi=27.1%, CTLA4-Ig=30.4%, and TNFi=36.2% (Cox P<0.001 between 4 groups), due to toxic adverse events was CTLA4-Ig=12.1%, aIL-6R=12.5%, TNFi=13.3%, and JAKi=14.6% (Cox P=0.369 between 4 groups). When categorized by RF (Figure 1a), adjusted discontinuation rates due to lack of effectiveness were listed in ascending order as follows, respectively; RF negative (aIL-6R, 16.2%; TNFi, 30.5%; CTLA4-Ig, 33.8%; JAKi, 39.9%; Cox P<0.001), low positive (aIL-6R, 19.6%; JAKi, 21.7%; CTLA4-Ig, 26.6%; TNFi, 29.9%; Cox P<0.001) and high positive (aIL-6R, 25.4%; JAKi, 28.1%; CTLA4-Ig, 31.2%; TNFi, 38.6%; Cox P<0.001). When categorized by ACPA (Figure 1b), discontinuation rates due to lack of effectiveness were listed in ascending order as follows, respectively; ACPA negative (aIL-6R, 20.9%; TNFi, 28.8%; JAKi, 30.7%; CTLA4-Ig, 43.4%; Cox P<0.001), low positive (aIL-6R, 19.2%; JAKi, 26.4%; CTLA4-Ig, 27.3%; TNFi, 33.6%; Cox P<0.001) and high positive (aIL-6R, 23.1%; JAKi, 25.6%; CTLA4-Ig, 29.7%; TNFi, 35.2%; Cox P<0.001).

Conclusion: Considering lack of effectiveness, aIL-6R showed highest continuation rates compared to other agents regardless of RF/ACPA positivity or titer levels. On the other hand, CTLA4-Ig and JAKi showed higher continuation rates, although TNFi showed lower continuation rates in RF/ACPA-positive (low or high titer) cases compared with RF/ACPA-negative cases.

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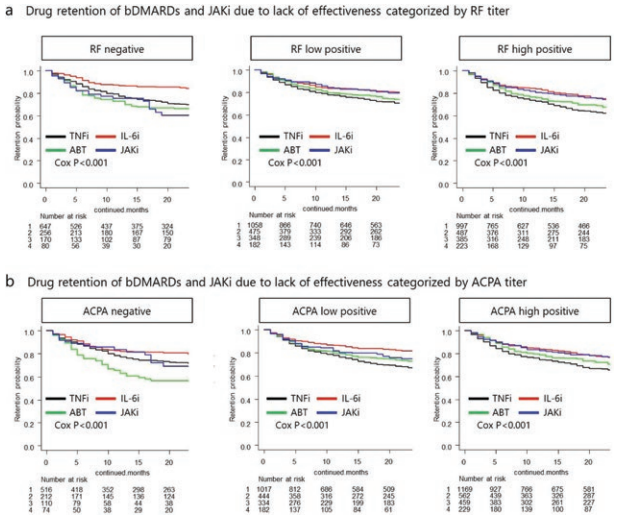


Figure 1.

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AB0408

DESCRIPTIVE STUDY ON USE OF BIOSIMILARS IN RHEUMATOID ARTHRITIS IN UNIVERSITY HOSPITALS PLYMOUTH, UNITED KINGDOM

Keywords: Descriptive Studies, Real-world evidence, bDMARD

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown etiology marked by a symmetric, peripheral polyarthritis. Treatment of RA should be aimed at reaching a target of sustained remission or Low Disease Activity (LDA) in every patient. [1] Given the heterogenicity of the disease, there are multiple disease modifying anti rheumatoid drugs (DMARDs) available including biologics and biosimilars with different modes of action to achieve disease remission or low disease activity. A biosimilar medicine is a biological medicine manufactured to be similar to an existing licensed "reference" biological medicine, with no meaningful differences from reference medicine in terms of quality, safety or efficacy. However, it has been observed significant number of patients going back on bio-originator drugs complaining either side effects or less efficacy of biosimilar. This study is aimed at looking at real rate of bio-similar (BS) switching back to bio- originator (BO) due to various reasons.

OBJECTIVES:

1)To look for rate of switching back to bio-original and reasons behind
2)Biosimilar persistence rate in RA and side effect profile
3)To look for any association between concurrent use of methotrexate with biosimilar persistence rate.

Methods: Descriptive study was done at department of rheumatology University Hospitals Plymouth (UHP). All patients with the diagnosis of Rheumatoid arthritis, treated with biological DMARDs were screened till October 2019. Data were gathered about switching back to BO from BS and if switched reason for switch, persistence rate of biosimilar, duration of biosimilar, disease activity measured by DAS 28 before and 6 weeks after biosimilar, side effects and concurrent use of methotrexate with biosimilar. Data were analyzed as percentages and chi-square is used to find associations.

Results: Total number of 590 patients with RA on biological DMARDs were screened. Most popular first choice of BS was etanercept (318) followed by rituximab (177), adalimumab (85) and infliximab [9]. Only 19 patients out of 318(5.9%) patients treated with etanercept BS went back to BO due to inefficacy and side effects. 222/318 (69.8%) remained on etanercept. Switching back rate of adalimumab BO was only 9.4% (8/85) while 73% remained on adalimumab BS. (62/85). For rituximab, 9 out of 177 (5.08%) patients went back to original; 6 due to inefficacy and 3 side effects. 147/177(83.05%) remained on BS rituximab. Only one patient out of 9 treated with infliximab went back on original drug due to inefficacy. Commonly observed side effects of BS are infections, allergic reactions, and gastrointestinal disturbances. Average DAS 28 score difference after 6 weeks of commencement of BS was calculated only for adalimumab and etanercept. There was 2.27 reduction of DAS 28 in adalimumab group (from 5.22 to 2.95) while the reduction was 1.67 for etanercept group (from 5.14 to 3.47). Looking at association between persistence rate of BS and concurrent use of methotrexate, only RA etanercept group showed a significant association with a *p value* of 0.000041.

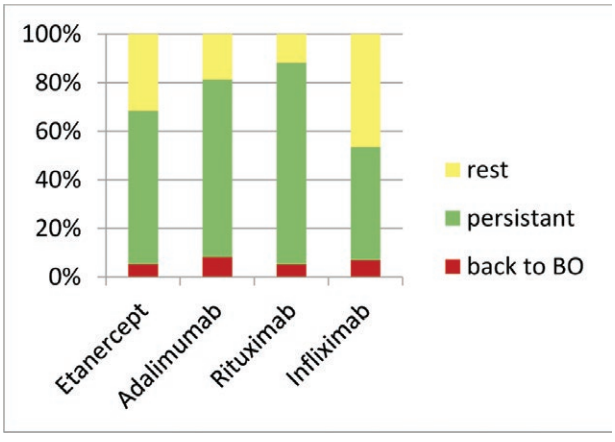


Figure 1.

Conclusion: Significant number of patients with RA are treated with biosimilar in UHP. Re switching to bio-originator is not very commonly seen. Most of the patients could tolerate biosimilar well and persistence rate is impressively high with good response reflected by reduction of average disease activity in studied cohorts. Among side effects infection, allergic reaction and GI side effects are common. Concurrent use of methotrexate showed positive correlation with persistent rate of biosimilar only in one group (RA treated with etanercept) but not others, hence does not give strong ground to the hypothesis that methotrexate minimizes immunogenicity for biosimilar.

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AB0409

TIME TO FIRST REMISSION AND PREVALENCE OF SUSTAINED REMISSION AFTER ETANERCEPT BIOSIMILAR (ETA-B) OR ORIGINATOR (ETA-O) INITIATION IN RHEUMATOID ARTHRITIS (RA)

Keywords: Real-world evidence, bDMARD, Rheumatoid arthritis

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Background: The first biosimilar etanercept (ETA-B) was approved in Canada in 2016, but real-world data comparing the effectiveness of ETA-B versus their equivalent originator (ETA-O) remains scarce.

Objectives: To compare time to remission throughout follow-up and sustained RA remission in the first 12 months.

Methods: We studied etanercept-naïve RA patients starting ETA-B or ETA-O between January 2015 and May 2022 from three prospective research cohorts related to the Early Undifferentiated Polyarthritis (Sherbrooke), RA Pharmacovigilance Program and Outcomes Research in Therapeutics (Edmonton), and RHUMADATA™ (Montreal) registries. We restricted analyses to RA patients with at least one follow-up visit after treatment initiation and with enough data to calculate remission. Remission was defined as Disease Activity Score 28-CRP or -ESR ≤2.6, Simplified Disease Activity Index ≤ 3.3, or Clinical Disease Activity Index ≤ 2.8. We used Cox regression to compare ETA-B versus ETA-O regarding time to first remission during follow-up (among those without remission at baseline) and logistic regression to assess sustained remission (remission in two consecutive visits) in the first 12 months of follow-up. Models were adjusted for sex, age, body mass index (BMI), RA duration, and smoking status at cohort entry. We also adjusted for high/moderate disease activity and the use of corticosteroids, methotrexate (MTX), or hydroxychloroquine (HCQ), all at etanercept initiation.

Results: We studied 150 RA patients initiating etanercept (65% on the biosimilar) between 2015-2022. Sex distribution was similar among ETA-B and ETA-O, but the biosimilar group has a longer disease duration and moderate/higher disease activity at baseline. Among 125 participants without remission at baseline, the median time to first remission was 8.7 months with ETA-B versus 14.5 with ETA-O. In the multivariate analysis (Table 1A), we were unable to detect a clear difference in time to achieve first remission when comparing ETA-B to ETA-O (hazard ratio, HR = 1.43, 95% confidence interval, CI 0.65-3.13). Obesity (BMI>30) was negatively associated with the outcome. Sustained remission in the first 12 months of follow-up was observed in 16.3% of ETA-B initiators versus 17.3% with ETA-O. After multivariate analysis (Table 1B), we were unable to establish any clear difference between ETA-B versus ETA-O (OR 1.16, 95% CI 0.31-4.74). HCQ was positively associated with sustained remission within the first 12 months.

Conclusion: In this pooled analysis of three Canadian RA cohorts, we were unable to detect clear differences in achievement or sustained remission when comparing ETA-B and ETA-O.

Table 1. – Cox proportional hazard ratios (HR) for time to remission and logistic regression model for sustained remission within first 12 months.

Baseline characteristics	Time to remission		Sustained remission (12 months)	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)[a]	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]
Biosimilar etanercept (versus originator)	1.10 (0.69, 1.74)	1.43 (0.65, 3.13)	0.93 (0.39-2.37)	1.16 (0.31-4.74)
Female sex	0.76 (0.46, 1.26)	1.03 (0.46, 2.31)	2.63 (0.84-11.6)	3.35 (0.68-25.8)
Age at RA diagnosis	1.00 (0.98, 1.01)	0.97 (0.95, 1.00)	0.98 (0.96-1.01)	1.00 (0.95-1.05)
Disease duration	0.99 (0.96, 1.01)	0.98 (0.94, 1.01)	0.97 (0.91-1.02)	0.98 (0.90-1.05)
Obese (Body mass index>30)	0.54 (0.28, 1.03)	0.52 (0.25, 0.96)	0.43 (0.13-1.25)	0.40 (0.10-1.40)
Current smoker	0.63 (0.31, 1.26)	0.40 (0.14, 1.21)	1.37 (0.42-3.91)	0.89 (0.18-3.71)
Moderate or high disease activity	0.64 (0.39, 1.04)	0.59 (0.26, 1.37)	1.38 (0.51-4.40)	3.82 (0.57-76.5)
Prednisone**	0.88 (0.53, 1.47)	1.04 (0.47, 2.28)	1.28 (0.48-3.18)	1.28 (0.31-4.95)
Methotrexate	1.07 (0.67, 1.69)	0.90 (0.42, 1.93)	2.01 (0.81-5.50)	2.44 (0.63-11.1)
Hydroxychloroquine	1.70 (1.05, 2.73)	1.88 (1.00, 4.51)	5.00 (1.78-17.9)	4.54 (1.00-34.9)

[a] Adjusted for all variables shown. *At etanercept initiation (unless otherwise specified) **Baseline current drugs

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AB0410 OBESITY AND ADIPOSE TISSUE CYTOKINES IN RHEUMATOID ARTRHITIS: DOES THE ROUTE OF ADMINISTRATION OF THE IL6 INHIBITORS MATTER?

Keywords: bDMARD, Rheumatoid arthritis, Comorbidities

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Background: Obesity has been associated with the response to biologic disease modifying anti-rheumatic drugs (bDMARDs). Obese patients have lower response to anti-TNF drugs than to other cytokine-targeted drugs, such as anti-IL6[1]. IL6 receptor inhibition is effective in the treatment of rheumatoid arthritis (RA), and there are two ways of administration: intravenous (IV) weight-adjusted tocilizumab and subcutaneous (SC) fixed-dose tocilizumab or sarilumab. However, evidence regarding the influence of body mass index (BMI) and these different routes of administration is still scarce.

Objectives: To analyze the role of BMI in the clinical response to antiIL6 therapy in its different routes of administration in patients with RA. To perform an in-depth analysis of the pathophysiology of obesity by assessing serum adipokine levels and their potential changes according to treatment.

Methods: This study involved 65 patients with RA starting IV tocilizumab at 8mg/kg every 4 weeks or SC antiIL6: tocilizumab 162mg/week or sarilumab 200mg/14days. Demographic and clinical characteristics before antiIL6 initiation (age, sex, smoking habit, age at diagnosis, concomitant and previous treatments and BMI) were collected. Laboratory parameters such as rheumatoid factor and anti-citrullinated peptide antibody were also assessed. Adipokine serum levels (leptin and adiponectin) were measured at baseline and after 6 months (6M) of treatment. Clinical response to treatment was assessed by Clinical Disease Activity Index (CDAI) 6M after initiation of the bDMARD. Differences between variables were assessed using the X2 test and Mann-Whitney test. Correlations between BMI, adipokines and other quantitative variables were assessed using the Pearson or Spearman coefficients. P-values <0.05 were considered statistically significant.

Results: Forty seven patients started IV antiIL6 (72.3%) and 18 SC (27.7%). Thirty six (55.4%) achieved low disease activity (LDA)/remission by CDAI: 24 patients from the IV group (51.4%) and 12 (66.7%) from the SC group without significant differences (p=0.19). No differences between BMI or serum adipokine levels were associated with the achievement of LDA/remission when patients were stratified according to the route of antiIL6 administration. Leptin levels in both groups (SC and IV) were very similar at baseline and 6M and regarding changes on adipokine profile between baseline and 6M, we observed a decrease in leptin and an increase in adiponectin levels both in SC and IV (Table 1).

	Serum adipokine levels (ng/mL)			
Route of administration		baseline	6 months	p
iv	Leptin	18.6 (10.4-30.9)	16.9 (7.2-29.2)	0.22
	Adiponectin	18310(13250-33890)	20610 (12690-33650)	0.39
sc	Leptin	17.9 (10.1-27.4)	16.3 (7.6-30.7)	0.22
	Adiponectin	28750 (20570-4394)	33350 (24157-49862)	0.35

BMI showed a significant positive correlation with leptin, overall and stratifying by route of administration, both at baseline and 6M. Adiponectin did not show a significant correlation with BMI.

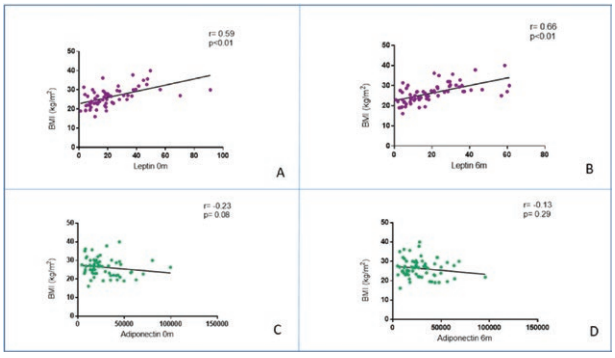


Figure 1.

Conclusion: Obesity and serum adipokines did not show association with the achievement of LDA/remission in patients treated with antiIL6 regardless the route of administration. Furthermore, IV and SC treatments could be used both in obese and normal-weight RA patients expecting the same efficacy.

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AB0411 ASSOCIATION BETWEEN ETHNICITY AND INITIAL RESPONSE TO TNF INHIBITORS IN PEOPLE WITH RHEUMATOID ARTHRITIS: RESULTS FROM THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTER FOR RHEUMATOID ARTHRITIS (BSRBR-RA)

Keywords: Rheumatoid arthritis, Epidemiology, bDMARD

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Department, Glasgow, United Kingdom; [8]*University of Sheffield, School of Health and Related Research, Faculty of Medicine, Dentistry and Health, Sheffield, United Kingdom*; [9]*Manchester University NHS Trust, NIHR Manchester Biomedical Research Centre, Manchester, United Kingdom*

Background: Little is known about the association between ethnicity and response to TNF inhibitors (TNFi) in people with rheumatoid arthritis (RA).
Objectives: This study examines the association between self-reported ethnicity and DAS28 response after 6 months of treatment in patients starting their first TNFi using data from the British Society for Rheumatology Biologics Register for RA.
Methods: 14133 RA patients with self-reported ethnicity starting their first TNFi were included. Due to a very low proportion of non-white patients, ethnicity was divided into white or non-white for analysis. Outcomes included the change in disease activity using DAS28, the proportion of patients who achieved DAS28 remission and EULAR response at month 6. Adjusted regression models appropriate to outcome were used to compare between the two groups. Multiple imputation was used to account for missing data.
Results: Of 14133 patients starting TNFi with recorded ethnicity, only 607 (4.3%) recorded themselves as non-white (389 Asian, 134 Black, 57 Mixed ethnicity and 27 other) (Table 1). At start of TNFi, non-white patients were younger (non-white vs. white: mean 51 vs. 57 years; p<0.001), with shorter disease duration (median 8 vs. 10 years; p<0.001), higher proportion of females (86% vs. 76%; p<0.001) and fewer current cigarette smokers (9% vs. 20%; p<0.001). Non-white patients had lesser improvement in DAS28 at month 6 (adjusted regression coefficient (95% confidence interval (95%CI)): 0.3 (0.04-0.5)). However, using the white patients as a reference, non-white patients were not associated with the achievement of DAS28 remission (adjusted odds ratio (95%CI): 0.7 (0.5-1.1)) or EULAR response (aOR (95%CI): 0.8 (0.7-1.0)) at month 6.

	White	Non-white	p
N	13515	607	
Age	57.0±12.0	51.4±12.3	**<0.001**
Female (%)	10262 (75.9%)	520 (85.7%)	**<0.001**
Ethnicity (%)			
White	13515 (100%)	-	
Black	-	134 (22.1%)	
Asian	-	389 (64.1%)	
Mixed ethnicity	-	57 (9.4%)	
Other	-	27 (4.4%)	
Disease duration (years)	10 (4-18)	8 (4-15)	**<0.001**
RF positive (%)	8341 (61.7%)	390 (67.5%)	0.08
DAS28	6.4±1.1	6.4±1.1	0.4
Tender joints	15 (10-21)	15 (9-21)	0.6
Swollen joints	10 (6-14)	9 (6-13)	**<0.001**
VAS	75 (61-86)	75 (61-88)	0.9
ESR	35 (19-58)	41 (25-65)	**<0.001**
CRP	24 (10-53)	19 (8-41)	**0.005**
HAQ	1.9±0.6	1.9±0.7	0.4
Biologic treatment (%)			
Adalimumab	4107 (30.4%)	165 (27.2%)	0.1
Certolizumab	875 (6.5%)	50 (8.2%)	
Etanercept	5322 (39.4%)	238 (39.2%)	
Infliximab	3211 (23.8%)	154 (25.4%)	
Concomitant csDMARDs (%)	7595 (56.2%)	340 (56%)	0.9
Methotrexate (%)	5512 (40.8%)	243 (40.0%)	0.7
Concomitant glucocorticoids (%)	5017 (37.1%)	199 (32.8%)	**0.03**
Current cigarette smoking (%)	2698 (20.0%)	57 (9.4%)	**<0.001**
Response to first-line TNFi at month 6			
DAS28 at month 6	4.7±1.8	5.0±1.8	**0.02**
ΔDAS28*	1 [reference]	0.3 [0.04-0.5]	**0.02**
DAS28 remission (%)	13%	11%	0.1
Odds of DAS remission*	1 [reference]	0.7 [0.5-1.1]	0.1
Good EULAR response (%)	18.2%	16.5%	
Moderate EULAR response (%)	33.7%	33.2%	
Odds of achieving higher EULAR response*	1 [reference]	0.8 [0.7-1.0]	

Data is expressed as mean±SD, median (interquartile range), number (percentage), adjusted regression coefficient [95% confidence interval] or adjusted odds ratio [95% confidence interval].*Adjusted for baseline age, gender, disease duration, concomitant csDMARDs, concomitant steroid, rheumatoid factor status, cigarette smoking status, DAS28 and HAQ

Conclusion: Recruitment to the BSRBR-RA of non-white patients was exceptionally low compared to expected population distribution – the reasons for this are not immediately evident. Among those recruited, there were no significant differences observed in initial treatment response although non-white patients were younger, more likely to be female, had shorter disease duration and less likely to be smokers. Further evaluation into both ways to increase representativeness in our national RA treatment register and influence of ethnic differences on longer term outcomes with biologic therapies is warranted.
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AB0412

COMPARISON OF THE EFFICACY AND SAFETY OF A PROPOSED BIOSIMILAR MSB11456 WITH TOCILIZUMAB REFERENCE PRODUCT IN MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS: RESULTS OF A RANDOMIZED DOUBLE-BLIND STUDY

Keywords: Rheumatoid arthritis, Randomized control trial, bDMARD

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Background: MSB11456 is a biosimilar to currently marketed originator tocilizumab. It has demonstrated pharmacologic, safety and immunogenic similarity to the US-licensed and EU-approved tocilizumab in healthy subjects.
Objectives: To evaluate the efficacy, immunogenicity and safety of MSB11456 versus EU-approved tocilizumab in patients with moderate to severe rheumatoid arthritis (RA) who had experienced inadequate clinical response to ≥1 disease-modifying antirheumatic drug and were receiving a stable dose of methotrexate.
Methods: Patients were randomised to double-blind subcutaneous injections of 162 mg MSB11456 or EU-approved tocilizumab for 24 weeks (W). At W24, patients receiving EU-approved tocilizumab were re-randomized to continue their treatment or to switch to MSB11456 up to W52. Those receiving MSB11456 continued MSB11456 for the 52W. Primary efficacy endpoint - change from baseline in Disease Activity Score-28 Joint Count (DAS28)-erythrocyte sedimentation rate (ESR) at W24 - was analysed using analysis of covariance to determine the least squares mean (LSM) difference between MSB11456 and EU-approved tocilizumab; MSB11456 was considered equivalent to EU-approved tocilizumab if the 95% confidence interval (CI) for this difference was entirely within the equivalence interval -0.6 to 0.6. Secondary endpoints were 20% improvement in American College of Rheumatology core set measures (ACR20) at W24 and DAS28-ESR at W12. Additional endpoints included ACR50/70, change in DAS28-C-reactive protein (CRP), Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI) at various time points up to W52, and evaluation of immunogenicity and safety. Results up to W24 are presented.
Results: Clinically relevant LSM decreases from baseline in DAS28-ESR were observed at W24 with MSB11456 and EU-approved tocilizumab (Table 1). As the 95% CI for the LSM difference in the change from baseline in DAS28-ESR between treatments was fully included within the predefined equivalence interval, therapeutic equivalence of MSB11456 and EU-approved tocilizumab was demonstrated. All sensitivity and other efficacy endpoint analyses supported

this finding. Immunogenicity results were similar in both treatment groups. Treatment-emergent adverse events (TEAEs) were usually mild or moderate and occurred at similar frequency with both drugs. There were no discernible patterns in terms of the nature, frequency or other characteristics of serious or treatment-related TEAEs to suggest a difference between drugs.

Conclusion: Equivalent efficacy, immunogenicity and safety at W24 of MSB11456 and EU-approved tocilizumab was demonstrated in patients with moderate to severe RA. Pharmacological and clinical similarity of these drugs was supported, therefore MSB11456 can be considered as biosimilar to EU-approved tocilizumab.

Efficacy endpoints – ITT	MSB11456 (N=302)	EU-approved tocilizumab (N=302)
DAS28-ESR change from baseline at W24, LSM (SE)[a]	-3.53 (0.11)	-3.54 (0.11)
LSM difference (95% CI)[a]	0.01 (-0.16, 0.18)	
ACR20 at W24, n (%)	244 (80.8)	256 (84.8)
Difference (95% CI)[b]	-3.94 (-9.97, 2.11)	
DAS28-ESR change from baseline at W12, LSM (SE)[a]	-3.13 (0.10)	-3.12 (0.10)
LSM difference (95% CI)[a]	0.01 (-0.21, 0.19)	
DAS28-CRP change from baseline at W24, mean (standard deviation)	-2.85 (1.22)	-2.88 (1.11)
ACR50 at W24, n (%)	183 (60.6)	188 (62.3)
ACR70 at W24, n (%)	118 (39.1)	116 (38.4)
DAS-ESR remission or LDA at W24, n/N (%)	182/277 (65.7)	191/285 (67.0)
DAS-CRP responder at W24, n/N (%)	46/276 (16.7)	55/285 (19.3)
CDAI remission or LDA at W24, n/N (%)	172/278 (61.9)	177/286 (61.9)
SDAI remission or LDA at W24, n/N (%)	174/276 (63.1)	181/285 (63.5)

[a]ANCOVA (analysis of covariance) model with fixed effects for treatment and previous biologic for RA exposure and baseline DAS28-ESR as covariate[b]95% stratified Newcombe CI adjusting for previous biologic for RA exposureITT, intent to treat; LDA, low disease activity; SE, standard error

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AB0413 COMPARISON OF THE EFFECTS OF TOCILIZUMAB AND TNF-A INHIBITORS ON HEMOGLOBIN AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS WITH ANEMIA

Keywords: bDMARD, Rheumatoid arthritis

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Background: Rheumatoid arthritis is a systemic disease with various extra-articular symptoms. Anemia is common comorbidity of RA.

Objectives: The purpose of this study is to compare the effect of tocilizumab and TNF-α inhibitors on hemoglobin changes and disease activity changes in RA patients. This study aims to determine whether tocilizumab is more effective in controlling hemoglobin elevation and disease activity in patients with anemia.

Methods: The data in this study derived from the Korean College of Rheumatology Biologics (KOBIO) registry. OF the patients registered in KOBIO registry, patients using tocilizumab and TNF-α inhibitors were enrolled in this study. To exclude the effects of previously used biologic DMARDs, patients who started the first biologic DMARDs and have been using one biologic DMARD for more than 1 year were included in this study. Anemia was defined as Hb levels <12.0g/dL in women and <13.0g/dL in men according to the World Health Organization (WHO) criteria at index date.

Results: Among rheumatoid arthritis patients with anemia, there were 126 patients in the tocilizumab group and 248 patients in the TNF-α inhibitor group. Initial and follow-up data collected after 1 year of biologic use were analyzed. After initiation of treatment, Hb and Hct were significantly elevated in tocilizumab group. Mean increases in Hb and Hct were 1.56 and 3.53 in tocilizumab group, 1.02 and 2.64 in TNF-α inhibitor group. DAS28-ESR and RAPID3 decreased significantly in tocilizumab group after using biologics. In tocilizumab group, DAS28-ESR decreased by 3.35 and RAPID3 decreased by 8.31. The changes in SJC, PGA, PhGA, SDAI and CDAI were not different between the two groups. Multivariate analysis was performed using the TNF-α inhibitor group as a control. Tocilizumab was more effective than TNF-α inhibitors in increasing Hb.

Conclusion: In RA patients with anemia, although tocilizumab was more effective than TNF inhibitors in increasing Hb, there was no difference between the two drugs in controlling disease activity. During the course of this research, the results of the DAS28-ESR and other outcome measures did not match. In patients treated tocilizumab, assessment of disease activity using the DAS28-ESR may be overestimated due to its effect on acute phase reactant values.

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AB0414 FACTORS PREDICTING THE INITIATION OF BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS FOR RHEUMATOID ARTHRITIS WITHIN THE FIRST THREE YEARS OF DIAGNOSIS

Keywords: bDMARD, Rheumatoid arthritis

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Background: Factors related to the use of biologic disease modifying anti-rheumatic drugs (bDMARDs) in rheumatoid arthritis (RA) have varied in prior studies.

Objectives: This study aims to identify characteristics at the time of diagnosis that may be related to the initiation of treatment with bDMARD within the first three years following diagnosis.

Methods: All patients with early RA diagnosed at the outpatient clinics of Skåne University Hospital in 2012-2016 were identified using the local patient administrative system. Diagnoses were validated in a structured review of the medical records. Patients with a confirmed RA diagnosis, aged ≥18 years with symptom duration <12 months at diagnosis, and who fulfilled the 2010 ACR/

Table 1. Comparison of hemoglobin and disease activity between initial and 1 year follow up in anemia patients

	Tocilizumab (n=126)		TNFi (n=248)			
Measurement	Baseline	1 year change	Baseline	1 year change	Between-Group Difference in Change	p-value[a]
HB	10.95 (10.77, 11.13)	1.56 (1.33, 1.80)	11.04 (10.93, 11.15)	1.02 (0.86, 1.18)	0.55 (-2.00, 3.09)	<.001
HCT	34.05 (33.60, 34.51)	3.53 (2.90, 4.17)	34.07 (33.76, 34.38)	2.64 (2.20, 3.09)	0.89 (-6.05, 7.84)	.013
TJC	7.63 (6.68, 8.58)	-5.97 (-6.92, -5.02)	9.40 (8.46, 10.35)	-7.43 (-8.32, -6.54)	1.46 (-10.79, 13.72)	.023
PTGA	7.14 (6.79, 7.48)	-3.76 (-4.20, -3.31)	6.88 (6.64, 7.13)	-3.51 (-3.86, -3.16)	-0.25 (-5.48, 4.98)	.370
PhGA	6.25 (5.93, 6.57)	-3.39 (-3.80, -2.98)	6.59 (6.35, 6.82)	-3.67 (-4.01, -3.32)	0.28 (-4.69, 5.24)	.288
ESR	53.84 (48.78, 58.90)	-43.31 (-48.37, -38.24)	55.7 (52.12, 59.28)	-26.85 (-30.59, -23.10)	-16.46 (-73.46, 40.54)	<.001
CRP	3.08 (2.47, 3.68)	-2.75 (-3.39, -2.12)	2.69 (2.33, 3.06)	-1.87 (-2.28, -1.47)	-0.88 (-7.56, 5.80)	.015
SDAI	29.8 (27.87, 31.73)	-20.68 (-22.74, -18.62)	30.27 (28.89, 31.65)	-20.64 (-22.18, -19.10)	-0.04 (-23.38, 23.30)	.914
CDAI	26.73 (24.94, 28.52)	-17.93 (-19.86, -16.00)	27.58 (26.29, 28.87)	-18.75 (-20.17, -17.33)	0.83 (-20.86, 22.51)	.377
SJC	6.62 (5.76, 7.48)	-5.57 (-6.45, -4.69)	7.53 (6.79, 8.26)	-6.37 (-7.07, -5.67)	0.80 (-9.52, 11.11)	.144
DAS28-ESR	5.68 (5.49, 5.87)	-3.35 (-3.58, -3.12)	5.77 (5.65, 5.89)	-2.59 (-2.77, -2.41)	-0.76 (-3.39, 1.87)	<.001
RAPID3	16.66 (15.63, 17.69)	-8.31 (-9.42, -7.19)	15.23 (14.5, 15.97)	-6.82 (-7.65, -5.99)	-1.49 (-14.09, 11.12)	.034

EULAR and/or the 1987 ACR classification criteria for RA, were included. Patients who started their first bDMARD in a clinical trial were excluded. Data on treatment were obtained from a national quality register, and from complementary case record reviews. Data on comorbidities were retrieved from a regional healthcare register, and data on level of formal education, country of origin and family background from national registers. The relation between characteristics at diagnosis and initiation of bDMARD within the first three years following diagnosis was examined in crude, age-adjusted and multivariable logistic regression models.

Results: Lower age, higher values for joint counts and DAS28-CRP3, and birth outside Europe were statistically significant baseline predictors of bDMARD start within the first 3 years after diagnosis in crude and age-adjusted analyses (Table 1). High level of education and absence of major comorbidities were predictive in crude but not in age-adjusted models. In multivariable logistic regression analysis, lower age (odds ratio (OR) 0.61 per SD; 95 % CI 0.46-0.83) and higher tender joint count (OR 1.56 per SD; 95% CI 1.18-2.10) were the only significant predictors of start of bDMARD ≤ 3 years after diagnosis.

Table 1: Predictors at RA diagnosis for a first bDMARD/tsDMARD start in patients with early RA within 3 years after diagnosis.
Logistic regression.

Variable	Crude OR (95% CI)	Age-adjusted OR (95% CI)
Male Sex	0.76 (0.44-1.31)	0.86 (0.49-1.51)
Age *	**0.60 (0.47-0.77)**	*N/A*
ACPA positive	1.39 (0.84-2.31)	1.23 (0.73-2.10)
RF positive	1.46 (0-87-2.44)	1.50 (0.89-2.55)
HAQ *	1.29 (0.97-1.71)	**1.50 (1.10-2.04)**
Tender joint count (of 28)*	**1.52 (1.20-1-93)**	**1.58 (1.23-2.03)**
Swollen joint count (of 28)*	**1.31 (1.04-1-65)**	**1.40 (1.10-1.78)**
DAS28-CRP-3**	**1.43 (1.11-1.85)**	**1.64 (1.24-2.16)**
CRP (mg/L) (quartiles)		
< 2.88	1 (ref)	1(ref)
2.89 - 7.95	1.30 (0.66-2.54)	1.68 (0.82-3.43)
7.96 – 24.0	1.38 (0.70-2.75)	1.97 (0.94-4.13)
> 24.0	1.41 (0.71-2.81)	**2.54 (1.17-5.51)**
ESR (mm/h) (quartiles)		
< 14	1(ref)	1(ref)
14 – 22	1.71 (0.85-3.44)	1.80 (0.87-3.70)
23 – 47	1.23 (0.61-2.50)	1.52 (0.72-3.18)
>47	1.35 (0.66-2.75)	2.07 (0.96-4.47)
Education		
≤ Lower secondary	1(ref)	1(ref)
Upper secondary / Short tertiary	1.70 (0.90-3.18)	1.21 (0.63-2.36)
≥ Bachelor's degree or equivalent	**2.11 (1.07-4-14)**	1.33 (0.64-2.75)
≥ 1 Psychiatric comorbidity	1.12 (0.67-1.88)	1.01 (0.59-1.71)
≥ 1 Pain related comorbidity	0.96 (0.60-1.54)	1.46 (0.86-2.46)
≥ 1 Other major comorbidity	**0.59 (0.37-0.94)**	0.85 (0.50-1.44)
Charlson's comorbidity index ≥1	0.79 (0.46-1.34)	1.23 (0.68-2.21)
Family background		
Both parents born in Sweden***	1(ref)	1(ref)
≥1 parent born abroad***	1.91 (0.97-3.77)	1.96 (0.98-3.93)
Subject born abroad	**2.33 (1.00-5.43)**	1.94 (0.82-4.60)
Country of birth		
Sweden	1(ref)	1(ref)
Europe outside Sweden	1.82 (0.61-5.43)	1.37 (0.45-4.26)
Rest of the world	**2.14 (1.21-3.76)**	**1.99 (1.12-3.56)**

*Estimates are per standard deviation. **Based on 3 variables – SJC, TJC and CRP
***Subject born in Sweden

Conclusion: Lower age and higher tender joint count at diagnosis were associated with an increased likelihood of starting bDMARD therapy within the first 3 years in early RA. The impact of age on the subsequent start of bDMARD therapy was not explained by other patient factors.

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AB0415

CAN WE PREDICT THE RISK FACTORS FOR SWITCHING IN THE FIRST YEAR OF THERAPY WITH BDMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS?

Keywords: bDMARD, Rheumatoid arthritis, Real-world evidence

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Background: Biological Disease-modifying Antirheumatic Drugs (bDMARD) have improved the clinical course and quality of life of patients with rheumatoid arthritis (RA). However, some patients failed to respond or have an insufficient response to bDMARD, early in the course of the treatment, and the reasons why this happens aren't fully understood.

Objectives: To determine the percentage of RA patients who failed to respond to bDMARD and need to switch in the first year of treatment, describe their characteristics, and identify specific baseline features as possible predictors of bDMARD early failure.

Methods: An observational monocentric retrospective cohort study was conducted with RA patients (according to 2010 ACR/EULAR criteria), registered in the national database (Reuma.pt) that started their first bDMARD between June 2000 and December 2021 and had a minimum follow-up of 12 months. Demographic data, disease characteristics, laboratory parameters and treatment at baseline were collected. Disease activity scores (CDAI, SDAI and DAS-28-CRP), functional scores (HAQ) and clinical response to treatment (according to EULAR and ACR response criteria) were collected at 3, 6 and 12 months after the start of bDMARD. The proportion of patients who failed to respond (according to treat-to-target strategies) and who switched to another bDMARD was calculated. Patients who discontinued treatment in the first year due to adverse events were excluded. Chi-square test, t-test and Mann-Whitney U test were conducted (categorical, normally and not normally distributed continuous variables, respectively). Also, a multivariate logistic regression analysis was performed. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. A p-value <0.05 was considered statistically significant.

Results: 437 (364 females, 83.3%) patients with RA were included. The mean age was 52.4 ± 11.4 years and the disease duration was 11.8 ± 8.8 years. The majority of these patients started an anti-TNF-α agent as their first bDMARD (n=315, 72.1%). The remaining patients started rituximab (n=66, 15.1%), tocilizumab (n=51, 11.7%) and abatacept (n=5, 1.1%). Forty-eight (11.0%) patients failed to respond to the bDMARD in the first year of treatment (mean duration of bDMARD treatment was 0.75 ± 0.3 years) and needed to switch to another bDMARD. Demographic characteristics were similar in the group of patients that switch due to ineffectiveness and patients that didn't switch in the first year. Disease activity scores (DAS-28-CPR, CDAI, SDAI) and HAQ at baseline were also similar in the two groups. There were significantly more current or former smokers in the group of patients that needed to switch in the first year of therapy (p=0.030). Moreover, depression was significantly more frequent in the switch group (p=0.003). Positivity for rheumatoid factor at baseline was also significantly more frequent in the switch group (p=0.014). Regarding the type of bDMARD, patients in the switch group were more frequently treated with anti-TNF-α agents than patients that didn't switch (p<0.001). In the multivariate analysis, anti-TNF-α agents use (versus non-anti-TNF-α agents) (OR 8.3, 95% CI 2.4-28.8, p=0.001), tobacco exposure (OR 2.3, 95% CI 1.1-4.8, p=0.02) and history of depression (OR 3.1, 95% CI 1.3-7.7) seem to predict the bDMARD early failure and the need to switch in the first year of treatment.

Conclusion: In our study, anti-TNF-α agents were associated with a higher switch rate due to ineffectiveness in the first year of treatment in RA patients, when comparing to non-anti-TNF-α agents. Moreover, current and former smokers, patients with depression and with positive rheumatoid factor had a higher switch rate due to ineffectiveness. This study reinforces the importance of RA patients quit smoking, as tobacco may interfere with clinical response to bDMARD. Furthermore, routine screening for depression should be included in daily clinical practice and a multidisciplinary treatment approach should be offered to these patients.

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AB0416

SUBCUTANEUS VS INTRAVENOUS ABATACEPT IN RHEUMATOID ARTHRITIS-INTERSTITIAL LUNG DISEASE. NATIONAL MULTICENTER STUDY OF 392 PATIENTS

Keywords: Rheumatoid arthritis, Disease-modifying Drugs (DMARDs), Lungs

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Background: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). Abatacept (ABA) has demonstrated efficacy in RA-ILD **[1-2].** Clinical trials have shown equivalence in subcutaneous (SC) and intravenous (IV) administration of ABA for articular manifestations **[3].** However, it has not been studied in RA-ILD.

Objectives: to compare the effectiveness of ABA in RA-ILD patients according to the route of administration (IV-ABA vs SC-ABA).

Methods: National multicenter study of RA-ILD patients on treatment with ABA. They were divided into 2 groups according to the route of administration: a) IV, and b) SC. We analyzed from baseline the following outcomes in both groups: **a)** forced vital capacity (FVC), **b)** diffusing capacity of the lungs for carbon monoxide (DLCO), **c)** chest high resolution computed tomography (HRCT), **d)** dyspnea (assessed with the modified Medical Research Council scale), **e)** arthritis activity (assessed with DAS28-ESR or described in clinical records), and **f)** sparing corticosteroids effect.

Results: We studied a total of 392 [SC-ABA/IV-AB; 288/91(available data)] patients. Baseline demographic and clinical characteristics are shown in **Table 1**. Patients were followed-up for a median [IQR] of 24 [10-48] months. FVC and DLCO remain stable during the first 24 months in both SC-ABA and IV-ABA **[Figure 1].** Dyspnea stabilized or improved in 85% of patients (89% of IV-ABA; 83% of SC-ABA). ABA was withdrawn in 80 patients: 60 (39%) in SC-ABA group and 20 (22%) in IV-ABA group. ILD worsening and articular inefficacy were the most common reasons of ABA discontinuation.

Conclusion: In RA-ILD, ABA seems equally effective and safe regardless of the route of administration IV or SC.

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Table 1. Main general features at baseline of RA-ILD patients with subcutaneous vs intravenous ABA.

	All ABA (n=392)	ABA IV (n=91)	ABA SC (n=288)	p
Age, years mean±SD	65 ± 10	66 ± 10	66 ± 10	0.85
Women n (%)	226 (58)	54 (59)	166 (58)	0.77
Smoker ever n (%)	210 (54)	49 (54)	154 (53)	0.95
ILD duration up to ABA, months, median [IQR]	11 (3-38)	11 (2-48)	10 (3-36)	0.65
RF n (%)	347 (89)	78 (86)	256 (89)	0.41
ACPA n (%)	344 (89)	76 (85)	256 (90)	0.25
DAS28-ESR	4.35±1.58	4.19±1.52	4.38±1.53	0.35
ILD pattern n (%)				
NIU	172 (44)	47 (52)	122 (42)	
NINE	117 (30)	20 (22)	94 (33)	0.14
Other	98 (25)	23 (26)	72 (25)	
FVC (% of the predicted) mean±SD	87 ± 21	82 ± 22	88 ± 21	0.26
DLCO (% of the predicted) mean±SD	67 ± 20	67 ± 20	67 ± 19	0.97
Prednisone at baseline, mg/ day, median [IQR]	5 (5-10)	7.5 (5-10)	5 (5-10)	0.34

ACPA, anti-citrullinated protein antibodies; DLCO, diffusing capacity of the lung for carbon monoxide; FVC, forced vital capacity; RF, rheumatoid factor; UIP, usual interstitial pneumonia.

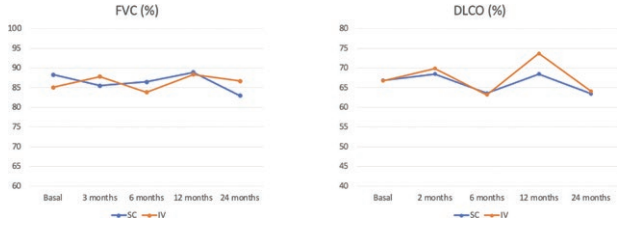


Figure 1. Evolution of pulmonary function tests (mean % of the predicted FVC and DLCO) in RA-ILD patients with SC-ABA vs IV-ABA therapy at baseline and 24 months.

Members of the Spanish Collaborative Group of Abatacept in RA-ILD patients: Luis Arboleya-Rodríguez, Javier Narváez, Juan Carlos Fernández, Belén Miguel, Iván Cabezas, Andrea García Valle, Clara Aguilera Cros, S. Romero-Yuste, Ignacio Villa Blanco, Sabela Fernández Aguado, Raquel Almodóvar, C. Ojeda-García, C. Aguilera-Cros, B. García-Magallón, Antonio Juan Mas, M. J. Moreno-Ramos, A. Ruibal-Escribano, Rosa Expósito, José Antonio Bernal, Evelin C. Cervantes, S. Rodríguez-García, R. Castellanos-Moreira, Iván Castellví, Manuel Rodríguez, Eva Salgado, Enrique Raya, Pilar Morales, Lorena Expósito, Mª Noelia Álvarez, José Luis Andreu, E. F. Vicente-Rabaneda, A. M. López-Robles, M. López-Corbeto, C. Hidalgo-Calleja, J.C. Fernández-López, Alejandro Olivé, S. Rodríguez-Muguruza, Iñigo Hernández, N. Quillis-Marti, J.A. Bernal-Vidal, A. García-Aparicio, S. Castro-Oreiro, J. Fernández-Melón, P. Vela Casasempere, María C. Fito, M. Rodríguez-Gómez, D. Palma-Sánchez, L. Expósito-Pérez, José María Andreu.

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AB0417 JAK INHIBITORS AND LIVER INVOLVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: RISK ASSESSMENT OF NAFLD AND SAFETY PROFILE IN HBV INFECTIONS

Keywords: bDMARD, Rheumatoid arthritis

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Background: Janus kinase inhibitors (JAK-i) are increasingly used in the treatment of Rheumatoid Arthritis (AR). Hypertransaminasemia is one of the described side effects of this class of drugs.
Objectives: The aim of the study is to evaluate the possible hepatotoxicity, the risk of NAFLD onset, and the reactivation of HBV and HCV in patients with AR and JAK-i therapy.
Methods: 78 patients with AR (81%F) were enrolled with an average disease duration of 15±7 years, BMI 26±4. The inclusion criteria were age > 18 years, fulfillment of ACR/EULAR 2010 criteria for AR, and stable intake for at least 3 months of JAK-i in monotherapy or combined therapy with methotrexate (MTX) and/or steroid.
Results: The average therapy duration of JAK-i treatment (Baricitinib, Filgotinib, Tofacitinib or Upadacitinib) was of 67±50 weeks. 32% of patients were on combined therapy with MTX and 22% took steroids (mean dose in prednisone equivalents of 5.5±2.5 mg/day). No patients had positivity for HCV antibodies at the beginning of JAK-i therapy, and no one reported alcohol abuse. At the beginning of JAK-i therapy, 9% of patients had hepatic steatosis on abdominal ultrasound and 26% had occult HBV infection. 8% of patients had hypertransaminasemia before starting therapy with JAK-i. During treatment with JAK-i, hypertransaminasemia occurred in 6% of patients; of these 20% had already known hepatic steatosis, 40% were occult HBV carriers and 40% were with combined therapy with MTX. Particularly, hypertransaminasemia was detected in 8% of patients treated with Baricitinib and in 8% of patients with Tofacitinib. No patients treated with Filgotinib and Upadacitinib developed hypertransaminasemia during follow-up. JAK-i treatment was not stopped in any patient with hypertransaminasemia. 14% had NAFLD during treatment with JAK-i, and no patients had hepatic steatosis with hypertransaminasemia above 3 times normal values. Among patients who developed NAFLD after JAK-i treatment, 18% were overweight, 36% were obese, 27% were in therapy with steroids, and 18% were with combined therapy with MTX. NAFLD has been detected in 16% of patients treated with Baricitinib, 8% of patients treated with Tofacitinib, and 15% of patients treated with Upadacitinib, no patients treated with Filgotinib showed onset of NAFLD. Among patients with previous episodes of hypertransaminesia for other reasons, JAK-i treatment didn't cause alterations of bio-humoral indexes of hepatic function. No HBV reactivation occurred in patients with occult HBV infection during treatment with JAK-i.
Conclusion: JAK-i treatment in patients with occult HBV infection or previous NAFLD has a good safety profile. In terms of hypertransaminasemia with or without NAFLD, the risk of liver dysfunction appears to be very low during JAK-i treatment, both in monotherapy or in MTX combination treatment.

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Disclosure of Interests: None Declared.
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AB0418 ELEVATED ANA AS A PREDICTOR OF THERAPEUTIC FAILURE TO BIOLOGICAL ANTI-TNF AGENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: bDMARD, Autoantibodies, Rheumatoid arthritis

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Background: Currently there is no way to distinguish or predict therapeutic failure of Tumor Necrosis Factor (TNF) inhibitors in patients with autoimmune diseases, especially rheumatoid arthritis (RA). Elevated Antinuclear Antibodies (ANA) have been linked as potential markers of therapeutic failure to iTNF.
Objectives: To analyze a possible relationship between high levels of ANA and the presence of therapeutic failure to infliximab (IFX) and Etanercept (ETN) in patients with RA.
Methods: Retrospective cohort study. Two groups were formed: 135 patients with RA and elevated ANA (> 1/80) and 135 patients with RA and negative ANA (< 1/80). All patients received IFX or ETN therapy. ANA was measured before starting therapy. Each group had 60 patients using IFX and 75 using ETN. The appearance of therapeutic failure was expected (DAS28 > 3.2 after at least 3 months of treatment with iTNF). The number of therapeutic failures in each group was counted and then a logistic regression analysis was used with the variables elevated ANA and existence of iTNF therapeutic failure.
Results: Thirty-two therapeutic failures were counted in the elevated ANA group and 16 in the negative ANA group. A higher percentage of failures was observed in IFX users. A higher percentage of therapeutic failure was also observed at a higher ANA level. No relationship was found between the ANA pattern and the presence of failure. The presence of an elevated ANA multiplies by 2.4 the risk of presenting therapeutic failure to IFX or ETN in patients with RA.
Conclusion: An elevated ANA is a predictor of therapeutic failure to IFX or ETN in patients with RA.
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Table 1.

Elevated ANA as a predictor of therapeutic failure to IFX or ETN

	p	Odds ratio	I.C. 95%: OR	
			Lower	Higher
Woman	0.075	0.436	0.175	1.088
ANA +	0.009	2.434	1.25	4.741
iTNF	0.305	0.715	0.376	1.358
Age	0.369	0.986	0.955	1.017

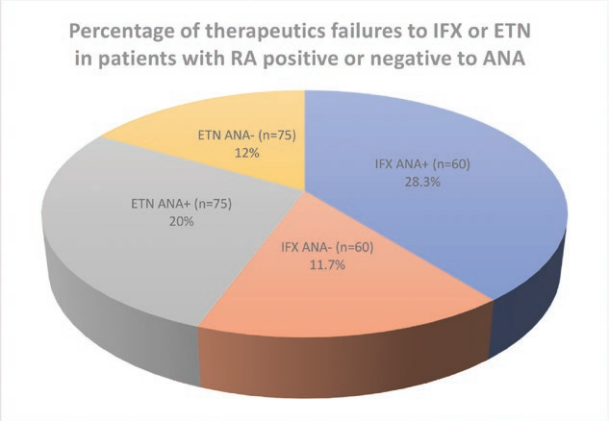


Figure 1.

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AB0419

OUTCOMES OF THE SELF-INJECTION ASSESSMENT QUESTIONNAIRE IN RHEUMATOID ARTHRITIS, AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS RECEIVING GP2015 (ETANERCEPT BIOSIMILAR) IN A REAL-WORLD STUDY: FINAL RESULTS FROM COMPACT STUDY

Keywords: Rheumatoid arthritis, Spondyloarthritis, Patient reported outcomes

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Background: COMPACT is an international, non-interventional cohort study evaluating the effectiveness, safety and quality of life in patients (pts) with rheumatoid arthritis (RA), axial-spondyloarthritis (axSpA) or psoriatic arthritis (PsA) treated with GP2015, an approved etanercept (ETN) biosimilar, in real-world conditions.
Objectives: To assess patient usage behaviour and feelings of self-administered injection with auto-injector device using the Self-Injection Assessment Questionnaire (SIAQ) in pts with RA, axSpA and PsA receiving GP2015.
Methods: Pts aged ≥18 years from Germany and UK who initiated treatment with GP2015 were enrolled in this study. The SIAQ, a questionnaire developed to assess overall pt experience with subcutaneous self-injection was used to assess the perceived self-confidence on self-injection, potential barriers as well as satisfaction with self-injection via device before the first self-injection (PRE module) and after dosing (POST module).[1] In COMPACT study, the POST module was assessed which comprised of 21 items grouped into 6 hypothetical domains: "feelings about injection", "self-image", "self-confidence", "skin reaction" (injection-site reactions), "ease of use of self-injection device", and "patient satisfaction". Domain scores were rated on a 10-point scale, i.e., 0 (worst experience) to 10 (best experience). Data was analysed from the first collected SIAQ responses during the study and was summarised using descriptive statistics. The final SIAQ scores by domain in pts with RA, PsA and axSpA and by study group in pts with RA are reported here.
Results: A total of 458 pts from Germany (RA: 285, PsA: 79, axSpA: 94) and 273 pts from UK (RA: 174, PsA: 54, axSpA: 45) responded to the questionnaire. Overall, each domain showed high SIAQ scores which were consistent across all indications. The "self-image" and the "skin reaction" domains were scored highest (**Figure 1**). RA pts who had prior experience with biologic or non-ETN targeted medication (Group A + B) had mean scores mostly higher than or equal to those of biologic-naïve pts (Group C + D). RA pts who switched from iETN (reference ETN or biosimilar ETN other than GP2015) to GP2015 treatment (Group A) reported high SIAQ scores in all domains, which can be explained by good patient experience with the device (**Table 1**).
Conclusion: The SIAQ showed high acceptance of the auto-injector device in both countries where the survey was performed across all indications. Most RA pts were satisfied with auto-injector device usability after switching from iETN to GP2015, demonstrating no major concerns after switching.

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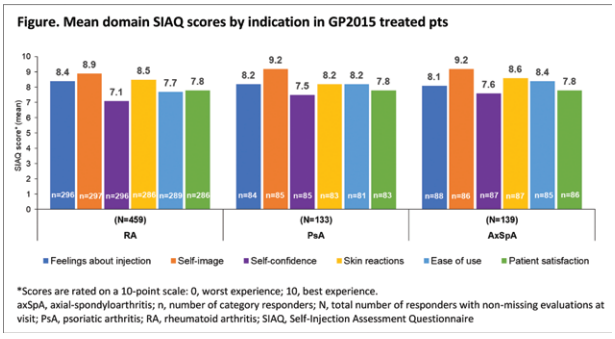


Table 1. Mean domain SIAQ scores by study group in pts with RA in GP2015 treated pts

Mean domain scores*	Group A (N=177)	Group A + B (N=206)	Group C + D (N=253)
Feelings about injections	9.1	9.0	7.9
Self-image	9.0	9.1	8.8
Self-confidence	7.7	7.5	6.9
Skin reactions	8.5	8.5	8.5
Ease of use	7.7	7.6	7.8
Patient satisfaction	8.0	7.8	7.7

*Scores are rated on a 10-point scale: 0, worst experience; 10, best experience. Study groups are defined as RA pts who were treated with iETN and switched to GP2015 (Group A) or pts who received non-ETN targeted therapies and switched to GP2015 (Group B) or biologic-naïve (Group C) or DMARDs-naïve pts who started GP2015 as a first biologic therapy (Group D). N, total number of responders with non-missing evaluations at visit

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Rheumatoid arthritis - biological DMARDs

AB0420 MATERNAL AND NEONATAL ANTIBODY LEVELS UPON PERTUSSIS VACCINATION IN PREGNANT WOMEN ON IMMUNE-MODULATING THERAPY FOR RHEUMATIC DISEASE

Keywords: Vaccination/Immunization, bDMARD, Pregnancy and reproduction

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Background: While protection against pertussis following maternal tetanus-diphtheria-and-acellular-pertussis (Tdap) vaccination has been demonstrated in term-born infants from healthy mothers[1], no evidence is available on Tdap vaccination in combination with immune-modulating therapy during pregnancy.
Objectives: In this pilot-study, we explored whether treatment with Tumor Necrosis Factor alpha inhibitors (TNFis) in pregnant patients with rheumatic disease interferes with Tdap vaccine responses and/or affects maternal IgG antibody concentrations against the relevant antigens in the newborns.
Methods: Patients included by a rheumatologist during pregnancy received a Tdap vaccination in their late-second or early-third trimester. Blood samples were drawn during the first trimester, three months after delivery and from the umbilical cord. IgG antibody levels against Tdap-included antigens were measured using a bead-based multiplex immunoassay. Findings on patients exposed to TNFis were compared with those from TNFi-unexposed patients and with data from a historical comparator study among healthy Tdap vaccinated mother-infant-pairs (n=53). [2]
Results: 66 patients (46 exposed and 20 unexposed to TNFIs) were enrolled. No differences in IgG antibody levels against Tdap-included antigens were observed between TNFi-exposed and unexposed patients before and after Tdap vaccination (Figure 1). In cord sera however, antibody levels against pertussis toxin were significantly lower after TNFi-treatment (35.94IU/mL, 95%CI 20.68-62.45) compared with no TNFis (94.61IU/mL, 95%CI 48.89-183.07) and with cord blood from the comparison cohort of healthy women-infant-pairs (125.12IU/mL, 95%CI 90.75-172.50). We observed similar differences for filamentous hemagglutinin, pertactin, tetanus toxoid, and diphtheria toxoid.
Conclusion: These preliminary data indicate no reduced IgG antibody response upon maternal Tdap vaccination in pregnant women following immune-modulating treatment, although our findings suggest that TNFis during pregnancy induce lower maternal antibody levels against Tdap-included antigens in newborns.
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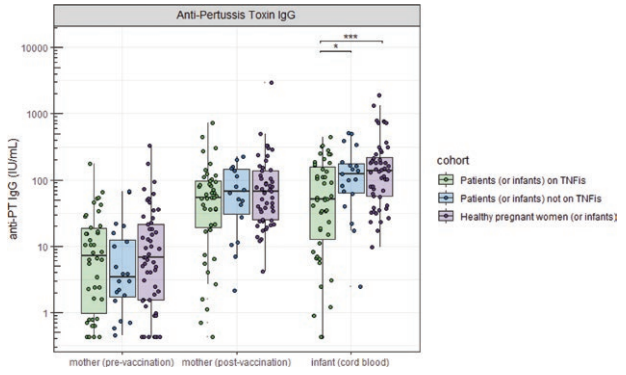


Figure 1. Anti-Pertussis toxin (anti-PT IgG) concentrations (IU/mL) before and after vaccination and in cord sera, represented for women exposed or unexposed to TNFis, or healthy pregnant women, including their offspring. X-axis: type and time-point of blood sample draw. Y-axis: IgG antibody concentration against pertussis toxin (IU/mL). Significance *p<0.05, **p<0.01, ***p<0.001.

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Disclosure of Interests: Nafise Ghalandari Grant/research support from: Financial support for printing PhD book from UCB Pharma., Employee of: From June 2022 till February 2023 worked as a medical science liaison (MSL) at UCB Pharma., Maarten Immink: None declared, Esther Röder: None declared, Patricia Bruijning-Verhagen: None declared, Hieronymus TW Smeele: None declared, Hubertina Johanna Maria Josephina Crijns: None declared, Nicoline van der Maas: None declared, Mireille Bekker: None declared, Lieke Sanders: None declared, Radboud Dolhain Speakers bureau: from AbbVie, AstraZeneca, Eli Lily, Galapagos, Novartis, Roche, UCB., Grant/research support from: an unrestricted grant from Galapagos, UCB Pharma B.V.
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AB0421 REAL-WORLD EFFECTIVENESS OF UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Real-world evidence

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Background: The Janus Kinase (JAK) inhibitor Upadacitinib (UPA) has shown efficacy in rheumatoid arthritis (RA) in trials, yet real-world evidence is lacking.
Objectives: We aimed to assess short-term effectiveness of UPA for standard of care for RA.
Methods: Data from participants included in the electronic platform "Tool for Administrative Reimbursement Drug Information Sharing" (TARDIS) were analysed. TARDIS collects data from all Belgian RA patients on advanced therapy during submissions of reimbursement requests for drug initiation or prolongation. Patients initiating UPA between 01/11/2020-31/12/2021, ≥18 years and DAS28>3.7 were included. Effectiveness was based on drug retention, proportion of patients achieving remission (DAS-28 <2.6), low disease activity (LDA, DAS-28 ≤3.2), HAQ-DI≤0.25 (HAQ25), HAQ-DI≤0.50 (HAQ50) as well as a clinical meaningful HAQ-DI-decrease (MCID_HAQ) since baseline of 0.22 at the first follow-up moment at 3 months. Sensitivity analyses by 1st, 2nd or 3rd+-line advanced therapy were performed.
Results: From 13 175 patients in TARDIS in the relevant time period, 996 patients on UPA could be included. Table 1 details this population. Of 871 patients with drug information at next follow-up, 783 (90%) continued UPA, and 42 (5%), 22 (3%), and 18 (2%) changed to a TNFi, non-TNFi and other JAKi respectively. In other effectiveness analyses, 705/996 (71%) patients were included. Remission and LDA were reached in 60% (421/705) and 74% (521/705) of patients respectively. HAQ25, HAQ50 and MCID_HAQ were reached in 11% (78/705), 26% (183/705) and 67% (475/705) of patients. Effectiveness slightly decreased with increasing line of therapy (Figure 1).

Table 1. Baseline characteristics of TARDIS patients on UPA

	Total UPA population
Number	996
Age (mean ±SD, years)	57.5 ±12.7
Disease duration (mean ±SD, years)	9.3 ±9.5
ESR (mean ±SD, mm/hour)	24.3 ±19.9
CRP (mean ±SD, mg/L)	13.1 ±15.5
SJC28 (mean ±SD)	6.5 ±4.5
TJC28 (mean ±SD)	9.2 ±5.4
DAS28 (mean ±SD, years)	5.0 ±0.8
HAQ-DI (mean ±SD, 0-3)*	1.3 ±0.8
PGA (mean ±SD, 0-100)	67.5 ±18.3
Advanced treatment naïve (yes)	434/996 (43.6%)
Advanced treatment Experienced (yes)	562/996 (56.4%)
2nd line	247/562 (24.8%)
3th line +	315/562 (31.6%)
Previous advanced treatment type**	
TNFi,	268/562 (48.2%)
Non-TNFi,	177/562 (31.8%)
JAKi	111/562 (20.0%)

Legend: Numbers given are mean ± SD or number, proportion. TNFi = tumour necrosis factor inhibitor, JAKi = Janus Kinase inhibitor, HAQ= health assessment questionnaire, PGA= Patient Global assessment; CRP= C-reactive protein; ESR= erythrocyte sedimentation rate; TJC= tender joint count; SJC= Swollen joint Count; DAS28 = disease activity score based on the 28joints. *Missing HAQ(0-3) scores were imputed by regression using age and HAQ(0-60) scores. **for 6 patients this was undefined.

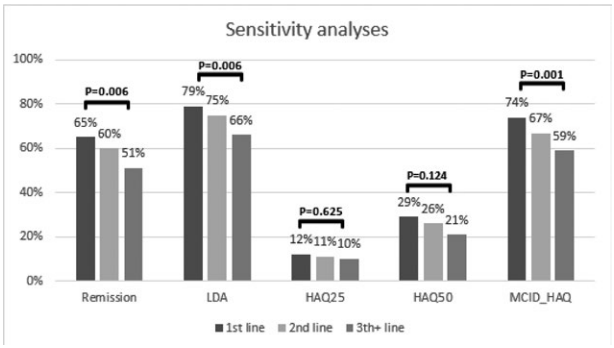


Figure 1. Effectiveness outcomes at 3 months of UPA per treatment line. remission (DAS-28 <2.6), LDA - low disease activity (DAS-28 ≤3.2), HAQ-DI≤0.25 (HAQ25), HAQ-DI≤0.50 (HAQ50) and minimum HAQ-DI-decrease (MCID_HAQ) since baseline of 0.22

Conclusion: Most patients continued UPA treatment. UPA improved clinical outcomes after 3 months in patients with moderately to severely active RA in a real-world setting, even in 3rd line of advanced therapy.

Acknowledgements: On behalf of the Royal Belgian Society for Rheumatology. AbbVie sponsored the study and contributed to the design. AbbVie participated in the reviewing and approval of the final version. No honoraria or payments were made for authorship.

Disclosure of Interests: None Declared.

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AB0422 THE EFFECTS OF CONCOMITANT USE OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SARILUMAB

Keywords: Real-world evidence, Rheumatoid arthritis, bDMARD

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Background: Sarilumab was launched the second interleukin 6 receptor inhibitor (IL-6Ri) as a treatment for patients with rheumatoid arthritis (RA) in Japan. Tocilizumab, that was known as first IL-6Ri, showed excellent therapeutic effect without methotrexate (MTX) for RA. However, it was unknown that the effect on concomitant use of MTX in RA patients treated with sarilumab.

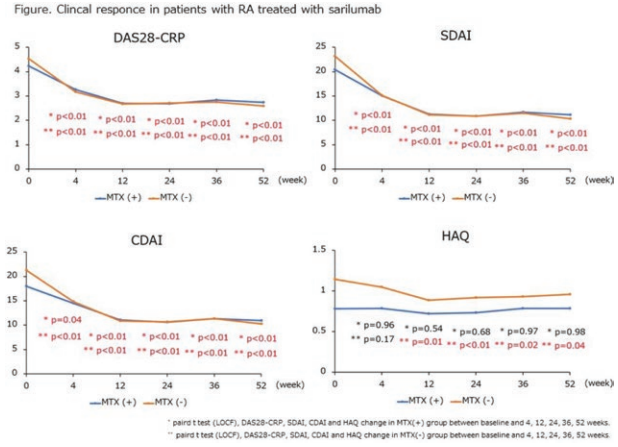
Objectives: We evaluated the effect on concomitant use of MTX in RA patients treated with sarilumab.

Methods: This study used a multicenter database included 673 RA patients treated with b/tsDMARDs. We finally analyzed 72 RA patients treated with sarilumab. Thirty-three RA patients were combined with MTX (MTX group) and 39 RA patients were not combined with MTX (non-MTX group). The continuation rate and efficacy at 52 weeks after sarilumab treatment in each group was evaluated.

Results: Non-MTX group was older, longer disease duration, and lower eGFR than MTX group (Table 1). The continuation rate at 52 weeks was not different between MTX group and non-MTX group (56.4 vs 74.4%, p=0.08). DAS28-CRP, SDAI, CDAI were decreased at 4, 12, 24, 36, 52 weeks after sarilumab treatment compared to baseline in both MTX group and non-MTX group (Figure 1). Improvement rate of DAS28-CRP, SDAI and CDAI at 4, 12, 24, 36, 52 weeks after sarilumab treatment were not different between groups (DAS28-CRP: p=0.36, p=0.53, p=0.56, p=0.46, p=0.29; SDAI: p=0.58, p=0.93, p=0.90, p=0.63, p=0.56; CDAI: p=0.65, p=0.98, p=0.99, p=0.61, p=0.47; respectively). HAQ was not improved in MTX group, but improved in non-MTX group during 52 weeks sarilumab treatment (MTX group, p=0.98; non-NTX group, p=0.04). In all patients, 49 RA patients were treated sarilumab as 2nd and more line biological/ targeted synthetic disease-modifying anti rheumatic dugs (b/tsDMARDs). DAS28-CRP, SDAI and CDAI at baseline in RA patients treated with sarilumab as 2nd and more line b/tsDMARDs were 4.1, 18.9, 16.4 in MTX group (n=23), and 4.6, 24.3, 22.6 in non-MTX group (n=26). DAS28-CRP, SDAI and CDAI were decreased at 4, 12, 24, 36, 52 weeks after sarilumab as 2nd and more line treatment compared to baseline in both MTX group (DAS28-CRP: 3.0, 2.5, 2.5, 2.7, 2.7, p<0.01, respectively; SDAI: 12.5, 9.6, 9.3, 10.6, 10.3, p<0.01, respectively; CDAI: 12.2, 9.4, 9.0, 10.2, 10.1, p<0.01, respectively) and non-MTX group (DAS28-CRP: 3.3, 2.8, 2.8, 2.8, 2.6, p<0.01, respectively; SDAI: 15.6, 11.5, 11.4, 11.1, 9.9, p<0.01, respectively; CDAI: 15.2, 11.1, 11.1, 11.0, 9.7, p<0.01, respectively). Improvement rate of DAS28-CRP, SDAI and CDAI at 4, 12, 24, 36, 52 weeks after sarilumab as 2nd and more line treatment were not different between groups (DAS28-CRP: p=0.99, p=0.96, p=0.83, p=0.94, p=0.53; SDAI: p=0.10, p=0.65, p=0.79, p=0.87, p=0.68; CDAI: p=0.95, p=0.72, p=0.76, p=0.74, p=0.53; respectively).

Table 1. Baseline characteristics of RA patients treated with sarilumab

	MTX (+) group (n=33)	MTX (-) group (n=39)	p
Age (years)	61.51 ± 13.68	69.51 ± 13.12	< 0.01
Male/ Female ratio	10/23	8/31	0.5
Disease durations (years)	9.30 ± 10.22	17.39 ± 11.33	< 0.01
RF positive ratio (%)	81.82	79.49	1.0
CCP positive ratio (%)	77.42	82.86	0.85
CRP (mg/dl)	2.44 ± 2.82	1.90 ± 2.06	0.65
MMP-3 (ng/ml)	271.57 ± 314.38	342.34 ± 327.87	0.047
eGFR	79.78 ± 27.50	58.22 ± 27.52	<0.01
DAS28-CRP	4.23 ± 1.31	4.53 ± 1.0	0.26
SDAI	20.41 ± 12.07	23.17 ± 9.66	0.17
CDAI	17.97 ± 10.71	21.27 ± 9.25	0.08
HAQ	0.78 ± 0.78	1.14 ± 0.88	0.02
MTX (mg/week)	8.58 ± 3.58	0 ± 0	<0.01
Glucocorticoid use (%)	18.18 (6/33)	38.46 (15/39)	0.1
Glucocorticoid dose (mg/day)	7.17 ± 3.19	5.83 ± 3.24	0.37
Number of past use of b/tsDMARD			
0 (%)	30.3	33.3	
1 (%)	51.5	33.3	
2 (%)	12.1	15.4	
3(%)	6.1	10.3	
4 (%)	0	5.1	
5 (%)	0	2.6	
Interstitial pneumonia	2/33	7/39	0.17



Conclusion: Sarilumab improved disease activity in patients with RA regardless of concomitant use of MTX.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0423 IMPROVEMENT OF ULTRASONOGRAPHIC FINDINGS IN JAK INHIBITOR TREATED JAPANESE RHEUMATOID ARTHRITIS PATIENTS COMPARISON WITH TNF INHIBITOR THERAPY

Keywords: Rheumatoid arthritis, Ultrasound, bDMARD

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Background: JAK inhibitor (JAKi) and TNF inhibitor (TNFi) are the important therapeutic agent for the treatment of rheumatoid arthritis (RA). However there is still few studies of improvement of ultrasonographic findings in RA treats comparison with JAKi and TNFi.

Objectives: To evaluate the improvement of ultrasonographic findings in JAKi treated RA patients comparison with TNFi.

Methods: Participants comprised 40 and 43 Japanese RA patients who had recently received each JAKi (BAR26, PEF9, UPA5) and TNFi (CZP30, ADA5, ETN4, GLM4). All patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria. Patients underwent clinical and laboratory assessments every 4 weeks from baseline to 24 weeks, and US assessments at baseline, 4, 12 and 24 weeks. Gray scale (GS) and power doppler (PD) signals were scored using a semi-quantitative scale from 0 to 3 at 26 (0-78) synovial sites (22 joints) in the following joints: bilateral first to fifth metacarpopharangeal (MCP) joints (dorsal recess); first interphalangeal (IP) and second to fifth proximal interphalangeal (PIP) (dorsal recess) joints; and the wrists (dorsal radial, median and ulnar). We evaluated the improvement of GS and PD score from baseline to week 24.
Results: In the patients receiving JAKi (n=40) and TNFi (n=43), the mean age was 56.0 vs 54.0 years old (p=0.514), disease duration was 7.3 vs 5.9 years (p=0.343), the rate of MTX use was 70% vs 86% (p=0.076), the mean MTX dose was 10.0 vs 9.9 mg/w (p=0.888), the rate of ACPA positive was 90% vs 79% (p=0.171), the rate of b/ts DMARDs naïve patients was 65% vs 91% (p=0.005), DAS28-ESR was 5.03 vs 4.69 (p=0.102), CDAI was 24.5 vs 19.2 (p=0.038), GS score was 22.1 vs 18.3 (p=0.535) and PD score was 15.1 vs 11.1 (p=0.625). The degree of improvement respective changes in GS and PD score from baseline to 4, 12 and 24 weeks were as follows: GS: -5.7 vs -4.7 (p=0.762) and PD: -6.6 vs -3.1 (p=0.489) after 4 weeks, GS: -9.3 vs -6.7 (p=0.975) and PD: -8.7 vs -4.6 (p=0.340) after 12 weeks, GS: -11.5 vs -9.7 (p=0.732) and PD: -9.5 vs -7.1 (p=0.802) after 24 weeks between JAKi and TNFi (Figure 1, 2). Next, The improvement rate of respective changes in GS and PD score after 4, 12 and 24 weeks were as follows: GS: -16.2% vs -20.7% (p=0.463) and PD: -29.7% vs -20.8% (p=0.414) after 4 weeks, GS: -30.2% vs -27.9% (p=0.884) and PD: -34.0% vs -33.0% (p=0.830) after 12 weeks, GS: -42.4% vs -39.4% (p=0.712) and PD: -41.6% vs -54.0% (p=0.865) after 24 weeks between JAKi and TNFi. Next, we evaluated the improvement of ultrasonographic findings between b/ts DMARDs naïve and switch, with and without MTX in the JAKi-treated patients. The degree of improvement respective changes in GS and PD score from baseline to 24 weeks were as follows: GS: -13.8 vs -7.1 (p=0.313) and PD: -10.8 vs -6.9 (p=0.334) between b/ts DMARDs naïve and switch patients, GS: -11.7 vs -11.0 (p=0.988) and PD: -9.2 vs -10.0 (p=0.658) between with and without MTX patients.
Conclusion: The present study provides evidence supporting the improvement in ultrasonographic findings in RA was similar for both JAKi and TNFi. Also In the JAKi-treated patients, similar improvement in ultrasonographic findings was observed regardless of whether the patients were naive or switch, with and without MTX.

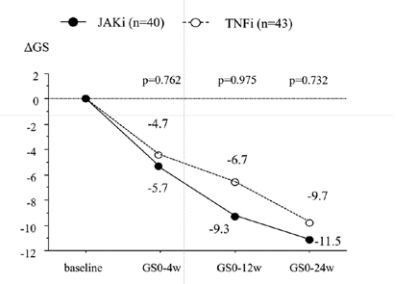


Figure 1 : The degree of improvement respective changesin GS score from baseline to Week 24 between JAKi and TNFi patients

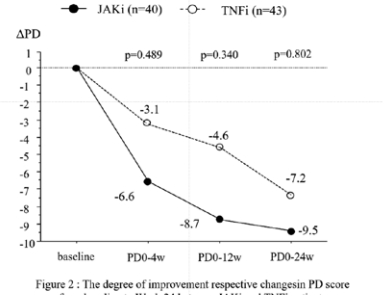


Figure 2 : The degree of improvement respective changesin PD score from baseline to Week 24 between JAKi and TNFi patients

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Yasuhide Kanayama Speakers bureau: YK has received speakers' fees from AbbVie, Astellas, Asahi Kasei, Daiichi-Sankyo, Eisai, Eli Lilly, Ono and UCB Japan., Atsushi Nagata: None declared, Miyuki Shimotake: None declared, Fumiko Miyachi: None declared, Keisuke Fujita: None declared, Mai Koyama: None declared, Shiho Uno: None declared, Kyosuke Hattori: None declared.
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AB0424

IMPACT OF BASELINE RHEUMATOID FACTOR TITERS AND ANTI-TNF MOLECULAR STRUCTURE ON THE RETENTION RATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: bDMARD, Real-world evidence, Rheumatoid arthritis

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Background: Rheumatoid Factor (RF) is an antibody against the Fc portion of IgG forming immune complexes that contribute to the Rheumatoid Arthritis (RA) process. RF also binds the Fc region of many monoclonal antibodies (mAB), leading to lower drug levels and potential early withdrawal. Conversely, the absence of Fc portion in Certolizumab Pegol (PEG) may lead to a higher retention rate in comparison with other drugs in RA patients with higher RF titers.
Objectives: a) To evaluate the retention rate to any anti-TNF according to the baseline RF titers in patients with RA and b) to compare the retention rate to PEG vs. other anti-TNF in patients with high RF titers.
Methods: Longitudinal, retrospective and unicentre study including patients with a diagnosis of RA and treated with any anti-TNF (mAB (Adalimumab, Golimumab and Infliximab), fusion protein (Etanercept) or PEG (Certolizumab Pegol)) between 2007 and 2022. RF levels before anti-TNF initiation as well as the dates of both initiation and treatment withdrawal were collected. Log-rank test and Kaplan-Meier curves were conducted to evaluate the retention rate to the treatment in RF positive vs. negative, and between RF <110 IU/ml vs RF ≥110 IU/ml (considering the median titre of RF (110 IU/ml) as the cut-off). In addition, the retention rate to each molecular structure were compared in patients with high RF titres (≥110 IU/ml).
Results: A total of 356 patients with RA treated with anti-TNF and with available titres of RF were included. Mean age was 52.0 (11.2) years and 80.1% were female. A total of 254 (71.3%) were RF positive. Retention rate to any anti-TNF was similar in RF- vs RF+ (median 4.30 vs. 3.91 years, p-value 0.580). However, considering the titres of RF, those with baseline RF ≥110 IU/ml showed a shorter retention rate in comparison with RF <110 IU/ml (median 2.78 vs. 6.13 years, p=0.016). In patients with high RF titres (RF ≥110 IU/ml), a longer retention rate was found with PEG in comparison with fusion protein and mAB, although these differences were not significant (median 4.08 in PEG, 2.33 in fusion protein and 1.24 in mAB, respectively; p=0.460).
Conclusion: Higher RF titers before anti-TNF initiation were associated with a shorter retention rate in patients with RA. However, no differences were found between molecular structures, although patients treated with PEG seem to have a longer retention rate. These results confirm the possible effect of the RF in binding the Fc portion of the drug.

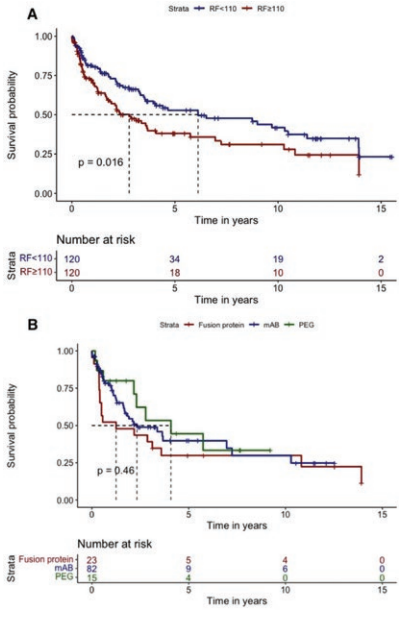


Figure 1. Retention rate to any anti-TNF according to the RF titers (A) and retention rate of each molecular structure in patients with high titers levels (≥110 UI/L) (B).

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0425 REAL-WORLD EFFECTIVENESS OF FILGOTINIB IN BELGIAN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Real-world evidence, Rheumatoid arthritis, Targeted synthetic drugs

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Background: Filgotinib (FIL), a preferential Janus Kinase (JAK) inhibitor targeting the JAK1 enzyme, has demonstrated efficacy in rheumatoid arthritis (RA) in clinical trials. FIL is reimbursed in Belgium since August 2021 for adult patients with moderate to severe RA with a DAS28 score >3.7 and inadequate response or intolerance to 2 conventional DMARDs including Methotrexate. Today, limited data exist on the real-world effectiveness of FIL in RA.
Objectives: Our aim was to examine the short-term effectiveness of FIL in a heterogeneous RA population.
Methods: Patients were included from the electronic platform "Tool for Administrative Reimbursement Drug Information Sharing" (TARDIS). Data from all Belgian RA patients on biologic and targeted therapy are collected in this platform during the submission of a request for initiation or prolongation of reimbursement of these drugs. The study population included adult patients ≥18 years starting FIL between August 2021 and November 2022. Baseline characteristics (demographics, clinical characteristics, treatment history) of Belgian RA patients treated with FIL were registered. Effectiveness of FIL was determined by the patient proportion achieving remission (DAS28 <2.6), low disease activity (DAS28 ≤3.2), HAQ-DI≤0.25 (HAQ25) and minimum HAQ-DI-decrease (MCID_HAQ) since baseline of 0.22, at the first follow-up moment, structurally planned in TARDIS after 3 months. Sensitivity analyses were performed in patients starting FIL as 1st, 2nd or 3th+-line advanced therapy.
Results: In total, 405 RA patients on FIL were included, representing all newly initiated FIL patients. Table 1 gives detailed information on the demographics, clinical characteristics and treatment history. Of the 228 patients with information on treatment at the next follow-up moment, 210 (92%) continued FIL, and 6 (3%), 9 (4%), and 3 (1%) changed to a TNFi, non-TNFi and JAKi respectively. In total, 193/405 (48%) patients could be included in the effectiveness analysis. Remission and low disease activity were reached in 61% (117/193) and 81% (156/193) of patients respectively. Baseline mean ±SD DAS28 was 4.9 ±0.8. The DAS28 change was 2.5 ±1.2, resulting in a mean ±SD DAS28 of 2.4 ±1.1 at first follow-up. HAQ25 and MCID_HAQ were reached in 21% (41/193) and 70% (136/193) of patients. FIL efficacy slightly decreased with increasing line of therapy (Figure 1).

Table 1. Baseline characteristics of TARDIS patients on FIL

	Total FIL population
Number	405
Age (mean ±SD, years)	58.3 ±13.7
Disease duration (mean ±SD, years)	10.0 ±9.5
ESR (mean ±SD, mm/hour)	24.9 ±20.9
CRP (mean ±SD, mg/L)	12.4 ±15.7
SJC28 (mean ±SD)	6.5 ±4.2
TJC28 (mean ±SD)	9.0 ±5.6
DAS28 (mean ±SD, years)	4.9 ±0.9
HAQ-DI (mean ±SD, 0-3)*	1.6 ±0.6
PGA (mean ±SD, 0-100)	65.6 ±18.9
Advanced Therapy Naive yes	148/405 (36,5%)
Advanced Therapy Experienced yes	257/405 (63.5%)
2nd line	113/405 (27.9%)
3th line +	144/405 (35.5%)
Previous advanced treatment**	
TNFi,	77/226 (34.0%)
Non-TNFi,	97/226 (42.9%)
JAKi	52/226 (23.0%)

Legend: Number given are mean ± SD or number, proportion. TNFi = tumour necrosis factor inhibitor, JAKi = Janus Kinase inhibitor, HAQ= health assessment questionnaire, PGA= Patient Global assessment; CRP= C-reactive protein; ESR= erythrocyte sedimentation rate; TJC= tender joint count; SJC= Swollen joint Count; DAS28 = disease activity score based on the 28joints. Advanced Therapy naive patients were patients starting FIL as first advanced therapy. *Missing HAQ(0-3) scores were imputed by regression using age and HAQ(0-60) scores. **for 31 of 257 Advanced Therapy Experienced patients this was undefined.

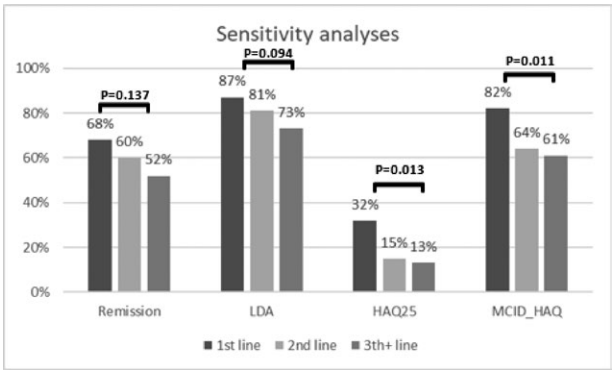


Figure 1. Effectiveness outcomes of FIL per treatment line

Conclusion: FIL treatment offered promising clinical outcomes after 3 months in most patients with moderately to severely active RA in a real-world setting.
Acknowledgements: on behalf of the Royal Belgian Society for Rheumatology. This work was financially supported by Galapagos.
Disclosure of Interests: None Declared.
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AB0426 PROFILE OF REFRACTORY RA PATIENTS FOR TARGETED THERAPIES IN REAL LIFE

Keywords: bDMARD, Rheumatoid arthritis, Targeted synthetic drugs

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Background: A proportion of RA patients fails to respond to their first targeted therapy (TT), and response decreases with increasing TTs exposures. EULAR have defined refractory RA (refRA) patients as a failure of two or more TTs of differing mechanisms of action.
Objectives: We aimed to determine the clinical and therapeutic profile of refRA and describe the patterns of drug sequencing.
Methods: Cross-sectional, observational study with RA patients diagnosed according to ACR/EULAR 2010 criteria, and exposed to TT over the last 20 years was performed. We classified patients in 1) non-refRA (1 or 2 TTs) and 2) refRA (at least 3 TTs). We analyzed the different lines of treatment with TTs, its duration treatment and reasons for discontinuation of treatment.
Results: 544 RA patients undergoing TTs were included, 122 from them were considered as refRA (at least 3 lines of TTs). RefRA patients showed younger age at diagnosis than non-refRA (P<0.001) but there is no differences on time of disease evolution until de 1st TT in both groups. Anti-TNF was the treatment of choice for the 1stline therapy, however is less likely to be administered in non-refRA rather than refRA (P<0.001) (table 1). "Cycling" after the first-line TTs was frequent in refRA (P<0.001), but from the 3rd-line of treatment "switching" is the main choice and different TTs differing mechanisms of action were used. The absence of conventional DMARD treatment is more likely in refRA, as well as a reduction in the treatment duration as increase the number of treatment lines administered. Secondary non-response in 1st and 2nd TTs were the main reason for discontinuing treatment (P<0.001) in refRA, being the adverse event more frequent as cause of discontinuing treatment in non-refRA (P=0.005). Analyzing the reason for discontinuing treatment and excluding the "other reasons", if the cause of discontinuing treatment in refRA is a primary non-response, near of the 30% of patients discontinue in 2nd-line by the same reason; and if the cause for discontinuation in 1st-line is an adverse effect, the 33% of patients discontinue in 2nd-line by the same reason (see image).
Conclusion: RefRA patients showed lower age at diagnosis. Anti-TNF was the most frequent TT both in 1st and 2nd line of treatment; and as from the 3rd-line there is a switching for TTs with mechanisms of action. Despite to secondary non-response is the most common cause of discontinuation in first and second-line in refRA, we observed a tendency to reiterate in the second-line of treatment the reason for discontinuation of the first-line of treatment.

	Non-refRA		RefRA							
Variable	**1st line N=422**	**2nd line N=136**	**1st line N=122**	**2nd line N=122**	**3rd line N=122**	**4th line N=71**	**5th line N=29**	**6th line N=13**	**7th line N=6**	**8th line N=3**
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
TTs:										
ANTI-IL6	54 (12.8)	19 (13.9)	10 (8.2)	16 (13.1)	32 (26.2)	22 (30.9)	4 (13.8)	2 (15.4)	0 (0)	0 (0)
ANTI-JAK	73 (17.3)	27 (19.9)	3 (2.5)	9 (7.4)	24 (19.7)	18 (25.4)	10 (34.5)	8 (61.5)	4 (66.7)	2 (66.7)
ANTI-TNF	257 (60.9)	52 (38.2)	101 (82.8)	80 (65.6)	35 (28.7)	10 (14.1)	3 (10.3)	1 (7.7)	2 (33.3)	1 (33.3)
Others	38 (9)	38 (27.9)	8 (6.5)	17 (13.9)	31 (25.4)	21 (29.6)	12 (41.4)	2 (15.4)	0 (0)	0 (0)
Cycling	0 (0)	45 (33.1)	0 (0)	73 (59.8)	35 (28.7)	8 (11.3)	1 (3.5)	2 (15.4)	4 (66.7)	1 (33.3)
Switching	0 (0)	91 (66.9)	0 (0)	49 (40.2)	87 (71.3)	63 (88.7)	28 (96.5)	11 (84.6)	2 (33.3)	2 (66.7)
Conventional DMARD										
No DMARD	150 (35.7)	24 (19.7)	45 (33.1)	29 (23.8)	32 (26.2)	20 (28.2)	8 (27.6)	5 (38.5)	5 (83.3)	1 (33.3)
Methotrexate	202 (47.9)	64 (52.5)	67 (49.3)	59 (48.4)	56 (45.9)	28 (39.4)	12 (41.4)	4 (30.8)	1 (16.7)	2 (66.7)
Leflunomide	55 (13)	29 (23.8)	17 (12.5)	29 (23.8)	25 (20.5)	12 (16.9)	3 (10.3)	1 (7.7)	0 (0)	0 (0)
Others	15 (3.5)	5 (4.1)	7 (5.2)	5 (5)	9 (7.4)	11 (15.5)	6 (20.7)	3 (23.1)	0 (0)	0 (0)
Discontinued treatment by:										
Primary non-response	19 (9.4)	3 (6.5)	15 (12.3)	28 (22.9)	14 (17.5)	7 (20)	3 (20)	3 (33.3)	1 (33.3)	0 (0)
Secondary non-response	68 (33.5)	2 (4.4)	69 (56.6)	62 (50.9)	44 (55)	14 (40)	7 (46.7)	2 (22.2)	2 (66.7)	0 (0)
Adverse events	71 (34.9)	18 (39.1)	35 (28.7)	28 (22.9)	22 (27.5)	12 (34.3)	4 (26.7)	4 (44.5)	0 (0)	1 (100)
Other causes*	45 (22.2)	23 (50)	3 (2.4)	4 (3.3)	0 (0)	2 (5.7)	1 (6.6)	0 (0)	0 (0)	0 (0)

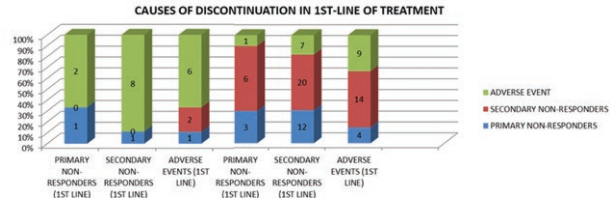


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4014

AB0427 ADHERENCE ANALYSIS OF REAL-WORLD EVIDENCE FOR ADALIMUMAB BIOSIMILAR MSB11022 THERAPY IN RHEUMATOLOGIC DISEASES

Keywords: Rheumatoid arthritis, Real-world evidence, bDMARD

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Background: Phase III clinical trial results demonstrated evidence of safety and efficacy data are similar between MSB11022 (an adalimumab biosimilar) and reference adalimumab in patients with moderate to severe rheumatoid arthritis (RA)[1]. Adherence to biologic treatments is often indicative of disease control and good patient treatment experience. However, evidence on the adherence for MSB11022 in rheumatology diseases is lacking in real-world clinical care setting.
Objectives: The objective of this project was to analyze real-world data collected by Fresenius Kabi patient-support program (PSP, KabiCare) on adherence to MSB11022. Patients with RA, psoriatic arthritis (PsA), and ankylosing spondylitis (AS) were included in this analysis.
Methods: Patients with RA, PsA and AS enrolled in KabiCare and received at least one dose of adalimumab biosimilar, MSB 11022, were follow-up from Feb 2021 to Nov 2022 in Canada. Medication initiation date and stop date, disease types and patient treatment (categorized by naïve to biologic or, switched from other biologics) were recorded in the database. The stop date was the date when KabiCare was informed that medication was discontinued. The patients continuing medication were censored at the maximal follow-up date of analysis, November 9, 2022. Log-rank tests were used for KM (Kaplan-Meier) plot comparison to examine if there were differences in medication adherence among RA, PsA and AS, and between naïve group vs. switch group by disease.
Results: The analysis sample consisted of 2049 patients, 879 of whom had RA, 514 had PsA and 656 had AS. Naïve group included 448 RA, 192 PsA and 256 AS patients. KabiCare followed patients for a median time of 260 days (interquartile range: 169-383 days; maximum: 609 days). At 500 days (approximately 18 months) post initiation of medication, the adherence probability was similar for patients with RA, PsA and AS (At day-500: 75.3%, 82.8% and 81.9%, P=0.096). The adherence probability was higher with switch group compared to naïve group (At day-500: 79.9.8% vs. 70.7%, P=0.027 in RA, 88.1% vs. 72.0%, P=0.0011 in PsA, and 85.8% vs. 74.9%, P=0.0057 in AS).
Conclusion: MSB11022 adherence probability for naïve group ranged between 70%-74.9%; and for switched group ranged from 79.9% - 88.1% for RA, PsA, and AS patients combined at 18 months after initiating MSB11022 biologic therapy. This real-world evidence analysis suggests that patients switching to MSB11022, adalimumab biosimilar, will more likely maintain on therapy when compared to patients initiating MSB11022 therapy. In both cases, inflammatory arthritis patients had high adherence to MSB11022 therapy.

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Disclosure of Interests: Sun Cheung Employee of: Fresenius Kabi Canada, Don Truong Employee of: Fresenius Kabi Canada.
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AB0428 SAFETY AND PERSISTENCE OF TREATMENT WITH GOLIMUMAB VERSUS CERTOLIZUMAB IN RHEUMATOID ARTHRITIS: RESULTS FROM BIOBADABRASIL COHORT STUDY.

Keywords: Real-world evidence, Safety, Registries

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Background: Golimumab and certolizumab were the last original anti-TNF agents approved in Brazil for the treatment rheumatoid arthritis (RA). Recent studies indicate that certolizumab is associated with higher risk of infections [1] and golimumab with better drug survival compared to the other anti-TNF agents [2], although they have not been compared in head-to-head trials.
Objectives: To evaluate the risk of adverse effects and survival of treatment course in RA patients treated with certolizumab or golimumab.
Methods: BiobadaBrasil is a multicentric registry-based cohort study of Brazilian patients with rheumatic diseases starting their first biologic disease modifying anti-rheumatic drug [3]. The present analysis includes RA patients recruited from Jan 2009 to Oct 2019, followed-up over one or two courses of treatment (latest date, Nov 19, 2019). A treatment course is defined as a period during which the medication scheme does not change. The primary outcome was the incidence of serious adverse events (AEs) and total AEs. System-specific AEs, treatment interruption for any reason, interruption due to AEs and due to inefficacy served as secondary outcomes. Negative binomial regression with generalized estimating equations (to calculate multivariate incidence rate ratios [mIRRs]) and extended (frailty) Cox proportional hazards models were used for statistical analyses (both types of analyses allowing time-fixed and time-varying covariates over multiple courses of treatment).
Results: In total, 227 patients (120 courses, 269.1 patient-years [PY] on treatment with certolizumab and 119 courses, 287.4 PY on golimumab therapy) were enrolled. Patients' features (female: 88.3%; seropositivity: 14.6%; mean age, 52.5 years; mean disease duration, 10.1 years) were comparable between the groups, but start of treatment with certolizumab was on average one year later than golimumab. The

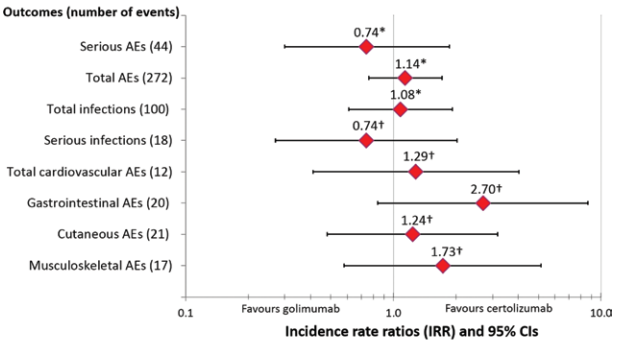
crude incidence of serious AEs was 9.2/100PY for certolizumab and 6.6/100 PY for golimumab. The incidence of any (total) AEs was 37.1/100 PY for certolizumab and 59.8/100 PY for golimumab. The risk of serious and total AEs (primary outcomes) did not differ significantly between the study groups (Figure 1). There was also no significant difference in the risk of infections and other secondary outcomes. Persistence of treatment and reasons for interruption of therapy course also were not significantly different between certolizumab and golimumab (Table 1).

Table 1. Results of univariate and multivariate frailty Cox proportional hazards models estimating the hazard of treatment interruption with golimumab versus certolizumab users (reference). Results are hazard ratios, 95% CIs, and P values.

Cause of interruption (number of events)	Crude analysis	Adjusted for covariates*
Interruption for any reason (111)†	1.58, 0.96 to 2.60, P=0.069	1.45, 0.88 to 2.40, P=0.150
Interruption due to adverse events (24)	1.93, 0.59 to 6.34, P=0.280	1.78, 0.48 to 6.56, P=0.380
Interruption due to inefficacy (65)	0.97, 0.54 to 1.74 P=0.920	0.92, 0.44 to 1.91, P=0.820

*Adjusted for time-fixed covariates (gender, smoking, seropositivity for RF or anti-CCP, history of malignancy, interstitial lung disease, diabetes, hypertension, renal failure, ischemic cardiomyopathy, chronic obstructive pulmonary disease, heart failure, hypercholesterolemia, osteoporosis, and hepatitis B and C; recorded at baseline) and time-varying covariates (age, baseline DAS28, disease duration, starting year, order of treatment, concurrent use of sulfasalazine, methotrexate, leflunomide, cyclosporine and corticosteroids; recorded at the start of each course). †Except for pregnancy or disease remission.

Figure 1. Safety of golimumab versus certolizumab in RA



*Multivariate IRR, adjusted for the same variables described in Table 1.
†Univariate IRR.

Conclusion: In this cohort study of Brazilian RA patients, we did not observe significant differences between certolizumab and golimumab in relation to safety outcomes and persistence of treatment course.

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Disclosure of Interests: None Declared.

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AB0429

EIGHT-MONTH FOLLOW-UP OF THE NON-MEDICAL SWITCH FROM ETANERCEPT BIO-ORIGINATOR TO GP-2015 OR SB4 ETANERCEPT BIOSIMILARS IN PATIENTS WITH CHRONIC INFLAMMATORY ARTHROPATHIES: A MONOCENTRIC OBSERVATIONAL STUDY

Keywords: bDMARD, Rheumatoid arthritis, Spondyloarthritis

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Background: After the expiration of bio-originators' licenses, the development of less expensive biosimilars has prompted the switch to these drugs. Data on the switch from etanercept (ETA) bio-originators to biosimilars are reassuring [1-2] but still limited.

Objectives: This observational study evaluated the real-life effectiveness of a non-medical switch from ETA bio-originator to GP-2015 or SB4 biosimilars in our cohort of patients with inflammatory chronic arthritis.

Methods: We enrolled consecutive adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) classified according to standard criteria switched from ETA bio-originator to GP-2015 or SB4 biosimilars for administrative/economic reasons. The date of the switch was the baseline (T0). Patients were reassessed after 4 (T4) and 8 months (T8). At T0, T4, and T8, data on demographic and clinical/laboratory features were registered. Patient-reported outcomes (PROs), such as visual analog scale (VAS 0-10) for pain and global assessment (PGA) and functional status by Health Assessment Questionnaire (HAQ) were used, together with disease-specific scores (DAS28-CRP for RA, DAPSA for PsA, ASDAS-CRP and BASDAI for AS). We assessed the same data at the time of early discontinuation for inefficacy (loss or lack of efficacy – LoE or LaE) or adverse events (AEs).

Results: One hundred and twelve patients switched from ETA bio-originator to GP-2015 [45 RA, F:M=33:12, median age 67 years (IQR 24), median disease duration 214 months (IQR 180), median exposure to bio-originator 126 months (IQR 97); 48 PsA, F:M=18:30, median age 59 years (IQR 18), median disease duration 168 months (IQR 120), median exposure to bio-originator 120 months (IQR 96); 19 AS, F:M=7:12, median age 55 years (IQR 16), median disease duration 162 months (IQR 245), median exposure to bio-originator 132 months (IQR 82)]. No differences were found in the clinical and laboratory parameters compared to T0 in RA and PsA, while AS patients showed an improvement of BASDAI at T8 compared to T4 (p=0.0273). Interestingly, at T8 RA patients experienced a worsening in the HAQ (p=0.0313) with respect to T0 (figure 1A) and PsA patients had a worsening of VAS pain compared to T4 (p=0.0371) (figure 1B). Four (8.8%) RA patients discontinued GP-2015 at T4 due to AEs (1 for recurrent infection of upper airways, 1 for injection site reaction, 1 for skin cancer, 1 for breast cancer). One (2%) PsA patient discontinued GP-2015 at T4 due to AE (oral ulcers). Twenty-eight patients switched from ETA bio-originator to SB4 [14 RA, F:M=13:1, median age 63.5 years (IQR 33), median disease duration 144 months (IQR 206), median exposure to bio-originator 84 months (IQR 96); 11 PsA, F:M=6:5, median age 54 years (IQR 12), median disease duration 205 months (IQR 198), median exposure to bio-originator 177 months (IQR 164); 3 AS, F:M=0:3; median age 56 years, median disease duration 210 months, median exposure to bio-originator 120 months]. An improvement of DAPSA at T4 compared to T0 was observed in PsA patients (p=0.0469). At T8, no differences were found compared to T0. One (9%) PsA patient experienced LoE at T4.

Conclusion: Our data indicate that the switch to GP-2015 or SB4 ETA biosimilars from ETA bio-originator does not bear clinical and laboratory differences in patients with chronic arthropathies. The worse outcome in PROs, which we also observed in the adalimumab bio-originator to biosimilar switch (3), does not reflect a worsening of disease activity indexes and could indicate a possible nocebo response.

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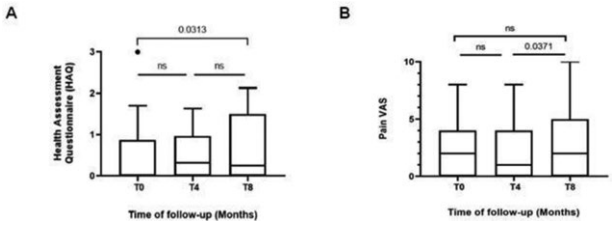


Figure 1. - Change in the HAQ in RA patients switching from ETA bio-originator to GP-2015 (A); change in the pain VAS score (0-10) in PsA patients switching from ETA bio-originator to GP-2015 (B)

Data are shown as Tukey boxplots; lines represent the median level with 25th-75th percentile; dots represent outliers.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0430

MEDICATION ADHERENCE IN PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS TREATED WITH BIOLOGIC OR TARGET SYNTETIC -DMARDS: EVALUATION OF PREDICTIVE FACTORS IN AN ITALIAN MONOCENTRIC COHORT

Keywords: Quality of care, Patient information and education, Rheumatoid arthritis

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Background: In rheumatoid arthritis(RA), medication non-adherence can be considered one of the primary determinants of therapeutic failure.
Objectives: To evaluate 1)the prevalence of treatment adherence in RA patients(pts) treated with biologic(b) or target synthetic(ts)-DMARDs followed in a tertiary rheumatologic center and 2)the factors associated to a better treatment adherence.
Methods: An observational retrospective single center study was conducted enrolling adult RA pts treated with b/ts-DMARDs, in monotherapy or in combination with methotrexate. Demographic data, clinical characteristics and outcomes measures were collected. To evaluate the comorbidities the Rheumatic Disease Comorbidity Index(RDCI) was used. Treatment adherence was assessed through self-reported adherence rate(SRAR) rated on a visual analogue scale (VAS, 0-100 mm) and 5-item Compliance Questionnaire for Rheumatology(CQR5). Pts were considered adherent if SRAR ≥80/100. All the participants were required to complete: VAS pain questionnaire, Patient Global Assessment(PGA), Health Assessment Questionnaire(HAQ), Depression Anxiety Stress Scales(DASS21), Insomnia Severity Index and self-reported VAS therapy satisfaction scale (0-100 mm, higher values indicate higher satisfaction).
Results: Among the 116 pts (Table 1) evaluated, 57% described themselves as being adherent to their treatment (median SRAR: 80 [60-90]; median satisfaction level: 80 [60-90]). According to CQR5, 97% of the pts presented a high adherence level; 28/116 pts declared a treatment suspension during the previous month; in most cases the withdrawal was reasonable (due to vaccinations, infections, surgery). The comparison between adherent and non-adherent pts is shown in Table 1: a significative association between non-adherence and higher DAS28, HAQ and VAS pain scores was observed; in addition, an association was found between adherence and treatment satisfaction level. No significant differences in demographic features, educational level, work status, comorbidities and therapeutic formulation/plan/type were found. Patient's reported outcomes scores regarding insomnia/anxiety/depression/stress were higher in non-adherent pts but not statistically different.
Conclusion: Treatment adherence is still a complex process difficult to measure. Our data show a discrepancy between SRAR and CQR5 adherence assessment (57% vs 97%). In our cohort of pts, regularly followed-up in a tertiary outpatient clinic, the prevalence of adherence is overall higher as compared with that reported in literature (medication adherence in RA pts: 30-80%)[1]. In this study, treatment adherence seems to be associated with a higher therapy satisfaction level and a lower disease activity, pain perception, and physical disability. However, a cause-effect relationship still remains difficult to analyze.

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Table 1.

	adherent pts SRAR≥80 n: 66	non-adherent pts SRAR<80 n: 50	p value
Age, years	57 [48-67]	59 [53-68]	0.16
Female sex	53 (80)	37 (74)	0.42
Worker	33 (50)	26 (52)	0.83
High educational level	36 (55)	21 (42)	0.75
Disease duration, years	11 [7-18]	12 [6-18]	0.71
FR+ and anti-CCP+	44 (67)	30 (60)	0.46
Combination with methotrexate	35 (53)	29 (58)	0.59
bDMARD (sc)	40 (61)	25 (50)	0.25
tsDMARD (os)	26 (39)	25 (50)	0.25
RDCI [0-9]	1 [0-2]	1 [0-2]	0.67
Therapy Satisfaction level [0-100]	90 [80-100]	70 [60-80]	***<0.01***
PGA [0-100]	30 [10-50]	50 [30-70]	***<0.01***
VAS pain [0-100]	30 [10-58]	60 [40-70]	***<0.01***
DAS28 [0.96-9.04]	1.8 [1.5-3.3]	2.5 [1.9-3.6]	***<0.01***
HAQ [0-3]	0.3 [0.0-0.6]	0.7 [0.25-1.1]	***0.01***
Insomnia Severity Index [0-28]	7 [3-12]	9 [6-14]	*0.09*
DASS 21 depression [0-42]	6 [2-12]	8 [4-12]	*0.22*
DASS 21 anxiety [0-42]	4 [2-8]	8 [2-12]	*0.07*
DASS 21 stress [0-42]	9 [4-16]	12 [7-18]	*0.07*

Continuous variables are expressed as median [IQR] and compared with Mann Whitney test; categorical variables are expressed as n (%) and compared with Chi squared test/ Fisher exact.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.

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AB0431

CANAKINUMAB AS FIRST-LINE BIOLOGICAL THERAPY IN STILL'S DISEASE AND DIFFERENCES BETWEEN THE SYSTEMIC AND THE CHRONIC-ARTICULAR COURSES: REAL-LIFE EXPERIENCE FROM THE INTERNATIONAL AIDA REGISTRY

Keywords: Inflammatory arthritides, Registries, bDMARD

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Background: Treatment with biotechnological anti-interleukin (IL)-1 agents is recommended in patients with Still's disease especially in cases refractory to glucocorticoids and conventional disease modifying anti-rheumatic drugs (cDMARDs), avoiding a long-term glucocorticoids exposure. In cases with refractory arthritis, IL-6 inhibitors have shown to be effective on articular inflammatory involvement.
Objectives: The objective of the present study is to evaluate any difference in the effectiveness of the IL-1β antagonist canakinumab prescribed as first-line biologic agent between the systemic and the chronic-articular Still's disease.

Methods: Data were drawn from the retrospective phase of the AutoInflammatory Disease Alliance (AIDA) international registry dedicated to Still's disease. Patients affected by Still's disease classified according to internationally accepted criteria (Yamaguchi criteria and/or Fautrel criteria) and treated with canakinumab as first-line biologic agent were enrolled.
Results: A total of 26 patients (17 females, 9 males; 18 patients developing Still's disease after the age of 16 years) were enrolled; 16 (61.5%) patients suffered from the systemic pattern of the disease; 10 (38.5%) patients suffered from the chronic-articular type. No differences were observed between the systemic and the chronic-articular Still's disease in the frequency of complete response, of flares after the start of canakinumab (p=0.701) and in the persistence in therapy (p=0.62). No statistical differences were observed between the two groups after 3 months, 12 months and at the last assessment in the decrease of: the systemic activity score (p=0.06, p=0.17, p=0.17, respectively); the disease activity score on 28 joints (p=0.54, p=0.77, p=0.98, respectively); the glucocorticoid dosage (p=0.15, p=0.50, and p=0.50, respectively); the use of concomitant disease modifying anti-rheumatic drugs (p=0.10, p=1.00, and p=1.00, respectively). No statistically significant differences were observed in the decrease of erythrocyte sedimentation rate (p=0.34), C reactive protein (p=0.48), and serum ferritin levels (p=0.34) after the start of canakinumab.
Conclusion: Canakinumab employed for Still's disease has been effective in controlling both clinical and laboratory manifestations disregarding the type of disease course when used as first-line biotechnological agent. These excellent results might have been further improved by the early start of IL-1 inhibition.
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AB0432 COMPARISON OF SYMPTOMATIC AND DISEASE-MODIFYING TREATMENT IN RHEUMATOID ARTHRITIS WITH CONCOMITANT FIBROMYALGIA

Keywords: Disease-modifying Drugs (DMARDs), Rheumatoid arthritis, Fibromyalgia

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Background: There is evidence that concomitant fibromyalgia (FM) among rheumatoid arthritis (RA) patients make the management of RA challenging by inflating subjective disease activity parameters.
Objectives: Thus, the aim of this study was to compare symptomatic and disease-modifying treatments in RA patients with and without concomitant FM.
Methods: This was a cross-sectional study including patients with an established RA according to the 2010 ACR/EULAR criteria. All patients were screened for concomitant FM by 2016 ACR criteria. Patients were divided into 2 groups: RA and RA+FM. Demographic and RA characteristics were collected. P<0.05 was accepted for significance. Multiple linear regression analysis performed, adjusting for clinical and demographic variables.
Results: Eighty patients distributed into 40 patients in each group were recruited. Epidemiological characteristics, RA characteristics and disease activity scores were. comparable between groups. Coxitis and atlantoaxial subluxation were significantly more frequent in RA+FM group (p=0.006 and p=0.049 respectively). No significant difference in corticosteroids prescription was found between the groups (p=0.88), nor in non Non-steroidal anti-inflammatory drugs prescription (p=0.48). Of the RA patients with concomitant FM, 52% were treated with biological therapy vs. 18% of RA patients without concomitant FM (p = 0.04). Tumor necrosis factor inhibitors were the most frequently prescripted in the two groups (47.5% of RA patients with FM vs 12.5 in RA patients, p=0.03). No significant difference was noted between the groups regarding conventional Disease-modifying antirheumatic drugs (DMARDs) prescription (p=0.052). Multiple linear regression in RA+FM group showed that FM is an independent factor for biological DMARDs prescription (B=0.284, p=0.018).
Conclusion: Our study showed that concomitant FM in patients with RA was associated with a higher use of biological treatments. This raises the question of whether the more frequent use of biologics in these patients is justified by inflammation, or by persistent pain and other centrally mediated symptoms.
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AB0433 BIOLOGICAL THERAPIES SURVIVAL FOR RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS SPONDYLOARTHRITIS AND JUVENILE ONSET ARTHRITIS. A COHORT STUDY FROM BIOBADAGUAY

Keywords: Inflammatory arthritides, bDMARD

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Background: BIOBADAGUAY is the Paraguayan/Uruguayan registry of adverse events in patients with inflammatory rheumatic conditions under biologic therapy (BT). The registry includes patients with different diagnosis that share similar biological therapies indication. However, different pathogenesis, patients' characteristics and treatment options can affect the survival of the BT.
Objectives: To analyze survival of biological therapies among patients with chronic inflammatory arthritis in the BIOBADAGUAY registry.
Methods: Patients with chronic inflammatory arthritis (CIA) such us rheumatoid arthritis (RA), spondylarthritis (SpA), psoriatic arthritis (PsA) and juvenile onset arthritis (JIA) enrolled in BIOBADAGUAY where analyzed. Other diseases included in the registry were grouped as others. Drug survival and clinical and epidemiological predictors were studied. Fewer than BT 25 registries were not included in the study. Survival analysis was performed using Kaplan-Meier estimators, and Cox proportional hazard models were used to estimate hazard ratios (HRs).
Results: A total of 1378 treatments (876 RA, 176 SpA, 40 JIA, 88 PsA, 98 others) were included. The mean BT survival according to diagnosis was 300.9 (95%CI, 230.6-444.4) weeks (wks) for RA; 541.6 (95%CI, 409.6-541.6) wks for SpA; 154.1 (95%CI, 125.0-194.7) wks for JIA and 555.3 (95%CI, 282.1-611.6) wks for PsA. In the general analysis, when survival was compared between different diagnosis, it was found that BT survival for SpA patients (p˂0.05; HR=1.23 [95% CI 0.97-1.56]) was higher than other CIA. On the other hand, JIA diagnosis was significantly associated with a lower BT survival (p˂0.05; HR=1.85 [95% CI 1.36–2.52]). In the general analysis, no significant differences between BT were found (p>0.05). When each drug survival was analyzed according to diagnosis, adalimumab showed a significant difference in SpA patients (p˂0,05; HR=0.55 [95% CI, 0.39-0.76]) and JIA patients (p=<0.005; HR=1.8 [95% CI 1.36–2.52]). Etanercept had a significant difference in RA (p <0.005; HR=0.57 [95% CI, 0.40-0.82]) and JIA patients (p=<0.005; HR=2.07 [95% CI, 1.39–3.06]). Following these results we analyzed JIA patients and found that remission was the principal reason of discontinuation in this group of patients (p<0.005, HR=10.700 [95% CI, 5.91–19.36]). Multivariable analysis showed that the number of previous BTs (p=0.01, HR=1.18 [95% CI, 1.03-1.34), corticosteroid treatment (p=0.05; HR=1.18 [95% CI; 0.99–1.40), SpA (p=0.01; HR=0.688 [95% CI 0.51-0.91) and JIA diagnosis (p=0.02; HR=1.4 [95% CI, 1.06-2.02]) where associated with BT survival.
Conclusion: In this study we found different survival profiles according to diagnosis. This could be related to different pathogenesis, discontinuation motives and treatment options in different health systems.
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AB0434 RHEUMATOID FACTOR AS PREDICTOR OF RESPONSE TO RITUXIMAB

Keywords: bDMARD, Rheumatoid arthritis

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Background: In Rheumatoid Arthritis (RA), the presence of rheumatoid factor (RF) indicate poor prognosis. Strategies searching biomarkers that predict response to biologic therapies allowing the selection of patients with the highest

chance for response are pertinent. Whether RF is a biomarker of response to RTX is disputed. [1]

Objectives: To investigate whether high rheumatoid factor (3 times normal) is predictive of a good therapeutic response in RA patients treated with Rituximab (RTX).

Methods: We conducted a Retrospective study in a single rheumatology hospital in Morocco. All patients satisfied the ACR-EULAR 2010 RA classification criteria. Socio-demographic data, comorbidities, disease-related variables (duration, characteristics, and drugs) were collected. The endpoint was a decrease in DAS28 greater than 1.2 at 6 month after RTX therapy. Statistical analysis were performed with SPSS 20.

Results: We included 129 patients with a mean age of 58.45 ± 11.99 years. The sex ratio F/M was 8:1. The mean duration of RA was 17.73 ± 8.34 years. The mean age at diagnosis was 44.13 ± 13.91 years, 87% of patients were seropositive. The positivity of rheumatoid factor and ACPA was in 82% and 69% of the patients respectively. RF was highly elevated in 48.4% of patients. In bivariate analysis, strong RF positivity was significantly associated with a good response as assessed by DAS28 (p=0.002), and to a high initial IgM level (p= 0.018).

Conclusion: In our study, RA patients with strong positive rheumatoid factor had a better therapeutic response as assessed by DAS28. These results should be taken into account when making therapeutic choices.

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AB0435 ADHERENCE TO BIOLOGIC THERAPIES IN INFLAMMATORY RHEUMATIC DISEASES: INFLUENCE OF ROUTE OF ADMINISTRATION

Keywords: Spondyloarthritis, bDMARD, Rheumatoid arthritis

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Background: Inflammatory rheumatic diseases are a debilitating disease affecting the joints and periarticular structures and leading, more or less rapidly, to cartilage and bone destruction. It is a major source of chronic pain and physical, psychological, and social disability, it affect approximately 1% of the world's population [1]. For more than 20 years, biotherapies have revolutionized the treatment of these inflammatory diseases and have largely contributed to the improvement of their prognosis [2]. Adherence to biologic therapies conditions the effectiveness of the treatments then the improvement of patients' quality of life [3].

Objectives: To evaluate and compare adherence to biologic disease-modifying antirheumatic drugs (bDMARDs) according to the route of administration and the molecule used (Infliximab, Tocilizumab, Etanercept, Adalimumab, Certolizumab, and Golimumab) in patients with inflammatory rheumatic diseases.

Methods: This is a descriptive cross-sectional study with repeated data collection, bi-centric carried out in the rheumatology departments and outpatient clinics at Charles Nicolle Hospital and Rabta Hospital in Tunis and conducted over a period of 01 year and 02 months between 02/02/2021 and 30/04/2022. 71 adult patients with rheumatoid arthritis, spondyloarthritis or juvenile idiopathic arthritis were recruited, their adherence rate in the last 3 months before inclusion should be ≥80%. The collection of socio-demographic, clinical and therapeutic data was established with the help of a pre-established form, from medical files completed by questioning the patients during a direct interview or through a telephone communication. Adherence rate was calculated by determining the ratio of treatments cures (number of biologic injections taken during a year divided by the number of annual biologic injections prescribed).

Results: Within the study population, adherence was estimated at 85.9%; in the group of patients using intravenous biotherapy was 82.1% (Infliximab 86%, Tocilizumab 75% p=0.04) and in the group of patients using subcutaneous treatment was 89.9% (Golimumab 94%, Etanercept 92%, Certolizumab 89%, Adalimumab 87% p=0.3). Adherence to biologic therapy was significantly higher in the subcutaneous group than in the intravenous group (p=0.01). The causes of poor adherence presented by the patients in this study were: stock-outs of biological treatment and delay in renewal by the national health insurance (CNAM) in thirty-eight cases (54%p<0.001), intercurrent infections in thirty-three cases (46% p=0.005) and the COVID 19 pandemic and its consequences in thirty patients (42%,p=0.28).

Conclusion: Adherence to biologic treatment is influenced by the route of administration, drugs type, intercurrent infections and drugs availability. All this factors must be treated to improve therapeutic adherence then the efficiency of the biologic therapy which conditions the preservation of physical capacities and an improvement in the quality of life.

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AB0436 THE IMPROVEMENT OF THE DAS28 SCORE AT THREE MONTHS PREDICTS BIOLOGIC DRUGS TOLERANCE AND SURVIVAL IN RHEUMATOID ARTHRITIS

Keywords: bDMARD

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Background: The treat-to-target strategy has been established as a guiding principle for the treatment of rheumatoid arthritis (RA). Nevertheless, data on the degree to which the improvement of the DAS28 score impacts the survival of biologic drugs is rarely studied.

Objectives: Our objective in this study was to assess the influence of the improvement of the DAS28 score at 3 months on biologics tolerance and survival.

Methods: We conducted a cross-sectional and observational study. Files of patients with RA on biologics drugs (archived from the files of patients on the National Health Insurance Fund of Tunis) were studied. Epidemiological characteristics such as age, sex, and comorbidities, were collected. RA activity was assessed by the composite score 'Disease Activity Score 28' (DAS28). Patient follow-up was done at 3 months by the DAS28 disease activity score. We specified the ΔDAS28, between the initiation of biotherapy and the value at 3 months. The therapeutic maintenance rate at 3 months as well as the biologics survival was analyzed using Kaplan-Meier survival curves and compared using the Log-Rank test.

Results: Three hundred and seventy-four files were selected. The average age of our cohort was 55±12.54 years [20-90]. A female predominance was noted with a sex ratio M/F=0.147. The average duration of RA was 11.7±6.76 years [2-41]. The first biotherapy prescribed was certolizumab pegol 13%, adalimumab in 14% of cases, infliximab 6%, tocilizumab 6%, etanercept in 54% of cases, and rituximab in 7% of cases. The average DAS28 at the initiation of the biological treatment was 6.02 ± 0.89. The median was 6 [5.37–6.50]. We noted that the higher the delta DAS28 at 3 months of treatment, the lower the risk of interrupting the biological treatment, as evidenced by the HR = 0.709 (p < 10-3). For patients with a moderate to good response the maintenance rate was 45.35 months [43.06-47.64]; for patients with no response; therapeutic maintenance was 28.55 months [22.41-34.69].

Conclusion: Efficient and rapid management of RA remains the most appropriate strategy to achieve control of the disease. The rapid improvement of DAS28 under biologics would be, according to our results, a factor influencing the survival of these treatments. Larger-scale studies will be needed to confirm these results.

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AB0437 IMMUNOGENICITY ANALYSIS FROM THE VOLTAIRE TRIALS IN PATIENTS WITH RHEUMATOID ARTHRITIS, CROHN'S DISEASE, AND CHRONIC PLAQUE PSORIASIS

Keywords: Rheumatoid arthritis, Safety, Disease-modifying Drugs (DMARDs)

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Background: The VOLTAIRE trials program compared safety, efficacy, and immunogenicity of biosimilar BI 695501 with adalimumab reference product (RP) for indications including moderate-severely active rheumatoid arthritis (RA), Crohn's disease (CD), and chronic plaque psoriasis (PsO). Details of each active-comparator, randomized controlled trial (RCT) are published. [1,2,3]
Objectives: Here we compare immunogenicity across these indications and by patient sex.
Methods: Immunogenicity was assessed at various timepoints by the proportion of patients with anti-drug antibodies (ADAs) and neutralising antibodies (nAbs), using acid dissociation followed by an electrochemiluminescence assay (ECL; MSD platform; Meso Scale Diagnostics LLC, USA).[4] Assay sensitivity was 50 ng/mL, and drug tolerance ≥30 µg/mL (free drug) at the low positive control level.
Results: Data are presented in **Table 1**.

Table 1. Immunogenicity data

	VOLTAIRE-RA		VOLTAIRE-CD		VOLTAIRE-PsO	
	BI 695501	**RP**	**BI 695501**	**RP**	**BI 695501**	**RP**
Antibody first detectable						
ADA	Baseline	Baseline	Baseline	Week 4 [a]	Baseline	Baseline
nAb	Baseline	Baseline	Week 4 [a]	Week 4 [a]	Baseline	Baseline
ADA titre at primary endpoint, mean (SD)	54.1 (93.54) at wk 12 163.2 (753.96) at wk 24	353.5 (1816.96) at wk 12 294.7 (1555.05) at wk 24	647.9 (2176.14) at wk 4	17.5 (31.03) at wk 4	32.0 (1, 16384) at wk 16 [b]	32.0 (1, 8192) at wk 16 [b]
Proportion of patients with antibodies (ADAs and nAbs) over time						
ADA positive	[c]	[c]				
Baseline	3.4% (11/323)	6.5% (21/321)	4.3% (3/69)	0% (0/74)	10.7% (17/159)	10.8% (17/158)
Day 7 (Wk 1)	5.7% (18/317)	9.3% (29/311)				
Day 14 (Wk 2)	10.1% (32/318)	16.0% (51/318)				
Day 28 (Wk 4)	20.1% (64/319)	19.7% (62/315)	20.6% (14/68) [b]	5.5% (4/73) [b]		
Day 84 (Wk 12)	32.4% (101/312)	34.9% (106/304)				
Day 113 (Wk 16)					68.2% (101/148)	71.8% (107/149)
Day 168 (Wk 24)	43.2% (127/294)	47.8% (144/301)				
nAb positive	[c]	[c]				
Baseline	2.8% (9/323)	5.0% (16/321)	0% (0/69)	0% (0/74)	0.6% (1/159)	1.9% (3/158)
Day 7 (Wk 1)	2.5% (8/317)	3.9% (12/311)				
Day 14 (Wk 2)	3.1% (10/318)	8.2% (26/318)				
Day 28 (Wk 4)	6.9% (22/319)	7.3% (23/315)	8.8% (6/68) [a]	2.7% (2/73) [a]		
Day 84 (Wk 12)	13.1% (41/312)	16.8% (51/304)				
Day 113 (Wk 16)					54.1% (80/148)	55.7% (83/149)
Day 168 (Wk 24)	16.0% (47/294)	20.6% (62/301)				
Proportion of patients with ADA antibodies by subgroup						
Sex	Wk 12 Male (13/53) 24.5% Female (88/259) 34.0% Wk 24 Male (19/50) 38.0% Female (110/246) 44.7%	Wk 12 Male (18/47) 38.3% Female (88/257) 34.2% Wk 24 Male (25/47) 53.2% Female (119/254) 46.9%	Wk 4 Male (8/37) 21.6% Female (6/31) 19.4%	Wk 4 Male (2/42) 4.8% Female (2/31) 6.5%	Wk 16 Male (65/93) 69.9% Female (36/55) 65.5%	Wk 16 Male (66/97) 68.0% Female (41/52) 78.8%

a. Wk 4 = Day 29 in CD trial; b. Median (minimum, maximum); c. Reported by randomisation completed at baseline

Conclusion: Minor differences in immunogenicity (ADAs, ADA titres and nAbs) between BI 695501 and adalimumab RP were observed across these 3 indications. The proportion of ADA- and nAb-positive patients increased from baseline in all 3 RCTs, and were similar in RA and CD RCTs, but rates were higher in PsO RCT. Subgroup analysis by patient sex showed the same trend. These differences may be partially explained by concomitant background therapy (MTX) in RA trial, stable doses of AZA, 6-MP or MTX in 36% of CD patients and the absence of background therapy in PsO RCT. Comparisons are limited by different visit schedules in the trials. Historical comparisons to RP data are complicated by recent differences in regulatory requirements for increased ADA assay sensitivity and stringency for biosimilar products than those originally used for the RP. Acid dissociation followed by the more sensitive ECL assay for detection of ADAs is not dependent on serum drug concentrations. In conclusion, these analyses confirm the biosimilarity of BI 695501 with the adalimumab RP across RA, CD, and PsO.

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AB0438 TAPERING BIOLOGICAL DMARD IN RHEUMATOID ARTHRITIS: REAL-WORLD EVIDENCE.

Keywords: bDMARD, Remission, Tapering

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Background: biological DMARDs have revolutionized the treatment of rheumatoid arthritis (RA), demonstrating effectiveness in terms of symptom control, improvement in quality of life and radiographic progression. However, their high-cost impacts global health systems. Therefore, tapering strategies are important therapeutic strategies to consider in patients with sustained remission. It is estimated that up to 50% of patients with bDMARDs and sustained response would be successful upon biologic therapy optimization [1].
Objectives: to estimate the relapse rate in patients with RA on tapering bDMARD protocol.
Methods: This is an observational cohort study of established RA patients followed in Medicarte, a Colombian specialized outpatient clinic, between 2014 and 2022. Selection criteria included patients ≥18 years of age, with a diagnosis of RA according to the 2010 EULAR classification criteria, who has been in remission for at least 12 months and agreed to enter the bDMARD reduction strategy either by reducing the dose or increasing the interval between doses. Relapse was defined according to the consensus of the Spanish Society of Rheumatology: mild relapse as an increase in DAS28>0.6 and final DAS28 >3.2, and severe relapse as an increase in DAS28 >1.2 [2]. Quantitative variables are presented as medians (interquartile range, IQR), while the qualitative variables as frequencies (percentages). Kaplan Meier was used to estimate the survival drug, according to tapering medication strategy and incidence density. A p value <0.05 was considered statistically significant.
Results: 167 patients [82.6% women, median (IQR) age of 59 years (52-65), and median (IQR) disease duration of 13.7 years (7.7-20.8)] were included. They have been in the tapering strategy for 2.4 years (IQR: 2-3.7). The median (IQR) of DAS 28 -CRP before start of tapering was 1.2 (0–1.6) and at the end of follow-up was 2.12 (IQR 1.54–2.77). Increasing the interval between doses was used as a tapering strategy in 70.1% of the patients. The most frequently bDMARD used was etanercept [n=57 (34.1%)], followed by tocilizumab 27.5% [n=46, subcutaneous and intravenous (27.5%)], adalimumab [n=27 (16.2%)], abatacept 8.4% [n=14, subcutaneous and intravenous (8.4%)], certolizumab 4.2% [n=7 (4.2%)], subcutaneous golimumab [n=11 (6.6%)], rituximab [(n=4 (2.4%)], and Infliximab [n=1

(0.6%)]. Relapses were observed in 24 (14.4%) patients while on biologic therapy optimization, being more frequent with certolizumab and abatacept. The lowest rates of relapse were observed with infliximab, adalimumab and etanercept, while certolizumab and abatacept had the shorter time to relapse (table 1). Overall, the relapse rate was 5.5 per 100 patient-years with RA at risk (p=0.021) (figure 1).

Conclusion: Tapering bDMARD strategy was effective in our large RA cohort with 85.6% of patients remaining in remission during the follow up. Adalimumab, etanercept and tocilizumab were the bDMARDs with the longest time to relapse. These findings support the use of the tapering strategy in patients with established RA.

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Table 1. Median (IQR) time to relapse (years) according to bDMARD

Total (n=167)	2.5 (1.2 a 3.3)
Abatacept (n=14)	1.9 (1.4 a 2.9)
Adalimumab (n=27)	2.8 (1.6 a 3.0)
Certolizumab (n=7)	1.1 (0.7 a 1.6)
Etanercept (n=57)	3.2 (1.8 a 3.7)
Golimumab (n=11)	1.2 (1.1 a 2.7)
Infliximab (n=1)	8.2 (8.2 a 8.3)
Rituximab (n=4)	1.4 (1.2 a 1.8)
Tocilizumab (n=46)	1.7 (1.2 a 3.2)

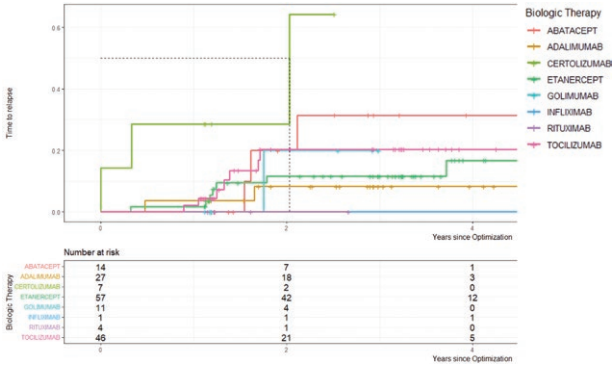


Figure 1. Relapse rate according to bDMARD

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AB0439

ADALIMUMAB AND NUMBER OF PREVIOUS BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS AS PREDICTIVE FACTORS FOR THE DEVELOPMENT OF IMMUNE-MEDIATED SKIN LESIONS

Keywords: Skin, bDMARD

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Background: Treatment of inflammatory rheumatic diseases has dramatically changed with the introduction of biologic disease modifying anti-rheumatic drugs (bDMARDs). However, these drugs aren't exempt from risks and skin lesions are the most frequent adverse reactions. Among the possible adverse skin reactions, immune-mediated skin lesions (IMSL) may occur. Risk factors associated with the occurrence of IMSL in rheumatic patients under bDMARDs are poorly known and studied.

Objectives: To identify predictive factors for IMSL in patients with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) under bDMARD therapy.

Methods: A retrospective single-center cohort study including patients with RA, axSpA and PsA followed at the Department of Rheumatology of a University Hospital Center between April 2000 and December 2021, treated with at least one bDMARD for at least 6 months was conducted. Data were collected from a national register of rheumatic patients (Reuma.pt) and medical records. Sociodemographic characteristics, disease duration, age at diagnosis, smoking and drinking habits, concomitant immunosuppressive medications, type and duration of the bDMARD treatment and number of previous bDMARD were collected. IMSL development were also collected. Independent samples t-test for normally distributed continuous data and chi-square tests for categorical variables was performed. Also, a multivariate logistic regression analysis was performed to identify possible predictive factors for the occurrence of IMSL. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Statistical significance was set at a p-value <0.05.

Results: From a total of 441 patients with RA, 386 with axSpA and 162 with PsA, 27 developed IMSL related to bDMARD (2.7%). Comparing the groups with and without IMSL, no differences were found regarding age, gender, BMI, presence of concomitant csDMARD or type of rheumatic disease. Patients with IMSL have a significant younger age at diagnosis (p=0.038), a longer disease duration (p=0.018) and a longer duration of bDMARD treatment (p=0.008). Patients with IMSL also have a higher number of previous bDMARDs (p<0.001) and adalimumab was the bDMARD with the higher risk of IMSL development (p<0.001). Table 1 described the demographic and clinical features of these two groups.

Table 1. Demographic and clinical features in patients with and without IMSL.

	With IMSL (n=27)	Without IMSL (n=962)	p-value
Age, mean ± SD, years	55.5 ± 14.0	52.2 ± 12.7	0.605
Female, n (%)	15 (55.6)	612 (63.6)	0.391
BMI, mean ± SD	25.4 ± 4.8	27.2 ± 7.5	0.227
Current/Former smoker, n (%)	10 (37.0)	327 (34.0)	0.477
Alcohol consumption, n (%)	4 (14.8)	140 (14.6)	0.599
Disease duration, mean ± SD, years	24.4 ± 12.7	19.2 ± 11.1	**0.018**
Duration of bDMARD treatment, mean ± SD, years	9.3 ± 4.4	6.6 ± 5.3	**0.008**
Age at diagnosis, mean ± SD, years	29.4 ± 12.8	35.0 ± 13.2	**0.038**
Number of previous bDMARDs, mean ± SD	1.6 ± 1.1	0.74 ± 0.84	**<0.001**
Presence of concomitant csDMARD, n (%)	10 (37.0)	467 (48.5)	0.238
Adalimumab vs other bDMARD, n (%)	14 (51.9)	211 (21.9)	**<0.001**

In a multivariate regression model, number of previous bDMARDs (OR 2.13, 95% CI 1.47 to 3.10, p<0.001) and treatment with adalimumab (OR 4.60, 95% CI 1.96 to 10.80, p<0.001) were statistically significant predictive factors for IMSL development.

Conclusion: In our cohort, we found that a younger age at diagnosis, longer disease duration, longer duration of bDMARD treatment, higher number of previous bDMARDs and treatment with adalimumab were independently associated with an increased risk of IMSL development. In the multivariate regression model, number of previous bDMARDs and exposure to adalimumab were statistically significant predictive factors for IMSL development. Further research is required to better understand and recognize the risk factors for IMSL.

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AB0440

CHANGES IN BONE BIOCHEMICAL MARKERS DUE TO THE INFLUENCE OF RISK FACTORS FOR OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TUMOR NECROSIS FACTOR INHIBITORS

Keywords: Rheumatoid arthritis, bDMARD, Biomarkers

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Background: Rheumatoid arthritis (RA) is an independent risk factor for osteoporosis which influences bone remodeling processes via increased production of proinflammatory cytokines, especially tumor necrosis factor-α (TNF-α), or through hormone-mediated mechanisms. The presence of other classical risk factors for osteoporosis additionally raises the risk of changes in bone tissue. Some of the most commonly used biological drugs in the osteoporosis treatment are those that inhibit TNF-α action. Apart from reducing inflammation, these TNF-inhibitors suppress osteoclast activity.
Objectives: To determine the impact of osteoporosis risk factors on the bone turnover marker levels in RA patients treated with TNF-inhibitors.
Methods: This 12-month-long study included 50 patients with RA who received a drug from the TNF-inhibitor group. In order to enter the study, patients had to fulfill certain inclusion/exclusion criteria considering the RA duration, the RA treatment method, the degree of joint damage, and the presence of other diseases affecting bone tissue. Data regarding traditional risk factors for osteoporosis and fractures were collected, such as menopause length, body mass index (BMI), previous fractures due to minor trauma, family history of osteoporosis and osteoporotic fractures, reduced physical activity, cigarette smoking, and alcohol consumption. Serum levels of the bone synthesis marker procollagen type I N propeptide (P1NP), and the bone resorption marker beta C-terminal telopeptide of type I collagen (b-CTX) were assessed via ECLIA method at the baseline and upon TNF-inhibitor therapy completion.
Results: The mean age in this cohort was 51.6 years. A higher percentage increase in P1NP and b-CTX was recorded in patients aged below 50 years, as well as those of normal weight (BMI = 18.50–24.99 kg/m², P1NP: Wilk's lambda =0.83, F = 9.56, p = 0.003; b-CTKS: Wilk's lambda = 0.77, F = 14.16, p = 0.000). A greater increase in the P1NP and b-CTX levels was also observed in non-smokers (28.70% and 27.50%) relative to smokers (27.50% and 7.75%). Menopause length had a statistically significant effect on both P1NP (Wilk's lambda = 0.84, F = 8.18, p = 0.006) and b-CTX (Wilk's lambda = 0.77, F = 13.31, p = 0.001) concentrations, whereby the highest percentage increase in P1NP (29.85%) was related to menopause duration below 2 years. On the other hand, the greatest b-CTX increase (10.2%) was recorded in patients that had entered menopause 2–3 years ago. Physical activity had a significant effect on changes in P1NP (Wilk's lambda = 0.84, F = 8.57, p = 0.005) as well as b-CTX (Wilk's lambda = 0.78, F = 13.30, p = 0.001) values. Further, P1NP percentage increase was higher in patients without family history of osteoporosis, while the opposite was true for the b-CTX levels. Finally, number of previous fractures was inversely correlated with the P1NP and b-CTX percentage increase.
Conclusion: After 12-month TNF-inhibitor treatment, although a significant increase in both bone turnover markers was achieved, it was greater in the bone synthesis marker P1NP. Younger age, normal body weight, shorter menopause duration, greater physical activity, negative osteoporosis family history, and non-smoking emerged as the most important factors associated with the P1NP percentage increase.
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Disclosure of Interests: None declared.
Changes in bone biochemical markers due to the influence of osteoporosis risk factors in patients with rheumatoid arthritis treated with tumor necrosis factor inhibitors.
Disclosure of Interests: None Declared.
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AB0441 JANUS KINASES INHIBITORS THERAPY FOR THE TREATMENT OF RHEUMATOID ARTHRITIS: AN OVERVIEW OF SYSTEMATIC REVIEWS AND META-ANALYSES

Keywords: Rheumatoid arthritis, Qualitative research methods

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Background: Janus kinases (JAK) inhibitors are a family of intracellular tyrosine kinases that act as hubs in the signaling process of many cytokine receptors, mediating inflammation and autoimmune diseases. It was reported that JAK inhibitors played an important role in inhibiting bone destruction by inhibiting the phosphorylation of proteins. In recent years, JAK inhibitors have been widely used to treat Rheumatoid Arthritis(RA).and proved to have an obvious curative effect. However, the efficacy and safety of the clinical use of JAK inhibitors need to be further verified.
Objectives: To access the methodological, reporting and evidence quality of systematic reviews and meta-analyses of JAK inhibitors for RA.
Methods: We comprehensively searched the literature in CNKI, Wanfang Data, VIP, PubMed, Web of Science databases from inception to November 2022. A Measurement Tool to Assess systematic Reviews (AMSTAR-2) tool and the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) were used to access the methodological and reporting quality. The level of evidence quality was evaluated by employing the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) scale.
Results: The AMSTAR-2 tool showed that half of the included literature had low quality, and the other 6 literatures had a very low quality. The study process lacked certain normativity, which had a certain impact on the implementation of the study and the evaluation of outcomes. The PRISMA statement showed that there were numerous vulnerabilities in the methodology module of each document, which was mainly manifested in the scheme and registration. The GRADE analyses showed that the quality of the evidence for the outcome measures was moderate to low. The results showed that JAK inhibitors had certain advantages in the proportion of patients with ACR20, 50 and 70 after treatment for 3 months or 6 months. In addition, this study found that JAK inhibitors could alleviate adverse reactions. Furthermore, all the included literature had certain deficiencies in randomization, blinding, allocation, etc. There was a risk of bias, which directly reduced the evidence level of RCT trials and showed that the included studies had defects in the design of trial protocols.
Conclusion: The effectiveness of JAK inhibitors for RA has certain advantages compared with placebo, and more studies need to be demonstrated than other drugs. However, the safety is uncertain and need further explored.
Keywords: JAK inhibitors Rheumatoid arthritis; AMSTAR-2; PRISMA; GRADE.
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AB0442 RETROSPECTIVE ANALYSIS ON JAK INHIBITORS AT SINGLE CENTRE IN THE UK

Keywords: Safety, Rheumatoid arthritis, Targeted synthetic drugs

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Background: There are limited real world data on the use of JAK inhibitors (JAKi). In 2022, the EMA suggested that JAKi should only be used if alternative therapies are not available in patients over 65 years, smokers or in those with cardiovascular or cancer risk factors.
Objectives: We conducted a retrospective study to describe the demographics, duration of therapy and adverse events profile of patients prescribed JAKi.
Methods: Baseline data including age, gender, smoking status, ethnicity, co-morbidities, cardiovascular risk factors, rheumatic diagnosis, concomitant csDMARD use and prior biological therapies was collected. Duration on therapy and reasons for stopping JAKi were identified. A Cox proportional hazard model was used to plot survival of drug therapy, by JAKi drug. Data was analysed on the STATA platform.
Results: In total, 151 patients were prescribed a JAKi since 2017. The average age was 55, with a female predominance, (n=125, 83%), and the majority had rheumatoid arthritis. Baricitinib and Filgotinib represented the most commonly prescribed JAKi. Over ¼ of the cohort were using JAKi monotherapy (28%). For those on combination therapy, methotrexate was the most commonly prescribed (53%). The median number of prior biologics was 1 (IQR 1-2), with TNFi the most frequently prescribed (66%). 48% had cardiovascular risk factors or cardiovascular disease; this was more prevalent in patients prescribed baricitinib or tofacitinib compared to upadacitinib or filgotinib (57%) versus (39%). During JAKi therapy 3 patients developed cancer, 2 had VTEs (both on Baricitinib) and 5

Table 1.

		Total	Baricitinib	Filgotinib	Tofacitinib	Upadacitinib	
		N=151	N=43	N=43	N=32	N=33	P value
Age, (median, SD)		55 (14)	54 (16)	57 (13)	58 (11)	51 (13)	0.10
Gender, female (n,%)		125 (82.8%)	36 (83.7%)	37 (86.0%)	28 (87.5%)	24 (72.7%)	0.36
Smoking status, (n, %)	Ex-smoker	9 (6.0%)	3 (7.0%)	3 (7.0%)	1 (3.1%)	2 (6.2%)	0.36
	Current Smoker	8 (5.3%)	4 (9.3%)	0	3 (9.4%)	1 (3.1%)	0.46
Ethnicity, (n, %)	White	69 (47.3%)	24 (58.5%)	18 (41.9%)	14 (46.7%)	13 (40.6%)	0.25
	Black	28 (19.2%)	7 (17.1%)	9 (20.9%)	9 (30.0%)	3 (9.4%)	
	South Asian	26 (17.8%)	5 (12.2%)	7 (16.3%)	5 (16.7%)	9 (28.1%)	
	Mixed	23 (15.8%)	5 (12.2%)	9 (20.9%)	2 (6.7%)	7 (21.9%)	
Diagnosis, (n,%)	RA	146 (96.7%)	42 (97.7%)	43 (100.0%)	30 (93.8%)	31 (93.9%)	0.27
	Other - PsA	3 (2.0%)	0	0	1 (3.1%)	2 (6.1%)	
	Ank Spon	1 (0.7%)	0	0	1 (3.1%)	0	
	CTD overlap	1 (0.7%)	1 (2.3%)	0	0	0	
Year JAK commenced		2017	2017	2021	2017	2019	<0.001
CVS risk factor/disease	ex/current smoker, DM, Chol	73 (48.3%)	25 (58.1%)	21 (48.8%)	18 (56.2%)	9 (27.3%)	0.04
Prior JAK comorbidity	VTE	4 (2.6%)	0	2 (4.7%)	2 (6.2%)	1 (3.0)	0.23
	Cancer	9 (6.0%)	4 (9.3%)	1 (2.3%)	1 (3.1%)	3 (9.1%)	0.41
	Mental health	33 (21.9%)	7 (16.3%)	11 (25.6%)	8 (25.0%)	7 (21.2%)	0.72
Post JAK new comorbidity	Cholesterol	11 (7.3%)	4 (9.3%)	0	3 (9.4%)	4 (12.1%)	0.17
	Diabetes	3 (2.0%)	2 (4.7%)	0	0	1 (3.0%)	0.35
	IHD	1 (0.7%)	1 (2.3%)	0	0	0	0.47
	VTE	2 (1.3%)	0	0	2 (6.2%)	0	0.06
	Cancer	3 (2.0%)	1 (2.3%)	0	2 (6.2%)	0	0.21
	Mental health	5 (3.3%)	1 (2.3%)	1 (2.3%)	0	3 (9.1%)	0.19
JAKi therapy stopped		56 (37.0%)	25 (58.1%)	3 (6.9%)	20 (62.5%)	8 (24.2%)	<0.001
Reason for stopping	AE	25 (44.6%)	7 (28.0%)	1 (33.3%)	15 (75.0%)	2 (25.0%)	0.028
	Primary failure	14 (25.0%)	7 (28.0%)	1 (33.3%)	2 (10.0%)	4 (50.0%)	
	Secondary failure	12 (21.4%)	8 (32.0%)	0 (0.0%)	2 (10.0%)	2 (25.0%)	
	Death	2 (3.6%)	1 (4.0%)	1 (33.3%)	0 (0.0%)	0 (0.0%)	
	Not documented	3 (5.4%)	2 (8.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	

had new mental health diagnoses. The reason for stopping therapy was equally spilt between drug failure (46%) and adverse events (45%). Drug survival over 2 years was numerically higher for Filgotinib and Upadacitinib. Cycling between JAKi occurred in 28 patients. Patients prescribed a second JAKi (n=26) or a third JAKi (n=2) had cycled through more prior biologics than patients prescribed their first JAKi [median number prior biologics 2 (IQR 1-3) versus 1 (IQR 1-2) p=0.007].
Conclusion: Our real world experience of JAKi is broadly similar to expectations from clinical trials. The differences in patient characteristics and drug survival between individual JAKi are likely to reflect drug availability and emergence of safety warnings over time.

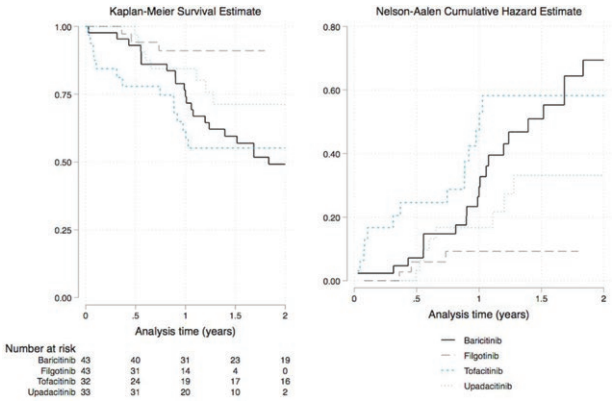


Figure 1.

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AB0443

REAL-WORLD EXPERIENCE OF BIOSIMILAR RITUXIMAB GP2013 IN RHEUMATOID ARTHRITIS PATIENTS NAÏVE TO OR SWITCHED FROM REFERENCE RITUXIMAB

Keywords: bDMARD, Real-world evidence, Outcome measures

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Background: Randomized controlled trials showed high comparability of biosimilar rituximab (bs-RTX) GP2013 to biologic originator RTX (bo-RTX) in terms of physicochemical and functional properties, pharmacokinetics, efficacy and safety [1,2]. Data on effectiveness of switching from bo-RTX to bs-RTX, starting therapy with bs-RTX and bs-RTX drug survival in real-world setting is sparse.
Objectives: To explore long-term drug effectiveness and survival of bs-RTX GP2013 in rheumatoid arthritis (RA) patients both naïve to and mandatory switched from bo-RTX in ordinary outpatient clinic.
Methods: Retrospective observational cohort study including adult RA patients treated with bs-RTX between 2018 and 2021 in Norway. Patients were examined and monitored with recommended disease activity measures and patient-reported outcomes (PROs). Drug survival was assessed with Kaplan-Meier survival analysis.
Results: 110 RA patients (71.8% women) treated with bs-RTX were identified (88 mandatory switched from bo-RTX, 22 RTX-naïve), baseline median (IQR) age was 68.0 (59.0-76.0) years, disease duration 13.0 (7.4-18.7) years, 93.6% were RF and 96.3% ACPA positive, 30.0% currently used csDMARDs (26.4% methotrexate). Statistically significant difference between bs-RTX-naïve and bs-RTX-switched patients was found for disease duration (3.0 vs 14.2 years, p<0.01), current steroids use (68.2% vs 35.2%, p=0.01) and first cycle bs-RTX dose: 90.9% bs-RTX-naïve received 2000 mg, while 85.3% bs-RTX-switched 1000 mg or 500 mg. During 2-year follow-up disease activity and PROs measures remained stable in switchers and improved in those starting naïve on RTX (Table 1).

Table 1. Changes in disease activity and PROs, median (IQR)

	Baseline		1 year-period		2 year-period	
	bs-RTX switched n=88	bs-RTX naïve n=22	bs-RTX switched n=88	bs-RTX naïve n=22	bs-RTX switched n=74	bs-RTX naïve n=13
CRP, mg/L	2.00 (1.00-5.00)	8.50 (4.00-17.50)	2.00 (1.00-5.00)	7.00 (2.75-9.00)	3.50 (1.00-6.00)	6.00 (2.00-16.00)
ESR, mm/hr	7.50 (4.00-14.00)	24.00 (19.00-38.00)	7.00 (2.00-12.00)	14.50 (7.00-26.00)	7.00 (4.00-10.00)	10.00 (6.00-21.00)
SJC28, 0-28	0.00 (0.00-0.00)	2.50 (0.00-9.50)	0.00 (0.00-0.00)	1.25 (0.00-3.00)	0.00 (0.00-0.50)	0.50 (0.00-1.00)
TJC28, 0-28	0.00 (0.00-1.00)	5.00 (1.50-9.00)	0.00 (0.00-1.00)	0.00 (0.00-3.00)	0.00 (0.00-1.00)	1.75 (0.00-3.00)
DAS28-ESR	2.00 (1.30-2.70)	4.35 (3.75-5.20)	1.80 (1.30-2.25)	2.20 (2.10-3.00)	2.10 (1.60-2.60)	2.50 (1.30-3.70)
DAS28-CRP	2.00 (1.30-2.70)	4.35 (3.75-5.20)	1.90 (1.50-2.40)	2.25 (1.80-2.90)	2.00 (1.70-3.00)	2.43 (2.19-3.25)
CDAI	2.65 (1.00-5.60)	15.50 (10.00-29.20)	2.65 (0.90-5.50)	6.90 (2.30-10.20)	3.80 (1.60-6.50)	4.53 (3.38-10.20)
PGA, 0-100mm	20.00 (8.00-33.00)	51.00 (40.00-67.00)	20.00 (8.00-37.50)	40.00 (15.50-57.00)	30.00 (12.00-50.00)	35.00 (23.50-46.50)
MHAQ, 0-3	0.32 (0.00-0.75)	0.57 (0.38-0.88)	0.38 (0.00-0.63)	0.25 (0.07-0.50)	0.38 (0.00-0.63)	0.13 (0.00-0.38)

Overall drug survival for bs-RTX was 80.0% (95% CI 71.2-86.3%) after 1 year and 57.7% (95% CI 47.8-66.3%) after 2 years. Drug survival in bs-RTX-switched patients was significantly higher than in bs-RTX-naïve (Figure 1).

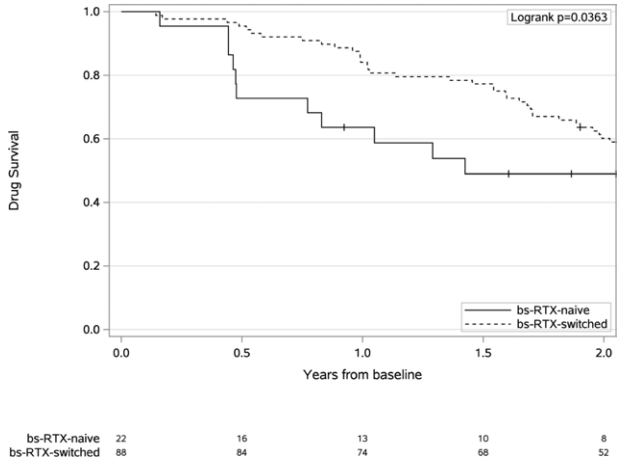


Figure 1. Kaplan-Meier plots of treatment retention rates

Conclusion: For the first time real-life data on drug effectiveness for GP2013 bs-RTX in RA is presented. Non-medical switch to bs-RTX is largely effective, no deterioration in disease activity outcomes was observed. Response in RTX-naïve patients was satisfactory and effect remains stable after 2-year follow-up. Drug survival was similar to published data for originator RTX.

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AB0444

SAFETY PROFILE OF BIOLOGICAL THERAPY IN RHEUMATOID ARTHRITIS IN MOROCCO. DATA FROM THE RBSMR

Keywords: bDMARD, Rheumatoid arthritis

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Background: In North African countries, few data are available on the safety of biotherapies.

Objectives: To evaluate safety of biological therapy (excluding infections) in a population with rheumatoid arthritis (RA) followed in the RBSMR (Registry of Biological therapies in rheumatic diseases of the Moroccan Society of Rheumatology).

Methods: This work was based on data from inclusion and 3 years of follow-up. It concerns 223 patients with RA receiving biotherapies, included between May 2017 and December 2018. safety was evaluated at inclusion and every 6 months for 3 years. Serious adverse events were defined as those that are life-threatening, that required hospitalization or permanent stopping of current biological agent.

Results: 223 patients were included in the study, the mean age was 51.8 ± 11.3 years, 87.4% were females, average duration of RA was 20.8 [13.9 - 31.3] months, The median duration of exposure to biotherapy was 3.1 [0 - 18.23] months. Patients were receiving anti-TNFα in 16.6% (37/223) of case, Rituximab (RTX) in 59.6% (133/223) and Tocilizumab (TCZ) in 23.8% (53/223). About 70% (155/223) of patients had an association with a csDMARDs. At inclusion, 19.73% (44/223) of patients had previously developed 59 adverse events (AEs) on current biotherapy. The 44 noninfectious AEs are occurred in 14.8% (33/223) of patients: 19 infusion reactions, 2 liver toxicities, 7 hematological disorders, 7 dyslipidemias and 9 other AEs. The global incidence of AEs was 24.81 per 100 patient-years (PA). The incidence of noninfectious AEs was 11.06 per 100 PA (Table I), The incidence of serious non-infectious AEs was 2.09 per 100 PA (n=14). The occurrence of noninfectious AEs differs depending the biological agent: anti-TNF=27% (10/37), RTX =27.3% (36/133) et TCZ =37.7% (20/53); with no statistically significant difference in frequency between these molecules (p=0,454). In logistic regression, no factors were associated with serious adverse events. The percentage of patients who changed their biological agent was 13.9% (31/223). During the 3 years of follow-up, 8 patients died, 4 of which by non-infectious AEs (lymphoma, heart rhythm disorder, unexplained deterioration of general condition, decompensated cirrhosis). Because of non-infectious AEs, biotherapy was discontinued in 3.58% (8/223) of patients. The percentage of patients lost to follow-up was 9.86% (22/223).

Conclusion: In RA, biological agents have a positive benefit/risk ratio. However, non-infectious side effects are not rare, they are multifactorial and can be potentially serious.

Table I non-infectious adverse events in the RBSMR

Type of adverse events	Incidence per 100 patient-years	Number of adverse events	Biological agents
Infusion reactions	1,19	8	RTX (n=6) TCZ (n=2)
Paradoxical reactions	0,29	2	Uveitis under TCZ (n=1) Paradoxical arthritis under Golimumab (n=1)
Drug-induced lupus	0,14	1	RTX
Cancers	0,44	3	Urothelial carcinoma under TCZ having already received RTX (n=1) Breast carcinoma under TCZ having already received RTX (n=1) Non-Hodgkin's lymphoma under TCZ (n=1)
Liver toxicities	1,79	12	TCZ (n=7) RTX (n=5)
Hematological disorders	3,13	21	TCZ (n=14) RTX (n=5) Anti-TNFα (n=2)
Dyslipidemias	1,94	13	TCZ (n=8) RTX (n=4) Golimumab (n=1)
Severe heart rhythm disorder	0,14	1	TCZ
Phlebitis	0,14	1	Etanercept
Other AEs (injection site reactions, myalgia, depression…)	2,69	16	RTX (n=7) Anti-TNFα (n=5) TCZ (n=4)

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AB0445 CHARACTERISTICS OF FIRST-LINE UPADACITINIB INITIATORS AND FACTORS CONTRIBUTING TO PRESCRIBING UPADACITINIB AS FIRST-LINE B/TSDMARD

Keywords: Disease-modifying Drugs (DMARDs), Real-world evidence, Rheumatoid arthritis

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Background: EULAR guidelines recommend switching to or adding a b/tsDMARD in patients with rheumatoid arthritis (RA) who do not respond or have an inadequate response to csDMARDs. Traditionally, TNF inhibitors (TNFi) are prescribed as the first b/tsDMARD. In Dec 2021, the upadacitinib (UPA) label in the US was updated to restrict use to those who have had an inadequate response or intolerance to one or more TNFi.

Objectives: In the period prior to the UPA label change in the US (through Jan 2022), to (1) compare characteristics of patients with RA receiving UPA as first b/tsDMARD with those who initiated TNFi as their first b/tsDMARD, and (2) explore the reasons why UPA was chosen as first-line advanced therapy.

Methods: Using CorEvitas RA registry data from Aug 2019 to Jan 2022, patients who initiated UPA or TNFi at or after enrollment in the registry with no history of prior b/tsDMARD use were evaluated. The patients' providers indicated which factors (they could choose more than one) contributed to prescribing UPA as first-line advanced therapy based on medical record chart review.

Results: Few differences in demographics, comorbidities, and disease activity at initiation were observed between the 815 TNFi initiators and 142 UPA initiators identified. UPA initiators were older (mean [SD] age 58.9 [12.8] vs 56.7 [13.9] yrs), had a higher proportion of White patients (87% vs 83%), and were less likely to be working (44% vs. 53%), and have private insurance (73% vs. 68%). UPA initiators had more frequent history of cardiovascular disease (16% vs 10%), joint deformity (17% vs 12%), and subcutaneous nodules (13% vs 10%), but less frequent history of anxiety/depression (29% vs 34%) than TNFi initiators. UPA initiators had greater disease severity, including mean CDAI (23.7 [14.9] vs 19.0 [13.0]), and tender (8.4 [7.7] vs 6.6 [6.7]) and swollen (6.1 [5.1] vs 4.3 [5.1]) joint counts, self-reported pain (54.5 [28.7] vs 50.3 [28.3]), and proportion with morning stiffness (89% vs 85%). UPA initiators were more likely to have a history of multiple csDMARDs (43% vs 35%), monotherapy b/tsDMARD initiation (32% vs 22%) and use of NSAIDs (53% vs 48%). For 142 patients initiating UPA as first-line, 34 providers (87% response rate) indicated major factors in the choice of prescribing UPA as first-line advanced therapy were the patient's level of disease activity (75%), patient's disease progression (61%), patient preference (51%), and patient's disease profile (43%). These reasons contributed to any part of the prescription decision in 99%, 96%, 77%, and 79% of patients, respectively. Oral delivery was indicated as a contributing factor by almost all (91%) of the 109 patients that were prescribed UPA as first-line therapy and indicated patient preference was a factor in prescribing UPA. Side effects were not a concern when deciding to prescribe UPA in at least 50% of the patients included in this study.

Conclusion: In a real-world cohort of patients with RA initiating a first-line b/tsDMARD, those who received UPA were more likely to have previously failed multiple csDMARDs, to initiate as monotherapy, and to have had greater disease activity based on both physician and patient measures compared to patients who received TNFi. Clinical factors including disease activity, disease progression, and disease profile influenced the prescribing decision by providers as well as patient preference.

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AB0446 SAFETY OF BIOLOGICAL THERAPIES: DATA FROM THE BIOBADAGUAY REGISTRY

Keywords: Registries, Safety, bDMARD

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Background: BIOBADAGUAY is the Paraguayan/Uruguayan registry of adverse events (AE) in patients with inflammatory rheumatic conditions under biologic therapy (BT).

Objectives: Determine the frequency and severity of AE of patients under BT in the BIOBADAGUAY registry.

Methods: Prospective, observational study of undetermined length to verify the efficacy, safety, and survival of the BT. The methodology applied is available at https://biobadaguay.ser.es. For the present study epidemiological and clinical variables, BT, type, and severity of AE were analyzed. The incidence rate (IR) was calculated as the total number of adverse events per 1000 patients/year and the incidence rate ratio (IRR) was analyzed using the Poisson regression model. (Significance value 0,05)

Results: 1104 patients with TB were analyzed, between 2016 and 2022. 73.28% were women, mean age at treatment initiation was 42±17.1 years. The most frequent diagnosis was rheumatoid arthritis (RA): 686 patients (62.4%). There were 1375 treatment cycles. 1365 AE were observed, 1191 (87.2%) were non-severe, 161 (11.8%) severe and 13 (0.95%) mortal. The IR of AE was 251.75 (238.6-265.8), for severe AE 32.1 (27.5-37.2). Infection was the most frequent AE in 731/1365 (55% of total AA): non-severe 661 (88%), 86 (11.5%) severe and 4 (0.5%) mortal. The IR of infections was 138.4 (126.69-265.47), 32.1 (27.48-37.2%) for severe infections. When analyzing the IR of AE according to diagnosis, it was observed that RA is associated with a higher IR of global AE when compared to other diagnoses (IRR=1.35 [95% CI,1.1-1.7] p=0.0088), and severe AE (IRR=1.72 [95% CI,1.2-2.5] p=0.006). Psoriatic arthritis (PsA) and ankylosing spondylitis (AS) were associated with lower overall IR of global AE: IRR=0.57 [95% CI,0.4-0.9] (p=0.007) and IRR=0.66 [95% CI,0.5-1] (p=0.04), respectively. corticosteroid use was associated with a higher global AE IR (IRR=1.46 [95% CI,1.2-1.8] p=0.0009). When IR was analyzed according to severity, it was observed that the second and subsequent cycles of BT were significantly associated with a higher IR of global and non-severe AE compared to the first cycle of BT (Table 1). Treatment with anti-TNF was significantly associated with lower IR of global and mortal AE compared to non-anti-TNF (Table 1).

INCIDENCE RATE OF ADVERSE EVENTS ACCORDING TO SEVERITY

First Cycle		Follow Cycles		
Adverse Event	Incidence Rate	Incidence Rate	Incidence Rate Ratio	P
Global	233.22 (219.28, 247.80)	339.2 (303.1, 378.3)	1.45 (1.14, 1.85)	**0.0024**
Not Serious	201.27 (188.34, 214.85)	306.50 (272.29, 343,82)	1.52 (1.18, 1.197)	**0.0014**
Serious	30.16 (25.26, 35.69)	27.39 (17.89, 40.13)	0.91 (0.55, 1.51)	0.7101
Mortal	1.79 (0,77, 3.52)	5.27 (1.71, 12,29)	2.95 (0.96-9.56)	0,0588
Non-antiTNF		AntiTNF		
Adverse Event	Incidence Rate	Incidence Rate	IRR	P
Global	306.31 (276.92, 337.98)	234.63 (220.09, 249.88)	0,77 (0.61, 0.97)	0,**0262**
Not Serious	261.56 (234.46, 290.94)	206.54 (192.91, 220.88)	0.79 (0.61, 1.02)	0.0695
Serious	38.58 (28.63, 50.86)	26.88 (22.11, 32.37)	0,70 (0.47, 1.04)	0,0758
Mortal	6.17 (2.66, 12.16)	1.21 (0.39, 2.83)	0.20 (0.06, 2.83)	**0.0043**

Conclusion: AE were in general non-severe, and infections were the most frequent. RA and concomitant treatment corticosteroid presented a higher IRR of global AE, whereas PsA and AS a lower IRR of AE. Second and Subsequent cycles of BT presented a higher IRR of global an AE. The RA diagnosis presented a higher rate of severe AE.

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AB0447 MEDICATION BELIEFS DURING THE PRECONCEPTION PERIOD AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Safety, Disease-modifying Drugs (DMARDs), Rheumatoid arthritis

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Background: Treatment maintenance in young women with rheumatoid arthritis (RA) may be influenced by factors such as fears of side effects on fertility and conception.

Objectives: We aimed to assess the therapeutic beliefs of patients with RA during the preconception period and to investigate associated factors.

Methods: We conducted a cross-sectional study including patients diagnosed with RA before menopause. We assessed beliefs about treatment during the preconception period using the French version of Beliefs about Medicines Questionnaire (BMQ). The questionnaire assessing specific beliefs is composed of 10 items: 5 items to assess beliefs regarding the necessity for treatment and 5 items to assess concerns.

Results: We included 31 females (mean age: 49.7±10.4 years). RA was erosive in 93% of cases. Coxitis was noted in 6 patients (19%) and atloido-axial dislocation in 2 patients (6%). The average number of gestation and parity was, respectively, 3 [0-9] and 2 [0-7]. Contraception was used by 20 patients (64%). The contraceptive method was progestin-only pill (10 patients), intrauterine device (6 patients), condoms (2 patients), and calendar method (2 patients). The mean beliefs' score regarding treatment necessity and concerns were 18.8±3.3 [10-23] and 12.3±5.9 [5-23], respectively. The score of therapeutic necessity was higher in patients without desire to conceive, but the difference was not significant (19.1±3.1 vs 17.2±4.8, p=0.246). The presence of erosions had an influence on therapeutic necessity (19±3 vs 16.5±7.7, p=0.03). The therapeutic necessity score was statistically higher in patients with coxitis (20.1±1.6 vs 18.5±3.6, p=0.05). The conception desire had no influence on concerns. The disease duration had a statistically negative correlation with concern score (r=-0.480, p=0.006). Contraception use was not influenced by either therapeutic necessity or concerns (p=0.129 and p=0.140, respectively).

Conclusion: This study showed that beliefs about therapeutic necessity during the preconception period were more important than concerns. We emphasize the importance of therapeutic patient education to fight against negative beliefs.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0448 THE IMPACT OF ACPAS ON THE RESPONSE TO BIOLOGICAL THERAPY IN RHEUMATOID ARTHRITIS

Keywords: bDMARD

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Background: Rheumatoid arthritis (RA) is a chronic, debilitating disease associated with reduced quality of life. It is characterized by the positivity of various antibodies, the most specific being autoantibodies against citrullinated antigens (ACPA). Those antibodies are associated with severe erosive phenotype and higher mortality rate comparisons to seronegative RA. Moreover, ACPA status is known to be associated with a favorable response to biologics drugs.

Objectives: Our objective in this study was to investigate whether ACPA positivity in RA can predict treatment responses to biologic therapies in Tunisian patients with rheumatoid arthritis.

Methods: We conducted a cross-sectional and observational study. Files of patients with RA on biologics drugs (archived from the files of patients on the National Health Insurance Fund of Tunis) were studied. ACPA and rheumatoid factor assays were performed. RA activity was assessed by the composite score 'Disease Activity Score 28' (DAS28). Patient follow-up was done with the DAS28 disease activity score. The therapeutic maintenance rate as well as the biologics survival was analyzed using Kaplan-Meier survival curves and compared using the Log-Rank test.

Results: Three hundred and seventy-four files were selected. Their average age was 55±12.54 years [20-90]. A female predominance was noted with a sex ratio M/F=0.147. The average duration of RA was 11.7±6.76 years [2-41]. Rheumatoid serology specified in 324 patients (86%), was positive in 79% of cases. Anti-citrullinated protein antibodies (ACPA) data were available in the records for 267 patients (71%). These were positive in 72% of patients. Anti-nuclear antibodies (ANA) were only positive in 12% of our population. Native anti DNA and anti Sm were respectively positive in one patient. First biogics prescription was: etanercept 54%, adalimumab 14%, certolizumab pegol 13%, infliximab 6%, tocilizumab 6% and rituximab 7%. In patients with positive rheumatoid factors, survival after 4 years of the first biological treatment was 58.8% versus 35.5% in FR negative patients. Mean therapeutic maintenance was 42.15 months and 34.97 months respectively for the two groups. For ACPA negatives, the 4-year survival was 52.05% versus 49.2% for ACPA positives. These antibodies did not influence the survival of the biotherapy with an HR = 1.004 (p=0.987).

Conclusion: Our study did not reveal any impact of ACPA positivity on the therapeutic response to biologics. These results are inconsistent with most of those in the literature. A larger-scale study is needed to confirm our results.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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Rheumatoid arthritis - non biologic treatment and small molecules

AB0449 ASSOCIATION OF OPG, OPN AND OCN PROTEINS WITH THE RISK OF RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Genetics/epigenetics, Biomarkers

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterised by joint swelling, joint compression and synovial joint destruction, where inflammation and bone destruction can lead to significant functional impairment. Recently, several studies have reported the identification of new biomarkers of RA, such as osteoprotegerin (OPG), osteocalcin (OCN) and osteopontin (OPN)[1], all three of which play a significant role in regulating bone metabolism and influencing osteoclast synthesis and secretion. Although OPG, OCN and OPN are strongly correlated with RA, it is not clear whether there is a causal relationship between them.
Objectives: The aim of this study was to assess whether OPG, OPN and OCN are causally related to the risk of RA in a Two-Sample Mendelian randomisation(TSMR).
Methods: The genetic instrumental variables (IVs) for OPG, OPN and OCN exposure from a large genome-wide association study (GWAS) meta-analysis including 21,758, 1322 and 3301 participants, respectively. The GWAS data for RA were selected from an independent RA GWAS analysis that included 29,880 RA cases of European ancestry and 73,758 controls.Significant ($P < 5 \times 10\text{-}6$) and independent ($r2 < 0.001$) SNP in genome-wide association studies were selected as IVs for performing MR analyses. The causal relationship between OPN、OPG、OCN and RA risk was assessed by TSMR analysis using inverse variance weighting (IVW) methods as the primary analysis, supplemented by weighted median, MR-Egger. MR-Egger regression, Leave-one-out analysis and Mendelian Randomization Pleiotropy RESidual Sum and Outlier (MR-PRESSO) were used to detect and correct for the effects of horizontal multi-effects[2].
Results: The Eighteen,seven and nine SNPs were selected as IVs for OPN, OPG and OCN respectively. The results of theIVW method (OPN:OR = 1.0191, 95% CI: 0.9800-1.0597, p = 0.3440; OPG: OR = 1.0396, 95% CI: 0.9327- 1.1588, p = 0.4827;OCN: OR = 1.077, 95% CI: 0.990- 1.077, p = 0.812) showed that there was no strong evidence of a relationship between the production of OPN, OPG and OCN in people of European ancestry and RA risk. Further sensitivity analyses verified the robustness of the above associations, with MR-Egger regressions showing no evidence of pleiotropy (OPN:p = 0.8703; OPG:p = 0.7043;OCN:p = 0.6356) and heterogeneity analyses showing no heterogeneity (OPN:p = 0.7880; OPG:p = 0.2451;OCN:p =0.5651). The leave-one-out method analysis indicated that genetically determined PN, OPG and OCN were not driven by any single SNP in association with RA risk.
Conclusion: We did not find any evidence of a causal relationship between OPN, OPG,OCN and RA risk. Further research is needed to elucidate the potential mechanisms underlying the role of OPN, OPG and OCN in the development of RA.

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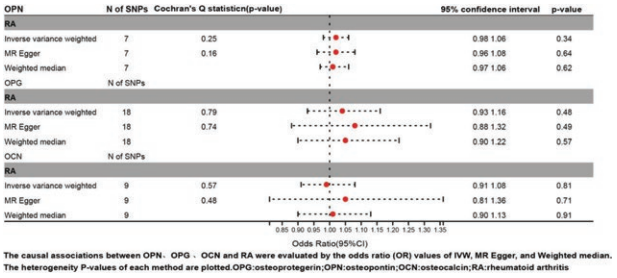


Figure 1.

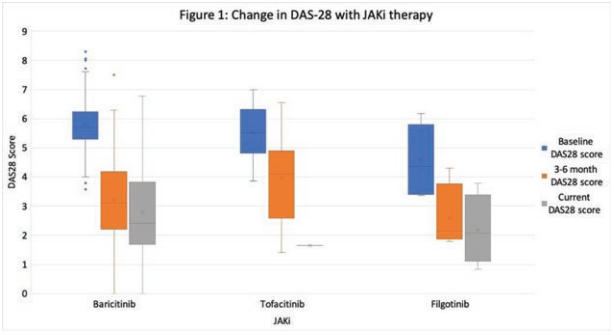
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0450 REAL-WORLD USE OF JAK INHIBITORS IN RHEUMATOLOGICAL PRACTICE IN SOUTH LONDON

Keywords: Targeted synthetic drugs, Rheumatoid arthritis, Psoriatic arthritis

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Background: Janus Kinase inhibitors (JAKi) are targeted synthetic disease modifying anti-rheumatic drugs (tsDMARDs) used in the treatment of inflammatory arthritis. Whilst evidence for their efficacy and side-effect profile is supported by data from randomised control studies, real world data is lacking.
Objectives: The objectives of the study were to evaluate the efficacy and safety of JAKi in real-world clinical rheumatological practice in the South London region.
Methods: Data was collected from two hospitals; St Georges University Hospitals NHS Trust (SGH; a tertiary centre) and Kingston Hospital NHS Foundation Trust (KH; a district general hospital). All rheumatology patients who were prescribed JAKi between January 2017 and June 2022 were included in the analysis. Baseline patient demographic data included age, gender, rheumatological diagnosis and comorbidities. A retrospective analysis evaluated prescribing practice, drug efficacy (measured using the Disease Activity Score (DAS-28)), adverse events and drug discontinuation rates.
Results: A total of 288 patients were included in the analysis; 184 from SGH and 104 from KH. The average age was 55.6 (range 20-82), 87% were female. Baricitinib was the most frequently prescribed JAKi (231 patients), followed by tofacitinib, filgotinib and upadacitinib (49, 7 and 1 patients respectively). Baricitinib was most prescribed for patients with seropositive rheumatoid arthritis (RA) (62%), seronegative RA (17%) and seronegative inflammatory arthritis (10%). 73% on tofacitinib had a diagnosis of psoriatic arthritis, 20% had RA. All patients on filgotinib had RA and the one patient on upadacitinib had overlap RA/systemic lupus erythematosus. In 53% of patients, JAKi was prescribed following biological DMARD (bDMARD) therapy. In these patients; 32%, 13%, 5% and 3% had previously received 1, 2, 3 and 4 bDMARDs respectively. Median DAS-28 scores improved with all JAKi therapy. This is summarised in Figure 1.



The most frequent documented adverse events included bacterial infection (25) hypercholesterolaemia (18), gastrointestinal side effects (18), viral infection (15) and deranged liver function tests (LFTs) [10]. These are summarised in Table 1.

Table 1.

Adverse events	Number of events		
	Baricitinib (n=231)	Tofacitinib (n=49)	Filgotinib (n=7)
Gastrointestinal side effects	**18**	**0**	**0**
Bacterial infection	**19**	**4**	**2**
Lower respiratory tract	10	1	1
Urinary tract	5	1	0
Genitourinary	1	0	0
Skin	1	1	1
Not specified	2	1	0
Viral/fungal infection	**15**	**1**	**1**
Shingles	6	0	1
COVID-19	4	0	0
Upper respiratory tract	2	0	0
Fungal nail infection	2	0	0
Herpes Simplex Virus	1	0	0
Biochemical abnormalities	**22**	**6**	**0**
Hypercholesterolaemia	14	4	0
Deranged Liver functions tests (LFTs)	8	2	0
Neutropenia	**2**	**0**	**0**
Venous thromboembolism (VTE)	**1**	**1**	**0**
Other side effects	**11**	**1**	**0**

10 patients died whilst on JAKi therapy (8 on baricitinib, 2 on tofacitinib). 5 died from COVID-19, 1 from pancreatic cancer and 4 with unknown cause of death. Excluding deceased patients, 77 discontinued JAKi therapy (56 on baricitinib, 19 on tofacitinib, 2 on filogitinib). Mean duration to discontinuation was 9.3 months (baricitinib), 11.7 months (tofacitinib) and 4.5 months (filgotinib). For all JAKis, drug inefficacy was the most commonly reported reason for discontinuation (40 patients). Other reasons included bacterial infection [8], deranged LFTs [6], perceived high risk for VTE [4], shingles [2] and other side effects [8].

Conclusion: JAKi are effective across a range of rheumatological diagnoses in a South London real-world analysis, including patients with bDMARD-naïve and bDMARD-refractory disease. JAKi are generally well tolerated and adverse events in this study were in keeping with the current literature.

REFERENCES: NIL.

Acknowledgements: NIL.

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AB0451 FRENCH REAL LIFE SAFETY DATA ON THE USE OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: OBSERVATIONAL STUDY, DEFACTO

Keywords: Safety, Real-world evidence, Targeted synthetic drugs

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Background: Tofacitinib, an oral Janus Kinase inhibitor, is indicated for the treatment of adult patients with moderate to severe active rheumatoid arthritis (RA).

Objectives: To describe the safety profile of Tofacitinib in a French prospective observational study DeFacTo.

Methods: The safety profile of tofacitinib was assessed using interim data from a descriptive analysis of patients who took at least one dose of tofacitinib in the DeFacTo study.

Results: Among 314 patients enrolled in the study, 306 received tofacitinib and were included in the safety analysis, including 274 patients with a follow-up ≥ 18 months (POP2) on 03/15/22 date of analysis) with a median exposure duration of 538 [Q1; Q3: 381; 554] days. 113 patients (41.2%) were still on tofacitinib (39 discontinued, 122 missing data regarding prescription). At inclusion, 78.3% of the 306 pts were women with a mean (± standard deviation) age of 59.5 ± 11.5 years, median disease duration of 8.9 years [Q1; Q3: 4.1; 18.9]. There was a history of cardiovascular (CV) disease in 11.9% of cases (including 4.6% myocardial infarction (MI), 5.0% stroke/transient ischemic attack (TIA), 1.7% heart failure, and 1.7% peripheral arterial disease); 5.6% history of cancer, 16.8% history of infection, and 46.6% smoker/former smoker. Tofacitinib was prescribed in combination with a csDMARD in 61.1% of patients and corticosteroids in 56.2% of cases. The results showed that adverse events (AEs) were reported in 54.2% of the 306 patients, 14.4% were considered as serious. Infections were found in 22.2% of patients, no deaths were reported (Table 1).

Table 1. Real-life and age-specific safety data for tofacitinib

N, (%)	< 65 ans (n=193)	≥ 65 ans (n=111)	Total (n=306*)
Adverse events (AEs)	104 (53.9)	62 (55.9)	166 (54.2)
Serious adverse events	21 (10.9)	23 (20.7)	44 (14.4)
Infection	41 (21.2)	27 (24.3)	68 (22.2)
Herpes Zoster	6 (3.1)	6 (5.4)	12 (3.9)
Serious AEs of special interest			
Serious infection	5 (2.6)	4 (3.6)	9 (2.9)
Herpes zoster	1 (0.5)	0 (0.0)	1 (0.3)
Tuberculosis	0 (0.0)	2 (1.8)	2 (0.7)
Cancer	1 (0.5)	1 (0.9)	2 (0.7)
CV event†	1 (0.5)	1 (0.9)	2 (0.7)
VTE‡	0 (0.0)	2 (1.8)	2 (0.7)
Death	0 (0.0)	0 (0.0)	0 (0.0)

*2 patients with missing age but counted in the total. † cardiovascular event (Evt): non-fatal MI and stroke + CV death. ‡ VTE (venous thromboembolic disease): deep vein thrombosis + pulmonary embolism.

Conclusion: These intermediate, descriptive results show a safety profile of tofacitinib in real-life RA similar to the one previously reported in clinical and observational studies. [1-2]

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Disclosure of Interests: Cécile Gaujoux-Viala Speakers bureau: AbbVie; Amgen; Bristol-Myers Squibb; Celgene; Eli Lilly; Galapagos; Gilead Sciences, Inc.; Janssen; Medac; Merck-Serono; Mylan; Nordic Pharma; Novartis; Pfizer; Roche; Sandoz; Sanofi; and UCB, Consultant of: AbbVie; Amgen; Bristol-Myers Squibb; Celgene; Eli Lilly; Galapagos; Gilead Sciences, Inc.; Janssen; Medac; Merck-Serono; Mylan; Nordic Pharma; Novartis; Pfizer; Roche; Sandoz; Sanofi; and UCB, Andre BASCH Consultant of: Janssen, Novartis, Amgen, BMS, Abbvie, Lilly, Pfizer, MSD, UCB, Slim Lassoued: None declared, Fabienne COURY-LUCAS Consultant of: AbbVie, Bristol-Myers Squibb, Janssen, Lilly, MSD, Novartis and Pfizer, Grant/research support from: AbbVie, Biogen, Roche Chugai, Pfizer, and UCB, Meriem Kessouri Shareholder of: Pfizer, Employee of: Pfizer, Yves Brault Shareholder of: Pfizer, Employee of: Pfizer, Thierry Lequerre Consultant of: Abbvie, BMS, Boeringher, Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Roche – Chugai, Sanofi, UCB, Carine Salliot Consultant of: Biogen, Lilly, Novartis, Roche Chugai, Pfizer.

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AB0452 SURVIVAL RATE OF BARICITINIB IN A LARGE COHORT OF RHEUMATOID ARTHRITIS PATIENTS: ANALYSIS OF REAL-WORLD DATA

Keywords: Safety, Rheumatoid arthritis, Outcome measures

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Background: Recently, the new class of drugs, namely targeted synthetic (ts) DMARDs, has broadened the possibilities of treating rheumatoid arthritis (RA). In particular, Janus Kinase inhibitors (JAKi) are used in RA and are currently represented by four drugs: baricitinib, tofacitinib, upadacitinib and filgotinib. One of the first to be used in Italy was baricitinib, a JAKi acting on JAK1 and JAK2.

Objectives: The aim of this study was to evaluate the clinical efficacy of baricitinib in a real-life setting in a cohort of RA patients.
Methods: This multicenter retrospective observational study included patients from 25 rheumatology centers diagnosed with RA and treated with baricitinib. The following were recorded for each patient: gender; age; duration of disease; presence of rheumatoid factor and anti-citrulline antibodies; concomitant treatment with conventional synthetic (cs) DMARDs; previous treatments with biological (b) or ts DMARDs. In order to evaluate the clinical efficacy, the retention rate was evaluated, calculated by means of the Kaplan-Meier method. The variables under examination were reported as frequencies and median with relative interquartile range.
Results: We included 478 patients of which 380 (79.5%) were female. 286 (60.1%) patients tested positive for rheumatoid factor (RF) and 264 (55,2%) for anti-citrulline antibody (ACPA). The parameters analyzed are shown in Table 1. 105 (22.0%) patients were treated with baricitnib as first line (after csDMARD), the remaining patients had failed at least one bDMARD and 9 (1.9%) also failed a tsDMARD. In 34,7% of cases baricitinib was used as monotherapy, the most frequently used csDMARD was methotrexate (29.2%). The median period of therapy was 674 days (298-1087). The survival rate at 6 months was 94.6%, at 12 months it was 87,9%, at 24 months was 81.7% and at 48 months was 53.4% (Figure 1). The main causes that led to the discontinuation of baricitinib therapy were: primary ineffectiveness (7,3%), secondary ineffectiveness (4.2%) and adverse events (3,7% 5 TEP/DVT). The concomitant steroid therapy seems to be a negative prognostic factor (HR 1,65 95% CI 1.03-2.63; p=0.035) as well as the line of therapy (HR 1.35 95% CI 1.15-1.58; p=0.000).

Table 1.

Characteristics		Value
M:F		98:380
Age, median [IQR] yrs		60 [51-70]
Smokers, n (%) (**)	Yes	84 (18,8)
	Former	76 (17,0)
	No	288 (64,2)
Body Mass Index, median [IQR] kg/m^2 (*)		24,8 [23,0-27,0]
Disease Duration, median [IQR], months		78 [32-163]
RF positivity, n (%)		286 (60,1)
ACPA positivity, n (%)		264 (55,2)
SJC, median [IQR]		5 [3-8]
TJC, median [IQR]		8 [4-12]
ESR, median [IQR], mm/h		33 [20-46]
CRP, median [IQR], mg/dl		1,3 [0,5-2,9]
VAS Patient (0-100), median [IQR]		70 [50-80]
DAS28, median [IQR]		5,4 [4,8-6,1]
Line of treatment, [IQR]		2 [2-3]
Concomitant csDMARDs use, n (%)	MTX	140 (29,2)
	LFN	11 (2,3)
	SSZ	3 (0,6)
	HCQ	12 (2,5)
Concomitant steroids use, n (%)		237 (49,6)
Steroids dose (PDN-Eq), median, mg/die		5 [4-5]
Prior bDMARDs use, n (%)	TNFi	164 (34,3)
	IL6i	84 (17,6)
	IL1i	0
	CD20i	8 (1,7)
	CD80i	54 (11,3)
Prior tsDMARDs use, n (%)	Tofacitinib	9 (1,9)
Concomitant relevant disease, n (%)	Diabetes	36 (7,5)
	Hypercholesterolemia	119 (24,9)
	MACE	28 (5,9)
	Arterial Hypertension	179 (37,4)
	Cancer	24 (5,0)

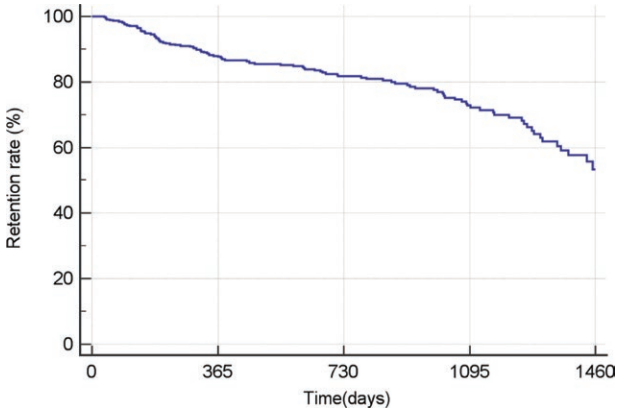


Figure 1. 4 year retention rate of baricitinib

Conclusion: The efficacy of baricitinib in the treatment of RA in a real-life context appears consistent with what was reported by the pivotal studies. Furthermore, from this preliminary experience, seropositivity and combo therapy seems to not correlate with a better retention rate, while concomitant steroid therapy and line of treatment are a negative prognostic factor.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0453 ARE WE DOING A CORRECT METHOTREXATE MONITORING?

Keywords: Rheumatoid arthritis, Disease-modifying drugs (DMARDs)

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Background: Methotrexate (MTX) is an antimetabolite of folic acid commonly used for the treatment of Rheumatoid Arthritis (RA). Despite its recognized benefit in controlling the activity of the disease, it can cause side effects, such as hepatic and hematologic toxicity. This makes necessary to carry out periodic analytical controls. According to the recommendations of ACR_1 and $EULAR_2$ on the monitoring of MTX toxicity, the most appropriate frequency for analytical controls in patients starting treatment with MTX would be 4-6 weeks, and it could be spaced up to every 3 months when reaching a stable dose. We consider this study in view of the perception in our real clinical practice of a low frequency of analytical abnormalities that lead to modify the treatment with MTX in our patients with RA.
Objectives: To evaluate the frequency of analytical abnormalities in patients with RA who start treatment with Methotrexate and to review the modifications in the treatments carried out based on these analytical abnormalities.
Methods: Retrospective descriptive study on patients with RA who had started treatment with MTX (15 mg per week) between 2001 and 2021. The results of hematological parameters and liver function tests, obtained in the analytical controls carried out, were collected from the beginning of the treatment and during the following two years. These controls were carried out before starting MTX, one month later, at 3 months, and subsequently every 3-4 months; according to the recommendations of the clinical guidelines. The parameters collected were aspartate aminotransferase (AST), alanine aminotransferase (ALT), hemoglobin (Hb), neutrophils, and lymphocytes. Only patients treated with MTX in monotherapy, with or without corticosteroids, were included in the study. The frequency of the analytical abnormalities found was calculated and the therapeutic changes made were reviewed in the medical records.
Results: 97 patients were included, of whom 67% were women and 33% men with a mean age of 55.94 (±12.9) years. Significant new-onset abnormalities in transaminases (>2-fold normal value: 68 U/L) were found in 8 patients (8.2%) during the 2-year monitoring. Of these, the MTX dose was modified in 6 patients (6.1%) and it was stopped in 2 patients (2.1%) due to ALT/AST>3-fold normal (102 U/L). After the suspension, the two patients normalized analytical values. Regarding the hematological parameters, anemia was observed (Hb <13 g/dl in men, <12 g/dl in women) in 10 patients (9.7%). However, none of them presented Hb < 10 g/dl and there was no treatment modification due to this alteration. Lymphopenia (lymphocytes < 0.9 x10^3/µL) was observed in 3 patients (3.1%) and neutropenia (neutrophils < 1.9 x10^3/µL) in 4 patients (4.1%). None of these patients required modifications in the treatment.
Conclusion: The low incidence of analytical abnormalities found in our study makes us reconsider the frequency of analytical controls in monitoring MTX, not only to avoid unnecessary repeated venipuncture, but also the visits to health centers. On the other hand, we must not forget the cost of health and human resources that these procedures entail. Larger studies are required to elucidate the most optimal time interval required to monitor MTX toxicity in the management of patients with RA.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0454

SAFETY OF FILGOTINIB IN PATIENTS WITH RA: LABORATORY ANALYSIS RESULTS FROM A LONG-TERM EXTENSION STUDY

Keywords: Clinical trials, Rheumatoid arthritis, Disease-modifying drugs (DMARDs)

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Background: Filgotinib (FIL) is a Janus kinase (JAK) 1 preferential inhibitor, approved for treatment of moderate to severe active RA in Europe, the UK, and Japan. Graded laboratory abnormalities from placebo-controlled analyses and long-term data on lymphocytes have been reported previously.

Objectives: Report the effect of FIL on laboratory parameters in the FINCH 4 long-term extension (LTE).

Methods: Safety was assessed from LTE baseline (BL) to data cutoff (1 Jun 2020) in patients (pts) receiving ≥1 FIL dose (FIL 200 mg [FIL200] or 100 mg [FIL100]) in FINCH 4 (NCT03025308). Laboratory abnormalities were graded per Common Terminology Criteria for Adverse Events v4.03. Frequencies and exposure-adjusted incidence rates (EAIRs)/100 pt-years of exposure (PYE) for graded abnormalities are reported. Median laboratory parameters are reported to LTE Week (W) 48.

Results: In FINCH 4, 2729 pts received FIL for 4198.08 PYE (mean 80.3 weeks); exposure was similar between dose groups. Frequency and EAIR of laboratory abnormalities were similar for anemia, decreased platelets, and increased alanine aminotransferase (ALT), aspartate aminotransferase (AST), and serum creatinine, and higher in the FIL200 vs FIL100 group for neutropenia, increased creatinine kinase (CK), hypophosphatemia, and cholesterol (high) (**Table 1**; graded data not shown). No Grade 4 decreased phosphate laboratory abnormalities were observed and hypophosphatemia was not associated with adverse events. Laboratory abnormalities led to discontinuation of FIL in 7 pts: ALT and AST increased, 3 (0.2%, FIL 200); ALT increased, 1 (<0.1%, FIL 100); and neutropenia 3 (0.3%, FIL 100). From LTE BL to W48, hemoglobin, platelets, ALT, and AST were relatively stable, with no clear differences between doses, or between pts with or without prior FIL. Neutrophil count was relatively stable from LTE BL to W48. Neutrophils decreased for the FIL200 group with no prior FIL exposure, remaining stable from W24. CK and serum creatinine were relatively stable from LTE BL to W48 in pts with prior FIL exposure; in pts with no prior FIL, initial increases plateaued by W6 and W12, respectively, remaining stable. Changes in phosphate levels from LTE BL were small, remaining within normal range (2.2–5.1 mg/dL). Triglycerides were stable over time with no differences between groups. Total cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels were stable in pts with prior FIL exposure. In pts with no prior FIL exposure, small increases in total cholesterol, HDL, and LDL plateaued by W24, remaining stable. The LDL:HDL ratio was stable, with no differences between groups (**Figure 1**).

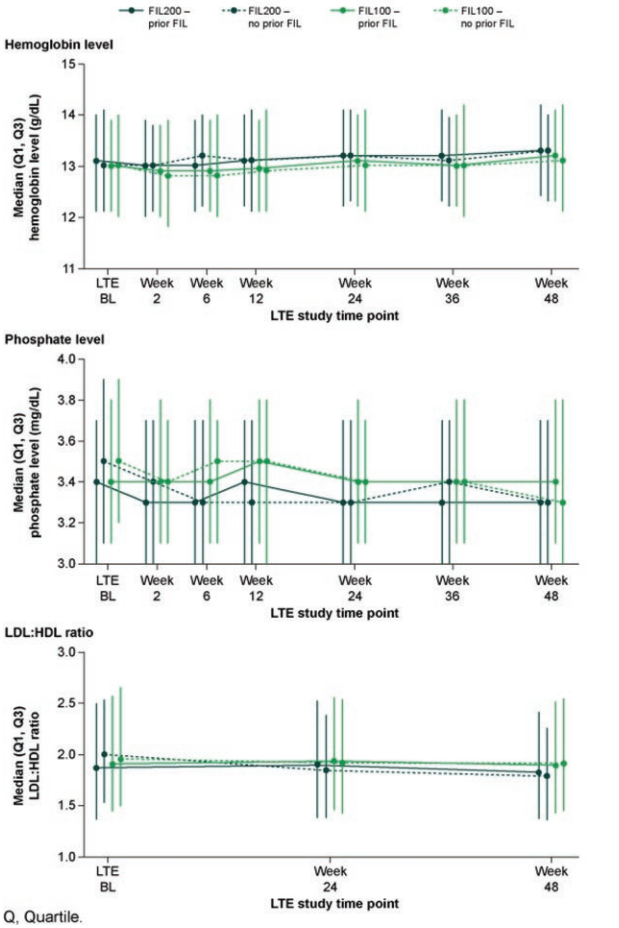
Conclusion: Laboratory abnormalities were generally mild to moderate, similar to previous observations. Frequency and EAIR were higher in the FIL200 vs FIL100 group for neutropenia, increased CK, hypophosphatemia, and high cholesterol.

Table 1. Treatment-emergent laboratory abnormalities* (any Grade ≥1; safety analysis set†)

n/N (%); EAIR (95% confidence interval)	FIL200 (n=1530; PYE=2346.0)	FIL100 (n=1199; PYE=1852.1)
Anemia	264/1526 (17.3); 11.3 (10.0, 12.7)	227/1193 (19.0); 12.3 (10.8, 14.0)
Platelets (decreased)	44/1525 (2.9); 1.9 (1.4, 2.5)	24/1189 (2.0); 1.3 (0.9, 1.9)
Neutropenia	194/1526 (12.7); 8.3 (7.2, 9.5)	101/1193 (8.5); 5.5 (4.5, 6.6)
ALT (increased)	349/1526 (22.9); 14.9 (13.4, 16.5)	287/1193 (24.1); 15.5 (13.8, 17.4)
AST (increased)	338/1526 (22.1); 14.4 (13.0, 16.0)	273/1193 (22.9); 14.7 (13.1, 16.6)
Serum creatinine (increased)	80/1526 (5.2); 3.4 (2.7, 4.2)	62/1193 (5.2); 3.3 (2.6, 4.3)
Creatine kinase (increased)	448/1526 (29.4); 19.1 (17.4, 20.9)	259/1193 (21.7); 14.0 (12.4, 15.8)
Hypophosphatemia	103/1526 (6.7); 4.4 (3.6, 5.3)	50/1193 (4.2); 2.7 (2.0, 3.6)
Hypertriglyceridemia	307/1497 (20.5); 13.1 (11.7, 14.6)	268/1164 (23.0); 14.5 (12.8, 16.3)
Cholesterol (high)	125/1497 (8.4); 5.3 (4.5, 6.3)	73/1164 (6.3); 3.9 (3.1, 5.0)

*Defined as an increase of ≥1 toxicity grade from BL up to 30 days post last study drug dose; †Pts who received ≥1 dose of study drug.

Figure. Median hemoglobin levels, phosphate levels, and LDL:HDL ratio over time



Q, Quartile.

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Disclosure of Interests: Ennio Giulio Favalli Speakers bureau: AbbVie, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Consultant of: AbbVie, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Maya H Buch Speakers bureau: AbbVie (paid to host institution), Consultant of: AbbVie, CESAS Medical, Galapagos, Gilead, Pfizer (all paid to host institution), Grant/research support from: Gilead (paid to host institution), James Galloway Speakers bureau: AbbVie, Biogen, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Roche, UCB, Consultant of: AbbVie, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Grant/research support from: AstraZeneca, Celgene, Gilead, Janssen, Medicago, Novavax, Pfizer, Arnaud Constantin Speakers bureau: AbbVie, Amgen, Biogen, BMS, Boehringer, Celltrion, Fresenius-Kabi, Galapagos, Janssen, Lilly, Medac, MSD, Novartis, Pfizer, Roche, Sanofi, Sandoz, UCB, Viatris, Consultant of: AbbVie, Boehringer, Celltrion, Galapagos, Janssen, Lilly, Novartis, Pfizer, UCB, Patrick Durez Speakers bureau: AbbVie, Eli Lilly, Galapagos, Paul Van Hoek Consultant of: Galapagos, Aspen, AOP Health, Sanofi-Genzyme, Astellas, Employee of: Schering Plough, MSD, Janssen, Chris Watson Shareholder of: Galapagos, Employee of: Galapagos, Pieter-Jan Stiers Employee of: Galapagos, Vijay Rajendran Shareholder of: Galapagos, Employee of: Galapagos, Katrien Van Beneden Shareholder of: Galapagos, Employee of: Galapagos, Tsutomu Takeuchi Speakers bureau: AbbVie GK, AYUMI, BMS, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Gilead Sciences, Inc., Janssen Pharm KK, Mitsubishi Tanabe, Pfizer Japan, Sanofi KK, Consultant of: AbbVie GK, Astellas, Chugai, Eli Lilly Japan, Gilead Sciences, Inc., Janssen Pharm KK, Mitsubishi Tanabe, Pfizer Japan, Grant/research support from: Astellas, AYUMI, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, AbbVie GK, Asahi Kasei Pharma, Mitsubishi Tanabe, Nippon Kayaku, UCB Japan, Bernard Combe Speakers bureau: AbbVie, Celltrion, Galapagos, Janssen, Lilly, Pfizer, Roche-Chugai, Consultant of: AbbVie, Galapagos, Gilead, Janssen, Lilly, Novartis, Roche-Chugai.
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AB0455

BARICITINIB IN THE TREATMENT OF PATIENTS WITH MODERATE TO SEVERE ACTIVE RHEUMATOID ARTHRITIS IN CHINA: 24-WEEK RESULTS OF POST-MARKETING SAFETY STUDY

Keywords: Real-world evidence, Safety, Rheumatoid arthritis

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Background: Baricitinib, an orally selective inhibitor of JAK1 and JAK2, was approved for adult patients with moderate-to-severe rheumatoid arthritis (RA) in China. The recommended dose is 2mg once daily and 4mg once daily in patients who have inadequately responded to baricitinib 2mg once daily (for 3 months) or TNF inhibitors. A single-arm, prospective, non-interventional post-marketing safety study (PMSS) was conducted in Chinese RA patients to describe the safety and effectiveness of baricitinib at 24 weeks.
Objectives: To describe the safety and effectiveness of baricitinib in real-world setting of treating patients with moderate to severe active RA.
Methods: This PMSS (starting July 2020) included 667 patients with RA treated with baricitinib (2 mg or/and 4mg/day) and followed up for 24 weeks. Safety and effectiveness (disease activity) were assessed for 24 weeks. All statistical analyses are descriptive.
Results: Safety analyses included 667 patients (females=82.3%, mean age=53.3 years, mean RA duration 86.9 months). 106 (15.9%) were ≥65 and <75years and 19 (2.8%) were ≥75 years. 29 (4.3%) had previously received biologic therapy. Baricitinib dose regimen was as follows: 2 mg/day, n = 580 (87.0%); 4 mg/day, n = 53 (7.9%); 2/4 mg, n = 34 (5.1%). Concomitant use of MTX and leflunomide occurred in 54.3% and 35.5%, respectively. The overall exposure of baricitinib was 262.1 patient-years; 197 (29.5%) patients withdrew from the study, mostly for patient's decision (n = 101). Adverse events (AEs) occurred in 250 (37.5%) patients [serious: 28 (4.2%)]. Two patients (0.3%) died: one of pneumonia and one with no cause reported. The incidence of serious infection, herpes zoster and hepatotoxicity was 0.6%, 1.0%, and 3.4%, respectively. No case met laboratory criteria for potential Hy's Law (ALT/AST ≥3 x ULN and TBL ≥2 x ULN). Malignancy occurred in one patient (thyroid cancer). No venous thromboembolism (VTE) or major adverse cardiovascular event (MACE) were reported during the study observation period (**Table 1**). In the effectiveness analysis at Week 24, the proportions of patients achieving remission/ low disease activity were 66.6% (235/353) for DAS28-CRP, 64.6% (228/353) for SDAI, and 63.5% (242/381) for CDAI (**Figure 1**).
Conclusion: In conclusion, the safety and effectiveness profile of baricitinib in this Chinese PMSS was generally similar to that in the global RA population with no VTEs or MACE reported and no new safety signals.
REFERENCES: NIL.

Table 1. Safety summary among patients with RA treated with baricitinib

	Safety Population (N=667)	
n (%) PYE[EAIR]	**12 weeks**	**24 weeks**
AE	214 (32.08)	250 (37.48)
	124.04 [172.52]	198.58 [125.89]
AEs related to study treatment	95 (14.24)	120 (17.99)
as judged by the investigator	139.99 [67.86]	236.65 [50.71]
Death	/	2 (0.30)
		261.30 [0.77]
SAE	22 (3.30)	28 (4.20)
	147.03 [14.96]	256.72 [10.91]
SAEs related to study treatment	8 (1.20)	10 (1.50)
as judged by the investigator	148.32 [5.39]	260.30 [3.84]
Treatment discontinuation due to AEs	20 (3.00)	24 (3.60)
	148.18 [13.50]	260.79 [9.20]
AESI		
Serious infection	3 (0.45)	4 (0.60)
	148.52 [2.02]	260.99 [1.53]
Hepatotoxicity	16 (2.40)	23 (3.45)
	147.13 [10.87]	256.76 [8.96]
VTE	0	0
	148.63 [0.00]	261.30 [0.00]
Herpes zoster, n (%)	3 (0.45)	7 (1.05)
Malignancy, n (%)	1 (0.15)	1 (0.15)
MACE, n (%)	0	0

Abbreviations: AE= adverse event; AESI= adverse event with special interest; EAIR= exposure-adjusted incidence rate; MACE= major adverse cardiovascular events; N= number of patients in the safety analysis set; n= number of patients in the specified category; PYE= patient-years of exposure; RA= rheumatoid arthritis; SAE= serious adverse event; VTE= venous thromboembolismUsed EAIR per 100 PYE (patient exposure censored at the event).AESI was based on the judgement of investigator recorded in eCRF (electronic case report form)MACE included myocardial infarction, cardiovascular death, and stroke.

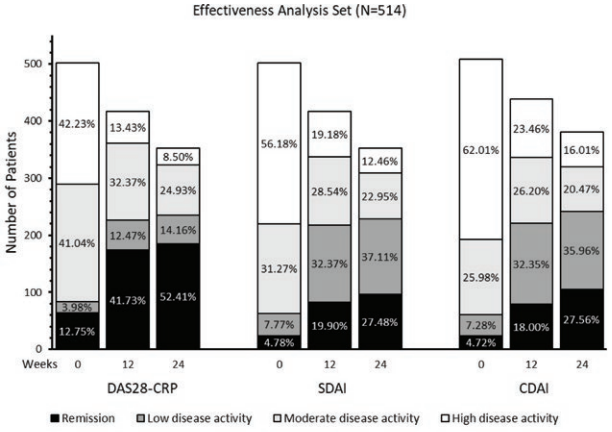


Figure1. The number of patients with known remission (black), low disease activity (dark grey), moderate disease activity (light grey), and high disease activity (white) based on DAS28-CRP, SDAI, and CDAI at each time point is plotted. The percentage of patients in each category, using the total number of applicable patients for each measure at each time point as the denominator, is shown within the columns. Patients with unknown effectiveness scores are not included in the analysis.

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AB0456

BARICITINIB AS MONOTHERAPY FOR TREATMENT OF RHEUMATOID ARTHRITIS: SUMMARY OF DATA FROM FIVE REAL-WORLD DATA SOURCES

Keywords: Disease-modifying drugs (DMARDs), Rheumatoid arthritis, Real-world evidence

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Background: EULAR recommendations suggest that use of interleukin-6 inhibitors and Janus kinase (JAK) inhibitors are preferred in rheumatoid arthritis (RA) when combination therapy with conventional synthetic disease modifying antirheumatic drugs (csDMARDs) is not indicated due to intolerance of csDMARDs. Monotherapy data for the JAK1/JAK2 inhibitor baricitinib (BARI) in patients with inadequate response to csDMARDs or biologic DMARDS (bDMARDs) are limited.

Objectives: To present an overview of baseline characteristics and effectiveness outcomes for patients with moderate-to-severe RA receiving BARI as monotherapy and combination therapy for up to 1 year in real world European settings.

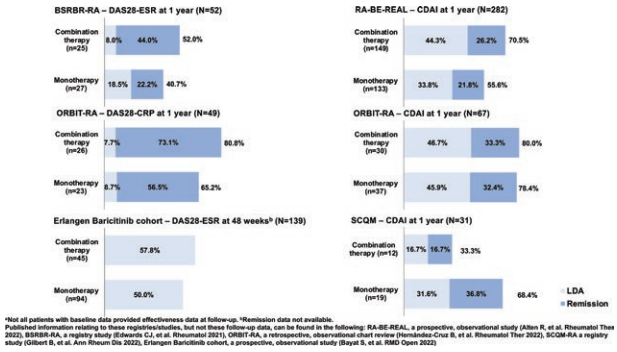
Methods: BARI-related real-world data from available European registries, long-term observational studies and retrospective chart review, obtained from published sources or investigators, were reviewed. Baseline and effectiveness data, separately from each source, were reviewed for patients who received BARI as monotherapy and for those receiving BARI in combination with csDMARDs with findings presented descriptively as mean ± standard deviation (SD) or number (%) of patients. No statistical modelling was applied. Disease activity score for 28-joint count (DAS-28) low disease activity (LDA) and remission data were collected in ORBIT-RA, BSRBR-RA and the Erlangen Baricitinib cohort; and Clinical Disease Activity Index (CDAI) LDA and remission data were collected in RA-BE-REAL, ORBIT-RA and SCQM-RA.

Results: In BARI cohorts, monotherapy was used by 51.0% of patients in RA-BE-REAL, 61.5% in ORBIT-RA, 60.1% in SCQM-RA, 39.4% in BSRBR-RA and 67.6% in the Erlangen Baricitinib cohort. Across all databases, most patients were female, and in general, patients who received BARI as monotherapy appeared to be older, with a longer disease duration and numerically larger likelihood of previous treatment with a bDMARD than those who received the drug in combination (Table 1). Available LDA and remission rates from patients with data in the different databases are shown in the Figure 1; 40.7–78.4% of patients receiving BARI monotherapy and 33.3–80.8% receiving BARI in combination achieved either LDA or remission states at 1 year.

Conclusion: Approximately 40–78% of patients achieved LDA or remission after up to 1 year of monotherapy across the different data sources and populations with RA, although the numbers of patients with data to up to 1 year were small for most registries. These findings suggest that BARI monotherapy is a suitable treatment option for patients with RA.

REFERENCE:

[1] Gilbert B, et al. Ann Rheum Dis 2022



[b]Not all patients with baseline data provided effectiveness data at follow-up. [a]Remission data not available.
Published information relating to these registries/studies, but not these follow-up data, can be found in the following: RA-BE-REAL, a prospective, observational study (Alten R, et al. Rheumatol Ther 2022), BSRBR-RA, a registry study (Edwards CJ, et al. Rheumatol 2021), ORBIT-RA, a retrospective, observational chart review (Hernández-Cruz B, et al. Rheumatol Ther 2022), SCQM-RA a registry study (Gilbert B, et al. Ann Rheum Dis 2022), Erlangen Baricitinib cohort, a prospective, observational study (Bayat S, et al. RMD Open 2022)

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Disclosure of Interests: Christopher John Edwards Speakers bureau: Abbvie, BMS, Biogen, Celgene, Fresenius Kabi, Galapagos, Gilead, Janssen, Lilly, Pfizer, MSD, Novartis, Roche, Samsung, Sandoz, Sanofi, UCB, Consultant of: Has received honoraria and has attended advisory boards from/for Abbvie, BMS, Biogen, Celgene, Fresenius Kabi, Galapagos, Gilead, Janssen, Lilly, Pfizer, MSD, Novartis, Roche, Samsung, Sandoz, Sanofi, UCB, Grant/research support from: Abbvie, BMS, Biogen, Celgene, Fresenius Kabi, Galapagos, Gilead, Janssen, Lilly, Pfizer, MSD, Novartis, Roche, Samsung, Sandoz, Sanofi, UCB, Axel Finckh Speakers bureau: Abbvie, BMS, Eli-Lilly, Galapagos, Pfizer, MSD, Novartis, Sandoz, and UCB, Consultant of: Has received honoraria and has attended advisory boards from/for Abbvie, BMS, Eli-Lilly, Galapagos, Pfizer, MSD, Novartis, Sandoz, and UCB, Grant/research support from: Abbvie, BMS, Eli-Lilly, Galapagos, Pfizer, MSD, Novartis, Sandoz, and UCB, Tsutomu Takeuchi Speakers bureau: AbbVie, Astellas Pharma, Eisai, Eli Lilly Japan, Gilead, and Pfizer Japan, Consultant of: Has received consulting fees from AbbVie, Astellas Pharma, Eli Lilly Japan, and Gilead, and has received honoraria from AbbVie, Astellas Pharma, Eisai, Eli Lilly Japan, Gilead, and Pfizer Japan, Arnd Kleyer Speakers bureau: Abbvie, BMS, Eli-Lilly, Galapagos, Pfizer, Novartis, and UCB, Consultant of: Has received honoraria and has attended advisory boards from/for Abbvie, BMS, Eli-Lilly, Galapagos, Pfizer, Novartis, and UCB, Grant/research support from: Abbvie, BMS, Eli-Lilly, Galapagos, Pfizer, Novartis, and UCB, Ewa Haladyj Shareholder of: Minor shareholder of Eli Lilly and Company, the manufacturer of baricitinib, Employee of: Employee of Eli Lilly and Company, Cedric Laedermann Shareholder of: Minor shareholder of Eli Lilly and Company, the manufacturer of baricitinib, Employee of: Employee of Eli Lilly and Company, Jens Gerwien Shareholder of: Minor shareholder of Eli Lilly and Company, the manufacturer of baricitinib, Employee of: Employee of Eli Lilly and Company, Tamas Treuer Shareholder of: Minor shareholder of Eli Lilly and Company, the manufacturer of baricitinib, Employee of: Employee of Eli Lilly and Company, Liliana Zaremba-Pechmann Consultant of: Contractor at HaaPACS GmbH providing services to Eli Lilly and Company., Employee of: Contractor at HaaPACS GmbH providing services to Eli Lilly and Company., Josef S. Smolen Speakers bureau: Has received honoraria for speaking engagements from Abbvie, Galapagos/Gilead, Novartis-Sandoz, BMS, MSD, Samsung, Sanofi, Celltrion, Chugai, R-Pharma and Lilly, Consultant of: Has received honoraria for consultations from Abbvie, Galapagos/Gilead, Novartis-Sandoz, BMS, MSD, Samsung, Sanofi, Celltrion, Chugai, R-Pharma and Lilly, Grant/research support from: Has received research grants to his institution from Abbvie, Astra-Zeneca and Lilly.

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Table 1. Baseline demographics and characteristics of patients receiving baricitinib and enrolled in real-world databases

Database	RA-BE-REAL		ORBIT-RA		SCQM-RA[1]		BSRBR-RA		Erlangen Baricitinib cohort	
Location	France, Germany, Italy, Spain, UK		Spain		Switzerland		UK		Germany	
Therapy	Mono-	Combi	Mono-	Combi	Mono-	Combi	Mono-	Combi	Mono-	Combi
Patients, n (%)	260 (51.0)	250 (49.0)	115 (61.5)	72 (38.5)	164 (60.1)	109 (39.9)	221 (39.4)	340 (60.6)	94 (67.6)	45 (32.4)
Mean±SD age, years	60.4±13.9	57.8±12.4	NR	NR	60±15	57±11	62.1±11.4	58.6±12.2	58.5±12.6	58.1±13.3
Female, n (%)	210 (80.8)	180 (72.0)	NR	NR	NR (82)	NR (73)	168 (76.0)	261 (76.8)	72 (76.6)	26 (57.8)
Mean±SD disease duration, years	10.6±8.8	9.5±9.3	NR	NR	13±10	12±9	14.0±10.4	12.6±10.2	10.2±9.5	8.8±6.5
Previously treated (MTX),[a] n (%)	0	203 (81.2)	NR	NR	NR	NR (50)	0	237 (69.7)	58 (74.4)	15 (41.7)
Previously treated (bDMARD), n (%)	136 (52.3)	112 (44.8)	NR	NR	NR (83)	NR (82)	144 (65.2)	159 (46.8)	NR	NR
Concomitant corticosteroid use, n (%)	100 (38.5)	119 (47.6)	NR	NR	NR (21)	NR (24)	66 (29.9)	76 (22.4)	5 (6.4)	2 (5.6)

[a]For RA-BE-REAL, BSRBR and SCQM-RA, this was treatment at baseline; for the Erlangen Baricitinib cohort this was treatment before or at baseline.[b]DMARD, biologic disease-modifying antirheumatic drug; Combi, combination; MTX, methotrexate; NR, not reported; SD, standard deviation.

AB0457

JAK INHIBITORS IN REFRACTORY AND AT-RISK COMORBID PATIENTS WITH RHEUMATOID ARTHRITIS IN CLINICAL PRACTICE

Keywords: Rheumatoid arthritis, Real-world evidence, Comorbidities

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Background: The use of JAK inhibitors (JAKi) may be challenged in rheumatoid arthritis (RA) by the multiplicity of previous treatment lines and the presence of comorbidities that may trigger the occurrence of potentially severe side effects.
Objectives: To assess the efficacy and safety profile of JAKi in active RA patients with refractory disease and/or risk factors for JAKi.
Methods: Retrospective routine care study carried out between 2018 and 2022 in the Rheumatology department of Cochin Hospital. We selected from our electronic medical report database RA patients initiating a JAKi between 2018 and 2021 who presented active disease (i.e. by a DAS28 >3.2) and at least one of the following criteria: age ≥65 years, presence of comorbidities (cardiovascular risk factors including active smoking, obesity, atherosclerotic cardiovascular (CV) disease, history of venous thromboembolism (VTE), previous malignancy, severe infection including herpes zoster), failure to at least two targeted biological therapies and inability to taper corticosteroids below 7.5 mg/day. Efficacy was assessed at the first visit following the initiation of treatment and at the last available visit up to December 2022. The number and causes of treatment discontinuations were collected during the exposition period.
Results: We included 83 RA (68 females, 82%) initiating a JAKi, with a mean age of 58±14 years and a mean disease duration of 16±13 years. Patients had a mean DAS28 of 4.60±1.42, they had received 3±2 previous lines of biologics, 63% belonged to the group "age ≥65 years and/or presence of at least one CV risk factor" and 20% received corticosteroids ≥7.5 mg/day. The first treatment visit was scheduled 3 or 6 months following JAKi initiation, and the last visit occurred 15±10 months after the baseline visit. The DAS28 and other parameters assessing disease activity were markedly reduced at the first and the last available visit compared to the baseline visit (**Table 1**). Low disease activity (DAS28 <3.2) was reached in 51% of patients at the first visit and 47% at the last visit. No difference of efficacy was observed according to the treatment line. A total of 35 patients (42%) discontinued the JAKi during a mean observation period of 20±10 months (**Figure 1**). The mean time to discontinuation was 10±8 months. Treatment retention was 70% at 12 months and 58% at the last visit. Discontinuations were related to inefficacy (n=21, 25%), side effects (n=11, 13%) and desire for pregnancy (n=3, 4%). The side effects leading to discontinuation were: VTE (n=2), myocardial infarction (n=2) (these 4 events occurred in the group of patients aged ≥65 years with or without presence of at least one CV risk factor), non-severe infections (n=2), allergy (n=2), gastrointestinal symptoms (n=2) and headache (n=1). No cancer was recorded during the observation period.
Conclusion: In a population o RA enriched with refractory and at-risk comorbid patients, JAKi demonstrated potent efficacy with a safety profile consistent with this population. Our results support the statement from the PRAC to use with caution JAKi in patients aged ≥65 years and/or with at least one CV risk factor.

Table 1. Efficacy of JAK inhibitors in D2TRA

	baseline	First visit	Last visit	Difference First visit-baseline	p-value	Difference last visit-baseline	p-value
Tender joints, mean±SD	5.6±5.5	2.7±3.7	2.7±3.9	-2.6±4.8	<0.001	-2.9±5.0	<0.001
Swollen joints, mean±SD	5.4±4.3	2.3±3.4	2.7±4.3	-1.5±3.6	0.002	-1.5±4.2	0.002
VAS pain (/100), mean±SD	59±26	34±22	41±29	-29±27	<0.001	-20±29	<0.001
VAS fatigue (/100), mean±SD	63±28	50±23	52±27	-21±28	<0.001	-13±33	0.040
PGA (/100), mean±SD	61±24	35±22	42±27	-26±28	<0.001	-17±31	<0.001
ESR (mm H1), mean±SD	29±24	27±26	32±29	-2.7±22	0.27	+2.6±29	0.29
CRP (mg/L), mean±SD	9.2±13.1	5.8±13.3	7.72±12.1	-2.7±7.6	0.004	-1.5±1.6	0.071
DAS28, mean±SD	4.60±1.41	3.41±1.59	3.74±1.74	-1.20±1.46	<0.001	-0.79±1.87	0.005
DAS28-CRP, mean±SD	4.06±1.21	2.91±1.17	3.17±1.5	-1.69±1.31	<0.001	-0,77±1.67	<0.001

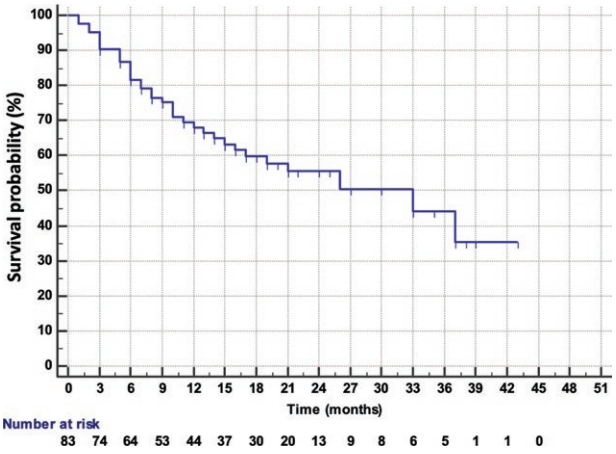


Figure 1. Time to JAKi discontinuation during the observation period

REFERENCES: NIL.
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AB0458

STEROIDS IN RHEUMATOID ARTHRITIS - TIME FOR REPREAVAL

Keywords: Cardiovascular disease, Tapering, Rheumatoid arthritis

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Background: The usage of steroids in the management of Rheumatoid Arthritis (RA) has been questioned after the ACR-2021 guidelines while short-term steroid use has been advocated by EULAR-2022.In usual clinical practices steroid has a major role in the management. The adverse events associated with the steroid use is a major limiting factor.
Objectives: To assess the steroid use in routine clinical practice and review the occurrence of Diabetes(T2DM), Hypertension(HTN),Osteoporosis,CoronaryArteryDisease(CAD),Avascular necrosis (AVN), Cataract, Infections.
Methods: All patients diagnosed with RA from 2014 to 2019 with regular follow up of minimum one year duration were taken for analysis. Demographics, weight recordings, steroid prescribed and baseline characteristics were noted.The presence of complications like DM, HTN, cataract, osteoporosis, CAD, AVN,infections before and after steroids were noted.
Results: A total of 967 patients were included in the analysis,826(85.4%) were given steroids and 141 (14.6%) were managed without steroids. The mean age was 53.58 (10.94) yrs the mean disease duration was 4.73 (5.21) for patient with steroids and 6.104 (6.05%) yrs for patients without steroids Patients who were given steroids had increased occurrence of HTN(8.7%), Infections(6%), cataract(5.3%), diabetes(3.6%), osteoporosis(1.2%), AVN(0.8%), CAD(0.7%). In non-steroids group this was 1.4% each in diabetes and infection, 0.7% HTN while 0% in other categories(**Table 1**).In the 826 patients steroids were stopped in 567 (58.6%) but the risk of HTN(8.2%), Infections(5.46%), cataract(4.9%), DM(4.05%),Osteoporosis(0.8%),AVN(0.7%)and CAD (0.8%) still remained high.
Conclusion: RA patients treated with Steroids have a increased chance of developing HTN, Infection followed by cataract, diabetes, with minimal increase in osteoporosis, CAD and AVN and this persists even after stopping steroids.
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[1] Smolen JS. recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. Ann Rheum Dis [Internet]. 2023;82. Available from: http://dx.doi.org/10.1136/ard-2022-223356 EULAR

Table 1.

STEROIDS	N	Age	F:M	DISEASE DURATION	HTN	INFECTION	CATARACT	DM	OSTEOPOROSIS	AVN	CAD
YES	826	53.58 (10.94)	868:99	4.739 (5.21)	72 (8.7%)	50 (6%)	44 (5.3%)	30 (3.6%)	10 (1.2%)	7 (0.8%)	6 (0.7%)
No	141	53.56 (10.89)	123:18	6.104 (6.058)	1 (0.7%)	2 (1.4%)	0	2 (1.4%)	0	0	0
p value		0.98		0.06							
Stopped	567	53.2 (11)	506:61	4.51 (5.02)	47 (8.2%)	31 (5.46%)	28 (4.9%)	23 (4.05%)	5 (0.8%)	4 (0.7%)	5 (0.8%)

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0459 RELATIONSHIP BETWEEN FISH CONSUMPTION AND RESPONSE TO TREATMENT WITH MOLECULAR TARGETED THERAPIES IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Remission, Non-pharmacological interventions, Rheumatoid arthritis

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Background: The use of molecular targeted therapies has improved the clinical course and quality of life of patients with rheumatoid arthritis (RA); however, a percentage of patients experience treatment failure (non-responders), which is a particular challenge for clinicians. Diet and nutrients are potential environmental factors that are likely to influence the course and the response to pharmacological therapies in RA. The Mediterranean diet or omega-3 polyunsaturated fatty acids (n-3 PUFAs) supplementation have been shown to have a favorable effect on the reduction of RA symptom. A higher intake of fish, the main source of PUFAs, was associated with lower disease activity in RA patients. Several factors have been identified that may affect treatment response in RA; however, the effect of fish consumption on treatment response in RA patients has not been clarified.
Objectives: To explore the relationship between fish consumption and response to targeted therapies in RA patients with two dietary patterns characterized by high fish consumption.
Methods: The study is a collaborative international cross-sectional retrospective study involving RA patients on treatment with biologics or Janus kinase inhibitors (JAKi) attending Hokkaido University Hospital (Japan) or Hospital Virgen de las Nieves (Spain). Patients complete a brief-type self-administered diet history questionnaire (BDHQ) and a detailed food frequency questionnaire (DFFQ) to assess fish consumption in the previous month. At study entry, qualified rheumatologists assessed RA disease activity. Demographic, clinical/laboratory data were collected retrospectively from the medical records. Descriptive analysis was performed in each cohort.
Results: One-hundred-twenty-four Japanese RA patients, 100 females, median age at entry 66 yrs [IQR 54-72], median disease duration 12 yrs [IQR 7-20] were included. One-hundred-seven (86%) patients were on biologics and 17 (14%) on JAKi, median treatment duration of 4 yrs [IQR 1-7]. Concomitant treatment with conventional synthetic disease modifying anti rheumatic drugs (csDMARDs) and glucocorticoids were reported in 84% and 53% of patients, respectively. Ninety-six (77%) patients were responders to treatment defined as disease activity score 28 (DAS28)-ESR <3.2 and DAS28-CRP <2.7. All patients had fish consumption in the last month and 82% reported intake of n-3 PUFA rich fish (fatty fish) (<1 time/week 33%, ≧1 time/week 49%). A higher estimated daily intake of n-3 PUFAs from fish was found in the responder group compared to the non-responder group [median grams, 1.01 (IQR 0.47-1.44) vs 0.51 (IQR 0.34-1.14), p=0.044]. The Spanish cohort comprised of 62 RA patients, 47 females, median age at entry 58 yrs [IQR 49-66], median disease duration 12 yrs [IQR 5-21]. Fifty-nine (95%) patients were on biologic therapies and three (5%) on JAKi, median treatment duration of 3 yrs [IQR 1-8]. Concomitant treatment with csDMARDs and glucocorticoids were reported in 38% and 42% of patients, respectively. Thirty-four (55%) patients were responders to treatment. All patients had consumption of fish in the last month and 77% had consumed fatty fish (<1 time/week 31%, ≧1 time/week 46%). No difference in estimated intake of n-3 PUFAs from fish was observed in this cohort.
Conclusion: Fish consumption may have a positive effect on the response to treatment of Japanese RA patients receiving targeted therapy.
REFERENCES: NIL.
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AB0460 JAK INHIBITOR DISCONTINUATION RATES: RETROSPECTIVE REAL-WORLD DATA FROM A TERTIARY CENTRE

Keywords: Real-world evidence, Targeted synthetic drugs, Inflammatory arthritides

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Background: JAK inhibitor uptake has increased in recent years, and recent NICE (National Institute for Health and Care Excellence) approval of certain JAK inhibitors for moderate rheumatoid arthritis disease activity will likely increase this further. The EULAR guidance on the management of rheumatoid arthritis recommends JAK inhibitors as part of the treat-to-target strategy, provided certain risk factors are considered [1]. However, there remains limited data on discontinuation rates for this drug class.
Objectives: This retrospective study aimed to measure the discontinuation rates of the four UK approved JAK inhibitors in a multi-ethnic population at a UK tertiary centre, thereby providing real-world data on the durability of the different JAK inhibitors.
Methods: All patients ever prescribed a JAK inhibitor at University Hospitals of Leicester were identified on a drug monitoring database. Discontinuation rates were calculated for each JAK inhibitor, as well as the median duration of time on each drug prior to discontinuation. The baseline characteristics of the patients who discontinued a JAK inhibitor were documented, as well as reason for discontinuation. These were categorized as either primary inefficacy, secondary inefficacy, toxic adverse events, non-toxic reasons, and disease remission.
Results: In total, 375 patients had been prescribed a JAK inhibitor since 2018. Discontinuation rates and duration of time prior to discontinuation for each drug are shown in Table 1.

Table 1. JAK inhibitor discontinuation rates and duration of use.

			Duration prior to discontinuation (weeks)							
Drug	Number of patients	Proportion discontinued	Median	Minimum	Q1	Q3	Maximum	Mean	Standard deviation	Standard error of mean
Baricitinib	233	51/233 (21.89%)	35.00	0.86	18.43	68.14	230.10	49.55	48.68	6.82
Tofacitinib	61	33/61 (54.09%)	70.29	5.29	37.86	96.93	161.10	72.35	43.29	7.54
Filgotinib	51	4/51 (7.84%)	13.50	4.71	6.54	15.86	16.14	11.96	5.14	2.57
Upadacitinib	30	0/30 (0%)	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

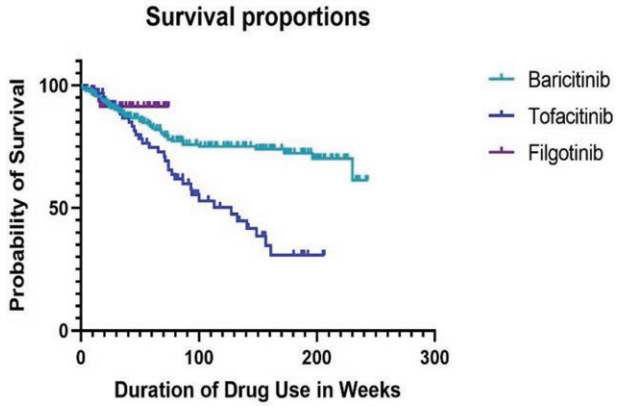


Figure 1. JAK inhibitor survival proportions.

Of the 88 patients who discontinued a JAK inhibitor, 86% were female and 14% male. Median age was 60 years (IQR 53-70 years), and median duration of drug intake was 45.60 weeks (IQR 19.29-74.07). Of these 88 patients, 77% were Caucasian, 20% from the Indian subcontinent, and the remaining patients mixed race, Asian other, and not stated. Furthermore, 65.9% of patients were on concomitant DMARDs, 71.6% had received a previous biologic drug (median number of previous biologics was 1 [0-2]). Diagnosis was seropositive RA (rheumatoid arthritis) in 59.1%, seronegative RA in 27.3%, PsA (psoriatic arthritis) in 11.4%, and 2.2% in RA/PsA overlap. Of the 88 patients where the JAK inhibitor was discontinued, reasons included primary inefficacy 37.5%, toxic adverse events 35.23%, non-toxic reasons 17.05%, secondary inefficacy 5.68%, disease remission 1.14%, and not stated 3.41%. Adverse events of interest included viral infections 6.81%, non-viral infections 4.54%, malignancy 2.27%, and MHRA alerts 9.09%. In this multi-ethnic population, there were no discontinuations for venous thromboembolism, or major adverse cardiovascular events, although patients are screened for risk factors prior to commencement, and MHRA alerts led to discontinuation if risk factors developed during treatment.

Conclusion: In this real-world population, tofacitinib followed by baricitinib had the highest discontinuation rates. While discontinuation rates for the 2nd generation JAK inhibitors appear more promising, patient numbers were lower. The most common reasons for discontinuation were primary inefficacy and toxic adverse events. Further real-world observational data is needed, particularly from multi-ethnic patient populations, to increase confidence levels in JAK inhibitor prescribing.

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AB0461

WHAT HAPPENS TO CORTICOSTEROID THERAPY, ONE YEAR AFTER THE INTRODUCTION OF TARGETED THERAPY IN RA? RESULTS OF THE STRATEGE 2 STUDY

Keywords: Rheumatoid arthritis, Disease-modifying drugs (DMARDs), Treat to target

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Background: The EULAR 2022 guidelines for the management of rheumatoid arthritis (RA) recommends methotrexate (MTX) combined with short-term corticoids (CS) as a 1st line standard of care [1]. In the event of an inadequate response to MTX and the presence of a poor RA prognosis factor, recommendations include initiation of biological (bDMARD) or synthetic (tsDMARD) targeted therapy in combination with MTX. Corticoids should be tapered as clinically feasible.

Objectives: Based on inclusion results of STRATEGE 2, we explore the evolution of therapeutic strategies after the initiation of a 1st b/tsDMARD, focusing on CS. Then patients' profiles with or without CS were investigated.

Methods: STRATEGE2 is a non-interventional, prospective study including RA patients treated with MTX for at least 3 months and requiring initiation of a first b/tsDMARD due to disease activity. Evolution of main treatments was followed during 12 months. Data regarding therapeutic strategies were collected at inclusion (baseline treatment and end-of-visit prescription) and at 12 months (treatment at the 12 months visit entry and the end-of-visit prescription).

Results: Between Feb. 2019 and Dec. 2020, 186 RA patients were included, among them 173 being reviewed at the 12 months visit. Cohort baseline conditions: 75.1% female, mean age 56.1 ±13.7 years, mean diagnostic oldness of 5.6 ±7.3 years, MTX treatment since 4.3 ±5.4 years. At the end of the inclusion visit, rheumatologists initiated a first targeted therapy. Then, patients were reviewed 12 months after inclusion (377.8 ±41.5 days). Patients' clinical conditions and treatments prescriptions are presented in the Table 1 here after.

Table 1.

	Inclusion consultation N = 173		12 months after inclusion N= 171	
	Baseline condition	After b/tsDMARD Prescription	Entry	After prescription
Mean DAS28	4.3 ±1.2		2.6 ±1.1	
Radiographic features, n (%)	82 (47.7)		NA	
Radiographic progression, n (%)	NA		5 (3.3)	
Extra-articular manifestations, n (%)	27 (16.2)		11 (6.7)	
Mean HAQ	1.0 ±0.7		0.7 ±0.7	
MTX (N + Discontinued)	173	169+4	143+28	141+30
→ Mean dosage (mg/week)	18.8 ±4.2	17.9 ±4.4	16.4 ±4.5	16.0 ±4.5
→ SC (%)	71.7	66.9	59.4	59.4
b/tsDMARD (N*+ Discontinued)	NA	173	149*+18	148*+19
Corticosteroids therapy (N*)	172	172	170*	170*
→ Yes, n (%)	86 (50.0)	80 (46.5)	66 (38.8)	68 (40.0)
→ Mean dosage (mg/day)	9.6 ±6.0	8.6 ±4.9	9.1 ±9.0	9.7 ±10.9
→ Median (Q1-Q3)	7.5 (5.0-10.0)	7.5 (5.0-10.0)	5.0	5.0 (5.0-10.0)
→ Min-Max	2.5-30.0	2.5-20.0	(5.0-10.0) 2.0-60.0	2.5-60.0

N* excludes missing data

Differences between patients' profiles with or without CS were investigated. At baseline, profiles tend to show some differences between patients treated by CS vs others compared to the full population: Age (57.4 ±14.1 vs 54.9 ±13.2; full population mean: 56.1 ±13.7), unemployed (50.0% vs 34.9%; full: 43.9%), normal body mass index (38.4% vs 51.2%; full: 44.6%), at least one comorbidity (48.8% vs 54.7%; full: 51.4%) and DAS28 score (4.5 ±1.1 vs 4.1 ±1.2; full: 4.3 ±1.2). At 12 months, the number of patients treated by CS decrease (from 50 to 40%). Patients' profiles still treated by CS are similar to inclusion except for "at least one comorbidity" (54.4% vs 50.0%; full: 51.4%).

Conclusion: One year after the initiation of a b/tsDMARD the proportion of patients treated by CS is still important with high doses. These patients are older, present comorbidities and active disease. This long-term maintenance of CS is not in line with the Eular guidelines which recommend discontinuing CS as rapidly as clinically feasible. Further analyses on patients' profiles are ongoing and supplementary data on 24 months follow-up may help to better understand the use of long-term CS in those patients.

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AB0462 COMPARING INJECTION OF LOCAL ANESTHESIA IN OVERLYING SKIN TO NOT GIVING IT PRIOR TO INTRAARTICULAR INJECTION OF GLUCOCORTICOID - A RANDOMIZED CONTROLLED TRIAL

Keywords: Rheumatoid arthritis, Pain, Inflammatory arthritides

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Background: There is no consensus among rheumatologists on giving local anesthesia to the overlying skin prior to an intra-articular injection of glucocorticoid.
Objectives: Compare procedural pain in intra-articular injection between using local anesthesia to overlying skin or not.
Methods: Open label randomized controlled trial included patients with rheumatoid arthritis or spondyloarthritis undergoing intra-articular injections (of glucocorticoid) to paired medium-large joints. First the left joint was injected followed by right joint after a gap of 10-minutes. Randomization was done by online software using serial permuted blocks of varying sizes (4, 6 and 8) whether local anesthesia (5ml of 2% Lignocaine using a 23G needle) would be given to the left or right joint. Primary endpoint was immediate procedural pain felt by the patient using the 'Numerical Rating Scale and Faces Pain Scale-Revised. Secondary endpoints were 1-hour pain assessment, patient preference and complications. Paired t-test and Wilcoxon Signed Ranked test was used (paired data). Trial#CTRI/2021/07/034777
Results: This study included 42 patients undergoing paired joint injections (84 joints); joints were knee (21 patients. 42 joints), wrists (14 patients, 28 joints), ankles (5 patients, 10 joints) and elbows (2 patients, 4 joints). In 21 patients, the left joint was given local anesthesia and in the other 21 patients, the right Joint was given local anesthesia. Most had rheumatoid arthritis (37) and minority had spondyloarthritis [5]. Their mean age (±SD) was 44.6 ± 14 years and 71% were females. There was a significantly lower immediate procedural pain in the joint over which the skin was given local anaesthesia compared to that not (4.7 (1.7), 5.6 (1.6), p<0.01, difference -1.1, 95% CI -1.5 to -0.7) (Table 1, Figure 1A). This was also reduced pain at 1-hour post procedure (3.3 (1.4), 4.0 (1.6), p<0.01). Majority of patients (78.6%) preferred the procedure with local anaesthesia (Figure 1B). There was no difference in complications of hypopigmentation or purpura nor in residual pain prick-site at 1-month.
Conclusion: Local anaesthesia of the overlying skin led to a definite but modest reduction in pain felt by the patient during intraarticular injection.

Table 1. Procedural pain felt by patients in their joint injected with or without local anesthesia at immediate (0 hour) and 1 hour post procedure

Pain using NRS-FPS	Joint with local anesthesia, n=42 Mean (SD)	Joint without LA, n=42 Mean (SD)	p-value
0 Hours	4.7 (1.7)	5.6 (1.6)	<0.01
1 Hour	3.3 (1.4)	4.0 (1.6)	<0.01

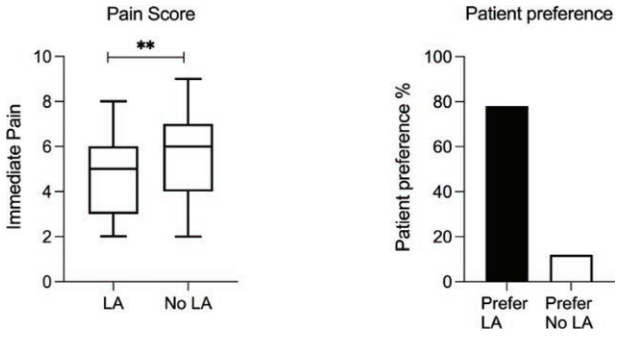


Figure 1. Procedural pain felt by patients in their joint injected with or without local anesthesia at immediate (0 hour) and the patient preference for future injections with or without local anesthesia

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.

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AB0463 THE IMPACT OF PHARMACOVIGILANCE RISK ASSESSMENT COMMITTEE (PRAC) RECOMMENDATIONS ON THE REAL-LIFE USE OF JANUS KINASES INHIBITORS FOR RHEUMATOID ARTHRITIS

Keywords: Comorbidities, Targeted synthetic drugs, Rheumatoid arthritis

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Background: In November 2022 the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) recommended measures to minimize the risk of serious adverse events associated with the use of Janus kinase inhibitors (JAKis).
Objectives: The aim of the study was to evaluate in a real-life cohort the impact of PRAC recommendations on the use of JAKis for the treatment of patients with rheumatoid arthritis (RA) and to describe their clinical characteristics. The rate of JAKi discontinuation because of major cardiovascular (CV) events (MACE), venous thromboembolism (VTE), or cancer was also analyzed according to PRAC limitations.
Methods: We conducted a retrospective analysis of RA patients treated with a JAKi from a single-centre, tertiary care hospital. The study population was stratified into patients eligible or not to JAKis in accordance with PRAC indications. We considered as ineligible: patients >65 years old; current or former long-term smokers; patients carrying increased risk of MACE (defined according to ORAL SURVEILLANCE trial[1] inclusion criteria [>50 years old and having at least one CV risk factor]), VTE (according to International Society on Thrombosis and Haemostasis categorization[2]), or cancer (defined as previous history of malignancy). In the ineligible group, a descriptive analysis of individual reasons for contraindication to JAKis was conducted. An analysis of reasons for JAKi discontinuation was performed in the whole population over a mean follow-up period of 20.9 months.
Results: Of 194 patients enrolled, 114 (57.9%) were classified as ineligible according to the PRAC definition (n=39 [34.2%] >65 years old; n=80 [70.2%] at increased risk of MACE; n=35 [30.7%] smokers; n=23 [20.2%] at increased risk of VTE, n=8 [7.0%] with history of malignancy). As detailed in Table 1, 52 (45.6%) patients fulfilled only one, 49 (43.0%) two, and 13 (11.4%) three or more PRAC criteria. Among patients ineligible for a single factor, this was high risk of MACE in 42.3% of cases. Compared with eligible ones, ineligible patients were more often obese (18.4% vs 0%; *p*<0,001), had a higher mean disease duration (15 vs 12 years; *p*=0.01), JAKis therapy duration (17.5 vs 10 months; p=0.02), mean HAQ score (1 vs 0.125; *p*<0.001), and prevalence of arterial hypertension (43% vs 12.5%; *p*<0.001), non-ischaemic heart disease (13.2% vs 3.8%; *p*=0.03), hyperlipidemia (53.5% vs 12.5%; *p*<0.001), and diabetes (7.9% vs 1,3%; p=0.04). The discontinuation rate due to adverse events was similar in eligible (5.0%) and non-eligible (7.0%) patients (p=0.57). We observed two withdrawals for VTE, one withdrawal for non-fatal stroke and one for solid malignancy (all in the ineligible group).
Conclusion: Our analysis shows that rigorous application of PRAC recommendations in a real-life setting would result in a large proportion of RA patients being excluded from treatment with JAKis, apparently without a consequent significant reduction in the rate of serious adverse events. A better quantification of the risk for MACE, VTE, and malignancy is advocated to improve our decision-making process in the management of RA.

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Table 1. Classification of ineligible patients according to PRAC recommendationsPRAC, Pharmacovigilance Risk Assessment Committee; MACE, major cardiovascular events

1 factor PRAC ineligibles (N=52)	N.
Current Smoking	9
Thrombophilia	9
History of malignancy	2
Age > 65 years	10
MACE risk	22
2 factors PRAC ineligibles (N=49)	
MACE risk + Age > 65 years	18
MACE risk + History of malignancy	2
MACE risk + Thrombophilia	7
MACE risk + Current smoking	19
Age > 65 years + Thrombophilia	1
Age > 65 years + History of malignancy	1
Current smoking + Thrombophilia	1
3 factors PRAC ineligibles (N=13)	
MACE risk + Age > 65 years + Thrombophilia	3
MACE risk + Age > 65 years + History of thrombosis	1
MACE risk + Age > 65 years + Current smoking	5
MACE risk + Age > 65% + History of malignancy	1
MACE risk + History of malignancy + Current smoking	3

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Disclosure of Interests: Ennio Giulio Favalli Speakers bureau: AbbVie, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Consultant of: AbbVie, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Matteo Ferrito: None declared, Raffaele Di Taranto: None declared, Martina Biggioggero Speakers bureau: Galapagos, Francesco Orsini: None declared, Sabino Germinario: None declared, Gilberto Cincinelli: None declared, Roberto Caporali Speakers bureau: AbbVie, Amgen, BMS, Celltrion, Fresenius, Galapagos, Janssen, Lilly, Novartis, Pfizer, UCB, Consultant of: AbbVie, Fresenius, Galapagos, Lilly, Novartis, Pfizer, UCB.
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AB0464 EFFICACY OF ANTI-FIBROTIC AGENTS IN RHEUMATOID ARTHRITIS ASSOCIATED INTERSTITIAL LUNG DISEASE: SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Rheumatoid arthritis, Systematic review, Lungs

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Background: The management of rheumatoid arthritis associated interstitial lung disease (RA-ILD) is mainly carried out with RA treatment. Anti-fibrotic drugs have been approved for idiopathic pulmonary fibrosis (IPF), decreasing peogression of the disease. The similarities between IPF and RA-ILD support the potential benefit of anti-fibrotic drugs, highlighting that nintedanib has been approved for other chronic fibrosing ILD.[1,2,3]
Objectives: To assess the efficacy of Nintedanib and Pirfenidone in RA-ILD patients.
Methods: A systematic review of the literature was performed in Medline, Cochrane Library, Web of Science and Embase databases and abstracts from EULAR and ACR were also screened. Language (English and Spanish) was the only limit for the search strategy. After eliminating duplicates and a first screening by title and abstract, records were included in the final selection for complete reading. Finally, papers included fitted inclusion criteria (RA-ILD diagnosis and anti-fibrotic treatment). A meta-analysis was performed when at least 2 comparable results were found in different studies.
Results: 24 records fitted inclusion criteria, of which 7 correspond to 2 randomized controlled clinical trials, 1 prospective case series, 4 case reports and 12 bibliographic reviews. Regarding quantitative summary, a significant less mean forced vital capacity (FVC) decrement in RA-ILD patients under anti-fibrotic treatment was found in comparison to placebo (SMD -3.42; 95%CI -4.19,-2.64; p=0.000) (Figure 1).
Conclusion: We found statistically differences between anti-fibrotic drugs and placebo concerning FVC improvement in RA-ILD patients. There does not seem to be differences between deaths and perceived quality of life. More studies with major capacity for statistical inference are needed.
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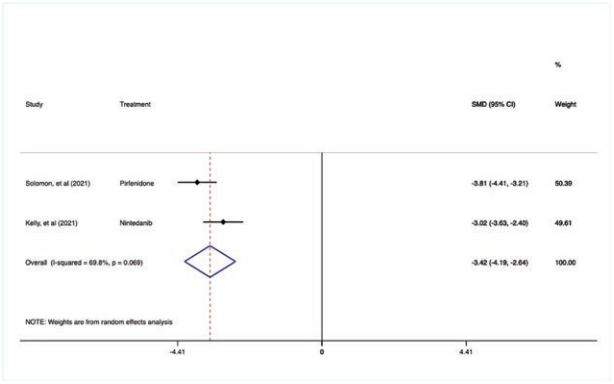


Figure 1. meta-analysis of less mean FVC decrement in RA-ILD patients treated with anti-fibrotic drugs.

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Disclosure of Interests: None Declared.
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AB0465 EFFICACY AND SAFETY OF LOW-DOSE IL-2 IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Cytokines and chemokines, Rheumatoid arthritis

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Background: Interleukin (IL)-2 is a key cytokine for tipping the balance of Treg and effector T cells, which can effectively relieve rheumatoid arthritis(RA).
Objectives: This study aimed to systematically evaluate the efficacy and safety of low-dose IL-2 therapy in RA.
Methods: Systematic searches of PubMed, EMBASE, Web of Science, the Cochrane Library and Medline, CNKI, CBM, and Technology Journal Database were performed. Original case reports, case series, observational studies, and clinical trials reporting the efficacy or safety data on RA patients treated with IL-2 were included. A random-effects meta-analysis was performed to calculate the pooled efficacy. Inconsistency was evaluated by using the I[2], and Egger tests were used for the evaluation of potential publication bias (STATA v.12.0)
Results: Thirteen studies comprising 1161 patients were identified (Table 1). After the low-dose IL-2 treatment, there were significant decreases in diseases activity measures such a DAS28[SMD=- 2.631, 95%CI (-3.526,-1.737), P<0.001], SJC[SMD=- 1.066, 95%CI (-1.467,-0.664), P<0.001], TJC[SMD=- 1.032, 95%CI (-1.193,-0.871), P<0.001], ESR[SMD=- 1.315, 95%CI (-1.883,-0.748), P<0.001], and CRP [SMD=- 0.824, 95%CI (-0.997,-0.652), P<0.001]. The values of BUN were increasedand the values of Cr was no statistical differences. The value of ALT was increased while the value of AST was decreased.Blood cell counts such as WBC, PLT and LY were significantly increased and RBC was no statistical difference. Meanwhile, the value of Hb was also no statistical difference(Figure 1). Besides, the numbers of CD4+T cells, CD8+T cells, Th1 cells, Th2 cells, Th17 cells and Tregs were significantly increased after IL-2 injection [SMD=0.819, 95%CI (0.692,0.946), P<0.001; SMD=0.388, 95%CI(0.222,0.554), P<0.001;SMD=0.634, 95%CI (0.436,0.832), P<0.001; SMD=0.521, 95%CI(0.366,0.676), P<0.001;SMD=0.626, 95%CI (0.475,0.776), P<0.001; SMD=1.177, 95%CI(0.941,1.412), P<0.001], while there were no statistical differences in the number of NK cells after IL-2 treatment. Importantly,the ratio of Th17/Tregs was significantly decreased[SMD=-0.700, 95%CI (-0.852,-0.549), P<0.001] and the radio of Th1/Th2 was no statistical difference(Figure 2).After the low-dose IL-2 treatment,the serious adverse event rate reported among all these studies was 0.083 (95%CI 0.051-0.114)(Figure 3).

Table 1. Available evidence including patients with RA treated with low-dose IL-2.

Study.Year.	Patients (include in analysis)	Gender (female %)	Dosage	DAS28	SJC	TJC
Xiaoying Zhang. 2022.	47(23)	86.96	1 million IU every other day	NA	NA	NA
Shengxiao Zhang. 2021.	888(233)	NA	0.5 million IU per day for 5 days	before:5.44 ± 1.34 after: 3.66 ± 1.09	before:6.40 ± 7.63 after: 1.70 ± 3.32	before:10.07 ± 7.97 after: 3.94 ± 4.76
C H Chien. 1990.	11(11)	54.55	10 to 50 thousand IU per kilogram	NA	NA	NA
F. Y. Hu. 2018.	267(267)	79.40	0.5 million IU per day for 5 days	NA	NA	NA
X. Jia. 2018.	75(75)	NA	0.5 million IU per day for 5 days	NA	NA	NA
ShengXiao Zhang. 2016.	41(26)	NA	0.5 million IU per day for 5 days	before:3.60±0.96 after: 2.85±0.67	before:1.40±1.64 after: 0.42±0.70	before:3.73±2.79 after: 0.94±1.00
Z. Li. 2017.	58(38)	NA	0.5 million IU per day for 5 days	before:3.34±0.81 after:2.36±0.97	NA	NA
张升校. 2018.	41(26)	57.69	0.5 million IU per day for 5 days	before:5.31±1.18 after:2.85±0.67	before:4.15±5.03 after:0.42±0.70	before:10.54±8.79 after: 0.94±1.00
X. Jia. 2018.	304(156)	NA	0.5 million IU per day for 5 days	NA	NA	NA
Ming Yan. 2018.	839(233)	NA	0.5 million IU per day for 5 days	NA	NA	NA
王佳. 2019.	41(26)	57.69	0.5 million IU per day for 5 days	before:5.3±0.89 after:2.7±0.67	before:2.5±1.48 after:0±0.74	before:6.5±10.37 after: 1±1.48
丁汀汀. 2022.	41(21)	66.67	0.5 million IU per day for 5 days	before:6.91±0.43 after:2.23±0.23	NA	NA
Jia Wang. 2022.	41(26)	57.69	0.5 million IU per day for 5 days	before:5.31±1.18 after:2.85±0.67	before:4.15±5.03 after:0.94±1.00	before:10.54±8.79 after:0.4±0.70

Conclusion: Low-dose IL-2 was promising and well-tolerated in the treatment of RA, which could promote the proliferation and functional recovery of Tregs.



Figure 1:Efficacy of IL-2 in patients with rheumatoid arthritis.(A) DAS28 scores.(B) TJC scores.(C) SJC scores.(D) ESR.(E) CRP.(F) Cr.(G) BUN.(H) ALT.(I) AST.(J) WBC.(K) RBC.(L) PLT.(M) LY.(N) Hb.

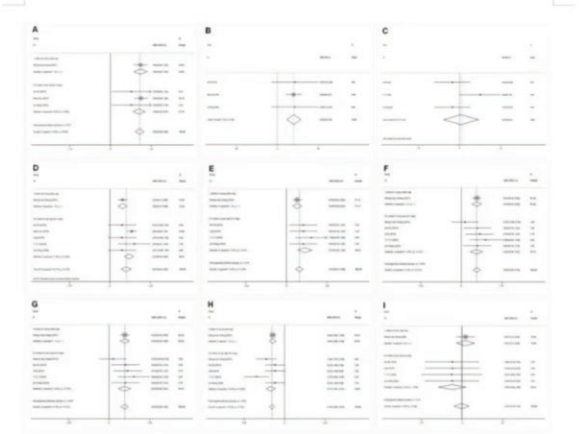


Figure 2: Changes in the subsets of lymphocytes after IL-2 in patients with rheumatoid arthritis.(A-G) the number of $CD8^+$T,$CD4^+$ T,NK,Th1,Th2,Th17 and Tregs cells before and after low-dose IL-2 treatment.(H)Th17/Tregs. (I) Th1/Th2.

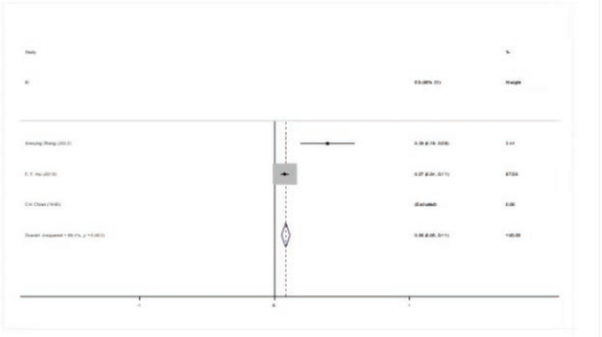


Figure 3:Safety of IL-2 in patients with rheumatoid arthritis.

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Disclosure of Interests: None Declared.
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AB0466

IDENTIFICATION OF POTENTIAL BLOOD BIOMARKERS FOR JAK INHIBITOR TREATMENT-RELATED PATHWAYS THROUGH BULK RNA SEQUENCING ANALYSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Genetics/epigenetics, Targeted synthetic drugs

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Background: Targeted small molecule therapy that inhibits receptor-mediated signaling via Janus kinase (JAK)–signal transducer and activator of transcription (STAT) pathways has become an established strategy for the treatment of rheumatoid arthritis (RA). The rationale for using these inhibitors is that JAKs have critical roles in specific pathological mechanisms and thus their targeted inhibition can lead to effective disease control. Despite JAK inhibitors (JAKi) having been approved for the treatment of RA and other systemic or organ-specific autoimmune diseases, the DAS28 response to JAKi is highly variable, emphasizing the need for reliable biomarkers.
Objectives: To reveal the potential impact of JAKi on treating RA patients, we aim to identify the biomarkers related to the responses of JAKi from blood bulk RNA-seq.

Methods: To better understand the molecular mechanisms of JAKi, we analyzed the global transcriptomics profile (using bulk RNA-seq) in peripheral blood mononuclear cells (PBMCs) that were collected from three RA patients before and after the treatment of JAKi.
Results: Comparing the responder and non-responder groups, we identified 1366 upregulated differentially expressed genes (DEGs) and 1366 upregulated differentially expressed genes (DEGs), and 1630 DEGs. To reveal further insight into the biological roles of the DEGs, we performed GO pathway analysis. Compared with responders, we found that the non-responders have a higher inflammation rate. In addition, non-responders have higher expression of genes that are involved in the JAKs signaling pathway. Specifically, gene profiling of non-responder represents higher Type I and II interferon pathway. In contrast, gene profiling of the responder represents a higher IL-12 pathway.

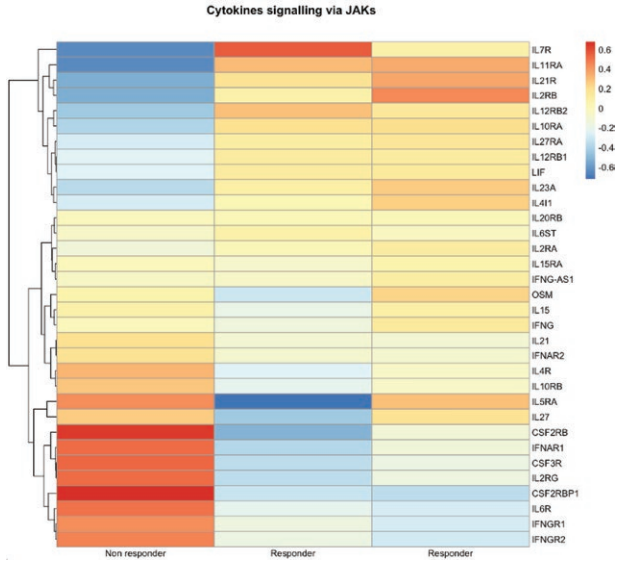


Figure 1.

Conclusion: These changes were accompanied by changes in broader immune cell composition, based on the deconvolution of bulk RNA-sequencing data. In summary, our study revealed several phenotypic and cellular changes that underlie the clinical improvement with JAKi.
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Disclosure of Interests: None Declared.
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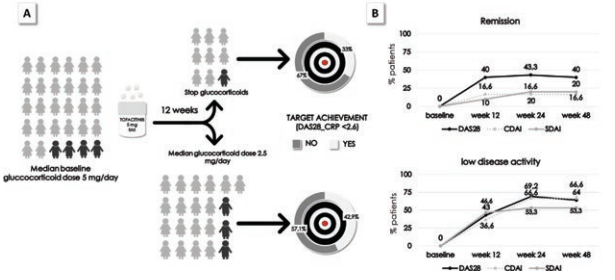
AB0467 STEROID-SPARING EFFECT OF TOFACITINIB. TAPERING AND WITHDRAWAL OF GLUCOCORTICOIDS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Targeted synthetic drugs, Clinical trials, Tapering

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Background: The 2022 updated EULAR recommendations for the management of Rheumatoid Arthritis (RA) suggest tapering and discontinuation of oral glucocorticoids (GC), as rapidly as clinically feasible [1]. Considering GC as a "bridging therapy" to promptly reduce symptoms and control inflammation until the maximum effect of the Disease Modifying Anti-Rheumatic Drugs (DMARDs) is reached, the rapid effect of Janus Kinase (JAK) inhibitors could allow a fast and safe tapering of GC.
Objectives: We aimed to evaluate the steroid-sparing effect of adding tofacitinib in RA patients with inadequate response to MTX.
Methods: In this open label study, we enrolled patients with moderate-to-severe RA, on stable prednisone dose (5-12.5 mg/day) starting tofacitinib. After 1 month, in patients achieving at least a moderate EUALR response (>1.2 points reduction in DAS28 score), GC was tapered according to pre-specified schedule until complete withdrawal at week-12. The sample size of 30 patients was estimated assuming a 12-weeks response rate of 30% with a confidence interval of 90% and a margin of error of 15%. Disease activity was assessed after 4, 12, 24 and 48 weeks of treatment. The primary endpoint of the study was the percentage of patients discontinuing GCs after 12 weeks of treatment with tofacitinib. Secondary endpoints were: 1) the percentage of patients requiring a new GC course during the 12-months follow-up, 2) the percentage of patients in clinical remission or low disease activity at week 12, 24 and 48. At each visit laboratory tests, complete physical examination and other safety assessments were performed with particular interest to serious infections, Varicella Zoster virus reactivation, Major Cardiovascular Adverse Events (MACE), thromboembolic events and malignancy. Adverse events leading withdrawal of tofacitinib were also recorded.
Results: We enrolled 30 patients (26F: 4M, mean age 60±13 years, mean disease duration 13.2±7.8 years). The primary endpoint was achieved: 9 patients (30%) discontinued GC at week-12. At week 24 and 48, 12 patients (40%) had discontinued prednisone. The median prednisone dose decreased from a median dose of 5 mg/day (interquartile range 5-10 mg) to 2.5 (0-5), 2.5(0-5) mg/day at week 12 and 48 ($p<0.00001$ vs baseline). Multivariate analysis showed that factors negatively associated with GC withdrawal after 12 weeks were age ($p=0.014$), disease duration ($p=0.045$), and baseline PGA ($p=0.028$). During the follow up 4 patients had to increase the dose of GC from 1.2 (IQR 1-25-2.5) to 5; one more patient had to reintroduce 5 mg of prednisone after stopping at week 12. Discontinuation of glucocorticoids did not affect target achievement at week 12: a similar percentage of patients who discontinued or not discontinued GC achieved remission or low disease activity at week 12 (Figure 1A), and the percentage of patients who achieved the target increased throughout follow-up with no difference according to glucocorticoid therapy (Figure 1B). Three out of the 30 patients discontinued tofacitinib for adverse events (one for the onset of endometrial malignancy after 5 months of treatment, one for serious infection and one for paresthesia). As for the adverse events of special interest, none of the patients reported Varicella Zoster reactivation and no case of MACE nor thromboembolic events were recorded.
Conclusion: The rapid effect of tofacitinib in long standing RA patients allowed a significant reduction of the daily prednisone dose leading to the discontinuation of glucocorticoids in up to 30% of patients, without limiting the drug effectiveness.
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Figure 1. Percentage of patients achieving the treatment target at week 12 according to glucocorticoids discontinuation (A) and target achievement up to 48-weeks follow up (B)



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AB0468 DRUG RETENTION AND SAFETY OF JANUS KINASE INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS - REAL WORLD EXPERIENCE FROM A SINGLE CENTRE IN UK

Keywords: Rheumatoid arthritis, Real-world evidence, Disease-modifying drugs (DMARDs)

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Background: Tofacitinib, baricitinib, upadacitinib and filgotinib are the Janus kinase inhibitors (JAKi) approved for the treatment of rheumatoid arthritis (RA) in the UK. We report our real-world experience in a cohort of RA patients commenced on JAKi in a regional centre in the UK.
Objectives: To study drug retention rates and adverse events of JAKi in RA patients in the real- world scenario.
Methods: Data of patients with RA initiated on JAKi from February 2018 to August 2022 were retrospectively collected from hospital and primary care records. Kaplan-Meier curve was plotted for the cumulative drug retention rate. Crude event rates for various adverse events were calculated per 100 patient-years. Hazard ratios were calculated for adverse events for tofacitinib vs baricitinib after adjusting for baseline variability using inverse probability of treatment weighting (IPTW). Statistical analysis was done using R studio.
Results: During the study period 356 patients were initiated on JAKi (Baricitinib: 266, Tofacitinib: 48, Upadacitinib: 33 and Filgotinib: 9). Baseline characteristics of patients are given in Table 1. Over 734.6 patient-years follow up 92 (25.6%) discontinued JAKi. Drug retention rate at 2 years, 3 years and 4 years was 74.2%, 67.5% and 61.5% respectively (Figure 1). Most common reason for discontinuation was lack/loss of response (42.3%). Infections led to discontinuation in 13 patients and cardiovascular events in 5 patients. Lymphopenia, rash, oral ulcer, anemia, weight gain, high cholesterol, diverticulitis, and lymphedema were the other adverse events which resulted in discontinuation. Ten patients died while on treatment with JAKi. Six patients had a major adverse cardiovascular event (MACE) - 4 acute coronary events and 2 strokes. Nine patients had a venous thromboembolic event (VTE) while one patient had central retinal artery occlusion. Event rates for MACE and VTE were 0.8(0.3-1.7) and 1.2(0.5-2.3) respectively. Herpes zoster (HZ) occurred in 13 patients with an event rate of 1.8(1.0-3.1). Incident malignancies were noted in 14 patients on JAKi. Event rate was 1.1(0.5-2.2) for malignancies excluding 6 non-melanoma skin cancers. There were no statistically significant differences in the incidence of adverse events between tofacitinib and baricitinib. Hazard ratios for discontinuation, MACE, Pulmonary embolism, HZ, and malignancy were 0.7 (0.4-1.4), 2.0 (0.3-10.8), 0.2(0.02-1.4), 0.8(0.2-3.3) and 1.2(0.3-5.0) respectively for tofacitinib compared to baricitinib. Upadacitinib and filgotinib had shorter follow up duration to draw any meaningful conclusion.
Conclusion: JAKi in this real-world population of RA patients had high persistence rates. MACE, VTE, HZ and infections remain adverse events of concern.

Table 1. Baseline characteristics of patients

	All (n=356)	Tofacitinib (n=48)	Baricitinib (n=266)	Upadacitinib (n=33)	Filgotinib (n=9)
Age					
Mean- in years	59.2±12.6	61.5±12.1	58.9±12.6	57.7±12.5	60.7±14.7
Female sex	284 (79.8)	36(75.0)	211(79.3)	31(93.9)	6(66.7)
RA duration, years	11.7± 9.6	13.2±10.1	11.7±9.6	11.1±9.9	12.3±8.5
RF	167 (58.4)	20(50.0)	122(57.5)	23(85.2)	2(28.6)
Anti CCP	194 (70.0)	31(75.6)	138(68.0)	23 (85.2)	2(33.3)
Base line DAS	5.91 ±0.92	5.96±0.96	5.92±0.89	6.02±0.95	4.99±1.2
Smoking status					
Current	51(17.3)	6(13.6)	40(18.6)	4(14.3)	1(14.3)
Ever	130(44.2)	17(38.6)	101(47.0)	10(35.7)	2(28.6)
Hypertension	112 (31.7)	20(41.7)	81(30.7)	9 (27.3)	2 (22.2)
Diabetes	43 (12.2)	6(12.2)	30 (11.5)	5 (15.2)	2(22.2)
Previous CV event	23 (6.5)	4(8.3)	16 (6.0)	1 (3.0)	2 (22.2)
AF	16 (4.5)	3 (6.3)	13 (4.9)	0 (0.0)	0(0.0)
TCh/HDL>4	66(18.5)	13(26.5)	45(16.9)	6(18.2)	2(22.2)
Any DMARD	209 (59.5)	22(45.8)	161(61.7)	23 (69.7)	3(33.3)
Number of previous biologics	1.0±1.1	1.4 ± 1.1	0.9 ±1.2	1.0±1.1	0.4±0.5
Biologic naïve	162(45.4)	14(28.6)	129(48.5)	14(28.6)	5(55.6)

RF: Rheumatoid factor, CCP: cyclic citrullinated peptide, AF: Atrial fibrillation, TCh: Total cholesterol, HDL: High density lipoproteins

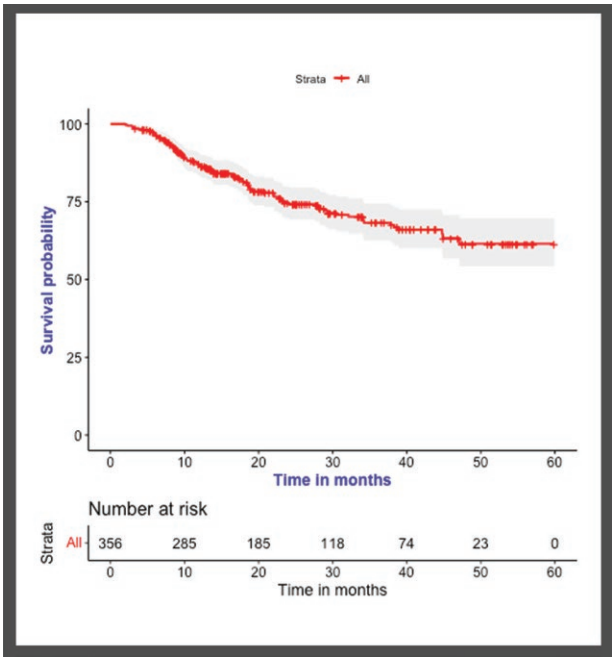


Figure 1. Kaplan Meier plot showing drug retention with JAKi

REFERENCES: NIL.
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AB0469

BASELINE MODIFIED TOTAL SHARP SCORE MAY BE A PREDICTOR FOR FLARE AND SUCCESSIVE JOINT DAMAGE IN TAPERING OF METHOTREXATE

Keywords: Prognostic factors, Rheumatoid arthritis

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Background: Many studies have reported the reduction or discontinuation of biologics in the treatment of rheumatoid arthritis (RA). In contrast, studies on tapering methotrexate (MTX) have been limited [1,2]. We prospectively reported whether bone destruction will progress at 48 weeks after tapering or discontinuing MTX in 79 RA patients in this meeting[3]. 34 patients (total 113 patients) were added for further analysis.
Objectives: According to tapering response, predictors for successful tapering MTX and progression of bone destruction were determined.
Methods: The subjects were RA patients who had maintained low disease activity or lower for 24 weeks or more in DAS28-CRP after MTX administration. Patients having PDUS Grade 2 or 3 per site by bilateral hand ultrasonography (26 areas) were excluded in this study owing to risk for joint destruction. Tapering of MTX dose was done every 2-3 months based on “shared decision between the patient and doctor.” The joint destruction was evaluated by joint X-ray evaluation by modified total Sharp scoring (mTSS) at 1 year after the start

of tapering MTX. Evaluation of clinical disease activity, severe adverse events, and the continuation rate during MTX tapering were also evaluated. According to tapering response, predictors for successful tapering MTX and progression of bone destruction were determined. Statistical analysis was performed by t-test, Mann-Whitney U test or one-way analysis of variance using EZR ver 1.37[4].

Results: Patients' demographic data were as follows, mean age:60.8 yrs, female: male: 88 pts:25pts, disease duration: 66.1 months, mean MTX dose: 8.51mg/week, mean DAS28-CRP: 1.55, ACPA:179.9 U/ml, ACPA positive(%): 72.6, RF: 48.1 IU/ml, RF(%):48.1, mean mTSS:17.6, ΔmTSS>1: 8.8% (10 cases) According to previous report, 113 RA patients were divided into three groups; Flared (F) group (22 patients), Less tapering (L) group, (37 patients) Good tapering (G) group (54 patients). As shown in Table 1A, significant differences were observed among the three groups in MTX dose at 6M(F vs G, P<0.01, L vs G, P<0.01), MTX dose at 12M(F vs L, P=0.01. F vs G, P<0.01, L vs G <0.01), DAS28-CRP at 12M (F vs L,G,P<0.05), ΔmTSS/y(Fvs G, P<0.05), baseline CDAI value (L vs G group, P<0.05), CDAI, SDAI at 12M(F vs G, P<0.05, F vs L, P<0.05), D-VAS at 12M(F vs L,G, P<0.01). Table 1B shows significant differences between F group and unflared (L+G) group in baseline mTSS (P<0.05), ΔmTSS/y(P<0.01), CDAI,SDAI, doctor VAS at 12M(P<0.01), MMP3 at 12M(P<0.05). Severe adverse events; cancer(stomach, lung) 2, MTX associated lymphoma(brain) 1, pneumoniae 1. These results indicated baseline mTSS may be a predictor for flare and flare response may be a predictor for joint destruction. Baseline CDAI may be a predictor for good response.

Conclusion: Baseline mTSS may be a predictor for flare successive joint damage in MTX tapering. Keeping low CDAI not DAS28 is important for good tapering.

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Table 1A.

	Flared group(N=22	Less tapering group(N=37)	Good tapering group(N=54)	P value
sex(F,M)	16,6	30,7	42,12	N.S
age	56.8(+-12.0)	62.4(+-10.3)	61.2(+-12.7)	N.S
duration(month)	71.5(+-56.0)	68.1(+-57.8)	66.5(+-55.8)	N.S
LDA(month)	30.4(+-28.6)	30.2(+-23.7)	31.2(+-23.9)	N.S
MTX dose baseline	8.35(+-2.39)	8.95(+-2.19)	8.31(+-2.91)	N.S
3M	6.09(+-2.37)	6.65(+-1.89)	5.55(+-2.40)	N.S
6M	6.34(+-2.59)	6.54(+-1.74)	4.58(+-2.22)	F vs L N.S, F vs G <0.01, L vs G
12M	7.65(+-2.31)	6.19(+-1.58)	2.87(+-2.0)	F vs L =0.01, F vs G <0.01, L vs G
GSS 0M	2.26(+-2.77)	2.65(+-3.08)	2.25(+-3.00)	N.S
PDS 0M	0.52(+-1.08)	0.75(+-1.50)	0.51(+-1.07)	N.S
PSL 0M	0.18(+-0.59)	0.33(+-1.10)	0.59(+-1.12)	N.S
ACPA	189.3(+-292.6)	194.4(+-351.9)	166.0(+-295.4)	N.S
RF 0M	42.9(+-42.9)	67.6(+-92.9)	37.1(+-50.6)	N.S
DAS28-CRP 0M	2.02(+-2.18)	1.63(+-1.64)	1.49(+-0.37)	N.S
mTSS 0M	21.8(+-19.4)	15.2(+-13.6)	17.6(+-20.0)	N.S
ΔmTSS/Y	0.35(+-0.77)	0.07(+-0.42)	- 0.02(+-0.36)	F vs G P<0.05
CDAI0	2.20(+-2.02)	2.55(+-2.24)	1.59(+-1.51)	L vs G P<0.05
SDAI0	2.36(+-2.01)	2.75(+-2.24)	1.81(+-1.62)	N.S
MMP-3 0	51.6(+-26.1)	47.7(+-28.2)	55.6(+-31.2)	N.S

Table 1B.

	Flared group(N=22	not flared group(N=91)	P value
sex(F,M)	16,6	72,19	N.S
age	57.5(+-11.8)	61.6(+-11.7)	N.S
duration(month)	54(36.0-80.8)	44(22.5-95.5)	N.S
LDA(month)	22.5(9.25-33.75)	23.0(13.25-44.75)	N.S
MTX dose baseline	8.36(+-2.44)	8.55(+-2.66)	N.S
3M	6.18(+-2.38)	5.95(+-2.24)	N.S
6M	6.5(+-2.54)	5.34(+-2.24)	P<0.05
12M	7.55(+-2.30)	4.20(+-2.46)	P<0.01
GSS 0M	1.5(0-9)	1.0(0-13)	N.S
PDS 0M	0(0-0)	0(0-1)	N.S
PSL 0M	0.18(+-0.59)	0.48(+-1.12)	N.S
ACPA 0 M	44.7(11.9-276.5)	31.5(0.95-187.7)	N.S
RF 0M	37.5(15-45)	22.0(9-64)	N.S
DAS28-CRP 0M	1.6(1.35-1.68)	1.5(1.20-1.80)	N.S
mTSS 0M	13.75(11-23)	10.50(6-19)	P<0.05
ΔmTSS/Y	0.35(+-0.77)	0.02(+-0.38)	P<0.01
CDAI0	1.5(1.5-2.5)	1.5(0.5-3.0)	N.S
SDAI0	2.05(1.60-2.60)	1.60(0.65-3.15)	N.S
MMP-3 0	49.3(34.95-58.0)	41.2(32.70-65.9)	N.S

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Disclosure of Interests: None Declared.
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AB0470 EFFECT OF TOFACITINIB IN MODULATING PLATELET FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Safety, Targeted synthetic drugs

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Background: Recent data suggested an association between Tofacitinib treatment and increased cardiovascular events in patients with Rheumatoid arthritis. Janus Kinase inhibitors (JAKi), specifically JAK3, have been demonstrated to be one of the regulators of platelet function. Treating platelets with thrombin induces tyrosine phosphorylation of the JAK3 target substrates STAT1 and STAT3, and JAK3 deficiency in mice reduces platelet aggregation and improves event-free survival in thromboplastin-induced thromboembolism.

Objectives: This study aimed to study the ability of the JAK1/JAK3 inhibitor, Tofacitinib, to influence platelet activity in patients with Rheumatoid Arthritis.

Methods: We enrolled patients with a diagnosis of RA according to the ACR/EULAR 2010 ACR/EULAR criteria. Peripheral blood was obtained from RA patients at the baseline and after 1, 3 and 6 months of Tofacitinib therapy.
Platelet aggregation assay was performed by optical aggregometry stimulated with the thromboxane A_2 receptor in RA patients and controls. The aggregation test was performed before starting the therapy with Tofacitinib and after one month, three months and six months.

Results: 25 RA patients treated with Tofacitinib were recruited, 86% female and 14 % male, with a mean age of 56.5 years (SD 9.7 yrs.), mean disease duration of 16.3 years, mean ESR 28.2 mm, mean CRP 0.9 mg/dl, mean SDAI 18.2 and mean prednisone equivalent dose 3.75 mg/die. 78% of the patients were positive for Rheumatoid factor and 57.1% for ACPA. Looking at the classical risk factors, 35.7 had hypertension, 21.4% had hypercholesterolemia, 16.2% had diabetes, and 14.2% were smokers.; only one patient had a previous cardiovascular event. The platelet aggregation was not influenced by Tofacitinib treatment at any time points (T1, T3 and T6) at any Thromboxane dose (5uM and 20 uM), furthermore did not differ from patients and controls basally (64%, SD 15.84% vs 62%, SD 10.5%).

Conclusion: In conclusion, Tofacitinib does not increase platelet aggregation in patients treated for Rheumatoid Arthritis.

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AB0471 FEASIBILITY STUDY OF METHOTREXATE USE IMPROVEMENT IN RHEUMATOID ARTHRITIS (MIRA) USING BIOMARKER FEEDBACK: QUALITATIVE RESULTS FROM PATIENT INTERVIEWS

Keywords: Biomarkers, Rheumatoid arthritis, Qualitative research methods

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Background: MTX non-adherence is associated with reduced response, increased healthcare costs to the NHS and reduced quality of life for the patient. Often the prescriber is unable to determine if a patient is taking their medication as prescribed. There is a need to measure adherence directly to facilitate more precise and objective measurements of adherence to add to the clinicians tools and help to open up honest discussions and supportive interventions with patients. Our group has previously developed a sensitive biochemical assay for the detection of MTX adherence, MIRA is a feasibility trial designed to assess the feasibility of a randomised controlled trial of MTX biochemical adherence biofeedback. This paper reports on the patients' perspectives on adherence monitoring.

Objectives: MIRA is a prospective multi-centre randomised controlled trial to examine the feasibility of a fully powered randomised controlled trial to examine if

a biochemical adherence guided intervention is superior to standard clinical care in RA patients prescribed MTX.

Methods: RA patients prescribed oral MTX for ≥ two years were randomised 1:1 to receive biochemical adherence biofeedback or control. Clinico-demographics, biochemical MTX adherence and DAS-28 and were measured at baseline and three months. Participants in the intervention cohort were telephoned with their biochemical adherence results and adherence was explored. The semi-structured interviews were used to evaluate a sample of patient perspectives about and engagement with the intervention (n=10, visit 4). Ethical approval for MIRA was given by the North West - Haydock Research Ethics Committee (19/NW/0047) and all participants provided written informed consent.

Results: 57 trial participants were recruited, withdrawal rate was 14% and reasons given were intercurrent illness, lost contact, withdrawn consent and one patient died during follow-up leaving full outcome data available for 49 participants. A total of nine semi-structured interviews were recorded and analysed in the qualitative arm of the study. The themes from the interviews were grouped in relation to the core concepts of normalisation process theory, these were: coherence, cognitive participation, collective action, reflexive monitoring. Density mapping of the themes suggested that *comprehension* of the study purpose might have been limited. However, there were high levels of *reflexive monitoring* and most of the reflections were of a positive nature. Additionally, the intensity of data relating to *cognitive participation* and *collective action* suggest that participants were fully engaged in the trial and were supportive of the intervention and trial process.

Conclusion: The results of the MIRA trial have demonstrated that the use of a biochemical adherence blood test with biofeedback is feasible as part of a clinical trial. Qualitative findings suggested that participants reported that they were happy to take part in the trial. In contrast to expectations, participants were happy to have their MTX adherence monitored.

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Disclosure of Interests: None Declared.

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AB0472 FILGOTINIB FOR RHEUMATOID ARTHRITIS - AN OBSERVATIONAL STUDY TO ASSESS CLINICAL EFFECTIVENESS IN NHS LOTHIAN

Keywords: Real-world evidence, Targeted synthetic drugs, Rheumatoid arthritis

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Background: Filgotinib (Jyseleca) is a Janus-kinase (JAK) inhibitor which in 2021 was approved for use in the UK in moderate or severe rheumatoid arthritis (RA) either as monotherapy or in combination with Methotrexate. A reduced dose of 100 mg is recommended for patients aged 75 years or over, or with moderate or severe renal impairment. Clinical efficacy of filgotinib alongside a conventional disease-modifying anti-rheumatic drug (cDMARD) was demonstrated in the FINCH 1 and FINCH 2 trials [1,2] but evidence of real-world effectiveness is currently limited.

Objectives: To describe a cohort of patients prescribed filgotinib (Jyseleca) for RA in NHS Lothian and assess clinical response and discontinuation rates in regular clinical practice.

Methods: The electronic patient record was reviewed for patients prescribed filgotinib in NHS Lothian between December 2021 and August 2022. Baseline data was recorded including time since diagnosis of RA, previous and concurrent treatment, duration of treatment with filgotnib and discontinuation reason if applicable. Comorbidities of interstitial lung disease (ILD), prior venous thromboembolism (VTE), major adverse cardiovascular events (MACE) or malignancy were recorded. Steroid prescriptions at the time of commencing filgotinib were recorded. DAS-28 scores within 6 months prior to starting filgotinib were recorded where they had been performed, along with most recent DAS-28 scores.

Results: 145 patients were prescribed filgotinib for RA; 106 females and 39 males. Median age was 64 years. Median treatment duration was 213 days. 35 (24.1%) patients were treated with the reduced 100mg dose. 14 (9.7%) discontinued treatment. 120 (82.8%) were previously treated with an alternative biologic DMARD. 59 (40.7%) had failed multiple biologic DMARDs of different classes. 19 (13.1%) switched directly to filgotinib from an alternative JAK inhibitor. Pre-treatment DAS-28 scores were recorded in 53 (36.6%), with a mean score of 5.07. DAS-28 scores following commencement of filgotinib were recorded in 29 (20.0%), with a mean score of 3.50. Pre-treatment tender (TJC) and swollen (SJC) joint counts were recorded in 86 (59.3%), with mean TJC 10.35 and SJC 6.50. Post-treatment counts were recorded in 46 (31.7%), with mean TJC 4.65 and SJC 2.91. Pre-treatment patient visual assessment score (VAS) of global health was recorded in 71 (49.0%), with mean VAS 62. Post-treatment VAS was recorded in 32 (22.1%), with mean VAS 43. 12 (8.3%) patients had DAS-28 scores recorded before and after. 7 were classed as a good response by EULAR criteria, 2 were a moderate response, and 3 were non-responders.

Conclusion: The drug survival rate of 90.3% after efficacy assessment at clinical review suggests a good tolerance, patient acceptability and clinical effectiveness. This Edinburgh-based, real-world, unselected patient cohort includes a high rate of multidrug-resistant RA yet sustains a high drug survival rate at 6 months. The cohort is limited by the lack of accurate DAS-28 recording in the clinical record. This may in part reflect the Lothian model of treating imaging-confirmed synovitis in the absence of a DAS-28 result.

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Title: Filgotinib for Rheumatoid Arthritis - an observational study to assess clinical effectiveness in NHS Lothian.

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AB0473 THE EFFICACY OF METHOTREXATE MONOTHERAPY STRATEGY CHOSEN AS FIRST-LINE DMARD THERAPY IN PATIENTS WITH NEWLY DIAGNOSED RHEUMATOID ARTHRITIS: RETROSPECTIVE EVALUATION OF SINGLE TERTIARY CENTER EXPERIENCE

Keywords: Remission, Disease-modifying drugs (DMARDs), Rheumatoid arthritis

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Background: Rheumatoid Arthritis (RA) is a chronic systemic disease in which immunologically mediated inflammation of synovia-lined joints can disrupt joint structure and function. Methotrexate is the first recommended conventional disease-modifying antirheumatic drugs (DMARD) when diagnosed in patients with RA. The goal of treatment is low disease activity or remission [1].

Objectives: It was aimed to retrospectively evaluate the response of patients who received methotrexate (MTX) monotherapy as a first-line DMARD strategy in newly diagnosed RA patients.

Methods: Between January 2018-September 2022, 642 patients diagnosed with RA in the Department of Internal Medicine Rheumatology of Sakarya University were retrospectively analyzed. All patients fulfilled the criteria for the 2010 Rheumatoid arthritis classification. Patients with newly diagnosed RA and obtaining MTX monotherapy as the first conventional DMARD strategy were included in the study. Patients diagnosed in another center and initially started conventional DMARD combination therapy were excluded from the study. Patients who discontinued treatment due to side effects were excluded and 73 were included in the study. Age, gender, rheumatoid factor and anticitrulized peptide antibody levels of the patients were recorded. Disease activity was evaluated at 0-3-6 months with the Disease Activity Score Calculator for Rheumatoid Arthritis (DAS-28). Data were analyzed using the computer program SPSS 21. Wilcoxon Signed Rank test and Friedman test were used from non-parametric tests. $p<0.05$ was considered statistically significant.

Results: The mean age of the patients was 54.82±11.65 years. Before MTX treatment, 27 (37.0%) patients had moderate DAS-28 scores and 46 (63.0%) patients had high disease activity. In the third months after MTX treatment, 44 (60.3%) patients were in remission or low disease activity, and 29 (39.7%) patients were moderate or high disease activity. In the sixth months after MTX treatment, 61 (83.6%) patients were in remission or low disease activity, and 12 (16.4%) patients were moderate or high disease activity (Table 1). The median DAS-28 score of the patients before MTX treatment was 5.51 (min-max: 3.49-7.77), the median score of the third months after treatment was 2.86 (min-max: 0.77-5.63) and the sixth months after treatment was 2.33 (min-max: 0.77-5.24). A significant improvement was observed in the DAS-28 score evaluated during the

treatment (p<0.001). When the patients were divided into two groups, seronegative and seropositive, DAS-28 scores were found to be significantly decreased after treatment in both groups.

Table 1. Disease activity rates before and after treatment.

Disease activity	Before MTX treatment (n, %)	MTX treatment 3rd month (n, %)	MTX treatment 6th month (n, %)
Remission	0	30 (%41.0)	48 (%65.8)
Low	0	14 (%19.3)	13 (%17.8)
Moderate	27 (%37.0)	26 (%35.6)	11 (%15.1)
High	46 (%63.0)	3 (%4.1)	1 (%1.3)
	73	73	73
Remission + Low	0	44 (%60.3)	61 (%83.6)
Moderate + High	73 (%100)	29 (%39.7)	12 (%16.4)
	73	73	73

Conclusion: Methotrexate is the first recommended conventional DMARD when diagnosed in patients with rheumatoid arthritis. However, clinical practice for monotherapy or combination use is quite heterogeneous. In this study, it was shown that the efficacy of MTX monotherapy was high in patients who were planned as the first conventional DMARD strategy, and the rate of patients who achieved the goal the sixth months increased.

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AB0474 REAL-WORLD SINGLE CENTER USE OF UPADACITINIB IN RHEUMATOID ARTHRITIS PATIENTS, INCLUDING THOSE REFRACTORY TO FIRST-GENERATION JAK INHIBITORS

Keywords: Rheumatoid arthritis, Targeted synthetic drugs, Real-world evidence

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Background: In practice, bDMARDs and subsequent first-generation JAK inhibitors (JAKi) have significantly improved the management of rheumatoid arthritis (RA), but there are still patients refractory or intolerant to multiple b/tsDMARDs. The fact that first-generation JAKi inhibit more than one JAK molecule has given rise to hopes that second-generation JAKi with enhanced kinase selectivity may maximize efficacy and enable a safer profile. Although a matched-adjusted indirect comparative study, differences in efficacy between some of the two JAKi drugs have been demonstrated, suggesting that second-generation JAKi may be effective for RA patients who are intolerant or have inadequate responses to first-generation JAKi.

Objectives: We evaluated the real-world course of upadacitinib (UPA), a second-generation JAKi, in a single-center cohort of RA patients, including refractory patients with resistance to first-generation JAK inhibitors.

Methods: All RA patients who started UPA between May 2021 and June 2022, including those who had previously received tofacitinib (TOF) and/or baricitinib (BAR), were eligible for the study. Kaplan-Meier survival rates were calculated based on ineffectiveness or intolerance as the reason for discontinuation. DAS28-ESR score, PRO (VAS for pain and stiffness), and patient satisfaction on a 7-point scale were recorded at baseline, 3 months, and 6 months. In addition, RF factor antibody titers before and after UPA administration, concomitant MTX and PSL doses, and UPA dose at 6 months were recorded. The above items were evaluated in subgroups of JAKi-non-use cases and the number of JAKi used in the past. In addition, reasons for discontinuation of administration were also investigated.

Results: UPA was administered to 122 patients, 85.2% of whom were female, age (S.D.) 69.7 (11.9) years, weight 52.5 (8.4) kg, duration of RA (S.D.) 15.8 (10.3) years, and 97.5% of whom were RF or anti-CCP antibody positive. A median of 2.5 bDMARDs had been administered, including 37 patients who received IL-6 inhibitors. 52 patients (1st JAKi group) did not use any JAKi, 51 patients (2nd JAKi group) used one type (15 TOF, 36 BAR), and 19 patients (3rd JAKi group) used two types. Survival rates at 6 months were 92.3%, 90.2%, and 94.7% (P=0.83) in each group, and none of the 82 patients who could be followed for more than 12 months discontinued between 6 and 12 months. The mean DAS28-ESR (S.D.) at baseline was 3.91 (0.78) overall, but significantly improved to 2.79 (0.82) at 6 months (P<0.05). 67.3%, 70.6% and 47.4% of patients in each group had low disease activity. The VAS for pain and stiffness improved significantly in the 1st and 2nd JAKi groups, including treatment satisfaction. 88% of patients had decreased RF factor antibody titer. 62.5% of patients received UPA less than 7.5 mg/day at 6 months, including those who received UPA every other day. The rate of concomitant use of PSL (<5 mg) remained unchanged at 10.7%, and the rate of MTX decreased from 27.7% to 7.1%, mainly in the 1st JAKi group. 4 patients developed herpes zoster within 6 months and UPA was resumed after a temporary suspension. 2 patients discontinued UPA due to inadequate efficacy and 8 due to adverse events. Adverse events requiring hospitalization were bacterial pneumonia, putaminal hemorrhage, and sudden death with suspected acute myocardial infarction.

Conclusion: UPA was effective in RA patients, including first-generation JAKi-resistant patients, with few cases of discontinuation due to inadequate efficacy. Although some Japanese patients taper off UPA due to their light weight, advanced age, or complications, more than 60% of patients maintained efficacy with UPA at 7.5 mg/day or less, suggesting that taper-off is feasible. After disease activity decreased, tapering or discontinuation of concomitant MTX was prioritized, but there were no cases of apparent flares, again confirming the efficacy of UPA alone. In addition to the long-term safety of UPA, head-to-head between JAKi and JAKi to bDMARDs should be considered in the future.

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AB0475 TRANSCRANIAL DIRECT CURRENT STIMULATION DECREASES CHRONIC PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS: A RANDOMIZED, CONTROLLED, DOUBLE-BLIND CLINICAL TRIAL

Keywords: Rheumatoid arthritis, Pain

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Background: Rheumatoid Arthritis (RA) patients often present chronic pain that may persist beyond therapeutic control of objective signs of inflammation [1] and may cause significant physical and psychological impairments. Complex mechanisms encompassing peripheral and central sensitization seem to be involved [2]. In fibromyalgia patients, Transcranial Direct Current Stimulation (tDCS) appears to be effective for decreasing chronic pain symptoms [3].

Objectives: To verify the effect of active tDCS on pain and clinical symptoms in RA patients.

Methods: This double-blind randomized pilot clinical trial recruited women aged between 18 and 70 years diagnosed with RA and stable (3 months) low inflammatory status (CRP < 10 mg/L, ESR < 20 mm/h, swollen joint count ≤ 1) and persistent pain (VAS-pain > 4cm), from the Rheumatology ambulatory clinic of Hospital de Clínicas de Porto Alegre/Brazil. The patients were randomized into two different groups: active tDCS (A-tDCS) and Sham (S-tDCS). The 20 sessions of tDCS (2mA) were applied at home daily, for 20 min, 5 days/week. Main outcome was pain by visual analogue scale (VAS cm) after 4 weeks. Additional evaluations: pressure pain threshold (PPT,Kg), disease activity (DAS28-CRP), physical function (HAQ-DI), fatigue (FACIT-F), central sensitisation (Central Sensitization Inventory - CSI), and safety. The Paired-sample t test, the Wilcoxon test, the T-tests for independent samples, the Mann-Whitney test and the Generalized estimating equations (GEE) were performed using a gamma model were performed (accepted at p ≤0.05).

Results: Twelve patients have completed this pilot study (A-tDCS, n=6 and S-tDCS, n=6). At baseline, there are no differences in clinical features between groups (Table 1). After the 4-week intervention, the time of intervention was associated with changes on VAS-pain (p=0.004). There was between groups a trend towards a statistically significant difference for the A-tDCS group (p=0.063). Both groups had improvements on HAQ-DI, FACIT-F and CSI. On the other hand, the CRP, DAS28-CRP and PPT did not change (p>0.05) in both groups (Table 1). All patients reported low intensity of itch as an adverse effect during the session of tDCS.

Table 1. Results at baseline and after 4 weeks of tDCS intervention within and between groups.

Variable	Baseline		After tDCS	
	A-tDCS(n=6)	S-tDCS(n=6)	A-tDCS(n=6)	S-tDCS(n=6)
Age (years), mean	54.3±11.1	57.3±9.1	-	-
Disease duration, median	8.0 (5.0-10.2)	11 (6.2-30.5)	-	-
CRP, median (mg/L)	3.5(2.0-10.0)	2.0(1.0-3.7)	3.0(1.7-7.0)	2.5(1.7-8.7)
DAS28-CRP, mean	2.9±1.0	2.3±0.5	2.5±0.9	2.2±0.4
HAQ-DI, mean	1.7±0.4	1.6±0.5	1.0±0.5*	1.1±0.6*
FACIT-F, mean	22.0±10.0	28.6±9.2	16.3±9.9*	13.3±11.1*
CSI, mean	50.6±8.2	63.7±10.5	29.6±14.4*	30.6±13.1*
PPT (Kg), median	2.2(2.0-2.9)	2.3(1.8-4.2)	2.6(2.8-2.8)	1.9(1.1-4.2)
VAS (cm), median	6.5(1.7-7.0)	6.0(1.7-8.7)	5.0(2.5-6.0)*	5.0(3.5-7.0)
Leflunomida, n (%)	2.0 (33,3)	2.0 (33,3)	-	-
MTX, n (%)	2.0 (33,3)	5.0 (83,3)	-	-
bDMARDS, n (%)	1.0 (16.7)	0.0 (0.0)	-	-

p, Difference value at baseline and after intervention with tDCS (within groups)(p≤0.05)*.

Conclusion: These preliminary findings revealed that daily treatment with tDCS compared to sham stimulation over 4 weeks may improve the chronic pain in RA patients, despite the placebo effect observed for physical function, fatigue, PPT and central sensitization. The intervention was well tolerated. Thus, tDCS appears to be a promising auxiliary tool in the treatment of patients with low-inflammation RA who have chronic pain, but larger and longer studies are needed to confirm this observation and optimize it.

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AB0476 AFTER JAK INHIBITOR FAILURE, 'SWITCHING' OR 'CYCLING'?

Keywords: Rheumatoid arthritis, Targeted synthetic drugs

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Background: The appearance of JAK inhibitors (JAKi) in the last few years has proved a great clinical application in rheumatic pathology and it has become an innovative and widely used therapeutic line. Nevertheless, the evidence of therapeutic alternatives in real life after the failure of a first JAK inhibitor is limited: a second JAKi or the change in therapeutic target.

Objectives: To analyze the treatment alternatives after JAKi failure in real life conditions.

Methods: Retrospective longitudinal observational study of patients that started JAKi treatment later discontinued between 2013 and 2022. Demographic and clinical variables were collected from the electronic medical record. 'Switching' and 'cycling' were analyzed depending on the prescribed therapy after the JAKi, classifying them in the following targets: anti-TNF, anti-IL6, anti-CTLA4, anti-IL12/23, anti-IL17, anti-IL23, another JAKi or other situations.

Results: Out of 265 JAKi prescriptions, 95 failures to JAKi treatment were included in this study. The most recurrent indication was Rheumatoid Arthritis (n=71), and the JAKi with higher failure rate was tofacitinib (n=61), with an average follow-up of 6 months (see Table 1). The most frequent cause of end of treatment was adverse reaction (34.74%), followed by secondary failure (28.42%) and primary failure (21.05%). After all the JAKi failures, cycling another JAKi was the most frequent therapeutical choice (n=25), followed by a switching to other families like anti-TNF (n=16) or anti-IL6 (n=15).

Conclusion: After a first JAKi failure, cycling another JAKi is the most recurrent alternative in our series, used most frequently in patients that present a secondary failure. Switching was the most frequent alternative used with patients who stopped receiving the treatment due to side effects.

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AB0477 EFFICACY AND SAFETY OF UPADACITINIB IN RHEUMATHOID ARTHRITIS: REAL-LIFE EXPERIENCE FROM A MULTICENTRIC ITALIAN STUDY

Keywords: Targeted synthetic drugs, Ultrasound, Real-world evidence

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Background: Upadacitinib (UPA), a JAK inhibitor engineered for a greater selectivity towards JAK1, has demonstrated a favourable benefit-to-risk profile in rheumatoid arthritis (RA) patients with an inadequate response to cDMARDs and biologic agents in randomized clinical trials. However, real-life data on its efficacy and safety are limited. We herein provide the first prospective multicentre experience on UPA efficacy and safety profile in RA in a real-life context, focusing on clinimetric and ultrasonographic (US) data.

Objectives: The primary aim of the study was to assess changes in clinimetric and US scores between different time point observations (baseline, 1 month, 3 months and 6 months). Secondary aims were to: (i) estimate the impact of biologic line of treatment and of concomitant therapies on response to therapy;

Table 1.

Patients n=95	JAKi n=25	Anti-TNF n=16	Anti-IL6 n=15	Anti-CTLA4 n=7	Anti-IL12/23 n=1	Anti-IL17 n=2	Anti-IL23 n=3	Others n=13	No n=5
Age when JAKi starts-years (sd)	51.56 (12.21)	52.81 (16.19)	55.07 (10.31)	62.57 (12.93)	69 (NA)	50.5 (7.78)	56.33 (4.16)	47.69 (16.6)	63.6 (16.46)
Female – n (%)	24 (96)	11 (68.75)	12 (80)	6 (85.71)	1 (100)	1 (50)	1 (33.33)	9 (69.23)	5 (100)
Diagnosis - n (%)	21 (84)	12 (75)	14 (93.33)	6 (86)	0 (0)	0 (0)	0 (0)	8(62)	3 (60)
Rheumatoid Arthritis	0 (0)	2 (12,5)	0 (0)	0 (0)	0 (0)	0 (0)	1 (33)	0 (0)	2 (40)
Axial spondyloarthritis	2 (8)	1(6.25)	1(6.67)	1 (14)	1(100)	2(100)	2(67)	2(15)	0(0)
Psoriatic arthritis	1 (4)	1(6.25)	0(0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (23)	0 (0)
Juvenile Idiopathic Arthritis	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Others									
Previous bDMARD - n (%)	3 (12.5)	4 (30.8)	5 (36)	2(33)	1 (100)	0 (0)	0 (0)	1 (7.7)	1 (20)
Failure to 1	4 (16)	1 (7.7)	5 (38)	2(33)	0 (0)	0 (0)	1 (33)	0 (0)	0 (0)
Failure to 2	9 (37.5)	5 (33.33)	3 (21)	1 (17)	0 (0)	2 (100)	2 (67)	10 (77)	2 (40)
Failure to 3									
Original JAKi -	17 (68)	12 (75)	8 (53)	6 (85.71)	1 (100)	2 (100)	1 (33.33)	6 (46.15)	2 (40)
n (%)	7 (28)	1 (6.25)	7 (47)	0 (0)	0 (0)	0 (0)	0 (0)	6 (46.15)	1 (20)
Tofacitinib	1 (4)	3 (18.75)	0 (0)	1 (14.29)	0 (0)	0 (0)	2 (66.67)	1 (7.69)	2 (40)
Baricitinib									
Upadacitinib									
Cause of failure - n (%)	3(12)	7 (43.75)	4 (26.67)	1 (14.29)	0 (0)	0 (0)	1 (33.33)	3 (23.07)	0 (0)
Primary	14 (56)	2 (11.76)	3 (20)	1 (14.29)	0 (0)	1 (50)	1 (33.33)	5 (38.46)	0 (0)
Secondary	6 (24)	5 (32.73)	6 (40)	4 (57.13)	1 (100)	1 (50)	1 (33.33)	4 (30.77)	3 (60)
Side effects	2 (8)	2 (11.76)	2 (13.33)	1 (14.29)	0 (0)	0 (0)	0 (0)	1 (7.7)	2 (40)
Others									

(ii) explore changes in laboratory parameters; (iii) find potential predictive factors associated with response to therapy.
Methods: Medical records of consecutive RA patients treated with UPA and referred to three Italian tertiary Centers were prospectively reviewed. Adult patients meeting ACR/EULAR classification criteria for RA were enrolled.
Results: Our real-life experience confirms the efficacy in terms of clinical and US improvement as well as displaying a good safety profile. The combination therapy with a conventional immunosuppressants predicts a significantly lower clinical and US improvement, likely reflecting a more severe and aggressive course worthy of ad-hoc and more in-depth investigation. An improvement in the SDAI and DAS28CRP was observed, already from the first month of therapy and has been maintained over time. In conclusion, these results demonstrated the short term efficacy of Upadacitinib 15 mg for up to 6 months and providing a prompt improvement of PROs. Even if further studies are needed to clarify those results, these novel findings may provide new insight for the management of UPA treatment in clinical practice.
Conclusion: Our real-life experience confirms the efficacy in terms of clinical and US improvement as well as displaying a good safety profile. The combination therapy with a conventional immunosuppressants predicts a significantly lower clinical and US improvement, likely reflecting a more severe and aggressive course worthy of ad-hoc and more in-depth investigation. An improvement in the SDAI and DAS-28CRP was observed, already from the first month of therapy and has been maintained over time. In conclusion, these results demonstrated the short term efficacy of Upadacitinib 15 mg for up to 6 months and providing a prompt improvement of PROs. Even if further studies are needed to clarify those results, these novel findings may provide new insight for the management of UPA treatment in clinical practice.

Table 1. Changes in clinimetric and ultrasonographic scores throughout the study period and significance levels (*p* values) for single comparisons between different observations in time.

Endpoint	Overall significance	T0 vs T1	T0 vs T3	T0 vs T6	T1 vs T3	T1 vs T6	T3 vs T6
Synovitis grade	**< 0.001**	0.804	0.090	**<0.001**	**< 0.001**	**< 0.001**	**< 0.001**
PD signal grading	**0.029**	0.914	0.320	**0.026**	**0.029**	**0.009**	0.066
Tenosinovitis grading	**0.012**	0.968	0.370	**0,031**	**0,018**	**0,009**	0,059
DAS28-CRP	**0.005**	**0.014**	**< 0.001**	**< 0.001**	0.220	**0.015**	**0.035**
SDAI index	**< 0.001**	**0.003**	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**

List of abbreviation: *DAS28-CRP* Disease Activity Score 28 – C-reactive protein, PD power Doppler, *SDAI* Simplified Clinical Activity Index, *T0* baseline, *T1* 1 month evaluation, *T3* 3 month evaluation, *T6* 6 month evaluation

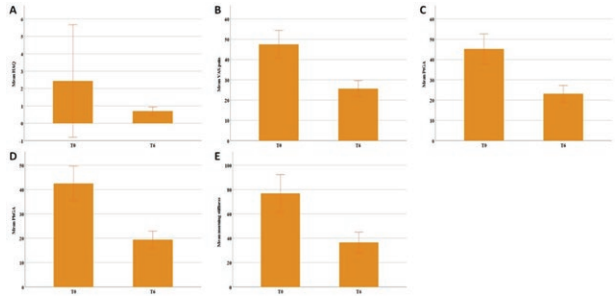


Figure 1.

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Disclosure of Interests: None Declared.
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AB0478

FRENCH REAL-LIFE DATA ON THE 18-MONTH EFFECTIVENESS OF TOFACITINIB ACCORDING TO CONCOMITANT USE OF CSDMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS: INTERIM RESULTS OF THE OBSERVATIONAL STUDY, DEFACTO

Keywords: Targeted synthetic drugs, Real-world evidence, Rheumatoid arthritis

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Background: Tofacitinib, an oral JAK inhibitor, is indicated for the treatment of adult patients with moderate to severe active rheumatoid arthritis (RA) for which we have no real-life effectiveness data in a French RA population.
Objectives: To describe tofacitinib effectiveness profile according to concomitant use of csDMARD in a French prospective observational study, DeFacTo.
Methods: DeFacTo, is an ongoing observational study with the primary objective of identifying predictive factors of Tofacitinib maintenance in real-life RA patients. The results described here are based on a descriptive interim analysis of its effectiveness at 18 months.
Results: Among 314 pts enrolled in the study, 301 (POP1) were included in this effectiveness analysis, including 274 (POP2) patients with follow-up ≥ 18 months on 03/15/2022 (date of analysis) with a median exposure duration of 538 [Q1; Q3: 381; 554] days. At baseline, among POP2: 168 (POP3) patients were treated with tofacitinib used concomitantly with at least one csDMARDs vs 106 (POP4) tofacitinib monotherapy. In POP3 vs POP4 respectively, 76.8% vs 84.9% were female, with a mean (± SD) age of 59.5 (10.8) vs 59.9 (12.1), median disease duration of 8.6 years [Q1;Q3: 3.2; 18.6] vs 11.1 [Q1;Q3: 5.3; 19.4)], 40.3% vs 52.4% patients had erosions, 80.5% vs 76.5% had FR+ and 77.7% vs 75.0% had ACPA+. Median CRP was 7.0 [Q1;Q3: 2.9; 18.0] vs 8.0 [Q1;Q3: 3.0; 18.1], and mean DAS28-4 CRP was 4.4 ±1.1 vs 4.7 ±1.0, in POP3 and POP4 respectively. Result showed a decrease in inflammatory markers, pain, and DAS28-CRP activity scores in both groups. At 18 months of follow-up, 24.4% and 24.5% of the pts achieved DAS28-CRP remission in POP 3 and POP 4 respectively (Table 1). Note that missing data and treatment discontinuation were considered as failures which resulted in an underestimation of LDA and remission at 18 months.

Table 1. Characteristics at inclusion and effectiveness at 18 months

	Baseline, n=274		At 18 month, n=274		Difference from baseline to M18	
Variables in LS mean ± SE or % of pts	Patients with at least one concomitant csDMARD treatment (N=168)	Patients without concomitant csDMARD treatment (N=106)	Patients with at least one concomitant csDMARD treatment (N=168)	Patients without concomitant csDMARD treatment (N=106)	Patients with at least one concomitant csDMARD treatment (N=168)	Patients without concomitant csDMARD treatment (N=106)
PtGA*	57.78 ± 1.67	61.43 ± 2.09	29.68 ± 2.97	35.40 ± 3.38	-28.10± 3.15	-26.03± 3.87
CRP* (mg/l)	15.25± 1.88	13.67± 1.45	5.16± 0.97	4.87± 0.82	-10.09 ± 2.00	-8.80 ± 1.52
DAS28-4 CRP*	4.38 ±0.09	4.68 ±0.10	2.49 ± 0.14	2.85 ± 0.13	-1.88 ± 0.15	-1.83 ± 0.16
ACR-EULAR boolean criteria†	3.0	0.9	12.5	14.2	9.5	13.3
LDA†, % pts	11.9	3.8	35.7	37.7	23.8	33.9
- DAS28 CRP ≤3,2	7.1	2.8	23.2	25.5	16.1	22.7
- DAS28 VS ≤3,2						
Remission†, % pts	5.4	2.8	24.4	24.5	19.0	21.7
- DAS28 CRP <2,6	3.6	1.9	16.1	12.3	12.5	10.4
- DAS28 VS <2,6						

* Missing data handled with mixed models for repeated measures ǂ Missing data and treatment discontinuations considered failures (122 patients with missing data, 39 treatment discontinuations).

Conclusion: This intermediate analysis from real-life study showed that tofacitinib in RA patients is effective with or without csDMARD.
Acknowledgements: This study was sponsored by Pfizer.
Disclosure of Interests: Cécile Gaujoux-Viala Speakers bureau: AbbVie; Amgen; Bristol-Myers Squibb; Celgene; Eli Lilly; Galapagos; Gilead Sciences, Inc.; Janssen; Medac; Merck-Serono; Mylan; Nordic Pharma; Novartis; Pfizer; Roche; Sandoz; Sanofi; and UCB, Consultant of: AbbVie; Amgen; Bristol-Myers Squibb; Celgene; Eli Lilly; Galapagos; Gilead Sciences, Inc.; Janssen; Medac; Merck-Serono; Mylan; Nordic Pharma; Novartis; Pfizer; Roche; Sandoz; Sanofi; and UCB, Andre BASCH Consultant of: Janssen, Novartis, Amgen, BMS, Abbvie, Lilly, Pfizer, MSD, UCB, Slim Lassoued: None declared, Fabienne COURY-LUCAS Consultant of: AbbVie, Bristol-Myers Squibb, Janssen, Lilly, MSD, Novartis and Pfizer, Grant/research support from: AbbVie, Biogen, Roche Chugai, Pfizer, and UCB, Meriem Kessouri Shareholder of: Pfizer, Employee of: Pfizer, Amine Saighi Shareholder of: Pfizer, Employee of: Pfizer, Yves Brault Shareholder of: Pfizer, Employee of: Pfizer, Pierre-Alexandre Squara Shareholder of: Pfizer, Employee of: Pfizer, Thierry Lequerre Consultant of: Abbvie, BMS, Boeringher, Lilly, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Roche – Chugai, Sanofi, UCB, Carine Salliot Consultant of: Biogen, Lilly, Novartis, Roche Chugai, Pfizer.
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Rheumatoid arthritis - non biologic treatment and small molecules

AB0479 **BARICITINIB AND UPADACITINIB AFFECT THE LEVELS OF BONE DESTRUCTION MARKERS AND BONE FORMATION INDICATORS IN PATIENTS WITH RHEUMATOID ARTHRITIS**

Keywords: Rheumatoid arthritis, Bone diseases, Disease-modifying drugs (DMARDs)

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Background: Janus kinase inhibitors (JAKis) baricitinib and upadacitinib inhibit the radiographic progression of joint damage in patients with rheumatoid arthritis (RA) [1-3]. Recent findings indicate that treatment with JAKi can lead to the repair of arthritic bone erosions [4]. However, although the immunomodulatory effects of JAKis have been extensively studied in inflammatory diseases, the effects of JAKis on bone metabolism in patients with RA are not fully understood.
Objectives: To investigate the effect of baricitinib and upadacitinib on the levels of bone destruction markers and bone formation indicators in the peripheral blood of patients with RA.
Methods: The study included 14 patients with RA (all women, aged 23–65 years, mean age 47.7 ± 12.4 years) with high disease activity at baseline (median DAS 28-ESR 5.625, range: 5.11–7.17); median ESR 11.50 mm/h (range 5.00–60.00 mm/h); median CRP 12.15 mg/ml (range 1.00–40.00 mg/ml). Peripheral blood plasma samples were collected from patients prior to JAKi treatment, and during therapy with baricitinib 4 mg once daily (n=9) or upadacitinib 15 mg once daily (n=5). Concentrations of C-telopeptide fragments of type I collagen (CTX-I), osteocalcin, Receptor Activator for Nuclear Factor κ B Ligand (RANKL), and osteoprotegerin (OPG) were measured in plasma by the enzyme-linked immunosorbent assays. Changes in the variables were assessed using paired Student t-test or Wilcoxon matched-pair signed rank test (depending on the type of data distribution). P-values <0,05 were considered significant.
Results: The median duration of treatment with JAKi was 12 months (range 7–18 months). Eleven (78.6%) patients were treated for more than 12 months. The effects of JAKis were analyzed in two-time intervals: after 5-8 months of therapy and after 12 months of therapy. The median DAS 28-ESR decreased to 2.83 (range 1.13–7.56, p=0,014), after 5-8 months of therapy, and to 2.53 (range 0.75–7.34, p=0.002) after 12 months of therapy. The concentration of bone turnover marker CTX-I decreased gradually during JAKi treatment from a median pre-treatment level of 247.1 ng/ml (range 50.0–1228.0 ng/ml) to 186.0 ng/ml (range 0.0–394.0 ng/ml) after 5-8 months of therapy, and 78.0 ng/ml (range 0.0–481.0; p=0.031) after 12 months of therapy. Conversely, treatment with JAKi resulted in a gradual increase in the median osteocalcin concentration from a pre-treatment level of 17.0 ng/ml (5.0–37.0 ng/ml) to 24.0 ng/ml (6–92 ng/ml) and 28.6 ng/ml (11.0–43.0 ng/ml) after 5-8 months and 12 months of therapy (p=0.027), respectively. In a subgroup of 6 patients (2 treated with upadacitinib and 4 treated with baricitinib), a decrease in RANKL/OPG concentration ratios were observed after 5-8 months or/and after 12 months of therapy (from pre-treatment median ratio of 0.23, range: 0.09–1.26 to 0.11, range: 0.00–0.87 after therapy; p=0.03). In 5 patients, the RANKL/OPG ratio did not change during treatment with baricitinib or upadacitinib.
Conclusion: The decrease in the concentration of CTX-I, a marker of bone destruction, with a simultaneous increase in the concentration of osteocalcin, a marker of bone formation, and a decrease (at least in a subgroup of patients) in the concentration of RANKL, a stimulator of bone resorption, in relation to its receptor-decoy OPG, suggests that treatment with baricitinib and upadacitinib may promote bone anabolic processes in patients with RA.
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AB0480 **IS TRADITIONAL CHINESE MEDICINE A GOOD OPTION IN METHOTREXATE-BASED COMBINATION THERAPIES IN RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND BAYESIAN NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS**

Keywords: Clinical Trials, Randomized control trial, Rheumatoid arthritis

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Background: Former findings suggested that MTX-based combination therapies show improved efficacy and safety compared to monotherapy [1]. Several studies [2] have been conducted analysis on MTX-based combination therapies, but there is a lack of systematic analysis involving MTX+TCM (Traditional Chinese medicine) therapies.
Objectives: To assess the effectiveness and adverse events of Methotrexate-based (MTX-based) combination therapies(especially MTX + TCM therapies) in rheumatoid arthritis (RA) treatment.
Methods: A comprehensive search of PubMed, Embase, the Cochrane Library, China National Knowledge Infrastructure (CNKI), the Database for Chinese Technical Periodicals and Wanfang data was done without language restriction. A systematic review and network meta-analysis included randomized controlled trials of MTX-based combination therapies and methotrexate monotherapy. The ability of different regimens to reduce rheumatoid factors and inflammatory indicators and the probability of adverse reactions were compared. This study has been registered with PROSPERO under the number CRD42022265799.
Results: A total of 37 studies, including 3119 patients, were eligible for inclusion. Meta-analysis results showed that methotrexate combined with other DMARDs or Traditional Chinese Medicine (TCM) could reduce serum Rheumatoid Factor (RF) and C-reactive protein (CRP) levels to some extent, but the therapies combined with TCM were more effective and had a lower rate of adverse effects. The results of RF reducing ability were ranked in ascending order: MTX-+LEF+TCM > MTX+SSZ+HCQ > MTX+LEF >MTX+TCM >MTX+HCQ >MTX. While the results of CRP reducing ability were ranked in ascending order: MTX+LEF+TCM>MTX+SSZ+HCQ>MTX+LEF>MTX+TCM>MTX+HCQ.
Conclusion: Overall, MTX-based combination therapies are an effective treatment, and the combination of TCM and MTX-based combination therapies is more effective and safer. For treating rheumatoid arthritis or patients with an inadequate response to MTX, MTX-based combination therapies remain an alternative, cost-effective option. To support and validate the potential of TCM and MTX-based combination therapies in treating RA, large-scale, high-quality RCTs should be conducted in the future to provide more accurate and complete data.
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Disclosure of Interests: None declared.

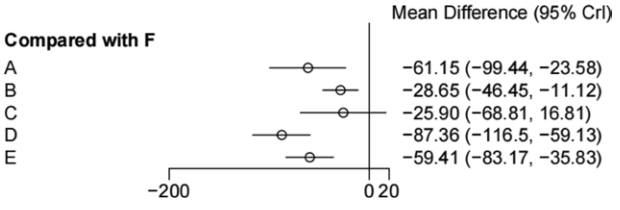


Figure 1. Forest plot of RF reducing ability (A, MTX+SSZ+HCQ; B,MTX+TCM; C,MTX-+HCQ; D,MTX+LEF+TCM; E,MTX+LEF; F,MTX)

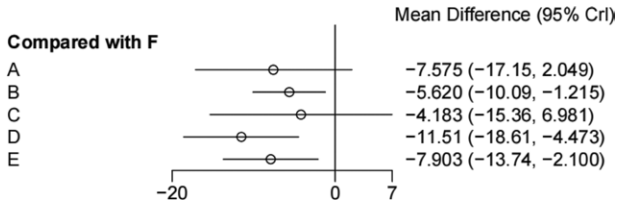


Figure 2. Forest plot of CRP reducing ability (A, MTX+SSZ+HCQ; B,MTX+TCM; C,MTX-+HCQ; D,MTX+LEF+TCM; E,MTX+LEF; F,MTX)

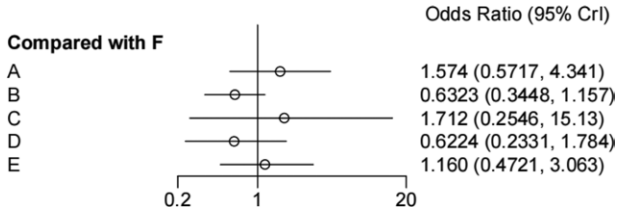


Figure 3. Forest plot of gastrointestinal adverse events (A, MTX+SSZ+HCQ; B,MTX-+TCM; C,MTX+HCQ; D,MTX+LEF+TCM; E,MTX+LEF; F,MTX)

Disclosure of Interests: None Declared.
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AB0481

UPADICITINIB EFFECTIVENESS IN RHEUMATOID ARTHRITIS: OBSERVATION FROM AN ITALIAN MULTI-CENTRIC COHORT

Keywords: Real-world evidence, Rheumatoid arthritis

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Background: Janus kinase (JAK) inhibitors have been approved for the treatment of Rheumatoid Arthitis (RA) and other systemic or organ-specific autoimmune diseases. Sustained remission or low disease activity are target treatments recomended by European League Against Rheumatism (EULAR) in RA patients [1]. Upadacitinib (UPA), a reversible, oral JAK inhibitor, has been engineered to have a greater selectivity for JAK1 vs JAK2, JAK3, and tyrosine kinase. In the Phase 3 SELECT clinical trial program, UPA has been shown to be effective and well tollerate in patients with RA [2]. However, data on the use of UPA in real-world clinical practice are limited.

Objectives: To evaluate UPA effectiveness in RA patients and to report the main reasons of suspension and the most relevant factor related to treatment persistence.

Methods: In 25 Italian rheumatological referral centers, all RA consecutive patients who received UPA were enrolled. Anamnestic data, treatment history and RA disease activity at baseline were recorded. The 6 and 12 months UPA retention rate was assessed with the Kaplan-Meier curve methods. The Cox analysis investigated the effect of age, sex, smoke habit, ACPA/RF presence, disease duration, DAS28-CRP, line of treatment, concomitant csDMARD treatment on UPA retention rate. A p-value < 0.05 was considered statistically significant.

Results: The one-hundred-eleven enrolled patients median age 57 (IQR 50-65 yrs); M:F 28:83; disease duration 78 (IQR 40-170 months). The median observation period was 6.1 (IQR 3.2-10.2) months. The observation lasted 812 patients-months. The majority of patients (54.0%) were in mono-therapy and received steroids (respectively 54.0% and 58.6%) (Table 1). The UPA retention rate at 6, 12 months was, respectively 90.4% and 74.7% (Figure 1). The main discontinuation reason was lack of efficacy (42% of interruptions), cancer onset and infections (both 11%). No thromboembolic events were reported. According to the Cox analysis, no one of the above mentioned parameters were associated to high risk of treatment interruption.

Table 1. Baseline characteristics UPA

Characteristics		Value
M:F		28:83
Age, median [IQR] yrs		58 [50-65]
Smokers, n (%) (**)	Yes	16 (16,5)
	Former	17 (17,5)
	No	64 (66,0)
Body Mass Index, median [IQR] kg/m^2 (*)		24,7 [22,4-27,7]
Disease Duration, median [IQR], months		78 [40-170]
RF positivity, n (%)		72 (64,9)
ACPA positivity, n (%)		68 (61,3)
SJC, median [IQR]		4 [3-8]
TJC, median [IQR]		8 [5-11]
ESR, median [IQR], mm/h		32 [20-53]
CRP, median [IQR], mg/dl		1,2 [0,5-3,3]
VAS Patient (0-100), median [IQR]		70 [50-80]
DAS28, median [IQR]		5,5 [4,9-5,9]
Line of treatment, [IQR]		3 [2-4]
Concomitant csDMARDs use, n (%)	MTX	41 (36,9)
	LFN	3 (2,7)
	SSZ	1 (0,9)
	HCQ	5 (4,5)
Concomitant steroids use, n (%)		65 (58,6)
Steroids dose (PDN-Eq), median, mg/die		5 [5-6]
Prior bDMARDs use, n (%)	TNFi	53 (47,7)
	IL6i	13 (11,7)
	IL1i	0
	CD20i	2 (1,8)
	CD80i	11 (9,9)
Prior tsDMARDs use, n (%)	Baricitinib	9 (8,1)
	Tofacitinib	2 (1,8)
Concomitant relevant disease, n (%)	Diabetes	12 (10,8)
	Hypercholesterolemia	23 (20,7)
	MACE	5 (4,5)
	Arterial Hypertension	34 (30,6)
	Cancer	4 (3,6)

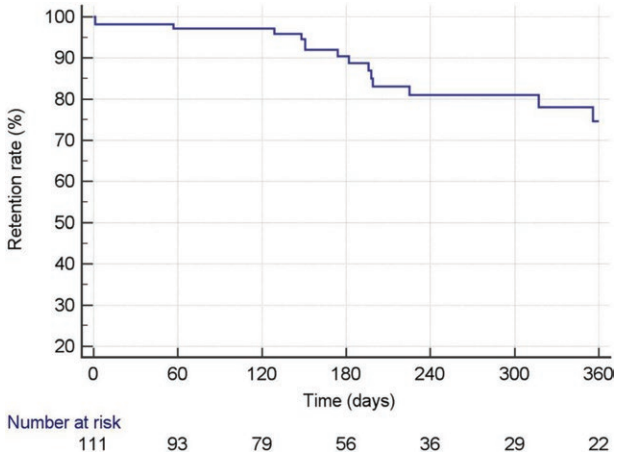


Figure 1.

Conclusion: UPA effectiveness appears to be confirmed. The safety profile of UPA 15 mg in real-world practice is consistent with data from Phase 3 SELECT trials, with no new safety signals.

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AB0482 CLINICAL SAFETY AND FEASIBILITY OF A NOVEL IMPLANTABLE NEUROIMMUNE MODULATION DEVICE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Randomized control trial, Non-pharmacological interventions

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Background: An urgent need exists for differentiated RA therapies that are safer and cost-effective to expand treatment approaches for non-responders to disease-modifying anti-rheumatic drugs (DMARDs). Electrical stimulation of the vagus nerve activates the inflammatory reflex and has been shown to inhibit the production and release of inflammatory cytokines and decrease clinical signs and symptoms in chronic inflammatory diseases, including rheumatoid arthritis [1].

Objectives: The RESET-RA Study (NCT04539964) was designed to determine the safety and efficacy of a novel neuroimmune modulation device for treating rheumatoid arthritis. Presented here are data on the safety of the surgical implantation and use of this device in the first 60 human subjects enrolled in the study.

Methods: The RESET-RA study is a randomized, double-blind, sham-controlled, multi-center, two-stage pivotal study to evaluate the safety and efficacy of a novel neuroimmune modulation device in patients with moderate-to-severe RA who are incomplete responders or are intolerant to one or more biologic or targeted synthetic DMARDs. The device system (*SetPoint Medical*, Valencia, CA) consists of 2 implanted components: a miniature, rechargeable, leadless pulse generator that is surgically implanted in the neck on the left vagus nerve and a silicon sleeve referred to as a positioning and orientation device (POD) that holds the generator in close approximation to the nerve; and two external components: a wireless charger and an iPad application for programming the pulse generation. All subjects were implanted with the study device. One to three weeks after the implant procedure, subjects were randomly assigned (1:1) to receive either active or sham stimulation (control). The safety of the surgical procedure, device, and device stimulation was blindly assessed after 12 weeks of stimulation therapy.

Results: All device implant procedures were completed with no intraoperative complications, infections, or surgical revisions. No unanticipated adverse events (AEs) were reported during the perioperative period and at the end of 12 weeks of follow-up. No study discontinuations were due to AEs, and no subjects died during the study. There were no serious AEs related to the device, stimulation, or explant procedures. There were two serious AEs related to the implant procedure: vocal cord paresis and prolonged hoarseness were reported in two subjects and are known risks of implanting a device on the vagus nerve. The vocal cord paresis resolved following vocal cord augmentation with injectable filler and speech therapy; the other SAE is ongoing and improving with speech therapy.

Conclusion: Initial results demonstrated that implantation and programming of the novel neuroimmune modulation device was safe, and the surgical procedure and device were well tolerated. Full results from this study, including the clinical efficacy, will be presented after the study is fully enrolled and data is analyzed to determine potential of neuroimmune modulation for treating rheumatoid arthritis.

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AB0483 FILGOTINIB IS EFFECTIVE AND SAFE IN RA PATIENTS AFTER FAILURE TO MULTIPLE BDMARDS AND TO OTHER JAK INHIBITORS: DATA FROM A MONOCENTRIC PERSPECTIVE COHORT STUDY

Keywords: Rheumatoid arthritis, Real-world evidence, Targeted synthetic drugs

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Background: The JAK-1 inhibitor filgotinib has been recently licensed for Rheumatoid Arthritis (RA), thus real-world evidence is lacking.

Objectives: Our aim was to assess safety and efficacy of filgotinib in a real-world setting.

Methods: In this prospective monocentric study, we included all patients with RA (ACR/EULAR 2010 criteria) regularly followed-up (every 2-6 months), undergoing therapy with filgotinib between 09/2021-01/2023. Disease activity was measured by DAS28-CRP, CDAI, and SDAI; TJC, SJC, patients (Pt) and physician (Ph) global assessment (0-10), the proportion of patients achieving DAS28-remission, concomitant csDMARDs and glucocorticoids (GC), comorbidities, and adverse events (AE) during filgotinib treatment were collected. Discontinuations for inefficacy or AE were recorded.

Results: We enrolled 58 RA patients: 33 (62%) on filgotinib monotherapy, 5 (9%) b/tsDMARD-naïve, 15 (26%) already treated with ≥ 2 classes of bDMARDs (multi-failure), 9 (17%) previously treated with JAK-inhibitors. Mean±SD follow-up was 9±5 months, with 30 (52%) and 8 (14%) patients having ≥6 and ≥12-month follow-up (fu). Among patients with ≥6 months of follow up there was a significant improvement in swollen and tender joint counts, PtGA, PhGA and composite disease activity measures (Table 1). Seventeen patients (57%) achieved DAS28-CRP remission. Compared to the general cohort's data, multi-failure patients and those failing a prior JAKi showed a similar DAS28-CRP response; in addition, multi-failure and filgotinib monotherapy patients reached comparable DAS28-CRP remission rates (Table 1). Among patients reaching 12 month fu, response rates were maintained (Table 1). During filgotinib therapy there was a trend towards a reduction in both GC users and mean GC dose (Table 1). Overall, 17 patients (29%) experienced ≥1 AE, of whom 2 (3%) were SAE (1 ILD progression, 1 death due to pneumonia). Six patients (10%) discontinued

Table 1. Characteristics of AR patients treated with filgotinib at baseline, t6, t12

Demographics and RA history			Baseline	6 months	p- value (m0 vs m6)	12 months	p-value (m6 vs m12)
N of patients	58	N of patients	30	30		8	
Age, y	60 ± 12	TJC, mean SD±	7 ± 6	4 ± 5	.20	1 ± 2	n.s.
Caucasian	47 (88%)	SJC mean ± SD	4 ± 4	2 ± 3	.31	1 ± 2	n.s.
Sex – female n(%)	45 (84%)	PGA mean ± SD	6 ± 3	4 ± 2	.003	3 ± 2	n.s.
BMI	23 ± 3	PhGA mean ± SD	6 ± 2	3 ± 2	<.001	2 ± 1	n.s.
RF+/ACPA+ n(%)	38 (71%)/32 (60%)	CDAI, mean±SD	22.5 ± 10.8	13.4 ± 11.1	.018	11.4 ± 8.5	n.s.
Symptoms duration, y	18 ± 11	SDAI, mean±SD	25 ± 11.9	16.2 ± 11.5	.073	9.7 ± 4.4	n.s.
Charlson	3.33 ± 1.7	DAS28-CRP, mean±SD	3.5 ± 1.3	2.6 ± 0.9	.003	2.2 ± 0.9	n.s.
Erosions n(%)	38 (71%)	Multifailure	3.9 ± 1.5	2 ± 0.9	<.001	n.c.	/
Extra-articular disease n(%)	16 (30%)	Previous JAK-i	4.2 ± 1.5	2.7 ± 0.9	.032	n.c.	/
Lung n(%)	7 (13%)	DAS28-CRP remission n(%)	5 (17%)	17 (57%)	.0017	4 (50%)	n.s
Rheumatoid nodules n(%)	4 (8%)	Multifailure	2 (7%)	8 (27%)	.030	n.c.	
Peripheral neuropathy n(%)	2 (4%)	Previous JAK-i	1 (12.5%)	5 (32.5%)	n.s.	n.c.	
Eye disease n(%)	4 (8%)	Monotherapy	2 (11%)	10 (55%)	.0116	n.c.	
Cardiovascular n(%)	1 (2%)	GC users n(%)	18 (60%)	14 (46%)	n.s.	3 (37%)	n.s.
		GC Dose * mean ± SD (mg of prednisone equivalent)	6.2 ± 3.6	4.7 ± 2.5	n.s.	2.5 ± 0.5	n.s.

n.c. not calculated; n.s. not significant

filgotinib: 1 (2%) due to primary inefficacy, 5 for AE/SAE (9%). No cardiovascular events were recorded.

Conclusion: Real-world treatment with filgotinib was associated with clinical improvement and low AE rate. Multi-failure and JAKi experienced patients benefited from filgotinib therapy. In this cohort of RA patients with low prevalence of comorbidities, no MACE or venous thrombotic events were observed.

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AB0484 DO JAK INHIBITORS IMPROVE PATIENT FATIGUE IN RHEUMATOID ARTHRITIS? RESULTS FROM A PATIENT SURVEY

Keywords: Inflammatory arthritides, Rheumatoid arthritis, bDMARD

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Background: Fatigue is a common symptom reported by up to three-quarters of patients with Rheumatoid Arthritis (RA) [1]. There is often no clear correlation between fatigue and RA disease activity [2]. There is a paucity of data on treatment of fatigue in patients with RA [2]. Fatigue remains one of the key unmet needs in patients with RA. Janus Kinase inhibitors (JAKi) are a group of targeted synthetic treatments used in RA with good clinical efficacy data in randomised controlled trials. There is clinical data to suggest that JAKi treatment can improve several patient-reported outcomes including fatigue [3].

Objectives: The aim was to establish whether fatigue was 'significantly improved' after at least 12 weeks of JAKi treatment. Only patients with a diagnosis of Rheumatoid Arthritis and features or a history of fatigue were included. A second question was incorporated to assess whether any improvement seen was noticed within the first 2 weeks of treatment.

Methods: A simple clinic-based patient survey was undertaken in patients with RA on a JAKi treatment. The first 20 patients with RA and fatigue are included in this sample. The following binary question(s) were asked: 1)Has your fatigue 'significantly improved' on JAKi treatment? 2)If so, was the improvement seen within 2 weeks of starting JAKi treatment? All patients had been on JAKi treatment for at least 12 weeks. The questions were asked prospectively to patients whilst being reviewed for their routine rheumatology outpatient clinic appointments.

Results: 13 out of 20 (65%) patients said that their fatigue had 'significantly improved' on JAKi treatment. 7 out of these 13 (54%) patients said that the improvement occurred within 2 weeks of starting JAKi treatment. Out of the 20 patients included in this sample, 11 were on Baricitinib, 5 on Upadacitinib and 4 on Filgotinib. No patients in in this sample were on Tofacitinib (Tofacitinib was not excluded by design). The majority of the patients included in this survey had been on prior biological treatment(s) or targeted synthetic disease modifying treatment. Most of the patients had one or more co-morbidities and over half of the patients were taking concomitant disease-modifying treatments for their RA. It is important to note that factors around fatigue in RA, such as; comorbidities (including chronic pain and fibromyalgia), sleep pattern, and features of low mood were beyond the scope of the survey and thus not asked about.

Conclusion: Whilst acknowledging the modest sample size and simplicity of our patient survey, our data suggests some benefit of JAKi treatment on fatigue in patients with RA. The benefits seen are broadly in keeping with what is seen in our wider local clinical practice. Our survey suggests that the improvement in fatigue can occur rapidly, with the majority of patients noting improvement within just 2 weeks. More detailed (including qualitative) data would be useful to support these initial findings from this patient survey and explore the role of JAKi treatment on fatigue in patients with RA.

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AB0485 SAFETY ANALYSIS OF JAKINIBS IN REAL CLINICAL PRACTICE IN A COHORT OF 116 PATIENTS

Keywords: Safety, Disease-modifying drugs (DMARDs), Rheumatoid arthritis

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Background: Janus kinase inhibitors (JAKinibs) have demonstrated efficacy in the treatment of rheumatoid arthritis (RA) and spondyloarthritis (SpA), although their safety profile continues to be analysed due to the possible increase in adverse events (AEs) in relation to anti-TNFs (mild and severe infections, haematological alterations, thromboembolism, increase in neoplasms).

Objectives: To evaluate in real clinical practice the AEs of JAKinibs in a cohort of patients with RA and SpA. In addition, adherence and reasons for discontinuation (1st or 2nd failure, AE) are analysed.

Methods: Observational study of 116 patients diagnosed with RA or SpA who received treatment with JAKinibis (tofacitinib, baricitinib, upadacitinib) after failure of treatment with different classical synthetic (FAMEsc) or biological (FAMEb) disease-modifying drugs. The following data were analysed: demographic characteristics of the patients, years of disease progression, 1st or 2nd failures and AE.

Results: Mean age was 52 years, with Baricitinib being older (60 years -SD 13.6), higher prevalence of females in all groups, and a disease progression time of about 10 years. Mean number of FAMEsc was 1.6 and mean number of FAMEb was 2,3 to Tofacitinib(Tofa), 2,76 to Baricitinib(Bari) and 4,4 to Upadacitinib(Upa). 71 (63%) patients had active corticosteroid therapy. The median treatment time with Tofa was 8.8 months, Bari 9.5 and Upa 2.4 months. Most frequent AEs with Tofa were urinary tract infections(UTI) (11.9%, 7 cases) and headaches (8.47%, 5 cases). There were 3 cases of herpes zoster (5.1%), one of which was recurrent, and 2 cases respectively of tachycardia and gastrointestinal intolerance (3.4%). With Baricitnib, 2(5%) cases of UTI and 2(5%) of influenza A were reported. Most

frequent AEs related to Upadacitinb are gastrointestinal intolerance, labialis and facial herpes, anterior uveitis and recurrent UTI, with 1 case for each adverse event. There were 4 success with Baricitinib treatment: 2 due to severe COVID, 1 influenza A and 1 due to stroke. 17 patients had 1st failure to Tofa(28.81%), 8 to Bari20.0%) and 3 to Upa(18.75%); 7(11.86%) and 2(5%) patients had 2nd failure to Tofa and Bari respectively, no with Upa. Mean CRP to Tofa-SD 18.9-was 17.19, 20-SD 22.7- to Bari and 24.2-SD 27.40- to Upa. Mean ESR-SD 15.3- was 25.4, -SD 26.4 and 44.3 -SD 32-, respectively. At 6 months, 36(62%) were continuing on Tofa, 22(56%) on Bari and 4(27%) on Upa. At 12 months, 27(46.6%) were still on Tofa and 12 on Bari(30.8%) and no patients were on upa.

Table 1.

	Tofa	Bari	Upa
Mean age	49	60	47
Male	19%	18%	20%
Female	81%	82%	80%
Time course of disease(years)	8	11	11
Permanence 6 months	62%	56%	27%
Permanence 12 months	46,6%	31%	0%
Patients with corticotherapy	62%	64%	60%
Previous biological drugs	2,3 SD 2	2,8 SD 2,3	4,4 SD 2,9
Patients who discontinued the drug	62%	59%	33%
Mean CRP at the end of treatment	17	20	24
Mean end-of-treatment ESR	25	26	44
Repeated AEs	UTI(7) Headache(5) Shingles(3) Nephritic colic(2) Gastrointestinal intolerance(2) Tachycardia(2)	UTI(4) Headache(2)	
Serious AEs	Shingles (3)	Varicella encephalopathy(1) Stroke(1) Shingles (1)	
1st failure	28,8%	20%	18,7%
2nd failure	11,9%	5%	0%
Success		SARS-Cov2(2) Influenza(1) Stroke(1)	

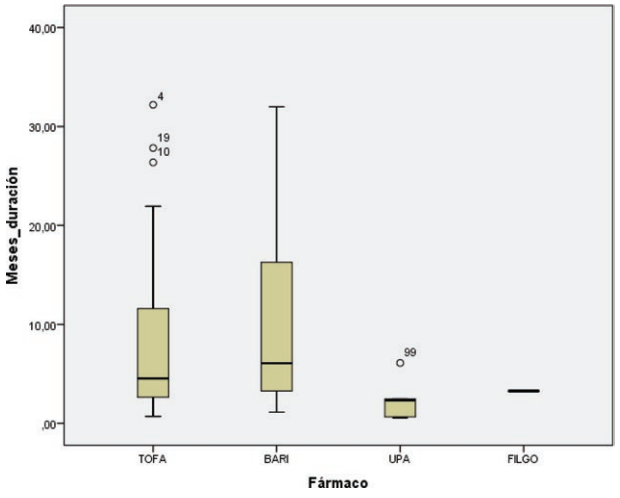


Figure 1. *Months stay pharmaco*

Conclusion: Most frequent adverse events with JAKinibs are mild infections, except gastrointestinal complaints with upadacitinib. Serious adverse events, including 3 deaths from viral infections, were observed, mostly in patients over 65 years. Most frequent cause of discontinuation was treatment failure. We believe that further observational studies are needed to stratify and profile the risk of infection with JAKinibs.

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AB0486 LIVER FIBROSIS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH METHOTREXATE: HYPOALBUMINEMIA, THE BIOLOGICAL PITFALL

Keywords: Rheumatoid arthritis

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Background: The relationship between hepatic fibrosis and cumulative doses of methotrexate (MTX) in rheumatoid arthritis (RA) patients is an emerging discussion. Hypoalbuminemia is known to be a potential risk factor for toxicity by methotrexate, mainly hematological toxicity and myelosuppression.

Objectives: The aim of our study was to investigate the biological associated factors with liver fibrosis in RA patients treated with MTX.

Methods: It was a cross-sectional study over nine months [April-December 2021], including RA patients under MTX, recruited from the Rheumatology department of Military Hospital. Liver stiffness was assessed by Fibroscan. Fibrosis and significant liver fibrosis were defined as liver stiffness higher than 6 and 8kPa, respectively. Liver enzymes (AST and ALT), alkaline phosphatase (ALP) and albuminemia were measured. Statistical analyses were performed using SPSS.

Results: Sixty-eight patients were included. The mean age was 51.60+11.82 years. The male-to-female ratio was 0.45. The mean disease duration was 8.29 + 6.48 years. The mean weekly intake of methotrexate was 13.76+3.91mg. The mean cumulative dose was 3508.87+3390.48 mg. The mean values of albuminemia were: 35.39 + 5.18 g/L [16.20 – 43.40]; AST 20.50 + 8.32 IU [11-52]; ALT 19.52 + 9.42 IU [5 -46] and ALP: 82.95 + 38.82 IU [10-240] and were all in the normal range. Four patients (6%) had elevated AST and ALP in 4 (6%) cases. Hypoalbuminemia was noted in 34% (n=23) of the cases. Mean liver stiffness was 4.50 + 1.53kPa. Nine patients had fibrosis, and 4 had significant fibrosis. On the univariate study, we found that hypoalbuminemia was associated with liver stiffness (OR=4.941,$CI_{95\%}$[1.107–22.057],p=0.034), along with increased ALP (OR=5.002, IC95% [1.086–67.252], p=0.025). We did not find correlation between and liver stiffness and albuminemia (r: -0.132, p=0.665), liver enzymes: AST (r: 0.036, p= 0.335) ALT (0.086, p= 0.476), nor ALP (r:0.111, p= 0.560).

Conclusion: Hypoalbuminemia leads to an increase in unbound MTX. It is this fraction that contribute to the development of liver damage. Along with the biological liver function, a particular attention is then needed to serum albumin when treating RA patients with MTX.

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Disclosure of Interests: None Declared.

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AB0487 EVALUATION OF EFFICACY OF PEFICITINIB FOR RHEUMATOID ARTHRITIS: A MULTICENTER, RETROSPECTIVE STUDY IN JAPAN

Keywords: Safety, Targeted synthetic drugs, Rheumatoid arthritis

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Background: Peficitinib (PEF) is the third Janus-kinase inhibitor (JAKi) approved for rheumatoid arthritis (RA) in Japan. Although PEF has the characteristic action of inhibiting all JAK subtypes, mainly JAK3, in vitro [1,2], there is slightly less variety of clinical studies showing the efficacy of PEF for RA compared with other JAKi; it is necessary to verify the clinical efficacy and safety [3,4].

Objectives: To examine the efficacy and safety of PEF for RA and explore the predictive factors related to the discontinuation due to the inadequately effective.

Methods: Patients who received PEF for RA at Yokohama Minami Kyosai Hospital and Saiseikai Yokohamashi Nanbu Hospital from July 2019 to December 2022 were included in the study. Patient background, clinical parameters, administration period of PEF, reason for discontinuation of PEF were collected retrospectively from the electronic medical records. All analyses were performed using SPSS. The log-rank test was used to compare continuation rates, and binomial

logistic analysis was used to explore predictive factors related to the discontinuation of PEF due to the inadequately effective.

Results: Fifty-seven patients were included in the study. The mean age at PEF initiation and DAS28-ESR were 75.6 ± 15.3 years old and 4.9 ± 1.3, respectively, and DAS28-ESR was significantly improved by 3.1 ± 1.1 at six months after ($p < 0.005$). The 1-year continuation rate of PEF among all patients was 42.8 %, and the rate among patients who had not previously used biologics and JAKi (NAÏVE) was significantly higher than among those who had previously used them (EXPERIENCE) (Figure 1). Univariate analysis of factors associated with discontinuation of PEF due to inadequate response identified the following factors: younger age at PEF initiation, seropositivity for anti-CCP antibodies (ACPA), and EXPERIENCE (Table 1). Of these factors, multivariate analysis showed significant differences in age at PEF initiation and ACPA seropositivity (Table 1), but no significant differences in persistence rates were found between patients with and without ACPA in sera in this analysis population (1-year continuation rate: 42.9% vs. 76.9%, $p = 0.081$). There were several limitations in this study as follows; the race of the patients was Japanese only, the study was retrospective, validation by a multiracial prospective study would have been desirable, and the small number of cases may have resulted in the imprecision of statistically significant differences, and further accumulation of cases is desirable.

Conclusion: PEF demonstrated certain effects on the elderly RA population in real-world clinical practice in Japan. This study suggests that patient characteristics that could be expected to be effective, being particularly elderly and ACPA-negative, were suggested, but in addition, patients who had not previously used biologics and JAKi were shown to have a higher continuation rate.

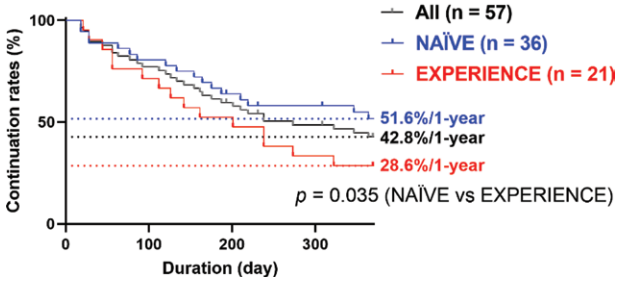
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Table 1. Uni and Multivariate analyses about predictive factors of discontinuation due to ineffectiveness of PEF.

	Univariable			Multivariable		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Female	0.505	0.10-2.45	0.397			
Age at PEF initiation	0.900	0.83-0.98	0.013	0.893	0.82-0.98	0.012
Age at onset	0.956	0.91-1.00	0.065			
BMI	0.995	0.82-1.20	0.959			
ACPA positive	4.722	1.07-20.89	0.041	5.884	1.07-32.33	0.041
RF positive	1.200	0.30-4.74	0.795			
EXPERIENCE	4.533	1.21-16.96	0.025			
PSL use	1.641	0.45-5.94	0.451			
MTX use	1.071	0.30-3.84	0.916			
DAS28-ESR	1.469	0.54-3.30	0.353			

Figure 1. Continuation rates of PEF



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AB0488 COMPARISON OF TWO METHOTREXATE INITIATION STRATEGIES IN RHEUMATOID ARTHRITIS IN CURRENT PRACTICE

Keywords: Treat to target, Disease-modifying drugs (DMARDs), Rheumatoid arthritis

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Objectives: To compare the efficacy and tolerance at 3 and 6 months of two methotrexate (MTX) initiation strategies in rheumatoid arthritis (RA).

Methods: Retrospective, monocentric, cross-sectional study including patients with RA who initiated MTX as first-line therapy during the last 2 years according to one of the following 2 strategies: a "classic" strategy defined by an initiation of oral MTX a dose of 10-15 mg/week or an "aggressive" strategy, defined by an initiation of subcutaneous (SC) MTX at a dose of 15 mg/week SC or >15 mg/week either orally or SC. Each strategy allowed the possibility to increase the doses and/or switch to the SC route at 3 months. Efficacy was assessed at 3 and 6 months using the DAS28-CRP. The tolerance of each strategy was also assessed at month 3 and 6.

Results: We included 101 patients (85 women) with a mean age of 55±12 years and disease duration of 5±6 months. The frequency of rheumatoid factors, anti-CCP antibodies and erosions was 83%, 81% and 38% respectively. 61 patients initiated MTX according to the "classic" strategy, with an increase of dose and/or a switch to the SC route at 3 months for 31 patients, and 40 patients started treatment according to the "aggressive" strategy, with an increase of dose and/or switch to the SC route at 3 months for 14 patients. There was no difference between these 2 groups in terms of age, gender, disease duration, antibody status, frequency of bone erosions, body mass index, comorbidities and disease activity at baseline. Efficacy at 3 months was significantly higher with the "aggressive" strategy (reduction of the DAS28-CRP from 4.34±0.91 to 2.39±0.75, mean difference of 1.95±1.21, p<0.001) compared to the "classic" strategy (reduction of the DAS28-CRP from 4.09±0.62 to 2.88±0.73, mean difference of 1.21±0.90, p=0.12) (**Figure 1**). The improvement of tender/swollen joint counts, patient global assessment and CRP levels was also significantly more important at 3 months with the "aggressive" strategy (**Table 1**). At 6 months, although the DAS28-CRP was similar in the 2 groups (**Figure 1**), less patients from the "aggressive" strategy subgroup required an escalation to a targeted biologic/synthetic therapy compared to the "classic" strategy (12/40, 30% vs. 29/61, 48%, p=0.073). The frequency of digestive side effects at 3 months was significantly lower in the "aggressive" strategy (3/40, 7,5% vs. 16/61, 26%, p=0.021). The frequency of hepatic cytolysis at 3 month was higher in the aggressive strategy (4/40, 10% vs. 1/61, 1,6%, p=0.057). The frequency of asthenia at 3 months was similar in both groups (7/4, 18% vs. 6/61, 10%, p=0.25). Only one infection was observed in the "classic" strategy and no hematological side effect was recorded. At 6 months, the cumulative incidence of side effects was 23% with the "aggressive" strategy compared to 46% with the "classic" strategy (p=0.015). Only one treatment discontinuation was noted in the "aggressive" subgroup vs. 9 in the "classic" subgroup (p=0.042).

Conclusion: This study suggests that it is possible to use a more aggressive initiation strategy of MTX in RA in routine clinical practice. This strategy allows to obtain an earlier clinical response and it is associated with a better tolerance than the classic strategy. These results need to be confirmed in prospective studies.

Table 1. Evaluation of efficacy parameter at 3 months according to the methotrexate initiation strategy

	"Classic" strategy (n=61)	"Aggressive" strategy (n=40)	p-value
Variation of tender joint count	-2.6±3.4	-4.4±4.9	0.032
Variation of swollen joint count	-2.0±5	-4.7±4.0	0.005
Variation of PGA-VAS	-24±25	-40±35	0.009
Variation of CRP (mg/L)	-1.8±13	-15±20	<0.001

PGA-VAS: patient Global Assessment - Visual Analogic Scale

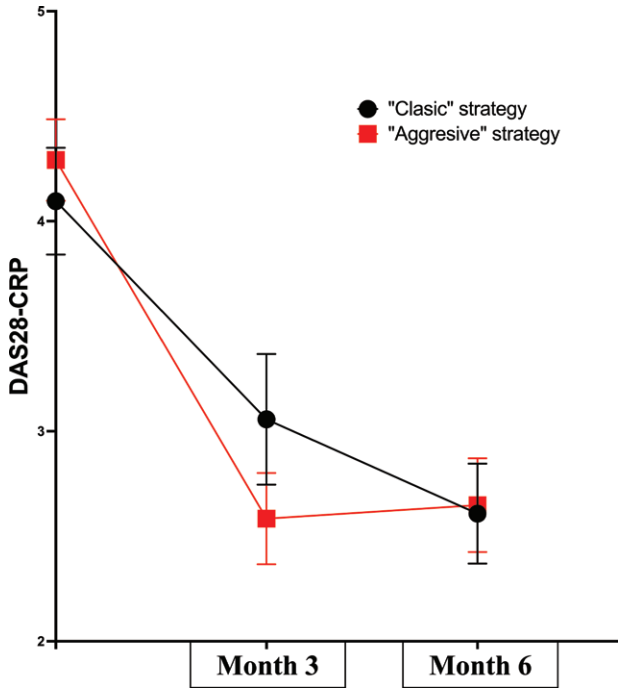


Figure 1. Evolution at 3 and 6 months of DAS28-CRP index according to the methotrexate initiation strategy

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AB0489

MAJOR ADVERSE CARDIOVASCULAR EVENTS AND MALIGNANCY POST JAK INHIBITORS INITIATION, A 4-YEAR EXPERIENCE FROM QATAR POPULATION

Keywords: Malignancy, Targeted synthetic drugs, Cardiovascular disease

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Background: In contrast to ORAL Surveillance data, reports from real world data did not show difference in rates of major adverse cardiovascular events (MACE) and malignancy between tofacitinib and biologic disease modifying anti-rheumatic drugs (b-DMARDs) [1-3].
Objectives: Investigate the rate of MACE and malignancy post janus kinase inhibitors (JAK-i) initiation in Qatar population.
Methods: All JAK-i prescriptions were captured electronically from the database of the pharmacy of Hamad Medical Corporation (HMC) from January 2018 to November 2022. Patients with non-dispensed prescriptions were excluded from the analysis. Electronic medical records of patients who received any class of JAK-i were reviewed retrospectively to identify demographic and clinical characteristics, starting and stopping date of JAK-i, MACE and malignancy events post JAK-i initiation.
Results: 219 JAK-i course therapies (tofacitinib 193, upadacitinib 14 and baricitinib 12) were identified from the database of the pharmacy of HMC. Six patients were excluded from the analysis as they were prescribed with JAK-i but their prescriptions were not dispensed. Five patients received two classes of JAK-i due to treatment failure. Mean (standard deviation [SD]) time of JAK-i exposure was 25 (17) months. A total of 208 patients included in the analysis with mean (SD) age at JAK-i initiation was 45.9 (14) years. Females were 72% of the cohort. JAK-i was prescribed for the following indications: rheumatoid arthritis 129 (60%), psoriatic arthritis 28 (13.1%), alopecia 29 (13.6%), spondyloarthropathy (SPA) 16 (7.5%), inflammatory bowel disease (IBD) 8 (3.8%), other rheumatic diseases 5 (2.3%). Two patients were having IBD with peripheral and axial SPA involvement. In patients with rheumatic diseases, JAK-i was received in 102 (55%) b-DMARDs naïve patients, post one b-DMARDs in 38 (20%) and post ≥ 2 in 46 (25%) patients. The comorbidity profile (hypertension, dyslipidemia, diabetes mellitus, and coronary artery disease) was 27%,25%, 23%, and 5.6%, respectively. New cancer diagnosis (follicular thyroid) was confirmed in one patient post tofacitinib and one patient developed lymphoma relapse after tofacitinib initiation. One ischemic cerebrovascular accident (CVA) identified post tofacitinib initiation. This patient was in atrial fibrillation when CVA occurred. No venous thromboembolism events reported from this cohort.
Conclusion: MACE and malignancy rates are very low in JAK-i users in Qatar population. Comparator group is needed for further evaluation the association of the use of JAK-i and risk of MACE and malignancy.
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AB0490

PREVALENCE OF RISK FACTORS FOR CARDIOVASCULAR EVENTS, MALIGNANCY OR THROMBOEMBOLIC EVENTS IN RHEUMATOID ARTHRITIS UNDER JAK INHIBITORS IN A REAL-LIFE MONOCENTRIC COHORT

Keywords: Comorbidities, Real-world evidence, Safety

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Background: Rheumatoid arthritis (RA) is an inflammatory, autoimmune disease, characterized by joint inflammation that can lead to irreversible joint damage and significant disability. The immunomodulatory therapies have dramatically changed the patient management, and the introduction of Janus kinase inhibitors (JAKi) leads the way to an oral, efficacious treatment for RA. Among JAKi, tofacitinib and baricitinib are considered as pan-JAKi (pJAKi) while upadacitinib and filgotinib as selective JAKi (sJAKi) drugs. However, recent safety issue has been highlighted, and the 2022 update of the EULAR recommendations for the management of RA suggests to consider the use of a JAKi only after risk assessment [1].
Objectives: This study aims to describe a monocentric experience of JAKi treatment in RA patients in a real-life setting, focusing on the prevalence of emerging risk factors.
Methods: Patients diagnosed with RA according to 2010 ACR/EULAR criteria and treated in a routine clinical setting with JAKi were retrospectively recruited from our rheumatologic clinic from May 2017 to August 2022. We evaluated the risk assessment according to the 2022 update of the recommendation, as reported below, to describe a real-life experience in the use of JAKi. In details we evaluated: age (over 65 years), smoking status, cardiovascular risk factors (such as diabetes, obesity, hypertension), risk factors for malignancy (current or previous history of malignancy other than successfully treated non-melanoma skin cancer), risk factors for thromboembolic events (history of myocardial infarction or heart failure, cancer, inherited blood clotting disorders or a history of blood clots, as well as patients taking combined hormonal contraceptives or hormone replacement therapy, undergoing major surgery or immobile).
Results: 205 RA patients treated with JAKi were included in our study. 133 underwent pJAK treatment, and 77 underwent sJAK treatment. Overall, 167 JAKi treatments were started in female patients. 128 were positive for rheumatoid factor, and 102 for anti–citrullinated protein antibody. 96/205 JAKi treatments were started in patients over 65 (46,8%), 45 were smokers (22%), 76 presented

cardiovascular risk factors (37%), 20 showed risk for malignancy (9,8%) and 21 for risk factors for thromboembolic events (10,2%). More details are reported in Table 1. At least 2 risk factors were reported in 30,7% of the population, and 11,7% presented at least 3 risk factors.

Conclusion: This study highlights the relative high prevalence of risk factors in a real-life population of RA patients treated with JAKi. The clinical effectiveness of JAKi has already been assessed by clinical trial and real-life experience, whereas the safety issue still remains to be further explored. Further studies are needed to define the RA sub-populations at highest risk for safety, and those patients who could benefit from an early JAKi treatment.

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Table 1.

	pJAKi (n=133)	sJAKi (n=72)
Age over 65 years, n (%)	65 (48,8%)	31 (43%)
Current smoking, n (%)	38 (28,6%)	7 (9,7%)
Major cardiovascular disease, n (%)	47 (35,3%)	29 (40,3%)
Previous malignancy, n (%)	16 (12%)	4 (5,5%)
Previous thromboembolic event, thrombophilia, n (%)	12 (9%)	9 (12,5%)

Acknowledgements: NIL.

Disclosure of Interests: Ivan Giovannini Speakers bureau: not relevant for this type of study, Roberto Agarinis: None declared, Sofia Cacioppo: None declared, Stefania Sacco: None declared, Ginevra De Marchi: None declared, EMMA DI POI: None declared, Alen Zabotti Speakers bureau: not relevant for this type of study, Luca Quartuccio Speakers bureau: not relevant for this type of study, Salvatore De Vita Speakers bureau: not relevant for this type of study.

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AB0491 COMPARATIVE STUDY ON THE SHORT-TERM EFFICACY AND OUTCOME OF JANUS KINASE INHIBITORS: A SINGLE-CENTER RETROSPECTIVE OBSERVATIONAL STUDY

Keywords: Rheumatoid arthritis, Targeted synthetic drugs, Safety

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Background: In recent years the use of Janus Kinase Inhibitors (JAK-Is) in rheumatoid arthritis (RA) has entered daily practice.In vitro studies they have shown a different selectivity [1], which however has not yet been confirmed in real life studies. Furthermore, considering recent developments, an in-depth study regarding the global safety of these drugs is needed.

Objectives: To address potential differences in the safety of Janus kinase inhibitors and short-term efficacy on disease activity we characterized their safety profile in RA patient population.

Methods: Single center retrospective observational study. The sample consisted of 68 patients receiving any of the following JAK-is: Tofacitinib, Upadacitinib, Filgotinib, Baricitinib, with a mean of 19.3 months of therapy and a diagnosis of RA according to the ACR/EULAR 2010 criteria. We collected and recorded the clinical features; any infections or adverse reactions during therapy; clinimetry at time 0 and at 6 months. For the statistical analysis, the $\chi 2$ (chi-square) test was used to evaluate whether there were statistical differences with respect to categorical variables, Anova one-way to evaluate any statistical difference with respect to continuous variables; mixed effects model and paired t-test for clinimetry comparison.

Results: We found no statistically significant differences between JAK-Is in the following outcomes: symptomatic Covid, p=0.388, new malignancies p=0.348, cardiovascular events p=0.788, thrombocytosis p=0.681, neutropenia p=0.962, lymphopenia p=0.935, anemia p=0.227, need to use glucocorticoids p=0.13, need to use Dmards p= 0.217, permanent discontinuation of therapy = 0.353. In our sample we had only development of 2 cardiovascular events, 1 DVT and a new diagnosis of cancer. Anova one-way showed no difference in the number zoster episodes (p=0.587), or other serious infections (p=0.193). The paired t-test showed that there was a class effect on the reduction of activity indices already after 6 months of therapy (DAS 28 pcr p=0.017, SDAI p=0.054, CDAI p=0.021). However, the mixed effects model showed that there was no molecule more effective in reducing disease activity considering the outcomes at 6 months (DAS 28 pcr p=0.445, SDAI p=0.639, CDAI p=0.467).

Table 1. Correlation with JAK-Is and outcomes.

	Number of events	Correlation with JAK-Is (p value)
Symptomatic covid	19	0.388
New malignancies	1	0.348
Cardiovascular events	2	0.788
DVT	1	0.348
Thrombocytosis	3	0.681
Neutropenia	4	0.962
Lymphopenia	1	0.935
Anemia	20	0.227
Need to use glucocorticoids	29	0.130
Dmard	8	0.217
Permanent discontinuation of therapy	35	0.353
Total number of zoster episodes	45	0.587
Total number of serious infections	60	0.193

Conclusion: The originality of our study was to compare the four different molecules in a real-life study. We prove that JAK inhibition is effective in a real-world population of RA patients. The lack of diversity between JAK-Is in efficacy outcomes, adverse reactions and infections could be explained by considering that their selectivity has only been demonstrated in vitro-studies. Meta-analyses performed on clinical trials confirmed lack of diversity in outcomes [2]. Furthermore, JAK is known to dimerize when activated in biological systems, but the percentage of different dimers is unknown. Therefore, further comparative studies are needed to verify their selectivity in real-life studies.

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Disclosure of Interests: None Declared.

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AB0492 ANEMIA IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH JAK INHIBITORS

Keywords: Rheumatoid arthritis, Targeted synthetic drugs, Safety

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Background: Recently, the safety of JAK inhibitors in the treatment of rheumatoid arthritis(RA) about malignancy and major adverse cardiac events has been highlighted [1], but there are still few reports on their effects on anemia. Filgotinib (FIL) is known to be a highly JAK1-selective agent with little effect on EPO-mediated JAK2 signaling [2].

Objectives: We investigated the effect of FIL on anemia in RA patients treated with JAK inhibitors at our hospital, comparing with other JAK inhibitors (non-FIL).

Methods: 73 patients who used 4 JAK inhibitors (filgotinib, tofacitinib, baricitinib, upadacitinib) after 2013 were divided into FIL group (16 patients) and non-FIL group (57 patients) respectively. Hemoglobin (Hb) trends at 3 and 6 months after the start of JAK inhibitors were investigated retrospectively. Subsequently, the investigation was performed with propensity score matching by age, gender, baseline Hb, CRP, s-Cre, presence of anemia treatments, presence of corticosterids/DMARDs, and history of previous bDMARDs/JAK inhibitor use. And, among the FIL group, we also examined whether there was a difference in Hb change depending on the history of JAK inhibitor use.

Results: Hb levels at the baseline were 10.5 g/dl in the FIL group and 11.6 g/dl in the non-FIL group, but there was no significant difference. The patients in the FIL group were significantly more likely to have used bDMARDs, other JAK inhibitors, and anemia treatments on starting FIL. Both at 3 and 6 months, although Hb levels were significantly increased in the FIL group ($P<0.05$), the anemia progressed over time in the non-FIL group despite exclusion of hemorrhagic anemia (Figures 1,2). The results after propensity score matching were also similar ($P<0.05$). There were no differences in CRP or RA disease activity at 0, 3, and 6 months. And then, compared to the FIL group with no history of JAK inhibitor use, the group that switched to FIL as a 2nd JAK inhibitor showed a significant Hb increase ($P<0.05$).

Conclusion: Compared to other JAK inhibitors, FIL did not reduce Hb levels and that could be maintained for a long time. In patients with anemia concerned with JAK inhibitors, switching to FIL is possible to make RA treatment safer and more successful.

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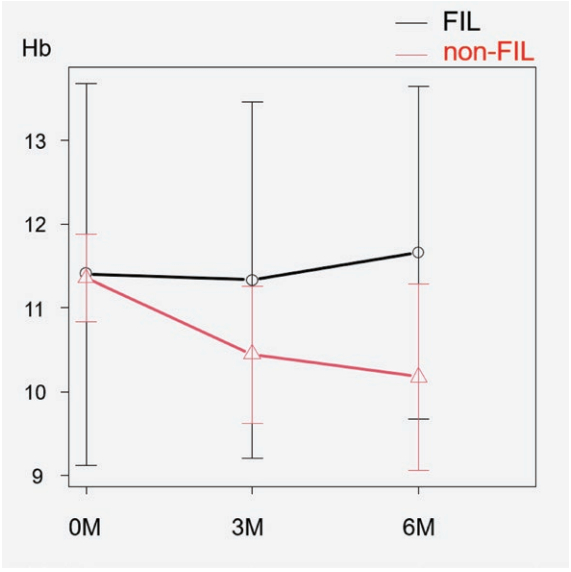


Figure 1.

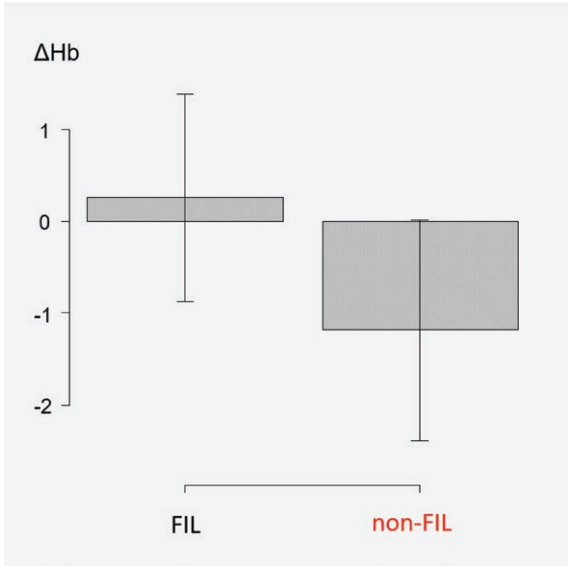


Figure 2.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0493

THE EFFICACY AND SAFETY OF TOFACITINIB IN THE TREATMENT OF DMARDS NAIVE RHEUMATOID ARTHRITIS PATIENTS (EASTERN STUDY)

Keywords: Rheumatoid arthritis, Targeted synthetic drugs

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Background: Janus kinase (JAK) inhibitor is a great addition to the therapeutic options for rheumatoid arthritis (RA). However, the the clinical efficacy and safety of tofacitinib comparing with methotrexate (MTX) was not elucidated.

Objectives: We conducted a controlled randomized clinical trial in treatment naive rheumatoid arthritis (RA) patients to explore the clinical efficacy and safety of tofacitinib (TOFA) comparing with MTX.

Methods: In this open-label, randomized, and controlled clinical trial, treatment naive RA patients at the status of medium or high disease activity [simplified disease activity index (SDAI)>3.3] were randomized at 1:1 ratio into TOFA and MTX groups. Patients in TOFA group received tofacitinib 5 mg twice per day and patients in MTX group received MTX 10-15 mg once per week plus betamethasone 1ml muscle injection at enrollment. The rate of disease activity improvement (defined as SDAI decreased >50% against baseline or at least 10) at week 12 was taken as primary outcome. Patients who did not achieve improvement transferred to the other group. Secondary outcomes included the rates of remission, low disease activity (LDA) and change of disease activity scores.

Results: 100 patients were enrolled in the study with 49 in TOFA group and 51 in MTX group. The improvement rate was much higher in TOFA group than in MTX group [29.3% (12/41) vs 7.5% (3/40), p=0.025]. The rate of remission and low disease activity at week 4 and week 12 were comparable between the two groups. The change of SDAI [17.9 (7.3-30.3) vs 10.8 (5.5-17.4), p=0.062], CDAI [7 (4.8-16) vs 15 (7.5-26), p=0.011], DAS28-CRP [2.1 (1.2-3.4) vs 1.4 (0.7-2.1), p=0.010] and DAS28-ESR [3.8 (2.5-5.2) vs 2.7 (1.8-3.9), p=0.005] at week 12 were all more significant in TOFA group than in MTX group. The total adverse event rate was high in MTX group than in TOFA group [28% (14/50) vs % (4/49), p=0.022]. Considering specific adverse events, the rates of liver damage [16% (8/50) vs 0, p=0.001] and dizzy [6% (3/50) vs 0, p=0.041] were higher in MTX group than in TOFA group.

Conclusion: For treatment naive RA patients, tofacitinib can bring higher rate of improvement of disease activity.

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AB0494

ADIPOSITY SEEMS TO NOT INTERFERE WITH THE JAK INHIBITORS RESPONSE IN RHEUMATOID ARTHRITIS: AN EXPLORATORY STUDY

Keywords: Targeted synthetic drugs, Rheumatoid arthritis, Prognostic factors

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Background: Cumulative data show how an excess body weight may hamper the activity of some anti-rheumatic drugs in rheumatoid arthritis (RA), but we lack studies in this regard on the new JAK-kinase inhibitors (JAKinibs).
Objectives: To prospectively evaluate the impact of adiposity on the anti-inflammatory response of JAKinibs in RA.
Methods: Observational, prospective, single-center exploratory study. We sequentially included adult patients from tertiary center clinics, with a clinical diagnosis of RA and a new JAKinib prescription by their treating rheumatologists. Only JAKinibs-naïve patients were allowed. For this analysis, during the follow up, csDMARD was required to remain unchanged. Patients participating in weight loss or bariatric surgery programs were also excluded. We used three different definitions for *adiposity*: A) body mass index (BMI), as kg/m2; B) body fat percentage, measured by impedancemetry; and C) blood levels of LDL and HDL cholesterol and triglycerides. We defined dyslipidemia as total cholesterol >200mg/dl and/or triglycerides >150mg/dl at blood tests. The potential modulating effect of adiposity on the effectiveness of JAKinib therapy was assessed on the change of DAS28-CRP and DAS28-ESR between baseline and 3 months later (when the peak action of JAKinibs is theoretically met). ANOVA regression was used to compare changes in DAS28 CRP/ESR regarding adiposity variables. When significant associations were found, a multivariate linear regression model was built. Software R v.4.2.1 was used.
Results: From an initial sample of 20 patients, 4 were excluded from analysis (2 stopping JAKinib due to intolerance, 2 as the cDMARD dose was modified), which finally left 16 participants. Median age was 57years (IQR 50.75 to 65.5) and 75% were females. Four patients were bDMARD-naïve and 9 were on concurrent csDMARD. 75% (n=12) of the subjects received 4mg baricitinib daily, the remaining 4 cases received 15mg upadacitinib daily. Median BMI was 27.7kg/m^2 (IQR 26.25 to 31.38), being 31.5% thus obese. Median body fat percentage was 34.95% (31.38 to 40.55). Ten patients achieved the dyslipidemia cutoff, 75 % of whom received lipid lowering treatment. Patients had mostly moderate-high activity measured by DAS28 at baseline (81.25%), while after 3 months no patient was on high activity and 62.5% and 56.25% (CRP/ESR) showed low activity and remission, respectively. The results for the association analyses between adiposity and changes in DAS28-ESR are given in **Table 1**. No association was found neither for BMI or body fat percentage, while a positive, independent relation with triglycerides was noted (not with LDL o HDL). No adiposity variables were found associated with changes in DAS28-CRP.

Table 1. DAS28-ESR regression analysis. Covariates included on multivariate model were JAKinib choice, time between visits and concurrent cDMARD.

	Univariate		Multivariate	
	β (95%CI)	p	β (95%CI)	p
BMI	-0.019 (-0.397 to 0.048)	0.694		
Body Fat %	-0.050 (-1.353 to 0.037)	0.186		
HDL-ch	-0.026 (-1.812 to 0.014)	0.080		
LDL-ch	0.007 (-0.952 to 0.007)	0.349		
Tryglicerides	0.007 (0.003 to 2.250)	0.032	0.01 (0.004 to 0.015)	0.004

Conclusion: No relevant impact of adiposity was noted on the anti-inflammatory effect of JAKinibs after three months of use in RA patients. Our findings support no dose adjustment for JAKinibs, independently of their weight or adiposity. This study should be replicated in larger studies to confirm our observations.
Acknowledgements: The realization of this study was possible thanks to the funding granted by ISABIAL.
Disclosure of Interests: Ernesto Tovar-Sugrañes Speakers bureau: UCB and Amgen, Mariano Andrés Speakers bureau: Lilly, Vega Jovani: None declared, Silvia Gomez-Sabater: None declared, Rocio Caño-Alameda: None declared, Paloma Vela Casasempere Speakers bureau: Pfizer, Lilly, Abbvie, Grant/research support from: Pfizer, Lilly, Abbvie.
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AB0495 **EFFICACY AND SAFETY OF VITAMIND IN PATIENTS WITH RHEUMATOID ARTHRITIS**

Keywords: Rheumatoid arthritis, Vitamin D

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory/autoimmune arthritis that causes pain, stiffness, swelling, loss of joint function, and a rise in acute-phase reactant levels. Vitamin D(VD) deficiency is linked to RA.
Objectives: The aim of this study was to summarize the association between serum vitamin D levels and RA and systematically evaluate the efficacy of VD supplementation in RA treatment.
Methods: Literature searches were conducted using PubMed, EMBASE, Web of Science, Clinical Trials.gov, Wanfang database, Weipu database, Chinese National Knowledge Infrastructure and Cochrane databases to identify available articles (up to January 1, 2023). Stata v.12.0 was used for the meta-analysis. And the results are presented both tabulated and graphically.
Results: In the study between serum vitamin D levels and RA, 26 studies, including 3,328 patients and 2,223 healthy controls, were identified (Table 2). Compared with the control group, the serum vitamin D level in the RA group was significantly reduced[SMD=-1.523, 95%CI (-1.590,-1.457), P=0.000]. Vitamin D was inversely correlated with disease activity. About the efficacy of VD supplementation in RA treatment, 7 studies comprising 392 patients were identified (Table 1). After the VD treatment, 91.28% of patients had distinct clinical remission, 47.72% were completely cured. After receiving VD therapy, patients with RA had significant decreases in DAS-28[SMD= -2.19, 95%CI (-2.58,-1.80), P=0.000], ESR [SMD=-2.12, 95%CI (-2.50,-1.74), P=0.000], CRP [SMD=- 1.84, 95%CI (-2.22,-1.45), P=0.000], SJC [SMD=-2.53, 95%CI (-2.71,-2.34), P=0.000], TJC [SMD=-3.45, 95%CI (-3.67,-3.23), P=0.000], and the Morning stiffness time [SMD=- 2.32, 95%CI (-2.72,-1.92), P=0.000]. None serious adverse events were reported among all these studies. Meta-analysis of 2 studies, including 420 patients with RA, showed that the incidence of adverse events was 19.46%.
Conclusion: Patients with RA had vitamin D deficiency, which was associated with the activity. Vitamin D supplementation did statistically significantly improve the RA.
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Table 1. Available evidence including patients with RA treated with VD.

Study. Year.	Patients (include in analysis)	Gender (female %)	Dosage	DAS-28	Remission, n(%)	CR,n(%)
Chawla,H.K.S. 2022	96(48)	83.33	60000 IU every week	NA	NA	NA
Aung,K.T.Z.M. 2020	58(31)	96.30	1000 IU every day	0w:5.27 12w:2.79	30(96.77%)	NA
ZhangChi Sun. 2021	100(50)	62.00	400 IU every day	NA	45(90.00%)	20(40.00%)
Lei Cao. 2019	320(160)	63.75	400 IU every day	NA	145(90.6%)	82(51.2%)
XiaoBin Yang. 2017	89(45)	66.67	200 IU every day	0m:5.82±0.3 3m:5.64±0.60 6m:4.65±0.37 12m:3.56±0.42	NA	NA
Nakamura, Y. 2017	43(21)	100.00	200 IU every day	0m:3.0±1.38 12m:2.7±1.41	NA	NA
XiaoFei Shi. 2019	72(37)	70.27	20 IU every day	0w:3.83±0.91 12w:2.99±0.79 24w:1.23±0.93	NA	NA

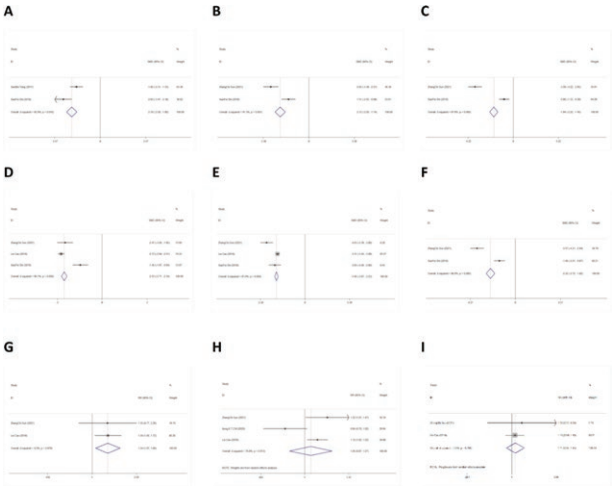


Figure 1. Efficacy and safety of Vitamin D in patients with rheumatoid arthritis (A) The DAS-28. (B) The ESR. (C) The CRP. (D) The SJC. (E) The TJC.(F) The Morning stiffness time.(G) The CR.(H) Remission. (I) Forest plot of the incidence of adverse events.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0496 TREATMENT WITH UPADACITINIB IN RA PATIENTS FOR WHICH BIOLOGICAL THERAPY FAILED

Keywords: Rheumatoid arthritis, Patient reported outcomes, Disease-modifying Drugs (DMARDs)

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Background: Upadacitinib is a JAK inhibitor recently approved for rheumatoid arthritis treatment with promising results in its studies for severe moderate RA for which conventional therapies failed.
Objectives: To study and describe the evolution of patients diagnosed with RA and treated with Upadacitinib who had inadequate response to biological therapy in association or not with DMARDs and GC for 1 year.
Methods: A population of 23 patients (19 of them female) with RA on treatment with Upadacitinib was analyzed over 1 year. Using patient-reported outcomes (PROs) to measure disease activity by visual analogue scale (VAS), the HAQ Disability Index (HAQ-DI), Disease Activity Score (DAS28), and morning stiffness duration. The age´s (average ± SD) = 53 ± 10 years and time of disease evolution (average ± SD) = 17.6 ± 23.3 years. Pretreatment DAS28 was (average ± SD) = 7.32 ± 2.41. The initial VAS was (average ± SD) = 7.32 ± 1.88. HAQ (average ± SD) = 2.2 ± 0.5. All patients received previous biologic treatments and 61% (14 patients) combined therapy with DMARDs. Only 2 cases had no glucocorticoid treatment prior to treatment with Upadacitinib.
Results: In 3 months time, most patients (81%, n = 21) treated with Upadacitinib were able to reduce GC dose, and this reduction was maintained 6 months from the beginning of the treatment. After one year of treatment (n = 14), 71% of patients reduce the dose of GC by 53% with respect to the initial dose. Upadacitinib enabled 50% of patients who initiated treatment to discontinue corticosteroid therapy completely. After 3 months of treatment, most patients experienced an enhancement in DAS28 (89%, n = 18), with an average improvement in DAS28 (average ± SD) = 1.87±1.09 units. After one year of treatment most patients (92%, n = 14) achieve a reduction in DAS28 (average ± SD) = 3.813 ± 1.56 units from baseline. Disease remission (DAS28 <3.2) was achieved in up to 25% of patients who initiated treatment with Upadacitinib. Regarding the pain (VAS), 67% of the patients showed improvement after 3 months (n=18), reaching 71% after 6 months (n=17). After 12 months of treatment (n = 14), 85% of patients experienced an improvement in pain, with the final (average ± SD) VAS being 5 ± 2.32 points. Sixty-eight percent of treated patients showed a reduction in morning stiffness after 3 months (n = 19), and this improvement increased up to 84% of treated patients at 6 months (n = 19) and remained so until 12 months (n = 14). Side effects were observed in five patients, consisting of dizziness and nausea. In no case were they a reason for the withdrawal of the drug. Treatment was withdrawn in three patients due to primary failure.
Conclusion: Treatment with Upadacitinib allows GS dose reduction, as well as an improvement in DAS28, VAS and morning stiffness at three months and six of treatment. These data are in line with the evidence published in Upadacitinib pivotal studies, meaning a good alternative in the treatment of patients with moderate or severe RA.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0497 THE ROLE OF CORTICOSTEROIDS (PREDNISONE) IN THE TREATMENT OF NEWLY DIAGNOSED RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis

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Background: The use of corticosteroids (CSs) in patients with newly diagnosed rheumatoid arthritis (RA) is important in order to reduce the inflammation as well as bridging until achieving the full effect of the basic therapy. In previous years, there were recommendations for the use of different doses of CSs [1-2].
Objectives: To compare the therapeutic effect of initially higher doses of CSs, prednisone (0.3-0.5 mg/kg) with a standard low-dose daily therapy (7.5 mg) in patients with newly diagnosed RA.
Methods: Two groups of 50 patients each with newly diagnosed RA were followed up for a period of 24 months. The groups were homogeneous in terms of sex, age and BMI. The group one (I) consisted of 50 patients who were initially treated with doses of prednisone 0.3-0.5 mg/kg (average initial dose 25mg) by bridging until achieving the full effect of basic therapy with Methotrexate (MTX) (in an average dose of 15 mg/week). The group two (II) consisted of 50 patients who were treated according to standard recommendations with an initial dose of an average of 7.5 mg of prednisone with MTX in an average dose of up to 15 mg/week. In both groups, the doses of prednisone were gradually reduced over a period of 3-6 months. During a period of 24 months (at 6, 12 and 24 months), the following parameters were monitored in all patients: DAS28, HAQ, VAS, CDAI. We also compared the number of corticosteroid-independent patients after 6, 12 and 24 months in both groups, the percentage of patients in remission (DAS28<2.6) and the percentage of patients with a good EULAR DAS28 response (CRP<3.2 or change in DAS28 by >1.2). The number of newly discovered comorbidities during the mentioned therapy, such as newly discovered hypertension, osteoporosis and diabetes mellitus (DM) type II, was also monitored.
Results: Highly statistically significantly lower values of the DAS28 score ($p<0.01$) were found in the group I of patients, treated initially with higher doses of CS after 6 and 12 months, as well as statistically significantly lower values after 24 months ($p<0.5$). Statistically significantly lower HAQ values were also found in group I after 6, highly statistically significantly lower after 12 and statistically significantly lower after 24 months of follow-up ($p<0.5$). For pain VAS, statistically significantly lower values in group I after 6 and 12 months ($p<0.01$) and statistically significantly lower values after 24 months. CDAI values were also statistically significantly lower in group I after 6 and 12 months. A statistically significantly higher percentage of patients were in remission and had a better EULAR response in the group I after 6, 12 and 24 months from the start of therapy ($p<0.05$). Also in the group I which was initially treated with higher doses of CSs, statistically significantly lower number of patients were corticosteroid-dependent after 6, 12 and 24 months. A special difference between the groups is represented by a highly statistically significantly lower number of comorbidities in group I after 24 months from the start of therapy, such as newly discovered hypertension, DM type II and osteoporosis.
Conclusion: The initial use of higher doses of corticosteroids (0.3-0.5 mg/kg) compared to the recommended daily doses of up to 7.5 mg in patients with newly diagnosed rheumatoid arthritis, provide significantly better clinical response in all the parameters DAS28, VAS, CDAI, HAQ, a higher level of corticosteroid-independent patients as well as a lower number of side effects such as newly discovered hypertension, osteoporosis and diabetes mellitus type II, 24 months after starting basic therapy.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0498 PREDICTIVE BIOMARKERS OF TOFACITINIB THERAPY IN RHEUMATOID ARTHRITIS: REAL WORLD DATA FROM MALAYSIAN RHEUMATOLOGY BIOLOGIC REGISTRY (MARBLE)

Keywords: Targeted synthetic drugs, Rheumatoid arthritis, Biomarkers

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Background: Targeted synthetic therapies brought revolutionary progress in rheumatoid arthritis (RA) management and culminated a paradigm shift over a decade. However, only a subset of patients responded clinically and achieved sustained remission. The interindividual factors may vary resulting in failure of therapeutic target and clinical response.
Objectives: We investigated the clinical and sociodemographic predictors of Tofacitinib response in RA patients at three, six and twelve months.
Methods: This retrospective study included 164 RA patients from the nationwide MARBLE registry who received Tofacitinib. Patients' clinical data were extracted from medical records. The response to Tofacitinib in terms of clinical remission, low disease activity (LDA) and DAS28 improvement (EULAR response) were measured at baseline, 3 months, 6 months and 12 months of therapy based on disease activity score (DAS)28 for RA. Factors predicting treatment response were analysed using binary logistic regression analysis.
Results: Our data revealed that at 3-month, 6-month and 12-month of Tofacitinib treatment, 17.7%(n=29), 67.7%(n=111) and 60.4%(n=99) RA patients achieved low disease activity/clinical remission. Further analysis demonstrated that anti-cyclic citrullinated peptide antibody (anti-CCP)-positivity and joint erosion were independently associated with unsatisfactory EULAR response (ie., anti-CCP at 3-month, OR=2.270, p<0.05; 6-month, OR=7.773, p<0.0001; and 12-month, OR=4.645, p<0.0001). Lower frequencies of clinical remission were associated with the presence of erosive joint throughout the three follow-up periods of treatment (OR=2.040 to 3.868; p<0.05), while only anti-CCP positive was found to be significantly associated with lower frequencies of LDA at 6-month and 12-month of treatment (anti-CCP positive, 6-month OR=3.659, p<0.0001 and 12-month OR=2.130; p<0.0001)
Conclusion: Our data suggest that joint erosion and anti-CCP positivity are strong predictive biomarkers for lower achievement of clinical remission, LDA and satisfactory EULAR response in patients with RA receiving tofacitinib treatment.
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AB0499

STEP-DOWN APPROACH IN METHOTREXATE USE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS (STEMETRA): A PILOT STUDY DEMONSTRATING EFFICACY AND SAFETY OF SHORT-TERM HIGH DOSE METHOTREXATE

Keywords: Disease-modifying drugs (DMARDs)

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Background: Methotrexate (MTX) is the cornerstone of Rheumatoid Arthritis (RA) treatment, showing a suitable efficacy-safety profile, relatively low-cost, and versatile routes and dosage administration. However, there are no clear indications yet on the optimal use of MTX in RA, whereas existing recommendations disagree on relevant aspects (eg. route, starting and maximal dose, titration increase/decrease, and intervals to monitor toxicity) [1].
Objectives: To evaluate the efficacy and the safety of a step-down strategy to use subcutaneous (sc) MTX in patients with RA.
Methods: STEMETRA is a 16-week open-label, monocentric, pilot study. The protocol treatment schedule consisted of the administration of MTX 50 mg sc/week for 4 consecutive weeks, followed by 25 mg/week for 4 weeks, and then 15 mg/week for 4 weeks. All patients received oral supplementation of folinic acid (leucovorin) 12 mg, 12 hours after the injection of MTX.
Results: Fifteen patients (10 females and 5 males; mean age, 60 years (±11)) diagnosed with RA according to 2010 ACR/EULAR classification criteria and naïve to any RA treatment were enrolled. One patient was lost to follow-up after week 12; 4 patients withdrew because of adverse events; therefore, 10 patients concluded the study. A total of 14 adverse events occurred in 7 patients; 7 were of mild entity and tolerated by patients, 3 solved, and 4 were persistent and lead to withdrawal of the drug (Table 1). Mean DAS28(CRP) at baseline was 5.6 (±1.4), whereas, at week 16, mean DAS28(CRP) was 1.6(±1). Most patients who concluded the study achieved ACR70 response and the state of remission (7 out of 10), whereas 3 still showed moderate disease activity.
Conclusion: In this study, step-down MTX approach was effective in inducing remission in most of the patients enrolled. According to data reported in other studies (2,3), one third of them showed adverse events leading to the withdrawal of the drug. On the contrary, different studies in which MTX was used as in current clinical practice (at lower dosages) showed lower efficacy: in the ORAL START study, ACR70 response was reached only in 12% of naïve patients 6 months after MTX monotherapy (4), whereas in the PREMIER study, 26% of patients receiving MTX monotherapy obtained ACR70 response after one year [5]. Thus, short-term higher dose MTX usage could be more effective in order to reach remission earlier. Nonetheless these results should be confirmed in larger populations of patients. In conclusion, this approach could be considered as a valid regimen for a more optimal use of MTX.
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Table 1. Adverse events

ADVERSE EVENT	N (%)	Grade/withdrawal (week of appearance)
Headache	1 (6.6)	Mild (W4)
Cutaneous local reaction	1 (6.6)	Mild (W4)
Nausea	2 (13.3)	Mild (W4)
Diarrhoea	1(6.6)	Moderate/Withdrawal (W8)
Lack of appetite	1 (6.6)	Mild (W8)
Dizziness	1 (6.6)	Moderate/Withdrawal (W12)
Fatigue	2 (13.3)	Mild (W16)
Urinary tract infection	4 (24)	Moderate/Withdrawal (2 out of 4 patients) (W12) Moderate (2 out of 4 patients) (W4)
Increased transaminases	1 (6.6)	Moderate (W2, solved in W8) – alcohol abuse

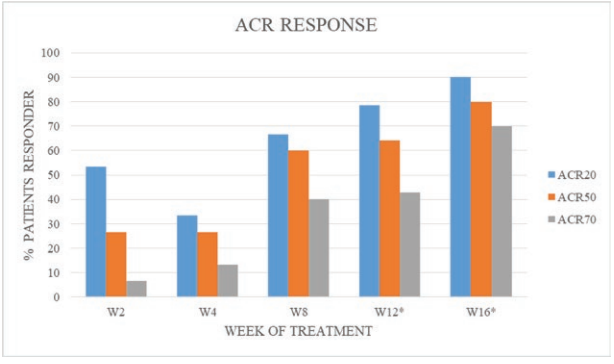


Figure 1. Percentage of patients in ACR response.*W12: total patients: 14. *W16: total patients: 10 patients

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0500 STUDY OF THE USE AND PRESCRIPTION OF ANALGESICS DURING RHEUMATOID ARTHRITIS (RA)

Keywords: Rheumatoid arthritis, Pain

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Background: In rheumatoid arthritis, pain is the major complaint for patients. Analgesic drugs are considered adjuvant treatments and their prescription is generally left to the patient's discretion.
Objectives: The objective was to determine the actual use of analgesics during RA.
Methods: This is a 5-month cross-sectional survey including patients with rheumatoid arthritis, meeting the ACR/EULAR 2010 criteria consulted during the study period were included The use of analgesics was evaluated via a questionnaire with 14 questions. Data was processed by statistical analysis using SPSS 2021 Software.
Results: There are 168 patients, including 24 men and 144 women. The average age was 49.91± 12.96 [20–90]. The average age at onset was 41.69 ±14.65. The average age of diagnosis for RA was 47.17 ±13.71 years. The average DAS28 was 5.32 ±1.35. Only 89 patients were taking analgesics The majority of patients were on disease modifying drug (DMARD) (78%), 145 (86%) were on corticosteroids, 46 (27.38%) were on non-steroidal anti-inflammatory drugs and 89 (53%) were taking analgesics. At the time of the survey 79 patients were not taking analgesics, 69 patients were taking a Tier 1 analgesic, 20 patients were taking a Tier 2 analgesic, none of the patients were taking a Tier 3 analgesic. Analgesics were never used alone. The difference between a pure analgesic and a non-steroidal anti-inflammatory was only known by 45 patients (27%). The difference between central and peripheral analgesic was only known by 15 patients (9%). For only 25 patients, analgesics were effective on diurnal pain in 25 patients and for 64 patients (72%) on nocturnal pain. Only 14 patients, or 15% were taking pain relievers at a fixed time, 60 (67%) only during flare-ups, and 15 (16%) were taking pain relievers at a fixed time with increased dose in case of flare-ups. The prescription of analgesics was the fact of the rheumatologist in 89% of cases, and self-medication in only 11% of cases.
Conclusion: In RA, as in all chronic painful diseases involving functional prognosis, pain is the essential symptom to treat. In our study the use of analgesics was 53%.
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Disclosure of Interests: None Declared.
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AB0501 ANALYSIS OF ADVERSE EFFECTS IN IMMUNE-MEDIATED INFLAMMATORY DISEASES TREATED WITH JAK INHIBITORS IN A SINGLE CENTER

Keywords: Rheumatoid arthritis, Disease-modifying drugs (DMARDs), Safety

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Background: Janus kinase (JAK)-inhibitors (JAKi) are anti-cytokine monoclonals against cellular targets and small molecule inhibitors of the JAK pathway approved for the treatment of diverse immune-mediated inflammatory diseases, such as rheumatoid arthritis (RA), spondyloarthritis (SpA) or psoriatic arthritis (PsA). Safety data comes mostly from randomized controlled trials, with scarce long-term registry data. Therefore, we aimed to evaluate the major adverse events in patients treated with Janus kinase inhibitors in various immune-mediated inflammatory diseases (RA, PsA and SpA).
Objectives: To evaluate adverse events in patients treated with Janus kinase inhibitors in various immune-mediated inflammatory diseases (RA, PsA and SpA).
Methods: We reviewed 203 patients in Rheumatology department at Navarra University Hospital who underwent treatment with JAKi (Baricitinib, Filgotinib, Tofacitinib and Upadacitinib) and the significant adverse events occurred.
Results: Of our sample of 203 patients, 81,2% were diagnosed RA, 8,8% with PsA, 7,5% with SpA and the remaining 2,5% were indeterminate arthritis. We found that out of the patients diagnosed with RA, 10,83 % had a significant adverse event (22 events in total). A 0,5% had a myocardial infarction, 1,5% stroke, 2,1% arterial thrombosis, 2,1% venous thrombosis, 1,5% developed some type of malignancy and 3,6% reactivation of herpes zoster. One arterial thrombosis happened in the indeterminate arthritis group.
Conclusion: In our series, out of 203 patients treated with JAKi, 11,33% had a significant adverse event. The most common adverse event was the herpes zoster reactivation (3,44%), followed by arterial and venous thrombosis (2,46 and 1,97% respectively). Longer-term follow-up and greater number of patients are necessary to ratify these data.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0502 PREVALENCE AND ASSOCIATED FACTORS FOR CONVENTIONAL DISEASE MODIFYING ANTI RHEUMATOID DRUG FAILURE IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A TERTIARY CARE HOSPITAL IN SOUTHERN SRI LANKA

Keywords: Treat to target, Disease-modifying drugs (DMARDs), Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown etiology marked by a symmetric, peripheral polyarthritis. It is the most common form of chronic inflammatory arthritis and often results in joint damage and physical disability [1]. Among limited studies available in Sri Lanka the community prevalence of early rheumatoid arthritis is 0.7% [2].
Treatment should be aimed at reaching a target of sustained remission or Low Disease Activity (LDA) in every patient [3]. Achieving this target begins with convensional disease modyfying antirheumatic drugs (cDMARDS) and only limited number of biological DMARDS (bDMARD) is available in Sri Lanka.
DMARD failure is a recognized problem in treating patients with rheumatoid arthritis. The poor response to cDMARDs once assessed in individual basis has variety of causes. The next step in managing patients with cDMARD failure is to offer bDMARDs. Biological DMARDs are expensive and give a major cost impact to the health budget especially during the background of economic crisis and the shortage of medicinal drugs. Knowing the prevalence of cDMARD failure is helpful in estimating costs for bDMARDs.
Objectives:
1. To describe the prevalence of cDMARD failure among patients with RA attending the Department of rheumatology and rehabilitation- Teaching Hospital Karapitiya, Galle, sri Lanka
2. To determine the factors associated with cDMARDs failure
3. To describe the distribution of side effects of cDMARD

Methods: This study was carried out in 429 patients with RA attending a Department of Rheumatology & Rehabilitation, Teaching Hospital Karapitiya, Southern Sri Lanka. Disease activity was measured by DAS28 of which moderate or high disease activity taken as a cDMARD failure sample and compared with non-failure sample (low disease activity/remission) to assess possible associated factors for poor response.
Results: Twenty-five point two out of 100 patients (25.2%) were found to have failed respond to cDMARDs, and females showed higher failure rate (17.2%) than males (4.2%). Except for 2.9% of those, all the others had been offered Methotrexate. Discontinuation of methotrexate due to side effects were observed in 5.7% in failure sample. Factors such as age, disease duration, education level, smoking had no significant impact on failure rate.
Conclusion: This study gives an insight to cDMARD failure prevalence which enables to predict the need of biologic DMARDs and impact on health budget. Furthermore, introduction of proper patient education program either individually or as groups would have account for minimum drug discontinuation which in turn

helps with good response rate for cDMARDs. Introduction of injectable version of methotrexate could have helped in some intolerable side effects of methotrexate however, efficacy of this measure will depend on several factors such as cost, willingness of patients to self-inject etc. Finally, conventional DMARDS still play a significant role in the management of this debilitating disease with a comparatively low cost and an acceptable side effect profile.

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AB0503 GENICULAR ARTERY EMBOLIZATION IN THE MANAGEMENT OF PERSISTENT JUVENILE IDIOPATHIC ARTHRITIS OF THE KNEE: A CASE REPORT

Keywords: Synovium, Non-pharmacological interventions, Inflammatory arthritides

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Background: Genicular artery embolization (GAE) is rapidly gaining popularity for treatment of patients with recurrent hemarthrosis following knee arthroplasty, and for pain relief in mild-to-moderate osteoarthritis (OA) [1]. Despite the growing evidence of the safety and efficacy of GAE in improving pain and disability in OA, it has yet to be reported in the treatment of patients with inflammatory arthropathy, such as rheumatoid arthritis (RA) or juvenile idiopathic arthritis (JIA).

Objectives: To apply GAE on an adult patient with oligoarticular JIA of the knee and refractory to biologic therapy, and measure improvement of pain symptoms.

Methods: A 40-year-old woman with history of oligoarticular JIA presented with progressively worsening right knee pain and swelling. She had tried several treatments in the past including oral analgesia (NSAIDS, acetaminophen, and opioids), multiple intra-articular steroid injections, therapeutic arthrocentesis, multiple DMARDs (MTX, SSZ, LEF), and had been on biologic therapy (adalimbumab) for the past 8 months, with no noticeable improvement from any of these strategies. Prior to GAE she had pain score of 8/10 on VAS, and Oxford Knee Score (OKS) of 25. The GAE procedure was subsequently performed on an outpatient basis under conscious sedation. A four French angled tip catheter was advanced into the distal SFA and angiography was performed. This demonstrated characteristic synovial hyperemia ("blush") of the synovium along the medial joint space supplied by the musculoarticular branch of the descending genicular artery (DGA), as well as the lateral synovium supplied by the inferior lateral genicular artery (ILGA). Super-selection of the DGA was performed using a 1.9 French microcatheter, with repeat angiogram confirming synovial hyperemia. After administration of intra-arterial nitroglycerin, the DGA was then embolized with 1.0 cc of 100 – 300 µm Embospheres (Merit Medical Systems, South Jordan, UT). Post-embolization super-selective angiogram confirmed a "pruned-tree" appearance of the DGA branches, with no further hyperemia, in keeping with a successful embolization.

Results: The patient tolerated the procedure well and was discharged home same-day. At 6 and 12 months follow-up, the patient continued to report substantial improvement in her symptoms with a pain rating of 1 out of 10 on both rest and mobalization. Her OKS was 35 at 12 months. Her right knee remained in remission on Adalimumab for 12 months post procedure. Figure 1 shows the comparison of the pre and post GAE fat saturated T1 image. Pre GAE, there were synovial thickening and enhancement of the knee capsule. As shown in Figure 1, at 12 months post GAE significant retraction and devascularisation of the synovium has occurred.

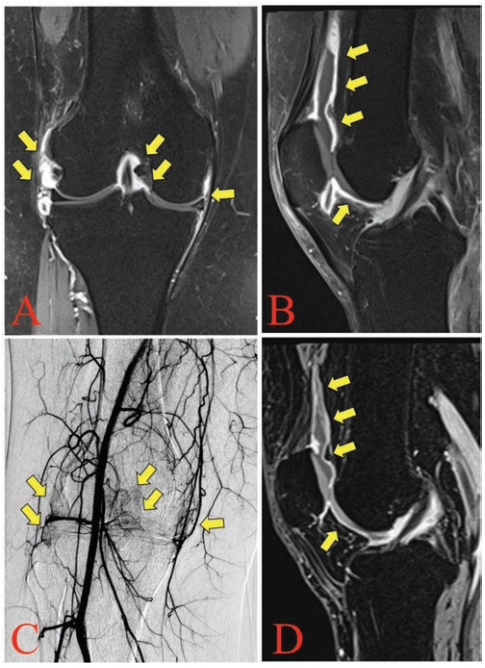


Figure 1. Modulation of Synovitis Pre and Post GAE: Pre GAE sagittal and coronal post contrast (gadolinium) fat saturated T1 image demonstrated synovial thickening and enhancement of the knee capsule (A+B). Coronal digital subtraction angiogram demonstrating corresponding arterial neovascularization/synovitis blush targeted by GAE (C). Post GAE (12 month) sagittal post contrast (gadolinium) T1 fat saturated image demonstrating significant retraction and devascularisation of the synovium (D).

Conclusion: We report the first case of GAE in a patient with inflammatory arthropathy, which showed dramatic and sustained reduction in pain. Though the efficacy, safety, and long-term clinical durability still need further evaluation in the context of inflammatory arthropathy, the positive result in this case posits an exciting avenue for further investigation into the role of transarterial embolization in rheumatologic disease.

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AB0504 CARDIOVASCULAR AND ADVERSE EVENTS RISK WITH TOFACITINIB IN RHEUMATOID ARTHRITIS IN THE DOMINICAN REPUBLIC

Keywords: Targeted synthetic drugs, Rheumatoid arthritis, Cardiovascular disease

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune inflammatory disease that affects the synovial membrane of small joints. Tofacitinib (TOF) is the first Janus Kinase Inhibitor (JAKi's) approved by the European Medicines Agency and the Food and Drug Administration for the treatment of RA. This inhibits JAK1 and JAK3 involved in cytokine signaling proinflammatory in RA. Concepcion et al. [1] found that 16% of the patients on TOF presented adverse effects (AEs) and the most frequent of these was dyslipidemia, followed by elevated liver enzymes. Ytterberg et al found an increased risk of MACE with the use of tofacitinib recently [2].

Objectives: To evaluate the risk of cardiovascular and adverse events with tofacitinib in rheumatoid arthritis.

Methods: Retrospective, longitudinal, descriptive. Records from the database of the Rheumatology service of the Hospital Docente Padre Billini were reviewed between January 2016 and December 2021. Inclusion criteria: ≥18 years, diagnosis of RA according to the ACR/EULAR 2010 criteria, TOF 5mg every 12h ≥ 3 months. Exclusion criteria: patients with ≤ 3 months of treatment, history of cardiovascular event, liver disease, moderate anemia, severe neutropenia, history of herpes, absence of > 2 visits. A descriptive analysis of AEs and Major Adverse Cardiovascular Events (MACE) were performed using SPSSv23.
Results: 215 met inclusion criteria. 87% (187) female. Mean age 57 + 11.5 years. Mean disease duration 7.6±2.3 years. HTA 49.8% (107), IMC>30 kg/m2 12.6% (27), DM 11.6% (25). Mean treatment with TOF 5±1.7 years. AEs and MACE 54%(101). AEs 73.3%(74): Hypercholesterolemia 26.7% (27), ALT or AST >3ULN 12.9% (13), herpes virus infection 8.9% (9), PMN: >500 8.9%(9), < 500: 7.9% (8), UTI 4.0% (4), severe anemia 4.0% (4). MACE 26.7%(27): mean age 60.2 + 9.1 years [Acute myocardial infarction (AMI) 63%(17), deep vein thrombosis 29.6%(8), cerebrovascular accident 7.4%(2)].
Conclusion: In our review, AEs were found in half of the patients evaluated. Most of MACE events were associated with older age; the most frequent was AMI. Infections were found in a lower proportion. Little risk of infectious processes is demonstrated with the use of TOF. We must take precaution in those over 55 years of age and with cardiovascular risk comorbidities with the use of TOF consistent with that reported in the world literature.
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AB0505 INTEGRATIVE MEDICINE APPROACH TO SUSTAIN LONG-TERM CONTROL IN CHRONIC RA: AN OBSERVATIONAL PROSPECTIVE STUDY OF A COMBINATION REGIMEN OF CONVENTIONAL DMARD AND AYURVEDIC HERBAL DRUG

Keywords: Tapering, Rheumatoid arthritis, Safety

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Background: Prolonged drug treatment in RA is complicated by related toxicity, inadequate efficacy, other health issues, cost, and compliance. Ayurveda (India) drugs (Ayur) have popularly treated arthritis since ancient times. Few controlled/extended drug studies, both as mono or combination (Ayur plus modern medicine/M-Med) showed impressive outcomes (especially safety). In 2018, we introduced limited integrative treatment in rheumatology practice (community) to improve the outcome of long-drawn chronic RA. We present preliminary experience.
Objectives: To evaluate the one-year outcome of a combination treatment of conventional DMARD with standardized Ayur (herbal drug)
Methods: Consenting patients of chronic RA and clinically well-controlled disease (last 6 months) were selected in no particular order; supervised ongoing standard care with DMARD with/without steroids (previous period, median 5.5 years). SC-1 (Ayur) was added in a fixed stable dose (1 gm tablet, bid); standardized medicinal plant extracts (1 tab contained 50 mg Withania somnifera, 500 mg Boswellia serrata, 50 mg Curcuma longa, 400 mg Phyllanthus emblica), as per Ayurveda pharmacopeia. M-Med (RA) were adjusted at 12-16 weeks intervals based on clinical judgment. Standard follow-up (FU) procedures included a predetermined routine drug toxicity checklist. An Excel (Microsoft) based analysis was performed; standard deviation in parentheses, single sample paired T-test (P, two-tailed). Disease activity was classified according to the standard DAS 28 score. 453 patients qualified (one-year uninterrupted combination treatment and sufficient data) for analysis: 32% remission, 38% low activity (LDA), and 30% borderline moderate activity (MDA). Six months prior, 51% of the latter cohort (mean DAS=3.33 (0.95) were in remission/LDA.
Results: At baseline, the median of age and RA symptom duration respectively was 56 years (12.5) and 11 years (7.4); 80% seropositive RF; 91 % erosive/RA deformity; mean pain VAS(10 cm line)=2.78(1.23), mean HAQ (validated Indian version, maximum score 24)=3.17 (2.95), mean DAS 28= 2.9(0.76), 47% steroids (mean daily dose ≤5 mg pred), median ESR=30(19.4), 22% Hydroxychloroquine, 22% Sulfasalazine,74% Methotrexate (mean 16.3 mg weekly (4.48), and Combo DMARD 23%. At 1 year FU, 57% were in remission, 31% in LDA, and 12 % MDA; median ESR=30 mm (18.8), mean DAS= 2.35 (0.87) (p=0.000), 14% Sulfasalazine, 18% Hydroxychloroquine, 49% steroid, 70 % Methotrexate (mean 15.5 mg (4.6). Though statistically significant, several changes (core variables) were small and clinically considered unimportant. 32% cohort reported brief arthritis flares (1-3) versus 40% in the previous year. 409 clinical adverse events/AE (none serious/hospitalization) were reported during the study period; 121 non-related (drugs), 68 unspecified drugs, 34 Hydroxychloroquine, 25 Sulfasalazine, 136 Methotrexate, and 21 SC-1 (mostly gut and dyspepsia, infrequent mild transaminitis); correspondingly 472 AE were reported in the previous year (non-SC-1). FU data will be presented. The absence of control, placebo response, and floor and ceiling effect (outcome) may complicate the clinical interpretation of the results. Patients continued to be followed till date.
Conclusion: SC-1 (Ayurveda) further improved disease control, albeit modest, and safety in long-drawn chronic RA when combined with ongoing standard modern drugs under prolonged rheumatology care. This augurs well for the future. But first, controlled evaluation (integrative medicine) studies are warranted.
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AB0506 DOES JANUS KINASE INHIBITOR INCREASE THE RISK OF HERPES ZOSTER IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SAUDI ARABIA? A MULTICENTER RETROSPECTIVE COHORT STUDY

Keywords: Rheumatoid arthritis, Safety, Infection-related RMDs

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Background: Currently, there is an advancing interest in the Janus kinase (JAK) intracellular pathway since targeted inhibitors are proving to be excellent in the treatment of Rheumatoid arthritis (RA). Nevertheless, this new therapeutic era of small molecules comes at a cost, JAKi is associated with a heightened risk of reactivation of dormant infections herpes zoster (HZ) virus infection. Furthermore, the incidence of HZ in rheumatoid arthritis using JAKi is higher in eastern Asian countries making this study essential for the assessment of its safety among the middle eastern population in a real-world setting.
Objectives: To evaluate the risk of serious infection (SI) and herpes zoster (HZ) in rheumatoid arthritis patients receiving JAK inhibitors.
Methods: Multicenter retrospective cohort study in Saudi Arabia. Rheumatoid arthritis patients aged 18 and above from the period of 2007-2022 were included. Medical records were reviewed, and patients were phone interviewed during 2022 to register an outcome of HZ infection. Chi-square was used to assess for the correlation between various risk factors and HZ infection.
Results: From a total of 308 patients, 108 were on JAKi. JAKi didn't significantly increase the risk of HZ development (OR1.97, 95% CI 0.71- 4.67). Rather, patients on Etanercept had higher risk of HZ (OR 2.88, 95% CI 1.65-2.83). 3 out of the 7 cases who developed HZ were on chronic corticosteroid. However, it wasn't significantly associated with HZ devolvement. Patients with Asian ethnicity were significantly more predisposed to HZ infection (OR 1.2, 95% CI 0.8-4.37). None of the patients received the vaccine prior to HZ infection.
Conclusion: In this multicenter study in Saudi Arabia, JAKi were not associated with the development of HZ among Rheumatoid Arthritis patients in real world setting. Asian ethnicity and etanercept usage were significantly associated with HZ infection.
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Table 1. Comparison between cases with HZ infection and controls regarding medication history among the participating RA patients (n=308)

	Total %	Patients with HZ infection (n=7)		Patients who didn't develop HZ (n=301)		P-value
		n	%	n	n	%
JAK inhibitors	35.1%	2	1.9%	106	98.1%	0.716
Adalimumab	20.5%	0	0.0%	63	100.0%	0.175
Methotrexate	88.0%	7	2.6%	264	97.4%	0.323
Rituximab	6.5%	0	0.0%	20	100.0%	0.481
Hydroxychloroquine	29.2%	1	1.1%	89	98.9%	0.379
Etanercept	10.1%	3	9.7%	28	90.3%	**0.004**
Chronically low dose corticosteroids	59.1%	5	2.7%	177	97.3%	0.502
60 mg or higher of Corticosteroids	37.7%	4	3.4%	112	96.6%	0.554

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AB0507 FILGOTINIB MAY BE USEFUL THERAPY FOR RAPID RADIOGRAPHIC PROGRESSION BY REDUCING BONE EDEMA

Keywords: Targeted synthetic drugs, Rheumatoid arthritis

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Background: Filgotinib is well-known to inhibit bone destruction in patients with RA, particularly those with poor prognostic factors. Recently, Filgotinib, especially at dose 200mg/d has been reported to have good results to inhibiting joint damage in patients with rapid radiographic progression (RRP) condition compared to non-RRP condition in post-hoc study of Finch1(Methotrexate (MTX) iR) or Finch 3(MTX naive) trial [1]. However, little has been reported about the joint protective activity by Filgotinib in the real world. On the other hand, we previously demonstrated that extensive MRI bone edema (BE) in the hand is a prognostic factor for RRP [2].
Objectives: To clarify, filgotinib action for inhibiting RRP, 10 patients who have extensive BE in hands or feet are analyzed for radiographic study for joint destruction from 32 patients treated with Filgotinib+MTX.
Methods: All 32 patients with inadequate response to MTX/Biologics/JAKi who were treated with filgotinib were examined to check for extensive BE in their most painful joints before treatment by MRI(Canon,1.5T).
Blood examination, DAS28-ESR, patient pain and doctor's VAS, mHAQ were routinely examined.
Results: As shown in Table 1, most of the patients were treated with filgotinib 200mg/d +MTX. Patients 1-4 (12 months) and patients 5,6 (2-3 months) had extensive BE in hand and RRP condition at baseline. Finally, the RRPs in all patients improved and BE almost disappeared (patients 1,2). Especially, patient 5 suffered severe BE and RRP during 4 months who was treated with IL-6inhibitor +MTX6mg/w, are tremendously recovering by filgotinib and denosumab (for osteoporosis) from severe joint damage (Figure 1). Patients 7-10 had extensive BE in mid-tarsal (2), toe (1), shoulder (1) and patients 7-9 had disappeared BE and symptoms and patient 10 had disappeared pain (not MRI checked). Finally, most of the patients showed clinical improvement (DAS28-ESR, VAS,HAQ).
Conclusion: Filgotinib (200mg/d)+MTX may be useful therapy for RRP by reducing BE.
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Table 1.

No	sex	age	Duration	RF	ACPA	class	stage	FILGOTINIB	pre BIO	pre JAK	MTX(mg/W)	CRP	MRI-BE	mTSS
1	f	60	408	11	12.8	3	4	200	IFX,TCZ	0	0	6.48	hand	348
2	f	68	252	19	42	3	4	200	0	0	12	2.57	hand	90
3	f	65	108	111	702	3	4	200	CZP	Pef,Bari	8	0.05	hand	60
4	f	63	192	18	4.7	3	4	200	ETA	TOF	8	0.48	hand	75
5	f	54	36	29	197	2	3	200	SAR	0	6	0.05	hand	28
6	m	73	8	38	95.4	2	3	200	0	0	16	0.06	hand	8
7	f	56	168	24	740	3	3	200	0	0	0	0.13	mid-tarsal	/
8	f	75	120	119	27.6	2	3	100	ADA	0	8	0.05	mid-tarsal	/
9	f	67	0	129	324	2	3	200	0	0	8	0.19	toe	/
10	f	88	42	33	0.6	3	3	200-100	0	0	8	1.11	shoulder	/
		66.9	133.4	53.1	214.61	2.6	3.4				7.4	1.117		

No	DAS28-E0	DAS28-EJ	DAS28-E2	Pat-VAS0	Pat-VAS1	Pat-VAS2	Pain-VAS0	Pain-VAS12	Pain-VAS2	D-VAS0	D-VAS12	D-VAS24	HAQDI-0	HAQDI1
1	4.9	4.4	3.8	80	40	40	80	35	40	50	15	15	1.5	1.5
2	4	2.6	2.5	50	50	65	70	65	75	40	20	10	1.8	1.6
3	3.5	3.7	3.9	5	5	5	20	10	20	70	40	25	1.1	1.1
4	4.9	3.3	3.2	50	45	65	30	60	60	45	30	40	1.3	1.3
5	1	/	/	10	/	/	50	/	/	10	/	/	1.5	/
6	2.6	/	/	20	/	/	50	/	/	65	/	/	1	/
7	4.8	4.3	3.7	50	70	50	80	60	40	65	20	25	1.1	0.8
8	2.5	0.8	1.6	5	5	0	70	70	15	50	20	10	NT	NT
9	3.5	2.2	3.1	30	20	25	30	10	10	35	5	20	0.6	0.4
10	5.1	3.2	3.9	20	0	30	80	60	50	30	20	10	2.4	2
	3.68	3.0625	3.2125	32	29.375	35	56	46.25	38.75	46	21.25	19.375	1.36666667	1.2428

Figure 1 Recover from RRP by Filgotinib (200mg/d)+ Denosumab therapy



Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5289

AB0508 EFFICACY OF SULFASALAZINE MONOTHERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO HAD FACTORS ASSOCIATED WITH PREFERENCE FOR SULFASALAZINE OVER METHOTREXATE AS THE FIRST-LINE DRUG

Keywords: Rheumatoid arthritis

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Background: Methotrexate (MTX) is the first-line drug in treating patients with rheumatoid arthritis (RA) [1], while some patients have baseline factors and comorbidities which discourage use of MTX. While treatment with sulfasalazine (SSZ) is often performed in these cases, the efficacy of SSZ monotherapy was not well evaluated using recent disease activity assessment measures such as DAS28-CRP, CDAI and HAQ-DI.
Objectives: The aim of this research is to evaluate the efficacy of SSZ monotherapy in RA patients who had baseline factors and comorbidities associated with preference for SSZ over methotrexate as the first-line drug.
Methods: 78 treatment-naïve RA patients who started treatment with SSZ were included. We compared outcomes of SSZ monotherapy in patients with and without each of the following baseline factors and comorbidities: age 75 years or more, seronegative RA, moderate disease activity or less (DAS28-CRP, CDAI and HAQ-DI), and presence of comorbidities in lung, renal and liver.
Results: Baseline disease activity was higher among patients with 75 years old or more compared with those with under 75 years old (DAS28-CRP as 4.9 and 3.9, CDAI as 24 and 17 and HAQ-DI as 1.4 and 0.8), while those were similar at week 24 (DAS28-CRP as 3.3 and 3.2, CDAI as 14 and 12 and HAQ-DI as 0.8 and 0.5). There was no significant difference in disease activity at baseline and week 24 regardless seronegative or seropositive RA. There were also no significant differences in disease activity at baseline and week 24 regardless presence or absence of comorbidities in lung, renal and liver. Disease activity at week 24 tended to be high among patients with high disease activity at baseline comparing to those with moderate or less disease activity at baseline, whereas no statistically significant difference was observed (baseline DAS28-CRP as 5.0 and 3.3 and DAS28-CRP at week 24 as 3.5 and 2.9).
Conclusion: SSZ was similarly effective in treating elderly RA patients, patients with seronegative RA and RA patients with comorbidities in lung, renal and liver, comparing in treating those without any baseline factors and comorbidities.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5991

AB0509

CLINICAL EQUIVALENCE OF GENERIC AND BRANDED TOFACITINIB IN REAL-WORLD: A PROSPECTIVE LONGITUDINAL COHORT STUDY IN RHEUMATOID ARTHRITIS PATIENTS

Keywords: Real-world evidence, Rheumatoid arthritis

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Background: The efficacy and safety of Xeljanz® have also been confirmed in RA patients. Varieties of generic tofacitinib have been developed in different countries. However, there is no study comparing the efficacy and safety between generic and brand-name tofacitinib yet.
Objectives: In the current study, we compared the efficacy, safety, and cost-effectiveness between a Chinese generic tofacitinib Kelejia® and the brand-name tofacitinib Xeljanz® in RA patients from a prospective real-world cohort.
Methods: RA patients receiving tofacitinib, either generic (Kelejia®, generic group) or branded (Xeljanz®, branded group) were enrolled. All the patients were followed up until the discontinuation of tofacitinib or last visit. Primary outcome was simplified disease activity index (SDAI) defined remission rate at month 6. Secondary outcomes included the rates of remission and low disease activity (LDA) defined by other composite scores; EULAR response rate and ultrasonic synovitis scores at month 1, 3, 6 and 12. Cost-effectiveness was investigated. Propensity score-based inverse probability of treatment weighting (IPTW) was adopted to reduce selection bias.
Results: 204 patients were enrolled, with 59 in generic group and 145 in branded group. The SDAI defined remission was achieved in 41.1% and 39.2% patients in generic group and branded group at month 6, respectively (p=0.854). The rates of remission and LDA achievement, the changes of clinical disease activity scores, power doppler (PD) and gray scale (GS) synovitis scores at months 1, 3, 6 and 12 from baseline were all comparable between two groups. Similar proportions of patients in two groups achieved moderate/good response. Rates of drug retention (78.0% vs 77.2%, p=0.911) and adverse effect (5.1% vs. 4.8%, p=1.000) were also similar in two groups. Both Kelejia® and Xeljanz® were cost-effective, but Kelejia® had lower average cost-effectiveness ratio.
Conclusion: Generic tofacitinib (Keljia®) showed equivalent clinical efficacy and safety, and better cost-effectiveness comparing with its originator (Xeljanz®). Keljia® can be an alternative to brand-name Tofacitinib.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2267

AB0510

COST-EFFECTIVE ANALYSIS OF GENERIC TARGETED SYNTHETIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUG - TOFACITINIB IN RHEUMATOID ARTHRITIS (TIRA CEA STUDY)

Keywords: Rheumatoid arthritis, Targeted synthetic drugs

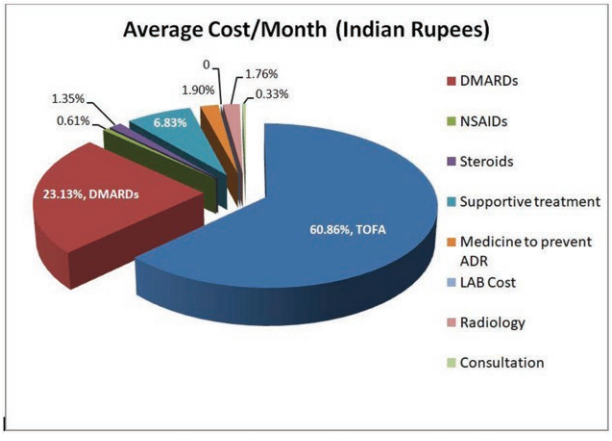
D. Syngle[1], I. Verma[2], K. Chauhan[3], S. Patyal[3], A. Syngle[3,4]. *[1]Healing Touch Foundation, Research & Innovations, Chandigarh, India; [2]MM College of Pharmacy, MMU, Pharmacy Practice, Mullana, India; [3]Healing Touch City Clinic, Internal Medicine & Rheumatology, Chandigarh, India; [4]Fortis Hospital Mohali, Internal Medicine & Rheumatology, Sahibzada Ajit Singh Nagar, India*

Background: With the introduction of generic version of tsDMARD tofacitinib in different parts of the world, its important to perform a cost-effective analysis of introducing generic tofacitinib to the current treatment sequence for patients with moderate-to-severe rheumatoid arthritis who have inadequate response or intolerance to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs-IR).
Objectives: Perform pharmacoeconomic analysis of introducing generic tofacitinib into the current treatment sequence for patients with moderate-to-severe rheumatoid arthritis who are csDMARDs-IR.
Methods: A prospective, observational study was conducted in 55 consecutive RA Indian patients (Table 1) meeting 2010 Rheumatoid Arthritis Classification Criteria with active disease and an inadequate response or intolerance to conventional disease-modifying antirheumatic drugs randomized to receive tofacitinib 5 mg bd as an add on therapy. All study patients attended the rheumatology OPD with 3 months follow-up. Average cost effectiveness analysis was done by taking HAQ-DI score as a measure of effectiveness. Total cost estimation included cost of the treatment, monitoring cost and adverse effect management.

Table 1. Demographic, clinical and biochemical characteristics of 55 Rheumatoid Arthritis patients

Age (years)	54.93 ± 8.92
Gender: M/F (n)	10/45
BMI (kg/m^2)	24.52 ± 4.58
Disease Duration (yrs)	14.11 ± 6.96
RF Positive	27 (49%)
Anti CCP	12 (21%)
Systolic Blood Pressure (mm Hg)	125.0 ± 10.34
Diastolic Blood Pressure (mm Hg)	84.56 ± 10.44
Disease Duration (years)	5.78 ± 4.84
ESR (mm 1st hr)	36.86 ± 16.47
CRP (mg/dl)	18.47± 19.19
DAS-28	5.31 ± 2.16
HAQ-DI	1.39 ± 0.60

Results: RA patients included in study had established disease with 18.18% males and 81.81% females and 49% were seropositive. Majority of the study RA patients (89%) were on a background regimen of two synthetic DMARDs (MTX and HCQ-80%, MTX and LEF-5.45%, SSZ and HCQ-3.63%,) and 1.81% of the RA patients were on a combination of three sDMARDs. After 3 months treatment with generic tofacitinib and other csDMARDS, the DAS-28 score improved from 5.31 ± 2.16 to 3.81±1.21, p≤0.001 and the mean disability index estimated by HAQ-DI reduced from 1.39± 0.60 to 0.62 ± 0.37, p<0.001. The direct medical cost of treatment of RA per month is 3032.81 rupees (34.39 Euro or 37.31 USD). The average cost effectiveness ratio for the treatment with generic tofacitinib and continuing the use of csDMARDs was Rs 3,938.71 (equivalent to 44.67 Euro or 48.48 USD) to gain or improve one unit of HAQ-DI score. Cost percentage for each head is depicted in Graph 1.
Conclusion: Treatment with generic tofacitinib is effective to control the disease activity and improves disability in RA. Incorporating generic tofacitinib into the csDMARD treatment sequence in active RA patients who have inadequate response or intolerance to csDMARDs is effective to improve the disability index. These results, reflecting the additional costs associated with deteriorating health condition, support the importance of using generic tofacitinib.



Graph 1.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5306

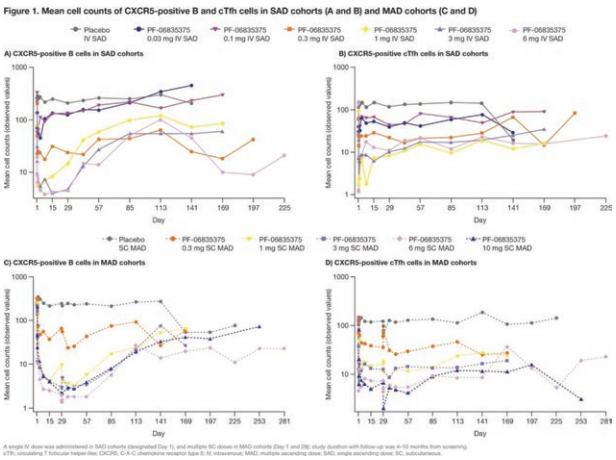
SLE, Sjön's and APS - treatment

AB0511 A PHASE 1, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, SINGLE- AND MULTIPLE-DOSE ESCALATION STUDY TO EVALUATE THE SAFETY, PHARMACOKINETICS AND PHARMACODYNAMICS OF PF-06835375 IN PATIENTS WITH SEROPOSITIVE SYSTEMIC LUPUS ERYTHEMATOSUS OR RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Clinical trials, Systemic lupus erythematosus

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Background: PF-06835375 is a humanised, afucosyl IgG1 antibody selective against C-X-C chemokine receptor type 5 (CXCR5), a receptor expressed on B cells, bona fide T follicular helper (Tfh) cells and circulating T follicular helper-like (cTfh) cells. PF-06835375 is in development for autoimmune diseases through depletion of CXCR5-positive B and Tfh cells and antagonism of C-X-C motif chemokine ligand 13-dependent signalling.
Objectives: This first-in-human study evaluated the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of PF-06835375 in patients with seropositive systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA).
Methods: This multi-centre, double-blind, placebo-controlled Phase 1 study enrolled patients aged 18–70 years with seropositive SLE (diagnosed by Systemic Lupus International Collaborating Clinics classification criteria, and positive anti-nuclear antibody titres ≥1:80 and/or anti-dsDNA and/or anti-Smith antibodies) or RA (diagnosed by 2010 ACR/EULAR criteria and positive rheumatoid factor and/or anti-citrullinated peptide antibody), with no minimum disease activity requirement. Patients were randomised to intravenous (IV) PF-06835375 (0.03, 0.1, 0.3, 1, 3 or 6 mg) or placebo in 6 sequential single ascending dose (SAD) cohorts, or to subcutaneous (SC) PF-06835375 (0.3, 1, 3, 6 or 10 mg) or placebo administered on Days 1 and 29 in 5 multiple ascending dose (MAD) cohorts. Pre-and post-dose corticosteroids were permitted to manage infusion or injection reactions at the investigator's discretion. Primary endpoints were incidence of treatment-emergent adverse events (TEAEs) of all casualties, infections and laboratory, vital sign and electrocardiogram (ECG) abnormalities. Secondary endpoints were PK parameters, change in circulating CXCR5-positive B- and cTfh-cell counts and incidence of anti-drug antibodies (ADAs).
Results: In total, 74 patients were randomised and 73 were treated (SAD cohorts: SLE, n=17; RA, n=14; MAD cohorts: SLE, n=22; RA, n=20). Corticosteroids were given in PF-06835375 3 and 6 mg IV cohorts and 3, 6 and 10 mg SC cohorts. Mean (standard deviation) age was 53.3 (10.7) years. Most patients were female (n=65, 89.0%) and White (n=54, 74.0%). In total, 62 patients (84.9%) experienced TEAEs; most were mild or moderate. Serious adverse events were reported in 3 patients (9.7%). One patient (1.4%) discontinued due to a TEAE of disease progression (placebo SC cohort). The most common TEAEs were headache (n=18, 24.7%), pyrexia (n=11, 15.1%) and urinary tract infection (n=9, 12.3%). All infections were mild or moderate. Laboratory abnormalities (placebo IV SAD, PF-06835375 1 mg IV SAD and PF-06835375 3 mg SC MAD) and ECG abnormalities (PF-06835375 0.1, 1 and 6 mg IV SAD) were reported as TEAEs in individual patients. No deaths occurred. In IV SAD cohorts, median T_{max} ranged from 2–4 h and mean CL ranged from 0.021–0.313 L/h. Exposure (AUC_{inf} and C_{max}) generally increased dose-proportionally for doses ≤1 mg and more than dose-proportionally for doses >1 mg. In SC MAD cohorts, median T_{max} ranged from 121–171 h and mean CL/F ranged from 0.07847–0.1171 L/h. Exposure (AUC_{tau} and C_{max}) generally increased dose-proportionally. B- and cTfh-cell counts generally showed dose-dependent reductions across cohorts (range of mean maximum depletion: 67.3–99.3% and 62.4–98.7%, respectively, in SAD, and 91.1–99.6% and 89.5–98.1%, respectively, in MAD cohorts; Figure 1). Mean duration of B- and cTfh-cell depletion extended up to 71.6 and 62.0 days, respectively, in SAD, and 78.5 and 109.5 days, respectively, in MAD cohorts. ADA data did not suggest any clinically relevant impact on PK, PD or safety.



Conclusion: PF-06835375 was generally well tolerated in patients with seropositive SLE and RA with potent and prolonged B- and cTfh-cell depletion, supporting further development as a treatment for autoimmune diseases.
Acknowledgements: This study was sponsored by Pfizer Inc. Medical writing support, under the direction of the authors, was provided by Sonya Frazier, PhD, CMC Connect, a division of IPG Health Medical Communications, and was funded by Pfizer Inc, New York, NY, USA, in accordance with Good Publication Practice (GPP 2022) guidelines (Ann Intern Med 2022; 175: 1298-1304).
Disclosure of Interests: Stanley Cohen Consultant of: Pfizer Inc, Jean Beebe Employee of: Former employee of Pfizer Inc, Vishala Chindalore: None declared, Shunjie Guan Employee of: Employee of Pfizer Inc, Mina Hassan-Zahraee Employee of: Employee of Pfizer Inc, Craig Hyde Employee of: Employee of Pfizer Inc, Sarita Koride Employee of: Employee of Pfizer Inc, Robert Levin Speakers bureau: AbbVie and GlaxoSmithKline, Consultant of: AbbVie, AstraZeneca and Janssen, Shannon Lubaczewski Employee of: Employee of Pfizer Inc, Mikhail Salganik Employee of: Employee of Pfizer Inc, Abigail Sloan Employee of: Employee of Pfizer Inc, Erin Stevens Employee of: Employee of Pfizer Inc, Elena Peeva Employee of: Employee of Pfizer Inc, Michael Vincent Shareholder of: Pfizer Inc, Employee of: Employee of Pfizer Inc, David Martin Employee of: Employee of Pfizer Inc, Myron Chu Employee of: Employee of Pfizer Inc.
DOI: 10.1136/annrheumdis-2023-eular.95

AB0512 INCIDENCE, PREVALENCE AND CURRENT TREATMENT PRACTICE OF SYSTEMIC LUPUS ERYTHEMATOSUS: A GERMAN CLAIMS DATA ANALYSIS

Keywords: Epidemiology, Real-world evidence, Systemic lupus erythematosus

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Background: Despite recent advances in the management of systemic lupus erythematosus (SLE), patients still suffer from reduced quality of life and increased mortality compared to the general population [1]. The latest data for Germany report a prevalence of 38.6 - 55.8 cases per 100,000 between 2009 and 2014, however more recent data as well as investigations on treatment algorithms in a real world setting are limited [2].
Objectives: To investigate incidence and prevalence of SLE for Germany and to evaluate treatment sequences in adult patients with SLE in Germany.
Methods: In this retrospective claims data analysis, 3017 patients with SLE diagnosis between January 2012 and December 2019 were identified for incidence and prevalence analysis. Out of these, 941 incident patients between January 2012 and December 2017 were selected for analysis of current treatment practice. For this analysis, only patients initiating SLE treatment according to guidelines were considered [1]. The date of the earliest prescription for SLE treatment on or following the SLE diagnosis (index date) was defined as start of sequence of therapy (SOT) 1. A new treatment added or switched to resulted in a new SOT. Up to 3 SOTs were measured during follow-up. SLE severity was recorded as previously described [2].

Results: Incidence rates were stable in both genders in Germany between 2012 and 2019, with women showing 3-4 fold higher incidence rates than men. In contrast, prevalence was rising from 40.5 in 2012 to 59.9 per 100,000 people in 2019, with a stronger trend in female patients (Figure 1). The mean (SD) age of the 941 incident patients identified for the treatment practice analysis was 50.6 (15.5) years, 74.4% were female and the mean (SD) follow-up duration was 1836 (634) days. 681 (70.3%) patients initiated SLE treatment (SOT1), with 246 (26.1%) progressing on to SOT2 and 113 (16.6%) on to SOT3. Monotherapies were most commonly prescribed in SOT1 (52.4%), while the use of combination therapies increases with SOT (SOT1 47.6%, SOT2 76.8%, SOT3 77.9%). Antimalarials in combination with corticosteroids were the most prescribed therapy during SOT1 (30.1%), immunosuppressants combined with corticosteroids during SOT2 (32.5%) and antimalarials combined with immunosuppressants and corticosteroids in SOT3 (36.3%). Combination therapies with biologics were used in 2.5% of patients in SOT2 and 8.8% of patients in SOT3 (Table 1). Disease severity increases with SOT.

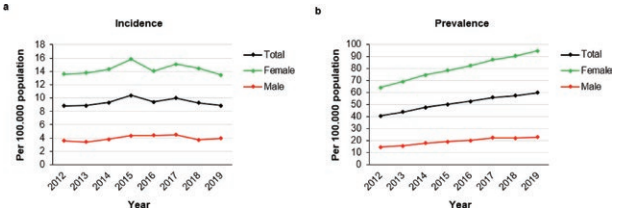


Figure 1

Table 1

Type of therapy	SOT1 (n=681)	SOT2 (n=246)	SOT3 (n=113)
Monotherapy - n(%)	**357(52.42%)**	**57(23.17%)**	**25(22.12%)**
Antimalarials	129(18.94%)	28(11.38%)	10(8.85%)
Immunosuppressants	15(2.20%)	25(10.16%)	14(12.39%)
Biologics	1(0.15%)	4(1.63%)	1(0.88%)
Intravenous Immunoglobulins	1(0.15%)	0(0.00%)	0(0.00%)
Corticosteroids	211(30.98%)	0(0.00%)	0(0.00%)
Combination therapies - n(%)	**324(47.58%)**	**189(76.83%)**	**88(77.88%)**
Antimalarials + IS	7(1.03%)	4(1.63%)	2(1.77%)
Antimalarials + IS + CS	42(6.17%)	49(19.92%)	41(36.28%)
Antimalarials + biologics + CS	1(0.15%)	1(0.41%)	3(2.65%)
Antimalarials + biologics	0(0.00%)	0(0.00%)	1(0.88%)
Antimalarials + CS	205(30.10%)	50(20.33%)	15(13.27%)
Antimalarials + IS + biologics + CS	0(0.00%)	3(1.22%)	0(0.00%)
IS + CS	68(9.99%)	80(32.52%)	20(17.70%)
IS + biologics	0(0.00%)	0(0.00%)	1(0.88%)
IS + biologics + CS	1(0.15%)	1(0.41%)	0(0.00%)
Biologics + CS	0(0.00%)	1(0.41%)	5(4.42%)

IS … Immunosuppressants, CS … Corticosteroids

Conclusion: While incidence of SLE is stable, prevalence is rising among German patients with statutory health insurance. Our data show that for newly diagnosed patients a combination of medication frequently including corticosteroids is required over time to control their disease. These data suggest a persistent unmet need for more effective treatment strategies for better SLE disease management and complement a recent US claims data analysis [3].

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Disclosure of Interests: Tobias Alexander Speakers bureau: Abbvie, Amgen, AstraZeneca, Bayer, GSK, Lilly, Medac, Roche, Consultant of: Abbvie, Amgen, Bayer, GSK, Lilly, Grant/research support from: Amgen, Janssen, Miltenyi, Marcus Schulte Shareholder of: AMGEN Inc., Employee of: AMGEN GmbH, Julia Borchert: None declared, Tarcyane Garcia: None declared, Eva Schrom Shareholder of: Amgen Inc., Employee of: Amgen GmbH.

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AB0513 SCREENING FOR HYDROXYCHLOROQUINE-INDUCED CARDIOMYOPATHY: A PROSPECTIVE OBSERVATION IN PATIENTS WITH CONNECTIVE TISSUE DISEASE WHO HAVE BEEN ON TREATMENT FOR MORE THAN 5 YEARS

Keywords: Disease-modifying drugs (DMARDs), Safety

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Background: Antimalarial-induced cardiomyopathy is a rare complication of prolonged use of antimalarial treatment. It can present with a conduction disorder, heart failure, or ventricular hypertrophy [1]. A systematic review has highlighted that early recognition and drug withdrawal are crucial and can potentially lead to recovery of cardiac function in up to 45% of patients. Despite this, there remains a significant risk of irreversible damage and death despite discontinuation (12.9% and 30.8% respectively) [2].

Objectives: After identifying our first case of Hydroxychloroquine-induced cardiomyopathy in our department [3], we decided to review the prevalence of this complication in a cohort of patients to determine the need for a screening tool to assess the cardiovascular risk in patients prescribed Hydroxychloroquine for longer than 5 years duration.

Methods: We identified a selection of patients with a diagnosis of a Connective Tissue Disease who had been prescribed Hydroxychloroquine for longer than 5 years. We performed cardiac screening including N-terminal-pro-BNP (NT-pro-BNP), Troponin I (TnI), Creatine Kinase (CK) and an Electrocardiogram (ECG). A basic tool was used to determine the need for further investigations (Echocardiogram +/- Cardiac magnetic resonance imaging) to evaluate the presence or absence of Hydroxychloroquine-induced cardiomyopathy.

Results: A total of 124 patients met the specified criteria of which 115 were female (92.7%) and 9 were male (7.3%) with a mean age of 48 years. The underlying diagnoses included Systemic Lupus Erythematosus (n=103, 83.1%), Mixed CTD (n=9, 7.3%), Sjögren's Syndrome (n=6, 4.8%), Undifferentiated CTD (n=5, 4.0%), and Systemic Sclerosis (n=1, 0.8%). A total of 40 patients (32.3%) had been prescribed Hydroxychloroquine for 5-10 years duration compared to 84 patients (67.7%) who had been prescribed for over 10 years duration. Daily Hydroxychloroquine dose varied from 0-200mg (n=15, 12.1%), 200mg (n=55, 44.3%), 200-400mg (n=13, 10.5%), and 400mg (n=41, 33.1%). Abnormal results which warranted further investigation included raised levels of NT-pro-BNP (7.6%), TnI (4.2%), and CK (11.7%), and specific features seen on ECG (19.3%). A total of 31 patients were investigated using Echocardiography and none of these patients exhibited features suggestive of cardiomyopathy.

Conclusion: We did not identify any patients within this cohort with features suggestive of Hydroxychloroquine-induced cardiomyopathy. Despite the condition being rare, the true prevalence is unknown. Clinicians should remain vigilant and consider including a cardiovascular risk assessment in the long-term management of patients taking Hydroxychloroquine especially in high-risk patients such as those with a high cumulative dose of the medication [3].

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AB0514 LABORATORY MARKER IMPROVEMENTS FOLLOWING LONG-TERM TREATMENT WITH ANIFROLUMAB IN ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN THE PLACEBO-CONTROLLED TULIP EXTENSION STUDY

Keywords: Biomarkers, Randomized control trial, Systemic lupus erythematosus

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Background: Anifrolumab is a type I interferon (IFN) receptor antagonist approved for treating adults with moderate to severe SLE [1]. The efficacy and safety of anifrolumab was evaluated in two 1-year phase 3 TULIP studies (NCT02446912, NCT02446899), and patients completing treatment in TULIP-1/-2 could enter the 3-year, placebo-controlled long-term extension (LTE) study (NCT02794285) [2-4]. Multiple serological markers are available to monitor SLE; notably, lymphopenia is associated with higher SLE disease activity and damage [5]. Assessing the long-term impact of anifrolumab on lymphocytes and other laboratory markers is of clinical interest.
Objectives: To compare the change over time of laboratory markers in blood samples from adults with SLE treated with anifrolumab vs placebo over the 4-year TULIP-LTE period.
Methods: Eligible patients fulfilled 1997 ACR criteria for SLE at TULIP entry, completed the TULIP treatment periods, and reconsented to participate in the LTE study. Here, we analyze data from patients who were randomized to anifrolumab 300 mg or placebo at TULIP entry and who did not change treatment over the TULIP+LTE period. Blood samples were collected from baseline (BL) until Week 208. Laboratory measures (lymphocytes, hemoglobin, platelets, complement C3 and C4, anti–double-stranded DNA antibodies) were analyzed using standard cell count and enzyme-linked immunosorbent assays. Mean changes from BL to Week 208 were analyzed descriptively.
Results: We present data on 536 patients (anifrolumab 300 mg, n=358; placebo, n=178). Assessing lymphocytes over time revealed a numerically greater increase in the anifrolumab vs placebo group during the TULIP studies which was maintained through the 3-year LTE period (Figure 1). BL laboratory characteristics and changes from BL to Week 208 are shown in the Table 1. Numerically greater increases in hemoglobin levels and platelet counts from BL to Week 208 were observed in patients treated with anifrolumab compared with placebo; mean platelet and hemoglobin levels remained in the normal range at BL and Week 208. Among patients with low C3 levels at BL, there was a numerically greater mean improvement in C3 levels to Week 208 with anifrolumab vs placebo.
Conclusion: Long-term improvement of lymphocytes and other laboratory markers, compared with placebo, indicates that type I IFN inhibition with anifrolumab normalizes SLE-related hematological parameters in patients with SLE. This normalization may relate to disease activity reduction and be relevant to long-term health outcomes and complications.
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Figure. Lymphocyte counts over time in the 4-year TULIP-LTE study

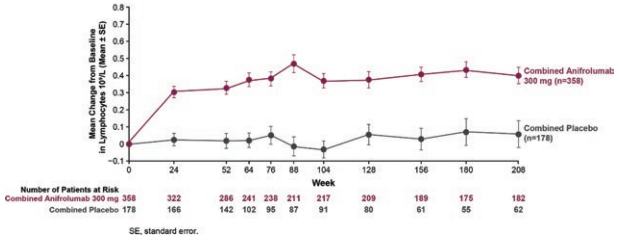


Table 1. Laboratory markers from the 4-year TULIP-LTE study

Treatment	Anifrolumab 300 mg (n=358)			Placebo (n=178)		
	N (BL, Week 208)	BL	Change from BL to Week 208	n (BL, Week 208)	BL	Change from BL to Week 208
		Mean (SE)			Mean (SE)	
Lymphocytes, 10^9/L	358, 182	1.27 (0.034)	+0.40 (0.048)	178, 62	1.26 (0.048)	+0.06 (0.078)
Hemoglobin, g/L	358, 182	125.1 (0.78)	+3.8 (0.95)	178, 62	126.7 (1.18)	−2.3 (1.46)
Platelets, 10^9/L	358, 182	239.9 (4.14)	+24.9 (4.38)	178, 61	248.2 (5.74)	+3.6 (6.25)
C3, g/L[a]	129, 64	0.690 (0.0132)	+0.192 (0.0284)	63, 18	0.712 (0.0187)	+0.085 (0.0579)
C4, g/L[b]	83, 36	0.073 (0.0018)	+0.050 (0.0103)	37, 10	0.073 (0.0022)	+0.012 (0.0093)
Anti-dsDNA, U/mL[c]	165, 79	129.6 (20.47)	−22.1 (45.64)	69, 20	115.3 (20.03)	+15.6 (28.66)

anti-dsDNA, anti–double-stranded DNA; BL, baseline; C3/C4, complement 3/4; LTE, long-term extension; SE, standard error. Baseline is defined as baseline of the phase 3 feeder studies (the last measurement prior to dose administration on Day 1). Only patients with [a]low C3 [<0.9 g/L], [b]low C4 [<0.1 g/L], or [c]positive anti-dsDNA [>15 U/mL], respectively, at baseline are included in this analysis.

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AB0515

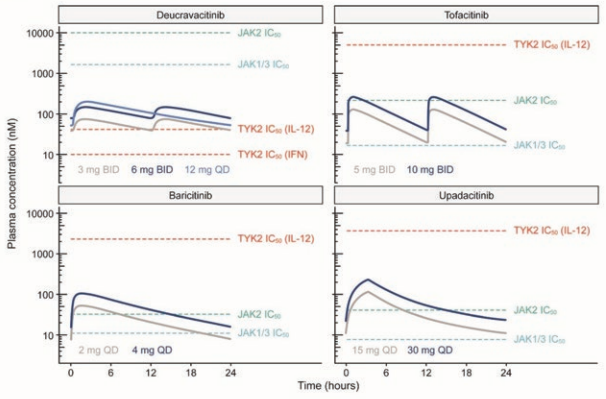
PHARMACOKINETICS, SELECTIVITY PROFILE, AND EXPOSURE-RESPONSE RELATIONSHIP FOR EFFICACY AND SAFETY IN A PHASE 2 STUDY OF DEUCRAVACITINIB, AN ORAL, SELECTIVE, ALLOSTERIC TYK2 INHIBITOR, IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Targeted synthetic drugs

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Background: Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis [1,2]. Deucravacitinib binds to the unique TYK2 regulatory domain, conferring greater functional selectivity vs JAK inhibitors, which bind to the catalytic domain. Deucravacitinib showed superior efficacy vs placebo in a phase 2 trial in SLE (NCT03252587) [3].
Objectives: This analysis assessed the pharmacokinetics (PK), selectivity profile compared to JAK inhibitors, and exposure-response (E-R) relationship for efficacy and safety of deucravacitinib in SLE.
Methods: In the phase 2 trial, patients with active SLE were randomized 1:1:1:1 to placebo or deucravacitinib (3 mg BID, 6 mg BID, 12 mg QD). PK analysis included pooled concentration data from 266 SLE patients and 328 phase 1 participants. IC_{50} was determined by *in vitro* whole blood assays and plotted against PK profiles. E-R analyses included data from 356 patients. Logistic regression analyses assessed the relationship between deucravacitinib exposure and probability of achieving efficacy endpoints and safety events at weeks 32 and 48.
Results: Deucravacitinib PK in SLE patients was not meaningfully different from that in phase 1 participants. At 12 mg QD, deucravacitinib C_{max} was 8-fold lower than JAK 1/3 IC_{50} and 47-fold lower than JAK 2/2 IC_{50} (**Figure 1**). In the E-R analyses, the probability of achieving SRI(4) and BICLA at week 32 increased with increasing deucravacitinib C_{minSS}, with 3 mg BID providing near-maximal response. The E-R relationship for infection and infestation was relatively flat, while skin and subcutaneous tissue disorders increased with increasing deucravacitinib C_{minSS}. These E-R relationships were similar at week 48.
Conclusion: Deucravacitinib PK in SLE patients is not meaningfully different from that in phase 1 participants. At clinically relevant exposures, deucravacitinib demonstrates highly selective inhibition of TYK2 vs JAK 1/2/3. The deucravacitinib E-R relationships are well characterized for various efficacy endpoints and safety events.
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Figure. Plasma concentration-time profile of deucravacitinib, baricitinib, tofacitinib, and upadacitinib along with their respective whole blood IC_{50} curves



BID, twice daily; IC_{50}, half-maximal inhibitory concentration; IFN, interferon; IL-interleukin; JAK, Janus kinase; QD, once daily; TYK2, tyrosine kinase 2.

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AB0516 **WITHDRAWN**

AB0518 **EFFECT OF LITIFILIMAB ON TYPE I INTERFERON (IFN) BIOMARKERS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) OR CUTANEOUS LUPUS ERYTHEMATOSUS (CLE): RESULT OF THE LILAC PHASE 2 STUDY**

Keywords: Biomarkers, Systemic lupus erythematosus, Clinical trials

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Background: Litifilimab (BIIB059) is a humanised IgG1 monoclonal antibody targeting BDCA2, a receptor predominantly expressed on plasmacytoid dendritic cells, that negatively regulates production of Type I IFN and proinflammatory chemokines and cytokines [1,2]. Both Part A (SLE) and Part B (CLE) of the randomised, placebo-controlled Phase 2 LILAC study of litifilimab (NCT02847598) met their primary efficacy endpoints at Weeks 24 and 16, respectively [1,2].
Objectives: To evaluate the effect of litifilimab treatment on IFN gene signature (IFNGS) scores and IFNα levels in LILAC participants.
Methods: Expression of a 22-IFNGS and IFNα concentrations were examined over time in whole blood and serum samples, respectively, from the LILAC modified intent-to-treat population (mITT; Part A N=120, Part B N=132) with a baseline biomarker value and at least one post-baseline value. Treatment effects were estimated using a mixed-effects model repeated measures approach (MMRM) and the dose-response relationship was estimated in Part B using a previously described MCP-Mod method [2].
Results: Few participants had low baseline IFNGS scores, so only data for participants with high baseline IFNGS scores are described here.
At the earliest post-baseline timepoint in Part A (Week 1) a sharp reduction in the mean IFNGS score was observed in the litifilimab 450-mg group vs placebo, which was sustained through Week 24 **(Figure 1; Table 1)**. At the earliest timepoint in Part B (Week 2), reductions in mean IFNGS scores were greater than placebo in all three litifilimab dose groups, and the dose effects were sustained through Week 16 **(Figure 1; Table 1)**. A similar pattern of reductions and dose effects was observed with the corresponding IFNα concentrations **(Table 1)**. Statistically significant (P<0.05) changes from baseline in IFNGS scores and IFNα levels were demonstrated for litifilimab 450 mg in Part A and for the 150-mg and 450-mg groups in Part B **(Table 1)**.
In Part B, the IFNGS-high subgroup's IFNGS scores and IFNα concentrations showed a similar dose-response relationship as was observed for the mITT's CLE clinical responses [2].
Conclusion: Litifilimab treatment induced sustained reductions in 22-IFNGS and IFNα concentrations in participants with SLE and CLE.

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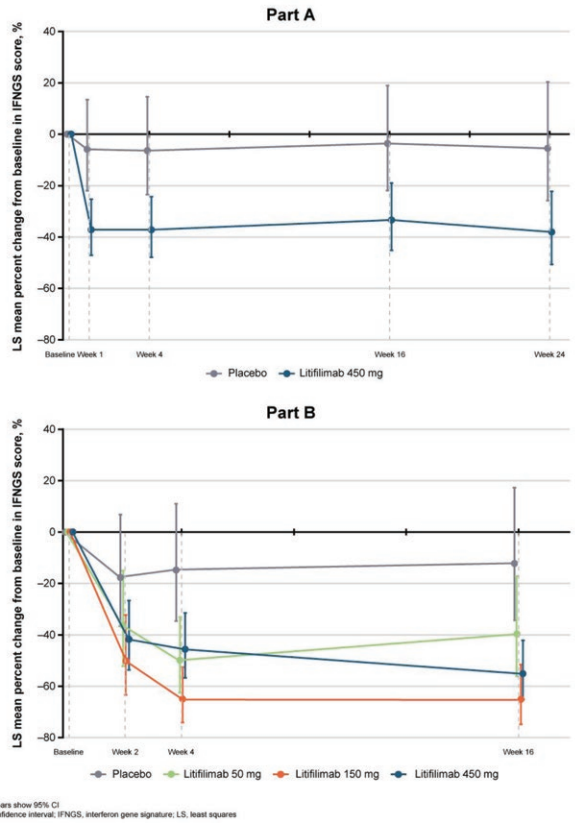
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Table 1. Primary efficacy endpoints and changes from baseline in IFNGS and IFNα levels for the IFNGS-high subgroup (mITT population)

Part A	**PBO**		**450 mg**	
n*	35		42	
Primary endpoint: Change in number of active joints† at Week 24, n	−11		−15	
n	45		49	
Change in IFNGS score, %				
Week 1	−6		−37	
Week 24	−5		−38	
IFNGS GMR‡ vs PBO at Week 24 (95% CI)			0.66 (0.48, 0.89) P=0.0072	
n	41		48	
Change in IFNα levels, %				
Week 1	5		−77	
Week 24	17		−74	
IFNα GMR vs PBO at Week 24 (95% CI)			0.22 (0.11, 0.44) P<0.0001	
Part B	**PBO**	**50 mg**	**150 mg**	**450 mg**
n	29	24	23	40§
Primary endpoint: Change in CLASI-A score at Week 16, %	−11	−41	−50	−44
n	29	24	23	39
Change in IFNGS score, %				
Week 2	−18	−36	−50	−42
Week 16	−12	−40	−65	−55
IFNGS GMR‡ vs PBO at Week 16 (95% CI)		0.69 (0.45, 1.05) P=0.0805	0.40 (0.26, 0.61) P<0.0001	0.51 (0.35, 0.75) P=0.0006
n	28	24	23	40
Change in IFNα levels, %				
Week 1	−14	−64	−75	−64
Week 16	−31	−63	−82	−73
IFNα GMR vs PBO at Week 16 (95% CI)		0.54 (0.25, 1.18) P=0.1225	0.26 (0.12, 0.58) P=0.0012	0.40 (0.20, 0.79) P=0.0088

Data are LS means unless otherwise specified*Assessed in participants who met the joint count inclusion criterion described in Furie 2022[1]†Total active joint count is the sum of the tender joint count and the swollen joint count‡Ratios between the GM fold change from baseline in the litifilimab arm and the GM fold change from baseline in the placebo arm; values <1 favour litifilimab§One participant had missing baseline biomarkers dataCI, confidence interval; CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index–Activity; GM, geometric mean; GMR, geometric mean ratio; IFN, interferon; IFNGS, IFN gene signature; LS, least squares; mITT, modified intent-to-treat; PBO, placebo

Figure. LS mean percent change from baseline in IFNGS score for Part A and Part B participants with a high IFNGS score at baseline



Error bars show 95% CI
CI, confidence interval; IFNGS, interferon gene signature; LS, least squares

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AB0519

LONG-TERM SAFETY OF BELIMUMAB AMONG ADULT PATIENTS WITH SLE: POOLED DATA FROM THREE OPEN-LABEL EXTENSION STUDIES OVER 11+ YEARS

Keywords: Clinical trials, Safety, Systemic lupus erythematosus

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Background: Belimumab is approved for the treatment of systemic lupus erythematosus (SLE) in >75 countries [1]. Clinical trials and long-term extension (LTE) studies have demonstrated the consistent safety profile of belimumab in patients with SLE receiving standard therapy (ST) [2-4]. A pooled analysis of LTE studies could provide a more robust dataset to explore the long-term safety of belimumab.

Objectives: To evaluate the long-term safety of belimumab in adult patients with SLE using pooled data from three multicentre, LTE studies.

Methods: This post hoc analysis pooled data from three belimumab LTE studies: LBSL02 LTE (Phase 2; GSK Study 112626) [2], BLISS-76 LTE (including US patients only; Phase 3; GSK Study 112233) [3], and BLISS-52 + BLISS-76 LTE (excluding US patients from BLISS-76; Phase 3; GSK Study 112234) [4]. Patients were eligible for LTE studies if they completed treatment through Week 72 (LBSL02 and BLISS-76 trials), or Week 48 (BLISS-52 trial). LBSL02 LTE also required an improvement in physician global assessment at Week 72 or 68 versus at first belimumab dose. From the start of each LTE, all enrolled patients received open-label belimumab 10 mg/kg intravenously every 28 days plus ST, regardless of study drug allocation in prior trials. Adverse events (AEs) were assessed at each infusion visit and summarised (based on observed data) any time post baseline (first belimumab dose in prior trial or LTE), and in each year.

Results: In total, 1304 patients were enrolled into the three LTE studies and 1299 (99.6%) received ≥1 dose of study drug (pooled safety population). Cumulative belimumab treated patient-years was 7040.1. Overall, 604 (46.5%) patients completed their respective studies. The main reasons for withdrawal included 'withdrawal by patient' (18.3%) and 'AE' (10.6%). In the pooled safety population, 1054 (81.1%) and 618 (47.6%) patients received steroids and immunosuppressants at baseline, respectively. Over 11+ years, 1267 (97.5%) patients had ≥1 AE (incidence generally decreased yearly; **Table 1**), while 525 (40.4%) had ≥1 serious AE (SAE) and 139 (10.7%) experienced ≥1 AE resulting in study drug discontinuation (incidence of each was stable over time). By system organ class, infections and infestations were the most frequent AE, SAE, and AE resulting in study drug discontinuation. The most common AE of special interest was post-infusion systemic reactions (9.7 events per 100 patient-years). There were 21 (1.6%) deaths in total, 3 (0.2%) were considered possibly related to study drug (cardiogenic shock, lung infection pseudomonal, and pneumonia cytomegaloviral [all n=1]).

Conclusion: Among a large, pooled population of patients with SLE treated with belimumab plus ST for over 11+ years, the incidence of AEs generally decreased or remained stable over time. No new safety concerns were observed. This analysis was limited by use of a self-selected population that had not withdrawn from prior trials, and the open-label nature of the study.

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Table 1. Incidence of treatment-emergent AEs over time* (pooled safety population, N=1299)

n (%)	Any time post baseline† (N=1299)	Year 0–1 (N=1299)	Year 2–3 (N=1140)	Year 4–5 (N=867)	Year 6–7 (N=541)	Year 8–9 (N=175)	Year 10–11 (N=131)	Year 11+ (N=88)
AEs	1267 (97.5)	1168 (89.9)	907 (79.6)	631 (72.8)	361 (66.7)	160 (91.4)	105 (80.2)	45 (51.1)
Serious AEs	525 (40.4)	152 (11.7)	141 (12.4)	91 (10.5)	59 (10.9)	28 (16.0)	14 (10.7)	7 (8.0)
AEs resulting in study drug discontinuation	139 (10.7)	18 (1.4)	30 (2.6)	12 (1.4)	8 (1.5)	3 (1.7)	2 (1.5)	0 (0.0)
Deaths	21 (1.6)	3 (0.2)	3 (0.3)	2 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

*AEs occurred on or after first belimumab dose (in prior trial or LTE); post hoc data shown for every other year†Post-baseline data include follow-up visits. Data from Year 0 up to last visit in the treatment period are shown by years of study participation. Note: patients may be counted in ≥1 year interval

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AB0520

TREATMENT OF PRIMARY SJÖGREN'S SYNDROME BY INHIBITING FCRN: A PHASE 2 RANDOMIZED, PLACEBO CONTROLLED, DOUBLE-BLIND, PROOF OF CONCEPT STUDY WITH EFGARTIGIMOD

Keywords: Sjögren syndrome, Biomarkers, Randomized control trial

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Background: Primary Sjögren's syndrome (pSS) is a chronic, progressive autoimmune disease, characterized by lymphocytic infiltration and progressive destruction of exocrine glands. B cells play a pivotal role in the development of the disease and this results amongst others in production of IgG autoantibodies (especially those which target SSA/Ro, SSB/La ribonuclear complexes) and rheumatoid factor, as well as elevated levels of serum IgG. In addition to symptoms of dry eyes, dry mouth, chronic pain and fatigue, a substantial subset of patients suffer from extraglandular systemic disease. There are no systemic disease-modifying treatments currently registered for the treatment of pSS. Circulating IgGs are rescued from lysosomal degradation via the neonatal Fc receptor (FcRn), extending their half-life. Efgartigimod is a human IgG Fc fragment engineered to block FcRn, thereby reducing serum IgG levels without impacting other immunoglobulins that are not recycled by FcRn. In phase II and III studies across a range of indications, efgartigimod decreased serum concentrations of total IgG, including pathogenic autoantibodies, without reducing albumin levels. Efgartigimod is well tolerated, and most adverse events were mild.

Objectives: We hypothesize that a reduction in autoantibodies by efgartigimod will target the underlying pathogenesis of pSS and will result in reduced systemic disease activity and symptoms. We present a phase II multicenter, randomized, placebo-controlled, double-blind, proof-of-mechanism study initiated to evaluate the safety and efficacy of efgartigimod in adult participants with pSS.

Methods: Adult patients with pSS fulfilling the ACR-EULAR classification criteria, time since diagnosis of ≤7 years, anti-SSA/Ro positivity, presence of residual salivary flow (UWSF rate >0 and/or SWSF rate >0.10) and moderate to high systemic disease activity (ESSDAI score ≥5) are eligible for participation in the study. Approximately 30 patients will be randomly allocated (2:1) to receive weekly intravenous efgartigimod or placebo for 24 weeks. At the end of the treatment period, participants who complete the study may roll over into an open-label extension (OLE).

Results: The primary endpoint is the proportion of responders to the Composite of Relevant Endpoints for Sjögren's Syndrome (CRESS; response on ≥3 out of 5 items) at week 24. Key secondary endpoints include proportion of responders to the Sjögren's Tool for Assessing Response (STAR) and change from baseline in the clinESSDAI, ESSDAI, and ESSPRI scores. Additional endpoints include changes in parotid gland pathology to understand the effects of efgartigimod on pSS disease pathology and blood-based biomarkers to explore the effect on innate and adaptive immune response. Safety will be assessed by incidence and severity of adverse events and laboratory evaluations.

Conclusion: This phase II study of efgartigimod will evaluate the effect of FcRn inhibition on disease pathology and the potential for therapeutic benefit in patients with pSS.

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AB0521

IDENTIFICATION OF AN INTERFERON 5-GENE SIGNATURE SCORE AS A PHARMACODYNAMIC AND POTENTIAL PREDICTIVE BIOMARKER FOR DEUCRAVACITINIB TREATMENT IN A PHASE 2 TRIAL IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Biomarkers, Systemic lupus erythematosus, Targeted synthetic drugs

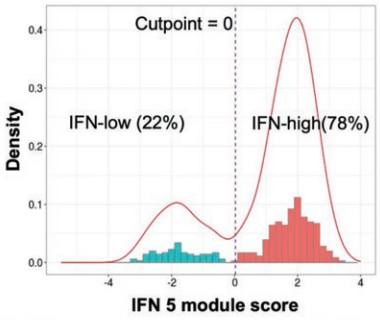
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Background: Tyrosine kinase 2 (TYK2) mediates cytokine pathways (eg, Type I IFN) linked with systemic lupus erythematosus (SLE) pathogenesis. Deucravacitinib is a first-in-class, oral, selective, allosteric TYK2 inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis [1,2]. Deucravacitinib was efficacious compared with placebo in a phase 2 SLE trial [3].
Objectives: To develop a customized IFN 5-gene signature score, assess the pharmacodynamic effects of deucravacitinib on the IFN score, and evaluate the score's association with SLE disease activity and clinical response in the phase 2 trial.
Methods: Patients with active SLE were randomized equally to oral placebo or deucravacitinib (3 mg BID, 6 mg BID, or 12 mg QD). DxTerity chemical ligation-dependent probe amplification was used to measure 51 immune system-related genes from whole blood. IFN genes were selected based on distribution, correlations, hierarchical clustering, and consistency of k-means clusters. Serum proteins, blood cell subsets, and antibody profiles were measured by immunoassays and flow cytometry. SRI(4) and BICLA were measured at weeks 32 and 48.
Results: An IFN 5-gene (*MX1*, *HERC5*, *IFIT1*, *RSAD2*, and *EIF2AK2*) signature score was identified and used to classify patients into IFN-high or IFN-low subgroups (**Figure 1**). Higher baseline IFN score was associated with higher baseline SLEDAI and CLASI disease activity scores, higher levels of IFN activity biomarker (eg, IFNα, IFNλ, BAFF, CXCL10) and anti-dsDNA, and lower complement and lymphocyte counts. Baseline IFN score was not predictive of SRI(4) response. A higher baseline IFN score was associated with a significantly higher probability of BICLA response with deucravacitinib 3 mg BID relative to placebo (P=0.014). Deucravacitinib reduced the IFN score from weeks 4 through 44 by >50%.
Conclusion: These data support the IFN 5-gene signature score as a biomarker to classify patients with SLE into IFN-high or IFN-low subgroups; however, clinical response by IFN score was inconsistently improved (**Table 1**). IFN-regulated gene expression performs well as a pharmacodynamic biomarker to confirm deucravacitinib mechanism of action and to aid in phase 3 dose selection.

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Figure: IFN 5-gene signature score with k-means clustering-derived cutpoint in the PAISLEY trial



IFN 5 genes: *MX1, HERC5, IFIT1, RSAD2, EIF2AK2*

N = 358 samples from the screening phase of the PAISLEY ITT population

Percentage of patients, out of 358, that were in the IFN-low or IFN-high subgroup at screening is shown.
IFN, interferon; ITT, intent to treat.

Table 1. Clinical response at week 32

	Placebo N = 90	Deucravacitinib 3 mg BID N = 91	Deucravacitinib 6 mg BID N = 93	Deucravacitinib 12 mg QD N = 89
SRI(4) response rate, n/N (%)				
IFN High	21/65 (32.3)	47/76 (61.8)	37/73 (50.7)	35/69 (50.7)
IFN Low	10/25 (40.0)	8/15 (53.3)	11/20 (55.0)	5/20 (25.0)
BICLA response rate, n/N (%)				
IFN High	18/65 (27.7)	39/76 (51.3)	31/73 (42.5)	30/69 (43.5)
IFN Low	13/25 (52.0)	7/15 (46.7)	13/20 (65.0)	7/20 (35.0)

BICLA, British Isles Lupus Assessment Group–Based Composite Lupus Assessment; BID, twice daily; IFN, interferon; QD, once daily; SRI, Systemic Lupus Erythematosus Responder Index.

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AB0522

EVALUATING GLOBAL PATTERNS IN TREATMENT AND PREVALENCE OF COMORBIDITIES IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Comorbidities

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Background: Regional disparities in the management of systemic lupus erythematosus (SLE) are frequently described. Governance, funding, logistic barriers, and physician choice may be important determinants though scarce data from underrepresented regions limits our understanding.

Objectives: To evaluate global patterns in treatment of SLE and identify the prevalence of comorbidities.

Methods: We identified SLE patients from the COVAD 2 database, consisting of over 20,000 respondents worldwide. Healthy controls (HC) were included to assess population comorbidity levels. Demographics, treatment i.e., corticosteroids (CS), antimalarials, immunosuppressants (IS), cyclophosphamide and biologics plus comorbidity data was recorded. Country Human Development Index (HDI) classification, a composite index formulated by the United Nations to rank countries into tiers of development, was utilised.

Results: 3323 HCs and 1167 SLE patients were included in analysis. Patients from low/medium HDI (lmHDI) countries were younger than those from high/very high HDI (hvhHDI) countries (median age 32, IQR 27-41 vs 41, IQR 32-52 years, p<0.0001). Disease duration was shorter in lmHDI countries (median 5, IQR 3-10 vs 10, IQR 5-19 years, p<0.0001). A higher proportion of SLE patients from lmHDI countries were on CS (73% vs 59%, p=0.0002), antimalarials (81% vs 68%, p=0.0002) and IS (66% vs 53%, p=0.0009) compared with patients from hvhHDI countries. Choice of IS varied with azathioprine prescribed more frequently in lmHDI countries (p=0.049). Biologics use was more common in hvhHDI countries (7% vs 2%, p=0.0055). Comorbidity prevalence was similar between groups, however when adjusted for age, patients with chronic kidney disease were significantly younger in lmHDI countries (36.67 vs 44.64 years, p=0.015), as were patients with coronary artery disease (35.7 vs. 44.6 years, p=0.015) and hypertension (41.5 vs 49.8 years, p=0.003). Results are detailed in Table 1.

Conclusion: To our knowledge, this is the largest study evaluating treatment and comorbidity incidence in SLE populations based on country HDI. We identified striking differences in pharmacological management globally. Cardiovascular comorbidities were seen in younger patients and earlier in the disease course in lmHDI countries, suggestive of premature organ damage. This could be due to limited global access to high-cost medication and increasing access may improve outcomes. Our results call for review of cardiovascular risk guidelines and regional approaches to preventive action as well as pharmacological and non-pharmacological management of patients with established cardiovascular comorbidity.

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Table 1

	Low HDI (n=50)		Medium HDI (n=163)		High HDI (n=265)		Very High HDI (n=689)		All SLE Patients (n=1167)		p value (SLE lmHDI vs hvhHDI)
Immunosuppressants, n (%)	**36 (72)**		**104 (64)**		**169 (64)**		**339 (49)**		**648 (56)**		**0.0009*****
Methotrexate, n (%)	5 (10)		27 (17)		35 (13)		91 (13)		158 (14)		ns
Mycophenolate Mofetil, n (%)	*9 (18)*		*45 (28)*		*70 (26)*		*127 (18)*		*251 (22)*		ns
Azathioprine, n (%)	*21 (42)*		*32 (20)*		*65 (25)*		*113 (16)*		*231 (20)*		***0.049****
Cyclophosphamide, n (%)	**0 (0)**		**3 (2)**		**2 (1)**		**9 (1)**		**14 (1)**		ns
Corticosteroids, n (%)	**37 (74)**		**119 (73)**		**159 (60)**		**404 (59)**		**719 (62)**		**0.0002*****
No Steroids, n (%)	7 (14)		20 (12)		50 (19)		92 (13)		169 (15)		ns
<10 mg/day, n (%)	*17 (34)*		*58 (36)*		*89 (34)*		*184 (27)*		*348 (30)*		*0.057 (ns)*
10-20 mg/day, n (%)	*9 (18)*		*19 (12)*		*20 (8)*		*47 (7)*		*95 (8)*		***0.003****
>20 mg/day, n (%)	*3 (6)*		*7 (4)*		*10 (4)*		*16 (2)*		*36 (3)*		*ns*
Antimalarials, n (%)	**40 (80)**		**133 (82)**		**182 (69)**		**469 (68)**		**824 (71)**		**0.0002*****
Biological treatments, n (%)	**1 (2)**		**3 (2)**		**19 (7)**		**48 (7)**		**71 (6)**		**0.005****
Comorbidities	**SLE**	**HC**	**SLE**	**HC**	**SLE**	**HC**	**SLE**	**HC**	**SLE**	**HC**	
Chronic Kidney Disease, n (%)	***5**** *(10)*	*0 (0)*	***13**** *(8)*	*7 (0.8)*	***31**** *(12)*	*5 (0.4)*	***76**** *(11)*	*4 (0.4)*	***125**** *(11)*	*16 (0.5)*	*Ns*
Coronary Heart disease, n (%)	*1 (2)*	*1 (0.5)*	*2 (1)*	*8 (0.9)*	***11**** *(4)*	*6 (0.4)*	*15 (2)*	*15 (1.6)*	***29**** *(2)*	*30 (1)*	*Ns*
Diabetes, n (%)	*2 (4)*	*11 (0.5)*	*4 (2)*	*51 (5.5)*	*7 (3)*	*33 (3)*	*28 (4)*	*29 (3)*	*41 (4)*	*124 (4)*	*Ns*
Hypercholesterolaemia, n (%)	*2 (4)*	*5 (2)*	*6 (4)*	*48 (5)*	*17 (6)*	*91 (7)*	*75 (11)*	*77 (8)*	***100**** *(9)*	*221 (7)*	***0.0055****
Hypertension, n (%)	*8 (16)*	*28 (13)*	*24 (15)*	*95 (10)*	***37**** *(14)*	*122 (10)*	***122**** *(18)*	*77 (8)*	*191 (16)*	*212 (6)*	*Ns*

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AB0523 TOXIC EPIDERMAL NECROLYSIS(TEN) IN SYSTEMIC LUPUS ERYTHEMATOSUS(SLE): RESULTS FROM A MULTI-INSTITUTIONAL COHORT FROM INDIA

Keywords: Skin, Systemic lupus erythematosus, Descriptive Studies

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Background: Toxic Epidermal Necrolysis(TEN) is a rare but life-threatening manifestation of Systemic Lupus Erythematosus (SLE). Epidermal necrolysis (EN), including Stevens–Johnson syndrome and TEN, is commonly drug induced. Furthermore, flares of SLE may present as EN (TEN-like LE). To the best of our knowledge, this is the largest series of SLE-TEN.

Objectives: The current study aimed to study the clinical characteristics and outcome of SLE-related TEN in the Indian population.

Methods: All patients satisfying ACR/EULAR 2019 criteria for SLE and clinically diagnosed with TEN were retrospectively reviewed and compiled from 7 rheumatology centres across India. Drug-induced TEN were excluded from the analysis.

Results: 16 patients (1 child) were included in the study. The majority of patients were females (13/81.25%). The median age of presentation was 25 (8-50) years, and one-third of patients (5/31.5%) presented with TEN as one of their first manifestations. All patients of TEN had active lupus in more than one domain (Median SLEDAI, 20.5). Involvement of constitutional domain followed by hematological was most common (Figure 1). Involvement of other domains is described in Figure 1. Most patients had low complements (14/87.5%), positive anti-dsDNA (13/81.25%) and anti-SSA positivity (12/75%). Management was dictated by activity in various domains and all patients had received steroids (1mg/kg in 13 and 0.5mg/kg in 3). Half of them received intravenous (IV) pulse steroid therapy and one-fourth were administered IV Immunoglobulins (IVIG). All but one patient were put on a steroid-sparing agent (Table 1). Outcomes were good, with all patients recovering from the TEN episode. Two patients who were lost to follow up, had died at their home and exact cause of death could not be ascertained.

Conclusion: TEN was a presenting manifestation in one-third of the patients with active disease in more than one domain. More than half of the patients had renal involvement and a quarter had Neuropsychiatric lupus (NPSLE). Anti-dsDNA, Anti-SSA positivity and low complements were common in patients with SLE-TEN. All patients required high-dose steroids for acute management of TEN, with maintenance therapy being guided by other domains involved. Though IVIG is often mentioned in literature as the treatment of choice for TEN, Most patients with SLE-TEN did well with pulse and oral Steroids suggesting IVIG could be reserved for patients with severe, resistant disease or in patients with concomitant sepsis.

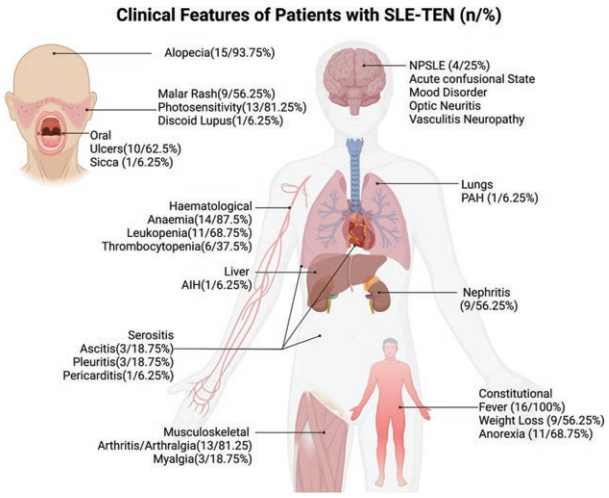


Figure 1. Clinical features of Patients with SLE-TEN (Created with Biorender.com)

Table 1. Serological and Treatment details of Patients with SLE-TEN

Lab Features			Treatment Details		
N=16	No.	%	Acute Management		
DCT	4	25	N=16	No.	%
ANA	16	100	IVIG	4	25%
Anti-DsDNA	13	81.25	Pulse	7	43.75
Low C3	14	87.5	1mg/kg	13	81.25
Low C4	11	68.75	0.5mg/kg	3	18.75
Anti-Sm	5	31.25	Maintenance therapy		
Anti-RNP	5	31.25	AZR	7	43.75
Anti-La	4	25	MMF	2	12.5
Anti-Ro 52	10	62.5	RTX	2	12.5
Anti-Ro60	10	62.5	CYC	4	25
Anti-SSA	12	75	Steroids	1	6.25
Anti Nucleosome	3	18.75	IVIG	7	43.75
Anti-Histone, Anti-RibosomalP, Anti SCL 70*	2	12.5	Pulse methylprednisolone	2	12.5

*- each of the antibody was present in two patients (might not be the same patient)

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0524 IN SLE PATIENTS TREATED WITH BELIMUMAB TYPE I INTERFERON AND BAFF GENE SIGNATURES PREDICT CLINICAL RESPONSE: EVIDENCE FOR REVERSAL OF MOLECULAR PATHWAYS LINKED TO ACTIVITY AND SEVERITY UPON TREATMENT

Keywords: bDMARD, Systemic lupus erythematosus

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Background: Belimumab, a monoclonal antibody against B-cell activating factor (BAFF), is the first biological agent approved in patients with systemic lupus erythematosus (SLE) with persistently active or flaring disease [1].

Objectives: To determine molecular signatures that may predict response to therapy based on RNA sequencing analysis and the impact of belimumab on previously defined molecular signatures of SLE activity and severity [2,3].
Methods: Whole blood transcriptome samples were obtained from 38 patients with active moderate to severe SLE at baseline and 6 months after initiation of treatment with belimumab. Disease activity was determined using the SLE-DAI-2K while response to treatment was defined as the achievement of lupus low disease activity state (LLDAS) at 6 months (M6). DESeq2 was used to call differentially expressed genes (DEGs) and weighted correlation network analysis (WGCNA) was applied to uncover gene module-traits associations. The impact of the belimumab treatment on the SLE severity signature was evaluated [2].
Results: From 38 patients treated with belimumab, 35 (97,2%) were women, mean age (SD) was 48,2 (±13,5) years and mean SLEDAI-2K (SD) at baseline was 7,2 (±2,1). A total of 44,4% achieved LLDAS at M6. Both, the presence of a molecular signature of type I interferon signaling and the upregulation of BAFF expression correlated with response to treatment at M6 ($p = 0.05$ and $p = 0.02$ respectively). Treatment with belimumab reversed the innate and adaptive immune system signatures in responders at 6-months. Within the non-responders, baseline transcriptome, disturbances related to metabolic processes and rRNA biogenesis were predominantly enriched. A tendency towards downregulation of the severity disease transcriptional signature upon treatment with belimumab was also observed in 6-month responders ($p = 0.3203$).
Conclusion: Both the presence of type I interferon and BAFF gene expression signatures at baseline correlates with response to treatment with belimumab while metabolic processes and rRNA biogenesis correlate with no response. Treatment with belimumab might ameliorate the molecular signatures indicative of disease severity in the 6 month-responders. These data provide a mechanistic basis for the response to treatment.
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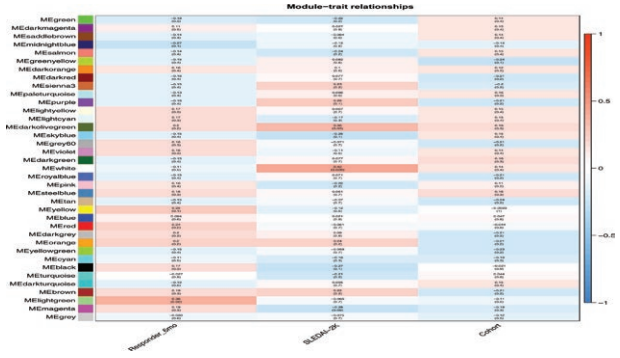


Figure 1. Correlation between the groups of differentially expressed genes from the WGCNA analysis and response to belimumab and SLEDAI at M6.

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*Georgia-Savina Moysidou and Panagiotis Garantziotis contributed equally to the abstract.
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AB0525 **SUSTAINED RESPONSES TO ANTI-CD38 TREATMENT WITH DARATUMUMAB IN A PATIENT WITH REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS**

Keywords: Systemic lupus erythematosus, Adaptive immunity

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Background: Given their contribution to the chronicity of autoimmune response, long-lived plasma cells (PCs) resemble an attractive treatment target in systemic lupus erythematosus (SLE) and other autoantibody-mediated diseases. We have recently reported the successful treatment of daratumumab, a CD38-targeting human monoclonal antibody, in two refractory patients with SLE [1], demonstrating a clinically relevant depletion of long-lived plasma cells with marked reduction of anti-double-stranded DNA (dsDNA) antibodies and marked clinical improvement in both cases over a follow-up period of 12 months.
Objectives: Here, we describe the long-term clinical and serologic responses of daratumumab treatment in one patient with SLE with a follow-up of 36 months.
Methods: A 51-year-old woman, who suffered from active lupus nephritis WHO class-III/V with nephrotic syndrome, pericarditis, arthritis and skin rash despite treatment with mycophenolate mofetil (MMF), cyclosporine A (CsA), hydroxychloroquine (HCQ) and glucocorticoids (GC), had received 4 weekly intravenous doses of 16mg/kg daratumumab as add on to background medication, which was complemented by subcutaneous 200mg belimumab weekly, starting 4 months after the initiation of daratumumab. Autoantibodies were investigated with ELISA and type-I interferon (IFN-I) activity investigated by measuring SIGLEC-I expression on monocytes with flow cytometry.
Results: During follow-up, the patients´ Urinary Protein/Creatinine Ratio (UPCR) declined from 1197 mg/g at 12 months to 467mg/g Creatinine at the last follow-up, while serum creatinine remained within normal levels (Figure 1A). No flares or novel disease manifestations occurred during the 3-year observation period, although the dosage of MMF was tapered to 1g daily at 21 months and prednisolone discontinued at 33 months, respectively, after the first daratumumab administration. Serologically, serum anti-dsDNA antibodies further decreased from 254 IE/ml at the 12 months follow-up to 38 IE/ml at 36 months (Figure 1B), and complement levels for C3 were consistently within the normal range (Figure 1C). Serum IgG levels remained stable after previous substitution with two doses of 30g intravenous immunoglobulins (Figure 1D). In addition, her initially increased type-I interferon activity, determined by the flow cytometric assessment of SIGLEC-1 on freshly isolated monocytes, completely normalized during follow-up, an effect most strongly observed during the first weeks following daratumumab that further substantiated under belimumab therapy (Figure 1E). At the last follow-up, she was in complete clinical remission, with a SLEDAI-2K of 2 due to slightly elevated dsDNA antibodies (Figure 1F). No severe adverse events occurred during follow-up, and no hospitalization was required for the management of SLE, infections or comorbidities.
Conclusion: Our data demonstrate that the administration of daratumumab as induction therapy for refractory and serologically active SLE may provide sustained clinical responses, when combined with immunosuppression and/or belimumab as maintenance therapy to prevent recurrence of autoreactive PCs. Apparently, depletion of long-lived PCs resulted in a therapeutically relevant reduction of autoantibodies and IFN-I activity, indicating a profound disease modification with resetting the chronic autoreactive immune system into an earlier stage of development, regaining responsiveness to standard therapies. These data suggest further studies to investigate the safety and efficacy of daratumumab in SLE and other autoantibody-mediated autoimmune diseases.
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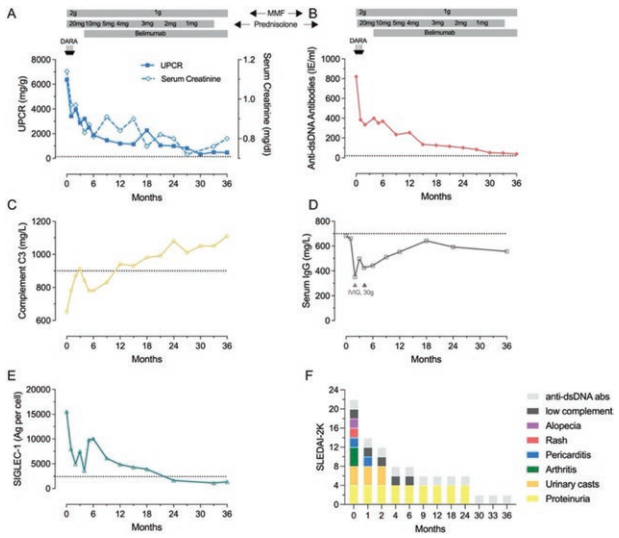


Figure 1. Clinical and serologic responses to daratumumab in one patient with SLE.

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Disclosure of Interests: Tobias Alexander Grant/research support from: Janssen, Lennard Ostendorf: None declared, Robert Biesen: None declared, Andreas Radbruch: None declared, Gerd Rüdiger Burmester: None declared, Falk Hiepe: None declared.
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AB0526

EVALUATION OF SATISFACTION AND EFFICACY OF SWITCHING FROM INTRAVENOUS TO SUBCUTANEOUS BELIMUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN DAILY CLINICAL PRACTICE

Keywords: bDMARD, Patient reported outcomes, Systemic lupus erythematosus

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Background: In 2017, Belimumab (BEL) was approved in subcutaneous (SC) version [1]. The effectiveness after switching from intravenous (IV) to SC and patient satisfaction in daily clinical practice has not been studied. During the pandemic, patient follow-up and treatment were significantly affected, including the administration of IV biologic therapies. In some patients, a change from IV to SC, including BEL therapy, was required [2].
Objectives: Our aim was to evaluate in daily clinical practice satisfaction to BEL SC therapy in patients previously treated IV BEL. We hypothesized that SC BEL in SLE patients previously treated with IV BEL was similar in effectiveness and conferred higher satisfaction.
Methods: Observational, multicenter study, conducted in 7 reference centres in Catalonia (Spain). Inclusion criteria: Stable SLE patients (EULAR/ACR 2019) on treatment with BEL SC and previous use of BEL IV (at least 3 months of treatment with BEL IV before switching). Since there are no well-validated tools for SC BEL treatment satisfaction, we used RASQ-SC, validated in patients with lymphoma who switched from Rituximab IV to SC treatment [3], modified for BEL treatment.
Results: Twenty-seven patients were included. Demographic and general characteristics are summarized in Table 1. The mean time from treatment with BEL IV before switch to SC was 26 (SD 21) months. 84% of patients reported confidence in BEL SC. 80% felt that treatment with BEL SC was convenient or very convenient. 85% felt they had gained time with the change. 89% would recommend the SC injection to other patients (Figure 1a,b,c,d). Disease activity (mean SLEDAI) and remission rates remain stable after switching. Patients did not require higher doses of glucocorticoids after the switch (Table 1). No major new side effects were reported.

TABLE 1. Clinical and demographic characteristics

DEMOGRAPHIC	
Age at inclusion (years), n (%)	45,9 (12,5)
Female, n (%)	23 (85,2)
Ethnicity, n (%)	
Caucasian	22 (81,5)
Mestizo	4 (14,8)
Maghrebi	1 (3,7)
Current smoker, n (%)	10 (37)
DISEASE CHARACTERISTIC	
Age at diagnosis (years), mean (sd)	28,8 (13,4)
SLICC at the time of inclusion, mean (sd)	0,67 (0,88)
Cumulative manifestations, n (%)	
Fever	10 (37)
Skin manifestation	
Malar rash	17 (63)
Discoid lupus	4 (14,8)
Lupus tumidus	1 (3,7)
Acute cutaneous lupus	11 (40,7)
Ulcers	17 (63,0)
Alopecia	6 (22,2)
Articular	
Arthralgias	27 (100)
Arthritis	26 (96,3)
Renal	
Proteinuria	3 (11,1)
Serositis	
Pericarditis	4 (14,8)
Pleuritis	11 (40,7)
Neurological	
Myelitis	1 (3,7)
Acute confusional state	1 (3,7)
Hematological	
Leukopenia	18 (66,7)
Lymphopenia	15 (55,6)
Thrombocytopenia	2 (7,4)
INMUNOLOGICAL	
ANA	27 (100)
Anti-dsDNA	25 (92,6)
Anti-Sm	10 (37)
Lupus anticoagulant	5 (18,5)
aCL	4 (14,8)
Anti-B2GP1	4 (14,8)
Low C3	21 (77,8)
Low C4	20 (74,1)
CHARACTERISTICS AT THE MOMENT OF LAST BELIMUMAB IV ADMINISTRATION	
Disease duration at the moment of initiation of BEL IV (months), mean (Sd)	153,4 (114,6)
SLEDAI, mean (sd)	2,96 (2,4)
Glucocorticoid treatment, n (%)	19 (70,4)
Prednisone equivalent mg/d, mean (sd)	4,8 (6,3)
Clinical remission, n (%)	19 (70,4)
Serological remission, n (%)	10 (37)
Complete remission, n (%)	8 (29,6)
Mean time from treatment with BEL IV before switch to SC (months), mean (sd)	26,35 (21,3)
LAST VISIT WITH BELIMUMAB SC	
Time since change (months), mean (sd)	30,9 (7,8)
SLEDAI, mean (sd)	1,82 (2,02)
Glucocorticoid treatment, n (%)	17 (63)
Prednisone equivalent mg/d, mean (sd)	3,57 (2,34)
Clinical remission BEL SC, n (%)	20 (74,1)
Serological remission BEL SC, n (%)	14 (51,9)
Complete remission BEL SC, n (%)	12 (44,4)

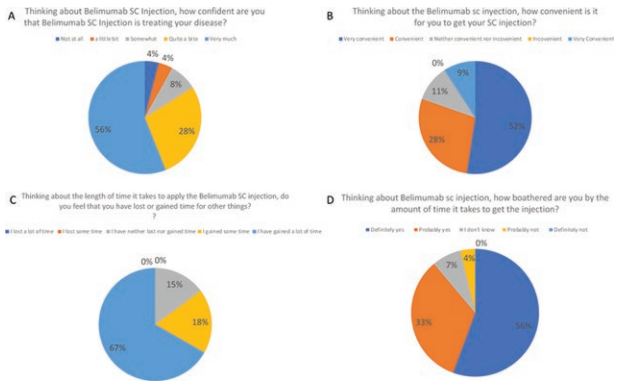


Figure 1. RASQ-SC modified

Conclusion: Overall satisfaction, satisfaction with via of administration and satisfaction with the time taken to receive BEL were higher for SC BEL treatment. A switching SC strategy is a reasonable alternative for BEL patients.

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Disclosure of Interests: None Declared.
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AB0527 FACTORS ASSOCIATED WITH GLUCOCORTICOID-FREE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS TREATED WITH BELIMUMAB IN THE REAL-WORLD SETTINGS: A SINGLE-CENTER RETROSPECTIVE COHORT STUDY IN JAPAN

Keywords: Real-world evidence, Tapering, Systemic lupus erythematosus

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Background: The treatment of patients with systemic lupus erythematosus (SLE) involves the progression of organ damage due to both the disease itself and glucocorticoid-induced adverse events [1]. Therefore, achieving glucocorticoid-free status is one of the most important goals in the treatment of SLE [2]. Belimumab has been reported to be effective in SLE patients, particularly with high disease activity, by inhibiting the B-lymphocyte stimulator (BLyS) to reduce disease activity, relapse rate, organ damage, and steroid dosage [3,4]

Objectives: Review the profile of patients who can achieve glucocorticoid-free status with belimumab administration, retrospectively.

Methods: We retrospectively reviewed 47 Japanese SLE patients who received belimumab for at least 1 year in addition to standard of care, including glucocorticoids. Patients were classified into two groups: glucocorticoid-free (GC free) and others (GC continuation) as of August 2022. Trends in C3, C4, and dsDNA antibody titers, SLEDAI-2K scores, and daily glucocorticoid dosage were examined at the start of belimumab and thereafter; at months 12 and 24. At the time of belimumab initiation, differences between the two groups were also examined for age, duration of disease, time from onset or last relapse to belimumab initiation, C3, C4, dsDNA antibody titer, daily glucocorticoid dose, SLEDAI-2K, with or without concomitant hydroxychloroquine and concomitant immunosuppressive drugs, and duration of belimumab treatment. Incidence of adverse event or relapse during the course were also followed. P values were determined using Wilcoxon's signed rank test, Mann-Whitney U test, and Fisher's exact test.

Results: 9 patients (19%) were classified as GC free. In overall patients, C3, C4, dsDNA antibody titer, and SLEDAI score showed significant improvement at 12 and 24 months compared to the baseline. The daily GC dosage was significantly reduced while it was increased in 2 patients (5%). Though there was no significant difference in SLEDAI, C3 was significantly higher in the GC free group at the baseline (P=0.032). There were no cases of discontinuation of belimumab due to adverse events or relapse during the course.

Conclusion: Although low C3 patients are more likely to benefit from belimumab because of higher serum BLyS levels [5], it is worthwhile to introduce belimumab for GC-free even in patients with high C3 levels.

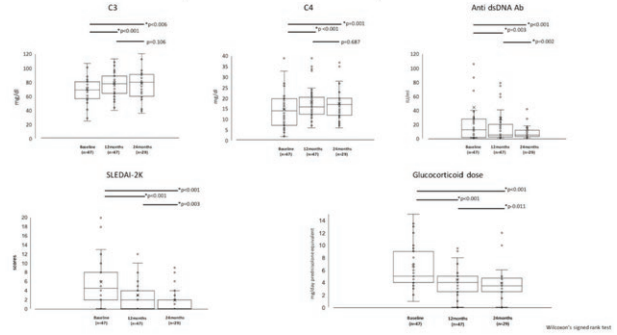
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Characters from table content including title and footnotes: Characteristics of the patients at baseline, according to current glucocorticoid administration status. Data are shown by median [quartile] or n (%). P values were determined by Mann-Whitney U test or Fisher's exact test. *P<0.05.

Table 1.

	GC free N=9	GC continue N=38	P value
Age (year)	**37 (33-46)**	**45 (39-54)**	**0.056**
Female sex	**7 (78)**	**35 (92)**	**0.240**
Disease duration (year)	**9 (2-16)**	**14 (5-21)**	**0.448**
Glucocorticoid dose (mg/day prednisolone equivalent)	**4 (2-9)**	**5 (4-9)**	**0.086**
C3 (mg/dl)	**81 (69-88)**	**67 (56-78)**	**0.032**
C4 (mg/dl)	**18 (11-26)**	**13 (7-18)**	**0.181**
Anti dsDNA antibody (IU/ml)	**24 (3-27)**	**11 (2-37)**	**0.720**
SLEDAI-2K	**6 (2-6)**	**4 (2-10)**	**0.905**
SLEDAI-2K ≧10	**0 (0)**	**10 (26)**	**0.093**
Duration from onset or relapse to start of Belimumab (months)	**12 (10 -24)**	**24 (6-60)**	**0.392**
History of relapse	**6 (67)**	**27 (71)**	**0.497**
Concomitant use of HCQ	**9 (100)**	**34 (89)**	**0.414**
Concomitant use of immunosuppressant	**7 (78)**	**34 (89)**	**0.322**
Duration of treatment with Belimumab (months)	**27 (20-38)**	**26 (17-38)**	**1.0**

Figure



Acknowledgements: NIL.
Disclosure of Interests: Takashi Yamane Speakers bureau: I have received a speaker's fee from GlaxoSmithKline, Akira Hashiramoto Grant/research support from: I have received support grants from ASAHI KASEI PHARMA, CHUGAI PHARMACEUTICAL CO., LTD and Eli Lilly Japan K.K.
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AB0528 BASELINE PROFILE OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS ON TREATMENT WITH BELIMUMAB OF A SPANISH MULTICENTER COHORT

Keywords: bDMARD, Systemic lupus erythematosus, Descriptive Studies

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Background: Belimumab (BLM) is a recombinant human IgG-1λ monoclonal antibody that inhibits B-cell activating factor. It is commonly used for treatment of systemic lupus erythematosus (SLE) patients with inadequate control to first-line treatments and inability to taper GC daily dose to acceptable levels. More recently it has been approved for patients with active lupus nephritis.
Objectives: To report baseline profile of SLE patients treated with BLM enrolled in a SLE Spanish registry.
Methods: Multicenter retrospective and longitudinal cohort study including SLE patients treated with BLM in 18 Spanish rheumatology units. Demographic, clinical data and treatments were collected at baseline, 6, 12 months and in the last visit available. Patients starting BLM in different periods (2010-2015 and 2016-2021) were compared regarding the reason of prescription of the drug.
Results: 324 patients (91% female, 84,8% caucasian) were enrolled. Mean (±SD) age at diagnosis: 31.8 years (±11.9); mean disease duration of 8.7 years (±9.07) and mean follow-up 3.8 (±2.7). A total of 319 (98.45%) subjects met SLE 1997 ACR or SLICC 2012 criteria; 217 (68.2%) were anti-dsDNA positive and 224 (69.8%) had low complement levels. At baseline, the mean SLEDAI-2K score was 10.4 (±5.25); 152 (47.5%) of patients had damage with a mean SDI score of 0.83 (±1.2). A total of 289 patients (89.2%) had received disease modifying anti-rheumatic drugs (DMARDs) before BLM: conventional (cDMARDS) in 282 patients (87%) and biologic DMARDs (bDMARDs) in 74 patients (22.8%); 164 (51.9%) had received more than one cDMARDs, methotrexate being the most frequently used (44.4%). Other cDMARDs used were: mycophenolate mofetil in 104 (37.01%), azathioprine in 91 (32.38%), leflunomide in 29 (10.32%), cyclophosphamide in 28 (9.92%) and calcineurin inhibitors in 13 (4.6%) of patients. The most frequent bDMARDs used was Rituximab in 80%. Most patients were receiving antimalarials (83,2%) and glucocorticoids (GC) (91.2%), with a mean dose of 12.3 mg/day. A total of 209 (67.9%) patients were receiving more than 5 mg/day and 180 (58.4%) more than 7.5 mg/day of prednisone. BLM was used in monotherapy in 99 (30.5%) subjects. It was initiated due to disease activity in 307 patients (95%) and/or as a GC sparing agent in 191 patients (59%). Most patients initiated BLM for several concurrent reason; only a few patients received BLM just for maintenance (4/322) or save GC (8/322). At baseline, only 6 patients (1.9%) were in DORIS-21-remission and LLDAS. The main reasons of prescription for ongoing activity were arthritis (65.4%), cutaneous (40.7 %) or both (81%). There were no statistically significant differences in any of the prescription reasons when comparing the periods 2010-2015 and 2016-2021.

Table 1. Type and reasons of prescription of Belimumab

	N (%) or mean (± SD) (n = 324 patients)
Age at prescription of Belimumab (years)	42.3 (± 12.9)
Intravenous Belimumab	215 (66.35%)
Subcutaneous Belimumab	110 (33%)
Reasons of prescription* (multiple response allowed)	
Disease activity	307 (95%)
Maintenance	197 (61%)
Glucocorticoid sparing	191 (59 %)
Activity	
Cutaneous	132 (40.7 %)
Articular	212 (65.4%)
Renal	58 (17,9%)
Hematological	60 (18.5%)
Serosal	47 (14.5%)
Other	29 (8.82%)

Conclusion: In the majority of patients, belimumab was prescribed after the use of other DMARDs and more than 50% of patients had received at least 2 DMARDs and were receiving GC at medium doses. One third of patients received BLM as monotherapy. It was prescribed due to active disease in the vast majority of patients and/or as GC sparing agent. Activity in articular and cutaneous domains were the main reasons of indication. No changes in prescription habits were identified over time.
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Acknowledgements: NIL.
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AB0529

GLUCOCORTICOIDS WITHDRAWN IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH SEROLOGICALLY ACTIVE CLINICALLY QUIESCENT STATE: A DESIRABLE GOAL

Keywords: Systemic lupus erythematosus, Organ damage, Remission

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Background: Serologically active clinically quiescent (SACQ) is a clinical state of systemic lupus erythematosus (SLE) characterized by high levels of serologic markers without clinical activity. The outcome and treatment strategy after SACQ achievement remains unclear. After achieving the treatment goal, maintaining low-dose glucocorticoids has always been both a blessing and a curse [1,2]. Whether glucocorticoids discontinuation is a desirable goal in patients achieved SACQ was controversial.
Objectives: In this multi-center prospective study, we aimed to identify the risk of flares, organ damage accumulation, and the low-dose glucocorticoids discontinuation feasibility of SLE patients who achieved the clinical state as SACQ.
Methods: This observational study was conducted based on data from the Chinese SLE treatment and research (CSTAR) registry. Demographic characteristics, autoantibody profiles, clinical manifestations, disease activity status, organ damage, and treatment profile were collected at recruitment and during follow-up. SACQ was defined as at least a 6-months period with persistent serologic activity (positive anti-dsDNA antibody, and/or hypocomplementemia), and without clinical activity. Serologically quiescent clinically quiescent (SQCQ) was defined as at least a 6-months period without serologic or clinical activity. The flare was measured according to the SELENA-SLEDAI flare index (SFI). Organ damage is principally assessed using the SLICC damage index (SDI).
Results: Of 4107 SLE patients, 1889 reached the clinical quiescent stage (990 achieved the clinical state as SACQ, and 899 patients achieved SQCQ). Among 990 SACQ patients, 364 (36.7%) underwent flares, 163(16.5%) showed organ damage, 47 (4.7%) developed renal damage, and 21 (2.1%) died during a mean follow-up of 7.30 years. Compared with patients who achieved SQCQ, SACQ patients were at a higher risk of flares (HR=1.47, 95% CI 1.25-1.73 , p<0.001) and renal damage accumulation (HR=2.02, 95% CI 1.23-3.33, p=0.004). Furthermore, 224 (22.6%) SACQ patients withdraw low-dose glucocorticoids and 125 (55.8%) of them did not flare during follow-up. Low-dose glucocorticoids discontinuation was a favorable factor of long-term survival (HR=0.22, 85% CI, 0.05-0.96, P=0.044). As shown in the Figure 1, withdrawing glucocorticoids can reduce organ damage (p=0.0075), especially renal damage accumulation (p=0.045), even experience flares after discontinuation.
(A) (B)

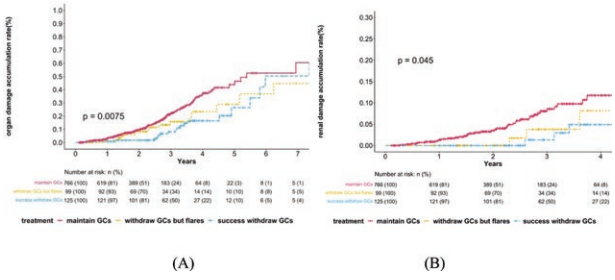


Figure 1. Cumulative probability of new-onset organ damage (A) and renal damage (B) in SACQ patients maintain glucocorticoids, withdraw glucocorticoids but flares, and successful withdraw glucocorticoids.

Conclusion: Our results suggest that low-dose glucocorticoids withdrawal under tight survallance could be considered after achieving the clinical state as SACQ to prevent the accrual of renal damage.
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AB0530

DESIGN OF 2 PHASE 3, DOUBLE-BLIND, PLACEBO-CONTROLLED, GLOBAL TRIALS OF DEUCRAVACITINIB, AN ORAL, SELECTIVE, ALLOSTERIC TYROSINE KINASE 2 (TYK2) INHIBITOR, IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Clinical Trials, Systemic lupus erythematosus

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Background: Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis [1,2]. Deucravacitinib demonstrated efficacy across the primary endpoint and all key secondary endpoints in a phase 2 trial in patients with systemic lupus erythematosus (SLE) [3].
Objectives: Here, we describe 2 phase 3 trials currently underway to assess the efficacy and safety of deucravacitinib in patients with active SLE. These phase 3 trials have been designed to replicate the successful elements of the phase 2 trial, including its glucocorticoid-tapering strategy and rigorous management structure [3].
Methods: In these phase 3, randomized, double-blind, placebo-controlled, global trials (POETYK SLE-1 [NCT05617677], POETYK SLE-2 [NCT05620407]), adults (aged 18-75) with active SLE on background standard-of-care treatment will be randomized (1:1) to placebo or deucravacitinib for 52 weeks of double-blind treatment (**Figure 1**). Patients on glucocorticoids will be instructed to taper, unless significant disease activity is present, to a threshold dose level during the double-blind treatment period. At week 52, patients may choose to continue in a 104-week open-label extension phase, in which all patients receive deucravacitinib. Key eligibility criteria and study design are depicted below (**Figure 1**). The primary endpoint of SLE Responder Index (SRI[4]) and all secondary endpoints will be assessed at week 52 (**Table 1**). Safety and tolerability will be assessed throughout the trial.
Results: Planned randomization in each trial includes 490 patients (245 per treatment group) in 27 countries across North and South America, Europe, and Asia-Pacific.
Conclusion: The phase 3 POETYK SLE trials will further evaluate the efficacy and safety of deucravacitinib, an oral, selective, TYK2 inhibitor, in patients with active SLE.

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Figure: POETYK SLE-1 and POETYK SLE-2 Trial Design

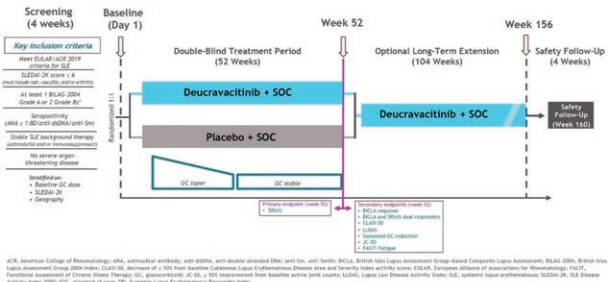


Table 1. Primary and Secondary Endpoints Assessed at Week 52

Primary Endpoint
• Proportion of patients who achieve an SLE Responder Index (SRI[4]) response
Secondary Endpoints
• Proportion of patients who achieve a British Isles Lupus Assessment Group-based Composite Lupus Assessment (BICLA) response
• Proportion of patients with simultaneous achievement of SRI(4) and BICLA response (dual responders)
• Proportion of patients who achieve a ≥ 50% reduction in Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI-50) among patients with CLASI activity score ≥ 10 at baseline
• Proportion of patients who achieve Lupus Low Disease Activity State (LLDAS)
• Proportion of patients maintaining ≤ 7.5 mg/day glucocorticoid dose from weeks 24 to 52
• Proportion of patients who achieve a ≥ 50% reduction in active joints (Joint-Count 50) among patients with ≥ 6 active joints at baseline
• Change from baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score

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AB0531

APPLYING THE WORKING DEFINITION OF THE DISEASE MODIFICATION CRITERIA TO LUPUS NEPHRITIS TREATMENTS FROM THE PUBLISHED LITERATURE

Keywords: Kidneys, Organ damage, Outcome measures

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Background: We have recently published a working definition of disease modification in lupus nephritis (LN) as 'minimising disease activity with the fewest treatment-associated toxicities and slowing progression to end-stage kidney disease' [1]. As an increasing number of LN medications become available, classification of treatments as disease-modifying is critical in informing treatment decisions.
Objectives: To apply the proposed disease modification criteria to LN treatments.
Methods: Based on a review of a selection of LN clinical trial (n=21) and practice/observational publications (n=18) and authors' clinical experience, we determined whether the LN treatments satisfied the renal disease activity and organ damage disease modification criteria. The proposed disease modification criteria were examined at three time points as shown in the **Table 1**.
Results: All LN treatments met at least one of the renal disease modification criteria at any time point (**Table 1**), with hydroxychloroquine meeting the criteria for confirmed disease modification at >5 years (no change in Systemic Lupus International Collaborating Clinics/American College of Rheumatology Disease Index [SDI] or delayed progression beyond 5 years). Belimumab met more criteria across the three time points than any other biologic treatment. Based on the reviewed literature, many criteria were inconclusive or not available for evaluation. Glucocorticoids did not meet the disease modification criteria beyond 5 years given their negative impact on organ damage progression.
Conclusion: We examined the evidence in the literature for the disease modification potential of LN therapies at 1, 2–5, and >5 years. Categorisation of treatments as disease-modifying is challenging, as studies use multiple agents, and study designs, patient populations, and endpoints/definition of renal response are not consistent between studies. The criteria allowed for the differentiation between LN therapies; future studies will evaluate the minimum number of criteria required to designate disease modification at each of the three time points, so that disease modification can be considered in the care of patients with LN and LN trial design.
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Table 1. Application of the proposed matrix for renal-specific immunoinflammatory and organ damage disease modification criteria

Product	DISEASE MODIFICATION POTENTIAL		DISEASE MODIFICATION CONFIRMED (BEYOND 5 YEARS)
	Outcomes Year 1	Outcomes Years 2–5	Outcomes Year >5
	❶ Significant improvement in uPCR or kidney activity index via biopsy ❷ Minimise eGFR decline (i.e., ≤30%) ❸ Significant reduction in renal flare ❹ Reduction in use of steroids* and/or immunosuppressants	❶ Sustained improvement in uPCR ❷ Minimise decline in eGFR (i.e., ≤30%) ❸ Prevention of renal flares ❹ Continued reduction in steroids* and/or immunosuppressants **Provisional:** no worsening in kidney chronicity index via biopsy	No change in SDI or delayed progression
Glucocorticoids	1 2 3 4	1 2 3 4	†●
Hydroxychloroquine	1 2 3 4	1 2 3 4	●
Azathioprine	1 2 3 4	1 2 3 4	●
Cyclophosphamide	1 2 3 4	1 2 3 4	●
Leflunomide	1 2 3 4	1 2 3 4	●
Mizoribine	1 2 3 4	1 2 3 4	●
Mycophenolate mofetil	1 2 3 4	1 2 3 4	●
Cyclosporine	1 2 3 4	1 2 3 4	●
Tacrolimus	1 2 3 4	1 2 3 4	●
Voclosporin	1 2 3 4	1 2 3 4	●
Belimumab	1 2 3 4	1 2 3 4	●
Rituximab	1 2 3 4	1 2 3 4	●
Obinutuzumab	1 2 3 4	1 2 3 4	●

●, criterion met; ●, inconclusive; ●, data not available in the literature

*≤7.5 mg/day per 2019 EULAR SLE treatment guidelines and LLDAS; ≤5 mg/day per DORIS remission definition
†Data were available in the literature but the criterion was not met

DORIS, definition of remission in SLE; eGFR, estimated glomerular filtration rate; LLDAS, Lupus Low Disease Activity State; SLE systemic lupus erythematosus; uPCR, urine protein/creatinine ratio

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AB0532

THE USE OF BDMARDS IS ASSOCIATED WITH A LOWER PREVALENCE OF BILATERAL CAROTID PLAQUE IN PSA

Keywords: Cardiovascular disease, bDMARD

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Background: Psoriatic arthritis (PsA) is an autoimmune rheumatic disease (ARD) [1]. PsA have excessive cardiovascular risk (CVR) because of systematic inflammation that triggers endothelial dysfunction, which in turn induces atherosclerosis and CV disease [2]. Possible beneficial effects of biologic disease modifying antirheumatic drugs (bDMARDs) in patients with ARDs have been seen, particularly those with rheumatoid arthritis. Treatment with TNF inhibitors seems to improve endothelial dysfunction and atherosclerosis [3].
Objectives: To evaluate the presence of carotid disease in patients with PsA using biologics or non-biologics.
Methods: This was a cross-sectional, descriptive study. PsA patients aged 40-75 years, who fulfilled the 2006 CASPAR criteria were recruited. Carotid ultrasound was performed on all study participants, and the presence of carotid plaque (CP), defined as carotid intima-media thickness (cIMT) ≥1.2mm or focal thickness ≥0.5mm, was assessed. Patients were divided into 2 groups according to whether they use bDMARDs or not. Comparisons were done with Chi-square test, Student´s T test and Mann-Whitney's U-test. A p-value ≤0.05 was considered significant.
Results: A total of 67 patients were recruited. Demographic characteristics are shown in Table 1. Twenty-seven were under bDMARD treatment, twenty-five of these were using an anti-TNF. We found a difference in C-reactive protein (CRP) levels (p=0.004), lower in patients with bDMARDs and in the presence of bilateral CP (p=0.041), less prevalent in patients with bDMARDs. The rest of the variables studied did not show significant differences.
Conclusion: We found that PsA patients under bDMARDs therapy had lower levels of CRP and less prevalence of bilateral CP in PsA, therefore strengthens the theory that the less inflammation the less bilateral carotid plaque is present.
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Table 1. Demographic, laboratory and carotid Doppler characteristics.

	Characteristics	PsA patients with bDMARDs	PsA patients without bDMARDs	*p*
		(n= 27)	(n=40)	
Demographic	Age, years, mean (DE)	52.00 (7.24)	57.98 (8.93)	0.004
	Women, n (%)	13 (19.4)	18 (26.86)	NS
	Disease duration, years, median (iQR)	8.0 (4.0-14.0)	6.0 (3.0-10.7)	NS
	BMI, median (iQR)	29.4 (25.86-34.57)	28.46 (26.59- 31.75)	NS
	SBP, mean (DE)	128.59 (14.76)	129 (21.48)	NS
	DBP, mean (DE)	85.15 (10.54)	78.53 (11.78)	0.019
Laboratory profile	Cholesterol, mg/dL. mean (DE)	187.7 (39.51)	171.7 (36.59)	NS
	Triglycerids, mg/dL. median (iQR)	141.7 (100.3-199.7)	128.4 (94.8-173.9)	NS
	HDL, mg/dL, mean (DE)	48.1 (10.83)	47.5 (15.00)	NS
	LDL, mg/dL, mean (DE)	106.3 (30.73)	94.2 (34.31)	NS
	CRP, mg/dL. median (iQR)	0.34 (0.28-0.94)	0.62 (0.36-1.09)	0.05
	ESR, mm/H, median (iQR)	14.0 (8.0-18.0)	18.0 (11.0-31.5)	NS
Carotid Doppler	Unilateral CP, n	9	6	NS
	Bilateral CP, n	2	11	0.041

BMI body mass index, SBP systolic blood preassure, DBP diastolic blood preassure, CRP C-reactive protein, ESR erythrocyte sedimentation rate, CP carotid plaque

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3978

AB0533 EFFECT OF RENIN-ANGIOTENSIN SYSTEM INHIBITORS ON RENAL REMISSION IN LUPUS NEPHRITIS: A REAL-WORLD SINGLE-CENTER STUDY

Keywords: Clinical trials, Systemic lupus erythematosus, Kidneys

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Background: Renin-angiotensin-system inhibitors (RASi) reduce urinary protein excretion and protect renal function in both diabetic and nondiabetic nephropathy. Few studies have focused on RASi in LN patients.
Objectives: The study aimed to provide real-world evidence to assess the effect of RASi in LN patients.
Methods: A total of 233 LN patients were included; 155 were RASi users, and 78 were not. The rate of proteinuria partial recovery (PPR), complete remission (CR), total remission (TR), the decline and decline rate of proteinuria at 6 and 12 months were compared by Chi-square test and Kaplan–Meier analysis. Propensity score matching (PSM) and Cox regression analysis was performed.
Results: The cumulative rates of PRR, TR and CR were 133 (85.8%), 103 (66.9%), and 53 (34.2%) in the RASi group compared to 66 (87.7%), 55 (71.1%), and 44 (57.2%) in the no RASi group at 6 months, respectively. At 12 months, the cumulative rates of PRR, TR and CR were 144 (99.4%), 115 (76.1%), and 83 (56.0%) in the RASi group and 73 (97.3%), 64 (83.5%) and 54 (71.3%) in the no RASi group, respectively. There was no statistically significant difference in cumulative PRR and TR rates between the two groups (p=0.601 and 0.203). The cumulative CR rate was significantly higher in the no RASi group (p=0.001). The UTP level of the RASi group was consistently higher than that of the no RASi group at 6 [0.5(0.2,1.6) vs. 0.3(0.1,0.7), p=0.003) and 12 months [0.2(0.1,0.6) vs. 0.1(0.1,0.3), p=0.008]. However, the ΔUTP was significantly higher in the RASi group [6 months: 2.6 (1.3, 5.1) vs. 1.2 (0.8, 2.4), p=0.001; 12 months: 3.3 (1.6, 5.4) vs 1.4 (0.9, 2.9), p=0.001], and the decline rate did not reach significance. Meanwhile, the serum SCr showed no difference between the two groups. The results were similar after PSM. Only HCQ usage was a prognostic predictor of PRR (HR 2.110, 95% CI: 1.223, 3.642, p=0.007).
Conclusion: RASi may not benefit the renal remission of LN, and the results need to be interpreted with caution. However, RASi may help to decrease urinary protein. Further high-quality randomized controlled trials are required to evaluate the RASi effects on proteinuria and renal prognosis.

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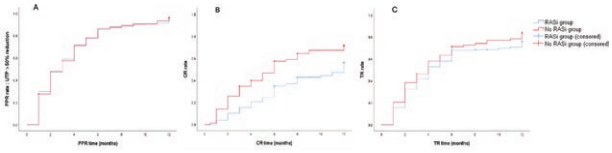


Figure 1. Kaplan–Meier plot of the cumulative rate of PPR (A), CR (B) and TR (C).

Table 1. Comparison of kidney indexes between the two groups at 3, 6, 9 and 12 months

	Before PSM			After PSM		
	RASi group	No RASi group	p value	RASi group	No RASi group	
3 months						
UTP	1.1 (0.4, 2.6)	0.5 (0.2, 1.5)	0.006	1.1 (0.5, 2.3)	0.8 (0.2, 1.7)	0.066
Alb	34.6±6.1	36.6±5.2	0.029	34.7±5.8	36.5±5.6	0.104
SCr	76.0 (66.0, 88.5)	74.5 (66.5, 82.5)	0.688	73.5 (65.0, 85.0)	77.0 (69.0, 83.0)	0.376
ΔUTP	2.3 (1.0, 4.6)	1.0 (0.5, 1.8)	0.001	1.9 (0.7, 4.2)	1.1 (0.5, 2.0)	0.021
6 months						
UTP	0.5 (0.2, 1.6)	0.3 (0.1, 0.7)	0.003	0.5 (0.2, 1.7)	0.3 (0.1, 0.7)	0.040
Alb	37.7±5.8	39.9±4.3	0.826	37.9±5.5	40.0±4.5	0.025
SCr	77.0 (67.0, 92.0)	74.0 (68.0, 84.0)	0.298	75.0 (65.0, 88.5)	73.5 (68.0, 84.8)	0.727
ΔUTP	2.6 (1.3, 5.1)	1.2 (0.8, 2.4)	0.001	2.2 (1.1, 4.5)	1.4 (1.0, 2.6)	0.054
9 months						
UTP	0.3 (0.1, 1.0)	0.2 (0.1, 0.5)	0.007	0.3 (0.1, 0.8)	0.2 (0.1, 0.7)	0.026
Alb	38.9±5.7	41.3±4.3	0.009	38.9±5.8	41.4±4.8	0.032
SCr	77.0 (66.0, 88.3)	81.0 (72.0, 86.0)	0.244	75.5 (66.3, 88.8)	81.5 (73.3, 86.0)	0.125
ΔUTP	2.8 (1.4, 5.2)	1.2 (0.7, 2.7)	0.001	2.7 (1.3, 4.7)	1.3 (0.9, 3.3)	0.021
12 months						
UTP	0.2 (0.1, 0.6)	0.1 (0.1, 0.3)	0.008	0.2 (0.1, 0.6)	0.1 (0.1, 0.4)	0.065
Alb	40.5±4.4	41.0±4.2	0.462	40.7±4.4	41.3±4.6	0.429
SCr	77.0 (68.0, 89.8)	74.0 (68.0, 82.0)	0.198	76.0 (68.0, 88.9)	75.0 (69.0, 85.0)	0.622
ΔUTP	3.3 (1.6, 5.4)	1.4 (0.9, 2.9)	0.001	2.7 (1.4, 5.0)	1.5 (1.0, 3.4)	0.015

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0534 TREATING SYSTEMIC LUPUS ERYTHEMATOSUS IN THE 21ST CENTURY: COMBINING RITUXIMAB WITH BELIMUMAB

Keywords: Systemic lupus erythematosus, Treat to target

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Objectives: efficacy of combination therapy with rituximab and belimumab in patients with systemic lupus erythematosus.
Methods: The study included 15 SLE pts (1M/14F) criteria with high (SLEDAI2K≥10 – 12pts.) and moderate (SLEDAI2K<10- 3pts.) disease activity; out of them 4 patients had lupus nephritis, 2- vasculitis. 1 pts had kidney damage, cerebrovasculitis and vasculitis. All patients fulfilled the Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) disease classification criteria [1] for SLE Others have predominantly mucocutaneous and articular manifestations of SLE. The dose of oral glucocorticoids (GC) was: 60 mg in one patient with vasculitis, LN, cerebrovasculitis, and one patient with vasculitis received 20 mg of prednisone; in 11 patients from 10 to 5 mg; in 2 patients without oral glucocorticoids. All patients with SLE with kidney damage and vasculitis received mycophenolate mofetil or cyclophosphamide. Rituximab (RTM) was administered at a dose of 500-2000 mg, followed by the addition of belimumab (BLM) after 1-6 months at a standard dose of 10 mg/ kg once a month - a total of 7 infusions. The following parameters were evaluated: the effectiveness of therapy, the concentration of autoantibodies, the dose of oral corticosteroids initially at the time of RTM administration and then every 3 months after the initiation of BLM therapy.
Results: 13 pts demonstrated the decrease in clinical and laboratory SLE activity, starting from 3mo of follow-up. After the start of BLM infusions, a decrease in SLE activity was observed in all patients. Among them, 10 had SLEDAI-2K activity of less than 4 points. SLEDAI-2k Me 10 [10;16], after treatment of RTM and BLM 4[2;6]. Only one patient (№4) had an relapse of SLE, due to the delay

in receiving the infusion of BLM. He was receiving standard GC doses. In dynamics, a decrease anti-double DNA titres (Me 101 [36;200]U/ml vs 28 [8;67]Ед/мл), C3 (0,49 [0,42;0,78]g/l vs 0,71 [0,59;0,87] g/l), C4 (0,06 [0,045;0,1] g/l vs 0,12 [0,07;0,14] g/l) was registered. The GC dose was reduced in most patients (Table 1), but the previously prescribed immunosuppressive therapy continued. There were no cases of severe infection. We have not detected any new organ damage.

Table 1. Dose of oral glucocorticoids, mg

№ patient	Before RTM, mg	1st injection of BLM, mg	7th injection of BLM, mg	
1	20 mg	20 mg	15 mg	↓
2	7,5 mg	5 mg	5 mg	↓
3	5 mg	5 mg	5 mg	=
4	10 mg	10 mg	10 mg	=
5	5 mg	5 mg	5 mg	=
6	60 mg	7,5 mg	2,5 mg	↓↓↓
7	10 mg	2,5 mg	0 mg	↓↓↓
8	10 mg	10 mg	5 mg	↓
9	2,5 mg	2,5 mg	2,5 mg	=
10	10 mg	10 mg	5 mg	↓
11	0 mg	0 mg	0 mg	=
12	0 mg	0 mg	0 mg	=
13	15	15	10	↓
14	15	5	3,75	↓↓
15	20	10	10	↓

Conclusion: Combination therapy allows to gain control over disease activity in short time, due to the effect of RTM, while added BLM provides further prolongation of the effect achieved, minimizing the risk of flare. The use of such therapy contributes to a rapid and effective reduction in the activity of the disease, improvement of laboratory markers of SLE (at to ds-DNA, C3, C4), the use of lower doses of oral GCs. This combination may be used as a method of choice in pts with severe SLE involving vital organs, and in persistent cutaneous-articular disease and high immunological activity.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0535 EFFICACY AND SAFETY OF BELIMUMAB IN PATIENTS WITH CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS:A SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Systematic review, Systemic lupus erythematosus, Targeted synthetic drugs

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Background: Childhood-onset systemic lupus erythematosus (cSLE) is associated with higher disease severity than adult-onset lupus. Abnormal activation of B cells is a crucial link in their pathogenesis. Belimumab is a specific inhibitor of the soluble B lymphocyte stimulator and inhibits its binding to receptors and thus its activity [1,2]. However, the current clinical research evidence of this drug in children is insufficient, the relevant clinical data are mostly from prospective studies in adults,and there are no exact guidelines for clinical application in children.

Objectives: This study aimed to investigate the efficacy and safety of belimumab for treating children with cSLE.

Methods: We systematically searched PubMed, EMBASE, Wan Fang Data,Web of Science, the Cochrane Library, and Medline for randomized controlled trials, original case reports, and case series that described belimumab's efficacy in treating cSLE. A random-effects meta-analysis was performed to calculate its efficacy. Inconsistency was evaluated using the I2 and Egger tests to evaluate potential publication bias (STATA v.12.0).

Results: Five studies with 325 patients were included in the meta-analysis (Table 1). The age range of the included participants was less than 18 years; most were women. All patients received belimumab at a dosage of 10mg/kg every 2 weeks for the first three doses, then every 4 weeks thereafter. SLEDAI-2K was the main score,which was significantly reduced compared with the baseline[SMD= -1.106, 95%CI (-1.311,-0.901), P<0.001]. The number of oral corticosteroids was significantly decreased after the belimumab therapy[SMD = -1.21,95%CI (-1.72, -0.70), P<0.001]. Both Anti-double stranded DNA (Anti-dsDNA) and anti-nuclear antibodies (ANA) positive patients also decreased obviously[RR= 0.56, 95%CI (0.37,0.85), P=0.007; RR= 0.90, 95%CI (0.83,0.98), P=0.012]. Infection and thrush were the main adverse effects with rates of 26% and 4%,respectively, but all were classified as mild-moderate treatment-emergent adverse events. Serious adverse reactions are rarely reported.

Conclusion: Belimumab treatment in cSLE minimizes the use of hormones, and the incidence of adverse events such as infections was low, suggesting belimumab can effectively reduce disease activity safely and reliably. Long-term efficacy and safety still need a multicenter, large sample, long-term, in-depth research.

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Table 1. Available evidence including patients with cSLE treated with belimumab.

Study. Year.	Patients (include in analysis)	Age (year)	Gender (female %)	SLEDAI-2K	Dosage of hormone mg/d(mg/(kg·d))
Hermine I Brunner 2020	93(53)	14±0.75	94.6	NA	0w:7.5±3.81 52w:5.84±3.81
Ping Zeng 2021	256(169)	12.17±2.79	79.3	0w:12.06±7.38 28w:4.18±4.04	0w:35.02±18.88 28w:10.69±8.57 0w:(1.08±1.73) 28w:(0.27±0.2)
Dahai Wang 2022	26(26)	10.3±2.4	80.8	0w:10.33±10.27 4w:5±7.11 24w:4±3.16	0w:36.67±23.7 24w:11.67±11.85 52w:4.17±7.9
Qiong Wu 2022	60(60)	10.94±2.41	58.3	NA	NA
Yutong Gao 2022	17(17)	12.1±2.3	70.6	0w:10.67±11.32 4w:2.67±1.62 24w:1±2.43 28w:0.67±1.62	0w:(0.83±0.4) 28w:(0.27±0.08)

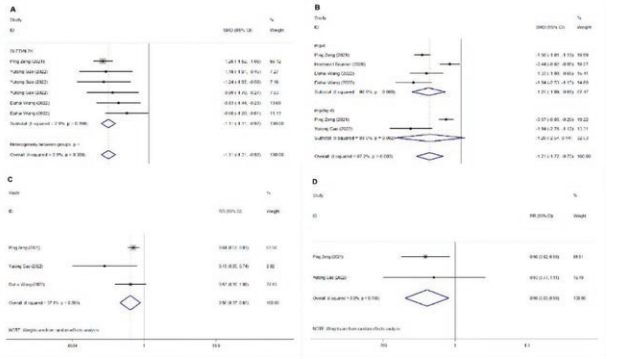


Figure 1. Efficacy of belimumab in patients with cSLE. (A) SLEDAI-2K scores. (B) oral hormone doses patients received. (C) dsDNA positive people. (D) ANA positive people. (A) - (D) are all changes before and after belimumab treatment.

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Disclosure of Interests: None Declared.

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AB0536

CORRECTION OF OMEGA-3 FATTY ACID DEFICIENCY AND IMPROVEMENT IN DISEASE ACTIVITY IN SLE PATIENTS TREATED WITH A CONCENTRATED EXTRACT OF KRILL OIL (AKM-3031)

Keywords: Diet and Nutrition, Systemic lupus erythematosus, Randomized control trial

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Background: Omega-3 fatty acids play a critical role in regulating inflammation. Patients with SLE have been reported to be deficient in omega-3 fatty acids, and deficiency could play a role in the ongoing inflammation characteristic of this disease. Previous work has produced conflicting results regarding the capacity of Omega-3 supplementation to control SLE disease activity.
Objectives: The goals of this study were to determine the level of omega-3 deficiency in SLE patients and to determine whether supplementation with a concentrated extract of krill oil rich in omega-3 fatty acids (AKBM-3031) could overcome the deficiency in SLE patients and decrease disease activity.
Methods: This was a randomized double blind controlled multicenter study of patients with active SLE (SLEDAI >/= 6). Patients meeting entry criteria were randomized to receive AKBM-3031 (4 grams/day) or identical placebo capsules containing mixed oils simulating that in a western diet (NCT03626311). Patients received investigational product or placebo daily for 24 weeks, at which time placebo patients could opt to receive AKBM-3031 for the subsequent 24 weeks, whereas those receiving AKBM-3031 continued on the medication. The primary outcome was the correction of the red blood cell omega-3 index determined by OmegaQuant. Changes in clinical features and adverse events were collected throughout the trial.
Results: 79 subjects were enrolled in the study; 97% of the patients were women and 56% were of European and 35% of African Ancestry. At baseline, the mean omega-3 index was 4.65+/- 1.09, below the lower limits of normal for the North American population (6.0). After 4 weeks of treatment with AKBM-3031, the Omega-3 index significantly increased from 4.65+/- 1.09 to 7.21+/-1.37, (p < 0.0001), whereas no significant change was noted in the patients receiving placebo. Increases in the Omega-3 index in AKBM-3031 treated patients persisted throughout the 48 weeks of the trial. Notably, when patients were changed from placebo to AKBM-3031 at 24 weeks, there was a rapid increase in the Omega-3 index (4.62+/-1.39 to 6.58+/- 1.85, p=0.0001). The total number of adverse events was less in the AKMB-3031group (186) than in the placebo group (342), most were mild or moderate and no serious adverse events were noted. Although there were no significant changes in disease activity when the entire groups were examined, there was a significant decrease in disease activity measured by SLEDAI-2K at 4, 8 and 16 weeks (p=0.0007, 0.04, 0.02, respectively) in the patients receiving AKBM-3031with high disease activity at baseline (SLEDAI >/=9).
Conclusion: Treatment of SLE patients with AKBM-3031 rapidly corrects the Omega-3 deficiency characteristic of these patients. AKBM-3031 was safe and decreased disease activity in those with more active SLE. These results suggest benefit of Omega-3 deficiency correction with AKBM-3031 in SLE patients with active disease and warrant a more extensive evaluation.

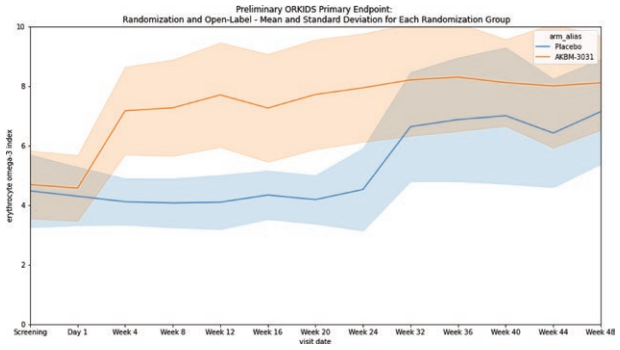


Figure 1.

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Disclosure of Interests: None declared
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AB0537

RITUXIMAB THERAPY IN LUPUS NEPHRITIS RESISTANT TO CONVENTIONAL THERAPY – A SINGLE CENTER EXPERIENCE (CASE SERIES)

Keywords: Systemic lupus erythematosus, Real-world evidence, Safety

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Background: Lupus nephritis(LN) can be a cause of morbidity and mortality in a significant portion of patients. The treatment of lupus nephritis can be challenging in some patients who are resistant to conventional immunosuppressive treatment.
Objectives: Rituximab is a promising agent for treating resistant LN patients. We evaluated the response of LN patients who were treated with rituximab treatment in our clinic retrospectively.
Methods: We evaluated LN patients who were followed and treated with at least one course of rituximab in our clinic between 2010-2022. LN was confirmed by renal biopsy. Creatinine clearence, serum creatinine, 24- hour proteinuria and Systemic Lupus Erythematosus- Disease Activity Index- 2000 (SLE-DAI-2K) were analyzed before and after Rituximab treatment. Primary end point was current prednisolone dose ≤5mg and 24-hour proteinuria ≤ 500mg. Also, we evaluated the side effect of rituximab.
Results: Forty seven patients (34 F, 13 M) were treated with rituximab. All patients had active lupus nephritis at initiation. Mean of disease duration was 10.44 ± 6.9 years. All patients were initally treated with high dose steroids. The other medications, the patients were previously treated with, were cyclophosphamide (n= 35), mycophenolate mofetil (n= 31), azathioprine (n= 6), cyclosporine (n= 2). Patients received an average of 4.1 ± 3.68 courses of rituximab (Table 1). The median value of pre-treatment proteinuria was 3050 (1370, 5175) mg/day. The median value of proteinuria after the final course was 747 (396, 1500) mg/day (p< 0.01). Serum creatinine level was changed from 0.94 ± 0.59 to 0.98 ± 0.68 (p= 0.53). Mean serum creatinine clearence was increased from 102.01 ± 43.2 to 109.1 ± 51.3 (p=0.28). Mean SLE-DAI-2K was reduced from 16.3 ± 6.2 to 7.2 ± 4.8 (p< 0.01). While initial steroid dose was 24.13 ± 18.47 mg/day, steroid dose at last rituximab course was 7.5 ± 5.8 mg/day (p< 0.01). End stage renal disease was developed in 3 (%6) patients. For primary end point of view, currrent prednisolone dose ≤ 5mg and 24-hour proteinuria ≤ 500 mg were achieved in %53.1, %36.1 of patients respectively. Both criteria was met by %25.5 of patients. During the treatment, 2 patients had serum reaction, 3 had pneumonia, 3 had herpes zoster. Three patients had hippogamaglobulinemia and treated with intravenous immunoglobulin. No one was died of lupus nephritis.
Conclusion: In lupus nephritis patients resistant to conventional therapy, rituximab can be tried as an alternative treatment choice. In our single center, most of the patients were class IV nephritis whom we observed the efficacy of rituximab. Generally, the side effects were acceptable. Rituximab could be a good option as a steroid reducing agent and exhibit a favorable clinical response in these patients.

Table 1. Characteristics of patients

Age, mean ± SD years	42.3 ± 11.1
Gender, n (%)	34 (64.2)
Female	13 (24.5)
Male	
Disease duration, mean ± SD, years	10.44 ± 6.9
*ISN/RPS Classification, n (%)	5 (10.6)
Class II	7 (14.8)
Class III	16 (34)
Class IV	6 (12.7)
Class V	7 (14.8)
Class III+V	6 (12.7)
Class IV+V	
RTX treatment courses mean ± SD	4.1 ± 3.68
Previous treatments, n	35
Cyclophosphamide	31
Mycophenolate mofetil	6
Azathioprine	2
Cyclosporine	

*ISN/RPS Classification: International Society of Nephrology/Renal Pathology Society Classification

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0538

LOW-DOSE BELIMUMAB AND ANTIMALARIAL AGENTS PREVENT RENAL FLARES IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM FOUR RANDOMISED CLINICAL TRIALS

Keywords: Systemic lupus erythematosus, bDMARD, Kidneys

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Background: Lupus nephritis (LN) is one of the most severe manifestations in systemic lupus erythematosus (SLE), constituting a substantial cause of end-stage kidney disease, dialysis, and mortality. Prompt and adequate treatment of LN, and prevention of renal flares are key components of disease management towards improved outcomes in patients with SLE.
Objectives: We aimed to determine the effect of the use of antimalarial agents (AMA) and different doses and pharmaceutical forms of belimumab on preventing renal flares in patients with active SLE.
Methods: We pooled data from the BLISS-52, BLISS-76, BLISS-SC and BLISS-Northeast Asia randomised clinical trials of belimumab (N=3225), that included patients with seropositive (antinuclear antibody titres ≥1:80 and/or anti-dsDNA levels ≥30 IU/mL), active SLE yet no severe ongoing renal disease. Participants were allocated to receive intravenous (IV) belimumab 1 mg/kg (N=559), IV belimumab 10 mg/kg (N=1033), subcutaneous (SC) belimumab 200 mg (N=556) or placebo (N=1077) in addition to standard therapy. Additionally, we classified patients as AMA users if they had received hydroxychloroquine, chloroquine, mepacrine, or quinine sulphate in stable doses for at least 30 days prior to the trial commencement. The outcome of the present post-hoc analysis was development of renal flares, defined according to the analysis plan within the BLISS programme. The hazard of renal flare was assessed with Cox proportional hazards regression models, adjusted for age, sex, ethnicity, previous renal involvement, baseline proteinuria and glomerular filtration rate, and use of glucocorticoids and immunosuppressants.
Results: In total, 192 patients developed a renal flare after a median of 197 days. In multivariable Cox regression analysis, use of AMA was associated with a lower risk of renal flares (HR: 0.64; 95% CI: 0.54–0.96; p=0.026). Compared with placebo, the risk of renal flares was lower among patients receiving IV belimumab 1 mg/kg (HR: 0.44; 95% CI: 0.25–0.79; p=0.006) and IV belimumab 10 mg/kg (HR: 0.63; 95% CI: 0.45–0.87; p=0.005), but not SC belimumab 200 mg (HR: 0.90; 95% CI: 0.57–1.42; p=0.648). When analysing all study arms with and without antimalarials separately, patients receiving IV belimumab 1 mg/kg along with AMA experienced the lowest rate of renal flares (18.5 (7.4–38.1) cases per 1000 person-years). Using patients who received placebo but not AMA as the reference comparator, patients receiving IV belimumab 1 mg/kg (OR: 0.30; 95% CI: 0.13–0.70; p=0.005) and patients receiving IV belimumab 10 mg (OR: 0.45; 95% CI: 0.27–0.75; p=0.002) were protected against renal flares only when belimumab use was combined with AMA.
Conclusion: In this RCT setting, belimumab and AMA protected against renal flares in patients with active seropositive SLE yet no ongoing severe renal involvement. The protective effect of IV belimumab against renal flares appeared optimal when belimumab was combined with AMA. The prominent effect of low-dose belimumab motivates investigation of the efficacy of intermediate doses of belimumab.
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AB0539 ANIFROLUMAB FOR REFRACTORY SKIN DISEASE IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A SINGLE CENTER CASE SERIES

Keywords: Systemic lupus erythematosus, Skin, bDMARD

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Background: Anifrolumab (ANI) a human monoclonal antibody to type I interferon receptor subunit 1 has been recently approved for the treatment of SLE. In SLE, the skin is not only a target but also a key- driver of the autoimmune response via the production of type I IFN.
Objectives: To evaluate the efficacy of ANI in real-life under the early access program (09/2021 – 03.2022).
Methods: A total of seven patients (all female, mean age 50 years, disease duration 15 years) with SLE- diagnosis based on ACR1997 or SLICC or EULAR/ACR 2019 classification criteria for SLE and inadequate response to prior immunosuppressive therapies received ANI from 09/2021 until 03.2022 as part of an early access program. Patients' demographics, clinical and laboratory characteristics, disease activity (SLEDAI-2K, CLASI) were recorded at baseline and first months of the administration of ANI.
Results: Active skin disease was the dominant clinical manifestation of all patients for the administration of ANI (subacute cutaneous lupus in 6/7, discoid lupus in 3/7, severe chemeltular lesions in one patient). Patients had received an average of 5.1 immunosuppressive drugs before ANI, with an inadequate response. The mean (SD) SLEDAI index at baseline was 6.9 (1.1) and the mean (SD) prednisone dose 2.7 (2.8) mg/day. In reference to the skin disease, mean (SD) CLASI (Activity/Damage) before first administration of ANI was 9.9/1.4 (6.3)/(2.2). A rapid response of the skin disease, especially the subacute cutaneous lupus lesions, was observed from the first injection of ANI. As expected, the results were less prominent in patients who had discoid lupus lesions, although patients reported subjective improvement. The mean (SD) SLEDAI, CLASI and daily prednisone dose are 3.4 (1.8), 3/1.4 (1.4/2.2) and 2.5 (2.5) mg, respectively. After a mean (SD) follow-up of 5.7 (2.0) months, one patient discontinued ANI due to VZV infection.
Conclusion: IFN inhibition is effective for the treatment of refractory cutaneous lupus manifestations. The prompt response of the dermatologic disease to ANI likely reflects the beneficial effects of neutralization of IFN on the autoimmune and vasculopathic processes in SLE.
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AB0540 COAGULATION AND HAEMOSTASIS PARAMETERS IN PREGNANT WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND HEALTHY CONTROLS WITH AND WITHOUT PREECLAMPSIA

Keywords: Pregnancy and reproduction, Systemic lupus erythematosus

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Background: Women living with Systemic Lupus Erythematosus (SLE) are at increased risk of pregnancy complications, including preeclampsia (PE). Placental dysfunction is the key pathogenic event, but the underlying mechanisms are scarcely known.
Objectives: This study aimed to investigate global hemostatic assays in pregnant SLE patients in relation to PE and the use of anti-thrombotic prophylaxis.
Methods: Patients with SLE were sampled during the third trimester of gestation for coagulation and haemostasis (C&H) assays: 1) overall coagulation potential (OCP); 2) overall haemostatic potential (OHP); 3) overall fibrinolysis potential (OFP), plasma levels of fibrinogen and D-dimer. Pregnant healthy controls (HC) with and without PE were also analysed.
Results: Twenty-two consecutive pregnant SLE patients, 80 pregnant HC without PE, and 42 pregnant HC with PE were analysed. Disease characteristics, pregnancy features, and coagulation parameters are reported in Table 1. No thrombotic or bleeding events occurred in SLE patients. Four SLE patients experienced PE (18.2%) despite treatment with low dose acetylsalicylic acid (LDASA) ± low molecular weight heparin (LMWH). These patients displayed significantly lower OCP and OFP, but not OHP, as compared to SLE without PE. Among 4 SLE+PE patients, the 2 treated with LMWH tended to have lower OCP, OHP, and OFP values as compared to the 2 untreated patients (134.9±190.7 vs 372.3±24.6; 90.6±128.2 vs 202.2±24.1; 16.4±23.3 vs 45.4±10.1). Among SLE patients treated with LMWH, undetectable

Table 1. Characteristics and coagulation parameters of SLE patients and HC. Abbreviations: aPL: antiphospholipid antibodies; APS: antiphospholipid syndrome; IQR: interquartile range; NA: not applicable; Continuous variables are expressed as mean±SD. [g, i, l, n]=p<0.05; [a, b, c, d, e, f, h, m]=p<0.01. (*) Prophylactic dose; (#) Anticoagulant dose.

	Pregnant SLE patients (n=22)	Pregnant SLE without PE (n=18)	Pregnant SLE with PE (n=4)	Pregnant SLE patients without LMWH therapy (n=14)	Pregnant SLE patients with LMWH therapy (n=8)	Pregnant HC without PE (n=80)	Pregnant HC with PE (N=42)
Age, years	32.5±3.6	32.1±3.4	34.5±4.8	32.6±4.2	32.4±4.2	30.1±4.9	31.2±6.6
Disease duration, years	10.7±7.9	9.8±7.2	15±10.4	10.9±9.3	10.5±4.8	NA	NA
Lupus nephritis, n (%)	6 (27.3)	4 (22.2)	2 (50)	5 (35.7)	1 (12.5)	NA	NA
APS, n (%)	1 (4.5)	0	1 (25)	0	1 (12.5)	NA	NA
aPL carrier, n (%)	7 (31.8)	5 (27.8)[c]	2 (50)[d]	2 (14.3)	5 (62.5)	2[c]	0[d]
Disease flare during pregnancy, n (%)	5 (22.7)	4 (22.2)	1 (25)	2 (14.3)	3 (37.5)	NA	NA
Preeclampsia, n (%)	4 (18.2)	0	4 (100)	2 (14.3)	2 (25)	0	42 (100)
LDASA only, n (%)	14 (63.6)	12 (66.7)[e]	2 (50)[f]	14 (100)	0	0[e]	0[f]
LDASA + LMWH, n (%)	8 (36.4)	6 (33.3) 5*; 1#	2 (50) 0*; 2#	0	8 (100)	0	2 (4.8)
Oral Glucocorticoids, n (%)	8 (36.4)	5 (27.8)	3 (75)	3 (21.4)	5 (62.5)	NA	NA
Hydroxychloroquine, n (%)	19 (86.4)	15 (83.3)	4 (100)	11 (78.6)	8 (100)	NA	NA
Other immunosuppressants, n (%)	7 (31.8)	6 (33.3)	2 (50)	4 (28.6)	3 (37.5)	NA	NA
Fibrinogen (g/L)	4.9±1	4.8±0.9	5.5±1.5	4.7±0,9	5.2±1.2	4.6±1.2	5.0±1.0
D-dimer (mg/L FEU)	1.5±0.5	1.5±0.6	1.1±0.3	1.5±0.5	1.4±0.6	1.4±0.5	1.6±0.8
OCP (Abs-sum)	368.9±135.8	394.6±116[g;h]	253.6±176.4[g]	427.2±50.7[i]	298.9±173[i]	242.2±36.1[h]	231.6±40.6
OHP (Abs-sum)	187.4±83.8	196.5±80.4	146.4±99.1	204.4±64.8	166.9±102	173.1±46.0	195.2±36.7
OFP %	44.7±18.6	47.8±16.9[l]	30.9±22.2[m]	53±10.1[n]	34.8±21.9 [n]	29.2±12.4[l]	15.3±9.2[m]

OCP, OHP, and OFP were found in 1 out of 2 SLE+PE and 1 out of 6 SLE without PE. No differences across groups were found for fibrinogen and D-dimer levels.

Conclusion: C&H parameters were altered in SLE pregnancy as compared to HC pregnancy, either in pregnancies complicated by PE or not. LWWH is expected to reduce to zero the values of OCP, OHP, and OFP, but this phenomenon was not observed in all SLE treated patients, suggesting that the response to LMWH can be variable among SLE pregnant patients. Larger and longitudinal studies across trimesters of gestation will clarify whether C&H parameters are useful to monitor treatment effects and improve the management of SLE pregnancy.

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AB0541 EFFICACY OF DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN PRIMARY SJÖGREN'S SYNDROME-RELATED INTERSTITIAL LUNG DISEASE

Keywords: Disease-modifying drugs (DMARDs), Clinical trials, Sjögren syndrome

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Background: Primary Sjögren's syndrome (pSS) is mainly characterized by dry mouth and eyes due to loss of secretory function of exocrine glands, and systemic involvement can be seen [1]. One of the most important causes of morbidity and mortality in pSS is interstitial lung disease (ILD) [2]. Primary SS-related ILD (pSS-ILD) treatment is usually based on the clinician's experiences since there are insufficient clinical studies.

Objectives: To evaluate the treatment modalities applied to patients with pSS-ILD and the functional response to the treatment.

Methods: A retrospective analysis was performed, of patients with pSS-ILD, who received conventional or biological disease-modifying antirheumatic drugs between January 2004 and August 2022. Forced vital capacity (FVC%) and diffusing capacity of carbon monoxide (DLCO%) performed within 1 month before treatment and within 1 month after treatment cessation, were analyzed. The effects of DMARDs on pulmonary function and whether there was a difference in their effectiveness were evaluated.

Results: The prevalence of pSS-ILD was 7.2%. The mean age of 27 patients included in the study was 62.6±10.8, and 20 (74.1%) of the patients were female. Among all DMARDs (19/47) and first-line treatments (16/27), AZA was the most frequently used agent. Other agents used were MMF (n=11), RTX (n=8), CyC (n=5), and MTX (n=4). There was an increase in FVC% (from 80.20±22.1 to 81.6±23.0) and FEV1% (from 73.8±20.6 to 75.3±22.8) and a decrease in DLCO% (from 53.7±15.3 to 52.2±19.3) with DMARDs treatment, but the difference was not statistically significant (p=0.434, p=0.463, and p=0.652, respectively). There was a statistically non-significant decrease in %FVC with AZA and an increase with MMF, RTX, and CyC (Table 1). Also, there was no significant change in DLCO% values with AZA, MMF, and RTX (Table 1). The HRCT patterns were UIP in 13 (48.1%) patients, NSIP in 9 (33.3%), LIP in 2 (7.4%), and unclassified in 3 (11.1%). There were no significant differences in FVC% and DLCO% parameters with DMARDs treatment in patients with UIP and NSIP patterns.

Conclusion: DMARDs can stabilize pulmonary functions and delay worsening in patients with pSS-ILD.

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Disclosure of Interests: None Declared.

Table 1. Mean change in FVC(%) and DLCO(%) values with DMARDs treatment

	Number of analyzes	Bazal	Posttreatment	Change	P value
DMARDs, n=47					
FVC	39/47	80.20±22.1	81.6±23.0	+1.40	0.434
DLCO	19/47	53.7±15.3	52.2±19.3	-1.50	0.652
AZA, n=19					
FVC	19/19	73.3±13.8	70.2±15.6	-3.14	0.263
DLCO	11/19	53.5±13.6	52.6±20.5	-0.91	0.868
MMF, n=11					
FVC	8/11	80.9±26.1	82.9±27.0	+2.0	0.492
DLCO	4/11	49.3±18.8	48.3±24.5	-1.0	0.812
RTX, n=8					
FVC	6/8	65.9±15.1	68.7±14.9	+2.72	0.534
DLCO	3/8	66.3±14.2	60.7±9.8	-5.67	0.392
CYC, n=5					
FVC	3/5	80.0±48.8	96.0±42.2	+16.0	0.086
DLCO	-	-	-	-	-

Disclosure of Interests: None Declared.

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AB0542 PRIMARY SJÖGREN'S SYNDROME AND INTERSTITIAL LUNG DISEASE. RESULTS OF AN OBSERVATIONAL COHORT

Keywords: Lungs, Disease-modifying drugs (DMARDs), Sjögren syndrome

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Background: Primary Sjögren's Syndrome (pSS) is a chronic systemic autoimmune disease of unknown etiology, with an estimated prevalence of 0.25% (0.15-0.43). It has a broad clinical spectrum and extraglandular manifestations such as Interstitial Lung Disease (ILD), being one of the main contributors to morbidity and mortality in patients with pSS [1].

Objectives: Analyze the clinical characteristics of patients with pSS and ILD, describe the patterns of lung involvement and the evolution of the disease as well as the treatments that were used.

Methods: Observational, retrospective, single-center study, in the *Hospital Universitario Virgen Macarena* Rheumatology department, from 2010 to 2022, including patients with pSS according to EULAR/ACR criteria and ILD. The data obtained from the medical records was analyzed by the statistical software SPSS v28. This study has been approved by the CEIC.
Results: 19 patients were included, 17 (89.5%) women, with a mean age of 66.4 years (62-71). All presented antinuclear and anti-SSA antibodies, 31.6% (6) anti-SSB antibodies and 43.8% (7) Rheumatoid Factor, 63.2% (12) hypergammaglobulinemia and none hypocomplementemia. 36.8% (7) were former smokers. The extraglandular manifestations and comorbidities are shown in Table 1. The mean age at diagnosis of ILD was 60.1 years (53.3-65.8). The time elapsed until the diagnosis was 93 months (12-198), however, in 52.6% (10) the diagnosis of ILD was prior to pSS diagnosis for approximately 17 months (6-27). The most common radiological pattern with 63.2% (12) is non-specific interstitial pneumonia, two patients presented lymphocytic interstitial pneumonia, two usual interstitial pneumonia, one organizing pneumonia and the rest of them other patterns. Two patients required lung biopsy. Prior to diagnosis, 3 patients were being treated with hydroxychloroquine, the rest had not required treatment with immunomodulators. Once diagnosed, 52.6% (10) required immunosuppressants (Graph 1). 80% (8) continue in treatment, 7 with mycophenolate mofetil with a mean duration of 48 months (20-75). 47.4% (9) required oral glucocorticoids at some point. 88.2% (15) improved or remained radiologically stable by HRCT, 73.3% (11) according to respiratory function tests (decrease in FVC <10% and DLCO <15%) and 72% (13) dyspnea remained stable or improved according to the MRC scale, with no significant differences between patients with and without treatment. The mean evolution time of ILD was 77.3 months (63-91). There were 2 deaths, one due to progression of the disease and the other due to a head trauma.
Conclusion: Interstitial lung disease is an extraglandular manifestation present in patients with pSS, therefore being essential the early diagnosis. In our case, after the diagnosis of ILD, half of the patients required immunosuppressive treatment to prevent the progression of the disease, with a large number of patients remaining currently stable.
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Table 1. Extraglandular manifestations and comorbidities.

	N	%
Arthralgias	5	26.3
Arthritis	3	15.8
Cytopenias	5	26.3
Lymphadenopathy	4	21.1
Parotidomegaly	4	21.1
Raynaud	3	15.8
Primary biliary cholangitis	2	10.5
Tubulointerstitial nephritis	1	5.3
Autoinmune hypothyroidism	3	15.8
Myasthenia gravis	1	5.3
Thrombocytopenic púrpura	2	10.5
Osteoporosis	5	26.3
Cardiovascular Disease	7	36,8
Hypertension	8	42.1
Dyslipemia	7	36.8
Diabetes Mellitus	3	15.8
Obesity	7	36.8
Asthma/ Copd	3	15.8
Pulmonary Hypertension	4	21.1

Pacients	Previuos Treatments	Current Treatments
1	Rituximab	Hydroxychloroquine + Mycophenolate
2	-	Mycophenolate
3	-	Hydroxychloroquine + Mycophenolate
4	-	Hydroxychloroquine + Mycophenolate
5	Cyclophosphamide	-
6		Hydroxychloroquine + Mycophenolate
7	Azathioprine Cyclophosphamide Rituximab	Mycophenolate
8	-	Nintedanib
9	-	Mycophenolate
10	Rituximab	-

Graph 1. Treatments used.

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AB0543

CHARACTERISTICS AND TREATMENT OUTCOMES OF ASIAN SLE PATIENTS WITH CONCOMITANT GENITOURINARY AND GASTROINTESTINAL INVOLVEMENT

Keywords: Kidneys, Gastrointestinal tract, Systemic lupus erythematosus

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Background: SLE is a chronic autoimmune disorder which affects multi-organ systems. We report a case series of SLE with concomitant genitourinary (GU) and gastrointestinal (GI) activity in our centre.
Objectives: To describe the characteristics, treatment response and outcomes of these cases.
Methods: The clinical notes were reviewed and descriptive statistical tests were used.
Results: 7 cases were recorded from 2019 to 2022. All were females with median age of onset 23 +/- 18.9 years old. Case 5 and 6 had prior diagnosis of SLE with lupus nephritis (LN). The initial symptoms were episodic abdominal pain, associated with vomiting and/or diarrhea. 2 cases had urinary symptoms too. The mean duration of symptoms was 4 months. All cases had severe GU and GI activity (Both BILAG A). Nearly all had clinically or biopsy-proven proliferative LN (mean 24 hour urine protein = 4.99 g/d). 3 patients also had ureterohydronephrosis and/or interstitial cystitis. Intestinal pseudo-obstruction (IPO) and lupus mesenteric vasculitis (LMV) were found in 2 and 5 cases, respectively. Serositis and mucocutaneous lesions were more frequent too. Almost all cases had high titres of ANA (≥ 1:320) and dsDNA, with prevalent positive anti-Ro. Other remarkable findings were low complements (especially C3) and normal ESR/CRP. Antiphospholipid antibodies were negative in all but one cases. Treatment wise, all had IV hydrocortisone and high dose prednisolone. 6 cases had pulsed methylprednisolone and IV cyclophosphamide therapy (NIH regimen). Case 7 had concurrent C. difficile infection and received mycophenolate mofetil (MMF) therapy once the infection resolved. In all cases, the extra renal features and urinary symptoms fully resolved. In term of LN, 4 patients did not achieve remission with NIH regimen and needed MMF therapy; and only 50% attained complete remission subsequently. In general, the outcomes of all patients were good except for Case 1 who developed contracted urinary bladder needing ileal conduit urinary diversion.
Conclusion: Concomitant IPO/LMV with LN and urinary tract abnormalities are rare clinical syndromes in SLE. Our patients shared similar clinical features as reported by Echeverry et al [1]. The treatment response was generally good with no recurrence of IPO/LMV and favourable renal outcomes.
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Table 1. Clinical profile of all cases

Patient	1	2	3	4	5	6	7
Age, year	28	23	18	21	20	53	66
Sx	Abd pain, V Urinary	Abd pain, V, D	Abd pain, V	Abd pain, V, D Urinary	Abd pain, D	Abd pain, D	Abd pain, D
Duration, month	8	4	4	2	2	6	2
Gut	IPO	LMV	LMV	IPO	LMV	LMV	LMV
LN & etc	III + V HN + HU Cystitis	No Bx HN Cystitis	II	No Bx Cystitis	IV	No Bx	No Bx
24HUP (g/d)	16.9	2.4	2.6	2.3	1.1	7.2	2.4
Other organ	Serositis	NPSLE Serositis MC	Cytopenia MC	NPSLE MC	Cytopenia MC Serositis	Serositis	Cytopenia Serositis
ANA	+	+	+	+	+	+	+
dsDNA	+	+	+	NA	+	+	+
ENA	+ Ro, La	+ Rib. P	+ Sm, RNP, Ro	+ RNP, Ro, Rib. P	+ RNP, Ro, La	+ Sm, Ro, Scl 70	-
C3, C4	N	L	L	L (C3)	L	L	L (C3)
APL	-	-	-	-	-	-	+ LA
ESR, CRP	N	N	N	N	N	N	N
Therapy	MTP	MTP	MTP	MTP	MTP	MTP	HCT
GC	HCT Pred 1mg	HCT Pred 0.8mg	HCT Pred 1mg	HCT Pred 0.8mg	HCT Pred 0.7mg	HCT Pred 1mg	Pred 1mg
IV CYC, NIH	Y	Y	Y	Y	Y	Y	No (MMF)
Outcomes	Failed	CR	CR	PR	PR	PR	(< 6 mth)
Renal (LN)	>> MMF	Rslv	Rslv	>> MMF	>> MMF	>> MMF	Rslv
Non-renal	(PR) Rslv			(CR) Rslv	(PR) Rslv	(CR) Rslv	

Abbrev. - Sx: Symptoms; Abd: Abdominal; V: Vomit; D: Diarrhea; IPO: Intestinal pseudo-obstruction; LMV: Lupus mesenteric vasculitis; LN: Lupus nephritis; Bx: Biopsy; HN: Hydronephrosis; HU: Hydroureter; 24HUP: 24 hour urine protein; NPSLE: Neuropsychiatric SLE; MC: cutaneous;; NA: Not available; APL: Antiphospholipid antibodies; LA: Lupus anticoagulant; N: Normal; L: Low; GC: Glucocorticoid; MTP: Pulsed methylprednisolone; Pred: Prednisolone (mg/kg/d); HCT: IV Hydrocortisone; CYC: Cyclophosphamide; Y: Yes; PR: Partial remission; CR: Complete remission; MMF: Mycophenolate mofetil; Rslv: Resolved.

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Disclosure of Interests: None Declared.
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AB0544

PHENOTYPING ON MUCOSAL MOLECULAR SIGNITURE OF PATIENTS WITH ULCERATIVE COLITIS ANALYSIS

Keywords: Gastrointestinal tract, Autoantibodies, -Omics

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Background: Ulcerative colitis (UC) is an inflammatory bowel disease characterized by idiopathic and recurrent mucosal inflammation, whereas disease heterogeneity has not sufficiently translated into current clinical subclassifications [1].
Objectives: This study aims to Identify and characterize subgroups of patients with similar target status and molecular biomarkers to reliably predict treatment response which is of great interest for the treatment of UC patients.
Methods: 16 microarray datasets including 602 colon tissue samples (455 patients with UC and 147 healthy controls) were both obtained from GEO database. Depend on up-regulated differentially expressed genes (DEGs),unsupervised clustering [2] was applied to group the samples and pathways and biomarkers associated with UC was unearthed by gene-set enrichment analysis. Xgboost classifier was used for evaluating the efficacy of different biologics in patients with UC.
Results: According to the 267 upregulated DEGs of UC, colon tissue samples were classified into three subtypes(A-C) with distinct molecular and cellular characteristics. Subtype A is designated as epithelial hyperplastic subtype with epithelial features while subtype C was characterized by the immune activation subtype with prominent immune cells and proinflammatory signatures. The subtype B is named mixed, which is in between the above two and is moderately activated in all signaling pathways. It is worth noting that, compared with subtype C as refractory UC patients, subtype A shows stronger correlation with the excellent reactions of biological agents such as golimumab(80%in A vs 37.5%in C), infliximab(100%in A vs 16.7%in C), vedolizumab(33.3%in A vs 0% in C) and ustekinumab(22.4%in A vs 3%in C).
Conclusion: These results, based on the most comprehensive microarray provide an in-depth understanding of the pathophysiological characteristics of UC, and build an accurate typing model for ulcerative colitis, which can benefit clinical treatment.

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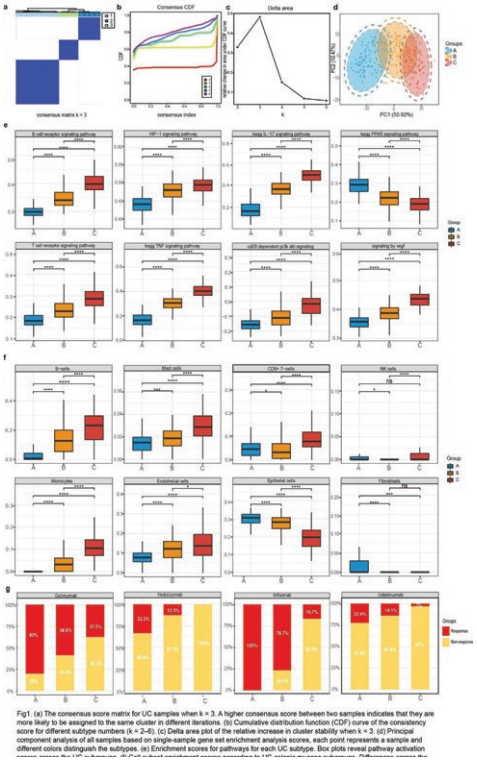


Fig1. (a) The consensus score matrix for UC samples when k = 3. A higher consensus score between two samples indicates that they are more likely to be assigned to the same cluster in different iterations. (b) Cumulative distribution function (CDF) curve of the consistency score for different subtype numbers (k = 2–6). (c) Delta area plot of the relative increase in cluster stability when k = 3. (d) Principal component analysis of all samples based on single-sample gene set enrichment analysis scores, each point represents a sample and different colors distinguish the subtypes. (e) Enrichment scores for pathways for each UC subtype. Box plots reveal pathway activation

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Disclosure of Interests: None Declared.
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AB0545

EFFECT OF BELIMUMAB ON CLINICAL PROFILES AND DAILY LIVING SCORE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Keywords: Biomarkers, bDMARD, Mental health

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Background: Belimumab (BE) was shown to decrease disease activity, glucocorticoid intake, and flare rates, thereby suppression of damage progression, and also has been included in the 2019 EULAR recommendations on SLE management as an approved biological drug to be used in patients with a refractory response to a standard of care regimen.
Objectives: We have examined the effect of belimumab on activities of daily living score (AS), immunological data, disease activities and dose of PSL in patients with SLE.
Methods: We selected 36 cases (F/M 30/6) from 2018 to 2022 in patients with SLE treated with BE (iv or sc) to clarify the effect of BE on immunological data, disease activities (SLEDAI), AS (Lupus 26: 849, 2017), and dose of PSL after treatment for 6 months (M), 12 M and 24M.
Results: Mean BMI and duration of disease were 20.5±3.7 kg/m2 and 15.7±13.8 years. Two cases could not continue due to arthralgia and loss of hair within 24 M. After treatment with BE for 6 M and 12 M, anti-dsDNA antibodies (AU/ml) were significantly decreased for 12 M and 24 M, respectively ($p<0.05$, before 61±103, 6M 28±48, 12 M 19±23), and C3, C4 and CH50 (U/ml) were significantly increased ($p<0.05$, before 76±26, 14±7 and 28.7±10.8, 6 M 186±18, 18±7 and 35.3±9.2, 12M 85±18, 18±7 and 135.3±9.2). Levels of SLEDAI score were significantly decreased ($p<0.01$, before 12±7, 6M 5±3, 12 M 4±3 and Doses of PSL (mg) were significantly decreased ($p<0.05$-0.02, before 10.8±10.6, 6 M 6.1±3.7, 12 M 5.7±3.0). AS scores were also significantly improved ($p<0.01$-0.05), before 28.4±14.2, 12 M 14.8±15.8, 24 M 16.8±10.9). Especially, anxiety, depression and loss of concentration, which were important marker for activities of living score, were not significantly changed.
Conclusion: Effects of BE on immunological data, disease activities, and daily living scores, induction of clinical remission and dose reduction of prednisolone were tolerable without major adverse effects in patients with SLE.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1367

AB0546

DESIGN OF ANIFROLUMAB STUDY OF TREATMENT EFFECTIVENESS IN THE REAL WORLD (ASTER): A MULTI-NATIONAL, OBSERVATIONAL, POST-LAUNCH STUDY TO DESCRIBE THE CLINICAL EFFECTIVENESS OF ANIFROLUMAB IN ROUTINE CLINICAL PRACTICE IN PATIENTS WITH SLE

Keywords: Real-world evidence, Quality of life, Systemic lupus erythematosus

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Background: Real-world evidence (RWE) on prescription medication use for systemic lupus erythematosus (SLE) is limited, and no real-world studies to date have investigated medication use post-launch with anifrolumab, a type I interferon receptor inhibitor. ASTER is the first multi-national, real-world study to examine patients with SLE receiving standard therapy who initiate anifrolumab treatment as an add-on biologic.
Objectives: To describe the study design of ASTER.
Methods: ASTER (NCT05637112) is a longitudinal, observational cohort study with 1 year of retrospective baseline data and 3 years of follow-up after first anifrolumab initiation until patient discontinuation, death, loss to follow-up or end of study (whichever occurs first). Adults with an SLE diagnosis per the 2019 European

League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) criteria for SLE who start anifrolumab per the approved country-specific label are eligible. Patients who are anifrolumab experienced, currently in anifrolumab early access/compassionate use programs, or in a clinical trial with an investigational product are excluded. Eligible patients will be enrolled at a routine clinical visit before the first anifrolumab infusion. Key study measures and data collection methods are presented in the Table 1. Patient-reported outcomes (PROs) and diaries are selected and designed based on patient feedback. Key endpoints of disease activity and the proportion of patients attaining a Lupus Low Disease Activity State will be assessed. For patients who discontinue anifrolumab, data collection will continue for the entire follow-up period, unless they withdraw consent.

Results: About 500 patients are expected to be enrolled from Austria, Canada, Denmark, France, Germany, Israel, Italy, Norway, Spain, and Sweden, with 15–200 patients per country. The study will be open for enrollment in 2023 and data collection is expected to finish in 2029. Data will be collected at baseline and at quarterly (Year 1) or biannual visits (Years 2 and 3). Electronic case report forms will be used to record patient information using the Medidata RAVE system. MyReco® software will be used to record PROs via a mobile application and collect physician-completed assessments via a web platform. Results will primarily be descriptive.

Conclusion: ASTER will provide physicians with valuable insights into the effectiveness of anifrolumab in patients with SLE in routine clinical practice. ASTER will generate comprehensive RWE of anifrolumab to inform patients about its impact on disease activity and health-related quality of life outcomes in global real-world settings.

Table 1. Key study measures

Demographics (age, sex, ethnicity, insurance type)[a]
Clinical characteristics (comorbidities, medical history, adverse events/drug reactions[b], lab results)[a]
SLE treatment history (steroids, antimalarials, immunosuppressants, NSAIDs, biologics)[a]
SLE flares[a]
Healthcare resource use[a]
Clinical assessments[c]
Physician's Global Assessment[d]
SLE Disease Activity Index 2000[d]
Cutaneous Lupus Erythematosus Disease Area and Severity Index
Systemic Lupus International Collaborating Clinics/ACR Damage Index[a]
Low Lupus Disease Activity State[d]
PROs[c]
Functional Assessment of Chronic Illness Therapy–Fatigue
Lupus Quality of Life
Patient Global Assessment
European Quality of Life 5-Dimension Health Questionnaire 5 Level
Work Productivity and Activity Impairment: Lupus
Pain Numerical Rating Scale
Diaries (e.g, medication use, pain, fatigue, sleep quality)[e]

ACR, American College of Rheumatology; NSAIDs, non-steroidal anti-inflammatory drugs; PRO, patient-reported outcome; SLE, systemic lupus erythematosus. [a]Collected at baseline and biannually in Years 1–3. [b]Collected throughout the study. [c]Collected at baseline, quarterly in Year 1, and biannually in Years 2–3. [d]Primary objective. [e]Collected at baseline, weekly in Year 1 only.

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Disclosure of Interests: Marta Mosca Speakers bureau: AstraZeneca, GSK, Janssen, Lilly, Consultant of: AstraZeneca, AbbVie, GSK, UCB, Lilly, Cathy Emmas Shareholder of: AstraZeneca, Employee of: AstraZeneca, Cassandra Nan Shareholder of: AstraZeneca, GSK, Employee of: AstraZeneca, Heide Stirnadel-Farrant Shareholder of: AstraZeneca, GSK, Employee of: AstraZeneca, Samuel Chen Shareholder of: AstraZeneca, Employee of: AstraZeneca, Lucy Carty Employee of: Currently employed by AstraZeneca as a contractor, Barnabas Desta Shareholder of: AstraZeneca, Employee of: AstraZeneca, Caroline Seo Shareholder of: AstraZeneca, Consultant of: HEOR consulting firm (Pharmerit-an OPEN Health Company), Employee of: AstraZeneca, Stephanie Chen Shareholder of: AstraZeneca, Employee of: AstraZeneca, Alessandro Sorrentino Shareholder of: Abbott Laboratories, Galapagos, Gilead, Kontigo Care, Moderna, Employee of: AstraZeneca; Before: Janssen and Sanofi.

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AB0547 EVALUATION OF THE CLINICAL OUTCOME, PRESCRIPTION PATTERNS AND COST OF TREATMENT IN PATIENTS WITH LUPUS NEPHRITIS IN A TERTIARY CARE HOSPITAL

Keywords: Systemic lupus erythematosus, Rare/orphan diseases

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Background: Lupus nephritis (LN), a rare but severe renal manifestation of Systemic Lupus Erythematosus (SLE), has one of the most unsatisfactory renal disease outcomes, posing a great challenge for treatment. The clinical outcomes with various treatment regimens in LN have been studied globally in many randomized controlled trials (RCT). However, there is a paucity of data on clinical outcomes with various treatment regimens in Indian LN patients despite these regimens being extensively used in clinical practice. Only a few studies have analyzed prescription patterns in LN but none of these studies were conducted in India. Also, there is a substantial economic burden associated with SLE and LN in terms of healthcare resource utilization. The economic burden on Indian LN patients is not known and the cost of illness studies is not reported in the literature.

Objectives: The objectives of the study were to assess the clinical outcome in terms of disease activity in patients with LN at the end of induction therapy and at the end of maintenance therapy of 12 months, and to evaluate prescription patterns and cost of the treatment in patients with LN.

Methods: A prospective, observational, single-center study was conducted in the rheumatology department of a tertiary care hospital. The study was conducted in two parts. Part- 1 was cross-sectional, where the clinical outcome in LN patients at the end of maintenance therapy of 12 months was assessed (based on American College of Rheumatology- Renal Response Criteria (ACR – RRC)), while part- 2 was a longitudinal study where clinical outcome at the end of induction therapy or at the end of 6 months was assessed along with prescription patterns and cost of treatment.

Results: A total of 64 LN patients with 41 patients in Part-1 (cross-sectional) and 23 patients in Part-2 (longitudinal) satisfying the eligibility criteria were included in the final analysis. In the cross-sectional part of the study, all 41 patients showed a response to treatment at the end of maintenance therapy for 12 months (Table 1). In the longitudinal part of the study, most of the LN patients (65.21%) showed a partial response at the end of induction therapy. The prescription pattern analysis showed that 66 (57.40%) prescriptions out of a total of 115 prescriptions were complete with the average number of drugs prescribed per encounter being 10.77 ± 1.85 (Mean ± Standard Deviation). The most prescribed immunosuppressant was MMF (59%). The direct costs incurred by the patient {Rs.24001.01 (11204.36– 29110.02), (Median (interquartile range)} were much higher as compared to the indirect costs {Rs. 3000 (2000-3150), (Median (interquartile range)} due to the higher cost borne by the patient for drug therapy {Rs.16429.49 (5260.07 – 22585.04), (Median (interquartile range)}.

Table. 1. Clinical outcome in the various treatment regimens (at the end of maintenance therapy of 12 months)

Clinical Outcome	MMF	NIH	Euro lupus	Change in regimen	Total n (%)
Complete response	4	9	6	3	22 (53.70%)
Partial response	1	11	2	5	19 (46.34%)
Total	5 (12.19%)	20 (48.79%)	8 (19.51%)	8 (19.51%)	41

Conclusion: The clinical outcome at the end of 12 months of maintenance therapy was found to be satisfactory, with all the LN patients being responders to treatment. The MMF regimen was the preferred treatment regimen over the equally efficacious cyclophosphamide-based regimens due to the ease of administration and non-requirement of hospitalization during the period of the COVID pandemic. The high cost of MMF increased the direct cost borne by the patient due to its unavailability in the hospital pharmacy. Hence there is a need to review the hospital pharmacy stock at regular intervals and streamline the procurement system for drugs during public health emergencies such as the pandemic.

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Disclosure of Interests: None Declared.

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AB0548 EFFICACY AND SAFETY OF NIPOCALIMAB IN ADULT PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS: DESIGN OF A PHASE 2 STUDY

Keywords: Systemic lupus erythematosus, Safety, Autoantibodies

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Background: Systemic lupus erythematosus (SLE) is a chronic, progressive, autoimmune disorder characterized by chronic inflammation of multiple organs and tissues; mediated by autoantibodies and immune complexes. Approved treatments are few and associated with limitations including suboptimal response. Nipocalimab is a novel high affinity, fully human, aglycosylated, immunoglobulin G1 (IgG1) monoclonal antibody that selectively blocks the neonatal Fc receptor (FcRn) and displays no effector function. Clinical studies conducted with nipocalimab in healthy volunteers (NCT02828046) and in adult generalized myasthenia gravis patients (NCT03896295) demonstrated rapid and durable serum IgG and pathogenic autoantibody reductions.
Objectives: To describe the protocol of a Phase 2 study evaluating the efficacy and safety of nipocalimab in patients with active SLE (NCT04882878).
Methods: This is a phase 2, multicenter, randomized, placebo-controlled, double-blind, parallel-group study enrolling adults with active, autoantibody-positive SLE with an inadequate response to one or more standard of care treatments. The study consists of a ≤6-week screening period, a 52-week double-blind treatment period, and a 6-week follow-up period. A target of approximately 225 participants will be enrolled. Participants will be randomized in a 1:1:1 ratio to receive nipocalimab dose 1, dose 2 or placebo intravenously every 2 weeks through Week 50.
Results: The primary efficacy endpoint is the percentage of participants achieving an SLE Responder Index (SRI)-4 composite response at Week 24. Secondary efficacy endpoints assessed at Week 24 include the percentage of participants achieving: ≥50% reduction in Cutaneous Lupus Erythematosus Disease Area and Severity Index Activity score (CLASI), ≥50% reduction in active joints, ≥4 points improvement in SLE Disease Activity Index 2000 (SLEDAI 2K), and British Isles Lupus Assessment Group Composite Lupus Assessment response (BICLA); time to first disease flare; and reduction in corticosteroid use. The percentage of participants achieving an SRI-4 composite response at Week 52 will also be assessed. Safety endpoints include adverse events (AEs), serious AEs, AEs of special interest (severe infections, Grade ≥3 hypoalbuminemia), and AEs leading to treatment discontinuation through Week 58. Additional assessments include pharmacokinetic, pharmacodynamic, and immunogenicity evaluations.
Conclusion: This ongoing phase 2 study will evaluate the safety and efficacy of nipocalimab in adults with active SLE, using multiple clinical outcome measures.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Fang Liu-Walsh Employee of: Janssen Research & Development, LLC and may own stock or stock options in Johnson & Johnson., Bart van Hartingsveldt Employee of: Janssen Biologics Europe, Leiden, Netherlands and may own stock or stock options in Johnson & Johnson., Qing Zuraw Employee of: Janssen Research & Development, LLC and may own stock or stock options in Johnson & Johnson., Robert W. Hoffman Employee of: Janssen Research & Development, LLC and may own stock or stock options in Johnson & Johnson., Terence Rooney Employee of: Janssen Research & Development, LLC and may own stock or stock options in Johnson & Johnson., Sheng Gao Employee of: Janssen Research & Development, LLC and may own stock or stock options in Johnson & Johnson., George Karpouzas Speakers bureau: Sanofi-Genzyme-Regeneron, Janssen, and Bristol-Meyer-Squibb, Consultant of: Sanofi-Genzyme-Regeneron, Janssen, and Bristol-Meyer-Squibb, Grant/research support from: Pfizer, Robert Gordon Employee of: Janssen Research & Development, LLC and may own stock or stock options in Johnson & Johnson., Jocelyn H Leu Employee of: Janssen Research & Development, LLC and may own stock or stock options in Johnson & Johnson., Cesar Calderon Employee of: Janssen Research & Development, LLC and may own stock or stock options in Johnson & Johnson., Federico Zazzetti Employee of: Janssen-Cilag Argentina and may own stock or stock options in Johnson & Johnson., Anne M. Stevens Employee of: Janssen Research & Development, LLC and may own stock or stock options in Johnson & Johnson., George Vratsanos Employee of: Janssen Research & Development, LLC and may own stock or stock options in Johnson & Johnson.
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AB0551 INTRAVENOUS IMMUNOGLOBULIN IN PREGNANT WOMEN WITH SEVERE ACTIVE LUPUS: A CASE SERIES

Keywords: Systemic lupus erythematosus, Pregnancy and reproduction

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Background: Evidence on the management of pregnant patients with lupus activity is limited. The choice of pharmacological treatment is decisive for an adequate outcome.
Objectives: To show the experience of management with intravenous immunoglobulin (IVIG) in pregnant patients with severe active lupus.
Methods: Case series from January 2020 to November 2022 of pregnant patients being managed with IVIG in a hospital in Bogotá, Colombia.
Results: Out a total of 33 pregnant patients evaluated during the period, three cases of the use of IVIG in pregnant patients with severe lupus were found (Figure 1). The main involvement of lupus was renal (increased proteinuria), hematological (thrombocytopenia) and vascular [Intrauterine growth restriction (IUGR) and threatened abortion]. Average age was 30.3 years. One of the patients was diagnosed de novo with the disease during pregnancy, IVIG was given due to thrombocytopenia with resolution, but she presented fetal loss due to sepsis, in addition she had maternal vascular complications due to polyautoimmunity with antiphospholipid syndrome. The other two patients underwent IVIG at 24 weeks, one of them reached week 30 without considering new immunoglobulin applications, in the second case due to persistent proteinuria she received two additional cycles reaching 33 weeks of gestation. In both cases, a cesarean section was performed by IUGR at 30 and 33 weeks respectively. There were no complications associated with the newborns, with good response to proteinuria and resolution of cytopenias (See Table 1). There were no adverse drug events reported in any case.
Conclusion: IVIG can be a useful medication for the treatment of severe active lupus in pregnant patients, mainly in those with renal and hematological involvement. It is important to highlight IVIG has high safety and few side effects, on the mothers with lupus and their offspring's.

Table 1. Characteristics of Patients

Characteristics	Case 1	Case 2	Case 3
Patients Age, years	32	34	25
Pregnancy weeks at the start IVIG	7	24,1	24
Body weight, kg	65	68	66
Number of prior miscarriage	0	0	0
Serology	1/640	1/1280	1/320
ANAS	homogeneous	homogeneous	speckled
Patern	Negative	129/130 (+)	Negative
Ro/La	Negative	Negative	Negative
SM/RNP	Double positive	Negative	Negative
APS profile			
Indication IVIG	Severe active lupus Thrombocytopenia	Severe active lupus Nephritis	Severe active lupus Nephritis
Posology IVIG	65 g (1g/kg), Single dose	136 g (2 g/kg), Single dose	132 g (2 g/kg), monthly (3 doses)
Days administration IVIG	2	5	4
Side effects with IVIG	None	None	None
Platelets (Before IVIG)	2,100	112,000	153,000
Proteinuria, g/24h (Before IVIG)	0.13	13.2	24.7
	Outcomes		
Plaquettes	250,000	207,000	388,000
Proteinuria, g/24h	-	9 (2 week after IVIG)	10.6 (1 week after last IVIG)
Gestational age at miscarriage/delivery, weeks	7, Septic Miscarriage	30, Cesarean for IUGR	33, Cesarean for IUGR
Pregnancy complications	Stroke, Carotid dissection	No, Healthy premature Newborn	No, Healthy premature Newborn
Breastfeeding	-	Yes, until 3rd month	>3 months

ANA: Antinuclear antibodies, APS: antiphospholipid antibody syndrome, IUGR: Intrauterine growth restriction, IVIG: Intravenous Immunoglobulin,

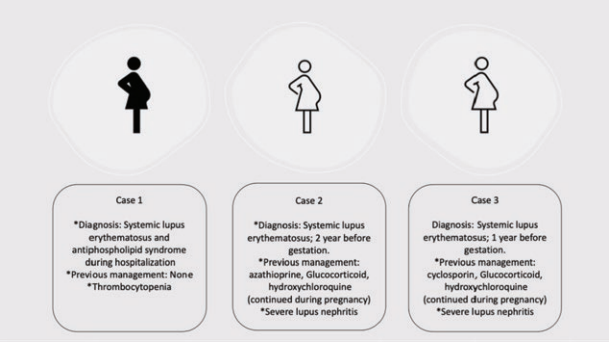


Figure 1. Patients' backgrounds

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0552 EFFECT OF BELIMUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS TREATED WITH MINIMAL OR NO STEROID

Keywords: Systemic lupus erythematosus

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Background: Belimumab is the only biologic agent approved for systemic lupus erythematosus (SLE). In cornerstone clinical trials, belimumab demonstrated SRI-4 response in patients with moderate disease activity, and real-world studies showed consistent findings (1¬3). In these studies, SRI-4 was significantly associated with baseline features including high SELENA-SLEDAI, dose of steroid, smoking status, BLyS level, and combining polyarthritis (2, 3). However, most previous studies have been conducted in patients with use of steroids, with mean prednisolone-equivalent dose of approximately 10 mg/day (1¬3). Therefore, the effect of belimumab has been focused on the steroid sparing.

Objectives: Here, we aimed to identify the effect of belimumab in SLE patients treated with minimal or no steroid with mild-to-moderate activity.

Methods: We retrospectively reviewed the electronic medical records of patients (age ≥ 18 years) who first received belimumab from May 2021 to June 2022 and maintained use at least 6 months. We only included patients who received prednisolone-equivalent ≤5mg or without steroid (for more than 1 year). The primary endpoint was SRI-4 response at 6 months, and secondary endpoint was improvement in serology, including C3, C4, and anti-ds DNA, at 6 months. Analysis Of Variance (ANOVA) with Bonferroni's post hoc analysis were performed to compare the continuous variables.

Results: In total, 31 patients were included, with 12 minimal steroid users and 19 non-steroid users. The mean age was 39.2 (±11.4) years, and 90.3% were female. Baseline SELENA-SLEDAI was 6.0 (4.0¬9.0). The primary endpoint was seen in 32.3% (10/31). Anemia (p=0.025), C4 level (p<0.001), and SELENA-SLEDAI (p=0.016) showed significant improvement over time during treatment. Univariable analysis showed baseline SELENA-SLEDAI and arthritis were significantly associated with SRI-4 response at 6 months, and SELENA-SLEDAI only remained significant in multivariable logistic regression analysis.

Conclusion: In our cohort study, belimumab was shown to be effective in improving SELENA-SLEDAI, anemia and low C4 in patients who did not use or did use minimal dose of steroids. Therefore, the effect of belimumab can be expected even in patients not taking steroids.

Table 1. Changes in clinical parameters in SLE patients treated with belimumab (no or low dose of steroid)

	Baseline	△0–3 months	△0–6 months	P-value	Post hoc test		
					P-value*	P-value†	P-value
CBC							
WBC							
Leukopenia (+)	2713.3 (±597.5)	246.7 (±639.0)	333.3 (±882.1)	0.143	0.246	1.000	0.430
Leukopenia (-)	5356.3 (±1141.3)	-387.5 (±831.8)	-368.8 (955.5)	0.165	0.471	1.000	0.496
Hb							
Anemia (+)	10.56 (±1.13)	0.17 (±0.87)	0.40 (±0.73)	**0.025**	1.000	0.424	0.074
Anemia ()	13.06 (±0.72)	-0.37 (±0.87)	-0.22 (±1.15)	0.543	0.557	1.000	1.000
Platelet, x10^3/μL							
Thrombocytopenia (+)	106.0 (±30.4)	24.0 (±29.8)	21.5 (±49.4)	0.153	0.240	1.000	0.459
Thrombocytopenia (-)	232.6 (±45.2)	9.6 (±46.1)	8.9 (±34.0)	0.301	1.000	0.899	0.902
Serology							
C3, mg/dL	59.13 (±15.46)	1.16 (±9.95)	6.24 (±21.51)	0.117	1.000	0.505	0.351
C4, mg/dL	10.25 (±5.14)	2.15 (±2.56)	3.21 (±4.57)	**<0.001**	**<0.001**	0.278	**0.001**
Anti-dsDNA, IU/mL	138.41 (±159.56)	-45.76 (±104.46)	-36.70 (±174.88)	0.252	0.063	1.000	0.755
Renal profile							
Creatinine, mg/dL	0.79 (±0.22)	0.04 (0.12)	0.02 (±0.09)	0.168	0.243	1.000	0.503
eGFR, mL/min/1.73m²	80.71 (±13.67)	-1.90 (±6.10)	-2.13 (±6.44)	0.076	0.277	1.000	0.227
UPCR, mg/g	418.10 (±777.02)	-108.02 (±350.99)	-100.15 (±413.98)	0.306	0.423	1.000	0.917
SELENA-SLEDAI	7.58 (±4.23)	-2.00 (±3.25)	-1.87 (±4.08)	**0.016**	**0.005**	1.000	**0.048**

* analysis of baseline and 3-month values; † analysis of 3- and 6-month values; ¶ analysis of baseline and 6-month values; SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index; anti-dsDNA, anti-double stranded DNA; eGFR, estimated glomerular filtration rate; UPCR, urine protein/creatinine ratio

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AB0554 LOW-DOSE IL-2 CHANGED THE PROPRTION OF LYMPHOCYTE SUBSETS IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

Keywords: Sjögren syndrome, Cytokines and chemokines

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Background: Primary Sjögren's syndrome (pSS) is a chronic inflammatory autoimmune illness characterized by various immune abnormalities. Abnormalities in the proportions of blood T lymphocyte subtype, that is Th17/Treg, were detected in pSS patients. Interleukin (IL)-2 is a crucial cytokine for tipping the balance of regulatory T(Treg) cells and effector T cells, which can effectively relieve pSS.

Objectives: This study aimed to systematically evaluate the changes in the number of lymphocyte subsets after low-dose IL-2 therapy for pSS.

Methods: Systematic searches of PubMed, EMBASE, Web of Science, the Cochrane Library and Medline, CNKI, CBM, and Technology Journal Database were performed. Original case reports, case series, observational studies, and clinical trials reporting the changes in lymphocyte subsets on pSS patients treated with IL-2 were included. A random-effects meta-analysis was performed to calculate the pooled efficacy. Inconsistency was evaluated by using the I [2], and Egger tests were used for the evaluation of potential publication bias (STATA v.12.0)

Results: A total of 3 studies comprising 929 patients were identified(Table 1). The numbers of Th17 cells and Tregs were significantly increased after IL-2 injection [SMD=0.325, 95%CI (0.060,0.590), P=0.016; SMD=1.085, 95%CI(0.469,1.701), P=0.001], while there were no statistical differences in the ratio of Th17/Tregs[SMD=-0.263, 95%CI (-0.602,0.076), P=0.129]between before and after IL-2 treatment(Figure 1).

Conclusion: Low-dose IL-2 was promising in treating pSS, which could promote the proliferation and functional recovery of Tregs and regulate the balance between Treg cells and effector T cells towards Treg cells.

Table 1. Available evidence, including patients with pSS treated with low-dose IL-2.

Study. Year.	Patients (include in analysis)	Gender (female %)	Dosage	Tregs	Th17	Th17/Tregs
J.-Y. Yang. 2020.	1221(759)	NA	NA	before:17.9±17.4 after: 34.5±36.7	before:7.5±7.4 after: 8.5±7.0	before:0.4±0.6 after: 0.4±0.5
Miao Miao. 2018.	169(82)	NA	0.5 million IU per day for 5 days	before:21.02±15.29 after:81.21±58.28	before:8.44±7.32 after:11.47±8.12	before:0.68±1.5 after: 0.22±0.27
M. Miao. 2017.	100(82)	NA	0.5 million IU per day for 5 days	before:16.67±12.35 after:66.67±52.47	before:6.49±5.29 after:9.74±6.74	before:0.33±0.32 after:0.22±0.16

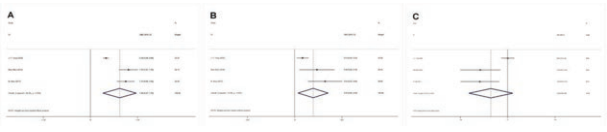


Figure 1. Changes in numbers of lymphocyte subsets after low-dose IL-2 therapy in pSS.(A-B) the number of Tregs and Th17 cells before and after low-dose IL-2 treatment. (C)Th17/Tregs.

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AB0555 CHARACTERISTICS OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AT THE START OF BIOLOGICAL THERAPY AND AT FIRST FOLLOW-UP

Keywords: bDMARD, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by heterogeneity of clinical manifestations ranging from mild skin and joint disease to severe, organ or life-threatening manifestations. It has an unpredictable tendency to flare up. Given the complex pathogenesis of SLE, involving both the adaptive and innate immune systems, the efficacy of steroids, antimalarials and immunosuppressants is limited in some cases, highlighting the need for new therapies with a targeted mechanism of action. Belimumab (BEL) is approved as an add-on therapy for active LES with positive autoantibodies despite standard treatment, while Rituximab (RTX) remains for off-label use in severe manifestations in many European countries.
Objectives: The aim of the current study is to describe the characteristics of SLE patients receiving biologic therapy with Belimumab or Rituximab at baseline and at first follow-up visit in a tertiary rheumatology center.
Methods: We retrospectively analyzed the electronic medical records of patients with SLE who started treatment with BEL and/or RTX. Demographic, clinical and paraclinical data as well as disease activity score at the time of starting treatment with biologics and at first follow-up visit were collected.
Results: Eighteen SLE patients were analyzed: 88.88% female, mean age at diagnosis 32±15 years, mean disease duration 7±5 years. The first follow-up visit was performed between 4 to 6 months after baseline. Eleven (61.1%) patients were treated with BEL, 5 (27.77%) RTX and 2 (11.11%) with both BEL and RTX. Hydroxychloroquine (HQ) was co-prescribed with biologics in 16/18 patients (88.88%). Azathioprine was prescribed in 6 patients (33.33%) and mycophenolate mofetil in 4 patients (22.22%). At the start of the biological treatment, all patients received steroids with a mean dose of 20±17 mg prednisone/day. One patient was able to discontinue the steroid, while in the others the mean prednisone dose decreased to 8.5±4.8 mg/day after 4-6 months. RTX was prescribed in 5 (71.42%) patients for lupus nephritis. All patients previously received cyclophosphamide. In one case, RTX was prescribed for severe thrombocytopenia, in another because of an overlap with active rheumatoid arthritis. Belimumab was prescribed in patients with more pronounced constitutional, articular, cutaneous and hematological features and mild renal involvement. In one case, BEL was prescribed for lupic enteritis. The mean SLEDAI score before starting treatment with the biologic was 12±3; the mean SLEDAI score at the first follow-up visit was 3±2.Anti-double-stranded DNA antibodies were positive in 16 (88.88%). At the time of initiating treatment with biologics and at follow-up, C3 hypocomplementemia was present in 13 (81.25%) and 8 (50%) patients, while C4 hypocomplementemia in 8 (50%) and 5 (31.25%) respectively. No serious adverse events were reported. One patient discontinued BEL due to inefficacy.
Conclusion: Biological therapy has been shown to control the disease activity and to reduce the need for steroids in SLE patients. RTX was used in patients with more severe manifestations such as lupus nephritis and severe thrombocytopenia.
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AB0556 OFF LABEL USE OF TARGETED THERAPIES IN SLE: SINGLE CENTER EXPERIENCE FROM THE ATTIKON LUPUS COHORT

Keywords: Systemic lupus erythematosus, Disease-modifying drugs (DMARDs)

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Background: Despite recent advances in the management of rheumatic diseases with the emergence of new targeted therapies, treatment options remain limited in systemic lupus erythematosus (SLE) [1] and disease may be refractory to conventional treatment.
Objectives: To evaluate the off-label use of biologics in a large cohort of lupus patients, its safety and efficacy.
Methods: Retrospective analysis of the Attikon SLE lupus cohort comprising over 800 patients in total in order to identify patients receiving off-label targeted therapies. Indication of the treatment, clinical characteristics and outcomes were recorded.
Results: A total of 52 patients received 54 off-label targeted therapies. Most of them were women (86.3%). Mean age (SD) at SLE diagnosis was 46.4 (15.2) years and mean disease duration (SD) at off-label treatment initiation was 8.8 (10.8) years. Mean SLEDAI (SD) before treatment initiation was 6.6 (3.7). The most frequently used off-label treatment was rituximab (84.6%) followed by tocilizumab (9.6%) and jak inhibitors (5.8%). The main indications were persistent, severe, refractory musculoskeletal and mucocutaneous activity (44.2%), neuropsychiatrical SLE (23.1%), hematological disease (13.5%) and lupus nephritis (11.5%).Six months after treatment, mean SLEDAI decreased in all patients to a mean of 4.3 (2.7). Mean drug survival was 2.2 (1.2) years. The dose of corticosteroids after 6 months of treatment was substantially decreased to 4.3 mg (versus 12.7 at baseline). No moderate/severe adverse effects were recorded.
Conclusion: The use of off-label targeted therapies allows disease activity improvement with a corticoid sparing effect even in a subset of patients with long-standing, refractory manifestations.
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Table 1. Patients' clinical characteristics

Women (N,%)	44(86.3)
Age at diagnosis (years,SD)	46.4 (15.2)
Mean disease duration at off label treatment initiation(years)	8.8 (10.8)
ANA (N,%)	52(100)
Low C3 or C4	27 (51.9)
High anti-ds DNA titers	17 (32.7)
Most frequent clinical manifestations (N,%)	Acute cutaneous lupus: 49 (94.2) Synovitis: 43 (82.7) Alopecia: 30 (57.7) Mouth or nasal ulcers: 23 (44.2) Lupus nephritis: 18 (34.6)
Previous and/or concomitant treatment (N,%)	Hydroxychloroquine: 52 (100) Belimumab: 11 (21.1) MMF: 7 (13.5) Azathioprine: 13 (25) Cyclophosphamide: 16 (30.8) Other: 26 (50)

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Disclosure of Interests: None Declared.
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AB0557 PERIPARTAL-ONSET OF LUPUS VASCULITIS WITH COMPLICATIONS OF ANTI-PHOSPHOLIPID SYNDROME-A CASE-BASED REVIEW

Keywords: Disease-modifying drugs (DMARDs), Anti-phospholipid syndrome, Autoantibodies

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Background: Lupus vasculitis (LV) [1] is one of the secondary vasculitides occurring in the setting of systemic lupus erythematosus most commonly affecting small vessels or medium vessels, rarely large vessels. LV is commonly associated with anti-phospholipid syndrome [2]
Objectives: Case Report 42year old female, 10weeks peripartal with twin-gestation presenting with progressive difficulty in walking with associated numbness and paraesthesia of the lower limbs [3], difficulty in breathing, Fever, non-erosive polyarthralgia and polyarthritis. Her symptoms started after delivery of her set of twins after 10years of secondary infertility. On examination; generalised cutaneous vasculitic rashes, left foot drop, bilateral lower limb swelling, coarse crepitations at the lung bases, reduced power at both lower limbs2/5, reduced tone and reflexes. Reduced sensation to light and deep touch at the left foot.
Methods: To access practicable treatment modalities in resource poor settings-Nigeria.
Results: Electromyelography-Mononeuritis multiplex, HRCT-pulmonary embolism in bilateral pulmonary artery extending into the segmental artery, Doppler USS of both lower limbs-Acute deep vein thrombosis of the left internal jugular vein, ENA panel-positive dsDNA, anti-smith, anti-Ro/Anti-La, Antiphospholipid antibody panel [4]- Positive aCL, anti-B2GP1, LAC, thrombocytopenia, anaemia. Renal parameters marginally deranged. Elevated inflammatory markers.
Management High dose corticosteroids, Rescue therapy low dose Rituximab @ days 0,15 patient had minimal response, maintained on low dose prednisolone, azathioprine and physiotherapy. Trial of EUROLUPUS regimen (6 courses) of low dose cyclophosphamide [5]. Rivaroxaban for PE & DVT. Inferior venae cavae filter for DVT.
Outcome: Regained full power, tone and reflexes of her lower limbs and walked without support after 6 courses of cyclophosphamide. however, she has residual left foot drop undergoing physiotherapy. Renal parameters marginally resolved. Pulmonary embolism and deep vein thrombosis resolved.
Conclusion: Lupus Vasculitis can affect any organ systems. Modalities for treatment are according to the presentation and severity of the disease.
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AB0558 ANIFROLUMAB IN REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS: A REAL-LIFE, MULTICENTER STUDY

Keywords: bDMARD, Systemic lupus erythematosus, Real-world evidence

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Background: Anifrolumab (ANI) is a monoclonal antibody to the type I interferon receptor recently approved by EMA as an add-on therapy for the treatment of moderate to severe SLE. As of this writing, real world data on its use are still lacking.
Objectives: To depict the clinical phenotype of refractory SLE patients treated with ANI. To evaluate short-term effectiveness and safety of ANI in clinical practice.
Methods: Multicenter prospective cohort study on adult patients with SLE treated with ANI for compassionate use. Demographic data, clinical and treatment history, and SLICC Damage Index (SDI) were retrieved from clinical charts. SLEDAI-2K, SLE-DAS, daily prednisone dose, number of tender (Tj) and swollen (Sj) joints, Cutaneous LE Disease area and severity index (CLASI-A), and Physician Global Assessment (PGA) were recorded at baseline, 1, 3, and 6 months of follow-up. Remission (according to 2021 DORIS definition) [1] and low disease activity (according to LLDAS definition) [2] were assessed at 6 months. Adverse events (AE) were recorded at each visit.
Results: 20 patients (90% female, 90% Caucasian, median age 48 (range 24-68), median disease duration 12 (4-27) years from 9 referral centers were included. 100% of patients had a history of articular involvement, 95% of skin rash, 50% of hematological involvement, 30% of nephritis, 25% of serositis, and 10% of neuropsychiatric involvement. Fifteen percent had a concomitant antiphospholipid syndrome and 10% Sjogren's syndrome. At baseline, 65% had an SDI>0 (median 2, 1-5). The median number of previous immunosuppressive therapies was 4 (1-7), while the median cumulative dose of prednisone was 10.3 g (5-90). Reasons for adding ANI to treatment were persistently active disease (83.3%) or disease flare (16.7%). Main active manifestations were: muco-cutaneous (70%), articular (40%), and hematological (25%). Concomitant therapies were glucocorticoids in 94.1% (pred-eq median daily dose 7.5 mg, range 0-25), conventional DMARD in 84% (31% mycophenolate, 16% azathioprine, 32% methotrexate, 5% cyclosporine), and hydroxychloroquine in 74% of cases. At 1 month after starting ANI, a significant decrease in all the activity indices was recorded: mean±SD SLEDAI from 7.6±4.2 at baseline to 6.1±3.5 (p=0.02), CLASI-A from 8.8±9.7 to 3.6±5.2 (p=0.01), and PGA from 1.3±0.5 to 1±0.5, (p=0.005), SLE-DAS from 9.6 ±6.5 to 6.8 ±5.2 (p=0.04), SJ from 1.6 ±0.6 to 0.5±0.2 (p=0.02). The improvement was maintained trough the 6 months of follow-up. A reduction in the mean daily dose of glucocorticoids was observed at all time points, but statistical significance was not reached (Table 1). LLDAS and remission were achieved by 75% of patients at 6 months of follow-up. One patient discontinued treatment after 2 infusions due to a lack of response. Nine AE were recorded, mainly mild viral infections including one herpes zoster reactivation. Only one AE (thromboembolism) led to treatment discontinuation.
Conclusion: ANI demonstrated a rapid efficacy on skin manifestation, arthritis, and overall disease activity in patients with SLE refractory to the standard of care. The good safety profile is also confirmed in this real-world analysis.
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Table 1.

Mean ±SD Median (range)	Baseline	At 1 month	At 3 months	At 6 months
SLEDAI-2K	7.2±4.3 6 (1-18)	6.1±3.5 6 (2-14)	4.5 ± 2.9 5 (0-10)	1±0.8 1 (0-2)
SLE-DAS	9.4±6.1 5.96 (4.45-27.4)	7.1±5.4 5.5 (3.5-21)	4.3 ± 3.7 3.5 (0.37-14)	0.9±0.6 0.85 (0.37-1.5)
CLASI-A	9.3±9.8 7 (0-27)	3.6±5.2 2 (0-17)	3.2 ±5.1 1 (0-17)	0.5±1 0 (0-2)
Tj	3.8±4.7 2 (0-15)	4.6±4.8 3 (0-14)	3 ± 4.9 0 (0-15)	7.5±11.9 2.5 (0-25)
Sj	1.2±2 0 (0-6)	0.6± 0.8 0 (0-2)	0.3±0.6 0 (0-2)	0 0
PGA	1.3±0.4 1 (1-2)	1±0.5 1 (0-2)	0.8±0.6 0.7 (0-2)	0.3±0.2 0.4 (0-0.5)
Prednisone daily dose (mg)	8.2± 5.3 7.5 (0-25)	8±6 6.25 (0-25)	6.7 ± 3.2 6.25 (0-12.5)	5±4.1 5 (0-10)
LLDAS n° (%)				3 (75%)
Remission n° (%)				3 (75%)

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AB0559 **EFFICACY AND SAFETY OF RITUXIMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

Keywords: Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with multisystem involvement characterized by the production of multiple autoantibodies and the consumption of complements. Rituximab, a chimeric anti-CD20 antibody, was already approved for treating B-cell lymphoma and autoimmune diseases.
Objectives: This study aimed to systematically evaluate the efficacy and safety of rituximab in treating SLE.
Methods: We systematically searched PubMed, EMBASE, Web of Science, Cochrane Library, CNKI, FDA.gov, Clinical trials.gov, Wanfang database, and Weipu database (from database inception to January 1, 2023) for studies of rituximab in the treatment of SLE. Observational studies, case series, and randomized controlled trials reporting the efficacy or safety data on SLE treated with rituximab were included in this meta-analysis. We selected the effect model according to the heterogeneity of the meta-analysis. If I2 < 50, a fixed effect model was used.
Results: A total of 8 studies with a total of 353 patients were included. After treatment with rituximab, the SLEDAI scores were significantly decreased [SMD=2.289, 95%CI (1.411,3.167), I2=64.5%, p<0.001]. Four studies mentioned clinical responses, 91.9% of patients with SLE who received rituximab had distinct clinical remission compared with 72.1% of patients with SLE who received conventional medication. The incidence of adverse events was 7.61% and 21.83%, in which pulmonary infection and gastrointestinal disease were the most common events, and no serious adverse events were reported among all these studies. Besides, we observed not only remarkable increases in complement C3 and C4 after rituximab injection [SMD=-0.838, 95%CI (-1.099,-0.577), I2=0.0%, p<0.001; SMD=-0.811, 95%CI(-1.071,-0.550), I2=0.0%, p<0.001], but also significant decreases in IgA and IgG [SMD=1.372, 95%CI (0.322,2.422), I2=95.5%, p=0.010; SMD=1.102, 95%CI(0.102,2.103), I2=93.6%, p<0.05],while there were no statistical differences in the ESR and IgM between before and after rituximab treatment (p>0.05)(Figure 1).
Conclusion: Rituximab was effective and well-tolerated for the treatment of SLE, which had a low incidence of adverse events.
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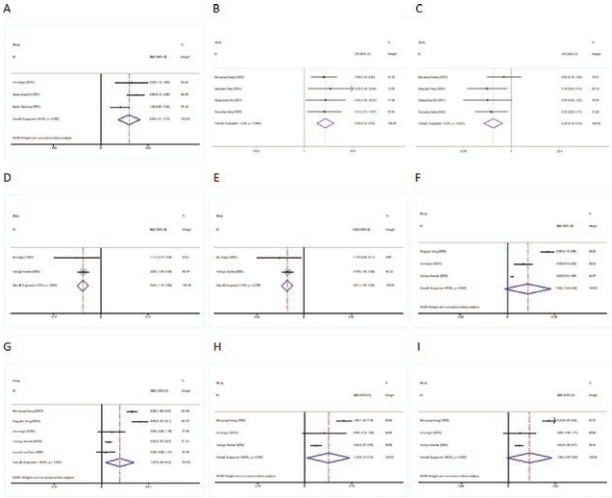


Figure 1. Efficacy and safety of rituximab in patients with SLE. (A) SLEDAI scores. (B) Remission. (C) Forest plot of the incidence of adverse events. (D) The complement C3. (E) The complement C4. (F) ESR. (G) Immunoglobulin A (IgA). (H) Immunoglobulin G (IgG). (I) Immunoglobulin M (IgM).

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0560 **EFFECT OF UPADACITINIB IN A PATIENT WITH PRIMARY SJOGREN SYNDROME: A CASE REPORT**

Keywords: Sjögren syndrome, Targeted synthetic drugs

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Background: Primary Sjogren syndrome (pSS) is a chronic autoimmune multisystem disease characterized by inflammation of exocrine glands, particularly the lacrimal and salivary glands, as well as multiple extraglandular involvements. Treatment is often challenging, and till now, no Disease-Modifying Antirheumatic Drugs (DMARD) have been approved for this condition. There is a lack of data about the efficacy of Janus kinase inhibitors in pSS. Here we report a patient with pSS successfully responding to upadacitinib.
Objectives: To see the efficacy of upadacitinib in the management of primary Sjogren syndrome.
Methods: A 68-year-old woman presented with pain in multiple joints for 16 years with intermittent use of NSAIDs. She had no low back pain and no self or family history of psoriasis or red eye. She denied dry mouth but required frequent water drinking during meals to aid swallowing and occasionally used artificial tears. MTX was started for her two-month articular flare and positive rheumatoid factor (RF). MTX caused severe vomiting and hyponatremia, and she was hospitalized. After the correction of hyponatremia, she was put on tofacitinib. We reevaluated the case when she came to us. She had grade 2-3 tenderness of most peripheral joints and was bedridden. Immunological parameters revealed RF 127 IU/ml (reference value <14), anti-SSA antibody 147 U/ml (normal <3.2), anti-SSB antibody 149 U/ml (reference value <8) and anti-CCP antibody; ANA, anti-ds-DNA Ab were negative. There was no erosion on the X-ray hands. Schirmer's test was positive (3 mm bilaterally). Unstimulated salivary flow after five minutes was 0.04 ml/min (≤0.1 ml/min indicates salivary hypofunction). She fulfilled the 2016 ACR/EULAR classification criteria, and we diagnosed her with primary Sjogren syndrome. Considering her age, she was switched to upadacitinib, as European Medicines Agency restricted the use of tofacitinib beyond 65 years.
Results: Her EULAR Sjogren Syndrome's Disease Activity Index (ESSDAI) [1] was six at baseline, indicating moderate disease activity. Her joint pain improved significantly within two months with infrequent use of pilocarpine in the sixth month. Six months after treatment with upadacitinib, ESSDAI came down to 2; the Patient's Global Assessment score was 02 and achieved STAR (Sjogren's Tool for Assessing Response) response 7 (STAR responder if score ≥5) [2].
Conclusion: To our knowledge, this is the first case report on the efficacy of upadacitinib in pSS. Further high-quality clinical trials are required to confirm the benefit of upadacitinib in pSS.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0561 **RITUXIMAB EFFICACY IN LUPUS NEPHRITIS: SYSTEMATIC REVIEW OF THE LITERATURE AND META-ANALYSIS**

Keywords: bDMARD, Systemic lupus erythematosus, Kidneys

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Background: Lupus nephritis (LN) is one of the most harmful clinical manifestation in systemic lupus erythematosus (SLE) patients. Despite of the existence of standard treatment protocols, a percentage of patients cannot be controlled with classical immunosuppresant drugs. This is the reason for exploring new therapies, such rituximab (RTX), in order to achieve a better management of LN [1,2].
Objectives: To assess the efficacy of RTX in LN treatment.
Methods: A systematic review was performed using Medline, Embase, Cochrane Library and Web of Science databases. Two independent reviewers selected the records that fitted the inclusion and exclusion criteria. Statistical analysis was carried out with Stata 15.1 for MacOS (StataCorp). Relating to meta-analysis, odds ratio (OR) was chose as measure of association in registries with control group and a prevalence meta-analysis was conducted in those registries without it.
Results: 436 papers were obtained from the search, finally 32 articles were analysed. Meta-analysis of registries with control group showed a significant higher rate of total response in LN patients treated with RTX, compared to control group (OR 2.154, 95%CI 1.271-3.650, p=0.004) after 52 weeks of follow-up (Figure 1). As well, a non-significant higher rate of complete response in LN patients treated with RTX, compared to control group (p=0.062) was found after 52 weeks of follow-up. A non-significant lower rate of partial response in LN patients treated with RTX compared to control group was found. Prevalence meta-analysis of registries without control group showed response in more than 50% of LN patients treated with RTX.
Conclusion: RTX seems to be effective in long-term treatment LN patients (52 weeks). More clinical trials are needed for clear indication of RTX for SLE treatment and its inclusion in general clinical practice.

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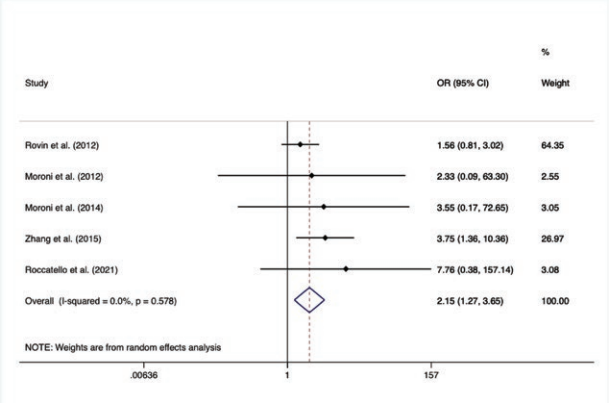


Figure 1. meta-analysis of LN patients treated with RTX in registries with control group and 52 weeks of follow-up.

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Disclosure of Interests: None Declared.
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AB0562 **BELIMUMAB FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS IN REAL WORLD: A SINGLE CENTER STUDY**

Keywords: Real-world evidence, Kidneys, Systemic lupus erythematosus

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Background: Belimumab efficacy and safety has been studied through randomized controlled trials in Systemic Lupus Erythematosus (SLE) patients even in cases with kidney involvement. However, more evidence is needed not only from long-term trials but also from real world conditions especially in Lupus Nephritis (LN) patients.
Objectives: To analyze the effectiveness and safety of Belimumab in SLE patients with data from a Real-World cohort.
Methods: A single center observational study was performed including SLE patients who had initiated treatment with Belimumab from September 2017 to January 2023. Demographic, clinical, laboratory, effectiveness and safety variables were collected. Effectiveness was evaluated according to changes from the baseline in SLEDAI-2K and disease activity markers (proteinuria, complement consumption and/or Anti DNAds). Safety data was collected including any adverse event (AE) due to any cause. AE was considered serious (SAE) if it was life-threatening or result in hospitalization, disability or in death.
Results: Overall, 15 patients were included in the study, whom baseline characteristics are exposed in the Table 1. Nine patients were still receiving the drug with a mean drug survival of 15.6 months. Belimumab allowed steroid tapering in all cases, but treatment was discontinued just in 1 patient (7%). Treatment also improved disease activity markers in all (100%) patients. Belimumab was well tolerated, and the AE reported were infection (14 events) and malaise in 1 patient. In 11 cases, infection was mild (9 upper respiratory tract infection, 1 urinary tract infection and 1 gastroenteritis). 3 severe infections were registered (1 pneumonia, 1 pyelonephritis and 1 meningitis).
Regarding LN patients, treatment exposure achieved was 10.85 patients/year. Renal Biopsy demonstrated class III in a patient (20%) and class IV in 4 patients (80%). Mean proteinuria at baseline was 6.66g/24h. In 3 cases, Belimumab was started in the first 6 months after LN diagnosis was established. In 4 cases (80%), Belimumab addition allowed significant reduction of proteinuria and corticosteroids. In 2 out 5 (40%) treatment was discontinued, one case due to an insufficient response and in the other, to a SAE (*Cryptococcus neoformans* meningitis).
Conclusion: Belimumab maintained an acceptable safety profile and an adequate effectiveness. Intravenous and subcutaneous formulations showed similar performance. Belimumab addition resulted in reduction in proteinuria and corticosteroid use.

Table 1. BASELINE CHARACTERISTICS

Characteristic	All SLE patients n=15 (100%)	No Lupus Nephritis N=10 (37%)	Lupus Nephritis n=5 (51%)
Age – years (ds)	36.4 (11.4)	30.5 (6.9)	48.2 (9.2)
Female sex – number (%)	14 (%)	10 (100%)	4 (%)
Race – number (%)	13 (86.7%)	10 (100%)	3 (60%)
White	1 (6.67%)	0 (0%)	1 (20%)
Hispanic	1 (6.67%)	0 (0%)	1 (20%)
Asian			
Formulation use at baseline – number (%)	5 (33.3%)	3 (30%)	(40%)
Intravenous	10 (66.7%)	7 (70%)	3 (60%)
Subcutaneous			
Disease features – number (%)	3 (20%)	2 (20%)	1 (20%)
Neuropsiquiatric involvement	5 (33.3%)	0 (0%)	5 (100%)
History of Lupus Nephritis	10 (66.7%)	7 (70)	3 (60%)
Arthritis	7 (46.7%)	4 (40%)	3 (60%)
Cutaneous	4 (26.7%)	2 (20%)	2 (40%)
Mucosal Ulcers	13 (86.7%)	8 (80%)	5 (100%)
Hematological	2 (13.3)	1 (10%)	1 (20%)
Serositis			
Steroid treatment - Number	15 (100%)	10 (100%)	5 (100%)
Mean glucocorticoid dosage – mg of prednisone or equivalent	24.4 (18.03)	15.2 (7.6)	35.4 (20.62)
Concomitant medication– number (%)	14 (93.3%)	9 (90%)	5 (100%)
Antimalarial	5 (33.3%)	5 (50%)	0 (0%)
Methotrexate	4 (26.7%)	4 (40%)	0 (%)
Azathioprine	5 (33.3%)	0 (0%)	5 (100%)
Mycophenolate	1 (6.67%)	0(0%)	1 (20%)
Cyclophosphamide			
SLEDAI – mean total score	15.7 (5.4)	14.6 (6.01)	18 (4.2)
SLE immunological tests	15 (100%)	10 (100%)	5 (100%)
ANA positivity	15 (100%)	10 (100%)	5 (100%)
Complement component 3	15 (100%)	10 (100%)	5 (100%)
Complement component 4	15 (100%)	10 (100%)	5 (100%)
Anti-double strained DNA positivity	204.08 (220.6)	59.2 (29.6)	431.2 (206.75)
Anti-double strained DNA titters			

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Disclosure of Interests: None Declared.
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SLE, Sjön's and APS - clinical aspects (other than treatment)

AB0563 "WELL CONTROLLED" SLE PATIENTS – PHYSICIAN PERCEPTION VS PATIENT REALITY

Keywords: Patient reported outcomes, Outcome measures, Systemic lupus erythematosus

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Background: SLE patients present significant challenges in the management of their condition.
Objectives: This study aims to uncover differences in physician perceptions and real-world treatment patterns and outcomes among moderate to severely active patients in the EU5 (France, Italy, Spain, Germany, and UK).
Methods: 1,279 moderate-to-severe (M/S) adult SLE patient records were collected in collaboration with 289 EU5 rheumatologists via an online survey platform from November 2021 through January 2022.
Results: 22% of moderate-to-severe EU5 SLE patients in the chart audit were receiving belimumab to treat their SLE. In half of those cases where patients were NOT on belimumab they were not considered good candidates for the therapy. The key reason for not initiating belimumab treatment being that patients were "well-controlled" on their current pharmacologic regimen. Closer inspection of these "well-controlled" patients (n=228) at the chart level revealed clinical aspects that highlight a potential gap in patient care: The majority of SLE patients in the "well-controlled" subset had moderately active disease, but over one-in-ten were classified with severe disease. On average, 40% of "well controlled" SLE patients had one or more flares over the past year. One-third of the "well controlled" patient subset suffers from at least one moderate-to-severe manifestation of their SLE, with musculoskeletal, dermatologic, and renal manifestations being most prevalent. 29% of "well-controlled" patients have at least one moderate-to-severe symptom of their disease. These include pain/stiffness, fatigue, synovitis, malar rash, photosensitivity, edema, fever, and alopecia.

Table 1.

SLE Disease Severity	Moderate		Severe	
"Well-controlled" patients	89%		**11%**	
SLE Flares (past year)	None	1 flare	2 flares	3 flares
"Well-controlled" patients	60%	**30%**	**8%**	**2%**
Severe SLE Manifestations	Has at least one moderate-to-severe manifestation			
"Well-controlled" patients	**32%**			
SLE Manifestation	*Moderate-to-Severe Manifestation Severity*			
Musculoskeletal	**24%**			
Dermatologic	**11%**			
Renal	**6%**			
Pulmonary	**5%**			
Severe Symptoms	Has at least one moderate-to-severe symptom			
"Well-controlled" patients	**29%**			
Symptom	*Moderate-to-Severe Symptom Severity*			
Pain, stiffness	**19%**			
Fatigue	**16%**			
Synovitis	**7%**			
Malar rash	**6%**			
Photosensitivity	**6%**			
Edema	**4%**			

- Further, one-third of "well controlled" SLE patients are on steroids, with 40% on a higher dose (>5mg/day) to control their disease. The mean overall dosage of the group was 9.4mg/day, a potentially harmful dosage particularly if used long term.

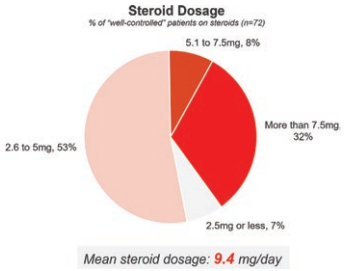


Figure 1.

Conclusion: EU5 physicians' perception of "well controlled" SLE may not align with some patients' clinical reality. Use of belimumab or other advanced therapies [1] in these cases may lead to improved patient outcomes and less reliance on steroids, which are often associated with adverse effects, even at low doses [2].

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Disclosure of Interests: Ryan Rex: None declared, Emily Hettel: None declared, Vibeke Strand Consultant of: AbbVie, Amgen, Aria, AstraZeneca, Bayer, Bioventus, Blackrock, BMS, Boehringer Ingelheim, Celltrion, Chemocentryx, Equillium, Gilead, Genentech/Roche, Glenmark, GSK, Horizon, Inmedix, Janssen, Kiniksa, Kypha, Lilly, Merck, MiMedx, Novartis, Pfizer, Priovant, Regeneron, Rheos, R-Pharma, Samsung, Sandoz, Sanofi, Scipher, Setpoint, Sorrento, Spherix, Tonix, Sawyer May: None declared.
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AB0564 TIGIT ACTIVATOR ALLEVIATES SYSTEMIC LUPUS ERYTHEMATOSUS BY NEGATIVELY REGULATING TH1-LIKE TREG CELL DIFFERENTIATION

Keywords: Treat to target, Cell biology, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous inflammatory chronic autoimmune disorder characterized by autoimmune tolerance deficiency [1]. T Regulatory cells (Tregs) play an important role in maintaining immune homeostasis. In inflammatory setting, the plasticity of Tregs increased with acquiring effector T helper (Th) phenotype, resulting in the reduction of immunosuppressive ability. It is reported that the frequency of Th1-like Treg cells, which has low suppressive function, increased in autoimmune diseases [2]. T cells Immunoglobulin and TIMI domain (TIGIT) is a co-inhibitory receptor, which can suppress the response of effector T cells. It is identified that the expression of TIGIT on Tregs significantly decreased in SLE [3-4]. Interferon-α (IFN-α) is a crucial pleiotropic cytokine with a high level in SLE and can promote type I immune response. IFN-α depends on AKT/mTOR signaling while phosphorylating JAK/STAT pathway to regulate the polarization of Th1 [5].
Objectives: The study is to evaluate the characteristics and differentiation mechanisms of Th1-like Treg cells in SLE patients and the role of TIGIT in regulating immunosuppressive function.
Methods: The frequency of $Foxp3^+T\text{-}bet^+$Th1-like Tregs of peripheral blood mononuclear cells (PBMCs) from SLE patients and healthy controls were analyzed by flow cytometry. PBMCs and $CD4^+$T cells were isolated and cultured under stimulation of IFN-α and/or TIGIT activator. The expression of characteristic markers of Th1-like Tregs, and the activation of AKT/mTOR/STAT pathway were assessed using flow cytometry and PCR.
Results: Th1-like Tregs with low TIGIT expression expanded in SLE patients. IFN-α promoted the conversation of Tregs to Th1-like Tregs through phosphorylated STAT4. TIGIT reactivation reversed the polarization of Th1-like Tregs and plasmablast differentiation induced by IFN-α through AKT/mTOR/STAT4 pathway.
Conclusion: Our findings indicate that the expansion of Th1-like Tregs and the decreased expression of TIGIT may contribute to the tolerance deficiency in SLE. TIGIT can reverse IFN-α-induced Th1-like Tregs and the impairment of immunosuppressive function, which is a potential therapeutic target for SLE.

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Disclosure of Interests: None Declared.
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AB0565 URIC ACID LEVELS, CARDIOVASCULAR RISK AND DISEASE ACTIVITY: THE BERMUDA TRIANGLE IN PRIMARY SJÖGREN'S SYNDROME

Keywords: Cardiovascular disease, Sjögren syndrome

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Background: Over the last decade, several observational studies provided evidence on the association between serum uric acid (SUA) levels and cardiovascular (CV) risk in the general population and identified SUA as a risk factor worth assessing in the setting of CV prevention also in patients without gout. Patients with primary Sjögren's syndrome (pSS), as those with other systemic autoimmune diseases, have a higher CV risk compared to the general population but studies assessing the role of SUA levels in the CV scenario of pSS are lacking.
Objectives: To explore the relationship between SUA levels, CV risk and CV events in patients with pSS and without gout and/or nephrolithiasis.
Methods: We retrospectively investigated pSS patients fulfilling the 2016 ACR/EULAR classification criteria. We recorded clinical, serological and CV-related variables while SUA levels were assessed at enrollment. In eligible patients (European individuals without previous CV events or diabetes) the 10-year risk of fatal and non-fatal CV disease events was calculated using the SCORE2 (individual aged 40-69 years) and SCORE2-OP (individuals aged over 70 years) risk prediction algorithms. Adherence to the Mediterranean Diet in the previous 12 months was also measured.
Results: We observed a strong relationship between disease activity, interstitial lung disease (ILD) and the occurrence of previous CV events in a cohort of 105 pSS patients. The association between ILD and CV events was dependent on higher SUA levels but independent on other traditional CV risk factors and on adherence to the Mediterranean diet. All 3 cases of previous non-fatal stroke were reported by female patients aged <65 years, with higher SUA levels and 2 of them also had pSS-ILD. Forty (51%) of the 79 patients eligible for the calculation of the 10-year risk of fatal and non-fatal CV risk had a risk higher than the cut-off recommended for their age, 6 (7%) have the same value as the cut-off level and 33 (42%) had risk values below the cut-off recommended for their age. The 2021 update of the ESC guidelines for CV prevention, reinforced the importance that in patients with chronic inflammatory conditions such as rheumatoid arthritis, multiplication of calculated total CV disease risk by a factor of 1.5 should be considered. For speculation purposes we applied this correction factor to our cohort and observed that 10 out of 33 patients were reclassified above the cut-off level recommended by guidelines for their age while 23 remained below. Among the 33 patients with a non-corrected risk below the cut-off level recommended by guidelines (N=33), those with the highest SUA values were reclassified above the cut-off level following the application of the 1.5 correction factor. The 23 patients whose SCORE remained below the cut-off regardless of the correction factor were the youngest and showed the lowest levels of total cholesterol, LDL cholesterol and triglycerides (all p<0.05). Only 10/23 (43%) patients have at least one CV risk factor and none of them showed more than 2 CV risk factors.
Conclusion: This study is the first to investigate in depth the role of SUA in the CV scenario of pSS. Our findings underpin the importance of assessing SUA levels in pSS in addition to the other traditional CV risk factors and are in line with the ESC advise that although evidence to use the 1.5 correction factor in connective tissue diseases is not yet solid enough to inform recommendations, it seems prudent to take into account the presence of such conditions when there is doubt regarding initiation of preventive interventions to ultimately achieve a better stratification and management of CV risk.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0566 A COMPARATIVE ANALYSIS OF CLINICAL CHARACTERISTICS OF 86 CASES WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ASEPTIC NECROSIS OF THE FEMORAL HEAD OR NON-FEMORAL HEAD AVASCULAR NECROSIS

Keywords: Comorbidities, Systemic lupus erythematosus

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Background: Symptomatic osteonecrosis of the femoral head (ONFH) and avascular osteonecrosis (AVN) are two types of osteonecrosis which is a serious complication of systemic lupus erythematosus (SLE). Even their pathophysiology of them is similar, though the onset timing, symptoms and signs, and other clinical characteristics are different.
Objectives: To compare the clinical characteristics of SLE combined with symptomatic ONFH and AVN.
Methods: We retrospectively analyzed the clinical data of 86 cases of SLE with symptomatic ONFH and AVN treated in the Department of Rheumatology and Immunology of The First Affiliated Hospital of Xi'an Jiaotong University from April 2013 to December 2021, and compared the similarities and differences between them.
Results: A total of 2730 patients with SLE were reviewed, including 60 patients combined with ONFH (male 9, female 51) and 26 patients combined with AVN (male 2, female 24). Morbility of ONFH was significantly higher than AVN. Compared with AVN group, the course of SLE was longer [(71.33±53.32) vs (48.69±35.11) months] , the time of glucocorticoids (GCs) use was longer [(67.47±51.71) vs (37.77±42.73) months], and the cumulative dosage of GCs was larger [(9.17±5.46) vs (6.02±6.66) g] in ONFH group. SLEDAI score was lower in ONFH group than in AVN group [(2.57±3.39) vs (4.46±4.81)]. The ONFH group had more Raynaud's phenomenon and lower serum Vitamin-D3 level compared with AVN group. Anti-cardiolipin antibodies (ACA) positive (15.38%) and edema as the initial symptom (46.15%) were more common in AVN group. Bilateral lesions were more common in ONFH group (68.33% vs 42.31%). All of the above differences were significant ($P < 0.05$).
Conclusion: Our results indicate that the long time and large cumulative dosage exposure of GCs, stable SLE state, Raynaud's phenomenon and low Vit-D3 value are more suggestive of ONFH than AVN. ACA positive and edema as an initial symptom are just the reverse.
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AB0567 SEXUAL DYSFUNCTION IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Quality of life, Real-world evidence

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Background: Due to its multisystemic involvement, systemic lupus erythematosus (SLE) can have a significant impact on patients' quality of life (QoL). Sexual (dis)function is a key component of QoL but is often underappreciated. Little is known about sexual disfunction in SLE patients, a condition that primarily affects women during their fertile age.
Objectives: We aimed at determining the prevalence of sexual dysfunction among women with SLE and predictors thereof.
Methods: We performed a cross-sectional multicenter study in which women (18-70 years-old) with a clinical diagnosis of SLE (according to their treating rheumatologist) were included. An anonymous online questionnaire

was perfomed where data on demographics (e.g., age), symptoms of depression and anxiety [Hospital Anxiety and Depression Scale (HADS)), health-related QoL (Short Form Health Survey Index 36 Item (SF36)]) and sexual function [Female Sexual Function Index (FSFI) - a 19-item patient-report outcome that assesses female sexual function]) were collected. Data on clinical features [disease activity according to the Safety of Estrogens in Lupus National Assessment-SLE Disease Activity Index (SELENA-SLEDAI), organ involvement and evaluation of comorbidity (Charlson Comorbidity Index)] and on treatment status were collected from medical records. The main outcome was sexual dysfunction, defined as FSFI<26.5 (validated cut-off). A multivariable logistic regression was perfomed to test the association of clinical and demographic characteristics with sexual dysfunction (present vs absent).

Results: In total, 194 female patients with SLE were included (mean age 44 years-old [standard deviation (SD) 11]). The mean SELENA-SLEDAI score was 1.7 (SD: 2.2), corresponding to low disease activity, and 94% of patients were on classical disease-modifying antirheumatic drugs. The mean value of HADS was 9 (0-21), for both depression and anxiety scores. Regarding SF36, the mental component had a mean value of 61 (0-100) and the physical one of 70 (0-100). Sexual disfunction was present in 128 (66%) patients. In the multivariable analysis (Table 1), older age (OR: 1.04; 95%CI: 1.01; 1.07), higher SELENA-SLEDAI (OR: 1.18; 95%CI: 1.01; 1.40), higher HADS depression score (OR: 1.20; 95%CI: 1.01; 1.43), as well as a lower (that is, worse) SF36 mental component score (OR: 0.97; 95%CI: 0.95; 0.98) were independently associated with sexual dysfunction.

Conclusion: Sexual disfunction is common in women with SLE and is influenced by both physical and mental health components. Clinicians should consider both for the optimal management of their patients in order to improve their sexual QoL.

Table 1. Factors associated with sexual dysfunction in female patients with SLE

	Univariable analysis OR (95% CI) (N=192-194)	p-value	Multivariable analysis OR (95% CI) (N=193)
Age	1.04 (1.01; 1.07)	0.01	1.04 (1.01; 1.07)
Menopause (yes vs no)	2.38 (1.11; 5.61)	0.03	†
SELENA-SLEDAI	1.09 (0.94; 1.28)	0.24	1.18 (1.01; 1.40)
CCI	1.39 (1.00; 2.02)	0.06	†
bDMARDs (yes vs no)	0.85 (0.30; 2.59)	0.76	*
cDMARDs (yes vs no)	0.16 (0.01; 0.87)	0.09	†
Glucocorticoids (yes vs no)	1.15 (0.63; 2.09)	0.66	*
HADS Depression	1.20 (1.03; 1.42)	0.02	1.20 (1.01; 1.43)
HADS Anxiety	1.19 (1.04; 1.38)	0.02	†
SF36 Mental	0.97 (0.95; 0.98)	< 0.01	0.97 (0.95; 0.98)
SF36 Physical	0.99 (0.98;1.00)	0.03	†

* Not selected in the univariable model (p>0.25)† Not selected in the multivariable model (p>0.05)CCI, Charlson Comorbidity IndexbDMARDs, biologic disease-modifying anti-rheumatic drugscDMARDs, classic disease-modifying anti-rheumatic drugs

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AB0568 CLINICAL USE OF ACTIVATED LEUKOCYTE CELL ADHESION MOLECULE, HEMOPEXIN, AND PEROXIREDOXIN 6: A POTENTIAL URINE BIOMARKER FOR KOREAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Biomarkers, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is sometimes difficult to make a prompt and accurate diagnosis due to the heterogeneity of various clinical manifestations and autoantibody expression. Therefore, the development of surrogate markers specific to the diagnosis of SLE is necessary. Among biological samples, urine is non-invasive means with the advantage of being easily obtained.

Objectives: This study aimed to evaluate the ability of Activated Leukocyte Cell Adhesion Molecule (ALCAM), Hemopexin, and Peroxiredoxin (PRDX) 6 as urine biomarkers in Korean patients with SLE.

Methods: Urine samples were collected from 138 patients with SLE and 39 healthy controls (HC) with clinical data. The level of urine biomarkers were measured by enzyme-linked immunosorbent assay kits specific for ALCAM, hemopexin and PRDX 6, respectively, according to the manufacturer's protocols. The diagnostic utility of urine biomarkers was evaluated using receiver operating characteristic (ROC) curve analysis, and Pearson's correlation analysis was performed to assess the relationships between disease activity and urine biomarkers.

Results: Urinary ALCAM level was 6,760.5 ± 2,826.4 pg/ml and 1,192.6 ± 577 pg/ml in patients with SLE and HCs ($p < 0.001$). The mean levels in urinary hemopexin and PRDX6 were also significantly higher in patients with SLE compared to HCs (hemopexin, 649.8 ng/ml vs. 202 ng/ml, $p < 0.001$; PRDX6, 0.78 ng/ml vs. 0.17 ng/ml, $p = 0.003$). In patients with lupus nephritis (LN), ALCAM, hemopexin, and PRDX6 showed more significant diagnostic value, and the area under the ROC for LN was 0.850 for ALCAM (95% CI, 0.778–0.921), 0.781 for hemopexin (95% CI, 0.695–0.867), and 0.714 for salivary S100A8 (95% CI, 0.617–0.812). In addition, all urine biomarkers were significantly associated with anti-double stranded DNA (ALCAM, $r = 0.350$, $p < 0.001$; hemopexin, $r = 0.346$, $p < 0.001$; PRDX6, $r = 0.191$, $p = 0.026$) and SLEDAI (ALCAM, $r = 0.526$, $p < 0.001$; hemopexin, $r = 0.479$, $p < 0.001$; PRDX6, $r = 0.262$, $p = 0.002$) in correlation analysis.

Conclusion: Urinary ALCAM, hemopexin and PRDX 6 were significantly increased in patients with SLE compared to HCs. Thus, we propose that urinary ALCAM, hemopexin and PRDX 6 can be potential biomarkers for SLE, especially valuable in the diagnosis of LN.

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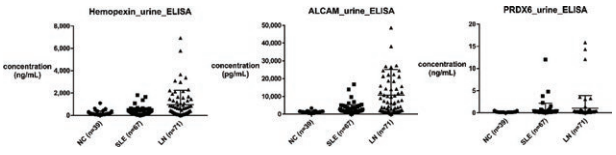


Figure 1. Urinary ALCAM, hemopexin and PRDX6 in patients with SLE and HCs

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AB0569 THE APPLICATION AND INFLUENCE FACTORS OF FACIT FATIGUE SCALE IN SLE PATIENTS

Keywords: Systemic lupus erythematosus, Quality of life

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Background: Fatigue is a frequent, disabling issue in systemic lupus erythematosus (SLE). It is, however, difficult to quantify. The Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale has been validated in SLE and has been successfully used to assess fatigue.

Objectives: To evaluate the application and influence factors of the Functional Assessment of Chronic Illness Therapy (FACIT-Fatigue) scale in patients with systemic lupus erythematosus (SLE)

Methods: 1061 SLE pts who fulfilled SLICC 2012 [1] criteria were enrolled into the study. The SLEDAI 2K index activity, SLICC damage index, fatigue was assessed by the FACIT-Fatigue scale from 0 to 52 (no or little fatigue 40-52, some fatigue 27-39, quite a lot of fatigue 14-26, extreme fatigue 0-13) [2]

Results: 1061 Lupus pts were studied, respectively. The pts were predominantly female (92%) and of indigenous nationality (Kazakh 10%,/ Kirghiz 54%/Russian 36%)with a mean±SD age 34,6±11,8 years. The mean disease duration (Me) was 4 [1;9], the disease activity (SLEDAI 2K) 13,23±8,74, SLICC damage index 1,36±0,82. Fatigue was detected in 828 (79%) of 1061 patients with SLE. 1061 pts were divided into two groups. The first group included 447 pts with quite a lot of fatigue and extreme fatigue (from 26 up to 0 by Facit -fatigue scale). The second one included 615 SLE pts with no or little fatigue and some fatigue). The first group pts were with higher SLE activity by SLEDAI 2 K (16,4±9,3 versus

11,5±8,4; p=0,0001), had a higher level of dsDNA (131,7±23,9 versus 94,5 ± 11,7; p=0,002), were treated with higher doses of glucocorticoids (22,33±12,3 versus 19,5±17,0 mg per day; p=0,001).

Table 1. Frequency of fatigue in different ethnic groups

Facit fatigue, Score	Russian [1], N = 386, n (%)	Kirghiz [2], N = 573, n (%)	P [1-2]	Kazakh [3], N = 102, n (%)	P [1-3]	All pts, N = 1061, n (%)
no or little fatigue, 52–40	146 (37%)	81 (14%)	< 0,0001	6 (6%)	< 0,0001	233 (21%)
some fatigue, 39–27	147 (38%)	222 (39%)	–	13 (13%)	< 0,0001	382 (37%)
quite a lot of fatigue, 26–14	80 (21%)	172 (30%)	0,01	52 (51%)	< 0,0001	304 (29%)
extreme fatigue, 13–0	13 (4%)	99 (17%)	< 0,0001	31 (30%)	< 0,0001	143 (13%)

Fatigue was significantly more common among Kazakhs (94%) and Kyrgyz (86%) than among Russians (63%) pts (Table 1). Extreme fatigue was significantly more common among Kazakhs (30%) than among Russians (4%) and Kyrgyz (17%) pts.

Conclusion: Fatigue are common (79%) in SLE pts and significantly higher among Asians pts (86-94%). Fatigue strongly associated with SLE activity.

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AB0570 RELATIONSHIPS AMONG ANXIETY, DEPRESSION AND DESEASE ACTIVITY IN ASIANS SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS FROM KAZAKHSTAN AND KIRGHIZSTAN

Keywords: Quality of life, Systemic lupus erythematosus

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Background: Depression and anxiety cause severe loss of quality of life for patients with systemic lupus erythematosus. The causes and factors that contribute to these psychological manifestations in lupus are difficult to disentangle.

Objectives: The aim of this study was to determine factors associated with anxiety and depression in Asians systemic lupus erythematosus patients (pts) from Kazakhstan and Kirghizstan.

Methods: 1060 SLE pts who fulfilled SLICC 2012 criteria were enrolled into the study. The SLEDAI 2K index activity, SLICC damage index, depressive and anxiety symptoms were assessed by the Hospital Anxiety and Depression (HAD) scale (0-21 points).

Results: 1060 Lupus pts were studied, respectively. The pts were predominantly female (92%) and of indigenous nationality (Kazakh 10%,/ Kirghiz 54%/Russian 36%)with a mean±SD age 34,6±11,8 years. The mean disease duration (Me) was 4 [1;9], the disease activity (SLEDAI 2K) 13,23±8,74, SLICC damage index 1,36±0,82. More than half of the pts (619 [58.3%]) had abnormal points by HADS scale. 1060 pts were divided into two groups. The first group included 619 SLE pts with abnormal HADS (HADS-A ≥ 8 points; HADS-D ≥ 8 points; HADS-D ≥ 8 points and HADS-A ≥ 8 points). The second one included 441 SLE pts with normal HADS. The most common were anxiety and depression (HADS-D ≥ 8 points and HADS-T ≥ 8 points) - in 346 (32.6%) pts, the second most common was anxiety disorder (HADS-T ≥ 8 points) - in 230 (22%) pts, the third - depressive disorder (HADS-D ≥ 8 points) - in 43 (4%). Such factors as age of the pts, age of SLE onset, duration of illness, SLICC damage index, SLEDAI 2 K, and dosage of corticosteroids. The pts with abnormal HADS were older (36,04±12,11 versus 29,94±11,49 years; p=0,003), with less disease duration (3,1 [0,9;8] versus 4,7 [1,5; 10]; p=0,01), with disease onset at a more later age (31,55±11,86 versus 26,43±11,39 years; p=0,0002), with higher SLE activity by SLEDAI 2 K (14,78±8,59 versus 12,22±8,30; p=0,01). The pts with abnormal HADS were treated with higher doses of glucocorticoids (22,33±12,6 versus 18,5±12,0 mg per day; p=0,005).

Table 1. Frequency of anxiety and depression in different ethnic groups

HADS score	Russian [1], n = 384, n (%)	Kirghiz 2, n = 574, n (%)	P [1-2]	Kazakh [3], n = 102, n (%)	P [1-3]	All pts, n = 1060, n (%)
Normal HADS	228 (59%)	153 (27%)	< 0,0001	60 (59%)	–	441 (42%)
Abnormal HADS	156 (41%)	421 (73%)	< 0,0001	42 (41%)	–	619 (58%)
Only HADS-A ≥ 8 points	78 (20%)	130(23%)	–	22 (21%)	–	230 (22%)
Oly HADS-D ≥ 8 points	10 (3%)	28 (5%)	–	5 (5%)	–	43 (4%)
HADS-D ≥ 8 points and HADS-A ≥ 8 points	68 (18%)	263 (46%)	< 0,0001	15 (15%)	–	346 (32%)

The frequency of anxiety and depression was significantly higher among the Kyrgyz pts (46%) than Russian (18%) and Kazakh pts (15%) (Table 1).

Conclusion: Depressive and anxiety symptoms are common (58,3%) in SLE pts and significantly higher among Asians pts (46%). Such factors as pts age, age of SLE onset, duration of illness, SLEDAI 2 K, and dosage of corticosteroids were strongly associated with abnormal HADS.

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AB0571 DO ADULT WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS REACH FITNESS STANDARDS FOR MAINTAINING PHYSICAL INDEPENDENCE IN LATER YEARS? ASSOCIATIONS WITH FATIGUE AT 2-YEAR FOLLOW-UP

Keywords: Non-pharmacological interventions, Systemic lupus erythematosus, Lifestyles

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Background: Maintaining physical fitness (i.e. muscle strength and cardiorespiratory fitness) is a key factor in preserving independence in later years [1]. Because people with systemic lupus erythematosus (SLE) present with reduced fitness levels [2,3], this population could be at risk of premature loss of independence. In addition, higher levels of physical fitness have been related to better SLE symptomatology, including fatigue [2,3], one of the most limiting symptoms. However, it is unclear whether physical fitness have a predictive role on future levels of fatigue in this population.

Objectives: This study aimed to analyze, in a sample of adult women with SLE: i) the proportion of participants that reach the proposed standards of fitness for muscle strength and cardiorespiratory fitness to maintain independence in the later life and ii) the association between reaching these standards of fitness and fatigue levels at 2-year follow-up.

Methods: This follow-up study included a total of 26 women with SLE (age: 41.3 ± 13.3 years) with low disease activity index (Systemic lupus erythematosus disease activity index [SLEDAI]: mean 1.0 ± 1.9). The 30-s chair stand and 6-min walk tests from the Senior Fitness Test Battery were used to assess muscle strength and cardiorespiratory fitness. The percentage of participants reaching the criterion-reference for women 60-64 years old (15 repetitions [in the 30-sec chair stand test] and 571,5 meters [in the 6-min walk test]) was calculated. Linear regression models adjusted by age were used to analyze the association of reaching the fitness criterion-reference and fatigue levels at 2-year follow up. Five dimensions of fatigue (general, physical, reduced activity, reduced motivation and mental fatigue) were assessed using the multidimensional Fatigue Inventory (MFI).

Results: A total of 42.3 % participants did not reach the criterion-reference for muscle strength and 50 % of participants did not reach the criterion-reference for cardiorespiratory fitness. Reaching the criterion-reference for cardiorespiratory fitness was associated with lower physical fatigue at 2-year follow-up (β=-0.55, P<0.05). There was no association with other dimensions of fatigue or reaching the criterion-reference for muscle strength.

Conclusion: In this relatively small sample of adult women with SLE, up to half of participants have reduced physical fitness that exposed them to a premature loss of functioning and independence in their later life. Reaching a minimum level for cardiorespiratory fitness, but not for muscle strength, predicted lower physical fatigue in the future. Exercise interventions aimed at increasing physical fitness

could be a promising approach to reduce the decline in functioning and contribute to lower fatigue in this population.

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AB0572 DIFFERENTIAL BACKGROUND OF CLINICAL AND IMMUNOHISTOLOGICAL CHARACTRSITICS IN SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS COMPLICATED WITH HEART DISEASE

Keywords: Cardiovascular disease, Systemic lupus erythematosus, Rheumatoid arthritis

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Background: Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are often complicated by heart disease. In severe cases, heart surgery is required, but little is known about clinical background and immunohistological pathology of diseases.

Objectives: The differences in clinical and immunohistological backgrounds of each disease were examined by comparing cases of heart disease associated with SLE and RA.

Methods: From 2012 to 2021, we observed 45 patients with SLE (32 patients underwent surgery), 67 patients with RA (33 patients underwent surgery), and 8 patients with overlapping SLE/RA (3 patients underwent surgery), all complicated with heart disease. The heart disease cases were divided into the aortic valve disease (Av), mitral valve disease (Mv), ischemic heart disease (I), and aortic aneurysm disease (Aa) groups, all from patients who had visited our hospital. The SLE (S) group consisted of Av, Mv, I, and Aa in 5, 6, 11, and 13 respective cases (10 duplicate cases), and in the RA (R) group there were 24, 12, 15, and 10 respective cases (6 duplicate cases). Immunohistological analysis of patients with left atrial appendage tissue (seven SLE, six RA, and two overlapping SLE/RA patients) was performed on left atrial cardiomyocytes for anti-human IgG, IgM, and C3 antibodies. Left atrial cardiomyocytes of eight cases of heart disease with non-connective tissue disease were used as the control.

Results: The age (in years) at diagnosis of heart disease in the S and R groups was S/R: 57.6/71.5 (p=0.057), and the duration (in years) from onset of the connective tissue disease to onset of the heart disease was S/R: 22.6/10.1 (p<0.001). Anti-SS-A antibody (P=0.041), anti-U1RNP antibody (p=0.0044), and anti-CLβ2GP1 antibody (p=0.022) showed a high positivity rate in the S group. In disease I, the age at the time of diagnosis of heart disease was S/R: 51.6/70.9 years (p = 0.0083); and in disease Aa, the age and duration of disease were S/R: 63.5/74.8 years (p = 0.0088) and 29.6/7.0 years (p = 0.0013), respectively. There was no significant difference in S/R in patients suffering from diabetes, hypertension, and hyperlipidemia. Immunohistological analysis revealed IgG deposition in the cardiomyocytes in six of the seven patients in the S-alone group, while no IgG deposition was observed in six patients in the R-alone group. In two patients with overlapping S-R, IgG deposition was observed in both. In the S group, two or more antibodies of antiphospholipid antibodies, anti-Ro/SSA or anti-U1RNP antibodies, were positive in five out of the seven patients, and preoperative anti-DNA antibody elevation or complement reduction was seen in only two patients. Two of the seven patients in the S group were negative for either antibody, and a patient showed no IgG deposition uniquely in the S group. Both patients with overlapping S-R were positive for anti-CL antibody and anti-Ro/SSA antibody. In the R group, all antibodies were negative within the measured range.

Conclusion: A comparison of SLE and RA patients complicated with heart disease revealed that the SLE patients tend to be younger at diagnosis than RA patients and had a longer morbidity period. It is possible that various autoantibodies, such as antiphospholipid antibodies, anti-Ro/SSA antibodies, and anti-U1RNP antibodies were involved and had immunological effects on the myocardial tissue. In contrast, in RA patients complicated with heart disease, the autoantibodies observed in SLE were negative, and immunoglobulins were not deposited in the myocardial tissue of the RA patients who underwent surgery, suggesting that immunological involvement was poor and older diagnostic age was involved.

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Figure 1 :Immunohistochemical staining of left atrial appendage

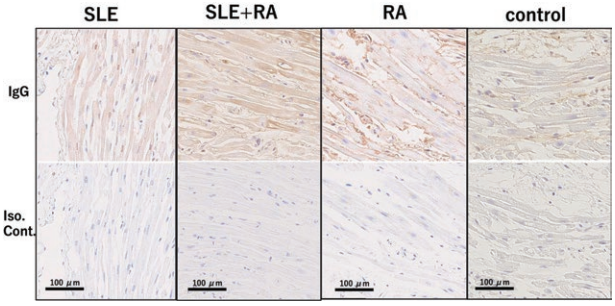


Table 1: Clinical and Tissue analysis of LA appendage

	Subjects of operation	age	sex	myocardial fibers IgG	myocardial fibers IgM	myocardial fibers C3	CL,β2GPI	CL	LAC	SS-A	RNP	Sm	DNAab (pre operation)	CH50 (post operation)
SLE	AS, AR	43	M	+	–	–	+	+	–	+	–	–	19	15.4
	AS, MR	70	F	+	–	–	–	–	–	–	–	–	–	39.3
	MR	67	F	–	–	–	–	–	–	–	–	–	–	45.3
	IHD	39	F	+++	++	±	+	+	+	+	+	–	–	45
	IHD	34	F	+	+	N/A	–	+	+	–	+	–	90	46.5
	IHD	59	F	+	+	N/A	+	+	–	–	+	–	–	52.4
	AR, AscAo dilatation	41	F	+	N/A	N/A	–	–	–	+	+	–	–	41.6
RA	MR	67	F	–	N/A		N/A		–	+	–	–	N/A	
	MR	78	M	±			N/A		N/A	N/A	N/A	N/A		
	MR	67	F	–			–	N/A	–	–	–	–		
	AS	79	F	–			N/A		–	–	N/A	N/A		
	AS	70	F	–			–		–	N/A	N/A	N/A		
	IHD	64	F	–			–		N/A	–	–	–		
SLE+RA	MR	61	F	++	N/A	N/A	–	+	–	+	–	–	–	33.9
	IHD, MR	74	F	++			–	+	–	+	–	–	25	26.2
control	MR	54	F	–	–	–	N/A							
	MR	52	M	–	–	–								
	MR	52	F	–	–	–								
	MR	42	M	–	–	–								
	AS	54	F	–	–	–								
	AS	58	F	–	–	–								
	IHD	52	M	–	–	–								
	IHD	66	F	++										

AS : Aortic valve stenosis, MR : Mitral regurgitation, IHD : Ischemic heart disease
AR : Aortic regurgitation, AscAo : Ascending aorta, N/A : Not applicable

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Disclosure of Interests: None Declared.

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AB0573 REASONS FOR BREASTFEEDING AVOIDANCE: A MULTICENTER INSIGHT IN MOTHERS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Patient reported outcomes, Pregnancy and reproduction

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Background: Even though the health benefits of breast milk are well established, only a small number of research have looked at breastfeeding in people with systemic lupus erythematosus, with mixed findings. In a previous multicenter cohort investigating 119 SLE pregnancies, one-third of patients did not breastfeed after giving birth.
Objectives: To study the causes of breastfeeding avoidance with the purpose to increase the standard of care of SLE women.
Methods: A priori questionnaire was created and administered to patients by structured-phone interview (Table 1). Pregnancy outcomes were retrospectively collected.
Results: A total of 22 questionnaires of women who did not breastfeed after first birth were collected. Twelve out of 22 (54.5%) patients experienced a disease flare in the 24 months following the delivery. Healthcare professional advice (36.4%) was the most frequently reported reason for not breastfeeding, followed by the mothers' fear that medications (drugs) taken during pregnancy (22.7%) and/or the circulating autoantibodies (4.5%) could be passed onto the baby and therefore harm the new-born. In 10 (45%) cases, breastfeeding was not possible because of mother's or neonatal clinical complications. One woman did not breastfeed for a personal choice. After giving birth, only nine out of 22 patients (40.9%) declared to have had adequate breastfeeding training, with 58% of women reporting a breastfeeding-training time of less than 5 minutes in those without an adequate counselling. Most patients (21 out of 22, 95.5%) stated that they would have breastfed their child if they could.
Conclusion: Breastfeeding avoidance in women with SLE is frequently the result of a confluence of individual preference, clinical advice, and the societal context. An implementation of patients-to-patients network, together with an update of health practitioners, may help to increase the frequency of breastfeeding in women with SLE and subsequently improve patients' care.
In Figure 1 implementation points suggested by patients.

Table 1.

1. Have you received pre-conceptional counselling?	Y N
2. For how long were you able to discuss about pregnancy planning with your HP?	-One session -Multiple session
3. In pre-conceptional counselling, were you informed on breastfeeding?	Y N
4. Why did you not breastfeed?	-Healthcare professional advice -Fear that the undertaken drugs could be delivered to the baby -Fear that the autoantibodies and the disease might have been transferred to the baby -N/A
5. Who, among HP, advised you not to breastfeed	-GP -Rheumatologist -Gynecologist -Nurse/obstetrician -Training physician -N/A
6. Did you seek out different medical opinions?	Y N
7. After you gave birth, did you receive detailed information on how to breastfeed, and were you trained to do it?	Y N
8. For how long have HP informed and trained you about breastfeeding	-Less than 5 minutes -15 minutes -30 minutes -Multiple times during my hospitalization -I received training and support for several days after being discharged from the hospital
9. Were informative materials on breastfeeding provided to you by HP?	Y N
10. If you not breastfed because of temporary neonatal complications, were you trained and supported in milk production maintenance?	Y N N/A
11. The choice of not breastfeeding was influenced by society's demands?	Y N
12. Your choice of not breastfeeding was influenced by:	-Work-related issue (lack of space and time to breastfeed) -Lack of support from family members and friends -None of the aforementioned
13. Have you felt overwhelmed by the delivery and the first days that came after it?	Y N
14. Your choice of not breastfeeding was influenced by the belief that formula milk was healthier for the baby compared to the mother's milk?	Y N
15. Would you have breastfed if you could have?	Y N
16. Do you think dedicated counseling could have changed your approach to breastfeeding?	Y N
17. Do you have any suggestions on how to implement breastfeeding awareness?	

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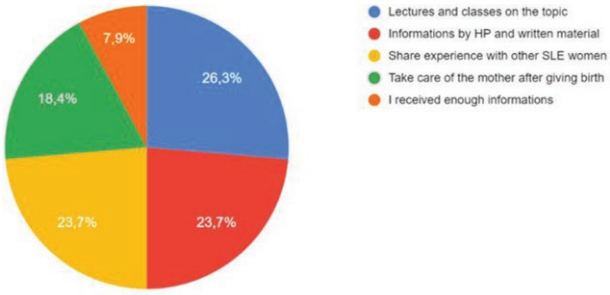


Figure 1.

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AB0574

LEVEL OF AGREEMENT ON CORE SIGNS OF CUTANEOUS LUPUS ERYTHEMATOSUS (CLE) SUBTYPES AMONG DERMATOLOGISTS AND RHEUMATOLOGISTS AND DEVELOPMENT OF A CONCEPTUAL MODEL FOR CLE

Keywords: Outcome measures, Health services research, Skin

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Background: CLE can present as an isolated skin disease or with systemic lupus erythematosus (SLE) and is classified as chronic (CCLE; primarily discoid [DLE]), subacute (SCLE), intermittent (ICLE), or acute (ACLE). Except for erythema, skin-related signs/symptoms may vary by subtype. We conducted mixed methods research to refine and develop an optimal clinician-reported outcome measure for CLE trials.
Objectives: Evaluate the level of agreement among dermatologists and rheumatologists on CLE signs/symptoms and develop a conceptual model for CLE.
Methods: We conducted one-to-one interviews with practicing, board-certified dermatologists or rheumatologists followed by a rank-and-sort exercise, and a

literature review. Interviews included open-ended and semi-structured questions on CLE diagnosis and their patients' signs/symptoms, and data were evaluated by thematic analysis. Two quantitative activities were conducted: first, clinicians sorted a list of skin signs/symptoms as 1) not characteristic, 2) moderately characteristic, or 3) highly characteristic of CLE or cutaneous SLE disease activity. Second, they classified CLE signs/symptoms as most closely associated with CCLE/DLE, SCLE or ACLE. Data were analyzed using an informal (ranking task) or formal (classification task) consensus model.

Results: Eleven dermatologists and 10 rheumatologists (US n=13; Europe n=8) were interviewed. Most dermatologists (70%) had 5–10 years' experience managing/treating patients with CLE; 56% of rheumatologists had 21–25 years' experience. The most frequently mentioned signs included erythema/rash (100%), malar rash (71%), palpable lesions (57%) and scale (57%). Photosensitivity (76%), itch (62%) and skin pain (57%) were the most frequently mentioned symptoms. Of the 33 skin signs presented, both specialties ranked photosensitive rash (weighted average: dermatologists 3.00; rheumatologists 2.85) and erythema (2.92 and 2.81) highest. However, some key differences were identified. For example, dermatologists ranked polycyclic (2.72) and annular (2.61) lesions (typical of SCLE) as highly characteristic of CLE, but rheumatologists ranked them as low or moderately characteristic (1.55 and 2.23, respectively). Also, dermatologists ranked markers of DLE, such as follicular plugging (2.88 and 2.36), higher than rheumatologists. Consensus analysis showed robust agreement between dermatologists (eigenvalue ratio 17.95; average competence 0.86) and modest agreement between rheumatologists (6.13; 0.67) in classifying skin manifestations by CLE subtype. Manifestations with the strongest agreement included acute alopecia (ACLE n=20; SCLE n=0; CCLE/DLE n=1), malar rash (n=21; n=0; n=0, respectively), dyspigmentation without scarring (n=1; n=18; n=2), psoriasiform annular plaques (n=0; n=20; n=1), dyspigmentation with scarring (n=0; n=0; n=21), and irreversible scarring alopecia (n=0; n=0; n=21). Variation was evident for signs more often associated with SCLE, including non-scarring photosensitive dermatitis (n=8; n=13; n=0). Multidimensional scaling showed notable differences in consensus between dermatologists and rheumatologists; while coherent clusters of symptoms were mapped to the CLE subtypes by dermatologists, the pattern for rheumatologists was more diffuse, suggesting a less consistent conceptualization of SCLE and CCLE. These results, together with the literature review, were used to develop a conceptual model for evaluating CLE.

Conclusion: Despite agreement on the importance of erythema and characterization of CLE as a photosensitive rash, differences between the specialties were apparent when rating CLE signs that typically accompany non-systemic, cutaneous disease. This might reflect increased training among dermatologists in clinical-histopathologic description of lesions. The conceptual model proposed will facilitate efforts to design measurement approaches to evaluate disease activity in clinical research and practice.

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AB0575 IMPACT OF PATIENT-REPORTED DISEASE ACTIVITY ON HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS. DATA FROM THE ALMENARA LUPUS COHORT

Keywords: Patient reported outcomes, Quality of life, Systemic lupus erythematosus

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Background: Health-related quality of life (HRQoL) is impaired in systemic lupus erythematosus (SLE) patients, but its association with physicians reported disease activity is modest to none.

Objectives: To determine the impact of patients reported disease activity on their HRQoL.

Methods: We evaluated patient-reported disease activity on SLE patients from the Almenara Lupus Cohort. Disease activity was assessed using the Lupus Foundation of America Rapid Evaluation of Activity in Lupus (LFA-REAL) patient-reported outcome (PRO) which ranges between 0 and 1200 (the higher the score is, the worse the activity is); HRQoL was ascertained using the LupusQoL which ranges between 0 and 100 (the higher the score is, the better the HRQoL). Generalized estimating equations were performed for each domain of the LupusQoL and the LFA-REAL PRO measured at the previous visit; multivariable models were adjusted for possible confounders (age at diagnosis, gender, educational level, disease duration, SLEDAI-2K, SDI, prednisone dose, antimalarials and immunosuppressive drug use and the same domain of LupusQoL) measured at the same visit as the LFA-REAL PRO. B was reported per 10 units increase of the LFA-REAL PRO.

Results: A total of 259 patients and 582 visits were included. Mean (SD) LFA-REAL PRO was 242.91 (178.92). The most affected LupusQoL domains at baseline were burden to others 57.5 (SD 31.5), intimate relationship 64.1 (SD 33.1) and body image 62.6 (SD 30.7). LFA-REAL PRO predicted a worse HRQoL in all domains, even after adjustment by possible confounders (Table 1).

Conclusion: A higher patient-reported disease activity predicted a worse HRQoL in SLE patients, even after adjustment for possible confounders. Strategies to improve how the patients feel and manage their disease could be useful to improve their HRQoL. Patient-reported disease activity should be included in the evaluation of SLE patients on a regular basis.

Table 1. Impact of LFA-REAL PRO per 10-unit increase on HRQoL in SLE patients

HRQoL domains	Univariable		Multivariable*	
	B (SE)	p value	B (SE)	p value
Physical health	-0.74 (0.06)	<0.001	-0.40 (0.05)	<0.001
Pain	-0.89 (0.06)	<0.001	-0.63 (0.06)	<0.001
Planning	-0.81 (0.06)	<0.001	-0.47 (0.06)	<0.001
Intimate relationship	-0.58 (0.10)	<0.001	-0.36 (0.08)	<0.001
Burden to others	-0.72 (0.08)	<0.001	-0.40 (0.07)	<0.001
Emotional health	-0.70 (0.07)	<0.001	-0.43 (0.06)	<0.001
Body image	-0.47 (0.09)	<0.001	-0.35 (0.08)	<0.001
Fatigue	-0.77 (0.06)	<0.001	-0.42 (0.06)	<0.001

SE: Standard error. * Multivariable models were adjusted by age at diagnosis, gender, educational level, disease duration, SLEDAI-2K, SDI, prednisone dose, antimalarials and immunosuppressive drug use and the same domain of LupusQoL

REFERENCES: NIL.

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AB0576 DEFINING INTERFERON MEDIATED CONDITIONS (DEFINITION): IFN ASSAYS AND CLINICAL FEATURES OF ESTABLISHED ANA-ASSOCIATED AUTOIMMUNE DISEASES

Keywords: Sjögren syndrome, Systemic lupus erythematosus, Undifferentiated connective tissue disease

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Background: A large body of evidence has shown that type I IFN (IFN-I) biomarkers are associated with worse clinical features within each ANA-associated rheumatic disease (ARMD). IFN-I biomarkers also predict response to IFN-targeted and other therapies. DEFINITION is an observational study to explore the clinical associations of IFN biomarkers across the disease course and spectrum of ARMDs. This is a preliminary analysis for the subsection on the spectrum of established ARMD.
Objectives: To determine whether patients with high IFN-I biomarkers have greater impact of disease including disease activity, functional impairment and quality of life.
Methods: Adults with current or previous positive ANA and either criteria for any ARMD (SLE, pSS, IIM, SSc, MCTD) or consultant diagnosis of ARMD (may be undifferentiated if symptoms>12 months and/or treated with immunosuppressants. We collected demographics, deprivation, participation, cardiovascular risk and comorbidity variables, diagnostic criteria for each ARMD, quality of life and other patient-reported outcome measures, and therapies. Disease activity was summarised using a composite of validated instruments to classify each organ system as severe, moderate, mild or inactive (equivalent to BILAG A-D/E for SLE). IFN-I pathway activation was measured using gene expression IFN Score A and B and memory B cell tetherin. We used Spearman correlations and unsupervised hierarchical clustering and to find associations between clinical outcomes and IFN-I biomarkers.
Results: Of 294 patients, 23/294 (18%) were male, mean (SD) age was 50 (14), index of multiple deprivation decile 4.9 (3.1), Charlson comorbidity index 2.1 (1.5). Current therapy was prednisolone (24.5%), hydroxychloroquine (45.2%), methotrexate (17.7%), mycophenolate (11.9%), azathioprine (10.2%), rituximab (8.5%), cyclophosphamide (0.3%). 104 patients had SLE, 111 had UCTD, 33 and pSS, 19 had myositis, 14 had SSc and 13 had MCTD. There was a significant association between ARMD diagnosis and IFN Score A (F= 2.52, p=0.030) and memory B cell tetherin (F= 4.34, p<0.001) but not IFN Score B (F=0.66, p=0.653). In pairwise correlations only one weak relationship between SF36 PCS and memory B cell tetherin was found (R=0.33, p<0.001). No substantive relationship was found between gene expression scores and clinical features. However, unsupervised hierarchical clustering across all ARMD patients yielded 5 clusters of patients with a significant role for sociodemographic variables that revealed further relationships between IFN biomarkers and disease activity. Cluster 1: mild symptoms, low comorbidity, high affluence; Cluster 2: older, high comorbidity, high affluence; Cluster 3: younger, low affluence, poor QoL; Cluster 4: high tetherin and BILAG; Cluster 5: low IFN and BILAG.
Conclusion: There are complex relationships between IFN and clinical features across the spectrum of ARMDs. This is confounded by socioeconomic variables, which must be considered in stratification studies.
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AB0577 LEFT VENTRICULAR DYSSYNCHRONY IN SUBJECTS WITH DIFFERENT SLE PHENOTYPES

Keywords: Cardiovascular disease

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with highly heterogenous clinical presentation involving, e.g., skin, joints, kidneys and the cardiovascular system. In prospective studies, the incidence rates of myocardial infarction and stroke in patients with SLE have been shown to be high, but more knowledge is needed regarding early myocardial involvement and affection of the right ventricle in different SLE phenotypes.
Objectives: The aim of the present study was to investigate differences of left- and right ventricular systolic function in three, well-defined SLE phenotypes, i.e. skin- and joint involvement, lupus nephritis antiphospholipid syndrome (APS), respectively.
Methods: Transthoracic echocardiograms were performed in 60 subjects with SLE (three age- and sex-matched groups of subjects with either skin- and joint involvement, lupus nephritis or APS, respectively) included in the SLEVASK [1] cohort which represents a subgroup of the regional quality register *Clinical Lupus Register in North-Eastern Gothia* (Swedish acronym: KLURING). There were 54 women and 6 men, and the median age was 48.5 (range 28-68y) years. Left- and right ventricular dimensions and standard systolic function parameters were measured according to international guidelines. Left and right ventricular longitudinal strain and left ventricular mechanical dispersion, defined as the standard deviation of time to maximal myocardial shortening were measured by a commercially available software. Three subjects with clinically manifest heart failure were excluded.
Results: There were no significant differences in left- or right ventricular dimensions, left ventricular ejection fraction or measures of right ventricular systolic function between the three groups. Left ventricular global longitudinal strain was reduced in subjects with nephritis (p=0.012), as compared to those with skin- and joint involvement and there was a trend for lower strain also among subjects with APS (p=0.078). Left ventricular mechanical dispersion was increased among subjects with APS (p=0.015) and nephritis (p=0.032), as compared to those with skin- and joint involvement (Table 1).
Conclusion: Reduced left ventricular global longitudinal strain and greater mechanical dispersion, a sign of a more heterogonous contraction, among SLE patients with nephritis and APS indicate more severe cardiac involvement, as compared to those with skin- and joint involvement. A greater degree of mechanical dispersion is thought to reflect myocardial fibrosis and future studies should investigate the pathogenesis of such sub-clinical impairment of cardiac function in SLE and its impact on long-term prognosis.
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Table 1.

	Lupus nephritis	APS	Joint- and skin involvement	p-value
LVEDDI (mm/m^2)	26 (25-28)	26 (24-27)	27 (26-28)	p=ns
LVEDVI (ml/m^2)	58 (46-65)	53 (55-62)	57 (49-67)	p=ns
LVEF (%)	57 (56-59)	57 (55-59)	58 (56-61)	p=ns
LV-GLS (%)	-20 (-21--18)	-20 (-21--19)	-21 (-23--20)	p=0.030
LVMD (ms)	38 (31-46)	38 (32-50)	32 (27-35)	p=0.037
RVOTD (mm)	32 (27-34)	31 (27-36)	28 (26-31)	p=ns
RVITD (mm)	35 (31-36)	36 (31-38)	33 (31-37)	p=ns
TAPSE (mm)	23 (20-25)	22 (20-25)	22 (21-25)	p=ns
RV s' (cm/s)	13 (11-16)	13 (11-15)	15 (12-16)	p=ns
RV-GLS (%)	-22 (-24--20)	-21 (-23--19)	-23 (-24--21)	p=ns
RV-FWS (%)	-26 (-27--24)	-25 (-27--23)	-26 (-30--24)	p=ns

Values are median with interquartile range (IQR). Abbreviations: LVEDDI = left ventricular end-diastolic diameter index; LVEDVI = left ventricular end-diastolic volume index; LVEF = left ventricular ejection fraction; LV-GLS = left ventricular global longitudinal stain; LVMD = left ventricular mechanical dispersion; ns = not significant; RVOT = Right ventricular outflow tract diameter; RVITD = Right ventricular inflow tract diameter; TAPSE = tricuspid annular plane systolic

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AB0578 LATIN-AMERICAN SYSTEMIC LUPUS ERYTHEMATOSUS CLUSTERS

Keywords: Autoantibodies, Registries, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is heterogeneous autoimmune disease. Identification of patient clusters may be useful for the management of the disease.

Objectives: To describe different SLE clusters according to sociodemographic, clinical and serological variables.

Methods: GLADEL 2.0 is an ongoing Latin-American observational cohort initiated in 2019. Variables chosen at cohort entry to stratify patients and construct clusters were selected from sociodemographic and cumulative clinical and serological variables. Hierarchical cluster analyses were performed by the Ward method on a distance matrix using the Gower's method.

Results: A total of 560 SLE patients were included in this analysis. Three clusters were identified. Cluster 1 (n=269) was characterized by more cutaneous, articular, renal and serosal involvement; serological manifestation was positive anti-dsDNA. Cluster 2 (n=194) was represented by patients who rarely had renal involvement and the most frequent clinical manifestations were cutaneous and hematological; the most frequent serological manifestations were the presence of antiphospholipid antibodies (aPLs). Cluster 3 (n=97) was characterized by a lower frequency of clinical and serological involvements, with the exception of neurological domain. Clusters 1 and 2 share hematologic manifestations and hypocomplementemia (Table 1).

Conclusion: In this cohort, three patient clusters were identified. Cluster 1 patients were characterized by renal, articular, cutaneous and serositis involvement, anti-dsDNA antibodies and hypocomplementemia, Cluster 2 patients were characterized by hematologic, cutaneous involvement, aPLs and hypocomplementemia. Cluster 3 patients presented fewer serological findings but a higher frequency of neurological involvement. Follow up of these patients will allow for elucidation of relationship of these clusters with SLE outcomes.

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Table 1. Clustering of GLADEL 2.0 SLE patients into three clusters by cluster analysis based on sociodemographic, serological and clinical variables

Variable	Cluster 1 (n=269)	Cluster 2 (n=194)	Cluster 3 (n=97)	p value	Variable	Cluster 1 (n=269)	Cluster 2 (n=194)	Cluster 3 (n=97)	p value
Female, n(%)	239 (88.8)	173 (89.2)	88 (90.7)	0.92	**Arthritis, n(%)**	230 (85.5)	151 (77.8)	73 (75.3)	0.03
Age at diagnosis, median (IQR)	26 (21-33)	26 (19-34)	29 (22-40)	0.12	**Acute cutaneous lupus, n(%)**	140 (52)	87 (44.8)	28 (28.9)	0.89
Ethnicity, n(%)					**Oral ulcer, n(%)**	124 (46.1)	89 (45.9)	42 (43.3)	0.07
Afro-Latin American	16 (5.9)	7 (3.6)	4 (4.1)	0.26	**Alopecia, n(%)**	185 (68.8)	114 (58.8)	59 (60.8)	0.02
Caucasian	61 (22.7)	59 (30.6)	21 (21.6)		**Delirium, n(%)**	7 (2.6)	0	4 (4.1)	0.29
Indigenous	3 (1.1)	4 (2.1)	0		**Psychosis, n(%)**	11 (4.1)	4 (2.1)	5 (5.2)	0.74
Mestizo	188 (69.9)	123 (63.7)	71 (73.2)		**Seizures, n(%)**	14 (5.2)	7 (3.6)	4 (4.1)	0.04
GLADEL 2.0 Groups of patients n(%)					**Mononeuritis multiplex, n(%)**	0	2 (1)	2 (2.1)	
Group I (LN never)	4 (1.5)	162 (83.5)	63 (64.9)	<0.001	**Peripheral/cranial neuropathy n(%)**	6 (2.2)	9 (4.6)	6 (6.2)	0.12
Group II (inactive LN)	79 (29.4)	15 (7.7)	19 (19.6)		**Acute confusional state, n(%)**	7 (2.6)	3 (1.5)	2 (2.1)	0.80
Group III (active prevalent LN)	99 (36.8)	14 (7.2)	13 (13.4)		**Hemolytic anemia, n(%)**	31 (11.5)	28 (14.4)	7 (7.2)	0.19
Group IV (active incident LN)	87 (32.3)	3 (1.5)	2 (2.1)		**Leukopenia, n(%)**	123 (45.7)	106 (54.6)	32 (33)	0.01
Persistent proteinuria, n(%)	240 (89.2)	24 (12.4)	28 (28.9)	<0.001	**Lymphopenia, n(%)**	151 (56.1)	111 (57.2)	38 (39.2)	0.01
Urinary cylinders, n(%)	122 (45.4)	16 (8.2)	8 (8.2)	<0.001	**Thrombocytopenia, n(%)**	54 (20.1)	48 (24.7)	19 (19.6)	0.43
NL (II o V class), n(%)	80 (29.7)	7 (3.6)	12 (12.4)	<0.001	**ANA +, n(%)**	268 (99.6)	192 (99)	94 (96.9)	0.09
NL (III o IV class), n(%)	203 (75.5)	21 (10.8)	20 (20.6)	<0.001	**Anti-dsDNA, n(%)**	255 (94.8)	142 (73.2)	53 (54.6)	<0.001
Pleuritis, n(%)	81 (30.1)	50 (25.8)	25 (25.8)	0.53	**aPLs, n(%)**	62 (23)	75 (38.7)	24 (24.7)	0.001
Pericarditis, n(%)	63 (23.4)	29 (14.9)	13 (13.4)	0.03	**Hypocomplementemia*, n(%)**	268 (99.6)	194 (100)	11 (11.3)	<0.001

IR (Interquartile range); NL (Lupus nephritis); aPLs (Antiphospholipid antibodies); *(decreased C3 or C4)

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AB0579 ASSOCIATION OF RACE OR ETHNICITY WITH MEDICATION ADHERENCE IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Gender/diversity issues, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) causes significant disease burden. Racial and ethnic differences in outcomes have been recognized, with increased morbidity and mortality in Black and Hispanic individuals, compared to non-Hispanic White referents. Financial barriers to treatment, such as copayments (or copays), may affect adherence to essential pharmacologic therapies, contributing to increased health adversity. Determining the contribution of copays to adherence may identify disparities in medication access and pathways to improve adherence.

Objectives: To examine the association between race or ethnicity and medication adherence.

Methods: We used administrative health claims data (Optum's De-identified Clinformatics® Data Mart Database, 2007-2021) to identify individuals with incident SLE (2 ICD-9/10 codes within 30-365 days) between 2010-19 receiving hydroxychloroquine (HCQ), azathioprine (AZA), mycophenolate mofetil (MMF), methotrexate (MTX), or combination therapy (HCQ with AZA, MMF, or MTX). Race or ethnicity were categorized as Asian, Black, Hispanic, White, or unknown. We dichotomized copays as low (<$10/30 days) or high (≥$10/30 days). Adherence was defined as proportion of days covered (PDC) ≥80%. We examined the association between race or ethnicity and adherence with multivariable-adjusted logistic regression models, using White individuals as referent. Results were then stratified by copay categories.

Results: We identified 12,510 individuals: age 54.2±15.5 years; 88.2% women; 63.2% (7910) White, 14.9% (1860) Black, and 13.8% (1729) Hispanic. A total of 9510 (76%) were on HCQ and 15% on combination therapy. Median (IQR) 30-day copays were $8 (4, 10) for HCQ, $7 (2, 10) for AZA, $10 (5, 20) for MMF, and $8 (3, 11) for MTX. Black individuals had 51% (95% CI 0.31-0.80), 30% (95% CI 0.61-0.81), and 35% (95% CI 0.45-0.94) lower odds of adhering to AZA, HCQ, and combination therapy, respectively. Hispanic individuals had 27% (95% CI 0.63-0.94) lower odds of adhering to HCQ. When stratified by low or high copay, the association between race or ethnicity and adherence did not change, and the interaction of copayment on the association between race or ethnicity and adherence was not significant (**Table 1**).

Conclusion: In this large cohort, Black and Hispanic individuals had decreased odds of adherence to SLE medications even after adjusting for several socioeconomic factors and comorbidities. The detrimental associations between copay and adherence were consistent across copay strata, suggesting that other factors contribute to racial and ethnic disparities. Factors such as polypharmacy, pharmacy deserts, transportation, mental health, cultural barriers, and health care access merit examination for their relation to adherence.

Table 1. Association of Race or Ethnicity and Odds of Medication Adherence

	Asian	Black	Hispanic
OR (95% CI); P value			
AZA (n=690)	0.67 (0.23-1.94); 0.46	0.50 (0.30-0.80); 0.004	1.00 (0.57-1.75); 0.99
HCQ (n=8629)	1.15 (0.87-1.53); 0.33	0.70 (0.61-0.81); <0.0001	0.73 (0.63-0.85); <0.0001
MMF (n=756)	1.53 (0.66-3.53); 0.32	0.73 (0.50-1.13); 0.16	0.82 (0.52-1.30); 0.40
MTX (n=518)	0.75 (0.20-3.43); 0.71	1.11 (0.57-2.15); 0.77	1.36 (0.67-2.76); 0.41
Combination Therapy* (n=1720)	1.04 (0.53-2.02); 0.91	0.65 (0.55-0.94); 0.02	0.70 (0.48-1.03); 0.97

Reference group: White individuals.

Table 2. Stratification by Copayment

≥$10 vs <$10 Copay				
OR (95% CI); P value				
	Asian	**Black**	**Hispanic**	**Interaction p value**
AZA	0.18 (0.02-1.54); 0.18	0.37 (0.17-0.81); 0.01	0.43 (0.17-1.11); 0.08	0.79
HCQ	0.52 (0.30-0.90); 0.02	0.72 (0.56-0.93); 0.01	0.57 (0.44-0.73); <0.0001	0.51
MMF	0.68 (0.13-3.44); 0.64	0.85 (0.42-1.75); 0.66	0.83 (0.39-1.75); 0.62	0.78
MTX	0.41 (0.02-9.51); 0.58	0.75 (0.25-2.30); 0.62	2.00 (0.50-8.04); 0.33	0.67
Combination Therapy	1.70 (0.45-6.45); 0.43	1.25 (0.69-2.27); 0.46	0.61 (0.32-1.16); 0.13	0.14

Adjusted for age, sex, Elixhauser comorbidities, tobacco use, antiphospholipid syndrome, educational attainment, annual household income, insurance type, and US geographic region.

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AB0580 PREGNANCY OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): DATA FROM A MULTIETHNIC, MULTINATIONAL LATIN AMERICAN COHORT

Keywords: Anti-phospholipid syndrome, Pregnancy and reproduction, Systemic lupus erythematosus

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Background: Obstetric morbidity (OM) is higher in SLE women than in healthy ones. Few data on SLE pregnancy outcomes in Latin America (LA) have been reported.

Objectives: To study SLE pregnancy outcomes in LA.

Methods: GLADEL 2.0 is an observational prevalent/incident cohort started in 2019. To date, 43 centers from 10 LA countries have enrolled 1030 SLE patients (1982/1997 ACR or SLICC criteria). Women with ≥1 pregnancy were included. Past and ongoing (6, 12, 24 months follow-up) OM (miscarriages, fetal deaths, preeclampsia, prematurity, neonatal lupus) were evaluated.

Results: At inclusion, 329 women have had at least one pregnancy [median (IQR): 2 (1-3)]: Table 1. Of them, 293 (89.1%) had ≥1 live birth and 183 (55.6%) developed OM. Preeclampsia occurred in 49 (14.9%). Among 71 (21.6%) women with anti-SS-A(Ro)/SS-B(La) antibodies, 3 (4.2%) developed neonatal lupus (no cardiac involvement). Antiphospholipid syndrome (APS) was associated with higher risk of OM (52.2% vs 10.0%; p< 0.001). Of the 755 pregnancies reported, 551 (73.0%) resulted in live births, of which 79 (14.3%) were premature. The remaining pregnancies ended in 178 (23.6%) miscarriages and 41 (5.4%) fetal deaths. During 2-follow-up years (Figure 1), 24 singles pregnancies occurred. All were under antimalarials; 16 (66.7%) resulted in live births, 4 (25.0%) premature; 12 (50.0%) developed OM. There were seven (29.2%) miscarriages and one fetal loss (4.2%) related to severe preeclampsia. One cholestasis gravidarum (4.2%) lead to prematurity. There were no new cases of neonatal lupus.

Conclusion: In GLADEL 2.0 cohort, around half of the studied women presented OM being frequently related to APS. Miscarriages, prematurity, preeclampsia and fetal deaths were the most common pregnancy complications. The incidence of neonatal lupus was lower than previously reported [1].

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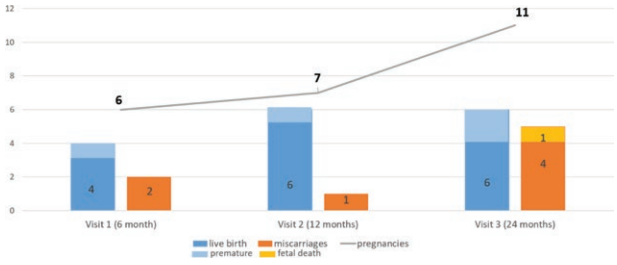


Figure 1. SLE pregnancy outcome 2-year follow-up.

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Table 1. Characteristics of SLE women with ≥1 pregnancy at cohort inclusion related to OM[1].

VARIABLES	OM[1]		p value[2]	VARIABLES	OM[1]		p value[2]
Epidemiological/Comorbidities	**No (n=146)**	**Yes (n=183)**		**SLE background**	**No (n=146)**	**Yes (n=183)**	
Age (years)[3]	41 (34-47)	39 (31.5-50)	0.542	Disease duration (months)[3]	76 (28-153)	100 (36.5-162.5)	0.136
Education (years)[3]	12 (10.2-15)	12 (10-15)	0.664	Antiphospholipid syndrome	**3/30 (10%)**	**24/46 (52.2%)**	**0.001**
Ethnicity			0.299	**Laboratory**			
Afro-Latin American	14/146 (9.6%)	8/183 (4.4%)		Anti-dsDNA antibodies	107/134 (79.9%)	139/172 (80.8%)	0.885
White	30/146 (20.5%)	42/183 (23.0%)		Anti-Ro antibodies	51/109 (46.8%)	57/135 (42.2%)	0.518
Amerindian	3/146 (2.1%)	4/183 (2.2%)		Anti-La antibodies	20/107 (18.7%)	18/132 (13.6%)	0.293
Mestizo	99/146 (67.8%)	129/183 (70.5%)		C3 and/or C4, low	117/141 (83.0%)	147/174 (84.5%)	0.760
Socioeconomic level			0.184	Lupus anticoagulant	17/92 (18.5%)	34/121 (28.1%)	0.109
High	29/143 (20.3%)	41/181 (22.7%)		aCL[4] IgG	21/101 (20.8%)	34/129 (26.4%)	0.353
Medium	42/143 (29.4%)	67/181 (37.0%)		aCL[4] IgM	15/101 (14.9%)	33/130 (25.4%)	0.071
Low	72/143 (50.3%)	73/181 (40.3%)		Anti-ß2GP1[5] IgG	11/79 (13.9%)	15/95 (15.8%)	0.832
Medical coverage			0.260	Anti-ß2GP1[5] IgM	10/79 (12.7%)	15/95 (15.8%)	0.666
Complete/partial	94/141 (66.7%)	133/182 (73.1%)		**Treatment**			
No Coverage	47/141 (33.3%)	49/182 (26.9%)		Corticosteroids	143/146 (97.9%)	176/181 (97.2%)	0.736
Hypertension	47/83 (56.6%)	73/110 (66.4%)	0.180	Antimalarials	141/146 (96.6%)	177/181 (97.8%)	0.520
Diabetes mellitus	9/83 (10.8%)	6/110 (5.5%)	0.184	Immunosuppressors	118/146 (80.8%)	152/179 (84.9%)	0.373
Dyslipidemia	23/78 (29.5%)	31/109 (28.4%)	0.872	Aspirin	30/42 (71.4%)	53/65 (81.5%)	0.243
Smoking	22/50 (44.0%)	34/58 (58.6%)	0.176	Anticoagulation	18/42 (42.9%)	33/66 (50.0%)	0.554

[1] Obstetric morbidity; [2] statistically significance: p < 0.05; [3] median (interquartile range); [4] anti-cardiolipin antibodies; [5] beta-2 glycoprotein I antibodies.

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AB0581

CLINICAL AND RENAL PATHOLOGICAL FEATURES PREDICTING COMPLETE CLINICAL RESPONSE IN CRESCENTIC LUPUS NEPHRITIS

Keywords: Prognostic factors, Systemic lupus erythematosus, Kidneys

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Background: Lupus nephritis (LN) is one of the major manifestations of systemic lupus erythematosus, which develops in approximately 40% of patients with systemic lupus erythematosus. Clinical presentation of LN varies between patients, from asymptomatic proteinuria to rapidly progressive glomerulonephritis. Due to improvements in treatment strategy, risk of developing end-stage kidney disease (ESKD) decreased to less than 10% in developed countries, but some patients still progress to ESKD and require renal replacement therapy. Crescent formation is considered as a poor prognostic factor in LN, however pathological features correlating with clinical response and long-term renal outcome has not been fully investigated.

Objectives: To determine clinical and pathological features predicting complete clinical response (CCR) after induction therapy in crescentic lupus nephritis (CLN) comparing with non-CLN.

Methods: Patients with biopsy proven class III or IV LN from 2008 to 2017 and who could be observed more than 5-years after induction therapy were selected. They were divided into two groups according to the presence of cellular crescentic lesions. Individual pathological lesions defined in modified NIH activity and chronicity indices were evaluated. CCR was defined as urinary protein-to-creatinine ratio (UPCR) less than 0.7g/day after 12 months of treatment, according to the 2019 EULAR/ERA-EDTA recommendations for LN. Cumulative CCR rates for 5-years were compared between the two groups, and independent factors associated with CCR were investigated.

Results: Seventy-three patients (CLN, 30 patients and non-CLN, 43 patients) were included in the analysis. There was no significant difference in age (42.8 ± 2.6 vs 44.4 ± 2.1 years, p=0.63), disease duration (10.9 ± 1.9 vs 11.4 ± 1.7 years, p=0.85), eGFR (70.7 ± 4.9 vs 66.0 ± 4.1 ml/min/1.73m^2, p=0.47), and UPCR (2.3 ± 0.5 vs 2.5 ± 0.4 g/gCr, p=0.72) between the CLN and non-CL groups. Cumulative CCR rates for 5-years were not different between CLN and non-CLN groups (83% vs 84%, p=0.96). In the non-CLN group, patients who achieved CCR had lower glomerular sclerosis (0.93 ± 0.16 vs 1.75 ± 0.27, p=0.01) and interstitial fibrosis score (0.77 ± 0.12 vs 1.25 ± 0.20, p=0.049) than those who did not achieve CCR. In the CLN group, patients who achieved CCR had lower interstitial fibrosis (0.94 ± 0.14 vs 1.67 ± 0.17, p<0.01) and tubular atrophy score (0.78 ± 0.15 vs 1.58 ± 0.19, p<0.01) than those who achieved CCR, while cellular or fibrotic crescentic score did not differ between them (2.33 ± 0.23 vs 2.50 ± 0.23, p=0.65). Multivariable analysis revealed that interstitial fibrosis was negatively associated with CCR in both CLN and non-CLN groups (odds ratio [OR] 0.11, p<0.01; OR 0.33, p=0.04, respectively). We next divided CLN patients into two groups according to the interstitial fibrosis less than 25% or not, and found significantly higher cumulative CCR rate in patients with interstitial fibrosis less than 25% (p<0.01).

Conclusion: Crescent formation in the kidney pathology was not associated with cumulative CCR rates in patients with class III or IV LN, while interstitial lesion was shared by both CLN and non-CLN as a significant prognostic factor for CCR after induction therapy.

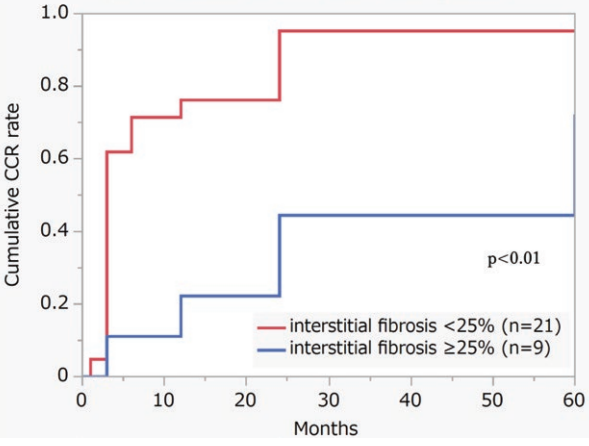
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Figure1. Cumulative CCR rate of CLN patients



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AB0582

DESCRIPTION OF ASYMPTOMATIC ANTI-PHOSPHOLIPID CARRIERS IN A FRENCH MULTICENTER COHORT STUDY

Keywords: Descriptive studies, Biomarkers, Anti-phospholipid syndrome

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Background: Anti-phospholipid antibodies (APL) are associated with thrombotic events or pregnancy complications leading to the so-called anti-phospholipid syndrome (APS) according to the classification criteria last updated in Sydney in 2006. APL can be found in asymptomatic patients.
Objectives: We observed the clinical, biological characteristics and association with other diseases of asymptomatic APL carriers group, and we compared them with an APS patients group.
Methods: In this French multicentric retrospective cohort study we analyzed the data of 507 patients with persistent positive APL measured between 2012 and 2019. Clinical and laboratory data were collected retrospectively. Data are expressed as numbers with frequencies and medians with interquartile ranges (IQR). Qualitative and quantitative variables were compared using Fisher and Kruskal-Wallis tests. Cumulative incidence curves of relapse event were generated using Kaplan-Meier. We used Cox model to obtain Hazard Ratio (HR). Proportional hazard assumption was checked using Schoenfeld residuals. Two-sided testing was used, with p ≤0.05 considered statistically significant.
Results: We observed a majority of female patients of a younger age in the APS group when compared to the APL carriers group. Cardiovascular risk factors were similar in both groups. Systemic lupus erythematosus was more frequently associated with the APS group, but interestingly rheumatoid arthritis, ankylosing spondylarthritis and chronic kidney disease were more frequently associated with asymptomatic APL carriers. At biological level, anti-cardiolipin IgG and beta-2-glycoprotein 1 IgG positivity rates were higher in APS group than in APL carriers group, but not for lupus anticoagulant positivity. Triple-positive APL were more frequent in APS group as expected, but we found up to 13.9% of triple-positive APL in APL carriers group. We also observed a higher prevalence of ANA, anti-dsDNA, anti-SSA/SSB in the APS group. At prognostic level patients from APL carriers group had a lower mortality (2.9 % vs 9.1%, p=0.006) but the observation period for this group was slightly shorter. No thrombotic event was observed in this group during the follow-up period, while 38.8% of APS patients had a relapse (thrombotic or obstetrical event during follow-up). In our subgroup analysis comparing primary and secondary APL carriers, we observed less women than men, an older age and a higher prevalence of cancer in primary APL carriers group. Interestingly, we observed a higher rate of atypical APL in primary APL carriers subgroup, with a trend toward a significant intergroup difference (31.1% vs 21.2%, p=0.075). There was no difference in mortality among groups.
Conclusion: APL carriers group was associated with the presence of autoimmune disease, infection and cancer. We did not observe any thrombotic events in the APL carriers group during the evaluation period. APS group had a higher mortality as expected. Interestingly, we observed a higher rate of atypical APL in primary APL carriers subgroup, with a trend toward a significant intergroup difference (31.1% vs 20.2%, p=0.075). We did not find a difference in mortality between primary and secondary APL carriers subgroups.
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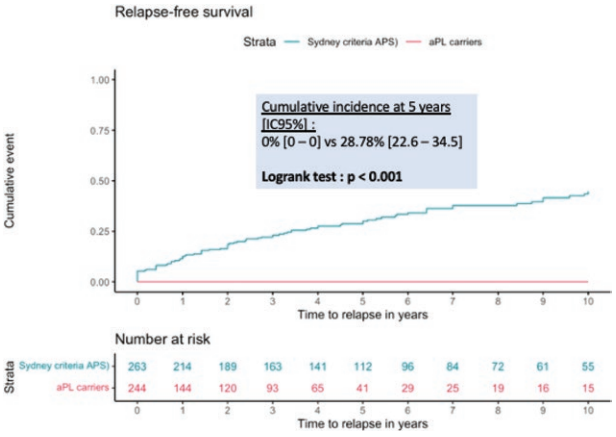


Figure 1. Cumulative incidence of thrombotic events over 5 years in APS patients group and asymptomatic APL carriers group.

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AB0583

CONCENTRATIONS OF SERUM ADVANCED GLYCATION END PRODUCTS (AGES) CARBOXYETHYLLYSINE CORRELATE WITH INDICES OF ACTIVITY AND SPECIFIC MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Biomarkers, Systemic lupus erythematosus

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Background: Studies postulate that advanced glycation end products (AGEs) could have a relevant role as inducers in the chronic inflammatory pathway present in various diseases, including systemic lupus erythematosus (SLE), and that AGEs concentration could be related to disease parameters such us activity or accumulated damage. To date, these studies show conflicting results.
Objectives: To estimate correlations between the concentrations of the blood AGE carboxyethyllysine (CEL) and disease-related parameters in a population of SLE patients.
Methods: Serum CEL concentrations were determined using a specific AGEs competitive ELISA Kit in accordance with the manufacturer's instructions in 113 SLE patients. We correlated demographic and clinical data with the results, and adjusted for age and smoking status as possible confounding factors, based on previous analysis (CEL AGEs decreased significantly with age and presence of smoking habits). The indices were analyzed both as quantitative and categorized variables according to previously established categories in the literature or to medians/tertiles depending on the distribution of the variable in our sample. CEL concentrations were classified into tertiles.
Results: Table 1 shows the distribution and correlations of our cohort characteristics according to CEL tertiles. Disease duration was inversely statistically correlated with CEL concentrations, as well as haematological alterations while alopecia was directly correlated. CEL values were statistically correlated with several markers of SLE activity: SLE disease activity index (SLEDAI), erythrocyte sedimentation rate, serum IL-6, and the count of swollen joints at the moment of the blood extraction (both in the Disease Activity Score 28 and 68). No associations were found with autoantibodies, other disease questionnaires, or different blood AGEs and AGEs receptor.
Conclusion: The correlation of CEL AGEs values with different disease activity markers in SLE could indicate their potential use as a biomarker of activity in this disease and an associated specific phenotype with less haematological manifestations and more alopecia.
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Table 1. Correlations of our cohort characteristics according to carboxyethyllysine tertiales. c: categorized; M1: adjusted for age; M2 adjusted for age and tobacco. Bold indicates statistically significant differences (p<0.05).

	All patients	1st tertile [0.823, 2.57)	2nd tertile [2.569, 4.19]	3rd tertile [4.191,27.76]	p-value M1	p-value M2
	N = 113	*N = 38*	*N = 38*	*N = 37*		
Disease duration (y)	10.0 [4.00;16.0]	12.0 [6.00;19.8]	9.00 [4.00;16.0]	10.0 [1.00;17.0]	0.007	0.030
Smoker	**29 (25.7%)**	**2 (5.26%)**	**8 (21.1%)**	**19 (51.4%)**	**<0.001**	
cSLEDAI:					**0.031**	**0.043**
0- Remission	**22 (19.5%)**	**12 (31.6%)**	**5 (13.2%)**	**5 (13.5%)**		
1- Mild	**39 (34.5%)**	**11 (28.9%)**	**13 (34.2%)**	**15 (40.5%)**		
2- Moderate	**41 (36.3%)**	**14 (36.8%)**	**17 (44.7%)**	**10 (27.0%)**		
3- Serious	**11 (9.73%)**	**1 (2.63%)**	**3 (7.89%)**	**7 (18.9%)**		
Alopecia	**51 (45.1%)**	**17 (44.7%)**	**16 (42.1%)**	**18 (48.6%)**	**0.125**	**0.033**
Haematological alterations	**82 (72.6%)**	**30 (78.9%)**	**30 (78.9%)**	**22 (59.5%)**	**<0.001**	**0.005**
ESR	**9.50 [5.00;18.2]**	**8.00 [3.25;19.8]**	**11.0 [6.00;15.0]**	**11.0 [4.00;19.0]**	**0.064**	**0.015**
ESR tertiles:					**0.036**	**0.015**
[2, 7]	**42 (37.5%)**	**18 (47.4%)**	**12 (32.4%)**	**12 (32.4%)**		
[7,17]	**39 (34.8%)**	**8 (21.1%)**	**17 (45.9%)**	**14 (37.8%)**		
[17,81]	**31 (27.7%)**	**12 (31.6%)**	**8 (21.6%)**	**11 (29.7%)**		
Serum interleukin-6	**2.27 [1.51;3.89]**	**1.94 [1.40;3.71]**	**2.08 [1.81;2.96]**	**2.88 [1.86;4.63]**	**<0.001**	**<0.001**
Swollen joints/28	**20 (17.7%)**	**6 (15.8%)**	**4 (10.5%)**	**10 (27.0%)**	**0.012**	**0.021**
Swollen joints/68	**21 (18.6%)**	**6 (15.8%)**	**4 (10.5%)**	**11 (29.7%)**	**0.012**	**0.032**

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AB0584

NOT ALL SJÖGREN IS DRY – PRESERVED GLANDULAR FUNCTION IN A SUBGROUP OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Descriptive studies

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Background: Lymphocytic infiltration of the salivary and lachrymal glands is a hallmark of primary Sjögren's Syndrome (PSS). Chronic inflammation leads to progressive destruction of the glands resulting in dryness of the eyes and mouth termed sicca. The course and pace of sicca development in PSS is elusive.

Objectives: To explore the effect of symptom duration on sicca and disease activity.

Methods: Data of patients from the PSS registry of the Medical University of Graz fulfilling the 2016 ACR/EULAR classification criteria for PSS were analysed. We analysed disease duration and total duration of sicca symptoms, Schirmer's test, unstimulated salivary flow test (USF), stimulated salivary flow test (SSF) and ESSDAI (EULAR Sjögren's Syndrome disease activity index), Evaluators Global Assessment (EGA), and focus score of the initial lip salivary gland biopsy. In addition, salivary gland ultrasound (SGUS) was performed using the De Vita scoring system. Free light chains (FLC) κ and λ, IgG, rheumatoid factor (RF) IgA were determined. The patient's perspective was analysed by ESSPRI and PSS-QoL.

Results: Data from 159 PSS patients were analysed, of whom 92.6% (n=148) were female. The mean age was 59.3±12.2 years (± standard deviation), with a mean disease duration of 5.5±5.4 years and a mean sicca duration of 11.6±7.4 years. Interestingly, results of USF, SSF, and Schirmer's Test did not decrease with duration of disease or sicca. The lack of correlation was probably caused by a subset of patients in whom glandular function remained stable 10 to 33 years after the onset of sicca. We defined this subgroup of patients by an SSF >0.5ml/min and with a symptom duration >10 years (SFSD10). 19.5% (n=31) of our PSS patient were categorised into this group. SFSD10 showed a significantly higher Schirmers test (median 0 (0-35] vs 3[3-35], p<0.01), lower ESSPRI-dryness (7 [1-10] vs. 5[1-10], p<0.05), PSS-QoL dryness (11[2-22] vs. 8 [3-15], p<0.01), lower IgG (15.5 [7.4-38.1] vs. 11.2 [6.5-30.5], p<0.05) and FLC-K (25 [3.9-134] vs. 20.2 [10.3-63.6], p<0.05) compared to non-SFSD10-group. SGUS De Vita score was significantly lower in the SFSD10 subgroup (median 1 [0-2] vs. 2 [1-3], p=0.045). We found no difference in ESSDAI, focus score, antibody status, pain, fatigue or HRQL between the two groups.

Conclusion: Our results indicate the presence of a subgroup of PSS patients with preserved glandular function despite long-standing disease.

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Disclosure of Interests: None Declared.

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AB0585

COMORBIDITY CLUSTERS AND THEIR RELATIONSHIP WITH SEVERITY AND OUTCOMES OF THE INDEX DISEASES, IN A LARGE MULTICENTER SYSTEMIC LUPUS ERYTHEMATOSUS COHORT (RELESSER REGISTER)

Keywords: Systemic lupus erythematosus, Comorbidities

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Background: Patients with Systemic lupus erythematosus (SLE) have a well-known increased risk of major comorbidities, but they are also very heterogeneous in term of prevalence of comorbid conditions. The relationship of the comorbidities with the outcomes and the severity of index disease is less known.
Objectives: Evaluate the interactions between comorbid conditions, on a large multicenter SLE cohort from RELESSER register, and its impact in severity and outcomes.
Methods: Data about 14 cumulative comorbidities, as previously defined [1], where derived from patients with SLE (ACR-97 criteria) included in the retrospective phase of RELESSER. Severity Katz Index (SKI) and SLICC/ACR Damage Index (SDI) were calculated. An unsupervised cluster analysis using K-means method was implemented to define clusters. ANOVA and Tukey tests were used to compare continuous numerical variables; Kruskal-Wallis test to discrete variables and the Chi-square test (or Fisher's exact test) to categorical ones.
Results: A total of 3658 SLE patients (ACR-97 criteria) were included. Median SKI: 2 (interquartile range (IQR):1-3); median SDI:1(IQR:0-2). Demographic data are shown in Table 1. The comorbidities considered and their prevalence were: Thyroiditis (8.3%), peptic ulcer (3.8%), severe hepatopathy (1.0%), obstructive pulmonary disease (2.7%), Diabetes (5.0%), cardiovascular event (CVE) (11.0%), cardiac arrhythmia (4.2%), pulmonary embolism (3.4%), dementia (0.7%), malignancy (5.9%); serious infection (19.3%), end stage renal disease (2.8%), osteoporosis (7.3%) and depression (17.1%). Four cluster, with markedly different comorbidity profiles and outcomes were identified (table 3): one subgroup was clustered around depression (100% of the cases) (cluster 2), another cluster (cluster 3) with > 1 serious infection (100%) and cluster 4, with 100% of CVE. In cluster 1, no patient had any of the 3 defining comorbidities in the rest of the clusters. There were no statistically significant differences between clusters in death by SLE. The clusters are characterized in more detail in table 1, where a just summary of the main comorbidities included in the analysis is displayed.
Conclusion: Cluster analysis identifies well-differentiated subgroups of SLE patients as regard comorbidities and associated mortality and severity of the disease.

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Table 1. Cluster of comorbidities and outcomes, N (%) unless specified

	Cluster 1 [d]	Cluster 2 [a]	Cluster 3 [b]	Cluster 4 [c]	*p*-value
Age, mean (SD)	44.8 (14.1)	49.8 (14.1)	46.7 (14.3)	46.7 (14.3)	<0.001
Male sex	214 (9.2) [a,c]	25 (4.8)	51 (12.2) [a]	63 (16.3) [a,d]	<0.001
Time with SLE (years), mean (SD)	129.2 (95.9)	159.3 (101.4) [d]	170.3 (100.3) [d]	169 (113) [d]	<0.001
Cardiovascular event	0 (0) [c]	0 (0) [c]	0 (0) [c]	**388 (100)**	<0.001
Cardiac arrhythmia	53 (2.3) [b,c]	17 (3.3) [c]	19 (4.5) [c,d]	61 (15.7)	<0.001
Malignancy	110 (4.7) [a,c]	46 (8.9) [d]	25 (6.0)	31 (8.0) [d]	0.001
Serious infection	0 (0)	122 (23.6)	**418 (100)**	165 (42.5)	<0.001
End stage renal disease	27 (1.2) [b,c]	11 (2.1) [b,c]	26 (6.2) [a,d]	34 (8.8) [a,d]	<0.001
Osteoporosis	79 (3.4)	71 (13.8) [d]	41 (9.8) [c,d]	69 (17.8) [b,d]	<0.001
Depression	0 (0) [a,c]	**516 (100)**	0 (0) [a,c]	94 (24.4)	<0.001
Glucocorticoids	1890 (86)	451 (91.3) [b,d]	400 (98)	354 (93.2) [b,d]	<0.001
Cyclophosphamide or mycophenolate	501 (23.5)	145 (29.7)	216 (54.3)	139 (37.4)	<0.001
Antimalarials	1869 (85.4) [b,c]	433 (86.9) [b,c]	317 (78.3)	263 (71.1)	<0.001
SKI*, mean (SD)	2.3 (1.4)	2.8 (1.8)	3.5 (1.8) [a,d]	3.5 (2) [a,d]	<0.001
SDI**, mean (SD)	0.7 (1)	1.3 (1.8)	1.6 (1.8)	3.3 (2.5)	<0.001
Death	46 (2.2)	27 (5.6)	45 (11.6)	90 (25.2)	<0.001
Death by lupus	14 (36.8) [#]	8 (40) [#]	8 (19.5) [#]	24 (30.4) [#]	0.27

*Severity Katz Index; ** SLICC/ACR Damage Index. Regarding age, the p-value for the comparation between group 1 and 3 is 0.0498. [#]: no significant. [a,b,c or d] means the only significant comparison.

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AB0586 **SERUM/ URINE LEVELS AND EXPRESSION OF CD163 IN LUPUS NEPHRITIS**

Keywords: Biomarkers, Systemic lupus erythematosus, Clinical trials

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Background: CD163 is a glycosylated membrane protein expressed in monocytes and macrophages that phagocytize the hemoglobin/haptoglobin complex. As a result of proinflammatory stimuli, CD163 is shedded from the cell membrane and becomes soluble CD163. Therefore, it has been shown that serum (s) and urine (u) levels of soluble CD163 increase in acute or chronic inflammatory diseases. sCD163 and uCD163 are considered as potential biomarkers reflecting disease activity in patients with systemic lupus erythematosus (SLE).
Objectives: We aimed to investigate the association of serum and urine soluble CD163 levels and renal CD163 expression with disease activity in patients with lupus nephritis (LN).
Methods: Serum and urine levels of CD163 of 45 SLE patients (active renal 20, active non-renal 15, inactive 10) and 20 healthy volunteers were tested by ELISA. Control samples were taken from 12 active renal patients after six months of treatment and 30 renal biopsy specimens were examined for CD163 expression.
Results: Of 45 participants, 37 (82.2%) were female, with a median disease duration of 113 (1-436) months and a mean age of 38,9±13 (18-68) years. Both the frequency of uCD163 positivity and its levels were significantly higher in the active LN group compared to the inactive LN (p=0,007 and 0.02 respectively) and active non-renal SLE (p=0,001 and 0.023 respectively) groups (Table 1). sCD163 and uCD163 levels of 12 patients with active LN were significantly reduced after treatment (p=0,04 and p=0,006) (Figure 1). CD163+ macrophage expression in kidney biopsies of patients with active LN correlated with sCD163 (r= 0.597 and p=0.01) and uCD163 (r=0.507 and p=0.045) levels.
Conclusion: uCD163 is a promising biomarker that can differentiate active LN from inactive LN and active extrarenal SLE changing in line with treatment response. Correlation of both s and uCD163 with CD163+ macrophage expression in biopsies suggests that it may be used as an activity parameter in patients with lupus nephritis histopathologically. Further studies are awaited to confirm these results (This study was funded by Istanbul University with the project number TTU-2021-38289)

Figure 1. Serum and urine levels of CD163 after treatment

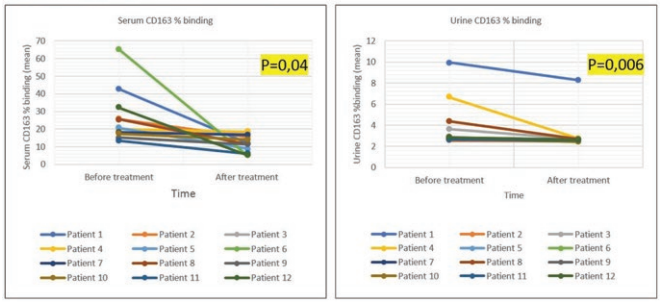


Table 1. Serum and urine levels of CD163 across study groups

Biomarker	Active LN (n=20)	Inactive LN (n=10)	P	Extrarenal active SLE (n=15)	P	Healthy control (n=20)	P
Serum CD163 % binding (mean+SD)	26,7±17,6	22,8±18,8	0,54	22,06±9,6	0,3	17,03±15,6	0,4
Serum CD163 positivity n (%)	%75	%50	0,2	%73	0,9	%40	**0,05**
Urine CD163 % binding (mean+SD)	3,9±2,4	2,6±0,04	**0,02**	2,5±0,1	**0,023**	2,6±0,5	**0,03**
Urine CD163 positivity n (%)	%90	%40	**0,007**	%33	**0,001**	%12	**<0,001**

LN lupus nephritis, SLE systemic lupus erythematosus, SD standard deviation

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AB0587

IN-HOSPITAL MORTALITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A STUDY FROM 2010-2020

Keywords: Systemic lupus erythematosus

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Background: SLE mortality depends on epidemiological, sociodemographic and clinical factors. These vary amongst different regions.
Objectives: To determine the factors predicting disease-associated mortality compared with factors affecting Infection associated mortality in SLE patients.
Methods: This was a retrospective study involving SLE patients admitted from February 2010 to January 2020. Demographic, clinical details, laboratory parameters, treatment received, and complications during the stay in the hospital were entered in a proforma. The cause of death was classified as disease-related, infection-associated, or both.
Results: There were 1156 SLE admissions and 135 in-hospital mortalities. 24 patients were excluded because of inadequate parameters or wrong codes. Among the 111 patients, 102 (91.9%) were females. Mean age at the diagnosis and mean duration of hospitalisation was 29.7 years (27.6-31.7) and 11 days (8.7-13.3) respectively. More than three-fourths of the total patients had skin (76.6%), Musculoskeletal (74.8%), Renal (81.1%) or Hematological (73%) involvement. Nearly half of the patients had Respiratory (42.3%) or Neurological (49.5%) involvement. Mortality was primarily due to disease activity (43.2%; n = 48) followed by mixed (infection and disease activity) (36%; n = 40). Isolated infection-associated mortality was less than the active disease (19.8%; n=22). A subgroup analysis of the study participants based on mortality showed that cardiac (50%) and haematological (75%) involvement were more common among the participants with disease activity. There was no significant difference between the baseline investigations and treatment administered between the groups. The details are shown in Table 1. The most common infections were due to gram-negative bacteria. Among the study participants, 45 patients (48.6%) died within six months of diagnosis. Pulmonary involvement (51.9%; n=28/54) was more common in the first six months compared to death after six months (33.3%; n=19/57) (p-value=0.04). Cardiac involvement in the form of myocarditis was more common in the later part of the disease compared to the first six months (18.5% vs 40.4%; n=10/54 vs n= 23/40.4; p-value = 0.01).
Conclusion: Disease activity alone or in combination with infection contributes more to hospital mortality than infections alone. Though patients with disease activity-associated mortality have more haematological and cardiac involvement at presentation, there are no differences in various laboratory parameters, including complement levels among the patients in the three groups.

Table 1. Comparison of Organ involvement, Investigations, and treatment administered among mortality subgroups

	Total (n=111)	Disease Activity (n=48)	Infection (n=22)	Mixed (n=40)	p-value
Age	29.7 (27.6-31.7)	29.7 (26.6-32.2)	30.2 (24.7-35.7)	29 (25.6-32.5)	0.92
Female Sex	102 (91.9)	47 (97.9)	21 (95.5)	34 (85)	0.07
Organ Involved					
Skin	85 (76.6)	40 (83.3)	20 (90.9)	24 (60)	0.01
Musculoskeletal	83 (74.8)	40 (83.3)	17 (77.3)	25 (62.5)	0.08
Renal	90 (81.1)	36 (75)	16 (72.7)	37 (92.5)	0.05
Neurological	55 (49.5)	25 (52.1)	7 (31.8)	23 (57.5)	0.15
Pulmonary	47 (42.3)	18 (37.5)	8 (36.4)	21 (52.5)	0.31
Cardiac	42 (37.8)	**24 (50)**	**3 (13.6)**	**15 (37.5)**	**0.01**
Haematological	81 (73)	**36 (75)**	**11 (50)**	**34 (85)**	**0.01**
Gastrointestinal	13 (11.7)	5 (10.4)	3 (13.6)	5 (12.5)	0.93
Vascular	8 (7.2)	3 (6.3)	2 (9.1)	3 (7.5)	0.90
Investigations at admission					
Haemoglobin, g/dL	8.3 (7.9-8.6)	8.5 (8.0-9.0)	8.4 (7.1-9.7)	7.9 (7.4-8.4)	0.36
Total Leucocyte Count, cells/ µL	9750 (7917-11584)	9272 (7166-11380)	9991 (6025-13959)	10300 (6251-14348)	0.88
Platelet count, × 10^3 cells/µL	126 (105-152)	139 (102-175)	168 (89-247)	95 (69-121)	0.07
Serum creatinine, mg/dL	2.5 (2.1-2.8)	2.1 (1.6-2.7)	2.9 (1.8-3.9)	2.6 (2.0-3.2)	0.28
Serum albumin, mg/dL*	2.4 (2.2-2.6)	2.4 (2.2-2.7)	2.5 (2.1-2.9)	2.3 (2.1-2.5)	0.62
Low C3/C4^	74/83 (89.2)	29/33 (87.9)	12/14 (85.7)	33/36 (91.7)	0.79

The values are presented as mean (95% confidence interval) or numbers (percentage) *n=102, ^n=83

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0588

ADALIMUMAB FOR IMMUNE RELATED INFERTILITY: EFFICACY AND SAFETY FROM PROSPECTIVE FRENCH MULTICENTER REGISTRY

Keywords: Pregnancy and reproduction, Autoantibodies, Anti-phospholipid syndrome

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Background: Recurrent miscarriage (RM) is a frequent condition affecting about 1–3 % of couples and is one of the most frustrating and difficult areas in reproductive medicine since the etiology is often unknown and evidence-based diagnosis and treatment strategies are scarce. Likewise, recurrent implantation failure (RIF) is considered after at least 3 unsuccessful transfers of good quality embryos, and remains unexplained in 45 % of infertile couples.
Objectives: The primary objective of this study was to describe a real-life prospective cohort of women with unexplained RM and/or RIF under adalimumab, to analyze the impact of the treatment on live birth rates and to evaluate its safety.
Methods: The French infertility multicenter FALCO registry is an ongoing registry from 2017 including patients with unexplained recurrent miscarriages and implantation failures from several university hospitals. Inclusion criteria were [1] at least 3 recurrent miscarriages before 12 weeks of gestation and/or at least 3 implantation failures of at least 2 good quality embryos transfers; [2] absence of any cause for recurrent miscarriages and implantation failures such as uterine, genetic, infectious, hormonal, thrombophilia and autoimmune diseases. The following data was collected:

- Clinical data including age, number of pregnancies, number of consecutive miscarriages, body mass index, tobacco and alcohol use, tea or coffee consumption during pregnancy, dietary habits, presence of endometriosis, adenomyosis and assessment of the uterine cavity by hysteroscopy or hysterosonography.
- Laboratory analysis of usual recurrent miscarriages etiological screening: parental karyotypes, ovarian reserve parameters (FSH (IU/L), LH (IU/L), Estradiol (pg/ml), AFC (Antral Follicular Count), AMH rate (ng/ml)), thyroid-stimulating hormone (TSH) levels (mUI/l) and biomarkers of immune origin (antinuclear antibodies, anti TPO/TG).

Results: Overall, between 2017 and December 2022, 2686 pregnancies from 395 patients were included with prospective follow-up. These women had history of recurrent implantation failure for 102 (26%), recurrent miscarriage for 275 (70%) and both for 18 (4%). The median gravidity was 4 [2-6]. Regarding the presence of immunity biomarkers, 263 had various autoantibodies (66,6%): 130 patients (33%) with antinuclear antibodies (>1/80e), 18 patients with antiphospholipid antibodies (5%), 44 patients with positive anti thyroid peroxidase antibodies (11%), 24 with positive anti-thyroglobulin antibodies (11%), 4 with anti-transglutaminase antibodies (11%). Most recent AMH count median was 1.73 [0.87, 3.24]. Among overall pregnancies, there were 1384 miscarriages (73,6%), 269 live births (14,3%), 89 abortions (4,7%), 24 medical terminations of pregnancies (1,3%), 55 pregnancies over 12 weeks of gestation (2,9%) and 58 extrauterine pregnancies (3,1%) Among 2686 pregnancies, 494 were treated and received immunomodulatory treatment. Among these pregnancies under therapies: steroids in 332 cases (12,4%), hydroxychloroquine in 185 cases (7%), intralipids in 102 cases (3,8%), and adalimumab in 69 cases (2,6%). Patients with pregnancy under adalimumab treatment had a significantly higher rate of cumulative live birth rate than those with untreated ones: OR: 3.52 [1.63 - 7.61]; p < 0.01 after adjustment of age, pregnancy, associated treatment (progesterone, aspirin, vitamin D, prednisone). Adverse events in Adalimumab treated pregnancies were reported in 7 women: herpes and zoster reactivation in 3 cases, cystitis and bronchitis in 4 cases, and no congenital malformation and no maternal deaths.
Conclusion: In this large prospective French cohort of women with unexplained immune origin RM and/or RIF, adalimumab has been effective to obtain a live birth pregnancy.
REFERENCE:
[1] Adalimumab for immune related infertility: efficacy and safety from prospective French multicenter registry

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0589 CANCER PREVALENCE IN SYSTEMIC LUPUS ERYTHEMATOSUS: A PORTUGUESE COHORT STUDY WITH 15 YEARS OF FOLLOW-UP

Keywords: Systemic lupus erythematosus, Malignancy, Epidemiology

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Background: An increased risk of malignancy was reported in patients with Systemic Lupus Erythematosus (SLE) [1-3].
Objectives: To estimate the prevalence of cancer in a Portuguese cohort of patients with SLE over long term follow-up.
Methods: Patients followed up between 01/01/2006 and 31/10/2021 at the Centro Universitário de Coimbra Lupus Clinic were included. All patients fulfilling SLE classification criteria (EULAR/ACR 2019 or SLICC 2012 or ACR 1999) and assessed at least in two visits were included. Cancer cases were only considered if the diagnosis was established after SLE diagnosis. Patient and SLE clinical and treatment data were collect from the cohort electronic database. Disease activity was assessed with the SLE Disease Activity Score (SLE-DAS) and organ damage with the SLICC/ACR Damage Index (SDI). Associations with malignancy were tested using the *Chi-square test*, *Fisher exact test*, *Student's t-test,* or *Mann-Whitney U test*, as appropriate. Statistical significance with Bonferroni adjustment accounting for multiple comparisons was considered for p<0.005
Results: In total, 438 patients were included (mean age: 49.6±15.8 years-old; female: 85.4%; mean disease duration: 14.2±9.8 years). At the last study visit, 68.8% were in remission, and mean SLE-DAS was 1.9±2.5. The total cumulative prevalence for cancer was 7.1% (n=31), with 4 patients presenting metastatic disease at the time of cancer diagnosis. The most common malignancies were non-melanoma skin cancer (1.1%), colorectal (1.1%), hematologic (1.1%), lung (0.7%), and breast cancer (0.7%). Cancer patients were older (64.5±14.9 vs. 48.5 years, p<0.001) and had higher any-cause mortality (35.5% vs. 5.9%, p<0.001). There were no significant differences regarding disease activity at last visit, disease duration, organ damage or cumulative immunosuppressive therapy usage (38.7% vs 54%, p=0.099). Death as a direct result of malignancy occurred in 8 (72.7%) patients, accounting for 22.9% of death in our cohort.
Conclusion: This is the first study reporting cancer prevalence in a Portuguese SLE cohort. Our results are similar to those reported by Sultan et all (5.4%) (2), but substantially lower than those reported in a Finish cohort (22%) (3).
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Acknowledgements: NIL.
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AB0590 CROSS-SECTIONAL ASSESSMENT OF THE QUALITY OF LIFE IN SLE PATIENTS: ROLE OF DISEASE ACTIVITY, CHRONIC DAMAGE, FIBROMYALGIA SYNDROME AND MOOD DISORDERS

Keywords: Quality of life, Patient reported outcomes, Systemic lupus erythematosus

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by a wide spectrum of manifestations, potentially involving every system. This heterogeneity may influence different aspects of patients' daily life, including physical ability, working and social life, thus impacting the quality of life (QoL). Among all the SLE-related manifestations, cutaneous involvement may lead to insecurity and isolation, negatively resulting in QoL.
Objectives: The aim of the present study was to analyse the QoL in a SLE cohort, determining the potential influence of disease activity, chronic damage, comorbidities, and mood disorders.
Methods: We enrolled consecutive SLE patients, diagnosed according to 2019 ACR/EULAR criteria. Clinical and laboratory data were collected, and disease activity and chronic damage were assessed by SLEDAI-2k and SDI. As controls, we enrolled patients affected by Discoid Lupus Erythematosus (DLE) and Undifferentiated Connective Tissue Disease (UCTD). The fibromyalgia diagnosis was made according to the 2016 ACR Classification Criteria. Quality of life was evaluated by using the Lupus Quality of Life questionnaire (LupusQoL); furthermore, each patient filled out the Hospital Anxiety and Depression Scale (HADS) questionnaire.
Results: We enrolled 237 SLE patients (M/F 18/219; median age 46 years [IQR 19.5], median disease duration 156 months [IQR 180]), 24 CLE patients (M/F 5/19; median age 61.5 years [IQR 29.5], median disease duration 92.1 months, [IQR 128.5]). and 25 UCTD (M/F 1/24; median age 40 years, [IQR 21.25]; median disease duration 66 months [QR 103.9]). In SLE patients the median SLEDAI-2k value was 0 (IQR 2) and the SDI was 0 (IQR 1). Fibromyalgia was diagnosed in 69 SLE patients (29.1%), 5 CLE (20.8%), and 7 UCTD (28%). The comparison among these three groups of patients revealed for SLE and CLE patients a significantly lower mean values in the LupusQoL domain related to Body Image (BI) (73.9±27.7 and 71.3±30.9, respectively) compared to UCTD patients (87.2±19.0) [p=0.01 and p=0.03, respectively]. Focusing on SLE patients, females showed significantly lower mean values compared to males for almost all domains: Pain (P, [p=0.02]), Intimate Relationship (IR; [p=0.001]), Burden to Others (BtO [p=0.029]), Emotional Health (EH; [p=0.012]), Body Image (BI; [p=0.033]) and Fatigue (F; [p=0.002]). As expected, fibromyalgia patients had lower values in all the domains of the LupusQoL when compared to patients without this condition (p<0.001 for all comparisons, except for BI p=0.006). Moreover, as reported in Figure 1, SDI values negatively correlated with all the LupusQoL domains (Figure 1A); conversely, we found a positive correlation between SDI and both HADS domains (Anxiety [r=0.16; p=0.015]; Depression [r=0.21; p=0.0009]). As expected, a strong negative correlation was identified between LupusQoL score in each domain and both Anxiety [(BH r=-0,58, P p=-0.53, Planning p=-0.52, IR p=-0.62, EH= -0.75, BI= -0.52, F=-0.64, BtO r=-0.62); p < 0.0001 for all the analysis] and Depression [(BH r=-0,61, P p=-0.58, Planning p=-0.63, IR p=-0.61, EH= -0.55, BI= -0.60, F=-0.69, BtO r=-0.55]; p < 0.0001 for all the analysis).
Conclusion: The presented results confirmed the negative impact of SLE on the quality of life. Among the analyzed variables, female sex and fibromyalgia deeply influenced the outcome. The chronic damage showed to be one of the main determinants of impairment of the QoL in SLE patients and of the development of Anxiety and Depression, measured through the HADS questionnaire. Lastly, Anxiety and Depression may contribute to the worst QoL in SLE, underlying the need for comprehensive evaluation and management of the SLE-associated comorbidities.

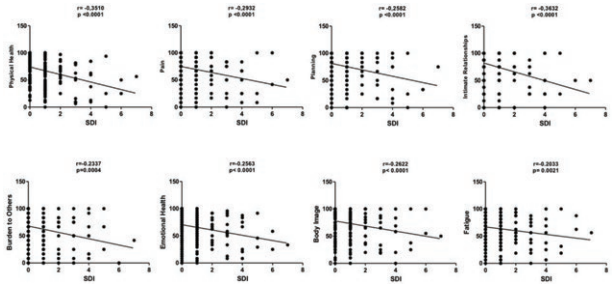


Figure 1. Correlations between HADS and LupusQoL domains

REFERENCES: NIL.
Acknowledgements: NIL.
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AB0591 COVID-19 VACCINE SAFETY DURING PREGNANCY IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: COVID, Pregnancy and reproduction, Systemic lupus erythematosus

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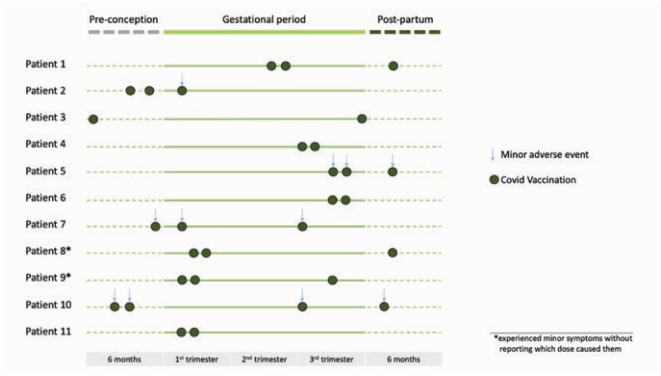


Figure 1. Timeline showing COVID-19 vaccination and vaccination-related minor adverse events in relation to gestational and post-partum periods in eleven pregnant/lactating women with systemic lupus erythematosus.

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Background: Vaccinations comprise a part of the antenatal care of pregnant women, including patients with systemic lupus erythematosus (SLE) who are at increased risk of adverse pregnancy outcomes (APOs). While COVID-19 vaccination has been shown to be safe in patients with SLE, data on vaccine-associated adverse events (AEs) during the antenatal and lactation period are scarce or lacking.
Objectives: To investigate the association between COVID-19 vaccination and AEs in pregnant SLE patients.
Methods: A total of 9201 complete responses were extracted on June 21st, 2022 from the COVID-19 Vaccination in Autoimmune Diseases (COVAD) 2 database, a global e-survey involving 157 collaborators from 106 countries. Among respondents, 6787 (73.8%) were women. We identified 70 (1.1%) women who were exposed to at least one COVID-19 vaccine dose during pregnancy, among those 11 with SLE. Delayed onset (>7 days) vaccine-related AEs were extracted and triangulated with disease activity, treatment changes due to flare after vaccination, and COVID-19 infections in vaccinated pregnant women with SLE. Additionally, information on health-related quality of life and physical function was recorded using PROMIS at the time of survey completion.
Results: The age of patients ranged from 28 to 39 years; 5/11 women were of Asian origin. None of these patients reported major vaccine AEs, including four patients with self-reported active SLE prior to the vaccination. None of them reported any change in the status of their autoimmune disease, and no hospitalisation or special treatment was recorded. Six women experienced minor vaccine AEs; two of them had active disease prior to vaccination. Four patients reported COVID-19 infection; two of them while they were pregnant and post-vaccination and two prior to pregnancy and vaccination. All four patients experienced symptoms of their disease, but no overt SLE flare was reported. At the time of survey completion, all patients reported their general health as being good to excellent in all aspects evaluated. Importantly, no APOs were reported. None of the patients reported thrombotic events post-vaccination, which provides some reassurance regarding COVID-19 vaccination in a patient population with a high risk for cardiovascular comorbidity and thrombosis, especially in the presence of antiphospholipid antibodies or in patients diagnosed with the antiphospholipid syndrome, a considerable portion within SLE populations. Moreover, it was reassuring to note an absence of association between experienced vaccine AEs and active disease prior to vaccination. Although minor AEs were common, they did not impair daily functioning, and the symptoms resolved in all patients after a median of 3 (IQR: 2.5–5.0) days.
Conclusion: Our report adds relevant evidence concerning the sensitive issue of COVID-19 vaccine AEs and flares in SLE patients during the antenatal and lactation period. Despite the small sample size, the findings provide some reassurance and can contribute to informed decisions regarding vaccination in patients with SLE and high-risk pregnancies due to their background autoimmune disease. Based on the present data, the risk/benefit ration of COVID-19 vaccination appears favourable, with vaccines both providing passive immunisation to the fetus and active immunisation to the mother with no signals of exacerbation of the mother's autoimmune disease.
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AB0592

COMPARATIVE CARDIOVASCULAR RISK IN PATIENTS WITH OLDER-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: A NATIONWIDE RETROSPECTIVE COHORT STUDY IN KOREA

Keywords: Cardiovascular disease, Systemic lupus erythematosus

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Background: Patients with systemic lupus erythematosus (SLE) have increased mortality related to cardiovascular disease (CVD) and the age is one of important risk factors for the development of CVDs. However, the comparative risk of CVDs in patients with older onset SLE has not been well studied.
Objectives: This study aims to compare the CVD risk in patients with SLE occurred after the age of 40 compared to those with DM.
Methods: Incident SLE patients aged over 40 years and age-sex matched (1:4:4) controls with DM or general population were identified from the nationwide claims database in Korea between 2008 and 2018. We defined CVD risk as ischemic heart disease, stroke, and cardiac death. The incidence rates (IR) and incidence rate ratio (IRR), and adjusted hazard ratio (HR) of CVDs were calculated using generalized estimating equation models.
Results: We identified 4,272 SLE, 17,003 DM, and 17,088 general population patients aged over 40 years. Their mean age was 53.1 (±9.7) and 81.7% of them were female. The IR per 1,000 person-years (PYs) of CVDs for SLE, DM, and general population were 16.8, 11.7, and 5.7, respectively. Compared to general population, patients with SLE (IRR 3.27, 95% CI 2.78-3.85) and DM (IRR 2.77, 95% CI 2.02-2.56) showed higher CVD risk compared to general population. Increased risk of CVDs in SLE patients was highest in their forties (IRR 4.13, 95% CI 3.06, 5.59). After adjusting confounders, the CVD risk of SLE (HR 1.99, 95% CI 1.66-2.38) was higher than DM (HR 1.39, 95% CI 1.22-1.58) patients.
Conclusion: Older onset SLE patients had increased CVD risk compared to general population. Even after adjustment for confounders, SLE patients showed higher CVD risk than DM patients in Korea.
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Disclosure of Interests: None Declared.
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SLE, Sjön's and APS - clinical aspects (other than treatment)

AB0593 **RISK FACTORS FOR HOSPITALIZATION IN SYSTEMIC ERYTHEMATOSUS LUPUS (SLE). WHAT IS AT STAKE IN THE FIRST YEAR OF THE DISEASE?**

Keywords: Prognostic factors, Systemic lupus erythematosus

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Background: Several risk factors for hospitalization have been identified among clinical, demographic, and laboratory features in SLE patients. However, less is known about how and how much disease expression in the first year since diagnosis may impact the outcome or predict disease course in the following years.
Objectives: To define early risk factors for hospitalization in SLE.
Methods: Observational, retrospective analysis in a monocentric cohort of SLE patients, regularly followed at our Unit. Demographics, clinical manifestations, hospitalizations over time, SLE flares and treatments at disease onset and during follow-up were collected. In particular, number and type of immunosuppressants (IS), daily and cumulative doses of glucocorticoids (GCs) at o 1 and 5 years of follow-up. Disease activity was evaluated by SLEDAI-2K score at baseline, at 1 and 5 years of follow-up while organ damage was assessed by the SLICC/ACR damage index (SDI). Disease state as modified Lupus Low Disease Activity status (LLDAS) without PGA, was evaluated at one year from SLE diagnosis. T-test and chi square test were used to estimate association between at least one hospitalization within the fifth years of disease and sex, age, and clinical manifestations at disease onset.
Results: Among 422 Caucasian SLE patients regularly followed in our centre, (87% female, mean age 47±13.2 years, follow-up duration 10.5±9.3 years) 263 (62%) had at least one hospitalization due to SLE disease activity or disease related complications within five years from disease onset. Similar hospitalization incidence rate at five years and at the last visit were found (0.19 and 0.21 patient-years respectively). Characteristics of hospitalized patients at 5 years with respect to non-hospitalized ones are reported in Table 1. Disease onset with nephritis or constitutional symptoms (fever, lymphadenopathies) and not being in LLDAs at one year were significantly associated to hospitalization within five years (p values <0.01). Moreover, number of IS, cumulative GC dose at 1 and 5 years and SDI at 5 years of follow-up resulted significantly associated with hospitalizations (p values<0.01). No correlations were found between age at disease onset, sex, diagnostic delay, other manifestations at disease onset, SDI at 1 year and the risk of hospitalization over time.
Conclusion: Hospitalizations for disease activity and its complications are frequent in SLE patients, not only in the first years of the disease. A more aggressive SLE phenotype and treatments at onset are associated with higher risk for future hospitalizations; on the other hand, being on LLDAS within one year from disease onset seems to be protective. Therefore, our data suggest that disease expression within the first year from diagnosis could be crucial to predict SLE course over time and to stratify patients at lower or higher risk for severe disease.

Table 1. Cohort characteristics

	Overall	Hospitalized patients at 5 years	Non hospitalized patients	P value
F Sex (%)	87,4	87.0	89.1	0.5
Age at onset (mean, sd)	29.1±11.8	28.7±12.2	29.9±11.2	0.3
Diagnostic delay (years, mean sd)	2.2±4.2	1.9±0.9	2.6±1.6	0.08
Renal at onset (%)	14.9	90.4	9.5	**<0.01**
Serositis at onset (%)	8.0	76.4	23.5	0.08
Constitutional at onset (%)	20.6	75.8	24.1	**<0.05**
Cutaneous at onset (%)	39.5	37.0	44.5	0.2
Articular at onset (%)	55.4	51.9	62.4	0.036
No LLDAS at one year (%)	30.6	78.5	21.4	**<0.01**
Cum. GC dose at 1 year (g, mean, sd)	2.9±2.4	3.7±2.6	1.6±1.4	**<0.01**
Cum. GC dose at 5 years (g, mean, sd)	9.2±6.3	10.8±6.5	6.3±4.7	**<0.01**
Number of flares at 5 years (mean, sd)	0.5±0.9	0.7±1.0	0.2±0.6	**<0.01**
Number of IS at 1 year (mean, sd)	0.7±0.8	0.9±0.8	0.3±0.5	**<0.01**
Number of IS at 5 years (mean, sd)	1.0±1.2	1.3±1.3	0.4±0.7	**<0.01**
SLICC-DI at 1 year >0 (%)	6.8%	11.2%	6.7%	0.1
SLICC-DI at 5 years >0 (%)	11.1%	21.4%	9.1%	**<0.01**

REFERENCES: NIL.
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Disclosure of Interests: None Declared.
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AB0594 **CLINICAL SIGNIFICANCE OF ANTI-LA ANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS**

Keywords: Systemic lupus erythematosus, Autoantibodies

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by a wide spectrum of clinical manifestations and the presence of various antibodies against antigens of the nucleus, cytoplasm, or membrane cell. Anti-La antibodies are present in 7-45% of SLE patients, usually accompanied by anti-Ro antibodies. Double anti-La and anti-Ro positivity is associated with a milder disease profile, with a lower risk of seizures and nephritis, as well as a higher frequency of arthritis. Studies analyzing the prevalence and clinical characteristics of patients with isolated anti-La+ in the absence of anti-Ro are lacking.
Objectives: To describe the demographic, clinical and serological characteristics and severity indices of anti-Ro-/La+ patients in a retrospective cohort of SLE patients and compare them with the rest of the patients.
Methods: Retrospective cross-sectional study, in which all patients with SLE (> 4 ACR-1997 criteria) registered in the RELESSER registry were included. Sociodemographic, clinical, serological and comorbidities variables were collected, as well as indicators of disease activity and severity. Patients were divided into 4 groups according to the presence of anti-Ro and anti-La: anti-Ro-/La+ group, anti-Ro+/La- group, anti-Ro+/La+ group and anti-Ro-/La- group. The anti-Ro-/La+ group was compared with the other groups.
Results: Out of 3619 SLE patients, 44 (1.2%) had anti-Ro-/La+. The mean (± SD) age was 33.77 (±16.52) years, 88.6% were female, 90.5% were Caucasian and the mean (± SD) disease duration was 135.36 (±88.46) months. The most frequent comorbidities were: smoking 48.8 %, dyslipidaemia 47.7 % and hypertension 31.8 %. 22.13% of patients had anti-Ro+/La-, 18.98% anti-La+/Ro+ and 64.02% anti-La-/Ro-. Photosensitivity and oral ulcers were observed more frequently in anti-Ro-/La+ patients compared to anti-Ro-/La- patients (60.2% vs 52.6% p=0.0471 and 59.1% vs 40.7% p=0.0194 respectively). Arthritis occurred in 77.3% of anti-Ro-/La+ patients, without significant differences with the other groups: 75.3% in anti-Ro+/La- (p=0.8588), 73.9% in anti-Ro+/La+ (p=0.7240) and 75.1% in anti-Ro+/La- (p=0.810). Twenty-five per cent of patients with isolated anti-La had lupus nephritis, with no significant differences compared to the other groups (29.5% in anti-Ro+/La- p=0.6116, 22.9% in Ro+/La+ p=0.7144 and 28.6% in Ro-/La- p=0.7364). 11.4% of anti-Ro-/La+ patients had seizures

vs 4.4% anti-Ro+/La-(p=0.0510), vs 3.3% in anti-Ro+/La+ (p=0.0218) and vs 5.2 % in anti-Ro-/La- (p=0.799). Cognitive impairment was observed in 7% of anti-Ro-/La+ patients vs 2.8% in anti-Ro+/La- (p=0.1315) vs 1.5% in anti-Ro+/la+ (p=0.0370) and vs 3.1% in anti-Ro-/La- (p=0.1492). No differences were observed in other SLE-associated clinical variables, immunological profile, degree of SLE activity or Katz severity index.

Conclusion: The prevalence of anti-La in the absence of anti-Ro in our SLE cohort was 1.2%. This group of patients presented a higher frequency of clinical manifestations such as photosensitivity and oral aphthous ulcers compared to patients with neither anti-Ro nor anti-La. In contrast with previous studies the isolated presence of anti-La is associated with greater neurological involvement in the form of seizures or cognitive impairment compared to the association of anti-Ro and anti-La or the isolated presence of anti-Ro.

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Disclosure of Interests: None Declared.

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AB0595 TESTING A NEW FATIGUE CHECKLIST IN SLE PATIENTS FOR EVERYDAY CLINICAL PRACTICE - AN INTERIM ANALYSIS

Keywords: Patient reported outcomes, Systemic lupus erythematosus, Quality of life

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Background: Fatigue is a difficult subject for both physicians and patients. It is barely addressed during consultations and can therefore burden patient-physician-relations. To improve communication regarding fatigue, we developed a checklist that includes suggestions for evaluating possible causes for fatigue. In this analysis, we describe our study population and report first results 3 and 6 months after using the checklist.

Objectives: The aims of our study are to validate the use of our newly developed fatigue checklist and to demonstrate that addressing fatigue in daily clinical practice and offering possible interventions can improve fatigue.

Methods: We recruited n=110 SLE patients with fatigue from our university hospital-based lupus reference centre in Duesseldorf. Fatigue was measured using the FSS (Fatigue Severity Scale). Our checklist included signs of depression and anxiety using the PHQ-4 (Patient Health Questionnaire), BMI (body mass index), physical activity, anemia, hypothyroidism and vitamin D deficiency. For each applicable cause, we listed possible interventions for free selection by the treating physician, such as replacement therapy (vitamin D, vitamin B12, iron, folic acid, erythropoietin), physical activity programs and psychosomatic consultations that were discussed with the patients. We re-evaluated our patients after 3 (T1) and 6 months (T2).

Results: Baseline characteristics of patients are summarized in Table 1.

Table 1. BMI=body mass index, TSH=thyroidea stimulating hormone, PHQ4=patient health questionnaire (cut-off >3 points), HAQ=health assessment questionnaire, IMET= Index for measuring restrictions on social participation (higher scores point towards more restrictions on social participation), FSS=fatigue severity scale (≥4 points equal severe fatigue)

N = 110

	n (%)	Mean (SD)
Age (years)		49.0 (12.34)
Female sex	99.0 (90.0)	
BMI (kg/m^2)		25.9 (5.55)
Disease duration (years)		19.1 (10.05)
TSH (µIU/ml)		1.5 (1.05)
25-OH-Vitamin D (ng/ml)		39.5 (15.35)
Haemoglobin (g/dl)		13.0 (1.64)
Sports activities		
>4h/week	6.0 (5.5)	
2-4h/week	18.0 (16.4)	
1-2h/week	16.0 (14.5)	
<1h/week	28.0 (25.5)	
No sport	42.0 (38.2)	
Depression (PHQ4 score)		2.3 (1.63)
Anxiety (PHQ4 score)		2.0 (1.71)
Functional status (HAQ score)		0.8 (0.49)
Participation (IMET score)		2.8 (2.31)
Fatigue (FSS score)		5.3 (1.35)

After 3 and 6 months, we re-evaluated 83 patients and saw a significant reduction in fatigue measured by the FSS score (T1: mean difference estimate 0.367 and p-value <0.001; T2: mean difference estimate 0.305; p-value <0.005).

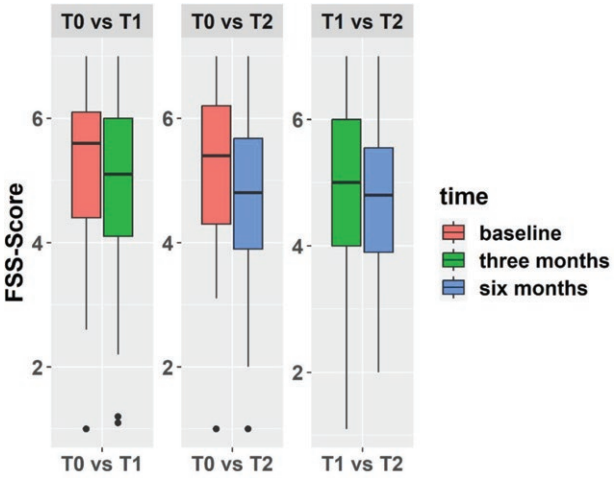


Figure 1. Comparing FSS-Scores from T0, T1 and T2

Conclusion: The preliminary analysis of our study shows for the first time that incorporation of a checklist procedure into the management of patients with fatigue may improve short-term outcome after 3 and 6 months of observation. The improvement of symptoms documented in our study occurred even though the suggested exercise program and psychosomatic counseling sessions were not available for use during the current observation period because of the COVID-19 pandemic. At present, the mechanisms behind the observed effect remain unclear. Our ongoing analysis will clarify whether an additional effect on fatigue will occur after all suggested interventions resulting from the use of the checklist have been executed. Finally, it will demonstrate whether the incorporation of our checklist into routine clinical practice is capable to reduce fatigue over a prolonged time period.

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AB0596 APPLICABILITY OF THE ACR-1997, SLICC-2012, AND EULAR/ACR2019 CLASSIFICATION CRITERIA IN ADULT-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS AND CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Diagnostic tests, Systemic lupus erythematosus

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Background: Over the past few decades, several classification criteria have been proposed for systemic lupus erythematosus (SLE), including the American College of Rheumatology (ACR)-1997, Systemic Lupus International Collaborating Clinics (SLICC)-2012, and European Alliance of Associations for Rheumatology (EULAR)/ACR-2019. The sensitivity and specificity of these classification criteria are inconsistent for the various races of SLE patients [1-3]. Patients with SLE who are younger than 18 year old are called childhood-onset SLE (c-SLE), which differ from adult-onset SLE (a-SLE) in several ways. The applicability of classification criteria for c-SLE of different races were also inconsistent [4-6]. Now, there is a lack of data to verify the applicability of classification criteria in a-SLE or c-SLE in northern China.

Objectives: This study is to verify the applicability of classification criteria in a-SLE and c-SLE in northern China, and explore the most applicable disease evaluation standards.

Methods: 81 c-SLE vs 59 pediatric controls, 80 a-SLE vs 76 adult controls were included in the study. All the participants are Chinese descent living in northern China. The control groups were diagnosed with other rheumatic diseases. The diagnosis of these patients was determined by two or more rheumatologists. We reviewed the clinical manifestations and laboratory tests of these patients with respect to three classification criteria.

Results: The sensitivity of EULAR/ACR-2019 and SLICC-2012 was higher than that of ACR-1997 in a-SLE group, but there was no significant difference in the specificity, with AUCs of EULAR/ACR-2019 (0.863), SLICC-2012 (0.895), and ACR-1997 (0.865). In c-SLE group, the sensitivity of SLICC-2012 was higher than that of ACR-1997, and the specificity was not significantly different, with AUCs of EULAR/ACR-2019 (0.94), SLICC-2012 (0.945), and ACR-1997 (0.899). Increasing the threshold of EULAR/ACR-2019 from 10 to 11 can improve the specificity and accuracy for a-SLE, while from 10 to 14 can improve those for c-SLE.
Conclusion: EULAR/ACR-2019 and SLICC-2012 are the most appropriate classification criteria for a-SLE, and SLICC-2012 is more applicable for c-SLE from northern China. Adjusting the threshold of EULAR/ACR-2019 can improve the specificity and accuracy for a-SLE and c-SLE.
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AB0597

CLINICAL SIGNIFICANCE OF ANTI-RHEUMATOID ARTHRITIS 33 ANTIBODY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Autoantibodies, Diagnostic tests, Clinical trials

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Background: Evidence initially showed that anti-rheumatoid arthritis (RA) 33 antibodies were highly specific for the diagnosis of RA [1]. Later studies reported that anti-RA33 was present in various connective tissue diseases (CTDs) [2]. However, the clinical significance of anti-RA33 antibodies in CTDs is still obscure.
Objectives: To explore the clinical significance and diagnostic value of anti-RA33 antibodies in CTDs, especially systemic lupus erythematosus (SLE).
Methods: A total of 565 patients with positive anti-nuclear antibodies who had been tested for anti-RA33 antibodies were included in the study. These patients were classified into RA33-positive and RA33-negative groups according to the anti-RA33 results. The association between anti-RA33 and the clinical features of CTDs was examined. Additionally, receiver operating characteristic (ROC) analysis was performed to explore the diagnostic value of anti-RA33 antibodies in SLE and SLE-related organ involvement.
Results: SLE was the most common disease in CTD patients positive for anti-RA33 (48.8%). Compared with the RA33-negative group, the proportion of patients with SLE was significantly higher in the RA33-positive group (64.3% vs. 47.1%, p=0.0164). Compared with those negative for anti-RA33, CTD patients positive for anti-RA33 had significantly higher percentages of SLE-associated antibodies (**Figure 1**). Higher proportions of SLE patients with a high disease activity (41.7% vs. 24.7%) as well as lower levels of serum complement components (50.0% vs. 27.7%) were observed in the RA33-positive group (Both p<0.05) (**Table 1**). Furthermore, CTD patients with positive anti-RA33 were more likely to suffer from mucocutaneous (46.4% vs. 33.2%, p=0.0361) and haematological involvement (51.8% vs. 35.6%, p=0.0200) as well as interstitial lung disease (25.0% vs. 11.8%, p=0.0108). ROC analysis revealed an area under the curve value of 0.634 (95% CI: 0.587 to 0.681) for anti-RA33 in the diagnosis of SLE, with a specificity and sensitivity of 92.9% and 13.5%, respectively.
Conclusion: This study reveals a significant association between anti-RA33 and the clinical features of CTDs, especially SLE, indicating a potential clinical significance of anti-RA33 in the management of SLE.
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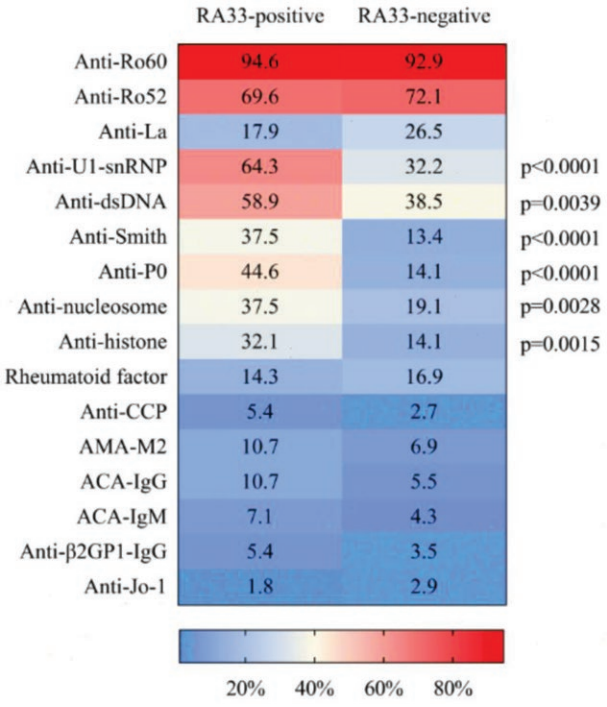


Figure 1. Association between anti-RA33 and coexistent autoantibodiesAbbreviations: anti-RA33, anti-rheumatoid arthritis 33; anti-U1-snRNP, anti-U1 nuclear ribonucleoproteins; anti-dsDNA, anti-double-stranded DNA; anti-P0, anti-ribosomal P protein; anti-CCP, anti-cyclic citrullinated peptide; AMA-M2, anti-mitochondrial antibody M2 subtype; ACA, anti-cardiolipin antibody; anti-β2GP1-IgG, anti-beta 2 glycoprotein 1 antibody.

Table 1. Laboratory characteristics of patients with CTDs

Parameters	RA33-positive (n=56)	RA33-negative (n=491)	p Value
IgG>18 g/L	32(57.1)	161(32.8)	0.0006
IgM>2.5 g/L	6(10.7)	41(8.4)	0.6122
C3<0.80 g/L	28(50.0)	136(27.7)	0.0011
C4<0.15g/L	29(51.8)	173(35.2)	0.0190
CRP>5mg/L	19(33.9)	149(30.4)	0.6467
ESR>20mm/h	40(71.4)	261(53.2)	0.0104
ALB<35g/L	20(35.7)	156(31.8)	0.5488
WBC<4×10^9/L	16(28.6)	111(22.6)	0.3188
PLT<100×10^9/L	7(12.5)	35(7.1)	0.1795
Hb<110g/L(female) or <120g/L(male)	21(37.5)	122(24.9)	0.0531

Abbreviations: anti-RA33, anti-rheumatoid arthritis 33; IgG, immunoglobulin G; IgM, immunoglobulin M; C3, complement 3; C4, complement 4; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ALB, serum albumin; WBC, white blood cell; PLT, platelet; Hb, hemoglobin.

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AB0598

SYSTEMIC LUPUS ERYTHEMATOSUS WITH CEREBRAL HEMORRHAGE DUE TO AUTOIMMUNE ACQUIRED COAGULATION FXIII/13 FACTOR DEFICIENCY: A CASE STUDY AND LITERATURE REVIEW

Keywords: Comorbidities, Systemic lupus erythematosus

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Background: Autoimmune acquired coagulation FXIII/13 factor deficiency (AiF13D) is a rare bleeding disorder characterized by the formation of autoantibody to F13. The treatment of AiF13D requires immunosuppressive (IS) therapy in addition to hemostatic therapy. Japanese guidance recommends high-dose glucocorticoid (GC) as initial therapy while cyclophosphamide (CPA), rituximab (RIT), and ciclosporin (CYA) are administered in refractory cases. Ichinose reported that 16 of 93 (17%) AiF13D patients had autoimmune diseases (AIDs) such as systemic lupus erythematosus (SLE) [1]. The guidance recommends that IS therapy for patients with underlying AIDs should be selected based on treatment guidelines for AIDs; however, recommendations for the choice of IS drugs are unavailable.
Objectives: To report the case of our patient and to analyze the reported cases of SLE complicated AiF13D.
Methods: We searched PubMed, Google Scholar, and Ichushi Web for articles or abstracts written in English and Japanese using the following terms: [acquired FXIII/13 factor deficiency or inhibitors] and SLE.
Results: A 24-year-old woman from Southeast Asia presented to the emergency department with headache and nausea; a hematoma was noted in the right temporal lobe on head CT. Her PT, APTT, platelet count, and bleeding time were normal. She developed impaired consciousness and underwent an emergency craniotomy to remove the hematoma. During surgery, no abnormal blood vessels were noted in the brain, and the hematoma was removed. However, recurrent hemorrhages occurred on days 2 and 13 after hospitalization, and she underwent reoperation. On day 18, F13 activity was found to be less than 3%, and an F13 preparation (Fibrogamin P) was administered. A positive cross-mixing test with normal plasma was positive for the F13 inhibitor, and a diagnosis of AiF13D was made [2]. In addition, she was diagnosed with SLE based on positive antinuclear and anti-dsDNA antibodies (Ab), hypocomplementemia, and lymphopenia. PSL 50 mg (1mg/kg/day) was prescribed. Owing to the local infection after cranioplasty, no IS drugs were used. hydroxychloroquine (HCQ) and belimumab were added, while tapering PSL. During 1 year period, anti-dsDNA Ab decreased and F13 activity remained above 40% without administering Fibrogamin P (Figure 1). The reported 11 cases of SLE complicated AiF13D and this case are summarized in the Table 1. IS therapy included CPA, CPA, and RIT besides GC; belimumab was administered only in our case.
Conclusion: The prognosis of patients with AiF13D is poor. Even after weaning from acute hemorrhage, long-term IS therapy is often necessary and death by infection is common. Based on our experience, we suggest belimumab as a therapy option for SLE complicated AiF13D.
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Table 1. Reported cases of SLE complicated AiF13D

	Age (Years)	Sex	Bleeding sites	Inhibitor /F13 %	Diagnosis of SLE	Immunosuppressive treatment	Out-come	Year
1	30	F	SC , IM	+/1%	10y prior	PSL60mg/day, plasmapheresis	Death	1996
2	22	F	ICH	+/NR	NR	CPA	PR	2002
3	28	F	IM	+/<1%	prior	GC, CPA, plasmapheresis, RIT	CR	2009
4	31	F	SC , IM	+/<1%	6y prior	PSL, IVCY, CYA	PR	2011
5	40	F	ICH	NR/<1%	9y prior	HCQ, IVCY	PR	2013
6	70	M	SC , IM	+/<4%	Same time	PSL0.8mg/kg/day, mPSL-P, RIT,	CR	2014
7	17	F	SC , IM	+/<1%	prior	PSL, IVIG, plasmapheresis,	PR	2017
8	52	M	IM	+/ NR	10y prior	mycophenolate mofetil	Death	2017
9	43	F	SDH	+/NR	Same time	PSL, mPSL-P, HCQ	CR	2021
10	41	F	SC , IM	+/0%	NR	GC, mPSL-P, CPA , RIT	CR	2021
11	85	F	SC , IM	+/0%	NR	GC, CPA	CR	2021
12	24	F	ICH	+/<3%	Same time	PSL50mg/day, HCQ, belimumab	PR	Our case

Intravenous high-dose immunoglobulin therapy , IVIG; intravenous cyclophosphamide , IVCY; mPSL-P, methylprednisolone pulse; rituximab, RIT; ICH: intracranial hematoma, SC, subcutaneous, IM, intramuscular; SDH, subdural hemorrhage; CR, complete remission; PR, partial remission; NR, Not Reported

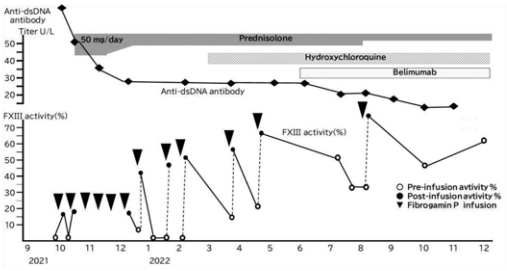


Figure 1. Anti-dsDNA antibody and F13 activity after hospitalization

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AB0599 CLINICAL AND SEROLOGICAL CHARACTERISTICS OF SERONEGATIVE PRIMARY SJÖGREN'S SYNDROME PATIENTS

Keywords: Sjögren syndrome

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Background: Sjögren's syndrome (SS) is accompanied by a number of autoantibodies as a result of B cell aberrant activation. The clinical manifestations, laboratory findings and evolution in seronegativity of a pSS patient changes compared to a seropositive pSS patient.
Objectives: This study compared the clinical and serological characteristics of seronegative and seropositive primary Sjögren syndrome (pSS) patients and the differences in terms of treatment recommended during the follow-up period.
Methods: We performed a retrospective study in a single center, with 131 patients (128 women and 3 men) diagnosed with pSS. Clinical examinations, complete blood count, inflammatory and immunological parameters were determined at the initial visit. The patients were divided into two groups through the presence or absence of pathology-specific antibodies.
Results: Nineteen of the 131 pSS patients (14.5%) were triple seronegative for ANA, anti-Ro, and anti-La autoantibodies. pSS patients with the specific antibodies absence performed accessory salivary gland biopsy and based on focus score they were diagnosed seronegative. No significant statistical differences were observed for age, sex distribution, disease activity scores and the administrated treatment, between the two groups. In terms of laboratory findings, only total proteins, RF and IgG were statistically lower in seronegative pSS patients ($p < 0.05$). While from glandular and extraglandular manifestations, singular xerostomia revealed a statistically significant between the two groups of pSS patients ($p < 0.001$). Cellular ratio, NLR was positively correlated with ESSDAI score and MLR, and negatively correlated with PLR, ESR, total proteins, IgG, C3 and C4, in seronegative pSS patients ($p < 0.05$).
Conclusion: The extraglandular manifestations and the administrated treatment, were similar for the two groups of pSS patients, while only the glandular manifestation, xerostomia, has a statistically significant difference. The hematological parameter, NLR, was statistically correlated with disease activity score and immunological markers in triple seronegative pSS patients.
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AB0600 THE FOLLOW-UP OF PSS PATIENTS WITH PERIPHERAL NEUROLOGIC INVOLVEMENT IN A TERTIARY CENTER

Keywords: Sjögren syndrome

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Background: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease mainly affecting exocrine glands. Extraglandular manifestations play a major role in the long-term prognosis of the disease, and neurological manifestations seem common in pSS. The early detection of haematological and immunological parameters might improve the disease evolution of patients.
Objectives: The study aimed to evaluate the predictive potential of clinical, haematological and immunological elements for the development of neurologic manifestations in pSS patients, followed for 12 months.
Methods: We performed a retrospective study in a single center, with a total of 265 patients (131 pSS patients and 134 healthy controls). Clinical examinations, complete blood count, inflammatory and immunological parameters were registered at baseline, 6 months and 12 months, for 131 pSS patients.
Results: In pSS patients, cellular count, complement fractions, and Vitamin B12 values were significantly decreased compared to healthy subjects ($p < 0.001$), while, cellular ratio- NLR, PLR, immunological and inflammatory parameters were significantly increased ($p < 0.001$) in the pSS patients. Likewise, the comparison at baseline and at every 6 months, of cellular ratios, total proteins, and gammaglobulins and disease scores revealed exponentially increased values, in pSS patients with PN. The occurrence of PN was positively correlated with neutrophils and platelets ($p < 0.05$), and negatively correlated with lymphocytes ($p < 0.05$). NLR and PLR also revealed significant positive correlations with the emergence of PN in pSS ($p < 0.05$), while for total proteins, and Vitamin B12 the correlation was negative ($p < 0.05$). The multivariate analysis confirmed the independent predictive character for PN emergence in pSS for NLR (CI95% 0.034 to 0.254, $p < 0.010$), gammaglobulins (CI95% -0.409 to -0.114, $p < 0.001$) and vitamin B12 (CI95% -0.001 to -0.001, $p < 0.001$).
Conclusion: High values for hematologic and immunological parameters were identified at baseline, while their persistent modifications during the follow-up period were observed in pSS patients with PN. NLR, gammaglobulins and vitamin B12, parameters that could become predictors for the early detection of patients at risk for the development of PN.

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AB0601 **THE MENTAL HEALTH IMPACT OF SEXUAL DYSFUNCTION IN SJÖGREN'S DISEASE: A SOCIAL MEDIA APPROACH TO REAL-WORLD EVIDENCE**

Keywords: Sjögren syndrome, Mental health, Real-world evidence

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Background: To obtain a comprehensive understanding of the needs of individuals in a particular community, it is essential to actively listen to and interpret the patient experience. A proprietary artificial intelligence (AI) analytics engine was applied to social media conversations from an online community for those living with Sjögren's disease (SjD). Sjögren's disease is an autoimmune disease characterized by inflammation of exocrine glands, most often presenting with dryness of the eyes and mouth (sicca). Some women with SjD also report vaginal dryness and discomfort [1] lthough individuals with SjD have an increased risk for poor mental health outcomes (e.g., anxiety, depression), the unique role of vaginal dryness and the resulting mental health impact are not well understood.
Objectives: The objective of the current study was to identify specific mental health impacts associated with vaginal dryness in SjD. We also aimed to explore common topics shared by community members discussing these symptoms to understand their impact on daily living.
Methods: Data included the public subreddit r/sjogrens, which contained 3779 users and 41,406 posts/comments from October 2012 to March 2022. The proprietary AI engine used for analysis leverages natural language processing techniques to analyze text-based social media data sources. First, the engine used entity recognition to identify the most frequent clinical findings mentioned across all posts/comments. Anxiety and depression were among the most frequently mentioned mental health symptoms in conversations. The engine then extracted the most frequent dryness-related symptoms from the data, which included dry eyes, mouth, throat, and vagina. We then fit 2 logistic regression models where dryness mentions (e.g., 'dry eyes', 'vaginal dryness') predicted mentions of 'anxiety' (model 1) or 'depression' (model 2). For our exploratory analysis, we used a guided topic modeling approach to extract conversations about vaginal dryness. This involved providing a list of seed terms (e.g., 'vaginal dryness', 'vaginal pain') around which the model could converge in identifying word clusters.
Results: In total, topic modeling revealed 563 posts/comments from 345 users regarding vaginal dryness. "Vaginal dryness" was a significant predictor ($P < .001$) in both regression models, with adjusted odds ratios between 2.2 and 2.8 (95% CI, 1.9-4.2), suggesting that users mentioning vaginal dryness are 2 to 3 times more likely to mention a negative mental health outcome. Our guided topic modeling approach yielded 3 subtopics within the primary vaginal dryness topic. These included conversational topics about 'sexual discomfort', 'lubrication', and 'marital impacts' across 141 users.
Conclusion: These findings suggest that vaginal dryness and sexual dysfunction in SjD are prevalent and associated with specific negative mental health symptoms. Potential daily impacts were illuminated when topic modeling showed conversations centered on physical pain during sex (i.e., dyspareunia) and adverse impacts on marriage/relationships. This social listening approach also revealed management techniques (e.g., lubrication) for individuals experiencing sexual discomfort. Interrogating social media conversations can be invaluable to elucidating patient-reported mental health challenges in rare diseases. It remains unknown how these conversational references to negative mental health symptoms directly translate to specific mental health diagnoses (e.g., anxiety disorder) or treatment challenges in patients with SjD. Future work should comprehensively explore these symptoms so clinicians, caregivers, and patients can better understand and manage mental health in the context of chronic disease.

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Novartis, Monica Converse Grant/research support from: Our clients are pharmaceutical and biotechnology companies including, but not limited to Horizon Therapeutics, Chiesi Global Rare Disease, Novartis, Harmony Biosciences, and Avadel. TREND Community: employee, Kristina Davidson Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Brian LaMoreaux Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Anthony Amatucci Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Jessica Massengale Grant/research support from: Our clients are pharmaceutical and biotechnology companies including, but not limited to Horizon Therapeutics, Chiesi Global Rare Disease, Novartis, Harmony Biosciences, and Avadel. TREND Community: employee, Julia Taylor Shareholder of: Horizon Therapeutics, Employee of: Horizon Therapeutics, Wei Li Grant/research support from: Our clients are pharmaceutical and biotechnology companies including, but not limited to Horizon Therapeutics, Chiesi Global Rare Disease, Novartis, Harmony Biosciences, and Avadel. TREND Community: employee, Christopher DeFelice Grant/research support from: Our clients are pharmaceutical and biotechnology companies including, but not limited to Horizon Therapeutics, Chiesi Global Rare Disease, Novartis, Harmony Biosciences, and Avadel. TREND Community: Owner., Maria Picone Grant/research support from: Our clients are pharmaceutical and biotechnology companies including, but not limited to Horizon Therapeutics, Chiesi Global Rare Disease, Novartis, Harmony Biosciences, and Avadel. TREND Community: Owner., E. Robert Wassman Grant/research support from: Our clients are pharmaceutical and biotechnology companies including, but not limited to Horizon Therapeutics, Chiesi Global Rare Disease, Novartis, Harmony Biosciences, and Avadel. TREND Community: employee.

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AB0602 SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN ISRAEL: GENDER DIFFERENCES IN MANIFESTATIONS, MANAGEMENT AND COMORBIDITIES

Keywords: Descriptive Studies, Systemic lupus erythematosus, Epidemiology

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Background: Prevalence, incidence, demographic and clinical characteristics of SLE are affected by race, ethnicity and socioeconomic status. The epidemiology of SLE in Israel is not well defined.
Objectives: We aimed to assess the prevalence of SLE and to describe the demographic and clinical characteristics of SLE patients.
Methods: A retrospective study using the computerized database of Maccabi Healthcare Services (MHS), a large health maintenance organization. Prevalent SLE patients on Dec 31 2020 were defined by: ICD-9 code 710.0 (≥2 diagnoses by a rheumatologist/immunologist and/or/≥3 diagnoses by a primary care physician/pediatrician and/or ≥2 diagnoses from a hospital); ≥1 a positive antinuclear antibody (ANA) test; ≥1 dispensed hydroxychloroquine (HCQ) prescription. All SLE patients were ≥10 years-old when first diagnosed; first diagnosed before Dec 31 2018; MHS members for ≥12 months before and ≥24 months after the first diagnosis of SLE. Patients diagnosed with dermatomyositis and/or systemic sclerosis were excluded. SLE patients were matched to controls from the general population of MHS members for age, sex and socio-economic status at a ratio of 1:5.
Results: We identified 1073 eligible SLE patients (prevalence rate of 55.6 per 100,000) and 5365 controls. The mean age on Dec 31 2020 was 50.7 (±14.9) and 942 SLE patients (87.8%) were female. Mean age at diagnosis was 37.2 (± 14.4). The prevalence of SLE disease manifestations is shown in Figure 1A. Since 2015 over 90% of SLE patients had ≥1 dispensed HCQ within 12 months of diagnosis, compared to only 50-70% among those diagnosed before 2015. In 2020 only 67.5% of the patients were still treated with HCQ, 24% were not taking any SLE medication, and 3.8% were treated with systemic glucocorticosteroids (GCs) alone. GCs were prescribed at least once for 74.8% of all patients, and for 30.8% in 2020. The median cumulative prednisone dose per disease year was 283 mg (IQR 0-1297.1), and was higher for males than females (630 mg [IQR 45-2028], 251.7 mg [IQR, 0-1183], respectively, P = 0.001). Compared to females, male SLE patients had a significantly higher prevalence of comorbidities (Figure 1B). Despite a similar prevalence of osteoporosis (OP) (P=0.828), use of OP medications was lower among men (M-16.2%, F-32.3%, P =0.046). Cardiovascular comorbidity and osteoporosis (OP) were more prevalent in SLE patients compared to controls (6.3% vs. 2.9%, respectively, P ≤0.001; (29.8% vs. 11.2%, respectively, P ≤0.001).
Conclusion: The prevalence of SLE in MHS in this study was found to be 1:1790. Prescription of HCQ within the first year after diagnosis has increased since 2015, however HCQ uptake decreased in the years following diagnosis, possibly due to waning compliance. GC cumulative doses were generally low, although it was three times higher in male than in female patients. Cardiovascular comorbidity and OP were more prevalent in SLE patients than in the general population, and more prevalent in male SLE patients, who usually bear a worse prognosis. Moreover, male SLE patients may be undertreated for comorbidities as manifested by higher GC doses and less OP treatment.

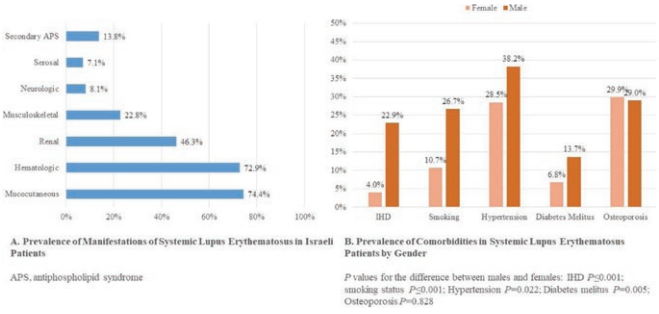


Figure 1.

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AB0603 WORKING TOWARDS A CORE MINIMAL DATASET FOR SYSTEMIC LUPUS ERYTHEMATOSUS STUDIES

Keywords: Clinical trials, Systemic lupus erythematosus

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Background: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease and its heterogeneity means that many cohorts and clinical trials do not collect the same data, making comparative studies difficult.
Objectives: We aimed to ascertain what data is commonly collected in SLE registries/trials. Our ultimate goal is to generate a core minimal dataset for future SLE studies.#8232;
Methods: We designed and distributed a questionnaire to members of the Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) as well as additional research active centres in China. Our survey included 26 questions about the types of data that are routinely collected for research. Data collected by ≥ 75% of participating centres was used as a threshold for concordance.#8232;
Results: Eighteen centres; eight from USA/Canada, five from China and five from Europe responded. Table 1 shows the data that ≥ 75% centres collected. Notably, the EULAR/ACR 2019 criteria was collected by 33.3% and even the most commonly collected patient reported outcome (PRO) - the SF36, was only collected by 53.3%. The SLICC/ACR SLE damage index did not reach our threshold (68.4%). Current treatment data collected did include drug name, dose, frequency and start date. Previous treatment reason for cessation was collected only pertaining to antimalarials. Baseline anti-dsDNA (ELISA) and Crithidia were collected by 70.6% and 52.9% respectively and baseline immunoglobulins were measured by 70.6%. Follow-up blood counts and complement C3/4 were collected by ≥ 75% of centres.

Table 1. Data that ≥ 75% centres collected

Sociodemographic	Racial background,Educational attainment,Occupation,Smoking status,Alcohol consumption,Contraception use,Pregnancy history (number of pregnancies, miscarriage, stillbirth and neonatal death)
SLE specific	Date at and age of diagnosis,Disease duration,Family history of SLE,ACR 1997 classification criteria,SLEDAI-2000 disease activity measure
Comorbidity	Diabetes,Hypertension,Bone disease/osteoporosis,Cerebrovascular disease,Ischaemic heart disease,Renal disease,Infection,Malignancy, Cardiovascular risk factors: smoking status, diabetes, hypertension and obesity, Renal data: renal biopsy, BP, serum creatinine, Urine Protein-Creatinine Ratio and estimated GFR
Baseline bloods	FBC,Complement C3/4,ESR,LFTS
Baseline immunology	Anti-cardiolipin antibody,ANA (IIF),ENA,Lupus anticoagulant,Anti-Beta2 glycoprotein
Treatment data	Current:Biologic (Name, Dose, Frequency, Start date),Immunosuppressant (Name, Dose, Frequency, Start date),Antimalarial (Name, Dose, Frequency, Start date),IV/PO Glucocorticoid (Name, Dose, Frequency, Start date),NSAID (Name only) Previous:Biologic (Name only),Immunosuppressant (Name only),PO Glucocorticoid (Name, Dose, Start date, End date),Antimalarial (Name, Start date, End Date, Reason for cessation)

Conclusion: An initial set of commonly collected data was identified. This forms the basis to start to consider a core minimum dataset for SLE. Development and further refinement of this dataset is needed, as will common definitions of each data field to allow widespread use.

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AB0604 IDENTIFYING THE RISK FACTORS AND INCREASING MORTALITY OF PULMONARY ARTERIAL HYPERTENSION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Prognostic factors, Systemic lupus erythematosus, Epidemiology

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Background: Patients with systemic lupus erythematosus (SLE) have a risk of pulmonary arterial hypertension (PAH), which could be fatal.
Objectives: The goal of this study was to identify the risk factors for mortality in patients with PAH.
Methods: Patients with SLE treated at Chang Gung Memorial Hospital were included in this retrospective cohort study. Univariate and multivariate COX regression, as well as Kaplan–Meier survival curve analysis were conducted to investigate risks in SLE patients.
Results: The average age at diagnosis was 40.78 ± 15.92 years. A total of 42 (6.1%) of the 689 patients had PAH. Patients with PAH exhibited shorter follow-up duration, higher disease activities, higher incidence rates of comorbidities patients without PAH. Physicians preferred to use more Cyclophosphamide and less hydroxychloroquine in PAH patients. Cox regression adjusted analysis indicated that PAH (hazard ratio = 2.709, 95% CI = 1.631, 4.499, p <0.001), old age at diagnosis (HR = 1.057, 95% CI = 1.045, 1.070, p < 0.001), high SLEDAI score (HR = 1.074, 95% CI = 1.040, 1.109, p < 0.001), end-stage kidney disease (ESKD) (HR = 2.533, 95% CI = 1.620, 3.961, p < 0.001) and Cyclophosphamide treatment (HR = 1.687, 95% CI = 1.058, 2.689, p < 0.028) were all linked to increased mortality. Moreover, the Kaplan–Meier survival curve analysis revealed that patients with pericarditis had a higher mortality rate (log-rank test, p < 0.001).
Conclusion: A 6.1% proportion of SLE patients have manifestations of PAH. Moreover, SLE patients with PAH have a greater risk of mortality. Therefore, these patients need intense screening and treatment of PAH.

REFERENCES: NIL.

Table. Multivariate Cox regression analysis: adjusted hazard ratio for the risk factors of mortality in SLE patients

Risk factor	Hazard ratio	95% Confidence interval	*p*-value
Male vs. Female	1.329	0.800-2.208	0.272
Age	1.057	1.045-1.070	<0.001*
Pulmonary arterial hypertension	2.709	1.631-4.499	<0.001*
SLEDAI score	1.074	1.040-1.109	<0.001*
Hypertension	0.984	0.661-1.465	0.936
Cardiovascular event	0.534	0.661-1.465	0.044*
End stage renal disease	2.489	1.559-3.973	<0.001*
Hydroxychloroquine	0.704	0.479-1.036	0.075
Cyclophosphamide	1.687	1.058-2.689	0.028*

SLEDAI, systemic lupus erythematosus disease activity index; SD, standard deviation; *, p<0.05.

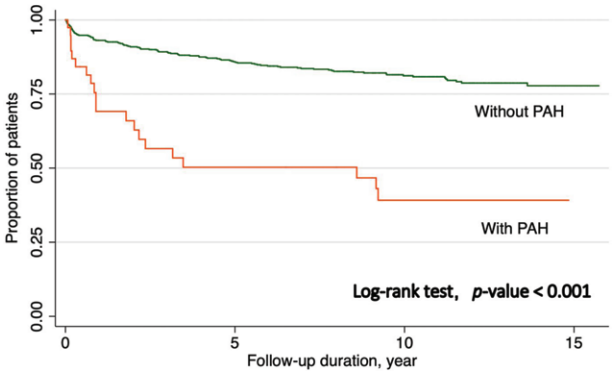


Figure 1. Survival curves of SLE patients with and without PAH. Abbreviations: SLE, systemic lupus erythematosus; PAH, pulmonary arterial hypertension

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AB0605 ALTERNATION OF FUNCTIONAL CONNECTIVITY BETWEEN THE RIGHT INSULAR CORTEX AND RIGHT THALAMUS IS RELEVANT TO FATIGUE IN SYSTEMIC LUPUS ERYTHEMATOSUS: A PRELIMINARY STUDY

Keywords: Imaging, Systemic lupus erythematosus

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Background: Fatigue is one of the most common symptoms in patients with systemic lupus erythematosus (SLE) [1]. Resting-state functional magnetic resonance imaging (rs-fMRI) has emerged as a powerful tool for mapping large-scale networks in the human brain. To explore the neural mechanism of fatigue, several studies evaluated the functional connectivity between brain region of interests using rs-fMRI. However, there are still few reports on patients with SLE.
Objectives: To identify the fatigue-specific functional connectivity in patients with SLE.
Methods: rs-fMRI data were acquired from SLE patients with fatigue and healthy controls (HCs). Functional connectivity of SLE patients and HCs were analyzed and compared by ANCOVA, adjusted for age and sex. On the day of rs-fMRI imaging, SLE Disease Activity Index score with the Safety of Estrogens in SLE National Assessment modification (SELENA-SLEDAI) was assessed, and the Chalder fatigue scale, fatigue assessment questionnaire, was collected. The association among SELENA-SLEDAI, the results of the questionnaire, and functional connectivity was evaluated by correlation analysis.

Results: A total of 10 SLE patients (90% female; median age: 44 years, IQR: 33-61) and 16 HCs (63% female; median age: 41 years, IQR: 34-46) were included. In SLE patients, the median SELENA-SLEDAI was 4 (IQR: 0-10) and the median prednisolone dose was 4 mg/day (IQR: 0-10). SLE patients with fatigue showed increased functional connectivity between the right insular cortex and right thalamus compared to HCs (p=0.03). The functional connectivity between the right insular cortex and right thalamus was significantly correlated with Chalder fatigue scale, an index evaluating fatigue, in patients with SLE (r=0.71, p=0.03), whereas it did not correlated with SELENA-SLEDAI. No correlation was observed between Chalder fatigue scale and SELENA-SLEDAI.

Conclusion: We identified a specific functional connectivity between the right insular cortex and right thalamus which may be associated with fatigue in SLE patients.

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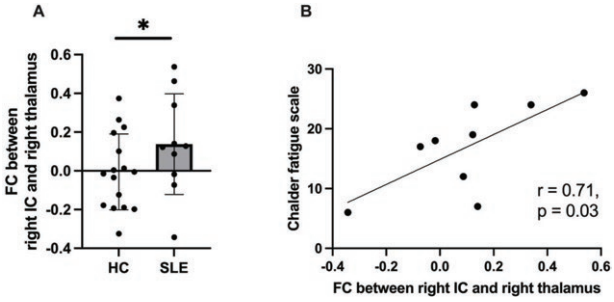


Figure 1. The specific functional connectivity (FC) between the right insular cortex (IC) and right thalamus in SLE patients. (A) FC value between right IC and right thalamus in healthy controls (HCs) and SLE patients. *p<0.05, ANCOVA, adjusted for age and sex. (B) Correlation analysis between the FC and Chalder fatigue scale.

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Disclosure of Interests: None Declared.

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AB0606 NODULAR MUCINOSIS AS INITIAL PRESENTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Skin, Systemic lupus erythematosus

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Background: Cutaneous mucinoses comprise a wide group of disorders characterized by aberrant accumulation of glycosaminoglycans between collagen bundles, that share clinical and histological characteristics, and are classified as primary and secondary [1-3]. Nodular mucinosis associated with lupus is a primary mucinosis first described in 1954 by Gold [4]. It is a distinctive but unusual cutaneous manifestation, with an incidence of 1.5%, that presents as asymptomatic, skin-colored papules or nodules on the trunk and upper extremities [2]. It can occur in patients with discoid lupus, subacute cutaneous lupus or systemic lupus erythematosus (SLE) (2,5,6). The temporal relationship with the development of SLE is variable, since in some cases it precedes it, while in others it occurs later or simultaneously, with clinical variations according to disease activity and antibody levels [6,7].

Objectives: Describe an infrequent cutaneous manifestation of SLE.

Methods: We describe a case of nodular mucinosis as an isolated clinical manifestation of SLE in a middle aged woman, with clinical improvement with methotrexate therapy.

Results: A 67-year-old female patient presented with an 8-month history of multiple skin-colored, asymptomatic nodules in face, trunk and extremities. Some of the nodules had a central depression (Figure 1 A and B). The clinical examination was otherwise unremarkable. Histological analysis of a biopsy specimen showed a circumscribed, non-encapsulated neoformation in the reticular dermis, composed of spindle cells in a storiform pattern, mixed with hyalinized collagen fibers (Figure 1 C). Alcian blue staining confirmed the presence of abundant interstitial, superficial and deep mucin, thus integrating the diagnosis of nodular mucinosis (Figure 1 D). Laboratory tests were positive for antinuclear antibodies (1:1000, coarse speckled pattern), anti-double stranded DNA (47.1 IU/ml), anti-nucleosome, anti-SSA/Ro, anti-RNP, anti-Sm antibodies and lupus anticoagulant, with a lymphocyte count of 3.6 cells/mm3 and hypocomplementemia (C4 of 15 mg/dL). A final diagnosis of nodular mucinosis associated with SLE was made and treatment was started with hydroxychloroquine 200 mg/day and prednisone 1 mg/kg/day. Improvement of skin lesions was observed after the addition of methotrexate 15 mg/weekly.

Conclusion: Our case presents a challenge to the clinician due to the atypical presentation and the absence of other systemic symptoms of SLE, as well as histologic findings similar or almost identical to other cutaneous mucinoses. This case demonstrates the importance of thorough dermatologic examination, high suspicion and directed complementary studies for the correct interdisciplinary approach to this entity.

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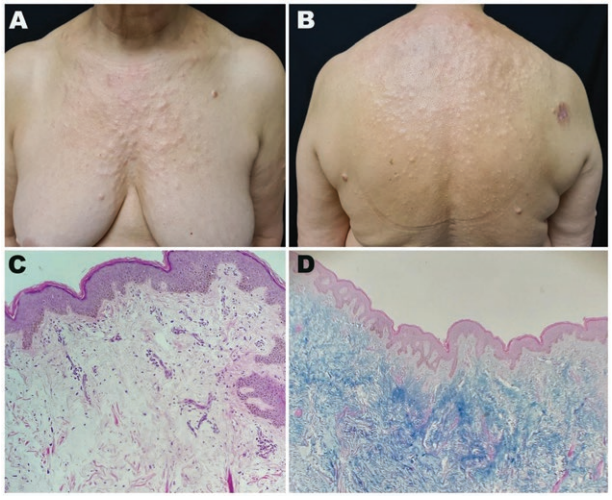


Figure 1. A and B. Multiple skin-colored nodules on the chest and back. **C.** Skin biopsy with pallor in reticular dermis, spindle cells in storiform arrangement and hyalinized collagen fibers (Hematoxylin and eosin. x10). **D.** Abundant interstitial mucin (Alcian blue stain. x10)

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Disclosure of Interests: None Declared.
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AB0607 ANALYSIS OF NAILFOLD CAPILLAROSCOPY FINDINGS AND CLINICAL FEATURES OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND PULMONARY ARTERIAL HYPERTENSION

Keywords: Autoantibodies, Biomarkers, Systemic lupus erythematosus

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Table 1. Demographic and clinical characteristics of study population

	SLE no PAH n=68	SLE PAH n=20	p-value
Age, years (median [IQR])	43.80 [33.48, 52.83]	42.30 [34.32, 49.71]	0.46
Female sex, n (%)	49 (72.1)	20 (100.0)	**0.01**
Disease duration, years (median [IQR])	13.35 [6.35, 19.53]	17.40 [7.33, 20.77]	0.34
Serology, n (%):	13 (19.1)	6 (30.0)	0.46
anti-Sm			
anti-RNP	12 (17.6)	9 (45.0)	**0.02**
anti-Ro	32 (47.1)	10 (50.0)	1
anti-La	5 (7.4)	3 (15.0)	0.54
LAC	13 (19.1)	9 (45.0)	**0.03**
anti-β2GPI IgG/IgM	11 (16.2)	2 (10.5)	1
anti-CL IgG/IgM	14 (20.6)	5 (25.0)	0.75
Clinical, n (%):	25 (36.8)	13 (65.0)	**0.04**
Mucocutaneous			
Serositis	11 (16.2)	7 (35.0)	0.12
Heamatological	38 (55.9)	15 (75.0)	0.20
Musculoskeletal	33 (48.5)	9 (47.4)	1
Neurological	5 (7.4)	5 (25.0)	**0.04**
Lupus nephritis	15 (22.1)	7 (35.0)	0.37
APS diagnosis	9 (13.2)	5 (27.8)	0.15
Raynaud phenomenon	11 (16.2)	12 (60.0)	**<0.001**
SD pattern at NVC, n (%)	7/68 (10.3)	6/9 (66.7)	**<0.001**
Capillary density, cap/mm (sd)	8.86 (1.38)	7.48 (1.09)	**0.004**
Presence of megacapillaries, n (%)	6 (8.8)	6 (66.7)	**<0.001**

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease affecting different organs and causing significant morbidity and mortality. Pulmonary arterial hypertension (PAH) is a rare manifestation of SLE. The prevalence of PAH in patients with SLE varies between 0.5 to 5% [1]. No screening algorithms have been developed in patients with SLE.

In patients with SSc, PAH is characterized by changes in the pulmonary vasculature and endothelial dysfunction. These microvascular changes are also present in periphery, observed with nailfold video-capillaroscopy (NVC) [2]. NVC findings may help to identify patients at a significant high risk of future development of PAH [3].

Objectives: The aim of our work is to analyze the clinical and demographic features and nailfold capillary changes of patients with SLE-related PAH compared to a group of SLE patients without PAH.

Methods: We identified and selected 20 patients with SLE and type I PAH and collected demographic, clinical and laboratory features from 8 rheumatology centers across Europe. We could perform NVC on 9 patients. We selected as controls 68 patients with SLE who underwent cardiopulmonary screening to exclude PAH: we collected demographic, clinical and laboratory features and performed NVC. The presence of SD pattern was assessed as previously described [4]. Patients satisfied the 2019 EULAR/ACR SLE classification criteria. We excluded patients with a diagnosis of mixed tissue disease and overlap syndrome.

Results: Demographic and clinical features of patients with SLE-PAH and SLE controls are shown in Table 1. All patients with SLE-PAH were female, age and disease duration were not different between the 2 groups. LAC+ and anti-RNP+ was more prevalent in patients with SLE-PAH. No differences were observed for anti-Sm, anti-Ro, anti-La and anti-phospholipid antibodies. Of clinical features, skin and CNS involvement were more prevalent in patients with SLE-PAH than in SLE controls. Raynaud's phenomenon was more prevalent in patients with SLE-PAH than in SLE controls. In patients with SLE-PAH we observed a significantly higher prevalence of scleroderma pattern at NVC than in controls: patients with SLE-PAH showed a lower number of capillary density and a higher frequency of megacapillaries. In multivariate analysis, Raynaud phenomenon and anti-RNP are predictors of PAH in patients with SLE. The McFadden's R-squared for the model is 0.30.

Conclusion: Our data show that LAC+, RNP+, Raynaud's, Skin and CNS involvement and a SD pattern at NVC is more prevalent in patients with SLE PAH than in patients with SLE without PAH. Our results point to a generalized microvascular involvement and a hypercoagulation state in patients with SLE PAH. The variables we identified could be used to implement a screening algorithm to identify patients with SLE with a high risk of developing PAH.

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*LC and MS are co-last authors.

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AB0608 CIRCULATING LEVELS OF TNF/TNFR SUPERFAMILY FACTORS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID RELATED SYNDROMES

Keywords: Biomarkers, Anti-phospholipid syndrome, Systemic lupus erythematosus

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Background: B-cell tolerance checkpoint defects are part of the pathomechanism in humoral autoimmune disorders, such as Systemic Lupus Erythematosus (SLE) and Antiphospholipid Syndrome (APS) [1]. In APS, despite the strong evidence of antibody mediated pathogenesis (aPL), specific B cell phenotype abnormalities, and the development of the disease in patients with inborn errors of immunity involving B cell ontogeny, data on the use of therapies directed toward B cells are still lacking and anticoagulation remains the corner stone of management [2].

Objectives: The aim of this study was to measure serum levels of TNF/TNFR superfamily factors which are involved in B-cell homeostasis, looking for differences among diseases.

Methods: Two hundred and twenty-seven patients [75 SLE, 62 SLE+aPL, 36 SLE+APS and 54 primary APS (PAPS)] were enrolled. The dosage was performed by high-sensitivity ELISA. Data are expressed in median (pg/ml or ng/ml for sBCMA) (1^{st}-3^{rd} quartile). P values≤0.05 were considered statistically significant (*).

Results: SLE patients had BAFF serum levels=316.61 (200.96-579.87) vs 359.26 (SLE+aPL), 615.87* (351.22-893) (SLE+APS), 483.31* (328.02-745.5) (PAPS); APRIL=4563.53 (3028.04-6236.94) vs 5080.33, 3142.60, 3424.06* (1278.25-5800.38); sBCMA=11891.15 (8859.21-15630.50) vs 14991.55, 10372.41, 14632.88; sTACI=357.37 (255.05-905.78) vs 450.51, 424.00, 486.43; sCD40L=1355.97 (651.77-2673.81) vs 985.42* (498.92-1746.94), 1023.00, 691.96* (258.19-1329.79); TWEAK=2477.49 (1772.76-3069.27) vs 2454.60, 1683.09* (583-2814.55), 2171.18. In a linear regression model including sBCMA, sTACI, BAFF, sCD40L and TWEAK as predictors, only sBCMA was associated positively with IgG anticardiolipin (p=0.003) and IgG antibeta2-glycoprotein I (p<0.001). In second approach a linear regression model was built, including diagnoses as predictor for respective TNFF member and potential cofounders BMI, gender, CRP, leukocyte levels, hormonal status and prednisone (mg/week). Levels of BAFF, sBCMA and sCD40L were clearly associated with the underlying diagnosis [predicted values for BAFF in SLE, SLE+aPL, SLE+APS, PAPS: 778.18 (p=0.007), 637.40 (p=0.035), 946.16 (p=0.002), 919.63 (p=0.005); for sBCMA: 9068.08 (p=0.004), 10655.50 (p=0.001), 8806.06 (p=0.009), 12131.52 (p=0.001); for sCD40L: 2464.84 (p<0.001), 2025.37 (p=0.001), 2018.68 (p=0.001), 1943.45 (p=0.002)]. TWEAK was not associated with diagnosis or any of the other variables included in this model. APRIL was only associated with the diagnosis of SLE [3017.76 (p=0.016)] and SLE+APL [3531.74 (p=0.007)].

Conclusion: Our study shows an association of TNF-family members with underlying diagnosis, which underscores the contribution of TNF-family members to pathogenesis. On the other hand, TNF-family members are also directly associated to certain anti-phospholipid antibodies with a significant positive association of the plasma cell activation marker sBCMA with IgG anticardiolipin and IgG antibeta2-glycoprotein I antibodies. Taken together, our results reinforcing the possible use of anti-B cell therapies in antiphospholipid related syndromes.

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AB0609

DESIGN OF A PHASE 2, DOUBLE-BLIND, PLACEBO-CONTROLLED, GLOBAL TRIAL OF DEUCRAVACITINIB, AN ORAL, SELECTIVE, ALLOSTERIC TYROSINE KINASE 2 (TYK2) INHIBITOR, IN PATIENTS WITH ACTIVE DISCOID AND/OR SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Clinical trials

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Background: Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis [1,2]. Deucravacitinib demonstrated efficacy across multiple outcome measures, including achievement of ≥50% reduction in Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity score (CLASI-50), in a phase 2 trial in patients with systemic lupus erythematosus (SLE) [3] and is being investigated in two phase 3 trials (NCT05617677; NCT05620407). Patients with discoid and/or subacute cutaneous lupus erythematosus (DLE/SCLE) have elevated expression of Type I interferons (IFN) [4]. Deucravacitinib mediates signaling of Type I IFN, IL-12, and IL-23 and may be an effective treatment for patients with DLE/SCLE [5].
Objectives: Results of this ongoing phase 2 trial (NCT04857034) will characterize the efficacy and safety of deucravacitinib compared with placebo in patients with active DLE/SCLE with or without SLE.
Methods: This phase 2, global, randomized, double-blind, placebo-controlled trial is enrolling adults (aged 18-75) with biopsy-confirmed clinical diagnosis of DLE/SCLE. Key eligibility criteria and study design are depicted below (**Figure 1**). Eligible patients will be randomized (1:1:1) to treatment with placebo or deucravacitinib (dose 1 or 2) for 16 weeks. At week 16, all patients randomized to placebo will be rerandomized (1:1) to treatment with deucravacitinib dose 1 or 2 until week 52. Patients originally randomized to deucravacitinib will continue treatment until week 52. The primary and secondary endpoints are depicted below (**Table 1**). This trial will also assess the safety and tolerability of 2 doses of deucravacitinib, exploratory efficacy endpoints, patient-reported outcomes, and pharmacodynamics.
Results: Planned enrollment is 75 total patients (25 per double-blind treatment group) in 8 countries in North and South America, Europe, and Asia-Pacific regions.
Conclusion: This phase 2 trial will characterize the efficacy, safety, and tolerability of deucravacitinib in patients with active DLE/SCLE.

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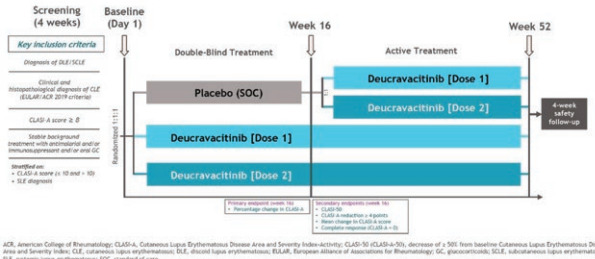
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Table 1. Primary and Secondary Endpoints Assessed at Week 16

Primary Endpoint
• Mean percentage change from baseline in CLASI-A score
Secondary Endpoints
• Percentage of patients who achieve a ≥ 50% reduction in CLASI-A score (CLASI-50) from baseline
• Percentage of patients who achieve a ≥ 4-point improvement in CLASI-A from baseline
• Mean change from baseline in CLASI-A score
• Percentage of patients who achieve a complete response (defined as a CLASI-A score of 0)

CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity.

Figure. Trial Design



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Disclosure of Interests: Victoria P. Werth Consultant of: Celgene, Medimmune, Resolve, Genentech, Idera, Janssen, Lilly, Biogen, Bristol Myers Squibb, Gilead, Amgen, Medscape, Nektar, Incyte, EMD Serono, CSL Behring, Principia, Crisalis, Viela Bio, Argenx, Kirin, AstraZeneca, AbbVie, GSK, Cugene, UCB, Corcept, and Beacon Bioscience, Grant/research support from: Celgene, Janssen, Biogen, Gilead, AstraZeneca, Viela, Amgen, and Lupus Research Alliance/BMS, Joseph F. Merola Consultant of: AbbVie, Amgen, Biogen, Bristol Myers Squibb, Dermavant, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB., Jörg Wenzel Consultant of: GSK, Incyte, Spirig, AstraZeneca, Bristol Myers Squibb, Medac, Biogen, Novartis, LEO, Kyowa Kirin, Janssen, Bayer, Merck/Serono, Roche, Pfizer, ArrayBio, and Amgen, Nikolay Delev Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Harini Kothari Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Richard Meier Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Shalabh Singhal Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Malavi Madireddi Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Shimon Korish Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb.
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AB0610

CHARACTERIZATION OF DISEASE SEVERITY AND ORGAN SYSTEM INVOLVEMENT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN SRI LANKA-ESTABLISHING A COUNTRY-WIDE LUPUS COHORT

Keywords: Organ damage, Systemic lupus erythematosus, Geographical differences

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune connective tissue disease with varying degrees of disease severity and organ system involvement. Disease phenotype and severity are shown to be different based on ethnicity [1,2] where Asians have been shown to have a more severe disease phenotype compared to Caucasians [2]. Infections, active SLE and cardiovascular involvement are identified as leading causes of death among Asian patients [3]. However, there is no consensus on whether this represents a more severe disease phenotype or a socioeconomically less fortunate population, owing to lack of contemporary studies in Asian settings. This study aims to explore the disease severity and organ involvement of Asian counterparts while establishing a lupus cohort in the region for follow up and future studies.
Objectives: To assess the disease severity and organ system involvement among patients with SLE in Sri Lanka based on an ongoing national multicentre lupus database.
Methods: This is a multi-centre descriptive follow-up study with plans to establish a national lupus database in Sri Lanka. 258 patients are recruited so far with a clinical diagnosis of SLE at 14 state hospitals which provide specialist rheumatology services across the country. Disease severity is assessed using the British Isles Lupus Assessment Group-2004 (BILAG-2004).
Results: Of 258 patients, 96.5% were females. Mean (SD) age of the sample was 36.1(12.7) years. Majority fulfilled ACR/EULAR 2019 criteria for classification (86.0%). Renal involvement was seen in 42.6% with 25% having active disease at the time of recruitment. Neurological involvement was seen in 18.6%. Percentages of other domain involvement were mucocutaneous 83.7%, musculoskeletal 74.4%, haematological 65.4%, constitutional 61.6%, cardiorespiratory 8.5%, gastrointestinal 2.8% and ophthalmological 1.2%. Nearly 44% had moderate or severe system involvement (BILAG A or B) in at least one organ system at the time of recruitment. Mean SLICC Damage score was 0.9 (0-8). Disease severity was not significantly determined by the fact that whether the classification criteria were met or not (p=0.17)
Conclusion: Disease severity at time of recruitment and the prevalence of major organ system involvement during the course of illness are commoner among the study population. This is in keeping with higher disease severity and organ involvement reported in the limited available studies among Asians when compared with available data for North American and European populations. This study highlights the importance of early detection and treatment with close

surveillance of disease activity among Asian patients and encourages further research on disease behaviour.

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AB0611 A RANDOMISED OPEN-LABEL PILOT STUDY OF PROBIOTICS AS AN ADJUNCTIVE THERAPY FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOUS (SLE)

Keywords: Real-world evidence, Randomized control trial, Systemic lupus erythematosus

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Background: SLE is a complex inflammatory multiorgan disease that leads to multiple comorbidities and mortality. Probiotics were shown to be successful in lowering the pro-inflammatory cytokines in animal SLE models.

Objectives: This study looked at probiotics' effect on disease activity and pro-inflammatory cytokine interleukin-6 (IL-6) among SLE patients.

Methods: We performed a prospective randomised probiotic controlled analysis of those aged 18 years old and above with mild to moderate disease activity (Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score < 13) visiting Hospital Canselor Tuanku Muhriz (HCTM) SLE clinic between December 2021 to February 2022. Patients were prescribed either twice daily probiotics (Lactobacillus spp. and Bifidobacterium spp) to ongoing therapy or maintain ongoing treatment for three months. Baseline and post-treatment Interleukin 6, disease activity score [SLEDAI 2K, Systemic Lupus International Collaborating Clinics American College of Rheumatology (SLICC/ACR) Damage index], and adverse effects following treatment were documented.

Results: There was a 7% reduction of the median (IQR) IL-6 concentration among the probiotic group, 2.28 (4.85)pg/ml at baseline versus 2.12 (2.56) pg/ml at three months; this was not statistically significant (p=0.145). In control group shows increase in level of IL-6 by 48.9% at end of treatment [1.94 (3.59) vs 2.89 (2.83), p = 0.723]. There was a substantial reduction in SLEDAI 2K among the probiotic group by 64.3%, with the mean (SD) baseline of 4.94 (3.09) versus 1.76 (3.15) at three months (p=0.01), while the reduction in the control group were 23.7 %, with the mean(SD) baseline of 4.17 (3.20) versus 3.18 (2.50) at three months (p=0.077). There were no adverse effects noted among the probiotic group.

Conclusion: The use of probiotics reduced clinical disease activity, as demonstrated by the SLEDAI 2K score reduction. The level of IL-6 reduction was insignificant statistically. However, it shows a beneficial effect of probiotics in stabilising IL-6 compared to the control group, which has increased serum IL-6 at three months. The probiotics are relatively safe to consume. These findings warrant further studies with a larger sample size, longer duration, and analysis of multiple cytokines profiles.

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AB0612 THE RELATIONSHIP BETWEEN SYSTEMATIC LUPUS ERYTHEMATOSUS DISEASE ACTIVITY INDEX (SLEDAI) AND HEALTHCARE RESOURCE UTILIZATION AND COSTS IN LUPUS PATIENTS

Keywords: Real-world evidence, Systemic lupus erythematosus

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Background: Standard sources of healthcare resource utilization (HCRU) for systematic lupus erythematosus (SLE) patients lack granular clinical information and longitudinal follow-up. Due to the heterogeneous nature of SLE, in which disease activity fluctuates with time and acute events such as flares and remissions are common, little is known about the relationship between disease activity and HCRU.

Objectives: In this study, we assess the relationship between disease activity and HCRU in patients with SLE.

Methods: We combined data from the longstanding Johns Hopkins Lupus Cohort, where SLE Disease Activity Index (SLEDAI) was collected at minimum every six-months during standardized protocol visits, with health system cost data (Casemix). Patient resource utilization and registry data were included each calendar half-year where at least 1-registry visit and 1-Casemix item was observed. We computed the annual HCRU and cost of care by type of utilization: outpatient (OP), inpatient (IP), emergency room (ER) and pharmaceutical (Rx). We described the impact of disease activity (based on the worst SLEDAI score observed in each period) on utilization and costs using mixed effect generalized linear models where categorized SLEDAI score 0 (no activity), 1-5 (mild), 6-10 (moderate), 11+ (high) is used as a predictor of outcomes, adjusted for patients fixed effects and disease characteristics.

Results: 1,111 patients contributing 5,094 patient years between 2013-2019 were included in our analysis. The average annual cost of care (and SD) by type was $5,337 (12,997), $3,896 (25,297), $215 (1,062), $3,251 (7,721) for OP, IP, ER and Rx. Regressions showed that total costs in 6-month period was 14% higher for mild, 32% higher for moderate and 76% higher for severe relative to SLEDAI score of 0 (no activity), (all p<0.001).

Conclusion: Using detailed clinical data collected via registry, combined with comprehensive utilization and costs, we have described the relationship between disease activity and HCRU over time. These estimates explain the clinical burden of the disease and can inform cost estimates in future studies of treatments that impact SLEDAI score.

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AB0613 ETIOLOGY, OUTCOME AND PREDICTORS OF MORTALITY AMONG SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS PRESENTING TO EMERGENCY DEPARTMENT: A SINGLE CENTRE PROSPECTIVE STUDY

Keywords: Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) patients can present to emergency department (ED) with acute manifestations that require immediate evaluation and initiation of appropriate therapy. The reasons for ED visits could be due to disease activity or various complications arising due to therapy. However, there is paucity of data on the reasons and outcomes of SLE patients who present to ED.
Objectives: To determine the reason, 3 month outcomes and the predictors of mortality among the SLE patients who present to ED.
Methods: Single centre prospective observational study was being performed between July 2021 and December 2022. Patients of SLE fulfilling the SLICC or the 2019 ACR/EULAR classification criteria and aged above 18 years and presenting to ED were included. Written informed consent was obtained from all the subjects. Clinical and laboratory details were noted at the time of presentation to ED. The reasons for ED visits were classified into disease activity or infection or both or non-SLE related. Outcomes of death and disease activity (by SLEDAI2K) at 3 months were noted. The study was approved by the Institute Ethics Committee.
Results: A total of 61 patients were included in the study. Median age was 28 years (IQR: 24-35) and 55 (90.2%) were females. Twenty (32.8%) patients were newly diagnosed with SLE after presentation to ED, and the median duration of illness among previously diagnosed patients was 24 months (IQR: 12-48). Disease activity alone (n=41; 67.2%) was the commonest reason for ED visit followed by disease activity co-existing with infection (n=15; 24.6%) and infections alone (n=5; 8.2%). Among the 56 patients with disease activity at presentation, active disease manifestations were noted in following organs: renal (57.1%), musculoskeletal (53.6%), skin (51.8%), haematological (42.9%), serositis (39.3%), neurological (28.6%), cardiac (26.8%), gastrointestinal (14.3%) and lung (5.4%). Among the 20 patients with infections at presentation, lower respiratory tract infections were the commonest, seen in 7 (35%) patients followed by CNS infections (15%). UTI, skin and soft tissue, ear and sino-nasal and sepsis with un-identified focus were seen in 2 (10%) patients each. Infective colitis and bacterial peritonitis were identified in 1 (5%) patient each. At 3 months of follow up, 21 (34.4%) patients died, with majority (n=18; 85.7%) dying within 1 month of presentation. Deaths were significantly more in patients who presented with both disease activity and infection compared to patients who presented with only disease activity or infection (p=0.0001). Among the remaining 40 patients, 15 (37.5%) were in remission, 13 (32.5%) were in low disease activity and 12 (30%) were in moderate to high disease activity. On multiple regression analysis, presence of hypoxia (p=0.046), serum albumin less than 2.5g/dl (p=0.006) and infection (p=0.001) at presentation predicted mortality at three months (Table 1).
Conclusion: The commonest cause of ED visit by SLE patients is disease activity alone followed by disease activity and co-existing infections. Infections were present at the time of ED admission in one-third of SLE patients. Three month mortality rate was high (34.4%) and presence of hypoxia, low serum albumin and infection at presentation predicted mortality at three months.

Table 1. Multiple regression analysis for prediction of mortality.

Parameter	p value
Gender	0.164
New onset disease	0.646
Hypotension at presentation	0.074
Hypoxia at presentation	**0.046**
Severe anaemia	0.386
Low complements	0.179
Serum creatinine >1.5mg/dl	0.451
Serum albumin <2.5 g/dl	**0.006**
Renal involvement	0.359
Need of haemodialysis at presentation	0.527
Myocarditis	0.112
Diffuse alveolar haemorrhage	0.092
Haematological involvement	0.557
Neurological involvement	0.333
Enteritis	0.119
Serositis	0.721
Infections at presentation	**0.001**

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0614 EFFECT OF COVID-19 INFECTION ON DISEASE FLARES AND HERPES ZOSTER REACTIVATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE-CONTROL STUDY

Keywords: Clinical trials, Systemic lupus erythematosus

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Background: Whether COVID-19 infection worsens SLE activity is uncertain.
Objectives: To study the effect of COVID-19 infection on disease flares and herpes zoster (HZ) reactivation in patients with systemic lupus erythematosus (SLE).
Methods: Patients who fulfilled the ACR or SLICC criteria for SLE and were followed in our rheumatology clinics were retrospectively studied. We identified patients who had documented COVID-19 infection (Omicron and its variants) between February and November 2022 and a group of SLE controls who did not have COVID-19 infection randomly matched for age, sex and the time period of COVID-19 infection in a 1:2 ratio. The primary outcomes of interest were SLE flares (clinical or serological) and the occurrence of HZ infection within 90 days of COVID-19 infection. SLE flares were assessed by the SELENA flare instruments, with modifications (mild/moderate or severe). HZ infection was a clinical diagnosis based on history and physical signs by attending physicians. The rates of SLE flares and HZ reactivation were compared between COVID-infected SLE patients and controls.
Results: 91 SLE patients with COVID-19 infection (age 48.6±14.0 years; 95.6% women; SLE duration 14.2±8.3 years; 53% history of lupus nephritis) and 182 SLE controls not infected by COVID-19 (age 48.7±13.8 years; 95.6% women; SLE duration 15.2±9.0 years) were studied. Eleven of 90 (12.2%) COVID-infected patients had serious manifestations (oxygen requirement, use of mechanical ventilator, lung infiltrates on imaging studies or admission to the intensive care unit). Patients with mild COVID-19 infection were treated symptomatically or oral anti-viral agents whereas those with serious COVID-19 infection was treated with intravenous remdesivir, dexamethasone and/or biologic/targeted agents. One (1.1%) of our patients died and 7(7.7%) patients developed severe complications. Within 90 days of COVID-19 infection, 14 (15.4%) patients developed mild/moderate SLE flares and 2 (2.2%) patients had severe SLE flares. The incidence of SLE flares in COVID-19-infected patients was significantly higher than those without (17.6% vs 5.5%; p=0.001). The changes in anti-dsDNA and complement C3 levels, however, were not significantly different between the two groups. Among COVID-19 infected SLE patients, those with clinical SLE flares had significantly lower C3 values (p=0.004) but non-significantly higher anti-dsDNA titer (p=0.32) before COVID-19 infection than those without SLE flares. HZ reactivation occurred in 2 patients (2.2%) with COVID-19 infection, which was numerically higher than those not infected by COVID-19 (2 patients, 1.1%; p=0.48). No particular risk factors were identified for HZ reactivation after COVID-19 infection.
Conclusion: In this retrospective case-control study, clinical flares within 90 days were significantly more common in patients infected with COVID-19 than age and gender matched non-infected SLE controls. SLE patients with lower C3 levels were more likely to flare after COVID-19 infection. HZ reactivation occurred at a numerically higher rate after COVID-19 infection in SLE patients than controls. The results from our study support the hypothesis for a viral trigger for disease exacerbation in SLE.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0615 COMPLEX RELATIONSHIPS BETWEEN INFLAMMATORY/TYPE 1 AND TYPE 2 SYMPTOMS IN SYSTEMIC LUPUS ERYTHEMATOSUS AND OTHER RHEUMATIC DISEASES: A LITERATURE REVIEW AND ANALYSIS

Keywords: Patient reported outcomes, Systemic lupus erythematosus, Quality of life

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Background: A better clinical stratification of patient is essential in order to propose personalized therapeutic management for patients with complex autoimmune conditions [1]. Recently, a new stratification has been proposed in Systemic Lupus Erythematous (SLE), which distinguishes different types of symptoms: those directly related to the inflammatory process or type 1 symptoms and type 2 symptoms including fatigue, pain and anxiety-depression [2].
Objectives: Our aim was to characterize the nature of the relation between type 1 symptoms, through disease activity, and type 2 symptoms, including their impact on health-related quality of life (HRQoL), in SLE, as well as in other

rheumatic diseases such as rheumatoid arthritis (RA), primary Sjögren's syndrome (pSS) and systemic sclerosis (SSc).
Methods: A narrative literature review was conducted on disease activity and type 2 symptoms. The appropriate medical subject heading (MESH) term was used for each disease and combined with the MESH terms for fatigue, depression, anxiety, pain and quality of life as well as the term "disease activity" to give the proper search keywords. Articles in English published after 2000 and related to adult patients were located on Medline via Pubmed. The selected articles had to evaluate at least one type 2 symptom and/or HRQoL using a validated scale. Similarly, disease activity had to be assessed by a validated method (usually a clinical score). Within each study, the relationship between disease activity (type 1) and type 2 symptoms or HRQoL was analyzed and classified depending on whether the correlation was present, absent, or weak.
Results: Overall, 287 articles were analysed, corresponding to 157 765 patients. For SLE (n=115 studies including 21 randomized controlled trials), we found that inflammatory activity/type 1 symptoms were mostly uncorrelated with type 2 symptoms and/or HRQoL, with several studies even showing an inverse correlation. No correlation was observed in 67.7% (64.7%), 60% (51.5%), 25% (11.2%), and 60% (53.6%) of studies (patients), and a weak correlation in 17.6% (27.9%), 16.7% (22.9%), 12.5% (61.9%), and 17.5% (34.4%) of studies (patients) for fatigue, anxiety-depression, pain, and HRQoL, respectively. These results were consistent in the other rheumatic diseases studied. Indeed, type 2 symptoms were mostly uncorrelated with disease activity/type 1 symptoms and this seemed even more pronounced for pain. There was no correlation in 45.2-92% (55.9-95%), 56.4-100% (54-100%), 66.7-100% (94-100%), 23-75% (43.4-55%) of studies (patients) and a weak correlation in 0-28.6% (0-34.4%), 0-31.2% (0-43%), 0-33.3% (0-6%), 25-28.6% (16-45%) of studies (patients) for fatigue, anxiety-depression, pain and HROQL respectively.
Conclusion: Type 2 symptoms are poorly correlated with inflammatory activity/type 1 symptoms in SLE as well as in other autoimmune rheumatic diseases. These results have important implications for clinical care and therapeutic evaluation.
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AB0616 GREATER SOCIAL VULNERABILITY ASSOCIATED WITH GREATER GLUCOCORTICOID USE IN PATIENTS WITH SLE

Keywords: Systemic lupus erythematosus

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Background: Patients with SLE experience substantial health disparities. Studying the effect of spatial context on health outcomes has become a focus in health disparities research. The CDC Social Vulnerability Index (SVI) characterizes census tracts by individual dimensions of social vulnerability, which create a cumulative SVI capable of identifying communities where social determinants lead to higher levels of morbidity and mortality.
Objectives: We sought to understand the level of social vulnerability where patients with SLE reside and determine if specific dimensions of social vulnerability were associated with disease activity and prednisone utilization.
Methods: At the Washington University Lupus Clinic, 324 consented subjects who met either ACR or SLICC classification criteria for SLE were enrolled and longitudinally assessed from April 2014 to August 2020. Participant addresses were recorded for each clinic visit. The census tract code was determined for the address listed for each patient's index visit which corresponds to a SVI available in the CDC database. Participants with addresses which did not correspond to a census tract code were excluded. SVI ranges from 0 to 1 with 1 being the most vulnerable; any tract with a SVI greater than the mean of 0.5 can be seen as a socially vulnerable area. Specific dimensions of SVI (socioeconomic status, household composition, race/ethnicity/language, and housing/transportation) are further elaborated in Table 1. Prednisone dosing was organized into four categories (none, >0-7.5 mg, 8-20 mg, >20 mg). SLEDAI-2000 Responder Index-50 (S2K RI-50) assessed SLE disease activity (>4 indicated active SLE). A multinomial logistic regression model analysis was used to determine association.
Results: The number of patients with SVI and prednisone data available was 272 patients. There was no significant correlation between cumulative SVI and disease activity (OR 1.15, 95% CI=0.67-1.99, p=0.6128). When examining prednisone utilization, 175 patients were not prescribed any prednisone at their index visit while 66 were on supraphysiologic doses. Average cumulative SVI was 0.511. Compared to patients with invulnerable cumulative SVI, vulnerable patients were 2.31 times as likely to have higher dose of prednisone (95% CI 1.36-3.92; p=0.0019). Of the specific dimensions, patients vulnerable in terms of socioeconomic status (OR 2.47, 95% CI 1.43-4.27, p=0.0012) and household composition (OR 2.21, 95% CI 1.28-3.83, p=0.0047) were also more likely to have higher doses of prednisone. Patients vulnerable in terms of race/ethnicity/language (OR 1.57, 95% CI 0.92-2.68, p=0.095) and housing/transportation (1.08, 95% CI 0.65-1.80, p=0.7537) were not statistically significantly likely to have higher doses of prednisone.
Conclusion: Patients who live in more socially vulnerable areas are more likely to be prescribed higher doses of prednisone, specifically patients vulnerable in terms of socioeconomic status and household composition. This is worrisome as this likely will contribute to a higher burden of damage. Consistent with other findings, our work highlights that access to social determinants is associated with health inequities.

Table 1.

SVI Dimensions	Census variables included
Socioeconomic status	Income, poverty, employment, education
Household Composition	Age, single parenting, disability
Race/ethnicity/language	Race, ethnicity, English language proficiency
Housing/transportation	Housing structure, crowding, vehicle access

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AB0617 PREDICTION OF MORTALITY USING CLUSTERS BASED ON CLINICAL AND LAB PARAMETERS: DATA FROM 2072 PATIENTS FROM INSPIRE COHORT

Keywords: Systemic lupus erythematosus

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Background: Lupus is a heterogenous diseases which results in significant premature mortality. Most studies have evaluated risk factors for lupus mortality using regression models which considers the phenotype in isolation. Identifying clusters of patients on the other hand may help overcome the limitations of such analyses.
Objectives: The objectives of this study were to describe the causes of mortality and to analyze survival across clusters based on clinical phenotype and autoantibodies in patients of the Indian SLE Inception cohort for Research (INSPIRE)
Methods: Out of all patients, enrolled in the INSPIRE database till March 3st 2022, those who had <10% missing variables in the clustering variables were included in the study. The cause of mortality and duration between the recruitment into the cohort and mortality was calculated. Agglomerative unsupervised hierarchical cluster analysis was performed using 25 variables that define SLE phenotype in clinical practice. The number of clusters were fixed using the elbow and silhouette methods. Survival rates were examined using Cox proportional

hazards models: unadjusted, adjusted for age at disease onset, socio-economic status, steroid pulse, CYC, MMF usage and cluster of the patients.

Results: Indian patients with lupus have significant early mortality and the majority of deaths occurs outside the hospital setting.Out of 2211 patients in the cohort, 2072 were included into the analysis. The median (IQR) age of the patients was 26 (20-33) years and 91.7% were females. There were 288 (13.1%) patients with juvenile onset lupus. The median (range) duration of follow up of the patients was 37 (6-42) months. There were 170 deaths, with only 77 deaths occurring in a health care setting. Death within 6 months of enrollment occured in in 80 (47.1%) patients. Majority (n=87) succumbed to disease activity, 23 to infections, 24 to coexisting disease activity and infection and 21 to other causes. Pneumonia was the leading cause of death (n=24). Pneumococcal infection led to death in 11 patients and SARS-COV2 infection in 7 patients. The hierarchical clustering resulted in 4 clusters and the characteristics of these clusters are represented in a heatmap (Figure-1A,B). The mean (95% confidence interval [95% CI] survival was 39.17 (38.45-39.90), 39.52 (38.71-40.34), 37.73 (36.77-38.70) and 35.80 (34.10-37.49) months (p<0.001) in clusters 1, 2, 3 and 4, respectively with an HR (95% CI) of 2.34 (1.56, 3.49) for cluster 4 with cluster 1 as reference(-Figure 1C). The adjusted model showed an HR (95%CI) for cluster 4 of 2.22 (1.48, 3.22) with an HR(95%CI) of 1.78 (1.29, 2.45) for low socioeconomic status as opposed to a high socioeconomic status (Table 1).

Conclusion: Indian patients with lupus have significant early mortality and the majority of deaths occurs outside the hospital setting. Disease activity as determined by the traditional activity measures may not be sufficient to understand the true magnitude of organ involvement resulting in mortality. Clinically relevant clusters can help clinicians identify those at high risk for mortality with greater accuracy.

Table 1. Univariate and multivariate Cox regression models predicting mortality

		Univariate		Multivariate	
Variables		**Hazard ratio (95% Confidence interval)**	**P value**	**Hazard ratio (95% Confidence interval)**	**P value**
Cluster	1	Reference	-	Reference	-
	2	0.87 (0.57, 1.34)	0.532	0.89 (0.57, 1.38)	0.598
	3	1.22 (0.81, 1.84)	0.337	1.15 (0.76, 1.73)	0.513
	4	2.34 (1.56, 3.49)	<0.001	2.22(1.48, 3.22)	**<0.001**
Socioeconomic status	Lower			1.78 (1.29, 2.45)	**<0.001**
Pulse steroid	Yes			1.6 (0.99, 2.58)	0.051
MMF	Yes			0.71 (0.48, 1.05)	0.083
CYC	Yes			1.42 (0.99, 2.02)	0.052
Proliferative LN	Yes			0.99 (0.62, 1.56)	0.952
Date of birth age				0.99 (0.98, 1.01)	0.657

CYC- cyclophosphamide, MMF- Mycophenolate mofetil

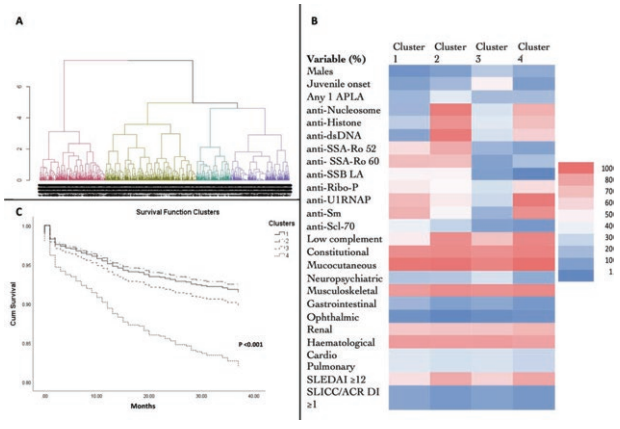


Figure 1. A. Agglomerative clustering dendrogram depicting the formation of four clusters. B.Heatmap depicting distribution of variables used in clustering C. Kaplan-Meier curve showing the survival function across the 4 clusters

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Disclosure of Interests: None Declared.

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AB0618

DELAY TO DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS IMPACT ON CUMULATIVE DAMAGE AND MORTALITY: DATA FROM A MULTIETHNIC LATIN AMERICAN COHORT

Keywords: Autoantibodies, Registries, Systemic lupus erythematosus

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Table 1. Comparison between the two patient groups in relation at the time to SLE diagnosis.

Variable	**Time to SLE Diagnosis**		
	< 6 months (n=716)	**≥ 6 months (n=721)**	**p value**
Age at diagnosis, years (median, IQR)	25.6 (16.2)	30.4 (15.6)	<0.001
Follow-up time, months (median, IQR)	54(44.1)	53(48.6)	0.302
Female, n %	628 (87.7)	662 (91.8)	0.010
Ethnicity, n %	306 (42.7)	339 (47.0)	0.001
Mestizo	116 (16.2)	70 (9.71)	
African Latin Americans	294 (41.1)	312 (43.3)	
Caucasian			
Education level, years, n%	216 (30.2)	237 (32.9)	0.541
0-7 years	329 (45.9)	320 (44.4)	
8-12 years	171 (23.9)	164 (22.7)	
>12 years			
Have medical insurance*[(13)], n%	606 (84.6)	573 (79.5)	0.020
Socioeconomic status, n%	436 (61.2)	437 (60.6)	0.955
Low	204 (28.7)	208 (28.8)	
Middle	72 (10.1)	76 (10.6)	
High			
Clinical manifestations§, n%	376 (52.5)	186 (25.8)	0.900
Malar rash	70 (9.8)	72 (10.0)	0.894
Discoid lupus	327 (45.7)	379 (52.6)	0.009
Photosensitivity	239 (33.4)	226 (31.4)	0.409
Oral ulcers	611 (85.3)	634 (87.9)	0.148
Arthritis/ Arthralgia	124 (17.3)	104 (14.4)	0.133
Pleuritis	92 (12.9)	61 (8.5)	0.007
Pericarditis	39 (5.5)	60 (8.3)	0.031
Psychosis/ seizures	372 (52.0)	403 (55.9)	0.134
Hematological disorder	254 (35.5)	202 (28.0)	0.002
Proteinuria/ cylindruria	403 (56.3)	303 (42.0)	<0.001
Fever	97 (13.6)	67 (9.3)	0.011
Lymphadenopathy	32 (4.5)	52 (7.2)	0.027
Livedo reticularis	125 (17.5)	190 (26.4)	<0.001
Raynaud's phenomenon	21 (2.9)	52 (7.2)	0.002
Sicca syndrome	6 (0.8)	0 (0.0)	0.014
Cardiac tamponade	14 (2.0)	28 (3.9)	0.030
Vascular thrombosis	4 (0.6)	12 (1.7)	0.046
Stroke (ischemic)	24 (3.4)	14 (1.9)	0.096
Pulmonary involvement	9 (1.3)	1 (0.1)	0.011
Peritoneal serositis			
Hypocomplementemia§, n%	487 (68.0)	385 (53.4)	<0.001
Antiphospholipid antibodies§, n%	363 (50.7)	375 (52)	0.795
SLEDAI† at diagnosis, median (RIQ)*[(257)]	12.0 (10.0)	9.0 (9.0)	<0.001
SDI at the last visit‡ ≥ 1	494 (69.0)	484 (67.1)	0.448
Death during follow-up, n%	39 (5.5)	45 (6.2)	0.521

SD (standard deviation); IQR (Interquartile range); § Before SLE diagnosis; † Systemic Lupus Erythematosus Disease Activity Index; ‡ SDI (Systemic Lupus International Collaborating Clinics) Damage Index;*(Missing data)

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Background: Systemic lupus erythematosus (SLE) SLE often mimics the symptoms of other diseases, and the interval between symptom onset and diagnosis remains long in these patients.
Objectives: To examine the variables associated with a delay to diagnosis and their impact in damage accrual and mortality in patients with SLE.
Methods: GLADEL a multi-ethnic, multi-national Latin-American SLE inception cohort was studied. Patients were recruited based on the physicians' diagnosis but 97% fulfilled the ACR criteria. Delay to diagnosis was defined as ≥6 months from the first ACR criterion to SLE diagnosis. Socio-demographic, clinical/laboratory, disease activity, damage and mortality were compared using descriptive statistical tests. Multivariable Cox regression (HR) model with damage accrual and mortality as the end points were performed.
Results: Of the 1437 included in this analysis, the median delay to diagnosis was 5.9 months (Q1-Q3 2.4–16.1) and 721 (50.2%) had ≥6 months delay in SLE diagnosis. Patients with delay in diagnosis were more frequently of female gender, older age at diagnosis, mestizo ethnicity and without medical insurance. The characteristics of patients according to delay in diagnosis are depicted in Table 1. Delay to diagnosis did not impact on disease outcome: damage accrual [HR 1.21 (IC 95% 0.78-1.88; p=0.39)] and mortality [HR 1.30, CI 95% 0.84-2.01; p= 0.24)], after adjusting for age at SLE diagnosis, gender, ethnicity and socioeconomic status.
Conclusion: In the GLADEL cohort, delay to diagnosis was associated to sex, age, thrombosis, sicca syndrome, cutaneous and neurological involvement. Furthermore, delay to diagnosis had no apparent negative impact on disease outcome (damage accrual and mortality). Early referral when there are suspicious clinical manifestations of SLE is crucial to reduce the diagnostic delay.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0619

PREDICTORS FOR FUTURE DEVELOPMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS IN KOREAN SJÖGREN'S SYNDROME PATIENTS

Keywords: Systemic lupus erythematosus, Sjögren syndrome

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Background: Sjögren's syndrome (SS) can occur alone or in combination with other autoimmune diseases. Systemic lupus erythematosus (SLE) is the most common autoimmune disease associated with SS. The prognosis of SS is generally better than that of SLE. However, the onset of SLE in these patients may be one of the factors that increase mortality.
Objectives: This study determined the impact of demographic factors, clinical manifestations, disease activity, and serological tests at baseline on future SLE development in Sjögren's syndrome (SS) patients.
Methods: This retrospective study assessed 1,082 SS patients without other autoimmune diseases at baseline who visited our hospital between January 2012 and March 2021. We analyzed demographic features, extra-glandular manifestations (EGMs), clinical indices, and laboratory values at baseline between the two groups divided per future SLE development (SS/SLE group vs. SS group). The probability and predictors of SLE development in SS patients were estimated using the Kaplan–Meier method and Cox proportional hazards models.
Results: The median follow-up duration was 1083.5 days. Forty-nine patients (4.5%) developed SLE that met the 2012 Systemic Lupus International Collaborating Clinics or 2019 EULAR/ACR classification criteria. The baseline EULAR SS disease activity index (ESSDAI) score was significantly higher in the SS/SLE group (p<0.001). The SS/SLE group had more lymphadenopathy and renal involvement (p=0.015 and p=0.017, respectively). Shorter SS disease duration (<3 years) (hazard ratio [HR]=2.61, p=0.012), high ESSDAI (HR=3.04, p=0.024), leukopenia (HR=2.20, p=0.017), hypocomplementemia (HR=17.40, p<0.0001), and positive for anti-dsDNA (HR=19.93, p<0.0001), anti-ribonucleoprotein (RNP) (HR=2.96, p=0.025), and anti-ribosomal P (HR=2.74, p=0.048) at baseline were SLE development predictors in SS patients.
Conclusion: Shorter disease duration and higher disease activity of SS at baseline may be risk factors for future SLE development. Serologic predictors of SLE development are hypocomplementemia, leukopenia, and positivity for anti-dsDNA, anti-RNP, and anti-ribosomal P antibodies. If the above factors are observed, close monitoring will be necessary during the follow-up period, considering the possibility of future SLE development.
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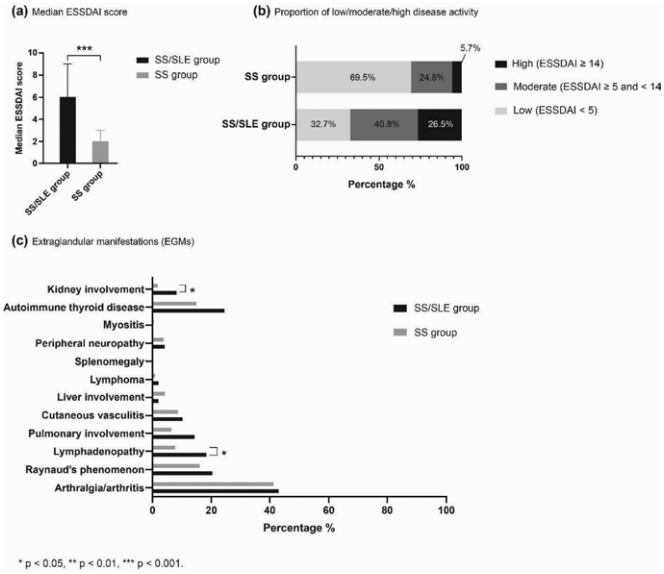


Figure 1. Comparison of disease activity (by ESSDAI score) and extraglandular manifestations (EGMs) at baseline between SS/SLE group and SS group.

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AB0620

IMMUNE THROMBOCYTOPENIC PURPURA AND SUBSEQUENT DEVELOPMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Prognostic factors, Systemic lupus erythematosus

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Background: Immune Thrombocytopenic Purpura (ITP) is an immune-mediated disorder, characterized by isolated thrombocytopenia (<100,000/mm^3). It is part of Systemic Lupus Erythematosus (SLE) classification criteria, and may be one of the first manifestations of the disease, often occurring years before its diagnosis.
Objectives: To assess the incidence of SLE in a cohort of patients with ITP, and to identify predictors for its development.
Methods: Retrospective cohort study. We included patients with ITP treated in a University Hospital between 2000 and 2018, with at least one year of follow-up. Patients with SLE or other secondary causes of ITP were excluded. Demographic, clinical, laboratory and treatment data were recorded. Patients meeting SLE classification criteria (ACR 1997/ SLICC 2012) during the follow-up were identified, and incidence density of SLE was calculated. Patients with ITP were grouped according to the development or non-development of SLE, and comparisons were made. Univariate analysis was performed to identify factors associated with the future development of SLE.
Results: 186 patients were included, 64.5% women, with a median age of 27.2 years (IQR 6.3-63.9). After a follow-up of 1801.4 person/years (py), 10 patients (5.4%) developed SLE, with a median time of 22.9 months (IQR 9.8-60.9) between ITP diagnosis and development of SLE. The incidence density of SLE was 5.6/1000 py (95% CI 2.9-9.9/1000 py). Patients who developed SLE had significantly higher proportion of chronic ITP (80% vs 40.3%; p 0.01), lower proportion of complete response (10% vs 54.6%; p 0.006), and more relapses (60%

Table 1. Baseline characteristics at ITP diagnosis and comparison between groups.

	ITP developing SLE (n= 10)	**ITP non-developing SLE** (n= 176)	p
Age, years, median (IQR)	19.0 (12.4-31.6)	28.3 (5.8-64.5)	0.36
Female gender, n, (%, 95% CI)	9 (90.0, 50.1-98.8)	111 (63.1, 55.6-69.9)	0.08
Follow-up time, years, median (IQR)	6.9 (4.9-10.1)	10.2 (4.6-14.8)	0.49
Rheumatologist evaluation at ITP diagnosis, n (%, 95% CI)	8 (80.0, 43.6-95.4)	23 (13.1, 8.8-18.9)	**<0.001**
ANA positivity, n (%, 95% CI)	10 (100)	35 (30.7, 22.8-39.9)	**<0.001**
Hypocomplementemia, n (%, 95% CI)	6 (60.0, 27.9-85.3)	7 (10.1, 4.8-20.1)	**<0.001**
Lupus anticoagulant, n (%, 95% CI)	4 (40.0, 14.7-71.9)	6 (6.1, 2.7-13.1)	**<0.001**
Polyclonal hypergammaglobulinemia, n (%, 95% CI)	5 (55.6, 23.4-83.6)	14 (11.6, 6.9-18.7)	**<0.001**
Splenomegaly, n (%, 95% CI)	3 (33.3, 10.2-68.8)	17 (12.8, 8.0-19-7)	0.09
Megakaryocytic hyperplasia in bone marrow, n (%, 95% CI)	4 (80.0, 24.9-97.9)	47 (64.4, 52.5-74.7)	0.48
Hemolytic anemia, n (%, 95% CI)	1 (10.0, 1.2-49.9)	1 (0.6, 0.1-3.9)	**0.005**
Leukopenia, n (%, 95% CI)	3 (30.0, 9.3-64.3)	11 (6.3, 3.5-10.9)	**0.006**
Rituximab therapy, n (%, 95% CI)	5 (50.0, 21.2-78.8)	40 (22.7, 17.1-29.6)	**0.05**
Hydroxychloroquine therapy, n (%, 95% CI)	7 (70.0, 35.7-90.7)	4 (2.3, 0.8-5.9)	**<0.001**
Splenectomy, n (%, 95% CI)	2 (20.0, 4.6-56.4)	15 (8.5, 5.2-13.7)	0.22
Duration of ITP treatment, months, median (IQR)	67.5 (40-113)	4 (1-14.5)	**<0.001**
Newly diagnosed ITP (<3 months), n (%, 95% CI)	1 (10.0, 1.2-49.9)	82 (46.6, 39.3-54.1)	**0.02**
Persistent ITP (3-12 months), n (%, 95% CI)	1 (10.0, 1.2-49.9)	23 (13.1, 8.8-18.9)	0.78
Chronic ITP (>12 months), n (%, 95% CI)	8 (80.0, 43.6-95.4)	71 (40.3, 33.3-47.8)	**0.01**

vs 30.6%; p 0.05). The median duration of ITP in SLE patients was significantly longer (67.5 vs 4 months, p<0.001). The presence of ANA (p<0.001), nuclear homogeneous pattern (p<0.001), ANA titres >1/640 (p 0.02), hypocomplementemia (p<0.001), LAC (p<0.001), hypergammaglobulinemia (p<0.001), leukopenia (p 0.006) and hemolytic anemia (p 0.005) were significantly associated with the future development of SLE.

Conclusion: In this cohort of ITP patients, the more refractory course of ITP, as well as the presence of high titre - nuclear homogeneous ANA, hypocomplementemia, LAC, hypergammaglobulinemia and other cytopenias were associated with the subsequent development of SLE.

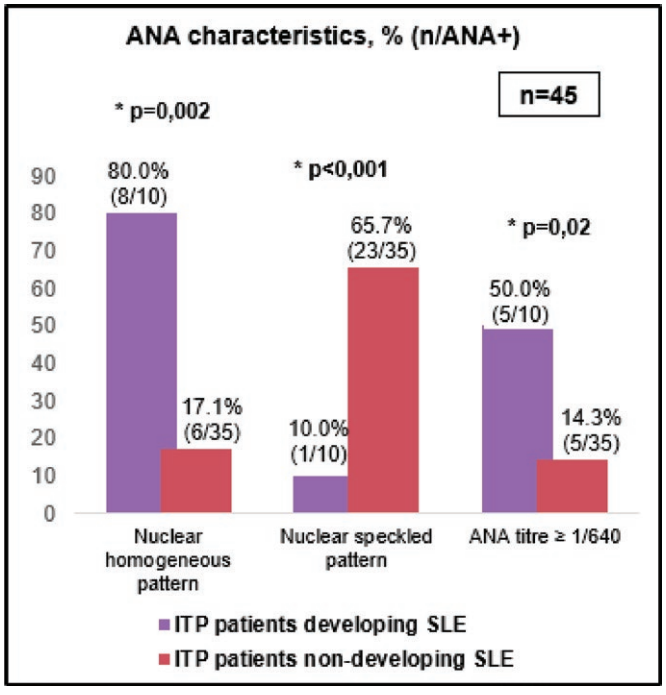


Figure 1. ANA characteristics at ITP diagnosis.

REFERENCES: NIL.

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AB0621

DISEASE ACTIVITY PATTERNS OVER TIME IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: IMPACT ON HEALTH-RELATED QUALITY OF LIFE

Keywords: Patient reported outcomes, Systemic lupus erythematosus, Quality of life

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Background: Health-Related Quality of Life (HRQoL) in patients with autoimmune systemic diseases has a multifactorial origin. In particular, data from the literature show that in patients with Systemic Lupus Erythematosus (SLE) the correlation between HRQoL and disease manifestations is quite controversial.

Objectives: to evaluate the impact of different disease activity patterns on HRQoL and patients' perception of disease activity in a monocentric cohort of patients with SLE.

Methods: a retrospective analysis of prospectively collected data from adult consecutive patients with a diagnosis of SLE, regularly followed at the Rheumatology Unit of Pisa. For each patient, the following data were collected: demographics, disease duration, clinical and laboratory data, SELENA-SLEDAI for disease activity and SLICC-DI for organ damage, comorbidities and ongoing treatment. Three different disease patterns were defined based on disease activity status during the year before enrollment: long quiescent (LQ) if patients were in remission in each visit; chronically active (CA) if they were not in remission in each visit; relapsing-remitting (RR) if patients presented periods of remission interspersed with periods of disease activity. Only patients with at least two visits in the year before enrollment were included. We excluded patients with a major clinical event/hospitalization not SLE-related during the year before enrolment that could influence their health status. At enrollment, each patient completed the following Patient Reported Outcomes (PROs): SF-36, FACIT-F, Lupus Impact Tracker (LIT), SLAQ, Hospital Anxiety and Depression Scale (HADS).

Results: 242 SLE outpatients were enrolled, mainly female (91.7%) and of Caucasian ethnicity (96.7%); mean age 44.2.6 ± 13 years, with a median disease duration of 12 years (IQR 6 – 21). 48.8% had at least one item of organ damage with a median SLICC-DI of 1 (IQR 1-2). Moreover, 15.3% of patients had a concomitant fibromyalgia. At enrollment, median SLEDAI in the entire cohort was 2 (IQR 0-4); the most frequent active disease manifestation was skin involvement (36/242); 12 patients had active arthritis and 11 active renal disease. Almost half of the cohort (51,2%) was on a low dose of glucocorticoids (mean daily dose 4.1 ± 2.9 mg of 6-methylprednisolone); 83.9% were on Hydroxychloroquine and 52.5% on immunosuppressive therapy. We applied the disease pattern definition criteria and we found that the LQ was the most represented pattern in our cohort (63.9% of patients), followed by the RR (22%) and CA (14.1%). No significant

differences in SF-36, HADS, LIT and FACIT results were observed between the 3 groups. Only SLAQ scores resulted significantly higher in the RR group compared with the LQ one (p<0.01) (Table 1).

Conclusion: our study shows that HRQoL in SLE is not significantly influenced by disease course over time, confirming that disease activity does not represent the major determinant of patients' perception of health status. However, we found that patients' self-evaluation of disease activity is affected by the disease pattern over time. Particularly, it seems that alternating periods of disease activity to periods of remission over time may worsen the patient's evaluation of disease status, even more than a mild chronically active disease.

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Table 1. Results of PROs among disease activity pattern groups in the SLE cohort.

	CA	LQ	RR	p value
PCS	44.54 ± 8.7	48.22 ± 10.5	46.7 ± 9.2	p=0.16 * p=0.95 § p=1 +
MCS	43.2 ± 11.9	44.2 ± 12.5	42 ± 10.7	p=1 * p=1 § p=0.7 +
LIT	29 ± 18.7	24.1 ± 20.5	29.7 ± 24.4	p=0.73 * p=1 § p=0.35 +
FACIT	36 ± 11.6	39 ± 9.6	36 ± 11.1	p=1 * p=1 § p=0.12 +
HADS anxiety	7.4 ± 4.5	6.5 ± 3.9	6.7 ± 3.4	p=1 * p=1 § p=1 +
HADS depression	5.7 ± 3.7	5.1 ± 3.6	5.8 ± 3.7	p=1 * p=1 § p=1 +
SLAQ	11 ± 7.9	8.6 ± 6.8	13 ± 9.6	p=0.67 * p=0.73 § **p<0.01** +

*CA vs LQ, §CA vs RR, +LQ vs RR

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.4887

AB0622

LUPUS NEPHRITIS: IS THE KIDNEY BIOPSY CURRENTLY NECESSARY IN THE MANAGEMENT OF LUPUS NEPHRITIS?

Keywords: Systemic lupus erythematosus, Kidneys

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Background: Lupus Nephritis (LN) is an immune-complex mediated glomerulonephritis affecting up to 60% of all SLE patients during the disease course. A kidney biopsy is indicated in SLE patients when proteinuria stably reaches or overcomes the level of 500 mg/24 h or spot urine protein to creatinine ratio (UPCR) >500 mg/g (50 mg/mmol), especially with impaired renal function or active urinary sediment, and is generally recommended to evaluate the inflammatory findings but also to rule out other etiologies of renal involvement and to guide the need of immunosuppressive therapy.

Objectives: To investigate the histopathologic findings in first-time renal biopsies from SLE patients and evaluate the type and occurrence of histopathological findings other than LN as these may lead to a risk of inadequate therapeutic interventions.

Methods: 64 SLE patients who had a first-time onset of renal involvement from 24/11/2020 up to 24/10/2022 and subsequent renal biopsy were included in the study. All patients fulfilled the Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) disease classification criteria (1) for SLE and were biopsied on clinical indication, i.e., proteinuria > 0.5 g/day or active SLE in combination with a rise in plasma creatinine, decrease in glomerular function or new onset proteinuria with concurrent active urine sediment.

Results: In total, 64 patients (female 51 (76%), Male (15 (24%) with first time presentation of renal involvement who had been subject to renal biopsy were included.. The median age at the time of biopsy was 35,34± 11,19 years. For more patient baseline characteristics, see Table 1.Fifty two (81%) had findings consistent with LN according to ISN/RPS classification system [2]. Four patients (6 %) had class I - II, 19 (30%) -class III, 13 (20%) - class IV, 8 (12%) - Class V, 2 (3%) - Class VI, 3 (4%) - Class III ± V, 3 (4% - Class IV ± V. Tvelwe patients (19%) did not have histological changes in accordance with LN. Of these, 3 had thrombotic microangiopathy, 5 had IgA nephropathy, 4 were later found to be ANCA-positive and were re-diagnosed with concomitant ANCA-associated vasculitis. Of the 12 non-LN patients, all had proteinuria > 0.5 g/day, 2 had new-onset low-grade proteinuria and concurrent active urine sediment, 2 had new-onset low-grade proteinuria with concurrent increasing SLE disease activity, and 5 patients had isolated persistent low-grade proteinuria.

Table 1. Baseline characteristics, 64 patients

Age (years) Mean (SD	
SLE duration at biopsy (years); M (IQR)	0.7 (0.4 – 7.3)
Systolic blood pressure (mm Hg); Mean (SD)	127.5 (20.8)
Ethnicity	
Caucasian; n (%)	58 (90%)
Asian; n (%)	6 (10%)
Diagnosis according to ISN/RPS	
Class I-II	4 (6%)
Class III	19 (30%)
Class IV	13 (20%)
Class V	8 (12%)
Class VI	2 (3%)
Class III ± V	3 (4%)
Class IV ± V	3 (4%)
TMA	3 (4%)
Vasculitis	4 (6%)
IgA nephropathy	5 (7%)

Conclusion: We demonstrate that renal histopathology confirmed other causes than LN in a significant proportion (19 %) of SLE patients with signs of renal involvement. Since these patients may need other therapeutic interventions than patients with classic LN, we can conclude that the renal biopsy is important in order to guide the choice of therapeutics.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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SLE, Sjön's and APS - clinical aspects (other than treatment)

AB0623 RELATIONSHIP BETWEEN NUMBER OF DMARS USED AND BODY COMPOSITION IN RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Diet and Nutrition, Rheumatoid arthritis

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Background: Chronic inflammation in rheumatologic diseases alters body fat distribution and response to treatment, requiring higher doses or amounts of disease-modifying antirheumatic drugs (DMARDs) [1].
Objectives: To describe body composition of patients with rheumatoid arthtritis (RA) and systemic lupus erythematosus (SLE) and its association with the number of DMARDs used and use of corticosteroids.
Methods: A cross-sectional and descriptive study was carried out in the rheumatology service of the University Hospital ¨Dr. José Eleuterio González¨. Patients over 18 years old with diagnosis of RA or SLE were included. Body composition was assessed with InnerScan TANITA BC-533 monitor (Yesod, Japan) which uses single frequency bioelectrical impedance analysis (BIA). We report frequencies and percentages for categorical variables. For quantitative variables, we measured center trend and dispersion (means and standard deviation).
Results: We included 323 patients, 248 (79.1%) with rheumatoid arthritis (RA) and 75 (20.89%) with systemic lupus erythematosus (SLE) with an average age of 51.79 (±12.7) and 42 (±14.8) years respectively. In the RA group, BMI <25kg/m² was found in 64 (25.8%) and BMI >25kg/m² in 183 (73.8%), high total fat in 148 (59.7%), high visceral fat in 40 (16.1%), low muscle mass in 212 (85.5%), low body water in 155 (62.5%), 148 (59.7%) patients met 2 of 3 criteria for sarcopenic obesity (no muscle strength assessment) and abdominal obesity in 163 (65.7%). Details of anthropometric evaluation and DMARD schemes are shown in Table 1. We found a relationship between the 2 DMARD combined scheme with being obese type 2 (p=0.02) and prednisone use with type 3 obesity (p=0.005). In SLE group BMI <25kg/m² was found in 18 (24%) and >25kg/m² in 57 (76%), high total fat in 45 (60%), low muscle mass in 61 (81.3%), low body water in 46 (61.3%) and abdominal obesity in 51 (68%).. Being obese type 3 and having high visceral fat was related with the use of 3 DMARDs combined (p=<0.001) and having an older metabolic age was associated with intramuscular steroid use (p=0.012).
Conclusion: Sixty percent of our population met 2 of 3 criteria for sarcopenic obesity and more than 80% had low muscle mass. These parameters may increase with disease activity and the number of drugs required for control. Reference: [1] Liu, Y., Hazlewood, G. S., Kaplan, G. G., Eksteen, B., & Barnabe, C. (2017). Impact of Obesity on Remission and Disease Activity in Rheumatoid Arthritis: A Systematic Review and Meta-Analysis. *Arthritis Care and Research*, *69*(2), 157–165. https://doi.org/10.1002/acr.22932

Table 1. Anthropometric parameters in patients with AR and SLE

	RA (n=248/ 100%)	SLE (n=75/ 100%)
Age	51.79 (±12.7)	42 (±14.8)
Anthropometric parameters		
Weight, kg, mean, (SD)	70.93 (±16.26)	71.99 (±18.84)
BMI	29.03 (±6.69)	29.02 (±7.35)
Waist, cm, mean, (SD)	92.09 (±16.19)	91.68 (±18.05)
Hip, mean, (SD)	109.94 (±64.30)	105.10 (±14.12)
WHR	0.86 (±0.11)	0.86 (±0.12)
BMI classification, n (%)		
Low	8 (3.2)	6 (8.0)
Normal	56 (22.6)	12 (16.0)
Overweight	85 (34.3)	29 (38.7)
Obesity type 1	56 (22.6)	12 (16.0)
Obesity type 2	28 (11.3)	10 (13.3)
Obesity type 3	14 (5.6)	6 (8.0)
EBI parameters		
% Fat, (SD)	36.11 (±8.9)	34.87 (±11.99)
% Water, (SD)	44.59 (±5.9)	46.16 (±8.27)
Kg Muscle, (SD)	41.94 (7.5)	43.25 (±6.93)
Kg bone mass, (SD)	2.25 (±0.36)	2.29 (±0.32)
Metabolic age, years, (SD)	43.52 (±11)	40.62 (±14.01)
Alterations in body composition n, (%)		
High total fat	148 (59.7)	45 (60)
High visceral fat	40 (16.1)	12 (16)
Low muscle mass	212 (85.5)	61 (81.3)
Metabolic age > chronological age	67 (27.0)	35 (46.7)
Low body water	155 (62.5)	46 (61.3)
2 out of 3 criteria for sarcopenic obesity	148 (59.7)	45 (60.0)
Abdominal obesity	163 (65.7)	51 (68.0)
Treatment schemes, n (%)		
	n= 233 (100)	n= 70 (100)
1 DMARD	117 (47.2)	22 (29.3)
2 DMARD	78 (31.5)	38 (50.7)
3 DMARD	27 (10.9)	7 (9.3)
Prednisone	132 (53.2)	43 (57.3)
Intramuscular steroid	42 (16.9)	7 (9.3)

RA=rheumatoid arthritis, SLE=systemic lupus erythematosus, BMI=body mass index, HWI=hip to waist index

Acknowledgements: No acknowledgements to declare.
Disclosure of Interests: None Declared.
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AB0624 DUAL TRAJECTORIES OF DSDNA AND C3 CORRELATED WITH MORTALITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Real-world evidence

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by diverse clinical manifestations with multi-organ damage and an increased risk of mortality. Several clinical characteristics have been identified as predictors of overall mortality in patietns with SLE, including oragan damage, time from onset to diagnosis > 1 year, nephropathy, male gender, older age of onset, high Systemic Lupus Eythematosus Disease Activity Index (SLEDAI) scores and high Age-adjusted Charlson Comorbidity Index (ACCI) scores. However, whether trajectories of dsDNA and C3, two of the frequently monitored immune profiles, are associated with mortality among patients with SLE is still unknow. We aimed to assess the association of mortality with dual trajectories of dsDNA and C3 within two years in a large Taiwanese lupus cohort.
Objectives: We aimed to assess the association of mortality with dual trajectories of dsDNA and C3 within two years in a large Taiwanese lupus cohort.
Methods: The study linked electronic medical record data at Taichung Veterans Genral hospital to the file of Cause of Death Data from the National Health Insurance Research Database managed by Center for Helath and Welfare Data Science in Taiwan. From Jan 1, 2000 to Mar 31, 2021, we identified 4850 patients with SLE who were followed up at TCVGH. We excluded 131 patients who were dead and 364 patients who were lost to follow-up withing 2 years. We also excluded 1999 patients who did not have at less 2 records of paired dsDNA and C3 data ever 3 months during the first two-years. We finally included 2,356 patients for trajectories analysis. The first 2 years of follow-up was used to establish trajectories of dsDNA and C3. We calculated the man ± standard deviation of dsDNA and C3 for the eight 3-month intervals and we used these data separately for trajectory determination, which was by group-based trajectory analysis with a latent class growth model, fitting the SAS Proc Traj procedure. We classified patients with SLE into 4 groups (G) based on dual trajectories of dsDNA and C3: G1- lowest dsDNA and second highest C3 trajectory (41.6%); G2- lowest dsDNA and highest C3 trajectory (32.0%); G3- second highest dsDNA and second highest C3 trajectory (19.2%); group 4, highest dsDNA and lowest C3 trajectory (7.1%). The relative risk of mortality was estimated using Cox proportional hazard model adjusting for age, gender, hypertension, diabetes mellitus and hyperlipidemia, shown as hazard ratios (HRs) with 95% confidence intervals (CIs).
Results: The proportions of female in G1-G4 were 88.0%, 87.0%, 86.7% and 84.0% respectively. The mean age in G1-G4 were 37.6 years, 41.3 years, 36.4 years and 34.7 years respectively. The mortality rates were highest in G1 (6.24 cases per 1,000 person-years), followed by G2 (5.90 cases per 1,000 person-years), G3 (5.04 cases per 1,000 person-years) and G4 (4.19 cases per 1,000 person-years). After adjusting for potential confounders, the risk of mortality in G1 was significantly higher in G2 (HR, 1.67; 95% CI, 1.10–2.53; p = 0.016), but not in G3 (HR, 1.16; 95% CI, 0.66–2.05; p = 0.605) and G4 (HR, 1.22; 95% CI, 0.51–2.91; p = 0.659) as compared to that in G2. Other significant independent predictors of mortality included age (HR, 1.05; 95% CI, 1.04–1.06; p < 0.001) and hypertension (HR, 1.83; 95% CI, 1.14–2.95; p = 0.013).

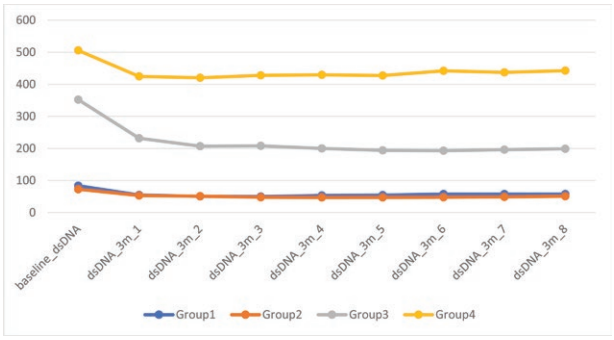


Figure 1. Trajectories of dsDNA during the first two years in four groups.

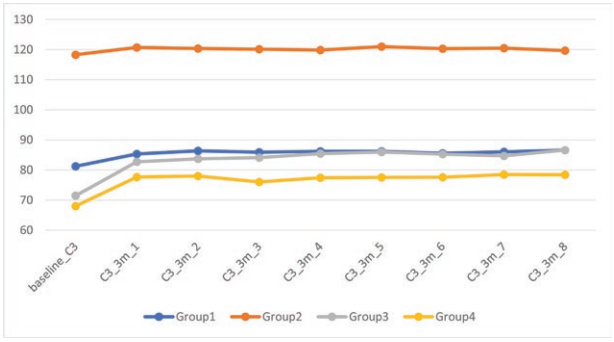


Figure 2. Trajectories of C3 during the first two years in four groups.

Conclusion: This single center study revealed that SLE patients with lowest dsDNA and second highest C3 trajectory had a significantly higher risk of mortality than SLE patients with lowest dsDNA and highest C3 trajectory.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0625 THE ATTRIBUTION OF NEUROPSYCHIATRIC EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM "ATTIKON" LUPUS COHORT

Keywords: Registries

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Background: The attribution of neuropsychiatric manifestations to systemic lupus erythematosus (SLE) or unrelated causes is often obscure.
Objectives: The attribution of neuropsychiatric events to lupus (SLE related) or other causes (non-SLE related) in a large SLE cohort.
Methods: Retrospective study of 707 SLE patients from "Attikon" lupus cohort [1,2]. Neuropsychiatric manifestations were classified as either primary neuropsychiatric SLE (SLE related; attributed to SLE using a combination of multidisciplinary physician judgment with attribution models [3]) or secondary NPSLE (non-SLE related; neuropsychiatric manifestations not attributed to SLE) or manifestations of uncertain attribution.
Results: 258 patients developed 345 NP events in total. Among them, 140 (40.6%) were attributed to SLE, while 148 (42.9%) were classified as secondary NPSLE. In 57 NP events, the attribution remained uncertain. Among primary NP manifestations, cerebrovascular events (n=34, 24.3%), seizures (n=25, 17.8%) and cranial neuropathies (n=18, 5.2%) were the most common, while mood disorders (n=69, 46.6%) and headache (n=22, 14.9%) were the most common secondary NPSLE. The extra-CNS clinical and serological phenotype do not differ between primary and secondary NPSLE. Patients with primary NPSLE as compared to secondary NPSLE, were more likely to accrue irreversible damage (SLICC damage index > 0) (OR=2.88, 95%CI 1.67-4.96) and develop additional neuropsychiatric manifestations (OR=3.74, 95%CI 1.98-7.09).
Conclusion: A significant proportion of NP events cannot classified as primary or secondary NPSLE. Cerebrovascular eventσ and seizures are the most common primary NP manifestations in SLE. The primary NPSLE is associated with accrual of irreversible damage and increased risk of developing additional NP manifestations.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5996

AB0626 DIFFERENTIALLY EXPRESSED GENES (DEGS) OVERLAP AMONG BLOOD SAMPLES DATASETS FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) THROUGH INTEGRATIVE BIOINFORMATICS METANALYSIS

Keywords: -Omics, Biomarkers, Systemic lupus erythematosus

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Background: Systemic Lupus Erythematosus is an autoimmune chronic disease mainly characterized by the presence of auto-autoantibodies, and periods of flares and remission [1]. Understanding the mechanisms of physiopathology is still being the aim for several researchers. In the last 20 years multiple studies tried to look for molecular mechanisms associated to the disease using biomolecular techniques [2]. Specifically, the gene expression patterns play an important role in the pathophysiology of this disease, in which the interferon signature has been widely found in SLE patients, but also in other autoimmune diseases like rheumatoid arthritis and Sjögren's syndrome [3]. However, there is a discordance in which genes from the interferon signature are specific biomarkers for SLE, since there are multiple studies that describe the interferon signature but with different differentially expressed genes.
Objectives: We aimed to identify differentially expressed genes that overlap across different datasets of gene expression from blood samples of SLE patients using an integrative bioinformatics metanalysis.
Methods: We design a search strategy in the Gene Expression Omnibus platform to identify data sets of gene expression profile by array from blood samples of patients with SLA. The inclusion criteria were: 1) assays performed in humans, 2) the dataset include SLE patients and healthy controls, 3) expression profiling by array, 4) data analysis using GEO2R, 5) samples from blood. The exclusion criteria was: 1) incomplete information of the genes, 2) gene expression by RNAseq. Differentially expressed genes were selected when logfold change was >2 with p <0.05. Integrative bioinformatics strategy was applied. Using the platforms GeneMania and DAVID we identify overlapped genes among datasets and functional enrichment analysis of the differentially expressed genes.
Results: We selected 3 datasets that fulfill the inclusion criteria: GSE110174, GSE10325, and GSE154851. A total of 29 up-regulated genes were identified among datasets. Venn diagram shows 3 genes overlapped among all the datasets, and 1 or 2 genes overlapped between different pairs of datasets (Figure 1).

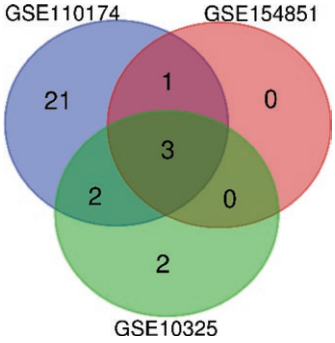


Figure 1. Venn diagram of the 3 datasets.

A prediction analysis yielded 20 co-expressed genes, that interact with the overlapped genes. A functional enrichment analysis yielded the 3 principal biological processes involving those genes: 17 genes participate in defense response to virus; 13 genes associated to response to virus; and 8 genes involved in negative regulation of viral genome replication (Table 1). Most of the genes identified belong to the interferon signature.

Table 1. Functional enrichment Analysis of the Co-Expressed genes.

Functional Enrichment Analysis		
Process	**Gene Count**	***p* Value**
Defense Response to Virus	17	8,1E-26
Response to Virus	13	1,8E-21
Negative Regulation of Viral Genome Replication	8	9,1E-14

Conclusion: We aimed to obtain upregulated genes and their co-expressed pairs through transcriptomic and functional enrichment analysis. 6 genes appeared upregulated across the 3 datasets, and 20 genes were listed as their co-expressed pairs. Those genes were involved in the processes of Defense Response to Virus, Response to virus, and Negative Regulation of Viral Genome Replication. These genes can serve as possible biomarkers for early diagnosis, and maybe even possible therapeutic targets.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.207

AB0627 CLINICAL PROFILE OF PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN A TERTIARY LEVEL HOSPITAL IN THE PHILIPPINES, YEAR 2015-2021

Keywords: Systemic lupus erythematosus

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Background: Pediatric Lupus Erythematosus is a chronic systemic autoimmune disease with a higher risk of disease damage than adults with SLE.
Objectives: To profile the clinical and laboratory features and manifestations of pediatric SLE patients seen and admitted at Region 1 Medical Center from January 2015 to December 2021 and assess the association of the clinical profile with complications and mortality.
Methods: A retrospective review of medical records of all pediatric SLE patients age <18 years, admitted at Region 1 Medical Center from January 2015 to December 2021. Charts were reviewed for clinical and laboratory data extraction. Clinical data were analyzed using descriptive statistical analysis. Fisher's exact test was utilized to analyze the association of clinical profile to morbidity and mortality. Odds ratio was used to determine the degree and direction of association among significantly associated variables in the study.
Results: A total of 29 patients who fulfilled the inclusion criteria were included in the study. Average age of diagnosis is 16 years with predominance of female. The most common presenting symptom is malar rash(27.6%) followed by joint pains (10.3%) and pallor (10.3%). Patients with pediatric SLE commonly manifested with acute cutaneous rash(79.3%). Thrombocytopenia (69%) is the most common laboratory finding. Complications of SLE include renal (51.7), infection (27.6%), and cardiovascular (17.2%). Oral corticosteroid is the most common treatment which was administered to all participants. Mortality rate of 34.5% is associated to the most common cause which is SLE in activity (80%) followed by infection (60%). Neurologic manifestation and increase creatinine were found to be associated with mortality with odds ratio of >1.
Conclusion: Malar rash is the most common clinical presentation among Filipino pediatric SLE. The most common complication is renal involvement. Neurologic manifestation and non-scarring alopecia increase mortality.

REFERENCE:

[1] PubMed Central, ResearchGate, Journals, World Health Organization website

Table 1. Odds ratio of significant associations between clinical and laboratory findings, and morbidity and mortality among eligible SLE patients in Region 1 Medical Center: 2015-2021

SIGNIFICANT ASSOCIATION	ODDS RATIO	P-VALUE
Neurologic disorder and morbidity	1.0	N/A
Neurologic disorder and mortality	8.5	0.029**
Non-scarring alopecia and mortality	0.2	0.030**
Increased creatinine and morbidity	1.0	N/A
Increased creatinine and mortality	5.1	0.056*

Note: * - significant at alpha = 10%; ** - significant at alpha = 5%

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.528

AB0628 IMPACT OF SOLAR RADIATION FROM SUN EXPOSURE AND PHOTOPROTECTION PRACTICES ON DISEASE ACTIVITY AMONG SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS IN MALAYSIA

Keywords: Comorbidities, Systemic lupus erythematosus, Epidemiology

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Background: Systemic Lupus erythematous (SLE) is an autoimmune disease which is characterized by remission and flares. Experimental studies demonstrate that sun exposure can trigger immunomodulatory response, however, there is lacking of strong epidemiologic data regarding its role in triggering SLE flare. Malaysia has a tropical climate and hence get more exposure to the sun.
Objectives: To determine the correlations between disease activity with exposure to sun measured with solar radiation [1h (W/m^2)], and photoprotection practices among SLE patients in Malaysia.
Methods: This was a cross-sectional study involving SLE patients conducted in Universiti Kebangsaan Malaysia and Sarawak General Hospital from January 2019 until December 2019. During the study visit, disease activity was measured using Modified Systemic Lupus Erythematosus Disease Activity Index (M-SLEDAI) and The British Isles Lupus Assessment Group 2004 (BILAG). Sun Exposure and Protection Index (SEPI) was used to assessed their photoprotection practices, and patients who reported no change in their photoprotection practices for the last 2 years were included. A high SEPI score reflects an increased risk of sun exposure. Their medical records were also reviewed for retrospective assessments of the disease activity from the past 2 years (2017-2019). Clinic visits with presence of infection or recent change of immunosuppressive treatment of ≤ 3 months were excluded. Sun exposure was determined by calculating the average of daily solar radiation (mean) and the maximum solar radiation (max) within 30 days preceding the clinic visits. The hourly and daily solar radiation data was obtained from the Department of Environment (DOE) Malaysia. Correlations between the solar radiation mean, max and SEPI scores with M-SLEDAI and BILAG were determined using the Pearson's correlation coefficient correlation; while their associations with severe SLE flares (presence of BILAG A or B) were performed using Student's t-test. The associations between the effects of solar radiation and SEPI on M-SLEDAI and BILAG scores were analyzed using the generalized estimating equation (GEE) model, while considering fixed effects for repeated measures.
Results: A total of 87 patients were recruited with 514 clinic visits were recorded. There was significant correlation between the mean solar radiation with M-SLEDAI scores (rs=0.303, p<0.001). SEPI scores were significantly correlated with M-SLEDAI and BILAG scores (rs=0.098, p=0.03 and 0.421, p<0.001 respectively). Patients who had severe flare (BILAG A or B) had a higher exposure to the mean solar radiation (154.6 ± 35.9 vs 148.7 ± 19.1, p=0.011). In the GEE analysis, mean solar radiation and SEPI scores were still significantly correlated with M-SLEDAI scores; and significantly associated with severe flares p<0.05.
Conclusion: These results suggest that solar radiation has a significant impact on SLE disease activity and flare. Patients should be emphasized on the importance of photoprotection practices as this is one of the modifiable risk factors of active disease and flare.

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AB0629 DEMOGRAPHIC, CLINICAL AND SEROLOGICAL CHARACTERISTICS OF SJÖGREN'S SYNDROME PATIENTS

Keywords: Real-world evidence, Sjögren syndrome

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Background: Sjogren's syndrome (SS); is a chronic multisystem inflammatory autoimmune disease characterized by dry eyes and mouth, involving lymphocytic infiltration of the lacrimal and salivary glands. Glandular involvement and extraglandular symptoms involving various organs and systems can be seen in patients. It can be seen in all age groups, although it is most common in those aged 45-50 years. The average female/male incidence rate is 9/1.

Objectives: Our aim in this study is to present the demographic, clinical and serological characteristics of patients diagnosed with SS.

Methods: Our study included 466 patients diagnosed with SS according to the 2016 ACR/EULAR Classification Criteria. Age, gender, primary/secondary SS status of the patients; organ involvement, salivary gland biopsy and serological features were recorded. Descriptive statistics were given as mean±standard deviation, frequency (n), and percent (%).

Results: The mean age of 466 (433 females, 33 males) patients in the study was 55.4±13.5 years. The female/male ratio was 13/1. There were 408 (87.5%) patients with primary SS diagnosis and 58 (12.5%) patients with secondary SS diagnosis. 67% of patients with a diagnosis of secondary SS had rheumatoid arthritis. The most common clinical presentation complaints were dry eye (86%) and dry mouth (67.8%). In our study, anti-nuclear antibody positivity was found to be 83.4%, rheumatoid factor positivity was 22.1%. Ro-52 antibody was positive in 56.4% of the patients. As a result of the evaluation in terms of organ/system involvement; pulmonary involvement was found in 45 patients (9.6%). Moreover; primary biliary cirrhosis in 18 (3.8%) patients, adrenal insufficiency in 1 (0.2%) patient, chronic tubulointerstitial nephritis in 2 (0.4%) patients, crescentic glomerulonephritis in 1 (0.2%) patient, optic neuropathy was found in 1 (0.4%) patient, and lymphoma was found in 1 (0.2%) patient (Table 1).

Conclusion: Sjögren's syndrome can affect almost any organ system, thus various systemic manifestations may occur. The disease is characterized by pleomorphic clinical manifestations, which can vary greatly in features and severity from one patient to another. Diagnosis of the disease is based on characteristic clinical signs and symptoms as well as specific tests including salivary gland histopathology and autoantibodies.

Table 1. Demographic, Clinical and Serological Characteristics of Sjögren's Syndrome Patients

	n	%
Primary SS	408	87,5
Secondary SS	58	12,5
• *Rheumatoid Arthritis*	39	67,2
• *Systemic Sclerosis*	11	18,9
• *Systemic Lupus Erythematosus*	8	13,7
Salivary gland biopsy positivity	247	53
Dry mouth	316	67,8
Dry eye	401	86
Locomotor system	165	35,4
• *Arthritis/arthralgia*		
Organ/system involvement	45	9,6
• *Pulmonary İnvolvement*	18	3,8
• *Primary Biliary Cirrhosis*	3	0,6
• *Autoimmune Hepatitis*	4	0,8
• *Vasculitis*	1	0,2
• *Amyloidosis*	2	0,4
• *Chronic Tubulointestial Nephritis*	1	0,2
• *Kresentik Glomerülonefrit*	1	0,2
• *Adrenal İnsufficiency*	1	0,2
• *Optic Neuropathy*		
• *Lymphoma*		
Anti-Nuclear Antibody positivity	389	83,4
Ro-52 positivity	263	56,4
Rheumatoid factor positivity	103	22,1

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0630 PREGNANCY IN AUTOIMMUNE DISEASES: THE IMPACT OF PREGNANCY PLANNING ON REPRODUCTIVE OUTCOMES IN A MULTIDISCIPLINARY PRECONCEPTION OUTPATIENT CLINIC

Keywords: Pregnancy and reproduction, Systemic lupus erythematosus, Real-world evidence

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Table 1.

	Total (n=41)
Sociodemographic data	
Age at visit, mean±SD	35.7±4.43
Age at diagnosis, mean±SD	28.5±7.65
Diagnosis, n (%):	19 (46.34%)
- SLE	2 (4.88%)
- APS	15 (36.59%)
- Other CTDs	2 (4.88%)
- Inflammatory arthritis	3 (7.32%)
- Autoinflammatory	
Before preconception counselling	16 (39%)
Median nº of pregnancies, n (%)	16 (39%)
- 0	7 (17%)
- 1	2 (4.9%)
- 2	
- 3	
Abortion, n (%)	21 (61.8%)
- 0	10 (29.4%)
- 1	3 (8.8%)
- 2	2 (4.88%)
Preterm, n (%)	2 (11.7%)
Low-weight at birth, n(%)	
Treatment, n (%)	11 (26.83%)
- c/tsDMARD	8 (19.5%)
- HCQ	11 (26.83%)
- bDMARDs	11 (26.83%)
- None	
Glucocorticoid dose, n (%)	18 (43.9%)
- <7.5 mg/day	3 (7.3%)
- >7.5 mg/day	5 (12.2%)
Previous Cyclophosphamide, n (%)	
Multidisciplinary team evaluation:	21 (51.2%)
Pregnancy risk, n (%)	16 (39.02%)
- Low	4 (9.76%)
- Moderate	
- High	
Assessment, n (%):	19 (46.34%)
- Fit to conception	10 (24.4%)
- Not fit to conception	5 (12.2%)
- Fit with medication change	7 (17.07%)
- Pregnant at first visit	
After preconception counselling	2 (13.3%)
Fertility assistance, n (%)	13 (86.7%)
- Assisted	4 (9.76%)
- Non-assisted	1 (11.1%)
Abortion	2 (4.88%)
Low-weight at birth	
Preterm birth	
Treatment	12 (29.3%)
- c/tsDMARDs	6 (14.6%)
- bDMARDs	10 (24.4%)
- HCQ	13 (31.7%)
- None	
Glucocorticoid dose	19 (46.3%)
- <7.5 mg/day	22 (53.7%)
- None	

Background: Pregnancy in patients with systemic autoimmune diseases (SADs) are known to be at high risk for the occurrence of adverse pregnancy outcomes. Pre-conception counselling and risk stratification performed in a multidisciplinary clinical setting are essential for improving pregnancy outcomes and reducing maternal and perinatal complications in patients with SADs.
Objectives: To describe clinical, obstetric and maternal comorbidities and pregnancy outcomes in patients with SADs.
Methods: A retrospective cohort study was conducted. Inclusion criteria were patients diagnosed with SADs that were examined by the multidisciplinary pregnancy clinic. Clinical, maternal and obstetric variables were collected. The multidisciplinary team evaluated if the risk of pregnancy was high, moderate or low. Data related to pregnancy outcomes were also collected. Mean, standard deviation and proportions were calculated.
Results: A total of 41 patients interested in getting pregnancy attended our outpatient preconception clinic, with a mean age at first visit of 35.7±4.43 years. The ethnicity of the patients was: 75.6% Caucasian, 19.5% Hispanic and 4.9% Asian. Sociodemographic, clinical, treatment data, maternal and obstetric comorbidities are summarized in Table 1. Prior to preconception counselling, history of live births occurred in 61%, pregnancy loss in 32%, preterm birth in 10.5% and low-weight at birth in 11.7% of patients. 53.66% of patients were under treatment with c/tsDMARDs and/or bDMARDs and 19.5% with hydroxychloroquine. As much as 43.9% were taking ≤7.5 mg of prednisolone/day and 7.3% were taking >7.5 mg/day. After evaluation by the multidisciplinary pregnancy clinic, 51.2% of patients were classified as low risk, 39% as moderate and 9.8% as high risk for adverse pregnancy outcomes. The final assessment was conception without treatment changes for 46.3% of the patients, treatment changes before conception for 12.2%, postponement of pregnancy for 24.4% and 17% of patients were pregnant at their first visit. Of these women, 15 conceived (36.6%) after a median time of 6.25±4.5 months. Medical and obstetric complications occurred in 13% and 20% of the patients. Abortion occurred in 9.76%, preterm birth in 4.88% and low-weight at birth in 11.1% of patients.
Conclusion: 46% of patients attending our pregnancy outpatient clinic had a diagnosis of SLE. Out of the 41 patients assessed, 59% were advised to conceive and 12% were discouraged. 36.6% of patients were able to get pregnant, with a reduction in maternal and perinatal complications after preconception counselling. Well-planned pregnancies, adequate treatment and pre-conception evaluation will contribute to an improved outcome, both for the mother and the child.
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Acknowledgements: NIL.
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AB0631 THE RELATIONSHIP OF LOWER URINARY SYSTEM SYMPTOMS WITH DEPRESSION AND ANXIETY IN PATIENTS WITH SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Patient reported outcomes, Descriptive Studies

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Background: Sjögren's syndrome (SS) is a multisystem autoimmune disease characterized by hypofunction of salivary and lacrimal glands and possible systemic multi-organ manifestations [1]. The prevalence and severity of lower urinary tract symptoms(LUTS) are higher in autoimmune diseases such as SS [2,3]. Likewise, the prevalence of anxiety and depression is increased in patients with Primary SS [4].
Objectives: It was aimed to investigate the frequency of LUTS in patients with SS and to evaluate the coexistence of depression and anxiety in patients with and without LUTS.
Methods: Sixty-three patients, including sixty women diagnosed with Sjögren's Syndrome at Sakarya University Faculty of Medicine, Internal Medicine Rheumatology Department, were included in the study after their informed consent was obtained. All patients fulfilled the criteria for the 2016 ACR/EULAR Classification for Primary Sjögren's Syndrome. The International Prostate Symptom Score (IPSS) was used in the evaluation of LUTS, and the Beck Depression and Anxiety Scale were used for the assessment of depression and anxiety. Data were analyzed using the computer program SPSS 21. Relationships between categorical variables were evaluated with Chi-square analysis. The relationship between IPSS and Beck Depression/Beck Anxiety scale was assessed by spearman correlation analysis. p<0.05 was considered statistically significant.
Results: The mean age of the patients was 53.6±11.6 years. The median disease duration was four years (min-max: 0-40). 58 (92.1%) patients had at least one LUTS. Of the patients with LUTS, 32 (55.1%) were mild, 21 (36.2%) moderate, and 5 (8.7%) severe. Anxiety was found in 31 (49.2%) patients, and depression was found in 37 (58.7%) patients. The frequency of depression was significantly higher in patients with LUTS. Depression and anxiety were not observed in patients without LUTS. When the severity of LUTS was compared with the presence of anxiety and depression, a significant difference was found in both groups (p=0.033; p=0.032, respectively) (Table 1). There was a moderate positive correlation between the IPSS score and the Beck Depression and Beck Anxiety Scale (r:0.429 p:<0.001; r:0.481 p:0.001, respectively).

Table 1. Association of LUTS severity and anxiety/depression.

		Mild n (%)	Moderate n (%)	Severe n (%)	p value
Depression	Present	16 (50.0)	16 (76.2)	5 (100)	**0,032**
	Absent	16 (50.0)	5 (23.8)	0 (0)	
Anxiety	Present	13 (40.6)	16 (76.2)	2 (40.0)	**0,033**
	Absent	19 (59.4)	5 (23.8)	3 (60.0)	

Conclusion: In conclusion, questioning the presence of LUTS in patients with SS and referral for treatment may reduced the frequency of depression and anxiety.
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AB0632 THE ASSOCIATION OF NEUROPATHIC PAIN WITH LOWER URINARY SYMPTOM SEVERITY IN PRIMARY SJÖGREN'S PATIENTS

Keywords: Descriptive studies, Patient reported outcomes, Sjögren syndrome

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Background: Primary Sjögren's syndrome(PSS) is a systemic autoimmune disease characterized by xerophthalmia and xerostomia and is associated with systemic visceral involvement. A wide variety of neurological complications also are characteristic features of PSS [1]. Patients with PSS can suffer from severe neuropathic pain with small fiber neuropathy.
Objectives: It is aimed to investigate the presence of neuropathic pain in patients with SS and to evaluate the severity of lower urinary tract symptoms (LUTS) in patients with or without neuropathic pain.
Methods: Sixty-two patients, including fifty-nine women diagnosed with Sjögren's Syndrome at Sakarya University Faculty of Medicine, Internal Medicine Rheumatology Department, were included in the study after their informed consent was obtained. All patients fulfilled the criteria for the 2016 ACR/EULAR Classification for Primary Sjögren's Syndrome. Neuropathic pain was divided into two groups, present and absent. International Prostate Symptom Score (IPSS) was used in the evaluation of LUTS and The Leeds Assessment of Neuropathic Symptoms and Sign Pain Scale (LANSS Pain Scale) was used for the assessment of neuropathic pain. Data were analyzed using the computer program SPSS 21. Relationships between categorical variables were evaluated with Chi-square analysis. The relationship between IPSS and LANSS Pain Scale was evaluated by spearman correlation analysis. p<0.05 was considered statistically significant.
Results: The mean age of the patients was 53.4±11.6 years. The median disease duration was seven years (min-max: 0-40). Neuropathic pain (LANSS Pain Scale>12) was observed in 18 (29%) patients. According to the LUTS questionnaire, 35(56.5%) patients were in the mild LUTS(IPSS<8), and 27(43.5%) patients were in the moderate and severe LUTS(IPSS≥8) group. The severity of LUTS was significantly higher in patients with neuropathic pain (Table 1). There was a moderate positive correlation between the IPSS score and the LANSS Pain scale (r=0.359 p=0.004).

Table 1. Association of LUTS severity and neuropathic pain.

	Neuropathic pain Present (n=18)	Neuropathic pain Absent (n=44)	p-value
IPSS<8	6 (%33.3)	29 (%65.9)	**0.019**
IPSS≥8	12 (%66.7)	15 (%34.1)	

Conclusion: In conclusion, LUTS should be questioned when neuropathic pain is observed in SS patients. Initiation of neuropathic pain treatment in SS patients may prevent the symptom severity of LUTS.

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AB0633 PREGNANCY IN SYSTEMIC LUPUS ERYTHEMATOSUS: DESCRIPTION AND COMPARISON OF COMORBIDITIES WITH OTHER SYSTEMIC AUTOIMMUNE DISEASES FROM A RHEUMATOLOGY PREGNANCY CLINIC

Keywords: Pregnancy and reproduction, Systemic lupus erythematosus, Real-world evidence

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Background: Pregnancy in patients with systemic lupus erythematosus (SLE) are known to be at high risk for the occurrence of adverse pregnancy outcomes. Pre-conception counselling and risk stratification performed in a multidisciplinary clinical setting with rheumatologists, obstetricians and nephrologists are essential for improving pregnancy outcomes and reducing maternal and perinatal complications in patients with SLE.

Objectives: To describe clinical, obstetric and maternal comorbidities and pregnancy in patients with SLE and patients with other systemic autoimmune diseases (SADs).

Methods: A retrospective cohort study was conducted including patients diagnosed with SLE attending our multidisciplinary pregnancy clinic. Clinical, immunological and obstetric variables were collected. Data related to pregnancy outcomes, delivery and disease activity were also collected. Description of the sample and comparison of groups were carried out. Shapiro-Wilk test was used for variable distribution.

Table 1.

	SLE (n=19)	Non-SLE (n=22)	P value
Sociodemographic data	36.8±4.61	34.4±3.93	0.08
Age at visit (year)	24.7±9.6	31.7±6.7	**0.02**
Age at diagnosis (year)	9.78±5.95	5.09±6.09	**0.004**
Diagnosis-1st visit (years)	48±41.76	19.4±32.5	**0.01**
Last flare-1st visit (months)			
Before preconception counselling	6 (33.3)	7 (45.75)	0.987
Abortion (n, %)	5 (71.43)	0	0.06
Preterm (n, %)	2 (28.5)	0	0.239
Low-weight at birth (n%)			
Treatment, n (%)	8 (42.1)	3 (13.64)	**0.049**
- c/tsDMARD	8 (26.3)	3 (13.64)	**0.049**
- HCQ	2 (26.3)	9 (40.41)	**0.04**
- bDMARDs			
Glucocorticoids (n, %)	14 (73.7)	7 (31.82)	**0.009**
Previous CYC (n, %)	5 (26.3)	0	0.06
Pregnancy risk (n, %)	8 (42.1)	13 (59.1)	0.28
- Low	8 (42.1)	8 (36.4)	0.71
- Moderate	3 (15.8)	1 (4.55)	0.25
- High			
After preconception counselling	7 (36.8)	12 (54.6)	0.26
Assessment (n, %)	6 (31.58)	4 (18.2)	0.32
- Fit to conception	3 (15.8)	2 (9.1)	0.52
- Not fit to conception	3 (15.8)	4 (18.2)	0.83
- Fit to conception after treatment change			
- Pregnant at 1st visit			
Complications in pregnancy (n,%):	2 (15.5)	0	0.24
- Medical	0	3 (10.7)	
- Obstetrical			
Abortion (n, %)	1 (7.69)	0	0.44
Preterm (n, %)	2 (10.5)	0	0.24
Low weight at birth (n, %)	2 (10.5)	0	0.24

Results: A total of 41 patients attended our outpatient preconception clinic. Comparison and description of the comorbidities, preconception counseling and pregnancy outcomes are summarized in Table 1. A total of 19 (43.2%) patients were diagnosed with SLE. Lupus nephritis was observed in 47% of the patients and 11% had received kidney transplant. Moderate SLEDAI activity (>4) was observed in 44.4%. There were 7 (37%) pregnancies after a mean time of 7.3±6 months since the first visit. SLE patients were significantly older when evaluated at the pregnancy clinic than patients with other SADs. Also, SLE patients exhibited a longer time since the last flare when evaluated at the pregnancy clinic. Significant differences were observed in treatment between both groups: more hydroxychloroquine, synthetic DMARDs and steroids were used in the SLE group. No significant differences in preconception counseling or adverse pregnancy outcomes were observed.

Conclusion: Patients with SLE took longer time since diagnosis and flare to seek pregnancy than patients with other SAD. No differences in pregnancy outcomes or risk profile were observed.

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AB0634 BASELINE CLINICAL – EPIDEMIOLOGICAL CHARACTERISTICS OF THE PATIENTS IN THE IMMEX COHORT

Keywords: Descriptive studies, Systemic lupus erythematosus, Diagnostic tests

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease with a wide clinical and evolutionary spectrum. The correct classification and study of the behavior of this type of population helps to constantly improve the approach and prognosis of patients with this disease.

Objectives: Describe the clinical and epidemiological characteristics of patients with SLE included in a cohort in Mexico.

Methods: Retrospective descriptive observational study based on the clinical-epidemiological historical review on the day of inclusion in the LUPUS-IM-Mex registry. Normality tests were applied, the frequencies and percentages were calculated for the categorical variables and the means with their standard deviation or medians with interquartile range (IQR) for the continuous variables depending on their distribution. A comparison of compliance with diagnostic scores was made according to three classification criteria (ACR 1997, SLICC 2012 and EULAR 2019) according to the manifestations of each patient at the time of incorporation into the cohort.

Results: 121 patients with a diagnosis of SLE according to the 2019 EULAR (European League Against Rheumatism) criteria were included, a review of records from the period 2006 to 2022 was carried out. They were 33 years old (IQR 26–41), 81% were female, 87.6% came from the metropolitan area, 49.1% with a basic educational level. Median age at diagnosis 28 years (IQR 23-37). The time of evolution of the disease until admission to the registry was 3 years (IQR 1-5). 17.48% reported a family history of autoimmune diseases and 27.86% presented concomitant allergies to some drug. The patients underwent a comparison of the classification criteria at the first medical care contact, where it was found that 81.81% met the lupus criteria according to ACR, 94.21% by SLICC and 100% by EULAR. Regarding clinical manifestations, the presence of joint alterations was the most frequent, being present in 61.48% of the patients at the time of diagnosis, followed by mucocutaneous manifestations in 57.38%, hematological manifestations in 49.18%, renal manifestations in 45.90%, fever in 24.59%, serous in 21.31% and lastly neuropsychiatric manifestations in 4.92%. The presence of hypocomplementemia was the most frequent data (72.12%) followed by SLE-specific antibodies and finally antiphospholipid antibodies.

Conclusion: Patients with SLE at our center have both clinical and epidemiological characteristics like those reported by other cohorts. Renal involvement is greater compared to European cohorts but less than that reported in Asian cohorts. The correct and adequate classification of each patient is fundamental to improve the prognosis and correct diagnosis. Although the availability of data in our environment is limited, it is necessary to continue with the constant obtaining of information regarding the subject to be able to be on a par with international cohorts.

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Table 1. Baseline characteristics at the time of diagnosis

Quantitative variables	*Median*	*RIC (25 – 75)*
Age (years)	33	26 – 41
Weight (kilograms)*	62.07	±14.50
Size (meters)	1.60	1.54 – 1.65
BMI (kg/m2)	24.22	±4.63
C3 (mg/dL)	48.95	32 – 74.10
C4 (mg/dL)	6.15	2.90 – 10.75
Hemoglobin (mg/dL)*	10.85	±2.95
Platelets (103/mm3)	228	143 – 306.50
Leukocytes (/mm3)	4,470	3,470 – 7,400
Lymphocytes (/mm3)	935	682.50 – 1442.50
Creatinine (mg/dL)	0.82	0.65 – 1.29
Lactic dehydrogenase (IU/L)	322.50	222.50 – 449
C-reactive protein (g/dL)	1.03	0.29 – 10.35
Qualitative variables	*Frequency*	*Percentage (%)*
Sex		
Feminine	98	81
Male	23	19
Metropolitan area resident	106	87.60
Family history of autoimmune diseases	19	15.57
Allergies to medications	3. 4	27.86

* Variables with normal distribution. Interquartile Range (IQR), Kilograms (Kg), meters (m), grams (g), milligrams (mg), deciliters (dL), complement (C), international units (UI).

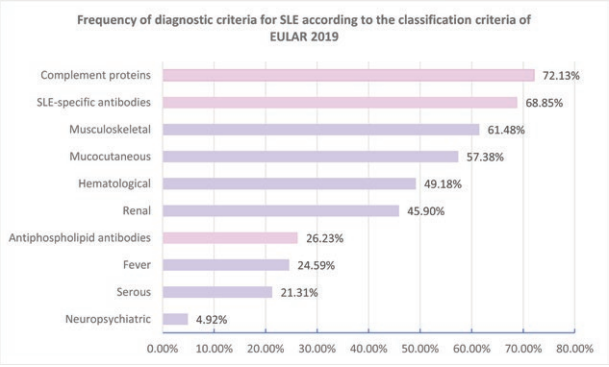


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2127

AB0635 HAEMATOLOGICAL MANIFESTATIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: REAL WORLD DATA FROM A CENTRE IN NORTHERN ITALY

Keywords: Systemic lupus erythematosus, Comorbidities, Descriptive studies

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder characterized by a variety of signs and symptoms; it manly affects women of childbearing age, with an estimated prevalence of 24/100,000 people in Europe and North America. Among other clinical manifestations, haematological involvement is one of the most common in SLE as it includes anaemia, leukopenia, lymphopenia, thrombocytopenia, lymphadenopathy and splenomegaly; furthermore, it is usually challenging to discriminate whether such manifestations are caused by disease or by immunosuppressants. To date, few studies tried to evaluate them using real world data.
Objectives: To evaluate haematological manifestations in patients with SLE by using real world data.
Methods: A retrospective study was performed by gathering real world data. 2019 EULAR/ACR Classification Criteria for SLE were used to discern haematological involvements in patients with a diagnosis of SLE; leukopenia, thrombocytopenia and autoimmune haemolytic anaemia (AIHA) were considered for this study. Six subgroups were formed as each condition alone and their combinations were analyzed. Logistic regression was used to calculate the odds ratio (OR) and a 95% confidence interval (CI) was chosen to assess statistical significance.
Results: One hundred and forty-two patients affected by SLE were enrolled in this study (N=142); among these, thirty met the inclusion criteria for haematological manifestations (n=30, 52 ±12.4 years, 28 F, 2 M). Three patients showed AIHA alone (10.0%), six had thrombocytopenia only (20.0%) and 8 displayed leukopenia alone (26.7%). Thirteen patients showed a combination as 6 people had both AIHA and thrombocytopenia (20.0%) and 4 manifested AIHA in association with leukopenia (13.3%); lastly, 3 patients showed thrombocytopenia with leukopenia (10.0%). The latter proved to be the most common manifestation as leukopenia was present in 15 out of 30 patients (50.0%) (Figure 4). Azathioprine (AZA), in association with hydroxychloroquine (HCQ), was used in 8 patients (26.6%), while a combination of Mycophenolate Mofetil (MMF) and HCQ was found in 5 out of 30 patients (16.7%); seventeen patients received either HCQ alone or a biologic drug (Belimumab). Among patients in therapy with AZA or MMF, the former proved to be more frequently associated with leukopenia vs MMF (OR_1=2.5); however, the result was not statistically significant ($CI_1$95% 0.77; 8;04); a similar result was observed for both patients in therapy with MMF or AZA when compared to HCQ alone or HCQ + Belimumab (OR_2=1.16, OR_3=0.46, respectively) since they did not reach statistical significance.
Conclusion: In this preliminary study, real-world data proved essential to analyze patients affected by SLE. Among many haematological manifestations, leukopenia showed to be the most frequent in agreement with data published in literature, strictly followed by thrombocytopenia and AIHA. AZA was linked with a higher percentage of leukopenia compared to MMF or other therapies but the result was not statistically significant. This study has some limitations (number of enrolled patients, possible selection bias) which require further evaluations to be properly assessed.

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Disclosure of Interests: None Declared.
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AB0636 FREQUENCY OF TROPICAL INFECTIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN A MEDIUM INCOME COUNTRY, USING DATA ANALYTICS TECHNIQUES

Keywords: Systemic lupus erythematosus, Artificial intelligence, Infection-related RMDs

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Background: The co-occurrence of lupus (SLE) and tropical infections has been poor studied, this group of infections, prevalent in the tropics could simulate or trigger disease activity, however, some studies suggest that malaria infection could confer protection from the development of SLE, that is for this reason, studies are required to characterize this population.
Objectives: The objective of our study was to estimate de frequency of tropical infections in patients with SLE using administrative databases in Colombia.
Methods: This study was carried out using databases generated based on technical studies conducted by the Colombian Ministry of health. For the present study, databases provided contained information from 2014 to 2017, and contains the information of approximately 20 million affiliates. A person in the database was considered a patient with SLE if she met the following operative definition: a patient who has been classified with an ICD-10 diagnosis code which corresponds to SLE in an inpatient claim or if she has been classified at least two times in outpatient claims, with a difference of minimum 30 days and less than 2 years, with a ICD-10 diagnosis code corresponding to SLE. In turn, a control group matched by age and sex was randomly selected to evaluate the difference in the frequency of tropical infections in both groups. The variables considered in this part of the study were classified in two main groups: demographic, and clinical. Demographic variables include age, sex, and department (territorial entity). As for tropical infections we use the ICD-10 diagnosis code and to estimate the prevalence of tropical infections.
Results: Using the operative definition of SLE, 5527 patients were selected, and 22108 controls paired by sex and age, the average age was 43 years old in both groups, the frequency of tropical infections was low in both groups, however, we documented a higher frequency of malaria and dengue in the group of subjects with SLE when compared to controls.
Conclusion: SLE patients had similar frequency of tropical infections compared to matched controls, except for malaria and dengue infections.

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Table 1. Prevalence of tropical infections by group

Variable	Non SLE 22 108 n (%)	SLE 5 532 n (%)
Malaria	20 (0.09)	**206 (3.72)**
Leishmania	2 (0.01)	3(0.05)
Chagas	15 (0.07)	7 (0.13)
Dengue	161(0.73)	**84 (1.52)**
Chicunguya	463 (2.09)	124 (2.24)
Zika	166 (0.75)	50 (0.90)
Yellow fever	2 (0.01)	0 (0.00)

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2876

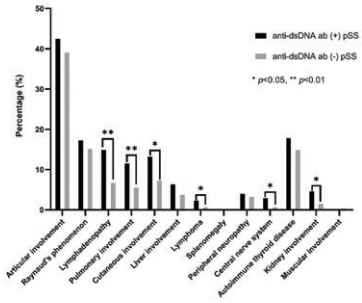
AB0637 THE CLINICAL CHARACTERISTICS OF KOREAN PRIMARY SJÖGREN'S SYNDROME (PSS) PATIENTS WITH POSITIVE ANTI-DOUBLE-STRANDED DNA (ANTI-DSDNA) ANTIBODY BY THE FARR METHOD

Keywords: Sjögren syndrome

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Background: Anti-Ro/SSA antibody is considered to play a crucial role in distinguishing the clinical features of pSS. However, the association of anti-dsDNA antibody on the characteristics and prognosis of pSS is not well known.
Objectives: We aimed to clarify the clinical characteristics of pSS patients presenting with positive anti-dsDNA antibody.
Methods: This retrospective study assessed 1255 pSS patients, fulfilling the classification criteria proposed by the American–European Consensus Group in 2002 or American College of Rheumatology/European League Against Rheumatism (EULAR) in 2016, who regularly visited Seoul St. Mary's Hospital between 2013 and 2021. Patients with other autoimmune diseases including SLE were excluded from this study. Of the total 1255 patients, 174 were in the anti-dsDNA antibody positive group (measured by using Farr assay, cut-off = 7 IU/ml) and 1081 were in the negative group. Data were compared between the two groups, including demographic features, extra-glandular manifestations (EGMs), clinical indices, and laboratory values at baseline.
Results: Patients in the anti-dsDNA (+) pSS group were younger (p = 0.015), and had higher proportion of positive finding in ocular staining score (OSS) by Sjögren's International Collaborative Clinical Alliance (SICCA) method (OSS ≥ 5) and minor salivary gland biopsy (Focus score ≥ 1) (p = 0.021 and p = 0.040, respectively). Among the EGMs, more frequent lymphadenopathy, lymphoma, pulmonary, cutaneous, renal, and CNS involvement were observed at baseline in the anti-dsDNA (+) pSS group. Total EULAR Sjögren's syndrome disease activity index (ESSDAI) scores were also higher in the anti-dsDNA (+) pSS group (median value [IQR]: 5.9 [5.1-6.7] vs 3.7 [3.4-3.9], p = 0.001). More frequency of leukopenia (p = 0.001), anemia (p = 0.001), rheumatoid factor positivity (p < 0.001), anti-Ro/SSA antibody positivity (p < 0.001), low C3 (p =0.024), low C4 (p=0.003) and hypergammaglobulinemia (p < 0.001) were found in the laboratory data in the anti-dsDNA (+) pSS group.
Conclusion: Korean pSS patients with positive anti-dsDNA antibody by Farr method showed distinct clinical characteristics at baseline including higher disease activity of SS, frequent several types of EGMs, and difference of laboratory data. Close monitoring for development of above clinical features in anti-dsDNA positive pSS patients is necessary.
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Figure 1. Comparison of EGMs between anti dsDNA ab (+) pSS and (-) pSS groups.



Acknowledgements: No acknowledgments to declare.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3594

AB0638 NEUROLOGICAL INVOLVEMENT IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: A RETROSPECTIVE CROSS-SECTIONAL STUDY

Keywords: Sjögren syndrome

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Background: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease that primarily affects the exocrine glands and eventually leads to xerophthalmia and xerostomia [1]. Up to 75% of pSS patients may experience extraglandular involvement ranging from mild arthralgia to life-threatening vasculitis [2,3]. Neurological involvement, one of the most common extraglandular manifestations associated with pSS, is classified into two subgroups: peripheral nervous system (PNS) involvement and central nervous system (CNS) involvement.
Objectives: The aim of this study is to identify the types of PNS and CNS involvement in pSS patients, as well as to investigate any relationships between clinical and immunological features and neurological involvement.
Methods: We retrospectively assessed 2127 patients with an ICD-10 code for Sjögren recorded in hospital database.Among these patients, those meeting the pSS classification criteria and having neurological symptoms and an objective evaluation accordingly were enrolled.After comparing the patients with and without neurological involvement, peripheral and central involvement subtypes were also compared within themselves.
Results: A total of 199 pSS patients were enrolled and neurological involvement was found in 31.6%. Patients with neurological involvement had a higher frequency of Schirmer's test, anti-Ro/SS-A and anti-La/SS-B positivity and presence of interstitial lung disease, articular involvement, lymphadenopathy, anemia and hypocomplementemia than patients without those. In multivariate regression analysis, only articular involvement had a higher risk for the development of neurologic involvement [OR 10.01 (4.18–23.97), p0.0001]. Among the patients with PNS, the frequency of anti-Ro/SS-A positivity, low C3 and Schirmer's test positivity were statistically increased compared to those who were not in PNS (p=0.032, p=0.044, and p=0.029, respectively). In comparison to CNS involvement, patients with CNS involvement were younger, had a shorter disease duration, and had a higher frequency of anti-Ro/SS-A positivity than patients without those (p=0.041, p=0.027, and p=0.046, respectively).
Conclusion: In our study, it was shown that one third of the symptomatic pSS patients had objective neurological involvement. The presence of neurological symptoms should be considered, especially in patients with articular involvement in pSS.
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Table 1. Comparison of clinical and immunological features of pSS patients with and without neurologic involvement

	Without neurologic involvement, n=136	With neurologic involvement, n=63	p
Female, n (%)	131 (96.3)	58 (92.1)	0.201
Age, years, mean (SD)	53.8 (10.8)	54.4 (13.1)	0.755
Age of diagnosis, years, mean (SD)	48.6 (10.6)	48.8 (13.2)	0.911
Positive Schirmer'stest, n (%)	107 (78.7)	58 (92.1)	0.020
Interstitial lung disease, n (%)	5 (3.7)	8 (12.7)	0.017
Articular involvement, n (%)	57 (41.9)	55 (87.3)	<0.001
Positive anti-Ro/SS-A, n (%)	77 (56.6)	46 (73.0)	0.021
Positive anti-La/SS-B, n (%)	40 (29.4)	25 (39.7)	0.151
Low C3, n (%)	11(8.1)	10 (15.9)	0.096

ANA: Antinuclear antibodies, Anti-SSA:Anti-Sjögren's syndrome type A antibodies, AntiSSB: Anti-Sjögren's syndrome type B antibodies

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0639 PREVALENCE OF MACE AMONG SAUDI WITH SLE

Keywords: Heart, Cardiovascular disease, Systemic lupus erythematosus

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Background: Cardiovascular diseases represent a major contributor to the increased mortality. Risk factors varies according to the subtypes of cardiovascular events and perhaps racial background. Little is known about the risk of major cardiovascular events (MACE) in Saudi lupus Population.
Objectives: This study aim to examine the prevalence of MACE among Saudi SLE compared to general population and factors associated with such outcome.
Methods: This a cross-sectional study nested within two prospective cohorts to assess the period prevalence of any MACE among SLE patients who were enrolled in national prospective cohort of SLE, Saudi Arabia since its initiation in 2020. As a comparison, Prospective Urban Rural Epidemiology Study Saudi sub-cohort (PURE-Saudi) for participants who have been enrolled during the same follow up period. Participants in both studies were followed using standardized published protocol. MACE was defined as the diagnosis of Myocardial infraction, stroke or Angina. We adjust for demographics, traditional cardiovascular risk factors and the diagnosis of SLE using logistic regression models.
Results: A total of 488 with SLE and 746 from PURE were included. SLE patients were younger (40.7±12.5 compared to 49.5±8.6) and female predominant (90.6% compared to. 41.6%). Prevalence of traditional risk factors were less in SLE patients including dyslipidemia (28.9% compared to 49.4%), obesity (63% compared to 85%) diabetes (7.8% compared to 27.2%) but not HTN (19.3 compared to 18.8%). Odds of MACE were significantly related to Age and Lupus diagnosis (OR: 1.08, 95% CI: 1.04-1.11, p=0.00) and (OR: 7.64, 95% CI: 2.65-22.07, p=0.00) but not CVS risk factors (OR: 0.8, 95% CI: 0.10-6.39, p=0.83).
Conclusion: SLE patients at significant risk of MACE compared to general population. This risk is not well explained by traditional risk factors which may explain the failure of CVS risk scores to adequately stratify SLE patients. Further work is needed to understand the pathogenesis of CVS risk in SLE and subsequently mitigate it.
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Disclosure of Interests: None Declared.
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AB0640 PREVALENCE OF COMORBIDITIES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN A MEDIUM INCOME COUNTRY, USING DATA ANALYTICS TECHNIQUES

Keywords: Systemic lupus erythematosus, Artificial intelligence, Comorbidities

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Background: Comorbidities and multimorbidity, often complicate the disease course of patients with systemic lupus erythematosus.
Objectives: The objetive was to estimate de prevalence of comorbidities in patients with systemic lupus. erythematosus using administrative databases in Colombia.
Methods: This study was carried out using databases generated based on technical studies conducted by the Colombian Ministry of health. A person in the database was considered a patient with SLE if she met the following operative definition: a patient who has been classified with an ICD-10 diagnosis code which corresponds to SLE in an inpatient claim or if she has been classified at least two times in outpatient claims, with a difference of minimum 30 days and less than 2 years, with a ICD-10 diagnosis code corresponding to SLE. In turn, a control group matched by age and sex was randomly selected to evaluate the difference in the frequency of comorbidities in both groups.
Results: We previously published the prevalence of patients with SLE, that ranges between 41.65 and 54.47 (cases/100 000), which is lower than other Latin American countries. Using the operative definition of SLE, 5527 patients were selected, and 22108 controls paired by sex and age, the average age was 43 years old in both groups, the average of comorbidities was 3.5 (SD 1.8) for SLE patients and 1.7 (SD 1.5) for control group, we found a higher prevalence for. most comorbidities, particularly those related to cardiovascular disease, kidney disease and depressive disorders in subjects with SLE compared to the control group Table 1. Table Prevalence of comorbidities by group.
Conclusion: SLE patients had a burden of comorbidities, and the prevalence of multiple comorbidities were higher compared to matched controls.
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Table 1. Prevalence of comorbidities by group

Variable	Non SLE 22 108 n (%)	SLE 5 532 n (%)
IC*	1 022 (4.62)	**720 (13.02)**
Congestive heart failure	463 (2.09)	**383 (6.92)**
PVD**	364 (1.65)	**306 (5.53)**
Cerebrovascular Disease	432 (1.95)	**290 (5.24)**
Dementia	320 (1.45)	**194 (3.51)**
COPD	2975 (13.45)	**951 (17.19)**
Peptic ulcer	146 (0.66)	53 (0.96)
Mild hepatic disease	455 (2.06)	**315 (5.69)**
Hypertension	8 683 (39.28)	**3 603 (65.13)**
Diabetes mellitus	6 333 (28.65)	**2 458 (44.43)**
Hemiplegia	157 (0.71)	**122 (2.21)**
Kidney disease	2 490 (11.26)	**2 019 (36.50)**
Tumors	2 991 (13.53)	791 (14.30)
Leukemia	374 (1.69)	**268 (4.84)**
Cirrhosis	500 (2.26)	**362 (6.54)**
Sida	468 (2.12)	160 (2.89)
Depresive disorder	1 285 (5.81)	**884 (15.98)**

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4198

AB0641 CLINICAL BACKGROUND FACTORS RELATED TO SILENT OSTEONECROSIS OF THE FEMORAL HEAD UPON INITIATION OF STEROID THERAPY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Safety, Systemic lupus erythematosus, Organ damage

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Background: Osteonecrosis of the femoral head (ONF) occurs frequently (3-40%) in patients who are treated with corticosteroids for SLE. MRI can correctly visualize pathological abnormalities of the femoral head, and it is much more sensitive than plain radiography. To analyze the risk factors associated with steroid-induced ONF, it seems important to detect early changes in the femoral head by MRI and early clinical events caused by steroid therapy. For treatment of SLE, several strategies have been selected according to the clinical conditions of patients, and there are slight differences between multicenter hospitals. In this study, the treatment performed at

two hospitals, and the treatment strategy, selection of steroid, initial dose of steroid and drugs used together with steroid have been quite similar. Therefore, it should be possible to clarify the background factors associated with ONF.

Objectives: The purpose of this study were to clarify the factors related to silent ONF in patients with SLE and, in case of ONF, to clarify the clinical characteristics between unilateral and bilateral.

Methods: One hundred thirty-two patients (18 males and 114 females) with SLE were selected on the basis of having been newly diagnosed and requiring high-dose prednisolone, including pulse therapy with methylprednisolone, as the initial treatment. All the patients initially underwent plain radiography and MRI at the start of corticosteroids to detect any early changes in the femoral head. Subsequently these examinations were performed three months thereafter. The laboratory parameters were evaluated at the beginning of steroid treatment and at one month thereafter. All statistical analyses were performed with SPSS v. 13 (SPSS Inc., Chicago, IL, USA). Statistical tests were considered significant at a P (two sided) < 0.05, and marginal significant at P = 0.05–0.10. Tests were 2-tailed, and differences at p < 0.05 were considered significant.

Results: By three months after the start of corticosteroid treatment, asymptomatic ONF was diagnosed by MRI in 33 patients (25.0%), being bilateral in 21 patients and unilateral in 12. Serological activity (C3, C4, CH50 and anti-ds DNA antibody), renal function (eGFR, serum creatinine and urinary protein), anti-phospholipid antibodies, and SLEDAI were not correlated with asymptomatic ONF. BMI, BSA, and the initial dose of prednisolone per unit body weight, BMI and BSA were not correlated with silent ONF. Additionally, the occurrence of ION was not related to SLEDAI. However, patients with angiitis tended to increase the incidence of ONF (p=0.069). Patients with a higher triglyceride level both of before (p=0.002) and 4 weeks after the start of steroid treatment (p=0.004) and total cholesterol level 4 weeks after the start of steroid treatment (p=0.036) showed a significantly higher in patients with asymptomatic ONF. In patients with ONF, the level of creatinine clearance was tended to lower (p=0.062). In unilateral and bilateral studies, both anti-ds DNA antibody and C3 were not correlated. However, despite no difference in initial steroid dosage, CH50 was significantly lower and C4 was tended to lower in patients with unilateral ONF.

Conclusion: Asymptomatic ONF is common in patients with SLE. Both of high triglyceride and total cholesterol levels are important risk factors for ONF. In unilateral and bilateral studies, excess steroid dosage relative to serologic activity of SLE might contribute to the development of bilateral ONF. In the pathogenesis ONF, it was suggested that SLE activity and steroids are closely related.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0642 ANTI-SSA POSITIVITY AND SALIVARY GLAND ULTRASOUND AS SCREENING TOOLS FOR PRIMARY SJÖGREN'S SYNDROME IN PATIENTS WITH SICCA SYMPTOMS

Keywords: Imaging, Sjögren syndrome, Ultrasound

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Background: Salivary Gland ultrasound is a sensitive point of care investigation for the assessment of salivary gland dysfunction. It can be abnormal in patients with primary Sjögren's syndrome(pSS), Sarcoidosis, IgG4 disease, Systemic sclerosis, Infections and Tumors.

Objectives: To understand the utility of Anti-SSA, ANA and Anti-SSA/SSB and Salivary gland ultrasound for diagnosing primary Sjögren's Syndrome in patients with Sicca symptoms.

Methods: In the current study, In patients referred to the department of Clinical Immunology and Rheumatology, King George's Medical University, with Sicca Symptoms, a salivary Gland Ultrasound was performed and in those with abnormal ultrasound (Hocevar Score ≥1) Clinical and serological evaluation were performed. The Sensitivity and Specificity of Salivary Gland ultrasound with a Hocevar score ≥17 to diagnose primary Sjögren's Syndrome was assessed, and the utility of ANA, Anti-SSA and Anti-SSB positivity in patients with abnormal ultrasound was assessed.

Results: A total of 78 patients with sicca symptoms and abnormal salivary gland ultrasound (Hocevar Score ≥1) were included of these, 36 were diagnosed with primary Sjögren's syndrome and 42 with other diseases, including 12 with Rheumatoid arthritis, 8 with Systemic lupus erythematosus, 7 with systemic sclerosis, 4 with IgG4 related disease and 4 with Sarcoidosis. 7 patients did not have any autoimmune rheumatic disease after evaluation. The mean age of pSS patients was 36.42 ±11.68 and for non-pSS patients was 44.45 ±15.31. A Hocevar score ≥17 has a sensitivity and specificity of 80.56% and 78.57%, respectively. Adding ANA to the screening protocol improved the sensitivity but reduced the specificity while adding Anti-SSA to the screening protocol improved sensitivity, specificity, positive likelihood ration, accuracy and area under curve for diagnosing pSS.

Conclusion: Anti-SSA positivity and abnormal salivary gland ultrasound in patients with Sicca symptoms can be effective screening tools for diagnosis primary Sjögren's Syndrome.

Table 1. Performance of different Screening methods in pSS Screening

	Ultrasound	Ultrasound + ANA	Ultrasound + Anti SSA/ Anti SSB	Ultrasound + Anti SSA
Sensitivity	*80.56%*	*82.35%*	*82.35%*	*82.35%*
Specificity	*78.57%*	*60.87%*	*90.00%*	*90.00%*
Positive Likelihood Ratio	*3.7593*	*2.1046*	*8.2353*	*8.2353*
Negative Likelihood Ratio	*0.2475*	*0.2899*	*0.1961*	*0.1961*
Accuracy	*79.49%*	*73.68%*	*84.09%*	*84.09%*
Area Under curve	*0.7956*	*0.7161*	*0.8618*	*0.8618*

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0643 THE ANALYSIS OF RISK FACTORS FOR PRETERM BIRTH AND LOW BIRTH WEIGHT IN SLE PATIENTS WITH OR WITHOUT ATTAINED LLDAS AT THE CONCEPTION

Keywords: Systemic lupus erythematosus, Pregnancy and reproduction

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Background: Women with systemic lupus erythematosus (SLE) have a higher risk for adverse pregnancy outcomes (APOs) including preterm birth (PB) and low birth weight (LBW) [1]. These APOs are revealed to be related to uncontrolled higher disease activity during pregnancy [2]. Currently, lupus low disease activity state (LLDAS), which is a comprehensive disease activity index, is suggested to be the treatment target to control damage accumulation. However, it is controversial whether achieving LLDAS during pregnancy can be a sufficient therapeutic target to prevent APOs.

Objectives: We analyze the risk factors for PB and LBW in SLE patients with or without achieving LLDAS at conception.

Methods: We used the data of SLE patients who have been treated at the planning for pregnancy from a single center cohort. We divided into LLDAS achieved

Table 1. Risk factor for PB and LBW with or without LLDAS achievement

	Achieved LLDAS			Not achieved LLDAS		
	PB (+) (n=5)	PB (-) (n=33)	P value	PB (+) (n=7)	PB (-) (n=12)	P value
Glucocorticoid use[##]	4 (80.0)	25 (75.8)	1.00	7 (100.0)	11 (91.7)	1.00
Mean glucocorticoid dose, mg/day	7.8±2.1	4.8±1.7	0.02*	14.9±4.2	10.5±2.0	0.01*
C3, md/dl[#]	86.6±18.0	95.0±21.9	0.53	70.7±17.9	96.8±18.8	<0.01*
C4, mg/dl[#]	20.0±5.5	19.6±6.5	0.88	12.8±10.4	19.3±5.6	0.06
CH50, IU/l[#]	40.9±9.4	41.8±9.2	0.78	34.2±11.3	43.1±8.4	0.09
Anti-dsDNA antibody, IU/l[#]	15.1±26.0	1.8±4.5	0.07	44.9±87.9	13.5±16.2	0.46
	LBW (+) (n=12)	LBW (-) (n=26)		LBW (+) (n=7)	LBW (-) (n=12)	
Glucocorticoid use[##]	12 (100.0)	17 (65.4)	0.04*	7 (100.0)	11 (91.7)	1.00
Mean glucocorticoid dose, mg/dl[#]	6.7±1.6	4.1±1.5	<0.01*	13.8±4.4	11.2±2.9	0.17
C3, mg/dl[#]	83.6±15.6	99.4±22.3	0.045*	75.1±17.5	94.0±22.4	0.07
C4, mg/dl[#]	18.8±3.9	20.2±7.3	0.99	15.2±9.6	18.0±7.3	0.29
CH50, IU/l[#]	36.3±4.6	44.4±9.7	0.02*	36.8±10.5	41.1±10.3	0.36
Anti-dsDNA antibody, IU/l[#]	6.9±17.4	2.1±5.0	0.54	44.4±88.1	13.8±16.2	0.58

(Values are presented as mean ± standard deviation or number (%). [#]Wilcoxon rank sum test; [##]Fisher's exact test; *P < 0.05.)

group and LLDAS non-achieved group, and evaluated the rate of pregnancy outcomes, especially in preterm birth and low birth weight. We also analyzed the risk factors for PB and LBW from therapeutic agents (glucocorticoid use and their doses), and serum immunological parameters (C3, C4, CH50 levels and the titer of anti-dsDNA antibody).

Results: In 66 pregnancies complicated with SLE, 42 cases (63.6%) achieved LLDAS at conception, while the other 24 cases (36.4%) did not. Table 1 showed the risk factors for PB and LBW by analyzed separately for LLDAS attained group and not-achieved LLDAS group. As for PB, mean glucocorticoid dose became a risk factor in both LLDAS attained group and not-attained LLDAS group (P=0.02 and 0.01). In addition, only for the group that did not achieve LLDAS, serum C3 levels were associated with the rate of PB. On the other hand, in the group achieving LLDAS, glucocorticoid use, mean glucocorticoid dose, and serum CH50 levels were identified as risk factors for LBW in addition to serum C3 levels (P=0.04, <0.01, 0.02, and 0.045). None of these factors were associated with LBW in the SLE patients without LLDAS achievement.

Conclusion: We revealed that glucocorticoid dose during pregnancy was found to be a risk factor for PB, regardless of whether or not the LLDAS was achieved at conception. As for LBW, low levels of C3 and CH50 was shown to be a risk factor even if LLDAS could be achieved at conception. Therefore, it is important to control the immunological disease activity parameters strictly for improving pregnancy outcomes, even if LLDAS, a comprehensive disease activity index, is achieved at conception.

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AB0644 OUTCOMES AND FACTORS PREDICTING MORTALITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ADMITTED TO INTENSIVE CARE UNIT

Keywords: Prognostic factors, Systemic lupus erythematosus, Descriptive studies

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Background: SLE is a chronic autoimmune disease; the course of illness is interspersed with disease flares, infections, adverse drug events which may warrant intensive care admission. Outcomes and factors affecting mortality in these patients are not well established.

Objectives: The primary objective is to describe the outcomes and causes of mortality of SLE patients admitted to ICU. Secondary objective is to analyse factors associated with mortality.

Methods: Single centre retrospective observational study from Krishna Institute of Medical Sciences, a tertiary care hospital in South India. Patient with SLE admitted to intensive care unit due to any cause between 2016 and 2021 were included. Data was collected about the characteristics of disease prior to their admission to the ICU, as well as the clinical features, laboratory values and therapeutic measures during ICU stay. Statistical analysis was done with SPSS.

Results: Eighty seven patients were included in the study. Mean age was 33.16 ± 12.6 years and 87% were females. Most common causes for admission were infection in 51 (58%) and disease flare-up in 31 (35%) patients; 34 (39%) patients had a combination of disease flare and infection. Mean APACHE II score at admission was 17.32 and mean SLEDAI-2k score at presentation was 15.16. The mean duration of ICU stay was 6.02 ± 6.58 days. Mechanical ventilation was needed for 45 patients (51%), inotropic support in 36 patients (41%) and dialysis in 19 patients (21%). The mortality rate was 21% (19 cases), 18/19 patients had both very high disease activity and sepsis. Factors correlating with mortality (on multivariate analysis) included higher APACHE II score at presentation, presence of fever, acute kidney injury, low serum albumin, low hematocrit, low glasgow coma scale, sepsis, need for mechanical ventilation, inotropic support and renal replacement therapy.

Conclusion: Mortality rate in our study population was 21%, which is in line with observed trend in last 2 decades. The leading cause of admission to ICU in our cohort was disease flare resulting from poor compliance and infections. Mortality resulted from a combination of high disease activity with infection; a difficult to manage situation for the rheumatologist and the intensivist.

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Table 1. Factors affecting mortality in our study subjects (n=87).

Parameter	p Value	r2	Correlation
Age	0.43	0.0073	No
Duration of SLE	0.45	0.006	No
Duration of current illness	0.84	0.004	No
SLEDAI-2k score	0.72	0.0014	No
Fever	**0.0019**	0.037	**Yes**
Mean arterial pressure	0.61	0.002	No
Pulse rate	0.59	0.003	No
Respiratory rate	0.74	0.0012	No
Serum Creatinine	**0.02**	0.05	**Yes**
Hematocrit	**0.0092**	0.032	**Yes**
WBC count	0.78	0.0008	No
Platelet count	0.12	0.02	No
ESR	0.24	0.016	No
Anti ds-DNA titre	0.75	0.011	No
Serum Albumin	0.03	0.049	No
GCS	**0.0015**	0.111	**Yes**
Sepsis	**0.009**	0.077	**Yes**
Disease flare	0.23	0.016	No
Mechanical ventilation	**0.00008**	0.166	**Yes**
Renal replacement therapy	**0.00007**	0.168	**Yes**
Inotropic support	**0.00003**	0.183	**Yes**

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AB0645 PREVALENCE AND DESCRIPTION OF AUTOIMMUNE POLYENDOCRINE SYNDROMES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: EXPERIENCE OF A SINGLE CENTER

Keywords: Systemic lupus erythematosus, Comorbidities, Epidemiology

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Background: Autoimmune polyendocrine syndromes (APS) are a heterogeneous group of clinical conditions characterized by functional alteration of one or more endocrine glands and often associated with other systemic autoimmune diseases. Four types of APS have been described. APS-1 is a rare autosomal recessive disease due to mutation in the AIRE gene and characterized by at least two of the following manifestations: chronic mucocutaneous candidiasis, hypoparathyroidism and Addison's Disease (AD). APS-2 is characterized by AD associated with Diabetes Mellitus Type 1 (DM1) and/or autoimmune thyroid disease. APS-3 involves the association of autoimmune thyroiditis and other organic or systemic autoimmune manifestations, excluding hypoparathyroidism and AD. APS-4 is characterized by autoimmune activity against an endocrine organ in combination with at least one more endocrine or non-endocrine organ. In literature, data regarding prevalence and incidence of APS are poor, especially in the Rheumatology field.

Objectives: The primary objective of the work is to describe the prevalence of APS in a cohort of patients with Systemic Lupus Erythematosus (SLE) followed in our Department and to assess the possible association between organic autoimmune diseases and SLE. The secondary aim is to describe the timing of onset of the different autoimmune diseases and the presence of associated comorbidities and/or any feature that may predict the development of APS.

Methods: In this retrospective observational study we included the medical history, biochemical, and immunological data of patients older than 18 years of age with SLE who are actively followed at the Department of Rheumatology and Clinical Immunology of our hospital. Patients who, in addition to the diagnosis of SLE, had at least one other autoimmune disorder against an endocrine organ were included in the study.

Results: The total number of SLE patients examined is 423, with a mean age at the last evaluation of 53 (±13), 393 were female (93%) and 30 male (7%). Forty-eight patients (11.3%) have at least one other endocrinological autoimmune disease that would allow the diagnosis of APS. The sample examined is composed of 46 (96%) females and 2 (4%) males (F:M=23:1). The mean age of the patients is 52 (±14) years; the mean age of SLE onset is 36 (±14) years. No cases of APS-1 nor APS-2 were found; 45 (94%) patients are affected by APS-3; while 3 (6%) by APS-4. Forty-three (90%) patients presented two autoimmune diseases and 5 (10%) presented three autoimmune diseases. The mean age at onset of the first disease is 31 (±12) years; the second manifestation is 39 (±13) years and the third manifestation is 37 (±11) years. Concerning the timing of the onset, SLE was the first manifestation in 17/48 patients, the second manifestation in 25 patients, the third manifestation in 1 patient and in 5 patients the diseases were diagnosed at the same time. **Figure 1** shows the different conditions according to the time of onset. The mean latency between the onset of the first manifestation and the onset of the second is 9 (±9) years. The mean latency between the onset of the second manifestation and the onset of the third is 4 (±3) years.

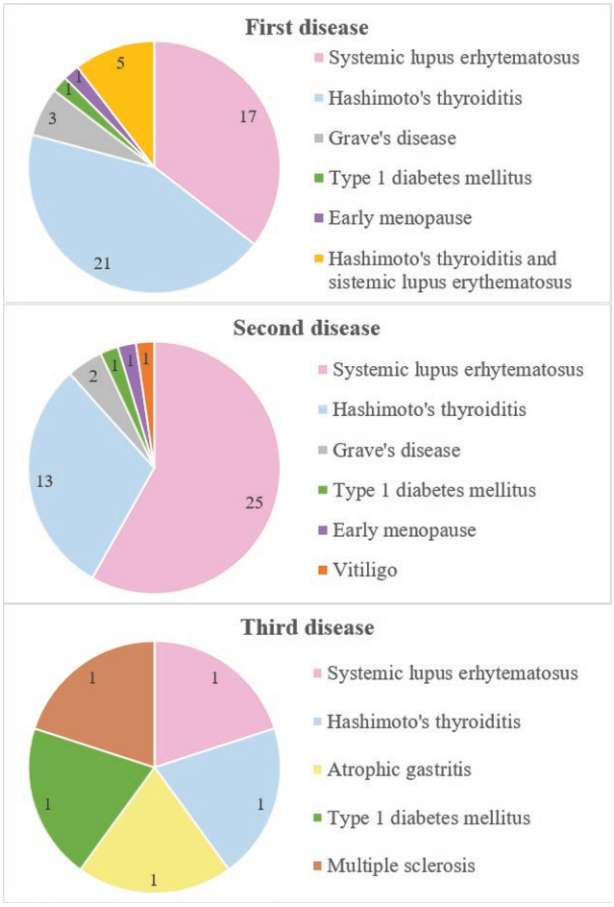


Figure 1. Time of onset of APS different pathologies

Conclusion: In our cohort of SLE patients, the prevalence of APS is quite high and occurs proportionally more in females than in males. Hashimoto's Thyroiditis (HT) is the most represented disease, followed by Graves' disease and DM1. In most cases, SLE is not the first autoimmune disease that appears in these patients. In most cases, the onset pathology is autoimmune thyroiditis. Furthermore, although the available data are scarce, in our cohort the latency between the onset of the first and second autoimmune pathology is significantly longer than the latency between the second and third manifestation.

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AB0646

CONCORDANCE OF THE DIAGNOSIS AND CLASSIFICATION OF SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Clinical trials, Autoantibodies, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a chronic, multisystemic autoimmune disease of unknown etiology. A defining characteristic is its immunological anomalies such as the production of antinuclear antibodies (ANA). Polymorphic clinical manifestations, the absence of pathognomonic signs and the absence of specific laboratory tests for SLE, make the diagnosis difficult. Although they have been developed for the homogenization of patients included in clinical trials, the SLE 2019 EULAR (European Alliance of Associations for Rheumatology)/ACR (American College of Rheumatology) classification criteria [1] can serve as a guide or diagnostic verification in individual cases from current medical practice.

Objectives: The study assessed the characteristics and consistency of the diagnosis and classification of SLE in order to measure a potential patient pool for inclusion in clinical trials.

Methods: The study retrospectively evaluated the conformity of the 2019 EULAR/ACR classification criteria in patients discharged from a single-center tertiary university rheumatology center between February 2020 and February 2022, diagnosed with SLE according to their attending rheumatologists and identified by international classification of diseases (ICD10) codes. Normally-distributed continuous variables are reported as "mean ± standard deviation". The correlation of continuous variables was studied with Spearman tests. Differences of continuous variables between nominal dichotomous subgroups were evaluated with Mann Whitney tests. Statistics were considered significant if $p < 0.05$.

Results: The study included 146 patients, of whom 92.5% were women, with an average age of 48.3 ± 13.3 years. Approximatively 7.5% of patients had negative ANA (including at repeated measurements) and 12.3% had an unknown ANA status. The method for determining ANA was ELISA (enzyme-linked immunosorbent assay; 75.3%), indirect immuno-fluorescence (2.7%) or undetermined (21.9%). Men scored a significantly higher median number of classification points than women (i.e., 21 points versus 16 points; $p = 0.020$) and they had a higher prevalence of class 3/4 nephritis (18.2% versus 3.0%; $p = 0.014$), pleuritis/pericarditis (36.4% versus 14.8%; $p = 0.064$) and oral ulcers (27.3% versus 9.6%; $p = 0.072$). Only 63.7% of SLE diagnoses also met the 2019 EULAR/ACR classification criteria. The most common manifestations not complying with these classification criteria were proteinuria (59.5% discordance), thrombocytopenia (13.6% discordance) and joint involvement (9.3% discordance). The median number of classification points correlated significantly with the median titer of ANA (*rho* = 0.301; $p = 0.001$) measured by ELISA.

Conclusion: Diagnostic reality includes ANA-negative SLE, which should be further investigated. In clinical practice, ANA are preferably determined by ELISA and their titer seems to be proportionally associated with more classifiable SLE clinical characteristics. Clinical trials have a maximum eligible SLE population of 63.7% of patients to whom additional inclusion/exclusion criteria could be applied.

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AB0647

THE SIGNIFICANCE OF A COMPREHENSIVE EXAMINATION OF DRY EYE DISEASE IN PRIMARY SJÖGREN SYNDROME AND ITS RELATIONSHIP TO EXTRAOCULAR MANIFESTATIONS

Keywords: Sjögren syndrome, Patient reported outcomes

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Background: Inflammation of the lacrimal glands leads to ocular dryness, an important cause of decreased quality of life in primary Sjögren's syndrome (pSS) patients [1]. Limited data focuses on dry eye disease (DED) in pSS. Previous studies did not conduct a comprehensive evaluation of DED using tests to measure tear film volume or instability, ocular surface damage, meibomian gland dysfunction, and patient-reported outcomes, and the disease activity parameters were not compared with these ocular findings in pSS [2].

Objectives: The aim of this study is to conduct a comprehensive evaluation of DED features in pSS patients using various methods and compare them to pSS disease characteristics and activity.

Methods: Thirty-four patients classified as pSS according to 2016 ACR/EULAR classification criteria[1] that are followed up in rheumatology clinic were included

in the study. The patients had an ophthalmologic examination and DED evaluation on the day of their routine follow-up appointments. ESSPRI scores was recorded and laboratory tests, salivary flow rate and salivary gland ultrasonography(USG) scores of the patients were recorded from the patients' files. The ophthalmologic examination includes Schirmer's test, BUT, ocular surface staining (Oxford score), Marx's line, and noninvasive BUT (NIBUT) with the Scheimplug-Placido disk system. Ocular surface disease index (OSDI) and dry eye questionnaire-5 (DEQ-5) were used for patient-reported outcomes. The relationship between the pSS-related parameters and the ophthalmologic findings was evaluated.

Results: The patient characteristics are given in Table 1. According to the TFOS-DEWSII definition and classification report, all patients have definite DED [3]. The mean Schirmer's test, BUT, and NIBUT were 3.4±5.2 mm, 5.9±3.0 sec, and 5.9±3.9 sec, respectively. The mean OSDI score was 38.2±22.7, indicating severe DED symptoms, and the mean DEQ-5 score was 10.3±6.0. Oxford score was positive in 25 (73.5%) patients. Marx's line grading that shows meibomian gland dysfunction was 3.2±2.3. The mean ESSPRI score for dryness, pain, and fatigue were 6.5±2.1, 5.4±3.2, and 5.3±3.1, respectively. There was a significant positive correlation between the ESSPRI-dryness score and OSDI (p=0.001), DEQ-5 (p=0.004), and Oxford score (p=0.03).Also, there was a significant negative correlation between patient global assessment (PGA) of general health and DEQ-5 scores (p=0.007). And there was a significant positive correlation between PGA of disease activity and OSDI and DEQ-5 scores (p=0.02 and p=0.001). Although seventeen (50%) of the patients have decreased unstimulated salivary flow rate with a median of 0.16 (0.24) ml/min, no significant correlation was observed with DED. The results of salivary gland USG were present in 12 (35.2%) of the patients, and there were 7 patients with at least one gland with an OMERACT USG score ≥2. No significant difference was found between OMERACT USG score and DED parameters, although it remained within the statistical siginificant limit for OSDI score and OMERACT USG score ≥2 in the submandibular glands (p=0.054). There was no significant difference between the DED parameters and other pSS clinical parameters.

Conclusion: Patient-reported outcomes such as ESSPRI-dryness score, PGA of general health, and disease activity worsen as DED severity increases in pSS patients.

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Table 1. The characteristics of the study population

Age, years, mean±sd	49.5± 13.3
Sex, female, n (%)	33 (97.1)
Disease duration, months, median (IQR)	73.5 (76.5)
Treatment, n (%)	24 (70.6)
Hydroxychloroquine	6 (17.6)
Methotrexate	6 (17.6)
Leflunomide	4 (11.8)
Azathioprine	2 (5.9)
Mycophenolate mofetil	2 (5.9)
Rituximab	
Disease manifestations, n (%)	31 (91.2)
Arthralgia	11 (32.4)
Arthritis	2 (5.9)
Parotitis	4 (11.3)
Interstitial lung disease	7 (20.6)
Lymphopenia	12 (35.3)
Hypergammaglobulinemia	4 (11.8)
Hypocomplementemia	

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AB0648

CYTOKINE AND CARDIOVASCULAR BIOMARKER PROFILES IN SOUTH AFRICAN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH SUBCLINICAL CARDIOVASCULAR INVOLVEMENT CHARACTERISED BY MULTIMODAL IMAGING

Keywords: Biomarkers, Heart, Systemic lupus erythematosus

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Background: Cardiovascular disease (CVD) is a leading cause of morbidity and mortality in systemic lupus erythematosus (SLE). Traditional risk tools underestimate CVD risk in young SLE patients. Identification of biomarkers may have utility in predicting CV involvement in SLE.

Objectives: To profile cytokine and CV biomarkers, associated with immune activation, fibrosis, CV dysfunction, and myocardial and vascular injury, in ambulatory South African SLE patients with subclinical CV involvement.

Methods: SLE patients, without known CVD, were recruited from rheumatology clinics at an academic hospital in Cape Town, and compared to controls matched for age, gender and ethnicity. All patients underwent echocardiography, carotid Duplex ultrasound, ankle brachial index and cardiovascular magnetic resonance (CMR) to characterise early CV involvement. Blood samples were obtained and stored at -80°C. Commercially available sandwich high sensitivity (hs) ELISA and Luminex multiplex bead assays were performed according to manufacturer's protocols to quantify biomarkers. Continuous variables were compared using Independent Samples t Test or Mann Whitney U Test. Regression analysis determined the strength and direction of associations between variables using Spearman's correlation co-efficient.

Results: 49 SLE patients attending routine outpatient follow-up, and 24 controls, were enrolled. SLE patients were 35±9 years old; 90% were women; and predominantly of mixed (69%) or black African (27%) ancestry. Median disease duration was 5 (IQR:3-8) years and patients had moderate disease activity (SLEDAI-2K=7 [IQR:4-12]) and low damage scores (SLICC-DI=1 [IQR:0-1]). On CMR, a substantial proportion (86%) of SLE patients were found to have subclinical CVD, with predominantly myocardial (78%) and pericardial (27%) involvement. We observed that despite having low C-reactive protein levels (2.54mg/L vs 2.90mg/L, p=0.36), compared to controls, SLE patients had significantly increased cytokine responses, including IL 1B, IL 6, TNFa & IFNg levels (p<0.001 for all, Table 1). Markers of fibrosis were significantly different in SLE, showing elevations in TIMP 1 (p<0.001) and galectin-3 (p=0.016), and decreased levels of MMP-9 (p<0.001). On regression analysis, MMP 9 showed an inverse relationship to all CMR parameters of myocardial fibrosis, including native myocardial T1 time, extracellular volume fraction and late gadolinium enhancement percentage (Figure 1), albeit with low co-efficient values. There were no significant correlations between hs troponin T, N-terminal prohormone of brain natriuretic peptide (NT proBNP) and soluble ST2 with parameters of myocardial dysfunction nor did cytokines measured correlate with indices of disease activity. In addition, VCAM 1, a marker of vascular injury was significantly elevated in SLE (p<0.001) but did not correlate with carotid intima media thickness or ankle brachial indices. Similar to previous studies, adiponectin showed an inverse correlation with BMI, but did not correlate with any manifestations of subclinical CVD.

Conclusion: In this cohort of young South African patients with stable SLE and subclinical CVD, we found evidence of ongoing immune activation. Low MMP 9 levels may be an early signal of myocardial disease. Plasma biomarkers may be useful in predicting CVD in SLE but larger prospective studies in SLE patients with CVD are needed.

Table 1.

Cardiovascular biomarkers	SLE (n=49)	Controls (n=24)	P value
pg/ml	**median (Q1-Q3)**	**median (Q1-Q3)**	
hs TNFa	2 (1,32-2,93)	0,58 (0,35-0,98)	<0,001
hs IFNg	3,37 (1,74-5,46)	1,25 (0,40-2,69)	<0,001
hs IL 1B	0,73 (0,46-0,93)	0,32 (0,05-0,55)	<0,001
hs IL 6	2,20 (1,33-5,51)	0,90 (0,47-1,38)	<0,001
TIMP 1	30418 (29756; 31132)	27660 (24284-30294)	<0,001
MMP 9	34791 (18583-47858)	57451 (43422-65112)	<0,001
VCAM 1	930979 (708295-1484550)	489223 (397266-733182)	<0,001

MMP matrix metalloproteinase; TIMP tissue inhibitor of MMP; VCAM vascular cell adhesion molecule

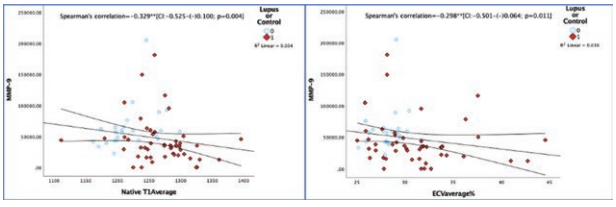


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5313

AB0649 PERIPHERAL B CELLS IMMUNOPHENOTYING IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

Keywords: Systemic lupus erythematosus, Cell biology, Biomarkers

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Background: B cells play a central role in systemic lupus erythematosus (SLE) pathogenesis connecting innate with adaptative immunity.
Objectives: To investigate the peripheral blood B cell phenotype in a cohort of SLE patients with renal (LN-SLE) and non-renal (NR-SLE) involvement compared to healthy controls.
Methods: Ninety-nine SLE patients, 76 with active renal involvement (30 at disease onset-Early and 46 in whom LN occurred after the disease onset-Long) and 23 with non-renal disease (articular and/or cutaneous) were enrolled. Thirty-seven healthy controls were included. Clinical, laboratory and demographic data were collected at baseline and at 6 and 12 months of follow-up. Disease activity was recorded using SLEDAI-2K. The memory B cells immunophenotyping (IgD/CD27 classification) was analyzed in peripheral blood through flow cytometry. To clarify the role of key molecules in the B cells activation, IL-6 and BAFF serum levels were assayed by Enzyme-linked immunosorbent assay (ELISA).
Results: Studying the B cell subsets, a lower percentage of $CD19^{pos}$ and unswitched memory ($IgD^{pos}CD27^{pos}$) in the whole SLE cohort compared to controls (8.7±6.8% *vs* 10.5±3.5%; *p=0.002* and 10.7±13.7% *vs* 15.3±8.0%; *p<0.01,* respectively) was observed. In addition, we found higher levels of double-negative memory B cells ($IgD^{neg}CD27^{neg}$) and plasmablasts ($CD27^{pos}CD38^{pos}$) in SLE than in controls [($CD27^{neg}IgD^{neg}$ 10.3±8.3% *vs* 4.1±1.9%; *p<0.01*) ($CD27^{pos}CD38^{pos}$ 6.1±7.9% *vs* 1.0±0.5%; *p<0.01*)]. Furthermore, $CD19^{pos}$ negatively correlated with BAFF (R=-0.322; *p=0.01)*. No correlation was found between B cell subsets and the disease activity parameters. According to the organ involvement, LN-SLE and RN-SLE showed a lower percentage of $CD19^{pos}$, $IgD^{pos}CD27^{pos}$ and plasmacells and higher levels of $IgD^{neg}CD27^{neg}$ than controls [($CD19^{pos}$: LN-SLE:9.1±7.4% *vs* 10.5±4.6%; *p=0.005;* NR-SLE: 7.7±4.6%; *p=0.008*)($IgD^{pos}CD27^{pos}$:LN-SLE 10.4±14.9% *vs* 15.3±8.0%; *p<0.001;* NR-SLE: 11.8±8.6%; *p=0.006*) ($CD27^{pos}CD38^{pos}$: LN-SLE 7.5±8.4% *vs* 0.9±0.5%; *p<0.001;* NR-SLE: 1.6±2.2%; *p=0.001)* ($IgD^{neg}CD27^{neg}$: LN-SLE 10.6±8.5% *vs* 4.1±1.9%; *p<0.001;* NR-SLE: 9.6±7.3%; *p=0.006*]. According to the onset of renal symptoms, there were no differences in the distribution of the renal classes and in activity and chronicity indexes in the two groups. Analyzing the B cells subsets the Long-LN-SLE showed a lower percentage of $CD19^{pos}$ and unswitched memory ($IgD^{pos}CD27^{pos}$) compared to controls (8.6±6.5% *vs* 10.5±3.5%; *p=0.004* and 9.7±6.9% *vs* 15.3±8.0%;*p=0.001,* respectively) and higher levels of $IgD^{neg}CD27^{neg}$ (12.1±8.4%) than Early LN-SLE (8.3±8.3%;p=*0.027)*, NR-SLE (9.6±7.3%;p=*0.001)* and controls(4.1±1.9%;p<*0.001)*. Furthermore, a direct correlation was observed between serum IL-6 levels and SLEDAI in Long-LN-SLE patients (r=0.380; p=0.004).
Conclusion: Data on memory B cells immunophenotyping reveals a distinct B cells subset of SLE patients when compared to healthy controls, confirming an alteration of B cells subsets in SLE patients and strengthening the hypothesis of the pathogenetic role played by B lymphocytes in the course of LN. In particular, the higher levels of DN B cells observed in patients in which renal damage occurs after the onset of SLE reinforcing the data that these cells represents a B memory subsets characteristic of immune system overactivation conditions.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5395

AB0650 PREVALENCE OF FATIGUE AND ITS IMPACT ON QUALITY OF LIFE IN THE PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

Keywords: Quality of life, Sjögren syndrome

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Background: Among the extra-glandular symptoms in primary sjogren's syndrome (pSS), fatigue and pain are the most common. Fatigue is a poorly understood phenomenon with multi-faceted involvement. Therefore, it is important to assess the severity of fatigue and describe its various dimensions while assessing fatigue. On the other hand, fatigue is also one of the predictors of reduced health and quality of life in pSS.
Objectives: To assess fatigue by Fatigue Severity Scale (FSS) and Profile of fatigue (ProF) questionnaires and quality of life (QoL) with Health Assessment Questionnaire- Disability Index (HAQ-DI) and to know the association between the two in patients with pSS.
Methods: Patients fulfilling AECG 2002 and/or ACR-EULAR 2016 classification criteria for pSS were included in this prospective observational study between January 2021 to June 2022. Fatigue was assessed with FSS and ProF and QoL was assessed with HAQ-DI. Depression and somatoform disorder were assessed using PHQ9 and PHQ15 respectively. Associations with fatigue was compared using multivariate regression analysis. Written informed consent was obtained from all subjects included in the study and the study was approved by Institute Ethics Committee.
Results: Out of 125 patients, 114 (91.2%) were female and 11 (8.8%) were male with a female to male ratio of 9.6: 1. The median age at the time of inclusion into the study was 41(32-50) years. The median duration of the disease was 36 (12-60) months. The median ESSDAI and ESSPRI score were 2 (1-3) and 6 (2-9) respectively. Fifty seven (45.6%) patients had fatigue, defined as FSS of ≥4 and/or ProF ≥2 in either of the domains. Among the patients with fatigue, 12 (21%) patients scored less than 4 on FSS, 36 (63.1%) had mild fatigue, 7 (12.2%) had moderate fatigue and only 2 (3.5%) patients had severe fatigue. The mean FSS score in the cohort was 2.9 ± 1.5. The ProF mean scores were 2.7 ± 0.6 for somatic fatigue and 2.9 ± 1.3 for mental fatigue. The median HAQ-DI in patients with fatigue was significantly more compared to non-fatigue patients (0.1 vs 0.5; p <0.001; Figure 1). There was a positive correlation between fatigue score and HAQ-DI score (rpb = 0.36, n = 125, p = <0.001). The prevalence of depression and somatoform disorder were 15.2% and 28% respectively. The ESSPRI pain score, ProFAD Ocular & Oral dryness score and PHQ-9 score were positively associated with higher fatigue score.
Conclusion: Fatigue was seen in nearly half of the patients with pSS and patients with fatigue had impaired QoL as assessed by HAQ-DI. The pain, dryness and presence of depression are the predictors of fatigue in patients with pSS.

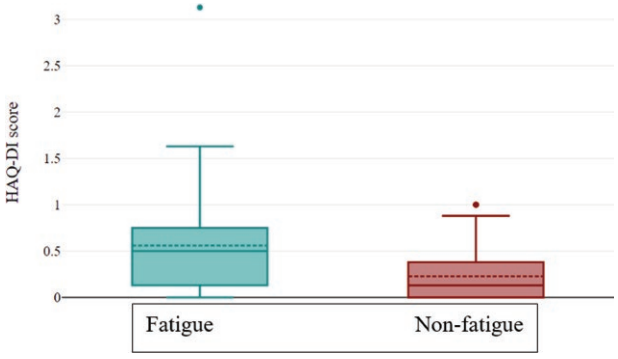


Figure 1. Median HAQ-DI among pSS patients with and without fatigue

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0651 INDIRECT HEALTH RELATED COST IN PSS PATIENTS IN RELATION TO SYMPTOM BASED ENDOTYPES

Keywords: Patient reported outcomes, Work-related issues, Sjögren syndrome

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Background: Primary Sjögren's Syndrome (pSS) is characterised by oral and ocular dryness, possible development of systemic manifestations, increased lymphoma risk, and a highly diverse patient burden. To address this heterogeneity Tarn identified four endotypes based on patient-reported symptoms of dryness, fatigue, pain, anxiety and depression: low symptom burden (LSB), pain dominant with fatigue (PDF), dryness dominant with fatigue (DDF) and high symptom burden (HSB).(1)
Objectives: The aim of this study was to explore indirect health related costs in relation to symptom-based endotypes in a cohort of patients with definite and suspected pSS.
Methods: Data from the Belgian Sjögren's Syndrome Transition Trial (BeSSTT) were used in which patients positive for at least one of the 2016 ACR/EULAR classification criteria, were enrolled. Patients were considered 'definite pSS' when fulfilling these criteria, and 'suspected pSS' otherwise. The Newcastle Sjögren's Stratification Tool (NSST), developed and provided by Tarn et al., was applied to stratify the cohort into endotypes. Patients reported their current work status and sick leave in the past year and completed the Work Productivity and Activity Impairment questionnaire (WPAI).
Results: Application of the NSST tool resulted in 4 endotypes, both in definite (LSB n=23, DDF n=33, PDF n=82, HSB n=30) and suspected pSS (LSB n=14, DDF n=22, PDF n=48, HSB n=21). The majority of definite pSS patients were female (158, 88.8%) with a mean±SD age of 53.4±14.7, with no significant differences between endotypes (p=0.365 and p=0.415). Definite pSS LSB patients reported significantly less invalidity (p=0.020). A numerically higher proportion of working PDF and HSB patients reported part time employment due to health (p=0.063). However, reported working hours did not differ between endotypes. In contrast, HSB pSS patients reported significantly more productivity loss during their job than those with LSB and DDF endotypes (p<0.001), which led to a significantly higher total work impairment (p<0.001). In addition, definite pSS patients with HSB endotype reported significantly more productivity loss during daily activities besides their job (69%, p<0.001). No significant differences concerning job characteristics were observed between definite and suspected pSS patients with the same endotype.
Conclusion: Definite pSS patients with a HSB endotype encounter significantly more work impairment than those with other endotypes, which is due to a significantly higher productivity loss while working. In addition, these patients report significantly more productivity loss during daily activities besides paid work, which entails large indirect health related costs as pSS is a predominantly female disease. Moreover, the burden associated with the HSB endotype appears to influence work ability independent of a definite pSS diagnosis.
REFERENCE:
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Table 1. Job characteristics of definite pSS patients per endotype. Continuous data presented as mean (SD), categorical data as number of patients (%).

Definite pSS without job	LSB (n=10)	DDF (n=18)	PDF (n=44)	HSB (n=17)	p
Student/retired	10 (100.0)	9 (50.0)	17 (38.6)	6 (35.3)	0.004
Unemployed	0	5 (27.8)	6 (13.6)	5 (29.4)	0.143
Invalidity	0	4 (22.2)	21 (47.7)	6 (35.3)	0.020
Definite pSS with current job	**LSB (n=13)**	**DDF (n=15)**	**PDF (n=38)**	**HSB (n=13)**	**p**
Part time due to health	1 (7.7)	4 (26.7)	20 (52.6)	7 (53.8)	0.063
Working hours past week	0 (0.0)	2.9 (9.4)	3.0 (7.5)	3.1 (6.9)	0.216
Absent: health	6.5 (11.7)	1.7 (3.1)	3.8 (7.8)	13.7 (30.8)	0.472
Absent: other	28.7 (13.6)	30.5 (10.5)	22.0 (14.1)	28.8 (15.0)	0.109
Worked	0.12 (0.18)	0.17 (0.21)	0.34 (0.29)	0.60 (0.20)	<0.001
Lost productivity due to health					
Total work impairment	0.1 (0.1)	0.2 (0.2)	0.3 (0.3)	0.6 (0.2)	<0.001

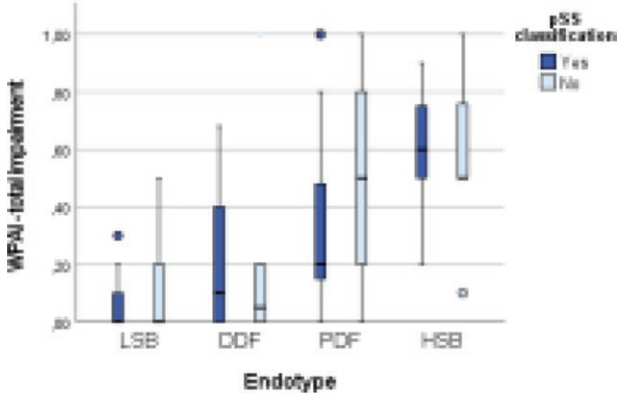


Figure 1. Box-plot visualizing total work impairment, assessed by WPAI, of definite and suspected pSS patients in relation to symptom-based endotypes. A score of 0.00 indicates no impairment, while 1.00 corresponds with total impairment.

Acknowledgements: We want to thank all BeSSTT patients for their participation.
Disclosure of Interests: None Declared.
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AB0652

HISTOLOGICAL RENAL FEATURES AND CYTOKINES ASSESSMENT AS POSSIBLE BIOMARKERS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND LUPUS NEPHRITIS

Keywords: Biomarkers, Cell biology, Systemic lupus erythematosus

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Background: Lupus Nephritis (LN) management remains a challenge for the inadequacy of the traditional parameters in identifying more severe disease and preventing renal damage.
Objectives: To identify a multipanel biomarkers matrix, from histological to molecular level, aiming to improve prognostic stratification and therapeutic protocol of LN patients.
Methods: 45 SLE patients with active disease (age: 40.5 ± 11.0 years) at disease onset or at disease flare were enrolled. 6 patients with LN in persistent remission (R-LN) (age: 43.5 ± 11.9 years) were included as controls. 28 patients had an active LN and underwent ultrasound-guided renal biopsy while 15 patients with non-renal SLE (NR-SLE) displayed cutaneous or articular manifestations. Laboratory, immunological and disease activity data were collected at baseline and then at 6(T6) and 12(T12) months. Renal biopsies were evaluated according to ISN/RPS classification, assessing the activity and chronicity indexes and the active interstitial infiltrate (II) using the BANFF score system. Serum level of BAFF, IL-2, L-6, IL-17 and IFN-α were assayed in the study cohort by ELLA panel at each timepoint.
Results: Considering LN cohort, 66% of the renal biopsies belonged to class III and IV; 71.8% of LN patients had a II>5%. Performing univariate analysis for each renal outcome, focusing on histological assessment, a significant association between higher activity index and worse renal prognosis in terms of remission achievement at 12 months (*p= 0,04*), proteinuria and chronic renal damage development (*p= 0,04* and *p= 0,03* respectively) was observed. Through the ROC curve analysis, a cut-off value of activity index of 7.5 was identified (sensitivity 72.7%, specificity 66.7%) [AUC: 0.77; 95% CI, 0.56-0.98; p= 0.04] for remission achievement within 12 months and proteinuria development. Furthermore, LN patients with presence of II>5% were not only less likely to achieve early remission (*p= 0,04*) as well as those with at least one antiphospholipid antibody (ApL) positivity (*p= 0,05*), but displayed a worse renal outcome overall, though without reaching statistical significance. The analysis of circulating cytokines revealed that serum levels of IL-6 were significantly higher in patients with active disease as compared to R-LN patients, independently from renal involvement (LN: 7.6 ± 10.0 vs R- LN: 2.1 ± 2.1, *p=0.02*; NR-SLE: 11.4 ± 17.8 vs R-LN: 2.1 ± 2.1, *p=0.02*). Moreover, baseline serum level of IFNα was significantly increased in LN patients compared to R-LN (12.1 ± 36.8 vs 1.5 ± 3.6, *p=0.01*). Serum levels of IL-6 in LN patients positively correlated with disease activity index (R=0.819; p<0.001), and negatively with C3 (R= -0.608; p=0.003) and C4 (R= -0.675; p=0.01). Furthermore, serum levels of IL-6 were associated with histological severity being significantly higher in patients with II>5% (*p= 0.01*) and positively correlating with activity index (R=0.695; *p=0.01*). The evaluation of cytokines serum levels in relation to outcome achievement revealed that NR-SLE patients with favorable course had baseline higher serum level of IL-2 than those with active disease (0.6 ± 0.2 vs 0.1 ± 0.1, p=0.01). Finally, LN patients with higher serum levels of IL-6 during the follow-up were less likely to reach remission (3.7 ± 1.8 vs 2.1 ± 1.4, p=0.02) as well as LN patients with higher serum level of IL-17 (3.4 ± 8.0 vs 0.9 ± 0.3, p=0.01*).* In particular, higher baseline serum levels of IL-17 were observed in patients who developed persistent proteinuria than those who did not (2.3 ± 2.3 vs 0.7 ± 0.5, p=0.02) and tended to remain higher also during FU, together with IL-6 serum level.
Conclusion: II>5%, higher disease activity index and Apl+ represent in our study the strongest predictors of worse renal outcome, among traditional parameters. Higher IL-6 and IL-17 serum levels, at baseline and during FU, emerge as negative prognostic factor suggesting a possible role as biomarkers of more aggressive LN. IL-2 seems to have a protective role in extra renal disease.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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SLE, Sjön's and APS - clinical aspects (other than treatment)

AB0653 PRESEPSIN IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: CLINICAL AND SEROLOGICAL ASSOCIATIONS

Keywords: Biomarkers, Systemic lupus erythematosus

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Background: Presepsin (soluble CD14 subtype) is a newly recognized biomarker of sepsis. Recently it has been reported that presepsin levels are elevated in patients with systemic lupus erythematosus (SLE) without infection, possibly due to phagocytosis of neutrophil extracellular traps by monocytes/macrophages [1]. However, the clinical significance of presepsin in SLE remains uncertain [2].
Objectives: This study aims to evaluate the relation between serum presepsin levels and clinical manifestations, disease activity and laboratory parameters in SLE patients.
Methods: A total of 78 SLE patients (aged 38.9±12.8 years; 87.2% females) and 16 age- and sex-matched healthy controls were enrolled. Patients with infections were not included in the study. Serum presepsin levels were determined by ELISA and were analyzed in relation to SLE organ and system involvement, routine laboratory tests, inflammatory markers, serum complement levels, autoantibody spectrum, and the overall disease activity assessed by Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Mann-Whitney test, Spearman and Pearson correlation tests were used for statistical analysis.
Results: The median serum presepsin level was significantly higher in patients with SLE than in healthy controls (137 (95-197) pg/ml vs 66 (62-77) pg/ml, p<0.001). SLE males had higher presepsin concentration compared with females (180 (140-156) pg/ml vs 130 (90-170) pg/ml, p=0.02). Presepsin levels were significantly lower in SLE patients with involvement of skin (124 (84-157) pg/ml) and musculoskeletal system (111 (87-153) pg/ml) compared to those without such manifestations (164 (110-210) pg/ml, p=0.032 and 145 (122-175) pg/ml, p=0.041, respectively). However, SLE patients with fever (215 (170-1606) pg/ml vs 130 (93-166) pg/ml, p=0.004), nephritis (145 (110-197) pg/ml vs 102 (82-146) pg/ml, p=0.011), anemia (170 (126-280) pg/ml vs 130 (92-280) pg/ml, p=0.04) and thrombocytopenia (198 (170-280) vs 130 (92-161) pg/ml, p=0.049) had higher presepsin levels than those without such symptoms. Significant correlation was found between presepsin concentration and estimated glomerular filtration rate (r=-0.440, p=0.017). Presepsin levels did not correlate with white blood cell count, C3, C4, C-reactive protein, erythrocyte sedimentation rate and procalcitonin levels. Presepsin levels in patients with lupus nephritis significantly correlated with SLEDAI score (r=0.461, p=0.008) and anti-dsDNA levels (r=0.545, p<0.01); no such associations were found in SLE patients without kidney involvement.
Conclusion: Higher serum presepsin levels in SLE patients are associated with male gender, fever, kidney involvement, anemia and thrombocytopenia. Further research focused on clinical use of presepsin in SLE is warranted.
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Disclosure of Interests: None declared
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AB0654 PHOSPHATIDYLSERINE PROTHROMBIN COMPLEX ANTIBODIES UTILITY IN PLACENTAL INSUFFICIENCY MANAGEMENT. A CASE CONTROL STUDY IN A GENERAL OBSTETRIC CARE UNIT

Keywords: Diagnostic tests, Pregnancy and reproduction, Anti-phospholipid syndrome

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Background: The clinical utility of new antiphospholipid antibodies in cases of adverse obstetric outcomes is not well known[1].
Objectives: To assess the performance of antibodies against the phosphatidylserine prothrombin complex (IgM and IgG), onwards "anti-PS/PT" in preeclampsia or foetal growth restriction.
Methods: A case control study was performed in a private maternal general care unit. Cases were patients with preeclampsia or foetal growth restriction developed before the 37th weeks of gestation. The full sample was calculated in 92 cases and 192 controls. Controls were patients who were hospitalized in the third trimester of gestation, with age +/- 5 years old respect to the controls, without known autoimmune diseases or history of adverse obstetric outcomes. All patients were studied with general laboratory, doppler, classical antiphospholipid antibodies and anti-PS/PT IgG and IgM. We present demographic characteristics and media comparisons which were performed with T test. Categorical variables were compared with Chi square test or Fisher test if applicable. The statistical significance was established in 5% (p<0.05). Informed consent from the patients as well as approval from the institutional ethics committee were obtained.
Results: Two hundred and eighty-four pregnant women were included (192 controls and 92 cases). Demographic and clinical data of the groups are presented in Table 1. The median (IQR) anti-PS/PT IgM titles were 8 (8) MPL U/ml in cases and 9 (9) MPL U/ml in controls, p>0,05. Regarding to anti-PS/PT IgG test, the median (IQR) titles were 5.5 (3) GPL U/ml in cases and 5 (5) GPL U/ml in controls, p>0,05
Conclusion: We did not find association between ant-PS/PT both IgG or IgM in cases of foetal growth restriction or preeclampsia. It is worth to note that this study was performed in a general care maternity, therefore, high risk cases were not included. Further analysis may show the utility of this biomarkers in obstetric adverse pregnancy outcomes management, particularly in other contexts as recurrent pregnancy loss, foetal death, or early severe preeclampsia[1,2].
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Table 1. Demographic and clinical data of cases and controls.

	Cases (n=92)	Controls (n=192)	p value
Maternal age (years) (mean, SD)	29.2 (6.1)	30.6 (5.7)	>0.05
Gestational age at inclusion (weeks) (mean, SD)	34.8 (3.3)	37.4 (4.3)	<0.001
Systolic blood pressure at inclusion (mmHg) (mean, SD)	130.6 (19.6)	116.14 (12.5)	<0.001
Diastolic blood pressure at inclusion (mmHg) (mean, SD)	79.1 (14.4)	68.9 (10.4)	<0.001
Foetal growth restriction (n, %)	52 (56.5%)	0	<0.001
Severe preeclampsia (n, %)	17 (18.4%)	0	<0.001
Weight of newborns (grams) (mean, SD)	2395 (681)	3314.6 (503.6)	<0.001

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Disclosure of Interests: None declared
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AB0655 PREVALENCE AND RISK FACTORS ASSOCIATED WITH THROMBOCYTOPENIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AT HOSPITAL DEL MAR

Keywords: Descriptive studies, Anti-phospholipid syndrome, Systemic lupus erythematosus

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease with a variety of manifestations, one of which is immune thrombocytopenia (ITP). Immune thrombocytopenia has been reported in 7-40% of SLE patients [1,2].
Objectives: To determine the prevalence of ITP in SLE patients and identify risk factors that correlate with ITP.
Methods: Retrospective case-control study. 407 medical records of SLE patients were reviewed: 34 patients were diagnosed with ITP (cases) and were age- and

sex-matched with 2 controls with SLE without ITP. Differences between cases and controls were analysed as well as factors associated with ITP.

Results: ITP prevalence in our cohort was 8.35% and was diagnosed at age 43.35±17.70 years (mean±st dev). No significant differences were found in demographic variables. At lupus diagnosis, controls had a higher prevalence of arthritis (p-val= 0.02), while cases presented a higher proportion of haemolytic anaemia (p-val=0.04). Along SLE disease, cases had higher antiphospholipid syndrome (APS) antibodies (lupus anticoagulant, p-val=0.01; anti-cardiolipin, p-val=0.044, anti-β2GP1, p-val=0.003). Cases presented a significantly higher SLICC than controls (p-val=0.02). Regarding treatments, cases received mycophenolate (p-val=0.02) and azathioprine (p-val=0.045) more frequently than controls.

Table 1. Characteristics of cases and controls.

VARIABLES	CASES (34)	CONTROLS (68)	P-VAL
Photosensitivity[a]	13/34 (38.2%)	37/68 (54.4%)	0.14
Arthritis[a]	17/34 (50.0%)	50/68 (73.5%)	0.02 (*)
Haemolytic anaemia[a]	4/34 (11.8%)	1/68 (1.5%)	0.04 (*)
Raynaud's phenomenon[a]	1/34 (2.9%)	10/68 (14.9%)	0.09
Low C3[a]	13/32 (40.6%)	14/64 (21.9%)	0.09
Low C4[a]	7/31 (22.9%)	6/64 (9.4%)	0.11
Low CH50[a]	5/31 (16.1%)	4/61 (6.7%)	0.15
Antinuclear antibodies[b]	34/34 (100%)	68/68 (100%)	1
Anti-dsDNA[b]	20/34 (58.8%)	41/68 (60.3%)	1
Anti-RNP[b]	5/33 (15.2%)	20/67 (29.9%)	0.14
Anti-cardiolipin[b]	15/33 (45.5%)	17/68 (25.0%)	0.04 (*)
Anti-β2GP1[b]	13/33 (39.4%)	8/66 (12.1%)	0.003(*)
Lupus anticoagulant[b]	10/33 (30.0%)	6/66 (9.1%)	0.01 (*)
Actual SLEDAI[c,d]	2.12 (Min=0, Max=13)	1.75 (Min=0, Max=12)	0.20
Actual SLICC[c]	1.12 (Min=0, Max=6)	0.41 (Min=0, Max=3)	0.02 (*)
Corticoids[e]	23/34 (67.7%)	48/68 (70.6%)	0.82
Mycophenolate[e]	14/34 (41.2%)	12/68 (17.7%)	0.02 (*)
Azathioprine[e]	9/34 (26.5%)	7/68 (10.3%)	0.045 (*)
Rituximab[e]	6/34 (17.7%)	3/68 (4.4%)	0.06

(*) Indicates statistically significant differences between cases and controls (level of confidence 95%). [a] Clinic and biochemical parameters at SLE diagnosis. [b] Immunologic parameters along SLE course. [c] Indicates mean and range. [d] SLEDAI-1 in cases. [e] Treatments along SLE course. Anti-β2GP1: Anti- β2-Glycoprotein 1. SLEDAI: SLE disease activity index. SLICC: SLE damage index

Conclusion: Patients with SLE that develop ITP seem to have a different phenotype than those without ITP, presenting less arthritis and more haemolytic anaemia at SLE disease onset, and more APS syndrome and APS antibodies along the disease. In addition, ITP was associated with a higher SLICC and with more frequent use of mycophenolate and azathioprine, possibly indicating a more severe disease, which would warrant the need of a more careful follow-up on these patients in the patients with the previously described associated characteristics.

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AB0656

PERFORMANCE OF CONVENTIONAL CARDIOVASCULAR RISK SCORES IN IDENTIFYING SUBCLINICAL ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Autoantibodies, Cardiovascular disease, Systemic lupus erythematosus

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Background: Cardiovascular disease (CVD) is a major cause of mortality in systemic lupus erythematosus (SLE) with a standardized mortality ratio of 2.4, that is underestimated by conventional CVD risk scores. Subclinical atherosclerosis, a major predictor of cardiovascular morbidity is an important target for primary prevention. Carotid intima media thickness (cIMT) and plaques are frequently used measures of subclinical atherosclerosis. Role of conventional risk scores which look at cardiovascular events, in assessment and risk stratification of subclinical atherosclerosis in SLE is not fully established.

Objectives: Assess performance of QRESEARCH database risk score-3 (QRISK3), systemic coronary risk evaluation (SCORE) and WHO (World Health Organization) CVD risk scores in assessing subclinical atherosclerosis in SLE and healthy controls. Compare SLE disease parameters between those with and without subclinical atherosclerosis.

Methods: This is a single centre cross-sectional analytical study. 79 patients with SLE without CVD and 76 age and gender matched healthy controls were enrolled. Demography, disease activity indices, autoantibodies, steroid dose were noted. Subclinical atherosclerosis (any carotid plaque or abnormal cIMT) was assessed. CVD risk was calculated by QRISK3, SCORE and WHO scores. Sensitivity, specificity, positive and negative predictive values were assessed. Agreement between scores was determined using kappa coefficient. Presence of subclinical atherosclerosis was compared with SLE disease manifestations.

Results: Subclinical atherosclerosis was seen in 52% of SLE (abnormal cIMT in 47% and carotid plaque in 8%) and 53% of healthy controls (abnormal cIMT in 47% and plaque 12%). Mean age of SLE and controls was 45±6 and 46±6 years respectively with 99% females. Average SLE duration was 96±64 months, SLEDAI was 1 ±2.3 and median SLICC ACR DI was 1 (0-2). SCORE, WHO and QRISK3 had a sensitivity of 0%, 10% and 28% in detecting subclinical atherosclerosis in SLE, 20%, 22% and 5% in controls while specificity was 0%, 82% and 79% in SLE and 97%, 91% and 100% in controls respectively. Kappa agreement was 0 for SCORE with others, 31% between QRISK3 and WHO 68% for plaque and 31% for cIMT in SLE. In healthy controls Kappa agreement was 0 for SCORE with others, 0 between QRISK 3 and WHO 15% for plaque and 31% for cIMT. SLE disease parameters were comparable among those with and without subclinical atherosclerosis. Anticardiolipin IgG (14.6% vs 2.6%) and any APLA positivity (41.5% vs 21%) were numerically higher in SLE with atherosclerosis but not statistically significant (p >0.05).

Conclusion: Sensitivity of conventional CVD scores in detecting subclinical atherosclerosis was very poor in SLE with QRISK3 and WHO score having good specificity. Hence until further scores are validated, screening for subclinical atherosclerosis using carotid ultrasound remains gold standard.

Table 1. Comparison of disease parameters among SLE patients with and without Subclinical Atherosclerosis

	SC Atherosclerosis n=41	No SC atherosclerosis n=38	P Value
Age years (Mean± SD)	42±6	45±6.1	0.38
Anti ACLA IgG n(%)	**6(14.6)**	**1(2.6)**	**0.07**
Any APLA positive n(%)	**17(41.5)**	**8(21)**	**0.9**
Disease duration months (Mean± SD)	92±57	101±71	0.77
Clinical SLEDAI (Mean± SD)	0.5±1.4	0.7±1.8	0.33
SLICC ACR DI (Median + IQR)	0(0-1)	0(0-1)	0.46
Standardized steroid dose mg (Mean±SD)	183±70	161±81	0.20
SCORE (Median + IQR)	0(0-2)	0(0-2)	0.86
WHO (Mean± SD)	2.56±1.6	2.86±2	0.85
QRISK 3(Mean± SD)	7.7±3.6	8.4±6	0.33

SC- subclinical

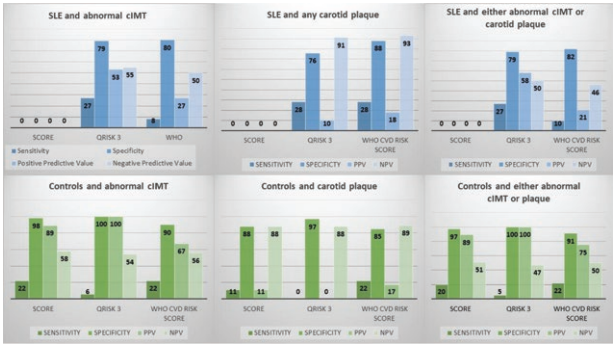


Figure 1. Sensitivity, specificity, positive and negative predictive values of scores in SLE and control

Disclosure of Interests: None declared

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AB0657

VALIDITY OF THE SLE DISEASE ACTIVITY SCORE (SLE-DAS) IN A COHORT OF EGYPTIAN JUVENILE-ONSET SLE PATIENTS

Keywords: Systemic lupus erythematosus

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Background: Juvenile-onset SLE patients (JSLE) are commonly characterized by a more severe and deleterious disease. Hence, treating-to-target is crucial to attain favorable outcomes, and it relies on several factors including optimal disease activity assessment. However, data about evaluating disease activity in JSLE patients is mostly extrapolated from adult-onset patients, with data about the validity of the SLE-DAS[1] among JSLE patients lacking, to the best of our knowledge.
Objectives: Assess the SLE-DAS as a potential activity assessment tool among JSLE patients.
Methods: This cross-sectional study included 108 JSLE patients (≤16 years) managed at the rheumatology departments of Cairo University in November 2022. Adult patients with juvenile onset were not included. The SLEDAI-2K[2] was set as the gold standard. The SLE-DAS was measured through its online designed calculator (http://sle-das.eu/?)[3]. Validity and agreement between the SLE-DAS and the SLEDAI-2K were assessed through Spearmen's rho correlation and Bland-Altman plot, respectively. The correlation between both scores was evaluated among patients with and without high disease activity (HDA ≥10)[4]. Damage was measured utilizing the SLICC/SDI[5].
Results: Of 108 patients, 95 (87.9%) were females. Age at onset and assessment were 9.8 ± 2.6 and 10.8 ± 2.4 years, respectively; whereas the mean disease duration was 43.8 ± 28.1 months (Median: 36). The most common cumulative manifestations included constitutional (71.8%), renal (65%), hematologic (55.1%), and mucocutaneous (47.6%) involvement. Serositis, arthritis, and neuropsychiatric manifestations were present in 35.5%, 27.3%, and 24.5% patients, respectively. The mean SLEDAI-2K was 14.4 ± 6.8 (Median: 14), whereas the mean SLE-DAS was 25.3 ± 14.4 (Median: 23.3). 80 (74%) patients demonstrated HDA. There was a significant correlation between both the SLE-DAS and SLEDAI-2K (rho = 0.24; p=0.001). There was a significant, yet lower, positive correlation (rho= 0.24; p = 0.03) between the two scores among patients with HDA, whereas there was no significant correlation between them among those with lower disease activity [rho = - 0.2; p = 0.19]. The mean difference of agreement between both scores was 9.3 + -1.02*Average-of-Scores [Bland-Altman plot (Figure 1)]. Cross-sectionally, there was a significant correlation between the SLICC/SDI and both the SLEDAI-2K (p = 0.001) and SLE-DAS (p < 0.0001).
Conclusion: Our preliminary findings denote that the SLE-DAS could be utilized to assess disease activity among JSLE patients. Yet, its implementation among JSLE patients with lower levels of disease activity should be carefully interpreted.
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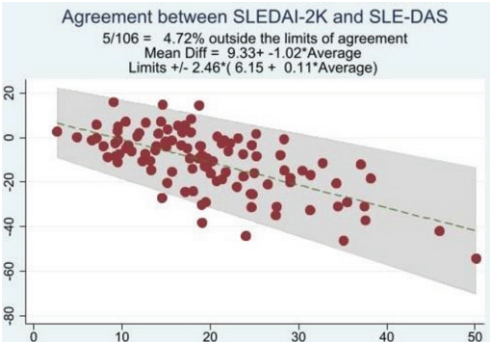


Figure 1. Bland-Altman Plot to show agreement between the SLEDAI-2K and SLE-DAS.

Disclosure of Interests: None declared
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AB0658

PREVALENCE AND ASSOCIATION OF AUTOANTIBODIES WITH LATENT TUBERCULOSIS IN FIRST-DEGREE RELATIVES OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Autoantibodies, Systemic lupus erythematosus

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Background: Systemic Lupus Erythematosus (SLE) patients have a higher risk of tuberculosis (TB). Detection of latent TB (LTBI) by mycobacterium tuberculosis (TB) IFN-γ release assay (TB-IGRA) is an important step to retard progression to overt TB. Among IGRA positive persons, studies have noted a dose-response relationship, where those with lower baseline levels IFN-γ have lesser risk of progression to over TB. A family history of SLE exerts an increased risk of other autoimmune diseases. Although several studies reported autoantibodies in first-degree relatives (FDR) of SLE patients, association between LTBI and antibodies is not clear. The current study focused on the role of antibodies and LTBI in FDRs of SLE.
Objectives: Study the prevalence of autoantibody levels and LTBI in FDRs of SLE. Evaluate whether seropositivity of autoantibodies confers any risk of TB.
Methods: This is a single centre cross sectional study. FDRs of SLE with no past h/o TB were recruited (n=167). Demography, comorbidity and various autoantibodies were measured by Enzyme Linked Immunosorbent Assay. LTBI was assessed using TB-IGRA. Based on the results of TB-IGRA and seropositivity to antibodies, FDR were divided into 4 groups- Autoantibody positive and negative groups with and without LTBI. Basal IFN-γ and Mtb antigen specific IFN-γ levels were assessed in the unstimulated and Mtb antigen stimulated tubes.
Results: In FDRs, prevalence of autoantibodies and LTBI were 24.5% (n=41) and 25.7% (n=43) respectively. Seropositivity of various autoantibodies were comparable between those with and without LTBI. Among the antibody positive FDR, prevalence of LTBI was 34%, which is higher than the general population cohort. Next, we measured the basal IFN-γ levels in the 4 groups, where the IGRA and autoantibodies positive group had significantly (p=0.014) reduced levels of basal IFN-γ compared to IGRA positive antibody negative group. In the Mtb specific antigen tubes also, the antibody and IGRA positive group showed significantly reduced response compared to the IGRA positive and autoantibody negative group.
Conclusion: The present study showed higher prevalence of LTBI (34%) in the antibody positive FDRs of SLE. Basal and stimulated levels IFN-γ were lower in antibody positive group in contrast to SLE patients who have higher basal IFN-γ. Further longitudinal studies would be required to see the effect of these autoantibodies on LTBI and the risk of progression to TB.

Table 1. Demography and autoantibody in first degree relatives of SLE

		Total(n-167)	IGRA Negative (n=124)	IGRA Positive(n=43)	P Value
Age (years)	Mean(±SD)	39.1(±12.7)	38.5 (±12.5)	41 (±12.9)	0.26
Gender	Male	65 (38.9%)	46 (37.1%)	19 (44.2%)	0.41
	Female	102 (61.1%)	78 (62.9%)	24 (55.8%)	
Antibody	Negative	126 (75.4%)	97 (78.2%)	29 (67.4%)	0.16
status	Positive	41 (24.6%)	27 (21.8%)	14 (32.6%)	
Antibodies	Cardiolipin IgG	3 (1.8%)	2 (1.6%)	1 (2.3%)	0.76
	Cardiolipin IgM	9 (5.4%)	5 (4.0%)	4 (9.3%)	0.189
	Glycoprotein IgG	5 (3.0%)	3 (2.4%)	2 (4.7%)	0.5
	Glycoprotein IgM	0 (0%)	0 (0%)	0 (0%)	
	Anti-thyroid peroxidase	10 (6%)	7 (5.6%)	3 (7%)	0.75
	Anti-cyclic citrullinated polypeptide	3 (1.8%)	2 (1.6%)	1 (2.3%)	0.76
	SERINE	3 (1.8%)	3 (2.4%)	0 (0%)	0.30
	Anti-glutamic acid decarboxylase	3 (1.8%)	2 (1.6%)	1 (2.3%)	0.76
	Anti-islet antigen 2	3 (0.8%)	1 (4.7%)	2 (1.8%)	0.10
	Antinuclear antibody	21 (13%)	15 (12.5%)	6 (14.6%)	0.73

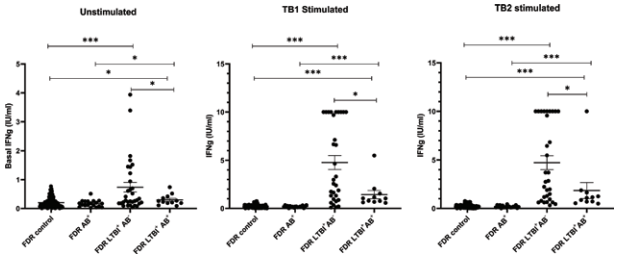


Figure 1. IFN-γ levels in unstimulated and Mtb antigen stimulated tubes

Disclosure of Interests: None declared
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AB0659 **EXTREMELY LOW FREQUENCY OF CHRONIC HEPATITIS B INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS**

Keywords: Clinical trials, Systemic lupus erythematosus

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Background: There are few studies evaluating the frequency of chronic hepatitis B virus (HBV) infection in systemic lupus erythematosus (SLE) patients (1).
Objectives: Aim of this study is to determine the HBV seroprevalence in SLE patients and to compare it with normal population and patient control groups (rheumatoid arthritis and spondyloarthritis).
Methods: HBV serology tests [hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), hepatitis B core antibody (HBcAb)] performed during the diagnosis of 278 SLE patient and the control group [consist of 125 rhomatoid arthritis (RA) and 125 spondhyloarthritis patient (SpA)] were analyzed retrospectively between 2005-2022 in two different centers. Patients with SLE responding to the 2019 ACR/EULAR criteria were included. HBV serology characteristics of SLE patients were compared with those of the normal population and control groups. The categorical data were presented as numbers (in percent). The chi-square test or Fisher's exact test was used to analyze the categorical variables. We compared 95% confidence intervals (95% CI) for the HBV infection rate of each variable; 95% CI which did not overlap were considered as statistically significant. Statistical significance was considered as p<0.05.
Results: HBsAg was positive in 2/278 (0.7%) in SLE patients, 6/125 (4.8%) in RA patients, and 9/125 (7.2%) in SpA patients. HBsAg positivity rate in SLE patients was lower than two different national normal population analysis [%4, (218/5960), %4,57, p=0,008] and RA (p=0,019) and SpA patients (P=0,003) (2,3). HBcAb positivity rate in SLE patients (%15) was significantly lower than both normal population (%30.6) and RA (%42.7) and SpA (%30.6) patients (Table 1). Analysis of SLE patients clinical outcomes showed that less oral ulceration (5/38 vs 57/210, p=0.067) and skin lesions (18/38 vs 140/208, p=0.018) occured in the HBcAb positive patients compared to negative patients. There was no relationship between other clinical findings and the HBcAb positivity. The HBcAb positive SLE patients were older than negative patients (51±10 vs 42±13, p<0.001).

Table 1. Hepatitis B seroprevalence of SLE and control groups

	SLE	RA	P_{SLE-RA}	SpA	$P_{SLE-SpA}$	Normal population (TURHEP)	$P_{SLE-normal\ population}$
HBsAg positive	2/278 (%0.7)	6/125 (%4,8)	**0,019**	9/125 (%7,2)	**0,003**	218/5960 (%4)	**0,008**
HBcAb positive	41/273 (%15)	44/103 (%42,7)	**<0,001**	37/121 (%30,6)	**<0.001**	1670/5460 (%30,6)	**<0,001**
HBsAb positive	107/278 (%38.5)	62/117 (%53)	**0.008**	51/122 (%41,8)	0,43	1746/5460 (%31,9)	**0.023**
HBsAb positive and HBcAb negative	77/273 (%28.2)	26/103 (%25,2)	0,33	25/121 (%20 ,7)	0,11	463/5460 (%8,4)	**<0,001**
HBsAb and HBcAb positive	30/273 (%11)	30/103 (%29,1)	**<0.001**	25/121 (%20 ,7)	**0,01**	1212/5460 (%22,2)	**<0,001**
HBsAb negative and HBcAb positive	11/273 (%4)	14/103 (%13,6)	**<0,001**	12/121 (%9,9)	**0,02**	251/5459 (%4,6)	0.659

Conclusion: The positivity rate of HBsAg and HBcAb was lower in SLE patients than both normal population and other inflammatory disease subgroups such as SpA or RA. Lower HBsAg and HBcAb seroprevelance in SLE patients compared to normal population and also to other inflammatory diseases (SpA and RA), maybe due to specific protective mechanisms in SLE pathogenesis (like the association of familial mediterrenian fever and pestilence). This mechanism can be explained with the high interferon levels in SLE patients. To properly understand these mechanisims we need more prospective and molecular studies.
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AB0660 **PREDICTIVE PARAMETERS FOR THE DEVELOPMENT OF PERIPHERAL NEUROPATHIES IN PRIMARY SJÖGREN'S SYNDROME**

Keywords: Sjögren syndrome

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Background: Sjögren's syndrome is a heterogeneous inflammatory disorder frequently involving peripheral nerves with a significant clinical and prognostic impact. The early detection of hematological and immunological parameters might improve disease control and even patients' survival.
Objectives: The objective of this study was to evaluate the predictive potential of hematological and immunological elements for the development of peripheral neuropathies (PN) in pSS patients.
Methods: In this single-centre, retrospective study, a total of 252 participants were included (131 pSS patients and 121 healthy controls). According to the neurologic examination and the result of the neuro electrophysiological examination, these patients were divided into two groups, with and without PN. Complete blood count, inflammatory and immunological parameters were determined at the initial visit. All patients underwent a periodical follow-up program when disease progression and response to therapy were monitored, including the emergence of PN.
Results: In pSS patients, cellular count, Vitamin B12 and D values were significantly decreased compared to healthy subjects ($p < 0.001$), whereas cellular ratio- NLR, PLR, immunological and inflammatory parameters were significantly increased ($p < 0.001$). In the PN patients group (41 patients 31.29%), gammaglobulins negatively correlated with vitamin B12 and total proteins ($p < 0.05$), while ESSDAI scores positively correlated with NLR and PLR ($p < 0.05$). The multivariate analysis confirmed the independent predictive character for PN emergence in pSS for NLR (CI95% 0.034 to 0.254, $p < 0.010$), gammaglobulins (CI95% -0.409 to -0.114, $p < 0.001$), vitamin B12 (CI95% -0.001 to -0.001, $p < 0.001$) and vitamin D (CI95% -0.018 to -0.006, $p < 0.001$).
Conclusion: Standard hematological and immunological parameters, widely used in assessing pSS patients, such as NLR, gammaglobulins, vitamin B12 and D, could become valid elements that might be used for the early detection of patients at risk for the development of PN. The hematological parameters related to platelets appear to be modified in patients with SS and cutaneous manifestations. However, only the neutrophil-to-lymphocyte ratio is independently associated with cutaneous involvement in these patients.
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Disclosure of Interests: None declared

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AB0661 CHANGES OF LYMPHOCYTE SUBSETS IN CONNECTIVE TISSUE DISEASE(CTD) WITH DIFFERENT TYPES OF PATHOGEN BLOODSTREAM INFECTIONS

Keywords: Adaptive immunity, Systemic lupus erythematosus

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Background: The underlying cause of autoimmune diseases is not known,infections, especially viral infections, is thought to be a possible reason[1].Disorder of CD4+T cells have been linked to autoimmunity, they are key players in various autoimmune diseases but are also crucial for immunity against different infections[2]. However, the immune response status of different types of infections in the context of autoimmune diseases is poorly understood.

Objectives: To evaluate the differences of lymphocyte subsets in connective tissue disease(CTD) with different types of pathogen bloodstream infections.

Methods: We analyzed 40 CTD patients with bloodstream infections, including 11 with virus infections,7 with fungal infections,13 with Gram negative bacteria infections(G- infection), 9 with Gram positive bacteria infections(G+infection), and 10 newly diagnosed CTD patients without co-infection were included as controls.The percentage and absolute numbers of lymphocyte phenotypes and CD4+ T subsets in peripheral blood were examined by flow cytometry.

Results: There were no significant difference in the percentage and absolute value of T,B,NK,CD4+T,CD8+T cells in different types of infection groups and no-infection group. Among comparison of the CD4+T subsets, the percentage of Th2 in the fungal infection was decreased than G- infection group and no-infection group,while the G- infection was increased than G+infection,and the virus infection was increased than fungal infection. The percentage of Th1,Th17 and Treg had no significant difference between different groups. Whereas for the absolute value comparison, the absolute value of Treg cells in the virus infection was higher than the fungal infection,G- infection and G+ infection, meanwhile the the fungal infection was obvious lower than no infection group. But there was no significant difference in Th1 and 17 among all groups.

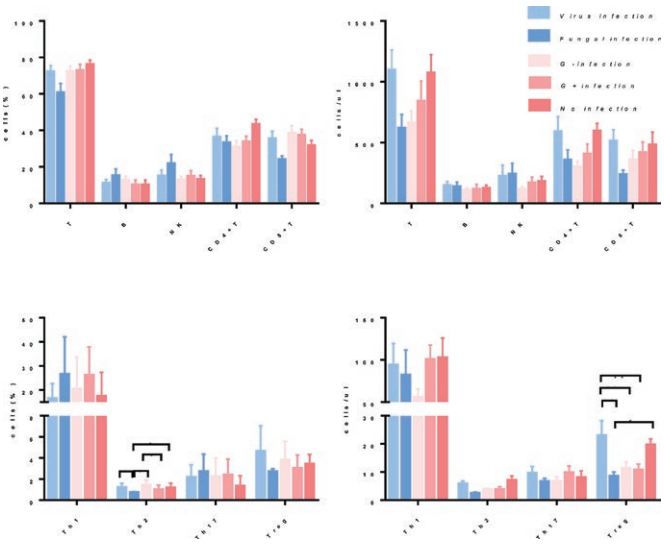


Figure 1. The comparsion about the lymphocyte subsets in different CTD groups.(*p<0.05,** p<0.001).G- infection: Gram negative bacteria infections.G+ infection:Gram positive bacteria infections.

Conclusion: Different types of pathgen blood may lead to development of specific immunological dysbalance,especially in the case of autoimmune disease hosts. CTD patients with fungal infection had lower Th2 response, higher Treg cells may be a characteristic of CTD combined with virus infection compare with other types of infection.

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AB0662 PERIPHERAL PLATELET-GENERATING MEGAKARYOCYTE REDUCED IN PRIMARY SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome

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Background: Primary Sjogren's Syndrome (pSS) is a complex and heterogeneous systemic autoimmune disease characterized by dysfunction of the secretory glands following chronic inflammation of lymphocytic infiltration.[1] Megakaryocytes (MKs), the precursor cells responsible for platelet production, act across the immune continuum.[2] However, the underlying pathogenesis of pSS involving megakaryocytes (MKs) is still to be elucidated.

Objectives: This study aimed to determine the changes in megakaryocyte subsets in pSS patients and to explore the role of different subsets in the pathogenesis of pSS.

Methods: The scRNA-seq dataset of five patients with pSS and five HCs were obtained from the GEO database to identify megakaryocytes (MKs) among PBMCs and further define the subpopulations. Then, cellular identity was determined by identifying the DEGs for each cluster using the Wilcoxon rank-sum test with the FindAllMarkers function and comparing the markers to known cell-type-specific genes from previous datasets. Finally, to investigate the hierarchy and developmental relationship between MK subpopulations, the monocle3 analysis was used to reconstruct pseudotime trajectories.

Results: First, four putative subpopulations (MK1-MK4) of MKs were identified by sub-clustering (Figure 1A). MK3 referred to as platelet-generating MKs, expressed key genes involved in hemostasis, cell-extracellular matrix interactions and so on. (Figure 1B) MK2 shared the same marker as MK3, but exhibited lower expression, which means MK2 may be an early stage of MK3, known as proplatelet-generating MKs. Then, compared with other MKs, MK2 and MK3 had the highest platelet activation-related and platelet aggregation-related pathways scores generated by ssGSEA (Figure 1F). Remarkably, the inflammatory response subpopulation (MK4), consisting of MKs expressing LSP11 and CD53 at high levels, was enriched in Immune system development and T-cell activation (Figure 1D). And, the proportion of the MK1, MK2, and MK4 subpopulations increased and that of the MK3 subpopulation was reduced in patients with pSS vs. HCs (Figure 1C), indicating the impaired maturation of platelet-generating MKs in pSS patients. Finally, with the trajectory analysis, we inferred that MK4 could exist independently of other MK subpopulations, and MK1 may characterize the point of initiation of a developmental trajectory (Figure 1E).

Conclusion: In summary, we have presented evidence for the reduction of peripheral platelet-generating MKs in patients with pSS, and identified changes in platelet-generating MKs via scRNA-seq analyses. The findings provide clues to the impaired maturation of platelet-generating MKs in the pathogenesis of pSS.

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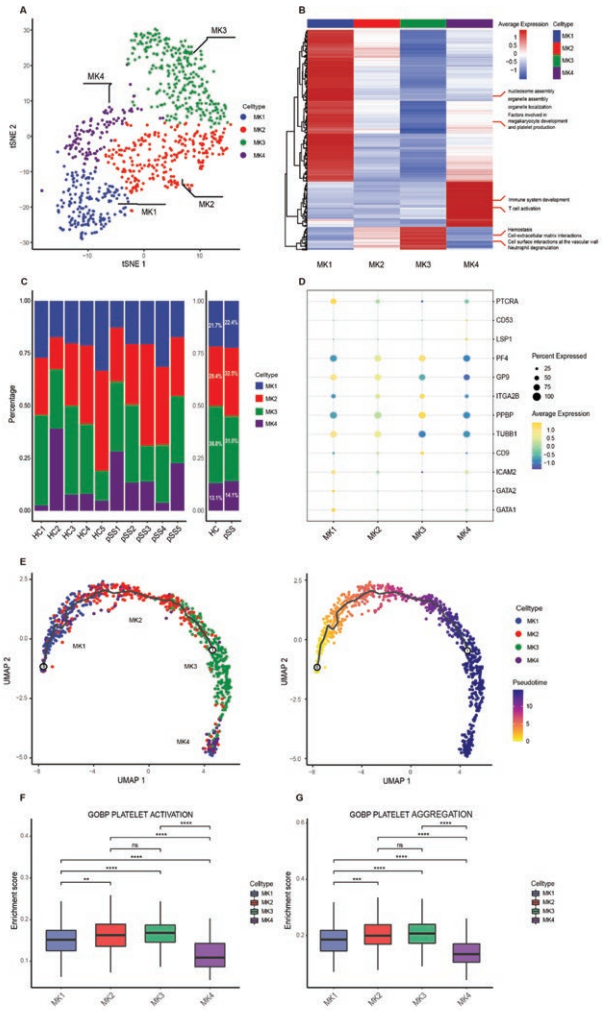


Fig. (A) The t-SNE plot highlighted the four MK subpopulations across patients with pSS and HCs. **(B)** Heatmap showing the markers and enriched biological processes and signalling pathways of each MK subpopulation. **(C)** Stacked bar charts showing the percentage of each MK subpopulation among total MKs in patients with pSS and HCs. **(D)** The dot plot shows the expression percentages and expression levels of canonical marker genes of different clusters of MKs. **(E)** Monocle pseudotime trajectory analysis of MKs, indicating only one developmental direction. MK subpopulations along the branching trajectories (left). The inferred pseudotime for each cell is shown (right). **(F-G)** box plots indicating the significantly enriched platelet-related pathway scores generated by ssGSEA across each MK subpopulation.

Figure 1.

Disclosure of Interests: None declared
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AB0663 **FOLLOW-UP FREQUENCY IN PATIENTS WITH SLE, 'ONE SIZE DOES NOT FIT ALL'**

Keywords: Systemic lupus erythematosus, Health services research, Real-world evidence

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Background: The recommended frequency of follow-up for SLE patients ranges from monthly to yearly, although once every 3 months seems common practice. Recommendations are based on expert opinion; data on frequency of follow-up in SLE patients and its impact are very scarce. (1,2,3)
Objectives: To assess the frequency of follow-up visits in SLE patients and its relation to clinical and sociodemographic characteristics.
Methods: Patients with SLE based on the '97 ACR criteria (4), who were treated at our regional teaching hospital between 2012 and 2021, were included in the study. Frequency of follow-up was defined by the frequency at which blood tests (Hb as a key indicator) were performed for disease assessment. This frequency was related to clinical characteristics. Kruskal–Wallis and Fisher's exact test were performed.

Results: 238 SLE patients were included in the cohort; 117 patients (49%) had follow-up at an average of three months (interval 60-120 days), 59 patients (25%) had follow-up at a low intensity (interval >120), and 62 (26%) at a high intensity (interval <60 days). Characteristics of these groups are shown in Table 1. The patients with high intensity follow-up were younger, more often non-white and had more severe disease at diagnosis. Upon evaluation, these patients had a more severe disease course as demonstrated by more treatment intensifications, hospitalizations, ER visits, a higher SLICC damage index and more frequent renal involvement. Conversely, the patients that were monitored at a low intensity were older had longer disease duration and showed a more quiescent disease with less negative health outcomes. Figure 1 shows the linear relationship between the frequency of tests and the number of abnormal results in Hb.
Conclusion: This study shows that the frequency of follow-up varies substantially between SLE patients. A majority of patients had follow-up at a frequency of 3 months, patients that differed from this norm had distinct features. At this moment frequency of follow-up depends on clinical judgment of the physician. Potentially, this process might be captured in prognostic modelling. Patients at high risk should be identified and have a high frequency of follow-up, while in other patients resources could be spared.

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Table 1. Characteristics per follow-up group

	Low intensity (n = 59)	Average (n = 117)	High intensity (n = 62)	
Age, mn (SD)	54 (16.3)	52 (14.6)	46 (14.7)	**0.005**
Non-white (%)	15 (26)	48 (41)	36 (58)	**0.008**
Number of ACR-criteria at diagnosis, m (IQR)	4 (4-5)	4 (4-6)	5 (4-6)	**0.006**
Disease duration in years at baseline, m (IQR)	6 (1-17)	6 (1-16)	3 (0-10)	**0.014**
% abnormal values – Hb, mn (IQR)	0 (0 - 25)	27 (3 - 63)	47 (15 - 76)	**<0.001**
% abnormal values - urine, mn (IQR)	2 (0 - 11)	8 (1 - 22)	22 (10 - 50)	**<0.001**
Kidney biopsy, n (%)	3 (5)	21 (18)	24 (39)	**<0.001**
Intensification of therapy per yr, m (%)				**<0.001**
≥2	1 (2)	10 (9)	13 (21)	
Hospitalizations per yr, m (%)				**<0.001**
0	55 (93)	86 (74)	33 (53)	
≥2	1 (2)	4 (3)	13 (21)	
ER visits per yr, m (%)				**<0.001**
0	54 (91)	90 (77)	38 (61)	
≥2	1 (2)	3 (3)	8 (13)	
SLICC DI, n (%)				**0.035**
≥2	11 (19)	41 (35)	22 (35)	

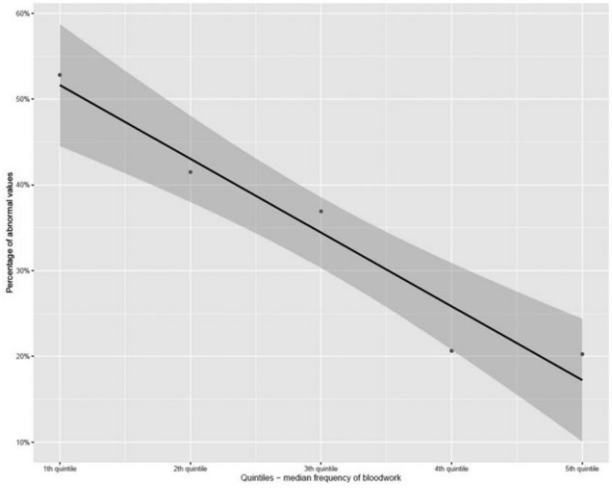


Figure 1. Relationship between frequency and number of abnormal blood tests

Disclosure of Interests: Selinde Snoeck Henkemans: None declared, Annelies Berden: None declared, Geeke Waverijn: None declared, Iris Verberk-Jonkers: None declared, Marc Kok: None declared, Els Zirkzee Consultant of: Yes, GSK 2018 advisory board
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AB0664 COMORBIDITIES IN PRIMARY SJÖGREN'S SYNDROME: A CROSS-SECTIONAL STUDY

Keywords: Comorbidities, Sjögren syndrome

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Background: Patients suffering from autoimmune diseases have a higher risk of developing comorbidities compared to the general population. The screening of these comorbidities is important, for it affects the patient's quality of life as well as the physician's therapeutic decisions. The epidemiological data concerning the comorbidities associated with the primary Sjögren syndrome pSS are heterogenous, and to our knowledge, no such study exists on the scale of the Lebanese population.
Objectives: The aim of this study is to expand the knowledge around the comorbidities associated with the pSS, in a cohort of Lebanese patients. This goal is achieved by analyzing the frequency of these comorbidities and their association with the patients' biological profile.
Methods: It's a cross-sectional study conducted on a population of 61 Lebanese patients, followed in a rheumatology clinic inside of Hôtel Dieu de France University Hospital in Beirut. The mean age of this population is 54 years, and 60 out of 61 participants are women. All of these patients meet the pSS classification criteria of the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR), established in 2016. On the one hand, the prevalence of each comorbidity is calculated, and on the other hand, the association between the patient's biological profile and the existing comorbidities has been analyzed.
Results: The most common comorbidities are: dyslipidemia (34.43%, 95% CI 23%-46%), hypertension (32.79%, 95% CI 21%-45%), obesity (26.23%, 95% CI 15%-37%), and hypothyroidism (18.03%, 95% CI 8%-28%). A significant correlation exists between hypocomplementemia (C3 and/or C4) and diabetes (p-value = 0.0026), as well as between hypocomplementemia and hypothyroidism (p-value = 0.024). Another significant correlation is noted between the presence of the rheumatoid factor and each of the following comorbidities: dyslipidemia (p-value = 0.005), diabetes (p-value = 0.0026), hypertension (p-value = 0.005), and hypothyroidism (p-value = 0.0037).
Conclusion: The Lebanese patients followed for pSS in our cohort form a population who is at risk of developing a metabolic syndrome alongside a thyroid disorder. In the light of these findings, these patients should benefit from a close cardiovascular risk factors and thyroid dysfunction screening and management, especially those presenting a particular biological profile like the presence of hypocomplementemia or the positivity of the rheumatoid factor.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2023-eular.1682

AB0665 LONG-TERM EXPOSURE TO PM10 AND SYSTEMIC-LUPUS-ERYTHEMATOSUS-RELATED MORTALITY IN THE KOREAN POPULATION

Keywords: Systemic lupus erythematosus

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Background: The effect of air pollutants on the risk or progression of systemic lupus erythematosus (SLE) has been evaluated in several studies. However, their results were inconsistent and large-scale investigations are lacking.
Objectives: We evaluated the effect of particulate matter (PM) 10 on the risk or prognosis of SLE in a cohort drawn from a very large number of SLE cases registered in a nationwide database.
Methods: A case-cohort study consisting of 23,511 SLE cases and 204,521 cohorts was conducted using NHIS customized data. The district-specific annual average PM10 concentration for the year 2004 was estimated using a land-use regression model. A mixed Cox proportional hazard regression with random intercepts for districts was performed to evaluate the association between PM10 and the SLE risk for the general population and between PM10 and mortality for SLE patients.
Results: There was no significant association between PM10 exposure and SLE risk. However, the plot of the association between PM10 exposure and mortality in male SLE patients followed an inverted U-shape. Compared to the first quintile, the hazard ratios of mortality for the second, third, fourth, and fifth quintiles were 1.541 (95% confidence interval [CI]: 1.049–2.185), 1.278 (95% CI: 0.893–1.829), 1.395 (95% CI: 0.972–2.002), and 1.266 (95% CI: 0.881–1.818). Those associations were not significant in females.
Conclusion: A past PM10 exposure was associated with high mortality in male SLE patients. Further studies of the risk associated with a higher than average PM exposure level are needed.
Disclosure of Interests: None declared
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AB0666 THE RELATIONSHIP BETWEEN NEUROPATHIC PAIN AND AUTOANTIBODY POSITIVITY AND SALIVARY GLAND BIOPSY IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Autoantibodies

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Background: Sjögren's syndrome (SjS) is an autoimmune disease characterized by exocrine gland inflammation (1). Extraglandular manifestations are common in SjS. Some articles reported neuropathic pain in 40% of patients with SjS (2). Autoantibodies (SS-A, SS-B, Anti Ro-52) and salivary gland biopsy are used to diagnose SjS. The relationship between autoantibody, salivary gland biopsy results, and neurological involvement is unclear.
Objectives: In this study, autoantibody positivity and salivary gland biopsy results were compared with the frequency of neuropathic pain.
Methods: Patients with a diagnosis of Primary SjS who visited the rheumatology outpatient clinic of Sakarya University between August 2021 and August 2022 were included in the study. The results of salivary gland biopsy and autoantibody (ANA, SS-A, SS-B, Anti-Ro 52) were analyzed. The LANSS (The Leeds Assessment of Neuropathic Symptoms and Signs) pain scale was used to define neuropathic pain. Obtained data were evaluated with Chi-Square and Mann-Whitney U test.
Results: Sixty-six patients were included in the study. Patients' age (mean): 53.5±11.3 years; genders were 3 (4.5%) male and 63 (95.5%) female. While 18 (27.3%) patients have neuropathic pain, 48 (72.7%) patients did not have neuropathic pain. No statistically significant difference was found between neuropathic pain and disease duration (p=0.584). There was no difference in neuropathic pain in terms of gender (p=0.178). While the rate of neuropathic pain was 25.6% in patients with a focus on biopsy, it was 45.5% in patients without focus, and the difference was not statistically significant (p=0.270). No statistically significant correlation was found between anti-SSA, Anti-SSB, and Anti-Ro52 positivity and neuropathic pain. In ANA-negative patients, the increase in the frequency of neuropathic pain was statistically significant (p=0.031).

Table 1.

	Neuropathic Pain Present	Neuropathic Pain Absent	p
ANA			
positive n(%)	8(18,6)	35(81,4)	0,031
negative n(%)	10(43,5)	13(56,5)	
Anti-SSA			
positive n(%)	3 (13)	20(87)	0,098
negative n(%)	13 (31,7)	28 (68,3)	
Anti-SSB			
positive n(%)	1 (8,3)	11 (91,7)	0,266
negative n(%)	15 (28,8)	37 (71,2)	
Anti-Ro52			
positive n(%)	5 (22,7)	17 (77,3)	0,670
negative n(%)	10 (27,8)	26 (72,2)	

Conclusion: In this study, we did not find a relationship between antibody positivity, focus score, and the frequency of neuropathic pain.
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Disclosure of Interests: None declared
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AB0667 CHARACTERIZING ULTRASOUND-PROVEN ENTHESITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS: PREVALENCE AND IDENTIFICATION OF DISEASE SUBSET WITH LESS FREQUENT RENAL INVOLVEMENT

Keywords: Systemic lupus erythematosus, Ultrasound, Epidemiology

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Background: Musculoskeletal inflammation is a frequent and debilitating feature of Systemic Lupus Erythematosus (SLE) that can involve all components of the joint, including extra-synovial sites such as the entheses[1]. In previous reports, enthesitis could be clearly demonstrated by musculoskeletal ultrasound (US) in small cohorts of patients with SLE[2,3]. However, SLE-enthesitis remains frequently overlooked and its prevalence in real-life cohorts as well as its clinical significance for disease classification and therapy remain to be determined.
Objectives: To assess the prevalence of US-confirmed enthesitis in a monocentric cohort of patients with SLE and to analyze the clinical associations to enthesitis during the course of disease.
Methods: Ultrasound examinations of SLE patients presenting with tender and/or swollen joints at the Lupus Unit of the Careggi University Hospital in Florence (Italy) were retrospectively analyzed to assess the presence of enthesitis. Patients with US-proven enthesitis were compared with SLE controls who showed no US-evidence of enthesitis. Clinical features and therapies were compared between the two groups at disease onset and throughout follow-up.
Results: We assessed 400 patients fulfilling EULAR/ACR classification criteria for SLE. In 106 of them, an US examination of the joints was performed. Evidence of enthesitis was found in 31/106 (29.2%) patients. Four participants were excluded due to lack of follow-up data. The remaining 71 patients without US-enthesitis were included as control group (**Figure 1**). At disease onset, all clinical features were comparable between enthesitis cases and controls. Clinical manifestations and therapy from disease onset to the last available follow-up are reported in **Table 1**. The median follow-up was of 10.0 (IQR 8.3-23.3) years for cases and 12.4 (IQR 7.2-13.3) years for controls. Patients with enthesitis were less likely to develop renal involvement (22.6% vs 46.5%, p<0.05), had more arthritis (100.0% vs 81.7%, p<0.01) and failed B-cell depleting therapies more frequently (75.0% vs 0%).
Conclusion: In SLE patients with tender or swollen joints, enthesitis is a fairly common finding. Enthesitis in SLE could be the hallmark of a distinct disease subset with less frequent renal involvement, more arthritis, and poor response to B-cell depletion, potentially requiring alternative treatments.
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Table 1. Clinical and demographic characteristics.

	Cases of SLE with US enthesitis	SLE controls without US enthesitis	p-value
N	**31**	**71**	
Female, N (%)	26 (83.9%)	67 (94.4%)	0.126
Age at US-assessment, median (years) (IQR)	50.0 (45.4-51.6)	51.3 (43.9-59.4)	0.456
Disease manifestations from SLE onset to LFU			
Musculoskeletal, N (%)	31 (100.0%)	58 (81.7%)	0.009*
Cutaneous, N (%)	23 (74.2%)	44 (62.0%)	0.264
Hematologic, N (%)	25 (80.7%)	46 (64.8%)	0.160
Mucosal, N (%)	8 (25.8%)	12 (16.9%)	0.416
Neurological, N (%)	8 (25.8%)	16 (22.5%)	0.801
Renal, N (%)	7 (22.6%)	33 (46.5%)	0.028*
Serositic, N (%)	7 (22.6%)	19 (26.8%)	0.806
Gastrointestinal, N (%)	5 (16.1%)	6 (8.5%)	0.302
Therapy from SLE onset to LFU			
Corticosteroids +/- HCQ, N (%)	12 (38.7%)	21 (29.6%)	0.369
Therapy, N (%)	-	-	-
MMF, N (%)	7 (22.6%)	18 (25.4%)	1.000
MTX, N (%)	6 (19.4%)	15 (21.1%)	1.000
AZA, N (%)	6 (19.4%)	11 (15.5%)	0.773
CSA, N (%)	4 (12.9%)	4 (5.6%)	0.241
CYC, N (%)	4 (12.9%)	4 (5.6%)	0.241
RTX, N (%)	8 (25.8%)	12 (16.9%)	0.416
Belimumab, N (%)	8 (25.8%)	20 (28.2%)	1.000

*statistically significant for p<0.05.SLE: systemic lupus erythematosus; IQR: interquartile range; SD: standard deviation; US: ultrasound; LFU: last follow-up; AZA: azathioprine; HCQ: hydroxychloroquine; MMF: mycophenolate mofetil; CCY: cyclophosphamide; CSA: cyclosporine; MTX: methotrexate; RTX: rituximab.

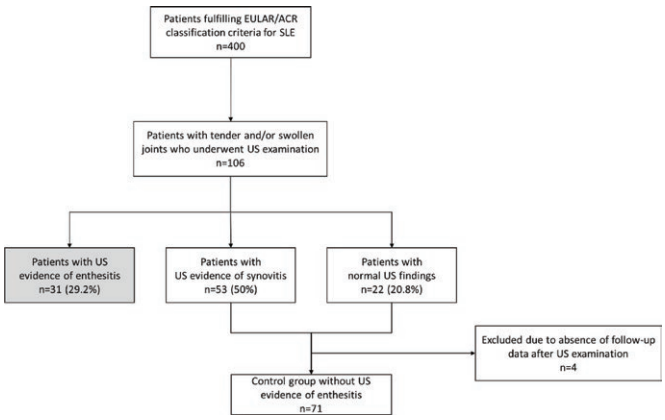


Figure 1. Flow-chart of the patient selection processSLE: Systemic Lupus Erythematosus; US: ultrasound

Disclosure of Interests: None declared
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AB0668 **BENEFITS OF ANA SCREENING FOR NPSLE IN PATIENTS ADMITTED TO THE DEPARTMENT OF PSYCHIATRY**

Keywords: Systemic lupus erythematosus, Diagnostic tests, Autoantibodies

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Background: Neuropsychiatric systemic lupus erythematosus (NPSLE) presenting with mood disorder, headache, psychosis, and cognitive impairment appears within 1 year of SLE diagnosis in more than half of cases (1, 2). Most studies have focused on the epidemiology of neuropsychiatric manifestations in patients with established SLE (3). Therefore, diagnosing NPSLE in patients who have visited the hospital with psychiatric symptoms is challenging. Although some studies have conducted anti-nuclear antibody (ANA) screening in psychiatric patients, none have occurred in an Asian population (4, 5).
Objectives: We aimed to determine the benefits of ANA screening for NPSLE in patients admitted to the department of psychiatry in Korea.
Methods: We investigated patients admitted to the department of psychiatry who underwent ANA testing between January 2015 and December 2021 at a single tertiary center in Korea. Patients diagnosed with SLE before admission were excluded from this study. Electronic medical records, including ANA titer, extractable nuclear antigen (ENA), complement, brain magnetic resonance imaging, electroencephalogram, and cerebrospinal fluid analysis, were reviewed retrospectively. Diagnosis at psychiatric hospitalization was classified according to the International Classification of Diseases (ICD)-10.
Results: Throughout the study period, 2523 patients were hospitalized, 1355 of whom underwent ANA testing. Three patients with SLE were excluded. The median age of all patients was 40 (27–58), and 897 (66.2%) were female. Of the 1355 patients, 96 (7.1%) were positive with a titer of ≥1:80, and 61 (4.5%) were positive with a titer of ≥1:160. Among the 17 patients who underwent ENA testing, 1 was positive for anti-Ro and anti-La, eventually diagnosed with Sjogren's syndrome. According to the diagnostic classification of admission, there was no significant difference in the ANA positivity rate (p=0.205).
Conclusion: There was no difference in the positivity rate of ANA in the general population when testing was performed for screening purposes on patients admitted to the psychiatric department. Additionally, none of the 1355 patients were diagnosed with NPSLE after undergoing ANA screening. Thus, the benefits of performing routine screening appear to be limited.
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Table 1. Baseline characteristics of patients admitted to the department of psychiatry who underwent ANA testing

	N = 1355
Female	897 (66.2)
Age, years	40 (27-58)
ANA titer	
1:80	35 (36.5)
1:160	37 (38.5)
1:320	12 (12.5)
1:640	8 (8.3)
1:1280	4 (4.2)
ANA fluorescence	
Nucleolar	25 (26.0)
Speckled	36 (37.5)
Discrete speckled	11 (11.5)
Homogeneous	24 (25.0)
Diagnosis at hospitalization	
Organic, including symptomatic, mental disorders	44 (3.2)
Mental and behavioral disorders due to psychoactive substance use	47 (3.5)
Schizophrenia, schizotypal and delusional disorders	324 (23.9)
Mood disorders	748 (55.2)
Neurotic, stress-related and somatoform disorders	166 (12.3)

Values are n (%), or median (interquartile range); ANA: anti-nuclear antibody

Disclosure of Interests: None declared

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AB0669 CUTANEOUS LUPUS ERYTHEMATOSUS OVER THE COVID MAJOR PANDEMIC PERIOD, INCIDENCE AND CLINICAL CHARACTERISTICS

Keywords: Systemic lupus erythematosus, COVID

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Background: Cutaneous Lupus Erythematosus (CLE) is a chronic inflammatory autoimmune disease with a broad spectrum of clinical manifestations and a variable course, often induced by exogenous factors. CLE is classified in specific and non-specific manifestations with the former divided in acute cutaneous LE (ACLE), subacute cutaneous LE (SCLE), chronic cutaneous LE (CCLE) and intermittent cutaneous LE (ICLE).

Objectives: To assess clinical features of CLE patients over the major pandemic period and its impact on disease characteristics.

Methods: Multi-center retrospective study conducted on consecutive CLE outpatients referring to the Rheumatology and Dermatology Units of Tor Vergata Hospital and San Gallicano Institute (Rome, Italy).

Inclusion criteria: diagnosis of CLE, age ≥ 18 years, and 4 years continuous follow-up from Mar 2018.

Data from every visit performed between Mar '18 - Feb '22 were registered for each patient, including: number of visits performed/skipped, demographics, therapy, number of skin flares (yes/no, via BILAG score) and systemic flares (yes/no, SLEDAI-2K increase ≥4 points), type of cutaneous manifestation, Sars-CoV2 infection and SLICC damage index score (SDI).

Number of visits, clinical course of disease, occurrence of Sars-CoV2 infection and therapy were compared in two periods: pre-pandemic outbreak (1 Mar 2018-29 Feb 2020) and first-wave pandemic (01 Mar 2020-28 Feb 2022).

Results: 80 patients were enrolled, 65 females, aged 55.2±14.3 with a disease duration of 32.1±19.8 (Tab 1). In the 1st period 398 visits were performed while only 180 resulted in 2nd with a number of visits/patient/year of 1.9 vs 1.1. Skipped and telemedicine visits amounted to 11 and 1 in the 1st period e to 31 and 21 in 2nd period respectively.

Statistical significant differences emerged in number of documented cutaneous flares: 28 (8.8%) in 1st period vs 42 (23.3%) in 2nd (p=0.03). A higher incidence in the 2nd period of ACLE (15% vs 30%, p<0.01), cutaneous calcinosis (0% vs 10%, p<0.01) and livedo reticularis (10% vs 1.2%, p<0.03) and a lower incidence of CCLE (13% vs 2.5% (p=0.02) were observed compared to the 1st pre-pandemic period.

Although mean SLEDAI-2k resulted significantly lower in the 2nd period (2.67 vs 2.13, p=0.02) compared to the 1st one, SLEDAI-2k score related to skin was higher in the 2nd period compared to the 1st (0.8 vs 1.1 (p=0.04). A significant reduction in the percentage of patients treated with topical therapy was registered in 2nd period (p=0.008) while other medications remained stable.

30 patients (37.5%) contracted Sars-CoV2 infection, no differences were registered between patients with infection and those that did not contract infection regarding number of visits, skin and systemic flares, SLEDAI-2K and SDI, therapy and clinical characteristics.

Conclusion: We reported how the major pandemic period – with general reduction in outpatients' medical assistance – consisted in a conspicuous increase in cutaneous flares as quantifiable in higher ACLE incidence and reduced topical treatment. At the same time, incidence of systemic flares – along with systemic treatments – remained substantially stable. In conclusion, it appears that patients suffered a burden of cutaneous manifestations after the pandemic period not associated to any systemic impact.

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Table 1. Measures as m±ds and % (n) when appropriate.

Patients	N=80		p
	1st period	2nd period	
N° cutaneous flares	8.8 (28)	23.3 (42)	0.03
N° systemic flares	27.5 (22)	16.2 (13)	-
Specific CLE: ACLE	15 (12)	30% (24)	0.03
SCLE	2.5 (2)	6.2 (5)	-
CCLE	13.7 (11)	2.5 (2)	0.01
Non-specific CLE: Livedo	10 (8)	1.2 (1%)	0.03
Raynaud's	6.2 (5)	11.2 (9)	-
Purpura	3.7 (3)	6.2 (5)	-
Alopecia	15 (12)	6.2 (5)	-
Cutaneous calcinosis	0	10 (8)	0.001
SLEDAI2K	2.6±1.1	2.1±0.9	0.02
SLEDAI2K skin domains	0.8±0.83	1.1±0.9	0.04
SDI	1.4±1.2	1.1±1.3	-
Prednisone, mg	2.6±2	2.8±2.1	-
Prednisone	67.5 (54)	63.7 (51)	-
Topical therapy	31.2 (25)	13.7 (11)	0.008
HCQ	78.7 (63)	80 (64)	-
csDMARDs	13.7 (11)	8.7 (7)	-
bDMARDs	6.2 (5)	8.7 (7)	-

Disclosure of Interests: None declared

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AB0670 MYOSITIS IN PRIMARY SJÖGREN'S SYNDROME: DATA FROM A MULTICENTRE COHORT

Keywords: Sjögren syndrome, Epidemiology, Myositis

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Background: Primary Sjögren's syndrome (pSS) is a multisystem autoimmune disease characterised by lymphocytic infiltration of the exocrine glands and their resultant dysfunction.

Muscle involvement has been given the highest weightage in the ESSDAI score Given the significant variation in prevalence (0.85–14%) and characteristics of myositis patients with pSS across studies (Owing to heterogeneous definitions and assessment) it is vital for us to understand myositis in pSS better.

Objectives: The aim of this study was to describe the prevalence of myositis in a multicentre Indian pSS cohort and to address the clinical manifestations and therapeutic strategies.

Methods: Clinical and serological data from a pSS cohort of patients were retrospectively collected and analysed. Those fulfilling the ACR/EULAR 2017 criteria for myositis and the ACR/EULAR 2012 Criteria for pSS were included. Patients with overlap features of other autoimmune rheumatic diseases were excluded.

Results: 12 (2.7%) out of 444 patients of pSS had Myositis. The mean age was 36.83 ±12.16 years, and the mean duration of follow-up was 5,46 ±5.23 years. All patients were females with a high prevalence of ANA positivity and Ro52, and Ro60 in these patients. Myositis was the presenting manifestation in 11/12 patients. Arthritis/Arthralgia (8/66%), Glandular enlargement/ Parotitis (7/58%), Lung Involvement (ILD) (5/41%), and Haematological abnormalities were also common in patients with myositis and primary Sjögren's syndrome. The 5-year survival was good, with 11/12 patients completing the 5-year follow-up. About a half patients received pulse methylprednisolone therapy followed by 1mg/kg steroid, with few patients requiring lower doses of steroids. Methotrexate was the steroid sparing drug of choice for patients with pSS myositis without lung

involvement and Cyclophosphamide in patients with lung involvement followed by Azathioprine or Rituximab maintenance, one patient was induced and maintained with low dose rituximab. Details of second-line therapy was not available for three patients. The mean ESSDAI and ESSPRI scores were high. None of our patients had Signs, symptoms or histopathological findings suggestive of IBM.

Conclusion: pSS patients with myositis had a younger age of onset with active Disease and High ESSDAI and ESSPRI scores. Myositis was the presenting manifestation in most, the proportion of patients with lung involvement in pSS myositis was much higher than is usually seen in patients with pSS and should prompt the clinician to look for clinical/subclinical lung involvement in pSS myositis patients. The Response to therapy was usually good. Unlike other cohorts, we didn't find any IBM in our set of patients – this may be due to referral bias or the rarity of IBM in the Indian population.

Table 1. Characteristics of pSS Myositis patients

N=12	n	%
Age [mean±SD(Range)]	36.83 ± 12.16(18-51)	
Females	12	100
Presenting Manifestation	11	91.67
Follow Up duration in years [mean±SD(Range)]	5.46 ± 5.23(1-15)	
Schirmer's Positive	11	91.67
USFM	9	75
Lip Biopsy	4	33.33
ANA	11	91.67
Ro52	11	91.67
Ro60	9	75
La	4	33.33
Constitutional features	2	16.67
Lymphadenopathy	1	8.33
Parotitis/ Glandular enlargement	7	58.33
Arthritis/Arthralgia	8	66.67
Rash/purpura	5	41.67
ILD	5	41.67
Renal	0	0
Neuropathy	1	8.33
Haematological	4	33.33
Fibromyalgia	2	16.67
ESSDAI (mean±SD)	21.75 ± 12.59	
ESSPRI (mean±SD)	15.75 ± 4.61	
Treatment Details		
Pulse Steroids	5	41.67
1mg/kg	7	58.33
0.5 mg/kg	3	25
< 0.5 mg/kg	2	16.67
Second line Immunosuppressants		
Methotrexate	5	41.67
Cyclophosphamide	3	33.33
Azathioprine	2	25
Rituximab	2	8.33

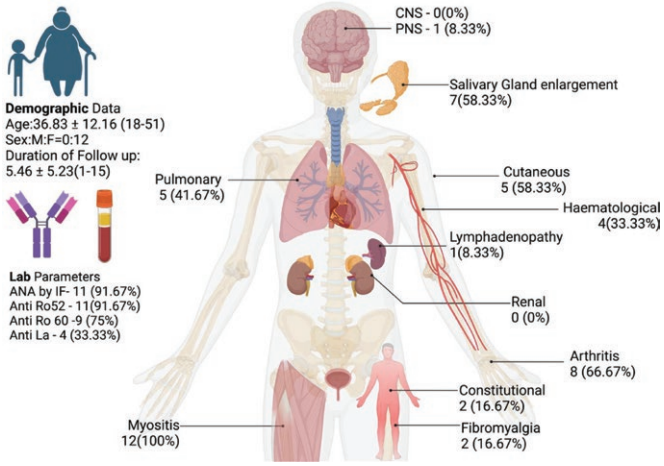


Figure 1. Demographic, Clinical and Serological data of patients with Sjögren's Myositis (created using biorender.com)

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2023-eular.4287

AB0671 LONGITUDINAL ASSESSMENT OF HAND AND WRIST BONE DESTRUCTION BY ULTRASOUND, AND ITS ASSOCIATION WITH DISEASE ACTIVITY IN PRIMARY SJÖGREN'S SYNDROME

Keywords: Ultrasound, Inflammatory arthritides, Sjögren syndrome

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Background: Primary Sjögren's syndrome (pSS) is a chronic systemic inflammatory autoimmune disease primarily affecting the exocrine glands (1). Joint damage is the main extra-glandular manifestation, usually described in 11% of patients as non-erosive polyarthritis of small joints, mainly of the upper limbs (2). Although articular bone erosion is a rare finding on hands' radiography, hand and wrist ultrasound (US) is an emerging technology in the rheumatology field used for diagnosis and follow-up disease activity through the assessment of bone articular erosions, synovitis and tissue power doppler (3).

Objectives: To evaluate joint damage by hand and wrist ultrasound, and its association with disease activity in primary Sjögren's syndrome patients in a longitudinal setting.

Methods: Ninety-seven consecutive pSS patients according to the American College of Rheumatology (ACR) and European Alliance of Associations for Rheumatology (EULAR) criteria without meeting the ACR criteria (1987) for rheumatoid arthritis were evaluated by hand and wrist ultrasound and clinical activity disease index previously by our group (3). Twelve patients of this initial evaluation were followed with hand and wrist ultrasound and clinical activity disease index. Disease activity was assessed by EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI). The US was performed by one expert blinded. Data were analyzed by Wilcoxon signed-rank test. Significance level was set at $P<0.05$.

Results: All patients were female and 8 (66.6%) were white. The time between the first and the second evaluation was 9.5 ± 1.6 years. At the first evaluation, only 1 (8.3%) patient had wrist erosion, 5 (41.6%) patients had synovitis and 4 (33.3%) patients had tissue power doppler in the US. The mean ESSDAI was 6.83 ± 5.70. At the second evaluation, 5 (41.6%) patients had wrist erosion (P=0.059), 10 (83.3%) patients had synovitis (P=0.010) and 7 (58.3%) patients had tissue power doppler in the US (P = 0.014). The mean ESSDAI was 2.33 ± 4.05 (P = 0.022). After the follow-up period, despite the improvement in the disease activity score, there was an increase in the number of erosions, mainly of the wrists, presence of tissue power doppler and synovitis.

Conclusion: This study describes a longitudinal evaluation of a small sample size of pSS. The findings show a worsening of joint assessments despite low-activity disease, indicating possible local inflammation in addition to systemic involvement.

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AB0672 DETECTION OF MACROPHAGE MIGRATION INHIBITORY FACTOR IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS COMPLAINING PAINFUL DISTURBANCES: A SINGLE CENTER STUDY

Keywords: Systemic lupus erythematosus, Pain, Biomarkers

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Background: Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) is considered one of the preeminent diagnostic and therapeutic challenges for the rheumatologist, not only due to the wide clinical heterogeneity but also because of the lack of specific diagnostic tools and biomarkers. Macrophage migration inhibitory factor (MIF) is a pleiotropic inflammatory cytokine associated with inflammatory neuropathy and neuropathic pain. This protein acts as an innate immunity modulator by promoting host inflammatory responses through induction of pro-inflammatory cytokines (including TNF and IL-6), regulating cellular processes such as T-cell proliferation, apoptosis and counter regulation of the immunosuppressive actions of glucocorticoids.
Objectives: In the present study we aimed at evaluating the serum titers of MIF in SLE patients with painful disturbances, screened for neuropathic pain, compared with healthy controls (HC) and identifying significant associations with clinical and other laboratory disease features.
Methods: Consecutive SLE patients (according to ACR 1987 criteria), with painful disturbances, were screened for neuropathic pain through a specific questionnaire (Douleur Neuropathique en 4 Questions-DN4). Subjects were enrolled in the presence of bilateral limb pain and one of the following: hypoesthesia to touch or prick; pain caused or increased by brushing; tingling, numbness and itching; electric shocks, painful cold or burning pain. We excluded SLE patients with other possible explanation for neuropathic pain including diabetes, Sjogren's syndrome and kidney impairment (eGFR <30 ml/m). For each patient the following data were collected: demographics, medical history (focusing particularly on other NPSLE manifestations), treatments, disease activity (SLEDAI-2K) chronic damage (SLICC *damage index)*, clinical and laboratory main disease data. Each patient enrolled underwent different tools specific for neuropathic pain (DN4, Neuropathic Pain Symptoms Inventory Questionnaire, Composite Autonomic Symptom Score-31 and Small Fiber Neuropathy-Symptoms Inventory Questionnaire). A concomitant fibromyalgia (FM) was evaluated by different tools including FIRST, FibroDetect and ACR 2016 criteria. MIF levels were determined by ELISA, following manufacturer's instructions in SLE patients and 38 HC matched for age and gender (Quantikine ELISA, Human MIF Immunoassay, Catalog Number DMF00B- R&D Systems).
Results: We excluded 58 subjects because of confounding factors and 25 declined the study. Therefore we enrolled 34 patients (M/F 2/32, median age 50.0 years, IQR 21.0; median disease duration 150.0 months, IQR 190.5; median SLEDAI-2k 0, IQR 2 and median SDI 1, IQR 2). MIF levels were not different between SLE and HC, median 42.8 ng/ml (IQR 49.3) and 38.3 ng/ml (IQR 46.4), respectively. FM was identified in 79.4% of SLE patients according to ACR criteria. Neuropathic pain was diagnosed according DN4 (>3) in 58.8% of SLE patients, but no significant difference in MIF levels were found between the groups. NPSLE was recorded in 35.3% of cohort (mild cognitive dysfunction in 5 subjects, headache and polyneuropathy in 3, movement disorders, psychosis, epilepsy, myasthenia and cerebrovascular accident in only one). Interestingly higher MIF serum levels were found in patients with NPSLE than in patients without overt neuropsychiatric involvement (p=0.037, Figure 1).
Conclusion: This study suggests that MIF could be a potential biomarker in NPSLE patients, however further studies are warranted to confirm this preliminary result.

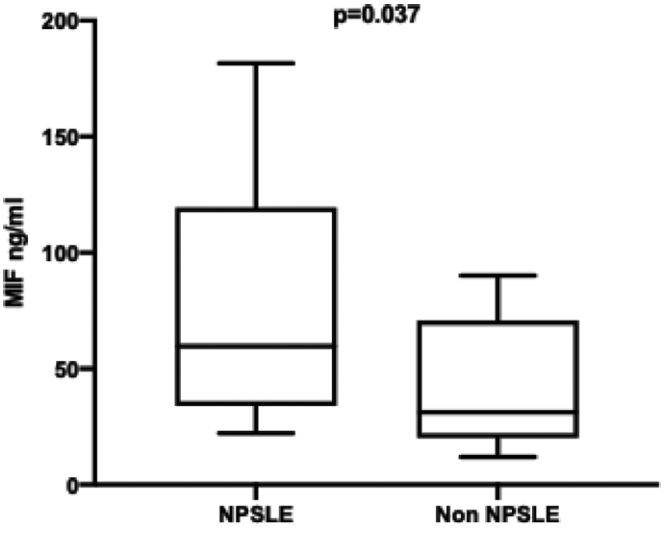


Figure 1. MIF serum titers in NPSLE patients compared with patients without neuropsychiatric involvementLegend: MIF: Macrophage Migration Inhibitory Factor; NPSLE: NeuroPsychiatric Systemic Lupus Erythematosus

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2023-eular.4651

AB0673 **SERUM 25 (OH) VITAMIN D LEVELS AND BONE MINERAL DENSITY IN SYSTEMIC LUPUS ERYTHEMATOSUS**

Keywords: Osteoporosis, Systemic lupus erythematosus, Vitamin D

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Background: Several disease- and treatment-related factors, such as proinflammatory cytokines, corticosteroid treatment, lupus nephritis, and impaired renal function affect serum vitamin D levels and cause accelerated osteoporosis in patients with systemic lupus erythematosus (SLE).
Objectives: We investigated serum 25(OH) vitamin D levels and bone mineral density (BMD) in female Caucasian patients with SLE. Further, we explored which treatment- and disease-related factors are most strongly associated with those measurements.
Methods: We enrolled female Caucasian SLE patients and controls in this cross-sectional study. A rheumatologist and a nurse gathered information about demographical and disease characteristics, evaluated disease activity and damage scores, and collected blood samples at the time of inclusion. SLE patients underwent DXA within one year after inclusion.
Results: A total of 325 SLE patients and 289 controls were enrolled, mean age (47 and 48 respectively, p>0,05), body mass index (BMI), smoking status, and the fraction of postmenopausal individuals did not differ between groups. 179 patients and 2 controls were on corticosteroids. Moreover, 172 patients and 14 controls were using vitamin D supplements. The SLE patients as a group had higher levels of 25(OH) vitamin D than the controls (64,2 nmol/L vs 59,4 nmol/L respectively, p=0.0021). Among SLE patients using vitamin D supplementation, those on corticosteroids had lower serum levels of 25(OH) vitamin D; this difference was not present in the supplementation naïve group. (p: 0,02, p: 0,69 respectively). In the SLE and control groups, not taking supplementation, serum 25(OH) vitamin D levels did not differ according to menopausal status (p= 0.22). Nephritis status (ever yes/no) did not affect 25(OH) vitamin D levels. Patients taking

Table 1. Univariate and multivariate regression analysis with standardized beta coefficients of variables related to BMD.

	Lumbar Spine		Total Hip		Femoral Neck	
Univariate regression analysis						
	Pre-menopausal Std B	Post-menopausal Std B	Pre-menopausal Std B	Post-menopausal Std B	Pre-menopausal Std B	Post-menopausal Std B
Age	0.15*	– 0,17*	ns	– 0,31 ***	ns	– 0,37 ***
BMI (kg/m²)	0,26**	0,19*	0,29**	0,29**	0,19*	0,27**
Disease duration (years)	ns	ns	– 0,17*	– 0,18*	– 0,24 **	– 0,22 **
Years since menopause	-	– 0,17*	-	– 0,19*	-	– 0,21*
SLICC/ACR	ns	– 0,18*	ns	– 0,16	ns	ns
Bisphosphonate treatment (yes/no)	– 0,16*	ns	– 0,17*	– 0,17*	ns	– 0,21 **
Corticosteroid treatment (months)	– 0,28 **	ns	– 0,3**	ns	– 0,38 **	ns
Smoking ever	ns	ns	ns	– 0,21 **	ns	– 0,24 **
Multivariate Regression analysis						
Age	ns	ns	ns	– 0,3*	ns	– 0,25 *
BMI (kg/m²)	0,24 **	0,19*	0,29**	0,31***	0,2*	0,27 **
Disease duration (years)	ni	ni	ns	ns	– 0,19 *	– 0,16 *
SLICC/ACR[a]	ni	– 0,18 *	ni	ns	ni	ni
Bisphosphonate treatment (yes/no)	ni	ni	ni	ni	ni	ni
Corticosteroid treatment (months)	ns	ni	ns	ni	ns	ni
Smoking ever	ni	ni	ni	– 0,24 **	ni	– 0,29 **
R^2	0,08	0,09	0,13	0,24	0,09	0,23

*P < 0.05, **P < 0.01 ***P < 0.001, [a] excluding osteoporosis item*ns*, not significant; *ni*, not included in the model; R2, coefficient of determination; Std B, standardized regression coefficient; BMD, bone mineral density.

supplements with higher disease activity (SLEDAI≥4, SLAM≥6) and more damage (SLICC/ACR Damage Index (SDI) >1) had lower serum 25(OH) vitamin D levels than those with lower disease activity/damage (*p*: 0,029, *p*: 0,049, *p*: 0,002).

Premenopausal SLE patients had higher T-scores than the postmenopausal in all measured locations (lumbar spine *p*: 0.0002, femoral neck: *p*<0,0001, total hip *p*<0,0001). Neither T-scores in the whole group, nor Z-scores in the group <40 years were correlated to serum 25(OH) vitamin D levels. (*p*> 0,05 in all locations). Variables affecting body mass index (BMD) are presented in Table 1, stratified for menopausal status.

Conclusion: Serum 25(OH) vitamin D levels are affected mainly by supplements, corticosteroid treatment, and organ damage in SLE patients. We found no correlation between serum 25(OH) vitamin D levels and BMD. Low BMD was in multivariable analyses associated with low BMI, older age, smoking, longer disease duration, and higher damage.

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AB0674 PRIMARY SJOGREN SYNDROME WITH ANTICENTROMERE ANTIBODIES - A CLINICALLY DISTINCT PHENOTYPE OR AN OVERLAP SYNDROME?

Keywords: Autoantibodies, Sjögren syndrome, Cardiovascular disease

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Background: Anticentromere antibodies (ACA) have been reported in primary Sjogren syndrome (pSS) at lower frequencies but have recently been suggested as another clinically important marker in this disease[1]. Although several papers have been published on ACA-positive pSS, the results have been conflicting[2,3].

Objectives: To evaluate the correlation between presence of ACA and associated symptomatology, especially related to microvascular dysfunction in a Romanian cohort of patients with ACA-positive pSS.

Methods: We assessed 132 patients who met the 2016 American College of Rheumatology/European League Against Rheumatism classification criteria for pSS. For all ACA+ patients, we collected data on the presence of sclerodactyly, puffy hands, Raynaud's phenomenon, calcinosis, telangiectasia, esophageal involvement, interstitial lung disease, digital ulcerations/pitting scars, pulmonary hypertension and nailfold capillaroscopy findings.

Results: The prevalence of ACA in our pSS cohort was 13%. ACA - positive pSS patients were older than the ACA-negative patients (median, 59 years [IQR, 48 to 62] vs median, 50 years [IQR, 45 to 60]; p = 0.042), with a shorter disease duration (53 months vs 260 months, p=0.073). Most patients were female (98.7%) and had ocular and oral symptoms of dryness (98.1% and 97.8%, respectively). Among the patients with pSS, 5 patients had ACA and limited cutaneous systemic sclerosis (lcSSc). Although there was no statistical differences between the two groups, ACA-positive patients were characterized by higher prevalence of associated symptomatology related to microvascular dysfunction: RP (Raynaud's phenomenon) and telangiectasias were present in 50% of the patients (5/10), sclerodactyly and digital ulcerations (DUs) in 33% (3/10); digital gangrene was not found. 60% (6/10) of ACA+ pSS patients had abnormal findings on nailfold capillaroscopy, which were nonspecific in 2 patients (crossed capillaries), while in the remaining 1 patient had an early-pattern, 1 had an active-pattern and 2 patients had late scleroderma-pattern. The presence of ACA was positively correlated with the presence of RP (p = 0.024), DUs (p = 0.034). In our study, patients showed similar severities in extraglandular manifestations compared to the ACA-negative group. Nonetheless, we noticed that even if not statistically significant, the use of vasodilators was more common in the ACA - positive pSS patients (66.7% vs 12.2%, p = 0.911) thus supporting the hypothesis of a symptomatic microvascular dysfunction. A higher proportion of ACA+ pSS (64% vs 42%) was treated with immunosuppressive agents. No differences in mortality were found between the groups.

Conclusion: Patients in the ACA-positive group were older, had more frequent RP and digital ulcers. In our cohort, ACA - positivity had little impact on the severity of extraglandular manifestations in pSS patients. Although there were no significant differences, use of vasodilators and immunosuppressants agents was more common. This study is the first to investigate the impact of ACA positivity on the vascular manifestations of Romanian pSS patients.

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AB0675 AVASCULAR NECROSIS IN A COHORT OF SLE PATIENTS IN AN AFRICAN CONTEXT

Keywords: Pain, Systemic lupus erythematosus

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Background: There is lack of recent data in South Africa describing the burden of AVN among SLE patients. Joint replacement in South Africa remains a challenge with more than 500 days of delay in some cases hence identification of potential clinical associations for AVN development among SLE patients is an important undertaking for prevention, early detection and treatment.

OBJECTIVES:

1.To determine the current prevalence of AVN among SLE patients at Tygerberg Hospital.

2.To determine associations between the development of AVN in SLE patients and SLE related factors, complications, treatment and other comorbidities.

3.To assess the outcomes of AVN in SLE patients.

Methods: This was a retrospective case-control study. All SLE patients (N=755) seen at Tygerberg Hospital, Rheumatology Clinic over a 8 years period (2013 – 2020) were screened for inclusion. The inclusion criteria consisted an age of 18 years with a proven diagnosis of SLE using the 2019 EULAR/ACR classification criteria, and a radiological diagnosis of AVN. The clinical data, radiological data and blood investigation data were collected for analysis. The radiological data (x-rays, MRI and CT scans) were reviewed by a radiologist for the diagnosis and grading of AVN using the Ficat and Arlet method.

Results: The prevalence of AVN among the SLE population at Tygerberg Hospital was 3.4%. The median SLEDAI-2K score six months prior to the radiological diagnosis of AVN (p < 0.001) and the SDI (p < 0.001) scores were individually found to be statistically significant between the two groups. The MRI Ficat and Arlet grading (p= 0.013) was found to be more advanced when compared with x-ray grading of the same joints, although done at different points in time with a median delay of 2 months (IQR:1-5). Only 26.3% of affected joints underwent a joint replacement with a median delay of 23 months (IQR:13-52).

Conclusion: The prevalence of AVN among SLE patients at Tygerberg Hospital is slightly lower than the international and the previously reported local data. High SLEDAI-2K and SDI scores were associated with AVN development in SLE. The delay in the acquisition of MRI scan for AVN diagnosis and grading, and that of joint replacement remain as significant challenges that require special attention in the state healthcare sector.

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AB0676 DELAYS IN CARE SEEKING AND DIAGNOSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS IMPACT ON DISEASE ACTIVITY AND DAMAGE

Keywords: Systemic lupus erythematosus, Epidemiology, Organ damage

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that presents with heterogeneous manifestations, some of which can delay access to specialized attention and according to the symptom, also lead to greater damage. (1)
Objectives: Compare initial symptoms/signs and disease damage or activity in patients with SLE with medical attention or diagnostic delays.
Methods: We performed a cross-sectional study in the lupus clinic in Hospital Universitario Dr. José Eleuterio González. Patients over 15 years old with an SLE diagnosis according to the EULAR/ACR 2019 criteria and a disease duration > 1 year were included in this study. Data from current EULAR/ACR 2019 disease classification, SLE Disease Activity Index (SLEDAI), and SLICC Damage Index were collected from patient files. Delay was defined as ≥ 6 months to request medical assistance or disease diagnosis. The timeline studied was divided into time from symptom onset to first medical assessment, and time from first medical assessment to SLE diagnosis. We compared demographics and initial symptoms, SLEDAI, and SDI scores between groups with and without delays.
Results: Fifty-five patients were evaluated, 96.4% were female, mean age at diagnosis was 30.44 years +/- 12.484, and the mean disease duration was 7.25 years. The most frequent symptom in both groups was arthritis/arthralgia, followed by mucocutaneous manifestations (Table 1). Mean time for requesting medical assistance was 483.4 days +/- 959.741 and for diagnosis 91.67 days +/- 194.417. 41.98% had a delay in medical attention, 52.72% had a delay in diagnosis, and 60% (33) of all patients presented some type of delay ≥ 6 months. No statistical difference was found in SLEDAI score (mean of 2.424 +/- 3.699) (p=.740 or SLICC score (mean 0.57 +/- 0.902) (p=.587) between groups. In the group with a delay in diagnosis, the patients were older, and in the group without a delay in diagnosis lupus nephritis was more prevalent.
Conclusion: Two out of 3 patients report delay ≥ 6 months in seeking medical assistance and/or a definitive diagnosis, although no statistical difference was found in disease activity or damage scores. Younger age and renal involvement were related to a prompt diagnosis.

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Table 1. Group demographics and clinical manifestations

	TIME FOR MEDICAL ATTENTION			TIME FOR DIAGNOSIS		
	<6 months	>6 months	p	<6 months	>6 months	p
	n=32	n=23		n=26	n=29	
Demographics						
Age, mean (SD)	35.25 (13.75)	41.22 (16.47)	NS	32.30 (11.60)	43 (16.36)	0.007
Female sex, n (%)	31 (96.87)	22 (95.65)		26 (96.2)	27 (96.43)	
First clinical manifestation, n (%)						
Arthritis/arthralgia	14 (43.75)	14 (60.8)	NS	12 (46.08)	16 (55.04)	NS
Mucocutaneous	7 (21.87)	4 (17.36)	NS	5 (24.2)	6 (20.64)	NS
Constitutional	0	2 (8.68)	NS	2 (9.68)	0	NS
Hematologic	4 (12.5)	2 (8.68)	NS	2 (9.68)	3 (10.32)	NS
Pulmonar	2 (6.25)	0	NS	0	2 (6.88)	NS
Renal	4 (12.5)	0	NS	4 (19.36)	0	0.034
Miositis	0	1 (4.34)	NS	0	1 (3.44)	NS
Neurologic	1 (3.12)	0	NS	0	1 (3.44)	NS
Clinical Scores						
SLEDAI, mean (SD)	2.19(3.26)	2.70(4.07)	NS	2.15 (3.278)	2.64 (3.92)	NS
SLICC, SDI mean (SD)	0.81 (1.14)	.52 (.898)	NS	0.70 (1.171)	.68 (.945)	NS

SD Standard Deviation, SLEDAI Systemic Lupus Erythematosus Disease Activity Index, SLICC SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology) Damage Index for Systemic Lupus Erythematosus. Pearson's chi-squared test for group comparison. T-test for demographics and clinical scores.

Disclosure of Interests: None declared
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AB0677 CUT OFF POINT OF NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A MARKER OF DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS AT HAJ ALSAFFE HOSPITAL LUPUS CLINIC FROM JUNE 2021 TO SEPTEMBER 2021

Keywords: Systemic lupus erythematosus, Prognostic factors

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Background: Systemic lupus erythematosus (SLE) is a chronic systematic autoimmune disease with high heterogeneity. SLEDAI is the standardized method to determine disease activity, neutrophils to lymphocytes ratio emerge as new method to detect disease activity. The study aim is to study the neutrophil-to-lymphocyte ratio as a marker of active disease in SLE patients.
Objectives: This study aimed to assess cut off point of neutrophil-to-lymphocyte ratio as a marker of disease activity in systemic lupus erythematosus.

Methods: A cross sectional study was conducted in Haj Al-Safi hospital. A 53 patients were studied using pretested questionnaire, a SLEDAI assessment was conducted to each patient's individually. NLR were measured from collected CBC at the time of the study. Inclusion criteria were: people aged 18 or older, SLE patient diagnosed and confirmed by new 2019 criteria, and exclude any patients with infections, malignancies, and other inflammatory diseases recorded in registry. Data were collected and analyzed using SPSS.

Results: The mean age of patients was (± SD) 39.85 (± 14.07), SLEDI score assessment was conducted for the patients, 48 (90.6 %) scored > 4 and were considered active disease according to the score, 5 (9.4 %) scored <4 and were inactive. The NLR was calculated and the mean was 2.9 (± 2.08). Receiver Operating Characteristic (ROC) was conducted, cut-off (COV) was 2.48. Area Under Curve (AUC) and was AUC=0.402 (95% CI: 0.232 to 0.572, p=0.475).The sensitivity was 47%, and the specificity was 60%.

Conclusion: This findings indicated that the Neutrophil-to-lymphocyte ratio, with a cut-off value (COV) of 2.48, could be utilized to identify the disease activity of systemic lupus erythematosus. Furthermore, by applying this NLR COV.

Disclosure of Interests: None declared
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AB0678 INTERLEUKIN-18 AS A PREDICTOR OF SUBCLINICAL CARDIOVASCULAR AFFECTION AND DISEASE ACTIVITY IN SYSTEMIC LUPUS PATIENTS

Keywords: Biomarkers, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease which has variable clinical manifestations and causes severe organ damage [(1)]. Interleukin-18 (il-18) is a pro-inflammatory
cytokine which plays a key role in many inflammatory and cardiovascular diseases [(2)].

Objectives: Evaluation of plasma level of IL-18 in SLE patients and correlate it with the subclinical cardiovascular affection and disease activity.

Methods: Thirty lupus patients (G I), and 30 healthy age and sex matched volunteers as control group (G II) were recruited for this case control study. All participants were subjected to complete history taking and clinical assessment, lupus disease activity was measure using SLE disease activity index 2000 (SLEDAI-2K), Serum IL-18 level, CRP, C3, C4, anti dsDNA, and lipid profiles were measured. Cardiovascular assessments were done using echocardiography, flow mediated dilatation of the brachial artery (FMD), and carotid intima-media thickness (cIMT). Plasma levels of IL-18 were measured and correlated with different parameters.

Results: There were no significant differences between the patients and controls regarding demographic data (P>0.05). The mean SLEDAI-2K was 3.5±2.1. The mean plasma level of IL-18 was 432.85±165.37 pg/ml in lupus patients, while IL-18 was 195.65±82.91 pg/ml in healthy volunteers, there was significant elevation of il-18 level in lupus patients in comparison with controls. There were significantly lowering levels of C3, & C4 in lupus patients. Regarding cardiovascular assessment; SLE patients showed significantly higher lipid profile, & cIMT measures and revealed lower FMD as well as detecting echocardiographic abnormalities compared to controls. (These date were summarized in Table 1).

Serum IL-18 was positively correlated with cIMT and SLEDAI-2K, also IL-18 was negatively correlated with FMD, C3 & C4.

Table 1. Comparison between lupus patients and controls regarding different parameters

	Lupus patients (30)	Controls (30)	P value
C3 (mg/dL)	78.9±22.9	116.8±18.6	< 0.0001
C4 (mg/dL)	9.6±4.8	25.7±4.6	< 0.0001
SLEDAI-2K	3.5±2.1	-	-
cIMT (mm)	0.91±0.27	0.68±0.21	0.0005
FMD%	5.92±2.25	7.65±2.16	0.0036
IL-18 (pg/ml)	432.85±165.37	195.65±82.91	< 0.001

Conclusion: IL-18 was an independent predictor of cardiovascular events in SLE patients, also it was correlated with lupus activity.

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AB0679 OPHTHALMOLOGICAL FINDINGS BY STRUCTURAL SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Autoantibodies, Descriptive studies, Systemic lupus erythematosus

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Background: Systemic Lupus Erythematosus represents the prototype of autoimmune systemic disease, its etiology involves aberrant interactions between genetic, immunological and environmental factors, affecting multiple organs and systems; about a third of patients present ocular alterations, with a variable degree of severity from mild clinical manifestations involving external and anterior ocular segments, to severe sight-threatening disease involving posterior eye segments.

Objectives: Describe and correlate ocular and clinical findings, as well as the positivity of autoantibodies in patients with Systemic Lupus Erythematosus using structural Spectral-Domain Optical Coherence Tomography (SD-OCT).

Methods: Cross-sectional single-center study, descriptive statistics and correlation analysis were performed using Spearman's test of the ocular findings determined by (SD-OCT) and serological determinations of antiphospholipid autoantibodies, anti-nuclear antibodies, anti-DNAds and anti-Smith antibodies in patients with Lupus during the months of January 2020 to December 2020, performing general ophthalmological examination and structural Spectral-Domain Optical Coherence Tomography.

Results: 29 patients were included, 26 women and 3 men, positive antiphospholipid antibodies in 56% of the population, lupus nephritis was found by renal biopsy in 49% of the population, disease activity was determined by MEX-SLEDAI, finding >9 points in 11% and <9 points in 89% of the population.

Maculopathy was found in 24% of patients; the correlations between autoantibodies and ophthalmological abnormalities determined by SD-OCT were: Lupus anticoagulant/Maculopathy p=0.008, anticardiolipin antibodies/maculopathy p= 0.026, anti Smith/choriocapillaritis p=0.014, decreased capillary perfusion/choriocapillaritis p= 0.003 and choroiditis p= 0.012, decreased perfusion by quadrants/maculopathy p=0.043. A decrease in retinal thickness was found in 65% of the population, also in the density of ganglion and macular cells and in the density of the optic nerve head.

Conclusion: Findings in our study were predominantly choroidal, macular and capillary alterations; a specific serological correlation was found between maculopathy and chorioretinitis with positive Lupus Anticoagulant, as well as alterations in capillary perfusion in patients with positive antiphospholipid and anti-Smith antibodies.

The use of SD-OCT can provide valuable and early information on the ocular microstructure and biological system in SLE and other autoimmune diseases affecting the eyes.

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Table 1.

Correlation Findings in Spectral Domain Optical Tomography (SD-OCT) rho Spearman

aPL LA aCL	Choriocapillaritis	Chorioretinitis	Altered retinal perfusion	Maculopathy
	rho p	**rho p**	**rho p**	**rho p**
	NS	-0.392 0.036	-0.556 0.002	0.553 0.008
	NS		-0.530 0.005	-0.414 0.026
Decreased capillary perfusion	0.512 0.003	0.458 0.012	NS	NS
Decreased overall perfusion	0.558 0.001	-0.480 0.008	NS	0.435 0.043
Decreased retinal fiber layer.	-0.406 0.029	NS	NS	NS
Anti Smith	0.450 0.014	NS	NS	NS

aPL: Antiphospholipids LA: Lupus Anticoagulant, aCL: Anticardiolipins, NS: Not Significant.

Disclosure of Interests: None declared
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AB0680

THE EFFECT OF DEPRESSION, ANXIETY, AND FIBROMYALGIA ON SEXUAL DYSFUNCTION IN FEMALE PATIENTS WITH SJÖGREN'S SYNDROME

Keywords: Fibromyalgia, Sjögren syndrome

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Background: Sjogren's Syndrome is a systemic autoimmune disease that mainly affects the exocrine glands.[1] The most common clinical symptoms of Sjogren's syndrome are dry mouth and eyes. Vaginal dryness and dyspareunia may be seen in the disease, as the female genital mucosa is also affected.[2]
Objectives: To compare the results by using the female sexual function scale in patients with Sjögren's Syndrome with and without depression, anxiety, and fibromyalgia and to evaluate the patients in terms of sexual dysfunction.
Methods: Twenty-five female patients diagnosed with Sjögren's Syndrome, according to the 2016 ACR-EULAR criteria, followed in the Internal Medicine, Rheumatology Clinic of Sakarya University Faculty of Medicine, were included in the study after their consent was obtained. Beck Depression Inventory, Beck Anxiety Inventory, and Female Sexual Function Scale were administered simultaneously to the patients. The presence of fibromyalgia was evaluated according to the 2016 Modified ACR diagnostic criteria. The relationship between depression, anxiety scale scores, the presence of fibromyalgia, and female sexual function was investigated.
Results: The mean age of the patients was 49±8.1 years, and the median duration of the disease was four years. 15 (60%) patients were primary school graduates, 2 (8%) patients were secondary school graduates, 4 (16%) patients were high school graduates, and 4 (16%) patients were university graduates. 11 (44%) of the patients were in menopause. Sexual dysfunction was found in 21 (84%) patients diagnosed with Sjögren's Syndrome. There was no statistically significant difference in sexual function scale scores between those with and without menopause. No statistical difference was found in disease duration, age, and scale scores in the presence of fibromyalgia. Sexual dysfunction was more pronounced in those with depression and anxiety (p=0.003; p=0.045, respectively) (Table 1).

Table 1. Comparison of depression and anxiety and sexual function scale scores

Sjogren Patients	Depression (+)	Depression (-)	p	Anxiety (+)	Anxiety (-)	p
Female Sexual Dysfunction score Median (IQR)	17.7 (8.6)	24.4 (7.1)	**0.003**	18.4 (6.9)	23.7 (6.2)	**0.045**
Desire score	1.8 (1.8)	3.0 (1.8)	0.107	2.1 (1.8)	2.7 (2.1)	0.319
Arousal score	2.2 (2.3)	3.6 (1.8)	**0.011**	2.7 (2.1)	3.6 (2.0)	0.089
Lubrication score	3.4 (1.3)	4.2 (1.5)	0.066	3.6 (1.0)	3.9 (1.6)	0.378
Orgasm score	2.8 (2.1)	4.0 (1.2)	**0.001**	2.8 (1.9)	4.0 (1.4)	0.052
Satisfaction score	2.8 (3.0)	4.4 (1.2)	**0.033**	3.0 (2.7)	4.6 (1.5)	0.101
Pain score	3.8 (3.3)	4.2 (4.8)	0.244	4.0 (3.3)	3.6 (4.8)	0.932

Conclusion: Depression and anxiety cause lower sexual function scores in female patients diagnosed with Sjogren's syndrome. The effect of fibromyalgia has not been demonstrated, but due to the limited number of patients, studies with a larger population will be more enlightening.
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AB0681

HISTORY OF ABORTION AND MULTIPARITY IN SYSTEMIC AUTOIMMUNE DISEASES: RESULTS FROM A MULTIDISCIPLINARY PREGNANCY CLINIC (GYNECOLOGY, RHEUMATOLOGY AND NEPHROLOGY)

Keywords: Real-world evidence, Pregnancy and reproduction, Systemic lupus erythematosus

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Background: Pre-conception counselling and risk stratification performed in a multidisciplinary clinical setting with rheumatologists, obstetricians and nephrologists may improve pregnancy outcomes in systemic autoimmune disease (SAD).
Objectives: To compare clinical, obstetrical comorbidities and pregnancy outcomes in patients with SAD with history of pregnancy loss with patients without history of pregnancy loss.
Methods: A retrospective cohort study was conducted. A total of 41 patients with SADs that attended the multidisciplinary preconception outpatient clinic were included. Variables related to SADs, obstetric comorbidities and pregnancy outcomes were collected. Description of the sample and comparison of groups were carried out. Shapiro-Wilk test was used to study normality.
Results: The description and comparison of the comorbidities, preconception counselling and pregnancy outcomes are summarized in Table 1. A total of 18 (46%) patients had a history of pregnancy loss. Fewer patients with history of pregnancy loss, 38.5% were fit for conception compared to 54.3% of patients with a history of pregnancy loss. Deferment of pregnancy was advised for 38.5% of patients with history of pregnancy loss and 54.3% in patients without history of pregnancy loss. Patients with a history of pregnancy loss had significantly higher anti-DNAds, antiphospholipid positivity and longer time since last flare.There was no significant difference for adverse pregnancy outcomes, disease activity or treatment. Interestingly, the distribution of risk profile for adverse pregnancy was different between both groups: there were more moderate and high risk for adverse pregnancy in patients with a history of pregnancy loss.
Conclusion: Patients with a history of pregnancy loss present delay to plan a new pregnancy, higher anti-DNA and antiphospholipid positivity. No worse pregnancy outcomes were observed.
Disclosure of Interests: None declared
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Table 1.

	Patients with previous abortion (n=13)	Patients without previous abortions (n=28)	P value
Sociodemographic data			
Age at visit (year)	36.8±4.61	34.4±3.93	0.43
Age at diagnosis (year)	28.31±2.48	28.617±1.35	0.9
Diagnosis-1st visit (years)	8±6.71	6.93±5.5	0.58
Last flare-1st visit (months)	47±39.45	27±38.59	**0.049**
Immunological data			
Anti-DNAds	61.17±52.46	42.62±52.46	**0.043**
LA, n (%)	11 (84.6)	5 (17.9)	**0.004**
Anti-cardiolipin, n (%)	9 (69.2)	5 (17.9)	**0.003**
Ro52, n (%)	3 (23.1)	4 (14.3)	0.49
Ro60, n (%)	1 (7.7)	4 (14.3)	0.55
Diagnosis, n (%):			
-SLE	6 (46.2)	13 (46.4)	0.99
-APS	1 (7.5)	1 (3.57)	0.58
-Autoinflammatory	0	3 (10.71)	0.39
-Other	6 (46.2)	11 (39.3)	0.68
Before preconception counselling			0.39
Treatment, n (%)			
-c/tsDMARD	4 (30.8)	7 (25)	
-HCQ	3 (23.1)	5 (7.9)	
-bDMARDs	2 (15.4)	9 (32)	
GC (n, %)	7 (53.9)	14 (49.9)	0.82
CYC (n, %)	2 (15.4)	3 (10.7)	0.67
After preconception counselling			0.24
Complications in pregnancy (n,%):			
-Medical	2 (15.4)	0	
-Obstetrical	0	3 (10.7)	
Fertility assistance (n, %)			0.73
-Assisted	0	1 (8.3)	
Non-assisted	11 (100)	11 (91.7)	
Abortion (n, %)	1 (7.69)	0	0.44

AB0682

DISEASE BURDEN AND UNMET NEED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS TREATED WITH ADVANCED THERAPY: RESULTS FROM A REAL-WORLD SURVEY IN EUROPE AND THE UNITED STATES

Keywords: Systemic lupus erythematosus, Real-world evidence, Outcome measures

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Background: Unmet medical need continues to be significant in patients with systemic lupus erythematosus (SLE) despite the use of advanced therapies (AT) to control active disease. Fatigue, end-organ damage, and low health-related quality of life (HRQOL) remain characteristic of the disease even among those treated with AT.

Objectives: In this analysis we measured the burden of unmet medical need in SLE patients prescribed AT for ≥12 months in real-world clinical settings.

Methods: Data were drawn from the Adelphi Real World Lupus Disease Specific Programme™, a cross-sectional survey with elements of retrospective data collection of rheumatologists and their consulting patients with SLE in France, Germany, Italy, Spain, the United Kingdom, and the United States in 2021.

Rheumatologists provided information on patient demographics, clinical status, and treatment history for their next six consulting SLE patients. The same patients completed the EQ-5D-5L, Functional Assessment of Chronic Illness Therapy Fatigue Subscale (FACIT-Fatigue), and Work Productivity and Activity Impairment questionnaire (WPAI) instruments. Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) scores were derived through physician assessment of patients' current clinical manifestations. AT was defined as biologics or off-label Janus kinase inhibitors.

All data were analysed descriptively.

Results: The sample included 234 patients seen by 125 physicians. Most patients (85%) were female and the mean participant age was 45.8 (SD:13.2) years. Mean duration since diagnosis was 6.6 (5.3) years and mean duration on their current regimen was 3.3 (3.0) years.

Despite receiving AT for ≥12 months, patients continued to have moderate-high levels of disease activity. Nearly half (48%) had SLEDAI scores ≥ 10 (Mean SLEDAI = 11.4 (11.2)). Many (37%) were assessed by physicians to have moderate/severe disease. Most (62%) continued to receive steroids, with 41% of patients prescribed oral/subcutaneous steroids receiving prednisone or equivalent doses of ≥7.5 mg/day. The majority of patients (56%) were 'currently experiencing' musculoskeletal symptoms including joint tenderness and swelling; while 37% and 19% respectively, were currently experiencing mucocutaneous and renal symptoms.

Mean EQ5D-5L score was 0.70 (0.27). Mean FACIT-Fatigue score was 32.4 (12.4), compared to US general population norm of 43.6 (9.4)[1]. Overall work impairment and mean daily activity impairment measured by the WPAI were 27.4% (20.4%) and 34.9% (25.3%) respectively.

Table 1. Unmet patient need in SLE patients prescribed AT for ≥ 12 months

			Patients on AT ≥12 months (n=234)
Physician-reported patient clinical status	Mean [SD] Derived SLEDAI score		11.4 [11.2]
	Organs/body areas affected, n(%)	Musculoskeletal	131 (56%)
		Mucocutaneous	87 (37%)
		Renal	44 (19%)
Steroid use	Steroid use, n(%)		145 (62%)
	Prednisone equivalent dose, n(%)ǂ	<7.5 mg/day	n=131
		≥7.5 mg/day	77 (59%)
			54 (41%)
Patient-reported outcomes†	Mean [SD] EQ5D-5L Utility score (0= death to 1= full health) [US value set]		n=99 0.70 [0.27]
	Mean [SD] FACIT-Fatigue score (0= worst fatigue to 52= no fatigue)		n=101 32.4 [12.4]
	Mean [SD] WPAI, percentage overall work impairment*		n=45 27.4 [20.4]
	Mean [SD] WPAI, percentage activity impairment		n=98 34.9 [25.3]

ǂPatients receiving oral/subcutaneous steroids only (n=14 excluded)†Patients with incomplete or unavailable responses were excluded*Working patients only; EQ-5D-5L, EuroQol-5 Dimension-5 Level; AT, advanced therapy; FACIT, Functional Assessment of Chronic Illness Therapy; mg, milligram; SLE, systemic lupus erythematosus; US, United States; WPAI, Work Productivity and Activity Impairment

Conclusion: Unmet medical need in SLE patients remained high despite long term use of AT. Study results suggest the need for more efficacious treatment options that reduce disease activity, reduce reliance on high-dose steroids, and improve quality of life.

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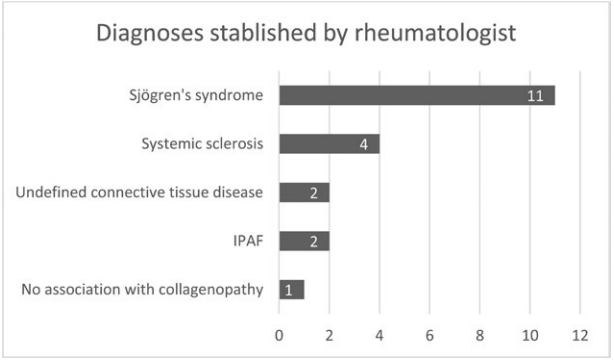
SLE, Sjön's and APS - clinical aspects (other than treatment)

AB0683 USEFULNESS OF A MONOGRAPHIC CONSULTATION RHEUMATOLOGY - PNEUMOLOGY

Keywords: Lungs, Work-related issues

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Background: Some rheumatological diseases may involve the lungs. This is something that the rheumatologist and pulmonologist must take into account in their clinical practice.
Objectives: To describe the characteristics of a group of patients with diffuse interstitial lung disease (ILD) that are being followed-up in a Rheumatology-Pneumology monographic consultation and study the usefulness of this consultation.
Methods: We reviewed the medical records of patients with a diagnosis of ILD that were being studied by both services in a monographic consultation in a tertiary hospital. A descriptive study was performed.
Results: A total of 40 patients were studied: 16 with nonspecific interstitial pneumonia (NSIP), 15 with usual interstitial pneumonia (UIP), 5 with fibrotic NSIP, 2 with cryptogenic organizing pneumonia (COP) and 2 with undefined ILD. 60% were women and the mean age was 64 years (40-80 years). Twenty patients with ILD were referred from pneumology to rheumatology. The primary reason for referral was the determination of positive antibodies (60%). Other reasons were arthritis (15%), other symptoms suggestive of connective tissue disease (15%) or the screening for collagenopathy in patients with poor outcome (10%). Ninety-five percent of patients with ILD referred to rheumatology were diagnosed with a connective tissue disease (Graph 1 and Table 1), which led to a change in treatment in 68.4% of them, with mycophenolate being the most prescribed drug, followed by rituximab. Twelve patients followed up in rheumatology with diagnosis of systemic sclerosis (n=6), rheumatoid arthritis (n=3), Sjögren's syndrome (n=2) and anti-synthetase syndrome (n=1) were referred to pneumology. The reasons for referral were the appearance of a pattern of interstitial involvement in imaging tests (chest X-ray or CT) and/or the alterations in respiratory function tests requested routinely (in the case of scleroderma) or due to respiratory symptoms (cough, dyspnea or crackles on chest auscultation). Follow-up by the pulmonologist implied a modification in the treatment in 5 out of 12 patients (41.7%) which consisted in the addition of an antifibrotic, Nintedanib in all cases. The reason for initiation was a decline in lung function demonstrated by pulmonary function tests. In 8 patients, the diagnosis of ILD and rheumatologic disease had been made in another center and they were referred for follow-up.
Conclusion: Ninety-five percent of patients with ILD referred to rheumatology were diagnosed with a connective tissue disease, which led to a change in treatment in 68.4% of them, with mycophenolate being the most frequently prescribed drug, followed by rituximab. The diagnosis of ILD in patients with rheumatologic disease was possible thanks to pulmonary auscultation, anamnesis on respiratory symptoms and the performance of imaging and functional tests. Referral of these patients to pneumology service allowed a better characterization of their pulmonary disease and the initiation of antifibrotic drugs in those with progressive fibrosing disease.



Graph 1.

Table 1.

Characteristics of patients diagnosed with Sjögren's disease

Antibodies	Saxon's test	Schirmer's test	Salivary gland biopsy
-	+	+	Compatible
-	+	+	Compatible
ANA speckled	+	+	Compatible
antiRo52	+	+	Compatible
ANA speckled	+	+	Compatible
Rheumatoid factor	-	+	Compatible
-	+	-	Compatible
ANA speckled	+	+	Compatible
-	+	+	Compatible
antiRo52, antiLa	-	-	Compatible
antiRo52, antiRo60	+	-	Not done

Saxon's test +: <2.75g unstimulated saliva in 2 minutes; Schirmer's test +: ≤ 5 mm in 5 min in at least one eye.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0684 RETROSPECTIVE STUDY ON SENSITIVITY AND SPECIFICITY OF VARIOUS CLASSIFICATION CRITERIA IN EARLY DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS AND LINK TO DISEASE OUTCOMES

Keywords: Outcome measures, Systemic lupus erythematosus, Descriptive studies

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Background: Systemic lupus erythematosus (SLE) is a multisystem inflammatory disease with heterogeneous clinical manifestations, making the diagnosis of disease challenging. To date, study on comparison of sensitivity and specificity of various SLE classification criteria among multiracial Malaysians is limited.
Objectives: To compare the sensitivity and specificity of various SLE classification criteria among multiracial Malaysians.
Methods: A retrospective study on data obtained from medical records of SLE and control cases. The sensitivity and specificity of 1997 American College of Rheumatology (ACR) revised criteria, Boston Weighted (BW) criteria, 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria, and 2019 European League Against Rheumatism (EULAR)/ACR classification criteria was calculated at baseline and at one year follow up. The link of diagnostic criteria to disease outcomes five years after diagnosis [disease damage, cardiovascular (CV) outcomes, and mortality] was studied.
Results: 420 SLE cases and 420 control cases were recruited. At baseline, the sensitivity and specificity of 1997 ACR criteria, BW criteria, 2012 SLICC criteria, and 2019 EULAR/ACR classification criteria were 69.3% and 99.3%, 89.5% and 96.7%, 94% and 97,6%, 96.4% and 96.5%, respectively. At one year follow up, sensitivity and specificity of the1997 ACR criteria, BW criteria, 2012 SLICC criteria, and 2019 EULAR/ACR classification criteria improved to 72.9% and 99.3%, 91.4% and 96.7%, 97.1% and 97,6%, 100% and 96.9%, respectively. There is statistical correlation between the 2019 EULAR/ACR classification criteria and SLICC/ACR damage index (DI), and disease relapses.
Conclusion: 2019 EULAR/ACR classification criteria demonstrated the highest sensitivity to diagnose SLE, with comparable specificity to other diagnostic criteria.
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AB0685

DESCRIPTIVE STUDY OF A COHORT OF PATIENTS WITH NEUROPSYCHIATRIC MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS IN A TERTIARY HOSPITAL

Keywords: Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) affects 0.1% of the world population; its neuropsychiatric expressions include, from vascular headache, mood disturbances to cognitive and other severe disorders such as transverse myelitis. It represents a diagnostic challenge, since none of the syndromes is exclusive of SLE and up to 40% is attributed to other causes; specifically it is necessary to rule out central nervous system infection, uremia, thrombotic thrombocytopenic purpura, posterior reversible encephalopathy, steroid psychosis and hypertension.
Objectives: To describe the neurological/neuropsychiatric manifestations in patients with systemic lupus erythematosus, diagnostic tests used and therapeutic possibilities in a cohort of patients in a tertiary level hospital.
Methods: Retrospective descriptive study of a cohort of patients with neuropsychiatric manifestations in the context of SLE in the Rheumatology Department of the Hospital Universitario Virgen del Rocio Sevilla (2017-2022).
Results: 12 patients with neuropsychiatric manifestations were included in our study, 8 (66.6%) women, 4 (33.4%) men, with a mean age of 30 ± 6 years and mean time of diagnosis of systemic lupus erythematosus of 3.5 years. Nine (75%) SLE with joint/cutaneous involvement and 3(25%) SLE with renal involvement (focal proliferative glomerulonephritis and segmental). In 9 (75%) of the cases imaging studies both cranial MRI and PET showed inconclusive lesions and as for specific antibodies: 4 (33.3%) anti-NMDAR, 3 (25%) anti-ribosome P. Among the most frequent clinical manifestations 6 (50%) presented persistent headache, 3 (25%) psychosis, 3 (25%) memory and mood disturbances. 9 (75%) of the cases responded to anti-CD20 (rituximab) and 3 (25%) to intravenous immunoglobulin infusion.
Conclusion: The data obtained from the clinical histories were conclusive with current scientific publications. It is an entity whose diagnosis is a challenge for the clinician, and both analytical tests and imaging studies are usually non-specific. The most frequent manifestations are headache, cognitive manifestations and mood alterations (anxiety attacks, panic, euphoria). Further studies are needed to classify the risk of this entity and the relationship with specific neuronal autoantibodies.
REFERENCES: NIL.
Acknowledgements: NIL.
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AB0686

THE NEUTROPHIL-TO-C3 RATIO (NC3R) WAS AN INFLAMMATORY MARKER IN THE ASSESSMENT OF LUPUS NEPHRITIS AND OCULAR VESSEL DENSITY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

Keywords: Biomarkers, Systemic lupus erythematosus, Kidneys

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Background: Lupus nephritis (LN) is one of the most serious complications of systemic lupus erythematosus (SLE). An increased neutrophil to C3 ratio (NC3R) may reflect LN. NC3R is a promising predictor of LN and ocular involvement in SLE patients.
Objectives: To explore the relationship between NC3R and LN patients and ocular vessel density in SLE patients.
Methods: This retrospective study included 53 patients with LN and 80 SLE patients without kidney involvement. The differences in NC3R between patients with and without LN were evaluated. Correlations between NC3R and other variables in SLE patients were assessed. Receiver operating characteristic curves (ROC) was constructed in NC3R to predict LN. Multivariate logistic regression analysis was used to analyze the independent factor of LN. We also investigate the role of NC3R in ocular involvement in SLE patients.
Results: NC3R was increased significantly in the LN group as compared with those SLE patients without LN(7.7 vs 4.5, P=0.002). NC3R were positively correlated with 24-hour proteinuria (r=0.437, P<0.001), and SLEDAI score(r=0.389, P<0.001), and negatively correlated with C3(r=-0.346, P<0.001) and C4(r=-0.293, P=0.001). Multiple regression analysis suggested that NC3R was an independent risk factor of LN[OR: 4.41 (1.64~11.91), P=0.003]. NC3R [AUC: 0.642, 95%CI(0.540~0.744)] was useful in differentiating LN patients, and the optimal cutoff was 4.56 (sensitivity: 79.6%, specificity: 49.2%). In the high NC3R group patients, there was increased superficial vessel density.
Conclusion: NC3R was a plausible indicator to predict LN and ocular involvement. Therefore, evaluating NC3R before treatment could help clinicians to identify potential organ involvement in patients with SLE.
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AB0687

CHRONIC SCLEROSING SIALADENITIS, IS IT A SJÖGREN'S SYNDROME OR NOT?

Keywords: Sjögren syndrome, Epidemiology, Descriptive studies

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Background: The Sjögren's syndrome (SS) is a chronic autoimmune disease. The classification criteria of SS have been evolved through the decades. Recent in 2016, American college of rheumatology (ACR)–European Alliance of Associations for Rheumatology (EULAR) classification requires at least one positive finding in either the labial salivary gland biopsy or anti-Ro (SSA) serology for the confirmation of SS. Chronic sclerosing sialadenitis (CSS) is unusual, underrecognized condition that affects the salivary gland, reported by H. Kutter at first. [1] Though the CSS already has been eliminated from the diagnostic criteria of SS, there is controversy in the meaning of CSS in SS. And that makes it difficult to determine whether the patient who suffers from sicca symptom is SS or not.
Objectives: Investigating the clinical meaning of CSS in association with SS by comparing the clinical and laboratory findings, we provide the extent of understanding CSS, the rare pathologic condition of salivary gland.
Methods: This study is a single center retrospective study, including patients confirmed as CSS via biopsy in Seoul St. Mary's Hospital from 2000 to 2022. (1) Patients with history of head and neck radiation, (2) graft-versus-host disease (GVHD), (3) IgG4-RD, (4) positive biopsy result in IgG4 immunohistochemistry

(IHC) staining, and (4) insufficient pathologic result to distinguish IgG4-RD from CSS were excluded. 21 of 27 CSS patients were eligible to our analysis. 4 of positivity with IgG4 in IHC staining positivity, 1 of GVHD, and 1 of prior head and neck radiation were excluded. We assessed 239 patients from 341 of the Korean Initiative of primary SS (KISS) prospective cohort study as SS control group, eligible to 2016 classification.

Results: In CSS group, only 1 of 21 was diagnosed as SS. Table 1 summarizes the result. 'CSS as SS' consisted of CSS patients meeting 2016 criteria, assuming that the CSS could be a part of SS pathology.

Table 1. The clinical characteristics of chronic sclerosing sialadenitis.

	CSS (n=21)	SS (n=239)	N	*p*	CSS as SS (n=15)	N	*p*
Female sex	19 (90.5%)	237 (99.2%)	260	**0.034**	15 (100.0%)	254	1.000
Age at diagnosis	50.6 ± 12.2	61.9 ± 9.5	260	**<0.001**	64.1 ± 6.8	254	**<0.001**
BMI (kg/m^2)	22.1 ± 3.7	22.2 ± 2.9	260	0.843	21.6 ± 3.2	254	0.873
Sicca symptom							
Dry eye	15 (71.4%)	223 (93.3%)	260	**0.004**	11 (73.3%)	254	**0.022**
Dry mouth	18 (85.7%)	227 (95.0 %)	260	0.110	13 (86.7%)	254	0.196
Diagnostic items for SS							
Salivary gland biopsy	0 (0.0%)	215 (90.0%)	260	**<0.001**		-	
Anti-Ro (SSA) Ab	2 (10.0%)	185 (84.1%)	240	**<0.001**	1 (6.7%)	235	**<0.001**
Schirmer test	1 (14.3%)	169 (72.2%)	241	**0.003**	1 (25.0%)	238	0.072
Ocular staining score	0 (0.0%)	64 (43.2%)	155	**0.042**	0 (0.0%)	152	0.139
Unstimulated salivary flow test	15 (78.9%)	78 (82.1%)	114	0.750	15 (100.0%)	110	0.121
Unstimulated salivary flow rate (ml/min)	0.08 ± 0.10	0.10 ± 0.19	107	0.856	0.035 ± 0.033	103	0.311
EGM	0.4 ± 0.7	1.1 ± 1.0	260	**0.001**	0.4± 0.7	254	**0.006**
ESSDAI	1.0 ± 2.5	3.1 ± 3.7	259	**<0.001**	1.3 ± 2.8	254	**0.005**
ESSPRI	4.8 ± 1.6	5.4 ± 1.8	206	0.131	4.6 ± 1.7	200	**0.004**
ANA	9 (45.0%)	165	205	**<0.001**	8 (53.3%)	200	**0.001**
Titer	220 ± 560	(89.2%) 610 ± 670	204	**<0.001**	280 ± 640	199	**<0.001**
Anti-La (SSB) Ab	1 (8.3%)	112 (51.1%)	231	**0.010**	0 (0.0%)	228	**0.003**
Rheumatoid factor	4 (22.2%)	125	208	**0.001**	4 (28.6%)	204	**0.012**
Titer	12.0 ± 18.7	(65.8%) 98.9 ± 206.2	208	**<0.001**	14.8 ± 20.4	204	**0.001**
Anti-CCP Ab	0.2 ± 0.3	23.2 ± 82.4	200	**<0.001**	0.1 ± 0.3	199	**<0.001**
Stimulated salivary flow rate (ml/min)	0.65 ± 0.57	0.54 ± 1.15	103	**<0.001**	0.50 ± 0.41	99	**0.006**

Abbreviations: BMI, body mass index; Ab, antibody; EGM, extraglandular manifestations; ESSDAI, EULAR Sjögren's syndrome disease activity index; ESSPRI. EULAR Sjogren's syndrome patient reported index.

Conclusion: The CSS were once inculeded in pathologic category of SS. However, it is a distinct phenotype separated from SS in such aspects of the (1) age of onset, (2) proportion of occular manifestation, (3) autoimmune profiles, and (4) stimulated salivary flow rate. Thus, physicians should also consider the possibility of CSS in old age patient with xerostomia.

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AB0688 QUALITY INDICATORS AND SATISFACTION WITH CARE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Patient reported outcomes, Systemic lupus erythematosus, Quality of care

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Background: Quality indicators (QI) for patients with SLE were developed based on the 2019 EULAR recommendations [1]. Measuring quality of care (QOC) may provide recognition of gaps and challenges in clinical practice. Improving QOC may relate to high satisfaction with care. Satisfaction might be considered a valuable indicator to measure the success of provided care. Evidence about the relationship between quality of care and satisfaction perceived by SLE patients is scarce.

Objectives: To correlate adherence to QIs based on the 2019 EULAR recommendations and satisfaction with care in SLE patients.

Methods: We conducted a cross-sectional and retrospective study in a Lupus Clinic in Northeast Mexico. We included patients at least 18 years old who met the ACR/EULAR 2019 classification criteria for SLE. Consecutive patients were interviewed by the researchers on their last visit to assess the adherence to quality indicators developed by Chavatza et. al., based on 2019 EULAR recommendations. Medical records were revised to assess demographic data, disease activity, treatment, organ involvement, and cumulative damage. Adherence was achieved if the patient met all components of the QI. We calculated adherence as the number of fulfilled patients divided by the number of eligible patients per indicator. Satisfaction with care was evaluated with the satisfaction domain of the LupusPRO 1.7 version. The distribution was assessed with Kolmogorov-Smirnov. The Spearman correlation coefficient was obtained to determine the relationship between quality of care and satisfaction with care.

Results: Seventy patients were included with a median age of 33 (IQR, 23-48), and 90% were female. Global adherence to the 18-QIs and Satisfaction with Care score revealed no correlation using the Spearman correlation coefficient (r = 0.064, p= 0.599). Overall adherence was 62.29%. The median satisfaction with care was 100. The results of each indicator are shown in Table 1.

Conclusion: In conclusion, we did not find a correlation between satisfaction with care and QOC. The areas of quality of care that performed the lowest were the measurement of the SLEDAI-2K and the SLICC/ ACR damage index, which was an area of opportunity for improvement.

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Table 1. Adherence to quality indicators

Indicator	Eligible patients n (%)	Fulfilled n (%)
1.Laboratory test	70 (100)	68 (97)
2.LN follow-up	65 (92.9)	45 (69.2)
3.Kidney biopsy	32 (45.7)	27 (84.3)
4.CVD risk stratification	70 (100)	47 (67.1)
5.Osteoporosis evaluation	58 (82.9)	20 (34.4)
6.Hydroxychloroquine monitoring	62 (88.5)	29 (46.7)
7.Tapering prednisone	46 (65)	18 (38.2)
8.Immunosuppressants in LN	30 (42.9)	26 (86.6)
9.ACE inhibitors or ARB in LN	27 (38.5)	19 (70.3)
10.Low-dose aspirin in pregnancy	2 (100)	2 (100)
11.SLEDAI evaluation	70 (100)	8 (11.4)
12.Annual SLICC damage index evaluation	70 (100)	17 (24.2)
13.Treat to achieve LDA or remission	70 (100)	50 (71.4)
14.Drug toxicity monitoring	70 (100)	68 (97.1)
15.Photoprotection	70 (100)	60 (85.7)
16.Vaccination	70 (100)	49 (70)
17.Fertility counseling	41 (58.6)	27 (68.5)
18.Pregnancy counseling	29 (41.4)	13 (44.8)
Global adherence	952	593 (62.29)

Adapted from Chavatza et al. (2021) LN, lupus nephritis; CVD, cardiovascular; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blockers; LDA, low disease activity

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AB0689 LIFESTYLE AND NUTRITIONAL STATUS IN ITALIAN PATIENTS WITH ISOLATED SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Lifestyles, Diet and nutrition

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Background: Dietary habits and Physical Activity (PA) are two pivotal features of healthy life in terms of the prevention and treatment of metabolic and chronic disease [1]. Few data are available concerning these issues in isolated Sjögren's syndrome (SS) patients [2].
Objectives: Aim of the study was to assess the level of PA, the adherence to Mediterranean diet (MD) and the nutritional status of Italian patients with SS.
Methods: Consecutive patients with SS (AECG criteria 2002) were enrolled. For each patient ESSDAI, ESSPRI, SSDDI were calculated. The value of focus score was obtained in the minor salivary gland biopsy (MSG), when performed. The International Physical Activity Questionnaire (IPAQ) was administered to assess the level of physical activity; the Mediterranean Diet (MDiet) score [3] was employed to analyse adherence to Mediterranean diet (the score spans from 0 - no adherence - to 55 - maximum adherence). In a subgroup of 26 patients, the dietary habits were evaluated with a daily food diary. Sarcopenia, a muscle failure that accrue across a lifetime, was identified by a diagnostic algorithm [4] with age-differentiated cut-offs; the Hand Grip test (HGT) and the Chair Stand test (CST) were used as screening tests, the Dual Energy X-ray Absorptiometry (DEXA) was employed to confirm and to quantify Appendicular Skeletal Mass (ASM, kg/m^2). The muscular performance (6-minutes Walking Test – 6MWT) was measured to grading sarcopenia. Statistical analysis was performed with SPSS.
Results: The 130 pSS patients enrolled showed a moderate adherence to the Mediterranean Diet (median MDiet = 33, third quintile) and played a moderately PA (median MET x min/wk in the second tertile). No significant associations were found between BMI, PA, MDiet and clinimetric index of pSS (ESSDAI, ESSPRI, SSDDI). BMI was higher in older patients (R ^{2} 0.96, p 0.02). 16 out of the 26 subjects of the subgroup (61%) showed a reduction in muscle strength (HGT and/or CST) and therefore a condition of probable sarcopenia but only 6 (23%) subjects were found to be sarcopenic (ASM). Only one sarcopenic patient had a 6MWT less than 10% of the predicted value and a reduced PA in MET x min/wk. Patients' daily diet consisted of 43% of total energy coming from carbohydrate, fat represented 40% of total energy intake, the remaining 17% daily energy coming from proteins. Fat consumption is higher and complex carbohydrates intake is lower compared to the levels of energy and nutrient intake for the Italian population [5].
Conclusion: This preliminary study considering Italian women with SS shows a moderate adherence to the MD similar to what previously reported in the general female population in Europe (32.5 ± 5 DS) [6]. Moreover, considering the results obtained in the subgroup, SS patients seem to have an unbalanced diet because of an intake of fat foods higher than that recommended in the Mediterranean Diet. A possible explanation for the higher fats intake may be a lubricating effect aiding mastication and swallowing. It can be hypothesized that an unbalanced diet might be partly responsible for increasing chronic damage and the associated reduction in muscle mass.

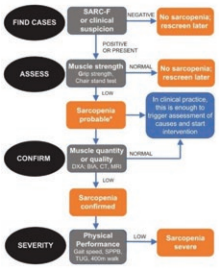
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Table 1. Features of population

Charateristics	N (%) or median (IQR) (130 patitents)	N (%) or median (IQR) (26 patitents)
F/M	125 (96%)	26 (100%)
Age	57 (35)	57 (17.5)
Disease duration (month)	48 (99)	12 (27)
ESSDAI	2 (5)	4 (15.4%)
ESSDAI (articular)	38 (29%)	1 (4%)
ESSDAI (muscular)	1 (0.07%)	0 (0%)
ESSPRI	5.6 (2.7)	5.3 (2.5)
ESSPRI (fatigue)	6 (4)	5 (3.5)
ESSPRI (pain)	5 (4.25)	5 (4)
SSDDI	1 (1)	1 (1.25)
Smoke	39 (30%)	4 (15.4%)
Alcohol	39 (30%)	7 (27%)
Hypertension	31 (24%)	4 (15.4%)
Cardiovascular event	6 (5%)	1 (3.8%)
Diabetes	10 (8%)	1 (3.8%)
Dislipidemia	15 (11%)	2 (7.7%)
BMI	23 (6)	25 (10.9)
MDiet	33 (6.5)	33 (4.25)
IPAQ (MET x min/wk)	1305 (2190)	1386 (2246)
IPAQ Low PA	45 (35%)	8 (30%)
IPAQ Moderately PA	49 (38%)	9 (35%)
IPAQ HighPA	36 (27%)	9 (35%)
Reduced Hand Grip and/or CST	-	16 (61%)
Sarcopenia (reduced ASM, kg/m^2)	-	6 (23%)
6MWT (metres)	-	595 (122)

Figure 1. Sarcopenia algorithm



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AB0690

SUBCLINICAL JOINT INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS: ROLE OF ULTRASOUND EVALUATION

Keywords: Ultrasound, Systemic lupus erythematosus, Prognostic factors

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Background: Patients with Systemic lupus erythematosus (SLE) experience musculoskeletal involvement in up to 90% of cases. Clinical presentation includes arthralgia, non-erosive arthritis, erosive arthritis and Jaccoud's arthropathy [1]. Recently, thanks to the use of ultrasound (US), several studies have demonstrated the presence of a subclinical joint and peri-articular inflammatory state, especially in patients with non-specific symptoms [2]. However, studies involved a small number of patients and there is a lack of predictive factors of disease progression to more aggressive forms as well of specific and validated clinimetric indices in patients with SLE.
Objectives: To evaluate joint and peri-articular involvement in SLE patients with different patter of musculoskeletal involvement by US. To evaluate the strength of the clinimetric indices already validated in other rheumatologic diseases (DAS28, CDAI, SDAI) in patients with SLE. To analyse the predictive value of laboratory data (autoantibody profile, complement levels, acute phase reactants) in joint involvement.
Methods: Consecutive SLE patients (18-65 years old), who fulfilled the EULAR/ACR 2019 criteria, were enrolled: 20 without symptomatic musculoskeletal involvement (Group 1) 19 with arthralgias without structural joint alterations (Group 2), 11 patients with estabilshed musculoskeletal involvement (Group 3). All patients undergo ultrasound evaluation with Esaote MyLab70 device with a 6-18 mmHz linear probe; wrists, metacarpophalangeal and proximal interphalangea joints, all finger flexors, wrist extensors and flexors at the hands, elbows, long head of the biceps and Achilles tendon were evaluated. All abnormalities were defined according to OMERACT EULAR Score System. [9]. DAS28 CDAI and SDAI and the most recent blood tests (ANA ENA FR anti CCP anti DNA ESR CRP C3 C4) were recorded; hands and wrists X-ray were performed according to good clinical practice.

Results: Fifty females were enrolled. Clinical characteristics during the disease course and serological and clinimeric scores at the time of enrollement are reported in Table 1. Group 1: US detected synovitis (grade 1–3) in 7 (35%) patients, mainly wrists and hands, Group 2: US detected synovitis (grade 1–3) in 5 (26.3%) patients mainly hands, elbows and wrists. Group 3: US detected synovitis (grade 1–3) in 7 (63.7%) patients, mainly knees elbows Achilles tendon, hands.

Conclusion: Our study confirmed that the musculoskeletal involvement in SLE is underestimated. Although not statistically significant, the groups showed differences in synovitis involvement. The percentage of asymptomatic patients with ultrasound signs of synovitis, especially of the hands and wrists, is higher than expected and almost comparable with symptomatic arthralgia patients. No association with clinimetric and laboratory tests were highlighted. As expected, the group of patients with known arthritis more frequently had ultrasonographic changes and signs of systemic disease activity.Our study suggests how necessary and interesting it is to prospectively evaluate in the future how the joint disease will progress in asymptomatic patients, and who will develop, for example, bone erosions or Jaccoud's arthropathy.

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Table 1. clinical characteristics of patients and disease activity at the time of observation

	GROUP 1	GROUP 2	GROUP 3
AGE (yr, median)	42,2	40,48	47,2
AGE AT DIAGNOSIS (yr, median)	29,6	22,3	29,4
DISEASE DURATION (months, mean)	150,3	217,5	218,2
MUCOCUTANEOUS involvement % (EVER)	60	50	55
NEPHRITIS % (EVER)	40	35	45
NPSLE involvement % (EVER)	25	10	20
SEROSITIS% (EVER)	20	15	10
HAEMATOLOGICAL involvement % (EVER)	50	60	55
CONSTITUTIONAL involvement % (EVER)	50	70	65
Disease activity at **at the time of US positive anti dsDNA %**	40	40	70
LOW C3/C4 %	45/55	50/45	65/70
SLEDAI median	2.63	1.53	4.86
DAS28 mean	1.53	1.57	2.24
SDAI mean	1.21	3.74	11.37
CDAI mean	1	3.47	6.55
CPR (mg/dl) mean	0.32	2.05	4.75

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AB0691 RESTLESS LEG SYNDROME AMONG PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A COMMON NEUROLOGIC MANIFESTATION

Keywords: Quality of life, Systemic lupus erythematosus, Comorbidities

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Background: Restless leg syndrome (RLS) is a common neurologic condition, affecting 5 to 10 percent of adults, that can be seen in patients with autoimmune diseases, like rheumatoid arthritis; however, data in patients with systemic lupus erythematosus (SLE) are scarce. Sleep disturbances are common in the SLE population, but few studies, with a small number of patients, investigated RLS. A deeper understanding of the relationship between SLE and RLS will allow us to promptly diagnose and manage RLS.

Objectives: The aim of this study is to determine the prevalence of RLS among patients with SLE, describe the clinical characteristics of RLS, examine its impact on health-related quality of life (HRQoL), and evaluate its association with depression.

Methods: We recruited SLE patients who met the SLICC-2012 criteria from September 2020 to September 2022. Demographic data, clinical characteristics, and pain level based on a visual analogue scale (0-10) were recorded. RLS diagnosis was based on the international restless leg syndrome study group criteria, and depression was assessed by the patient health questionnaire (PHQ)-9, with scores ≥10 indicating major depressive disorder (MDD). Patient global assessment was scored from 0 to 10, with higher numbers indicating active disease. HRQOL was assessed by a disease-specific validated questionnaire, the LupusQoL; scores ranged between 0-100, with higher scores indicating better QoL. These variables were compared between SLE patients with RLS and without RLS using t-tests or Wilcoxon non-parametric tests for continuous variables, as appropriate, and the chi-square test of independence for categorical variables. A p-value ≤ 0.05 was considered statistically significant and all tests performed were two-sided.

Results: Among the 144 SLE patients included in the study, 108 were women (87.1%), with a mean age of 49 ± 15 years (range 19 - 80) and a mean disease duration of 14 ± 12 years. Forty (32%) of them met the criteria for RLS and were more likely to experience a delay in diagnosis (mean 4.6 vs 2.2 years; p=0.019) and were less likely to work (65% vs 45%, p=0.040) compared to non-RLS patients. RLS patients were more likely to have coexisting MDD (45% vs 24%, p=0.019), higher level of pain (mean 3.9 vs 2.5, p=0.007) and disease activity based on patient global assessment (mean 4.2 vs 3.2, p=0.025). Further, all the domains of LupusQoL were significantly lower in the RLS patients group suggesting worse HRQoL (Table 1).

Conclusion: One of every three SLE patients had RLS, which negative impacted the patient's HRQoL. In addition, RLS was associated with depression, higher levels of pain, and worse perceived disease activity. Therefore, clinicians should be vigilant to recognize and manage RLS in SLE patients.

Table 1. LupusQol domain scores (median (Q1, Q3)) among patients SLE patients with and without RLS

LupusQoL Domains	All patients	No RLS	RLS	P-value
Pain	75.0 (41.6, 100.0)	83.3 (58.3, 100.0)	45.8 (25.0, 75.0)	<.001
Emotional health	79.1 (58.3, 91.6)	83.3 (66.6, 95.8)	66.6 (43.7, 85.4)	0.008
Physical health	71.8 (46.8, 90.6)	78.1 (56.2, 96.8)	64.1 (31.2, 78.1)	0.001
Planning	75.0 (41.6, 100.0)	91.6 (58.3, 100.0)	66.6 (33.3, 91.6)	0.017
Intimacy	75.0 (37.5, 75.0)	75.0 (50.0, 100)	62.5 (25.0, 75.0)	0.056
Burden to others	75.0 (58.3, 100.0)	83.3 (66.6, 100.0)	66.6 (41.6, 87.5)	0.006
Body image	88.8 (66.6, 100.0)	91.6 (70.0, 100.0)	77.5 (55.0, 100.0)	0.059
Fatigue	68.7 (50.0, 87.5)	81.2 (62.5, 93.7)	50.0 (31.2, 62.5)	<.001

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AB0692 SERUM INTERFERON A (IFNA) LEVELS AND SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) DISEASE ACTIVITY IN SLE PATIENTS IN ESTONIA. A PROSPECTIVE COHORT STUDY OF 40 SLE PATIENTS IN ESTONIA

Keywords: Systemic lupus erythematosus, Real-world evidence, Descriptive studies

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Background: SLE is a rare chronic autoimmune disease with polymorphic clinical manifestation. It has been found that the interferon signature is detectable in 80% of SLE patients. With the implementation of measuring IFNα levels, additional method to evaluate SLE has been provided.

Objectives: The aim of the present study is to characterize a sample of Estonian SLE patients.

Methods: Consecutive outpatient and inpatient patients with rheumatologist diagnosed SLE (≥20 years) were enrolled in East-Tallinn Central Hospital. Two study visits were done with 6 months apart to evaluate disease activity, current treatment, organ involvement, immunological findings and comorbidities. In addition, data from medical records were collected: organ involvement and immunological findings at the time of diagnosis and initial treatment. SLE disease activity was measured using SLEDAI 2K (Systemic Lupus Erythematosus Disease Activity Index 2K) score. Blood tests were taken to measure interferon levels using Simoa (Single Molecul Array) method. To evaluate the extent of the deviation of IFNα levels in patients with SLE compared to non-autoimmune individuals, age and gender matched control group was used. Interferon score was calculated according to interferon induced gene expression in blood cells collected to RNA stabilizing tubes. Spearman correlation was used for correlation analyses and chi-square and Fisher test for the group comparison.

Results: Among 40 patients (mean age 50 (standard deviation ±12.4) years, mean disease duration 12 (±9.9) years, mean SLEDAI 2K at diagnosis 10 (±3.9)) 92.5% were females. Mean SLEDAI 2K value at entering into the study was 4 (±3.4) similar to the value after six months 4 (±5.0). Median IFNα levels during first and second study visits were respectively 133 fg/ml (IQR=560) and 117 fg/ml (IQR=477). At first and second study visit respectively 48% and 45% of patients had low IFNα levels (<100 fg/ml), 35% and 37% had high IFNα levels (100-1000 fg/ml) and 18% of patients had very high IFNα levels (>1000 fg/ml). IFNα levels correlated poorly or not significantly in either time point with SLEDAI 2K (r=0.3280, p=0.04 and r=0.5460, p=0.0004), organ involvement (for joints r= 0.2352, p=0.14 and r=0.3433, p=0.03; for skin r=0.0216, p=0.89 and r=-0.0532, p=0.76), Rituximab treatment (r=0.2061, p=0.20 and r=0.3201, p=0.05). IFNα levels correlated strongly with IFN score (r=0.9325, p<0.0005) and 78% of patients had elevated IFNa levels compared to 98 percentile of healthy controls (median IFNα level 0.5605 fg/ml, IQR=1.77). There was no statistical difference in regards of Rituximab treatment during the study in low and in high IFNα level group, respectively 16% and 38% (p=0.22) at first study visit and 12% and 43% (p=0.07) at second study visit.
Conclusion: The first analysis of Estonian SLE patients' IFNα levels and disease activity shows that measuring IFNα levels can give additional information in some SLE patients in the light of new treatments targeting IFNα, although the general correlation with disease activity and available treatment so far is low. Further studies are in progress to evaluate IFNα levels in larger Estonian SLE population to better understand possible pathogenetic mechanisms in different SLE subpopulations.
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AB0693 IN-OFFICE LACRIMAL BIOMARKERS IN PRIMARY SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Outcome measures, Descriptive studies

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Background: Dry eye disease (DED) is characterized by loss of homeostasis of the tear film, ocular surface inflammation, ocular symptoms and neurosensory abnormalities. [1] The exposure of epithelial surface triggers a series of cellular processes that culminate in an inflammatory mediator increase, which can be measured non-invasively and affordably in a medical office. [2]
Objectives: To compare tear film osmolarity (Osm) and matrix metalloproteinase-9 (MMP-9) inflammatory biomarkers between primary Sjögren's syndrome (pSS) patients and a control group.
Methods: A prospective, cross-sectional and comparative study was conducted as part of a dry eye screening cohort by the ophthalmology and rheumatology services of the Hospital Universitario "Dr. José Eleuterio González". pSS diagnosis was made according to ACR/EULAR 2016 criteria. Control group participants were recruited as part of dry eye screening evaluations in general population. Patients under 18 years old, history of ocular disease not related to pSS, ocular surgery in the last 3 months and contact lenses wearers were excluded. All participants underwent the following dry eye tests: tear film Osm, tear film MMP-9, ocular surface disease index (OSDI) questionnaire, tear breakup time (TBUT), sicca ocular staining score (OSS), Schirmer without anesthesia (SCH) and corneal sensitivity.
Results: One eye per patient was included, 76 with pSS and 76 age- and sex-matched controls. Mean age was 53.0 ± 12.7 and 53.4 ± 16.2 (p=0.955) in pSS and control group respectively. The majority were women in pSS (74, 97.4%) and controls (74, 97.4%). We found a significant difference in the prevalence of comorbidities, with hypothyroidism (12, 18.8% vs. 1, 1.3% *p*=0.002) and depression (7, 9.2% vs 0 *p*=0.007) being more frequent in the pSS group than controls. In pSS and controls, Osm was 316.05 ± 25.54 vs 305.13±17.22 (p=0.010), positive MMP-9 in 19 (25.0%) vs 7 (9.2%) (p=0.017), OSDI was 43.52 ± 24.09 vs 34.09 ± 21.15 (p=0.012), TBUT 5.04 ± 3.36 vs 6.48 ± 2.76 (p <0.001), OSS 7.12 ± 3.50 vs 1.83 ± 1.70 (p<0.001), SCH 10.91 ± 10.05 vs 15.70 ± 9.60 (p<0.001) and sensitivity 5.56 ± 1.01 vs 5.91 ± 0.28 (p=0.032) respectively. No significant correlation was found between Osm and other dry eye variables.
Conclusion: Patients with pSS had higher Osm and OSDI, as well as more prevalence of MMP-9 detection than controls, and lower TBUT, Schirmer and corneal sensitivity. More information is needed to determine the role of tear film osmolarity and MMP-9 in the tear in the diagnosis and prognosis of pSS. However, biomarker tests are useful for the diagnosis and severity stratification of DED, being non-invasive, affordable and easy to use in the medical office.

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AB0694 CORRELATION BETWEEN PATHOLOGICAL FINDINGS AND SALIVARY GLAND ULTRASOUND IN PATIENTS WITH CLINICAL SUSPICION OF SJÖGREN'S SYNDROME IN A TERTIARY HOSPITAL

Keywords: Sjögren syndrome, Ultrasound

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Background: Sjögren's syndrome (SS) is a chronic systemic autoimmune disease that presents a great clinical heterogeneity, which condition a significant delay in its diagnosis. The current 2016 classification criteria for SS, according to ACR/EULAR, are based on five objective tests/data, including minor salivary gland biopsy (MSGB). These criteria do not include any imaging tests2. Ultrasound of the major salivary glands (MSGU) has been consolidated in Rheumatology as a rapid, non-invasive, accessible and cost-effective test that could be useful in the evaluation of patients with Sjogren's syndrome, both for diagnosis and follow-up of these patients.
Objectives: To evaluate the correlation between the histological results obtained from the minor salivary gland biopsy (MSGB) and the findings of the major salivary gland ultrasound (MSGU) in patients with suspected Sjögren's syndrome.
Methods: It is a cross-sectional study in a consecutive cohort of patients evaluated in the rheumatology clinics of a tertiary hospital for ten months with suspicion of SS who underwent a MSGB as part of the of the usual diagnostic process and who are proposed to perform an MSGU (parotid and submandibular, bilaterally). We used the ultrasound scoring system proposed by OMERACT in 2019 that is based on the homogeneity of the glandular parenchyma individually (0-3) and a total score (0-12) is made. Demographic, clinical, and histological data were collected from the patient's clinical history after performing the ultrasound. A descriptive and inferential analysis of data is carried out.
Results: Fifty-seven patients were included, with a mean age of 56.8 years, 87% being women. Of these, 31 patients were diagnosed with Sjogren's syndrome. The rest of the patients, 26 individuals, were considered the control group. Of the 22 patients with MSGB consistent with SS, 14 had pathologic MSGU. A total ultrasound score >5 showed a sensitivity of 96% for the SS group with a negative predictive value (NPV) of 94%. The ultrasound total score was significantly higher in patients with positive SMGB and in patients diagnosed with SS compared to those with a negative BGSM and in patients not finally diagnosed with SS, respectively. The correlation between MSGB and MSGU presents a direct and significant (P< 0.01) moderate (value=0.628) association.
Conclusion: The results of our study show a moderate positive correlation between ultrasonographic and histological findings, which supports the role of ultrasonography of major salivary glands in the diagnosis of Sjogren's syndrome.
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AB0695 **SJÖGREN'S SYNDROME: ORAL MANIFESTATIONS, ITS IMPACT ON ORAL QUALITY OF LIFE AND RELATIONSHIP WITH DAMAGE AND DISEASE ACTIVITY**

Keywords: Sjögren syndrome, Quality of life

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Background: Involvement of oral cavity have been described in patients with primary Sjögren Syndrome (pSS). Research about how oral health affects the quality of life in pSS is lacking, for this reason we conducted this study.
Objectives: 1-To establish the presence and characteristics of oral involvement in patients with pSS. 2-To assess the quality of life related to oral health. 3-To assess relationship between the quality of life related to oral health and saliva production, disease activity, and damage.
Methods: An observational, analytical and cross-sectional study was conducted. Patients aged ≥18 years who met the European-American 2002 and/or ACR-EULAR 2016 classification criteria for pSS were included. Patients with another rheumatic disease and/or conditions that favor the appearance of caries were excluded. The quality of life related to oral health was evaluated by the abbreviated version of OHIP Oral Health Impact Profile questionnaire (Oral Health Impact Profile-OHIP14sp) validated in its Spanish version, a self-administered generic questionnaire (score 0-56 meaning the highest, the worst). A rheumatologist performed visual analogue scale (VAS) for xerostomia (0-100mm) ESSPRI (EULAR Sjogren's Syndrome Patient Reported Index) ESSDAI (EULAR Sjögren's Syndrome Disease Activity Index) and SSDDI (Sjögren's Syndrome Disease Damage Index). A dentist assessed oral health using the DMFT (number of Decayed, Missing, and Filled Permanent Teeth) index, it quantifies the prevalence of caries and its results are expressed as follows: 0-1.1 very low prevalence; 1.2-2.6 low, 2.7-4.4 moderate, 4.5-6.5 high and ≥6.6 very high). The O'Leary index and Loe & Silnes index were also calculated (the first evaluates dental hygiene, a value of > 10% determines poor hygiene; and the second one measures bacterial plaque categorized as 0,1,2 and 3, category 3 represents the greatest thickness and extension). Continuous variables were reported as mean and standard deviation or median and interquartile range, according to distribution. Categorical variables were reported as percentage. A multiple linear regression model was performed, taking OHIP14sp as the dependent variable, adjusted for possible confounders.
Results: 51 patients were included, 98% were female, mean age 54 (±13 years). The OHIP-14sp median was: 16 (6-25), xerostomia VAS median was 60 [30-80]. Mean of ESSPRI was 4 (± 2.6), ESSDAI median was 0 (0-2), SSDDI median was 3 [2-4]. Unstimulated saliva flow rate was positive in 75% of patients, the median was 0.7 ml (0.5-1). ANAs were positive in 90%, Anti-Ro autoantibodies were positive in 74.5%. Regardless treatment, 56% were treated with conventional DMARDs (75% received hydroxychloroquine), 4% DMARDb, and 9.8% received glucocorticoids with a median dose of 10mg/day [5-20]. 60% were treated for xerostomia xerostomia (M agonists or salivary substitute). Oral involvement occurred in 100% of patients, DMFT median was 22 [14-28]. 88% had poor dental status, O'Leary index median was 21 [13-30]. The Loe & Silnes index was 1 in 51%, 2 in 18.9% and 3 in 8%. In the univariate analysis, OHIP14sp was significantly associated with ESSPRI (β coefficient: 2.04 95% CI 0.72-3.3), xerostomia VAS (β coefficient: 0.19 95% CI 0.08-0.29) and category 2 of the Loe & Silnes index (β coefficient: 18 95% CI: 5-31). In the multivariate analysis, OHIP14sp was independently and significantly associated with xerostomia VAS (β ccoefficient: 0.19 95% CI 0.09–0.29) and category 2 of the Loe & Silnes index (β coefficient: 19 95% CI:7.7-29.7)
Conclusion: In our study the entire population included had oral involvement, with impaired oral quality of life, and related significantly with the degree of dryness measured by xerostomia. Our findings support the importance of multidisciplinary treatment with dentists to improve the degree of xerostomia, hygiene and oral condition.

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AB0696 **EULAR SJOGREN'S SYNDROME PATIENT REPORTED INDEX (ESSPRI) AND OTHER PATIENT-REPORTED OUTCOMES IN ASSESSMENT OF GLANDULAR DYSFUNCTION IN SJÖGREN'S SYNDROME**

Keywords: Outcome measures, Patient reported outcomes, Sjögren syndrome

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Background: Sjögren's syndrome (SS) constitutes a common autoimmune disease in which the exocrine glands, especially salivary and lacrimal glands, produce excessive immune responses with the resultant tissue damage leading to mucosal dryness. For assessment of disease activity, the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI), ESSPRI, and other patient-reported outcomes (PROs), such as visual analog scale (VAS) for symptoms, and EULAR sicca score (ESS), are performed. ESSPRI, ocular staining score (OSS), salivary flow rate (SFR), salivary gland scintigraphy (SGS), and minor salivary gland (MSG) pathology have a cooperative relationship with regard to the evaluation of glandular function and inflammation in SS, its diagnosis and therapeutic management, and patient follow-up. However, although ESSPRI is reported to show a significant correlation with PROs, the relationship between ESSPRI or RPOs and objective parameters of glandular dysfunction, especially salivary and ocular glands, is not well defined.
Objectives: To investigate whether ESSPRI or other PROs are correlated with objective parameters of glandular dysfunction in primary SS (pSS).
Methods: A total of 70 patients with pSS were included in the present study. Disease activity indexes including ESSPRI, EULAR sicca score (ESS), VAS scores for symptoms, and ESSDAI, serologic markers, SFRs, SGS, MSG biopsy, and OSS were evaluated. Correlations were calculated with the Spearman correlation coefficient.
Results: ESSPRI was a significantly correlated with its domains (dryness domain, r=0.661 p<0.001; fatigue domain, r=0.859, p<0.001; pain domain, r=0.849, p<0.001). ESSPRI showed a significant correlation with ESS (r=0.639, p<0.001), oral (r=0.522, p<0.001) and ocular dryness VAS (r=0.482, p<0.001), acute phase reactant levels (ESR, r=0.271, p=0.028; CRP, r=0.322, p=0.008), serum IgG level (r=0.322. p=0.033), and ESSDAI (r=0.371, p=0.002), while it was not correlated with SFRs, data of SGS, focus score (FS) and OSS. ESSPRI dryness domain was significantly correlated with ESS (r=0.969, p<0.001), SFRs (unstimulated, r=-0.281 p=0.025; stimulated, r=-0.263, p=0.037), data of SGS (parotid gland [PG] uptake ratio [UR], r=-0.252, p=0.044; submandibular gland (SMG) UR, r=-0.357, p=0.004; SMG ejection fraction [EF], r=-0.325, p=0.009), FS (r=0.261, p=0.050) and OSS (r=0.386, p=0.002). However, it did not demonstrate the correlation with ESSDAI, acute phase reactant levels, and serum IgG level. ESS was closely correlated with SFRs (unstimulated, r=-0.400, p=0.001; stimulated, r=-0.364, p=0.003), data of SGS (PG UR, r=-0.325, p=0.009; PG EF, r=-0.285, p=0.023; SMG UR, r=-0.424, p<0.001; SMG EF, r=-0.356, p=0.004), FS (r=0.284, p=0.032), and OSS (r=0.340, p=0.007), but not with ESSDAI, acute phase reactant levels, and serum IgG level. Oral dryness VAS was also correlated with SFRs (unstimulated, r=-0.527, p<0.001; stimulated, r=-0.470, p<0.001), data of SGS (PG UR, r=-0.417, p=0.001; PG EF, r=-0.366, p=0.003; SMG UR, r=-0.467, p<0.001; SMG EF, r=-0.377, p=0.002), and FS (r=0.288, p=0.030) but not with OSS. Ocular dryness VAS showed a significant correlation with OSS (r=0.422, p=0.001), but not with parameters of salivary gland dysfunction.
Conclusion: The present study demonstrated that ESSPRI dryness domain, ESS, and VAS for symptoms, but not ESSPRI, reflected the glandular dysfunction in SS.

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AB0697 **COMPARISON OF COVID-19 VACCINATION WITH INFLUENZA VACCINATION IN KOREAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: PERCEPTION, ADVERSE EVENTS, AND FLARES FROM THE CIVIL STUDY**

Keywords: Systemic lupus erythematosus

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Background: Vaccines are widely credited for their role in reducing the incidence and the severity of various infections. Although the safety profiles of vaccines have been proved, there still remain gaps between healthy individuals and patients with autoimmune diseases in the efficacy and adverse events of vaccinations.
Objectives: The aim of the **C**OVID-19 and **I**nfluenza **V**accine **I**n **L**upus (CIVIL) study was to compare the perception and safety profile between COVID-19 vaccine and influenza vaccine in Korean patients with systemic lupus erythematosus (SLE).
Methods: We conducted a cross-sectional study based on a 34-question web-based survey on COVID-19 and influenza vaccination in 207 medically confirmed SLE patients. Patients were recruited from 13 academic hospitals affiliated with Korean society of SLE research (KSSR) from DEC 2022 to JAN 2023. The primary outcome was the perception of patients and physicians on the vaccines, and the occurrence of side effects including flare.
Results: 94.1% of two hundred respondents were females aged in 20's (19.8%), 30's (24.3%), 40's (27.7%), 50's (16.8%), and 52% was treated more than 10 years. More than 50% of patients were in stable condition for recent 6 months (below 20mm in 100mm visual analogue scale with lower than 10mg prednisolone equivalent dose). COVID-19 vaccine (Pfizer, Moderna, AstraZeneca, Novavax) and influenza vaccine were completed in 77.7% and 87.6% of SLE patients, respectively. Reasons for willing not vaccinated included fear of lupus flare (56.3% vs 24.5%), worried about side effects (52.1% vs 26.6%), and not recommended from physicians (35.4% vs 7.4%) on COVID-19 and influenza vaccines, respectively. Adverse events (AEs) occurred much higher in COVID-19 vaccine (65.8%) than influenza vaccine (12.4%). However, only 4.4% of patients experiencing AEs from COVID-19 vaccine required hospitalization. Most common AEs were pain/redness on injection site, myalgia and/or arthralgia, fatigue, febrile sense, irregularity in menstrual period. 10.3% of patients taking COVID-19 vaccine experienced lupus flare (arthralgia, skin rash, hair loss, and deterioration of proteinuria/laboratory parameter), which lead to medication change or hospitalization.
Conclusion: COVID-19 vaccine has a worse perception and higher adverse events compared to influenza vaccine in Korean SLE patients.
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Table 1. Reasons of vaccination unwillingness

Covid-19	
Fear of lupus flare	56.3%
Fear of AEs	52.1%
Recommended not to be vaccinated by medical staff	35.4%
Not sure vaccine has a preventive effect	18.8%
Recommended not to be vaccinated by peer	6.3%
Just do not want to be injected	2.1%
Influenza	
Not sure vaccine has a preventive effect	27.7%
Fear of AEs	26.6%
Fear of lupus flare	24.5%
Recommended not to be vaccinated by medical staff	7.4%
Recommended not to be vaccinated by peer	1.1%
others	10%

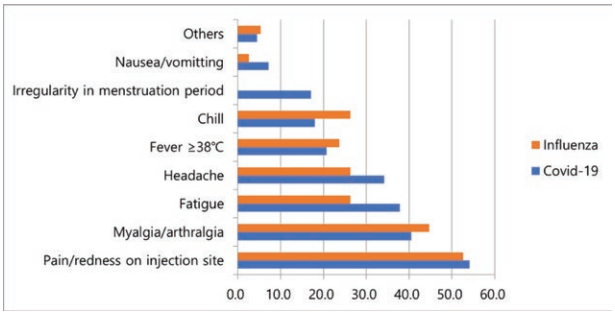


Figure 1. Common vaccination-related AEs

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AB0698

SYSTEMIC LUPUS ERYTHEMATOSUS OVER 80 YEARS OF AGE: A RETROSPECTIVE COHORT OF VERY LATE-ONSET IN A THIRD LEVEL HOSPITAL

Keywords: Systemic lupus erythematosus, Epidemiology

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Background: Late-onset systemic lupus erythematosus (SLE) is designated as that developing after the age of 50 [1], [2]. It has been associated with a different prevalence of clinical manifestations, disease activity, and mortality compared to early-onset SLE.
Objectives: - To describe the clinical expression and epidemiological features of our patients diagnosed with SLE from the age of 80.
- To delimit the average survival time and mortality, as well as the main cause of death in case of it is present.
Methods: A retrospective cohort of 31 patients diagnosed with SLE with an age of onset older than 80 years and followed up at the Hospital de León between 1997-2022. All fulfill the 1992 ACR and 2012 SLICC classification criteria.
Results: The patients were mostly women, with a female/male ratio of 2.1, and a mean age at diagnosis of 84.32 ± 2.79 years. The most prevalent clinical manifestations were arthritis and inflammatory arthralgia (48.4%) and dermatological involvement (45.1%), such as acute cutaneous lupus (35.7%), discoid (7.1%) and other reactions of unspecified photosensitivity (57.1%). Leuko-lymphopenia (45.1%) and thrombocytopenia (29.3%) were also relevant. On the other hand, the cases of alopecia (3.2%), hemolytic anemia (6.45%), interstitial lung disease (ILD) with a usual interstitial pneumonia (UIP) pattern (3.2%), sensory polyneuropathy (3.2%) and chorea (3.2%). Oral ulcers were present in 12.9% of patients, as were cases of renal involvement (1 with microscopic hematuria, 1 with proteinuria > 0.5 mg/dL, 1 nephrotic syndrome, and 1 nephritic syndrome). Raynaud's phenomenon affected 16.1%, as well as serositis (4 patients with pleuritis and 2 with pericarditis). No one reported *sicca* syndrome or thrombotic events. Regarding immunological criteria, the most important findings were: ANA 97%, DNA 38%, Sm 10% and hypocomplementemia 29%. Antiphospholipid antibodies were present in 42%, and 6,5 % have triple positivity). The average survival time was 4.5 years, with a statistically significant difference in favor of women (7 vs 3.4 years; p-value = 0.0024). There were 11 losses to follow-up and 10 deaths (7 men). The fundamental causes of death were certified in 4 of the cases as infectious etiology, one due to heart failure and another due to global respiratory failure. In 4 cases the cause of death was unknown.
Conclusion: - Late-onset SLE diagnosed in people over 80 years of age is more frequent in women (2.1:1), although there is a higher proportion of men than in cases of earlier debut [1].
- The most frequent manifestations in our cohort were joint, skin, and hematological involvement.
- The main cause of death was of infectious origin.
- The average survival time was 4.5 years.
- The male sex was associated with a worse prognosis in our patients, with higher mortality (70%) and significantly lower survival.
- More research is needed to broaden our knowledge of SLE in this age group, as well as to clarify to what extent excess male mortality may be due to disease burden or is influenced by other factors (lower life expectancy, toxic habits, etc.).

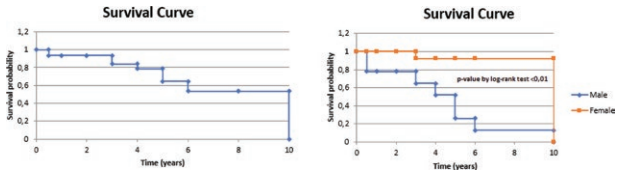


Figure 1. Average Survival Curve using Kaplan-Meier method in all patients (left) and segregated by sex (right).

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AB0699

IS AUTONOMIC DYSFUNCTION MORE COMMON IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME WITH FIBROMYALGIA THAN IN PATIENTS WITHOUT FIBROMYALGIA?

Keywords: Fibromyalgia, Sjögren syndrome

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Background: Primary Sjögren's syndrome (pSS) is an autoimmune disease that primarily affects the exocrine glands, but other organs, including the nervous system, may also be affected [1]. Many studies provide evidence of autonomic dysfunction in pSS [2,3]. Although the etiology of fibromyalgia (FM) is not fully understood, data suggest that FM may be caused by autonomic nervous system dysfunction [4].

Objectives: In this study, we aimed to reveal the incidence of autonomic dysfunction in patients with pSS compared to those without fibromyalgia.

Methods: In this cross-sectional study, 64 patients who admitted to our Sakarya University Faculty of Medicine rheumatology outpatient clinic between November 2021 and August 2022 and were followed up with the diagnosis of pSS were included. The patients were divided into two groups 35 (54.7%) with fibromyalgia and 29 (45.3%) without fibromyalgia. Patients were evaluated with the Composite Autonomic Symptom Score-31 (COMPASS-31), which consists of 6 subsections including autonomic dysfunction, orthostatic, vasomotor, secretomotor, gastrointestinal, bladder and pupillomotor functions. Mann-Whitney U test and Chi-square test were used to compare the groups.

Results: The mean age of the patients was 53.8±11.3 years. There was no difference between the groups regarding sex and age (p = 0.586 and p = 0.580, respectively). The median disease duration (IQR) was 4(5) years. The mean total COMPASS-31 score was significantly higher in patients with fibromyalgia than in those without fibromyalgia (0.014). Among its subgroups, secretory dysfunction was significantly higher in patients with fibromyalgia (p=0.001). Vasomotor dysfunction is more common in patients with FM (p=0.016) (Table 1).

Conclusion: In our study, patients with pSS with fibromyalgia had a higher COMPASS-31 score than those without FM, and especially the secretory dysfunction score was higher. Since both diseases can cause autonomic dysfunction separately, it seems reasonable to have a high total COMPASS-31 score in patients with both. In addition, vasomotor dysfunction is more common in patients with FM.

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Table 1. Comparison of COMPASS-31 score and subtypes of autonomic dysfunction according to the presence of fibromyalgia.

	Fibromyalgia +	Fibromyalgia -	p
COMPASS-31, total	33 (32)	20.6 (20)	*0.014*
Orthostatic	8 (24)	0 (16)	0.177
Vasomotor	0 (3)	0 (0)	*0.016*
Secretomotor	6.4 (2)	4.3 (4)	*0.001*
Gastrointestinal	5.4 (8)	3.6 (8)	0.187
Bladder	2.2 (2)	1.1 (3)	0.337
Pupillomotor	2.3 (2)	2 (2)	0.477

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AB0700

HISTOPATHOLOGICAL FINDINGS IN RENAL BIOPSY OF PATIENTS WITH LUPUS NEPHROPATHY AS THE INITIAL MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS AND LONG-TERM RENAL OUTCOME IN MEXICAN POPULATION

Keywords: Systemic lupus erythematosus, Epidemiology, Descriptive studies

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Background: Renal biopsy is essential in Lupus nephritis (LN) to guide treatment of lupus nephritis and provides information on classes and prognosis of lupus nephritis. Activity and chronicity index can be used as a guide for lupus nephritis treatment although little has been considered the percentage of fibrosis and tubular atrophy in the renal prognosis.

Objectives: Describe the histopathological findings in biopsies performed in patients with LN as an initial manifestation of SLE and the long-term renal outcome.

Methods: Retrospective descriptive observational study. Data on baseline demographic, biopsy records, laboratory results and treatment regime were extracted from the case notes. Normality tests were applied, the frequencies and percentages were calculated for the categorical variables and the means with their standard deviation or medians with minimums and maximums for the continuous variables depending on their distribution.

Results: Of the 61 patients who presented LN at the diagnosis of SLE, renal biopsies were performed in 80% (n=54). The median age was 30 (19-66) years, females predominated (77%). The frequencies of different classes of lupus nephropathy as well as their index of activity and chronicity and treatment used are described in Table 1. Only 30 of renal biopsies (65%) described tubulo-interstitial findings and 60% had no immunofluorescence. Another additional finding found in the renal biopsy were fibrocellular crescents, membranoproliferative pattern and podocytopathy. At the diagnosis of LN, median serum creatinine (CrS) was 0.8 (1-6) mg/dl and proteinuria 1355 (90-9450) mg/24 hrs. The remission induction treatment frequently used was the combination of mycophenolate and prednisone. However, in the second and third relapse cyclophosphamide and rituximab was preferred. Ten patients had a second relapse with complete remission in 40%, partial remission in 40%, and no response in 20%. Seven patients had more than 3 relapses and correlationate with a percentage of tubulointerstitial fibrosis greater than 25% (r=0.34, p<0.05), three of them progressed to end-stage renal disease (5%), all of them with class IV of LN. The main reasons why patients did not finish treatment were infectious processes (37%), myelotoxicity (25%), loss of social security (19%) and poor adherence (19%).

Conclusion: Frequency of class IV LN in our population is like that reported worldwide, however a higher percentage of mixed forms (IV+V) is reported. Combination of mycophenolate and prednisone was used as remission induction treatment. Although the complete remission rates are much lower than those reported (33% vs 58%). Presence of fibrosis in more than 25% is associated with progression to end-stage renal disease.

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Table 1. Demographic characteristics and renal biopsy findings in the population

	N=54
Edad	30 (19-66)
Sexo	14 (23%)
Hombre	47 (77%)
Mujer	
Indice de actividad	8 (15%)
Sin reporte	33 (61%)
≤6	9 (17%)
7-9	4 (7%)
≥10	
Indice de cronicidad	6 (11%)
0	38 (70%)
≤6	10 (19%)
≥7	
Fibrosis tubulointersticial	24 (44%)
Sin reporte	24 (44%)
≤25%	6 (12%)
25-50%	

		Tratamiento de Inducción a la remisión		
Clase histológica	3 (6%)	**INH**	**EL**	**MFM+PDN**
I ó II	8 (15%)	33%	-	67%
III	25 (46%)	-	-	75%
IV	13 (24%)	24%	8%	36%
IV + V	5 (8%)	-	8%	77%
V	1 (1%)	20%	-	70%
VI		100%		-
Remisión completa	18 (33%)			
Remisión parcial	23 (43%)			
Sin remisión	13 (24%)			

	Tratamiento de Inducción primera recaída				
Clase histológica	**INH**	**EL**	**MFM+PDN**	**Rituximab**	**Multitarget**
I ó II	34%	67%	-	-	-
III	-	-	12%	-	-
IV	4%	-	28%	8%	-
IV + V	8%	-	15%	-	8%
V	20%	-	20%	20%	-
VI	100%	-	-	-	-
	-	-	-	-	-

INH: Institute National Health, **EL:** Eurolupus, **MFM:** Mycophenolate *Mofetil*, **PDN**: prednisone

Acknowledgements: NIL.
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AB0701

PERFORMANCE OF DRAFT 2022 ACR/EULAR CLASSIFICATION CRITERIA IN A TURKISH COHORT OF APL ANTIBODY POSITIVE PATIENTS

Keywords: Epidemiology, Anti-phospholipid syndrome, Autoantibodies

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Background: Revised Sapporo classification criteria is the most commonly used criteria set for the classification of antiphospholipid syndrome (APS) patients [1]. Since its revision in 2006, various other clinical and laboratory manifestations have been reported in the literature. Among these are livedo reticularis (racemosa), cutaneous ulcers, thrombocytopenia, cardiac, pulmonary and renal involvement [2]. In 2022 American College of Rheumatology Convergence meeting, new draft classification criteria have been presented [3].

Objectives: Comparing the performance of the new draft classification criteria for antiphospholipid syndrome with the revised Sapporo criteria in a Turkish cohort of antiphospholipid antibody positive patients.

Methods: Patients with a positive antiphospholipid antibody (LAC, aCL IgM or IgG, aB2GPI IgM or IgG) followed since 2016 in our institution have been included. Demographic, clinical, laboratory and radiological features of the patients were recorded retrospectively. All parameters were evaluated with reference to the 2006 revised Sapporo and 2022 draft criteria.

Results: 40 patients were included our study. 80% (N=32) of the patients were female. Average age of the patients at diagnosis or first antibody positivity was 33.9 years. 27.5% of patients (N=11) were screened for hereditary thrombophilia, with only one patient having heterozygous factor V Leiden mutation. 37% of patients (N=13) had ever smoked prior to their inclusion in the cohort. 57.5% of patients (N=23) had secondary APS, 12.5% had primary APS, 30% had isolated antiphospholipid antibody positivity. Among the secondary APS patients, vast majority had SLE (N=20). 47,5% of the patients (N=19) had a history of vascular thrombosis. 16 patients had venous and 5 patients had arterial thrombosis. Among the 32 female patients, 62,5% (N=20) had an obstetric morbidity associated with APS. 20,5% of patients (N=8) had a skin finding consistent with APS, the most common one being livedo racemosa (N=7). 50% of patients had thrombocytopenia. 20% of patients (N=8) had developed autoimmune hemolytic anemia. Only a single patients had a history of catastrophic APS. 17,5% of cases (N=7) had a positive lupus anticoagulant. Most commonly positive aPL antibody was anti-cardiolipin IgG (55%, N=22), followed by anti-B2GP-I IgG (28%, N=11). 82% of patients (N=33) had a positive ANA test, 62,5% (N=25) had low C3 and C4. Overall, 42,5% (N=17) of patients fulfilled 2006 revised Sapporo criteria, whereas 40% (N=16) ultimately fulfilled the 2022 draft criteria for classification. There was a large level of agreement between the two criteria sets, with one patient not fulfilling 2006 criteria fulfilling 2022 criteria and two patients fulfilling 2022 criteria without fulfilling 2006 criteria.

Conclusion: Our cohort of patients had a high prevalence of thrombocytopenia, as well as a significant minority having livedo racemose and autoimmune thrombocytopenia. None of the patients with isolated aPL antibody positivity were classified as APS, despite many of the fulfilling the initial screening step of the draft criteria. Longer term follow-up of patients fulfilling 2022 screening criteria may yield additional information in the future.

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Disclosure of Interests: None Declared.
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Vasculitis - large vessel vasculitis

AB0702 THE INCIDENCE OF LARGE VESSEL VASCULITIS IN NORFOLK, UK

Keywords: Epidemiology, Vasculitis, Real-world evidence

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Background: There are no data on the collective incidence of the large vessel vasculitides. The data of incidence of GCA and Takayasu arteritis in the UK has been based on clinical coding in routine administrative datasets. There are no data on the incidence of these diseases based on clinically verified diagnoses. We studied the incidence of the large vessel vasculitides in a stable population with a predominant Northern European ancestry.
Objectives: To report the incidence of large vessel vasculitis and its subsets in Norfolk, UK.
Methods: Individuals attending a secondary care hospital with a clinically verified diagnosis of primary systemic vasculitis made between 2011-2020, who lived within the NR postcode districts of Norfolk County borders were included if they met classification criteria (ACR 1990 or ACR/EULAR 2022) for GCA/ Takayasu arteritis [1-4], or had definite tissue or imaging evidence of large vessel vasculitis. The population data from the 2011 census, available from the office of national statistics was used as the denominator. If classification criteria for both GCA and TAK were met, a clinical decision was taken to decide on the subtype.
Results: 272 individuals were diagnosed with a large vessel vasculitis in a population of 454,316 above the age of 18. The annual incidence of large vessel vasculitis in Norfolk is 59.9/million in population above the age of 18. The annual incidence of giant cell arteritis is 9.9/100000 in population above the age of 50 using the ACR 1990 criteria and 10.6/100000 using the ACR/EULAR 2022 criteria. There is a marked rise in the incidence from 2017 onwards when a fast-track pathway was formally established (Table 1). There is dip in the incidence in 2020 when services were suspended during the SARS-COV2 pandemic. The annual incidence peaks at 168.5/100000 in the 9th decade of life and is commoner in females (12.3/100000) than males (7.3/100000). The annual incidence of Takayasu arteritis is 3.3/million in population above the age of 18 using the ACR 1990 criteria and 1.1/million using the ACR/EULAR 2022 criteria.
Conclusion: This is the first study that reports the incidence of all objectively diagnosed large vessel vasculitis from a secondary centre which provides services to a large stable population in the East of England. The incidence of GCA rose with the establishment of a fast-track pathway and its peak may have been affected by the SARS-COV2 pandemic. GCA is commoner in females and peaks in the 8th and 9th decades.

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Table 1. Incidence of GCA by age, gender and year using the ACR 1990 criteria

	Number of cases	Incidence (per 100000 in age >50)
Age		
6th decade	9	9.9
7th decade	53	54.4
8th decade	109	166.4
9th decade	63	168.5
10th decade	6	78.7
Gender		
Female	150	12.3
Male	79	7.3
Year of diagnosis		
2011	14	6.1
2012	14	6.1
2013	14	6.1
2014	21	9.1
2015	11	4.8
2016	16	6.9
2017	29	12.6
2018	40	17.3
2019	43	18.6
2020	27	11.7

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AB0703 TOWARDS TREAT-TO-TARGET PATIENT CENTRED CARE: DEVELOPMENT OF MULTIDIMENSIONAL DISEASE SPECIFIC PATIENT REPORTED OUTCOME MEASURES QUESTIONNAIRE FOR GIANT CELL ARTERITIS

Keywords: Remission, Patient reported outcomes, Vasculitis

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Background: Giant Cell Arteritis (GCA) is the commonest form of systemic vasculitis in people over the age of 50. In 2017, the OMERACT Vasculitis Working Group published a core set of domains and outcome measures for use in clinical trials in large vessel vasculitis [1] and highlighted the lack of a disease-specific patient reported outcomes (PROMs) for GCA. The OMERACT group proposed a draft core set of domains for GCA, including disease specific domains, organ and arterial function, psychosocial impact and physical function biomarkers, fatigue, pain, as well as death.
Objectives: To assess the validity, reliability and responsiveness to change of a patient self-reported questionnaire to assess for the construct outcome measures, co-morbidities and the impact of GCA and its treatment on health-related quality of life in GCA patients.
Methods: The PROMs-GCA was conceptualized based on frameworks used by the WHO Quality of Life tool and the PROMIS. Initially, cognitive interviews were conducted to identify item pool of questions. Item selection and reduction was achieved based on patients as well as an interdisciplinary group of specialists. Rasch and internal consistency reliability analyses were implemented. The questionnaire included the GCA specific physical and psychological symptoms, sense of self, symptoms severity using numerical visual analogue scale (0-10) in addition to assessment of functional disability, quality of life (QoL), review of the systems, glucocorticoids benefit:risks, comorbidities as well as motivation [2]. In addition, every patient completed HAQ and EQ-5D questionnaires.
Results: A total of 52 GCA patients completed the questionnaire. The PROMs-GCA questionnaire was reliable as demonstrated by a high standardized alpha (0.867-0.941). Content construct assessment of the PROMs-GCA/functional disability and QoL revealed significant correlation ($p< 0.01$) with both HAQ and EQ-5D. Changes in functional disability, QoL showed significant ($p< 0.01$) variation with diseases activity status in response to therapy.
Conclusion: The developed PROMs-GCA questionnaire is a reliable and valid instrument for assessment of patients living with GCA. A phased treatment regimen depending on the severity of GCA as well as the patient's preferences and comorbidities are the best approach to tailored patient management.

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Disclosure of Interests: None Declared.
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AB0704 EVALUATION OF THE OF THE 2022 ACR/EULAR CLASSIFICATION CRITERIA FOR GCA IN A GERMAN PATIENT COHORT

Keywords: Diagnostic tests, Ultrasound, Vasculitis

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Background: In 2022, the ACR and the EULAR proposed new classification criteria for Giant Cell Arteritis (GCA). While the previous classification criteria from 1990 were based on clinical and histological findings only, the new classification criteria also consider several types of imaging.
Objectives: To assess and compare the sensitivity and specificity of the ACR 1990 (1990CC) and the ACR/EULAR-2022 classification criteria (2022CC) for GCA.
Methods: In a retrospective analysis, we classified 210 patients (33 % males, median age 68 years) with suspected GCA according to the 1990CC and 2022CC. All patients attended the Klinikum Ludwigshafen between 2018 and 2022 and were examined with either ultrasound, MRI, or PET-CT. The results were compared with the final clinical diagnosis made by the attending physician.
Results: Of 210 patients under consideration, 94 had GCA. Of these 94 patients, 54 met the 1990CC, while 90 met the 2022CC (Table 1). Of the 116 non-GCA patients, 110 did not meet the 1990CC and 112 did not meet the 2022CC, amounting to a sensitivity and specificity of 0.57 and 0.96 for the 1990CC versus 0.96 and 0.97 for the 2022CC, respectively (Table 1). Overall, the correct classification proportion was 0.78 for the 1990CC and 0.96 for the 2022CC (Table 1). It was noticeable that 21 GCA patients had no cranial symptoms like temporal headache, jaw claudication, or striking temporal arteries. 18 of these patients were correctly classified by the 2022CC, but all of them were misclassified by the 1990CC. Moreover, 81 of 94 patients showed a typical ultrasound halo in at least one vessel section, which increased the sensitivity of the 2022CC.
Conclusion: Our results demonstrate that the inclusion of imaging methods increase the sensitivity of the 2022CC compared with the 1990CC, while the specificity of > 0.95 remains similar. The 1990CC were primarily developed for the classification of giant cell temporal arteritis, causing a frequent misclassification of patients with isolated extracranial large vessel vasculitis. Moreover, the 1990CC classified GCA patients without cranial symptoms only accurately in case of a positive temporal biopsy.

Table 1. Sensitivity and specificity of the 1990-ACR-Classification Criteria and 2022-ACR/EULAR-Classification criteria for GCA compared with the final clinical diagnosis of GCA.

		Clinical diagnosis positive	Clinical Diagnosis negative	Sensitivity	Specificity	Correctly classified proportion
	n=	94	116			
1990 ACR - Criteria positive	59	54	5	0.57	0.96	0.78
1990 ACR - Criteria negative	151	40	111			
2022 EULAR/ACR-Criteria positive	94	90	4	0.96	0.97	0.96
2022 EULAR/ACR-Criteria negative	115	4	112			
		ACR 1990 positive	ACR 1990 negative			
		59	151			
2022 EULAR/ACR-Criteria positive	94	56	38			
2022 EULAR/ACR-Criteria negative	116	3	113			

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Acknowledgements: NIL.
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AB0705

LONG TERM SAFETY OF CONVENTIONAL AND BIOLOGIC IL-6RI IMMUNOMODULATORS AS SECOND-LINE (2L) OR THIRD-LINE (3L) TREATMENT OF POLYMYALGIA RHEUMATICA

Keywords: Safety, Vasculitis, Disease-modifying drugs (DMARDs)

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Background: In polymyalgia rheumatica (PMR), IL-6Ri therapy has been studied in limited number of patients in RCTs, with exposure up to 16-52 weeks, [1-3] while patients may require longer treatment in real world. Data are presented on safety of IL-6Ri and conventional immunomodulatory (CIM) therapy for up to 2 years (Y) in patients with PMR.
Objectives: Evaluate safety of IL-6Ri and CIM therapy in 2L or 3L treatment of PMR.
Methods: This was a retrospective study in US adults ≥50Y, with 1 inpatient/2 outpatient claims with PMR diagnosis ≥30 days apart, from national fee-for-service Medicare data (3/29/2016 - 6/30/2020). Patients were on ≤25 mg prednisone (PS) equivalent and started IL-6Ri (tocilizumab/sarilumab) or CIM (methotrexate/leflunomide/azathioprine) as 2L/3L therapy and had continuous enrollment ≥180 days prior to index. For 2L, index date was start of IL-6Ri/CIM with no prior use of IL-6Ri/CIM. For 3L, index date was start of IL-6Ri (with/without background CIM) or new CIM, after prior CIM. Follow-up was until the earliest of end of enrollment, death, treatment switch, or 2Y. Patients with seropositive RA, other arthritis or connective tissue disease, giant cell arteritis, organ transplant, or malignancy undergoing treatment were excluded. Stratifying by line of therapy, IL-6Ri patients were direct matched using 1:3 variable ratio matching on age, sex, index date and baseline PS equivalent dose category (<2.5, 2.5-<5, 5-<10, 10-<15, 15-<20, 20-25 mg), recency of prior CIM (3L only; 1-60, 61-180, 180+days), and then 1:1 propensity score matched using multivariate logistic regression to identify variables with SMD >0.1. We examined hospitalized infection (any and primary diagnosis), gastrointestinal perforation, major adverse cardiac events, malignancy, and drug induced liver injury. Except for infection, patients with prior events were excluded from each outcome-specific analysis. Outcomes were identified using validated or previously used claims-based algorithms. Incidence rates were reported per 100 patient-years through 2Y of follow-up, using exact Poisson for 95% CI, if events <5. Cox proportional hazards model was used to estimate adjusted hazard ratios (aHR) for infections (given paucity of other events). Sensitivity analyses examined events in Y1 and Y2 separately and stratified by 2L vs 3L.
Results: In final cohort, covariate balance for 451 matched patients (2L: 183; 3L: 268) in each arm was good. Residual imbalances were small for disability status, steroid dose category, and chronic obstructive pulmonary disease. Incidence rates and aHRs for events are shown in Table 1; aHRs were not significant for IL-6Ri vs CIM. Sensitivity analyses were consistent with primary results and generally showed incidence was similar, or numerically lower for IL-6Ri vs CIM in Y2 and lower for CIM vs IL-6Ri in Y1, for most outcomes.

Table 1. Pooled incidence rates and aHR stratified by 2L/3L of safety events for IL-6Ri and CIM-treated patients with up to 2Y exposure

Outcome	Exposure Group	Events/100PY	aHR (95% CI) IL-6Ri vs CIM
Hospitalized Infection, any	IL-6Ri	14.4 (11.8 - 17.7)	1.05 (0.79 - 1.41)
	CIM	13.4 (10.8 - 16.6)	
Hospitalized infection, primary diagnosis	IL-6Ri	9.8 (7.7 - 12.5)	1.16 (0.82 - 1.65)
	CIM	8.4 (6.4 - 11.0)	
Malignancy	IL-6Ri	0.8 (0.3 - 1.9)	NE
	CIM	2.0 (1.1 - 3.5)	
Major adverse cardiac events	IL-6Ri	2.1 (1.2 - 3.7)	NE
	CIM	2.1 (1.2 - 3.7)	
Gastrointestinal perforation	IL-6Ri	0.1 (0.0 - 0.8)	NE
	CIM	0.1 (0.0 - 0.8)	
Drug induced liver injury	IL-6Ri	0.0 (0.0 - 0.5)	NE
	CIM	0.0 (0.0 - 0.5)	

aHR, adjusted hazard ratios, controlling for covariates imbalanced with SMD >0.10; CI, confidence interval; CIM, conventional immunomodulatory therapy; NE, not estimated, inadequate sample size; PY, patient-years; IL-6Ri, interleukin-6 receptor inhibitor

Conclusion: Rates of serious adverse events for IL-6Ri vs CIM therapy with up to 2Y exposure were comparable in PMR.
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Disclosure of Interests: Ara Dikranian Speakers bureau: AbbVie, Amgen, GlaxoSmithKline Eli Lilly, Mallinckrodt, Pfizer Inc, and Sanofi, Consultant of: AbbVie, Boehringer Ingelheim, Eli Lilly, Glaxo SmithKline, Janssen, Mallinckrodt, Novartis, Pfizer Inc, Sanofi, UCB, cassandra calabrese: None declared, Clifton Bingham Consultant of: AbbVie, Janssen, Lilly, Pfizer, and Sanofi, Grant/research support from: BMS, Stefano Fiore Shareholder of: Sanofi and may hold stock/stock option, Employee of: Sanofi, Kerri Ford Shareholder of: Sanofi and may hold stock/stock option, Employee of: Sanofi, Lita Araujo Shareholder of: Sanofi and may hold stock/stock option, Employee of: Sanofi, Fenglong Xie: None declared, Jeffrey Curtis Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, CorEvitas, Janssen, Lilly, Myriad, Pfizer, Regeneron, Roche, and UCB.

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AB0706 AGGLOMERATIVE HIERARCHICAL CLUSTER ANALYSIS IDENTIFIES TWO CLUSTERS OF TAKAYASU ARTERITIS BASED ON CLINICAL PHENOTYPE WHICH PREDICT ANGIOGRAPHIC FINDINGS AND MORTALITY IN A COHORT OF 200 PATIENTS

Keywords: Vasculitis, Registries

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Background: Cluster analysis is a data-driven approach to identify natural patterns of disease which may help better understand the phenotype of Takayasu arteritis (TAK), a rare large vessel vasculitis.

Objectives: To evaluate whether clusters based on clinical phenotypes of TAK predict angiographic patterns of disease or mortality.

Methods: From a retrospective cohort of TAK, agglomerative hierarchical clustering using Ward method was performed using clinical features. Optimal number of clusters were identified using elbow method and silhouette method. The hitherto identified clusters were compared for differences in clinical features, vascular involvement, and Hata's angiographic subtypes using odds ratios (OR, with 95% confidence intervals), and for survival (crude, using Kaplan-Meier curves; adjusted for gender and age of disease onset using Cox regression analyses) using STATA 16.1 I/C.

Results: Optimal number of clusters was two [Ward agglomerative coefficient 0.989; Cluster 1: 111 TAK, mean (SD) age 25.06 (9.97) years, 80.2% females; Cluster 2: 89 TAK, mean (SD) age 25.54 (10.38) years, 65.2% females]. Carotidynia, pulse or BP inequality, pulse loss, vascular bruits, upper limb claudication, lower limb claudication, and chest pain were more common in cluster 1, whereas, hypertension, renal failure, and stroke/TIA were more common in cluster 2 (Table 1). Involvement of subclavian and carotid arteries, left vertebral, brachiocephalic, ascending aorta, arch of aorta, descending thoracic aorta were more common in cluster 1, whereas, abdominal aorta, celiac, superior mesenteric, inferior mesenteric, left and right renal arteries were similar in both clusters. Hata's angiographic subtype V was more common in cluster 1 (OR 0.45, 95%CI 0.25 – 0.80), whereas, subtype IV was more common in cluster 2 (OR 6.16, 95%CI 1.70 – 22.35). Over 697 person-years of follow-up (193 patients), cluster 1 had worse survival than cluster 2 (log-rank p value 0.027, Figure 1), even after adjustment for gender and age of onset (adjusted Hazard ratio cluster 2 vs cluster 1 0.09, 95%CI 0.01 – 0.78).

Conclusion: Clinical features corresponded to vascular territories which were more common in cluster 1. Hypertension and renal failure were more common in cluster 2, which correspond to more frequent Hata's subtype IV in this cluster. Clusters based on clinical features could predict well the patterns of vascular involvement. Higher adjusted mortality rate in cluster 1 requires validation in other cohorts of TAK.

Table 1. Clinical and angiographic involvement in the two clusters

Clinical features	OR (95%CI) Cluster 2: Cluster 1	Arterial involvement	OR (95%CI) Cluster 2: Cluster 1
Constitutional	1.15 (0.66 – 2.03)	Right subclavian	0.48 (0.27 – 0.86)
Carotidynia	0.18 (0.05 – 0.63)	Left subclavian	0.49 (0.26 – 0.92)
Syncope/dizziness/ vertigo	0.64 (0.31 – 1.32)	Right carotid	0.44 (0.24 – 0.79)
Stroke/TIA	11.04 (3.68 – 33.09)	Left carotid	0.36 (0.20 – 0.64)
Vision blurring or loss	1.76 (0.82 – 3.77)	Right vertebral	-*
Pulse/BP inequality	0.18 (0.10 – 0.34)	Left vertebral	0.31 (0.11 – 0.86)
Pulse loss	0.12 (0.06 – 0.23)	Brachiocephalic	0.42 (0.21 – 0.84)
Vascular bruits	0.13 (0.07 – 0.27)	Ascending aorta	0.46 (0.22 – 0.97)
Upper limb claudication	0.09 (0.03 – 0.21)	Arch of aorta	0.44 (0.24 – 0.81)
Lower limb claudication	0.31 (0.14 – 0.68)	Descending thoracic aorta	0.38 (0.21 – 0.67)
Hypertension	2.75 (1.29 – 5.85)	Abdominal aorta	0.65 (0.37 – 1.14)
Aortic regurgitation	0.45 (0.12 – 1.75)	Celiac trunk	0.70 (0.37 – 1.32)
Renal failure	3.96 (1.37 – 11.46)	Superior mesenteric artery	0.73 (0.38 – 1.41)
Abdominal angina	0.61 (0.15 – 2.51)	Inferior mesenteric artery	0.82 (0.23 – 3.01)
Chest pain	0.18 (0.05 – 0.63)	Right renal	1.11 (0.63 – 1.95)
Heart failure	0.43 (0.16 – 1.15)	Left renal	1.09 (0.62 – 1.92)
		Pulmonary	1.27 (0.39 – 4.07)
		Coronary	-*

*Only involved in Cluster 1

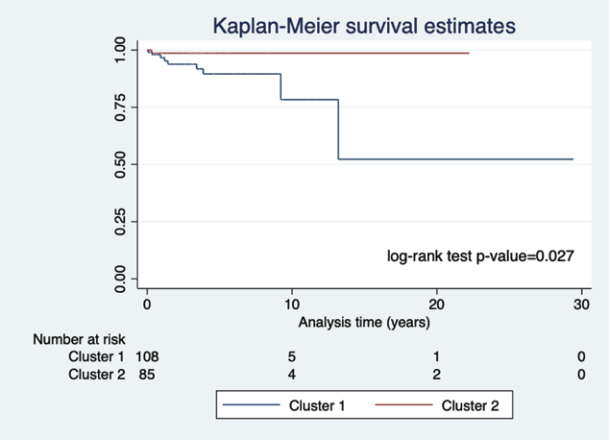


Figure 1. Kaplan-Meier survival curve based on the clusters identified on clinical phenotypes

REFERENCES: NIL.

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AB0707 PREDICTIVE FACTORS OF RELAPSE IN GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB

Keywords: Vasculitis, bDMARD

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Background: Tocilizumab (TCZ) is the only biologic therapy approved for giant cell arteritis (GCA). Clinical trials with TCZ in GCA was performed with intravenous (iv) TCZ in a phase 2 trial [1], and with subcutaneous (sc) TCZ in the phase 3 GiACTA [2]. There is general agreement on the initial/maintenance dose, but duration of TCZ therapy is not well established. In GiACTA trial, after one year on TCZ, most patients had GCA relapse after withdrawal.

Objectives: To assess the predictive factors of relapse in GCA in a clinical practice scenario.

Methods: Multicentre observational study of 471 patients with GCA. The diagnosis of GCA was performed between 2016 and 2021 according to: **a)** ACR criteria, and/or **b)** temporal artery biopsy, and/or **c)** imaging techniques.

Relapse was defined according to EULAR consensus definition [3].

From the 471 patients, we selected the patients who had available the data on relapse during follow-up. Multivariable study was conducted to identify the best set of predictors for the appearance of a relapse.

Results: GCA relapses were observed in 63 of 405 (15%) patients for whom such data was available **(Table 1).** No significant differences were observed between the two groups in demographic, clinical and laboratory characteristics or in prednisone dose at initiation of TCZ. The set of variables associated with GCA relapses were prior use of synthetic conventional disease-modifying antirheumatic drugs (scDMARDs), use of iv.TCZ, shorter time on TCZ therapy and optimization of TCZ dose **(Figure 1).**

Conclusion: GCA relapse seems related mainly to TCZ schedule and was associated with iv TCZ, and a shorter treatment time and optimization.

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Table 1. Main features of the patients with GCA according to relapses.

	No relapsing GCA (n=342)	Relapsing GCA (n= 63)	p
Age at GCA diagnosis (mean±SD)	72±9	70±9	0.12
Women/Men (% de women)	246/96 (72)	47/16 (75)	0.57
Phenotype			
cGCA	152 (44)	31 (48)	0.63
ecGCA	62 (18)	12 (18)	0.95
mixGCA	128 (37)	22 (34)	0.58
Cardiovascular risk factors			
High blood pressure, n (%)	212 (63)	37 (60)	0.65
Dyslipidemia, n (%)	193 (57)	33 (53)	0.57
Diabetes, n (%)	63 (19)	12 (19)	0.89
Previous or current smoking history, n (%)	33 (10)	9 (14)	0.28
Ischemic manifestations			
Headache, n (%)	189 (55)	36 (58)	0.70
Jaw claudication, n (%)	84 (26)	11 (19)	0.25
Visual manifestations, n (%)	56 (16)	13 (20)	0.48
Systemic manifestations			
Fever, n (%)	39 (11)	12 (19)	0.11
Constitutional syndrome, n (%)	139 (41)	27 (42)	0.83
PmR, n (%)	210 (62)	43 (68)	0.32
Laboratory			
ESR, mm/1a hora, median [IQR]	36 [14-56]	14 [6-42]	0.85
CRP (mg/dL), median [IQR]	1.6 [0.3-3.0]	0.8 [0.4-2.9]	0.21
Previous treatment			
scDMARDs, n (%)	171 (50)	53 (82)	<0.001
bDMARDs, n (%)	4 (1)	4 (6)	<0.001
Prednisone dose (mg/day), median [IQR]	20 [10-40]	20 [10-30]	0.86
TCZ			
IV/SC, (%IV)	171/171 (50)	45/18 (69)	0.004
Mono/combo, (%mono)	263/79 (77)	43/20 (66)	0.066
Optimization, n (%)	123 (39)	38 (62)	<0.001
Months receiving TCZ	27 [18-43]	4 [2-12]	<0.001

Abbreviations: bDMARDs: biologic disease-modifying antirheumatic drugs,GCA, CRP: C-reactive protein, giant cell arteritis, ESR: erythrocyte sedimentation rate, IQR: interquartile range [25th-75th], JAKINIB: Janus kinase inhibitors, scDMARDs: synthetic conventional disease-modifying antirheumatic drugs, SD: standard deviation

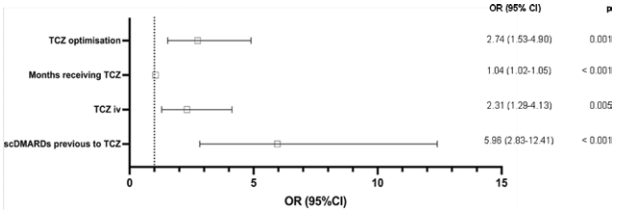


Figure 1. Forest plot of the multivariable analysis.

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AB0708 PHYSICAL ACTIVITY AND POLYMYALGIA RHEUMATICA RISK: A MENDELIAN RANDOMIZATION STUDY

Keywords: Fibromyalgia, Non-pharmacological interventions, Genetics/epigenetics

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Background: Polymyalgia rheumatica (PRM)is a chronic inflammatory disorder characterized by pain and long-term morning stiffness of the neck, shoulders, hips, upper arms, and thighs [1]. Prolonged unaccustomed exercise involving muscle lengthening (eccentric) movements can lead to ultrastructural muscle destruction, impaired excitation-contraction coupling, inflammation, and muscle protein degradation to produce muscle pain [2]. This muscle pain due to exercise may be associated with muscle pain in PRM.

Objectives: This study aims to discover whether physical activity affects PRM.

Methods: We obtained GWAS data for sedentary: Time spent watching television (n=91,084), time spent using a computer (n=360,895), and time spent driving (n=310,555). Types of physical activity included moderate physical activity 10+ minutes (n= 440,266), vigorous physical exercise 10+ minutes (n=440,512), tachometer-based physical activity, Vigorous physical activity, and moderate to vigorous physical activity (UK Biobank). GWAS of PRM included 213,145 European individuals. Single nucleotide polymorphisms (SNPs) that were independent ($r^2 < 0.001$) and were strongly related to accelerometer-measured physical activity ($p < 5\times10^{-8}$, $F > 10$) were selected as instrumental variables. The inverse-variance weighted (IVW) method was the primary method, to evaluate the causal association. The weighted median, and MR-Egger were applied for further MR analysis. Cochran's Q test, MR-Egger intercept analysis, the funnel plot, and the leave-one-out analysis were used for sensitivity analysis.

Results: There was an inverse association between time spent using a computer with PRM (IVW OR: 0.32, 95% CI: 0.15–0.70, *p*: 0.004). No directional pleiotropy was revealed by the MR-Egger intercept analysis (*p*: 0.797). On the flip side, tachometer-based physical activity, vigorous physical activity, moderate to vigorous physical activity, moderate physical activity 10+ minutes, vigorous physical activity 10+ minutes, time spent watching TV (TV), and driving time were not associated with PRM(*p*>0.05). (Figure 1)

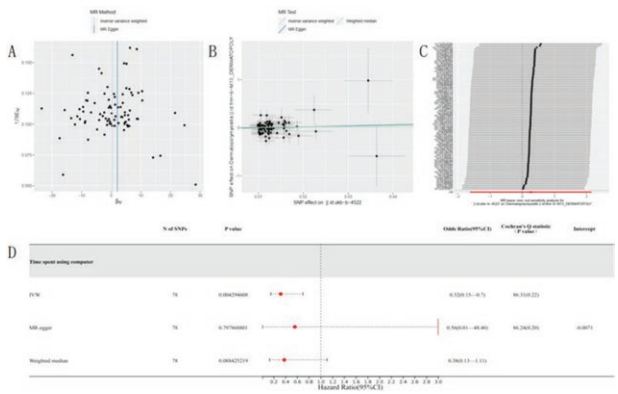


Figure 1. The causal associations between PA and PRM were evaluated by the odds ratio (OR) values of IVW, MR-Egger, and Weighted median. (A)Funnel plot, (B)scatter plot, (C) leave-one-out analysis, and (D)forest plot.

Conclusion: Computer time spent is a protective factor for PRM. Conversely, excessive exercise may be a risk factor, providing new insights into the pathogenesis of PRM.

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AB0709

EFFECTIVENESS OF JANUS KINASE INHIBITORS IN GIANT CELL ARTERITIS IN CLINICAL PRACTICE. REAL-WORLD CLINICAL PRACTICE STUDY AND LITERATURE REVIEW

Keywords: Vasculitis, Real-world evidence

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Background: Patients with giant cell arteritis (GCA) can relapse despite glucocorticoids, methotrexate and tocilizumab treatment. The JAK/STAT signalling pathway is involved in the pathogenesis of GCA, and JAK inhibitors (JAKi) are a potential treatment alternative. Baricitinib showed positive results in a small uncontrolled study [1].

Objectives: To evaluate the effectiveness of JAKi in GCA.

Methods: Real-world, retrospective clinical practice study of patients with GCA treated with JAKi. Outcomes assessed included disease relapse and safety. A literature search for other JAKi-treated GCA cases was conducted in PubMed, Embase and the Cochrane library from inception to 12/31/2022. We compared results of the previous baricitinib study **(1)** and the baricitinib recipients in our series.

Results: We present 32 patients (27 females [84%], mean age, 72.4 years, relapsing disease 32 [100%]) that received JAKi. The initial JAKi was baricitinib (n=12), tofacitinib (n=10) and upadacitinib (n=10) (**Table 1 and Figure 1**). After a median [IQR] follow-up of 6 [3-15] months, 23 (72%) achieved and maintained remission, and 9 (28%) patients discontinued the initial JAKi due to relapse (n=7, 22%) or severe adverse events (SAEs) (n=2, 6%) including liver dysfunction and dyspnea/palpitations. The 9 patients failing the initial JAKi were switched to an alternative [JAKi (n=4) or to another immunosuppressant (n=5)]. The literature review identified another 21 GCA patients (17 females, mean age 74.2 years) treated with JAKi, mostly with baricitinib (n=18). Most of these patients benefited from JAKi therapy (**Table 1**). Patients in our series receiving baricitinib had longer disease duration (median [IQR]36 [24-48] vs 9 [7-21] months; p=0.001) and had received biologics (83% vs 6.7%; p<0.001) more frequently than those in the previous baricitinib study [1]. Remaining baseline features were similar.

Conclusion: This real-world analysis suggests that JAKi could be effective in GCA, including patients failing other immunosuppressive therapies. The results of an ongoing phase 3 randomized controlled trial are awaited to confirm or rule out this observation.

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Table 1. Current series and literature review of patients with GCA treated with JAKi.

Reference	Cases	Sex	Mean age	JAKi	Previous csDMARDs	Previous bDMARDs	Follow-up (months), mean±SD	Outcome
Herlihy. Br J Haematol. 2019	1	Female	75	Ruxolitinib	Methotrexate, Mycophenolate mofetil	None	9	Missing data
Prigent. Clin Nucl Med. 2021	1	Female	76	Baricitinib	Methotrexate	Tocilizumab	12	Clinical improvement
Camellino. Ann Rheum Dis.2022	3	Female	74	Baricitinib (3)	Methotrexate (2), Hydroxychloroquine (1), Sulfasalazine (1), Cyclosporine (1), Mycophenolate mofetil (1)	Tocilizumab (2)	8.5±4.9; Missing data (1)	Clinical improvement (1), Missing data (2)
Koster. Ann Rheum Dis. 2021	15	Female (11)	72.4	Baricitinib (15)	Methotrexate (2), Cyclosporine (1)	Sirukumab (1)	11.3±2.3	Clinical improvement (13); No improvement (1); MIssing data (1)
Sanada. Rheumatology (Oxford). 2022	1	Female	72	Upadacitinib	Sulfasalazine	None	7.5	Clinical improvement
Current series	32	Female (27)	72.4	Baricitinib (12), Tofacitinib (10), Upadacitinib (10)	Methotrexate (19), Hydroxychloroquine (3), Leflunomide (1)	Tocilizumab (26), Sarilumab (2), Abatacept (8), Adalimumab (1), Ustekinumab (1)	9.2±7.9	Clinical improvement (23); No improvement (7); JAKi discontinued due to safety (2)

Abbreviations: csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; bDMARDs, biologic disease-modifying antirheumatic drugs; JAKi, JAK inhibitor.

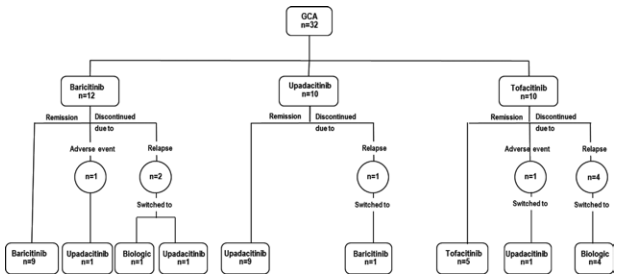


Figure 1. Flow chart of the 32 GCA patients treated with JAKi.

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AB0710 MIXED RESPONSE TO TOFACITINIB IN INDIAN PATIENTS WITH REFRACTORY TAKAYASU ARTERITIS: A MULTI-CENTER STUDY

Keywords: Targeted synthetic drugs, Vasculitis

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Background: Treatment of patients with Takayasu arteritis (TAK) is challenging in-spite of the use of conventional cytotoxic agents and biologics. Tofacitinib has been reported to be effective in inducing and maintaining remission in around 80% of patients with refractory TAK [1].
Objectives: To assess the efficacy and safety of tofacitinib in Indian patients with TAK.
Methods: In this retrospective study, medical records of consecutive patients with TAK being treated with either originator or generic tofacitinib at 4 centres in India were studied. Details regarding demographics, clinical presentation, disease duration, Indian Takayasu Activity score (ITAS), laboratory markers angiography treatment and response to treatment were recorded. The disease was considered active if the patient had evidence of activity in any two of the following three domains: new clinical symptoms as evidenced by ITAS >1; persistently raised C-reactive protein (CRP) for 2 consecutive visits; new areas of arterial wall thickening or active uptake in angiography or 18FDG PETCT respectively. Good response was defined as the absence of activity in at least 2 of the 3 above-mentioned domains. In contrast, presence of carotidynia or new areas of arterial narrowing were considered as standalone indicators of disease activity. In the absence of follow up imaging, a rise in CRP from baseline visit on 2 consecutive occasions was also considered as active disease. The data is presented as mean± SD or median (Interquartile range) according to distribution of data. Fischer's exact test or Mann Whitney test was used to compare the parameters between patients with good response and no response to treatment.
Results: Twenty-seven patients (24, 88.9% females; age 30.4 ± 8.13 years) with median disease duration 48 (20-72) months were included. At diagnosis, 13 (48.1%), 6 (22.2%), 15 (55.6%) and 7 (25.9%) patients presented with constitutional symptoms, carotidynia, ischemia features and aortic regurgitation respectively. All patients had active disease while all except 1, had received a median of 3 (1-4) lines of immunosuppressants including biologics in 16 (59.3%). All patients received prior systemic steroids. The indication of switching to tofacitinib were clinical, laboratory and imaging wise activity in 19, 17 and 4 patients respectively. The median ESR, CRP, ITAS score and steroid dose at initiation of tofacitinib was 46 (25-72) mm/1st hr, 25 (16.5-44) mg/L, 0 (0-2) and 7.5 (5-10) mg/day respectively. At median follow up of 10 (5-12) months, clinically stable disease was observed in 18 (72%), normalisation of CRP in 9 (36%), decrease in CRP in 8 (32%) and non-progression of new lesions in angiography (available in 10 patients) in 8 patients. Overall, 14 (51.9%) had good response in 2 domains and were classified as responders. The responders trended to have significantly higher median disease duration as compared with non-responders (median: 60 (41-96) months vs 27 (6-63) months), p= 0.054. None of the other clinical parameters differentiated the two groups. Four patients discontinued the drug due to side effects while one patient had sudden death within 3 months of initiation on tofacitinib.
Conclusion: The response to tofacitinib was modest in Indian patients with difficult to treat TAK. Further multi-ethnic studies are required to ascertain its effectiveness in TAK.
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AB0711 VASCULAR CALCIFICATIONS IN LARGE VESSEL VASCULITIS

Keywords: Imaging, Vasculitis

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Background: Arterial wall calcifications are a hallmark of atherosclerosis and represent an important cardiovascular risk factor. Accelerated atherosclerosis and vascular calcifications have been reported in large vessel vasculitis (LVV), but data are scarce about the amount and localizations [1].
Objectives: The aim of this study was to compare the prevalence, amount, and local distribution of arterial wall calcification evaluated on CT scan in LVVs versus lymphoma patients matched for age, sex, and year of diagnosis.
Methods: All consecutive patients diagnosed at our institution with LVVs from 2007 to 2018 with an available baseline PET-CT scan were included. Lymphoma patients were matched based on age, sex, and year of baseline PET-CT. CT images derived from baseline PET-CT scans of both patient groups were retrospectively reviewed by a single radiologist who, after setting a threshold of minimum 130 HU, semi-automatically computed vascular calcifications in three separate sites (coronaries, thoracic and abdominal arteries), quantified as Agatston, volume and mass scores. Calcifications in the two groups were compared for each site by using paired T-test. The effect of patient group was evaluated on the presence of calcifications in each site by means of adjusted conditional logistic regressions, and on the score of thoracic calcifications by means of adjusted regression.
Results: 258 patients were enrolled, including Takayasu's arteritis n=57, giant cell arteritis n=72 and lymphoma n=129. Thoracic artery calcifications were more represented in LVV patients, when compared with lymphoma patients (mean volume 2026 in LVVs vs 1014 in lymphomas, p=0.054). Coronary calcifications were higher in lymphoma patients (mean volume 104 in LVVs and 198 in lymphomas, p=0.13), whereas abdominal artery calcifications were equally distributed (mean volume 3220 in LVVs and 2712 in lymphomas). A diagnosis of LVV was associated with the presence of thoracic calcifications after adjusting by age and year of diagnosis (OR=4.13, 95%CI= 1.35-12.66; p=0.013), and with the volume score in the thoracic arteries (p=0.048).
Conclusion: When compared with lymphoma patients matched by age, sex, and year of diagnosis, LVV patients have higher calcification in the thoracic arteries, but not in coronary and abdominal arteries.
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AB0712 INFLUENCE OF GLUCOCORTICOID THERAPY ON TEMPORAL ARTERY BIOPSY. EXPERIENCE IN A REFERRAL HOSPITAL

Keywords: Best practices, Vasculitis, Tapering

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Background: The relationship between corticosteroid (GCs) treatment prior to temporal artery biopsy (TAB) and a negative result in giant cell arteritis (GCA) is controversial.
Objectives: To assess whether cumulative GCs dose and time of steroid exposure influence in TAB result.
Methods: Observational study of 191 patients diagnosed with GCA from a clinical practice of a referral center between January 2016 and December 2022 who underwent TAB. The diagnosis of GCA was made according to **a)** ACR criteria, and/or **b)** temporal artery biopsy, and/or **c)** EULAR/ACR2022 criteria, and/or **d)** imaging techniques. The biopsies were transversally sectioned into pieces and were cut from paraffin blocks and stained with hematoxilyn-eosin. A comparative study between patients with positive TAB and those with negative TAB was performed.
Results: The 191 GCA patients were divided into 2 subgroups: **a)** patients with positive TAB (n=52), and **b)** patients with negative TAB (n=139) **(Table 1)** of whom 26 (13.6%) had not received prior corticosteroid therapy versus 165 (86.4%) patients who did. Patients with positive TAB had more frequently visual symptoms and/or jaw/lingual claudication, while polymyalgia rheumatica (PmR) was less frequent. The median dose [interquartile range (IQR) 25th-75th] in the negative TAB group was 40 [25-40] mg/day and also 40 [35-60] mg/day in the positive TAB group. The median duration [IQR] of treatment in the first group was 11 [4-24] days. while in the second group it was 7 [3-13] days. The percentage of positive TAB was higher the shorter the delay between GCs treatment onset and the TAB, decreasing after 15 days from GCs therapy onset **(Figure 1)**. Finally, the cumulative pre-biopsy GCs dose was calculated with a median [IQR 25th-75th] of 484 [225-1295] mg for negative TAB patients while it was 760 [360-2185] mg in positive TAB cases.
Conclusion: Most patients with GCA were receiving GCs at the time of the TAB. Longer exposure to GCs increases the likelihood of a negative TAB, especially after 15 fays from GCs therapy onset.

Table 1. Main characteristics of patients with GCA according to biopsy result.

	Positive TAB (n=52)	Negative TAB (n=139)	p
Age (years), mean±SD	77±8	74.2±10	0.11
Sex, female/male (% females)	28/24(54)	92/47(66)	0.12
Length of TAB (mm), mean±SD	17±6	16.±6	0.36
Number of biopsy slices, mean±SD	29±7	28±7	0.44
Ischemic manifestations, n (%)			
Headache	45(87)	107(77)	0.15
Scalp tenderness	14(27)	34(24)	0.73
Abnormal examination of TA	30(58)	59(42)	0.06
Visual symptoms	32(62)	44(32)	**<0.001**
Jaw/lingual claudication	21(40)	29(21)	**0.006**
Systemic manifestations, n (%)			
PmR	20(38)	93(67)	**<0.001**
Fever	7(13)	20(14)	0.87
Prednisone therapy			
Dose (mg/day), median [IQR]	40± [35-60]	40± [25-40]	0.053
Cumulative dose (mg), median [IQR]	760± [360-2185]	484± [225-1295]	0.36
Time (days) from GC onset and TAB, median [IQR]	7± [3-13]	11± [4-24]	0.13

Abbreviations: GC: glucocorticosteroids, GCA: giant cell arteritis, IQR: interquartile range [25th-75th] PmR: polymyalgia rheumatica, TA: temporal artery, TAB: temporal artery biopsy

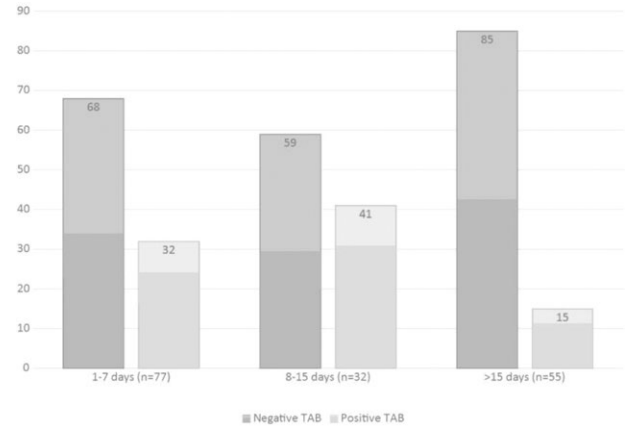


Figure 1. Positivity of TAB according to time from GC onset and TAB. 164 patients were treated with GCs prior TAB. All data are in % (n).

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AB0713

FREQUENCY OF TUBERCULOSIS AND ASSOCIATED RISK FACTORS IN PATIENTS WITH BEHÇET'S SYNDROME

Keywords: bDMARD, Spondyloarthritis, Behcet's disease

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Background: A considerable number of patients with Behçet's syndrome (BS) have vitreous cells on slit lamp examination at the time of diagnosis. However, the prognostic importance of vitreous cells (VC) and their association with the development of posterior uveitis (PU) requiring immunosuppressive treatment is unknown.
Objectives: We aimed to determine the prognostic importance of VU in BS patients.
Methods: The charts of 572 consecutive BS patients fulfilling ISG criteria who were registered between 2010 and 2012 were reviewed. At baseline visit 164 patients had VC in one eye or both eyes. Among the remaining patients, 229 had no eye involvement, 116 patients had bilateral pan or posterior uveitis, 14 had unilateral pan or posterior uveitis and no eye involvement in the other eye, 20 had isolated anterior uveitis, and 29 had insufficient data in their medical records. Among the 164 patients with VC, 110 patients with a follow-up of ≥2 years were included in this study (Figure 1).
Results: At baseline, among the 111 included patients (68 men, mean ± SD age: 31±9 years), 61 had VC in both eyes, 34 had VC in only one eye, and 15 had VC in one eye and PU in the other eye. There was anterior uveitis (AU) in addition to VC in the same eye in 13 patients at baseline (Figure 1). New PU developed in 26 (24%) patients during a mean follow-up of 1.9±1.1 years.7 patients that developed PU in the eye with VC had had PU in the contralateral eye at baseline. This means 7 of 15 patients with VC in one eye and PU in the contralateral eye developed bilateral PU despite treatment. 2 of these 7 patients had developed AU before they developed PU. Additionally, 6 patients that developed PU in the eye with VC had anterior uveitis in the same eye at baseline.
Conclusion: Careful follow-up is required for patients with VC since one quarter developed PU within 2 years. The presence of PU in the contralateral eye and AU in the same eye may be risk factors for the development of PU in patients with VC.

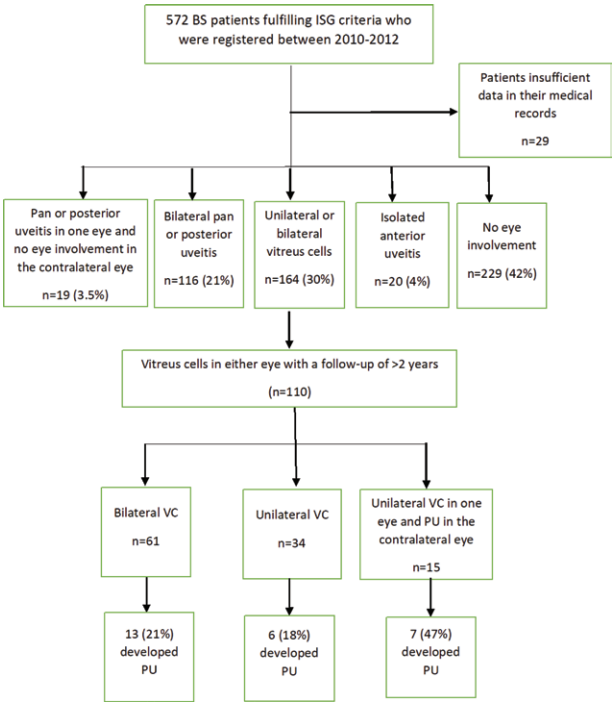


Figure 1.

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AB0714 CLINICAL CHARACTERISTICS AND RISK FACTORS ANALYSIS IN PATIENTS OF TA WITH CORONARY ARTERY CALCIFICATION

Keywords: Cardiovascular disease, Vasculitis

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Background: Takayasu arteritis(TA) is a chronic inflammatory disease mainly involving large vessels, including the aorta and its main branches, pulmonary arteries and coronary arteries, which can usually lead to stenosis, occlusion, expansion, or aneurysm formation of the affected vessels [1-2].Studies have shown that 10-20% of patients with TA have coronary lesions detected by angiography.In fact, this situation is still underestimated, because most TA patients do not complete the coronary angiography examination due to the lack of cardiac symptoms, such as palpitations and chest pain [3]. Coronary artery involvement is a serious adverse factor of poor prognosis and increases mortality in TA patients, specifically showing coronary artery stenosis, occlusion, and coronary artery calcification(cac) [4]. Patients with high coronary calcification scores have an extensive coronary plaque burden, with a high risk of stress-induced ischemic events [5].
Objectives: The aim of our study is to investigate the risk factors of cac in TA patients.
Methods: This retrospective study enrolled a total of 120 TA patients.All patients were divided into two groups according to the absence or presence of cac in TA patients (90 vs 30). we measured the Agatston score and compare clinical characteristics and ancillary findings between the two groups.A logistic model was applied to determine the risk factors associated with the incidence of cac in TA patients.
Results: A total of 30 patients with TA (25%) had cac.Age,medical history of hypertension and type of Numano V are the independent risk factors for developing cac in TA patients (OR [95% CI]1.080[1.020-1.143], p = 0.008; 5.457 [1.818-16.379], p = 0.002;7.827 [1.822-33.615], p = 0.006). However it's not associated with disease activity and clinical symptom. We counted the number of risk factors for each patient and measured the integral values of the cac, and found that the integral value of cac increased with the number of risk factors.We also counted the medication status of patients before admission,and found that patients with cac had a greater proportion of statin(50%vs. 28.9%, P=0.035) than patients without it.But there was no difference in using glucocorticoid and aspirin between the two groups. Glucocorticoid accumulation was also not statistically significant.
Conclusion: Age, hypertension and Numano type V are risk factors for developing cac in TA patients.It is recommended that arteria coronaria screen in TA patients with Numano type V should be actively treated as early as possible. The severity of cac will increase with the number of risk factors, and TA patients should be actively treated and strictly controlled with blood pressure levels.

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Table 1. Logistics regression analysis of risk factors in TA patients with cac.

Variables	OR(95%CI)	P value
Age	1.080(1.020,1.143)	0.008
Disease duration	0.998(0.994,1.003)	0.506
Hypertension	5.457(1.818,16.379)	0.002
Hyperlipidemia	2.447(0.648,9.242)	0.187
Numano V	7.827(1.822,33.615)	0.006
BP difference	1.868(0.624,5.591)	0.264

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AB0715 THE LONG-TERM PROGNOSTIC VALUE OF THE "2022 ACR/EULAR CLASSIFICATION CRITERIA FOR TAKAYASU ARTERITIS": DATA FROM A LARGE MONOCENTRIC COHORT

Keywords: Vasculitis, Real-world evidence, Prognostic factors

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Background: The "2022 classification criteria" for Takayasu arteritis (TAK) have been developed for the purpose of classifying patients with TAK. These criteria provide a score from 0 to 22; a score ≥5 allows to classify a patient.
Objectives: To investigate whether the "2022 classification criteria" score correlates with long-term outcomes of patients with TAK.
Methods: Data of patients with TAK followed up for ≥1 year and evaluated at least once within the last year at our Vasculitis Clinic were reviewed. For each patient, the score provided by the "2022 classification criteria" at baseline was calculated and the following outcomes at 24, 60, 120 months were evaluated: glucocorticoid (GC) suspension, introduction of a conventional disease-modifying anti-rheumatic drug (cDMARD), introduction of a biologic DMARD (bDMARD), need for vascular procedure, total number of bDMARDs received. Correlation of these outcomes with the score and with different thresholds (scores ≥5, ≥6, ≥7) was evaluated. Statistical tests were performed as appropriate.
Results: 120 TAK patients were included (103 women, 87.3%); mean follow-up duration was 154±113.8 months (24 months, n=110, 60 months, n=88, 120 months, n=60). Mean age at diagnosis was 37.3±13.6 years. 112 patients (93%) were classified as having TAK (mean score, 9.5±3). Seven patients (5.8%) were only treated with GC; 110 patients (91.6%) received at least one cDMARD (mean, 1.6±1), after a mean of 23.6±61.1 months; 80 patients (66.7%) received at least one bDMARD (mean, 1.2±1.5), after a mean of 40.1±64.5 months. GCs were suspended in 44 patients (36.7%), after a mean of 102.3±93.7 months. Forty-four patients (36.7%) underwent at least one vascular procedure (mean, 0.9±1.5). No significant correlation between the five outcomes and the score was found at all three timepoints (Table 1). No significant correlation between GC suspension, introduction of a csDMARD or a bDMARD, need for a vascular procedure and a score ≥5, ≥6, or ≥7 was found at all three timepoints (Table 1). A significant correlation between the total number of bDMARDs received at 120 months and both scores ≥6 and ≥7 was found (1.3±1.5 vs 0.6±0.8, p=0.045, and 1.3±1.6 vs 0.6±0.7, p=0.035, respectively).
Conclusion: Although the "2022 classification criteria for TAK" do not seem to correlate with the long-term prognosis, in our cohort we found that a higher baseline score (≥6) is associated with a higher number of bDMARDs received during follow-up. This suggests that the score might allow to identify TAK patients with

Table 1. Correlations between basline score and long-term outcomes

	GC suspension	csDMARD introduction	bDMARD introduction	Vascular procedure
24 months (n=110)				
Total score	10.3±2.8 vs 10.6±2.3 p=0.65	9.7±2.9 vs 9.6±3.4 p=0.89	9.5±2.9 vs 9.8±3.1 p=0.65	10.1±3.1 vs 9.5±3.1 p=0.28
Score ≥5 n=103	11/103 vs 0/7 p=0.99	77/103 vs 5/7 p=0.99	46/103 vs 3/7 p=0.99	32/103 vs 2/7 p=0.99
Score ≥6 n=99	11/99 vs 0/11 p=0.59	75/99 vs 7/11 p=0.47	45/99 vs 4/11 p=0.75	31/99 vs 3/11 p=0.75
Score ≥7 n=96	11/96 vs 0/14 p=0.35	73/96 vs 9/14 p=0.54	43/96 vs 6/14 p=0.99	30/96 vs 4/14 p=0.99
60 months (n=88)				
Totale	9.6±2.5 vs 10±3.1 p=0.29	10.1±2.8 vs 9.4±3.5 p=0.53	10.2±2.8 vs 9.8±3.2 p=0.83	10.1±3.1 vs 9.9±2.9 p=0.61
Score ≥5 n=84	17/84 vs 0/4 p=0.99	67/84 vs 3/4 p=0.99	46/84 vs 2/4 p=0.99	33/84 vs 2/4 p=0.99
Score ≥6 n=81	16/81 vs 1/7 p=0.99	66/81 vs 4/7 p=0.15	45/81 vs 3/7 p=0.69	32/81 vs 3/7 p=0.69
Score ≥7 n=80	16/80 vs 1/8 p=0.99	66/80 vs 4/8 p=0.05	45/80 vs 3/8 p=0.46	32/80 vs 3/8 p=0.46
120 months (n=60)				
Total score	9.6±3.1 vs 10.5±2.9 p=0.28	10.4±2.7 vs 9.9±3.8 p=0.87	10.5±2.8 vs 10.1±3.1 p=0.68	10.2±3.3 vs 10.4±2.7 p=0.90
Score ≥5 N=58	14/58 vs 1/2 p=0.44	45/58 vs 1/2 p=0.42	27/58 vs 1/2 p=0.99	26/58 vs 2/2 p=0.21
Score ≥6 n=55	13/55 vs 2/5 p=0.59	44/55 vs 2/5 p=0.08	26/55 vs 2/5 p=0.99	25/55 vs 3/5 p=0.66
Score ≥7 n=54	13/54 vs 2/6 p=0.64	43/54 vs 3/6 p=0.13	26/54 vs 2/6 p=0.67	25/54 vs 3/6 p=0.99

a more refractory disease. These preliminary data need to be replicated in larger cohorts.

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Disclosure of Interests: None Declared.

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AB0716 CLINICAL FACTORS ASSOCIATED WITH VASCULAR COMPLICATIONS (ANEURYSMS, THROMBOSIS, DISSECTION OR SURGERY) IN PATIENTS WITH GIANT CELL ARTERITIS

Keywords: Vasculitis, Real-world evidence, Imaging

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Background: Giant cell arteritis (GCA) typically affects cranial vessels, but it can also affect large vessels in a high percentage of patients. Vascular inflammation of the aorta and/or its main branches can cause complications of high morbidity and mortality such as aneurysms, dissection, thrombosis and/or require aortic surgery. The analysis of the different clinical and imaging patterns in patients with GCA and aortitis and their relationship with the prognosis needs more investigation. Early identification of patients with the highest risk of mortality could help predict deaths and vascular complications.

Objectives: To evaluate the clinical characteristics of patients with giant cell arteritis (GCA) who present vascular complications.

To evaluate prognostic factors associated with vascular complications in patients with GCA.

Methods: A retrospective cohort study was carried out including patients diagnosed of GCA by a multidisciplinary expert committee in aortic pathologies. A total of 71 patients followed between the years 2011-2021 who had a PET-CT at onset before receiving treatment were included. Other causes of aortitis were excluded. Vascular complication was defined as the presence of aneurysm, dissection, thrombosis, or aortic surgery during the disease. Demographic, clinical, analytical and imaging variables were collected. A descriptive study of the sample and a groups comparison, according to the presence of vascular complication, was carried out. The Shapiro-Wilk test was used to study the normality of the variables. Univariate logistic regression was performed to assess predictive factors.

Results: A total of 71 patients were included, 73.2% were female and the mean age was 79.3 (±6.7) years. During the disease, 13 patients presented aortic vascular complication. Jaw claudication (p<0.0001), fever of unknown origin (p<0.0001), anemia (p=0.001), constitutional syndrome (p<0.0001) and use of pulses of glucocorticoids (p=0.014) were associated with a higher occurrence of vascular complications. On the contrary, ischemic stroke prior to or at onset of disease (p=0.035) was the only variable associated with fewer complications with statistical significance. Cardiovascular risk factors and acute phase reactants were not associated with the appearance of complication, and either the delay of diagnosis and start of therapy. The details of the sample characteristics are described in Table 1.

Table 1. Demographic and clinical characteristics of patients according to the presence or not of vascular complication.

	Complication (n=13)	No complication (n=58)	p
GCA Classification (%)		18.9	0.944
- Cranial	15.3	24.1	
- Extracranial	23.1	56.9	
- Both	61.5		
Clinical presentation (%)			
Headache	30.77	31.58	0.945
Jaw claudication	84.6	61.4	**<0.000**
Ophtalmological signs	53.8	73.6	0.159
Scalp tenderness	61.5	80.7	0.138
Fever of unknown origin	76.9	71.9	**<0.000**
Polymyalgia rheumatica	53.8	59.6	0.702
Anemia	23	71.9	**0.001**
Constitutional syndrome	61.5	60.5	**<0.000**
Complications at onset (%)			
Aortic surgery	0 0	6.8	**0.049**
Ischemic stroke	1 7.6	5.1	**0.035**
Vascular complication	0	13.7	0.383
IV pulse GC mg/kg/d (%)	46.1	15.5	**0.014**

The univariate analysis to identify predictive factors showed that anemia (OR: 0.11 [0.02-0.48], p=0.003) was a protective factor against the occurrence of vascular complication.

Conclusion: Occurrence of new vascular complications was observed in 18.3% of patients with GCA included in our study. Jaw claudication, fever of unknown origin, anemia and constitutional syndrome, and the use of pulses glucocorticoids as treatment were associated with a greater appearance of complications, while ischemic stroke with fewer complications. Anemia proved to be a protective factor against the occurrence of vascular complications.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0717 DIAGNOSIS OF CRANIAL GIANT CELL ARTERITIS IN JAPAN USING VASCULAR ULTRASONOGRAPHY COMBINED WITH OTHER COMPLEMENTARY IMAGING METHODS

Keywords: Imaging, Ultrasound, Vasculitis

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Background: The utility of vascular ultrasonography (v-US) was proved recently in European countries, due to which the technology, diagnosis, and classification methods have been spreading. However, the use of v-US is not prevalent in Japan. Therefore, giant cell arteritis (GCA) is usually diagnosed by combining v-US with other imaging methods scrupulously. Furthermore, progressive Computed Tomography Angiography (CTA) technologies, increased use of Positron Emission Tomography (PET-CT), and a high population with Takayasu disease are found in Japan.

Objectives: Giant cell arteritis of cranial type (c-GCA) can quickly lead to blindness and stroke. Therefore, a rapid and appropriate diagnostic method is required to differentiate between c-GCA cases and those mimicking c-GCA. Thus, we aimed to construct a diagnostic method for c-GCA by optimizing the available imaging methods in Japan and using v-US as a diagnosing method from Europe.

Methods: We targeted 56 patients with suspected GCA, who visited our hospital from 2019 to 2022. v-US had been performed previously in all patients and 23 patients were diagnosed with GCA. These GCA patients were classified as c-GCA vs c-GCA + Large vessel (LV)-GCA vs LV-GCA in the ratio 11: 6: 6. In this study, we established 17 cases as c-GCA, and the other 39 as mimic cases using clinical and imaging methods. Furthermore, we analyzed and compared 31 patients evaluated with v-US from 2021 to 2022 using a vascular map, which was originally made by us and we were making maps for blood flow and writing down clinical symptoms evaluated at three stages.

Results: The sensitivity of the imaging methods to c-GCA patients was high for v-US (82.3%), Temporal artery biopsy (TAB) (78.6%), and CTA (71.4%) and low for PET-CT (50.0%) and Magnetic resonance imaging angiography (MRI/A) (38.5%). However, we did not use a contrast agent for MRI/A because our main objective to perform MRI/A was to distinguish cerebral infarction. The match rate of the imaging methods between v-US and PET-CT was 87.5% (CTA: 71.4%, TAB and v-US: 64.3%, and CTA: 63.6%). Among the 39 mimic cases, 15 cases were found to be Polymyalgia Rheumatica (PMR), 6 cases were LV-GCA, 5 cases were chronic headache, and others were collagen diseases, including 2 cases of Takayasu diseases. In 31 cases (10 cases of c-GCA and 21 mimic cases) from 2021 to 2022, halo sign of v-US (p-value: 0.01), jaw claudication (p-value: 0.02), and temporal headache on both sides (p-value: 0.01) were significant statistically.

Conclusion: In this study, we constructed a flowchart to diagnose c-GCA in Japan using v-US and other complementary imaging methods. First, we distinguished GCA cases from mimic cases with high precision. Thereafter, we combined imaging methods, which contributed highly to diagnosis in our results. Lastly, we considered the accommodation of TAB. We have started using this flowchart, and this contribute to be higher rate of diagnosing GCA and decreasing blindness and stroke.

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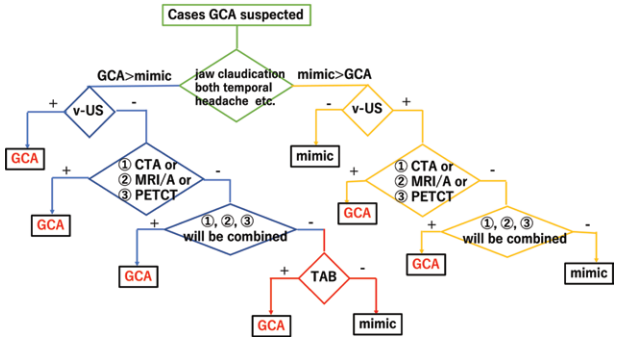
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Table 1: Characteristics of patients

	all patient	c-GCA	mimic	p-value
n	56	17	39	
Age (years)	70.5	76.4	68.0	0.0113
Female (%)	67.9	76.5	64.1	0.3724
Cranial type (%)	30.4 (17/56)	100(17/17)	0	
LV type (%)	10.7(6/56)	0	15.4 (6/39)	
Cranial + LV type (%)	10.7(6/56)	35.3(6/17)	0	
Ocular findings(%)	17.8(10/56)	29.4(5/17)	12.8(5/39)	0.136
PMR (%)	39.3(22/56)	41.2(7/17)	38.5(15/39)	0.407
Jaw claudication(%)	17.9(10/56)	47.1(8/17)	5.1(2/39)	0.0102
Headache (%)	60.7(34/56)	76.5(13/17)	53.8(21/39)	0.484
Temporal	48.2(27/56)	64.7(11/17)	41.0(16/39)	0.0833
Temporal両側	25.0(14/56)	58.8(10/17)	10.3(4/39)	0.0001
Occipital	33.9(19/56)	35.3(6/17)	25.6(10/39)	0.372
max CRP (mg/dl)	6.92	7.92	6.92	0.63
max ESR (mm/hr)	86.8	97.8	81.9	0.0737

Figure 1: a flowchart to diagnose c-GCA using v-US and imaging methods



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AB0718 LEVELS OF PHOSPHO-STAT3 ASSOCIATE WITH TREATMENT DURATION IN GIANT CELL ARTERITIS

Keywords: Adaptive immunity, Biomarkers, Vasculitis

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Background: Giant Cell Arteritis (GCA) is a granulomatous inflammation of medium and large arteries, that occurs in elderly individuals. Evidence on the immunopathology of GCA indicates that the IL-6 IL-23 Th17 axis is one of the dominant pathways and the Janus kinase (JAK)/signal transducers and activators of transcription (STAT) acts downstream of this axis. Targeted IL-6 receptor blockade by tocilizumab (TCZ) emerges as a promising treatment option. However, there is no further data on which patients would benefit most. The therapeutic effect of TCZ in a substantial group of GCA patients suggests that the vasculitis is driven by the JAK/STAT pathway in these patients.
Objectives: To investigate whether phosphorylated STAT (pSTAT) signatures in GCA patients can aid the stratification of patients for personalized treatment in GCA.
Methods: To investigate the expression of pSTAT, a phosphoflow method combined with a fluorescent cell barcoding technique (FCB) was developed. Frozen peripheral mononuclear cells (PBMCs) from treatment-naive GCA patients (n=18), infection controls (INF, n=11) and age-matched healthy controls (HC, n=15) were included in this study. PBMCs were incubated with IL-6 for 30 minutes. Cells were stained for T-cell markers (CD3, CD4, CD8, CD19, CD45RO) and STAT signature markers (pSTAT1, pSTAT3, pSTAT5). Serum IL-6 levels were measured by Luminex assay. The baseline inflammation markers and pSTAT3 in prospectively followed GCA patients was assessed by Kaplan-Meier curves for prognostic analysis. The pSTAT3 activity after treatment was evaluated in paired baseline, 3 months and 1-year samples.
Results: After IL-6 stimulation, we found a lowered proportion of pSTAT3 in CD4+ memory T-cells of GCA patients and INF controls compared to HCs. In GCA patients, proportion of pSTAT3 in CD4+ memory T cells was negatively associated with ESR at diagnosis (p=0.001, r=-0.729). Considering the link between IL-6 and ESR, we stratified GCA patients according to high (>1.5pg/mL) and low (≤1.5pg/mL) serum IL-6 levels and found that that the decrease in pSTAT3 in CD4+ memory T cells was especially found in GCA patients with high serum IL-6 levels. Importantly, we found that GCA patients with low ESR and high pSTAT3 at the time of diagnosis significantly predicted long-term glucocorticoid requirement. Levels of pSTAT3 in patients with high serum IL-6 levels at diagnosis normalized after 1 year of treatment.
Conclusion: We demonstrate a relation between serum IL-6 levels and in vitro pSTAT3 expression in GCA. Importantly, our results suggest that pSTAT3 can be an important prognostic marker in GCA.

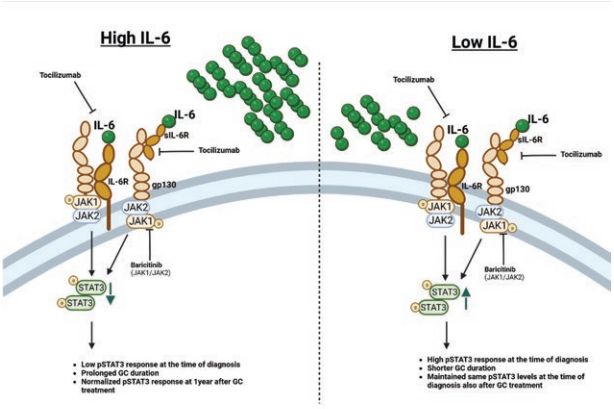


Figure 1.

Disclosure of Interests: Idil Esen: None declared, Maria Sandovici: None declared, Peter Heeringa: None declared, Annemieke Boots: None declared, Elisabeth Brouwer Consultant of: speaker/consulting fees from Roche, Yannick van Sleen: None declared, Wayel Abdulahad: None declared.
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AB0719 IS AORTIC 18FDG-UPTAKE PREVALENCE UNDERESTIMATED? DATA FROM A LARGE HOSPITAL-BASED COHORT

Keywords: Epidemiology, Real-world evidence, Imaging

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Background: Giant cell arteritis (GCA) and Takayasu arteritis (TAK) are the most common rheumatologic cause of aortitis, but it is still debated whether clinically isolated aortitis (CIA) represents a variant of such conditions or a nosologically different entity. CIA real frequency may be underestimated since it may occur without specific clinical manifestations.
Objectives: The aim of the present study was to assess the frequency of vasculitic aortic uptake in patients who undergo 18FDG-PET for any kind of clinical reason.
Methods: One-thousand consecutive patients who underwent a whole-body 18FDG-PET at the Nuclear Medicine Department of Pisa Hospital for whatsoever clinical question since January 1st, 2019 were enrolled. All the 1000 reports were separately reviewed searching for abnormal uptake of the aorta, and for the doubtful cases the images were revised with an experienced specialist in nuclear medicine. Demographic data, clinical question and provenience was collected; in case of aortic uptake, Meller grade and other sites of abnormal uptake were registered.
Results: The cohort included 439 males and 561 females with a mean age of 62.75 years. The clinical suspicion was neoplasm in 875 cases, infectious process in 55, vasculitis in 25, fever of unknown origin (FUO) in 12, lymphadenopathy

in 11, aneurysm in 4 and some other in 18. Thirteen patients (8 males and 5 females, mean age 59.69 years) showed positive aortic uptake. Among them, 6 patients underwent examination for a suspected vasculitis and 7 (53.8%) for other clinical questions (e.g. neoplasm, FUO, polymyalgia rheumatica). Of all the patients who underwent 18FDG-PET for a suspected vasculitis, 7/25 (28%) showed abnormal vascular uptake. Moreover, among the 13 positive patients, three showed isolated aortic uptake while the others also presented other large vessel involvement. Interestingly, in none of the isolated aortitis vasculitis was the clinical question for the examination (arthritis, FUO, myocarditis).
Conclusion: To our knowledge, this is the first hospital-based study aimed to assess the prevalence of 18FDG-PET aortic uptake on such a large-scale cohort. According to our results, 18FDG-PET may result positive despite the absence of clinical vasculitis-related manifestations, especially in case of CIA. For this reason, the actual prevalence of aortic uptake may be underestimated and further wide-scale studies, which are currently ongoing, are expected to better identify the characteristics of CIA patients and their long-term course.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0720 DEVELOPMENT OF RESPONSE CRITERIA FOR GCA: AN SLR INFORMING AN INTERNATIONAL TASK FORCE

Keywords: Systematic review, Remission, Vasculitis

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Background: Giant cell arteritis (GCA) is the most common form of large vessel vasculitis. While remission and relapse are common primary endpoints in randomized clinical trials (RCTs), a definition of response is missing. We conducted a systematic literature review (SLR) to inform an international task force developing new response criteria in GCA.
Objectives: To identify descriptors used to measure response to treatment and change of disease activity in GCA in RCTs and longitudinal observational studies (LOS).
Methods: An SLR was conducted using Ovid Medline, Embase, and Cochrane Central. The research question was formulated according to the PICO framework: the population included patients with GCA, any intervention or comparator was considered, and the outcomes addressed were active disease, improvement/response, remission, worsening, relapse, flare, or recurrence. RCTs and LOS with > 20 subjects and studies on qualitative research were included. Titles screening and full data extraction were performed by 2-3 reviewers. Discordant cases were discussed among reviewers until a final consensus; if not achieved, a methodologist was consulted. In case of multiple publications from the same trial and LOS, they were only considered if separate, pre-specified outcomes were reported.
Results: 10,593 studies were retrieved in the search, of which 116 were finally included. The descriptors used for the different outcomes' definition were extracted and grouped into different categories (Figure 1). Active disease was reported in 11/11 (100%) RCTs and 20/104 (19%) LOS. Active disease was predominantly defined as a combination of clinical and laboratory components. The clinical component was described as the presence of symptoms of GCA while the laboratory component mainly included ESR and CRP. Remission was reported in 8/11 (73%) RCTs and 44/104 (42%) LOS. Remission was predominantly defined as a combination of clinical and laboratory components. The clinical component was described as the resolution of clinical signs/symptoms of GCA. The laboratory component (ESR/CRP) was only considered when associated with the resolution of signs/symptoms of GCA. Relapse was reported in 11/11 (100%) RCTs and 90/104 (87%) LOS. Relapse was predominantly defined as a combination of clinical, laboratory and treatment components. The clinical component was defined as the recurrence of clinical signs/symptoms of GCA. The laboratory component included the elevation of ESR and/or CRP. The treatment component (reinstitution or increase in glucocorticoids dose) was frequently considered as a criterion for relapse. No standardized definition of response was found across studies. Most RCTs used composite endpoints (including treatment tapering/discontinuation, maintenance of remission, and absence of relapse over a certain time frame) to assess the primary endpoint – response. Fourteen imaging studies were analyzed (10 prospective and 4 retrospectives). PET-CT was the most studied imaging (n= 10), followed by ultrasound (n=3). PET activity was evaluated thorough qualitative or semiquantitative scores. Ultrasound evaluated presence of disease activity based on the intimal wall thickness/halo sign. **Conclusion:** The results of this SLR showed that an internationally accepted definition of response in GCA is elusive so far. RCTs and LOS mainly defined the extremes of the spectrum of GCA disease activity (remission and relapse) as primary endpoints. The descriptors identified will be incorporated in future phases of an international task force for the development of response criteria for GCA.

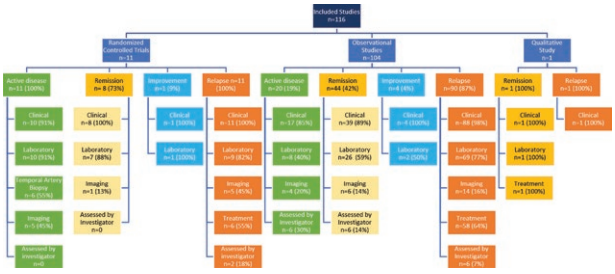


Figure 1. Components assessed in the definitions of active disease, remission, improvement, and relapse across the included studies

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AB0721 CHARACTERISTICS AND LONG-TERM OUTCOME OF DISEASE PHENOTYPES IN TAKAYASU ARTERITIS WITH SUPRA-AORTIC INVOLVEMENT

Keywords: Vasculitis, Cardiovascular disease

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Background: Supra-aortic involvement was most commonly seen in Takayasu arteritis (TA), ranging from 40% to 84%. [1, 2]. The clinical manifestations were heterogeneous and prognosis differed greatly in TA with supra-aortic involvement [3, 4].
Objectives: To explore the characteristics and long-term outcomes in different phenotypes of the East China Takayasu arteritis (ECTA) cohort with supra-aortic involvement.
Methods: Patients with supra-aortic involvement were enrolled from the ongoing ECTA cohort from July 2009 to December 2021 and followed up until June 30, 2022. Patients were assigned to four phenotypes: asymptomatic (AS), constitutional symptoms (CSs), vascular-associated symptoms (VASs), and neurological severe ischemic events (SIEs). Pattern differences in clinical features were analyzed, and the cumulative incidence of severe adverse events (SAEs) was evaluated. We performed multiple logistic regression analysis to compare the phenotypes.

Results: Six hundred fifty-seven TA patients with supra-aortic involvement were included: 54 (8.2%), 72 (11.0%), 303 (46.1%), and 228 (34.7%) patients with AS, CSs, VASs, and neurological SIEs, respectively. Compared to other phenotypes, CSs had significantly higher levels of inflammatory indicators. Neurological SIEs experienced poor treatment response including lower 6-month clinical remission rate and higher drug change rate. The median follow-up period was 3.0 (1.5–13.3) years. The 5-, and 10-year cumulative SAEs incidence rates in neurological SIEs (26.0% [18.7–32.1%], and 61.5 % [30.3–78.7%]) were significantly higher than those in other patients (Figure 1). The occurrence of SAEs was 5.9 folds (3.4–10.1; p < 0.001) in patients with neurological SIEs history compared with that in those without neurological SIEs history.

Conclusion: Our findings provide new insights into the characteristics and prognosis of different phenotypes in TA with supra-aortic involvement, which may be critical for early detection strategies and stratification management of heterogeneous diseases.

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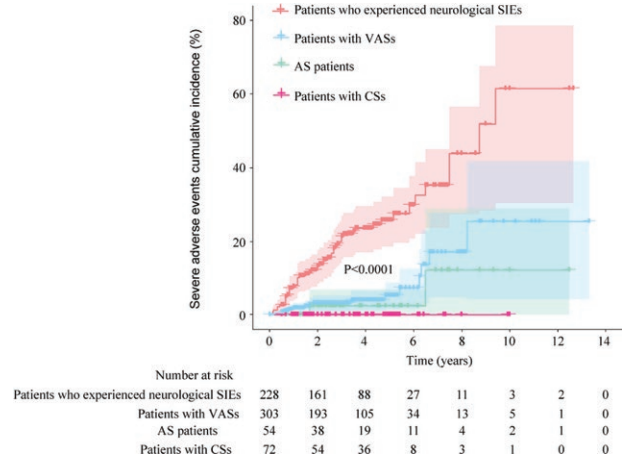


Figure 1. Cumulative incidence of severe adverse events based on different phenotypes of supra-aortic involvement. The shaded area indicates the 95% confidence interval (CI). AS, asymptomatic; CSs, constitutional symptoms; VASs, vascular-associated symptoms; SIEs, severe ischemic events.

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AB0722

ULTRASOUND HALO COUNT IN THE DIFFERENTIAL DIAGNOSIS OF ATHEROSCLEROSIS AND LARGE VESSEL GIANT CELL ARTERITIS

Keywords: Vasculitis, Cardiovascular disease, Ultrasound

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Background: Giant cell arteritis (GCA) is the most common vasculitis in the elderly and large vessel involvement occurs in up to 50% of cases. Otherwise, atherosclerosis is frequent in older patients; therefore, ultrasound (US) diagnosis of GCA in these patients may be challenging.

Objectives: To determine the diagnostic discriminant validity between large vessel giant cell arteritis (LV-GCA) and atherosclerosis using US with intima-media thickness (IMT) measurements.

Methods: We included 44 patients, paired by age and sex, with LV-GCA and 42 with high-risk atherosclerosis. US examinations of the axillary, subclavian and common carotid arteries (CCA) were systematically performed using a MylabX8 system (Genoa, Italy) with a 4-15 MHz probe. IMT ≥1mm was accepted as pathological.

Results: The LV-GCA cohort included 24 females and 20 males with a mean age of 72.8±7.6 years. The atherosclerosis group included 25 males and 17 females with a mean age of 70.8±6.5 years. Mean IMT values of all arteries included were significantly higher in LV-GCA than in atherosclerosis. The frequency and localization data are shown in Table 1. Among LV-GCA patients IMT ≥1mm was seen in 31 axillary, 30 subclavian and 28 CCA. In the atherosclerotic cohort, 17 (38.6%) had IMT ≥1mm with axillary involvement in 2 patients, subclavian in 3 patients, carotid distal in 14 patients (5 bilateral) and isolated carotid proximal affectation in 1 case. A cut-off point of at least 1 pathological vessel in the summative count of axillary and subclavian arteries or at least 3 vessels in the count of six vessels, including CCA, showed a precision upper 95% for GCA diagnosis in front of atherosclerosis.

Conclusion: The IMT is higher in LV-GCA than in atherosclerosis. The proposed US halo count achieves an accuracy >95% for the differential diagnosis between LV-GCA and atherosclerosis. The axillary and subclavian arteries have higher discriminatory power, while carotid involvement is less specific in the differential diagnosis. *This study was presented in November 2022 at the ACR Convergence.

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Table 1. Number of arteries with intima media thickness (IMT) ≥1 mm in GCA and atherosclerosis patients

	GCA (n=44)		Atherosclerosis (n=42)	
Axillary	Right	27	Right	2
	Left	23	Left	1
	Bilateral	19	Bilateral	1
	Any	31	Any	2
Subclavian	Right	20	Right	2
	Left	25	Left	1
	Bilateral	20	Bilateral	0
	Any	30	Any	3
Common Carotid Distal	Right	21	Right	8
	Left	19	Left	11
	Bilateral	12	Bilateral	5
	Any	28	Any	14
Common Carotid Proximal	Right	4	Right	3
	Left	9	Left	3
	Bilateral	2	Bilateral	1
	Any	11	Any	5

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Disclosure of Interests: Irene Monjo Speakers bureau: Roche, Novartis, UCB, Gedeon.
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AB0723 TAKAYASU ARTERITIS AND LARGE-VESSEL GIANT CELL ARTERITIS IN ITALIAN POPULATION. A RETROSPECTIVE COHORT STUDY

Keywords: Vasculitis

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Background: There are few studies comparing clinical, laboratory, and imaging characteristics, and treatment of LV-GCA and TAK [1-3].

Objectives: To compare clinical and imaging characteristics in patients with Takayasu arteritis (TAK) and large vessel-giant cell arteritis (LV-GCA) in an Italian population.

Methods: We conducted a retrospective monocenter study comparing characteristics and outcomes of a cohort of 59 patients with TAK and a cohort of 127 patients with LV-GCA diagnosed between 1996 and 2016 and followed up for at least 24 months at Reggio Emilia Hospital (Italy).

Results: LV-GCA patients had a higher prevalence of males (p=0.003), and more frequently presented with cranial symptoms (p=0.001), fever>38°C (p=0.007), polymyalgia rheumatica (p=0.001), and hypertension.

(p=0.001), and they had higher ESR levels at diagnosis (p=0.0001). Differently, TAK patients had longer delay to diagnosis from the beginning of symptoms (p=0.048), they presented more frequently with loss of pulses of large arteries (p=0.0001), vascular bruits (p=0.001), limb claudication (p=0.003), myocardial infarction/angina (p=0.03), and hypertension induced by renal artery stenosis (p=0.001). Regarding treatment, TAK patients received a higher total and at 1 year cumulative prednisone doses (0.0001 and 0.001, respectively), they had a longer duration of prednisone therapy (p=0.008), and received during follow-up more frequently traditional immunosuppressants (p=0.0001) and biological agents (p=0.0001). Flares were more frequently observed in TAK patient (p=0.001), while no differences were observed for long-term remission. New vascular procedures during the follow-up were more frequently performedin TAK. patients (p=0.0001). Regarding imaging at diagnosis, TAK patients had more frequently vascular stenosis/occlusion (p=0.0001) and a higher number of vessels with structural damage per person (p=0.0001), while LV-GCA patients had a higher number of inflamed vessels per person (p=0.0001). Comparing the involved vascular districts at diagnosis for the presence of vessel inflammation and/or arterial damage, patients with LV-GCA had a more frequent involvement of thoracic and abdominal aorta (p=0.024 and p=0.007, respectively), and axillary, iliac and femoral arteries (p=0.018, p=0.002, and p=0.0001. respectively), while in TAK patients, brachiocephalic, celiac, mesenteric and renal arteries were more frequently involved (p=0.011, p=0.019, p=0.019, and p=0.005, respectively). At imaging arterial damage at diagnosis was more frequently observed in TAK patients, specifically at common carotid, brachiocephalic, and subclavian arteries (p=0.0001, p=0.006, p=0.0001, respectively) and descending aorta. (p=0.022). Regarding imaging during the follow-up, TAK patients developed more frequently new vascular stenosis/occlusion (p=0.0001) and new vascular thickening (p=0.002), no differences were observed for the development of new dilatation/aneurysm between the two vasculitis. In the literature review, we identified 7 papers comparing clinical and imaging characteristics of LV-GCA and TAK. Similarities and differences were found comparing our results with those of previous studies.

Conclusion: Patients with TAK and LV-GCA show a number of similarities and also differences. Indeed, it is unclear whether they are part of the same disease spectrum or they are different conditions. As more information regarding the pathogenesis and etiology becomes known, answers to these questions are like to be forthcoming.

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AB0724 THE VALUE OF [18F]FDG PET/CT FOR MONITORING AND TREATMENT DECISION GUIDANCE IN LARGE VESSELL VASCULITIS: IS IT TELLING TOO LITTLE, OR MAYBE TOO MUCH?

Keywords: Imaging, Vasculitis

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Background: Large Vessel Vasculitis (LVV) are vasculitides affecting large arteries, including aorta and its major branches. LVV can cause systemic and vascular inflammation that could result in long term complications such as artery stenosis, aneurysm formation and artery dissection. LVV include giant cell arteritis (GCA) and Takayasu. CGA typycally affects people aged over 50 and involves superficial temporal arteries. Meanwhile its cranial manifestations are well recognized and can be easily diagnosed by vascular ultrasound, it has been appreciated that GCA can extend beyond the superficial cranial arteries in up to 80% of patients or even spare the temporale arteries, and ultrasound is of limited diagnostic value in these cases. The usefulness of [^{18}F]FDG PET/CT in supporting the diagnosis of LVV is well known, particularly in patients with less specific manifestations such as fever or unexplained weight loss. However, the role of [^{18}F]FDG PET/CT in monitoring the course of the disease and its complications is less well established.

Objectives: To investigate the findings of repeated [^{18}F]FDG PET/CT scan in a cohort of patients with LVV in clinical and biochemical remission.

Methods: We have evaluated 30 pts (female 67%, age 75±9) with a diagnosis of LVV based on clinical features and serological tests (T0). The diagnosis was also supported by a positive [^{18}F]FDG PET/CT scan (arterial uptake equal or superior to the liver at the aorta or at least one of its major branches). 16 patients (53%) had also GCA confirmed by positive ultrasound of the temporal arteries. All patients were started on Prednisolone (PRED) 1 mg/kg according to standard guidelines, and some were subsequently started on Tocilizumab (TCZ) due to either relapse on steroid tapering or contraindications to long term use of steroids. After at least 6 months of effective treatment and while on clinical and biological controlled disease (T1), patients were reassessed clinically and biochemically; 14 pts aldo had a repeated [^{18}F]FDG PET/CT scan. We have used a binary grading to score the second scan: 1. negative (improved compared to first study) or 2. positive (not improved compared to first study), where improvement has been defined as no uptake or uptake inferior to the liver in the same areas that were highly metabolically active at previous study, and no new sites of vascular uptake detected. Images have been assessed by a nuclear medicine doctor and reviewed by 2 rheumatologists with recognised experience in the field of vasculitides, with excellent interobserver agreement.

Results: Inflammatory markers significantly dropped between the 2 timepoints (ESR 48±28 vs 6±4 and CRP 5.9±5.4 vs 0.4±1.2, p=0.0004). Among the 14 patients that had a repeated scan, 9 (65%) showed a negative and 5 (35%) a still positive scan despite being in clinical and biochemical remission. The number of metabolically active sites was reduced with a statistically significant difference between the 2 groups (8±4 vs 3±3, p=0.02). Of the 5 pts that had a positive scan, only 1 (20%) had a positive ultrasound of the temporal arteries at the time of the diagnosis.

Conclusion: Our study revealed persistent vascular uptake on repeated [^{18}F] FDG PET/CT scan in over 1/3 of LVV patients with clinical and biological controlled disease. The significance of this residual uptake and its prognostic value is currently unknown. Therefore the routine use of [^{18}F]FDG PET/CT alone in monitoring disease activity and treatment response may be not appropriate and therapy should not be modified based on scan results only. Further research is needed in order to place the correct use of imaging in the long term monitoring of LVV.

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Disclosure of Interests: None Declared.

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AB0725 BARICITINIB FOR THE TREATMENT OF REFRACTORY VASCULAR BEHÇET'S DISEASE: A PILOT STUDY IN CHINA

Keywords: Targeted synthetic drugs, Vasculitis, Behcet's disease

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Background: Major vessel involvement in Behçet's Disease (BD) profoundly affects morbidity and mortality. Monoclonal anti-TNF antibodies are recommended for severe and (or) refractory vascular BD (VBD) beyond glucocorticoids (GCs) and immunosuppressants (IS), while some patients are still struggling due to inadequate response and relative contraindications. Our group has previously reported the efficacy of JAK1/JAK3 inhibitor tofacitinib for treating VBD[1]. We hypothesized that the JAK1/JAK2 inhibitor baricitinib might be a potential therapeutic choice in VBD patients through a broader panel of cytokine inhibition.

Objectives: This is a single-center, one-arm, self-controlled, open-label pilot study aimed at evaluating the effectiveness and safety of the JAK1/JAK2 inhibitor baricitinib in BD patients with refractory vascular involvement.

Methods: We consecutively enrolled refractory VBD patients who received baricitinib treatment (2 mg/ day) at Peking Union Medical College Hospital between Mar 2020 and Jan 2022. Efficacy assessment mainly depends on the proportion of clinical remission after 3-month treatment. Other outcomes include disease activity, organ damage evaluation, GCs and IS-sparing effects, and side effects.

Results: A total of 17 patients (12 males) were included, with a mean age of 37.9 ± 11.9 years and a mean follow-up of 10.5±5.4 months (Table 1). Before enrollment, all patients had insufficient response or intolerance to conventional therapies and (or) biologics (five patients failed first-line anti-TNF mAb using infliximab/ adalimumab/golimumab, and two patients had second-line therapy with other anti-TNF mAb, but still responded inadequately). At the 3-month follow-up, 13 (76.5%) patients achieved a complete response and the proportion increased to 88.2% (15/17) at the last visit. Laboratory parameters ESR (13 (IQR 7–40.5) vs 8 (IQR 2–17.5) mm/h, p<0.01) and CRP (11.8 (IQR 2.5–18.5) vs 1.2 (IQR 0.6–5.2) mg/L, p<0.0001) decreased significantly 3 months after baricitinib use (Figure 1), as well as the Behçet's Disease Current Activity Form (BDCAF) score (1 (IQR 0–2) vs 0 (IQR 0–1), p<0.01) and Birmingham Vasculitis Activity Score (BVAS) (2 (IQR 0–4.5) vs 2 (IQR 0–2), p<0.01). The vasculitis damage index (VDI) and Behçet's Syndrome Overall Damage Index (BODI) remained stable (p>0.05). At the last visit, baricitinib showed a GCs-sparing effect (7.5 (IQR 5–11.3) vs 5 (IQR 3.1–10) mg/d, p<0.05), and 9 patients (52.9%) discontinued or maintained 5 mg or lower daily of GCs dosage. In addition, IS were reduced in number and dosage in 5 (29.4%) and 9 (52.9%) patients, respectively. During follow-up, baricitinib dosage was tapered to 1 mg/day or less in 6 cases (35.3%) with sustained remission. No serious adverse events were noted during the follow-up.

Conclusion: Our study suggests that baricitinib is well tolerated and effective in refractory BD patients with multi-vessel involvement. Further prospective controlled study is warranted to access the utility of bariticinib in VBD.

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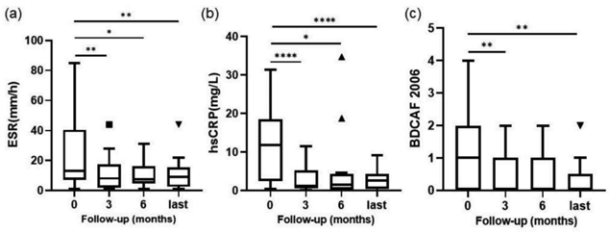


Figure 1. Outcomes of baricitinib treatment. Change in (a) ESR, (b) hsCRP, and (c) BDCAF score during follow-up.

Table 1. Baseline demographic and clinical characteristics of enrolled patients.

Characteristics	VBD (n=17)
Sex (male), n (%)	12 (70.6)
Age at enrollment, mean ± SD (years)	37.9 ± 11.9
Duration of vascular involvement, median (IQR) (months)	29 (IQR 20.5-73.0)
Follow-up, mean ± SD (months)	10.5 ± 5.4
Venous lesion, n (%)	5 (23.5)
Inferior vena cava syndrome	3 (17.6)
Deep venous thrombosis	3 (17.6)
Cerebral venous sinus thrombosis	2 (11.8)
Artery lesion, n (%)	6 (35.3)
Multiple arterial occlusion/stenosis	3 (17.6)
Aneurysms/ pseudoaneurysm	4 (23.5)
Pulmonary artery involvement, n (%)	1 (5.9)
Pulmonary thromboembolism	1 (5.9)
Cardiac lesion, n (%)	8(47.1)
Valve regurgitation	7 (41.2)
Right heart thrombus	1 (5.9)
Coronary artery lesion	2 (11.8)

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Disclosure of Interests: None Declared.

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AB0726 C-REACTIVE PROTEIN GENE POLYMORPHISMS IN BIOPSY PROVEN GIANT CELL ARTERITIS IN NORTHERN ITALY

Keywords: Vasculitis

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Background: Previous studies have reported that four functional C-reactive protein (CRP) gene polymorphisms, namely rs1417938, rs1800947, rs1205, and rs3093059 variants, were associated with plasma CRP levels, but not with clinical manifestations of giant cell arteritis (GCA) (1)

Objectives: Aim of our study was to investigate potential associations between two other functional variants of CRP gene at position 3872G/A (rs2015) and 4741G>C (rs3093068) with susceptibility to biopsy-proven GCA, baseline clinical and laboratory findings, treatment, and disease outcomes.

Methods: 164 patients with biopsy-proven GCA, resident in Reggio Emilia area (Italy), and 198 healthy controls from the same geographic area were genotyped for 3872G/A (rs2015) and 4741G>C (rs3093068) CRP gene polymorphisms by molecular methods. Data collected for all cases included comprehensive information about clinical findings, laboratory tests, histological data, imaging, therapies, and flares. Long-term remission was defined as permanent discontinuation

of glucocorticoids without flares for at least 1 year. All patients were followed according to a standardized predefined follow-up and therapeutic protocol. At the end of the follow up period, we evaluated for each patient the number of flares, long term remission, the duration of steroid treatment and the cumulative glucocorticoid dose.

Results: Association analysis of 3872G>A polymorphism showed that allele A homozygosity was significantly more frequent in cases than in healthy controls (OR =2.32, 95% CI: 1.26-4.27, p=0.006). Association analysis of 4741G>C polymorphism showed that allele G carried by CG and GG genotypes was significantly lower in GCA patients than in controls (OR =0.35, 95% CI: 0.17-0.70, p=0.002).No significant associations were found between these 2 polymorphisms and baseline clinical manifestations. Patients homozigous for the allele A had a significantly lower frequency of CRP values >5 mg/dl at diagnosis compared to patients carrying GA or GG genotypes (44.5% vs 72.4%, p=0.018, OR 0.31, 95% CI: 0.11-0.85). Considering 4741G>C CRP gene polymorphism, patients carring G allele had at diagnosis significantly higher levels of CRP (13.2 + 5.5 vs 8.9 + 6.3 mg/dl, p=0.037) and ESR (105 + 30.6 vs 86.6 + 29.0 1st hour, p=0.040), and lower levels of Hb (10.3 + 1.2 vs 11.3 + 1.5 g/dl, p=0.044). At histological examination of temporal artery biopsy (TAB), patients homozigous for the allele A had significantly more frequent eosinophilic infiltration of the arterial wall (21.4% vs 6.0%, p=0.010, OR 4.28, 95% CI: 1.31-13.98) than patients carring allele G. Furthermore, patients carring the allele A had lower steroid treatment duration (52 + 56 vs 79 + 78 months, p=0.041), lower cumulative steroid dose (11146 + 7162 vs 18.520 + 19659 mg, p=0.017), higher frequency of steroid treatment withdrawal (61.5 % vs 39.6%, p=0.016) and of longterm remission (60.3 % vs 39.6%, p=0.024). Survival analyses demonstrated a significative differences for the duration of steroid treatment and the frequency of long term remission between the three AA, AG and GG genotypes (p=0.033 and p=0.031 respectively).

Conclusion: Single nucleotide polymorphisms of PCR gene at position 3872G/A (rs2015) and 4741G>C (rs3093068) have impact on susceptibility and outcomes of biopsy-proven GCA.

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Disclosure of Interests: None Declared.

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AB0727 A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL GROUP STUDY TO EVALUATE THE EFFICACY OF METHOTREXATE AS REMISSION MAINTENANCE THERAPY AFTER REMISSION-INDUCTION THERAPY WITH TOCILIZUMAB AND GLUCOCORTICOIDS IN SUBJECTS WITH GIANT CELL ARTERITIS (METEORITICS TRIAL): STUDY PROTOCOL

Keywords: Disease-modifying drugs (DMARDs), Vasculitis, Clinical trials

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Background: Giant cell arteritis (GCA) is the most common systemic vasculitis found in adults over 50 years of age and affects medium and large vessels. The standard treatment is glucocorticoids (GC). Because of the negative side effects of GC and the high prevalence of relapses GC should be combined with other immunosuppressive or immunomodulatory agents. Since the GIACTA Trial and other randomized controlled trials (RCT) assigned tocilizumab (TCZ) a GC-sparing effect, higher remission rates compared to placebo and the potency to maintain remission even without GC this biologic is a promising option to treat GCA. Due to the high costs of the TCZ treatment and the increased risk of infections, other treatment options are needed in the long term. An RCT published by Adler et al. showed that only 55% of patients remained in remission after discontinuation of intravenous TCZ therapy. It highlights the need for options to maintain remission after discontinuation of TCZ. The combination of methotrexate (MTX) and GC was also effective in reducing relapse rate and the cumulative GC doses in new or relapsing GCA.

Objectives: The primary objective of the study is to investigate whether MTX is useful for maintaining remission after remission-induction with TCZ and GC in patients with GCA. In addition, we evaluate patient and investigator reported outcomes, prevalence of aortitis, number of vasculitic vessels and change of intima-media-values during the study.

Methods: This monocentric, randomized, double-blind, placebo-controlled study estimates the efficacy of MTX through a treatment period of 12 months and a six-months follow-up. Patients who are in stable remission after treatment with GC and at least six months of treatment with TCZ for new-onset or relapsing giant cell arteritis are eligible for inclusion. Forty participants will be randomly assigned to the treatment arm (N=20) and the placebo arm (N=20). The treatment consists of 17.5 mg MTX subcutaneous weekly for 12 months as a monotherapy. In case of intolerance, elevated liver enzymes or low glomerular filtration rate a dose reduction is possible. In event of relapse an escape treatment with GC on a tapering regimen is added to the study medication. Assessments are conducted eight times during the treatment period and twice during the follow-up. An ultrasound examination takes place on every study visit to measure the intima-media-values of several arteries. Magnetic resonance imaging is performed on baseline, month 12 and 18 to detect aortitis. The primary endpoint is the time to first relapse during the 12 months therapy.

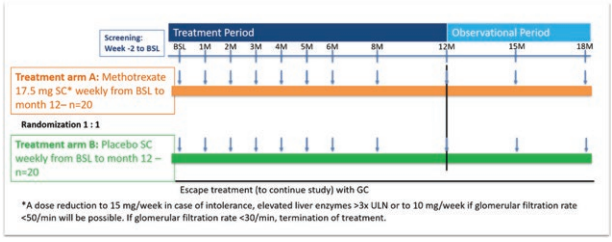


Figure 1. Study design

Arrows indicate study visits mg, milligram; SC, subcutaneous; BSL, baseline; M, month; GC, glucocorticoids; ULN, upper limit of normal.

Results: No results are available yet.

Conclusion: This is the first study that evaluate MTX as remission maintenance therapy after stable remission has been induced by GC and TCZ in GCA. MTX could be an effective, safe, inexpensive therapy agent after discontinuation of TCZ.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0728 AORTITIS SPECTRUM. STUDY OF 82 PATIENTS FROM A SINGLE REFERRAL CENTER

Keywords: Real-world evidence, Vasculitis

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Background: Aortitis is the inflammation of the aortic wall, and can be idiopathic or associated with a cluster of infectious and non-infectious diseases. Giant-cell arteritis (GCA) and Takayasu arteritis (TA) are the most common underlying [1,2].

Objectives: To assess the causes and the main features of patients with aortitis.

Methods: Observational study of patients with aortitis from a large-vessel vasculitis monographic consultation at a referral hospital from June 2022 to December 2022. Aortitis was diagnosed by imaging techniques.

Results: We present 82 patients (52 female/ 30 male) (mean±SD age; 60.2±12.6 years). The different subtypes of aortitis were: GCA (n=69), Takayasu arteritis (n=6), other inflammatory autoimmune diseases (n=3), IgG4-related disease (IgG4-RD) (n=2), syphilis (n=1) and isolated aortitis

(n=1). The imaging techniques used for the diagnosis of aortitis were: PET/TAC (n=81), TAC (n=23), RMN (n=20) and arteriography (n=10). The main features of the patients are summarized in **Table 1**. Aortitis was most frequent in women. 50% patients had high blood pressure and dyslipidaemia. Polymyalgia rheumatica and asthenia were more frequent manifestations. The underlying diseases in the group of aortitis related to other inflammatory autoimmune diseases were: ulcerative colitis (n=1), idiopathic retroperitoneal fibrosis (n=1), and polyarteritis nodosa (n=1). The ascending thoracic aorta and the supraaortic trunks were the most frequently involved segments **(Figure 1)**.

Conclusion: Aortitis is an entity which can be isolated or secondary to infectious and non-infectious process. Among the non-infectious causes, GCA and TA are the most frequent, being common the presence of PmR and asthenia. The ascending thoracic aorta and the supraaortic trunks seems to be the most frequently involved segments.

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Table 1. Main features of the patients with aortitis.

FEATURES	OVERALL (n=82)	GCA PATIENTS (n=69)	TA PATIENT(n=6)	RELATED TO OTHER INFLAMMATORY DISEASES (n=3)	IgG4-RD (n=2)
Age (years), mean±SD	60.2±12.6	66.1±10.0	41.8±14.1	52±18.7	51.5±7.8
Female/Male (% female)	52/30 (63)	43/26 (62)	6/0 (100)	2/1 (67)	1/1 (50)
High blood pressure, n (%)	41 (50)	34 (49)	4 (67)	2 (67)	1 (50)
Dyslipidaemia, n (%)	41 (50)	33 (48)	4 (67)	2 (67)	0 (0)
Diabetes mellitus, n (%)	12 (15)	12 (17)	0 (0)	0 (0)	0 (0)
Active smoker or ex-smoker, n (%)	27 (33)	20 (29)	5 (83)	0 (0)	0 (0)
Asthenia, n (%)	39 (48)	33 (48)	4 (67)	0 (0)	2 (100)
Weight loss, n (%)	22 (27)	19 (27)	2 (33)	0 (0)	1 (50)
PmR, n (%)	40 (49)	39 (56)	0 (0)	0 (0)	1 (50)
Fever, n (%)	11 (13)	9 (13)	1 (17)	1 (33)	0 (0)
Headache, n (%)	32 (39)	29 (42)	2 (33)	0 (0)	1 (50)
Visual symptoms, n (%)	14 (17)	12 (17)	1 (17)	0 (0)	1 (50)
Jaw claudication, n (%)	10 (12)	10 (14)	0(0)	0 (0)	0 (0)
Lumbar pain, n (%)	25 (30)	22 (32)	2 (33)	0 (0)	1 (50)
Pain in thighs, n (%)	18 (22)	17 (25)	1 (17)	0 (0)	0 (0)
Upper Limb claudication, n (%)	21 (26)	19 (27)	2 (33)	0 (0)	0 (0)
Lower limb claudication	17 (21)	14 (20)	2 (33)	1 (33)	0 (0)
CRP (mg/dL), median [IQR]	0.4 [0.4-1.6]	0.5 [0.4-1.7]	0.4 [0.2-2.0]	0.4 [0.3-0.4]	1.5 [0.9-2.0]
ESR (mm/1h), median [IQR]	13 [5-45.2]	14 [5-48]	16.5 [3.5-32.5]	12 [7-24]	7.5 [6.7-8.2

Abbreviations: CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, GCA: giant cell arteritis, IgG4-RD: IgG4-related disease, PmR: polymyalgia rheumatica, TA: Takayasu arteritis

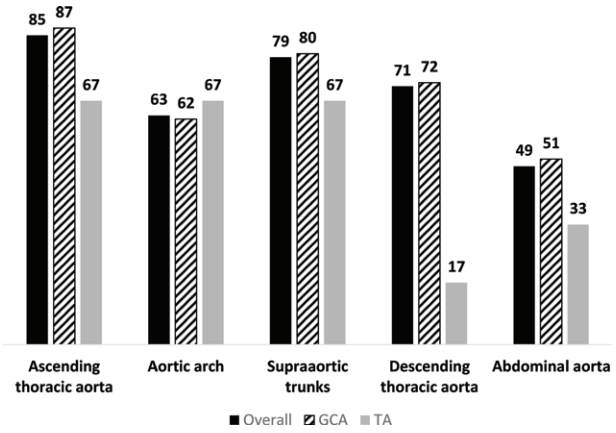


Figure 1. Segments of the aorta affected. All data are in %.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0729

EVALUATION OF DIFFERENT TREATMENT REGIMENS IN TAKAYASU'S ARTERITIS: A SINGLE CENTER STUDY

Keywords: bDMARD, Vasculitis, Disease-modifying drugs (DMARDs)

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Background: Takayasu's arteritis (TAK) is a large-vessel vasculitis associated with high morbidity and mortality. Although new biological immunosuppressive drugs have been introduced in recent years, there is no strong evidence on which therapy is most effective to obtain a faster and lasting remission.

Objectives: The aim of the present study is to evaluate how different treatment approaches could provide better results in terms of disease activity, imaging improvement, glucocorticoids (GC) sparing and damage progression.

Methods: Inpatients and outpatients, classified as TAK, referred to our third level rare diseases center, were retrospectively assessed. We included all patients with complete clinical data and that underwent at least three consecutive visits. Patients were subdivided and compared according to five different treatment approaches: GC monotherapy, conventional disease modifying antirheumatic drugs (cDMARDs) monotherapy, anti-tumor necrosis factor (anti-TNF) monotherapy, combination therapy with cDMARDs+anti-TNF and Tocilizumab (TCZ). Demographic, clinical and laboratory data were collected. Imaging features (PET scan, magnetic resonance angiography, CT angiography, ultrasonography) were evaluated and registered. Clinical activity was assessed using the Indian Takayasu Clinical Activity Score (ITAS2010) (1) while damage according to the Large-Vessel Vasculitis Index of Damage (LVVID) [2].

Table 1. Demographic and clinical features, previous and concomitant treatment in refractory Behçet's uveitis patients treated with tocilizumab.

No	Sex/Age	Uveitis duration before TCZ (year)	Previous therapy	Indications	Concomitant medications	Number of attacks	VA (before TCZ)		VA (after TCZ)		Response to TCZ treatment
							R	L	R	L	
1	M/30	4	cs, aza, CsA, ifn, inx, ada, czp, tac	induction	cs, aza, CsA	3	1/10	CF at 3 m	CF at 0.5 m	2/10	active
2	F/44	15	Cs, aza, CsA, ifn, inx, ada, mmf, czp	induction	cs, CsA, mmf	3	TD	4/10	TD	9/10	active
3*	M/45	18	cs, aza, CsA, ifn, inx	induction	Anti-tuberculosis	0	1/10	1/10	1/10	2/10	remission
4¥	M/35	1	cs, aza, ada	Contraindication for TNF inhibitors	cs, mmf	0	10/10	10/10	10/10	10/10	remission
5	M/42	3	cs, aza, CsA, ifn, inx, mmf, ada	induction	cs	1	1/10	1/10	1/10	HM	active
6	M/42	4	colchicine, cs, aza, CsA, inx, anr, ifn, chlorambucil	induction	cs	5	5/10	HM	8/10	LP	active

cs: corticosteroids, aza: azathioprine, CsA: cyclosporine A, ifn: interferon alpha, inx: infliximab, ada: adalimumab, czp: certolizumab, tac: tacrolimus, mmf: mycophenolate mofetil, anr: anakinra, tcz: tocilizumab, VA: visual acuity, CF: counting fingers, m: meter, TD: terminal disease, HM: hand motion, LP: light perception, R: right, L: left*: The patient had pulmonary tuberculosis under infliximab treatment and was switched to tocilizumab. While uveitis was in remission, tocilizumab was discontinued due to the development of tuberculous lymphadenitis.¥: The patient had interstitial lung disease under infliximab treatment and was switched to tocilizumab.

Results: The study included 31 TAK patients (age 28 [21-48], 87% female) exposed to a total of 52 treatment regimens (n=4 GC monotherapy, n=17 cDMARDs, n=5 anti TNF, n=20 cDMARDs+antiTNF, n=6 TCZ). Overall clinical remission rate during the follow-up was 75% in GC treated patients, 70.6% in cDMARDs-treated, 100% in anti-TNF-treated, 80% in cDMARDs+anti-TNF-treated and 100% in TCZ-treated. Persistence of treatment was 19[8-30.75] months in GC group, 10[5.5-26.5] in cDMARDs group, 15[12-44] in anti-TNF group, 21[12.75-81.75] in cDMARDs+antiTNF group and 4 [17-64.5] in TCZ group. Treatment with cDMARDs+antiTNF and TCZ led to significant reduction of acute phase reactants (C-Reactive Protein: cDMARDs+antiTNF 31[9.1-93] vs2.9[0.4-16] mg/L, <0.001; TCZ 31.5[10.5-59]vs2.9[0.2-8.75] mg/L, 0.009) (Erythrocyte Sedimentation Rate: cDMARDs+antiTNF 43[14-84]vs17.5[10-25.75] mmh, 0.017; TCZ 15[5-55]vs5.5 [2-11.75]). Daily GC dose at last follow-up was 0 in cDMARDs+antiTNF group (25vs0 mg, p<0.001) and TCZ (11.25vs 0 mg, p<0.007). All the therapeutic regimens led to a significant reduction of disease activity at last follow-up (ITAS2010 in GC-treated 0 [0-1.5], in cDMARDs-treated 0 [0-1], in anti-TNF treated 0 [0-1], in cDMARDs+antiTNF 0 [0-0], in TCZ 0 [0-0]). LVVID did not significantly increase during follow-up in patients treated with cDMARDs, anti-TNF, cDMARDs+anti-TNF and in TCZ. Imaging data shown an improvement in metabolic activity at LFU in 33.3% of TCZ-treated patientsp and in 40% of cDMARDs+anti-TNF treated patients.

Conclusion: Anti-TNF, cDMARDs+anti-TNF and TCZ led to a statistically significant reduction in GC dosage, allowing steroid sparing. Compared to monotherapy, treatment regimens with cDMARDs+anti-TNF and TCZ could lead to a better disease control in terms of clinical activity and inflammatory markers and overall is the only therapeutic lines that provides an improvement in metabolic activity on imaging.

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AB0730 TOCILIZUMAB TREATMENT IN SEVERE AND REFRACTORY BEHÇET'S SYNDROME: A CASE SERIES

Keywords: Behcet's disease, bDMARD

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Background: Tocilizumab may be an alternative for patients with Behçet's Syndrome (BS) refractory to conventional immunosuppressives and TNF inhibitors.

Objectives: We aimed to report our experience with tocilizumab in patients with BS.

Methods: We identified BS patients who were treated with tocilizumab for eye, nervous system and arterial involvement, and amyloidosis, using our hospital's electronic medical records. Demographic and clinical features, previous therapy, treatment response, outcomes, and adverse events were retrieved from patient charts.

Results: A total of 12 patients with BS (M/F: 9/3, mean age 44.4±10.3 years) were treated with tocilizumab for uveitis (n=6), parenchymal nervous system involvement (n=2), aortitis (n=2) and amyloidosis (n=2) between 2014-2022. Previous treatment modalities and treatment response for uveitis are shown in Table 1. Only 2 of the 6 patients with uveitis obtained remission with tocilizumab. Both patients with neurological involvement were refractory to tocilizumab treatment. They had previously used colchicine, steroids, azathioprine, interferon-alpha, infliximab, and adalimumab. Additionally, one had used cyclophosphamide and the other methotrexate and mycophenolate mofetil. One of the patients with amyloidosis was unresponsive and underwent kidney transplantation. The other had improvement in proteinuria, but she developed Crohn disease and infliximab was started. One patient with aortitis had used steroids, colchicine, azathioprine, cyclophosphamide, infliximab and the other had used steroids, colchicine, azathioprine, interferon-alpha and methotrexate. Both patients with aortitis obtained remission. One of them discontinued tocilizumab voluntarily, and the other due to dyslipidemia. Overall, tocilizumab was discontinued in 10/12 patients after 10.1±7.8 months. Adverse events were increased mucocutaneous lesions in one and dyslipidemia in another patient.

Conclusion: BS patients with aortitis benefitted from tocilizumab. However, our experience with tocilizumab in patients with eye and nervous system involvement was not as favorable as reported in previous case series. This may be partly due to the long disease duration before tocilizumab and the patient's 'being difficult-to-treat patients, refractory to several previous biologics including TNF inhibitors and interferon-alpha.

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Acknowledgements: none.

Disclosure of Interests: None Declared.

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AB0731 CUTANEOUS AND ARTICULAR MANIFESTATIONS OF BEHÇET'S DISEASE

Keywords: Behcet's disease

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Background: Behçet's disease is a chronic inflammatory disease evolving by relapses whose etiopathogeny remains poorly elucidated. It is characterized by polymorphism and a clinical heterogeneity associating oral and genital aphthosis with systemic manifestations, notably cutaneous and articular.

Objectives: The aim of this study is to describe the epidemiological and clinical aspects of the articular and cutaneous-mucosal manifestations during Behçet's disease.

Methods: This was a monocentric, retrospective, and descriptive study. It was conducted over a period of 30 years and included all patients with Behcet's disease followed at the internal medicine department and meeting the international criteria for Behcet's disease.

Results: We collected 98 patients. A male predominance was observed (sex ratio of 2.5) with an average age of onset of the disease of 31 years. Familial forms were observed in 5.1%. Oral aphthosis was constant. The different localizations were on the inner side of the lip in 17 cases (68%), the inner side of the cheek in six cases (24%), the tongue in two cases (8%), and the gums in one case (4%). Genital aphthosis was found in 81 cases. Other manifestations were pseudofolliculitis (61 cases), erythema nodosum (7 cases), cutaneous aphthosis (4 cases), acneiform lesions (2 cases), cutaneous vasculitis (2 cases), and erythema multiforme (1 case). The pathergy test was performed in 30 cases. It was positive in 23 cases (76%). Joint involvement was present in 47 patients. The average age of diagnosis of joint involvement was 34 years. The mean time to diagnosis was 25 months. The involvement was peripheral in the majority of cases (95.7%), with the predominant site being the knees (67%). It was in the form of inflammatory arthralgias in 45 patients, associated with arthritis in 14 cases. Other manifestations were: low back pain (2 cases), sacroiliitis (1 case), bone erosion involving the hand (1 case), and popliteal cyst (1 case).

Conclusion: In Behçet's disease, the clinical manifestations are very polymorphic. Its polymorphic and non-specific clinical presentation can be a source of confusion with other pathologies. Cutaneous and articular manifestations are the most frequent.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.5995

Vasculitis - large vessel vasculitis

AB0732 OUTCOMES OF PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY IN TAKAYASU ARTERITIS: A SINGLE CENTER EXPERIENCE

Keywords: Vasculitis

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Background: Revascularization endovascular techniques have been used with success in Takayasu arteritis (TA), but relapses sometimes appear. (1) There is much debate regarding optimal management and outcomes of patients who underwent these procedures. (2,3)
Objectives: The aim of the study was to investigate the long-term efficacy of percutaneous transluminal angioplasty (PTA) in patients with TA from a Romanian tertiary rheumatology center and factors that might influence it.
Methods: Data from clinical charts of patients with a diagnosis of TA established in the last 15 years who underwent interventional revascularization procedures were retrospectively studied. Symptoms, laboratory investigation results, data about treatment and outcome were analyzed at baseline and follow-up.
Results: There were 11 interventions of PTA in 6 patients with a diagnosis of TAK, all of them in women. The mean follow-up period was 59 months. Cardiologists were the ones who diagnosed the disease in 83% of the patients included. The mean delay in diagnosis was 74 months, while the biggest delay was of 242 months. Hypertension was the first sign of disease in 3 of the patients, while the rest complained of limb claudication (2 patients) and acute limb ischemia phenomenon (1 patient). The average disease duration until PTA was 65 months and most of them were done at the time of diagnosis (54%). PTA was performed while the disease was active in 100% of cases and biological inflammatory syndrome was present in 45% of cases. Symptoms relief was seen in all patients. Restenosis was seen in 3 cases – two of them in patients with lack of treatment adherence and one in a patient who wasn't given immunosuppression (due to delay in diagnosis). Restenosis was experienced 52 months after PTA, on average. Symptoms included relapse of limb claudication in 2 patients and hypertension and renal failure in a patient with renal artery restenosis. Inflammatory markers were raised in two cases. Clinical improvement was seen in all the patients after reintervention.
Conclusion: PTA is a valuable intervention in TA patients that significantly improves clinical symptoms. Relapses may appear especially in patients with deficient immunosuppression, and they may need revascularization interventions.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6130

AB0733 CONCORDANCE BETWEEN THE 1990 ACR CLASSIFICATION CRITERIA AND THE NEW 2022 ACR/EULAR 2022 CRITERIA IN GIANT CELL ARTERITIS

Keywords: Diagnostic tests, Vasculitis, Epidemiology

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Background: Classification criteria for vasculitis, including giant cell arteritis (GCA) are under constant revision. In 2022, the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria were presented, renewing those published by ACR in 1990. They include wider range of clinical criteria and imaging tests, such as ultrasonography (US) and Positron emission tomography (PET), which has contributed to the diagnosis of a higher number of cases.
Objectives: To assess the concordance between recent 2022 ACR/EULAR giant cell arteritis classification criteria and the criteria of ACR 1990 [1,2].
Methods: Observational study of patients diagnosed with GCA who underwent temporal artery biopsy (TAB) between 2016 and 2022 in an university hospital. Concordance between both sets of criteria were analyzed with Cohen's kappa index.
Results: We present 191 patients (120 female/71 male) (mean±SD; 75±10 years). The main characteristics of the patients are shown in **Table 1**.
The Kappa index between both criteria weighted by prevalence and bias was 0.654 (moderate-high degree of agreement). Global agreement of 83% was observed, with a higher specific agreement for negative results (88%) than for positive results (67%).
Disagreement was observed in 16% of patients who were considered negative for ACR 1990 criteria but positive for ACR/EULAR 2022 criteria and in 2% who were considered positive for ACR 1990 criteria but negative for ACR/EULAR 2022. 2022 ACR/EULAR showed a higher sensitivity, and 27 additional patients were classified as GCA with these classification criteria.
Conclusion: Moderate-high concordance was found between 2022 ACR/EULAR and 1990 ACR classification criteria. However, the 2022 ACR/EULAR criteria consider a wider range of factors than the 1990 ACR criteria by introducing US and PET findings, thus increasing sensitivity and allowing a larger number of patients to be diagnosed. Cranial GCA was the most frequent phenotype observed.
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Table 1. Main characteristics according to TAB result

	Suspected diagnosis of GCA (n=191)	ACR 1990 Criteria (n=128)	ACR/EULAR 2022 Criteria (n=155)	Negative ACR1990 Criteria Positive ACR/EULAR 2022 Criteria (n=30)
Age (years), mean±SD*¶	75 ± 10	75 ± 10	75 ± 10	73 ± 10
Sex, female/male	120/71	78/50	96/59	10/20
TAB+, n (%) *¶	52 (27)	51 (39)	52 (34)	1 (3)
Halo sign on temporal artery US, n (%) ¶	37 (19)	29 (23)	37 (24)	10 (59)
Bilateral axillary involvement on US, n (%) ¶	12 (18)	8 (19)	12 (20)	4 (24)
FDG-PET activity throughout aorta, n (%) ¶	43 (43)	30 (48)	37 (44)	7 (33)
GCA Phenotype, n (%)				
Cranial GCA	127 (66)	95 (74)	108 (70)	16 (53)
Extracranial GCA	28 (15)	6 (5)	14 (9)	8 (27)
Mixed GCA	36 (19)	27 (21)	33 (21)	6 (20)
Ischemic manifestations, n (%)				
Headache*¶	152 (80)	117 (91)	134 (86)	20 (67)
Scalp tenderness¶	48 (25)	39 (30)	46 (30)	7 (23)
Jaw/lingual claudication¶	50 (26)	39 (30)	49 (32)	10 (33)
Visual symptoms	76 (40)	58 (45)	66 (43)	8 (27)
Sudden visual loss ¶	44 (23)	35 (27)	40 (26)	5 (17)
Blindness	16 (8)	12 (9)	14 (9)	2 (7)
Abnormal examination of TA*¶	89 (47)	81 (63)	85 (55)	6 (20)
Systemic manifestations, n (%)				
Fever	27 (14)	20 (16)	20 (13)	1 (3)
PmR¶	113 (59)	71 (55)	91 (59)	20 (67)
Laboratory				
CRP, mg/dL, median [IQR] ¶	2.5 [0.5-7.7]	4.2 [1.3-9.0]	3.4 [0.7-7.8]	0.6 [0.4-2.2]
ESR 1h, median [IQR]* ¶	52 [29-82]	63 [41-88]	57 [33-84]	29 [10-44]
Hb, mean ±SD	12.4 ± 1.4	12.3 ± 1.4	12.4 ± 1.3	12.6 ± 1.3

* Criteria evaluated in ACR1990¶ Criteria evaluated in ACR/EULAR 2022**Abbreviations:** ACR: American College of Rheumatology, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, EULAR: European League Against Rheumatism, FDG-PET: fluorodeoxyglucose positron emission tomography, GCA: giant cell arteritis, Hb: Hemoglobin, PmR: polymyalgia rheumatica, TA: temporal artery, TAB: temporal artery biopsy, US: ultrasound.

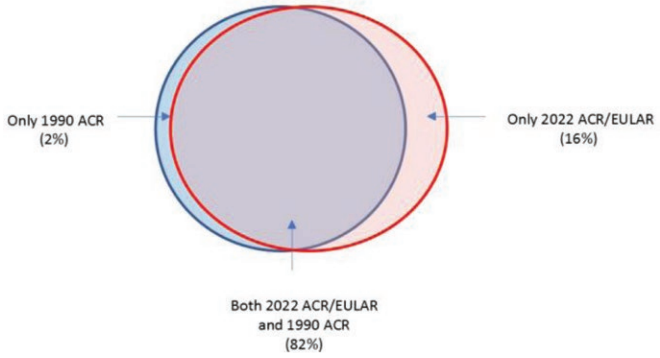


Figure 1. % of patients who met the different classification criteria.

Disclosure of Interests: None Declared.
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AB0734 POLYPHARMACY AND COMORBIDITIES ARE NOT INCREASED AT DIAGNOSIS IN PATIENTS WITH POLYMYALGIA RHEUMATICA

Keywords: Malignancy, Comorbidities

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Background: Polypharmacy, the prescription of multiple drugs for an individual patient, is increasing especially in ageing individuals with comorbidities. Polymyalgia rheumatica (PMR) is an inflammatory disease of the elderly causing pain and stiffness in the girdles. A recent systematic review showed that cardiovascular disease and lymphoproliferative disorders could be possibly increased in PMR patients, but the quality of the included studies was relatively poor. In addition, some comorbidities could be caused by PMR treatment and not by the disease itself.
Objectives: Our study is concerned with an evaluation of polypharmacy and comorbidities in PMR patients at diagnosis.
Methods: Patients were enrolled if they fulfilled the 2012 EULAR/ACR provisional criteria for PMR. Sex and age-matched controls were patients with hand OA diagnosed according to the 1990 ACR clinical criteria and seen in the same private outpatient clinic as patients. Both groups were interviewed at the time of diagnosis for the type and number of assumed drugs and comorbidities by the same investigator. The rheumatic diseases comorbidity index (RCDI) was used.
Results: 83 PMR patients (median 75 years, range 50-88 years, 65.1% women) and 83 controls (median 72 years, range 53-90 years, 65.1% women) were studied. Median disease duration was 2 months (0.3-8 months) and median glucocorticoid dose before assessment was 0 mg (0-750 mg). The mean number of drugs assumed by PMR patients was 2.5±2.1 in comparison with 3.0±2.2 of controls (p=0.129). PMR patients with hip pain assumed less drugs (2.1±1.8 vs. 3.7±2.3, p=0.008) and those with morning stiffness >45 minutes assumed more drugs (2.8±2.1 vs. 2.8±2.1, p=0.001). The mean RDCI was 1.58±1.29 in PMR patients and 1.45±1.36 in controls (p=0.52). The frequency of the individual comorbidities in PMR patients and controls is reported in Table 1. No difference was observed in cancer type. Number of assumed drugs and RDCI significantly correlated (r=0.58; p<0.001), and both were directly associated with age (p<0.001). At multiple logistic regression, with number of assumed drugs as dependent variable and variables which showed in univariate analysis p<0.1 as independent ones, age (p=0.007) directly, whereas hip pain (p=0.006) and fever (p=0.014) indirectly predicted number of assumed drugs. With RDCI as dependent variable, age (p=0.04) and WBC (p=0.02) directly, whereas fever (p=0.019) indirectly predicted RDCI.
Conclusion: When considered at the time of diagnosis, PMR patients do not show an increased comorbidity index nor number of assumed drugs in comparison with OA controls. Only gastric disease was lower, possibly due to the increased NSAIDs use in OA patients.

Table 1. Frequency of the individual comorbidities in PMR patients and controls (Co).

Comorbidity	PMR (n=83)	Co (n=83)	p
pneumological	11 (13.3)	9 (10.8)	0.63
CV/ictus	19 (22.9)	14 (16.9)	0.33
hypertension	45 (54.2)	39 (47)	0.35
fracture	8 (9.6)	7 (8.4)	0.79
depression	2 (2.4)	5 (6)	0.25
cancer	13 (15.7)	11 (13.3)	0.66
diabetes	7 (8.4)	5 (6)	0.55
gastric	6 (7.2)	15 (18.1)	0.036

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0735 THE EFFECT OF NEW CLASSIFICATION CRITERIA ON THE DIAGNOSIS OF LARGE VESSEL VASCULITIS

Keywords: Vasculitis, Rare/orphan diseases, Epidemiology

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Background: GCA and Takayasu arteritis are the two recognised forms of LVV. In addition, there is recognition of LVV which are not easily classified into the two forms. Classification criteria have been proposed since 1990 and have been recently updated. Classification criteria should be able to minimise the number of cases that are unclassifiable and the number of cases that are classified into more than one set. We used both sets of criteria to test their performance in our cohort.
Objectives: To study the performance of large vessel vasculitis classification criteria in a real world cohort.
Methods: Between January 2011 to December 2020, 270 individuals were diagnosed as having LVV by virtue of having either a positive biopsy, ultrasonography, or PET scan. The ACR 1990 and the ACR/EULAR 2022 classification criteria were applied on our cohort.
Results: The mean age was 74. 181 were female. Using the 1990 criteria, 2 individuals met both classifications and 30 did not meet either. Using the 2022 criteria, 3 individuals met both classifications and 24 did not meet either. The numbers classified as having TAK has reduced from 13/270 to 2/270. The numbers classified as GCA have increased from 225/270 to 241/270. (Figure 1)
Conclusion: The new classification criteria have expanded the phenotype recognised as having GCA by including previously unclassified individuals, and narrowed the phenotype recognised as having Takayasu mostly by declassifying it as not meeting any criteria. Overall, the new criteria improve classification for 5/270 (1.8%) cases.
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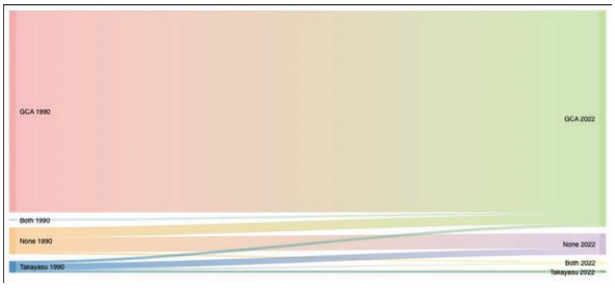


Figure 1. The effect of classification criteria on our cohort of 270 individuals with large vessel vasculitis

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.309

AB0736 EPIDEMIOLOGY OF CLINICALLY ISOLATED AORTITIS: A POPULATION-BASED STUDY

Keywords: Vasculitis, Epidemiology

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Background: Clinically isolated aortitis (CIA) refers to inflammation of the aorta without signs of systemic vasculitis or infection [1]. The diagnosis of CIA generally relies on histopathologic evaluation of aortic tissue obtained during thoracic aortic aneurysm surgery making the diagnosis more challenging. Recent studies suggest that CIA might be a limited presentation of giant cell arteritis [2]. Population-based data on the epidemiology of CIA in North America is lacking.
Objectives: The objectives of this study were to evaluate the epidemiology, clinical characteristics, and outcomes of patients with CIA.
Methods: In a defined geographical area, all possible subjects were screened for thoracic aortic aneurysm procedures with current procedural terminology (CPT) codes between January 1, 2000, and December 31, 2021. The medical records of all patients were manually reviewed. CIA was defined as histopathologically confirmed active aortitis diagnosed by evaluation of aortic tissue obtained during thoracic aortic aneurysm surgery in the absence of any infection, rheumatic disease, or systemic vasculitis. Incidence rates were age and sex adjusted to the 2020 United States total population. Mortality rates were estimated using the Kaplan-Meier method and were compared with expected mortality rates for persons of the same age, sex, and calendar year estimated using Minnesota population life tables.
Results: Eight incident cases of CIA were diagnosed during the study period (Figure 1); 6 (75%) of them were female. Median (IQR) age at diagnosis of CIA was 78.3 (70.2- 78.9) years; all were diagnosed following ascending aortic aneurysm repair. The overall age and sex adjusted annual incidence rate of CIA was 8.9 (95% CI, 2.7- 15.1) per 1,000,000 individuals over age 50 years. Histopathological evaluation demonstrated giant cell aortitis in 7 (88%) patients and lymphoplasmacytic aortitis in 1 (13%) patient. Five (63%) patients were seen by a rheumatologist and 2 (25%) were treated with glucocorticoids after the diagnosis of CIA. Most of the patients had cardiovascular signs and symptoms prior to the surgery. One patient presented with aortic dissection and contained rupture. The median (IQR) duration of follow-up was 8.7 (1.2- 12.0) years. Five (63%) patients died during follow-up; 1 (13%) within one week of surgery. The overall mortality compared to the age and sex matched general population did not differ (standardized mortality ratio: 1.58; 95% CI, 0.51 3.68).
Conclusion: This is the first population-based epidemiologic study of CIA in North America. CIA predominantly affects older women and is quite rare. In this small cohort, survival following a diagnosis of CIA was not significantly different than the general population.
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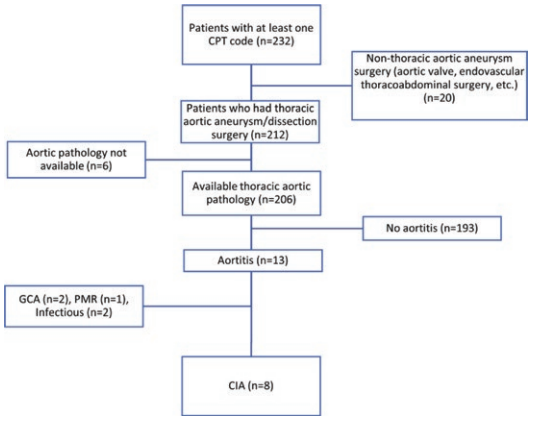


Figure 1. Flowchart for identification of the cohort

Acknowledgements: NIL.
Disclosure of Interests: Mahmut Kaymakci: None declared, Mohanad Elfishawi: None declared, Hannah Langenfeld: None declared, Cynthia S. Crowson: None declared, Weyand Cornelia: None declared, Matthew Koster: None declared, Kenneth J Warrington Consultant of: Chemocentryx, Sanofi, Grant/research support from: Eli Lilly, Kiniksa, GSK.
DOI: 10.1136/annrheumdis-2023-eular.1062

AB0737 FAST TRACK PATHWAY: A GIANT STEP FOR THE DIAGNOSIS AND MANAGEMENT OF GIANT CELL ARTERITIS

Keywords: Vasculitis, Patient reported outcomes, Validation

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Background: Giant cell arteritis (GCA), a medium and large vessel vasculitis remains a formidable disease. Through feed-forward loops and a multitude of vascular complications, GCA impacts seriously negatively on both the patient's vision as well as life. In 2018, Darent Valley Hospital published its GCA management pathway [1] and launched a fast track GCA clinic in 2019. This included clinical assessment along with US examination in the rheumatology outpatients' clinic. The pathway enabled direct access to both general practitioners in primary care as well as health care professionals in secondary care to this service. Education sessions for both the primary and secondary care teams were carried out to inform them of the referral criteria and the service pathway.
Objectives: To evaluate the impact of implementing the GCA-fast track pathway on prompt diagnosis and treatment of GCA.
Methods: Retrospective cohort analysis of patients referred to the Fast Track GCA clinic. A cohort of patients with new suspected diagnosis of GCA along with acute flare ups of diagnosed GCA cases were referred to the clinic according to a set up referral criteria. All the patients referred to the clinic were offered an appointment within 24-hours and had blood tests for inflammatory markers and basic rheumatology blood profile done prior to their assessment. Diagnosis of GCA was made based on clinical examination, laboratory results and US assessment [2]. Presence of 'halo' sign, which is a non-compressible hypo-echoic ring around the artery lumen reflecting inflammation of the vessel wall was considered as a positive US finding. Steroid therapy was commenced on the same day of the diagnosis. If steroid infusion is indicated, the patient is referred to the AEC/ AMU to have the steroid infusion on the same day. Outcomes of management were assessed by GCA-patient reported outcomes as well as US assessment. The service was audited twice.
Results: During the evaluation period, 56 patients were referred to the Fast track GCA clinic. Age range 57-87 years old. 78.6% of these patients were females. 85.7% (48/56) of these patients were offered an appointment and assessed within one working day (24-hours), whereas the remaining 14.3% (8/56) were reviewed within 24-72 hours. All the patients (100%) had US examination of the temporal artery within the targeted time of maximum 72-hours from the referral date and less than 2-weeks of presenting with the temporal headache. Six patients were diagnosed as non-GCA, 5-patients migraine, 1-patient trigeminal neuralgia, 2-patients with large vessel vasculitis, 3-patients with PMR and 2-patients had flare of their previous PMR. 37-patients (66.1%) were diagnosed with GCA. No biopsies were performed. 9-patients (24.3%) required IV steroid infusion, whereas 28-patients (75.7%) started oral steroids. None of the patients included in the study suffered GCA related sight loss. No hospital admissions were required for these patients. There was significant improvement in the GCA patient reported outcomes in response to therapy, US measures as well as the inflammatory markers.
Conclusion: The developed Fast Track GCA clinic has significantly facilitated early and prompt diagnosis as well as management of GCA. Majority of the patients were reviewed within 24-hours with immediate initiation of steroid therapy. The fast-track referral pathway, combined with GP education, resulted in a significant reduction of incidences of permanent sight loss attributed to GCA (which would have resulted in loss of independence and mobility which subsequent increase health care use) and has proven to be a cost-effective practice as number of admitted patients was reduced.
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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1108

AB0738

ELEVATED PLATELET COUNT IS A RISK FACTOR FOR REFRACTORY TAKAYASU ARTERITIS

Keywords: Biomarkers, Vasculitis

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Background: Takayasu arteritis (TAK) is a chronic systemic vasculitis that mainly affects the aorta and its major branches. This chronic relapsing disease is relevant to significant morbidity and treatment remains challenging [1]. Early identification of refractory TAK is helpful to improve the long-term prognosis of the disease. In recent years, platelets have been recognized as important markers for various types of diseases [2]. Platelet counts may indicate the activity of autoimmune disease as well as responsiveness to anti-inflammatory therapy and presence of various comorbidities [3]. Multiple studies have demonstrated that platelet count of TAK patients was significantly increased, especially in the active phase, which was significantly higher than that in the inactive phase [4-8].
Objectives: Platelets have been recognized as important markers for various types of diseases. The aim of our study was to investigate whether platelet count could be the risk factor of refractory Takayasu arteritis (TAK).
Methods: In this retrospective study, 57 patients were divided into groups with or without refractory TAK. We compared the clinical manifestations, laboratory parameters, and medication between the two groups. The logistic regression analysis was used to identify the risk factors of refractory TAK.
Results: Among the 57 patients, 18 cases (31.6%) were considered to have refractory TAK within 1 year of initiation of medication in our hospital. Refractory TAK patients had higher level of platelet (PLT) than non-refractory TAK patients (305.5 vs. 272.0, 10^9/L, P=0.043). PLT was positively correlated with ESR (r=0.502, p < 0.001), hs-CRP (r=0.529, p < 0.001), IgA (r=0.322, p=0.016), IgG (r=0.419, p=0.001), IgM (r=0.343, p=0.010), C3 (r=0.554, p < 0.001). For PLT, the area under the ROC curve was 0.668 (95% CI 0.515 to 0.822, p=0.043) and the best cut-off value was 296.5×10^9/L. The level of PLT greater than 296.5×10^9/L was found to be statistically related to refractory TAK (OR [95%CI] 4.000 [1.233-12.974], p=0.021).
Conclusion: Clinicians should pay close attention to platelet levels in patients with TAK. For TAK patients with elevated platelet levels, earlier and more aggressive treatment is needed, and antiplatelet therapy is recommended as appropriate.

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Disclosure of Interests: None Declared.
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AB0739

PERFORMANCE OF THE 2022 AMERICAN COLLEGE OF RHEUMATOLOGY/EULAR CLASSIFICATION CRITERIA FOR GIANT CELL ARTERITIS IN A COHORT OF PATIENTS WITH SUSPICION OF HAVING GIANT CELL ARTERITIS

Keywords: Vasculitis

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Background: The new ACR/EULAR 2022 classification criteria for giant cell arteritis (GCA) use weighted items and incorporate findings from vessel imaging to reflect the current clinical standard. Although intended to define homogenous patient populations for research purposes when a diagnosis of medium- or large-vessel vasculitis has been made, the 2022 criteria were developed including non-vasculitis comparators. Hence, in the absence of a sensitive diagnostic gold standard, the criteria bear potential to be used for GCA diagnosis.
Objectives: To evaluate the performance of the new 2022 ACR/EULAR classification criteria for GCA when used for GCA diagnosis.
Methods: Retrospective analysis of a cohort of patients suspected of having GCA who underwent ultrasound between 12/2006 and 05/2021. GCA was diagnosed if temporal artery biopsy was positive, if the 1990 ACR criteria were fulfilled, or if at least 2/5 ACR criteria were fulfilled in combination with vasculitis on imaging.
Results: 276 patients were diagnosed with GCA, and 400 patients had a condition that mimics GCA. When applying the 2022 criteria as diagnostic criteria, sensitivity remained high with 87.3% (95% CI 82.8%–91.0%), whereas specificity was lower with 70.3% (95% CI 65.5% to 74.7%). In 35 patients (12.7%) with GCA, the criteria were not met (Table 1). These were mainly patients without cranial symptoms but having typical imaging findings in vascular territories not considered in the criteria. 119 non-GCA patients (29.8%) scored ≥6 points. Polymyalgia rheumatica (PMR) (31.9%) followed by non-vasculitic ophthalmologic diseases (15.1%) were the most frequent diagnoses among those.
Conclusion: The inclusion of polymyalgic symptoms and heavy weighting of sudden visual loss in the score led to false classification of patients with PMR and ophthalmologic diseases as GCA. For diagnostic purposes, the scoring of the criteria could potentially be adapted by applying a higher cut-off for the diagnosis of GCA or a lower weighting for polymyalgic and visual symptoms.

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Table 1. 2022 American College of Rheumatology/ EULAR classification criteria for giant cell arteritis in patients with GCA and non-GCA

	Total number of patients (n=676)	GCA patients with <6 points (n=35)	GCA patients with ≥6 points (n=241)	p-value	Non-GCA patients <6 points (n=281)	Non-GCA patients ≥6 points (n=119)	p-value
Age, mean (±SD)	71.8 (9.7)	71.3 (8.7)	73.5 (8.4)	0.167	71.2 (10.2)	70.2 (11.0)	0.393
Female, n (%)	398 (58.9)	21 (60.)	150 (62.2)	0.799	155 (55.2)	72 (60.5)	0.324
ACR/EULAR criteria							
Morning stiffness in shoulders/neck, n (%)	287 (42.5)	8 (22.9)	98 (40.7)	0.004	104 (37.0)	77 (64.7)	<0.001
Sudden visual loss, n (%)	78 (11.5)	0 (0.0)	36 (14.9)	0.01	21 (7.5)	21 (17.6)	0.002
Jaw or tongue claudication, n (%)	147 (21.7)	0 (0.0)	110 (45.6)	<0.001	9 (3.2)	28 (23.5)	<0.001
New temporal headache, n (%)	347 (51.3)	11 (31.4)	158 (65.6)	<0.001	84 (29.9)	94 (79.0)	<0.001
Scalp tenderness, n (%)	139 (20.6)	1 (2.9)	95 (39.4)	<0.001	9 (3.2)	34 (28.6)	<0.001
Abnormal examination of the temporal artery, n (%)	111 (16.4)	1 (2.9)	83 (34.4)	<0.001	7 (2.5)	20 (16.8)	<0.001
Maximum ESR ≥50 mm/hour or maximum CRP ≥10 mg/liter, n (%)	504 (74.6)	29 (82.9)	226 (93.8)	0.004	150 (53.4)	99 (83.2)	<0.001
Positive temporal artery biopsy or halo sign on temporal artery ultrasound, n (%)	194 (28.7)	2 (5.7)	186 (77.2)	<0.001	0 (0.0)	6 (5.0)	<0.001
Bilateral axillary involvement, n (%)	38 (5.6)	2 (5.7)	35 (14.5)	0.191	0 (0.0)	1 (0.8)	0.3
FDG-PET activity throughout aorta, n (%)	52 (7.7)	5 (14.3)	36 (14.9)	0.919	8 (2.8)	3 (2.5)	1

CRP=C-reactive protein; ESR=erythrocyte sedimentation rate; FDG-PET=fluorodeoxyglucose-positron emission tomography; IQR=interquartile range; n=number; PMR=Polymyalgia rheumatica; SD=standard deviation; TA=temporal artery, TAB=temporal artery biopsy.

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AB0740 DESCRIPTION AND PROGNOSTIC FACTORS FOR AORTITIS RELAPSE IN PATIENTS WITH GIANT CELL ARTERITIS

Keywords: Real-world evidence, Vasculitis, Imaging

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Background: Giant cell arteritis (GCA) is the most common systemic vasculitis in individuals ≥ 50 years of age. It typically affects cranial vessels, but it can also affect large vessels in a high percentage of patients. Vascular inflammation of the aorta and/or its main branches can cause complications of high morbidity and mortality, and the presence of relapses is associated to more complications. The analysis of the different clinical and imaging patterns in patients with GCA and aortitis and their relationship with the prognosis needs more investigation. Early identification of patients with the highest risk of mortality could help predict deaths and vascular complications.
Objectives: To evaluate the demographic and clinical characteristics of patients with giant cell arteritis (GCA) who present a relapse.
To evaluate prognostic factors associated with GCA relapse.
Methods: A retrospective cohort study was carried out including patients diagnosed of GCA by a multidisciplinary expert committee in aortic pathologies. A total of 71 patients followed in the vasculitis clinic between 2011-2021 who had a PET-CT at onset before receiving treatment were included. Other causes of aortitis were excluded. Relapse was defined as a new episode of vasculitis confirmed by analysis and/or imaging test. Demographic, clinical, analytical and imaging variables were collected. A descriptive study of the sample and a groups comparison, according to the presence of vascular complication, was carried out. The Shapiro-Wilk test was used to study the normality of the variables. The relapse-free survival was analyzed using the Kaplan-Meier method. Univariate logistic regression was performed to assess predictive factors.
Results: A total of 71 patients were included, 73.2% were female and the mean age was 79.3 (±6.7) years. During the follow-up of the disease, 22 (30%) patients presented a relapse. Scalp tenderness (p<0.0001) and the complications prior to or at onset (aortic surgery [p=0.0003], ischemic stroke [p=0.0001], aneurysm/dissection/thrombosis [p=0.012]) presented a significant association with relapse. Cardiovascular risk factors and acute phase reactants were not associated with relapse during the disease, and either the diagnostic delay and start of treatment. Details of the demographic and clinical characteristics of the sample are described in Table 1.

Table 1. Characteristics of the sample according to the occurrence or not of relapse.

	Relapse (n=22)	No relapse (n=49)	p
GCA Classification (%)			0.375
- Cranial	18.2	18.3	
- Extracranial	13.6	28.5	
- Both	68.2	53.1	
Clinical presentation (%)			
Headache	22.7	35.4	0.433
Jaw claudication	63.6	66.6	0.804
Ophtalmological signs	72.7	68.7	0.736
Scalp tenderness	81.8	75	**<0.000**
Fever of unknown origin	72.7	72.9	0.987
Polymyalgia rheumatica	59.1	58.3	0.952
Anemia	72.7	58.3	0.247
Constitutional syndrome	63.6	77.1	0.240
Complications at onset (%)			
Aortic surgery	4.5	6.2	**0.000**
Ischemic stroke	9.1	4.1	**0.000**
Vascular complication	4.5	14.5	**0.012**
Treatment			
IV pulse GC mg/kg/d (%)	22.7	20.4	0.247
Oral GC, mean (SD)	48.6 (±16.4)	50.8 (±18.1)	0.631
sDMARD +/- bDMARD (%)	45.5	34.7	0.174

The relapse-free survival time in patients with GCA is shown in Figure 1. The median time (months) in relapse was 14-4 (IQR 36.1).

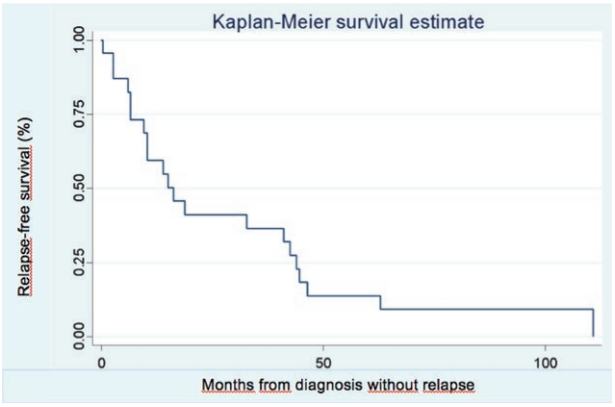


Figure 1. Kaplan-Meier curve of relapse-free survival in patients with GCA.

The univariate analysis to identify prognostic factors showed that the use of synthetic or biological disease-modifying anti-rheumathic drugs (sDMARD, bDMARD) was a protective factor against the occurrence of disease relapse, presenting a risk of relapse in untreated patients versus treated 64% higher (RR=0.64).
Conclusion: Disease relapse was observed in 30.9% of patients with GCA included in our study.
Scalp tenderness and the presence of vascular complications prior to or at onset of the disease were associated with greater occurrence of relapse. Our study suggests a possible protective effect of immunosuppressive drugs against relapse in GCA patients.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0741 CAN NORMAL ERYTHROCYTE SEDIMENTATION RATE AND C-REACTIVE PROTEIN LEVEL BE A REASON FOR DIAGNOSTIC DELAY IN POLYMYALGIA RHEUMATICA?

Keywords: Vasculitis, Diagnostic tests, Real-world evidence

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Background: Polymyalgia Rheumatica (PMR) is an inflammatory disease which does not have specific diagnostic tests or pathological symptoms and is defined with clinical characteristics. Among the acute phase reactants (APR), erythrocyte sedimentation rate (ESR) and C-Reactive Protein (CRP) are laboratory findings used in the diagnosis and follow-up. Although abnormal ESR and CRP levels are included in the criteria for the classification of PMR, ESR and CRP can be observed as normal in 13% of PMR patients.
Objectives: In the study, it was aimed to determine the incidence of normal APR rates in patients diagnosed with PMR and to identify the distinguishing characteristics of these patients.
Methods: PMR patients who were clinically diagnosed at a single center were reviewed. After the presence of bursitis was demonstrated with ultrasonography (USG) in patients with normal ESR and CRP rates, they were accepted to have PMR. Patients with normal rates of ESR and CRP were compared against patients with high levels of ESR and/or CRP.
Results: In all 54 patients who were diagnosed with PMR (63% female, and mean age 65.39±7.39 years), >45 minute morning stiffness was present. Symptom duration median (IQR) was 3.5 (3) months, and ESR and CRP were found to be high in 72.2% and 83.3% of the patients, respectively. ESR and CRP were normal in 8 patients (14%), and serum amyloid A (SAA) was determined to be high in all these patients. At the time of the diagnosis, 51 patients (94%) had shoulder pain, and 41 patients (75%) suffered from hip pain. At the time of the diagnosis, median (IQR) ESR was found as 59.5 (49) mm/hour and CRP as 16.25 (38) mg/L. In 20 patients, SAA median (IQR) was 36 (26) U/L. The initial median (IQR) steroid dosage at the beginning of the treatment was prednisolone 20 mg/day. As steroid sparing therapy, methotrexate was started in 27 patients, and azathioprine was started in 4 patients. In the group with normal levels

of ESR and CRP, diagnosis median (IQR) ESR was 28 (4) mm/hour and CRP was 3.9 (1) mg/L, while in the group with high levels of ESR and CRP, diagnosis median (IQR) ESR was 76.5 (26) mm/hour, and CRP was 35.5 (60) mg/L. When the groups with normal and high levels of ESR and CRP were compared, it was found that diagnosis age was lower (p=0.027) in the normal ESR and CRP group, while the symptom duration was longer (p<0.001). When the patients were evaluated in terms of presence of at least one comorbidity, comorbidity was determined to be significantly lower in this group (p=0.01). Rheumatoid factor positivity, presence of anemia, and platelet count at the time of diagnosis and PMR exacerbation and giant cell arthritis development in the follow-up were similar. In the multiple regression analysis, when diagnosis age, symptom duration, and comorbidity were evaluated together, long symptom duration was independently associated with PMR with ESR and CRP normal levels (OR=0.045, %95 CI 0.03-0.676, p=0.025).

Table 1. Comparison between the characteristics of the patients with normal levels of ESR and CRP and those with high levels of ESR and CRP

	ESR and CRP Normal n:8	ESR and/or CRP High n:46	p
Diagnosis age, mean (±SD) (year)	61.8 (8.3)	68.57 (7.5)	***0.027***
Symptom duration, median (IQR) (month)	6 (1)	3 (1)	***<0.001***
Gender, female, n (%)	7 (87.5)	27 (58.7)	0.234
Anemia at the time of diagnosis, n (%)	3 (37.5)	23 (50)	0.706
Platelet count at the time of diagnosis, median (IQR)	315 (85)	288 (103)	0.495
SAA at the time of diagnosis, median (IQR)*	33 (34)	51.6 (94)	0.165
Rheumatoid factor, n (%)	1 (12.5)	2 (4.3)	0.388
Presence of at least one comorbidity, median (IQR)	3 (37.5)	39 (84.8)	***0.010***
Exacerbation of PMR, n (%)	0 (0)	15 (32.6)	0.089
Giant cell arthritis development, n (%)	0 (0)	3 (6.5)	1

**SAA was measured in 20 patients.*

Conclusion: Significantly younger age of diagnosis, longer symptom duration and less comorbidity were determined in the group with normal levels of ESR and CRP compared to the group with high levels of ESR and CRP. While bursitis can be demonstrated with USG in patients who are clinically evaluated to have PMR, APRs such as SAA other than ESR and CRP can also be used.

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AB0742 STEROID-SPARING EFFECT OF METHOTREXATE IN PATIENTS WITH STEROID-RESISTANT POLYMYALGIA RHEUMATICA: MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY

Keywords: Pain, Rare/orphan diseases, Disease-modifying drugs (DMARDs)

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Background: Polymyalgia rheumatica is a common inflammatory rheumatic disease affecting people older than 50. It is characterized by simmetrical pain and stiffness of the neck, shoulder, and pelvic girdle and associated with an increase in the concentration of positive acute phase reactants. The diagnosis is based on a clinical picture. Initial treatment consists of corticosteroids, and initial doses of 15 to 20 mg of prednisone or equivalent are usually adequate in most cases. The subgroup of patients that responds only partially to corticosteroids or develops corticosteroid resistance usually requires the introduction of a corticosteroid-sparing drug, methotrexate being the most widely used in routine clinical practice.

Objectives: To evaluate the efficacy and safety of methotrexate in patients with steroid-resistant polymyalgia rheumatica in real clinical practice.

Methods: Retrospective multicenter descriptive study of patients diagnosed with polymyalgia rheumatica in three hospitals in Madrid (Spain) treated with methotrexate as a corticosteroid-sparing agent. Clinical and demographic characteristics of the sample were analyzed and laboratory data evolution were evaluated by collecting positive acute phase reactants (ARF) (erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)) at baseline, at 6 and 12 months of treatment. Descriptive statistics were used for data presentation. The Wilcoxon test for paired data was used to contrast statistical significance, with a p<0.05 being considered significant.

Results: Overall, 58 patients were included: 26 men (44.83%) and 32 women (55.17%), with a mean age of 78.58 (±7.3) years, mean disease duration of 7.46. (±5.78) years. The mean values of CRP, ESR, dose of prednisone and MTX at baseline, at 6 and 12 months of treatment are shown in Table 1. In 52 (89.66%) patients it was possible to reduce the dose of prednisone to <5mg/24h after 12 months of treatment. No significant liver function abnormalities were observed in any of the patients.

Table 1.

	Baseline	6 months	12 months	Baseline vs 12 months p<0,05
Prednisone, mean ± SD	8,28(±4,2) mg/24h v.o	3,75(±2,8) mg/24h v.o.	2,11(± 2,63)	< 0.001
Metotrexato, mean ± SD	11,98(±3,92) mg/sem	13,19(±3,9) mg/sem	13,75(±4,23) mg/sem	0.008
PCR, mean ± SD	13,26 (±20,96) mg/dl	5,11 (±8,72) mg/dl	5,84(±7,02) mg/dl	0.124
VSG, mean ± SD	31,93(±22,4) mm	23,35(±23,07) mm	19,83(±21,6) mm	0.106

Conclusion: As a therapeutic option in steroid-resistant polymyalgia rheumatica, methotrexate seems to offer a steroid-sparing effect at 6 and 12 months of treatment. The treatment is well tolerated.

References: no.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0743 THE IMPACT OF GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA ON FRAILTY, DAILY FUNCTIONING AND QUALITY OF LIFE IN A PROSPECTIVE LONGITUDINAL STANDARD-OF-CARE COHORT

Keywords: Patient reported outcomes, Disease-modifying drugs (DMARDs), Vasculitis

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Background: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are often overlapping inflammatory diseases that occur in people older than 50 years. Both diseases can affect the quality of life, due to the burden of vascular inflammation and ischemia-related symptoms (GCA), joint symptoms (PMR) and systemic symptoms (GCA and PMR), in addition to the side-effects of long-term treatment with glucocorticoids.

Objectives: The goal of this study was to analyze patient reported outcome measures (PROMs), including the quality of life, in patients with GCA and PMR at the time of diagnosis and during 5 years of follow-up, in comparison with age- and sex-matched healthy controls (HCs).

Methods: We prospectively followed treatment-naïve GCA (n=56) and PMR (n=42) patients since diagnosis for up to five years in our observational GPS (GCA, PMR, SENEX) cohort. At each visit, frailty was assessed with the Groningen Frailty Indicator (GFI), daily functioning with the Health Assessment Questionnaire-Disability Index (HAQ-DI) and health-related quality of life with the Short Form (SF)-36. Data were compared to HCs (n=70) selected based on frequency matching of 10-year age cohorts stratified for gender, who were also followed for up to five years.

Results: At diagnosis, PROMs were substantially worse in GCA and PMR patients compared to HCs. GCA patients reported worse scores on the General Health domain than PMR patients, but better scores on the Physical Functioning domain, Pain domain and the HAQ. During the 5-year follow-up, we recorded a partial improvement in PROMs during the first year, which however never reached levels similar to that of HCs in most of the outcomes (Figure 1). Next, we aimed to identify the clinical factors that are most strongly associated with the

PROMs at diagnosis and during follow-up. We found that weight loss at diagnosis was associated with particularly low PROM scores, whereas inflammatory markers did not (PMR) or only moderately (GCA) associate with PROMs. Surprisingly, the physician general disease assessment (GDA) score showed no association with PROMs at diagnosis or at the 2-year visit. PROMs at the 2-year visit did correlate with the Fatigue score and patient GDA. Equivalent to the baseline visit, laboratory markers such as CRP correlated with PROMs in GCA, but not PMR patients. Finally, at the 2-year visit the use of glucocorticoids in GCA patients associated with worse PROMs, but in PMR patients with better scores on the SF-36. MTX use was associated with better PROMs, but only in GCA patients.
Conclusion: GCA and PMR patients experience both short-term and long-term impact on their frailty, daily functioning and quality of life. Medication use appears to be important in determining the patient's quality of life, although surprisingly, glucocorticoid and methotrexate use appear to affect GCA and PMR patients differently. Importantly, the physician GDA or inflammatory markers do not associate strongly with PROMs, particularly in PMR patients, indicating a need for better understanding of the disease and treatment impact on patient's life.

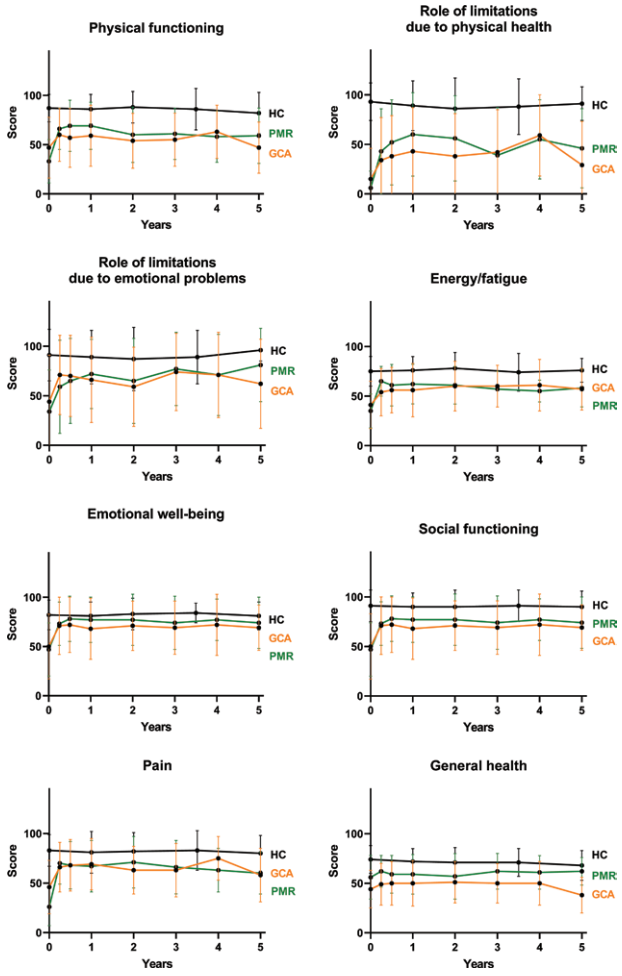


Figure 1. Scores of the eight domains of the SF-36 throughout the disease course in GCA and PMR patients.

Data, expressed as median and interquartile range, are compared to age and sex-matched HCs. Scores range from 0-100; a score of 100 indicates the most healthy outcome.
REFERENCES: NIL.
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Disclosure of Interests: Yannick van Sleen: None declared, Suzanne Arends Consultant of: Argenx and Novartis, Kornelis van der Geest Speakers bureau: Roche, Grant/research support from: Abbvie, Maria Sandovici: None declared, Elisabeth Brouwer: None declared.
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AB0744 HYPERTENSION AND AGE ARE RISK FACTORS FOR VISUAL IMPAIRMENT IN GIANT CELL ARTERITIS

Keywords: Vasculitis

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Background: Permanent vision loss is a feared complication and a leading cause of morbidity in Giant Cell Arteritis (GCA). Prompt recognition of patients with visual manifestation is fundamental to reduce permanent vision loss occurrence.
Objectives: The study aims to evaluate risk factors for visual manifestations at disease onset in an Italian monocentric cohort of patients with Giant Cell Arteritis (GCA).
Methods: We identified 128 patients with GCA diagnosed between 2011 and 2021 in our Center. All patients were older than 50 years of age, met the 1990 ACR criteria for GCA or had a positive temporal artery biopsy or ultrasound. Medical records of all patients were reviewed and demographic, clinical, and laboratory data were collected.
Results: Fifty-five patients (43%) presented at diagnosis visual ischemic manifestations: blurred vision in 6 pts, diplopia in 6 pts, amaurosis fugax in 5 pts, partial visual loss in 23 pts and complete vision loss in 1 or 2 eyes in 12 and 3 pts respectively. Out of 38 patients with partial or complete visual loss, 36 presented Arteritic Anterior Ischemic Optic Neuropathy (AION), and 2 presented Central Retinal Artery Occlusion (CRAO). Patients with visual manifestations had a median age of 77 (IQR 73-81) years, significantly older if compared to patients without ocular symptoms (72 (67-76) years, p<0.001). Patients with ocular involvement presented more often hypertension (67 vs 44%, p: 0.009) and chronic kidney disease (7 vs 0%, p: 0.031) as comorbidity at diagnosis, while no differences were found in diabetes, cancer, coronary heart disease and dyslipidemia incidence comparing patients with and without visual manifestations. No associations between visual impairment and other cranial symptoms (headache, jaw claudication, scalp tenderness) were found, but peripheral arthritis was negatively associated with ocular manifestations. No laboratory variables were associated with ocular involvement.
Conclusion: In this large cohort of patients with GCA, partial or complete visual loss were the most frequent visual manifestations. No associations between ocular involvement and other cranial symptoms were found, while patients with peripheral arthritis had a lower risk of developing visual impairment. Age and hypertension at disease onset seem to be the most important risk factors for visual ischemic manifestations in GCA patients.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3686

AB0745 [18F]-FDG PET/CT IN LARGE VESSEL VASCULITIS: SEMI-QUANTITATIVE [18F]-FDG PET/CT ANALYSIS AND CORRELATION WITH DISEASE ACTIVITY

Keywords: Vasculitis, Descriptive studies, Imaging

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Background: [18F]-FDG PET/CT in a useful tool to assist diagnosis and therapy of large vessel vasculitis (LVV). Visual grading methods are commonly used in clinical practice, but these may lead to interpretation mistakes because of the confounding factors due to atherosclerosis and basal setting of the exam, reducing diagnostic accuracy for detecting active disease. Therefore, a semi-quantitative analysis based on normalization of the arterial wall uptake to the background activity or grading the arterial inflammation against a reference background, were introduced in the context of clinical studies in the last years.
Objectives: To review a series of [18F]-FDG PET/CT of LVV by applying a semi-quantitative analysis that included the standardized uptake value (SUV) and a target-to-background ratio (TBR) to evaluate possible correlations between FDG uptake, considering also a TBR cut-off, haematological inflammatory markers and the CT angiography (CTA) findings.

Methods: We reviewed our internal database for [18F]-FDG PET/CT among patients with LVV (GCA, Takayasu). Were selected [18F]-FDG PET/CT with available blood inflammatory markers and a CTA performed during the same period (permitted a range of 7 days for blood tests or 30 days for CTA), patients were all out of therapy or on stable therapy. As controls were taken ten patients undergoing PET/CT for oncologic diagnostics. The SUV maximum (SUV max) was considered that in the aortic arch or in the vascular region with higher levels of SUV. Target-to-background ratio was calculated considering average SUV in the right hepatic lobe (SUV max/SUV liver ratio). Non parametric test for correlation analysis were performed between SUV max, SUV max/SUV liver ratio and CRP (mg/dl). According previous data a cut-off of SUV max/SUV liver ratio >1.2 was considered and was then compared with CRP, for disease activity, and with CTA, to find agreement with vessel wall thickness and contrast enhancement.
Results: 33 [18F]-FDG PET/CT from 21 patients, 4 Takayasu and 17 GCA, 9M/12F, mean age 61,2 years were available for analysis, 13 out of them had at least one CTA to compare (total 21 CTA). SUV max and SUV max/SUV liver ratio in LVV resulted statistically higher than controls (Mann-Whitney test respectively U= 21, p = 0.00001 and U=76, p=0.027). Linear correlation between SUV max and CRP resulted highly significant (Spearman: r= 0,51 p = 0,006) but also correlation for SUX max/SUV liver ratio resulted significant (Spearman: r = 0,47, p = 0,011). Applying a cut-off for SUV max/SUV liver >1,2 we found a statistically significant agreement with CRP (Mann-Whitney U=43 p =0.0015). Less correlation was found when [18F]-FDG PET/CT SUV was compared with contrast enhancement and vessel wall thickening of CTAs, probably, because of the increased vessel thickness remains even in the inactive disease stages.
Conclusion: Although further studies are expected, semi-quantitative [18F]-FDG PET/CT scoring methods and simple cut off scores based on TBR analysis seems to correlate with disease activity and they could be used in the clinical practice, together with inflammation indices and other radiological imaging techniques, to offer a reliable and repeatable tool to help clinicians in managing LVV.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0746 CHANGES IN DIAGNOSING GIANT CELL ARTERITIS OF THE TEMPORAL ARTERY OVER A 7.7 YEAR PERIOD

Keywords: Vasculitis, Imaging, Clinical trials

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Background: Temporal artery biopsy (TAB) was the diagnostic reference standard for decades in giant cell arteritis (GCA). Evidence-based EULAR recommendations regarding the use of imaging techniques in diagnosing GCA have been published in 2018 [1]. Accordingly, the use of colour Doppler ultrasonography (CDUS) should "complement the clinical criteria for diagnosing GCA, assuming high expertise and prompt availability of the imaging technique" [1]. However, sensitivity and specificity of CDUS showed substantial variation between studies (2), with the investigator's expertise assumed to be a major contributing factor [1].
Objectives: To study changes in the use of CDUS and TAB as diagnostic procedures for suspected GCA of the temporal artery over a period of 7.7 years in a single rheumatological centre.
Methods: Patients who presented to our rheumatological department between 10/2014 and 06/2022 were retrospectively identified either via a final diagnosis of GCA (ICD-10 codes M.31.4, M31.5, M31.6) or by the coded procedure of TAB (OPS 1-587.0 or 1-587.x). CDUS was performed by rheumatologists using GE Healthcare S5 machine from 2014 until spring 2016, and thereafter GE Healthcare LogiqE9 machine. A positive CDUS was defined by a non-compressible halo sign and hypoechogenic thickened vessel wall in any of the temporal arteries. We compared the frequency of use and results of CDUS and of TAB for confirming a clinical diagnosis of GCA of the temporal artery in three time periods of 2-3 years each (2014-2016, P1; 2017-2019, P2; 2020-2022, P3). Statistical significance of changes in relative frequencies was assessed via Fisher's exact test.
Results: Of 158 patients, we excluded 48 patients for the following reasons: diagnosis of aortitis or Takayasu vasculitis by other diagnostic means (n=16), final diagnosis other than GCA but undergoing TAB (n=24), already existing diagnosis of GCA with affection of the temporal artery prior to first presentation (n=7), and incomplete data sets (n=1). Of 110 GCA patients analysed, the mean age was 76.2 yrs (range 55 to 91 yrs), and 72 patients (65.5%) were female. All but one patient underwent CDUS (99.1%). Over the entire study period, the proportion of positive CDUS findings increased from 45.8% in P1 to 80.6% in P3. Conversely, the proportion of TAB evaluations decreased from 88% in P1 to 71.4% in P2 to 16.7 % in P3. In all three time periods, conducted TAB evaluations were largely positive: 77.3% in P1, 74.3% in P2, and 83.3% in P3 (Figure 1).

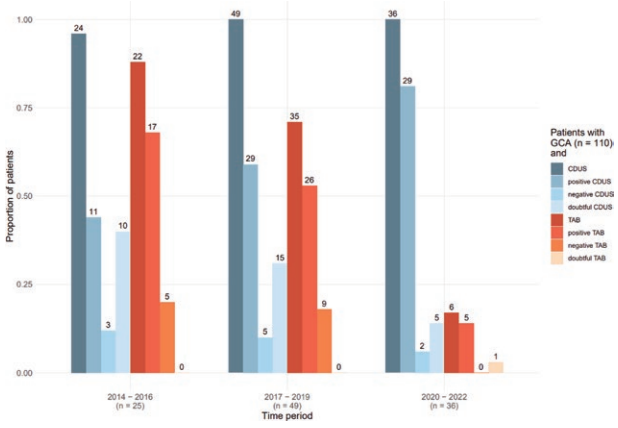


Figure 1.

In P3, 29 out of 36 (80.6%) GCA patients had a positive CDUS and were diagnosed based on CDUS alone, all of them without consecutive TAB. Only 6/36 patients (16.7%) underwent TAB: 5 patients received a positive TAB after doubtful CDUS, 1 patient received a doubtful TAB after negative CDUS. The proportion of patients who were diagnosed with GCA after positive CDUS and without TAB among all GCA-diagnosed patients that underwent CDUS of the temporal artery significantly increased when comparing P3 vs. P1 ($p<0.001$) and P3 vs. P2 ($p<0.001$), but not for P1 vs. P2 ($p=0.2$). Due to small sample size and involvement of several rheumatologists who gained experience in CDUS over the study period, an independent effect of exchanging the ultrasound machine could statistically not be assessed.
Conclusion: A significant change in using CDUS alone for diagnosing GCA of the temporal artery has taken place between 2014 and 2022, with substantial reduction of TAB evaluations especially after having obtained positive CDUS results. This change is likely due to increased expertise and confidence of the examiners (rheumatologists) in CDUS evaluations on appropriate ultrasound machines over time. Yet, data from the most recent time period indicate the ongoing need for TAB as an effective diagnostic tool in the few cases of inconclusive CDUS and high clinical suspicion of GCA.
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AB0747 NON-INFECTIOUS AORTITIS: CLINICAL AND HISTOLOGICAL CORRELATION

Keywords: Imaging, Vasculitis

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Background: Isolated aortitis is considered a single organ vasculitis in the latest 2012 International Chapel Hill Consensus Conference revision. Despite being an increasingly diagnosed condition thanks to imaging tests, given the difficulty in completing the histological study, it is frequently unknown whether it is an isolated entity or a clinical manifestation of other vasculitis or rheumatologic entities.
Objectives: To describe the histological findings in samples of inflammatory aortic aneurysms and correlate them with their clinical presentation.
Methods: A descriptive cross-sectional study was performed. Aortic biopsies from elective aortic aneurysm surgery performed at a university hospital from 2019 to 2021 were reviewed. The samples with a non-infectious inflammatory pattern were selected. Cases of aortitis secondary to infection and/or atherosclerosis were excluded. The samples were reviewed again by a pathologist specialized in vascular wall disease and classified according to the 2015 consensus on surgical pathology of the aorta of the Society for Cardiovascular Pathology and the European Association of Cardiovascular Diseases in granulomatous pattern, lymphoplasmacytic pattern and mixed inflammatory pattern. Likewise, the pathologist, taking into account the previous classification and the findings, assigned a diagnostic orientation, only taking into account the histological findings. Demographic, clinical, laboratory data and the diagnostic orientation of the rheumatologist were collected.
Results: Of the 116 aortic tissue samples reviewed, inflammatory findings were observed in 10 (9%) of the biopsies. Characteristics of the patients whose biopsies were included are shown in Table 1. 80% of the samples came from the proximal aorta, 10% from the aortic arch, and the remaining 10% from the abdominal aorta. The mean diameter of the aneurysm was 61.7 ± 21 millimeters. The rheumatologist's clinical diagnosis for the patients included was: 1 patient with Giant Cell Arteritis, 1 patient with Takayasu's disease, 1 patient with Behçet's disease, 1 patient with HLA-B27-associated spondyloarthropathy, and 6 patients with idiopathic aortitis. Histologically, 8 patients presented a lymphoplasmacytic pattern, 1 patient a granulomatous pattern, and 1 patient a mixed inflammatory pattern. The diagnostic orientation of the pathologist coincided with the clinician in 9/10 of the cases. The most frequent final diagnosis was nonspecific isolated aortitis (7/10), followed by Giant Cell Arteritis (1/10), Takayasu's arteritis (1/10) and Behçet's disease (1/10). There is a concordance between the histological pattern and the diagnostic orientation of the pathologist with the diagnostic orientation of the clinician in 9 of the 10 cases.
Conclusion: There is a high concordance between histopathologic and clinical diagnosis in the patients included in this study. Despite this, there is a high prevalence of non-specific aortitis, yet to be identified. Non-granulomatous lymphoplasmacytic pattern is the most reported in our series of cases.

Table 1. Demographic, clinical data, aortic parameters and other analytical results

Variables	N = 10
Male, n (%)	7 (70)
Age at diagnosis (years), median ± SD	69.4 ± 18
CV risk factors	
Smoking history	7 (70)
Diabetes	1 (10)
Dyslipidaemia	4 (40)
Arterial hypertension	4 (40)
Coronary Disease, n (%)	1 (10)
BMI (kg/m²), median ± SD	29.4±10.2
Treatment, n (%)	
Aspirin	1 (10)
Antihypertensive	5 (50)
Statins	4 (40)
Beta-blockers	3 (30)
Anticoagulant	1 (10)
Symptoms, n (%)	
Cranial symptoms	0 (0)
PMR	2 (20)
Constitutional symptoms	3 (30)
Thoracic pain	4 (40)
Analytical variables at baseline, median ± SD	
CRP (mg/L)	37.7±18.5
ESR (mm/h)	87.3±33
TG (mg/dL)	108.3±64
Cholesterol (mg/dL)	147.1±21
LDL (mg/dL)	95.8±24
HDL (mg/dL)	45.2±12

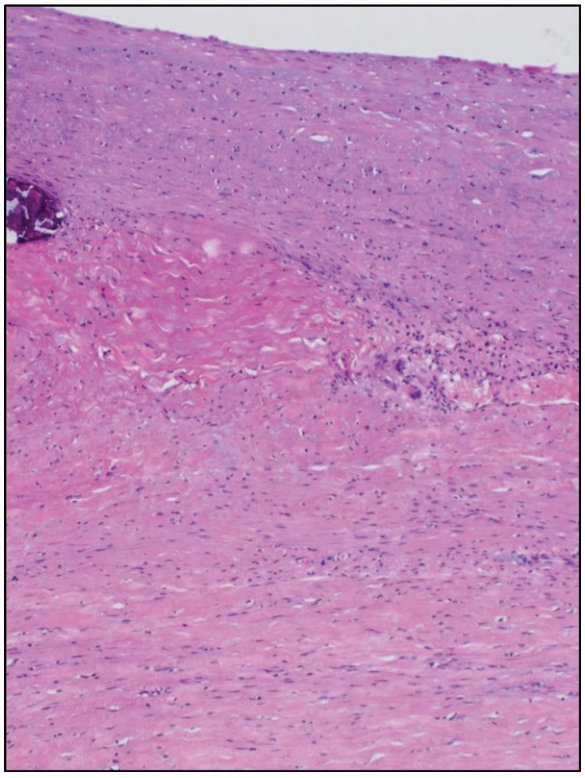


Image 1. Biopsy of the aorta: Complete scarring of the elastic fibres of the media layer with granulomatous inflammation and presence of giant cells. Intimal hyperplasia.

REFERENCES: NIL.
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AB0748 **COGNITIVE FUNCTION IN POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS**

Keywords: Vasculitis, Cognitive Function, Patient reported outcomes

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Background: In the past decade our understanding of the prevalence, and indeed impact of cognitive impairment in rheumatic diseases has increased.[1, 2] An aging population, coupled with systemic inflammation have been postulated as key drivers of increased cognitive decline in these conditions. Intact cognitive function is imperative not only for quality of life and maintenance of one's functional capacity, but also for the successful therapeutic management of disease, namely the adherence to treatment regimens. Both giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) occur in those over 50 years of age, and are associated with a significant systemic inflammatory response. [3] To date, the prevalence of cognitive impairment in these conditions has not been studied.
Objectives: To explore the prevalence and possible predictors of cognitive impairment in those with PMR and/or GCA.
Methods: Participants from a multicentre longitudinal cohort study of PMR and/or GCA participated in a study visit that included an assessment of cognitive function. Cognitive function was evaluated using the Montreal Cognitive Assessment (MoCA) test which was conducted by trained interviewers. Demographics, clinical and laboratory data related to disease activity (PMR-Activity Score), neuropsychiatric symptoms (DASS-21) and patient reported outcomes (Visual analogue scale (VAS) and health assessment questionnaire (HAQ-DI)) were collected. Cognitive impairment was defined by the previously validated MoCA cut-off score of <26. A two tailed t-test, and independent chi squared test were used to analyse continuous and categorical variables respectively. A multivariable linear regression analysis was then performed.
Results: A total of 55 participants with a mean age of 70.5 (SD 7.61) were suitable for inclusion. 29 (52.7%) were female. 29 (52.7%) had isolated PMR, 8 (14.5%) had subclinical GCA with PMR, and 18 (32%) had isolated GCA. 34

(61.8%) participants were cognitively impaired, with executive skills, verbal fluency and abstraction the most affected domains. Advancing age demonstrated a statistically significant association with cognitive impairment (OR 1.12, 95% CI 1.016- 1.233, p<0.05). Notably, our analyses did not show a statistically significant association between cognitive performance and gender, BMI, functional limitation, VAS scores, neuropsychiatric symptoms, serum interleukin-6 levels or disease activity scores. Moreover, there was no statistically significant increased risk of cognitive impairment in those with GCA/ subclinical GCA versus those with isolated PMR.

Table 1. Results

Variable	Cognitively Impaired (n=34)	Normal Cognition (n=21)
Mean Age (+/- SD)	72.29 (7.66)	67.62(6.73)
Female (n)	19	10
Mean BMI (+/- SD)	28.5 (5.65)	27.83 (5.39)
Mean VAS (+/-SD)	1.26 (1.76)	1.33 (1.93)
Mean HAQ-DI score (+/- SD)	0.223 (0.455)	0.2281 (0.359)
Mean PMR- AS (+/- SD)	1.987 (2.91)	2.46 (2.81)
Mean C-reactive protein levels (mg/L) (+/- SD)	5.16 (6.93)	7.76 (7.98)
Mean Erythrocyte sedimentation rate (mm/h) (+/- SD)	14.18 (16.98)	21.05 (18.97)
Mean serum Interleukin-6 levels (pg/ml) (+/- SD)	57.6 (23.1)	16.8 (23.1)

Conclusion: The findings of our study show for the first time that the prevalence of cognitive impairment in those with PMR and/or GCA is significant. We highlight the need to address cognitive health in those with PMR and/or GCA, both in clinical settings and also future large scale research.

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AB0749 FAST TRACK GIANT CELL ARTERITIS SERVICE IN A DISTRICT GENERAL HOSPITAL USING ULTRASOUND DOPPLER IMAGING

Keywords: Vasculitis, Ultrasound, Diagnostic tests

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Background: Giant Cell Arteritis (GCA) is the commonest large and medium artery vasculitis affecting patients aged 50 or above. It is a multisystem, inflammatory condition that can result in significant comorbidity, even mortality. Corticosteroids form the mainstay in remission induction and play a vital role in maintenance therapy. Complications can arise either due to delayed treatment, or unnecessary treatment of GCA mimics due to steroid side effects. This renders quick diagnosis a pivotal first step in its management. Temporal Artery Biopsy (TAB) has traditionally been the golden standard diagnostic modality, but it requires a surgical setting, resulting in delays. On the other hand, temporal artery Ultrasound Doppler Scan (USS) under an expert clinician has been incorporated by both BSR and EULAR in their recommendations. This offers a diagnostic tool with high specificity and sensitivity.

Objectives:

1. To set up a Fast Track GCA clinic and a referral pathway to allow timely diagnosis in an one-stop-shop outpatient (OPD) clinical setting with inhouse USS
2. To limit dependence of GCA diagnosis on TAB

Methods: We set up a weekly dedicated GCA OPD clinic at Eastbourne District General Hospital (EDGH) aiming to see patients within five days of referral. Upon review, patients were categorised to low, moderate or high GCA risk via a pretest probability score. Patients scoring high, moderate, or low but with diagnostic uncertainty, had temporal artery USS by an expert Rheumatologist on the day. We collected data on number of USS performed, scan outcomes, and TAB requests over a six-month period between May and December 2022.

Results: Total number of referred patients with suspected GCA was 50, 18 male and 32 female. Referral source was mainly via General Practice (GP) and Ophthalmology. Out of the 50 total, 49 had already been commenced on corticosteroids. All patients (100%) were seen within five days of the referral and had their pretest probability scores worked out in the clinic. Overall, 42 patients (84%) had USS and 6 (12%) were scanned within 72 hours of steroid commencement by the referrer. Eight patients (16%) were not scanned: six of them had very low probability score and were given alternative diagnoses without a diagnostic test; one was out of the window for diagnostics due to the timing of steroid commencement; one could not be scanned due to technical reasons, so a TAB was requested. Crucially, this was the only TAB requested during this period. GCA diagnosis was comfortably made for 21 out of the 42 patients scanned (50%). We ruled out GCA in the rest of the scanned patients (50%).

Conclusion: A pilot Fast Track clinic at EDGH facilitated prompt diagnosis of GCA with the use of USS. In a period of six months, we were able to confidently diagnose or rule out GCA in 100% of our scanned patients, without the need for a TAB. Such a set up enables prompt diagnosis of GCA and timely commencement of the appropriate steroid-weaning regimen, thus avoiding any future complications. Crucially, it allows the timely discontinuation of GP-commenced steroid therapy in patients with excluded GCA, thus minimising side effects of an unnecessary treatment. Typically, it takes more than three weeks to arrange a TAB. USS use also avoids an invasive procedure with potential for surgical complications. Additionally, from a Healthcare System point of view, there are certain cost-saving implications in using USS for GCA diagnosis. These range from reduced OPD clinic time and diminished demand for theatre slots and staff, to minimisation of future complications from timely commencement or discontinuation of steroid management. We also observed improved patient experience. This study confirms the integral role of USS in a Fast Track GCA Service.

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AB0750 PREGNANCY DURING TAKAYASU VASCULITIS: ABOUT 24 PREGNANCIES

Keywords: Vasculitis, Pregnancy and reproduction

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Background: TAKAYASU vasculitis is a vasculitis of the large trunks mainly affecting women of childbearing age. Pregnancy during TAKAYASU disease may be associated with maternal and/or materno-fetal complications as well as a flare-up of this vasculitis. Adequate management of TAKAYASU disease as well as regular monitoring of pregnancy is necessary.
in order to avoid these complications which can affect the maternal-fetal prognosis.

Methods: We conducted a descriptive, analytical and observational retrospective study, spanning 36 years (1984 -2020) at the internal medicine department of the UHC IBN SINA.102 patients are being followed up for Takayasu disease. We have listed the pregnancies carried out in patients during their follow-up for TAKAYASU disease.

Results: During their follow-up for TAKAYASU's disease;10 patients carried out 24 pregnancies. Their mean age was estimated at 31.78 ±12.2 years (16-51 years).2 patients had taking oral hormonal contraception. Hypertension is found in 5 patients at the time of diagnosis of TAKAYASU's disease. It was secondary to bilateral stenosis of the renal arteries in one patient. 53% pregnancies are carried to term without fetal complications in 5 patients with inactive TAKAYASU vasculitis during their pregnancies, 23% were complicated by fetal death in utero,15% termination of pregnancy (voluntary and therapeutic and spontaneous), and 12.5% growth retardation in utero. 3 (33%) patients presented with pre-eclampsia, and one (10%) patient presented with pregnancy-induced hypertension and another patient (10%)

had a hemorrhagic stroke. Only one premature delivery was performed in front of a fetal distress by caesarean section. The vaginal delivery was ensured in 45.83%, and the caesarean in 8.3%. Fetal extraction was performed vaginally for death feat in utero and pregnancy terminations. The pregnancy was responsible for a flare-up of TAKAYASU's vasculitis which went from an inactive status (NIH stage 1-2) to an active status (NIH stage 3-4) in 2/10 (20%) of the patients and was statistically linked to relapse with a significant p (p=0.009). TAKAYASU vasculitis type I was predominant (50%) followed by type V (30%).Statistical analysis showed a statistically significant link between pregnancy and carotid artery disease (P= 0.01). 8/10 patients (80%) were treated by corticosteroids and platelet aggregation inhibitor during 13/24 pregnancies (54.16%). Before the pregnancies, 7 patients had received immunosuppressive treatment such as methotrexate, cyclophosphamide in one patient and another was treated by adalumimab. Only 5 patients needed recourse to immunosuppressive therapy during their pregnancies (azathioprine). Statistical analyzes objectified a significant link between pregnancy and the use of azathioprine (p= 0.02). 4 patients received antihypertensive treatment; one patient had undergone vascular surgery for bilateral stenosis of the renal arteries.

Conclusion: TAKAYASU's vasculitis does not affect the fertility of patients with this disease. But a pregnancy carried out during the progressive form of this vasculitis can be responsible for serious maternal and fetal complications. Our study suggests links between pregnancy and relapse of TAKAYASU vasculitis, TAKAYASU's type I protective factor, and the interest of using azathioprine during pregnancies evolving on active TAKAYASU vasculitis.

We propose an internist-obstetrician collaboration in order to better manage this delicate medical situation on the maternal and fetal medical strategy.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0751 AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH GASTROINTESTINAL INVOLVEMENT OF BEHÇET SYNDROME

Keywords: Gastrointestinal tract, Behcet's disease, Spondyloarthritis

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Background: Despite attempts to lump Behçet syndrome (BS) with spondyloarthritides, controlled studies have shown that radiographic sacroiliitis is not increased in BS (BS). However, gastrointestinal involvement of Behçet syndrome (GIBS) shares common features with inflammatory bowel disease which, in turn, can be associated with spondyloarthritis.

Objectives: We wanted to test whether GIBS patients have an increased frequency of radiographic sacroiliitis or non-radiographic axial spondyloarthropathy (nr-AxSpA) compared to BS patients without major organ involvement who have only mucocutaneous and/or joint involvement.

Methods: We included 67 GIBS patients and 55 consecutive BS patients without major organ involvement. Patients were screened for axial spondyloarthritis (axSpA) using the Assessment of Spondyloarthritis International Society (ASAS) criteria. First they were questioned for chronic back pain, defined by ASAS as the presence of chronic back pain for more than 3 months with an age at onset of <45 years. Patients with chronic back pain were questioned for other spondyloarthritis features and underwent HLA-B27 testing, C-reactive protein testing, and X-ray and magnetic resonance imaging of the sacroiliac joints.

Results: Chronic back pain was reported by 24 (35%) GIBS patients and 16 (29%) BS patients without major organ involvement. Eight (12%) GIBS patients and 4 (7%) controls met ASAS criteria for axSpA (p=0.39). Four (6%) GIBS patients and 1 (2%) patient in the control group had radiographic axSpA (also termed ankylosing spondylitis), whereas 4 GIBS patients and 3 patients among the controls had nr-AxSpA. HLA B27 was positive in 2 (8%) of the GIBS patients and in 3 (19%) of the controls (p=0.33) (Table 1).

Conclusion: There was some, statistically insignificant increase in the frequency of axSpA among the GIBS patients. While the frequency of ankylosing spondylitis was consistent with previous studies, the frequency of axSpA according to the more recent ASAS criteria was found in 9.8% of the total group of BS patients. To the best of our knowledge ASAS criteria have not previously been tested in BS. They, perhaps need to be studied in a larger group of BS patients, including those with acne associated arthritis- previously shown to be associated with enthesitis (1) - together with healthy and diseased controls.

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Table 1. Demographics and characteristics of the patients

	GIBS (n=67)	BS without major organ involvement (n=55)
Male	36 (54%)	20 (36%)
Mean age	45 ±12	40 ± 13
AxSpA according to ASAS criteria	8 (12%)	4 (7%)
Clinical arm	2	2
Imaging arm	6	2
Chronic back pain	24 (35%)	16 (29%)
Inflammatory back pain	13 (19%)	10 (18%)
SpA features among patients with chronic back pain		
Inflammatory back pain	13 (54%)	10 (62.5%)
HLA-B27	2 (8%)	3 (19%)
Arthritis	11 (46%)	6 (37.5%)
Enthesitis	9 (37.5%)	5 (31%)
Dactylitis	2	0
Psoriasis	1	0
Good response to NSAID	16 (67%)	9 (56%)
Family history for SpA	2	4
Elevated CRP	6	1

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Disclosure of Interests: None Declared.

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AB0752 REMAINING UNMET NEEDS FOR THE TREATMENT AND MANAGEMENT OF GIANT CELL ARTERITIS

Keywords: bDMARD, Vasculitis, Disease-modifying drugs (DMARDs)

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Background: Rheumatologists face significant challenges in the management of giant cell arteritis (GCA), with a limited armamentarium of treatment options. Physicians are largely dependent on the use of glucocorticoids, with tocilizumab being the only available advanced systemic agent for the treatment of giant cell arteritis.

Methods: An independent market analytics firm collaborated with 102 US rheumatologists to conduct an analysis of the GCA market. Data were collected via an online survey and supplemented with 8 qualitative interviews, all fielded June 16 through July 13, 2022. Research stimuli included physician demographics, patient management, use and perceptions of current treatments, as well as perceptions of potential new assets in development for GCA.

Results: The desire to minimize use of glucocorticoids is currently the greatest treatment challenge in the management of GCA. Although rheumatologists recognize the benefits of initiating newly diagnosed patients on glucocorticoids for the prevention of disease progression, including blindness caused by GCA, the negative side effects caused by long-term use gives physicians concern. While tocilizumab is used in patients with and without cerebral or ocular symptoms, most rheumatologists still rely heavily on the use of glucocorticoids, accounting for 89% of patient prescriptions in GCA, an aspect largely driven by a lack of availability for other advanced therapies. Of patients prescribed tocilizumab, 65% of patients were initiated on the drug in combination with glucocorticoids. Interviewed prescribers indicate difficulty in tapering glucocorticoids for patients on combination therapy, aiding in the desire for more steroid-sparing treatment options.

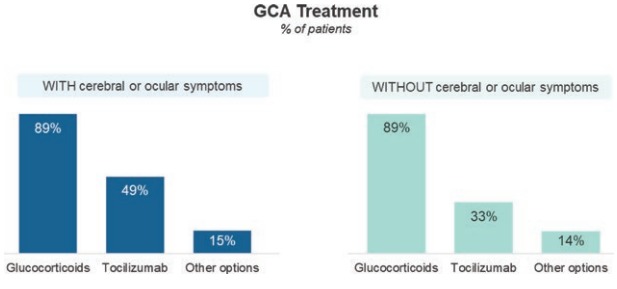


Figure 1.

Rheumatologists are excited to see new agents in development for GCA. Preference is highest for an IL-17A inhibitor, making secukinumab the leading drug of interest. Physicians also perceive secukinumab to be more of an advance over tocilizumab than upadacitinib or guselkumab.

Table 1. Product Profile Perceptions

	Considered an advance in treatment *% of respondents*	Strong level of interest *% of respondents*	% of GCA patients considered candidates
Secukinumab	52%	58%	29%
Guselkumab	42%	44%	26%
Upadacitinib	44%	41%	25%

Conclusion: With rheumatologists continuing to use tocilizumab in GCA, there is still a high need to reduce the use of steroids and for new mechanisms of actions to become available for this patient population. Physicians are eager to expand the current GCA armamentarium and anticipate these potential new agents to make have a positive impact on their management of GCA.

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[1] Kara Murray, Emily Hettel and Maxine Yarnall are employees of Spherix Global Insights, an independent market intelligence firm, and have received no industry funding to conduct and report on this study.

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Disclosure of Interests: None Declared.

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AB0753 EFFICACY AND SAFETY OF TOCILIZUMAB IN PATIENTS WITH VASCULITIS

Keywords: Systematic review, bDMARD, Vasculitis

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Background: Vasculitis is characterized by inflammation of blood vessels, leading to potential long-term sequelae, including vision loss, aneurysm formation, and kidney failure. Large vessel vasculitis encompasses Takayasu arteritis and giant cell arteritis, which cause inflammation of the aorta and its major branches. Tocilizumab, a humanized monoclonal antibody against the interleukin-6 receptor, has been associated with rapid induction and maintenance of remission in patients with vasculitis.

Objectives: This study aimed to systematically evaluate the efficacy and safety of tocilizumab therapy in vasculitis.

Methods: Eight databases (PubMed, Web of Science, Embase, Cochrane Library, Web of Knowledge, MEDLINE, Clinical Trials.gov, and FDA.gov) were searched for studies on tocilizumab treatment of vasculitis published from the date of establishment of the database to January 1, 2023. We used Stata 12.0 software to conduct a meta-analysis of the efficacy and safety of tocilizumab in patients with vasculitis using a random effect model.

Results: A total of 8 studies with a total of 823 patients were included. Either doses 162mg/week or 8mg/kg/4weeks, compared with placebo, tocilizumab significantly both promoted remission of vasculitis(RR=0.909, 95%CI: 0.768-1.075, P<0.001; RR=0.639, 95%CI: 0.410-0.994, P<0.042)(Figure 1A). No significant difference was observed in the probability of disease relapse in subgroup analysis based on different diseases(Figure 1B). In subgroup analysis based on dose, 8mg/kg/4 weeks doses significantly reduced the probability of disease relapse (RR=0.639, 95% CI: 0.410-0.994, P=0.047)(Figure 1C). The results of subgroup analysis about the rate of adverse events (AE) and serious adverse events (SAE) according to different diseases and different doses, our meta-analysis found that there was no statistical significance between tocilizumab and placebo(Figure 1E-H). It demonstrated the safety of tocilizumab therapy in vasculitis treatment.

Conclusion: Tocilizumab treatment was effective and well-tolerated in vasculitis patients.

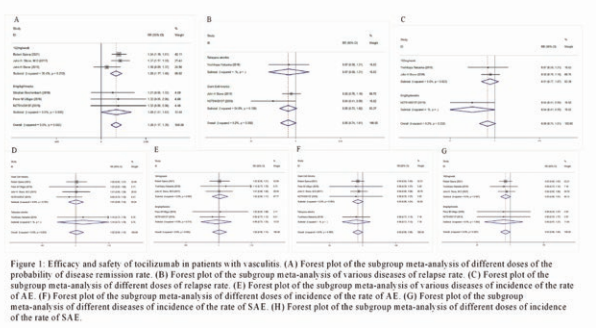


Figure 1. Efficacy and safety of tocilizumab in patients with vasculitis. (A) Forest plot of the subgroup meta-analysis of different doses of the probability of disease remission rate. (B) Forest plot of the subgroup meta-analysis of various diseases of relapse rate. (C) Forest plot of the subgroup meta-analysis of different doses of relapse rate. (E) Forest plot of the subgroup meta-analysis of various diseases of incidence of the rate of AE. (F) Forest plot of the subgroup meta-analysis of different doses of incidence of the rate of AE. (G) Forest plot of the subgroup meta-analysis of different diseases of incidence of the rate of SAE. (H) Forest plot of the subgroup meta-analysis of different doses of incidence of the rate of SAE.

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Disclosure of Interests: None Declared.

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AB0754 CLUSTER ANALYSIS OF ARTERIES INVOLVED IN TAKAYASU ARTERITIS

Keywords: Vasculitis

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Background: Takayasu's arteritis (TAK) is a chronic, large-vessel vasculitis that mostly affects young Asian women[1-4]. Vascular inflammation in TAK primarily invades the aorta and its major branches and often leads to arterial stenosis and aneurysms. At present, there is no relevant research report on how to identify the vascular lesions of organs in the early stage and the relationship between the affected vessels.

Objectives: To investigate the correlation of arterial involvement sites in Takayasu arteritis.

Methods: We retrospectively investigated data of 144 TAK patients. The clinical and image data of the patients were analyzed. We performed cluster analysis according to the affected artery.

Results: cluster analysis revealed five clusters of patients. In cluster one was named "abdominal aortic type". It was characterized by the involvement of arteries in the abdominal aorta, renal artery, coeliac trunk, superior mesenteric artery. In cluster two was named "cardio-cerebral arteries type". It was characterized by the involvement of arteries in the intracranial artery, coronary artery. In cluster three was named "thoracic aorta type". It was characterized by the involvement of arteries in the thoracic aorta and pulmonary artery was observed. In cluster four was named "vertebral artery type". It was characterized by the involvement of arteries in the left vertebral artery, right vertebral artery. In cluster five was named "carotid artery type". It was characterized by the involvement of arteries in the right common carotid artery, left common carotid artery, right subclavian artery, left subclavian artery, innominate artery.

Conclusion: Cluster analysis of the involved sites of Takayasu arteritis could be divided into 5 categories. It is abdominal aortic type, cardio-cerebral arteries type, thoracic aorta type, vertebral artery type and carotid artery type.

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AB0755

INVESTIGATING CYTOGLOBIN IN GIANT CELL ARTERITIS: ITS ROLE IN THE PATHOGENESIS AND POTENTIAL AS A BIOMARKER

Keywords: Diagnostic tests, Biomarkers, Vasculitis

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Background: Cytoglobin (CYBG) is a non-erythroid globin that is found in medial smooth muscle cells (SMCs) of human vessels. Recent studies have postulated that CYGB act as a pro-survival factor during conditions associated with increased oxidative stress, by upregulating anti-apoptotic factors and antioxidant pathways. In this study, we hypothesized that CYGB regulates the inflammatory and antioxidant response associated with GCA pathogenesis.
Objectives: The purpose of this study is to evaluate giant cell arteritis (GCA) vascular lesions for the expression of CYGB and its association with specific molecular markers of cellular damage. We would also like to investigate the association of CYGB with GCA pathogenesis, symptomatology, degree of systemic inflammation, patient demographics, and response to treatment.
Methods: We obtained 29 temporal artery biopsy samples, 14-biopsy positive and 15-biopsy negative, from patients who underwent temporal artery biopsy for GCA diagnosis **(Table 1)**. Inclusion criteria for the experimental group included patients over the age of 18 who had histologic evidence of GCA and met the ACR 1990 classification criteria. The control group included patients who were biopsy negative for GCA. Immunofluorescence staining for CYGB will be done on all samples to assess differential expression across the experimental and control groups. Proximity ligation assays (PLA) will be done to assess binding between cytoglobin and known pro-inflammatory markers to establish mechanistic insights for CYGB in the pathogenesis of GCA. We will also obtain clinical data including signs and symptoms at presentation, levels of serum inflammatory markers, treatment, clinical course, and outcomes.
Results: We are currently conducting validation studies of the immunofluorescence and PLA staining for specific molecular markers on temporal artery biopsy samples. Thus far, we were able to validate the immunofluorescence staining for CYGB **(Figure 1)** and the PLA for CYGB and HMGB2. Once we have established robust and reliable staining protocols for other markers, we will implement these protocols in our control and GCA groups and move forward with the analysis.
Conclusion: We previously demonstrated that overexpressing CYGB in human cardiac stem/progenitor cells (HCPCS) led to an increase in cell survival in response to oxidative stress. Whereas, silencing of CYGB in these cells, increased the rate of cell death. Similarly in rat and mouse models, it was found that CYGB contributes to vascular remodeling following injury, and the absence of CYGB led to accelerated cell death and inhibition of neointima formation. Based on these studies, we hypothesized that CYGB may play a role in the pathogenesis of different vasculitis including GCA. Once we develop this correlation, we will use this data to identify cellular and serum markers for the diagnosis of GCA. [1,2]

Table 1. Demographic and clinical features of patients who underwent temporal artery biopsy

DIAGNOSIS	GCA, 14	Non-GCA, 15
Sex (F/M)	11 F/3 M	9 F/6 M
Age (avg. years)	77.1	73.1
Ethnicity		
Caucasian	13	14
African American	0	1
Asian	1	0
CLINICAL FEAUTURES		
Abnormal visual changes	12	5
New Onset Headaches	9	8
Temporal Tenderness	4	5
Jaw Claudication	3	1
Fever (◦C)	14	1
PMR symptoms	1	0
Initial CRP (Avg.)(<8.0mg/L)	46.2	43.7
ESR (Avg.)(0-25 mm/h)	57	40.4
THERAPY		
Steroid therapy	13	5
Tocilizumab therapy	5	0
Methotrexate therapy	1	2

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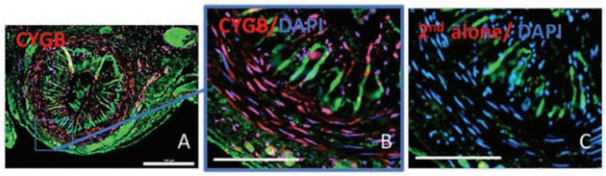


Figure 1. Validation of the immunofluorescence staining for cytoglobin (CYGB) on temporal artery biopsy specimen

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0756

IDENTIFICATION OF HISTOPATHOLOGIC FINDINGS OF PATIENTS WITH GIANT CELL ARTERITIS: A MULTICENTRE STUDY IN THE ERA OF 2022 ACR/ EULAR CLASSIFICATION CRITERIA FOR GCA

Keywords: Diagnostic tests, Validation, Vasculitis

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Background: Although temporal artery biopsy (TAB) is the gold standard in the diagnosis of giant cell arteritis (GCA), the specific histopathological findings and their relationship with clinical diagnosis have not been well discussed. In recent 2022 ACR/EULAR GCA classification criteria, the presence of giant cells, predominantly mononuclear cell infiltration, and fragmentation in the internal elastic lamina have been defined for the interpretation of definitive vasculitis. [1]
Objectives: To re-evaluate TAB histopathological findings of patients with GCA recruited from 4 tertiary centres in Ankara according to the2022 ACR/EULAR Classification criteria and compare frequencies of these items with DCVAS study [2].
Methods: TAB reports of patients with GCA from 4 tertiary centres between March 2004 and February 2022 were retrospectively reviewed according to the histopathological items defined in the updated criteria. TAB reports were classified by the local physicians as normal, nondiagnostic, consistent with vasculitis but not definite, and definite vasculitis.
Results: Totally, TAB histopathologic reports of 88 patients with GCA were reviewed. The mean age of the patients at the time of TAB was 69.7(±8.5) years and 46(52.2%) were female. Twenty-eight reports without microscopic details were excluded and reports of 60 patients were reanalysed. Of the 60 patients,

46 (76.6%) met one of the defined histopathological findings of updated criteria (Figure 1). Histopathological findings of all patients with microscopic findings were detailed in the Table 1. 17(28.3%) patients had at least two histopathological findings.

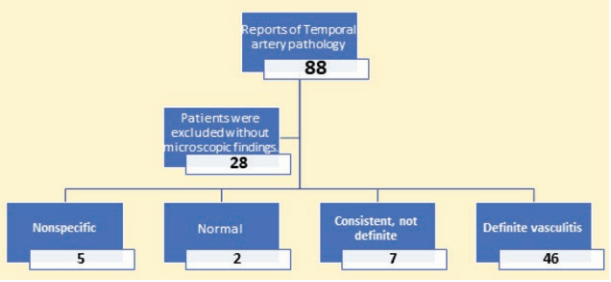


Figure 1.

Table 1. Specific histopathological findings of patients who underwent biopsy with a preliminary diagnosis of giant cell arteritis

Demographic and Histopathologic findings	DCVAS (n=705)	Our study (n=60)
Mean age,SD	73.5 ± (8.5)	69.7(±8.5)
Sex, female	**455(65)**	**46(52.2)**
Giant cells,n(%)	303(51)	18(30)
Internal elastic lamina fragmentation, n(%)	242(41)	22(36.6)
Mononuclear leukocytes (no definition of intimal/adventitial), n(%)	198193(32)	26(43.3)
Intimal thickening, n(%)	198(33)	21(35)
At least one of the defined histopathologic findings for definitive vasculitis *		46(76.6)
>=2 defined histopathologic findings for definitive vasculitis*		17(28.3%)
Vascular thrombosis, n(%)	26(4)	2(3.3)
Granuloma, n(%)	23(4)	1(1.6)
Perivascular inflammation only, n(%)	8(2)	-
Medial calcinosis, n(%)	NA	5(8.3)
Myxoid degeneration, n(%)	NA	6(10)
Adventitial mononuclear infiltration, n(%)	NA	3(5)

NA: Not applicable* defined histopathologic features are giant cells, predominantly mononuclear cell infiltration, and fragmentation in the internal elastic lamina for definitive vasculitis

Conclusion: Even giant cells were reported less in our study, updated histopathological definitions for GCA seem an excellent option to diagnose vasculitis definitively.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0757 TAKAYASU DISEASE: ABOUT 109 CASES

Keywords: Vasculitis

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Background: TAKAYASU disease is an inflammatory vasculitis of the means and large caliber, which affects th aorta and its main branches, and which leads to the formation of arterial stenosis, thromboses and aneurysms. Touching preferably young women, it may be responsible for complications severe visceral events that may be life-threatening.

Methods: We conducted a 38-year, single-centric retrospective study (1984 and 2022) in patients followed for TAKAYASU vasculitis at the department of internal medicine and the department of vascular surgery of the Ibn Sina Hospital in Rabat. Statistical data were analyzed using SPSS 20. 0 software and KHI- DEUX analytical test.

Results: We collected 109 files. The sex ratio (F/M) was 7. 3 (96 women/ 13 men). 11. 92% of patients were male. The mean age was 34. 8 ±11. 9 (12 – 62 years). Patients who had juvenile takayasu diagnosed before 20 years of age were 11 (10%) and patients who had late-diagnosed takayasu to over 50 years of age were 14 (12. 88%). HTA was present in 44 (40. 7%) of patients at diagnosis, 11 (10. 1) of patients were taking oral contraceptives. Inflammatory syndrome was associated in 72 (66. 1%) with no statistically significant difference with a P=0. 6. Vascular symptomatology was present in 103 (95. 4%) of the cases o vascular murmur (66. 1%), pulse suppression (62. 4%), intermittent claudication (49. 5%) and ischemia (10. 1%). Extravascular symptoms were present in 47. 6% of the patients dominated by inflammatory arthralgia (18. 3%). Only one patient had asymptomatic TAKAYASU vasculitis discovered by chance during ultrasound examination for a thyroid nodule. Cardiac involvement occurred in 36 (33%) of patients and consisted mainly of valvulopathy (20. 2%) and cardiomyopathy (17. 4%). Central neurological involvement was present in 17 patients. (15. 6%) of patients with complicated HAI in 13 patients. Renal impairment was present in 35 patients (32. 11%). Ophthalmologic involvement in 26 (23. 9%) of patients was mainly represented by retinal vasculitis and optic nerve involvement. In addition, 10 patients had 24 pregnancies, 4 patients had preeclampsia, we recorded 9 abortions and half of our patients had full term pregnancies. The type of injury in our series was mainly stenosis and was found in 73 (67%) of cases. Occlusion was recovered in 21 (19. 3%) patients. Thrombosis was found in 26 (23. 9%) of patients and aneurysms in 19 (17. 4%) of patients. TAKAYASU vasculitis was Type I in 42 (38. 5%) patients, followed by Type V in 39 (35. 8%). Type IIa was present in 7 patients (6. 4%), type IIb in 4 patients (3. 7%), type III in 2 patients (1. 8%), and type IV in 14 patients (12. 8%). Most patients 104 (95. 4%) received corticosteroids and 77 (70. 6%) received immunosuppressive therapy including one on mycophenolate mofetil. 2 patients received anti-TNF therapy (adalimumab) and 1 patient received Tocilizumab. At the surgical level; 9 (8. 3%) of patients had angioplasty; A further 6 (8. 3%) underwent cardiac surgery (5 aortic valve replacement and closed-heart commissurotomy) and 15 (13. 8%) had vascular surgery. The outcome was favourable in the majority of patients. Late relapses > 6 months were reported in 25 (23. 1%) patients. There was only one death from global heart failure. We analyzed several associations such as vascular and cardiac disease, vascular and neurological disease. None returned significant with P ranging from 0. 3 to 1.

Conclusion: The results of our study are consistent with the literature and confirm the predominance of women and the stenosing nature of this vasculitis. Early diagnosis and management of the disease significantly improves the progression profile of the disease.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0758 TAKAYASU DISEASE IN JUVENILE FORM: ABOUT 11 CASES

Keywords: Vasculitis

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Background: Takayasu disease is a non-specific inflammatory vasculitis of the large and medium caliber arteries occurring during the 2nd or 3rd decade. Attachment before the age of 20 is rare.

Methods: This is a retrospective descriptive study including patients with aged less than 20 years with Takayasu disease out of a series of 109 patients between 1984 and 2022 in a department of internal medicine and vascular surgery at the CHU INB SINA of Rabat.

Results: We identified 11 cases of patients under 20 years of age with a Takayasu disease with a sex ratio of 1 man to 2. 6 woman (8 women/ 3 men) The mean age of patients was 17 years ±2. 8 (12 - 20 years). (45. 5%) had hypertension at diagnosis, 10 patients (90. 9%) had symptomatology type of vascular murmur (54. 5. %), pulse suppression (63. 6%), lameness. intermittent (36. 4%), no ischemia (23. 1%) and one patient had extravascular: headache, fever, altered general condition... Inflammatory syndrome was present at diagnosis in 8 of our patients (72. 7%) Aortic involvement was found in 7 patients (63. 63%) predominantly due to abdominal aorta (6 patients). We identified 4 cases (36. 36. %) of arterial damage. 3 cases of cerebral arteries (27. 27%). The most common arterial disorders stenosis (72. 7%), thickening (54. 5%), thrombosis (9. 1%) and aneurysm (9. 1%). 6 patients (54. 54%) had heart disease as part of the study. Takayasu disease dominated by cardiomyopathies (4 cases), 2 cases of valvulopathy, and 1 only case of pericarditis. Associated in two cases with rhythm disturbances. 3 patients

(27. 28%) had stroke-type neurological disease, which accounted for 18. 75% of cases (16 cases/109 cases) in the global series and 3 patients had (27. 3%) two cases of blindness and one case of optic nerve damage. TAKAYASU vasculitis was type V in 5 patients (45. 5%), followed by type I in 4 patients (36. 4%). Type II and IV were present in 1 patient each; type I and IV have not been described in any of the patients. All patients received corticosteroid therapy, 9 patients (81. 8%) were initiated immunosuppressant and one patient received adalimumab, five of the patients received a. angioplasty and/ or one or more vascular surgeries, two complicated cases of restenosis. stunt artery and 1 complicated case of aorto-abdominal fistula. Four patients (45. 5%) had. had one or more relapses during their evolution. We also noted a case of tuberculosis meningoencephalitis associated with bilateral blindness in a 16-year-old patient and. two concepts of coarctation of the non-dilated aorta in a 12-year-old patient and in a. 18-year-old patient.

Conclusion: Our study is consistent with the literature and illustrates the seriousness of the juvenile takayasu as the common combination with severe heart disease, neurological and ophthalmological.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0759 CAN GLUCOCORTICOIDS WITHDRAWAL REPRESENT A CHALLENGE IN BEHÇET'S DISEASE? A CATEGORICAL DATA ANALYSIS IN A MONOCENTRIC COHORT

Keywords: Behcet's disease

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Background: When active manifestations occur in Behçet's disease (BD), systemic glucocorticoids (GCs) are essential to induce remission. Scarce evidence is available about how frequently GCs are used in the long-term as well as the reason of their withdrawal-failure.

Objectives: The aims of the study were: i) to characterize the profile of BD patients taking GCs at the last evaluation, including the reasons behind the withdrawal-failure and ii) to compare their profile with patients not taking GCs.

Methods: One-hundred patients regularly followed-up for at least 24 months were consecutively enrolled. Demographic, clinical and therapeutic data was collected, including GC assumption, daily dosage, and duration; patients were identified as GCs + or GCs -. A categorical data analysis was performed to explore the reasons of non-withdrawal in GCs+ group: recent BD relapse, inability to reduce current dosage for disease recurrence, and steroid addiction (meant as occurrence of manifestations non-BD-related).

Results: GCs+ group included 40 patients, while 60 patients were GCs- at the last evaluation. Both groups were mainly represented by females (75% GCs+, 62% GCs-). Overall mean age was 49 years and disease duration was most commonly 3–10 years. GCs+ group showed higher rates of colchicine and immunosuppressive therapy, while no significant differences were observed in terms of organ involvement. In the GCs+ group 32 patients (80%) assumed a daily prednisone equivalent dose ≤ 5 mg, because of recent relapse in 30% of cases, disease recurrence at tapering in 30% and steroid addiction in 40%. The mean cumulative GC duration in the last 2 years in GCs+ and GCs- patients was 17.3 and 1.8 months, respectively.

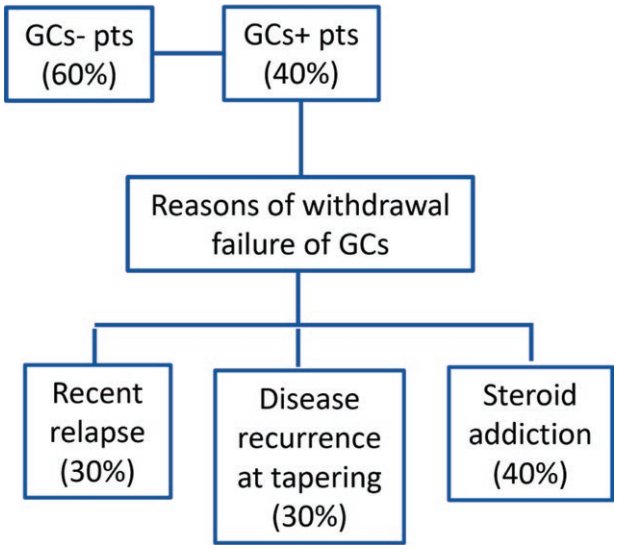


Figure 1.

Conclusion: Despite a similar control of disease activity, the main reason for GCs assumption seems to be represented by the occurrence of manifestations non-BD-related. Such acknowledgement highlights the need to improve the therapeutic approach in BD patients allowing stable steroid discontinuation, as well as stable disease remission.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0760 EVOLUTION OF PATIENTS WITH GIANT CELL ARTERITIS: BEFORE AND AFTER THE BIOLOGICAL ERA

Keywords: bDMARD, Vasculitis

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Background: Giant cell arteritis (GCA) is the most common form of systemic vasculitis. The standard treatment to induce and maintain remission of GCA is based on the use of glucocorticoids (GC), often requiring high doses and for long periods of time. It has been associated with adverse events, sometimes severe, in up to 95% of cases (fractures, diabetes mellitus, hypertension, sepsis). In 2017, the first specific drug for this entity, tocilizumab (TCZ), an anti-IL-6 antibody, was approved. To date, there are few communications in clinical practice comparing the classical treatment scheme with the use of TCZ early.

Objectives: To compare patients treated with the standard regimen (corticosteroid monotherapy) versus those treated early with TCZ, in terms of the dose of corticosteroid received, use of immunosuppressants, and adverse events.

Methods: A retrospective observational study was carried out. Patients diagnosed with GCA in the Rheumatology section of the HGU Dr. Balmis during the period January 1, 2011, to November 1, 2021, were selected. Until 2017, patients received the standard regimen (corticosteroid monotherapy); from 2017, TCZ was associated early. Demographic data, treatment data (prednisone doses at months 1,3,6,12,18 and 24; use of immunosuppressants), and adverse events were collected. A descriptive analysis of the different variables was performed. The $\chi 2$ test or Fisher's exact test was used for the association between qualitative variables. For quantitative variables, mean comparison was performed using the t-student test.

Results: We obtained 73 patients (37% male and 63% female) with a mean age at diagnosis of 74.47 ± 8.4 years. All received initial corticosteroid treatment; 28 were also administered early TCZ (38.4%), the preferred route being subcutaneous (96.4%). The time between diagnosis and initiation of steroid treatment was a median of 0 days (median, IC 0-0), being 60 days for TCZ (IC 30-97). The use of immunosuppressants was higher in the glucocorticoid-only group than in the group treated with TCZ (57.8% vs. 21.4%, p=0.002). Prednisone dose was higher in the standard group at all follow-up time points (p<0.001). No differences were found in the occurrence of adverse events, except infections, which were more frequent in the standard treatment group (standard 28.9% vs TCZ 3.6%, p=0.008).

Conclusion: Tocilizumab allows a greater and faster reduction of corticosteroids, compared to standard corticosteroid monotherapy, lower use of other immunosuppressants, and is associated with a lower frequency of infections.

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Vasculitis - small vessel vasculitis

AB0761 **MULTICENTRIC SPANISH ANALYSIS OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS PATIENTS TREATED WITH MEPOLIZUMAB**

Keywords: bDMARD, Vasculitis

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Background: inophilic granulomatosis with polyangiitis (EGPA), formerly called Churg-Strauss syndrome, is an ANCA-associated vasculitis which is mainly mediated by eosinophils. Mepolizumab (MPZ) is an anti-interleukin-5 monoclonal antibody that reduces the total number of eosinophils in peripheral blood and tissues, and its use has been approved in EGPA.
Objectives: To analyze the effectiveness and safety of MPZ in EGPA in a real life multicenter Spanish cohort.
Methods: We retrospectively analyzed the epidemiological data, comorbidities, clinical evolution and adverse effects of patients who have received MPZ in 13 Rheumatology Spanish services, through electronic medical records up to November 2022.
Results: A total of 27 patients with EGPA treated with MPZ have been analyzed. Median age at diagnosis was 53 years old, fifteen were men (55.6%), 21(77.8%) were Caucasian, 5 (18.5%) Arabic and 1 Hispanic. At diagnosis, 3 (11.1%) patients had arterial hypertension and 4 dyslipidemia (14.8%); ten patients were or had been smokers (37%). A total of 14 (51.8%) patients were ANCA positive. The Five Factor Score (FFS) was calculated just in 20 patients, and from them, 14 had a 0 result (70%) and 6 a 1 result (30%); the mean Birmingham Vasculitis Activity Score (BVAS) at diagnosis was 15. EULAR severity index was 0 in 2 patients (7.7%), 1 in 10 patients (38.5%), 2 in 9 (34.6%) and 3 in 5 patients (19.2%). Up to 23 patients (85.2%) had rhinosinusal symptoms and 19 (70.4%), had lung involvement of which 16 patients had interstitial lung disease. Sixteen (59.3%) patients had general symptoms 14 (51.9%) skin involvement and 11 (40.7%) peripheral nervous system involvement. Nine (33.3%) patients had musculoskeletal symptoms, 5 eye involvement and 5 cardiac involvement (18.5%). Regarding treatments, the mean starting dose of daily prednisone was 45 mg, 9 patients received intravenous methylprednisolone pulses (33.3%) and 16 (59.3%) required an immunosuppressant for induction, of which in 11 it was cyclophosphamide. The mean disease duration of the EGPA when MPZ was started was 51 months, and the mean follow-up during the treatment with MPZ was 16 months. The mean Birmingham Vasculitis Activity Score (BVAS) before MPZ was 9, after one month of MPZ, it dropped down to 5.4, and three months later to 4.6. The mean C reactive protein (CRP) before treatment with MPZ was 19.9 mg/L, and three months later, it was 3.3 mg/L. Before MPZ, the patients had a mean eosinophils number per microliter of 753, and after three months of treatment, it was 59 eos/µL. The mean Vasculitis Damage Index (VDI) before treatment with MPZ was 4.5 and after treatment with mepolizumab, it worsened only in 3 patients (11.1%). Twenty patients achieved a 50% clinical response according to global physician criteria (74.1%) and 12 achieved clinical remission (44.4%). The mean final prednisone dose was 2.5 mg/d. No patients had serious infections during treatment, one developed a neoplasm, and one of them withdrew MPZ due to musculoskeletal pain, switching to benralizumab (anti-IL5-receptor). Only one patient died from causes unrelated to the drug or the disease.
Conclusion: Our data about the use of MPZ in EGPA in real world practice suggest that is a quite effective and safe drug, allowing to save corticosteroids. Moreover, it seems to prevent the progression of the damage associated with the disease.

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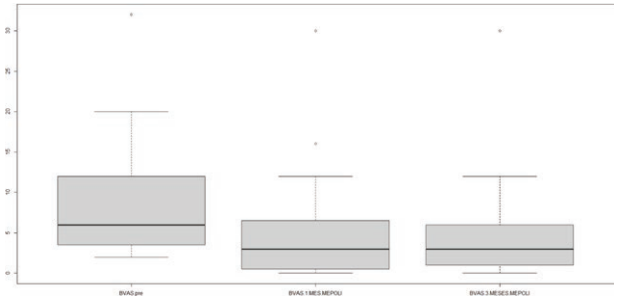


Figure.

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1044

AB0762 **DIAGNOSTIC YIELD OF BIOPSIES IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS: A SINGLE CENTRE EXPERIENCE**

Keywords: Descriptive Studies, Diagnostic Tests, Vasculitis

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Background: Recently published classification criteria for eosinophilic granulomatosis with polyangiitis (EGPA) [1] require, to be applied, a diagnosis of small- or medium-vessel vasculitis, without specifying how that diagnosis should be made. Histologically, EGPA is characterized by eosinophil-rich and necrotizing granulomatous inflammation together with necrotizing vasculitis, predominantly affecting small to medium vessels. Some of these features are not specific for EGPA and may be seen in other forms of ANCA associated vasculitis (AAV). Current guidelines on the management of AAV recommend biopsies to assist in establishing a new diagnosis and for further evaluation of patients with suspected relapse [2]. Therefore, biopsies are essential tools for the diagnosis, classification and management of these diseases.
Objectives: To describe the histopathological findings, diagnostic yield and the most common localizations of biopsies performed to assist in the diagnosis and follow-up of patients with EGPA.
Methods: Medical charts of patients with EGPA regularly followed at our department were reviewed to retrieve the number and localization of biopsies, as well as biopsy findings including proportion of a) eosinophil-rich extravascular inflammation, b) granulomas and/or c) necrotizing vasculitis. Biopsies were performed if patients presented symptoms in any given and most accessible localization (at diagnosis) or if they were necessary to confirm active disease (during follow-up).
Results: Among 59 EGPA patients regularly controlled at our department, a total of 163 biopsies were performed on 54 of them. In 44 patients (81.5%), 89 biopsies were performed at diagnosis and in 27 (50%), 74 biopsies were performed during follow-up. A total of 37 biopsies in 26 patients (48.1%) had proven vasculitis. A total of 7 biopsies in 5 patients (9.3%) had proven granuloma. A total of 87 biopsies in 42 patients (77.8%) had proven eosinophil-rich extravascular inflammation. The main localizations were: ear, nose and throat (ENT, 49 biopsies), respiratory (31), skin (25), gastrointestinal (GI, 18), muscular (14), nerve (12), bone marrow (8), renal (4) and temporal artery biopsy (TAB, 2). Among them, at least 1 typical histological feature detailed above was found in: ENT 38/49 biopsies (sensitivity of 77.6%), respiratory 15/31 (48.4%), skin 23/25 (92%), GI 10/18 (55.6%), muscular

4/14 (28.6%), nerve 5/12 (41.7%), bone marrow 6/8 (75%), renal 4/4 (100%) and TAB 1/2 (50%). A total of 57 biopsies performed in 29 patients (53.7%) showed none of the typical findings described above, although only 6 patients had all their biopsies without abnormal findings. These results are summarized in Table 1.

Conclusion: Multiple tissues are biopsied in clinical practice to assist in the diagnosis and evaluation of patients with EGPA, according to the multi-organ nature of this disease. Biopsies are more frequently obtained from accessible sites such as ENT or skin and usually dictated by clinical manifestations. In our cohort, the highest sensitivity was obtained from kidney, skin, ENT, bone marrow? and GI tract.

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[2] Yates et al, Ann Rheum Dis 2016

Table 1.

Biopsies in the EGPA cohort (N=59)			
Patients with biopsy: 54 (91.5%) **At diagnosis: 44 (81.5%); 89 biopsies** **During follow-up: 27 (50%); 74 biopsies**			
Histological findings			
Vasculitis			
Patients with vasculitis: 26 (48.1%) **At diagnosis: 22 (40.7%)** **During follow-up: 5 (9.3%)**			
Granuloma			
Patients with granuloma: 5 (9.3%) **At diagnosis: 3 (5.6%)** **During follow-up: 2 (3.7%)**			
Eosinophil-rich inflammation			
Patients with eosinophil-rich inflammation: 42 (77.8%) **At diagnosis: 31 (57.4%)** **During follow-up: 23 (42.6%)**			
Main localizations of biopsies, n (with at least 1 histological finding, n)			
	At diagnosis	**During follow-up**	**Total**
ENT	**21 (16)**	**28 (22)**	**49 (38)**
Respiratory	**13 (6)**	**18 (9)**	**31 (15)**
Skin	**15 (14)**	**10 (9)**	**25 (23)**
Gastrointestinal	**3 (3)**	**15 (7)**	**18 (10)**
Muscular	**13 (4)**	**1 (0)**	**14 (4)**
Nerve	**12 (5)**	**0 (0)**	**12 (5)**
Bone marrow	**6 (5)**	**2 (1)**	**8 (6)**
Renal	**4 (4)**	**0 (0)**	**4 (4)**
Vascular (temporal artery biopsy)	**2 (1)**	**0 (0)**	**2 (1)**

Acknowledgements: This study was supported by Instituto de Salud Carlos III (ISCIII) through the project PI18/00461, part of Plan Estatal de Investigación Científica y Técnica y de Innovación 2013–2016, and co-funded by the European Union. Roberto Ríos-Garcés is a recipient of a Río Hortega grant from Instituto de Salud Carlos III, Spain (CM19/00032).

Disclosure of Interests: Roberto Ríos-Garcés: None declared, José Hernández-Rodríguez: None declared, Sergio Prieto-González: None declared, Maria C. Cid Paid instructor for: Vifor, GSK, Consultant of: GSK, Abbvie and Janssen, Grant/research support from: Kiniksa, Georgina Espígol-Frigolé Consultant of: Janssen.

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AB0763

CHARACTERISTICS OF RELAPSES IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS. A SINGLE CENTRE EXPERIENCE

Keywords: Descriptive Studies, Outcome measures, Vasculitis

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is a heterogeneous disease with a variable, relapsing course. Real-world data regarding specific characteristics of relapses in this patients are scarce.

Objectives: We aim to describe and analyse the relapses presented in a single-center cohort of EGPA patients.

Methods: Medical charts of EGPA patients regularly controlled at our department were reviewed to describe demographics, clinical characteristics at diagnosis and at relapse, number of relapses, disease activity at relapse, treatment of the relapses, damage accrual, and laboratory results. The definition of relapse was the same used in the MIRRA trial: a) active vasculitis (BVAS >0), b) active asthma or active nasal or paranasal sinus disease leading either to an increase in the dose of prednisone > 4mg/day, initiation of or increase in immunosuppressive therapy, or hospitalization [1].

Results: A total of 59 EGPA patients were followed regularly at our department. All fulfilled either ACR 1990 and/or MIRRA trial inclusion criteria for EGPA. The mean age at diagnosis was 51.6 years, 59.3% were female and 91.5% were Caucasian. Among them, 76.3% were ANCA positive and 23.7% were ANCA negative. The mean time of follow-up was 10.7 ± 8.2 years. During the follow-up, a total of 324 relapses were diagnosed in 47 patients, with 12 patients experiencing no relapse. A relapse-free survival analysis showed that 35% of patients had a relapse in the first year, 51% at 2 years, 59% at 3 years and 64% at 5 years. The main clinical symptoms at relapse were asthma (in 248 flares, 76.5% of them), followed by rhinitis (100, 30.9%), sinusitis (60, 18.5%), skin involvement (19, 5.9%), fever (18, 5.6%), arthralgia (16, 4.9%), lung infiltrates (15, 4.6%), myalgia (12, 3.7%), peripheral nervous system involvement (11, 3.4%), cardiac involvement (6, 1.9%), arthritis (3, 0.9%), weight loss (2, 0.6%), alveolar hemorrhage (2, 0.6%), gastrointestinal involvement (2, 0.6%) and central nervous system involvement (2, 0.6%). No renal involvement was seen at flare. Median BVAS at relapse was 2 (IQR 2-4, range 0-28). When determined, median blood eosinophils at relapse were 500 cells/mm^3 (IQR 100-1000) and in 73% of the measures eosinophils did not reach 10% of the total leucocyte count. Median CRP was 0.6 mg/dl (IQR 0.2-2.4) and median ESR 14 mm/h (IQR 8-32). ANCA were measured in 37 relapses only, being positive in 14 of them. The median prednisone dose at relapse was 6.25mg/day and the median increase for treating the relapse was 30 mg/day. In 53 relapses, patients were already taking azathioprine. In 47, mepolizumab. In 36, methotrexate. In 11, mofetil mycophenolate. When comparing patients who relapsed vs. those who did not, and those who relapsed less than 1 time every 2 years vs those who relapsed more than 1 time every 2 years, no predictive factor of relapse was seen.

Conclusion: After a mean follow-up of 10.7 years, 324 relapses were diagnosed in 59 patients. First relapse occurred in 35% of patients at 1 year and in 64% at 5 years. The clinical spectrum of relapses was predominantly asthma, followed by ear, nose and throat, being vasculitic manifestations much less frequent. No predictive factors of relapse were identified.

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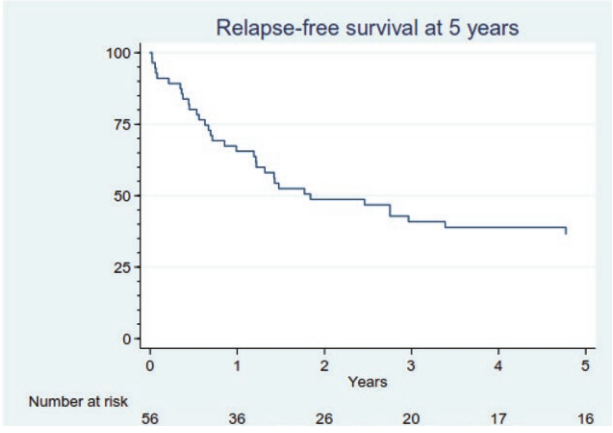


Figure.

Acknowledgements: This study was supported by Instituto de Salud Carlos III (ISCIII) through the project PI18/00461, part of Plan Estatal de Investigación Científica y Técnica y de Innovación 2013–2016, and co-funded by the European Union. Roberto Ríos-Garcés is a recipient of a Río Hortega grant from Instituto de Salud Carlos III, Spain (CM19/00032).

Disclosure of Interests: Roberto Ríos-Garcés: None declared, José Hernández-Rodríguez: None declared, Sergio Prieto-González: None declared, Maria C. Cid Paid instructor for: Vifor and GSK, Consultant of: GSK, Abbvie and Janssen, Grant/research support from: Kiniksa, Georgina Espígol-Frigolé Consultant of: Janssen.

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AB0764

EVALUATION OF THE APPLICABILITY OF THE 2022 AMERICAN COLLEGE OF RHEUMATOLOGY-EUROPEAN ALLIANCE OF ASSOCIATIONS FOR RHEUMATOLOGY CLASSIFICATION CRITERIA FOR ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS TO AN ASIAN POPULATION

Keywords: Organ damage, Vasculitis

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Background: The 2012 Chapel Hill Consensus Conference (CHCC) definitions and the 2007 European Medicines Agency (EMA) algorithm have been commonly used for the diagnosis of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) as a conventional and reliable method. Recently the 2022 American College of Rheumatology (ACR)-European Alliance of Associations for Rheumatology (EULAR) classification criteria for AAV have been released. It is well-known that patients with granulomatosis with polyangiitis (GPA) are predominantly proteinase 3 (PR3)-ANCA-positive in the U.S. and Europe, but myeloperoxidase (MPO)-ANCA-positive patients with GPA are more prevalent in Japan. However, very few studies have been available on the evaluation of the applicability of the new criteria to an Asian population.
Objectives: This study aimed to assess the applicability of the 2022 ACR/EULAR classification criteria to AAV patients from an Asian background.
Methods: This study included a total of 415 patients (mean age = 64.2 years, standard deviation [SD] = 16.3 years) diagnosed with AAV by the conventional method at three medical institutions in Japan between 2000 and 2022. Only Asians accounted for the whole population comprising 139, 128, and 148 patients (mean age = 65.2 years, SD = 15.7 years; mean age = 70.8 years, SD = 13.8 years; mean age = 56.1 years, SD = 15.8 years) diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA), GPA, and microscopic polyangiitis (MPA) by the conventional method, respectively. The applicability of the new criteria to AAV patients in Japan was assessed through the verification of the consistency with the conventional diagnoses. Additionally, phenotypes of organ involvement were analyzed in each reclassified group from the conventionally-diagnosed GPA population.
Results: The patients diagnosed with EGPA and MPA by the conventional method were significantly more likely to be reclassified into the same AAV subphenotype (138 out of 139 patients [99.3%] and 145 out of 148 patients [98.0%], respectively). On the other hand, the patients diagnosed with GPA by the conventional method were less likely to be reclassified into the same AAV subphenotype (91 out of 128 patients [71.1%]). In the conventionally-diagnosed GPA population, 71 patients were reclassified as GPA, not as MPA, 20 were reclassified not only as GPA but also as MPA, and 36 were reclassified not as GPA but rather as MPA. In the group reclassified only as GPA, there were 59 patients with sinusitis, including ten patients with orbital mass lesions. In the group reclassified both as GPA and as MPA, there were 20 patients with severe organ involvement, including 15 patients with pauci-immune glomerulonephritis (PIGN).
Conclusion: The new criteria gave more weight to ANCA serology than histology and surrogate markers compared with the conventional method, which kept diagnostic consistency in the conventionally-diagnosed EGPA and MPA populations. At the same time, the new criteria occasionally led to a big diagnostic contradiction in the conventionally-diagnosed GPA population from an Asian background. In the conventionally-diagnosed GPA population, the new criteria were likely to reclassify MPO-ANCA-positive patients as MPA. However, it is noteworthy that the new criteria were still beneficial in extracting GPA patients with recurrent or severe organ involvement, including orbital masses and PIGN.

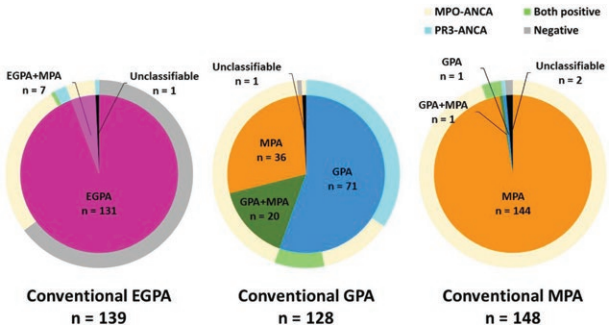


Figure. Reclassification of the conventionally-diagnosed AAV patients according to the 2022 ACR/EULAR classification criteria for AAV, including the distribution of ANCA serotypes. AAV, antineutrophil cytoplasmic antibody-associated vasculitis; ANCA, antineutrophil cytoplasmic antibody; MPO, myeloperoxidase; PR3, proteinase 3; EGPA, eosinophilic granulomatosis with polyangiitis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0765

DIFFUSE ALVEOLAR HAEMORRHAGE IS ASSOCIATED WITH HIGH DISEASE ACTIVITY AND HIGH MORTALITY IN AAV PATIENTS: PROSPECTIVE OBSERVATIONAL STUDY

Keywords: Vasculitis

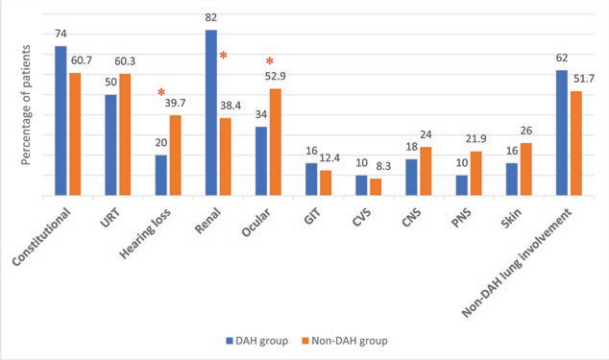
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Background: Diffuse alveolar haemorrhage (DAH) is a life-threatening emergency in patients with anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitides (AAV).
Objectives: To describe the clinical features and outcomes of AAV patients with DAH and compare them with non-DAH AAV patients.
Methods: Observational cohort study based on the prospective Indian Vasculitis Registry. 292 AAV patients were included in the study. DAH was diagnosed based on the clinical features and radiology findings. Fischer's exact test and Mann-Whitney U test were used for comparison. A p value of <0.05 was considered as significant.
Results: Fifty (17%) patients had DAH. Median age was 40.5 years and males constituted 54%. GPA, MPA and EGPA were the diagnoses in 39, 10 and 1 patients, respectively. Prevalence of DAH was higher in MPA (37.05%) than GPA (15.5%; p=0.0132). Haemoptysis was present in only 70% of patients while cough (76%) and breathlessness (62%) were the other respiratory symptoms. Six (12%) patients did not have any of these clinical features and were diagnosed with DAH based on radiology. DAH patients had more renal involvement (82% vs 38.4%; p<0.00001), less ocular involvement (34% vs 52.9%; p=0.0193) and hearing loss (20% vs 39.7%; p=0.0094) and higher BVASv3 score at presentation (21.6 vs 15.4; p=0.00026). Table 1 and Figure 1 shows the comparison of clinical features between the two groups. Remission induction agents used were glucocorticoids (100%), cyclophosphamide (62%) and rituximab (38%). PLEX was used in only 5 (10%) patients. Eleven (22%) patients died during follow up compared to 17 (7%) in patients without DAH (p=0.0028).
Conclusion: Presence of DAH in AAV patients was associated with high disease activity and higher mortality on follow up. Haemoptysis may be absent in a significant number of patients with DAH and hence, high index of suspicion is required to suspect and diagnose it early.

Table 1 : Clinical features of patients included in the study.

Clinical feature	DAH group (n=50)	Non-DAH group (n=242)	P value
Age	40.5 (17-80) years	44 (14-80) years	0.06876
Females	23 (46%)	146 (60.3%)	0.0828
Diagnosis			0.1143
GPA	39 (78%)	212 (87.6%)	
MPA	10 (20%)	17 (7%)	
EGPA	1 (2%)	13 (5.4%)	
Pulmonary symptoms			
Haemoptysis	35 (70%)	27 (11.2%)	<0.00001
Breathlessness	31 (62%)	41 (16.9%)	<0.00001
Cough	38 (76%)	81 (33.5%)	<0.00001
ANCA positivity	44 (88%)	189 (78.1%)	0.1253
PR3 ANCA	30 (68.2%)	153 (81%)	
MPO ANCA	14 (31.8%)	21 (11.1%)	
BVASv3 at presentation	21 (8-37)	13 (0-47)	0.00026
Induction therapy			-
Cyclophosphamide	31 (62%)	152 (62.8%)	1.0
Rituximab	19 (38%)	88 (36.4%)	0.8724
Plasma Exchange	5 (10%)	4 (1.7%)	0.0089
Others	1 (2%)	39 (16.1%)	0.0057
Deaths	11 (22%)	17 (7%)	0.0028

Figure 1: Organ manifestations due to AAV in both the groups.



* p < 0.05

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0766 STEP-DOWN TREATMENT WITH MEPOLIZUMAB FOR EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA). REAL-LIFE EXPERIENCE OF A SINGLE-CENTER COHORT

Keywords: Vasculitis

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Background: Mepolizumab is an anti-interleukin-5 (IL-5) agent approved for EGPA at the dose of 300 mg every 4 weeks. However, from real-life studies, evidence is accruing of its comparable effectiveness at "asthma-dose" of 100 mg every 4 weeks. The preferred approach at our center is to start mepolizumab 300 mg/4 weeks and to reduce to 100 mg/4 weeks once remission is achieved (Birmingham Vasculitis Activity Score - BVAS=0), asthma is controlled (Asthma Control Test – ACT >20), eosinophil count is normalized and glucocorticoids are withdrawn (step-down approach).

Table 1

		STEP-UP STRATEGY		STEP DOWN STRATEGY	
		100 ->100	100 ->300	300 ->100	300 ->300
N° of patients (%)		6 (16%)	1 (2%)	9 (24%)	22 (58%)
Sex (female)		4 (67%)	1 (100%)	7 (78%)	10 (5 %)
Median age at the starting of MEPO		59 (57-72)	48	52 (50-58)	56 (49-64)
START of MEPO	Disease duration at MEPO start	90,5 (51,25-165)	144	50 (21-91)	75 (34-108)
	ACT	22 (19-25)	10	19 (15-19)	19 (14,5-25)
	BVAS	4,5 (3,3-5,8)	4	2 (2-3)	3,5 (2-5)
	EOS	550 (365-697,5)	400	600 (390-665)	590 (400-1040)
	PDN dose	5 (3,7-5)	25	5 (5-7,5)	8,75 (5-23,75)
	asthma exac./6 months before MEPO start	0,5 (0-1)	4	1 (1-1,5)	1 (0-3)
	n° of patients treated with immunosuppressants	3 (50%)	1 (100%)	7 (78%)	15 (68%)
END of F-UP	Total months of FUP	33 (22-40)	46	48 (38-89)	33 (12-50)
	ACT	25 (25-25)	13	25 (25-25)**	25 (25-25)**
	BVAS	1,5 (0,25-3,5)	5	0 (0-2)**	0 (0-2)**
	EOS	77,5 (56,25-95)*	300	75 (48-108)**	40 (0-100)**
	PDN dose	0 (0-0)	7,5	0 (0-0)**	0 (0-2,5) **
	n° of pts experienced asthma exac	0 (0%)	1 (100%)	1 (11,1%)	4 (18%)
	n° of pts experienced ENT exac	0 (0%)	1 (100%)	3 (33,3%)	2 (9%)
	n° of pts experienced non respiratory EGPA exac	0 (0%)	0	0 (0%)	4 (18%)
	n° of pts treated with immunosuppressants	2 (33,3%)	1 (100%)	3 (33,3%)	14 (64%)

ACT: Asthma Control Test; BVAS: Birmingham Vasculitis Activity Score; EOS: eosinophils;EXAC: exacerbation; F-UP: follow-up; MEPO: mepolizumab; PDN: prednisone; PTS: patients; *:p < 0.05 for START vs END analysis, ** p<0.01 for START vs END analysis

Objectives: To assess the long term-efficacy of step-down treatment with mepolizumab in EGPA.
Methods: We reviewed medical charts of patients with EGPA treated with mepolizumab from April 2014 to December 2022. We divided patients by homogeneous dosing schedule and compared disease activity and characteristics at baseline and over time.
Results: We treated 38 patients for a median follow up of 38 months (IQR 29-53). Seven patients underwent a step-up approach (starting with mepolizumab 100 mg/4w and subsequent switching to mepolizumab 300 mg/4w in case of failure). Among them, only 1 patient (17%) needed a dose increase due to uncontrolled respiratory symptoms. Mepolizumab 300 mg/4w was started in 31 patients allowing a step-down in 9 (29%), without any patient having to increase the dose again. Both subgroups of the step-down strategy showed significant reduction in terms of BVAS, ACT, serum eosinophils and daily prednisone dose at last follow-up. At the same time presented a high proportion of nasal exacerbations (33 vs. 9% p=0.31). [Table 1]
Conclusion: In our experience, a step-down approach with mepolizumab in EGPA is reasonable and allows to safely reach the low-dose regimen in a great proportion of patients. Nasal polyps are the new challenge for physicians treating EGPA in an age where a steroid-free remission is an achievable target.
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Disclosure of Interests: None Declared.
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AB0767 OUTCOMES OF SARS-COV-2 INFECTION IN PATIENTS WITH ASSOCIATED ANCA VASCULITIS. DATA FROM THE NATIONAL SAR-COVID REGISTRY

Keywords: Vasculitis, COVID, Real-world evidence

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Background: Systemic vasculitis are rare autoimmune diseases that can lead to multiple organs and systems involvement. ANCA-associated vasculitis presents characteristics that differentiate them from other vasculitides. There is evidence that infection by (SARS-CoV-2) impacts differently in patients with various underlying diseases and different comorbidities, even generating differences in the morbidity and mortality of the viral infection.
Objectives: To describe the clinical characteristics and outcomes of SARS-CoV-2 infection in patients with systemic vasculitis.
Methods: Observational, multicenter, cross-sectional analytical study in patients 18 or older diagnosed with systemic vasculitis with confirmed SARS-CoV-2 infection (RT-PCR or serology) included in the SAR-COVID registry. Patients were evaluated from July 2020 to February 2022. Patients diagnosed with ANCA-associated vasculitis (AAV), other systemic vasculitides (Giant cell arteritis, Takayasu), and a control group of patients with other rheumatological diseases matched by age, sex, comorbidities, and date of SARS-CoV-2 infection. The survival curve of the groups was studied by Kaplan-Meier and compared through the Log-Rank Test. A Cox regression model will be performed to adjust survival for different variables (sex, age, treatments for underlying disease, treatments for viral infection, smoking, obesity, d-dimer level, and disease activity).
Results: A total of 282 out of 2694 patients in the SAR-COVID registry were included, 57.4% women with a mean age of 55.7 years (SD 14.1). Fifty-four patients in the AAV group, 32 in the other vasculitis group, and 196 controls were studied. In 51.1% of the cases, one or more comorbidities were observed. We found caucasian ethnicity at 50.7%, mestizo at 39.7%, and other ethnic groups at

9.6%. PCR made the diagnosis of COVID-19 in 81.2% of the cases. The controls had treatment with corticosteroids before the onset of symptoms in 30.1% of the cases, while 64.8% and 68.8% in the AAV group and other vasculitides, respectively ($p < 0.001$). Hospitalization was required in 53.7% of the AAV group, 37.5% in other vasculitides, and 26.2% in the control group. 5.6% of patients in the control group presented acute respiratory distress syndrome (ARDS), 15.6% in the other vasculitis group, and 22.2% in the AAV group ($p<0.001$), requiring invasive mechanical ventilation in 13% of the control group. 33.3% of the other vasculitis group and 57% of the patients in the AAV group ($p<0.001$) Complete recovery was observed in 82.3% of patients in the control group, 75% in the other vasculitis group, and 63% in the AAV group. We observed that 5.7% of the patients in the control group died from COVID-19, 9.4% from other vasculitides, and 27.8% in the AAV group ($p<0.001$). We found a lower survival in the AAV group compared to the control group ($p <0.005$). In the multivariate Cox regression model, we can see that older age (HR:1.05 IC95% 1.01-1.09 p=0.01), BMI>40 (HR:13.2 IC95% 2.1-83.2 p=0.01), and high activity of the underlying disease (HR:16 95% CI 3.7-69.4 $p<0.005$) were associated with lower survival.

Conclusion: In conclusion, we can mention that patients diagnosed with AAV presented a worse evolution of the disease caused by SARS-CoV-2 with a more frequent requirement for invasive mechanical ventilation. Likewise, these patients showed lower survival compared to other autoimmune diseases.

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AB0768

NEW INSIGHTS ON EPIDEMIOLOGICAL DATA AND IMPACT OF THE COVID-19 PANDEMIC ON IGA VASCULITIS IN CHILDREN AND ADULTS IN FRANCE: A NATIONWIDE COHORT

Keywords: COVID, Vasculitis, Epidemiology

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Background: IgA vasculitis (IgAV) is a rare autoimmune disease affecting small vessels. It is well established that the incidence is higher in children (3 to 26 per 100,000 children/year,) [1] than in adults (0.1 to 1.8 per 100,000 individuals/year) [1]. However others epidemiological data and impact of the COVID-19 on IgAV remain overlooked [2].

Objectives: To collect and analyze epidemiological data on IgAV in both adults and children in France.

Methods: We conducted an observational study using a national database called "BNDMR" [3] (Banque Nationale de Données Maladies Rares) on IgA vasculitis (code ORPHA761), which gathered patients managed in the French rare disease expert network. The incidence was estimated from the date of diagnosis, and we calculated the median annual incidence over the period 2010-2022. We specifically assessed the north/south gradient (latitude of the residence higher/lower than the median of the latitudes), the seasonality, and the impact of the COVID-19 pandemic compared to other patients reported within the same period and addressed in the same expert centers used as controls.

Results: During this 12-year period, 1988 patients with IgAV were reported (1498 children; 490 adults). The male to female ratio was 1.57 for adults and 1.05 for children. The median IgAV annual incidence was 15 cases/year [IQR 9-30] and 82 cases/year [IQR 72-86] for adult and children cases respectively. Time to diagnosis was less than 1 month for both. Compared with other patients reported in the same expert centers, IgAV was more frequently reported in the southern part of France than in the north (OR 4.88 [95% confidence intervals: 4.17 - 5.74] in adults and OR 1.51 [1.35 - 1.68] in children). IgAV was also more frequently observed in winter than during the rest of the year in both adults (OR 1.60 [1.39 - 1.82]) and children (OR 1.22 [1.01 - 1.48]). The incidence of IgAV decreased during the COVID-19 pandemic period (from March 2020 to September 2022) in children (OR 0.62 [0.47 - 0.81]) but not in the adult population (OR 0.90 [0.76 - 1.06]).

Conclusion: Our study confirms the winter seasonality and sex ratio in IgAV [4,5], but suggests that the incidence or the reporting of IgAV decreased in children during the COVID19 pandemia, possibly due to barrier measures [6]. The observed north/south gradient need confirmation. The main limitation of this study is a possible IgAV under-reporting as this study rely only on cases addressed in expert centers.

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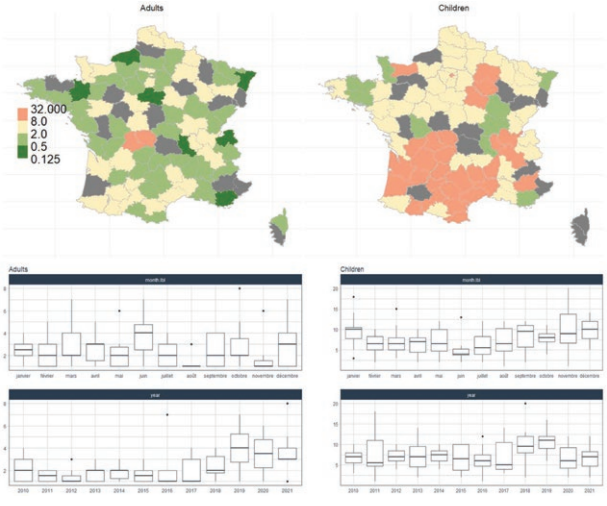


Figure.

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AB0769

CARDIAC AND PULMONARY INVOLVEMENTS IN BEHCET'S SYNDROME: A CASE SERIES OF 93 PATIENTS

Keywords: Cardiovascular disease, Behcet's disease, Lungs

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Background: Behçet syndrome (BS) is a multisystemic vasculitis of unknown etiology, frequently observed in the Mediterranean region and the Middle east. Pulmonary involvement (PI) and cardiac involvement (CI) are rarely described in BS, with a prevalence of less than 5%. However, they are entailed to high morbidity and mortality.
Objectives: Our work aims to describe the profile and outcomes of BS patients presenting with cardiopulmonary lesions.
Methods: We retrospectively conducted a descriptive and monocentric study, between 2020 and 2022, including 576 BS patients.
Results: 93 patients were enrolled (16%). The sex ratio (M/F) was 4.8 and the mean age was 3 ± 6 years [19-51]. Cardiovascular risk factors comprised smoking (26%), high blood pressure (10%), and diabetes (9%). Patients were often asymptomatic (78%) or presented with chest pain (23%), dyspnea (11.5%), dry cough (5%), and hemoptysis (5%). On chest CT angiography, we observed pulmonary artery aneurysms (70%), pulmonary artery thrombosis (24%), and alveolar hemorrhage (1%). Cardiac involvement (46%) included right intracardiac thrombosis (24%), pericarditis (10%), coronary thrombosis (4%), myocarditis (1%), and endomyocardial fibrosis (1%). Deep vein thrombosis was reported (28%) in the superior vena cava (14%), inferior vena cava (11%), and lower extremities (8%). Extravascular involvements were mostly mucocutaneous (79%), ocular (40%), articular (31%), and neurological (15%). Patients were treated with colchicine (83%), glucocorticoids (92%), curative anticoagulation (77%), cyclophosphamide (42%), azathioprine (36%), Infliximab (8%) and ciclosporin (1%). Surgery was performed for 8% of the patients. Relapse and death were recorded in respectively 15% and 7% of the cases.
Conclusion: PI and CI are serious complications of BS, often lately discovered and underdiagnosed, due to their discrete evolution. Systematic screening should thus be considered in at-risk patients, especially young males presenting with mucocutaneous lesions and venous thrombosis. Prompt and adequate immunosuppressive therapy is usually linked to favorable outcomes.
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AB0770 MANAGING MEDICATION WITHDRAWAL IN ANCA ASSOCIATED VASCULITIS, A SINGLE CENTRE STUDY

Keywords: Vasculitis, Tapering, Safety

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Background: While ANCA- associated vasculitis (AAV) can be a life-threatening condition, once patients achieve sustained remission, it is possible to withdraw glucocorticoids (GC) and immunosuppressive therapy successfully. British [1] and European [2] guidelines advocate withdrawal of therapy in sustained remission. However, robust definitions of remission and risk of relapse on drug withdrawal are active research areas within the vasculitis community. Therefore, we took the opportunity to review & compare the clinical practice at our Tertiary Vasculitis Centre to guidelines published by the British Society for Rheumatology (BSR) [1].
Objectives: To describe the proportion of patients in remission and rates of drug withdrawal in line with BSR guidelines and evaluate if any characteristics were associated with GC-dependent remission.
Methods: We conducted a retrospective records review of all AAV patients (clinical diagnosis regardless of classification criteria) in our centre who attended for their routine care between July 2015 – August 2020. Those who lost or lacked significant follow-up information were excluded. Approval by the local clinical audit department was granted. Remission was defined per BSR guidance as a well-controlled disease by physician assessment on drug or drug-free remission. SPSS v.25 was used for statistical analysis.
Results: Sixty-five patients were included, 58% female, mean (SD) age at diagnosis of 60.7 (13.2), and 92% were Caucasians. The median (range) disease duration was five years (0.5 – 43). 33.8% were classified as GPA, 29.2% as EGPA. 55.4% had life or organ threatening disease, and 50.8% with a relapsing disease (table 1). At the time of the study, 60% of patients remained on GCs and 89% on immunosuppressive therapy. 48/65 (74%) were in clinical remission, of whom 19/48 (39.6%) were on GC plus immunosuppression, 21/48 (43.8%) were on immunosuppression alone, and 5/48 (10.4%) were in drug-free remission. In those with disease duration ≥ 10 years (n=14), 50% were deemed high relapse risk or poorly controlled and remained on a median dose of 10mg prednisolone. On univariate and multiple logistic regression analysis (reference=GC-dependent), skin involvement and a positive biopsy (83.3% non-renal) were associated with a statistically significant lower odds (OR 0.127 *P*=0.006, OR 0.207 *P*=0.04 respectively) of remaining on long term GC. In contrast, the relapsing disease was associated with increased odds (OR 4.006, *P*=0.026) of GC-dependent remission (figure 1).
Conclusion: Withdrawing treatment in AAV is challenging and achievable in a minority of patients, while the vast majority remain on long-term treatment. Skin involvement and non-renal positive biopsy may carry a positive prospect toward GC-free remission. Age, gender, disease type, ANCA status or persistent ANCA did not significantly influence the potential to stay on GC. Having a relapsing disease is the single most crucial factor significantly associated with long term treatment.
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Table.1 Cohort characteristics

Total number	65
Age at diagnosis, mean (SD) years	60.7 (13.2)
Female, n (%)	38 (58.5%)
Caucasians	60 (92%)
GPA, n (%)	22 (33.8%)
EGPA, n (%)	19 (29.2%)
Other AAV, n (%)	24 (36.9%)
ANCA positive, n (%)	41 (63.1%)
Duration in years, median (range)	5 (0.5-43)
Disease duration ≥ 5 years, n (%)	29 (45%)
Disease duration ≥ 10 years, n (%)	14 (21.5%)
Organ/ life-threatening, n (%)	35 (55.4%)
Relapsing (once or more), n (%)	33 (50.8%)
Still on Glucocorticoids, n (%)	39 (60%)
Still on immunosuppression, n (%)	58 (89%)
GC withdrawn 12 months following remission, n (%)	15 (23.1%)
Off immunosuppression and GC, n (%)	5 (7.7%)

Variable	Univariate OR (95% CI)	*P value* *	Multivariate OR (95% CI)	*P value* *
Age at diagnosis	0.975 (0.934 – 1.0119)	0.261		
Disease duration	1.025 (0.946 – 1.110)	0.546		
Male gender	2.137 (0.753 – 6.066)	0.153		
Disease type - GPA	1.444 (0.450 – 4.641)	0.537		
Disease type – EGPA	2.80 (0.765 – 10.246)	0.120		
Negative ANCA	2.073 (0.618 – 6.954)	0.238		
Positive biopsy	0.257 (0.068 – 0.970)	0.045	0.207 (0.046 – 0.930)	0.040
Persistently positive PR3/MPO	1.149 (0.360 – 3.672)	0.814		
Relapsing disease	3.022 (1.075 – 8.499)	0.036	4.006 (1.178 – 13.632)	0.026
Skin involvement	0.235 (0.069 – 0.803)	0.021	0.127 (0.030 – 0.547)	0.006
ENT involvement	1.867 (0.607 – 5.736)	0.276		
Pulmonary involvement	1.6 (0.587 – 4.365)	0.359		
Neurological involvement	1.109 (0.409 – 3.008)	0.839		
Renal involvement	0.350 (0.076 – 1.615)	0.178		
Organ or life threatening	1.00 (0.370 – 2.706)	1.000		

* Logistic regression

Figure.1 Factors associated with Glucocorticoid-dependent remission

Acknowledgements: Data team and the clinical audit department at the RUH NHS trust, Bath.
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AB0771 FEMALE GENDER AND STEROID TREATMENT AS MAIN INFLUENCING FACTORS IN THE PERCEPTION OF QUALITY OF LIFE IN ANCA-ASSOCIATED VASCULITIS: FINAL RESULTS FROM THE ITALIAN VERSION OF ANCA-ASSOCIATED VASCULITIS PATIENT-REPORTED OUTCOME (AAV-PRO_ITA) QUESTIONNAIRE

Keywords: Quality of life, Vasculitis, Patient reported outcomes

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Background: The ANCA-associated vasculitis patient-reported outcome (AAV-PRO) questionnaire is a 29-item disease-specific PRO measure for AAV [1]. Originally only available in English, it has been translated into several languages in recent years to spread its use. The Italian version of the AAV-PRO questionnaire (AAV-PRO_ita) was translated in collaboration with Oxford and Bristol University (UK) and, after a preliminarily test on a single-center Italian cohort [2], it was evaluated on a large Italian cohort [3].

Objectives: To assess the internal consistency, feasibility, and reliability of the AAV-PRO_ita in the multicentric cohort of Italian AAV patients belonging to the Vasculitis Study Group of the Italian Society of Rheumatology.

Methods: The AAV-PRO_ita is describes the following disease domains: (1) organ-specific and systemic symptoms and signs(SSS); (2) physical function(PF); (3)social and emotional impact(SEI). In this study, Italian-speaking AAV patients were recruited from Italian Centres (N=17) with a large experience in the diagnosis and treatment of systemic vasculitis, belonging to the Vasculitis Study Group of the SIR. Inclusion criteria were: a confirmed diagnosis of GPA, MPA, or EGPA; ANCA positivity in at least once occasion or biopsy-proven AAV; and age ≥18 years old. Participants completed the AAV-PRO_ita at three different time-points: baseline, after 5-7 days, and at month 3.

Results: 276 AAV-patients (56.5% women) with a median age of 61 (IQR 51.5-71.6) were recruited and completed the questionnaires. The subtype of AAV was mainly GPA (146, 52.9%), followed by EGPA (77, 27.9%), and MPA (53, 19.2%). Median BVASv3 at baseline was 0 (IQR 0-3), whereas the median BVASv3 at the onset of disease was 13 (IQR 8-18). Participants had a median duration of disease of 62 (IQR 23.8-118.5) months. Patients who experienced at least one relapse, one hospitalization, and one severe infection were 41.7%, 53.3%, and 22.1%, respectively. 81.2% of the patients were on immunosuppressant therapy and 72.1% were still receiving GCs. AAV-PRO_ita questionnaire had good internal consistency (Cronbach's Alpha range 0.81-0.93) and good test-retest reliability (ICCs range 0.93-0.96). Item response rates were high overall (maximum 1.8% missing data), supporting the feasibility of the questionnaire. Concerning the domains of the questionnaire, female AAV patients scored higher (i.e. worse) in all 3 domains, especially in the SEI domain (p-value<0.001). There were also differences between patients on steroid therapy (n=199) and patients without steroid therapy (n=77), in fact, the former had higher scores on all domains, especially in the PF domain (p-value<0.001). Furthermore, patients who had at least one relapse of disease (n=114) had higher scores compared with who had never had one (n=161) on all domains (p-value<0.05). Differently, there were no differences in median scores between younger and older responders and between AAV subtypes. Duration of disease, previous hospitalizations and/or infections, BVASv3 and VDI at baseline did not influence the scores.

Conclusion: The AAV-PRO_ita questionnaire is a new 29-item, disease-specific PRO measure for use in AAV in the Italian language. It is a self-administered Italian questionnaire with good internal consistency, feasibility, and reliability. Research on treatment strategies based on steroid-sparing regimen and spreading awareness of the existence of gender differences in medicine may improve the perceived QoL of AAV patients, reducing the psychosocial impact of the chronic disease.

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AB0772

AZATHIOPRINE VERSUS METHOTREXATE AS INDUCTION AND MAINTENANCE THERAPY IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA): A MONOCENTRIC RETROSPECTIVE STUDY

Keywords: Vasculitis, Disease-modifying Drugs (DMARDs), Outcome measures

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Background: Despite the clinical differences between EGPA and the other AAVs, treatment guidelines are mostly based on the evidence available for patients with MPA and GPA, due to the lack of enough randomized controlled trials on patients with EGPA [1].

Objectives: The aim of our study is to analyse the efficacy, safety and steroid-sparing effect of azathioprine (AZA) and methotrexate (MTX) as induction and maintenance therapy in EGPA.

Methods: We collected data from 57 retrospective patients divided in 4 groups according to the treatment received (MTX/AZA as 1st line agents in patients with non-severe EGPA or as 2nd line agents in patients with severe EGPA previously treated with cyclophosphamide or rituximab). We analysed the data collected during five years of follow up from the initiation of AZA/MTX and compared

Table 1. Baseline characteristic of the population and statistical differences between therapy groups

	Total	MTX 1st line	AZA 1st line	P-value	MTX 2nd line	AZA 2nd line	P-value
ANCA	31 (54%)	20 (80%)	3 (38%)	0.01	3 (28%)	5 (38%)	0.6
Negative	21 (37%)	5 (20%)	4 (50%)		4 (36%)	8 (62%)	
MPO	5 (9%)	0	1 (12%)		4 (36%)	0	
Unknown							
Creatinine (mg/dl)	1.44 (SD 1.69; min 0.48; max 8.62)	0.77 (SD 0.13; min 0.48; max 0,99)	1.05 (SD 0.5; min 0.53; max 1.8)	0.02	2.94 (SD 1.32; min 0.79; max 8.72)	1.85 (SD 1.77; min 0.55; max 6)	0.2
Eosinophil count ($x10^9/l$)	8.33 (SD 7.1; min 0.18; max 27.67)	7.32 (SD 9.33; min 0.18, max 27.62)	6.34 (SD 5.64, min 0.53; max 11.8)	0.8	9.89 (SD 4.81; min 3.8; max 14.4)	9.94 (SD 4.32; min 5.46; max 17)	1
C-reactive protein (mg/dl)	5.67 (SD 5.81; min 0; max 17.4)	3.94 (SD 5.92; min 0; max 14)	4.08 (SD 5.51; min 0.02; max 14.1)	0.9	6.77 (SD 6.27; min 1.17; max 17.4)	9.53 (SD 4.66; min 0.62; max 13.16)	0.3
BVAS/63	13.59 (SD 7.3; min 0; max 29)	9.16 (SD 4.23; min 4; max 20)	13.12 (SD 4.39; min 8; max 21)	ns	18.55 (SD 6.39; min 5; max 25)	19.69 (SD 6.01; min 8; max 29)	ns
Asthma	41 (72%)	21 (84%)	6 (75%)	ns	5 (45%)	9 (69%)	ns
Sinusitis	37 (65%)	19 (76%)	6 (75%)	ns	7 (63%)	5 (38%)	ns
Pulmonary nodules	24 (42%)	9 (36%)	2 (25%)	ns	6 (54%)	7 (53%)	ns
Cardiomyopathy	16 (28%)	6 (24%)	0	ns	4 (36%)	6 (46%)	ns
Mononeuritis multiplex	12 (21%)	3 (12%)	3 (37%)	ns	2 (18%)	4 (30%)	ns
Purpura	9 (16%)	1 (4%)	4 (50%)	0.0019	1 (9%)	3 (23%)	ns
Biopsy proven glomerulonephritis	6 (11%)	0	0		3 (27%)	3 (25%)	ns
Peritonitis	1 (2%)	0	0	ns	0	1 (7%)	ns

the patient groups according to time to first relapse, percentage of patients in remission (defined as R1: BVAS=0, R2: BVAS=0 with prednisone ≤5mg/day, R3: BVAS=0 with prednisone ≤ 3,75mg/day – following the MIRRA definition(2)), persistence on therapy, percentage of patients with side effects and average cumulative steroid dose.

Results: There were no significant differences in the time-to-first relapse. No statistically significant differences were found in R1 remission analysis; a higher percentage of patients receiving MTX as 1st line therapy obtained R2 remission in the first 6 months (54% vs 12%, p=0,04), R3 remission wasn't achieved by any patient receiving AZA as 1st line treatment in the first 18 months of follow up (vs 35% in the MTX group, p=0.07). MTX was correlated with more adverse events (68% vs 33%, p=0.0049) still, persistence on therapy was higher for MTX (median time of suspension was >60months vs 12 months, p=0.03). The average cumulative steroid dose was lower in patients receiving MTX as a maintenance therapy compared to those receiving AZA (6g vs 10g at 5 years-follow up, p=0,039).

Conclusion: This study shows that MTX as 2nd line therapy has a better steroid-sparing effect and allows a better persistence on therapy, while as 1st line therapy it allows an earlier remission on lower prednisone dose.

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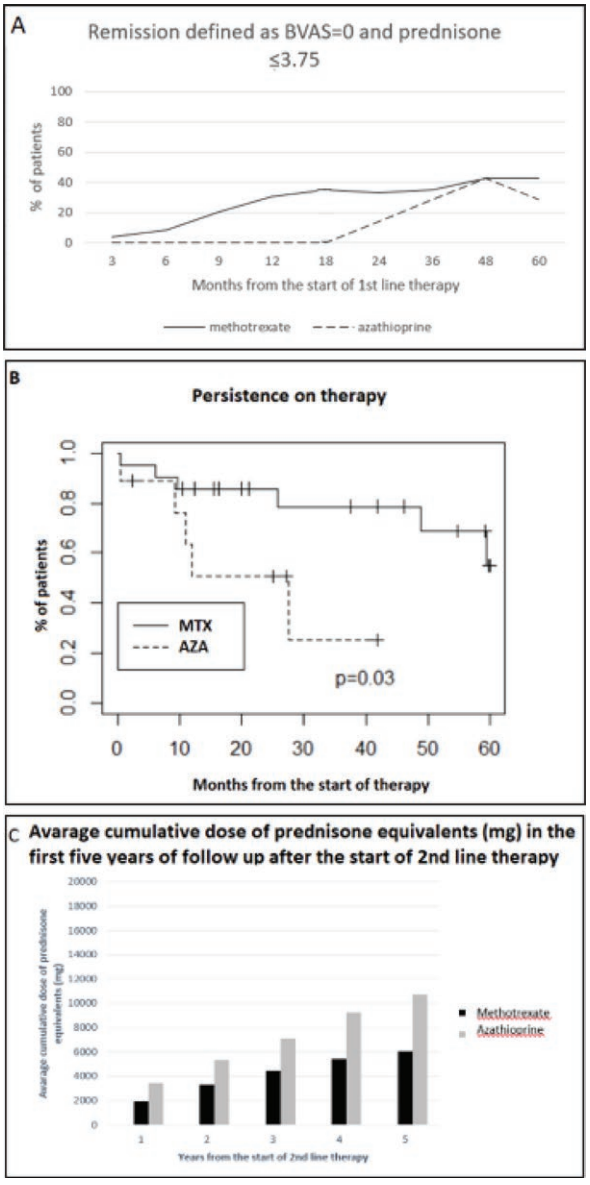


Image 1. A) Remission analysis B) Persistence on therapy C) Avarage cumulative prednisone-dose

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0773 IMPROVING ADHERENCE TO TREATMENT IN BEHÇET'S DISEASE - THE MULTI-STAKEHOLDER IMPACT_BD INTERNATIONAL STUDY

Keywords: Behcet's disease

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Background: Behçet's disease (BD) is a rare, and severe, multisystemic inflammatory disease characterized by recurrent oral aphthous ulcers, genital ulcers, skin lesions, and both anterior and posterior uveitis; articular, vascular, gastroenteric and neurological involvement may also occur. The multi-organ involvement and the wide spectrum of clinical manifestations make the diagnosis of BD challenging. The lack of medication adherence leads to poorer health outcomes for the patients, which affect quality of life, generate economic loss for the healthcare system and trigger uncertainty for the healthcare prescribers in dealing with the disease treatment. This challenge is particularly important in BD, and for this reason, worldwide experts in BD and patient representatives living with BD gathered to launch the IMPACT_BD study.

Objectives: The objectives of IMPACT_BD are to explore the unmet needs in treatment adherence and the main reasons for low- or non-adherence, to create a tool aimed at identifying and monitoring the reasons of low treatment adherence and to plan specific actions aimed at improving treatment adherence in BD.

Methods: The methodology includes 5 phases. *Phase A. Panel creation* - The first step created a multi-stakeholder panel that included clinicians, BD patient's representatives, BD caregiver representatives and other experts (economists, psychologist, pharmacists, etc). *Phase B. Co-design process* – Ad hoc surveys were created in co-design with the different stakeholders to capture the different dimensions, barriers and needs related to treatment adherence. The survey was translated into 8 languages and launched across Social Media (*Phase C. Launch of the survey*). *Phase D. Data analysis, workshop and agreement* – Answers to the survey questions will be elaborated to identify the main barriers and unmet needs in treatment adherence. An online workshop will be organized to co-design a tool that will enable the identification and the monitoring of BD treatment adherence during the clinical follow-up of BD patients. *Phase E. Pilot phase for validation* – The final tool will be translated into different languages and will be adopted in a pilot study. The results of the pilot phase will be discussed and

refined within the panel. A list of future actions aimed at improving treatment adherence in BD patients will also be produced with the support of members of the co-design panel.

Results: The main results of the study will be represented by: the identification of the main barriers and unmet needs related to treatment adherence in BD patients, caregivers and families; the creation of a co-designed tool aimed at assessing the causes and barriers of low- or non-adherence in BD patients; and the planning of future initiatives aimed at improving treatment adherence in BD patients.

Conclusion: Assessing the barriers causing low or non-adherence in BD will provide relevant information that will support the clinicians and the other health-care professionals caring for BD patients, by improving the clinical management of the disease; by taking tangible actions aimed at increasing adherence to treatment; and therefore by improving the wellbeing of BD patients, caregivers and families.

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Acknowledgements: NIL.

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AB0774 URINARY INTERLEUKIN (IL)-16 IN ANTI – NEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA)- ASSOCIATED VASCULITIS WITH KIDNEY INVOLVEMENT

Keywords: Biomarkers, Vasculitis, Kidneys

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Background: The pro-inflammatory interleukin (IL)-16 can be released by different immune cells and has been shown to be an inflammatory mediator in rheumatic diseases. Urinary (u-) IL-16 has recently been found to be associated with proliferative nephritis in systemic lupus erythematosus (SLE) and is expressed in inflammatory foci in the kidney [1,2]. However, data on u-IL-16 in other immune-mediated kidney diseases including Antineutrophil Antibody Associated Vasculitis (AAV) is lacking.

Objectives: To investigate levels of u- IL16 in AAV patients with kidney involvement compared to controls and to assess associations of u-IL16 with clinical variables.

Methods: Urine samples from 43 AAV patients were collected at the time of kidney biopsy on clinical indication. The biopsies were classified according to histopathological class [3]. Clinical variables were extracted from medical records. Forty-eight population controls were included. The u-IL16 was measured using a commercial sandwich ELISA. The cut-off for detectable IL-16 was set to ≥ 10 pg/mL. Vasculitis disease activity at the time of kidney biopsy was assessed using the Birmingham Vasculitis Activity Score (BVAS 3.0).

Results: In the AAV group, there were 25 males (58.1%), the median age was 61 years, and 22 (51.2%) were anti-PR3 positive while 21 (48.8%) were anti-MPO positive. There were 25 (58.1%) patients with GPA and 18 (41.9%) with MPA in the study. Median BVAS was 16 (interquartile range 13-21). Thirty-nine (90.7%) patients had biopsy-proven kidney involvement, whereas four patients had no histopathological signs of vasculitis. Mean eGFR (SD) was 51.1(31.9) in the AAV group and 91.6 (11.9) in the control group, respectively (p=<0.001). At inclusion and urine sampling 35 (81.4%) patients were on immunosuppressive treatment. In all, 15/43 (34.9%) patients had detectable levels of u-IL16, all of whom had biopsy-proven vasculitis (Figure). The AAV patients had significantly higher levels of u-IL16 compared to controls (p=0.027, 95% CI 1.79 – 27.6). Two controls had detectable levels of u-IL16. u-IL16 levels did not differ with respect to diagnosis (GPA/MPA) or ANCA-serotype. A positive correlation was seen between u-IL16 and BVAS (r=0.326, p=0.03), and there was a negative correlation between u-IL16 and eGFR (r= -0.330, p=0.03). Thirty-seven kidney biopsies were classified according to Berden: Focal (n=20), Crescentic (n=8), Mixed (n=6), and Sclerotic (n=3). There was a significant difference in u-IL16 levels between these groups (H (3)=8.68, p =0.034) with the highest proportion of patients with detectable u-IL16 in the sclerotic (66.7%) and crescentic (62.5%) classes. Levels of u-IL16 were not statistically significantly different between patients with or without ongoing treatment. The sensitivity for u-IL16 to correctly classify occurrence of kidney involvement in AAV patients was 38% (specificity 100%, PPV 100%, NPV 14%).

Conclusion: Urinary IL-16 was detectable in a significant proportion of AAV patients with kidney involvement and reflected disease activity and severity. As similar findings have been described in SLE, u-IL16 may be a marker of kidney inflammation in systemic immune-mediated kidney diseases. Further research is warranted to evaluate the pathogenic role of IL-16, the possible use of u-IL16 as a biomarker in clinical practice, as well as its potential as treatment target.

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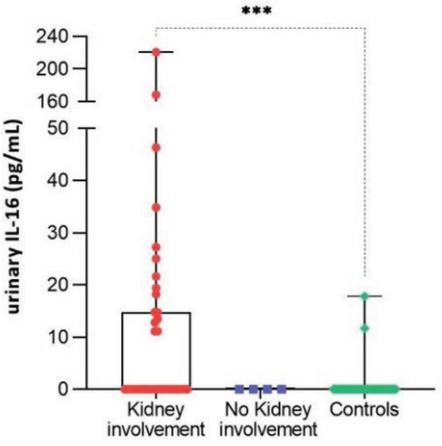


Figure. Urinary IL-16 in patients with ANCA associated vasculitis with and without biopsy-proven kidney involvement.

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Disclosure of Interests: None Declared.

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AB0775 EFFECTIVENESS AND SAFETY OF NON-MEDICAL SWITCH FROM RITUXIMAB ORIGINATOR TO AND AMONG BIOSIMILARS IN SMALL VESSEL VASCULITIDES PATIENTS: REAL WORLD DATA FROM A RETROSPECTIVE MONOCENTRIC STUDY

Keywords: bDMARD, Safety, Vasculitis

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Background: Rituximab (RTX) is indicated for treatment of severe small vessel vasculitides (SVV), namely granulomatosis with polyangiitis (GPA) microscopic polyangiitis (MPA) and cryoglobulinemic vasculitis (CV). Currently available RTX molecules include the originator drug (RTX-Or) and two biosimilars, CT-P10 and GP2013. SVV are rare and only few studies evaluated safety and efficacy of non-medical switch (NMS) from RTX-Or to CT-P10 [1,2,3]. No data are available about clinical use of GP2013 and switching strategies between RTX biosimilars in these conditions.

Objectives: The aim of our study was to obtain real world data about effectiveness and safety of different RTX molecules, and to evaluate switching strategies from RTX-Or to and among biosimilars for treatment of patients affected by GPA, MPA and CV.

Methods: We retrospectively evaluated clinical and laboratory data of patients affected by GPA, MPA and CV, according to specific classification criteria, and treated with RTX based on expert rheumatologist indication between 2018, date of biosimilars availability, and 2022. Specifically, C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), gamma globulins, C3, C4, Five Factor Score (FFS), Birmingham Vasculitis Activity Score version 3 (BVASv3) and concomitant rheumatologic therapy were recorded. Autoimmunity was assessed as anti-neutrophil cytoplasmic antibody (ANCA) positivity for GPA and MPA and as presence of cryoglobulins in CV. All patients were followed-up for at least 12 months and received at least two cycles of therapy with RTX-Or, CT-P10 or GP2013. NMS to RTX biosimilars was performed when clinically feasible and accepted by the patient. Any safety issue associated with RTX treatment was recorded. Clinical and laboratory data were analyzed using appropriate statistical tests with SPSS.
Results: Data on 29 patients (female No. 19 - 65,5%; mean age 56.3±15.7 years old; mean disease duration 52.3±20.1 months) were available. Ten patients started therapy with RTX-Or, and all accepted NMS to CT-P10. Nine patients were treated with CT-P10 and six accepted NMS to GP2013. Twelve patients started treatment with GP2013. At baseline and during follow-up no significant differences among laboratory and clinical data of patients treated with any RTX molecule was highlighted. All patients achieved a statistically significant reduction of mean corticosteroid dose used from 20.4±12.8 mg/day of prednisone equivalents at baseline to 5.0±2.8 mg/day at 12 months (p=0.00016), and of mean BVASv3 from 20.0±4.5 at baseline to 4.7±2.3 after 12 months (p<0.00001). On average, a reduction of CRP and ESR levels, despite a small decrement of gamma globulins level was also observed. Mean C3 and C4 level resulted normal over time. ANCA positive patients decreased from 83.3% at baseline to 35.3% after one year (p=0.0059). Cryoglobulins were still detectable in 36.4% of patients after one year of RTX treatment (p=0.0039). No severe AEs were recorded, and only two CV patients treated with CT-P10 presented mild AEs: moderate lymphopenia, resolved after temporary drug withdrawal in one subject, and mild urticaria after infusion, with no new AEs after CT-P10 retreatment in the other. Of note, no AEs were observed in our cohort after NMS.
Conclusion: Our study demonstrated comparable effectiveness and safety of RTX-Or and its two biosimilars both for induction and maintenance of remission. The effectiveness and safety of NMS for RTX in SVV is confirmed, and our results grant first time evidence for safety and maintained effectiveness of treatment in such patients also after NMS between biosimilars. This practice allows economic sustainability for healthcare systems and represents a hot topic in clinical practice.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0776 REAL-WORLD EVIDENCE ON THE LONG-TERM USE AND DRUG SURVIVAL OF MEPOLIZUMAB IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA)

Keywords: Vasculitis, Descriptive Studies, Real-world evidence

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare form of ANCA-associated vasculitis in which it is frequently difficult to achieve glucocorticoid (GC) tapering without relapse. Mepolizumab (MEPO) is an approved anti-IL5 agent for EGPA but real-world evidence of its long-term efficacy and survival is scarce.
Objectives: To study the efficacy, safety, and survival of MEPO for EGPA in daily clinical practice.
Methods: Retrospective study of all patients with EGPA who received MEPO in two academic Rheumatology centers up until January 10, 2023. Demographic and clinical data were recorded at baseline (start of MEPO) and at last follow up visit.
Results: 16 patients with EGPA treated with MEPO (females: 87.5%, mean age: 52.4 years, mean disease duration at MEPO start: 4.4 years, ANCA+: 25%) were included in the study. At baseline, the median (IQR) BVASv3 was 6 (7) and the history of EGPA systemic involvement was: lung 94%, ENT 94%, musculoskeletal 50%, heart 50%, peripheral nervous system 37.5%, skin 25% and gastrointestinal 25%. The median number of EGPA relapses before MEPO use was 2, while 11/16 (69%) had previously failed various immunosuppressive (IS) (MTX, AZA, MMF, CYC) and 3/16 (18%) omalizumab treatment. At MEPO start, all patients were on GCs (median prednisolone dose: 12.5 mg/day), while 62.5% were on IS (MMF=6, MTX=2, RTX=2). During follow-up [median (IQR)=12 (19) months], there was a statistically significant reduction in GC dose (median, from 12.5 to 2.5mg/day, p=0.002, while 3/16 (19%) patients discontinued GCs), absolute eosinophil count (mean, from 1603±1163 to 84±42, p<0.001) and BVASv3 (median, from 6 to 0, p=0.007). The cumulative drug survival at 6, 12 and 18 months was 100%, 100% and 83% respectively (Figure 1). MEPO was discontinued in 2 patients due to relapsing disease, while it was well tolerated in all patients without withdrawals for safety issues. Of note, in 3 subjects (19%) MEPO was used concurrently with rituximab (RTX) with good tolerability.
Conclusion: In this real-world study of EGPA patients, MEPO was efficacious and safe, with a high retention rate and significant GC-sparing effects. Furthermore, in almost one out of five patients it was used successfully in combination with RTX. These findings confirm the RCT data in real-life, difficult to treat patients.

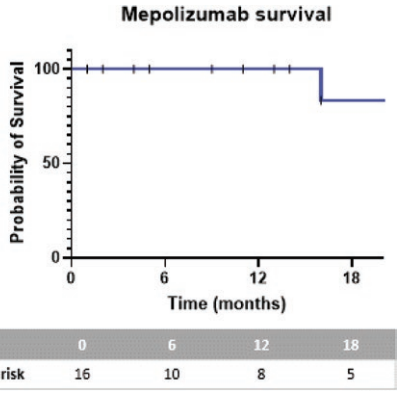


Figure 1. Mepolizumab survival (Kaplan-Meier analysis) in real-life EGPA patients

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AB0777 PERFORMANCE OF 2022 ACR/EULAR GPA, EGPA AND MPA CLASSIFICATION CRITERIA IN TURKISH VASCULITIS STUDY GROUP PROSPECTIVE COHORT (TRVAS)

Keywords: Validation, Vasculitis, Registries

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Background: External validation of the 2022 ACR/EULAR GPA, EGPA and MPA Classification Criteria is recommended by the DCVAS study group [1-3].
Objectives: Turkish Vasculitis Study (TRVaS) prospective cohort is an electronic database including 15 centres from all over Turkey. We aimed to test performance of the recent criteria sets in TRVaS cohort.
Methods: Patients diagnosed according to physicians' decisions have been recruited prospectively in TRVaS (in total 3730 patients by January 2023). 2022 ACR/EULAR and 1990 ACR Classification Criteria sets were applied to all of the patients with AAV [GPA (n=533), EGPA (n=112), MPA (n=105), and unclassified AAV (n=70)], poliarteritis nodosa (PAN, n=47) and IgA Vasculitis (n=76). Performances were analysed using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy.
Results: For the patients with GPA, 2022 criteria had higher sensitivity and specifity compared to 1990's (83.6% vs. 71.0% and 95.6% vs. 88.6%, respectively in Table). A significant increase was observed in sensitivity for 2022 criteria for patients with EGPA (86.4% vs.59.1%) with no change in specificity. Sensitivity and specificity of 2022 MPA criteria was calculated as 83.8% and 89.8%, respectively. Using the 2022 criteria to the patients with unclassified AAV, led to classify seven (10.0%) patients as GPA and 29 (41.0%) patients as MPA. Of 47 patients with PAN, one patient fulfilled 1990 ACR and another fulfilled 2022 GPA criteria. Others were not classified as EGPA or MPA. None of the patients with IgA vasculitis fulfilled 2022 AAV criteria. Of 533 patients with GPA, 1.5% fulfilled both 2022 GPA and MPA criteria and 7.7% fulfilled only MPA criteria (Figure). In each clinically diagnosed AAVs, around 10% of patients were not classified by any 2022 criteria.
Conclusion: Using 2022 ACR/EULAR Classification Criteria, improved sensitivity and specifity for GPA and sensitivity for EGPA were observed. Additionally, half of the unclassified AAV patients could be classified as either GPA or MPA. These criteria functioned well for the discrimination of patients with AAV from other small/medium vessel vasculitides such as PAN and IgA vasculitis. In total, over 80% of the patients with AAV were accordingly classified in paralel to the clinical diagnosis in each GPA/EGPA/MPA.
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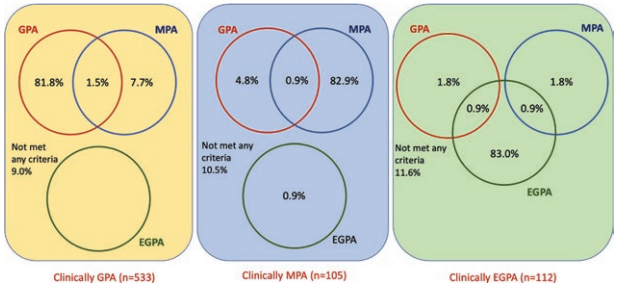


Figure. Classification of clinically diagnosed GPA/EGPA/MPA patients using 2022 ACR/EULAR criteria sets

Table. Performance of 1990 ACR and 2022 ACR/EULAR criteria

		GPA	Non-GPA AAV	EGPA	Non-EGPA AAV	MPA	Non-MPA AAV	PAN + IgAV
1990 ACR Wegener criteria	Sn/Sp	71/88.6	71/84	-	-	-	-	71/99.2
	PPV/NPV	89.3/69.6	89.6/60	-	-	-	-	99.7/44
	Accuracy	78.6	75.4	-	-	-	-	76.3
2022 ACR/ EULAR GPA	Sn/Sp	83.6/95.6	83.6/94.1	-	-	-	-	83.6/99.2
	PPV/NPV	96.3/81.2	96.5/74.5	-	-	-	-	99.8/58.2
	Accuracy	88.7	87.1	-	-	-	-	86.5
1990 Churg-Strauss criteria	Sn/Sp	-	-	59.1/100	59.1/100	-	-	59.1/100
	PPV/NPV	-	-	100/94.6	100/93.7	-	-	100/73.1
	Accuracy	-	-	95	94.2	-	-	80.6
2022 ACR/ EULAR EGPA	Sn/Sp	-	-	86.4/99.8	86.4/99.8	-	-	86.4/100
	PPV/NPV	-	-	98.9/98.1	98.9/97.81	-	-	100/89.1
	Accuracy	-	-	98.2	97.9	-	-	93.5
2022 ACR/ EULAR MPA	Sn/Sp	-	-	-	-	83.8/89.8	83.8/87.9	83.8/100
	PPV/NPV	-	-	-	-	52.1/97.7	52.1/97.2	100/87.8
	Accuracy	-	-	-	-	89.1	87.4	92.5

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AB0778

HISTOPATHOLOGIC FEATURES AND CLINICAL OUTCOMES IN PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

Keywords: Vasculitis, Clinical Trials

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Background: The main histological features of eosinophilic granulomatosis with polyangiitis (EGPA) are tissue eosinophilia (TE), small-vessel vasculitis (SVV), and extravascular granuloma. However, the relationship between these pathological findings and treatment response is not known.
Objectives: To explore the associations between pathological features of TE or SVV and the clinical parameters and treatment response in EGPA patients.
Methods: This is a single-center, retrospective, cohort study. Subjects who met the following were included for analysis: 1) those who fulfilled the 1990 ACR criteria and/or the 2012 revised CHCC criteria and/or the ACR/EULAR 2022 criteria, 2) those who were treated for at least 2 years in our hospital since 1/1/2010, 3) those who had undergone tissue biopsy at any site during their initial diagnostic workup. All available slides of biopsies were reviewed by a blinded pathologist expertise with vasculitis. Based on the EULAR recommendations, remission was defined as the absence of vasculitis activity (BVAS=0) with daily doses of prednisolone <=7.5mg after 2 years of treatment and refractory disease was defined as failure to attain remission.
Results: Among 37 patients diagnosed with EGPA, 30 patients were included. Total 84 biopsies (muscle 36, skin 15, nose 9, colon 8, stomach/duodenum 4, nerve 4, kidney 3, lung 2, heart 1, small intestine 1, and temporal artery 1) were reviewed. SVV, TE, and extravascular granuloma were found in 17 (56.5 %) patients, 16 (53.3 %) patients and 3 (10 %) patients, respectively. (Fig.1) SVV was associated with refractory disease (47.1 % vs 0 %, p=0.04). TE was associated with skin lesions (56.2 % vs 14.3%, p = 0.021) and inversely associated with severe peripheral neuropathy (43.8 % vs 85.8 %, p = 0.021). (Table.1) ANCA was present in 11 (36.7 %) patients. ANCA was not associated with refractory diseases (ANCA positive 36.3% vs ANCA negative 21.1%, p=0.31)
Conclusion: In EGPA, pathological evidence of SVV may be better predict poor treatment response than ANCA positivity.

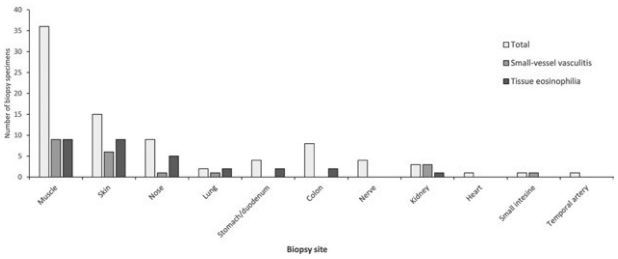


Fig.1 Biopsy sites and each number of positive pathological finding.

Table.1 Characteristics of EGPA patients with or without pathological findings.

Characteristics	Small-vessel vasculitis (SVV)			Tissue eosinophilia (TE)		
	Pts with SVV (n=17)	Pts without SVV (n=13)	P value	Pts with TE (n=16)	Pts without TE (n=14)	P value
Female sex, n (%)	9 (52.9)	9 (69.2)	0.465	8 (50.0)	10 (71.4)	0.206
Age, years, median (IQR)	62 (55-71)	57 (54-63)	0.173	60 (55-71)	58 (50-66)	0.270
Anti-MPO ANCA, n (%)	7 (41.2)	3 (23)	0.259	6 (37.5)	4 (28.6)	0.450
Anti-PR3 ANCA, n (%)	1 (5.9)	0 (0)	0.567	1 (6.3)	0 (0)	0.533
BVAS, median (IQR)	22 (13-26)	18 (15-22)	0.476	22 (13-26)	18 (15-22)	0.538
Clinical features, n (%)						
Myalgia	13 (76.5)	10 (76.9)	0.660	11 (68.8)	12 (85.7)	0.256
Cutaneous involvement	8 (47.1)	3 (23.1)	0.167	9 (56.3)	2 (14.3)	0.021
ENT involvement	15 (88.2)	8 (61.5)	0.101	13 (81.3)	10 (71.4)	0.419
Cardiac involvement	9 (52.9)	6 (46.2)	0.500	9 (56.3)	6 (42.9)	0.358
Pulmonary infiltrates	10 (58.8)	8 (61.5)	0.590	9 (56.3)	9 (64.3)	0.471
Glomerulonephritis	3 (17.6)	0 (0)	0.167	3 (18.8)	0 (0)	0.167
Gastrointestinal involvement	3 (17.6)	3 (23.1)	0.531	2 (12.5)	4 (28.6)	0.261
Severe peripheral neuropathy (MMT≦3)	10 (58.8)	9 (69.2)	0.421	7 (43.8)	12 (85.8)	0.021
Treatment response, n (%)						
Refractory disease	8 (47.1)	0 (0)	0.040	5 (31.2)	3 (21.4)	0.426

REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0779 NAILFOLD VIDEOCAPILLAROSCOPY IN ANCA-ASSOCIATED VASCULITIS

Keywords: Diagnostic Tests, Prognostic factors, Vasculitis

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Background: Nailfold videocapillaroscopy (NVC) is a simple and noninvasive tool utilized by rheumatologists for monitoring of systemic sclerosis, dermatomyositis, and Raynaud's phenomenon [1]. A capillaroscope is utilized to view the nailfold capillaries and evaluate for evidence of small vessel abnormalities, which can be seen with the aforementioned disorders. Other forms of rheumatologic disease such as ANCA-associated vasculitis (AAV) are already known to cause capillaritis. This is the proposed mechanism for some of the disease manifestations including pulmonary alveolar hemorrhage and glomerulonephritis(2, 3). We sought to clarify whether patients with AAV would have corresponding abnormalities on NVC.

Objectives:

1. Characterize NVC characteristics in patients with AAV.
2. Define the prevalence of dilated capillaries, microhemorrhages, ramifications, disorganization, and decreased density in patients with AAV compared to controls.

Methods: Patients over the age of 18 with a diagnosis of small vessel vasculitis based on Chapel Hill Criteria or confirmed on biopsy were identified for inclusion in the trial and invited to participate. Patients with co-existing disorders that are felt to impact NVC results were excluded: dialysis dependence, type 2 diabetes mellitus, Raynaud's phenomenon, CTD, acrocyanosis, erythromelalgia, recent manicure or hand trauma, routine use of vibratory tools, psoriasis, bleeding disorder, or exposure to toluene or benzoyl. NVC was performed at the time of enrollment. A semiquantitative scale calculated by 2 providers was used to score several parameters including enlarged or giant capillaries, hemorrhages, capillary density, disorganization, or ramifications. We compared baseline characteristics and NVC Scores of patients with AAV to non-AAV controls using a Wilcoxon rank sum test for continuous and ordered variables. Fisher's exact test was utilized for categorical variables.

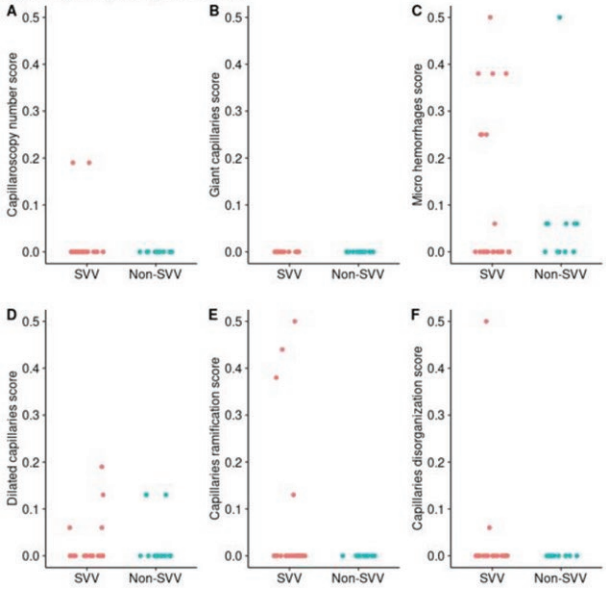
Results: Twenty-four patients with small vessel vasculitis and 13 control patients were enrolled. One patient with cryoglobulinemic vasculitis was excluded. Baseline assessment reported in ***Table 1***. Patients with AAV tended to be older than the non-AAV controls (median 58 years vs. 40 years). Among patients with AAV, 58% were female, 83% ANCA positive. C-ANCA present in 43%, PR3 in 48%, P-ANCA in 35% and MPO in 35%. Four of the 23 patients (17.4%) had an active flare within 90 days prior to NVC assessment. We did not observe any statistically significant difference in NVC scores between AAV patients and non-AAV controls (all P>0.12, ***Table 2***, ***Figure 1***). Some non-specific NVC changes were observed in the AAV group such as ramifications and decreased density which were not observed in the control group though these did not reach statistical significance.

Conclusion: ANCA-associated vasculitis was not strongly associated with NVC abnormalities. Some non-specific changes were observed, and further research may help identify whether these abnormalities correlate with specific disease manifestations or disease activity.

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Figure 1. Jitter plots of NVC scores



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Disclosure of Interests: None Declared.
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AB0780 TIME MANAGEMENT AND RISK FACTORS IN LIFE-THREATENING ANCA-VASCULITIS

Keywords: Vasculitis, Prognostic factors, Organ damage

Table 1. Baseline characteristics

	Small Vessel Vasculitis (SVV) (N = 23)	Control (non-SVV) (N = 13)	p value
Age			0.004
Median (Q1, Q3)	56 (48,66)	40 (34, 50)	
Ethnicity			1.000
Hispanic or Latino	1 (4%)	0 (0%)	
Non-Hispanic or Latino	21 (91%)	13 (100%)	
Unknown or not reported	1 (4%)	0 (0%)	
Gender			0.501
Male	10 (43%)	4 (31%)	
Female	13 (57%)	9 (69%)	
Diagnosis			
GPA	13 (57%)		
EGPA	4 (17%)		
MPA	3 (13%)		
Unspecified AAV	3 (13%)		
ANCA Positive	19 (83%)		
C-ANCA	10 (43%)		
PR3	11 (48%)		
P-ANCA	8 (35%)		
MPO	8 (35%)		

GPA – granulomatosis with polyangiitis; EGPA – eosinophilic granulomatosis with polyangiitis; MPA – microscopic polyangiitis; AAV – ANCA associated vasculitis; PR3 – Proteinase 3; MPO – Myeloperoxidase

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Background: Accuracy of diagnosis and prompt therapeutic intervention are the mainstay in patients with ANCA-associated vasculitis(AAV) suffering from life-threatening complications [1].However, there is no definition of therapeutic window in vital AAV, nor its impact on patient outcome regarding length of hospital stay, intensive care unit(ICU) admission or survival.
Objectives: The aim of the study is to analyze the process of care from the perspective of time management in vital organ involvement AAV patients and to identify potential risk factors for ICU admission.
Methods: A retrospective multicenter study identified AAV patients with life-threatening organ involvement, defined as alveolar hemorrhage, rapidly progressive renal failure, myocarditis and cerebral granuloma. Demographic data was collected. Key time frames were recorded, namely the interval from acute symptom onset to hospital presentation, days until imaging(plain X-ray, cardiac ultrasound, CT-scan), time to therapeutic intervention with corticosteroids or biologic/non-biologic immunosuppression(cyclophosphamide or rituximab) and to renal replacement therapy(RRT) or plasmapheresis. Time to ICU admission, hospital length-of-stay, Birmingham Vasculitis Activity Score(BVAS) were also noted. Statistical analysis was performed using SPSS and Chi-square and Pearson correlation tests were applied.
Results: 66 patients with AAV were enrolled, out of which 17 fulfilled inclusion criteria. Mean age in the study group was 58.6±11.1 years old,10 patients(58.8%) were females and 7 (41.2%) males.11(64.7%) patients were c-ANCA positive, while 6 (35.3%) had p-ANCA and all were diagnosed with AAV prior to life-threatening event. Two patients had COVID-19 triggered AAV.In the study group, the most frequent critical organ suffering was rapidly progressive renal failure(12), followed by alveolar hemorrhages(10), 2 cerebral granulomas and one acute myocarditis. Three patients(17.6%) had more than one vital manifestation. Ten patients(58.8%) had more than three additional non-organ-threatening manifestations. Mean interval from AAV diagnosis to emergency admission was 30.1± 61.1 days, median 3 and from severe episode onset to hospitalization 1.65±0.18 days, median 1. There was only one death in the study group. Three patients were admitted in the ICU in 0.59±1.5 days following hospital presentation and required either RRT or plasma exchange within 2.66 days. Imaging examination was performed unanimously the day upon hospital admission. All patients received corticosteroids in the first 5.95±14.3 days, while immunosuppression was given to 13(76.5%) patients within 11.5±15.5 days from hospitalization.12 patients(70.5%) suffered from associated infections. Mean BVAS(13.6±6.76) correlated to ICU admission(p 0.013, r 0.58).Patients in ICU revealed higher BVAS(22±9.53) versus non-ICU(11.8±4.76).Hospital length of stay was 14.7±10.7 days(median 14) and showed no relationship to the type of severe organ involvement. The need for ICU caring was dominant in males(p 0.05) and confirmed in patients with proteinuria(p 0.012) and at least two major organ damage.
Conclusion: This study shows that severity risk factors for potential ICU admission for life-threatening AAV appear to be male gender, proteinuria and the number of affected organs.Moreover, BVAS should be considered a useful tool to predict patients' risk for intensive care management since a higher score indicates a more aggressive disease.However, time to investigational or therapeutic intervention did not correlate to patient outcome in AAV.
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AB0781 LARGE VESSEL INVOLVEMENT IN ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

Keywords: Vasculitis, Outcome measures, Descriptive Studies

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Background: Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) is currently categorized under the small vessel vasculitides and includes granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA) [1]. There is limited knowledge about large vessel involvement in AAV (L-AAV); mainly described in case reports and small series. L-AAV can involve temporal arteries (TA-AAV), aorta (A-AAV), and periaortic soft tissue (PA-AAV).
Objectives: The objective of this study was to investigate the characteristics of L-AAV.
Methods: Patients older than 18 years at diagnosis of TA-AAV, A-AAV and PA-AAV seen at a single institution between January 1, 2000, and December 31, 2021, were identified through a proprietary medical text search algorithm. Patients were included if diagnosed with L-AAV by the treating physician, fulfilled 2022 American College of Rheumatology/ European Alliance of Associations for Rheumatology classification criteria for GPA, MPA or EGPA, had positive ANCA, and had more than one outpatient or inpatient visit. Arteritis of the temporal artery was based on histopathology whereas the diagnosis of aortitis and periaortitis could be either based on radiology or histopathology.
Results: The study cohort consists of 36 patients with L-AAV. Of those, 23 had p-ANCA/ MPO-ANCA and 13 had c-ANCA/ PR3- ANCA. Mean (SD) age at AAV diagnosis was 63.4 (12.79); 20 (56%) were male. Seventeen patients had TA-AAV, 10 had A-AAV and 9 had PA-AAV (Table 1). Most of the patients (n=25, 69%) were diagnosed with large vessel involvement and AAV within a one-year timespan. Inflammatory markers were elevated at the time of diagnosis of large vessel involvement. Twenty-five (69%) patients had histopathologic confirmation of AAV diagnosis. There was no overlap between TA-AAV, A-AAV and PA-AAV groups. Of the 17 patients with TA-AAV, 6 had inflammation of a temporal artery branch vessel. The most frequent site of involvement in the A-AAV group was the ascending thoracic aorta, whereas in the PA-AAV group, the abdominal aorta was most frequently involved. Glucocorticoids (36/36), rituximab (19/36), and methotrexate (18/36) were the most frequent treatments. During the study period 8 patients died (4 in TA-AAV, 3 in A-AAV, and 1 in PA-AAV). There was no difference in mortality between this cohort of L-AAV patients and the general population (standardized mortality ratio: 0.98; 95% CI, 0.42- 1.93).
Conclusion: This is the largest single-center cohort of patients with L-AAV to date. Clinicians should consider L-AAV in the differential diagnosis of vasculitides especially in the context of positive ANCA and atypical organ manifestations.
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Table 1. Features of L-AAV cohort

	Temporal Artery Vasculitis (N=17)	Aortitis (N=10)	Periaortitis (N=9)	Total (N=36)
Demographics				
Mean (SD) age at AAV diagnosis	68.8 (7.07)	56.2 (16.64)	61.2 (13.05)	63.4 (12.79)
Sex, male n (%)	9 (53)	4 (40)	7 (78)	20 (56)
Race, white n (%)	17 (100)	9 (90)	7 (78)	33 (92)
Duration of follow-up from AAV diagnosis years, median (IQR)	4.5 (0.1- 12.6)	9.5 (2.2 – 16.9)	4.7 (1.8 – 6.2)	4.7 (1.0 – 11.8)
AAV				
GPA, n (%)	3 (18)	6 (60)	6 (67)	15 (42)
MPA, n (%)	13 (76)	4 (40)	3 (33)	20 (56)
EGPA, n (%)	1 (6)	0 (0)	0 (0)	1 (3)
Histological confirmation of AAV, n (%) *	11 (65)	6 (60)	8 (89)	25 (69)
Clinical manifestations before or at AAV diagnosis				
Constitutional symptoms, n (%)	16 (94)	6 (60)	7 (78)	29 (81)
Cutaneous, n (%)	1 (6)	1 (10)	0 (0)	2 (6)
Mucous membranes/ eyes, n (%)	1 (6)	2 (20)	1 (11)	4 (11)
ENT, n (%)	5 (29)	8 (80)	5 (56)	18 (50)
Cardiovascular, n (%)	1 (6)	0 (0)	0 (0)	1 (3)
Gastrointestinal, n (%)	0 (0)	1 (10)	0 (0)	1 (3)
Pulmonary, n (%)	5 (29)	2 (20)	5 (56)	12 (33)
Renal, n (%)	6 (35)	0 (0)	4 (44)	10 (28)
Nervous system, n (%)	8 (47)	1 (10)	0 (0)	9 (25)

*Histological confirmation of AAV, other than large vessel pathology

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Johnson & Johnson, Consultant of: AstraZeneca, ChemoCentryx, Grant/research support from: Genentech, AstraZeneca, GSK, Bristol Myer Squibb, Kenneth J Warrington Consultant of: Chemocentryx, Sanofi, Grant/research support from: Eli Lilly, Kiniksa, GSK.

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AB0782 RISK FACTORS FOR SERIOUS INFECTION IN PATIENTS WITH MICROSCOPIC POLYANGIITIS: RESULTS FROM THE REVEAL COHORT

Keywords: Real-world evidence, Vasculitis

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Background: Many studies have reported risk factors for infection in ANCA-associated vasculitis, but the consistency of these risk factors varies between studies [1-5]. In addition, few reports have focused specifically on patients with microscopic polyangiitis (MPA) or have focused on the impact of glucocorticoids (GC) reduction on the risk of infection.

Objectives: In this study, we aimed to examine risk factors of serious infections (SI) in patients with MPA in the REVEAL cohort, a Japanese multicenter cohort. As one of the risk factors, we also focused on the pace of GC reduction.

Methods: 181 MPA patients hospitalized for induction therapy and followed for at least three months were recruited from the REVEAL cohort. We evaluated the demographic, clinical, and laboratory findings, and treatments. To assess the pace of GC reduction, GC doses at 3, 12, and 24 months were extracted, and the ratio of each to the initial dose was calculated. Univariate analysis and COX regression analysis were performed to identify risk factors for SI, defined as infections requiring hospitalization in these patients. Gray test was performed for the comparison of the cumulative incidence of SI between groups.

Results: There were 115 patients without SI and 66 patients with SI. Univariate analysis showed that age, smoking index, CRP, and GC dose ratio (3 months/initial dose) were associated with SI. In the COX regression analysis (shown in Table 1), age, CRP, and GC dose ratio (3 months/initial dose) were identified as significant risk factors (p values are <0.005, <0.005, and 0.04, respectively). In addition, the group with GC dose ratio (3 months/initial dose) ≥ 0.4 had significantly higher cumulative incidence of SI than the other group (p=0.032) (shown in Figure 1).

Conclusion: Age, CRP, and GC dose ratio (3 months/initial dose) were identified as risk factors for SI in MPA patients.

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Table 1

	Odds ratio [95% CI]	p value
Age (years)	**1.08 [1.04-1.12]**	**<0.005**
Sex (Female)	**0.57 [0.30-1.07]**	**0.08**
Smoking index	**1.00 [1.00-1.00]**	**0.26**
CRP	**1.08 [1.03-1.13]**	**<0.005**
GC dose ratio (3 months/initial dose)	**6.53 [1.08-39.52]**	**0.04**

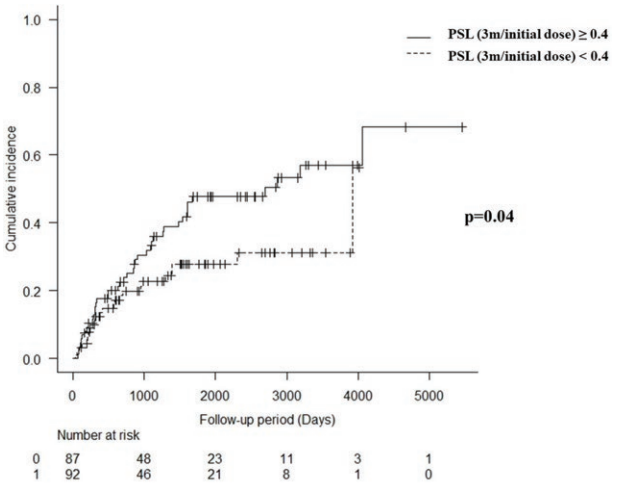


Figure 1

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AB0783 RISK FACTORS IN HENOCH-SCHÖNLEIN PURPURA NEPHRITIS

Keywords: Vasculitis, Prognostic factors, Kidneys

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Background: Henoch - Schönlein purpura (HSP) is an immuno-mediated small-vessel vasculitis that manifests as non—thrombocytopenic purpura, arthritis or arthralgia, abdominal pain and/or kidney involvement. HSP nephritis can presented is micro- or macroscopic hematuria, proteinuria, nephrotic or nephritic syndrome, as well as acute renal failure {1,2}.

Objectives: The aim of the study is to identify risk factors associated with unfavorable outcomes in patients with HSP nephritis.

Methods: This retrospective study enrolled 68 patients with HSP nephritis. Renal and extra-renal symptoms were analyzed. A diagnosis of HSP nephritis was made when hematuria and/or proteinuria, and/or renal failure was associated with a palpable purpuric eruption or abdominal or joint pains (at least two of these three clinical signs) and predominant mesangial IgA immune deposits, confirmed by renal biopsy. The patients were subdivided into five classes according to the renal manifestation at onset of disease: 1) micro- or macroscopic hematuria; 2) mild proteinuria (<1 g/L) ± hematuria; 3) acute nephritic syndrome, defined as moderate proteinuria, hematuria, increased serum creatinine and/or hypertension; 4) nephrotic syndrome; 5) mixed nephritic-nephrotic syndrome.

Results: Of 68 patients with HSP nephritis, diagnosed by kidney biopsy, 41 (60,29 %) were male and 27 (39,71 %) - female. Age of onset was between 18 and 66 years (mean 37,28 ± 9,34). Duration of follow-up was between 2 and 28 years. 29 patients had histories of infection preceding presentation. At onset all patients had palpable purpura and urinary abnormalities (only hematuria - in 16,18 %; mild proteinuria ± hematuria – in 44,12 %; moderate or severe proteinuria and hematuria – in 39,70 %). Arthralgias were present in 49 patients (72,06 %), gastrointestinal involvement – in 32 patients (47,05 %). Renal function was impaired in 26,47 % of patients, and 51,47 % were hypertensive. Mesangial hypercellularity lesions were found in most patients (97,06 %), endocapillary proliferation – in 20,58 %, segmental sclerosis – in 32,35 %, tubular atrophy/interstitial fibrosis – in 38,23 %. Corticosteroids and cyclophosphamide were prescribed in patients who presented with severe clinical and histological features and/or rapidly progressing renal disease. During follow-up classical extra-renal organ diseases were seen in 55,88 % of patients, and hematuria and/or proteinuria – in 77,94 %. At final review 26,47 % had progression of renal failure. Risk factors for renal failure were moderate or severe proteinuria during follow-up ($p<0,001$), renal impairment at presentation ($p<0,001$), hypertension at presentation and during follow up ($p<0,05$), crescents, interstitial fibrosis and tubular atrophy ($p<0,001$). No significant difference in renal outcome was observed between patients who had relapses in extra-renal organs versus in those who did not.

Conclusion: Our results indicated that lower GFR, nephrotic syndrome, nephritic-nephrotic syndrome and crescentic nephritis were risk factors for unfavorable outcomes.

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Disclosure of Interests: None Declared.

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AB0784 SKULL BASE INFILTRATION AS A MANIFESTATION OF GRANULOMATOSIS WITH POLYANGIITIS

Keywords: Rare/orphan diseases, Organ damage, Vasculitis

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Background: Although upper respiratory symptoms are the most frequent localization of granulomatosis with polyangiitis (GPA) [1], infiltration of the skull base is rare.

Objectives: The aim of this analysis was the clinical characteristic of GPA patients' skull base involvement.

Methods: The retrospective analysis was performed on patients diagnosed in tertiary academic referral center (Medical University of Gdansk, Poland) between 1990 and 2022 due to GPA. Medical database of 232 GPA vasculitis patients were retrospectively reviewed, and demographics, serological, and clinical features of the patients presenting skull base infiltration throughout the disease course were recorded. Comparisons of disease characteristics and long-term outcomes were performed between patients with and without this manifestation.

Results: Among 232 patients (121 males, median age 52,5 years, 87% ANCA positive, 12,5% localized, 87,5% systemic), seven patients presented skull base infiltrations as a manifestation of GPA. It was 4 women and 3 men, aged between 27 and 72. Four patients were cANCA positive, 1 patient had atypical pANCA and 2 patients were ANCA negative. In six of them it was a first manifestation of vasculitis. Clinical characteristic of patients is summarized in table. Statistical analysis showed that patients with skull base involvement and those without this manifestation differed only in the frequency of ocular involvement - in patients with skull base infiltration, ocular involvement occurred in all cases, while among patients without infiltration it occurred in only 34.5 per cent of subjects. In terms of other parameters, there were no statistically significant differences between the groups.

Conclusion: Skull base infiltrations presenting mainly as cranial nerve palsies is rare presentation of GPA. In most of patients it is one of the first symptoms of vasculitis. It can occur in both ANCA positive and ANCA negative cases.

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Table. Clinical characteristics of 7 patients with skull base infiltrations.

Case no.	Age (years)	sex	ANCA status	Clinical manifestation	CN palsy	Organ involvement	Histopathological confirmation (localization)	Treatment	Outcome
1	46	F	cANCA	headache, dizziness, double vision	III, V, VI	N, S, E, L, SK, eye, J	Yes (nose)	GKS, CYC	remission
2	52	F	cANCA	hearing loss, blindness, headache	II	E, SK, eye	No	GKS, CYC	remission
3	39	F	Atypical pANCA (anti elastase)	headache, dizziness, hearing loss, dysphagia	V, IX, X, XI, XII	L, SK, eye	No	GKS, CYC	remission
4	39	M	cANCA	headache, loss of smell	VII, IX	O, J, eye	Yes (oral cavity)	GKS, CYC	remission
5	72	M	ANCA negative	Headache, dizziness, double vision Hearing loss	II, VI,	S, E, SK, CNS, eye	No	GKS, CYC, RTX	death (infectious)
6	27	F	cANCA	Headache, dizziness, loss of smell, dysphagia	IX, X	P, E, O, L, J, eye	Yes (lungs)	GKS, CYC	death (active GPA)
7	35	M	ANCA negative	exophthalmos, headache, eyelid infiltration	no	K, N, S, J, SK, eye	Yes (sinus, eyelid, tumor orbitea)	GKS, CYC, radiotherapy	death (gastrointestinal bleeding)

N – nose, S – sinuses, E – ear, O – oral cavity, P – pharynx, PNS – peripheral nervous system, CNS – central nervous system, L – lungs, K – kidney, SK – skin, J – joints; GKS – corticosteroids, CYC – cyclophosphamide, RTX – rituximab; CN – central nerve; F - female, M – male; ANCA - anti-neutrophil cytoplasmic antibodies, cANCA - cytoplasmic ANCA, pANCA - perinuclear ANCA

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0785 ASSOCIATED FACTORS TO REMISSION IN PATIENTS WITH UVEITIS RELATED TO BEHÇET DISEASE TO THE FIRST THERAPEUTIC SCHEME

Keywords: Behcet's disease, Uveitis, Remission

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Background: Behcet's disease (BE) is a systemic venous and arterial vasculitis of unknown etiology [1]. Ocular involvement is common, affecting 40-70% of patients [2], and is the main cause of morbidity. Uveitis is the most frequent common ocular clinical presentation, with a prevalence that can reach up to 90% of cases, affecting the anterior and posterior segments of the eye. Among 16-25% of the cases end in blindness, so early detection and treatment are essential [3].

Objectives: To describe the characteristics of uveitis in EB, extraocular manifestations, therapeutic lines used, and to compare the factors associated with uveitis remission to the first therapeutic scheme. In addition, evaluate the adherence to the EULAR 2018 recommendations.

Methods: Multicenter, observational, retrospective cohort study. Patients over 18 years of age with EB according to the 2014 ICBD criteria and uveitis according to the Uveitis Nomenclature Standardization Working Group (SUN). Disease remission was defined if the patient met the SUN criteria for ocular remission and if the rheumatologist did not have to change the immunosuppressant due to extraocular involvement.

Results: Fifty-five patients were included, 69.1% were men, with a mean age at diagnosis of 33.7 (SD 11.4) years old, mean age at uveitis presentation

of 37.1 (SD 19.6) years old, and a median follow-up of 2.5 (IQR 7.2) years. HLA-b51 was positive in 13/15 (86.7%). The most frequent presentation was panuveitis (49%), bilateral (69.1%) and chronic (59.6%) affectation; the first-line treatment was azathioprine (45%). According to the variables studied, acute presentations responded better to the initial therapeutic scheme (41% vs 8.3%, p 0.01) and a history of thrombosis was associated with greater refractoriness (16.7% vs 0%, p 0.03). Table 1 shows the comparison in terms of remission or refractoriness to the first therapeutic line. In relation to the year of uveitis diagnosis, 21 cases occurred after the publication of the recommendations, and adherence to the first line was observed in 66.7%. Also, a comparison was made to find out if the physician who adhered to the EULAR recommendations had a higher probability of remission, but this was not statistically significant (66.7% vs 42.9%; p 0.99). Sequelae were observed in 11/44 patients: 1 glaucoma, 3 retinal scars, 3 blindness, and 4 cataracts. The mean visual acuity of the right eye and left eye at the first visit was 6.8 (SD 3.6) and 6.6 (SD 3.7); and in the last visit, 7.4 (DE 3.5) and 7.1 (DE 3.4), respectively.

Table 1.

Characteristics	Refractory to the first scheme n= 24 (43.6%)	Remission with first scheme n= 31 (56.4%)	p value
Anterior. U, n (%)	6 (25)	12 (38.7)	0.28
Intermediate. U, n (%)	3 (12.5)	6 (19.3)	0.49
Posterior. U, n (%)	0	1 (3.2)	0.99
Panuveitis. U, n (%)	15 (62.5)	12 (38.7)	0.08
Bilateral, n (%)	19 (82.6)	19 (61.3)	0.13
Súbita, n (%)	14 (58.3)	7 (33.3)	0.09
Acute, n (%)	2 (8.3)	13 (41.9)	0.01
Chronic, n (%)	17 (70.8)	14 (45.16)	0.06
Recurrent, n (%)	5 (20.8)	1 (3.2)	0.07
Thrombosis, n (%)	4 (16.7)	0	0.03
Azathioprine, n (%)	14 (58.3)	13 (41.9)	0.22

Conclusion: In this multicenter cohort of patients with uveitis associated with EB, the most frequent form of presentation was panuveitis, as well as bilateral involvement and chronic forms. Approximately half of the patients achieved remission with the first therapeutic scheme line, regardless of the selected immunosuppressant. The acute forms could be associated with a higher probability of remission, while the history or presence of thrombosis would seem to be related to greater refractoriness. The therapeutic management presented high consistency with the current recommendations.

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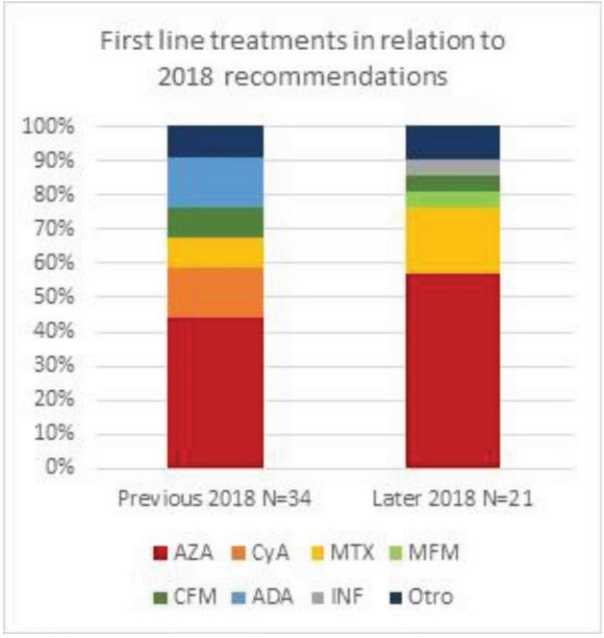


Figure 1

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AB0786

INDUCTION THERAPY WITH RITUXIMAB ENABLES SUSTAINED REMISSION IN ELDERLY PATIENTS WITH RELAPSED ANCA-ASSOCIATED VASCULITIS: A RETROSPECTIVE ANALYSIS FROM J-CANVAS, A JAPANESE MULTICENTRE-COHORT

Keywords: Vasculitis

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Background: Rituximab (RTX) is widely used in both remission induction and maintenance therapy for the new-onset ANCA-associated vasculitis (AAV)[1]. However, few studies have reported the efficacy and safety of RTX against relapsed AAV, especially in elderly patients.
Objectives: To clarify the effectiveness and safety of RTX as a remission induction therapy after relapse in elderly AAV.
Methods: We retrospectively extracted elderly (≥65 years) patients who relapsed granulomatosis with polyangiitis or microscopic polyangiitis and received remission induction therapy from J-CANVAS, a Japanese multicentre-cohort. The main exposure was the usage of RTX in the therapy. Clinical and laboratory variables at relapse and complete remission (CR) rates at week 24 and 48 after starting induction therapy were compared between patients treated with RTX (RTX group) and those with the other conventional immunosuppressive therapies (non-RTX group). The primary outcome was the CR rates at week 24, which was defined as Birmingham Vasculitis Activity Score (BVAS) version3 = 0. In addition, we performed a multivariate logistic regression analysis after adjusting for the potentially confounding factors of age, AAV-subtype, and ANCA-serotype. Patients whose data were missing at week 24 or 48 were treated as non-CR.

Results: A total of 71 patients were enrolled; 30(42%) in RTX group and 41(58%) in non-RTX group. Baseline characteristics were comparable between two groups as shown in Table1. The median age was 74 vs. 76 years with the PR3-ANCA positivity rate of 23% vs. 17%, and the median BVAS score was 11 vs. 12 points, respectively. The CR rate at week 24 was higher in the RTX group than in the non-RTX group [21(70.0%) vs 27(65.8%), p = 0.308)] and that at week 48 was significantly higher in the RTX-group [24(80.0%) vs 19(46.3%), p = 0.004)] (shown in Figure 1), with comparable doses of concomitant glucocorticoids. The adjusted odds ratios of RTX use for CR at week 24 and 48 were 1.09 (95%CI 0.38-3.10) and 4.01 (95%CI1.29-12.30). The incidence of serious infection was similar in both groups: [4(13.3%) vs 4(9.8%), p=0.638)].

Conclusion: RTX may be superior, with well tolerability, to the other conventional immunosuppressive therapies as an induction therapy in elderly patients with relapsed AAV.

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Table 1: Baseline characteristics of the enrolled patients

	Overall (N=71)	RTX group (N=30)	Non–RTX group (N=41)	P-value
Age (years), median (IQR)	75(71-80)	74(71-80)	76(71-82.5)	.263
Sex (female), n (%)	37(52.1)	13(43.3)	24(58.5)	.205
AAV subtype, n (%)				.133
GPA	26(36.6)	14(46.7)	12(29.3)	
MPA	45(63.4)	16(53.3)	29(70.7)	
ANCA serotype, n (%)				.782
PR3-ANCA	14(19.7)	7(23.3)	7(17.1)	
MPO-ANCA	54(76.1)	22(73.3)	32(78.0)	
both negative	3 (4.2)	1(3.3)	2(4.9)	
Glucocorticoid dose (PSL equivalent), median(IQR)	9(5-15)	8.3(5-11.8)	10(5.5-15)	.373
Prior treatment regimen, n(%)				
Cyclophosphamide	4(5.6)	3(10.0)	1(2.4)	.172
Mycophenolate mofetil	14(19.7)	2(6.7)	2(4.8)	.747
Azathioprine	18(25.4)	10(33.3)	8(19.5)	.186
Methotrexate	3(4.2)	2(6.7)	1(2.4)	.382
Mizoribine	5(7.0)	1(3.3)	4(9.8)	.296

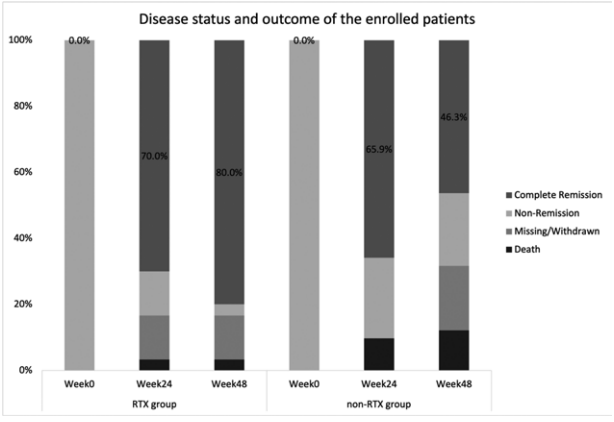


Figure1 : Disease status and outcome of the enrolled patients

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0787

INTRAVENOUS IMMUNOGLOBULIN IN ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS. BIRMINGHAM VASCULITIS ACTIVITY SCORE OUTCOME IN THE DIFFERENT SUBTYPES

Keywords: Outcome measures, Vasculitis, Patient reported outcomes

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Background: Anti-neutrophil cytoplasmic antibodies (ANCA) associated vasculitis (AAV) includes granulomatosis with polyangiitis (GPA), Eosinophilic granulomatosis with polyangiitis (EGPA) and microscopic polyarteritis (MPA). AAV may be refractory to standard immunosuppressive treatment, that also may be accompanied by significant adverse events. Intravenous immunoglobulins (IVIG) may constitute a therapeutic alternative in these cases.

Objectives: To compare the effectiveness and safety of IVIG in the Birmingham Vasculitis Activity Score (BVAS) outcome on each type of clinical phenotype (GPA, EGPA and MPA).

Methods: Observational study of patients with AAV from a referral center treated with IVIG from January 2000 to December 2021. AAV diagnosis was based on a compatible clinical presentation, positive ANCA serology and/or histology. Disease activity was assessed with the Birmingham Vasculitis Activity Score (BVAS). All of them were measured at 1 month, 6 months, 1 and 2 years after IVIG onset. IVIG schedule was 2g/kg administered in 1-5 days.

Results: We included a total of 28 patients (13 females/15 males) with a mean±SD age of 57.1±18 years. The most frequent type of AAV was GPA (n=15, 53.6%), followed by MPA (n=10; 35.7%) and EGPA (n=3, 10.7%). The main features are summarized in **Table**. The reasons for using IVIG were: **a)** relapse or refractory disease (n=25); **b)** the presence (or suspicion) of infection (n=3); and **c)** both causes (n=5). The doses of IVIG were: 0.4 g/kg/day (5 days) (n=16), 0.5 g/kg/day (4 days) (n=8), and 1 g/kg/day (2 days) (n=4). There was an important, rapid and similar improvement on the BVAS score rate on each clinical phenotype **(Figure).** Three (10.7%) patients developed mild adverse events: headache (n=2), hypertension (n=1), and cutaneous rash (n=2). One patient developed congestive cardiac failure and had to stop the IVIG therapy.

Conclusion: IVIG are equally effective in AAV regardless of the vasculitis subtype.

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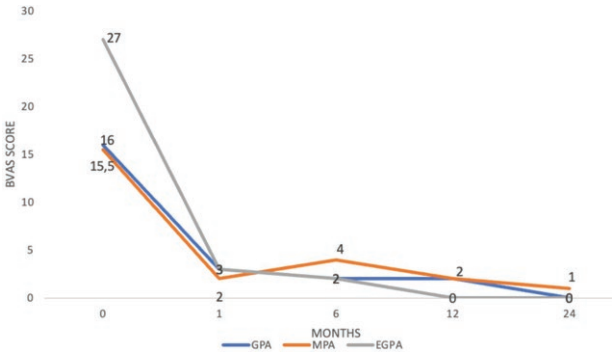


Figure. BVAS outcome accordingly to AAV phenotype.

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TABLE. General features of 28 patients with AAV treated with IGIV.

GENERAL FEATURES	ALL SERIES n=28	GPA n=15	MPA n= 10	EGPA n= 3
Age (years) of diagnosis of AAV, mean±SD	57.1±18	51.8±16.9	68.5±14.8	45.7±17.9
Men/ Women; n, (% men)	15/13 (53.6)	7/8 (46.7)	5/5(50)	3/0
FFS at AAV diagnosis, n (%)				
0	10 (35.7)	9(60)	1 (10)	0
≥1	18 (64.3)	6(40)	9(90)	3 (100)
ANALITICAL FINDINGS				
CRP (mg/dL), median [IQR]	11.5 [3.2-23.8]	10.3[0.6-16.5]	15.4[6.45-29]	13.1[2.2-19]
ESR, mm/1st hour, median [IQR]	61 [47-110]	54[33-80]	87[56.2-125.5]	65[48-112]
Anti PR3-ANCA, n (%)	11 (39.3)	11(73.4)	0	0
Anti MPO-ANCA, n (%)	12 (42.8)	2(13.3)	8(80)	2(66.7)
ANCA negative, n (%)	5 (17.8)	2(13.3)	2(20)	1(33.3)
BVAS, median [IQR]	16.5 [12-20]	16[11-19]	15.5[12-17.8]	27[25.5-28.5]
IVIG THERAPEUTIC REGIMENS, n (%)				
IVIG alone	7 (25)	5(33.3)	1(10)	1(33.3)
IVIG with corticosteroids	7 (25)	3(20)	4(40)	0
IVIG with other therapies	14 (50)	7(46.7)	5(50)	2(66.4)

AAV: anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis; ANCA: Antineutrophil cytoplasmic antibody; BVAS: Birmingham Vasculitis Activity Score; CRP: C-Reactive protein; dL: deciliter; EGPA= Eosinophilic granulomatosis with polyangiitis; ESR: erythrocyte sedimentation rate; FFS: Five-Factors Score; GPA=Granulomatosis with polyangiitis (Wegener`s disease); IQR: Interquartile range; IVIG= Intravenous immunoglobulins; mg: milligram; mm: millimeter; MPA= Microscopic polyangiitis; MPO-ANCA= ANCA specific for myeloperoxidase; n=Number; PR3-ANCA= ANCA specific for proteinase 3; SD: Standard Deviation.

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AB0788

FLOW CYTOMETRY ANALYSIS OF IMMUNE CELLS IN PATIENTS WITH BEHCET'S SYNDROME: A REAL-WORLD STUDY IN CHINA

Keywords: Real-world evidence, Behcet's disease

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Background: Behcet's syndrome (BS) is an autoimmune disease characterized by recurrent mucocutaneous ulcerations, vascular and nervous system involvement. While there have been a lot of researches proving that immune cells play a vital role in rheumatic disease, opinions on the effect of different immune cell subsets on BS is inconsistent. Therefore, we performed this real-world study to explore the role of immune cells in the pathogenesis of BS.

Objectives: To investigate the changes in the levels of several immune cell subsets in BS, and the correlation between the levels of different immune cell subsets and clinical features in patients with BS.

Methods: This is a retrospective, single-center study conducted in Beijing. 136 patients diagnosed with BS in rheumatology and immunology department of Peking University People's Hospital from 2018 to 2021 and 114 healthy controls (HCs) were enrolled. All patients met the International Criteria for Behcet's Disease (ICBD). We utilized flow cytometry to test the levels of $CD4^+$ T cells, $CD8^+$ T cells, B cells, NK cells and several subsets of $CD4^+$ T cells. Wilcoxon rank test and student's *t*-test were used and a P-value <0.05 was considered statistically significant.

Results: Compared to HCs, there is a decrease in the count of $CD4^+$ T cells, B cells and NK cells in BS patients. A significant increase in the frequency of IFN-γ, IL-2 and IL-4 producing $CD4^+$ T cell in BS patients were observed, which accompanied by a decreased frequency of Naïve $CD4^+$T cells. The frequency of $Foxp3^+$ Treg cells was notably increased while the proportion of CLA^+ Treg in Treg cells was significantly decreased in BS patients. BS patients' frequency of follicular helper T cells were apparently lower than HCs. There was a significant reduction of the frequency of Treg in patients with vascular involvement. The frequency of follicular helper T cells were positively correlated with joint involvement and negatively correlated with nerve involvement in BS patients. Patients with gastrointestinal involvement had a increased frequency of TNF-α, IFN-γ, IL-2 and IL-4 producing $CD4^+$ T cells and a decreased level of B cell count. Elevated level of NK cell count and decreased frequency of TNF-α, IL-2 producing $CD4^+$ T cells were found in patients with skin-mucosa involvement alone.

Conclusion: Our study confirmed that Th1 cells, Th2 cells, Treg cells, follicular helper T cells, B cells and NK cells contribute a lot to the pathogenesis of BS.

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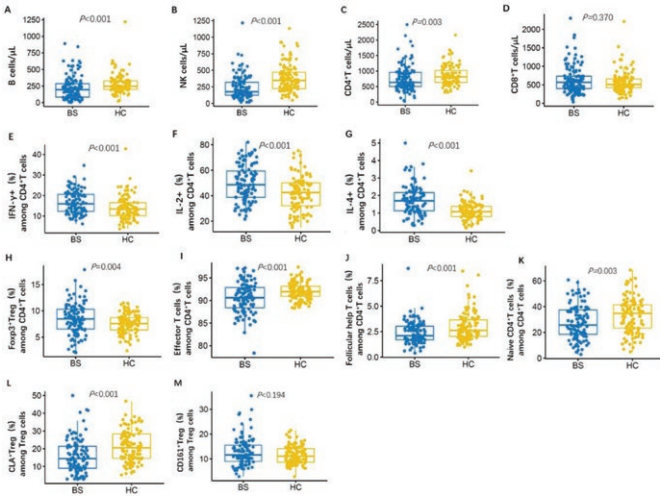


Figure : The level of different immune cells in patients with BS and healthy controls.

Table : Correlation of immune cells and clinical manifestation in patients with BS.

	Patients with skin-mucosa involvement alone	Patients with more than skin-mucosa involvement	*P*
TNF-α (%)	33.17±11.31	44.20±12.37	0.010
IL-2 (%)	43.58±14.46	52.41±13.63	0.004
NK cell (/μL)	302.86±222.00	209.89±148.46	0.006
	Patients with joint involvement	**Patients without joint involvement**	
Follicular helper T cell (%)	2.97±1.42	2.18±0.93	0.002
	Patients with nerve involvement	**Patients without nerve involvement**	
Follicular helper T cell (%)	1.83±0.84	2.52±1.15	0.006
	Patients with gastrointestinal involvement	**Patients without gastrointestinal involvement**	
TNF-α (%)	49.53±11.72	40.74±11.71	0.002
IFN-γ (%)	18.94±6.52	16.04±5.00	0.039
IL-2 (%)	56.94±15.26	47.81±13.46	0.005
IL-4 (%)	2.10±0.88	1.60±0.76	0.010
B cell (/μL)	160.48±141.41	232.64±177.21	0.028
	Patients with vascular involvement	**Patients without vascular involvement**	
Treg (%)	7.75±2.27	9.14±3.41	0.019

(Results without significance are not listed)

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AB0789

AVACOPAN IN THE REAL-LIFE PRACTICE: EVALUATION OF EFFICACY, SAFETY, AND IMPACT ON QUALITY OF LIFE IN THE EARLY STAGES OF TREATMENT

Keywords: Safety, Vasculitis, Remission

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Background: Avacopan is a new approved treatment for granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA). Compared with glucocorticoids (GCs) added to standard immunosuppression with cyclophosphamide (CYC) or rituximab (RTX), avacopan proved to be non-inferior for treatment response at 26 weeks, whereas was found to be superior for sustaining remission at 52 weeks compared with a prednisone tapering schedule of 20 weeks [1].
Objectives: The aim of this prospective multicenter study was to assess efficacy and safety of avacopan in the real-life practice in GPA or MPA patients in the setting of a compassionate use program. A secondary objective was to describe the change in perceived quality of life before and during treatment.
Methods: We prospectively collected clinical and laboratory data of GPA and MPA patients who started treatment with avacopan from May 2022. Patients were recruited from Rheumatology/Nephrology Units belonging to the Vasculitis Study Group of the Italian Society of Rheumatology (SIR). At least 3 months of follow-up from start of treatment were required for data analysis. Clinical remission was defined as BVASv3 equal to 0. Patients self-completed the Italian version of the AAV-PRO questionnaire (AAV-PRO_ita) at baseline and after 3 months [2].
Results: A total of 12 patients (7 females, 5 males) with a median age of 64 (IQR 48-66.3) were recruited from 9 Italian Rheumatology/Nephrology departments. Avacopan was mainly used in relapsing disease (8/12, 66.7%) and in GPA (9/12, 75%), compared with new-onset disease (4/12, 33.3%) and MPA (3/12, 25%). The relapsed patients had a median disease duration of 12 (IQR 4.3-15.3) years and had been previously treated with other immunosuppressants, including RTX (5/8, 62.5%), CYC (5/8, 62.5%), AZA (3/8, 37.5%), MTX (2/8, 25%), and MMF (1/8, 12.5%). At the start of avacopan treatment, the median BVASv3 and VDI were 12 (IQR 8-20.8) and 2.5 (IQR 1.5-3.3), respectively. 9 out of 12 (75%) patients had renal involvement, of which 5/9 (55.6%) had rapidly progressive glomerulonephritis. Other disease involvements were ENT (5/12, 41.7%), and pulmonary (5/12, 41.7%), of which 3/5 (60%) patients had alveolar haemorrhage. Treatment was initiated with a median steroid dose of 50 (IQR 6.9-50) mg prednisone equivalent (PN-eq) and in combination with RTX at a dose of 1 gram every 2 weeks (9/12 75%) or 375 mg/m2 weekly for 4 consecutive weeks (3/12, 25%). Two patients also received 1 gram of CYC before RTX. After month 3, 10/12 (83.3%) patients were in clinical remission and the median steroid dose had decreased to 5 (IQR 2.2-10.6) mg PN-eq (**Figure 1**). The median value of creatinine did not differ from baseline (1.7 [IQR 1.3-2.4] mg/dL *versus* 1.8 [IQR 1.2-3.2] mg/dL), whereas the median value of 24-hour urine protein had decreased from 680.5 (IQR 408-2300) mg per day to 254 (IQR 169.5-488) mg per day. A total of 3 adverse events (AEs) were recorded: 1 urinary tract infection (AE grade 2), resulting in temporary suspension of avacopan, 1 herpes simplex infection and 1 dyspnea/fatigue that was self-limiting (AEs grade 1). Regarding the AAV-PRO_ita questionnaire, the percentage of the three higher severity levels in all domains had decreased from 57.2% at baseline to 31.8% at month 3. In particular, fatigue was reported by 80% of patients *versus* 55.6% of patients at baseline and at month 3, respectively.
Conclusion: Our study described the real-life practice of avacopan in GPA and MPA patients, especially relapsing patients. The clinical added value of avacopan as steroid-sparing strategy can be observed already in the early stages of therapy. Overall, avacopan appears to be an effective and safe adjunctive therapy in the active AAV.

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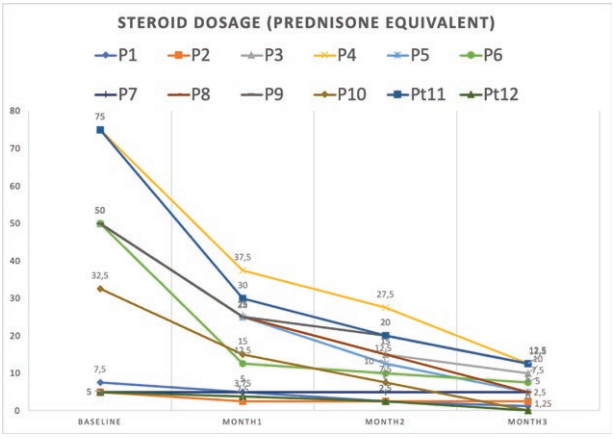


Figure 1.

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Disclosure of Interests: None Declared.
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AB0790

UNILATERAL RELAPSING PRIMARY CENTRAL NERVOUS SYSTEM VASCULITIS: DESCRIPTION OF 3 CASES FROM A SINGLE INSTITUTIONAL COHORT OF 216 CASES

Keywords: Vasculitis

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Background: Some cases of unilateral primary central nervous system vasculitis (PCNSV) with relapsing disease involving the same brain hemisphere have been described [1].
Objectives: The aim of this study was to define the frequency and characteristics of patients with unilateral relapsing involvement in a large cohort of patients with PCNSV.
Methods: We retrospectively studied a cohort of 216 patients with PCNSV seen at the Mayo Clinic, Rochester, MN from 1983 to 2022. Data collected for all cases included comprehensive information about clinical findings, laboratory tests, imaging, CNS biopsy or autopsy, therapies, flares, follow-up functional status and cause of death. Cerebral biopsy specimens were reviewed by one neuropathologist (CG). Angiograms and MRIs were reviewed by a neuroradiologist. For the present study, we specifically identified those patients with at least two flares and imaging at diagnosis and at follow-up showing vasculitis confined to one cerebral hemisphere.
Results: Twenty-five patients (19.8%) had at least two flares. 3 of them (1.4%) had unilateral relapsing vasculitis. All 3 patients had angiography-negative and biopsy-positive PCNSV. One patient had amyloid beta-related angiitis (ABRA), while the other 2 patients had granulomatous-necrotizing and lymphocitic vasculitides, respectively. Hemisphere involvement occurred on the left in two, and on the right in one. In all three patients the main presenting clinical manifestation at diagnosis and at the time of flares was seizures. All had multiple flares (from 4 to 10) and were treated with different traditional immunodepressive drugs and rituximab (RTX) for the steroid-resistance. They received long-term treatment (more than 2 years) with fixed high-dose prednisone (PDN) (in one 40 mg/daily, in the other two 20 mg/daily) because the vasculitic process flared when the PDN dose was reduced. One patient had at MRI prominent leptomeningeal enhancement, while the other two had cerebral lesions with gadolinium enhancement. In all three patients the vasculitic process was confined to the same cerebral

hemisphere at diagnosis and during the flares, and at the last available brain MRI performed 35 months, 167 months, and 65 months after the diagnosis, respectively. All 3 patients at last follow-up had slight disability with mild cognitive impairment; one case also had mild left hemiparesis. Spinal fluid examination at diagnosis was normal in 2 patients.

Conclusion: Unilateral relapsing involvement represents a rare subset of PCNSV with peculiar characteristics and can be observed in all neuropathological patterns.

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AB0791 EVALUATION OF THE EFFICACY AND COMPLICATIONS OF PLASMA EXCHANGE IN ANCA-ASSOCIATED VASCULITIS: RESULTS OF PROPENSITY SCORE MATCHING ANALYSIS IN HIGH-RISK PATIENTS

Keywords: Vasculitis

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Background: Therapeutic plasma exchange (PE) is applied in addition to standard induction therapy for patients with severe organ or system involvement in ANCA-associated vasculitis (AAV). However, prognostic significance of this approach is questioned.

Objectives: We aimed to evaluate both short- and long-term efficacy and safety of PE in our established single center cohort.

Methods: In this study, we evaluated the clinical and laboratory data of 128 patients diagnosed with AAV between 2011 and 2021. Data of patients with GFR <50 ml/min with or without diffuse alveolar hemorrhage (DAH) at the time of admission were included into the analysis. Disease activity, laboratory and follow-up data of patients who underwent PE were compared with those who did not. The analyses were repeated in the groups formed after the propensity score matching (PSM) performed according to the presence of DAH, age, gender, baseline GFR and BVAS scores.

Results: Seventy-one (55.5%) patients (F/M: 32/39, mean age± SD: 54.6±12.9) were included into the study. Thirty-nine (54.9%) patients had C-ANCA/PR3, 29 (40.8-%) patients had p-ANCA/MPO positivity. The mean follow-up was 53.6±34.7 months. In addition to high-dose corticosteroid treatment during induction therapy, IV cyclophosphamide (CYC) was used in 66 (92.9%) and rituximab was used in 3 (4.3%) patients. PE was applied in 33 (46.5%) patients. All patients who underwent PE had received CYC for induction. The median number of PE sessions was 7 (2-12). Fresh frozen plasma was used in 22 patients (66.6%) and albumin was used in 11 patients (33.3%). In patients who underwent PE, DAH and GFR<50ml/min were present in 20(28.2%) and 64(90.1%) patients, respectively. Hypotension in 3 patients, hypocalcemia in one, catheter-related thrombosis in one and transfusion reactions in 2 patients were recorded as short-term complications. In patients who underwent PD, the remission rate was low in the sixth month, and the development of severe infections and ESRD was high in the first year (Table 1). In the PSM analysis, creatinine values during the follow-up were higher in the patients who underwent PE. In both analyses, remission rates were lower in the PE group at six months, and the number of serious infections, ESRD development, and total VDI score were higher at twelve months.

Conclusion: In this retrospective study, positive effect of PE on remission and mortality in AAV could not be demonstrated. Efficacy against the development chronic renal failure and ESRD was also not observed. Despite low short-term complication rates related to PE, increased risk of severe infection which became evident with PSM analysis, was remarkable. In conclusion, these findings raise concern and should lead to careful patient selection for PE. Although an important therapeutic option for AAV patients with severe disease, limited long term benefits should be well balanced with risks.

Table 1. Comparison of patients who did or did not undergo plasmapheresis in patients with AAV

	DAH or GFR<50 ml/min (n=71)			PSM analysis groups (n=48)		
	TPE group (n=38) (%)	Standard induction (n=33) (%)	p	TPE group (n=24) (%)	Standard induction (n=24) (%)	p
Age	53.3±13.2	55.7±12.8	0.4	55.8±10.9	54.4±12.5	0.7
Baseline BVAS	19.7±6.9	17.6±5.5	0.3	20.8±7.1	17.2±5.8	0.2
Baseline GFR ml/min	28.7±23	30.2±31	0.8	18.6±11.6	19.5±8.2	0.8
Remission (6th mo) (n=53)	12/22	25/31	0.04	8/16	17/21	0.045
Mortality (6th mo)	2	0	0.12	1	0	0.3
Creatinine mg/dl (6th mo)	2.1±1.6	1.6±1.3	0.08	2.2±1.7	1.28±0.4	0.02
Proteinuria >0.5 gr/day (6th mo) (n=31)	8/17	14/30	0.9	7/16	8/20	0.7
Creatinine mg/dl (12th mo)	2.6±2.8	1.3±0.3	0.03	2.8±3	1.3±0.4	0.045
Proteinuria >0.5 gr/day (12th mo) (n=33)	5/16	9/26	0.82	5/13	5/17	0.6
Cumulative prednisolone dose (12th mo) (g) (median / IQR)	6.5 (25)	7.7 (46)	0.8	5 (45)	7.9 (39)	0.87
Cumulative CYC dose gr (long term)	3 (3.3)	3 (3)	0.2	2.4 (4)	3 (3.7)	0.29
Severe infection (first year)	11	66	0.02	10	2	0.003
End stage kidney disease (first year)	4	0	0.01	4	0	0.03
VDI score (overall)	3.6±2.2	2.6±1.8	0.03	3.2±1.3	2.2±0.4	0.6

REFERENCES: NIL.

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Disclosure of Interests: None Declared.

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AB0792 ADULT-ONSET IGA VASCULITIS WİTH RENAL INVOLVEMENT

Keywords: Vasculitis, Kidneys, Prognostic factors

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Background: Systemic Immunoglobuline A vasculitis (IgAV) often presents glomerulonephritis accompanying palpable purpura. Unlike children, renal involvement can be severe in adults. Especially, in the chronic period, renal involvement determines the prognosis. A significant proportion of the patients initially have pathological renal findings, while pathological renal findings may occur later in some patients.

Objectives: It was aimed to compare the clinical features of patients with renal involvement at the beginning and those with subsequent renal involvement, to determine the predictors of renal involvement and to determine the factors affecting renal prognosis.

Methods: A total of 42 adult patients with IgA vasculitis nephritis with followed between January 2018 and August 2022 in two tertiary hospitals were included in the study. The patients were divided into 2 groups as those with and without IgA vasculitis nephritis findings at the beginning. Patients' clinical and laboratory data were collected at baseline and at follow-up. and were analyzed retrospectively.

Results: Thirty (%71) of 42 patients had signs of IgA vasculitis nephritis at baseline and 12 (%29) patients, signs of nephritis appeared later. The median time between first visit and development of nephritis was 18 [IQR:6-44] days in patients whose nephritis findings appeared later. In the binary logistic regression analysis, it was determined that gastrointestinal involvement at the baseline predicted the later development of renal involvement [OR:9,399, 95% CI=1,800-49,079, p = 0,009]. Comparative results of the 2 groups with and without IgA vasculitis nephritis findings at baseline in terms of clinical features are presented in Table 1.

Table 1 : Comperative characteristics of patients presented with and without renal findings

	Patients with renal findings at initially N=30	Patients without renal findings at initially, N=12	*P*-value
Age, mean (S.D.),years	44.2 (15,4)	51.9 (14,3)	0,406
Female sex, n/N (%)	12 (40)	4 (33,3)	0,740
Joint involvement, n/N (%)	11 (36,6)	6 (50)	0,498
Gastrointestinal involvement, n/N (%)	6 (20)	8 (66,7)	***0,009***
Renal involvement type,			
Nephrotic proteinuria-hematuria, n/N (%)	4 (13,3)	1 (8.3)	1,000
Non-nephrotic proteinuria-hematuria, n/N (%)	19 (63,3)	9 (75)	0,719
Isolated hematuria, n/N (%)	6 (20)	1 (8,3)	0,651
Isolated proteinuria, n/N (%)	1 (3,3)	1 (8,3)	0,495
Acute renal injury, n/N (%)	11 (36,7)	4 (33,3)	0,522
İnitial laboratory features,			
Gfr, median, (Min-Max), mL/min/1.73m^2	92 (11-142)	94 (68-120)	0,978
Crp level, median, (Min-Max), mg/dl	27,3 (1-416)	37 (6-172)	0,559
ESR level, mean, (S.D.), mm/hr	41,7 (27,1)	42,2 (26,7)	0,939
IgA level, mean, (S.D.), g/L	3,4 (1,4)	2,2 (1,1)	0,339
Renal remission rate at 3 months, n/N (%)	19 (63)	7 (58)	1,000
Renal remission rate at 12 months, n/N (%)	14/18 (77)	8/8 (100)	0,205
İnitial steroid dosing, median, (Min-Max), mg/day	290 (0-1000)	64 (20-1000)	0,786

S.D.: Standard Deviation**Gfr:** Glomerular filtration rate**Crp:** C-reactive Protein**ESR:** Erythrocyte Sedimantation Rate**IgA:** Immunoglobuline A

Conclusion: A significant proportion of patients with IgA vasculitis who do not have pathological renal findings at baseline may appear glomerulonephritis findings in the later follow-up period. Clinicians should be careful in terms of renal involvement. Similar to previous studies, our study revealed that gastrointestinal involvement is a risk factor for renal involvement.(1,2) Patients with initial gastrointestinal symptoms but no pathological renal findings should be followed more frequently and regularly.

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Disclosure of Interests: None Declared.

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AB0793

SERUM C3 LEVELS ARE ASSOCIATED WITH DISEASE PATHOLOGY IN MICROSCOPIC POLYANGIITIS: RESULTS FROM THE REVEAL COHORT

Keywords: Real-world evidence, Vasculitis

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Background: Recent studies have shown that complement C5a receptor antagonist is highly effective for treating microscopic polyangiitis (MPA), suggesting that complement is substantially involved in the pathogenesis.

Objectives: In this study, we aimed to examine whether serum C3 levels were associated with clinical characteristics, disease severity, treatment, and prognosis in the Japanese multicenter cohort.

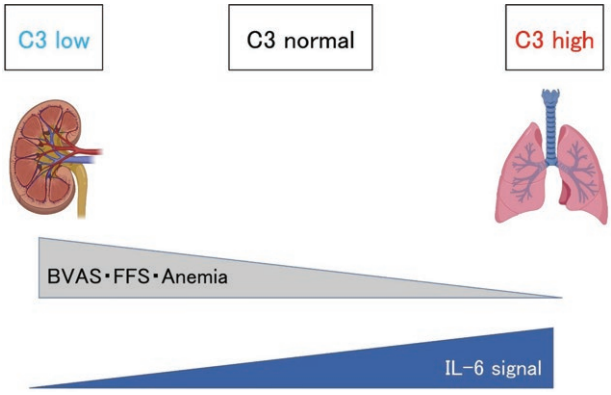
Methods: Patients with MPA whose C3 levels were measured at diagnosis were enrolled. The diagnosis of MPA was based on the 2012 revised Chapel Hill consensus criteria. Patients were divided into three groups: low C3 (<86 mg/dL), normal C3 (86-130 mg/dL), and high C3 (>130 mg/dL) groups to compare clinical characteristics. Analysis of variance or the Kruskal–Wallis test was used when the variates were numeric, while the chi-squared test or Fisher's exact test was used when variates were categorical.

Results: A total of 158 patients (low C3: 28, normal C3: 90, high C3: 40 patients) were enrolled. Baseline characteristics did not differ between the three groups in age at onset, sex, smoking history, and MPO-ANCA positivity. Serum C3 levels (P<0.001) as well as C4 (P<0.001) and CH50 levels (P=0.0013) were significantly lower in the low C3 group. In addition, hemoglobin (P=0.0058), platelets (P<0.001), and serum CRP levels (P=0.002) were significantly lower in the low C3 group, while serum creatinine levels (P=0.001), BVAS (P=0.039), and five factor scores (P=0.005) were significantly higher in the low C3 group. Notably, the proportion of patients who fulfilled the 2022 revised ACR/EULAR classification criteria for MPA was significantly lower in the low C3 group (P=0.039). Initial prednisolone dose and survival did not differ between the three groups.

Conclusion: Low C3 levels are associated with severe disease and renal dysfunction, while high C3 levels are associated with elevated CRP levels. Serum C3 levels are closely associated with disease pathology.

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Figure

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AB0794

A PROSPECTIVE STUDY ON RENAL INVOLVEMENT IN INDIAN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

Keywords: Outcome measures, Real-world evidence, Vasculitis

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Background: The ANCA-associated vasculitides (AAV) are systemic autoimmune diseases affecting small and medium-sized blood vessels. Upper airways, lungs, and kidneys are variably involved in the different types of AAV, and the consequences of a missed or delayed diagnosis of renal vasculitis are potentially life-threatening. AAV may be classified into clinical syndromes or based on their serology (Anti-PR3 or Anti-MPO). Patient survival and the risk of end-stage renal disease are closely associated with renal functional status.

Objectives: This study was undertaken to study the disease characteristics and outcomes in patients of AAV based on the presence or absence of renal involvement.

Methods: This was a longitudinal, observational study conducted at a tertiary care hospital in Northern India. Between February 2020 and December 2021, all consecutive adult patients diagnosed with AAV based on their autoantibody profiles (using indirect immunofluorescence and Line ImmunoAssay) and clinical features were included in this study after taking their informed consent. Demographic details, clinical features, laboratory parameters, disease activity, and mortality or morbidity outcomes of patients were analysed prospectively. All outcomes were compared between patients with and without renal involvement.

Results: A total of 112 patients were included in our study, with a median age of 51.5 years. 74 (66%) patients had renal involvement either in the form of Nephritic

syndrome, Nephrotic syndrome, RPRF (Rapidly progressive renal failure), Nephritic nephrotic syndrome, or Asymptomatic Urinary Sediments. c-ANCA and PR3 positivity were seen in more than two-thirds of our population, without any significant correlation with organ involvement. Patients with renal disease had a significantly higher proportion with diffuse alveolar haemorrhage (32.4% vs 10.5%, p=0.05) and palpable purpura (19.6% vs 7.9%, p-0.025), but significantly lower occurrences of nasal pathology (14% vs 42%, p=0.001) and subglottic stenosis (1.4% vs 18.4%, p=0.001). Mean BVAS at enrolment was significantly higher in the renal group (20.9 vs 12.89). Remission was achieved in 50% and 47.4% of the patients with and without renal involvement respectively. Rates of relapse (19/74 vs 14/38), refractory disease, and mortality were not significantly different among the two subgroups. The commonest organ involvement in disease flare was pulmonary involvement. 21.6% of the patients developed CKD over a median follow-up period of 18 months.

Conclusion: Kidney involvement is one of the commonest manifestations of AAV. Patients with renal involvement may have higher mean BVAS scores and an increased risk of developing alveolar haemorrhage and purpuric skin rash; while nasal pathology and subglottic stenosis occurred more frequently in patients without renal disease. Rates of remission, refractory disease, and mortality were almost similar, regardless of renal involvement, while relapses were numerically more in the non-renal AAV patients.

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AB0795 MPO-ANCA ANTIBODIES: ASSOCIATED DISEASES, SPECIFICTY, AND RELATION WITH SEVERITY AND PROGNOSIS OF UNDERLYING VASCULITIS. STUDY FROM A SINGLE UNIVERSITY HOSPITAL

Keywords: Autoantibodies, Vasculitis

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Background: Anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) include Granulomatosis with polyangiitis GPA), Microscopic polyangiitis (MPA), and Eosinophilic granulomatosis with polyangiitis (EGPA). Anti-myeloperoxidase (anti-MPO) or anti-proteinase 3 are the two main ANCA subtypes. Anti MPO specificity and correlation with the severity and prognosis of underlying vasculitis is contradictory [1].

Objectives: To assess, in patients with positive anti-MPO, **a)** associated diseases, **b)** specificity in diagnosing AAV and, **c)** relation with severity and prognosis of underlying vasculitis in a single university hospital.

Methods: Study of patients with positive anti-MPO from a University Hospital, from 2003 to 2022. ANCA was determined by standard inmunohistochemistry. The specificity of anti-MPO for diagnosis and relation with severity and prognosis of underlying vasculitis were evaluated with Receiver Operating Characteristics (ROC) curves. At diagnosis severe AAV were considered cases with renal disease (hematuria and/or proteinuria) and pulmonary involvement. In follow-up, worst prognosis was considered if the patient needed dialysis, a transplant or died.

Results: We study 101 patients with positive anti-MPO. **Table** summarizes the prevalence of these antibodies in vasculitis and non-vasculitis diseases. Most of them (76.23%) had an underlying AAV, being the most frequent MPA (33.7%). The non-vasculitis disease more frequent was neoplasm (4,9%). For anti-MPO antibodies with a diagnosis of AAV (n=77), an area under the curve (AUC) was calculated (AUC=0.8084), and a cut-off point of 41.5 IU/ml was determined (**Figure**). When the analysis was restricted to exclusively MPA (n=34), the cut-off point was 36.5 IU/ml with an AUC of 0.6435. For severity of AAV, there were significant differences in anti-MPO levels between patients with renal or pulmonary dysfunction (n=65) versus those without them (n=36) (p=0.0003), and a cut-off threshold of 60 IU/ml was established. Finally, after evaluating the illness's prognosis, an AUC= 0.5546 was found, being no significant differences between those patients who had a worse disease progression (n=19) and those who did not (n=82) (p=0.4643).

Conclusion: MPO antibodies levels, at the moment of diagnosis, may be associated to AAV diagnosis (specificity) and severity but not with disease outcome.

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Table. Underlying associated Diseases with positive anti-MPO antibodies (n=101).

Group	Disease	Number (n)	Frequency (%)
Vasculitis (n=77; 76.23%)	Microscopic polyangiitis	34	33.7
	Pauci-immune glomerulonephritis	13	12.9
	Unclassified vasculitis	11	10.9
	Granulomatosis with polyangiitis	10	9.8
	Eosinophilic granulomatosis with polyangiitis	9	9.9
No vasculitis (n=24; 23.76%)	Neoplasm	5	4.9
	Ulcerative colitis	4	3.9
	Infection	3	2.9
	Rheumatoid arthritis	2	1.9
	Chron's disease	1	0.9
	Intestinal ischemia	2	1.9
	Sjogren's syndrome	1	0.9
	Autoimmune hepatitis	1	0.9
	Psoriasis	1	0.9
	Lung fibrosis	1	0.9
	Pleural effusion	1	0.9
	Silicosis	1	0.9
	Pachymeningitis	1	0.9

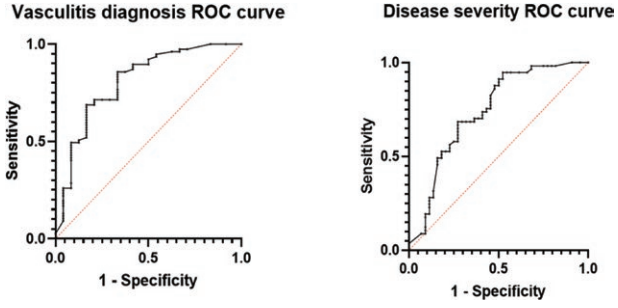


Figure. Receiver Operating Characteristic (ROC) plots for AAV and positive MPO-antibodies (AUC=0.8084) and disease severity at diagnosis (AUC=0.7160).

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AB0796 CANVASC CONSENSUS RECOMMENDATIONS FOR THE USE OF AVACOPAN IN ANTINEUTROPHIL CYTOPLASM ANTIBODY-ASSOCIATED VASCULITIS: 2022 ADDENDUM

Keywords: Vasculitis

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Background: In 2020, the Canadian Vasculitis Research Network (CanVasc) published their updated recommendations for the management of antineutrophil cytoplasm antibody (ANCA)-associated vasculitides (AAV). Since then, clinical data on the complement C5a receptor inhibitor avacopan (formerly, CCX168) has continued to expand.

Objectives: The current addendum provides further recommendations regarding the use of avacopan in AAV based on a review of newly available evidence.

Methods: An updated systematic literature review on avacopan using Medline, Embase, and the Cochrane Library was performed for publications up to September 2022. New recommendations were developed and categorized according to the EULAR grading levels, as done for previous CanVasc recommendations. A modified Delphi procedure and videoconferences were used to reach ≥80% consensus on the inclusion, wording and grading of each recommendation.

Results: Three new recommendations were developed. They focus on avacopan therapy indication and duration, as well as timely glucocorticoid tapering.

Conclusion: These 2022 addended recommendations provide rheumatologists, nephrologists, and other specialists caring for patients with AAV with guidance for the use of avacopan, based on current evidence and consensus from Canadian experts.

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Disclosure of Interests: David Turgeon: None declared, Volodko Bakowsky Speakers bureau: Abbvie, Consultant of: Advisory board attendance from Abbvie, Apotex, Eli Lily, Novartis, Pfizer, Jamp, and Sandoz UCB, Corisande Baldwin: None declared, David Cabral: None declared, Marie Clements-Baker Speakers bureau: Honoraria from Abbvie, Novartis, Boehringer Ingleheim and Otsuka, Alison Clifford Speakers bureau: Hoffman La-Roche Limited, Consultant of: Participation in clinical trials with Abbvie and UCB, Jan Willem Cohen Tervaert Speakers bureau: Pfizer, Sanofi, AbbVie, Hoffmann-La Roche, Medexus, and GSK, Paid instructor for: Chair IDMC InflaRx (2017-2022), Consultant of: Merck, Novartis, and Mallinckrodt Pharmaceuticals, Natasha Dehghan: None declared, Daniel Ennis: None declared, LEILANI FAMORCA: None declared, Aurore Fifi-Mah Speakers bureau: ChemoCentryx, Grant/research support from: Roche, Louis-Philippe Girard: None declared, Frédéric Lefebvre: None declared, Patrick Liang Grant/research support from: Roche, Amgen, Janssen, Abbvie, BMS, and Novartis, Jean-Paul Makhzoum Speakers bureau: Teva, Otsuka Pfizer, GKS, and Jansenn, David Massicotte-Azarniouch: None declared, Arielle Mendel: None declared, Nataliya Milman Consultant of: Otsuka, Heather Reich Consultant of: Calliditas, Novartis, Pfizer, Eledon, Omeros, Travere and Chinnook, David Robinson: None declared, Carolyn Ross: None declared, Dax G. Rumsey Consultant of: AbbVie, Mylan, and Novartis, Grant/research support from: Pfizer, Medha Soowamber: None declared, Tanveer Towheed: None declared, Judith Trudeau Consultant of: Hoffman-Laroche, Medexus, and ChemoCentryx, Marinka Twilt: None declared, Elaine Yacyshyn: None declared, Gozde Yardimci: None declared, [Nader Khalidi} Consultant of: Roche, Bristol Meyers Squibb, Lillian Barra Consultant of: Roche, Bristol-Myers Squibb, Boehringer-Ingelheim, Otsuka and Pfizer, Grant/research support from: Pfizer, Christian Pagnoux Speakers bureau: ChemoCentryx, Astra-Zeneca, and InflaRx GmbH, Grant/research support from: Roche, GSK, Otsuka, Pfizer.

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AB0797

ABSTRACT TITLE: OCULAR INVOLVEMENT AS AN INITIAL PRESENTATION IN SYSTEMIC VASCULITIS: AN OBSERVATIONAL STUDY

Keywords: Uveitis, Vasculitis, Behcet's disease

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Background: Systemic Vasculitides are a heterogenous group of immune mediated vascular inflammatory pathologies that contributes to vessel wall necrosis and damage. Ocular manifestation with systemic vasculitides isn't uncommon as an initial presentation. Identifying the patterns of ocular involvement associated with a specific diagnosis of vasculitis might guide the diagnosis at early encounter, while if underdiagnosed or improperly treated might contribute to devastating complications [1-3].

Objectives: to survey the patterns of ocular manifestations as the initial presentation in a population of patients with systemic vasculitides.

Methods: This is an observational cohort study in which data regarding ocular involvement were retrieved from medical records. The inclusion criteria: medical records of adult patients > 18 years with the diagnosis of any form of vasculitis according to the internationally recognized criteria having ocular involvement as confirmed by an expert ophthalmologist. Exclusion Criteria: patients with additional diagnosis whether endocrinal, metabolic, neoplastic and infectious diseases.

Results: The study included a total of 328 patients with the different diagnoses of vasculitis (68.9% males and 31.1% females, their mean ages were 38.58± 11.96 years, mean disease duration of 65.35±75.84 months). Figure 1 Ocular involvement was reported in 46% of the included cases with vasculitis at initial encounter, uveitis was diagnosed in 31.1% (7.3% anterior uveitis, 10.7% posterior uveitis, 13.1% pan uveitis), optic neuritis in 3.5%, retinal vasculitis in 17%, retinal artery thrombosis was reported in 1.8%, retinal vein thrombosis in 5.4%, orbital pseudotumor in one patient with granulomatosis with polyangiitis, scleritis one patient and episcleritis one patient with granulomatosis with polyangiitis. Ocular involvement was found in 61.3% of cases with BD (uveitis in 48.2%, retinal vasculitis in 18.4) at initial encounter with uveitis being the most common.

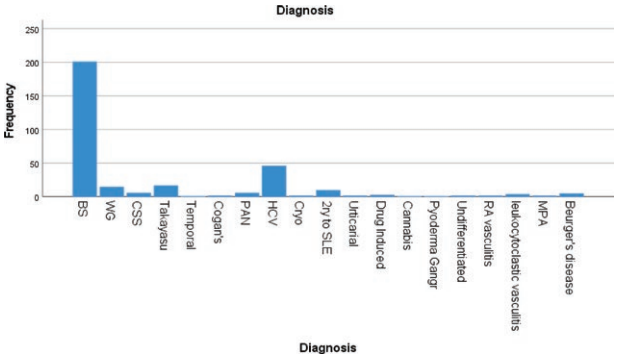


Figure1 : The Frequency of the different diagnoses of vasculitis in the Study population.

Conclusion: The patterns of ocular involvement at initial presentation might guide the diagnosis of one form of vasculitis over the other especially with incomplete forms.

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Disclosure of Interests: None Declared.
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AB0798 PREVALENCE AND CLINICAL SPECTRUM OF CARDIAC INVOLVEMENT IN BEHÇET'S SYNDROME: A SINGLE CENTER RETROSPECTIVE STUDY

Keywords: Cardiovascular disease, Behcet's disease, Heart

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Background: Behçet's Syndrome (BS) is a systemic vasculitis, which main clinical features include mucocutaneous manifestations, pan-uveitis, non-deforming arthritis, thrombosis, central nervous system (CNS) and gastrointestinal (GI) involvement [1].
Despite being increasingly recognized as part of the clinical spectrum in BS [2,3,4], cardiac involvement has not been systematically described.
Objectives: To investigate the prevalence and clinical spectrum of cardiac manifestation in a cohort of BS patients.
Methods: Three hundred and twelve patients were retrospectively studied. All patients fulfilled the International Classification Criteria for BS [5]. Demographic, clinical, therapeutic features, and specific data on cardiac involvement were collected.
Results: Cardiac involvement was observed in 46 out of 312 patients (13.2%). The mean age at cardiac involvement diagnosis was 43 years (SD ± 13.2). Mean BS duration before cardiac manifestation onset was 5.35 years (SD ± 6.86). Female to male ratio was 1.42. Among 46 patients with cardiac involvement, 37 (80.4%) displayed a single manifestation, while 9 (19.5%) showed two or more cardiac events. BS related cardiac lesions included arrhythmias (n=12; 26%), pericarditis (n=12; 26%), ischemic heart disease (n=7; 15%), acute myocarditis (n=5; 10.8%), valvular abnormalities (n=8; 17.3%), and pulmonary hypertension (n=2; 4.3%) **(Figure 1)**. Thirteen patients (28.2%) had cardiac abnormalities classified as "other", which included patent foramen ovale, Takotsubo syndrome, cardiac amyloidosis, and aortic root aneurysm **(Figure 1)**. After the first event, remission of cardiac manifestations was achieved by all patients. Cardiac relapse occurred in 9 patients (19.5%), due to recurrent pericarditis (n=7), myocarditis (n=1), and arrhythmic manifestation (n=1). Overall clinical manifestations of BS are shown in **Table 1**. Muco-cutaneous manifestations were present in almost all patients, specifically oral aftosis was present in 45/46 (98%), genital aftosis in 26/46 (56.5), and skin manifestations in 35/46 (76%). A significant proportion of patients displayed vascular involvement (n=20; 43,4%), CNS involvement (n=20; 43.4%), and GI involvement (n=32; 69.5%). At the time of cardiac events 21/46 (45.6%) patients were receiving oral corticosteroids, 16/46 (34.7%) were receiving colchicine, 13/46 (28.2%) were receiving a traditional DMARD, while 19/46 (41.3%) were receiving a biologic DMARD **(Table 1)**.
Conclusion: Our study indicates that cardiac events are a fairly common manifestation in BS patients, pointing out the need for a routine screening of such involvement. As previously described [2], our study suggests the association between cardiac abnormalities and vascular involvement in BS. Furthermore, we found a significant proportion of patients presenting with other major organ manifestations, such as CNS and GI involvement, suggesting that cardiac involvement may reflect a more severe and systemic disease course.

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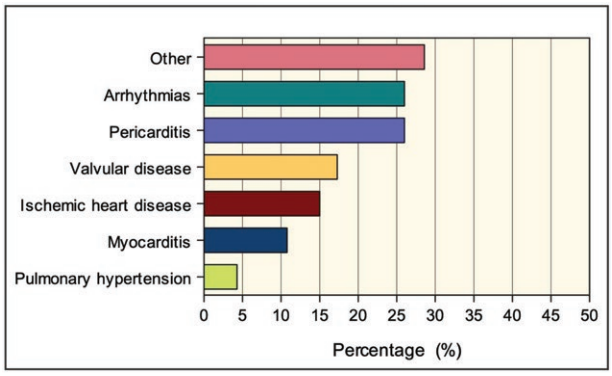


Figure 1. Spectrum of cardiac lesions in a monocentric cohort of BS patients

Table 1. Demographic and clinical features of BS patients with cardiac involvement

	BS patients (46)
Female N (%)	27 (58.6%)
Age (mean ± SD)	43 (± 13.2)
Cardiovascular risk factors N (%)	
Smoking habit	7 (15.2%)
Dyslipidemia	11 (24%)
Hypertension	10 (21.7%)
Diabetes	2 (4.3%)
Clinical manifestations N (%)	
Oral aftosis	45 (98%)
Genital aftosis	26 (56.5%)
Ocular involvement	12 (26%)
Skin manifestations	35 (76%)
Positive pathergy test	11 (24%)
Vascular involvement	20 (43.4%)
CNS involvement	20 (43.4%)
GI involvement	32 (69.5%)
Articular involvement	33 (71.7%)
HLA-B51 positivity	30 (65.2%)
Treatment N (%)	
Corticosteroids	21 (45.6%)
Colchicine	16 (34.7%)
Traditional DMARDs	13 (28.2%)
Biologic DMARDs	19 (41.3%)

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AB0799 ASSOCIATION BETWEEN MUSCLE QUALITY AND MORTALITY IN PATIENTS WITH ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

Keywords: Vasculitis

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Background: Decreased muscle mass is frequently observed in patients with autoimmune rheumatic diseases; however, the relationship between muscle quality and patient outcomes has not been well understood.
Objectives: This study evaluated the influence of muscle quality on the outcomes of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV).
Methods: Records of patients with AAV (microscopic polyangiitis, granulomatosis with polyangiitis, and eosinophilic granulomatosis with polyangiitis) at the Severance Hospital having computed tomography (CT) images at disease diagnosis were retrospectively reviewed. For muscle quality measures, normal attenuation muscle area (NAMA), low attenuation muscle area (LAMA), total abdominal muscle area (TAMA), and intramuscular adipose tissue (IMAT) in the axial muscles of the middle third lumbar vertebra level was calculated. Correlations between NAMA, LAMA, and IMAT and patient characteristics and outcomes were assessed.

Results: A total of 136 patients with CT images at AAV diagnosis were identified. Correlation analyses revealed that age, female sex, total cholesterol, and alanine aminotransferase were significantly associated with NAMA. LAMA was associated with age, body mass index (BMI), five-factor score (FFS), and C-reactive protein, while a relationship between IMAT and age and BMI was observed. Cox-proportional hazard analysis demonstrated that NAMA/TAMA≤0.46 (odds ratio [OR] 5.612, 95% confidence interval [CI] 1.758-17.909, p=0.004), female sex (OR 0.228, 95% CI 0.075, 0.684, p=0.008), dyslipidemia (OR 3.819, 95% CI 1.380, 10.571, p=0.010), and FFS (OR 2.160, 1.298-3.595, p=0.003), were independent factors associated with mortality.
Conclusion: Higher mortality was observed in patients with AAV with NAMA/TAMA ≤ 0.46, indicating that cautious monitoring is required in these patients.
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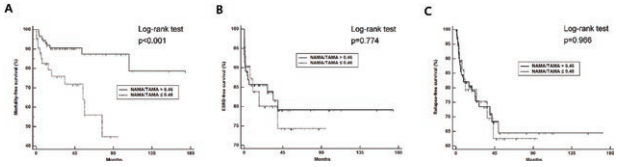


Figure : Kaplan Meier-analysis with clinical outcomes according to NAMA/TAMA cut-off value of 0.46.

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AB0800 EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS CLINICAL MANIFESTATIONS AND OUTCOMES: A RETROSPECTIVE COHORT ANALYSIS OF 38 PATIENTS FROM RUSH UNIVERSITY MEDICAL CENTER CHICAGO, IL, USA

Keywords: Prognostic factors, Organ damage, Vasculitis

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is the rarest anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis according to incidence and prevalence reports in the literature [1]. Typical manifestations include obstructive airway disease, nasal polyps, mononeuritis multiplex, eosinophilia, and eosinophilic-predominant inflammation on biopsy [2]. Studies have been published that describe the clinical manifestations and disease outcomes but these are limited [3]. Further studies are necessary to better understand this disease.
Objectives: This study characterized the clinical manifestations and outcomes of a cohort of Rush University Medical Center (RUMC) patients with EGPA.
Methods: Retrospective cohort analysis of EGPA patients at RUMC from 1/1/2010-12/31/2021. Clinical characteristics, treatment, and outcome were analyzed, using Fisher's Exact Test and Chi-Square Test to perform comparisons.
Results: This cohort included 38 patients with EGPA. 55% were female, 68% were Caucasian, and mean age at diagnosis was 57.7 (+/- 16.3). 95% had pulmonary involvement. 37% were (ANCA) positive. There was no statistically significant difference in clinical characteristics, treatment strategies, or outcomes when comparing ANCA positive to ANCA negative patients.
Conclusion: This analysis describes the clinical characteristics, treatment, and outcomes of a cohort of RUMC patients with EGPA. Prevalence of pulmonary involvement and ANCA positivity was similar to that reported in the literature. Unlike previous studies which reported higher prevalence of neurologic and kidney involvement in ANCA positive EGPA patients our study did not find a statistically significant difference in characteristics of ANCA positive patients when compared to ANCA negative patients.
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Disclosure of Interests: None Declared.
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AB0801 NEW DIAGNOSTIC TOOL IN BEHCET'S DISEASE

Keywords: Behcet's disease

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Background: Behcet's disease (BD) is characterized by oral, genital, and gastrointestinal manifestations. The pathergy test is used as a diagnostic tool, but this is not specific to BD, since it can be found in other diseases and can equally be negative even having the disease. Another characteristic of BD is the vascular compromise, predominantly venous. In a study, the measurement of the thickness of the common femoral vein (CVF) proved to be a diagnostic test with sensitivity and specificity greater than 80% for the cut-off value of 0.5 mm.
Objectives: To evaluate the diagnostic performance of the thickness of the posterior wall of the common femoral vein, measured by Doppler ultrasound for the diagnosis of Behcet's disease.
Methods: A multicenter pilot study was carried out to evaluate a diagnostic test. Data were collected by reviewing medical records collected from patients who met the 2014 International Criteria for Behcet's Disease (ICBD), and healthy controls. Venous Doppler ultrasound of the lower limbs was performed in both groups using an ultrasound evaluation protocol, considering posterior wall thickness of the CFV ≥ 0.5 mm as positive.
Results: 19 patients with EB and 19 healthy controls were included. The mean age of patients with DB was 47 (SD 12.6), and the median age of healthy patients was 41 years (IQR 36.5-48.5). 57.89% were mestizo in the BD group and 68.42% in the control group. The median delay in diagnosis was 19 months (IQR 11-36). The presence of HLA B51 was 63.15% and the positive pathergy test was found in 31.57%. At the time of the study, 42.10% had disease activity and a mean of 8.8 years of disease. (Table 1) The ultrasound was positive in 89.4% of patients with BD and 10.5% in the healthy group, observing a sensitivity of 94.1% and a specificity of 94.7%, with an area under the curve 0.89 ($p < 0.0001$), PPV 94.1% and NPV 94.7%. (Fig. 1) We observe a post-test probability of 0.059. The test presents LR + 17.8 (95%CI 2.5-127) and LR - 0.06 (95%CI 0.008-0.4)
Conclusion: The diagnosis of Behcet's disease is difficult because it is based mainly on clinical manifestations, so this ultrasound test has a good capacity to be used as part of the diagnosis in patients with clinical suspicion, since it has a good sensitivity and specificity profile, low cost and simplicity.
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Table 1 Demographic, clinical and treatment characteristics.

	BD n = 19	Control n = 19
Female (n (%))	11 (58)	8 (42)
Age	Mean 47 (SD 12.6)	Median 41 (IQR 36.5-48.5)
Smoking (n (%))	5 (26.3)	6 (31.5)
Ethnic groups		
Mestizo (n (%))	11 (58)	13 (68.5)
White (n (%))	8 (42)	6 (31.6)
African-Latin Americans (n (%))	0	0
Amerindians (n (%))	0	0
Clinical Manifestations	EB n = 19	
Oral ulcers (n (%))	18 (95)	N/A
Genital ulcers (n (%))	15 (79)	N/A
Eye compromise (n (%))	8 (42)	N/A
Skin compromise (n (%))	4 (63)	N/A
Neurological compromise (n (%))	2 (10.5)	N/A
Positive pathergy (n (%))	6 (31.6)	N/A
Positive HLA B51 (n (%))	12 (63)	N/A
Activity (n (%))	8 (42)	N/A
Delay to diagnosis (Months)	Median 19 (RIC 11-36)	N/A
Treatment		
Without treatment (n (%))	4 (21)	N/A
Colchicine (n (%))	4 (21)	N/A
Immunomodulators (n (%))	7 (37)	N/A
Both (n (%))	4 (21)	N/A
Corticosteroid (n (%))	10 (52.6)	N/A

N/A: not applicable

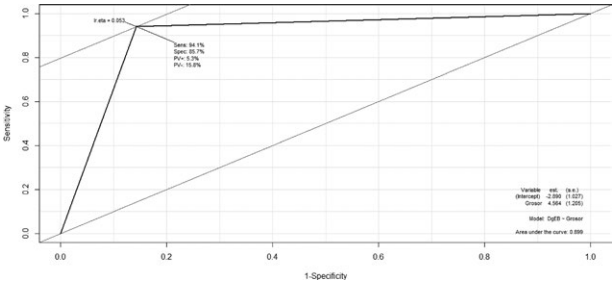


Fig. 1 ROC Curve

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AB0802

PRESENCE OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS IN PATIENTS WITH NASAL POLYPS AND ASTHMA. STUDY OF A SINGLE REFERRAL CENTER

Keywords: Vasculitis, Outcome measures, Biomarkers

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is included in anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV). It mainly affects patients with asthma, sinusitis, allergic rhinitis, and nasal polyposis.
Objectives: To assess **a)** prevalence of clinical features of EGPA in patients with clinical history of nasal polyps and asthma, and **b)** proportion of positive ANCA (+ANCA) test in those patients.
Methods: Retrospective study of patients with clinical history of asthma and nasal polyps with histologic study from a referral center between 2021 and 2022. The measurement of ANCA were performed by chemiluminescence assay using IO-FLASH (Inova, San Diego, CA). Diagnosis of EGPA was based on ACR/EULAR 2022 criteria [**1].** Disease activity was assessed with Birmingham Vasculitis Activity Score (BVAS). All biopsies of nasal polyps were examined by the same expert pathologist to assess the presence of eosinophil aggregates.
Results: A total of 123 biopsies with eosinophil aggregates were studied between 2021 and 2022. Twenty-three patients (19%) had history of asthma. Of them, we objectified EGPA criteria in 12 patients (10% of the series of 123 patients). General features of these 12 patients are summarized in **Table**. Seven patients had more than 20 eosinophil aggregates per field in polyp biopsy. The median [IQR] BVAS score was 0[0-0]; just 2 patients showed activity measured by BVAS score (with a mean of 3 points). ANCA test was positive in 1 (8.3%) patient.
Conclusion: According to data from our series, approximately 10% of patients with nasal polyps with biopsy meet EGPA criteria.

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TABLE. General features of 12 patients with Nasal polyps and EGPA

FEATURES	Results (n=12)
Age, mean±SD	47±14
Male/ Female n, (% male)	6/6 (50)
Clinical manifestations, n (%)	
Ocular	2(16.6)
CNS/PNS	2(16.6)
ENT	1(8.3)
MSK	1(8.3)
Pulmonary	1 (8.3)
ANCA-test specificity, n (%)	
MPO-ANCA	1(8.3)
PR3-ANCA	0
None	11(91.7)
CRP (mg/dL), median [IQR]	0.5 [0.4-0.7]
ESR, mm/1st hours, median [IQR]	15 [8.5-33.2]
Serum eosinophilia (mg/dL), median [IQR]	0.4 [0.2-0.6]
BVAS, mean±SD	0.8±1.9
FFS, n (%)	
0	10(83.4)
≥1	2(16.6)
Eosinophils infiltrate concentration in polyps >20 cell, n(%)	7 (58.3)

Abbreviations in alphabetical order:ANCA: Antineutrophil cytoplasmic antibody; BVAS: Birmingham Vasculitis Activity Score; CNS: central nervous system; CRP: C-Reactive protein; dL: deciliter; ENT: ear, nose, throat; ESR: erythrocyte sedimentation rate; FFS: Five-Factors Score; g; IQR: Interquartile range; mg: milligram; mm: millimeter; MSK: musculoskeletal; MPO-ANCA= ANCA specific for myeloperoxidase; n=Number; PNS: peripheral nervous system; PR3-ANCA= ANCA specific for proteinase 3; SD: Standard Deviation.

Acknowledgements: NIL.
Disclosure of Interests: Fabricio Benavides-Villanueva: None declared, J. Loricera Speakers bureau: Dr. J. Loricera had participation in company-sponsored speaker´s bureau from Roche, Novartis, Galápagos, UCB Pharma, MSD, Celgene, and Grünenthal and received support for attending meetings and/or travel from Janssen, Abbvie, Roche, Novartis, MSD, UCB Pharma, Celgene, Lilly, Pfizer, Galápagos., Vanesa Calvo-Río: None declared, Ricardo Blanco Speakers bureau: Speakers bureau: Abbvie, Pfizer, Roche, lilly, Bristol-Myers, Janssen, Galapagos and MSD., Consultant of: Consultant of: Abbvie, Pfizer, Roche, lilly, Bristol-Myers, Janssen and MSD, Grant/research support from: Grant/research support from: Abbvie, MSD, novartis and Roche.
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AB0803

ANCA-ASSOCIATED VASCULITIS (AAV) AND RENAL DISEASE IN A MULTIDISCIPLINARY OUTPATIENT CLINIC IN NORTHERN SPAIN

Keywords: Vasculitis, Kidneys

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Background: The severity of clinical features and outcomes in previous series of patients reported with renal disease related to ANCA-associated vasculitis (AAV) vary greatly, probably due to selection bias.
Objectives: To establish the actual clinical spectrum of renal disease due to AAV in a multidisciplinary outpatient clinic in Northern Spain.
Methods: Review of 132 patients classified as having AAV between 1994 to 2022; Granulomatosis with polyangiitis (GPA), Microscopic polyangiitis (MPA) or Eosinophilic Granulomatosis polyangiitis (EGPA) was classified according to 2022 ACR/EULAR classification criteria.

Results: Renal disease was observed in 82 of 132 (62.1%) AAV (38 men/44 women), median age 61.37 years (24-87 years). **Table** reflects the main clinical findings and outcomes. Renal biopsy was performed in 44 patients (36 patients showing a pauci-immune crescentic glomerulonephritis). The remaining 38 patients were not biopsied due to patient disagreement, mild renal disease or contraindication for biopsy. The most frequent ANCA antibody specificity was MPO (64.6%) followed by PR3 (26.8%) and double positivity in 3 patients (2 MPO and PR3 and 1 MPO and MBG). 43 patients were classified as MPA (52.4%), of those, 18 patients (21.9%) had renal limited vasculitis, 27 GPA (32.9%), and 4 EGPA (4.9%). The rest of the patients had other renal disease (5 microhematuria, 1 amyloidosis, 1 diabetes nephropathy and 1 nephroangiosclerosis). Nephritic syndrome was the most common renal manifestation when the vasculitis was fully established (56.1%). The most frequent therapies used were corticosteroids (68.3%), Cyclophosphamide (46.3%), Azathioprine (35.4%), Rituximab (34.1%) and mycophenolate mofetil (23.2%). After a median follow-up of 6.23 years (7 days-22.9 years) the last median creatinine and glomerular filtration rate (GFR) was 1.4 mg/dl and 43 ml/min, respectively. Renal function worsened compared to baseline in 78.3% of MPO positive and only in 33% of PR3 positive (p=0.005). During the first 12 months follow-up, stabilization or normalization GFR (median GFR at 1 year: 50 ml/min) was observed in 47.1% with no statistical differences among ANCA groups (p=0.303). Renal outcome at the end of follow-up was poorer in MPA than GPA or EGPA (76.3%, 47.4% and 50% respectively worsened GFR from baseline). 16 patients (19.5%) needed dialysis at any moment. Total remission was achieved in 25 patients (30.5%) while relapses were observed in 17 patients (20.7%). Severe infectious was the main severe side-effect, reported in 26 patients (31.7%).

Conclusion: Most AAV patients had some grade of renal disease during follow-up and almost 20% ended up needing dialysis. Therefore this multi-systemic disease should be managed in a multidisciplinary way to establish an early diagnosis and adequate treatment, limiting chronic disease.

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Table. Main clinical findings and outcomes of patients with AAV and renal disease.

	AAV with renal disease (n=82)
Renal biopsy; n, (%)	44, (53.66%)
ANCA; n, (%)	
MPO	53, (64.6%)
PR3	22, (26.8%)
double positivity	3, (3.65%)
Diagnosis; n, (%)	
MPA	43, (52.4%)
GPA	27, (32.9%)
EGPA	4, (4.9%)
Other diseases	8, (9.8%)
Renal involvement; n, (%)	
nephritic syndrome	46 (56.1%)
proteinuria > 3.5 g/24h	3 (3.6%)
isolated hematuria	5 (6.1%)
Outcome; n, (%)	
dialysis	16, (19.5%)
total remission	25, (30.5%)
relapses	17, (20.7%)

Abbreviations: ANCA-associated vasculitis (AAV), Granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA) or microscopic polyarteritis (MPA)

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AB0804 THE PERFORMANCE OF ACR 1990 AND ACR/EULAR 2022 CRITERIA IN THE DIAGNOSIS OF GPA AND EGPA

Keywords: Vasculitis

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Background: ANCA-associated vasculitis (AAV) are systemic disorders with involvement of multiple organs that may lead to severe damage. An early diagnosis and often an aggressive treatment is necessary to preserve organ function, but the diagnosis can be difficult at disease onset when non-specific symptoms are predominant.

To address this issue, classification criteria have been developed in 1990 and recently updated.

Objectives: To evaluate the performance of ACR 1990 and ACR/EULAR 2022 criteria in the diagnosis of GPA and EGPA.

Methods: Patients with certain or suspected diagnosis of EGPA and GPA, followed in the Rheumatology and Clinical Immunology units, have been selected for the study. Concordance has been evaluated by means of the K Cohen coefficient.

Results: Out of 50 patients with the diagnosis of GPA, 36 (72%) fulfill the ACR 1990 criteria and 41 (82%) the ACR/EULAR 2022 criteria. Out of 31 patients with the diagnosis of suspected GPA, 17 (55%) fulfill the ACR 1990 criteria and 16 (52%) the ACR/EULAR 2022 criteria. Concordance is low (K=0,1). Analyzing discordant cases, 14 patients positive only for 1990 criteria have lung involvement and in half of the cases renal involvement. Eighteen patients positive only for 2022 criteria have anti PR3 ANCA, one third nasal involvement, one third lung involvement. This reflects the higher weight of pathology, renal and lung involvement in 1990 criteria, the weight of ANCA positivity and upper airway involvement in 2022 criteria. Out of 40 patients with the diagnosis of EGPA, 13 (33%) fulfill the ACR 1990 criteria and 36 (90%) the ACR/EULAR 2022 criteria. Out of 30 patients with the diagnosis of suspected EGPA, 1 (3%) fulfill the ACR 1990 criteria and 19 (63%) the ACR/EULAR 2022 criteria. Concordance is low (K=0,13). Analyzing discordant cases, 18 patients positive only for 2022 criteria have asthma and hypereosinophilia and in half of the cases nasal poliposis. This reflects the higher weight of asthma and hypereosinophilia in 2022 criteria.

Conclusion: These data clearly indicate a higher sensitivity of the ACR/EULAR 2022 criteria, that take into account ANCA detection by the currently available sensitive and specific techniques. On the other hand, the data confirm that classification criteria can be applied only to well selected cohorts of patients, when a careful clinical and laboratory workup has excluded other diagnosis and suggested a systemic vasculitis.

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Scleroderma, myositis and related syndromes

AB0805 DESCRIPTION IN FLOW IN EARLY VERSUS CLINICALLY OVERT SYSTEMIC SCLEROSIS. LASER SPECKLE CONTRAST ANALYSIS: A DESCRIPTIVE STUDY ON THE PERIPHERAL BLOOD OF THE DIFFERENT SUBTYPES OF SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Descriptive Studies, Imaging

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Background: Description of flow, measured by laser speckle contrast analysis (LASCA), in 'early' systemic sclerosis (SSc) versus 'clinically overt' SSc (diffuse cutaneous SSc [DcSSc] and limited cutaneous SSc [LcSSc]) has not yet been described [1].
Objectives: To investigate in an unselected, SSc cohort if baseline LASCA PBP-measurements differ between 'early' SSc and 'clinically overt' SSc.
Methods: Between September 2019 and December 2022, patients with SSc (as defined by the 2013 ACR/EULAR criteria and/or the 2001 LeRoy and Medsger criteria) were included [1,2]. A group of 20 consecutive 'early' SSc, LcSSc and DcSSc patients were recruited. Vasoactive medication was continued. LASCA was performed at baseline in standardized instrumental and environmental conditions [3]. PBP was assessed by marking regions of interest (ROI's) with fixed 1 cm diameters at the fingertips of the 2nd through 5th digit volary bilaterally. The adjusted mean PBP was calculated (expressed in perfusion units [PU]). A linear mixed model was fit with a random intercept per patient, together with a linear covariance structure to capture the residual correlations between fingers. Fixed effect terms included subset, side, finger, vasoactive medication, active smoking, history or presence of digital trophic lesions (DTL), and disease duration. Significance level was set at 0.05 and no correction for multiple testing was applied.
Results: Sixty patients with SSc (75% female, mean age 53 years, mean disease duration 73.1 months) were enrolled (table 1). Comparing the adjusted mean PBP at baseline in 'early' versus 'clinically overt' SSc, no statistical significant difference was found (144 vs. 150 PU, p=0.77) (figure 1A). Additionally within the 'clinically overt' group no significant difference was perceived between DcSSc and LcSSc (157 vs. 141, p=0.53). A wide variability was noted when observing the individual measurements of each subset (figure 1B).
Conclusion: This study with an unselected day-to-day SSc population, where patients were allowed to continue their vasoactive medication, showed there was no difference in PBP at baseline between 'early' SSc and 'clinically overt SSc' when corrected for subset, vasoactive medication, active smoking, history or presence of DTL and disease duration. Interestingly a wide variation of individual datapoints was noted in each subset, which emphasizes the heterogeneity of SSc. In conclusion, there is no inter-individual variation between the different subsets of SSc, as measured with LASCA. Future investigation is needed to enlighten us about the intra-individual changes over time.

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Table 1. Baseline characteristics of the study population (n = 60).

Baseline characteristics general				
Age (years), mean ± SD			53 ± 12.6	
Gender (♂/♀), n (%)			15 (25)/ 45 (75)	
Disease duration (months), mean ± SD			73.1 ± 89	
Raynaud, n (%)			60 (100)	
Active smoking, n (%)			10 (16.6)	
LeRoy subset; 'early' SSc, LcSSc, DcSSc, n (%)			20 (33.3), 20 (33.3), 20 (33.3)	
Baseline characteristics per subset				
Subset (n)	Total (60)	Early SSc (20)	LcSSc (20)	DcSSc (20)
SSc-specific Ab, n (%)	29 (48.3)	7 (35.0)	11 (55.0)	11 (55.0)
Anticentromere Ab, n (%)	13 (21.7)	4 (20.0)	8 (40.0)	1 (5.0)
Anti-topoisomerase-1 Ab, n (%)	14 (23.3)	2 (10.0)	3 (15.0)	9 (45.0)
Anti-RNA-polymerase III Ab, n (%)	2 (3.3)	1 (5.0)	0 (0.0)	1 (5.0)
Vasoactive medication, n (%)	20 (33.3)	3 (15.0)	6 (30.0)	11 (55.0)
History of digital trophic lesions, n (%)	16 (26.7)	0 (0.0)	5 (0.25)	11 (55.0)

Ab: antibody; DcSSc: diffuse cutaneous systemic sclerosis; LcSSc: limited cutaneous systemic sclerosis; SSc: systemic sclerosis.

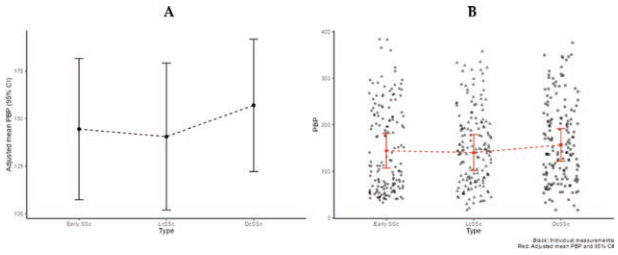


Figure 1. Peripheral blood perfusion (PBP) per subset. (**A**): Adjusted mean PBP and 95% CI. (**B**): Individual measurements.

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Disclosure of Interests: None Declared.
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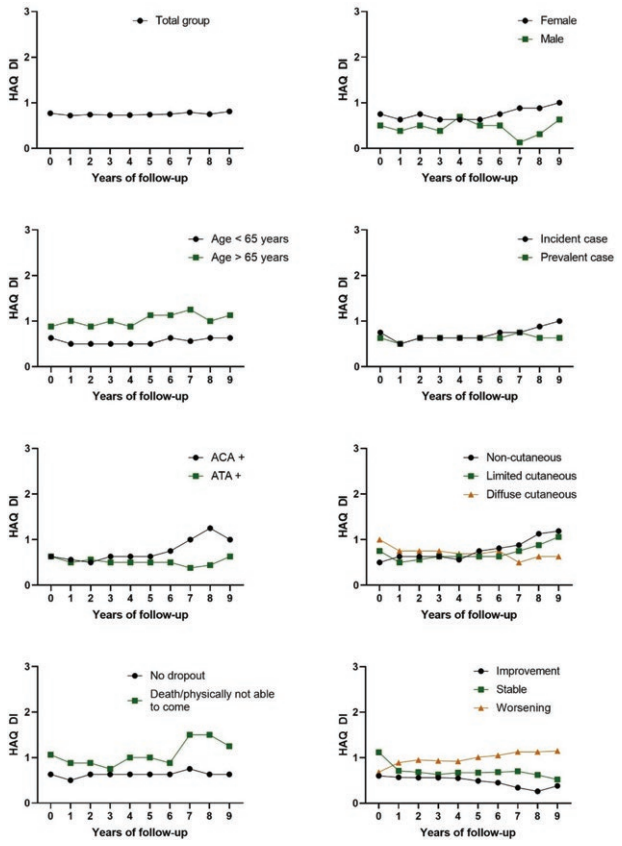
AB0806 THE LONG-TERM COURSE OF THE HEALTH ASSESSMENT QUESTIONNAIRE IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Patient reported outcomes

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Background: Functional disability in patients with systemic sclerosis (SSc) greatly influences quality of life. The Health Assessment Questionnaire-Disability Index (HAQ-DI) is an important outcome reflecting functional disability, but knowledge on its course over time in SS) is scarce.
Objectives: To describe the long-term course of functional disability in SSc patients, most importantly to investigate which patients have a worsening functional ability, and investigate its associations with disease characteristics.
Methods: SSc patients, fulfilling the ACR/EULAR 2013 criteria, were included from the Leiden CCISS cohort with annual assessments including the Scleroderma HAQ. The Scleroderma HAQ consists of the HAQ-DI (range: 0 [no difficulties] to 3 [maximum difficulties]) and five SSc-related VAS scores: Raynaud's Phenomenon, digital ulcers, gastrointestinal, pulmonary and general disease burden (range: 0 to 100). The HAQ-DI course was evaluated over the total follow-up (baseline to last available HAQ-DI) and between yearly visits. Based on a minimal clinical important difference of 0.22, patients were categorized into worsening, stable, or improvement. Baseline SSc characteristics were compared between patients with a worsening or improvement of the HAQ-DI using logistic regression. The change of the HAQ-DI and the SSc-related VAS scores over time was evaluated with linear mixed models.
Results: 517 SSc-patients were included (Table 1). The median follow-up duration was 7 years (IQR:4; 9). The mean baseline HAQ was 0.77 (SD:0.65). On group level, the HAQ-DI increased annually with 0.019 (95% CI:0.011; 0.027). Patients ≥65 years (β 0.27, 95% CI: 0.1; 0.4) and patients who died/were physically not able to come during follow-up (β 0.34, 95% CI: 0.2; 0.5) had a significantly higher HAQ-DI over time than respectively patients younger than 65 years old and patients who did not die (Figure 1). Between baseline and the last follow-up, the proportions of patients with a worsening, stable or improved HAQ-DI were 35%, 42% and 23%, respectively. Logistic regressions, adjusted for age, sex and disease duration, revealed that, at baseline, the use of immunosuppressive medication (OR: 0.5, 95% CI: 0.3; 0.9) and gastrointestinal involvement (OR: 0.6, 95% CI: 0.4; 0.9) decreased the chance of a worsening overall HAQ-DI course, whereas presence of anti-centromere autoantibodies (OR: 1.4, 95% CI: 0.8; 2.3) and pulmonary arterial hypertension (OR: 2.3, 95% CI: 0.3; 20.8) increased this. For all the VAS scores, the β of the longitudinal course for the total group was stable. Over time, most importantly, patients who died/were physically not able to come during follow-up had a 18.8 point higher pulmonary VAS (95% CI: 12.9; 24.8) and a 13.3 higher general burden of SSc VAS (95% CI: 6.5; 20.2) compared to patients who survived.
Conclusion: Over time, the average course of the HAQ-DI is stable in SSc-patients, but individual trajectories vary, with worsening occurring in one third. Importantly, use of immunosuppressives decreased the chance of worsening while presence of anti-centromere antibodies increases the chance of worsening.

and



Figure

Disclosure of Interests: Sophie Liem: None declared, Sytske Anne Bergstra: None declared, Jacopo Ciaffi: None declared, Coen van der Meulen: None declared, David Ueckert: None declared, Rita Schriemer: None declared, Thomas Huizinga: None declared, T.P.M. Vliet Vlieland: None declared, Jeska de Vries-Bouwstra Grant/research support from: JVB received research grants from Roche, Galapagos and Janssen and consulting fees from Abbvie, Janssen and Boehringer Ingelheim. All was paid to her institution.

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AB0807

PATIENT-REPORTED OUTCOMES ABOUT QUALITY OF LIFE IN PATIENTS WITH IDIOPATHIC INFLAMMATION MYOPATHY

Keywords: Quality of life, Patient reported outcomes, Work-related issues

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Background: Idiopathic inflammation myopathy (IIM) defines a group of chronic autoimmune-mediated diseases that most commonly affect the skin, muscles, and lungs [1]. Despite considerable advances over the past decades in improving life expectancy compared with the general population, IIM patients still experience substantially impaired health-related quality of life (HRQoL) [2].

The value of incorporating patient-reported outcomes in clinical trials is increasingly appreciated. The 36-item Short-Form Health Status Survey (SF-36) has been proposed to evaluate HR-QoL in IIM patients. However, because it is very time-consuming, the actual completion rate of the questionnaire is extremely low, and the SF-36 cannot be used directly in cost-effectiveness analyses. The EuroQol 5-Dimension (EQ-5D) is another tool for assessing HR-QoL and has been used extensively for chronic diseases. Wolfe et al. [3] verified the association between EQ-5D and SF-36 in rheumatic diseases. Moreover, workforce losses in patients with IIM are underestimated, and even health-related absenteeism imposes an economic burden on society [4].

Objectives: To explore the feasibility and validity of the EuroQol 5-dimension (EQ-5D) and Work Productivity and Activity Impairment (WPAI) surveys as patient-reported outcomes of health-related quality of life (HR-QoL) in Idiopathic inflammation myopathy (IIM).

Methods: This cross-sectional study surveyed patient's outcomes using the Manual Muscle Testing-8 (MMT-8), Myositis Disease Activity Assessment Visual Analog Scale (MYOACT), Myositis Damage Index (MDI), Disease Activity Score (DAS), and Physician/Patient Global Assessment (PGA/PtGA). HR-QoL was determined using EQ-5D, 36-item Short-Form Health Status Survey (SF-36), and WPAI questionnaire. The relationship between IIM-related parameters and HR-QoL was assessed using ordinal logistic and quantile regression.

Results: We enrolled 189 patients with IIM. Decreased MMT-8 and increased MYOACT, DAS, MDI-global, and PGA/PtGA were associated with higher EQ-5D values. For the 25^{th}–75^{th} percentile of WPAI, greater activity impairment was associated with lower MMT-8 and higher age of onset and PGA. Poorer overall working productivity impairment was associated with higher MYOACT (cutaneous and skeletal). MDI-global and PtGA were associated with increased activity and overall working productivity impairment in most quantiles ($P < 0.05$).

Conclusion: The EQ-5D and WPAI may be valid patient-reported outcomes to evaluate HR-QoL in ambulatory patients with IIM.

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AB0808

A PROOF OF BIOLOGICAL CONCEPT TRIAL OF CM101 TO TARGET CCL24 IN SYSTEMIC SCLEROSIS: A BIOMARKER INFORMED, PRECISION MEDICINE APPROACH

Keywords: Systemic sclerosis, Biomarkers, Clinical Trials

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Background: Systemic sclerosis (SSc) is an inflammatory and fibrosing autoimmune disease of unknown etiology. However, it has been established that endothelial cells, immune cells, and fibroblasts play important roles in SSc initation and progression. CCL24 (eotaxin-2) is a chemokine secreted by fibroblasts and endothelial cells, which promotes trafficking of profibrotic immune cells through the CCR3 receptor. Levels of CCL24 and CCR3 in the skin and serum of patients with SSc were found to be upregulated compared with healthy controls [1]. Serum CCL24 levels have been shown to correlate with extracellular matrix turnover biomarkers, to predict decline in forced vital capacity (FVC) and the diffusion capacity of the lungs for carbon monoxide (DLCO), and to be associated with a worse digital ulcer burden in patients with SSc [1]. Blockade of CCL24 with CM101, a humanized IgG1 anti-human CCL24 monoclonal antibody, significantly reduced endothelial cell activation in vitro and in skin and lung immune cell infiltration and fibrosis in experimental SSc animal models.

Objectives: To present an innovative trial design which allows for comprehensive disease assessment and determination of the biological activity of CM101 in patients with SSc.

Methods: Informed by the predictive value of CCL24 on vascular and fibrotic clinical outcomes in a large SSc observational cohort, the CM101 clinical development team aims to bridge biomarker science and clinical trial design by implementing a phase 2a clinical trial that includes evaluation of the

biology of CCL24, effects of CCL24 blockade on biological and clinical markers of SSc activity, with comprehensive safety and efficacy assessments in patients with SSc.

Results: A biomarker driven, phase 2a, multicenter, randomized, double-blind, placebo-controlled, proof of biology study was designed to evaluate the safety, tolerability, and activity of CM101 in patients with SSc. Approximately 45 patients will be enrolled and randomized in a 2:1 ratio to receive either 10 mg/kg CM101 IV every 3 weeks (N=30 patients) or placebo (N=15 patients) for 8 treatments in the double-blind treatment period (24 weeks). All patients will have the option to receive 8 active treatments (CM101 20mg/kg IV every 3 weeks) in the open-label treatment period (24 weeks), with a follow-up period of 12 weeks. To elucidate the role of CCL24 in SSc, adults with early limited or diffuse cutaneous SSc are required to have elevated serum levels of CCL24 and clinical evidence of active disease, defined as modified Rodnan Skin Score (mRSS) ≥ 15 or presence of interstitial lung disease or current digital ulcer along with elevated C-reactive protein, erythrocyte sedimentation rate, or platelets, at trial entry. CM101 biological activity will be evaluated through a pre-defined biomarker analysis. Along with safety assessment, the clinical activity of CM101 on the vascular, dermatological, and pulmonary systems will be evaluated by nailfold video capillaroscopy, Digital Artery Volume index (DAVIX©), Digital Ulcer Clinical Assessment Score, mRSS, and FVC. The global response will be assessed by the revised Composite Response Index Systemic Sclerosis (CRISS) in conjunction with patient-reported outcomes.

Conclusion: This novel, biomarker enriched clinical trial, will determine the biological activity of CM101 in patients with active vascular or fibrotic SSc, across limited and cutaneous subsets, and inform future development of CM101 in SSc. Bridging biomarker science with clinical trial design carries the opportunity of improving the efficiency in subsequent clinical development and allows for a targetted treatment approach.

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AB0809

INTERSTITIAL LUNG DISEASE SECONDARY TO ANTI SYNTHETASE SYNDROME AND SYSTEMIC SCLEROSIS: DIFFERENCES IN CHARACTERISTICS AND IMMUNOSUPPRESSIVE TREATMENT RESPONSE

Keywords: Systemic sclerosis, Myositis, Lungs

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Background: Anti synthetase syndrome (ASS) is an inflammatory myositis with autoantibodies against one of the aminoacyl transfer RNA synthetase. Interstitial lung disease (ILD) is a main clinical feature which dictates the prognosis and treatment. Since there are no randomized controlled trials to guide therapy, treatment strategies are extrapolated from other connective tissue diseases-related-ILD (CTD-ILD), mainly systemic sclerosis (SSc).

Objectives: Our aim was to evaluate the effect of immunosuppressive treatment (IS) on ASS-related ILD, compared with SSc-related ILD.

Methods: A multicenter observational registry, including 45 patients with CTD-ILD (ASS (n=18) and SSc (n=27)) from 3 medical centers in Israel, between 2017-2021. During follow up, 12 patients did not receive any IS, while 17 patients started IS treatment shortly after the 1st visit and 16 after a period of follow up. We compared the **monthly** change in diffusion capacity for carbon monoxide (DLCO) and forced vital capacity (FVC) percent predicted between ASS and SSc. Further analysis included a comparison between non-IS and IS treated patients. Mann-Whitney test was used to compare medians, with a p value of <0.05 considered significant.

Results: The mean±SD age was 62.9±10 and 31 (69%) were females. ILD as the presenting disease feature was more common in ASS, compared with SSc (61% vs. 11%, p<0.001). DLCO% was lower at baseline among ASS patients (44 ±13 vs. 57 ±14, p=0.004), while other lung function measures were not significantly different (table 1). Overall, 32 patients (71%) received an IS therapy. As expected, glucocorticoid treatment was more prevalent in the ASS group (n=14) compared to the SSc group (n=8) (78% vs. 30%, p=0.002). The most prevalent non-steroidal IS was mycophenolate mofetil (MMF) (96%). Two ASS and one SSc received azathioprine. There was a trend towards a monthly improvement of DLCO% among treated patients with ASS compared with SSc (median change of 0.30 vs. -0.17 percentage points, p=0.053), while among non-IS treated patients there was no difference in the decline (-0.27 vs. -0.29, p=0.853) (figure 1). When comparing CTD-ILD treated with IS, with non-treated patients among patients with ASS, IS was associated with a monthly increase in DLCO% (0.3 vs. -0.27 without IS, p=0.001), and in SSc – a lower rate of decline (-0.17 vs. -0.29, p=0.041); However, the positive change of FVC% in both ASS (0.12 vs. 0.33, p=0.217) and SSc (-0.38 vs. 0, p=0.79) patients was not statistically significant.

Table 1 , demographic and clinical characteristics of the study cohort

Variable, number (%)	ASS n=18 (%)	SSC n=27 (%)	p
Age, years (mean±SD)	65 ±12	62 ±10	0.378
Female sex	13 (72)	18 (67)	0.693
Ever smokers	8 (44)	6 (22)	0.115
Heart failure	2 (11)	1 (4)	0.329
Interstitial lung disease onset[a]			**<0.001**
Before systemic symptoms	11 (61)	3 (11)	
Concurrent	7 (39)	8 (30)	
After systemic symptoms	0	16 (59)	
Glucocorticoid treatment, number (%)	14 (78)	8 (30)	**0.002**
Non-steroidal Immunosuppression	10 (56)	18 (67)	0.451
Lung functions at diagnosis [b] % predicted (mean±SD)			
FEV1	73 ±20	79 ±15	0.324
FVC	75 ±20	81 ±15	0.256
FEV1/FVC	81 ±11	78 ±8	0.370
TLC	80 ±17	85 ±14	0.285
DLCO	44 ±13	57 ±14	**0.004**

ASS, anti-synthetase syndrome; SSC, systemic sclerosis; FEV1, forced expiratory volume in first second; FVC, forced vital capacity; TLC, total lung capacity; DLCO, Diffusing capacity for carbon monoxide.[a] Onset of interstitial lung disease is divided into more than 6 months before other systemic symptoms, under 6 months before or after the appearance of systemic symptoms, and after more than 6 months from systemic symptoms.[b] First documented lung functions after diagnosis.

Table : CRP, ESR, KL-6 and their combinations for predicting ILD progression

	dcSSc						SSc-ILD					
	PF-ILD			**PPF**			**PF-ILD**			**PPF**		
	AUC	**Sensitivity**	**Specificity**	**AUC**	**Sensitivity**	**Specificity**	**AUC**	**Sensitivity**	**Specificity**	**AUC**	**Sensitivity**	**Specificity**
CRP	**0.52**	**16.0**	**88.0**	**0.48**	**9.1**	**86.0**	**0.51**	**14.0**	**87.9**	**0.49**	**11.1**	**86.7**
ESR	**0.47**	**13.6**	**80.3**	**0.45**	**10.5**	**79.7**	**0.44**	**14.7**	**73.6**	**0.44**	**14.3**	**74.4**
KL-6	**0.58**	**29.2**	**86.4**	**0.57**	**28.6**	**85.7**	**0.64**	**45.2**	**82.8**	**0.61**	**42.9**	**79.8**
CRP or ESR	**0.49**	**22.7**	**76.1**	**0.45**	**15.8**	**62.4**	**0.46**	**25.7**	**66.7**	**0.45**	**24.1**	**66.7**
CRP or KL-6	**0.60**	**41.7**	**77.8**	**0.57**	**38.1**	**76.2**	**0.62**	**52.4**	**72.4**	**0.59**	**48.6**	**69.1**
ESR or KL-6	**0.51**	**31.8**	**70.0**	**0.51**	**31.6**	**69.9**	**0.57**	**52.5**	**60.8**	**0.55**	**51.5**	**59.3**
CRP or ESR or KL-6	**0.53**	**40.9**	**65.7**	**0.51**	**36.8**	**64.4**	**0.56**	**57.5**	**54.1**	**0.53**	**54.5**	**51.9**

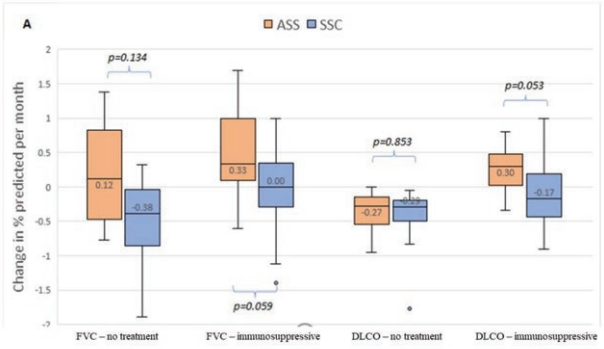


Figure 1. Median monthly change (in percentage points) of FVC% and DLCO% in ASS and SSc patients with (n=28) and without (n=28) immunosuppressive treatment. Five patients (3 SSc and 2 ASS) were excluded from this analysis due to lack of serial lung functions.

ASS, anti-synthetase syndrome; SSC, systemic sclerosis; FVC, forced vital capacity; DLCO, Diffusing capacity for carbon monoxide.

Conclusion: Immunosuppressive therapy, and specifically MMF, was associated with an improvement in DLCO% in patients with ASS and lower rate of decline in SSc. ILD in the context of ASS may responds better to immunosuppressive treatment compared to ILD in SSc. These encouraging results need to be validated in larger scaled randomized prospective studies to assess the role of MMF in ILD related to ASS.

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AB0810 PERFORMANCE OF CIRCULATING BIOMARKERS FOR PREDICTING PROGRESSION OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Biomarkers

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Background: In patients with systemic sclerosis (SSc), progression of interstitial lung disease (ILD) is associated with an increased risk of mortality. Since the course of SSc-ILD is variable, it is critical to predict progression of ILD in clinical practice as well as in designing clinical trials. Risk factors for ILD progression include short SSc duration, male, elevated inflammatory markers and Krebs von den Lungen-6 (KL-6), and progression of skin thickness in diffuse cutaneous SSc (dcSSc).

Objectives: To investigate if inflammatory markers and KL-6 at baseline are useful to efficiently capture patients who subsequently experience ILD progression in patients with dcSSc or SSc-ILD using a single-center cohort.

Methods: Patients with dcSSc or SSc-ILD were selected from the prospective SSc registry. C-reactive protein (CRP) ≥6 mg/L and erythrocyte sedimentation rate (ESR) ≥28 mm/hour were used as inflammatory markers [1], and a cutoff level of KL-6 was provisionally set at 1,000 U/ml. ILD progression was defined as the first event developing progressive fibrosing ILD (PF-ILD) [2] or progressive pulmonary fibrosis (PPF) [3]. Receiver operating characteristic curve (ROC) analysis was used to determine the sensitivity, specificity, and area under the curve (AUC) values of individual biomarkers and their combinations for predicting ILD progression. Cumulative rates free from ILD progression were assessed using Kaplan-Meier analysis and were compared using log-rank test.

Results: We enrolled 109 patients with dcSSc and 136 patients with SSc-ILD. The median disease duration at baseline was 15 and 17.5 months for dcSSc and SSc-ILD, respectively, and 87 patients with SSc-ILD (64%) had dcSSc. During median of 37 months of follow-up of dcSSc patients, 27 (25%) and 22 (20%) developed PF-ILD and PPF, respectively; and during median of 44.5 months of follow-up of SSc-ILD patients, 43 (31%) and 36 (26%) developed PF-ILD and PPF, respectively. As shown in Table, specificity of CRP, ESR and KL-6 for predicting ILD progression was favorable (73.6-88%), but sensitivity of CRP and ESR was low (9.1-16%). KL-6 provided better sensitivity (29.2-45.2%). The combination of CRP/KL-6 showed the AUC value (0.57-0.60), with sensitivity of 38.1-52.4% amd specificity of 69.1-77.8%. Kaplan-Meier analysis found that ILD progression occurred more frequently in patients with increased KL-6 than in those without irrespective of definition of ILD progression (P = 0.0001-0.03). The same trend was observed when combination of CRP/KL-6 was used (P = 0.001-0.14).

Conclusion: Increased KL-6 at baseline is the best biomarker for predicting ILD progression in patients with dcSSc or SSc-ILD. When KL-6 was combined with CRP, sensitivity was increased by maintaining acceptable specificity, proposing use of this combination as inclusion criteria for enriching an "at risk" patients in clinical trials for dcSSc or SSc-ILD.

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AB0811 NAILFOLD CAPILLAROSCOPY FINDINGS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES AND ITS ASSOCIATION TO AUTOANTIBODIES: A CASE-CONTROL STUDY

Keywords: Biomarkers, Autoantibodies, Myositis

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Background: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of acquired muscle diseases, which have distinct clinical, pathological and histological features. Autoantibodies are clinically useful biomarkers to help the diagnosis of IIM. Raynaud's phenomenon is very frequent and the presence of microvascular changes in IIM have been described however, the role of nailfold videocapillaroscopy NVC) for diagnosis and prognosis in IIM is not clearly established.

Objectives: The aim of this study was to study the relationship between clinical and immunological characteristics and nailfold videocapillaroscopy (NVC) abnormalities in patients with idiopathic inflammatory myopathies (IIMs).

Methods: We performed a retrospective study of IIM patients followed in a University Hospital. Patients underwent a NVC at 200x magnification. Epidemiological, clinical data and antibody status, including myositis and scleroderma antibody panel of all patients was retrieved. NVC findings including loss of capillary density, enlarged and giant capillaries, ramified capillaries, haemorrhages, thrombosis, avascular areas, disorganization of capillary architecture and subpapillary venous plexus presence were recollected, if present. For the comparison of qualitative and/or quantitative variables Fisher's exact Test or T-test was performed when necessary.

Results: 95 patients with NVC performed during the follow-up were included (66% female) with a median age at inclusion of 55.3±24 years. Median IIM duration was 6.8±7 years. 39% had Raynaud's phenomenon at first clinical evaluation and 58% of them showed NVC pathological findings. Table 1 Summarizes the epidemiological, clinical, and autoantibody status of the patients. We found an association between the presence of dysphagia and avascular areas (p=0.02) or abnormal capillary organization (p<0.01) on NVC. ILD was associated with capillary loss (p=0.04) and avascular areas (p=0.004). Anti-MDA5+ was associated with capillary loss (p=0.03), thrombosis (p=0.02) and ramified capillaries (p=0.04). Anti-Mi2+ and anti-Th/To was associated with abnormal capillary organization (p=0.017 and p=0.001). The presence of haemorrhages was associated with anti-Ku+ (p=0.048) and anti-PL12+ (p=0.046). The presence of enlarged capillaries was associated with anti-RNA-pol III (p=0.04) and anti-NXP2 (p=0.044). A significant association between anti-Ro52 (OR 2.69, CI 95% 1.05-6.8, p 0.03) and anti-Jo1 (OR 7.03 CI 95% 1.46-33.7, p 0.01) with ILD was found. Anti-PML (OR 4.32 CI 95% 1.35-10.42, p 0.038) and anti-Th/To (OR 5.82 CI 95% 1.89-13.24, p 0.04) were associated with dysphagia. Anti-MDA5 (OR 5.85 CI 95% 1.92-14.21, p 0.044) was associated with skin involvement.

Conclusion: The presence of certain autoantibodies is related to the degree of microangiopathy in IIM and associates with capillaroscopic changes. Studying the association between capillaroscopic changes with diagnostic and pathogenic autoantibodies in IIM can provide useful information regarding the current knowledge about pathogenesis, classification, and prognosis of the disease.

Table 1 : Epidemiological, clinical, immunological and NFC features and autoantibody status from patients with IIM

Clinical features	
Muscle weakness	79 (83%)
Skin findings	30 (32%)
ILD	47 (49%)
Dysphagia	18 (19%)
Raynaud's phenomenon	37 (39%)
CK elevation	45 (47%)
Cardiac disease	4 (4%)
NFC features	
Loss of capillary density	27 (28%)
Enlarged and giant capillaries	37 (39%)
Haemorrhages	36 (38%)
Thrombosis	19 (20%)
Avascular areas	26 (27%)
Disorganization of capillary architecture	24 (25%)
Subpapillary venous plexus	36 (38%)
Antibody status	
Disease-specific antibodies	
Anti-MDA5	8 (8%)
Anti-TIF1G	11 (12%)
Anti-MI2	11 (12%)
Anti-NXP2	6 (6%)
Anti-synthetase antibodies	
Anti-Jo1	13 (14%)
Anti-PL7	9 (9%)
Anti-PL12	5 (5%)
Disease-associated antibodies	
Anti-Ro52	27 (28%)
Anti-KU	6 (6%)
Antinuclear antibodies	
Others (EJ, SRP, PM-SCL75, PM-SCL100, CN1A)	61 (64%)
	22 (23%)

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AB0812

GASTROINTESTINAL DISORDERS IN SYSTEMIC SCLEROSIS: CLUSTER ANALYSIS AND SEVERE INVOLVEMENT PREDICTION

Keywords: Motor function, Mixed connective tissue disease, Gender/diversity issues

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Background: Gastrointestinal tract (GIT) is the second most common organ involved in Systemic Sclerosis (SSc) after the skin, and is responsible for alteration of quality of life and SSc-related mortality.
Objectives: Since early development of organ failure is associated with poor prognosis, we need to identify risk factors associated with severe GIT involvement to prevent apparition of severe form of the disease.
Methods: We conducted an observational prospective and monocentric study which included 90 patients followed for SSc, from 26 December 2019 to 14 September 2021.
Results: We included 90 patients in this study, with 76 female sex (84.4 %) and a median age of 55.7 years (IQR 44.3-64.4). 64 had a limited cutaneous SSc (lcSSc) (71.1 %) and 26 had a diffuse cutaneous SSc (dcSSc) (28.9 %). We observed 28 patients (31.1 %) with a malnutrition and 9 patients (10 %) with at least one episode of digestive hemorrhage or small intestinal bacterial overgrowth or chronic intestinal pseudo-obstruction. The patients with malnutrition had less limited cutaneous SSc form (53.6 % vs 79 %, p = 0.027), more interstitial lung disease (57.1 % vs 27.4 %, p = 0.013) and more cardiac disease (39.3 % vs 11.3 %, p = 0.005). No patient without malnutrition died at the end of the follow-up whereas 4 patients with malnutrition died (p = 0.013). Clustering of individuals on the basis of the selected variables yielded a number of 3 clusters. Cluster 1, "Limited cutaneous systemic sclerosis" (n = 25) was only composed of lcSSc patients, presenting more frequently anti-centromeres antibodies (n = 22, 88% vs n = 9, 34.6%, p<0.001 and n = 2, 6.1%, p<0.001 in cluster 2 and 3 respectively). They had less frequently intestinal (n = 11, 44%) or anorectal involvement (n = 1, 4%) than cluster 2 (n = 24, 88.9% and n =16, 59.3%, p = 0.003 and p<0.01, respectively). They also had a better diffusing capacity for carbone monoxide (median [IQR]: 78.50 [70.25, 84.00], p < 0.001). Cluster 2 "SSc with cardio-digestive involvement" (n = 27) was composed of 20 patients with lcSSc (74.1%), less frequently than cluster 1 (n = 25, 100%, p = 0.02) and tends to be more frequently than cluster 3 (n = 19, 50%, p = 0.09). They had more frequently intestinal (n = 24, 88.9%) or anorectal involvement (n = 16, 59.3%). Regarding heart status, patients from cluster 2 had more frequently heart involvement (n = 12, 44.4 % vs n = 1, 4%, p = 0.002 and n = 5, 13.2%, p = 0.01 vs cluster 1 and 3 respectively) with higher BNP levels (median [IQR]: 91.0 [27.0, 244.5] vs 44.0 [20.0, 85.0], p = 0.03 and 27.0 [19.0, 42.0], p = 0.01 vs cluster 1 and cluster 3 respectively). They also had higher troponin levels than cluster 1 (median [IQR]: 8.5 [3.0, 21.5] vs 3.0 [2.0, 8.0], p = 0.04) and more frequently pericardial effusion (n = 7, 26.9% vs 0, 0.0% p < 0.01). Regarding treatment, they had more frequently aspirin (n = 7, 26.9% vs n = 0, 0%, p = 0.02 and n = 1, 2.6, p = 0.01 in cluster 1 and 3 respectively) and more frequently statin (n = 9, 34.6% vs n = 1, 4%, p = 0.02 and n = 1, 2.6%, p < 0.01). Cluster 3 "SSc with cutaneous and pulmonary involvement", composed of 38 patients, including 19 patients (50%) with diffuse cutaneous systemic sclerosis. They had higher modified Rodnan score (median [IQR]: 10.0 [8.0, 17.0] vs 3.0 [0.0, 6.0], p <0.001 and 7.0 [3.0, 15.0], p = 0.04 in cluster 1 and 2 respectively). They had more interstitial lung disease according to the CT-scan compared to cluster 1 (n = 24, 61.1% vs n = 5, 20%, p < 0.001) and tends to have more compared to cluster 2 (n = 24, 61.1% vs n = 11, 40.7%, p = 0.095). They also had more frequently immunosuppressive treatments than cluster 2 (n = 26, 68.4% vs n = 10, 37%, p = 0.02) but less frequently biotherapy (n = 3, 7.9% vs n = 9, 34.6%, p = 0.02)
Conclusion: This study reported the gastrointestinal manifestations in a cohort of 90 patients with SSc, with a predominance of gastro-esophageal involvement and in particular for the first time described a cluster analysis allowing classification of various clinical GIT phenotypes.

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AB0813

MULTICENTER ASSESSMENT OF ACRO-OSTEOLYSIS IN PORTUGUESE PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Autoantibodies, Systemic sclerosis

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Background: Acro-osteolysis is a disabling manifestation of Systemic Sclerosis (SSc). Few is known about its prevalence and clinical associations.
Objectives: To define the prevalence of acro-osteolysis among Portuguese SSc patients, to determine the most sensitive radiological location for its diagnosis and to clarify the phenotype of SSc patients with acro-osteolysis.
Methods: A cross-sectional multicenter study was conducted evaluating SSc patients from 14 Portuguese centers, registered in the Rheumatic Diseases Portuguese Registry (Reuma.pt), that fulfilled Leroy/Medsger 2001 or ACR/EULAR classification criteria for SSc. The presence of acro-osteolysis was assessed through systematic plain radiographs of hands and feet. Statistical analysis with

independent parametric or non-parametric tests, multivariate logistic regression of the significant variables in univariate analysis and sensitivity calculation of each radiographed site for the diagnosis of acro-osteolysis were performed.

Results: We included 195 patients, of whom 167 (85.6%) were female, with a median [min, max] age of 64 [20, 90] years-old and a median [min, max] disease duration of 11.2 [2, 57] years. Regarding disease classification, 146 (75.3%) patients had limited SSc, 32 (16.5%) had diffuse SSc, 9 (4.6%) had *sine scleroderma* SSc and 7 (3.6%) had early SSc. Acro-osteolysis was present in 62 (31.8 %) patients, with the hands (n=49, 25.1%) being more frequently affected than the feet (n=22, 11.3%). The most sensitive location to detect acro-osteolysis was the hand (79.0%). The presence of overall acro-osteolysis was significantly associated with digital ulcers (p=0.001), flexion contractures (p=0.031), oesophageal (p=0.006), gastric (p=0.014) and lung (p=0.004) involvements, higher mRSS score (p<0.001), anti-topoisomerase I positivity (p=0.034) and radiological calcinosis (p=0.018). Patients with hand acro-osteolysis had longer disease duration (p=0.02) and were more often affected by digital ulcers (p=0.004), flexion contractures (p=0.041), oesophageal (p=0.001), gastric (p=0.015) and lung (p=0.001) involvements, higher mRSS score (p<0.001), anti-topoisomerase I positivity (p=0.004) and radiological calcinosis (p=0.008). No significant differences were found between patients with and without feet acro-osteolysis. In multivariate analysis, anti-topoisomerase I positivity (OR 4.6, 95%CI 1.3-16.4, p=0.017) was predictor of hand acro-osteolysis.

Conclusion: The prevalence of acro-osteolysis found in Portuguese SSc patients is within the range found in the literature (20-40%) [1]. The hands were the most sensitive location to detect acro-osteolysis – a novel aspect since, to our knowledge, this is the first study evaluating acro-osteolysis in the feet besides the hands. Our data replicated some previously reported associations between acro-osteolysis and other hand involvements (digital ulcers, calcinosis and flexion contractures) and systemic complications (esophagogastric and pulmonary systems) [2-4]. Anti-topoisomerase I positivity appears to increase the risk for hand acro-osteolysis.

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AB0815

CLINICAL PHENOTYPE AND ANTIBODY CORRELATIONS USING IMMUNOPRECIPITATION IN INDIAN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES FROM THE MYOCITE COHORT

Keywords: Myositis, Epidemiology, Autoantibodies

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Background: There is a lack of epidemiological studies in idiopathic inflammatory myositis (IIM) to identify geographical and clinical disease variations between populations. Reviewing disease prevalence in different populations and clinical presentations may help improve our understanding of rare diseases.

Objectives: We reviewed the clinic-serological profile of 148 patients from a well-characterised MyoCite cohort of juvenile and adult patients with IIM from Lucknow, India, to determine significant clinical characteristics associated with different myositis-specific antibodies (MSA).

Methods: The MyoCite cohort is a retro-prospective dataset of adult and juvenile IIM patients (2017 ACR/EULAR criteria or diagnosed by two rheumatologists) enrolled in Lucknow, India, between 2017-2020. (1) The cohort is well-characterised with a detailed case record form and glossary outlining clinical characteristics and disease outcomes with biospecimen archiving. Sera were shipped to the NMH lab in Bath, and autoantibody status was determined using immunoprecipitation (IP). Sera with 140kDa band were characterised for NXP2 versus MDA5 using ELISA. Clinical associations for specific autoantibodies on IP were analysed by comparing each MSA to the rest of the cohort. We conducted univariate and multivariate logistic regressions, with results reported as odds ratios with 95% confidence intervals (CI). We selected variables as candidates for the multivariate logistic regression which scored a p-value ≤0.3 in the univariate analysis. A stepwise procedure was to select the final multivariate models which achieved the best fit, measured using AIC.

Results: Of 148 patients, one had dual MSA antibody specificity (Jo1/NXP2) and was excluded from analysis. The median age of onset was 35.5, with 75.2% being women. Muscle weakness was present in 88.9% of patients; 61.5% had a rash consistent with dermatomyositis (DM), 35% were diagnosed with ILD, and 41.3% experienced arthritis. Underlying malignancy was present in 1.4% at the time of enrolment. Dermatomyositis (DM) (30%) was the most common subtype of IIM, followed by anti-synthetase syndrome (ARS) (20%), overlap myositis (16%) and juvenile DM (14%). Anti-Jo1 (10.9%) was the most common MSA detected, followed by MDA5 (9.5%) (figure 1), and 43.5% of patients were seronegative. Mechanic's hands were associated with anti-Jo1 (OR 20.5 95%CI 5-77.7) and ARS antibodies (OR 11.9 95%CI 3.8-36.9). Heliotrope rash (OR 6.4 95%CI 1.5-26.7) and gottron's sign (OR 5 95%CI 1.2-20.9) were associated with anti-MDA5 (Table 1). ARS antibodies were negatively associated with weakness and heliotrope rash. NXP2 was associated with dysphonia (OR 29.1 95%CI 3.5-243), while Mi2 was associated positively with a V-sign rash (OR 7 95%CI 1.4-34.7) and negatively with fever. SAE antibodies were associated with dysphagia (OR 9.3 95%CI 1.1-76.6). Seronegative IIM was associated with hyperpigmentation (OR 4.3 95%CI 1.6-11.7) and erythematous changes (OR 2.8 95%CI 1.2-6.5) and was negatively associated with arthritis and fatigue.

Conclusion: Autoantibodies are present in nearly two-thirds of Indian patients with IIM, commensurate with other populations (Figure 1), although the prevalence of individual MSA differs. The frequency of ILD is closer to those previously reported in European cohorts than in East Asian populations. Most MSAs exhibited association with prominent cutaneous manifestations, including mechanics hands, heliotrope rash, Gottron's sign, V-sign, hyperpigmentation and erythematous changes. These differences in antibody profile and clinical characteristics from the MyoCite cohort compared to that of different geographical and ethnic populations previously reported suggest the potential influence of genetics and/or environmental factors.

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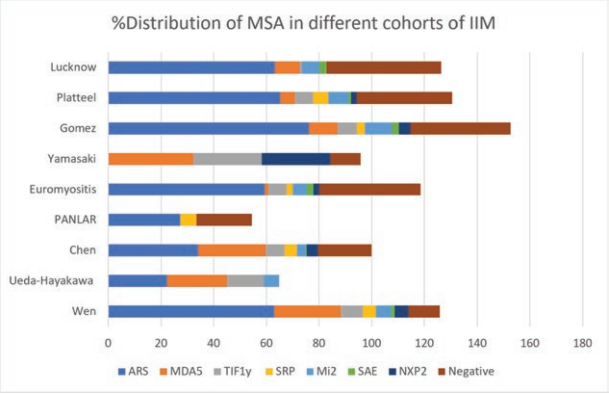


Figure 1.

Table 1 Multivariate Logistic Regression for MSA and significant results

	Positive Clinical Associations				Negative Clinical Associations			
Antibody	**Symptom**	**Odds Ratio**	**95% CI**	**p-value**	**Symptom**	**Odds Ratio**	**95% CI**	**p-value**
Jo1	Mechanic's Hand	20.5	5-77.7	<0.001				
ARS	Mechanic's Hand	11.9	3.8-36.9	<0.001	Heliotrope	0.1	0.001-0.6	0.02
					Weakness	0.2	0.05-0.96	0.04
PL-7/PL-12					Weakness	0.1	0.02-0.5	0.01
MDA5	Heliotrope	6.4	1.5-26.7	0.01				
	Gottron's Sign	5	1.2-20.9	0.03				
NXP2	Dysphonia	29.1	3.5-243	0.001				
Mi2	V-sign	7	1.4-34.7	0.02	Fever	0.07	0.008-0.6	0.02
SAE	Dysphagia	9.3	1.1-76.6	0.04				
Negative/ Unknown	Erythematous Changes	2.8	1.2-6.5	0.001	Arthritis	0.4	0.2-0.8	0.01
	Hyper-pigmentation	4.3	1.6-11.7	0.005	Fatigue	0.3	0.1-0.8	0.02

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AB0816 TREATMENT OF A PATIENT WITH SEVERE DIFFUSE SYSTEMIC SCLEROSIS (SSC) USING CD19-TARGETING CAR-T-CELLS

Keywords: Systemic sclerosis, Autoantibodies

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Background: Several data suggest a role of B-cells in SSc-pathogenesis: disturbed B-cell homeostasis with expansion of naïve and decrease of memory B-cells (1), increased levels of B-cell stimulating factors [2] and anti-fibrotic effects of B-cell-depletion in murine fibrosis models [3]. Although first randomized controlled trials show promising effects of the CD20-targeting antibody rituximab (RTX) in SSc (4,5), the role of B-cell targeting treatments remains controversial. A possible explanation is the limited B-cell repertoire targeted by CD20-depleting antibodies that spare early B-cell precursors, which are particularly expanded in SSc, as well as plasmablasts responsible for autoantibody production. Hence, deeper and wider B-cell-depletion may be effective in SSc treatment. Recently, CD19-targeting CAR-T-cells, that are used to deeply deplete B-cells in refractory lymphoma and leukemia, showed remarkable effects in refractory systemic lupus erythematosus patients, suggesting the principle feasibility to intercept with autoimmune disease via CD19-targeting CAR-T-cells.
Objectives: To test the feasibility of treating severe SSc with CD19-targeting CAR-T-cells. Outcomes: B-cell -, absolute and relative CAR-T-cell counts, ANA-titer, SSc-specific antibodies, ^{68}Ga-FAPI-04-uptake, carpal MRI, EUSTAR activity index, mRSS, TJC, forced vital capacity (FVC), diffusion coefficient (DLCO).
Methods: This is a case study of compassionate use of CD19-targeting CAR-T-cells in a 60-year old male patient with severe, diffuse SSc (year of diagnosis 2020 (first non-Raynaud manifestation, mRSS 24 at baseline) with diffuse myocardial fibrosis, lung fibrosis, Raynaud´s phenomenon and carpal arthritis who previously failed several standard therapies including methotrexate and mycophenolate. CAR-T-cell-infusion was performed upon lymphodepletion with fludarabine (25 mg/m^2 on days -5, -4, -3) and cyclophosphamide (1g/m2 on day -3) in August 2020 as single infusion. Immunosuppressive treatment was stopped before. Main outcomes were assessed before baseline and three months after CAR-T-cell infusion.
Results: CAR-T-cells expanded remarkably and fast *in vivo* from day 3 (0.3 cells/µl; 0.1% CARs of CD3+ T cells) until day 9 (0.30.19 (1275/µl; 66,35% CARs of CD3+ T cells) and were measurable until day 51 after infusion. B-cells were completely depleted by day 7 and were not detectable until day 77. Serum-IgG levels endured above 600mg/dl. CAR-T-cell therapy was well tolerated without signs of cytokine release syndrome or cell-associated neurotoxicity syndrome. ANA titers (before baseline: 1:320) and SSc-specific antibodies (anti-RNAP III antibodies, antigen RP11) were no longer detectable three months after CAR-T-cell-infusion. In parallel, myocardial tracer uptake was reduced by 30% in ^{68}Ga-FAPI-04-PET-CT imaging, a novel imaging technique that allows the molecular assessment of fibroblast activation *in vivo*. The extent of lung fibrosis on CT scan and pulmonary function test parameters was stable or slightly improved. As analyzed by contrast supported hand-MRI, carpal arthritis improved three months after CAR-T-cell therapy. Consistently, tender joint counts improved from n=22 at baseline to n=3 at 3 months follow up. In addition, tendon friction rubs were no longer present consistent with reduction of EUSTAR activity index. Skin fibrosis showed a tendency of improvement after 3 months as analyzed by two independent assessors.
Conclusion: We show for the first time, that CAR-T-cell therapy can result in the fast loss of SSc-specific autoimmunity in a patient with severe, diffuse SSc and is paralleled by amelioration of clinical manifestations including skin- and heart-fibrosis and arthritis. Further studies with longer follow-up times and more patients will help to further characterize the role of CAR-T-cell therapy in SSc.
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AB0817 CLINICAL ASSOCIATION OF ANTI-RO52 ANTIBODIES IN SYSTEMIC SCLEROSIS: A SINGLE CENTRE COHORT PRELIMINARY ANALYSIS

Keywords: Autoantibodies, Systemic sclerosis

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Background: Anti-Ro52 antibodies may be detected in several Rheumatic disorders, with different clinical significances. They may occur also in systemic sclerosis (SSc), but with clinical correlates not completely established, with some reports showing their association with pulmonary arterial hypertension (PAH), and other with interstitial lung disease (ILD).
Objectives: To evaluate the clinical characteristics of anti-Ro52 positive SSc patients.
Methods: Patients aged more than 18 years, satisfying the 2017 ACR EULAR criteria for SSc referring to our SSc Unit and with at least one follow-up visit between October 2021 and October 2022 were evaluated for study participation. All patients positive for anti-Ro52 antibodes by ELISA were then included. Clinical characteristics were retrospectively collected and analysed. Pulmonary arterial hypertension (PAH) was defined by right heart catheterization, and ILD by chest high resolution computed tomography (HRCT).
Results: between the 420 SSc patients assessed, we identified 76 patients (18%) positive for anti-Ro antibodies. Only 29 patients were characterized for anti-Ro52 antibody, and 26 were positive. These patients were in prevalence females (21; 81%), with a median age at the onset of 60.5 years (Interquartile range, IQR, 48-71) and a median follow-up of 96 months (IQR 48-180). ANA were positive in 23 patients (88%), and the 2 most observed pattern were anticentromere (10; 38%) and nucleolar (9; 35%); 6 patients (23%) had cytoplasmic positivity of the ANA test. Six patients (23%) were concomitantly anti-La positive. Anti-Scl70 were found in 2 cases (8%). Other systemic sclerosis associated antibodies were positive in 6 cases (23%): anti-RNA polymerase III antibodies, and anti-Ku antibodies, in 2 cases (8%), anti-Th/To, and anti-PM-Scl100 in one case (4%). Patients had mainly limited cutaneous SSc subset (13; 50%), 5 had diffuse cutaneous SSc (19%), and the remaining 8 (31%) had no scleroderma. SSc was in overlap with other rheumatic diseases in the 50% of cases. The overlap was with Rheumatoid arthritis (RA) in 4 cases (15%), and with Sjogren syndrome (SjS) in 10 cases (38%), with one case diagnosed with both conditions. Most patients had Raynaud's phenomenon (RP) (24, 96%). The 2 patients without RP had puffy finger (PF), that were observed in 9 cases (35%). All patients performed nailfold capillaroscopy (NVC), showing scleroderma pattern in 22 cases (85%; early, 13, 50%; active 7, 27%; late 2, 8%). ILD was observed in 12 patients (46%), the HRCT pattern was mainly NSIP (10, 83%), with a cellular phenotype in the 50% of cases. Only 2 patients (17%) had UIP pattern. Ten patients (38%) had an history of smoke, but only 3 had ILD. PAH was identified in 7 patients (27%), in 3 cases concomitantly to mild ILD. Four patients (15%) had myocarditis. Dyspnoea was reported in 10 cases (38%; NYHA class: I 2, 20%; II 5, 50%; III 3, 30%).
Conclusion: In our cohort, anti-Ro52 positive patients with SSc had only rarely the diffuse subset of the disease. Clinically, these patients may have ILD, PAH, and myocarditis. The pattern of ILD was mainly NSIP, and only rarely UIP. The main overlap conditions were RA and SjS, and not rarely these patients were positive for some rare SSc rare autoantibodies, suggesting the need of a careful autoantibody profiling in this subset of patients. The characterization of anti-Ro52 antibodies in patients till now not assessed is ongoing.
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AB0818

SCLERODERMA RENAL CRISIS TREATMENT WITH C5 INHIBITOR ECULIZUMAB – A REVIEW OF LITERATURE

Keywords: bDMARD, Systemic sclerosis, Targeted synthetic drugs

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Background: Scleroderma renal crisis (SRC) occurs in about 10% of SSc patients and is characterized by abrupt onset of hypertension, thrombotic microangiopathy (TMA), and acute kidney injury. Although prognosis has improved with the use of angiotensin-converting enzyme inhibitors (ACE-i), 40% of SRC patients still require dialysis, and 20-25% die within 1 year. The pathogenesis of SRC remains poorly understood but a growing body of evidence suggests that activation of the complement system may be involved in the disease [1]. It is hypothesized that injury to the endothelium due to persistent stimulation by the complement system creates a pathological loop responsible for thrombotic microangiopathy and target organ injury. Several case reports have shown that Eculizumab (humanized recombinant immunoglobulin G2/4 monoclonal antibody directed against the complement component C5) is effective in treating patients with SRC who presented with symptoms of thrombotic microangiopathy [2,3].

Objectives: In this study, we aimed to characterize the presentation and outcome of patients with SRC who were treated with C5 inhibitor, Eculizumab.

Methods: A literature search was conducted on PubMed and Cochrane from inception to December 2022 using MeSH terms for 'scleroderma', 'systemic sclerosis' 'scleroderma renal crisis', 'Eculizumab', and 'Solaris'. We included case reports, case series, observational studies, and literature reviews. We included patients with treatment refractory SRC who did not show improvement with ACE inhibitors or patients who had evidence of thrombotic microangiopathy (SRC-TMA).

Results: The initial search revealed 27 articles. After exclusion of non-relevant articles, data was included from 11 articles and 16 patients. The median age was 51 years, sex distribution was 4 males (33.3%) and 12 females (66.6%). Treatment with ACE-i was reported in 11 (68.75%), plasmapheresis (PLEX) in 8 (50%), steroids in 5 (31.25%), cyclophosphamide (CYC) in 3 (18.75%), calcium channel blockers (CCB) in 2 (12.5%) and Rituximab (RTX) in 2 (12.5%) of the patients. Renal replacement therapy (RRT) was required in 10 patients (62.5%). 8 out of 10 patients (80%) were reported to have clinical improvement with Eculizumab (Eculi) therapy **(Table 1).**

Conclusion: Recent clinical studies have focused on the role of complement activation in the pathogenesis of SRC and results suggest the use of C5 inhibitor in the treatment of refractory SRC. Serum complement levels and renal histological findings could help us identify patients who could benefit from Eculizumab. These findings should prompt testing on a larger cohort of SRC-TMA patients. However, based on the positive anecdotal evidence, it is reasonable to treat SRC patients with eculizumab in whom complement-mediated TMA is suspected.

Table 1 : Characteristics of patients included in the study

Author	No. of cases (n)	Sex M/F	Age (Y)	Treatment	RRT	Improvement	Outcome
Devresse et al	1	F	28	Eculi, ACEi CCB, PLEX	Y	Y	Death
Uriarte et al	1	F	40	Eculi, ACEi CCB, PLEX	Y	Y	Alive
Riley et al	1	M	47	Eculi, ACEi	Y	Y	Alive
Saba et al	1	F	52	Eculi, ACEi	N	Y	Alive
Rhoads et al	1	F	58	Eculi, PLEX	N	Y	Alive
Nakamura et al	1	M	61	Eculi, PLEX steroids	Y	N	Alive
Thomas et al	1	F	46	Eculi, ACEi PLEX, steroids	N	Y	Alive
Skonieczny et al	1	M	46	Eculi, steroids FFP	Y	Y	Alive
Arneson et al	1	F	51	Eculi, ACEi	Y	N	Alive
Shahoub et al	1	F	NA	Eculi, ACEi, PLEX, steroids, CYC	N	Y	NA
Gouin et al	6	F	73	Eculi, PLEX steroids	Y	NA	Death
		M	80	Eculi, RTX	Y	NA	Death
		F	44	Eculi, ACEi	Y	NA	Death
		F	64	Eculi, ACEi, PLEX, CYC	N	NA	Alive
		F	80	Eculi, ACEi RTX	Y	NA	Alive
		F	43	Eculi, ACEi CYC	N	NA	Alive

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AB0819

CLINICAL AND IMMUNOLOGICAL PROFILES OF PATIENTS WITH ANTI-SYNTHETASE SYNDROME: A RETROSPECTIVE COHORT STUDY FROM A TERTIARY CENTRE

Keywords: Autoantibodies, COVID, Myositis

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Background: Anti-synthetase syndrome (ASS) is a rare auto-immune condition that combines autoantibodies and specifics clinical manifestations, including myositis, interstitial lung disease (ILD), polyarthritis, mechanic's hands, Raynaud's phenomenon, and unexplained fever. The hallmark of this syndrome is the presence of anti-aminoacyl-tRNA-synthetase (ARS) antibodies. Several anti-ARS antibodies have been described, anti-Jo1 being the most common, followed by anti-PL7, anti-PL12, anti-OJ, anti-EJ, anti-KS, anti-YRS, and anti-Zo. According to a recent epidemiological survey, the rising number of patients with autoimmune diseases, including idiopathic inflammatory myopathies (IIM) coincides with the COVID-19 pandemic.

Objectives: To evaluate the clinical characteristics of ASS patients with different anti-ARS antibodies from a tertiary rheumatology center.

Methods: We conducted a retrospective, single-centered study on consecutive patients diagnosed with ASS from 1 January 2015 to 31 December 2022. Clinical and serologic data were obtained by medical records review from hospital database. Myositis-specific antibodies (MSA) and myositis-associated antibodies (MAA) were tested using commercial ELISA kits. We included all patients fulfilling Connor's criteria for ASS.

Results: Sixty-one patients (44 females) with mean age 54.4 (13.8) years were included. The most frequently reported clinical manifestation was arthralgia (68.8%), followed by Raynaud's phenomenon (67.2%), ILD (65.6%), myositis (46%), mechanic's hands (44.3%), arthritis (39.3%), and fever (18.0%). The typical triad for ASS, including myositis, arthritis and ILD was present in 17 patients. Twenty-eight (45.9%) patients were PL7+, 21 (34.4%) were Jo1+, 3 (4.9%) were PL12+, and 2 (3.2%) were OJ+. Seven patients were positive for more than two anti-ARS antibodies. The most frequently found MAA was anti-Ro52 (n=23, 37.7%). Of the 61 patients included, 41 (67.2%) patients were diagnosed in the last 3 years (COVID-19 pandemic). The most frequently detected MSA in ASS patients diagnosed during COVID-19 pandemic was anti-PL7 (25/28), while anti-Jo1 was the most common MSA in ASS patients diagnosed before 2020 ($p<0.05$) (Fig 1). The anti-Jo1+ patients were younger, have significantly more frequent muscle involvement and significantly higher levels of CK than anti-PL7+ patients ($p<0.05$). The co-occurance of anti-Ro52 antibodies was more frequently observed in anti-Jo1+ patients (n=11, 52.4%) than in anti-PL7+ patients (n=6, 21.4%) ($p<0.05$). We did not find statistically significant differences between ASS groups regarding sex, disease duration, clinical manifestations including dermatologic lesions, Raynaud's phenomenon, arthralgia/arthritis, ILD, fever, and cancers (all $p>0.05$).

Conclusion: ASS patients have heterogenous manifestations, and different types of anti-ARS antibodies are associated to distinct clinical and immunological features. The COVID-19 pandemic led to increase prevalence of ASS cases and to a remarkable shift in the anti-ARS antibodies profile, with increased frequency of anti-PL7 antibodies. Further studies are needed to investigate the link between SARS-CoV-2 infections and myositis.

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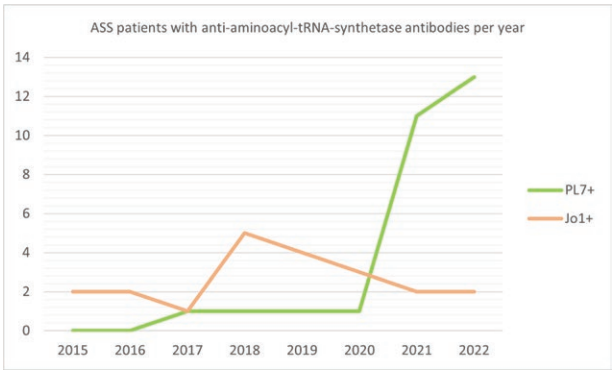


Figure 1. ASS patients with positive anti-ARS antibodies per year (from 2015 to 2022). The green line shows the PL7+ patients; and the orange line shows the Jo1+ cases.

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AB0820 THE RISK OF MALNUTRITION IS A PROBLEM ASSOCIATED WITH SYSTEMIC SCLEROSIS

Keywords: Diet and Nutrition, Patient reported outcomes, Systemic sclerosis

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Background: Malnutrition is a serious health problem that worsens comorbid processes, increases hospital stays, infections and mortality. In addition, in chronic patients, it increases the complexity of the processes and the fragility of the patient who suffers from it.
Objectives: To describe the prevalence of malnutrition and malnutrition risk and its associated factors in a series of patients with Systemic Sclerosis (SSc).
Methods: Design: Cross-sectional descriptive study. **Participants**: consecutive recruitment of patients with SSc (ACR/EULAR 2013 criteria) followed up in our unit. Follow-up of these patients is usually carried out every 3 to 6 months in consultation and all patients were registered in a database. 90% of the patients accepted and signed the consent, the rest refused due to travel or work difficulties. **Variables:** The main variable was malnutrition or risk of malnutrition defined according to the Mini Nutritional Assessment (MNA) questionnaire, malnutrition was defined with a score less than or equal to 7, risk of malnutrition with scores between 8 and 11, and normal nutrition with values greater than 11. Clinical data, anthropometric and laboratory values were collected, as well as sarcopenia according to the European Working Group on Sarcopenia in Older People (EWGSOPII) and Short Physical Performance Battery (SPPB) criteria. **Statistical analysis:** descriptive, bivariate and a multiple linear regression model to identify factors associated with malnutrition and risk of malnutrition.
Results: 52 patients were included, of whom 51 (98.1%) were women, with a mean (SD) age of 60.8 (11.0) years. 17/52 patients (32.7%) were at risk of malnutrition and 1/52 patients (1.9%) were malnourished (Table 1). Patients at risk of malnutrition and malnutrition compared with patients with normal nutritional status, more frequently had diffuse skin involvement (38.9% vs 14.7%; p= 0.05), sarcopenia (44.4% vs 11.8%; p=0.01), severe sarcopenia (27.8 vs 2.9; p=0.01), weight loss (100.0 vs 55.6%; p<0.001) and polypharmacy (94.4% vs. 67.6%, p=0.02). Likewise, patients at risk of malnutrition and malnutrition had lower mean values (SD) in calcium levels (8.7 [2.1] vs 9.2 [0.42]; p=0.05), circumference lesser left calf (32.8 [3.0] vs 35.4 [6.0]; p = 0.03), and in the SPPB functional grade (8.1 [4.2] vs 9.8 [2.9]; p = 0.06) and higher PCR values (10.5 [11.1] vs 7.1 [7.0]; p = 0.06). In multivariate analysis, the only factor associated with malnutrition in SSc was sarcopenia (B [95% CI], -2.521 [-4.867, -0.175]; p=0.036) (R2=0.115).
Conclusion: Malnutrition has serious consequences for the health of people with SSc, including the development of sarcopenia, a condition that predicts disability, hospitalization, and premature death.

Table 1. Clinical-epidemiological characteristics of the 52 patients in SSc

Variable	ES n=52
Woman, n (%)	51 (98,1)
Age, mean (SD)	60,8 (11,0)
Limited skin patern, n (%)	40 (76,9)
Disseminated skin patern, n (%)	12 (23,1)
DILD, n (%)	17 (32,7)
HTAP, n (%)	5 (9,6)
Anti-Centromere, n (%)	28 (53,8)
Anti-Sl70, n (%)	10 (19,2)
Other antibodies, n (%)	9 (17,3)
MNA Normal nutritional status n (%)	34 (64,5)
MNA Risk of malnutrition, n (%)	17 (32,7)
MNA malnutrition, n (%)	1 (1,9)
Sarcopenia, n (%)	12 (23,1)
Sarcopenia severe, n (%)	6(11,5)
Right calf circumference, mean (SD)	34,5 (5,5)
Left calf circumference, mean(SD)	34,5 (5,3)
Weight loss >1kg in the last 3 months, n (%)	25 (48,1)
Polypharmacy, n (%)	12 (23,1)
CPR mg/dl, mean (SD)	8,3 (8,7)
Calcium mg/L mean (SD)	9 (1,2)
Prealbúmin mg/dl, mean (SD)	21,4 (4,6)

Abreviaturas. SSc: sistemic sclerosis; DE: standard deviation; DILD: diffuse interstitial lung disease; HTAP: pulmonary arterial hypertension; MNA: mini nutritional assesment; CPR: c reactive protein.

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AB0821 VALIDITY AND RELIABILITY OF MEASUREMENT OF PERIPHERAL OXYGEN SATURATION DURING THE 6-MINUTE WALK TEST IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Lungs, Validation, Systemic sclerosis

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Background: The 6-Minute Walk Test (6MWT) is a standardised method routinely used to screen for and monitor interstitiel lunge disease and/or pulmonary arterial hypertension in patients with systemic sclerosis (SSc). Studies shows that esaturations during the 6MWT are associated with severity of pulmonary manifestations in patients with SSc [1]. Digital sensors are commonly used to measure peripheral oxygen saturation (SpO_2) during the 6MWT. However, digital-based sensors may have important limitations in patients with SSc due to disease-related microangiopathy, Raynaud's phenomenon, sclerodactyly and motion artifacts during the 6MWT [2]. Sensors located at more central body positions may therefore be more accurate as these as less prone to Raynaud attacks.
Objectives: To determine the validity and re-test reliability of peripheral oxygen saturation measured at the finger, forehead, and ear during the 6MWT in patients with SSc.
Methods: 82 patients with SSc had an arterial line placed while performing the 6MWT. Peripheral oxygen saturation was simultaneously measured by finger, forehead, and earlobe sensors and compared to the arterial oxygen saturation (SaO_2) measured before and after the 6MWT. 40 patients repeated the 6MWT one week later. We used Bland-Altman plots to display the agreement between SpO_2 and SaO_2, and between the minimal SpO_2 ($minSpO_2$) one week apart. The intraclass correlation coefficient (ICC, 95% confidence interval 95% CI]) for repeated measurement of minSpO2 was calculated.
Results: The mean difference (SpO_2 - SaO_2, ± standard deviation [SD]) after the 6MWT was –3.3% (±4.82), 0.15% (±1.55), and 1.36% (±1.93) for the finger, forehead, and earlobe, respectively (Table 1).
The finger $minSpO_2$ also demonstrated the poorest re-test reliability: The mean difference in $minSpO_2$ (visit2-visit1, ±SD) was 1.28% (±5.3), 0.74% (±4.36) and –1.10% (±2.87),). The ICC (95% CI) showed good agreement using the ear and forehead probe (ICC_{ear} = 0.89 [0.80; 0.94]; $ICC_{forehead}$ = 0.88 [0.60; 0.87]), while a modest reliability was found using the finger probe (ICC_{finger} = 0.65 [0.43; 0.80]).
Conclusion: Peripheral oxygen saturation should be measured using either the earlobe or forehead during the 6MWT in patients with SSc.
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Table 1. Validity and re-test reliability of peripheral oxygen during the 6MWT (n= 82)

	Finger probe	Forehead probe	Ear probe
Mean difference SpO2 - SaO2			
Mean difference $_{pre\text{-}test}$ (+/-SD)	–0.68% (±1.88)	0.13% (±1.26)	1.54% (±0.69)
Mean difference $_{post\text{-}test}$ (+/-SD)	–3.30% (±4.82)	0.15% (±1.55)	1.36% (±1.93)
Mean difference of the minSpO$_{2\ (visit2\text{-}visit1)}$			
Mean difference (±SD)	1.28% (±5.3)	0.74% (±4.36)	1.10% (±2.87)

Abbreviations: SpO_2, Peripheral oxygen saturation; SaO_2, Arterial oxygen saturation; SD, Standard deviation.

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AB0822 SYSTEMIC SCLEROSIS ASSOCIATED ANTIBODIES POSITIVITY IN SYSTEMIC SCLEROSIS PATIENTS: SINGLE VS. COMBINATION

Keywords: Systemic sclerosis, Biomarkers, Autoantibodies

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Background: Autoantibodies (abs) are one of the most widely used tools currently in systemic sclerosis (SSc) as biomarkers. It has been described that 95% of patients with SSc have at least one ab and ≈5% >1. When looking only at abs associated with SSc (SSc-ab) that prevalence is reduced to 2.6%. The combination usually confers different clinical characteristics compared to those with positivity for a single ab.
Objectives: To determine the prevalence of the combination of SSc-ab in a series of patients diagnosed with SSc, and to analyze the clinical differences between those with positivity for a single vs multiple SSc-ab.
Methods: Retrospective study of 134 patients with SSc in whom the SSc-ab profile was systematically determined by an immunoblot (Euroimmun®) which included anti-topoisomerase (ATA), anti-centromere (ACA), anti RNA-Polymerase III (ARA), anti-U3-RNP (U3), anti-Th/To (Th/To), anti-Ku (Ku), anti-PmScl (PmScl) and anti-U1-RNP (U1) abs. Demographic and clinical differences were studied between those with positivity for a single ab vs those with more than one. Differences were identified using Fisher's exact test, and Mann-Whitney.
Results: Table 1 shows the SSc-ab profile of our patients: 128/134 (96%) were ANA+, 111 (82%) had 1 SSc-ab, 8 (8%) had 2 and 3 (2.3%) had 3 concomitant SSc-ab. Ku was found in combination with other ab in all patients and was present in the 3 patients with 3 ab. When analyzing patients with combined vs sole abs, we found the following statistically significant differences: the limited cutaneous SSc subtype associated with ACA was lost in the combinations ACA-U1-Ku+ and ACA-Ku+, being 0/1 patients (0%, p=0.038) and 0/1 patients (0%, p=0.039), respectively). Patients with ATA-ARA+ had a higher modified Rodnan skin score vs ATA+ (18.33 ± 2.08 vs 9.67 ± 5.59, p=0.036). No other statistically significant differences were found in any other characteristics in the patients with ≥1 vs 1 ab, although a trend toward some clinical differences was seen in ACA-U1-Ku+ patients, with more digestive symptoms and interstitial lung disease, and less myositis than ACA+. Additionally, patients ACA-PmScl-Ku+ seemed to have less myositis than those with PmScl+, and patients ACA-Ku+ less myositis than those ACA+.
Conclusion: The concomitant presence of more than 1 SSc-ab is more frequent in our cohort than initially described (8%), likely due to the systematic detection carried out in our study. Anti-Ku was the most frequent ab in combination to others. The combination of abs may change the characteristic clinical phenotypes associated to them when found in isolation. We saw some differences in our study, although conclusions cannot be drawn due to the limiting sample size. The implementation of routine immunoblots as ab screening to achieve a better characterization of patients could be a helpful tool for medical professionals, as these combinations of SSc-ab may have prognostic implications.
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Table 1 : Profile of antibodies. Numbers in brackets indicate total number of patients.

	Total	Coexistence	%	Overlapping antibodies	
				2	3
Anti-Ku (Ku)	5	5	100%	ATA (1), ACA (1)	PmScl-ACA (1), U1-ACA (1), Th/To-U1 (1)
Anti-U1-RNP (U1)	4	2	50%	-	ACA-Ku (1), Th/To-Ku (1)
Anti-Th/To (Th/To)	4	2	50%	ACA (1)	U1-Ku (1)
Anti-PmScl (PmScl)	7	3	43%	ATA (1), ACA (1)	ACA-Ku (1)
Anti-topoisomerase (ATA)	22	5	23%	ARA (3), PMScl (1), Ku (1)	-
Anti-RNApolymerase III (ARA)	13	3	23%	ATA (3)	-
Anti-centromere (ACA)	61	5	8%	PmScl (1), Th/To (1), Ku (1)	U1-Ku (1), PmScl-Ku (1)
Anti-U3-RNP	1	0	0%	-	-

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AB0823 A BAYESIAN APPROACH TO DETERMINE THE ROLE OF ORAL ANTICOAGULANTS FOR THE OCCURRENCE OF DIGITAL ULCERS IN SYSTEMIC SCLEROSIS – A EUSTAR OBSERVATIONAL STUDY

Keywords: Systemic sclerosis, Artificial Intelligence, Rare/orphan diseases

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Background: In systemic sclerosis (SSc), the role of oral anticoagulants (OACs) for treating or preventing the occurrence of digital ulcers (DUs) is not well understood. Given the low prevalence of OACs used in these patients, standard frequentist statistics are not suitable to capture the effect of OACs on DUs conclusively. However, a Bayesian statistical approach, which incorporates prior knowledge, can deal with a low prevalence of outcome or exposure and might provide conclusive evidence.

Objectives: To assess the effectiveness of a therapy with OACs on DUs in patients with SSc.
Methods: This study used prospectively collected data from the European Scleroderma Trials and Research group (EUSTAR) registry. Patients fulfilling the 2013 ACR/EULAR SSc classification criteria with complete longitudinal data on the presence of DUs and OACs were included in the analysis. The Bayesian prior probability distribution was created by capturing SSc experts' opinion on the probability of absence of DUs with and without OACs and their degree of uncertainty using a questionnaire. In addition, participants ranked factors that influence the presence or absence of DUs as confounding factors using a numeric rating scale. The outcome was the absence of DUs at the last follow-up visit in SSc patients from the EUSTAR cohort, after one year of exposure to OAC. A nearest neighbor matching algorithm using Bayesian Additive Regression Trees with uniform priors generated a cohort with two groups of patients (treated and non-treated with OACs), which were balanced for age, sex, anti-Scl-70 antibody positivity, joint contractures, use of platelet inhibitors, use of prostacyclin analogues, use of any endothelin receptors antagonists or any phosphodiesterase type 5 inhibitor. The matching algorithm generated two balanced groups of treated and untreated patients (imbalance < 10%). A Bayesian logistic regression was implemented to estimate the effect of OACs on DUs. This model incorporated the priors elicited from experts' beliefs and was adjusted for the above mentioned factors that influence the absence of DUs, as well as modified Rodnan skin score, disease duration, season, left ventricular ejection fraction, presence of pulmonary hypertension, C-reactive protein elevation, arterial hypertension and any previous DUs.
Results: Of the 6,424 patients enrolled in the EUSTAR registry, 663 (10.3%) had current digital ulcers, 2556 (39.8%) had previous DUs and 143 (2.2%) were exposed to OACs at their last follow-up visit. Mean age was 59 (SD: 13.6) years, 933 (14.5%) were males, mean disease duration was 13.1 (SD: 8.7) years, 4,454 (69.3%) had a limited *cutaneous SSc and* 1510 (23.5%) had C-reactive protein elevation. The median probability for the absence of DUs after exposure of one year to OACs was 70-75%, the pessimistic and optimistic probability were 70-75% and 80-85% respectively. After incorporation of the prior experts' opinion, the unadjusted analysis revealed that the use of OACs was associated with absence of DUs at the last follow-up visit (OR 2.05, 95%CrI 1.63 to 2.46). In the adjusted analysis, the effect is OACs was slightly stronger (OR 2.15, 95%CrI, 1.71 to 2.52). The results of the analysis where the priors from experts were withheld (and uniform priors were set) are illustrated in figure 1.
Conclusion: This study indicates with incorporation of Bayesian priors that represent experts' beliefs, a positive effect of OACs for the DUs in SSc.

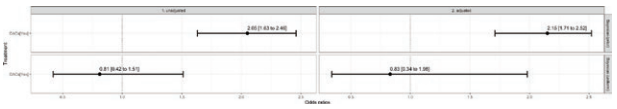


Figure 1. Effect of OACs on the absence DUs related to SSc at the last follow-up visit. Bayesian (priors): Analysis where the prior knowledge from the experts was incorporated into the model. Bayesian (uniform): Analysis where the prior knowledge from the experts was not incorporated into the model and a uniform/uninformative/neutral prior was used. OACs: Oral anticoagulants.

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AB0824

THE ROLE OF IMMUNOSUPPRESSIVE THERAPY IN GASTROINTESTINAL INVOLVEMENT AND ITS IMPACT ON QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC SCLEROSIS - A COHORT STUDY

Keywords: Systemic sclerosis, Gastrointestinal tract

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Background: Gastrointestinal (GI) disease is a major cause of morbimortality in systemic sclerosis (SSc) and affects up to 90% of patients. GI manifestations are frequently unrecognized in early phases and there are few data suggesting the potential effect of immunosuppression (IS) in GI tract.
Objectives: The aim of this study was to evaluate the role of IS in GI involvement and its impact on health-related quality of life (HRQoL) in SSc patients.
Methods: A cross-sectional multicenter study was conducted, enrolling SSc patients that fulfilled the 2013ACR/EULAR criteria or presented the EUSTAR criteria for very early diagnosis of SSc (VEDOSS). Patients were requested to answer UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract, SHAQ and Short Form Health Survey (SF36) measures. Social-demographic and clinical data were collected. GI involvement was determined by the presence of one of the following: GI symptoms for at least 3 of the last 7 days, abnormalities in GI exams and/or use of GI pharmacological therapies. IS was defined as exposure to at least one of the following: mycophenolate mofetil (MMF), cyclophosphamide (CYC), methotrexate (MTX), azathioprine (AZA), leflunomide, glucocorticoids (>10mg/d prednisone-equivalent), rituximab, tocilizumab, and abatacept, for more than 6 months. General descriptive analysis and independent parametric or non-parametric tests were performed using SPSSv26.
Results: One-hundred and one patients were included, 83 female (82.2%), with a mean age of 56.8±12.39 years-old and a mean duration of disease of 67.2±72.5 months. Sixty-four patients (63.4%) had limited SSc, 30 (29.7%) diffuse and 7 (6.9%) presented VEDOSS. Forty patients were under IS therapy, being the MTX the most frequent drug in 21.8%, followed by MMF in 11.9% and AZA in 5.9%. Seventy-two patients (71.3%) had GI involvement, where clinical manifestations were present in 72.2% patients, abnormalities in GI exams in 44.4% and GI pharmacotherapy was used in 41.7% patients. Patients with GI involvement were significantly more frequent under IS therapy (p=0.044), although no differences were found in severity of symptoms in UCLA domains between patients with and without IS. On the other hand, patients without GI involvement and under IS therapy presented significantly higher total UCLA score (mean 0.10±0.11 vs 0.11±0.18 for patients with and without IS therapy respectively, p=0.046). IS group was significantly more frequent under GI pharmacotherapy (p=0.006), being the proton pump inhibitors (PPI) the most significantly prescribed drug (55% vs 16.4% for patients with and without IS respectively, p<0.01). IS group had significantly higher SHAQ scores in total item (p=0.001) and overall disease severity VAS (p=0.009). Regarding HRQoL patients under IS present significantly lower SF36 scores for physical functioning (p=0.001), physical role functioning (p=0.002), physical component summary (p=0.001) and general health perception (p=0.036).
Conclusion: Patients with GI involvement were more frequent under IS, although no differences were found in severity of symptoms in UCLA domains when compared to those without IS. IS therapy was associated with worst HRQoL probably due to more severe multi-organ disease and were treated more often with PPI. Investigation is needed to evaluate the potential effects of IS in GI tract, as

patients with absence of GI involvement presented higher UCLA scores when IS therapy was given, which may reflect the potential GI complaints as an adverse effect by therapy, rather than involvement by the SSc.

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AB0825 EFFICACY OF AUTOLOGOUS PLATELET RICH PLASMA ON MORPHEA: A COMPARATIVE CLINICAL AND ULTRASONOGRAPHIC FOLLOW UP STUDY

Keywords: Ultrasound, Skin, Systemic sclerosis

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Background: Morphea is a subtype of limited scleroderma characterized by atrophic changes. There are multiple treatment modalities for morphea, but all have limited success to restore atrophy.

Objectives: To evaluate the efficacy and safety of paltelet rich plasma (PRP) to restore skin changes in morphea such as (skin atrophy, dyspigmentation and adnexal destruction) by ultrasound and Localized Scleroderma Cutaneous Assessment Tool (LoSCAT).

Methods: Nine morphea patients (21 lesions) were diagnosed clinically and by histopathology. Intradermal PRP was injected into morphea lesion once weekly for 12 sessions. The disease severity and damage were evaluated at baseline, after the last session (3 months later) and at 6 months follow up using (LoSCAT). Echogenicity and skin layer thickness were measured by musculoskeletal ultrasound with high frequency linear probe.

Results: The mean age of our patients was 21.8 ± 8.4 years (range: 11 to 36 years). The mean duration of morphea lesions was 5.96 ± 2.4 years (range: three months to 20 years). The LoSCAT score showed a significant improvement with a mean reduction from 13 ± 7.3 up to 7.33 ± 6.8 after therapeutic endpoint (at 3 months) reaching to 6.44 ± 7.1 after 6 months follow up with p-value = 0.008 and 0.014 respectively. The activity index (LoSAI) also showed a significant lowering in the score at both timepoints with p-value =0.02 and 0.04 respectively. The significant difference in size between morphea lesions and healthy control areas by US (1.77± 1.13 vs 3.29 ± 1.72; p = 0.007) has been vanished after treatment (at 3 month; p= 0.17 and at 6 month; p=0.53). There was a significant positive correlation between the duration of the lesion and the improvement assessed by ultrasound with p-value = 0.01. As regard adverse effects all patients reported having pain during PRP injection, transient edema of face reported by 4 patients (45%) and only 2 patients showed transient erythema. fig 1.

Conclusion: Autologous PRP is a safe technique with great aesthetic outcomes as filling up of contour defects and correction of both hyper and hypopigmentation in addition to softening of the indurated lesions.

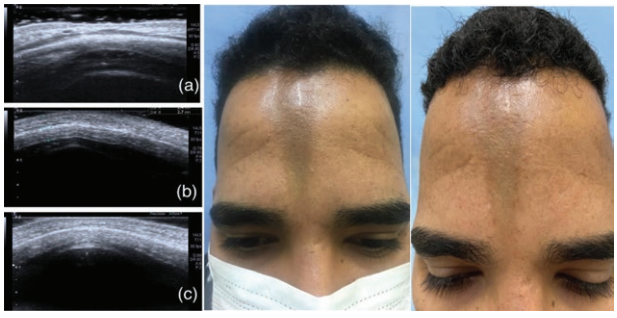


Figure Ultrasound (greyscale; transverse view) (a) before treatment shows morphea lesion in between two healthy areas. The lesion shows dermal and subcutaneous atrophy at end-stages with Loss of the border between dermis and subcutaneous tissue. (b) after treatment shows marked increase in dermal and subcutaneous thickness (c) remained improvement after 6 months of the end of treatment (d& e: photos for the same patient before treatment & at six-month follow up).

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AB0826 EXPLORING THE POTENTIAL GENDER DIFFERENCE IN MYOSITIS: DISEASE PHENOTYPE AND ANTIBODY PROFILE FROM A SINGLE-CENTER ITALIAN COHORT

Keywords: Autoantibodies, Myositis, Gender/diversity issues

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Background: Idiopathic inflammatory myopathies (IMM) include a heterogeneous group of rare autoimmune diseases with a large spectrum of muscular and systemic manifestations, mainly involving skin and lung [1,2]. Myositis specific antibodies (MSA) and myositis associated antibodies (MAA) have been described in IMM patients potentially correlating to disease outcome [3]. As well documented, autoimmune diseases present with a clear gender bias with a greater prevalence among women. To our knowledge, no studies has explored the potential gender difference in IIM patients.

Objectives: The aim of the study was to explore differences in disease features, clinical outcome, antibody profile, and treatments in IMM patients according to the gender.

Methods: In an observational study, we included patients with a defined IIM diagnosis who were referred to 3rd level Rheumatology Unit "Tor Vergata" University Hospital in Rome (Italy) for the past 5 yrs (to Dec 2022). Inclusion criteria were i. a defined diagnosis of dermatomyositis (DM), polymyositis (PM), and anti-synthetase syndrome (ASS), in accordance with the 2017 EULAR/ACR criteria, ii. age ≥ 18 y.o., iii. availability of medical records and consent to study. Data comprised: disease duration and diagnostic delay, clinical phenotype, treatments, and autoantibodies including anti-nuclear antibodies (ANA), MSAs (anti -MDA5, -NXP2, -SAE, Mi2, -TIF1, anti-tRNA synthetase, -Jo1, -PL7, -EJ), and MAAs (anti-PM/Scl, -Ro52, -Ku, U1RNP).

Results: The study cohort comprised 31 patients who met the inclusion criteria, with a similar gender distribution [n= 17 (54.8%) females and n=14 (45.2%) males]. The median age at symptoms onset was similar in both groups (59±13.3 vs 58.6±12.6 yrs) while males experienced slightly longer diagnostic delay (10.7±14.4 vs 8.7±9.6 months) and disease duration (30±29 vs 21±20 months) than females (P <0.05 for both). No significant difference in the distribution of IIM occurred between the two groups with a half of patients affecting mostly by DM (F 76.5% *vs* M 50%). However, both PM (F 6.5% *vs* M 21.4%) and ASS (F 6.5% vs M 28.6%) were moderately prevalent in males. Skin involvement occurred similarly in both groups while lung disease occurred about twofold in males (57.1%) than females (29.4%). Most patients in the cohort showed ANA titre≥ 1:160, with a comparable rate in females and males (64.7% vs 64.3%), and a positivity for at least one MSA and MAA. A double positivity of MSA occurred in 6.5% of the cohort, all females (MDA5/anti NXP2 and MDA5/EJ). The whole cohort had undergone steroids as 1st line therapy: as steroid-sparing agents, the main difference on treatments occurred for the mycophenolate mofetil which resulted significantly more administered in males (57.14%) than females (6%, P 0.002). Furthermore, among patients with lung involvement (n=13), the need to treat the progression of interstitial lung disease, by using the antifibrotic agent (nintetanib), resulted only in males (15%).

Conclusion: Our preliminary findings suggest that IMM can present a gender difference in disease outcome by showing a longer diagnostic delay and a higher respiratory involvement in male patients. These data might highlight a possible gender-oriented approach in accordance with a different disease profile and treatment strategies but require further investigations in a larger cohort.

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Disclosure of Interests: None Declared.

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AB0827 CLINICAL SIGNIFICANCE OF SERUM FERRITIN IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis

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Background: The main systemic sclerosis (SSc) manifestations are skin thickening, microangiopathy and ischemic changes in tissues, fibrotic damage to the lungs, heart, kidneys, and digestive system, arthritis, and myopathy. Acute phase reactants (APR) like erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) reflect inflammation activity in various inflammatory conditions. Ferritin is a protein bound to iron; low serum ferritin indicates iron deficiency and/or anemia. Instead, high ferritin levels are associated with inflammatory and non-inflammatory conditions such as dermatomyositis, pulmonary fibrosis, lupus, systemic COVID-19, vasculitis, tissue damage, thromboembolic complications, and metastatic cancer. The possible role of ferritin in SSc as APR is unclear.
Objectives: We aimed to assess whether ferritin levels can reflect the severity of SSc and predict the outcome.
Methods: 241 files of SSc patients with information on serum ferritin level (ferritin over 300 mg/dL is considered elevated) who visited the Rambam Rheumatology Institute in the years 2004-2021were used for retrospective analysis. Patients' demographic, clinical, laboratory, imaging, and respiratory function data were collected from electronic hospital files. Statistics included Student's T-test, Pearson's chi-squared test, and Kaplan-Meier curve; statistical significance was determined as p<0.05.
Results: 36 patients (FerEl-SSc) had elevated ferritin values; the rest (n=205) represented the second group (FerNor-SSc). Significant differences were seen in gender (male 44.4% - 15.6%), disease duration (4.56 - 7.7 years), modified Rodnan skin score (12.3 - 6.9), as well as in incidence of lung (65.7% - 38.7%), heart (51.4% - 21.1%), and renal (28.6% - 5.9%) involvement. Increased ferritin correlated with elevated ESR, CRP, creatinine, creatine kinase, troponin, and reduced hemoglobin, impaired pulmonary function tests and reduced left ventricular ejection fraction on echocardiography. Patients with elevated ferritin had a significant increase in mortality rates (52.8% and 35.1%) and non-significant reduction in survival.
Conclusion: Our study demonstrated that ferritin has a potential as a sensitive marker for SSc severity in term of skin thickening, vital organ complications, and mortality. The ferritin test is simple and inexpensive, it can add to the complex SSc assessment and contribute to treatment decision-making in complicated SSc.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0828 THE DIAGNOSTIC AND PROGNOSTIC VALUE OF COMMERCIAL LINE BLOT ASSAY IN TAIWANESE PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Autoantibodies, Diagnostic Tests

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Background: Emerging evidence has demonstrated the clinical utility of scleroderma-specific autoantibodies in systemic sclerosis (SSc) [1]. However, the diagnostic performance and prognostic value of line bot assay (LIA) in Taiwanese patients was unknown.
Objectives: Our aim is to evaluate the diagnostic performance of a commercial LIA and the prognostic value of SSc-specific antibodies and anti-Ro52 in Taiwanese population.
Methods: We retrospectively enrolled all individuals tested by the LIA with 13 antigens between 2020 and 2021 in Taichung Veterans General Hospital. The diagnosis of the scleroderma was based on the 2013 ACR/EULAR classification criteria. The positive result of the semi-quantitative test was presented as +, ++ and +++ based on the signal intensity. If multiple antibodies were detected, the patient will be categorized according to the antibody with the highest signal intensity. Multivariable logistic regression was used to evaluate the association between autoantibody subtype and clinical phenotype.
Results: A total of 896 patients (209 SSc, 293 non-SSc CTD, 394 non-CTD) were retrospectively analyzed. ROC analysis of LIA showed numerically higher AUC excluding anti-Ro52 in comparison with whole panel. After excluding anti-Ro52, the LIA exhibited sensitivities of 79.9%, 65.1%, 56.0% and specificity of 44.8%, 65.2%, 72.8% for diagnosis of SSc at different cutoff values respectively (signal intensities 1+, 2+ and 3+). An overall diagnosis performance of AUC 0.674, 65.36% accuracy, 36.36% positive predictive value (PPV), 86.18% negative predictive value (NPV), 1.89 positive likelihood ratio (LR+), 0.53 negative likelihood ratio (LR-) was determined at the optimal cutoff of 2+. For SSc patients, we observed significantly higher risk of diffuse-type scleroderma in participants with negative autoantibodies, anti-Scl-70, anti-RNA polymerase III and anti-Ro-52 positive (OR: 12.28, 95% CI: 3.19-47.19, p <0.001; OR: 33.56, 95% CI:8.91-126.51, p <0.001; OR:18.32, 95% CI:4.16-80.71, p <0.001; OR:2.00, 95% CI:1.05-3.83, p=0.036, respectively, Table1) as compared to the counterparts. Development of ILD was more frequently seen in SSc patients with autoantibody negative, anti-Scl-70, and anti-Ro52 positive (OR: 8.48, 95% CI: 2.79-25.75, p < 0.001; OR:16.91, 95% CI: 5.61-50.95, p <0.001; OR:2.58, 95% CI: 1.35-4.96, p=0.004, respectively) as compared to counterparts. Anti-Ro52 positive was also associated with PAH and GI tract involvement (OR 3.26, 95% CI: 1.18-8.99, P=0.023; OR: 2.86, 95% CI: 1.28-6.39, p=0.011). In addition, we found combination of anti-Scl-70 and anti-Ro52 positive was associated with the highest rate of ILD (Figure 1).
Conclusion: We demonstrated the diagnostic performance of LIA in Taiwanese patients with optimal cutoff defined and also the prognostic values of autoantibodies. Moreover, anti-Ro52 was associated with higher risk of various organs involvement including ILD, PAH and GI tract involvement.
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Table 1. The association of autoantibodies status with disease manifestation.

Phenotype and organ involvement	OR	95%CI		*p* value
Diffuse type				
Centromere	Reference			
Negative	12.28	(3.19-	47.19)	<0.001**
Scl-70	33.56	(8.91-	126.51)	<0.001**
RNA polymerase III	18.32	(4.16-	80.71)	<0.001**
Ro52-	Reference			
Ro52+	2.00	(1.05-	3.83)	0.036*
ILD				
Centromere	Reference			
Negative	8.48	(2.79-	25.75)	<0.001**
Scl-70	16.91	(5.61-	50.95)	<0.001**
Ro52-	Reference			
Ro52+	2.58	(1.35-	4.96)	0.004**
PAH				
Ro52-	Reference			
Ro52+	3.26	(1.18-	8.99)	0.023*
GI tract				
Ro52-	Reference			
Ro52+	2.86	(1.28-	6.39)	0.011*

OR: odds ratio; CI: confidence interval; ILD: interstitial lung disease; PAH: Pulmonary Arterial Hypertension; GI: gastrointestinal.

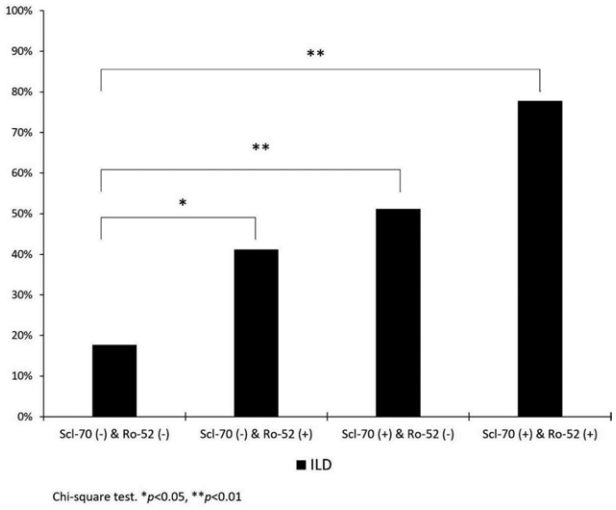


Figure 1. The association of anti-Scl-70 and anti-Ro52 with occurrence of ILD in patients with SSc.

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Disclosure of Interests: None Declared.
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AB0829 PROGRESSION OF ILD (INTERSTITIAL LUNG DISEASE) IN PFT (PULMONARY FUNCTION TEST) AND HRCT (HIGH RESOLUTION COMPUTERIZED TOMOGRAPHY) ACCORDING TO CTD (CONNECTIVE TISSUE DISEASE) IN 12 MONTHS

Keywords: Systemic sclerosis, Rheumatoid arthritis, Lungs

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Background: ILD is an important cause of morbidity and mortality in CTD. Moreover, it can be the first clinical feature of a CTD.
Objectives: To evaluate progression of ILD in 12 months through HRCT and PFT according to the kind of CTD (systemic sclerosis, myositis, Sjögren's syndrome, rheumatoid arthritis, mixed connective tissue disease, systemic lupus erythematosus), vasculitis, sarcoidosis and interstitial pneumonia with autoimmune features (IPAF).
Methods: A restrospective single tertiary center cohort study in CTD-ILD outpatients seen between 2012 and 2022. Sociodemographic, clinical and serological data, PFT and HRCT results were collected. ILD patterns were classified into usual interstitial pneumonia (UIP), inconsistent UIP, nonspecific interstitial pneumonia (NSIP), fibrosing NSIP, organizing pneumonia (OP), interstitial lymphoid pneumonia and associated to sarcoidosis. Progression of ILD was defined in PFT as: decline ≥ 10% in FVC ≥ 15% in DLCO. Progression of ILD in HRCT was considered according to radiologists'criteria.
Results: Data regarding 83 ILD-CTD patients is shown in Table 1. 54,1% of the patients complained of dyspnea at diagnosis of ILD. Immunosuppression prescribed is shown in Table 1. Treatment was not required in all cases at. diagnosis of ILD. Pulse steroids, mycophenolate and rituximab are some of the most prescribed treatments. UIP was the most prevalent pattern in 40% of the patients with RA (rheumatoid arthritis) but also was present in 28% of non-RA patients. 40% of RA and 28% of non-RA had UIP.

Table 1.

Sociodemographic & Baseline Characteristics		**Clinical features/affection**	**n** *(%)*
Total - n *(%)*	83 *(100)*	Raynaud	36
Age at dx. Of CTD- years- mean *(IQR)*	57 *(21-82)*	Skin	*(43,4)*
Age at dx. Of ILD- years- mean *(IQR)*	62 *(32-87)*	Arthritis	36
Female - n *(%)*	65 *(78,3)*	Ocular	*(43,4)*
Smoking status	15 *(18,1)*	PHT	27
Current - n *(%)*	18 *(21,7)*	Esophagus	*(32,5)*
Former - n *(%)*	50 *(60,2)*	Myositis	18
Never - n *(%)*	28 *(33,7)*	Hematological	*(21,7)*
Hypertension - n *(%)*	8 *(9,6)*	Renal	10 *(12)*
Diabetes Mellitus - n *(%)*	5 *(6)*	Neuropathy	10 *(12)*
Ischaemic cardiopathy - n *(%)*	9 *(10,8)*		9 *(10,8)*
POCD - n *(%)*			6 *(7,2)*
			3 *(3,6)*
			2 *(2,4)*
Antibodies	**n *(%)***	**Type of CTD associated to ILD**	**n *(%)***
ANA	55 *(66,3)*	Systemic Sclerosis	22
RF	33 *(39,8)*	Rheumatoid Arthritis	*(26,5)*
Ro	33 *(39,8)*	Sjögren's Syndrome	21
Anti Sclero	21 *(25,3)*	Inflammatory Myopathy	*(25,3)*
Anti Myositis	19 *(22,9)*	Sarcoidosis	11 *(13,2)*
Anti Synthetase	7 *(8,4)*	IPAF	11 *(13,2)*
		MCTD	8 *(9,6)*
		SLE	5 *(6)*
		Vasculitis	4 *(4,8)*
			2 *(2,4)*
			2 *(2,4)*
Pattern HRCT	**n *(%)***	**Immunosuppresion**	**n *(%)***
UIP	26 *(31,3)*	Mehthotrexate	31 *(37,3)*
NSIP	22 *(26,5)*	Hydroxicloroquine	26
INCONS UIP	18 *(21,7)*	MMF	*(31,3)*
NSIP-FIB	5 *(6)*	Pulses MP	23*(27,7)*
Sarco	8 *(9,6)*	Rituximab	20 *(24)*
OP	2 *(2,4)*	Azathioprine	18
LIP	2 *(2,4)*	TNFinhibitor	*(21,7)*
		Abatacept	14
		Leflunomide	*(16,9)*
		Tacrolimus	9 *(10,8)*
		Cyclophosphamide	8 *(9,6)*
		Nintedanib	8 *(9,6)*
		Tocilizumab	5 *(6)*
			5 *(6)*
			2 *(2,4)*
			2 *(2,4)*

POCD = Pulmonary Obstructive Chronic DiseaseANA = Antinuclear AntibodiesRF = Rheumatoid FactorAnti Sclero = SclerodermaSLE = Systemic Lupus ErythematosusMCTD = Mixed Connective Tissue DiseaseRA = Rheumatoid ArthritisIPAF = Insterstitial Pneumonia with Autoimmune FeaturesPHT= Pulmonary HypertensionUIP = Usual Interstitial PneumoniaIncons-UIP = Inconsistent Usual Interstitial PneumoniaNSIP = Nonspecific Interstitial PneumoniaFib-NSIP = Fibrosing Nonspecific Interstitial PneumoniaSarco = SarcoidOP = Organizing PneumoniaLIP = Lymphoid Interstitial PneumoniaMMF = Mycophenolate MophetilMP = Methylprednisolone

Image 1 shows progression in HRCT and PFT per CTD. Globally, 21,7% (n 14) of the patients progressed according to HRCT criteria and 16,7% (n 12) according to PFT criteria.

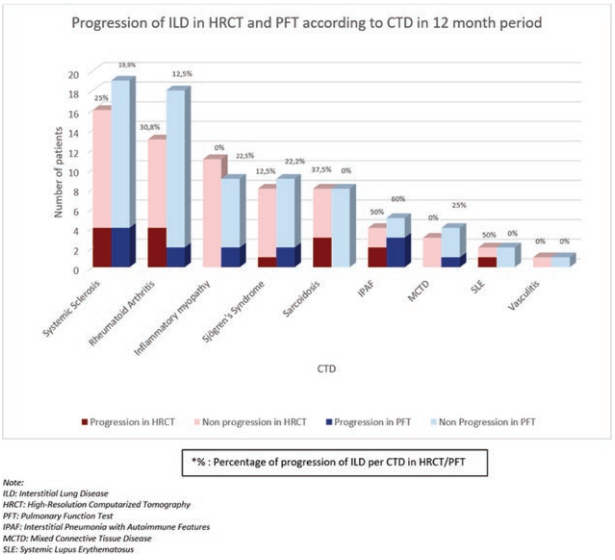


Image 1.

Conclusion: Close follow-up and treatment show non-progression in approximately 80% of the patients. In our series, patients with more progression (as found in literature) are systemic sclerosis, RA and IPAF. More studies must be done to identify best treatments and predictors to avoid progression of ILD.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0830

EXAMINATION OF EXERCISE STRESS ECHOCARDIOGRAPHY AND BIOMARKERS IN SYSTEMIC SCLEROSIS PATIENTS FOR THE EARLY DETECTION OF PULMONARY ARTERIAL HYPERTENSION AND MYOCARDIAL INVOLVEMENT

Keywords: Systemic sclerosis

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Background: The leading causes of death in patients suffering from systemic sclerosis are interstitial lung disease, malignancy and pulmonary arterial hypertension, but several other cardiovascular complications affect their quality of life.
Objectives: Our investigation aimed to examine biomarkers relating to active fibrotic changes in the myocardium and pulmonary vasculature and to find potential correlations with pathological findings detected by exercise stress echocardiography.
Methods: 28 consecutive systemic sclerosis patients attending our outpatient clinic underwent complete physical examination and routine blood tests. At the same day, resting and stress echocardiography were performed with supine bicycle exercise stress, and serum NT-proBNP, galectin-3 and soluble suppression of tumorigenesis-2 (sST-2) levels were measured. Patients with defined cardiological disease (systemic sclerosis-related manifestation or co-morbidity), interstitial lung disease, overt pulmonary hypertension or severe musculoskeletal disorder (active myositis, arthritis and severe lower limb osteoarthrosis) were excluded from the cohort.
Results: 27 female and 1 male patient participated in the study, aged 55,09±13,05 years. Median serum galectin-3 level was 58.57±31.48 ng/ml, in 24 patients, it was found to be elevated (normal range: >22,1 ng/ml, 85.71%). The sST-2 median level was 108,39±44,06 ng/ml, increased in 27 patients (normal range>35 ng/ml, 96,43%). Elevated levels of NT-proBNP were found in 24 patients. On echocardiography performed at rest, normal pulmonary arterial pressure was calculated in all 28 patients, while in the majority of them (in 23 patients), stress-induced pulmonary arterial hypertension (SIPAH) occurred at different grades of bicycle exercise. In those patients, the NT-proBNP level was also significantly higher (161,4± 85 vs 93,5± 61

pg/ml in those without SIPAH, p <0,05). Serum galectin -3 level showed a negative correlation with the peak heart rate measured at the maximal stress (r=0,48, p<0,05), and Tricuspid Annulus Plane Systolic Excursion (TAPSE) was lower at rest and on exertion in all patients whose galectin-3 level was found to be elevated. (p<0,05)

Conclusion: Biomarkers such as galectin-3 and NP-proBNP provide objective information about the ongoing pathophysiological changes of the myocardium in systemic sclerosis patients. A subset of patients with normal pulmonary arterial pressure at resting echocardiography develops SIPAH. The combination of echocardiographic findings with serum levels of NT-proBNP and galectin-3 may help to identify systemic sclerosis patients with a higher risk of progressive pulmonary arterial or myocardial involvement. Our ongoing project is to follow up these patients with annual examinations.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0831 CLINICAL PHENOTYPE OF ANTINUCLEAR ANTIBODY NEGATIVE SYSTEMIC SCLEROSIS IN A COHORT OF SYSTEMIC SCLEROSIS ROMANIAN PATIENTS

Keywords: Autoantibodies, Systemic sclerosis, Organ damage

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Background: Autoantibody formation is one of the hallmarks of systemic sclerosis (SSc). Previous studies suggested that SSc patients who are antinuclear antibody (ANA) negative constitute a distinct subset of SSc patients associated with a better prognosis, defined by male dominance, less vasculopathy and more frequent lower gastrointestinal involvement [1,2].

Objectives: To examine clinical and serologic correlations of Romanian SSc patients without ANA/SSc-related autoantibodies (Abs).

Methods: This was a single-center retrospective study which enrolled 270 SSc. The presence for both circulating SSc-related autoAbs and ANA was screened. Demographic and clinical features, symptoms and parameters related to a specific organ involvement according to MEDS evaluation sheets, were evaluated.

Results: We identified a population of 32 (12%) patients who had neither SSc-related autoAbs nor ANA. The group comprised 27 females and 5 males, with a mean age of 59.7 (±14.3) years, most of them with diffuse subset (25/32). ANA/SSc-related autoAbs negative patients had a significantly younger disease onset (48 [8-76] vs 60.5 [20-81] years, P <.005), longer disease duration (6 [0.1-50] vs 2 [0.1-25] years, P <.001), lower mRSS (7 [2-21] vs 9 [1-23], P <.001) but higher European Scleroderma Study Group (ESSG) activity index (5.3 [0.1-50] vs 2.9 [0.1-25] P <.001), higher proportion of synovitis (42% vs 16%, P <.001) and calcinosis (42% vs 17%, P <.001). For organ involvement, although the absence of SSc-related autoAbs was positively correlated with presence of digital ulcers (P < 0.001), heart and severe pulmonary involvement (P < 0.001), we didn't find a statistically significant difference between the two groups. Patients negative for ANA/SSc-related autoAbs more frequently received corticosteroids (58% vs 14%, P <.0001) and immunosuppressants (16% vs 0.5%, P <.0001) than those positive SSc-related Abs. No differences in mortality were found between the groups.

Conclusion: Our data revealed that ANA/SSc-related autoAbs negative patients are younger and have more frequently diffuse skin involvement, inflammatory arthritis, and calcinosis. Although digital ulcers, severe pulmonary and heart involvement were more common, there was no statistically difference between the two groups. Even though overall disease activity index was significantly higher in seronegative SSc patients, no difference in mortality were found between the groups. Whether the absence of detectable autoAbs persists and is to be viewed as a favorable prognostic factor are questions to be addressed by future studies.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0832 CHRONIC INTESTINAL PSEUDO-OBSTRUCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Gastrointestinal tract, Systemic sclerosis, Diet and Nutrition

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Background: Chronic intestinal pseudo-obstruction (CIPO) is one of the gastrointestinal manifestations related to systemic sclerosis (SSc). Despite its low incidence (5%), it burdens a high morbimortality.

Objectives: The objective of the present study was to analyse a selected cohort of patients with SSc and CIPO and to describe the treatments they received, the response to them and the clinical outcome.

Methods: SSc patients diagnosed with CIPO were selected for the study. There was analysed the baseline clinical variables, the period between the diagnosis of SSc and CIPO, the received therapies, and the clinical outcome.

Results: All the seven cases we studied were women, with a median (interquartile range, IQR) age at SSc diagnosis of 46.2 years (34-52). All of them met the ACR/EULAR 2013 classification criteria for SSc. Five (71.4%) of the patients presented diffuse cutaneous SSc (dcSSc), while the other two had the limited cutaneous SSc (lcSSc) subset. The median period between the SSc diagnosis and CIPO was 7.1 years (1.84-15.96). Concerning basal characteristics, 4 (57.1%) patients presented cardiac involvement, 3 (42.8%) arthritis, 3 (42.8%) interstitial lung disease, and 1 (14.2%) pulmonary arterial hypertension. Regarding specific SSc autoantibodies, anti-centromere antibodies were detected in 2 (28.6%) patients, anti-U1RNP in 2 (28.6%) and anti-RNA polymerase III in 1 (14.2%). Six (85.7%) had concomitant small intestinal bacterial growth (SIBO), with positive response to courses of antibiotics. Regarding CIPO treatment, all of them received dietetic recommendations, 6 (85.7%) prokinetics (cinitapride, prucalopride or erythromycin) and 4 (57.1%) the somatostatin analogue octreotide subcutaneous (sc). At CIPO onset, 3 (42.8%) patients had serious oral intolerance, two of them required parenteral nutrition (PTN), while the other received intravenous immunoglobulins (IVIG) and percutaneous endoscopic gastrostomy. During the first year of follow-up after an adequate initial response to treatment, 5 (71.7%) patients had a relapse into CIPO symptoms. Among them, one improved after initiating octreotide sc, 3 required PTN, 2 IVIG and 1 case was treated with adalimumab. Four (57.1%) patients died during the follow-up, three of them as a consequence of gastrointestinal complications related to CIPO, and the fourth because of sudden death.

Conclusion: CIPO is a gastrointestinal manifestation of SSc, that despite its low prevalence, it represents a high morbi-mortality. Patients with dcSSc might have a higher susceptibility for CIPO. There is a substantial variability period between the SSc onset and the appearance of CIPO related symptoms. Diet recommendations, prokinetics and octreotide are common initial therapies, reserving IVIG and PTN for refractory cases or with more aggressive onset. Notwithstanding, the mortality related to this gastrointestinal involvement is certainly significant.

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Disclosure of Interests: None declared

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AB0834 VALIDITY AND PSYCHOMETRIC CHARACTERISTICS OF THE DURUÖZ HAND INDEX IN TURKISH PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Outcome measures, Systemic sclerosis, Validation

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Background: The Duruöz Hand Index (DHI) is a self-report questionnaire that was developed for evaluating the functional status of hands in patients with

rheumatoid arthritis and subsequently validated in many cultures and various rheumatic patient groups [1].

Objectives: The aim of the study was to investigate the validity and psychometric properties of DHI in patients with systemic sclerosis (SSc).

Methods: Patients diagnosed with SSc according to the EULAR/ACR 2013 system were included [2]. Demographic and clinical characteristics of the patients were recorded. Functional assessments of the hands were evaluated with DHI, Keitel Functional Index (KFI), visual analog scale (VAS) for disability, VAS-Handicap for handicap, and Health Assessment Questionnaire (HAQ). Short Form-36 (SF36) was used for assessing quality of life. Disease activity was assessed with European Scleroderma Study Group (EScSG) activity index and VAS doctor's opinion for activity. Modified Rodnan skin score (mRSS), VAS-Hand pain, VAS-Raynoud, swollen joint count (SJC), tender joint count (TJC), Pittsburgh sleep quality index (PSQI), and CRP levels were also noted. For the reliability analysis, internal consistency (Cronbach's alpha) and test-retest reliability (ICC); and for the validity analysis face, content, convergent, and divergent validities were applied. Face and content validities were evaluated via cognitive debriefing interviews with the patients. The correlations of the DHI with KFI, VAS-disability, VAS-Handicap, and HAQ were analyzed for convergent validity. The correlations of the DHI with other measurements (non-functional) were analyzed for divergent validity.

Results: Seventy-three patients with a mean age of 48.6 (SD 12.8) years were recruited and 57 of them were women. Cognitive debriefing showed the DHI to be clear, understandable, and relevant. It was easy to complete and calculate, with the 5 minutes and 30 seconds, respectively. The Cronbach's alpha coefficient for internal consistency was 0.973 and ICC for test-retest reliability was 0.993 (95%CI 0.981-0.997). DHI showed good to moderate correlations with the functional measurements indicating its convergent validity and moderate to non-significant correlations with the non-functional parameters supporting its divergent validity (Table 1).

Conclusion: DHI is a quite practical, reliable, and valid instrument to assess hand function in patients with SSc.

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Table 1. Spearman's correlation coefficients of Duruöz Hand Index with the other parameters for convergent and divergent validity

Functional Parameters (Convergent)	Rho	Non-functional Parameters (Divergent)	Rho
KFI	0.970**	Age	-0.124
VAS-Disability	0.524**	Disease duration	0.347*
VAS-Handicap	0.567**	CRP	0.246*
HAQ	0.395*	SJC	0.273*
		TJC	0.464**
		mRSS	0.495**
		EScSG	0.535**
		VAS-raynoud	0.419**
		VAS-Hand pain	0.512**
		VAS-Doctor's activity opinion	0.484**
		SF36 Physical functioning	-0.338*
		SF36 Physical role limitations	-0.525**
		SF36 Emotional role limitations	-0.375*
		SF36 Vitality	-0.164
		SF36 Emotional well-being	-0.085
		SF36 Social functioning	-0.336*
		SF36 Pain	-0.259*
		PSQI	0.305*

** p<0.001, *p: 0.001-0.049.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0835 CAPILLAROSCOPIC FINDINGS IN PATIENTS WITH SJÖGREN'S SYNDROME, SYSTEMIC SCLEROSIS, AND PRIMARY RAYNAUD'S PHENOMENON IN A HIGH-COMPLEXITY CENTER IN MEDELLÍN, COLOMBIA 2016-2022

Keywords: Sjögren syndrome, Real-world evidence, Systemic sclerosis

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Background: In Sjögren's syndrome (SS), it has been suggested that capillaroscopy could be useful to identify patients with characteristics of overlap syndromes and risk of evolving into another connective tissue disease, in addition to determine extraglandular systemic involvement. The published information is scarce, as its comparison with systemic sclerosis (SSc) and primary Raynaud's phenomenon (pRP); in addition, different optical instruments other than the videocapillaroscope with 200x magnification have been used.

Objectives: To assess capillaroscopic findings in patients with SS compared to subjects with SSc and pRP at a national capillaroscopy reference center in Medellín, Colombia, between 2016 and 2022.

Methods: An analytical cross-sectional observational study was carried out. Patients over 18 years who met 2016 ACR/EULAR, 2013 ACR/EULAR, and 2014 international criteria for SS, SSc, and pRP, respectively, confirmed by a rheumatologist, were included. Capillaroscopic variables were analyzed (number of capillaries per millimeter, dilated capillaries, megacapillaries, abnormal capillaries, microhemorrhages, avascular zones, arborescent capillaries, capillary disorganization, and capillaroscopic pattern). Qualitative variables were expressed by absolute and relative frequencies and the quantitative by the median and interquartile range (IQR) due to the heterogeneous distribution of data.

Results: In total, there were 195 patients, of which 181 (92.8%) were female; the median age was 53 years (IQR:39-62). The most frequent capillaroscopic finding in SS was the presence of dilated capillaries (n=36; 55.4%). A higher frequency of global capillaroscopic abnormalities was observed in the SSc group compared to the other groups (p<0.0001 in all comparisons). There was no difference in the frequency of arborescent capillaries between the SS and SSc groups. In the SS group, either scleroderma pattern was found in 18.5% (n=12) (Table).

Table. Capillaroscopic findings in 195 patients with Sjögren's syndrome, systemic sclerosis, and primary Raynaud's phenomenon in a capillaroscopy reference center in Medellín, Colombia.

Findings	SS (n=65) n (%)	SSc (n=65) n (%)	RF (n=65) n (%)	p-value **
Decreased capillary density	8 (12.3)	28 (43.1)	0 (0)	<0.0001
Dilated capillaries	36 (55.4)	51 (78.5)	9 (13.8)	<0.0001
Megacapillaries	10 (15.4)	31 (47.7)	0 (0)	<0.0001
Abnormal capillaries	22 (33.8)	36 (55.4)	6 (9.2)	<0.0001
Microhemorrhages	16 (24.6)	33 (51.6)	1 (1.5)	<0.0001
Avascular zones	12 (18.5)	29 (44.6)	0(0)	<0.0001
Arborescent capillaries*	3 (10.7)	2 (10.5)	0 (0)	0.254
Capillary disorganization	22 (33.8)	33 (50.8)	5 (7.7)	<0.0001
Highest capillary diameter (um+)	21.4 (16.9-34.0)	41 (21.4-97.0)	15 (13.1-17.6)	<0.0001 ++
Capillaroscopic pattern				<0.0001
No scleroderma – normal	32 (49.2)	14 (21.5)	65 (100)	
Non-specific abnormalities	21 (32.3)	21 (32.3)	0 (0)	
Early scleroderma	3 (4.6)	3 (4.6)	0 (0)	
Active scleroderma	8 (12.3)	18 (27.7)	0 (0)	
Late scleroderma	1 (1.5)	9 (13.8)	0 (0)	

*Total (n=61), Sjögren's syndrome (n=28), Systemic sclerosis (n=19), Primary Raynaud's phenomenon (n=14)+Median (p25-p75), Raynaud's phenomenon (n=64)** Chi square test ++ Kruskal-Wallis test

Conclusion: Patients with SSc and SS have a high prevalence of capillaroscopic abnormalities with statistically significant differences compared to the pRP group. The high frequency of dilated capillaries in SS stands out, as well as common arborescent capillaries and scleroderma patterns.

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Disclosure of Interests: None Declared.

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AB0836 ANTI-SAE ANTIBODY-POSITIVE DERMATOMYOSITIS: CLINICAL CHARACTERISTICS FROM AN ITALIAN COHORT

Keywords: Myositis

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Background: Anti-small ubiquitin-like modifier-1 activating enzyme (anti-SAE) antibodies are rare myositis-specific antibodies, which are mainly associated with cutaneous involvement in inflammatory myositis (IIM).
Objectives: To analyse clinical characteristics of anti-SAE positive Dermatomyositis (DM) patients in a monocentric cohort. We focused on clinical manifestations and type of organ involvement.
Methods: In a monocentric cohort of 169 patients with IIM, anti-SAE antibody positive patients were included in the study. Anti-SAE antibodies were investigated by immunoblotting. We considered the presentation symptoms at disease onset and during follow-up, focusing on musculoskeletal, cutaneous and pulmonary domains. Muscular involvement was evaluated by Manual Muscle Test-8 and creatin kinase (CK) levels. To determine interstitial lung disease (ILD), high-resolution computed tomography (HRCT) was performed at diagnosis and during follow-up and evaluated by an expert radiologist. Skin and joint involvement was evaluated by clinical judgment. Therapeutic approach was also considered.
Results: Of the 169 patients with IIM, 6 were positive for anti-SAE antibodies (3,5%). Among them, five were female and one male. The mean age at onset of symptoms was 46.3 years (range 5-78 years). Cutaneous manifestations were the most prevalent clinical features at disease onset. Indeed, all of the patients had photosensitive rash, heliotrope rash and Gottron papules. Mechanic's hands were noted only in one patient with ILD. Four (70%) had arthritis. Muscular involvement, which was mostly mild, was evidenced by muscular weakness and high levels of CK (mean value 538 U/l) in 30% of patients (n=2). Three patients (50%) had radiological evidence of ILD at onset or during follow-up. Non-specific Interstitial Pneumonia (NSIP) was the main pattern found. Story of malignancy was noted only in the male patient. Half of the patients (n=3) were treated with methotrexate (MTX). Because of drug intolerance, MTX was substituted by mycophenolate mophetil (MMF) in two of them. One patient received intravenous immunonoglobulin (IGIV) and cyclophosphamide (CYC) for persistent cutaneous disease activity.
Conclusion: In our small cohort of patients, anti-SAE antibodies were strongly associated with skin disease, in one case severe. Lung involvement was another common clinical feature described and malignancy was noted in one case.

Table 1. Clinical and serological characteristics of anti-SAE positive patients

Parameters		Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age of onset (years)		5	61	45	32	78	57
Age at diagnosis (years)		6	61	47	32	78	58
Gender		F	M	F	F	F	F
Presentation	Fever	–	+	+	+	–	–
	Muscle weakness	+	–	–	–	+	–
	Dysphagia	+	–	–	+	+	–
	Photosensitive rash	+	+	+	+	+	+
	Voice change	–	–	–	+	–	–
	Dyspnea	–	–	+	+	+	–
	Myalgia	+	–	–	+	–	–
	Arthritis	+	–	+	+	–	+
	Heliotrope rash	+	+	+	+	+	+
	Gottron papule	+	+	+	+	+	+
	Mechanic's hand	–	–	–	–	+	–
	Skin ulcer	–	–	–	–	–	–
	Malignancy	–	+	–	–	–	–
	Interstitial lung disease	–	–	+	–	+	+
Laboratory values	CK (U/L)	NA	564	110	100	512	128
	AST (U/L)	NA	27	49	20	NA	NA
	LDH (U/L)	NA	70	80	386	NA	NA
	ANA	+	+	+	+	+	+
	ENA		PM-Scl-100		Tif-1-gamma		
Treatment		MTX MMF	MMF	MTX, IgIV, CYC, MMF	MTX	NA	NA

CK creatine kinase, AST aspartate transaminase, LDH lactate dehydrogenase, ANA anti-nuclear antibody,MMF mycophenolate mofetil, MTX methotrexate, IgIV intravenous immunoglobulin, CYC cyclophosphamide

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0837

EFFECTIVENESS AND SAFETY OF RITUXIMAB AND MYCOPHENOLATE MOFETIL COMBINATION THERAPY FOR IDIOPATHIC INFLAMMATORY MYOPATHIES: A MONOCENTRIC REAL-LIFE STUDY

Keywords: Myositis, bDMARD, Lungs

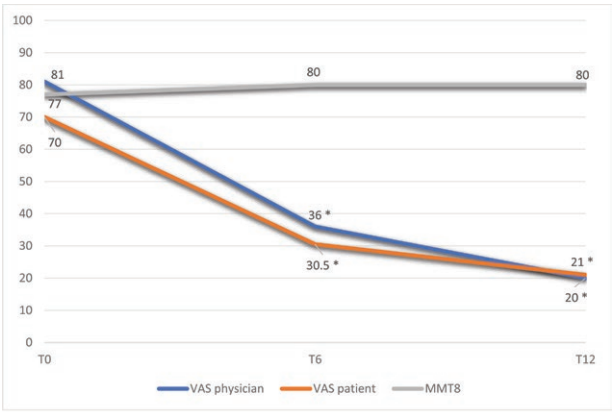
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Background: Due to a lack of robust clinical evidence, no defined recommendations for the treatment of refractory idiopathic immune myopathies (IIMs) exist. Hence, management of IIMs is still challenging.
Objectives: To assess the real-life effectiveness and safety of rituximab (RTX) and mycophenolate mofetil (MMF) combination therapy in severe and refractory IIMs.
Methods: Adult patients with IIMs ('2017 EULAR/ACR classification criteria'[1]) followed up at our Myositis Clinic and treated with a combination of RTX and MMF were identified. IMACS six core set measures (i.e., VAS physician; VAS patient; MMT8; HAQ; muscle enzymes; extramuscular assessment, including MITAX, MYOACT scores) were recorded at three different time points (baseline, 6-month, and 12-month after first RTX infusion). Subgroup analyses according to the involvement of specific organs (heart, lung) were performed. Safety was evaluated.
Results: We identified 20 IIM patients (ASS, n=12; dermatomyositis, n=2; polymyositis, n=2; immune-mediated necrotizing myopathy, n=1; overlap myositis, n=3). Median age was 61 (48-71) years; 14 patients were women (70%). Myocarditis and interstitial lung disease (ILD) were identified in 7 (35%) and 15 (75%) patients, respectively; 6 patients (30%) had arthritis and 3 (15%) had dysphagia. MMF was started after a median of 2 (0-76) months since diagnosis. RTX was always started after MMF (after a median of 22.5 (10-122) months), and administered at a dose of 1 g 2-week apart repeated 6 monthly. MMF dose was reduced in all patients (to 1 g daily, n=3, 15%; to 2 g daily, n=17, 85%) after RTX introduction. Adjunctive treatments were glucocorticoids (n=17), hydroxychloroquine (n=5), intravenous immunoglobulins (n=3). At 6 months, IMACS core set measures significantly improved all but MMT8 (**Figure**). A significant reduction of CPK and CRP levels and of prednisone (PDN) daily dose was observed (**Table**). In addition, a reduction in troponin T levels in patients with myocarditis and a stabilization of functional parameters in patients with ILD were observed (**Table**). At 12 months, a further reduction in the PDN dose and a further significant reduction in troponin T levels in patients with myocarditis were observed (**Table**). No patient had severe infections; 10 patients (50%) had mild infections (the most common upper respiratory tract infection, n=6).
Conclusion: Combination treatment with RTX and MMF could represent an effective and safe option in patients with severe and refractory IIMs.
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Table. Baseline and follow-up parameters in IIM patients treated with RTX + MMF

Variable	Baseline	6 months	p-value	12 months	p-value (versus 6 months)
PDN dose, mg daily median (IQR)	8.75 (5-12.5)	5 (0 – 5)	**0.008**	0 (0 – 5)	0.357
CPK (U/L) median (IQR)	439 (129 - 971)	141 (73 -299)	**0.002**	131 (74-342)	0.397
CRP (mg/L) median (IQR)	4.0 (0.9-19.7)	1.2 (0.8-1.9)	**0.034**	1.2 (0.7-1.4)	0.373
Troponin T (ng/L)* median (IQR)	56.5 (23-142)	24 (19 -47)	**0.046**	19.9 (13 -44)	**0.028**
FVC (%)**	79 (67 -96)	77 (68 – 90)	0.600	84 (74-100)	0.128
FEV1 (%)**	83 (73-98)	71 (69 – 88)	0.461	75 (75-109)	0.236
DLCO (%)**	69 (45-82)	42 (32 – 80)	0.115	40 (39-76)	0.173

*only among patients with cardiac involvement**only among patients with ILD



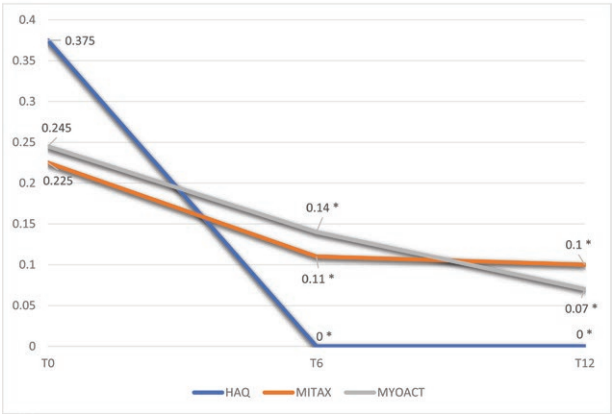


Figure. IMACS core set measures at 6 and 12 months in IIMs patients who received RTX and MMF combination treatment. * = P value < 0.05

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Disclosure of Interests: None Declared.
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AB0838

PULMONARY AND CARDIOVASCULAR MANIFESTATIONS IN SYSTEMIC SCLEROSIS: RESULTS FROM A SSC PATIENTS COHORT AT A TERTIARY CENTRE OF NW GREECE

Keywords: Lungs, Cardiovascular disease, Systemic sclerosis

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Background: Systemic Sclerosis (SSc) is a connective tissue disease affecting multiple systems, including the respiratory and cardiovascular systems. Among the various disease complications, interstitial lung disease (ILD), pulmonary arterial hypertension (PAH) and -lately recognized- myocardial fibrosis (MF), are those mainly related to reduced life expectancy.
Objectives: We aimed to evaluate the prevalence of SSc complications and to investigate possible associations with patients' clinical and serological characteristics.
Methods: Patients fulfilling the ACR/EULAR 2013 Scleroderma criteria, who were followed at our tertiary rheumatology centre between January 2018 and December 2022, were included in our cohort. Demographic, clinical, and serological characteristics, as well as imaging data (high-resolution chest CT, cardiac MRI) were used in our retrospective analysis.
Results: Ninety-one patients were included in our study, with 39.6% of them having diffuse cutaneous SSc. Most patients were female (81.3%), with a mean age at diagnosis 50.3 ±14.5 years and a mean disease duration 10.2 ±9.0 years. Leaving aside Raynaud's phenomenon and sclerodactyly, gastrointestinal involvement (71.4%), ulcers (46.2%) and arthritis (45.1%) were among the most prevalent clinical manifestations. Mean baseline FEV1 and FVC values were normal (83.4%±16.8 and 84.4%±18.5 respectively, while mean baseline DLCO was pathological (62.6±18.9). All patients underwent a high-resolution CT early at diagnosis and upon rheumatologist's/pulmonologist's judgement afterwards. Eighty-one patients (89.0%) were diagnosed with interstitial lung disease (76.0% had NSIP pattern, 24.0% UIP pattern). Patients with NSIP had better scores in lung function tests than those with UIP pattern (Mean difference in FEV1, FVC and DLCO were 13,3%, 17,7%, and 12% respectively, p<0.05 for all comparisons). Positivity for anti-topoisomerase antibody (Scl-70) presented an OR=24.9 (p=0.001) for ILD, while ACA and anti-CENP-B were negatively associated (OR=0.114, p=0.003 and OR=0.164, p=0.024, respectively). Pulmonary hypertension based on echocardiogram findings was reported in 18/91 patients (19,8%), however PAH based on right heart catheterization (RHC) was confirmed in 11 of them (12,1% of total patients). Anti-Ro52 positivity was associated with PH (OR=4.45, p=0,005) and PH-ILD coexistence (OR=5.18, p=0,002), however no association was found for ILD presence in this cohort. There was also a trend for PAH-RHC, but it did not reach statistical significance. Cardiac MRI was performed in 24 patients, and non-ischemic myocardial fibrosis (compatible with SSc involvement) was identified in 18/24. The mean disease duration in MF group was longer (8.7 ±7.3 vs 3.3 ±4.3, p=0.040). Gastrointestinal involvement seems to confer an increased risk for this complication (OR=10.0, p=0.038).
Conclusion: The estimated ILD prevalence in our study is significantly higher than the one reported in the literature. As a referral centre, the patients reaching to our department probably have worse organ involvement than the average patient of primacy care setting. In addition, universal screening with a baseline HRCT and close monitoring lead to an earlier identification of this population. Anti-Ro52 has been recently reported as an independent risk factor for PAH. Our results could not verify this observation, probably due to the relatively small number of PAH patients in our study. Cardiac MRI availability and radiologist's experience are essential for MF diagnosis. It is our belief that larger studies are necessary to evaluate this population.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5554

AB0839

SAFETY OF LOW-DOSE ACETYL SALICYLIC ACID IN PATIENTS WITH SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY

Keywords: Safety, Cardiovascular disease, Systemic sclerosis

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Background: The low-dose acetyl salicylic acid (ASA) is often used among patients with Systemic sclerosis (SSc) in clinical practice since its use is not mentioned in any official document concerning the management of SSc [1]. Recently, a study from EUSTAR database demonstrated that anti-platelet therapy is a protective factor for digital ulcers onset, while Valentini et al associated the use of ASA with a lower incidence of primary cardiac involvement in SSc patients [2,3]. On the other hand SSc has been shown to be one of the autoimmune diseases with the highest CV risk [4]. The publication of 2022 EULAR Recommendations on cardiovascular (CV) involvement in rheumatic diseases asserting that *"the use of ASA in SSc is not recommended for primary prevention"* because of "*data about this topic were not find"* caused uncertainty to justify the use of this drug [5].
Objectives: Aim of our study was to evaluate the safety of ASA in a cohort of pts affected by SSc.
Methods: We retrospectively analyzed data from patients with SSc, fulfilling the 2013 ACR/EULAR classification criteria [6], followed in our Scleroderma Clinic, receiving ASA. Analysis included data from subjects that were not treated with ASA, as control group. Exclusion criteria were CV disorders and/or major bleeding occurred before the evaluation, treatment with ASA started before the diagnosis of SSc, Helicobacter pylori-related gastritis or other causes of gastritis not SSc-related, tumors, anticoagulant or other anti-platelet therapies. Demographic, clinical, ongoing therapies data were examined; conventional cardiovascular risk factors, instrumental and laboratory assessments were collected and the CV risk was calculated using the SCORE2 and/or SCORE2-OP [7]. All data were collected for a follow-up time variable from 2 to 10 years since ASA was prescribed (for *cases*) and since the first rheumatologic visit after diagnosis was done for *controls* (T0). Safety data included the following variables:

- major bleeding (requiring blood transfusion and/or leading to death)
- minor bleeding
- intracranial hemorrhage
- ocular hemorrhage requiring immediate treatment
- gastroenteric tract hemorrhage
- gastroenteric tract neoplasm
- gastric ulcer

- allergy to ASA

Results: Data were collected from 121 SSc pts, 71 *cases* and 50 *controls*. From the analysis of gastroenteric involvement at T0 *control* pts showed more frequently endoscopic gastroenteric lesions of the upper gastroenteric tract respect to *cases* (N-% *controls vs cases*: 8-16% vs 4-6%; p-value 0.0039). Among traditional CV risk factors we found that *cases* were more frequently smokers than *control*s (N-% *cases* vs *controls*: 15-21% vs 2-4%; p-value 0.007), but no difference was found with either of the other traditional CV risk factors or with the CV risk scores, calculated with SCORE2, between *cases* and *controls.* Our analysis didn't reveal any significant difference on the occurrence of adverse events concerning ASA safety between the two groups: after 1 year of treatment with ASA, 4 subjects showed minor bleeding and in one case a gastric neoplasm was diagnosed; after 2 years of treatment 2 pts reported minor bleeding, while just 1 case showed minor bleeding after 5 years of treatment. Among *controls*, the onset of gastric ulcers in one subject only was reported after 2 years of follow-up.
Conclusion: Despite the long period of ASA treatment, we didn't find a significative increase in the frequency of related adverse events in our pts. ASA seems to be a manageable therapy and, since the high CV risk associated with SSc [4], very similar to that showed by pts with diabetes mellitus where in some cases the use of ASA in primary prevention is recommended, we suggest a reassessment of EULAR Recommendations together with other studies on larger cohort of SSc pts, in order to confirm the safety of ASA.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5666

AB0840

ACUTE VASCULAR EFFECTS OF INTRAVENOUS ILOPROST IN SCLERODERMA PATIENTS CAN BE DETECTED BY POWER DOPPLER EXAMINATION OF THE FINGER SUBCUTANEOUS TISSUE

Keywords: Systemic sclerosis, Imaging

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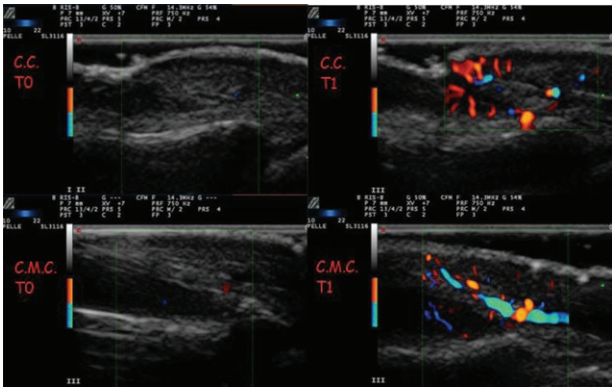
Background: Intravenous iloprost (ILO) is used in the treatment of refractory Raynaud phenomenon and scleroderma (SSc) digital ulcers. To date, there are no recommended imaging modalities to monitor ILO vascular effects. So far few studies explored ultrasound (US) as a tool to assess vascular subcutaneous involvement in patients affected by SSc.
Objectives: We aim to evaluate the acute vascular effects of intravenous ILO infusion by power Doppler US (PDUS) examination at periungual (PU) and finger pulp (FP) subcutaneous areas in a consecutive series of SSc patients.
Methods: Ten consecutive SSc patients who met the ACR/EULAR criteria for SSc referring to our tertiary center for ILO infusions were enrolled in the study. FP and PU vascularization of the 1st, 2nd and 3rd finger of the dominant hand were evaluated before and after ILO infusion (dosage 0.5-2.0ng/kg/min for 4-6 hours) using an Esaote MylabClassC, (Genoa, Italy) machine equipped with a 22-8 Mhz multifrequency linear probe. All the exams were performed after at least 30 minutes of acclimation in a room with an ambient temperature ranging from 20 to 22C by the same operator (PM). All the images with the highest presence of PD signal were stored for subsequent examination by a rheumatologist (ST) blind to the sequency of the images. The presence of PD signal in every image was scored according to a semiquantitative 0-3 scale (grade 0 no vessels; grade 1: 1-2 visible vessels; grade 2: 3 to 5 vessels, and grade 3 more than 5 vessels). The value of each finger (FP & PU) were summed up to obtain a total patient PD score and values before and after ILO treatment were compared by T-test for paired samples. Single fingers PD improvements after infusion were summed obtaining total improvement respectively for the PU and FP areas.
Results: Clinical and laboratory features of the enrolled patients are reported in Table 1. Mean total PU PD score was 4.2±2.2 at T0 and increased to 7.3±2.5 after treatment **(p=0.012).** Mean FP total PD score was 2,2±1,81 at T0 and remained unchanged (2,8±1,68) at T1 (p= 0,475). The median number of fingers/patient with PU PD improvement after treatment was 2 (1-3), while the median number of fingers/patient with FP PD improvement was 0,5 [0-3].
Conclusion: PDUS examination of the PU area could demonstrate an ILO acute effect in SSc patients with long-lasting disease.

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Table 1. Clinical, laboratory and power doppler ultrasound characteristics of our patients, before and after iloprost treatment. SD: standard deviation; ERA: endothelin receptors antagonists; CCB: calcium channel blockers; PDE5i: Phosphodiesterase type 5 inhibitors; ENA: extractable nuclear antigen; ACA: Anti-centromere antibody; RNA: ribonucleic acid; PD: power doppler; PU: periungual; FP: finger pulp.

	number (%)	Mean ± SD	Median (range)	P value
Total patients	10 (100%)	\	\	\
Age (years)	\	56,5±14,54	56,5 (32-79)	\
Sex	2(20%)	\	\	
Male	8(80%)			
Female				
Iloprost therapy duration (years)	\	10,57±8,16	10 (0,2-25)	\
Concomitant vasoactive therapy		\	\	\
ERA	6(60%)			
CCB	3 (30%)			
PDE5i	0			
Infusion rate (ml/h)		17,1±6,9	16,5 (10-30)	\
ENA antibodies		\	\	\
Topoisomerase I	6 (60%)			
Negative	2 (20%)			
ACA	1 (10%)			
RNA polymerase III	1 (10%)			
Cutaneous subset of disease		\	\	\
Diffuse	8(80%)			
Limited	2(20%)			
Ultrasound PD features	\		\	**0,012**
Total PU PD T0		4,2±2,2		0,475
Total PU PD T1		7,3±2,49		
Total FP PD T0		2,2±1,81		
Total FP PD T1		2,8±1,68		
PU PD improvement		1,9±0,88	2 (1-3)	\
1 finger	4 (40%)			
2 fingers	3 (30%)			
3 fingers	3 (30%)			
FP PD improvement		0,9±1,1	0,5 (0-3)	\
0 finger	5 (50%)			
1 finger	2 (20%)			
2 fingers	2 (20%)			
3 fingers	1 (10%)			



Figure

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0841

CONCORDANCE AND PROGNOSTIC RELEVANCE OF DIFFERENT DEFINITIONS OF SYSTEMIC SCLEROSIS INTERSTITIAL LUNG DISEASE PROGRESSION

Keywords: Systemic sclerosis, Lungs, Outcome measures

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Background: Interstitial lung disease (ILD) is a common complication of systemic sclerosis (SSc) with a variable natural history and prognosis. Several definitions of SSc-ILD progression have been proposed including minimal clinical important worsening of forced vital capacity (FVC MCIW), EUropean Scleroderma Trials and Research group (EUSTAR) progression, Outcome Measures in Rheumatology Clinical Trials (OMERACT) progression, and Erice ILD working group progression. The aim of the study was to assess concordance and prognostic value of these different definitions in SSc-ILD patients overall and specific clinical subsets.
Objectives: Progression status was assessed in consecutive SSc-ILD patients over a period of 24 months and the mortality related to SSc-ILD was compared between progressors and non-progressors according to different definitions in the subsequent 60 months. Severe baseline pulmonary functional impairment was defined for a combination of FVC<80% and alveolar diffusion of CO (DLco) <60% of predicted.
Methods: Progression status was assessed in consecutive SSc-ILD patients over a period of 24 months and the mortality related to SSc-ILD was compared between progressors and non-progressors according to different definitions in the subsequent 60 months. Severe baseline pulmonary functional impairment was defined for a combination of FVC<80% and alveolar diffusion of CO (DLco) <60% of predicted.
Results: The retrospective analysis included 245 SSc-ILD patients (age 54.6±13.2 years, male 18.8%) with a 54.7% prevalence od diffuse cutaneous variant and a median disease duration of 4 years (IQR 2-8). Disease duration ≤ 3 years, severe pulmonary functional impairment, and pulmonary artery systolic pressure (PASP) 40 mmHg were reported in the 47.8%, 18.0% and 17.1% of patients, respectively. Twenty-six deaths were reported among enrolled patients and progression according to FVC MCIW (HR 2.27, 95% IC 1.03 - 4.97, p=0.041), OMERACT (HR 2.90, 95% IC 1.28 - 6.57, p=0.011), and Erice criteria (HR 11.02, 95% IC 2.38 - 51.08, p=0.002) were associated with mortality in the whole cohort. Prognosis prediction, considering the 4 different definitions of progression status, was challenging (independently from the adopted criteria) in patients with disease duration >3 years, mild pulmonary function test impairment, and PASP ≥40 mmHg. Erice criteria performed better in patients with disease duration ≤3 years, limited cutaneous variant, and PASP <40 mmHg, while OMERACT criteria in patients with diffuse cutaneous variant, and severe baseline pulmonary functional impairment.
Conclusion: The proposed progression definitions of SSc-ILD are not interchangeable, since up to one third of progressors could be misdiagnosed using different criteria. Regardless of the criteria used, progressor patients presented more frequently a diffuse skin variant of the disease, a shorter disease duration and worse baseline functional impairment of the lung.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0842 HIGH BRONCHOALVEOLAR FLUID NEUTROPHILS INDEPENDENTLY PREDICT 15-YEAR MORTALITY IN SCLERODERMA PATIENTS WITH INTERSTITIAL LUNG DISEASE NAIVE TO IMMUNOSUPPRESSANT

Keywords: Lungs, Innate immunity, Systemic sclerosis

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Background: Scleroderma interstitial lung disease (SSc-ILD) has a variable and poorly predictable course. Data on independent role of bronchoalveolar lavage fluid (BALF) analysis in prognostic stratification of SSc-ILD patients are conflicting. We wanted to retrospectively evaluate the role of BALF analysis to predict severe course of disease in our cohort of SSc-ILD.
Objectives: We wanted to retrospectively evaluate the role of BALF analysis to predict severe course of disease in our cohort of SSc-ILD.
Methods: Forty SSc-ILD patients naive to immunosuppressants underwent comprehensive clinical evaluation, bronchoalveolar fluid analysis with total and differential leukocyte count, pulmonary function tests (PFTs), high-resolution computed tomography (HRCT). All the patients had fibrosing lung disease affecting more than 10% of lung volume on HRCT. Baseline alveolar (AS) and interstitial score (IS) on HRCT were computed. The 15-year crude mortality rate was retrospectively assessed.
Results: The enrolled patients (pts) (male 20.0%, aged 53.9±13.0 years) had a disease duration of 4.3±3.4 years. Diffuse LeRoy variant was reported in 47.5% of patients and anti-Scl70 and anti-centromere antibodies were detected in 57.5% and 12.5% of pts, respectively. The average AS and IS were 6.5±4.8 and 6.2±2.7, respectively, while 25.0% had FVC≤80% and 35.0% had DLco≤50%. During follow-up 18 pts received immunosuppressants. BALF neutrophilia (≥3.0%), eosinophilia (≥1.0%) and lymphocytosis (≥15.0%) were reported in 40.0%, 16.0% and 5.0% of patients, respectively. Twenty-five pts (62.5%) died within 15 years after bronchoscopy with a mean survival of 12.7 years (95% IC 11.5-13.9) overall. Fifteen-year mortality was predicted by BALF alveolitis (HR 2.87, 95% IC 1.26-6.56), and neutrophilia (HR 3.74, 95% IC 1.64-8.55), log-transformed absolute count of total cells (HR 2.52, 95% IC 1.12-5.58), neutrophils (HR 1.80, 95% IC 1.28-2.54), and eosinophils (HR 1.31, 95% IC 1.05-1.62), and percentages of neutrophils (HR 1.8, 95% IC 1.26-2.73) and eosinophils (HR 1.32, 95% IC 1.01-1.73). Only absolute and relative neutrophil counts were independently associated with mortality also in all models adjusted for demographics (age, gender), main disease traits (diffuse LeRoy variant, anti-Scl70 positivity), baseline pulmonary function tests (FVC, DLco), baseline HRCT involvement (AS, IS) and presence of vascular involvement (pulmonary hypertension, digital ulcers).
Conclusion: High BALF neutrophils were associated with high 15-year mortality independently from other established clinical risk factors. Given the negative prognosis of SSc-ILD, its poorly predictable clinical course, and the availability of new promising biomarkers, BALF analysis may be considered in assessing these pts to improve prognosis prediction.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0843 THE EXPRESSION PROFILING OF CIRCULATING MIRNAS IN SYSTEMIC SCLEROSIS

Keywords: Genetics/Epigenetics, Systemic sclerosis

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Title: The expression profiling of circulating miRNAs in systemic sclerosis.
Background: Systemic sclerosis (SSc) is a rare chronic disease of unknown etiology. Genetics plays an important role in SSc's pathogenesis; however, considering genetic factors alone does not explain the disease's occurrence, epigenetic influences are also believed to contribute to SSc development [1]. miRNAs are reported to be aberrantly expressed in SSc patients and, therefore, potential contributors to its pathogenesis. The role of miRNAs in SSc is just beginning to unravel [2].
Objectives: To investigate the expression profile of circulating miRNAs in SSc.
Method: Whole blood miRNA (84 miRNAs involved in human fibrosis) transcripts were identified by miScript miRNA PCR Array using RT-qPCR.
Results: Fourteen miRNAs (6 upregulated -hsa-miR-145-5p, hsa-miR-150-5p, hsa-miR-18a-5p, hsa-miR-195-5p, hsa-miR-223-3p, hsa-miR-29c-3p; 8 down-regulated- hsa-miR-211-5p, hsa-miR-217, hsa-miR-31-5p, hsa-miR-328-3p, hsa-miR-335-5p, hsa-miR-382-5p, hsa-miR-449a, and hsa-miR-661) showed differential expression compared to controls. IPA (Ingenuity Pathway Analysis) predicted miRNA-mRNA targets gene (hsa-miR-145-5p, hsa-miR-18a-5p, and hsa-miR-449a- TGFβ1), were validated through qRT-PCR and found to be dysregulated in the SSc patients. DIANA-Mir Path v3.0 pathway analysis showed dysregulated miRNAs were associated with pathways implicated in SSc's pathogenesis (Figure 1).
Conclusion: The differentially expressed miRNA and their putative mRNA targets and associated pathways may provide diagnostic biomarkers as well as point to therapeutic targets for SSc treatments.
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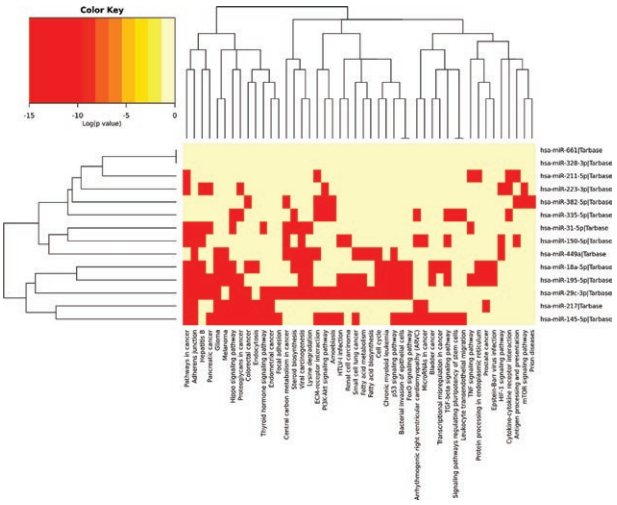


Figure 1. Through DIANA-miRPath v3.0, we generated hierarchical clustering of miRNAs and pathways based on their interaction levels.

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Disclosure of Interests: None Declared.
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AB0844 ARTERIAL ISCHEMIC EVENTS AND VENOUS THROMBOSIS IN SYSTEMIC SCLEROSIS: DATA FROM A MONO-CENTRIC STUDY

Keywords: Cardiovascular disease, Comorbidities, Systemic sclerosis

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Background: Systemic sclerosis is a systemic autoimmune disease characterized by vasculopathy (Raynaud phenomena), pulmonary arterial hypertension (PAH), and renal crisis), fibrosis of skin and visceral organs (notably the gut, heart, and lungs), and musculoskeletal inflammation (joints, muscles, and tendons) **[1].** Inflammation drives atherosclerosis and contributes to cardiovascular (CV) disease **[2]**. A few studies have examined the incidence of individual macrovascular manifestations such as myocardial infarction, stroke, peripheral artery disease, and venous thromboembolism **[3-4-5].**
Objectives: Our aim to estimate the incidence and the **arterial ischemic events and venous thrombosis** rates of SSc in our database. We also investigated underlying **the classical risk factors for venous thromboembolism (VTE)** unprovoked (deep venous thrombosis and pulmonary emboli not associated with cancer, recent surgery, hospitalization, fracture and pregnancy) and ASCVD (myocardial infarction and stroke).
Methods: In a retrospective cohort of SSc patients between 2005 and 2017, arterial ischemic events (myocardial infarction, ischemic stroke), venous thrombosis, risk Factor (Hyperlipidemia, Smoking, Diabetes, hypertension, abdominal obesity), classical risk factors for venous thromboembolism, as well as cardiac, cutaneous and immunological characteristics were assessed.
Results: The study population comprised 212 patients (86 % female) with a diagnosis of SSc. We identified a total of 7 (3%) and 26 (12%) patients have respectively an only arterial ischemic events or venous thrombosis, and 6 (3%) additional patients have both arterial and venous thrombosis, with an event during median 10(5-34) and 6 (0-55) years of follow-up. Venous thrombosis (VT) is present in 26 patients (12 %), active or historic neoplasia is present in 4 patients (15%) of VT. In comparison of patient without VT, 20 patients (11%) have a neoplasia. Arterial ischemic events are also most frequent in female sex n=6 (86 %) with all patients (100%) have a limited sclerosis, antinuclear antibodies and Raynaud phenomena, but no difference with the control group without thrombotic events. The prevalence of most cardiovascular disorders was found to be higher in the SSc with limited sclerosis than in diffuse sclerosis. The tobacco use, alcohol is not associated of increase risk of thromboembolic events. The presence of other autoimmune tissue disorders is not significant (p>0.0003) associated of increase rate among patients with SSc with thrombotic events than without. Further adjustment for medications (aspirin, NSAIDs, glucocorticoids, statins, oral anticoagulants, and platelet inhibitors) and comorbidities yielded results similar to the main analyses, except for ischemic stroke.
Conclusion: In this monocentric study, SSc was associated with greater risks of venous thrombosis and ischemic events, with a mortality rate in group with arterial ischemic events. There is no significant statistic difference associated of the classical risk factors of venous thromboembolism, comorbidity and the arterial ischemic events and venous thrombosis in systemic sclerosis.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5924

AB0845 A NOVEL MARKER IN SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: PEROXIREDOXIN-4

Keywords: Biomarkers, Systemic sclerosis, Lungs

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Background: Krebs von den Lungen-6 (KL-6) and surfactant protein D (SP-D) are suggested as useful markers for the evaluation of systemic sclerosis associated interstitial lung disease(SSc-ILD)[1-3]. Increased expression of Peroxiredoxin-4(PRDX-4) mRNA had been demonstrated in the lung tissue of patients with ILD[4]. PRDX-4, a member of peroxidases family, has not been studied as a marker in SSc-ILD before.
Objectives: Aim of this study was to assess the clinical significance of serum PRDX-4 as a viable alternative to KL-6 and SP-D in patients with SSc-ILD.
Methods: The serum PRDX-4, KL-6 and SP-D levels were determined by ELISA in 61 patients with SSc(34 with ILD and 27 without ILD) and 28 healthy controls. Lung function parameters were assessed, the extent of ILD was measured by a HRCT score.
Results: PRDX-4 levels were significantly higher in patients with SSc-ILD than in SSc without ILD patients and controls[14.27(26.14) vs. 10.17(3.22) vs. 9.68(2.06)ng/ml, median,(IQR), p=0.001). KL-6 levels were also remarkbly different between groups[134.25(224.28) vs. 103.90(34.81) vs. 92.84(29.16) U/ml, median,(IQR), p=0.002)]. Moreover PRDX-4, KL-6 and SP-D levels in patients with progressive ILD were significantly higher in stable ILD patients(p<0.001). PRDX-4, KL-6 and SP-D were correlated each other(p<0.01). Receiver operator characteristic curve analysis demonstrated high sensitivity and specificity of PRDX-4 for the determination of SSc-ILD and progressive pulmonary fibrosis. (AUC:0.705, p<0.01 and AUC:0.936, p<0.001).
Conclusion: PRDX-4 is more sensitive and spesific than KL-6 and SP-D and it is a potentially useful marker in assessing interstitial lung disease and progressive pulmonary fibrosis in patients with SSc.
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Table 1. Baseline characteristics of study population

Number of population	*N*=89
Female *n*, (%)	81 (91)
Age (mean±SD, years)	50.81±12.71
Limited/diffuse SSc *n,* (%)	43(70.5)/ 18(29.5)
Groups *n,* (%)	
SSc with ILD	34(38.2)
SSc without ILD	27(30.3)
Controls	28(31.5)
ILD Paterns on HRCT *n,* (%)	
Usual interstitial pneumonia	2(5.9)
Fibrotic Non-spesific interstitial pneumonia	28(82.4)
Celular Non-spesific interstitial pneumonia	3(8.8)
Lymphocytic interstitial pneumonia	1(2.9)

Abbreviations: *SSc* systemic sclerosis, *ILD* interstitial lung disease, *HRCT* high resolution computer tomography

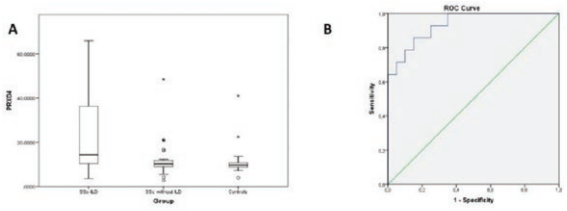


Figure 1. A. PRDX-4 levels in groups. Boxes show 75th and 25th percentiles; horizontal bar=median; outliers show maximum and minimum. B. PRXD-4 in presence of progressive pulmonary fibrosis, sensitivity and specificity, area under ROC curve (AUC)=0.936.

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Disclosure of Interests: None Declared.
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AB0846

EFFICACY OF RITUXIMAB IN IDIOPATHIC INFLAMMATORY MYOPATHIES. EXPERIENCE ON 36 PATIENTS FROM A PROSPECTIVE MONOCENTRIC COHORT

Keywords: Myositis

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Background: Idiopathic inflammatory myopathies are a heterogeneous group of autoimmune disorders characterized by muscle inflammation frequently associated with the involvement of other organ systems. Due to variety of presentations and severity degree, treatment of inflammatory myopathies is challenging. Considering the immunopathogenic role of B cell in myositis, Rituximab (RTX), as B cell depleting agent, could be an effective therapy in patients refractory to others immunomodulatory drugs.
Objectives: The aim of the present study is to demonstrate the efficacy of RTX for the treatment of idiopathic inflammatory myopathies in multi refractory patients. We also considered the effectiveness of a low-dose RTX as a remission-maintenance therapy.
Methods: From a monocentric cohort of patients with inflammatory myopathies, we considered all patients who have been treated with RTX (2 infusions of 1 gram, week 0-2). We also considered low-dose RTX as a single dose of 1g every 6 months. The response to RTX was considered based on physician judgement (complete CR, partial PR, no-response NR), focused on muscle and lung manifestations. Improvement in muscle involvement was based on reduction of 30% of creatine kinase levels and/or an increase in Manual Muscle Test score (MMT-8) of 20%. Interstitial Lung disease (ILD) was evaluated by pneumologist judgement based on chest computer tomography and spirometry. A response was considered partial if it was maintained less than 6 months from RTX administration and complete if it persisted more than 6 months.
Results: Thirty-six patients were included, 15 with diagnosis of polymyositis, 13 with antisynthetase syndrome, 6 with dermatomyositis, 1 with inclusion body myositis and 1 with necrotizing myopathy. Anti-Jo1 autoantibodies were found in 12 patients, anti-SSA in 9, anti-SRP in 5, anti-PM/Scl 75 in 2, anti-Mi2 in 2, anti-PL7 in 1, anti-PL 12 in 1, anti-SSB in 1, anti-TIF1-γ in 1, anti Ku in 1 and anti Sp100 in 1. Most patients (50 %, n=18) were treated with RTX for muscle involvement, 17 % (n= 6) for ILD, 33 % (n=12) for both muscular and lung disease. All patients received oral glucocorticoid before starting RTX administration. The others previous therapies were: methotrexate in 72% of patients, mycophenolate mofetil in 50%, IVIG in 27%, azathioprine in 22%, hydroxychloroquine in 14%, cyclosporine in 14%, leflunomide in 11%, tacrolimus in 3%, cyclophosphamide in 3%. We observed CR to RTX in 70% of patients, PR in 19%, NR in 11%. In the subgroup treated for muscle involvement (n=18), we found a CR in 10 patients, a PR in 5 and NR in 3. In patients with ILD, 5 patients got a CR and 1 PR. In the group of patients with both lung and muscle manifestations, we observed 10 CR, 1 with PR and 1 with NR. Five patients were treated with a low dose maintenance therapy after having achieved remission with standard dose. Three patients had a diagnosis of polymyositis, one of dermatomyositis and one of antisynthetase syndrome. Patients received a minimum of 3 infusions and a maximum of 5 infusions of low dose RTX.Therapy was administrated for an average of 3 years. All of them maintained a CR to RTX.
Conclusion: In our cohort, RTX was effective in 89% multi-drug refractory patients and the low-dose was efficacious as a maintenance therapy in all cases.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5986

AB0847

COMORBIDITIES IN IDIOPATHIC INFLAMMATORY MYOPATHIES: DATA FROM THE MYOCITE COHORT

Keywords: Autoantibodies, Myositis, Comorbidities

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Background: Patients affected by idiopathic inflammatory myopathies (IIM) may suffer from comorbidities such as cancer and cardiovascular diseases, calling for optimized evaluation and additional management(1, 2).
Objectives: We aimed to explore the prevalence and profile of comorbidities in a cohort of Indian patients diagnosed with IIM, and to explore their association with a disease subtype and autoantibodies.
Methods: Information on demographics, disease subtype and autoantibodies in Indian patients with IIM were extracted from the MyoCite dataset. Comorbidities were classified as autoimmune, cardiovascular, cancer, infections, Diabetes Mellitus and others. Pearson's chi-square and Fisher's exact test were used to assess differences in the occurrence of any comorbidity between the various IIM subtypes and antibodies.
Results: Of 250 patients (F:M 3.9:1, median age 36.0 ± 15.4), the majority (110, 44.0%) were diagnosed with dermatomyositis (DM), followed by overlap myositis (OM) (59, 23.6%) and anti-synthetase syndrome (ASS) (45, 18.0%). Patients with comorbidities had a higher median age (40 ± 13.9 years) compared to patients without comorbidities (35 ± 16 years) without any statistical significance. A statistically significant increase (P<0.001) in female to male ratio was observed in patients with comorbidities (10.5:1) compared to patients without comorbidities (2.3:1). Female gender was associated with higher odds of any comorbidity (OR = 4.58; 95 CI = 2.17-9.65). Comorbidities were identified in nearly half (115, 46.0%) of the patients, with autoimmune comorbidities being the most common (72/115, 62.6%) followed by cardiovascular (38/115, 33.0%) and infections (24/115, 20.9%). Hypertension was identified as the most common comorbidity (38/115 33.0%) overall, followed by thyroiditis (26/115, 22.6%) and mixed connective tissue disease (23/115, 20.0%). Statistically significant differences (P<0.001) in frequency of comorbidities was observed in DM (OR = 0.21; 95 CI = 0.12-0.36) and OM (OR = 136.3; 95 CI = 18.44-1008.45).
Conclusion: Despite younger population with IIM, comorbidities are frequently reported in nearly half of Indian patients with IIM. It is noteworthy that autoimmune comorbidities and infections are fairly common with substantial cardiovascular risk calling for optimized assessment and care.
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Table 1 : Comparison of patients with comorbidities and without comorbidities in the Myocite cohort

Parameter	Patients with comorbidities (n=115)	Patients without comorbidities (n=135)	P-Value
Median age (years)	40 ± 13.9	35 ± 16	0.217
Female	105 (91.3%)	94 (69.6%)	<0.001
Male	10 (8.7%)	41(30.4%)	<0.001
Disease Subtype			
Dermatomyositis 110/250 (44.0%)	28 (24.3%)	82 (60.7%)	<0.001
Overlap Myositis 59/250 (23.6%)	58 (50.5%)	1 (0.7%)	<0.001
Antisynthetase syndrome 45/250 (18.0%)	17 (14.8%)	28 (20.7%)	0.222
Juvenile Dermatomyositis 33/250 (13.2%)	7 (6.1%)	26 (19.3%)	0.002
Polymyositis 27/250 (10.8%)	7 (6.1%)	20 (14.8%)	0.027
Cancer-Associated Myositis 9/250 (3.6%)	7 (6.1%)	2 (1.5%)	0.085
Juvenile Overlap Myositis 3/250 (1.2%)	3 (2.6%)	0	0.096
Necrotizing Autoimmune Myositis 3/250 (1.2%)	0	3 (2.2%)	0.252
Clinically Amyopathic Dermatomyositis 1/250 (0.4%)	0	1 (0.7%)	1.000
Antibodies			
Anti-Nuclear Antibodies 173/250 (69.2%)	84 (73.0%)	89 (65.9%)	0.224
Myositis-Specific Antibodies 93/250 (37.2%)	33 (28.7%)	60 (44.4%)	0.010
Myositis-Associated Antibodies 86/250 (34.4%)	40 (34.8%)	46 (34.1%)	0.906
Anti-Aminoacyl tRNA Synthetase Antibodies 33/250 (13.2%)	12 (10.4%)	21 (15.6%)	0.233

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Disclosure of Interests: None Declared.
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AB0848 DISEASE BURDEN IS ASSOCIATED WITH POOR PATIENT-REPORTED OUTCOMES IN WOMEN'S HEALTH-RELATED DOMAINS OF QUALITY OF LIFE IN SYSTEMIC SCLEROSIS: A STUDY ON 100 PATIENTS BY A MULTIDIMENSIONAL QUESTIONNAIRE

Keywords: Systemic sclerosis, Quality of life, Gender/diversity issues

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Background: Systemic Sclerosis (SSc) affects mostly women, with a significant impact on different domains of their quality of life (QoL).
Objectives: We aimed to identify clinical and demographic features of SSc women associated with impairment in specific QoL domains related to women's health (gynecological issues, sexual dysfunction, family planning), by means of a multidimensional ad hoc-created questionnaire [1].
Methods: The questionnaire was administered to consecutive SSc female patients attending our Unit over one year (May 2021-January 2022). The Female Sexual Function Index (FSFI) questionnaire was also administered. Clinical and demographic data were retrieved from clinical charts.
Results: One hundred women were enrolled, with a median [IQR] age of 59 [43-67] years, median disease duration of 11 [6-17] years; 75% had limited cutaneous involvement (lcSSc); 43% had anti-centromere antibodies; 48% had received diagnosis during reproductive age (<45 years). Non-regular gynecological follow-up visits were reported by 40% of patients. They were older at diagnosis and at questionnaire, more frequently post-menopausal (p:0.003, OR 4.96, 95%CI 1.68-16.6) and required immunosuppression more frequently (p:0.006, OR 2.37, 95%CI 1.02-5.50) than those regularly attending visits (Table 1). A negative impact of SSc on sexual function was reported by 60% of patients. Among the 39 patients who compiled the FSFI questionnaire, 24 (62%) displayed sexual dysfunction (score ≤26.55). These women were older and more treated (p:0.013, OR 7.50, 95%CI 1.69-33.3) as compared to patients with normal sexual function (Table 1). Among 48 patients who were diagnosed during reproductive age, 54% wished for a pregnancy after diagnosis and 30% did not reach the desired family size. These were more frequently affected by digital ulcers (p:0.040, OR 10.3, 95%CI 1.03-103) as compared to those who satisfied their family plan (Table 1).
Conclusion: Older age at diagnosis, digital ulcers, and immunosuppressive treatment were associated with a negative impact on women's health-related domains of QoL in SSc patients. The disease burden impairs sexual function and adherence to regular gynecological visits and receiving diagnosis during reproductive age increases the likelihood for a reduced family size. Clinicians caring for SSc women should be aware of the relevance of these domains of QoL, not usually considered in everyday practice as treatment targets.

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Table 1. Clinical and demographic features of the 100 SSc women, according to the presence of impairment in specific areas of QoL.

	NON regular gynecological visits n=38/94	Sexual dysfunction (FSFI ≤26.55) n=26/39	Desired family size NOT satisfied n=9/25
Age at onset, years	**52.0 (44.0-63.0)***	42.0 (28.0-52.0)	27.0 (23.0-32.0)
Age at questionnaires, years	**67.0 (57.8-70.3)***	**57.0 (43.0-67.0)°**	41.0 (37.0-57.0)
Disease duration at questionnaire, years	11.0 (6.0-17.0)	13.0 (7.0-17.0)	11.0 (10.0-25.0)
Anti-topoisomerase 1+	16/38 (41.1)	6/26 (23.1)	3/9 (33.3)
Diffuse cutaneous subset	10/38 (26.3)	4/26 (15.4)	4/9 (44.4)
History of digital ulcers	**31/37 (83.8)***	**18/25 (72.0)°**	**8/9 (88.9)^**
Sicca symptoms	11/38 (28.9)	7/26 (26.9)	2/9 (22.2)
Gastrointestinal involvement	**22/38 (57.9)***	9/26 (34.6)	3/9 (33.3)
Cardiac involvement	16/38 (42.1)	10/26 (38.5)	3/9 (33.3)
Interstitial lung disease	19/38 (50.0)	1/26 (3.8)	4/9 (44.4)
Immunosuppressants	**23/38 (60.5)***	**20/26 (76.9)°**	6/9 (66.6)

*Continuous variables: median (IQR), compared with Mann-Whitney test; categorical variables: number/number of available data (%), compared with Chi Squared/Exact Fisher test. Significant associations (p<0.05) as compared to patients: * with regular gynecological follow-up; ^ who satisfied the desired family size after SSc diagnosis; °with FSFI >26.55.*

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Disclosure of Interests: None Declared.
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AB0849 JAK INHIBITORS IMPROVE SEROPOSITIVE REFRACTORY MYOSITIS: SINGLE CENTER EXPERIENCE

Keywords: Myositis, Targeted synthetic drugs, Safety

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Background: Inflammatory myopathies are heterogeneous with variable clinical course and prognosis [1]. Despite conventional treatment, some patients are refractory [2].
Objectives: To describe the efficacy and safety of JAK inhibitors (JAKi) in patients with refractory dermatomyositis (DM).
Methods: Retrospective analysis of 6 patients with active DM, refractory to previous immunosuppressive treatment including methotrexate, rituximab, mycophenolate mofetil, cyclophosphamide and intravenous immunoglobulin. Demographical, clinical characteristics, outcomes and adverse events after JAKi administration were recorded.
Results: 83.3% of the patients were women, with mean age 62.4±10.9 years. All patients had long-standing disease with mean disease duration 9±8.1 years. Three patients were seropositive: one with positive anti-MDA5 antibodies, one with association of anti-Jo1 and anti-Ro52 antibodies and the latter with positive anti-Ro52 antibodies. The most frequently used JAKi was upadacitinib (50%), followed by tofacitinib (33.3%) and baricitinib (16,6%). Mean daily dose of corticosteroids at baseline was 8. 5mg.Prior to treatment with JAKi, mean muscle strength was 108±35, with mean CPK levels of 997±2244. Four patients had active skin rash. After a mean follow-up period of 7.6 months, all four patients with persistent skin involvement had clinical response (MMT-8=127±30). Muscle strength was improved in 4 patients (66.6%). Of note, the two patients that did not respond to JAKi were seronegative with marked muscular atrophy. One patient discontinued treatment due to severe thrombocytopenia. No other adverse events were recorded.
Conclusion: In this case series, JAKi treatment resulted in clinical improvement in seropositive patients with longstanding, refractory DM with acceptable safety profile. Prospective data are necessary to confirm these preliminary findings and define the subset of DM patients most likely to benefit from JAKi treatment.

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Disclosure of Interests: None Declared.

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AB0850

EQ5D-5L BASED HEALTH UTILITY SCORES AND QUALITY ADJUSTED LIFE YEARS(QALY) IN IDIOPATHIC INFLAMMATORY MYOSITIS: A PROSPECTIVE STUDY

Keywords: Descriptive Studies

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Background: Idiopathic inflammatory myopathies (IIM) are a heterogenous group of diseases manifesting with involvement of the musculoskeletal, mucocutaneous and pulmonary domains. Studies have shown that the health-related quality of life (HQoL) in IIM is poorer than that in the general population with decreased muscle strength being associated with low HQoL [1]. However, majority of the studies are cross sectional and the data on the use of EQ5D-5L based health utility measures in myositis is sparse.

Objectives: To quantify the EQ5D-5L based health utilisation scores and QALY in a cohort of IIM. To identify the determinants of gain in QALY in IIM.

Methods: This was a single center prospective study involving patients with IIM classified using the 2017 EULAR/ACR classification criteria. Patients were recruited between 2018 February and July 2022. All the patients were evaluated at 3 and 6 months with Manual muscle testing of 8 muscle groups (MMT-8), Functional index 3(FI3) and 2 minute walk distance (2MWD), besides the other components in the core set measures. EQ5D-5L was administered to all the patients during each of their visits. The health utility scores for EQ5D-5L health states specific for Indian population was used and QALY was calculated across three time points (0, 3 and 6 months). Individuals with MMT8 of <55 or those who had extra muscular disease activity of > 6 were considered severe disease. Those who had an MMT8 of > 74 and extramacular disease activity VAS of <2 were considered inactive disease and the rest as moderate disease. Linear regression models for identifying the role of change in MMT8, FI3 in predicting gain in health utility scores at 3 and 6 months were constructed.

Results: There were 54 patients with IIM included in this study. The mean ±SD age of the cohort was 37.35±10.15 years and 41 of them were females. Interstitial lung disease was present in 24 patients. There were 30 dermatomyositis, 18 antisynthetase syndromes, 3 immune meditated necrotizing myopathies and 3 polymyositis. The median (IQR) of extra-muscular disease activity in the cohort was 2.3 [0-5]. Fourteen patients had severe myositis and 16 had inactive disease at baseline. The baseline and change in health-related quality and the impact of achieving early disease response is represented in Figure 1. Upon linear regression modelling with change in health utility scores as dependent variable, both between 0-3 months and 6 to-12 months the severity of disease at baseline determined the change. Improvement in MMT-8 and FI3 had significant predictability between 0-3 months but only change in MMT-8 had significant effect on improvement in health utility score between 3 and 6 months when adjusted for age and baseline disease status (Table 1).

Conclusion: The health-related quality of life at baseline and its improvement on follow up is extremely low in individuals with severe IIM. Achieving inactive disease status within 3 months results in significant QALY gain. Improvement in muscle power significantly determines improvement in health related quality of life when adjusted for other factors.

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Table: 1 Determinants of gain in health utility scores of patients across time points

		Change in health utility 0-3 months				Change in health utility 3-6 months			
SN	Characteristics	R square	Beta	95% CI	P value	R square	Beta	95% CI	P value
1.	Age	0.59	0.09	-0.003 to 0.02	0.13	0.63	0.9	-0.001 to 0.003	0.002
2.	Baseline disease status		-0.35	-0.54 to -0.17	<0.001		-0.067	-0.10 to -0.04	<0.001
3.	Change in MMT8		0.02	0.004 to 0.032	0.01		0.01	0.006 to 0.015	<0.001
4.	Change in FI3		0.01	0.001 to 0.013	0.02		0.0001	-0.001 to 0.001	0.58

FI3- functional index 3, MMT8- Manual muscle testing 8 muscles

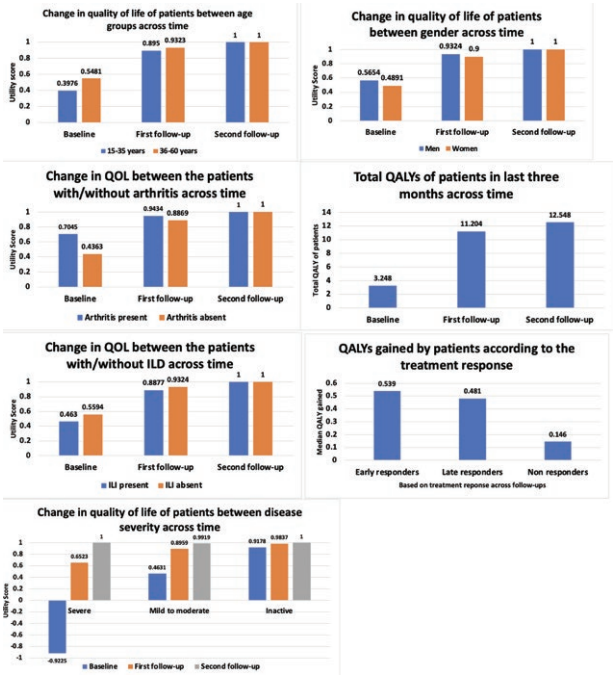


Figure 1 : Baseline and change in health-related quality and the impact of achieving early disease

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AB0851

AUTOLOGOUS HEMATOPOIETIC STEM–CELL TRANSPLANTATION IN SEVERE AND REFRACTORY SYSTEMIC SCLEROSIS. LONG-TERM MULTICENTRE STUDY

Keywords: Systemic sclerosis, Skin, Lungs

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Background: Pharmacological therapy does not reverse the natural course of systemic sclerosis (SS). Autologous hematopoietic stem-cell transplantation (AHSCT) has been used in refractory autoimmune diseases, including SS. The

AHSCT is based on the ablation of the immunoreactive system with high doses of chemotherapy and a subsequent regeneration of the immune system.
Objectives: Study of the efficacy of AHSCT in a multicentric cohort of patients with SS.
Methods: Descriptive study of patients with SS (ACR/EULAR 2013 criteria) treated with AHSCT between 2002 and 2022. These clinical variables were reviewed (Raynaud's phenomenon, pulmonary interstitial involvement, digital ulcers, presence of sclerodermic renal crisis) and activity index variables (Modified Rodnan Score, HAQ-DI).
Results: We included 11 patients with a mean age of 43±12.1 years, with a mean time of disease of 17±12.6 months. In all cases but one, the initial diagnosis was diffuse cutaneous SS, refractory to corticosteroids and at least one DMARD (Methotrexate n=7, Rituximab n=4, Azathioprine n=3, Tocilizumab n=1). One patient had a limited cutaneous SS and was treated with AHSCT due to a concomitant Hodgkin lymphoma. All patients (100%) had positivity for anti-nuclear antibodies and 8 (72.7%) for anti-Scl70. 11 patients (100%) presented Raynaud's phenomenon and sclerodactyly and 9 (81.8%) suffered from skin ulcers. 7 patients (63.6%) had interstitial lung disease and 1 patient had history of sclerodermic renal crisis. The conditioning treatment for the AHSCT was cyclophosphamide and anti-thymocyte globulin with the exception of 1 patient who developed an infusion reaction (in which the globulin was stopped) and 1 patient with Hodgkin lymphoma (who received a different chemotherapy schedule). After the AHSCT, 1 patient (9.1%) died of cardiorespiratory arrest after acute pulmonary edema the day +45. Other adverse events observed where febrile neutropenia (n=8, 72.7%), mucositis (n=4, 36.4%), confirmed infection (n=3, 27.3%) and serum sickness (n=3, 27.3%). The response of AHSCT is summarized in **table**. An improvement in Modified Rodnan Score, skin ulcers and HAQ-DI was observed.
Conclusion: AHSCT can be a therapeutic option in refractory and severe SS. These hopeful data must be ratified in larger studies.

Table.

	BASAL	6 MONTHS	12 MONTHS
Skin involvement			
Raynaud – n (%)	11 (100)	10 (90.1)	9 (81.8)
Sclerodactylya – n (%)	11 (100)	9 (81.8)	9 (81.8)
Ulcers – n (%)	9 (81.8)	0 (0)	1 (0.9)
Modified Rodnan Score	22.6±11.6	8.5±6.6	11.7±8.6
Pulmonary Function tests:			
FVC – mean % ± SD	89.0±11.9	94.2±9.9	90.9±17.2
FEV1 – mean % ± SD	89.2±15.2	96.3±9.7	92.9±19.9
DLCO – mean % ± SD	76.9±26.7	64.7±15.1	74.0±15.6
Laboratory tests			
CRP (mg/dl) – mean ± SD	3.1±3.0	0.5±0.4	0.48±0.29
ESR – mean ± SD	23.0±11.9	3.3±0.5	3.33±1.15
Creatinine – mean ± SD	0.7±0.2	0.8±0.2	0.70±0.2
Glomerular filtration rate – mean ± SD	100.7±15.3	99.3±13.5	98.7±16.0
Functional index			
HAQ-DI – mean ± SD/ median [ICR]	2.7 ± 0.3	0.25 [0-0.50]	0.25 [0-0.38]

CRP= C-Reactive Protein; DLCO=Diffusing capacity; ESR=Erythrocyte Sedimentation Rate; FVC=Forced vital capacity; FEV1=Forced expiratory volume in 1 second; HAQ-DI=Health Assessment Questionnaire Disability Index

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0852 CLINICAL CHARACTERISTICS, MYOSITIS AUTOANTIBODY PROFILE AND EARLY TREATMENT RESPONSE IN IDIOPATHIC INFLAMMATORY MYOSITIS - A SINGLE CENTRE EXPERIENCE FROM SOUTH INDIA

Keywords: Myositis, Autoantibodies

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Background: Idiopathic inflammatory myopathies (IIM) is a rare heterogenous group of diseases with varying involvement of muscle, skin, joints and lung. There is a paucity of prospective cohort studies in IIMs from India which assess the treatment response and clinico serological profile of patients with IIM.
Objectives: To describe the clinical characteristics, autoantibody profile and early treatment response in a prospective cohort of patients with IIM attending the Rheumatology clinic of a tertiary care teaching hospital in South India between October 2020 and June 2022. To compare IIM patients with interstitial lung disease (ILD) and IIM patients without ILD.
Methods: A prospective cohort of 37 consecutive adult patients fulfilling the 2017 EULAR ACR classification criteria of IIM was studied. The demographic data and clinical characteristics was recorded using a structured proforma. Muscle power was assessed by manual muscle testing (MMT8) in all patients. Myositis specific autoantibodies (MSA)and myositis associated autoantibodies (MAA) to 16 antigens were performed in all patients by line blot assay using Euroimmun (Luebec, Germany) as per manufacturer's instruction. All patients with MMRC grade 2 or more dyspnoea and/or dry cough and a restrictive pulmonary function test underwent HRCT chest for the diagnosis of ILD. Treatment response was assessed at 6 months based on the 2016 ACR/EULAR criteria for minimal, moderate and major clinical response. The various demographic, clinical and serological parameters were compared between patients with ILD and those without ILD. Comparisons between groups were made with the chi-squared test/Fisher's exact test when testing categorical variables and the Mann-Whitney *U* test or Independent samples' t test for continuous data. Multivariate analysis was done to find the independent factors associated with interstitial lung disease.
Results: 24 patients were female (64.9%) and the mean age of the study population was 46.7 ± 14 years. The median disease duration was 8 months (13 months). The most common symptoms were dyspnoea (59.5% of patients), proximal muscle weakness (56.8%), SICCA (35.1%) and photosensitive rash (32.4%). Mechanics hand was seen in 29.7% of patients, heliotrope rash in 24.3%, Gottron's papule in 18.9% and Gottron's sign was seen in 16.2% of patients. The median creatinine kinase (CK) level was 309 Units/L (1794) and median MMT 8 score was 78. 15/37 patients (40.5%) had dermatomyositis, 13/37 (35.1%) patients had anti synthetase syndrome, 4/37(10.8%) had biopsy proven necrotizing myopathy, 3/37 (8.1%) had overlap myositis and 2/37 (5.4%) had pure polymyositis. The most common MSA was anti Jo1 (7/37, 18.9%) followed by anti MDA5 (5/37, 13.5%) and anti PL12 (4/37, 10.8%) and the most common MAA was Ro52 (6/37,16.2%). 7/37 patients (18.9%) were negative for any of the MSA/MAA. Clinically amyopathic myositis was seen in 19/37 (51.4% of patients). ILD was seen in 20/37 patients (54.1%) and rapidly progressive ILD (RP ILD) was seen in 5/20 ILD patients (25%). The most common immunosuppressive agent used was corticosteroid (37/37) followed by mycophenolate mofetil (17/37,45.9%), methotrexate (9/37, 24.3%) and Rituximab (7/37,18.9%). After 6 months of treatment, 13/37 (35.1%) patients showed major response, 16/37 (43.2%) moderate response and 3/37(8.1%) patients showed minimal response. There were 5 deaths, 3 of which was due to pneumonia, 1 due to RP ILD, and 1 due to respiratory muscle weakness. On univariate analysis median disease duration, arthritis, CK levels, MDA 5 positivity and MSA/MAA positive status were associated with ILD. However, on multivariate analysis none of the factors showed any significant association with ILD.
Conclusion: The frequency of ILD is high in our cohort of IIM patients and as a significant proportion had no objective muscle weakness, the use of myositis autoantibody panel is warranted for early detection of such cases.
Acknowledgements: Department of Pulmonary Medicine, Government Medical College Kottayam, Kerala, India.
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AB0853 ENDOTHELIAL DISFUNCTION MARKERS CAN BE REDUCED IN SYSTEMIC SCLEROSIS PATIENTS BY NUTRITIONAL TREATMENT

Keywords: Systemic sclerosis, Diet and Nutrition

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Background: Systemic sclerosis is a chronic autoimmune disease which is represented by progressive fibrosis, vascular impairment and immune abnormalities. In recent years metabolic and endothelial factors were reported as elements which play role in pathogenesis of systemic sclerosis (SSc). Adipokines, mediators secreted by adpiose tissue, depends on fat mass and nutritional status. Ghrelin, a gut hormone, is a key regulator of metabolism of glucose, meal initiation and appetite. Another metabolic factor myostatin, is a myokine produced by muscles and is negative regulator of muscle growth. Endothelial factors auch as endothelin 1 (endogenous vasoconstrictor, mainly secreted by endothelial cells) and asymmetric dimethylarginine (ADMA, endogenous nitric oxide inhibitor) are important markers for vascular dysfunction.
Objectives: The aim of the study was to evaluate serum concentration of ghrelin, myostatin, adiponectin, wisfatin, chemerin, leptin, interleukin 6 (IL-6), endothelin 1 and ADMA in relation to the nutritional status of patients with SSc, and impact of nutritional treatmet on their levels.
Methods: Study population consisted of 56 SSc patients (47 females, 9 males) and 49 healthy persons (42 females and 7 males). Demographic and clinical

data were recorded. Assessment of nutrition based on 7-SGA and laboratory tests were done.

Results: SSc patients had significantly higher levels of nonacylated ghrelin (478,5±289,9 vs 347,7 ±294,8 pg/ml; p=0,018), IL-6 (30,7±29,7 vs 3,16±26,15 ng/ml; p=0,001), endothelin 1 (2,71±1,67 vs 1,96±1,02 pg/ml; p=0,002) and ADMA (1,37±0,45 vs 1,23±0,23 um/l; p=0,025) than control population. From 56 SSc patients 40 (71%) were well-nourished and 16 (29%) had nutritional disbalance. In those subgroups significantly higher levels of endothelin 1 (3,32±2,02 vs 2,58±1,71 pg/ml, p=0,043) and ADMA (3,32±2,02 vs 2,58±1,71 um/l, p=0,043) had malnourished patients. No statistically significant results in other parameters were observed. Dietary recommendations and high protein oral nutritional suplement (200 ml/day, containing 250 kcal and 19 g of protein) were given for 3 months to all 16 SSc patients with nutritional disorder. After 3 and 12 months patients were re-evaluated. Significantly higher levels of myostatin were noticed after 1 year after initial assesment (p=0,001). Opposite effect were seen with endothelin 1 and wisfatin, where in last evaluation both gain the lowest results (p<0,001,p=0,039).

Conclusion: Higher levels of endothelin 1 and ADMA confirm that vascular damage is crucial in SSc patients. Proper nutritional treatment in undernourished SSc patients can reduce levels of markers involved in endothelial disfunction, such as endothelin 1 and wisafatin.

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AB0854 CLINICAL CHARACTERISTICS OF PATIENTS WITH AMINOACYL-TRNA SYNTHETASES COMPARED WITH OTHER MYOSITIS ANTIBODIES IN A COHORT OF INFLAMMATORY MYOSITIS

Keywords: Autoantibodies, Myositis, Epidemiology

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Background: The Idiopathic Inflammatory Myositis (IIM) are heterogeneous with different clinical profiles associated with various myositis autoantibodies. Among the Myositis specific antibodies (MSA), antibodies against aminoacyl-tRNA synthetases(ARS) is related to the clinically unique IIM subsets, Antisynthetase syndrome(ASS).

Objectives: The aim of this study was to identify the prevalence and clinical features of patients with ARS autoantibodies compared with other myositis antibodies in a single center cohort of IIM in Korea.

Methods: Adult patients diagnosed with IIM and positive for myositis antibodies were recruited in the myositis cohort from January 2020 to December 2022. Retrospective analysis was performed based on the clinical data including clinical features, laboratory data, high-resolution CT (HRCT) findings, and pulmonary function manifestations.

Results: Among 82 patients, 25 patients were positive for ARS autoantibodies and 57 patients had other myositis antibodies. The most common ARS antibody was anti-EJ (n=10) followed by anti-PL-7 (n=8). MSA other than ARS antibodies included anti-SRP (n=6), anti-TIF1γ (n=11) and anti-MDA-5(n=19). Anti-Ro52 was detected in 48 patients and 79.2% of which were accompanied by other antibodies. The most common clinical manifestations of patients with ARS antibodies were respiratory symptoms, more commonly experienced than patients with other myositis antibodies (84% vs. 47.4%, p=0.002). Meanwhile, muscle weakness (32.0% vs. 61.4%) and dysphagia (8.0% vs. 33.3%) were less frequently exhibited compared with those with other myositis antibodies. In regard to laboratory findings, the ARS antibodies positive group showed higher inflammatory markers than other myositis antibodies group, the mean (SD) of erythrocyte sedimentation rate (ESR) was 53.6 (34.6) and 33.8 (24.3), respectively. Anti-Ro52 and anti-nuclear antibodies (ANA) cytoplasmic pattern were more detected in the ARS antibodies positive group. Interstitial lung disease (ILD) was also more commonly detected in patients with ARS antibodies than other myositis antibodies group (88.0% vs. 59.6%) and non-specific interstitial pneumonia (NSIP) was the most frequent pattern of ILD. However, there were no significant differences in the baseline pulmonary function between the two groups.

Conclusion: Patients with ARS antibodies experienced more respiratory symptoms while muscle weakness is less common clinical manifestations than patients with other myositis antibodies. Moreover, higher inflammatory markers and ANA cytoplasmic pattern along with Anti-Ro52 were more commonly detected in the ARS antibodies positive group.

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Table 1. Baseline characteristics of patients with ARS antibodies compared to those with other myositis antibodies (n=82)

	ARS Ab(+) (n=25)	Other myositis Ab(+) (n=57)	P
Clinical feature, n (%)			
DOE	21 (84.0)	27 (47.4)	0.002
Weakness	8 (32.0)	35 (61.4)	0.014
Dysphagia	2 (8.0)	19 (33.3)	0.016
Fever	7 (28.0)	8 (14.0)	0.132
Mechanic's hand	11 (44.0)	17 (29.8)	0.213
Raynaud phenomenon	8 (32.0)	16 (28.1)	0.719
Arthritis	7 (28.0)	13 (22.8)	0.614
Laboratory findings			
ANA, cytoplasmic Ab(+)	9 (36.0)	7 (13.0)	0.014
Ro52	22 (88.0)	26 (45.6)	<0.001
ESR	53.56 ± 34.59	33.78 ± 24.17	0.014
CRP	1.90± 2.19	0.76 ± 1.62	0.028
PFT			
FVC	72.0 ± 16.3	73.3 ± 18.9	0.772
FEV1	75.5 ± 14.1	81.5 ± 21.0	0.152
DLCO	62.6 ± 21.9	62.8 ± 23.0	0.969
ILD, n(%)	22 (88.0)	34 (59.6)	0.011
NSIP	17 (70.8)	22 (44.9)	0.037

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Disclosure of Interests: None Declared.

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AB0855 BASELINE DEMOGRAPHICS AND DISEASE CHARACTERISTICS IN A PHASE 2 STUDY TO EVALUATE EFFICACY, SAFETY, AND TOLERABILITY OF MT-7117 IN SUBJECTS WITH DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

Keywords: Rare/orphan diseases, Randomized control trial, Systemic sclerosis

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Background: Dersimelagon (MT-7117), a novel synthetic, oral, selective melanocortin-1 receptor agonist, demonstrated disease-modifying effects in preclinical models of systemic sclerosis (SSc). MT-7117 reduces inflammation, vascular dysfunction, and fibrosis through its pleiotropic effects on inflammatory cells, endothelial cells, and fibroblastsis, and is as a potential therapeutic agent for the treatment of SSc. A phase 2 proof of concept clinical trial (MT-7117-G02) in subjects with diffuse cutaneous SSc (dcSSc) is ongoing (NCT04440592). 73 subjects (target 72) were enrolled over 22 months at 33 sites in 8 countries.

Objectives: Evaluate the demographics, baseline disease characteristics and the standard of care of the subjects randomized in MT-7117-G02 study to examine variability of these parameters by the geographic regions (North America [NA], Europe [excluding Poland], and Poland). Population in Poland was analyzed separately due to delayed inclusion in the study and the highest enrollment rate.

Methods: MT-7117-G02 is a Phase 2, multi-center, randomized, double-blind, placebo-controlled, 52-week parallel-group study to evaluate the efficacy, safety, and tolerability of MT-7117 in subjects with dcSSc. Eligible subjects were randomized 1:1 to either MT-7117 QD or matching placebo and stratified by the autoantibody status of anti-RNA Polymerase III at screening (positive or negative). The primary endpoint

is the American College of Rheumatology Combined Response Index in Diffuse Cutaneous Systemic Sclerosis (ACR CRISS) composite score at Week 52. The study included subjects who have been diagnosed with dcSSc ≥ 18 years of age and a disease duration ≤ 5 years who are on a stable standard of care treatment, receiving one stable concomitant immunosuppressant (Mycophenolate/Mycophenolic acid [MMF], Methotrexate [MTX], Hydroxychloroquine [HCQ], or Azathioprine [AZA]). Eligibility included the baseline Modified Rodnan skin score (mRSS) of 15-45 units and Forced Vital Capacity (FVC%) predicted > 50%.

Results: Most of enrolled subjects were middle-aged White females and approximately half received one immunosuppressant (Table 1). MMF was the most frequently used immunosuppressant followed by MTX. Approximately ¾ of the subjects had normal CRP with comparable distribution across the regions. There were neither regional differences in the baseline mRSS nor in the predicted FVC%. The overall average frequency of anti-RNA Polymerase III antibody positivity was 20.5%, with the lowest proportion in Poland (15.4%). The average frequency of anti-Scl-70 positivity was 50.7% with the lowest proportion in NA (23.5%). Subjects in NA were more likely to be on MMF.

Table 1 : Baseline demographics and disease characteristics by Regions (Blinded)

	Mean (SD) or n (%)			
	Overall	North America*	Europe†	Poland
Number	73 (100 %)	17 (23.3 %)	30 (41.1 %)	26 (35.6 %)
Age (yrs)	51.6 ± 12.4	54.7 ± 12.5	52.2 ± 10.6	48.9 ± 14.2
Disease duration (yrs)	2.0 ± 1.4	1.7 ± 1.4	1.9 ± 1.3	2.2 ± 1.6
Female	55 (75.3 %)	15 (88.2 %)	22 (73.3 %)	18 (69.2 %)
White	65 (89.0 %)	11 (64.7 %)	28 (93.3 %)	26 (100 %)
Anti-RNA-Poly III positive	15 (20.5 %)	4 (23.5 %)	7 (23.3 %)	4 (15.4 %)
Anti- Scl-70 positive	37 (50.7 %)	4 (23.5 %)	16 (53.3 %)	17 (65.4 %)
Normal CRP (≤ 5.0 mg/L)	58 (79.5 %)	13 (76.5 %)	22 (73.3 %)	23 (88.5 %)
Any immunosuppressant‡	41 (56.2 %)	10 (58.8 %)	17 (56.7 %)	14 (53.8 %)
MMF	24 (32.9 %)	7 (41.2 %)	9 (30.0 %)	8 (30.8 %)
MTX	14 (19.2 %)	1 (5.9 %)	7 (23.3 %)	6 (23.1 %)
HCQ	7 (9.6 %)	1 (5.9 %)	4 (13.3 %)	2 (7.7 %)
AZA	2 (2.7 %)	1 (5.9 %)	1 (3.3 %)	0
mRSS (0-51)	24.8 ± 7.9	23.1 ± 9.2	25.3 ± 7.9	25.2 ± 7.2
FVC% predicted	88.0 ± 17.9	88.7 ± 20.2	82.0 ± 16.9	94.4 ± 15.5

*US and Canada† UK, Germany, Spain, Italy, and Belgium‡ Includes MMF, MTX, HCQ, and AZA

Conclusion: There were no major differences in the baseline demographics such as disease duration, sex and age, and no major differences in disease severity as well as the percentage of use of immunosuppressants among the regions although some variation in SSc autoantibody specificity were observed.

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AB0856

A MULTI-NATIONAL SURVEY TO IDENTIFY THE CLINICIANS' PERSPECTIVES CONCERNING PROTON PUMP INHIBITORS IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Gastrointestinal tract

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Background: Proton Pump Inhibitors (PPIs) are widely used in the management of gastro-oesophageal problems in SSc. However, there is little evidence to support their empirical use in SSc, and long-term safety concerns have been highlighted in the general population [1,2].

Objectives: To examine clinicians' perspectives concerning PPI use in patients with SSc.

Methods: An online survey in the English language targeting healthcare providers (HCP) involved in the care of patients with SSc was developed and distributed through international physician networks and social media. The survey was lauched on 27th November 2022 and kept open for 3 weeks.

Results: Responses from 227 HCP from 36 countries were obtained. The majority (86.3%) were between 30-70 years old. Female and male gender were equally represented (M:48%, F:52%). Most respondents practiced in a university hospital (86%), the most common specialties represented were rheumatology (70.5%), internal medicine (10.6%), and gastroenterology (7.5%). The majority of respondents (87%) agreed that gastroesophageal reflux disease (GERD) is a major cause of morbidity in SSc. Lifestyle modifications/non-pharmacological approaches alone were seldom (16%) considered as effective in controlling GERD symptoms. Only half of responders either 'agreed' (43%) or 'strongly agreed' (11%) that solid evidence supports PPI efficacy in SSc. PPIs were prescribed by 93% of HCP with the most commonly prescribed compounds being pantoprazole (74%), esomeprazole (72%), omeprazole (72%), and lansoprazole (68%). PPIs were mainly prescribed for: 1) symptomatic GERD unresponsive to lifestyle modification (95%); 2) objective evidence of GERD (e.g., on endoscopy) (82%); 3) hoarseness or respiratory symptoms where GERD is implicated (71%). Over 80% reported prescribing the "maximum (or even higher)" PPI dose in patients with refractory GERD, and said they would initiate combination therapy (e.g., PPI plus prokinetic agent) in case of dysphagia and/or evidence of dysmotility (84%). Over 80% reported that they would perform further diagnostic investigation/s to better characterize the GI manifestations in such cases (69% would perform H. Pylori test). There was significant heterogeneity regarding safety of long-term treatment with PPI in SSc: 34% agree that side effects are a major concern, 25% disagree and 36% were neutral. The three potential PPI adverse events of highest concern among the group were: 1) small intestinal bacterial overgrowth (5.5), osteoporosis and increased risk of fracture (5.4), and 3) drug interactions (5.2), (0-10, where 10 is 'very concerned'). There was no clear consensus whether PPI dose and/or frequency should be reduced in patients with refractory calcinosis: 'disagree' = 25.3%, 'neutral' = 48.4%, and 'agree' = 22.6%. In addition, around half of responders considered that patients should be on high-dose PPI long-term after lung transplantation ('agree' or 'strongly agree' = 49.8%) or were 'neutral' (42.9%) There were differences in attitudes towards the use of GI surgery for refractory GERD where 45.2% of respondents agreed and 45.6% considered their opinion 'neutral'. Half of the responders agreed that GI surgery in SSc is associated with frequent complications, such as worsening of dysphagia.

Conclusion: Various PPIs are often prescribed at maximum doses to control symptoms of GERD in SSc. Potential concerns about long-term side effects are acknowledged by prescribing physicians. There is a significant heterogeneity in attitudes towards surgical intervention for refractory GERD and still need to be better defined. Further research and practical treatment recommendations pertaining to PPIs in SSc are urgently warranted.

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AB0857

ANTI-THYMOCYTE GLOBULIN EXPOSURE IS ASSOCIATED WITH TREATMENT RESPONSE IN PATIENTS WITH DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS UNDERGOING AUTOLOGOUS HAEMATOPOIETIC STEM CELL TRANSPLANTATION

Keywords: Biomarkers, Systemic sclerosis

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Background: Autologous haematopoietic stem cell transplantation (HSCT) ameliorates event-free survival, skin thickening and lung function in patients with progressive diffuse cutaneous systemic sclerosis (dcSSc). Anti-thymocyte globulin (ATG) is a key lymphoablative constituent of conditioning protocols and is administered in a body weight-based dose. Response to HSCT and occurrence of infections is still highly variable across dcSSc patients. Studies in haemato-oncological patients suggest that ATG exposure varies across subjects and impacts outcomes [1].
Objectives: To explore the relation between rabbit derived ATG exposure, lymphocyte reconstitution and clinical outcomes in patients with dcSSc undergoing autologous HSCT.
Methods: We retrospectively analysed patients with dcSSc undergoing autologous HSCT between 2014 and 2020. ATG levels were measured in cryopreserved serum samples at four time points (day 1 and week 1, 2 and 4) after stem cell reinfusion. ATG exposure was estimated using population pharmacokinetics models [1]. Treatment response was defined as pulmonary stabilisation (with no decline more than 10% in forced vital capacity and 15% in diffusing capacity for carbon monoxide) and/or skin improvement (modified Rodnan skin score reduction of more than 30%). Differences between groups were examined with Wilcoxon rank-sum test for contentious variables and Fisher exact test for categorical variables.
Results: Fifteen patients were included in this study with median age 43 years-old (IQR 37–50). During a median follow-up of 45 months (IQR 19—66), 73% (n=11) of patients had a treatment response, and 27% (n=4) were non-responders. Eight (73%) responders achieved long-term remission and three (27%) responders had progressive disease in the follow-up, at a median time of eight months (IQR 5—17) post-HSCT. Although all patients received the same weight-based ATG dosage (7.5 mg/kg), ATG exposure varied across patients. ATG exposure was higher in responders than non-responders (p = 0.026, Table 1) but was not correlated with lymphocyte reconstitution or infection rate.
Conclusion: In our study, ATG exposure highly varied across dcSSc patients undergoing HSCT despite the same weight-based dosage. Responders had a higher ATG exposure than non-responders. More research into optimal ATG dosing is needed to improve HSCT outcomes.
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Table 1. ATG-exposure comparison on outcomes

	Yes	No	p-value
	Response to aHSCT		
Total exposure	163 (153—183)	137 (101—149)	0.026*
Exposure before stem cell reinfusion	30 (30—33)	27 (23—30)	0.226
Exposure after stem cell reinfusion	130 (120—153)	108 (78—117)	0.026*
	Progressive disease following initial treatment response		
Total exposure	178 (164—180)	153 (141—168)	0.536
Exposure before stem cell reinfusion	30 (30—32)	30 (27—32)	0.840
Exposure after stem cell reinfusion	148 (132—150)	121 (114—136)	0.633

The median (interquartile range) anti-thymocyte globulin (ATG) exposure was presented in the cumulative area under the concentration–time curves (AU*day/mL).
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AB0858

PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS: A NATIONAL INPATIENT ANALYSIS

Keywords: Lungs, Systemic sclerosis

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Background: Pulmonary arterial hypertension (PAH) is a chronic, progressive, and eventually fatal complication of Systemic Sclerosis (SS), affecting the prognosis and quality of life. Risk of PAH in SS is substantially high, and it causes early mortality. Non-specific manifestations of PAH can result in delayed diagnosis and result in poorer outcomes.
Objectives: We aim to study the prevalence and epidemiology of pulmonary arterial hypertension in SS, and impact of PAH on adult scleroderma hospitalizations in the United States population. We also aim to estimate the effect of PAH in SS on utilization of healthcare resources.
Methods: We utilized the National Inpatient Sample (NIS) to obtain pertinent data. Total adult hospitalizations with primary diagnosis of SS and coexistent comorbidity of PAH were extracted from 2016-2019. We studied the demographic and epidemiological differences as well as mortality outcomes. Healthcare burden was estimated from total hospital charges (THC) and length of stay (LOS). Secondary outcomes including pulmonary embolism, atrial flutter/fibrillation, pneumonia, sepsis, cardiac & renal failure and ventilator requirements were also studied. Statistical analysis was performed on STATA, with linear and logistic regression analyses.
Results: Out of 126,685 adult scleroderma hospitalizations between 2016-19, 21930 (17%) presented with concurrent pulmonary hypertension. Females were significantly more in this group compared to patients with SS without PAH, representing approximately 85% of total admissions. Patients with PAH had a higher mean age (64.85±13.29 vs 62.56±14.51, P 0.000) as well. In terms of racial demographics, there was a significantly higher proportion of African American and significantly less Asians in the study group. Charlson comorbidity index was also higher >3 in the PAH group. PAH was associated with higher adjusted odds ratio (aOR) for mortality (aOR: 1.39, p<0.001), increased LOS (6.64 vs 6.0 days, p<0.001) increased THC ($83813 vs $71016, p <0.001). It was also associated with significantly higher odds for cardiac failure (aOR 3.13) and ventilator requirement (aOR 2.15). Secondary outcomes of kidney failure, Pulmonary embolism, atrial flutter/fibrillation, and pneumonia recorded a significantly higher aOR for patients with PAH. No significant difference in cardiac arrest, sepsis, or respiratory failure was noted.
Conclusion: Pulmonary arterial hypertension in scleroderma is associated with worse overall outcomes in terms of mortality and morbidity, as well as much higher healthcare burden compared to SS without PAH. Also, PAH disproportionately affects African-american & Asian populations. Although advancements have been made in the treatment of PAH in SS, there still remains room for efforts directed towards early diagnosis and management to further improve outcomes for scleroderma patients.
References: none.

Table 1. Characteristics and Outcomes of adult scleroderma hospitalizations with & without PAH

Hospitalization Characteristics and Outcomes	SCL without PAH N = 104755	SCL with PAH N = 21930	P-Value Odds ratio (OR)
Female	87,829 (83.84%)	18,730 (85.4%)	0.023 OR 1.12
Age (Mean/SD)	62.56/14.51	64.85/13.29	0.000
Race			
White	68774 (65.6%)	13450 (61.3%)	0.000 OR 0.82
African American	15370 (14.6%)	4290 (19.5%)	0.000 OR 1.41
Hispanic	11735 (11.2%)	2505 (11.4%)	0.721
Asian PI	18884 (18%)	615 (2.8%)	0.000 OR 1.57
Native American	870 (0.8%)	194 (0.88%)	0.699
Total died	1410 (6.43%)	4250 (4.01%)	0.000 (1.39)
Length of Stay (LOS) (Mean/SD)	6.00 (7.72)	6.64 (7.3)	0.000
Total hospital charges	71016	83813	0.000
Secondary outcomes		**Odds ratio**	**P-value**
Heart failure		3.13	0.000
Pulmonary embolism		1.84	0.000
Cerebral infarction		0.44	0.000
Atrial Flutter/Atrial Fibrillation		1.86/1.56	0.000/0.000
Sepsis		0.96	0.658
Pneumonia		1.22	0.000
Ventilator		2.15	0.000

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AB0859 CLINICAL COURSES AND PREDICTORS OF LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN SYSTEMIC SCLEROSIS

Keywords: Cardiovascular disease, Systemic sclerosis, Prognostic factors

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Background: Left ventricular systolic dysfunction (LVSD) is a cardiac involvement, resulting in its being the leading cause of death among patients with systemic sclerosis (SSc). Currently, no predictor of LVSD has been defined by longitudinal data for follow-up among SSc patients.
Objectives: We aimed to define the clinical course and predictors of LVSD among SSc patients.
Methods: We conducted a cohort study among adult SSc patients who were followed up at the Scleroderma Clinic, Khon Kaen University, between 2013 and 2020. Semi-parametric Cox regression analysis with robustness clustering by cohort identification number was used for evaluating the predictors of LVSD.
Results: Among the 55,056 person-years, LVSD was defined in 35 of 419 SSc patients for an incidence of 0.25 per 100 person-years. The majority were female (23 cases) with diffuse cutaneous SSc (dcSSc) (26 cases). The median duration of the disease was 8.5 (IQR 4.9-12.9) years. Every 1-point increase in the modified Rodnan skin score (mRSS) and salt and pepper skin were strong predictors of LVSD, with a respective adjusted hazard ratio (HR) of 1.05 and 3.17. During follow-up, 26 cases (74.3%) had worsening LVSD. The strong predictors of the worsening of LVSD were every 1-point increase in mRSS (HR 1.05), every 1 mg increase in prednisolone treatment (HR 1.05), and every 1 U/L increase in creatine kinase (CK) (HR 1.001). Meanwhile, mycophenolate treatment was a protective factor against the worsening of LVSD in SSc (HR 0.15).
Conclusion: LVSD was frequently found in dcSSc, and most cases worsened during follow-up. The severity of skin thickness increases the risk of LVSD. High mRSS, steroid use, and high CK were predictors of worsening LVSD, while mycophenolate treatment might prevent the progression of LVSD. Steroids should be prescribed with caution to patients with longer disease duration.

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AB0860 DISEASE ACTIVITY IS ASSOCIATED WITH LOW QUADRICEPS MUSCLE THICKNESS IN WOMEN WITH SYSTEMIC SCLEROSIS: PRELIMINARY DATA

Keywords: Ultrasound, Quality of life, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is an autoimmune connective tissue disease characterized by progressive cutaneous and visceral fibrosis, and disseminated vasculopathy [1]. Due to clinical features, SSc patients may present low muscle mass, which impacts negatively on their daily activities and physical function [2,3]. There are several methods to assess muscle mass such as magnetic resonance imaging (MRI), computed tomography (CT) and dual-energy radiological absorptiometry (DXA). However, the high costs of the equipment and the lack of portability make them uncommon tools in clinical practice. In this sense, ultrasonography has been used to evaluate muscle mass in different populations [4].
Objectives: To assess the quadriceps muscle thickness and to verify associations with clinical features, muscle strength and physical performance in SSc women.
Methods: In this cross-sectional study, patients with SSc according to the 2013 ACR-EULAR classification criteria were included. Age in years (y), disease duration (y), modified Rodnan skin score (mRSS), the European Scleroderma Trials and Research Group (EUSTAR) SSc activity index (EScSG-AI), and the health assessment questionnaire (HAQ) were assessed. The muscle thickness was assessed by a real-time ultrasound device (Esaote S.p.A MyLab 50 X Vision; SãoPaulo, Brazil). An experienced ultrasound evaluator analyzed the muscle thickness of vastus lateralis (VL, cm), rectus femoris (RF,cm), vastus intermedius (VI,cm), and vastus medialis (VM,cm). Muscle strength was assessed by handgrip (HGS,kg) and physical performance was assessed by short physical performance battery (SPPB,points). Frequency analysis and Pearson's or Spearman's correlation coefficients were explored as appropriate. The significance was considered when $p<0.05$.
Results: We included 45 patients with SSc, 32 (71.1%) with diffuse disease. The median age was 62.00 (54.50-66.50) years and the disease duration was 10.91 (4.88-18.68) years. The median of EScSG-AI was 1.33 (0.33-2.34), the mRSS was 4.00 (2.00-8.00) and the HAQ was 0.62 (0.25-1.06). The mean of muscle thickness were: VL 1.38 + 0.32 cm, RF 1.06±0.35 cm, VM 1.16±0.47 cm, and VI 1.17±0.33 cm. The mean of HGS was 18.64±9.71kg and the median SPPB was 10.00 (9.00-11.50) points. The disease activity by EScSG-AI was negatively associated with VL ($r = -0.410$, $p = 0.016$) and VI ($r= -0.394$, $p = 0.021$). In addition, HGS was positively associated with VM ($r= 0.435$, $p = 0.003$) and SPPB was positively associated with VL ($r= 0.354$, $p = 0.017$).
Conclusion: Low quadriceps muscle thickness is associated with higher disease activity. As expected, our findings suggest that there are positive associations between muscle thickness with strength and physical performance in SSc women. Our findings highlight the importance of aiming for disease activity control because it may indirectly influence the muscle mass of SSc women.

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AB0861 INCIDENCE AND PREVALENCE OF SYSTEMIC SCLEROSIS IN THAILAND IN YEAR 2017-2020: A DATABASE FROM THE MINISTRY OF PUBLIC HEALTH

Keywords: Epidemiology, Systemic sclerosis

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Background: A better understanding of the epidemiological profile of systemic sclerosis (SSc) in Thais could improve care, human resource deployment, and public health budgeting.
Objectives: We aimed to determine the incidence and prevalence of SSc in Thailand between 2017 and 2020.
Methods: A descriptive epidemiological study was performed using the Information and Communication Technology Center, Ministry of Public Health database, comprising all types of healthcare providers during the study period. Demographic data of patients having a primary diagnosis of M34 systemic sclerosis and over 18 years of age between 2017 and 2020 were reviewed. The incidence and prevalence of SSc were calculated as well as their respective 95% confidence intervals (CIs).
Results: The number of SSc cases in 2017 was 15,920 from a total Thai population of 65,204,797. The prevalence of SSc in 2017 was 24.4 per 100,000 populations (95% CI 24.0-24.8). The prevalence of SSc among women was 2 times greater than among men (32.7 vs. 15.8 per 100,000). The incidence of SSc was stable from 2018 to 2019 but dropped slightly in 2020 (7.2, 7.6, and 6.8 per 100,000 person-years, respectively). Most SSc cases were in northeastern Thailand (11.6, 12.1, and 11.1 per 100,000 person-years from 2018-2020, respectively) and the peak was between 60-69 years of age (24.6, 23.8, and 20.9 per 100,000 person-years from 2018 to 2020, respectively).
Conclusion: SSc is a rare disease among Thais. The disease was commonly revealed in late middle-aged women with a peak at age 60-69 years, mainly from the Northeast regions. The incidence remained stable during the study period, albeit during the emergence of the coronavirus pandemic a slight decline was recorded.

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AB0862 NAILFOLD CAPILLAROSCOPY FOR PREDICTION OF NOVEL SEVERE ORGAN INVOLVEMENT IN SYSTEMIC SCLEROSIS

Keywords: Organ damage, Prognostic factors, Systemic sclerosis

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Background: Nailfold capillaroscopy (NFC) has been suggested as a potential biomarker of disease severity in systemic sclerosis (SSc). Several studies report the association between capillary loss and disease severity however, the association of NFC abnormalities with novel severe organ involvement/progression in SSc has not been evaluated.
Objectives: We aim to evaluate the association of nailfold capillaroscopy (NFC) with novel major organ involvement/progression in SSc.
Methods: Follow-up data from patients with SSc registered between 2000 and 2022 were analysed. Patients underwent NFC at baseline. Novel severe organ involvement/progression was defined as new or progressive involvement of peripheral vasculature, lungs, heart, skin, gastrointestinal, kidney, musculoskeletal at 12 and 24 months of follow-up. The following NFC parameters were evaluated: capillary density, haemorrhages, enlarged and giant capillaries, avascular areas, organization of capillary architecture and scleroderma pattern (early/active/late). Logistic regression modelling was run to assess associations between NFC parameters and the occurrence of novel severe organ involvement and/or progression and risk factors.
Results: 113 patients with SSc were included, 70 patients (61%) developed novel overall severe organ involvement/progression: 39 patients (56%) during the first 12 months and 31 patients (44%) from 12 to 24 months of follow-up. 11% of patients developed novel peripheral vascular involvement, 21% developed novel interstitial lung disease (ILD), 11% had progression of known ILD, 6% had novel pulmonary hypertension, 11% had skin progression, 10% had novel heart involvement, 10% had novel gastrointestinal involvement, 6% had scleroderma renal crisis and 13% had novel musculoskeletal involvement. Table 1 summarizes the significant associations between NFC and novel severe organ involvement/progression during follow-up. Loss of capillary density was associated with overall severe organ involvement (p 0.002), peripheral vascular involvement (p 0.03), new ILD (p 0.04) and skin progression (p 0.01); avascular areas were associated with overall severe organ involvement (p 0.03), new ILD (p 0.03) and progression of ILD (p 0.02) and scleroderma pattern was associated with overall severe organ involvement (p 0.03), peripheral vascular involvement (OR p 0.04), new ILD (p 0.004), progression of ILD (p 0.03) and skin progression (p 0.04).
Conclusion: NFC may be a potential biomarker in SSc for predicting novel severe organ involvement and/or progression. Abnormal capillary density, avascular areas and scleroderma pattern are predictors of overall severe organ involvement, peripheral vascular involvement, novel and progression of ILD and skin progression.

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Disclosure of Interests: None Declared.
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AB0863 SERUM ANTI-MITOCHONDRIAL-AMA, ANTI-TIF1GAMMA, ANTI-RO52 AUTOANTIBODIES CHARACTERIZE CANCER-ASSOCIATED DERMATOMYOSITIS

Keywords: Autoantibodies, Malignancy, Myositis

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Table 1. Associations between NFC and novel severe organ involvement/progression during follow-up

Novel severe involvement or progression	Loss of capillary density	P value	Haemorrhages	P value	Enlarged capillaries	P value	Avascular areas	P value	Scleroderma pattern	P value
Overall future organ involvement	**3.21 (1.02-5.45)**	**0.002**	1.82 (0.82-4.52)	0.82	1.09 (0.52-3.23)	0.72	**2.1 (1.34-6.23)**	**0.03**	**1.82 (1.12-4.25)**	**0.03**
Peripheral vascular involvement	**1.7 (1.10-3.19)**	**0.03**	1.72 (0.82-2.72)	0.62	1.92 (0.64-4.2)	0.52	2.62 (0.72-3.2)	0.72	**1.82 (1.2-3.9)**	**0.04**
New ILD	**2.45 (1.32-4.23)**	**0.04**	1.2 (0.52-3.21)	0.75	1.32 (0.72-4.21)	0.82	**1.82 (1.12-3.42)**	**0.03**	**1.98 (1.32-3.42)**	**0.004**
Progression of ILD	0.98 (0.23-2.14)	0.32	0.45 (0.14-1.98)	0.45	0.78 (0.21-2.34)	0.72	**1.32 (1.10-3.52)**	**0.02**	**1.45 (1.12-3.82)**	**0.03**
New PAH	0.72 (0.14-1.98)	0.42	0.32 (0.15-1.67)	0.62	0.34 (0.21-1.52)	0.65	0.85 (0.62-2.14)	0.73	0.92 (0.52-1.45)	0.62
Skin progression	**1.42 (1.12-3.29)**	**0.01**	1.32 (0.62-2.81)	0.34	0.72 (0.32-1.30)	0.39	1.19 (0.63-3.62)	0.06	**2.3 (1.45-3.14)**	**0.04**

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Background: Cancer-associated myositis (CAM) remains a clinical challenge and established risk factors include older age, male sex, dermatomyositis (DM), and specific antibodies, including anti-TIF1gamma and -MJ/NXP2 [1]. However, a recent report suggests a lower risk of malignancy in -TIF1gamma positive patients with other concurrent autoantibodies (2,3), whereas the protective role against malignancy of antisynthetase or anti-Mi-2 antibodies is being questioned [1].
Objectives: To describe the demographic, clinical, and serological characteristics of a cohort of patients with CAM in a specific autoantibody profile.
Methods: Retrospective cohort analysis on electronic clinical charts, autoantibody analysis by serum immunoprecipitation and ELISA.
Results: Malignancy was observed in 17/73 (23%) patients with IIM, in 13/17 (76%) within 5 years before or after IIM diagnosis and cancer relapse or progression in 7 cases; 2/17 were men with a median age of 56 years. Breast cancer was the most frequent, followed by lung, thyroid, ovarian, and lymphoma. Four patients died, three for cancer-related complications and one for severe refractory IIM. Muscle injury was observed in 13/17 (76%) while 2/17 experienced dysphagia. Skin lesions were present in 14/17 (82%) patients, while ILD (24%) and arthritis (18%) rarely occurred; no cases of myocardial involvement were described. Anti-Ro52 was the most common antibody (5/17 – 29%) in our cohort, detected as the only specificity in 2/5 cases. Anti-TIF1gamma was described in 4/17 (24%, one case with concurrent -Ro52), followed by antisynthetase (3 – 18%), -Mi-2 (2 – 12%), -MJ/NXP2, -SAE1, -SRP (1 each – 6%). Combined anti-E2/E3 PDH (AMA) and anti-Ro positivity was found in a patient who developed lymphoma and cholangiocarcinoma within two years from IIM. We compared CAM patients with (n=4) and without (n=13) serum anti-TIF1gamma (Table 1). Albeit not reaching statistical significance, dysphagia and skin disease were more frequently observed with anti-TIF1gamma, whereas arthritis, Raynaud's phenomenon, and capillaroscopy alterations were rarer in such group. Prevalence of early-stage cancer seemed more frequent with anti-TIF1gamma. 3/13 patients without anti-TIF1gamma died due to cancer-related causes; the only death observed in the TIF1gamma positive group was due to progressive IIM, and occurred in a patient with complete cancer remission.
Conclusion: We observed that DM remains the most common clinical subset of CAM, but other myositis phenotypes can be also observed. Anti-TIF1gamma remains the more prevalent autoantibody in CAM along with anti-Ro52. The role of AMA positivity may warrant further investigation, particularly in patients with seronegative CAM.
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Table Clinical features of patients with (+) and without (–) anti-TIF-1gamma antibodies

	Anti-TIF1gamma+ (n=4)	Anti-TIF1gamma– (n=13)	p
Advanced cancer at diagnosis, n.(%)	0 (0)	3 (23.1)	.3041
Dysphagia, n.(%)	1 (25)	1 (7.7)	.3624
Skin rash, n.(%)	4 (100)	10 (76.9)	.3041
Gottron, n.(%)	3 (75)	6 (46.2)	.3276
Raynaud, n.(%)	0 (0)	4 (30.8)	.2181
Capillaroscopy alterations, n.(%)	1 (25)	9 (69.2)	.1276
Arthritis, n.(%)	0 (0)	3 (23.1)	.3041

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AB0864 IDIOPATHIC INFLAMMATORY MYOPATHIES AND CANCER RISK STRATIFICATION

Keywords: Myositis, Malignancy

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Background: Patients with idiopathic inflammatory myopathies (IIMs) are at increased risk of cancer, particularly in the first ±3 years of the disease, and a cancer risk stratification was proposed recently [1], to improve cancer screening in IIMs.
Objectives: The aim of our retrospective study was to determine the frequency, temporal relations, and cancer types, as well as to evaluate the performance of proposed cancer risk stratification tool in our well-defined IIM cohort.
Methods: We analyzed medical records of IIM patients diagnosed between January 2005 and December 2020 and followed at our rheumatology centre of a median (IQR) 72.6 (35.1; 126.9) months. The development of cancer, its location and temporal relationship to IIM diagnosis were extracted. We applied the proposed cancer risk stratification [1] in a cohort of our patients.
Results: In a cohort of 175 IIM patients (122 females, 69.7%), 38 patients (21.7%; 24 females (19.7%) and 14 males (26.4%)) developed 41 cancers. Fifteen cancers (39.5%) were diagnosed or were active/relapsing within the two years prior to diagnosis of IIM, 10 cancers (26.3%) were diagnosed concurrently with IIM, and 16 (39.0%) cancers were diagnosed during the IIM follow up (9 (22.0%) of them during the first 3 years of the follow up) (Figure 1, Panel A). The most frequently diagnosed cancers were breast and gynaecologic cancers in females (20.0% each), and urogenital cancers in men (43.8%). The cancer location (overall and sex stratified) is presented in Table 1. The Figure 1, panel B shows the stratification of patients to their estimated risk of developing cancer, and the actual proportion of patients who develop cancer. Based on the estimated risk, 6.3%, 46.3% and 47.4% IIM patients were allocated into low-, intermediate- and high-risk group, respectively. While there were no episodes of cancer from -2 years to +3 years of follow up in the low-risk group, 12.5% patients in the intermediate-risk group, and 31.3% in the high-risk group developed cancer during this time interval.

Table 1. Location of cancer in IIM patients

Cancer location/type	All cancers (41 episodes)	Cancer in males (16 episodes)	Cancer in females (25 episodes)
Head and Neck	4 (9.8%)	2 (12.5%)	2 (8.0%)
Lung	4 (9.8%)	1 (6.3%)	3 (12.0%)
Breast	5 (12.2%)	0	5 (20.0%)
Colonic	3 (7.3%)	0	3 (12.0%)
Renal	2 (4.9%)	2 (12.5%)	0
Bladder	1 (2.4%)	1 (6.3%)	0
Gynaecologic	5 (12.2%)	-	5 (20.0%)
Prostatic	2 (4.9%)	2 (12.5%)	-
Testicular	2 (4.9%)	2 (12.5%)	-
Skin – melanoma	4 (9.8%)	1 (6.3)	3 (12.0%)
Skin – NMSC	2 (4.9%)	1 (6.3%)	1 (4.0%)
Lymphoma	2 (4.9%)	2 (12.5%)	0
Leukaemia	1 (2.4%)	1 (6.3%)	0
Unknown origin	4 (9.8%)	1 (6.3%)	3 (12.0%)

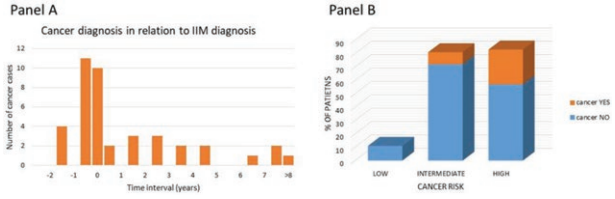


Figure 1. Panel A: Diagnosis of cancer in time relation to IIM. Panel B: Cancer risk stratification and actual development of cancer Legend: Panel A: time interval between the diagnosis of cancer in relation to the diagnosis of idiopathic inflammatory myopathy (Time 0).

Conclusion: Cancer affected a fifth of our IIMs patients. Almost a third of patients who were at high risk of cancer had cancer associated myositis.
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AB0865 BODY COMPOSITION ASSESSMENT IN PATIENTS WITH SYSTEMIC SCLERODERMA

Keywords: Systemic sclerosis, Sarcopenia

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Background:
Objectives: To assess the body composition in patients with systemic scleroderma (SS) and to determine the frequency of sarcopenia (SP).
Methods: 43 patients with SS were included (90% women), mean age 49.75±7.3 years. The patients underwent: dual-energy X-ray absorptiometry of the whole body (DXA), assessment of muscle strength (carpal dynamometry, lifting from a chair 5 times) and functional state of the muscles (short set of tests for assessing physical fitness (SST APF), determination of body mass index (BMI). In order to interpret the results of the study, appendicular muscle mass (AMM) - the sum of the muscle mass of the legs and arms, appendicular muscle index (AMI) - the ratio of AMM (kg) to height squared (m2) was determined. The diagnosis of sarcopenia was made in accordance with the updated EWGSOP2 criteria.
Results: In patients with SS, the average content of bone mineral was 2.0±0,1 kg, and adipose tissue - 25.0±1,9 kg, which turned out to be an average of 28.0% of the total weight of patients. Among the examined individuals, the frequency of obesity according to DXA (fat > 35% of body weight) was 50%, while obesity calculated by BMI (≥30 kg/m2) was detected in 6 (14.2%), and overweight (25-30 kg/m2) - in 16 (35.8%) patients. The content of total muscle mass averaged 42.7 kg, and AMM -18.2 kg, while the average AMI was 6.7 kg/m2. Low AMM was found in 4 (9.5%), and a decrease in AMM and AMI was found in 6 (14.2%) individuals. Low muscle strength according to the results of carpal dynamometry and/or the "Get up from the chair" test was found in 22 patients (52.3%), while confirmed SP (decrease in muscle strength and muscle mass) was diagnosed in 14 (33.3%) patients. When assessing the functional state of the muscles in 18 (42.8%) patients, the walking speed was <0.8 m/s, and the SST APF was less than 8 points in 24 (57.1%) patients. Severe SP (low muscle strength, low muscle mass and low physical capacity) was confirmed in 8 people (19.4% of the entire group of patients and 75% of confirmed SP). One patient with SP had a fat content of more than 35%, thus diagnosing sarcopenic obesity.
Conclusion: The results of the pilot study showed that 50% of patients with SS were obese, 33.3% - SP and 4.7% sarcopenic obesity. Thus, 12% of patients with SS had SP, which requires further study of this problem in order to identify specific risk factors for SP and develop methods for its prevention in patients with SJS.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0866 **SEASONAL VARIATION OF SERUM KL-6 LEVELS IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED WITH INTERSTITIAL LUNG DISEASE**

Keywords: Systemic sclerosis

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Background: Recent studies have shown that serum KL-6 levels were useful for diagnosing and estimating prognosis in patients with systemic sclerosis-associated with interstitial lung disease (SSc-ILD) [1-4]. Additionally, KL-6 has the potential for assessing the activity of SSc-ILD; however, it may fluctuate irrespective of disease activity [5]. Identifying the reasons for fluctuation will lead to the utilization of this non-invasive tool. Based on our clinical experience, serum KL-6 levels may have seasonal variations.
Objectives: We aimed to evaluate whether serum KL-6 levels are affected by season in patients with SSc with ILD (SSc-ILD).
Methods: This is a single-center, retrospective observational study. The diagnosis of SSc was according to the 2013 ACR/ EULAR classification criteria, and the presence of ILD was confirmed by computed tomography (CT) or high-resolution CT (HRCT). We defined summer as July to September and winter as December to January. SSc-ILD patients with data of serum KL-6 levels in the 2015 winter (from December 2014 to January 2015), 2015 summer, and 2016 winter were included. Patients with comorbidities that could affect serum KL-6 levels, such as malignancy, pneumocystis pneumonia and alveolar proteinosis, and patients who did not confirm the change in the extent of ILD by chest CT during the observational period were excluded. The extent of ILD was calculated as the average of CT images at the five predefined levels [6], and scoring was blinded. Differences in serum KL-6 levels between summer and winter were analyzed by the Wilcoxon signed-rank test, followed by the Bonferroni correction for adjusting multiple comparisons.
Results: Sixty patients with SSc-ILD were included. 53 (88%) patients were female. At baseline, the median age was 61 (interquartile range [IQR]: 44–66) years, and the median disease duration was 7.7 (IQR: 4.2–13) years. 34 (57%) patients had diffuse cutaneous SSc (Table 1). Regarding the extent of ILD, 18 (30) patients had a lesion area greater than 20%. Eight (15.4%) patients had changed in the extent of ILD, and 52 (84.6%) patients were unchanged. Serum KL-6 levels were significantly higher in the winter than in the summer (2015 summer vs 2015 winter: 585 IU/L vs 648 IU/L, $p < 0.0001$; 2015 summer vs 2016 winter: 585 IU/L vs 690 IU/L, $p < 0.0001$). However, there was no difference between the 2015 winter and 2016 winter ($p=0.62$) (Figure 1). Regarding 52 patients with stable ILD, similar results were obtained (2015 summer vs 2015 winter: 736 IU/L vs 860 IU/L, $p < 0.0001$; 2015 summer vs 2016 winter: 736 IU/L vs 815 IU/L, $p < 0.0001$; 2015 winter vs 2016 winter: 815 IU/L vs 860 IU/L, $p =0.63$).
Conclusion: Serum KL-6 levels may fluctuate regardless of the activity of SSc-ILD. The result of our study may aid the interpretation of serum KL-6 testing.
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Table 1. Patients characteristics

	Overall (n=60)	ILD change (+) (n=8)	ILD change (-) (n=52)
Female, n (%)	53 (88)	7 (88)	46 (88)
Age, years (IQR)	61 (44–66)	58 (46–71)	61 (42–65)
Disease duration, years (IQR)	7.7 (4.2–13)	8.0 (2.0–11)	8.0 (4.8–14)
Modified Rodnan skin score (IQR)	12 (4–15)	15 (12–23)	11 (4–14)
Diffuse SSc, n (%)	34 (57)	5 (63)	29 (56)
SSc-related autoantibody, n (%)			
Anti-topoisomeraseIantibody, n (%)	36 (60.0)	6 (75)	30 (58)
Anti-centromere antibody, n (%)	7 (11.7)	1 (13)	6 (12)
Anti-U1-RNP antibody, n (%)	7 (11.7)	0 (0)	7 (14)
Anti-RNA polymerase III antibody, n (%)	2 (3.3)	0 (0)	2 (4.0)
Treatment			
Prednisolone use, n (%)	42 (70.0)	7 (88)	35 (67)
Cyclophosphamide, n (%)	28 (46.7)	6 (75)	22 (42.3)
Other immunosuppressive agents, n (%)	26 (43.3)	3 (37)	23 (44.2)

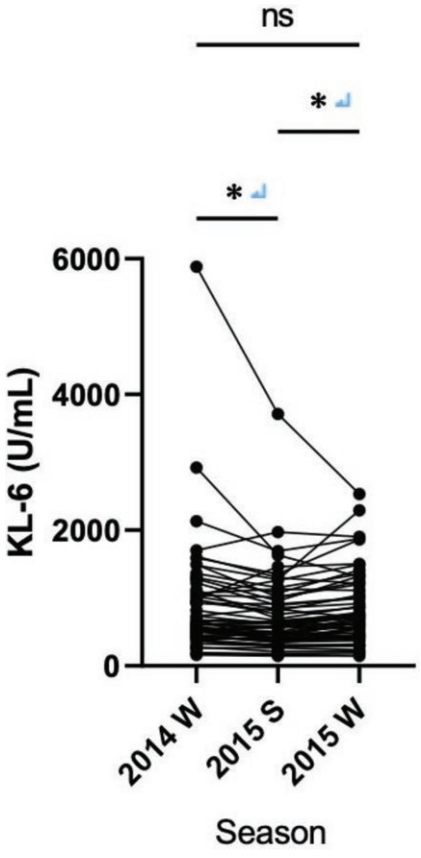


Figure 1. Seasonal variation of serum KL-6 levels in the study population. ns: not significant; *: $p < 0.0001$.

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AB0867 LOW STARTING DOSE AND TITRATION OF NINTEDANIB FOR SSC-ILD: ANALYSIS OF TOLERABILITY IN A SINGLE-CENTER COHORT

Keywords: Systemic sclerosis, Real-world evidence, Lungs

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Background: Interstitial lung disease (SSc-ILD) is a common manifestation of Systemic Sclerosis (SSc) and to date few therapies are available [1]. Nintedanib (NTD) is a promising drug, but its use is often limited by intolerance, mainly by gastrointestinal adverse events (GI AEs). As reported in the SENSCIS trial [2] GI AEs related to NTD treatment (150mg bid) occur in >70% of cases, in particular diarrhea (75.7%), nausea (36.7%), vomit (24.7%), weight loss (11.8%), abdominal pain (11.5%) and alterations of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (13.9%).
Objectives: We investigated the safety and tolerability of an up-titration strategy of NTD until the maximum tolerated dose (max 150mg bid) in our cohort of SSc-ILD patients.
Methods: Evaluation of SSc patients followed at our Rheumatology Unit, treated with NTD according to clinical indication with a dose escalation regimen: 100mg die for 7 days, then 100mg bid for 7 days, then 150mg + 100mg/die for 7 days, and finally 150mg bid. At baseline, demographic, clinical and disease features were collected. NTD GI tolerability was clinically evaluated at 1 (T1), 3 (T3) and 6 (T6) months from the beginning of the treatment.
Results: 12 SSc-ILD patients were enrolled, all females, with a mean age of 62.5 ± 12.7 years and disease duration of 9.2 ± 6.8 years (from the first non-Raynaud symptom). The more frequent disease specific antibody was anti-topoisomerase I (50%) followed by anti-centromere (8.3%). ILD pattern at HRCT was non-specific interstitial pneumonia (NSIP) in 25% of the patients, fibrosing NSIP in 50% and usual interstitial pneumonia (UIP) in 25%. The mean FVC % predicted was 71.2% (± 15.9%) and the mean DLCO 50.4% (± 14.4%). Indications for NTD prescription were fibrosis >10% (25%), FVC decline 5-10% + clinical or imaging worsening (33.3%), clinical and/or imaging worsening (41.7%). GI involvement due to SSc at baseline was present in 75% of patients: gastrointestinal reflux in 66.7%, dysmotility, vomit, and dyspepsia in 8.3% each. Table 1 shows GI AEs at T1, T3 and T6 from NTD beginning. At T6 50% of patients had nausea, 50% diarrhea, 37.5% abdominal pain and 25% referred weight loss. No one showed vomit and AST/ALT alterations. Only 3 patients reached 150mg bid (Figure 1), while 4 got at least to 100 mg bid and 1 patient suspended the drug after 3 months due to vomit.
Conclusion: These data, although limited to a small cohort, suggest that a gradual dose escalation of NTD in SSc-ILD may improve the tolerability of the drug, with a lower incidence of GI AEs (≤50%) and AST/ALT elevation. Although only 3 patients reached the maximum dose, most of the cohort managed to do at least 100 mg bid. This approach can be a good compromise in the management of ILD in SSc patients, knowing that the dose reduction to 100 mg bid does not significantly compromise the efficacy of NTD in reducing disease progression [3]–[5]. Studies of larger populations are needed to support these data.
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Table 1. GI AEs during NTD treatment

	T1 (n=12)	T3 (n=12)	T6 (n=8)
Nausea, n (%)			
Not present	9 (75%)	7 (58.3%)	4 (50%)
New onset	3 (25%)	2 (16.7%)	2 (25%)
Stable		1 (8.3%)	1 (12.5%)
Improved			1 (12.5%)
Worsened		2 (16.7%)	
Vomit, n (%)			
Not present	10 (83.4%)	9 (75%)	8 (100%)
New onset	2 (16.6%)	1 (8.3%)	
Stable			
Improved			
Worsened		2 (16.7%)	
Diarrhea, n (%)	1		
Not present	2 (100%)	11 (91.6%)	4 (50%)
New onset		1 (8.3%)	3 (37.5%)
Stable			
Improved			
Worsened			1 (12.5%)
Abdominal pain, n (%)			
Not present	9 (75%)	9 (75%)	5 (62.5%)
New onset	3 (25%)	1 (8.3%)	1 (12.5%)
Stable		1 (8.3%)	1 (12.5%)
Improved		1 (8.3%)	
Worsened			1 (12.5%)
AST/ALT elevation, n (%)	0	0	0
Weight loss, n (%)	0	2 (16.7%)	2 (≠ from the T3) (25%)

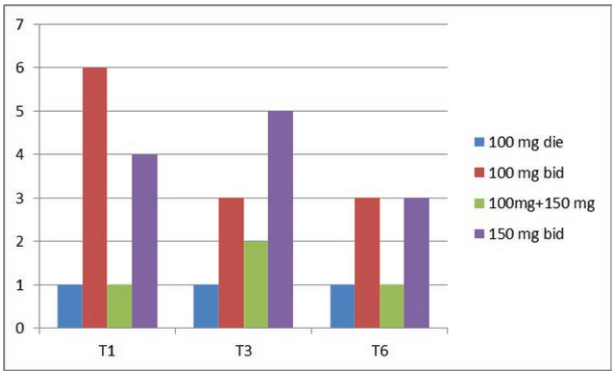


Figure 1. NTD dosages

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Disclosure of Interests: None Declared.
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AB0868 IMMUNE CHECKPOINT INHIBITOR-ASSOCIATED MYOPATHY

Keywords: Myositis, Targeted synthetic drugs

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Background: In recent decades, immunotherapy has changed the management and prognosis of cancer patients. Immune checkpoint inhibitors, such as those targeting PD-1 and PD-L1, are used for some types of cancer; however, their use has been associated with the appearance of immune-mediated adverse events. Among these, those related to the field of rheumatology are relatively frequent, joint involvement being the most common, followed by muscle involvement (myalgias 4%, myositis 1%).
Objectives: To describe oncologic patients who developed immune checkpoint inhibitors- related myositis.
Methods: All patients from the oncology department of a tertiary hospital, referred to rheumatology and diagnosed with immune-mediated myositis due to immune checkpoint inhibitors were collected. A descriptive analysis was performed.
Results: Five patients were analyzed, 60% male, with a mean age of 65.8 years (56-78 years). The types of cancer were: melanoma (n=2), gastroesophageal

junction cancer (n=1), cavum cancer (n=1) and pancreatic cancer (n=1); all in advanced stages with lymph node and/or metastatic involvement. The immunotherapy employed was: Nivolumab (PD-1 inhibitor) in three patients, Pembrolizumab (PD-1 inhibitor) in one patient and Darvalumab (PD-L1 inhibitor) in one patient; all at standard doses. Mean time from onset of symptoms was 4 months from drug initiation (1-10 months). In all 5 cases, the drug was discontinued with the onset of clinical symptoms and oral prednisone was prescribed at a dose between 10 and 20 mg per day. The symptom present in all patients was pain and weakness of proximal limbs (100%). In addition, one patient had ankle arthritis and another had dermatomyositis with typical cutaneous involvement (heliotrope erythema, V sign). In 3 patients there was an elevation of CK levels that resolved one month after discontinuation of the drug. Also, 3 patients, developed myositis-specific antibodies (AntiPM75 and Anti MI2, anti-PL7 and anti-TIF1gamma) that disappeared with drug withdrawal. One patient had anti-Ro52 and Ro60 antibodies that remain positive. Two patients underwent muscle MRI: one showed fatty infiltration in the gluteal musculature and atrophy with fatty infiltration in the right rectus femoris (image); in the other patient, signs of inflammatory myositis in the bilateral adductor group and in the right gluteus medius and gluteus minimus and fibrosing myositis in the iliac muscle was described. In both cases, the signs of myositis had disappeared in the control PET scan 5 months after drug discontinuation. In 4 patients, symptoms subsided in less than one month. One patient required the association of methotrexate to achieve corticosteroid withdrawal.

Conclusion: In our hospital, a total of 5 patients undergoing oncological treatment with immune checkpoint inhibitors have developed, in a mean time of 4 months from the start of the drug, a myopathy associated in 60% with the appearance of myositis-specific antibodies. This represents 1.8% of the total number of patients treated with these three drugs in our hospital.

Withdrawal of the drug and treatment with prednisone at intermediate doses allowed clinical remission and normalization of laboratory and imaging tests.



Image 1. MRI: SPAIR technique and fat suppression.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0869 ANTI-NUCLEAR AUTOANTIBODIES IN ANTI-U1RNP POSITIVE SYSTEMIC SCLERODERMA PATIENTS

Keywords: Systemic sclerosis

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Background: In patients with systemic scleroderma (SSD) with overproduction of anti-U1ribonucleoprotein, there are features in the clinical picture and course of the disease.

Objectives: The aim of the study is to study the level of major autoantibodies in patients with systemic scleroderma who are positive for anti-U1ribonucleoprotein.

Methods: The study included 55 patients (48 women and 7 men, mean age 41.5±11.5 years), positive for anti-U1ribonucleoprotein and meeting the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) 2013 classification criteria for systemic scleroderma. Defined autoantibodies (AT): rheumatoid factor (RF), antibodies to cyclic citrullinated peptide (ACCP), anticentromeric antibodies (ACA), antibodies to the nonhistone chromosomal protein Scl-70 (anti-Scl-70), antibodies to RNA polymerase III (anti-RNAP III), antibodies to cytoplasmic antigen (anti-Ro), antibodies to cytoplasmic antigen SS-B (La) associated with RNA polymerase III (anti-La), antibodies against DNA (anti-DNA), antibodies to U1-, U2-, U4-ribonucleoproteins (anti-Sm (Smith)), antibodies to cardiolipin (AKL), anti-synthetase antibodies to cytoplasmic antigen (anti-Jo1). After 2 years of complex therapy, these patients were examined.

Results: In patients of the study group, the clinical picture was dominated by inflammatory lesions of the joints and muscles, and skin manifestations were not very pronounced. Interstitial lung disease was detected in 47% of cases. Intersections with diseases (rheumatoid arthritis, systemic lupus erythematosus) were detected in 23% of cases and a combination with Sjögren's syndrome in 21.3%. Other antibodies were often detected: RF (27%), anti-Ro (31%), anti-DNA (32%), rarely - anti-Sm (13%), ACCP (7%), anti-La (5%), ACA (7%), anti-Scl70 (4%), ACL (3%). Anti-Jo1 and anti-RNAP-III were not detected in any of the patients. In patients with systemic scleroderma, highly positive for anti-U1RNP (more than two upper limits of normal) compared with low positive, RF, anti-Ro, anti-DNA were significantly more common (p=0.00). In dynamics after 2 years, high titers of anti-U1RNP persisted in 65% of patients, while other autoantibodies were detected with the same frequency. In patients with an initially low titer of anti-U1RNP, their disappearance was noted.

Conclusion: In patients with systemic scleroderma and overproduction of anti-U1RNP, inflammatory musculoskeletal manifestations predominate and are often associated with Sjögren's syndrome and overlap syndrome. High positivity for antiU1RNP was accompanied by a persistent increase in the levels of RF, anti-Ro, and anti-DNA.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0870 ANTI-HMGCR AUTOANTIBODY LEVELS IN THE FOLLOW-UP OF STATIN-INDUCED IMMUNE-MEDIATED NECROTIZING MYOPATHY. MULTICENTRIC STUDY OF 24 PATIENTS

Keywords: Myositis, Autoantibodies, Diagnostic Tests

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Background: Statin-induced immune-mediated necrotizing myopathy (IMNM) is associated with anti-3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) autoantibodies. It is characterized by elevated creatine kinase (CK) levels, and severe muscle weakness. Measuring disease activity is problematic, since it is challenging to differentiate it from damage. The utility of the quantitative analysis of anti-HMGCR autoantibodies during the follow-up has not been thoroughly studied.

Objectives: To assess the usefulness of measuring the levels of anti-HMGCR autoantibodies in relation to response to treatment.

Methods: We included patients all consecutive patients diagnosed with statin-induced IMNM according to the definition of the European Neuromuscular International Workshop 2016 (1) and positivity for anti-HMGCR autoantibodies in two centers from Spain and Sweden from January 2017 to November 2022. All patients were followed for at least 3 months to be included. Clinical data was extracted retrospectively from the patients' clinical records. Remission was defined as no disease activity assessed by expert rheumatologists according to 2016 ACR/EULAR response criteria in myositis. Moderate and high disease activity was defined when physician global activity score was higher than 2 or 3 (on a Likert scale) respectively [2,3]. Anti-HMGCR autoantibodies level was measured at the time of diagnosis and at a variable period of time after treatment.

Results were obtained using the chemiluminescence immunoassay (CLIA) method. Negative anti-HMGCR was considered as levels lower than 20 U/ml.

Results: Our group combined of 24 patients. Main features of the patients are summarized in the **TABLE 1**. 21 (87.5%) patients reached clinical remission or low disease activity. However, 3 patients (12.5%) remained with moderate activity of the disease. None of the patients had high disease activity. Anti-HMGCR levels at diagnosis were higher than 100 U/ml in 23 patients (95.8%) and above 200 in 11 patients (45.8%). However, anti-HMGCR levels after treatment were significantly lower in patients in remission (p=0.035). Numeric levels in patients at diagnosis of the disease and after treatment are shown in the **FIGURE 1**. Most of the patients at diagnosis (with high activity of the disease) had high anti-HMGCR levels (22 patients, 91.7% had levels above 100 U/ml). After treatment, most patients in remission had low (n=3, 14.3%) or negative (n=9, 42.9%), while patients with moderate activity had higher levels (n=2, 66.7% with levels above 100 U/ml). However, 6 patients in remission (28.6%) still had levels above 100 U/ml.

Conclusion: Anti-HMGCR autoantibodies levels evaluation can be used in parallel with other tools to accurately measure disease activity in patients with statin-induced IMNM. However, more studies are needed to confirm these results.

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Table 1. General features of 24 patients diagnosed with anti-HMGCR positive IMNM

Variables	Total (n=24)	Remission/ low activity (n=21)	Moderate activity (n=3)	P (remission vs no remission)
Age (years), mean ± SD	68.2 ± 7.2	67.6 ± 7.1	67.3 ± 10.1	0.95
Sex (women), n (%)	10 (42)	9 (42.9)	1 (33.3)	0.89
Analytical values, mean ±SD				
CK (ukat/L) at diagnosis	114.3 ± 103.9	103.5 ± 100	230.7 ± 84.5	0.51
Anti-HMGCR levels at diagnosis	214.6 ± 110.8	212.2 ± 89.7	295 ± 127.8	0.24
Anti-HMGCR levels after treatment	83.8 ± 89	74 ± 80.4	190 ± 100.1	**0.035***
Muscle strength assessment, mean ±SD				
MMT-8 at diagnosis	64.4 ± 12	65.4 ± 12.7	62.7 ± 12.5	0.73
MMT-8 after treatment	77.6 ± 4.2	78.6 ± 3.1	74.3 ± 8.1	0.1

CK: Creatine kinase. Upper limit for CK: < 4.7 ukat/L for men and 3.5 ukat/L for women.*: p < 0.05

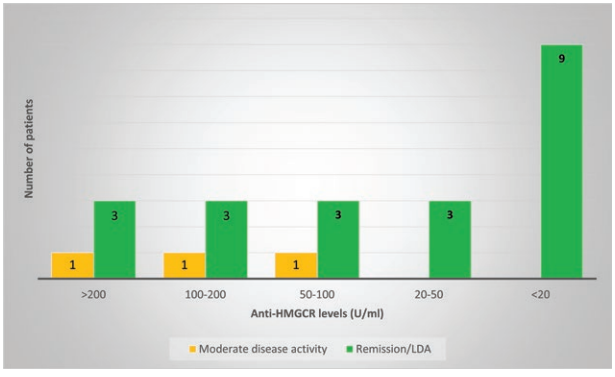


Figure 1. Anti-HMGCR autoantibodies levels according to disease activity after treatment in 24 patients with IMNM. LDA: Low disease activity

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AB0871

REMISSION IN ANTI-HMGCR POSITIVE IMMUNE-MEDIATED NECROTIZING MYOPATHY WITHOUT THE USE OF GLUCOCORTICOIDS: A MULTICENTRIC STUDY OF 24 PATIENTS

Keywords: Comorbidities, Myositis, Safety

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Background: Statin-induced immune mediated necrotizing myopathy (IMNM) is a subtype of inflammatory myopathy associated with anti-3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) autoantibodies. This condition is characterized by progressive muscle weakness leading to severe disability. Treatment is not well established, but usually includes high doses of glucocorticoids (GCs). Therapeutic effects are often disappointing. Side effects are common and related to the high doses of GCs. Intravenous immunoglobulins (IVIG) may be effective in the treatment of IMNM.

Objectives: To compare two therapeutic protocols in IMNM; **a)** standard therapy including high doses of GCs, and **b)** a GC-free protocol.

Methods: Patients consecutively diagnosed with statin-induced IMNM in our centers from January 2017 to November 2022 and followed for at least 3 months were included. IMNM was diagnosed according to the definition of the European Neuromuscular International Workshop 2016 [1]. Clinical data was extracted retrospectively from the patients' clinical records. Remission was defined as no disease activity according to 2016 ACR/EULAR response criteria in myositis [2,3].

Table 1. General features of 24 patients diagnosed with HMGCR positive IMNM.

Variables	Total (n=24)	Glucocorticoid group (n=19)	Glucocorticoid-free group (n=5)	P (steroids vs no steroid)
Age (years), mean ± SD	68.2 ± 7.2	69.2 ± 6.9	64.4 ± 8	0.2
Sex (women), n (%)	10 (42)	8 (42.1)	2 (40)	0.7
Comorbidities (n, %)				
Hypertension	17 (70.8)	13 (68.4)	4 (80)	0.96
Diabetes mellitus	15 (62.5)	11 (57.9)	4 (80)	0.7
Cardiovascular disease	7 (29.2)	6 (31.6)	1 (20)	0.96
Analytical values at diagnosis, mean ±SD				
CK (ukat/L)	114 ± 104	134± 108	40 ± 34	0.07
Treatments, n (%)				
Intravenous GC	8 (33.3)	8 (42.1)	0	0.2
Oral GC	19 (79.2)	19 (100)	0	**0,0001***
MTX	18 (75)	15 (78.9)	3 (60)	0,8
AZA	3 (12.5)	3 (15.8)	0	0,8
IVIG	18 (75)	13 (68.4)	5(100)	0,4
RTX	4 (16.7)	3 (15.8)	1 (20)	0,7
Muscle strength assessment				
MMT-8 at diagnosis	64.4 ± 12	63.7 ± 10.4	67.3 ± 19.4	0.6
MMT-8 after treatment	77.6 ± 4.2	77.2 ± 4.6	79.5 ± 1.5	0,3
Remission				
Patients achieving remission, n (%)	21 (87.5)	16 (84.2)	5 (100)	0.8
Time to clinical remission (months), mean ± SD	5.2 ± 2.3	5.5 ± 2.5	4.1 ± 1.1	0.2
Time to CK normalization (months), mean ± SD	4.1 ± 1.6	3.9 ± 1.7	4.9 ± 1.3	0.3

AZA: Azathioprine; CK: Creatine kinase; GC: Glucocorticoids; IVIG: Intravenous immunoglobulins; MTX: Methotrexate; RTX: Rituximab Upper limit for CK: < 4.7 ukat/L for men and 3.5 ukat/L for women.*: p < 0.05

Treatment was assigned to the patients considering the current recommendations and contraindications of the therapies available. In patients with comorbidities that limit the use of glucocorticoids, a steroid-free regime was agreed through a shared decision between the physician and the patient.

Results: We included 24 anti-HMGCR positive patients. Main features and treatment of the patients are summarized in **TABLE 1**. A GC-free regimen based on the use of IVIG 2g/kg every month for at least 3 months was used in 5 (20.8%) patients. The remaining received standard treatment including GCs. At baseline, general demographic data, MMT-8 and CK levels were similar in both groups. Comorbidities were higher in patients treated with the GCs free protocol. Remission or low disease activity was achieved in 21 patients (87.5%), including all 5 patients who did not receive GCs (after a mean of 4.1 ± 1.1 months). However, 3 (15.8%) of the 19 patients receiving glucocorticoids did not achieve remission or low disease activity. The time to remission or CK normalization was similar in both groups.

Conclusion: In our series of patients with anti-HMGCR positive IMNM, we found that patients can achieve remission without glucocorticoid treatment.

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[3] Rider LG, et al. Arthritis Care Res (Hoboken). 2011 Nov;63 Suppl 11(0 11):S118-57.

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Disclosure of Interests: David Martínez-López: None declared, Diana Prieto-Peña Grant/research support from: UCB, Roche, Pfizer, Amgen, Janssen, AbbVie/Abbott, Novartis, Eli Lilly, Cristina Corrales-Selaya: None declared, Piotr Szczęsny: None declared, Antonella Notarnicola: None declared, Ricardo Blanco Grant/research support from: RB received grants/research supports from AbbVie, MSD, and Roche, and had consultation fees/participation in company-sponsored speaker's bureau from AbbVie, Pfizer, Roche, Bristol-Myers, Lilly, Janssen, and MSD and received support for attending meetings and/or travel from AbbVie, Pfizer, Roche, Bristol-Myers, Lilly, Janssen, and MSD., Ingrid E. Lundberg Grant/research support from: Argenx, AstraZeneca, Bristol Myers Squibb, Novartis, Corbus, EMD Serono, Roche, Pfizer, Orphazyme, Octapharma, Kezar, Janssen, Maryam Dastmalchi: None declared.

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AB0872 RELAPSES OF 129 PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Keywords: Disease-modifying Drugs (DMARDs), Prognostic factors, Myositis

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Background: A high dose of glucocorticoid is suggested as initial management of Idiopathic inflammatory myopathies(IIMs), and immunosuppressive agents are added in severe cases [1]. However, since the diseases are rarely diagnosed, few studies have addressed the issue regarding the use of immunosuppressive agents with limited evidence [2]. The treatment of IIMs largely relies on empirical evidence and small studies [3]. As a results, The immunosuppressives have been indeed administered at the discretion of the physicians in practice. The initial glucocorticoid treatment usually leads to a stable phase for IIMs where clinical symptoms are improved, and glucocorticoids are tapered to low doses. A relapse is occasionally observed in clinical practice as the recurrence of muscle or cutaneous manifestations during and after glucocorticoids tapering, although there is no consensus on the definition regarding the relapse of IIMs [4]. Therefore, it is poorly understood which factors are essential to predicting the relapse of IIMs.

Objectives: Few studies have assessed risks for the relapse of idiopathic inflammatory myopathies (IIMs). We investigated relapse in patients with IIMs.

Methods: Patients who were newly diagnosed with IIMs and underwent muscle biopsy between 2000 and 2017 were retrospectively reviewed. The relapse of IIMs was defined as the recurrence of muscle or cutaneous manifestations after reaching the stable phase, leading to ≥50 % increase in the glucocorticoid dosage. The factors associated with the relapse of IIMs were investigated by Cox proportional hazards analysis.

Results: Of the 105 patients with IIMs, relapse was observed in 65 patients (62%). The titer of an antinuclear antibody (ANA) was higher in the relapse group than in the non-relapse group (P = 0.033). In multivariable analysis, three factors were associated with the relapse of IIMs: histopathologic features consistent with IIMs (model 1; HR, 1.69; 95% CI, 1.01-2.83, P = 0.0453) and the use of immunosuppressants before relapse (model 2; HR, 0.50; 95% CI, 0.29-0.86, P = 0.0132). Doubling of ANA titer showed a trend toward an association with relapse albeit without statistical significance (model 1; HR, 1.13; 95% CI, 1.00-1.27, P = 0.0517).

Conclusion: The use of immunosuppressants during a period of tapering glucocorticoid in the initial treatment would help reduce the risk of relapse of IIMs.

Table 1. Factors associated with the relapse of Idiopathic inflammatory myopathies in univariate and multivariable analyses.

	Model 1			Model 2			Model 3		
Factors	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*
Histopathologic features consistent with IIMs	1.69	1.01-2.83	0.0453	1.59	0.95-2.67	0.0791	1.59	0.95-2.67	0.0791
ANA titer[a] (reference: ANA negative)	1.13	1.00-1.27	0.0517	1.10	0.98-1.25	0.1135	1.10	0.98-1.25	0.1135
Immunosuppressant before relapse				0.50	0.29-0.86	0.0132	0.50	0.29-0.86	0.0132

Model 1: adjusted for factors at baseline Model 2: adjusted for factors at baseline and treatments Model 3: adjusted for factors at baseline, treatments, and follow-up laboratory findings[a] doubling titer starting from 1:40

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AB0873 WHOLE BODY INSULIN SENSITIVITY IS INCREASED IN SYSTEMIC SCLEROSIS

Keywords: Diet and Nutrition, Cardiovascular disease, Systemic sclerosis

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Background: The prevalence of type 2 diabetes (T2D) is increased in rheumatoid arthritis (RA) and other inflammatory diseases, while the available evidence suggests that in systemic sclerosis (SSc) it is lower than in the general population [1]. Insulin resistance and ß-cell dysfunction are the main mechanisms in the pathophysiology of T2D. However, mechanisms underlying the negative association between SSc and T2D have not been elucidated.

Objectives: We aimed to evaluate whole-body insulin sensitivity in SSc patients and to compare the results with controls with no autoimmune rheumatic disease (non-ARD) and with patients affected by RA. Additionally, we investigated whether insulin sensitivity was associated with SSc characteristics.

Methods: The study population was composed of consecutive adult SSc patients. For comparison, non-ARD and RA patients were included. All were screened for T2D before inclusion. Individuals with a diagnosis of diabetes and those using corticosteroids or insulin-sensitizing agents were excluded. The whole-body insulin sensitivity index (ISI) was estimated from glucose and insulin concentrations obtained during the oral glucose tolerance test (OGTT) using the equation proposed by Matsuda [2], which is validated against euglycemic insulin clamp and provides reliable estimates of glucose homeostasis. Insulin resistance (HOMA-IR) was calculated.

Results: A total of 41 SSc patients, 41 individuals with RA and 82 non-ARD control patients were recruited. SSc patients were significantly older and had lower BMI than controls with RA, but had comparable characteristics with non-ARD patients (Table 1). The ISI was significantly higher in SSc patients compared with RA controls [8.01 (4.85 – 12.62) vs 3.39 (1.93 – 6.14), p <0.001] and with non-ARD patients [8.01 (4.85 – 12.62) vs 4.38 (3.39 – 6.37), p <0.001]. Significant differences emerged also when analysing the HOMA-IR, which was lower in SSc patients than in RA [0.98 (0.66 – 1.52) vs 2.02 (1.36 – 3.63), p <0.001] and non-ARD [0.98 (0.66 – 1.52) vs 1.74 (1.28 – 2.28), p <0.001]. In normal weight individuals (BMI from 18.5 to 24.9), median ISI was higher in the SSc group than in RA (p =0.007) and non-ARD controls (p <0.001). In overweight and obese cases (BMI ≥25) ISI was also higher in the SSc group than in RA (p =0.003) and non-ARD controls (p =0.017) (Figure 1). In the SSc group, patients with diffuse cutaneous disease had significantly higher ISI than individuals with limited cutaneous SSc [11.60 (8.59 – 20.13) vs 6.58 (4.91 – 11.63), p = 0.027]. In univariate analysis, ISI was significantly correlated with BMI (rho= -0.468, p= 0.002), fasting insulin (rho= -0.715, p <0.001), and modified Rodnan skin score (rho= 0.422, p= 0.006. In multiple linear regression model adjusted for BMI and fasting plasma insulin, the association between ISI and modified Rodnan skin score was lost (r^2 = 0.27, p= 0.095).

Conclusion: The findings of our study suggest that patients with SSc are more insulin sensitive than those with RA and even than individuals without inflammatory diseases. This is the first time that whole-body insulin sensitivity is assessed in SSc using a validated and reliable method, contributing unique data to the knowledge about glucose homeostasis in SSc.

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Table 1. Characteristics of patients and glucose metabolism in SSc and controls.

	SSc (n=41) [a]	RA (n=41) [b]	Non-ARD (n=82) [c]	p-value
Female, n (%)	34 (82.9)	27 (65.9)	65 (79.3)	0.077 [ab] 0.629 [ac]
Age, years	59.4 ± 13.1	53.8 ± 11.4	58.3 ± 8.4	0.041 [ab] 0.546 [ac]
BMI, kg/m^2	24.0 ± 3.4	27.8 ± 6.5	24.3 ± 2.2	0.002 [ab] 0.559 [ac]
ISI	8.01 (4.85 – 12.62)	3.39 (1.93 – 6.14)	4.38 (3.39 – 6.37)	< 0.001 [ab] < 0.001 [ac]
HOMA-IR	0.98 (0.66 – 1.52)	2.02 (1.36 – 3.63)	1.74 (1.28 – 2.28)	< 0.001 [ab] < 0.001 [ac]

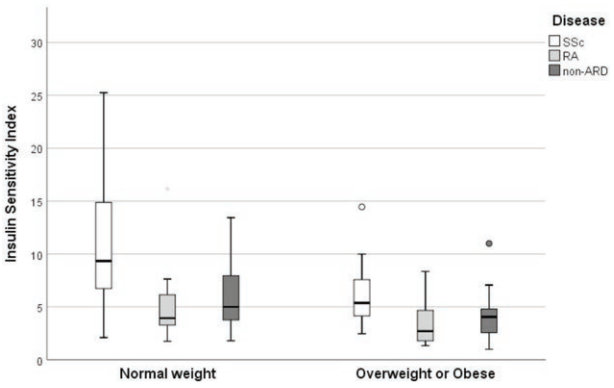


Figure 1. Insulin sensitivity stratified according to BMI

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Disclosure of Interests: None Declared.

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AB0874

EPIDEMIOLOGY AND CLINICAL FEATURES OF IDIOPATHIC INFLAMMATORY MYOPATHIES IN SINGLE REGION IN NORTHERN SPAIN

Keywords: Descriptive Studies, Myositis, Epidemiology

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Background: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of disorders characterized by proximal muscle weakness and inflammation. The main subtypes of IIM are dermatomyositis (DM), polymyositis (PM), inclusion body myositis (IBM), immune-mediated necrotizing myopathy (IMNM) and antisynthetase syndrome (ASS). Prevalence and incidence vary depending on the geographic location.

Objectives: To describe the epidemiological and clinical features of IIM in a single region in northern Spain.

Methods: We included all consecutive patients diagnosed with IIM in the region of Cantabria, excluding IBM, from January 2000 to December 2022. IIM was diagnosed by expert rheumatologists according to **a)** EULAR/ACR 2017 classification criteria of IIM in PM and DM, **b)** Definition of the European Neuromuscular International Workshop 2016 in IMNM and **c)** Connor's criteria in ASS.

Table 1. Main demographic, clinical features, laboratory findings and treatments in 63 patients diagnosed with IIM.

	Dermatomyositis (n=34)	Polymyositis (n=5)	Immune-mediated Necrotizing Myopathy (n=9)	Antisynthetase Syndrome (n=15)		DM (n=34)	PM (n=5)	IMNM (n=9)	ASS (n=15)
Age at diagnosis (years), mean ± SD	53.9 ± 18.6. (*) DMJ 5.5 ± 1.7	54.8 ± 11.6	64.5 ± 7	52.7 ± 11.7	**LDH mg/dl, mean ± SD**	489.5 ± 223.7	1360 ± 992.7	654 ± 258	343.6 ± 151.2
Sex (women), n (%)	26 (76.5)	3 (60)	6 (66.7)	9 (60)	**AntiJo1/Mi2/MDA5, n (%)**	1 (2.9)/1 (2.9)/3 (8.8)	2 (40)/0/ 0	0	4 (26.7)/ 0/ 0
Dyslipidemia, n (%)	10 (29.4)	2 (40)	9 (100)	4 (26.7)	**PL7/PL12/EJ, n (%)**	0/0/1 (2.9)	0	0	7 (46.7)/ 4 (26.7)/ 0
Hypertension, n (%)	9 (26.5)	1 (20)	7 (77.8)	1 (6.66)	**HMGCR/ Ro52, n (%)**	0/3 (8.8)	0	9 (100)/ 0	0/ 8 (53.3)
Diabetes Mellitus, n (%)	4 (11.8)	.	7 (77.8)	.	**Edema/Atrophy RMI, n (%)**	12 (100)/ 2 (16.7)	2 (100)/ 0	5 (55.6)/ 3 (33.3)	1(11.1)/ 0
Cancer, n (%)	6 (17.7)	.	.	.	**Oral/ Intravenous Corticosteroids, n (%)**	34 (100)/ 18 (52.9)	5 (100)/ 1 (20)	7 (77.8)/ 3 (33.3)	15 (100)/ 5 (33.3)
Muscle weakness, n (%)	26 (76.5)	3 (60)	9 (100)	3 (20)	**Methotrexate/ Azathioprine, n (%)**	15 (44.1)/ 15 (44.1)	2 (40)/ 4 (80)	3 (33.3)/ 3 (33.3)	2 (13.3)/ 8 (53.3)
Myalgia, n (%)	11 (32.4)	2 (40)	4 (44.4)	4 (26.7)	**Mycophenolate/ Cyclophosphamide n (%)**	4 (11.8)// 4 (11.8)	0/ 1 (20)	.	9 (60)/ 4 (26.7)
Gottron papule/ Sign/Heliothrope rash, n (%)	27 (79.4)/25 (73.5)/11(32.3)	.	.	1 (6.7)/./.	**Calcineurin Inhibitors, n (%)**	5 (14.7)/ 4 (11.8)	.	.	2 (13.3)
Arthritis/ Raynaud, n (%)	9 (26.5)/ 3 (8.8)	1 (20)/ 1 (20)	.	4 (26.7)/ 9 (60)	**Hydroxychloroquine, n (%)**	15 (44.1)	.	.	3 (20)
Interstitial Lung Disease, n (%)	5 (14.7)	2 (40)	.	14 (93,3)	**Intravenous Immunoglobulins, n (%)**	21 (61.8)	1 (20)	6 (66.7)	1 (6.7)
Dysphagia/ Calcinosis, n (%)	15 (44.1)/ 6 (17.6)	.	3 (33.3)/.	2 (13.3)/.	**Rituximab, n (%)**	13 (38.2)	1 (20)	3 (33.3)	12 (80)
Creatin-Kinase (UI/L), median [IQR]	533 [226.5-1325.5]	3360 [3158-4100]	4977 [3273-9271]	57 [35-550]					

Data regarding demographics features, clinical findings, laboratory tests and treatments were extracted from the patients' clinical records.
Results: We included a total of 63 patients, mean age at diagnosis 52.1±19.3 years. Most of the patients were women (n=44, 69.8%). Main features are shown in **TABLE 1**. Prevalence of IIM was 10.8/100.000 population. The incidence rate was 4.9 cases per million persons per year. An upward trend in annual incidence was observed from 1.7 in 2000 to 15.4 per million in 2018 **(FIGURE 1)**. The most common IIM subtype was DM (n=34, 54%). Gottron papules, muscle weakness and Interstitial lung disease were the most frequent manifestations in DM, IMNM and ASS group, respectively. The most frequent autoantibody was anti-Ro 52 (n=12, 19%), however in 28 patients (44.4%) none was detected. Most used treatments were glucocorticoids (n=61, 96.8%), azathioprine (n=30, 47.6%), intravenous immunoglobulins (n=29, 46%) and rituximab (n=29, 46%).
Conclusion: We describe the prevalence, incidence rate, clinical features and main treatments used in IIM in our area. An upward trend in annual incidence was observed in our study.

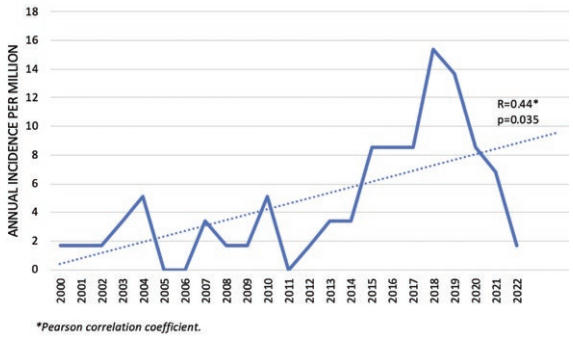


Figure 1. Annual incidence of IIM from 2000 to 2022.

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AB0875 CANCER, DYSPHAGIA, AND HEART INVOLVEMENT IN PATIENTS WITH INFLAMMATORY MYOSITIS AND INTERSTITIAL LUNG DISEASE

Keywords: Lungs, Heart, Myositis

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Background: Interstitial lung disease (ILD) is a leading cause of morbidity and mortality in patients with inflammatory myositis (IIM) [1]. The risk of ILD is higher with myositis-specific (MSA, e.g. antisynthetase, MDA5) and -associated antibodies (MAA, e.g. Ro52) [2], while negatively associated to malignancy [3]. IIM specific clinical phenotypes and ILD are treated with glucocorticoids, mycophenolate mofetil or rituximab (4), and characterizing IIM organ involvement is a major task to optimize diagnostic and therapeutic choices. In particular, cardiomyopathy is emerging as a leading cause of morbidity in IIM [5].
Objectives: To assess the demographic, clinical, and serological features of patients with IIM-associated ILD.
Methods: We retrospectively analyzed clinical data of 73 patients with IIM followed at our center in 2015-2022; sera were analyzed for autoantibodies (ANA-HEp-2 IFA; ENA; MSA/MAA and anti-E2/E3 PDH by immunoprecipitation) as per protocol. ILD was defined by positive high-resolution computed tomography (CT) scan; heart magnetic resonance imaging (MRI) was performed when symptoms, ECG, or echocardiographic alterations were present.
Results: ILD was detected by high-resolution CT scan in 33/73 (45%) patients (Table 1), with no significant differences in terms of age, sex, and smoking history. Serum ANA were detected in 60/73 (82%) patients, with no difference between ILD and no-ILD groups. Arthritis was more frequent in patients with ILD; there was no difference in terms of muscle damage, skin lesions (heliotrope rash, Gottron's papules, periungeual erythema), and Raynaud's phenomenon according to the presence of ILD. Dysphagia and heart disease at MRI were more prevalent in patients with ILD. Patients with ILD also had lower prevalence of malignancy. Anti-Ro52 and antisynthetase antibodies were significantly associated with ILD. Anti-MJ/NXP2 antibodies were observed only in the group without ILD, but such association was not statistically significant. The prevalence of anti-TIF-1gamma antibodies did not differ between the two groups; 3/5 (60%) patients in the group without ILD developed malignancy vs only 1/4 (25%) in patients with ILD.
Conclusion: There is a higher prevalence of dysphagia and heart involvement in patients with IIM and ILD, a highly prevalent manifestations of IIM, thus suggesting dedicated therapeutic strategies. ILD correlates with antisynthetase and -Ro52 positivity, with a negative association with malignancy, particularly in anti-TIF1gamma positive patients.
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Table 1. Main features of patients with and without ILD and inflammatory myositis.

		Total (N=73)	With ILD (N=33)	Without ILD (N=40)	p
Demographic	Age [mean (SD)]	51 (17)	51 (17)	50 (18)	.8110
	Female (%)	57 (78)	27 (81.8)	30 (75)	.4876
	Smoke (%)	32 (44)	16 (48.5)	16 (40)	.4694
	Malignancy (%)	18 (25)	4 (12.1)	14 (35)	**.0248**
	Overlap autoimmune (%)	18 (25)	6 (18.2)	12 (30)	.2477
Clinical	Myositis (%)	57 (78)	24 (72.7)	33 (82.5)	.3172
	Dysphagia (%)	17 (23)	11 (33.3)	6 (15)	*.0674*
	Skin (%)	53 (73)	26 (78.8)	27 (67.5)	.2846
	Gottron (%)	25 (34)	8 (24.2)	17 (42.5)	.1034
	Raynaud (%)	29 (40)	16 (48.5)	13 (32.5)	.1673
	Arthritis (%)	23 (32)	15 (45.5)	8 (20)	**.0205**
	Cardiomyopathy (%)	8 (11)	6 (18.2)	2 (5)	*.0744*
Serology	ANA (%)	60 (82)	27 (81.8)	33 (82.5)	.9384
	Ro52 (%)	15 (21)	13 (39.4)	2 (5)	**.0003**
	Antisynthetase (%)	15 (21)	13 (39.4)	2 (5)	**.0003**
	TIF1gamma (%)	9 (12)	4 (12.1)	5 (12.5)	.9590
	NXP2 (%)	4 (5)	0 (0)	4 (10)	*.0635*

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AB0876 IMPACT OF AUTOANTIBODY PROFILE ON FUTURE ORGAN INVOLVEMENT IN SYSTEMIC SCLEROSIS: DISEASE FREE SURVIVAL IN DIFFERENT PATIENT GROUPS

Keywords: Systemic sclerosis, Autoantibodies

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Background: Some specific autoantibodies were known to be associated with cutaneous subtype, type of organ involvement and prognosis in systemic sclerosis (SSc).
Objectives: The aim of our study was to evaluate the impact of autoantibody profile on the course of SSc regarding new organ involvement over time.
Methods: The data of 206 consequitive patients (189 women) with SSc who were followed up at least 12 months were retrospectively analyzed. Associations between the autoantibodies (anti-nuclear antibody (ANA) (27.7%, n=57), anti-Scl70 (47.1%, n=97) and anti-centromere (ACA) (22.3%, n=46)) and disease-free survival (without new organ involvement) were evaluated in SSc patients with a mean follow-up time of 101.26±71.02 months.
Results: Anti-Scl70 was associated with diffuse cutaneous disease involvement, digital ulcers, arrhythmia, and interstitial lung disease (ILD) (OR:3.43, p<0.001, OR:1.835, p=0.033, OR:4.06, p=0.038 and OR:2.393, p=0.006, respectively). ACA was associated with PAH (OR:3.319, p=0.040) and protective against diffuse skin involvement, flexion contractures and ILD (OR:0.203, p=0.001,

OR:0.251, p=0.012 and OR:0.288, p=0.008, respectively). In ACA (+) group, new organ involvement was observed less frequently (HR: 0.523 (95% CI (0.29-0.94), p=0.030) and after a longer time period when compred to ACA (-) group (82.65±14.5 vs 53.98±5.49 months, p=0.026). At the 5th and 8th years of the follow-up, half of the ACA(+) patients did not develop new organ involvement. In the ACA(-)[(ANA(+) or antiScl70(+)] group, new organ involvement was detected in >67% within 5 years and in >80% within 8 years (figure-1, table-1).

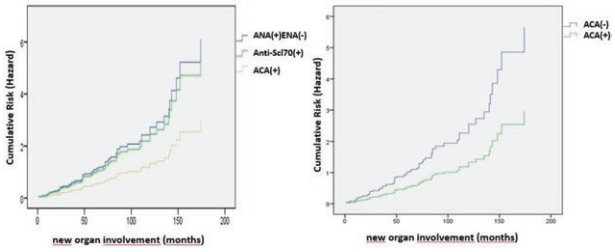


Figure 1. Cumulative risk of the new organ involvement for different systemic sclerosis patient groups according to autoantibody profile over time.

Table-1 Time to New Organ Involvement and Disease-Free Survival according to Autoantibody Profile in SSc Patients

	Time to New Organ Involvement		Disease-Free Survival without New Organ Involvement		
	Mean (months)	CI 95%	2.year	5.year	8.year
ACA(+) (n=17)	82,65±14,5	54,25±111,1	%76.5(±10.3)	%52.9(±12.1)	%47.1(±12.1)
ANA(+)-ENA(-) (n=18)*	52,06±9,31	33,82±70,29	% 61.1(±11.5)	%33.3(±11.1)	%16.7(±8.8)
Anti-scl70(+) (n=36)	54,95±6,88	41,45±68,44	%72.2(±7.5)	%38.9(±8.1)	%16.7(±6.2)
*ACA(-)(n=54)^*	*53,98±5,49*	*43,22±64,75*	*%68.5 (±6.3)*	*%37.0 (±6.6)*	*%11.1 (±4.3)*

* p=0,026, ^p=0,026 compared to ACA(+) patients, Log Rank (Mantel-Cox)test

Conclusion: Although ACA(+) patients are considered to have a better prognosis, some patients may develop new or worsening manifestations after a longer time period. The prognosis of ANA or anti-Scl70(+) patients was shown to be more severe and most patients had new organ involvement within the first 5 years of the disease, warranting a careful evaluation and efficacious treatment at this period.

REFERENCES: NIL.

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Disclosure of Interests: None Declared.

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AB0877 TARGETING VASCULOPATHY TO SLOW FIBROSIS IN SYSTEMIC SCLEROSIS (SSC): DESIGN OF A PHASE II STUDY WITH A SOLUBLE GUANYLATE CYCLASE ACTIVATOR (SGCA)

Keywords: Systemic sclerosis, Biomarkers, Randomized control trial

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Background: The pathophysiology of SSc involves a complex interplay between immune dysfunction, vasculopathy, and fibrosis. The soluble guanylate cyclase (sGC) pathway has been shown to improve vascular endothelial function. We designed a Phase II study to test whether treatment of vasculopathy with an sGCa could slow the progression of fibrosis in patients with early progressive SSc and vasculopathy.

Objectives: To design a randomized, double-blind, placebo-controlled trial to evaluate the progression of fibrosis in patients with SSc treated with an sGCa.

Methods: We reviewed criteria used in published clinical trials to define early progressive disease, as well as clinical and biomarker features from existing studies and registries that are predictive of more rapid progression of fibrosis [1, 2]. Specifically, we looked for features of vasculopathy associated with progression of skin and lung fibrosis [3]. We performed a rigorous review of investigator- and patient-reported outcomes to test the hypothesis that amelioration of vascular symptoms could slow the progression of fibrosis in patients with SSc.

Results: Progressive disease was defined as having diffuse cutaneous SSc with evidence of active disease as defined by clinical and biomarker criteria. The clinical criteria were similar to those used in previous trials, but we developed a novel biomarker strategy using KL-6 in addition to C-reactive protein (CRP) and erythrocyte sedimentation rate. These biomarkers identify additional patients at risk for progressive lung fibrosis. Significant vasculopathy was defined as having digital ulcers or a history of digital ulcers and/or Raynaud's phenomenon requiring medical treatment or associated with elevated CRP. We developed a hierarchy of primary, key secondary, and secondary endpoints, including forced vital capacity, modified Rodnan skin score, revised Composite Response Index in Systemic Sclerosis, Health Assessment Questionnaire-Disability Index, digital ulcer burden, and Raynaud's symptom scoring, to investigate whether amelioration of vascular symptoms could slow decline in lung function over 48 weeks and reduce the progression of skin fibrosis and other disabilities associated with SSc. We determined that a sample size of 100 patients was sufficient to obtain 80% power to observe changes in lung and skin fibrosis.

Conclusion: We designed a 48-week randomized, double-blind, placebo-controlled Phase II trial enrolling 200 patients with early progressive SSc and significant vasculopathy to test whether targeting vasculopathy with a novel sGCa can slow the progression of fibrosis in patients with SSc. The trial is now active, and additional details are available at NCT05559580.

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AB0878 SAFETY AND EFFICACY OF MESENCHYMAL STEM CELLS TRANSPLANTATION IN SYSTEMIC SCLEROSIS

Keywords: Safety, Systemic sclerosis, Clinical Trials

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease characterised by vasculopathy and tissue fibrosis of the skin and various internal organs. Currently available treatments for SSc have limited efficacy, and the disease still has poor prognosis. New therapeutic approaches such as mesenchymal stem cell (MSC) transplantation are of great interest. MSCs are known as multi-potent progenitor stromal cells that self-renew and differentiate toward multiple mesenchymal cell lineages [1, 2].

Objectives: to evaluate the efficacy and safety of bone marrow MSCs transplantation in SSc.

Methods: Twenty-five patients with a reliable diagnosis of SSc refractory to classical immunosuppressive therapy were divided between main and control group. Patients from the main group underwent transplantation of MSCs in combination with high-dose immunosuppressive therapy (HIST) (n=14), while the control group was observed on the background of traditional immunosuppressive therapy without cell transplantation (n=11). Both groups were comparable in age, gender

of patients, duration and severity of the disease. The degree of induration of the skin was evaluated using the modified Rodnan skin score (mRSS). The disease activity was assessed using the EScSG scale. Anti-nuclear antibodies (ANA), anti-SCL-70 were examined by indirect immunofluorescence, cytokines (IL-1B, IL-6, IL-10, TNF-α) - by ELISA. All patients underwent CT scan of the thoracic segment, echocardiography with determination of mean pulmonary artery pressure (mPAP) and spirography. Statistical analysis was carried out by GraphPad Prism version 8.
Results: Before MSC transplantation, SSc patients in both groups demonstrated an increase in ANA, C-reactive protein (CRP), IL-1, IL-6, TNFα, with the background of severe skin induration. After transplantation of MSCs with HIST a pronounced clinical effect was noted: induration and dense swelling of skin, muscle contractures, vasospasm attacks (Raynaud syndrome) significantly decreased, dysphagia was relieved. In addition, a significant decline in skin density according to mRSS was observed (from 22.13±2, 52 to 9.8±0.93, p=0.03). A significant reduction in EScSG was registered from 3.21 to 2.48 points (p=0.05). Six months after transplantation patients with SSc demonstrated a decrease in CRP from 10.14±2.01 to 3.28±1.31. Parameters of the cytokine profile with a moderate decrease for IL-1, IL-6 and TNFα (p<0.05). According to the results obtained patients who underwent BM-MSCs transplantation demonstrated 54% decrease in mPAP, from 41.4 ± 10.87 to 26.8 ± 3.27. In SSc patients in the control group high levels of cytokines, mRSS, and mPAP were recorded during the observation period. No cases of death or severe complications associated with MSCs transplantation with HIST have been registered.
Conclusion: The conducted research demonstrated the therapeutic effect of MSC transplantation consisted in the decrease of the induration of skin, the activity of SSc and the severity of pulmonary hypertension, as well as normalizing the levels of proinflammatory cytokines.
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AB0879 SAFETY AND EFFECTIVENESS OF RITUXIMAB TREATMENT FOR SYSTEMIC SCLEROSIS: AN UPDATE OF OUR CLINICAL EXPERIENCE

Keywords: bDMARD, Systemic sclerosis

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Background: The treatment of systemic sclerosis-SSc is challenging because of its complex pathogenesis. Data on Rituximab-RTX use in SSc are still conflicting but information from case reports or non-randomized clinical trials are somehow promising.
Objectives: According to our previous experience, we newly evaluated the safety and effectiveness of rituximab (RTX) in systemic sclerosis (SSc) patients. In addition, we compared the efficacy of RTX taken alone or in combination with Mycophenolate mofetil (MMF).
Methods: We collected data from 43 SSc subjects referred to the Scleroderma Units of Modena and Reggio Emilia (M/F 10/33, age 54,19±13,75SD years, disease duration 10,5±6,56SD years, lc/dcSSc 19/24). Our patients were treated with RTX (4 weekly/infusions/375 mg/m^2) between January 2004 and January 2022. The main indications to RTX treatment were: interstitial lung disease, skin fibrosis, and/or articular involvement unresponsive to previous therapies. Clinical information and blood exams were evaluated before (T0), 6 months (T1), and 12 months (T2) after RTX administration. Pulmonary function tests-PFTs, high-resolution computed tomography-HRCT of the lungs, and echocardiogram were performed at T0 and T2.
Results: The extent of skin sclerosis measured by means of modified Rodnan skin score-mRSS decreased from 14,83±10,37SD at T0 to 11,56±7,91SD at T2, and this result was more evident in diffuse cutaneous subsets. Melanodermia and skin tightening significantly improved during follow-up (p<0.0001). Arthritis revealed a good response too leading to a marked reduction of swollen/tender joints (p<0.0001). HAQ and NRS scores also showed a significant amelioration from T0 to T2 (p<0.0001). Inflammatory indices (ESR and CRP) normalized in almost all subjects (p<0.0001). Lung fibrosis at chest-CT remained stable during the entire follow-up. DLCO % improving was more evident in patients with combination RTX+MMF (p<0.0001). No pulmonary arterial hypertension-PAH progression was observed in subjects with a previous diagnosis, while no patient presented a new diagnosis of PAH. No significant side effects were observed.
Conclusion: Our results further support the effectiveness and safety of RTX in the treatment of SSc patients. The improvement of skin sclerosis, arthritis, and pulmonary function were the main results. The role of the association RTX-+MMF is intriguing for the preliminary correlations with SSc cardio-pulmonary involvement. Immunomodulatory therapies are successful and encouraging in the management of SSc, and the correct positioning of these drugs is worthy of further investigations.
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AB0880 CORRELATION BETWEEN THE RESULTS OF NAIL FOLD CAPILLAROSCOPY AND OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Diagnostic Tests

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Background: Vasculopathy of blood vessels are, apart from immunological disorders, an important.
common pathogenetic link of dangerous organ complications in systemic sclerosis (SSc). Endothelial damage is one of the mechanisms leading to disorders of vascular hemostasis, platelet activation, thrombosis causing coagulopathy and microangiopathy. Nailfold capillaroscopy (NC) is a non-invasive diagnostic tool for the detection and monitoring patients with SSc and current methods of the assessment of microcirculation and capillary structure within the nail folds. Although vascular pathologies can occur in other organs including the organ of vision. Optical coherence tomography angiography (OCT A) is a noninvasive imaging method of microvasculature of the retina and choroid providing the assessment of retinal perfusion.
Objectives: The aim of the study was to evaluate the correlation between the optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) parameters and capillaroscopic results.
Objectives: The aim of the study was to evaluate the correlation between the optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) parameters and capillaroscopic results.
Methods: 31 patients (pts) with SSc diagnosed were included to the study. Mean age of the patients was 35,1 (8,3). Capillaroscopy was performed. The modified Rodnan Skin Score (mRSS) examination was taken by one assessor at the time of the study. There were measured HRCT, proBNP. echocardiography. Finger ulcers were observed in physical examination. OCTA scans were collected from 31 patients. 61 eyes were included to the study to assess changes in retinal microcirculation. Foveal avascular zone (FAZ) in superficial plexus and deep plexus, parafoveal mean superficial vessel density and parafoveal mean deep vessel density were correlated to NF findings and other parameters used in rheumatic examination. All the statistical procedures were performed by using STATGRAPHICS Centurion, version 19.4 (Statgraphics Technologies, Inc., The Plains, Virginia, USA).
Results: In our study group 74 % has diffuse Scc, 26% has limited SSc. InNC: 5 pts has early pattern, 12 has active pattern,9 pts has late pattern. Only one person has pulmonary arterial hypertension (PAH) and 8 pts have active finger ulcers. Interstitial lung disease was observed in 12 pts. (67% has non-specific interstitial pneumonia (NSIP) and 33% usual interstitial pneumonia (UIP)). Elevated proBNP were detect in 17,8% The parafoveal mean superficial vessel density correlated positively and statistically significantly with mRSS (p=0,0460). Patients with early scleroderma pattern in capillaroscopy showed larger superficial FAZ (0,4± 0,07 mm^2) than pts with active (0,24 ± 0,09 mm^2) and late (0,22 ±0,09 mm^2). There was correlation between deep FAZ area and scleroderma pattern showing larger FAZ in pts with active (0,46±0,14 mm^2) than pts with active

(0,2 ±0,12 mm^2) and late (0,17±0,13 mm^2). Statistically significant difference was found between interstitial lung disease NSIP and UIP in correlation with deep FAZ area. Pts with NSIP had larger FAZ (0,32 ±0,14 mm^2) than UIP pts (0,17 ±0,12 mm^2). Moreover, NSIP pts had higher parafoveal mean superficial vessel density (42,21% ±1,69) than UIP (39,89 ±1,23). NSIP pts had also higher mean parafoveal deep vessel density (43,58 ±1,5 %) than UIP pts (41,72 ±1,55 %).

Conclusion: In conclusion, our findings indicate ocular vascular abnormalities in patient with SSc. The results show the important role of OCTA in diagnosis, monitoring and prognosis of microvascular changes in SSc. Moreover, NF correlate with FAZ.

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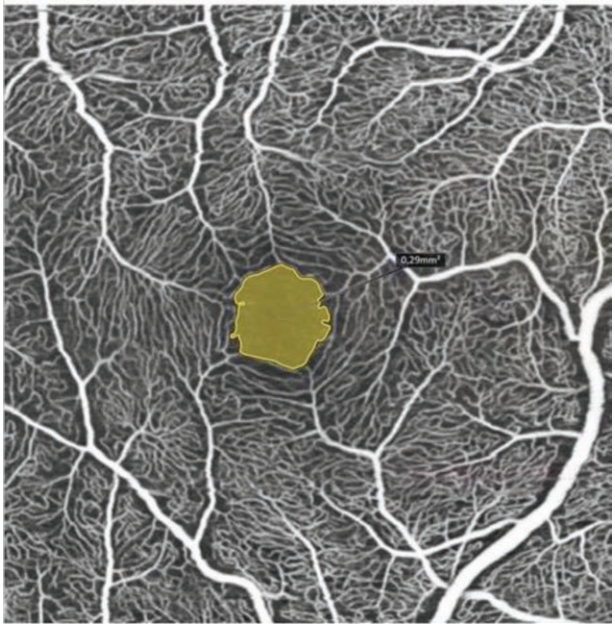


Figure 1. OCTA image of foveal avascular zone area in the right eye of the patient with systemic sclerosis.

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AB0881 CLINICAL TRAJECTORIES OF MULTIFACTORIAL HAND FUNCTION DETERIORATION IN SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Patient reported outcomes, Clinical Trials

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Background: Hand function deterioration is a major multifactorial driver of disability in Systemic Sclerosis (SSc) whose rate has been poorly described.

Objectives: The aim of this study is to describe incidence and risk factors of hand functional worsening in a longitudinal, multicenter, observational SSc cohort.

Methods: Hand involvement and disability were evaluated in consecutively enrolled patients for 24 months. Patient-reported hand impairment was captured with Cochin Hand Disability Score (CHFS) and the corresponding minimal clinical important differences (MCID) and patient acceptable symptom state (PASS). Clinical association with CHFS change over time and clinically meaningful worsening (MCID-Worsening) were investigated.

Results: Three-hundred-ninety-six patients from 10 centres were evaluated and 201 SSc (age 55.7±12.2 years, male 13.4%) were included in the final analysis. Median (IQR) disease duration was 5 (2-11) years while the proportion of patients with diffuse cutaneous variant was the 29.9%. Fifty-six (27.8%) patients had a CHFS ≥PASS at baseline. CHFS increased over time 35.8% of patients reaching CHFS≥PASS ($p<0.001$), and 52.2% of patients reporting MCID-Worsening at 24 months. A LASSO model simultaneously exploring the effects of multiple baseline clinical variables showed that MCID-Worsening was associated with male gender, LeRoy diffuse variant, late capillaroscopy pattern, shorter disease duration, absence of digital ulcers, presence of tenosynovitis, pain, Raynaud's phenomenon, and global and hand disability severity, together with treatment with immunosuppressants, vasoactive medications, and second-line analgesics.

Conclusion: Hand function tends to deteriorate over time in one SSc patient in two despite available therapies and clinical assessment support risk stratification. These results pave the way to inform design of intervention studies aimed at improving the outcome of this major driver of disability in SSc.

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AB0882 ADVANCED GLYCATION END PRODUCTS IN SYSTEMIC SCLEROSIS

Keywords: Prognostic factors, Organ damage, Biomarkers

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Background: Studies have postulated that advanced glycation end products (AGEs) could have a relevant role as inducers in the chronic inflammatory pathway present in various diseases -- including systemic sclerosis (SSc). Similarly, that the concentration of AGEs maybe related to nailfold capillaroscopy SSc changes, the diffuse skin subtype, or calcinosis. Validation studies have shown that skin autofluorescence is strongly related to AGEs levels in skin biopsies.

Objectives: To characterize and identify association between the concentrations of AGEs, measured by cutaneous autofluorescence, and disease parameters in SSc patients.

Methods: AGEs concentrations were measured by skin autofluorescence (Age Reader Mu Connect from Diagnostics Technologies BV®) in 179 SSc patients and correlated with demographic and clinical data. Cumulated AGEs were distributed in tertiles. Categorical data was described with frequencies, whereas continuous variables were displayed as mean (standard deviation). ANOVA tests were conducted to explore the linear association of demographics and clinical features with the cumulated AGEs value. Regression models were adjusted by age (M1), and also by smoking status (M2 = M1 + smoker).

Results: Table 1 shows the distribution and correlation of the most relevant patients characteristics studied according to AGEs levels classified in tertiles. Male gender (p-value M1=0.008, M2=0.003) and anticentromere antibodies (ACA) (p-value M1=0.010, M2=0.034) were statistically significant associated with higher AGEs levels. In addition, AGEs levels were inversely correlated with obesity as a categorical variable with statistical significance (p-value M1=0.036, M2=0.022). Although not statistically significant, there was a trend towards higher values of AGES (p-value 0.05 - 0.1) in patients with esophageal involvement and skin manifestations (either diffuse or limited cutaneous subtype) and lower prevalence of anti-topoisomerase antibodies (ATA). No associations with other characteristics were found.

Conclusion: Higher AGEs levels were independently associated to male gender, ACA positivity and inversely with obesity. AGEs might be involved in the

aethiopathological pathways leading to skin and esophageal manifestations. Finally, the disease mechanism in obese SSc patients might indicate a milder disease, as they present lower AGEs values, opposing to what has been described in healthy subjects. This could indicate less severe gastrointestinal disease leading to malnourishment.

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Table 1. Correlations of our cohort characteristics according to advanced glycation end products levels. c: categorized; M1: adjusted for age; M2 adjusted for age and tobacco. BMI: body mass index. * Not adjusted age. Bold indicates statistically significant differences (p<0.05).

	All	First tertile [1.4,2.4)	Second tertile [2.4,2.9]	Third tertile [2.9,6.7]	p-value M1	p-value M2
	N=179	*N=60*	*N=62*	*N=57*		
Gender (Male)	17 (9.5%)	4 (6.7%)	5 (8%)	8 (14%)	**0.008**	**0.003**
Age	61.0 (12.6)	55.7 (13.4)	61.7 (11.9)	65.8 (10.4)	**0.000***	
Smoking status	16 (8.94%)	2 (3.33%)	6 (9.68%)	8 (14.0%)	**0.031**	
Skin involvement	161 (89.9%)	50 (83.3%)	58 (93.5%)	53 (93.0%)	0.100	0.085
Esophageal involvement	155 (86,6)	49 (81,7%)	55 (88,7%)	51 (89,5%)	0.113	0.078
Anti-topoisomerase antibodies	21 (14.7%)	10 (20.4%)	6 (11.8%)	5 (11.6%)	0.076	0.071
Anti-centromere antibodies	70 (47.3%)	21 (41.2%)	26 (50.0%)	23 (51.1%)	**0.010**	**0.034**
Obesity	39 (21.8%)	15 (25.0%)	14 (22.6%)	10 (17.5%)	**0.036**	**0.022**
BMI	26.0 (5.42)	26.4 (6.20)	25.8 (4.91)	25.8 (5.13)	0.457	0.603
cBMI:					0.370	0.387
Healthy	84 (47.5%)	28 (46.7%)	29 (48.3%)	27 (47.4%)		
Overweight	66 (37.3%)	21 (35.0%)	22 (36.7%)	23 (40.4%)		
Obesity	27 (15.3%)	11 (18.3%)	9 (15.0%)	7 (12.3%)		

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AB0883 IDIOPATHIC OPHTHALMIC MYOSITIS: CLINICAL PRESENTATION, THERAPEUTIC APPROACH AND IMAGING DIFFERENTIATION FROM GRAVES OPHTHALMOPATHY

Keywords: Myositis

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Background: Idiopathic ophthalmic myositis (IOM) represents a rare autoimmune ophthalmoplegia of unknown etiology, that may mimic predominantly Graves' ophthalmopathy (GO). IOM is characterized by pronounced inflammatory infiltration of extraocular muscles leading to fibrosis and eye-threatening complications, if remains untreated [1,2]. The rarity and clinical heterogeneity of the disease pose diagnostic and therapeutic challenges.

Objectives: To describe the clinical phenotype, therapeutic interventions and clinical course of IOM and to define the distinct imaging features that differentiate IOM from GO.

Methods: This is a single-center, retrospective, observational study of 14 consecutive patients with IOM followed-up between 2017 and 2022. Cumulative clinical, laboratory and imaging data from the medical records until last follow-up were analyzed. The detailed orbital magnetic resonance (MRI) findings of 11 IOM patients were compared to those of 16 age- and sex-matched GO patients.

Results: IOM patients studied (men: 9/14, median age at disease onset: 46 years, median follow-up time: 15.5 months), presented subacute clinical course in 57%, whereas most common clinical manifestations were unilateral exophthalmos (79%), diplopia (71%), eyelid drop and/or swelling (50%). Extraocular muscle inflammation most commonly involved horizontal recti (median number of affected muscles: 2) and predominantly caused restrictive motility disturbance (71%). Anemia of chronic disease occurred in 36% of patients, however, erythrocyte sedimentation rate and c-reactive protein levels were found within normal limits. Myositis specific or other autoantibodies were not detected. Orbital MRI assessments revealed significantly more frequent occurrence of intraconal/extraconal fat edema (in at least one eye) in IOM patients (64.0%), compared to GO patients (25.0%, p-value 0.01). In addition, the abnormal contrast enhancement in extraocular muscles was present in 91.0% and 75.0% of IOM and GO patients, respectively, whereas tendon involvement was observed exclusively in IOM patients (18.2%). In all patients, the mainstay of therapy was steroids. IOM patients were treated with various combinations of corticosteroids and c-DMRD/b-DMRD (methotrexate, mycophenolate-mofetil, azathioprine, rituximab, tocilizumab), whereas GO patients mainly received corticosteroids with/or without tocilizumab.

Conclusion: IOM is a potentially severe organ-specific disease with heterogeneous clinical presentation. Early diagnosis and aggressive immunosuppressive treatment are required to prevent permanent eye-threatening complications. IOM should be considered in the differential diagnosis of exophthalmos, while MRI-imaging may help in differentiating IOM from GO. Studies are underway to delineate tissue-specific alterations of the inflamed extraocular muscles and involving larger series of patients.

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AB0884 THE IMPORTANCE OF RENAL IMPAIRMENT IN SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Kidneys

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Background: Systemic sclerosis (SS) is an autoimmune disease characterized by fibrosis and vascular abnormalities. Studies have shown that renal impairment is increased in SS, but this fact is neglected during diagnostic evaluation [1]. As a control group, patients with rheumatoid arthritis (RA) were selected because the renal involvement was as high as 9% although the kidneys were not the target organs in the disease [2]. Comparation of renal function (RF) between patients with SS and RA have not yet been described.

Objectives: The main goal was to detect correlation between clinical features and renal impairment in SS and to compare the renal impairment in patients with SS to patients with RA.

Methods: The 30 patients diagnosed with SS were included in the study. The demographics, modified Rodnan skin score (mRSS), EUSTAR DAI, diffusing capacity for carbon monoxide (DLCO) and immunology parameters were collected. Evaluation of RF was done by using: serum creatinine (SC), creatinine clearance (CC), proteinuria from 24h urine specimen and renal parenchym thickness (RPT) with abdominal ultrasound. To compare the renal impairment, the 30 patients diagnosed with RA without history of glomerulonephritis, diabetes mellitus, hypertension or urinary tract infection were enrolled as a control group.

Results: The 86.7% patients were female, mean age was 57.07±10.41 and mean disease duration was 73.6±68.73 months. Raynaud phenomen had 93.3% patients, digital ulcers (DU) 43.3% and the mean of mRSS was 21.43±9.5. Antinuclear antibodies had 83.3% patients, 46.7% had anti-Scl-70 antibodies and 43.3% had anticentromere B antibodies. The mean of EUSTAR DAI was 4.85±2.56 and DLCO 60.57±16.60. Regarding RF, the mean value of SC was 70.67µmol/l, CC 83.08 ml/min, proteinuria 0.17 g/l and RPT was reduced in 46.7% patients. We correlated clinical features with RF parameters in patients with SS. Significantly reduced RPT was observed in patients with higher mRSS (p=0.035) and in patents with DU (p=0.05). No association was observed between RF and other clinical features. Our results showed significant difference in all RF parameters, between patient and control group. SC (p=0.004) and proteinuria (p=0.03) were significantly higher in SS compared with RA. CC was significantly higher in RA than in patients with SS (p=0.005). RPT was significantly reduced (p=0.000) in SS compared to patients with RA. The results are displayed in Table 1.

Table 1. RF parameters in SS and RA group

	SS	RA	p
Gender F (%)	26 (86.7)	27 (90)	/
Age	57.07±10.41	50.07 ± 10.31	/
Serum creatinine	70.67 ± 17.77	59.87 ± 8.25	**0.040**
Creatinine clearance	83.08 ± 26.16	99.49 ± 16.59	**0.005**
Proteins/24h urine	0.17 ± 0.19	0.09 ± 0.05	**0.030**
Parenchymal thickness (%)	14 (46.7)	1 (3.3%)	**0.000**

RF-renal function; SS-systemic sclerosis; RA-rheumatoid arthritis

Conclusion: Presence of DU and high values of mRSS can be asocciated with renal damage and that indicates the need for evaluation of the RF. The renal impairment in our study was more significant in patients with SS than in those with RA. More studies are necessary to establish this correlation.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0885 HIGH RESOLUTION IMPEDANCE MANOMETRY IN DERMATOMYOSITIS ALLOWS THE CHARACTERIZATION OF ESOPHAGEAL DYSMOTILITY AND THE PROFILING OF DIFFERENT CLINICAL AND SEROLOGICAL SUBSETS

Keywords: Diagnostic Tests, Gastrointestinal tract, Myositis

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Background: Esophageal involvement is common in dermatomyositis (DM), occurring in up to 54% of patients [1]. It can lead to severe complications, such as malnutrition and aspiration pneumonia. Therefore, esophageal assessment is of foremost importance to drive patients management. Recently, high-resolution impedance manometry (HRiM) has emerged as a promising technique to assess esophageal motility and has already been tested in systemic sclerosis [2].

Objectives: To evaluate esophageal motility by HRiM in DM and correlate the alterations to clinical and serological disease domains.

Methods: We analyzed HRiM findings in 15 consecutive DM patients enrolled in our clinic between December 2021 and December 2022. All patients received a rheumatological assessment, including screening questions for dysphagia, and underwent HRiM. All HRiM parameters (Integrated relaxation pressure (IRP), percentage of LES relaxation, distal contractile integral (DCI), distal latency (DL), upper esophageal sphincter (UES) pressure) were studied, coupled with impedance findings (esophageal clearing and bolus transit time). The report followed the Chicago Classification v.4.0 for esophageal motility disorders. The associations between HRiM findings and DM features were evaluated.

Results: DM patients were divided according to their serological status: 5 Mi2 (33%), 6 MDA5 (40%), 2 Ku (13%), 1 NXP2 (6.6%), 6 Ro52 (40%). Asymptomatic patients presenting at least one HRiM alterations were 4 (26.7%). Among HRiM parameters, 83.3% MDA5 patients and 50% Ro52 patients showed high UES pressure (Figure 1), in contrast to the other serological groups. Among impedance findings, incomplete bolus clearance was detected in MDA5 (67%) and in Ro52 patients (50%). Notably, the only NXP2 patient showed 100% of incomplete bolus clearance. Considering the Chicago classification v.4.0, only 16.7% of MDA5 patients had a normal esophageal motility, the rest presenting absent contractility (33.3%) and ineffective esophageal motility (IEM) (50%). Distal esophageal spasm was evidenced only in Mi2 patients (40%). All patients with concomitant manometric and impedance alterations were MDA5 positive. DM patients with high UES, IEM or impedance abnormalities presented higher rate of lung involvement and active Raynaud's phenomenon (Table 1). No relation with ongoing treatment emerged.

Conclusion: We describe for the first time HRiM findings in DM. Anti-MDA5 patients appear to have a more severe esophageal involvement, even in absence of reported dysphagia, followed by anti-Ro52 patients. Interestingly, the same subsets show higher prevalence of lung involvement and Raynaud's phenomenon, suggesting a possible pathogenetic link between esophageal, lung and microvascular disease. Asymptomatic patients may present occult esophageal motility disorders detected by HRiM. Further validation of our findings are required to definitely include HRiM in the workup of DM patients as a diagnostic, prognostic and monitoring tool.

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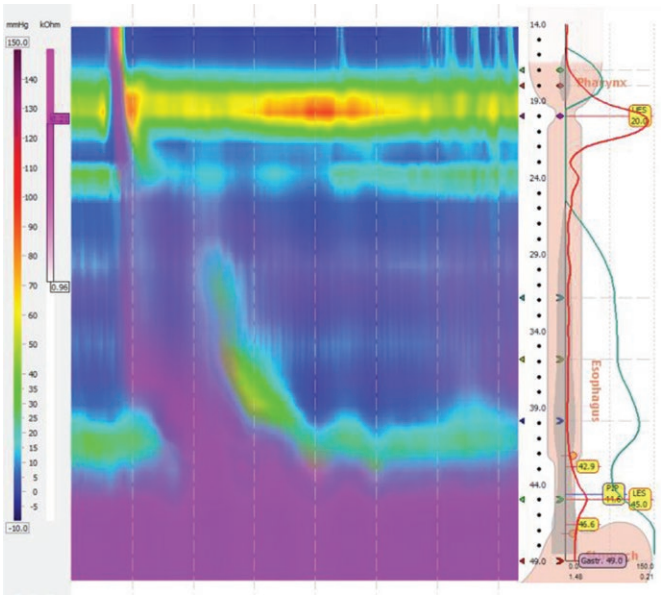


Figure 1. Representative HRiM plot of a MDA5+ patient

Table 1. HRiM abnormalities and features of DM patients

	High UES (*n* = 6)	IEM (*n* = 3)	Incomplete bolus clearance/altered flow time (*n* = 7)	Combination (*n* = 3)
Anti-Mi2	2 (33.3%)	0 (0%)	0 (0%)	0 (0%)
Anti-MDA5	5 (83.3%)	3 (100%)	4 (57.1%)	3 (100%)
Anti-Ro52	3 (50%)	1 (33.3%)	3 (42.8%)	1 (%)
Anti-Ku	1 (16.6%)	1 (33.3%)	1 (14.3%)	1 (33.3%)
Anti-NXP2	0 (0%)	0 (0%)	1 (14.3%)	0 (0%)
DLCO < 80% predicted	5 (83.3%)	3 (100%)	6 (85.7%)	3 (100%)
ILD	4 (66.6%)	3 (100%)	4 (57.1%)	3 (100%)
Dysphagia	2 (33.3%)	1 (33.3%)	3 (42.8%)	1 (33.3%)
Raynaud's phenomenon	4 (66.6%)	2 (66.6%)	6 (85.7%)	2 (66.6%)

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AB0886 PROGRESSIVE INTERSTITIAL LUNG DISEASE IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

Keywords: Systemic sclerosis

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Background: A subset of patients with systemic sclerosis associated interstitial lung disease (SSc-ILD) develop progressive ILD, which is associated with higher mortality, but the prevalence of progressive ILD and the overall disease course and patterns of SSc-ILD are unknown. Current clinical practice emphasises treatment initiation. of SSc-ILD patients with progressive ILD.

Objectives: To identify progression patterns and risk factors predictive for progressive interstitial lung disease (ILD) in patients with systemic sclerosis-associated ILD (SSc-ILD)

Methods: Within our database, patients included since 2000 aged ≥18 years fulfilled the SSc classification criteria and had lung imaging data available and had measurements of forced vital capacity (FVC) at baseline and after 12±3 months. **A** decline in FVC of ≥10%, or a decline in FVC of 5% to 10% along with a decline in DLCO of 15%, is a proposed definition of progressive fibrosis.

Results: From our database of the 813 patients included 210 (25.8%) had evidence of SSc-ILD on imaging, 134 (63.8%) at basal and 76 (36.2%) over time. The proportion of

patients with SSc-ILD who experienced progressive ILD during the initial 12±3-month period was 30.9% (65 pt) (FVC), either moderate 35 pts 53.8% (FVC decline 5% to 10%) or significant 30 pts 46.2% (FVC decline >10%), 76 (36.2%) were stable and 69 (32.8%) had improvement. In our population, the strongest predictive factors for FVC decline over 12 months were higher modified Rodnan skin score at basal.

Conclusion: Novel treatment concepts, with treatment initiation before FVC decline occurs, should. aim for prevention of progression to avoid irreversible organ damage in SSc-ILD that shows a heterogeneous and variable disease course, and thus monitoring all patients closely is important.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0887 THE EFFECTIVENESS AND SAFETY OF MESENCHYMAL STEM CELLS IN TREATMENT OF SYSTEMIC SCLEROSIS: SYSTEMATIC REVIEW

Keywords: Systemic sclerosis, Systematic review

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Background: Systemic scleroderma, or systemic sclerosis (SSc) is an autoimmune disease with high morbidity and mortality, characterised by fibrosis of the skin and internal organs. In the last decade, alternative methods of treatment of SSc resistant to standard immunosuppressive therapy have been actively studied. Of interest are the data about mesenchymal stem cells (MSCs) with their immunomodulatory properties, the ability to self-renew and differentiation.

Objectives: to evaluate the safety and effectiveness of MSCs transplantation in SSc refractory to standart therapy by a systematic review.

Methods: The search was conducted on PubMed and Google Scholar platforms using the following strategy: "Systemic sclerosis" + "Mesenchymal stem cells". All articles presented in the public domain published before 01.12.2022 in the format of case descriptions, clinical and multicenter studies (Case Reports, Clinical Studies, Clinical Trials, Multicentre Studies) were analyzed. The effectiveness of MSCs was evaluated using the index of systemic sclerosis activity and the modified Rodnan skin score (mRSS), diffusing Capacity of the lungs for carbon monoxide (DLCO), the Mouth Handicap in Systemic Sclerosis (MHISS), the Cochin Hand Functional Disability Scale (CHFS),left ventricular ejection fraction (LVEF), EASTAR 2017 Disease Activity Index, visual analog scale (VAS), manifestations of Raynaud's syndrome, laboratory parameters (ESR, CRP), immunological parameters (ANA, Scl-70). The safety assessment included the registration of various adverse events during and after transplantation.

Results: For the period from 2010-2022, fifty publications were found on the topic of MSCs transplantation in SSc, of which 15 publications met the above criteria and were included in the study. The data of 417 patients who underwent transplantation of MSCs obtained from various biological sources (bone marrow - 7, adipose tissue - 5, umbilical cord - 1) were analyzed. The average age of the patients was 42.42 ± 10.79 y.o. The results obtained suggested that there was a significant decrease in the activity of SSc compared to the baseline level of mRSS scale from 21.81± 7.2 to 4.5 ± 5.4, the number of finger ulcers decreased, there was an improvement in mouth opening assessed by the MHISS scale, 2.5 fold decrease in the level of Scl-70, and 2-fold decrease in VAS (p=0.05). The assessment of all patients (n=417) who underwent MSCs transplantation revealed a few side effects, such as postoperative consequences (bruising, swelling and soreness of the donor site, resolved within 14 days), a superficial wound infection (1 patient), which succumbed to oral antibacterial therapy and no further surgical intervention was required. Pulmonary hypertension was diagnosed in 5 patients 24 months after MSCs transplantation; ventricular arrhythmias requiring treatment with carvedilol was observed in 1 patient four months after MSCs transplantation. Restrictive cardiomyopathy and chronic fibrosing myocarditis developed in 1 patient. 6 patients who underwent liposuction had transient paresthesia, which was completely eliminated after a few weeks; 1 patient dropped out due to dizziness after lidocaine injection. 2 patients complained about digital ulcers developed within 24 months. No tumor-related events were observed. The mortality rate consisted in 1.19%, the survival rate was 98.81%. Cause of death (5 cases in total): pneumonia- 1, lung cancer- 1, unknown – 2 patients. One patient died from sudden cardiac arrest due to ventricular fibrillation.

Conclusion: According to the analysis of data from different up-to-date research, MSCs transplantation in SSc patients improved the degree of skin thickening, lung function and mouth opening, as well as relieved ulcers and finger pain without serious side effects. Thus, MSCs can be suggested as an effective and promising therapeutical approach for patients with SSc resistant to standard immunosuppressive therapy.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0888 CLINICAL CHARACTERISTICS OF ANTI HMGCOA REDUCTASE ANTIBODY POSITIVE IMMUNE MEDIATED NECROTIZING MYOPATHY: CASE SERIES OF 5 PATIENTS FROM A TERTIARY CENTRE

Keywords: Myositis, Autoantibodies

Case	1	2	3	4	5
Gender	Female	Male	Male	Female	Male
Age (Years)	54	63	66	57	54
Statin use	Simvastatin and then Atorvastatin (10 years of statin use)	Simvastatin changed to Atorvastatin/ Pravastatin (6 years of statins prior to myopathy)	Atorvastatin 20mg daily (for 2 years) and dose increased 8 months prior to onset of myopathy	Atorvastatin 10 mg stopped 6 months before IMNM due to myalgia	Atorvastatin for 4 years
Muscles involved	Proximal muscle weakness	No proximal muscle weakness	Proximal muscle weakness	Proximal muscle weakness Including neck flexors, dysphagia and respiratory failure	Proximal muscle weakness in lower limbs
Other Manifestations - skin, myocarditis	None	None	None	None	None
CK on presentation	4341	10491	9383	31666	8009
Inflammatory markers	ESR 66 CRP <3	ESR 24 CRP 13	ESR 113 CRP 60	ESR 62 CRP 100	ESR 20 CRP 140
ANA	Negative	Negative	Negative	Negative	Negative
Anti HMGCoA reductase antibodies	>200	359.5	>200	Positive	>200
Associated conditions	CLL	None	None	None	Atypical lipoma
EMG pattern	Myopathic	No myopathy/ myositis	Myositis	Myositis	Myopathic
Biopsy	Necrosis with minimal inflammation	Recovery phase of necrotising myopathy	Necrotising features with foci of sparse inflammatory cells	Necrotic and regenerative fibres, paucity of cellular infiltrates	Not done
MRI	Muscle oedema of thighs	Not done	Proximal muscle oedema	Muscle oedema of thighs	Muscle oedema in thighs
Treatment	Oral	Oral	IV followed by oral	IV followed by oral	Oral
Steroids					
DMARD	None – patient declined	MMF & IvIG	Methotrexate IvIG	Cyclophosphomide IvIG Maintenance with Mycophenolate mofetil	Combination of Mycophenolate mofetil and methotrexate
Outcome	44	190	64	64	124
CK					
Muscle power	Thighs - +4/5 Shoulders 5/5	Normal	Normal	Hip flexors – 4/5	Normal

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Background: Immune Mediated Necrotizing Myopathy is a type of autoimmune myopathy which is commonly associated with the use of statins. Common antibody detected in these patients would be HMGCoA reductase antibodies. Significant muscle necrosis with paucity of cellular infiltration is the characteristic histological feature.
Objectives: To describe clinical and therapeutic characteristics of anti HMGCoA reductase antibody positive necrotizing myopathy.
Methods: Cohort of patients with myositis were selected. The myositis antibody panel was assessed and patients with HMGCoA reductase antibody were selected. Diagnosis was made based on the 2017 EULAR/ ACR criteria [1]. Clinical manifestations, statin use, investigations, treatment offered, and outcome were described.
Results: Of the selected 5 cases, all the patients were middle aged with 3 males and 2 female patients. All 5 patients were on statins and 3 of them were on statins for many years prior to development of myopathy. None of the cases had other systemic involvement including dermatological or cardiac involvement. All 5 patients were positive for HMGCOA reductase antibodies. One patient had CLL which never required any specific treatment and another was incidentally found to have an atypical lipoma which was managed conversatively. All patients required steroids with either Methotrexate and Mycophenolate mofetil. Three of the patients received intravenous immunoglobulin therapy with good response. All of the patients had made a complete recovery though 2 of them required prolonged rehabilitation.
Conclusion: Statin induced necrotising myopathy patients could develop the disease after many years of statin therapy. It is possible that changes in the drug or the dose could act as a precipitant. This cohort of patients tend to be treated with intravenous immunoglobulin in addition to other conventional treatments. In spite of having very severe disease at the onset, with timely and appropriate immunosuppression and rehabilitation patients appeared to have a good outcome.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5438

AB0889 FILGOTINIB FOR THE TREATMENT OF SYSTEMIC SCLEROSIS OVERLAP RHEUMATOID ARTHRITIS: DATA FROM OUR PRELIMINARY EXPERIENCE

Keywords: Targeted synthetic drugs, Systemic sclerosis, Rheumatoid arthritis

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Background: Systemic sclerosis is a connective tissue disease characterized by endothelial disfunction and fibrosis of the skin and internal organs. JAK inhibitors has shown efficacy in reducing cutaneous and pulmonary fibrosis in mice models of SSc, but only few case reports and no RCTs are reported in literature. SSc is frequently associated with other autoimmune diseases and SSc- Rheumatoid arthritis (RA) is one of the most common SSc-Overlap Syndrome. Filgotinib is an oral selective JAK1 inhibitor, recently approved for the treatment of RA.
Objectives: The aim of our work was to assess efficacy and safety of Filgotinib for the treatment of cutaneous, visceral and articular involvement in patients affected by SSc overlap RA.
Methods: Prospective, open-label, monocentric study in which 5 patients affected by SSc overlap RA (M/F 0/5, age 57,80±16,62DS years, disease duration 11,6±7,89 DS years, limited/diffuse subset 3/2) referring to the Scleroderma Units of Modena and Reggio Emilia between October 2021 and July 2022, were enrolled. All patients satisfied both ACR/EULAR criteria for SSc and RA and were already in treatment with standard therapy (prostanoids, calcium-channel blockers a/o endothelin-receptors inhibitors a/o phosphodiesterase type 5 inhibitors) and had an inadequate response or were intolerant or had contraindication to one or more DMARDs or bDMARDs. Patients received Filgotinib 200 mg once daily for a period of 24 weeks. Articular, cutaneous and visceral involvement were assessed according to clinical practice at the baseline and at 12th and 24th week after the start of the treatment.
Results: All patients showed a significant improvement in articular involvement at 24th week, in particular a significant reduction in tender joint count (TJ, p=0,003), SDAI/CDAI (p=0,012/0,008) and pain numerical rating scale (NRS, p=0,035) was reported. A trend of improvement of DAS28 (p=0,055) was also observed. Notably a significant reduction in TJ (p=0,023) and a trend of improvement of SDAI/CDAI (p=0,059/0,051) was already seen at 12th week. The extent and severity of skin involvement assessed through modified Rodnan Skin Score (mRSS) remained stable during follow-up (p=0,918). No improvement or worsening of exertional dyspnea measured by means of Borg scale was reported. No drug-related side effects were recorded during follow-up and none of the patients discontinued the treatment. No deaths were reported.
Conclusion: According to our preliminary data, Filgotinib was effective, safe and well tolerated in the treatment of articular involvement in patients affected by SSc overlap RA. Further analysis on a larger number of patients and control group are needed to confirm our data. Patients' enrollment with assessment of efficacy on skin and lung involvement is currently ongoing.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0890 EARLY SYSTEMIC SCLEROSIS PATIENTS SHOW A SLOW DISEASE COURSE

Keywords: Systemic sclerosis, Epidemiology

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Background: Systemic sclerosis is a heterogenous immune-mediated connective tissue disease characterized by vasculopathy and progressive tissue and organ fibrosis. [1]
Objectives: Our aim was to determine characteristics of Finnish patients with systemic sclerosis (SSc) and early SSc that were followed during 1996-2018 in two university hospitals in Finland.
Methods: The data of patients with SSc with ICD-10 diagnostic code (M34) were collected retrospectively from medical registers. The patients were reclassified into different subsets based on the ACR/ EULAR (American College of Rheumatology and European League Against Rheumatism) 2013 classification criteria of the SSc. Early SSc was defined as a condition that did not fulfil the classification criteria (less than 9 points). Diffuse (dcSSC), limited cutaneous (lcSSc), overlap and sine scleroderma subsets were differentiated by their clinical phenotype.
Results: 336 patients were obtained after re-evaluation of data. Out of 336 patients 40 (11.9%) patients had dcSSc, 222 (66.1 %) lcSSc, 16 (4.8%) SSc-overlap syndrome, 2 (0.6%) SSc sine scleroderma and 56 (16.7%) early SSc. The early SSc group did not develop any of the most severe manifestations such as interstitial lung disease (ILD), the incidence of which was 32.7/1000 patient years in the whole SSc group, n=280, pulmonary arterial hypertension (PAH) (14.3/1000 patient years), renal crisis (RC) (3.5/1000 patient years), myocarditis (1.2/1000 patient years) during the 4.3 [IQR 1.9-6.7] years of follow-up. The SSc group had significantly more other manifestations as digital ulcers (41.1 vs. 6.7/1000 patient years, p<0.001, SSc and early SSc, respectively), reduced mouth opening (44.3 vs. 10.1, p<0.001) and manometry positive oesophageal dysmotility (21.1 vs. 10.3, p=0.007) than patients with early SSc. ILD was diagnosed 2.8 (SD 4.5) years, PAH 5.6 (SD 8.7) years and RC 0.2 (SD 0.3) years after the onset of the first non-Raynaud's phenomenon symptom in SSc patients. The patients with dcSSc had worse survival than lcSSc patients (after 5 years 81.9% vs 91.6%,

after 10 years 67.3% vs 82.9%, p<0.001 and HR=2.7 (1,6-4,4), p<0.001). The SSc-overlap and early SSc subsets did not have difference in survival when compared to lcSSc subset.

Conclusion: Disease course of patient with early SSc was slow or mild since none of them developed any severe complication during the median follow-up time of 4.3 years.

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Table 1. The rates of different organ manifestations as reported cases per patient year for SSc and early SSc patients

	SSc	Events/1000 py	Early SSc	Events/1000 py	p-value
Patients	280		56		
Vasculitis	4/275 (1.5)	1.6	0/55 (0)	0.0	0.611
Gangrene	18/274 (6.6)	7.5	1/54 (1.8)	3.3	0.218
Amputation	20/274 (7.3)	8.0	1/55 (1.8)	3.2	0.147
Digital ulcer	81/275 (29.5)	41.1	2/55 (3.6)	6.7	<0.001
Decreased mouth opening	79/274 (28.8)	44.3	3/55 (5.2)	10.1	<0.001
Arthritis	60/273 (22.0)	29.3	14/55 (25.5)	57.3	0.597
Myositis	3/273 (1.1)	1.2	0/55 (0)	0.0	0.650
Cardiac	9/273 (3.3)	3.5	0/55 (0)	0.0	0.234
Gastrointestinal	105/275 (38.2)	67.3	15/55 (27.3)	72.7	0.166
Manometry positive	46/57 (80.7)	21.1	3/9 (33.3)	10.3	0.007
Renal crisis	9/274 (3.3)	3.5	0/54 (0)	0.0	0.365
ILD	68/276 (24.6)	32.7	0/55 (0)	0.0	<0.001
ILD and transplantation	1/67 (1.5)	0.4	-	-	-
PAH	35/275 (12.7)	14.3	0/55(0)	0.0	0.007
PAH and transplantation	1/35 (2.9)	0.4	-	-	-
Calcinosis	60/275 (21.8)	29.7	9/55 (16.4)	34.0	0.468
Acro-osteolysis	18/275 (6.5)	7.7	0/55 (0)	0.0	0.094

Results are expressed as n (%) for qualitative variables

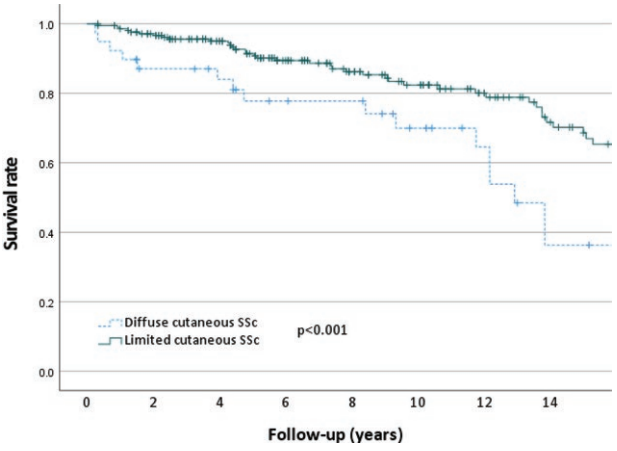


Figure 1. Kaplan-Meier survival curves from the first non-Raynaud's phenomenon symptom for lcSSc and dcSSc patients

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AB0891

PROOF OF CONCEPT OF THE USE OF CO-DESIGNED 3D PRINTED ASSISTIVE DEVICES WITHIN AN OCCUPATIONAL THERAPY INTERVENTION IN SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Physical therapy/Physiotherapy, Health Services Research

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Background: Despite the positive impact of assistive devices (ADs) on the daily lives of people with disabilities, many of them are initially adopted and then regrettably abandoned. Even though the AD of an individual patient might fit his/her needs, up to 7 out of 10 people stop using it. On the one hand this may be linked to an improvement in their health, on the other, the devices may not be ergonomically suitable for long-term use. Previous studies have highlighted the possibility that co-designed and customised 3D printed assistive devices can benefit patients with rheumatic diseases which impair daily activities, especially manual ones. Among the 29 patients with Systemic Sclerosis who took part in the joint prevention clinic workshop at the University-Hospital of Modena (Italy), in 2019 4 patients actively joined the 3D printing project for the co-designing of ADs.

Objectives: This work has two main goals: firstly, to check whether in the short term the co-design approach is able to guarantee better acceptance of ADs and a lower abandonment rate. Secondly, to check during follow-ups, if the patients are satisfied and regularly use their ADs and if their daily activities remain unchanged.

Methods: The development of the ADs begins with co-design sessions which involve the patient, an Occupational Therapist and a designer. The AD is digitally modelled and 3D printed. Subsequently it is delivered to the patient following a number of training sessions. Using standardized tests such as PIADS (Psychosocial Impact of Assistive Devices Scale) and QUEST (Quebec User Evaluation of Satisfaction with assistive Technology) at the time of delivery of the ADs, then after 3 years, we assessed the level of satisfaction of the 4 patients enrolled, the condition of the ADs and their actual use.

Results: In 2019 each of the 4 patients received at least one AD, which they used on a regular daily basis [i.e. a device to open a moka pot (an Italian coffee machine); a token for a shopping trolley; a pen grip handle; a multiple key turner]. The results of the PIADS following delivery and in the 3-years follow-up were positive. The QUEST results were also positive. After 3 years the ADs were still being used regularly. Moreover, in 2022, 2 patients co-designed and 3D printed new ADs in response to new or altered needs.

Conclusion: In both the long and short term, ADs are still being used regularly and patients are still enjoying the benefits. After 3 years none of the ADs displayed any significant wear or breakage, thus their effectiveness was not compromised. Finally, the satisfaction of the patients with the co-designed ADs remained unaltered over time. Co-design 3D printed devices have therefore proven to effectively reduce the AD abandonment rate.

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AB0892

SMOKING DOES NOT REPRESENT A SUSCEPTIBILITY FACTOR FOR THE DEVELOPMENT OF SYSTEMIC SCLEROSIS: AN ANALYSIS OF THE LEIDEN CCISS COHORT

Keywords: Systemic sclerosis, Lifestyles, Epidemiology

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Table 1. Comparison of prevalence of ever-smoking men and women in the Dutch population and in the Leiden systemic sclerosis (SSc) CCISS cohort int the years 2015 and 2021.

2015						2021					
Men						**Men**					
Age range (years)	Size of the general population	Ever smokers	SSc patients (number)	Ever smokers	p-value	Age range (years)	Size of the general population	Ever smokers	SSc patients (number)	Ever smokers	p-value
25-45	2.126.000	55,4%	12	75%	0,172	25-45	2.193.000	51,8%	15	66,7%	0,249
45-65	2.385.000	65,2%	34	64,7%	0,952	45-65	2.409.000	59,5%	68	63,2%	0,530
>65	1.362.000	79,1%	13	69,2%	0,381	>65	1.604.000	76,7%	28	75%	0,831
Women						**Women**					
Age range (years)	Size of the general population	Ever smokers	SSc patients (number)	Ever smokers	p-value	Age range (years)	Size of the general population	Ever smokers	SSc patients (number)	Ever smokers	p-value
25-45	2.154.000	43,2%	62	46,8%	0,570	25-45	2.116.000	47,8%	58	43,1%	0,474
45-65	2.413.000	53,6%	213	47,7%	0,095	45-65	2.369.000	60,8%	134	53,7%	0,112
>65	1.849.000	55%	186	51,6%	0,353	>65	1.644.000	52,2%	88	51,1%	0,842

Background: A proinflammatory and immunosuppressive role of cigarette smoking has been suggested in rheumatic and autoimmune conditions, with former and current smokers having increased susceptibility to the development of several diseases [1]. Conversely, a study from the United States showed that ever-smoking was not associated with a significant risk to develop systemic sclerosis (SSc) [2]. Up to date, no other study addressed smoking as a possible risk factor for developing SSc.

Objectives: The aim of our study was to investigate whether smoking is a risk factor for disease susceptibility in SSc in the Dutch population.

Methods: At Leiden University Medical Center, the prospective Combined Care in Systemic Sclerosis (CCISS) cohort was initiated in 2009 and, as of January 2022, 708 SSc patients have been included. Information about smoking history was collected at time of enrolment in the cohort, allowing patients to be categorized into never-smokers and ever-smokers. Data about smoking habits in the Dutch population from 2014 to 2021, stratified for sex and age (12-25; 25-45; 45-65; >65 years) are accessible from the Dutch Central Bureau of Statistics website (https://opendata.cbs.nl/#/CBS/nl/dataset/ 83385NED/table?dl=6A354). The prevalence of ever-smokers in the CCISS cohort was compared with the prevalence of ever-smokers in the general Dutch population using chi-square tests. Due to the limited number of young SSc patients, only individuals aged 25 or above were included in the analysis. In order not to miss potentially relevant differences attributable to changes in smoking habits during time, two index years were chosen for the current analysis, 2015 and 2021. Age of the SSc patients who were enrolled in the CCISS cohort at the time of the index years was calculated. Patients who had died before each index year were excluded from the relative analysis. Official data about the Dutch population size and age composition were retrieved from the Dutch Central Bureau of Statistics website (https://www.cbs.nl/visualisaties/dashboard-bevolking/bevolkingspiramide).

Results: Details about the population size in each age range and the number of patients included in the study are reported in Table 1. No statistically significant differences emerged in the comparison of ever-smoking rates between SSc patients and the general Dutch population both in men and women and in each of the three age categories (all p-values > 0.05).

Conclusion: Our study demonstrates that the percentage of ever-smoking individuals is comparable in SSc patients and in the Dutch population. Although the stratification might have decreased the statistical power of our analysis, we can conclude that smoking does not confer an increased risk for the development of SSc in the Netherlands.

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AB0893

CORRELATIONS BETWEEN CT SCAN, CLINICAL AND RESPIRATORY FUNCTIONAL DATA IN SYSTEMIC SCLEROSIS ASSOCIATED INTERSTITIAL LUNG DISEASE

Keywords: Systemic sclerosis, Imaging, Lungs

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Background: The role of computed tomography (CT) in the assessment of pulmonary involvement in systemic sclerosis is witnessing constant updates with the development of scores and tools.

Objectives: The aim of our study was to look for a correlation between CT scan, clinical and respiratory functional data and to evaluate the severity of diffuse infiltrative lung disease using the Goh' score.

Methods: It was a retrospective and descriptive study carried out at the Internal Medicine Department of Mongi Slim Hospital. It included data of patients with SSc with pulmonary involvement. We used the Goh CT score and the modified Goh score (with 6 levels) to assess the severity of lung involvement.

Results: 31 patients were included. The mean age of our patients was 50 years. The predominant elemental lesions on chest CT were ground-glass opacities (78%), septal thickening (77%) and traction bronchiectasis or bronchiolectasis (70%). The most common type of interstitial lung disease was non-specific interstitial pneumonia (65%) followed by usual interstitial pneumonia (23%). The statistical analysis showed associations between clinical, respiratory functional and imaging data. Decreased forced vital capacity was statistically associated with honeycomb (p=0.04) and non-specific interstitial pneumonia (p=0.05). It was also associated with the extent of lesions according to Goh score (p=0.031) and the modified 6-level Goh score (p=0.024). Crackles at the bases of lungs were associated with the degree of the reticulation extent according to the modified Goh score (p=0.022). A statistically significant relationship was also noted between cough and the extent of ground-glass opacities according to the modified Goh score (p=0.022).

Conclusion: Chest CT allows the assessment of the severity of lung involvement in SSc using semi-quantitative CT scores. We have concluded that the modified Goh score correlates better with clinical abnormalities.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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Scleroderma, myositis and related syndromes

AB0894 SYMPTOMS OF GASTROINTESTINAL INVOLVEMENT IN PATIENTS WITH LIMITED AND DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS EVALUATED WITH TWO DIFFERENT SELF-ASSESSMENT TOOLS

Keywords: Gastrointestinal tract, Systemic sclerosis, Patient reported outcomes

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Background: Gastrointestinal (GI) tract is the second most affected organ in systemic sclerosis (SSc).
Objectives: This study aims to analyze the frequency and severity of GI symptoms and their impact on health-related quality of life among patients with limited cutaneous (lcSSc) and diffuse cutaneous systemic sclerosis (dcSSc), as well as in patients with anti-centromere autoantibodies (ACA) and anti-topoisomerase I autoantibodies (ATA).
Methods: Eighty-six consecutive patients with SSc (mean age 59.5 yrs, mean disease duration 11.7 ± 7.9 yrs) were included in this study. LcSSc have had 65 (75.6%) of patients, whilst 21(24.4%) had diffuse form of the disease. ACA were detected in 48 patients (55.8%), ATA in 25 patients (29.1%), two of them had both ACA and ATA (2.3%) and 11 (12.8%) of them had positive antinuclear antibodies (ANA) without specific autoantibodies. We used two self-assessment questionnaires to evaluate the presence and severity of GI symptoms: UCLA-SCTC-GIT 2.0 (1) and the SAQ [2].
Results: There was no difference in percentage of patients with lcSSc and dcSSc who used proton pump inhibitors (41.5%/52.3%), as well as in patients with positive ACA or ATA (45.8%/52%). Symptoms of gastroesophageal reflux (lcSSc: dSSc = 70.7%: 71.4%), distension/bloating (lcSSc: dSSc = 72.3%: 61.9%), diarrhea (lcSSc: dSSc = 27.7%: 42.8%), constipation (lcSSc: dSSc = 44.6%: 33.3%) and fecal soilage (lcSSc: dSSc = 9.2%: 14.3%) were found equally frequent (p>0.05) in patients with lcSSc and dcSSc. GI symptoms were equally common (p>0.05) in patients with ACA and ATA as follows: reflux (ACA: ATA = 70.8%: 80%), distension (ACA: ATA = 77.1%: 64%), diarrhea (ACA: ATA = 33.3%: 28%), constipation (ACA: ATA = 47.9%: 40%) and fecal soilage (ACA: ATA = 8.3%: 16%). Reflux and distension were most frequently present categories, with the highest mean index scores, implicating that these symptoms were most common and severe in our patients. We did not notice significant difference in prevalence and severity of GI symptoms in patients with lcSSc and dcSSc, as well as in patients with ACA and ATA (Table 1). Total GIT score correlated positively with all SAQ indices. Interestingly, index of reflux correlated with the Index of respiratory status (IRS), a distinct domain within the SAQ questionnaire, related to respiratory symptoms, implicating that patients with severe reflux have more serious respiratory symptoms.
Conclusion: Gastrointestinal impairment is very frequent and affects the quality of life in patients with SSc, with no difference regarding the disease subtype or autoantibodies, emphasizing the importance of early diagnose and treatment. These questionnaires may be helpful in early detection of GI involvement.

Table 1. Severity of GI symptoms in different disease subtypes and autoantibodies present. Differences among the groups were not statistically significant (p>0.05).

	lcSSc (n=65)	dcSSc (n=21)	ACA (n=48)	ATA (n=25)
UCLA GIT 2.0 (mean±SD)				
Reflux	0.49 ± 0.53	0.52 ± 0.6	0.51 ± 0.57	0.55 ± 0.52
Distension/Bloating	0.88 ± 0.84	0.52 ± 0.6	0.97 ± 0.85	0.61 ± 0.77
Diarrhea	0.2 ± 0.36	0.43 ± 0.52	0.24 ± 0.39	0.25 ± 0.42
Constipation	0.35 ± 0.48	0.14 ± 0.26	0.36 ± 0.49	0.22 ± 0.35
Fecal soilage	0.15 ± 0.56	0.24 ± 0.62	0.12 ± 0.49	0.3 ± 0.74
Social functioning	0.31 ± 0.4	0.3 ± 0.45	0.35 ± 0.39	0.25 ± 0.4
Emotional well-being	0.32 ± 0.43	0.35 ± 0.63	0.33 ± 0.43	0.26 ± 0.38
Total GIT score	0.45 ± 0.73	0.4 ± 0.47	0.5 ± 0.83	0.37 ± 0.39

dcSSc - diffuse cutaneous systemic sclerosis, lcSSc- limited cutaneous systemic sclerosis, ACA – anti-centromere autoantibodies, ATA – anti-topoisomerase I autoantibodies.

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AB0895 SUBCUTANEOUS IMMUNOGLOBULINS IN IDIOPATHIC INFLAMMATORY MYOPATHIES: IS IT TIME FOR A THERAPY DISCONTINUATION SCHEDULE?

Keywords: Myositis, Outcome measures, Quality of care

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Background: Subcutaneous immunoglobulins (SCIg) therapy is effective in patients with Idiopathic Inflammatory Myopathies (IIMs), especially in severe and refractory forms of the disease; however, its use is burdened by high costs. Although it is now known that the dosage to be used for the immunomodulatory effect is 2g/kg per month, there are no standardised tapering or discontinuation schemes to date.
Objectives: The aim of the study was to assess whether there are differences in terms of clinical outcomes and patient Quality of Life (QoL) between two different SCIg treatment regimens, involving discontinuation of therapy after the first six months or continuation of the drug for a further six months.
Methods: Within the cohort of IIM patients (2017 EULAR/ACR criteria) followed at our Myositis Clinic, we selected those who were treated with SCIg and, dividing them into two groups according to whether they discontinued therapy after the first six months, we performed a retrospective analysis on data prospectively collected. For each patient, demographic and clinical data (age, sex, disease subset and duration, organ involvement, comorbidities, treatment) were collected from medical charts. The International Myositis Assessment & Clinical Studies Group Disease Activity Core Set Measures (IMACS-CSMs) [Physician Global Activity (PhGA), Patient Global Activity (PGA), 8-items Manual Muscle Testing (MMT8), Health Assessment Questionnaire (HAQ), serological muscle enzymes values] were used to assess the disease activity at baseline and to evaluate the clinical outcomes after six and twelve months from the start of SCIg therapy. Patients' perspective was evaluated also by administration of Patient Reported Outcomes (PROs) not included in the IMACS-CSMs: Short-Form 36 Items Health Survey (SF-36), Functional Assessment of Chronic Illness Therapy Fatigue Subscale (FACIT-F), Hospital Anxiety and Depression Scale (HADS). We then compared the delta of IMACS-CSMs and PROs between the 12-month (12m) and 6-month (6m) assessments to detect any significant changes in patients' health status following the discontinuation of SCIg therapy.
Results: We included 18 patients (12 dermatomyositis, 6 polymyositis; 61.1% female) with a mean age at the beginning of SCIg therapy of 63.8±14.8 years. Of these, 10 (55.6%) discontinued SCIg therapy after 6 months of treatment while 8 (44.4%) continued it for at least one year. We found no differences between the two groups in terms of disease activity and patients' QoL at baseline. At 12 months evaluation, there were no statistically significant differences in PhGA (2.9±1.7 vs 2.5±2.0), MMT8 (67.9±8.0 vs 75.1±6.1) and serum values of muscle enzymes (CPK, LDH, aldolase) between those who had discontinued SCIg after the first 6 months and those who continued the treatment. Patients' QoL was also found not to differ between the two groups, as no statistically significant differences emerged between the scores of HAQ, all SF-36 domains, FACIT-F and HADS anxiety and depression subscales. The delta 12m-6m of QoL assessment parameters showed no differences between the two groups, while there was a worsening of mean PhGA (1.5±1.4 vs -0.5±1.8, p=0.026) and MMT8 (-5.9±6.6 vs 3.3±2.8, p=0.010) in those who discontinued therapy compared with those who continued SCIg.
Conclusion: Although preliminary and with the limitations inherent to the retrospective nature of the study, these data seem to suggest that there are no significant differences in outcomes assessed by IMACS-CSMs and in patient's perception of the disease between different treatment regimens concerning the discontinuation of SCIg. If our findings will be confirmed by future studies on larger cohort of IIM patients, although it appears that there may be a slightly deterioration in muscle function, discontinuing SCIg therapy after the first six months of treatment could reduce health costs, without the risk of significantly compromising patients' quality of care.
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AB0896 BEYOND CLINICAL TRIALS: EFFICACY AND SAFETY OF NINTEDANIB IN IPF AND PROGRESSIVE FIBROSING INTERSTITIAL LUNG DISEASES IN CLINICAL PRACTICE

Keywords: Organ damage, Lungs, Real-world evidence

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Background: Since publication of clinical trials regarding the efficacy of nintedanib in fibrosing ILD, including the ILD associated with autoimmune diseases, its clinical use has increased but not enough real-world data has been published.
Objectives: The aim of our study was to evaluate the efficacy and safety of nintedanib in patients with interstitial lung diseases (ILDs) progressively fibrosing of several etiologies in a spanish third-level hospital.
Methods: A retrospective study was designed to collect clinical and radiological data of 31 patients under treatment with nintedanib, followed up by Internal Medicine, Rheumatology, or Pneumology specialists since 2016.
Results: Chacteristics of the study population are collected in Table 1. The indications for nintedanib were a fibrosis progression in the previous 24 months, determined as a decrease of Forced Vital Capacity higher than 10% in 25 patients (41,67%) or a decrease of 5-10% in 5 patients (8,33%). The increase of fibrosis in CT in 17 patients (28,33%) and a clinical worsening in 25 patients (41,67%) were also indications for treatment, as in pivotal trials. The mean time with nintedanib was 12,58 months (± 13,20). The drug was stopped in 9 patients (29%), 1 of them due to progression and 8 due to adverse effects, none of them severe, being the most frequent gastrointestinal. 12 patients died during follow-up. 7 (58,33%) were diagnosed with IFP, 4 with progressive fibrosis ILD, and 1 with ILD associated with systemic sclerosis. No significant differences between groups were found. Spirometric values were collected before treatment as well as at 3, 6, 12, and 24 months after starting treatment to compare the mean values of FVC (ml), FEV1 (ml), Tiffenau index and DLCO (%). The evolution of spirometric parameters is shown in graphic 1. No significant differences were found between them at baseline and after treatment, in accordance with the expected slowing of the progression to fibrosis. Regarding the evolution in radiological studies, fibrosis progression was only observed in a small percentage of patients.
Conclusion: Nintedanib was one of the first anti-fibrotic drugs with indication in fibrosis ILD. Not only for IPF but also for ILD of diverse aetiology, including those associated with autoimmune diseases, after the publication of clinical trials. Therefore, its use is increasing despite limited inclusion criteria in trials and scarce real-life clinical data. Our real-world study, even with its limitations, shows consistent results with those of the clinical trials, stabilising progression of pulmonary fibrosis in our population for the next 24 months after its start.

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Table 1.

CHARACTERISTICS (n: 31)	N	%		N	%
Men	20	64,52			
Years (SD)	74,35 (±1,63)				
Ex-smoker	16	51,61			
No smoker	8	25,81			
Comorbidities:			**Concomitant treatment**		
HTN	17	54,84	Antihypertensives	16	51,61
Dyslipidemia	14	45,16	PPI	15	48, 39
GERD	7	22,58	Bronchodilator	16	51, 61
Cardiopathy	6	19,35	Statin	11	35,48
SAD	5	16,13	ASA	2	6,45
COPD	4	12,90	Anticoagulant	3	9,68
DM	4	12,90	Oral antidiabetic	2	6,45
Other	7	22,58			
Main diagnosis			**Radiologic findings**		
IPF	16	51, 61	UIP	20	64,52
PF-ILD	10	32,26	NSIP	10	32,26
IPAF	*10*	*16,13*			
AD-ILD	5	16,13	BOOP	1	3,23
SSc	*3*	*9,68*			
RA	*1*	*3,23*			
Sjögren	*1*	*3,23*			

HTN: hypertension, GERD: gastroesophageal reflux disease hipertensión arterial, AD: autoinmune disease, COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, PPI: Proton pump inhibitors, ASA: Acetylsalicylic acid, UIP: usual interstitial pneumonia, NSIP: Nonspecific interstitial pneumonia, BOOP: bronchiolitis obliterans with organizing pneumonia, FPI: idiopathic pulmonary fibrosis, PF-ILD: progressive fibrosing interstitial lung diseases, AD-ILD: interstitial lung disease associated with autoimmune diseases. RA: rheumatoid arthritis

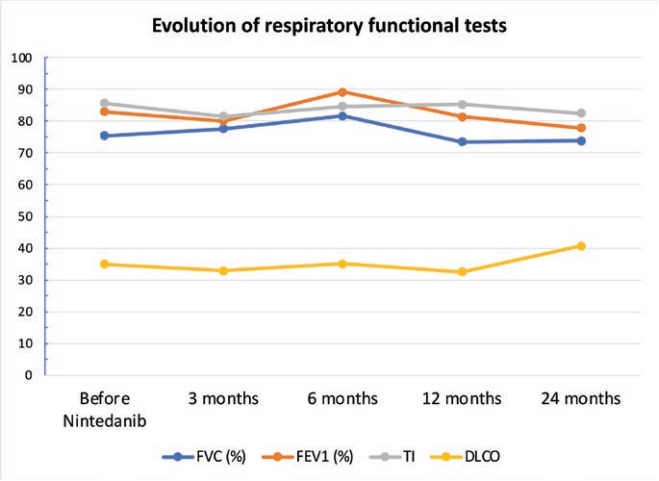


Figure 1.

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AB0897

THE PRESENCE OF ANTI-U1-RNP ANTIBODY HAS A MILD BUT APPARENT IMPACT ON INTERSTITIAL LUNG DISEASE IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Lungs, Systemic sclerosis, Autoantibodies

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Background: Interstitial lung disease (ILD) is the leading cause of systemic sclerosis (SSc)-related death[1]. With the availability of antifibrotic agents to slow the progression of SSc-ILD[2], it is important for clinicians to be aware of the antibody profile predicting the severity and progression of SSc-ILD.
Objectives: To determine the impact of anti-U1 ribonucleoprotein antibody (αRNPab) in addition to anti-topoisomerase 1 antibody (ATA) on SSc related interstitial lung disease (ILD).
Methods: Patients with SSc who visited Mie University Hospital between December 2020 to December 2021 were consecutively registered. The severity and progression of ILD on chest computed tomography (CT) were assessed based on the ILD and traction bronchiectasis (TBE) scores, evaluated by using established method [3] with minor modification. We hypothesized that ATA had the greatest impact on ILD, followed by αRNPab, and accordingly stratified patients into three groups: group 1, ATA-positive; group 2, αRNPab-positive; and group 3, double-negative. At registration, patient characteristics were compared according to the presence of ILD, and the severity of ILD were compared among three groups. For patients who had earlier CT scans available, ILD progression was assessed.
Results: Among 48 patients (ILD/non-ILD; n=25/23), αRNPab positivity was significantly higher in the ILD than in the non-ILD group (32%, 0%, p<0.01). In 47 patients, the percentage of patients whose ILD score ≥ 20% was 83.3, 28.5 and 5.8% in groups 1, 2 and 3 (n = 6/7/34), respectively (p<0.01). In 25 patients, the percentage of patients with progressive ILD whose ILD score increased by ≥ 5% was 80.0, 50.0 and 14.3% in groups 1, 2 and 3 (n = 5/6/14), respectively (p<0.01).
Conclusion: The presence of αRNPab significantly affects the presence, severity and progression of SSc-ILD, although the effect is milder than that of ATA.

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Table 1. Frequency and characteristics of SSc-ILD based on ATA and αRNPab positivity.

	ATA positive group	αRNPab positive group	Double-negative group	P value
	n = 6	n = 7	n = 34	
ILD present, n (%)	5 (83.3%)	7 (100%)	12 (35.2%)	<0.01*
Extensive ILD (ILD score ≥ 20%), n (%)	5 (83.3%)	2 (28.5%)	2 (5.8%)	<0.01*
HRCT score				
ILD score (%), median [IQR]	40.17 [16.83, 59.02]	16.55 [9.55, 30.35]	0 [0, 9.9]	<0.01*
TBE score (%), median [IQR]	2.25 [0.75, 2.62]	0.50 [0, 2.00]	0 [0. 0]	<0.01*
Longitudinal analysis	n = 5	n = 6	n = 14	
Delta TBE score ≥ 1, n (%)	4 (80.0%)	3 (50.0%)	2 (14.3%)	<0.01*
Progressive ILD condition 1 (the ILD score incrased by ≥ 5%), n (%)	4 (80.0%)	3 (50.0%)	2 (14.3%)	<0.01*
Progressive ILD condition 2 (the ILD score increased by ≥ 10%), n (%)	4 (80.0%)	1 (16.7%)	1 (7.1%)	<0.01*
Progressive ILD condition 3 (the ILD score increased by ≥ 5% and/or the TBE score increased by ≥ 1), n (%)	4 (80.0%)	3 (50.0%)	3 (21.4%)	<0.01*
Progressive ILD condition 4 (the ILD score increased by ≥ 10% and/ or the TBE score increased by ≥ 1), n (%)	4 (80.0%)	3 (50.0%)	2 (14.3%)	<0.01*

* p<0.05. Abbreviations; ATA, anti-topoisomerase 1 antibody; αRNPab, anti-U1 ribonucleoprotein antibody; HRCT, high resolution computed tomography; ILD, interstitial lung disease; IQR, interquartile range; SSc, systemic sclerosis; TBE, traction bronchiectasis;

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AB0898 LUNG ULTRASONOGRAPHY FOR THE SCREENING AND PROGNOSTIC STRATIFICATION OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS: RESULTS FROM A SYSTEMATIC LITERATURE REVIEW

Keywords: Systematic review, Ultrasound, Systemic sclerosis

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Background: Interstitial lung disease (ILD) affects almost all systemic sclerosis (SSc) patients and is the major cause of morbidity and mortality. Chest high resolution computed tomography (HRCT) is today the gold standard imaging method to diagnose and disclose the characteristic SSc ILD features. More than a decade ago, ultrasonography (US) has been shown to be a less invasive and radiation-free methodology to screen and show the lung involvement in SSc.
Objectives: To evaluate and confirm the reliability of lung US as a screening tool for SSc ILD.
Methods: A systematic literature search in several databases was conducted following the PICO framework on July 2022. Two researchers independently screened abstracts and titles and full texts were subsequently reviewed to determine eligibility (original research articles enrolling adult SSc patients undergoing lung US and HRCT). Data from eligible articles were extracted and risk of bias (RoB) was assessed with validated tools. Owing to extensive interstudy heterogeneity, narrative summaries had to be used to present the data.
Results: Out of 1656 retrieved articles, only 95 were selected for full text evaluation, and only 15 were considered eligible for inclusion. In these15 studies, published between 2014 and 2022, only 3 of these enrolled a control group of normal subjects. 14 studies had a cross-sectional design and 1 study was a prospective longitudinal study. In 10 studies, information about patient characteristics (SSc subset and/or autoantibody positivity) were lacking (67%). The studies were highly heterogeneous in terms of type of US probe used (2,5-3,5 MHz vs 7-10 MHz), number of scanned sites (ranging between 18 to 72) and US score/threshold to classify the US findings as ILD. The sensitivity of lung US ranged between 73.58 and 100% while the specificity ranged between 55 to 92.3%: 7 studies did not report either sensitivity or specificity or both, and it was not possible to calculate it on the basis of data provided. In 7 studies, feasibility was explored, showing that the scanning of up to 72 sites always took less than 10 minutes. In 3 studies, a good to very good reproducibility (intraclass correlation coefficients=0.95-0.96 and Cohen's k=0.72) was detected. The concordance between US and HRCT in identifying ILD pathological findings was around 80%. The only longitudinal study revealed that the number of B-lines at baseline was correlated with the change of the diffusing capacity for carbon monoxide (DLCO) after 12 months.
Conclusion: The results of our Systematic Literature Review confirm that lung US is a useful screening tool for SScILD. However, the data on the prognostic value of lung US are still too few to draw any definite conclusions. The implementation of routine lung US might allow an early identification and prompt treatment of SSc-ILD patients. However, the lung US procedure still need to be unified and harmonised (e.g. type of probe, number of scanned sites) together with the scoring systems/threshold to allow a comparison of research studies and a broad implementation of lung US in clinical practice.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0899 RITUXIMAB IN INFLAMMATORY MYOPATHIES: A SINGLE CENTER EXPERIENCE

Keywords: Myositis

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Background: Rituximab (RTX) is currently the most widely used biologic agent in the treatment of IIM. The main indications for treatment with RTX in IIM are refractory muscle, lung, and skin involvement. There is growing evidence that biologic therapy in IIM has the potential to benefit patients with refractory disease. (1)

Table 1: Features

	Patients n: (14)
Gender	
Female	10 (71 %)
Male	4 (29%)
Age (years) at diagnosis	50 ± DS 17
Comorbidity	
Diabetes	1/14 (7%)
Arterial hypertension	1/14 (7%)
dyslipidemia	2/14 (14%)
Statin use	1/14 (7%)
smoking	1/14 (7%)
Alcohol	1/14 (7%)
Neoplasma	1/14 (7%
Inflammatory myopathy (subtypes)	
Dermatomyositis	9/14 (64 %)
Polymyostis	3/14 (21%)
Necrotizing myopathy	1/14 (7%)
Overlap myopathy	1/14 (7%)
Clinical features	
Symmetric proximal muscle weakness	12/14 (71%)
Respiratory muscle weakness	3/14 (21%)
Neck muscle weakness	7/14 (50%)
Dysphagia	9/4 (64%)
Skin manifestations	
skin compromise	10/14 (71%)
Gottron's papules	8/10 (80%)
Heliotrope erythema	7/10 (70%)
Signs of the Shawl	8/10 (80%)
Sign of the "v"	8/10 (80%)
Raynaud	7/14 (50%)
Interstitial lung involvement	0/14 (0%)
Complementary studies	
Muscle biopsy	6/14 (42%)
Electromyogram	8/14 (57%)
Video swallowing	9/14 (64%)
Skin biopsy	6/14 (42,5%)
Immunological Laboratory	
ANA positive	11/14 (78,5%)
SSB-Ro	2/13 (15%)
RNP	1/12 (8,3%)
Anticentromere	1/4 (25%)
Jo1	0/10 (0%)
Myopathies Panel	0/4 (0%)

Objectives: Describe and analyze the clinical indications for RTX in a cohort of patients with IIM. Describe adverse effects associated with RTX and clinical response to RTX.
Methods: Descriptive, retrospective study, in a single center of patients diagnosed with IIM (Bohan and Peter-ACR/EULAR 2017), who received RTX (1993 to 2022). Patients with follow-up of at least 6 months after first infusion of RTX were included. The following variables were considered: myopathy subtype, clinical manifestations, RTX indication, RTX administration regimen, and adverse events. Significant clinical response to RTX was defined as improvement in organ function or symptoms, or halting of disease progression, or prevention of relapses, such that the patient did not require further immunosuppression or was maintained on stable immunosuppressive therapy, and no more than 10 mg prednisolone/day or additional doses of RTX were given to treat disease relapses or to maintain initial clinical benefit.
Results: Of 138 patients registered with MMII, 17 (12.3%) patients received treatment with RTX. Fourteen (14) patients (10.4%) were included in the analysis. Table 1 describes demographics and clinical characteristics. The main reason for indication was refractory disease (50%) (Table 2). One hundred percent (100%) of patients received glucocorticoids during RTX use at an average daily dose of 25 mg. Methotrexate was co-administered with RTX in the majority of patients and was also the most widely used drug before RTX. Regarding safety, 5 infectious adverse effects (35%) were recorded in 4 patients (28%), 3 of which were deemed as serious (21%). The clinical response to RXT at 3 months was 78.5%, and 71 % at 6 months.

Table 2 -Rituximab

	n 14 (%)
Rituximab Dosage Guidelines:	
A: (1 gr every 15 days) average dose: 1357 gr ± 420	8/14 (57%)
B: (375 mg/m2/body sup) average dose 1730 ±710	6/14 (43%)
Infusion of hospitalized patients	4/14 (28,5%)
Infusion center	10/14 (71,4%)
Main reason for indication:	
Severity of diseases	4/14 (28,5%)
Refractory disease	7/14 (50%)
Both situations	3/14 (21,5%)
Indication of organic involvement (frequency)	
Dysphagia	8/14 (57%)
Cutaneous	5/14 (37,5%)
Peripheral muscles	5/14 (37,5%)
Respiratory muscles	2/14 (14%)

Conclusion: In this cohort of patients with IIM, 12.3% received treatment with RTX and the main indications were dysphagia and refractory disease.
Adverse effects were recorded in 28% of the cases, all infectious, of which 21% were serious. Clinical response was obtained in 78.5% 3 months after the first indication of rituximab, which was maintained in 71% of the patients at 6 months.
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AB0900 NINTEDANIB DOES NOT IMPROVE NAILFOLD CAPILLARY ABNORMALITIES IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Lungs, Imaging, Systemic sclerosis

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Background: The pathogenesis of SSc consists of three aspects: fibrosis, angiopathy, and immune abnormalities. Nintedanib has been shown to be effective against interstitial lung disease (ILD) as an antifibrotic drug, but it may also have effects on vascular disorders due to its inhibitory effects on FGF, PDGF, and VEGF. While nailfold capillary abnormalities in patients with systemic sclerosis (SSc) may improve with immunosuppressive therapy, no reports have evaluated whether nintedanib improves nailfold capillary abnormalities.
Objectives: To clarify whether nintedanib improves nailfold capillary abnormalities in patients with SSc complicated by ILD.
Methods: This study is a prospective observational study. Among patients diagnosed as having SSc according to the 2013 ACR/EULAR classification criteria, those who started to treat with nintedanib for ILD at our hospital from March 2020 to July 2022 were consecutively registered. The nailfold capillaries were evaluated using a nailfold videocapillaroscopy (NVC), capable of observation at 200x magnification. The evaluation was carried out using the current standardized method. [1] NVC was performed before drug induction and 1 year after drug induction. Only patients who had NVC testing up to 1 year later were included in the evaluation. At the same time, blood tests such as KL-6, SP-A, and SP-D, and respiratory function tests were evaluated. This study has been pre-approved by the Hiroshima University Hospital Ethics Committee. (OySTeR study: Optimal strategy in SSc Treatment for Recovery, approval number: E-1940-1)
Results: Eight patients were analyzed. The mean age was 59 ± 17 years. Female were 7 (87.5%). Six patients (75%) were positive for anti-Scl-70 antibodies. Details of other cases are listed in Table 1. Seven patients (87.5%) had a history of treatment with immunosuppressive therapies. The disease duration was less than 6 years in 5 patients, and 6 years or longer in the remaining 3. Five patients were able to continue nintedanib for 52 weeks: 1 patient discontinued nintedanib after 1 month due to abnormal liver function, 1 patient with diarrhea discontinued after 10 months. All of the patients who were able to continue oral administration were also reduced to 200 mg/day due to diarrhea. Baseline mean FVC, KL-6, SP-A, and SP-D are described in Table 1. The results by NVC pattern were Normal in 1 case, Early in 2 cases, Active in 1 case, Late in 3 cases, and Non-specific in 1 case. Quantitative baseline results for the NVC tests were capillary density (number of capillaries) 5.8 ± 2.2/mm, enlarged capillary score 0.91 ± 0.83, giant capillary score 0.31 ± 0.30, and hemorrhage score 0.22 ± 0.27. 1 year later, the NVC pattern deteriorated from early to active in only one case, but the others remained unchanged. Quantitative results for the NVC test were capillary density 5.8 ± 2.3/mm, enlarged capillary score 0.98 ± 0.95, giant capillary score 0.38 ± 0.48, and hemorrhage score 0.20 ± 0.33. Mean FVC, KL-6, SP-A, and SP-D after 1 year are also shown in Table 1.
Conclusion: Nintedanib tended to improve ILD biomarkers and pulmonary function test results in patients with SSc, but did not improve nailfold capillary abnormalities. Based on this result, combination therapy is preferable to nintedanib alone for improving the pathology of SSc.
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Table 1. Comparison of laboratory data and NVC test results at baseline and after 1 year

	Baseline (N=8)	1 year later (N=8)
Age(year)	**59 ± 17**	**60 ± 17**
Sex	**Female: 7 (87.5%)**	
Antibody	**Anti-Scl-70: 6(75%)**	
	Anti-RNA polymerase III: 1 (12.5%)	
	Negative: 1 (12.5%)	
FVC (mL)	**1673 ± 465**	**1722 ± 504**
KL-6 (U/mL)	**1241 ± 824**	**977 ± 732**
SP-A (ng/mL)	**49.4 ± 15.7**	**51.5 ± 12.6**
SP-D (ng/mL)	**179 ± 105**	**147 ± 95**
NVC pattern		
Normal	**1**	**1**
Early	**2**	**1**
Active	**1**	**2**
Late	**3**	**3**
Non-specific	**1**	**1**
Density (/mm)	**5.8 ± 2.2**	**5.8 ± 2.3**
Enlarged	**0.91 ± 0.83**	**0.98 ± 0.95**
Giant	**0.31 ± 0.30**	**0.38 ± 0.48**
Hemorrhage	**0.22 ± 0.27**	**0.20 ± 0.33**

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AB0901 FUNCTIONAL CAPACITY, BODY COMPOSITION AND DISEASE ACTIVITY ARE ASSOCIATED WITH QUALITY OF LIFE IN PATIENTS WITH MYOSITIS

Keywords: Outcome measures, Quality of life, Myositis

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Background: Idiopathic inflammatory myopathies – or briefly myositis – has cardinal traits of muscle weakness [1] and decreased muscle endurance [2] in addition to reduced quality of life (QoL) [3]. However, QoL is complex, and it is unclear which factors affect QoL in patients with myositis. Knowledge of these factors and potential associations to QoL is of importance for evoking changes to a better life for patients with myositis.
Objectives: To investigate the influence of functional capacity, muscle strength, body composition and disease activity and damage on QoL in patients with myositis.
Methods: Measures of functional capacity (functional index 3, 2-minute walk test, timed-up-and- go and 30-s sit-to-stand), muscle strength (5 repetitions maximum strength in leg press, bench press, cable row, knee extension, biceps curl and static handgrip strength; all expressed relative to body mass), leg extensor power (Nottingham Power Rig, relative to body mass), body composition (height adjusted appendicular lean mass and fat mass) and IMACS (International Myositis Assessment & Clinical Studies Group) disease activity and disease damage core set measures were analysed to investigate the impact on QoL (physical- and mental component summary in the Short Form 36 questionnaire (SF-36)).
Results: All functional capacity measures were positively correlated with the physical component summary (PCS); functional index 3 (r^2=0.15, p=0.03), 2-minute walk test (r^2=0.26, p=0.003), timed-up-and-go (r^2=0.14, p=0.03) and 30-sit-to-stand performance (r^2=0.15, p=0.03). Only leg press (r^2=0.15, p=0.04) showed a positive correlation with PCS for measures of muscle strength and power. For body composition, height-adjusted fat mass correlated negatively with PCS (r^2=0.20, p=0.01). Of the IMACS disease activity and disease damage core set measures, Health Assessment Questionnaire (r^2=0.40, p=0.0001), Physician Global Assessment of Disease Damage (r^2=0.44, p<0.001) and Patient Global Assessment of Disease Damage (r^2=0.18, p=0.02) were negatively correlated with PCS. In contrast, none of the investigated outcome parameters were correlated with the mental component summary of SF-36.
Conclusion: In the present group of patients with myositis, functional capacity and muscle strength had positive associations with the physical component summary of the QoL, indicating that future interventions should be directed to improve these factors to ultimately improve QoL. The Health Assessment Questionnaire and Patient/Physician Global Assessment of Disease Damage revealed strong correlations with PCS, supporting that both patient-reported outcome measures (PROMS) and clinician-reported outcomes are highly relevant QoL-related monitoring parameters in patients with myositis.
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AB0902

LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IS RARE BUT PROGNOSTICALLY IMPORTANT IN SYSTEMIC SCLEROSIS

Keywords: Cardiovascular disease, Systemic sclerosis, Heart

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Background: Reduced left ventricular ejection fraction (LVEF) occurs in only around 5% of unselected SSc cohorts [1]. Subclinical LV systolic dysfunction (LVSD) defined by advanced echocardiographic measures including global longitudinal strain (GLS) may be more prevalent [2].
Objectives: To quantify the frequency of LVSD in SSc as measured by LVEF and LV GLS, and its impact on survival and physical function.
Methods: Included participants in the Australian Scleroderma Cohort Study met ACR/EULAR criteria for SSc and had ≥1 echocardiographic LVEF measurement. Those with secondary causes of LVSD (ischaemia, valvular disease and PAH) were excluded. Chi squared tests, two sample t-tests or Kruskal Wallis tests were used for between group comparison as appropriate. Generalised estimating equations were used to model longitudinal data. Survival analyses were performed using Kaplan-Meier and Cox proportional hazard models.
Results: Of 1145 participants, 2.5% recorded a reduced of LVEF<50% during follow up; 14% had borderline LVEF of ≥50% but <55%; and 83% always a LVEF ≥55%. Only 0.6% ever had a LVEF≤40%. LVEF returned to normal in 66% of those who had recorded a LVEF<50%. Compared to those with normal LVEF, those with reduced LVEF were similar in age, more frequently male (p=0.01), with dcSSc (p<0.01), SSc renal crisis (p=0.02), synovitis (p=0.04) and higher inflammatory markers (p<0.02). Those with reduced LVEF more commonly had myositis (p<0.01), muscle atrophy (p=0.01) and proximal weakness (p<0.01). Use of prednisolone (p=0.03), IVIG (p<0.01), and cyclophosphamide (p<0.01) were more common in those with reduced LVEF. Survival was worse in those with reduced LVEF (Figure 1). Reduced LVEF was associated with a 2.8-fold increased risk of death (95% CI 1.3-6.3, p=0.01: Table 1). Physical function and quality of life were worse in those with reduced LVEF. Multivariate analyses identified shorter six minute walk distance (p=0.01), higher Health Assessment Questionnaire Disability Index scores (p<0.01) and lower Short Form 36 Physical Component Summary scores (p=0.02) in those with reduced LVEF. Participants with reduced LVEF were 3.9-times more likely to record WHO Class III/IV dyspnoea (95%CI 1.8-8.1, p<0.01). LV GLS data were available for 90% of participants at one centre (n=219). Abnormal LV GLS (> -17%) was seen in 30% of those with normal LVEF and 53% with borderline LVEF. LV GLS was lowest in those with reduced LVEF (-17.2%; IQR -14.9 – -18.0%) compared to those with normal (-19.5%; IQR -18.0 – -20.8%) or borderline LVEF (-18.3%; IQR -16.6 – -19.5%; p<0.01). Worst recorded GLS was associated with increased mortality (HR 1.3, 95%CI 1.0-1.6, p=0.02), although this association was attenuated in multivariate analyses (HR 1.2, 95%CI 1.0-1.5, p=0.10).
Conclusion: After excluding secondary causes, reduced LVEF in SSc is rare. Despite the relative infrequency, LVEF<50% is associated with a specific SSc phenotype, worse survival and physical function. Abnormal LV GLS is more prevalent in SSc, seen in 30-50% of those with persistent LVEF≥50%. Further data are required to define the threshold of LVSD in SSc, and to explore the utility of measures of subclinical LVSD such as LV GLS.
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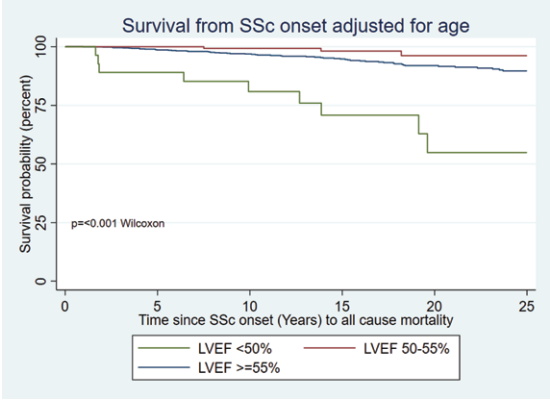


Figure 1. Age adjusted survival from SSc onset

Table 1. Cox proportional hazard model for all cause mortality

Disease feature	HR	95% CI	p value
Model 1 – Reduced LVEF			
LVEF<50%	2.8	1.8 - 6.3	0.01
Age at SSc onset (y)	1.1	1.1 - 1.1	<0.01
Male	2.4	1.3 - 4.5	0.01
LcSSc	0.4	0.2 - 0.7	<0.01
Raised CRP	1.6	1.0 - 2.7	0.08
SSc Renal Crisis	1.6	0.7 - 4.0	0.28
Peak RVSP	1.02	1.01 - 1.04	0.01
Model 2 – LV GLS			
Lowest LV GLS	1.2	1.0 - 1.5	0.10
Age at SSc onset (y)	1.1	1.0 - 1.1	0.01
Male	10.6	2.2 - 52.3	<0.01

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AB0903

EFFICACY AND SAFETY OF NINTEDANIB IN COMBINATION WITH IMMUNOSUPPRESSIVE AGENTS FOR PROGRESSIVE FIBROSING CTD-ILD IN CLINICAL PRACTICE

Keywords: Lungs

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Background: Nintedanib (NTB), a multitargeted tyrosine kinase inhibitor, has been approved in Japan for progressive fibrosing interstitial lung disease (PF-ILD) since May 2020 based on the results of the INBUILD trial [1]. This also made it a new treatment option for connective tissue disease (CTD) that are frequently complicated by ILD. On the other hand, the use of immunosuppressive agents in the treatment of ILD and primary diseases varies by disease type and country.

Objectives: The purpose of this study is to evaluate the efficacy and safety of NTB for progressive fibrosing CTD-ILD treated with immunosuppressive agents at a single center in Japan.

Methods: CTD-ILD patients who received NTB at our institution between 2020 and 2022 were extracted. Among CTD-ILD patients who received NTB, those who met the criteria for PF-ILD (1) were included in this analysis. Efficacy was evaluated by changes in forced vital capacity (FVC), and the monthly rate of decline in FVC (ΔFVC %/M) before and after the initiation of NTB. Changes in KL-6 (Krebs von den Lungen 6), a serum biomarker for ILD, were also analyzed. In addition, these efficacy parameters were compared between two groups; one group that received additional immunosuppressive agents at the same time as NTB administration (NTB+IS group), and the other group that received only NTB (NTB group). Safety was evaluated by the occurrence of adverse events within 12 months.

Results: There were 24 CTD-ILD patients (8 males and 16 females) who received NTB, all of whom met the criteria for PF-ILD. Patient characteristics are shown in Table 1. The most common primary disease was systemic sclerosis in 8 patients (33.3%), followed by polymyositis/dermatomyositis in 6 patients (25.0%). The mean FVC were 56.8±15.1 % and 1600.0±600.1 mL. Mean FVC increased at 6 and 12 months (ΔFVC %: +6.4 %/6M; +8.1 %/12M) and ΔFVC %/M improved from -0.65 %/M to +1.06 %/M after the initiation of NTB. Serum KL-6 decreased significantly at 6 and 12 months (ΔKL-6 U/mL: -233.7 U/mL/6M; -401.4 U/mL/12M). Eleven of the 24 patients received additional immunosuppressive agents at the same time as NTB administration (NTB+IS group). The immunosuppressive agents administrated concurrently were rituximab in 5 patients, glucocorticoids (>20 mg/day prednisone or equivalent) in 4, cyclophosphamide in 2, abatacept in 2, and mycophenolate mofetil in 1. In NTB + IS group, ΔFVC %/M was significantly improved compared with the 13 patients who received only NTB (NTB group) (+1.81%/M vs. +0.20%/M, respectively) (Figure 1). Adverse events (AEs) considered to be related to treatment were diarrhea in 13 patients, nausea in 2 patients, elevations in liver enzymes in 2 patients, and headache in 1 patient, and the dose of NTB was reduced in 11 patients. No patient discontinued NTB due to AEs.

Conclusion: NTB for progressive fibrosing CTD-ILD appeared to be effective and safe in clinical practice. The results also suggested that the combination of NTB and immunosuppressive agents may be an effective treatment strategy. Because this was a small, single-center, observational study, further research is needed to clarify the type and timing of immunosuppressive agents to be used in combination.

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Table 1. Patient characteristics (n =24).

Age, mean±SD, years	65.3±10.7
Sex, Female, number (%)	16 (66.7)
Disease duration, mean±SD, years	8.5±7.7
Primary connective tissue diseases	
Systemic sclerosis, n (%)	8 (33.3)
Polymyositis, Dermatomyositis, n (%)	6 (25.0)
Rheumatoid arthritis, n (%)	4 (16.7)
Microscopic polyangiitis, n (%)	3 (12.5)
Others, n (%)	3 (12.5)
KL-6, mean±SD, U/mL	1479.0±967.9
FVC % of predicted value, mean±SD, %	56.8±15.1
FVC mL, mean±SD, mL	1600.0±600.1
Concomitant immunosuppressive agents	
Glucocorticoids , number (%)	19 (79.1)
Tacrolimus, n (%)	7 (29.2)
Mycophenolate mofetil, n (%)	5 (20.8)
Rituximab, n (%)	5 (20.8)
Azathioprine, n (%)	3 (12.5)
Abatacept, n (%)	2 (8.3)
Cyclophosphamide, n (%)	1 (4.2)

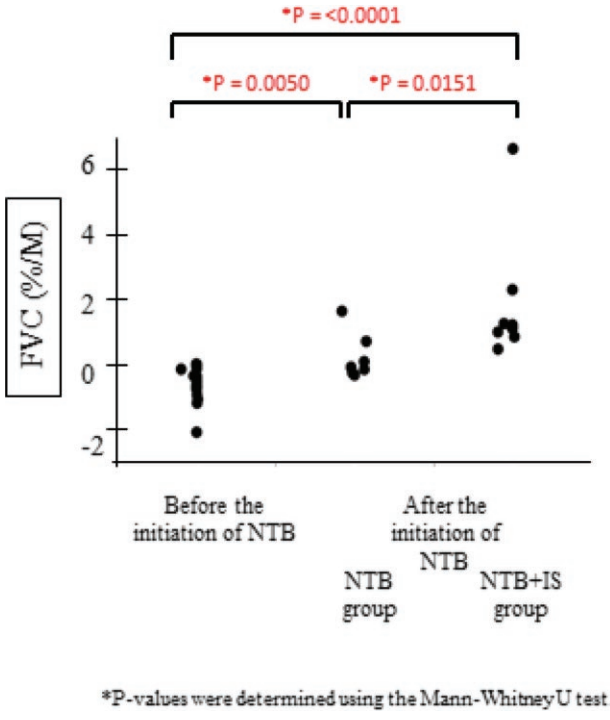


Figure 1. The monthly rate of decline in FVC before and after the initiation of NTB.

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AB0904

BELIMUMAB FOR THE TREATMENT OF INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS: A PHASE 2/3, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Keywords: Randomized control trial, Lungs, Systemic sclerosis

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Background: There is a breadth of evidence supporting a key role for abnormal B-cell function in the pathogenesis of systemic sclerosis and associated interstitial lung disease (SSc-ILD) [1,2]. A previous pilot study investigated the efficacy of belimumab, a recombinant human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody that binds to and neutralises B-lymphocyte stimulator (BLyS) subsequently inhibiting the survival of B cells [3], in reducing modified Rodnan skin score (mRSS) in 20 patients with SSc [4]. Belimumab is well tolerated and is approved for the treatment of patients with active systemic lupus erythematosus and active lupus nephritis receiving standard therapy [5]. We hypothesise that by reducing the number of B cells and dampening B-cell effector functions in the circulation and tissue, belimumab will reduce inflammation and fibrosis across multiple organ systems in patients with SSc. This will result in the stabilisation of, and/or reduction in, lung function decline and skin thickening in SSc, and improvements in patients' quality of life.

Objectives: To present the design of a randomised controlled trial that will evaluate the efficacy and safety of subcutaneous (SC) belimumab versus placebo in adult patients with SSc-ILD.

Methods: In this global, parallel-group, Phase 2/3, randomised, double-blind, placebo-controlled, two-arm, 52-week study (GSK Study 218224), eligible adults with a documented diagnosis of SSc and ILD (as confirmed by high-resolution computed tomography) will be randomised 1:1 to receive either belimumab 200 mg SC weekly (Arm 1), or matching SC placebo weekly (Arm 2), for 52 weeks (**Figure 1**). Participants will be permitted to continue their stable doses of standard therapy throughout the study. The primary endpoint of the study is absolute change from baseline in forced vital capacity (ml) at Week 52. Key secondary endpoints, analysed at Week 52, include: absolute change from baseline in mRSS, absolute change from baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score, and SSc progression or death. Patient-reported outcomes (listed in the **Figure 1**) will also be assessed. A comprehensive biomarker approach will be implemented to evaluate the belimumab modulating effects on key biological processes involved in SSc pathogenesis (fibrosis and inflammation) in circulation and in skin biopsies. Safety will be monitored throughout the study.

Results: Target sample size is planned to be approximately 300 patients, with 150 patients per arm.

Conclusion: We present the design of a global Phase 2/3 study that will test the efficacy and safety of SC belimumab in patients with SSc-ILD. Together, the study endpoints enable the assessment of the efficacy of belimumab on a broad range of disease manifestations, disease progression, and impact on patient burden and survival.

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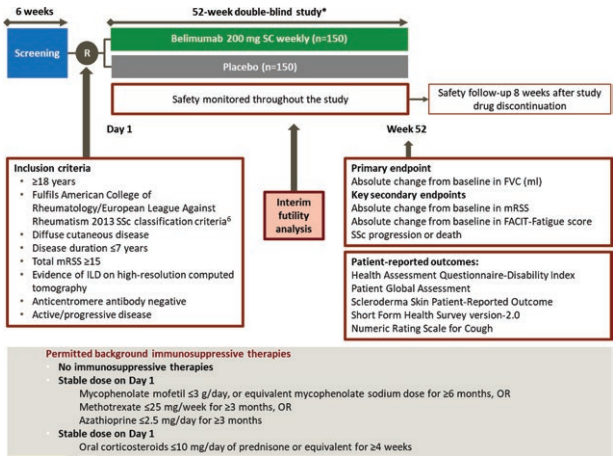


Figure 1. Study design *An open-label extension will be performed. FVC, forced vital capacity; R, randomisation

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AB0905

DEVELOPMENT OF A NEW COMPREHENSIVE ASSAY KIT FOR MYOSITIS-ASSOCIATED ANTIBODIES AND MYOSITIS-SPECIFIC ANTIBODIES EXAMINATION OF CLINICAL USEFULNESS IN INFLAMMATORY MUSCLE DISEASES

Keywords: Autoantibodies, Myositis

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Background: Inflammatory muscle diseases are systemic inflammatory disorders that affect not only muscles but also skin, joints, lungs, and heart. Dermatomyositis (DM) and polymyositis (PM) are characterized by the production of antibodies. Measurement of these antibodies is useful for diagnosis, classification of disease type, evaluation of disease activity, prognosis prediction, and determination of therapeutic strategy. However, the sensitivity and specificity vary depending on the measurement method, and some autoantibodies can only be measured in limited laboratories.

Objectives: We developed a novel comprehensive assay kit for myositis-associated antibodies with the aim of developing a rapid and simple detection method for myositis-specific or related autoantibodies. we used a proteome-wide antibody screening and quantification with wet protein arrays consisting of proteins synthesized from proteome-wide human cDNA library (HuPEX). We examined whether this assay kit is clinically useful compared to enzyme-linked immunosolbent assay (ELISA).

Methods: Sera from 47 patients diagnosed or suspected of inflammatory muscle disease were used to measure myositis-specific autoantibodies (anti-ARS, anti-MDA5, anti-TIF1-γ, anti-Mi-2, and anti-SRP, antibodies) and myositis-related autoantibodies (anti-U1RNP, anti-Ku, and anti-PM-Scl, anti-mitochondria antibodies) were measured using a proteome-wide antibody screening and quantification with wet protein arrays consisting of proteins synthesized from proteome-wide human cDNA library (HuPEX) and compared with the results of ELISA, which is commercially available and immunoprecipitation with some autoantibodies (anti-OJ, anti-Zo antibodies). Autoantibodies that were undetectable by the ELISA and positive only on the array were subjected to immunoprecipitation. In immunoprecipitation, primary antibody added to a solution containing an antigen to form an antigen-antibody complex in the solution. Next, a secondary antibody immobilized on the beads is added to adsorb the antigen-antibody complex to the beads. Finally, the antigen was eluted from the beads using SDS and analyzed using SDS-PAGE.

Results: In the 47 cases, the clinical diagnosis was DM in 26 cases, PM in 20 cases, and inclusion body myositis in 1 case. In the ELISA commercially available, 20 cases of anti-ARS antibody (17 cases of DM, 3 cases of PM), 5 cases of anti-MDA5 antibody (Amyopathic DM), 1 case of anti-TIF1-γ antibody (DM), 2 cases of Mi-2 antibody (1 case of DM, 1 case of PM), 2 cases of anti-RNP antibody (PM), and 2 cases of anti-mitochondria antibody (PM).

Compared with the results measured by the ELISA commercially available, eighteen of the 20 cases were positive for anti-ARS antibodies using the proteome-wide antibody screening system and all other autoantibodies were 100% concordant.

In addition, 1 case of DM in which autoantibodies could not be detected by the ELISA was positive for anti-OJ antibody by the proteome-wide antibody screening system. Of the 6 PM cases whose autoantibodies could not be detected by the ELISA, 1 was anti-HMGCR antibody-positive and 1 was anti-Zo antibody-positive, consistent with the clinical diagnosis. Furthermore, among the 4 PM cases who were positive only for anti-SS-A antibody by ELISA, 2 were anti-SRP antibody positive, 1 was anti-Ku antibody positive, and 1 was anti-Ki antibody positive by the proteome-wide antibody screening system. Those samples that could be detected by the array were also confirmed to be positive by immunoprecipitation.

Conclusion: Collectively, proteome-wide screening of antibodies using the *in vitro* proteome can reveal the myositis-associated antibodies of patients and may provide novel clinical biomarkers.

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AB0906 SEVERITY OF DIGESTIVE AFFECTATION IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Gastrointestinal tract

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Background: Almost 90% of patients with systemic sclerosis (SSc), both the diffuse and limited forms, have gastrointestinal (GI) involvement, which leads to increased morbidity and mortality. The UCLA SCTC GIT 2.0 questionnaire has been used to assess the severity of digestive involvement in patients with SSc.

Objectives: To describe the severity of digestive involvement in a series of patients with SSc and identify factors associated with the severity of digestive involvement.

Methods: ***Design***: Cross-sectional study of a series of cases with SSc from the Regional University Hospital of Malaga recruited between January and December 2022. ***Protocol***: Patients with SSc are regularly followed up in rheumatology clinic, are registered in a database, and they were consecutively invited to participate in this study. The study was approved by the Ethics Committee (Code 1719-N-15) following the recommendations of the Declaration of Helsinki and current legal regulations for Good Clinical Practice. ***The main outcome***: severity of digestive involvement measured by the UCLA SCTC GIT 2.0 questionnaire (total GIT). This questionnaire includes 34 items and 7 multi-item scales (reflux, bloating/swelling, diarrhoea, fecal soiling, constipation, emotional well-being and social functioning) and a total GIT score to assess health-related quality of life (HRQoL) and the severity of GI symptoms in SSc. Total GIT was categorized as follows: (1) none to mild severity from 0.00 to 0.49; (2) moderate from 0.5 to 1.0; and (3) severe to very severe from 1.01 to 3.0. ***Other variables*** included were: epidemiological characteristics, clinical and analytical manifestations, including modified Rodnan skin score (mRSS). ***Statistical analysis***: descriptive, bivariate and multivariate to identify factors associated with the severity of digestive involvement in patients with SSc.

Results: 52 patients were included, 98.1% were women with a mean (SD) age of 60.8 (11.1) years. The clinical-epidemiological characteristics of the included patients are shown in Table 1. A total of 49/51 patients (94.2%) had digestive involvement, of which 18/49 (34.6%) had mild involvement (UCLA 0.01-0.49), 14/49 (26.9%) moderate (UCLA 0.50-1.00) and 17/49 (32.7%) severe or very severe (UCLA 1.01-3.00). Correlations of total GIT were observed with skin thickness measured by mRSS (r=-0.394; p=0.004) and with HRQoL measured with VAS-EQ-5D (r=-3.77; p=0.006). The baseline variables that were independently associated with the severity of digestive involvement measured by UCLA were: skin extension measured by mRSS (β [95% CI] 0.026 [0.008-0.043]; p=0.004), quality of life measured by VAS-EQ-5D (β [95% CI] -0.009 [0.13, -0.15]; p=0.013]) and sex (β [95% CI] -0.942 [0.513, 1.370]; p< 0.001]).

Conclusion: Digestive involvement in SSc patients was frequent, and in almost a third of patients the involvement was severe or very severe. The variables associated with a greater severity of digestive involvement were male gender, low VAS-EQ-5D, and high mRSS.

Table 1. Clinical-epidemiological characteristics of patients with SSc.

Variable	SSc n= 52
Baseline clinical-epidemiological characteristics	
Sex, women, n (%)	51 (98.1)
Age, years, mean (SD)	60.83 (11.1)
Race, Caucasian, n (%)	52 (100.0)
Smoking history	
No smoker, n (%)	35 (67.3)
Smoker, n (%)	3 (5.8)
Ex-smoker, n (%)	14 (26.9)
Modified Rodnan skin score, mean (SD)	10.88 (9.1)
ANA, n (%)	50 (96.2)
Anticentromere, n (%)	28 (53.8)
AntiScl70, n (%)	10 (19.2)
Skin pattern	
Limited, n (%)	40 (76.9)
Diffuse, n (%)	12 (23.1)
BMI, Kg/m^2, mean (SD)	25.59 (4.6)
EQ-5D, mean (SD)	0.59 (0.25)
VAS-EQ-5D, mean (SD)	0.54 (21.6)
Weigh, mean (SD)	62.9 (10.6)
No weightloss, n (%)	27 (51.9)
Weightloss 1-3 Kg, n (%)	17 (32.7)
Weightloss > 3 Kg, n (%)	8 (15.4)
ILD, n (%)	17 (32.7)
PAH, n (%)	5 (9.6)

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Disclosure of Interests: None Declared.

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AB0907 HIGH EXPRESSION LEVELS OF TYPE I INTERFERON AND IP-10 IN ANTI-MDA5 ANTIBODY-POSITIVE DERMATOMYOSITIS AND ITS IMPLICATION IN THE PATHOGENESIS

Keywords: Myositis, Cytokines and chemokines, Biomarkers

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Background: Dermatomyositis (DM) patients with anti-melanoma differentiation-associated protein 5 (MDA5) antibodies (Ab) are likely to have rapidly progressing interstitial lung disease and a poor prognosis. Thus, it is important to understand the pathogenesis of the disease.
Objectives: The aim of this study was to identify humoral factor(s) that characterize anti-MDA5 Ab^+ DM and to analyze the cells that produce these factors.
Methods: Twenty-eight cytokines in the serum of patients with anti-MDA5 Ab^+ DM patients were screened and compared with the results of patients with other collagen vascular diseases. We also performed an immunohistochemical analysis of skin rashes (Gottron's signs) from two patients.
Results: Serum levels of interferon gamma-induced protein 10 (IP-10, CXCL10), one of CXCR3 chemokines, were significantly higher in anti-$MDA5^+$ DM patients than in SLE and anti-MDA5 Ab^- DM patients. Moreover, serum interferon (IFN) α2 levels were also higher in anti-$MDA5^+$ DM patients. After initiation of immunosuppressive therapy, IP-10 and IFN-α2 levels decreased rapidly, whereas those of IFN-γ and CXCL9, another CXCR3 chemokine, did not substantially decrease. Skin samples revealed that the IP-10 positive cells in the dermis were positive for CD68 antigen, a monocyte/macrophage marker. In contrast, they contained a few $CD8^+$ cells and almost no $CD4^+$ cells. We also stimulated monocytes from healthy controls with type I and II IFNs *in vitro* and demonstrated that IP-10 was produced in the culture supernatant in a dose-dependent manner.
Conclusion: Our results indicate that IP-10 is highly produced in DM patients with ant-MDA5 Abs. The levels of type I IFN were also high and even exceeded those of SLE. Several reports have shown that not only type II IFN but also type I IFN induces IP-10. Thus, type I IFN/IP-10 axis may play an important role in the pathogenesis of anti-MDA5 Ab^+ DM. Our immunohistochemical analysis of the skin also revealed that IP-10 released from macrophages may prompt infiltration of macrophages themselves, constituting a positive feedback loop in the skin inflammation. Further analyses are required to prove the usefulness of IP-10 as a disease activity and/or prognostic marker of DM with anti-MDA5 Abs.
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Disclosure of Interests: Kojiro Sato Grant/research support from: Asahi Kasei Pharma, Boehringer-Ingelheim, Teijin Pharma, Tanabe-Mitsubishi, and Chugai, Ayako Kokuzawa: None declared, Jun Nakamura: None declared, Yasuyuki Kamata: None declared.
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AB0908 SCREENING AND ANALYSIS OF POSSIBLE DRUGS BINDING TO PDGFRA: A MOLECULAR MODELING STUDY

Keywords: Targeted synthetic drugs, Systemic sclerosis, Disease-modifying Drugs (DMARDs)

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Background: The platelet-derived growth factor receptor (PDGFR) is a membrane tyrosine kinase receptor involved in several metabolic pathways, mainly in tumor progression [1, 2], immune-mediated diseases [3-4], and viral diseases [5].
Objectives: Considering this macromolecule as a druggable target for modulation/inhibition of these conditions, the aim of this work was to find new ligands or new information to design novel effective drugs.
Methods: We performed an initial interaction screening with the human intracellular PDGFRα of about 7200 drugs and natural compounds contained in five independent databases/libraries, implemented in the MTiOpenScreen web server. After selection of 27 compounds, a structural analysis (in particular, molecular docking and molecular dynamics analysis, using SwissDock based on EADock DSS algorithm [6, 7] and GROMACS [8], respectively) of the complexes obtained was performed. Three-dimensional quantitative structure–activity relationship and ADMET analyses were also performed to understand physicochemical properties of that compound to increase affinity and selectivity.
Results: Among these 27 compounds, the drugs Bafetinib, Radotinib, Flumatinib and Imatinib showed the higher affinity for this tyrosine kinase receptor, lying in the nanomolar order, while the natural products, such as curcumin, luteolin and EGCG, included in this group showed submicromolar affinities. All these compounds, through the QSAR and ADMET analysis, provided physicochemical information about an ideal best ligand for PDGFRα.
Conclusion: Although experimental studies are recommended, the structural information obtained could provide useful insight into the future development of PDGFRα inhibitors.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0909 IMMUNOEXPRESSION OF TGFB1 IN SKIN IN SYSTEMIC SCLEROSIS

Keywords: Prognostic factors, Systemic sclerosis, Diagnostic Tests

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Background: TGF-β pleiotropic functions in inflammation, fibrosis, and vascular remodeling suggest that TGF-β signaling could play a central role as a link between fibrosis and vasculopathy characteristic of SSc. Moreover high mRNA level of TGF β1 in whole blood and high immunoexpression in tissues in SSc patients confirms its role in the SSc pathogenesis.
Objectives: The aim of this study was to determine TGFβ1 immunoexpression in the skin of patients with systemic sclerosis.
Methods: Skin biopsies from 14 patients with SSc (7 female and 7 male) at median age 60 years (19-69) were analyzed by immunohistochemistry method using anti-TGFβ1 primary mouse monoclonal antibody IgG (Abcam, Cambridge, UK; ab190503). Morphological analysis has been conducted by Hematoxylin and eosin (H&E) staining and Masson trichrome staining. The sections were examined using a light microscope Olympus BX 41 (Olympus, Hamburg, Germany). **Patients**. Women and men in the study group did

not statistically differ in age. Men were characterized by significantly higher CRP (p=0.03) but not ESR (p>0.99). In the study group, women were more often characterized by irreversible fibrotic lesions in lungs (HRCT=5), but the frequency of occurence was not statistically significant (p=0.56). Men were characterized by higher mRSS than women, but the difference was not statistically significant (p=0.14).

Results: Histological analysis of the human skin biopsies from patients with systemic sclerosis revealed perivascular edemas, flattening of the dermal papilla and excessive accumulation of collagen in the papillary and reticular layers of the dermis (Figure 1A, B). The fibrosis of the dermis was manifested by the presence of numerous bunches of irregularly distributed collagen fibers (Figure 1B). Moreover, perivascular focal infiltrations of inflammatory cells and reduction of blood vessel density were observed. In the human skin biopsies from patients with systemic sclerosis TGFβ1-positive cells were observed (Figure 1C, D, E). The cells showed various cytoplasmic immunoexpression of TGFβ1 (brown-stained cytoplasm) in keratinocytes (mainly in the basal layer of epidermis) and in fibroblasts of the dermis.

Conclusion: High immunoexpression of TGFβ1 is correlated with mRNA level observed in whole blood in patients with SSc. Patients with limited SSc are characterized by weaker staining in skin biopsy than patients with diffuse SSc. Determination of mRNA TGF β1 level in whole blood seems to be a good diagnostic marker of SSc.

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[1] AB0603 PDGFA AS A POTENTIAL BLOOD MARKER IN DSSC

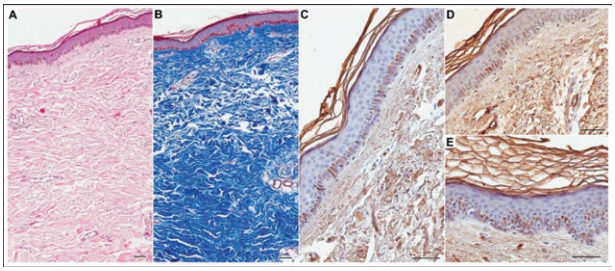


Figure 1. Representative light micrographs of H&E-stained (A), Masson trichrome-stained (B) and TGFβ1 immunostained (C, D, E) human skin biopsies from patients with systemic sclerosis. Skin of patients with systemic sclerosis was characterized by flattening of dermal papilla (A) and fibrosis in papillary and reticular layers of dermis – blue-stained collagen fibers (B). The cytoplasmic immunolocalization of TGFβ1 (brown color) was revealed in the fibroblasts localized in the dermis and keratinocytes in the basal layer of the epidermis. Scale bar - 50 µm.

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Disclosure of Interests: None Declared.

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AB0910 GASTRIC DYSRHYTHMIAS IN PATIENTS WITH EARLY SYSTEMIC SCLEROSIS PROSPECTIVE CROSS-SECTIONAL STUDY

Keywords: Systemic sclerosis, Gastrointestinal tract, Descriptive Studies

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Background: Systemic sclerosis (SSc) is an autoimmune disorder characterized by vasculopathy and fibrosis of skin and internal organs. Gastrointestinal (GI) system is affected in up to 90% of patients and dysmotility is the primary abnormality [1]. Gastric dismotility contributes to esophageal symptoms and causes nausea, vomiting, abdominal bloating, and early satiety. It also impacts quality of life and when severe is associated with increased mortality [2]. GI dysmotility can be evaluated with Electrogastrography (EGG), a non-invasive and safe test. It measures gastric myoelectrical activity, and when impaired it predicts delayed gastric emptying with an accuracy of 85% [3]. To the date gastric involvement in patients with early SSc has not been directly studied.

Objectives: Describe the prevalence of gastric dysrhythmias in early SSc and the association between GI symptoms and GI dysmotility.

Methods: SSc patients fulfilling the 2013 ACR/EULAR classification criteria with early disease (≤ 3 years from the first non-Raynaud symptom) were included and cross-sectionally assessed. Pregnancy and Diabetes Mellitus were exclusion criteria. All patients signed informed consent. GI symptoms were assessed using the UCLA GIT 2.0 questionnaire [4]. Gastric myoelectrical activity was measured using surface EGG and informed as preprandial, postprandial or continuous brady or tachygastria. Continuous bradygastria was considered a severe abnormality. It was informed by an expert gastroenterologist blinded to patient characteristics. Statistical analyses: Categorical variables were described as frequencies and percentages, and quantitative variables as mean, SD and IQR. The associations between variables were analyzed using the Fisher exact test. Statistical significancy was defined as $p < 0,05$

Results: 30 patients were included, 96,6 % were female, with a mean age of 48.7 years (25–72 years). SSc was limited in 76.6%. 14/28 patients had an anticentromere antinuclear antibody pattern and 6 had anti Scl 70. Organ involvement was interstitial lung disease in 7/29, altered echocardiogram in 10/25 and erosive esophagitis in 11/15. Half of the patients were under immunosuppressive treatment, 43% on methotrexate and 50% mycophenolate. EGG was abnormal in 28/29 patients, 71.4% had bradygastria, 10.7% tachygastria an 17.8% mixed. Bradygastria was mostly preprandial (45%) and continuous (50%). According to the UCLA GIT 2.0 questionnaire, two thirds of the patients had a moderate to severe GI involvement. Other score items are described in Table 1. There was no correlation between symptoms and severity of the gastric motility disorder, but the presence of bradygastria was associated to a worse social functioning score (p 0,018).

Conclusion: Gastric dysrhythmias, especially bradygastria occurs early in systemic sclerosis. Bradygastria was associated with a worse social functioning score.

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Table 1. UCLA STCT GIT 2.0 Score results

Scales	None to mild	Moderate	Severe
Total GIT Score	11 (36,7%)	12 (40%)	7 (23,3%)
Reflux	14 (46,7%)	9 (30%)	7 (23,3%)
Distension bloating	13 (43,3%)	4 (13,4%)	13 (43,3%)
Emotional wellbeing	13 (43,3%)	6 (20%)	11 (36,7%)
Social functioning	13 (43,3%)	14 (46,7%)	3 (10%)

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0911 EFFICACY OF LOW-DOSE IL-2 IN PATIENTS WITH MYOSITIS

Keywords: Cytokines and chemokines, Myositis

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Background: Idiopathic inflammatory myopathies (IIMs) are a group of rare and heterogeneous muscle inflammatory diseases characterized by disturbances of regulatory T(Treg) cells. Interleukin (IL)-2 has been rediscovered as a pivotal cell population in the control of autoimmunity, which effectively relieves idiopathic inflammatory myopathies(IIMs) such as polymyositis(PM) and dermatomyositis (DM).

Objectives: This study aimed to systematically evaluate the efficacy of low-dose IL-2 therapy in PM, DM, and IIMs.

Methods: Systematic searches of PubMed, EMBASE, Web of Science, the Cochrane Library and Medline, CNKI, CBM, and Technology Journal Database were performed. Original case reports, case series, observational studies, and clinical trials reporting the changes in the numbers of lymphocyte subsets on

PM, DM, and IIMs patients treated with IL-2 were included. A random-effects meta-analysis was performed to calculate the pooled efficacy. Inconsistency was evaluated by using the I^2, and Egger tests were used for the evaluation of potential publication bias (STATA v.12.0)

Results: A total of 5 studies comprising 401 patients were identified(Table 1).The CDASI scores were significantly decreased after IL-2 treatment[SMD=-1.146, 95%CI (-1.591,-0.700), P<0.001].Besides, the number of Tregs cells was significantly increased[SMD=-1.146, 95%CI (-1.591,-0.700), P=0.007], and the subgroup analysis was performed based on the dose of IL-2(Figure 1).

Conclusion: Low-dose IL-2 was promising in the treatment of DM, PM, and IMMs, which could promote the proliferation and functional recovery of Tregs.

Table 1. Available evidence including patients with DM, PM, and IIMs treated with low-dose IL-2.

Study.Year.	Patients (include in analysis)	Gender (female %)	Types of disease	Dosage	CDASI	Tregs
Yunzhi 2022.	13(13)	NA	IIMs	1 million IU every other day	before:12±7.04 after:3±4.07	NA
Min Feng. 2019.	35(35)	NA	DM	0.5 million IU per day for 5 days	NA	before:8.1±7.59 after:20.71±14.47
M. T. Qiu. 2020.	320(320)	NA	PM/DM	NA	before:7.14±5.72 after:10±7.14	before:25.71±22.85 after:31.43±25.72
M.Miao. 2020.	15(15)	NA	IIMs	1 million IU every other day	before:7±5.19 after:2±2.96	before:8.18±4.27 after:15.2±2.69
Miao Miao. 2021.	18(18)	NA	IIMs	1 million IU every other day	before:7±6.30 after:2±5.19	before:52.01±8.21 after:84.31±20.25

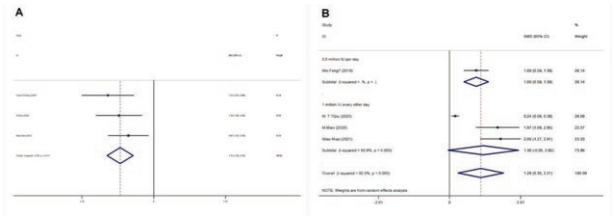


Figure 1. The efficacy of low-dose IL-2 therapy in PM, DM and IIMs treatment.(A) CDASI scores.(B) the numbers of Tregs cells.

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AB0912

RP-ILD IN PATIENTS WITH ANTI-MDA5 POSITIVE ANTIBODIES: CLINICAL EVALUATION AND PROGNOSIS. RETROSPECTIVE DATA FROM A SINGLE CENTER COHORT

Keywords: Lungs, Myositis

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Background: Patients with anti-melanoma differentiation-associated gene 5 antibody-positive (anti-MDA5+) dermatomyositis (DM) often develop a rapidly progressive interstitial lung disease (RP-ILD) associated with high mortality [1].

Objectives: to evaluate clinical features and prognosis of patients with anti-MDA5+ DM who developed RP-ILD.

Methods: Anti-MDA5+ patients were selected from a single center cohort of 198 idiopathic inflammatory myopathies (IIM) patients. Data were collected retrospectively. Onset clinical manifestations considered were muscle, joint, skin and lung involvement. All patients underwent chest high resolution computed tomography (HRCT). RP-ILD was defined by hypoxemia and dyspnea associated with radiological worsening within 3 months from pulmonary symptoms onset [2]. The dosage of ferritin during the follow up was also evaluated. Muscle involvement was assessed by myocytolysis indexes and Manual Muscle Test 8 (MMT-8). Joint and skin involvement was defined by clinical judgment. The therapeutic approach and the clinical outcome were also considered for each patient.

Results: based on inclusion criteria 11 patients were identified, 7 males and 4 females, aged between 30 and 67 years (mean age 55.54±9.58 years). The duration of the follow-up was 19.9±24.25 months. Cutaneous, pulmonary, joint and muscle involvement at onset were 63%, 36%, 36% and 9% respectively. Complete clinical and serological data are shown in Table 1. Ten patients (91%) develop ILD and the most frequently observed radiological pattern was organizing pneumonia (OP) found in 60% of cases, followed by OP/Nonspecific interstitial pneumonia (NSIP) (30%), NSIP (10%). During the disease course, 60% of patients with ILD developed RP-ILD with a mean time of 7.8±7.13 months from onset. RP-ILD patients showed a higher mean ferritin level than in those without (mean 13506±2219.05 vs 473±538.33 ug/L). Immunosuppressive therapy in all RP-ILD patients was based on cyclophosphamide plus tacrolimus and/or plasmapheresis. Two patients underwent extracorporeal membrane oxygenation. Four patients with RP-ILD died (66%), one from SARS-CoV-2 infection and three from respiratory failure. None of the patients with non-RP-ILD died.

Conclusion: in our cohort RP-ILD occurred in 60% of patients with MDA5+ ILD and was characterized by elevated ferritin levels. An intense immunosuppressive combination therapeutic scheme was always required. Nevertheless, mortality rate remained high.

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Table 1. Patient's clinical and serological features

Patient	Sex	Age	Associated antibodies	Clinical manifestations		ILD		Ferritin (ug/L)	Induction therapy				Outcome		
				At onset	During follow-up	Radiological pattern	RP ILD		Steroid Pulses* (mg)	N° of Cyc infusions **	Tacrolimus/ die (mg)	Plasmapheresis (n° of session)	ECMO	Alive	Improved	PM
1	F	51	Anti-Ro52, ACPA	C	A	-	N	1091	250	-	-	-	-	Y	Y	N
2	M	59	Anti-Ro52	C	P	OP/NSIP	N	-	-	6	-	-	-	Y	Y	N
3	M	67	Anti-Ro52	C, P	-	OP/NSIP	Y	5777	1000	1	-	3	N	N	-	N
4	F	48	Anti-Ro52	A	C	OP #	N	-	500	6	-	-	-	Y	Y	Y
5	M	30	-	C	P	OP	Y	1566	500	6	4	-	N	Y	Y	Y
6	M	55	Anti-Ro52, RF, ACPA	P, C	-	OP	Y	5879	500	1	4	6	N	N	-	Y
7	F	61	-	P	C, A	OP/NSIP	Y	743	500	6	4	5	N	Y	Y	N
8	F	56	-	P	C, A	OP	N	222	125	-	4	-	-	Y	Y	N
9	M	60	RF, ACPA	A	P	NSIP	Y	2400	1000	2	-	3	Y	N	-	N
10	M	55	Anti Jo-1	C, A	-	OP #	N	106	125	-	2	-	-	Y	Y	N
11	M	58	Anti-Ro52	C, A, M	P	OP	Y	4670	500	1	-	7	Y	N	-	N

RF, rheumatoid factor; **ACPA,** anti-citrullinated protein antibodies; **OP,** organizing pneumonia; **NSIP**, nonspecific interstitial pneumonia; **C,** Cutaneous; **A,** Articular; **P,** Pulmonary; **Cyc,** cyclophosphamide **750 mg/m2/month; **MMF,** mycophenolate mofetil; **ECMO,** Extracorporeal Membrane Oxygenation; **PM,** pneumomediastinum; *Administered for three consecutive days; # Asymptomatic ILD; **Y,** Yes; **N,** No.

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Disclosure of Interests: None Declared.
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AB0913

MORTALITY AND ASSOCIATED FACTORS IN 44 PATIENTS WITH SYSTEMIC SCLEROSIS ASSOCIATED PULMONARY ARTERIAL HYPERTENSION FROM TURKEY

Keywords: Systemic sclerosis

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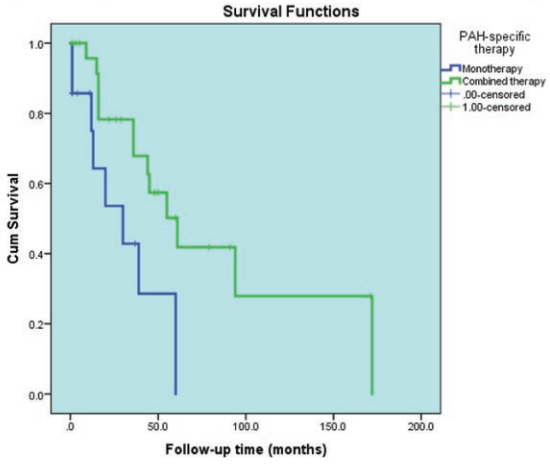
Background: Pulmonary arterial hypertension (PAH) is a severe complication of systemic sclerosis with high mortality. Although new drugs and treatment strategies developed in the last years, the prognosis of prevalent patients has not been sufficiently improved.
Objectives: We aimed to analyze the prevalence, mortality, and prognostic factors in patients with SSc-PAH from our single-center SSc cohort.
Methods: We retrospectively evaluated the association between mortality and demographics, transthoracic echocardiography, right heart catheterization (RHC) and pulmonary function parameters at baseline, and treatment modalities in patients with SSc-PAH that have been assessed and followed up by a multi-disciplinary team.
Results: Forty-four (10.6%) out of 415 patients with SSc were diagnosed as SSc-PAH in 2008-2022. The mean age was 56.6±13.5 years, and 23 (52.3%) patients were deceased during a median follow-up of 45 months. The survival rates were 91% for the first year, 75% for 2 years, 68% for 3 years, and 43.1% for 5 years. The available causes of death were a cardiopulmonary failure in 6 (26%), infection in 6 (26.1%) including one with COVİD-19, and malignancy in 3 (13%) patients. Clinical and hemodynamic findings of the patients were given in Table 1.

Table 1. Demographic, serologic, clinical, and hemodynamic findings of SSc-PAH patients.

Demographics (n)			SSc-PAH
Men			2
Women			42
Clinical Characteristics (n)			
LcSSc			10
DcSSc			34
Digital ulcer			20
Gastrointestinal involvement			27
Arthritis			7
Renal crisis			2
Specific auto-antibodies (n)			
Anti-centromere			8
Anti-Scl 70			22
	Survived	**Died**	
Patient number (n,%) 21 (47.7) 23 (52.3)			
Pulmonary findings			**P-value**
Nonspecific interstitial pneumonia (NSIP)	8	7	**0.01**
Usual interstitial pneumonia (UIP)	2	7	
Echocardiography			
ePASP (mmHg)	49.3±12.2	67.0±26.9	**0.01**
RHC findings			
Systolic PAP (mm Hg), mean (SD)	49.7±15.1	56.2±15.9	0.15
Diastolic PAP (mm Hg), mean (SD)	16.6±3.3	19.6±8.2	0.15
mPAP (mm Hg), mean (SD)	30.7±6.2	34.1±10	0.18
RAP (mm Hg), mean (SD)	7.0±3.5	6.9±2.2	0.95
PVR WU	4.9±3.9	5.3±2.1	0.74
PCWP (mm Hg), mean (SD	11.5±3.0	11.2±3.6	0.70
CO (L/min), mean (SD)	5.0±1.3	3.9±1.2	**0.02**
CI (L/min/m2), mean (SD)	2.7±0.6	2.2±0.8	0.13
Respiratory function tests			
FVC (mL), mean (SD)	2241.7±460.7	1769.2±269.7	**0.001**
DLCO (%), mean (SD)	51.1±22.5	42±11	0.1
6 MWT, mean (SD)	270±160	200±164	0.23

The initial ePASP was significantly high, and cardiac output (CO), and FVC values were significantly lower in deceased patients. The patients who died had more UIP patterns compared to survived patients (Table 1). Initial PAH-specific therapy was monotherapy in 31 (70.5%) and dual therapy in 11 (25%) patients. Fifteen (34%) patients were switched to combined (dual or triple) therapy from monotherapy. Nine/fourteen (22.5%) patients on monotherapy and 13/26 (32.5%) patients on combined therapy died. Four patients could not be given specific therapy for various reasons. Bosentan (11.4%) as monotherapy, ambrisentan and tadalafil (9.1%) as combined therapy were more preferred during follow-up. Median survival time was significantly better on combined therapy compared to monotherapy (44 vs. 61 months, p=0.01) (Figure 1).
Conclusion: Our SSc-PAH cohort consisted of severe patients with a significant number of DcSSc group, ILD especially UIP pattern, anti-Scl-70 positivity, and low baseline FVC and DLCO values. FVC, CO, and 6-MWT were the parameters affecting survival during follow-up. Although combined therapy had better survival rates, poor long-term survival rates warranted the need for early and effective treatment modalities.

Figure 1: Kaplan-Meier survival curve of treatment in SSc-PAH patients.



REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0914

CARDIOVASCULAR RISK FACTORS ARE ASSOCIATED WITH INCREASED CRP LEVELS IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Cardiovascular disease, Comorbidities

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Background: Patients with systemic sclerosis (SSc) are known to have an elevated risk for cardiovascular diseases. Approximately 20-25% of all SSc patients have permanently elevated C-reactive protein (CRP) levels [1,2]. Higher CRP levels are known to be associated with metabolic syndrome and diabetes mellitus (DM) (3), two factors that contribute to cardiovascular risk.
Objectives: To investigate if permanently elevated CRP levels are associated with higher cardiovascular risk in a cohort of 65 patients with SSc.
Methods: Data analysis was carried out in R 4.1 using the packages dplyr, ggplot2, mice and MASS. 65 patients were enrolled in the study; 20 had permanently elevated CRP levels over two years before enrollment (CRP+ group), and 45 had normal CRP levels over 2 year prior enrollment (CRP- group). The following cardiovascular risk factors were selected as candidate predictors of CRP status: The Framingham Score, left and right carotid intima-media thickness (CIMT) on bilateral carotid ultrasound, pathological status of both carotids, presence of plaques in both carotids, number of plaques (0 if none), extent of largest plaque (0 if none), height, weight, body mass index (BMI), presence of arterial hypertension, history of smoking, packyears, DM type 2, chronic kidney disease, and a positive family history (cardiovascular event before the age of 65). We tested each variable as a bivariate predictor of CRP status in a logistic regression model. Subsequently, we used stepwise logistic regression based on the Akaike Information Criterion (AIC) to determine the optimal set of predictors. AIC evaluates model deviance in relation to the number of variables in the model, i.e., it can be used to find the optimal trade-off between model performance (predictive accuracy) and model complexity (number of predictors). Prior to logistic regression analysis, missing values in the dataset were replaced by means of multiple imputation.
Results: In the bivariate logistic regression analyses (Table 1), only the Framingham Score and DM2 were identified as significant predictors, both with a positive weight, i.e., a higher Framingham Score and the presence of DM2 in a given patient were predictive of permanently positive CRP status, respectively. However, due to relatively low sample size, model sensitivity was 65%, and specificity was 86.7%.

Cardiovascular risk factor	*OR*	*t-value*	*p-value*
Age [years]	1.00	0.34	.734
Framingham Score	1.02	2.18	**.033**
CIMT right/ left	1.28/ 1.20	0.84/ 0.86	.402/.395
CIMT pathological right/ left	0.86/ 1.03	-0.78/ 0.18	.440/.860
plaque right/ left	1.16/ 1.19	1.32/ 1.50	.191/.140
number of plaques right/ left	1.12/ 1.11	1.24/ 1.03	.221/.307
largest plaque right/ left [cm]	1.08/ 1.01	1.62/ 0.30	.110/.763
height [m]	1.20	0.29	.772
weight [kg]	1.01	1.75	.085
BMI [kg/m²]	1.02	1.76	.082
arterial hypertension	1.03	0.24	.808
history of smoking	1.14	1.12	.269
Packyears	1.00	0.48	.631
DM 2	1.49	2.03	**.046**
chronic kidney disease	1.12	0.68	.499
positive family history	1.07	0.45	.657

Conclusion: Permanently increased CRP levels are associated with higher Framingham scores and DM type 2 in SSc-patients. These findings are going to be validated in larger and longitudinal cohorts.

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Characters from table 1:

Title: Results of bivariate logistic regression analyses.

Footnotes: For each candidate predictor variable, the odds ratio (OR) along with its t-value and p-value are given. An OR greater than 1 indicates that a higher value in the respective candidate predictor variable (or response 'yes' for categorical candidate predictor variables) is associated with a higher probability of belonging to CRP-positive group.

Acknowledgements: We thank Dr. Marius Keute, an employee of Ortmann Statistics, for his support with statistical calculations.

Disclosure of Interests: Mohamed Gamal Abdelzaher: None declared, Daria Feldmann: None declared, Ursula Heilmeier: None declared, Ilona Jandova: None declared, Florian Kollert Employee of: Novartis, Reinhard Voll Speakers bureau: Novartis, Roche, Janssen, Galapagos, Pfizer, Astra Zeneca, Böhringer Ingelheim, Consultant of: Novartis, Roche, Janssen, Galapagos, Astra Zeneca, Böhringer Ingelheim, Grant/research support from: Novartis, Pfizer, BMS, Stephanie Finzel Speakers bureau: Novartis, Galapagos, Amgen, Abbvie, Paid instructor for: Novartis, Galapagos, Amgen, Abbvie, Consultant of: Novartis, Amgen, Novonordisk, Grant/research support from: Novartis, Sobi.

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AB0915 A STUDY ON THE ASSESSMENT OF CARDIOVASCULAR RISK AND CIMT IN PATIENTS OF SYSTEMIC SCLEROSIS AND CORRELATION OF CIMT WITH QRISK 3 AND DISEASE SEVERITY SCORE

Keywords: Comorbidities, Systemic sclerosis, Autoantibodies

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Background: Accelerated atherosclerosis is well-known in connective tissue disease however is less reported in Systemic Sclerosis. There is evidence that atherosclerosis occurs prematurely in Systemic sclerosis. The micro vascular disease is characteristic of SSc, but there is growing evidence of macro vascular disease in SSc patients. Several studies have evaluated the prevalence of atherosclerosis in carotid arteries in patients with SSc by ultrasonography. Increased CIMT and conventional CVD risk factors have well known association with future events of stroke and coronary heart disease.

Objectives:

1. To study the Cardiovascular risk and Carotid Intima medial thickness in patients of Systemic sclerosis and their correlation
2. To assess the Disease Severity by using MEDS score and its correlation with CIMT

Methods: Data of 72 patients including clinical, serological profile and treatment were recorded. Cardiovascular risk by QRISK 3 calculator, CIMT by Ultrasonography are used. Correlation between Cardiovascular profile with CIMT and disease severity were seen. Medsger disease severity score was used to estimate the disease severity. Thirty-four age comparable controls were included.

Results: A total of 72 SSc patients (lcSSc -27, dcSSc -45) were included in the study. F> M (11:1). The median duration of disease enrolled was 2.9 years and time to referral to a specialist was 1.28 years. On patient in our study developed Scleroderma renal crisis and one patient was diagnosed with Adenocarcinoma of lung. Lipid profile showed low HDL, high LDL, TG, Cholesterol as compared to controls. The mean CIMT of the patients showed a significant difference when compared to controls (0.58± 0.09 **vs** 0.56 ±0.10; p=<0.01).The mean mRSS was 23.99±10.44 and mean MEDS score was 8.68±2.76. Forty-three patients (59.7%) out of 72 had ILD documented by HRCT. NSIP in 22 (30.6%) and UIP in 21 (29.2%) patterns on HRCT were observed. The Severity of PAH (Mpap >20 mm Hg) is greater in lcSSc vs dcSSc (30.33±10.50 vs 28.42 ± 7.38). Cyclophosphamide, MMF were used as induction therapies mainly for treatment of ILD. The mean CIMT (0.58± 0.09) showed a significant positive correlation with QRISK3 however it is weak with rho=0.575, p value <0.001. The mean CIMT (0.58± 0.09 mm) showed a negative correlation with mRSS with rho = -0.145 and p value 0.224.

Conclusion: CIMT had positive correlation with PAH (significant, p=0.034) and QRISK3 (significant, p=<0.01). CIMT had negative correlation with mRSS. The mean CIMT showed no correlation with MEDS score.

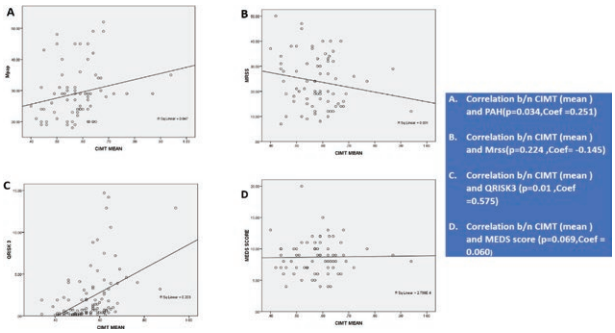


Figure 1. Spearman Correlation of CIMT with Mpap, Mrss, QRISK 3 and MEDS score

Table 1. Clinical parameters and frequency in SSc Subsets:

Parameter	Lcssc n=27 (%)	Dcssc n=45 (%)	P value
Raynaud's phenomenon	25 (92.6%)	45(100%)	0.137
Weight loss	6(22.2%)	16(35.6%)	0.234
GERD	20(74.1%)	30(66.7%)	0.509
Dysphagia	9(33.3%)	12(26.7%)	0.547
Digital ulcers	7(25.9%)	19(42.2%)	0.163
Arthritis	8 (29.6%)	13(28.9%)	0.947
Cardiac conduction block	2(7.4%)	6(13.3%)	0.439
Renal disease	0	1(SRC)	
ILD	17(63%)	26(57.8%)	0.664
NSIP	6/17 (35.2%)	16/26(61.5%)	
UIP	11/17(65.8%)	10/26(38.4%)	
Hypertension	2(7.4%)	3(6.7%)	1.000
Hypothyroid	5 (18.5%)	8(17.8%)	0.937
Malignancy	0	1(Adenocarcinoma of lung)	
Resorption of digits	6(22.2%)	16(35.6%)	0.234
Tendon friction rub	0	6(13.3%)	**0.048**
Calcinosis	6(22.2%)	13(28.9%)	0.534
Digital pitting scars	12(44.4%)	27(60%)	0.200
Gangrene	3(11.1%)	13(28.9%)	0.079

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0916 IDIOPATHIC INFLAMMATORY MYOPATHIES: ABOUT 50 CASES

Keywords: Motor function, Myositis, Autoantibodies

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Background: Idiopathic inflammatory myopathies are rare autoimmune diseases that affect between two and ten people per million.
Objectives: The aim of our work is to describe the epidemiological, clinical and paraclinical characteristics of autoimmune inflammatory myopathies as well as the therapeutic modalities.
Methods: This is a retrospective study involving 50 inflammatory myopathy patients admitted to Ibn Sina Hospital's internal medicine department between January 2015 and June 2022.
Results: There were 50 patients, 37 women and 13 men (gender ratio M/F: 0. 35). The mean age of onset of symptoms was 45.8 years old, the mean age of diagnosis was 47.6 years old (extremes: 23 and 80 years old) and the mean time between onset of symptoms and positive diagnosis was 14.9 months. The main reason for hospitalization was muscle impairment in 98% of our patients. It was dominated by muscle weakness with a mean score of 3/5 and myalgia. Proximal involvement was predominant. No facial musculature involvement was reported. At the time of diagnosis, dysphagia was present in 42% of cases, and no dysphonia was reported. Cutaneous signs were observed in 78% of cases with erythroderma type 22%, Gottron's papules 20% and manicure sign 16%. General signs were found in 56% of cases predominantly asthenia and weight loss, arthralgia was present in 34.7% of cases. 20% of patients had heart disease, myocarditis type, pericarditis, and arrhythmia in 2 cases each, neurological disease was found in 16% of cases (pyramidal syndrome type in 5 (10%) cases and neurogenic disease in 3 (6%) cases). PID-type pulmonary disease was present in 24% of cases, with complications of pulmonary fibrosis in 4% of cases. Creatine phosphokinase was elevated in 76% of cases with a mean value of 2553 IU/L and extremes between 26 and 25000 IU/L. Fifteen patients at the time of diagnosis had normal CPK contrasting with clinical signs. LDH was increased in 73%, liver cytolysis in 73%, and biologic inflammatory syndrome in 51%. Electromyograms were performed in 80% of cases, showing a myogenic pattern in 82.5% of cases, associated with neurogenic involvement in 25% of cases. Muscle biopsy (performed in 75% of cases) confirmed the diagnosis in 27 patients (77.1%) and in 8 patients the biopsy was normal. Antinuclear antibodies were positive in 70% of the cases, anti-JO1 positive in 26% of the cases, 26.7% of the patients were anti-SSA positive, and 10% of the cases were anti-MI2 positive. The diagnosis was dermatomyositis in 36% of cases, anti-synthetase syndrome in 20% of cases and cancer-associated myositis in 10% (in 5 patients), and overlapping myositis in 28% of cases. No cases of necrotizing myopathies or inclusion myopathies have been reported. The types of neoplasia revealed by idiopathic inflammatory myopathies in our study were: poorly differentiated carcinoma in 3 cases on lymph node biopsies, poorly differentiated adenocarcinoma of metastatic lung in 1 case and one case had Hodgkin's lymphoma. The treatment was based on corticosteroid therapy for all cases. Corticosteroid therapy was associated with an immunosuppressant in 58% of cases (methotrexate in 38% of patients, cyclophosphamide in 20% of patients, azathioprine in 4 patients and 2 patients on MMF). In 32% of patients, IV immunoglobulin therapy was prescribed, and in 8%, Rituximab was prescribed. We found no deaths in our series, with 38% of cases going into complete remission.
Conclusion: The classification criteria for idiopathic inflammatory myopathies have been constantly changing. The diagnosis of inflammatory myopathy can currently be made in common practice when a patient's clinical, muscular histology, and serology support the diagnosis. The elimination of an associated cancer remains a challenge for the practitioner.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0917

A RANDOMIZED CONTROLLED PROSPECTIVE SINGLE-CENTER FEASIBILITY STUDY OF RHEOPHERESIS FOR RAYNAUD'S SYNDROME AND DIGITAL ULCERS IN SYSTEMIC SCLEROSIS (RHEACT) - PRESENTATION OF FIRST INTERIM RESULTS

Keywords: Randomized control trial, Systemic sclerosis

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Background: Raynaud's phenomenon (RP) and digital ulcers (DU) are frequent manifestations of Systemic Sclerosis (SSc). There are very few available approved drugs with varying efficacy. Rheopheresis (RheoP) is an extracorporeal apheresis technique used to treat microcirculatory disorders by improving blood viscosity. The effect of RheoP in SSc is currently unknown, and here, we report the interim results of the first patients.
Objectives: To determine the efficacy of RheoP compared to Standard of Care (SoC) intravenous iloprost on RCS and DU healing.
Methods: A *randomized controlled prospective single-center feasibility study of Rheopheresis for Raynaud's syndrome and Digital Ulcers in Systemic Sclerosis (RHEACT)* aims to investigate the efficacy of RheoP on the Raynaud Condition Score (RCS) as the primary outcome measure after 16 weeks from baseline. A planned number of 30 patients will be randomized in a 1:1:1 ratio to one of two RheoP treatment groups or assigned to the SoC control group.
Results: We here report the results of the first seven patients. The patient assigned to the RheoP1 group had a baseline Raynaud Condition Score (RCS of 8, which improved to 0 after 16 weeks (the primary endpoint). The two patients randomized to the RheoP2 had a baseline RCS of 8 and 6, respectively, which improved to 4 and stayed unchanged at 6 in the second patient. The four patients assigned to SoC had only minimal improvement. RheoP1 had a significantly lower RCS compared to RheoP2 and SoC at week 16 (*p<0.05). Furthermore, DU completely healed in patients with DU at baseline with either RheoP therapy and avoided amputation in one patient. Exemplary images are shown in figure 2 (A, baseline; B, at week 16).
Conclusion: RheoP improved the RCS and DU better than SoC (Iloprost) treatment alone and avoided amputation in one patient.

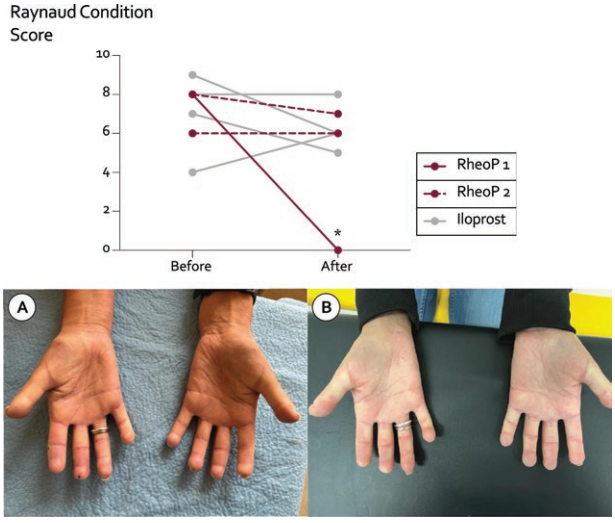


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
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AB0918

CLINICAL AND SEROLOGICAL FEATURES OF DERMATOMYOSITIS IN TUNISIA

Keywords: Myositis, Autoantibodies, Motor function

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Background: The spectrum of dermatomyositis (DM), as all idiopathic inflammatory myopathies (IIM), has been evolving steadily from a pathology characterized by muscle weakness and cutaneous rash to a disease with a wide range of systemic manifestations and various muscular phenotypes.
Objectives: The aim of our study was to describe the epidemiological, clinical and paraclinical features of DM in a Tunisian cohort.
Methods: We conducted a retrospective and monocentric study, over a 21-year period. All patients who fulfilled the 2017 ACR/EULAR classification criteria for IIM and were classified among the group "DM" were included.
Results: Among 85 patients with IIM, 46 were classified with DM (54%). The gender ratio (M/F) was 0,4. The mean age at diagnosis was 48,4 ± 14.8 years. Cutaneous manifestations revealed the diagnosis of DM in 82% of cases. Other revealing symptoms were: muscular weakness (20%), joint involvement (18%), pulmonary involvement (11%) and general symptoms (2.6%). Muscular weakness was noted in all patients, myalgia in 87% and amyotrophy in 11% of patients. Motor deficit was predominantly proximal and symmetric in all patients, affecting the hip flexors in 98% of cases, upper limbs in 87% and/or axial muscles in 28%. Distal muscles were affected in 11% of patients. Other involved muscle groups were: oesophageal muscles (59%), laryngeal muscles (15%) and myocardium (4%). High Creatine kinase levels were noted in 87 % of cases with a median level of 1896 IU/L [IQQ=861-4952]. Muscle biopsy, performed in 37 patients, showed perimysial infiltrate (44%), necrosis/regeneration foci (34%), endomysial infiltrate (31%), microangiopathy (16%), muscular atrophy (13%), perifascicular atrophy (9%) and interstitial fibrosis (6%). Cutaneous signs (100%) included eyelid erythema (85%), heliotropic rash (72%), Gottron's papules (61%), manicure sign (30%), Gottron's sign (22%), psoriasiform rash (22%), Raynaud syndrome (20%), vasculitis lesions (15%), telangiectasia (9%), skin ulcerations (9%), calcinosis (9%), skin necrosis (7%), panniculitis (7%) and mechanic's hands (2%). Pulmonary involvement (26%) was represented by diffuse infiltrative lung disease (17%) and inhalation pneumopathy (9%). Arthralgias were noted in 37% of patients and synovitis in 13%. Antinuclear antibodies were found in 65% of patients. Myositis specific antibodies were found in 16 patients (for n=21 available data): anti RNA synthetase (n=6), anti SRP (n=2), anti Mi-2 (n=4), anti-TIF1-γ (n=2), anti MDA5 (n=1) and anti NXP2 (n=1). Twelve patients (26%) were diagnosed with cancer associated myositis. In terms of therapy, all patients were treated with oral corticosteroids. Immunosuppressive therapy, employed in 85% of patients, was indicated for muscular manifestations (90%) and ILD (10%). Intravenous immunoglobulin was administered in seven patients (15%). The median duration of follow up was 44,5 months. On the date of the last consultation, complete clinical and biological remission of muscular manifestations was noted in 70%. Clinical and radiological stability of ILD was noted in seven patients and regression of radiological infiltrates in one patient. Clinical remission of skin manifestations was noted in 87% of patients, at the cost of cutaneous sequelae in 9%. Overall, a relapse was noted in 57% of patients. Seven patients (15%) have died, after a median period of 12 months.
Conclusion: This study highlighted the heterogeneity among DM patients, as evidenced by the variety of systemic manifestations at onset and during the disease course and of immunological data.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0919 DYNAMIC OPTICAL COHERENCE TOMOGRAPHY MIGHT BE A VALUABLE TOOL TO ASSESS THERAPEUTIC EFFICACY OF VASOACTIVE THERAPY IN SYSTEMIC SCLEROSIS

Keywords: Diagnostic Tests, Patient reported outcomes

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Background: Systemic sclerosis is a rare connective tissue disorder characterized by a triad of inflammation, vasculopathy, and fibrosis. Vasculopathic disease manifestations occur early in disease development and include Raynaud's phenomenon, acral ulcers, necrosis, and pulmonary arterial hypertension. Currently, acral vasculopathy is assessed in clinical practice by nailfold capillary microscopy. However, nailfold capillary microscopy is limited to the nailfold and cannot assess the deeper vascular plexus, changes in dynamic perfusion, or inflammatory and fibrotic disease manifestations. These limitations do not occur with dynamic optical coherence tomography (D-OCT). D-OCT is an imaging technique based on an infrared laser. It allows simultaneous three-dimensional, high-resolution imaging of fibrotic and inflammatory changes as well as vasculopathy in systemic sclerosis [1].
Objectives: The aim of this study was to characterize vascular alterations in the skin of patients with systemic sclerosis and to assess dynamic changes in skin perfusion under vasoactive therapies.
Methods: Twenty-six patients diagnosed with systemic sclerosis according to ACR/EULAR classification criteria 2013 were included in this study. Patients diagnosed with systemic sclerosis received a treatment with iloprost infusion for a duration of five days. Alterations in dynamic perfusion were assessed daily in six locations (nailfold, finger, hand, lower arm, upper arm, ear) using VivoSight OCT. Moreover, alterations in dynamic skin perfusion were assessed under topical treatment with diltiazem (n=13) as well as warmth (n=17). Dynamic perfusion was characterized by the parameters vessel density and vessel diameter. In addition, patients filled questionnaires to assess the severity of vasculopathic disease symptoms and to assess subjective treatment response to iloprost infusion.
Results: Patients were mainly female (73.1%) and of a mean age of 53.6 ± 12.6 years. The majority of the patients were characterized as limited cutaneous systemic sclerosis (76.9%). Seven patients had digital ulcers at the time of study inclusion. Moreover, patients reported that Raynaud's phenomenon occurred with a median frequency of 3.5 attacks per day and the mean duration of Raynaud's phenomenon was 36.9 minutes per day. On a visual analogue scale ranging from 0 to 100, patients rated limitations in daily life due to Raynaud's phenomenon with 48.3 ± 37.3. Whereas the majority of patients (83.3%) reported a subjective benefit, 8.3% reported no change and 8.3% of patients a worsening of acral perfusion under treatment with iloprost infusions. Wilcoxon matched pairs signed rank test did not reveal a significant increase in vessel diameter (p=0.4609) and vessel density (p=0.0681) after topical application of diltiazem. Application of warmth led to a significant increase in vessel diameter ($p < 0.0001$) and vessel density ($p < 0.0001$). Interestingly, therapeutic efficacy assessed by increase in vessel diameter and vessel density differed markedly between individual patients. Prospective assessment of vessel diameter and vessel density under therapy with iloprost infusions yielded heterogeneous regarding the therapeutic efficacy at different sites and timepoints for individual patients.
Conclusion: D-OCT might be a valuable tool to assess vasculopathic alterations and response to vasoactive therapies in the skin of patients with systemic sclerosis. Further studies are required to investigate whether D-OCT might be a technology enabling individual vasoactive treatment in systemic sclerosis in the direction of precision medicine.
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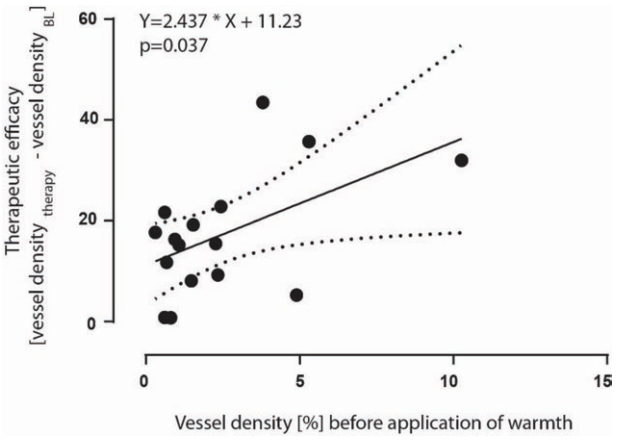


Figure 1. Linear regression analysis revealed a reduced therapeutic efficacy in patients with low baseline vessel density.

Acknowledgements: NIL.
Disclosure of Interests: Hanna Grasshoff Speakers bureau: Abbvie, Katja Adriany: None declared, Linh Ha-Wissel: None declared, Tanja Lange: None declared, Jennifer Hundt: None declared, Gabriela Riemekasten: None declared.

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AB0920 THE MDA5 ANTIBODY AND ITS RELATIONSHIP WITH AMYOPATHIC DERMATOMYOSITIS

Keywords: Myositis, Autoantibodies

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Background: The antibody directed against the protein encoded by melanoma differentiation-associated gene 5 (anti-MDA5) is associated with a subgroup of rare inflammatory myopathies characterized by skin lesions typical of classic dermatomyositis with no or minimal involvement of the proximal musculature. The importance of early diagnosis and treatment lies in the rapidly progressive interstitial lung disease that can develop in 50-100% of cases. This can lead to a poor prognosis with a mortality rate between 33 and 66% six months after diagnosis. In less than 5% of cases it is associated with neoplastic disease.
Objectives: To describe the clinical and evolutive characteristics of patients presenting positivity against MDA5 antibody in our hospital.
Methods: An active search for positive MDA5 antibodies in the service of Rheumatology in a 3th level Hospital was performed by collecting epidemiological, clinical and radiological data between the years 2021-2022.
Results: We identified 10 patients with a mean age of 56.8 years (32-86 years), 60% being female (6) and 40% male [4]. Of the total number of patients, only 30% were diagnosed with dermatomyositis. Three patients presented other autoimmune rheumatologic diseases (two of them were diagnosed with systemic lupus erythematosus and one with rheumatoid arthritis), two exclusively with pulmonary involvement, and in two cases no pathology was found. As for the patients diagnosed with dermatomyositis, 100% presented diffuse interstitial lung disease (DIDP) and classic dermatomyositis skin involvement. Arthritis was present in 66.6%, 33.3% were related to incipient breast carcinoma, and 33.3% presented muscular involvement. In all cases treatment was started early with intravenous methylprednisolone boluses associated in 66.6% of cases with intravenous cyclophosphamide and in 66.6% of cases with Tacrolimus. One death was reported due to respiratory failure, probably secondary to progression of the pulmonary disease related to the disease. The rest of the cases presented favorable evolution with remission of skin and joint involvement, as well as stability of pulmonary involvement.
Conclusion: The frequency of hypo- or amyopathic dermatomyositis with positive MDA5 is low. 100% of the cases presented pulmonary involvement at diagnosis, only 30% presented muscular involvement and 30% were associated with neoplasia. One third of the patients with MDA5-positive dermatomyositis died.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6298

AB0921 EFFICACY AND SAFETY OF MACITENTAN IN REFRACTORY DIGITAL ULCERS

Keywords: Systemic sclerosis, Safety, Real-world evidence

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Background: Raynaud's phenomenon (Rp) is used to describe a symptom complex caused by digital vascular involvement. The presence of digital ulcerations (DU) should prompt further evaluation for secondary causes of Rp. Among the conditions that may be associated with Rp are Systemic Autoimmune Rheumatic Diseases (SARDs), especially Systemic Sclerosis (SSc). DU are a major cause of morbidity and have a high recurrence rate in most patients and may be refractory to multiple treatments. Macitentan is a dual endothelin receptor antagonist authorized to treat pulmonary hypertension. Its efficacy in the treatment of DU associated to SSc has been assessed in two clinical trials (DUAL-1 and DUAL-2)[1], without any visible effects on their prevention or reduction. However, these trials have been criticized on the methodology and profile of the patients included.
Objectives: To assess efficacy and safety of Macitentan in patients suffering from SARDs and refractory DU.
Methods: Spanish observational multicentric study. Data were retrospectively obtained from medical records of 10 patients suffering from SARDs and refractory DU secondary to severe Rp treated with Macitentan 10mg/daily. Total response was defined as the complete healing of DU and partial improvement as the reduction of the number or size of ulcers. Patients with ischemic ulcers caused by other factors were excluded.
Results: We identified 10 patients who has received treatment with Macitentan for DU, median age 59 years (IQR 51-68), 80% female, with a median Rp and DU duration of 56 (IQR 14-214) and 25 (IQR 9-215) months (Table 1). Eight patients were diagnosed with limited SSc; anti-nuclear abs, anti-centromere abs and anti-phospholipidic abs were positive in 90%, 80% and 20% of the patients. Most patients (90%) had received previously treatment with Bosentan, and the reason for withdrawal was inefficacy in 4 cases (44%) and adverse effects (liver toxicity) in 5 (56%). 8 patients had received Intravenous prostanoids with no response. In the beginning of Macitentan the number of DU was 5.5 (IQR 2.3-6) and digital gangrene was reported in one case. Two patients were treated with Macitentan in monotherapy, 6 in combination with calcium antagonists and 2 received triple therapy (Macitentan + Calcium antagonists + PDE5 inhibitor). Just one patient stopped the treatment for adverse effects (lower limb edema). Median follow-up of patients who didn't discontinue the treatment was 3.9 (IQR 2.4-5.7) years. 78% (7/9) of patients had a sustained complete response and 22% (2/9) had a partial response.
Conclusion: Our data show that Macitentan is an effective agent for ischemic digital refractory ulcers in patients suffering from SARDs with a favorable safety profile in clinical practice.
REFERENCE:
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Table 1. Baseline characteristics patients.

Clinical characteristics*	n 10
Female	8 (80%)
Age#	59 (51-68)
Raynaud duration (m)#	56 (14-214)
Diagnosis	
Limited systemic sclerosis	8 (80%)
Undifferentiated connective tissue	2 (20%)
Anticentromere abs (+)	7 (70%)
Current smoker#	3 (30%)
Capillaroscopic features	
Cutolo "early" pattern	1 (10%)
Cutolo "active" pattern	2 (20%)
Cutolo "late" pattern	5 (50%)
Unspecific	3 (30%)
Duration of DU (m)#	25 (9-215)
Number of DU#	
<5	4 (40%)
≥5-10	5 (50%)
>10	1(10%)
Localization of DU#	
Hands	5 (50%)
Hands and feet	5 (50%)
Previous or current therapy	
Calcium antagonist	10 (100%)
PDE5 inhibitor	4 (40%)
Bosentan	9 (90%)
Intravenous prostanoids	8 (80%)
Antibiotics	5 (50%)
Statin	5 (50%)
Acetylsalicylic acid	8 (80%)
Systemic therapy	3 (30%)
Amputation	3 (30%)
Surgical sympathectomy	3 (30%)

* Data represent median (IQR), or number (%)
\# At start of Macitentan

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Disclosure of Interests: None Declared.

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AB0922 CLINICAL CHARACTERISTICS AND CLINICAL OUTCOME OF SYSTEMIC SCLEROSIS OVERLAP SYNDROME (SSC-OS) IN TURKISH PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Lungs, Systemic sclerosis, Epidemiology

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Background: Systemic sclerosis (SSc, scleroderma) is a systemic autoimmune connective tissue disease (CTD). Disease subsetting specific to the extent of skin sclerosis subdivides SSc into the three following main subtypes: (1) limited cutaneous SSc (lcSSc); (2) diffuse cutaneous SSc (dcSSc) and (3) sine scleroderma SSc (ssSSc). Any SSc subgroup can also have features of one or more other CTDs [1]. When a patient has features of any two CTDs, this satisfies the criteria for SSc-overlap syndrome (SSc-OS)[2].
Objectives: The aim of this study was to determine the clinical, serological features and clinical outcome of systemic sclerosis (SSc) and SSc-overlap syndromes(SSc-OS).
Methods: This study included patients enrolled in the Gazi University Systemic Sclerosis Cohort registry during January 2005 to December 2022. SSc-OS was defined as SSc patients who also met criteria for rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), dermatomyositis (DM), polymyositis (PM) and Sjogren syndrome. Baseline and last follow up characteristics were compared between SSc and SSc-OS.
Results: 41 patients (age 54.0 ± 15.8 years, 90% female, disease duration 8.2 years, 43.9% diffuse cutaneous subset, 26.8% limited cutaneous subset, 41.4 % anti-Scl-70 positivity) were included. SSc-OS were classified 29.2% of patients and 4.8%, 7.3%, 2.4%, and 14.6% of patients were classified as SSc-RA, SSc-SLE, SSc-myositis, SSc-Sjogren. SSc-OS had a higher prevalence of arthralgia/arthritis(p=0.029) and SSc had a higher prevalence of interstitial lung disease(p=0.014).
Conclusion: SSc-OS is associated with prevalance of arthralgia/arthritis. SSc-Sjogren syndrome is the most common overlap syndrome. Primary diffuse SSc patients had a greater decrease DLCO compared with the SSc-overlap patients.
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AB0923 COST-EFFECTIVENESS OF ALGINIC ACID IN COMBINATION WITH PROTON PUMP INHIBITOR FOR THE TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE IN SYSTEMIC SCLEROSIS PATIENTS

Keywords: Gastrointestinal tract, Systemic sclerosis

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Background: Systemic sclerosis (SSc) patients often become refractory to proton pump inhibitor (PPI)—a standard treatment for gastroesophageal reflux disease (GERD)—and intolerant to PPI in combination with domperidone. PPI with alginic acid is an alternative treatment option, but alginic acid is costly.
Objectives: We compared the costs and effectiveness of alginic acid plus proton pump inhibitor (PPI) versus standard treatments (PPI with/without antacids as needed and lifestyle modifications) for gastroesophageal reflux disease (GERD) in systemic sclerosis (SSc) patients unsuitable for, or intolerant to, domperidone.
Methods: An economic evaluation using the Markov model was conducted among SSc patients between 40 and 65 with GERD, having a partial or non-response to 4 weeks of standard-dose omeprazole (40 mg/d) and being unsuitable for or intolerance to domperidone. Using a societal perspective, we computed the incremental cost-effectiveness ratios (ICERs) in terms of Thai baht (THB) per quality-adjusted life-years (QALY) between a combination of alginic acid plus PPI and standard treatment for GERD. The lifetime time horizon was used.
Results: The ICER for alginic acid plus PPI versus standard treatments was 377,101THB/QALY. According to the one-way sensitivity analysis, the cost of alginic acid was the most impactful parameter. If the market prices of alginic acid plus PPI were reduced by 61%, this treatment option would become cost-effective at the willingness-to-pay threshold of 160,000THB/QALY (34.71 THB/USD data on 3 December 2022). Furthermore, if alginic acid were included in the public health insurance program, the national budget would be increased by 66,313THB per patient resulting in an overall budget increase of 5,106,101 to 8,885,942THB compared to the standard treatment.
Conclusion: Alginic acid plus PPI does not represent good value for money compared to the standard treatment among such SSc patients in Thailand unless its price is reduced significantly.
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AB0924 SMART PILL TECHNOLOGY PROVIDES SAFE AND EFFECTIVE ASSESSMENT OF GASTROINTESTINAL FUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Gastrointestinal tract, Systemic sclerosis

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Background: Gastrointestinal dysmotility is a common complication in systemic sclerosis (Sc) patients including slow colonic transit leading to gastrointestinal tract (GIT) symptoms. Fecal microbiota transplantation (FMT) with ACHIM did not improve lower or total GIT symptoms in SSc patients compared to placebo enrolled in the Norwegian multicenter, double-blind, randomized, placebo-controlled ReSScue trial. It is unclear if transit times were impacted by FMT. The SmartPill wireless motility capsule (SmartPill®), measures transit times and peristalsis in patients and was given to a subgroup of patients in the ReSScue trial.
Objectives: To estimate gut transit time and safety of SmartPill® in patients with SSc and predominant lower GIT symptoms.
Methods: Ten patients from the ReSScue trial were included in this SmartPill substudy. The patients followed the required diets and procedures prior swallowing a pH calibrated SmartPill capsule. Two infusions of ACHIM or placebo at week 0 and 2 were given to all participants. SmartPill was given by all participants at week 0 and 11. The primary outcome of this study was the change of transit times in patients with ACHIM and placebo from week 0 to week 11 and safety.
Results: Ten patients were enrolled to receive a SmartPill®, six patients in the placebo group and four patients in the ACHIM group. Baseline characteristics in the placebo and ACHIM groups were comparable, with 2 (20%) males and 8 (80%) females, 90% with limited systemic sclerosis and a median age of 51 and 53, respectively. At week 0 the placebo group had a whole gut transit time (WGT) 35.8 hours ± 13.2 (mean ± SD) compared to 40 hours± 8.1 in the ACHIM group. At week 12 the WGT for the placebo group was 38.1 hours±7.2 compared to 73.5 hours±49.8 in the ACHIM group. There was no significant difference in the change of estimated gut transit time between placebo and ACHIM group regarding whole gut transit time, p=0.158 for week 0 and p=0.752 for week 12. (Figure 1). One patient experienced a delayed transit time after receiving ACHIM, with 254 hours from ingestion to body exit for the SmartPill®. In four cases, the activation of the capsule failed. These patients were included in the trial with new, functional capsules. The reason for the malfunction remained unclear.
Conclusion: FMT with ACHIM did not improve gastrointestinal transit times in patients with SSc and lower GIT symptoms. Our study demonstrates that the SmartPill® is safe to use for patients with SSc, but we experienced a high number of malfunction.

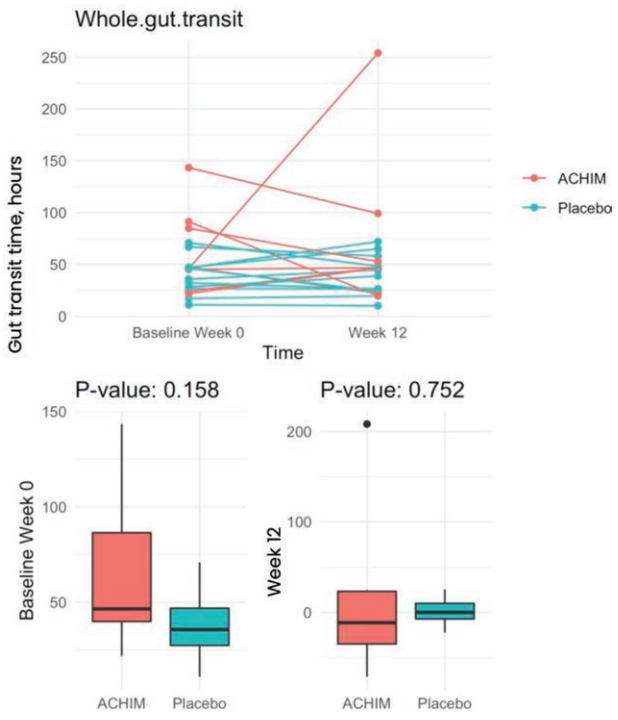


Figure 1.

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AB0925 DERMATOMYOSITIS AS A PARANEOPLASTIC SYNDROME OF TONSILLAR CARCINOMA: FIRST REPORTED CASE IN THE UK

Keywords: Myositis, Malignancy, Imaging

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Background: Dermatomyositis (DM) has a strong association with Malignancy, with one study showing risk up to five times that of the general population and is the leading cause of death [1]. Occult cancer can result in resistant disease, and early diagnosis can improve patient outcomes. We report a case of occult tonsillar cancer associated with severe DM.
Objectives: Our report sought to report the presentation of occult tonsillar cancer with severe dermatomyositis.
Methods: A 60-year-old usually fit and well gentleman presented with a 4-month history of progressive proximal muscle weakness of upper and lower limbs and a characteristic erythematous rash suggestive of DM. Investigations showed a CK of 6813 U/L typical myositis changes on MRI and positive myositis specific Anti-NXP ab. An initial malignancy screen, including CT TAP, was negative for underlying malignancy. He was commenced on oral Prednisolone at 1mg/kg and was discharged with urgent rheumatology follow-up. However, he was admitted a week later with severe dysphagia and ongoing muscle weakness. An urgent OGD excluded a structural upper GI lesion, and Nasogastric feeding was commenced. He was administered IV methyl Pred 500 mg over three days along with IVIG (2g/kg) but failed to respond with ongoing muscle weakness and dysphagia. A subsequent PET scan showed a right tonsillar mass, later confirmed as tonsillar cancer on biopsy. Following this, the ENT team proceeded with robotic surgery and radical surgical resection of tonsillar cancer. We repeated IVIG every four weeks along with IV Methyl pred 50 mg OD and a PEG tube inserted to meet his nutritional needs. Gradually he started to show signs of improvement with improved mobility, muscle strength, and normal CK levels. He received six cycles of IVIG, and azathioprine was commenced with the weaning of prednisolone to 10 mg after discharge. 6 months after the initial presentation, he mobilized independently with improved swallowing to liquids and a soft diet.
Results: Head and neck cancers are rarely associated with Dermatomyositis, with tonsillar cancer extremely rare. To our knowledge, this is the first reported case of occult tonsillar cancer associated with treatment-resistant DM. Detecting occult cancer can be difficult, especially in cases where the DM symptoms precede cancer diagnosis. The usual first-line cancer screening in inflammatory myopathies includes CT TAP, which can miss a malignancy of the head and neck region. Current evidence does not show a definite benefit of PET scanning over conventional CT for cancer identification [2]. But PET scanning can be very useful in selected patients with a high index of clinical suspicion. Recently published BSR guidelines recommend considering PET scanning for cancer screening [3].
Conclusion: Increased vigilance is required to look for occult cancer, including head and neck cancers, especially in patients with treatment-resistant DM. PET scanning can potentially aid in early cancer diagnosis and guide definitive treatment.
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AB0926 LA DISFAGIA EN LA ESCLEROSIS SISTÉMICA SE ASOCIA CON PROBLEMAS NUTRICIONALES Y MALA CALIDAD DE VIDA

Keywords: Systemic sclerosis, Patient reported outcomes, Gastrointestinal tract

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Background: Digestive involvement is one of the most prevalent manifestations of systemic sclerosis (SSc) with great significance for the health and quality of life of patients.

Objectives: To describe the prevalence of dysphagia and the nutritional status of a series of patients with SSc.

Methods: Design: Cross-sectional descriptive study. Participants: consecutive recruitment of patients with SSc (ACR/EULAR 2013 criteria) followed up in our unit. Follow-up of these patients is carried out every 3 to 6 months in consultation and all patients were registered in a database. 90% of the patients accepted and signed the consent, the rest refused due to travel or work difficulties. Variables: The main variable was dysphagia, defined according to the EAT10 questionnaire (positive ≥3). The dysphagia risk factors evaluated were: malnutrition according to the Mini Nutritional Assessment (MNA) (continuous: 0-14, considering 14 better nutritional status), sarcopenia defined according to the European Working Group on Sarcopenia in Older People (EWGSOP) criteria, prealbumin, polypharmacy (if they take >3 drugs), weight loss of at least 1 kg in the last 3 months, quality of life according to EQ-5D and Steinbrocker functional status. Statistical analysis: descriptive and logistic regression (VD: dysphagia) to identify associated factors.

Results: 52 patients were included, of whom 51 (98.1%) were women, with a mean (SD) age of 60.8 (11.0) years. 32/52 patients (61.5%) had dysphagia (EAT≥3) and 12/52 patients (23.1%) were referred to endocrinology for severe dysphagia (EAT≥20) Table 1. Patients with dysphagia compared with the rest had sarcopenia more frequently (37.5% vs 0.0%; p=0.001), weight loss (65.6% vs 20.0%, p= 0.004) and more polymedicated (87.5% vs 60.0%, p=0.022). Likewise, patients with dysphagia (EAT≥3) had lower values (mean [SD]) of nutrition per MNA screening (11.0 [1.2] vs 13.1 [2.3]; p = 0.001), of EQ5D (0.5 [0.2] vs 0.7 [0.2]; p = 0.004), EVA-EQ5D (48.6 [22.3] vs 62.5 [17.6]; p = 0.023) and in Steinbrocker's functional grade (2.3 [1.0] vs 1.3 [0.6]; p = 0.001). The multivariate analysis identified that MNA screening (0-14) (OR [95% CI], 0.511 [0.317-0.824]; p=0.006) and EQ5D (OR [95% CI], 0.965 [0.932-0.998]; p= 0.036) (R2=0.397) were independently associated with dysphagia (EAT ≥3).

Conclusion: Dysphagia is a common problem in systemic sclerosis and is associated with poorer quality of life and a lower probability of reaching a normal nutritional status. The serious nutritional implications associated with dysphagia must be diagnosed in order to intervene nutritionally in these patients.

Table 1. Clinical-epidemiological characteristics of the 52 patients in SSc

Variable	SS n=52
Woman n (%)	51 (98,1%)
Age mean (SD)	60,8 (11,0)
Limited skin patern n (%)	40 (76,9%)
Disseminated skin patern n (%)	12 (23,1%)
DILD n (%)	17 (32,7%)
HTAP n (%)	5 (9,6%)
Anti-Centromere antibodies n (%)	28 (53,8%)
Anti-Sl70 antibodies n (%)	10 (19,2%)
Other antibodies n (%)	9 (17,3%)
Sarcopenia n (%)	12 (23,1%)
MNA Normal nutritional status n (%)	34 (64,5%)
MNA Risk of malnutrition n (%)	17 (32,7%)
MNA malnutrition n (%)	1 (1,9%)
Weight loss >1kg in the last 3 months n (%)	25 (48,1%)
Polypharmacy n (%)	12(23,1%)
Steinbrocker mean (SD)	1,94 (1,03)
EQ5D mean (SD)	0,593 (0,25)
VAS EQ5D mean (SD)	54 (21,56)

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Acknowledgements: NIL.

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AB0927 SYSTEMIC SCLERODERMA: ABOUT 60 CASES

Keywords: Autoantibodies, Systemic sclerosis, Rare/orphan diseases

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Background: Systemic scleroderma is a relatively rare and potentially serious and debilitating connectivitis. It also seems to be different from other diseases in this group, by its pathogenic process that involves several successive or concurrent disorders involving fibroblastic, vascular and dysimmune phenomena. Some impairments condition the functional prognosis and may affect the life-threatening prognosis.

Methods: We conducted a 10-year, single-centric retrospective study (2011 and 2021) of 60 patients followed up for systemic scleroderma at the Internal Medicine Department of the Ibn Sina Hospital in Rabat. We analyzed the statistical data using JAMOVI 2. 2. 5.

Results: We collected 60 files. The sex ratio (F/H) was 5 (50 women/ 10 men), with a mean age of 51±12. 6 (26-76 years). The mean time to diagnosis was 9. 5±38. 9 months (1–180 months). General signs were present in 23 cases (38. 3%) Skin involvement was constant. Raynaud's syndrome was reported in 49 cases (81. 7%) sclerodactyly in 23 cases (38. 3), trophic disorders in 19 cases (31. 7%), telangiectasis in 13 cases (21. 7%) and subcutaneous calcinosis in 5 cases (8. 3%). Rodnan's modified score at admission ranged from 1 to 47/51. Joint manifestations were noted in 36 patients (60%). Lung involvement was objectified in 40 cases (66. 7%), revealing in 22 cases (36%). Interstitial syndrome was observed in 13 cases (21. 7%). Respiratory functional explorations revealed a restrictive syndrome in 23 cases (40%). Chest CT showed diffuse interstitial lung disease in 29 cases (48. 3%), pulmonary fibrosis in 12 cases (20. 3%). Cardiac involvement was detected in 26 cases (43. 3%): pulmonary arterial hypertension in 20 cases (33. 3%); pericarditis in 5 cases (8. 3%); heart failure in 5 cases (8. 3%); and rhythm disturbance in 1 case. Digestive involvement was noted in 17 patients (28. 3%), dominated by oesophageal involvement in all cases, associated with gastric involvement in 6 cases (10%). duodenal garstro esophageal fibroscopy objectified esophagitis and its complications in 17 cases (28. 3%). Neurological involvement was present in 3 cases. Kidney damage was absent from our series. Inflammatory syndrome was present in 37 cases. Anti-nuclear antibodies were positive in 42 cases, anti-Scl70 in 28 cases, anti-centromere in 5 cases, anti-RNP in 6 cases and anti-PM-Scl in 6 cases. An association with another autoimmune disease was noted in 18 patients: Gougerot Sjorgen Syndrome was noted in 5 cases, rheumatoid arthritis in 5 cases, disseminated lupus erythematosus in 5 cases, anti-phospholipid syndrome in 4 cases, primary biliary cirrhosis in 2 cases, hashimoto's thyroiditis in 2 cases, inflammatory myopathy in 1 case and Bullous linear dermatosis to igA in 1 case. Neoplasmic pathology occurred during progression in 3 cases: 1 case of marginal lymphoma and 2 cases of lung cancer. Colchicine was prescribed in 24 cases, D-Penicillamine in 1 case, calcium inhibitors in 31 cases. Corticosteroid therapy was prescribed in 29 cases. Forty-five patients received immunosuppressive therapy and three patients received anti-CD20 (Rituximab) for one patient indicated for rheumatoid arthritis. Complications of immunosuppressive therapy were predominantly infection and impaired liver function. The outcome was favourable in the majority of patients. Late relapses > 6 months were reported in 12 patients, including 8 pulmonary relapses, 1 skin relapses and 1 muscle relapses. The outcome of lung disease was unfavourable in 3 cases. And six patients died. We analyzed several associations such as: lung and heart disease, lung and digestive disease, and heart and digestive disease, the only significant revenue was the association of lung and cardiac disease that was significant (p = 0. 025)

Conclusion: The results of our study are consistent with the literature and confirm the predominance of women and the relatively high incidence of skin, joint, lung and cardiac involvement. Vital prognosis is conditioned by severe visceral damage, especially pulmonary and cardiac.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0928 USE OF RITUXIMAB IN SYSTEMIC SCLEROSIS PATIENTS WITH PULMONARY AND DIFFUSE CUTANEOUS INVOLVEMENT. A SERIES OF 15 CASES

Keywords: Real-world evidence, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is often difficult to treat and the evidence in support of many of the usual therapies is limited. Abnormalities in B-cell function in SSc are thought to play a role in disease pathology. Furthermore, B-cell infiltrates have been demonstrated in both the skin and lung specimens in SSc. Rituximab (RTX) is a chimeric monoclonal antibody inhibiting CD20-mediated B-cell proliferation and differentiation that has shown promising results for pulmonary and cutaneous involvement of SSc.
Objectives: Our aim was to assess RTX for pulmonary and diffuse cutaneous involvement in real-life patients diagnosed of SSc.
Methods: Retrospective observational study of a wide and unselected series of patients diagnosed as SSc from a single university hospital from 2011 to 2022. Patients were classified as SSc following 2013 ACR/EULAR classification criteria. We reviewed pulmonary function through conventional spirometry and diffusing capacity of lung for carbon monoxide (DLCO). Pulmonary involvement was also assessed by high-resolution chest-CT test. Cutaneous involvement was assessed by modified Rodnan skin score (MRSS).
Results: We included 15 patients with a median [range] age (at the onset of RTX) of 53 [41-78] years (80% women; 20% men). The median [range] of time since diagnosis and treatment onset was 3 [0-12] years. At the diagnosis of SSc, no one of our patients evidenced a restrictive ventilatory pattern. DLCO was below normal limits in 12 patients (80%). Small airway obstruction expressed according decreased maximal (mid-) expiratory flow (MMEF) 25-75 was present in 1 patient (6.7%). Regarding cutaneous involvement, median MRSS at diagnosis was 18.3 [range 4-26]. RTX intravenous treatment regimen employed was 1000 mg (Day 1, followed by 1000 mg on day 15), with a repeat cycle every 6 months if required. After a median [range] follow-up period of 31 [6-100] months, 12 (80%) patients completed a total of 4 RTX cycles. An analysis of the pulmonary function showed that, after RTX, DLCO decreased in 2 of 15 patients (13.3%) and none presented worsening of MMEF 25-75. In all patients there was an improvement of cutaneous involvement. After a median follow-up of 31 [6-100] months during RTX therapy none of the patients presented any new relapse of cutaneous involvement or MRSS progression. The mean difference between MRSS measurement before and after RTX was 6.4±1.2. Only 2 of the patients (13.3%) had to discontinue RTX in the first term due to infusion-related reaction. After RTX treatment, 4 patients (26.7%) died (prostate cancer, SARS-COV-2 pneumonia, sudden cardiac arrest and ictus) has been well tolerated and no severe infections were reported.
Conclusion: In our experience, RTX seems to be a great option in real-life for those patients with pulmonary and diffuse cutaneous involvement due to SSc. However, cardiovascular, infectious and neoplastic complications should be assessed.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0929 CLINICALLY AMYOPATHIC DERMATOMYOSITIS (CADM) WITH ANTI–MELANOMA DIFFERENTIATION-ASSOCIATED GENE 5 ANTIBODY POSITIVE: UNDERSTANDING IT'S CLINICAL PRESENTATION AND EXTENT OF LUNG INVOLVEMENT

Keywords: Myositis

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Background: CADM is a subset of dermatomyositis with cutaneous manifestation in the absence of myositis. Myositis-specific autoantibodies (MSA) permits the delineation of homogenous subgroups of DM. CADM associated with anti-melanoma differentiation-associated gene-5 antibody positive (anti-MDA5+) is typically characterized by the presence of dermatomyositis (DM) skin rash and polyarthralgia and interstitial lung disease (ILD)
Objectives: To elaborate on clinical features and management of two patients presenting with MDA-5 positive CADM and associated interstitial lung disease.
Methods: Patient's clinical notes including laboratory results and images were reviewed.
Results: First Case: 59-year-old lady with underlying hypertension presented with inflammatory symmetrical polyarthritis associated with high rheumatoid factor value for 5 months duration. She was initially diagnosed as seropositive Rheumatoid arthritis and treated with T. Methotrexate 15mg/weekly. She achieved clinical remission within two months of treatment. However, eight months later, she developed progressive shortness of breath and reduce effort tolerance (MMRC III). Examination revealed palmar papules and periungual erythema on bilateral hands, and fine crepitations on lung auscultation. No proximal myopathy and active synovitis. ANA 1:1280 (speckled) and MSA panel revealed MDA-5positive.She was unable to perform the lung function test (weak blow) and high-resolution computed tomography (HRCT) showed fibrotic nonspecific interstitial pneumonia (NSIP). She was started on high dose prednisolone (1mg/kg) and oral cyclosporin 100mg daily. One month post treatment, her reduced effort tolerance improved (MMRC II).
Second Case: 32-year-old lady presented with symmetrical arthritis of proximal interphalangeal joints for one year associated with diffuse erythematous rash over the face and neck for five months. She had one month history of steroid exposure. No associated proximal weakness or reduced effort tolerance. Examination revealed hyperpigmentation over the face and Gottron papule over bilateral hands. Auscultation of lung was clear and no synovitis was noted. ANA 1:80 (speckled) and MSA panel revealed MDA-5 positive. Lung function test was normal, however, high-resolution computed tomography (HRCT) revealed interstitial lung disease with organizing pneumonia. She was started on prednisolone 0.3mg/kg for her cutaneous manifestation. Assessment four months later, showed good effort tolerance and complete resolution of cutaneous manifestation.
Conclusion: Myositis-specific autoantibodies have been found to correlate with clinical features and have also served as a diagnostic and prognostic marker. We suggest all patients with MDA-5 positive to undergo CT imaging irrespective of their respiratory symptoms.
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Acknowledgements: NIL.
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AB0930 THE VALUE OF THE CURRENT DIAGNOSTIC TOOLS IN THE DIAGNOSIS OF INFLAMMATORY MYOPATHIES: A MULTICENTRE STUDY

Keywords: Diagnostic Tests, Myositis, Biomarkers

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Background: traditionally, the diagnosis of inflammatory myopathies has been based on clinical signs and symptoms (muscle weakness and characteristic skin involvement, especially in dermatomyositis), increased muscle enzymes, electromyographic findings, skin or muscle biopsy, as well as anti-Jo1 antibodies (antisynthetase syndrome). However, this approach has led to significant diagnostic gaps in atypical cases such as in those of pure lung involvement.
Objectives: to evaluate the diagnostic yield of each procedure in a sample of 61 patients who were diagnosed, followed-up and treated in two tertiary university rheumatology clinics in Greece.

Methods: serum samples tested using a myositis panel (Mi-2α, Mi-2β, Ku, PM-Scl100, PM-Scl 75, SRP, Jo-1, PL-7, PL-12, OJ, EJ, Ro-52, TIF1γ, MDA5, NXP2, SAE1) and muscle enzymes (CK, aldolase, LDH, SGOT, SGPT). Electromyography has been carried out in all patients, whereas in 27 with elevated muscle enzymes or muscle weakness an MRI-guided muscle biopsy has been done. In addition, in 8 patients, a skin biopsy has been performed and in all patients a detailed examination (determination of muscle strength) has been performed in all muscle groups.
Results: in 42 cases the diagnosis has been made after a positive myositis panel, while in 20 cases there was also a histological confirmation. In 8 cases, the diagnosis has been made on the grounds of positive clinical features and characteristic findings on the electromyogram. Only 4 patients have been diagnosed on the basis of histological findings in the absence of other laboratory and clinical findings **(table 1)**. The most common autoantibodies in patients with lung involvement were Jo-1, PL-12 and PL-7.
Conclusion: based on the aforementioned results, a myositis panel seems a reasonable and reliable diagnostic strategy as it improves significantly the diagnostic yield of an inflammatory myopathy. In addition, it gives a diagnostic "alibi" for the therapeutic approaches that otherwise can be administered only by histological confirmation. Finally, in patients with atypical signs and symptoms such as lung fibrosis that cannot be attributed elsewhere, a myositis panel should be performed.
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Table 1.

	Positive MP	Positive EMG	Positive histology	Muscle biopsy	Skin biopsy
Number of patients	42/61	8/61	20/61	27/61	8/61

MP: myositis panel; EMG: electromyography; ME: muscle enzymes

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0931 NUTRITIONAL STATUS EVALUATED BY BIOELCTRICAL IMPEDANCE IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis

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Background: Systemic sclerosis (SSc) is a multi-organ disease with significant morbidity and mortality., Gastrointestinal disorders in patients with SSc may play a significant role in deteriorating nutritional status, sometimes the diagnosis of malnutrition is difficult.
Objectives: The aim of the study was to assess the nutritional status of patients with SSc.
Methods: The study included 87 patients (72 female) with diagnosed SSc, mean age 56.7±12.2 years, median 56 years (range 21-76). Anthropometric measurements were performed in all SSc patients and body composition was assessed using electrical bioimpedance (BIA).
Results: Moderate obesity was diagnosed in 7 patients (8%), mild obesity was diagnosed in 7 patients (8%), over-weight in 29 patients (33%), normal-weight in 40 patients (46%) and 5 (5.7%) patients under-weight. By Spearman Rank Correlation we correlated Fat Free Mass (FFM), Visceral Fat Index (VFI), Total Body Water (TBW), Intra-cellular Water (ICW), Extra-cellular Water (ECW) and Body Mass Index (BMI) with age, use of immunosoppressive drugs (DMARD's), use of OH-clorochine, use of corticosteroids, interstitial lung disease (ILD), activity index (AI), diastolic dysfunction (E/A). The results are reported in table 1.
Conclusion: our study shows the importance of the parameters assessed with BIA, particularly the intra and extra-cellular water composition which may represent a prognostic factor for the development of cardiac and pulmonary fibrosis. There is a need to define that of randomized controlled trials on larger case series. Nutritional disorders are common in patients with SSc. The most common disturbance in nutritional status in SSc patients was overweight/obese, which was present in 50% of patients.
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Table 1.Correlations between the parameters of the BIA and the clinical parameters of the ssc (Spearman Rank Correlation)

	Age	DMARD's	corticosteroids	OH-Clorochina	ILD	Activity index	E/A
	p	P	p	p	p	P	p
FFM	ns	0.02	ns	ns	ns	0.08*	ns
	ns	0.04	ns	ns	0.075*	0.0069	0.039
TBW	ns	0.03	ns	ns	ns	ns	ns
	<0.0001	ns	ns	0.058*	ns	ns	0.0003
ECW	0.053*	ns	0.059*	0.026	0.04	ns	0.0081
	ns	0.05	ns	ns	0.04	ns	ns

Fat Free Mass (FFM), Visceral Fat Index (VFI), Total Body Water (TBW), Intra-cellular Water (ICW), Extra-cellular Water (ECW) and Body Mass Index (BMI) interstitial lung disease (ILD), activity index (AI), diastolic dysfunction (E/A).
p significative <0.05; *p not quite significant

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0932 LONG-TERM CORTICOSTEROID THERAPY WAS ASSOCIATED WITH SIGNIFICANT LIVER FIBROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis

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Background: Fibrotic changes of the internal organs, such as lungs, heart, kidneys, and gastrointestinal tract, characterize the clinical course of both limited (lcSSc) and diffuse cutaneous SSc (dcSSc), potentially leading to organ dysfunction. However, liver involvement is less defined.
Objectives: In a cross-sectional study we investigated the prevalence and predictors of significant liver fibrosis in patients with systemic sclerosis (SSc) who had no evidence of liver diseases due to heavy alcohol consumption, viral infection, drug.
Methods: A total of 65 SSc patients were recruited, satisfied the 2013 ACR)/(EULAR) classification. In addition to the clinical and laboratory data, modified Rodnan skin score (mRSS), and activity index, video-capillaroscopy, echocardiography, and lung function were analysed. Liver stiffness (LS) was measured using transient elastography to assess the degree of liver fibrosis and 7.4 kPa was adopted as the cut-off value for significant liver fibrosis and liver steatosis with CAP values ≥ 248 dB/m were considered consistent with mild steatosis (S1), ≥268 dB/m with moderate steatosis (S2) and ≥280 dB/m with severe steatosis (s3)
Results: The median age of patients (60 women) was 50.5 years (range 20-80) and the median disease duration was 5.5 years (range 1-10). The median LS value was 4.65 kPa (range 3.1-8.3); the median CAP value was 220.5 (164-327). By Spearman Rank Correlation LS value vs age has a p value 0.02 (CI 95% 0.290.64), vs corticosteroid use has a p value 0.0032 (CI95% 0.179-0.731). On the contrary Cap value vs age has a p value 0.026 (CI 95% 0.04-0.64). Forty-six

(70.8%) patients had no fibrosis (F=0); 17 (26%) had a LS value from 5.2 and 7.4; 3 patient (4.6%) LS>7.4 (F3) significant liver fibrosis. Eight patients (12.3%) had mild liver steatosis (CAP value was ≥ 248 dB/m) and 6 patient (9.2%) had moderate steatosis (S2) (CAP value ≥268 dB/m)

Conclusion: In our study **t**he prevalence of significant liver fibrosis was relatively low (4.6%). Long-term corticosteroid therapy was associated with increased liver stiffness on Fibroscan. T**he** low number of patients is a limitation of the study, we await the data relating to a more representative population.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0933 RAYNAUD´S PHENOMENON AND RELATED SYNDROMES CLINIC: CHARACTERIZATION OF NEWLY REFERRED PATIENTS AND DIFFERENCES BETWEEN PRIMARY AND SECONDARY RAYNAUD´S PHENOMENON

Keywords: Autoantibodies, Systemic sclerosis, Diagnostic Tests

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Background: The Raynaud´s Phenomenon (RP) and Related Syndromes Clinic was created in the Rheumatology Department at Hospital de Braga in order to provide differentiated health care to the population with RP, emerging as a unique outpatient clinic in the country. The aim of this Clinic is to evaluate patients who present with this clinical manifestation in a prompt and multidisciplinary approach, considering the differential diagnosis between the primary and secondary etiology. In this way, adequate monitoring can be carried out, such as performing a Nailfold Videocapillaroscopy (NVC) and early and targeted therapy instituted.

Objectives: Characterize the individuals evaluated in first RP and Related Syndromes Clinic appointments and determine predictive factors allowing to distinguish primary and secondary RP.

Methods: Retrospective, single center study, including patients who were evaluated in first RP and Related Syndromes appointments between February 2021 and December 2022. Sociodemographic variables, clinical data and the results of the complementary study such as anti-nuclear antibodies (ANA) profile and NVC pattern were analyzed. Statistical analysis of the data was performed using SPSS, using the Chi-square and the t-Test independent samples tests, as appropriate. A p value < 0.05 was considered statistically significant.

Results: Fifty four patients were included (female 88,89%, male 11,11%; mean age 52,48±17,06 years), referred to this clinic with the following main reasons: suspected RP (64,82%), suspected connective tissue disease (CTD) (31,48%) and laboratory tests changes (3,7%). Among these patients, 43 patients had RP: primary in 12 (27,91%) and secondary in 31 (72,09%). A total of 42 NVC were performed: normal pattern in 30,95%; nonspecific changes in 28,57%; early scleroderma pattern in 21,43% and active scleroderma pattern in 19,05%. The diagnosis established in the 54 patients evaluated were: acrocyanosis (1,85%), erythema pernio (7,41%), frostbite (1,85%), Achenbach Syndrome (1,85%), Systemic Sclerosis (SSc) (31,48%) - 11,76% Very Early Diagnosis Of SSc; 5,88% SSc diffuse cutaneous form; 82,35% SSc limited cutaneous form -, undifferentiated CTD (3,70%), primary RP (22,22%) and secondary RP non-CTD (22,22%) - includes patients with RP secondary to tobacco, betablockers, SARS-Cov2 infection or autoimunne thyroiditis. 7,42% of the patients didn´t have RP or a rheumatic disease. Ten patients were discharged, with the remaining patients being followed regularly. Table 1 summarizes the characterization of patients with primary and secondary RP. Comparing patients with primary RP with patients with secondary RP, we found that older age, ANA´s positivity, taking betablockers and an altered NVC pattern was statistically significantly associated with the diagnosis of a secondary RP.

Conclusion: With this work, we emphasize the importance of RP investigation in order to establish a definitive diagnosis and an adequate follow up, showing a higher probability of secondary RP in patients with older age, positive ANA´s and who were taking betablockers. It reinforces, as well, the importance of NVC in the evaluation of patients with RP, as significant differences are found between primary and secondary RP, with scleroderma pattern raising the hypothesis of a secondary RP.

Table 1. Characterization of patients with primary and secondary RP and p-value of statistical tests used to compare patients with primary RP and secondary RP for each variable in study.

	Primary RP (n=12)	Secondary RP (n=31)	p-value
Age (years)	43.92 (±18.38)	58.68 (±13.29)	**0.006**
Sex			0.300
Feminine	12	26	-
Masculine	0	5	-
RP duration (years)	11.88	8.51	0.453
Active smoking	2	7	1.000
Beta-blockers	0	10	**0.040**
RP symmetry			0.500
Symmetric	8	16	-
Assymetric	4	15	-
History of digital ulcers	0	6	0.163
ANA			**<0.001**
Negative	11	6	-
Positive	1	25	-
NVC Pattern			**<0.001**
Normal	10	2	-
Inespecific chages	2	8	-
Early stage scleroderma	0	9	-
Active stage scleroderma	0	8	-

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0934 SYSTEMIC SCLERODERMA IN MEN: A CASE REPORT OF 10 PATIENTS

Keywords: Epidemiology, Rare/orphan diseases, Systemic sclerosis

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Background: Systemic scleroderma is a connective tissue disease that is common in women and characterized by vascular alterations associated with skin fibrosis and visceral manifestations. Several particularities of this connectivitis in men are discussed. We propose to show these particularities in men through 10 cases.

OBJECTIVES:

Methods: We identified 10 cases of systemic scleroderma in men among 60 cases of systemic scleroderma collected for our descriptive restrospective study in the internal medicine department of the IBN SINA University Hospital in Rabat. The search for clinical or subclinical visceral involvement was performed in all our patients.

Results: The average age of the patients was 61 ±14.1 years (extremes: 28-74 years) with a delay in diagnosis of 8 months. General signs were found in 3 patients (30%), the skin involvement was made of diffuse sclerosis in 6 cases (60%) and limited in 4 cases (40%); Raynaud's phenomenon was noted in 7 cases (70%). Pulpal ischemia and digital ulcer were noted in 1 and 3 cases respectively. Telangiectasias in 1 case. Joint involvement was present in half of the cases. Pulmonary involvement was present in 6 cases (60%). Pulmonary fibrosis was found in 1 case. Cardiac involvement was found in 6 cases (60%), of which 4 cases had PAH, one case of pericarditis and one case

of heart failure. Esophageal involvement was found in 4 cases (40%). Biologically, an inflammatory syndrome was noted in 4 patients (40%). Antinuclear antibodies were positive in 7 cases (70%). Anti-Scl70 was detected in 4 cases (40%). Capillaroscopy showed lesions suggestive of organic microangiopathy in 2 cases (20%). 4 of our patients were treated with colchicine. Corticosteroids were prescribed in 2 cases. Half of our patients received immunosuppressive treatment, including 3 cases who received monthly courses of cyclophosphamides with relay by Imurel, and 3 patients received treatment by mycophenolate mofetil, stopped in one patient due to hepatic cholestasis. The association with autoimmune diseases was noted in 2 patients, including one with rheumatoid arthritis and one with primary biliary cholangitis 2 cases of neoplasia were observed in our series, the first one was a marginal zone lymphoma and the second one was a pulmonary adenocarcinoma. 3 deaths were reported, one by pulmonary embolism, and the 2 patients who presented a neoplastic pathology.

Conclusion: Despite the small number of our patients, our results agree with those of the literature. The male sex seems to be associated with more severe forms with a shorter diagnostic delay, diffuse skin involvement, severe Raynaud's phenomenon, and early and severe pulmonary involvement.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0935 THE MIMIC THAT CAUGHT EVERYONE BY SURPRISE!

Keywords: Skin, Systemic sclerosis, Rare/orphan diseases

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Background: 57-year-old gentleman, a previous smoker, presented with a 12-month history of gradually progressive anasarca that started initially with bilateral lower limbs and involved face, abdomen and entire body over 3-4 months. Four months into his illness, the patient noticed skin changes in the form of hyperpigmentation initially over anterior chest that progressed to involve the face, bilateral upper limbs, abdomen, and lower limbs over next 3 months. It was associated with increased friability, subcutaneous oedema, and spontaneous ecchymosis. Gradually he developed progressive motor weakness, initially in both upper limbs proximally which progressed to involve distal, bilateral lower limbs and trunk with sparing of bowel and bladder functions severely limiting his activities of daily living. Over the next 15 days patient became breathless with rapidly worsening dyspnoea of exertion, dry cough and left sided pleuritic chest pain. There was history of loss of appetite and significant loss of weight 18 kgs over 4 months. General physical examination was suggestive of pallor, diffusely hyperpigmented and fragile skin over the face, neck, upper limbs, hands, back, anterior abdomen, lower limbs with multiple ecchymotic spots and subcutaneous edema with anasarca. Breath sounds were decreased bilaterally over intrascapular, axillary, infra-axillary areas and JVP elevated on Cardio-Respiratory system examination. CNS examination revealed bilateral external ophthalmoplegia with pure motor quadriparesis involving limbs and trunk without sensory, cranial nerve or autonomic involvement, Generalised wasting with asymmetric swelling over right shoulder was seen with reduced active and passive range of movements.

Objectives: Differentials:

1)Scleredema

2)Diffuse cutaneous systemic sclerosis

Methods:

CBC	12/4800/170
Total protein/albumin	6.1/3(g/dl)
ANA/ENA	negative
Urine R/M	normal
FreeT4/TSH/FSH/ Prolactin/HbAIC	normal
CECT chest+ abdomen	B/ pleural effusion with Hepatosplenomegaly
Pleural fluid	Transudative with negative malignant cytology
NCS	Sensorimotor axonal polyneuropathy
SPEP	Light chain myeloma with predominant IgG lamba
Serum free lambda chains	50(5-26)
Serum VEGF	658 (0-200 pg/ml)
Skin biopsy	Amyloidosis (Congo Red stain positive)
Bone marrow exam	Scattered CD 138 positive plasma cells
2D Echo and Cardiac MRI	Restrictive cardiomyopathy
MRI right shoulder	diffuse contrast enhancement in all muscles of right shoulder with subcutaneous edema and scattered fatty changes?infiltrative

Results:

Final diagnosis:

POEMS syndrome with primary amyloidosis.

International Myeloma Working Group criteria fulfilled:

Mandatory criteria-

Polyneuropathy

Monoclonal plasma cell proliferative disorder

Atleast 1 major criteria:

Elevated VEGF levels

Minor criteria:

Organomegaly

Extravascular volume overload

Skin changes

Hematological involvement

Conclusion: The patient was started on treatment after Clinical haematology reference but died due to cardiogenic shock. This interesting case highlights POEMS as a great mimic of changes associated with various autoimmune disorders including scleroderma, SLE and vasculitis syndromes.

REFERENCES: NIL.

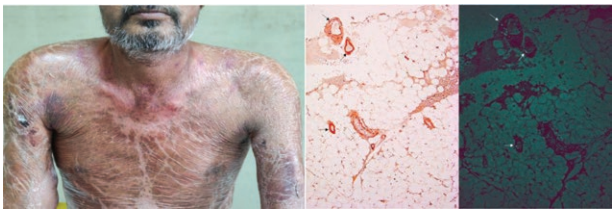


Image 1. Cutaneous changes, shoulder pad sign and skin biopsy showing Congo red stain and apple green biriferengence

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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Spondyloarthritis - treatment

AB0936 IMPACT OF DIFFERENT BDMARDS ON PATIENT REPORTED OUTCOMES IN AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW OF THE LITERATURE AND META-ANALYSIS

Keywords: bDMARD, Pain, Spondyloarthritis

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Background: Pain, fatigue and altered quality of life are frequent complaints in axial spondyloarthritis (axSpA), with an impact on disease activity evaluation, regardless of radiographic or non-radiographic phenotype. No study compares face to face the effects of biologic DMARDs (bDMARDs) on patient reported outcomes (PROs).
Objectives: To evaluate the impact of biologic DMARDs (bDMARDs: anti-TNF and anti-IL17) on three PROs (pain, fatigue, quality of life) in patients with axial spondyloarthritis (axSpA).
Methods: A systematic review was performed in PubMed, Embase until May 2022, and abstracts from EULAR and ACR meetings for the past 3 years. The search included all randomized controlled trials of bDMARDS with outcomes reporting data on pain ("total back pain", "nocturnal back pain"), fatigue (FACIT-F) and quality of life (ASQoL and SF36 PCS and MCS) in patients with axSpA.
Statistical analysis used the inverse variance method to obtain results as mean differences, which were visualized by forest plot. Variation between studies was assessed by calculating the heterogeneity (I^2) with Cochran's Q test.
Results: A total of 25 studies were included in the final analysis, with a total number of 8457 patients. Compared to placebo, treatment with bDMARDs was associated with a significant improvement in pain, fatigue and quality of life. The mean differences were -1.47 (95% CI (-1.72, -1.22)) for total back pain, -1.67 (95% CI (-2.06, -1.28)) for nocturnal back pain, 4.47 (95% CI (3.23, 5. 72)) for FACIT-F, -2.59 (95% CI (-2.68, -2.49)) for ASQoL, 3.68 (95% CI (3.21, 4.15)) for SF36 PCS and 2.79 (95% CI (1.83, 3.75)) for SF36 MCS. For the subgroup analysis comparing the different bDMARDs, the effects on pain were numerically superior with anti-TNF, but the difference was not significant because of the confidence intervals overlapping. There was no difference for the other PROs between anti-TNF and anti-IL17. Heterogeneity was weak except for the "nocturnal back pain" scale. For the subgroup analysis comparing axSpA phenotypes, the improvement of PROs on bDMARDs between radiographic and non-radiographic axSpA was not different, except for the mental component of the SF36 score less improved in the non-radiographic axSpA.
Conclusion: bDMARDs (anti-TNF and anti-IL17) significantly improve pain, fatigue and quality of life compared to placebo in patients with axSpA. No significant difference was observed between anti-TNF and anti-IL-17, nor between radiographic and non-radiographic axSpA, except for the mental component of the SF36.
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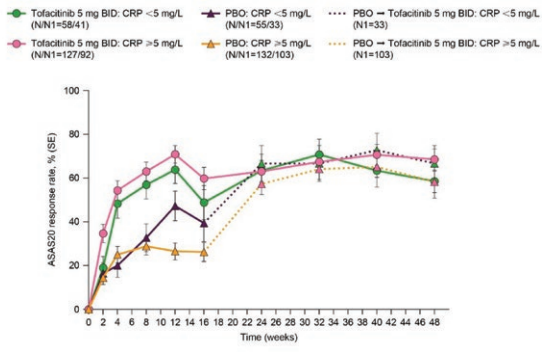
AB0937 TOFACITINIB EFFICACY AND SAFETY IN PATIENTS WITH ANKYLOSING SPONDYLITIS BY BASELINE C-REACTIVE PROTEIN LEVELS: A POST HOC ANALYSIS

Keywords: Randomized control trial, Targeted synthetic drugs, Spondyloarthritis

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Background: Elevated baseline (BL) C-reactive protein (CRP) levels can predict treatment response in patients (pts) with ankylosing spondylitis (AS). Tofacitinib is a Janus kinase inhibitor for the treatment of AS.
Objectives: To evaluate the impact of BL CRP levels on tofacitinib efficacy and safety in pts with AS.
Methods: Post hoc analysis of pooled data from placebo (PBO)-controlled, randomised, double-blind trials (NCT01786668, Phase [P]2, 16 weeks; NCT03502616, P3, 48 weeks) in pts with AS on ≥1 dose of tofacitinib or PBO (P3: PBO-treated pts switched to tofacitinib after Week [W]16), by BL CRP: normal (NML) <5 mg/L; elevated (ELV) ≥5 mg/L. Tofacitinib 5 mg twice daily (BID) efficacy was assessed to W12/W16–48 (P3). Endpoints: Assessment of SpondyloArthritis international Society (ASAS) 20/40, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50, AS-Disease Activity Score-CRP inactive disease (ASDAS-CRP ID), least squares mean change from BL (Δ) in nocturnal pain and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F). Safety was assessed to W16 and W48.
Results: Of 372 pts, 30.4/69.6% had NML/ELV BL CRP. Both groups had generally similar BL characteristics; more pts with ELV CRP were male, current smokers and had prior biologic disease-modifying antirheumatic drug use. At W12, ASAS20 response was greater for tofacitinib vs PBO in both groups (Figure 1); efficacy maintained to W48. At W12, the difference in response from PBO for tofacitinib was numerically greater for ELV vs NML CRP for ASAS20 (44.7% vs 15.9%), ASAS40 (34.6% vs 17.3%), BASDAI50 (33.8% vs 15.3%), ASDAS-CRP ID (9.5% vs 8.2%), Δnocturnal spinal pain (-2.1 vs -1.4) and ΔFACIT-F (5.2 vs 3.5). For tofacitinib, rates of treatment-emergent adverse events (TEAEs) and infections to W16 trended numerically higher for tofacitinib vs PBO in pts with NML CRP, but were similar to PBO in pts with ELV CRP (Table 1). There were few serious AEs (SAEs), serious infections (SIs) or herpes zoster (HZ) across groups and no deaths. Limitations: small sample size, differences in BL characteristics.

Figure. ASAS20 response rates over time by BL CRP



N, pooled pts in P2 and P3 from BL–W16; N1, pts from P3 from W24–48; SE, standard error

Conclusion: Regardless of BL CRP, at W12, tofacitinib was more efficacious vs PBO; and across endpoints, the differences in response from PBO for tofacitinib were numerically greater in pts with ELV vs NML CRP. Tofacitinib safety rates were consistent with PBO in pts with ELV CRP, but trended higher for tofacitinib vs PBO in pts with NML CRP.
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Table 1. Safety outcomes by BL CRP (NML <5 mg/L; ELV ≥5 mg/L)

n (%) IR[d] [95% CI]	To W16				To W48			
	Tofacitinib 5 mg BID[a]		PBO		All tofacitinib 5 mg BID[b]		All tofacitinib[c]	
	NML N=58	ELV N=127	NML N=55	ELV N=132	NML N=91	ELV N=225	NML N=129	ELV N=291
TEAEs	39 (67.2) 365.4 [259.9, 499.6]	61 (48.0) 222.7 [170.4, 286.1]	27 (49.1) 240.7 [158.6, 350.2]	64 (48.5) 235.4 [181.3, 300.6]	60 (65.9) 188.2 [143.7, 242.3]	138 (61.3) 146.5 [123.1, 173.1]	80 (62.0) 202.5 [160.6, 252.0]	168 (57.7) 155.6 [133.0, 181.0]
SAEs	1 (1.7) 5.6 [0.1, 31.0]	2 (1.6) 5.1 [0.6, 18.6]	0 0.0 [0.0, 21.9]	1 (0.8) 2.5 [0.1, 14.0]	5 (5.5) 7.8 [2.5, 18.2]	3 (1.3) 1.8 [0.4, 5.3]	5 (3.9) 6.6 [2.1, 15.4]	4 (1.4) 2.2 [0.6, 5.5]
All infections	23 (39.7) 158.0 [100.2, 237.1]	28 (22.0) 81.5 [54.2, 117.8]	13 (23.6) 87.9 [46.8, 150.2]	30 (22.7) 83.9 [56.6, 119.8]	37 (40.7) 82.1 [57.8, 113.2]	74 (32.9) 56.7 [44.5, 71.2]	46 (35.7) 84.1 [61.6, 112.2]	86 (29.6) 58.0 [46.4, 71.6]
SIs	1 (1.7) 5.6 [0.1, 31.0]	0 0.0 [0.0, 9.5]	0 0.0 [0.0, 21.9]	0 0.0 [0.0, 9.2]	1 (1.1) 1.5 [0.0, 8.5]	0 0.0 [0.0, 2.2]	1 (0.8) 1.3 [0.0, 7.3]	0 0.0 [0.0, 2.0]
HZ	0 0.0 [0.0, 20.4]	0 0.0 [0.0, 9.5]	0 0.0 [0.0, 21.9]	0 0.0 [0.0, 9.2]	2 (2.2) 3.1 [0.4, 11.1]	3 (1.3) 1.8 [0.4, 5.3]	3 (2.3) 3.9 [0.8, 11.5]	4 (1.4) 2.2 [0.6, 5.5]
Discontinuation due to AEs	1 (1.7) 5.6 [0.1, 31.0]	3 (2.4) 7.7 [1.6, 22.6]	2 (3.6) 11.9 [1.4, 43.0]	2 (1.5) 5.0 [0.6, 18.0]	4 (4.4) 6.1 [1.6, 15.7]	7 (3.1) 4.2 [1.7, 8.7]	4 (3.1) 5.2 [1.4, 13.4]	8 (2.7) 4.3 [1.9, 8.5]

[a]To W12: P2; W16: P3 [b]To W12: P2; W48: P3 [c]P2: tofacitinib 2, 5 or 10 mg BID to W12; P3: 5 mg BID to W48 [d]Pts with events/100 pt-years CI, confidence interval; n, number of pts with an event within risk period (on treatment); N, number of pts in safety analysis set

AB0938

SAFETY PROFILE OF BIMEKIZUMAB AT WEEK 16 IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS: RESULTS FROM FOUR PLACEBO-CONTROLLED PHASE 3 STUDIES

Keywords: Safety, Psoriatic arthritis, Spondyloarthritis

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Background: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.
Objectives: To report Week (Wk) 0–16 safety of BKZ and placebo (PBO) in 2 axial spondyloarthritis (axSpA) and 2 psoriatic arthritis (PsA) phase 3 studies.
Methods: Patients (pts) in 2 safety pools received ≥1 dose of subcutaneous BKZ 160 mg or PBO every 4 wks during Wks 0–16 (double-blind phase) of BE MOBILE 1 + BE MOBILE 2 in axSpA (NCT03928704; 03928743); BE OPTIMAL + BE COMPLETE in PsA (NCT03895203; 03896581) (**Figure 1**) [1-4].
Results: Wk 16 completion rates: 95.8% (PBO), 97.1% (BKZ) in axSpA; 95.9% (PBO), 97.1% (BKZ) in PsA. Most frequently reported treatment-emergent adverse events in ≥3% pts on BKZ were nasopharyngitis, upper respiratory tract infection, oral candidiasis and headache (**Table 1**). See **Table** for adverse events of special interest. Serious infections occurred in 5 pts (axSpA: 1 [0.4%] PBO, 1 [0.3%] BKZ; PsA: 0 PBO, 3 [0.4%] BKZ). Fungal infections were all local and reported as mild/moderate by investigators; more *Candida* infections were seen on BKZ (axSpA: 15 pts [4.3%]; PsA: 18 [2.6%]) than PBO (axSpA: 0; PsA: 2 [0.5%]) and led to discontinuation by 3 pts on BKZ (1 axSpA, 2 PsA). In axSpA pts, uveitis occurred in 11 (4.6%) on PBO and 2 (0.6%) on BKZ; inflammatory bowel disease occurred in 1 (0.4%) pt on PBO, 2 (0.6%) on BKZ. No uveitis/IBD cases in PsA by Wk 16 (PBO or BKZ). No deaths, active tuberculosis, suicidal ideation/behaviour, or major adverse cardiac events were reported in any study to Wk 16.
Conclusion: The overall safety profile of BKZ was in line with previous phase 2 trials in axSpA and PsA, with a low rate of discontinuation. As expected, due to inhibition of IL-17, there was a higher rate of oral candidiasis compared to PBO.

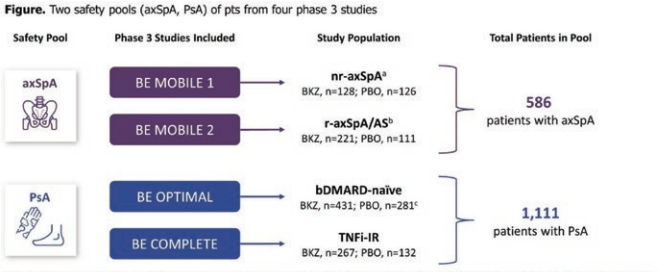


Figure. Two safety pools (axSpA, PsA) of pts from four phase 3 studies

[a]Patients included in BE MOBILE 1 met ASAS classification criteria. Patients with radiographic sacroiliitis were excluded; [b]Patients included in BE MOBILE 2 met modified New York criteria and ASAS classification criteria, therefore the terms r-axSpA and AS may be used interchangeably; [c]BE OPTIMAL also included an adalimumab treatment arm. Patients randomised to this arm are not included in the PsA safety pool.

Abbreviations: AESI: adverse events of special interest; AS: ankylosing spondylitis; ASAS: Assessment of SpondyloArthritis international Society; axSpA: axial spondyloarthritis; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; IBD: inflammatory bowel disease; nr-axSpA: non-radiographic axSpA; PBO: placebo; PsA: psoriatic arthritis; pt: patient; Q4W: every 4 weeks; r-axSpA: radiographic axSpA; TEAE: treatment-emergent adverse event; TNFi-IR: tumour necrosis factor inhibitor-inadequate response.

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Table 1. Summary of TEAEs to Wk 16

	axSpA BE MOBILE 1 [nr-axSpA] + BE MOBILE 2 [r-axSpA/AS] (N=586)		PsA BE OPTIMAL [bDMARD-naïve] + BE COMPLETE [TNFi-IR] (N=1,111)	
TEAEs, n (%) MedDRA v19.0	PBO (N=237)	BKZ 160 mg Q4W (N=349)	PBO (N=413)	BKZ 160 mg Q4W (N=698)
Pt-years at risk	73.0	108.6	128.5	218.7
All	119 (50.2)	200 (57.3)	183 (44.3)	365 (52.3)
Severe	1 (0.4)	3 (0.9)	0	9 (1.3)
Led to study discontinuation	5 (2.1)	8 (2.3)	3 (0.7)	10 (1.4)
Drug-related[a]	37 (15.6)	97 (27.8)	39 (9.4)	136 (19.5)
Serious	2 (0.8)	4 (1.1)	3 (0.7)	12 (1.7)
Most common[b]				
Nasopharyngitis	10 (4.2)	29 (8.3)	14 (3.4)	50 (7.2)
Upper respiratory tract infection	16 (6.8)	15 (4.3)	20 (4.8)	27 (3.9)
Oral candidiasis	0	13 (3.7)	0	16 (2.3)
Headache	7 (3.0)	12 (3.4)	7 (1.7)	25 (3.6)
AESI				
Serious infections	1[c] (0.4)	1[d] (0.3)	0	3[e] (0.4)
Fungal infections[f]	0	22 (6.3)	4 (1.0)	32 (4.6)
Candida infections	0	15[g] (4.3)	2 (0.5)	18 (2.6)
Oral candidiasis[h]	0	13 (3.7)	0	16 (2.3)
Liver function test changes/enzyme elevations	6 (2.5)	15 (4.3)	11 (2.7)	22 (3.2)
Alanine aminotransferase	1 (0.4)	5 (1.4)	3 (0.7)	5 (0.7)
Aspartate aminotransaminase	0	6 (1.7)	2 (0.5)	3 (0.4)
Hepatic enzyme increased	1 (0.4)	1 (0.3)	3 (0.7)	4 (0.6)
Malignancies	0	0	2[i] (0.5)	1[i] (0.1)
Adjudicated IBD[j]	1 (0.4)	2 (0.6)	0	0
Crohn's disease	0	1 (0.3)	0	0
Ulcerative colitis	1 (0.4)	1 (0.3)	0	0
Uveitis	11 (4.6)	2 (0.6)	0	0
With prior history	9 (3.8)	1 (0.3)	0	0
No prior history	2 (0.8)	1 (0.3)	0	0
Neutropenia	0	2 (0.6)	1 (0.2)	9 (1.3)
Injection site reactions	4 (1.7)	12 (3.4)	3 (0.7)	8 (1.1)

[a]Per investigator assessment; [b]Occurring in ≥3% BKZ-treated pts; [c]Unknown viral infection; [d]Hepatitis A infection; [e]2 pneumonia, 1 bronchitis; [f]None systemic, all localised mucocutaneous and none serious; [g]One infection classified as opportunistic (oropharyngeal candidiasis); [h]*Candida* infection preferred terms occurring in >1 BKZ-treated patient are reported; [i]Breast cancer stage I, basal cell carcinoma; [j]Basal cell carcinoma; [h]Definite/probable, 0 cases with prior history.

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AB0939

BONE-RELATED OUTCOME DURING TWO YEARS OF SECUKINUMAB TREATMENT IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RADIOGRAPHIC SPINAL AND FACET INVOLVEMENT, BONE MINERAL DENSITY, VERTEBRAL FRACTURES AND BONE TURNOVER MARKERS

Keywords: Outcome measures, Bone diseases, Spondyloarthritis

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Background: IL17 inhibitors have proven to reduce disease activity in patients with ankylosing spondylitis (AS). AS is an intriguing disease which is characterized by both excessive bone formation and bone loss. Data on the effect of IL17 inhibitors on the different aspects of bone formation as well as bone resorption is still limited.

Objectives: To evaluate radiographic progression of the spine and cervical facet joints, bone mineral density (BMD), vertebral fractures (VF) and serum markers of bone resorption, formation, and mineralization during 2 year of secukinumab treatment in AS patients in daily clinical practice.

Methods: In this explorative study, consecutive AS outpatients from the GLAS cohort who were treated with secukinumab for 2 years were included. Standardized follow-up visits were performed at baseline (before start of secukinumab) and after 3/6 months, 1 and 2 years of treatment. Bone-related outcome was assessed at baseline and after 2 years. Radiographs were blinded for patient characteristics and scored in chronological time order by 2 independent trained readers. Spinal radiographic damage was assessed using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS; 0-72) and cervical facet joint involvement according the 'de Vlam' method (0-15). Radiographic VF were assessed using the Genant method and bone mineral density (BMD) with DEXA. Serum levels of BTM reflecting collagen resorption, collagen formation and facilitation of bone mineralization (sCTX, PINP and BALP, respectively) were measured at all visits. BTM Z-scores were calculated using a healthy reference population to correct for the normal influence of age and gender. Bone-related outcomes were explored using descriptive statistics. Generalized estimating equations were used to analyze BTM over time within patients.

Results: In total, 17 AS patients were eligible for analyses; 53% were male, mean age was 46.6±14.6 years, 82% were HLA-B27 positive, mean ASDAS at baseline was 3.9±1.2, median CRP was 5 (IQR 3 - 26) mg/L, 53% were biological naïve, and median time between diagnosis and start of secukinumab was 5.0 (IQR 1.5-12.0) years. After 2 years of secukinumab treatment, mean ASDAS was 2.2±1.1. At baseline, median mSASSS was 3.3 (IQR 1.3 - 10.2). 10 patients had mSASSS and facet joint data available at baseline and 2 years. Median progression rate was 1.1 units in 2 years and 4 patients (40%) showed progression of ≥2.0 mSASSS units or ≥1 new syndesmophyte. At baseline, median facet joint score was 1.5 (IQR 0.0 - 2.8), with partial or complete ankylosis in 7 (8%) individual facet joints in 5 patients. Median progression rate was 0.5 and 6 (12%) facet joints in 4 patients showed progression to partial or complete ankylosis. At baseline, there were no signs of VF. One traumatic VF (grade 3) occurred during 2 years of follow-up. At baseline, median BMD Z-score (n=12) was -0.6 (-1.5 - -0.4) for the lumbar spine and -0.1 (-1.8 - 0.1) for the hip and BMD remained stable over time. Before secukinumab treatment, median sCTX, PINP and BALP Z-scores were +0.0, -0.60 and +1.2 SD, respectively. The course of sCTX and PINP did not change significantly during follow-up, BALP Z-scores, however, significantly decreased at 2 years compared to baseline (Figure 1).

Conclusion: This explorative study in daily clinical practice with assessments of both new bone formation and bone resorption in AS patients treated with secukinumab showed that there was low radiographic damage at baseline, with little change during 2 years of treatment. Serum BTM levels reflecting the actual bone turnover process corrected for normal influence of age and gender showed high BALP at baseline, indicative for mineralization, which decreased during 2 years of secukinumab treatment.

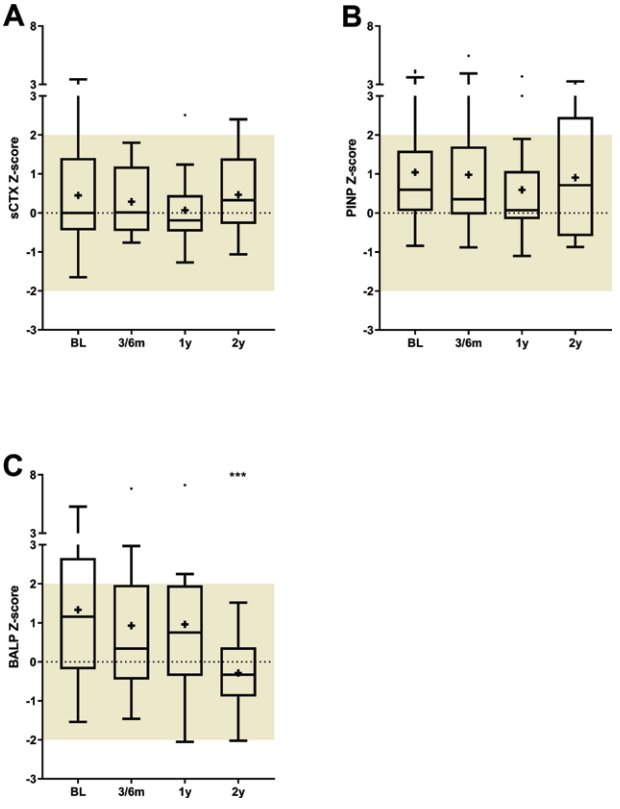


Figure 1. The effect of 2 year of secukinumab treatment on markers of bone turnover sCTX (A), PINP (B) and BALP (C) in patients with AS (n=17). Bar indicates median value.

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Disclosure of Interests: Mark Siderius Consultant of: Novartis., Suzanne Arends: None declared, Freke Wink Consultant of: Janssen., Anneke Spoorenberg Consultant of: Abbvie, Pfizer, MSD, UCB, and Novartis., Grant/research support from: Abbvie, Pfizer, UCB.

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AB0940

TITLE: CHOICE OF BDMARD AFTER TNFI: DOES IT MATTER IN THE TREATMENT OF SPONDYLOARTHRITIS?

Keywords: bDMARD, Spondyloarthritis

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Background: Following the failure of initial biological treatment in spondyloarthritis, switching to an alternative biological drug is possible. However, the data regarding the choice of the drug is limited. ASAS/EULAR guideline on axial spondyloarthritis does not make a distinction between TNFi, IL-17i or JAKi, with certain precautions regarding JAKi [1]. On the other hand, ACR/SAA/SPARTAN guideline recommends IL-17i over a different TNFi in primary failure, based on the assumption that TNF is not the key inflammatory mediator in these patients [2].

Objectives: Our main objective was to compare and contrast the clinical and laboratory features of the patients who received either a TNFi or IL-17i following the failure of the initial biologic treatment in our cohort of spondyloarthritis patients.
Methods: Spondyloarthritis patients followed in our institution between 2014 and 2022 who received a secondary bDMARD following primary or secondary biologic failure were included in our study. ASAS criteria were used to classify patients as having axial or peripheral SpA. Failure was defined as lack of clinical improvement following at least 12 weeks of therapy. Demographic, clinical, laboratory and radiological features of the patients, along with clinical and laboratory response following the second line bDMARD treatment were recorded.
Results: 90 patients were included in our study. 51% were female (N=46), mean age at diagnosis was 35 (SD: 11.9, %95 CI: 32.5–37.6), median duration of disease was 9 years (IQR: 10, minimum: 2 years, maximum: 38 years). 76% (N=68) of patients were classified as axial SpA, remaining 22 were classsifed as peripheral SpA. 68% (N=58) were HLA-B27 positive. Median ASDAS-CRP before the intial bDMARD was 3.7 (IQR: 1.3, min-max: 2.6–5.9). Adalimumab was the most used initial TNFi (48%, N=43). Most common reason of treatment switch was secondary failure (51%, N=41), followed by primary failure (25%, N=20) and side effects (19%, N=15). Following initial treatment failure, 30% of patients (N=27) were switched to a drug with an alternative pathway, with most of them being secukinumab (N=22). Median ASDAS-CRP after initial treatment failure was 3.8 (IQR: 1.0, min-max: 2.5–6.0). There was no difference in type of spondylarthritis, HLA-B27 positivity, ASDAS-CRP score and choice of bDMARD between primary and secondary failure groups. 24% of patients (N=22) achieved clinical remision in the secondary line of bDMARD treatment. The rate of clinical remission was 5% for TNFi and 75% for IL-17i (P<0.001). Duration of disease was shorter for responders (median 4 years vs. 11 years, P=0,03). Gender, HLA-B27 status, presence of enthesitis, dactylitis, uveitis, skin involvement, gastrointestinal involvement and initial ASDAS-CRP score did not differ between responders and non-responders (Table 1).

Table 1. Characteristics of responders and non-responders to secondary line treatment

	Secondary bDMARD		P
	Non-responder	Responder	
Disease duration	11 years (IQR: 12)	4 years (IQR: 5)	**0.033**
SpA classification			
Ax-SpA	52 (77%)	23 (24%)	0.722
Per-SpA	16 (72%)	6 (27%)	
HLA-B27			
Negative	18 (67%)	9 (33%)	0.285
Positive	45 (78%)	13 (22%)	
Second line bDMARD			
TNFi	59 (95%)	3 (5%)	**<0.001**
IL-17i	6 (25%)	18 (75%)	
Other	3 (%75)	1 (%25)	
Second line TNFi			
ADA	12 (86%)	2 (%14)	0.116
ETN	26 (100%)	0	
GOL	4 (80%)	1 (20%)	
IFX	9 (100%)	0	
CZP	8 (100%)	0	

Conclusion: The rate of remission for IL-17i was significantly higher than TNFi following the failure of initial bDMARD failure. There was no difference between clinical and laboratory features of responders and non-responders, except for duration of disease. These findings suggest using an alternative pathway in case of TNFi failure may be preferable.

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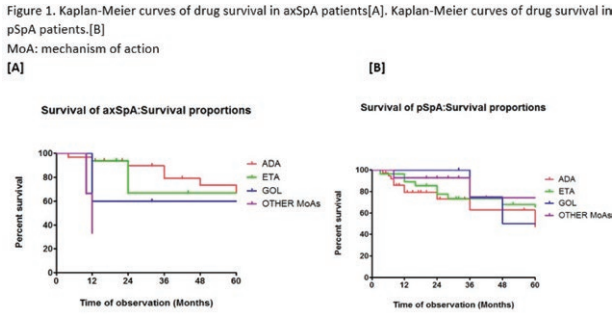
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4280

AB0941 REAL-LIFE ANALYSIS ON SURVIVAL TO TREATMENT AND REASONS FOR SWITCHING OF BIOLOGICAL DMARDS IN PATIENTS WITH SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, bDMARD

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Background: Studies on drug survival in patients with spondyloarthritis (SpA) in a real-life context are scant.
Objectives: We aimed to examine the real-life data of survival and the reasons for discontinuation or switching of biologic DMARDs (bDMARDs) in patients with axial and peripheral SpA (axSpA and pSpA).
Methods: This is a single-center retrospective longitudinal study in adult consecutive patients with axSpA and pSpA according to ASAS criteria treated with at least one bDMARD. Data are presented as medians (interquartile range [IQR]) for continuous data or as numbers (percentages) for categorical variables. Drug survival distribution curves were computed by the Kaplan-Meier method.
Results: A total of 141 patients (M/F: 72/69), median age 56 years [IQR 15], median disease duration 112 months [IQR 140] were enrolled. Among 57 patients with axSpA, 30 (53%) were HLA-B27-positive, 11 (19%) had had at least one uveitis episode, 4 (7%) were also affected by inflammatory bowel disease; 14 (24%) were taking NSAIDs and 2 (6%) glucocorticoids (GCs). Among 84 patients with pSpA, 50 (66%) were affected by psoriasis, 2 (5%) had had at least one uveitis episode; 16 (18%) were taking NSAIDs, 14 (16%) GCs and 33 (39%) csDMARD. The median duration of follow-up was 28 months (IQR 46). In the axSpA group, the median treatment duration was 32 months (IQR 60), while in the pSpA group was 25 months (IQR 37). Among axSpA patients, adalimumab (ADA) was the most common current bDMARD (58%) followed by etanercept (ETA) (28%), golimumab (GOL) (9%), ustekinumab (UST) (1%), and secukinumab (SEC) (4%). During a follow-up of five years, the comparison between survival curves of these bDMARDs showed significant differences (p= 0.015) (figure 1 A). The reasons for bDMARDs switching were primary failure (PF, 50%), secondary failure (SF, 25%), side effects (SE, 20% - mostly infections). In the pSpA groups, the most common current therapy was ADA (44%) followed by ETA (33%), SEC (12 %),GOL (6%), UST (5 %). As shown in figure 1 B, no significant differences (p= 0.49) in drug survival were found among patients treated with these bDMARDs. The reasons for bDMARDs switching were PF (38%), SF (38%), SE (8% - mostly infections).
Conclusion: In our experience, ADA was the most frequently prescribed bDMARDs as the first choice in patients with axSpA and pSpA. Despite PF and SF being the main causes of treatment discontinuation, a second anti-TNF agent was the preferred option in most cases.



REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0942 ANTI-IL17 TREATMENT AND INCIDENCE OF INFLAMMATORY BOWEL DISEASE: SYSTEMATIC REVIEW AND META-ANALYSIS OF CLINICAL TRIALS

Keywords: Psoriatic arthritis, Spondyloarthritis, bDMARD

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Background: A warning about appearance or worsening of inflammatory bowel disease (IBD) during treatment with anti-IL17 agents has been launched by regulatory agencies in the last years. This caution is based on the relationship between bowel (IBD), joint (spondyloarthritis [SpA]) and skin (psoriasis [Ps]);

regarding immune aspects. As well, anti-IL17 drugs have been proved ineffective in IBD treatment. [1,2]

Objectives: To analyze the incidence of IBD in patients with SpA or Ps treated with anti-IL17 drugs.

Methods: A systematic review about clinical trials has been performed using 4 databases (Medline, Embase, Web of Science, Cochrane Library). There were identified papers assessing the appearance of IBD in clinical trial's participants, previously diagnosed of Ps or SpA, treated with anti-IL17 drugs. A global incidence rate (IR), incidence rate ratio (IRR) and relative risks (RR) were estimated in this population, in paralell and crossover studies. Heterogeneity and risk of bias were also evaluated.

Results: 53 papers were finally selected for performing this meta-analysis. A global IR of IBD diagnosis in Ps/SpA patients under treatment with anti-IL17 was 0.3/100 patients-year (95%CI 0.24-0.37). An IRR of IBD diagnosis in Ps/SpA patients under treatment with anti-IL17 was 0.56 (95%CI 0.34-0.9, p<0.01). A RR of IBD diagnosis in Ps/SpA patients under treatment with anti-IL17 in crossover trials was 0.73 (95%CI 0.27-1.99, p=0.54) (Figure 1).

Conclusion: We cannot afirm that anti-IL17 agents increase the global risk of IBD appearance in Ps or SpA patients. Anti-IL17 drugs may not be avoided in clinical practice concerning Ps and SpA patients, due to IBD prevention.

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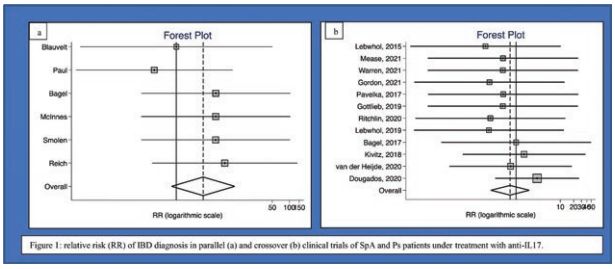


Figure 1: relative risk (RR) of IBD diagnosis in parallel (a) and crossover (b) clinical trials of SpA and Ps patients under treatment with anti-IL17.

Figure 1. Relative risk (RR) of IBD diagnosis in parallel (a) and crossover (b) clinical trials of SpA and Ps patients under treatment with anti-IL17.

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Disclosure of Interests: None Declared.
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AB0943

EVALUATION OF THE EFFECT OF TUMOR NECROSIS FACTOR - A THERAPY ON 24-HOUR AMBULATORY BLOOD PRESSURE MEASUREMENT AND SLEEP QUALITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Cardiovascular disease, Spondyloarthritis

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Background: Increased cardiovascular mortality has been reported in AS patients. There are studies showing the positive effects of anti-TNF-α therapy on both cardiovascular mortality and sleep quality. (1,2)

Objectives: To determine the changes in sleep quality and 24-hour blood pressure readings in patients with axial spondiloarthritis (axSpA) after treatment with anti- tumor necrosis factor TNF-α therapy.

Methods: Patients with axSpA who were admitted to Hacettepe University Hospital Rheumatology outpatient clinic between 01.03.2021 and 01.12.2021, anti-TNF-naive and without a history of cardiovascular disease were included. Disease activitiy assesment (ESR, CRP, BASDAI and BASFI), ambulatory blood pressure measurement (AMBP) and sleep quality evaluated by pittsburgh sleep quality index questionare (PSQI) were assessed before ant-TNF therapy (0.month) and after anti-TNF-α therapy (3.month).

Results: Totally, 28 patients with axSpA (mean (SD) age 40.0 (10.4) years, female:16(57.1%) patients) were included in to this study (table-1). The 0th and 3th month ABPM measurements of the patients in our study were within the normotensive limits. Both disease activity scores and median PSQI scores [8.5 (4.0-12.8)] were high and sleep quality was poor in 71% of the patients. Although there was a significant decrease in disease activity scores and a significant improvement in sleep quality at the 3. month after anti-TNF- α therapy, no significant changes were observed in ABPM parameters such as Ambulatory Arterial Stiffness İndex (AASI), Average real Variability (ARV), Pulse Pressure İndex (PPI), Sleeptroughsurge and Prewaking surge compared to pre-treatment. While after anti- anti-TNF-α therapy the percentage of patients with dipper phenomena increased in the 3. month, this increase was not statistically significant (46.4% (0. month) vs. 60.7% (3. month); p=0.388). Furthermore, the change in nighttime systolic blood pressure reduction was statistically significant respectively ([4.8% ((-7) – 9.2) (0. month) vs. 9.2% (4.7-11.1) (3. month); p=0.020], while there was no statistically significant difference in the change in nighttime diastolic blood pressure reduction respectively ([6.4% (1.5-14.7) vs. 9.6% (5.0-15.8); p=0.112] (table-2).

Conclusion: This study shows that anti-TNF-α treatment has positive effects on modifiable cardiovascular risk factors by increasing sleep quality and increasing nighttime blood pressure reduction. Prospective and long-term studies are needed.

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Table 1. Baseline demographic and clinical characteristics of the patients

Men/ Women n (%)		12 (42.9%)/ 16 (57.1%)
Age* years		40.0±10.4
Disease duration** years		6,5 (4-11)
HLA-B27 positivity n (%)		13(59,1%)
Peripheral manifestations n (%)		1 (3,6%)
Uveitis n (%)		-
Psoriasis n (%)		-
Dactilitis n (%)		-
Entesithis n (%)		-
IBD n (%)		-
VAS-Pain**		7.5 (5.3 – 9.0)
BASDAI** (0-10)		5.8 (3.5-7.1)
BASFI** (0-10)		6.4 (3.6-7.3)
ESR** (mm/h)		14.0 (6.3-30.0)
CRP** (mg/dL)		0.8 (0.3-2.3)
BMI* (kg/m^2)		27.2±5.6
LDL (mg/dL)*		123.7±38.4
HDL (mg/dL)*		50.2±10.1
Triglycerides (mg/dL)*		117.7±71.9
Smoking n (%)		13 (46.4%)
Obese n (%)		9 (32,1%)
Medicaitons*	NSAID n (%)	28 (100%)
	kDMARD n(%)	17 (60,7%)
	Steroid# n(%)	4 (14.3%)

Mean±standard deviation **(Median 25%-75%) # <7.5 mg prednisone or equivalent BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), BASFI (Bath Ankylosing Spondylitis Functional Index), IBD (Inflammatory bowel disease), ESR (Erythrocyte-Sedimentation Rate), CRP (C-reactive protein), BMI (Body mass index), NSAID (Non-steroidal anti-inflammatory drug), kDMARD (conventional DMARD), steroid (users under <7.5 mg). Those who were obese were considered as having a BMI >30.

Table 2 Comparison of dipper/non-dipper ratios (0.and 3.month) (n=28)

Variable		0.month	3.month	p
Sleep quality* n (%)	Good	8 (28.6%)	16 (57.1%)	0.008**
	Poor	20 (71.4%)	12 (42.9%)	
Sleep quality point [Median (25%-75%)]		8.5 (4.0-12.8)	4.0 (1.0-5.8)	<0.001 &
Dipper n (%)		13 (46.4%)	17 (60.7%)	0.388*
Non-dipper/Reverse dipper n (%)		15 (53.6%)	11 (39.3%)	
Reduction in systolic blood pressure% Median (25%-75%)		4.8 ((-7) -9.2)	9.2 (4.7-11.1)	0.020**
Reduction in diastolic blood pressure % Median (25%-75%)		6.4 (1.5-14.7)	9.6 (5.0-15.8)	0.112**

* Assesed by Pittsburg quality index ** Mc Nemar test & Wilcoxon test *** T-test in dependent groups

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0944

COMORBIDITIES IN THE SPONDYLOARTHRITIS GISEA COHORT: AN AVERAGE TREATMENT EFFECT ANALYSIS ON PATIENTS TREATED WITH BDMARDS

Keywords: bDMARD, Comorbidities, Artificial Intelligence

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Background: The treatment of Spondyloarthritis (SpA) has enormously improved thanks to bDMARDs, which are usually safe but they still require some caution because of their interference with the immune system homeostasis. ATE is a still evolving method designed to study the causal relationship between treatment and outcome.

Objectives: We endeavoured to investigate the impact of TNF-inhibitors (TNFi), anti-interleukin17 or interleukin12/23 monoclonal antibodies (anti-IL) on comorbidities among SpA patients enrolled in the Italian GISEA Registry, using an average treatment effect (ATE) analysis.

Methods: SpA patients from the GISEA Registry were divided into groups according to pharmacological exposure: no treatment (G0), TNFi (G1) and anti-IL (G2). In each group, the prevalence and incidence of infectious, cardiopulmonary, endocrinological, non-inflammatory gastrointestinal disease (NIGID), oncologic, renal and neurologic comorbidities were evaluated. Thus, each comorbidity was fitted for ATE and baseline features were evaluated for importance.

Results: This multi-centre Italian GISEA study comprised 4458 SpA patients (G0=495 patients, G1=3113 patients, G2=815 patients). Cardiovascular disease was the most prevalent and incident comorbidity in all groups, with no significant difference between groups. ATE showed no increased risk of solid cancer in G1 and G2 (G1 vs. G0 = 0,42 95% CI 0,20-0,85; G2 vs. G0 = 0,26 95% CI 0,08-0,71), but significantly higher prevalence and incidence in G0 (14.07/1000 patient-years, p=0,0001). Conversely, a significantly higher risk of NIGID and fibromyalgia was found in G1 and G2 vs. G0 (NIGID: G1 vs. G0 =1.56 95% CI 1.06-2.33, G2 vs. G0 =1.91 95% CI 1.05-3.24; fibromyalgia: G1 vs. G0 1.69 95% CI 1.05-2.68, G2 vs. G0 2.13 95% CI 1.14-3.41). No treatment risk modification was observed concerning haematological malignancies, cardiovascular events and endocrinological comorbidities.

Conclusion: Overall, this study reveals that bDMARDs have only a slight interference of the occurrence of comorbidities in SpA patients, underlining the appropriateness of the use of bDMARDs in current clinical practice. Some caveats pertain to NIGID and fibromyalgia. Importantly, causality may yield more reliable and relevant clinical information, flattening the unbalance between observational data and clinical trials.

Table 1. Prevalence and incidence of selected comorbidities in the GISEA Cohort and results of the Average Treatment Effect Analysis (ATE).

Incidence of comorbidities (number of events; events/1000 patient-years)

Comorbidity	No treatment (G0) N=494	TNFi (G1) N =3113	AntiIL (G2) N=815	P value (ANOVA)
Cardiovascular disease	10 events; 16.90	114 events; 28.81	26 events; 26.44	0,0794
Endocrinological disease	7 events; 11.35	60 events; 9.30	15 events; 13.83	0,6678
Fibromyalgia	5 events; 6.72	102 events; 13.42	33 events; 25.19	**0,0095**
Gastrointestinal (non IBD) disease	8 events; 12.41	110 events; 16.48	33 events; 19.68	**0,0408**
Haematologic malignancy	0 events; 0	2 events; 0.26	0 events; 0	0,6498
Solid cancer	10 events; 14.07	13 events; 1.71	5 events; 3.79	**0,0001**

Average treatment effect (ATE) analysis

Outcome (comorbidity) RR (CI 95%)	TNFi vs. no treatment (G1 vs. G0)	antiIL vs. no treatment (G2 vs. G0)	antiIL vs. TNFi (G2 vs. G1)
Cardiovascular	1.41 (0.99-1.99)	1.66 (1-2.97)	1.16 (0.91-1.55)
Endocrinologic	1.27 (0.76-2.05)	1.41 (0.68-2.72)	1.09 (0.74-1.54)
Fibromyalgia	**1.69 (1.05-2.68)**	**2.13 (1.14-3.41)**	1.25 (0.95-1.51)
GI (non IBD)	**1.56 (1.06-2.33)**	**1.91 (1.05-3.24)**	1.21 (0.92-1.51)
Haematologic malignancy	0.78 (0.14-2.88)	0.81 (0.04-4.67)	0.78 (0.20-1.96)
Solid cancer	**0.42 (0.20-0.85)**	**0.26 (0.08-0.71)**	**0.61 (0.33-0.96)**

Legend: G0= Group 0, no treatment= no biologic DMARD, G1= Group 1, TNFi= Tumour necrosis factor inhibitors, G2= Group 2, antiIL= anti-interleukin17 and anti-interleukin17/23 monoclonal antibodies, N= numerosity of the group, IBD= inflammatory bowel disease, RR= relative risk, CI 95%= confidence interval 95%. Significant results are in bold characters.

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AB0945

ASSESSMENT OF THE RISK OF LIVER FIBROSIS IN SPONDYLOARTHRITIS TREATED WITH SECUKINUMAB: A SINGLE-CENTER RETROSPECTIVE OBSERVATIONAL STUDY

Keywords: Disease-modifying Drugs (DMARDs), Spondyloarthritis, Psoriatic arthritis

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Background: The prevalence of non-alcoholic steatopathy (NAFLD) is increasing in chronic inflammatory rheumatisms. NAFLD may favor the development of liver fibrosis, which may lead to cirrhosis and its complications including hepatocellular carcinoma. The process of hepatic fibrogenesis involves inflammatory mechanisms with an overexpression of TNF but also of IL 17. Thus, the use of anti-TNF alpha is associated with a decrease in the incidence of hepatic fibrosis. Anti-IL-17 could also have an effect on fibrogenesis but this has not been studied in spondyloarthritis.

Objectives: The aim of this study was to assess, non-invasively, the risk of liver fibrosis using the FIB-4 score, in patients treated with anti-IL-17.

Methods: A single-center retrospective observational study was performed. We included all consecutive patients followed between 2015 and 2022 for axial spondyloarthritis (axSpA) meeting the ASAS 2009 criteria or psoriatic arthritis (PsA) meeting the CASPAR criteria, treated for at least 12 months with secukinumab, and for whom at least 12 months of biological follow-up was available. For each patient, we collected demographic data, clinical data, associated treatments, and levels of AST, ALT, platelets at initiation of treatment and after 12 months of treatment. We assessed the FIB-4 score (age(years) * ASAT (U/L))/(platelets (109/L)*√ALAT (U/L))at M0, M12, and M24. Fischer's exact test was used for comparison between categorical variables and Student's t test for quantitative variables.

Results: 38 patients, (20 PsA, 18 axSpA; 60% women in both groups; mean age 57 years in PsA group and 46 years in axSpA group (p<0.01)) were included. The mean disease duration was 10 ± 4 years in the PsA group and 11 ± 5 years in the axSpA group. 78% of axSpA were HLA B27 positive versus 20% of PsA (p<0.01). There was a trend towards a higher prevalence of NAFLD (30% vs. 5%, p=0.09) and previous methotrexate use was more frequent (100% VS 39%, p<0.01) in PsA. The FIB4 score was higher in the PsA group at baseline (1.30 ± 0.24 VS 0.74 ± 0.05; p=0.04). This difference remained significant after 12 months of treatment (1.34 ± 0.25 vs. 0.79 ± 0.06; p=0.048). At M0, no axSpA patient had a FIB4 > 1.3 vs. 6 in the PsA group. At M12, one axSpA patient had a FIB4>1.3 (and <2.0) vs. 6 in the PsA group (including 4 patients with a FIB4>2.0). At M24, one axSpA patient out of 6 had a FIB4>1.3 (and <2.0) versus 3 in the PsA group out of 13 (including 1 patient with FiB4>2.0 and 1 with FiB4<1.3 at inclusion). The overall change in FiB-4 score at 1 year was not different in the PsA and axSpA groups (-0.62 ± 0.25 vs. -0.59 ± 0.27; p=NS). Finally, PsA patients suffer from NAFLD did not worsen their FiB4 score (2.08 ±1.6 at M0 VS 2.02 ± 1.07 at M12; p=NS).

Conclusion: In PsA and axSpA, 1-year treatment with secukinumab is not associated with an increase in FIB-4 even in patients known to have NAFLD. This study requires confirmation in a larger cohort.

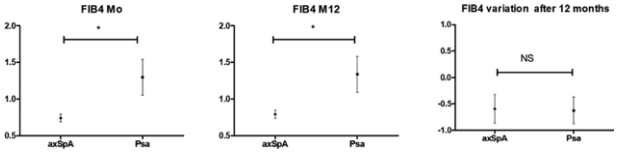


Figure 1.

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AB0946

A META-ANALYSIS TO EVALUATE THE EFFICACY AND SAFETY OF IGURATIMOD ON ACTIVITY AX-SPA

Keywords: Spondyloarthritis, Disease-modifying Drugs (DMARDs)

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Background: Iguratimod is a newly-developed small molecular anti-rheumatic drug, which can inhibit the effects of prostaglandin E2, TNF-α and IL-17. Iguratimod had been reported to be effective in the treatment of SpA. Iguratimod was implied to be of potential efficacy on ax-SpA.
Objectives: This study was aimed to demonstrated the efficacy and safety of Iguratimod on activity ax-SpA (ASDAS>2.1).
Methods: We performed a meta-analysis to systemically evaluate the efficacy and safety of Iguratimod by gathering the published RCTs about the treatment of Iguratimod in ax-SpA, mean differences (MD) and 95% CI of the change of back pain, morning stiffness, PhGA, ASDAS, BASDAI, BASFI and concertation of TNF-α, ESR and CRP were calculated. Besides, the odds ratio (OR) and 95% CI of the ASAS 20, ASAS 40, partial remission of ASAS, ASAS 5/6 were calculated as well.
Results: 7 RCTs were admitted into the meta-analysis, including 186 cases in the control group and 208 cases in the Iguratimod group. The control group was treated with NSAIDs monotherapy or NSAIDs combined with DMARDs, and the range of follow-ups was 12-24 weeks. The improvement of back pain (MD -1.76, 95% CI: -2.33 ~ -1.20, P<0.001), morning stiffness (MD -11.27, 95% CI: -13.57 ~ -8.96, P<0.001), PhGA (MD -2.86, 95% CI: -5.45 ~ -0.26, P<0.05), ASDAS (MD -0.8, 95% CI: -1.26 ~ -0.33, P<0.001), BASDAI (MD -1.19, 95% CI: -1.59 ~ -0.78, P<0.001), BASFI (MD -0.92, 95% CI: -1.29 ~ -0.55, P<0.001), ASAS 20 (OR 11.94, 95% CI: 5.30 ~ 26.91, P<0.001), ASAS 40 (OR 4.46, 95% CI: 1.95 ~ 10.16, P<0.001), partial remission of ASAS (OR 17.69, 95% CI: 4.06 ~ 77.08, P<0.001) in the Iguratimod treatment group were better than those in the control group, as well as for concertation of ESR (MD -8.77, 95% CI: -15.37 ~ -2.18, P<0.001), CRP (MD -4.44, 95% CI: -6.66 ~ -2.23, P<0.001) and TNF-α (MD -6.98, 95% CI: -7.72 ~ -6.24, P<0.01). There was no significant difference in the reported adverse events between the two groups.
Conclusion: Iguratimod is effective and well-tolerated during the treatment and thus could be a new pharmaceutical option for activity ax-SpA patients.
REFERENCES: NIL.
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Disclosure of Interests: None Declared.
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AB0947

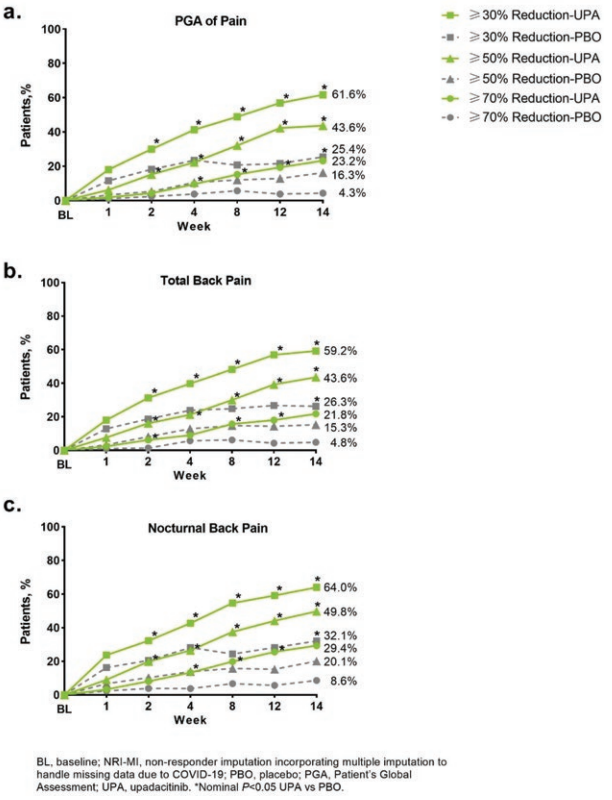
EFFECT OF UPADACITINIB ON REDUCING PAIN IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS AND INADEQUATE RESPONSE TO BIOLOGIC THERAPY

Keywords: Spondyloarthritis, Pain, bDMARD

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Background: Pain is a debilitating symptom of ankylosing spondylitis (AS) that negatively affects patients' lives. Upadacitinib (UPA), a Janus kinase inhibitor approved for the treatment of AS and other inflammatory diseases, showed significant efficacy vs placebo (PBO) in the phase 2/3 SELECT-AXIS 1 study in patients with AS who were biologic-naive and in the phase 3 SELECT-AXIS 2 study in patients with active AS who had an inadequate response (IR) to biological therapy [1,2]. Improvement in pain outcomes with UPA was also previously demonstrated in the SELECT-AXIS 1 study [3].
Objectives: The objective of this post-hoc analysis of SELECT-AXIS 2 was to evaluate the efficacy of UPA vs PBO on multiple pain assessments through 14 weeks in patients with IR to a biologic disease-modifying antirheumatic drug (bDMARD-IR).
Methods: SELECT-AXIS 2 (NCT04169373) enrolled adults with active AS with IR to biological therapy, including patients who discontinued biologics due to lack of efficacy or intolerance [1]. Patients were randomized 1:1 to UPA 15 mg once daily (QD) or PBO for 14 weeks. Pain endpoints evaluated here included the proportion of patients achieving ≥30%, ≥50%, and ≥70% reduction from baseline, minimal clinically important difference (MCID, defined as ≥1 point reduction or ≥15% reduction from baseline), and much better improvement (MBI, defined as ≥2 point reduction and ≥33% reduction from baseline) in Patient's Global Assessment (PGA) of pain, total back pain, and nocturnal back pain on a 0–10 numeric rating scale [3,4]. Non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19 was used.
Results: A total of 211 patients received UPA 15 mg QD and 209 patients received PBO. Higher proportions of patients receiving UPA vs PBO achieved ≥30% and ≥50% reductions in PGA of pain, total back pain, and nocturnal back pain as early as week 2 that were sustained at all time points through 14 weeks (nominal *P*<0.05; **Figure 1a-c**). Achievement of ≥70% reductions in PGA of pain and nocturnal back pain were higher at week 4 and sustained thereafter (**Figures 1a** and **1c**), and achievement of ≥70% reduction in total back pain was higher at week 2 and week 8, but not week 4, and sustained thereafter (**Figure 1b**). Results were similar for the proportion of patients achieving MCID and MBI, with improvements in PGA of pain, total back pain, and nocturnal back pain for UPA vs PBO as early as week 1 (MCID) or week 2 (MBI) that were sustained through week 14 (all nominal *P*<0.001; **Table 1**).

Figure 1. Proportion of Patients Achieving ⩾30%, ⩾50%, and ⩾70% Reduction in Pain Outcomes Over Time (NRI-MI)



BL, baseline; NRI-MI, non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; PBO, placebo; PGA, Patient's Global Assessment; UPA, upadacitinib. *Nominal *P*<0.05 UPA vs PBO.

Table 1. Achievement of MCID and MBI in Pain Outcomes at Week 14 (NRI-MI)

	Responder Rate (95% CI), %		
Pain Outcomes	**UPA 15 mg**	**PBO**	**Nominal *P* Value**
PGA of pain			
MCID	81.0 (75.8–86.3)	62.7 (56.1–69.2)	<0.0001
MBI	60.7 (54.1–67.3)	24.9 (19.0–30.7)	<0.0001
Total back pain			
MCID	80.1 (74.7–85.5)	65.1 (58.6–71.5)	0.0005
MBI	58.3 (51.6–64.9)	25.4 (19.5–31.3)	<0.0001
Nocturnal back pain			
MCID	82.9 (77.9–88.0)	61.3 (54.7–67.9)	<0.0001
MBI	61.6 (55.0–68.2)	32.1 (25.7–38.4)	<0.0001

MBI, much better improvement; MCID, minimal clinically important difference; NRI-MI, non-responder imputation incorporating multiple imputation to handle missing data due to COVID-19; PBO, placebo; PGA, Patient's Global Assessment; UPA, upadacitinib.

Conclusion: In patients with active AS who were bDMARD-IR, greater proportions of patients treated with UPA achieved rapid and clinically meaningful reductions in pain vs PBO as early as week 2 that were sustained through 14 weeks across multiple pain assessments.

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AB0948 SPERM PARAMETERS DIFFER AMONG DIFFERENT SPONDYLOARTHROPATHY CATEGORIES- A PROSPECTIVE CONTROLLED PILOT STUDY

Keywords: Pregnancy and reproduction, Inflammatory arthritides, Psoriatic arthritis

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Background: Fertility impairment may occur in men diagnosed with inflammatory arthritis. High disease activity, sex hormones imbalance and some disease modifying drugs are important factors considered to be involved in this phenomenon [1]. Sperm parameters assessment is of key importance in clinical practice. Studies focusing on fertility assessment in patients diagnosed with spondyloarthritides (SpA) showed discordant results [1]. Indeed, long term treatment with Methotrexate (MTX) raised concerns about its potential negative impact on male fertility although more recent studies do not confirm it [1,2].

Objectives: To identify potential differences in sperm analysis among patients with ankylosing spondylitis (AS) and psoriatic arthritis (PSA) and to assess the impact of long-term low and intermediate doses of MTX on sperm parameters.

Methods: Consecutive active SpA patients were recruited for sperm parameters assessment. Demographics, type of disease, disease duration, validated activity/skin scores, current therapies and sperm parameters were recorded. Patients in the PSA group underwent sperm parameters assessment at baseline and after chronic MTX treatment. A healthy age matched control group underwent parallel sperm parameters assessment.

Results: Out of 33 SpA patients, 20 patients accepted to undergo sperm parameters evaluation. 15 patients were diagnosed with AS (7 solely with axial involvement) and 5 patients were diagnosed with PSA. Table 1. presents the most important monitored parameters. All patients presented high disease activity measured by ASDAS and DAPSA. All patients had mild Psoriasis Area and Severity Index scores. Both AS patient groups (purely axial, and axial + peripheral) showed comparable sperm parameters to the control group. Chronic MTX therapy was given to 5 AS patients (refractory to Salazopyrin therapy). This subgroup presented normozoospermia. Sperm parameters were profoundly altered in all PSA patients, at baseline and during follow up, when compared to both the AS and control groups. Chronic MTX administration in the PSA group did not supplementarily alter the sperm parameters. On the contrary, in 2 patients a mild sperm concentration and motility increase was detected at follow up.

Table 1. Demographics, type of disease, disease duration, MTX exposure and sperm parameters in AS and PSA patients versus controls.

Demographics	Axial SpA (n=7)	Axial and peripheral SpA (n=8)	PSA (n=5)	Controls (n=25)
Age (years, mean±SD)	35.85±8.37	31.71±7.97	36±12.54	34.52±5.1
Disease duration (years, mean±SD)	4.14±2.11	4±2.5	3.22±1.74	-
Sperm characteristics				
Sperm concentration ($nx10^6$/ml, mean and limits, NV>15)	60.71(15-110)	43.25 (7-66)	6.025 (0.1-12)	61.32 (0-160)
Total motility (%, SD, NV>40)	65±15.81	62.57±10.81	33.12±19.19	51.68±21.49
Normal morphology (%, NV>4)	65±23.22	54±9.70	13.87±1.12	56.12±16.14
Normozoospermia (%)	85.71	87.50	0	68
Normoastenozoospermia (%)	0	0	0	20
Oligospermia (%)	14.28	0	40	12
Oligoastenozoospermia (%)	0	12.50	60	0
Treatment				
Methotrexate 15-20 mg/week (number of patients)	0	5	5	0

SD-standard deviation, NV-normal values

Conclusion: Our data suggest that PSA patients represent a distinct group inside the SpA disease spectrum and fertility impairment is already a manifestation of early disease. AS patients with early disease onset undergoing treatment (including MTX) have sperm parameters comparable to those of the controls. Chronic MTX therapy in dosages between 15-20 mg/week do not have a negative impact on sperm parameters.

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AB0949 COEXISTING INFLAMMATORY BOWEL DISEASE AND ANKYLOSING SPONDYLITIS: MANAGEMENT AND CLINICAL OUTCOMES

Keywords: Comorbidities, Gastrointestinal tract, Spondyloarthritis

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Background: Ankylosing spondylitis (AS), which occurs in about 10% of inflammatory bowel disease (IBD) patients [1], is more common in Crohn's disease and does not correlate with bowel activity [2]. The occurrence of IBD in patients with AS is 4-16% [3-5].

Objectives: To investigate the patterns of treatment modifications following newly diagnosed AS in patients with IBD or a new IBD diagnosis in patients with AS.

Methods: This is a retrospective observational study that included patients with coexisting IBD and AS that were followed simultaneously by the gastroenterology and the rheumatology departments of the Sheba Medical Center. Patients with a follow-up duration of at least 3 months since the second diagnosis were included.

Results: The cohort consisted of 68 patients, 41 with a first diagnosis of IBD (fIBD-group) and 27 with a first diagnosis of AS (fAS-group). Patients in the fAS-group were younger (median age of 36 years, inter quartile range (IQR) 25-48 vs. 43 years IQR 35-56, p=0.043), had more Crohn's disease (92.6% vs. 68.3%, p=0.016), had a shorter interval up to the second diagnosis (median of 3 years, IQR 1-6 vs. 6 years, IQR 2-11.5, p=0.03), and had an increased rate of past/current biologic treatment (81% vs. 51%, p=0.019) compared with the fIBD-group.

Therapy modifications rates were 78% in the fIBD-group and 96% in the fAS-group. The most common modification for the fIBD-group was initiation of biologic therapy in 18/32 patients (Adalimumab 44%, Infliximab 33%, Golimumab 5.75%, Etanercept 5.75%, Certolizumab pegol 5.75%, Ustekinumab 5.75%). In the fAS-group, switching biologic agent to Adalimumab or Infliximab (42%) and ceasing NSAIDs (27%) were the most common (Figure 1). At 1-year follow-up there were no significant differences in clinical outcomes (treatment failure, surgery/hospitalization, clinical remission) between fIBD and fAS groups. However, patients in both groups with treatment modifications, had a trend for higher rate of IBD clinical remission than patients without (72% vs. 40%, p=0.066). No difference was found in AS clinical outcome.

Conclusion: Treatment modifications are common among newly coexisting IBD and AS patients, preferably biologic drug modifications. These modifications may contribute to IBD clinical remission.

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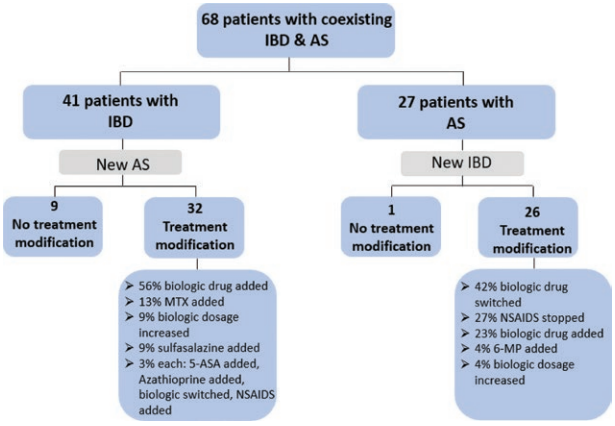


Figure 1. Cohort stratification by diagnoses and treatment modifications AS=ankylosing spondylitis; IBD= inflammatory bowel disease; MTX=methotrexate; 5-ASA=5-aminosalicylic acid; 6-MP=mercaptopurine; NSAIDS= non-steroidal anti-inflammatory drugs.

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AB0950 COST-EFFECTIVE THERAPY IN AXIAL SPONDYLARTHRITIS: A COMPARATIVE ANALYSIS OF TWO TREATMENT STRATEGIES

Keywords: Targeted synthetic drugs, Spondyloarthritis, Tapering

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Background: Biologic disease-modifying anti-rheumatic drugs (bDMARDs) remain inaccessible to a majority of patients in resource-poor countries due to high cost. Cost-saving strategies including the use of generic bDMARDs with an early de-escalation schedule instead of continued standard dose or using generic small molecules such as tofacitinib or baricitinib are being explored for the treatment of axial spondyloarthritis (AxSPA). The generic molecules are cheaper in India as compared with the rest of the world.

Objectives: To compare the efficacy, safety, and cost of generic tofacitinib and disease activity-directed early de-escalation schedule of intended copies of adalimumab (ADA), the most commonly used bDMARD available in India.

Methods: In this retrospective study, patients diagnosed with AxSpA in a tertiary care center in India, initiated on tofacitinib (TOFA), and had at least one follow-up visit from January 2021 to November 2022, were included. Patients who received ADA due to moderate to high disease activity with an early de-escalation schedule, during the same period were included as historical diseased controls. Early de-escalation was defined as increasing the interval between 2 doses of ADA by 1 week every 3 months within 12 months of initiation of the drug. The baseline demographic, clinical presentation, and response to treatment and adverse drug reactions were compared between patients on TOFA and ADA. An Ankylosing spondylitis disease activity score (ASDAS-CRP) of <2.1 was considered a good response to treatment. The descriptive data are presented as mean± SD or median (Interquartile range) or percentages. Fisher's exact test and Mann Whitney U test were used to compare categorical and continuous parameters, respectively, between TOFA and ADA. The average monthly cost of therapy was calculated for both groups.

Results: Among 240 patients who received TOFA, 155 patients satisfied the inclusion criteria, while 40 patients received early de-escalation of ADA. The age (33.0±951 and 33.6±13.3 years, p= 0.66), gender [males n=131 (86.8%) and 32 (80.0%), p = 0.32], median disease duration [7 (4-11) and 7 (4.3-11.0) years] and CRP [22.1 (10.2-44.5) and 23.85(14.48-71.50) mg/L, p= 0.32] were similar for patients who received TOFA and ADA, respectively. The frequency of uveitis, peripheral arthritis, and HLA B27 positivity was similar between the two therapies. Majority of patients [124(82.1%) in the TOFA group and 32 (80%) in the ADA group] in both the groups received concomitant conventional DMARDs, while 36 (23.8%) patients on TOFA received prior TNF inhibitors. During a follow-up period of 6 (3-9) months, 129 (86.7%) of 151 patients on TOFA achieved low disease activity or inactive disease status as compared with 37 patients (92.5%) who received ADA (p = 0.42). Adverse drug reaction requiring drug discontinuation was observed in 6 patients on TOFA (transaminitis in 3, herpes zoster in 2, 1 infective spondylodiscitis) and in 5 patients receiving ADA (transaminitis in 4 and abdominal tuberculosis in 1).

Conclusion: Tofacitinib therapy is comparable to the early dose de-escalation strategy of adalimumab in terms of treatment response and safety in Indian patients with AxSPA.

Acknowledgements: I have no acknowledgments to declare.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5901

AB0951 EFFICACY AND SAFETY OF UPADACITINIB IN ANKYLOSING SPONDYLITIS. REAL WORLD DATA

Keywords: Spondyloarthritis, bDMARD

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Background: Upadacitinib is a selective and reversible inhibitor of Janus Kinases (JAKs) that preferentially inhibits signaling via JAK1 or JAK1/3. JAK1 inhibition with upadacitinib modulates JAK-dependet cytokine signaling, thereby decreasing the inflammatory burden of different immune-mediated diseases. Upadacitinib is approved for the treatment of rheumatoid arthritis, psoriatic arthritis, non-radiographic axial spondyloarthritis, ankylosing spondylitis (radiographic axial spondyloarthritis), ulcerative colitis, and atopic dermatitis. In the case of ankylosing spondylitis, the drug has been approved for use in Spain since March 2022.

Objectives: The present study aims to evaluate the first data on safety and efficacy of upadacitinib use in ankylosing spondylitis in real clinical practice.

Methods: Retrospective observational multicenter study that included patients of 8 Spanish hospitals. Demographic data, personal history, and clinical course of patients diagnosed with ankylosing spondylitis treated with upadacitinib at participating centers were collected.

Results: Forty-four patients with ankylosing spondylitis who received upadacitinib for a mean time (SD) of 8.7 (7.4) months were included in the study. They had received previous biological treatments in 86 % of cases, 30% of patients at least 5. An improvement was observed in 70 % of patients as measured by subjective patient-reported improvement. The treatment was

suspended in the 27.3% of patients, the main reason for suspension was inefficacy. A higher percentage of suspension was found in patients who had received a greater number of previous biological treatments. Adverse effects were reported in 8 patients, the most serious being one episode of tachyarrhythmia, one episode of deep vein thrombosis, one episode of peptic ulcer and one episode of herpes zoster, and the most frequent adverse effect being headache.

Conclusion: 70% of patients with ankylosing spondylitis who received upadacitinib for a median time of 8.7 months experienced subjective improvement in their symptoms.

Acknowledgements: Acknowledgements to all collaborators.

Disclosure of Interests: None Declared.

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AB0952 COMPARISON OF THE EFFECT BETWEEN BISPHOSPHONATE AND DENOSUMAB ON BONE MINERAL DENSITY AND RADIOGRAPHIC PROGRESSION IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A PILOT STUDY

Keywords: Spondyloarthritis

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Background: Osteoporosis is a frequent complication of ankylosing spondylitis (AS). Althogh there are no clear guidelines for the treatment of this secondary osteoporosis in AS, antiosteoporotic agents including bisphosphonate were used according to the same guidelines for primary osteoporosis. Also, approved by European Medicines Agency (EMA) in 2010, denosumab is being widely used.

Objectives: To compare the effect between bisphosphonate and denosumab on bone mineral density and radiographic progression in patients with AS for one year.

Methods: Among twenty-four patients with AS, sixteen patients were treated with bisphosphonate and nine patients with denosumab. BMD in the lumbar spine and right femur was measured by dual energy x-ray absorptiometry (DEXA) at baseline and one year after treatment. Radiographic progression was scored using the modified Stoke AS Spinal Score (mSASSS). Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS), and bone markers (bone-specific alkaline phosphatase (ALP), Collagen type 1 cross-linked C-telopeptide) were used to assess disease activity.

Results: Mean BMD values in the lumbar spine and total hip at one year increased when compared to those at baseline in both the bisphosphnate and denosumab groups (P=0.006 and 0.007 in bisphosphonate group, 0.015 and 0.036 in denosumab group). The increment was greater in denosumab group. The mean BMD in L-spine and total hip increased by 11.0% and 4.9% in denosumab group, while 9.0% and 2.7% in bisphosphonate group. There were no differences in disease activities such as BASDAI, ASDAS-CRP, ESR, and CRP between two groups. mSASSS and number of syndesmophyte also revealed no significant differences, suggesting that denosumab does not adversely affect disease activity and radiographic scores compared to bisphosphonate.

Table 1. Comparisons of the changes of clinical measure and radiographic scores between bisphophonate and denosumab

Change from baseline to year one	Bisphosphonate (n=15)	Denosumab (n=9)	P-value
BASDAI	1.5 ± 2.4	2.9 ± 2.8	0.215
ASDAS-CRP	0.9± 1.2	1.7 ± 1.3	0.174
ESR, mm/h	17.2 ± 24.8	31.0 ± 35.9	0.519
CRP, mg/l	13.7 ± 31.5	24.5 ± 44.0	0.446
Bone-specific ALP, μg/l	-0.7 ± 14.6	4.2 ± 4.3	0.379
C-telopeptide, ng/ml	-0.7 ± 2.7	0.128 ± 0.1	0.411
mSASSS in C- and L-spine	0.7 ± 0.9	0.4 ± 1.4	0.411
Number of syndesmophytes in C- and L-spine[a]	0.1 ± 0.3	0.2 ± 0.4	0.558

Changes are calculated as base value subtracted from one year value. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index. ASDAS: Ankylosing Spondylitis Disease Activity Score. ALP: ankaline phosphatase. mSASSS: modified SASSS. C-: cervical. L-: lumbar.

Conclusion: Both bisphosphonate and denosumab increase L-spine and total hip BMD, while not affecting disease activity and spinal new bone formation. Further prospective studies with larger subject numbers are needed.

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Disclosure of Interests: None Declared.

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AB0953 THE EFFECTIVENESS OF IL-23 INHIBITORS ON AXIAL SPONDYLARTHRITIS AND AXIAL PSORIATIC ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Psoriatic arthritis, Spondyloarthritis

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Background: Axial spondylarthritis (axSpA) is an immune-mediated systemic chronic inflammatory arthritis involving the axial skeleton that may involve peripheral joints. Nonsteroidal anti-inflammatory drugs are first line therapy in the management of axSpA, however for many patients NSAID monotherapy is not sufficient to induce disease remission. Given the known efficacy of biologics in spondyloarthritis and the heterogenicity of these conditions, treatment choices should take into account all relevant disease domains. Interleukin-23 has been identified as a promising therapeutic target in SpA and PsA based on a significant body of evidence. Interleukin 23 inhibitors have produced inconsistent results when used to treat axial spondylarthritis and axial psoriatic arthritis.(1,2) Thus, there is a need for a holistic understanding of the use of IL23 inhibitors in axial conditions in particular spondylarthritis and psoriatic arthritis to provide appropriate evidence-based management and mitigate the growing burden of these diseases.

Objectives: To explore the latest reported literature on the effectiveness of IL 23 inhibitors in axial spondylarthritis and psoriatic arthritis.

Methods: A systematic literature review was conducted. The following databases were searched: Pubmed, Mendely EMBASE, MEDLINE (OVID), CINAHL, Cochrane Library (central) and Web of Science. The search strategy included terms related to the axial spondylarthritis and axial psoriatic arthritis and specifying the medications of study interest Ustekinumab, Risankizumab, Guselkumab or Tildrakizumab. The search was restricted to studies published in English from inception until June 2022. Randomized controlled trials, observational studies, or systematic reviews were eligible. Screening of titles, abstracts, and subsequent full text assessment were conducted independently by two independent reviewers. Outcomes assessed were BASDIA, BASDAI 50,modified BASDAI, BASFI and ASDAS.

Results: Total of 4456 studies were identified, 9 studies of which 5 studies examining axial spondylarthritis (Four RCTs and 1 prospective study) and 4 studies examining axial psoriatic arthritis (two prospective observational studies and two post hoc-analysis) were deemed suitable for inclusion. In contrast to one prospective observational study, 4 RCT (3 ustekinumab, 1 risankizumab) did not support the use of IL23 inhibitors in axSpA based on the analyzed outcome measures of interest. Pooling of results for the three ustekinumab trials (BASDAI50, BASFI, and ASDAS) (figure 1) demonstrated that the drug was not efficacious in treating axSpA. However, trials in axial PsA investigations showed an improvement in BASDAI, modified BASDAI, and ASDAS.

Conclusion: The results of this meta-analysis would support the use of IL-23 inhibiting medications in the treatment of axial PsA. However, this is not the case for axSpA, as these drugs failed to demonstrate a significant improvement in patient outcomes in axSpA patient populations. This meta-analysis raises several interesting questions regarding differences in pathogenesis of axSpA and axial PsA. It also supports the need for ongoing drug development in axSpA, as biologic options remain limited compared to other forms of inflammatory arthritis.

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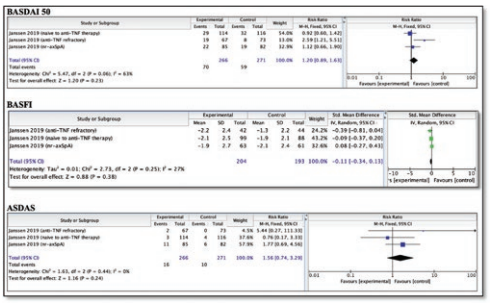


Figure 1.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0954

IMPACT OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH AS USING BIOLOGIC AGENTS

Keywords: Comorbidities, bDMARD, Spondyloarthritis

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Background: Although renal involvement is an rare extra-articular involvement in patients with ankylosing spondylitis (AS), medications and accopamyning comorbidities may adversly affect renal functions [1].
Objectives: To determine the frequency and impact of CKD in patients with AS using biologic disease modyfying anti-rheumatic drugs (bDMARDs).
Methods: Between 2005 and November 2021, 3207 patients diagnosed with AS according to the modified New York criteria were enrolled in the Hacettepe University biological database (HUR-BIO). The 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guideline was used for the definition of CKD to evaluate the renal function of patients. Glomerular filtration rate (GFR) was calculated with the MDRD (modified Modification of Diet in Renal Disease) formula, taking into account the creatinine value, age and gender parameters of the patients [2]. CKD was detected in 39 (1,2%) patients. Age-sex matched 41 non-CKD AS patients were selected as the control group. Demographic and clinical characteristics and mortality rates of AS patients with and without CKD were compared.
Results: Of 39 AS-CKD patients, 25 (64.1%) had CKD before the initation of bDMARD and and 14 (35.8%) developed CKD during follow-up after treatment was started. Patients with AS-CKD had longer duration of symptoms and disease (Table 1). Comorbidities such as hypertension, coronary artery disease and amyloidosis were more prevalent in patients with AS-CKD. At a median follow-up of 2.48(0.1-20.1) years, mortality was observed in 11(28.2%) patients in the AS-CKD group, while no mortality was observed in the age-sex matched AS-nonCKD group (p<0.001, Figure 1). The mortality rate in patients with AS-CKD was 12.6 per 1000 patient-years, and 4 (10.2%) of deaths were during the COVID-19 pandemia.

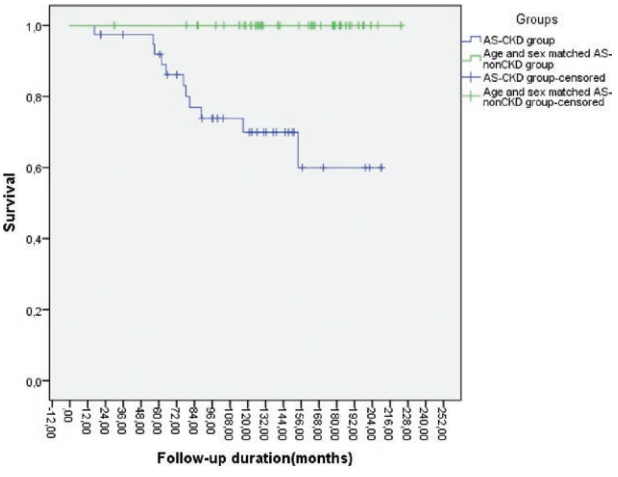


Figure 1.

Conclusion: Both comorbid disease burden and mortality seem to be increased in patients with AS-CKD. Increased mortality was more pronounced during the COVID-19 pandemia.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.

Table 1.

	AS-CKD group (n=39)	AS-nonCKD group (n=41)	P	Total AS patients, (n=3207)
Age, mean(SD), years	68.2 (12.0)	58.8(12.6)	-	47.9±(11.2)
Male, n(%)	27 (69.2)	27(65.9)	-	1716(53.5)53.1)
Symptom duration, years median (min-max)	20 (5-42)	11(2-30)	0.01	10(1-44)
Disease duration, years median (min-max)	14,5(5-42)	7(1-29)	0.04	6(1-37)
HLA-B27 positivity, n(%)	13(33.3)	12(29.2)	0.5	826/2014(41.0)
Uveitis, n(%)	6/35	4/36	0.2	339/2946(11.5)
Inflammatory bowel disease, n(%)	4/35	3/36	0.4	135/2946(4.58)
Smoking, ever, n(%)	22/34 (64.7)	20/36(55.5)	0.3	1781/2942(60.5)
BMI (kg/m^2), mean(SD)	28 (6.08)	28.2(5.01)	0.8	28.1(5.5)
Amiloidosis, n(%)	14/36(38.9)	1(2.4)	<0.001	33/2949(1.11)
Comotbidities n(%)				
• Diabetes Mellitus,	7/34(20.6)	4/36(11.1)	0.2	199/2949(6.7)
• Hypertension	27/34(79.4)	9/36(25)	<0.001	442/2949(14.9)
• CAD	8/21(38.1)	1/25(4)	0.005	110/1882(5.8)
• COPD	5/21(23.8)	0/24	0.004	117/1774(6.59)
CRP, med(min-max)	1.6(0.4-12.4)	1.77(0.1-23.6)	0.8	1.07(0.1-45)
• at the initiation of bDMARDs, at the last visit, ESR, med(min-max)	0.7(0.16-14)	0.55(0.1-7.5)	0.3	0.5(0.1-14)
• at the initiation of bDMARDs,	48(12-140)	30(2-96)	0.1	19(1-140)
• at the last visit, med(min-max)	25(3-93)	15(2-70)	0.1	13(1-110)
BASDAI, mean (SD)				
• At the initiation of bDMARDs	4.5(±2.1)	5.46(±2.07)	0.5	5.7(±2.04)
• At the last vizit	3.94(±2.35)	2.95(±2.33)	0.09	3.69(±2.5)

CAD: Coronary artery disease, COPD: Chronic Obstructive pulmonary disease, BMI: Body mass index, BASDAI: Bath AS Disease Activity Index

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AB0955

WITHDRAWAL FROM PROFESSIONAL LIFE DUE TO HIGH DISEASE ACTIVITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TUMOUR NECROSIS FACTOR INHIBITORS AND/OR NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN ROUTINE CARE: RESULTS FROM THE MULTINATIONAL "INVISIBLE" STUDY

Keywords: Spondyloarthritis, Descriptive Studies, Outcome measures

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Background: Ankylosing Spondylitis (AS) is an inflammatory rheumatic disease affecting the axial skeleton (1), with a prevalence of up to 0.5% in Europe (2; 3), and occurs equally in men and women [4]. Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and biological Disease-Modifying Antirheumatic Drugs (bDMARDs) such as Tumour Necrosis Factor inhibitors (TNFi) are the first choice in pharmacological treatments for AS patients (5; 6). Data on employment situation in correlation with disease activity and disease duration in AS patients treated in real life settings in Europe are limited.
Objectives: To evaluate the disease activity status and assess participation in professional life in relation to treatment response following at least 12 weeks of treatment with TNFi and/or NSAIDs.
Methods: INVISIBLE was a multinational, cross-sectional, non-interventional study in Germany, Austria and Belgium. Adult patients with confirmed diagnosis of AS for at least 6 months and ongoing treatment with TNFi and/or NSAIDs for at least 12 weeks prior to enrolment were included. Primary data were collected at a single visit using Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS) and collecting current demographic data including employment status using the categories employed, unemployed, parental leave, retired and sick leave (>6 weeks). Medical history data were collected from available patient files.
Results: 747 adult AS patients (67% male) were included in this analysis. The patients were 47.9±13.1 years of age. Symptom duration was 18.2±13.0 years. 22.9% of patients received NSAIDs, 41.6% TNFi, 29.7% both NSAIDs and TNFi, and 5.4% other treatment for at least 12 weeks prior to enrolment. BASDAI was

3.4±2.3 and ASDAS 2.2±1.0. Patient's disease activity assessment (Visual Analogue Scale 0-100) showed on average 35.8±27.5 and patients with BASDAI ≥4 reported significantly higher disease activity compared to patients with BASDAI <4 (59.7±20.7 vs. 20.7±19.7, p<0.001). 72.5% of patients were employed and 9.9% unemployed or in sick leave for >6 weeks. More patients with a BASDAI ≥4 were unemployed or in sick leave regardless of type of treatment and duration of symptoms compared to patients with a BASDAI <4 (see Table 1).

Conclusion: Results from the non-interventional study INVISIBLE showed that a higher proportion of AS patients receiving NSAIDs and/or TNFi with high disease activity according to BASDAI are not participating in professional life. These results suggest that in some patients, disease control and treatment response are suboptimal under current treatment strategy.

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Table 1. Participation in professional life in relation to disease activity

	BASDAI <4 (N = 445)					BASDAI ≥4 (N = 292)				
	N	Employed 333 (74.8%)		Unemployed* 29 (6.5%)		N	Employed 192 (65.7%)		Unemployed* 41 (14.0%)	
		n	%	n	%		n	%	n	%
Treatment										
- NSAID	85	71	83.5	2	2.4	82	63	76.8	6	7.3
- TNFi	200	144	72.0	19	9.5	99	63	63.6	14	14.1
- NSAID & TNFi	123	98	79.7	6	4.9	91	58	63.7	19	20.9
- Other	26	20	76.9	2	7.7	13	6	46.2	2	15.4
Duration of Symptoms										
- <5 years	57	51	89.5	4	7.0	45	37	82.2	6	13.3
- ≥5 years	375	281	74.9	25	6.7	242	155	64.0	35	14.5

* unemployed and sick leave >6 weeks

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Disclosure of Interests: Jan Brandt-Juergens Consultant of: Abbvie, Affibody, BMS, Gilead, Janssen, Lilly, Medac, MSD, Novartis, Pfizer, Roche, Sanofi-Aventis, UCB, Judith Haschka Speakers bureau: Eli Lilly, Amgen, Consultant of: Eli Lilly, Richard Finsterwalder Employee of: Novartis Pharma GmbH, Aurélie Casier Employee of: N.V. Novartis Pharma S.A., Angela Kill Employee of: Novartis Pharma GmbH, Stéphanie Dierckx: None declared.

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AB0956 APPLICATION OF THE DIFFICULT-TO-TREAT CONCEPT FOR AXIAL SPONDYLOARTHRITIS

Keywords: Real-world evidence, Spondyloarthritis, bDMARD

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Background: The term "Difficult-to-Treat" (D2T) includes those patients who have persistent disease activity despite of having undergone several guideline-based treatments. This concept has been defined by EULAR for rheumatoid arthritis (RA) [1], thus could be analogously used for patients with Axial Spondyloarthritis (axSpA). In a recent publication [2] authors suggest that, among other criteria, axSpA patients could be classified as D2T when they require three or more biological drugs (bDMARDs) to control their disease.

Objectives: To describe the characteristics of axSpA patients who have undergone treatment with bDMARDs from a third-level university hospital and compare those who have received a maximum of two bDMARDs (group A) versus those who have received three or more (group B).

Methods: Descriptive, retrospective and unicentric study. Patients with axSpA diagnosis based on ASAS classification criteria, from March 2011 to December 2022, pulled from a specific database were included. They were separated into two groups according to the number of bDMARDs they had been under. Sociodemographic, clinical, radiographic and therapeutic variables were gathered.

Results: A total of 193 patients met the ASAS criteria for the diagnosis of axSpA and had received at least one bDMARD. The studied variables for each group are summarised in Table 1. Out of 193 patients (71% men; mean age 46,4 +/- 14 years old) 158 (81,9%) belonged to group A and 35 (18,1%) belonged to group B. There were no statistically significant differences between both groups. However, a tendency towards history of psoriasis, positive HLA B27 and elevated CRP at diagnosis was observed in those patients from group B.

Conclusion: The need of three or more bDMARDs in SpA is not infrequent in patients with axSpA and has similar proportions to RA. There has not been an agreement on stablished criteria for a D2T axSpA, but they could resemble those already defined for RA. Describing D2T for axSpA would be useful to identify those interrelated factors that may be associated with an increased activity upon diagnosis (high CRP) or the presence of extra musculoskeletal manifestations (psoriasis).

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Table 1. Included patients' sociodemographic, clinical and therapeutic variables.

	Group A n= 158	Group B n= 35	p-value
Age (yr)			
Mean age	46,5 ± 14,2	48,8 ± 14	0.391
Age at beginning of symptoms	28,3 ± 10,7	27,7 ± 11,7	0.797
Age at diagnosis	34,3 ± 12,1	32,4 ± 11,8	0.384
Sex			
Male	118 (74,7%)	20 (57,1%)	0.038
Female	40 (40%)	15 (42,9 %)	
HLA B27			
Positive	111 (13%)	23 (65,7%)	0.387
Negative	41 (27%)	12 (34,3%)	
High CRP			
Yes	106 (67%)	29 (82,9%)	0.066
No	52 (32,9%)	6 (17,1%)	
Uveitis			
Yes	32 (20,3%)	6 (17,1%)	0.675
No	126 (79,8%)	29 (82,9%)	
Psoriasis			
Yes	12 (7,6%)	7 (20%)	0.026
No	146 (92,4 %)	28 (80%)	
Familiar history of axSpA			
Yes	31 (19,6%)	7 (20%)	0.959
No	127 (80,4%)	28 (80%)	
Peripheral arthritis			
Yes	67 (42,4%)	17 (48,6%)	0.506
No	91 (57,6%)	18 (51,4%)	
Enthesitis (heel)			
Yes	54 (34,2%)	10 (28,6%)	0.524
No	104 (65,8%)	25 (71,4%)	
Dactylitis			
Yes	8 (5%)	4 (11,4%)	0.158
No	150 (94,9%)	31 (88,6%)	
axSpA type			
r-axSpA (AS)	110 (69,6%)	21 (60%)	0.270
EnA	28 (17,7%)	7 (20%)	0.752
Juvenile SpA	4 (2,5%)	0 (0%)	0.341
Ps SpA	6 (3,8%)	4 (11,4%)	0.065
nr-axSpA	10 (6,3%)	3 (8,6%)	0.632
Smoking history			
Non-smoker	81	19	0.746
Ex-smoker or active smoker	77	16	

axSpA: axial Spondyloarthritis; CRP: C-Reactive Protein; r-axSpA: radiographic axial Spondyloarthritis; AS: Ankylosing Spondylitis; EnA: Entheropatic Arhtritis (Inflammatory Bowel Disease-Associated Spondyloarthritis); Juvenile SpA: Juvenile Spondyloarthritis; Ps SpA: Psoriasic Spondyloarthritis; nr-axSpA: non-radiographic Spondyloarthritis

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2648

AB0957 IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES AMONG PATIENTS WITH RESOLUTION OF ENTHESITIS AND/OR DACTYLITIS: POST HOC ANALYSES FROM THE KEEPSAKE 1 AND 2 TRIALS OF RISANKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

Keywords: Spondyloarthritis, Enthesitis, Pain

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Background: Enthesitis and dactylitis are associated with greater disease activity and reduced quality of life. Results from the phase 3 randomized, placebo-controlled KEEPsAKE 1 and 2 studies (NCT03675308; NCT03671148) of risankizumab in active PsA showed greater resolution of enthesitis and dactylitis with risankizumab 150 mg vs placebo at week 24.
Objectives: This post hoc analysis evaluated improvements in patient-reported outcomes (PROs) among patients who had enthesitis (n=444), dactylitis (n=188), or both (n=128) at baseline and achieved resolution of enthesitis, dactylitis, or both with blinded risankizumab at weeks 0, 4, 16, and open-label risankizumab every 12 weeks thereafter.
Methods: Assessments included achievement of minimal clinically important differences (MCID) in pain (≥10-mm decrease on visual analog scale), Health Assessment Questionnaire-Disability Index (HAQ-DI; ≥0.35-unit decrease), and Functional Assessment of Chronic Illness Therapy (FACIT-Fatigue; ≥4-point increase). Nonresponder imputation (with multiple imputation for COVID-19–related missing data at week 24) was used.
Results: Many patients who achieved resolution of enthesitis at week 24|week 52 also achieved MCID in pain (66.4%|71.4%), HAQ-DI (58.2%|63.4%), and FACIT-Fatigue (59.0%|72.1%). Many patients who achieved resolution of dactylitis at week 24|week 52 also achieved MCID in pain, (72.2%|81.7%), HAQ-DI (56.3%|66.2%), and FACIT-Fatigue (67.7%|69.9%). Many patients who achieved resolution of both enthesitis and dactylitis at week 24|week 52 also achieved MCID in pain (82.1%|86.4%) HAQ-DI (66.7%|69.2%), and FACIT-Fatigue (71.4%|74.6%). PRO results for patients for who did not achieve resolution of enthesitis and/or dactylitis will be presented.
Conclusion: Majority of patients who achieved resolution of enthesitis and/or dactylitis with risankizumab also reported improvements in pain, disability, and fatigue.
Acknowledgements: AbbVie and the authors thank the patients who participated in the study and all study investigators for their contributions. Medical writing assistance, funded by AbbVie, was provided by Lisa M Pitchford, PhD, of JB Ashtin.
Disclosure of Interests: Shawn Kwatra Consultant of: AbbVie, Aslan Pharmaceuticals, Arcutis, Celldex, Galderma, Genzada Pharmaceuticals, Incyte, Johnson & Johnson, Novartis, Pfizer, Regeneron, and Sanofi., Grant/research support from: Galderma, Incyte, Pfizer, and Sanofi., Saakshi Khattri Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, and UCB, Grant/research support from: Bristol Myers Squibb, LEO Pharma, Novartis, and Pfizer, Ahmad Amin Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Dermavant, Eli Lilly, Janssen, LEO Pharma, Regeneron, Sanofi/Genzyme, Pfizer, and UCB, Ran Liu Shareholder of: AbbVie, Employee of: AbbVie, Byron Padilla Shareholder of: AbbVie, Employee of: AbbVie, Ahmed M. Soliman Shareholder of: AbbVie, Employee of: AbbVie, Blair Kaplan Shareholder of: AbbVie, Employee of: AbbVie, Dennis McGonagle Speakers bureau: AbbVie, Janssen, Novartis, and Pfizer., Grant/research support from: AbbVie, Janssen, Novartis, and Pfizer, UCB, BMS, Celgene.
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AB0958 A STUDY ON EARLY TAPERING OF TOFACITINIB IN ANKYLOSING SPONDYLITIS: A HIT AND RUN STRATEGY

Keywords: Tapering, Spondyloarthritis, Targeted synthetic drugs

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Background: Tofacitinib is emerging as a cost-effective drug in managing ankylosing spondylitis (AS) [1]. Tofacitinib (XELJANZ) was FDA-approved for the use of active AS in December 2021. Safety concerns have been raised about the long-term use of Tofacitinib following the ORAL surveillance trial data [2]. However, in developing countries, the cost is a primary concern, and Tofacitinib, an oral drug, can be considered an alternative to biologicals. This study investigates whether early tapering can mitigate the safety risk and attain sustained remission.
Objectives: To assess the efficacy of early tapering of tofacitinib on disease activity in adult patients with active AS.
Methods: This observational study enrolled 22 consecutive patients aged ≥18 years diagnosed with active AS, meeting the ASAS criteria [3]. Patients received tofacitinib 10mg per day. ASDAS CRP was calculated at 0 and 6 months to monitor the response. The primary and secondary endpoints were early tapering of tofacitinib within six months of initiation and assessment of ASDAS CRP at six months, respectively. Assessment of the safety profile was done monthly.
Results: In our study, the mean ASDAS CRP at the initiation of tofacitinib was 2.24 (SD 1.13). After six months of treatment, the mean ASDAS CRP was 0.9 (SD 0.6), with remission in 77.27% (17 of 22). Tapering was initiated at a mean of 4.4 months (SD 3.18) and as early as one month. 41%of patients (9 of 22) had attained remission with early tapering of Tofacitinib and in 9%of patients (2 of 22), we could successfully stop Tofacitinib with sustained remission. Transaminitis occurred in 22% (5 of 22), of which in 2 patients drug had to be stopped.Two2 patients (9%) had to be switched to biologicals due to non-responsiveness. There were no deaths, malignancies, major adverse cardiovascular events, thromboembolic events, or opportunistic infections.
Conclusion: In our study of 22 patients, we find that Tofacitinib can be a cost-effective treatment option in patients with AS who cannot afford biologicals, especially in a developing economy like India. However, recent concerns about the drug's long-term safety preclude its optimal use. Early tapering of Tofacitinib demonstrates no increased incidence of flares and helps maintain remission. A hit-and-run strategy of early tapering of Tofacitinib would benefit patients with AS in the Indian context. We find that early tapering is effective in at least some of the patients, and it can reduce the cost of treatment as well as potential adverse reactions.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4367

AB0959 SECUKINUMAB SURVIVAL AND ASSOCIATED DEMOGRAPHIC CHARACTERISTICS IN PATIENTS WITH SPONDYLOARTHRITIS AND PSORIASIC ARTHRITIS IN A REAL CLINICAL SETTING

Keywords: Safety, Spondyloarthritis

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Background: Secukinumab (SCK) is a human monoclonal antibody (IgG1) directed against IL-17A, approved for the treatment of plaque psoriasis, psoriatic arthritis (PsA) and axial spondyloarthritis (AxSpA). Data from randomized controlled clinical trials (RCTs) have shown that SCK has a low frequency of treatment discontinuation. We currently have little consistent data on long-term survival of SCK in patients with AxSpA and PsA in regular clinical practice. Therefore, we aimed to evaluate the drug retention of SCK in actual clinical practice, causes for discontinuation and factors associated with SCK suspension in patients diagnosed with PsA or AxSpA who receive or have received such therapy.
Objectives: We aimed to evaluate the drug retention rate, causes for treatment discontinuation and factors associated with SCK persistence in patients with AxSpA and PsA in a real clinical setting.
Methods: A retrospective cohort study was carried out including patients diagnosed of axSpA fulfilling the ASAS classification criteria and PsA fulfilling the CASPAR classification criteria. A total of 90 patients were included in the study treated with SCK between 2016 and 2022 in the rheumatology service of the Hospital Universitario de Navarra. All patients included started SCK at least 12 months before the data extraction.
Drug survival in months was analyzed by Kaplan-Meier curves while predictive factors of discontinuation were evaluated using a Cox regression analysis. The reason of suspension was also recollected.
Results: We included 90 patients (46 AxSpA and 44 PsA). The mean age at diagnosis was 44.5 years (SD 11.1) and the mean age at SCK initiation was 51.6 (SD 11.4). The median time from diagnosis to onset of SCK was 4.2 months (IQR 9.8) (Table 1). Eighty-three (92.2%) patients were treated with one or more biologics prior to SCK, median number of previous biologics was 2 (IQR 0-5). The average treatment duration was 31.8 months (SD 75.1). The 1 and 2-year retention rates for SCK in the AxSpA group was 83 and 71%, respectively, while for the PsA group it was 69 and 52% respectively (Fig 1). Thirty-five (38.88%)

patients discontinued treatment, 29 (82,85%) due to inefficacy, 1 (2,85%) by their own decision, 4 (11,42%) due to persistent mechanical pain and 1 (2,85%) due to neoplasia. The factors associated with lower risk of discontinuation were higher IMC (p = 0.025) and diabetes (p = 0.04). None of the other clinical variables evaluated had a statistically significant association with a lower or higher risk of discontinuation or discontinuation. No patient presented infections that required discontinuation of the drug.

Conclusion: SCK showed a very high retention rate in a population that has been previously exposed to several biological therapies both in AxSpa and PsA groups. According to previous reports [1], cardiometabolic comorbidities such as obesity and diabetes appear to be associated with better SCK survival and therefore this drug could be an optimal therapy for patients with cardiometabolic risk factors.

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Table 1. Baseline characteristics

	AxSpA (n=46)	PsA (n=44)	Total (n=90)
Female	23 (51.1%)	22 (51.2%)	45(50%)
Hypertension	10 (21.7%)	15 (34.1%)	25 (27.8%)
Dyslipidaemia	16 (34.8%)	20(46.5%)	36 (40.4%)
Diabetes mellitus	5 (10.9%)	7 (15.9%)	12 (13.3%)
Body Mass Index	27.7 (SD5.1)	29 (SD7.2)	28.4 (SD6.4)
Tobacco	17 (37.8%)	15 (34.1%)	32 (36%)
Alcohol	2 (4.4%)	0 (0.0%)	2 (2.2%)
Cardiovascular disease	8 (17.4%)	5 (11.6%)	13 (14.6%)
Depression	5 (10.9%)	1 (2.3%)	6 (6.7%)
Number of previous biologics, median (IQR)	1 (1-2)	2 (1-3)	2(1-2)
Glucocorticoids	8 (18.2%)	21 (47.7%)	29 (33%)

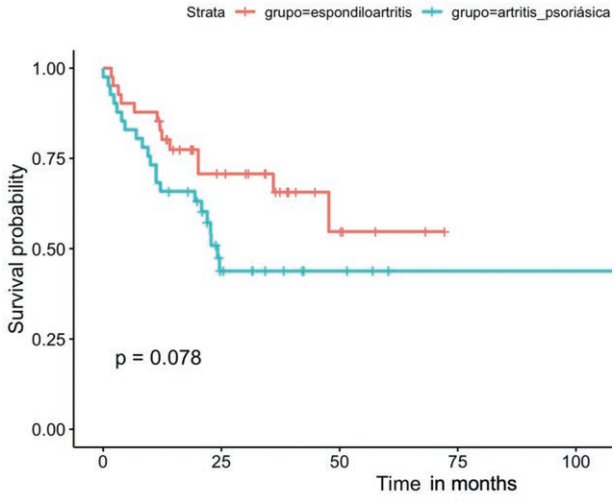


Figure 1. Kaplan-Meier survival estimate in months

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0960

EFFECT OF BODY MASS INDEX ON TREATMENT RESPONSE OF BIOLOGIC-/TARGETED SYNTHETIC DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS

Keywords: Inflammatory arthritides, bDMARD, Comorbidities

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Background: Overweight and/or obese patients with inflammatory arthritis (IA) have higher disease activity and lower chances of achieving as well as maintaining the treatment targets. Obesity also appears to negatively affect the response to tumor necrosis factor (TNF) inhibitors in patients with IA. The efficacy of other biologic (b) and of targeted-synthetic (ts) DMARDs in overweight/obese patients with IA, including rheumatoid arthritis –RA, psoriatic arthritis –PsA, axial spondyloarthritis –AxSpA, is unclear.

Objectives: To conduct a systematic literature review (SLR) to explore the effect of weight/body-mass-index (BMI) on the efficacy of all b-/ts-DMARDs approved for the treatment of RA, PsA and AxSpA.

Methods: For this PROSPERO-registered SLR, we searched PubMed, Scopus and Cohrane-Library up to June 21st 2022. PICO-format was as follows: Population: adults with RA, PsA or AxSpA and low/normal weight/BMI; Intervention: treatment with approved b-/ts-DMARDs; Comparator: adults with RA, PsA or AxSpA and high/abnormal weight/BMI; Outcome: any outcome used for the assessment of treatment response (e.g DAS28, ACR20, drug-survival). The search query included the following keywords in the article's title and/or abstract: ("psoriatic arthritis" OR "rheumatoid arthritis" OR "inflammatory arthritis" OR "ankylosing spondylitis" OR "axial spondyloarthritis" OR "non-radiographic axial spondyloarthritis") AND (DMARDs OR bDMARDs OR tsDMARDs OR tofacitinib OR upadacitinib OR baricitinib OR filgotinib OR apremilast OR anti-TNF OR etanercept OR infliximab OR adalimumab OR golimumab OR certolizumab OR abatacept OR rituximab OR tocilizumab OR anti-IL-6 OR anti-IL-17 OR anti-IL-23 OR anti-IL-12/23 OR ustekinumab OR guselkumab OR risankizumab OR secukinumab OR ixekizumab OR "janus kinase inhibitors" OR "JAK inhibitor") AND ("body mass index" OR BMI OR obes* OR weight). Clinical-trials and observational studies were included. The screening and selection process was conducted independently by two reviewers. Risk of bias (ROB) was assessed using the RoB2-Cochrane tool and Newcastle-Ottawa scale for randomized and non-randomized studies, respectively.

Results: Out of 996 references, 192 full-text articles were reviewed and 75 eventually fulfilled the inclusion criteria (of which 10 studies were retrieved through manual-search). Number of studies, most of which were of medium RoB, was: 34 for TNF-inhibitors, 4 for IL-12/23 inhibitors, 1 for IL-23 inhibitor, 7 for IL-17 inhibitors, 18 for tocilizumab, 8 for abatacept, 3 for rituximab and 5 for JAK-inhibitors. The efficacy of TNF-inhibitors was found to be affected by the BMI in all forms of IA with the effect being similar across various TNF-inhibitors. In contrast, the favorable results of IL-23 and IL-17 inhibitors do not appear to be influenced by increased BMI in patients with PsA or AxSpA. Similar evidence exists for tocilizumab and abatacept, while no conclusion can be drawn for rituximab. More data are needed for JAK-inhibitors, although the effect of weight/BMI does not seem to be significant so far (**Figure-1**).

Conclusion: Weight/BMI should be considered in the treatment-plan of patients with IA, with its effect being more pronounced for TNF-inhibitors compared to other b-/ts-DMARDs.

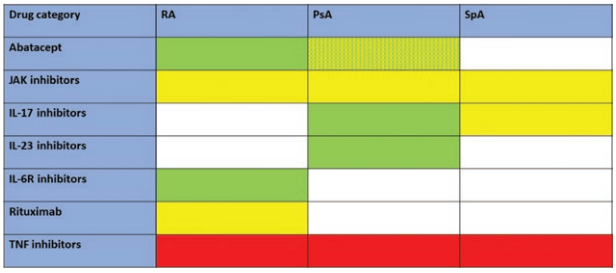


Figure -1 The effect of weight/BMI on the efficacy of the approved b- and ts-DMARDs for RA, PsA and AxSpA. Red color: negative effect, green color: no effect, yellow color: limited data, green/yellow knitting: possibly no effect but limited data, white: not applicable.

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AB0961

EFFICACY OF BIOTHERAPIES IN APS PATIENTS ACCORDING TO AGE OF DISEASE ONSET: DATA FROM THE MOROCCAN RBSMR REGISTRY

Keywords: Registries, Spondyloarthritis

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease most often affecting young adult males and linked to the HLA B27 antigen in more than 90% of cases. The classic age of onset of symptoms is in most cases between 20 and 30 years. However, it is known that the disease can start in early childhood and that there are cases appearing after 50 years.

The aim of this study is to compare the efficacy of biotherapy in juvenile onset spondyloarthritis and adult onset spondyloarthritis using data from the biotherapy registry of the Moroccan Society of Rheumatology BRSMR.

Objectives: To evaluate the real-life effectiveness of biologic therapies in patients with ankylosing spondylitis (AS) according to age of disease onset.

Methods: A cross-sectional multicenter observational study was conducted; the data source was the Moroccan Registry of Biological Therapies in Rheumatic Diseases (RBSMR Registry). Patients, included from May 2017 to January 2019, were all adult patients (age >18 years), with APS, according to the ASAS classification criteria for APS 2009. Therapeutic efficacy was assessed by ASDAS-CRP, a therapeutic response was defined by an ASDAS-CRP less than 1.3. The therapeutic response to biological treatment after 1, 2 and 3 years of evaluation was compared between two groups: group a: juvenile spondyloarthritis with age of onset less than 16 years and group b: spondyloarthritis in patients over 16 years.

Results: 194 patients were included in the study. Concerning group a (26 patients 13%): The mean age was 26.15 ± 7.05 years, the sex ratio was 4.2. 92.3% of the patients had axial involvement, 79.2% had peripheral involvement and 41.7% had enthesic involvement. The mean erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) on admission were 41.6±29.2 mm/h and 39.51 [6.98;58.25] respectively. HLA B27 was positive in 100% of patients. The mean ASDAS CRP was 3.6±1.14; 1.5±1.22; 1.8±1.3; 1.25 [0.85; 3.35] at baseline and then at 1 year,2 years and 3 years respectively. As for group b (120 patients 62%): The mean age was 44.61 ±12.14 years, the sex ratio was 1.4. 97.5% of the patients had axial involvement, 66.1% had peripheral involvement and 63.6% had enthesic involvement. The mean erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) at admission were 38.36 [16.55] and 26.43 [5.9; 40], respectively. HLA B27 was positive in 63.3% of patients. The mean ASDAS CRP was 3.35±1.5; 1.9±1.09; 1.6±1.3; 1.8±0.93 at baseline and then at 1 year,2 years and 3 years respectively. The analysis revealed no statistically significant difference between the two groups regarding the therapeutic response to biological treatment (p=0.16; p=0.73; p=0.26 at one, two and three years respectively).

Conclusion: Spondyloarthritis, whether it starts in childhood or in adulthood, has similar clinical and radiological manifestations. Similarly, the response to treatment is identical to that obtained in patients with an adult onset. Biotherapy opens a new avenue for the treatment of juvenile spondyloarthritis. Our study as well as the literature data confirm the efficacy of biotherapy and its good tolerance in our patients with APS whatever the age of onset of the disease.

Key words: spondyloarthritis, biotherapy, age of disease, RBSMR registry.

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Disclosure of Interests: None Declared.

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AB0962

COMPARISON BETWEEN SECUKINUMAB AND IXEKIZUMAB IN PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS: A SINGLE CENTER EXPERIENCE

Keywords: bDMARD, Psoriatic arthritis, Spondyloarthritis

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Background: The pathogenesis of SpA has not been completely elucidated, but several pieces of evidence suggest that interleukin (IL)17-A plays a pivotal role in this group of diseases. Both anti-IL-17A drugs Secukinumab (SEC) and Ixekizumab (IXE) have shown efficacy in treating multiple facets of SpA. (2)

Objectives: Our study aimed to compare the effect of SEC and IXE in our cohort of patients with PsA or axSpA.

Methods: We retrospective analyzed our clinical database, enrolling patients with PsA or axSpA treated with SEC or IXE. We collected disease activity scales and scores at baseline (0) and after 3, 6 and 12 months of treatment: BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), DAPSA (Disease Activity Index for Psoriatic Arthritis), VAS (Visual Analog Scale) for pain, PGA (Patient Global Assessment), and PHGA (Physician Global Assessment).

Results: We selected 73 patients, 55 with PsA (75.30%) and 18 with axSpA (24.70%). In the SEC cohort, we found 52 patients, mainly females (73.00%), mean age of 57.00 ± 11.47 years; in the IXE cohort, there were 21 patients, 71.43% females, mean age of 53.81 ±11.17 years. Peripheral involvement was present in the majority of patients (88.46% vs. 100%), while axial involvement was predominant in SEC treated patients (61.54% vs. 28.57%). The presence of dactylitis was similar in the two groups (15.38% vs. 14.29%), enthesitis prevailed in SEC cohort (75.00% vs. 57.14%) while cutaneous psoriasis in the IXE cohort (44.23% vs. 80.95%). During follow-up, BASDAI and DAPSA decreased significantly in both SEC and IXE groups, especially in the first trimester, with a similar trend during the

Table 1. BASDAI and DAPSA variations between SEC and IXE during follow up

Month	Drug	Change		Change difference		Change adj		Change difference adj	
		Estimate (CI95%)	*P*	Estimate (CI95%)	*p*	Estimate (CI95%)	*p*	Estimate (CI95%)	*p*
BASDAI									
0 vs 3	SEC	-1.20 (-1.64 - -0.76)	**<.0001**	0.73 (0.13 – 1.33)	**0.0174**	-0.81 (-1.21 - -0.41)	**<.0001**	0.20 (-0.37 - 0.77)	0.4894
	IXE	-0.47 (-0.88 - -0.06)	**0.0256**			-0.61 (-0.99 - -0.22)	**0.0019**		
3 vs 6	SEC	-0.71 (-1.21 - -0.21)	**0.0048**	0.41 (-0.16 – 0.99)	0.1620	-0.75 (-1.19 - -0.30)	**0.0009**	0.12 (-0.47 – 0.72)	0.6819
	IXE	-0.30 (-0.60 - 0.002)	0.0519			-0.62 (-1.01 - -0.25)	**0.0012**		
6 vs 12	SEC	-0.43 (-0.82 - -0.04)	**0.0287**	0.53 (-0.18 – 1.24)	0.1452	-0.76 (-1.28 - -0.23)	**0.0044**	0.43 (-0.32 – 1.18)	0.2609
	IXE	0.01 (-0.50 – 0.70)	0.7458			-0.33 (-1.01 – 0.34)	0.3392		
DAPSA									
0 vs 3	SEC	-7.11 (-8.51 - -5.71)	**<.0001**	0.87 (-3.59 – 5.34)	0.7002	-4.27 (-5.85 - -2.69)	**<.0001**	0.95 (-1.87 – 3.78)	0.5087
	IXE	-6.23 (-10.47 - -1.99)	**0.0040**			-3.32 (-5.42 - -1.21)	**0.0020**		
3 vs 6	SEC	-1.51 (-2.93 - -0.08)	**0.0374**	-0.95 (-3.82 – 1.91)	0.5160	-2.79 (-4.61 – 0.96)	**0.0027**	-0.35 (-2.77 – 2.07)	0.7776
	IXE	-2.46 (-4.95 – 0.03)	0.0529			-3.14 (-5.07 - -1.21)	**0.0014**		
6 vs 12	SEC	-0.11 (-1.77 – 1.54)	0.8918	2.45 (-3.79 – 8.69)	0.4422	-2.84 (-5.05 – 0.63)	**0.0116**	2.67 (-3.70 – 9.05)	0.4107
	IXE	2.33 (-3.68 – 8.35)	0.4475			-0.16 (-6.72 – 6.38)	0.9596		

second trimester (significant only for SEC). When compared with each other, SEC and IXE appeared to have a similar effect on both scales, except for a significantly greater reduction of BASDAI in the first trimester for SEC, which however was no longer present when the values were adjusted for the starting BASDAI value (Table 1). Analyzing PGA, PHGA, and VAS pain, we observed a significant trend in reduction in the first trimester for both drugs, then maintained only for SEC, significantly greater for SEC than IXE in both trimesters. The analysis of the adjusted values confirmed the significant decrease in BASDAI DAPSA PGA PHGA and VAS for both SEC and IXE, especially until 6 months after baseline.

Conclusion: Our data confirmed that SEC and IXE are both valid options for the treatment of PsA and axSpA, without significant differences when comparing the two drugs.

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AB0963 SAFETY OF DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN SPONDYLOARTHRITIS: A RETROSPECTIVE REVIEW FROM A SOUTH AFRICAN RHEUMATOLOGY CENTRE

Keywords: Spondyloarthritis, Disease-modifying Drugs (DMARDs)

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Background: The long-term immune-suppressive effects of Disease Modifying anti-Rheumatic Drugs (DMARDs) have long been a concern for serious adverse effects (SAE). Other developing countries, e.g. Brazil, used their registry to report a higher incidence of serious infections in the bDMARD treated patients compared with sDMARDs [1]. There are no published articles about the true incidence and nature of SAEs in Spondyloarthropathy (SpA) patients treated with bDMARDs in the South African context.

Objectives: To describe the incidence of SAEs amongst patients with SpA treated with b- and s-DMARDs at a rheumatology centre in the Western Cape, South Africa.

Methods: A retrospective medical record review was conducted, involving patients with SpA seen at a private rheumatology clinic in Stellenbosch, Western Cape, between the 1 January 2014 and 31 December 2021. Demographic, clinical, and patient reported SAEs were recorded for those treated with b- and s-DMARDs. Incidence of SAEs was calculated and presented with 95% confidence intervals.

Results: Incidence of SAEs recorded between 1 January 2014 and 31 December 2021. A total of 92 patients were included, 59 bDMARD exposed and 33 treated only with sDMARDs (bDMARD naïve). The accumulated exposure was 300 person-years (p-y) for those on bDMARDs and 140 p-y for those on sDMARDS only. Twenty two SAEs were reported during the study period: 14 infective, 4 major adverse cardiac events, 3 malignant (prostate, uterine, and thymoma), and 1 pulmonary complication. Twenty SAE's occurred whilst on a DMARD, one occurred 37 days after stopping etanercept, and a single SAE was excluded as it occurred 2 years after stopping infliximab. All SAEs were associated with hospitalisation and there were two deaths (one related to multi-organ failure, the other COVID-19 related). The SAE incidence for the sDMARD control group was 2.1/100 p-y (95% C.I. 0.5-5.8/100 p-y) and 6.0/100 p-y (95% C.I. 3.7-9.3/100 p-y) in the bDMARD study group. Of the anti-TNF inhibitors assessed, etanercept had the lowest SAE incidence at 3.8 events/100 p-y (95% C.I. 1.2-9.3/100 p-y) (see Table 1).

Table 1: Incidence of SAEs

	n	Person-years	Infective	CVS	Malignant	Other	Total SAEs	Incidence of SAEs per 100 person-years (95% C.I.)
Adalimumab	37	102,1	4	1	1		6	5.9 (2.4-12.2)
Etanercept	31	104,1	2	2			4	3.8 (1.2-9.3)
Golimumab	18	52,1	2		1		3	5.8 (1.5-15.7)
Infliximab	9	33,9	3			1	4	11.8 (3.7-28.5)
Secukinumab	6	7,2	1				1	13.9 (0.7-68.5)
Ustekinumab	1	0,6					0	-
sDMARDs only	33	139,8	1	1	1		3	2.1 (0.5-5.8)
Total			13	4	3	1	21	
bDMARD groups								
Monoclonal antibodies[a]	64	188.1	9	1	2	1	13	6.9 (3.8-11.5)
All anti-TNF[b]	95	292.2	11	3	2	1	17	5.8 (3.5-9.1)
All bDMARDs	101	299.2	12	3	2	1	18	6.0 (3.7-9.3)

2. [a]Adalimumab, Golimumab, Infliximab. [b]Adalimumab, Golimumab, Infliximab, Etanercept, *bDMARD – biologic Disease Modifying Anti-Rheumatic Drug; n – number; SAE – Serious Adverse Event; sDMARD- synthetic Disease Modifying Anti-Rheumatic Drug;*

Conclusion: The preliminary results of this retrospective review of SpA patients attending a private rheumatology clinic in a developing country suggests that infliximab treated patients were 5.5 times more likely to develop an SAE compared to patients on sDMARDs. Overall patients exposed to monoclonal antibodies were 3.2 times as likely to develop an SAE compared to those receiving sDMARDs, with respiratory infections the most commonly reported SAE.

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AB0964 THERAPEUTIC DRUG MONITORING OF INFLIXIMAB IN INFLAMMATORY RHEUMATIC DISEASES: REAL-LIFE DATA IN A COHORT OF PATIENTS

Keywords: Spondyloarthritis, bDMARD, Rheumatoid arthritis

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Background: Therapeutic drug monitoring (TDM) could be helpful in several clinical situations such as loss of response to therapy, the interpretation of side effects to therapy and to determine dose adjustments [1].

Objectives: To investigate the influence of demographic and clinical characteristics on circulating infliximab (IFX) levels and the clinical relevance of measuring IFX trough levels (ITL) in patients with inflammatory arthritis treated with IFX.

Methods: Unicentric observational retrospective study conducted in a tertiary hospital between January 2018 and December 2022. Patients with spondyloarthritis (SpA) and rheumatoid arthritis (RA) treated with IFX and having been performed a serum ITL determination during follow-up were included. Patients were classified into two groups depending on the disease activity, descriptive statistics and a comparative analysis were performed. The continuous data were compared using the Mann-Whitney U test or the Student t-test, and the frequency data with the Pearson $\chi 2$ or Fisher exact tests. Univariable and multivariable logistic regression models were employed to investigate the influence of demographic and clinical characteristics in ITL and immunogenicity. Serum dependent ROC curves were used to determine the ITL that best predicted good clinical response.

Results: A total of 91 patients, 78 SpA and 13 RA were included. Their demographic and clinical characteristics are shown in Table 1. All patients who had remission or low disease activity (LDA) in the ITL measurement remained without activity at 12 months. 34 of 41 (83%) patients with disease activity achieved remission or LDA at 12 months of ITL measurement with a significant improvement in the disease activity ($p < .001$). In the univariable analysis, the presence of rheumatoid factor (OR 0.1; CI95% 0.03 – 0.7), methotrexate use (4.5; 0.8 –2.5), sulfasalazine use (7.7; 1.3 – 4.4) and disease activity (0.06; 0.02 – 0.2) are associated with ITL ($p < .1$). Regarding immunogenicity, we observed an association with female sex (2.5; 0.8 – 7.6), rheumatoid factor (1.8; 3.7 – 8.6), ACPA positive (4.1; 0.9 – 1.9), disease duration (0.9; 0.9 – 1.0), IFX duration (0.8; 0.7 – 0.9), baseline SpA activity (2.9; 0.9 – 9.2) and disease activity (31.4; 3.9 – 2.5), all $p < .1$. However, in the multivariable analysis only was confirmed the association between ITL and immunogenicity with disease activity, and between immunogenicity with IFX duration ($p < .05$). In our cohort, the optimal cut-off of ITL in RA patients was 1.5 µg/mL and 6.7 µg/mL for SpA (Fig).

Conclusion: TDM appears to be a useful technique for the control of inflammatory arthritis. Demographic and clinical characteristics can influence drug levels that are important to know to decrease immunogenicity when possible. More studies still need to be carried out to analyze the therapeutic range of biologics.

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Table.

	All patients **(n=91)**	Remission/LDA **(n=50)**	Moderate/high activity **(n=41)**	p-value
Men, n (%)	49 (54)	29 (58)	20 (49)	0.7
Age (years)*	53 (13)	56 (15)	51 (11)	0.2
Body mass index (kg/m^2)*	28.3 (6)	27.4 (5)	29.3 (7)	0.08
Smoking, n (%)				
No	42 (46)	23 (46)	19 (46)	
Active	26 (29)	13 (26)	13 (32)	0.3
Ever-smoker	19 (21)	11 (22)	8 (20)	
Diagnosis, n (%)				
RA	13 (14)	4 (8)	9 (22)	0.1
SpA	78 (86)	46 (92)	32 (78)	
Disease duration (years)*	16 (11)	19 (11)	12 (9)	*0.009*
Rheumatoid factor +, n (%)	10/13 (77)	2/4 (50)	8/9 (89)	0.3
ACPA +, n (%)	11/13 (85)	3/4 (75)	8/9 (89)	0.8
HLAB27 +, n (%)	39/59 (66)	27/46 (59)	12/32 (38)	*0.03*
IFX duration (years)*	7 (5)	8 (5)	5 (5)	*0.009*
IFX levels (µg/mL)*	3.3 (4)	4.1 (3)	2.3 (4)	*0.02*
Immunogenicity, n (%)	17 (19)	1 (2)	16 (39)	*< 0.0001*
csDMARDs, n (%)				
None	9 (10)	5 (10)	4 (10)	
Methotrexate	39 (43)	20 (40)	19 (46)	0.8
Sulfasalazine	32 (35)	21 (42)	11 (27)	
Others	11 (12)	4 (8)	7 (17)	
MTX doses (mg/week)**	15 (7.5–25)	11,3 (7.5–20)	20 (7.5–25)	*0.003*
n previous biologics, n (%)				
0	68 (75)	39 (78)	29 (71)	
1	13 (14)	8 (16)	5 (12)	0.8
2 or more	10 (11)	3 (6)	7 (17)	

*mean (SD), **median (range). csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs

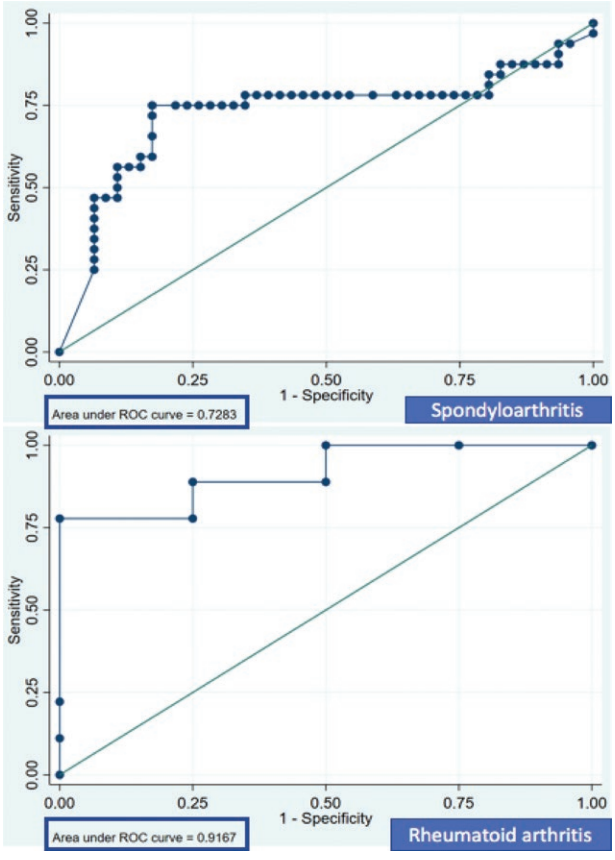


Figure 1. Optimal cut-off of ITL in RA and SpA patients

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Disclosure of Interests: None Declared.
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AB0965

EXTRA-AXIAL MANIFESTATIONS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: THE COURSE AND RESPONSE TO THERAPEUTIC AGENTS

Keywords: Remission, Disease-modifying Drugs (DMARDs), Spondyloarthritis

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease involving the axial skeleton and commonly include some coexisting extra-axial manifestations (EAMs) [1] which may have an influence on prognosis and treatment decisions [2].
Objectives: We aim to show the characteristics of EAMs in patients with axSpA and to assess the progress under different therapeutic agents.
Methods: In this retrospective cohort study; medical records of all patients with axSpA who fulfilled ASAS classification criteria and were followed up between 1980 to 2022 at our tertiary referral outpatient clinic were screened. The data of 201 (59.7% males) patients who had sacroiliitis (by using X-Ray or MRI) and coexisted EAMs was recorded into a pre-defined protocol. Demographics and progress of EAMs under different therapeutic agents were analysed.
Results: The mean age and duration of follow-up period were 34 years (IQR 25-43) and 144 months (IQR 84-213). Prevalence of family history and HLAB27 were 30.6% (38/124) and 77.4% (65/84). Non-radiographic sacroiliitis was observed in 21.9%. Peripheral arthritis (60%) was the most common EAM and followed by uveitis (46%), IBD (17%), psoriasis (14%), enthesitis (13%) and dactylitis (5%). Demographics and treatment details are shown in *Table 1* and *Figure 1*. Approximately, half of the patients were treatment naive at onset of each EAMs. Anterior uveitis and psoriasis were frequently occured despite using bDMARDs (31% and 39%). Fifty nine percentage of the patients with psoriasis and one third of patients with uveitis and dactylitis required a switch to bDMARDs.
Conclusion: In patients with axSpA, some of EAMs required treatment switches and relapses occured despite treatment optimization. Determining appropriate and efficaceous treatment algorithms according to presence of EAMs should be one of the main goals of axSpA management strategies.

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Table 1. Demographics and treatment details in patients with axSpA and coexisted extra-articular manifestations

	Arthritis (n=122)	Uveitis (n=94)	IBD (n=35)	Psoriasis (n=29)	Enthesitis (n=27)	Dactylitis (n=10)
Prevalence up the diagnosis of axSpA, %	40.6	21.9	13.3	13	35.7	50
Duration of onset of EAMs' to the diagnosis of AxSpA, months, med (min-max)	0 (-324-324)	0 (-192-528)	-12 (-276-144)	-12 (-312-180)	0 (-12-24)	12 (0-276)
Simultaneous axial activity, %	63.7	43.8	18.2	30.8	75	66.7
Treatment at onset of EAMsS, %						
Naive	57.6	47.2	57.9	53.8	46.7	57.1
NSAID	5.9	7.5	5.3	0	13.3	0
cDMARD	22.4	15.1	21.1	7.7	33.3	28.6
bDMARD	14.1	30.2	15.8	38.5	6.7	14.3
Treatment change for EAMs, %						
Unchanged	3.4	11.5	5	25	0	0
Switch to NSAİD	3.4	9.6	0	0	6.7	0
Switch to cDMARD	64.8	40.4	55	16.7	73.3	66.7
Switch to bDMARD	28.4	38.5	40	58.3	20	33.3
Response to first treatment agent without relapses, %						
NSAİD	67	40	-	-	0	-
cDMARD	54	30	55	50	67	75
bDMARD	56	63	57	57	100	100

(AxSpA: axial spondyloarthritis, EAM: extra-axial manifestation, IBD: inflammatory bowel disease, NSAID: nonsteroid anti inflammatory drugs, cDMARD: conventional disease modifying anti-rheumatic drugs, bDMARD: biologic DMARD)

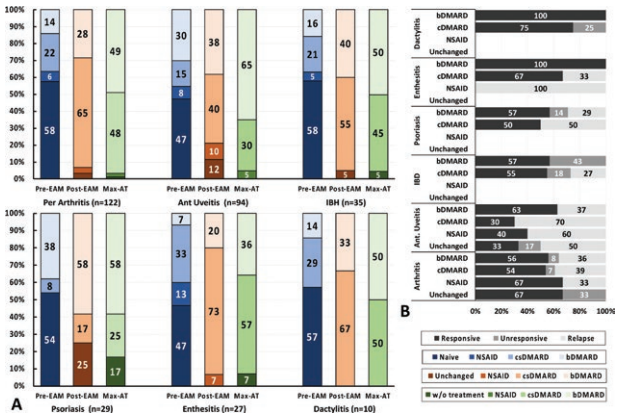


Figure 1. A. Treatment proportion of EAMs. **B.** Response to first-line treatment (EAM: extra-axial manifestation, Pre-EAM: treatment at onset of EAMs, Post-EAM: treatment change for EAMs, Max-AT: required maximum advanced treatment, w/o: without)

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AB0966

EFFICACY AND SAFETY OF SECUKINUMAB IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: SINGLE CENTER EXPERIENCE

Keywords: Disease-modifying Drugs (DMARDs), bDMARD, Spondyloarthritis

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Background: Secukinumab (SCK), the first-in-class human monoclonal antibody against interleukin-17A, has been approved for the treatment of AS in many countries, including the US and EU. The efficacy of subcutaneous secukinumab in the treatment of Ax-SpA was primarily evaluated in five multicenter, phase III studies that included four randomized double-blind studies (MEASURE Studies). However, there are few studies evaluating long-term SCK efficacy in real-life data in patients with AxSpA [1,2].
Objectives: Our aim in this study is to retrospectively evaluate the clinical findings and treatment response status of patients who were followed up with the diagnosis of Ax-SpA and using SCK.
Methods: A total of 60 patients who were followed up with the diagnosis of akSpA in our rheumatology clinic were included in the study. Demographic characteristics of the patients, comorbidities, duration of symptoms, delay in diagnosis, biologics and DMARDS were recorded. In the evaluation of the patients, BASDAI, BASFI, ASDAS, VAS pain, and VAS global scores were recorded as baseline, 3, 6, 12 and 24th months. The number and order of treatment before SEC in patients using bDMARDs were also examined, and SCK efficacy and drug retention characteristics were investigated between the biological treatment naive and resistant groups. Variables were analyzed at 95% confidence level, and p value less than 0.05 was considered significant.
Results: Follow-up data of 60 patients diagnosed with SpA (n=50 AS and n=10 nr-AxSpA) followed in a single center (inception cohort) were evaluated. Of these patients, 15 (25%) were bDMARD naive patients and 45 (75%) had used ≥1 bDMARD before SEC. The age and gender distribution was similar between the bDMARD naive and ≥1 bDMARD group. At 1-year follow-up, 1 and 7 patients discontinued their treatment in the ≥1 bDMARD group and the SCK group, respectively (p<0.001) (Table 1). The retention rate at 24 months was 80% and 49% in the naive and ≥1 bDMARD patients, respectively (p=0.026) (Figure 1). In our study, no significant drug-related serious adverse events or safety problems were encountered in the follow-up of secukinumab treatment for more than 36 months.
Conclusion: We found that SCK treatment in patients with Ax-SpA had better clinical response and higher drug survival rates in biologic naive patients, similar to TNFi treatment in real-life data. However, better drug retention rates were found in naive patients compared to patients using >1 bdmard, which is consistent with the results of previous studies.

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Table 1. Demographic and clinical characteristics of patients using secukinumab treatment.

		Naive (n=15)	≥ 1bDMARD (n=45)	Total (n=60)	p value
		n (%)	n (%)	n (%)	
Gender	male	9 (60)	24 (53.3)	33 (55)	0.263
Diagnosis	nr-AxSpA	5 (33.3)	5 (11.1)	10 (16.7)	**0.002**
	AS	10 (66.7)	40 (88.9)	50 (83.3)	
Smoking history	(+)	7 (46.7)	31 (68.9)	38 (63.3)	0.341
HLA B27	(+)	8 (57.1)	29 (65.9)	37 (63.8)	0.284
		Median (IQR)	**Median (IQR)**	**Median (IQR)**	
Age (year)		41 (33-65)	42 (20-75)	42 (20-75)	0.199
BMİ (kg/m^2)		25.1 (22.7-29.6)	26.8 (19.6-43.2)	26.7 (19.6-43.2)	0.350
Diagnosis Duration		72 (9-360)	84 (4-473)	84 (4-473)	0.130
Symptom duration (month)		6 (5-16)	16 (5-50)	15.5 (5-50)	**<0.001**
Symptom duration (year)		6 (5-12)	16 (11-20)	15.5 (9-20)	**<0.001**
Secukinumab treatment (month/ total)		12 (1-46)	13 (1-44)	12.5 (1-46)	**0.010**
BASDAI	Baseline	5.7 (5.3-6.5)	4.8 (3.1-5.6)	5 (3.1-5.8)	**0.018**
	6th month	1.2 (1.1-3)	4.1 (1.9-5)	3.1 (1.4-4.7)	**<0.001**
	12th month	2.4 (1.2-2.9)	3.2 (2.1-4.9)	3.1 (1.75-3.75)	0.325
VAS Pain	Baseline	2.8 (2.6-3)	5.9 (4.6-6.5)	5.6 (4.2-6.5)	**<0.001**
	6th month	1.6 (1-2.2)	5.2 (4-5.7)	4.8 (3.9-5.3)	0.046
	12th month	3 (0-6)	4.6 (4-6)	4.6 (4-6)	0.660
ASDAS-CRP	Baseline	2.7 (2.6-2.7)	3.2 (2.7-4)	3.2 (2.6-4)	**0.002**
	6th month	1.6 (0.9-2.3)	3.2 (2.4-3.8)	3.1 (2.4-3.7)	0.246
	12th month	2.1 (1.8-2.4)	2.7 (2.3-3.3)	2.4 (2.3-3)	0.148

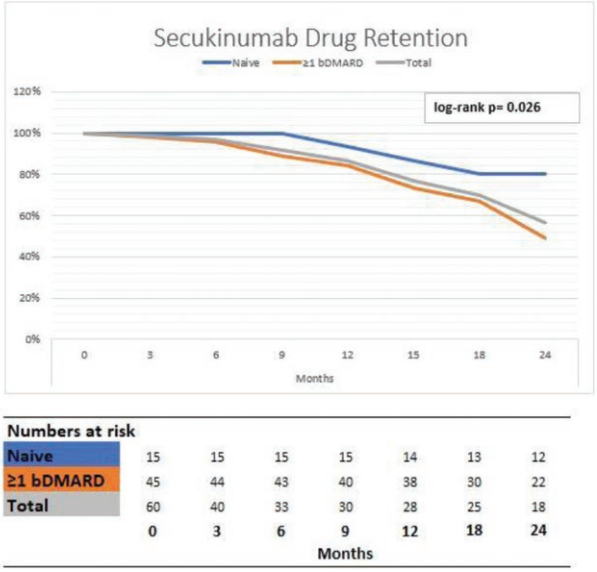


Figure 1. Secukinumab drug retention in naïve and ≥1bDMARD groups

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5978

AB0967

REFRACTORY ACHILLES ENTHESITIS SUCESSFULY TRAETED BY IXEKIZUMAB LOCAL INJECTION

Keywords: bDMARD, Spondyloarthritis, Enthesitis

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Background: Axial spondyloarthropathy (axSpA) is a chronic autoimmune inflammatory disease that involves the axial skeleton with inflammatory back pain as the most common presenting symptom. [1] Apart from the axial joints, enthesis are frequently involved in spondyloarthopathy (SPA) and clinical enthesitis reported to affects 10% – 60% of SPA patients. Enthesitis usually involves the lower limb and heel pain represents a significant clinical challenge due to frequent presence of Achilles enthesitis (AE), retrocalcaneal bursitis (RB) and plantar fasciitis, plus a

treatment challenge in refractory cases that usually not controlled by conventional DMARDs and fails to respond to biological treatment [2-4].
Objectives: To describe a successful management of refractory case of AE after US guided Ixekizumab injection to the RB.
Methods: Male 42 y old known case of axSpA for 22 y with +ve HLAB27 and bilateral AE. initially treated with salazopyrine, and NSAIIDs with no response and treatment escalated to Infleximab with secondary failure after 6 months, switched etanercept injection with primary failure. Patinet achived god clinical responce on adalimumab which was maintained up to 7y, followed by secondry faliure due to antidrug antibodies, resolved by addding Methotrexate. July 2019, developed hepatotoxicity due to methotrexate with discontinuation. December 2019, patient switched to Ixekizumab with successful control of his disease. Apart from the course of axial disease, January 2019 his heel pain becomes refractory to treatment VAS 8 with US assessment shows AE, RB, and tendinitis with positive Doppler signals. pain was partially responding to the added physiotherapy and NSAIDs with VAS fluctuating between 5 and 6 on both sides. February 2020, after initiation of Ixekizumab AE resoluted on the right-side VAS 0, while the left side still symptomatic VAS 6. US of the left Achilles insertion shows hypoechogenety of the tendon, distended RB, positive Doppler signals involving the bursa and extending to the tendon body. Figure 1 March 2020, an US guided injection with Triamcinolone acetate 20mg infiltrated to the RB failed to control pain with partial response for two weeks. July 2020, an US guided injection of the RB with Ixekizumab 80mg arranged two weeks after application of the systemic Ixekizumab.

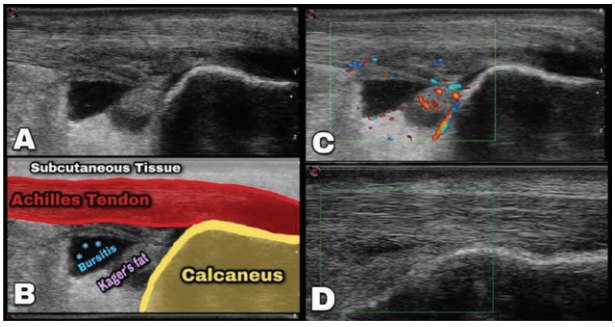


Figure 1. long axis scan of the left Achilles tendon; A: Grey scale shows hypoechogenecity of the tendon, with retrocalcaneal bursitis, B: corresponding Cartoon, C: positive color Doppler at the tendon and bursa, D: post Ixekizumab injection; resolution of the Doppler signals and bursitis.

Results: Three months after Ixekizumab local injection, heel pain drops to VAS 0, with radiological improvement in US; resolution of the Doppler signals and the RB. On follow up from July 2020 - January 2022; Resolution of heel pain, AE and RB persists since the application of Ixekizumab, with normalized Doppler and RB. Figure 1
Conclusion: US Guided local application of Ixekizumab successfully help to resolve pain and inflammation in a refractory case of AE.
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Acknowledgements: NIL.
Disclosure of Interests: Ahmed Abogamal Speakers bureau: Pfizer, Novartis, Lilly, Abbvie, Novartis, Astra-Zeneca, Amgen, Janssen.
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AB0968 RAPID ONSET OF EFFICACY IN CHINESE PATIENTS WITH ACTIVE RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS TREATED WITH IXEKIZUMAB: A PHASE 3 STUDY

Keywords: Outcome measures, Clinical Trials

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Background: Ixekizumab, a high-affinity monoclonal antibody that selectively targets interleukin-17A, has demonstrated efficacy in global clinical trials in patients with active radiographic axial spondyloarthritis (r-axSpA)/ankylosing spondylitis (AS) [1,2]. Rapid onset of clinical improvement is one of the most important needs of treatment for r-axSpA patients.
Objectives: To evaluate the onset time of ixekizumab in Chinese patients with r-axSpA.
Methods: This report evaluated efficacy onset time of r-axSpA patients treated with ixekizumab compared with placebo based on data from a phase 3 study in China. The major secondary efficacy measures in this report included Assessment of Spondyloarthritis International Society (ASAS) 40 response, ASAS 20 response, change from baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS), change from baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), change from baseline in Bath Ankylosing Spondylitis Functional Index (BASFI), and ASDAS <2.1 response. Other secondary efficacy measures in this report included change from baseline of ASAS individual components (like patient global, Spinal pain, Inflammation, high sensitivity C-reactive protein [hsCRP]), proportion of patients who experience clinically important improvement (change of ASDAS from baseline ≥1.1), major improvement (change of ASDAS from baseline ≥2.0), and BASDAI 50 response. All efficacy measures were evaluated from week 0 through week 52. A logistic regression model and mixed-effects model of repeated measures (MMRM) were used to analyze categorical and continuous measures from week 0 to 16 (placebo-controlled period), and categorical missing data were imputed using non-responder imputation (NRI).
Results: More patients achieved ASAS40 and ASAS20 response as early as week 1 ($p = 0.042$ and $p < 0.001$) in the ixekizumab-treated group compared with placebo. In addition, statistically significant ($p < 0.05$) improvements were observed as early as week 1 for the ixekizumab group compared to placebo in almost all efficacy measures mentioned above. For other outcomes including proportion of patients who experience major improvement and BASDAI 50 response, differences were evident ($p < 0.05$) by week 2 in the ixekizumab group compared with placebo. Furthermore, ixekizumab sustained high efficacy in all efficacy measures through 52 weeks.
Conclusion: Ixekizumab demonstrated a rapid onset of efficacy improvements on ASAS response, ASAS core set values, disease activity and function in Chinese patients with r-axSpA.
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Disclosure of Interests: YU XUE Consultant of: Yu Xue has been investigator of Eli Lilly and Company, Jiankang Hu Consultant of: Jiankang Hu has been investigator of Eli Lilly and Company, Dongzhou Liu Consultant of: DongZhou Liu has been investigator of Eli Lilly and Company, Jingyang Li Consultant of: Jingyang Li has been investigator of Eli Lilly and Company, Huaxiang Wu Consultant of: Huaxiang Wu has been investigator of Eli Lilly and Company, Chunyu Tan Consultant of: Chunyu Tan has been investigator of Eli Lilly and Company, Lie Dai Consultant of: Lie Dai has been investigator of Eli Lilly and Company, Yan Yan Employee of: Yan Yan is employee of Eli Lilly and Company, Hongying Li Shareholder of: HongYing Li is minor stockholder of Eli lilly and Company, Employee of: HongYing Li is employee of Eli Lilly and Company, Hejian Zou Consultant of: Hejian Zou has been investigator of Eli Lilly and Company.
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AB0969 FAILURE OF THE FIRST BIOLOGIC IN PATIENTS WITH SPONDYLOARTHRITIS: DATA FROM THE MOROCCAN RBSMR REGISTRY

Keywords: bDMARD, Spondyloarthritis

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Background: Spondyloarthritis is a group of chronic inflammatory rheumatism most often affecting young adults. Biological background treatments have revolutionized their care, although some patients have failed these treatments.
Objectives: To estimate the prevalence of failure of the first biological treatment during spondyloarthritis and the factors associated with this failure.
Methods: Our study included patients with Spondyloarthritis retained according to the ASAS criteria, having an age > 18 years, treated with biological treatment, having given their written informed consent, in the 10 rheumatology departments in Morocco, collected from the RBSMR registry, a multicenter historical-prospective registry. Primary failure was defined as failure at 6 months of treatment and secondary failure as failure at more than 6 months of treatment. Patients were assessed every six months with a scheduled follow-up of three years. Inclusion began in June 2017 and ended in January 2019, when the database was first frozen.
Results: 194 patients included. The average age was 40.23 years +/- 13.68, the sex ratio was 1.73 M/F, the average duration of evolution was 615.9 weeks +/- 349.12. An HLA B27 antigen was positive in 66% of patients. Peripheral involvement was found in 70% of patients, axial involvement in 96.4% of patients and enthesic involvement in 61.5% of patients. Radiographic sacroiliitis was present in 87.6% of patients, radiographic coxitis in 40.7% and sonographic coxitis in 19.8%. Regarding extra-articular manifestations, 14.5% of patients had anterior uveitis, 6.9% had cutaneous psoriasis, and 10.7% had associated chronic inflammatory bowel disease. The ASDAS CRP was in high activity in 50.9% of the patients and the BASDAI (spondyloarthritis activity index) more than 4 in 79.2% of the patients. At the first visit, 22.5% of patients were taking corticosteroid therapy and 53.8% were taking csDMARDs. The most widely used biological was Etanercept with a percentage of 33%. Over a follow-up period of 03 years, 05 primary failures were objectified and 17 secondary failures to the first biological treatment (08 failures at the 12th month, 06 failures at the 18th month and 03 failures at the 24th month), the prevalence of failure of the first biological was 8.76%. In bivariate analysis, no statistically significant factors were observed associated with the failure of the first biological during the visit of the 6th month, the 12th month or that of the 24th month. At the visit of the 18th month, the average BASDAI as well as that of the C reactive protein (CRP) was statistically higher in patients who failed the first biological.
Conclusion: The failure of the first biological is a rather rare situation in our study. Certain factors were significantly associated with this failure and must be taken into account when managing patients, namely high values of BASDAI and CRP. Higher values of the Bath Spondylitis Functional Index (BASFI) or CRP at baseline are predictors of a greater risk of failure of the first biological found in the literature.

REFERENCES: NIL.

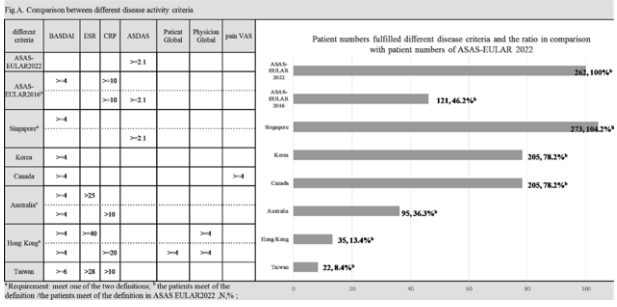
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0970 GREAT DIVERSITY IN B/TSDMARD TREATMENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AROUND THE WORLD AND THE COMPARISONS WITH THE 2022 UPDATED ASAS-EULAR RECOMMENDATIONS

Keywords: Spondyloarthritis, bDMARD, Treat to target

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Background: The 2022 updated ASAS-EULAR recommendations for the management of axial spondyloarthritis (SpA) uses the Ankylosing Spondylitis Disease Activity Scores(ASDAS) ≥2.1 as the single disease activity index indicated for the using of b/tDMARDs. Unlike the care of rheumatoid arthritis, there is a diversity in the disease activity criteria for b/tsDMARDs in axSpA worldwide, which is worthy of note.
Objectives: This study aimed to **investigate the diversity of b/tsDMARDs using in axSpA care worldwide** in the light of the 2022 ASAS-EULAR recommendations for SpA, by comparing the population fulfilled each disease activity criteria indicated for b/tsDMARDs.
Methods: Biologic-naïve patients fulfilled the ASAS axSpA criteria were recruited in the rheumatology clinic in the Shuang-Ho Hospital from 2018 to 2020. In each visit, disease activity including BASDAI, ASDAS-CRP, ESR and CRP were recorded and the fulfillment of different disease activity criteria indicated for b/tsDMARDs were labelled, including the latest two versions of ASAS-EULAR recommendations and the reimbursement criteria of Australia, Singapore, Korea, Hong Kong, Canada and Taiwan. The data having the highest disease activity of each patient were selected for analysis, and the complete data including every visit recorded were also analyzed as sensitivity test. The population size fulfilled different activity criteria were compared.
Results: This study recruited 396 biologic-naive patients with axSpA with 1390 disease activity data totally. The mean age was 41 years, and among the cohort, 129(32.6%) were female. In the 396 disease activity measures, there were 262(66.2%) patients met the disease activity criteria for b/tsDMARDs according to the 2022 ASAS-EULAR recommendations, which was more than twice the population (121) indicated by the activity criteria of the prior version. In comparison with the 2022 recommendations, the disease activity criteria of many countries are stricter leading to less b/tsDMARDs using. Using the population indicated by the 2022 recommendations as reference, the rate of patients eligible by the disease activity criteria in different countries varied greatly, which ranged from as low as 8.40% in Taiwan to 100% in Singapore. The result was consistent in analyzing the whole 1390 dataset.
Conclusion: There is a great expansion of the population indicated for b/tsDMARDs brought by the 2022 update, in comparison with the 2016 version. There is a great diversity for b/tsDMARDs using in axSpA care around the world. In some countries, a surprisingly huge disparity in b/tsDMARDs using was noted. Only less than 10% patients indicated for b/tsDMARDs using by the 2022 ASAS-EULAR recommendation met the reimbursement criteria in Taiwan, analyzed in the single measure setting.



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Disclosure of Interests: None Declared.
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AB0971 EFFECTIVENESS OF IGURATIMOD IN THE TREATMENT OF AXIAL SPONDYLOARTHRITIS-REAL WORLD DATA FROM CHINA

Keywords: Spondyloarthritis, Real-world evidence, Disease-modifying Drugs (DMARDs)

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Background: Axial spondyloarthritis (ax-SpA) is a group of chronic auto-inflammatory diseases. Tumor necrosis factor-alpha (TNF-α) and interleukin-17 (IL-17) were demonstrated to play an irreplaceable role in the pathogenesis of ax-SpA. Iguratimod is a newly-developed small molecular anti-rheumatic drug, which can inhibit the effects of prostaglandin E2, TNF-α and IL-17 [1]. The efficacy and safety of Iguratimod in the treatment of rheumatoid arthritis (RA) have been fully studied and approved to the treatment of active RA in China and Japan [2]. Iguratimod had been reported to be effective in the treatment of ax-SpA [3], despite those studies were limited and of small-example size.

Objectives: In consideration of the efficacy of Iguratimod in the treatment of RA and the overlap of disease pathogenesis between RA and SpA, Iguratimod was implied to be of potential efficacy on ax-SpA. This study was aimed to demonstrated the efficacy and safety of Iguratimod on ax-SpA in the real word from China.

Methods: 1993 patients with ax-SpA who visited the outpatient rheumatology clinics in the First Medical Center of Chinese PLA General Hospital between April 2016 to June 2022, were collected and screened. Patients treated with NSAIDs only, combined with sulfasalazine (SSZ) or Iguratimod for over 6 months were admitted into analysis. Those three groups of patients were also matched by propensity score on a ratio of 1:1:1, by age, gender and ASDAS at baseline. Multilevel models for repeated measurement data were conducted to compare the differences of ASDAS, back pain, ESR and CRP level between the three groups of patients during the 18 months follow-ups.

Results: 302 patients with ax-SpA were included in the real-world study and they were followed at a mean 6-month interval for 3 times (median follow-up 17.55 months, interquartile range 16-20 months). 161, 96 and 45 patients fell into the NSAIDs only, NSAIDs combined with SSZ or Iguratimod group. At the baseline, those three groups of patients had significantly different back pain scores, PGA, PhGA, ASDAS, ESR and CRP level (P<0.05). At the end of follow-up, patients treated with Iguratimod had significant improvement on the primary endpoint (ASDAS, 1.51±0.67 vs. 2.07±0.90, P<0.001) and secondary endpoint (BASDAI, 1.48±0.94 vs. 1.98±1.49, *P*=0.027; Back pain scores, 1.91±1.14 vs. 2.64±1.69, *P*=0.007; PGA, 2.07±1.39 vs. 2.78±1.57, *P*=0.015; PhGA, 2.20±1.16 vs. 2.96±1.45, *P*=0.003; CRP, 3.47 mg/L vs. 5.20 mg/L, *P*=0.017) than that at the baseline. Patients treated with NSAIDs and Iguratimod had higher clinically important improvement rate that that treated with NSAIDs combined with SSZ (26.66% vs. 8.33%, *P*=0.008) or NSAIDs only (26.66% vs. 8.70%, *P*=0.004). 135 patients were matched by propensity score matching (45 patients on each group) and after adjusting for potential confounding factors, patients treated with NSAIDs and Iguratimod had greater improvement on ASDAS than that on patients treated with NSAIDs combined with SSZ (β<0.001, 95% CI: 0.000 ~ 0.001, *P*=0.043) or NSAIDs only (β<0.001, 95% CI: 0.000 ~ 0.001, *P*=0.033).

Conclusion: Iguratimod had significant add-on effect on the decrease of disease activity and alleviation of back pain than monotherapy of NSAIDs or NSAIDs combined with SSZ. Iguratimod is effective and well-tolerated during the treatment and thus could be a new pharmaceutical option for ax-SpA patients.

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Disclosure of Interests: None Declared.

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AB0972 EFFICACY OF TILDRAKIZUMAB IN PATIENTS WITH PSORIASIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Systematic review, Skin

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Background: Psoriasis is a common chronic inflammatory disease of the skin[1]. The IL-23/IL-17 immune pathway plays a vital role in promoting Psoriasis pathogenesis[2]. Tildrakizumab, a humanized IgG1 monoclonal antibody against interleukin 23 p19, is currently used in the treatment of patients with psoriasis.

Objectives: This study aimed to evaluate the efficacy of tildrakizumab in the treatment of psoriasis.

Methods: Five databases, including PubMed, Embase, Medline, Web of Science, and Cochrane Library, were retrieved from their establishment to January 2, 2023. We used the EndNote X9 software to filter the retrieved articles according to the inclusion and exclusion criteria. Heterogeneity was tested using I-squared (I2). When I2>50%, we choosed the random effects model for data analysis, conversely, a fixed effects model. Publication bias was assessed using the Egger test. All analyzes were performed in STATA 12.0.

Results: We included 6 studies, 2,395 patients in the Tildrakizumab group and 552 patients in the placebo group (Table 1). Results of the meta-analysis showed that 68% of patients with psoriasis met the PAIS75 remission criteria after taking Tildrakizumab [Rate =0.68 95%CI(0.66, 0.70), P<0.001], and they had significantly higher PASI75 response rates than the placebo group [RR=11.390, 95%CI (8.08, 16.06), P<0.001]. Compared to the placebo group, patients in the Tildrakizumab group had a significantly higher remission rate of PASI90 [RR=26.751, 95%CI (15.282,46.827), P<0.001]. In addition, patients taking Tildrakizumab had an average 15-point reduction in PASI scores [Rate=-14.854 95%CI(-19.146, -10.561), P<0.001], and 45% of patients achieved PASI100 remission criteria [Rate= 0.450, 95%CI (0.131, 0.769), P=0.006] (Figure 1).

Conclusion: This study showed that Tildrakizumab improved disease activity and increased clinical remission rates in patients with psoriasis, demonstrating a better therapeutic effect.

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Table 1. Population characteristics included in the study

Author (Year)	Population (include in analysis)		Age (Mean±SD)		Gender (male %)	
	TIL	PBO	TIL	PBO	TIL	PBO
Kristian Reich (2017)	617(617)	155(154)	46.65±13.14	47.9±13.5	70.2	64.5
K. Papp (2015)	309(102)	46(41)	44.79±13.04	45.9±11.7	75.1	82.5
Alessandra Narcisi. (2022)	237(121)	NA	48.6±14.6	NA	59.9	NA
Y Poulin (2020)	1413(1413)	357(357)	NA		72.1	70.0
Cantrell, W. (2021)	248(135)	NA	NA		NA	
T Graier (2022)	15(7)	NA	45.9±14.1	NA	73.3	NA

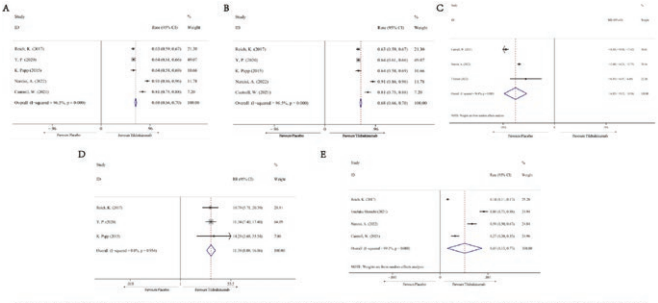


Figure 1: Forest plot of comparison Tildrakizumab versus placebo-efficacy in patients with Psoriasis using (A)PASI 75 and (B)PASI 90; Forest plot to evaluate the efficacy of Risankizumab in patients with psoriatic arthritis using (C)PASI, (D)PASI75 and (E)PASI100.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0973 REAL-WORLD EFFECTIVENESS AND SAFETY OF SECUKINUMAB IN SPONDYLOARTHRITIS AND PSORIASIC ARTHRITIS

Keywords: Real-world evidence, Psoriatic arthritis, Spondyloarthritis

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Background: Secukinumab (SEC) is a human monoclonal antibody (IgG1) aimed against IL-17A, a proinflammatory cytokine involved in the pathogenesis of psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA). It is already well known that C-reactive protein (CRP) is an important inflammatory biomarker and that it could be used as a variable of its efficacy. More recently, it has been published that the neutrophil lymphocyte ratio (NLR) [1] an inflammatory biomarker, could be predictive of CV events occurrence and all cause mortality. In this study, we intend to evaluate effectiveness and safety with SEC with conventional and non-conventional scales in patients with Spondiloartrhitis.
Objectives: To evaluate the long-term effectiveness and safety of SEC in patients with axSpA and PsA in an actual clinical setting.
Methods: We designed a single center retrospective and longitudinal observational study including patients diagnosed of axSpA fulfilling the ASAS classification criteria and PsA fulfilling the CASPAR classification criteria. Between 2016 and 2022, a total of 90 patients were included in the study treated with SEC in the rheumatology service of the Hospital Universitario de Navarra. All patients included started SEC treatment at least 1 year before the data extraction. For the axSpA CRP, the Ankylosing Spondylitis Disease Activity Score (ASDAS) scale, the patient's visual analog scale (VAS) and NLR [1] were analyzed. In the PsA group VAS, CRP and NLR were assessed. In both groups the variables were analyzed at baseline, 12 and 24 months. Safety was evaluated by analyzing intercurrent infections or neoplasms that required discontinuation.
Results: We included a total of 90 patients (46 axSpA and 44 PsA), 45(50%) of which were female. The mean age at diagnosis was 44.5 years (SD 11.1) while the mean age at SEC initiation was 51.6 (SD 11.4). The median time from diagnosis to onset of SEC was 5 years (IQR 2-11) (Table 1). Eighty-three (92.2%) patients were treated with one or more biologic drugs prior to SEC, median 2 (IQR 0-5). The mean CRP before starting SEC was 9mg/L (SD 17.6), VAS 7 (SD 2) and NLR 1.9 (SD 1). A statistically significant improvement was observed in both pathologies when it comes to CRP at 24 months (p 0.049) but not at 12 months (Table 1). VAS presented a statically significant improvement at 12 and 24 months of treatment (p 0.008 and 0.012 respectively). There were no statistically significant differences in NRL in any group. Regarding ASDAS in the axSpA group, 4,34% showed a great improvement while 26% of them showed clinical improvement. None of the baseline characteristics included in the analysis showed significant association with SEC performance on these variables. None of our patients experienced serious adverse reactions, infections or malignancies during the use of SEC.
Conclusion: In our cohort, SEC showed to be effective in axSpa and PsA patients, displaying statistically significant improvements in VAS at 12 and 24 months and CRP at 24 months. SEC safety profile in our cohort was consistent with the well-established safety profile of this drug.
REFERENCE:
[1] Merola Joseph, Mclnnes Iain et al. Effect of Secukinumab on Traditional Cardiovascular Risk Factors and Inflammatory Biomarkers: Post Hoc Analyses of Pooled Data Across Three Indications. *Rheumatology and Therapy* volume 9, pages 935–955 (2022)

Table 1. Baseline Characteristics

	AxSpA (n=46)	PsA(n=44)	Total (n=90)
Hypertension	10 (21.7%)	15 (34.1%)	25 (27.8%)
Dyslipidaemia	16 (34.8%)	20(46.5%)	36 (40.4%)
Diabetes mellitus	5 (10.9%)	7 (15.9%)	12 (13.3%)
Body Mass Index	27.7 (SD5.1)	29 (SD7.2)	28.4 (SD6.4)
Cardiovascular disease	8 (17.4%)	5 (11.6%)	13 (14.6%)
Number of previous biologics, median (IQR)	1 (1-2)	2 (1-3)	2(1-2)
CRP			
12 months	-4.7 (SD 13.3)	-4.6 (SD 17.6)	-4.6 (SD 15.2)
24 months	1.6 (SD 7.9)	-8.4 (SD 21.4)	-2.8 (SD 15.9) p 0.049
VAS			
12 months	-3.2 (SD 2.5)	-0.6 (SD 3.4)	-2.1 (SD 3.1) p 0.008
24 months	-6.6 (SD 2.3)	-2.6 (SD 1.5)	-4.6 (SD 2.8) p 0.012
NLR			
12 months	-0.0 (SD 0.8)	-0.4 (SD 1)	-0.2 (SD 0.9) p 0.123
24 months	-0.2 (SD 1.6)	-0.2 (SD 0.9)	-0.2 (SD 1.3) p 0.864

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0974 **TREATMENT OF AXIAL SPONDYLOARTHRITIS WITH SECUKINUMAB: A REAL-LIFE RETROSPECTIVE COHORT STUDY**

Keywords: bDMARD, Spondyloarthritis

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Background: Data from several large prospective studies have demonstrated that secukinumab is an efficient and safe treatment choice for axial spondyloarthritis (axSpA) [1].
Objectives: The aim of our study was to evaluate data from a real-life cohort of patients with axSpA treated with secukinumab.
Methods: We retrospectively analysed data from our institutional registry of axSpA patients (radiographic and non-radiographic) treated with secukinumab. We analysed the features of patients who continued secukinumab at their last visit and those who discontinued the drug over the follow-up period. We used the Kaplan-Meier curve to estimate the cumulative retention rate of secukinumab.
Results: A total of 57 patients were enrolled in our study. Among them, 26 (45,6%) were women, and 31 (54,4%) were men. The median age was 50 (22-71). There were 26 (45,6%) patients who were bDMARD naïve and 31 (54,4%) patients that had used at least one bDMARD before secukinumab. Among the naïve group, 4 (14,4%) patients discontinued secukinumab, whereas among the group with former bDMARD usage, 12 (38,7%) people discontinued treatment. The ineffectiveness of the drug was the most common reason for discontinuation in both groups. Regarding adverse effects, two people reported respiratory infections. We did not record significant drug safety complications in our cohort. The duration of treatment was 6,5 years. The survival rate of the drug was 91% after six months, 83,4% after 12 months, 75% after 24 months, and 66,6% after 48 months. Table 1 shows detailed clinical aspects of the cohort.
Conclusion: Our data confirmed a good survival rate of secukinumab in patients with axial spondyloarthritis. However, results showed that fewer biologically naïve patients discontinued the secukinumab treatment than those who received the drug after the failure of another biologic.
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Table 1. Clinical characteristics of the cohort

	Naive bDMARD **n=24**	≥1 bDMARD **n= 33**	Patients continuing the secukinumab **n=41**	Patients discontinuing the secukinumab **n=16**	Total **n=57**
	n(%)	**n(%)**	**n(%)**	**n(%)**	**n(%)**
Male	13 (54,2)	13 (39,4)	22 (53,7)	4 (17,9)	31 (54,4%)
Female	11 (45,8)	20 (60,6)	19 (46,3)	10 (43,5)	26 (45,6%)
HLAB27 positive	13 (54,2)	19 (57,6)	25 (61)	8 (50)	32 (56,1)
	Median (range)	**Median (range)**	**Median (range)**	**Median (range)**	**Median (range)**
Age (year)	48 (32-66)	52 (22-71)	50 (22-71)	50,5 (30-62)	50 (22-71)
Diagnosis duration (year)	8 (2-17)	12 (4-41)	9 (2-21)	12 (2-41)	9 (2-41)
Initial BASDAI	7,15 (3,10-9,4)	7,3 (1,9-9)	7,1 (1,4-9,4)	7,65 (4,2-8,9)	7,25 (1,4-9,4)
Δ BASDAI (3 months)	1,1	0,4	2,8	0,85	2,3
Initial BASFI	6,3 (3,4-8,9)	6,5 (0,6-9,6)	6,5 (3,4-9,4)	6,2 (0,6-8,6)	6,4 (0,6 -9,4)
Initial CRP	5,5 (0,8-44,4)	3,6 (0,3-115)	4,4 (0,3-44,4)	3,45 (1,4-115)	4 (0,3-115)
Δ CRP (3 months)	1,6	0,4	1,45	0,5	0,6
Secukinumab therapy duration (days)	883,5 (79-1973)	1127 (112-2359)	1413 (79-2359)	293,5 (112-1408)	1050 (79-2359)

Acknowledgements: NIL.
Disclosure of Interests: Ljiljana Smiljanic Tomicevic Speakers bureau: Novartis, Ely Lilly, Pliva, Pfizer, Abbvie, Ivan Padjen Speakers bureau: Novartis, Ely Lilly, Pliva, Pfizer, Abbvie, Matea Martinić: None declared, Miroslav Mayer Speakers bureau: Novartis, Ely Lilly, Pliva, Pfizer, Abbvie, Branimir Anić Speakers bureau: Novartis, Ely Lilly, Pliva, Pfizer, Abbvie.
DOI: 10.1136/annrheumdis-2023-eular.6035

Spondyloarthritis - clinical aspects (other than treatment)

AB0975 THE ACCURACY ON THE SELF-REPORTED DIAGNOSIS OF IMIDS IS LOWER AMONG RHEUMATIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

Keywords: Patient information and education

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Background: The association of several immune-mediated inflammatory diseases (IMIDs) in the same patient is well known[1]. Rheumatologic and dermatologic IMIDs are frequently diagnosed in patients with inflammatory bowel disease (IBD)[1]. However, the degree of knowledge that patients with IBD have about the coexistence of other IMIDs is little studied.
Objectives: Our aim was to evaluate the accuracy of self-reporting of IMIDs by patients with IBD.
Methods: Prospective, unicentric study that included patients attended in person at the IBD Unit of the Central University Hospital of Asturias (Oviedo-Spain) between August 2020 and December 2021. Patients were invited to participate in the study, and, after signing the informed consent, they answered a questionnaire about the presence or not of 50 IMIDs (self-reported diagnosis). The diagnosis of an IMID was confirmed in the medical records of each patient (reference diagnosis). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy (proportion of subjects correctly classified) of self-reporting was calculated. Statistical analyses were performed with R software version 4.0.2.
Results: A total of 1621 patients were included. Forty-four percent of patients had ulcerative colitis, 53% Crohn's disease and 3% an IBD-unclassified, sex distribution was 1:1, and the age at diagnosis of IBD was 38 ± 15.2 years. Seven hundred and twelve patients were receiving mesalazine, 67 corticosteroids, 394 immunomodulators and 532 biologics. Six hundred and twenty-seven (39%) patients were diagnosed with at least one IMID, 177 (10.9%) with two, 49 (3%) with three, and 17 (1%) with more than three. Sixteen percent of patients had a rheumatologic IMID and 15% a cutaneous IMID. Self-reporting of IMIDs by IBD patients showed a sensitivity, specificity, PPV, NPV and accuracy of 0.75 (95%CI 0.73-0,78), 0.89 (95%CI 0.86-0.91), 0.92 (95%CI 0.89-0.93), 0.69 (95%CI 0.66-0.73) and 0.81 (95%CI 0.79-0.83), respectively. Accuracy of self-reported diagnosis of IMIDs was lower among the rheumatic IMID group (Table 1).
Conclusion: Eighty-one percent of patients with IBD are able to correctly identify the coexistence or not of other IMIDs. It was observed that in the case of rheumatologic IMIDs there is a significant percentage of patients who do not know whether or not they suffer from one of these conditions.
REFERENCE:
[1] Inflamm Bowel Dis. 2022 Nov 2;28(11):1756-1765.

Table 1. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of self-reporting of immune-mediated inflammatory diseases (IMIDs) by patients with inflammatory bowel disease: results by IMID groups.

IMID group*	Reference/ Self-reporting (n/ n)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
Rheumatological	265/ 404	0.84 (0.79-0.88)	0.87 (0.85-0.88)	0.55 (0.5-0.6)	0.96 (0.95-0.97)	0.86 (0.84-0.88)
Cutaneous	244/276	0.77 (0.71-0.82)	0.94 (0.92-0.95)	0.68 (0.62-0.73)	0.96 (0.95-0.97)	0.91 (0.89-0.92)
Digestive	23/121	1 (0.85-1)	0.94 (0.93-0.95)	0.19 (0.12-0.27)	1 (1-1)	0.94 (0.93-0.95)
Endocrinological	69/ 108	0.97 (0.90-1)	0.97 (0.96-0.98)	0.62 (0.52-0.71)	1 (1-1)	0.97 (0.96-0.98)
Ocular	53/ 61	0.79 (0.66-0.89)	0.99 (0.98-0.99)	0.69 (0.56-0.8)	0.99 (0.99-1)	0.98 (0.97-0.99)
Others	160/ 209	0.86 (0.80-0.91)	0.95 (0.94-0.96)	0.66 (0.59-0.72)	0.98 (0.98-0.99)	0.94 (0.93-0.95)

*Rheumatologic IMIDs: rheumatoid arthritis, psoriatic arthritis, spondyloarthritis; cutaneous IMIDs: psoriasis, hidradenitis suppurativa, pyoderma gangrenosum, erythema nodosum, alopecia areata, vitiligo; digestive: primary sclerosing cholangitis, primary biliary cholangitis, autoimmune hepatitis; endocrinological: diabetes type 1, autoimmune hypothyroidism, hyperthyroidism; ocular: uveitis, episcleritis; others: asthma, multiple sclerosis, etc.n: number; IMID: immune-mediated inflammatory disease; PPV: positive predictive value; NPV: negative predictive value.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1042

AB0976 LOW SPINAL RADIOGRAPHIC PROGRESSION AFTER A MEAN OF 15 YEARS OF FOLLOW-UP IN A COHORT OF PATIENTS AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Descriptive Studies

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Background: Axial spondyloarthritis (axSpA) is characterized by progressive structural damage on the sacroiliac joints and/or the spine. The progression is assessed by conventional radiology through available scales such as the mSASSS (modified Stoke Ankylosing Spondylitis Spinal Score) in the spine. However, data on long-term radiographic progression and factors associated with such progression are scarce.
Objectives: To evaluate the radiographic progression of the spine in patients with axSpA after a mean of 15 years of follow-up as well as the factors associated with such progression.
Methods: Patients with axSpA included in 2006-2007 in the multicentre Spanish registry REGISPONSER and pertaining to the Reina Sofia Hospital were re-evaluated in 2021-2022. Spine (cervical and lumbar) radiographs were obtained with the aim to be compared with those obtained in 2007. Two trained blinded readers scored the mSASSS in radiographs from both visits (baseline and current). First, intraclass correlation coefficients (ICC) were calculated to evaluate the agreement between both readers in mSASSS. Mean mSASSS of both readers in both timepoints were calculated and the absolute progression (ΔmSASSS) was evaluated. In addition, we evaluated the mean and median progression per year dividing the ΔmSASSS by the years of follow-up in each patient. Then, the median progression per year was used to divide patients in "low progressors" and "high progressors". Baseline characteristics between these two groups were compared using univariate analysis.
Results: A total of 77 axSpA patients with both baseline and current radiographs were included. A total of 53 (68.8%) were male and the mean disease duration was 10.15 (SD 9.2) years. All of them were naïve to bDMARD at baseline and 38% had radiographic sacroiliitis. The mean years of follow-up (i.e, mean time separating the radiographs) was 15 years (SD 3.3). ICC between the two readers was moderate for mSASSS at baseline (0.73, 95%CI 0.26-0.88) and at the 15 years visit (0.65, 95%CI 0.11-0.84). After a mean of 15y of follow-up, the mean progression was 0.54 (SD 0.55) points in mSASSS per year and the median progression was 0.38 points per year. A total of 37 (48%) patients were considered "low progressors" (i.e., median progression <0.38 points per year) and 40 (52%) were considered as "high progressors" (i.e., median progression ≥0.38 points per year). The only significant variable associated with "high progression" was low back pain before the diagnosis (82.5% vs. 48.6%, p-value 0.003). Neither sex, smoking, disease duration, HLAB27 or c-reactive protein were associated with the "high progression" group.
Conclusion: In this stablished axSpA population, the mean and median progression were 0.54 and 0.38 points in mSASSS per year respectively, which is lower than what has been reported in similar cohorts (i.e., change in 2 points in mSASSS). Only low back pain was found as predictor of spinal radiographic progression.
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[1] Aouad K, Ziade N, Baraliakos X. Structural progression in axial spondyloarthritis. Joint Bone Spine. 2020;87(2):131-136. doi:10.1016/j.jbspin.2019.04.006
Acknowledgements: NIL.
Disclosure of Interests: Raquel Ena María Granados: None declared, Santiago Dans-Caballero: None declared, María Lourdes Ladehesa Pineda: None declared, María Ángeles Puche Larrubia: None declared, Desiree Ruíz-Vilchez: None declared, M. Carmen Ábalos-Aguilera: None declared, Alejandro Escudero Contreras: None declared, Eduardo Collantes Estevez Speakers bureau: Lilly, Consultant of: Lilly, Grant/research support from: Lilly, UCB, Abbvie, Clementina López-Medina Speakers bureau: AbbvVie, Eli, Lilly, Novartis, Janssen, UCB Pharma., Consultant of: Eli, Lilly, Novartis, UCB Pharma.
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AB0977 CHANGES IN ASDAS AND SYMPTOMS OF ANXIETY AND DEPRESSION IN AXIAL SPONDYLOARTHRITIS: LATENT TRAJECTORY ANALYSIS

Keywords: Spondyloarthritis, Epidemiology

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Background: Disease-assessment in axial spondyloarthritis (axSpA) includes subjective measures that do not necessarily reflect inflammatory processes in the spine and joints. Mental health comorbidities such as anxiety and depression can be secondary to inflammatory and non-inflammatory processes. There may be subgroups that respond differently to axSpA treatment, for example, discordance in these indices whereby disease activity improves but not mental health. Understanding such potential subgroups and their characteristics can support individualised care.

Objectives: To apply data-driven approaches to longitudinal disease activity (ASDAS) and Hospital Anxiety and Depression Scale (HADS) subscores for anxiety (HADS-A) and depression (HADS-D) to identify potential groups with discordant trajectories.

Methods: This was an ancillary analysis of the data collected for the Assessment of SpondyloArthritis international Society Health Index (ASAS HI) Validation Study. We included individuals who fulfilled ASAS criteria for axSpA and required a therapeutic change (initiation of NSAID, csDMARDs or TNFi) due to active disease. Those with diagnosis of peripheral SpA were excluded. Participants were assessed at baseline and one follow-up. Group-based trajectory models were used to group individuals based on shared trajectories of ASDAS, HADS-A and HADS-D. These three dependent variables were standardised (scale 0 to 10), then included in linear models with a time indicator (baseline or follow-up) as the independent variable. We selected the optimum number of groups through statistical fit. Individuals were assigned to the group with the highest posterior probability of membership. Patient and disease characteristics were compared across groups.

Results: Of 206 participants (mean age 37 years, 65% male), 73 (35%) started NSAIDs, 23 (11%) csDMARD and 109 (53%) TNFi (Table 1). The optimum number of trajectory groups was 4 (Figure 1). Three indices changed concordantly regardless of the number of latent groups. Group descriptions are relative: Group (G) 1 (54%) started with low scores for all three indices, G2 (34%) moderate, and G3 (5%) high. Mean improvements in ASDAS were numerically similar across these groups. G4 (7%) had the greatest improvement across all three indices. Initiated therapy differed with G3 and 4 more frequently starting TNFi.

Conclusion: Results of this study show that ASDAS and symptoms of anxiety and depression are closely related and change concordantly with treatment, and suggest that reported musculoskeletal and mental health symptoms influence each other. There were no clear differences in patient or disease characteristics across these groups except for age. Whether axSpA patients benefit from knowing that mental health symptoms generally improve jointly with disease activity when starting treatment remains to be shown.

Table 1. Clinical and disease characteristics across the four latent groups.

	Group 1 (n=112)	Group 2 (n=69)	Group 3 (n=11)	Group 4 (n=14)	p
Age (years)	33.8 (10.8)	41.4 (11.4)	44.4 (12.7)	35.1 (11.8)	<0.001
Male	76 (68)	40 (58)	7 (64)	11 (79)	0.38
Symptom duration (years)	10.6 (8.9)	13.0 (10.2)	15.2 (8.6)	9.1 (13.7)	0.17
HLA-B27 positive	86 (85)	39 (74)	8 (80)	8 (62)	0.10
r-axSpA*	65 (58)	46 (67)	8 (73)	9 (64)	0.58
Peripheral arthritis	44 (40)	32 (47)	6 (55)	4 (31)	0.54
Uveitis	21 (19)	12 (18)	2 (18)	4 (29)	0.78
Psoriasis	9 (8)	8 (12)	1 (9)	0	0.57
IBD	7 (6)	6 (9)	1 (10)	0	0.65
Baseline ASDAS	2.9 (0.8)	3.7 (1.0)	4.6 (0.6)	4.3 (1.1)	<0.001
Baseline HADS-D	4.2 (2.7)	8.9 (2.9)	14.4 (2.7)	12.3 (2.2)	<0.001
Baseline HADS-A	4.8 (2.4)	10.5 (3.0)	15.7 (3.4)	11.5 (3.4)	<0.001
Mean change ASDAS	-1.2 (0.9)	-1.3 (1.1)	-1.4 (1.1)	-2.8 (1.1)	<0.001
Mean change HADS-A	-1.4 (2.4)	-1.6 (3.2)	-0.6 (5.3)	-8.7 (4.5)	<0.001
Mean change HADS-D	-1.8 (2.9)	-1.2 (3.1)	-3.2 (5.1)	-11.4 (2.6)	<0.001
NSAIDs initiators	42 (38)	26 (38)	2 (18)	3 (21)	0.45
TNFi initiators	52 (46)	37 (54)	9 (82)	11 (79)	0.03
csDMARD initiators	17 (15)	6 (9)	0	0	0.15

Data shown as mean (SD) or n (%). *proportion of radiographic vs non-radiographic axSpA.

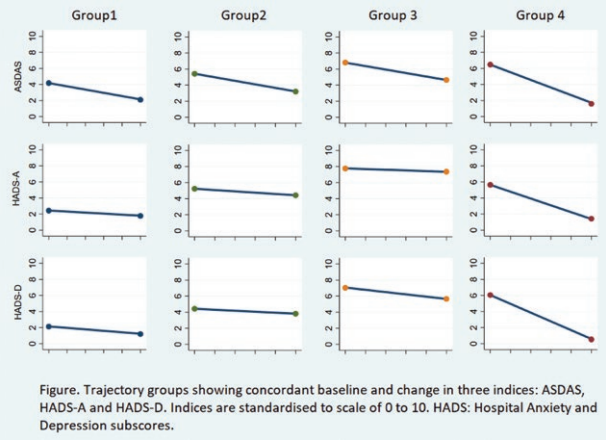


Figure. Trajectory groups showing concordant baseline and change in three indices: ASDAS, HADS-A and HADS-D. Indices are standardised to scale of 0 to 10. HADS: Hospital Anxiety and Depression subscores.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0978

ASSOCIATION OF SLEEP QUALITY WITH DISEASE ACTIVITY, INFLAMMATION, MOBILITY, AND FUNCTION AMONG PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Quality of life, Patient reported outcomes

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Background: Inflammation and ankylosis of the axial skeleton are two major features of axial spondyloarthritis (axSpA), which cause midnight pain and immobility of back, respectively. Both features may lead to sleep problem. Nevertheless, which of the two features influence sleep most is less studied. Moreover, there are many disease activity measurements, including BASDAI, ASDAS, ESR and CRP, among these measurements, which one could best predict sleep disturbance are still unknown.

Objectives: This pilot study aimed to discover the association between different measurements of axSpA and sleep disturbance.

Methods: This cross-sectional study recruited patients with axSpA from the rheumatology clinic in the Shuang-Ho hospital from 2018 to 2020. The Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep quality together with other clinical measurements, including BASDAI, ESR, CRP and ASDAS-CRP for disease activity, BASMI for mobility and BASFI for function. The features associated with poor sleep quality (PSQI > 5) were identified. All the domains of sleep disturbance were compared between patients with different level of disease activity classified by each activity measurement.

Results: This cross-sectional study recruited 322 patients with axSpA, among them 72% were male, and the mean age was 42 years. There were 249 (77.3%) patients had poor sleep quality (PSQI>5). Poor sleepers had significantly higher BASDAI, ASDAS-CRP and BASFI, while there was no significant difference in sex, age, ESR, CRP and BASMI. Patients with higher BASDAI had significantly poorer sleep quality in almost all domains of PSQI (figure 1A), while higher level of ESR or CRP could not discriminate poor sleeper in every domain of PSQI (figure 1C,1D). ASDAS-CRP had a moderate discriminability, which was believed brought by the integrated components of BASDAI in the index.

Conclusion: Lots of patients (77.3%) with axSpA were poor sleeper, which is worthy note in clinical care. Mobility seems to have less influence on sleep than disease activity. Although BASDAI was believed too subjective as a disease activity index, it performed the best to discriminate poorer sleep quality in almost all domains of sleep. Although ESR and CRP were more objective disease activity markers of axSpA and have better relevance to the MRI-demonstrated inflammation, both the inflammatory markers had no value in the care of sleep in axSpA patients surprisingly. In conclusion, BASDAI still had value in axSpA care, and the elements of BASDAI make ASDAS a more comprehensive index than ESR or CRP alone.

Table 1. Differences in characteristics and features between axial spondyloarthritis patients with different sleep quality

	Poor sleep quality (N=249)	Good sleep quality (N=73)	p-value
Male (n, %)	179 (72%)	57(78%)	0.89
Age (yr)	41.84(13.3)	39.3(13.32)	0.14
BASMI	1.83 (1.85)	1.42 (1.66)	0.0958
BASFI	1.95 (2.16)	1.26 (1.85)	<0.05
BASDAI	4.04 (2.24)	2.54 (1.92)	<0.001
ASDAS-CRP	2.46 (1.14)	1.97 (0.85)	<0.001
ESR (mm/hr)	16 (15.76)	15.5 (17.24)	0.8186
CRP (mg/dl)	9.36 (16.43)	8.6 (12.21)	0.67

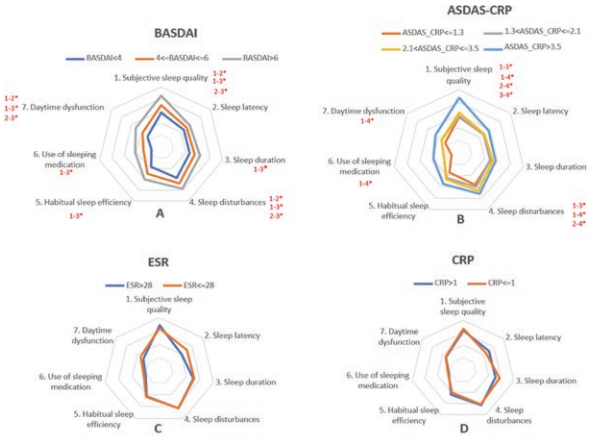


Figure 1. The discriminative power of different disease activity measurements to differentiate poor sleep quality in patients with axial spondyloarthritis

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AB0979

SELF-REPORTED AND PHYSICIAN´S ASSESSMENT OF INFLAMMATORY BACK PAIN ACCORDING TO ASAS CRITERIA: IS IT THE SAME? RESULTS FROM THE SHERPAS STUDY

Keywords: Spondyloarthritis, Health Services Research, Quality of care

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Background: Inflammatory back pain (IBP) is the core symptom in patients with axial spondyloarthritis (axSpA). For its assessment, experts recommend using the Assessment of SpondyloArthritis International Society (ASAS) criteria. Advances in telemedicine and online screening strategies require to evaluate whether self-reported perform equally to physicians' assessment.
Objectives: To assess the agreement and correlation between self-reported and physician´s assessments of ASAS IBP criteria and evaluate their performance compared with rheumatologist´s judgement for IBP.
Methods: The "Strategy for a Hospital Early Referral in Patients with Axial Spondyloarthritis" (SHERPAS) is a prospective ongoing study recruiting young patients (18 to 40 years) with chronic back pain asked to undergo an MRI of the spine by other specialists different than rheumatologists in a tertiary hospital, starting in September 2021. After inclusion, an additional MRI of the sacroiliac joints (SIJ), followed by a rheumatology visit and eligible blood tests were performed. IBP was assessed in 3 different independent ways: i) ASAS criteria asked verbatim by the rheumatologist (*ASAS-IBP-phy criteria*), ii) ASAS criteria embedded in a self-reported questionnaire (*ASAS-IBP-self reported*), and iii) according to rheumatologist judgement in the interview (*IBP-rheumatologist*). Dataset for this interim analysis was locked in October 2022. Kappa statistic (κ) and tetrachoric correlation coefficient (rt) were calculated to assess the agreement and correlation between ASAS-IBP-phy criteria and ASAS-IBP-self reported. Overall accuracy, sensitivity, specificity, positive and negative predictive values for each IBP assessment method were calculated, using IBP-rheumatologist as gold standard.
Results: Among 152 recruited patients, 85 (55.9%) were female; mean (SD) age was 34.2 (5.3) years. 66/152 (43.4%) patients reported IBP by at least one of the three assessments, and 24 (15.8%) patients presented back pain as assessed by the three methods altogether. Venn diagrams representing the overlap between the different IBP assessments are shown in **Figure 1**. A moderate agreement (κ =0.48) and strong correlation (rt=0.7) were found between ASAS-IBP-self reported and ASAS-IBP-phy criteria. While ASAS-IBP-phy criteria showed a strong level of agreement and very strong correlation with IBP-rheumatologist (κ = 0.74, rt= 0.94), ASAS-IBP-self reported showed a moderate agreement and moderate correlation with this outcome (κ = 0.44, rt=0.67). ASAS-IBP-phy criteria showed better performance than ASAS-IBP-self reported for capturing IBP- rheumatologist [accuracy of 0.89 (95%CI 0.83- 0.94) vs 0.77 (95%CI 0.70- 0.84)] **(Table 1)**.
Conclusion: ASAS criteria to define IBP show higher level of agreement and correlation with IBP rheumatologist overall judgement when assessed by physician as compared to a self-reported assessment. These results call for caution when extrapolating use of experts IBP criteria from clinical to online setting and suggest that clinicians should prioritize physician assessment over self-report to define this.

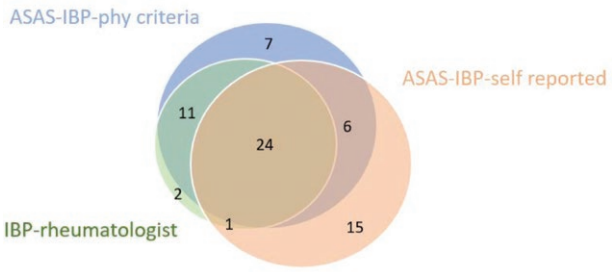


Figure 1. Number of patients showing IBP by each method of assessment

Table 1. Utility measures for each IBP assessment method to capture IBP according to rheumatologist judgement

	ASAS-IBP-phy criteria	ASAS-IBP-self reported
Accuracy	0.89	0.78
Sensitivity	0.89	0.81
Specificity	0.92	0.66
Negative Predictive Value	0.73	0.54
Positive Predictive Value	0.97	0.87

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AB0980

HOW DO SPONDYLOARTHRITIS START? IDENTIFICATION OF THE FIRST SYMPTOMS ACCORDING TO THE DIAGNOSIS AND HLA-B27. DATA FROM REGISPONSER AND RESPONDIA REGISTRIES

Keywords: Spondyloarthritis, Registries

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Background: The definition for early spondyloarthritis (SpA) implies the correct identification of the initial symptom of SpA. There is currently no consensus on whether only musculoskeletal manifestations (MM) or also extra-MM (EMM) should be considered as the onset of SpA.
Objectives: a) To describe the initial symptom (either MM or EMM) in the different SpA subtypes; b) to describe the initial symptom stratified by the clinical diagnosis and by the presence of HLA-B27; c) to analyze the clinical factors associated with different forms of initiation.
Methods: Observational, cross-sectional and multicenter study, including patients with a diagnosis of SpA (Ankylosing Spondylitis (AS), AS associated with Psoriasis (AS-Pso), AS associated with Inflammatory Bowel Disease (AS-IBD), Psoriatic Arthritis (PsA), Reactive Arthritis (ReA), Juvenile Spa (Juv-SpA), Arthritis associated with IBD (A-IBD) and undifferentiated SpA (u-SpA)) from REGISPONSER and RESPONDIA registries. Investigators responses to the question "Indicate the first sign or symptom attributable to the disease" have been recorded. The date of appearance of each MM and EMM feature was collected, allowing to determine the first symptom(s) in each patient. Differences in the first symptom across diagnosis and between HLA-B27 carriers were compared using the chi-square test. Finally, factors associated with the most prevalent initial symptom were evaluated.
Results: A total of 4411 patients were included. AS (54.9%), PsA (18.7%) and uSpA (11.1%) were the most prevalent diagnosis. In the overall population, low back pain (60.3%) was the most prevalent initial symptom followed by buttock pain (35.3%) and lower limbs arthritis (39.9%). The percentage of patients who started the disease with each symptom according to the diagnosis is represented in Figure 1. In AS patients, the absence of HLA-B27 lead to an increment in the probability of initiating the disease with cervical pain (25.6% vs. 15.5%), enthesitis (18.8% vs. 12.4%) and coxitis (15.7% vs. 8.4%) in comparison with HLA-B27 positives. In PsA, the initiation with upper limb arthritis (61% vs. 38.4%) and psoriasis (62.1% vs. 37%) was more prevalent in HLA-B27 negatives, while the initiation with low back pain (22.1% vs. 38.4%) and buttock pain 13.6% vs. 28.8%) was more prevalent in HLA-B27 positives. In AS-Pso, the absence of HLA-B27 was more frequently associated with peripheral features and psoriasis as first symptom. In the whole population, factors associated with cervical pain vs. low back pain as first symptom were cutaneous psoriasis, negative HLA-B27 and peripheral involvement (arthritis, enthesitis and dactylitis). On the other hand, factors associated with upper limbs arthritis vs. lower limbs arthritis as first symptom were female gender, cutaneous psoriasis, HLA-B27 negative and absence of axial symptoms.
Conclusion: In this SpA population, the most prevalent initial symptoms were musculoskeletal (i.e., low back pain, buttock pain and lower limbs arthritis), with differences across diagnosis and depending on the presence of HLA-B27 antigen. In AS patients the absence of the HLA-B27 seems to be associated with cervicalgia and peripheral involvement as first symptom, while in PsA it was associated with upper limbs involvement as initial symptom.
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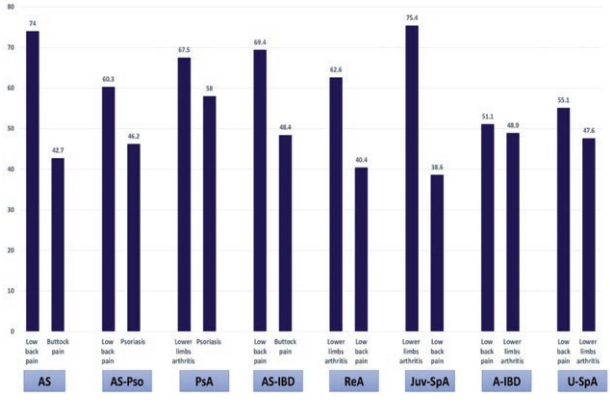


Figure 1. Description of the first symptoms according to the SpA diagnosis.

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AB0981

HIGH PREVALENCE OF IRRITABLE BOWEL SYNDROME IN AXIAL SPONDYLOARTHRITIS: A CROSS SECTIONAL MULTICENTRIC OBSERVATIONAL STUDY

Keywords: Gastrointestinal tract, Spondyloarthritis

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Background: Axial spondyloarthritis (ax-SpA) is a heterogeneous disease including extra-articular manifestations that can impact both disease severity and quality of life[1]. Among them, gastrointestinal symptoms can be related to inflammatory bowel disease (IBD), but also to functional disorder of the gastrointestinal tract such as irritable bowel syndrome (IBS)[2][3]. IBS and IBD are associated with multiple comorbidities and lifestyle behaviors including diet and physical activity.
Objectives: The objectives of this study were to evaluate the prevalence of IBS, IBD and associated factors including demographic and ax-SpA characteristics, treatments and adherence, lifestyle behaviors, and comorbidities.
Methods: A cross-sectional, multicenter study was conducted at rheumatology departments in 5 university hospitals (Bordeaux, Clermont-Ferrand, Limoges, Montpellier, and Toulouse). Patients with ax-SpA (ASAS criteria) treated by biologics were recruited from June 2021 to June 2022. Patients completed an anonymous self-questionnaire evaluating demographic data, lifestyle behaviors, treatment adherence (Girerd questionnaire) and IBS (Roma IV criteria). A medical questionnaire on ax-SpA characteristics, activity and treatments, was completed by rheumatologists.
Results: 500 patients were included in the study (mean age 49.5±13.8 years, 47 % women, mean disease duration 14.7±11 years, and mean BASDAI 3.6±2.1). Sacroiliitis was observed in 51 % on radiographs and 56 % on MRI, HLA-B27 positivity in 71 %. 86 % of the patients received TNF inhibitors, 13% IL17 inhibitors, 1% IL12/IL23 inhibitors, and 25 % NSAIDs. Good adherence (Girerd score = 0) was reported in 49 % of patients. A medical diet was followed by 26 patients (5%) and non-medical diet by 47 patients (9 %). Most of non-medical diets were lactose (22 patients) and gluten-free diets (11 patients). IBS was present in 124 patients (25 %). Female gender (60 %, p=0.001), unemployment (27 %, p=0.013), higher disease activity (BASDAI, p<0.001), worse functional score (BASFI, p<0.001), multiple lines of biologics (p=0.002), fibromyalgia (34%, p<0.001), anxiety (41%, p<0.001), depression (16%, p=0.037) and lower physical activity (p=0.001) were associated with IBS. No difference was noted regarding diet between patients with or without IBS. IBD was observed in 53 patients (11%). Among them, 41 had Crohn disease (77%), 12 ulcerative colitis (23%), 7/53 being considered active by rheumatologists (15%). Proportion of females was higher (63%, p=0.017) in patients with IBD, whereas HLA-B27 was less present (54%, p=0.016). Patients with IBD received less NSAIDs (p<0.001). The use of TNF inhibitors was as frequent as for patients with no IBD whereas IL17 and IL12/IL23 inhibitors were less frequently used (p=0.01). In contrast to IBS, there was no observed difference in comorbidities and physical activity. The prevalence of IBS was similar between patients with or without IBD (respectively 11/53 (21%) vs. 113/447 (25%)).
Conclusion: Prevalence of IBS is high in ax-SpA, accounting for a quarter of patients, and should be screened in the presence of gastrointestinal symptoms. The presence of IBS is not associated with IBD, nor diets. It is associated with female gender, anxiety, depression and fibromyalgia. Patients with IBS seem to have a more difficult to treat disease characterized by higher activity, worse functional scores, and multiple lines of treatments.
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AB0982 GISCASPA – STUDY OF SUBCLINICAL GUT INVOLVEMENT IN AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Gastrointestinal tract

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Background: Axial spondyloarthritis (axSpA) had a predilection for the axial skeleton and belong to the group of Spondyloarthritis, a set of inflammatory rheumatic diseases with common clinical, radiologic, and serologic features in which extraarticular manifestations are frequent, including inflammatory bowel disease (IBD). The link between SpA and IBD has been recognized for decades, with 5-10% of axial SpA patients suffering from concurrent IBD.[2] But, emerging evidence suggests that subclinical gut inflammation in patients with SpA is an important pathophysiological event that plays a role in disease pathogenesis. However, it is difficult to detect subclinical gut inflammation since it is largely asymptomatic. Faecal calprotectin (FC) is a very sensitive marker for inflammation in the gastrointestinal tract. The role of FC in patients with SpA is not clearly defined, but some studies suggest that FC levels may predict the onset of IBD and may be related to disease activity.
Objectives: To test the validity of FC as a marker of intestinal inflammation in patients with axSpA and to investigate factors associated with increased FC levels in patients with axSpA.
Methods: Patients involved fulfilled ASAS classification criteria for axSpA and were divided into two groups - ankylosing spondylitis (AS) or non-radiographic axSpA (nr-axSpA); a control group without rheumatologic diseases or IBD was also included. All patients and controls answered a structured questionnaire about the presence of gastrointestinal symptoms - Red Flags Questionnaire for IBD and underwent FC measurement with enzyme-linked immunosorbent assay (≥50 mg/g was considered positive). Patients treated with oral NSAIDs should undergo adequate washout (at least 3 weeks). In patients, BASDAI, BASFI, ASDAS-PCR and BASMI were recorded. A general analysis was performed; p-value ≤0.05 was statistically significant.
Results: We included 64 patients (34 with AS and 30 with nr-axSpA) and 25 controls. Demographic, clinical data is represented in table 1. In AS group, 2.9% had nocturnal diarrhoea, first-degree relative with confirmed IBD and rectal urgency; in nr-axSpA, 6.7% had abdominal pain 30-45 minutes after meals and 3.3% chronic abdominal pain; all controls were asymptomatic. Elevated FC was observed in 32.4% of AS patients (129.2±404.0), 23.3% of nr-axSpA patients (70.9±114.4) and 4.2% of controls (21.9±18.4). FC was significantly higher in each axSpA subtype vs controls (p=0.03). There were no statistically significant differences in ASDAS, BASDAI, BASFI or BASMI scores between axSpA patients with normal vs high FC levels.

Table 1. Characteristics of the population according to axSpA groups and controls.

	AS (n=34)	axSpA (n=30)	Controls (n=25)	*P**
Age (years), mean±SD	55.5±14.7	44.9±13.3	40.2±14.0	**0.004**
Sex (F/M)	15/19	18/12	13/11	0.205
Age at disease onset (years), mean±SD	11.8±7.7	5.4±3.3	-	**<0.001**
Comorbidities, n (%)				
Arterial Hypertension	13(38.2)	10(33.3)	1(4)	0.166
Dyslipidemia	8(23.5)	7(23.3)	2(8)	0.985
Diabetes Mellitus	3(8.8)	2(6.7)	0	0.748
Obesity	1(2.9)	1(3.3)	0	
Smoking status, n (%)	4(11.8)	1(3.3)	1(4)	0.850
Peripheral involvement, n (%)	9(26.5)	5(16.7)	-	0.344
Dactylitis (ever), n (%)	0	1(3.3)	-	0.283
Enthesitis (ever), n (%)	1(2.9)	2(6.7)	-	0.482
Uveitis (ever), n (%)	9(26.5)	4(13.3)	-	0.192
Positivity HLA-B27, n (%)	25(73.5)	13(43.3)	-	**0.014**
BASDAI, mean±SD	3.4±2.5	3.8±2.4	-	0.589
BASFI, mean±SD	3.3±2.5	3.3±2.1	-	0.981
ASDAS-PCR, mean±SD	2.3±1.0	2.4±1.1	-	0.070
BASMI, mean±SD	4.2±1.8	3.1±1.7	-	0.226
Therapeutic, n (%)			-	
AINEs**	16 (47.1)	14 (46.7)		0.124
cDMARDs	2 (5.9)	2 (6.7)		0.897
bDMARDs	9 (26.5)	11 (36.7)		0.408

*Comparison between nr-axSpA and AS groups.** washout before collecting stool.

Conclusion: In patients with axSpA, gut inflammation measured by FC was higher than among controls and it was also higher in patients with AS than in nr-axSpA. We also found that high FC values were not associated with more pronounced gastrointestinal symptoms. Thus, studies with a larger population and invasive studies are needed to assess the impact that this marker may have on the management of this pathology.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0983 THE DIFFERENCE IN DISEASE ACTIVITY SCORES AND TREATMENT RESPONSE ACCORDING TO GENDER IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Outcome measures

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Background: Measurement of disease activity of axial spondyloarthritis (axSpA) is mainly dependent on the patient reporting outcomes. It is known that there are differences in patient reporting outcomes between men and women.
Objectives: We investigated the differences in disease activity scores before and after treatment with biologic disease-modifying antirheumatic drugs (bDMARDs) between gender.
Methods: Data were retrieved from the Korean College of Rheumatology Biologics therapy (KOBIO) registry. axSpA patients from December 2012 to August 2021 were included in the study. Bath ankylosing spondylitis disease activity index (BASDAI) and ankylosing spondylitis disease activity score (ASDAS) at the first visit after starting bDMARDs were compared between male and female patients. Generalized linear model analyses were conducted to check the relationship between the change in disease activity scores and gender with the correction of other clinical variables.
Results: In total, 1,753 patients (1,343 male and 410 female patients) were included in the analyses. At baseline, male patients were younger, had longer disease duration, and had a higher ratio of HLA-B27 positive patients, higher ratio of radiographic disease, lower BASDAI, and higher CRP level. At the first follow-up

visit, male patients achieved BASDAI < 4 more significantly than female patients (79.57% vs. 71.54%, p < 0.0010). However, the proportion of patients who achieved ASDAS low disease activity (< 2.1) and ASDAS inactive disease (<1.3) were not significantly different between gender (71.14% vs. 71.5%, p = 0.8892; 38.82% vs. 39.44%, p = 0.8265, respectively). The difference in BASDAI between the first follow-up visit and baseline was statistically significantly related to gender after adjusting for other clinical information at baseline (p = 0.0033). In the same analysis, the difference in ASDAS was not significantly related to gender (p = 0.1303).
Conclusion: Depending on the method of calculating disease activity, the interpretation of treatment response of bDMARDs may differ between gender.

Table 1. The results of the multivariate generalized linear model of the relationship between the change in disease activity scores and clinical variables, including gender

	Gender	Age	Disease duration	HLA-B27	Radiographic disease	Smoking	Ex-smoker	Current smoker	Baseline value
BASDAI									
beta	0.4054	0.0190	0.0036	-0.4990	0.1918	.	0.1025	0.4557	-0.7609
SE	0.1377	0.0041	0.0089	0.1712	0.1758	.	0.1439	0.1298	0.0257
p	0.0033	0.0000	0.6888	0.0036	0.2752	0.0016	0.4764	0.0005	0.0000
ASDAS									
beta	0.1030	0.0079	0.0103	-0.2953	0.1022	.	0.0652	0.2964	-0.8320
SE	0.0680	0.0020	0.0045	0.0857	0.0880	.	0.0713	0.0647	0.0237
p	0.1303	0.0001	0.0214	0.0006	0.2459	0.0000	0.3609	0.0000	0.0000

BASDAI, Bath ankylosing spondylitis disease activity index; *ASDAS*, ankylosing spondylitis disease activity score; *SE*, standard error

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Disclosure of Interests: None Declared.
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AB0984 SACROILIAC MRI FINDINGS IN PATIENTS WHO WERE REQUESTED A SACROILIAC STUDY: SACROILIITIS AND OTHER DIAGNOSES

Keywords: Spondyloarthritis, Gender/diversity issues, Imaging

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Background: Magnetic resonance imaging (MRI) is the most sensitive imaging modality for the detection of sacroiliitis. Diagnosing sacroiliitis on MRI is not always straightforward and can be challenging in some cases.
Objectives: To evaluate the prevalence of sacroiliitis (according to ASAS criteria) and other diagnoses in sacroiliac MRI. To analyse/compare these diagnoses by sex, age and service requesting the study.
Methods: This is a cross-sectional, multicentre, descriptive, retrospective study in a hospital and/or specialised care setting. Consecutive MRI examinations (in adults) of the sacroiliac joints (SIJ) performed between 1 de Enero de 2019 y el 31 de Diciembre del 2019 were retrospectively evaluated for the presence of structural and active sacroiliitis findings according to the Assessment of SpondyloArthritis International Society guidelines. Alternative diagnoses, including degenerative changes, diffuse idiopathic skeletal hyperostosis (DISH), osteitis condensans ilii (OCI), septic sacroiliitis/discitis, stress reaction and anatomic variants, were registered.
Results: We evaluated 1,283 MRI examinations, 526 (41%) males, average age 46.7 ± 14 years. 71.6% of the requests are from the Rheumatology service, 15.8% from Orthopedic Surgery and Traumatology and 12.5% from other services. 70% of the MRIs were reported by a radiologist expert in the locomotor system. Findings suggestive of axial spondyloarthritis were found in 353 (27.5%). Sacroiliitis was found in 71 examinations (25%) and alternative diagnoses were suggested in 87 (31%) (OCI 8.9%, anatomic variants 5.3%, septic sacroiliitis/discitis 5.3%, degenerative findings 4.3%, DISH 1.5%, stress reaction 0.7%, tumor 0.3%). A normal examination was found in the remaining 123 examinations. Patients with alternative diagnoses were older than those with sacroiliitis (62 vs. 47 years of age, respectively, P > 0.05). Alternative diagnoses in the SIJ were significantly more common in females (66) than in males (21), P < 0.05.

Table 1.

MRI Diagnosis	Principal	2nd	3rd diagn
Without alterations	452 (35.2)	6 (0.5)	3 (0.2)
Degenerative changes of the SIJ	152 (11.8)	37 (2.9)	5 (0.4)
Sacroiliitis with erosions	147 (11.5)		
Sacroiliitis BME + erosions	157 (12.2)	11 (0.9)	
Degenerative disc disease L5-S1	103 (8)	141 (11)	12 (0.9)
BME (without ASAS criteria)	82 (6.4)	32 (2.5)	4 (0.3)
Sacroilitis with BME	73 (5.7)		
Other	40 (3.1)	29 (2.3)	7 (0.5)
Lumbosacral transition abnormality	18 (1.4)	27 (2.1)	10 (0.8)
Osteitis condensans ilii	17 (1.3)	7 (0.5)	2 (0.2)
Fracture	12 (0.9)	2 (0.2)	
Tumor	16 (1.2)	4 (0.3)	
Diffuse idiopathic skeletal hyperostosi (DISH)	6 (0.5)	1 (0.1)	1 (0.1)
Anatomical variants of SIJ	6 (0.5)	11 (0.9)	1 (0.1)
Septic Arthritis	2 (0.2)		
Gout		1 (0.1)	

Conclusion: A substantial proportion of patients with suspected sacroiliitis had normal SIJ while the rest were more commonly diagnosed with pathologies other than inflammatory sacroiliitis. A referral by an experienced rheumatologist may improve the sensitivity and specificity of this important examination.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2484

AB0985 COSTOVERTEBRAL AND COSTOTRANSVERSE JOINT INVOLVEMENT IN SPONDYLARTHRITIS BY ROUTINE CHEST COMPUTED TOMOGRAPHY

Keywords: Spondyloarthritis

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Background: In spondyloarthritis (SpA) patients, costovertebral (CV) and costotransverse (CTr) joint are affected however these involvements are not routinely examined in clinical practice. Clinical characteristics of these involvements need further assessment.
Objectives: In this study, we aimed to determine the characteristics of CV and CTr joint involvements in SpA patients by routine chest computed tomography (CT).
Methods: SpA patients who have been requested a chest CT for any reason between January 2010 and December 2020 were retrieved from medical records and included in this retrospective cross-sectional analysis. Of these subjects, 281 had a diagnosis of SpA confirmed with patients records and sacroiliac imaging. After the patient population was created, the patients were sorted according to the registration number and divided into groups of ten. One patient was selected from each group. Thirty age- and sex-matched rheumatoid arthritis (RA) patients and 30 healthy controls were selected. Thorax CT were re-examined for CV and CTr joints by an experienced radiologist. All joints were classified as: Normal (0); suspicious [1], mild [2], moderate [3], and severe [4]. A total of 44 joints were evaluated for each patient, 24 CV and 20 CTr joints.
Results: Of the SpA patients, 206 (73.3%) were diagnosed with AS, 63 (22.4%) with psoriatic arthritis (PsA), and 12 (4.3%) with non-radiographic axial SpA (nr-AxSpA). 34 (54%) of PsA patients had axial PsA. Total scores of CV joint were different between diseases (AS 35 (0-96), PsA 16 (0-73), axial PsA 16 (0-73), peripheral PsA 20 (1-53), nr-AxSpA 6.5 (0-42), RA 15.5 (0-50), healthy control 13 (0-48) (p<0.001))

(Figure 1). Similarly, total scores of CTr joint were different between diseases (AS 16 (0-80), PsA 13 (0-34), axial PsA 12 (0-34), peripheral PsA 14 (0-32), nr-AxSpA 14 (2-31), RA 6.5 (0-24), healthy control 4 (0-20) (p<0.001)). In AS patients, 123 were male and 83 were female. Male AS patients had higher CV and CTr scores than female AS patients (Male CV score:52 (0-96) CTr score:20 (0-80); Female CV score:22 (0-96), CTr score:12 (0-79), p<0.001). In male AS patients, strong negative correlations between chest expansion and joint involvement of CV (r=-0.612, p<0.001) and CTr (r=-0.618, p<0.001) were found. In addition, strong positive correlations were observed between CV joints and lumbar modified stoke ankylosing spondylitis spinal score (mSASSS) (r=0.742 p<0.001), CV joints and cervical mSASSS score (r=0.754 p<0.001), CTr joints and lumbar mSASSS score (r=0.638 p<0.001), CTr and cervical mSASSS score (r=0.654 p<0.001).

Conclusion: In this study, we have found that CV and CTr joint involvement on thorax CT were more severe in AS patients and were associated with mSASSS and it negatively affects chest expansion. In a study with 25 AS patients, CV and CTr joint involvements were 80% and 60%, respectively and negative correlation with chest expansion were observed [1]. Another study showed moderate correlation mSASSS and arthritis of CV or CTr joints in AxSpA patients with MRI [2]. Our results are in line with the literature. In the light of these results, it may be beneficial to evaluate these joints, which have the potential to be overlooked clinically, and to initiate patients with CTr and CV joint involvement in exercise programs in the early period.

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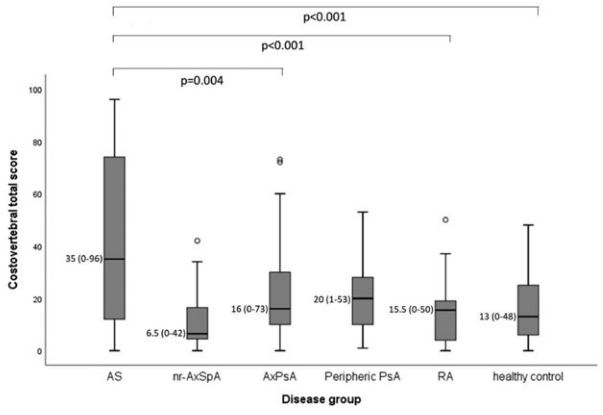


Figure 1. Distribution of costovertebral joint scores according to diseases AS: Ankylosing spondylitis, AxPsA: Axial psoriatic arthritis, nr-AxSpA: non-radiographic axial spondyloarthritis, PsA: psoriatic arthritis, RA: rheumatoid arthritis

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Disclosure of Interests: None Declared.
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AB0986 QUALITY STANDARDS FOR PATIENTS WITH AXSPA – STATUS QUO OF DIAGNOSTIC AND THERAPEUTIC MANAGEMENT OF AXSPA PATIENTS IN GERMANY

Keywords: Spondyloarthritis, Quality of care

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Background: Despite the availability of national and international recommendations for management of patients with axial spondyloarthritis (axSpA), shortcomings in the delivery of high level quality of care in daily practice likely exist in many health care systems. To optimize diagnostic and therapeutic approaches for axSpA patients, 9 quality standards (QS) were developed by ASAS (Assessment of SpondyloArthritis international Society) [1]. These international QS have been recently adapted in Germany [1, 2].

Objectives: To determine the status of quality of care delivered to axSpA patients in 2021 across Germany, with special reference to the new ASAS QS.

Methods: As part of a multicentre study, the Continuous Outcome Benchmarking in Rheumatology (KOBRA) project in Germany, patients with axSpA were surveyed regarding the 9 ASAS QS: QS1 - time until referral; QS2 - time to specialist; QS3 - time span of diagnostic work-up; QS4 - monitoring of disease activity; QS5 - discussion of biological treatment in case of insufficient NSAID therapy; QS6 - benefit of regular exercise; QS7 - offers for disease educational courses; QS8 - time to contact with the rheumatologist in case of flare or drug adverse events; QS9 - annual review.

Results: A total of 417 axSpA patients on an in-patient basis in 27 rheumatology clinics were surveyed; mean age 50.7 yrs; mean symptom duration 14.6 years; 53.4% had r-axSpA, 71.4% BASDAI>4, and 81.2% ASDAS>2.1. Regarding the 9 ASAS QS, 31.7% of the patients received a referral to a rheumatologist within 3 working days after initial suspicion of an axSpA (QS1). 36.0% of referred patients received an appointment with the rheumatologist within 3 weeks (QS2). The diagnostic work-up by the rheumatologist was completed within 2 months in 63.2% of the patients (QS3). Monitoring of the disease activity with validated scores at least once every 6 months was performed in 50.2% (QS4). 62.9% of patients were treated with NSAIDs, of whom 66.2% described therapy as insufficient. In 14.6% of patients, rheumatologist did not discuss a potential treatment escalation to biologics despite the insufficient response to NSAIDs (QS5). About ¾ of patients (72.6%) reported being informed about the positive effects of regular exercise (QS6). Only 35.7% received an offer for an educational course including disease management within 2 months after diagnosis (QS7). In case of flare or adverse events, urgent contact to rheumatology within 2 business days took place in only 35.1% of patients (QS8). 51.4% of patients have undergone an annual assessment of life circumstances and disease influencing cofactors (QS9). Of note, relevant gender differences were identified: the waiting time for an appointment with a rheumatologist was longer for women (>3 months, 32.3% vs. 18.0%), and female patients reported more often an insufficient NSAID therapy than males (71.3% vs. 59.8%) despite similar rates of NSAID use. In patients insufficiently treated with NSAIDs, therapy with a biologic was less often discussed with females (17.2% vs. 10.4%). Despite, more women were treated with a biologic (42.6% vs. 35.1%). Contact with the rheumatologist, if urgently needed, within <7 working days took place more often in women (60.5% vs. 45.9%).

Conclusion: This is the first project to assess the quality of care according to the ASAS QS among axSpA patients in Germany. The quality of care was acceptable in some areas (e.g. escalation to biological therapy) but needs improvement in others (e.g. rapid access to rheumatology for diagnosis and in case of urgent matters, educational offers). Relevant gender differences were identified. Overall, this data provides important guidance for the improvement of rheumatologic care in daily practice.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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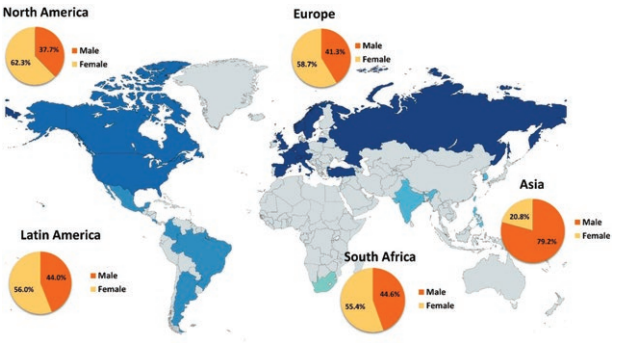
AB0987 FEMALES WITH AXIAL SPONDYLOARTHRITIS REPORT HIGHER BURDEN OF DISEASE AND WORSE PATIENT-REPORTED OUTCOMES. RESULTS FROM THE INTERNATIONAL MAP OF AXIAL SPONDYLOARTHRITIS (IMAS)

Keywords: Gender/diversity issues, Patient reported outcomes, Spondyloarthritis

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Background: There is increasing evidence of differences between males and females in axial spondyloarthritis (axSpA), but the source is restricted to specific geographic locations or populations.
Objectives: This analysis aims to assess gender differences in a large sample of patients included in the International Map of Axial Spondyloarthritis (IMAS) study from around the globe.
Methods: IMAS is a cross-sectional online survey (2017-2022) of 5,557 unselected axSpA patients from 27 countries. The current analysis looked at the differences in a variety of patient and disease characteristics/assessments between males and females. The factors evaluated were: sociodemographic (age, educational level, marital status, employment status, and patient organization membership), health behaviours (smoking, alcohol consumption, and physical activity), disease characteristics (age at symptom onset, diagnostic delay, HLA-B27, family history of axSpA, uveitis, inflammatory bowel disease), patient-reported outcomes (disease activity [0-10] on the BASDAI scale, spinal stiffness [3-12], functional limitation [0-54], and mental health [0-12] using GHQ-12 scale), mental comorbidities (anxiety, depression, and sleep disorders), and treatments (NSAIDs, csDMARDs and bDMARDs).
Results: Data from 5,555 patients reporting gender were analyzed: 3,492 from Europe, 769 from North America, 600 from Asia, 548 from Latin America, and 146 from Africa. Globally, 55.4% were females, with higher proportions in South Africa (82.2%) and lower in Asia (20.8%; **Figure 1**). Compared to males, females were of a younger age, more frequently university educated, more often divorced, more commonly on permanent sick leave, and less often members of patient organizations (**Table 1**). With respect to health behaviours, male participants smoked and drank more than females. Compared to males, diagnostic delay was significantly longer (by 2.4 years) while the rate of HLA-B27 positivity and family history with axSpA were lower in females. With respect to patient-reported outcomes, females presented with higher disease activity, greater functional limitation, and poorer mental health. The use of axSpA drug treatment was more common in females with a higher proportion having ever taken NSAIDs, csDMARDs and bDMARDS (**Table 1**).
Conclusion: Globally, females with axSpA practiced better health behaviors and reported lower frequency of HLA-B27 positivity but had longer diagnostic delay. Despite more frequently receiving medication, females presented with higher disease activity, greater functional limitation, and worse mental health. Reducing the disease burden and diagnostic delay in females is crucial to improving axSpA care around the world.



Map 1. Gender* proportion by region (N= 5,555)* Gender options in the survey were limited to males or females only

Table 1. Patient and disease characteristics in males and females with axSpA (N= 5,555)

	Mean ± SD or n (%)		P-value
	Male 2,475 (44.6%)	**Female** 3,080 (55.4%)	
Age	44.9 ± 13.6	43.2 ± 12.1	**<0.001**
Patient organization membership	1113 (45.0)	1293 (42.0)	**0.025**
Smoking	548 (23.3)	580 (19.7)	**0.002**
Alcohol consumption	823 (33.8)	808 (26.7)	**<0.001**
Diagnostic delay	6.1 ± 7.8	8.5 ± 9.7	**<0.001**
HLA-B27 Positive	1115 (78.9)	1348 (65.8)	**<0.001**
Family history of axSpA	459 (31.4)	752 (39.8)	**<0.001**
Uveitis	564 (25.3)	607 (21.5)	**0.002**
Psoriasis	172 (17.3)	289 (22.7)	**0.002**
Disease activity (0-10)	5.0 ± 2.2	5.7 ± 2.0	**<0.001**
Functional limitation (0-54)	18.1 ± 15.2	21.2 ± 15.3	**<0.001**
Mental health (0-12)	4.2 ± 4.0	5.1 ± 4.1	**<0.001**
Anxiety	623 (27.0)	1149 (39.2)	**<0.001**
Depression	620 (26.8)	1007 (34.4)	**<0.001**
Sleep disorders	696 (30.3)	1206 (41.4)	**<0.001**
NSAIDs	1729 (75.5)	2190 (81.2)	**<0.001**
csDMARDs	933 (41.3)	1206 (45.5)	**0.003**
bDMARDs	1093 (47.1)	1362 (50.2)	**0.030**

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Disclosure of Interests: Victoria Navarro-Compán Speakers bureau: AbbVie, Eli Lilly, Janssen, MSD, Novartis, Pfizer, UCB Pharma, Consultant of: AbbVie, Eli Lilly, Galapagos, MoonLake, MSD, Novartis, Pfizer, UCB Pharma, Grant/research support from: AbbVie, Novartis, Marco Garrido-Cumbrera Grant/research support from: Novartis, Denis Poddubnyy Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB, Grant/research support from: AbbVie, MSD, Novartis, and Pfizer, Christine Bundy Speakers bureau: AbbVie, Celgene, Janssen, Lilly, Novartis and Pfizer, Souzi Makri Consultant of: Novartis, GSK and Bayer, José Correa-Fernández: None declared, SHASHANK MURLIDHAR AKERKAR Speakers bureau: Pfizer, Novartis, Eli Lilly, Jansen, Lillann Wermskog Grant/research support from: No personal funding, but ASIF has received funding from Novartis, UCB, Lilly, Abbvie, Boehringer Ingleheim, Pfizer, Janssen, Elie Karam: None declared, Asif Siddiqui Employee of: Novartis employment and stock ownership, Fernando Sommerfleck Speakers bureau: Abbvie, Eli Lilly, Janssen, Novartis, Consultant of: Abbvie, Novartis, Janssen.
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AB0988

GENETIC EVIDENCE FOR A BIDIRECTIONAL CAUSAL RELATIONSHIP BETWEEN ANKYLOSING SPONDYLITIS AND CARDIOVASCULAR DISEASE

Keywords: Spondyloarthritis, Cardiovascular disease

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease[1]. Mounting evidence suggests an increased risk of cardiovascular disease (CVD) in patients with AS. And cardiovascular problems in AS patients have been identified as the primary cause of death[2]. Furthermore, few studies have examined whether CVD directly impacts AS, making the link between AS and CVD less complete. In this study, we conducted a bi-directional Mendelian randomization (MR) analysis to investigate the causal relationship between these two traits.
Objectives: This study aimed to investigate the bidirectional causal effects of AS and CVD.
Methods: Genetic instruments for AS were obtained from the Finnish database, including 2,252 cases and 227,388 controls. The summary data for 12 CVD were retrieved from genome-wide association studies (GWAS). We utilized the inverse variance weighted (IVW), MR-Egger regression and weighted-median (WME) analysis to test the casual relationship. Sensitivity analysis

is used for hypothesis testing and estimating the tangible impact between exposure and results.

Results: The study indicated that AS increased the genetic susceptibility to cardiogenic stroke (IVW:OR: 1.05, 95% CI: 1.01-1.10, p = 0.03), heart failure (HF) (IVW: OR=1.01, 95% CI=1.00-1.01, P=0.0004) and atrial fibrillation (AF) (IVW: OR= 1.01, 95% CI= 1.00-1.01, P= 0.007). Small vessel stroke (SVS) was positively associated with an increased risk of AS (IVW: OR=1.20, 95% CI=0.77-1.41, P=0.022).

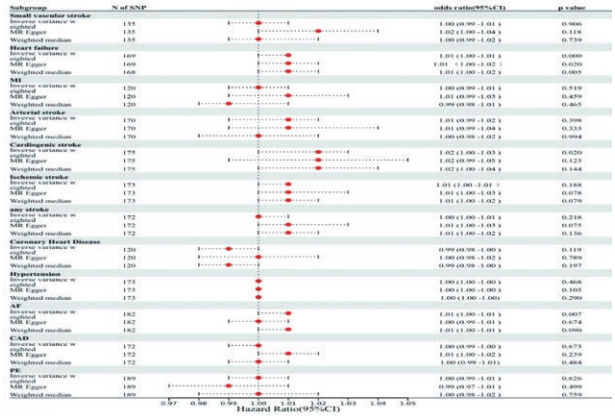
Conclusion: AS may be a risk factor for CVD such as cardiogenic stroke, HF, and AF. At the same time, for patients of SVS, the risk of developing AS was 1.20 times. Inflammation may be one of the main pathways linking this causality.

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(A)



(B)

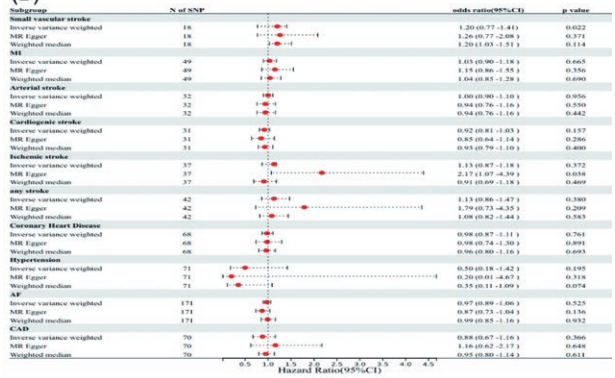


Figure 1: Odd ratio (OR) of Ankylosing spondylitis (AS) and cardiovascular disease (CVD). (A) OR of the associations of AS with the risk of CVD; (B) OR of the associations of CVD with the risk of AS. CI: confidence interval; SNP: single nucleotide polymorphism; IVW: the inverse variance-weighted.

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Disclosure of Interests: None Declared.

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AB0989 **ARE OSTEOPOROSIS AND FRACTURES NEGLECTED ISSUES IN AXIAL SPONDYLOARTHRITIS? DATA FROM A CROSS-SECTIONAL MONOCENTRIC STUDY**

Keywords: Spondyloarthritis, Comorbidities, Osteoporosis

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Background: Prevalence of osteoporosis (OP) and fractures (Fx) in spondyloarthritis (SpA) is frequently overlooked[1]. Axial (ax-) involvement, particularly in ankylosing spondylitis (AS), is associated with seeming increased lumbar spine bone mineral density (BMD) while vertebral fractures are present in up to 43% of patients with AS. Bone densitometry is considered the gold standard for osteoporosis diagnosis and fracture risk assessment.

Objectives: To investigate predictors of OP and prevalence of Fx in a population of ax-SpA patients.

Methods: Data were cross-sectionally extracted from a monocentric registry including SpA patients with axial involvement [AS, ax- Psoriatic Arthritis (ax-PsA), non-radiographic ax-SpA (nr-axSPA), IBD associated-SpA] at their last evaluation in a tertiary rheumatology center between August and December 2022. Comparisons were performed by T test and chi-square test; logistic regression was used to analyze the predictors of OP screening assessed by dual-energy x-ray absorptiometry (DXA) and other collected variables.

Results: The overall population included 385 patients (35.6% female; mean age±SD 48.5±12.7 yrs; 42.9% AS, 33% nr-axSpA, 20.5% ax-PsA, 3.6% IBD-SpA; 43.9% HLAB27 positive; 42.3% postmenopausal females; 7.8% patients with previous diagnosis of OP). Almost 10% of the entire population experienced Fx (n=38): 16 vertebral Fx, 2 femoral Fx, and 24 non-vertebral/ non femoral Fx. The presence of previous fragility Fx was significantly associated with menopause (39% vs 12.4%, p<0.001), older age (56.6±10.11 vs 47.6±12.65, p<0.001), elevated ESR (median 13 mm/h (IQR 7-24) vs 9 (5-19), p=0.04) and higher ASDAS-CRP (median 1.28 (1-2.6) vs 1.05 (0.6-1.7), p=0.03), and previous OP diagnosis (50% vs 3.1%, p<0.001). DXA was performed only in 11.7% of the population. DXA was mainly performed in females (64.5% vs 31.8%, p<0.001), post-menopausal women (57.8% vs 9.4%, p< 0.001), older patients (58.6±12.5 vs 47.2±8.9, p<0.001), patients with previous diagnosis of disthyroidism (11.1% vs 4.7%, p=0.08), OP (53.4% vs 1.8%, p<0.001), patients with previous Fx (46.7% vs 5%, p<0.001), both vertebral Fx (26.7% vs 1.2%, p<0.001) and non-vertebral/non femoral Fx (24.5% vs 3.9%, p<0.001). DXA was significantly more frequently performed in patients supplemented with vitamin D (86.7% vs 29.4%, p<0.001), calcium (53.4% vs 4.1%, p<0.001), and receiving bisphosphonate therapy (26.7% vs 1.8%, p<0.001) or on bone loss inducing drugs (44.4% vs 21.3, p=0.001). DXA was significantly less frequently evaluated in current smokers (1.5% vs 24.7%, p=0.04) and ax-PsA subtype (8.9% vs 22%, p=0.04). Factors associated with OP screening by DXA were menopause [OR 17.8, 95% CI 2.3-135, p=0.005], and bone loss inducing drugs (OR 3.2, 95% CI 1.12-9.16, p=0.030). Predictor of Fx was the presence of elevated disease burden expressed as ASDASCRP (OR 1.9, 95% CI 1.2-3.2, p=0.012).

Conclusion: Our data confirm that OP is an underestimated comorbidity in axSpA patients, particularly males or younger patients. Fragility Fx is related with disease burden, confirming that inflammation mostly triggers bone loss. Not all risk factors for OP are correctly addressed, such as active smoke. We should aim to better evaluate OP as a SpA comorbidity to early detect patients at high risk of fragility Fx to treat them properly.

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AB0990 **OBSTRUCTIVE SLEEP APNEA IS INCREASED IN PATIENTS WITH SPONDYLOARTHRITIS COMPARED TO HEALTHY CONTROLS**

Keywords: Spondyloarthritis, Cardiovascular disease, Epidemiology

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Background: Obstructive sleep apnea (OSA) is a common chronic disorder, characterized by recurrent collapse of the upper airway during sleep. OSA is associated with comorbidities, such as ischemic heart disease, hypertension, arrhythmias, and others. The spectrum of spondyloarthritis (SpA) encompasses several diseases, including ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease related arthropathy, reactive arthritis, and undifferentiated SpA, sharing common clinical manifestations. It is important to gather more data on the prevalence of OSA, as diagnosing and treating comorbidities is an essential part of the management of inflammatory diseases. There are several reports on the association between OSA and ankylosing spondylitis with conflicting results. To date, studies evaluating the association between OsA and broader spectrum of SpA are lacking.

Objectives: To examine the prevalence and severity of OSA in patients with SpA with or without axial involvement compared to healthy controls. Predictive factors for OSA, such as disease activity, SpA subtypes, axial involvement and medical treatment, were assessed as well.

Methods: This was a controlled cross-sectional study. The study cohort consisted of consecutive patients with SpA defined by the ASAS classification criteria. Clinical and demographic characteristics of the cohort were retrieved from patients' files. Disease activity scores and sleep quality questionnaires were administered at enrolment. All participants underwent a single night home sleeping test using a validated diagnostic device. OSA was defined as apnea-hypopnea index (AHI) ≥5, and moderate-severe OSA as AHI≥15.

Results: Forty-two consecutive patients with SpA and 33 healthy controls were recruited to this study. Patients' characteristics are shown in **table 1**. OSA was diagnosed in 34 patients (81%) with SpA compared to 15 (33%) in the control group (P<0.01) **figure, panel A**. Moderate-severe OSA was found in 14 (33%) patients in the SpA group vs. 1 (3%) in the healthy control group (P<0.01) **figure, panel B**. Other sleep indices, such as sleep efficiency, sleep stages and sleep latency, didn't show any significant difference between the groups. There was also no correlation between SpA activity scores, BASDAI and ASDAS, sleep scores, drug therapy and the presence of OSA. In a logistic regression analysis, older age, elevated body mass index and axial involvement were associated with the presence of OSA.

Conclusion: In this study, OSA, including moderate-severe OSA, was significantly more prevalent in patients with SpA in comparison with healthy controls. Axial involvement predicted the presence of OSA in SpA. Our study emphasizes the importance of sleep assessment and diagnosing OSA in patients with SpA, in order to provide treatment, improve the quality of life and reduce the impact of comorbidities.

Table 1. Patients and Controls Characteristics

	SpA	Controls
General Characteristics		
Age (years)	50.2 ± 13.2	43.8 ± 11.0
Male, n (%)	27 (64.3)	22 (66.7)
BMI, Kg/m²	29.5 ± 9.4	25.2 ± 2.9
Disease characteristics		
Mean disease duration (years ± SD)	12.2 ± 13.1	
ASDAS (mean ± SD)	2.48 ± 1.24	
BASDAI (mean ± SD)	6.25 ± 6.76	
Pain-VAS (mean ± SD)	51.6 ± 31.1	
HAQ (mean ± SD)	3.4 ± 2.81	0.41 ± 1.42
Axial involvement, n (%)	30 (71%)	
Sleep and Fibromyalgia Scores		
ESS, (mean ± SD)	6.8 ± 3.9	6.8 ±5.62
PSQI, (mean ± SD)	7.4 ± 4.42	7.7 ± 4.83
WPI, (mean ± SD)	4.5 ± 5.1	2.07 ± 3.32
SSS, (mean ± SD)	4.6 ± 3.4	3.03 ± 3.22

SpA, Spondyloarthritis; BMI, body mass index; SD, Standard Deviation; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Score; Pain-VAS, Pain Visual Analog Scale; HAQ, Health Assessment Questionaire; ESS, Epworth Sleepiness Scale; PSQI, Pittsburgh Sleep Quality Index; WPI, Widespread Pain Symptoms; SSS, Symptoms Severity Scores.

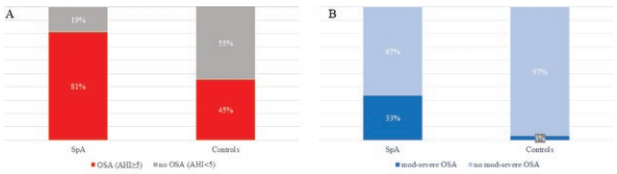


Figure. Panel A. obstructive sleep apnea in spondyloarthritis patients compared to healthy controls. p<0.01. Panel B. moderate to severe obstructive sleep apnea (AHI≥15) in spondyloarthritis patients compared to healthy controls. SpA, spondyloarthritis; OSA, obstructive sleep apnea, mod-severe, moderate-severe

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Disclosure of Interests: None Declared.

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AB0991 RADIOGRAPHIC EVALUATION OF FOOT SPURS IN SPONDYLOARTHRITIS

Keywords: Spondyloarthritis

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Background: Although bone spurs are frequently seen in non-inflammatory diseases, they can also be seen with inflammation of the enthesis areas, especially in spondyloarthritis (SpA).

Objectives: To investigate the radiological evaluation of foot spurs in SpA and compare the characteristics between the SpA and degenerative diseases.

Methods: This ongoing study included 168 (124 women) patients with radiographic plantar or achilles spur. Age, disease duration, and body mass indexes were recorded. Patients were categorized with inflammatory [non-radiographic SpA (nr-AxSpA), radiographic SpA (r-AxSpA), psoriatic arthritis (PsA), and other) and non-inflammatory [osteoarthritis (OA) and diffuse idiopathic skeletal hyperostosis (DISH)]. Foot radiographs of the plantar region, achilles, and other regions (anterior ankle, posterior ankle, and tarsal bones) were examined for the spurs. The spur caharacteristics were evaluated. Three measurements were taken from each radiograph: plantar spur base, mid-segment, and length in millimeters. The differences were compared between SpA patients and controls.

Results: The mean age of the patients was 50.8 (SD:11.3) years, and the mean disease duration was 55.1 (SD:55.8) months. One hundred twenthy eight (76.2%) were in the inflammatory group [PsA (n=56), r-axSpA (n=30), nr-axSpA (n=27), other SpA (n=14)], while 40 (23.8%) were in the non-inflammatory [OA (n=35), DISH (n=5)] group. Plantar spur base, midsegment, and length were higher in the non-inflammatory group than in the inflammatory group (p<0.05). Fluffy structure and erosion in the plantar spur were more common in the inflammatory group (p<0.05). The characteristics of the spurs were not different between diseases in the inflammatory group (p>0.05). Plantar spur lengths in the PsA patients were significantly higher than in the non-PsA SpA group (p=0.028 and 0.003); other spur features between groups were not different (p>0.05).

Conclusion: Spurs are smaller and erosion and fluffy appearance are more common in SpA patients compared to non-inflammatory conditions. Spur characteristics are not different among SpA group diseases; only the plantar spur lengths were higher in patients with PsA. Although calcaneal and achilles spurs are frequently evaluated in clinical practice, approximately half of the patients also have spurs in the tarsal bone.

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Table 1. Comparison of spurs in the inflammatory and non-inflammatory group

	Inflammatory Group	**Non-inflammatory Group**	*p*
Right			
Plantar spur, n (%)	98 (%76.6)	31 (%77.5)	0.32
Fluffy plantar spur, n (%)	28 (%21.9)	2 (%5)	**0.026**
Erosion in the plantar spur, n (%)	21 (%16.4)	1 (%2.5)	**0.008**
Plantar spur base, mean (SD)	5.49 (2.1)	7.01 (2.5)	**0.002**
Plantar spur mid-segment, mean (SD)	2.97 (1.32)	3.6 (1.6)	**0.045**
Plantar spur length, mean (SD)	4.2 (2.1)	5.9 (2.7)	**0.003**
Achilles spur, n (%)	69 (%53.9)	23 (%57.5)	0.24
Calcification in the achilles spur, n (%)	62 (%48.4)	23 (%57.5)	**0.08**
Erosion in the achilles spur, n (%)	10 (%7.8)	1 (%2.5)	0.12
Proliferation on the calcanela body, n (%)	51 (%39.8)	10 (%25)	0.237
Anterior ankle spur, n (%)	5 (%3.9)	1 (%2.5)	0.76
Posterior ankle spur, n (%)	9 (%7)	6 (%15)	0.09
Tarsal bone spur, n (%)	60 (%46.9)	15 (%37.5)	0.63
Left			
Plantar spur, n (%)	98 (%76.6)	37 (%92.5)	**0.043**
Fluffy plantar spur, n (%)	35 (%27.3)	2 (%5)	**0.002**
Erosion in the plantar spur, n (%)	16 (%12.5)	1 (%2.5)	**0.013**
Plantar spur base, mean (SD)	5.35 (2.1)	6.5 (2.2)	**0.006**
Plantar spur mid-segment, mean (SD)	2.98 (1.2)	3.3 (1.2)	0.055
Plantar spur length, mean (SD)	4.5 (2.2)	5.7 (2.7)	**0.011**
Achilles spur, n (%)	73 (%57)	23 (%57.5)	0.88
Calcification in the achilles spur, n (%)	63 (%49.2)	26 (%65)	0.13
Erosion in the achilles spur, n (%)	5 (%3.9)	1 (%2.5)	0.33
Proliferation on the calcanela body, n (%)	57 (%44.5)	15 (%37.5)	0.36
Anterior ankle spur, n (%)	5 (%3.9)	1 (%2.5)	0.65
Posterior ankle spur, n (%)	16 (%12.5)	7 (%17.5)	0.46
Tarsal bone spur, n (%)	59 (%46.1)	22 (%55)	0.406

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Disclosure of Interests: None Declared.
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AB0992 **THE POTENTIAL IMPACT OF HLA-B27 AND HLA-B51 HAPLOTYPE ON PATTERNS OF NON-INFECTIOUS UVEITIS**

Keywords: Spondyloarthritis, Behcet's disease, Uveitis

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Background: Non-infectious uveitis (NIU) include diseases characterized by the inflammation of the vascular tunica of the eye that can cause significant ocular impairment up to blindness, and systemic inflammatory rheumatic diseases (RDs) represent one of their major causes [1]. NIU can be widely heterogeneous in terms of course, laterality, and anatomical involvement, while their clinical presentation may be influenced by associated RDs and certain HLA haplotypes [2].
Objectives: To explore the potential impact of HLA-B27 and HLA-B51 haplotypes on clinical presentation of NIU from patients who were referred to a 3rd level Rheumatologic Clinic in Italy.
Methods: A cross-sectional study was conducted. Selection criteria consisted of having a diagnosis of NIU in an age of onset ≥ 18 years old regardless of etiology among patients who were admitted to the 3rd level Rheumatologic Clinic at "Tor Vergata" University Hospital (Rome, Italy) between January 2018 and October 2022. Data were collected from medical records: age of NIU onset, recurrence and anatomic patterns of affected eyes according to the Standardization of Uveitis Nomenclature (SUN) working group, HLA-B27 and HLA-B51 positivity, and associated RDs were analyzed.
Results: Among the NIU cohort (n= 144), 76 of them underwent HLA-B haplotype typing: 26 (34.2%) showed HLA-B27 positivity while 16 HLA-B51 positivity (21.1%), without a gender difference. Patients HLA-B27(+) had more frequently anterior NIU (AU, 88.5% vs 60%, p=0.01), acute course (69.2 vs 44%, p=0.03), and unilateral involvement (69.2% vs 42%, p=0.02) than patients HLA-B27(-) (Figure 1). HLA-B27(+)-NIU had a significantly prevalent diagnosis of axial-spondylarthritis (ax-SpA, 53.8% vs 6%, p<0.00001) than HLA-B27(-)-NIU. Differently, patients with HLA-B51(+) had mostly posterior NIU (PU, 68.8% vs 16.7%, p<0.00005), recurrent/chronic course (68.8% vs 40%, p=0.04), and bilateral involvement (81.3% vs 33.3%, p=0.0005) than patients HLA-B51(-) (Figure 1). A diagnosis of Behçet's Disease (BD) was performed more frequently in HLA-B51(+) than in HLA-B51(-) patients (75% vs 6.7%, p<0.00001). The age of NIU onset was significantly younger in HLA-B51(+) than in HLA-B51(-) (34.1±13.8 vs 41.1±13.2 yo, p=0.003), while there was no statistically significant difference in age of NIU onset between HLA-B27(+) and HLA-B27(-) (38.38±13.7 yo vs 40.49±13.5 yo. p>0.05).
Conclusion: Our population-based findings describe how HLA-B27 and HLA-B51 haplotypes can impact NIU patterns and suggest a relevant role of an early HLA typing study of NIU patients for the definition of targeted diagnostic and therapeutic strategies.

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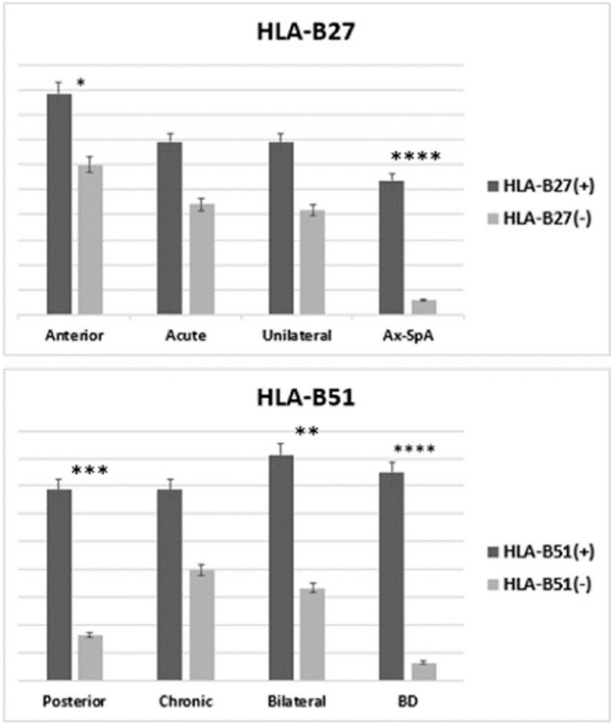


Figure 1. Ax-Spa, axial-spondyloarthritis; BD, Behçet Disease* p<0.01; **p<0.001; *** p<0.0001; ****p<0.00001

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0993 **CONTROL OF CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH SPONDYLOARTHROPATHIES VERSUS RHEUMATOID ARTHRITIS**

Keywords: Cardiovascular disease, Rheumatoid arthritis, Quality of care

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Background: It has been reported that management of cardiovascular (CV) risk factors is suboptimal in patients with rheumatoid arthritis (RA). Whether this also applies to psoriatic arthritis (PsA) or ankylosing spondylitis (AS) patients is unknown.
Objectives: The main objective of this study was to compare control of CV risk factors among disease groups.
Methods: Information on CV risk factors was collected in consecutive adult patients from rheumatology clinic, with RA, PsA or AS. Hypertension (HTN) was defined as systolic blood pressure (BP) ≥140 mmHg, diastolic BP ≥ 90 mmHg

and/or antihypertensive treatment, hypercholesterolemia as LDL-cholesterol ≥ 100 mg/L and/or lipid-lowering treatment. Treatment goals were defined according to European Society of Cardiology and EULAR guidelines.

Results: We included 520 patients (54% women; 46% RA, 22% PsA, 32% AS). Mean age and disease duration were 52.1±14.1 and 11.0±10.6 years, respectively. Out of 520 patients, 203 (39%) had HTN, among whom 140 (69%) were treated and 86 (42%) were controlled; 293 (56%) had HC, among whom 88 (30%) were treated and 51 (17%) were controlled; 30 (6%) had type 2 diabetes, among whom 18 (60%) were controlled. Current smoking was present in 100 patients (19%), obesity in 136 patients (26%) and increased waist circumference in 192 patients (37%). Compared to RA patients, patients with spondyloarthropathies were less often in remission (40% vs. 54%, p<0.005). Furthermore, patients with spondyloarthropathies differed from RA patients by a lower proportion of treated (56% vs. 84%, p<0.001) and treated-to-target (24% vs. 64% p<0.001) HTN, a higher proportion of active smokers (28% vs. 12%, p<0.01), and lower physical activity (29% vs. 46%, p<0.001). Control of LDL-cholesterol was poor in both groups (17% vs.18%, p=0.95). No significant difference between groups was found for diabetes, overweight and obesity.

Conclusion: Compared to patients with RA, patients with spondyloarthropathies were less well controlled both for disease activity and CV risk factors. Furthermore, lipid control was poor in both groups. If confirmed in a multicentre cohort, these results may help orienting CV prevention strategies and increasing awareness both in physicians and patients, with emphasis on spondyloarthropathies.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB0994 HOW SPONDYLOARTHRITIS PROFILE HAS EVOLVED OVERTIME: RESULTS FROM GESPA COLOMBIAN COHORT

Keywords: Geographical differences, Spondyloarthritis, Enthesitis

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Background: Over the last two decades, our knowledge of spondyloarthritis (SpA) has been improved. The awareness of this disease within the medical community and the implementation of advances in clinical practice are unclear, especially in some geographical regions less well represented in research studies.

Objectives: The aim of our study was to evaluate the changes overtime in disease profile in patients with SpA from a Colombian cohort.

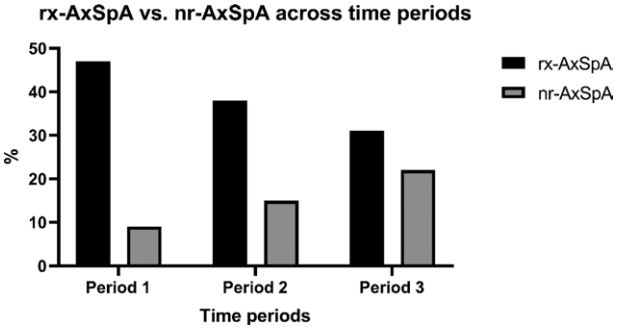
Methods: Data from 471 patients recruited in a prospective Colombian cohort of Spondyloarthritis patients (diagnosed according to rheumatologist), with registries from 90' to the date was analyzed. Three time periods were stablished for the analysis, the first period from the first registry until October 10, 2003; the second period from October 10, 2003 to October 26, 2010; and the third period from October 26, 2010 to December 31, 2021. The patients were reclassified according to ASAS classification using the information available, and judgment from a group of four expert rheumatologists.

Results: 471 patients were included in the study, period 1 (n = 158), period 2 (n = 150) and period 3 (n = 163). There were no differences in sex distribution across three periods. Time to diagnosis was shorter in period 1 than 3 (table 1). The frequency of r-AxSpA diagnosis was proportionally higher in period 1 (47.5%), than period 2 (38.2%), and 3 (31.3%), P = 0.013. For another hand, the frequency of nr-AxSpA diagnosis was lower in the period 1 (9.5%) than period 2 (15.1%), and 3 (22.1%) (view graphic). The frequency of peripheral SpA diagnosis was similar across the three periods (38% vs. 39.5% vs. 37.4%, for periods 1, 2 and 3 respectively, P = 0.8). The presence of dactylitis at physical examination was most common in the first period (10.8%) than the last two periods (3.3% and 3.7%), P = 0.007. There were no differences in frequency of dactylitis, arthritis or uveitis. There were no statistically significant differences in frequency of HLA-B27 (42.4% vs. 44.8% vs. 48.6%, for periods 1, 2 and 3, respectively, P = 0.2) or HLA-B15 (14.4% vs. 8.2% vs. 15%, for periods 1, 2 and 3, respectively, P = 0.2) across the three periods. The metrology analysis showed higher physical limitation in the first period (thoracic expansion < 2.5 cms and modified Schober < 5 cms) than in the last two period (view table 1). The history of psoriasis in SpA patients was higher in period 1 (7.6%) than period 2 (2.6%), and 3 (2.5%), P = 0.036. Infections preceding SpA symptoms onset were most frequent in period 1 (32.9%) than period 2 (29.6%) and 3 (16.6%), P = 0.002.

Conclusion: The profile of patients with SpA has evolved over time in Colombia. While the frequency of peripheral SpA has remained unchanged over time, the incidence of non-radiographic axial forms has increased over time. Furthermore, functional limitation in SpA, infections preceding symptoms, and dactylitis are less common than 20 years ago. These results highlight the impact of advances in rheumatology and the awareness of the medical community about this disease in Colombia, allowing an earlier diagnosis or the diagnosis of less evident forms of SpA.

Table 1.

Variable	< November 11, 2003	November 11, 2003 – October 26, 2010	> October 26, 2010	P value
Total	158	150	163	
Female	57 (36.1%)	47 (30.9%)	59 (36.2%)	0.5
Time to diagnosis (months)	12 (3 – 40.5)	18 (3 – 62)	49.5 (9.75 – 122)	0.00
ASAS axial	91 (57.6%)	82 (53.9%)	85 (52.1%)	0.4
ASAS peripheral	60 (38%)	60 (39.5%)	61 (37.4%)	0.4
HLA-B27	59 (42.4%)	60 (44.8%)	68 (486%)	0.22
HLA-B15	20 (14.4%)	11 (8.2%)	21 (15%)	0.22
VAS spinal pain	6 (3 - 8)	5 (3 - 8)	6 (2 - 8)	0.86
Disease activity by patient	6.5 (4.5 - 8.5)	6 (5 - 8)	6 (4- 8)	0.55
Occiput to wall distance	0 (0 - 0)	0 (0 - 0)	1 (0 - 3)	0.00
Right lateral flexion test	10 (3 - 19.75)	15 (10.38 - 19)	14 (10 - 17)	0.01
Left lateral flexion test	13 (3 - 20)	15-75 (11 - 18.25)	14 (11 - 17)	0.05
Limited thoracic expansion (< 2.5 cms)	28 (17.7%)	15 (10.5%)	16 (9.9%)	0.02
Limited lumbar Schober (< 5)	103 (71%)	90 (62.1%)	85 (53.1%)	0.01



Graphic 1. Three periods P value < 0.05
rx-axSpA: radiographic axial Spondyloarthritis; nr-AxSpA: non-radiographic axial Spondyloarthritis.

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Disclosure of Interests: None Declared.

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AB0995 ASSESSMENT OF MATRIX METALLOPROTEINASE-3 IN SPONDYLOARTHRITIS: CORRELATION WITH DISEASE ACTIVITY

Keywords: Biomarkers, Patient reported outcomes, Spondyloarthritis

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Background: Several studies showed that the activity of proteinases, including matrix metalloproteinases (MMPs), is increased in inflamed tissue, via the overproduction of pro-inflammatory cytokines, in spondyloarthritis (SpA) [1].

Objectives: Our study aimed to assess the correlation between serum levels of MMP-3 and disease activity in SpA.
Methods: We conducted a cross-sectional study including patients with SpA, diagnosed according to ASAS 2009 criteria. ELISA technique was used to measure MMP-3 serum levels. CRP and ESR were also measured. Disease activity was assessed with Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP). Pearson correlation coefficient was calculated.
Results: We included 82 patients. The mean age was 45.32 ± 13.41 years [20-80]. Male to female ratio was 3.82. The mean disease duration was 7.57 ± 7.79 years. Radiographic axial SpA (r-AxSpA) and psoriatic arthritis (PsA) were noted in 65.9% (n=54) and 34.1% (n=28) of cases, respectively. The mean MMP-3 serum levels were 64.14 + 187.31 ng/mL [1.75 – 1237.36]. The mean CRP and ESR levels were 20.64 + 24.52 mg/l and 35.46 + 31.69 mm, respectively. The mean BASDAI and ASDAS-CRP were 3.26 ± 1.89 and 2.98 ± 1.45, respectively. MMP-3 serum levels correlated significantly with inflammatory biomarkers: CRP (r=0.314, **p=0.004**) and ESR (r=0.291, **p=0.013**). A correlation was also found with ASDAS-CRP (r=0.245, **p=0.028**). However, no correlation was found between MMP-3 serum levels and BASDAI (r=0.204, p=0.070).
Conclusion: Our results showed that MMP-3 serum levels correlate significantly with inflammatory biomarkers (CRP and ESR) and with ASDAS-CRP. MMP-3 seems to be a promising biomarker for disease activity in SpA.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB0996 PERCEIVED EFFECTS OF HEALTH STATUS ON SEXUAL ACTIVITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS OVER A 5-YEAR PERIOD

Keywords: Spondyloarthritis, Patient reported outcomes, Outcome measures

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disorder of the axial skeleton and may involve peripheral joints, entheses and other organs, which may cause pain, fatigue, stiffness, loss of physical function. The persons health status may influence on sexual activity and enjoyment. Sexual activity is one of the key functions in human beings and affects both quality of life (QOL) and sexual QOL.
Objectives: To explore perceived effects of health status on sexual activity in patients with axSpA over a 5-year period.
Methods: Patients with axSpA were consecutively recruited from two public outpatient rheumatology clinics in Southern Norway (Martina Hansens Hospital (MHH), and Sørlandet Hospital (SSHF)). A broad specter of data was collected which included: demographic (age, weight, employment, education, married or cohabiting and if they had a partner to have sex with), disease activity and damage (MASES, CRP, BASMI, 68 tender and 66 swollen joints), current medication (NSAID, CsDMARD and bDMARD) and comorbidities (yes/no). A summed score was generated to reflect overall co-morbidity. Quality of life were measured by 15D, which also included a question on perceived influence of health status on sexual activity. Item 15 in the 15D questionnaire was used to study the effect of health status on sexual activity. with the following response options: My state of health: has no adverse effect on my sexual activity, slight effect, considerable effect, makes sexual activity almost impossible, makes sexual activity impossible to analyze the effects of health on sexual activity, we dichotomized the five responses to item 15 in the 15D instrument, which were related to sexual activity. Responses 1 and 2 were grouped into “no/little effects” and the other three categories were grouped into “large effects”. The same data collection performed at baseline was also performed at the five-year follow-up.
Results: A total of 245 patients (168 men and 77 women) with (At baseline the mean age was 46 years (SD ± 11.9) mean disease duration 13.9 years (SD ± 11.4). At 5-years follow-up 44 (18%) patients reported their health status to have large effects on their sexual activity, while 200 (82%) reported no/little effect. The same pattern was seen at baseline. However, 24 patients changed from reporting large effect at baseline to no/little effect at 5-year follow-up, while 26 patients changed from no/little effect to large effect. When comparing patients reporting their health status to have no/little effect on sexual activity versus the one with large effect on sexual activity, the same pattern of differences was seen at both baseline and 5-year follow-up. However, the differences seemed to be more prominent at 5-year follow-up. Focusing on 5-years follow-up differences; patients reporting their health status to have a large effect on sexual activity were older (54 (10) years vs 50 (11) years, p=0.014), fewer were employed (74% vs 47%, p<0.001), exercised less (77% vs 92%, p=0.003), had more co-morbidities (1.5 (1.3) vs 0.8 (1.1), p=0.002), higher CRP (10.2 (19.1) vs 4.6 (7.0), p=0.002), higher BASDAI (4.7 (2.2) vs 2.5 (2.0), p<0.001) higher BASFI (3.9 (2.2) vs 2.0 (2.0), p<0.001), higher BAS-G (5.3 (2.6) vs 2.6 (2.4), p<0.001 and higher HAQ (0.81 (0.45) vs 0.37 (0.4), p<0.001).
Conclusion: Approximately 20% of axSpA patients reported their health status to have a large negative effect on their sexual activity both at baseline and 5-year follow-up. From baseline to 5-year follow-up there has been an increase in comorbidities, and the increase has been larger in patients reporting the disease to have a large negative effect on sexual activity.
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Disclosure of Interests: None Declared.
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AB0997 THE RADIOGRAPHIC ENTHESIS INDEX (REI) FACILITATES THE DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS: RESULTS FROM GESPA COLOMBIAN COHORT

Keywords: Enthesitis, Diagnostic tests, Spondyloarthritis

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Background: Spondyloarthritis (SpA) refers to a group of related but phenotypically distinct disorders: psoriatic arthritis, arthritis related to inflammatory bowel disease, reactive arthritis, a subgroup of juvenile idiopathic arthritis, and ankylosing spondylitis. [1]. Patients with SpA can be distinguished, according to their clinical presentation, as axial SpA or peripheral SpA patients [2]. Each of these diseases is characterized by distinct clinical and laboratory characteristics, and each features a wide spectrum of clinical presentations, facts that highlight the dynamism and progression of SpA.
Objectives: To evaluate the diagnostic performance of radiography in the evaluation of enthesitis in the pelvis and its usefulness in the diagnosis of SpA.
Methods: This study was a historical cohort study from 2005 to 2020. Eligible patients were adults (≥18 years of age) with SpA according to the Assessment of Spondyloarthritis international Society (ASAS) criteria, and the control group were patients with chronic lumbar pain (more than three months) with non-inflammatory characteristics, without meeting ASAS criteria for SPA, and who assisted neurosurgery and rheumatology consultations in the Hospital Militar Central, Bogotá DC. The pelvic radiography had an anteroposterior view with gut preparation with laxative, the coccyx and pubic symphysis were aligned with the midline, and the distance between the tip of the coccyx and the upper limit of the coccyx was more than 2.5 cm. We used three zones of tendinous insertion in the pelvis. Zone one (ZI) is the iliopubic ramus; zone two (ZII) is the pubic symphysis; zone three (ZIII) is the ischiopubic ramus. In addition, a grading system was created from zero to four (grade 0: normal; grade I: periostial wishkering and/or osteopenia; grade II: periostial wishkering, osteopenia, sclerosis and erosions; and grade III: grade II findings in addition to the presence of ripple or waving patterns > 2 mm outside the cortex). The scores of each zone of the REI, without discriminating by laterality, were added to give the total REI as a result.
Results: The cohort have 450 patients, we selected 150 patients for the initial evaluation. Eleven (17.19%) were females and fifty-three (82.12%) were males. In the non-SpA, grade 0 was the most frequent in the three zones of REI, while grades II and III were more frequent in the SpA group; those outcomes were statistically significant. Zone III had the highest degree of enthesitis according to the REI classification (63.4%) in the SpA group, with a probability greater than 99% that these findings are related to SpA and not by chance.
Conclusion: Conventional pelvis radiography is still useful for SpA diagnosis, not just for sacroiliac joint and lumbar spine involvement assessment but also for the evaluation of the pelvic enthesis, which gives essential information for the diagnosis of SpA.
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AB0998 DIFFERENCES IN PSYCHOLOGICAL BURDEN AND IN QUALITY OF LIFE MEASURES BETWEEN GENDERS IN SPONDYLOARTHRITIS PATIENTS-ANALYSIS OF A MONOCENTRIC COHORT

Keywords: Gender/diversity issues, Quality of life, Spondyloarthritis

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Background: Spondyloarthropathies (SpA) are chronic inflammatory arthritis, characterized by both peripheral and axial skeletal involvement and some typical extra-articular marks; they tend to associate with several comorbidities and can increase the risk of an impaired quality of life (QoL). Already published data show SpA expression differs based on gender; in particular, women are at higher risk of a more pronounced peripheral disease activity and show a greater burden of the disease, thus having worse values of Patient Reported Outcomes (PROs). It is well known that a compromission in physical functioning and psychological sphere may compromise productivity of patients and subsequently increase health costs.
Objectives: The aim of our study was to assess the differences between male and female sex in the prevalence of mood disorders, fatigue and parameters of QoL in a monocentric cohort of patients with SpA.
Methods: Adult patients diagnosed with Psoriatic Arthritis (PsA) and Ankylosing Spondylitis (AS) according to the CASPAR (ClASsification criteria for Psoriatic Arthritis) and to Assessment of SpondyloArthritis international Society (ASAS) criteria, regularly followed at the SpA clinic of our unit, were consecutively enrolled from April to December 2022. Epidemiologic, clinic and clinimetric data were collected. Each patient filled in the following Patient Reported Outcomes: Hospital Anxiety and Depression Scale (HADS), FACIT-Fatigue (FACIT-F) and SHORT-FORM 36 (SF-36). Intergroups comparisons were assessed by using Chi-square, t-test and ANOVA. P values <0.05 were considered significant.
Results: A total of 200 patients were enrolled; 85 (42.5%) were women, with a mean age of 56.84±12.22 years and a mean disease duration of 12.91±10.3 years. One hundred and thirty-five patients (67.5%) had a diagnosis of PsA (M/F 79/56), while 59 (29.5%) had a diagnosis of AS (M/F 36/23) and 6 (3%) of Enteropathic Arthritis (M/F 0/6). Women showed worse FACIT-F values than men, (mean 35.20 vs 40.23, p-value 0.002) and a greater impairment of QoL expressed by statistically significant lower values of almost all the domains of SF-36 (exception for Global Health). Moreover, the values of HADS resulted higher in female sex both for the anxiety and depression domains (p-value <0.001 and 0.039 respectively).
Conclusion: The analysis of our cohort confirmed that women affected by SpA suffer from anxiety and depression more often than men, develop a higher level of fatigue and have an overall worse QoL in both psychological and physical domains. These data should sensitize rheumatologists in the assessment of this subgroup of patients. The clinician should not only focus on the disease activity evaluation and therapy or in managing of the comorbidities, but also on the psychological and functional status of the patients, developing strategies able to avoid or delay the onset of their impairment in daily life and to optimize with specific therapies, rehabilitation or psychological support their compromission, when already established. This approach could finally improve the social burden and health cost of women with SpA.

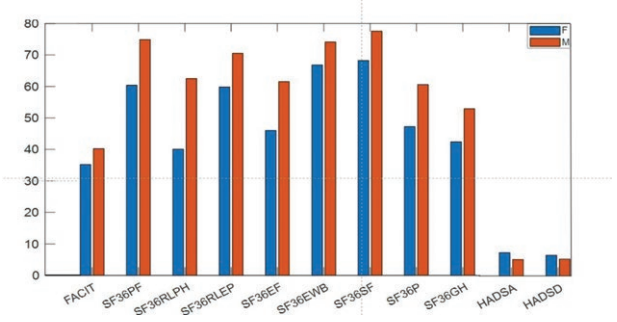


Figure 1.

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AB0999 RELIABILITY OF INFLAMMATORY BACK PAIN CRITERIA AS A TOOL FOR DIFFERENTIATION BETWEEN INFLAMMATORY AND MECHANICAL BACK PAIN AMONG EGYPTIAN PATIENTS

Keywords: Patient reported outcomes, Pain, Spondyloarthritis

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Background: Inflammatory back pain (IBP) is a key symptom of axial spondyloarthritis (AxSpA). Most items of the IBP criteria are subjective and liable to change depending on the patient's expression. (1)
Objectives: Assessment of the sensitivity, specificity, and reliability of IBP parameters and sets in patients with AxSpA.
Methods: This case-control study was conducted on 2 groups: the first group included 103 patients with AxSpA, and the other group included 103 patients with chronic mechanical back pain. A standardized questionnaire, addressing all items included in Calin, Berlin, and ASAS criteria sets, was applied by 2 rheumatologists (one senior and one junior) to both groups. The sensitivity, specificity, and reliability of the 3 sets and individual parameters were assessed.
Results: Morning stiffness > 30 minutes was the most specific parameter (81%), while the insidious onset was the most sensitive (98%). Calin set was the most sensitive set (88.1%), but it had the least specificity (60%). Adding the item of Morning stiffness > 30 minutes to Calin criteria resulted in improving the specificity of Calin criteria to 81%. Reliability of all parameters and the 3 sets showed moderate agreement (kappa 0.422–0.588) except for Morning stiffness > 30 minutes which showed good agreement (kappa 0.736) and night pain which showed fair agreement (kappa 0.388) (Table 1).

Table 1. Reliability of IBP parameters and criteria sets

IBP parameter	Kappa Agreement
Age of onset less than 40 years	1.000
Insidious onset	0.581
Morning stiffness	0.588
Morning stiffness more than 30 min	0.736
Improvement with exercise	0.566
No improvement with rest	0.422
Improvement with exercise and no improvement with rest	0.508
Night pain	0.388
Awakening in night due to pain	0.553
Buttock pain	0.504
Global Evaluation	0.951
Criteria	
Calin	0.556
Berlin	0.496
ASAS	0.455
modified. Calin	0.694

Conclusion: Most IBP parameters and criteria have moderate reliability and average sensitivity and specificity. There may be a need for an objective tool to differentiate between inflammatory and mechanical back pain.

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AB1000

ACHIEVEMENT OF INCREASINGLY STRINGENT CLINICAL RESPONSE CRITERIA AND LOWER LEVELS OF DISEASE ACTIVITY WAS ASSOCIATED WITH GREATER IMPROVEMENTS IN PHYSICAL FUNCTION AND HRQOL IN PATIENTS WITH ACTIVE AXIAL SPONDYLOARTHRITIS: 52-WEEK RESULTS FROM TWO PHASE 3 STUDIES ON BIMEKIZUMAB

Keywords: Quality of life, Patient reported outcomes, Spondyloarthritis

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Background: Patients with axial spondyloarthritis (axSpA) can experience a significant burden due to the pain, fatigue and impaired physical function resulting from the disease.[1]

Objectives: To assess how achievement of increasingly stringent clinical response criteria and lower disease activity levels translates into improvements in physical function, sleep and health-related quality of life (HRQoL) in patients with axSpA.

Methods: This post hoc analysis reports results from the phase 3 studies, BE MOBILE 1 (NCT03928704; non-radiographic axSpA [nr-axSpA]) and BE MOBILE 2 (NCT03928743; radiographic axSpA [r-axSpA], i.e., ankylosing spondylitis[2]) at Week (Wk) 52. In BE MOBILE 1, patients met the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA and had elevated C-reactive protein and/or MRI sacroiliitis. In BE MOBILE 2, patients had radiographic sacroiliitis, fulfilling modified New York criteria. All patients who completed Wk 52 and reached specified clinical response criteria (**ASAS**: ASAS20 not reached [<ASAS20], ASAS20 reached but not ASAS40 [ASAS20–<ASAS40], ASAS40 reached [ASAS40]; **ASAS-PR**: Yes, No; **BASDAI50**: Yes, No), **ASDAS** (≥2.1, ≥1.3–<2.1, <1.3) or **ASDAS responses** (major improvement [change from baseline ≥2.0], clinically important improvement [change ≥1.1 but <2.0], non-response [change <1.1]) were pooled regardless of their original treatment arm (placebo then BKZ from Wk 16 or continuous BKZ 160 mg Q4W; all subcutaneous BKZ), by study. Associations between achievement of these clinical responses and improvements in patient-reported measures of physical function (**BASFI**; **SF-36 PCS**), sleep (**MOS Sleep-R Index;** 12 item measure, higher scores reflect more of the attribute implied by the scale) and HRQoL (**ASQoL**) were assessed. Observed case data are reported.

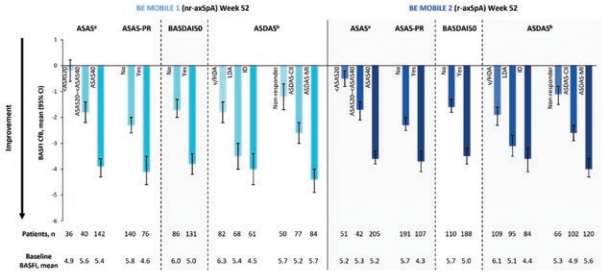
Results: Most patients completed Wk 52 (nr-axSpA: 220/254 [86.6%]; r-axSpA: 298/332 [89.8%]). Baseline demographics and disease characteristics were generally similar between nr-axSpA and r-axSpA patients, aside from gender, HLA-B27 status, symptom duration and time since first diagnosis, indicating similar burden of symptom severity, reduced physical function and HRQoL. Across studies, patients achieving increasingly stringent ASAS responses presented sequentially greater mean (95% confidence interval) improvements from baseline in BASFI (**Figure 1**) and SF-36 PCS score (nr-axSpA: <ASAS20: 5.1 [2.5, 7.7], ASAS20–<ASAS40: 9.5 [7.1, 11.8], ASAS40: 14.6 [13.1, 16.2]; r-axSpA: 5.9 [4.1, 7.7], 8.4 [6.6, 10.2], 14.6 [13.3, 15.9]). Achievement of higher ASAS response was also associated with sequentially greater mean improvements from baseline in MOS Sleep-R index scores (nr-axSpA: <ASAS20: 3.6 [1.3, 6.0], ASAS20–<ASAS40: 3.9 [1.6, 6.2], ASAS40: 9.0 [7.4, 10.6]; r-axSpA: 0.7 [−1.2, 2.6], 4.9 [2.5, 7.3], 8.2 [7.2, 9.3]) and ASQoL (nr-axSpA: <ASAS20: −2.2 [−3.7, −0.7], ASAS20–<ASAS40: −4.3 [−5.5, −3.2], ASAS40: −7.2 [−7.9, −6.5]; r-axSpA: −2.0 [−3.0, −1.1], −4.3 [−5.1, −3.4], −6.9 [−7.5, −6.3]). Similar sequential improvements from baseline in BASFI, SF-36 PCS, MOS-Sleep R index and ASQoL were observed with achievement of ASAS-PR, BASDAI50, and ASDAS-related outcome measures. Improvements in BASFI, SF-36 PCS, MOS Sleep-R index and ASQoL were of similar amplitude between nr-axSpA and r-axSpA patients.

Conclusion: Patients with nr-axSpA and r-axSpA who achieved increasingly stringent clinical response criteria and lower levels of disease activity at Wk 52 reported greater improvements in physical function, sleep function and HRQoL. Similar amplitudes of improvement for each response level were observed across the axSpA disease spectrum.

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Figure. Association between ASAS response criteria, ASAS -PR, BASDAI response, ASDAS status and ASDAS response at Wk 52 and mean change from baseline in physical function (BASFI) [OC]



Data reported as observed case. Categories are mutually exclusive. BASFI is a component of ASAS response criteria. [a]Patients were stratified into groups based on ASAS clinical response criteria: those who did not achieve ASAS20 (<20), those who achieved ASAS20 but not ASAS4 0 (20–<40) and those who achieved ASAS40 (≥40); [b]Levels of ASDAS disease activity were defined as very/high disease activity (v/HDA; ≥ 2 .1), low disease activity (LDA; ≥1.3–<2.1), inactive disease (ID; <1.3). Levels of ASDAS response were defined as ASDAS -MI (change from baseline [CfB] ≥2.0), ASDAS-CII (CfB ≥1.1 but <2.0) and non-response (CfB <1.1).

Abbreviations: ASAS: Assessment of SpondyloArthritis International Society; ASAS-PR: ASAS partial remission; ASDAS: Ankylosing Spondylitis Disease Activity Index; ASDAS-CII: ASDAS clinically important improvement; ASDAS-MI: ASDAS major improvement; ASQoL: Ankylosing Spondylitis Quality of Life; axSpA: axial spondyloarthritis; BASDAI50: Bath Ankylosing Spondylitis Disease Activity Index 50% improvement; BASFI: Bath Ankylosing Spondylitis Functional Index; BKZ: bimekizumab; CfB: change from baseline; CI: confidence interval; HDA: high disease activity; HLA-B27: human leukocyte antigen B27; HRQoL: health-related quality of life; ID: inactive disease; LDA: low disease activity; MOS: medical outcomes study; n: number; nr-axSpA: non-radiographic axial spondyloarthritis; PCS: physical component summary; Q4W: every four weeks; r-axSpA: radiographic axial spondyloarthritis; SF-36: short form -36; v: very; Wk: week.

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Disclosure of Interests: Marina Magrey Consultant of: AbbVie, Eli Lilly, Novartis, Pfizer and UCB Pharma, Grant/research support from: AbbVie and UCB Pharma, Atul Deodhar Speakers bureau: Janssen, Novartis and Pfizer, Consultant of: AbbVie, Amgen, Aurinia, BMS, Eli Lilly, Janssen, MoonLake, Novartis, Pfizer and UCB Pharma, Grant/research support from: AbbVie, BMS, Celgene, Eli Lilly, MoonLake, Novartis, Pfizer and UCB Pharma, Philip J Mease Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer and UCB Pharma, Consultant of: AbbVie, Acelyrin, Aclaris, Amgen, BMS, Boehringer Ingelheim, Eli Lilly, Galapagos, Gilead, GSK, Janssen, MoonLake, Novartis, Pfizer, Sun Pharma and UCB Pharma, Grant/research support from: AbbVie, Amgen, BMS, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Sun Pharma and UCB Pharma, Victoria Navarro-Compán Speakers bureau: AbbVie, Eli Lilly, Janssen, MSD, Novartis, Pfizer and UCB Pharma, Consultant of: AbbVie, Eli Lilly, Galapagos, Moonlake, MSD, Novartis, Pfizer and UCB Pharma, Grant/research support from: AbbVie and Novartis, Sofia Ramiro Consultant of: AbbVie, Eli Lilly, Novartis, Pfizer, Sanofi and UCB Pharma, Grant/research support from: AbbVie, Galapagos, MSD, Novartis, Pfizer, UCB Pharma, Martin Rudwaleit Speakers bureau: AbbVie, BMS, Boehringer Ingelheim, Chugai, Eli Lilly, Janssen, Novartis, Pfizer and UCB Pharma, Paid instructor for: Janssen, Novartis and UCB Pharma, Consultant of: AbbVie, Eli Lilly, Novartis and UCB Pharma, Christine de la Loge Consultant of: UCB Pharma, Carmen Fleurinck Employee of: UCB Pharma, Vanessa Taieb Employee of: UCB Pharma, Michael Morup Employee of: UCB Pharma, Marga Oortgiesen Shareholder of: UCB Pharma, Employee of: UCB Pharma, Jonathan Kay Consultant of: Alvotech Swiss AG, Boehringer Ingelheim GmbH, Organon, Ridgeline Discovery, Samsung Bioepis, Sandoz Inc., Scipher Medicine and UCB Pharma, Grant/research support from: Gilead and Novartis paid to institution.

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AB1001

PROPOSAL OF SIMPLIFIED CT SYNDESMOPHYTE SCORE (SCTSS) AND COMPARISON WITH CTSS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

Keywords: Bone diseases, Spondyloarthritis, Imaging

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Background: The CT syndesmophyte score (CTSS) can evaluate spinal progression more precisely than mSASSS in ankylosing spondylitis (AS); however, it is complex and time consuming.

Objectives: Here, we propose a simplified CTSS (sCTSS) for measuring spinal structural changes in AS.

Methods: Patients with AS were recruited from a single tertiary hospital. Baseline and 2-year follow-up whole spine CT images were used to calculate CTSS and sCTSS. The sCTSS used the anterior and posterior vertebral corners, and ranged 0–184. Intraclass correlation coefficients (ICC) were calculated, as well as the smallest detectable changes.

Results: Fifty AS patients were included. For reader 1, the mean sCTSS at baseline and 2-year follow-up were 11.7 ± 14.6 and 15.8 ± 16.1, whereas those for

reader 2 were 12.0 ± 12.5 and 15.8 ± 15.7, respectively. The ICCs for CTSS at baseline and at 2-year follow-up were 0.97 (95% confidence interval [CI] 0.96–0.99) and 0.98 (0.97–0.99), respectively, and that for changes over the 2 years was 0.48 (95% CI 0.23–0.67). For sCTSS, the ICCs were 0.96 (95% CI 0.92–0.97), 0.97 (95% CI 0.94–0.98), and 0.58 (95% CI 0.36–0.74), respectively. Detection rates for syndesmophyte progression were comparable between CTSS and sCTSS. The detection rate for syndesmophytes on only lateral side was 13.2 and 11.4%, and 11.4 and 15.2% at baseline and 2-year follow-up (reader 1 and 2).

Conclusion: sCTSS and CTSS showed similar detection rates for syndesmophyte progression. sCTSS may be a reliable method for evaluating spinal structural damage in AS.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.1068

AB1002 LONGER DIAGNOSTIC DELAY, SEVERE FATIGUE AND LESS USE OF TNF-INHIBITORS ARE ASSOCIATED WITH UNACCEPTABLE AXIAL PAIN IN 354 SWEDISH PATIENTS WITH ANKYLOSING SPONDYLITIS

Keywords: Spondyloarthritis, Pain

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Background: Pain has been shown to be the most important consequence of the disease in affecting health in patients with axial spondyloarthritis[1].

Objectives: To assess factors associated with unacceptable axial pain in patients with long-standing ankylosing spondylitis (AS) overall and by sex.

Methods: Patients with AS (modified NY-criteria) from two geographically separated regions in Sweden were included in this cross-sectional, observational study. Primary outcome was axial pain (question number 2 from Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)) dichotomised in VAS < or ≥ 4 based on patient unacceptable pain[2]. Independent variables were selected based on previous knowledge and hypotheses of factors associated with pain. Information was collected from questionnaires (demographics, lifestyle habits, fatigue (BASDAI question number 1), symptoms of depression (from EQ-5D), medications), calculation of body mass index (BMI), blood sample (C-reactive protein (CRP)), and lateral spinal radiographs (assessment of spinal new bone formation with modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS)). Univariate and multivariable logistic regression analyses (dependent variable VAS axial pain ≥ 4) were used overall and stratified by sex. Variables with univariate *p*-values ≤ 0.1 were included in the multivariable model if not too highly correlated.

Results: In total, 354 patients were included, 62 % men, mean (SD) age 52 (13) years, symptom duration 27 (13) years and delay in diagnosis 9 (8) years. Mean (SD) VAS axial pain was 4.2 (2.6) with no significant difference between men and women (p = 0.30). However, in patients with unacceptable axial pain (VAS ≥ 4), n=177 (50%), significantly higher proportion of women reported unacceptable pain compared to men, 57 % vs 46 %, p = 0.049. In univariate analyses, unacceptable axial pain was associated with longer disease duration, longer delay in diagnosis, more severe fatigue, more symptoms of depression, lower alcohol consumption and less treatment with TNF-inhibitors. There was no association between unacceptable axial pain and age, civil state single, educational level, BMI, smoking status, mSASSS, CRP or use of NSAIDs. In the multivariable analysis, unacceptable axial pain was independently associated with longer delay in diagnosis and more severe fatigue, whereas use of TNF-inhibitor reduced the risk of having unacceptable pain (Figure 1). In the multivariable analyses stratified by sex, the same variables were associated with unacceptable pain in men as in the whole group; OR (95 % CI) for delay in diagnosis 1.08 (1.03 to 1.14), fatigue 2.0 (1.65 to 2.41) and use of TNF-inhibitor 0.23 (0.09 to 0.61). In women, fatigue was the only factor independently associated with unacceptable axial pain, OR (95 % CI) 1.32 (1.12 to 1.56).

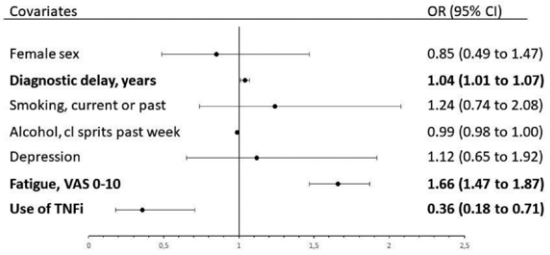
Conclusion: In this cross-sectional study of patients with long-standing AS, 50 % of the patients had unacceptable axial pain. Even though a higher proportion of the women were affected, female sex was not independently associated with unacceptable axial pain. There were some sex-differences. Delay in diagnosis was associated with higher risk, and use of TNF-inhibitor was associated with lower risk of unacceptable axial pain only in men. The sex-difference possibly due to few women using TNF-inhibitors. Fatigue was independently associated with axial pain in both sexes. This study underpins the importance of early diagnosis in AS.

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Figure. Multivariable logistic regression analysis assessing factors associated with unacceptable axial pain in 354 patiens with ankylosing spondylitis



TNFi, tumor necrosis factor inhibitor; VAS, visual analogue scale

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1003 IMPROVED CLINICAL OUTCOMES AND PATIENT ENGAGEMENT THROUGH AN INTEGRATED ELECTRONIC PATIENT REPORTED OUTCOME WITH THE HOSPITAL ELECTRONIC PATIENT RECORD IN SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Patient reported outcomes, Outcome measures

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Background: Patient-reported outcome measures (PROMs) have been at the forefront of the assessment of spondyloarthritis (SpA). With the increasing adoption of electronic health records (EHRs), collecting PROMs electronically (ePROMs) presents an opportunity for advancing patient care in SpA. ePROMs were incorporated into our SpA clinics at the Royal Berkshire Hospital since the start of 2018. Collecting patient data remotely brings the patients' perspective into routine clinical care without delay. Moreover, connection to EHRs have led to a seamless integrated optimised care process.

Objectives: The objective of this programme was to evaluate the clinical effectiveness and practicality of implementing a fully integrated ePROMs into the hospital EHR in real world clinic settings. The interoperability across different information technology (IT) modules was assessed. We also evaluated the interaction with the patients through the assessment of satisfaction and completion rates of ePROMs.

Methods: AxSpA patients meeting the ASAS criteria completed the outcome measures BASDAI, BASFI, Spinal NPRS, and BASG. PsA patients meeting the CASPAR criteria completed patient assessed tender joint, swollen joint, global assessment and PSAID-12. The period of the data collection for this study was January 2021 to December 2022. Patients were sent reminders to complete ePROMs through email or text messaging before each appointment and every 6 months. Ad-hoc scores went sent out according to clinical need. Appointments were expedited or deferred depending on the values and trends in the ePROMS. Time saved in clinic was measured.

Results: There were 1141 patients with AxSpA and PsA who were sent ePROMs over a 2 year period (2021-22). The mean (SD) age for AxSpA patients were 42.7(11.2) and PsA 52 (7.9) years. 536 (47%) patients were on biologics. At baseline, the completion of was 38% (437/1141). At month 12, it was 63% (722/1141) and at month 24, reached 73% (836/1141), Figure 1. Both AxSpA and PsA patients had similar rates of uptake of ePROMs between months 0 and 24 (40% to 72% in AxSpA and 35% to 73% in PsA). At group level, there was a trend to the reduction in mean (SD) ASDAS at months 0, 6, 12, 18 and 24 (3.8±1.2, 3.3±1.1, 3.0±1.5, 2.2±0.9, 1.9±1.0) and BASDAI (4.6±2.7, 4.5±1.9, 3.9±2.4, 3.8.±2.3, 3.6±1.2). In the PsA group, there was also a trend to the reduction in the mean (SD) PSAID-12 level (4.1±1.8, 3.8±0.8, 3.6±1.2, 3.4±1.1, 3.1±1.3). The reduction in ASDAS, BASDAI and PSAID-12 was most evident in patients on biologic treatments. In patients with an ASDAS of < 1.3 or PSAID-12 <2, appointments were moved from 6 to 12 monthly. In this group of

patients, the appointments were also switched from face to face to teleclinics. This resulted in a saving of 280 hours of clinical time. Over 90% of clinician and patient user rated the ePROMs as good to excellent. In patients not completing ePROMS (308/1141, 27%) paper forms were used. Factors for not completing ePROMs include multiple forms, frequency of forms sent, lack of understanding of process, data safety concerns, lack of IT access and patient choice.

Conclusion: The development of a clinician dashboard captured a range of multidimensional ePROMs that was used proactively to support patient management and patient-centric appointment scheduling. Using ePROMs increased the uptake and acceptability of completing patient outcomes. A trend based on ePROMs collated over a period of time was more informative, particularly when considered alongside interventions that were introduced into the clinics such as self-referral to physiotherapy, digital psychological therapy and biologic treatments. This enabled the clinical team use ePROMs as part of remote monitoring to implement patient-initiated follow up (PIFU) and schedule teleconsultations when clinically appropriate. The integrated ePROMS system allows clinical encounters where needed and more individualised care.

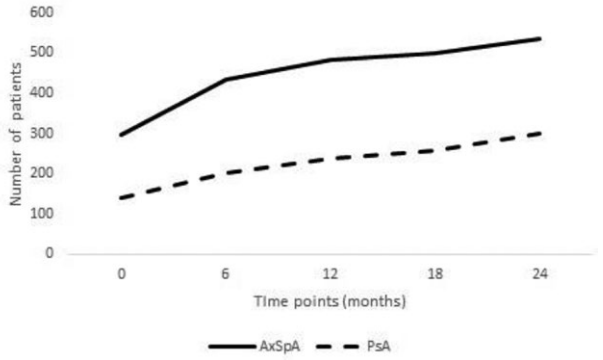


Figure 1. Number of AxSpA and PsA patients completing ePROMs at baseline (0), 6, 12, 18 and 24 months

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Antoni Chan Grant/research support from: A non-promotional grant was received from Novartis for the initial set up of the digital software for this programme, Kathryn Rigler: None declared, Liz Van Rossen: None declare.d.

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AB1004

ACCURACY OF ICD10-AM M45 CODE FOR ANKYLOSING SPONDYLITIS IN A WESTERN AUSTRALIAN HOSPITAL COHORT

Keywords: Descriptive studies, Spondyloarthritis

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Background: Administrative linked health data (ALHD) facilitates epidemiological research of Ankylosing Spondylitis (AS) but best practice requires dataset validation[1]. While ICD10-code M45 is used to identify AS populations internationally it is also used to code "Rheumatoid arthritis of the spine"[2]. Neither background AS nor Rheumatoid arthritis (RA) is captured in ICD coding, unless actively flaring whilst the patient is admitted.

Objectives: To define the accuracy of ICD 10 Australian Modification (ICD10AM) code M45 in identifying AS patients in a tertiary hospital.

Methods: Retrospective audit of patients with an electronic hospital discharge code M45 between 2000 and 2015. Patient records were manually reviewed to confirm presence of AS based on following criteria a) radiological evidence of Grade IV sacroiliitis or "bamboo spine" b) fulfilment of classification criteria (1984 Modified NY, 1991 AMOR, 2002 ESSG and 2009 ASAS criteria)[3] c) letter from treating rheumatologist confirming AS d) Biological DMARD (bDMARD) prescription for treating confirmed AS. Cases that were not able to meet AS criteria and had a likely alternative diagnosis documented by their treating team had this detail noted, but not assessed against formal criteria. All patients were then evaluated to for presence of an RA code ever during that patient's lifetime. Codes used to define RA included by codes M08.0* M8.2*, M8.3*, M8.4*, M8.8*, M8.9*, M05.*, M06.* (ICD10) or 714 (ICD9).

Results: Of 155 cases reviewed, eighty-six (55.4%) met audit criteria for AS. Of the 69 cases not meeting audit criteria for AS, 35 (72%) had RA ICD codes applied during their lifetime and a further 15 had background RA recorded in their notes. Five cases met AS audit criteria and had RA code applied. Excluding patients ever tagged with an RA code reduced AS case finding by 6% and raised overall accuracy to 67.5%. If background RA is also excluded, accuracy is 78.9%.

Conclusion: Overall raw accuracy of the ICD10AM M45 code in identifying AS patients was low, with RA acting as a significant confounder. This bears significant implications for international ALHD research reliant on this code for case finding. Excluding those ever coded with RA significantly improved accuracy and is recommended for future research. Our data support the call for scrutiny of international variations of ICD taxonomy[4].

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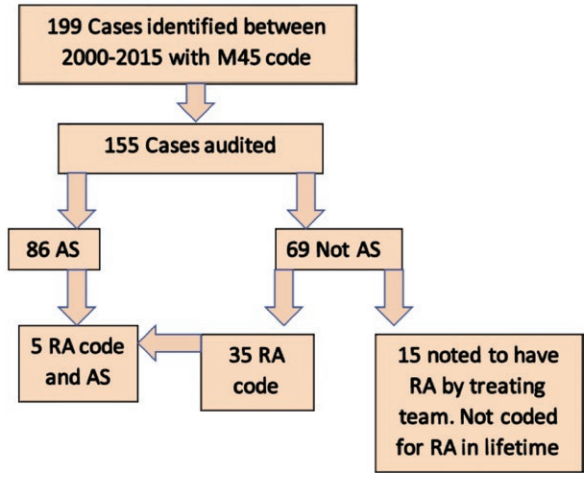
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Table 1.

	AS (%)
TOTALS	**86 (55)**
Male	56 (65)
Female	30 (35)
Mean age at diagnosis (years)	43
Met clinical criteria	37
Met Radiological criteria	31
Specialist diagnosis with or without bDMARD prescription	80

Figure 1. Audit Flowchart



Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.1352

Spondyloarthritis - clinical aspects (other than treatment)

AB1005 ASSOCIATION BETWEEN CHANGES IN SERUM ALKALINE PHOSPHATASE LEVELS AND RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS

Keywords: Biomarkers, Prognostic factors, Spondyloarthritis

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Background: The changes in bone metabolism may occur earlier than those that can be identified on radiography. Although studies have evaluated the changes in inflammatory markers that precede radiographic progression, no studies have evaluated the relationship between the timing of changes in bone metabolism and radiographic progression in patients with AS.
Objectives: To determine the relationship between serum alkaline phosphatase levels and radiographic changes over time in ankylosing spondylitis.
Methods: This retrospective study evaluated the electronic medical records of patients with ankylosing spondylitis between January 2001 and December 2018. Longitudinal data including serum alkaline phosphatase levels were imputed by linear interpolation at 3-month intervals. Among the serum alkaline phosphatase levels for 8 years prior to measurement of the modified Stoke Ankylosing Spondylitis Spinal Score, the serum alkaline phosphatase level having the highest beta coefficient with the modified Stoke Ankylosing Spondylitis Spinal Score was selected. Linear mixed models with the selected serum alkaline phosphatase levels and the modified Stoke Ankylosing Spondylitis Spinal Score, including clinical variables, were investigated.
Results: Overall, 1122 patients were included, with a mean follow-up period of 8.20 (standard deviation: 2.85) years. Of the series of serum alkaline phosphatase levels, the level in the previous 5 years and 3 months showed the highest beta coefficient with the modified Stoke Ankylosing Spondylitis Spinal Score (Figure 1). In the linear mixed model including clinical variables, the serum alkaline phosphatase level 5 years and 3 months before radiographic changes was significantly associated with the modified Stoke Ankylosing Spondylitis Spinal Score (β=0.021, 95% confidence interval: 0.017–0.025, p<.001).
Conclusion: Serum alkaline phosphatase levels measured at approximately 5 years before may be a surrogate marker for predicting spinal radiographic changes. Long-term prospective clinical and experimental studies of > 5 years are required for biomarker discovery or therapeutic research on the radiographic progression of ankylosing spondylitis.

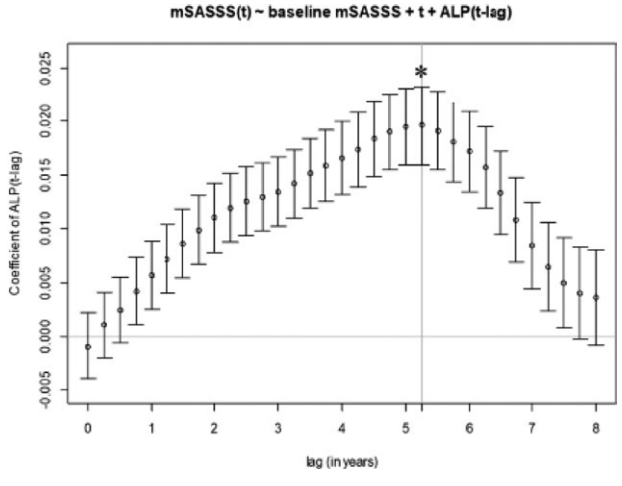


Figure 1. Beta coefficients of ALP levels to calculate the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). ALP levels 5 years and 3 months before measured mSASSS had the highest significant beta coefficient (0.020, 95% CI 0.016–0.023) with mSASSS (asterisk).mSASSS, the modified Stoke Ankylosing Spondylitis Spinal Score; ALP, alkaline phosphatase.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1472

AB1006 PULMONARY MANIFESTATIONS OF AXIAL SPONDYLOARTHRITIS (AXSPA): A SYSTEMATIC LITERATURE REVIEW

Keywords: Systematic review, Spondyloarthritis, Lungs

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Background: Common extra musculoskeletal manifestations (EMM) of axSpA include uveitis, inflammatory bowel disease, and psoriasis; and some of the uncommon manifestations include aortic incompetence, conduction abnormalities and IgA nephropathy. We felt that an updated and comprehensive review of pulmonary manifestations of axial spondyloarthritis was needed.
Objectives: To conduct a systematic literature review (SLR) using 2020 PRISMA guidelines on the spectrum of pulmonary manifestations in axial spondyloarthritis.
Methods: Using the 2020 PRISMA guidelines, we conducted a systematic literature review in the PubMed data base. The following MeSH combinations were used: (1) Ankylosing Spondylitis (AS) and interstitial lung disease, (2) AS and lung disease, (3) AS and obstructive sleep apnea, (4) non-radiographic axial spondyloarthritis (nr-axSpA)and lung disease (5) nr-axSpA and obstructive sleep apnea (6) nr-axSpA and interstitial lung disease (7) AS and/or axSpA and obstructive sleep apnea and/or thoracic wall disease. Our search timeline was limited to the past 40 years. The same combination terms were also hand searched. Reviewing of articles were divided between two authors.
Results: Our search led to a total of 10,948 articles and 10,919 were excluded based on relevance after title review (n=10,905), case report study design (n=6), and lack of access to the full manuscript (n=2). Additional 6 articles were excluded based on relevance after the entire manuscripts were read. Twenty nine full length manuscript were ultimately included for further study. All studies included patients with a diagnosis of AS rather than axSpA. The majority of studies were cross-sectional (n=12) followed by review articles (n=10 including one systematic review), and finally cohort studies (n=5 prospective and 1 retrospective). Mean disease duration range was 7.0-31 years. Average age of participants was 30.6 to 57.2, and majority were males (57.1-100%). The most common pulmonary manifestation (40-90%) was pleuro-parenchymal abnormalities noted on high resolution CT scan (HRCT) followed by abnormal pulmonary function tests (PFTs) (15-57%), chest wall movement restriction (50% with manubriosternal and sternoclavicular enthesitis and chest wall pain in 30-60%) and obstructive sleep apnea (OSA) (8.8%-47.8% of AS patients which was significantly higher than controls in all studies except one). OSA was associated with long disease duration and low age at onset of disease. HRCT abnormalities described were interstitial lung disease in 13.7-22%, spontaneous pneumothorax (0.29%), apical fibrosis (1.2%-19%), ground glass opacities (3.6-15%), nodules (3.8-40%), pleural thickening (3.8-45%), honey-combing (5.8%), parenchymal bands (5.8-41%), interlobular septal thickening (5.8-45%), bronchial wall thickening (7.1-41%), emphysema 9-45%, bronchiectasis (9.5-33%), subpleural bands (10.9-35%), tracheal dilation (11.1%), linear opacities (11.7%), and lymphadenopathy (16.7-28.6%). Frequency of apical fibrosis and bronchiectasis increased with disease duration. Subpleural nodules and parenchymal bands were found early in the disease course. Among those with abnormal PFTs, majority were restrictive in pattern (20-57%). A link between COPD and AS was found (46% in one cross-sectional study with 1.45 higher incidence compared to controls).
Conclusion: In our SLR, we identified various pulmonary manifestation in AS patient – the commonest being parenchymal lung disease as seen on HRCT – but there is a lack of controlled trials. Furthermore, there are no data in nr-axSpA patients which remains a major unmet need. No data were available on whether current advanced therapies are disease modifying from pulmonary perspective. Prospective studies are required to evaluate efficacy of novel treatments on lung disease.

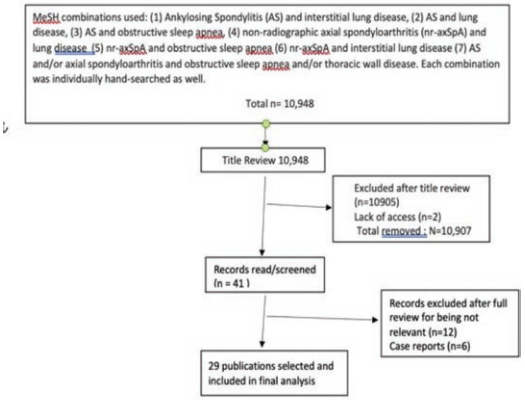


Figure 1: Flowchart summarizing the search process

REFERENCES: NIL.
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Disclosure of Interests: Kiana Vakil-Gilani: None declared, Tomas Cordova: None declared, Daniel Saifer: None declared, Atul Deodhar Consultant of: Consulting, advisory boards: AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Janssen, MoonLake, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Galvani, Eli Lilly, Janssen, MoonLake, Novartis, UCB.
DOI: 10.1136/annrheumdis-2023-eular.1901

AB1007 NEUROPATHIC PAIN AS A PREDICTOR OF FUNCTIONAL DISORDERS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

Keywords: Spondyloarthritis, Pain

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Background: Ankylosing spondylitis (AS) is one of the most actual problems in modern rheumatology. AS is characterized by a violation of functional abilities, which causes a decrease in the quality of life and invalidation of patients. The main symptom of AS is chronic pain, which persists in some cases not only due to inflammation, but also due to the neuropathic component of pain, however, this issue needs additional investigation [1].
Objectives: To assess functional status and its association with neuropathic pain in patients with AS.
Methods: Following the principles of biomedical ethics, on the basis of informed consent, we clinically examined 133 patients (men - 71%) diagnosed with AS according to the modified New York criteria. The presence of neuropathic pain (NP) was assessed by the Leeds Neuropathic Pain Rating Scale (LANSS) and by the Diagnostic Questionnaire for Neuropathic Pain (DN4). Disease activity was assessed by the BASDAI (Bath Ankylosing Spondylitis Disease Assessment Index) and ASDAS (Ankylosing Spondylitis Disease Activity Score). Functional disorders in AS were evaluated according to the BASFI (Bath AS Functional Index) and BASMI (Bath Ankylosing Spondylitis Metrology Index). The HAQ (Health Assessment Questionnaire) questionnaire was used to assess functional capabilities. Statistical analysis was carried out by the methods of variational statistics in the SPSS22 software package (©SPSS Inc.). Significance of differences between groups (p) was measured using the Mann-Whitney test. Results are presented as mean with standard deviation (M±SD).
Results: In patients with AS, the prevalence of NP according to the LANSS was 34.8%. Presence of NP in women was found significantly more often than in men: 52.3% versus 31.1%. According to DN4 data, 37.7% of patients have NP, and the ratio of women to men is 59.1 to 32.2. The NP according to both scales was found in 33.1% of AS patients, significantly more often in women than in men: 51.4% versus 29.7%. Moderate and high disease activity according to the BASDAI and ASDAS prevailed in our patients, and the average values were at the level of 5.5±1.7 and 3.54±0.83, respectively. Functional impairment according to the BASMI in patients with NP was significantly higher in comparing with the group without NP (4.0±2.1 versus 5.1±2.2; p<0.01). At the same time, according to the BASMI, it was established that among all patients with AS, the absence of functional disorders occurred only in 7.0% of patients, moderate disorders - in 68.3%, and severe disorders - in 24.7 % of patients. Pronounced functional disorders prevailed in the group of patients with NP (39.6% vs. 17%). Similar data were obtained by the BASFI (4.3±2.1 versus 6.6±1.6; p<0.01). The presence of functional disorders according to the BASFI was found in 70.7% of all AS patients. At the same time, functional disorders were found in 93.2% of patients with NP. The functional disability according to the HAQ in patients with NP was significantly higher than in the group without NP, which indicates that NP is associated with more pronounced functional disorders - 1.23±0.45 versus 0.91±0.51 (p<0, 01).
Conclusion: The presence of NP in AS patients is a common phenomenon. NP has a close relationship with functional abilities in patients with AS and can be consider as a predictor of severe functional disorders.
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AB1008 TIME, DURATION AND ORDER OF APPEARANCE OF EXTRA-ARTICULAR MANIFESTATIONS IN SPONDYLARTHRITIS: CLINICAL RISK FACTORS

Keywords: Spondyloarthritis, Epidemiology, Prognostic factors

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Background: Little is known about the chronologic order of appearance of extra-articular symptoms and spondylarthritis (SpA) symptoms and its effect in disease progression. Most information is based on population-based registries or big data that may lack precision.
Objectives: To describe duration, time until diagnosis and order of appearance of the articular and extra-articular (psoriasis, uveitis, or inflammatory bowel disease) symptoms. To evaluate factors associated with time from extra-articular symptoms onset until appearance of SpA symptoms.
Methods: A retrospective cohort study was conducted. Inclusion criteria were patients that met ASAS criteria visited at the SpA clinic between July – October 2022. Other autoimmune rheumatic diseases were excluded. Data were collected previously reviewing patient records available from the electronic and paper database of the hospital. Additional information was retrieved by the shared medical history database of the Catalan Institute of Health which attends the 99.2% of the population. Missing data were collected prospectively by patient interview. Univariate linear regression was conducted to study association.
Results: From 91 patients 54 (59.3%) were male and mean age was 63.9 (SD 14.3). There were 46 (50.5%) patients with exclusively peripheral SpA and 17 (16.5%) exclusively axial SpA. History of extraarticular symptoms were observed in 69 (76.6%) of the patients and 33 (37.1%) were HLA-B27 positive. In 49 (54.8%) patients extra-articular symptoms appeared before SpA. The median disease duration since SpA diagnosis was 11 year (IQR 14). Median time for SpA diagnosis since articular symptoms onset was 2 years (IQR 8). The median time from the extra-articular symptoms until the appearance of articular symptoms was 2 years (IQR 30). The associations of SpA features and time since first extra-articular symptoms until articular symptoms appearance is detailed in table 1. HLA-B27 positivity and axial disease showed a negative linear association while peripheral disease showed a positive linear association.

Table 1.

Variables	Coef (p)
Age (year)	0.15 (0.42)
Male	0.65 (0.91)
Smoker	-2.31 (0.54)
B27 positivity	**-21.4 (0.00)**
Elevate CRP	-1.16 (0.86)
Erosions	1.97 (0.77)
Radiographic sacroiliitis	-4.43 (0.24)
Peripheral SpA	**16 (0.03)**
Axial SpA	**-23.8 (0.01)**
Peripheral and Axial	**-13 (0.02)**

Conclusion: Most patients presented extra-articular manifestation before articular symptoms onset.
The median delay since first articular symptoms until SpA diagnosis was 2 years. Longer time between extra-articular manifestation and articular symptoms was liniarly associated with peripheral disease.
Axial disease and HLA-B27 were linearly associated with shorter time between the two symptoms.
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AB1009 INVERSE CORRELATION BETWEEN NONHDL CHOLESTEROL AND INFLAMMATORY BOWEL DISEASE IN SPONDYLOARTHRITIS: A NEW LIPID PARADOX

Keywords: Comorbidities, Spondyloarthritis, Cardiovascular disease

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Background: In Spondyloarthritis (SpA) a higher prevalence of cardiovascular comorbidities has been observed, such as diabetes mellitus (DM), arterial hypertension (AHT), dyslipidaemia (DLP), obesity and metabolic syndrome [1].

In recent years, several studies have established a causal relationship between non-HDL cholesterol (non-HDLC) levels and cardiovascular diseases. Non-HDLC offers a wide vision of proatherogenic lipoproteins containing apolipoprotein B (apoB) -VLDL, IDL, LDL, chylomicron remnants and Lp(a)- without being interfered by triglyceride concentrations. Thus, non-HDLC has become an innovative cardiovascular risk (CVR) biomarker. Therefore, the *Multinational Cardiovascular Risk Consortium* [2] recently published a set of recommendations estimating CVR based on non-HDLC levels. We have analyzed in a cohort of patients with SpA possible associations between clinic and laboratory data, and non-HDLC serum levels.

Objectives: To analyse in patients with SpA whether there is a relationship between disease-dependent variables (C-reactive protein [CRP] levels, erythrocyte sedimentation rate [ESR], presence of HLA-B27, axial or peripheral involvement, structural damage, and extra-articular manifestations) with non-HDLC serum levels.

Methods: Observational, cross-sectional, single-centre study, which included a sample of 104 patients with both radiographic and non-radiographic SpA, in whom each disease-dependent variable was analyzed individually for its possible association with non-HDLC serum levels. Classical CVR factors were also analyzed.

Results: Of 104 patients included most of them were women (54,8%), mean age was 43 years, 33,7% smoked, HLA-B27 was positive in 52,9% of patients, with mean CRP levels of 9,83 mg/L and ESR of 17,92 mm/h. Axial involvement prevailed over peripheral (92,3% vs 26%). Extra-articular manifestations were distributed as follows: 13,5% uveitis, 7,7% inflammatory bowel disease (IBD) and 4,8% psoriasis. 43,3% of patients had structural damage. None of these patients suffered from cardiovascular disease prior to diagnosis. Regarding the classic CVR factors: AHT was observed in 16,3%, DM in 1.92%, obesity (BMI >30) in 14.4%. Mean non-HDLC was 144.19 mg/dL (± 36,1), giving this population a 12,87% probability of suffering cardiovascular disease at the age of 75. For CVR estimation, we categorized non-HDLC levels according to low (100 - <145 mg/dL), moderate (145 - <185 mg/dL), high (185 - <220) and very high (≥220 mg/dL) levels. Lower mean concentrations of non-HDLC were found in those patients with IBD (117,6 ± 35,7 mg/dL), compared to those without intestinal involvement (146 ± 35,5 mg/dL) (p<0,05). No statistically significant relationships were observed between non-HDLC and the rest of disease-dependent variables.

Conclusion: In our cohort of patients, mean levels of non-HDLC were elevated (144 mg/dL), giving patients a 13% probability of suffering cardiovascular disease at the age of 75. Of clinical and laboratory features analyzed, we observed lower serum concentration of non-HDLC in patients with IBD. This could be explained by lipid malabsorption, as inflammatory damage of the intestinal epithelium decreases the synthesis of apo-B48, which is necessary for both chylomicron formation and hepatic synthesis of apo-B100 [3]. This may turn into lower serum levels of non-HDLC. Therefore, presence of IBD in patients with SpA should be kept in mind when defining non-HDLC levels as an estimator of CVR.

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AB1010

WHICH FACTORS ARE ASSOCIATED WITH CLINICALLY HIGH DISEASE ACTIVITY IN AXIAL SPONDYLOARTHRITIS? RESULTS FROM THE INTERNATIONAL MAP OF AXIAL SPONDYLOARTHRITIS (IMAS)

Keywords: Spondyloarthritis, Patient reported outcomes

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Background: Active axial spondyloarthritis (axSpA) is associated with poorer physical and mental health outcomes.

Objectives: This study aims to assess the prevalence of clinically active disease in axSpA and its associated factors in a large sample of patients from the International Map of Axial Spondyloarthritis (IMAS) study from around the globe.

Methods: IMAS is a cross-sectional online survey (2017-2022) including 5,557 unselected axSpA patients. Patients were divided between those with active disease (BASDAI < 4) and those without active disease (BASDAI ≥ 4). The factors evaluated were: age, gender, physical activity engagement, work-related issues, work choice and difficulty finding a job due to axSpA, number of self-reported symptomatic body regions, diagnostic delay, HLA-B27, extra-musculoskeletal manifestations, spinal stiffness (3-12), functional limitation (0-54), mental health using GHQ-12 scale (0-12), and treatments (NSAIDs, csDMARDs and bDMARDs). Mann-Whitney, chi-square test and logistic regression analysis were used to evaluate the possible association of the investigated factors with active disease in axSpA patients.

Results: 5,295 patients who had responded to the BASDAI scale in IMAS survey were included in the present study: 3,231 were from Europe, 770 from North America, 600 from Asia, 548 from Latin America, and 146 from Africa. The mean age was 43.8±12.9 years and 55.4% were females. Patient reported a mean BASDAI of 5.4 (**Figure 1**) with 75% having active disease (BASDAI≥4). In South Africa, 87.0% of patients reported having active disease, compared to 68.5% in Asia. Compared to patients with non-active disease, patients with active disease were more likely to be older, female, physically inactive, experience work-related issues, have greater difficulty finding a job and faced limited work choice due to axSpA, had higher number of self-reported symptomatic body regions, longer diagnostic delay, higher proportion of HLA-B27 negative, presence of inflammatory bowel disease, greater spinal stiffness, higher functional limitation, worse mental health, and greater use of csDMARDs. In the multivariable logistic regression, the factors associated with active disease were the presence of work-related issues due to axSpA, difficulty finding a job due to axSpA, higher number of self-reported symptomatic body regions, greater spinal stiffness, higher functional limitation, longer diagnostic delay, HLA-B27 negative, and worse mental health (**Table 1**).

Conclusion: Globally, three in four patients with axSpA reported clinically active disease, with higher proportion of patients with active disease in South Africa and lower in Asia. The causal relationship between the identified factors and clinical disease activity is complex and may vary from patient to patient. Our results underline the complexity of the clinical disease activity concept in axSpA and underline the need of a holistic approach in the patient management.

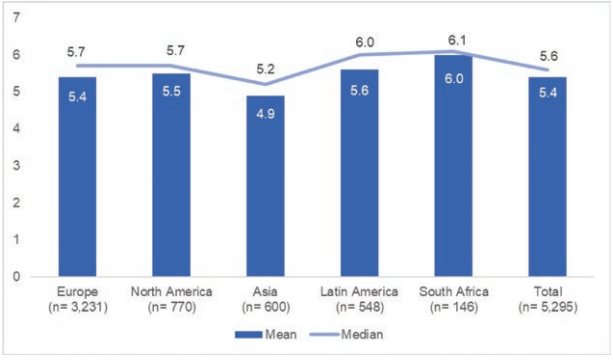


Figure 1. Mean and median of disease activity by region (N= 5,295)

Table 1. Logistic regression analysis to determine factors associated with active disease (N= 2,630)

	Univariable logistic regression		Multivariable logistic regression	
	OR	CI 95%	OR	CI 95%
Age	0.99	**0.98, 0.99**	0.99	0.98, 1.01
Gender. Female	1.95	**1.72, 2.21**	1.14	0.84, 1.56
Physical activity engagement. No	1.34	**1.12, 1.59**	1.19	0.77, 1.85
No. of self-reported symptomatic body regions	1.12	**1.11, 1.14**	1.08	**1.04, 1.11**
Spinal Stiffness (3-12)	1.39	**1.35, 1.43**	1.37	**1.27, 1.47**
Functional Limitation (0-54)	1.05	**1.04, 1.05**	1.02	**1.01, 1.03**
Diagnostic Delay	1.01	**1.01, 1.02**	0.98	**0.96, 0.99**
HLA-B27. Negative	1.47	**1.22 1.76**	1.48	**1.06, 2.08**
Inflammatory bowel disease. Yes	1.82	**1.48, 2.23**	1.43	0.90, 2.28
Difficulty finding a job due to axSpA. Yes	5.08	**4.38, 5.90**	1.92	**1.38, 2.68**
Work-related issues due to axSpA. Yes	3.16	**2.70, 3.69**	1.73	**1.22, 2.44**
Work choice due to axSpA. Yes	2.10	**1.84, 2.41**	1.03	0.75, 1.41
Mental health (0-12)	1.27	**1.24, 1.29**	1.20	**1.14, 1.26**
Use of csDMARDs	1.18	**1.03, 1.35**	1.11	0.82, 1.49

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AB1011

CO-DIAGNOSIS SPONDYLOARTHRITIS AND INFLAMMATORY BOWEL DISEASE: THE ENTRY MODE MATTERS

Keywords: Gastrointestinal tract, Descriptive studies, Spondyloarthritis

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Background: There is a clear pathophysiological link between spondyloarthritis (SpA) and Inflammatory Bowel Disease (IBD), so that 10% of IBD is estimated to have SpA and 10% of SpA is estimated to have IBD. Recently, Luchetti et al [1] demonstrated an increased level of bacterial translocation in cases of co-diagnosis of SpA and IBD compared to patients with IBD alone. These data suggest that the presence of this codiagnosis is associated with a more inflammatory and therefore a more active pathology.
Objectives: The aim of this study is to describe this population and to evaluate the impact of timing of diagnoses.
Methods: A single-centre retrospective observational study was conducted. We included all consecutive patients followed between 2015 and 2022 for spondyloarthritis (SpA) meeting the ASAS 2009 criteria and IBD histologically proven. For each patient, we collected demographics, smoking, extrarticular manifestations, imaging data and the number of bDMARDs used and bDMARD combinations. We then compared the populations according to first diagnosis, SpA or IBD. Fischer's exact test was used for comparison between categorical variables and Student's t test for quantitative variables.
Results: A total of 62 patients, 51% male and 67% HLA B27+, were included. In 61% of the cases, IBD was diagnosed first. The majority of IBD patients were diagnosed with Crohn's disease (68%) with a mean age at diagnosis of 35.7 (±12.9) years. Concerning spondyloarthritis, it was mostly axial (95%), 55% of which was radiographic axial, with a mean age at diagnosis of 36.8 (±13.4) years. Psoriasis was present in 24% and uveitis in 24% of cases, active smoking in 66%, and a physical job in 20% of cases. Patients had used an average of 3 bDMARDs and 10% are treated with a combination of bDMARDs. When SpA was diagnosed first, patient characteristics were different from those whose IBD was diagnosed first, with a mean age at diagnosis of SpA of 29.8 (±11.6) years (versus 41.6 (±12.6) years; P< 0.001) and a mean age at diagnosis of IBD of 31.9 (±11.8) years (versus 38.6 (+/-13) years; p= 0.043). When the codiagnosis was initiated by SpA, the prevalence of HLA B27 was 83% (versus 42%; p<0.01), psoriasis 17% (versus 29%; p=0.27) and uveitis 35% (versus 16%; p=0.087). Finally, radiographic damage was more frequent when SpA started first, with 86% of radiographic sacroiliitis (versus 34%; p< 0.001) and 44% of syndesmophytes (versus 13%; p= 0.036).
Conclusion: The population of patients with a co-diagnosis of SpA and IBD is a particular and difficult to treat population with an average of 3 different bDMARDs used and 10% of bDMARDs combination. Within this population, we identified two different clusters of patients according to the first diagnosis.
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Table 1.

	Global population (n=62)	SpA first (n=24)	IBD first (n=38)	P value
Gender (% male)	**51%**	**62%**	**39%**	**0.077**
Age at diagnosis of IBD	**35.7 (±12.9)**	**31.9 (±11.8)**	**38.6 (±13.0)**	**0.043**
Age at diagnosis of SpA	**36.8 (±13.4)**	**29.8 (±11.6)**	**41.6 (±12.6)**	**<0.001**
Disease duration IBD (years)	**17.1 (10.5)**	**11.9 (5.24)**	**20.0 (11.4)**	**<0.001**
Disease duration SpA (years)	**14.0 (9.84)**	**19.3 (8.14)**	**10.1 (8.44)**	**<0.001**
HLA B27+	63%	83%	42%	<0.01
axSpA	95%	96%	95%	1
Number of bDMARDs	2.8 (±1.7)	3.12 (±2.03)	2.61 (±1.55)	0.39
Association bDMARDs	9.5 %	4.2%	13%	0.39
Psoriaisis	24%	17%	29%	0.27
uveitis	**24%**	**35%**	**16%**	**0.087**
Sacroiliitis (Rx)	**55%**	**86%**	**34%**	**<0.001**
Sacroiliitis (MRI)	50%	81%	79%	1
Romanus (MRI)	50%	55%	50%	0.81
Syndesmophytes (Rx)	**27%**	**44%**	**13%**	**0.036**
Crohn disease	68%	71%	66%	0.38
Smoking	66%	64%	68%	0.76
Physical work	20%	19%	21%	1

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AB1012

AN INCREASED FREQUENCY OF ANKYLOSING SPONDYLITIS HAS BEEN FOUND IN THE SPOUSES OF SPONDYLOARTHRITIS/ANKYLOSING SPONDYLITIS PATIENTS: ENVIRONMENTAL FACTORS MAY PLAY A ROLE IN SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Epidemiology

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Background: It is known that genetic and environmental factors play a role in the pathogenesis of spondyloarthritis (SpA). [1] It can be thought that spouses living in the same house are exposed to similar environmental factors.
Objectives: This study aimed to investigate whether common living space increases the frequency of SpA development in unrelated spouses of SpA patients.
Methods: Between November 2021 and June 2022, 680 SpA patients who applied to the Hacettepe University rheumatology outpatient clinic were included. Patients were divided into ankylosing spondylitis (AS), non-radiographic SpA, and peripheral SpA. The patients were asked whether their spouses had SpA, and if they had SpA diagnosis, they were called to the outpatient clinic, and their diagnosis was confirmed. The family history of the patients and their use of bDMARDs were also noted. It was also checked whether the patients whose spouses had SpA findings fulfilled the AS criteria.
Results: 680 SpA patients were evaluated. There were 582(85.6%) AS, 72(10.6%) nr AxSpA, and 26 only peripheral SpA (3.8%). 49.4% of the patients

were male, and the mean age was 45.6 (10.4). The mean follow-up period of the patients was 10.6 (7.9) years. Of all patients, 468 (55.1%) were using a bDMARD at the time of evaluation. 12 SpA patients stated that their spouses had SpA. In the review of these patients, it was found that four patients did not have SpA, and one of them had PsA. Spouses of patients with nr AxSpA and peripheral SpA did not have AS/SpA AS was detected in the spouses of 7 patients. The incidence of AS in the entire SpA patient group was calculated as 7/695 (1.01% (0.4-2.1)). The incidence of AS in spouses of AS patients are 7/582 (1.20% (0.5-2.5)) calculated. 2 of 7 wives were cousins' children. The incidence of AS in unrelated spouses of AS patients are 5/580 (0.86% (0.3-2)). Only one of the spouses with AS knew her spouse's diagnosis at the time of marriage, while the other six were diagnosed after marriage. The median time for these patients to be diagnosed after marriage is 22 (7-32) years.

Conclusion: In the Turkish population, the frequency of AS was 0.49%, and the frequency of SpA was 1.05%. [2] The incidence of AS in the spouses of SpA patients has increased approximately two times compared to the average Turkish population. A 2.4-fold increased risk was found in AS patients. This situation may be related to environmental factors that play a role in the pathogenesis of SpA disease. However, the fact that half of the patients were using bDMARDs suggests that they were analyzed in the group with the potential for more severe disease. The results require confirmation in more extensive studies.

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AB1013 ARTIFICIAL INTELLIGENCE FOR DETECTION OF INFLAMMATORY SACROILIITIS IN MAGNETIC RESONANCE IMAGING IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Artificial intelligence, Imaging, Spondyloarthritis

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Background: Magnetic resonance imaging (MRI) is frequently used to evaluate active inflammatory sacroiliitis for early axial spondyloarthritis (axSpA) diagnosis. However, evaluation of sacroiliitis in MRI requires expertise because noninflammatory degenerative changes can mimic axSpA, and the semiquantitative diagnosis remains subject to significant variation. Artificial intelligence could function as assistance for inflammatory sacroiliitis detection.

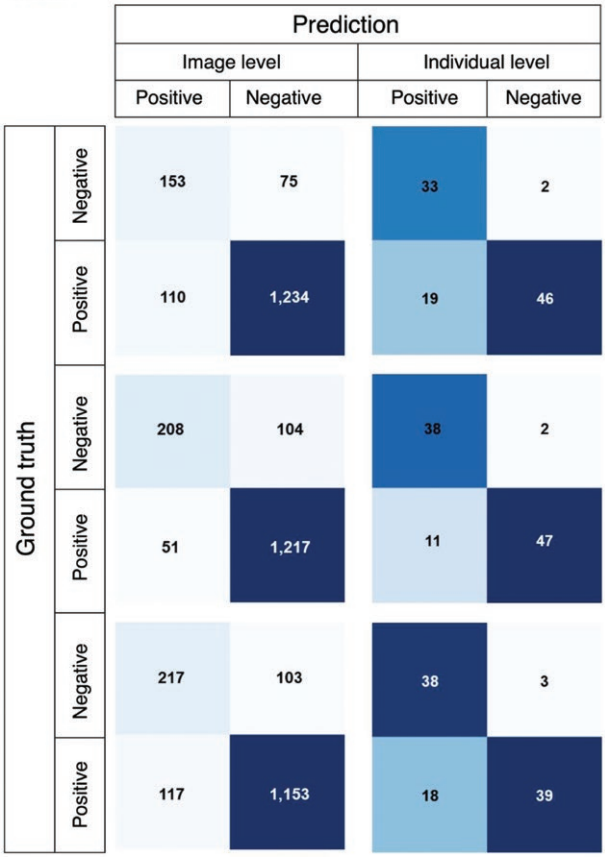
Objectives: This study aimed to develop artificial intelligence for detecting inflammatory sacroiliitis for axSpA in MRI.

Methods: This retrospective study included MRI examinations of patients with clinical suspicion of axSpA collected at Samsung Medical Center between January 2010 and December 2021. Only the patients who performed short tau inversion recovery (STIR) MRI of the sacroiliac joints were included. Active inflammatory lesions consisting of bone marrow edema (BME) were identified independently by a rheumatologist and a radiologist using the Assessment of SpondyloArthritis international Society (ASAS) definition of MRI sacroiliitis. We propose a two-stage deep learning framework that combines a sacroiliac joints (SIJs) localization network with a BME classification network. First, the Faster R-CNN network extracts regions of interest (ROI) to localize the SIJs using whole MR images. Here, Maximum Intensity Projection (MIP) using three consecutive images of SIJs ROI is applied to enhance the low intensity of BME and consider the contextual information between images. Second, the VGG-19 network determines the presence of BME on individual MR images of localized SIJs ROIs with a resolution of 128x256. During the training process, we augmented the positive dataset 6-fold using blurring, contrast, noise, rotation, and sharpening because of the smaller number of data than the negative dataset. The prediction models were evaluated using 3-round, 3-fold cross-validation. The performance of BME classification was measured using accuracy and area under the receiver operating characteristic curve (AUC-ROC) curve.

Results: A total of 296 participants with 4,746 MRI images were included in the study. Inflammatory sacroiliitis was identified in 864 MRI images from 119 participants. The mean average intersection over unions (IoU) of ROIs to localize the SIJs was 0.742 for the right side and 0.744 for the left side. The mean accuracy and AUC-ROC of inflammatory sacroiliitis were 0.898 and 0.830 for image level and 0.801 and 0.827 for patient level, respectively. The confusion matrices of inflammatory sacroiliitis prediction are shown in Figure 1. In the original model, without using MIP and dataset augmentation, the mean accuracy and AUC-ROC were 0.867 and 0.609 for image level and 0.717 and 0.620 for individual level. Compared to the original model, improved performances of inflammatory sacroiliitis could be observed.

Conclusion: Artificial intelligence can detect inflammatory sacroiliitis for axSpA according to the ASAS definition in MRI.

Figure 1. The confusion matrices of classification of inflammatory sacroiliitis prediction by image-based and individual-based in first round.



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Disclosure of Interests: None Declared.

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AB1014 RADIOGRAPHIC VERSUS NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: RESULTS FROM TREASURE DATABASE

Keywords: Real-world evidence, Outcome measures, Registries

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Background: Axial Spondyloarthritis is an umbrella term including radiographic (r-axSpA) and non-radiographic (nr-axSpA) forms which has been initially suggested by Assessment of SpondyloArthritis International Society (ASAS) as a different stages of the disease. Within time, studies have tried to answer whether these two entities represent distinct features, and the debate is still ongoing.

Objectives: The objective of this study is to define the similarities and differences of r-AxSpA and nr-AxSpA patients using a large national registry data.

Methods: TReasure is a national, multicentre, longitudinal, and observational database, initiated in Turkey in 2017 [1]. This database included patients with inflammatory arthritis, rheumatoid arthritis, axial-and peripheral SpA at the time of the first introduction of biological treatment. At the time of this analysis database consisted of 7015 SpA patients. All patients registered to the database fulfill the 2009 ASAS classification criteria. For this analysis, patients were categorized into r-AxSpA and nr-AxSpA and demographic and clinical characteristics of patients were determined.

Results: There were 4629 (86.7%) patients with r-AxSpA, 707 (13.3%) patients with nr-AxSpA patients. *Demographic differences*; r-AxSpA group were older (45 (16) vs 41 (14), p<0.001) and male predominant (59.6% vs 46.0%, p<0.001), with longer disease duration at bDMARD initiation (3.0 (6.9) vs 1.1 (3.4) years, p<0.001) and more smoker (61.4% vs 50.4%, p<0.001). *SpA clinic/genetic differences*; r-AxSpA group had less arthritis (7.7% vs 27.5%, p<0.001), heel pain (11.1% vs 40.8%, p<0.001), dactylitis (3.4% vs 8.1%, p<0.001), psoriasis (10.2% vs 14.5%, p<0.001), SpA family history (28.2% vs 40.8%, p<0.001), IBD (4.5% vs 7.4%, p=0.001) and more HLA-B27 positivity (58.2% vs 51.4%, p<0.001), similar uveitis rate (13.2% vs 14.8%). *SpA Outcome measures (bDMARD baseline) differences;* r-AxSpA group had worse functionality and quality of life measured by BASFI (5.0 (3.0) vs 4.0 (3.9), p<0.001), HAQ-DI 0.63 (0.40) vs 0.55 (0.65), p=0.029) respectively. Worse metrology by BASMI 3.2 (2.6) vs 1.7 (2.1), p<0.001) and high disease activity by ASDAS-CRP (3.64 (1.28) vs 3.24 (1.33), p<0.001) with higher CRP (12 (21.8) vs 7.3 (15.0) p<0.001) was observed. *SpA imaging differences;* r-AxSpA group had higher rate of `any syndesmophytes `(26.6% vs 5.4%, p<0.001), hip involvement (24.6% vs 4.5%, p<0.001), hip prosthesis (2.3% vs 0.3%, p<0.001), MRI structural lesions (63.6% vs 37.3%, p<0.001), and less active MRI lesions (74.6% vs 87.0%, p<0.001). No significant difference was observed in the physician decision on the b-DMARD choice at baseline (p=0.673).

Conclusion: A significant proportion of SpA patients who were initiated bDMARD have r-SpA. Although the two entities are seen as the continuum of each other, they have significant differences in terms of demographic, clinical, genetic, functional, metrology, activity and imaging characteristics. On the other hand, there is no difference in treatment choices at the stage of bDMARD initiation.

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AB1015

FETUIN-A: A NEW BIOMARKER OF BONE DAMAGE IN EARLY AXIAL SPONDYLARTHRITIS. RESULTS OF AN INTERIM ANALYSIS OF THE SPACE STUDY

Keywords: Diagnostic tests, Imaging, Spondyloarthritis

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Background: Fetuin-A serum levels have been variably associated with radiological damage in axial spondyloarthritis (axSpA).

Objectives: The aim of this study was to evaluate the association of fetuin-A with the presence of radiographical sacroiliitis and syndesmophytes in early axSpA and to identify predictors of radiological damage in the sacroiliac joints (SIJ) after 24 months.

Methods: Patients with axSpA in the Italian cohort of the SpondyloArthritis-Caught-Early (SPACE) study were included. Physical examinations, laboratory tests (including fetuin-A), SIJ and spinal plain radiographs and MRIs at T0 (diagnosis) and at T24 were considered. Radiological damage in the SIJ was defined according to modified New York (mNY) criteria.

Results: Fifty-seven patients were included (41.2% males, average chronic back pain duration of 13.2±6 months). Fetuin-A levels were lower in patients with radiological sacroiliitis compared to those without at T0 (205.7±59.7 vs 249.7±50.4 µg/mL, respectively, p <0.001) and at T24 (222.3±51.5vs 272.3±91.6 µg/mL, p=0.03) (Table 1). T0 fetuin-A levels significantly correlated with mNY score at T0 and at T24, and T24 fetuin-A levels with mNY at T24 (Figure 1). At T0, fetuin-A levels were significantly higher in non-smokers, in patients with heel enthesitis and in those with a family history of axSpA; at T24 levels were higher in females, in patients with higher ESR/CRP at T0 and in those with radiological sacroiliitis at T0 (Table 1). Following multivariable analysis, fetuin-A at T0 resulted negatively associated with the likelihood of radiological sacroiliitis (OR=0.9 per 10-unit increase (95%CI 0.8, 0.999), p=0.048); but not with syndesmophytes. Fetuin-A at T0 and T24 were associated with mNY at T0 (β -0.5, p<0.001) and at T24 (β -0.3, p<0.001), respectively; T0 fetuin-A levels did not achieve statistical significance in predicting mNY at T24 (β -0.9, p<0.001).

Conclusion: Fetuin-A levels were negatively associated with radiological damage of the SIJ, but not of the spine, in early axSpA and after 2 years of follow-up. Fetuin-A levels may serve as biomarker to identify patients with a more severe disease and early structural damage.

Table 1.

	All patients	No radiological sacroiliitis	Radiological Sig. sacroiliitis		No syndesmophytes	Syndesmophytes	Sig.
Number	57	36	21		51	6	
Males	24 (42.1)	12 (33.3)	12 (57.1)	0.08*	19 (37.3)	5 (83.3)	0.03**
BMI	24.1±4.3	24.1±4.7	24±3.7	0.92	23.5±3.5	29±7	0.05**
Smoking	19 (33.3)	9 (25)	10 (47.6)	0.08*	16 (31.4)	3 (50)	0.36
Age of onset chronic back pain(CBP)	29.2±8.3	29.8±8.9	28.1±7.4	0.49	28.1±7.9	38.3±6.6	0.01**
Duration CBP	13.2±6	12.9±5.7	13.6±6.7	0.75	12.9±6.2	15.7±4.6	0.25
HLA-B27	22 (38.6)	12 (33.3)	10 (47.6)	0.29	21 (41.2)	1 (16.7)	0.24
Heel enthesitis	46 (80.7)	32 (88.9)	14 (66.7)	0.04**	40 (78.4)	6 (100)	0.21
Peripheral arthritis	24 (42.1)	13 (36.1)	11 (52.4)	0.23	20 (39.2)	4 (66.7)	0.2
Family history	28 (49.1)	19 (52.8)	9 (42.9)	0.47	26 (51)	2 (33.3)	0.41
Response to NSAIDs	55 (96.5)	35 (97.2)	20 (95.2)	0.69	49 (96.1)	6 (100)	0.62
Fetuin-A, µg/mL	233.5±57.6	249.7±50.4	205.7±59.7	<0.001**	233.8±59.3	231.4±44.6	0.68
Elevated CRP or ESR	30 (52.6)	16 (44.4)	14 (66.7)	0.11	27 (52.9)	3 (50)	0.89
BASDAI	4.4±2.5	4.9±2.3	3.5±2.6	0.03**	4.5±2.5	3.2±2.9	0.2
BASMI	0.8±1	0.8±1.1	0.7±1	0.8	0.7±1	1±1.5	0.98
ASDAS	2.5±0.8	2.5±0.8	2.5±0.8	0.6	2.5±0.8	2.1±0.9	0.18
MASES	3.5±2.5	4±2.7	2.5±1.9	0.04**	3.5±2.6	2.8±2.4	0.53
Radiological sacroliliitis	0.4±0.5	0±0	1±0	-	0.4±0.5	0.3±0.5	0.85
Syndesmophytes	0.1±0.3	0.1±0.3	0.1±0.3	0.85	0±0	1±0	-
mNY	0.5±0.8	0.2±0.4	1.1±0.9	-	0.5±0.8	0.3±0.5	0.61
mSASSS	3.3±3.9	3.2±4.2	3.5±3.3	0.36	2.5±2.8	10±5.3	<0.001**
SPARCC SIJ	5.1±11.7	3.3±10.9	8.2±12.7	0.09†	5.3±12.3	3.7±4.8	0.89
SPARCC spine	9.6±13.4	6.8±9.8	14.2±17.2	0.09†	9.9±13.9	7±7.1	0.63

Scatterplots: association of Fetuin-A levels and radiological damage in the sacroiliac joints according to the modified New York (mNY) score

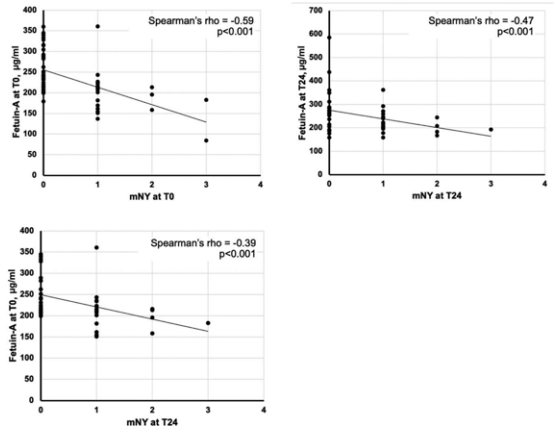


Figure 1.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1016 ERECTILE DYSFUNCTION IN ANKYLOSING SPONDYLITIS: ASSOCIATIONS WITH DISEASE-RELATED PARAMETERS

Keywords: Patient reported outcomes, Comorbidities, Spondyloarthritis

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Background: Ankylosing spondylitis (AS) is a chronic, inflammatory, autoimmune disease that dominantly affects younger men. (1) Patients with AS often experience chronic musculoskeletal pain, fatigue and stiffness, which may contribute to psychological distress and sexual dysfunction (SD). (2)
Objectives: The study aimed to assess prevalence of ED in patients with AS and identify potential associations between clinical parameters related to AS and the presence of ED.
Methods: This observational cross-sectional study was approved by the local Ethics Committee. Forty consecutive male patients with the AS (mean age 42.8 ± 8.9 years) and 60 healthy men (mean age 38.9 ± 10.9 years) were included. All subjects filled-in the International Index of Erectile Function (IIEF) questionnaire, as well as the Beck anxiety inventory (BAI) and the Beck depression inventory (BDI). In patients with AS disease activity was evaluated using the Ankylosing Spondylitis Disease Activity Score (ASDAS) and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), functional ability using the Bath Ankylosing Spondylitis Functional Index (BASFI), and quality of life using the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire.
Results: ED was significantly more frequent in patients with AS (21/40, 52.5%) compared to controls (52.5%: 25%, p=0.049). Moreover, the mean value of IIEF score was significantly (p=0.035) lower in AS patients (22.3 ± 8,9) than in the control group (25.7 ± 7.5). There was no significant difference in BAI and BDI scores between patients with AS and ED and patients with ED in the control group. Parameters reflecting disease activity (ASDAS, BASDAI, CRP) and functionality (BASFI) were somewhat higher in the patients with AS and ED in comparison to patients without ED. However, these findings were not statistically significant. According to ASQoL scores, patients with AS and ED had a worse quality of life compared to patients with AS but without ED (p=0.022). AS patients with ED had more severe symptoms of depression than AS patients without ED (p=0.034). Univariate logistic regression showed that BDI and ASQoL scores were associated with the presence of ED. However, multivariate logistic regression analysis showed that ASQoL was an independent prognostic factor for the presence of ED in patients with AS. The increase in one unit of ASQoL score increased the risk of having ED for 17.5% (p=0.035).
Conclusion: The prevalence of ED in patients with AS was higher than in healthy controls. Poor quality of life (according to ASQoL) was the only parameter, independently associated with the presence of ED. It is necessary to raise awareness of ED in patients with AS.

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AB1017 DETERMINANTS OF SLEEP DISORDERS IN AXIAL SPONDYLOARTHRITIS: A CONTROLLED STUDY

Keywords: Quality of life, Spondyloarthritis, Patient reported outcomes

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Background: Axial spondyloarthritis (axSpA) is a chronic joint disease, characterized by inflammation and damage of the axial skeleton. It is frequent for patients to experience pain during periods of rest, such as during night sleep. A limited number of studies address the relationship between axSpA and sleep quality (SQ), although it represents a major concern for patients. Moreover, most of these studies lack a control group and do not explore the different areas of sleep.
Objectives: To describe the prevalence of sleep disorders in patients with axSpA and compare it with a healthy population. To analyse the determinant factors associated with SQ in both populations. To analyse the effect of structural damage, disease activity and its specific treatments on sleep quality.
Methods: We conducted a cross-sectional study. The cohort was composed of adult axSpA patients followed in the Rheumatology outpatient clinic at Doctor Peset University Hospital, and age- and gender-matched healthy individuals. Participants with known sleep diseases were excluded. The following variables were collected for both patients and controls: age, gender, perceived health, weekly physical activity, employment situation, and annual level of income, history of anxiety and/or depression and active treatment for it. The following variables were collected for axSpA patients: year of diagnose, BASFI, BASDAI and ASAS-HI scores, current dosage of glucocorticoids, use of NSAIDs and conventional, biologic or targeted synthetic DMARDs, and presence of syndesmophytes on plain radiography. The Pittsburgh Sleep Quality Index (PSQI) questionnaire, which evaluates sleep quality and disturbances over a month time interval, was applied. This questionnaire studies 7 different sleep domains: subjective quality, latency, duration, efficiency, disturbances, use of sleeping medication, and daytime dysfunction. A regression model was created to estimate the influence of the collected variables on the results of this questionnaire.
Results: 57 axSpA patients and 50 healthy controls were included. There were no statistical differences in mean age and sex percentage between both groups. According PSQI scores, 87.72% of patients and a 62% of controls were classified as “poor” sleepers. SQ was related to axSpA (p = 0.002), anxiety (p = 0.003), perceived health (p = 0.001) and physical activity levels (p = 0.006). The domains of subjective sleep quality, latency, duration, efficiency and sleep disturbances were negatively affected by axSpA (p < 0.05). The estimated odds ratio of having a sleep disorder was 5.63 times higher in patients diagnosed with axSpA. With regards to AS patients; anxiety (p < 0,001), physical activity (p = 0,015), BASDAI scores (p = 0,001), BASFI scores (p = 0,038) and axial syndesmophytes (p=0,028) were found to affect the PSQI score.
Conclusion: Patients with axSpA have a poorer sleep quality when compared to healthy individuals. AxSpA affects subjective sleep quality, latency, duration, efficiency and sleep disturbances. Disease activity and the presence of syndesmophytes have a detrimental effect, whereas physical activity has a positive effect on SQ. Therefore, these factors must be considered when attending this area of our patient’s health. The PSQI questionnaire provides a complete approach to sleep health and should be considered a complementary tool for the management of axSpA patients.

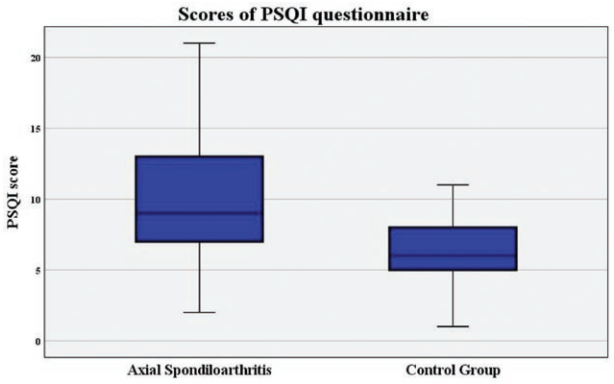


Figure 1.

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AB1018 BASELINE CHARACTERISTICS OF AN EARLY SPONDYLOARTHRITIS COHORT IN HONG KONG

Keywords: Geographical differences, Spondyloarthritis, Descriptive studies

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Background: Axial Spondyloarthritis (axSpA) is characterized by inflammation of the sacroiliac joint and the spine. It is a heterogeneous disease with variable musculoskeletal and extra-articular manifestations. The **Be**l**G**ian **I**nflammatory **A**rthritis and spo**N**dylitis cohor**T** (Be-Giant) is a cohort that recruited newly diagnosed SpA patients in Belgium and prospectively followed up the patients.

Objectives: Given the difference in genetic susceptibility and environmental exposure, we aimed to compare the disease nature, clinical presentation, and prognosis between Chinese and Caucasian axSpA patients.

Methods: The SPARK cohort (**SP**ondylo**AR**thritis in Hong **K**ong) resembled the Be-Giant cohort. Newly diagnosed, biologic naïve Chinese axSpA patients who fulfilled ASAS classification criteria were recruited. All patients underwent standardized clinical, laboratory and radiographic assessments as per Be-Giant protocol.

Results: A total of 53 newly diagnosed axSpA patients were recruited in the SPARK cohort (Table 1). The mean age at diagnosis (32 years old) and symptom duration (2 years) were comparable in both cohorts. There was a slight male predominance (59%) in the SPARK cohort as compared to the Be-Giant cohort (50%). More patients were HLAB27 positive in Chinese patients (SPARK 96% vs Be-Giant 71%). In both cohorts, less than one-fifth of the patients had radiographic sacroiliitis according to modified New York criteria (SPARK 17% vs Be-Giant 18%). Patients in the Be-Giant cohort and the SPARK cohort had similar disease activity clinically by ASDAS-CRP (SPARK 2.4 (SD 0.9) vs Be-Giant 2.6 (SD 1.0)) and radiographically by positive MRI SIJ according to the ASAS definition (SPARK 53% vs Be-Giant 87%). More patients in the SPARK cohort (37%) experienced uveitis compared to the Be-Giant cohort (12%). Around 9% and 5% of axSpA patients in Be-Giant cohort suffered from psoriasis and inflammatory bowel diseases (IBD) respectively while none in SPARK cohort did. Enthesitis (28%) and dactylitis (3.8%) were more common in Chinese as compared to Belgians. Whereas peripheral arthritis and dactylitis were more common in Belgians than Chinese axSpA patients.

Conclusion: Caucasian and Chinese axSpA patients display a similar burden regarding axial disease, yet appear to be different in the extent on peripheral and extra-musculoskeletal manifestations.

Table 1. Baseline demographic and clinical characteristics of newly diagnosed axial SpA patients

	Be-Giant cohort (n=257)	SPARK cohort (n=53)
Male, no %	128 (49.8%)	31 (58.5%)
Age at diagnosis, years	32 (8.3)	32(7.9)
Symptoms duration, months	27 (10-83)	24 (13-54)
Current smoker, no %	52 (20.5%)	10 (18.9%)
HLAB27, no %	181 (70.7%)	51 (96.2%)
Peripheral manifestation		
Enthesitis, no (%)	24 (9.3%)	15 (28.3%)
Arthritis, no. (%)	38 (14.8%)	6 (11.3%)
Dactylitis, no (%)	5 (1.9%)	2 (3.8%)
Extra-musculoskeletal manifestation (now/ever)		
Acute anterior uveitis	31 (12.1%)	20 (37.7%)
Psoriasis	23 (8.9%)	0
IBD	12 (4.7%)	0
ASDASCRP, mean+-SD	2.6 (1.0)	2.4 (0.93)
BASDAI, mean+-SD	4.3 (2.0)	3.7 (2.2)

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AB1019 ANALYSIS OF DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF ENTEROPATHIC SPONDYLOARTHRITIS IN A TERTIARY CARE HOSPITAL

Keywords: Spondyloarthritis, Epidemiology, Gastrointestinal tract

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Background: Enteropathic spondyloarthritis (eSpA), is a type of inflammatory joint disease that is related to inflammatory bowel diseases (IBD). Both spondyloarthritis (SpA) and IBD share clinical, genetic and immunological features. Arthritis can occur before, during or after IBD. The treatment of this disease is based on the use of NSAIDS and corticoids as well as the use of csDMARDs and bDMARDs.

Objectives: To describe the demographic, clinical and serological characteristics, as well as the onset pattern, radiological involvement, smoking habit, activity disease and comorbidities such as cardiovascular risk factors (CVRF) in patients with eSpA. To analize the most commonly used drugs in these patients and the therapeutic response.

Methods: We performed a descriptive observational study of patients with eSpA diagnosed in the Hospital of León between 1980 and 2022. The variables analysed were sex, date onset of IBD and SpA, time between the two diagnoses, pattern of SpA involvement, type of IBD, HLAB27, toxic habits, family history, arthralgias, uveítis, psoriasis, dactylitis, radiological involvement (sacroilitis, syndesmophytes) and treatments received. The activity disease was assessed by BASDAI Index.

Results: The patient´s features are shown in Table 1. We included 56 patients, half men and half women. The 57,1% of the cases debut with IBD. Crohn's Disease (CD) was the most represented IBD. The 41,1% had a peripheral SpA (16,1% oligoarticular arthritis and 25% polyarticular arthritis); the 32,1% patients presented an axial SpA and 26,8% had a mixed pattern. Peripheral SpA was the most represented form. The time elapsed between joint involvement and IBD was < 5 years in the 50% of the sample analyzed. HLAB27 was positive in 28,6% of the sample and the 35,7% showed BASDAI > 4. We found associated uveitis and psoriasis in 14,3% and 16,1% of the cases. The 57,1% of eSpA had CVRF, the most prevalent was dyslipemia (39,3%). The 53,6% had radiological involvement (sacroilitis 48.2%, syndesmophytes 21.4%). Radiological involvement was significantly greater in smoker patients (p=0.003), probably due to higher associated inflammatory activity. 78.6% of SpA were treated with cDMARDs and methotrexate was the most used (51.8%), followed by azathioprine, 5-ASA, and leflunomide. 73.2% of the cases received bDMARDs and anti-TNF was the most used (73.2%), followed by IL12-23 inhibitors, JAK inhibitors and anti-integrin.

The most frequent cause of discontinuation of methotrexate was side effects (16.1%), especially digestive intolerance; while in patients treated with anti-TNF was secondary failure (19.6%)

Table 1. Demographic, clinical, serological features, radiological involvement and treatments of the eSPA patients.

Characteristics	Patients (n=56) Median; IQR or n(%)
Sex F/M	28(50)/28(50)
Smoking	27(48,2)
Family history	12(21,4)
Previous onset of IBD	32 (57,1)
Previous onset of SpA	23 (41,1)
Type of IBD:	
- Ulcerative colitis (CU)	23(41,1)
- Crohn´s disease (CD)	33(58,9)
Pattern of SpA:	
- Axial	18(32,1)
- Peripheral	23(41,1)
Peripheral oligoarticular	9(16,1)
Peripheral polyarticular	14(25)
- Mixed	15(26,8)
Arthralgias	47(83,9)
HLAB27	16(28,6)
BASDAI (>4)	20(35,7)
Uveitis	8(14,3)
Psoriasis	9(16,1)
Dactylitis	0(0)
Radiological involvement	30(53,6)
- Sacroilitis	27(48,2)
- Syndesmophytes	12(21,4)
MRI lesions(sacroilitis)	28(50)
CVRF	32(57,1)
- HTA	18(32,1)
- Dyslipemia (DL)	22(39,3)
- Diabetes Mellitus (DM)	1(1,8)
- Obesity	6(10,7)
Treatment	
- Corticoids	40(71,6)
- NSAIDS	44(78,6)
- csDMARDs	51(91,1)
o Methotrexate	29(51,8)
o Azathioprine	21(37,5)
o 5-ASA	16(28,6)
o Leflunomide	1(1,8)
- bDMARDs	41(73,2)
o antiTNF	41(73,2)
o IL12-23 inhibitors	9(16,1)
o JAK inhibitors	7(12,5)
o antiintegrin	5(8,9)

Conclusion: In our study, most patients with enteropathic spondyloarthritis first presented intestinal symptoms. The most frequent patterns were peripheral spondyloarthritis and Chron's disease, and we found HLA B27+ in around a third of the sample. Smoking was associated with greater radiological involvement in the form of sacroiliitis and syndesmophytes.

Multidisciplinary work between gastroenterology and rheumatology is essential for the diagnosis and treatment of enteropathic spondyloarthritis. These results are consistent with the literature.

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AB1020 MUSCULOSKELETAL INVOLVEMENT IN INFLAMMATORY BOWEL DISEASE PATIENTS: A MONOCENTRIC EXPERIENCE

Keywords: Inflammatory arthritides, Spondyloarthritis

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Background: Musculoskeletal (MSK) symptoms, varying from arthralgia to arthritis are frequently reported by patients (pts) with inflammatory bowel diseases (IBD). A peripheral or axial joint involvement has been reported with a similar range from 5 to 30% and a definite spondyloarthritis (SpA) diagnosis is present in up to 46% of patients with IBD [1-8]. To date, a more comprehensive disease control is requested and the optimization of the treatment (choosing a mono or a combination therapy strategy) to improve both gastrointestinal and musculoskeletal is mandatory.

Objectives: To evaluate the rate of MSK involvement in a mono centric cohort of IBD pts and the consequent need to optimize their therapeutical schemes.

Methods: A gastroenterologist working in the IBD out-patient clinic had selected IBD patients who should be referred to the rheumatologic visit, on the basis of the results of a questionnaire aimed at highlighting the presence of clinical features suggestive of SpA. From January 1st 2017 to December 31st 2022 IBD pts have been evaluated by a rheumatologist expert in SpA. In case of doubts about the diagnosis, further examinations were requested. The diagnosis of SpA was made following the ASAS criteria of 2011.

Results: A total of 288 pts were sent to the rheumatologist (140 CD, 127 UC, 21 not defined IBD). One hundred sixty-eight pts received only one rheumatological visit while, one hundred two were evaluated twice or more times. To make a diagnosis, 37 MRI (30 for sacroiliac joints), 30 ultrasound assessment (mostly hands, wrists or feet), 19 X-rays and 23 blood tests were requested. Most of pts (196/288, 68%) were not classified as SpA; 50/288 (17.4%) were peripheral SpA and 24/288 (8.3%) were axial SpA, in 18/288 (6.3%) there was an isolated entheseal involvement. The rheumatologist recommended a therapeutical optimization in 138 IBD pts (47.9%). In particular, a DMARD was added in 59 pts and a bDMARD was prescribed in 6 for rheumatological indications; moreover, in 73 cases, a choice between two different therapeutical approaches was suggested to the gastroenterologist, in order to improve the control of MSK disease activity on the basis of IBD course.

Conclusion: Our results confirm the already published prevalence of MSK involvement in IBD patients. A relevant number of IBD pts, after the rheumatological evaluation, were classified as peripheral (17.4%) or axial (8.3%) SpA. In about half of IBD pts, a therapeutical modification was recommended by the rheumatologist, aiming at improving the control of MSK disease activity in the context of the IBD course. These data confirm the importance of a close collaboration between gastroenterologists and rheumatologists, to optimize the clinical assessment of IBD pts, thus improving their quality of care [9].

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AB1021 THE DISEASE BURDEN OF AXSPA: ARGENTINIAN DATA FROM THE INTERNATIONAL MAP OF AXIAL SPONDYLOARTHRITIS (IMAS)

Keywords: Spondyloarthritis

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Background: The term axial spondyloarthritis covers both patients with non-radiographic (nr-axSpA) and ankylosing spondylitis (AS). Axial spondyloarthritis (axSpA) is a chronic disease that typically affects the axial skeleton, and produces varying degrees of pain, stiffness, and fatigue [1-2].

Objectives: The aim of this study is to describe the burden of disease from the patient´s perspective who participated in the International Map of Axial Spondyloarthritis in Argentina.
Methods: IMAS is a cross-sectional online survey including axSpA patients from around the globe. In this study, Argentinian axSpA patients ≥ 18 years old with AS or nr-axSpA, who provided informed consent and participated in the IMAS survey, were included. To determine disease burden from patient´s perspective BASDAI and GHQ-12 scale were performed. In addition, data on demographic, clinical and treatment characteristics were included to describe the daily life of these patients. Numerical variables are expressed as mean (standard deviation) or median (interquartile range), while categorical variables are expressed as count and percentage.
Results: 115 individuals (67 men) were included. Mean ± SD age of surveyed participants was 46.9 ± 12.3 years. 76.5% reported being diagnosed with ankylosing spondylitis. Most of them (n: 98) live in Buenos Aires and surroundings. The median BASDAI score was 5.1 (IQR: 3.5), 66.1% had a BASDAI score > 4. The mental state (psychological distress) was affected in less than half, 41.7% of the participants showed a GHQ-12 >3. The delay in diagnosis was 4 years (SD 8). Biologics were prescribed in 88 out of 115 (76.5%) patients and 92% were on them at the time of the survey. The most frequently reported associated health conditions were anxiety and sleep disorders. The main hopes revealed by the respondents were to stop the disease (87%), recover quality of life (72%), and improve mobility (56%).
Conclusion: This is the first study of the International Map of Axial Spondyloarthritis in Argentina. In this sample of patients with axSpA, a substantial proportion were active in their disease, although most of them were under biological treatment. The delay in diagnosis was less than that reported in other series, and we should not underestimate the anxiety and sleep disorders suffered by these patients.
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AB1022 EARLY DIAGNOSIS OF SPONDYLOARTHRITIS AND OTHER RHEUMATIC DISEASES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE STUDY BASED ON A SCREENING QUESTIONNAIRE AND EARLY REFERRAL TO THE RHEUMATOLOGIST

Keywords: Spondyloarthritis, Gastrointestinal tract, Inflammatory arthritides

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Background: Patients (pts) with inflammatory bowel disease (IBD) frequently disclose muscoloskeletal (MSK) symptoms. About 15-20% of these pts are affected by spondyloartritis (SpA) and almost 50% have mechanical back pain and non-inflammatory arthralgyas [1]. Notably, up to 30% of them may have fibromyalgic syndrome (FMS) [2], although there are limited data on this issue. Early and accurate diagnosis of articular involvement in IBD pts is crucial to allow a personalized therapeutic approach and mostly an unmet need.
Objectives: Early diagnosis of axial-SpA (Ax-SpA) and peripheral SpA (p-SpA) in IBD pts with MSK symptoms and definition of other rheumatologic causes of pain in these complex pts.
Methods: A prospective cohort of IBD outpatients without a previous clear diagnosis of rheumatic disease was evaluated with the self-administered DETAIL questionnaire [3], which has been recently validated as a useful screening tool for early detection of SpA in IBD [4]. Pts with at least 3 out of 6 points of the score (the risk cohort) underwent a full clinical rheumatological evaluation and ultrasonographic (US) assessment of 6 enthesis (according to MASEI score). Pts fulfilling ASAS classification criteria were diagnosed as having p-Spa or ax-Spa. Rheumatoid arthritis (RA) and FMS were also diagnosed according to ACR 2010 criteria.
Results: 660 IBD pts were administered the questionnaire. Ninetytwo pts (14%) were selected for rheumatological evaluation: 69/92 pts (75%) were female, the median age was 48 (±12.7) years and the mean BMI was 23.8 (±3.7). Sixtyseven pts (73%) were affected by Crohn disease, 23 pts (25%) by ulcerative colitis and 2 pts (2%) had indeterminate colitis. The median disease duration was 11.6 (±9.3) years. Fiftytwo pts (56,5%) were in biologic therapy (77% with anti-TNF, 15,3% con Vedolizumab and 7,7% with Ustekinumab). Overall, 38/92 pts (41%) were classified as having arthritis [25 (66%) p-SpA, 11 (23%) ax-SpA, 3 (1%) RA. Notably, in 9 of these pts coexisted FMS. 54/92 pts (58.6%) of the risk cohort did not fullfill arthritis classification criteria: 32 pts (60%) were diagnosed as having osteoarthritis or aspecific arthralgias and 22 pts (41%) fullfilled FMS criteria. Notably, in the whole risk cohort there were 31 pts (41%) with FMS. Concerning US assessment, the statistical analysis only showed marginal correlation between MASEI score and ax-SpA diagnosis (p=0.086) but no correlation with p-SpA.
Conclusion: This study confirm that the DETAIL questionnaire may be a useful screening tool in order to select IBD pts needing rheumatologic evaluation and get an early diagnosis of SpA. However, our data also show that IBD pts with MSK symptoms often have other non-inflammatory rheumatic diseases. Notably, in our series US did not represent a sensitive method in identifying pts with SpA.
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AB1023 THE DIFFERENTIAL CHARACTERISTIC OF SPONDYLOARTHRITIS PATIENTS WHO CANNOT BE CLASSIFIED ACCORDING TO ASAS: RESULTS FROM THE GESPA COLOMBIAN COHORT

Keywords: Descriptive studies, Spondyloarthritis

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Background: The Assessment of SpondyloArthritis International Society (ASAS) classification criteria for SpA has changed the approach to the disease, enhancing the performance of the classification process. However, regardless of the ASAS classification criteria were developed according to a global cohort of patients, Latin American patients were not included in a significant number. SpA patients from our region have unique characteristics that may impact the SpA classification. Other alleles than HLA-B27 have been identified, the frequency of HLA-B15 was reported to be 19.1% in the Latin American SpA population [1], compared to 3.3% in the healthy population [2].
Objectives: The aims of our study were to describe the demographics, clinical, genetic characteristics, and metrology of patients diagnosed with SpA by a rheumatologist but who did not meet ASAS classification criteria and compare them to patients who fulfilled ASAS classification criteria.

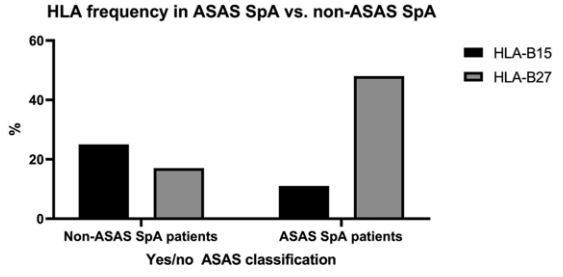
Methods: A longitudinal and analytic study was conducted on a cohort of Colombian SpA patients. Patients were evaluated in a SpA clinic at two institutions from 1990 to the present. All patients were classified according to ASAS. Patients included before 2011 were reclassified according to ASAS by a group of two rheumatologists.
Results: We enrolled 473 SpA patients; of these, 437 (92.39%) fulfilled ASAS classification criteria, and 37 (7.6%) had a diagnosis by rheumatologists but did not fulfil ASAS classification criteria for neither axial or peripheral SpA. There were no differences in gender distribution between both groups (table 1). Patients who did not fulfill ASAS classification had a lower frequency of enthesitis (36.1% vs. 79.2%, P = 0.00), dactylitis (5.6% vs. 19%, P = 0.04), arthritis (30.6 vs. 71.6%, P = 0.00), and lower frequency of history of infections preceding SpA onset (2.8% vs. 27.9%, P = 0.01) than patients classified by ASAS, respectively. There were no differences in the frequency of uveitis, psoriasis, inflammatory spinal pain, or familiar history of SpA (P = 0.3). The frequency of SpA with axial symptoms at the onset of the disease was higher in patients unclassified by ASAS (Table 1). Non-ASAS SpA patients had a higher frequency of HLA-B15 (25% vs. 11.8%, P = 0.01), and lower frequency of HLA-B27 (16.7% vs. 48.2%, P = 0.01) than ASAS SpA patients, respectively (Graphic 1). The BASFI and BASDAI were comparable between two groups (Table 1)
Conclusion: Most patients diagnosed as SpA by rheumatologists in a Colombian cohort fulfilled ASAS classification criteria. Only 7% did not fulfil the criteria. Of these patients, the demographic characteristics, disease activity and functional compromise were comparable to patients classified by ASAS. Interestingly, the frequency of HLA-B15 is high in both groups, but it is significantly higher in unclassified individuals. These results highlight the significance of HLA alleles other than HLA-B27 and their potential diagnostic value for SpA in LatinAmerica.

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Table 1.

		Not fulfilling ASAS criteria	Fulfilling ASAS criteria	P value
	Total	36	437	
	Female	11 (30.6%)	154 (35.2%)	0.57
	Age at symptoms onset	28 (24.8 - 38)	27 (21 - 35.7)	0.27
ASAS classification	Axial		257 (58.8%)	
	Peripheral		180 (41.2%)	
	History of infection	1 (2.8%)	122 (27.9%)	0.01
	Inflammatory spinal pain	15 (41.7%)	249 (57%)	0.08
Disease onset	Axial	20 (57.1%)	155 (35.5%)	0.02
	Peripheral	9 (25.7%)	164 (37.5%)	0.02
	Mixed	6 (17.1%)	118 (27%)	0.02
	BASFI	6.05 (3.3 - 7.9)	5.1 (3.2 - 6.9)	0.23
	BASDAI	6.2 (3.9 - 8.2)	5.6 (3.4 - 7.4)	0.30
	VSG	15 (5 - 21)	15 (7 - 29.8)	0.09
	PCR	0.335 (0.1 - 1.6)	0.53 (0.2 - 5.1)	0.13



Graphic 1.

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AB1024

IMPACT OF DISEASE ACTIVITY ON FUNCTIONAL IMPAIRMENT IN PATIENTS WITH SPONDYLOARTHRITIS IS DIFFERENT ACCORDING TO THE DEGREE OF RADIOGRAPHIC PROGRESSION: RESULT FROM SNUH-AS COHORT

Keywords: Spondyloarthritis, Motor function

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Background: Although previous studies suggested that physical functioning is largely driven by disease activity in patients with spondyloarthritis (SpA), its relationship to radiographic progression has not been thoroughly investigated.
Objectives: The aim of this study was to investigate whether the effect of disease activity on physical function varies according to the radiographic progression in SpA patients.
Methods: This cross-sectional study used baseline data from the patients in a single-center, prospective cohort of SpA. Disease activity was assessed through Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS). Physical function was measured using Bath Ankylosing Spondylitis Functional Index (BASFI) and functional impairment of the patients was defined as BASFI ≥4. Radiographic progression of SpA was assessed using modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). Clinical factors related to functional impairment of the patient were investigated using logistic regression analysis.
Results: A total of 221 patients were analyzed. Mean (SD) age at baseline was 43.4 (14.1) yeas and 176 (79.6%) were male. Mean (SD) disease duration of the included patients was 7.5 (9.5) years. Remission or low disease activity (LDA, ASDAS-CRP < 2.1) was achieved in 149 (67.4%) patients. Mean (SD) mSASSS was 19.5 (20.6) and 96 (43.4%) patients had at least one syndesmophyte on baseline spinal radiographs. At the baseline, functional impairment was present in 41 (18.6%) patients. Univariable analysis showed that older age at diagnosis, shorter disease duration based on two years, and higher ASDAS-CRP were associated with functional impairment. Although the effect of ASDAS-CRP on the outcome was consistent in the multivariable analysis (adjusted OR 2.46 [95% CI 1.70-3.58]), it was significantly different according to the severity of radiographic progression (*P* value for interaction = 0.001). In the absence of bridging syndesmophyte, increase in ASDAS-CRP was associated with more frequent functional impairment (adjusted OR 5.12 [2.61-10.05]). By contrast, in the subgroup of patients with bridging syndesmophyte, ASDAS-CRP did not increase the likelihood for functional impairment (adjusted OR 1.14 [0.70-1.86]). In fact, in the subgroup without bridging syndesmophyte, no patient with LDA showed a functional impairment. However, in advanced patients with bridging syndesmophyte, the rate of functional impairment was 23.8% despite achieving LDA. (Figure 1)

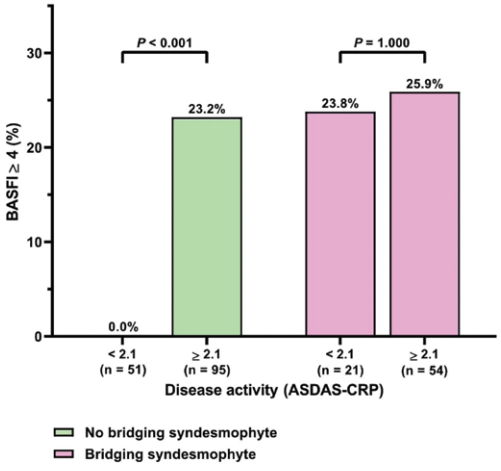


Figure 1.

Conclusion: In the presence of advanced radiographic progression, low disease activity was not significantly associated with less functional impairment in patients with SpA, which suggests that early diagnosis and optimal treatment are critical for better physical function.

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AB1025

ASSESSING THE DIFFERENCE BETWEEN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN A TWO-CENTER DESCRIPTIVE STUDY WITH MEXICAN PATIENTS

Keywords: Geographical differences, Spondyloarthritis, Descriptive Studies

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Background: Spondyloarthritis (SpA) is a group of inflammatory rheumatic diseases that have some key features in common. According to ASAS, this condition is classified into three main disease groups: radiographic axial SpA (r-AxSpA), non-radiographic axial SpA (nr-axSpA), and peripheral SpA (pSpA). All patients with SpA with predominantly axial involvement are considered to have axial SpA, patients with significant radiographic sacroiliitis according to the modified New York criteria have r-axSpA. Patients without radiographic sacroilitis but with axial disease have nr-axSpA. More information is needed about the difference between these groups, especially in other populations like ours.

Objectives: The objectives of this study are to systematically compare the demographic, clinical, and laboratory characteristics, disease onset, and physical examination findings of patients with r-AxSpA and nr-AxSpA; and identify factors that could predict a subtype of the disease.

Methods: Data from 148 patients over 18 years collected between 1998 and 2005 from Hospital General de México and Instituto Nacional de Ciencias Médicas y Nutrición. Patients classified according to ASAS criteria. We selected patients with nr-AxSpA and r-AxSpA and compared, clinical, demographic, and clinimetric variables. Logistic regression analysis was applied to identify the parameters associated with r-AxSpA or nr-AxSpA. Exclusion criteria included patients under biologic treatment.

Results: This study included 148 adult Mexican patients; general characteristics are exposed in table 1. HLA-B*27 was present in 57% of patients. Patients with nr – AxSpA were more women (41.4% vs 21.8%; P <0.05), with less presence of HLA-B27 (54.3% vs 92.7%, P < 0.05) compared to the r – axSpA group. R-AxSpA patients were younger at symptom onset (16 vs. 21 years; P < 0.01) than nr – axSpA (Image 1). Patients with nr – AxSpA had more history of infection preceding disease onset (32.9% vs 9.1%; P < 0.05), and less frequency of uveitis (10% vs 25.5% P < 0.05), more dactylitis (12.9% vs. 0%, P < 0.01), less painful entheses (3 vs. 6 P < 0.01), and less axial enthesopathy (1 vs. 4 P < 0.05) than r-AxSpA patients. The measures of thoracic expandability, modified Schober, right and left flexion test, were significantly lower in r-AxSpA group than in the nr-AxSpA group, p < 0.01). patients with r-AxSpA had higher Bath Ankylosing Spondylitis Functional Index (BASFI) (4.8 vs 2.9%; P < 0.01), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (5.2 vs 4.1; P < 0.01), Dougados functional index (14% vs 7%; P < 0.05) than nr – AxSpA. Logistic regression shows that the factors that most influence the presentation of r-AxSpA are the history of uveitis (OR 14, 95% CI 2.3-85), HLA-B27 (OR 7, 97, 95% CI, 2.96-122), gender (male) (OR 6.16, 95% CI, 1.47-25.7), axial enthesopathy count (OR 1.17 95% CI, 1.03-1.33). The history of infection is a protective factor against radiographic disease (OR 0.19, 95% CI 0,04 – 0,91).

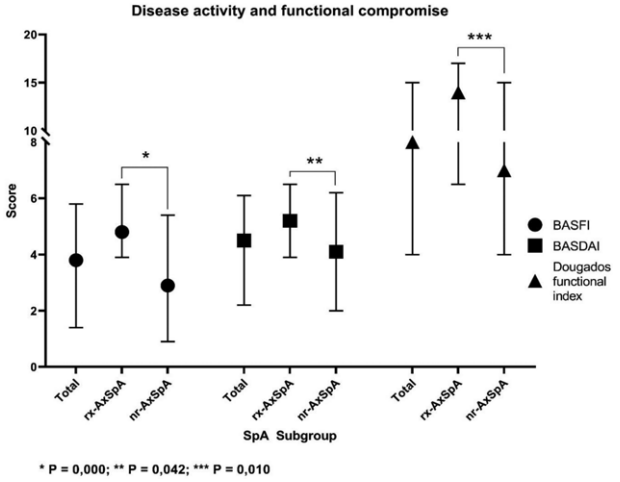
Conclusion: This study provides insight into the differences that may affect the prediction of radiographic progression in patients with nr-AxSpA. We found that patients with radiographic disease had a younger age of presentation, mostly male, higher prevalence of HLA-B27, more history of uveitis, fewer episodes of dactylitis, more axial enthesopathy, and higher disease activity.

Table 1

Table 1. Patient characteristics and disease course

	Total SpA	r-AxSpA	nr-AxSpA	pSpA
Total, n (%)	*148*	55 (37.2)	70 (47.3)	23 (15.5) Δ
Age at symptom onset (yrs)	*20 (14 – 26)*	16 (12 – 21) Δ	21 (17 – 28) Δ	24 (13 – 27) Δ
Age at diagnosis (yrs)	*23 (17 – 29)*	19 (16 – 26)	26 (18 – 33)	24 (17 – 30)
Delay in diagnosis (yrs)	*2 (0 – 5)* ◊	3.5 (0 – 7) ◊	1.5 (0 – 5)	1 (0 – 3)
Men (%)	103 (69.8)	43 (78.2) ¥	41 (58.6) ¥	19 (82.6)
Male:Female ratio	*2.3:1*	3.6:1	1.4:1	4.8:1
HLA-B27	*85 (57.4%)*	38 (92.7%) ¥	38 (54.3%) ¥	9 (60%) ¥

¥ P<0.05, † P<0.001, Δ P<0.0001, ◊ P>0.05 *BMI:* Body mass index; *r-AxSpA:* radiographic AxSpA*; nr-AxSpA:* non-radiographic AxSpA; *pSpA*: Peripheral SpA.



Graphic 1.

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Disclosure of Interests: None Declared.

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AB1026

THE TIME OF INTESTINAL BOWEL DISEASE ONSET IS ASSOCIATED WITH THE PHENOTYPE AND DIAGNOSIS IN PATIENTS WITH SPONDYLOARTHRITIS. RESULTS FROM REGISPONSER REGISTRY

Keywords: Gastrointestinal tract, Spondyloarthritis

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Background: Our group has evaluated the impact of the time of appearance of some extramusculoskeletal manifestations in spondyloarthritis. However, we still need to know more about the impact of both the inflammatory bowel disease (IBD) itself and its moment of appearance with respect to rheumatic symptoms.

Objectives: a) to compare SpA characteristics in patients with and without IBD and b) To compare the clinical characteristics and the rheumatologist's diagnosis in SpA patients with IBD according to the onset of IBD (before vs. after the appearance of rheumatic symptoms).

Methods: This was a cross-sectional study with data extracted from the REGISPONSER (Spondyloarthritis Registry of the Spanish Rheumatology Society) registry. Dates of SpA and IBD onset were available. Two groups were classified depending on the time of appearance of IBD (before or after rheumatic symptoms). The clinical characteristics, disease activity, radiographic damage, functional ability and rheumatologists' diagnoses were compared between the

two groups. Univariate and multivariate logistic regressions were conducted to evaluate the factors associated with each group and chi-square test to evaluate differences in phenotype and rheumatologists' diagnoses.
Results: A total of 123 of 2367 (5.2%) patients included in the REGISPONSER registry were diagnosed with IBD but 20 patients did not have available date of IBD onset. There was less prevalence of HLA-B27, psoriasis and dactylitis, and less frequency of uveitis in patients with IBD vs patients with SpA without IBD. Moreover, these patients were younger and had less disease duration, and less disease activity (by ASDAS and BASDAI indexes) and functional ability (by BASRI index). Among patients with IBD, 54 (52.4%) already had IBD at the moment of rheumatic symptoms onset, while 49 patients (47.6%) began with IBD after the SpA onset. Peripheral phenotype [10 (18.5%) vs 1 (2%)] was more frequently observed in patients who had been already diagnosed of IBD when rheumatic symptoms began while axial involvement had a lower prevalence [25 (46.3%) vs 33 (67.3%)]. There also were significant differences in rheumatologist's diagnosis in these patients, with a less frequency of ankylosing spondyloarthritis diagnosis [31 (57.5%) vs 42 (85.7%)] in the first group. After performing a multivariate analysis with demographic and clinical characteristics, we obtained a shorter diagnosis delay [0.90 (CI95% CI 0.82-0.98)] and a less prevalence of HLA-B27 antigen [0.19 (CI95 % 0.07-0.52)] in the former group.
Conclusion: SpA patients with IBD have a less severe disease with less prevalence of extramsuculoskeletal imanifestations. When IBD began before the rheumatic symptoms, it was associated to an earlier diagnosis and a more frequent peripheral phenotype.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1027 CHARACTERISTICS OF UVEITIS IN SPONDYLOARTHRITIS IN A MULTICENTER STUDY IN MOROCCO

Keywords: Uveitis, Spondyloarthritis

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Background: Uveitis is the most common extra-articular manifestation of Spondyloarthritis (SpA).
Objectives: The aim of this study was to determine the prevalence of uveitis in patients with SpA in a multicenter series and to identify factors associated with its occurrence.
Methods: A multicenter descriptive analytical study, including patients followed for SpA in 8 rheumatology departments from 6 different regions in Morocco. All data were measured by standard instruments. Demographic, clinical, paraclinical and therapeutic data of the disease were collected. Disease activity was assessed by BASDAI and ASDAS-CRP scores. Data analysis was done by SPSS.20 software, the p significance level was set at 0.05.
Results: The study had included 700 patients followed for SpA, 54% of whom were men. The mean age at diagnosis was 40.42 + 14.19 years. The average diagnosis delay was 59.76 months. The percentage of patients who smoked was 15.6%. A family history of SpA was noted in 11.7%. SpA was non-radiographic in 14% of cases. Bilateral sacroiliitis was described in 49.4%. Coxitis was present in 32.5%. Juvenile SpA represented 15.5% of cases. The prevalence of HLA-B27 was 65.51%. Systemic involvement was dominated by uveitis (11.3%), it was unilateral in 59.5%, bilateral in 28.6% and tilted in 11.9%, anterior in 95.7%. Evolution of the uveitis was acute in 88.9% and chronic in 11.1%. The mean of BASDAI and ASDAS ware 4.42 ±1.67 and 3.19 ±1.24 respectively. The mean CRP and erythrocyte sedimentation rate (ESR) were 35.5 mg/l and 43.3mm respectively. The mean BASDAI was significantly higher in SpA with uveitis (p=0.025). Biological treatments, in particular tumor necrosis factor-α (TNF-α) inhibitors were more prescribed in patients with uveitis; 47.5% versus 30.9% in SpA without uveitis, with a significant difference (p=0.006). Uveitis was less present in SpA associated with inflammatory bowel disease (p=0.004). However, we did not find a significant association with gender (p=0.61), age at diagnosis (p=0.69), age of onset of symptoms (p=0.8), diagnostic delay (p=0, 58), smoking (p=0.06), clinical forms of SpA (p=0.71), coxitis (p=0.6), HLA B27 antigen (p=0.17), ESR (p=0.56), CRP (p=0.99) and ASDAS-CRP (p=0.51).
Conclusion: In our study, the prevalence of uveitis was 11.3%. Its presence was associated with a higher activity according to the BASDAI, and it was associated with a higher use of biological treatments.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1028 IS THERE AN ASSOCIATION BETWEEN SERUM LEVELS OF BIOMARKERS OF OSTEOPROLIFERATION AND MARKERS OF INFLAMMATION IN SPONDYLOARTHRITIS?

Keywords: Spondyloarthritis, Biomarkers

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Background: The two most studied inhibitors of the Wnt signaling pathway in spondyloarthritis (SpA) are Dickkopf-1 (DKK-1) and Sclerostin. Their dysfunction would be responsible for bone formation phenomena. Osteoprotegerin (OPG), a potent inhibitor of osteoclasts and regulated by the Wnt pathway, has also been implicated in this osteoformation phenomenon.
Objectives: Our work aimed to determine the associations between serum levels of DKK-1, Sclerostin, OPG, and markers of inflammation in SpA.
Methods: It was a cross-sectional study including patients with SpA meeting ASAS criteria. Data collected included sociodemographic and disease characteristics, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). Biomarker assays were performed using an ELISA technique.
Results: One hundred and nine patients were included, 68 men and 41 women. The mean age of the patients was 43 ± 12 years [19-79]. The mean age of disease onset was 30.6 ± 11 years [5-56]. The mean duration of SpA at inclusion was 12.6 ± 9.8 years [1 - 62]. Forty-nine percent of patients had a biological inflammatory syndrome (BIS). The mean ESR was 28.6 ± 21.2 mm/h [10 - 110 mm/h], and the mean CRP value was 15.2 ± 23.4 mg/L [1 - 153 mg/L]. Median serum levels, in pg/mL, of DKK-1, Sclerostin, and OPG were 146.7 [0-455.3], 32.8 [0-488], and 471 [0-1613.6], respectively. The biological inflammatory syndrome was not associated with DKK1 level (p=0.800). It tended to be associated with OPG and Sclerostin levels (p=0.085 and p= 0.051, respectively). ESR was negatively correlated with Sclerostin (r=-0.222; p=0.022). The CRP level appeared to be negatively correlated with OPG (r=-0.161; p=0.099) and Sclerostin levels (r=-0.181; p=0.064).
Conclusion: An association between markers of inflammation and inhibitors of the wnt signaling pathway as well as OPG was shown by our study, suggesting that actors of systemic inflammation may influence the secretion of these biomarkers.
REFERENCES: NIL.
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Disclosure of Interests: None Declared.
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AB1029 THE RELATIONSHIP BETWEEN THE PRESENCE OF ISCHIAL ENTHESITIS AND OTHER RADIOLOGICAL INVOLVEMENTS AND PERIPHERAL ENTHESITIS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Enthesitis, Spondyloarthritis

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Background: Sacroiliac radiographs in axial spondyloarthritis (axSpA) allow the evaluation of sacroiliac and hip joint involvement, as well as the symphysis region and ischial enthesis regions. In this study.
Objectives: It is planned to test and review the relationship between the presence of ischial enthesitis and disease-related factors, the presence of peripheral enthesitis and other radiological features of involvement.
Methods: Of 355 patients with axSpA diagnosis and follow-up sacroiliac joint radiography evaluated for ischial enthesitis were included in the study. Since the presence of ischial enthesitis was detected in 1 patient in non-radiographic axSpA patients, the analysis was performed with radiographic axSpA patients. Demographic, clinical and laboratory characteristics of the patients were recorded. Irregular appearance in the region where tendons and ligaments attach to the bone (lower region) in the pubic arms in the sacroiliac joint X-ray was evaluated as ischial enthesitis. Radiological evaluation was performed by a rheumatologist (EDE) and a radiologist (AS). The relationship between the presence of ischial enthesitis and other factors was tested with both univariate and multivariate analysis methods.
Results: The mean age at diagnosis (±SD) was 42 (11.9) and 74% of the patients included in the study were male. Demographic and radiological characteristics of the study group are summarized in Table 1. Ischial enthesitis was detected in 57 (16.1%) patients. Gender (p=0.006), symptom duration (p<0.001), duration of diagnosis (p=0.002), HLA-B27 positivity (p=0.09), radiographic hip involvement (p=0.09) total sacroiliac joint score (p<0.001), baseline cervical mSASS score (p<0.001), basal lumbar mSASS score (p<0.001), presence of symphysis (p<0.001), serum CRP level (p=0.014) found to be associated with ischial enthesitis in univariate analysis. There was no correlation between the presence of ischial enthesitis and heel pain (p=0.61) or SPARCC enthesitis score (p=0.59). In the two models established in the multivariate analysis, serum CRP level (p=0.022), presence of cervical syndesmophyte (p=0.042), presence of total ankylosis in the sacroiliac joint (p=0.012) and SIE score (p=0.001) were found to be independent variables associated with the presence of ischial enthesis.
Conclusion: Although ischial enthesitis can be seen independently of clinical heel pain in axSpA patients, it can also be an indicator of radiographic damage.

Table 1. Demographic and radiological characteristics of axSpA patients

All patients (n=355)		İschial enthesitis(+) (n=57)	İschial enthesitis (-) (n=298)	p
Age at diagnosis, mean (SD)	42.0 (11.9)	35.3 (11.9)	35.2 (12.5)	0.99
Sex, male, %	74	88.9	71.3	0.006
HLA-B27 positivity,%	65.1	82.2	61.7	0.010
Duration of symptoms, median (IQR)	13 (13)	20 (12)	12 (14)	<0.001
SIE score, median (IQR)	6 (3)	8 (1)	6 (3)	<0.001
SIE ankylosis, %	33.5	68.4	26.8	<0.001
Servical mSASS score, median (IQR)	0 (8)	9 (18)	0 (4)	<0.001
Servical syndesmophitis (+), %	43.4	77.8	35.5	<0.001
Lumbal mSASS score, median (IQR)	0 (4)	6 (30)	0 (0)	<0.001
Lumbal syndesmophitis (+), %	29.0	55.8	24.4	<0.001
Hip involvement, %	15.9	38.2	11.8	<0.001
Serum CRP level, median (IQR)	10 (20)	14 (29)	9 (19)	0.014

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AB1030 FACTORS ASSOCIATED WITH CERVICAL INVOLVEMENT PROGRESSION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis

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Background: The evaluation of cervical, lumbar spinal structures and hip joint has been important and this is reflected in the variables in the scoring systems in patients with axial spondyloarthritis.
Objectives: In this study, it was aimed to investigate the factors affecting cervical spinal progression.
Methods: The patients with the diagnosis of axSpA who were followed-up at least two years, and whose cervical mSAS scores were evaluated by servical X-ray were included in the study. A change of 1 unit or more in the modified Stoke Ankylosing Spondylitis Spine score (mSASS) between two radiographs taken at least two years apart was considered progression. Radiological evaluation was done by a rheumatologist (EDE) and a radiologist (AS). Demographic, clinical and laboratory characteristics of the patients were recorded. The relationship between the presence of cervical progression and other factors was tested with both univariate and multivariate analysis.
Results: Of the 237 patients included in the study, 62% were male and the median age at diagnosis (IQR) was 33 (14) and 68.8% of the patients were radiographic axSpA. The demographic, clinical and laboratory characteristics of the study groups were summarized in Table 1. Cervical progression was detected in 42 of the patients (17.7%) with cervical radiography in the median (IQR) 3 (2) follow-up period. Presence of cervical progression was related with symptom duration (p=0.004), age at symptom onset (p=0.011), age at diagnosis (p<0.001), presence of total ankylosis in sacroiliac joint X-ray (SIE score=8) (p<0.001), cervical mSAS score (p<0.001), total SSI score (0-8) (p<0.001), baseline cervical mSAS score (p<0.001), presence of cervical syndesmophyte (p<0.001), baseline lumbal mSAS score (p<0.001), the presence of lumbal syndesmophyte (p<0.001). Cervical progression was not associated with HLA-B27, smoking, presence of either extramusculoskeletal or peripheral involvement, baseline disease activity scores (BASDAI, ASDAS-CRP). In two different models were established in multivariate analysis, age at diagnosis(p<0.001), presence of cervical syndesmophyte (p=0.014), sacroiliac joint score (p=0.004) were associated with cervical progression.
Conclusion: It should be kept in mind that the age at diagnosis, presence of spinal involvement and sacroiliac joint score may be predictors of cervical spinal progression in the follow-up of patients in axSpA.

Tablo 1. AxSpA hastalarının demografik ve radyolojik özellikleri

	All patients	Servical progression (+)	Servical progression (-)	p
Age at diagnosis, mean (SD)	33 (14)	40 (19)	32 (13)	<0.001
Sex, male, %	62.0	76.2	58.9	0.037
HLA-B27 positivity,%	63.3	68.6	62.1	0.56
Symptom duration, median (IQR)	10 (12.3)	15 (15)	10 (11)	0.004
mNY positivity, %	68.8	88.1	64.6	0.03
Total SİE score, median (IQR)	5 (5)	7 (2.3)	4 (4)	<0.001
Baselinel servical mSASS score, median (IQR)	0 (2)	6 (15)	0 (0)	<0.001
Bazal lumbal mSASS score, median (IQR)	0 (0)	0 (18)	0 (0)	<0.001
SIE ankylosis, %	24.1	52.4	17.9	<0.001
Servical syndesmophyte, %	30.7	73.8	20.8	<0.001
Lumbal syndesmophyte, %	16.3	48.6	9.6	<0.001

Table 2. Factors associated with presence of servical spinal progression

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1031 ENDOTHELIAL DYSFUNCTION AND SUBCLINICAL ATHEROSCLEROSIS IN RADIOGRAPHIC AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHROPATHY

Keywords: Comorbidities, Cardiovascular disease, Spondyloarthritis

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease which includes radiographic subtype [ankylosing spondylitis (AS)], and non-radiographic subtype (nr-axSpA)[1]. Chronic inflammatory disorders, such as axSpA, are associated with increasing cardiovascular (CV) risk which is mainly due to the inflammatory burden[2].
Objectives: Evaluation of endothelial dysfunction and subclinical atherosclerosis in axSpA and comparison between in AS and nr-axSpA regarding disease activity, functional status and Subclinical atherosclerotic disease.
Methods: Eighty Patients fulfilling the ASAS classification criteria plus 60 healthy individuals were included in this study. Patients were divided into two groups;

50 patients with AS (GI) and 30 patients with nr-axSpA (G II), while G III was the control group. Patients with nr-axSpA were defined as the absence of definite sacroiliac (SI) joint changes on plain radiograph but with active sacroiliitis on MRI and at least one of the characteristic traits of SpA according to the 2009 ASAS criteria[3]. Demographic data, duration of the disease, delay in diagnosis, extra-articular manifestations, smoking, comorbidities and detailed medication history were taken. Disease activity were assessed by Ankylosing Spondylitis Disease Activity Score (ASDAS) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Physical function was assessed by the Bath Ankylosing Spondylitis Functioning Index (BASFI) & patient-reported outcome measures (PROMs). Serum endothelin-1 and carotid intima-media thickness (cIMT) were measured to assess endothelial dysfunction and subclinical atherosclerosis.

Results: There was no significant difference between the GI & GII regarding age and gender (p>0.05), while AS patients had longer mean disease duration than nr-axSpA (6.6 years vs 3.7 years, P < 0.001). Forty-eight patients out of 50 in G I were receiving biological therapy while 23 patients from 30 in G II were receiving biological therapy with significant difference between the two groups (p=0.02). There were no significant differences between GI and GII regarding comorbidity, and smoking status (p>0.05). Regarding disease activity; we found no significant difference between GI and GII in ASDAS-CRP (2.0±0.9, & 2.2±1.02 respectively), also there was no significant difference between GI and GII in ASDAS (3.9±1.3, & 4.1±1.1 respectively). There was no notable differences between the AS and nr-axSpA neither in BASFI nor in PROMs (p>0.05). The serum endothelin-1 was significantly elevated in both patients' groups when compared with controls (GI: 2.3±1.5, GII: 2.05±1.3, controls: 0.76±0.5) with no significant difference between GI and GII (p>0.05). When we measured cIMT we noticed a significant increase in the thickness of cIM of patients in comparison with controls (P < 0.01), while there was no significant difference between the AS and nr-axSpA (p>0.05). We found 6 AS patients had atheromatus plaque, while 4 patients had atheromatus plaque in nr-axSpA group with no significant difference between the 2 groups (p= 0.86) There was positive correlation between endotheline-1, cIMT and both ASDAS-CRP & BASFI.

Conclusion: Axial spondyloarthritis patients (either AS or nr-axSpA) had higher risks for endothelial dysfunction and subclinical atherosclerosis. patients with AS & nr-axSpA shared a comparable disease activity, functional disability and endothelial dysfunction.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1032

COURSE OF AORTIC REGURGITATION IN ANKYLOSING SPONDYLITIS – A FOLLOW-UP STUDY OF 52 PATIENTS EXAMINED WITH ECHOCARDIOGRAPHY

Keywords: Heart, Spondyloarthritis

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Background: Ankylosing spondylitis (AS) is associated with cardiac manifestations such as aortic regurgitation. However, contemporary follow-up studies are lacking.

Objectives: To investigate the course of aortic regurgitation and proximal aortic root diameter in patients with AS examined with echocardiography at baseline (2009-2011) and at follow-up (2014).

Methods: At baseline, 187 patients with AS (56% men, mean age 50 years) were examined with echocardiography, of whom 34 (18%) had an aortic regurgitation of mild to severe grade[1]. Of these 34 patients, 26 agreed to participate in a follow-up with echocardiography in 2014. In addition, we re-assessed 26 sex- and age-matched patients from the same AS cohort, but without aortic regurgitation at baseline. The presence and severity of aortic regurgitation (none, mild, moderate, severe) as well as the proximal aortic root diameter were assessed. Related-samples Wilcoxon signed rank test was used to analyze the change (Δ) in aortic root diameter from baseline to follow-up, divided by patients with and without aortic regurgitation at baseline and stratified by sex. Mann-Whitney U test was used to compare the Δ aortic root diameter in patients with and without an aortic regurgitation at baseline.

Results: In total 52 patients (54% men, mean age (SD) 62 (11)) were re-examined in 2014. The time between the baseline and follow-up echocardiography examination ranged between 3.0 to 4.7 years with a median of 4.3 years. There were no statistically significant differences in aortic root diameter between baseline and follow-up as shown in Table 1. The distribution of Δ aortic root diameter was not statistically different in patients with an aortic regurgitation at baseline compared to the patients without. The change in aortic regurgitation grade from baseline to follow-up is presented in Figure 1. Of the 26 patients with aortic regurgitation at baseline, two had a more severe grade, eight had a lower grade, and 16 an unchanged grade of aortic regurgitation at follow-up. Of the 26 patients without aortic regurgitation at baseline, two had developed a mild grade of aortic regurgitation at follow-up.

Table 1.

	Patients with aortic regurgitation at baseline (n=26)	Patients without aortic regurgitation at baseline (n=26)
ΔAortic root diameter,mm		
Overall	-1 (-3, 0.25)	-1 (-2, 1.25)
Men	-1 (-3, 2.25)	-1 (-3.5, 1.25)
Women	-0.5 (-3, 0)	0 (-1.75, 1.75)

Δ, change in aortic root diameter from baseline to follow-up. The data is presented in median (25th percentile, 75th percentile).

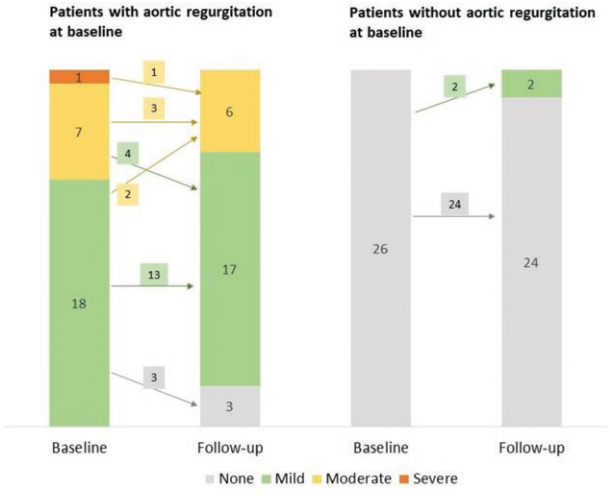


Figure 1.

Conclusion: Although aortic regurgitation like other AS related manifestations might vary over time, the majority of AS patients examined with echocardiography at baseline and after three to five years had an unchanged grade of aortic regurgitation at follow-up.

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Disclosure of Interests: Karin Bengtsson: None declared, Georgios Mourtzinis: None declared, Anna Deminger: None declared, Eva Klingberg: None declared,

Margareta Scharin Täng: None declared, Lennart T.H. Jacobsson Speakers bureau: LTHJ has received lecture and consulting fees from Novartis, Eli Lilly and Janssen (all outside the submitted work), Consultant of: LTHJ has received lecture and consulting fees from Novartis, Eli Lilly and Janssen (all outside the submitted work), Lennart Bergfeldt: None declared, Helena Forsblad-d'Elia: None declared.
DOI: 10.1136/annrheumdis-2023-eular.57

AB1033 THE RELATIONSHIP BETWEEN LONG-TERM USE OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS AND KIDNEY FUNCTION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

Keywords: Spondyloarthritis, Kidneys, Safety

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Background: Although nonsteroidal anti-inflammatory drugs (NSAIDs) are the first-line treatment for ankylosing spondylitis (AS), their effect on kidney function remains unclear.
Objectives: This longitudinal study investigated the correlation between long-term NSAID use and kidney function in patients with AS using electronic medical records.
Methods: The electronic medical records of 1,280 patients with AS collected from a single center between January 2001 and December 2018 were reviewed. The Assessment of Spondyloarthritis International Society (ASAS) NSAID Intake Score was used to determine the cumulative dose of all NSAIDs prescribed for a different time intervals. Each ASAS NSAID Intake Score was obtained for intervals of 6 months, 1 year, 2 years, 3 years, 5 years, and 10 years. The correlation between the ASAS NSAID Intake Score and final estimated glomerular filtration rate (eGFR) for each interval was investigated.
Results: The mean ASAS Intake Scores for 6-month, 1-year, 2-year, 3-year, 5-year, and 10-year intervals were 55.30, 49.28, 44.84, 44.14, 44.61, and 41.17, respectively (Figure 1). At each interval, the pearson correlation coefficients were -0.018 (95% CI: -0.031 – -0.006, p=0.004), -0.021 (95% CI: -0.039 – -0.004, p=0.018), -0.045 (95% CI: -0.071 – -0.019, p=0.001), -0.069 (95% CI: -0.102 – -0.037, p<0.001), -0.070 (95% CI: -0.114 – -0.026, p=0.002), -0.019 (95% CI: -0.099 – 0.062, p=0.645), respectively. There was a very weak negative relationship between ASAS Intake Score and eGFR at each interval.
Conclusion: Long-term NSAID use did not correlate with kidney function based on real-world data in patients with AS.

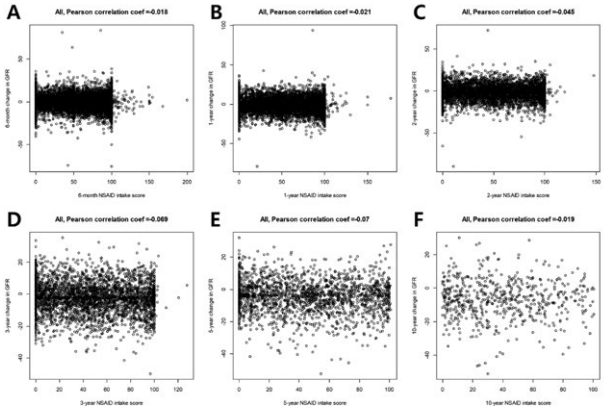


Figure 1. Scatter plots for NSAID intake score and eGFR changes of 6 months (A), 1 year (B), 2 years (C), 3 years (D), 5 years (E), and 10 years (F) interval in overall patients.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1034 COSTOVERTEBRAL JOINTS INVOLVEMENT IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: A CASE-SERIES COMPUTED TOMOGRAPHY STUDY

Keywords: Spondyloarthritis

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Background: The involvement of the costovertebral joints (CVJ) and its radiographic patterns in patients with radiographic axial spondyloarthritis (rAxSpA) and thoracic pain were described more than three decades ago, however the extent and details of structural damage in the CVJ have never been assessed.
Objectives: To evaluate structural changes of CVJ in patients with rAxSpA using available computed tomography (CT) studies.
Methods: Available chest or thoracic spine CT studies of 17 patients with rAxSpA and 17 patients with rheumatoid arthritis (RA) were analyzed. Ankylosis, erosions, joint space narrowing and osteophytes of both components of the CVJ, including head-vertebral joints (HVJ) and costotransverse joints (CTJ), were noted and compared between patient groups. The distribution of the structural changes of the CVJ along the thoracic spine was assessed.
Results: The groups were similar by patients' average age, but the rAxSpA group included more males (11/17) compared to the RA group (4/17, p=0.036). In all, 748 CVJ were assessed in each patient group, including 408 head-vertebral joints (HVJ) and 340 costotransverse joints (CTJ). rAxSpA patients had significantly more total CVJ lesions (p<0.001 for all comparisons), more lesions in the HVJ (p<0.001, for all comparisons), and more lesions in the CTJ (p≤0.005, for all comparisons, except for osteophytes), compared to RA group. All types of lesions, including ankylosis, erosions, narrowing, and osteophytes, were seen more frequently in rAxSpA patients. Joint space narrowing and ankylosis of the CVJ were the most frequently seen findings in rAxSpA and were distributed throughout the thoracic spine.
Conclusion: Structural pathology of the CVJ was more commonly observed in patients with rAxSpA than in RA patients in this study.
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Table 1. CVJ changes in patients with rAxSpA and RA

	All joints			Head-Vertebral joints			Costotransverse joints		
	rAxSpA	RA	*p*	rAxSpA	RA	*p*	rAxSpA	RA	*p*
Ankylosis	159	8	<0.001	91	5	<0.001	68	3	<0.001
Erosions	65	6	<0.001	47	6	<0.001	18	0	0.001
Narrowing	220	100	<0.001	150	58	<0.001	70	42	0.005
Osteophytes	77	32	<0.001	72	31	<0.001	5	1	NS
Scored joints	748	748		408	408		340	340	

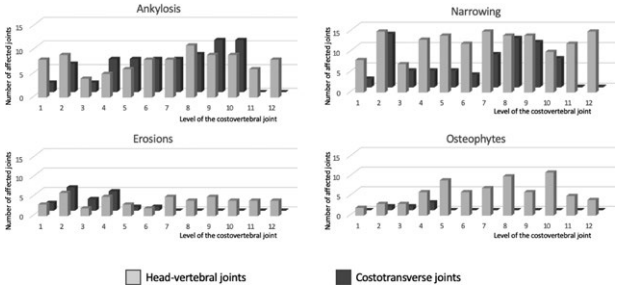


Figure 1. Involvement of CVJ in patients with rAxSpA, per thoracic vertebral level

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Spondyloarthritis - clinical aspects (other than treatment)

AB1035 TRANSLATION AND CROSS-CULTURAL ADAPTATION OF THE ASAS HEALTH INDEX ENVIRONMENTAL FACTORS ITEM SET INTO SWEDISH AND ASSESSMENT OF RELIABILITY OF THE SWEDISH VERSIONS OF ASAS HEALTH INDEX AND ENVIRONMENTAL FACTORS ITEM SET

Keywords: Outcome measures, Spondyloarthritis, Quality of life

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Background: The impact of axial spondyloarthritis (axSpA) on health-related quality of life can be substantial[1], affecting both physical and mental health[2]. There is a need to assess the effect with disease-specific instruments. A global collaboration developed the Assessments of SpondyloArthritis international Society Health Index (ASAS HI) and Environmental Factors Item Set (EFIS). These instruments measure everyday function and health across aspects typical and relevant for patients with axSpA[3]. These instruments have been translated into 35 languages[4] but only the ASAS HI component has been translated into Swedish.

Objectives: To translate and culturally adapt EFIS into Swedish, and to assess reliability of the Swedish ASAS HI and EFIS.

Methods: Patients with axSpA were recruited from the rheumatology clinic at Sahlgrenska University Hospital, Sweden. ASAS HI and EFIS contain 17 and 9 items respectively, with dichotomous response options; "I agree" or "I do not agree". The total sum of ASAS HI ranges from 0 to 17, lower score indicating better health status. EFIS does not provide a sum score due to its multidimensional nature. Translation and cultural adaptation of EFIS was carried out using a forward–backward procedure consisting of: Initial translation; synthesis of the translations; back translation; expert committee review; field testing with cognitive debriefing[5]. The translations were performed separately by translators with clinical perspective and professional translators with no medical or clinical background. Reliability was analysed by internal consistency, evaluated with the Cronbach's alpha coefficient for ASAS-HI, and test-retest reliability using the intraclass correlation coefficient (ICC) for ASAS-HI (sum-score) and EFIS (discrete items).

Results: Ten patients were recruited to the field test and 61 patients to the reliability study of which 53 (87%) returned a second questionnaire after 1 week and were included in the test-retest reliability study (Table 1). *Translation and cross-cultural adaptation of the EFIS*. The translators produced a prefinal Swedish version of EFIS. The field test was performed in 10 patients and resulted in minor rewording. *Internal consistency.* ASAS HI scores showed an acceptable internal consistency; Cronbach's alpha 0.79. *Test-retest reliability.* ASAS HI sum score showed excellent reliability; ICC (95% CI) 0.87 (0.78-0.93), P-value <0.001. ASAS EFIS individual items reliability ranged from poor for item 2, 3 and 8 to excellent for item 1 and 9; ICC (95% CI) from -0.43 (-0.83 to 0.41), P-value 0.56, to 0.89 (0.81 to 0.94), P-value <0.01.

Conclusion: A Swedish version of EFIS has been produced and uploaded on ASAS website[4]. The Swedish version of ASAS-HI showed acceptable internal consistency and excellent test- retest reliability. Test-retest reliability for individual items of EFIS varied from poor to excellent.

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Table 1. Description of the participating patients.

	Field test n=10	Internal consistency n=61	Test-retest reliability n=53
	Median (min-max)	Median (min-max)	Median (min-max)
Sex, male n (%)	5 (50%)	36 (59%)	33 (62%)
Age, years	58 (31-76)	63 (43-80)	63 (43-80)
BASDAI, score	4.4 (0.7-8.0)	3.3 (0.4-7.9)	3.2 (0.4-7.9)

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1036 FACTORS ASSOCIATED WITH HIP INVOLVEMENT IN SPONDYLOARTHRITIS

Keywords: Epidemiology, Enthesitis

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Background: Hip involvement in spondyloarthritis determines a large part of the functional prognosis and affects negatively the patient's life. Identifying these factors could influence our management strategy by developing specific therapeutic protocols.

Objectives: The objective of this work is to determine the factors associated with hip involvement during spondyloarthritis.

Methods: The study is a single-center prospective observational study, carried out during the period extending between January 2020 and January 2022. Spa patients meeting the criteria for ASAS were included. On a patient-by-patient basis, clinical, biological, and imaging data were collected.

Results: In total, 259 patients with consecutive spondyloarthritis were assessed. Of these, 80 patients (30.88%) had hip involvement associated with spondyloarthritis, including 66 men and 14 women (gender ratio = 4.7), with an average age of 37.66 and 11.3 years. It was bilateral in 70% of cases, and inaugural in over half of patients (55% of cases). The biological inflammatory syndrome was observed in 72.5% of cases and HLA B 27 was found in ¾ of patients. The anatomio-radiological forms observed were: the destructive form (36.76%), the condensant constructive form (22.05%), the initial form (24.26%), and the synostotic form (16.91%). TNF alpha treatment was initiated in 85% of cases, with a third of patients receiving PTH. Factors related to hip involvement were: functional impotence (BASFI), limitation of spinal and joint mobility (BASMI, inter-malleolar distance), structural damage to the SpA (total BASRI), presence of HLA B27, and initiation of anti-TNF alpha treatment. On the other hand, the age of hip involvement and spa, gender, bilateral involvement, high scores of the BASDAI and ASDAS indices, and the presence of a biological inflammatory syndrome did not seem to be involved.

Conclusion: The occurrence of hip involvement during spondyloarthritis seems to be frequent in our country. Hip involvement is one of the elements of poor prognosis and its presence predicts a severe form of the disease.

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Disclosure of Interests: None Declared.
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AB1037 ARE THE CLINICAL SCALES USED TO ASSESS DISEASE ACTIVITY AND FUNCTIONAL ABILITY IN AXIAL SPONDYLOARTHROPATHY REALLY RELIABLE?

Keywords: Spondyloarthritis

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Background: Evaluation of disease activity and functional impairment in Axial spondyloarthritis (AxSpA) are important in therapeutic plan. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS) and The Bath Ankylosing Spondylitis Functional Index (BASFI) scores are based largely on subjective measures, which liable to change depending on patient's expression, culture, and awareness.
Objectives: Assessment of reliability of BASFAI, BASDAI, ASDAS-ESR, and ASDAS-CRP as a total score and individual questions in patients with AxSpA.
Methods: This cross-sectional study was conducted on 103 patients with AxSpA according to the ASAS classification criteria for AxSpA. Each patient completed BASFAI, BASDAI, ASDAS-ESR, and ASDAS-CRP during their routine visit for follow up with one rheumatologist. Then the same patients completed the three questionnaires again in the same day or on the second day with another rheumatologist.
Results: Internal consistency and reliability of ASDAS-ESR, ASDAS-CRP, BASDAI, and BASFAI scores was good (ICC was 0.841, 0.820, 0.767, and 0.852 respectively). Reliability of BASFAI score was better than that of ASDAS-ESR, ASDAS-CRP, BASDAI scores, and that of ASDAS-ESR, ASDAS-CRP was better than reliability of BASDAI score.

Table 1. Interclass Correlation Coefficient of BASFAI in AxSpA patients reported by observer 1 and observer 2

Variables	Cronbach's Alpha	ICC	CI
1) Putting on your socks or tights without help or aids (e.g sock aid) (F1).	0.931	0.871	0.815-0.911
2) Bending from the waist to pick up a pen from the floor without aid (F2).	0.903	0.823	0.749-0.877
3) Reaching up to a high shelf without help or aids (e.g helping hand) (F3).	0.837	0.719	0.612-0.801
4) Getting up from an armless chair without your hands or any other help (F4).	0.751	0.601	0.462-0.711
5) Getting up off the floor without help from lying on your back(F5).	0.779	0.638	0.508-0.740
6)Standing unsupported for 10 minutes without discomfort (F6).	0.707	0.547	0.396-0.669
7) Climbing 12-15steps without using a handrail or walking aid (F7).	0.863	0.760	0.664-0.831
8) Looking over your shoulder without turning your body (F8).	0.887	0.798	0.715-0.858
9)Doing physically demanding activities (e.g physiotherapy exercises, gardening or sports) (F9).	0.817	0.690	0.573-0.779
10) Doing a full day's activities whether it be at home or at work (F10).	0.748	0.598	0.458-0.709
Total BASFAI Score	0.920	0.852	0.789-0.898

ICC (.21 to.4) was indicative of fair agreement, ICC (.41 to.6) was indicative of moderate agreement, ICC (.61 to.8) was indicative of substantial agreement, ICC (.81 to.99) was indicative of almost perfect agreement, and ICC (1) was indicative of perfect agreement.

Conclusion: Some questions of ASDAS, BASDAI, and BASFAI scores are more reliable than others, this depends on the question. The answers of the questions that assess sensation of pain, are liable to change. While the answers of other questions that assess stiffness or assess its duration are less liable to change. Questions that assess certain daily activity are more reliable than that assess the ability to do more than one activity.
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Acknowledgements: NIL.
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AB1038 RELATIONSHIP BETWEEN ANKYLOSIS AND PHYSICAL FUNCTION ASSESSMENT IN ANKYLOSING SPONDYLITIS

Keywords: Quality of life, Spondyloarthritis, Patient reported outcomes

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Background: Ankylosing spondylitis (AS) is a progressive inflammatory disease affecting the spine and large joints of the extremities. Ankylosis of the spine and sacroiliac joints affects patients not only physically but also psychologically and socially, resulting in a significant decline in quality of life (QOL) and disruption of daily activities [1]. However, it is unclear to what extent the progression of the disease affects physical function and patient subjective evaluation.
Objectives: The purpose of this study was to investigate the relationship between the degree of progression of ankylosis, physical function, and frailty in patients with AS.
Methods: Twenty-four patients with AS attending our hospital who underwent full spine computer tomography (CT) and physical function assessment were included in the study. The anterior-posterior, intervertebral joint, and interspinous process ankylosis sites and number of ankylosis (whole spine/cervical spine/thoracic spine/lumbar spine) and sacroiliac joint ankylosis were evaluated in each vertebra. Patient-objective measures of physical function included gait speed, grip strength, Timed Up and Go test (TUG), time of five sit-to-stand, and Bath Ankylosing Spondylitis Metrology Index (BASMI), and patient-subjective measures of physical function included Bath Ankylosing Spondylitis Functional Index (BASFI), Kihon Checklist (KCL), the 25-question Geriatric Locomotive Function Scale (GLFS-25), and Beck Depression Inventory (BDI-II) as subjective assessments. Spearman's rank correlation coefficient was used to analyze the correlation between the degree of progression of ankylosis and each of the assessment items.
Results: The mean age (± standard deviation) at the time of the study was 40±15 years, 79% were male, 50% were HLA-B27 positive, and the disease duration was 13±9 years. Age was significantly correlated with the number of thoracic spine ankylosis (r=0.449), and disease duration with the number of total spine/cervical spine/thoracic spine/sacroiliac joint ankylosis (r=0.600/0.553/0.635/0.510). BASMI, an objective patient assessment, showed a significant correlation with the number of total spine/cervical spine/thoracic spine/lumbar spine ankylosis (r=0.732/0.653/0.707/0.615), but not with walking speed, grip strength, TUG, or time of five sit-to-stand. BASFI, a subjective patient assessment, showed a significant correlation with the number of total spine/ cervical spine/ thoracic spine/ lumbar spine ankylosis(r=0.680/0.729/0.600/0.469), and the GLFS-25 (r=0.418/0.500) with the number of total spine/ cervical spine ankylosis. BDI-II, an assessment of psychiatric symptoms, and KCL, an assessment of frailty, showed no correlation with the number of ankylosis.
Conclusion: BASFI and GLFS-25, physical function assessments, were significantly correlated with spinal ankylosis in AS patients, and the degree of progression of spinal ankylosis was found to interfere with daily life.
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Table 1. Relationship between Ankylosis and Physical Function

	Total spine	Cervical spine	Thoracic spine	Lumbar spine	Sacroiliac joint
Age	.394	.449*	−.324	−.239	−.126
Disease duration	.600**	.553*	.635**	.332	.510*
BMI	.221	.180	.170	.272	−.093
BASFI	.680**	.729**	.600**	.469*	.219
BASMI	.732**	.653**	.707**	.615**	.364
Grip strength	.227	.180	.227	.009	−.060
five sit-to-stand	−.004	−.104	.023	.026	.295
Gait speed	.035	−.022	.068	−.218	.139
TUG	.370	.436	.287	.115	.330
BDI-Ⅱ	.145	.217	.079	−.001	.027
GLFS-25	.418**	.500**	.332	.289	.219
KCL	.329	.259	.287	.369	.301

BMI: Body mass index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; TUG: Timed Up and Go test; BDI-Ⅱ: Beck Depression Inventory-Ⅱ: GLFS-25: the 25-question Geriatric Locomotive Function Scale; KCL: Kihon Checklist.

* <0.05 ** <.001

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Disclosure of Interests: None Declared.
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AB1039 A COMPARATIVE STUDY TO ASSESS THE DIFFERENCES IN DISEASE CHARACTERISTICS IN PATIENTS WITH NON-RADIOGRAPHIC AND RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Descriptive studies, Inflammatory arthritides

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Background: Spondyloarthritis (SpA) is an umbrella term for a group of clinically heterogeneous chronic inflammatory diseases, with Ankylosing Spondylitis (AS) having the characteristic radiographic features of sacroiliitis and spinal deformities, while the other subtypes of SpA have some common as well as unique

articular and extra-articular manifestations. Recent advances in early diagnosis have differentiated axial SpA into radiographic and non-radiographic subsets but the exact differences between them are debatable.

Objectives: This study was conducted to assess and compare the clinical, laboratory, and radiologic characteristics of Indian patients with radiographic and non-radiographic axial SpA.

Methods: This was a cross-sectional, observational, comparative study conducted at a 1250-bedded tertiary care hospital. Between February 2020 and December 2021, all consecutive adult patients classified as having Axial Spondyloarthritis as per the Assessment of Spondyloarthritis international Society (ASAS) 2009 Classification Criteria and with symptom duration of at least 3 years were included in the study after taking their informed consent. Patients were classified as radiographic (AS) or non-radiographic Axial SpA (nr-Axial SpA) by two independent and blinded rheumatologists with over twenty years of experience in their field each, based on findings on anteroposterior plain radiographs in the supine position. Demographic details, articular and extra-articular manifestations, comorbidities, and relevant family history were assessed along with the levels of inflammatory markers and HLA B27 status. The study was approved by the Institutional Review Board and the Institutional Ethics Committee.

Results: 209 patients consented to this study, with 160 being classified as radiographic and 49 as non-radiographic axial SpA. 79.4% of the patients were male. The mean age at symptom onset was 27.69 ± 9.33 years for our cohort, with a median duration of 50 months. There was a significantly higher proportion of males (85% vs 15%, p <0.001), patients with enthesitis (74% vs 41%, p 0.05), and hypertension among the radiographic subgroup. 44% of our patients had bilateral Grade 2 changes on their sacroiliac joint radiographs according to the modified New York Criteria, and there was a significant positive correlation between increasing symptom duration and worsening radiographic grades of sacroiliitis, but there were no significant differences in the remaining clinical features, HLA B27 positivity, or age at symptom onset among the AS and nr-Axial SpA patients. Mean values of BASDAI, BASMI, and ASDAS-ESR scores were also significantly higher in patients with radiographic Axial SpA.

Conclusion: Data from our Indian cohort of axial Spondyloarthritis revealed a significant association of radiographic disease with male gender and the presence of enthesitis, as well as higher mean values of inflammatory markers and composite scores. However, non-radiographic axial SpA was similar to AS as far as most other features were concerned. With increasing symptom duration, the majority of patients may develop radiographic disease, and they may be considered as two ends of the same spectrum, justifying early therapy even in nr-axial SpA.

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AB1040 CHARACTERIZATION OF ANXIETY AND DEPRESSION AND THEIR IMPACT ON DISEASE ACTIVITY, FATIGUE AND QUALITY OF LIFE IN SPONDYLARTHRITIS PATIENTS TREATED WITH ANTI-TUMOR NECROSIS FACTOR ALPHA AGENTS

Keywords: bDMARD, Spondyloarthritis, Quality of life

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Background: The psychological health of patients with spondylarthritis (SpA) influences their response to anti-tumor necrosis factor alpha (anti-TNF-α) therapy. However, little is known about the correlation between anxiety and depression symptoms and clinical outcomes over time.

Objectives: Hence, based on clinical practice setting, this study, aimed to explore the impact of anxiety and depression symptoms on clinical outcomes in patients with SpA treated with anti-TNF-α agents over time.

Methods: An observational retrospective longitudinal cohort study was conducted. Adult patients with diagnosis of SpA according to Assessment of Spondylarthritis International Society (ASAS) classification criteria, who started their first anti-TNFα agent between 2002 and 2022 were included. Sociodemographic, clinical and laboratory data were obtained from the national register Reuma.pt at the time of initiation of the first anti-TNF-α agent and after 12 months (M). Anxiety and depression symptoms were assessed by Hospital Anxiety and Depression Scale (HADS). A score ≥8 on the HADS-Anxiety and HADS-Depression indicates the presence of clinically significant anxiety and depression symptoms, respectively. Ankylosing Spondylitis (AS) Disease Activity Score with CRP (ASDAS-CRP) and Bath AS Disease Activity Index (BASDAI) were assessed to measure disease activity. Pain Visual-Analogue-Scale (VAS), Bath AS Functional Index (BASFI) and Bath AS Metrological Index (BASMI) were also collected to assess pain severity and disability. To evaluate enthesitis the Maastricht AS enthesitis score (MASES) was performed. Clinical response was evaluated by ASDAS response. Fatigue was evaluated using Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue: score ≤ 39 indicates the presence of clinically significant fatigue and health-related quality of life with EQ-5D. In order to correlate anxiety and depression with clinical outcomes, Pearson coefficient was used. Linear regression models adjusted for age, gender and disease duration were used to assess the impact of anxiety and depression symptoms on clinical outcomes.

Results: A total of 130 patients with SpA (mean age of 40.6±10.8 years old; 85.4% female; 74% with AS) with a median disease duration of 7 [4-14] years were included. Nearly half (50.6%) of patients had anxiety, 33.8% depression and 30% had both anxiety and depression symptoms. At the baseline, the median of anxiety and depression symptoms was 8 [4.5-12] and 6 [3-8], respectively. At the baseline, there were statistically significant correlations between anxiety and depression symptoms and pain-VAS at night (r_p=0.47, p=0.03 and r_p=0.6, p=0.004, respectively); between depression symptoms and BASMI (r_p=-0.34, p=0.006) and between anxiety and depression symptoms and EQ-5D (r_p=-0.56, p=0.04 and r_p=-0.65, p=0.011, respectively). At 12M, there were statistically significant correlations between anxiety symptoms and BASDAI (r_p=0.23, p=0.03), FACIT-Fatigue (r_p=-0.68, p<0.001) and EQ-5D (r_p=-0.51, p=0.001); and between depression (r_p=-0.65, p<0.001) and EQ-5D (r_p=-0.59, p<0.001). In the multivariable regression models, depression symptoms at baseline moment predicted VAS at night (β=0.6, p=0.06). At 12M anxiety symptoms predicted BASDAI (β=0.2, p=0.027), FACIT-Fatigue (β=-0.7, p<0.001) and EQ-5D (β=-0.5, p<0.002); depression symptoms also predicted EQ-5D (β=-0.6, p<0.001).

Conclusion: Anxiety and depression are common conditions in patients with SpA treated with anti-TNF-α agents. After 12M of treatment, anxiety and depression symptoms predicted worse quality of life and anxiety also predicted higher disease activity and fatigue. Our results encourage the assessment and monitoring of anxiety and depression symptoms over time in these patients in order to design more individualized multidisciplinary approaches. Further longitudinal research is needed to explore the impact of anti-TNF-α agents on anxiety and depression symptoms.

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AB1041 AUTOMATED VERTEBRAL FRACTURE ASSESSMENT AS A SCREENING TOOL IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Outcome measures, Imaging, Spondyloarthritis

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Background: Bone loss reflected by low bone mineral density (BMD) is common in axial spondyloarthritis (axSpA) and often already noticed at early stages of disease. Severe bone loss may lead to vertebral fractures (VF). Prevalent VF, low BMD and older age are well-known risk factors for the development of new VF. Manual assessment of VF according to the method of Genant et al.1 is considered as the gold standard, however, this is time consuming in research and clinical settings. Nowadays, when performing BMD measurements an automated VF assessment (aVFA) can be generated which potentially could be a useful screening method for detecting VF in patients with axSpA.

Objectives: To investigate the performance of aVFA in comparison to manual assessment of radiographic VF according to Genant method in patients with axSpA.
Methods: In this pilot study, we included axSpA patients from the GLAS cohort who underwent DEXA with aVFA and had spinal radiographs available within 1 year. Two independent trained readers assessed the vertebral bodies on the lateral view of the thoracic and lumbar spine for radiographic VFs. Anterior, middle, and posterior heights of the 4th thoracic vertebra (Th4) to the 4th lumbar vertebra (L4) were exactly measured. VFA scans were analyzed from T4 to L4 by using a viewer (QDR, Hologic) with software supplied by the manufacturer in which a computer-aided fracture assessment semi-automatically performs total vertebral assessment for each vertebra (T4–L4) on a lateral VFA image. In both methods, radiographic VF were defined according to the method of Genant et al.[1]. A prevalent VF was defined as ≥20% reduction in any vertebral height. Vertebrae were categorized as grade 0 (normal, <20% height reduction), grade 1 (mild, ≥20-<25% reduction), grade 2 (moderate, ≥25-≤40% reduction) or grade 3 (severe, >40% reduction) fractures. Agreement was compared at vertebral level.
Results: In total, 40 axSpA patients were included; 58% were male, mean age was 46.2±14.2 years, mean symptom duration was 18.0±12.4, 80% were HLA-B27 positive, mean ASDAS was 2.1±1.0 and median mSASSS (n=35) was 5.2 (IQR 1.2-18.3). At group level, median BMD T-score and BMD Z-score of the lumbar spine was -0.5 (-1.3-0.8) and -0.1 (-1.0-1.7), respectively. Osteoporosis was found in 1 (2.6%) patient and 15 (38.5%) patients had osteopenia, of these 56% were male and mean age was 46.7 ± 14.1years. In 477 (91.7%) vertebrae, there was absolute agreement on the aVFA and manual assessment (missing, normal or fracture and accompanying grade and fracture shape). In total, manual assessment detected 2 radiographic VF in 2 patients and aVFA detected 10 VF in 6 patients. The 2 fractures found with the manual method were seen in the lumbar spine, both grade 2 and wedged or biconcave shaped). The 10 aVFA fractures were found in the thoracic (n=5) and lumbar (n=5) spine; grade 1 (n=5), grade 2 (n=4) or grade 3 (n=1) and wedged (n=4) or biconcave (n=6) shaped. The fractures detected with manual assessment were both also detected with aVFA, but the fracture grading was different for one of these fractures (manual grade 2 vs. aVFA grade 3). 8 fractures detected with aVFA were not found with manual assessment. In 6 of these cases, the patient had extensive radiographic damage. X-ray quality was low in the 2 remaining cases. Regarding vertebrae defined as missing; aVFA could not assess 26 (5%) vertebrae compared to 8 (1.5%) for manual assessment.
Conclusion: In this pilot study using data from our observational cohort, aVFA seems a good first screening tool for the detection of radiographic VF in axSpA patients, since no fractures were missed. However, these VF should be confirmed with manual assessment especially in axSpA patients with extensive radiographic damage. A larger study population in which more VF can be identified is needed to more reliably calculate sensitivity and specificity of aVFA.
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AB1042 PATIENT CHARACTERISTICS AND SPA FEATURES IN RECENTLY DIAGNOSED AXIAL SPONDYLOARTHRITIS PATIENTS STRATIFIED FOR CLINICAL DIAGNOSIS AND ASAS CLASSIFICATION CRITERIA; RESULTS FROM STANDARD-OF-CARE COHORT

Keywords: Gender/diversity issues, Spondyloarthritis, Epidemiology

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Background: In axial spondyloarthritis (axSpA), besides the characteristic symptoms of chronic (inflammatory) back pain and stiffness, patients may suffer from peripheral and extra-skeletal manifestations. Within axSpA, patients can be diagnosed with ankylosing spondylitis (AS) or non-radiographic axSpA (nr-axSpA) based upon the presence or absence of radiographic sacroiliitis. Furthermore, patients can be classified as axSpA according to the ASAS criteria into the imaging arm for which radiographic sacroiilitis and/or sacroiliitis on MRI is mandatory or into the clinical arm for which the presence of HLA-B27 is mandatory. Until now, little is known about patient characteristics in these subgroups of axSpA with a recent axSpA diagnosis.
Objectives: To explore patient characteristics and SpA features in recently diagnosed axSpA patients diagnosed as AS or nr-axSpA and in patients fulfilling the imaging or clinical arm of the ASAS classification criteria.
Methods: This cross-sectional analysis included consecutive axSpA patients between 2009 and 2019 diagnosed no more than 1 year before inclusion in the Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort. Demographic data and all SpA features based on the ASAS classification criteria (sacroiliitis on pelvic radiograph according to the modified New York criteria, sacroiliitis on MRI according to the ASAS criteria, inflammatory back pain (IBP) according to the ASAS criteria; peripheral manifestations (peripheral arthritis, enthesitis and dactylitis); extra-skeletal manifestations (uveitis, psoriasis, inflammatory bowel disease); good response to a NSAID; family history of SpA; HLA-B27 status and CRP level) were collected at the GLAS baseline visits. Characteristics and features of the following axSpA subgroups were analyzed: clinical diagnosis AS vs. nr-axSpA, imaging arm vs. clinical arm of the ASAS classification criteria, only axial disease vs. axSpA with ≥1 peripheral manifestation.
Results: In total, 319 aSpA patients were included, with a mean age of 38.2 ± 12.0 years, 175 (55%) were male, median symptom duration was 25 (19-34) years and 242 (76%) were HLA-B27 positive. 177 (55%) patients were diagnosed with AS and 142 (45%) with nr-axial SpA. AS patients were more often male (65% vs. 42%, p<0.001), had more often IBP (89% vs. 76%, p=0.004), more often a SpA family history (38% vs 22%, p=0.002) and higher CRP (median 5 vs. 2, p=0.001) compared to patients diagnosed with nr-axSpA. The number of SpA features was not significantly different between patients diagnosed with AS or nr-axSpA (median 3.7 vs. 3.7, p=0.73). 265 (83%) axSpA patients fulfilled the imaging arm and 54 (17%) patients fulfilled the clinical arm. Patients fulfilling the clinical arm were per definition all HLA-B27 positive (100% vs. 71%, p<0.001), had more often IBP (92% vs. 80%, p=0.040) and a positive SpA family history (51% vs. 25%, p<0.001) compared to patients fulfilling the imaging arm. Furthermore, patients from the clinical arm showed a higher CRP (median 4 vs. 2, p=0.028) and had more SpA features (median 4.1 vs. 3.6, p=0.019). 200 (64%) axSpA patients had only axial involvement without peripheral manifestations and 111 (36%) axSpA patients had ≥1 peripheral manifestations, of which 69% had a history of peripheral arthritis, 37% enthesitis and 17% dactylitis. Accordingly, axSpA patients with peripheral manifestations presented significantly more SpA features than patients with only axial involvement (median 4.5 vs. 3.2, p<0.001).
Conclusion: In this large cross-sectional study of recently diagnosed (<1 year) axSpA patients, the presence of IBP, positive family history and higher CRP occurred significantly more often in patients diagnosed with AS compared to patients diagnosed with nr-axSpA and in patients fulfilling the clinical arm compared to patients fulfilling the imaging arm of the ASAS classification criteria.
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AB1043 PRESENCE OF FAMILY HISTORY MAY CONTRIBUTE TO STRUCTURAL DAMAGE IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS UNLIKE RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis

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Background:
Objectives: Evaluation of the frequency of family history according to ASAS in patients with axial spondyloarthritis (axSpA) and review of its relationship with clinical features, activity and structural damage.
Methods: In total 578 patients (age: 39.9 ±11.5; male patient: 357, 61.8%) followed in a single center axSpA cohort were included in the study. The study group was consisting 65% radiographic axSpA (r-axSpA). Demographic data and disease related characteristics including disease activity, function, quality of life and spinal mobility were collected. Structural damage was evaluated by using modified Stoke Ankylosing Spondylitis Spine Score (mSASSS).
Results: A family history was found in 153 (26.4%) patients according to ASAS. AS (115; 75%) and psoriasis (54; 35.3%) were the most common diseases in family history. Female sex 45.1% vs 35.8%; p:0.042), longer symptom duration

(16.6 ± 11.7 vs 13.6 ± 9.4; p:0.045), higher body mass index (26.7 ± 4.6 vs 26.0 ± 4.8; p:0.043) and psoriasis (13.1% vs 3.8%; p<0.001) were more frequent in familial cases. HLA B27 positivity was higher tendency without statistical significance in patient with family history (66.4% vs 56.7%; p:0.60). In terms of structural damage, basal syndesmophyte, basal mSSASS, mSSASS progression and new syndesmophyte development could not differ between the groups. Family history was found in 30% of nr-axSpA patients. HLA B27 positivity, higher baseline mSSASS and basal syndesmophyte frequency were found more frequently in patient with family history among nr-AxSpA. And also more mSSASS progression was detected in the same group (Table 1). In the r-axSpA group, there was no difference in structural damage or radiological progression, except for longer symptom duration in those with a family history.

Conclusion: There was a significant frequency of family history in AxSpA and it might be contribute to the disease phenotype at different rates. The presence of family history in both baseline and follow-up data, especially in radiographic, seems to increase severity in disease subgroups.

Table 1. Comparison of family history in r-axSpA and nr-axSpA groups *

	r-axSpA			Nr-AxSpA		
Variables	Having Family History (n:92)	No Family History (n:285)	p	Having Family History (n:61)	No Family History (n:140)	p
Age, mean ±SD	43.0±12.35	41.5±11.7	0.26	36.0±10.09	36.3±10.07	0.92
Female sex, n%	27;29.3	70;24.6	0.36	42;68.9	82;58.6	0.16
Symptom duration,	17.5±12.25	14.1±9.62	**0.045**	9.1±8.76	7.1±7.34	0.13
Smoking, mean ±SD	69/92;75.0	210/278;75.5	0.91	36;59	81/137;59.1	0.98
BMI, mean ±SD	27.0±4.69	26.1±4.98	0.43	26.4±4.45	25.8±4.5	0.44
Psoriasis	14;15.2	14;4.9	**0.001**	6;9.8	2;1.4	**0.005**
IBD n;%	2/87;2.3	9/208;4.3	0.40	2/59;3.4	9/119;7.6	0.27
HLA B27 positivity	51/73;69.9	136/206;66.0	0.54	32/52;61.5	50/122;41.0	**0.013**
CRP mg/dl, mean ±SD	17.8±22.98	18.1±25.72	0.89	5.1±11.4	8.9±17.0	0.38
BASFI, mean ±SD	4.2±2.90	4.0±2.88	0.57	3.0±2.56	2.6±2.24	0.41
BASDAI, mean ±SD	4.4±2.38	4.3±2.32	0.83	4.1±2.22	4.0±2.12	0.75
ASDAS-CRP, mean ±SD	3.0±1.16	3.0±1.22	0.48	2.3±1.06	2.4±1.05	0.95
BASMI, mean ±SD	3.9±1.92	3.8±1.94	0.60	2.4±1.25	2.4±1.15	0.81
Basal mSSASS,** mean ±SD	15.5±22.0 1(34.5)	10.2±17.9 0(14)	0.18	0.64±1.41 0(0)	0.27±1.22 0(0)	**0.019**
mSSASS progression	4/31;12.9	34/103;33.0	0.029	4/22;18.2	1/46;2.2	**0.018**
Basal syndesmophyte	44/78;56.4	139/257;54.1	0.71	12/48;25.0	11/113;9.7	**0.011**

* Continuous variables mean ±SD; categorical variables are expressed as n;%.**Median (IQR)

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1044

SELF-REPORTED HIDRADENITIS SUPPURATIVA-LIKE SKIN SYMPTOMS IN PATIENTS WITH SPONDYLOARTHRITIS: RESULTS FROM AN ONLINE SURVEY

Keywords: Spondyloarthritis, Skin, Psoriatic arthritis

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Background: Hidradenitis suppurativa (HS) is a chronic immune-mediated disease with known associations with other chronic auto-inflammatory diseases, such as inflammatory bowel disease and spondyloarthritis (SpA).[1–3] However, real-world data on the occurrence of HS in patients with SpA are limited.

Objectives: To explore the proportion of patients with SpA who report having an HS diagnosis from a doctor or report having undiagnosed skin symptoms similar to HS.

Methods: An online survey with validated questions about HS diagnoses/symptoms was conducted from 1–22 September 2021 among users of the social network MySpondylitisTeam, aged ≥21 years and reporting a SpA diagnosis (principally ankylosing spondylitis [AS; also known as radiographic axial spondyloarthritis], non-radiographic axial spondyloarthritis [nr-axSpA], or psoriatic arthritis [PsA]), or a SpA diagnosis but without knowing the specific subtype.[1] Prototypical pictures of HS symptoms were included to help participants identify these symptoms.

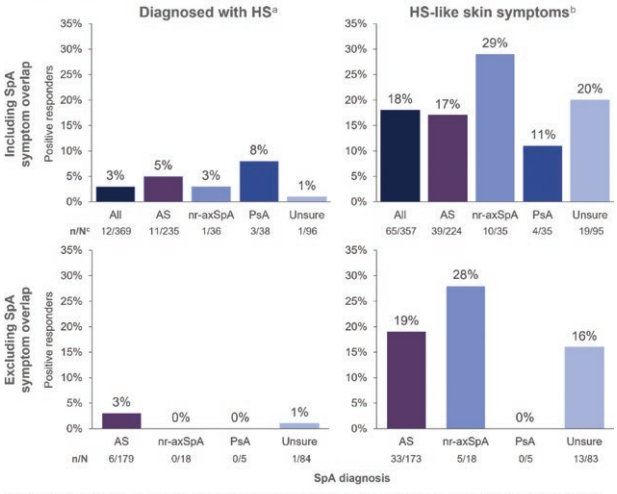
Results: 369/448 participants with self-reported SpA diagnoses completed the full survey; 81% were female, 69% aged 50–70 years and most from the US (87%; with a further 8% from the UK and 2% from Canada). While most participants reported that a doctor had diagnosed them with one SpA subtype, others reported diagnoses of >1 SpA subtype, potentially reflecting symptom overlap with different SpA subtypes (SpA symptom overlap) (**Figure 1**). Three percent (12/369) of participants reported an existing HS diagnosis; of the remaining 357 participants without an HS diagnosis, 18% (65/357) self-reported skin symptoms resembling HS. Among the principal SpA subtypes studied, an HS diagnosis was most frequent among participants with PsA (8%; 3/38), while undiagnosed HS-like skin symptoms were reported by 11% (4/35) of the participants with PsA who did not report an HS diagnosis. All participants with PsA and either an HS diagnosis or undiagnosed HS-like skin symptoms also reported having SpA symptom overlap (**Figure 1**). The participants with nr-axSpA exhibited the highest proportion of undiagnosed HS-like skin symptoms (29%; 10/35, including participants reporting SpA symptom overlap) while very low rates of HS diagnoses were reported (**Figure 1**). Among those reporting undiagnosed HS-like skin symptoms (or unsure if they have them), 48% (34/71) had previously discussed their skin symptoms with a healthcare professional. These participants mainly reported being told that their skin symptoms were due to infected hair follicles (44%; 15/34) or cysts (24%; 8/34).

Conclusion: Of the participants surveyed, very few reported an HS diagnosis while a considerably higher proportion reported skin symptoms resembling HS. Despite the limitations and potential biases inherent in online surveys, these results suggest that HS may be underdiagnosed in patients with SpA and highlight a need for further research and potentially, greater awareness of HS in the clinical care of patients with SpA.

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Figure. Participants with SpA who self-reported being diagnosed with HS by a doctor (left) or having skin symptoms resembling HS (right)



[a]Results taken from Q8 of the survey, which included the following text: 'Has a doctor ever diagnosed you with HS?'; [b]Results taken from Q9 of the survey, which included the following text and an example picture (not included here): 'We would like to understand whether you have had any signs of HS. HS is a chronic inflammation of the hair follicles. It can occur in the groin or buttocks area, in the armpits, under breasts, on the thighs, or on the back or neck. Signs of HS may not always look like this, but this photo is one example of how it may appear. Have you had painful, recurring abscesses, boils, or lesions on your skin in the past six months?' Participants who answered affirmatively to Q8 were asked not to respond to Q9; [c]Participants (N=369) reporting >1 SpA diagnosis feature in multiple SpA subtype categories.

Abbreviations: AS: ankylosing spondylitis; HS: hidradenitis suppurativa; nr-axSpA: non-radiographic axial spondyloarthritis; PsA: psoriatic arthritis; SpA: spondyloarthritis.

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Disclosure of Interests: Anneke Spoorenberg Consultant of: Abbvie, Eli Lilly, MSD, Novartis, Pfizer and UCB Pharma, Grant/research support from: Abbvie, Novartis, Pfizer, UCB Pharma, Mindy Kim Shareholder of: UCB, Employee of: UCB Pharma, Ingrid Pansar Shareholder of: UCB, Employee of: UCB Pharma, Heather Lapidus Glassner Grant/research support from: Employee of

MyHealthTeam, which received funding from UCB Pharma to conduct studies on the impact of HS.
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AB1045 IS IT POSSIBLE TO DETECT CHRONIC LESIONS ON MRI IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS?

Keywords: Imaging, Spondyloarthritis

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Background: The absence of categorical radiographic evidence of structural changes in the sacroiliac joints serves to distinguish AS from nr-axSpA. Both groups of patients are characterized by active inflammatory changes, established by magnetic resonance tomography (MRI) of the sacroiliac joints, which, with the progression of the disease, are structurally progressive.
Objectives: To determine whether it is possible to detect erosions, subchondral osteosclerosis and bone marrow metaplasia on a magnetic resonance imaging of the sacroiliac joints in patients with non-radiographic axial spondyloarthritis and symptom duration less than 3 years.
Methods: A cross-sectional survey was conducted with rheumatologists and their consulting patients in Bulgaria from February 2012 through April 2019. Patients who had a rheumatologist confirmed diagnosis of nr-axSpA were eligible to participate. All patients met ASAS criteria for IBP with duration from 3 months to 2 years. All patients had no changes reported after the conventional X-ray of the sacroiliac joints and a performed subsequent MRI. Sacroiliac joint inflammation was assessed using the Canadian Spondyloarthritis Research Consortium (SPARCC). The SPARCC scores of sacroiliac joint inflammation and sacroiliac joint structural damage (SSSD) (erosions, bony brain metaplasia and subchondral osteosclerosis) were evaluated by both - a radiologist and rheumatologist.
Results: A total of 98 patients with non-radiographic were included in this analysis. A higher proportion of patients were male patients (51% vs 37%). The mean age was 33.8±7.71 with mean symptoms duration 0.76±0.26 years. MRI showed bone marrow edema (BME) in all 98 patients and at least 1 structural lesion in 32 patients (92.5%). The most prevalent chronic lesions were erosive changes in 7.14% (n = 7) and narrowed joint space in 7.14% (n = 7). Fat metaplasia was found in 5.10% (n = 5) in the patients with nonradiographic spondyloarthritis. The mean values of SPARCC score in patients with the different arm of nr-ax SpA is 22.42 ± 15.18. The burden of disease activity measured by BASDAI, ASDAS-CRP and VAS as well as ASQoL did not differ in patients with SSSD compared with those with BME only (p>0.05)
Conclusion: Patients with nr-ax SpA are characterized by a short duration of symptoms. Regardless of this recent onset and initially normal X-ray image of the sacroiliac joints, in some patients there are objective data of previous inflammation of the sacroiliac joints that may had not be detected on X-ray. That arise the question of low sensitivity of conventional radiography as well as the presence of risk factors for rapid structural damage and progression in some patients with nr-ax SpA.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1046 LEVEL OF VITAMIN D IN MEN WITH ANKYLOSING SPONDYLITIS, CONNECTION WITH DISEASE ACTIVITY AND SEASONALITY

Keywords: Spondyloarthritis, Vitamin D

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Background: It is known that in ankylosing spondylitis (AS) there is a decrease in the level of vitamin D in blood serum. Its status in these patients can be determined by both exogenous (deficiencies in the diet of products that are its main sources) and endogenous (ecological problems, urbanization, seasonality) factors. In addition, the availability of vitamin D in this cohort of patients can be determined by the course of the disease. In particular, the role of vitamin D in suppressing the proliferation of T-cells and reducing the production of interleukin-2, interferon-γ, tumor necrosis factor-α, etc. is well-known. The frequency of vitamin D deficiency in the Ukrainian population of patients with AS is unknown, and the study of the relationship between vitamin D and disease activity and seasonality is also worthy of attention.
Objectives: To determine vitamin D availability in men with AS and to assess its relationship with seasonality and activity of the disease.
Methods: 81 men with AS were examined with an average age of 41,0±0,1 years and duration of the disease of 9,0±0,6 years. The diagnosis of AS was made according to the modified New York criteria (1984) and the ASAS criteria (2009). Seasonal measurements of vitamin D content in blood serum were carried out in the autumn-summer and winter-spring periods. Disease activity was determined on the basis of BASDAI and ASDAS-CRB indices.
Results: In men with AS, vitamin D deficiency was detected in 35 (43,2%) people, an insufficient level in 25 (30,9%) cases, and in 21 (25,9%) patients, it was within the normal range. In the control group, optimal levels of vitamin D wer.e. found in 7 (30,4%) examined patients, 9 (39,2%) patients showed insufficiency and 7 (30,4%) patients had vitamin D deficiency. It is shown that the share of people with vitamin D deficiency is the highest in the spring period (61,8%), and the winter and summer periods did not significantly affect vitamin D availability. Vitamin levels were also closely associated with high activity of the inflammatory process. In particular, in the group of patients with a high degree of activity (BASDAI > 4 points), vitamin D deficiency was detected in 52,6% of people, which is 2,5 times higher than in the group of patients with moderate activity of AS (20,8%). Similar regularities were found according to the ASDAS index. In addition, it is the activity of the inflammatory process that is key in the occurrence of vitamin D deficiency, since regardless of the season (winter/summer), reliable correlations are established between the level of the vitamin on the one hand and the activity according to ASDAS and BASDAI on the other hand (r = -0,30; -0,27 p<0,05).
Conclusion: Vitamin D deficiency occurs with a high frequency (43,2%) in men suffering from AS. Despite the fact that there are seasonal fluctuations in vitamin D levels, its status is determined precisely by the activity of the inflammatory process.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4088

AB1047 COMORBIDITY WITH FIBROMYALGIA IS ASSOCIATED WITH INCREASED JOINT SWELLING, HIGH DISEASE ACTIVITY AND REDUCED PRODUCTIVITY IN THAI PATIENTS WITH SPONDYLOARTHRITIS

Keywords: Fibromyalgia, Spondyloarthritis

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Background: Spondyloarthritis (SpA) is a chronic inflammatory disease and may present with diffuse pain. Fibromyalgia (FM) is a non-inflammatory diffuse pain syndrome and may be a co-morbid disease of SpA. No prior study of prevalence FM and its effect on Thai patients with SpA.
Objectives: To estimate the prevalence and explore the associated factor of fibromyalgia among patients with spondyloarthritis in Thailand.
Methods: This was a cross-sectional study. Thai patients with SpA were consecutively recruited. FM was diagnosed according to the 2016 revision of the 2010/ 2011 American College of Rheumatology diagnostic criteria. The characteristics of the patients, physical examination, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Work Productivity and Impairment Questionnaire and EuroQoL-5 dimensions (EQ5D) were collected. The Fischer exact test or the Mann-Whitney U test was used to compare the associated factors.
Results: Of the total of 218 patients with 113(51.8%) female, mean age of 49.5 years, and median disease duration of 6 years, 12 (5.5%) were diagnosed with FM. Pain areas and symptoms between the patients with and without FM was

shown at Figure 1. FM patients were associated with a higher median tender joint count [1.0 vs 0, *p*=0.020] and swollen joint count [1.5 vs 0, *p*=0.037], BASDAI>4/10 [7(58.3%) vs 34(16.5%), *p*=0.002], mean EQ5D index [0.6 vs 0.88, *p*=0.001], median overall work impairment [65 vs 10%, *p*=0.002], and activity impairment [50 vs 10%, *p*=0.001] than those without FM.

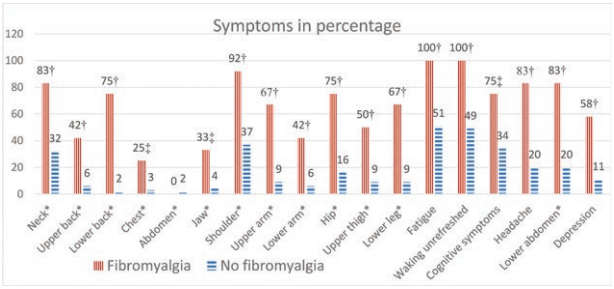


Figure 1. Pain areas and symptoms according to the 2016 Revisions fibromyalgia diagnostic criteria comparing participants with fibromyalgia and without fibromyalgia.*, pain; †, p-value <0.001; ‡, p-value <0.05 and >0.001

Conclusion: The prevalence of FM among Thai patients with SpA is low. However, it is important to identify and treat because it is associated with reduced productivity and poor quality of life. Active inflammation is associated with FM. Controlling SpA disease may also help to control FM.

Acknowledgements: This study was supported by a grant from the Siriraj Research Fund, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (grant no. R016331042). The authors gratefully acknowledge the patients that participated in this study; the EuroQol group for permission to use the Thai version of the EQ-5D-5L.

Disclosure of Interests: None Declared.

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AB1048 ENTHESAL ULTRASOUND ABNORMALITIES CAN PRECEDE SPA DEVELOPMENT IN ASYMPTOMATIC IBD PATIENTS. A RETROSPECTIVE STUDY

Keywords: Spondyloarthritis, Enthesitis, Ultrasound

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Background: Nearly four million people worldwide are affected by Inflammatory Bowel Diseases (IBD) and approximately 25-40% of them develop extra-intestinal manifestations, such as arthritis and enthesitis. Enthesis inflammation is a cornerstone in Spondyloarthritis (SpA) but there are few data concerning prevalence, clinical presentation and prognostic value of enthesitis in IBD patients. Ultrasound (US) assessment has emerged as a feasible, reliable and easily accessible technique for the detection of enthesis abnormalities. Recently a systematic review about the predictive value of the US elementary lesions in IBD patients was performed [1]. Multicenter studies performed on IBD patients without clinical signs of SpA demonstrated high prevalence of US entheses abnormalities such as dishomogeneous echostructure and Power Doppler (PD) positivity [2-3]. The predictive role of these abnormalities is up to now unknown.

Objectives: To find US abnormalities that can predict or frequently precede the development of SpA in a population of IBD patients asymptomatic for entheseal involvement.

Methods: We conducted a retrospective analysis of clinical and US enthesis data coming from 29 patients affected by IBD without clinical signs of SpA evaluated in the period between 2010 and 2012 at the combined Gastroenterology/Pediatrics/Rheumatology Clinic and still in follow up in the Gastroenterology and Rheumatologic Unit of L. Sacco University Hospital in 2022. After a long term follow-up from the first combined US (according to MASEI score with ESAOTE MyLab 70 linear probe 6-18 MHz) and clinical evaluation we retrospectively analyze the patient's clinical record in order to find which patients developed clinically a SpA according to the Assessment of SpondyloArthritis international Society (ASAS) criteria [4]. Medium MASEI score and the presence of US elementary entheseal lesions at baseline of patients that develop SpA were compared by chi-squared test with those without signs of joint involvement.

Results: After an average follow-up of ten years we evaluated data from 29 patients (19 F and 10 M) with a mean age of 33,38 (range 17-82) years and mean disease duration of 14,1 (range 11-33) years. Four patients out of 29 (14%) developed a SpA. Reviewing their US baseline evaluation and comparing it with those of patients that didn't develop the disease we have found that the medium MASEI score of those who developed a SpA was statistically higher (18 ± 13,3 Vs 8,2 ± 6,6 p=0,02). Focusing on US elementary lesions (Table 1) we can underline that all patients developing SpA had at baseline at least one entheses with a positive PD signal (Vs 9/25 of the comparing group (p=0,02).

Conclusion: MASEI score and PD US positivity at enthesal level are possible predicting factors for the development of SpA in IBD patients. Further investigations from long term prospective studies need to confirm these preliminary data.

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Table 1.

Presence in at least 1 enthesis of:	Patients that developed SpA	Patients that not developed SpA	
Power Doppler signal positivity	4 (100%)	9 (36%)	χ= 5,7 p = 0,02*
Erosions	0	1 (4%)	χ= 0,17 p = 0,7
Calcification	2 (50%)	7 (28%)	χ= 0,78 p = 0,3
Echostructure	4 (100%)	17 (68%)	χ= 1,7 p = 0,18
Structural thickness	4 (100%)	18 (72%)	χ= 1,5 p = 0,22

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1049 THE STATUS OF BREG CELLS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

Keywords: Spondyloarthritis, Biomarkers, Systematic review

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Background: Ankylosing spondylitis (AS) is a common chronic inflammatory autoimmune disease that primarily affects the sacroiliac joints, spine and peripheral joints, and attachments of ligaments. Regulatory B cells (Bregs) are unique subpopulations of B cells with immune-regulating properties. Interestingly, different subsets of Breg cells have distinct markers and phenotypes and participate in self-immune regulation in different ways. However, the level of Breg cells in AS remains debated.

Objectives: This study aims to clarify the proportions of Breg cells with unique, controversial cellular markers in AS patients.

Methods: We explored the proportion of Breg cells in AS patients by searching literature through January 10, 2023, from 11 Databases. Random effects model was used to pool data. Heterogeneity and risk of bias were examined with the I-squared index (I^2) statistic. Inconsistency was evaluated using the I^2 and Egger tests to evaluate potential publication bias (STATA v.12.0).

Results: A total of 7 case-control studies involving 278 AS patients and 237 healthy controls (HCs) were included in this study(Table 1). No significant difference in the proportions of Breg cells was evident between AS patients and

HCs[SMD=-0.324, 95%CI(-0.971, 0.323), P=0.327]. Because of a significant statistical heterogeneity observed [p<0.1, I^2=89.2%], we conducted sub-analyses based on individual definitions of Breg cells. We found that the proportions of $CD19^+CD24^{hi}CD38^{hi}$ Breg cells have no significant difference between AS and HCs [SMD=-0.546, 95%CI (-1.126, 0.034), P=0.065](Figure 1). The level of $CD19^+CD24^{hi}CD27^+$ Breg cells was increased in AS compared to that of HCs[SMD=0.965, 95%CI (0.339, 1.590), P=0.003] with no publication bias based on the Egger tests (t=1.35, p=0.236).

Conclusion: The levels of $CD19^+CD24^{hi}CD27^+$ Breg cells were significantly increased in AS patients, suggesting that the abnormalities of Breg cell numbers and function are the critical causes in the development of AS.

Table 1. Characteristics of the individual studies included in the meta-analysis.

Author	Publish year	Case number		Breg cells' definition	Breg cell ratio (mean/median±standard deviation)	Breg in PBMC/ $CD19^+B$ cells
		AS	HC			
Yu Zhang	2022	42	30	$CD19^+CD24^{hi}CD38^{hi}$	AS:6.125±4.219 HC:9.021±4.527	PBMC
Guo-Hui Xue	2015	38	30	$CD19^+CD24^{hi}CD38^{hi}$	AS:2.1±0.66 HC:3.44±0.8	PBMC
Xiao-Wan Huang	2014	10	18	$CD19^+CD24^{hi}CD38^{hi}$	AS:7.15±2.0277 HC:6.87748±1.9131	PBMC
Mingcan Yang	2020	67	50	$CD19^+CD24^{hi}CD38^{hi}$	AS:1.84812±2.1178 HC:2.03012±4.2419	PBMC
Maria-Belen Bautista-Caro1	2017	42	42	$CD19^+CD24^{hi}CD38^{hi}$	AS:3.412±1.011 HC:4.361±1.744	PBMC
Zhangyu	2020	42	30	$CD19^+CD24^{hi}CD38^{hi}$	AS:6.2±3.2 HC:8.6±4.0	PBMC
Zhukangxiang	2021	22	22	$CD19^+CD24^{hi}CD27^+$	AS:16.5±3.5 HC:13.4±2.9	PBMC
Chenmeng	2016	15	15	$CD19^+CD24^{hi}CD38^{hi}$	AS:9.8±1.1 HC:9±1.4	PBMC

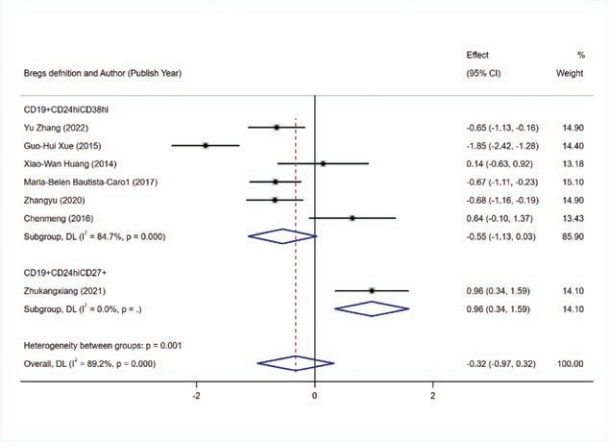


Figure 1. (A) Forest plot of the subgroup meta-analysis of individual definitions of peripheral Breg cell proportions between patients and HCs.

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Disclosure of Interests: None Declared.
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AB1050

THE LEVELS OF FECAL CALPROTECTIN, SERUM INTERLEUKIN 17/23, MALONDIALDEHYDE, GLUTATHIONE PEROXIDASE IN THE PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND THEIR CORRELATIONS WITH CLINICAL, LABORATORY PARAMETERS, DISEASE ACTIVITY SCALES

Keywords: Cytokines and chemokines, Spondyloarthritis, Gastrointestinal tract

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Background: Recent studies in the literature show that the fCal, some proinflammatory cytokines, oxidant/antioxidant markers are associated with disease activity in SpA(1,2,3).
Objectives: The aim of this study was to compare the levels of fCal, serum IL-17/23, malondialdehyde (MDA) and glutathione peroxidase (GPx) between the patients with axSpA treated with NSAID or anti-TNF and the control group; to evaluate the correlations of them with laboratory, clinical parameters, and disease activity scales.
Methods: 75 people from the outpatient clinic at Department of PMR Rheumatology Department, Ankara University were included in this cross-sectional study. Patients have met the ASAS classification criteria for axSpA. 25 volunteers participated in per group (NSAID group/anti-TNF group/the control group). The study was approved by the Clinical Research Ethics Committee, and all participants signed an informed consent form. Individuals participating in the study were evaluated with disease activity scales, ESR, and CRP. Via ELISA method, fCal level from stool samples and IL-17/23 level from serum samples; and via spectrophotometric method, the levels of MDA and GPx were measured.
Results: Fecal calprotectin level was found to be higher in the NSAID group than in anti-TNF group and to be at the lowest level in the control group, which is not statistically significant (p=0.05). In the anti-TNF group, the level of IL-23 is higher than that of the NSAID group (p=0.000). A weak positive correlation was detected between CRP and fCal level in the axSpA group (p=0.009/r=0.380). No relationship between fCal and disease activity scales was observed. It was detected that IL-17 has a weak positive correlation with BASDAI, ASDAS-CRP (p=0.035/r=0.311) and has a strong positive correlation with MASES (p=0.000/r=0.794). No relationship between IL-23 and disease activity scales was found. A weak positive correlation of MDA with BASFI and BASDAI was detected (p=0,018/r=0,355) (p=0,002/r=0,452). It was found a weak negative correlation between IL-23 and GPx (p=0,000/r=0,499), however no statistically significant relationship between the other levels was observed.
Conclusion: The fact that fCal level in the NSAID group is higher than the anti-TNF Group supports the literature that NSAIDs cause leaky gut syndrome by adversely affecting the gut microbiota. Higher fCal level in the NSAID group makes us think that in addition to intestinal inflammation caused by the disease, it is originated by the NSAID treatment[1]. In our study, the reason why the level of IL-23 in the NSAID group is lower may be the underlying mechanism through PGE2, and the reason why it is higher in the anti-TNF group may be that anti-TNF treatment has not had enough effect on the IL-17/23 pathway[2,4]. Especially the relationship of IL-17 level with MASES using for the clinical evaluation of the enthesitis areas, clinically shows us the role of the IL-17/23 pathway in the entheseal inflammation as well[5].

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AB1051

PREGNANCY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Pregnancy and reproduction

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Background: There is limited information available on the course of axial spondyloarthritis (AxSpA) during pregnancy, in contrast to other chronic inflammatory disorders. AxSpA poses a special set of challenges because it has anatomical and inflammatory consequences on pregnancy.
Objectives: The aim of this study was to evaluate the course of AxSpA during pregnancy.
Methods: In order to evaluate the course of AxSpA during pregnancy, an observational descriptive retrospective study was carried out at a private rheumatology clinic. Data were gathered using a self-administered questionnaire from 70 women who were diagnosed with AxSpA prior to pregnancy.
Results: The average age at disease onset was 23.6 years. Approximately one-third (35.7%) of patients said their AxSpA symptoms were worse during pregnancy, compared to 64.2% who said their symptoms got better. The postpartum flare was reported by 52.5% women. The mode of delivery was by cesarean section in 76% patients. Back pain and stiffness during pregnancy were the most prevalent symptoms. None of the patients had extra-articular manifestations during pregnancy or postpartum. Adverse pregnancy outcomes were reported by 15.7% patients. In our study, we found that the majority of women avoided using drugs even when they felt the need to do so out of concern for the foetus.
Conclusion: A large number of patients reported ease of symptoms during pregnancy. Due to the significant risk of flare, patients should be followed up during post-partum period. AxSpA females have an increased prevalence of cesarean sections.
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Table 1. Disease course of AS

	n	n%
Accompanying Conditions		
Peripheral Arthritis	17	24.28
Uveitis	12	17.14
IBD	4	5.70
Disease Activity		
Ease	45	64.28
Aggravation	25	35.71
Symptoms Experienced During Pregnancy		
Hip and Back pain	42	71.18
Morning stiffness	34	57.62
PREGNANCY OUTCOMES		
Mode Of Delivery		
Cesarean Section	40	76.27
Normal	19	32.20
Adverse Pregnancy Outcome		
Miscarriage	7	10.0
Congenital abnormalities	4	5.7

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Disclosure of Interests: None Declared.
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AB1052 COMPARISON OF HIP INVOLVEMENT IN ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLARTHRITIS- A RETROSPECTIVE STUDY

Keywords: Spondyloarthritis

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Background: Hip involvement is common in axial spondylarthritis (axSpA), with several studies reporting a prevalence as high as 36% in Ankylosing spondylitis (AS)[1,2]. Hip involvement represents a negative impact on the quality of life and daily functionality in these patients[2]. Although some studies identify radiographic sacroiliitis as a predictor of hip involvement in Spondylarthritis[2], there are no studies aiming to directly compare patients with AS and Non-radiographic axial spondylarthritis (Nr-axSpA).
Objectives: The purpose of our study is to compare the hip involvement between AS and Nr-axSpA and to evaluate predictors of hip involvement in axSpA.
Methods: A retrospective study was performed during the last trimester of 2022 including patients with axSpA (all patients fulfill ASAS criteria) followed in a Portuguese Rheumatology Center. Patients were divided into two groups: patients with AS (group 1) and patients with Nr-axSpA (group 2). Sociodemographic, clinical, and laboratory data were collected. Hip involvement was evaluated by imaging and defined by a BASRI-h >1. Descriptive analysis was performed using means and standard deviation (SD), medians, and Interquartile range (IQR) for continuous data, and frequencies and percentages for qualitative variables. Clinical, laboratory, and radiological findings were compared between patients with AS and Nr-axSpA using parametric and non-parametric tests. A multivariate analysis, with a stepwise backward binary logistic regression, was performed to identify risk factors independently associated with hip involvement. Significance was set at a p-value ≤ 0.05.
Results: 106 patients were enrolled in the study, 58 (54.7%) with AS and 48 (45.3%) with Nr-axSpA (mean age was 56.03 ±13.05 years, with 50% of females in AS group, and 43.96 ±11.31 years, with 64.58% females in Nr-axSpA group). AS patients were older and had longer disease duration (p<0.001). There were no differences regarding the presence of extra-articular manifestations, HLA-B27 positivity, inflammation markers, disease activity scores, treatment, or comorbidities between groups. Of all patients, 44.3% had hip involvement, and 26.4% were symptomatic (pain and/or limited mobilization). Hip involvement was significantly more prevalent among AS patients (60.34% Vs 25%, p< 0.001). On univariate analysis, age (p=0.001), disease duration (p<0.001), radiographic sacroiliitis (p<0.001), higher C reactive protein levels (p=0.03), high blood pressure (p=0.03) and type 2 *Diabetes Mellitus* (p=0.03) were associated with hip involvement in axSpA patients. Although, on multivariate analysis, only age and the presence of radiographic sacroiliitis were found as independent risk factors [age: OR1.04 CI(1.04-1.07), p=0.03; radiographic sacroiliitis: OR3.10 CI(1.25-7.68), p=0.01].
Conclusion: Our study suggests that hip involvement is frequent in axSpA, mainly in those with AS. Older age and the presence of radiographic sacroiliitis were potential independent risk factors for hip involvement, reinforcing the importance of closely monitoring this subset of patients, thus potentially minimizing its negative impact on patients' quality of life and functionality.
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Disclosure of Interests: None Declared.
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AB1053 MATRIX METALLOPROTEINASE-3: A BIOMARKER OF SPONDYLOARTHRITIS

Keywords: Biomarkers, Spondyloarthritis, Diagnostic tests

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Background: Several studies reported that matrix metalloproteinase 3 (MMP-3), an enzyme of the proteolytic system, is implicated in the pathogenesis and progression of several rheumatic diseases [1].
Objectives: We aimed to compare MMP-3 serum levels between spondyloarthritis (SpA) patients and healthy controls.
Methods: We conducted a case-control study, including 164 subjects divided into two groups, all matched for age and gender: G1 including 82 SpA patients, diagnosed according to ASAS 2009 criteria, and G0 including 82 healthy controls. ELISA technique was used to measure MMP-3 serum levels. Statistical analyses were carried out using SPSS software.
Results: Each group included 65 men. The mean age was 45.32 ± 13.41 years. The mean disease duration was 7.57 ± 7.79 years. Radiographic axial SoA (r-AxSpA) and psoriatic arthritis (PsA) were noted in 65.9% (n=54) and 34.1% (n=28) of cases, respectively. In G1, axial manifestations were noted in 81.7% (n=67). A peripheral syndrome was associated in 45% (n=18): arthritis in 42.7% (n=35) and enthesitis in 14.6% (n=12). The mean MMP-3 serum levels were statistically higher in G1 than in G0 (G1: 64.14 ± 187.31 [1.75 – 1237.36] versus G0: 12.06 ± 10.99 ng/mL [2.98 – 58.94], **p=0.01**). MMP-3 serum levels were significantly higher in PsA than in r-AxSpA patients (141.65 ± 306.33 [2- 1238] ng/mL versus 23.95 ± 31.67 [3 - 149] ng/mL, **p=0.006**). The cutoff of 10.43 ng/mL could discriminate G1 from G0 with a sensitivity and a specificity of 67.1% and 61% respectively (AUC: 0.647, p=0.001).
Conclusion: Our study showed that MMP-3 serum levels were significantly higher in SpA patients compared to controls. This finding suggests that MMP-3 plays a role in the pathogenesis of SpA. However, MMP-3 did not have high sensitivity and specificity in discriminating patients from healthy controls. Thus, MMP-3 was not a good biomarker for the diagnosis of SpA.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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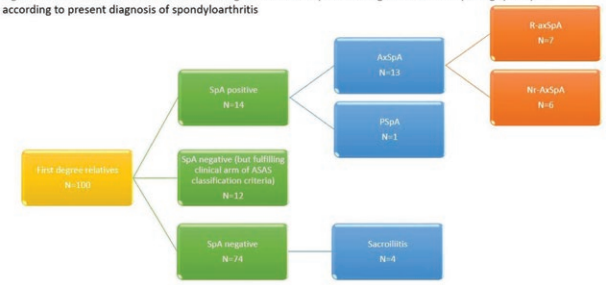
AB1054 SPONDYLOARTHRITIS IN FIRST DEGREE RELATIVES OF ANKYLOSING SPONDYLITIS PATIENTS

Keywords: Imaging, Spondyloarthritis, Genetics/epigenetics

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Background: Ankylosing spondylitis (AS) is a relatively common inflammatory rheumatic disease with a strong familial risk and heritability.
Objectives: The aim of this study was to examine first-degree relatives of patients diagnosed with AS to determine the presence of active sacroiliitis, fulfilment of Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axial and/or peripheral spondyloarthritis (SpA), and the clinical diagnosis of SpA.
Methods: One hundred subjects without a previous rheumatological diagnosis with a first-degree relative treated for AS were included in the study. Clinical data were collected and rheumatological examinations were performed by trained rheumatologists. Magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ) was read by a trained rheumatologist who was blinded to all patient data. Subjects were further divided into both SpA (according to ASAS classification criteria and clinician opinion) and non-SpA subgroups.
Results: A total of 26 subjects met ASAS classification criteria for SpA, of which the diagnosis of SpA was confirmed in 14 subjects (13 subjects met ASAS classification criteria for axial and 1 subject for peripheral SpA). In addition, 12 individuals met the clinical arm of the ASAS classification criteria for axSpA, but were not diagnosed with axSpA in the clinicians' opinion. Active sacroiliitis as defined by MRI was present in all 13 individuals diagnosed with axSpA, 7 (54%) of whom already had advanced radiographic changes on conventional radiographs of the SIJ. In addition, active sacroiliitis defined by MRI was also present in 4 individuals who did not have back pain. The data are shown in Figure 1. Analysis of clinical characteristics showed a significant difference in CRP and BASDAI between the SpA vs. non-SpA subgroups (8.8 (±10.5) vs. 2.3 (±4.1) mg/l, p=0.0048, and 3.1 (±1.8) vs. 1.76 (±1.78), respectively). Individuals diagnosed with SpA were more likely to be HLA-B27 positive and had inflammatory back pain compared to the non-SpA subgroup (87% vs. 43%, p=0.0069 and 57% vs. 9%, p=0.0002, respectively). Individuals who were not diagnosed with SpA but met the clinical arm of the ASAS classification criteria for axSpA were excluded from the analysis. Other clinical characteristics and differences between subgroups are shown in Table 1.
Conclusion: In this cross-sectional study, a quarter of the relatives of patients with first-degree AS met the classification criteria for SpA, and 14% were diagnosed with SpA based on physician opinion. These individuals had a significantly higher prevalence of HLA-B27, inflammatory back pain, and disease activity indices. It should be kept in mind that in a small proportion of individuals, active sacroiliitis may be present in relatives with first-degree AS even in the absence of back pain.

Figure 1: The distribution of examined first-degree relatives of patients diagnosed with ankylosing spondylitis according to present diagnosis of spondyloarthritis



Abbreviations: N, Number; SpA, Spondyloarthritis; ASAS, The Assessment of SpondyloArthritis international Society; AxSpA, Axial SpA; PSpA, Peripheral SpA, R-axSpA, Radiographic AxSpA; Nr-axSpA, Non-radiographic axSpA

Table 1. Patient characteristics and subgroups differences

Characteristic	All	SpA	Non-SpA	P
	N=100	N=14	N=74	SpA vs non-SpA
Age (years), *mean (SD)*	34.4 (11.3)	36.5 (10.5)	33.7 (11.4)	0.2956
Gender: Males, *number (%)*	54	7 (50)	40 (54)	>0.9999
BMI (kg/m2), *mean (SD)*	28.8 (38.9)	24.8 (4.9)	30.2 (45.1)	0.7069
BASDAI, mean (SD)	2.0 (1.8)	3.1 (1.8)	1.76 (1.78)	0.0054*
CRP (mg/L), *mean (SD)*	3.4 (6.0)	8.8 (10.5)	2.3 (4.1)	0.0048*
BP, *number (%)*	74	14 (100)	48 (65)	0.0082*
IBP, *number (%)*	25	8 (57)	7 (9)	0.0002*
Smokers, *number (%)*	44	7 (50)	20 (27)	0.1185
Spinal distances: Schober *(cm), mean (SD)*	4.8 (1.2)	4.5 (0.9)	4.9 (1.2)	0.276
chin-chest *(cm), mean (SD)*	0.5 (1.4)	0.6 (2.9)	0.4 (1.0)	0.0714
fléche *(cm), mean (SD)*	0.2 (1.0)	0.6 (1.6)	0.1 (1.0)	0.0873
chest expansion *(cm), mean (SD)*	5.4 (1.7)	6.0 (2.0)	5.3 (1.7)	0.2773
HLA-B27 positivity, *number (%)*	56	12 (86)	32 (43)	0.0069*

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, Body mass index; BP, back pain; CRP, C-reactive protein; HLA, human leukocyte antigen; IBP, inflammatory back pain, * P value < 0.05

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Acknowledgements: NIL.
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AB1055 COMORBIDITIES IN SPONDYLOARTHRITIS: DATA FROM THE MOROCCAN RBSMR REGISTRY

Keywords: Spondyloarthritis, Comorbidities

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Background: In addition to the extra-articular manifestations associated with spondyloarthritis such as IBD, psoriasis and uveitis, spondyloarthritis is linked to an increased risk of comorbidities.

Objectives: To study the prevalence of comorbidities in spondyloarthritis (SPA) at inclusion and 36-month follow-up and their influence on disease activity and functional outcome in a cohort of patients followed for SPA from the Moroccan registry of biological therapies in rheumatic diseases (RBSMR Registry).
Methods: Data were analyzed from cohort of 194 patients with SPA from the RBSMR Registry including comorbidities (hypertension, diabetes, dyslipidemia, obesity, osteoporosis, sedentary lifestyle, gastrointestinal ulcer, smoking, depression, fibromyalgia) and disease activity scores at inclusion (M0) and at 36-month follow-up (M36).
Results: The mean age was 40,23 ± 13,68 ans. The sex-ratio (M/W) was 1,73. 96.4 % of the patients had axial involvement, 70 % had peripheral involvement and 61.5 % had enthesitis. SPA was radiographic in 88.1 % of the cases. The mean duration of disease was 615,90 ± 349,12 weeks. 57,2% of patients had at least one comorbidity, among whom the median comorbidity count was 1 (range 1-5).

Table 1. comparison between prevalence of comorbidities at M0 and M36.

Comorbidity	Prevalence at inclusion (M0)	Prevalence at 36-month follow-up (M36)
Sedentary behaviour	29,4% (n=57)	31,4% (n=61)
Osteoporosis	11,3% (n=22)	13,4% (n=26)
Smoking	10,8% (n=21)	10,8% (n=21)
Hypertension	5,7% (n=11)	9,3% (n=18)
Obesity	8,2% (n=16)	8,2% (n=16)
Tuberculosis	6,7% (n=13)	11,34% (n=22)
Diabetes	5,2% (n=10)	6,2% (n=12)
Gastrointestinal ulcer	2,6% (n=5)	3,1% (n=6)
Dyslipidemia	1,5% (n=3)	2,6% (n=5)
Cancer	0% (n=0)	1,0%(n=2)
Depression	2,6% (n=5)	2,6% (n=5)
Fibromyalgia	2,1% (n=4)	2,1% (n=4)

Table 2. Comparison between patients with or without comorbidities.

Parameter	Patients with at least one comorbidity (57,2%)	Patients without comorbidities (42,8%)	p
ESR (mm/h)	36,24	36,97	0,163
CRP (mg/l)	42,14	27,00	**0,002**
ASDAS-CRP	3,67	2,50	**0,003**
BASDAI	5,10	4,50	0,098
BASFI	6,10	4,16	**0,028**

Conclusion: In our study, the presence of comorbidities was correlated with more severe disease activity. Better management of these comorbidities may result in better outcome of patients with SPA.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1056 ASSESSMENT OF PULMONARY CIRCULATION WITH STRESS ECHOCARDIOGRAPHY IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS

Keywords: Imaging, Cardiovascular disease, Spondyloarthritis

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Background: Extra-articular features are common in ankylosing spondylitis (AS) and in psoriatic arthritis PsA. Cardiac involvement are less frequent but may be severe. The anterior chest wall pain and sterno-costal arthritis can lead to reduced chest expansion, which may contribute to the progression of cardio-pulmonary manifestations. We aimed to assess the response of the pulmonary circulation unit during stress in AS and PsA patients.
OBJECTIVES:
Methods: A total of 71 patients were enrolled in the study: 28 of them had AS (age 50.8±11.8 years), 17 APs (age 52.1±13.5 years), and 26 were healthy individuals (age 54.23±9.9 years). 74,1 % of AS patient, 11,1 % of PsA patient had ankylosis at the time of assessment. To the maximally tolerated workload, all subjects underwent resting and exercise stress echocardiography on a supine bicycle ergometer. Echocardiographic measurements were taken at rest, at 50 watts workload, and at maximal exercise.
Results: AS patients had significantly higher pulmonary artery systolic pressure (PASP; AS: 32.6±16.8 mmHg, APs: 21.6±12.7 mmHg, p<0.05) and pulmonary vascular resistance (PVR; AS: 1.3±0.4 WU, PsA: 1.1±0.3 WU, p<0.05) at maximal workload, while the right ventricular-pulmonary arterial (RV-PA) coupling at peak stress was higher in APs patients (AS: 1.2±0.6 mm/mmHg, PsA: 1.8±1.1 mm/mmHg, p<0.05). Comparing to the control group, AS and PsA patients had significantly higher resting PASP (control: 12.6±6.4 mmHg; AS: 22.8±7.6 mmHg, p<0.001; PsA: 21.4±7.0 mmHg, p<0.001), lower resting RV-PA coupling (control: 2.7±1.4 mm/mmHg; AS: 1.3±0.4, p<0.001; PsA 1.3±0.4 mm/mmHg, p<0.001), and higher peak PVR (control: 0.6±0.4 WU; AS: 1.3±0.4, p<0.001; PsA: 1.1±0.3 WU, p<0.005). One-way analysis of variance of the three groups also showed significant differences in the resting PASP (p<0.001), peak PASP (p<0.05), resting RV-PA coupling (p<0.001), peak PVR (p<0.001). At maximal workload, the AS patient had higher E/e' in ankylosing group.
Conclusion: Stress echocardiography is a promising, radiation-free method for assessing the subclinical cardiopulmonary changes among AS and PsA patients. The changes of PVR during stress may highlight the pulmonary complications in the subclinical stage. Higher E/e' in ankylosing group can refer to the influence of ankylosis on the left ventricular filling.
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Disclosure of Interests: None Declared.
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AB1057 INTERPRETATION OF DISEASE-SPECIFIC QUESTIONNAIRES ON DISEASE ACTIVITY, FUNCTIONAL CAPACITY AND QUALITY OF LIFE IN DAILY PRACTICE IN AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Outcome measures, Patient reported outcomes

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Background: In axial spondyloarthritis (axSpA), assessment of disease activity and physical function in clinical studies relies on patient-reported outcomes (PRO) such as patient's global, BASDAI, ASDAS and BASFI. However, it still remains unclear how response criteria adequately reflects the patients' opinion on disease status in daily practice.
Objectives: Investigate whether the results of PROs used in clinical studies with axSpA are indeed related to patient's opinion on disease status as reported in daily clinical routine.
Methods: Data were retrieved from the very first and from the last five visits within a timeframe of 5 years. Patient´s clinical characteristics, physician's global assessment and PROs (ASDAS, BASDAI, BASFI) were assessed at each visit. Status and change of all assessed information during follow-up were compared with patient´s opinion on symptoms related to axSpA, categorized into absent, mild, severe or very severe.
Results: 3.120 visits with median follow-up (IQR) 4.7 (4.3) years from 557 axSpA patients were analyzed. Absent/mild symptoms were stated in 98.7% and 90.9% of visits with inactive or low ASDAS disease status, while in 67.9% and 39.3% of visits showing association to high or very high ASDAS disease activity status, respectively (Figure 1). In comparison, BASDAI<4 was found in 90.8% of visits with absent/mild symptoms, while BASDAI≥4 showed severe symptoms in 48.1% of visits (Figure 1). Achievement of ASAS40 was associated with 92.4% visits reporting absent/mild symptoms, while this was the case in 76.4% visits despite not reaching ASAS40. Similar data were observed for ASAS20. Severe symptoms were reported in 0.6% patients achieving vs. 30.1% patients not achieving ASAS partial remission (PR). BASFI correlated with patients' opinion regarding symptoms at each visit.
Conclusion: Low disease activity as assessed by ASDAS or BASDAI were associated with mild symptoms in the majority of visits over a period of up to 5 years. Interestingly, a large proportion of visits showed low disease activity even when not achieving ASAS20 or ASAS40 responses or ASAS-PR.

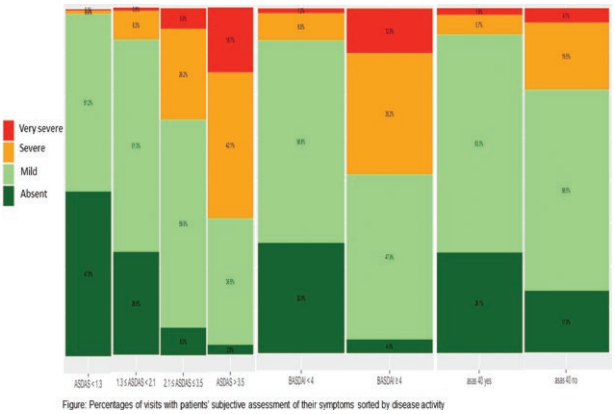


Figure: Percentages of visits with patients' subjective assessment of their symptoms sorted by disease activity

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Acknowledgements: NIL.
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AB1058 GENDER DIFFERENCES IN SPONDYLOARTHRITIS: FOCUS OF THE CLINICAL BURDEN OF DISEASE IN FEMALE PATIENTS

Keywords: Spondyloarthritis, Gender/diversity issues, Comorbidities

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Background: Spondyloarthritis (SpA) are a group of systemic autoimmune diseases, mainly affecting musculoskeletal system, with typical axial or peripheral forms. Recent data from the literature show significant differences in SpA subsets, levels of disease activity, drug efficacy and quality of life between male and female sex. [1, 2] It is well known how disease activity and comorbidities could compromise physical function and quality of life of SpA patients.
Objectives: To describe the clinical characteristics of women with SpA in our single-centre cohort compared to men, in relation to clinical characteristics, disease activity, therapy and comorbidities.
Methods: Adult patients with a diagnosis of Psoriatic Arthritis (PsA) and Axial Spondyloarthritis (AxSpA) according to CASPAR (ClASsification criteria for Psoriatic Arthritis) and to Assessment of SpondyloArthritis international Society (ASAS) criteria, regularly followed at the SpA clinic of our unit, were consecutively enrolled from April to December 2022. Their epidemiologic, clinic and clinimetric data were collected. Intergroups comparisons were assessed by using Chi-square, t-test and ANOVA. P values <0.05 were considered significant.
Results: A total of 200 patients were enrolled, 115 male (57.5%) and 85 female (42.5%) with comparable mean age values (M 56.13±14.48 years, F 56.84±12.22 years; p=0.508) and with a significantly shorter disease duration in women (12.9±10.3 years vs 17.05±12.08 years; p<0.001). No differences in the distribution of PsA or AxSpA based on gender were observed. Six patients had a diagnosis of enteropathic SpA; all of them were women. Taking into account the clinimetric evaluations, female patients show higher values of both Disease Activity Index for Psoriatic Arthritis DAPSA (15.63 vs 9.40; p=0.003), Leeds Enthesitis Index (LEI) (0.46 vs 0.16; p=0.02) and Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index (0.7 vs 0.4; p=0.05). The total number of drugs [both Biological disease modifying anti-rheumatic drugs (bDMARDs) and conventional synthetic DMARDs)] taken for disease control was 4.47±2.45 for women and 3.79±2.07 for men (p=0.012); no differences were observed between the 2 groups for any specific drug. Among the comorbidities, none of them was more prevalent in men, while osteoporosis (OP) (p=0,006), mood disorders (0,009), fibromyalgia (FM) (p<0,000015), osteoarthritis (OA) (0,007) and thyroid disease (p<0,000015) were significantly more frequent in women.
Conclusion: Women of our cohort show a significantly higher risk of developing an inflammatory bowel disease than men. Female patients have also higher levels of peripheral disease activity, both on joints and enthesis; moreover, they show a significantly lower persistence in drug therapy. Besides, they have a more complex disease, suffering more frequently of OP, OA, FM and thyroid diseases than men. Finally, it is very interesting to note how women tend to develop a much more complex disease, even with a significantly shorter disease duration than male patients. These data confirm how rheumatologists should focus on the assessment of women with SpA, aiming at promoting a closer monitoring of gastrointestinal symptoms, peripheral arthritis and enthesitis and at preventing the development of comorbid conditions, thus optimizing also their quality of life and physical functioning.
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AB1059 NETRIN-1 IN SPONDYLOARTHRITIS: A NOVEL MARKER TO PREDICT DISEASE ACTIVITY?

Keywords: Biomarkers, Real-world evidence, Spondyloarthritis

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Background: Netrin-1 is a chemorepulsant and inhibits the migration of monocytes, neutrophils and lymphocytes by activation of its receptors. It has been revealed that netrin-1 can limit the inflammatory response, reduce tissue damage due to hypoxia and simultaneously suppress apoptosis. Due to this immune regulatory role, it has been hypothesized that netrin-1 can be used as a biomarker in rheumatic diseases.
Objectives: To compare plasma netrin-1 levels in axial spondyloarthritis (SpA) patients with the healthy subjects and to evaluate its relationship with disease activity and other clinical and laboratory parameters.
Methods: Patients with axial SpA between the ages of 18-65 who applied to Ankara City Hospital Rheumatology outpatient clinic between November 2021 and January 2022 were consecutively enrolled upon acceptance to participate. Pregnant patients, patients with systemic disease other than axial SpA and patients who were taking regular medication other than axial SpA treatment were excluded. A control group was formed from healthy volunteers with similar age and gender characteristics. In both groups, in addition to regular laboratory tests netrin-1 level was measured by an Enzyme Linked ImmunoSorbent Assay (ELISA) kit with an analytical unit of pg/mL (Elabscience, Texas, USA, Catalog No: E-EL-H2328; Lot No: GZWTKZ5SWK).
Results: A total of 60 axial SpA patients and 56 healthy controls were included in the study. There was no statistically significant difference between the groups in terms of age, gender andnetrin-1 levels between patients and controls (Table 1). Data regarding clinical characteristics, HLA-B27 positivity, acute phase reactants at the time of evaluation and disease activity scores of the axial SpA group was presented in Table 1. No significant differences were observed in netrin-1 levels in any comparison among all axial SpA patients, in ankylosing spondylitis (AS) and nonradiographic axial spondyloarthritis (nr-ax SpA) patient subgroups, and in healthy controls (all axial SpA vs control p=0,361, AS vs nr-axSpA p=0,790, AS vs control p=0,360, nr-axSpA vs control p=0,700). Netrin-1 levels had a significant positive correlation with BASDAI (r=0,301 p=0,032), ASDAS CRP (r=0,320 p=0,022), VAS pain (r=0,340 p=0,015).
Conclusion: Our results demonstrated a positive correlation between netrin-1 levels and disease activity in axial SpA patients, implying that netrin-1 may come to the forefront as a novel biomarker to predict disease activity in axial SpA.
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Table 1. Demographics of subject groups, clinical and laboratory characteristics of axial SpA patients

	Axial SpA N=60	Control N=56	P
Age, years, mean ± SD	39,51 ± 10,88	44,57 ± 13,87	0,057
Gender, female, n (%)	37 (53,6)	32 (46,4)	0,620
Type of axial SpA, n (%)			
AS	49 (81,66)		
Nr-ax SpA	11 (18,33)		
HLA-B27 positivity, n (%)*	22 (64,7)		
CRP, mg/L, mean ± SD	8,09 ± 9,30		
ESR, mm/hour, years, mean ± SD	13,4 ± 10,95		
Morning stiffness time, hours, mean ± SD	1,6 ± 2,72		
VAS pain, mean ± SD	4,11 ± 2,75		
BASDAI, mean ± SD	3,00 ± 2,04		
ASDAS CRP, mean ± SD	2,30 ± 1,04		
Serum Netrin-1, pg/mL, mean (min-max)	74,436 (34,5-237,18)	61,904 (35,85-175,33)	0,361

* Out of 34 patients with a HLA-B27 test result, SpA: spondyloarthritis, AS: ankylosing spondylitis, Nr-ax SpA: non-raidographic axial spondyloarthritis, HLA-b27: human leukocyte antigen B27, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, VAS: visual analogue scale, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, ASDAS CRP: Ankylosing Spondylitis Disease Activity Score CRP

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Spondyloarthritis - clinical aspects (other than treatment)

AB1060 EXPLORING DISEASE ACTIVITY AND PATIENT CHARACTERISTICS IN ANKYLOSING SPONDYLITIS (AS) IN EUROPE

Keywords: Spondyloarthritis

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Background: Ankylosing Spondylitis (AS) is a form of arthritis that primarily affects the spine. It causes inflammation of the spinal joints that can lead to severe, chronic pain and discomfort[1]. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is the most frequently used patient-reported outcome to measure disease activity in axial spondyloarthritis. There is no validated definition for disease remission using BASDAI, although a threshold of ≤3 has been used in clinical trials for low disease activity[2].
Objectives: The objective of this study was to examine AS patient characteristics of those with low disease activity (LDA) (BASDAI score ≤3), highlighting any nuances in treating these patients.
Methods: A multi-centre online medical chart review study of patients with AS was conducted between July 2022 – September 2022 among UK, FR, DE, IT & ES rheumatologists practicing across hospital and private practices. Physicians were screened for practice duration and patient volume. Charts of patients prescribed with biologics were included in the analysis.
Results: 262 sampled physicians collectively reported 524 AS patients. From the reported AS patients, 277 were recorded as having achieved LDA ('LDA') and 165 were recorded as not having achieved LDA ('not LDA'). Among not LDA reported patients, a higher proportion were female vs the LDA cohort (32% vs 19%). Reported not LDA patients were more likely to suffer any additional co-morbidities vs LDA cohort (63% vs 44%). When analysing disease severity (physician-defined) status between these two patient groups, reported not LDA patients were more likely to be recorded as 'mild' at diagnosis vs LDA (14% vs 4%). In contrast, current (i.e. at time of consult) disease severity was more likely to be recorded as moderate/severe for the not LDA cohort vs the LDA cohort (76% vs 20%). In addition, reported not LDA patients recorded with higher mean disease and haematology scores.

Table 1. Reported patient disease and haematology scores (mean)

Reported AS patients	Tender joint count (TJC)	Swollen joint count (SJC)	C-reactive protein (CRP)	Erythrocyte Sedimentation Rate (ESR)
Achieved LDA	0.8	0.4	10.7	3.6
Not achieved LDA	3.4	2.2	28.9	15.5

The most prominent biologic therapy class used to treat both patient groups are still TNFis; notable JAKi usage is more prominent in the not LDA cohort vs the LDA cohort (9% vs 3%).

Conclusion: From the sample surveyed, it appears the not achieved LDA group are milder at diagnosis but show a greater disease severity/activity on their most recent consultation compared to the LDA cohort – it could be inferred that initial mild severity resulted in a lesser need to treat earlier and, as such, disease progression ensued. There may therefore be an argument to treat early with advanced therapies, regardless of initial disease severity. Further investigation using comparator cohort is warranted.

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AB1061 CORRELATION OF SERUM SUBFATIN, CTHRC1, CTRP3, CTRP6 LEVELS WITH DISEASE ACTIVITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Prognostic factors, Spondyloarthritis

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Background: It has been determined that biological treatments affect the serum concentration of these biomarkers independently of disease activity. As current adipokines and known modulators of inflammation, it may play a role in evaluating the efficacy of treatment, especially in cases using biologic agents.
Objectives: To analyze novel biomarkers from the C1q TNF superfamily and their function in autoimmune inflammatory rheumatic disorders, as well as to look for a biomarker capable of evaluating both the clinical disease activity and aiding in the evaluation of therapy efficacy.
Methods: Sixty-one AxSpa patients and 30 healthy controls were enrolled in the study. Serum biomarkers subfatin, CTHRC1, CTRP3, CTRP6, IL-6, IL-17, TNF-α and disease activity indexes BASDAI, BASFI, MASES, ASDAS-ESR/CRP were evaluated and compared. Patients were then classified, and their serum biomarkers were also assessed according to their disease activity scores, and further according to their treatment regimens.
Results: None of the examined biomarkers revealed a discernible difference between patients and healthy controls. Although the difference was not statistically significant, healthy controls were found to have lower median concentrations of serum subfatin, CTHRC1, CTRP3, CTRP6, IL-6, IL-17, and TNF-α. Furthermore, no association between the research biomarkers and clinical disease activity was seen once the patients were categorized according to the severity of their disease. Finally, it was discovered that biological therapies had an impact on these biomarkers' serum concentrations (Table 1) regardless of the disease's activity.
Conclusion: Circulating levels of subfatin, CTHRC1, CTRP3, CTRP6, IL-6, IL-17, and TNF-α, which are novel adipokines and well-known inflammatory mediators, may be important for determining treatment effectiveness, particularly in patients receiving biologics. We were unable to prove a connection between serum biomarker levels and clinical disease activity, though.

Table 1. The comparison between different treatment groups

	Biologics(n=43)	cDMARD(n=18)	p-value
Age (years)	43±9	34±9	**0.02**
ESR (mm/hr)	14 [8-35]	21 [9-34]	0.72
CRP (mg/L)	2 [2-9]	4.4 [2-10]	0.61
Subfatin (ng/mL)	0.57 [0.4-0.8]	0.89 [0.6-1.7]	**0.03**
CTHRC1 (ng/mL)	54 [39-89]	71 [40-181]	0.33
CTRP3 (ng/mL)	1.9 [1.7-2]	2.2 [1.8-3]	**0.03**
CTRP6 (ng/mL)	1.92 [1.1-2.6]	2.85 [1.5-6.8]	**0.03**
IL-6 (pg/mL)	70 [55-80]	73 [55-138]	0.35
IL-17 (pg/mL)	19 [15-32]	33 [21-55]	**0.04**
TNF-α (pg/mL)	93 [76-128]	118 [97-163]	**0.01**
ASDAS-CRP	2.4±1.0	2.8±0.9	0.16
BASDAI	3.4±1.8	4.1±1.7	0.21

*Data are given in median [25-75p] or mean±SD **ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; CTHRC1: Collagen triple helix repeat-containing protein-1; CTRP3: C1q/TNF-related protein-3; CTRP6: C1q/TNF-related protein-6; TNF: Tumor necrosis factor; BASDAI: Bath Ankylosing Spondylitis Disease Activity *Index*; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score-CRP

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1062 RENAL INVOLVEMENT IN SPONDYLOARTHRITIS

Keywords: Descriptive studies, Spondyloarthritis, Kidneys

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Background: Spondyloarthritis (SpA) encompasses a group of inflammatory diseases characterized by enthesitis, axial and eventually peripheral skeletal involvement. Extra-articular manifestations are common and important systemic features of SpA. The most common extra-articular manifestations are represented by uveitis, bowel disease, skin, heart, lung and kidney involvement. Renal complications are frequent among patients with SpA.
Objectives: The aim of the present study was to assess the epidemiologic, clinical, biological and histological features of renal diseases in SpA.
Methods: A retrospective monocentric study was performed including patients diagnosed with SpA according to the ASAS criteria. Baseline data were obtained during the period from 2002 to 2022. We reviewed sex, age, disease duration and results of laboratory examination and urinalysis in order to detect renal abnormalities.

Results: A total of 107 patients were enrolled in the study, including 78 men and 29 women. The median age was 42 years [16-74]. Renal abnormalities were diagnosed in 8 cases (7.4%), all of them were men. The median age of the patients at the time of diagnosing renal complications was 46 years [21-62]. Renal involvement onset was diagnosed after a mean follow-up of 9.6 years [1-21] from the SpA diagnosis. We noted nonsteroidal antiinflammatory agents (NSAID) intake in 4 cases. Three patients were treated with salazopyrin and one with azathioprine. Among the 8 patients who presented renal abnormalities, we noticed: proteinuria in 5 patients, microscopic hematuria in 2 patients, macroscopic hematuria in 1 patient, nephrotic syndrome in 2 patients and decreased renal function in 2 patients. Secondary renal amyloidosis (4 patients) and Immunoglobulin A nephropathy (2 patients) were the most common causes of renal involvement followed by nephrolithiasis (2 patients). Amyloid deposits were histologically proven by salivary gland biopsy in one case and by renal biopsy in 2 cases. Concerning the Immunoglobulin A nephropathy, the diagnosis was made by renal biopsy and the serum IgA level was normal. Six patients were treated with tumor necrosis factor (TNF)-alpha blocker therapy, with a good outcome only in 4 cases. Only one patient evolved to the end stage renal disease.
Conclusion: The finding of a significant renal abnormality in 7.4% of patients suggests that evidence of renal involvement should be actively sought in this disease by monitoring renal function and urinalysis at regular intervals.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1063 PREDICTORS OF ACTIVITY OF ANKYLOSING SPONDYLITIS DURING PREGNANCY

Keywords: Spondyloarthritis, Pregnancy and reproduction

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Background: The ratio of men and women suffering from ankylosing spondylitis (AS) approaches 1:1. Many women aged 30-40 think about motherhood, which makes it important to study the problem of pregnancy in AS.
Objectives: Assess predictors of AS activity during pregnancy.
Methods: The study included 38 pregnant women who met the New York criteria for ankylosing spondylitis, 1984. The average age of patients was 32.6±6.8 years, age at the onset of the disease was 22.8±12.9 years, disease duration was 132, 9±67.3 months The BASDAI index for 1-3 months before conception, in the I, II and III trimesters averaged 2.2±1.85; 2.7±1.72; 3.3±1.87 and 3.4±2.15, respectively. 11 (28.9%) patients received genetically engineered biological preparations (GEBP) 1–3 months before pregnancy, 8 (21.05%) patients in the month of conception, 4 (10, 5%), 4 (10.5%) and 1 (2.6%) women, respectively. Non-steroidal anti-inflammatory drugs in I, II and III (up to 32 weeks) trimesters were taken by 11 (28.9%), 23 (60.5%) and 16 (42.1%) women, respectively. 25 (65.7%) women planned an observed pregnancy. Most of the patients (n = 28) were included in the study in the first trimester of gestation, 7 - in the II, 1 - in the III trimester. The visits were carried out at 10-11, 20-21 and 31-32 weeks of pregnancy.
Results: In the first trimester of pregnancy with the level of activity according to BASDAI, there were the following significant correlation coefficients: the level of BASDAI (rs=0.71) and back pain (rs=0.71) 1-3 months before conception, smoking experience (rs=0, 39), pregnancy planning with a rheumatologist (rs=-0.35), p<0.05 in all cases. In the second trimester, we can talk about the effect on the activity of the level of BASDAI in the first trimester (rs=0.33) and the fact of pregnancy planning (rs=-0.79). In the third trimester, BASDAI activity was influenced by early follow-up with a rheumatologist (rs=-0.37), pregnancy planning (rs=-0.52), exercise therapy in the third trimester (rs=-0.37). Risk factors for high AS activity (BASDAI>4) were high AS activity 1-3 months before conception (odds ratio (OR) in the I and II trimesters - 23 and 7, respectively; 95% CI; p<0.01), lack of pregnancy planning (OR for trimesters 9.2; 32.5 and 15.9, respectively; 95% CI, p<0.01), the abolition of biologics on the eve of pregnancy and in the first trimester (OR in the II and III trimesters - 23.9 and 22.4, respectively; 95% CI, p<0.01). In addition, risk factors for high AS activity in the third trimester were BASDAI>4 in the first (OR - 7.1; CI 95%, p<0.05) and second trimesters of pregnancy (OR - 9.55; CI 95%, p <0.05).
Conclusion: Lack of pregnancy planning, the value of the BASDAI index at the time of conception and in the first trimester of pregnancy, the abolition of biologics 1-3 months before conception and in the first trimester are predictors of AS activity throughout the gestation period.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1064 THE RELATIONSHIP BETWEEN DISEASE ACTIVITY AND CENTRAL SENSITIZATION IN SPONDYLOARTHROPATHY PATIENTS RECEIVING BIOLOGICAL TREATMENT

Keywords: Spondyloarthritis

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Background: Spondyloarthritis (SpA) is a chronic systemic inflammatory disease. Most patients with SpA complain of chronic pain during the course of the disease. Chronic pain can be explained by central sensitization (SS).
Objectives: Our aim was to investigate the relationship between disease activity and SS in patients with SpA receiving biologic therapy.
Methods: 92 patients with SpA who met the ASAS criteria were included in this *retrospective* study. Demographic characteristics of patients, comorbidities, drug treatments used, Bath Ankylosing Spondylitis Metrology Index (BASMI), Bath Ankylosing Spondylitis Functional Index (BASFI), visual analog scale (VAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Index (ASDAS-CRP), Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), Central Sensitization Scale (SSS) were calculated. Patients were divided into 2 groups according to BASDAI score <4 low disease activity and ≥4 high disease activity. All parameters between groups were compared. The correlation between the patients' SSQ scores and their BASDAI and ASDAS-CRP scores was analyzed. In addition, ROC analysis was performed to estimate the disease activity of the SS value and the optimal threshold value was determined.
Results: The proportion of patients with high disease activity was 41.3% (n=38 patients). There was no statistically significant difference between the low disease activity (group 1) and high disease activity (group 2) groups in terms of age, gender, body mass index, comorbid diseases, and the medical treatment (NSAID, steroid, methotrexate, sulfasalazine). There was no statistically significant difference between the groups in ESH, CRP and vitamin D levels. SS, MASES, BASFI, and ASDAS-CRP were found to be significantly higher in group 2 patients, respectively (40.87 ± 12.26 vs. 26.78 ± 11.81, p < 0.001; 6.32 ± 3.60 vs. 3.69 ± 3.05, p = 0.001; 5.77 ± 2.12 against 2.80 ± 1.33, p < 0.001, 3.35 ± 0.70 versus 2.43 ± 0.45, p < 0.001). A moderate correlation was found between the SS scale and ASDAS-CRP (r:0.421; p<0.001) and BASDAI (r:0.581; p<0.001). ROC curve analysis showed that the optimal threshold value of the SS scale score for high disease activity was 31.5% with 78.3% sensitivity and 76.1% specificity (AUC: 0.802, 95% CI: 0.687-0.917, p<0.001) (Figure 1).
Conclusion: It has been shown that the central sensitization scale, which is a simple and applicable scale, can be used to evaluate disease activity in SpA patients receiving biologic therapy.
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Table 1.

	BASDAİ <4 (n:54)	BASDAİ ≥4 (n:38)	P value
Age, years	43.6 ± 9.3	44.7 ± 8.6	0.594
Female gender, n (%)	17 (31.5)	11 (28.9)	0.795
BMI, kg/m²	26.7 ± 4.0	27.1 ± 4.2	0.712
Marital status single, n (%)	8 (14.8)	2 (5.3)	0.187
Comorbidity			
Menopause, n (%)	2 (11.8)	2 (16.7)	0.706
Hypertension, n (%)	3 (5.6)	1 (2.6)	0.640
Diabetes Mellitus, n (%)	2 (3.7)	0 (0)	0.230
Hypothyroidism, n (%)	3 (5.6)	0 (0)	0.140
History of Cancer, n (%)	0 (0)	1 (2.6)	0.231
Amyloidosis, n (%)	0 (0)	1 (2.6)	0.231
History of Uveitis, n (%)	6 (11.4)	3 (7.9)	0.609
Laboratory			
CRP, mg/dl	8.10 ± 10.03	12.18 ± 15.84	0.134
25 (OH) Vitamin D, ng/ml	26.69 ± 42.36	21.68 ± 7.67	0.479
Treatment			
Methotrexate, n (%)	7 (13.0)	8 (21.1)	0.301
Steroid, n (%)	5 (9.3)	2 (5.3)	0.695
NSAID, n (%)	46 (85.2)	36 (94.7)	0.187
Hastalık Aktivite Skorları			
BASMİ	3.07 ± 1.70	3.34 ± 2.35	0.527
BASFİ	2.80 ± 1.33	5.77 ± 2.12	<0.001
VAS	50.46 ± 21.55	53.16 ± 16.45	0.518
BASDAİ	2.58 ± 0.86	5.87 ± 1.33	<0.001
ASDAS-CRP	2.43 ± 0.49	3.35 ± 0.70	<0.001
MASES	3.69 ± 3.05	6.32 ± 3.60	0.001
Central Sensitization Scale	26.78 ± 11.81	40.87 ± 12.26	<0.001

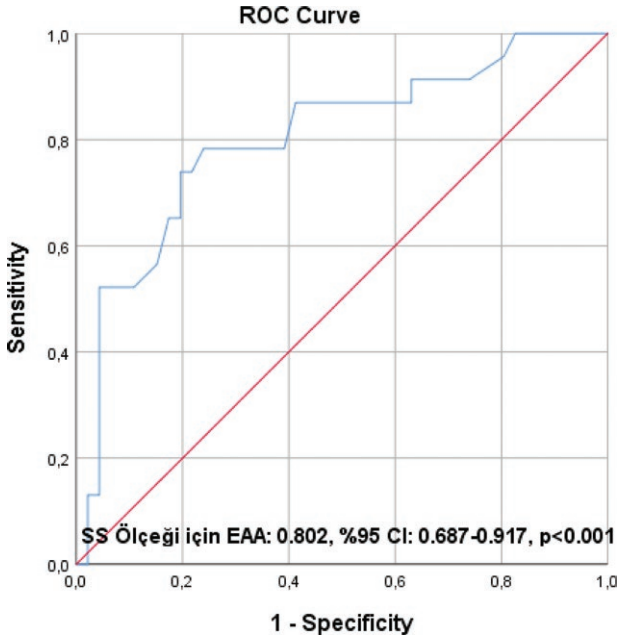


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1065 BERTOLOTTI SYNDROME: AN UNDER RECOGNIZED CAUSE OF INFLAMMATORY BACK PAIN?

Keywords: Spondyloarthritis, Pain, Quality of life

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Background: Bertolotti syndrome describes a lumbosacral transitional vertebra (LSTV) which causes symptoms, usually low back pain. LATV is a congenital anomaly where the L5 vertebra has an unusual morphology. Bertolotti syndrome is an under-recognised condition by clinicians.
Objectives: To clarify the presentation of Bertolotti syndrome, whether there are features of inflammatory back pain (IBP) and the effect on quality of life.
Methods: In this pilot study, 62 patients with LSTV were identified on imaging (plain x-ray). Imaging was performed for a variety of indications, predominently for back pain. In total, 34 patients agreed to take part, with 18 returning questionnaires. Questionnaires were selected for face vailidity and included: Calin IBP Questionnaire, EQ-5D Questionnaire, Visual analogue pain scale (VAS-P). In view of Covid restrictions all contact was by phone and questionnaires were completed online or returned via post. Plain X-rays visualising the lumbar spine were assessed for radiological features of LSTV.
Results: Seventeen (94%) of the participants (n=18) recorded a VAS-P score >3, indicating a clinically significant level of pain. The mean VAS-P score was 6 (range of 2-9). 89% of respondents scored at least 3/5 in the Calin questionnaire. Of the 5 features of inflammatory back pain in the Calin questionnaire, 4 out of the 5 were reported by most respondents. The exception was 'improvement on exercise', which was only reported by 18% of respondents. Quality of life was impaired-EQ-5D (mean: 0.503, range -0.074 to 0.796). The commonest radiological abnormality was enlarged transverse process (100%) followed by pseudoarticulation with the sacrum (83%) and scoliosis (33%). Presence of sclerosis and/or osteoarthritis at the pseudoarticulation was associated with worse pain scores. Female respondents reported worse pain.
Conclusion: These results suggest Bertolotti syndrome is associated with pain in the majority of patients and affects quality of life,. The character and site of the pain suggests that Bertollotti syndrome should be considered in the differential diagnosis of spondyloarthritis.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Simon Stebbings Consultant of: Abbvie. Janssen, Ciara White: None declared, Terence Doyle: None declared.
DOI: 10.1136/annrheumdis-2023-eular.2128

AB1066 DISEASE DURATION, AGE AND CLINICAL FEATURES RELATED TO AORTIC VALVE SCLEROSIS IN PATIENTS WITH SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Heart, Epidemiology

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Background: Valve degeneration is prevalent in Spondylarthritis (SpA) patients according to descriptive studies, but it is also common in general population. Disease burden may be a key factor for valve degeneration in SpA.
Objectives: Compare clinical, radiographic and laboratory parameters between patients with spondylarthritis (SpA) with aortic valve sclerosis (AVS)
Compare disease duration since onset of symptoms, diagnosis, and age in patients with AVS and patients without AVS.
Methods: A retrospective cohort study was conducted. Eligible patients were 219 SpA patients that met ASAS criteria visited the SpA clinic between July – October 2022. A total of 75 patients that had an echocardiography carried out after SpA diagnosis were included. Aortic valve surgery, rheumatic valve disease, endocarditis and bicuspid valves were excluded. Missing information about SpA were collected prospectively. Comparison between groups was conducted using t test or U-Mann Whitney test according to variable distribution. Proportions were compared using risk difference (RD) or odds ratio (OR).
Results: AVS was observed in 30 (39.5%) patients. Description and comparison of the sample is summarized in Table 1. Age had an OR of 1.17 (95% CI 1.1-1.3) with minor increase of risk for AVS. Duration of disease and delay in diagnosis were similar in both groups. Smoking had a protective effect for AVS with OR former smoker 0.36 (95% CI 0.12-1.11) and OR smokers 0.13 (95% CI 0.03-0.61). Other echocardiographic findings of the patients were: mild aortic insufficiency in 15 (19.5%) and moderate in 3 (3.9%). Mean aortic root diameter was 34.4mm (SD 3.67). Aortic root was dilated in 9 (11.7%).

Table 1.

Time related variables	All (n=75)	AVS (n=30)	No AVS (n=45)	p
Years from 1st symptom to diagnosis, p50 (IQR)	2 (9)	2 (12)	2 (9)	0.59
Years of disease duration since 1st symptom, p50 (IQR)	16.5 (16.5)	15 (19)	17 (16)	0.30
Years of disease duration since diagnosis, p50 (IQR)	11 (15)	9.5 (14)	11 (16)	0.65
Age, mean (SD)	60.9 (15.0)	71.0(9.9)	54.3(15.1)	**0.00**
Clinical variable, n (%)				
Male	30 (61.3)	17 (56.7)	29 (64.4)	0.50
Hypertension	47 (62.7)	22 (73.3)	25 (55.6)	0.12
Dyslipidemia	49 (65.3)	20 (66.7)	29 (64.4)	0.84
Diabetes	22 (29.3)	8 (26.7)	14 (31.3)	0.68
Ischemic heart disease	9 (12)	5 (16.7)	4 (8.9)	0.31
Non-smoker	21(28)	13(43.3)	8(17.8)	**0.02**
Former	35(46.7)	13(43.3)	22(48.9)	
Smoker	17(22.7)	3 (10)	14(31.1)	
B27	24 (35.3)	11 (39.3)	13 (32.5)	0.56
High CRP	49 (73.1)	20 (71.4)	29 (74.4)	0.79
Enthesitis	32 (42.7)	12 (40)	20 (44.4)	0.70
Uveitis	7 (9.3)	3 (10)	4 (8.9)	0.85
Psoriasis	44 (45.9)	20 (66.7)	24 (53.3)	0.34
Nail psoriasis	34 (45.3)	14 (46.7)	20 (44.4)	0.75
Inflammatory bowel disease	1 (1.3)	1 (3.3)	0	0.21

Conclusion: Age showed small but statistically significant association with AVS. Disease duration measured since diagnosis or onset of 1st symptom did not show significant association. Surprisingly, smokers showed less AVS.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1067 OPTIC NEURITIS IN SPONDYLARTHRITIS NAÏVE TO TNFA INHIBITORS: A SYSTEMATIC LITERATURE REVIEW

Keywords: Spondyloarthritis

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Background: Optic neuritis (ON) is the expression of many diseases: demyelinating (MS or NMOSD), autoimmune (sarcoidosis, systemic erythematous lupus, Sjogren's syndrome, etc.), infectious (syphilis, tuberculosis, toxoplasma etc.), or genetic disorders such as Leber's Hereditary Optic Neuropathy or Kjer's optic atrophy[1]. In spondyloarthropathies (SpA), ON occurs as a demyelinating adverse event to TNFα inhibitors; however, cases of ON in SpA naïve to TNFα also have been reported.
Objectives: We aimed to assess the directionality and/or causality between SpA and ON in patients naïve to TNFα inhibitors.
Methods: The systematic literature review was performed according to the PRISMA guidelines[2] in four databases (PubMed, Scopus, Embase and Ovid) for studies published from database inception until 01.12.2022. Additionally, we searched the electronic database of our Rheumatology Department for patients with a diagnosis of both SpA and ON. We excluded patients with ON secondary to therapy with TNFα inhibitors and pediatric cases.
Results: We identified 529 studies across the databases. After eliminating duplicates and applying exclusion criteria, we found eight publications (describing nine patients) eligible for review. We identified two additional cases in the electronic database of our center which met the requirements. Among the 11 patients with SpA and ON, 7 (63.63%) were female; the great majority had ankylosing spondylitis (90.9%) and one patient had psoriatic arthritis. HLA-B27 was positive in 8 (72.7%) patients. More than half of the cases (54.54%) were of Asian origin, two (18.18%) were Caucasian; in the rest, the origin was not specified. Bilateral eye involvement occurred in 6 patients, most of whom (83.33%) were HLA B27 positive. Six patients (54.54%) experienced at least one episode of relapse. The workup for demyelinating diseases included anti-MOG antibodies (performed in three, positive in one case) and anti-AQP4 antibodies (tested in six, positive in one). Oligoclonal bands were assessed in a limited number of cases (36%) and were reported positive in one of four tested patients; a diagnosis of demyelinating disease (NMO-SD or MS) was established in 3 (27%) patients. No thorough infectious disease screening was reported in any of the published cases. Various treatment protocols were employed in the management of ON; only 3/11 (27%) patients followed the standardized ON treatment regimen (ONTT)[3]. In seven patients, ON resulted in the complete loss of vision or perception of light.
Conclusion: Literature reports of the association of NO and SpA are scarce, pointing to the coexistence, rather than a causative association between the two diseases. Patients with SpA who develop ON should undergo a thorough screening for an underlying etiology. Timely standardized treatment for ON is mandatory to improve the outcome of patients with ON.
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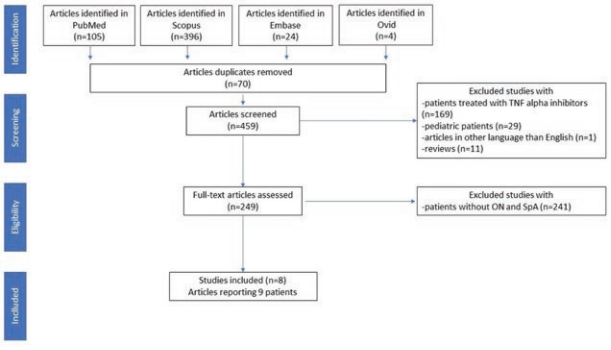


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1068

THE ROLE OF HEPCIDIN IN THE FORMATION OF ANEMICAL SYNDROME IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND ITS SIGNIFICANCE IN THE DIFFERENTIATION OF ANEMIA OF CHRONIC DISEASE, IRON DEFICIENCY ANEMIA AND THEIR COMBINATION

Keywords: Spondyloarthritis, Diagnostic tests

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Background: Anemia is a frequent comorbid condition in ankylosing spondylitis (AS) patients. Anemia of chronic disease (ACD), iron deficiency anemia (IDA) and their combination are most often found in patients. The differential diagnosis between ACD and IDA is important because they require different treatment and at the same time is complicated due to the presence of an inflammatory component.
Objectives: To establish the role of hepcidin in the formation of anemic syndrome in AS patients and its significance in differentiating anemia of chronic disease, iron deficiency anemia and their combination.
Methods: The study included 76 patients diagnosed with AS according to the modified New York criteria (1984) and 26 controls. Among them, there were 47 patients without anemia and 29 patients with anemia (IDA, n=7; ACD with iron deficiency, n=6; ACD, n=15, folate deficiency anemia, n=1). The diagnostic list included a complete blood count, serum iron, total iron-binding capacity, transferrin saturation, serum ferritin, soluble transferrin receptors (sTfR), and hepcidin. In the literature, there are no clear criteria for gradation of hepcidin levels, therefore, for further analysis, a percentile comparison was performed and indicators corresponding to P25 (up to 25 ng/ml), P25 - P75 (25-35 ng/ml) and P75 (above 35 ng/ml) were selected control group. The statistical processing of the obtained results was carried out using the Microsoft Office Excel 2007 statistical software package.
Results: In the group of AS patients, 41 patients (54%) had hepcidin levels >P75, 16 (21%) - <P25, and 19 (25%) within P25 - P75. Hepcidin levels in patients with anemia were 1.4 times higher (51.77 ± 4.62 ng/ml) than in people without anemia (36.08 ± 2.57 ng/ml). The level of hepcidin (35.84±7.50 ng/ml) in patients with IDA is practically comparable to the group of patients without anemia. The level of hepcidin (62.78±5.94 ng/ml) is 1.7 times higher in people with ACD than in people with IDA ($p<0.05$). Patients with ACD and iron deficiency in terms of hepcidin level occupy an intermediate place (48.53±9.50 ng/ml), which may indicate an important role in the pathogenesis of ACD and can be used as a diagnostic marker for the differential diagnosis of ACD and IDA. In the group of patients without anemia, we found no significant relationship between hepcidin and indicators of red blood and ferrokinetics. While in individuals with anemia we found the relationship of hepcidin with serum iron ($r=0.26$; $p<0.05$), soluble transferrin receptors ($r=-0.15$; $p<0.05$) and transferrin saturation coefficient ($r=0.17$; $p<0.05$).
Conclusion: For AS patients, for the early differential diagnosis of the types of anemia (ACD, IDA, and ACD with iron deficiency), in addition to traditional methods, the complex of laboratory tests should include determination of the hepcidin level in blood serum. A high level of hepcidin indicates the presence of ACD.
REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1069

GENDER DIFFERENCES IN PRESENTATION, CLASSIFICATION, AND DISEASE ACTIVITY OF SPONDYLOARTHRITIS: RESULTS FROM GESPA COLOMBIAN COHORT

Keywords: Spondyloarthritis, Geographical differences, Gender/diversity issues

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Background: Spondyloarthritis (SpA) is a chronic inflammatory rheumatic disorder composed of axial (AxSpA) and peripheral (pSpA) disease. AxSpA is further subdivided into radiographic AxSpA (r-AxSpA) and non-radiographic AxSpA (r-AxSpA). Historically, SpA was mostly a male disease. However, actual disease awareness has changed the approach, allowing women to be included to a greater extent.

Objectives: Few studies have explored the male and female disease features in Latin American population. The aim of this study was to examine the clinical presentation, disease onset characteristics, metrology, HLA frequency, and clinical characteristics of male and female SpA patients.
Methods: We used a cohort of Colombian SpA patients from 1990 to the current day. Patients were evaluated by rheumatologists, filled out validated questionaries, and were classified according to the Assessment of SpondyloArthritis International Society (ASAS) classification criteria at the time of diagnosis. Using the available information, patients enrolled before to 2011 were reclassified according to ASAS. We compared the features of both genders and used SPSS 26.0 to conduct statistical analysis.
Results: In this study, 469 SpA patients from a Colombian SpA cohort were included. There were 164 (34.9%) females and 305 (65.1%) males total. There were no statistically significant differences in ASAS classification; 61.2% of females and 50.6% of males had AxSpA, P = 0.3. However, nr-AxSpA was more prevalent among females (20.6%) than males (13.3%), P = 0.01. In all groups the frequency of HLA-B15 was comparable (15.9% vs. 11.2%, P = 0.1). And the prevalence of HLA-B27 was greater in men than in women (52.4% vs. 33.3%, P < 0.01). The symptoms at the onset of the disease had similar distribution in both sexes (table 1). Enthesopathy was more prevalent among women than males (82.4% vs. 72.4%, P = 0.02). but no arthritis, uveitis, psoriasis, and inflammatory bowel disease (table 1). In males, disease onset was more acute (40.7% vs. 27.3%, P = 0.04). Age at beginning of the disease was 32 (24.5 – 41.1) years for females and 24.89 (20.5 – 31.7) years for males (P < 0.01). The time to diagnosis (in months) was 39 (11.5 – 126) for females and 13 (3 – 71) for males (P < 0.01). Women had more functional impairment measured by BASFI, disease activity measured by BASDAI, and self-reported illness activity than men, although men had a higher C-reactive protein (CRP) (P < 0.01) (Table 1).
Conclusion: Nr-AxSpA is more frequent in women than in men, although radiographic disease is more prominent in men. The prevalence of HLA-B27 is higher in men with SpA. Males are older at the onset of the disease and were diagnosed sooner than females. Females had more disease activity as measured by BASDAI and functional impairment as measured by BASFI, whereas males have lower CRP levels.

Table 1.

		Female	Male	P value
	Total	164	305	
	Age at symptoms onset, median (IQR)	32 (24.5 – 41.1)	25 (20.5 – 31.7)	0.00
	HLA-B27	50 (33.1%)	140 (52.4%)	0.12
	HLA-B15	24 (15.9%)	30 (11.2%)	0.12
SpA Classification	Axial	101 (61.2%)	156 (50.6%)	0.27
	Peripheral	53 (32.1%)	127 (41.2%)	0.73
	Not classified	11 (6.7%)	15 (8.1%)	0.71
	r-AxSpA	67 (40.6%)	115 (37.3%)	0.01
	nr-AxSpA	34 (20.6%)	41 (13.3%)	0.01
Symptoms at disease onset	Arthritis	39 (23.6%)	102 (33.2%)	0.03
	Enthesopathy	10 (6.1%)	16 (5.2%)	0.70
	Lumbar pain	69 (41.8%)	112 (36.5%)	0.26
	Buttock pain	6 (3.6%)	6 (2%)	0.27
	Various initial symptoms	38 (23%)	67 (21.8%)	0.76
	Enthesitis history	136 (82.4%)	223 (72.4%)	0.02
	Dactylitis history	34 (20.6%)	51 (16.6%)	0.28
	Arthritis history	107 (64.8%)	217 (70.5%)	0.21
	Uveitis history	16 (9.7%)	29 (9.4%)	0.92
	CRP	0.3 (0.1 - 1.2)	0.7 (0.3 - 6)	<0.01
	BASFI	5.7 (3.8 - 7.2)	5 (2.7 - 6.8)	0.01
	BASDAI	6.2 (4.6 - 7.8)	5.2 (3.1 - 7.2)	0.00

ASAS: Assessment of Spondyloarthritis international Society; CRP: C-reactive protein; BASFI: Bath ankylosing Spondyloarthritis Functional index; BASDAI: Bath ankylosing Spondyloarthritis Disease Activity Index.

REFERENCES: NIL.
Acknowledgements: NIL.
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AB1070

CERVICAL SPINE INVOLVEMENT IN AXIAL SPONDYLOARTHRITIS. RADIOGRAPHIC CHARACTERISTICS AND ASSOCIATED FACTORS

Keywords: Imaging, Spondyloarthritis, Descriptive studies

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Background: The study of the cervical spine (CS) in axial spondyloarthritis (axSpA) and its radiographic characteristics including the zygapophyseal joints (ZJ) may be helpful for early diagnosis, establishing a prognosis and sharpening treatment choices.
Objectives: To describe the prevalence and characteristics of CS involvement in a cohort of patients with axSpA and its associated factors, who have been followed up in the Rheumatology Department of a third level university hospital.
Methods: Descriptive, retrospective and unicentric study. Patients with an axSpA diagnosis based on the ASAS classification criteria, from March 2011 to December 2022, retrieved from a dedicated axSpA database were included. Sociodemographic, clinical, radiographic and therapeutic variables were gathered. They were separated into two groups according to CS involvement; "CS group" as patients with BASRI≥2 in CS and/or a score ≥3 in ZJ measured by De Vlam method[1]; and "no CS group" as controls.
Results: A total of 340 patients were included (71.8% men; mean age 57,4 ± 14,9 years). CS involvement is common among axSpA (n=182; 53,5%). ZJ involvement was observed in 99 patients (29,1%), and of those, 21 did not show concomitant structural damage in the vertebral bodies. A total of 83 patients (24,4%) had damage in the vertebral bodies exclusively, and 37 (10,9%) had CS involvement without radiographic involvement of the lumbar spine (LS) (29,7% women). Patients from the CS group were predominantly men, older, had a higher BMI and higher prevalence of smoking (Table 1). They also showed higher disease activity (BASDAI and ASDAS CRP), worse function (BASFI), worse mobility in CS and LS, as well as more structural damage in both LS and sacroiliac joints. No differences were found between groups for positive HLA B27, age at diagnosis, familiar history, presence of arthritis, enthesitis, dactylitis or extra musculoskeletal manifestations (uveitis, psoriasis or IBD).
Conclusion: The radiographic evaluation of the CS is relevant in axSpA, and it should be performed routinely, as well as the evaluation of the ZJ, as they are commonly involved in axSpA and related to higher disease activity and worse function.
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Table 1. Characteristics of the CS and no CS group.

n=340		NoCS group (n=158)	CS group (n=182)	p-value
Sex	Male	91 (57.6%)	153 (84.1%)	<0.001
Smoking	Non smoker	74 (49.3%)	66 (37.3%)	0.001
Age		49.9 ± 13.5	63.9 ± 13	<0.001
BMI		25.1 ± 3.8	27.6 ± 4.4	<0.001
Age at the beggining of symptoms		27.6 ± 9.3	26.4 ± 9.1	0.238
Age at diagnosis		32.7 ± 10.5	33.5 ± 11.9	0.490
HLA B27	Positive	122 (78.2%)	153 (84.1%)	0.215
Familiar history of SpA		41 (25.9%)	38 (20.9%)	0.329
Uveitis		40 (25.3%)	39 (21.4%)	0.473
Psoriasis		15 (9.5%)	9 (4.9%)	0.155
IBD		16 (10.1%)	15 (8.2%)	0.679
Arthritis		42 (26.6%)	59 (32.4%)	0.291
Enthesitis		27 (17.1%)	41 (22.5%)	0.265
Dactylitis		6 (3.8%)	2 (1.1%)	0.152
axSpA type	r-axSpA	114 (72.2%)	166 (91.2%)	<0.001
	EnA	13 (8.2%)	10 (5.5%)	
	Ps SpA	8 (5.1%)	3 (1.6%)	
	nr-axSpA	23 (14.6%)	3 (1.6%)	
BASDAI		3.3 ± 2.1	3.8 ± 2.1	0.036
BASFI		2.7 ± 2.3	4.6 ± 2.7	<0.001
ASDAS CRP		2.1 ± 1	2.4 ± 1	0.006
CS mobility		81.0 ± 11.3	54.1 ± 24.6	<0.001
Schober 10		4.3 ± 1.2	2.7 ± 1.7	<0.001
Schober 15		6.4 ± 1.7	4.2 ± 2.3	<0.001
BASRI sacroiliac joints	0	9 (5.7%)	2 (1.1%)	<0.001
	1	15 (9.5%)	4 (2.2%)	
	2	57 (36.1%)	15 (8.2%)	
	3	52 (32.9%)	47 (25.8%)	
	4	25 (15.8%)	114 (62.6%)	
BASRI LS	0	108 (68.4%)	35 (19.3%)	<0.001
	1	5 (3.2%)	10 (5.5%)	
	2	33 (20.9%)	37 (20.4%)	
	3	8 (5.1%)	35 (19.3%)	
	4	4 (2.5%)	64 (35.4%)	
bDMARD		52 (32.9%)	75 (41.2%)	0.143

BMI: Body Mass Index; SpA: Spondyloarthritis; CRP: C-Reactive Protein; IBD: Inflammatory Bowel Disease; r-axSpA: radiographic axial Spondyloarthritis; EnA: Entheropatic Arhtritis (IBD-Associated Spondyloarthritis); Ps SpA: Psoriasic Spondyloarthritis; nr-axSpA: non-radiographic Spondyloarthritis; bDMARD: Biologic Disease-modifying Antirheumatic Drug

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AB1071

MICRONUTRIENTS DEFICIENCY IN ENTEROPATHIC SPONDYLOARTHRITIS: EXPLORING THE INTERPLAY BETWEEN JOINT AND GUT DISEASES IN A CASE-CONTROL STUDY

Keywords: Spondyloarthritis

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Background: Micronutrient deficiency (MND) is common among patients with certain chronic inflammatory diseases. MND is associated with a pro-inflammatory status and co-morbidities. Recent evidence documented a relevant prevalence of MND in Spondyloarthritis (SpA) and its interplay with gender and inflammatory-dependent dysmetabolism[1]. MND in patients with Enteropathic Spondyloarthritis (ESpA) has not been analyzed even though the concomitant occurrence of Inflammatory Bowel Disease (IBD) and SpA might strongly impact MNDs.
Objectives: In this study, we aimed at comparing for the first time the occurrence of anemia and deficiencies of ferritin (Fe), vitamin B12 (B12), folic acid (FA), and vitamin D [25(OH)D] in patients with ESpA, IBD without SpA, and isolated SpA.
Methods: In a prospective case-control study, consecutive subjects were enrolled among ESpA (Cases), IBD (Controls-1), and SpA (Controls-2) patients referring to combined gastro-rheumatologic outpatient Clinic at the "Tor Vergata" University Hospital (Rome, Italy). Each Case (ESpA) was retrospectively matched (1:1) for IBD type with one IBD subject from Controls-1 group. Inclusion criteria: 1) age ≥18 years; 2) follow up (≥2 visits/year); 3) recent (<3 mos) micronutrients data. Additional inclusion criteria for Cases: 1) diagnosis of SpA, 2) diagnosis of IBD. Additional inclusion criteria: 1) for Controls-1: diagnosis of IBD; 2) for Controls-2: diagnosis of SpA. Additional exclusion criteria: 1) for Controls-1: diagnosis of SpA; 2) for Controls-2: diagnosis of IBD. Mean and standard deviation (SD) express normally distributed variables; for non-symmetric distributed data, median and range were used. Continuous variables were compared by using either unpaired T test or the Mann-Whitney U test, as appropriate. Categorical variables were were compared using the Chi-squared test or Fisher's exact test, as appropriate. P value<0.05 was significant.
Results: One hundred ESpA (Cases) were enrolled and matched with 100 IBD (Controls-1, n=58 Crohn's Disease - CD, n=42 Ulcerative Colitis - UC), and 100 SpA including 81% psoriatic-SpA (Controls-2). The median age was comparable between groups (Cases, 50 [20-77]; Controls-1; 48.5 [19-86], Controls-2; 53 [26-77]), while male gender was more frequent in Controls-1 than Cases (P=0.0001). The median IBD duration was shorter in Cases than in Controls-1 (P<0.0001) while the frequency of IBD-related surgery was comparable between the two groups. In patients with CD (n=58 in both groups), lesions distribution was comparable between Cases and Controls-1; differently, penetrating CD was less frequent in Cases vs Controls-1 (P=0.02). Cases had a shorter SpA disease duration (P=0.004) and a higher rate of patients in moderate/high SpA disease activity than Controls-2 (P=0.02). Anemia (Hb≤12 g/dl) was slightly prevalent in Cases and Controls-1 (15% and 19%, respectively) than in Controls-2 (7%) while Fe deficiency (Fe≤15 ng/dL) was similar between Cases and Controls-1 and significantly prevalent in both Cases and Controls-1 than Controls-2 (P=0.001 for both). The B12 deficiency (≤200 pmol/l) was similar between Cases and Controls-1 but it resulted more frequent in Controls-1 than Controls-2 (P=0.04). The rate of folate defect (≤4 ng/ml) was similar between Cases and Controls-1 but it resulted less frequent in Controls-2 than in both Cases (P=0.002) and Controls-1 (P=0.00001). The 25(OH)D deficiency (≤20 ng/ml) was more frequent in Controls-2 than Cases (P=0.02).
Conclusion: In ESpA, MND results relevant and appears comparable with MND revealed in IBD patients without SpA. The isolated SpA seems to be related mainly with vitamin D deficiency that in turn might be linked to SpA disease duration and activity.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1072

ANKYLOSING SPONDYLITIS: UNEARTHING THE ASSOCIATION BETWEEN ACTIVE SACROILIITIS ON MRI AND C-REACTIVE PROTEIN AS A MARKER OF INFLAMMATION

Keywords: Imaging, Spondyloarthritis

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Background: Ankylosing spondylitis (AS) is a chronic autoimmune disorder that causes inflammation in the joints, particularly the sacroiliac joints. Magnetic resonance imaging (MRI) is a non-invasive and objective tool that can be used for early diagnosis of AS. C-reactive protein (CRP) is a biomarker that is commonly used to evaluate disease activity in AS patients, and is included in the Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS-CRP).
Objectives: The primary outcome of the study to investigate the association between active sacroiliitis on MRI and CRP levels in AS patients. The secondary outcome was to identify other parameters that may be associated with sacroiliitis activity in AS patients. The study was a retrospective analysis that included 140 AS patients who had MRI of their sacroiliac joints between January 2011 and March 2022.
Methods: Retrospective study was conducted on all SpA cases that were established between January 2011 and March 2022. The study aimed to explore the relationship between sacroiliitis as detected on MRI and C - reactive protein (CRP) levels in patients with Ankylosing Spondylitis. Magnetic Resonance Imaging (MRI) of the sacroiliac joints was performed on all patients using coronal oblique T1, T2 and STIR weighted sequences. Active sacroiliitis was defined as the presence of inflammatory lesions according to the ASAS (Assessment of SpondyloArthritis international Society) criteria. CRP was considered high if it was greater than or equal to 6 mg/L. The statistical analysis was performed using the Fisher and Chi-Squared test and a p-value of 0.05 was considered as the level of significance.
Results: MRI of the sacroiliac joints was performed in 140 patients; the mean age was 47.54± 14.46 years with a predominantly female sex ratio of 0.34 (M/F). The mean duration of evolution was 5.40± 5.13. Active sacroiliitis was found in 65% of the patients, it was bilateral in 31.4%, unilateral in 28.6% (15% left and 13.6% right). An elevated CRP was found in 60.3% of the patients, the mean CRP was 21.79± 44.68, and the mean sedimentation rate was 26.04± 26.12. Active sacroiliitis did not have a statically significant association with an elevated CRP level. For the other clinico-biological parameters, Young onset was significantly associated with active sacroiliitis (p<0.05).
Conclusion: In conclusion, this study did not demonstrate a significant association between CRP levels and active sacroiliitis on MRI in patients with AS. However, the study suggests that MRI may allow for an early diagnosis of AS in the absence of biological inflammation, and that young onset may be a risk factor for active sacroiliitis in AS patients. Further studies are needed to validate these findings and to better understand the relationship between CRP levels, imaging, and sacroiliitis activity in AS patients.
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Disclosure of Interests: None Declared.
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AB1073

IS THERE A RELATIONSHIP BETWEEN BONE TURNOVER MARKERS AND DISEASE ACTIVITY IN TUNISIAN SPONDYLOARTHRITIS PATIENTS?

Keywords: Spondyloarthritis, Vitamin D

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Background: It has been reported that disease activity was correlated to the alterations in vitamin D metabolism and increased bone resorption in patients with spondyloarthritis (SpA).
Objectives: To investigate the relationship between bone turnover markers, Vitamin D levels and disease activity in SpA patients.
Methods: In this cross-sectional study, we included patients with SpA.
In addition to the routine blood and urine tests, serum 25-(OH)D3, bone turnover markers (osteocalcin and Alkaline phosphatase (ALP) for formation, and serum C-terminal telopeptide (CTX) for resorption) of all participants were also measured. The disease activity was evaluated by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and AS disease activity scores (ASDAS-CRP) and the functional status by Bath Ankylosing Spondylitis Functional Index (BASFI).
Results: We included 79 patients (56 males, 23 females; mean age: 46.3 ± 1.9 years). The mean 25(OH)D, Calcium, Phosphor, ALP, PTH, Osteocalcin, CTX values were 17.7± 9.8 ng/ml, 89.70±12 (mg/l), 36.10 ±9.5 (mg/l), 84.6± 28.5(UI/l), 38.5 ±25.7 (pg/ml), 23.7± 9 (ng/ml), 0.57± 0.32(ng/ml), respectively. The mean

BASDAI, ASDAS-CRP, BASFI, and CRP were 4.13±2.11, 3.21±1.19, 4.5±2.25 and 20.97±12,5 mg/l respectively. There were negative correlation between PTH levels and disease duration (p: 0.029, r: -0.248), ASDAS-CRP (p=0.017, p=-0,433) and CRP levels (p=0.014, r=-0.332). The present study didn't show any correlation between both APL, osteocalcin levels and BASDAI, BASFI, ASDAS-CRP (p>0.05). We couldn't find any correlation between CTX and disease activity scores.

Conclusion: Bone formation markers (APL and osteocalcin) and bone resorption markers (CTX **I**) did not correlate with disease activity. However, PTH levels were negatively correlated with disease activity in patients with SpA.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1074 TO ASSESS ADHERENCE TO OMERACT/ASAS RECOMMENDATION FOR MRI PROTOCOL IN AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis

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Background: The interpretation of MRI in Axial Spondyloarthritis (AxSpA) has been a topic of much debate and controversy. The OMERACT/ASAS MRI group devised a list of recommendations for the protocol used in diagnostic MRI for AxSpA [1]. MRI of the sacroiliac joints (SIJs) is of crucial importance in confirming a diagnosis of AxSpA in patient presenting with back pain and a positive interpretation has a major impact on early diagnosis. The lack of agreement on a positive MRI and limited expertise in interpreting these MRI images [2] is the main stumbling block in the long diagnostic delay still seen in patient with AxSpA [3].

Objectives: We carried out a retrospective survey to assess the protocol being used in the Radiology department for requests for diagnostic MRI of spine and SIJs in patient presenting with features of inflammatory back pain. The recommended protocol is to perform short T1 inversion recovery (STIR)and T1 weighted sequences of the whole spine in sagittal view and coronal oblique views of the SIJs.

Methods: Data was collected retrospectively on 57 patients confirmed to have a diagnosis of AxSpA made by a rheumatologist, from 2015 to 2022. The protocol used for the MRi imaging was confirmed from the available radiological reports and where required further clarification of the protocol used was confirmed by the help of the performing and reporting radiologist. We also made note of the HLA-B27 status of this cohort and the use of NSAIDS and c DMARD and subsequent use of biological agents.

Results: Of the 57 patients included in this study, 25 were female and 32 were male. Just over one third of the patients (n= 23) were HLA-B27 positive, with under a third were HLA-B27 negative (n= 20), and in about a quarter of the cohort this had either not been checked or was not documented. In this cohort 16 patients were diagnosed within two years of onset of symptoms and about a third (n=23) within 5 years of onset of first symptoms. The duration of first onset of symptoms to diagnosis ranged from 7 months to a maximum of 10 years, giving a mean value of just over 7 years. Out of the 57 patients studied, about a third (n=26) had their first MRI according to the SpA protocol. A subsequent MRI was carried out in 19 patients and 11 of these were according to the SpA protocol.

Conclusion: The correct SpA protocol is still not being applied to all inflammatory back pain imaging requests. In this study we note that although this has improved in subsequent imaging, the fact remains, that not all Radiologists are fully compliant with the use of the correct SpA protocol. This is adding to the diagnostic delay and hence commencement of appropriate treatment to control the disease and prevent further progression and structural changes in the spine and SIJs. We recommend that all rheumatologists proactively and regularly audit their radiology department to improve the awareness and hence implement the correct protocol for MRI imaging in AxSpA.

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AB1075 CHARACTERISTICS OF COLOMBIAN PATIENTS WITH SPONDYLOARTHRITIS: DIFFERENCES BETWEEN AXIAL AND PERIPHERAL RESULTS FROM THE GESPA COLOMBIAN COHORT

Keywords: Spondyloarthritis, Epidemiology, Descriptive studies

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Background: Spondyloarthritis groups several diseases with similar clinical, biochemical, and imaging characteristics. These similarities have allowed this disease to be classified since 2009 as both axial or peripheral. The Latin American population with spondyloarthritis presents differential characteristics that do not allow it to be adequately classified by the current ASAS criteria, and because there are few latin cohorts of patients with spondyloarthritis, it is necessary to continue with the construction of said cohorts to improve the knowledge of the disease in our region, improving our participation in the construction of more inclusive criteria.

Objectives: To describe the clinical, biochemical, and imaging characteristics of Colombian patients diagnosed with spondyloarthritis at a reference institution in Bogotá DC.

Methods: Patients with a diagnosis of spondyloarthritis were chosen according to the assessment carried out by four expert rheumatologists at a reference institution in Bogotá DC, Colombia, between 2002 and 2015. They underwent a survey that included clinical, biochemical, and imaging characteristics and were followed up in a rheumatology clinic.

Results: 473 patients were recruited between 2002 and 2015, with 65.1% men, 83.7% being of mixed race, a mean age of onset of the disease of 29.5 years, and a median delay in the diagnosis of the disease of 24 months. According to the ASAS classification, there were 189 axial patients and 223 peripheral patients; there were no differences between the age of onset of symptoms, sex, race, or duration of the first symptom between both groups. The axial patients had the longest delay in diagnosis (P = 0.03); more low back pain and less arthritis as initial symptoms (P 0.001); a higher frequency of insidious onset of arthritis (P 0.001); greater pain in the spine, stiffness, and inflammatory characteristics of pain (P 0.001). Patients with axSpA presented with more enthesitis (P = 0.03), less arthritis (P = 0.02), limited chest expansion (P = 0.03), and sacroiliitis on physical examination (P = 0.001). Patients with pSpA have a lower frequency of HLA-B27 (P 0.001) but a higher frequency of other HLA alleles (P = 0.01), such as HLA-B15 (P = 0.001), with a higher ESR (P = 0.03).

Conclusion: Colombian patients with SpA are predominantly young men, with pSpA being the most frequent. AxSpA patients present a longer delay in diagnosis, more low back pain and less arthritis as initial symptoms, greater pain and stiffness of the spine compared to patients with pSpA spondyloarthritis, but the latter present more of the HLA-B15 allele, a higher frequency of previous infection and higher ESR than patients with axSpA.

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AB1076 SPECTRUM OF AXIAL SPONDYLOARTHRITIS IN COLOMBIAN'S PATIENTS: NON-RADIOGRAPHIC VS RADIOGRAPHIC AXIAL SPA. RESULTS FROM GESPA COLOMBIAN COHORT

Keywords: Epidemiology, Spondyloarthritis

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Background: Spondyloarthritis encompasses several diseases with similar clinical, biochemical, and imaging features. Since 2009, these characteristics have allowed this disease to be classified into axial and peripheral, with the presence of chronic spinal pain and the age of onset of the disease being important criteria for the classification of axial spondyloarthritis[1]. Interest in non-radiographic axial spondyloarthritis has recently increased [2], but this information is limited in our population.
Objectives: To differentiate the clinical, biochemical, and imaging characteristics of one Colombian cohort of patients with radiographic and non-radiographic axial spondyloarthritis.
Methods: Patients with axial spondyloarthritis were consecutively recruited at a reference institution in Colombia from 2002 to 2015. A structured survey was conducted at the time of the diagnosis of the disease, which included sociodemographic, clinical, biochemical, and imaging variables. The presence of sacroiliitis was evaluated by locar radiologist. Patients and disease characteristics were comparated nr-axSpA and r-axSpA.
Results: A total of 258 patients with axial spondyloarthritis were recruited between 2002 and 2015, of whom 69.6% (185 patients) were radiographic axial and the remaining 30.4% (73 patients) were non-radiographic axial. When comparing the two groups (radiographic vs. non-radiographic axial), not differences were observated in sex, the age of onset, the duration of the disease, initial symptom, number of swollen joints, duration of morning stiffness, number of painful entheses. Compared with r-axSpA, patients with nr-axSpA had greater presence of HLA-B15 (P=0,04), presence of inflammatory spinal pain (P=0,01), history of relatives with spondyloarthritis (P=0,03), longer duration of enthesitis (P=,001), low back pain (P=0,007) and gluteal pain (P=0,003) in the first episode, and greater chest expansion (P=0,001) and distance in the Schober test (P<0,001) in non-radiographic axial versus radiographic axial patients.
Conclusion: Colombian patients with non-radiographic axial spondyloarthritis have higher presence of HLA-B15, higher frequency of inflammatory spinal pain, family history of spondyloarthritis, low back pain, and gluteal pain during the first episode of the disease, greater chest expansion and distance on the Schober test than patients with radiographic axial spondyloarthritis.
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Table 1. Characteristics of Colombian's patients with SpA (n=258)

	Radiographic SpA (%) [DE] n= 185	Non radiographic SpA (%) n= 73	P-value
Sex	117 (63,2)	39 (53,4)	0,18
Man			
Age of onset disease	27 [20,6 – 38]	29 [22 – 34,3]	P= 0,71
Median			
Disease duration in months:	4 [2 – 12]	43 [9,5 – 121]	P=0,57
Median			
Initial symptom duration in months:			
Arthritis			
Median	3 [1 – 8]	3 [0.8 – 8]	P=0,57
Enthesitis			
Median	2 [0,3 – 6]	3 [0,3 – 9]	**P=0,001**
Lumbar pain:			
Median	5 [3 – 12]	6 [3 – 12]	**P=0,007**
Buttock pain:			
Median	1 [0 – 4]	2 [0 – 6]	**P=0,003**
Inflammatory back pain	127 (70,2)	62 (81,6)	**0,01**
Chest expansion	3,8 [DE±1,34]	4,5 [DE±1,54]	**P=0,001**
Mean			
Schober test	3,9 [DE±2,4]	6,89 [DE±5,58]	**P<0,001**
Mean			
HLA			
B27	94 (50,8)	38 (50,7)	0,98
B15	9 (4,9)	9 (12)	**0,04**
Other HLA	52 (33,8)	25 (34,7)	0,72

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AB1077 THE PREVALENCE AND ASSOCIATED FACTORS OF SARCOPENIA IN AXIAL SPONDYLOARTHRITIS

Keywords: Sarcopenia

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Background: Sarcopenia consists of decreasing muscle strength, muscle mass and physical performance. Muscle wasting is common in chronic inflammatory diseases, such as spondyloarthritis (SpA).
Objectives: This research aims to determine the prevalence and associated factors of sarcopenia in Thai ankylosing spondylitis patients.
Methods: A cross-sectional study was conducted at Phramongkutklao Hospital between January 2020 and February 2021. One hundred and four axial spondyloarthritis (ax-SpA) patients who met the 2009 ASAS criteria were enrolled. Sarcopenia related factors and disease characteristics were recorded. Sarcopenia was diagnosed according to the Asian Working Group for Sarcopenia 2019. Appendicular skeletal muscle mass was measured by antero-posterior dual-energy X-ray absorptiometry. Strength, Ambulation, Rising from a chair, Stair climbing and history of Falling (SARC-F) was evaluated. Muscle strength was measured by hand grip strength and chair stand time. Physical performance was assessed by 6-meter walk and time up and go tests. Logistic regression was performed to identify factors associated with sarcopenia.
Results: Most patients were male (77%) with the mean (standard deviation: SD) age and disease duration were 42.64 (12.19) and 8.3 (8.5) years. The mean BMI (SD) was 23.80 (4.44). The prevalence of sarcopenia was 22.1%. There was no difference in disease activities (BASDAI and ASDAS) between ax-SpA patients with and without sarcopenia. Factors independently associated with sarcopenia were age and low BMI with the adjusted odd ratios and 95% confidence interval of 27.319 (3.69-202) and 12.517 (1.67-93.76) respectively.
Conclusion: Sarcopenia is common in ax-SpA patients. It is independently associated with older age and low BMI, but not disease activity.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1078 SPONDYLOARTHRITIS AND INFLAMMATORY BOWEL DISEASE (IBD): CLINICAL AND PARACLINICAL CHARACTERISTICS

Keywords: Descriptive studies, Enthesitis, Comorbidities

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Background: Spondyloarthritis (SpA) is a group of chronic inflammatory rheumatic diseases characterized by enthesis involvement. SpA can be associated with extra-articular manifestations, in particular Inflammatory bowel disease (IBD)
Objectives: The objective of the study is to compare the clinical and paraclinical characteristics of a population of patients with spondyloarthritis (SpA) associated to IBD and patients without IBD.
Methods: Retrospective study conducted in the Rheumatology Department, including patients followed up for SpA for SpA between 2004 and 2021.
Results: Our study involved a population of 333 patients with SpA. he averages age was 40.5 years. Men constituted 54.1%. Smokers represented 13.5% of the cases, diabetics 7.5%, hypertensives 8.4% and 9.9% of patients had IBD. In univariate analysis: patients with SpA with IBD had more uveitis (p=0.001), more stage VI sacroiliitis (p=0.0001), more syndesmophytes p= 0.02) and a more active disease according to the BASDAI (p= 0.011). In multivariate analysis, SpA with IBD was associated with uveitis (OR 3.53) and to a BASDAI higher than 4 (OR 2.7).
Conclusion: In our study, uveitis, stage VI sacroiliitis, and syndesmophytes were more frequent in patients with SpA and IBD, with a more active disease.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1079 CLINICAL, RADIOLOGICAL AND BIOLOGICAL CHARACTERISTICS OF SPONDYLOARTHRITIS WITH COXITIS

Keywords: Spondyloarthritis, Prognostic factors

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Background: Spondyloarthritis (SpA) is the most common chronic inflammatory rheumatic disease with hip involvement, which is a marker of disease severity, given its major functional impact.
Objectives: Determine the clinical, biological and radiological characteristics of SpA with coxitis, and to determine the factors associated with its occurrence.
Methods: Retrospective and analytic study including patients with SpA. Clinical demographics, biological radiological data, and activity scores were collected. The significance threshold was set for a value of p<0.05.
Results: These were 333 patients, of which 54.1% were men. The mean age was 40.52±15.05 years, and the mean age at onset was 32.02±15.42. The percentage of smoking patients was 11.1%. HLA-B27 was positive in 57% and uveitis was present in 7.2% of patients. Coxitis was present in 25.52% of patients, it was inaugural in 10.5% and bilateral in 71.76% of cases. Coxitis was more common in men; the male gender accounted for 76.47% in SpA with coxitis versus 46.37% without coxitis (p<0.001). The mean age of SpA onset was lower in patients who developed coxitis (24.4±13.75 years versus 34.6±15.14 years; p = 0.014). Pure axial form and low back and buttock pain were more noted in patients with coxitis (18.8% versus 13.3% p=0.022, 31.7% versus 18.9% p=0.018 respectively). Enthesopathy was more common in SpA without coxitis (56.86% versus 35.3%, p=0.001). There was no significant difference between the two groups for CRP and erythrocyte sedimentation rate (p=0.91; p=0.35), nor for ASDAS and BASDAI (p=0.95; p=0.38 respectively). Also a frequency not modified by the presence or absence of coxitis was noted, in particular for the family history of SpA, smoking, HLA-B27, uveitis, the existence of radiographic sacroilitis.
In multivariate analysis, coxitis was associated with male gender, early age of onset, and pure axial form.
Conclusion: Our study showed that the presence of coxitis was associated with early disease onset, male sex and pure axial form of SpA.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1080 IS HLA-B27 ASSOCIATED WITH BIOMARKERS OF OSTEOFORMATION IN SPONDYLOARTHRITIS? RESULTS OF A STUDY FROM NORTH AFRICA

Keywords: Biomarkers, Spondyloarthritis

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Background: The Wnt signaling pathway is a signaling pathway regulating bone metabolism. Dickkopf1 (DKK-1) and Sclerostin are potent inhibitors of this pathway, and their dysfunction would be responsible for osteoformation phenomena in patients with spondyloarthritis (SpA). Osteoprotegerin (OPG), a potent inhibitor of osteoclasts and regulated by the Wnt pathway, has also been implicated in this osteoformation phenomenon.
Objectives: Our work aimed to determine the associations between serum levels of DKK-1, Sclerostin, OPG, and the HLA B-27 allele.
Methods: It was a cross-sectional study including patients with SpA (meeting ASAS criteria). Data collected included sociodemographic and disease characteristics. Biomarker assays were performed using an ELISA technique. Human leukocyte antigen typing was performed by a specific polymerase chain reaction.
Results: One hundred and nine patients were included, with a mean age of 43 ± 12 [19-79] years and a sex ratio M/F of 1.65. The mean age of onset of the disease was 30.6 ± 11 years. Seven patients had a juvenile onset of the disease. HLA B27 allele was present in 30 patients (27.52%). The respective medians [range] of serum levels, in pg/mL, of DKK-1, Sclerostin, and OPG were 146.7 [0-455,3], 32.8[0-488], and 471 [0-1613,6]. HLA B27 was not associated with any of these biomarkers (DKK-1; p=0.744), (Sclerostin; p=0.870), (OPG; p=0.835).
Conclusion: Our study suggests that there is no association between inhibitors of the Wnt signaling pathway as well as OPG and HLA B27.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1081 THE PRESENCE OF SYMPHYSIS IN PATIENTS WITH AXIAL SPONDYLITIS MAY BE A SIGN OF RADIOGRAPHIC DAMAGE

Keywords: Spondyloarthritis

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Background: Sacroiliac joint radiographs allow the evaluation of the symphysis region and ischial enthesis regions as well as the evaluation of the sacroiliac and hip joints in patients with axial spondyloarthritis (axSpA).
Objectives: In this study; It is planned to test and review the relationship between the presence of symphysis and disease-related factors and other radiological involvement features.
Methods: Of 384 patients with axSpA and whose sacroiliac joint radiographies were evaluated for symphysitis were included in the study. Since the presence of symphysis was not detected in non-radiographic axSpA patients in our cohort, the analysis was performed with radiographic axSpA patients. Demographic, clinical and laboratory characteristics of the patients were recorded. Irregular appearance in the symphysis pubis on the sacroiliac joint X-ray was evaluated as symphysis. Raiological evaluation were done by a rheumatologist (EDE) and a radiologist (AS). The relationship between the presence of symphysitis and other factors was tested with both univariate and multivariate analysis methods.
Results: The mean age at diagnosis (±SD) was 42.1 (±11.9) and 73.7% of the 384 patients included in the study were male. Demographic, clinical and laboratory characteristics of the study group were summarized in Table 1. Symphysitis was detected in 49 (12.8%) patients on the sacroiliac joint radiograph. The presence of symphysis were associated with duration of symptoms (p<0.001), duration of diagnosis (p<0.001), HLA-B27 positivity (p=0.001), radiographic hip involvement in the evaluated radiographs (p=0.006), total sacroiliac joint score (4-8) (p<0.001), baseline cervical mSAS score (p<0.001), basal lumbal mSAS score (p<0.001), serum CRP level (p=0.001), ASDAS-CRP score (p=0.030)). The presence of symphysitis was not found to be associated with gender, age at diagnosis, extramusculoskeletal and peripheral involvement. In multivariate analysis, the presence of radiological symphysitis was found to be associated with the presence of total ankylosis in the sacroiliac joints (p=0.034) and hip involvement(p=0.019).
Conclusion: Symphysitis in AxSpA patients may be an indicator of radiological damage as well as accompanying other involvements.

Table 1. Demographic and radiographic characteristics of patients with axial spondyloarthritis

All patients (n=384)		Symphysitis (+) (n=49)	Symphysitis(-) (n=335)	p
Age at diagnosis, mean (SD)	42.1 (11.9)	34.6 (11.7)	35.7 (17)	0.53
Sex, male, %	73.7	70.2	75.3	0.45
HLA-B27 positivity,%	65.3	83.8	62.3	0.010
Symptom duration, median (IQR)	13 (13)			<0.001
SIE score, median (IQR)	6 (3)	8 (2)	6 (4)	<0.001
SIE ankylosis, %	33.6	65.3	29.0	<0.001
Servikal mSASS, median (IQR)	0 (6)	6 (18)	0 (6)	<0.001
Servkal sindesmofit, %	43.2	71.1	37.5	<0.001
Lumbal mSASS, median (IQR)	0 (6)	6 (33)	0 (2)	<0.001
Lumbal syndesmophitis, %	28.8	48.6	26.6	0.005
Hip involvement, %	16.6	31.3	14.5	0.004
ASDAS- CRP score, median (IQR)	3.0 (1.8)	3.4 (1.4)	3.0 (1.8)	0.030
Serum CRP level, median (IQR)	9.7 (19.3)	18.0 (23.4)	8.4 (17.2)	0.001

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Psoriatic arthritis - treatment

AB1082 **EARLY CLINICAL RESPONSE AS A PREDICTOR OF LONG-TERM HEALTH-RELATED QUALITY OF LIFE IMPROVEMENTS IN PATIENTS WITH PSORIATIC ARTHRITIS AND TNFI-IR RECEIVING GUSELKUMAB (COSMOS)**

Keywords: Quality of life, Outcome measures, Psoriatic arthritis

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Background: Improvement in health-related quality of life (HRQoL) is a key goal of psoriatic arthritis (PsA) therapy.[1,2] Here, we assess whether early clinical response predicts long-term improvement in HRQoL for patients (pts) with PsA and inadequate response to 1–2 tumour necrosis factor inhibitors (TNFi-IR).
Objectives: Assess the association between early clinical response across various PsA domains and HRQoL at Week (W)48, as well as identify baseline (BL) characteristics that could predict early response in guselkumab (GUS)-treated TNFi-IR PsA pts in the Phase 3b COSMOS trial.
Methods: In the randomized controlled COSMOS trial (NCT03796858),[3] adults with active PsA (swollen/tender joint counts [SJC/TJC] each ≥3) and TNFi-IR were randomized 2:1 to receive subcutaneous injections of either GUS 100 mg (at W0, W4, then every 8 weeks through W44) or placebo (at W0, W4, W12, W20, followed by GUS at W16 [early escape] or at W24 [planned], W28, W36, W44). Only pts randomized to GUS were included in this analysis. Long-term improvements in HRQoL were defined as changes from BL to W48 in 36-item short-form survey (SF-36) physical and mental component summary (PCS and MCS) and Dermatology Life Quality Index (DLQI) scores. Early clinical response was defined as achievement of the following criteria at W4 or W8: American College of Rheumatology (ACR)20, pt pain on a visual analogue scale (VAS) ≤15, SJC ≤1, skin VAS ≤20, and health assessment questionnaire – disability index. (HAQ-DI) ≤0.5. In addition, Psoriasis Area and Severity Index (PASI) ≤1 was considered at W16 – the earliest PASI assessment. Analyses were restricted to pts not meeting the respective early response criteria at BL. Long-term HRQoL improvements were compared between pts achieving vs not achieving early response criteria by means of Student's. t-test and by multivariate linear regression models adjusting for demographic and BL pt disease characteristics. Results from the multivariate linear regression analyses are presented here. Demographic and BL pt disease characteristics predicting early clinical response were investigated using multivariate logistic regression.
Results: Overall, 189 pts were randomized to GUS, with a mean age of 49.1 years, and 45.5% were male. Among pts not meeting the respective early response criteria at BL, GUS led to. 2.7–19.0% and 4.3–38.4% of pts achieving one of the clinical responses of interest as early as W4 and W8, respectively. SF-36 PCS improvement from BL to W48 was significantly associated with ACR20 response, SJC ≤1 and HAQ-DI ≤0.5 achievement at W4 as well as at W8. There were no significant findings for SF-36 MCS. DLQI improvement from BL to W48 was significantly associated with ACR20 and skin VAS ≤20 at W8 (**Figure 1**). Improvements in SF-36 PCS, SF-36 MCS and DLQI at W48 were all significantly associated with achievement of PASI ≤1 at W16. Multivariate logistic regression identified significant (P<0.05) associations between males and early clinical response at W8 (ACR20: odds ratio [OR]=1.98; HAQ-DI ≤0.5: OR=3.71), BL SJC and. SJC ≤1 at W8 (OR=0.84), BL HAQ-DI and HAQ-DI ≤0.5 at W8 (OR=0.23), and BL skin VAS and skin VAS ≤20 at W8 (OR=0.98).
Conclusion: For pts receiving GUS, ACR20 response at W4 and W8 was positively associated with SF-36 PCS improvement from BL to W48, and also at W8 with DLQI improvement from BL to W48. Therefore, early clinical response is relevant for HRQoL improvements over time. These results may help in shared decision-making processes.

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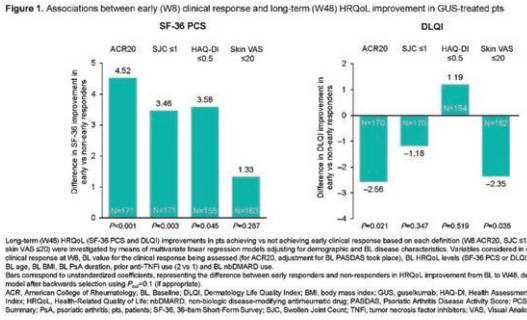


Figure 1. Associations between early (W8) clinical response and long-term (W48) HRQoL improvement in GUS-treated pts

Long-term (W48) HRQoL (SF-36 PCS and DLQI) improvements in pts achieving vs not achieving early clinical response based on each definition (W8 ACR20, SJC ≤1, HAQ-DI ≤0.5 and skin VAS ≤20) were investigated by means of multivariate linear regression models adjusting for demographic and BL disease characteristics. Variables considered in each model were: clinical response at W8, BL value for the clinical response being assessed (for ACR20, adjustment for BL PASDAS took place), BL HRQoL levels (SF-36 PCS or DLQI, accordingly), sex, BL age, BL BMI, BL PsA duration, prior anti-TNFi use (2 vs 1) and BL nbDMARD use.
Bars correspond to unstandardized coefficients, representing the difference between early responders and non-responders in HRQoL, improvement from BL to W48, derived from the best-fitting model after backwards selection using P_{out}=0.1 (if appropriate).
ACR, American College of Rheumatology; BL, Baseline; DLQI, Dermatology Life Quality Index; BMI, body mass index; GUS, guselkumab; HAQ-DI, Health Assessment Questionnaire – Disability Index; HRQoL, Health-Related Quality of Life; nbDMARD, non-biologic disease-modifying antirheumatic drug; PASDAS, Psoriatic Arthritis Disease Activity Score; PCS, Physical Component Summary; PsA, psoriatic arthritis; pts, patients; SF-36, 36-Item Short-Form Survey; SJC, Swollen Joint Count; TNFi, tumor necrosis factor inhibitors; VAS, Visual Analogue Scale; W, Week

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Disclosure of Interests: Laure Gossec Consultant of: AbbVie, Amgen, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sandoz, UCB, Grant/research support from: Sandoz, UCB, Daniel Aletaha Speakers bureau: Abbvie, Gilead, Galapagos, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sandoz, and Sanofi, Consultant of: Abbvie, Gilead, Galapagos, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sandoz, and Sanofi, Grant/research support from: Abbvie, Gilead, Galapagos, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sandoz, and Sanofi, Philipp Sewerin Speakers bureau: AXIOM Health, Amgen, AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Chugai Pharma Marketing Ltd./ Chugai Europe, Deutscher Psoriasis-Bund, Gilead Sciences, Hexal Pharma, Janssen-Cilag, Johnson & Johnson, Lilly/ Lilly Europe/ Lilly Global, medi-login, Mediri GmbH, Novartis Pharma, Onkowissen GmbH, Pfizer, Roche Pharma, Rheumazentrum Rhein-Ruhr, Sanofi-Genzyme, Spirit Medical Communications, Swedish Orphan Biovitrum, UCB Pharma, Consultant of: AXIOM Health, Amgen, AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Chugai Pharma Marketing Ltd./ Chugai Europe, Deutscher Psoriasis-Bund, Gilead Sciences, Hexal Pharma, Janssen-Cilag, Johnson & Johnson, Lilly/ Lilly Europe/ Lilly Global, medi-login, Mediri GmbH, Novartis Pharma, Onkowissen GmbH, Pfizer, Roche Pharma, Rheumazentrum Rhein-Ruhr, Sanofi-Genzyme, Spirit Medical Communications, Swedish Orphan Biovitrum, UCB Pharma, Grant/research support from: AXIOM Health, Amgen, AbbVie, Biogen, Bristol-Myers Squibb, Celgene, Chugai Pharma Marketing Ltd./ Chugai Europe, Deutscher Psoriasis-Bund, Gilead Sciences, Hexal Pharma, Janssen-Cilag, Johnson & Johnson, Lilly/ Lilly Europe/ Lilly Global, medi-login, Mediri GmbH, Novartis Pharma, Onkowissen GmbH, Pfizer, Roche Pharma, Rheumazentrum Rhein-Ruhr, Sanofi-Genzyme, Spirit Medical Communications, Swedish Orphan Biovitrum, UCB Pharma, Alen Zabotti Speakers bureau: AbbVie, Novartis, Janssen, Lilly, UCB, Amgen, Paid instructor for: AbbVie, Novartis, UCB, Filip van den Bosch Consultant of: AbbVie, Amgen, Eli Lilly, Galapagos, Janssen, Moonlake, Novartis, Pfizer and UCB, Michela Efficace Shareholder of: Janssen Pharmaceutical Companies of Johnson and Johnson, Employee of: Janssen Pharmaceutical Companies of Johnson and Johnson, Frederic Lavie Shareholder of: Johnson & Johnson, Abbvie, Employee of: The Janssen Pharmaceutical Companies of Johnson & Johnson, Miriam Zimmermann Employee of: Janssen Pharmaceutical Companies of Johnson and Johnson, Mohamed Sharaf Employee of: Janssen Pharmaceutical Companies of Johnson and Johnson, Iain McInnes Speakers bureau: Abbvie, Consultant of: Amgen Abbvie, Astra Zeneca, GSK, Lilly, Sanofi, Evelo, Compugen, Cabaletta, UCB, Novartis, BMS, Causeway Therapeutics, Gilead, Moonlake, Pfizer, Janssen, Grant/research support from: Amgen, AstraZeneca, BMS, Lilly Novartis, Janssen, GSK, UCB, Pfizer.
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AB1083 **HALF OF THE PSORIATIC ARTHRITIS PATIENTS IN A GERMAN CLAIMS DATA COHORT EXPERIENCE POLYPHARMACY**

Keywords: Psoriatic arthritis, Comorbidities, Health services research

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Background: Psoriatic arthritis (PsA) therapy and comorbidity almost inevitably lead to the issue of polypharmacy (intake of ≥ 5 medications daily), which may further challenge the management of the disease. There is a lack of data on polypharmacy in PsA.
Objectives: To assess polypharmacy in women and men with PsA.

Methods: From the German BARMER health insurance database, 11,984 persons with PsA and DMARD therapy in 2021 were included and compared to sex and age matched controls without inflammatory arthritis. Medications were grouped by Anatomical Therapeutic Chemical groups. Polypharmacy (≥ 5 concomitant drugs) was compared by sex, age and comorbidity using the Rheumatic disease comorbidity index (RDCI, range 0-9) and the Elixhauser comorbidity index (range 0-31). The mean difference in the medication number between persons with PsA and controls was estimated with a linear regression model.

Results: From all adult persons insured in 2021 (n=7.4 Mio.), 190,000 (2.6%) had a diagnosis of psoriasis (ICD-10-GM Code L40). Of those, 20,245 (11%) had a PsA diagnosis (L40.5 + M07.0-3) and 11,984 received any DMARD therapy. A total of 119,840 persons without diagnoses of inflammatory arthritis were included as controls. A total of 63% of all persons with PsA and DMARD therapy were women and the overall mean age was 60 years (Table 1).

Table 1. Characteristics and frequencies of comorbidities (%) of women and men with PsA and controls in 2021.

	Women	Men	Total	Controls
N	7,565	4,419	11,984	119,840
Female (%)			63	63
Age, mean in years	61 (13)	59 (13)	60 (13)	60 (13)
Comorbidities (%)				
RDCI, mean (SD), range 0-9	1.9 (1.6)	1.7 (1.6)	1.9 (1.6)	-
Elixhauser Score, mean (SD), range 0-31	3.8 (2.6)	3.4 (2.7)	3.6 (2.6)	2.2 (2.2)
Hypertension	56	58	57	42
Diabetes mellitus	20	22	21	13
Other cardiovascular disease	12	17	14	9.7
Stroke	0.9	0.2	0.7	0.3
Lung disease	22	16	20	13
Osteoarthritis	39	28	35	15
Depression	32	21	28	16
Hypothyroidism	26	9	19	14
Ulcer or stomach problem	13	10	12	6.3
Cancer	9.6	10	9.8	9.1
Renal failure	8.4	9.0	8.6	4.2
Osteoporosis	18	7	14	4.8
Fracture	5.5	2.1	4.2	1.5

Polypharmacy was significantly higher in PsA (49%) compared to controls (17%), more frequent in women (52%) compared to men (45%) and strongly increased with age (15% in 18 to 30 yrs., 78% in >80 yrs.) and comorbidity. Comorbidity was more frequent in PsA compared to controls (mean Elixhauser comorbidity score 3.6 vs. 2.2 in controls, table 1). This applies to the conditions of the metabolic syndrome: hypertension (57% vs. 42% in controls), dyslipidemia (32% vs. 27%), diabetes (21% vs. 13%) as well as to all other comorbidities, in particular osteoarthritis (35% vs. 15%) and depression (28% vs. 16%). Compared to controls, all ATC drug classes were significantly more frequent in persons with PsA, most commonly drugs for the musculoskeletal system (81% vs. 30%), immunomodulating agents (56% vs. 2.6%), cardiovasculars (62% vs. 48%), alimentary tract/metabolism (57% vs. 31%) and nervous system (50% vs. 31%) (frequencies for PsA see Figure 1). For each unit increase of the RDCI, the age-adjusted number of medications increased by 0.98 (95% CI 0.95; 1.01) units in men and 0.93 (0.90; 0.96) units in women. Compared to controls, the number of prescribed medications (mean 4.9 (2.8)) was 2.4 (2.34; 2.43) units higher in women and 2.3 (2.21; 2.35) units higher in men.

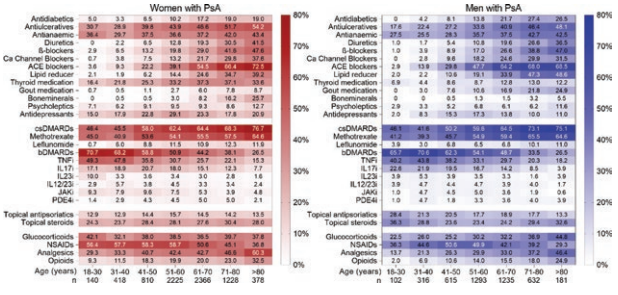


Figure 1. Prescription frequency of medications in 2021 in women and men with PsA by age groups.

Conclusion: Polypharmacy is common in PsA and is composed of PsA-specific medication as well as medication for frequent comorbidities, equally affecting women and men. While DMARD therapy is essential to prevent subsequent damage, systemic GC should be avoided in PsA and analgesics might be dispensable if PsA is well controlled. With regard to the elderly, more frequent therapy with bDMARDs should be discussed which may result in reduced use of analgesics, opioids, and other secondary-induced co-medication.

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AB1084

GUSELKUMAB PROVIDES RAPID CLINICALLY MEANINGFUL IMPROVEMENTS IN CLINICAL AND PATIENT REPORTED OUTCOMES AND SUSTAINED DISEASE CONTROL OF PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Quality of life, Patient reported outcomes

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Background: The Group for Research and Assessment of Psoriasis and PsA advocates addressing all aspects of disease, including optimizing functional status and improving health-related quality of life (HRQoL).[1] Guselkumab (GUS) has demonstrated robust efficacy across key PsA domains at week (W) 24, with effects sustained or further enhanced through 2 years.[2-4] Timing of clinically meaningful improvement in disease activity (DA), functional status, and HRQoL is of interest to PsA patients (pts) and providers.

Objectives: 1) Evaluate effect of GUS on time to minimally clinically important improvements (MCII) in pt reported outcomes and composite measures of DA; 2) Assess association between W4/W8 MCII achievement and later disease control (W24/W52).

Methods: This post hoc analysis evaluated 1120 adults with active PsA despite standard therapies from DISCOVER-1 (D1) (swollen & tender joint counts [SJC/TJC] ≥3 each, CRP ≥0.3 mg/dL, 1-2 prior TNF inhibitors [TNFi] in 31% of pts) and D2 (SJC/TJC ≥5 each, CRP ≥0.6 mg/dL, biologic-naïve). Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo (PBO)→GUS 100 mg Q4W at W24. Time to MCII in outcomes of interest, i.e., improvement in cDAPSA ≥5.7, Joint Visual Analogue Scale [VAS] ≥15mm, Pt Pain ≥15mm, HAQ-DI ≥0.35, PASDAS ≥0.8, PtGA ≥15mm, Skin VAS ≥15mm, FACIT-F ≥4, SF-36 PCS ≥5, was compared between GUS vs PBO with Cox regression adjusting for baseline (BL) levels of respective outcome, treatment group, prior TNFi use, and BL DMARD use. MCII achievement was determined using non-responder imputation and compared between GUS and PBO using logistic regression adjusting for the above covariates. The association between MCII achievement at W4/W8 and stringent clinical response at W24/W52 amongst GUS-treated pts was assessed with logistic regression adjusting for prior TNFi use and BL DMARD use.

Results: Time to achieve MCII in all studied outcomes was significantly shorter (hazard ratio range: 1.3-2.5; all p<0.01) for both GUS Q4W and Q8W vs PBO, including cDAPSA as a representative example (**Figure 1**), with curve separation occurring at the first timepoint assessed. MCII rates also were significantly higher with GUS vs PBO at the first timepoint assessed, i.e., W4 for cDAPSA, Joint VAS, Pt Pain, and HAQ-DI and W8 for PASDAS, PtGA, Skin VAS, FACIT-F, and SF-36 PCS (**Table 1**).

W4 achievement of MCII in cDAPSA, Joint VAS, Pt Pain, and HAQ-DI was associated with greater odds of achieving future disease control, defined as ACR50, ACR70, cDAPSA ≤13, PASDAS ≤3.2, and MDA, at W24 (odds ratio [OR] range: 1.5-3.6) and W52 (OR: 1.2-2.4). W8 achievement of MCII in all studied outcomes was also associated with greater odds of achieving disease control at W24 (OR: 1.4-17.2) and W52 (OR: 1.2-5.4).

Conclusion: In pts with active PsA, treatment with GUS was associated with more rapid MCII in both clinical and pt reported outcomes compared with PBO. As early as W4, achievement of MCII vs non-achievement in each studied outcome, particularly PASDAS and cDAPSA, was associated with greater odds of longer-term stringent DA control. Findings highlight the impact of these rapid improvements with GUS - as early as W4 - on the trajectory of long-term pt outcomes.

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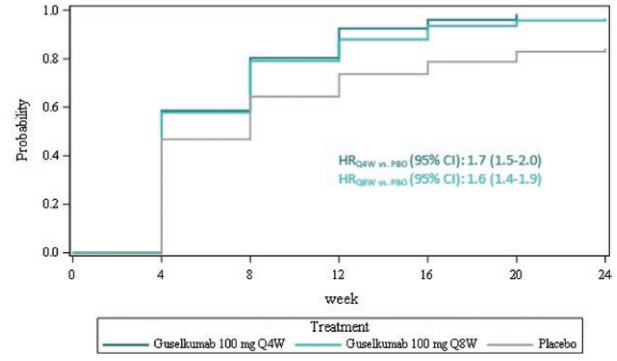
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Table 1. Proportions of Pts Achieving MCII

Endpoint with MCII	Week	GUS Q4W	GUS Q8W	PBO
cDAPSA	4¥	58.5%†	57.9%†	46.8%
	8	73.9%‡	72.1%‡	56.8%
Joint VAS	4¥	31.9%†	34.1%‡	21.1%
	8	45.3%‡	45.7%‡	30.7%
Pt Pain	4¥	27.8%†	29.4%†	18.9%
	8	44.7%‡	44.1%‡	28.1%
HAQ-DI	4¥	33.9%†	30.5%*	22.7%
	8	41.7%‡	42.6%‡	27.6%
PASDAS	8¥	68.4%‡	64.9%‡	44.0%
PtGA	8¥	53.4%‡	53.7%‡	32.9%
Skin VAS	8¥	64.0%‡	62.1%‡	35.2%
FACIT-F	8¥	51.1%*	53.1%†	43.4%
SF-36 PCS	8¥	43.2%†	41.6%	35.8%

*nominal p <0.05; †p <0.01; ‡p ≤0.0001 vs PBO. ¥First time point assessed.

Figure. Time to MCII in cDAPSA (Δ ≤ -5.7) Through W24



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AB1085

CHANGES IN SERUM CYTOKINES AND COLLAGEN PROTEINS CORRELATE WITH DURABILITY OF GUSELKUMAB EFFICACY AND CONTINUED DISEASE IMPROVEMENT THROUGH 2 YEARS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis

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Background: Guselkumab (GUS) is a fully human, selective interleukin (IL)-23p19 subunit inhibitor. In the phase 3 DISCOVER-2 study of biologic-naïve patients (pts) with active psoriatic arthritis (PsA), GUS significantly reduced the signs and symptoms of disease and radiographic progression vs placebo (PBO),[1] with durable response across multiple disease domains through 2 years.[2] GUS also significantly decreased serum levels of collagen turnover markers,[3] which are elevated in PsA pts vs healthy controls, consistent with diminished progression of structural damage. Further, changes in these and other serum cytokine levels through Week 24 (W24) of GUS treatment are associated with clinical response through 2 years.[4]

Objectives: Further assess effects of GUS on serum cytokine and collagen turnover biomarkers from W24 through W100 (2 years) and explore associations between biomarker levels and longer-term clinical response (W100).

Methods: In DISCOVER-2, biologic-naïve adults with active PsA (swollen joint count ≥5, tender joint count ≥5, C-reactive protein [CRP] ≥0.6 mg/dL) were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4 and then Q8W; or PBO with crossover to GUS Q4W at W24. Blood samples from consenting GUS-treated pts (Q4W and Q8W pooled) were assessed for serum cytokine levels (N=100), including Th17-related effector molecules (IL-17A, IL-17F, IL-22), β-defensin 2 (BD-2), acute phase proteins (CRP, serum amyloid A [SAA], IL-6), and serum collagen turnover biomarkers (N=174; C1M, C3M, C4M, C6M). Using Spearman linear regression and general linear models, pooled changes from baseline (BL) in biomarkers during GUS treatment, correlations between changes in biomarker levels and reductions from BL at three time points (W24, W52, W100) in disease activity (measured by changes in Disease Activity in Psoriatic Arthritis [DAPSA] score, Psoriatic Arthritis Disease Activity Score [PASDAS], Psoriasis Area and Severity Index [PASI] score) were assessed. Associations between biomarker changes and achievement of American College of Rheumatology (ACR)50 response at W100 were also assessed.

Results: Continued treatment with GUS led to significant and sustained reductions in serum cytokines from W24 through W100. Reductions in CRP and IL-6 were associated with changes in DAPSA score, with a similar trend observed for PASDAS. Reductions in BD-2, IL-17A, IL-17F and IL-22 from BL correlated with improvements in the PASI score, and reductions in collagen turnover biomarkers correlated with changes in the PASDAS (Table 1). Continued disease improvement with long-term GUS treatment, assessed clinically using ACR50 response, was supported by the further reductions in CRP, SAA, IL-6 and collagen turnover biomarkers in ACR50 responders at W100 who were ACR50 nonresponders at W24 (Figure 1). Among ACR50 responders at W24, mean reductions in CRP, SAA and IL-6 were sustained through W100.

Conclusion: These results provide molecular evidence that sustained reductions in serum acute phase proteins and collagen turnover biomarkers may contribute to the continuous, durable improvements in joint symptoms and that reductions in Th17-related effector molecules contribute to improvements in skin symptoms seen in PsA pts receiving GUS.

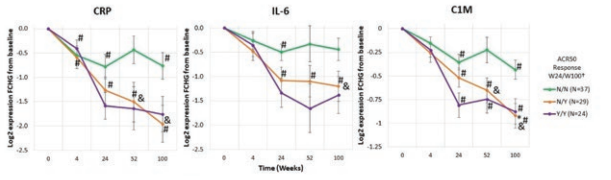
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Table 1. Correlation of Change in Serum Biomarker Levels With Change in PsA Disease Activity From BL Through 24, 52 or 100 Weeks of GUS Treatment

	DAPSA	PASDAS	PASI
BD-2	0.08	0.16	**0.58**[a]
CRP	**0.30**[a]	0.24	0.08
IL-17A	0.08	0.21	**0.46**[a]
IL-17F	0.00	0.11	**0.41**[a]
IL-22	0.17	0.22	**0.34**[a]
IL-6	**0.26**[a]	0.17	-0.03
SAA	0.20	0.20	0.14
TNF-α	0.16	0.19	0.14
C1M	**0.27**[a]	**0.27**[a]	0.07
C3M	0.24	**0.27**[a]	0.06
C4M	0.23	**0.27**[a]	0.06
C6M	**0.30**[a]	**0.31**[a]	0.04

[a]Significant correlation between biomarker expression and disease activity;r>0.25 and P<0.05.

Figure. Reduction in serum cytokine levels and collagen biomarkers in patients who achieved ACR50 response at W24 and through W100.



Statistics based on general linear model. No apparent differential expression was observed across groups at baseline.
*Indicates statistical significance compared to W24 by P<0.05 and |fold difference| ≥1.25.
#Indicates statistical significance compared with baseline by P<0.05 and |fold difference| ≥1.4.
&Indicates statistical significance of W24 nonresponder→W100 responder compared with W24 nonresponder→W100 nonresponder by P<0.05 and |fold difference| ≥1.4.
*Y/N group was not included in this analysis due to a limited number of subjects.

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AB1086

COVID-19–RELATED ADVERSE EVENTS IN THE PHASE 3 POETYK TRIALS OF THE ALLOSTERIC TYROSINE KINASE 2 INHIBITOR, DEUCRAVACITINIB, IN PATIENTS WITH MODERATE TO SEVERE PLAQUE PSORIASIS

Keywords: Targeted synthetic drugs, COVID

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Background: Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis. Deucravacitinib suppresses signaling of cytokines involved in the pathogenesis of immune-mediated diseases including psoriasis, psoriatic arthritis, and systemic lupus erythematosus. Deucravacitinib was efficacious compared with placebo in phase 2 trials in psoriatic arthritis and systemic lupus erythematosus.[1,2] In two phase 3 trials in patients with moderate to severe plaque psoriasis (POETYK PSO-1 [NCT03624127], PSO-2 [NCT03611751]), deucravacitinib showed superior efficacy versus placebo and apremilast.[3,4] Upon completion of either psoriasis trial, patients could enroll in the POETYK long-term extension (LTE) trial (NCT04036435).
Objectives: To evaluate the incidence rate and severity of adverse events (AEs) due to COVID-19 with deucravacitinib treatment in the POETYK PSO-1 and POETYK PSO-2 trials and open-label POETYK LTE trial.
Methods: In PSO-1 (N=666) and PSO-2 (N=1020), adult patients with moderate to severe plaque psoriasis were randomized 2:1:1 to deucravacitinib 6 mg once daily, placebo, or apremilast 30 mg twice daily. At Week 16, placebo patients in both trials switched to deucravacitinib. Based on their Week 24 PASI response, apremilast patients continued with apremilast or switched to placebo or deucravacitinib. In PSO-1, patients randomized to deucravacitinib continued treatment for 52 weeks; in PSO-2, some patients randomized to deucravacitinib had a randomized treatment withdrawal period. At Week 52, patients could enroll in the open-label LTE and receive deucravacitinib. Incidence rates and severity of COVID-19–related AEs in the POETYK trials (n=1364; 2076.7 person-years [PY] of follow-up) were compared with the Janssen/Johnson & Johnson COVID-19 vaccine trial placebo group (n=19,544; 3096.1 PY of follow-up). This reference population was selected due to the study design and timing of the trial, which occurred when variants were in circulation.
Results: As of October 1, 2021, 1519 patients received ≥1 dose of deucravacitinib over a 2-year follow-up period; 1364 patients met criteria for this analysis, with deucravacitinib exposure since the pandemic onset (estimated to be January 1, 2020). In total, 153 deucravacitinib patients reported a COVID-19–related AE, for an overall exposure-adjusted incidence rate (EAIR) of 7.4/100 PY (95% CI, 6.2–8.6). Serious COVID-19–related AEs occurred in 43 patients (EAIR, 2.1/100 PY; 95% CI, 1.5–2.8), including 30 with COVID-19 and 13 with COVID-19 pneumonia; this rate was within the margins of those for moderate to severe COVID-19 reported in the reference population (EAIR, 16.5/100 PY; 95% CI, 15.0–17.9). Deaths due to COVID-19 occurred in 6 patients (EAIR, 0.3/100 PY; 95% CI, 0.1–0.6), with the COVID-19–related mortality rate being consistent with the reference population (EAIR, 0.23/100 PY; 95% CI, 0.1–0.5). Treatment was discontinued due to COVID-19 or COVID-19 pneumonia in 7 patients, including the 6 patients who died due to COVID-19.
Conclusion: COVID-19 was among the most frequently reported AEs during the 2-year period of the pooled PSO-1, PSO-2, and LTE trials due to the temporal overlap of the pandemic with the trials. However, COVID-19 infection and death rates did not differ from the reference population; most infections were not serious and did not lead to treatment discontinuation. Based on this analysis, deucravacitinib did not appear to increase the risk of COVID-19 nor its progression to severe outcomes.

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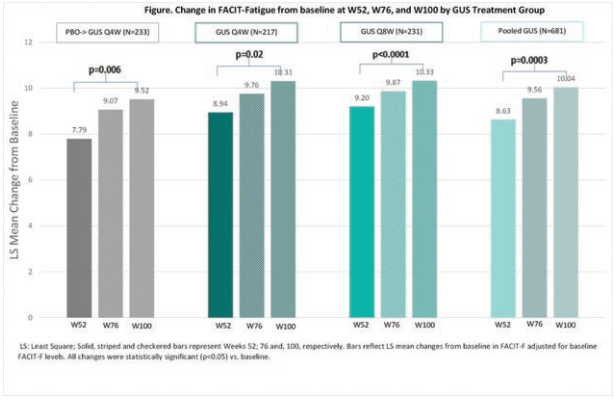
AB1087

LONG-TERM EFFICACY OF GUSELKUMAB IN FATIGUE AND IDENTIFICATION OF EARLY TREATMENT TARGETS: POST HOC ANALYSIS THROUGH 2 YEARS OF A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY CONDUCTED IN BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis

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Background: The IL-23p19-subunit inhibitor guselkumab (GUS) demonstrated clinically meaningful improvements in fatigue through one year of treatment[1] independent of its effects on American College of Rheumatology 20% (ACR20) improvement criteria and Minimal Disease Activity (MDA) achievement[2].
Objectives: In this post-hoc analysis, the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scale was used to: (a) evaluate the long-term effect of GUS in maintaining or further improving fatigue between week (W) 52 and W100, and to (b) identify potential early (W8) predictors, in terms of fatigue, for improved long-term fatigue outcomes.
Methods: DISCOVER-2 enrolled adult patients (pts) with active PsA (≥5 swollen and ≥5 tender joints and CRP ≥0.6 mg/dl) who were naïve to biologics/JAK inhibitors. Pts were randomized (1:1:1) and treated with GUS 100 mg every 4W (Q4W); GUS 100mg at W0, W4, then Q8W; or placebo (PBO→GUS Q4W; crossing over to GUS Q4W at W24). Pts with baseline (BL) fatigue levels lower than the normative value (FACIT-F score ≤43)[3] were included in these post hoc analyses (N=681). The proportions of pts with clinically meaningful improvement (≥4 points) from BL in FACIT-F and with normative FACIT-F levels between W52 and W100 were calculated using non-responder imputation (NRI) for missing data and compared over time within each treatment group with the McNemar test. Changes in FACIT-F over time were assessed with mixed models adjusting for time, treatment group, their interaction, and BL FACIT-F score. Receiver operating characteristics (ROC) analyses were conducted using Youden's index to determine optimal cutoffs at W8 for predicting achievement of normative scores and clinically meaningful FACIT-F responses at W100.
Results: At BL, the mean (SD) FACIT-F score was 28.3 (8.7) with similar levels across treatment groups. At W52, 66.1%, 69.6%, 68.0%, and 67.8% of pts in the PBO→GUS Q4W, GUS Q4W, GUS Q8W, and pooled GUS groups, respectively, achieved clinically meaningful improvements from BL in FACIT-F score; response rates were maintained through W100. Normative FACIT-F levels were achieved by 24.9%, 28.1%, 29.4% and 27.5% of pts in each treatment group, respectively, at W52, and by increasingly greater proportions of pts through W100. Significant improvements from BL in FACIT-F scores were observed at W52 (all nominal p<0.05), with further improvements seen from W52 to W100 across all GUS groups (Figure 1). ROC optimal cutoff in FACIT-F improvement from BL to W8 associated with a clinically meaningful improvement in FACIT-F at W100 was ≥2.0 (nominal p<0.0001); while for achieving normative FACIT-F levels at W100, the optimal cutoff in actual FACIT-F score at W8 was ≥39.5 (nominal p<0.0001).



Conclusion: The clinically meaningful improvements in fatigue seen after 1 year of GUS treatment were further enhanced through 2 years, at which time nearly a third of GUS-treated pts reported normative FACIT-F levels. Early targets in FACIT-F levels achieved with GUS were identified to aid in guiding treatment decisions in routine clinical practice.
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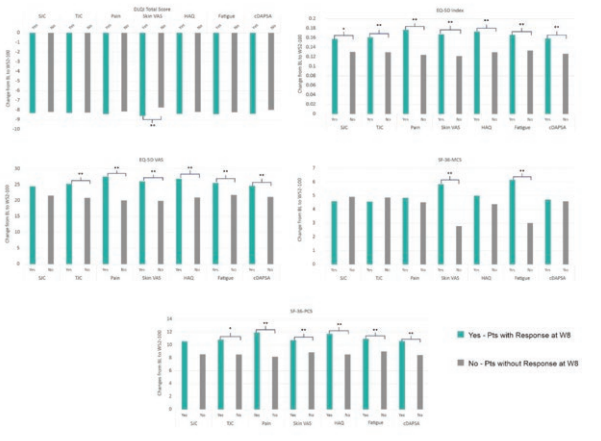
EARLY CLINICAL IMPROVEMENT AS PREDICTOR OF LONG-TERM HEALTH-RELATED QUALITY OF LIFE IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH GUSELKUMAB: POST-HOC ANALYSIS THROUGH 2 YEARS OF A PHASE-3 STUDY

Keywords: Quality of life, Psoriatic arthritis

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Background: Patients (pts) with psoriatic arthritis (PsA) experience lower quality of life than both the general population and pts with psoriasis alone[1,2]. Recent PsA treatment recommendations highlight the importance of maximizing long-term (LT) health-related quality of life (HRQoL) and social participation as primary goals of therapy[3].
Objectives: To determine whether early clinical improvement with guselkumab (GUS) predicts future attainment of enhanced HRQoL.
Methods: DISCOVER-2 enrolled adults naïve to biologics/JAK inhibitors who had active PsA defined as swollen joint count (SJC) ≥5, tender joint count (TJC) ≥5, and C-reactive protein (CRP) ≥0.6 mg/dL. 739 pts were randomized (1:1:1) and treated with GUS 100 mg every 4 weeks (Q4W; n=245); GUS 100 mg at W0, W4, then Q8W (n=248); or placebo (PBO) (n=246). In this post hoc analysis, pts treated with GUS Q4W and GUS Q8W were pooled. Early (W8) clinical improvement was defined as any of: (i) ≥20% improvement in SJC, TJC, pt pain, pt skin visual analog scale (VAS), and Health Assessment Questionnaire-Disability Index (HAQ-DI); (ii) ≥4-point improvement in the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score; (iii) minimally clinically important improvement (MCII) in clinical disease activity in PsA (cDAPSA; ≥5.7 points); (iv) change in Leeds enthesitis index (LEI) and dactylitis severity score (DSS) at W8 among pts with baseline (BL) enthesitis and dactylitis, respectively. Time-averaged changes in HRQoL estimates from BL to W52-100 were determined for Dermatology Life Quality Index (DLQI), EQ-5D Index & VAS, and SF-36 mental (MCS) and physical (PCS) component summary scores. The association between early clinical improvement at W8 and LT HRQoL among GUS-treated pts was assessed with mixed models.
Results: Clinical improvement by W8 was significantly greater among GUS-treated patients compared with PBO. Early clinical improvement with GUS was associated with greater increase in HRQoL (EQ-5D) at W52 through W100, with the exception of SJC on EQ-5D VAS (Figure 1; LEI & DSS results not shown). Similarly, pts achieving early clinical improvement in any domain except DSS and SJC experienced significantly greater benefits in physical function (SF-36 PCS) at W52-W100. Early improvements in skin disease and fatigue were associated with greater improvement in mental health (SF-36 MCS) at W52-W100, while for skin-specific HRQoL (DLQI), early pt skin VAS response was the only predictor of HRQoL at W52-W100. Although significantly lower than in pts with early clinical improvement, benefits in HRQoL were also observed in pts without clinical improvement at W8.
Conclusion: Clinical response at W8 with GUS was associated with significantly greater improvements in HRQoL from W52 through W100. Although pts without early clinical improvement demonstrated benefits in LT HRQoL, early response in distinct PsA domains differentially impacted more specific aspects of HRQoL over 2 years. In contrast, significantly greater improvements in overall and physical HRQoL were observed among responders across several PsA domains.

Figure. Associations Between Early (W8) Clinical Improvement and Long-term (W52-100) HRQoL Improvement in GUS-treated Patients



SJC: 20% improvement in SJC at W8; TJC: 20% improvement in TJC at W8; Pain: 20% improvement in Pain at W8; Skin VAS: 20% improvement in Skin VAS at W8; HAQ: 20% improvement in HAQ at W8; Fatigue: FACIT-fatigue response (≥4 point improvement) at W8; cDAPSA MCII: Minimal clinically important improvement in cDAPSA (≥5.7 point improvement) at W8. *p<0.05; **p< 001. P values represent comparison of early clinical response 'yes' vs. 'no'. 'Yes' bars refer to pts who presented a response as described above in the respective domain at W8. 'No' bars refer to pts who did not present the respective domain at W8. Long-term refers to the change from BL to W52-100 in each HRQoL outcome. Values represent time-averaged least-square mean (95% CI) changes in HRQoL from BL derived from repeated-measures mixed models including the change in HRQoL as the dependent variable and early clinical response, GUS regimen time, BL HRQoL, and BL stratification factors (DMARD use, CRP) as fixed factors.

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AB1089

BIMEKIZUMAB EFFICACY IN HIGH-IMPACT AREAS FOR PATIENTS WITH MODERATE TO SEVERE PLAQUE PSORIASIS: POOLED RESULTS THROUGH TWO YEARS FROM THE BE SURE AND BE RADIANT PHASE 3 TRIALS

Keywords: Skin, Outcome measures, Clinical trials

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Background: High levels of complete clearance of plaque psoriasis in high-impact areas such as the scalp, nails, palms and soles have been reported in patients (pts) after 1 year (yr) of bimekizumab (BKZ) treatment.[1]
Objectives: Assess scalp, nail and palmoplantar outcomes over 2 yrs from two BKZ phase 3 trials in moderate to severe plaque psoriasis.
Methods: Data were pooled over 2 yrs from the BE RADIANT phase 3b trial (NCT03536884), including Yr1 of its ongoing open-label extension (OLE), and the 1-yr BE SURE phase 3 trial (NCT03412747) with the ongoing OLE, BE BRIGHT (NCT03598790).[2,3] Pts included were randomised at baseline to BKZ 320 mg every 4 weeks (wks; Q4W) and then continued to receive BKZ Q4W or switched to BKZ every 8 wks (Q8W) at Wk16, and received the same dose on entering the OLE (Q4W/Q4W/Q4W or Q4W/Q8W/Q8W). Regional involvement was analysed using scalp Investigator's Global Assessment (scalp IGA; 5-point scale [0–4]), modified Nail Psoriasis Severity Index (mNAPSI; total fingernail score, 0–130 scale) and palmoplantar (pp)-IGA (5-point scale [0–4]). We report proportions of pts who achieved complete regional clearance (scalp IGA 0, mNAPSI 0, pp-IGA 0) through Yr2 (OLE Wk48) among pts with moderate to severe regional involvement at baseline (scalp IGA ≥3, mNAPSI >10, pp-IGA ≥3). Missing data were imputed as non-response (NRI).
Results: Of pts who entered the OLEs from BE SURE and BE RADIANT, 303 and 323 received BKZ Q4W/Q4W/Q4W and Q4W/Q8W/Q8W, respectively. Of these, 209 (69.0%) and 241 (74.6%) had baseline scalp IGA ≥3; 43 (14.2%) and 44 (13.6%) had pp-IGA ≥3; 100 (33.0%) and 111 (34.4%) had mNAPSI >10. Among pts with baseline scalp IGA ≥3, 78.0% and 81.7% treated with BKZ Q4W/Q4W/Q4W and Q4W/Q8W/Q8W achieved scalp IGA 0 at Wk16, respectively; 80.4% and 79.3% achieved scalp IGA 0 at Yr2 (OLE Wk48) (**Table 1**). Of pts with baseline pp-IGA ≥3, 60.5% and 81.8% treated with BKZ Q4W/Q4W/Q4W and Q4W/Q8W/Q8W achieved pp-IGA 0 at Wk16, respectively; 83.7% and 81.8% achieved pp-IGA 0 at Yr2 (**Table 1**). Of pts with baseline mNAPSI >10, 51.0% and 58.6% treated with BKZ Q4W/Q4W/Q4W and Q4W/Q8W/Q8W achieved mNAPSI 0 at Wk32, respectively; 40.0% and 59.5% achieved mNAPSI 0 at Yr2 (**Table 1**).
Conclusion: A high percentage of BKZ-treated pts achieved complete clearance of scalp and palmoplantar psoriasis at Wk16, which was sustained over 2 yrs. Complete nail clearance continued to increase through Yr1, reflecting the longer timescale required for nail growth, and was generally sustained through Yr2. Proportions of pts achieving complete nail, scalp and palmoplantar clearance were generally comparable between BKZ Q4W/Q4W/Q4W and Q4W/Q8W/Q8W dosing regimens.

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Table 1. Complete regional clearance of scalp, nail, or palmoplantar psoriasis over 2 years (NRI)

	BKZ 320 mg Q4W/Q4W/Q4W n (%)	BKZ 320 mg Q4W/Q8W/Q8W n (%)
Scalp IGA ≥3 at baseline	**N=209**	**N=241**
Scalp IGA 0 at Wk16	163 (78.0)	197 (81.7)
Scalp IGA 0 at Yr1[a]	186 (89.0)	206 (85.5)
Scalp IGA 0 at Yr2[b]	168 (80.4)	191 (79.3)
mNAPSI >10 at baseline	**N=100**	**N=111**
mNAPSI 0 at Wk32[c]	51 (51.0)	65 (58.6)
mNAPSI 0 at Yr1[a]	54 (54.0)	79 (71.2)
mNAPSI 0 at Yr2[b]	40 (40.0)	66 (59.5)
pp-IGA ≥3 at baseline	**N=43**	**N=44**
pp-IGA 0 at Wk16	26 (60.5)	36 (81.8)
pp-IGA 0 at Yr1[a]	35 (81.4)	41 (93.2)
pp-IGA 0 at Yr2[b]	36 (83.7)	36 (81.8)

[a]Wk48 of treatment; [b]OLE Wk48: BE RADIANT Wk96 and BE SURE/BE BRIGHT Wk104 of total treatment; [c]mNAPSI response initially reported at Wk32 due to the longer timescale required for nail growth vs skin clearance. Pts included had regional involvement at baseline and entered the OLE without switching maintenance dose. Treatment groups refer to BKZ dosing schedules in Wks: 0–16/16–48/OLE entry. BKZ: bimekizumab; IGA: Investigator's Global Assessment; mNAPSI: modified Nail Psoriasis Severity Index; NRI: non-responder imputation; OLE: open-label extension; pp: palmoplantar; pts: patients; Q4W: every 4 wks; Q8W: every 8 wks; wk: week; yr: year.

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AB1090

EFFICACY OF UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS STRATIFIED BY INVOLVEMENT OF WEIGHT-BEARING JOINT REGIONS: A POST HOC SUBGROUP ANALYSIS OF THE PHASE 3, RANDOMIZED, SELECT-PSA 1 AND SELECT-PSA 2 TRIALS

Keywords: Outcome measures, Randomized control trial, Psoriatic arthritis

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Background: Involvement of weight-bearing joints in patients with psoriatic arthritis (PsA) can be associated with reduced activities of daily living and quality of life. Upadacitinib (UPA) is an oral, reversible Janus kinase inhibitor approved for the treatment of active PsA in adults. In the SELECT-PsA 1 and SELECT-PsA 2 trials, treatment with once daily UPA 15 mg (UPA15) or 30 mg (UPA30) resulted in greater improvements in the number of swollen and tender joints as well as other patient- and physician-reported outcomes when compared with placebo.[1-3]

Objectives: To evaluate the long-term efficacy of UPA in patients with PsA and involvement in 1 or more regions of weight-bearing joints.

Methods: The SELECT-PsA 1 (NCT03104400) and SELECT-PsA 2 (NCT03104374) phase 3, randomized, controlled trials enrolled patients ≥ 18 years old with active PsA and intolerance or inadequate response to ≥ 1 nonbiologic disease modifying anti-rheumatic drug (DMARD; SELECT-PsA 1) or biologic DMARD (SELECT-PsA 2). This post hoc analysis of the 2 phase 3 trials stratified patients with involvement in 1 to 6 regions of weight-bearing joints (hips, knees, ankles, midfoot, metatarsophalangeal [MTP], or proximal interphalangeal [PIP]) who were randomized at baseline to receive either UPA15, placebo (PBO), or adalimumab (ADA; only in SELECT-PsA 1); at week 24, PBO-treated patients switched to UPA15 (PBO/UPA15). This analysis did not include patients who received UPA30 or PBO/UPA30. A mixed-effects model with repeated measures was used to analyze the change from baseline to week 104 in 4 patient-reported outcome measures (pain, Health Assessment Questionnaire-Disability Index [HAQ-DI], Work Productivity and Activity Impairment [WPAI] questionnaire, and EuroQol 5 Dimension 5 Level [EQ-5D-5L]) and 1 composite outcome measure (Disease Activity in Psoriatic Arthritis [DAPSA]). UPA safety results in patients with PsA have been previously reported.[1-3]

Results: A total of 1069 patients from the SELECT-PsA 1 trial and 317 patients from the SELECT-PsA 2 trial were included in the pooled analysis. Of all patients with any involvement in regions of weight-bearing joints, > 91% of patients had involvement in ≥ 2 regions. The most common weight-bearing joints with involvement were the PIP (SELECT-PsA 1, 79.8%; SELECT-PsA 2, 84.5%), MTP (71.1%; 73.8%), and knee (62.3%; 64.9%) joints. Improvements from baseline to week 104 were observed with UPA15 treatment in patient-reported outcomes of pain, HAQ-DI, WPAI, EQ-5D-5L, and the DAPSA score across all subgroups of patients with involvement in 1 to 6 regions of weight-bearing joints (**Figure 1**). In general, the magnitude of improvement in outcome scores with UPA15 was greater in patients with involvement in a higher number of regions. Similar improvements from baseline to week 104 in outcome scores were observed in patients who received PBO/UPA15 or ADA to week 104.

Conclusion: UPA15 treatment was associated with long-term improvements in pain, disability, work productivity, disease activity, and quality of life in patients with PsA and involvement in 1 or more regions of weight-bearing joints.

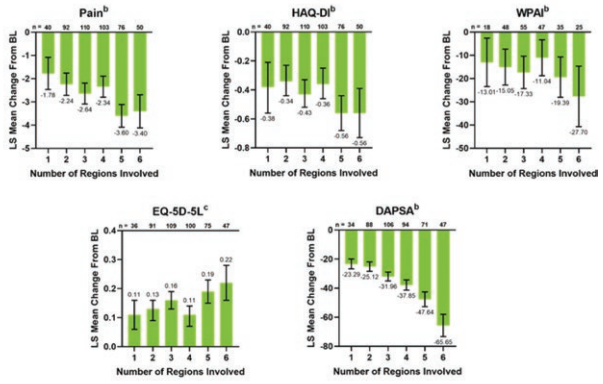
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Figure. Mean Change at Week 104 in Outcome Scores Among Subgroups of Patients With Psoriatic Arthritis and Involvement in 1 to 6 Regions of Weight-bearing Joints[a] Treated With UPA 15 mg



[a]Weight-bearing joints include hips, knees, ankles, midfoot, metatarsophalangeal (MTP), or proximal interphalangeal (PIP).
[b]Decrease in score indicates improvement.
[c]Increase in score indicates improvement.
BL, baseline; DAPSA, Disease Activity in Psoriatic Arthritis; EQ-5D-5L, EuroQol 5 Dimension 5 Level; HAQ-DI, Health Assessment Questionnaire-Disability Index; LS, least squares; UPA, upadacitinib; WPAI, Work Productivity and Activity Impairment questionnaire.

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AB1091 BIOLOGIC THERAPIES FOR PSORIASIS DECREASE THE RISK TO DEVELOP MAJOR DEPRESSIVE DISORDER

Keywords: bDMARD

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Background: Major depression is some of the numerous comorbidities associated with psoriasis (PsO) and psoriasis arthritis (PsA) [1].
Objectives: Assessing the risk of developing depression in patients with pre-existing PsO treated with different treatment regimens; topical treatment, conventional disease-modifying anti-rheumatic drugs (cDMARDs), and biologic disease-modifying anti-rheumatic drugs (bDMARDs), which had not previously studies sufficiently on real-world data.
Methods: We conducted a retrospective exploratory study with real-world data using the databases of the third largest Israeli health maintenance organization, 'Meuhedet' which covers approximately 1,300,000 subjects. All patients of 'Muehedat' diagnosed with PsO from January 2000 until January 2020 were included in the analysis. Overall, 61,003 patients with PsO were detected. In addition, each PsO patient was paired with four control subjects by gender, age, and ethnicity (general, Arabic, or Orthodox). We defined PsO and PsA according to physicians' diagnoses. Depression included patients with either Selective serotonin reuptake inhibitors (SSRI) treatment or the physicians' diagnoses of depression. The date of the depression incident was defined by the first occurrence of the first to occur. We classified the patients diagnosed with PsA into a separate group; thus, patients were categorized according to their diagnosis (control, PsO or PsA). Furthermore, we analyzed the patients by the most advanced treatment prescribed to the patient; sub-grouped 1- topical therapy, phototherapy, or no therapy, sub-grouped 2 - cDMARDs (methotrexate or sulfasalazine), sub-grouped 3 - bDMARDs (anti-TNF, anti-IL17, or anti-IL12/23 agents) (**Table 1**). The Incident cases of depression were analyzed according to the different lines of therapy mentioned above. In addition, Time-dependent Cox proportional hazard models were used to evaluate the adjusted risk of developing MACE by treatment group.
Results: 231,584 patients were included after exclusion by the defined criteria, contributing a total of 2,917,319 patient-years. Adjusted Cox proportional hazards regression analysis showed that the risk of developing depression in PsO patients treated with topical treatment and those treated with bDMARDs was significantly higher in comparison to controls (Topical, HR: 1.06, CI: 1.04 - 1.09, p-value: <0.001; bDMARDs, HR: 2.08, CI: 1.76 - 2.45, p-value: <0.001). Yet, the risk of developing depression in PsO patients treated with cDMARDs was significantly lower compared to controls (HR: 0.66, CI: 0.5 – 0.87, P-value: 0.003). Similarly, the risk of developing depression in PsA patients treated with topical treatment and those treated with bDMARDs was significantly higher in comparison to controls (Topical, HR: 1.67, CI: 1.56 - 1.78, p-value: <0.001; bDMARDs, HR: 1.86, CI: 1.66 – 2.1, p-value: <0.001). Yet, the risk of depression in PsA patients treated with cDMARDs was not significantly different compared to controls (HR: 0.91, CI: 0.77 – 1.08, p-value: 0.29). (**Figure 1**). This analysis was adjusted to gender, body mass index (BMI), and age of PsO diagnosis; notably, female gender, higher BMI, and older age were all associated with a greater risk of developing depression.
Conclusion: Despite the fact that psoriasis and arthritis severity is higher in patients treated with cDMARDs compared to those treated with topical therapy, cDMARDs have a protective effect on the risk of developing depression. On the contrary, biological treatment increases the risk of depression, possibly due to the high severity of the disease, yet also have a protective effect compared to those treated with topical therapy.

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AB1092 GUSELKUMAB RAPIDLY IMPROVES ACTIVITIES OF DAILY LIVING IN PATIENTS WITH ACTIVE PSA: POOLED ANALYSIS OF 2 PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED STUDIES

Keywords: Quality of life, Psoriatic arthritis, Patient reported outcomes

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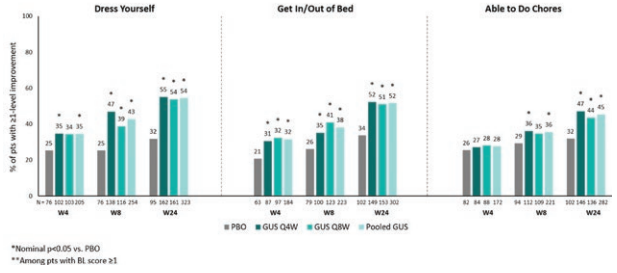
Background: Maintaining daily activities is a critical treatment goal for patients (pts) with psoriatic arthritis (PsA). The Health Assessment Questionnaire-Disability Index (HAQ-DI), a mainstay tool for evaluating physical function in pts with PsA, assesses 20 common activities of daily living that should be evaluated given the heterogeneous clinical presentation of PsA.
Objectives: In this post hoc analysis from DISCOVER (D)-1 and -2, we examined the level of impairment in individual activities of daily living assessed by the HAQ-DI, and the effect of guselkumab (GUS) on pts' ability to accomplish these activities, among pts with active PsA.
Methods: D1/D2 enrolled adults with active PsA despite standard therapies. D1 pts had ≥3 swollen and ≥3 tender joints (SJC/TJC), C-reactive protein (CRP) ≥0.3 mg/dL; 31% had 1-2 prior TNF inhibitors (TNFi). D2 pts had ≥5 SJC/TJC and CRP ≥0.6 mg/dL; all were biologic-naïve. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo (PBO). Scores for each of the 20 HAQ-DI items (range: 0-3; 0/1/2=no/some/much difficulty, 3=unable to do) at baseline (BL) and proportion of pts with scores ≥1 or ≥2 were summarized. Ability to achieve ≥1-level or ≥2-level improvement in each HAQ-DI item (in pts with BL score ≥1 or ≥2, respectively) during the 24W PBO-controlled period was compared between GUS- and PBO-treated pts using logistic regression adjusting for BL value, prior TNFi use, and BL DMARD use.
Results: At BL, the mean (SD) HAQ-DI score=1.2-1.3 (0.6) across treatment groups. The majority of pts (84.5%) had a score >0.5, indicating some functional limitation, and reported impairment in one or more activity, with the greatest impact on ability to do chores, dress oneself, and get in/out of bed (Table 1). The proportion of pts achieving ≥1-level improvement across HAQ-DI items was significantly higher with GUS vs. PBO as early as W4 and increased through W24 (Figure 1). Similar patterns were observed for achieving a ≥2-level improvement across HAQ items (data not shown). Responses were numerically similar between GUS Q4W and Q8W.
Conclusion: In the setting of PsA, GUS demonstrated improvements as early as W4 across all HAQ-DI items, including those most impaired at BL, with comparable responses between dosing regimens. These findings may assist the communication between pts and healthcare providers when establishing treatment goals during shared decision making.

Table 1. Summary of HAQ-DI Items at BL

	Mean (SD)			Score ≥1, %		
HAQ-DI Item*	**PBO (N=372)**	**GUS Q4W (N=373)**	**GUS Q8W (N=375)**	**PBO (N=372)**	**GUS Q4W (N=373)**	**GUS Q8W (N=375)**
Able to Do Chores	**1.3 (0.8)**	**1.2 (0.8)**	**1.2 (0.8)**	**86**	**83**	**84**
Dress Yourself	**1.0 (0.7)**	**1.0 (0.7)**	**1.1 (0.7)**	**80**	**79**	**80**
Get In/Out of Bed	**1.0 (0.6)**	**1.0 (0.7)**	**1.1 (0.7)**	**82**	**76**	**80**
Climb Up 5 Steps	1.1 (0.7)	0.9 (0.7)	1.0 (0.7)	77	72	74
Reach-Get Down 5 lb Object Above Head	1.1 (0.8)	0.9 (0.8)	1.0 (0.8)	75	66	71
Bend Down Pick Up Clothing - Floor	1.0 (0.7)	0.9 (0.7)	1.0 (0.7)	79	73	77
Take a Tub Bath	1.0 (0.8)	0.9 (0.8)	1.0 (0.9)	69	66	68
Stand Up from Straight Chair	1.0 (0.7)	0.9 (0.7)	0.9 (0.7)	77	72	73
Open Jars Previously Opened	1.0 (0.8)	0.9 (0.8)	0.9 (0.9)	69	67	63
Cut Your Meat	0.8 (0.8)	0.8 (0.8)	0.8 (0.8)	61	59	58
Walk Outdoors on Flat Ground	0.8 (0.7)	0.8 (0.7)	0.8 (0.7)	69	66	67
Shampoo Your Hair	0.7 (0.7)	0.7 (0.7)	0.7 (0.7)	61	57	59
Wash/Dry Your Body	0.7 (0.7)	0.7 (0.6)	0.7 (0.7)	63	60	63
Get On/Off the Toilet	0.7 (0.7)	0.7 (0.6)	0.7 (0.6)	60	56	61
Lift Full Cup or Glass to Mouth	*0.6 (0.7)*	*0.5 (0.6)*	*0.5 (0.6)*	*49*	*45*	*46*
Open Car Doors	*0.5 (0.7)*	*0.5 (0.6)*	*0.5 (0.6)*	*44*	*42*	*45*
Turn Faucets On/Off	*0.5 (0.6)*	*0.5 (0.6)*	*0.5 (0.7)*	*43*	*42*	*42*

Bold=highest impairment, italics=lowest impairment; 'Open a New Milk Carton', 'Get In/Out of a Car', and 'Run Errands/Shop', ranking in the middle in terms of impairment, not shown. *Ordered from highest to lowest mean impairment.

Figure. Proportion of pts achieving ≥1 level Improvement in HAQ-DI Items with highest impairment at BL**



*Nominal p<0.05 vs. PBO
**Among pts with BL score ≥1

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AB1093

LONG-TERM IMPROVEMENT IN INDIVIDUAL ACR RESPONSE CRITERIA AND RESIDUAL DISEASE IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH GUSELKUMAB: POST HOC ANALYSIS OF A PHASE 3 RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

Keywords: Clinical trials, Psoriatic arthritis, bDMARD

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Background: Treatment effects on PsA joint symptoms are assessed by ACR response rates, reflecting percentages of patients (pts) meeting a composite measure of improvement from baseline (BL) at specific timepoints. Alternatively, the ACR-numeric (ACR-N) is a continuous measure of improvement based on 7 ACR components.
Objectives: Contrast performance of ACR response rates with ACR-N in characterizing guselkumab (GUS) treatment effect in PsA and describe duration and extent of continuous improvement with GUS using ACR-N and ACR components through week (W) 100.
Methods: The phase 3 DISCOVER-2 trial enrolled bio-naïve adults with active PsA (swollen and tender joint counts [SJC/TJC] ≥5, C-reactive protein [CRP] ≥0.6 mg/dL). 739 pts were randomized (1:1:1) and treated with GUS 100 mg every 4W (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo (PBO) with crossover to GUS Q4W at W24. ACR20/50/70 response rates through W100 were determined using non-responder imputation (NRI) for missing data; GUS Q4W/Q8W and PBO rates were compared through W24. Duration of continuous improvement over 100W of GUS was assessed by contrasting least square mean (LSM) ACR-N and ACR component values between consecutive visits. Percent changes in SJC, TJC, physician global (MDGA), pt global (PtGA), health assessment quality disease index (HAQ-DI), CRP, and pt-pain were also assessed, adjusting for treatment group, BL use of csDMARDs, and respective BL scores.
Results: ACR response rates were significantly greater with GUS Q4W/Q8W vs PBO by W4 (ACR20), W8 (ACR50), and W8-12 (ACR70); significant differences in ACR-N between GUS Q4W/Q8W vs PBO were observed by W2 (GUS Q4W) or W8 (GUS Q8W) (Table 1; nominal p<0.05). Similar responses were observed with GUS Q4W and Q8W. Among GUS-treated pts, nominally significant improvements comparing ACR-N scores across consecutive visits were

observed by W2, with a positive trajectory through W100 (Figure 1). Individual ACR components also significantly improved by W2 and – apart from CRP levels that rapidly plateaued to means <1 mg/dL – continued to improve vs previous visit through W68-84 of GUS (nominal p<0.05).

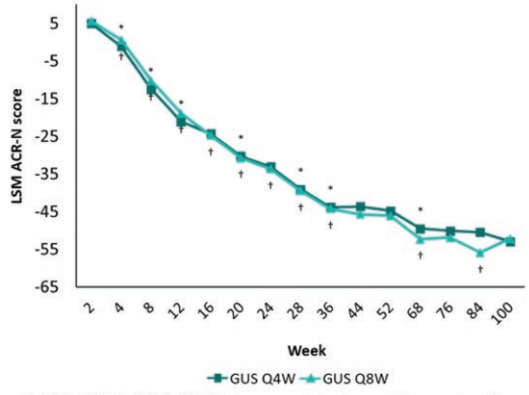
Conclusion: GUS rapidly improved PsA activity whether assessed by ACR response or ACR-N. Early response was apparent across ACR components, followed by a positive trajectory through 2 years of GUS that yielded low levels of residual disease.

Table 1. ACR Response Rates (NRI) and ACR-N Scores Over Time With GUS (Q4W/Q8W) vs PBO

	ACR20 Achievement (% of Pts)		ACR50 Achievement (% of Pts)		ACR70 Achievement (% of Pts)		ACR-N Score (LSM Estimate)	
W	Q4W (N=245)/ Q8W (N=248)	PBO →Q4W (N=246)	Q4W (N=245)/ Q8W (N=248)	PBO →Q4W (N=246)	Q4W (N=245)/ Q8W (N=248)	PBO →Q4W (N=246)	Q4W (N=245)/ Q8W (N=248)	PBO →Q4W (N=246)
2	10.6%/ 10.1%	8.1%	0.4%/ 1.6%	0.4%	0%/ 0%	0%	4.6/ 5.2	6.4
4	21.6%*/ 19.8%*	11.8%	3.3%/ 4.0%	1.2%	0.8%/ 0.4%	0.8%	-1.3*/ 0.2	5.4
8	40.4%*/ 39.1%*	17.5%	11.4%*/ 10.1%*	4.1%	2.4%/ 3.6%*	0.8%	-12.9*/ -10.6*	1.9
12	51.4%*/ 49.6%*	26.4%	17.1%*/ 19.0%*	6.1%	5.3%*/ 8.1%*	0.4%	-21.5*/ -19.2*	-3.3
16	56.7%*/ 55.2*%	34.6%	21.6%*/ 28.6%*	9.8%	8.6%*/ 13.7%*	0.8%	-24.7*/ -25.1*	-4.3
20	59.2%*/ 63.7%*	30.5%	30.2%*/ 31.9%*	16.7%	14.3%*/ 15.7%*	3.3%	-30.7*/ -31.2*	-4.7
24	64.9%*/ 64.9%*	34.6%	33.5%*/ 31.5%*	15.0%	13.5%*/ 18.5%*	4.5%	-33.5*/ -34.1*	-5.2
28	68.6%/ 67.7%	46.7%	38.8%/ 39.5%	22.0%	20.0%/ 20.2%	7.3%	-39.4/ -39.9	-17.8
36	73.9%/ 74.6%	64.6%	42.9%/ 42.3%	37.4%	23.3%/ 26.2%	14.6%	-44.2/ -44.6	-35.5
44	69.8%/ 74.6%	66.3%	44.5%/ 45.6%	41.9%	22.4%/ 28.2%	19.9%	-43.9/ -46.2	-38.0
52	71.0%/ 74.6%	64.2%	45.7%/ 48.4%	41.1%	26.1%/ 27.8%	17.9%	-45.0/ -46.4	-36.8
68	71.8%/ 78.6%	69.5%	52.7%/ 55.6%	44.7%	32.2%/ 32.7%	25.2%	-49.8/ -52.6	-43.3
76	75.1%/ 75.4%	67.9%	53.1%/ 50.8%	45.9%	29.8%/ 33.1%	25.2%	-50.4/ -52.2	-44.7
84	71.4%/ 75.8%	70.3%	51.4%/ 56.9%	49.2%	35.1%/ 38.3%	26.0%	-50.9/ -56.3	-48.9
100	75.9%/ 73.8%	68.3%	55.9%/ 54.8%	47.6%	34.7%/ 35.5%	29.7%	-53.0/ -52.4	-49.5

*p-value <0.05 vs PBO (assessed only for PBO-controlled period [grey shaded]).

Figure. Duration of Continuous Improvement from Previous Visit with GUS in ACR-N Through W100



*p<0.05 for Q4W. †p<0.05 for Q8W. P-values are nominal and represent the comparison of mean parameter levels at each visit with the previous visit. *LSM=least square mean estimate.*

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AB1094

GUSELKUMAB EFFECT ON INFLAMMATORY CARDIOVASCULAR (CV) RISK BIOMARKERS, EFFICACY, AND SAFETY IN PSORIATIC ARTHRITIS PATIENTS WITH CV RISK FACTORS: POST-HOC ANALYSIS OF 2 PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDIES

Keywords: Cardiovascular disease, Psoriatic arthritis, Outcome measures

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Background: PsA has been associated with an increased risk of cardiovascular disease (CVD), likely due to accelerated atherosclerosis secondary to chronic inflammation.[1] The number of CV risk factors has been shown to correlate with PsA disease activity (DA).[2]

Objectives: Describe effect of guselkumab (GUS) on inflammatory biomarkers that predict CVD, and its efficacy and safety, in patients (pts) with active PsA and concurrent CV risk factors.

Methods: DISCOVER (D)1&2 enrolled adults with active PsA despite standard therapies. D1 pts (31% received 1-2 prior TNF inhibitors [i]), had tender and swollen joint counts (TJC/SJC) each ≥3 and CRP ≥0.3 mg/dL; D2 pts (biologic-naïve) had TJC/SJC each ≥5 and CRP ≥0.6 mg/dL. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo (PBO)→GUS 100 mg Q4W at W24. Pts included in this analysis had ≥1 of the following CV risk factors: obesity; smoking (past or current); or history of hypertension, diabetes mellitus (DM), or hyperlipidemia. Changes in high-sensitivity (hs) CRP and neutrophil–lymphocyte ratio (NLR) were compared between GUS vs PBO with mixed models adjusting for baseline (BL) levels. Achievement of endpoints at W24 (missing data imputed as no response) was compared in GUS vs PBO with logistic regression adjusting for BL levels, prior TNFi use, and BL DMARD use: American College of Rheumatology (ACR) response criteria, Investigator's Global Assessment (IGA) of psoriasis score 0/1, DA Index for PsA (DAPSA) low DA (LDA)/remission, PsA DA Score (PASDAS) LDA, minimal DA (MDA), Psoriasis Area and Severity Index (PASI) responses, Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F) response, Health Assessment Questionnaire Disability Index (HAQ-DI) response, and enthesitis and dactylitis resolution. The incidence of major adverse CV events (MACE; cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke) was assessed through W100.

Results: Of 1120 enrolled pts, 758 had ≥1 CV risk factor (259 Q4W, 252 Q8W, 247 PBO); of these, 448 (59%) were obese, 420 (55%) had hypertension, 315 (42%) were smokers, 171 (23%) had hyperlipidemia, and 103 (14%) had DM.

Through W24, GUS significantly reduced hsCRP and NLR vs PBO (Figure 1). Response rates at W24 were significantly higher with GUS vs PBO for all assessed endpoints (Table 1). During the PBO-controlled period, one pt each had a MACE in the PBO (0.9 [95% CI: 0.0-4.9]/100 person-years [PY]) and pooled GUS (0.4; 0.0-2.4)/100PY groups. In the pooled GUS group, the incidence (95% CI) of MACE was 0.2 (0.0-0.8)/100PY over 1 year and 0.3 (0.1-1.0)/100PY over 2 years.

Conclusion: In the subgroup of PsA pts with concurrent CV risk factors, GUS was associated with significant reductions in hsCRP and NLR and significantly higher response rates vs PBO for all PsA domains assessed. MACE incidence was similar to that in the overall D1/D2 population.[3] These findings support the efficacy of GUS on systemic inflammation and its cardiovascular safety.

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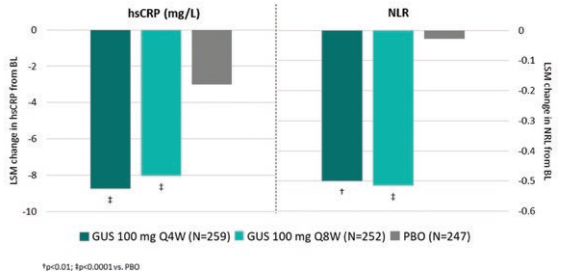
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Table 1. Achievement of Efficacy Endpoints at W24 in Pts With Concurrent CV Risk Factors

Parameter	GUS 100 mg Q4W (N=259)	GUS 100 mg Q8W (N=252)	PBO (N=247)
ACR20	62.9%‡	58.3%‡	30.4%
ACR50	32%‡	28.2%‡	11.7%
ACR70	13.5%†	13.1%†	4.0%
DAPSA LDA (Pts with BL DAPSA >14)	39.8%‡	40.3%‡	19.4%
PASI90	60.2%‡	56.3%‡	11.7%
PASI100	47.5%‡	36.5%‡	6.5%
IGA 0/1 (Pts with BL IGA >1)	88.6%‡	85.2%‡	33.7%
Dactylitis resolution (Pts with BL dactylitis)	64.8%†	62.5%*	44.6%
Enthesitis resolution (Pts with BL enthesitis)	43.7%†	48.1%†	29.1%
FACIT-F Response (Pts with BL FACIT-F ≤48)	65.3%‡	59.8%†	44.1%
HAQ-DI Response (Pts with BL HAQ-DI ≥0.35)	56.5%‡	50.4%‡	30.2%
MDA	23.2%‡	20.6%‡	7.3%
PASDAS LDA (Pts with BL PASDAS >3.2)	27.2%‡	29.3%‡	9.4%

*Nominal p<0.05; †p<0.01; ‡p<0.0001 vs PBO.

Figure. Least Square Mean (LSM) Changes From BL to W24 in hsCRP and NLR in Pts with Concurrent CV Risk Factors



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AB1095

IMPACT OF PSORIATIC ARTHRITIS MANIFESTATIONS ON PERCEPTION OF PAIN IMPROVEMENT: POOLED ANALYSIS OF TWO PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDIES WITH GUSELKUMAB

Keywords: bDMARD, Pain, Psoriatic arthritis

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Background: Pain in PsA has multifaceted origins (e.g., peripheral joint inflammation, axial involvement [axPsA], skin lesions, dactylitis, enthesitis, underlying conditions) and can be difficult to treat. Guselkumab (GUS), a fully human IL-23p19 subunit inhibitor, is effective in treating multiple PsA domains and elicited durable improvement in patient (pt)-reported pain (PtP) in the DISCOVER (D)-1&2 trials[1,2].

Objectives: Assess association between improvement in key PsA manifestations and PtP using 1-year D1&2 data.

Methods: D1&2 enrolled adults with active PsA despite standard therapies[3,4]. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo with crossover to GUS 100 mg Q4W at W24. Treatment groups were pooled (N=1120). Longitudinal associations of improvement in SJC (0-66), TJC (0-68), Leeds enthesitis index (LEI), dactylitis severity score (DSS), Psoriasis Area and Severity Index (PASI), axPsA (N=312), and improvement in overall PtP (0-100 mm) and spinal pain (BASDAI question 2 in pts with axPsA) were assessed. Longitudinal associations of improvement in these PsA manifestations with ≥30%/50%/70% improvements in PtP (PtP-30/50/70) were assessed.

Results: Mean (SD) BL PtP of 61.2 (19.8) indicated substantial burden. Upon adjusting for potential confounders, greater improvement in PASI, SJC, and TJC (mutually adjusted) were each associated with significantly greater improvement in PtP and higher odds of achieving PtP-30 through W52 **(Table 1)**. PASI reduction was also associated with greater odds of PtP-50, as was TJC improvement for PtP-50/70. In pts with BL enthesitis, LEI, PASI, and TJC improvements were each associated with greater PtP improvement and attaining PtP-30/50/70; SJC reduction was only associated with PtP-30. In pts with BL dactylitis, PASI and TJC reductions were significantly associated with PtP improvement. Overall, axPsA presence did not impact the extent of PtP improvement (data not shown). In pts with axPsA, significant associations were observed between spinal pain improvement and TJC and LEI improvement.

Conclusion: Improvements in key PsA manifestations were significantly associated with pain reduction, although to varying extents. TJC reduction had the greatest impact on PtP improvement, likely due to overlap of the construct measured. Psoriasis improvement had a greater impact on pain relief than SJC improvement, highlighting the sensory burden of skin lesions, while enthesitis improvement showed a significant association with both overall and spinal pain relief. These findings underscore the importance of utilizing treatments effective across manifestations to address recalcitrant PsA symptoms.

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Table 1. Adjusted[1] Associations Between Improvements in Key PsA Manifestations and Pain Improvement Through W52

Pt Population	Predictor (Δ)	Δ PtP (β)[2]	Odds Ratio (OR)[3]			Δ Spinal Pain (β)[2,4]
			PtP-30	PtP-50	PtP-70	
All	**PASI**	0.41‡	1.05†	1.04†	1.04	0.03
(N=1120)	**SJC**	0.28†	1.03*	1.03	1.06	0.03
	TJC	0.55‡	1.05‡	1.08‡	1.12‡	0.06‡
BL Enthesitis	**LEI**	1.62‡	1.19‡	1.25‡	1.32‡	0.18†
(N=728)	**PASI**	0.47‡	1.06†	1.06†	1.06*	0.02
	SJC	0.28†	1.03*	1.03	1.03	0.03
	TJC	0.39‡	1.04‡	1.05‡	1.08‡	0.05‡
BL Dactylitis	**DSS**	-0.04	0.97*	1.01	1.07	0.01
(N=473)	**PASI**	0.31†	1.04*	1.05*	1.05	0.02
	SJC	0.19	1.03	1.03	1.02	0.05*
	TJC	0.60‡	1.05‡	1.06‡	1.11‡	0.05†

*p<0.05; †p<0.01; ‡p≤0.0001 [1]Adjusted for BL values, age, gender, BMI, SF-36 Mental Component Summary score, presence of TJC – SJC ≥7 (central pain sensitization proxy), FACIT-Fatigue score, and treatment group[2] β correspond to the incremental increase in pain improvement; [3]ORs correspond to the incremental increase in the odds of achieving pain endpoints, for every increase in improvement in key PsA manifestations or in the presence (vs absence) of axPsA. Higher β = greater impact on pain improvement[4]N=312

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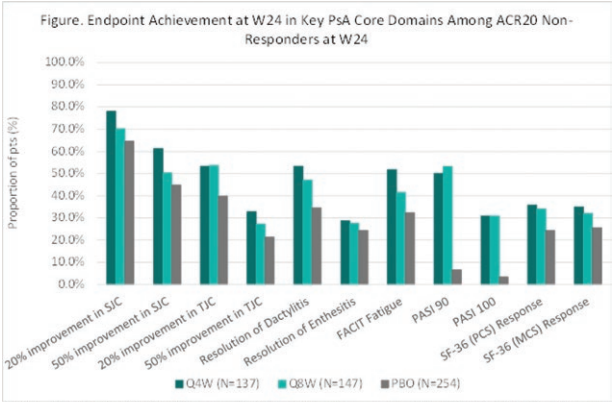
AB1096

IMPROVEMENT IN KEY PSORIATIC ARTHRITIS CORE DOMAINS WITH GUSELKUMAB TREATMENT IN AN ENRICHED POPULATION OF ACR20 NON-RESPONDERS AT WEEK 24: POST HOC ANALYSIS OF TWO PHASE 3 STUDIES

Keywords: Psoriatic arthritis, Quality of life

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Background: Despite available PsA treatments, a portion of PsA patients (pts) does not achieve improvements in PsA signs and symptoms according to the American College of Rheumatology (ACR) response criteria.
Objectives: Using data from the phase 3 DISCOVER-1 and DISCOVER-2 (D1/D2) studies in pts with active PsA, the purpose of this analysis was to describe the benefit of the IL-23p19 inhibitor, guselkumab (GUS), vs placebo (PBO) across key PsA domains, including those not comprising the core ACR measures, in pts not meeting ACR response criteria.
Methods: Pts enrolled in D1 and D2 were adults with active PsA despite standard therapies. D1 pts had ≥3 swollen and ≥3 tender joints (SJC; TJC), and C-reactive protein (CRP) ≥0.3 mg/dL; D2 pts had SJC ≥5, TJC ≥5, and CRP ≥0.6 mg/dL. In all, 31% of D1 pts received 1-2 prior tumor necrosis factor inhibitors (TNFi); D2 pts were biologic-naïve. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at Week (W)0, W4, then Q8W; or PBO; PBO pts crossed over to GUS 100 mg Q4W at W24. In this post hoc analysis, patients not meeting ≥20% improvement in ACR response criteria (ACR20) at W24 were included. Changes from baseline (BL) over 24 W in continuous outcomes of interest (SJC; TJC; enthesitis/dactylitis scores; psoriasis area and severity index [PASI] score; Functional Assessment of Chronic Illness Therapy [FACIT]-fatigue score; and 36-item Short Form survey [SF-36] physical [PCS] & mental [MCS] component summary scores) were assessed with repeated measures mixed models adjusting for treatment group, BL non-biologic disease-modifying antirheumatic drug (DMARD) use, and prior TNFi use. Descriptive statistics were produced for categorical outcomes at W24 (Figure 1) using non-responder imputation for missing data.
Results: Of the 1120 pooled D1/D2 pts, 538 did achieve an ACR20 response at W24, including 137 (36.7%) GUS Q4W, 147 (39.2%) GUS Q8W, and 254 (68.3%) PBO pts, and were included in this analysis. A consistently greater proportion of GUS- than PBO-treated pts achieved W24 categorical outcomes, including those relating to skin, tender joints, and dactylitis, with similar findings for GUS Q4W and Q8W (Figure 1). For continuous endpoints, the benefit of GUS was seen as early as W2 for SJC (W4 for Q8W), TJC, dactylitis (W4 for Q8W), and enthesitis (W4 for Q8W); W8 for FACIT-fatigue, SF-36 PCS, and SF-36 MCS (W16 for Q8W); and W16 for PASI; most endpoints continued to improve through W24. Across both GUS treatment groups, 43.5%-48.9% of W24 ACR20 non-responders achieved an ACR20 response by W52.
Conclusion: In this cohort of W24 ACR20 non-responders, GUS-treated pts experienced greater benefits than pts receiving PBO in improving both joint disease and other important PsA domains outside the ACR response criteria, which translated to significant improvements in health-related quality of life. These benefits occurred as early as W2 of GUS treatment, and showed continued improvement over 24 W, such that considerable proportions of W24 ACR non-responders achieved an ACR20 response by W52. Such improvements in key PsA domains over time among the minority of GUS W24 non-responders are consistent with the known immunomodulatory mechanism of GUS.



PASI90 and PASI100 refer to 90% and 100% improvement from BL, respectively, and were assessed in patients with IGA ≥2 and BSA ≥3% at BL. Resolution of dactylitis and enthesitis were assessed in patients with dactylitis and enthesitis at BL, respectively. FACIT-Fatigue Response refers to ≥4-point improvement from BL. SF-36 responses refer to ≥5-point improvement from BL. Number of evaluable ACR20 non-responders differed for Resolution of Dactylitis (Q4W: N=60; Q8W: N=66; PBO: N=107), Resolution of Enthesitis (Q4W: N=94; Q8W: N=91; and PBO: N=173), and PASI 90/100 (Q4W: N=94; Q8W: N=94; PBO: N=182). Mean (SD) SJC levels at BL were 12.7 (8.01), 11.1 (7.18) and 11.6 (7.28) and at W24 were 6.2 (6.76), 5.9 (7.02), 7.2 (7.39) for GUS Q4W, Q8W, and PBO, respectively.
ACR, American College of Rheumatology; BL, baseline; BSA, body surface area; FACIT, Functional Assessment of Chronic Illness Therapy; GUS, guselkumab; IGA, investigator's global assessment; MCS, mental component summary; PASI, psoriasis area and severity index; PBO, placebo; PCS, physical component summary; PsA, psoriatic arthritis; pts, patients; Q4W, every 4 weeks; Q8W, every 8 weeks; SD, standard deviation; SF-36, 36-item short form survey; SJC, swollen joint count; TJC, tender joint count; W, week

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AB1097

MALIGNANCIES WITH LONG-TERM USE OF IXEKIZUMAB IN ADULTS WITH PSORIASIS, PSORIATIC ARTHRITIS, OR AXIAL SPONDYLOARTHRITIS: A POST-HOC ANALYSIS OF DATA FROM 25 RANDOMIZED CLINICAL TRIALS

Keywords: Psoriatic arthritis, Spondyloarthritis

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Background: This integrated analysis examines long-term incidence rates (IRs) of malignancies in adults with psoriasis (PsO), psoriatic arthritis (PsA), or axial spondyloarthritis (axSpA) who received ≥1 dose of ixekizumab (IXE) up to 5 years (PsO) or 3 years (PsA, axSpA) in clinical trials.

OBJECTIVES:

Methods: IRs of malignancies were assessed across 25 randomized IXE clinical trials (17 PsO, 4 PsA, 4 axSpA). Malignancy rates were analyzed for pooled studies by years of therapy, through March 2022. Exposure-adjusted IRs per 100 patient-years (PY) are reported.

Results: 6892 patients with PsO, 1401 patients with PsA, and 932 patients with axSpA, with a cumulative IXE exposure of 18025.7 PY for PsO, 2247.7 PY for PsA, and 2097.7 PY for axSpA were included in this analysis. The IRs of malignancies at 1-year intervals up to 5 years for patients with PsO, and up to 3 years for patients with PsA and axSpA, remained low (≤1.2/100 PY) and constant. Malignancies occurred in 141/6892 patients with PsO (IR=0.8), 15/1410 patients with PsA (IR=0.7), and 9/932 patients with axSpA (IR=0.4). Of these cases, non-melanoma skin cancer (NMSC) was reported among 55 patients with PsO (IR=0.3) and 9 patients with PsA (IR=0.4). No incidences of NMSC were reported among patients with axSpA.

Conclusion: IRs of treatment-emergent malignancies were low and stable among adult patients with PsO, PsA or axSpA receiving IXE treatment in clinical trials over the time periods examined.

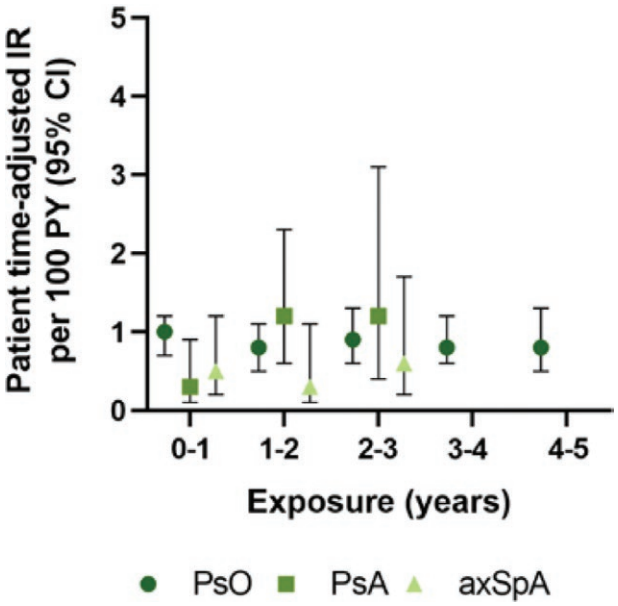


Figure 1. Exposure-adjusted incidence rates (IR) of malignancies across indications by yearly intervals. Data points on the graph are the IR (95% CI)/100 patient-years (PY) at successive year intervals from year 0-5 (PsO), 0-3 (PsA and axSpA). *CI = Confidence interval*.

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AB1098

DEUCRAVACITINIB IN PLAQUE PSORIASIS: 2-YEAR LABORATORY RESULTS FROM THE PHASE 3 POETYK PSO PROGRAM

Keywords: Safety, Targeted synthetic drugs, Clinical trials

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Background: Tyrosine kinase 2 (TYK2) is an intracellular enzyme involved in IL-23 signaling that is important in the pathogenesis of immune-mediated diseases, including psoriasis, psoriatic arthritis, and systemic lupus erythematosus (SLE). Deucravacitinib is a first-in-class, oral, selective, allosteric TYK2 inhibitor approved in multiple countries for the treatment of adults with plaque psoriasis. Deucravacitinib uniquely binds to the TYK2 regulatory domain rather than the more conserved catalytic domain at which Janus kinase (JAK) 1/2/3 inhibitors bind. Deucravacitinib was efficacious compared with placebo in phase 2 trials in psoriatic arthritis and SLE.[1,2] Furthermore, deucravacitinib was significantly more efficacious than placebo or apremilast and was well tolerated in patients with moderate to severe plaque psoriasis, as observed in the phase 3 POETYK PSO-1 and PSO-2 trials.[3,4] Patients who completed the psoriasis trials could enroll in the ongoing open-label, 240-week long-term extension (LTE) trial.

Objectives: This analysis examined whether changes occurred in blood laboratory parameters upon deucravacitinib treatment in the phase 3 POETYK PSO-1, PSO-2, and LTE trials and, if so, assessed how these compared with signature laboratory changes seen with JAK 1/2/3 inhibitors.

Methods: POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) were 52-week, double-blind trials that randomized patients with moderate to severe plaque psoriasis 2:1:1 to deucravacitinib 6 mg once daily, placebo, or apremilast 30 mg twice daily. Patients receiving placebo switched to deucravacitinib at Week 16, and patients receiving apremilast who failed to achieve ≥50% reduction from baseline in Psoriasis Area and Severity Index (PASI 50; PSO-1) or ≥75% reduction from baseline in PASI (PASI 75; PSO-2) at Week 24 switched to deucravacitinib. At Week 52, all eligible patients enrolled in the LTE trial (NCT04036435) and received open-label deucravacitinib 6 mg once daily. Changes from baseline in hematologic parameters (lymphocytes, neutrophils, platelets, hemoglobin) and lipid and chemistry parameters (cholesterol, creatinine, CPK, ALT) known to be impacted by JAK 1/2/3 inhibitors were assessed through Week 100 (LTE at Week 48). CTCAE grade ≥3 laboratory abnormalities and treatment discontinuations due to laboratory abnormalities were also evaluated.

Results: Patients (n=1519) received ≥1 dose of deucravacitinib in PSO-1, PSO-2, and/or the LTE through the cutoff date of 1 October 2021. In total, 1179 (77.6%) and 584 (38.4%) patients had ≥52 and ≥104 weeks, respectively, of continuous deucravacitinib exposure at the cutoff date, and the median duration of exposure was 682.0 days (97 weeks). No trends for clinically meaningful changes from baseline were observed in any laboratory parameters from Weeks 0–52 in PSO-1 or in the LTE. Grade 3 or 4 abnormalities over 100 weeks of deucravacitinib treatment were rare; incidence rates were comparable with placebo and apremilast through Week 52, and no increases were seen in the LTE. Two patients discontinued deucravacitinib treatment due to laboratory abnormalities (1 lymphopenia, 1 abnormal hepatic function).

Conclusion: No trends for clinically meaningful changes from baseline were observed with deucravacitinib treatment in hematologic, lipid, or chemistry parameters, including signature laboratory changes associated with JAK 1/2/3 inhibitors, for up to 100 weeks. Treatment discontinuations and grade 3 or 4 laboratory abnormalities were rare, consistent with those in the parent studies, and comparable to the incidence rates seen with placebo and apremilast. These results suggest that laboratory monitoring in patients with plaque psoriasis is not warranted with deucravacitinib treatment.

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AB1099

SUSTAINED EFFICACY OF BIMEKIZUMAB TREATMENT ASSESSED USING COMPOSITE DISEASE ACTIVITY MEASURES IN PATIENTS WITH PSORIATIC ARTHRITIS AND PRIOR INADEQUATE RESPONSE OR INTOLERANCE TO TUMOUR NECROSIS FACTOR INHIBITORS: RESULTS FROM THE PHASE 3 BE COMPLETE STUDY AND ITS OPEN LABEL EXTENSION UP TO 1 YEAR

Keywords: Clinical trials, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a disease characterised by heterogeneous joint and skin manifestations, so comprehensive treatment efficacy is best captured by assessment of a broad spectrum of affected domains using composite outcome measures.[1] Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated superior efficacy and tolerability to 16 weeks (wks) vs placebo (PBO) in patients (pts) with active PsA in the phase 3 BE OPTIMAL and BE COMPLETE studies.[2,3]

Objectives: To assess the long-term efficacy of BKZ treatment on disease activity using composite outcome measures in pts with active PsA and prior inadequate response or intolerance to tumour necrosis factor alpha inhibitors (TNFi-IR).

Methods: BE COMPLETE (NCT03896581) comprised a 16-wk double-blind, PBO-controlled period. Pts with PsA and TNFi-IR were randomised 2:1 to subcutaneous BKZ 160 mg every 4 wks or PBO. Pts who completed Wk 16 were eligible for entry into BE VITAL (NCT04009499), an open-label extension (OLE) study. Pts receiving PBO switched to BKZ at Wk 16 (PBO/BKZ). The BE VITAL OLE included pts from BE OPTIMAL and BE COMPLETE. Here, we report data up to 1 year for pts randomised at baseline (Wk 0) of BE COMPLETE (52 wks of study drug). Composite measure data up to Wk 52 are reported: minimal and very low disease activity (MDA/VLDA), the composite endpoint of ≥50% improvement in American College of Rheumatology criteria and 100% improvement in Psoriasis Area and Severity Index response (ACR50+PASI100) in pts with baseline psoriasis (≥3% body surface area [BSA]), Disease Activity Index for Psoriatic Arthritis (DAPSA), and Psoriatic Arthritis Disease Activity Score (PASDAS; collected up to Wk 40). Missing data were imputed using non-responder imputation (NRI) or worst-category imputation.

Results: 388/400 (97.0%) pts completed Wk 16 of BE COMPLETE; 377 (94.3%) entered BE VITAL and 347 (86.8%) completed Wk 52. At Wk 16, a higher proportion of BKZ-treated pts achieved composite disease activity thresholds vs PBO-treated pts. Across all composite outcome measures, efficacy was sustained to Wk 52 in pts randomised to BKZ treatment at Wk 0, and pts who switched to BKZ at Wk 16 demonstrated improvements in efficacy responses to Wk 52 (**Figure 1**, **Table 1**). At Wk 16, 6.0% PBO and 44.2% BKZ pts achieved MDA; at Wk 52, this proportion was sustained on BKZ treatment: 33.1% PBO/BKZ and 47.2% BKZ (NRI; **Figure 1**). Improved or sustained responses were also observed for the proportions of PBO/BKZ and BKZ pts achieving VLDA, ACR50+PASI100, DAPSA and PASDAS thresholds at Wk 52 (**Figure 1**; **Table 1**).

Conclusion: BKZ-treated pts with PsA and TNFi-IR demonstrated clinically meaningful improvements in composite measures of disease activity, comprising joint and skin domains, vs PBO at Wk 16. These improvements were sustained up to 1 year on BKZ. Pts who switched to BKZ at Wk 16 showed improvements in efficacy responses up to 1 year.

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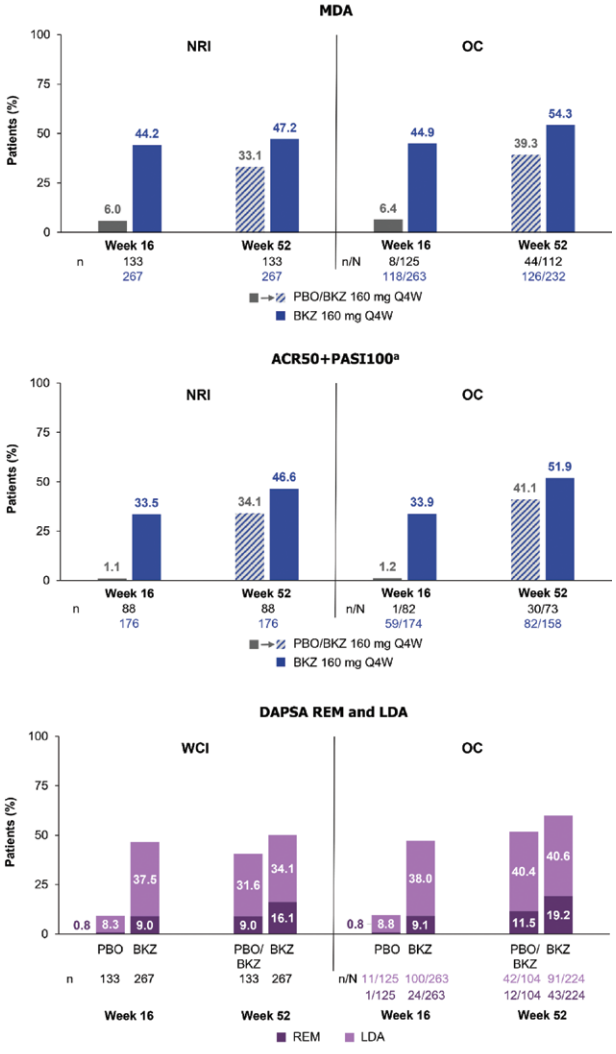
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Table 1. Pts achieving composite endpoints at Wk 16 and to Wk 52

	Wk 16		Wk 52	
n (%)	PBO N=133	BKZ 160 mg Q4W N=267	PBO/BKZ 160 mg Q4W N=133	BKZ 160 mg Q4W N=267
VLDA [NRI]	3 (2.3)	36 (13.5)	20 (15.0)	63 (23.6)
		Wk 16		Wk 40[a]
PASDAS REM+LDA [WCI]	14 (10.5)	126 (47.2)	53 (39.8)	146 (54.7)
PASDAS REM [WCI]	2 (1.5)	51 (19.1)	22 (16.5)	69 (25.8)

Randomised set. [a] Data not collected at Wk 52.

Figure. Pts achieving composite endpoints at Wk 16 and Wk 52



Randomised set. [a]In pts with psoriasis affecting ≥3% BSA at baseline.

Abbreviations: ACR50: ≥50% improvement in American College of Rheumatology criteria; BKZ: bimekizumab; BSA: body surface area; DAPSA: Disease Activity Index for Psoriatic Arthritis; LDA: low disease activity; MDA: minimal disease activity; NRI: non-responder imputation; OC: observed case; PASDAS: Psoriatic Arthritis Disease Activity Score; PASI100: 100% improvement in Psoriasis Area and Severity Index; PBO: placebo; Q4W: every four weeks; REM: remission; VLDA: very low disease activity; WCI: worst-category imputation; Wk: week.

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AB1100

ACHIEVEMENT OF INCREASINGLY STRINGENT CLINICAL DISEASE CONTROL CRITERIA WAS ASSOCIATED WITH GREATER IMPROVEMENTS IN PHYSICAL FUNCTION, PAIN AND FATIGUE IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: 52-WEEK RESULTS FROM BE OPTIMAL, A PHASE 3 RANDOMISED, PLACEBO-CONTROLLED STUDY

Keywords: Psoriatic arthritis, Clinical trials

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Background: The multiple joint and skin manifestations of psoriatic arthritis (PsA) place a substantial burden on patient quality of life.[1] Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A.

Objectives: To examine the association between achieving increasingly stringent clinical disease control criteria and patient-reported measures of physical function, pain and fatigue in patients (pts) with PsA, using Week (Wk) 52 data from BE OPTIMAL.

Methods: BE OPTIMAL (NCT03895203) comprised a 16-wk double-blind placebo (PBO)-controlled period and a 36-wk treatment blind period. Pts were ≥18 years, biologic disease-modifying antirheumatic drug naïve, with adult-onset, active PsA, ≥3 tender and ≥3 swollen joints. Pts were randomised 3:2:1, subcutaneous BKZ 160 mg every 4 weeks (Q4W):PBO:reference arm (adalimumab 40 mg Q2W). From Wk 16, PBO pts received BKZ 160mg Q4W. In this post hoc analysis, all pts who reached specified disease control criteria (**ACR**: ACR20 not reached [<ACR20], ACR20 reached but not ACR50 [ACR20–<ACR50], ACR50 reached but not ACR70 [ACR50–<ACR70], ACR70 reached [ACR70]; ACR50 and Psoriasis Area and Severity Index 100 [**ACR50+PASI100**]: non-responder, responder; Disease Activity in PsA [**DAPSA**]: high, moderate and low disease activity or remission [HDA, MoDA and LDA/REM, respectively]; Minimal Disease Activity [**MDA**]: non-MDA, MDA) at Wk 52 were pooled regardless of treatment arm. Associations between achieving these criteria and improvements in the following patient-reported physical function and symptom measures were assessed: Health Assessment Questionnaire Disability Index (**HAQ-DI**), Pt's Assessment of Arthritis Pain Visual Analog Scale (**Pain VAS**) and Functional Assessment of Chronic Illness Therapy-Fatigue subscale (**FACIT-Fatigue**). It should be noted that some aspects of the disease control criteria relate to aspects of HAQ-DI and PtAAP. Observed case data were reported.

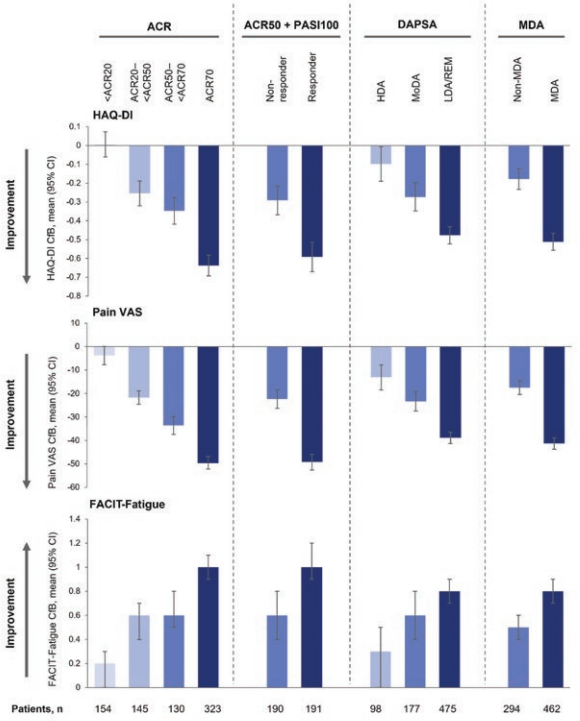
Results: 821/852 (96.4%) pts completed Wk 16; 761 (89.3%) completed Wk 52. Baseline mean (SD) HAQ-DI (0 [best] to 3 [worst]), Pain VAS (0 [best] to 100 [worst]) and FACIT-Fatigue (0 [worst] to 52 [best]) scores were 0.85 (0.59), 55.2 (23.9) and 37.0 (9.7). Pts achieving higher ACR response thresholds demonstrated sequentially greater mean (95% CI) improvements from baseline in HAQ-DI, Pain VAS and FACIT-Fatigue (**Figure 1**). Similar improvements from baseline in HAQ-DI, Pain VAS and FACIT-Fatigue were seen with the achievement of ACR50+PASI100, increasingly stringent DAPSA thresholds and the achievement of MDA (**Figure 1**).

Conclusion: Patients with active PsA who achieved increasingly stringent disease control criteria at Wk 52 reported concomitantly greater improvements in patient-reported measures of physical function, pain and fatigue.

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Figure. Association between ACR, ACR50 + PASI100[a], DAPSA[b] and MDA disease control states and improvements in HAQ-DI, Pain VAS and FACIT-Fatigue at Week 52



Randomised set. Data reported as observed case for both disease control states and patient-reported physical function and symptom measures. Categories are mutually exclusive. [a]PASI subgroups are defined on the subgroup of patients with baseline psoriasis affecting ≥3% body surface area; [b]HDA: >28; MoDA: >14 to ≤28; LDA/REM: ≤14.

Abbreviations: ACR: American College of Rheumatology; CfB: change from baseline; CI: confidence interval; DAPSA: Disease Activity in Psoriatic Arthritis; FACIT-Fatigue: Functional Assessment of Chronic Illness Therapy-Fatigue subscale; HAQ-DI: Health Assessment Questionnaire Disability Index; HDA: high disease activity; LDA: low disease activity; MDA: minimal disease activity; MoDA: moderate disease activity; Pain VAS: Patient's Assessment of Arthritis Pain Visual Analog Scale; PASI: Psoriasis Area and Severity Index.

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AB1101

THERAPEUTIC EFFECTS OF APREMILAST ON ENTHESITIS AND DACTYLITIS IN REAL CLINICAL SETTING: AN ITALIAN MULTICENTER STUDY

Keywords: Real-world evidence, Inflammatory arthritides, Psoriatic arthritis

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Background: To date only few real-world setting studies evaluated apremilast efficacy in psoriatic arthritis (PsA). Enthesitis and dactylitis are difficult-to-treat features of PsA leading to disability and affecting quality of life.

Objectives: The aims of this study is to evaluate the leed enthesitis index (LEI) and dactlitis index (DAI) at 6 and 12 month in patients on treatment with apremilast.

Methods: All PsA consecutive patients treated with apremilast in fifteen Italian rheumatological referral centers were enrolled. Anamnestic data, treatment history, and PsA disease activity (DAPSA), LEI, DAI at baseline (T0), 6 month (T1) and 12 months (T2) were recorded. The Mann-Whitney test and chi-squared tests assessed the differences between independent group, whereas the Wilcoxon matched pairs signed-rank test assessed the differences between dependent samples. A p-value<0.05 was considered statistically significant.

Results: the total cohort consisted of 209 patients (M/F 94/105) of whom 72 (34.4%) (M/F 29:43) patients had an enthesitis with a median LEI of 3 and 65 patients (31.1%) had dactylitis with a median of DAI of 1; DAPSA at base line was 24.1 in the enthesitis group, and 27.2 in the dactylitis group **(Table 1**). Prior DMARDs use and concomitant DMARDs drugs were more common in LEI groups with respect to DAI group. Compared to base line, Apremilast 30 mg two times per day demonstrated at 6 and 12 months a significantly improvements in LEI **(Figure 1a**; p<0.001 for both T1 vs T0, T2 vs T1), DAI (**Figure 1b;** p<0.001 for both T1 vs T0, T2 vs T1) and DAPSA (**Figure 1c**; p<0.001 for both T1 vs T0, T2 vs T1). In the LEI group, 29 patients (28.7%) reached a remission with LEI=0 at six months and 40 (44%) patients had a sustained improvement with LEI=0 at 12 months. In the DAI group 45 patients (52.9%) had a remission of dactylitis at 6 months and 43 patients (56.6%) had no dactylitis at T1.

Conclusion: Apremilast demonstrated significant and sustained efficacy in real-life Psa patients, including improvements in enthesitis and dactylitis for up to 12 months.

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Table 1.

Baseline Characteristic		Total Cohort	Dactylitis subgroup	Enthesitic subgroup
N		209	65	72
M:F		94:105	30:35	29:43
Age, median [IQR] yrs		60 [53-67]	59 [53-65]	59 [52-65]
Smokers, n (%)	Yes	36 (17,2)	13 (20,0)	11 (15,3)
	Former	27 (12,9)	10 (15,4)	14 (19,4)
	No	144 (68,9)	42 (64,6)	47 (65,3)
	Unknown	2 (1,0)	0	0
Body Mass Index, median [IQR] kg/m^2		26,5 [23,8-29,6] (*)	27,1 [23,7-29,9] (**)	26,1 [23,2-29,9] (***)
PsA Duration, median [IQR], months		50 [19-97]	42 [15-85]	51 [15-85]
PsO Duration, median [IQR], months		72 [28-140]	84 [21-141]	67 [17-142]
SJC, median [IQR]		3 [2-4]	3 [2-4]	3 [2-4]
TJC, median [IQR]		5 [3-8]	5 [3-7]	6 [4-12]
LEI, median [IQR],		-	-	3 [1-4]
Dactylitis, median [IQR], fingers		-	1 [1-2]	-
CRP, median [IQR], mg/dl		1,8 [0,7-4,8]	2,3 [1,0-5,0]	3,6 [0,9-6,7]
PGA Patient (0-10), median [IQR]		7 [6-8]	7 [6-8]	7 [5-8]
VAS pain (0-10), median [IQR]		7 [6-8]	7 [6-8]	7 [6-8]
DAPSA, median [IQR]		24,1 [19,4-31,5]	24,2 [19,5-31,2]	27,2 [22,9-35,6]
Concomitant csDMARDs use, n (%)		49 (23,4)	22 (33,8)	19 (26,3)
Prior bDMARDs use, n (%)		69 (33,1)	34 (52,3)	20 (27,8)
Concomitant relevant disease, n (%)		94 (44,8)	37 (56,9)	31 (43,1)

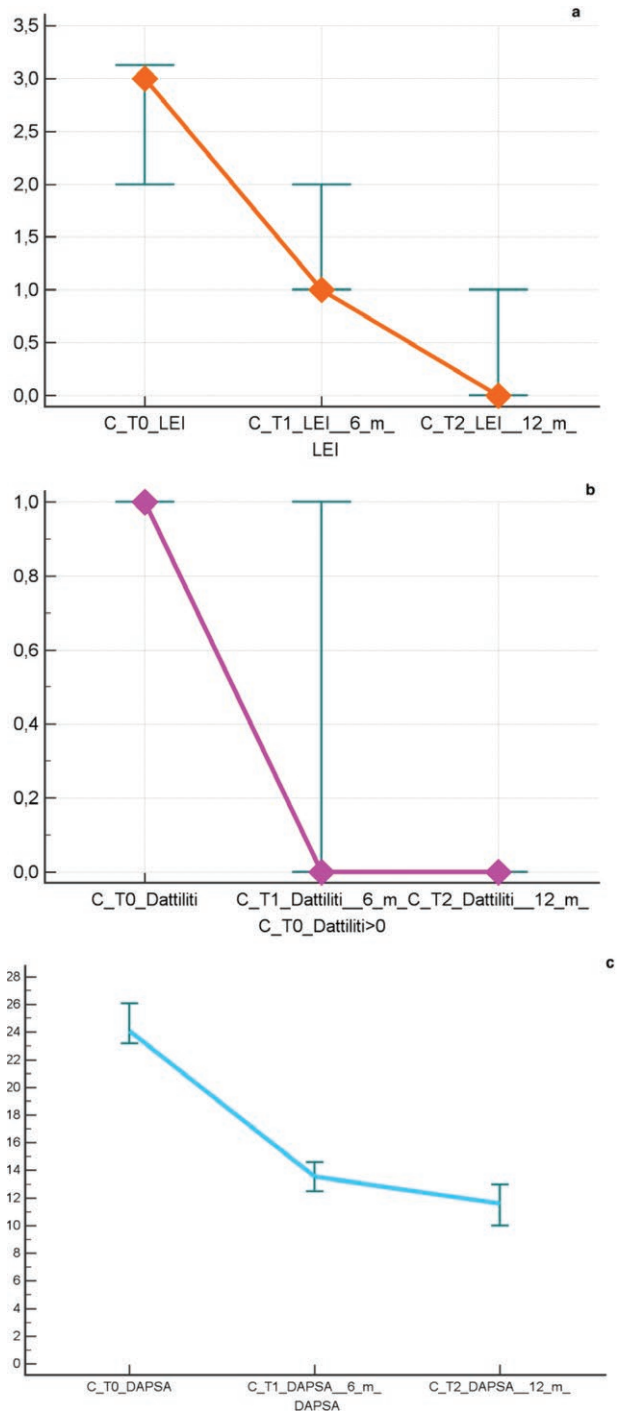


Figure 1.

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AB1103

UPADACITINIB REAL-LIFE EFFICACY AND SAFETY IN PSORIATIC ARTHRITIS: RESULTS AT 24 WEEKS OF A MULTICENTRIC ITALIAN STUDY (UP-REAL)

Keywords: Psoriatic arthritis, Targeted synthetic drugs, Real-world evidence

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Background: Psoriatic arthritis (PsA) is a chronic systemic inflammatory musculoskeletal disease whose heterogeneous manifestations are classified in multiple domains; moreover, PsA negatively influence many comorbid diseases.[1] As growing evidence suggests, it is important to research drugs active on multiple domains, trying to target therapy for every PsA manifestations. Upadacitinib (UPA) is a selective JAK inhibitor effective in many PsA domains according to randomized controlled trials.[2] However, real-world data on UPA performance in everyday clinical practice are currently lacking.

Objectives: This observational study aims to evaluate real-life efficacy and safety of UPA in the treatment of PsA in a large multicentre cohort. Secondary objectives are: **a.** to obtain the ideal patient profile for UPA therapy; **b.** to stratify clinimetric and laboratoristic responses according to patient manifestation and comorbidities.

Methods: Patients with either peripheral and/or axial PsA, classified according to CASPAR and ASAS criteria, who initiated UPA by clinical indication were enrolled at 10 Italian centers according to the following inclusion criteria: 1a. failure or intolerance towards at least one csDMARD for bio-naïve patients, or 1b. failure of at least one bDMARD for bio-failure patients; 2. active PsA disease, defined according to treat-to-target strategy by the absence of MDA (Minimal Disease Activity); 3. age > 18 years. Patients were assessed at baseline (T0) and at week 12 (T3) and 24 (T6), recording responses in the main clinimetric indices (i.e. TJC, SJC, LEI, DAPSA, ASDAS-CRP, MDA & VLDA) and a complete laboratory panel. Any type of adverse event was recorded at each visit. Data about assessment until week 56 (T12) for all patients will be presented in a future work.

Results: A total of 126 patients, 73 (69.5%) females and 32 (30.5%) males, started therapy with UPA: mean age 55.9±11.2 years, mean BMI 26.8±5.1, mean duration of disease 114.7±100.9 months. Most patients (n.124, 98.4%) show peripheral joint involvement: n.39 (31.4%) with oligoarticular and n.85 (68.6%) with polyarticular pattern. Axial involvement was found in n.56 (44.4%) patients. Most patients (n.89, 70.6%) had failed at least 1 bDMARD. At baseline, all patients show high disease activity (DAPSA 27.7±10.0; ASDAS-CRP 2.4±0.7). The following characteristics were notable: 1. cardio-metabolic diseases more represented in axial and polyarticular involvement; 2. baseline disease activity greater with polyarticular involvement, comorbidities, higher BMI and/or CRP; 3. patients with axial involvement showed a longer disease duration. Follow-up data are available for n.94 (74.6%) patients at T3 and n.66 (52.4%) patients at T6 evaluation, showing response in disease activity scores and patient-reported outcomes (Table 1, Figure 1). A subsequent multivariate logistic regression analysis shows that males (OR 2.53), bio-naïve (OR 4.12) and patients with high baseline CRP (OR 2.49) had the highest probability of MDA response at T6. A few patients (n.10, 7.9%) discontinued UPA during the study due to ineffectiveness (n.7) or adverse events (n.2 moderate thrombocytopenia; n.1 severe hypertension).

Conclusion: Preliminary data are confirming UPA effectiveness and safety in PsA real-life population. These findings will allow more targeted therapy based on patient profiling and disease domains.

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Table 1. Main disease activity scores at T0, T3, T6. Data are presented as mean±*DS*.

Parameters	T0	T3	p	T6	p
Patients (%)	126 (100.0)	94 (74.6)	/	66 (52.4)	/
DAPSA, mean ± SD	*27.7 ± 10.0*	*14.1 ± 9.6*	*<0.001*	*11.7 ± 10.7*	*<0.001*
ASDAS-CRP, mean ± SD	*2.40 ± 0.65*	*1.42 ± 0.74*	*<0.001*	*1.19 ± 0.74*	*<0.001*
LEI, mean ± SD	*0.91 ± 1.41*	*0.32 ± 0.77*	*<0.001*	*0.32 ± 0.77*	*0.003*
PASI, mean ± SD	*1.34 ± 4.17*	*0.44 ± 1.07*	*0.009*	*0.69 ± 3.15*	*0.03*
CRP (mg/dl), mean ± SD	*0.99 ± 1.8*	*0.40 ± 0.76*	*<0.001*	*0.35 ± 0.83*	*<0.001*
MDA nr. (%)	*0 (0.0)*	*29 (30.9)*	/	*31 (47.0)*	/
VLDA nr. (%)	*0 (0.0)*	*9 (9.6)*	/	*9 (13.6)*	/

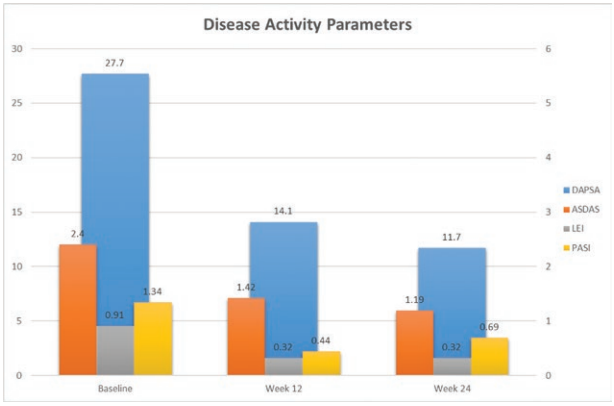


Figure 1. Disease activity scores trend

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AB1104

STRINGENT DISEASE ACTIVITY CONTROL AT 2 YEARS ACROSS PSORIATIC ARTHRITIS DOMAINS IRRESPECTIVE OF BASELINE CHARACTERISTICS IN PATIENTS TREATED WITH GUSELKUMAB: POST-HOC ANALYSIS OF A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

Keywords: Psoriatic arthritis

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Background: Guselkumab (GUS) is associated with robust and sustained improvement in psoriatic arthritis (PsA) signs and symptoms in subgroups of patients (pts) pooled from the phase 3 DISCOVER-1 and DISCOVER-2 trials, across a variety of baseline (BL) pt characteristics through 1[1], and 2 years (DISCOVER-2 only)[2].
Objectives: This post-hoc analysis using DISCOVER-2 data aimed to evaluate the efficacy of GUS in inducing long-term (Week [W]100) stringent disease control in Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA)-recommended domains across BL characteristics.
Methods: DISCOVER-2 enrolled biologic-naïve adults with active PsA defined as ≥5 swollen and ≥5 tender joint counts (SJC; TJC) and C-reactive protein (CRP) ≥0.6 mg/dL. 739 pts were randomized (1:1:1) and treated with GUS 100 mg every 4 weeks (Q4W; n=245); GUS 100 mg at Week 0, Week 4, then every 8 weeks (Q8W; n=248); or placebo (n=246) with crossover to GUS 100 mg Q4W at W24. In this analysis, only GUS-randomized pts were included (n=493). Achievement of the following outcomes at W100 was assessed: minimal disease activity (MDA), American College of Rheumatology 50% improvement (ACR50), ACR70, Investigator's Global Assessment score of 0 (clear skin) (IGA 0), Psoriatic Arthritis Disease Activity Score – low disease activity (PASDAS LDA), resolution of enthesitis and dactylitis, Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) response (≥4-point improvement), and Health Assessment Quality Disease Index (HAQ-DI) response (≥0.35-point improvement). BL characteristics of interest were pt sex, baseline body mass index (BMI), SJC, TJC, PsA duration, CRP, % body surface area (BSA) with psoriasis, and PASI score, and use of conventional synthetic (cs) DMARDs and methotrexate (MTX). Non-responder imputation was used for missing categorical response data.
Results: 442 (90%) GUS-randomized pts completed study treatment through W100. With few exceptions, achievement of MDA response (Figure 1) at Week 100 was demonstrated across a variety of baseline pt characteristics, without consistent differences in proportion of responders across pt subgroups of adequate sample size or between GUS dosing regimens. Similar trends were observed for achievement of ACR50, ACR70, IGA 0, PASDAS LDA, enthesitis resolution, dactylitis resolution, FACIT-F response, and HAQ-DI response.
Conclusion: Irrespective of dosing regimen, treatment with GUS resulted in sustained achievement of several stringent endpoints spanning key GRAPPA-recommended domains through 2 years across a variety of BL demographic and disease characteristics. These results further support the long-term efficacy of GUS across the full spectrum of PsA disease domains and diverse PsA populations.

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Figure 1. MDA Response at Week 100 by Treatment Group and BL Characteristics



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AB1105

LONG-TERM SAFETY OF IXEKIZUMAB TREATMENT IN ADULT PATIENTS WITH PSORIASIS, PSORIATIC ARTHRITIS, OR AXIAL SPONDYLOARTHRITIS: A POST-HOC ANALYSIS OF END-OF-STUDY PROGRAM DATA RELATING TO MAJOR ADVERSE CARDIOVASCULAR EVENTS

Keywords: Psoriatic arthritis, Spondyloarthritis

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Background:

Objectives: The objective of this study is to report long-term, end-of-study-program safety outcomes, relating to major adverse cardiovascular events (MACE), in adult patients with psoriasis (PsO), psoriatic arthritis (PsA), and axial spondyloarthritis (AxSpA) who received ≥1 dose of Ixekizumab (IXE) over 5 years (PsO) or 3 years (PsA, axSpA).

Methods: The incidence of MACE was assessed across 25 randomized clinical trials (17 PsO, 4 PsA, 4 axSpA) examining long-term safety of IXE. MACE rates were analyzed for pooled studies by years of therapy, through March 2022. Exposure-adjusted incidence rates (IRs) per 100 patient-years, at successive year intervals are reported.

Results: The incidence of MACE was low among patients with PsO (IR=0.5), PsA (IR=0.5), and axSpA (IR=0.3). In the PsO cohort, of the 103 reported MACE cases, 20 were fatal (19.4%), 57 recovered (55.3%), and 17 recovered with sequelae (16.5%). Of the 12 reported MACE cases in the PsA cohort, 2 were fatal (16.7%), 9 recovered (75.0%), and 1 recovered with sequelae (8.3%). All 6 MACE cases reported in the axSpA cohort recovered (100.0%). IRs were low and stable over the treatment periods. The most common types of MACE reported in the PsO, PsA and axSpA cohorts were non-fatal myocardial infarction (PsO: IR= 0.3; PsA: IR=0.3; axSpA: IR=0.3), nonfatal stroke (PsO: IR=0.1; PsA: IR=0.2) and vascular death (PsO: IR=0.1; PsA: IR=0.1). All MACE cases were confirmed by adjudication.

Conclusion: The incidence of MACE was low and stable over the IXE treatment periods examined.

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AB1106 EFFICACY OF RISANKIZUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS:A SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Psoriatic arthritis, Systematic review

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Background: Psoriatic arthritis (PsA) is a chronic autoimmune disease that is seen in nearly 30% of patients with psoriasis. As a new targeted treatment drug, risanzumab may provide a new treatment with fewer side effects for patients with psoriasis arthritis. However, there are currently discrepancies in the evaluation of the efficacy of Risankizumab in PsA patients.
Objectives: This study aims to systematically evaluate the efficacy of Risankizumabin patients with PsA.
Methods: We systematically searched PubMed, Embase, Web of Science, Cochrane Library, MEDLINE, Web of Knowledge, Clinical Trials. gov, FDA. gov and print databases (SSRN, bioRxiv, and MedRxiv) from the establishment of the database to January 2, 2023, and conducted data analysis in Stata 12.0. We used the I-squared (I2) to assess the heterogeneity of the included studies in order to select the appropriate model for statistical analysis. A random-effects model will be used when I2>50%, otherwise, a fixed-effect model will be applied. The publication bias was evaluated by using Egger test.
Results: We ultimately included 11 studies that included data on six outcome indexes. The results of the meta-analysis of ACR20 as our main outcome indicator of interest showed patients in the Risankizumab group had a significantly higher ACR20 response rate than those in the placebo group at 24 weeks [RR=1.768, 95%CI (1.572, 1.988), P<0.001]. In addition, compared with the placebo group, the MDA response rate of Risankizumab group significantly higher [RR=1.841, 95%CI 1.084-3.126, P<0.05]. Then, SF-36 score [SMD=0.508, 95%CI (0.337, 0.678), P<0.001] were improved in the Risankizumab group, which was statistically significantly different from the placebo group. For HAQ-DI, the Risankizumab group had significantly lower scores than the placebo group[SMD=-0.273, 95%CI (0.373, 0.172), P<0.001]. However, FACIT-F scores in the Risankizumab group were significantly higher than placebo group [SMD=0.270, 95%CI (0.177, 0.364), P<0.001]. For PASI, patients had an average reduction of 9.8 points after Risankizumab treatment [MD=-9.832, 95%CI (14.367, 5.298), P<0.001]. (Figure 1)
Conclusion: The overall results of the meta-analysis show that Risankizumab treatment can significantly improve the symptoms of PsA such as arthritis and skin symptoms, improve the clinical remission rate and the quality of life of patients. However, taking Risankizumab may also potentially increase fatigue levels in patients.

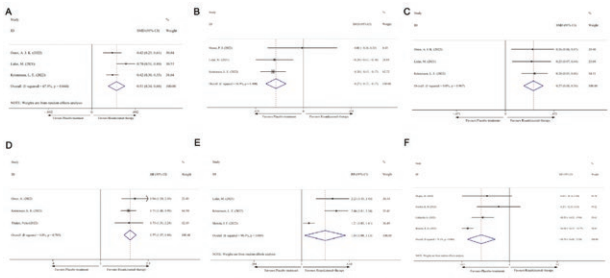


Figure 1: (A-E) Forest plot of comparison Risankizumab versus placebo-efficacy in patients with psoriatic arthritis using multiple outcome measures;A, Short Form 36 Questionnaire (SF-36) ; B, Health assessment questionnaire&Disability Index (HAQ-DI); C, Functional assessment of chronic illness therapy -fatigue (FACIT-F) ; D, American College of Rheumatology-20 (ACR20) ; E, Minimal Disease Activity (MDA); (F) Forest plot to evaluate the efficacy of Risankizumab in patients with psoriatic arthritis using PASI; PASI, Psoriasis Area and Severity Index.

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AB1107 PSORIATIC ARTHRITIS: IMPROVEMENT IN OUTCOMES BUT PERSISTENT SEX DIFFERENCE - 5 YEAR FOLLOW UP STUDY OF A NORWEGIAN OUTPATIENT CLINIC POPULATION

Keywords: Remission, Real-world evidence, Psoriatic arthritis

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Background: Improvement of pharmacological therapies and treatment approaches in psoriatic arthritis (PsA) have led to substantial progress in disease outcomes [1]. Despite this progress there is still a need for improvement in PsA treatment [2].
Objectives: To explore long-term (5 years) changes in disease activity, remission rates and sex-related differences in these outcomes in PsA patients treated in ordinary outpatient clinic.
Methods: Prospective longitudinal cohort study. DAS28, DAPSA, SDAI, CDAI, MDA and Boolean remission criteria for PsA were assessed. Parametric statistics for comparisons of patient characteristics and dependent t test for differences between observation times were used.
Results: 114 PsA patients (49.1% women), baseline mean±SD age was 51.4 ±9.4 years, disease duration 9.2±6.8 years, 24.8% were HLAB27(+), 32.7% currently used NSAIDs, 61.4% csDMARDs, 37.7% b/tsDMARDs. At 5-year follow-up numerical improvement was noted for multiple disease activity measures and PROs (Table 1). Statistically significant increase in remission rates was

Table 1. PROs and disease activity measures, mean±SD

	Baseline				5 years				
	All n=114	Women n=56	Men n=58	p-value[1]	All n=114	Women n=56	Men n=58	p-value[2]	p-value[3]
Pain, 0-100mm	32.0±22.0	36.3±22.4	27.8±21.0	0.04	30.1±23.0	34.6±25.0	25.6±20.1	0.04	0.42
PGA, 0-100mm	34.7±23.7	40.0±24.5	29.5±21.8	0.02	31.3±21.6	34.7±22.8	28.0±20.1	0.10	0.12
Fatigue, 0-100mm	44.5±31.6	53.5±31.6	35.7±29.2	<0.01	40.9±30.5	48.2±30.1	33.5±29.3	0.01	0.16
TJC 68	9.5 ±10.4	12.1±10.8	6.9±9.4	0.01	6.4±7.1	8.0±7.8	4.8±6.0	0.02	<0.01
SJC 66	0.6 ±1.0	0.6±0.9	0.5±1.1	0.84	0.3±0.8	0.2±0.6	0.4±0.9	0.20	0.03
CRP, mg/L	4.3±6.7	2.8±3.4	5.6±8.6	0.03	5.1±12.2	3.9±7.9	6.3±15.2	0.29	0.41
ESR, mm/h	14.9±11.1	17.7±12.0	12.2±9.5	0.01	10.9±12.9	13.8±12.8	8.3±12.6	0.02	0.02
DAPSA	17.1±12.9	20.6±13.4	13.8±11.6	<0.01	13.3±9.6	15.3±10.1	11.2±8.8	0.03	0.01
SDAI	8.9 ±6.7	10.7±7.4	7.2±5.4	0.01	6.3±4.7	7.2±5.1	5.5±4.0	0.04	<0.01
CDAI	8.5±6.5	10.4±7.3	6.7±5.1	<0.01	5.8±4.4	6.9±5.0	4.8±3.5	0.01	<0.01
DAS28 CRP	3.1 ±1.1	3.0±1.0	2.5±0.9	0.01	2.4±1.1	2.6±0.9	2.2±0.8	0.01	<0.01
DAS28 ESR	2.8±1.0	3.5±1.0	2.6±1.0	<0.01	2.4±0.8	2.9±1.0	2.0±±0.9	<0.01	<0.01
mHAQ, 0-3	0.40±0.35	0.47±0.36	0.34±0.33	0.05	0.38±0.38	0.45±0.42	0.31±0.32	0.04	0.72

[1]women vs men, baseline [2]women vs men, follow-up [3]baseline vs follow-up, all patients

observed for DAS28 and CDAI but not for MDA, SDAI, DAPSA, and Boolean remission for PsA (Figure 1).

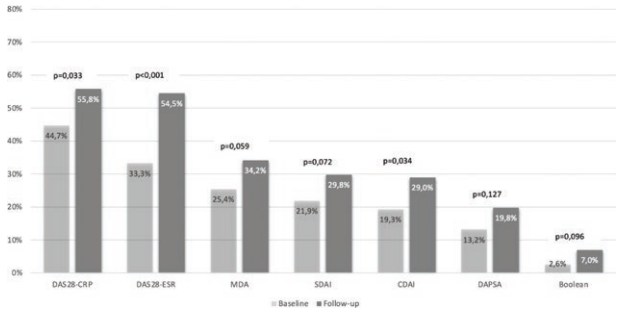


Figure 1. Proportions of PsA patients in remission (total cohort).

During follow-up number of b/tsDMARD users significantly increased (from 37.7% to 48.3% p=0.01), while number of NSAIDs and csDMARDs users significantly decreased (from 32.7% to 21.9% p=0.02, and from 61.4% to 46.5% p<0.01, respectively). Both at baseline and follow-up women reported higher levels of pain, PGA and fatigue, and had higher TJC68, DAPSA, SDAI, CDAI, DAS28 and mHAQ compared to men. Even though mean CRP was higher in men both at baseline and follow-up, men more often achieved remission, regardless which remission definition was applied. A higher proportion of men were treated with b/tsDMARDs (46.6% vs 28.6% at baseline, 60.3% vs 35.7% at follow-up).

Conclusion: Our study adds evidence that improvement in PsA outcome between 2013 and 2020 was achieved, most probably due to more intensified treatment with b/tsDMARDs. Women had higher PROs and disease activity indexes both at baseline and follow-up and were less likely to achieve remission. Despite obtained progress, the number of PsA patients in remission remains unsatisfactory. This may indicate further need to improve both therapeutic approaches and methods of assessing PsA activity and remission.

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AB1108

EFFECT OF GUSELKUMAB ADMINISTERED EVERY 8 WEEKS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS PERSISTS BETWEEN CONSECUTIVE DOSES AND IS DURABLE: POST HOC ANALYSIS OF A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

Keywords: Clinical trials, Psoriatic arthritis, Outcome measures

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Background: The efficacy of guselkumab (GUS), a fully human IL-23p19 subunit inhibitor, in patients (pts) with active psoriatic arthritis (PsA) has been previously shown across a variety of PsA domains and baseline (BL) pt characteristics[1-3]. Given the central role of the IL-23/Th17 pathway in PsA, it has been hypothesized that IL-23 inhibition with GUS may provide persistent and durable clinical responses between doses and over time when administered every 8 weeks (Q8W).

Objectives: To assess at the pt level the persistence of effect of GUS Q8W between doses and its durability of effect over time.

Methods: DISCOVER-2 was a phase 3, randomized, double-blind, placebo (PBO)-controlled study that enrolled pts with active PsA despite standard therapies. Pts were biologic-naïve, had tender and swollen joint counts (TJC/SJC) each ≥5, and C-reactive protein (CRP) ≥0.6 mg/dL. Pts were randomized 1:1:1 to GUS 100 mg Q4W; GUS 100 mg at W0, W4, then Q8W; or PBO with crossover to GUS 100 mg Q4W at W24. In the current analysis, only pts treated with GUS Q8W (N=248) were included. Persistence of effect between consecutive dosing visits was described with the proportion of pts maintaining response (as defined below) in outcomes assessed during dosing visits (Disease Activity index for PsA [DAPSA], clinical DAPSA [cDAPSA]). Durability of effect was assessed with the Kaplan Meier estimator of the survival function where each pt contributed follow-up from the first time of achievement of clinical response within the 24-week period and the time of loss of response or last available assessment through W100. Definitions of clinical response included achievement of clear/almost clear skin (investigator's global assessment [IGA] 0/1; among pts with BL IGA>1) or minimal clinically important improvements (MCII) in DAPSA (≥7.25), cDAPSA (≥5.7), skin visual analog scale (VAS; ≥15 mm), and PsA Disease Activity Score (PASDAS; ≥0.8).

Results: Between consecutive (Q8W) dosing visits through W52, the proportion of pts maintaining response ranged from 93.3% (DAPSA MCII between W4 and W12) to 99.1% (DAPSA/cDAPSA MCII between W28 and W36), depending on the time interval. Among pts showing clinical response within the first 24 weeks, the estimated mean (SE) duration of maintenance was 58.6 (2.2) weeks for DAPSA MCII, 52.4 (2.0) weeks for cDAPSA MCII, 75.7 (1.6) weeks for. IGA 0/1, 71.7 (1.9) weeks for skin VAS MCII, and 76.7 (1.4) weeks for PASDAS MCII (Figure 1). As estimated probabilities of maintenance of effect at W100 were between 65% (IGA 0/1) and 90% (PASDAS MCII) for all outcomes assessed, median duration of effect could not be calculated.

Conclusion: Treatment with GUS Q8W was associated with long-lasting effects in both joint- and skin-related outcomes, as well as in multi-domain composite outcomes, in individuals with PsA. These results highlight that, in addition to continuous improvement in clinical response rates over time, GUS Q8W provides consistent and highly durable responses between consecutive doses.

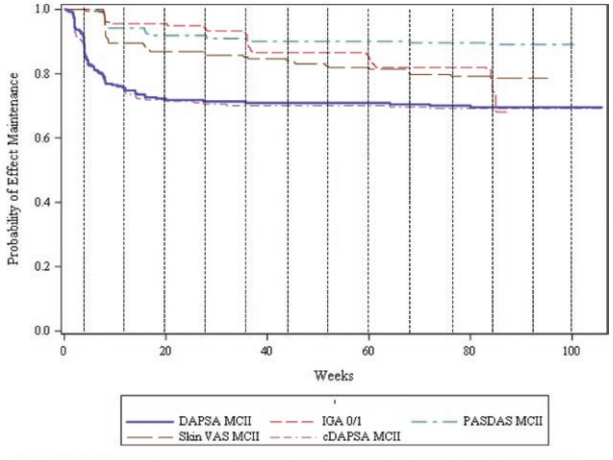
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Figure. Maintenance of Response Through W100 During Treatment with GUS Q8W



Note: Data shown represent time from first endpoint achievement to first loss of endpoint achievement. Vertical lines indicate dosing.

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AB1109

TREATMENT RETENTION AND SAFETY OF IXEKIZUMAB IN A POPULATION WITH PSORIATIC ARTHRITIS REFRACTORY TO BIOLOGIC AND TARGETED SYNTHETIC DMARDS

Keywords: Psoriatic arthritis

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Background: Information on the performance of ixekizumab (IXE) in patients with psoriatic arthritis (PsA) in clinical practice is scarce.
Objectives: We aimed to analyze the retention rate and safety of IXE in patients with PsA in routine clinical practice. The present study has analyzed drug survival and safety of IXE in patients with PsA under real clinical practice conditions. This information may complement that obtained from the RCTs done to date with this drug.
Methods: Retrospective longitudinal observational single-center study of all patients with PsA who had received at least one dose of IXE. Adverse events (AEs) and drug retention rate were considered the main variables. Survival was analyzed using Kaplan-Meier curves and predictive factors using multivariate Cox regression analysis. The Hazard Ratio (HR) was used as a measure of the association.
Results: Seventy-two patients were included (52 women and 20 men). Median disease duration was 5 years (IQR 3-9). More than 90% have received ≥ 2 biologic and/or targeted synthetic disease modifying anti-rheumatic drugs (DMARDs) prior to IXE. Ixekizumab showed a 1-year retention rate of 65% and a 2-year retention rate of 57% (Figure 1). Regarding discontinuation due to AEs, 0.18 AEs per person-year were identified. The number of previous biologics did not influence drug survival but prior use of methotrexate [HR 2.31 (95%CI 1.05-5.10), p < 0.05] and depression [HR 2.40 (95%CI 1.07-5.41), p < 0.05] increased the risk of IXE discontinuation (Table 1).
Conclusion: Ixekizumab demonstrated high drug persistence in a population of PsA mostly refractory to various lines of systemic therapy. In addition, the aspects that usually penalize the survival of most biologics in PsA (age, duration of disease, female gender, smoking, obesity, prior exposure to other biologics) did not affect drug persistence in this study.

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Table 1. Disease characteristics of the study population.

Characteristic	Psoriatic arthritis n = 72
Age (yrs), mean (SD)	50 (12)
Female, n (%)	52 (72.2)
Disease duration (yrs), median (IQR)	5 (3-9)
Anti-TNFα prior to IXE, n (%)	60 (83.3)
csDMARDs prior to IXE, n (%)	42 (58.3)
tsDMARDs prior to IXE, n (%)	24 (33.3)
Other biologics prior to IXE, n (%)	8 (11.1)
Weight, median (IQR)	77 (65-85)
Obesity (BMI>30), n (%)	20 (27.8)
Smoker, n (%)	31 (43.1)
Hypertension, n (%)	21 (29.2)
Dyslipidemia, n (%)	25 (34.7)
Diabetes, n (%)	10 (13.9)
COPD, n (%)	2 (2.7)
Cardiovascular disease*	2 (2.7)
Ischemic heart disease	4 (5.5)
Depression	39 (54.2)
Chronic kidney disease	2 (2.7)
Chronic liver disease	1 (1.4)
DAPSA, mean (SD)	9.8 (6.8)
PsAID, mean (SD)	2.7 (2.2)

SD: standard deviation, yrs: years, IQR: intercuartile range, TNF: tumor necrosis factor, IXE: ixekizumab, BMI: body mass index, csDMARDS: conventional-synthetic disease modifying anti-rheumatic drugs (methotrexate, leflunomide, sulphasalazine), tsDMARDS: targeted-synthetic disease modifying anti-rheumatic drugs (apremilast, tofacinitib), COPD: chronic obstructive pulmonary disease, DAPSA: disease activity index for psoriatic arthritis, PsAID: psoriatic arthritis impact of disease.* Myocardial infarction and/or cerebrovascular event.

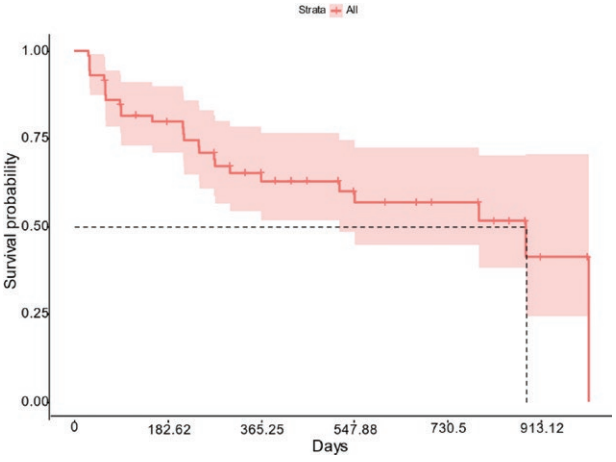


Figure 1. Median survival of Ixekizumab

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Disclosure of Interests: None Declared.
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AB1110 EXPLORING LEVELS OF PROTEIN BIOMARKERS IN RESPONSE TO TREATMENT FOR PSORIASIS AND PSORIATIC ARTHRITIS

Keywords: Disease-modifying drugs (DMARDs), Biomarkers, Psoriatic arthritis

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Background: Psoriatic Arthritis (PsA), an inflammatory arthritis, occurs in 30% of psoriasis patients[1]. Serum chemokine (C-X-C motif) ligand 10 (CXCL10) is elevated in psoriasis patients that will develop PsA[2]. MMP3 is associated with response to Tissue-necrosis factor inhibitor (TNFi) treatment[3]. S100A8, CCL2, and ACP5 are associated with PsA development[4,5,6]. We aimed to compare CXCL10, MMP3, S100A8, ACP5, and CCL2 levels in PsA patients before and after treatment with biologics and in cutaneous psoriasis without arthritis (PsC) patients on and off treatment with biologics.
Objectives: The objective of this study was to evaluate the levels of CXCL10, MMP3, S100A8, CCL2, and ACP5 in serum of psoriasis and PsA patients before and after treatment with biologic agents (TNFi and IL-17i).
Methods: PsA and PsC patients are followed prospectively at the Toronto Western Hospital psoriatic disease clinic. We identified 93 PsA patients on TNFi and 22 on IL-17 inhibitors (IL-17i) and retrieved serum samples before and after therapy. Samples from 30 patients with PsC treated with biologics were matched to 30 patients not treated with biologics were also retrieved from the databank. Using the Luminex Discovery assay we measured CXCL10, MMP3, S-100A8, CCL2, and ACP5 levels. Statistical analysis was performed using Wilcoxon Signed-rank test.
Results: CXCL10 (*P=0.0007*), MMP3 (*P<0.0001*), S100A8 (*P<0.0001*), ACP5 (*P<0.0001*), and CCL2 (*P=0.01*) significantly decreased after TNFi treatment in PsA patients. CXCL10 (*P=0.*04) and ACP5 (*P=0.02*) significantly increased after IL-17i treatment in PsA patients. There were no significant differences between treated and untreated PsC patients.
Conclusion: CXCL10, MMP3, S100A8, ACP5, and CCL2 are potential biomarkers for response to TNFi in PsA patients. CXCL10 and ACP5 are potential biomarkers for response to IL-17i treatment in PsA patients.
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AB1111 SUSTAINED RESPONSE TO GUSELKUMAB REGARDLESS OF BASELINE DEMOGRAPHIC, DISEASE, AND MEDICATION CHARACTERISTICS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND AN INADEQUATE RESPONSE TO TNF INHIBITORS: RESULTS FROM A PHASE 3B TRIAL

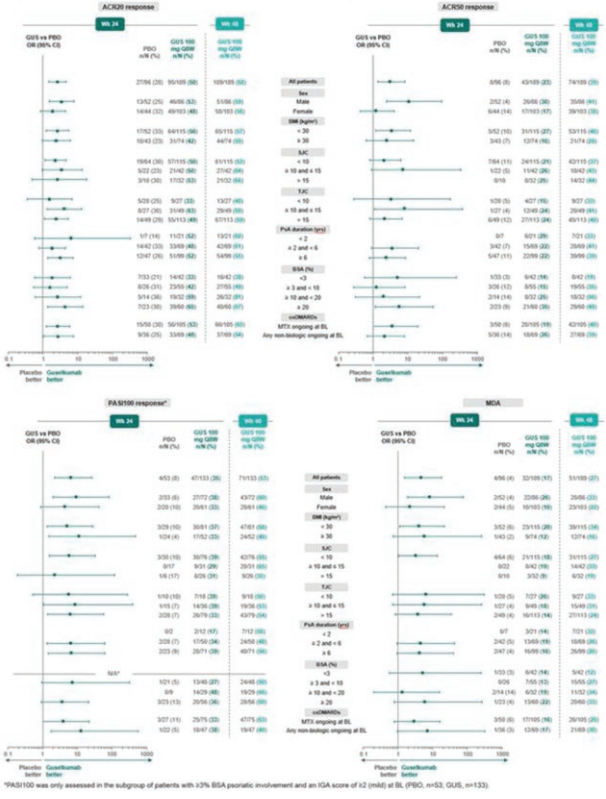
Keywords: Psoriatic arthritis

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Background: Guselkumab (GUS) is a human monoclonal antibody targeting the IL-23 p19 subunit. In the Phase 3b COSMOS trial (NCT03796858), GUS significantly improved disease signs/symptoms vs placebo (PBO) in patients (pts) with psoriatic arthritis (PsA) and an inadequate response (IR) to TNF inhibitor (TNFi) therapy. The primary endpoint of American College of Rheumatology 20% improvement (ACR20) response at Week (W)24 was achieved, with the benefit of GUS vs PBO consistent across subgroups.[1]
Objectives: In this post-hoc analysis, we evaluated if response to GUS across disease domains was maintained through 1 year across various subgroups of these TNFi-IR PsA pts.
Methods: In COSMOS, adults with active PsA (swollen joint count [SJC] ≥ 3 and tender joint count [TJC] ≥ 3) with a lack of efficacy/intolerance to 1–2 TNFi therapies were randomized (2:1) to GUS 100 mg or PBO. Pts in the GUS group were treated at W0, W4, then every 8 weeks (Q8W) to W44; those in the PBO group were treated at W0, W4, W12, and W20, with planned crossover to GUS 100 mg at W24 followed by GUS at W28, W36, and W44. Pts with < 5% improvement from baseline (BL) in SJC and TJC qualified for W16 early escape (EE); EE pts receiving GUS continued treatment, while pts receiving PBO crossed over to GUS. In this analysis, efficacy of GUS in subgroups was evaluated at W24 and W48 via joint (ACR20/50 response), skin (Psoriasis Area and Severity Index [PASI]100 response), and multi-domain (minimal disease activity [MDA] response) outcome measures. Subgroups were defined by selected demographics, disease characteristics, and ongoing medications at BL: sex, body mass index (BMI), SJC, TJC, PsA duration, % psoriatic body surface area (BSA), and conventional synthetic disease-modifying antirheumatic drug (csDMARD) use. Odds ratios (ORs) and 95% confidence intervals (CIs) based on Fisher's exact test for GUS vs PBO are shown overall and for each subgroup at W24. No treatment comparison was performed after W24. Pts who discontinued and/or correctly met EE criteria before W24 were imputed as nonresponders. Missing data were also imputed with no response through W48.
Results: Overall, 285 pts were randomized to GUS (n = 189) or PBO (n = 96). BL characteristics were generally similar between treatment groups, although numeric differences were observed for the proportion of females, joint symptoms, and skin involvement in GUS vs PBO pts. At W16, 39 (21%) pts in the GUS group and 45 (47%) pts in the PBO group were assigned to EE. In this analysis, joint, skin, and multi-domain response rates at W24 were numerically greater in GUS vs PBO pts, with the benefit of GUS consistent across all subgroups of adequate sample size (Figure 1). Response rates with GUS were maintained, or in most cases numerically increased, from W24 to W48, regardless of BL subgroup.
Conclusion: GUS 100 mg Q8W led to consistent improvements vs PBO in joint, skin, and multi-domain outcomes at W24 across subgroups of TNFi-IR PsA pts defined by selected demographics, disease characteristics, and ongoing medications at BL. Response to GUS was maintained or further improved through 1 year of treatment regardless of BL subgroup.
REFERENCE:

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Figure. ACR20, ACR50, PASI100, and MDA response at W24 and W48 per BL characteristics



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AB1112

DESCRIPTION OF THE REAL-WORLD TREATMENT PATTERNS OF GUSELKUMAB IN THE MANAGEMENT OF PSORIATIC ARTHRITIS IN AUSTRALIA: AN ANALYSIS FROM THE OPAL DATASET

Keywords: Real-world evidence, Psoriatic arthritis, bDMARD

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Background: Guselkumab (GUS) is a novel anti-interleukin 23 (IL-23) p19 antibody that acts as a selective and specific inhibitor of the IL-23 cytokine. GUS has been shown to significantly improve signs and symptoms of active psoriatic arthritis (PsA) and became available for the treatment of PsA in Australia in July 2021. Limited data from large real-world patient populations exist to describe the utilisation of GUS for the management of PsA.

Objectives: To describe the patient demographics and treatment patterns of GUS in a large real-world cohort of Australian adult patients with PsA.

Methods: The OPAL dataset is a collection of deidentified clinical data derived from the electronic medical records of 112 rheumatologists at 43 sites around Australia. Adult patients with a diagnosis of PsA who received at least one prescription of GUS or a biologic or targeted synthetic disease modifying anti-rheumatic drug (b/tsDMARD) between Jul 2021 and Jul 2022, were eligible for inclusion in the analysis. Results were summarised descriptively.

Results: A total of 1,868 patients with PsA, (GUS n=355, TNFi n=795, IL-17Ai n=371 and JAKi n=347) were eligible for inclusion in this study. The median [IQR] age of patients was 55 [44-63] years, and 70.1% were female. At baseline, median disease duration was 5[2-8], 2[1-6], 3[1-7] and 5[3-8] years, for patients treated with GUS, TNFi, IL-17Ai and JAKi, respectively. 17.7% of patients receiving GUS were first line compared with 58.7% of TNFi, 39.4% of IL-17Ai and 19.3% of JAKi treated patients (Table 1). At index, the majority of patients were treated as monotherapy.

Conclusion: These are the first data describing the demographics and treatment patterns of real-world Australian patients with PsA treated with GUS. In this preliminary analysis, a higher proportion of GUS and JAKi were used in later lines of therapy, and patients who initiated GUS or JAKi had a longer median disease duration. This may be due to the different time periods of availability of the different b/tsDMARD, as both GUS and JAKi are newer treatment options for PsA compared with TNFi and IL17Ai. Persistence among patients with PsA treated with GUS is currently being investigated.

Table 1. Demographic features of patients with psoriatic arthritis treated with GUS, TNFi, IL-17Ai or JAKi as any line of therapy.

Feature	Initiators of GUS (n=355)	Initiators of TNFi (n=795)	Initiators of IL-17Ai (n=371)	Initiators of JAKi (n=347)
Gender, Female (n, %)	250 (71.3%)	538 (69.2%)	240 (67%)	251 (73%)
Age at Index, years (median [IQR])	55 [45-63]	51 [41-61]	54 [45.5-64]	55 [48-64]
Duration of disease recorded in Audit4 at Index, years (median [IQR])	5 [2-8]	2 [1-6]	3 [1-7]	5 [3-8]
Line of therapy (n, %)				
Line 1	63 (17.7%)	467 (58.7%)	146 (39.4%)	67 (19.3%)
Line 2	57 (16.1%)	152 (19.1%)	99 (26.7%)	81 (23.3%)
Line 3+	235 (66.2%)	176 (22.1%)	126 (34%)	199 (57.3%)

GUS; guselkumab.

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Disclosure of Interests: Geoff Littlejohn: None declared, Nithila Anbumurali: None declared, Paul Bird Speakers bureau: GSK, AbbVie, Janssen, Eli-Lilly, Consultant of: AbbVie, Janssen, Pfizer, Eli-Lilly, GSK, BMS, Peter Youssef: None declared, Catherine OSullivan: None declared, Tegan Smith: None declared, Daniel Sumpton: None declared, Barry Kane: None declared, Andrew McGeachie Employee of: Current employee of Janssen Australia, Stefanie Spiers Employee of: Current employee of Janssen Australia, Claire Deakin: None declared.

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AB1113

REAL-WORLD USAGE OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN PATIENTS WITH PSORIATIC ARTHRITIS IN SWEDEN

Keywords: Disease-modifying drugs (DMARDs), Psoriatic arthritis, Real-world evidence

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Background: Given the growing number of treatment options for psoriatic arthritis (PsA) over the last decades, including a variety of biologic disease-modifying anti-rheumatic drugs (bDMARDs), selecting optimal treatment regimens is critical. Beyond clinical guidelines, understanding how physicians choose between available treatment options based on patient characteristics in real-world settings is of interest to both patients and health care providers.

Objectives: To reveal the patient characteristics (ie. demographics, comorbidities – including concomitant psoriasis [PSO], PsA+PSO and history of bDMARD exposure) in relation to bDMARD type and dosing in patients with PsA, treated in real-world clinical practice.

Methods: This retrospective observational cohort study utilised data from Swedish national administrative health care registers. Adult patients with an existing PsA diagnosis and a new bDMARD pharmacy dispensation between 2017–2021 were identified. Index date was that of the first observed dispensation qualifying as a new bDMARD, ie, without prior exposure to the index biologic. Prior bDMARD exposure and patient characteristics (including comorbidities) were screened for from 2005 and 2001, respectively. For patients initiating secukinumab (SEC), prescribed dosing was reported separately for patients with and without PSO manifestations given the variability in prescribing recommendations.

Results: This study identified 8,658 PsA patients initiating a new bDMARD during the study period, among which 2,706 (31.3%) were already bDMARD-experienced. Patients had a mean age of 52.3 years (SD=13.7), and 45.1% were male. The most frequently prescribed bDMARDs were adalimumab (45.3%), etanercept (31.8%), and SEC (11.3%). As expected, due to their recent market authorisations in PsA, the least frequently prescribed bDMARDs were guselkumab (0.8%) and risankizumab (0.4%). The most frequently observed prescriber speciality was rheumatologist (46.1%). The highest proportion of bDMARD-experienced patients was observed amongst interleukin-17 inhibitors initiators (82.4%), while 19.7% of tumour necrosis factor inhibitor initiators were bDMARD-experienced. Overall, 62.8% of patients had PsA+PSO. Other frequent non-inflammatory comorbidities included hypertension (22.0%), malignancies (12.6%), and depression (11.7%). The proportion of patients with anxiety and depression was higher among those initiating risankizumab compared to those initiating other bDMARDs. Other comorbidities were comparable between groups.

Amongst 981 SEC initiators, 679 (69.2%) had PsA+PSO. Maintenance dose data were available/could be analysed for 901 patients. Most PsA-only patients-initiated SEC at a dose of 150 mg (53.7%), and most PsA+PSO at 300 mg (65.0%). This was similar for maintenance period with 51.8% percent of PsA-only and 62.4% of PsA+PSO patients receiving a maintenance dose of 150 mg and 300 mg, respectively. A similar pattern was observed within bDMARD-naïve and bDMARD-experienced patients regardless of PSO manifestations.

Conclusion: This study provides information on the profiles of PsA patients treated with different bDMARDs and suggest that factors such as PSO manifestations and biologic-experience play important roles in the choice of bDMARD and dosing regimen. Future studies are warranted to identify patient outcomes associated with treatment patterns, including discontinuation and switches over time, which can assist in tailoring therapies to patient needs.

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AB1114 MUSCULOSKELETAL ULTRASOUND BASELINE ASSESSMENT IMPROVES THE RESPONSE TO APREMILAST IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM A MULTICENTER STUDY

Keywords: Ultrasound, Psoriatic arthritis, Imaging

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Background: Psoriatic arthritis (PsA) is an inflammatory rheumatic disease characterized by different phenotypes in terms of joint involvement. Apremilast, PDE4 competitive inhibitor, has been introduced in the treatment of adult psoriatic arthritis (PsA) with moderate disease activity. Musculoskeletal ultrasound (MUS) is useful in the assessment of disease, treatment response and follow up in PsA patients. Choosing an effective and safe treatment over time is an increasingly urgent goal given the greater availability of indicated drugs.

Objectives: The aim of this study is to evaluate if MUS assessment before apremilast treatment can improvement its retention rate.

Methods: We enrolled consecutive patients affected by PsA (according to the CASPAR Criteria) from 15 rheumatology centers. The following data were recorded for each patient: age, gender, duration of disease, DAPSA; smoke, comorbilities; concomitant treatment; duration of therapy with apremilast; reason of sospensione, PsA phenotype (poliarticular or oligoarticular) (Table 1). All patients were divided in two subset according to the presence of a MUS assessment before apremilast treatment. The differentes between two groups were calculated by means of the Mann-Whitney and Chi-quadro tests. The Kaplan Meier curve and Cox analysis assessed the retention rate and associated factors. P values < 0.05 were considered statistically significant.

Results: ON Three hundred and fifty patients (m/f: 198/152; median age 60 years, IQR 52-67 years), 40% received MUS examination. In the MUS group there was a moderate disease (medium 22,9 IQR 18,2-29 vs 26,9 IQR 20,3-33,9; p=0,0006) and a prevalence of the oligoarticular pattern (73% vs 44%, p<0,0001). The retention rate was statistically higher in MUS group (Figure 1) (HR 0,57 IC95% 0,35-0,95; p=0,03).

Table 1.

	No US	Yes US	P-value
Number	216	140	-
Age (years)	61 [54-69]	58 [50-65]	0,0016
Gender (M:F)	85:131	67:73	Nss
Smoke (%)	23,4	34,8	0,0198
BMI (kg/m^2)	25,7 [23,4-29,8]	26,1 [23,7-29,0]	nss
Duration of disese PsA (months)	44 [13-95]	37 [12-78]	nss
Duration of disese PsO (months)	13 [0-83]	30 [0-93}	nss
Comorbility (%)	47,7	39,3	nss
Swollen joints	8 [4-12]	4 [3-7]	<0,000001
Tender joints	3 [2-5]	2,5 [2-4]	0,0434
PCR (mg/dl)	2,9 [0,8-5,2]	1,0 [0,7-3,0]	0,0057
DAPSA	27,0 [20,4-34,2]	22,9 [18,2-29,0]	0,0004
Concomitant treatment (%)	13,4	27,1	0,0012
Naive biologic (%)	80,6	68,6	0,0100
Oligoarticolar pattern (%)	36,1	63,6	<0,0001

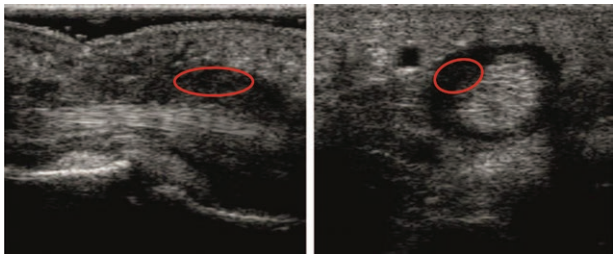


Figure 1. A: Psoriatic arthritis. Longitudinal volar scan of the interphalageal prossimal joint. Tenosinovitis of the flexor tendons ^{0}B: Psoriatic arthritis. Transversal volar scan of the interphalageal prossimal joint. Tenosinovitis of the flexor tendons ()

Conclusion: In PSA patients treated with apremilast, MUS assessment at baseline was associated with an higher retetion rate. MUS could be useful in the PsA treatment algorithm in order to better identify those patients whose characteristics are favourable to apremilast response.

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AB1115 STUDY DESIGN AND FULL BASELINE SAMPLE CHARACTERISTICS OF PATIENTS FROM THE 24-MONTH MULTINATIONAL PROSPECTIVE PSORIATIC ARTHRITIS OBSERVATIONAL STUDY OF PERSISTENCE OF TREATMENT (PRO-SPIRIT)

Keywords: Psoriatic arthritis

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Background: Ixekizumab (IXE), an Interleukin (IL)-17A inhibitor (i), approved for the treatment (tx) of Psoriasis (Pso), psoriatic arthritis (PsA) and axSpA (rad/non rad) have limited real-world data. PRO-SPIRIT is the first large, prospective observational study for IXE in patients (pts) with PsA who start a new biologic/targeted synthetic disease modifying anti-rheumatic drug (b/tsDMARD), with a primary endpoint of persistence at 24 months (M).
Objectives: To describe baseline (BL) characteristics of pts enrolled in PRO-SPIRIT.
Methods: PRO-SPIRIT enrolled pts December 2019-June 2022 in FR, ES, IT, DE, UK, and CA, who started a new b/tsDMARD, approved for PsA. Tx groups are; IXE, secukinumab (SEC), IL-12/-23i, IL-23i, tumor necrosis factor inhibitor (TNFi), Janus kinase inhibitors (JAKi), and Phosphodiesterase-4 inhibitor (PDE4i). Pts' demographic, disease activity, and tx characteristics were recorded at BL, effectiveness outcomes and tx changes at 3, 6,12,18, and 24M. BL descriptive statistics are shown.
Results: The analysis included 1207 pts (2 pts with other tx not shown below). Most were female, had mean age 52.4yrs, poly/oligo-arthritis and enthesitis/dactylitis in similar proportions except for enthesitis in IL12/23i and IL-23i pts.
Pts started on IXE had long disease duration (9.2yrs). Most had prior b/tsDMARDs (69.5%) and 38.7% had active PsO similar to SEC pts. For TNFi pts, mean disease duration was 6.5yrs, 30.8% had received prior b/tsDMARDs, and 30.4% had active PsO. IL-23i pts (n=57) were typified by long disease duration (8.7yrs), high proportions of PsO (50.9%)/nail PsO (50.9%) and prior b/tsDMARD use (78.9%). JAKi pts had long (9.2yrs) disease duration, 72.2% prior b/tsDMARDs experience, and 26.2% had active PsO. IXE and IL23i pts were more often treated on monotherapy.
Conclusion: In PRO-SPIRIT, pts starting IXE showed active PsA, with both joint and often skin involvement, and were mostly treated with monotherapy after failing several b/tsDMARDs. TNFis were often used as 1st line therapy alongside csDMARDs.
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Disclosure of Interests: Jacques Morel Speakers bureau: Biogen, Amgen, Bristol Myers Squib, Eli Lilly and Company, Novartis, Sanofi, MSD, Mylan, Fresenius Kabi, Roche, Union Chimique Belge, Janssen, Medac, and Nordic Pharma, Consultant of: Pfizer, AbbVie, Boerhinger Ingelheim, Galapagos, and GSK, Grant/research support from: Fresenius Kabi, Ennio Lubrano Speakers bureau: Abbvie, Janssen Cilag, Lilly, UCB, Pfizer, and Novartis, William Tillett Speakers bureau: AbbVie, Amgen, Eli Lilly and Company, GSK, Janssen, Novartis, Pfizer, and UCB., Consultant of: Abbvie, Amgen, Eli Lilly and Company, GSK, Janssen, Novartis, Ono Pharma, Pfizer, and UCB., Grant/research support from: Janssen, UCB, Pfizer, and Eli Lilly and Company., Rieke Alten Speakers bureau: AbbVie, BMS, Celltrion, Galapagos, Eli Lilly and Company, Novartis, Pfizer, Roche, and UCB, Consultant of: AbbVie, BMS, Celltrion, Galapagos, Eli Lilly and Company, Novartis, Pfizer, Roche, and UCB, Lars Erik Kristensen Speakers bureau: Pfizer, AbbVie, Amgen, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly and Company, and Janssen, Consultant of: Pfizer, AbbVie, Amgen, UCB, Gilead, Biogen, BMS, MSD, Novartis, Eli Lilly and Company, and Janssen, Grant/research support from: Pfizer, AbbVie, UCB, Gilead, Biogen, Novartis, Eli Lilly and Company, and Janssen, Vinod Chandran Consultant of: AbbVie, Eli Lilly, Novartis, Amgen, and Janssen, Grant/research support from: AbbVie, Tamas Treuer Shareholder of: Minor shareholder, Employee of: Eli Lilly and Company, Joanna Burke Employee of: Joanna Burke is contracted to Eli Lilly and Company, À Martínez-Ferrer Grant/research support from: Eli Lilly and Company, Thorsten Holzkaemper Shareholder of: Minor shareholder Eli Lilly and Company, Employee of: Eli Lilly and Company, Nicola Gullick Speakers bureau: AbbVie, Eli Lilly and Company, Janssen, Novartis, UCB, Consultant of: AbbVie, Janssen, Novartis, UCB, Grant/research support from: Astra Zeneca, AbbVie, Eli Lilly and Company, Izana, Novartis.
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AB1116

APREMILAST IN PSORIATIC ARTHRITIS. ULTRASOUND ANALYSIS (JOINT-ENTHESES-UNGUEAL INDEX) OF THE EFFICACY AND VARIABLES CORRELATION STUDY

Keywords: Psoriatic arthritis, Biomarkers, Ultrasound

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Background: We conducted a study using ultrasonography (US) to evidence inflammatory changes (joint-enthesis-ungueal) in active PsA (aPsA) patients who started Apremilast (A) in clinical practice.
Objectives: Obtain a 20, 50, 70 % reduction in the US index (UIC) at 12 months, and study correlation between variables.
Methods: *Phase IV, multicenter, prospective and open-label clinical trial* conducted *in 9 centres* from 2018 to 2021. All patients signed the informed consent. Approval by the ethical committee was obtained, code PSA-PI-006421. PsA patients (≥ 2 swollen joints), ≥ 2 joint US synovitis and ≥ 1 US enthesitis at screening were recruited. 52 weeks follow up (baseline, 1, 6, 9 & 12 months). US & clinic variables, and ESR & CRP were registered at each visit. US scans were scored according to Ficjan et al [1]. Ungueal nail plate (NP) and subungueal thickness (ST) US evaluation of 2nd, 3rd and 5th finger was done.
Results: 48 patients screened and 46 included (2 screening failure) in follow up. 26 completed the study. A 20 % (main objective) reduction in UIC was obtained, until 40%, but not 50/70%. Clinical and US variables were reduced, ESR and CRP did not change during follow-up (Table 1). Strong correlation was observed between UIC and SJC, moderate between UIC and TJC, PGA, PtGA, CRP. A reduction in clinical onychopathy, NP lesion, and slight relation between lesion, and high ST and ST with onychopathy was seen but didn't achieve statistical significance (reduced sample size). 75 adverse events in 33 patients

Table 1. Baseline Characteristics

			bDMARDs				tsDMARDs
	Ixekizumab	**Secukinumab**	**IL-12/23i**	**IL-23i**	**TNFi**	**JAKi**	**PDE4i**
	N=344	*N=169*	*N=36*	*N=57*	*N=441*	*N=126*	*N=32*
Age	53.9±12.1	52.4±12.0	51.2±12.1	53.0±11.5	51.0±12.4	52.9±12.3	54.8±9.2
Female, n(%)	224(65.1)	106(62.7)	19(52.8)	34(59.6)	265(60.1)	82(65.1)	20(62.5)
Yrs since PsA diagnosis	9.2±8.5	8.4±8.4	8.0±8.8	8.7±8.0	6.5±7.2	9.2±8.2	8.8±7.7
Prior b/tsDMARD, n(%)	239(69.5)	112(66.3)	26(72.2)	45(78.9)	136(30.8)	91(72.2)	6(18.8)
Tx as monotherapy, n(%)	218(63.4)	102(60.4)	28(77.8)	40(70.2)	198(44.9)	67(53.2)	24(75.0)
Tender Joint Count (0-68)*	8(0-60)	8(0-65)	6.5(0-32)	6.5(0-52)	7(0-65)	8(0-66)	4(0-47)
Swollen Joint Count (0-66)*	3(0-35)	2(0-39)	2(0-24)	2(0-21)	3(0-31)	4(0-53)	2(0-17)
Enthesitis, n(%)	142(41.3)	66 (39.1)	9(25.0)	33(57.9)	179(40.6)	55(43.7)	12(37.5)
Dactylitis, n(%)	67(19.5)	38 (22.5)	6(16.7)	13(22.8)	85(19.3)	26(20.6)	5(15.6)
BSA ≥3 n(%)	133(38.7)	62(36.7)	15(41.7)	29(50.9)	134(30.4)	33(26.2)	13(40.6)
Nail PsO, n(%)	131(38.1)	64(37.9)	10(27.8)	29(50.9)	160(36.3)	43(34.1)	15(46.9)
Physician Global assessment VAS	61.7±18.2	61.7±19.3	59.0±20.5	56.1±20.7	61.2±18.7	61.1±19.5	53.8±18.0
Patient Global Assessment VAS	60.7±21.2	61.0±22.3	55.3±25.1	63.9±22.7	57.7±23.2	61.4±22.2	53.2±23.5
Patient Assessment of (Joint) Pain VAS	62.9±21.5	63.2±22.6	53.5±27.4	62.8±22.1	59.7±23.6	62.8±24.0	55.5±25.1

Mean±SD, *Median(Range),unless stated*b=biologic; BSA=body surface area; cs=conventional synthetic; DMARD=Disease Modifying Arthritis Rheumatic Drug; i=inhibitor; IL=interleukin; JAK=janus kinase; N=number of patients; PDE4=phosphodiesterase 4; PsO=psoriasis; TNF=tumor necrosis factor; ts=targeted synthetic; VAS = Visual Analog Scale*

were registered, only 1 severe. Reasons for withdrawal were: 6 patients AE, 8 no efficacy, and 6 other reasons (loss of follow-up, withdrawal of consent).
Conclusion: Apremilast is a safe, well tolerated, and useful treatment in different patterns of PsA (joint, enthesis) demonstrated by an ultrasonography score. Ultrasound can identify nail disease in PsA patients.
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Table 1. Variables changes in aPsA patients treated with Apremilast

variable	0	1 m	6 m	9 m	12 m	p
PGA	45	45	31	27	26	**<0.001**
	5.6 (1.2)	4.1 (2)	2.4 (1.9)	2.4 (1.9)	2.6 (1.9)	
	CI[5.2; 6]	[3.5; 4.7]	[1.8; 3.1]	[1.7; 3.2]	[1.8; 3.4]	
PtGA	45	45	31	26	26	**<0.001**
	6.2 (1.9)	5.1 (2.5)	3.4 (1.9)	3.1 (2.4)	3.8 (2.1)	
	[5.6; 6.8]	[4.4; 5.9]	[2.7; 4.1]	[2.1; 4]	[3; 4.7]	
LEI	45	45	31	27	26	**0.01**
	1.4 (1.6)	1 (1.3)	0.9 (1.2)	0.5 (1.1)	0.8 (1.2)	
	[0.9; 1.9]]	[0.7; 1.4]]	[0.5; 1.4]	[0.1; 0.9]	[0.3; 1.3]	
NAD	45	45	31	27	26	**0.009**
	5.8 (5.8)	4.4 (4.8)	2.9 (4)	2.4 (3.6)	3 (4)	
	[4.1; 7.6]	[3; 5.8]	[1.4; 4.4]	[1; 3.8]	[1.4; 4.6]	
NAT	45	45	31	27	26	**0.001**
	3.2 (2.4)	2.1 (2.2)	0.9 (1.8)	1.1 (1.9)	1 (1.4)	
	[2.5; 3.9]	[1.4; 2.7]	[0.3; 1.6]	[0.4; 1.9]	[0.5; 1.6]	
CRP	43	42	29	27	26	**n.s**
	1.7 (3.7)	0.9 (1.9)	0.9 (1.4)	0.9 (1.3)	1 (1.7)	
	[0.6; 2.9]	[0.3; 1.5]	[0.4; 1.5]	[0.3; 1.4]	[0.3; 1.7]	
US joint	45	45	31	27	26	**0.006**
	17.6 (11)	12.4 (8.5)	9.2 (7.2)	7.9 (8.1)	7.5 (6.7)	
	[14.3; 20.9]	[9.8; 15]	[6.5; 11.8]	[4.7; 11.1]	[4.9; 10.2]	
US entheses	45	45	31	27	26	**<0.001**
	6 (3.9)	3.9 (3.1)	3.7 (2.8)	3.3 (3)	3.2 (2.5)	
	[4.9; 7.2]	[3; 4.9]	[2.7; 4.7]	[2.1; 4.5]	[2.2; 4.2]	
US total (UIC)	45	45	31	27	26	**<0.001**
	23.6 (12.6)	16.3 (9.8)	12.8 (8)	11.1 (9.5)	10.7 (7.6)	
	[19.9; 27.4]	[13.4; 19.3]	[9.9; 15.8]	[7.4; 14.9]	[7.7; 13.8]	
ESR	41	42	30	27	25	**n.s**
	18.3 (16.8)	16.7 (12.4)	17.6 (15.8)	12.7 (10.3)	15.7 (12)	
	[13; 23.6]	[12.8; 20.6]	[11.7; 23.5]	[8.6; 16.7]	[10.7; 20.6]	

PGA, physician global assessment; PtGA, patient global assessment; LEI, Leeds enthesitis index; SJC, swollen joint count; TJC, tender joint count, CRP, c reactive protein; ESR; erythrosedimentation rate

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AB1117 **DRUG SWITCHING IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH TUMOR NECROSIS FACTOR INHIBITOR.**

Keywords: bDMARD, Psoriatic arthritis, Epidemiology

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis, characterized by different clinical manifestations and associated comorbidities that requires targeted treatment. Therapy with Tumor necrosis factor inhibitor (TNFi) represents one of first therapeutic choices. However, PsA patients can experience TNFi failure, lack of efficacy, or adverse events. Although rheumatologists are now able to choose between several drugs, there is a lack of standard patient profiles or detailed treatment algorithms that can be followed when patients need to switch their therapy regimens.
Objectives: To evaluate the switching treatments regardless the cause in patients with PsA treated with TNFi as first biologic agent.
Methods: Retrospective longitudinal observational study. Subjects: Cohort of patients attended in the outpatient rheumatology clinic from January 2006 to December 2021, and followed up to June 2022, diagnosed with PsA according to ICD-10 code and on treatment with TNFi. Main outcome: Therapy regimens switching. Covariables: sociodemographic and clinics. Statistical analysis: Descriptive analysis of the switching therapy, global and stratified by treatment courses.
Results: 125 patients with a diagnosis of PsA and on treatment with TNFi were included, 52% were female, the mean age was 47.87 ± 13.29 years. 94 (75.20%) patients had a history psoriasis at baseline and 95 patients (76%) presented peripheral arthritis and 21 (16.80%) referred inflammatory low back pain as a main clinical domain, 50% of the patients presented at least three PsA domains. 232 courses of treatment were recorded throughout follow-up. As a whole, TNFi was the most used drug with 184 (79.31%) courses, adalimumab 78 (42.39), flowed by interleukin-17 inhibitors (IL-17i) with 30 (12.93%) courses of treatment. 82 (65.60%) patients were on concomitant treatment with conventional DMARDs. From the 125 patients, 49 recorded a switching to a second therapy regimen (32 switched to a second TNFi and 17 to another class of drugs, mainly IL-17i). Then, 28 presented a third change (16 to a different TNFi and 12 switched to another class of drugs) and finally 14 patients had a fourth switching (8 patients received a drug other than TNFi). TNFi switching data expressed in course of treatment is shown in Table 1. Switching after TNFi exposure was mainly due to lack of efficacy with 90 (84.11%) courses of treatment, followed by adverse events with 11 (10.28%).
Conclusion: In our study, although most of the TNFi switching was to a different TNFi, we observed a number of PsA patients receiving another class of drugs after TNFi exposure, and this action increased over the consequent treatment cycles.

Table 1. Courses of switching treatment in PsA patients treated with TNFi.

	Total Courses of treatment N (%)	Frist cycle Courses of treatment N (%)	Second cycle Courses of treatment N (%)	Third cycle Courses of treatment N (%)
Abatacept	2 (0.86)	0	0	0
Interleukin-17 inhibitors	30 (12.93)	0	3(5.26)	27(54)
Ustekinumab	4 (1.73)	0	0	4 (1.73)
Guselkumab	4 (1.73)	0	0	4 (1.73)
JAK inhibitors	8 (3.45)	0	0	8 (3.45)
Tumor necrosis factor inhibitors	184 (79.31)	125 (67.93)	54 (29.35)	5 (2.72)
Total	232 (100)	125 (53.88)	57 (24.57)	50 (21.55)

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AB1118 **EFFECT OF APREMILAST ON PSORIATIC DISEASE DOMAINS STRATIFIED BY EXTENT OF SKIN INVOLVEMENT IN PATIENTS WITH PSORIATIC ARTHRITIS**

Keywords: Skin, Psoriatic arthritis

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Background: It has been suggested that greater skin involvement in patients with psoriatic arthritis (PsA) may be associated with greater joint disease activity.
Objectives: To assess the impact of APR on PsA disease domains in patients with BSA <3% vs BSA ≥3% at 52 weeks using pooled data from 2 phase 3 trials.
Methods: PALACE 1 & 2 were randomized, placebo (PBO)-controlled, phase 3 studies in patients with active PsA. Eligible patients had ≥3 swollen and ≥3 tender joints despite prior treatment with a conventional systemic Disease Modifying Antirheumatic Drug (csDMARD) and/or biologic DMARD (bDMARD) or concurrent treatment with csDMARD. Patients were randomized to receive APR or PBO for up to 24 weeks, after which all patients received APR until Week 52. This ad-hoc analysis includes pooled data from patients randomized to APR 30 mg BID at Week 0 in these studies. Assessments included change from baseline at Week 52 in Clinical Disease Activity Index for Psoriatic Arthritis (cDAPSA), swollen joint count (SJC), tender joint count (TJC), patient assessment of pain visual analog scale (VAS), and Patient Global Assessment of Disease Activity (PtGA) VAS stratified by baseline psoriasis body surface area (BSA) involvement (<3% vs ≥3%).
Results: Of 330 patients randomized to APR 30 mg BID at Week 0, 171 had BSA <3% and 159 had BSA ≥3%. Of those with available data, 98.2% of patients with BSA <3% and 100% of patients with BSA ≥3% had a history of psoriasis; mean BSA at baseline was 1.2 in the <3% group and 14.3 in the ≥3% group. More patients with BSA ≥3% at baseline were men with higher rates of nail and SJC involvement, and slightly higher rates of oligoarthritis and TJC (**Table 1**). At Week 52, both subgroups showed mean decreases (improvement) from baseline in clinical parameters with APR treatment, including cDAPSA (BSA <3%: -18.0, BSA ≥3%: -23.3), SJC (BSA

<3%: -6.1, BSA ≥3%: -8.7), TJC (BSA <3%: -10.1, BSA ≥3%: -13.0), Patient Assessment of Pain (BSA <3%: -15.5, BSA ≥3%: -18.0), and PtGA (BSA <3%: -11.8, BSA ≥3%: -16.8) (**Table 1**). There were numerically greater decreases in these parameters among patients with baseline BSA ≥3% than those with BSA <3%. Improvements in enthesitis and dactylitis were also observed in both subgroups.

Conclusion: Patients with PsA in PALACE 1 & 2 with higher BSA had higher disease activity in some disease domains at baseline. Both BSA subgroups showed improvement with APR at Week 52 regardless of disease severity, although numerically greater improvements were seen in patients with BSA ≥3%. To our knowledge, this is a novel analysis assessing treatment efficacy in patients with PsA by level of skin involvement.

Table. Baseline Demographics, Disease Characteristics, and Change From Baseline in Efficacy Parameters to Week 52 by BSA Subgroups

Baseline Parameter	BSA <3% (n=171)	BSA ≥3% (n=159)
Age, mean (SD), y	52.4 (11.9)	49.4 (10.8)
Female, n (%)	114 (66.7)	73 (45.9)
BMI, mean (SD), kg/m²	30.3 (6.1)	29.5 (6.0)
Duration of PsA, mean (SD), y	7.3 (7.4)	7.7 (8.3)
Oligoarthritis, n (%)	41 (24.0)	46 (28.9)
History of nail psoriasis, n/m (%)	104/169 (61.5)	123/159 (77.4)
BSA, mean (SD), %	1.2 (0.7)	14.3 (18.8)
TJC (0–78), mean (SD)	21.9 (14.7)	23.1 (16.6)
SJC (0–76), mean (SD)	10.3 (6.2)	13.0 (9.4)
Patient Assessment of Pain (0–100 mm VAS), mean (SD)	56.8 (20.0)	57.7 (21.0)
PtGA (0–100 mm VAS), mean (SD)	56.1 (20.6)	56.1 (22.3)
Prior use of bDMARDs, n (%)	28 (16.4)	36 (22.6)
Mean (SD) Change From Baseline to Week 52*		
cDAPSA	-18.0 (16.4)	-23.3 (21.8)
TJC	-10.1 (10.5)	-13.0 (15.0)
SJC	-6.1 (7.1)	-8.7 (9.9)
Patient Assessment of Pain	-15.5 (25.5)	-18.0 (24.9)
PtGA	-11.8 (27.0)	-16.8 (25.4)

*Data as observed. Includes patients randomized to APR 30 mg BID at Week 0. m = the number of patients with non-missing data. Data availability for each individual parameter and time point may vary.
BMI, body mass index; BSA, body surface area; bDMARD, biologic disease-modifying antirheumatic drug; cDAPSA, Clinical Disease Activity Index for Psoriatic Arthritis; PsA, psoriatic arthritis; SJC, swollen joint count; TJC, tender joint count; VAS, visual analog scale.

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AB1119

GUSELKUMAB EFFICACY AND SAFETY ANALYSIS FOR PSA ACCORDING TO BASELINE CHARACTERISTICS AS GENDER, OBESITY OR PREVIOUS TREATMENT IN REAL LIFE AFTER 52 WEEKS

Keywords: Psoriatic arthritis, Real-world evidence, bDMARD

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Background: Guselkumab is a human IgG1λ monoclonal antibody that binds to interleukin 23, a regulatory cytokine that modifies the activity of T lymphocytes, intervening in pathogenic ways that initiate and maintain the activity of Psoriatic Arthritis (PsA). PsA has a wide spread of systemic manifestations where several profiles of disease exist depending on the predominant affection. Guselkumab has been used widely to treat cutaneous psoriatic disease (PsO) and PsA since 2020. Nevertheless, no long-term analysis have been done.

Objectives: To analyze the long term efficacy and safety of Guselkumab at 52 weeks (w). Likewise, relevant demographic data such as sex, weight or previous biological treatment was taken into account.

Methods: A prospective, unicentric, observational study was conducted in patients who met ACR criteria for PsA, who received treatment with Guselkumab for 52 w. Patient demographic and baseline data were recorded and response variables such as DAPSA and BSA index, presence of enthesitis and dactylitis, and drug persistence at 12, 24 and 52 w of treatment were statistically analyzed and compared between different groups of patients stratified by their demographic data and previous biological therapy using Student-T and ANOVA. In addition, adverse events were recorded.

Results: 45 patients with moderate-to-severe PsA were included: 60 % were female, they had a mean BMI of 28.87. Approximately, 60% of patients received Guselkumab in fourth to eighth line of treatment. According to their DAPSA index score, patients were classified into remission, low activity and active disease. 50% of the patients fell under the remission category at w52, with the majority of the remaining in low activity (44%). The percentage of enthesitis and dactylitis presented an important reduction, from 31% and 8.88% at baseline to both 0% at 52 w respectively. BSA also experimented a significant reduction. (Figure 1) At baseline both genders showed a similar mean value for DAPSA which decreased significantly when they reached w 52. There were not differences between genders at the end of the study, however women had an earlier response with significant differences at w 12. Moreover, when we analyzed the population regarding weight, we found that Guselkumab was effective both in normal weight and also in overweight patients being 8/13 of them obese. Finally, studying the previous biologic treatment profiles, we found that better results were expected after anti-TNF or IL-17 inhibitors compared to other drugs. Treatment persistence was 100% after 24 w and 85% after 52 w in those patients who received Guselkumab as 2nd or 3rd line of treatment, but 84% and 63% at 24 and 52 w in those who took it in 4th place or more. No adverse effects were reported and a total of 11 patients abandoned treatment, 10 of them due to primary failure and 1 due to secondary failure.

Conclusion: Guselkumab was effective and safe for the treatment of manifestations of PsA in a real world evidence cohort of patients for 52 w. In addition, Guselkumab was equally effective in men/women as well as overweight patients, showing better results when the patient had followed treatment previously with anti-TNF or IL-17 inhibitors probably because they were less bDMARD-experienced patients. According to this fact, Guselkumab demonstrated an increased survival when administered in the second or third line of treatment compared to advanced lines of treatment.

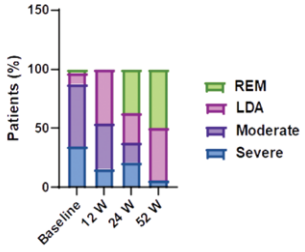


Figure 1. Percentage of patients reaching remission (REM), low disease activity (LDA) or active disease at baseline, 12, 24, and 52 weeks after Guselkumab treatment.

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Disclosure of Interests: VICTOR RUIZ DEL VALLE Speakers bureau: I have been paid for oral communications regarding medical topics by Janssen Pharmaceutica, Grant/research support from: Financial aid to pay study expenses as a statistician, Irene Martín Martín Grant/research support from: Financial aid to pay study expenses as a statistician., Míriam Navidad Fuentes Speakers bureau: She has been paid for oral communications regarding medical topics by Janssen Pharmaceutica, Grant/research support from: Financial aid to pay study expenses as a statistician., Laura Estepa Díaz Grant/research support from: Financial aid to pay study expenses as a statistician., Susana Quirosa Flores Grant/research support from: Financial aid to pay study expenses as a statistician.

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AB1120 REAL-LIFE EFFICACY AND SAFETY OF IXEKIZUMAB IN A COHORT OF PATIENTS WITH PSORIATIC ARTHRITIS: A SINGLE-CENTER RETROSPECTIVE STUDY

Keywords: Psoriatic arthritis, bDMARD, Real-world evidence

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Background: Ixekizumab is a high-affinity monoclonal antibody that selectively targets interleukin-17A and is indicated for psoriasis, psoriatic arthritis (PsA) and axial spondyloarthritis. Literature highlights efficacy and safety in real life in patients affected by psoriasis[1], instead little are data concerning PsA.[2]

Objectives: To retrospectively evaluate the effectiveness and safety of ixekizumab, in a cohort of patients with PsA.

Methods: Patients with a diagnosis of PsA and treated with ixekizumab who visited our outpatient clinic from October 2019 to December 2022 were included in the study. Clinical data were recorded since the first prescription of ixekizumab and at 6-month follow-up visit. Demographic, clinical and laboratory characteristics, treatment, and causes of discontinuation were analyzed. Differences between baseline and 6-months erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), tender joint count (TJC) and swollen joint count (SJC) were analysed.

Results: Main results are reported on Table 1. 76 patients were included in the study, with an average age at the prescription of ixekizumab (T0) of 57.1±13.0 years. Main comorbidities were: hypertension (44.7%), obesity and overweight (44.7%), cardiopathy (19.7%), hepatic steatosis (21.0%), diabetes (13.2%), and hyperlipemia (3.9%). 93.42% of patients presented peripheral arthritis, 30.6% axial involvement, and 42.1 % enthesitis. 28,9% of patients were biologic-naïve, 34,0% received one biologic agent before, and 31.5% two or more biologic agents. 88,2% of patients initiated ixekizumab in combination with a csDMARDs, mainly methotrexate. The indications for the prescription of ixekizumab as a first biologic agent were: multiple comorbidities, severe psoriasis, and intolerance to csDMARDs. 28.9% of patients stopped ixekizumab because of primary failure (31.8%), secondary failure (22.7%), or adverse events (45.5%). 40% of the adverse events were relevant skin reactions at the injection site. No severe adverse events were registered. 60 patients completed 6 months of treatment (T6). In those patients, a statistically significant decrease between the SJC and TJC at baseline and T6 was found (p-value 0.0011 and 0.0006 respectively). No difference in the values of ESR and CRP values between T0 and T6 was present.

Table 1. General characteristics of our cohort and clinical and laboratory findings at baseline and follow-up for patients who completed 6 months of treatment with ixekizumab.

Male/female n. (%)	22 (28.9%)/ 54 (71.1%)		
Mean age at diagnosis (years)	50.0		
Years from diagnosis at the first prescription of ixekizumab (years)	6.7		
Patients: n. 60	**T0**	**T6**	**p-value**
ESR (mm/h)	27.44±23.3	27.56±22.2	0.9741
CRP (mg/dl)	1.58±2.47	0.98±1.7	0.1569
TJC	9.17±6.98	5.02±6.65	0.0011
SJC	1.57±2.75	0.28±0.64	0.0006

Conclusion: There are few data in real life concerning efficacy and safety in patients affected by PsA. In our cohort, ixekizumab significantly improved peripheral arthritis, and it revealed a good safety profile, without severe adverse events during the follow up. Further real-life evaluations on axial involvement, which was not included in this study, are warranted.

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AB1121 EFFICACY AND DRUG PERSISTENCE OF NEWLY INITIATED BIOLOGICS IN PSORIATIC ARTHRITIS

Keywords: bDMARD, Real-world evidence, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a form of spondyloarthritis associated with psoriasis and characterized by joint, entheses and spine inflammation. Numerous therapeutic molecules have appeared in the last decade following breakthroughs in the pathogenesis of the disease [1].

Objectives: The study aimed to evaluate the effectiveness and persistence of first-line biological treatment in PsA in a real-life setting.

Methods: The study included retrospectively all the PsA patients initiated on biologics in a university single center real-life clinical practice between January 2018- December 2021, as reported in the Romanian Register of Rheumatic Diseases [2]. Differences of continuous variables among subgroups were assessed with Mann Whitney tests, while associations of categorical variables were assessed with χ^2 tests, considered significant if $p < 0.05$.

Results: The study included 38 patients with an average age at biologic initiation of 50 ± 16 years, of which 71.1% were women, 34.2% were obese and 10.5% were smoking. The patients had established disease, with an average PsA duration of 9 ± 9 years. Regarding treatment, 44.7% initiated tumor necrosis factor inhibitors (TNFi) and 55.3% interleukin 17 inhibitors (IL-17i). A fraction of 31.6% had biologic monotherapy. After the first 6 months of therapy, 55.3% reached the treatment target (Disease Activity in PSoriatic Arthritis - DAPSA < 14) with a drug persistence of 78.9%, while 65.8% reached target by 12 months with 68.4% drug persistence. There were no differences of DAPSA scores, target frequencies or persistence frequencies at 6 and 12 months between TNFi and IL17i ($p > 0.05$). An equal number of initiations was observed in the pre-pandemic period (2018-2019; 50%) versus the pandemic period (2020-2021; 50%).

Conclusion: Observations in a real-life setting show good efficacy persistence of both TNFi and IL17i in PsA at 6 and 12 months after their initiation. SARS-CoV-2 pandemic did not influence the number of biologic initiations in PsA patients.

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Disclosure of Interests: None Declared.

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AB1122

GUSELKUMAB VS GOLIMUMAB IN PSA TNFI-INADEQUATE RESPONDERS (EVOLUTION): FORMULATING A PRAGMATIC PHASE 3B RANDOMIZED TRIAL

Keywords: Randomized control trial, Psoriatic arthritis, Real-world evidence

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Background: Aside from the Tight Control in PsA (TICOPA) study, treatment strategy trials in psoriatic arthritis (PsA), and definitive guidance on managing patients (pts) with inadequate response (IR) to a first tumor necrosis factor inhibitor (TNFi), are lacking. Recent observational studies suggest potentially greater benefit from switching TNFi-IR pts to a new mechanism of action (MOA).[1]
Objectives: Design a pragmatic trial (EVOLUTION) to determine whether switching TNFi-IR PsA pts to a new MOA, specifically to the selective interleukin 23 inhibitor (IL-23i) guselkumab (GUS), is more effective than cycling to a 2nd TNFi (Figure 1).
Methods: To plan the EVOLUTION trial, we assessed pts receiving any biologic in the multicenter longitudinal observational Psoriatic Arthritis Research Consortium (PARC) study.[2] Findings informed expected mean changes in selected outcome measures, enrollment feasibility, and sample size estimates.
Results: 215 pts initiating a biologic in PARC (including later lines of therapy) had data for the outcomes of interest and a 3-6 month follow-up visit. At therapy initiation (baseline [BL]), mean age=50.4 (SD 14.4), 56% were female, 81% were White. Mean BL clinical disease activity in PsA (cDAPSA)=20.0 (15), mean body surface area (BSA)=2.0% (6), 21% were in minimal disease activity (MDA), 43% were in cDAPSA remission/low disease activity (LDA), and 70% had a BSA ≤1%. 113/215 (53%) pts met EVOLUTION's clinical enrollment criteria (Figure 1). Pts who would be eligible for EVOLUTION vs ineligible pts had higher disease activity (mean cDAPSA 29.0 vs 10.0, PtGA 5.6 vs 3.1, Psoriatic Arthritis Impact of Disease Questionnaire [PSAID-12] 5.1 vs 2.6, swollen joint count [SJC] 6.0 vs 0.8, tender joint count [TJC] 11.0 vs 2.4); age and sex distribution were similar. Among EVOLUTION-eligible pts not in MDA at BL, 21% achieved MDA at follow up. Also at follow-up in EVOLUTION-eligible pts not in response at BL, 38% achieved cDAPSA LDA, 38% achieved BSA ≤1%, 30% achieved both, and mean change (Δ) in PtGA= -1.0 (2.5), Δ pt pain= -1.4 (2.7), and Δ PSAID-12= -1.0 (1.9). EVOLUTION'S primary study outcome (cDAPSA LDA + IGA 0/1) will be assessed at 12 months (Table 1), and per clinical practice, pts will be enrolled at the time of switch vs post-washout. Assuming 24%, 45% and 50% of pts in the golimumab (GOL), GUS Q8W and GUS Q4W arms, respectively, would achieve the primary outcome, and a 20% pt dropout rate, a total sample size of 300 pts is anticipated to yield 80 pts per randomized group and provide 80% power to detect a difference in proportions of GUS Q4W vs GOL and GUS Q8W vs GOL pts achieving cDAPSA LDA + IGA 0/1.
Conclusion: The EVOLUTION trial will apply an innovative, pragmatic randomized trial approach to assessing therapy effectiveness by recruiting a treatment-refractory PsA population consistent with that seen in clinical practice. This also includes using a novel primary endpoint (cDAPSA LDA + IGA 0/1) with direct applicability to routine care. This first of its kind head-to-head comparative effectiveness trial in real-world PsA pts will address important knowledge gaps in the management of PsA related to switching from a TNFi to GUS vs cycling to a 2nd TNFi and will build on a longitudinal cohort study used to plan this study.

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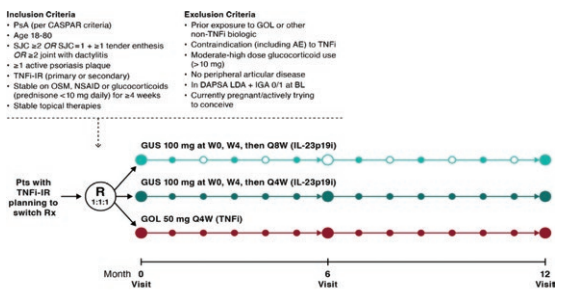


Figure. EVOLUTION Design. This is a 12-month, double-blind, randomized controlled trial with primary endpoint at 12 months. Large circles represent in-person visits (BL, 6 months, 12 months) while small circles indicate remote capture of PROs (W4, W8, etc); solid circles represent active treatment, while open circles represent matching placebo. AE = Adverse event; CASPAR = Classification criteria for Psoriatic Arthritis; NSAID = Non-steroidal anti-inflammatory drug; OSM = Oral small molecules; R = Randomization; Rx = Medication.

Table 1. EVOLUTION Endpoints

Primary outcome	cDAPSA LDA + IGA 0/1 at 12 months
Secondary endpoints at 6 and 12 months	cDAPSA LDA + IGA 0/1 (6 months) MDA, PSAID-12 <4, Δ PSAID-12, IGA 0/1 in pts with BSA >3% at BL, IGA in pts with IGA ≥2 at BL, Δ PROMIS-Fatigue, Δ DLQI, Δ BASDAI in pts with axial disease, dactylitis resolution, enthesitis resolution, drug retention, AE, tolerability
Qualitative process evaluation	Qualitative interviews on trial format, engagement and participation

PSAID-12 (PSAID <4 is the pt acceptable symptom state); Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); Dermatology Life Quality Index (DLQI); Pt-Reported Outcomes Measurement Information System (PROMIS)

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AB1123

EFFICACY AND SAFETY OF SECUKINUMAB IN PATIENTS WITH PSORIASIS

Keywords: Psoriatic arthritis, bDMARD

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Background: Psoriasis is a chronic, multisystem inflammatory disease with predominantly skin and joint involvement. The interleukin-(IL-)17 axis plays a vital role in the development of psoriasis. Secukinumab (Cosentyx) is a fully human monoclonal antibody that selectively targets IL-17A for the treatment of adult patients with psoriasis[1].
Objectives: This study aimed to systematically evaluate the efficacy and safety of secukinumab therapy in psoriasis.
Methods: Eight databases (PubMed, Web of Science, Embase, Cochrane Library, Web of Knowledge, MEDLINE, Clinical Trials.gov, and FDA.gov) were searched for studies on secukinumab treatment of psoriasis published from the date of establishment of the database to January 3, 2022. A random effect model was used to conduct a meta-analysis of the efficacy and safety of abatacept in patients with RA using (Stata 12.0).
Results: A total of 27 studies with a total of 4470 patients were included. After receiving secukinumab therapy for 12 weeks, The response rate of PASI 75 was 82.2% (95% CI 0.766–0.879,p<0.01), PASI 90 was 66.3%(95% CI 0.609–0.718,p<0.01), and PASI 100 was 42% (95% CI 0.343–0.497,p<0.01). The results showed that more than 80% of patients achieved skin lesion removal in 12 weeks. Considering PGA 0/1 as the secondary endpoint. The percentage of patients who achieved a PGA score of 0 or 1 was 72.3% at 12 weeks (95% CI 0.658–0.788,p=0.005). As for the safety, the incidence of adverse events was 63.7%. Infection is the main adverse effects, with rates of 19.4%. Most of the adverse events were mild and recovered quickly after discontinuation. (Figure 1)
Conclusion: Secukinumab is effective in patients with psoriasis and is generally well tolerated, and thus represents a useful treatment alternative to TNFi and other bDMARDs in adult patients with psoriasis.

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Table 1. Available evidence including patients with psoriasis treated with secukinumab.

Study. Year.	Patients (include in analysis)	Age (year)	Gender (female %)	PASI 75,n(%)	PASI 90,n(%)	PASI 100,n(%)	PGA, n(%)
Ulrich Mrowietz 2021	79(79)	50.6 ± 14.8	81.0	21(26.6)	NA	NA	NA
A Blauvelt 2015	59(59)	45.1 ± 12.57	64.4	45(75.9)	36(60.3)	26(43.1)	NA
Richard G Langley 2014	245(245)	44.9±13.5	31.0	200 (81.6)	145 (59.2)	70 (28.6)	NA
C Paul 2015	60(60)	46.6 ± 14.23	23.3	52(86.7)	NA	NA	NA
Nan-Lin Wu 2015	16(16)	38.1± 12.0	12.5	14(87.5)	11(68.8)	5(31.3)	NA
Mamitaro Ohtsuki 2014	29(29)	51.9 ± 11.77	10.3	24(82.8)	18(62.1)	8(27.6)	NA
Lin Cai 2020	221(221)	39.0±11.6	19.9	215(97.7)	179(81.0)	NA	NA
Xi-Bei Chen 2022	83(83)	39.43 ± 12.42	48.2	80(96)	73(88)	63(76)	NA
Gaojie Li 2022	87(87)	36.06 ± 11.82	34.5	79(90.59)	65(74.12)	NA	NA
Ilteris Oguz Topal 2022	229(229)	19 ± 7.8	39.3	206(89.9)	181(79)	110(48)	NA
Si-Man Zhu 2020	20(20)	NA	NA	17(87.5)	14(68.8)	9(43.8)	NA
Jing-Xin Zeng 2020	54(54)	36.5±3.6	24.1	52(96.3)	NA	NA	NA
José-María Ortiz-Salvador 2019	156(156)	28 ± 17.7	43	130(83.5)	97(62)	NA	NA
Diamant Thaçi 2015	334(334)	45.2 ± 13.96	32	307(91.8)	246(73.5)	131 (39.3)	NA
Richard G Langley2014	245(245)	44.9 ± 13.5	31	200(81.6)	145(59.2)	70 (28.6)	NA
Richard G Langley2014	323(323)	44.95± 13.2	31.5	249(77.1)	175(54.2)	78(24.1)	NA
Mamitaro Ohtsuki 2017	34(34)	51.50 ± 12.08	29.7	17(50)	17(50)	NA	NA
Diamant Thaçi2015	338(334)	45.2 ± 13.96	32	304(91.0)	243 (72.8)	130 (38.9)	NA
Jerry Bagel 2017	51(51)	42.7±13.4	47.1	NA	27(52.9)	18(35.3)	NA
J-P Lacour 2017	60(60)	46.6 ± 14.23	23.3	53(88)	33(55.6)	16(26.9)	NA
Iain B McInnes 2020	426(426)	48.5 ±12.38	51	NA	230(54)	NA	NA
Joel M. Gelfand 2020	46(46)	47.9 ±12.7	28.3	NA	34(74)	NA	NA
Nina Magnolo 2022	42(42)	NA	NA	NA	NA	23(54.8)	NA
Yu-Xin Zheng2022	22(22)	12.0±4.5	54.5	NA	NA	19(86.3)	NA
R B Warren 2021	163 (163)	46·8 ± 14·9	62.0	NA	NA	NA	108 (66.3)
M Augustin 2022	1756 (745)	48.4 ± 13.5	48.9	NA	NA	NA	578 (77.6)
Uta Kiltz 2022	534 (303)	52.5 ± 11.9	54.9	NA	NA	NA	216 (71.3)

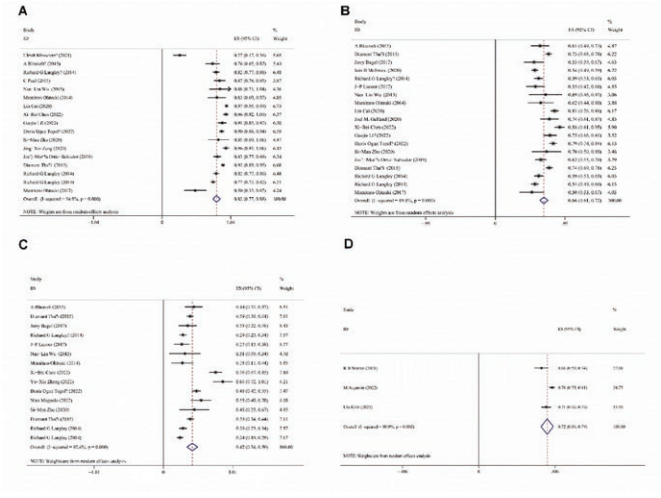


Figure 1. Efficacy of Secukinumab in patients with psoriasis (A) PASI 75 (B) PASI 90 (C) PASI 100 (D) PGA score of 0 or 1

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1124 TOFACITINIB IN PSORIATIC ARTHRITIS -WELL TOLERATED DRUG - REAL LIFE EXPERIENCE

Keywords: Psoriatic arthritis, Targeted synthetic drugs, Safety

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Background: Tofacitinib a small molecule JAK- inhibitors has been approved for use in psoriatic arthritis (PSA) since 2017 while it has shown to be effective in the clinical trials real life data is sparse.With increase in use there has been growing concern about the safety profiles and adverse events which makes it all the more important to have real life data.
Objectives: To review patient records who were treated with tofacitinib for psoriatic arthritis and to assess the tolerance and continuation rate and also assess the occurrence of adverse events like infections, coronary artery disease.
Methods: All PSA patients who were prescribed tofacitinib from JAN-2021 to JUNE 2022 with minimum of 6 months followup were included for analysis. Demographics, weight recordings, lab parameters and occurence of adverse events were noted.
Results: There were a total of 71 patients who were prescribed tofacitinib out of which 46 are continuing and 25 have stopped during this period. The mean age was 47.25 (10.9)yrs the mean disease duration was 4.182 (4.474)yrs The reason for stopping tofacitinib was better(52%) followed inefficacy(24%), and miscellaneous(24%)reasons..When analysing before and after tofacitninb one thing whihc was striking is the significant weight gain among patients with minimum of 3.52(3.06) kg weight gain and this weight gain was consistent even in stopped patients.in comparing the lab parameters before and after tofacitininb there was a significant redcution in CRP,ESR,PLATELET COUNT Table 1 and a minimal but insginificant rise in liver enzymes within the physiological range.When compared to before and after tofacitinib there was increased occurence of fatigue(18.3%), minor infections(11.2%), Gastrointerstinal adverse events (11.2%), alopecia (11.2%), Itching(10.4%), headache(9.8%), UTI(5.6%), cough (4.2%), transaminitis(2.8%), covid(1.7%), zoster(1.4%) and CAD(1.4%).
Conclusion: Tofacitinib in psoriatic arthritis is well tolerated with significant reduction in the inflammatory markers and weight gain but serious adverse events in lesser percentage eventhough it leads to significant weight gain.

Table 1.

PARAMTERS	Before	After	P value
Weight	70.15 (14.19)	72.31 (14.24)	0.000249
ESR	45.29 (28.26)	35.23 (28.33)	0.037
CRP	21.56 (16.38)	10.72 (11.98)	<.0001
PLATELET COUNT	332.92 (88.77)	307.09 (88.18)	0.0046
SGOT	30.33 (9.99)	35.69 (19.92)	0.125
SGPT	22.57 (12.96)	27.98 (20.17)	0.116

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Disclosure of Interests: None Declared.
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AB1125 TREATMENT WITH UPADACINITIB IN REFRACTORY PSORIATIC ARTHRITIS. MULTICENTER STUDY OF 101 PATIENTS OF CLINICAL PRACTICE

Keywords: Real-world evidence, Targeted synthetic drugs, Psoriatic arthritis

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Background: Upadacitinib (UPA) is an inhibitor of JAK kinases recently approved by EMA for the treatment of psoriatic arthritis (PsA) in Europe (January 2021) [1] UPA has shown efficacy in refractory patients to anti-TNF [2]
Objectives: A) to assess efficacy and safety of UPA in the first cases in Spain in clinical practice. **B)** to compare the profile of clinical practice (CP) patients with clinical trial (CT) of UPA in PsA refractory to biologics [2]
Methods: Study of 101 patients of CP with PsA treated with UPA in Spain. The diagnosis of PsA was made using CASPAR criteria. Patients who received one or more dose of UPA with at least one follow-up visit were included. Results are expressed as percentage, mean±SD or median [IRQ]
Results: 101 patients (73♀/28♂), mean age of 43.8 ± 12.1 years **(Table 1).** Pattern joint involvement was: peripheral (n=61) axial (8) and mixed (32) During the PsA evolution patients presented enthesitis (38.6%) nail involvement (22%) and dactylitis (25.7%) Prior to UPA most patients (71.3%) received oral prednisone or equivalent (mean maximum dose 12.04±6.98 mg/d), synthetic immunosuppressants (mean; 1.8±0.9) and biological therapy (TB) (3.4±2.2). TB were: etanercept (n=47), adalimumab (77), infliximab (23), golimumab (21), certolizumab (32), secukinumab (53), ixekizumab (32), ustekinumab (34), Abatacept [2], brodalumab [1] and guselkumab [2]. Apremilast was used in 23, Tofacitinib in 26 and filgotinib in 1 UPA was started (15 mg/24 h) after a mean follow-up of 9.9±7.8 years from PsA diagnosis. Prednisone was used in 47 cases (mean dose, 7.8±5.7 mg/d). UPA was combined with methotrexate (n=30), salazopyrin (7) and leflunomide (15); in the remaining 51 cases (50.50%) was used in monotherapy. At UPA initiation patients presented peripheral arthritis (78%), axial involvement (28,71%), skin involvement (22.8%), enthesitis (22.7%), and dactylitis (11%) Patients of CP compared with CT were younger, more frequently women, refractory to a greater number of TB and received more concomitant corticosteroid **(Table 1)** After a median follow-up of 5.72±4.64 months with UPA, patients showed a prompt improvement in activity indexes (DAS28, DAPSA) **(Figure 1)** and CRP mg/L decreased from a median 2.51 [1.0-8.0] to 1.00 [0.30-5.00] (p <0.006). Extra-articular manifestations also improved: dactylitis in 75% patients, enthesitis (55.56%) and skin involvement (60%) No serious Adverse events (AE) were reported. Minor side effects were observed in 20 patients (19.8%). UPA was discontinued in 31 (20 inefficiency, 4 patient decision, 2 infection, 2 thrombosis, 1 surgery, 1 pregnancy)
Conclusion: In this study, first patients of CP in Spain with UPA in PsA were younger, received concomitant corticosteroid more frequently and were refractory to a greater number of TB than those of CP. As in the UPA CT, it seems effective, rapid and relatively safe in daily CP for refractory Ps.A.

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Table 1.

	CLINICAL PRACTICE N=101	CLINICAL TRIAL N=211	p
Baseline demographic parameters			
Age years (mean±SD)	43.8±12.1	53.0 ± 12.0	**<0.001**
Sex n (%) female	73 (72.3)	113 (53.6)	**0.002**
Disease Characteristics			
Duration of PsA year (mean±SD)	9.94 ± 7.8	9.5 ± 8.4	0.658
HAQ-DI	0.97±0.65	1.10 ± 0.6	0.082
Swollen joint count mean±SD	4.33 ± 5.01	11.3 ± 8.2	**<0.001**
Painful joint count mean±SD	6.15 ± 5.68	24.9 ± 17.3	**<0.001**
Enthesitis n (%)	23 (22.7) MASES	172 (81.5) SPARCC	**<0.001**
Dactylitis n (%)	11 (11)	55(26.1)	**0.001**
PASI score mean±SD	0.95±1.64	10.1 ± 9.2	**<0.001**
CRP (mg/L)	8.72 ± 15.50	11.2 ± 18.5	0.245
Oral glucocorticoid use n (%)	47 (46.53)	22 (10.4)	**<0.001**
Concomitant synthetic DMARDs n (%)	50 (49.50)	98 (46,4)	0.613
Previous use of biological DMARDs n (%)	94 (93.1)	195 (92.4)	0.837
Number of prior failed biologic DMARDs n (%)			
1	16 (15,84)	135 (63.7)	**<0.001**
2	18 (17.82)	35 (16.5)	0.786
≥3	60 (59.40)	24 (11.3)	**<0.001**
UPA in monotherapy n (%)	51 (50.50)	113 (53.6)	0.613

HAQ-DI Health Assessment Questionnaire-Disability Index, PASI Psoriasis Area Severity Index, CRP C-reactive protein, DMARD disease-modifying antirheumatic drug

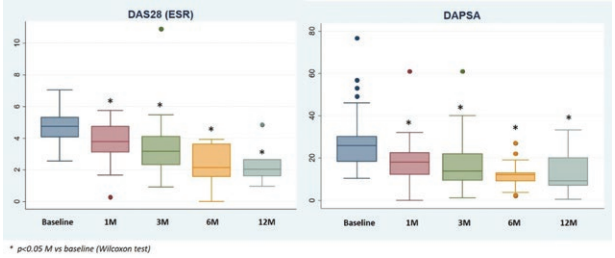


Figure 1.

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AB1126

LOW-DOSE IL-2 CHANGED LYMPHOCYTE SUBSETS IN PATIENTS WITH PSORIATIC ARTHRITIS.

Keywords: Psoriatic arthritis, Cytokines and chemokines

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Background: Psoriatic arthritis (PsA) is an autoimmune disease characterized by disturbances of regulatory cells, which were regulated by interleukin (IL)-2.
Objectives: The aim of this study was to systematically evaluate the changes in number of lymphocytes subsets after low-dose IL-2 therapy in psoriatic arthritis(PsA).
Methods: Systematic searches of PubMed, EMBASE, Web of Science, the Cochrane Library and Medline, CNKI, CBM and Technology Journal Database were performed. Original case reports, case series, observational studies and clinical trials reporting the changes in numbers of lymphocytes subsets on PsA patients treated with IL-2 were included. A random-effects meta-analysis was performed to calculate the pooled efficacy. Inconsistency was evaluated by using the I^2 and Egger tests were used for the evaluation of potential publication bias (STATA v.12.0)

Results: A total of 3 studies comprising 156 patients were identified(Table 1).The numbers of Tregs were increased after the treatment of IL-2[SMD=0.928, 95%CI (0.004,1.853), P=0.049]. Additionally, there were no statistical differences in the numbers of Th1, Th2 and Th17 cells[SMD=0.213, 95%CI (-0.198,0.623), P=0.310; SMD=0.137, 95%CI(-0.739,1.013), P=0.759;SMD=0.146, 95%CI (-0.430,0.722), P=0.619](Figure 1).
Conclusion: Low-dose IL-2 was promising in the treatment of PsA, which could promote the proliferation and functional recovery of Tregs.

Table 1. Available evidence including patients with PsA treated with low-dose IL-2.

Study.Year.	Patients (include in analysis)	Gender (female %)	Dosage	Tregs
Jia Wang. 2020.	22(22)	NA	0.5 million IU per day for 5 days	before:26.26±10.99 after:70.78±44.82
S. J. Guo. 2020.	112(112)	44.64	NA	before:32.18±18.56 after:37.13±35.89
ShengXiao Zhang. 2019.	22(22)	NA	0.5 million IU per day for 5 days	before:27.44±11.30 after: 71.65±44.04

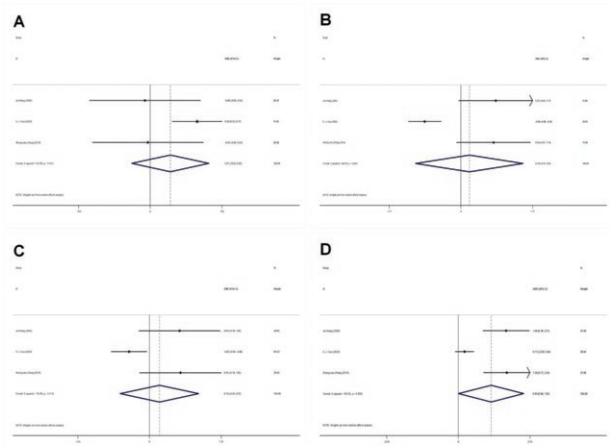


Figure 1. Changes in the subsets of lymphocytes after IL-2 in PsA patients.(A-D) the number of Th1,Th2,Th17 and Tregs cells after IL-2 injection.

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5113

AB1127

THE RETENTION RATE OF ETANERCEPT AND ADALIMUMAB IN FIRST-LINE AND AFTER NON-MEDICAL SWITCH IN PATIENTS WITH PSORIATIC ARTHRITIS: A COMPARISON BETWEEN ORIGINATORS AND BIOSIMILARS. A SINGLE-CENTER RETROSPECTIVE STUDY.

Keywords: Psoriatic arthritis, bDMARD

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Background: Psoriatic arthritis is a chronic immune-mediated disease that may appear with arthritis and/or enthesitis and systemic manifestations, affecting 0.1-1% of the general population and up to 30% of patients with psoriasis. A greater understanding of the pathogenesis has led to an increase of therapeutic options, namely biotechnological drugs which may prevent the progression of the disease and improve the quality of life by acting on specific pathways. Among these drugs, anti-TNFα agents play an important role. Adalimumab (ADA) and Etanecept (ETA) were the first developed ones, indeed they are defined as "originator" drugs. Subsequently, "biosimilars" have been developed. They are defined by the EMA as highly similar to other biological agents already on the market in terms of qualitative characteristics, biological activity, safety, and efficacy. Spending review and pharmaco-economic policies have almost "imposed" the use of non-medical switching (NMS).
Objectives: The aim of this study is to evaluate the retention rate of ETA and ADA originators, compared to their biosimilar counterparts, in the first line and after NMS, detecting discontinuation for adverse events (AEs) or ineffectiveness, in patients with psoriatic arthritis.
Methods: Fifty-four patients diagnosed with psoriatic arthritis were enrolled (F: 61%; mean age 53.4±13 years, BMI 24.9±3.6), Baseline disease activity was 4, 1 ± 1.1. Inclusion criteria were age >18 years, fulfillment of CASPAR 2006 criteria for PsA, therapy with originators or biosimilar etanercept or adalimumab in the first line, with the possibility of no NMS, stable combined therapy with methotrexate during the observation time. Statistical significance was set at $p \leq 0.05$.
Results: The retention rate of ETA and ADA originators was 541 ± 70 weeks and 486 ± 24 weeks, respectively. The retention rates of biosimilar ETA and biosimilar ADA in the first line were 265 ± 20 weeks and 79 ± 21 weeks, respectively (p=0.231). After NMS, the retention rate of biosimilar ETA and biosimilar ADA was 49.1 ± 13 weeks and 108 ± 12 weeks, respectively. Discontinuation due to AEs were recorded in 8.3% of patients receiving originator ETA, 5% of patients receiving originator ADA, and 31% of patients receiving biosimilar ADA. Discontinuation due to ineffectiveness occurred in 54% of patients treated with originator ETA, in 40% of patients treated with originator ADA, and in 44% of patients treated with biosimilar ADA. In patients treated with biosimilar ETA, no suspensions were recorded either for AEs or for ineffectiveness.
Conclusion: Our data show that the retention rate of originator drugs was higher than that of biosimilars, both when administered in the first line and after a NMS. A greater number of suspensions were recorded for AEs and, to a lesser extent, for ineffectiveness with biosimilar ADA compared to originator ADA, while in patients treated with biosimilar ETA no suspensions were recorded either for AEs or for ineffectiveness.
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Disclosure of Interests: None Declared.
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AB1128

METHOTREXATE MAINTENANCE THERAPY IN PSORIATIC ARTHRITIS

Keywords: Tapering, Disease-modifying drugs (DMARDs), Psoriatic arthritis

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Background: The management of psoriatic arthritis (PsA) is currently well codified. Methotrexate (MTX) remains the most frequently used DMARD in first-line treatment of peripheral joint disease.
Objectives: We aimed to identify the rate of therapeutic maintenance of MTX during PsA and to determine the date of first biotherapy.
Methods: We conducted a single-center, retrospective study including PsA patients with peripheral joint involvement. Patient and disease characteristics were recorded. We determined the MTX maintenance rate and tolerance profiles. We recorded data related to the first biotherapy.
Results: Twenty-two women and eleven men were included. The mean age was 52.31±12.98 years [21-78]. The mean disease duration was 10.90±5.91 years [1-21]. PsA had an articular peripheral onset in 68.8% of cases and axial and articular peripheral in 31.3% of patients. Psoriasis was present at diagnosis in 27 patients (81.8%). The mean age at diagnosis was 42.70±13.84 years [19-68]. MTX was initiated for all patients after a mean duration of 3.14±2.58 months [1-12]. It was prescribed orally in 86.7% of patients and intramuscularly in 13.3%. The mean duration of treatment was 7.83±5.90 years [1-21]. The maintenance rate at 1 year was 100%, at 2 years was 83.3%, and at 5 years was 70%. MTX was discontinued in 4 patients for adverse events: 3 cases of digestive intolerance and 1 case of liver toxicity. Biotherapy was prescribed for 10 patients (30.3%): Infliximab (2 cases), Adalimumab (2 cases), and Etanercept (6 cases). The time to prescription of the first biotherapy was 4±1.6 years [3-7]. Biotherapy was indicated but not prescribed in 5 patients (15.2%). Causes of non-prescription were mainly lack of social security coverage.
Conclusion: In our study, MTX was the first-line treatment for patients with PsA. The therapeutic maintenance seems to be good reflecting the effectiveness. However, this maintenance is certainly influenced by the socio-economic factors.
REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5591

Psoriatic arthritis - clinical aspects (other than treatment)

AB1129 **UTILITY OF LOW-DOSE COMPUTED TOMOGRAPHY (LDCT) FOR IDENTIFYING PATIENTS WITH AXIAL PSORIATIC ARTHRITIS (AXPSA) – A CROSS-SECTIONAL STUDY**

Keywords: Diagnostic tests, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a multicentric disease with axial involvement being a critical feature. As inflammatory back pain (IBP) may be atypical or even absent, axial PsA is often under diagnosed. Axial PsA (axPsA) is currently diagnosed by identifying sacroiliitis on radiography. However, the detection of radiographic sacroiliitis is not entirely reliable and is challenging in early disease. Recently, magnetic resonance imaging (MRI) has been used to diagnose sacroiliitis to good effect. Even more recently, low dose (<0.5mSv) computed tomography (LDCT) has been used to identify structural changes of sacroiliitis such as erosions and ankylosis. However, the usefulness of LDCT for diagnosing sacroiliitis in axPsA compared to radiography and MRI remains uncertain.
Objectives: To investigate the usefulness of LDCT in diagnosing axPsA-related sacroiliitis compared to radiography and MRI.
Methods: Consecutive biologic disease modifying anti-rheumatic drug (bDMARDs)-naïve patients who fulfilled CASPAR were recruited into this cross-sectional study, regardless of the presence of back pain. Radiographs of the pelvis, LDCT and MRI of the sacroiliac joints were performed.
Results: 33 patients (age: 45 ± 12 years, 23 (70%) male, disease duration: 3.0 ± 6.5 years) were recruited. The cohort had moderate peripheral joint disease (Disease Activity in Psoriatic Arthritis (DAPSA): 18.78 ±1 6.33) and skin disease (Psoriasis Area Severity Index (PASI): 5.40 ± 7.10). Axial disease activity (Ankylosing Spondylitis Disease Activity Score, ASDAS) was 2.52 ± 1.26. Twenty (61%) patients were on conventional synthetic DMARDs. Radiography revealed definite sacroiliitis according to modified New York criteria in 2 (6%) patients while 8 (24%) patients had possible sacroiliitis and 23 (70%) had no sacroiliitis. LDCT revealed sacroiliitis in 9 (27%) patients, including both patients with radiographic sacroiliitis, 7 (88%) of the 8 patients with possible radiographic sacroiliitis and 2 (4%) of 23 patients with normal radiographs (Figure 1). Patient with LDCT-sacroiliitis had longer symptom duration, higher patients' pain score, physician global, enthesitis scores and Bath Ankylosing Spondylitis Metrology Index (BASMI) (Table 1). The presence of human leukocyte antigen (HLA) B27, IBP, and fulfillment of the Assessment of SpondyloArthritis international Society (ASAS) 2009 criteria of axial spondylitis could not differentiate between patients with or without LDCT-sacroiliitis. LDCT had 100% agreement with MRI. MRI detected 9 patients with sacroiliitis, all of whom were identified by LDCT.
Conclusion: LCDT revealed sacroiliitis in 4 times more patients than radiographs. Patients with sacroiliitis had higher disease activity across various disease domains. LDCT had excellent agreement with MRI. LDCT is very helpful for diagnosing axPsA, especially when access to MRI is limited.

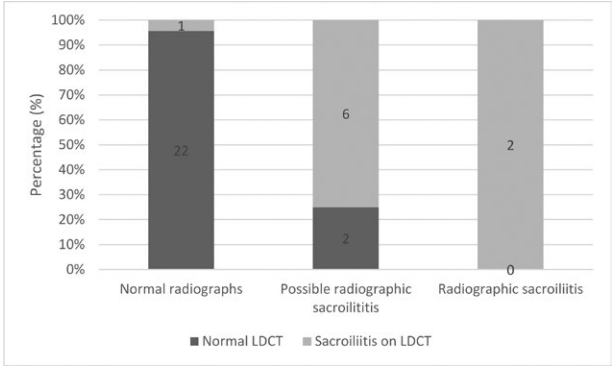


Figure 1. Prevalence of sacroiliitis detected by low dose CT (LDCT) in patients whose radiographs showed normal appearances, possible sacroiliitis and sacroiliitis

Table 1. Characteristics between patients with or without sacroiliitis detected by low-dose CT

	Normal LDCT (n=24)		Sacroiliitis detected by LDCT (n=9)		
Age	44	11	47	15	
Sex, male (n, %)	17	71%	6	67%	
PsA, symptom duration, years	1.2	1.4	3.4	2.9	*
Fullfiled ASAS criteria (n,%)	2	8%	3	33%	
HLA-B27 +ve (n,%)	1	4%	1	11%	
Presence of IBP (n,%)	3	13%	3	33%	
Presence of nail disease, (n,%)	16	67%	6	67%	
NRS pain	4	2	6	4	*
NRS ptga	5	3	6	3	
NRS phyga	5	3	6	4	*
Tender joint count	5	11	6	4	
Swollen joint count	3	4	4	3	
No. of dactylitis digit	0	1	1	1	
PASI	4.5	6.2	7.8	9.1	
SPRACC	0	0	1	1	*
BASMI	1	1	3	2	*
ESR, mm/hr	29	22	37	30	
CRP, mg/L	7.7	8.8	13.6	21.9	
DAPSA	16.94	16.87	23.69	14.54	
ASDAS	2.3	1.14	3.03	1.46	
BASDAI	3.5	2.4	5	2.4	

*p<0.05

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1130 **CAUSAL ASSOCIATION BETWEEN LOW-DENSITY LIPOPROTEIN CHOLESTEROL AND PSORIATIC ARTHRITIS**

Keywords: Psoriatic arthritis, Genetics/Epigenetics

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Background: Psoriatic arthritis (PsA) is an inflammatory disease that causes inflammation and swelling of the joints and entheses in addition to skin symptoms(PsA)[1]. Chronic psoriatic lesions may increase serum concentrations of low-density lipoprotein cholesterol (LDL-C) by producing large amounts of IL-6 and other pro-inflammatory cytokines, which release free fatty acids, cholesterol, and triglycerides from the adipose tissue[2]. However, whether LDL-C affects articular psoriasis is unclear.
Objectives: We used a two-sample Mendelian randomization (MR) analysis to investigate the causal associations of LDL-C with PsA.
Methods: Firstly, we obtained LDL-C-associated single-nucleotide polymorphisms (SNPs) from a GWAS published by the UK Biobank, including up to disequilibrium (LD) threshold for clumping was set to $r^2 < 0.001$. The clumping window size was set to 10000 kb, and we selected autosomal biallelic SNPs with P-values < 5×10^{-8}. Thirdly, as for MR analyses, F statistics were calculated to evaluate the strength of each instrument, the F-statistic of each SNP> 10, indicating a low risk of weak instrument bias. Inverse variance weighted (IVW) was the primary method to assess the association of genetically predicted LDL-C and PsA risk. Fourthly, MR-Egger and weighted median were applied to validate the results from IVW. The Cochrane Q test and funnel plots were used to test the possible heterogeneity. The directional pleiotropy was separated by intercepting from MR-Egger and MR-presso. Finally, a leave-one-out sensitivity analysis was also performed.
Results: With 158 LDL-C-associated SNPs, LDL-C was a hazard factor for PsA(OR =1.30,95%CI 1.02-1.65, P=0.032), which was consistent in direction with the weighted median(OR=1.38,95%CI,1.00-1.91, P=0.050) and MR-Egger(MR-Egger: OR=1.43, 95%CI 1.01-2.04, P=0.045). Heterogeneity existed in the results(P<0.05). But IVW could provide a robust causal estimate in the presence of heterogeneity[3]. No evidence of pleiotropy was observed (MR-Egger-intercept:

-0.0049, P=0.447), and leave-one-out sensitivity analysis showed that removing any SNP would not change the overall result, suggesting this finding was available. Details of the results were shown in Figure 1.

Figure 1

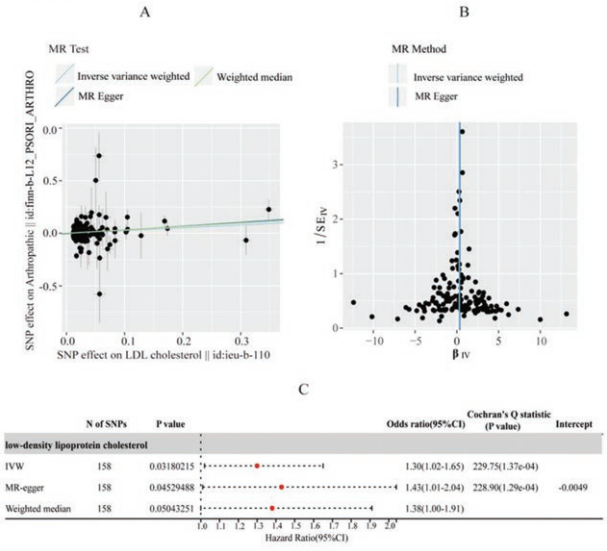


Figure 1. The causal associations between low-density lipoprotein cholesterol (LDL-C) and psoriatic arthritis (PsA) were evaluated by the odds ratio (OR) values of IVW, MR-Egger, and Weighted median. Scatter plot (A), funnel plot (B), and forest plot (C).

Conclusion: LDL-C was a hazard factor for PsA. Monitoring and lowering serum concentrations of LDL-C may make a difference in psoriasis treatment and slow down the process of PsA.

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Disclosure of Interests: None Declared.

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AB1131 PATIENT ACCEPTABLE SYMPTOMS STATE IN PSORIATIC ARTHRITIS: DOES IT DIFFER BETWEEN SEXES?

Keywords: Psoriatic arthritis, Outcome measures, Patient reported outcomes

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Background: Patient Acceptable Symptoms State (PASS) is a dichotomous and feasible tool recently validated for Psoriatic Arthritis (PsA). It assesses if the patient accepts her/his disease status by using a simple question: "Think about all the ways your PsA has affected you during the last 48 hours. If you were to remain in the next few months as you were during the last 48 hours, would this be acceptable to you?". A negative answer ("no") denotes a disease status not acceptable for the patient. Due to the recent introduction of PASS in PsA, there are not data about its difference between sexes.

Objectives: To assess PASS differences in PsA based on sexes, characterizing the factors associated with an unacceptable disease state (PASS "no").

Methods: This is a cross sectional study. Patients were consecutively enrolled from January 2022 to December 2022, in two outpatient clinics devoted to PsA. All enrolled patients were adult and had a PsA diagnosis (for at least six months). We assessed PASS and its difference between sexes (χ^2 test). Moreover, we performed two logistic regression models to assess which factors were associated with PASS "no", in both sexes.

Results: Two-hundred and forty-five patients were enrolled. Female less accepted their disease status, compared with male patients, PASS "no" was 49.1% vs 23.5%, (p<0.001) (Table1). The factor associated with a higher probability to have an unacceptable symptoms state was a higher disease activity (Table 2), both for male and female. In particular, for male patients, when DAPSA increases of 1 point, the probability to have a state of PASS "no" increases of 31% (OR 1.31, CI 95% 1.16-1.47), independently by age, disease durations, BMI and BSA. The same result was confirmed for female patients, but with a stronger association: when DAPSA increases of 1 points the probability to have a state of PASS "no" increase of 101% (OR 2.01, CI 95% 1.45-2.77), independently by age, disease durations, BMI, BSA and fibromyalgia. Moreover, fibromyalgia in female patients was not associated with PASS "no".

Table 1 Clinical and demographic characteristics, grouped by sexes.

	All patients n. 245	Female n. 119	Male n. 126	p value
Age, mean (SD)	55 (12)	55 (12)	56 (13)	0.553
Disease duration (months), median (IQR)	94 (49-164)	94 (51-157)	94 (47-165)	0.650
BMI, mean (SD)	27.4 (5.01)	26.7 (5.28)	28.0 (4.68)	0.044
DAPSA, median (IQR)	10.2 (4.3-17.65)	13.45 (6.70-20.70)	7.29 (4-14.42)	<0.001
PASS "no", n. (%)	82/227 (36.1)	55/112 (49.1)	27/115 (23.5)	<0.001
Fibromyalgia, n. (%)	27 (11)	22 (18.5)	5 (4)	<0.001

BMI: Body Mass Index, DAPSA: Disease Activity for Psoriatic Arthritis; IQR: Inter Quartile range; PASS: Patient Acceptable Symptoms State; SD: Standard Deviation.

Table 2 Logistic regression analysis. Factors associated with PASS "no".

	PASS "no"	
Model 1*(male patients)	**OR (CI 95%)**	**p value**
DAPSA	1.31 (1.16-1.47)	<0.001
	PASS "no"	
Model 2*(female patients)	**OR (CI 95%)**	**p value**
DAPSA	2.01 (1.45-2.77)	<0.001
Fibromyalgia (yes)	1.34 (0.21-8.30)	0.715

*Both models were corrected for: age, disease duration, BMI and BSA.
All these predictors did not show any statistically significant association with PASS "no".

Conclusion: Female patients perceive their disease acceptable less than male. A higher disease activity (assessed by DAPSA), in particular for female patients, is the main factor to predict a state of non-acceptance of the disease.

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AB1132 PSYCHOMETRIC PROPERTIES OF SCREENING INSTRUMENTS FOR PSORIATIC ARTHRITIS

Keywords: Diagnostic tests, Psoriatic arthritis

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Background: There is a considerable delay in the diagnosis of psoriatic arthritis (PsA) and several screening tools have been proposed for fascilitating the diagnosis of PsA among patients with psoriasis.
Objectives: We aimed to identify all instruments that were developed for screening PsA among psoriasis patients, and to analyze the psychometric properties of these instruments.
Methods: A systematic literature search was conducted to identify all studies for developing and validating instruments that evaluate the presence of psoriatic arthritis among psoriasis patients. Psychometric properties of each instrument including construct validity, reproducibility, internal consistency, sensitivity to change and feasibility were extracted. Additionally, the reasons for false positivity and false negativity with each instrument were tabulated. Literature review and data extraction were performed by two independant reviewers and inconsistencies were resolved by a senior investigator. The systematic review protocol was registered in PROSPERO (CRD42021231734).
Results: The systematic review revealed 15 screening instruments that were evaluated in a total of 42 studies. Psychometric evaluation was available for only 5 of the instruments, assessed in 8 studies. Table shows the psychometric properties of these 5 instruments. Main reasons for false positivity were rheumatoid arthritis, osteoarthritis, mechanical pain and fibromiyalgia for PASE, PEST, CONTEST and EARP, and ankylosing spondylitis and osteoarthritis for PASQ. Main reasons for false negatives were axial involvement for ToPAS and PEST, peripheral involvement for SiPAT, PASE and PAQ, enthesal involvement for PEST, PASE and ToPAS. Among these instruments, EARP had low false negativity and high false positivity rates, while ToPAS II had both low false positivity and low false negativity compared to the other instruments.
Conclusion: Overall, the psychometric properties of PsA screening tools have not been adequately evaluated. There is an unmet need for studies evaluating and comparing psychometric properties of different screening tools in a large patient population, including patients with various PsA features such as enthesitis, axial and peripheral involvement.

Table.

Instrument	Number of studies	Internal consistency	Test-retest reliability	Construct Validity	Criterion validity	Interrater reliability	Sensitivity to change	Feasibility
PASE	6	good	good	good	Not provided	moderate	good	moderate
PEST	2	moderate	Not provided	Not provided	Not provided	Not provided	Not provided	Not provided
EARP	3	good	Not provided	Not provided	Not provided	Not provided	Not provided	good
TOPAS II	1	Not provided	Not provided	Not provided	Not provided	Not provided	Not provided	good
PsA-Disk	1	good	good	good	moderate	Not provided	Not provided	Not provided

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1133 AXIAL PSORIATIC ARTHRITIS: ISOLATED ENTITY OR PHENOTYPE FORM ONLY

Keywords: Psoriatic arthritis, Spondyloarthritis

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Background: The latest literature data increasingly emphasizes the axial involvement of Psoriatic Arthritis (PsA). The clinical and radiographic characteristics suggest that it is a new entity compared to the axial involvement of Ankylosing Spondylitis (AS), while therapeutic advances and cytokine targets suggest that it is a clinical form only.
Objectives: The objective of our study is to compare the characteristics of patients with axial PsA (axPsA) and axial AS (axAS).
Methods: Patients≥18 years old, with axPsA or axAS, during registration in the prospective monocentric register, between August 2012 and August 2022. A rheumatological investigation including: clinical, laboratory and genetic assessments as well as imaging with conventional radiography of pelvic and spine was performed.
Results: Of 250 patients (58 PsA vs 192 AS) with axial involvement, isolated axPsA patients were older at diagnosis (age of diagnosis of axial involvement was 35.8 vs 29.4). Patients with isolated axPsA were more likely to have: Less clinical inflammatory back pain compared with patients with isolated axAS: less limited schöber index (10/14 vs 10/12), finger-to-ground distance often equal to 0 cm in axPsA, less contracture of the paravertebral muscles, less reduction in thoracic expansion (4 vs 2 cm). Less limitation of inguinal pain (hip flexion 100 vs 70), a higher dactylitis count ±SD (0.3±1.2 vs 0.1±0.8), more nail lesions which could suggest looking for an association between nail damage and the presence of dactylitis in PsA, less extensive skin psoriasis [PASI= 2-13] and less presence of uveitis (18.96% (11/58) vs 23,95% (46/192)). Human Leucocyte Antigen (HLAB27) positivity was negatively associated with isolated axPsA disease (20 vs 78%). AxPsA were less frequently had radiographic sacroiliitis with unilateral/asymmetric pattern [On the X-ray, the SI were either normal or slightly modified, deliberately asymmetrical, rarely grade 4, the syndesmophytes were most often asymmetrical, coarse and of lumbar location, the heels were affected in less severe involvement, most often represented by simple shielding] and average patients showed slight spinal/pelvic radiographic progression (OR: 0,14; 95% CI: 0,01, 0,58). Finally, AxPsA had lower BASDAI and HAQ scores (OR 0.10, 95% CI 0,01to 0.47/ OR 0.03, 95% CI 0,00 to 0.17) and lower PRO evaluation (PRO spine pain 39.65 vs 49.47% and PRO fatigue 50 vs 52.6%).
Conclusion: Isolated axial PsA and AS are uncommon, axPsA has different clinical and radiographical characteristics when compared to AS. AxPsA is largely independent of HLAB27, it was associated with distinct radiographic ax AS features, increased spinal progression and low grade radiographic sacroiliitis as well as lower disease activity and impact scores.
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Disclosure of Interests: None Declared.
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AB1134 IMPACT OF INFLAMMATORY BOWEL DISEASE ON DAPSA REMISSION IN PATIENTS WITH PSORIATIC ARTHRITIS: A PROPENSITY SCORE-MATCHED RETROSPECTIVE ANALYSIS OF "CROSS" MULTIDISCIPLINARY PROJECT PATIENTS'.

Keywords: Psoriatic arthritis, Remission

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Background: Psoriatic Arthritis (PsA) is a chronic inflammatory disease and patients with PsA have an increased risk of developing inflammatory bowel disease (IBD) [1]. It's not clear whether the coexistence of IBDs in PsA patients on bDMARDs is associated with the achievement of clinical outcome.
Objectives: The aim of this study was to identify whether IBDs may impact on 12-month remission of articular disease assessed by Disease Activity Index for Psoriatic Arthritis (DAPSA) in PsA patients on monoclonal anti-TNFα or anti-IL12/23 therapy.
Methods: Patients with classified PsA according to CASPAR criteria with active skin psoriasis who underwent monoclonal anti-TNFα or anti IL12/23 treatment were retrospectively analyzed from January 2019 to May 2021 in our CROSS multidisciplinary outpatient's clinic. Clinical and demographic characteristics as disease severity indices (Disease Activity in Psoriatic Arthritis (DAPSA), Psoriasis Area and severity index (PASI), and Leeds Enthesitis Index LEI) were recorded. We identified those with IBDs (either Chron's disease or Ulcerative Colitis) and assess the intestinal disease activity by specific symptoms (abdominal pain, diarrhoea, intestinal bleeding) or instrumental findings. Propensity score-nearest-neighbour (1:1; caliper= 0,2) algorithm was used to provide two comparable groups. Paired t-Test was used to identify differences between outcome of interest at different follow-up periods and univariate and multivariable logistic regression models were run to identify predictors of DAPSA remission at 12-month follow-up.
Results: Of 123 patients with PsA on monoclonal bDMARDs therapy, the algorithm retrieved a sample of 74 patients (IBD group 37 patients, control group 37 patients)

matched by gender, BMI, age and DAPSA at bDMARDs start. In the PsA+IBD group mean age (± SD) was 55,21 ± 12,73, mean BMI was 27,70 ± 7,75, mean DAPSA was 17,28 ± 13,86, mean HAQ was 0,90 ± 0,74 and mean PASI was 1,13 ± 2,99. In PsA-only group mean age was 47,19 ± 10,23, mean BMI was 27,24 ± 5,10, mean DAPSA was 20,21 ± 12,58, mean HAQ was 0,92 ± 0,77 and mean PASI was 0,94 ± 2,25. The final multivariate model included DAPSA at baseline (OR 0,89 95% CI 0,82-0,97), duration of joint involvement (months, OR 0,99 95% CI, 0,98-0,99), HAQ (OR 0,66 95% CI 0,22-1,93) and presence/absence of IBD. HAQ was retained in the model as a potential confounder. PsA-only patients were more likely to achieve DAPSA remission at 12 month-follow up (OR=7,37; 95% CI 1,58-34,37).
Conclusion: In the management of PsA patients with IBD undergoing monoclonal anti-TNFα or anti-IL12/23 therapy, intestinal involvement has a negative influence on the clinical response of articular disease. For these patients clinicians should consider a low DAPSA at baseline and a shorter PsA disease duration as a predictor of 12-month DAPSA remission.
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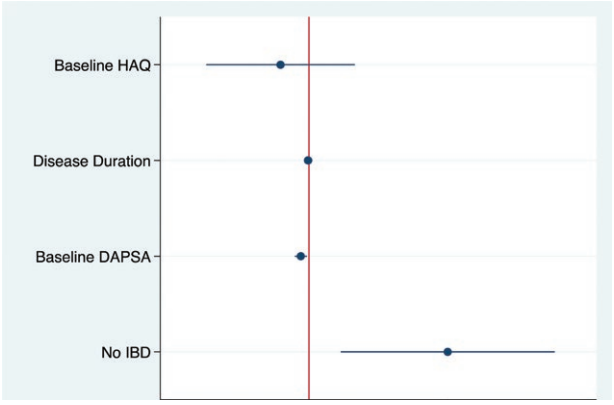


Figure 1.

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AB1135 CHARACTERIZING THE MINIMAL DISEASE ACTIVITY DOMAINS ACHIEVED BASED ON DIFFERENT TREATMENTS.

Keywords: Psoriatic arthritis, Outcome measures

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Background: Minimal Disease Activity (MDA) is a validated treatment response index for Psoriatic Arthritis (PsA). A status of MDA is reached when 5/7 domains are achieved. Even if MDA is worldwide used, both in clinical trials and in clinical practice, nowadays there are no studies that evaluated any differences in the MDA domains achievement based on various treatments.
Objectives: To characterize the MDA domains achieved based on treatment; to assess which treatment is associated with a higher probability to reach MDA status in clinical practice.
Methods: This is a cross sectional analysis of two longitudinal PsA cohorts. Inclusion criteria were: age ≥18 years, PsA diagnosis for at least 12 months, stable treatment for at least 6 months. Patients were grouped depending on the therapy: group 1: NSAIDs or COX2i or steroids, group 2: csDMARDs, group 3: TNFi, group 4: anti-IL 12-23 or 23, group 5: anti-IL17A, group 6: PD4i. For each group, MDA domains based on therapy were assessed. Logistic regression analysis was performed to assess the association between the treatment groups and the achievement of the MDA, independently by others confounding factors.
Results: Patients enrolled were 220. MDA was achieved in 45.8% of patients. In all treatment groups, the first three MDA domains more achieved were: BSA ≤3, SJC ≤1 and LEI ≤1, instead, in all groups (excepted for the PD4i) the MDA domains less frequently achieved were PtGA ≤2 cm and pain on VAS ≤1.5 cm (Table 1). Moreover, the logistic regression analysis showed a higher probability to achieve MDA for those patients in group 3 and 4 when compared with group 1, independently by age, sex and disease duration (Table 2).

Table 1. For each treatment group, table 1 shows the percentage of patients that achieved each domain.

Total patients n.220

	1st MDA achieved domain (%)	2nd MDA achieved domain (%)	3rd MDA achieved domain (%)	4th MDA achieved domain (%)	5th MDA achieved domain (%)	6th MDA achieved domain (%)	7th MDA achieved domain (%)
Group 1 n.23 (10.4%)	**BSA ≤ 3** (90.5)	**SJC ≤ 1** (77.3)	**LEI ≤ 1** (76.2)	**HAQ-DI ≤ 0.5** (61.9)	**TJC ≤ 1** (57.1)	**PtGA ≤ 2** (28.6)	**Pain on VAS ≤ 1.5** (19)
Group 2 n.24 (10.9%)	**LEI ≤ 1** (100)	**BSA ≤ 3** (90.9)	**SJC ≤ 1** (73.9)	**HAQ-DI ≤ 0.5** (59)	**TJC ≤ 1** (43.5)	**PtGA ≤ 2** (34.8)	**Pain on VAS ≤ 1.5** (30.4)
Group 3 n.89 (40.5%)	**LEI ≤ 1** (96.6)	**BSA ≤ 3** (87.6)	**SJC ≤ 1** (86.5)	**TJC ≤ 1** (58.4)	**HAQ-DI ≤ 0.5** (55.0)	**Pain on VAS ≤ 1.5** (40.4)	**PtGA ≤ 2** (32.6)
Group 4 n.14 (6.4%)	**LEI ≤ 1** (92.8)	**BSA ≤ 3** (85.7)	**SJC ≤ 1** (78.6)	**HAQ-DI ≤ 0.5** (64.3)	**TJC ≤ 1** (64.3)	**PtGA ≤ 2** (42.8)	**Pain on VAS ≤ 1.5** (42.8)
Group 5 n.59 (26.8%)	**SJC ≤ 1** (93.0)	**BSA ≤ 3** (91.2)	**LEI ≤ 1** (89.5)	**TJC ≤ 1** (56.1)	**HAQ-DI ≤ 0.5** (38.6)	**PtGA ≤ 2** (36.8)	**Pain on VAS ≤ 1.5** (24.6)
Group 6 n.11 (5.0%)	**LEI ≤ 1** (90)	**BSA ≤ 3** (90)	**SJC ≤ 1** (80)	**TJC ≤ 1** (40)	**PtGA < 2** (30)	**HAQ-DI ≤ 0.5** (20)	**Pain on VAS ≤ 1.5** (20)

BSA: Body Surface Area; HAQ-DI: Health Assessment Questionnaire Disability Index; LEI: Leeds Enthesitis Index; MDA: Minimal Disease Activity; VAS: Visual Analogue Scale, PtGA: Patient Global Assessment; SJC: Swollen Joint Count; TJC: tender Joint Count.

Table 2. Logistic regression analysis; dependent factor: MDA, independent factors: age, sex, disease duration treatment groups.

	MDA	
	OR (CI 95%)	**p value**
Age (years)	0.98 (0.96-1.01)	0.212
Sex (male)	3.54 (1.94-6.45)	<0.001
Disease durations (months)	0.99 (0.99-1.00)	0.337
Treatment group		
Group 2 (vs group 1)	2.10 (0.57-7.67)	0.260
Group 3 (vs group 1)	3.58 (1.26-10.20)	0.016
Group 4 (vs group 1)	5.47 (1.16-25.80)	0.031
Group 5 (vs group 1)	1.64 (0.54-4.89)	0.376
Group 6 (vs group 1)	1.37 (0.24-7.63)	0.719

Group 1: NSAIDs or COX2i or steroids, group 2: csDMARDs, group 3: TNFi, group 4: anti-IL 12-23 or anti-IL23, group 5: anti-IL17, group 6: PD4i; OR: Odds Ratio; CI 95%: Confidence Interval 95%.

Conclusion: In each treatment group, the MDA domains less frequently achieved were PtGA and pain, suggesting that the patient driven domains are still an unmet need. Moreover, the probability to achieve MDA status is higher in patients in group 3 and 4. However, larger and prospective studies needed to confirm these preliminary results, including also the newest therapies recently adopted for PsA.
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Acknowledgements: NIL.
Disclosure of Interests: silvia scriffignano: None declared, Fabio Massimo Perrotta Speakers bureau: Lilly, Novartis, AbbVie, Mauro Fatica: None declared, Paola Triggianese: None declared, Paola Conigliaro: None declared, Mario Ferraioli: None declared, Maria Sole Chimenti: None declared, Ennio Lubrano Speakers bureau: Lilly, Pfizer, AbbVie, Novartis, Janssen, Amgen, Consultant of: Lilly, Pfizer, AbbVie, Novartis, Janssen, Amgen.
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AB1136 MORTALITY IN PATIENTS WITH PSORIATIC ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Psoriatic arthritis, Prognostic factors

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Background: It remains debated whether patients with psoriatic arthritis (PsA) are at greater risk of mortality.

Objectives: We aimed to determine the magnitude of all-cause mortality risk in patients with PsA compared with the general population through a systematic review and meta-analysis.
Methods: We searched Pubmed, EMBASE and Cochrane Library for studies published from inception to April 2022. STATA meta-analysis software was used to calculate the pooled risk estimates for mortality (standardized mortality ratio, SMR). To address the potential heterogeneity, $\chi 2$ test, I2 statistics, subgroup analysis and sensitivity analysis were used.
Results: Our search identified 3235 articles, of which 18 studies with 134355 patients were eventually included for the analysis. A total of 7518 deaths were observed. Overall, we found a 1.13-fold increased risk of death in PsA patients when compared with the general population (meta-SMR: 1.13, 95% CI 1.03-1.25). Subgroup analyses showed that summary meta-SMR was higher in female patients (1.24 [95% CI 1.10-1.39]; I^2=49.7%) than male patients (0.92 [95% CI 0.62-1.37]; I^2=73.8%).
Conclusion: The existing data indicated approximately 13% increase of mortality among patients with PsA compared with the general population. More attention should be paid to those patients with risky characteristics.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3418

AB1137 BURDEN OF SKIN DISEASE IN PSORIATIC ARTHRITIS PATIENTS

Keywords: Patient reported outcomes, Psoriatic arthritis, Skin

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Background: Skin disease is one of the key domains of psoriatic disease (1) and most Psoriatic arthritis patients have skin psoriasis. However skin and joint disease are often managed separately by rheumatologists, dermatologists or primary care health care providers. This can lead to disjointed care, unmet need, and treatment decisions that don't take into account all aspects of this heterogeneous condition.
Objectives: We sought to evaluate how psoriatic skin disease is assessed and managed within our rheumatology services by identifying disease burden, approach to management and patient satisfaction.
Methods: In an existing psoriatic arthritis outpatient rheumatology clinic, patient swere asked to anonymously complete questionnaires on disease extent, management and satisfaction. Patients also completed dermatology quality of life index (DLQI) questionnaires. Case notes and clinic letters were reviewed to collect data relating to patient diagnosis, medications and extent of clinical assessment during consultations over a 4 month period.
Results: Questionnaires were returned by 30 patients. 72% reported problems with psoriasis, with scalp was the most commonly affected body area. 77% participants reported receiving medication to manage joints only, 4% for skin only, 19% for both joints and skin. 13 participants were receiving topical medication for PsA, with the majority being managed by their GP. From the survey, 47% of respondents were asked about their skin in the rheumatology clinic, and 30% were given advice on its management. Of the patients that completed DLQI questionnaires mean score was 3.9 (SD 3.4). Average satisfaction with psoriasis management was 5/10 (SDEV 3.6). Of the 59 consultations from which data was extracted, 54% of consultations discussed joints only, and 37% discussed both joints and skin (remainder no discussion documented). At 45% of appointments joints and skin were examined, and at 35% of appointments joints only were examined (remainder no examination documented).
Conclusion: Psoriatic skin disease appears to be a significant burden in this population of patients, affecting 72% of those surveyed. Over half of these patients required topical therapy to manage their psoriasis, with some requiring systemic treatments. Of these patients, most of the management of their skin condition was done by their GP, with the topic being brought up at rheumatology clinic in only half of cases. Less than half had skin examined at rheumatology clinic and less than a third were advised on management of their skin disease by their rheumatologist. Satisfaction levels with psoriasis management were fairly neutral overall. An integrated approach to care with a focus on opportunistic assessment should be encouraged and has potential to benefit both patient and clinician.
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Acknowledgements: NIL.
Disclosure of Interests: Michael Reed Speakers bureau: Novartis, Heather Boagey: None declared, Beatrice Milligan: None declared.
DOI: 10.1136/annrheumdis-2023-eular.3757

AB1138 DIFFICULT-TO-TREAT PSORIATIC ARTHRITIS: ANALYSIS OF A SINGLE-CENTER COHORT FROM NORTHERN ITALY

Keywords: Psoriatic arthritis, Descriptive studies, bDMARD

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Background: The multifaceted nature of psoriatic disease can potentially make its skin, articular, and extra-articular manifestation complex to manage. Biologic disease modifying anti-rheumatic drugs (bDMARDs) have dramatically improved the outcome of patients affected by chronic inflammatory arthritis. However, a satisfactory disease control is not achieved in a proportion of patients. While a "difficult-to-treat" (D2T) definition has been validated in rheumatoid arthritis (RA), it was only recently suggested for psoriatic arthritis (PsA) [1].
Objectives: Based on the proposed definition, we aimed to assess prevalence and characteristics of D2T-PsA in a single-center cohort.
Methods: We conducted a single-center, cross-sectional study. 269 consecutive, adult PsA patients receiving bDMARDs at a tertiary care, dedicated outpatient clinic were enrolled. Demographic, clinical, and clinimetric data, and the Health Assessment Questionnaire (HAQ) were gathered and depicted in Table 1. According to the aforementioned definition, D2T patients were identified as: 1) failure of ≥ 2 b/tsDMARDs (with different mechanisms of action- MoA) after failing csDMARD therapy; 2) signs suggestive of active/progressive disease (defined either as a DAPSA >14 or not achieving MDA; signs or symptoms suggestive of active disease; a rapid radiographic progression; a reduction of quality of life due to PsA symptoms); 3) disease management perceived as problematic by rheumatologists or patients (all three criteria must be met to define D2T patients). Comparison between D2T and non-D2T patients was performed with univariate analyses.
Results: Among 269 PsA patients, only 8 (2.9%) fulfilled D2T definition. In bivariate analysis, D2T patients presented higher rate of osteoarthritis (62.5% vs 24.9%; *p=0.03*), fibromyalgia (62.5% vs 14.94%; *p<0.004*), and therapy with steroids (50% vs 12.1%; *p=0.008*). Furthermore, D2T patients presented significantly higher patient global assessment (PGA 0-10) (7.5 vs 2.00; *p<0.001*) and VAS pain 0-10 (8.00 vs 2.00; *p<0.001*). Among non-D2T patients, 24 were in moderate disease activity (9.19%). Due to the unbalance between the groups numerosity, multivariate analysis was not feasible.
Conclusion: Only few patients satisfied the PsA-D2T definition in our cohort; application of a RA-like D2T definition to a heterogeneous disease as PsA should be discussed more broadly in the future.

Table 1.

	Study population (N=269)
Gender (male)	140 (52.0%)
Age (years)	52.63 ± 11.87
Smokers	68 (25.3%)
BMI	22.49 (CI 20.27 – 22.91)
Disease duration (months)	154.5 (CI 88.25 – 251,75)
Disease subset	
Axial	29 (10.8%)
Peripheral	194 (72.1%)
Axial+peripheral	37 (13.8%)
Enthesitic	9 (3.3%)
Skin psoriasis	205 (76.2%)
Vulgaris	167 (81.5%)
Scalp	37 (18.0%)
Nail	31 (15.1%)
Palmo-plantar	17 (8.3%)
Extra-articular manifestations	
IBD	4 (1.5%)
Uveitis	6 (2.2%)
Dactilitis	40 (14.9%)
Charlson Comorbidity Index	1 (CI 1 - 2)
Fibromyalgia	44 (16.4%)
DAPSA (median)	4.21 (CI 1.11 – 9.89)
Remission	120 (44.6%)
LDA	237 (88.1%)
MDA	238 (88.5%)
BSA>3%	9 (3.3%)
LEI <1	255 (94.8%)
HAQ (median)	0.125 (CI 0 – 0,375)
HAQ>0,5	59 (21.9%)
Steroid use	32 (11.9%)
csDMARD failure	178 (66.2%)
>2 previous bDMARDs	45 (16.7%)
>2 previous MoA	27 (10.0%)

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Acknowledgements: NIL.
Disclosure of Interests: Gilberto Cincinelli: None declared, Matteo Ferrito: None declared, Marco Pandolfi: None declared, Martina Biggioggero Speakers bureau: Galapagos, Silvia Casari: None declared, Martina Cornalba: None declared, Chiara Crotti: None declared, Francesca Desiati: None declared, Ennio Giulio Favalli Speakers bureau: AbbVie, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Consultant of: AbbVie, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB, Maria Manara Speakers bureau: Novartis, Angelini, Consultant of: Lilly, MSD, Roberto Caporali Speakers bureau: AbbVie, Amgen, BMS, Celltrion, Fresenius, Galapagos, Janssen, Lilly, Novartis, Pfizer, UCB, Consultant of: AbbVie, Fresenius, Galapagos, Lilly, Novartis, Pfizer, UCB.
DOI: 10.1136/annrheumdis-2023-eular.3948

AB1139 ASSOCIATION BETWEEN TRIGLYCERIDE-GLUCOSE INDEX AND CAROTID ATHEROSCLEROSIS IN PATIENTS WITH PSORIATIC ARTHRITIS: A CROSS-SECTIONAL STUDY

Keywords: Psoriatic arthritis, Epidemiology, Ultrasound

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Background: The triglyceride-glucose (TyG) index, proposed as a surrogate marker for insulin resistance, appeared to be a good indicator of clinically overt cardiovascular events and subclinical atherosclerosis in general population.
Objectives: We aimed to investigate the correlation of TyG index with atherosclerotic risk among patients with psoriatic arthritis (PsA).
Methods: This cross-sectional study included 165 consecutive PsA patients receiving carotid ultrasonography with integrated TyG index, calculated as ln [fasting triglycerides (mg/dL)×fasting glucose (mg/dL)/2]. Logistic regression models were applied to analyze the association of TyG index as continuous variables and tertiles with carotid atherosclerosis and carotid artery plaque.
Results: Overall, PsA patients with carotid atherosclerosis had substantially higher TyG index than those without (8.82±0.50 vs. 8.54±0.55, p=0.002). The frequency of carotid atherosclerosis was increased with increases in TyG index tertiles, showing 14.8%, 34.5%, 44.6% for tertile 1, 2 and 3, respectively (p=0.003). Multivariate logistic analyses showed that each 1-unit increase in TyG index was significantly associated with prevalent carotid atherosclerosis (unadjusted OR 2.65 [1.39-5.05]; fully-adjusted OR 2.69 [1.02-7.11]). Compared to patients with tertile 1 of TyG index, the unadjusted and fully-adjusted OR for occurrence of carotid atherosclerosis were 4.64 (1.85-11.60) and 5.10 (1.54-16.93) in patients with tertile 3. Similarly, higher prevalent carotid artery plaque was observed with increasing TyG index (unadjusted OR 3.11 [1.54-6.26]; fully-adjusted OR 3.61 [1.15-11.38]) or with tertile 3 vs. tertile 1 (unadjusted OR 10.20 [2.83-36.82]; fully-adjusted OR 17.89 [2.88-111.11]). Additionally, TyG index provided incremental predictive capacity beyond established risk factors, shown by an increase in discrimination ability (all P < 0.001).
Conclusion: TyG index was positively correlated with the burden of atherosclerosis in PsA patients, independent of traditional cardiovascular risk factors and psoriatic-related factors. These findings suggest that TyG index may be a promising atherosclerotic marker for PsA population.

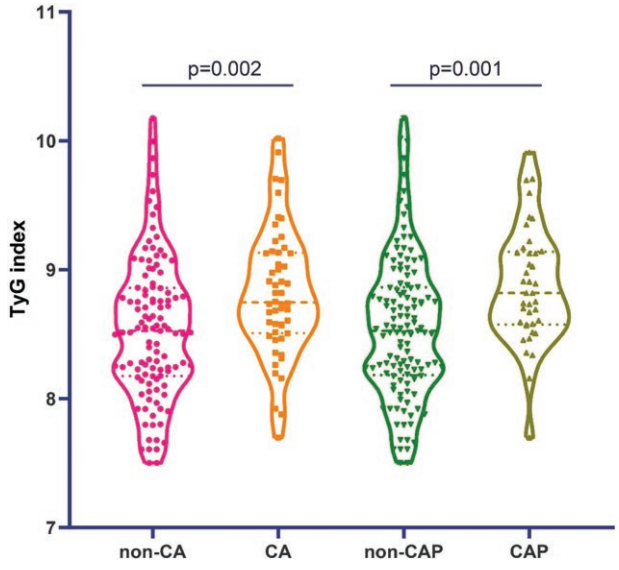


Figure 1. The level of TyG index in patients with psoriatic arthritis, stratified by carotid atherosclerosis (CA), carotid artery plaque (CAP).

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1140 TREATMENT WITH TNF AND IL17 INHIBITORS DIFFERENTLY AFFECTS SERUM LIPID PROFILE AND TH1/TH2 IMMUNE RESPONSE IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS.

Keywords: bDMARD, Psoriatic arthritis, Cardiovascular disease

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Background: Psoriatic arthritis (PsA) is a form of spondyloarthritis (SpA) associated with alterations to the serum lipid profile. Current research suggests that biological treatment with TNF and IL-17 inhibitors differently affects the lipid profile and Th cells populations in PsA and ankylosing spondylitis (AS)
Objectives: To investigate the relationship between lipid profile, disease activity and T-cells phenotype changes in patients with SpAs treated with TNF and IL-17 inhibitors.
Methods: A group of 36 SpA patients (AS 14, PsA 22) with high disease activity were assessed at the start and after 6 months of anti TNF (n=19) and anti IL17 (n=17) treatment. Serum lipid profile: triglycerides (TG), total cholesterol (TC), low (LDL), and high-density lipoproteins (HDL), nonHDL, VLDL levels and atherogenic index (AI) were evaluated. Frequency of Th1, Th2, Th1/Th17, Th17 and T regulatory cells (Tregs) was determined by flow cytometry. The Spearman's rank test was used for the statistical analysis of correlations, and the Wilcoxon rank test for dependent sample testing. All data are given as medians and the absolute and relative difference between two variables are expressed as delta.
Results: A significant reduction in disease activity was observed in all treated patients: DAPSA (32,5 vs 4); BASDAI (6,8 vs 1,5; p<0,01), ESR (15 vs 5mm/h; p<0,01) and CRP (6 vs 1mg/l; p=0,03). In all 36 patients, the reduction of disease activity was followed by a mild decrease of TC (205 vs 195mg/dL p<0,01), LDL (120 vs 110mg/dL p<0,02) and non-HDL levels (18 vs 5 vs 12mg/dL, p<0,05). In PsA patients treated with IL-17 inhibitor (n=13) we found a statistically significant, more pronounced decrease in lipid levels compared to AS and PsA patients treated with anti-TNFs i.e: delta of TC (19 vs 12 vs 12mg/dLp=0,03), LDL (23 vs 15 vs 10mg/dL p<0,05) and VLDL (11 vs 4 vs 4,5mg/dl p=0,02). In addition, in PsA group (n=22) after 6 months of treatment, we found reduction of TG (144 vs 94mg/dL p=0,05), VLDL (28,8 vs 20,6mg/dL p=0,04) levels and improvement of AI (4,4 vs 3,5 p=0,03), also deltas of DAPSA correlated positively with deltas of TC (rho=0,6 p=0,03) and nonHDL (rho=0,5 p=0,04). In flow cytometry after 6 months of treatment of all 36 patients we observed a rise of Th1 (11,3 vs 12,6% p=0,05) and a decrease of Th2 (5,7 vs 4,7% p=0,03) cells with almost no change in Treg cells (5,3 vs 5,35%). In PsA patients (n=22) we have found correlations (p<0,05) between decreases of CD4+CD25+ counts and levels of TC (rho=0,6), nonHDL (rho=0,5), AI (rho=0,6) and DAPSA (rho=0,5). Effectiveness of treatment with iTNFs and iIL-17s was comparable in PsA or AS, but some differences were observed in alterations to limphocyte profile. Patients treated with anti-IL-17 (PsA 13/ AS 4) showed a more pronounced increase in the Th1/Th17-like cell percentage (9,3 vs 13,5%; p=0,04) with a decrease of Th2 cells (7,3 vs 3,5%p=0,03) and concomitant increase in Th1 cells (11 vs 13,8%). In patients treated with IL-17 inhibitors increase of Th1 cells correlated negatively (p<0,05) with TG (rho=-0,6), nonHDL (rho=-0,7), LDL(rho=-0,6) levels, VLDL(rho=-0,6) and positively with HDL (rho=0,4). In PsA patients Th1 cells correlated with DAPSA (rho=-0,4). Patients treated with antiTNFs (AS 10/PsA 9) revealed an increase of Th1 cells (10,5 vs 12% p=0,04) and also a decrease of CD4+CD25+ (23 vs 14,5%; p=0,008), but no correlations with lipid profile were found.
Conclusion: Anti TNF and anti IL17 treatment distinctively affects lipid profile and T Cell balance especially in PsA. Patients with SpAs treated with biologics presented a tendency towards reduction of TC and LDL concentrations, but in PsA those changes were stronger with additional reduction of VLDL, non-HDL and TG levels. Alterations in the lipid profile correlate with disease activity in PsA and with a shift in Th cells (increase in the Th1/Th2 ratio with a decrease in the percentage of activated CD4+CD25+ T cells), which was not observed in AS.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1141 **PREDICTORS OF X-RAY PROGRESSION IN PATIENTS WITH PSORIATIC ARTHRITIS**

Keywords: Prognostic factors, Psoriatic arthritis, Biomarkers

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Background: Psoriasis arthritis (PsA) is a systemic chronic inflammatory disease, which leads to irreversible destruction of the joints. Multiple factors drive the development of this heterogeneous disease including genetic predisposition, environmental triggers, and immunologic dysfunction. Even structural damage differs significantly between patients, with a subset of patients suffering from severe and rapid (rheumatoid arthritis-like) bone destruction (arthritis mutilans), while others experience only modest signs of bone damage, or develop new bone formation.[1]
Objectives: The study aims to identify potential predictors for radiographic such as clinical, radiographic, and laboratory parameters.
Methods: In this retrospective data analysis 231 patients with PsA and at least two available x-rays were included. Radiographs were scored according to Sharp-van-der-Heijde-total Score (mSvdHTH) modified for PsA and a mean annual progression (MAP) rate was calculated by dividing the change in mSvdHTS between two x-rays number of years between them. For each patient, the median of the annual progression rates was calculated. Patients were grouped in no progressors (MAP ≤ 0.5), low progressors (MAP 0.5 < MAP ≤ 2.5) and high progressors (MAP > 2.5). Clinical data such as the clinical disease activity index (CDAI), radiographic data and laboratory data (CRP, ESR, C-terminal Telopeptide) were analysed for their predictive value of radiographic progression using parametric and non-parametric statistical analysis according to the distribution of data. For correlation analysis Spearman´s rank coefficient was used. For group analysis ANOVA was used. Dichotomous variables such as gender or nail involvement were analysed using χ^2-test. Multiple linear regression analysis was used to identify factors influencing radiographic progression.
Results: The mean baseline mSvdHTS in high progressors was 41.59 (43.53), 19.89 (34.93) in low progressors and 16.25 (26.77) in non-progressors. Baseline mSvdHTS was significantly correlated with MAP (ρ=0.27, p=0.002) rate. Group analysis comparing clinical and laboratory parameters in patients again showed significant difference baseline mSvdHTS. The high progression cohort also exhibits greater mean CRP, ESR, CDAI, median first year CDAI, TJC68, SJC66 and a higher percentage of nail involvement than low- or non-progressors but no statistically significant result was found. In a multiple linear regression analysis baseline SvdHS (β = 0.51, 95%CI 0.28-0.73, p=<0.001), median CDAI in the first year after baseline (β = 0.51, 95%CI 0.19-0.83, p=0.018) and CDAI at baseline (β = -0.62, 95%CI -1.05 – -0.19, p=0.043) were significantly associated with mean annual progression. No association was found between MAP and bone turnover markers.
Conclusion: This study shows a clear association of Sharp-van-der-Heijde score at baseline with future radiographic progression. Moreover, the median CDAI in the first year after baseline was associated with radiographic progression.
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AB1142 **DOES OBESITY PLAY A ROLE IN FOOT INVOLVEMENT IN PSORIATIC ARTHRITIS?**

Keywords: Spondyloarthritis, Comorbidities, Psoriatic arthritis

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Background: Several studies have reported a higher prevalence of obesity in Psoriatic Arthritis (PsA)[1]. Obesity may lead to more weight on the joints, namely on the ankle/foot joints, altered mechanics, and repetitive micro-trauma. Foot involvement is common in PsA, including arthritis, dystrophic nails, toe dactylitis and Achilles enthesitis. Obesity has been found to be associated with higher disease activity and worse functionality scores in PsA patients. [1]
Objectives: The purpose of this study was to evaluate the role of obesity in foot involvement in PsA patients.
Methods: A retrospective study including patients with PsA (all patients fulfill CASPAR criteria) followed from January to May 2022, from a Rheumatology Clinic. Patients were divided into two groups: with current or previous foot involvement (assessed clinically or by ultrasound) (group 1) and without current or previous foot involvement (group 2). Sociodemographic, clinical and laboratory data were collected. Obesity was defined as a body mass index greater than or equal to 30 Kg/m^2 and multimorbidity was defined as 2 or more comorbidities. Descriptive analysis was performed using means and standard deviation (SD), medians and Interquartile. range (IQR) for continuous data, and frequencies and percentages for qualitative variables. Clinical, laboratory and radiological findings were compared between patients with and without foot. involvement using parametric and non-parametric tests, with a p-value ≤ 0.05.
Results: A total of 154 patients were enrolled (mean age of 57.08 (±11.54) years and 39.6% were women). Foot involvement was found in 110 patients (71.40%). Obesity was more prevalent among patients with foot involvement – group 1 (40.90% VS 13.64%; p=0.001). Enthesitis was found in 35.10 % of patients with Achilles enthesitis (28%) as the most frequent manifestation. PsA patients in group 1 who were obese had higher prevalence of Achilles enthesitis (p= 0.01). 18.18% of patients had current/previous toe dactylitis and dystrophic nails were found in 37.7% of patients (no differences were encountered between obese and non-obese patients). Multimorbidity were more frequent in PsA patients with foot involvement- group 1 (p=0.04). We found a higher frequency of extra-articular manifestations and higher HAQ disability index values in patients with foot involvement (p=0.03 and p<0.001, respectively). Although we did not find statistically significant differences in the HAQ disability index between obese and non-obese patients with foot involvement, there was a predominance of disability in obese patients. PsA patients in group 1 who are obese have higher C-reactive protein (p=0.01) and higher consumption of non-steroidal anti-inflammatory drugs (p=0.02). We did not find statistically significant differences in swollen and tender joint counts, in conventional and biological DMARDS between obese and non-obese patients in group 1.
Conclusion: Obesity was more prevalent among PsA patients with foot involvement, suggesting its presence may enhance and contribute for foot complaints in these patients. Patients with foot involvement had higher HAQ disability index levels, reflecting the negative impact of foot involvement in daily functionality in these patients. Our study highlights the importance of obesity management in PsA patients with foot involvement. Further studies are needed to develop weight reduction strategies that can applied in clinical practice, in order to improve outcomes related to PsA.
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Disclosure of Interests: None Declared.
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AB1143 **MIR-10B EXPRESSION IN PSORIATIC ARTHRITIS PATIENTS WITH DAPSA SCORE REMISSION OR LOW DISEASE ACTIVITY**

Keywords: Biomarkers, Psoriatic arthritis

Keywords: Psoriatic arthritis, miRNA, Biomarkers

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Background: Psoriatic arthritis (PsA) is a heterogeneous inflammatory rheumatologic disease associated with psoriasis. The etiopathogenesis of PsA has not been fully elucidated. Although activity scores are used in the follow-up of patients, reliable biomarkers are not yet available. MicroRNAs (miRNA) are non-coding RNA oligonucleotides whose cellular expression levels change in inflammatory and autoimmune diseases and provide gene expression regulation. miRNAs are being investigated for their potential biomarker properties in the diagnosis and follow-up of psoriatic arthritis.
Objectives: In this context, the current study aimed to determine the changes in mir-10b expression level in patients with PsA who have remission/low disease activity according to DAPSA score and in age-sex matched healthy population.

Methods: Ethics committee approval was obtained from Sakarya University Ethics Committee for the study (E-71522473-050.01.04-15102135). RNA isolation, cDNA synthesis and RT-PCR analysis were performed in 30 PsA patients (19 Female and 11 Males) and age/sex matched control group (20 Females and 11 Males) with DAPSA scores in remission or low disease activity, who applied to Sakarya University Internal Medicine Rheumatology Clinic between January 2019 and February 21, miR-10b expression levels. U6 was used as internal control. IBM SPSS Statistics 26 program was used for statistical analysis.

Results: The mean age of the patients with psoriatic arthritis was 47.4±13.4, and the control group was 46.6±12.9 (p=0.78). No gender difference was analyzed between the two groups. (p=0.92).In addition, it was analyzed that the miR-10b expression level was 0.90-fold in PsA patients compared to the control group, and the expression level did not change significantly compared to the control group (p=0.53).

Conclusion: In our study, no statistically significant difference was observed in terms of miR-10b expression in PsA patients with DAPSA remission-low disease activity when compared to healthy controls. Further studies are needed in patients with moderate and high activity psoriatic arthritis.

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AB1144 PREVALENCE OF SECONDARY SJOGREN'S SYNDROME IN PSORIASIS AND PSORIATIC ARTHRITIS AND ITS RELATIONSHIP WITH DISEASE CHARACTERISTICS

Keywords: Sjögren syndrome, Psoriatic arthritis

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Background: Secondary Sjögren's syndrome (sSS) accompanies many systemic rheumatic diseases at certain rates, including axial spondyloarthritis (axSpA).[1] There are some case reports in which psoriasis or psoriatic arthritis (PsA) with sSS co-existence.[2] However, the prevalence of sSS in psoriasis (PsO) and PsA is not fully addressed. Additionally, clinical and laboratory features that may be associated with sSS, and whether arthritis and sSS are related are not known.

Objectives: This study aims to assess the prevalence of sSS in patients with non-arthritic psoriasis and PsA and illuminate disease features associated with sSS.

Methods: Psoriasis patients diagnosed by a dermatologist and patients classified as PsA who fulfilled the CASPAR criteria were questioned for sicca symptoms consistent with the 2002 American-European Sjogren's Syndrome Consensus Criteria (AECG). The salivary gland scintigraphy of the patients with oral dryness was performed and the unstimulated salivary flow rate (SFR) was measured. Schirmer's test was performed on patients with dry eyes. Anti-Ro antibodies were measured and minor salivary gland biopsies were performed in patients with sicca detected by objective measurements. After the evaluation of the patients, the sSS was classified according to the 2002 AECG. The frequency of sSS in non-arthritic psoriasis and PsA patients were compared. In addition, PsA patients were divided into two groups according to the presence and absence of sSS. PsA-specific characteristics in these two groups were compared.

Results: Of the 184 psoriasis patients who participated in the study, 112 had PsA, and 72 had psoriasis without arthritis. There was no significant age difference between non-arthritic psoriasis and PsA patients (48.3±11.9 and 49.4±13.5, respectively; p=0.59) Similarly, female to male ratio (rates (%): non-arthritic psoriasis: 43/29 (59.7/40.3) PsA: 82/30 (73/27), respectively; p= 0.08) and age of onset of psoriatic skin changes (mean (SD) of non-arthritic psoriasis: 30.3 ±10.9, PsA: 29.4 ±13.2, respectively; p=0.68) did not differ between non-arthritic psoriasis and PsA patients. sSS was more prevalent in PsA patients when compared with the non-arthritic psoriasis group (PsA: 20 (%17.9), non-arthritic psoriasis: 1 (%1.3), p<0.001). None of the patients had a previous diagnosis of sSS. Of the patients with sSS (n=20), 18 had salivary gland involvement detected in salivary gland scintigraphy, four Anti-Ro positivity, and three low unstimulated SFR. All PsA patients with sSS (sSS/PsA) had a positive Schirmer test. sSS/PsA patients were significantly more positive for ANA and had plantar fasciitis more frequently than PsA patients without sSS (Table 1). Although not statistically significant, the age of onset of joint involvement in sSS/PsA patients was higher and was treated less with biological therapy (Table 1).

Conclusion: Secondary Sjögren's syndrome is part of the clinical picture in a substantial proportion of PsA patients and its absence in non-arthritic PsO implies that sSS is arthritis associated. Whether the type of arthritis in sSS/PsA patients has a pattern necessitates larger patient numbers. A higher rate of ANA positivity may suggest the role of B lymphocytes in the progression from PsO to PsA.

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Table 1 - Comparison of PsA patients with and without sSS

	Presence of sSS n=20	Absence of sSS n=92	p
Age mean (SD)	53.9	48.4	0.09
Female/Male ratio	18/2	61/27	0.08
Age of onset of skin involvements mean (SD)	30.6	29.4	0.74
Age of onset of joint involvements mean (SD)	42.6	37.4	0.09
Axial Involvement n (%)	6 (35.3)	25 (29.4)	0.77
Polyarthritis n (%)	4 (22.2)	11 (14.9)	0.29
Heel Enthesitis n (%)	5 (31.3)	12 (21.4)	0.19
Plantar Fasciitis n (%)	5 (31.3)	6 (9)	***0.03***
RF positivity n (%)	1 (7.7)	1 (1.9)	0.36
ANA positivity n (%)	10 (55.6)	12 (27.2)	***0.04***
Biological therapy ever n (%)	10 (50)	63 (72.4)	0.06

sSS: Secondary Sjögren's syndrome, SD: Standard deviation, RF: Rheumatoid Factor, ANA: Anti-Nuclear Antibody, PsA: Psoriatic Arthritis

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Disclosure of Interests: None Declared.

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AB1145 QUALITY INDICATORS: APPLYING QUALITY MEASURES TO IMPROVE SERVICES AND PATIENT OUTCOMES. A QUALITY IMPROVEMENT INITIATIVE

Keywords: Rheumatoid arthritis, Quality of care, Psoriatic arthritis

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Background: The use of quality-of-care indicators is an important strategy to measure and evaluate if the care provided in the standard clinical setting adheres to current evidence informed best practices. Achievement of quality indicators is often reported as a quality score (%). Quality indicators are often developed from guidelines, systematic literature reviews, or expert panel consensus using a systematic approach. The recently developed national guidelines for inflammatory arthritis [1, 2] provided the fundamentals of quality indicators of inflammatory arthritis.
Objectives: To evaluate quality indicators for inflammatory, their use in routine clinical practice reflecting the processes of clinical care and improvement in outcomes.
Methods: Quality measurement was carried out across 5 centers based on six domains of quality: 1. Structure (Describes the innate characteristics of providers and the system and the organisational aspects of care), 2. Process (Assesses actual healthcare service delivered to patients by healthcare providers), 3. Patient experience (Describes the patient's perception of quality of care)[3], 4. Outcome (Assesses the end result or the final goals of the delivered care), 5. Access (Evaluates the provision of timely and appropriate healthcare), 6. Efficiency (Describes the relationship between clinical performance and resource use). Data were logged based on patients' recorded data.
Results: Inflammatory arthritis services are provided in 100% of the centers. 88.3% of the participants voted that they do implement "Treat to Target" approach and quality indicators for the management of inflammatory arthritis in their standard practice. Patient experience was rated positive in 63% whereas Timely treatment target was recorded in 74%. Efficiency evaluation revealed constrains attributed to lack of insurance cover of cost of some recommendations (72.7%).
Conclusion: Irrespective of resource and infrastructure constraints, assessment of all the relevant domains of care, revealed improvement and strengths of all the other measures. Results revealed that the treating rheumatologists not only do adhere to quality indicators required for the management of inflammatory arthritis, but also provide timely and appropriate healthcare that has been well received by the patients. Such results are vital as quality measurement in rheumatology is focused primarily on processes of care, consequently, process measurement facilitates implementing actionable targets for improvement instead of focussing solely on outcomes of care.
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AB1146 PHYSICIAN ADHERENCE TO CLINICAL GUIDELINES IN RHEUMATOLOGY: CAN IT HELP PROVIDING EVIDENCE-BASED, STANDARDIZED CLINICAL DECISIONS.

Keywords: Rheumatoid arthritis, Remission, Psoriatic arthritis

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Background: Clinical practice guidelines serve many targets, including guiding clinical decision-making process based on best evidence, standardized patient care, improving provider performance, setting standards of practice, and reducing variability in practice. Despite their vital role in standard practice, adherence to guidelines has been reported to be suboptimal. Overall, no information is available of how rheumatologists would interact with recently published national clinical practice guidelines [1, 2].
Objectives: To answer three principal research questions: (i) how far do rheumatologists deviate from the recommended clinical guidelines (ii) What are the major barriers to guidelines adherence? and (iii) What are the factors that would improve guideline adherence?
Methods: This was Cross sectional multi-center, survey-based study. Rheumatologists in 12-centers, covering both the north and south of Egypt, were invited to participate in the study. All outcomes were measured using a validated survey tool. The primary outcome of interest was barriers to guideline adherence. Secondary outcomes included general attitudes toward guidelines and factors that could improve adherence to guidelines. Outcomes were measured by the survey tool. All outcomes were reported on a numerical visual analogue scale (0-100). 55% was defined a priori as a threshold to infer strong association between physician responses and category of interest. P-value <0.05 was used for statistical significance.
Results: 77 rheumatologists participated in the survey. Analysis of the participants experience revealed a broad range of knowledge with 18.2% were still in training (residents), 10.4% have 1-3 years of experience, 14.3% have 3-5 years' experience, 24.7% have 5-10 years of experience whereas 32.5% had more than 10-years of experience. The majority 65% have not been ever involved in clinical guidelines development ($p < 0.001$). 74% agreed/ strongly agreed that they were adequately trained accessing and applying guidelines in their standard practice, whereas 6.5% only disagreed ($p< 0.001$). 58.4% rated their adherence to clinical practice guidelines as high/very high, whereas 38% rated it as average and 2.6% rated it as low ($p< 0.01$). In concordance, 88.3% of the participants voted that they do implement "Treat to Target" approach for the management in their standard practice ($p< 0.001$). Major barriers to guidelines adherence were time constrains due to clinical documents (53.2%), access to relevant guidelines at the point of care (48.1%) as well as lack of insurance cover of cost of some recommendations (72.7%). Factors that would improve guideline adherence included: improved focus on guidelines during training (88.3%), access to relevant guidelines at the point of care (87.4%)
Conclusion: Guidelines have enhanced physician adherence to management recommendations and provide evidence-based, standardized clinical decisions. Results of the work revealed significantly less tendency to deviate from the national guidelines among rheumatologists. Few areas of improvement have been identified including implementing the guidelines in trainee's education courses and consistent access to relevant guidelines at the points of care.
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[2] El Miedany Y. et al. Psoriatic arthritis treatment to the target: a consensus, evidence-based clinical practice recommendations for the management of psoriatic arthritis and its concomitant clinical manifestations. Egypt Rheumatol Rehabil 2022; 49: 32.
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Disclosure of Interests: None Declared.
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AB1147 THE COMPARATIVE PERFORMANCE OF THREE SCREENING QUESTIONNAIRES FOR PSORIATIC ARTHRITIS IN A PRIMARY CARE SURVEILLANCE PROGRAM

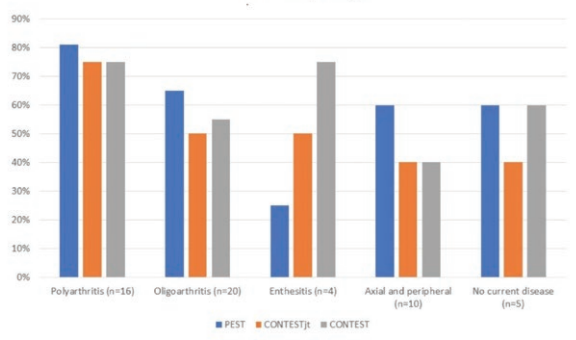
Keywords: Epidemiology, Non-pharmacological interventions, Psoriatic arthritis

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Background: There are considerable delays in the diagnosis of psoriatic arthritis (PsA) and earlier diagnosis is likely to lead to better outcomes.
Objectives: The aim of this study was to compare the performance of three PsA screening questionnaires in a primary care psoriasis surveillance program.
Methods: Participants with psoriasis, and not known to have psoriatic arthritis (PsA), were identified from general practice databases and invited to attend a secondary care centre for a clinical assessment. The three patient-completed screening questionnaires (PEST, CONTEST, and CONTEST with a manikin CONTESTjt) were administered along with other patient reported measures and

a clinical examination of skin and joints was performed. Participants who demonstrated signs of inflammatory arthritis suggestive of PsA were referred, via their GP, for a further assessment in a secondary care rheumatology clinic.
Results: A total of 791 participants attended the screening visit and 165 participants were judged to have signs and symptoms of inflammatory arthritis, of which 150 were referred for assessment. Of these 126 were seen and 48 were diagnosed with PsA. The results for each questionnaire were as follows: PEST: Sensitivity 0.625 (95% CI 0.482 to 0.749), specificity 0.757 (0.724 to 0.787). CONTEST: Sensitivity 0.604 (0.461 to 0.731), specificity 0.768 (0.736 to 0.798). CONTESTjt: Sensitivity 0.542 (0.401 to 0.676), specificity 0.834 (0.805 to 0.859). There was no evidence of any significant difference in sensitivity between questionnaires, but CONTESTjt demonstrated marginally superior specificity to PEST. However, the area under the ROC curve was similar for all three instruments. PEST was better at identifying cases of peripheral arthritis, including those with axial involvement, but the CONTEST questionnaires were better at identifying cases of peripheral enthesitis, though numbers were small (Figure 1).
Conclusion: Minimal differences in discriminative ability between the three screening questionnaires were found in this study and no specific recommendation can be made based on these results. The choice of which instrument to choose will depend on other factors, such as simplicity and low patient burden.
References: ni.l.

Figure one. Proportion of patients with PsA testing positive on screening questionnaires according to disease phenotype



No current disease Includes those with no current peripheral disease (1 with pure axial, 3 with no current peripheral disease or axial disease, 2 with no current peripheral disease and axial disease status not known)

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AB1148

PATIENT AND PHYSICIAN GLOBAL ASSESSMENT OF PSORIATIC ARTHRITIS APPEAR MORE IN AGREEMENT IN ARAB COUNTRIES THAN PREVIOUSLY REPORTED ELSEWHERE – AN INTERNATIONAL STUDY UNDER THE AEGIS OF ARLAR

Keywords: Psoriatic arthritis

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Background: In patients with psoriatic arthritis (PsA), discordance between physicians and patients when assessing disease activity has been described as frequent, mainly in European and North American studies. This discordance may negatively impact treatment adherence and shared decision-making processes. Culture and beliefs influence patients' perceptions of health.
Objectives: To evaluate the concordance between patient- (PGA) and physician-global assessment (PhGA) of PsA disease activity and its association with demographic and disease characteristics in a multinational group of patients from Arab countries.
Methods: This multicentric multinational cross-sectional study was conducted in thirteen Arab countries by the Arab League of Associations of Rheumatology (ArLAR) research group (ARCH). During a single routine visit, patients and physicians were requested to rate the PsA disease activity on a numeric scale from 0 (no activity) to 10 (worse activity). In addition, demographic and disease data were collected, as well as PGA and PhGA for psoriasis (PsO) activity, Health Assessment Questionnaire (HAQ), Fibromyalgia Rapid Screening Tool (FiRST), Patient Health Questionnaire (PHQ4) and Disease Activity in Psoriatic Arthritis (DAPSA). First, the correlation between PGA and PhGA for PsA and PsO disease activity was assessed statistically using the Spearman correlation coefficient (PsA and PsA) and graphically using the Bland and Altman method (PsA). Second, concordance between the PGA and PhGA PsA activity (defined as a difference between -2 and 2) was calculated and correlated with demographic and disease factors using multivariable binary logistic regression.
Results: The study included 554 patients from thirteen countries: mean age 45 years (SD 13), 57% females, median disease duration four years (IQR 2-9); 89.2% had skin PsO, and 43.5% had nail PsO. The disease was active overall: mean DAPSA was 19.3 (SD 16.1), HAQ 1.1 (SD 0.8), and PHQ4 3.3 (SD 2.9). The screening test for widespread pain was positive in 18.4% of patients. The mean PGA for PsA activity was 4.7 (SD 2.5), versus a PhGA of 3.9 (SD 2.4). Similarly, PGA for psoriasis activity was 4.0 (SD 2.8), and PhGA was 3.1 (SD 2.6). The correlation between PGA and PhGA was strong for PsA activity (r= 0.738) (with good agreement on Bland and Altman (Figure 1)) and moderate for psoriasis activity (r=0.613). Among 554 patients' measurements, 358 (84.2%) were in concordance with the physician's global assessment. In the multivariable analysis, concordance was independently associated with a high CRP (OR 2.32 [95%CI 1.33; 4.02] and DAPSA category (better concordance in patients in remission (OR 1.02 (95%CI 1.01; 1.03]).
Conclusion: In this unselected sample of patients from Arab countries, there was a strong concordance between PGA and PhGA of PsA activity. This raises questions about patient expectations and pain perceptions in Arab countries. Concordance was stronger for PsA than PsO, indicating that rheumatologists may be more comfortable assessing joints than skin. The patient's evaluation of disease activity needs to be taken into account when considering the disease management plan, especially in patients who are not in remission.

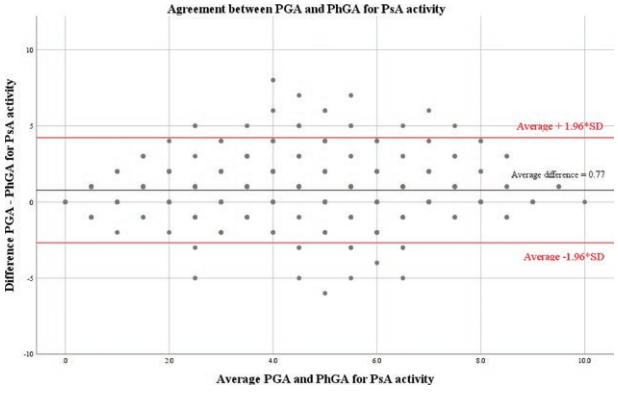


Figure 1. Agreement between PGA (Patient) and PhGA (Physician Global Assessment) of PsA activity using the Bland and Altman plot. Each dot is the difference between PGA and PhGA for a specific patient.

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Disclosure of Interests: None Declared.
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AB1149 **SEX DISTRIBUTION IN PSORIATIC ARTHRITIS: SYSTEMATIC LITERATURE REVIEW**

Keywords: Gender/diversity issues, Epidemiology, Psoriatic arthritis

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Background: The prevalence of psoriatic arthritis (PsA) is considered equal in male and female patients but recent studies in cohorts of PsA it has been observed that women are more dominant in sex distribution, and the female-male ratio varies between 1.2 and 2 [1]. It is not yet clear whether this is related to a change in the epidemiology of the disease.
Objectives: To assess the female-male ratios in recent PsA studies.
Methods: A systematic review of the literature (from January 2020 to September 2022) was performed using the Pubmed database with keywords and MeSH terms referring to psoriatic arthritis. Randomized controlled, cross-sectional, prospective, and retrospective cohort studies involving ≥20 patients and specifying the number of men and women were considered eligible. Only original articles in English were included. Two independent reviewers performed study selection and data collection. The number of female and male patients, study design, study center, and PsA clinical phenotypes were recorded.
Results: Total of 1469 articles were selected for full-text reading, of which 486 were included for analyses. Overall, the number of studies in which the F/M and M/F ratio ≥1.5 was 86 (17.7%) and 60 (12.4%), respectively. Comparing the study types, it was observed that the female gender was more dominant in cross-sectional studies (p=0.004), Table 1. The sex distribution was more heterogeneous in single-center studies than in multi-center studies. Studies were stratified according to continents; it was found that the number of studies in which the F/M ratio is ≥1.5 was higher in America than the multinational studies (27% vs. 4%). On the other hand, the studies from Asia had higher male predominance.
Conclusion: Although there were some differences observed in sex distribution by study design and continents, overall, the ratio of females to males was similar. The female predominance observed in some studies might be due to selection bias or greater access to the medical system.
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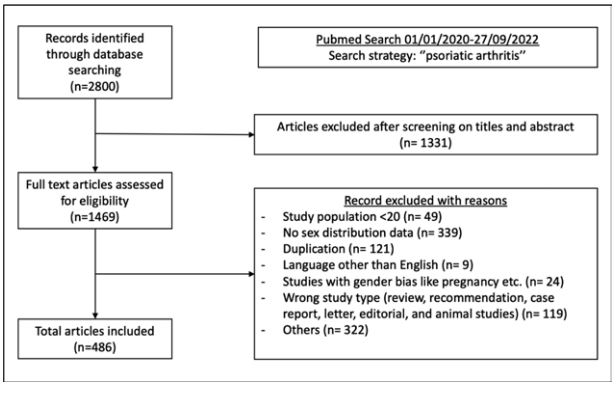


Figure 1. Flowchart

Table 1. Characteristics of studies included in analyses

	Female	Male	Total	F/M≥1.5		M/F≥1.5	
	N (%)	N (%)	N	N	*p*	N	*p*
Overall	490752	426581	917333				
Study type	(53.5%)	(46.5%)			0.004		0.563
Randomized controlled (n: 35)	7149 (51%)	6733 (49%)	13882	4/35 (11%)		3/35 (9%)	
Cross-sectional (n: 235)	123228 (51%)	117137 (49%)	240365	57/235 (24%)		32/235 (14%)	
Retrospective cohort (n: 127)	327651 (55%)	273494 (45%)	601145	15/127 (12%)		12/127 (9%)	
Prospective cohort (n: 89)	32724 (53%)	29217 (47%)	61941	10/89 (11%)		13/89 (15%)	
Center					0.001		0.004
Single-center (n: 224)	13568 (50%)	13468 (50%)	27036	54/224 (24%)		38/224 (17%)	
Multi-center (n: 262)	477184 (54%)	413113 (46%)	890297	32/262 (12%)		22/262 (8%)	
Continents					0.002		0.001
America (n: 85)	284128 (53%)	249383 (47%)	533511	23/85 (27%)		7/85 (8%)	
Europe (n: 275)	164655 (54%)	137880 (46%)	302535	52/275 (19%)		35/275 (12%)	
Asia (n: 60)	9896 (50%)	9838 (50%)	19734	7/60 (12%)		16/60 (27%)	
Africa (n: 6)	193 (51%)	188 (49%)	381	2/6 (33%)		0/6 (0%)	
Australia (n: 3)	88 (30%)	203 (70%)	291	0/3 (0%)		1/3 (33%)	
Multinational (n: 57)	31792 (52%)	29089 (48%)	60881	2/57 (4%)		1/57 (2%)	

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1150 **ORDER OF APPEARANCE OF PSORIASIS AND ARTHRITIS SYMPTOMS IN PSORIATIC ARTHRITIS: COMPARATIVE STUDY OF A RETROSPECTIVE COHORT**

Keywords: Prognostic factors, Epidemiology, Psoriatic arthritis

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Background: Little is known about the chronologic order of appearance of psoriasis (Pso) and psoriatic arthritis (PsA) symptoms and its effect on disease evolution. Most information is based on population-based registries or big data that may lack precision.
Objectives: To evaluate duration and chronologic order of appearance cutaneous and articular manifestations of PsA from 1st symptoms till diagnosis.
To compare differences between patients with symptoms and diagnosis of Pso before PsA with those that manifest Pso after PsA.
Methods: A retrospective cohort study was conducted. Eligible patients were 219 patients that met ASAS criteria visited the SpA clinic between July – October 2022. Finally, 129 patients that met CASPAR criteria and Pso diagnosis were included. Other autoimmune rheumatic diseases were excluded. Data were collected previously reviewing patient records available from the electronic

and paper database of the hospital. Additional information was retrieved by the shared medical history database of the Catalan Institute of Health which attends the 99.2% of the population. Missing data were collected prospectively by patient interview. ANOVA or Kruskall-Wallis test was carried out according to variable distribution.

Results: A total of 129 patients were included from which 98 had all time data related about disease appearance. There were 13.3% of missing data. The median disease evolution in years was 14 years with patients from 1 to 53 years of duration. The description and comparison of the clinical characteristics of each group is summarized in Table 1. Patients that begin with arthritis showed significant association with higher elevated C reactive protein and longer PsA disease duration. Longer time till arthritis appearance as well as more prevalence of Dactylitis was more observed in patients that begin with Pso before arthritis.

SpA related variables, n (%)	Pso before PsA (n=64)	Same time (n=16)	Pso after PsA (n=18)	p
Male	36 (56.3)	9 (56.3)	10 (55.5)	0.99
HLAB27+	12 (18.8)	2 (12.5)	1 (5.6)	0.45
Elevated CRP	29 (45.3)	11(68.8)	14 (77.8)	**0.03**
Nail Pso	40 (62.5)	9 (56.3)	12 (66.7)	0.93
Other Pso	27 (42.2)	8 (50%)	15 (83.3)	0.10
Enthesitis	27 (42.2)	8 (50)	7 (38.9)	0.69
Dactylitis	25 (39.1)	10 (62.5)	3 (16.7)	**0.03**
Uveitis	1 (1.6)	0	1 (5.6)	0.48
Inflammatory bowel disease	0	1 (6.25)	1 (5.6)	0.15
Axial affection	10 (15.6)	2 (12.5)	2 (11.1)	0.80
Family history of Pso	29 (45.3)	3 (18.8)	7 (38.9)	0.23
Family history of SpA	63 (98.4)	14 (87.5)	18 (100)	**0.04**
Time related variables, p50 (IQR)				
Age	59.7 (15.4)	58.5 (16.8)	60.3 (19.6)	0.38
Years from 1st till 2nd manifestation	24.5 (1)	0	8 (9)	**0.00**
Years of delay until PsA diagnosis	3 (0)	1 (7)	5.5 (8)	0.07
Years of disease duration	11 (8)	20 (18.5)	19 (15)	**0.01**

Conclusion: Significantly higher prevalence of CRP elevation in patients that begin with arthritis.

Higher prevalence of dactylitis and longer time until articular manifestation was observed in patients that begin with Pso.

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Disclosure of Interests: None Declared.

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AB1151 COMORBIDITY IN PSORIATIC ARTHRITIS (COMPASS) – INCIDENCE OF DEPRESSIVE SYMPTOMS AND ASSOCIATED FACTORS

Keywords: Epidemiology, Comorbidities, Psoriatic arthritis

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Background: Patients with psoriatic arthritis (PsA) demonstrate increased prevalence of several comorbidities, including mental health conditions.

Objectives: Aim of the study was to investigate the prevalence of self-reported depressive symptoms (SRDS) and diagnosis of depression among PsA patients treated at Centre for Rheumatology, Stockholm and investigate associated clinical, laboratory and psychosocial parameters.

Methods: 71 patients were included from prospective cross-sectional COMPASS study. Information regarding disease activity (joint assessment, enthesitis (SPARCC), psoriasis body surface area (BSA)% and psoriasis area severity index (PASI)) were collected. Patient Health Questionnaire-9 (PHQ-9) was used to assess SRDS. Dermatology Life quality Index (DLQI) was used to assess impact of cutaneous symptoms.

Results: 72% of included patients were females, mean age 53.9 years (SD 12.7) and 75% were included at first visit. 52 patients reported a PHQ-9 score of none to mild depression (ND group) and 19 patients a score equal to moderate or severe depression (D group). The D group had significantly more severe somatic disease, including higher swollen (p=0.006) and tender joint counts (p=0.003), higher enthesitis score (p=0.012) and VAS score (p=0.004). Multivariate analyses showed a positive correlation between severity of SRDS and pain (ρ=0.51, p<0.001), DLQI (ρ=0.40, p=0.001), tender/swollen joints (ρ=0.38, p-=0.001/ρ=0.34, p=0.004), enthesitis (ρ=0.27, p=0.032) and PASI (ρ=0.28, p=0.028). Patients reported that the mean time from the first joint symptom to the first visit to rheumatologist was 10.5 years (SD 13.2). Importantly, only those who received the PsA diagnosis and treatment later than 2 years since the onset of symptoms, reported depressive symptoms (PHQ>10 (mild or more severe) or 14 (moderately or severe)).

Conclusion: In our cohort up to 26% of PsA patients display medium to severe depressive symptoms. Importantly, delay of 2 years to the first visit to rheumatologist is associated with SRDS. A severity of SRDS correlates with severity of somatic disease.

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Disclosure of Interests: Aune Avik: None declared, Eva Waldheim: None declared, Sofia Geschwind: None declared, Aleksandra Antovic: None declared, Vilija Oke Speakers bureau: Novartis, Jansen, Lilly, Consultant of: Jansen, Lilly, Abbvie, UCB.

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AB1152 FATIGUE IN PATIENTS WITH PSORIATIC ARTHRITIS OF EMPLOYABLE AGE

Keywords: Psoriatic arthritis, Patient reported outcomes

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Background: Fatigue is an important and underrated multifactorial manifestation of psoriatic arthritis (PsA).

Objectives: The evaluation of frequency and relationship of fatigue with anthropometric, clinical, laboratory, ultrasound (US) data and quality of life (QoL) in patients with PsA of employable age.

Methods: The study included 92 patients with PsA aged 18-59 years. Assessment of fatigue was conducted using a fatigue subscale from the FACIT-F questionnaire. Severity of skin lesions and arthritis was determined with PASI and DAPSA, respectively, as well as anthropometric data, the number of painful and swollen joints and entheses, inflammatory biomarkers, the number of inflamed entheses and entheses with structural changes and the number of active and non-active synovitis detected by US, QoL by SF-36 and DLQI and functionality by HAQ-DI.

Results: In all 92 patients: male - 42 (45.7%), mean age 42.9±9.6 (SD) years (y), PsA duration was 7 (2; 11.8) y, DAPSA 15.2 (10.2; 21.4), PASI 3,8 (1,2; 9,6). Fatigue (FACIT-F values <34 points) was detected in 46 (50%) patients. It was associated with psoriasis (p<0.05) and PsA duration (p<0.01), DAPSA (p<0.01), and clinical enthesitis (p<0.01). At the same time, there was no relation between (b/w) age and anthropometric data (body mass index, waist and hip circumference, waist-to-hip ratio) (p>0.05). FACIT-F score was correlated with physical functioning (SF-36 subscale) and DLQI scores (p<0.01). These data are consistent with findings from other studies, especially with psoriasis burden, despite the fact that the relation b/w fatigue, PASI and psoriatic onychodystrophy (NAPSI) was not found (p>0.05). Association of fatigue with inflammatory markers (ESR, hs-CRP) and US articular and entheseal inflammation was not found (p>0.05). Probably this indicates a greater influence of clinical signs, rather than US that could be explained by the high incidence of asymptomatic course of these changes.

Conclusion: Fatigue was found in 46% of employable aged PsA patients and was associated with clinical signs of PsA, particularly, with its activity and duration. Fatigue has been linked to physical functioning and DLQI scores. Further research is needed to investigate the individual factors that make the greatest influence to the fatigue development. The results of this study may indicate the need for routine fatigue examination among people with active PsA.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1153 FATIGUE AND PSORIATIC ARTHRITIS: WHAT CHARACTERISTICS?

Keywords: Descriptive studies, Quality of life, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) can cause an impairment of patients' quality of life. Fatigue is a common and often underestimated symptom in PsA.

Objectives: We aimed to assess the characteristics of fatigue in PsA.

Methods: This was a cross-sectional study including patients with PsA meeting CASPAR criteria. Socio-demographic, clinical and biological data were collected. The FACIT fatigue score (Functional Assessment of Chronic Illness Therapy) was calculated for all patients. It is a 13-item questionnaire evaluated on a five-point scale (4 = no fatigue to 0 = extreme fatigue), with scores from 0 to 52, the highest scores correspond to less fatigue [1].

Results: There were 37 patients, the sex ratio M/F was 2.1. The mean age was 52.46±14.22 years, the mean age at disease onset was 41.32±14.69 years and the mean disease duration was 133.62±112.82 months. The mean BMI was 25.69±5.13 kg/m². The mean CRP was 31.63±37.95 mg/l. The patient global assessment (PGA) of the disease was 50.54±17.47. The mean DAS28-CRP score was 4.06±1.54. The mean BASDAI and ASDAS-CRP scores were 5.06±6.14 and 2.60±1.05, respectively. The mean DAPSA score was 38.31±35.05. The mean BASFI and HAQ were 4.91±2.59 and 1.30±0.93, respectively. The mean FACIT fatigue score was 16.11±11.99 [0-49]. It correlated with mean BMI value (r=0.444; p=0.044), age at disease onset (r=0.421; p=0.016), PGA (r=0.397; p=0.036), and HAQ (r=0.437; p=0.020). Patients with a BMI≥25 kg/m² had a higher FACIT fatigue score (19.94±13.20 vs. 11.00±8.12, p=0.049), In contrast, no correlation was identified with gender, age, smoking, disease duration, axial or peripheral involvement, extra-articular manifestations, high CRP levels, DAS28-CRP, BASDAI, ASDAS-CRP, DAPSA, BASFI, and hip involvement.

Conclusion: Fatigue is an important symptom in PsA and can be responsible for significant psychosocial impact and impairment of quality of life. Its assessment and management should be part of the overall management of PsA.

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Disclosure of Interests: None Declared.

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AB1154 NEW INFLAMMATION PARAMETERS IN PSORIATIC ARTHRITIS: NEUTROPHIL/LYMPHOCYTE AND PLATELET/LYMPHOCYTE RATIOS

Keywords: Psoriatic arthritis

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Background: Monitoring disease activity in patients with psoriatic arthritis (PsA) is crucial. Commonly used inflammation markers, including C-reactive protein (CRP), lack specificity and sensitivity. Other markers using complete blood count (CBC) parameters have been proposed: neutrophil/lymphocyte ratios (NLR), platelet/lymphocyte ratios (PLR).

Objectives: The aim of this study is to investigate these ratios in PsA.

Methods: A cross-sectional study including patients with PsA meeting CASPAR criteria. Socio-demographic, clinical and biological data were collected. NLR and PLR ratios were calculated from the CBC parameters.

Results: Thirty-seven patients were enrolled; the sex ratio M/F was 2.1. The mean age was 52.46±14.22 years, the mean age at symptoms onset was 41.32±14.69 years. Axial and peripheral involvement were noted in 21 and 31 cases, respectively. Rheumatoid factor, ACPA and ANA were positive in 10, 8 and 9 cases, respectively. At least one extra-articular manifestation was present in 18 cases. Hip involvement was noted in 11 cases. The mean CRP was 31.63±37.95 mg/L. The mean DAS28-CRP, BASDAI, ASDAS-CRP and DAPSA were 4.06±1.54, 5.06±6.14, 2.60±1.05 and 38.31±35.05, respectively. The mean values for leukocytes, neutrophils, and lymphocytes were 10.97±12.95 10^3/mm3, 5.22±2.04 10^3/mm3, and 2.36±0.96 10^3/mm3, respectively. The mean hemoglobin level was 12.73±1.57 g/dl. The mean platelet count was 315.03±119.01 10^3/mm3. The mean NLR and PLR were 2.52±1.31 and 58.05±91.69, respectively. Our statistical study identified a correlation of PLR with CRP (r=0.423; p=0.016), hemoglobin level (r=-0.524; p=0.002) and DAPSA (r=0.487; p=0.047). However, no correlation was found between PLR and age, disease chronology, axial or peripheral involvement, immunological profile, extra-articular manifestations, DAS28-CRP, BASDAI, ASDAS-CRP, and hip involvement. Furthermore, no correlation between NLR and any of the above variables was identified.

Conclusion: This study showed that PLR correlates with CRP, hemoglobin level, and disease activity. These new, inexpensive, and available inflammation markers may be useful in monitoring patients with PsA.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1155 SOLUBLE PROGRAMMED CELL DEATH-1 IN PSORIASIS AND PSORIATIC ARTHRITIS PATIENTS

Keywords: Psoriatic arthritis

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Background: psoriasis (PSO) and Psoriatic arthritis (PsA) are chronic, inflammatory, diseases that affect many sustems[1]. Soluble programmed cell death- 1 (sPD-1) block the PD-1/PD-L1 inhibitory pathway and associated with persistent activation of self-reactive T cells[2].

Objectives: Assess the plasma levels of sPD-1 in PSO and PsA patients and correlate it with the clinical, laboratory, radiological characteristics and disease activity.

Methods: This study included 30 PSO patients (G I), 30 PsA patients (G II), and 40 healthy control (G III). All studied groups were subjected to clinical assessment, PASI and DAPSA scores assessment, musculoskeletal ultrasound (MSUS) assessment of affected areas, laboratory evaluation in form of CBC, ESR, and CRP. Plasma levels of sPD-1 were measured and correlated with different parameters.

Results: There were no significant differences between the three groups regarding demographic data (P>0.05). 19 PSO patients were receiving biological treatment while 21 PsA patients were receiving biological therapy. The remaining patients were receiving conventional DMARDs. PASI score was 20.34± 8.63 & 21.62± 10.53 in GI & GII consequently with no significant difference between PSO & PsA groups (P=0.6). DAPSA score was 10.28±5.39 in G II. Plasma levels of sPD-1 were 465.64±251.16, 786.44±153.96, and 198.73±73.36 in the three groups respectively with significant increase in GI, & GII than controls (P<0.01), sPD-1 was significantly elevated in PsA patients when compared with PSO patients (P<0.01). s-PD-1 levels were elevated in patients who had active synovitis by MSUS. s-PD-1 levels were positively correlated with CRP, PASI score, and DAPSA score. Figure 1 demonstrates sPD-1 levels in the three groups.

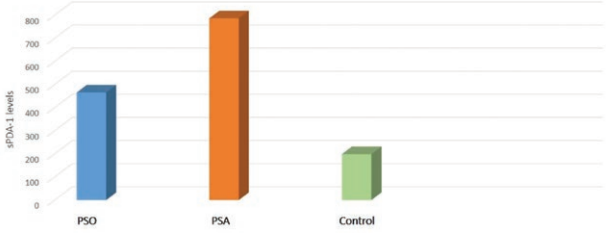
Conclusion: Plasma levels of sPD-1 were elevated in PSO and PsA patients and correlated with disease severity and activity. sPD-1 might be good predictor of PSO and PsA disease activity, a new biomarker or target for immunomodulatory therapy.

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Figure 1: sPDA-1 levels in the three studied groups



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AB1156 METABOLIC DISORDERS AND ABNORMAL DIETARY PATTERNS AND THEIR ASSOCIATION WITH PSORIATIC ARTHRITIS ACTIVITY: THE DIETARY INTERVENTION IN PSA (DIPSA) STUDY

Keywords: Clinical trials, Diet and nutrition, Psoriatic arthritis

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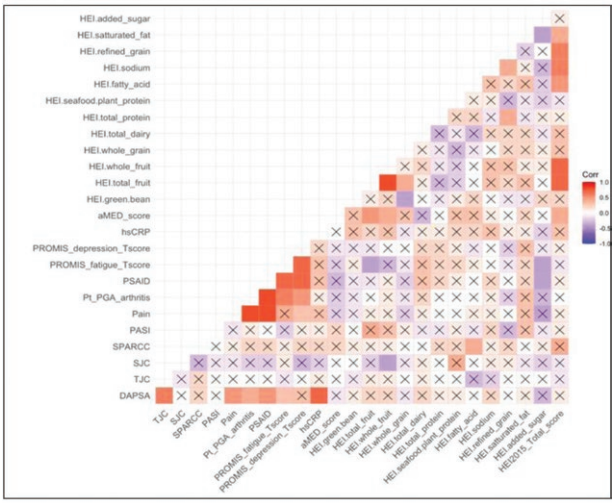
Background: Psoriatic Arthritis (PsA) is associated with obesity and its related metabolic abnormalities. The role of diet as an adjunct therapy in PsA remains unclear.
Objectives: We aimed to describe the prevalence of cardiometabolic abnormalities and adherence with healthy eating recommendations among patients participating in the DIPSA study and asses their association with measures of disease activity.
Methods: DIPSA is a randomized controlled trial (NCT04180904) that aims to compare the efficacy of Mediterranean diet and DASH-low caloric diet vs. standard of care as adjunct therapy in patients with PsA who are overweight or obese (BMI>25). Study participants must have Disease Activity in Psoriatic Arthritis (DAPSA) score >10 and be on stable therapy. Baseline information on the first 32 patients enrolled in the study (out of expected 90 patients) was analyzed. The presence of cardiometabolic abnormalities was assessed based on medical history, physical examination and laboratory tests. All participants completed a 24-h dietary recall of foods/beverages consumed during 3 separate weekdays. Healthy Eating Index (HEI) 2015, a diet quality score which evaluates adherence to dietary guidelines for Americans, was calculated. The score includes 13 food components (9 components encouraged, 4 to limit) with a range of 0 (low) to 5 or 10 (high). We describe the baseline cardiometabolic abnormalities and adherence with healthy diet scores and assess their correlation with PsA disease activity measures.
Results: The mean age of study participants was 53.3 years (71.9% females). The mean DAPSA, tender and swollen joint counts were 23.6, 6.6 and 1.1, respectively. A significant proportion of the patients had obesity (71.9%) and related metabolic abnormalities such as dyslipidemia (41.9%), hypertension (37.5%) metabolic syndrome (46.9%). Mean HEI-2015 was 59.3 with higher adherence scores (HEI-2015>50; 25%Q1) found in females than males (91% vs. 57%, respectively, p<0.05). No differences in HEI-2015 scores were found between age and level of education groups. Of the individual HEI-2015 food groups, the lowest adherence scores were found for whole grain and total sodium consumption (Table 1). Significant correlation was found between lower added sugar and both lower fatigue and lower PSAID scores (Figure 1), and correlation between greater whole fruit consumption and lower swollen joint count. Additionally, a correlation was found between the unsaturated than saturated fatty acids and higher enthesitis score.
Conclusion: High prevalence of metabolic abnormalities was found in patients with PsA starting a diet intervention study. Adherence with healthy diet eating recommendations at baseline was higher in female patients and individual foods, particularly sugar and whole fruit consumption, were associated with PsA measures of disease activity. The DIPSA study will determine the role of dietary interventions as adjunct therapy in PsA.

Table 1. Summary of adherence with healthy eating recommendations by Healthy Eating Index (HEI)* 2015 and its individual components (N=29); Mean±SD

HEI-2015 total score (0-100)	59.3±11.4
HEI-2015 total vegetable score (0-5)	4.2 ± 1.2
HEI-2015 total greens and bean score (0-5)	3.4 ± 1.7
HEI-2015 total fruit score (0-5)	2.7 ± 2.1
HEI-2015 whole fruit score (0-5)	2.9 ± 2.1
HEI-2015 total whole grain score (0-10)	2.9 ± 2.9
HEI-2015 total dairy score (0-10)	5.5 ± 2.6
HEI-2015 total protein score (0-5)	4.7 ± 0.7
HEI-2015 total seafood & plant protein score (0-5)	3.5 ± 2
HEI-2015 total fatty acid score (0-10)	5.6 ± 3.1
HEI-2015 total sodium score (0-10)	3.1 ± 2.9
HEI-2015 refined grains score (0-10)	6.8 ± 3.3
HEI-2015 saturated fatty acids score (0-10)	5.5 ± 3.1
HEI-2015 added sugars score (0-10)	8.6 ± 2.2

*Calculation of HEI-2015 was based on an average of self-administered dietary recalls from 3 separate weekdays (ASA24). HEI-2015 total score ranges from 0 (low) to 100 (high). Each individual component ranges from 0 (low) to 5 or 10 (high).

Figure 1: Correlation matrix of HEI (total and sub-scores) and PsA measures of activity. "X" represents p value>0.05.



aMED: adjusted Mediterranean Diet score; HEI: Healthy Eating Index; PASI: psoriasis area and severity index; PSAID: Psoriatic Arthritis Impact of Disease; Pt_PGA_Arthritis: Patient global assessment of PsA; SJC: Swollen joint count; SPARCC: total enthesitis count by SPARCC; TJC: tender joint count

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AB1157

HIGH PREVALENCE OF UNDIAGNOSED PSORIATIC ARTHRITIS AMONG PATIENTS WITH PSORIASIS: ALGERIAN MULTICENTER SCREENING SURVEY USING PURE4 QUESIONNAIRE AND CASPAR CRITERIA.

Keywords: Psoriatic arthritis, Epidemiology

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Background: Psoriatic arthritis (PsA) is a polymorphic disease, in term of clinical presentation, severity and evolution. Skin lesion precedes joint damage in 84%, therefore, a multidisciplinary approach associating dermatologist and rheumatologist provide an opportunity for earlier diagnosis, more timely therapy and prevention of disability.
Objectives: To provide Algerian epidemiological data on the Prevalence of undiagnosed PsA among psoriasis patients in dermatology practice. This multicenter screening survey is conduct in order to reduce diagnostic delay and prevent progressive joint involvement and disabilities.
Methods: Between 2019 and 2022, a multicenter cross-sectional trial conducted in four Dermatology Clinics in Algeria (Algiers, Blida, Bechar and Constantine); had recruited patients presenting with plaque psoriasis and no prior rheumatologist-confirmed PsA diagnosis. Patients were screened using the Psoriatic arthritis UnclutteRed screening Evaluation (PURE4) questionnaire and were referred to a rheumatologist for assessment of PsA using classification for psoriatic arthritis criteria CASPAR if they had a PURE 4 score ≥1.Psoriasis characteristics:

Body surface area, psoriasis types, area, severity index, and psoriasis disability index tools were used for assessing psoriasis patients.

Results: The study included 212 patients with psoriasis:64% were male and 36% female. Their median age was 48.12 yr ±11.74. Referring to the type of psoriasis, 72% presented with plaque psoriasis, 16% guttata 6% pustular and 24% with psoriasis of more than one type. Nail disease appeared in 24 % and scalp disease in 26%. PURE 4 was applied to all 212 psoriasis patients; among them n = 53 (25% of all tested patients) had a score ≥1. The sequential application of PURE4 and CASPAR criteria found a prevalence of undiagnosed PsA of 20.28% [95% CI: 9, 23.5]. The PPV of PURE 4 in this setting is 49.23% [95% CI: 39, 67]. Of these patients, 44% of patients with PsA had psoriatic nail disease and scalp involvement seen in 37%. With reference to the PsA type, 30% patients presented with polyarthritis,44% with oligoarthritis,39% with enthésites, dactylitis in 23% and 13%with axial arthritis. The subgroup of patients with PsA had significantly higher rates of obesity (42%) compared to non-PsA. Patients with severe psoriasis(P = 0.001), nail and scalp involvement (P = 0.003) with chronic plaque psoriasis (P = 0.001)associated with obesity (P = 0.0001)were identified as independent positive predictors of PsA.

Conclusion: Screening for PsA in Algerian patients with psoriasis revealed a significant number of undiagnosed cases (20.28%) that should be treated early. Severe psoriasis nail and scalp involvement, and obesity are factors predicting the PsA development.

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Disclosure of Interests: None Declared.

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AB1158 FATIGUE IN ANKYLOSING SPONDYLITIS IS ASSOCIATED WITH DISEASE ACTIVITY BUT NOT IN PSORIATIC ARTHRITIS

Keywords: Comorbidities, Patient reported outcomes

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Background: Fatigue is a common symptom in chronic inflammatory diseases. The mechanism by which fatigue occurs is multidimensional. Previous studies suggested that several factors, including physiology, psychology and behavior, may contribute to its pathogenesis. Fatigue is considered one of the most common symptoms in patients with psoriatic arthritis (PsA) and ankylosing spondylitis (AS) with an incidence of 50–70%. Fatigue is a major factor contributing to unsatisfactory treatment outcome and poor quality of life, or even disability. Therefore, from a clinical point of view, how to improve the symptom of fatigue remains a challenge. Identifying factors related to fatigue could be a key to the management of this complex symptom.

Objectives: To compare fatigue and its associated factors in patients with PsA and AS from two university hospitals.

Methods: A cross-sectional analysis was performed in 105 patients (May – December 2022) Fatigue was assessed using 3 instruments: the fatigue subscale of the Short-form 36 survey (fatigue-SF36), the Visual Analogue scale of fatigue (VASf) and the Functional Assessment of chronic illness Therapy Fatigue Scale (FACIT-F). T-test was used to compare mean fatigue between PsA and AS patients. To determine in each patient group the relationship between fatigue (assessed by FACIT-F) and the other variables (DAPSA or ASDAS, CPR, ESR, hemoglobin, HAQ, Hospital Anxiety and depression Scale [HAD] and Brief Pain Inventory [BPI]) a Spearman correlation was performed. A value of $p < 0.05$ was accepted as statistically significant.

Results: A total of 105 patients were included, 55 (52.4%) PsA patients and 50 (47.6%) AS patients. We found that mean fatigue (using 3 instruments) had not significant differences in patients with PsA and AS (Table 1). In patients with PsA and AS, fatigue correlated to HAD, HAQ and pain, but not with CRP, ESR and hemoglobin (Table 2). In AS patients, high disease activity (assess by ASDAS) correlated with high levels of fatigue (lower levels on FACIT-F). However, in patients with PsA, fatigue and disease activity (DAPSA) were not related.

Conclusion: In PsA and AS patients, fatigue seems to be related to subjective but not with objective (analytical) variables. In patients with AS, fatigue was related to disease activity, but in patients with PsA we found no correlation.

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Table 1. Mean of fatigue in PsA and AS patients

	PsA Mean (SD)	AS Mean (SD)	p-value
FACIT-F	38.1 (10.3)	37.7 (11.4)	0.88
VAS-F	3.8 (2.5)	4.29 (2.8)	0.396
SF36-Fatigue	53.4 (22)	56.7 (21.8)	0.45

Table 2. Fatigue correlations in PsA and AS patients

	PsA	p-value	AS	p-value
Disease activity	-0.19	0.164	-0.63	<0.001
PCR	0.01	0.947	0.01	0.30
VSG	0.05	0.680	0.04	0.325
Hemoglobin	-0.13	0.337	-0.15	0.46
HAQ	-0.50	<0.001	-0.67	<0.001
HAD depression	-0.75	<0.001	-0.61	<0.001
HAD anxiety	-0.70	<0.001	-0.47	<0.001
Pain (BPI)	-0.64	<0.001	-0.71	<0.001

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1159 THE SPANISH VERSION OF THE PURE-4 QUESTIONNAIRE USE FOR PSORIATIC ARTHRITIS SCREENING AFTER 1 YEAR OF FOLLOW-UP IN PATIENTS WITH PSORIASIS

Keywords: Psoriatic arthritis

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Background: The Psoriatic arthritis UnclutteRed screening Evaluation (PURE-4), culturally adapted to Spanish language following the standardized methodology,[1]

was recommended by experts due to the reduced number of items,[2] its high sensitivity/specificity and the feasibility to implement in clinical practice.

Objectives: To confirm the presence/absence of psoriatic arthritis (PsA) according to rheumatologist criteria in patients (pts) with psoriasis (Pso) 1 year after having answered the PURE-4 questionnaire in the dermatology consultation.

Methods: Cross-sectional, observational, multicenter study conducted with primary data collection under conditions of routine clinical practice in Spain. Adult pts (≥18 years old) with Pso diagnosis that voluntarily accepted to participate. Two cross-sectional evaluations. Assessment I allowed to validate the Spanish version of the PURE-4 questionnaire and its results were previously communicated.[3] Data from assessment II (pts without PsA in assessment I were evaluated by the rheumatologist 1 year ±2 months later and performed the PsA diagnostic confirmation according to her/his criteria and collected clinical characteristics) are presented here.

Results: 268 patients pts were included in assessment I, 223 (83.2%) of them without a PsA diagnosis. 219 pts were evaluable in assessment II, as they go to the second visit to rheumatologist: 56.2% male, with a mean (SD) age of 46.8 (12.5) years, a mean (SD) time from Pso diagnosis of 18.7 (12.8) years. Mean (SD) PURE-4 score was 2.4 (1.1) for pts with PsA and 1.2 (1.2) for pts without PsA diagnosis. Among pts who did assessment II, PsA diagnosis was confirmed in 12 (5.5%) pts. Area under the receiver-operating characteristic (ROC) curve was 0.7618 (95% CI: 0.6530, 0.8706) (n=217), confirming the good quality of the questionnaire (Figure 1). Using the Youden index, it was identified a score ≥2 indicative of a possible early presence of PsA, same as in assessment I. PURE-4 questionnaire showed a sensitivity of 75.0% and a specificity of 62.9%. In 63.6% of the cases, the PURE-4 questionnaire classified pts in the same way as the rheumatologist, with a negative predictive value of 97.7%.

Conclusion: Assessment II findings together with the assessment I results, demonstrate the good PsA screening properties of the PURE-4 questionnaire, starting with a ≥2 score, differing from the original questionnaire (≥1).[4] Questions of the PURE-4 questionnaire referring to dactylitis, both buttocks pain and peripheral joint pain with swelling (before age 50) were the most "discriminative" of PsA. The study reinforce the recommendation to assess annually, or ideally every 6 months, the possible PsA presence,[5] as early PsA identification thanks to simple tools such as PURE-4 could help to prevent irreversible joint damage of this disease.

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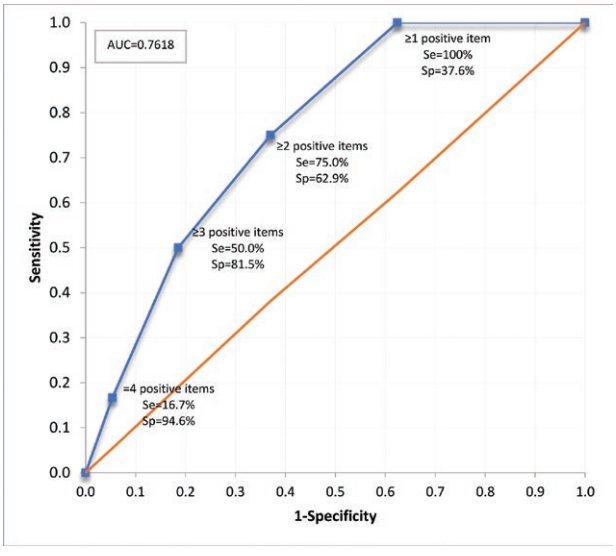


Figure 1. Area under the ROC curve (assessment II)AUC, area under the curve; Se, sensitivity; Sp, specificity.

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Pharmaceuticals Inc, Almirall SA, Lilly, AbbVie, Novartis, Celgene, Biogen, Amgen, Leo-Pharma, Pfizer-Wyeth, BMS, UCB and MSD, Anna Lopez-Ferrer Speakers bureau: advisor and/or researcher and/or speaker for Abbvie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Janssen, LEO Pharma, Lilly, MSD, Novartis, Pfizer, UCB, Consultant of: advisor and/or researcher and/or speaker for Abbvie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Janssen, LEO Pharma, Lilly, MSD, Novartis, Pfizer, UCB, Grant/research support from: advisor and/or researcher and/or speaker for Abbvie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Janssen, LEO Pharma, Lilly, MSD, Novartis, Pfizer, UCB, Marta Ferran i Farrés Speakers bureau: advisor and/or researcher and/or speaker for Abbvie, Almirall, Amgen, Janssen, LEO Pharma, Lilly, MSD, Novartis, Pfizer, UCB, Consultant of: advisor and/or researcher and/or speaker for Abbvie, Almirall, Amgen, Janssen, LEO Pharma, Lilly, MSD, Novartis, Pfizer, UCB, Grant/research 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AB1160

SOFT TISSUE EDEMA VISUALIZED ON MUSCULOSKELETAL ULTRASOUND AS A DIAGNOSTIC TEST FOR PSORIATIC ARTHRITIS: A PILOT COHORT STUDY

Keywords: Psoriatic arthritis, Ultrasound, Rheumatoid arthritis

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Background: Musculoskeletal ultrasound (MSKUS) is more sensitive than physical examination to detect inflammation in extra-articular structures in psoriatic arthritis (PsA).[1] Peritendinous soft tissue edema on MSKUS has shown to be more frequent in PsA when compared to rheumatoid arthritis (RA).[1,2,3]

Objectives: Here we assess the degree of association between the presence of flexor compartment (FC) soft tissue edema and the diagnosis of PsA with the aim of developing a soft tissue score to differentiate PsA from rheumatoid arthritis (RA).

Methods: This pilot prospective cohort study included 16 PsA and 40 RA patients from the Biologics Clinic at a single centre site in Ottawa. Patients are referred to the biologics clinic if they require initiation of, or changes to their biologic disease modifying antirheumatic drug (bDMARD). In addition to demographic and clinical data, eight MSKUS images were collected from each patient including one Grayscale (GS) and one power Doppler (PD) image of the FC of the 2nd and 3rd bilateral digits using a GE LogicE9 and a linear 15 MHz probe. Images were scored on a 0-2 semiquantitative scale to assess the degree of soft tissue edema, where 0 indicates absent, 1 indicates mild, and 2 indicates severe GS or PD. Following data collection, scoring was completed by two investigators blinded to the patients' diagnosis and in random order. Consensus decision was taken as the final score.

Results: Disease characteristics are provided in table 1. On MSKUS, PsA patients had a statistically significant higher total GS score compared to RA (7.0 vs 5.0, p=0.005). We found that numerically higher number of PsA patients had PD score of 2 in ≥3 fingers (20.0% PsA vs 2.5% RA, p=0.057) and GS score of 2 in ≥3 fingers (43.8% PsA and 22.5% RA, p=0.189). [Table 1]

Table : Patient demographics and disease characteristics

	PsA patients N:16 n(%)	RA patients N:40 n(%)	p
Age; mean±SD	49.8±13,1	59.4±15.3	**0.033**
Sex			
Male	6 (37.5%)	11 (27.5%)	0.527
Female	10 (62.5%)	29 (72,5%)	
Length of time since diagnosis; median (IQR)	4.5 (12.8)	14.5 (21.3)	**0.014**
Steroid current	3 (18.8%)	13 (32.5%)	0.350
Currently using csDMARDs	10 (62.5%)	27 (67.5%)	0.721
Previous bDMARD	7 (43.8%)	20 (50.0%)	0.672
SJC-66; median (IQR)	6.5 (7)	8 (6)	0.554
TJC-68; median (IQR)	15 (18)	8.5 (13)	0.253
CCP positive	2 (8.7)	21 (55.3%)	**0.013**
RF positive	2 (13.3)	28 (71.8%)	**<0.001**
Dactylitis current	2 (12.5)	-	N/A
BMI; median (IQR)	31.9 (12.0)	25.9 (7.4)	**0.042**
Total GS score*; median (IQR)	7.0 (3.0)	5.0 (2.0)	**0.005**[c]
Total PD Score*; median (IQR)	4.0 (3.0)	3.0 (2.0)	0.213
PD score =2 in four fingers*	1 (6.3%)	0 (0%)	0.273
GS score =2 in four fingers*	5 (31.3%)	5(12.5%)	0.129
PD score =2 in ≥3 fingers*	3 (20.0%)	1 (2.5%)	0.057
GS score =2 in at ≥3 fingers*	7 (43.8%)	9 (22.5%)	0.189

RA = rheumatoid arthritis, PsA = psoriatic arthritis GS = Grayscale, PD = power Doppler, csDMARD = conventional synthetic disease modifying antirheumatic drug, bDMARD = biologic disease modifying antirheumatic drug, TJC-66 = tender joint count using 66 joint count.
*Semiquantitative score of soft tissue edema (0-2) within the flexor compartment images in 2nd and 3rd digits

Conclusion: Our results suggest a possible role for FC soft tissue edema visualized on MSKUS in both GS and PD modes to differentiate PsA from RA. It is also important to understand the impact of soft tissue edema on disease pathogenesis and patient reported outcomes. While our sample size is small, some of the tests reaching reaching statistical significance using non-parametric testing encourages us to repeat this analysis again in the future as our cohort grows. When our sample size allows, we will assess for confounding effect of seropositivity, sex, age, BMI, previous therapy, and disease duration.

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AB1161

RACIAL AND GENDER - BASED DIFFERENCES IN THE PREVALENCE OF METABOLIC COMORBIDITIES AMONG PSORIATIC ARTHRITIS PATIENTS

Keywords: Gender/diversity issues, Comorbidities, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis that develops in at least 5% of patients with psoriasis. It affects women and men equally. Obesity, diabetes, hypertension and hypercholesterolemia always affect PsA patients.

Objectives: To study the gender and race effect on the prevalence of metabolic comorbidities among PsA patients in Malaysia.

Methods: This is a restrospective study. The medical records of all PsA patients under rheumatology clinic Hospital Sultan Ismail and Hospital Pakar Sultanah Fatimah follow up from 1/1/2009 to 31/12/2022 were reviewed. Data on demography, type of skin disease, joint manifestations and past medical history were obtained and analysed using Chi Square test in SPSS.

Results: We identified 226 patients. 110 were male patients (male to female ratio 0.95). The Malays (128/ 226) were the majority followed by the Chinese (57/226), Indian (38/226) and others (3/226). Most of them were plaque psoriasis (181/226). The commonest joint involvement was peripheral joint (174/226), followed by axial (25/226) and both (27/226). The prevalence of metabolic comorbidities according to gender (male vs female) were: [48/110, 44% vs 57/116, 49%; p =0.407] for hypertension, [35/110, 32% vs 37/116, 32%; p=0.990} for diabetes mellitus, [63/110, 57% vs 65/116, 56%; p= 0.851] for dyslipidemia. There was no association between gender and hypertension, diabetes mellitus and dyslipidemia. The prevalence of metabolic comorbidities according to races (Malay vs non Malay) were:[58/128, 45% vs 47/98, 48%; p=0.693] for hypertension, [40/128, 31% vs 32/98, 33%; p=0.822] for diabetes mellitus, [75/128, 58% vs 53/98, 54%; p= 0.498] for dyslipidemia. There was no association between ethnicity and metabolic comorbidities.

Conclusion: There was no difference in the prevalence of hypertension, diabetes mellitus and dyslipidemia between the gender and races in our patient cohort.

References: NA.

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AB1162

COMPARISON OF SERUM CXCL13 LEVELS BETWEEN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS

Keywords: Prognostic factors, Cytokines and chemokines, Psoriatic arthritis

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Background: Psoriasis is a chronic, autoimmune disease with predominantly skin and joint involvement. Factors leading to the progression of psoriasis to psoriatic arthritis (PsA) is still a mystery in spite of an increasing number of in vivo and in vitro studies. CXCL-13, a B cell chemokine, studied and emphasized in lymphoid pathways, immune responses and pathogenesis of many rheumatologic diseases [1-2]. Moreover, this chemokine is associated with systemic involvement of rheumatic diseases such as lupus nephritis [3].
Objectives: The aim of the study was to evaluate serum CXCL 13 levels in patients with psoriasis and psoriatic athritis and compare with healthy controls.
Methods: 54 patients with psoriasis and 47 patients with psoriatic arthritis and 19 controls were enrolled to the study. Blood samples from study participants were collected and serum CXCL-13 levels were analysed with ELISA method via Human BLC(CXCL 13) kit (BT Lab, Shangai, China).
Results: Age, body mass index and serum PASI scores were similar between two patient groups; but higher when compared to controls (Table 1). Median levels of CXCL-13 levels were significantly higher in patients with psoriatic arthritis and psoriasis when compared to control group (p= 0,001, Figure 1). But serum CXCL-13 levels were similar between psoriasis and psoriatic arthritis groups (p=0,251). Also levels of C reactive protein and sedimentation were higher in patients with psoriatic arthritis, followed by psoriasis and controls (p= 0.024 and 0.02, in order).
Conclusion: Many clinical studies showed that CXCL13 expression is elevated in many autoimmune conditions and related to activity, prognosis and symptomatic status of disease [4]. Also in SLE, this chemokine was associated with extraarticular involvement of disaese [5]. Also previous studies reported increased levels of serum and tissue CXCL-13 in psoriasis and associated with disease severity [6]. We conclude that serum levels of CXCL-13 is associated with psoriasis, but not related with articular involvement.

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	Psoriasis	Psoriatic arthritis	Healthy control	p
Age ((median (IQR)years))	42,5(24)	44(21)	28,5(17)	**<0,001**
Sex (female/male)	25/28	32/15	12/7	0,203
Body mass index (kg/m^2, median(min-max))	27,3(21,2-46,6)	28,6(19,3-48,8)	23,05(15,8-33,1)	**0,001**
Duration of disease(median(IQR), years)	12(3,5)	14(3,8)	NA	0,235
DAS-28	NA	3,32(0-6)	NA	NA
PASI score(median(min-max))	2,1(0-44)	1,2(0-8,8)	NA	**0,004**
CRP(mg/L, median(min-max))	4(1-24)	3(2-50)	3(1-7)	**0,02**
Sedimentation((median (min-max),mm/hour)	12(2-47)	13(3-96)	11(6-20)	**0,024**
CXCL-13 levels(pq/mL, median (min-max))	342,55(223,63)	378,5(167,40)	233,6(138,4)	**0,001**

IQR: inter quartile range, DAS-28: Disease activity score 28, PASI: Psoriasis activity and severity index, CRP: C reactive protein, min-max: minimum-maximum levels

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AB1163

INVESTIGATION OF SELECTED AUTOANTIBODIES IN PSORIATIC ARTHRITIS AND THEIR ASSOCIATION WITH COMORBIDITIES

Keywords: Psoriatic arthritis, Autoantibodies, Comorbidities

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory joint disease. It can result in severe joint destruction and cardiac or pulmonary involvement. So far, no specific autoantibodies have been identified that would simplify the diagnosis of PsA. HLA-B27 positivity is only detectable in 20% of PsA patients. It still takes several years until a diagnosis is established, which is crucial for the treatment. In addition, the disease is associated with a higher body mass index (BMI) and cardiovascular risk.
Objectives: The aim of the study was to identify possible PsA-associated autoantibodies which might enable earlier diagnosis, and to investigate possible associations of these selected autoantibodies with specific comorbidities.
Methods: Both, PsA patients and healthy individuals without known autoimmune disease were included in the study. Sociodemographic data (age, sex, BMI, waist circumference), current disease activity, current rheumatological therapy, cardiovascular diseases and fatigue were investigated. HLA-B27 status was determined and a radiological evaluation of PsA-typical changes in the hands and feet was performed. Serologically, antibodies against ADAMTSL-5, LL37, calpastatin and gliadin were investigated by ELISA.
Results: A total of 107 PsA patients (60% female) and 19 healthy controls (HC) were included. Median age of PsA patients was 59 years (21-80 years), 28% were HLA-B27 positive. Median BMI was 28 kg/m2 (19-48 kg/m2). Cardiovascular disease was present in 65% of patients, which included the following conditions: arterial hypertension, atherosclerosis, heart failure, coronary heart disease (CHD) and myocardial infarction. Antibodies to LL37 were present in 47% of patients compared to 30% of healthy individuals. Antibodies to ADAMTSL-5 were detectable in 47% of patients and 35% of healthy individuals. Calpastatin antibodies were present in 23% of patients and 11% of healthy individuals and against gliadin in 3% of patients and 5% of healthy individuals. In patients with antibodies against LL37, antibodies against ADAMSTL-5 could also be detected in most cases (p< 0.001). In patients with a treatment duration of <5 years more frequently antibodies against calpastatin were detectable compared to those with longer treatment duration (p<0.05).
Conclusion: In summary, none of the antibodies investigated were found to be significantly elevated in PsA-patients compared to HC. However, in the group of patients with a treatment duration <5 years, autoantibodies against calpastatin were detected more frequently. This could suggest that this autoantibody might play a role in the early phase of PsA and immunomodulatory treatment might diminish autoantibody levels.

	N	%
Female	65	60
Age (years, median, interval)	59 (21-80)	
HLA-B27 positive	34	32
Disease duration (years, median, interval)	15 (1-50)	
DAPSA (Median, Intervall)	41 (3-95)	
BMI (Median, Intervall)	28 (19-48)	
Waist circumference (median, interval)	100 (72-140)	
Nicotin abusus	72	68
Comorbidities		
Arterial hypertension	45	42
Myocardial infarction	7	7
Coronary heart disease	10	9
Heart failure	5	5
Uveitis	3	3
Diabetes mellitus	20	19
CED	5	5

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AB1164 PSAQOL (PSORIATIC ARTHRITIS QUALITY OF LIFE) QUESTIONNAIRE: TRANSLATION, CULTURAL ADAPTATION AND VALIDATION INTO ARABIC LANGUAGE

Keywords: Quality of life, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) is a multifaceted inflammatory disease that has a strong negativeimpact on the quality of life of patients. The Psoriatic Arthritis Quality of Life (PsAQoL)questionnaire was the first disease-specific patient derived instrument developed tomeasure the quality of life in patients with PsA.
Objectives: Our objective was to translate the PsAQol into Arabic language and evaluate its reliability and validity in patients with PsA.
Methods: This was a cross-sectional study including patients with PsA. A clinical and biologicalassessment of the patients was performed at inclusion. Translation of the original PsAQoL into Arabic was performed by professional bilingual and lay panel. Eight patients wereinterviewed to assess face and content validity. A separate sample of PsA patients (n=30)were invited to participate in a test-retest postal study in order to investigate reproducibilityand construct validity. One week separated the two administrations. The Arabic versionof Health Assessment Questionnaire (HAQ) was used as comparator instruments forconvergent validity.
Results: Face and content validity were satisfactory. The Arabic version of the PsAQoL was foundto be relevant, understandable and easy to complete in only a few minutes. One item wasexcluded (item 16). It showed having no correlation with neither the other 19 items nor the total score of PsAQol. The Arabic PsAQol had excellent internal consistency (Cronbach'sa=0.926), and test-retest reliability (r=0.982). There was a positive correlation betweenthe total score of the PsAQoL and the Arabic version of HAQ ((Spearman's r=0.838,p<10-3). Exploratory factor analysis had extracted two factors explaining 55% of the totalvariance.
Conclusion: Nineteen items were selected to compose the Arabic version of PsAQoL which was foundto be relevant, understandable and has excellent reliability and construct validity. The newmeasure will be a valuable new tool for use in routine for patients' assessment.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1165 ULTRASOUND AS A TOOL FOR EARLY DETECTION OF JUXTAARTICULAR NEW BONE FORMATION IN PSORIATIC ARTHRITIS AND THE ASSOCIATION OF SELECTED BIOMARKERS WITH NEW BONE FORMATION

Keywords: Psoriatic arthritis, Autoantibodies, Ultrasound

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Background:
Objectives: To investigate whether the new bone formation (NBF) that is typical of psoriatic arthritis (PsA) can also be detected by ultrasound. In addition, we aimed to investigate whether the presence of NBF and specific autoantibodies could facilitate an earlier diagnosis of psoriatic arthritis.
Methods: Patients fulfilling the CASPAR criteria (Classification Criteria for Psoriatic Arthritis) for PsA were included in the study. X-ray examinations of the hands and feet and standardized ultrasound examination of the hands and feet was performed. Antibody levels of calpastatin, LL37, gliadin, and ADAMTSL5 (Thrombospondin type-1 domain-containing protein 6) were determined by serum ELISA.
Results: Seventy-six patients (51% female) compared to 20 healthy controls (70% female) were included. The median age was 57 years (23-86) and the median disease duration was 10 years (1-54). HLA-B27 was positive in every fourth individual. By X-ray, NBFs were detectable in 55% (n=42) of the patients. In the ultrasound examination, these NBFs were also detectable (Figure 1). In addition, in 18 patients, signs of NBF were detectable due to the increased resolution of the ultrasound examination. Regarding the selected autoantibodies, none of the selected antibodies were associated with the presence of PsA or with PsA related NBFs.
Conclusion: In this study, NBFs were detectable radiographically as well as in the ultrasound examination. As ultrasonography is ubiquitously available in rheumatological offices and represents a gentle examination procedure for the patient, repeated X-ray examinations might be avoided, and regular ultrasound investigations might facilitate an earlier detection of PsA.

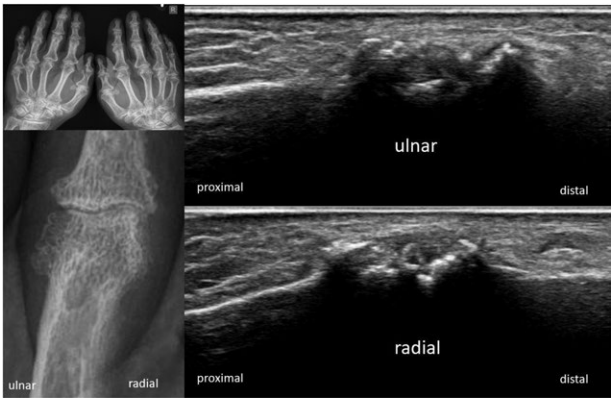


Figure 1. Proximal interphalangeal joint IV of the left hand

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AB1166 RANDOMIZED CONTROLLED TRIAL TO ANALYSE THE EFFECT OF BLOOD FLOW RESTRICTION TRAINING IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS COMPARED TO CONVENTIONAL RESISTANCE TRAINING – AN INTERIM ANALYSIS

Keywords: Rheumatoid arthritis, Psoriatic arthritis, Non-pharmacological interventions

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Background: Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are the two most common forms of arthritis with a prevalence of 1% and 0.5% in Europe. Physical activity exerts a major influence on disease activity, symptoms, quality of life, and increased cardiovascular risk [1,2]. In contrast to conventional strength training, Kaatsu blood flow restriction (BFR) training, which was initially developed in Japan as a rehabilitation measure, incorporates pneumatic cuffs

applied to the extremities, which are recurrently inflated with a defined pressure. The inherent blood flow modification promises a less weight-intensive and thus joint-protective strength training, while still preserving sufficient muscular hypertrophy stimulus [3].

Objectives: Ours is the first study in the world to compare the effect of Kaatsu blood flow restriction training to conventional resistance training in RA and PsA patients.

Methods: In this pilot study (ethical approval under Institutional Review Board #217/20), 40 RA and 40 PsA patients are individually randomized to one of three groups: Kaatsu-BFR training (20 patients each), conventional resistance training "CRT" (10 patients each), or the non-exercise group (10 patients each). Training is performed twice weekly over a 12-week period. Standardized recording of disease activity (via FFB-H-P, IPAQ, and DAS 28 or PSAID12, plus clinical examination and CRP), myokine levels, sonographic muscle diameter measurements, bioimpedance analysis and clinical characteristics is performed.

Results: The interim analysis of 9 BFR vs. 4 CRT patients with rheumatoid arthritis showed comparable CRP reduction (mean ± SD: BFR: -1.08 mg/L ± 1.33, CRT: -0.89 mg/L ± 1.94) and reduction in the number of painful joints (mean ± SD: BFR: -0.78 ± 2.44, CRT: -0.76 ± 1.71) during the training period. BFR group results surpassed CRT group results in terms of weight loss (mean ± SD: BFR: -2.9 kg ± 3.6, CRT: -1.9 kg ± 3.1) and body fat mass reduction (mean ± SD: BFR: -2.8 kg ± 5.3, CRT: -0.3 kg ± 2.5). The interim analysis of 4 BFR vs. 4 CRT patients with psoriatic arthritis showed a comparable PSAID reduction (mean ± SD: BFR: -5.1 ± 12.1), CRT: -4.3 ± 9.0) during the training period. BFR group results exceeded CRT group results with regards to CRP reduction (mean ± SD: BFR: -0.15 mg/L ±0.91, CRT: 1.27 mg/L ±2.7), weight loss (mean ± SD: BFR: -2.4 kg ±1.7, CRT: +1.3 kg ±0.7) and body fat mass reduction (mean ± SD: BFR: -2.5 kg ±1.2, CRT: +0.6 kg ±1.0).

Conclusion: These results provide preliminary evidence that 12-week Kaatsu blood flow restriction training exerts a positive effect on disease activity parameters in patients with arthritis. Furthermore, BFR training shows comparable, in parts even more favourable results than CRT, suggesting it as an effective alternative to conventional strength training. Completion of the study data set is expected in March 2023.

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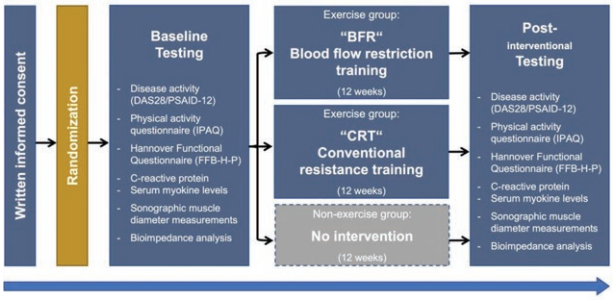


Figure 1. Study design

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1167 PREVALENCE OF OBESITY AND EVALUATION OF THE WAIST CIRCUMFERENCE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS IN A HOSPITAL.

Keywords: Psoriatic arthritis, Comorbidities, Rheumatoid arthritis

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Background: Obesity is a condition characterized by a chronic state of low-grade inflammation due to increased cytokine production in visceral adipose tissue [1].Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PSA) are both autoimmune diseases that share comorbidities such as a high prevalence of obesity, a comorbidity that leads to a lower response to treatment with biologic drugs such as Anti-TNFs [2]. PSA has a higher prevalence of abdominal obesity to RA according to some recent studies [3]. Current research has shown that excess adiposity contributes to the development of cutaneous psoriasis in some patients and suggests that obesity may also be a key factor in the transition from cutaneous psoriasis to arthritis [4], however, it has not been proven the etiological role of obesity in RA [5].

Objectives: To evaluate the waist circumference (WC) and the prevalence of obesity using the Body Mass Index (BMI) in a sample patients from the same hospital with a diagnosis of RA and PSA and to analyze the differences between both diseases.

Methods: It has been carried out an observational, retrospective, single center study. The population included in the study were patients from rheumatology clinic with a diagnosis of RA and PSA who were being treated with biological treatment. The variables analyzed were: age, sex, height (m), body mass (Kg) and WC (cm). The anthropometric variables were measured in the rheumatology nursing clinic. An anthropometric tape was used to measure the WC, taking the height of the navel as a reference in the patients. The BMI was calculated and the World Health Organization classification was used to categorize the patients. A descriptive analysis of the variables analyzed in the study was performed, including the mean and standard deviation (SD) of the continuous quantitative variables (BMI and WC). A one-factor ANOVA was performed to analyze the differences in the variables age, BMI, and WC between RA and PSA patients. Statistical significance was set a priori at $p<0.05$.

Results: In this study a total of 245 RA and 122 PSA patients were included. The WC and BMI data of only 207 patients (121 with RA and 86 with PSA) were completed. The patients with PSA showed higher values of WC, observing significant differences with the patients with RA (103.66±15.05 cm vs 99.38±14.90 cm, p=0.04). However both patients with PSA and with RA showed WC measurements above the recommended values (74.41% vs 74.38%). Regarding BMI, patients with PSA had a higher mean BMI (31.29±6.37 cm vs 28.85±5.84 cm, p<0.043) than patients with RA.

Table 1. Descriptive analysis.

	RA	PSA
N=207	121	86
Age (Mean±SD)	57,31±13,01	56,03±10,74
Sex	26 men (21,5%) 95 women(78,5%)	33 men(38,37%) 53 women (61,63%)
BMI (Mean±SD; min-máx)	28,85±5,84; 18,00-53,78	31,29±6,37; 19,00-49,15
WC (Mean±SD; min-máx)	103.66±15.05; 100,44-106,89	99.38±14.90; 96,70-102,06
WC		
• Men ≥ 102 cm	18 (69,23%)	19 (57,57%)
• Women ≥ 88 cm	72 (75,78%)	45 (84,90%)

Conclusion: In the present study, patients with PSA showed stadistical differences and had higher values of WC and BMI compared to patients with RA, coinciding with recent studies. More studies are necesary to characterize obesity in patiens wih RA and PSA and treat it adequately.

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AB1168 AXIAL INVOLVEMENT IN PSORIATIC ARTHRITIS: WHAT PARTICULARITIES?

Keywords: Psoriatic arthritis, Enthesitis, Disease-modifying drugs (DMARDs)

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory rheumatism belonging to the spondyloarthritis. It is characterised by a heterogeneous clinical presentation.
Objectives: The aim of our work is to evaluate the characteristics of axial involvement in RPso.
Methods: Retrospective study of 86 patients followed for RPso in the rheumatology department over a period of 7 years from 2014 to 2021. The patients were divided into 2 groups: group 1 (RPso with axial involvement) and group 2 (RPso without axial involvement).
Results: Our study involved a population of 86 patients with RPso, the average age was 44.7 years with a female predominance (58.6%), 16.1% of the patients were diabetics, 9.3% were hypertensive, 9.3% were smokers and 2.4% had a history of psoriasis in the family. Concerning the clinical manifestations, 95.3% of patients had polyarthralgia, 73.3% had polyarthritis, 29.4% had deformities and 86% had axial involvement. The bivariate analysis allowed us to identify the results summarised in the following Table 1:

Table 1.

	Group 1 (74 patients)	Group 2 (12 patients)	P value
Women (%)	63.5	33.3	**0.04**
Duration of evolution (years)	8.07	3.5	**0.012**
Psoriasis (%)	39.1	25	0.3
Polyarthralgias (%)	95.9	91.6	0.2
enthesic syndrome (%)	37.5	68.8	0.08
Dactylitis (%)	6.7	41.6	**0.003**
BASDAI >4	72.97	41.6	**0.03**
Average CRP	28.7	50.6	**0.032**
NSAIDs (%)	40.5	75	**0.026**

Logistic regression analysis identified that patients with axial involvement were more likely to have a longer duration of evolution (OR = 3.5) and elevated CRP (OR = 4.9).

Conclusion: Axial involvement in our study was present in 86 % of the patients and was associated with a long.
duration of evolution and a statistically significant higher average CRP.
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Table 1. Univariate analysis to the characteristics of the 2 groups.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1169 THE PRESENCE OF PSORİASİS MIGHT INCREASES STRUCTURAL DAMAGE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Psoriatic arthritis

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Background: Psoriasis is one of the most common extra-articular involvement in axial spondyloarthritis (axSpA) patients.
Objectives: To examine the effect of the presence of psoriasis on the clinical and radiological features of patients with axSpA.
Methods: In this single-center study, 657 axSpA patients (mean age; 39.9±11.7, male gender n:411 [62,7%,]) were included in this analysis, according to the criteria of the Assessment of Spondyloarthritis International Society (ASAS). In addition to the initial demographic, clinical and radiological characteristics of the patients, radiological damage and progression were also evaluated. Demographic and disease-related characteristics were reviewed according to the presence of psoriasis.
Results: In total 43 (6.5%) patients with axSpA had psoriasis. While patients with psoriasis had a higher mean age (44.8±12.4 vs 39.6±11.5; p:0.008), their gender distribution was similar (Table 1). According to the ASAS definition, positive family history (55.6% vs 24.5%; p<0.0001) and basal biological use (41.9% vs 25.9%; p:0.023) rates were also higher in psoriasis patients. While activity scores were found to be similar in patients with and without psoriasis; in the psoriasis group, patient-reported outcome measures (night and general low back pain) and function (BASFI) scores were found to be significantly higher. In addition to the presence of basal cervical (50% vs 31.6%; p:0.032), basal lumbar syndesmophytes (40% vs 18.8%; p<0.006), new syndesmophyte development in the lumbar spine (53.3% vs 10.1%); p<0.0001) rate was higher in axSpA patients with psoriasis. Although the baseline mSASS scores were higher in these patients, the difference did not reach statistical significance. There was no difference between the groups in terms of hip involvement frequency and progression.
Conclusion: Presence of psoriasis might contribute significantly to structural damage and function in axSpA patients, independent of activity.

Table 1. Demographic, some clinical and laboratory characteristics as well as structural characteristics of patients with axial spondyloarthritis with and without psoriasis

	Psöriasis (+) axSpA patients n:43	Psöriasis (-) axSpA patients n:614	*P*
r-axSpA, n(%)	34 (79,1)	397 (64,7)	0,54
Age, year, (mean ±SD)	44,8 (12,4)	39,6 (11,5)	**0,008**
Male sex, n(%)	30 (69,8)	381 (62,1)	0,323
Disease duration, (mean ±SD)	16,3 (14,4)	12,1 (10,0)	0,098
Smoking, ever, n(%)	15/20 (75)	232/332 (70)	0,627
ASAS family history, n(%)	20/36 (55,6)	134/547 (24,5)	**<0,0001**
HLA-B27, n(%)	17/31 (54,8)	282/491 (57,4)	0,777
Biological agent usage, n(%)	18 (41,9)	156/602 (25,9)	**0,023**
Peripheral arthritis, n(%)	17/38 (44,7)	192/558 (34,4)	0,197
Heel pain, n(%)	17/38 (44,7)	250/519 (48,2)	0,683
Hip involvement, n(%)	8/38 (21,1)	75/507 (14,8)	0,300
Uveitis, n(%)	5/38 (13,2)	70/567 (12,3)	0,883
Dactylitis, n(%)	3/39 (7,7)	13/567 (2,3)	0,077
IBD history, n(%)	1/37 (2,7)	11/510 (2,2)	0,628
Crohn		12/510 (2,4)	
Ulcerative colitis			
CRP, (mean ±SD)	20,1 (29,2)	13,8 (21,5)	0,422
ASDAS-CRP, (mean ±SD)	3,1 (1,2)	2,8 (1,2)	0,143
HAQ, (mean ±SD)	1,1 (0,8)	0,9 (0,7)	0,082
BAS-night, (mean ±SD)	5,5 (2,7)	4,4 (3,0)	**0,032**
BAS-G, (mean ±SD)	5,6 (2,7)	4,5 (3,0)	**0,029**
PGA, (mean ±SD)	5,4 (2,8)	4,8 (2,8)	0,220
BASFI, (mean ±SD)	4,6 (3,0)	3,6 (2,9)	**0,035**
BASDAI, (mean ±SD)	4,3 (2,3)	4,3 (2,3)	0,898
ASQol, (mean ±SD)	9,8 (5,3)	9,5 (8,9)	0,559
mSASS basal, (mean ±SD)	13,1 (21,4)	7,8 (16,4)	0,056
Basal cervical syndesmophyte, n(%)	16/32 (50)	143/453 (31,6)	**0,032**
Basal lumbar syndesmophyte, n(%)	12/30 (40)	94/500 (18,8)	**0,006**
Cervical new syndesmophyte, n(%)	5/20 (25)	39/235 (16,6)	0,340
Lumbar new syndesmophyte, n(%)	8/15 (53,3)	26/257 (10,1)	**<0,0001**
New syndesmophyte, n(%)	9/21 (48,8)	54/285 (18,9)	**0,009**
Hip involvement, n(%)	5/41 (12,2)	69/583 (11,8)	0,945
Hip progression, n(%)	1/24 (4,2)	19/322 (5,9)	0,725

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Osteoarthritis

AB1170 TRANSCUTANEOUS VAGUS NERVE STIMULATION AS A PAIN MODULATOR IN KNEE OSTEOARTHRITIS

Keywords: Osteoarthritis

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Background: We no longer consider Osteoarthritis (OA) as a degenerative disease, but rather as a multifactorial disorder in which low grade, chronic inflammation has a central role. In addition, evidence points to the presence of both peripheral and central nervous system sensitization as sources of pain in OA. Transcutaneous Vagus Nerve Stimulation (tVNS) has shown efficacy on pain, inflammation and central sensitization in other conditions such as fibromyalgia, pelvic pain, and headaches and therefore we hypothesized that tVNS could be an additional line of management for knee OA.
Objectives: To assess the efficacy and safety of tVNS on nociceptive pain, central sensitization, neuropathic pain, depression, anxiety, and physical function in individuals with knee OA.
Methods: Afferents of the auricular branch of vagus nerve were stimulated using an auricular electrode connected to a transcutaneous electrical nerve stimulation (TENS) device. We conducted 30 minutes session once a day for 3 days per week for 12 weeks. Sixty-eight patients with chronic knee OA were allocated randomly into active and sham group (34 patients in each group). The outcome measures included visual analogue scale (VAS), pressure pain threshold (PPT), PainDETECT and Douleur Neuropathique 4 (DN4) questionnaires, hospital anxiety and depression scale (HADS), and knee injury and osteoarthritis outcome score (KOOS). These outcome measures were assessed at baseline, at the end of the stimulation period then after 4 weeks later.
Results: There was a significant improvement in VAS for pain score in the active tVNS group between the baseline and first follow-up visit, and between the baseline and second follow-up visit (P <0.001). The median VAS improvement was 4.0 (3.0 – 5.0) in active group versus 1.0 (1.0 – 2.0) in sham group (p <0.001). PPT in right knee, left knee and right elbow was significantly improved compared to baseline in active tVNS and maintained till 4-weeks post-intervention. On the other hand, in the sham group tVNS, right knee PPT was improved but not maintained. PainDETECT and DN4 questionnaires were statistically improved in active tVNS (p <0.001). In contrast, DN4 questionnaire showed no improvement at all and PainDETECT showed improvement that was not maintained at the end of follow up in sham group. A statistically significant improvement in HADS immediately post intervention in active and sham tVNS (p <0.001), this improvement was maintained only in the active group 4 weeks after intervention. Regarding functional outcomes, the improvement in KOOS was significant in the active group only (31.44 ± 18.49, p > 0.001). No serious adverse events were reported in both study groups.
Conclusion: This study provides preliminary evidence for the beneficial effects of tVNS in OA and raises the possibility of using neuromodulation as an add-on treatment to existing pharmacological and non-pharmacological measures.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1171 BARRIERS AND ENABLERS TO UPTAKE OF EVIDENCE-BASED ONLINE EXERCISE TREATMENTS FOR OSTEOARTHRITIS

Keywords: Non-pharmacological interventions, Telemedicine, Osteoarthritis

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Background: Research suggests that delivering evidence-based exercise treatments (ET) for osteoarthritis (OA) online may improve healthcare access and quality of care (de Thurah et al. 2022). Further, such evidence-based online ET were found to be effective and comparable to evidence-based face-to-face ET (Cottrell et al. 2017). Understanding the barriers and enablers of people with OA (PwOA) and physiotherapists (PTs) to uptake of evidence-based online ET may inform efforts to encourage and successfully implement evidence-based practice in routine care for OA.
Objectives: To identify the barriers and enablers of PwOA and PTs to uptake of evidence-based online ET for OA, and to explore the influence of demographics on top-rated barriers and enablers.
Methods: An online survey was circulated to PwOA and PTs in Ireland from March-September 2021. Data items were sought for demographics, and barriers and enablers to evidence-based online ET for OA. Data analysis was performed using frequency distributions to illustrate demographics and the most frequently reported barriers and enablers. Multivariable logistic regression was used to explore the influence of demographics on top-rated barriers and enablers.
Results: 240 stakeholders responded (PwOA=86; PTs=154). PwOA barriers and enablers were related to personal beliefs (e.g., "Preference to wait until I can access face-to-face treatment") and service delivery (e.g., "Improved Wi-Fi and bandwidth"). PT barriers and enablers were related to patient characteristics (e.g., "Patients lack IT resources or knowledge) and organisational readiness (e.g., "Improved IT infrastructure in clinic (e.g., laptops, webcams)"). PTs uptake of evidence-based online ET for OA may be significantly influenced by their work setting (p < 0.05).
Conclusion: Barriers and enablers of PwOA and PTs influencing uptake of evidence-based online ET for OA were related to personal beliefs, service delivery, patient characteristics, and organisational readiness. Future research should examine whether implementation strategies addressing these factors improve uptake and evidence-based practice.
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AB1172 SHINS MUSCLE DYSFUNCTION IN FEMALE PATIENTS WITH KNEE OSTEOARTHRITIS

Keywords: Pain, Osteoarthritis

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Background: Knee osteoarthritis (OA) is a chronic disease known as a common source of pain and disability globally. OA is among the top 10 causes of physical disability in the elderly population. Loss of muscle mass and lower extremity muscle dysfunction are independently associated with progression of OA and reduction in health status.
Objectives: The investigation was aimed at studying the condition of flexor/extensor shin muscles in patients with knee OA, serum leptin concentrations and analyze correlations between them by statistical methods.
Methods: The study involved 71 patients with knee OA and 32 persons from the control group. There was measured the isometric strength of the flexor/extensor shin muscles and measured leptin serum levels. Muscle strength was measured by using an isokinetic device, approved by a state enterprise "Ukrainian Intellectual Property Institute" (patent #81950). All patients were performed common clinical investigations (complaints, medical history, physical examination data) laboratory, instrumental (knee joint X-ray) examinations, and statistical analysis methods were used.
Results: : It was established that the age of OA patients included in the study ranged from 30 to 76 years and averaged 57,60 ± 11,69 years, and 32 % of the examined patients had had the history disease from 6 to 10 years, and 90,4 % of them suffered from excessive body weight or obesity of a certain degree. The study of maximal isometric force of flexor/extensor muscles of both shins revealed a significant reduction in the muscle strength in OA patients compared

with the individuals from the control group. Thus, apparently healthy individuals had the strength of shin flexor muscles (min-max) within 9,6 – 16,9 kg, while the extensors muscles showed 12,6 – 22,5 kg. The OA patients had the strength of both shin muscle groups within the range of 0,7 – 12,1 kg for the flexor group, and 3,3 – 20,3 kg for extensor muscles. At the same time, like in the control group, the strength of the extensor muscles appeared to be higher than the one of the flexors. The calculated total muscle strength (the sum of the flexor and extensor muscle strength of both limbs) in OA patients was 31,97 ± 9,2 kg, whereas in the apparently healthy persons it was 58,65 ± 6,59 kg (p <0,001). The calculated specific muscle strength (the ratio of the total strength to the patient's BMI) in OA patients was 1,03 ± 0,32 kg against 2,21 ± 0,24 kg in the control group (p <0,001). The above data suggest that OA patients were characterized by a decrease in specific muscle strength, not only in total muscle strength. The total force of muscles of patients in relation to healthy individuals was 1,8 times less, the specific force was less 2,2 times. Using the correlation analysis, we established that there was no correlation between the total muscle strength and OA patients` blood leptin (r = -0,05, p>0,05), however, an inverse correlation between the specific force muscle and leptin concentration (r = -0,2, p = 0,09) was found. Instead, in the control group a statistically unreliable direct correlation between the total muscle strength and leptin level (r = 0,12, p>0,05), and the inverse statistically significant association between the specific strength and the leptin concentration (r = -0,412, p<0,05) were revealed. Such an inverse correlation undeniably suggests that the negative effect of leptin on the condition of muscle tissue and the blood elevation thereof is associated with a decrease in muscle strength. At the same time, a significantly lower coefficient of correlation between leptin concentrations and the specific strength of patients` muscles indicates that, in addition to leptin, the disease itself (OA) makes a significant contribution to the reduction of muscle strength.

Conclusion: Understanding the role of the flexor/extensor shin muscles dysfunction in the pathogenesis of knee OA may help to improve further management approaches.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1173 PARAFFIN BATH REDUCES PAIN IN PATIENTS WITH HAND OSTEOARTHRITIS

Keywords: Osteoarthritis, Non-pharmacological interventions, Clinical trials

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Background: In addition to the lack of disease modifying treatments in osteoarthritis (OA), there is also a need for safer and efficacious treatments for pain relief. Patients with hand osteoarthritis (HOA) experience pain that can be incapacitating, which is usually unresponsive to painkillers. Non-pharmacological alternatives are an interesting option for pain relief in HOA.

Objectives: to demonstrate that paraffin baths (PB) provide safe, significant, clinically meaningful pain relief in HOA patients.

Methods: (CAAE:07360819930015045) 67 patients with HOA diagnosis according to ACR criteria were prospectively recruited from March 2020 to August 2022 (interruptions due to COVID pandemic) in private rheumatology services and randomized to receive either 20 min daily sessions of PB, 3 times/week for 4 weeks or a leaflet with information for protection of hand joints (control, C). Baseline demographic, clinical and radiographic (Kellgren-Lawrence, KL score) data were registered. The evaluator was blinded to group allocation. Primary endpoint was 15% reduction of pain on movement (0-10 VAS, visual analogue scale) in the most affected joint of the hand at baseline as compared to pain value at 4w; secondary endpoints were sustained pain reduction at 12w as compared to baseline, increase in grip and pinch strength (KgF) as well as improvement in Cochin hand functional scale (CHFS), FIHOA, and SF-12 scores at 12w as compared to baseline.

Results: baseline characteristics of 34 paraffin and 33 control patients are shown in Table 1; three patients in each group did not return for follow up at 4 weeks; median disease duration was 58(range 3-360) months in both groups; Primary outcome was reached: baseline pain in PB (7.8±1.9) was reduced to 6.4±2.7 (p<0.017) whereas baseline pain in C (7.1±1.8) was not significantly reduced at 4w (6.9±1.9; p=0.7067); reduction of pain in PB was significantly sustained at 12w (6.3±2.9) (p=0.0196). Grip and pinch strength as well as CHFS, FIHOA, and SF-12 scores were similar both at baseline and at 12 weeks in both groups. There were no major adverse events.

Table 1. Baseline characteristics

	Control	PB	P value
Age	60±9	59±10	ns
Women	31(94)	32(94)	ns
BMI	26.6±4	28±5	ns
Month Family income <900 US$	14(42)	21(61)	
K-L>2	24(72)	26(76)	ns
CRP (mg/dL)	0.27±0.19	0.56±0.9	0.123

67 patients were randomized to PB or control treatment; data are mean(%) or SD; ns, non-significant.

Conclusion: PB in a single-blinded prospective randomized trial provided early and sustained pain reduction in HOA. Although larger trials are needed, we believe that spreading of this cheap, easy-to-use method, should be encouraged.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1174 BODY COMPOSITION IN POSTMENOPAUSAL WOMEN WITH CHRONIC KNEE PAIN

Keywords: Pain, Osteoarthritis

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Background: Among all the known risk factors, obesity is one of the important risk factors for the incidence and prevalence of osteoarthritis (OA). However, body mass index (BMI), which reflects the severity of obesity, measures only height and weight with no consideration of other obesity-related characteristics, such as fat distribution or deposition. The features of fat deposition and distribution may serve as better indices of the metabolic activity of adipose tissue and can have an important influence on the pain and disability of patients with OA.

Objectives: The study aimed to assess the body composition indices in postmenopausal women with chronic knee pain and its association with pain severity.

Methods: In the single-center study 230 females aged 50-89 years were examined and divided into groups depending on the intensity of chronic (>3 months) knee pain. Knee pain was assessed using the visual analog scale (VAS). Group I consisted of females with mild (VAS < 4 cm) pain (n = 87), group II - subjects with moderate (VAS more than 4, but less than 6 cm) pain (n = 111), and group III - women with severe (VAS ≥ 6 cm) pain (n = 33). The body composition (body weight (BW), height, body mass index (BMI), fat mass (FM), lean mass, appendicular lean mass (ALM) and appendicular lean mass index (ALMI, ALM/height), fat content (fat mass/BW), and ALM/BW) were assessed by dual-energy X-ray absorptiometry (Lunar, Prodigy). Sarcopenia was determined according to ALM (< 15 kg) or ALMI (< 6 kg/m2), obesity - as BMI > 30 kg/m^2, sarcopenic obesity as a combination of high-fat mass/BW (> 40 %) and low ALM/BW (< 23.47 % for females younger than 65 years old and < 19.4 % for females 65 years and older).

Results: All three groups did not significantly differ in age (F = 2.5, p > 0.05), age of menopause (F = 0.6, p > 0.05), and its duration (F = 0.4, p > 0.05). Women of different groups did not differ in height, however, BW was higher in group III than in groups II and I (84.6 ± 13.8 vs. 77.9 ± 13.9 and 73.0 ± 12.1 kg, F = 9.6, p < 0.0001), as BMI (30.6 ± 5.5 vs. 34.2±6.4, and 30.9±4.9 kg/m^2, F = 13.5, p < 0.00001). The females with chronic severe knee pain had higher ALM (P < 0.0001), ALMI (P < 0.000001), and FM/BW (P < 0.05) compared to the women with mild knee pain. The frequency of obesity was 36.8 % in women with mild pain, 52.2 % of subjects in group II and significantly higher among females with severe pain - 63.6 % (χ^2 = 4.5, p < 0.05 in comparison with group I). Sarcopenic obesity was registered in 18.4, 27.9, and 36.4 % of females of the I, II, and III groups, respectively. It was significantly more frequent among women with severe than mild pain (χ^2 = 4.3, p < 0.04). However, sarcopenia was found in 13.8 % of women in group I, 14.4 % of subjects of group II and 6% of group III according to ALM as well as in 11.5, 10.8, and 6 %, respectively according to ALMI without significant differences.

Conclusion: Women with severe chronic knee pain have significantly higher BW, BMI, ALM, and fat mass than females with mild pain. Despite the absence of differences in sarcopenia frequency, the subjects with severe knee pain have not only an increased frequency of obesity but also high sarcopenic obesity.

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AB1175 IS DISTAL ENTHESITIS OF EXTENSOR DIGITORUM TENDON A SPECIFIC ULTRASOUND FEATURE OF PSORIATIC ARTHRITIS?

Keywords: Ultrasound, Osteoarthritis, Psoriatic arthritis

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Background: Distal interphalangeal (DIP) joints are commonly affected in both hand osteoarthritis (OA) and psoriatic arthritis (PsA). However, enthesitis is well known to be a hallmark of spondyloarthritis including PsA.
Objectives: Our study aimed to assess distal enthesitis of extensor digitorum tendon in PsA and hand OA using ultrasonography (US).
Methods: We conducted a cross-sectional study including two groups: Group 1 included patients with hand OA fulfilling American College of Rheumatology criteria and Group 2 included patients with PsA according to CASPAR criteria. All patients underwent a physical examination followed by an US exam. US was performed in all DIP joints. For each joint, the following abnormalities were assessed: synovial thickening, osteophyte, enthesitis, and power Doppler signal (PDS). A quantitative score (0/1) was used for each lesion. Pearson correlation coefficient was calculated.
Results: We examined 160 DIP joints in 20 PsA patients (13 women and 7 men), with a mean age of 55.5 ± 12.1 years [33–77]. We also examined 80 DIP joints in 10 patients with hand OA (9 women and one man), with a mean age was 66±11 years [46–78]. The mean duration of hand OA and PsA symptoms were 4±3 years and 4±7 years, respectively. Synovial thickening of DIP joints was exclusively noted in PsA patients (**p=0.014**). Osteophytes were exclusively seen in hand OA patients (**p=0.08**). The number of enthesitis was significantly higher in the PsA group (2.79±1.75 versus 1.2±1.75, **p=0.028**).
Conclusion: Our study showed that distal enthesitis of extensor digitorum tendon was suggestive of PsA whereas osteophytes were exclusively observed in hand OA.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1176 DIAGNOSTIC YIELD OF CT-GUIDED BIOPSY IN SUSPECTED INFECTIOUS SPONDYLODISCITIS

Keywords: Imaging, Osteoarthritis

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Background: Infectious spondylodiscitis is a serious and morbid disease. It is often suspected after magnetic resonance (MR) imaging of the spine. Suspected spondylodiscitis requires further workup, in which computed tomography (CT)-guided needle biopsy plays a crucial role.
Objectives: The aim of this study was to examine the yield of CT-guided biopsy in patients with suspected infectious spondylodiscitis, and to identify factors associated with successful pathogen isolation.
Methods: This is a retrospective study involving infectious spondylodiscitis from January 2010 to december2021. All patients were identified with clinically and radiologically suspected infectious spondylodiscitis who underwent CT-guided biopsy of the vertebral lesion. Patient characteristics and clinical details were evaluated. Parameters were compared in patients with positive and negative microbiological and histologic results.
Results: A total of 42 patients (20 men, 22 women) was included. The mean age was 55.8 years (SD ± 16.7). The mean duration of symptoms was 60.2 days (SD ± 52.7). The final diagnosis was tuberculous spondylodiscitis in 15 patients (23.8%), brucellosis spondylodiscitis in 12 patients (28.6%) and pyogenic spondylodiscitis in 15 patients (47.6%). CT-guided biopsy has a diagnostic yield of 44.8% (13/42). Biopsy was contributory in identifying 8/13 patients (58%) with tuberculous spondylodiscitis, and 5/13 patients (42%) with pyogenic spondylodiscitis. Histological examination was the most sensitive diagnostic modality. The factors associated with successful microbe isolation was duration of symptoms (p=0.01) and not exposed to pre-biopsy antibiotics (p=0.02).
Conclusion: The CT-guided biopsy, as a diagnostic procedure for infectious spondylodiscitis, has a reasonably high diagnostic yield in this disease. A higher yield was identified in patients who has long duration of symptoms and not exposed to pre-biopsy antibiotics.
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AB1177 SPINAL EPIDURAL ABSCESS ASSOCIATED WITH INFECTIOUS SPONDYLODISCITIS

Keywords: Osteoarthritis

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Background: Infectious Spondylodiscitis and spinal epidural abscess (SEA) are relatively rare conditions that is rising in incidence. SEA is a challenging entity associated with high morbidity and mortality. That's why early diagnosis is critical in this disease.
Objectives: we aimed to describe the clinical characteristics and outcomes of patients with spinal epidural abscess associated with infectious spondylodiscitis (SEA).
Methods: we conducted a retrospective study from June 2010 to December 2022. We included 42 patients with clinically and radiologically suspected infectious spondylodiscitis. Patient characteristics and outcomes were retrospectively reviewed.
Results: We enrolled 42 patients (23men,19 women) with infectious spondylodiscitis. The mean age was 57.2 years (SD ± 15.7). Twenty-nine patients (72.5%) had SEA. All patients showed varying degrees of focal spinal pain. Fever occurred in 18 patients. Ten patients (34.7%) exhibited neurological deficits. Furthermore, 20 cases (69%) involved lumbar spine, 6 cases (20.7%) involved thoracic spine, and 3 cases (10.3%) involved cervical spine. Abscess locations was Anterior in 14 cases (48.3%), posterior in 5 cases (17,2%), and Circumferential in 10 cases (34.5%). Among 11 SEA patients, 12 cases (41.4%) had infection caused by Mycobacterium tuberculosis, 8 case had infection caused by brucellosis, 5 cases had infection caused by Staphylococcus aureus, one case had infection caused by Staphylococcus coagulase negative, one case had infection caused by Escherichia coli, one case had infection caused by candida albicans, and one case caused by Enterococcus faecalis. All patients underwent conservative treatment, two of which improved symptoms. Five cases undergo surgical treatment, one of which showed improved symptoms, 4 cases had left limb motor and sensitive dysfunction.
Conclusion: SEA is rare and is often difficult to diagnose in the early stage. Early diagnosis, followed by specific therapy is necessary to improve the prognosis of this disease.
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AB1178 THE COMPARISON OF PRP ALONE, SUPERVISED EXERCISE ALONE, AND PRP COMBINED WITH SUPERVISED EXERCISE IN MANAGEMENT OF KNEE OSTEOARTHRITIS

Keywords: Clinical trials, Physical therapy/Physiotherapy, Osteoarthritis

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Background: Platelet-rich plasma (PRP) has sparked widespread interest as a regenerative adjunct therapy, and it is increasingly being used to treat knee osteoarthritis (OA). There is a scarcity of reports on the characterization of injected products, as well as a scarcity of exercise protocols following PRP injections, despite the rising number of studies in the present PRP literature.
Objectives: The purpose of this study was to compare the efficacy of PRP with a supervised exercise program and reveal if the combination of the two treatments is effective in the management of knee OA.
Methods: This is a randomized, single-blinded, prospective, three-arm clinical trial. The PRP group received three weekly injections of fresh, leukocyte-poor PRP. The exercise group followed a structured and supervised exercise regimen for six weeks. These therapies were given in conjunction with the third group. The primary outcome was the change in overall average knee pain scores (on an 11-point numeric pain rating scale, with higher scores indicating worse pain) over a 24-week time period. The secondary outcomes were changes on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), durations of the functional performance tests, and health-related quality of life. For statistical analysis, the mixed model with repeated measurements (ANOVA) was performed.
Results: A total of eight-hundred four patients with mild to moderate knee osteoarthritis were randomly allocated to three groups. There was a significant group-by-time interaction for overall knee pain ($p<0.001$). Pain reduction from baseline to 24 weeks was greater in PRP&Exercise group (Δ -5.40, 95%CIs -5.28 to -4.39). There were significant group-by-time interactions on the WOMAC total score, durations of the functional performance tests, and physical component of SF-12 ($p<0.012$). Exercise group and PRP&Exercise group had statistically greater impact than PRP alone, with large to very large effect sizes in terms of pain, self-reported function and functional performance tests ($p<0.012$, $\eta p2>0.14$).
Conclusion: PRP demonstrated short-term efficacy comparable to exercise or a combination of PRP and exercise; however, when compared to the other groups, it demonstrated a negative tendency in terms of long-term clinical improvements. PRP alone is not as effective as supervised exercise; however, if a patient has difficulties maintaining exercise programs for any reason, PRP can be offered as an alternative option.

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AB1179

VARIATION OF INTER-RATER RELIABILITY FOR BONE MARROW LESION SCORES IN DIFFERENT REGIONS OF THE KNEE: A STUDY USING KIMRISS

Keywords: Osteoarthritis, Imaging

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Background: Semi-quantitative magnetic resonance imaging (MRI) scoring is more challenging in some anatomic regions than others. Bone marrow lesion (BML) is an important scoring feature and may be more closely related to clinical outcomes in arthritis in some anatomic regions than others. The Knee Inflammation MRI Scoring System (KIMRISS) scores BML and synovitis-effusion from fluid-sensitive sagittal MRI[1]. Via web-based interface, readers place ready-made overlays onto scorable portions of each bone, divided into grid squares which are scored dichotomously (yes/no) for presence of BML. The total KIMRISS BML score, which sums positive grid squares on all slices, has been previously shown to have high inter-rater reliability for both status and change.
Objectives: We aimed to evaluate patterns of regional variation in inter-rater reliability for BML across the knee via KIMRISS grid elements. This granular analysis serves as a foundation for further study of the relationship of precise BML location to clinical outcomes.
Methods: Baseline MRI from 61 patients in the Osteoarthritis Initiative (OAI) dataset were scored by 8 trained readers using KIMRISS scoring. Total scores for each of the 28 grid overlay regions (14 femur, 10 tibia, 4 patella) were calculated by adding up positive scores from all scorable MRI slices. We calculated descriptive statistics and interclass correlation coefficients (ICC) for all 28 reader pairs, then combined any neighbouring grid locations with ICC <0.5 before recalculating the ICC.
Results: The 8-reader mean (SD) BML scores at each scoring location (Table 1) showed that the mean reader pair ICC was very good (>=0.80) or good (0.70-0.80) for 17/28 (61%) of the grid regions (Figure 1). The lowest ICCs occurred at the inferior patella [P4; mean (SD) ICC=0.52 (0.19)], a small interior region of the femur [mean (SD) ICC=0.49 (0.26)], and the two most posterior regions of the tibia [mean (SD) ICC=0.41 (0.26) and 0.31 (0.33)]. Lower reliability was also found in regions of tibia not immediately adjacent to the tibiofemoral joint (ICC range: 0.60-0.67) as well as posterior non-articular regions of the femur (ICC range: 0.59-0.65). Combining the posterior tibial regions scores (T5+T55) slightly improved ICC compared to separate scores [mean (SD) ICC= 0.40 (0.29)].
Conclusion: Most individual KIMRISS grid squares were scored with high reliability. Decreased reliability in certain regions may be due to lower incidence of BML or anatomical features that lead to difficulty of interpretation at specific locations. Combining neighbouring regions with lower reliability, such as those at the posterior tibia, may increase reliability if discrepancy arises from assigning a positive score for the same lesion to different grid squares between readers. The patterns of reliability demonstrated here support further study of the impact of precise BML location status scores on clinical outcomes.

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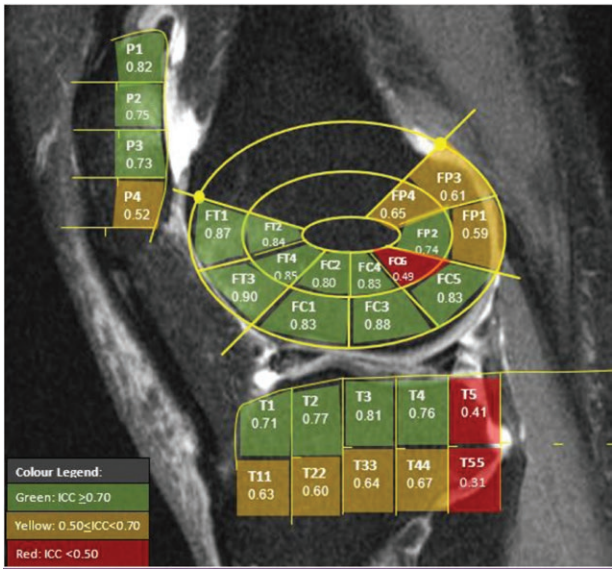


Figure 1. KIMRISS grid region labels with 8-reader mean ICC from baseline knee MRIs from the Osteoarthritis Initiative dataset (n=61).

Table 1. 8-reader mean (SD) BML score at each KIMRISS grid region (colour coded according to ICC in Fig 1.)

Patella		Femur			Tibia		
Region	Mean (SD)	Region		Mean (SD)	Region		Mean (SD)
P1	2.0 (2.5)	Trochlear	FT1	1.8 (2.7)	Subchondral Region	T1	1.6 (2.8)
P2	2.5 (2.6)		FT2	0.6 (2.0)		T2	1.8 (3.0)
P3	1.9 (2.3)		FT3	2.6 (3.0)		T3	1.9 (3.1)
P4	0.6 (1.1)		FT4	0.8 (2.1)		T4	1.4 (2.5)
		Weight-bearing	FC1	1.3 (2.2)		T5	0.5 (1.0)
			FC2	0.6 (1.9)	Below Subchondral Region	T11	0.6 (1.7)
			FC3	0.8 (2.0)		T22	0.8 (1.9)
			FC4	0.3 (1.4)		T33	0.8 (1.8)
			FC5	0.5 (1.6)		T44	0.6 (1.5)
			FC6	0.2 (0.8)		T55	0.2 (0.6)
		Posterior	FP1	0.4 (0.9)			
			FP2	0.2 (0.7)			
			FP3	0.2 (0.6)			
			FP4	0.1 (0.5)			

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AB1180

THE CHANGES OVER TIME OF KNEE STRENGTH AND FUNCTIONAL OUTCOMES BEFORE AND AFTER BILATERAL TOTAL KNEE ARTHROPLASTY

Keywords: Osteoarthritis, Rehabilitation

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Background: Knee osteoarthritis is the most common joint disorder and is associated with functional disability and pain. Total knee arthroplasty (TKA) is considered as an effective treatment for patients with end-stage knee osteoarthritis. However, most patients experienced deterioration in knee strength and functional outcomes immediately after surgery.
Objectives: The overall aim of this study was to investigate the change over time of knee strength and functional outcomes before and after bilateral total knee arthroplasty.
Methods: Retrospective cohort data of 308 patients who underwent primary bilateral TKA were analyzed. Patients underwent home-based preoperative rehabilitation program (3 times per week for 3 or 4 weeks) including strengthening and resistance training. After TKA, standard rehabilitation program was applied to all patients. Outcome measures were assessed 3 times, preoperatively and at 6 weeks and 3 months after surgery which included performance-based physical function test and self-reported physical function questionnaires. Assessment were included the isometric knee extensor and flexor strength of both knees, timed up-and-go (TUG) test, timed stair climbing test (SCT), 6-minute walk test, isometric knee extensor and flexor strength of both knees, knee flexion and extension range of motion, Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) for pain, stiffness, and functional levels. The knee flexion and extension range of motion (ROM) was assessed 5 times including at the beginning and end of standard rehabilitation.
Results: The knee extensor strength and ROM, and SCT of ascending were worsened at the 6 weeks after surgery, and these measures significantly improved following the 6 weeks. The ROM of knee flexion improved earlier than other physical functions and ROM of knee extension worsened after 6 weeks postoperatively. However, the result of self-reported physical function and other performance-based physical functions continued to improve significantly at 6 weeks and 3 months after surgery.
Conclusion: This study demonstrated that the patients who underwent bilateral TKA surpassed most of their physical functions in the 3 months before surgery. However, the recovery of performance-based physical function and self-reported physical function occurred at different times after surgery. Therefore, a rehabilitation treatment strategy according to these changes of physical functions is needed.

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Table 1. Demographic and Disease-Related Characteristics of the Subjects (N=308)

Variables	Values
Age (years)	69.3 ± 4.5
Sex, males/females	39 (12.7)/ 269 (87.3)
BMI (kg/m^2)	26.5 ± 3.2
K-L grades (Grade 3/Grade 4)*	
Right	42 (13.6)/ 266 (86.4)
Left	52 (16.9)/ 256 (83.1)
Comorbidities	
Diabetes mellitus	47 (15.3)
Hypertension	184 (59.7)
Cerebrovascular disease	20 (6.5)
Dyslipidemia	66 (21.4)
ASA PS Classification	
Class I	98 (31.8)
Class II	204 (66.2)
Class III	6 (1.9)

Values represent mean ± standard deviation or number (%) of cases Abbreviations: BMI, Body Mass Index; K-L, Kellgren-Lawrence; ASA PS, American Society of Anesthesiologists Classification Physical Status

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AB1181

INTRAMUSCULAR METHYLPREDNISOLONE ADMINISTRATION IN HAND OSTEOARTHRITIS PATIENTS: A FEASIBILITY STUDY TO INFORM A RANDOMIZED CONTROLLED TRIAL

Keywords: Osteoarthritis

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Background: Inflammation is thought to play an important role in hand osteoarthritis (HOA), which is further associated with pain and increased limitation of hand function [1,2]. Therapeutic options in HOA are scarce [3].
Objectives: The aim of this study was twofold: to explore the acceptability of treatment with intramuscular (IM) methylprednisolone (MP) in hand OA by both healthcare providers (HCPs) and hand OA patients, and to observe the response to a single IM MP injection in patients with symptomatic hand OA.
Methods: We adopted a mixed methods design. Firstly, in a qualitative study we examined the acceptability of intramuscular MP using questionnaires with open-ended questions for all health care providers of the Rheumatology Department of the Sint Maartenskliniek and a semi-structured interview for an a-selective group of patients with clinically diagnosed hand OA not previously treated with MP. Secondly, in a prospective observational study the course of symptoms was examined in patients with hand OA who received an intramuscular MP injection as part of routine care. Data on average pain and the intensity of pain in the hands and other joints (both assessed on a Numeric Rating Scale), OA related functional impairment (Functional Index of Hand Osteoarthritis questionnaire), use of analgesics and occurrence of adverse events was collected with a checklist within 3 days after the injection was administered (baseline) and at week 4, 8 and 12 after the injection.
Results: Fourteen health care providers (all rheumatologists) and 15 patients (93.3% female, mean age = 67 years) participated in the first part of the study. HCPs considered intramuscular MP therapy as an effective therapeutic intervention and most patients were very open to get this therapy, yet they all expressed

their concerns about the risk of long-term adverse events. Twenty-two patients with hand OA participated in the second part of the study. Intramuscular MP administration decreased hand pain with 1.96 (week 4), 1.59 (week 8) and 1.23 (week 12), as compared to baseline (Table 1). The average pain in other joints decreased at 4 weeks after MP administration with 0.73 and at 8 weeks HOA related functional impairment decreased with 2.19, as compared to baseline. A total of 13 patients reported 45 adverse events, of which almost half occurred within the first four weeks after MP administration.

Response to therapy	Baseline (n=22)	Week 4 (n=22)	Week 8 (n=21)	Week 12 (n=22)	P value Δ t0 to t4	P value Δ t0 to t8	P value Δ t0 to t12
Average hand pain (0-10), mean (±SD)	5.96 (± 1.43)	4.00 (±2.41)	4.37 (±2.28)	4.73 (±2.00)	0.001	0.002	0.002
Average pain in other joints (0-10), mean (±SD)	5.00 (±2.43)	4.27 (±2.29)	4.41 (±2.22)	4.59 (±2.11)	0.073	0.179	0.226
FIHOA-score (0-30), mean (±SD)	12.96 (± 5.65)	10.64 (±6.26)	10.77 (±5.26)	11.45 (±5.89)	0.052	0.018	0.225
Analgesics use, n (%)	21 (95,5)	19 (86,4)	18 (81,8)	20 (90,9)	0.024	0.021	0.003
Patients with adverse events, n (%)		13 (59)	12 (57)	12 (54,5)			

Conclusion: We found a high acceptability of intramuscular MP treatment for hand OA and our findings suggest that methylprednisolone may reduce pain and improve hand function as quick as 4 weeks after administration, with a persisting effect of almost 3 months. This suggests that it might be a valid long-term therapeutic option in these patients.

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AB1182 EFFECTIVENESS OF FATIGUE INTERVENTIONS IN OSTEOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Osteoarthritis, Physical therapy/Physiotherapy, Systematic review

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Background: Pain and physical function are common factors targeted for osteoarthritis (OA) management. However, fatigue has been reported as an important component of OA experience and a significant concern for people with OA (Power et al., 2008). Despite this, fatigue has received very little attention. However, with increasing interests in fatigue, it is expedient that fatigue be considered a top priority in clinical practice (Overman et al., 2016). Thus, there is dire need for evidence-based fatigue interventions in OA given the paucity of evidence in this area.
Objectives: To identify fatigue interventions and determine the effectiveness of the interventions in reducing fatigue immediately and over time in OA.
Methods: A review protocol was developed and registered with the PROSPERO database, with the ID-CRD42020163730. Studies included comprised peer-reviewed randomized controlled trials (RCTs) that examined the effects of any intervention in the management of fatigue or vitality outcomes in people with upper limb and lower limb OA. Studies that used spiritual, pharmacological or surgical interventions to manage fatigue in patients with upper limb and lower limb OA were excluded. The Cochrane Collaboration's tool for assessing the risk of bias (ROB) was used assess the quality of evidence for the included RCTs. Narrative synthesis was used to summarise the identified fatigue interventions while only studies on exercise interventions were used in the meta-analysis.
Results: Out of 2,586 studies identified from database search, 31 RCTs studies were included after screening for titles, abstracts and full texts. Of the 31 included RCTs, only nine studies were included in the meta-analysis comparing the effects of exercise versus non-exercise interventions on fatigue. From the ROB assessment, 11 RCTs were of low ROB whilst 11 had moderate and 9 high ROB respectively. The narrative synthesis identified 12 interventions for fatigue and these include activity pacing, cognitive behavioural therapy (CBT), yoga, exercise, acupuncture, moxibustion, pain-coping skills, BEMER therapy, modified shoes, massage/aromatherapy, education and thermotherapy. Exercises interventions included strengthening, balance, kinesthesia, and mobilization, hand-based, stretching, aquatic danced-based and web-based exercises. Activity pacing (mean difference [MD]=0.8; (standard deviation [SD]=0.3), CBT (MD=4.32; [SD]=1.85), moxibustion (vitality: MD=-2.61; [standard error]=-1.69) had statistically significant reductive immediate effect on fatigue. The meta-analysis pooled effects showed that exercise interventions on fatigue in OA was not statistically significant both immediately (SMD=-0.10; 95% CI -0.74, 0.54; I^2=94%) and overtime (SMD=-0.79; 95% CI -2.30, 0.73; I^2=98%), although the effects was in favour of exercise interventions relative to other comparison non-exercise interventions.
Conclusion: Activity pacing, CBT and moxibustion interventions showed beneficial effects on fatigue in OA immediately. Cumulatively, the pooled effect of exercise on fatigue was not statistically significant immediately and overtime but the effect was in favour of the exercise interventions relative to other control interventions. However, there is currently insufficient evidence regarding the effectiveness of majority of identified fatigue interventions in this review. Further, the findings of the meta-analysis may have been affected by high level of heterogeneity. Largely populated RCTs with low ROB are needed to ascertain the effectiveness of fatigue interventions in OA population.

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AB1183 NEUROPATHIC PAIN IN PRIMARY KNEE OSTEOARTHRITIS

Keywords: Osteoarthritis, Pain

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Background: Pain is a major symptom in primary knee osteoarthritis. The mechanisms of this pain are heterogeneous explaining the variable response to different treatments. The presence of a neuropathic pain (NP) may be associated with a different phenotype disease.
Objectives: The present study was conducted to identify the frequency of NP in patients with painful primary knee osteoarthritis, and to investigate its correlation with socio-demographic factors, anthropometric and postural features, physical function, quality of life, and disease severity.
Methods: The study included 200 patients with primary osteoarthritis of the knee who did not have co-morbid disorders and/or were taking drugs that may cause neuropathy. NP was assessed by both Douleur Neuropathique 4 questions (DN4) and painDETECT questionnaires.
Results: The mean age of the patients was 59.15 7.62 years. The majority were women (87.5%). The mean of the body mass index was 24,72±4, 84 kg/m^2. The mean of the quadriceps perimeter was 48,28±4,14cm. The mean of the waist circumference was 93,04±11,43 cm. The mean of the total Womac score was 53,61±4,93. NP was detected in 55.5% of patients according to DN4 questionnaire and in 46% according to painDETECT questionnaire. DN4 score was positively correlated with VAS (VAS Visual analogue Scale)-pain at rest (r_s=0,188; P=0,009), VAS pain on movement (rs=0.173; P=0.0017), Womac pain score (rs=0.157; p=0.030), Womac stiffness score (rs=0.253; p=0.000),

Physical function Womac score (rs=0.271; p=0.000), total Womac score (rs=0.305; p=0.000) and Lequesne index (rs=0.221; p=0.002), and it was negatively correlated with perimeter quadriceps (rs=-.210;p=0.008), while painDETECT score was positively correlated with VAS pain on movement (rs=0.220; p=0.002), Womac stiffness score (rs=0.147; p=0.043), Womac physical function score (rs=0.172; p=0.017), and total Womac score (rs=0.182; p=0.012). The risk factors of NP retained according to DN4 score were longer symptom duration (p=0,030) and a reduced quadriceps perimeter, whereas painDETECT score was associated with high VAS pain on movement (p=0.022).

Conclusion: NP is common in primary knee osteoarthritis. The presence of NP is associated with more painful pathology and extreme disability.

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AB1184 ANXIETY, DEPRESSION AND FIBROMYALGIA: SIMILAR PREVALENCE IN OSTEOARTHRITIS AS IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Osteoarthritis, Fibromyalgia

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Background: Non-articular comorbidities, including anxiety (ANX), depression (DEP) and fibromyalgia (FM), are common in patients with rheumatic diseases. Their presence may impact measures of disease activity and responses to treatment. The burden of ANX, DEP and FM has been described in many reports concerning patients with rheumatoid arthritis (RA), but far less information is available concerning these comorbidities in patients with osteoarthritis (OA). It is feasible to screen for these comorbidities in all patients seen in routine care using a multidimensional health assessment questionnaire (MDHAQ)[1,2], completed by patients in 5-10 minutes before seeing the rheumatologist, which includes screening indices for ANX, DEP, and FM.

Objectives: To analyze the prevalence of positive screening for ANX, DEP, and/or FM in patients with OA compared to RA in routine care at an academic rheumatology center.

Methods: All patients seen for routine rheumatology care are asked to complete an MDHAQ, which includes 0-3 physical function and ANX and DEP scales in the patient friendly HAQ format, three 0-10 visual numeric scales (VNS) for pain, fatigue and global status, self-report 0-54 RADAI painful joint count, 60-symptom checklist review of systems (ROS) including ANX and DEP, medical history queries, and 4 indices: RAPID3 (routine assessment of patient index data to assess patient status in all diseases studied), MDHAQ ANX screen (MAS2), MDHAQ DEP screen (MDS2)[1], and fibromyalgia assessment screening tool (FAST4) [2]. MAS2 and MDS2 are positive for ANX or DEP if 0-3 ANX or DEP response is ≥2 OR positive ANX or DEP on the symptom checklist. FAST4 is positive if 3/4: pain VNS ≥6/10, fatigue VNS ≥6/10, self-report painful joint count ≥16/54, and/or symptom checklist ≥16/60. Patients were classified as OA or RA according to primary ICD 10 diagnosis. An MDHAQ database was used to compute retrospectively medians and interquartile ranges (IQR).

Results: The study included 366 OA and 488 RA patients seen between 2013 and 2022. Patients were mostly female and OA patients were slightly older (Table 1). RAPID3 was similar in RA and OA patients. Positive screening for ANX was seen in 28.4% of OA and 21.9% of RA patients (p= 0.04, Table 1), for DEP in 21.6% of OA and 18% of RA patients (p>0.05), and for FM in 20.4% of OA and 20% of RA patients (p>0.05).

Conclusion: Positive ANX, DEP, and FM screening is seen in > 20% of routine care patients with primary diagnoses of OA or RA, at similar levels in OA and RA. Although definitive diagnosis requires a physician, MAS2, MDS2, and FAST4 agree more than 80% with reference standards which are highly associated with positive diagnoses. The results underscore a need for rheumatologists to aware of these comorbidities, easily screened for using an MDHAQ.

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Table 1. Positive anxiety, depression and fibromyalgia screening in routine care OA and RA patients

	Rheumatoid Arthritis	Osteoarthritis	p-value*
N	488	366	
RAPID3	13.3	14.0	0.48
median (IQR)	(13.2)	(10.1)	
MAS screening for anxiety	107	104	0.04
n (%)	(21.9%)	(28.4%)	
MDS screening for anxiety	88	79	0.23
n(%)	(18.0%)	(21.6%)	
FAST4 ≥3 screening for fibromyalgia	98	75	0.95
n(%)	(20%)	(20.4%)	

*Chi square test for comparison of proportions, Mood's median test for comparison of RAPID3

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AB1185 POLYACRYLAMIDE HYDROGEL FOR THE TREATMENT OF KNEE OSTEOARTHRITIS: 3 YEAR FOLLOW UP RESULTS OF A PROSPECTIVE CLINICAL STUDY

Keywords: Osteoarthritis

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Background: Polyacrylamide hydrogel (iPAAG), manufactured by Contura International, is CE marked for the symptomatic treatment of patients with knee osteoarthritis (OA). iPAAG fulfils an unmet clinical need for an effective, long-acting and safe non-surgical treatment that may postpone knee surgery for those with OA.

Objectives: To evaluate the efficacy and safety of a single injection of 6 ml intra-articular iPAAG on knee symptoms in participants with moderate to severe knee OA for up to 5 years after treatment.

Methods: In this prospective, multicentre study (3 sites in Denmark) participants received a single intra-articular injection of 6 mL Arthrosamid®. The initial 1-year study was extended to follow the participants for up to 5 years. The study was approved by the Danish Health authorities and the local Health Research Ethics committee. All participants provided informed consent prior to study activities and signed a new consent form to participate in the extension phase. Injections were given by an investigator experienced in administering intra-articular injections. Participants could continue analgesics (except 48 hours prior to visits) and non-pharmacological therapy, but topical (on target knee) and systemic corticosteroids or additional injections were not allowed. Outcomes included the WOMAC pain, stiffness and function subscales (0-100 score where 100 was worst) and Patient Global Assessment of disease impact (PGA). Changes from baseline in these outcomes were analysed using a mixed model for repeated measurement (MMRM) with a restricted maximum likelihood-based approach. The estimated changes based on the least square means were presented including 95% confidence limits and corresponding p-values. Additional sensitivity analyses were for the 3-year data. The MMRM analysis was repeated, but only data from the 35 participants that continued into the extension phase were included. In another analysis an ANCOVA model was used where missing values at 3 years were replaced by the participants baseline value (BOCF).

Results: 49 participants (31 females) with mean age of 70 years (range 44 – 86 years) were treated with iPAAG. 46 participants completed the 1-year assessment and 35 participants (22 females) continued into the extension phase. A site closure and the increased length of the study were the most common reasons for not continuing. 29 participants completed the 3-year follow-up.

The originally planned MMRM analysis including all available data from the 49 treated participants showed clinically relevant and statistically significant decreases from baseline to 3 years for each of the 3 WOMAC subscale scores and the PGA (Table 1).

Table 1. Analyses of change from baseline to 3 years in transformed (0-100) WOMAC subscales

	Number of participants		LSMean (95% CI)	p-value
	At baseline	At 3 years		
WOMAC pain subscale				
Planned analysis	49	29	-18.0 (-24.9; -11.1)	<0.0001
Extension participants	35	29	-17.7 (-24.7; -10.8)	<0.0001
Baseline carried forward	49	49	-12.1 (-17.0, -7.3)	<0.0001
WOMAC stiffness subscale	49	29	-16.4 (-22.5; -10.3)	<0.0001
WOMAC Phys. Function subscale	49	29	-14.9 (-21.4; -8.4)	<0.0001
Patient Global Assessment	49	29	-15.0 (-27.6; -2.4)	0.0223

The analysis only using the data from the extension phase participants showed a similar change from baseline in the WOMAC pain subscale compared to the result of the planned analysis (Table 1). The BOCF analysis also showed a clinically relevant and statistically significant decrease in the WOMAC pain subscale from baseline. 74 adverse events have been reported in the study including 19 new events reported between the 2-year and 3-year visits. None of the new events were assessed as related to treatment and Covid-19 infection was the most frequently reported AE in this period. 3 of the new events were SAEs (Covid-19 infection, pre-syncope, uterine prolapse).

Conclusion: Single injections of 6 ml intra-articular iPAAG are well tolerated and continue to provide clinically relevant and statistically significant effectiveness at 3 years after treatment.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1186 BODY MASS INDEX EFFECTS QUADRICEPS MUSCLE ARCHITECTURAL CHARACTERISTICS IN PATIENTS WITH KNEE OSTEOARTHRITIS

Keywords: Imaging, Osteoarthritis, Ultrasound

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Background: Sufficient lower extremity muscle mass is necessary for performing functional tasks. It is well known that body mass index (BMI) adversely effect knee cartilage health but in knees with osteoarthritis (OA) it is still unclear how BMI level effect knee muscle architectural characteristics.

Objectives: The aim of this study was to investigate effect of body mass index (BMI) level on quadriceps muscle architecture in patients with knee OA and healthy controls.

Methods: Nineteen patients with OA (mean age= 50.58±4.56 years, mean BMI=28.29±2.51 kg/m2,) and twenty healthy controls (mean age= 48.35±2.83 years, mean BMI=26.76±4.88 kg/m2) were included in the study. Rectus Femoris (RF), Vastus Medialis (VM) and Vastus Lateralis (VL) muscles thickness and pennation angle were evaluated using B-Mode ultrasonography (Esaote MyLab X8 eXP Ultrasound System, Florence, Italy). Ultrasound images were analyzed offline using an image analysis software (Image J, National Institutes of Health, Bethesda, MD, USA) program. When investigating the changes in muscle architecture by group, the effect of BMI was adjusted using covariance analysis (ANCOVA) tests.

Results: There were no differences between age (p=0.073) and BMI (p=0.10) in both groups. Interaction between groupXBMI represented in Table 1. Control group had higher RF muscle thickness, RF pennation angle, VM muscle thickness, VM pennation angle and VL muscle thickness than OA group. There was significant effect of BMI on VM and VL muscle thickness.

Conclusion: Patients with knee osteoarthritis has lower quadriceps muscle thickness and pennation angle than matched healthy controls and BMI was an important factor effecting muscle characteristics. The decrease in VM and VL muscle thickness were associated with increased BMI in knee OA group. These findings highlight the need of body weight control in order to restore muscle thickness in knee OA patients.

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Table 1. Muscle architectural characteristics of the groups and interaction between group and BMI.

	Parameters	OA Group (n=19, 27 knees) mean (SD)	Healthy Group (n=20, 39 knees) mean (SD)	Group effect p	BMI effect p
RF	Muscle thickness (cm)	1.78±0.35	1.99±0.30	**0.006**	0.153
	Pennation angle (°)	11.76±3.63	13.71±2.29	**0.008**	0.444
VM	Muscle thickness (cm)	1.6±0.37	1.88±0.28	**<0.001**	**0.032***
	Pennation angle (°)	10.08±3.62	13.05±2.7	**<0.001**	0.889
VL	Muscle thickness (cm)	1.84±0.5	2.05±0.33	**0.014**	**0.032***
	Pennation angle (°)	15.85± 2.96	15.71±2.83	0.899	0.770

OA: Osteoarthritis, RF: Rektus Femoris, VM: Vastus Medialis, VL: Vastus Lateralis, SD: Standard Deviation *p<0.05 Significant effect of BMI on groups.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1187 RELIABILITY AND VALIDITY OF THE CONE EVASION WALK TEST IN HIP OSTEOARTHRITIS

Keywords: Outcome measures, Pain, Osteoarthritis

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Background: Hip osteoarthritis (OA) is associated with joint pain and stiffness, reduced balance, impeded mobility, and loss of functional independence [1]. Falls are the leading cause of fatal and nonfatal injuries among older adults and people with hip OA. Fall-related injuries and circumstances such as hip fractures and subsequent arthroplasty procedures put a significant burden on financial resources and healthcare systems [2]. Therefore, the identification and prevention of falls are easier, cheaper, and more effective for all parties in healthcare. The Cone Evasion Walk Test (CEW) is a dual-tasked performance measurement that was designed for evaluating dynamic balance, proactive gait control, and fall risk by assessing the ability to evade obstacles [3].

Objectives: The aim of this study was to investigate the reliability and validity of the CEW in patients with hip OA and estimate the minimal clinically important difference (MCID) of the CEW.

Methods: Twenty-seven patients with hip OA were included in this study. Patients performed trials for the CEW and the Timed up and Go Test (TUG). Between the CEW trials, patients got to rest for an hour.

Results: The analysis showed that the CEW has excellent reliability and validity in hip OA (p<0.001). The relative (ICC coefficient) and absolute (SEM and SRD95) reliability of the CEW were 0.95, 0.53, and 1.46 respectively. The Spearman correlation coefficient with the TUG was 0.65.

Conclusion: The CEW was shown to be effective in terms of evaluating the function, dynamic balance, mobility, and fall risk with an additional attention-demanding task in patients with hip OA. The low MCID value (1.46) provides a sensitive measure of alterations in a patient's condition. Therefore, the CEW may be a better assessor of the proactive gait control, fall risk, mobility, and dynamic balance activities in the everyday community than the existing performance measures.

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AB1188

DYNAMICS OF PAIN SYNDROME DURING 180-DAY TREATMENT WITH UNDENATURED COLLAGEN TYPE II IN COMPARE TO GLUCOSAMINE AND CHONDROITIN COMBINATION

Keywords: Pain, Quality of life, Osteoarthritis

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Background: OA osteoarthritis is a heterogeneous group of diseases of different etiology with similar biological, morphological, clinical manifestations and consequences, which are based on damage to all articular structures (cartilage, subchondral bone, synovial membrane, ligaments, capsules, periarticular muscles). A key role in the pathogenesis of OA is played by an increase in the catabolic activity of various cytokines, as well as matrix metalloproteinases (MMP) of the cartilage itself.
Objectives: The purpose of the study was to compare the dynamics of pain syndrome (based on Western Ontario McMaster Osteoarthritis Index – WOMAC pain subscale) during 180-day treatment with undenatured collagen type II (UC-II) and glucosamine and chondroitin (G + Ch) combination in patients with Grade II knee OA.
Methods: Patients with Grade II knee OA were investigated. 20 patients were administrated the UC-II during 180-day period, 20 patients took the combination of G + Ch during the same period. WOMAC pain subscale was used to evaluate the effectiveness and was completed before the start of therapy and after 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 90, 120, 150, 180 day of treatment. Visual analog scale (VAS) from 0 to 10 was used for assessment the WOMAC subscale by patient. In this abstract we presented the dynamics of pain during walking and nocturnal pain.
Results: The initial data of pain during walking and nocturnal pain in UC-II group were 6.29±0.37 and 4.35±0.59, after treatment – 2.99±0.37 (-52.46 %, p <0.05) and 1.7±0.41 (-60.92 %, p <0.05). In G + Ch group initial data were 7.05±0.43 and 4.85±0.69, after therapy – 3.85±0.35 (-45.39 %, p <0.05) and 2.85±0.51 (-41.24 %, p <0.05). Comparing groups demonstrated the better results according to decrease of WOMAC pain subscale in the group of UC-II: reduce of pain during walking by 28.76 % and reduce of nocturnal pain by 67.65 % (p <0.05). The analysis of the graph of pain during walking has recorded the beginning of significant pain reducing after 30 day of treatment in both groups (Figure 1). The analysis of the graph of nocturnal pain has showed the beginning of significant pain reducing after 50 day of treatment in both groups. Dynamics of nocturnal pain reducing in the G + Ch group was more unstable with periods of reduced efficiency, while in the UC-II group the dynamics was smooth without fluctuations.

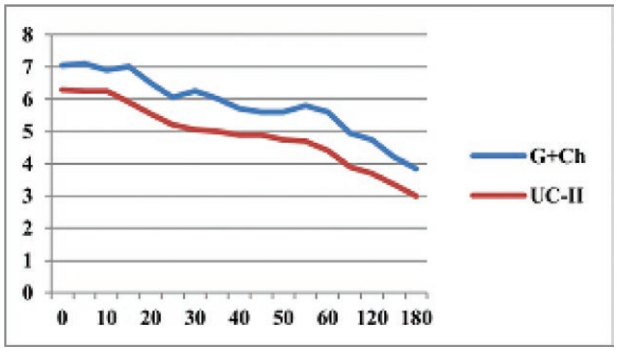


Figure 1.

Conclusion: The therapy of Grade II knee OA with UC-II during 180-day demonstrates the benefit in reducing of pain during walking and nocturnal pain in compare to G + Ch combination. The dynamics of nocturnal pain reducing in the UC-II group characterizes by gradual decline without significant fluctuations.

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AB1189

BOTULINUM TOXIN TYPE A OR SELECTIVE GENICULAR PULSED RADIOFREQUENCY FOR TREATING ADVANCED KNEE OSTEOARTHRITIS

Keywords: Randomized control trial, Pain, Osteoarthritis

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Background: Knee osteoarthritis was the most common type (6% of all adults). Developing osteoarthritis increases with age. Pain is a key symptom in the decision to seek medical care and is an important antecedent to disability.
Objectives: To discuss the effectiveness, indications, limitations and side effects of botulinum toxin type A and genicular nerves pulsed radiofrequancy for treating osteoarthritis to help clinicians choose the most appropriate treatment.
Methods: Randomized double blind controlled trial study, ***fifty two participants were recruited divided into 2 groups as follows:***Group I (Bx): 25 patients given intra-articular botulinum toxin type A 100 IU sonographically guided in patient with osteoarthritis knee according to American Collage of Rheumatology criteria and in stage 3 or 4 of the Kellgren_Lawrence classification Group II (RF): 27 patient get radiofrequncy ablation of genicular nerves. The primery outcome was Visual analogue pain score (VAS), secondry outcome was stiffness, physical function of each knee using Western Ontario and McMaster University Osteoarthritis Index (WOMAC), and Calculation of Oxford knee score at base line, 4,8,12 and 24 weeks.
Results: 16 female and 9 male in group I versus 10 female and 17 male in group II. The mean age were 54.36±7.8 years, there was significant difference in pain VAS between groups at 4th week (P value = 0.005). A significant difference in WOMAC pain at 4th and 12th weeks (P value > 0.001), WOMAC stiffness at 12th and 24th weeks (P value > 0.001), WOMAC function 4th, 12th and 24th weeks (P value > 0.001) and WOMAC total at 4th, 12th and 24th weeks (P > 0.001).However there were no significant difference in Oxford between the two groups.
Conclusion: Intra-articular Botulinum toxin type A 100 IU can reduce the overall pain and improve the function in Knee osteoarthritis with higher effecacy than Pulsed Radiofrequancy. However. Further research is needed to compare the effect of botulinum toxin type A and Radiofrequancy for the different stages of Osteoarthritis.

Variables	Group I (Botox) (n=25)	Group II (Radiofrequency) (n=27)	*P*-value
WOMAC pain preintervention	16 (1)	16 (1)	0.84
WOMAC pain 4 wk	5 (2) *	15 (5) *	<0.001
WOMAC pain 12 wk	5 (2) *	8 (6) *	<0.001
WOMAC pain 24 wk	5 (2) *	5 (11) *	0.77
WOMAC stiffness preintervention	7 (1.5)	7 (2)	0.88
WOMAC stiffness 4 wk	3 (1.5) *	3 (5) *	0.15
WOMAC stiffness 12 wk	3 (1.5) *	7 (2)	<0.001
WOMAC stiffness 24 wk	3 (1) *	7 (1)	<0.001
WOMAC function preintervention	50 (10)	51 (5)	0.42
WOMAC function 4 wk	16 (8) *	49 (26) *	<0.001
WOMAC function 12 wk	16 (7.5) *	50 (26) *	<0.001
WOMAC function 24 wk	16 (8.5) *	50 (17) *	<0.001
WOMAC total preintervention	73 (11.5) *	71 (6) *	0.38
WOMAC total 4 wk	23 (11)	68 (34)	<0.001
WOMAC total 12 wk	24 (10.5)	66 (33)	<0.001
WOMAC total 24 wk	24 (10.5)	64 (25)	<0.001

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1190

ATTITUDES AND BELIEFS REGARDING TREATMENT IN PATIENTS WITH OSTEOARTHRITIS

Keywords: Osteoarthritis, Patient information and education

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Background: Therapeutic decision is one of the essential procedures for coping with the disease, so adherence to treatment is one of the key elements of care, particularly in patients with degenerative musculoskeletal pathologies, in particular osteoarthritis.

These attitudes can be influenced by beliefs about drugs, which will affect the care and quality of life of patients.
Objectives: The objective of this study is to assess beliefs about medications as well as associated factors in patients with osteoarthritis.
Methods: This is a cross-sectional study that included any patient ≥ 18 years of age followed for knee osteoarthritis or digital osteoarthritis who presents to the rheumatology department. We excludedpatients with psychiatric or memory disorders or who refused to participate in the study. Sociodemographic data, comorbidities, information on functional impact and treatments received were collected. A validated questionnaire: Belief on Medicine Questionnaire (BMQ) specific which allows to evaluate the beliefs of the patients related to the need and the concerns towards the drugs was used. The specific BMQ is made up of two subscales: the first includes questions related to the necessity for treatment, the second includes questions about concerns related to the prescription. Each of the sections is made up of five graduated scales from 1 (strong disagreement) to 5 (strong agreement). The specific BMQ is therefore rendered as two scores ranging from 5 to 25 and can be expressed as a need-concern differential ranging from –20 to +20, which is an equivalent of the benefit-risk ratio perceived by the patient.
Results: We have included 221 patients. The average age was 59.4+-9.8, 88.7% of patients were women. 70.6% of patients were illiterate. 62.1% of patients had comorbidities. 80.5% were followed for knee osteoarthritis and 19.5% for digital osteoarthritis. The median duration of evolution was 8 [2-10] years. For the treatments, 53.8% of the patients in our study were on anti-osteoarthritis treatment, 44.7% had already received an NSAID and 11.7% had already received an injection. The mean of the BMQ- specific necessity was 16.92+-6.33 and 52% of patients strongly believed that drugs are essential to keep them healthy. The average of the BMQ-specific concerns were 14.69+-5.69 The main concerns of patients were the lack of information about the medications they were taking in 45.9% and 38% of patients were concerned about the potentially harmful consequences of their treatment. The median need-concern differential was 2 [-3 - 8] suggesting a positive risk-benefit ratio perceived by the patients. In multivariate linear regression, only functional disability is statistically significantly associated with the need-concern differential (OR=0.24, 95% CI [0.204-0.817], p=0.001).
Conclusion: Moroccan osteoarthritis patients have a positive perception of the benefit-risk ratio towards their treatments. Functional disability is the main factor incriminated in this perception. Therapeutic education must take more place in the management of osteoarthritis patients.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1191 FACTORS ASSOCIATED WITH WALKING SPEED IN PATIENTS WITH END-STAGE KNEE ARTHRITIS WHO ARE SCHEDULED FOR TOTAL KNEE ARTHROPLASTY

Keywords: Gastrointestinal tract

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Background: Patients with knee joint disorders have impaired mobility, which interferes with their daily lives, resulting in frailty. Various factors are assumed to contribute to the decline in walking speed, which is an indicator of mobility.
Objectives: In this study, we measured the gait speed of patients scheduled to undergo initial total knee arthroplasty (TKA) and examined the factors that correlate best with gait speed.
Methods: Patients with end-stage knee arthritis who underwent initial TKA at our hospital between July 2020 and October 2022, and whose gait speed was measured before surgery with written consent, were included in the study. We investigated the relationship between basic attributes such as age and gender at the time of the survey, pain VAS during walking, clinical evaluation of knee joint function (Knee Society Score: KSS), skeletal muscle mass of both lower limbs (whole-body mode Dual Xray Absorptiometry method), quadriceps muscle strength (flexion and extension strength by dynamometer), and range of motion (degree of flexion and extension), frailty, sarcopenia.
Results: 210 subjects (170 women, mean age 75.5 years) were included in the study. Multivariate analysis was performed using walking speed as the objective variable and age, gender, VAS for pain during walking, KSS, skeletal muscle mass of both lower limbs, quadriceps muscle strength(flexion and extension strength), range of motion(degree of flexion and extension), frailty and sarcopenia as dependent variables. The results showed that age and walking pain VAS and KSS were significantly and independently associated with walking speed (P=0.01, 0.04, 0.05). Gender, skeletal muscle mass of both lower limbs, quadriceps strength (flexion and extension), range of motion (degree of flexion and extension), frailty, and sarcopenia were not found to be significantly associated with walking speed (P = 0.79, 0.13, 0.65, 0.21, 0.68, 0.74, 0.34, 0.20).
Conclusion: Age was found to correlate most with walking speed, with walking speed slowing with increasing age. A correlation between lower quadriceps muscle extension and lower walking speed has been reported previously, but this study did not correlate. Nor did it correlate with lower limb skeletal muscle mass or range of motion. Pain during walking was observed in many cases, so it may not have been significant.
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Factor	Group	
disease (n)	osteoarthritis	213 (97%)
rheumatoid arthritis	7 (3.0%)	
body mass index (kg/m2)	26.22(4.60)	
pain VAS on walking	44.05 (30.35)	
total Knee Society Score	76.48 (27.89)	
range of motion (degree)	flexion	118.45 (13.8)
extension-10.43 (13.8)		
quadriceps power (N)	143.43 [34.00, 350.00]	
waling speed (m/sec)	0.88 (0.33)	
grip power (kg)	19.50 (6.48)	
skeletal muscle mass index (kg/m2)	appendicular	6.83 [3.35, 10.74]
lower limb5.56 [2.66, 8.36]		
Frailty (n)	none	36 (17.1%)
Pre-frail120 (57.1%)		
frail	54 (25.7%)	
Sarcopenia (n)	none	197 (93.8%)
sarcopenia6 (2.9%)		
severe sarcopenia7 (3.3%)		

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Disclosure of Interests: None Declared.
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AB1192 RESPONSE TO VISCOSUPPLEMENTATION WITH DIFFERENT TYPES OF INTRA-ARTICULAR HYALURONIC ACIDS IN OSTEOARTHRITIS OF THE KNEE – A RETROGRADE INDIAN COHORT STUDY OF MORE THAN 15 YEARS LONGITUDINAL DATA

Keywords: Outcome measures, Osteoarthritis

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Background: Knee osteoarthritis (OA) is a progressive degenerative condition resulting in functional loss, pain and discomfort. [1] The current aim of treatment is alleviation of symptoms, improvement of function and joint preservation. Viscosupplementation (VS) with Intra-articular hyaluronic acid (IAHA) injection has been shown to have protective physiochemical functions and may confer disease-modifying, long term effects in OA. [2][3] However, conflicting guidelines, pooling of results for different molecular weight products, and a paucity of long-term clinical studies has resulted in lack of confidence in the results of IAHA.
Objectives: To determine the primary and sustained response to VS with different types if IAHA in Bilateral Knee OA.
To identify whether the response is different for subgroups which are:

- Type of IAHA,
- Gender - Males (M) or Females (F), and
- Grade of OA treated.

Methods: We did a retrospective analysis of a 15-year cohort from a single Indian centre. The inclusion criteria were adults with bilateral knee OA with functional reduction and radiological KL Grade of III and IV, treated with Non-Animal Stabilized Hyaluronic Acid (NASHA) origin IAHA injections.

Subjects were stratified into two groups based on the molecular weight of the hyaluronic acid used:

- High Molecular Weight - 6-8 mg/ml – 6ml single injections (HMW-HA), or
- Very high Molecular weight – 20 mg/ml – 3 ml injections (VHMW-HA).

The primary outcome measure was responder rates determined by those with improvement in total WOMAC scores of > 30% from baseline versus non-responders. Responders with sustained response of at least 12 months or more were determined.

Results: A total of 2037 (F 1467 (72%) & M 570 (28%)) patients were treated.
The overall responder rate was 1496 (73.4%) (F 1099 (74.9%) & M 397 (69.6%)).
The Primary responder rate was similar for VHMW-HA (73.5% in Gr III OA & 77.0% in Gr IV OA) and HMW-HA (71.0% in Gr III OA & 68.6% in Gr IV OA).
The Sustained response in VHMW-HA was greater (60.5% in Gr III OA & 68.5% in Gr IV OA) versus HMW-HA (47.3% in Gr III OA & 46.7% in Gr IV OA).

Table 1. The results are summarized in Table -1: -

INTERVENTION TYPE		VHMW-HA	VHMW-HA	HMW-HA	HMW-HA	TOTAL	RATE
GRADE OF OA		Grade III OA	Grade IV OA	Grade III OA	Grade IV OA	N	%
TOTAL PATIENTS TREATED	Total (%)	684 (33.6%)	631 (31.0%)	480 (23.6%)	242 (11.9%)	**2037**	
	Females	509	418	352	188	**1467**	**72.0%**
	Males	175	213	128	54	**570**	**28.0%**
PRIMARY RESPONDERS	Total (%)	503 (73.5%)	486 (77.0%)	341 (71.0%)	166 (68.6%)	**1496**	**73.4%**
	Females	394	330	251	124	**1099**	**74.9%**
	Males	109	156	90	42	**397**	**69.6%**
SUSTAINED RESPONDERS	Total (%)	414 (60.5%)	432 (68.5%)	227 (47.3%)	113 (46.7%)	**1186**	**58.2%**
	Females	311	286	166	84	**847**	**77.1%**
	Males	103	146	61	29	**339**	**85.4%**
NON RESPONDERS	Total (%)	181 (26.5%)	145 (23.0%)	139 (29.0%)	76 (31.4%)	**541**	**26.6%**
	Females	115	88	101	64	**368**	**25.1%**
	Males	66	57	38	12	**173**	**30.4%**

Primary responders – Total WOMAC scores improvement of > 30% from baseline, Sustained responders - Sustained WOMAC improvement for >=12 mts., Non-responders - WOMAC change < 30% or Lost to follow up. OA-Osteoarthritis Knees, Grade III and IV OA - radiological KL Grade, VHMW-HA - Very high Molecular weight hyaluronic acid, HMW-HA -High molecular weight hyaluronic acid.

Conclusion: The responders to treatment of 73.4% justify treatment outcome.
The primary response to treatment was similar in all the subgroups – Type of IAHA, Grade of OA and Gender.
However, the sustained response for 12 months or more was far greater in VHMW-HA versus HMW-HA.

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AB1193

IS COMBINING BETTER THAN SINGLE GAIT PARAMETER CHANGES FOR PEOPLE WITH MEDIAL OF KNEE OSTEOARTHRITIS? A STUDY ON THE KINETIC CHANGES INDUCED BY GAIT RETRAINING

Keywords: Osteoarthritis

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Background: Gait retraining has been demonstrated to be effective in reducing the peak knee adduction moment (pKAM) in individuals with knee osteoarthritis (KOA). Since medial-compartment loading has been related to both the pKAM and the peak knee flexion moment (pKFM), reducing the pKAM without pondering the changes in pKFM does not ensure a decreased load in the knee. It is unknown whether combining multiple gait parameters is more effective than isolated gait parameter changes in achieving specific kinetic targets for the pKAM and pKFM.
Objectives: To characterize the individual changes in the pKAM and in the pKFM in patients with medial KOA walking with a combination of varied gait parameters. We hypothesised that the number of people achieving the dual kinetic change (2KC) of decreasing the pKAM of at least 10% without increasing the pKFM through a combined parameter gait changes is higher than the number of people achieving it through a single gait parameter change.
Methods: We recruited medial KOA patients (K-L I-III) had a diagnosis confirmed through x-ray. A motion capture system and floor-embedded force-plates were used to measure the kinetics (pKAM and pKFM) and the spatio-temporal parameters (foot progression angle (FPA), step width (SW), stride length (SL) and walking speed) during gait. Gait retraining method used was an augmented-reality system. Each patient performed 81 trials combining three different amplitudes of PFA, SW and SL. Gait speed was controlled. The gait modifications were toeing-in by 15° or 10° or normal, walking width narrower (0.10m) or wider (0.15m) or normal SW, and/or walking with shorter (0.10 or 0.15m 0.15m) or normal SL. Descriptive statistics was used. The data of 17 patients, mean 52.7 years old (SD 15.9), mean height 172.9cm (12.8) and mean BMI 24.9 Kg/m^2 (3.2) was compiled for statistical analysis.
Results: 76.5% of the patients achieved the 2KC with at least one of the combination (Figure 1). Changing one gait parameter led to a 2KC in 7 patients and changing a combination of multiple parameters led to a 2KC in 13 patients. Adding a third to a combination of two gait parameters change "only" added one patient to the total number of patients achieving the targeted 2KC. All patients achieving the 2KC with a single modification were also able to achieve it using two combined modifications. All patients achieving the 2KC with a combination of two gait parameters, achieved it too combining modifications in three parameters. 5.9% of patients achieved the 2KC with a combination of three gait parameters only.
Conclusion: When compared to single-parameter changes, gait-retraining through an augmented-reality setting using a combination of multiple gait parameter changes is more likely to achieve the targeted kinetic changes. Future research should assess the percentage of KOA people retaining the 2KC on both the shorter- and the longer-term.

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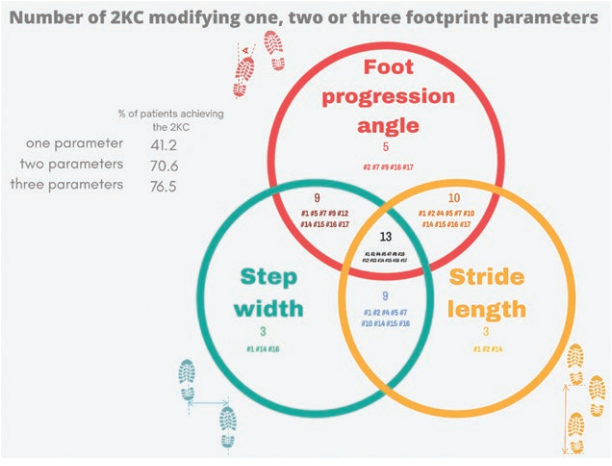


Figure 1.

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Disclosure of Interests: None Declared.
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AB1194 A PROOF OF PRINCIPLE DIETARY INTERVENTION TRIAL TO EXAMINE THE PROTECTIVE EFFECT OF BROCCOLI BIOACTIVES, (SPECIFICALLY SULFORAPHANE), ON OSTEOARTHRITIS

Keywords: Diet and nutrition, Pain, Osteoarthritis

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Background: Osteoarthritis (OA) accounts for more than a third of chronic moderate to severe pain in the UK. Sulforaphane (SFN) is a naturally occurring phytochemical derived from eating cruciferous vegetables, particularly broccoli. It has several biological activities that promote health, including anti-inflammatory properties. SFN has a potential role in limiting pain and cartilage destruction in OA.
Objectives: In a two centre, placebo-controlled, double-blind, two-arm parallel, RCT, proof of principle study with a primary outcome we evaluated whether dietary SFN (from consumption of broccoli) improves pain in participants with knee OA. Secondary objectives were to determine whether food containing SFN improves knee function, and the feasibility of the study design for an appropriately powered trial.
Methods: Participants with symptomatic and radiographic knee OA were recruited from regions of Norfolk and Leeds in the UK, were over 50 years of age with moderate to severe knee pain (at least 4 on 0-10 numeric rating scale), and radiological evidence of OA (Kellgren-Lawrence score 2-3). The intervention was a sensory-matched soup. Patients received either the intervention soup (300g high glucoraphanin soup (containing broccoli, and base vegetables)) or placebo soup (300g no glucoraphanin soup (base vegetables only)), once daily on 4 days per week. The study duration was 12 weeks with follow-up visits at 6 and 12 weeks. Knee pain and function outcome measures were obtained using WOMAC, an 11-point NRS, the ICOAP questionnaire and use of rescue analgesics/NSAIDS. Creatinine, metabolites of glucoraphanin, matrix metalloproteinase-3 and C-reactive protein were measured in plasma or 24-hour urine samples.
Results: Recruitment was severely curtailed due to the Covid-19 pandemic. In total n= 37 consented and n= 24 met screening criteria with one drop-out at week 12 (control n=17 and intervention n= 7), the recruitment aim was n= 64. Control group was 43% female, and mean age was 70.14 yrs [7.69 SD] (control), and 61.88 yrs [8.58 SD] (intervention). Mean BMI was 26.4[2.91 SD] (control) and 28.2[4.68 SD] (intervention). The intervention resulted in a trend towards a decrease in pain scores for each subscale of WOMAC, ICOAP and NRS measures: total WOMAC median difference from baseline (9.65 [CI:-0.78,20.09]), ICOAP constant (wk 12, 4.83 [CI: -1.99,11.64]) and intermittent pain (wk 12, 2.96 [CI: -0.31,6.24]), NRS overall pain (wk 12, 1.86 [CI: 0.13,3.58]), while a trend for increased satisfaction for knee function (wk12, -1.55 [CI: -3.55,0.44]) was also observed for this group. No change in rescue analgesics/NSAIDS for knee pain was seen in either group. Metabolites of glucoraphanin were detected in plasma and urine samples in the intervention group. Study compliance and intervention adherence was high (>70%-100%) while acceptability for randomisation was 100%.
Conclusion: Patient acceptability, adherence and retention was high and biomarkers and metabolites objectively confirming compliance with the intervention were detected. In this study, although underpowered to observe significant differences for pain, improving trends over time were observed across a range of clinical pain measures including the primary outcome, where the CI encompassed the minimal clinically important difference, requisite for progress to full trial. Given COVID impact on recruitment, the pilot achieved its aims, and we conclude that the intervention was feasible, and a full trial is justified.
Acknowledgements: Our thanks to the study participants, study team, research nurses, and doctors; Fiona Brudenell-Straw, Lisa Cook, Lizzy Daniel, Asim Ghouri, Robert Hindmarsh, Kiran Khokar, Teja Kodali, Angela Nauth, Iraklis Papageorgiou, Tracey Swingler, Rabia Thompson, Nicola Ward, and Celia Whitehouse, and Trial committee Simon Donell (Independent Chair), Sam Norton (Independent Biostatistician) and Trish Phillips (Independent member) for their tenacity and team spirit throughout such an unprecedented time. This work is supported by grants from Versus Arthritis and Action Arthritis.
Disclosure of Interests: Rose Davidson: None declared, Laura Watts: None declared, Gemma Beasy: None declared, Shikha Saha: None declared, Paul Kroon: None declared, Aedin Cassidy: None declared, Allan Clark: None declared, William Fraser Speakers bureau: Roche, Incstar/Diasorin, IDS, Sanofi, Siemens, Menarini, Abbott, Entera Bio, NPS pharmaceuticals and Alexis, Consultant of: Roche, Incstar/Diasorin, IDS, Sanofi, Siemens, Menarini, Abbott, Entera Bio, NPS pharmaceuticals and Alexis, Grant/research support from: Roche, Incstar/Diasorin, IDS, Sanofi, Siemens, Menarini, Abbott, Entera Bio, NPS pharmaceuticals and Alexis., Iain McNamara: None declared, Sarah Kingsbury: None declared, Philip G Conaghan Speakers bureau: AbbVie, Novartis, Consultant of: AbbVie, AstraZeneca, Biosplice, BMS, Eli Lilly, Galapagos, Genascence, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Stryker, and UCB, Ian Clark: None declared, Alex MacGregor: None declared.
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AB1195 KNEE OSTEOARTHRITIS AND NEUROPATHIC PAIN: IMPACT OF RADIOGRAPHIC SEVERITY

Keywords: Pain

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Background: Pain in knee osteoarthritis remains the main symptomatology, classically considered as nociceptive. A neuropathic component of this pain has recently been described. The identification of which is essential for adequate management.
Objectives: The objective of our study is to evaluate the relationship between the prevalence of neuropathic pain and the stages of radiographic severity in gonarthrosis.
Methods: This is a descriptive cross-sectional study of patients with clinically and radiographically retained knee osteoarthritis. The radiographic stage was determined by the Kellgren and Lawrence classification. Neuropathic pain was assessed by the DN4 questionnaire. The neuropathic nature of the pain was retained if the DN4>=4. The patients included were divided into 4 groups according to the radiographic stage.
Results: 173 patients were included. The average age was 58.0±9.19 years. 88.2% were women. 32.7% of patients had neuropathic pain. Average pain VAS was 4.4±2.1. The median duration of evolution was 3.8 years[1-23]. 5.6%, 64.4%, 25.6%, and 4.4%, of the patients studied were classified by radiography as caution, 1, 2, 3, and 4 respectively. The prevalence of neuropathic pain was 16.6%, 34.4%, 35.5% and 33.3% in patients with radiographic severity grade 1, 2, 3, and 4 respectively. When comparing the groups, there was no difference in the DN4 score according to the stage of radiographic severity (p=0.633).
Conclusion: The results of our study suggest that the stage of radiographic severity does not predispose to neuropathic pain in patients with gonarthrosis.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4516

AB1196 NEUROPATHIC PAIN IN GONARTHROSIS: PREVALENCE AND ASSOCIATED FACTORS

Keywords: Pain

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Background: Pain in knee osteoarthritis remains the main symptomatology, classically considered as nociceptive pain. A neuropathic component of this pain has recently been described. The identification of which is essential for appropriate management.
Objectives: The objective of our study is to evaluate the prevalence of neuropathic pain in patients with knee osteoarthritis, and to identify the associated factors.

Methods: This is a cross-sectional study involving patients with knee osteoarthritis. Sociodemographic and clinical data, including comorbidities, were collected. Neuropathic pain was assessed by the DN4 questionnaire. Neuropathic pain was defined by a DN4 >= 4. Depression, catastrophizing, and central sensitization were assessed by Arabic versions of validated questionnaires, PCS (Pain Catastrophizing Scale) for catastrophizing, and PHQ9 (Patient Health Questionnaire) for depression, CSI (central sensitization inventory) for central sensitization.
Results: 173 patients were included in our study. 88.2% are women. The average age was 58.0±9.19 years. 32.7% had neuropathic pain. VAS mean pain was 4.4±2.1. The median duration of evolution was 3.8 years [1-23]. The average lequesne index was 9.75±3.9. The median of the PCS score was 22 [0 –52], and the median of the PHQ9 score was 7 [0 – 24]. The average CSI score was 38.2±15. 72.6% of patients had comorbidities: 28.8% had obesity and 12.7% were diabetic. In multivariate analysis, only functional disability was associated with the presence of neuropathic pain p=0.04 (OR: 1.19, 95% CI [1.03 – 1.38]. However, pain severity, central sensitization, comorbidities including diabetes and obesity did not come out as associated factors.
Conclusion: Neuropathic pain is quite common in gonarthrosis. Functional disability seems to be an associated factor.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1197 CAN OSTEOARTHRITIS, SARCOPENIA AND BODY COMPOSITION PREDICT LOSS OF FUNCTION?

Keywords: Sarcopenia, Osteoarthritis

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Background: Elderly populations e growing in the majority of Countries in the World. Portugal in currently among the 5 most aged counties with 23,4% of it´s population over 65 and an ageing index of 182[1]. Osteoarthritis is the 3rd cause of responsible for severe disability in adults over 60 years in developed and developing countries[2]. Lack of data at a national or regional level in Portugal compromises the ability to prepare for both health and care need of aged population. Simultaneously the region of Algarve has particular geographic characteristics with 49% of the population living within 2 km from the cost (in 9% of the Algarve's Territory).
Objectives: Are aim was to study our regional population, namely the incidence of Osteoarthritis (OA) and the relation of function ability with OA, Sarcopenia and Body composition.
Methods: This study is a prospective, observational secondary analysis of data from the "*Sarcopenia Screening Study in the Algarve Region*". Subject were recruited through informative flyers that was distributed at Elderly Associations, Senior Universities,… in different areas of the region of Algarve. Subsequently, by appointment, the evaluations were performed. Until June 2022 a total of 270 participants have voluntarily participated. Subjects over 60 were eligible for the study. All gave their informed consent to participate. Clinical diagnose of OA was established according to the NICE Guidelines for knee osteoarthritis diagnose[3]. Functional ability was measures with the Lower Extremity Functional Scale (LEFS)[4], sarcopenia was measures with the SARC-F Questionnaire[5], body composition was evaluated by Medical Body Composition SECA® mBCA515. Data was treated with IBM-SPSS-Statistics version 26.
Results: Of the 270 subjects analyzed for this secondary analyze 75,2% were female (24,8% male), mean age in years 75,39 ± 6,75 (60-93). 70,5% had Knee OA. Statistical differences was found between groups (with and without OA), in LEFS (p<0,001), SARC-F (p<0,001), percentage of fat free mass (p<0,001). A multiple linear regression was carried out to see if having OA, Sarcopenia and percentage of fat free mass can predict LEFS, once all were significantly different within groups, creating a statistically significant model [Z(3,233)=155,957; p<0,001:R^2=0,668] were with having OA (ß=-0,121;t= -271;p=0,003), Sarcopenia (ß=-0,694;t= -16,258;p<0,001), and low muscular mass (ß=0,146;t=3,468 ;p<0,001), can significantly predict diminished lower extremity function.
Conclusion: Looking for the presence of OA, Sarcopenia and low percentage of fat free mass is important when monitoring elderly subjects over time once they can predict the decrease in functional ability.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5006

AB1198 CLINICAL PROFILE OF HAND OSTEOARTHRITIS IN A LOW INCOME POPULATION

Keywords: Descriptive studies, Osteoarthritis, Epidemiology

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Background: hand osteoarthritis (HOA) is a highly prevalent disease that may be impacted by social inequalities. However, there are few studies on HOA from underdeveloped regions.
Objectives: to present clinical characteristics of a HOA cohort from a low-income population.
Methods: clinical data and serum from 70 patients with a diagnosis of HOA fulfilling ACR criteria seen between March 2020 and December 2022 in Fortaleza/Brazil registering hypertension, diabetes, obesity (BMI>30 kg/m²), and concurrent diagnosis of knee or spine OA and "bunions"; pain (VAS, visual analogue scale), X-ray (Kellgren-Lawrence) and ultrasonography (US) [synovitis and power-doppler (PD) sign] of the most affected joint of the hand were recorded, as well as grip and pinch strength (KgF), Cochin hand functional scale (CHFS), FIHOA, and SF-12 scores. Social data included income, occupation [white (WCJ) *vs.* blue (BCJ) colar jobs], education level [>/≤ 8 school-years (SY)].
Results: 70 patients were included, comprising 66(94%) women, mean age 60.3±10.3 with 12(17.1%) below 50 years-old; median disease duration was 72(range 30-120) months. Pain on movement (VAS) was 7.4±1.9, grip strength 14.5±6.4, pinch strength 1.7±1, CHFS 21±14.8, FIHOA 10.3±6.2, and SF-12 32.1±3; 54(77.1%) had KL≥3. All but 2 out of 61 evaluated joints had synovitis at US with only 4(6.7%) displaying positive PD signal; 27(38.5%) had isolated HOA; 9(12.8%), 8(11.4%), and 5(7.1%) had concurrent spine or knee OA or bunions, respectively and 22(31.4%) had ≥2 sites other than HOA; 31(44.2%), 16(22.8%), and 7(10%) had hypertension, obesity and diabetes as comorbidities, respectively; 38(54.2%) declared <900 US$ monthly family earnings, 8(11.4%) had <8SY and 27(38.5%) had occupations classified as BCJ. Mean pain was similar regardless of occupation, literacy (SY) or monthly family income. Although pain in BCJ group (7.9±1.7) was higher than in WCJ group (7.1±2) it did not reach statistical significance (p=0.0576); CHFS, FIHOA and SF-12 scores were similar regardless of occupation, SY or income; total mean CRP was 0.41±0.64 mg/dL; mean CRP in those with concurrent knee OA (0.38±0.25 mg/dL) had a trend to be higher than in isolated HOA patients 0.24±0.1 mg/dL (p=0.0547).
Conclusion: Our results suggest that income and literacy did not influence disease severity in HOA in our low income cohort.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1199 PAIN ON WALKING AND PAIN AT REST IN PATIENTS WITH KNEE OSTEOARTHRITIS: IS THERE A DIFFERENCE?

Keywords: Osteoarthritis, Pain

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Background: The knee osteoarthritis (KOA) pain can be divided into two main categories: pain on walking and pain at rest. A thorough understanding of pain is essential for managing KOA. However, few studies have focused on these two types of pain.
Objectives: The objective of this study was to investigate possible factors associated with knee osteoarthritis pain with a focus on the differences between pain on walking and pain at rest.

Methods: Cross-sectional study including 87 patients. All demographic data and visual analog scale (VAS) score at walking, VAS score at rest, Kellgren and Lawrence (KL) stage on radiography, and results of clinical examination were collected. Exclusion criteria were the presence of a total knee prosthesis and patients followed for chronic inflammatory rheumatism. Statistical data analysis was performed using SPSS version 21 software.
Results: This study included 87 patients followed for KOA, with an average age of 63.67+/-5.8 years (46-83 years), and a female predominance (78.3%). In the univariate analyses, significant correlations were found between the VAS score at walking with age (r=0.56, p=0.037), body mass index (BMI) (r=0.61, p=0.023), KL grade (r=0.54, p=0.039) and patellar shock (r=0.46, p=0.044). While the VAS score at rest was only correlated with BMI (r=0.26, p=0.01). And an association between VAS at rest and skin hyperalgesia was noted (p=0.034). The multivariate analysis showed that the significant explanatory factors of the VAS score on walking were BMI > 25kg/m2 (p=0.03) and KL grade >3 (p=0.03). On the other hand, no significant explanatory factor for the VAS score at rest was found.
Conclusion: Predisposing factors were significantly different between the two types of pain, indicating the presence of different pain mechanisms. Pain on walking was more strongly associated with mechanical and structural factors, whereas pain at rest was associated with knee hyperalgesia.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5756

AB1200 WAIST CIRCUMFERENCE AND GONARTHROSIS

Keywords: Osteoarthritis

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Background: Overweight, translated into a high body mass index (BMI), is associated with a risk of gonarthrosis, thus, this risk is increased by 15% for each increase of a unit of body mass index (BMI). (1) Various studies indicate that the association of high BMI and abdominal obesity measured by waist circumference leads to increased morbidity especially in obese. But no study has so far shown a sufficiently strong association force between waist circumference and gonarthrosis.(2,3)
Objectives: The objective of our study is to assess the relationship between waist circumference and pain perception and gonarthrosis impact.
Methods: This work included patients followed in consultation for gonarthrosis. For each patient we specified next to the demographic data, the BMI, the waist circumference, and the existence or no pain of the knee or both. The intensity of pain was assessed by the Analog Visual Scale (EVA). Functional impact was assessed by the Lequesne index and Womac score. Knee X-rays were classified according to Kellgren Lawrence (KL) criteria.
Results: A total of 209 patients were included (24 men/185 women). The average age was 57.94± 9.01 years. The average body mass index was 25.15 ±5.47 kg/m2and the average TI was 93.45 ±12.35 cm. The average pain EVA at rest was 1.95 2.53 and at stress 7.89 ±1.30. Womac's average score was 12.3± 8.92 and Lequesne's average index was 6.71 3.20. WOMAC SCORE was significantly higher in gonarthrosis patients with a high waist circumference (p = 0.02). A positive correlation was found between the resting and stress pain EVA and the waist circumference of gonarthrosic patients with respectively (p=0.04, p=0.002). but it is statistically insignificant between the radiographic stages, the lesquene index and waist circumference with (p=0.11, p=0.06, respectively).
Conclusion: The the waist circumference seems to be a predictive factor of the presence of gonalgie and a significant functional impact.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5862

AB1201 DIGITAL SELF-MANAGEMENT, ANALGESIC USE AND PATIENT-REPORTED OUTCOMES IN KNEE OR HIP OSTEOARTHRITIS

Keywords: Telemedicine, Osteoarthritis, Self-management

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Background: Despite recommendations for exercise therapy, patient education and weight loss as the first-line treatment for osteoarthritis (OA), analgesics are commonly used to manage pain [1].
Objectives: To investigate analgesic use among participants of a digital first-line treatment for knee or hip OA. We also explored the associations between analgesics use and pain/function.
Methods: We included individuals participating in the treatment during December 2021–July 2022 with data on analgesic use at baseline and 12-week follow-up (N=4100, mean [SD] age 64.5 [9.3], 73.3% females). Using self-reported data on analgesic use (paracetamol, NSAIDs, opioids, other) during the past month at baseline and follow up, we created a 4-category variable: non-users ("no" at both), persistent users ("yes" at both), quitters ("yes" at baseline and "no" at follow-up) and new users ("no" at baseline and "yes" at follow-up). Data on NRS Pain (0-10, higher value = more pain) and function, measured by the Knee injury/the Hip disability and Osteoarthritis Outcome Score 12 (KOOS-12/HOOS-12) Function subscale (0-100, higher values = better function), were collected. The McNemar test was used to assess the change in analgesic use. Multivariable logistic regression was used to compare characteristics of analgesics users/non-users at baseline. We applied a linear random intercept model adjusted for baseline characteristics to investigate the associations between analgesics use and pain/ function.
Results: Among included participants, 2517 (61.4%) were analgesic users at baseline. Female sex, hip OA, lower education, higher body mass index, living outside three largest metropolitan cities, rheumatoid arthritis, and walking difficulties were associated with higher odds of analgesic use at baseline. From baseline to 12-week follow up, the proportion of analgesic users dropped by 12.0% (95% CI, 10.5, 13.5), from 61.4% to 49.4%. The results of linear random intercept model suggested that at both baseline and 12-week follow up, persons not using analgesics at the time had better outcomes (Table 1). Moreover, all groups but "new users" experienced improvements in their pain and function following participation in digital program with the greatest improvements observed among "quitters". Interestingly, the magnitude of improvements was comparable for "non-users" and "persistent users".
Conclusion: Participation in a digital self-management program for hip or knee OA was associated with 12% drop in analgesic use. Analgesic use was associated with worse pain and function in these people. Greatest improvements were seen for those who stopped analgesic use. Similar results were reported for a face-to-face first-line treatment in Denmark [1, 2]. These results highlight the importance of providing effective first-line treatment to people with hip or knee OA.
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Table 1. Predicted pain and KOOS12/HOOS12 Function subscale by analgesic use category (adjusted for sex, age, education, place of residence, index joint, physical activity, body mass index, co-existing conditions, fear of moving and walking difficulties).

	Baseline	12-week	Change
NRS Pain			
Non-users	4.5 (4.4, 4.6)	2.9 (2.8, 3.0)	-1.6 (-1.7, -1.5)
Persistent users	5.7 (5.6, 5.8)	4.1 (4.0, 4.2)	-1.6 (-1.7, -1.5)
Quitters	5.3 (5.2, 5.4)	2.6 (2.5, 2.8)	-2.7 (-2.8, -2.5)
New users	4.9 (4.7, 5.1)	4.2 (3.9, 4.4)	-0.8 (-1.0, -0.6)
KOOS12/HOOS12 Function			
Non-users	59.5 (58.6, 60.3)	66.3 (65.4, 67.1)	6.8 (6.0, 7.6)
Persistent users	47.1 (46.4, 47.7)	53.2 (52.5, 54.0)	6.2 (5.5, 6.9)
Quitters	51.6 (50.5, 52.7)	67.2 (66.0, 68.3)	15.5 (14.3, 16.8)
New users	54.7 (53.0, 56.4)	55.5 (53.6, 57.3)	0.8 (-0.9, 2.5)

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Disclosure of Interests: Ali Kiadaliri Employee of: I acted as a consultant for Joint Academy®, provider of a digital self-management program for osteoarthritis, from August 2021 to December 2022., Stefan Lohmander Employee of: I

acted as a consultant for Joint Academy®, provider of a digital self-management program for osteoarthritis, during 2020-2022., Leif Dahlberg Shareholder of: I am founder and chief medical officer at Joint Academy®, providing self-management treatment for osteoarthritis., Employee of: I act as chief medical officer at Joint Academy®, providing self-management treatment for osteoarthritis.

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AB1202 PARTICULARITIES OF KNEE OSTEOARTHRITIS FUNCTIONAL IMPACT IN A GERIATRIC POPULATION

Keywords: Osteoarthritis

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Background: Knee osteoarthritis (KOA) is the most common of osteoarticular diseases. Its increasing incidence with age means that the geriatric population is particularly exposed.

Objectives: The aim was to study the functional impact of knee OA in elderly subjects.

Methods: A cross-sectional study of 52 patients aged ≥65 years, followed for knee OA. Clinical characteristics of knee OA, pain intensity (VAS) were collected. Functional impact was assessed by the short form of the Knee Injury and Osteoarthritis Outcome Score (KOOS-PS) with a score ranging from 0 (no difficulty) to 100 (extreme difficulty). Radiographic severity was classified according to the Kellgren Lawrence criteria.

Results: The mean age was 73.7±7.8 years and the sex ratio (male/female) was 0.13. KOA was femoro-tibial in 79% and femoro-patellar in 21%, the internal compartment was affected in 98% of cases, and a bilateral involvement was found in 94% of cases. The knees were in varus in 30% of cases, in valgus in 23%. The VAS pain was 6.63±1.89. The mean KOOS-PS score was 48.04±19.1. The radiographic severity stages of KOA according to KL were classified as follows: stage 2 (17%), stage 3 (50%), and stage 4 (33%). A positive and significant correlation between the KOOS and VAS pain was found (r: 0.6; p<0.00). There was no correlation between the KOOS and the radiographic stage (p=0.17), the duration of evolution (p=0.43).

Conclusion: In elderly patients with knee OA, there is no concordance between radiographic severity and functional impact. The latter goes hand in hand with the pain experienced.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1203 EVALUATION OF THE URIC ACID AND HEMATOLOGICAL PARAMETERS IN PATIENTS WITH NODAL HAND OSTEOARTHRITIS

Keywords: Diagnostic tests, Osteoarthritis

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Background: Osteoarthritis (OA) is the most commonly seen joint disease worldwide. The frequency of OA is increased together with an increase in obesity and ageing. The hand is one of the most frequently involved areas, and hand OA is seen more often in females.

Objectives: To compare patients with symptomatic nodal hand osteoarthritis (OA) with a control group in respect of inflammation parameters, uric acid, and hematological parameters.

Methods: The study included 50 post-menopausal female patients, aged 40-80 years, diagnosed with symptomatic nodal hand OA, and a control group of 50 post-menopausal females in the same age range with no hand OA. Patient data including age, monocyte, neutrophil, lymphocyte, and thrombocyte counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, uric acid level, and the Kellgren-Lawrence (KL) score obtained from evaluations of hand radiographs, were recorded retrospectively from the hospital information system. The neutrophil-lymphocyte ratio (NLR), thrombocyte-lymphocyte ratio (PLR) were calculated. The data were compared between the two groups.

Results: The data of 100 females were compared, comprising a patient group of 50 patients with symptomatic nodal OA, and a control group of 50 females. Age, monocyte, neutrophil, lymphocyte, and thrombocyte counts, NLR, PLR, ESR, CRP, and uric acid level were compared. With the exception of ESR, no statistically significant difference was determined between the two groups. The ESR was determined to be statistically significantly higher in the patient group than in the control group (p<0.001). When patients with a KL score of 2 and 3 were compared, with the exception of age, no other difference was determined. Patients with a KL score of 3 were seen to be significantly older (p:0.032).

Conclusion: ESR was determined to be significantly higher in patients with symptomatic nodal OA. Clarification of the relationship between inflammation, uric acid, and hand OA, which is a heterogeneous disease, will be useful in the follow-up and treatment of patients.

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AB1204 THE COMPARISON OF THREE DIFFERENT MANAGEMENT STRATEGIES FOLLOWING PLATELET RICH PLASMA INJECTION IN PATIENTS WITH KNEE OA

Keywords: Osteoarthritis

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Background: The main symptoms of patients with knee osteoarthritis (OA) are defined as pain, muscle weakness and functional impairments. Muscle strengthening exercises are recommended in core treatment of conservative management of knee OA [1]. Recently, intraarticular platelet-rich plasma (PRP) injection has gained much attention for the management of knee OA. A combination of different approaches is also recommended for achieving better symptomatic relief.

Objectives: The aim of the study was to compare the effect of PRP plus supervised exercise, PRP plus home exercise and only PRP in patients with knee OA.

Methods: Patients with knee OA aged 45-70 years old were included. The demographic characteristics of the patients were recorded, and they were randomly divided into three groups: PRP plus supervised exercise group (PRP+SEG); PRP plus home exercise group (PRP+HEG); PRP group. The pain was assessed with visual analogue scale (VAS); knee functions were assessed with Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) and the stair test was assessed with a 10-step stair. The PRP+SEG performed the exercises under the supervision of a physiotherapist and PRP+HEG performed the same exercises at home. Both PRP+SEG and PRP+HEG performed a total of 6-week (3 times/week) strengthening exercises for knee and hip muscles. The PRP group received only PRP injection. All assessments were performed at 3rd day after PRP injection and at 6th week.

Results: A total of 41 female patients (mean age: 56.65±±6.64 years; mean BMI: 28.82±5.19 kg/m^2) were randomized (PRP+SEG (n=15); PRP+HEG (n=12); and PRP (n=14)). There was no significant difference between three groups at baseline (p>0.05). There was significant difference in VAS (p=0.001); WOMAC Pain (p=0.003); WOMAC-Function (p=0.001) and WOMAC Total (p=0.001) scores between three groups at 6th week. The PRP+SEG had greater relief in pain both VAS and WOMAC Pain scores and greater improvement in WOMAC Function and WOMAC Total scores compared to PRP+HEG and PRP at 6th week. There was no significant improvement in stair test and WOMAC Stiffness scores for all groups at 6th week (p>0.05) (Table 1).

Conclusion: A combination of supervised exercise with PRP injection resulted in better symptomatic relief in patients with knee OA. Clinicians should consider the

Table 1. Comparison of groups at baseline and at 6th week.

	Baseline				6th Week			
n=41	PRP+HEG (n=12)	PRP+SEG (n=15)	PRP (n=14)	p1	PRP+HEG (n=12)	PRP+SEG (n=15)	PRP (n=14)	p2
	Mean±SD	Mean±SD	Mean±±SD		Mean±SD	Mean±SD	Mean±SD	
VAS (cm)	7.42±1.81	7.38±1.79	5.98±1.95	.0.81	5.70±2.30	3.18±1.63	6.02±2.24	**.001*[a]**
Stair climbing (sec)	7.40±4.22	6.43±2.72	5.86±2.04	.446	5.92±3.21	4.08±0.82	5.54±1.93	.067
Stair descending (sec)	7.59±5.36	6.46±2.87	5.62±1.91	.380	6.25±4.41	3.77±0.91	6.05±2.82	.056
WOMAC Pain	9.08±3.44	9.13±3.83	8.57±2.92	.892	8.83±3.53	4.00±2.00	7.71±4.92	**.003*[b]**
WOMAC Stiffness	5.25±3.95	3.26±1.79	2.71±2.94	.087	2.16±2.51	1.26±1.16	2.21±2.42	.399
WOMAC Function	32.08±15.04	28.00±12.22	30.71±14.46	.736	34.58±15.93	13.53±7.93	29.42±16.06	**.001*[ab]**
WOMAC Total	48.35±17.47	42.08±15.83	43.75±18.83	.639	47.48±21.45	19.58±9.35	40.99±23.15	**.001*[ab]**

PRP: Platelet Rich Plasma, HEG: Home Exercise Group, SEG: Supervised Exercise Group, VAS: Visual Analog Scale, WOMAC: The Western Ontario and McMaster Universities, SD: Standard deviation, p1 and p2: OneWay-ANOVA, *p<0.05 [a]Pairwise comparison of PRP+SEG and PRP is significant (p<0.017), Bonferroni test [b]Pairwise comparison of PRP+HEG and PRP+SEG is significant (p<0.017), Bonferroni test

effectiveness of supervised strengthening exercises for providing better improvement in pain and knee function after PRP injection.

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AB1205 IMPACT OF CATASTROPHIZING ON PAIN, FUNCTION, AND PHYSICAL PERFORMANCE IN PATIENTS WITH KNEE OSTEOARTHRITIS

Keywords: Osteoarthritis, Pain

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Background: Osteoarthritis (OA) is the most common osteoarticular disease, with pain and functional discomfort being the main symptoms leading patients to consult. Catastrophism is defined as an exaggerated negative reaction to an anxiety-provoking stimulus. It is considered to be an important cognitive factor in painful conditions, particularly in osteoarthritis.

Objectives: The aim of this study was to assess the level of catastrophizing and to determine the relationship between catastrophizing and pain intensity, functional impact, and physical performance.

Methods: This is a cross-sectional study conducted in the rheumatology department. Sociodemographic information and comorbidities were collected. Pain was assessed by Visual Analogic Scale (VAS); functional impact by the Lequesne knee index and radiographic stage by the Kellgren and Lawrence scale. The level of catastrophizing was assessed by the validated Moroccan version of the Pain Catastrophizing Scale (PCS). A PCS $\geqslant$ 30 indicate high level of catastrophizing. Physical performance was assessed by the 06min walk test and IPAQ questionnaire.

Results: A total of 178 patients were included. The sociodemographic and clinical characteristics of the patients are presented in (Table 1).

Table 1. Demographic and clinical characteristics of patients

Parameters	PCS <30	PCS >30	P value
Number of patients = 178	105 (59 %)	64 (36 %)	—
Age (Mean ±SD)	59.3±9	57±10.7	*p=0.369*
Femal gender (%)	82.9%	95.3%	***P=0.013***
Comorbidity (%)	68.6%	73.4%	*P=0.654*
Analphabetic (%)	68.6%	71.9%	*P=0.150*
Lequesne score (±SD)	9.3±3.8	10.7±4	*P=0.189*
Radiological stage (±SD)	2.2±0.6	2.4±0.6	*P=0.228*
VAS pain (±SD)	4.1 ± 2.5	5.6 ± 2.8	*P=0.313*
Median time of evolution	3 years[1-7]	4 years[1-10]	*P=0.069*
The mean distance walked in 06 minutes	372 ± 137	355 ± 147	*P=0.586*
Patients with a physical disability	74.3%	80.7%	*P=0.427*

Univariate and multivariate analysis showed the Lequesne index (p=0.008) and anxiety (0.001) were statistically significantly associated with the level of catastrophizing.

Conclusion: The level of catastrophizing seems to have an impact on function and anxiety. However, there was no association between catastrophizing and the walking test. Catastrophism is an important factor to assess at the beginning of the management of a patient with OA.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1206 THE SOURCES OF DISEASE-RELATED INFORMATION FOR MOROCCO'S OSTEOARTHRITIS PATIENTS

Keywords: Osteoarthritis, Patient information and education

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Background: In osteoarthritis, the patients have an almost continuous need of information and communication. In addition to the information delivered by health professionals, patients tend to look for other sources to complete it.

Objectives: Our study aims to investigate the non-conventional sources of information used by osteoarthritis patients and to identify the possible associated factors.

Methods: This is a cross-sectional study, conducted in the rheumatology department at the University Hospital Center in Tangier, which included patients diagnosed with osteoarthritis.Data on sociodemographic characteristics, clinical presentations, comorbidities, and the health outcomes of patients were examined. Patients' beliefs and attitudes about disease-related sources of information were assessed by a questionnaire.A list of 12items was proposed to the patients who mentioned the different used sources, their level of trust, and their experience with the effectiveness of these sources. Binary logistic regression was conducted to identify the associated factors with the use of the disease-related sources of information.

Results: We included 221 patients. The mean age was 59.4 ± 9.8, 88.7% of the patients were female, and 69.2% had comorbidities. 80.5% were diagnosed with knee osteoarthritis and 19.5% with hand osteoarthritis. The median of disease duration was 8 [2-10] years. 31.2% of the patients sought information related to their osteoarthritis, the 3 main sources were: peers (21.7%), YouTube (17.2%) and television (13.1%). 12.7% have already applied some of this information. Only 10% of patients discussed the found information with their physicians and 85.4% would like to have health professionals in their online space to answer their questions. In uni and multivariate analysis, age (OR=0.959, IC95% [0.927-0.991], p=0.014) and level of education (OR=1.597, IC95% [1.146-2.224], p=0.006) were statistically significant with the use of non-conventional information sources.

Conclusion: Our study showed that Morocco's osteoarthritis patients, especially those with certain age and level of education, are seeking information about their disease. Rheumatologists need to invest more, especially on virtual spaces, to respond to these requests.

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AB1207

PREVALENCE OF NEUROPATHIC PAIN AND ITS ASSOCIATION WITH CLINICAL OUTCOMES IN PATIENTS WITH PRIMARY KNEE AND HIP OSTEOARTHRITIS

Keywords: Pain, Patient reported outcomes, Outcome measures

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Background: Osteoarthritis (OA) is a common musculoskeletal disease associated with significant chronic pain and physical disability. The presence of pain with a neuropathic component may be associated with different phenotypes of this condition.
Objectives: Thus, this study aimed to explore the prevalence of neuropathic pain (NP) and its association with sociodemographic characteristics and clinical outcomes (pain severity and disability), in patients with primary knee and hip OA.
Methods: A cross-sectional study involving adult patients with a primary knee and hip OA diagnosis according to American College of Rheumatology (ACR) was conducted. Sociodemographic variables, symptoms and disease duration and pain characteristics were obtained. Pain severity was assessed with Pain Visual Analog Scale (VAS) and functional disability with Health Assessment Questionnaire (HAQ). Western Ontario and McMaster Universities Arthritis Index (WOMAC) was used to assess pain, stiffness and physical function. The pain DETECT scale was used to evaluate NP in these patients. In order to correlate NP with sociodemographic, clinical and pain characteristics, a correlation coefficient was used- Pearson coefficient. Linear and logistic regression models adjusted for age, gender, symptom duration and diagnosis duration were applied to assess the main predictors of NP.
Results: A total of 36 patients (mean age of 65.1±8.9 years old; 72.2% female) with primary knee OA (n=13, 36.1%), hip OA (n=4, 11.1%) and both (n=19, 52.8%) were included. Patients had a mean symptoms duration of 13.3±8.7 years and a median disease duration of 5 [3-13] years. The mean Pain VAS was 5.0±3.4, and the median HAQ of 1 [0.65-1.91]. The mean of WOMAC- pain, -stiffness, -physical function and -total were 11.9±4.2, 4.5±2.2, 37.5±15.4 and 53.8±20, respectively. Characteristics of NP were found in 28 (77.8%) patients and the mean of PAINDETECT scale was 31.1±11.9. None of the patients had treatment aimed at NP. There were positive correlations between NP and Pain-VAS (r_p =0.63, p=0.001), HAQ (r_p =0.33, p=0.005), WOMAC-physical function (r_p =0.41, p=0.027) and WOMAC-total (r_p =0.38, p=0.049). In the multivariable model, Pain-VAS predicted NP (β=0.76, p=0.014).
Conclusion: Our study demonstrated that NP is common in patients with OA. The presence of this type of pain is associated with worse clinical outcomes, namely pain severity and functional disability. Hence, these findings encourage the screening of NP in all patients with knee and hip OA in order to implement more appropriated therapeutic strategies.
REFERENCES: NIL.
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AB1208

THE RELATIONSHIP BETWEEN KNEE MUSCLE STRENGTH WITH DISABILITY AND PAIN IN PATIENTS WITH KELLGREN-LAWRENCE GRADE III-IV KNEE OSTEOARTHRITIS: A PILOT STUDY

Keywords: Rehabilitation, Physical therapy/Physiotherapy, Osteoarthritis

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Background: Knee osteoarthritis (OA) is the most common chronic joint disease and is the main cause of disability and pain. It is important to better understand potentially modifiable risk factors that may reduce disability and pain in advanced knee osteoarthritis.
Objectives: The aim of this study was to investigate the relationship between knee muscle strength with disability and pain in patients with advanced OA.
Methods: Twenty-one patients (66.05 ± 8.02 years, 32.77 ± 5.37 kg/m^2) with Kellgren-Lawrence grade III-IV OA were included in this pilot study. Knee flexion and extension muscle strength were measured with Easy Force® isometric pull dynamometer in accordance with the make test procedure. Disability was measured with Knee Injury and Osteoarthritis Outcome Score (KOOS), and pain intensity was measured with VAS and Pain Catastrophizing Scale (PCS).
Results: The knee flexion strength of the patients was 75.52 ± 29.58 N, and the knee extension strength was 155.42 ± 49.84 N. Knee flexion strength was 17.85 ± 32.06 % and extension strength was 22.60 ± 21.10 % less than the other extremity. The total KOOS scores of the patients were 48.90 ± 24.78 %, PCS scores were 27.58 ± 15.82 and VAS were 8.42 ± 1.69. Flexion muscle strength of patients were moderately correlated with KOOS (r=0.44, p<0.05), but not with PCS and VAS scores. Extension muscle strength of patients was highly correlated with KOOS (r=0.70, p< 0.001), but not with PCS and VAS scores.
Conclusion: In advanced knee osteoarthritis, knee extension strength deteriorated more than knee flexion strength. Exercise interventions for knee extension strength training can provide superior outcomes in knee extensor strength and function but not in pain.
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AB1209

AN INVESTIGATION OF THE VARIABLES INFLUENCING PLATELET-RICH PLASMA FEATURES IN INDIVIDUALS WITH KNEE OSTEOARTHRITIS

Keywords: Synovium, Osteoarthritis, Gender/diversity issues

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Background: Platelet Rich Plasma (PRP) has drawn great interest as a regenerative adjunct therapy, and it is increasingly used in management of knee osteoarthritis (OA). The primary goal of PRP injections is to deliver a higher concentration of platelets to the target area than blood circulation does. The features and content of the injected substance are vital when evaluating the effectiveness of PRP.
Objectives: The objective of this study was to investigate the factors affecting the features of PRP in patients with knee OA.
Methods: Potential volunteers with diagnose of symptomatic knee OA were included if they had knee pain greater than 3 points on 11-point numerical pain rating scale. Exclusion criteria were i) lower hemoglobin count than 15g/dL, ii) ongoing anticoagulation therapy, iii) using non-steroidal anti-inflammatory drugs in previous 3 weeks before the participation, iv) previous operation in affected knee v) active infection or malignancy, and vi) impaired cognition. To perform complete cell counts for both whole blood and PRP, 20 ml of the whole blood was drawn from the ante-cubital vein of the patients under sterile conditions. PRP was prepared using a commercially available kit, tubes contains 3.20% concentrated 0,1M of sodium citrate to block the coagulation. After phlebotomy, the tubes were placed swing-out rotor centrifuging device and were centrifuged at 830g for 4 minutes. A correlation analysis was performed between the features of PRP and the patient-related variables, including age, gender, BMIs, smoking status, presence of other diseases, physical activity scores, duration of symptoms, and pain levels. Pearson's correlation coefficient, point bi-serial correlation, and paired sample t test were performed; alpha level was set at 0.05 in all analyses.
Results: A total of 62 patients (mean age: 56.68 ± 7.13 years) were included in the analysis. The dose of injected platelets was 3.25 billion, efficiency of the process was 77%, and the purity rate of the PRP was %98.4. These results indicated "high dose (B)", "medium platelet recovery rate (B)", and "very pure (A)". PRP platelet count was correlated with whole blood platelet count (r=0.81, p<0.001), whole blood WBC count (r=0.39, p=0.002), smoking status (r=0.56, p=0.03), smoking index (-r=0.63, p=0.002), and the presence of hypertension (r=-0.31, p=0.04). PRP WBC and purity of PRP were correlated with smoking status of the patients (r=0.52, p=0.01; r=0.64, p=0.003, respectively). In addition, smoking index for current smokers was shown a good correlation with PRP WBC (r=0.57, p=0.02) and a fair correlation with purity of PRP (r=0.35, p=0.04).

Conclusion: High dose and very pure PRP with medium efficiency was yielded with this PRP preparation procedure. Whole blood platelet count, the presence of hypertension, and the smoking status of the patients can affect the features of the yielded PRP in patients with OA. Considering these factors into account in the clinical decision is important for determining whether PRP is an option in the management of patients with knee osteoarthritis. These results may serve as a guide in terms of patient selection and avoiding unnecessary injections and their associated costs.

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AB1210 SEPTIC ARTHRITIS IN HEMODIALYSIS PATIENTS

Keywords: Kidneys, Infection-related RMDs, Descriptive studies

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Background: The frequency of musculoskeletal disorders in hemodialysis patients varies around 60% as the duration of their dialysis increases. Their physiopathology is complex and multifactorial. Septic arthritis represents 30% of these arthropathies.

Objectives: analyze the clinical, biological and radiological characteristics of septic arthritis in hemodialysis patients and to assess the results of the proposed treatment.

proposed treatment.

Methods: This is a retrospective study of 22 observations of septic arthritis in hemodialysis patients identified in our department over a 5-year period (2015-2022).

Results: The mean age was 43 years [22-60]. The sex ratio is equal to 1. The average duration of hemodialysis was 11.5 years [3 months-28 years]. Joint involvement was acute in 17 cases, with a mean duration of 4 days [1 day-1 week]. It was mono-articular, affecting the knee in18 cases and the elbow in 2 case, oligoarticular in 18 cases, and poly-articular in 2 case. Sacroiliitis was noted in 1 case. Biology: sedimentation rate, CRP and procalcitonin were increased in all patients. On standard radiography: obvious signs of arthritis were observed in 17 cases. Ultrasound showed joint effusion in 18 cases. Lumbar and sacral CT scans were performed in 1 case each and revealed multifocal destructive sacral arthropathy in 1 case and were consistent with unilateral sacral ilitis. Scintigraphy was requested twice. Joint biopsy was performed in 15 cases. Surgical treatment was required in 17 case.s. arthrotomy with joint lavage and biopsy of the synovium followed by an adapted antibiotic therapy according to the antibiogranmJe during 3 weeks by IV route relayed by an oral intake during 3 weeks while the antibiotic treatment alone after biopsy was practiced in 3 patients for two cases of polyartlu-itis and one case of deep localization.

Conclusion: Arthropathies of hemodialysis patients can have several clinical aspects. They occur on average after 10 years of hemodialysis.

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Disclosure of Interests: None Declared.

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AB1211 RISK FACTORS OF DEPRESSION IN PATIENTS WITH KNEE OSTEOARTHRITIS

Keywords: Osteoarthritis

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Background: Knee osteoarthritis (KOA) is among the mean sources of chronic pain and functional disability which may lead to anxiety and depression.

Objectives: The aim of this study was to determine risk factors of depression in patients with KOA.

Methods: We conducted an analytical cross-sectional study over a 3-month period, including patients presenting with KOA. Demographic data, history of KOA and Kellegren and Lawrence radiographic stage were collected. Functional discomfort was assessed by the Lequesne knee index and catastrophizing was assessed by the Pain Catastrophizing Scale (PCS) questionnaire. Psychological assessment was performed by the Hospital Anxiety and Depression (HAD) scale.

Results: Ninety patients with KOA were included. The mean age was 58.76 ± 9.1 years. The mean BMI was 30.19 ± 5.54. The average Lequesne index was 11.33 ± 3.53 and the average PCS was 23.91 ± 11.28. A high depression score was noted in 58.9% of patients. Depression was significantly associated with sex ($p = 0.001$), BMI ($p=0.03$), lequesne index ($p=0.02$) and PCS ($p=0.00009$).

Conclusion: Pain catastrophizing thoughts in KOA and obesity worsen patients' attitudes and psychological profile towards pain and may lead to depression.

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AB1212 OSTEOARTICULAR TUBERCULOSIS, A VERY CHALLENGING DIAGNOSIS

Keywords: Rare/orphan diseases, Bone diseases, Osteoarthritis

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Background: Osteoarticular Tuberculosis (TB) is an uncommon form of extrapulmonary TB, it comprises 2–5% of all TB cases in Tunisia. The most frequent sites of osteoarticular TB infection are the spine, hip, and knee. Diagnosis can be challenging owing to the non-specific and insidious nature of the clinical presentation.

Objectives: Describe clinical features, diagnosis and management of this uncommon clinical entity.

Methods: A retrospective clinical study of TB had been diagnosed in our hospital during the last five years. the diagnosis was made by bacteriological and histological examinations after imaging assessment (MRI, CT scan).

Results: Ten cases were included (6 males and 4 females). The mean age was **53 years (16-72 years**). The average time to diagnosis was 4 months (2-12months). The joints affected were the dorsolambur spine, shoulder, elbow, phalanges, the trochanter-femur and the metatarsal bones. The most common symptoms noted were pain, swelling and restricted motion of the involved joint. Cutaneous fistulas were visualized in one case. Fever and systemic symptoms were present in one case. Radiological findings varied, with lytic lesions, abscesses, and joint destruction observed. All patients presented with pathognomonic histological tubercle appearances, with caseous necrosis, lymphocytes, and Langhans giant cells present and TB-PCR in the pus samples was positive in one case. All patients were treated with anti-TB drugs for 12 months and three patients received corticosteroid therapy. The abscess was drained in six cases. We noted clinical and radiological recovery with medical tuberculosis treatment in all patients.

Conclusion: Osteoarticular TB is a common manifestation of extrapulmonary TB and must not be overlooked. Early detection of osteoarticular TB may prevent limb morbidity. Although anti-TB drugs are the primary treatment for osteoarticular TB, in some cases, surgery is required to establish a diagnosis and gain local infection control.

Reference: **Diagnosis of Osteoarticular Tuberculosis: Perceptions, Protocols, Practices, and Priorities in the Endemic and Non-Endemic Areas of theWorld—AWAIOT View.**
Vikas M. Agashe 1, Ashok N. Johari 2, Mudit Shah 3, Rashid Anjum 4,*, Carlo Romano 5, Lorenzo Drago 6, Hemant K. Sharma 7 and Thami Benzakour 8 Microorganisms **2020**, 8, 1312; doi:10.3390/microorganisms8091312
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AB1213 ILLNESS PERCEPTION IN PATIENTS WITH KNEE OSTEOARTHRITIS

Keywords: Cognitive function, Osteoarthritis, Pain

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Background: Knee osteoarthritis (OA) can be a source of pain and major functional handicap. If not relieved, it leads to an alteration of the patient's quality of life. The cognitive component of pain varies from one subject to another.
Objectives: The aim of this study was to evaluate the illness perception in patients suffering from knee OA.
Methods: We conducted a cross-sectional study in patients with knee OA. Illness perception was assessed using the French version of the Brief Illness Perception Questionnaire (BIPQ). This questionnaire was developed from the model of Leventhal et al. and aims to assess the different components of the disease. It includes 9 items: 8 quantitative questions on a numerical scale from 0 to 10 and a last item in the form of a qualitative question. The total score varies from 0 to 80, with no predefined thresholds. The higher the score, the more threatening the patient's perception of the disease is. A "p" value inferior to 0.05 was considered significant.
Results: Thirty patients with knee OA responded to the questionnaire. It was about 26 women (87%) and 4 men (13%) with a mean age of 60 years [42-71]. The average duration of the disease was 78 months [12-240]. All patients used tier 1 analgesics and NSAIDs, 33% used tier 2 analgesics and three patients had received corticosteroid knee injection. The mean visual analog scale (VAS) of pain was 6 cm [3-9]. The mean walking distance was 678m [100-1000]. None of the patients used a cane. The mean value of the Lequesne algofunctional index (AFI) was 8.8 [3-15]. Lameness was noted in 13% of patients. The patellar tap test was positive in 47% of cases. The mean values of body mass index (BMI) and waist circumference were 30kg/m² and 96cm, respectively. According to the Kellgren-Lawrence classification, knee OA was at grade 1 in 10% of the cases, grade 2 in 40% of the cases, grade 3 in 40% of the cases, and grade 4 in 10% of the cases. All patients completed the entire questionnaire with a mean score of 45 [36-54], and a mean maximum score of 6/10 for the first question assessing the impact of the disease on the patients' lives. Responses were incomplete for the 9th question which consists on listing 3 reasons that may cause the disease: only 15 patients (50%) cited 3 causes. The main reported factors causing knee OA according to patients were physical activity (83%), age (66%), prolonged standing (62%), and weight (51%). A statistically significant negative correlation was noted between the BIPQ, and age (r=-0.488, p=0.006) and disease duration (r=-0.583, p=0.001). This correlation was not significant with pain VAS, walking distance, BMI, waist circumference and the Lequesne AFI.
Conclusion: Illness perception in patients with knee OA is important to screen in order to deliver a more personalized management.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1214 PATIENT OUTCOMES AFTER TIBIAL HIGH OSTEOTOMY

Keywords: Epidemiology, Descriptive studies, Cartilage

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Background: At a time when total or partial arthroplasty is taking on a predominant role in the treatment of medial ferno-tibial gonarthrosis, tibial valgus osteotomy with internal opening and filling with a bone substitute filling with a bone substitute wedge remains for many authors an indication of choice in young patients.
Objectives: The aim of our work is to evaluate the functional and radiological results of this type of osteotomy and to assess the osseointegration and resorption of the bone substitute.
Methods: This was a single-centre retrospective study osteotomies performed in 63 patients, collected between June 2016 and June 2020. We evaluated the functional outcome. Lysholm-Tegner and assessed osseointegration of the classification of the GESTO.
Results: The mean age of our patients was 55.6 ± 8.1 years. The mean body mass index (BMI) was. (BMI) was 31.56 ± 4 Kg.m-': According to the Ahlback classification: stage II was found in 64.7% of cases, stage III and I were found in 23% and 7.7% of cases respectively. 3 patients had stage IV gonarthrosis. The average follow-up was 24 months. There was only one case of plaque sepsis. The Lysholm-Tegner score was improved (p<O,OOl) with a mean gain of 11.82/100. The mean internal laxity was reduced by 6o (p<O, 001). The mean angular correction was 2.65° (p<O,OOl). The postoperative tibial slope did not increase significantly: 5.98° ± 1.65° preoperatively and 6.38° ± 1.63° postoperatively(p=0.208). According to the GESTO classification: the rate of osseointegration rate was 18% at 3 months postoperatively and 98.5% at 6 months postoperatively. 98.5% at 6 months post-operatively. We had only one case of poor integration. At follow-up, no total resorption of the wedge was achieved less than 40% in 89% of cases and less than 60% in 19% of cases. The degree of satisfaction was good or excellent in 97%.
Conclusion: The use of wedges in the internal opening VTO was a determining factor in the determining factor in the accuracy of the correction. It also guarantees the bone capital thanks to its osteo-conductive effect and allows conductor effect and allows us to hope for greater simplicity in the event of a subsequent arthroplasty.
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AB1215 ASSOCIATED FACTORS TO POSTURAL BALANCE CONTROL IN KNEE OSTEOARTHRITIS AND COMMON LOW BACK PAIN PATIENTS

Keywords: Rehabilitation, Pain

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Background: Pain induces the alteration of postural balance (PB) mechanisms. Therefore, the PB control is an important element to consider when managing patients with degenerative musculoskeletal diseases(DMD).
Objectives: The aim of our study was to evaluate balance control in patients having knee osteoarthritis (KOA) or low back pain and to identify the associated factors.
Methods: A cross sectional study including patients suffering from common low back pain(LBP) and KOA. We collected the sociodemographic data. We evaluated the PB using a stabilometric platform, realized when the eyes were closed. Analyzed variables were the center of pressure(COP) in the mediolateral(ML) and anteroposterior(AP) axis, the surface area (S), the mean sway velocity(V) and the mean sway energy(E).We divided patients into 2 groups; G1:patients having postural imbalance and G2:patients with a good postural balance profile.
Results: We had 30 patients with a sex ratio at 1.3, a mean age of47±11.14 [23-65] years old. The mean BMI was 28.17±2.1[20.3-39.56]. Twelve patients (40%) suffered from KOA, 18(60%) of them had chronic low back pain, with a mean disease duration of 1.61±1.55[0.10-5] years. Postural profile evaluation revealed a mean S of 265.93±576.3 [1 - 3239]. COP position in the ML axis was 0.68±9.49[-15.7 -24.6] and in the AP: 21.4±21.70[-8.2 – 81.4]. Mean sway V was11.4±3.88 [7.2 – 22.9]. The E was 8.94±89.6[27 – 403]. We detected an abnormal S in 5% of participants, decreased E in 8% of patients. According to the ML axis the COP was: left in one patient and right in 5% of patients. The COP was anterior in 21% of cases. The mean sway V was pathological in 5% of cases. The comparison between both groups did not find any

significant difference concerning gender (p=0.43), the disease (p=0.65). We did not find a significant difference in the means of age (p=0.52), BMI (p=0.3) and underlying disease duration (p=0.31).
Conclusion: Half of the patients with DMD presented a postural imbalance which wasn't explained by sociodemographic or anthropometric parameters. The instrumental evaluation of PB, considering the fall's risk factor is then essential.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1216 SYMPTOMATIC SLOW-ACTING DRUGS FOR GONARTHROSIS: BETWEEN EXPECTATIONS AND REALITY

Keywords: Pain, Osteoarthritis

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Background: Osteoarthritis of the knee is the most common cause of chronic pain and disability in patients. In addition to non-steroidal anti-inflammatory drugs and analgesics, the symptomatic slow-acting anti-arthritic drugs (SAALs) define a specific class of medications used in the symptomatic treatment of osteoarthritis of the knee. With a delayed effect, this family of drugs is used to reduce the intensity of pain and functional discomfort caused by the destruction of cartilage.
Objectives: The objective of this study was to evaluate the fears and expectations of patients before the treatment and the response to the treatment as well as the degree of satisfaction after one year of treatment.
Methods: This study was conducted in the form of an individual questionnaire, 56 patients followed in consultation for a primary gonarthrosis without a period of congestive attack, the diagnosis of knee osteoarthritis was made by and radiography of the knee according to the classification of Kellgren and Lawrence, any patient with secondary osteoarthritis or very disabling gonarthrosis was excluded. Patients were questioned about their fears and expectations before the start of treatment. An evaluation of the therapeutic response after one year was done by different parameters: the visual analogue pain scale (VAS pain), the Lequesne index of the knee, and decrease in analgesic consumption, improvement in walking perimeter and side effects and pain reduction. Global satisfaction was evaluated by a likert scale composed of 7 degrees of satisfaction (from extremely satisfied to extremely dissatisfied).
Results: We included 56 patients, the average age was 44 years, the female sex represented 59%, the average educational level represented 20%. According to the classification of Kellgren and Lawrence, stage 2 represents (40%), stage 3 (52%) and stage 4 (8%). There were 30% of patients on chondroitin-based antiarthritis drugs, 60% on glucosamine and 10% on avocado-soybean unsaponifiable extract. The average VAS pain was 5 ± 1.1, the average Lequesne index (knee) was 7. Fear of pain exacerbation was noted in 15%, 20% were afraid of a functional handicap and 49% were afraid of a probable surgery, 16% had no fear. Before the initiation of treatment, 65% of the patients hoped for an improvement in their function, 49% feared a probable surgery and 16% had no fear. Before the initiation of treatment, 35% thought it was a placebo. The mean VAS pain after treatment was 3±2.2 vs 5 ±1.1 before treatment (p= 0.003), the mean Lequesne index after treatment was 4.9 vs 7 after treatment with a statistically significant difference (p= 0.003), an improvement of the gait perimeter was noted in 51%, 41% reported a reduction in the consumption of analgesics, 3% of patients had side effects such as nausea and and vomiting. After 1 year of treatment, 45% of patients were extremely satisfied with their treatment, 15% were extremely dissatisfied, 10% were satisfied and 30% were not very satisfied.
Conclusion: Patient expectations and satisfaction are important components in the evaluation of quality of care. This new approach is important to guarantee therapeutic adherence.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1217 COMORBIDITIES DURING GONARTHROSIS

Keywords: Quality of life, Comorbidities, Osteoarthritis

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Background: Osteoarthritis of the knee, together with that of the hip, is the most serious disease of osteoarthritis.
Long considered a benign disease, gonarthrosis is nevertheless associated with significant morbidity.
Objectives: To assess the prevalence of co-morbidities in gonarthrosis patients and to assess their impact on pain, functional impact and radiographic progression.
Methods: Our study involved patients with gonarthrosis. Comprehensive comorbidity screening was done. Pain intensity was assessed by the Analogue Visual Scale (EVA). The neuropathic component was assessed by the DN4 score. Functional impact was assessed by the Lequesne index and Womac score. Knee X-rays were classified according to Kellgren Lawrence (KL) criteria.
Results: A total of 215 patients were included (24 men/191 women). The average age was 58.02 ±9.11 years. The mean body mass index was 24.87± 5.39 kg/m2. The main comorbidities were:

COMORBIDITIES	PREVALENCE
Overweight and obesity	40,6%
Heart disease	37,4%
HTA	26%
Diabetes	24,2%
Dyslipidemia	11.2%
Anxiety	9,3%
Ostéoporosis	7,9%
Dysthyroidism	7%
Smoking	3,7%
Neoplasia	1,4%
Chronic kidney disease	0,9%

The visual analogic scale was 7.86± 1.31 and stress at 13.74 ±4.95. The average Womac score was 12.3 ±8.92. The average Lequesne score was 6.71 ±3.20. The average DN4 score was 18.81± 8.9. Comorbidities were associated with age (p = 0.02), DN4 score (p = 0.01), and KL radiographic grades (p = 0.02).
Conclusion: In this study, co-morbidity in gonarthrosis was associated with advanced age, a neuropathic component of pain, and severe structural impairment.
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Osteoporosis

AB1218 **ASSOCIATION BETWEEN OSTEOPOROSIS AND DISRUPTION OF GUT MICROBIOTA: A META-ANALYSIS**

Keywords: Osteoporosis

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Background: Osteoporosis(OP) is a systemic disease of the skeleton characterized by decreased bone mineral density and the imbalance of bone, resulting in an increased risk of fragility fractures[1]. Gut microbiota has a mutually beneficial and symbiotic relationship with the host and plays a vital role in the host's metabolism and immune regulation. An expanding body of studies asserts that gut microbiota has a role in bone metabolism and the pathogenesis of osteoporosis[2].
Objectives: This study aimed to confirm the changes of gut microbiota in osteoporosis through meta-analysis.
Methods: We searched PubMed, Embase, MEDLINE, Cochrane Library, CNKI, VIP, CBM, and Wanfang databases from the established to January 10 2023 on gut microbiota diversity in patients with OP. Standardized mean difference(SMD) and 95% confidence interval(CI) were used to evaluate the difference in microbial abundance between the OP and healthy control(HCs).
Results: A total of 16 studies were included in this meta-analysis, including 517 OP and 714 HCs. The summary results showed that there was no significant difference in α diversity index compared with HCs[Simpson index: SMD=0.120, 95%CI(-0.031~0.271), p=0.049; Shannon index: SMD=-0.039, 95%CI(-0.284~0.206), p=0.001; ACE: SMD=0.029; 95%CI(-0.647~0.706), p<0.001; Chao1: SMD=0.000, 95%CI(-0.446~0.446), p<0.001; Observed_species: SMD=0.134, 95%CI(-0.049~0.317), p=0.198]. To eliminate the heterogeneity caused by the difference of the observed species index by the sequencing method, we conducted a subgroup analysis of the observed species, and the results showed that the index obtained by high-throughput sequencing[SMD=0.490, 95%CI(0.084~0.896), p<0.001] was higher than that of HCs.
Conclusion: This study suggested that changes in intestinal microecology were related to OP. More studies should be conducted to explore the specific differences in gut microbiota in OP.

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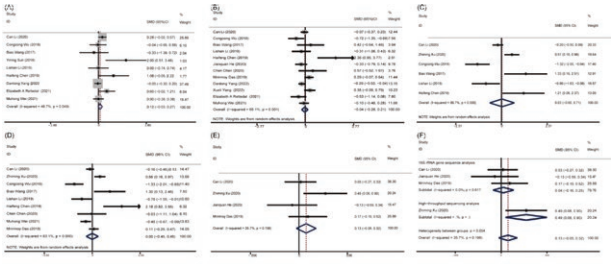


Figure 1: Forest map of intestinal flora α diversity in osteoporosis patients compared with healthy controls. (A)Simpson index; (B)Shannon index; (C)ACE; (D)Chao1; (E)Observed_species; (F)Observed_species grouped by sequencing method.

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AB1219 **HOW TO TAILOR THE ANTI-OSTEOPOROSIS TREATMENT IN PATIENTS WITH ADVANCED LIVER DISEASE? VARIATIONS OF RENAL FUNCTION BY CREATININE AND CYSTATIN C**

Keywords: Bone diseases, Biomarkers, Osteoporosis

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Background: A rapid bone loss and an increase in fractures have been described after liver transplantation, warranting focused management. Bisphosphonates are effective antiresorptive agents, but with a limited in patients with significant kidney disease, as the drugs are excreted by urine, accumulating and increasing the risk of adverse events (including at the kidney level). The evaluation of renal function in the patient with cirrhosis can be challenging and may be underestimated by standard methods[1]. This issue may impact the choice of the anti-osteoporosis (OP) agent.
Objectives: To compare the variations on bisphosphonate treatment indication across different glomerular filtration rate (GFR) equations in patients with advanced liver disease included in a pre-transplantation study.
Methods: Descriptive cross-sectional study of patients from a tertiary center selected for a multidisciplinary assessment before liver transplantation from February 2019 to December 2022. Sex, age, ethnicity, and serum creatinine and cystatin C (a more sensitive marker than creatinine for the estimation of GFR in patients with cirrhosis[2]) levels are collected. The indication for anti-OP treatment is established in the presence of T< -1.0 by densitometry (DXA), vertebral radiographic wedging or history of a fragility fracture. GFR adjusted by creatinine, cystatin C and creatinine-cystatin C was calculated using the online calculation tool MediCalc®. Results are later categorized as below or above 30ml/min^2 (usual cut-off to contraindicate the use of bisphosphonates[3]), finally comparing the rate of patients with GFR <30 ml/min across three methods. A descriptive study is presented. Comparison of variables are performed by Fisher's exact test. P-values of <0.05 are considered statistically significant.
Results: A total of 162 patients (75.9% men) were included, all Caucasian, with a mean age of 60 years (SD 7.6) and a mean BMI of 27.9 (SD 4.9). Seventy-six percent (n=120) were candidates to anti-OP therapy, and 68.5% (n=111) ultimately received it (88% bisphosphonates, 11% denosumab, and 1% teriparatide). Three percent (n=5) presented a fragility fracture, and 9.5% (n=17) showed a radiographic vertebral fracture. Fifty-one percent (n=80) had osteopenia and 22.9% (n=36) osteoporosis at DXA scans. Regarding renal function, mean serum levels of creatinine and cystatin C were 0.99 mg/dl (SD 1) and 1.7 mg/L (SD 1), respectively. The mean estimated GFR levels using creatinine, cystatin C and creatinine-cystatin were 87 ml/min (SD 24.8), 49.3 (SD 23.4) and 63.9 (SD 23.3), respectively. The percentage of patients with GFR <30ml/min was 1.9% measured by creatinine, 20.5% calculated by cystatin, and 5.6% calculated by creatinine-cystatin (Figure 1). Differences between rates were statistically significant. In this sense, anti-OP therapy was tailored accordingly in 12 patients (10.9%) with treatment indication, using denosumab instead of bisphosphonates. p 0,008 p <0,001

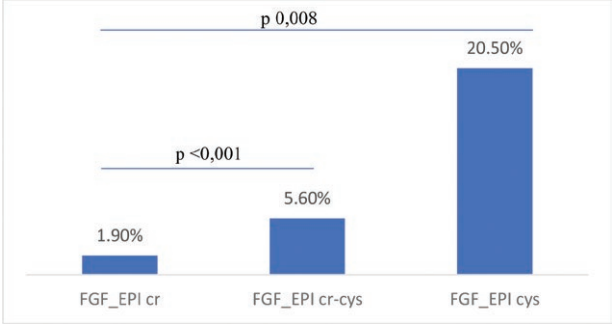


Figure 1. Patients with GFR <30 ml/min by different equations.

Conclusion: In a setting of advanced liver disease candidate to transplantation, renal function estimates significantly varied depending on the GFR equation used, thus largely modifying the rates of patients with contraindication for using bisphosphonates, despite the high fracture risk.
Further studies are necessary to establish the best method to assess the renal function in advanced liver disease patients, in order to tailor anti-OP strategies.

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AB1220

VERTEBRAL FRACTURE CHARACTERISTICS IN AN FLS UNIT ACCORDING TO THE IDENTIFICATION METHOD; EMERGENCY LIST, OUTPATIENT CLINIC OR VFA.

Keywords: Osteoporosis

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Background: The risk o subsequent fracture is very high after a vertebral fracture (VF)
Objectives: To analyze the characteristics of patients with VF seen in a Fracture Liaison Service (FLS).
Methods: Our FLS cares for patients from the emergency list (URG), referred by hospital or primary care doctors (HPC) with VF <12 months, and captured by DXA-VFA (Densitometry - VF Assessment) in patients with non-VF. The database included the FRAX items plus previous treatment and DXA results. Traumatic VFs or VFs with a known age > 1 year, infiltrative or neoplastic diseases, and patients with contraindications for treatment were excluded. The number and grade of VF (Genant's scale) were analyzed.
Results: 570 patients have been included (Table 1). The most frequent route of identification was HPCfollowed by the emergency registry and detection by DXA-VFA. The patients identified by VFA did not report a previous VF, as did 25 of the HPC cases, referred by a report of fracture by the radiologistst or by detection in the consultation by the rheumatologist. Figure 1 shows the identification of patients over the years.

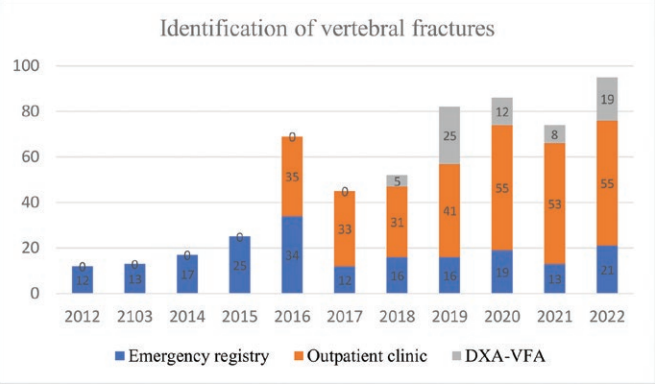


Figure 1.

We observed a higher percentage of grade 3 fractures in those identified in the emergency registry. Those identified by HPC had a higher average number of fractures and a higher percentage of osteoporosis by DXA. In this group there was a greater frequency of previous fracture, as well as rheumatoid arthritis and glucocorticoid use. Patients referred through HPC had a higher adherence to treatment compared with the other groups. The 69 patients detected by DXA-VFA consisted of 30 humerus fractures, 1 pelvic, and 38 forearm, mostly women with a single fracture and lower percentage of osteoporosis by DXA. The adherence to treatment has changed over the years. In 2021 and 2022 it was 93%, compared to 79% in 2012-2020.
Conclusion: All the ways to identify VF are important. The training campaign carried out in the healthcare area, including radiologists, has allowed us to improve the standard. The results will be helpful in the implementation and consolidation of the model based on FLS.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1169

Table 1. - Distribution according to identification group. Results represent n (%) and mean (SD) unless expressly indicated.

	All patients N=570	Emergency registry N=198	Outpatient N=303	VFA N=69	*p*
Age	73.6 (9.7)	75.5 (9.4)	72.6 (9.9)	72.4 (8.8)	0.003
Women	480 (84.2)	156 (78.7)	261 (86.1)	63 (91.3)	0.020
Time from fracture to visit (weeks)					
Mean	17 (11)	13 (8)	20 (12)	13 (8)	0.02
Median (IQR)	13 (8-20)	12 (8-16)	13 (8-28)	12 (8-16)	
<12 weeks	214 (37)	83 (42)	101 (33)	30 (43)	0.08
Vertebral fractures					
Number of VF					
mean	2.0 (1.6)	1.76 (1.4)	2.35 (1.8)	1.22 (0.5)	0.000
median (IQR)	1 (1-2)	1 (1-2)	2 (1-3)	1 (1-1)	
Only fractures grade 1	24 (4.2)	3 (1.5)	20 (6.6)	*	0.007
≥ 2 VF**	259 (45.7)	78 (39.3)	169 (56.1)	12 (17.4)	0.000
At least one grade 3 fracture***	274 (48.8)	124 (63.9)	141 (47.3)	9 (12.0)	0.000
Risk factors for fracture					
Previous fracture	155 (27.2)	51 (25.8)	89 (29.3)	15 (20.0)	0.362
Parental hip fracture	51 (8.9)	20 (10.1)	25 (8.2)	6 (8.0)	0.775
Active smoking	67 (11.7)	21 (10.6)	34 (11.2)	12 (16.0)	0.294
Glucocorticoids	51 (8.9)	9 (4.5)	40 (13.2)	2 (2.7)	0.001
Rheumatoid arthritis	22 (3.8)	5 (2.5)	17 (5.6)	0	0.045
Secondary osteoporosis	86 (15.0)	37 (18.6)	36 (11.8)	13 (17.3)	0.075
Alcohol	21 (3.6)	9 (4.5)	10 (3.3)	2 (2.7)	0.712
BMI	27.5 (5.0)	28.5 (4.7)	26.2 (5.3)	28.7 (5.1)	0.000
FRAX major	12.7 (8.6)	13.3 (9.6)	13.0 (11.0)	10.8 (7.9)	0.156
FRAX hip	5.6 (6.6)	6.0 (7.9)	5.9 (4.0)	4.3 (6.6)	0.231
DXA #					
Normal	46 (8.6)	18 (10.0)	18 (6.3)	10 (13.3)	0.000
Osteopenia	175 (32.8)	69 (38.5)	75 (26.3)	31 (41.3)	
Osteoporosis	312 (58.5)	92 (51.3)	192 (67.3)	28 (37.3)	
T-score lumbar	-2.29 (2.0)	-2.0 (1.7)	-2.5 (2.3)	-1.4 (1.5)	0.000
T-score femoral hip	-1.91 (1.0)	-1.8 (1.2)	-2.0 (1.0)	-1.5 (0.9)	0.003
Treatment&					
Previous treatment	124 (21.8)	35 (17.6)	80 (28.0)	9 (12.0)	0.012
Start within 6 months of the visit	474 (83.1)	161 (81.3)	265 (87.4)	48 (69.5)	0.001

* Only grade 2 and 3 fractures were considered. ** Available in 567 patients. ***Available in 561 patients. # Available in 533 patients. & Bisphosphonate, denosumab, SERM or teriparatide.

AB1221

CLINICLAL EFFICACY OF SEQUENTIAL TREATMENT AFTER ROMOSOZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARISON WITH PRIMARY OSTEOPOROSIS FOR 24 MONTHS

Keywords: Osteoporosis, Rheumatoid arthritis

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Background: Romosozumab (ROMO), a monoclonal antibody that binds sclerostin, increases bone formation and decreases bone resorption. And although it is a novel therapeutic agent for osteoporosis, which has shown high effects of increasing bone density and inhibiting fragile fracture in overseas clinical trials. However the clinical efficacy for rheumatoid arthritis complicated with osteoporosis (RA-OP) is unknown.
Objectives: To evaluate the clinical efficacy of ROMO for 12 months and denosumab (DMB) for 12 months in patients with RA-OP comparison with primary osteoporosis (P-OP) for 24 months.
Methods: RA patients diagnosed according to the 2010 ACR/EULAR criteria. All patients (RA-OP; 12 cases, P-OP; 19 cases) met at least one of the following criteria were eligible; a bone mineral density T score of -2.5 or less at the lumber spine or total hip and either one or more moderate or severe vertebral fractures or two or more mild vertebral fractures. All patients were initiated ROMO from between April, 2019 and July, 2020. The ROMO dose was 210mg at once every 1 months. After 12 months of ROMO, all cases were changed to DMB. In all cases native or activated vitamin D has been used. We reviewed the results for 24 months about the increase and decrease of bone mineral density (BMD) of lumbar spine(LS) and total hip(TH) by DEXA and bone turnover markers, intact n-terminal propeptide type I procollagen(PINP) and tartrate-resistant acid phopshatate form 5b(TRACP-5b).
Results: The gender was all female. Patient background at baseline in RA-OP (n=12) and P-OP (n=19) had a mean age of 72.8 ± 7.0 and 73.9 ± 9.7 (p=0.417); the body mass index were 19.5 ± 3.1 and 20.1 ± 3.6 (p=0.516); the FRAX were 36.0 ± 14.9 and 33.7 ± 16.6 (p=0.529); the number of previous fracture were 5cases (42%) and 13cases (68%) (p=0.142) and the number of previous drug for treatment osteoporosis use were 9cases (75%) and 7cases(38%) (p=0.038). The bone turnover markers and bone mineral density at baseline were as follows; P1NP 62.4 ± 36.2 and 94.6 ± 101.3 (p=0.656); TRACP-5b 485 ± 252 and

546 ± 278 (p=0.516); LS-BMD and T-score 0.79 ± 0.14 and 0.79 ± 0.12 g/cm^2 (p=0.903), -2.82 ± 0.99 and -2.87 ± 0.87 (p=0.919) and TH-BMD 0.55 ± 0.07 and 0.56 ± 0.07 g/cm^2 (p=0.621), -3.14 ± 0.53 and -3.06 ± 0.55 (p=0.682). Clinical findings related to RA-OP at baseline were as follows; disease duration 17.7 ± 16.5 years; CRP 1.25 ± 1.75; DAS28-CRP 3.45 ± 0.99; HAQ 1.56 ± 0.99. The rate of increased LS-BMD from baseline to 6, 12, 18 and 24 months between RA-OP and P-OP were 10.8 ± 8.0% and 11.6 ± 5.7%, (p=0.670) at 6 monts, 15.2 ± 9.5% and 16.4 ± 8.2% (p=0.584) at 12 months, 18.9 ± 10.4% and 21.8 ± 9.4% (p=0.598) at 18 months, 20.6 ± 11.7% and 22.7 ± 9.6% (p=0.730) at 24 months and TH-BMD were 4.1 ± 4.5% and 2.7 ± 3.9%, (p=0.389) at 6 monts, 5.7 ± 6.3% and 6.1 ± 6.0% (p=0.747) at 12 months, 8.4 ± 8.1% and 8.2 ± 5.3% (p=0.747) at 18 months, 8.4 ± 9.8% and 8.8 ± 5.0% (p=0.236) at 24 months (Figures 1, 2).

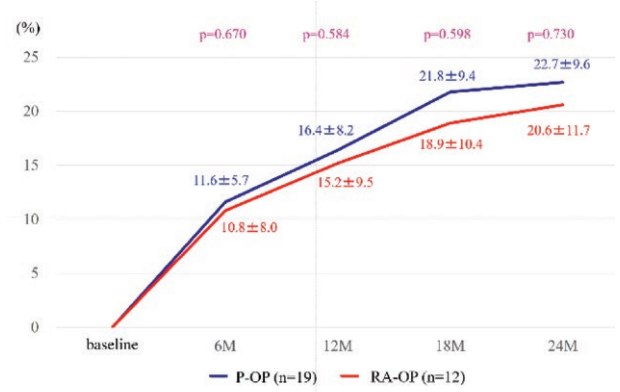


Figure 1 : The rate of increased LS-BMD from baseline to 24 month

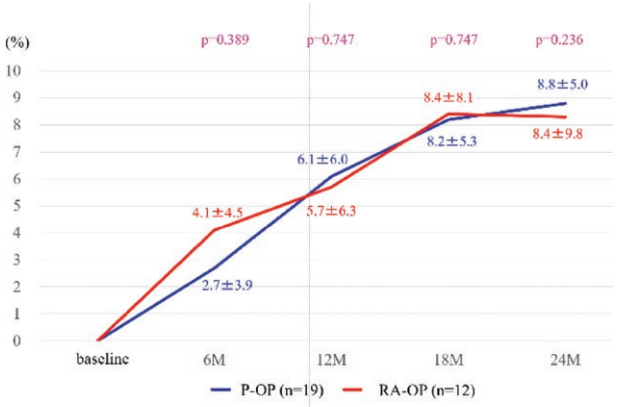


Figure 2 : The rate of increased TH-BMD from baseline to 24 month

Conclusion: Clinical efficacy of treatment with ROMO for 12months and DMB for 12months was extremely effective for RA-OP as well as for P-OP and has the high potential to be an important option in the treatment of RA-OP.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Yasuhide Kanayama Speakers bureau: YK has received speakers' fees from AbbVie, Astellas, Asahi Kasei, Daiichi-Sankyo, Eisai, Eli Lilly, Ono and UCB Japan., Kyosuke Hattori: None declared.

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AB1222

NEUTROPHIL TO LYMPHOCYTE RATIO (NLR) PREDICTS FRACTURE IN PATIENTS ON LONG-TERM GLUCOCORTICOID.

Keywords: Registries, Osteoporosis, Bone diseases

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Background: Long-term glucocorticoid (GC) exposure leads to systemic bone loss and fracture. In addition, GC is known to increase white blood cell (WBC) amount and change the distribution of differential count (DC). Neutrophil-to-Lymphocyte ratio (NLR) has been studied as an optimal marker of subclinical inflammation, predicting the prognosis of cardiovascular diseases, cancers and even covid-19 infection. For patients under long-term GC exposure, the hemogram change might be a potential parameter to predict prognosis.

Objectives: This pilot study aims to investigate if GC related WBC-DC change, including NLR, is associated with future fractures during 3 years follow-up.

Methods: This retrospective study is based on a registry, conducted in Kaohsiung Chang Gung Memorial Hospital, Taiwan, from September 2014 till April 2021, aimed to monitor bone mineral density (BMD) changes and fractures in patients with autoimmune diseases. All recruited patients were followed at least 3 years and took X-ray images annually to capture new fragility fracture, including morphometric vertebral fractures. We screened participants who used GC continuously at least 3 months before the index day. We recorded the complete blood count (CBC) and WBC-DC values at least twice during the period of 3 months before and after the index day, and excluded patients who were febrile, under infection status, diagnosed as cancers or cardiovascular diseases at the index day. The NLR was calculated by the absolute neutrophil count divided by absolute lymphocyte count individually.

Results: A total of 346 participants were enrolled in current study, and 101 (29.2%) suffered from new fragility fracture in 3 years. Among patients with fracture and non-fracture, conventional fracture risk factors, such as age, BMD, and previous fracture remained significantly different, while the WBC revealed no difference (Table 1). Nevertheless, the absolute neutrophil and lymphocyte count were significantly higher and lower in the fracture group, respectively, and no difference in the monocyte, eosinophil, and basophil count. We compared different WBC ratio, and NLR is significantly higher in the fracture group, providing the odds ratio of 1.24 (95% confidence interval 1.07-1.44, p=0.005). Figure 1 showed that the observed fracture risk raised as the NLR values increased.

Conclusion: In patients under long-term GC, NLR might be a helpful marker to predict fracture, and higher NLR indicates higher fracture risks.

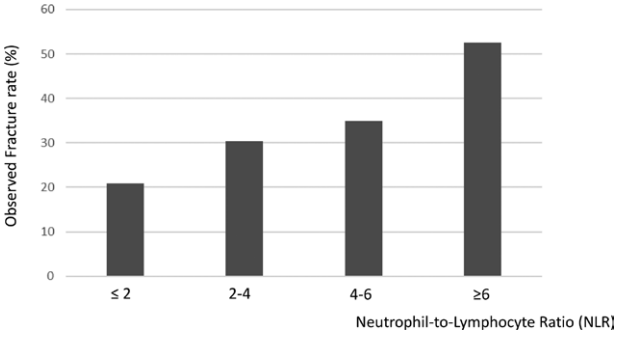


Figure 1. Observed fracture rate is associated with baseline NLR

Table 1. Demographic characteristics of enrolled patients on long-term glucocorticoid.

	Fracture N=101	No-Fracture N=245	p-value
Age	63.7 ± 9.0	56.5 ± 9.6	<0.001*
Sex(women)	89(88.1)	210(85.7)	0.55
BMI	24.1 ± 3.9	23.4 ± 3.9	0.14
Previous Fracture	64(63.4)	55(22.4)	<0.001*
Total hip BMD	0.738 ± 0.133	0.790 ± 0.122	0.001*
Femoral neck BMD	0.575 ± 0.113	0.626 ± 0.109	<0.001*
Lumbar BMD	0.841 ± 0.200	0.855 ± 0.150	0.49
WBC	7.3 ± 2.1	6.9 ±1.7	0.14
Hemoglobin	12.8 ± 1.5	12.9 ± 1.4	0.33
Platelet	239.2 ± 64.7	247.9 ± 71.4	0.30
Neutrophil	67.3 ± 9.7	64.3 ± 9.7	0.009*
Lymphocyte	24.3 ± 8.7	26.6 ± 9.5	0.04*
Monocyte	6.2 ± 1.8	6.3 ± 1.6	0.52
Eosinophil	1.8 ± 1.8	1.9 ± 1.3	0.77
Basophil	0.4 ± 0.2	0.4 ± 0.2	0.18
NLR (Neutrophil to lymphocyte)	3.3 ± 1.7	2.8 ± 1.4	0.004*
NMR (Neutrophil to monocyte)	11.9 ± 4.5	11.0 ± 3.6	0.04*
LMR (Lymphocyte to monocyte)	4.2 ± 1.7	4.5 ± 1.9	0.20

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Disclosure of Interests: None Declared.

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AB1223

WHAT ABOUT BONE MINERAL DENSITY IN RHEUMATOID ARTHRITIS PATIENTS USING GLUCOCORTICOIDS?

Keywords: Osteoporosis, Comorbidities, Rheumatoid arthritis

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Background: Osteoporosis is a major co-morbidity to screen for in patients with RA. Inflammation, low activity level, and treatments, particularly glucocorticoids, increase the risk of osteoporosis in RA patients and expose them to a high fracture risk. Few studies examined glucocorticoid-induced osteoporosis in patients with RA, especially in Africa.
Objectives: Our study aimed to compare the densitometric profile of RA patients receiving glucocorticoids with that of patients not receiving glucocorticoids, and to assess the fracture risk by the FRAX.
Methods: We conducted a retrospective observational study including patients with RA according to the ACR EULAR criteria in the rheumatology department of Kassab Institute of orthopaedics. General data, demographics, inflammation markers (sedimentation rate (SR) and C reactive protein (CRP)), and disease activity (DAS28 (CRP)) were collected. We compared the parameters of bone mineral density (BMD) and FRAX score for two groups: G1 patients who received glucocorticoids and G2 patients who did not.
Results: A total of 207 patients with RA (169 women and 38 men) were included. The mean age was 57±12.2 years [29-85]. The mean duration of disease progression was 7.1±7 years [0-41]. Sixty percent of RA patients had positive RF and/or ACPA. Obesity was noted in 34% of cases. The mean SR and CRP were 47.6±27mm, and 21.5±28mg/l, respectively. The mean DAS28 (CRP) was 6.23±4.49. Seventy percent of the patients (n=144) were using systemic corticosteroid therapy with a mean dose of 6.26mg±4.5 [0-15] prednisone equivalent with a mean duration of corticosteroid use of 14 months ±4.5. Forty-two percent of the patients had osteoporosis (T score≤ -2,5 DS), 37% had osteopenia (-2,5 DS <T score≤-1 DS), and 18% had normal BMD (T score>-1 DS). The Table 1 summarizes BMD parameters and Frax score in the two groups.
Conclusion: Patients receiving glucocorticoids had a lower bone density, T-score, and a higher fracture risk. Osteoporosis and the high incidence of osteoporotic fractures are dramatic consequences of glucocorticoid therapy in RA patients, leading to marked impairment of their quality of life.

Table 1: Comparison of the BMD parameters and Frax score in the two groups

		G1	G2	p
BMD	Vertebral site	0,91±0,19	1±0,22	0,008
T score	Vertebral site	-2,11± -1,51	-1,33± -1,62	0,002
BMD	Femoral site	0,79±0,16	0,89±0,18	0,001
T score	Femoral site	-1,88± -1,22	-1,03± -1,45	0,00
FRAX		2,21±2,8	0,93±1,07	0,002

G1: groupe1; G2: G2; BMD: bone mineral density

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1224

FREQUENCY OF OSTEOPOROTIC THORACIC VERTEBRAL FRACTURES DETECTED AS INCIDENTAL FINDINGS ON INPATIENT CT SCANS

Keywords: Osteoporosis, Imaging

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Background: Osteoporosis is one of the main public health problems, leading to the appearance of fragility fractures. Within these, there are vertebral fractures, which in their vast majority have an asymptomatic course, which is why they are presented as incidental findings in imaging studies.
Objectives: To estimate the prevalence of insufficiency fractures in the thoracic vertebrae in patients hospitalized for any cause in a Hospital in Bogotá (Colombia).
Methods: Cross-sectional study in a sub population of Latin American patients, older than 50 years with chest tomography indicated during hospitalization in 2020 for reasons other than suspicion of vertebral bone disease. Patients with secondary causes of vertebral fracture, trauma and spinal instrumentation were excluded. Reading by two independent expert researchers with Genant's semi-quantitative visual method and the ABQ method. Clinical and sociodemographic variables were captured (RedCap).Descriptive statistical analysis (STATA 17). The project was approved by the ethics committee.
Results: A total of 317 patients with a mean age of 69.4 years and a predominance of males (57.1%) were included. The most frequent personal history was active smoking (15.8%), use of glucocorticoids in the last 5 years (12.9%), and alcohol consumption (7.5%). A prevalence of vertebral fractures of 8.5% was found, being more frequent in women in 51.8% of the cases, with T11 as the most frequent location (See Table 1 and Figure 1). Only two vertebrae did not define a fracture according to the ABQ method compared to Genant. A disagreement was found in 77.7% of the cases with respect to the final report.
Conclusion: The prevalence of vertebral fractures reported here is lower than that reported in the literature when x-ray imaging is used; it is possible that the use of the tomography influences this result and possibly allows a more objective assessment. Careful evaluation of chest tomographic studies performed during the hospital stay may contribute to an opportune diagnosis of insufficiency fracture associated with osteoporosis.

Table 1. Fractured vertebrae characteristics, n= 42*

Fracture type		
Biconcave	27	64.3
Wedge	12	28.6
Crush	3	7.1
Fractured vertebra		
T3	1	3.7
T4	4	14.8
T5	2	7.4
T6	1	3.7
T7	5	18.5
T8	0	0
T9	2	7.4
T10	5	18.5
T11	14	51.8
T12	8	29.6

* In total, 44 fractured vertebrae were identified; only 42 are described in the table, since only 3 vertebrae were classified in the patient in whom 5 fractured vertebrae were detected.

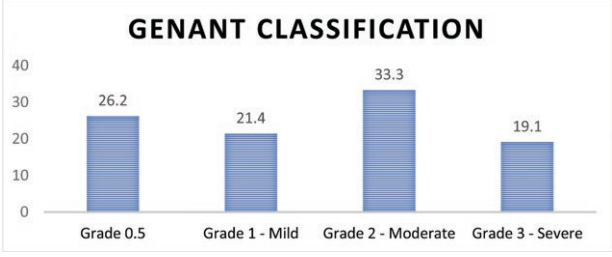


Figure 1. Fracture severity

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1225

ASSOCIATION BETWEEN BONE METABOLISM MARKERS AND INCREASES IN BONE MINERAL DENSITY IN PATIENTS WITH POSTMENOPAUSAL OSTEOPOROSIS TREATED WITH ROMOSOZUMAB

Keywords: Osteoporosis

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Background: Osteoporosis is a metabolic bone disorder characterized by a systemic impairment of bone mass and microarchitecture that results in fragility fractures [1]. Romosozumab (Rmab), a humanized monoclonal anti-sclerostin antibody, increases bone mineral density (BMD) and decreases fragility fractures in patients with postmenopausal osteoporosis (PMO) [2]. While an increase in type 1 amino-terminal propeptide (P1NP) and a decrease in tartrate-resistant acid phosphatase 5b (TRACP-5b) are observed early after administration of Rmab, the association between these changes in bone metabolic markers (BTMs) and increases in BMDs was still unknown.

Objectives: The aim of this research is to evaluate association between effect of Rmab on BMD and BTMs in patients with PMO.
Methods: Between March 2019 and August 2021, 34 patients with PMO, who were naïve to treatment of osteoporosis were included. The correlation between baseline characteristics, changes (%-) in BMDs in lumber (L-) and total hip (TH-) at 12 months (-M), and absolute values of P1NP and TRACP-5b and %P1NP and %TRACP-5b at 1, 3, 6M was calculated, respectively. Multiple regression analysis was performed on the factors that showed significant correlations to L- and TH-BMD, respectively.
Results: The mean age was 72.5 years old, mean BMI was 20.6 kg/m^2, mean vertebral fractures were 2.1, mean L- and Th-BMD were 0.762 g/cm^2 and 0.589 g/cm^2, and mean P1NP and TRACP-5b were 107.0 μg/L, and 640.3 mU/dL. %L- and %TH-BMD at 12M were 18.1% and 9.1%. %P1NP at 3M was positively correlated with %L-BMD at 12M, while %P1NP at 1 and 6M and TRACP-5b at each time point showed no significant correlation with %L-BMD at 12M. Multiple regression analysis confirmed that a great increase in P1NP at 3M was associated with a great increase in L-BMD at 12M. No correlation between either P1NP or TRACP-5b at each time point and %TH-BMD at 12M was observed.
Conclusion: We showed that a great increase in P1NP at 3M was a predictive factor of a great increase in L-BMD at 12M in patients with PMO treated with Rmab. On the other hand, there was no association between an increase in TH-BMD and BTMs including P1NP and TRACP-5b.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1226 CLINICAL SIGNIFICANCE OF A PATIENT COMPLIANCE IN PREVENTION OF SECONDARY FRACTURES

Keywords: Osteoporosis

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Objectives: to evaluate the effect of compliance in patients with osteoporosis on the incidence of new fragility fractures.
Methods: The study was performed in two stages. At the 1st stage, a retrospective analysis of outpatient records for the period from December 2019 to December 2021 was completed in the Volgograd Center of Osteoporosis. During Phase II of the study, in December 2022, researchers conducted a telephone survey to identify new fractures.
Results: The analysis included outpatient records of 2236 patients aged 40 to 92 years with DEXA scan. (1897 women and 339 men). 715 patients out of 2236 (control group or 31.98% of all included in the study) were found to have an abnormal DEXA, but lost follow up, among 715 patients from the control group, 509 (71%) patients were diagnosed with osteoporosis, 115 patients had a history of fragility fractures [1,2]. But these patients refused to attend the school for patients with osteoporosis and offered treatment. 158 patients in this group (26.51%) reported new low-traumatic fractures on a telephone survey. The remaining 1521 patients out of 2236 (68.02% of all included in the study) were followed up and treated in our Osteoporosis Center. Of these, 1262 patients (82.97%) were diagnosed with osteoporosis and treated with anti-resorptive therapy [2]. 784 out of 1262 patients (62.12%) were compliant with physician's recommendation, these patients constituted the II group of the study (highly compliant patients). Among these patients, only 11 new low-traumatic fractures (1.4%) were registered. Group III of the study (low compliance patients) consisted of 478 patients (37.88%) with a low physician's compliance.[3]. In this group, 42 new fragility fractures (8.79%) were identified.
Conclusion: 26.51% fragility fractures were registered in patients who refused monitoring and treatment. In the group of low compliance patients, 8.79% of new fractures were detected. While in the group of highly compliant patients, only 1.4% of new fractures were registered.
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Acknowledgements: Disclosure of Interests: **None Declared.**
DOI: 10.1136/annrheumdis-2023-eular.5857

AB1227 MINDFULNESS OF THE RISK OF FRACTURE IN OSTEOPOROSIS AND THERAPEUTIC ADHERENCE

Keywords: Patient reported outcomes, Osteoporosis, Outcome measures

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Background: Therapeutic adherence especially in chronic pathologies such as osteoporosis is of enormous importance, the foundation of which is based on close doctor-nurse-patient interaction, functional in informing the patient about the reasons for the proposed treatment and the possible side effects of a therapy that lasts for long periods of time.
Objectives: aim of this longitudinal study was to evaluate whether awareness of one's own fracture risk calculated using the DeFRA algorithm could improve adherence and persistence in anti-fracture treatment in an Italian population affected by osteoporosis and possibly reduce the fracture risk itself.
Methods: during 2018-2019, 309 menopausal women with osteoporosis (mean age 75 years ± 4.8) were enrolled in the present longitudinal study. The fracture risk was calculated with Defra algorithm and all were prescribed oral anti-readsorptive therapy for the first time (alendronate 70mg 1 tablet/week or risedronate 35mg 1 tablet/week). Two groups were therefore created: group A (134 subjects) represented by patients managed according to the Standard Clinical Practice and who were NOT given further information about their fracture risk and who were NOT given the risk card; group B (175 subjects) represented by patients who were provided with all the information regarding the risk of fracture according to the variables collected in the Defra algorithm and who were physically given the fracture risk card (Figure 1). After 18 months the patients had a new DXA densitometric data examined, the DeFRA fracture risk was recalculated and a therapy adherence questionnaire, the OS-MMAS (Osteoporosis-Specific Morisky Medication Adherence Scale). Patients with an OS-MMAS score <6 were categorized as "low adherence", otherwise as "high adherence"
Results: Mean age was not significantly different in the two groups: Group A 75yy±4.7, Group B 74.7yy±4.7 ($p>0.05$). The mean DeFRA value at baseline was 26.7 and 26.8 in Group A and Group B, respectively ($p>0.05$), while at the control it was 27.4 and 25.6 ($p<0.01$). The mean OS-MMAS score was significantly lower in group A than in group B (4.95±2.75 vs 8.25±2.85, $p<0.001$) (Figure 2 and Figure 3). 38.5% of the subjects fell into the "low adherence" category with an OS-MMAS score < 6, 61.5% fell into the "high adherence" category with a score ≥ 6. We found a significant correlation between the belonging group and the punctual values of Defra at 18 months and those of variation of Defra between baseline and 18 months (correlation between belonging to group B and Defra at 18 months -2.74, with the delta values of Defra at 18 months -2.72 respectively, $p<0.01$). The OS-MMAS score was shown to be correlated to belonging to group B (coeff Beta 0.5 $p<0.001$) in a linear regression model including the other variables collected age and Defra value at baseline. The same result was obtained by analyzing the data in terms of "low adherence" and "high adherence", where having an OS-MMAS score greater than or equal to 6 correlated to belonging to group B and not to age or DeFRA score baseline (ExpB 0.170 95% CI 0.103-0.281, $p<0.01$)) in a binary logistic regression model. In turn, the better OS-MMAS score correlated with the improvement over time of the DeFRA fracture risk recalculated at the follow-up visit on the basis of the control DXA data (Spearman's Rho -3.95 $p<0.001$)
Conclusion: The data collected in our study, although preliminary and with obvious limitations related to the smallness of the sample analysed, suggest that a greater awareness on the part of the patient of his or her risk of fracture (in the specific case providing detailed information about the result of the DeFRA algorithm provided during the baseline evaluation), may be associated with a greater long-term adherence to the suggested therapy and above all with a reduction in the risk of fracture over time, as evidenced by a reduction in the risk of DeFRA fracture at the 18-month follow-up.
References: none.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1228

RADIOFREQUENCY ECHOGRAPHIC MULTISPECTROMETRY COMPARED WITH DUAL X-RAY ABSORPTIOMETRY FOR OSTEOPOROSIS DIAGNOSIS ON LUMBAR SPINE AND FEMORAL NECK IN A COLOMBIAN POPULATION

Keywords: Osteoporosis, Diagnostic tests

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Background: An innovative non-ionizing ultrasound technique for osteoporosis diagnosis, which directly measures the BMD (Bone Mineral Density) of both the lumbar spine and the femoral neck, REMS, has shown significant correlations with BMD values and good levels of concordance with DXA-based diagnoses.
Objectives: Cross-sectional study to establish the concordance of BMD measurement between REMS and the gold standard (DXA) in Colombian adult patients receiving oral steroids.
Methods: Observational, analytical and descriptive, cross-sectional study in adults of both sexes who receive steroids and who attend a rheumatology center in Bogotá-Colombia. Inclusion criteria: Men and women over 18 years. Receiving steroids more than 2.5 mg of prednisone or its equivalent for 3 or more continuous months. Interpretable bone densitometry. Subjects who accepted their participation in the study and signed the informed consent. Exclusion criteria: History of prosthesis implantation in the abdomen and/or buttocks. Known physical deformities and/or previous lumbar spine surgery and/or bilateral hip replacement. Pregnant women. Subjects prevented from performing bone densitometry. The densitometric measurements were made with a compact high-performance equipment from General Electric, model iDXA, by the same technologist at the skeletal sites of interest. In a second moment, the same trained technologist performed the BMD measurement with REMS, using an EchoS machine (Echolight®), equipped with a 3.5 MHz convex transducer. This study was submitted and approved by the institutional ethics committee. The calculation of the sample size was carried out with the prevalence of osteoporosis induced by steroids, for n of 185 individuals. The concordance between the two technologies was evaluated with the weighted Cohen's Kappa index.
Results: 200 patients were included in the study, 162 were women. The median age of the entire cohort was 50.5 years (IQR: 22.2), with a minimum age of 20 and a maximum of 86 years. In women, the median age at menarche was 13 years (IQR: 2) and the median age for menopause was 47 years (IQR: 8), only 2.50% (n = 5) reported having fractures for fragility. 51% of the patients had rheumatoid arthritis, SLE 29% and other diagnoses 20%. Regarding the type of corticosteroid used, 92.5% received prednisolone. The last dose of corticosteroid used in median was 5 mg/day (IQR: 5). In the case of the accumulated dose in the last year, the median was 1825 mg/year (IQR: 1850). For the concordance analysis, 11 patients were excluded because the image of all the lumbar vertebral bodies could not be interpreted with both DXA and REMS techniques. Taking into account the diagnostic classification of each technology, a diagnostic concordance was obtained with the weighted Cohen's Kappa index of $\kappa\ \omega$= 0.72 95%CI: [0.63; 0.81] in the lumbar spine and $\kappa\ \omega$= 0.65 95% CI: [0.54; 0.74] in femoral neck.
Conclusion: In Colombian patients receiving steroids, the diagnostic concordance for BMD measurement between DXA and REMS is good; however, there are factors that affect the measurement, for which further training in REMS is required for the technologist to mitigate errors and improve the concordance between the techniques.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Edwin Jauregui Speakers bureau: Abbvie, Biopas, Amgen, Fresenius kabi, Consultant of: Abbvie, Amgen, Grant/research support from: Bristol myers Squibb, Katherine Gonzalez: None declared, Marcela Nuñez: None declared, Juan Londoño: None declared, Bibiana Corredor: None declared, Juan Huertas: None declared, Catalina Cabrera: None declared.
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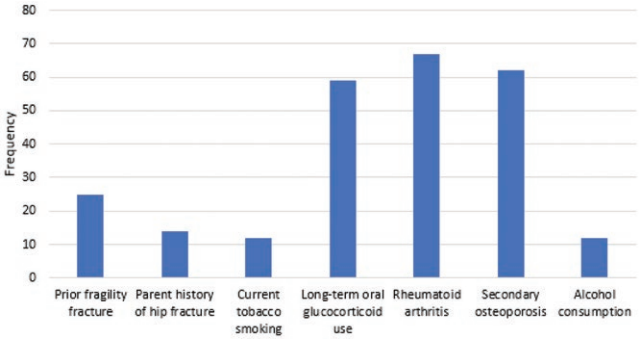
AB1229

COMPARISON OF FRACTURE RISK BY FRAX WITH AND WITHOUT BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATIC DISEASES

Keywords: Prognostic factors, Osteoporosis, Non-pharmacological interventions

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Background: FRAX is a well-validated instrument that calculates the probability of a major osteoporotic fracture over the following 10 years based on a set of risk factors such as age, body mass index (BMI), history of fragility fracture, steroid treatments used in patients with autoimmune rheumatic diseases (ARD) such as rheumatoid arthritis (RA), and secondary osteoporosis [1]. The FRAX score obtained without bone mineral density (BMD) is comparable to the fracture risk calculated using BMD values; it aims to identify patients who are likely to benefit from health interventions [2].
Objectives: To compare the fracture risk using FRAX with and without BMD in patients with ARD.
Methods: An observational, cross-sectional, prospective study was carried out at the Rheumatology Clinic in the University Hospital "Dr. José Eleuterio González" in Monterrey, Mexico from September to December 2022. We included > 40 years old ARD patients with a previous BMD test who were evaluated as part of a "Bone Health Program". The risk fracture scores were compared using FRAX with and without BMD. There were classified as low (<10% probability of a major fracture), intermediate (10% - 19% probability) and high risk (≥20% probability). Non-traditional risk factors such as visual problems, periodontal disease, 2 or more falls in the last year, lack of physical activity, the ARD diagnosis or the consumption of disease-modifying drugs (DMARDs), were collected using a semi-structured form. The Kolmogorov-Smirnov test was used to determine normality. Data were presented as percent frequency, mean ± standard deviation (SD), or median and interquartile range (IQR) as appropriate. We used the Mann–Whitney U or Chi-square to analyze the differences between groups. A $p<0.05$ was considered statistically significant. The statistical analysis was performed with SPSS v.25.
Results: A total of 146 patients were included: 142 (97.3%) were women and 4 (2.7%) were men with a mean age of 61.49 ± 9.22. The most frequent BMI was overweight (43.2%), followed by normal (31.5%), obesity grade 1 (13.7%), obesity grade 2 (10.3%) and obesity grade 3 (1.4%). The occupations were housewife (78.8%), employed (17.1%) and owned business (4.1%). The most prevalent main diagnosis was RA (45.9%) followed by osteoporosis (24.7%), osteoarthritis (14.4%), systemic lupus erythematosus (3.4%), Sjogren's syndrome (2.7%) and others (8.9%). The risk factors used by FRAX can be found in **Figure 1.** According to the non-traditional risk factors, 24.7% suffered 2 or more falls in the last year, 26% had periodontal disease, 71.9% were sedentary and 53.8% had visual problems. The median T-score spine was -1.7 [IQR (-2.5) - (-0.8)] and the mean T-score hip was -1.06 ± 1.21. The risk fracture scores using FRAX with and without BMD are in **Table 1**.
Conclusion: Higher hip fracture and major fracture risks were identified in the FRAX without BMD group. We found significant differences between the hip fracture risk of FRAX with and without BMD. Nevertheless, no differences were found in the major fracture risk of FRAX with and without BMD; this is of critical importance if all patients cannot have their BMD measured. The FRAX use makes it possible to offer a larger population a timely diagnosis.



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Table 1. Fracture risk by FRAX with and without BMD and risk classification.

	FRAX with BMD	FRAX without BMD	p value
Mayor fracture risk, median, (IQR)	9.30 (6.07 - 15.0)	9.85 (6.60 - 17.0)	0.313
Hip fracture risk, median, (IQR)	1.10 (0.40 - 3.10)	1.95 (0.80 - 4.73)	0.002
Risks of major osteoporotic fracture assessed by FRAX, n (%)			
Low	81 (27.7%)	73 (25%)	0.598
Intermediate	43 (29.5%)	46 (15.8%)	
High	22 (7.5%)	27 (9.2%)	

IQR: Interquartile range

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Disclosure of Interests: None Declared.
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AB1230 CHARACTERISTICS OF FRACTURES TREATED IN THE FIRST YEAR OF OPERATION OF THE FLS OF TUDELA. NAVARRA.

Keywords: Osteoporosis, Descriptive studies, Outcome measures

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Background: Osteoporosis is a common disease with a huge impact on public health due to the great morbidity and mortality and the impact on the quality of life of fractures.The main objective of its approach is to avoid the appearance of osteoporotic fractures, so it is important to devote efforts to diagnose and treat individuals who are most at risk of suffering this type of fractures. In our environment the approach to osteoporotic fracture was deficient, so a specific secondary prevention consultation was launched.
Objectives: To analyze the general characteristics of patients referred to the FLS consultation during their first year of operation at the Reina Sofia Hospital in Tudela. Navarra.
Methods: Retrospective descriptive study including patients referred to the secondary fracture prevention rheumatology (FLS) consultation, from November 2021 to November 2022. Epidemiological characteristics, risk factors, type of fracture, therapeutic acts and adherence to treatment at month, 6 months and 12 months are analyzed.
Results: During the indicated period, 200 patients were referred to FLS consultation from Traumatology, Internal Medicine and Rehabilitation, of which 67% (134) were evaluated during admission for hip fracture, of whom 11 died during admission. 33% of patients were treated on an outpatient basis -with a maximum delay of 6 weeks-, for low-impact fractures of radius (23), proximal humerus (15) and vertebral (28). The mean age of patients with hip fracture was 84.95 years, and that of the rest of osteoporotic fractures treated was 72.95 years, with a ratio of men/ women of 43/157, close to 1/5. The Barthel was also calculated with an average of 90.36. Regarding risk factors: the mean BMI of the patients was 25.56 kg/m2, 23 patients (11.5%) were active smokers, 8 of the women attended (4%) had early menopause, 2 women (1%) were on treatment with aromatase inhibitors, 48 patients (24%) had had a previous fracture and 57.5% of patients had hypovitaminosis D. Only 20 patients (10%) had taken or were being treated for osteoporosis prior to fracture. BMD was requested from 47% of patients. Regarding the treatment prescribed after evaluation in the FLS, 16% was not considered subsidiary to specific pharmacological treatment, but was always given non-pharmacological advice, as well as calcium and vitamin D supplements. Those who were prescribed specific therapy 64% were prescribed antiresorptive and 36% an osteoformer. Regarding adherence to treatment, only 4 patients did not take it within one month of their prescription. The rest followed a correct completion each review call per month, 6 months and one year, although at the time of writing the study there are pending review appointments of 6 and 12 months in patients recruited from the second semester of 2022.
Conclusion: The establishment of standardized units for secondary prevention of fracture is a necessity for the health of the population. In our sample, only 10% of patients treated for osteoporotic fracture had specific therapy before their fracture, but, after assessment in the FLS, the initiation of therapy after osteoporotic fracture was ensured in all subsidiary patients, as well as adequate adherence to treatment.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1776

AB1231 PROFILE OF OSTEOPOROSIS IN YOUNG WOMEN: EXPERIENCE FROM A POPULATION IN SOUTHERN MOROCCO

Keywords: Osteoporosis, Descriptive studies, Bone diseases

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Background: Osteoporosis is a generalized skeletal disease characterized by low bone density and alterations in bone microarchitecture. Current definitions and recommendations focus more on postmenopausal osteoporosis with a low number of studies in young pré-menopausal women, which makes it difficult to estimate the prevalence of osteoporosis in this population.
Objectives: To establish the prevalence and determine the etiologies of osteoporosis in young women and their management according to the experience of our department.
Methods: Retrospective descriptive and analytical study including 97 female patients aged less than 45 years, who performed a bone densitometry measurement between the years 2014 and 2022. Data were collected from the bone densitometry database. Osteoporosis was retained if a T score less than or equal to -2.5. Women older than 45 years and or followed for genetic osteopathy were excluded from this study.
Results: There were 97 patients with osteoporosis in this study. The average age was 25 years. Early menopause was found in 15% of cases (10% of cases after chemotherapy). Osteoporosis secondary to endocrinopathy was found in 17% of cases (5% diabetes, 10% primary hyperparathyroidism, 2% Cushing's syndrome). It was secondary to a systemic disease or chronic inflammatory rheumatism in 45% of cases (29% rheumatoid arthritis, 12% spondyloarthropathy, 3% systemic lupus erythematosus and 1 % Horton's disease). The other pathologies found were chronic renal failure in 3% of cases, a notion of prolonged use of corticosteroids in 21% and hormone therapy for breast neoplasia in 14%. 3% of the patients had at least one osteoporotic vertebral fracture. The mean bone mineral density (BMD) in both femurs was 0.727g/cm2. The mean BMD in the spine was 0.965g/cm2. 11% of these patients were treated with oral anti-osteoporotic drugs, 35% were supplemented with vitamin D and calcium.
Conclusion: The discovery of osteoporosis is rare in young women, hence the scarcity of studies in this category of women. It may be of metabolic or drug-induced origin or related to other chronic inflammatory diseases. It should be investigated in the presence of risk factors in order to limit the risk of bone fractures.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5765

AB1232 HIGHER PAIN SCORE MEASURED WITH VISUAL ANALOG SCALE HAS SIGNIFICANT HIGHER RISK OF INCIDENT BONE FRAGILITY FRACTURE

Keywords: Pain, Rheumatoid arthritis, Osteoporosis

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Background: Bone fragility fracture (BFF) is one of serious troublesome incident in treating patient with rheumatoid arthritis (RA). Previously, sustaining clinical remission with simplified disease activity index (SDAI) was clarified that prevents occurrence of incident BFF [1].
Objectives: We hypothesized that pain degree would correlates with occurrence of incident BFF, because that caused gait disability and bone fragility. The aim of this study is to clarify this issue.
Methods: A retrospective cohort study data was used in the study. Postmenopausal female patients who matched the EULAR/ACR classification criteria under the T2T since August 2010, have been treating RA and were measured bone mineral density (BMD) with dual-energy X-ray absorptiometry, were recruited. The initial target of therapy is the attainment of remission with SDAI within 6 months of initiation. The primary outcome was incident BFF. Follow-up started at BMD measurement (baseline) and continued until the development of the first fracture or censoring at death, loss to follow-up or end of the study. Binary logistic regression analyses (BLR) were determined for incident BFF incidence up to the last observation. Risks for the incidence of BFF was classified as RA specific and general candidate. In general candidate, comorbidities that might affect the incidence of BFF, such as lifestyle-related diseases, increased ability to fall, and pain score using visual analog scale (PS-VAS) were included. anti-citrullinated polypeptide antibodies and rheumatoid factor titers, SDAI score, Health Assessment Questionnaire Disability Index, and Sharp/van der Heijde score were included in RA specific candidate risks. Each evidence was evaluated using Cox regression analysis to identify significantly higher risk factors within 5% in univariate models and to evaluate using multivariate model. In the variants with significant higher risk ratio in the Cox regression analysis, Receiver

operation characteristics (ROC) was examined to determine cut-off index (COI). Finally, statistically evident variants in the ROC study was examined to clarify a validity of the variant as a risk factor using Kaplan-Meier survival curve analysis again.

Results: A total of 239 patients were recruited. Mean age was 73.6 years and mean follow up period was 52.4 months. Mean T-score in the lumbar spine and femoral neck were -2.10 and -1.85. Using BLR, PS-VAS, estimated glomerular filtration ratio based on cystatin C (eGFR_CysC), prevalent BFF (pr-BFF), and SDAI remission rate were significant correlation with incident BFF. In these, PS-VAS and pr-BFF demonstrated significant higher risk ratios using a multivariate cox regression analysis. In the ROC, COI of PS-VAS was 24.6 and the area-under-the-curve was 0.669 ($p<0.001$). Finally, PS-VAS ≥ 24.6 mm had 3.506 fold higher hazard ratio than PS-VAS < 24.6 mm using Kaplan-Meier survival curve analysis.

Conclusion: These results suggested pain control in treating RA is the important task in order to avoid incident BFF in postmenopausal female patients with RA.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1233 IMPACT OF RHEUMATOID ARTHRITIS ON THE DENSITOMETRIC STATUS OF WOMEN

Keywords: Rheumatoid arthritis, Osteoporosis

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Background: Rheumatoid arthritis (RA) is the most common chronic inflammatory rheumatic disease. It can be associated with several comorbidities including osteoporosis (OP). The origin of this bone loss is multifactorial. A fracture episode is the complication of osteoporotic disease and constitutes all the gravity of this disease.

Objectives: The objective of this work was to evaluate bone densitometry (BMD) in women with RA and to identify its relationship with disease parameters.

Methods: This was a cross-sectional study, including patients followed for RA meeting the ACR/EULAR 2010 criteria. For each patient, disease parameters (duration of progression, activity score (DAS28 VS), functional impact (HAQ), corticosteroid intake) were assessed and BMD of the lumbar spine and femoral neck was performed in all patients.

Results: A total of 76 women were included, 66% of whom were postmenopausal. The mean age of the patients was 52.5±9.7 years and the mean duration of RA progression was 11.3±7.9 years. The mean DAS28 VS score was 4.3±1.4 and the mean HAQ was 0.98±0.8. Corticosteroid use was noted in 62 patients (81.5%) at a mean dose of 8.6±3.2mg/day. Regarding the densitometric profile of the patients, the mean BMD values at the vertebral and femoral sites were -1.4±1.3DS and 0.8±1.1DS respectively, and the prevalence of osteoporosis and osteopenia were 21.6% and 46.6% respectively. Patients with osteoporosis (OP) were older (p=0.00), and there was a significant relationship between OP and menopausal status (p=0.007). In contrast, disease parameters (function, activity, duration and treatment) were not associated with the occurrence of osteoporosis in our series: HAQ (p=0.6), disease duration (p=0.3), disease activity (p=0.3) or corticosteroid use (p=0.9).

Conclusion: OP is a frequent comorbidity associated with RA. It should be systematically detected because of its functional and vital complications. In our study, the occurrence of OP was more frequent at an older age during RA and menopausal status. There was no relation with the disease parameters.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1234 THE BODY COMPOSITION IMPACT ON OSTEODENSITOMETRY VALUES IN PERSONS OLDER THAN 65 YEARS

Keywords: Diet and nutrition, Osteoporosis, Diagnostic tests

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Background: The aging process is a normal physiological phenomenon and has an impact on the body composition and physical fitness of the elderly. It is characterized by a progressive increase in total body fat mass, a decrease in muscle mass and changes in distribution in terms of an increase in abdominal fat tissue. These changes in the elderly have a great impact on health, functional capacity, and quality of life. The variability of body composition components contributes to the origin and progression of pathology and disability. Today osteodensitometric examination is considered one of the most versatile imaging techniques for assessing osteoporosis, sarcopenia, and obesity, and is currently the only technique capable of identifying all of these conditions at the same time. Osteoporosis is characterized by low bone mass and microarchitectural bone loss, leading to an increased risk of fracture caused by a minor trauma.

Objectives: To determine the presence of normal values of T score, osteopenia and osteoporosis, to determine the distribution of BMI and values of lean muscle mass, adipose tissue and visceral adipose tissue of the examined population.

Methods: In this retrospective study conducted from March to April 2019 at the University Clinical Center of Vojvodina, 699 respondents of both sexes over 65 participated. Exclusion criteria were established osteoporosis and treatment. The research consisted of collecting general information of the respondents (gender, age, smoking status, level of education, marital status). Body composition (BMD, FM, VAT, LM) was measured by osteodensitometric examination. Also, all subjects body weight, and height were measured and their body mass index (BMI) was determined.

Results: The average age of respondents was 71.92 ± 5.14, most respondents 50.6% have secondary education, 52.2% are married, 9.5% are smokers. The classification of the total T score shows a normal finding in 26.8%, with osteopenia 58.4% and with osteoporosis 14.8% of subjects. According to (BMI) with a normal finding is 16.5%, overweight is 38.5% and obese 45% of respondents. The average BMI of men is 28.79 ± 4.01, and for women the average BMI is 29.92 ± 4.91. The average value of VAT is 1,537 ± 0,820, FM 31,105 ± 9,152 and LM 43,735 ± 8,279. Men have higher average VAT values (2.06 ± 0.90) compared to women (1.32 ± 0.67). The average FM is higher in women (32.49 ± 8.88) than in men (27.60 ± 8.89). The average LM is higher in men (53.38 ± 7.05) than in women (39.92 ± 4.97). Subjects with normal findings were 61.5% obese, with osteopenia 40.2%, and with osteoporosis 28% obese. The measured value of LM in persons with normal findings is 47,921 ± 8,738, with osteopenia 42,342 ± 7,378, with osteoporosis 40,443 ± 6,949. The measured value of FM in persons with normal findings is 34.37 ± 9.51, with osteopenia 30.20 ± 8.75, and with osteoporosis 27.60 ± 7.14. The measured value of VAT in persons with normal findings is 34.37 ± 9.51, with osteopenia 34.37 ± 9.51, with osteoporosis 27.60 ± 7.14.

Conclusion: Higher values of BMI, LM, FM, and VAT have a positive effect on the hip and spine T score, and a protective role against osteoporosis.

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AB1235 PREVALENCE OF OSTEOPOROSIS IN AN ALGERIAN POPULATION WITH OSTEOARTHRITIS: CROSS-SECTIONAL STUDY

Keywords: Osteoporosis, Osteoarthritis, Descriptive studies

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Background: Osteoarthritis is a chronic degenerative rheumatism responsible for a structural modification of bone tissue which can alter its biomechanical qualities. Data are contradictory regarding the relationship between osteoarthritis (OA) and osteoporosis (OP) with some studies showing the increased risk of OP in OA especially in patients awaiting arthroplasty. Failure to consider bone loss in this osteoarthritis population can lead to serious complications such as fracture, which can considerably reduce the quality of life and expose this elderly population to excess mortality.
Objectives: This study aims to identify patients at risk of fracture in osteoarthritis Algerian population and evaluate postoperative bone loss complication in patients undergoing arthroplasty.
Methods: Descriptive, cross-sectional study in patients with knee osteoarthritis candidates for arthroplasty. All patients underwent a rheumatology exploration including clinical, radiological and biological evaluation with a measurement of bone mineral density (BMD) at spine and hip. The results are interpreted according to the WHO classification.
Results: Three hundred patients were recruited with a sex ratio=0.45, the mean age was 67.97 ± 6.78 years and the mean BMI was 30.81 ± 5.37 kg/m2. With regard to bone loss, osteoporosis was present in 26.7% (95% CI: 21.7%-32.1%), while ostepenia was found in 43.7% (CI 38.0%-49.5%).Factors associated with bone loss were: female sex ($P<10^{-6}$), urban habitat (P= 0,001) and age ≥ 60 years (P=0,003).
Conclusion: In this Algerian sample of severe osteoarthritis awaiting arthroplasty, osteoporosis and consequently the risk of fracture are prevalent. Identifying the population with bone loss in these patients could improve overall management and avoid postoperative fractures.

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AB1236

OSTEOPOROSIS AND FRACTURES IN PATIENTS UNDERGOING CHRONIC CORTICOSTEROID THERAPY

Keywords: Prognostic factors, Osteoporosis, Real-world evidence

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Background: Glucocorticoids are widely used for the treatment of various rheumatic diseases and are one of the major risk factors for bone fragility associated fractures. However, beyond randomized clinical trials, there is little evidence in actual clinical practice.
Objectives: Our aim is to evaluate the appearance of osteoporosis and fractures in patients undergoing corticosteroid therapy.
Methods: We performed an observational retrospective descriptive study with Vasculitis (several subtypes) or Polymyalgia Rheumatica (PMR) patients diagnosed, who had received corticosteroid regimens with doses of at least 5 mg/day of prednisone (or equivalent) for a period of not less than 3 months, and in which the appearance of fractures was monitored for the next 2 years.
Results: We included 234 patients (62.4% females) with a mean age at the onset of corticosteroids of 75.8 years and mean duration corticosteroid regimens of 58 months. The most represented disease was PMR, with 183 patients (78.2%), followed by Large Vessel Vasculitis (12.4%), ANCA positive Small Vessel Vasculitis (4.3%), ANCA negative Small Vessel Vasculitis (3.4%), with a lower proportion of Medium Vessel vasculitis and other diseases such as Relapsing Polychondritis. Furthermore, 29 patients (12.39%) had previous fragility fractures, while 32 patients (13.68%) suffered one or more fractures after the start of corticosteroid therapy, being hip its most frequent location (4.7%), followed by vertebrae (3.8%). Likewise, the mean duration of corticosteroid treatment until the onset of new fractures was 4.5 months. Even without reaching statistical significance, we observed a greater age (80.5 years), a higher presence of the female gender (81.25%) and a previous fracture (18.75%) in patients with new fractures. In addition, 32.91% of patients had densitometric osteoporosis at the beginning of corticosteroid therapy.

Table 1. Comparison between different therapeutic options

Treatment	Patients n (%)	New Fractures n (%)	Fracture-free time: average in years
Alendronate	31 (13.25)	5 (16.13)	5.39
Ibandronate	6 (2.57)	3 (50)	6.51
Risedronate	54 (23.07)	6 (11.11)	5
Zoledronate	8 (3.42)	5 (62.5)	5.03
Bazedoxifene	1 (0.43)	0 (0)	1.19
Denosumab	38 (16.24)	6 (15.79)	4.41
Teriparatide	10 (4.27)	4 (40)	5.2
No treatment	86 (36.75)	3 (3.49)	3.88

We observed an association between fractures and zoledronate treatment (P=0.012), and a tendency for ibandronate (P=0.07). The discreet entity of these differences could be explained by the statistical effect produced by the small number of new fractures, taking into account, moreover, the fact that in our Rheumatology Department we systematically carry out a fracture risk assessment to decide whether and when to start the treatment, and also prescribing more powerful therapeutic options to patients at higher risk of fracture. Finally, we did not observe significant differences in fracture-free time among the most frequent therapeutic options.
Conclusion: We observed a tendency to have a higher frequency of fractures in patients with previous fractures, older age and female gender. Less quantitative prevention of fractures was observed in patients with zoledronate and ibandronate, with no clear differences in fracture-free time.
REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Crystal diseases, metabolic bone diseases other than osteoporosis

AB1237 ASSOCIATION OF GUT MICROBIOTA WITH RISK OF GOUT

Keywords: Gout

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Background: Gout is a prevalent and painful inflammatory arthritis. Increasingly studies have shown that the gut microbiota is associated with gout [1-3]. However, whether these associations reflect a causal relationship is still being determined.
Objectives: To investigate whether there is a causal relationship between intestinal bacteria and gout, we used Mendelian randomization (MR) two-sample analysis.
Methods: Gout-related data were derived from the Integrated Epidemiology Unit (IEU) GWAS database, which included 2115 gout cases and 67259 controls [4]. The data on intestinal bacteria came from the website MRbase. We searched 173 species of bacteria and finally identified 5 genus species, which were the *Eubacterium brachy, Eubacterium hallii, Howardella, Sellimonas,* and *order Mollicutes RF9*. MR-Egger, weighted median, inverse variance weighting (IVW), and MR-PRESSO were used to conduct the double-sample MR analysis. Finally, we excluded the data related to poly-effect and heterogeneity to ensure the robustness of the results.
Results: Five kinds of gut microbiota (*Eubacterium brachy, Eubacterium hallii, Howardella, Sellimonas, and order Mollicutes RF9*) had a causal relationship with gout. According to inverse variance weighted estimation, *Eubacterium hallii*(odds ratio(OR) = 1.660, 95% confidence interval(CI): 1.073-2.569, P = 0.023), *Howardella*(OR = 1.391, 95% CI: 1.058-1.828, P = 0.018) and *Sellimonas*(OR = 1.384, 95% CI: 1.009-1.897, P = 0.044) were risk factors for gout. *Eubacterium brachy*(OR = 0.656, 95% CI: 0.469-0.917, P = 0.014) and *order Mollicutes RF9*(OR = 0.641, 95% CI: 0.471-0.874, P = 0.005) showed protective effect against gout (Figure 1).
Conclusion: This study suggested a causal relationship between these five gut microbiota and gout, providing new implications for future clinical trials on the association between microbiota and gout.

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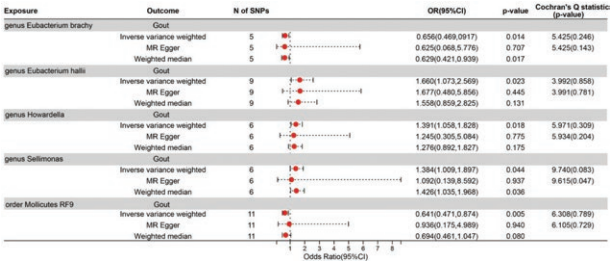


Figure 1. Forest plot of the results of mendelian randomization analysis between gut microbiota and gout

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Disclosure of Interests: None Declared.
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AB1238 LONG-TERM EFFECTIVENESS AND PREDICTORS OF NERIDRONATE TREATMENT OF TYPE I COMPLEX REGIONAL PAIN SYNDROME (CRPS)

Keywords: Rare/orphan diseases, Bone diseases, Pain

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Background: Complex Regional Pain Syndrome (CRPS) is a painful disease that can lead to chronic pain and disability. Bisphosphonates are largely used in the real-life for the treatment of CRPS, but data on long-term effectiveness and its predictors are lacking.
Objectives: The aim of the present study is to describe the real-life effectiveness of IV neridronate on both pain and long-term disability in patients with type I CRPS. Secondary objective is to determine the factors associated with long-term disability and response to treatment.
Methods: We conducted a longitudinal observational study on patients with type I CRPS treated with IV neridronate (400 mg over 4 days). Clinical and demographic characteristics were collected at baseline, after 3 months (M3) and after 12 months (M12) from treatment. Mixed-effect analysis was used to determine the effect of treatment on VAS pain. Multivariable logistic regression was employed to determine the factors associated with long-term response to treatment. We determined "responders" and "early responders" to be those who achieved a ≥50% VAS score reduction between (baseline/pretreatment) and M12 (responders) and M3 (early responders). We defined "excellent responders" based on full recovery from loss of motion at M12 AND VAS pain at M12 less than 20 mm (excellent responders were those patients with mild/moderate/severe loss of motion at baseline who had none loss of motion at M12 AND VAS pain less than 20 mm).
Results: 103 patients with type I CRPS treated with IV neridronate were included in the study. Mean VAS pain decreased significantly at M3 (79.1 mm to 33.1 mm, -45.9 mm, 95% CI 40.1 to 51.8) and M12 (79.1 mm to 17.5 mm, -61.6 mm, 95% CI 55.3 to 67.9) **Figure 1A**. Hyperalgesia and allodynia resolved in 84.3% and 88.1% of patients at M12. Loss of motion resolved in 53.5% of patients. The predictors of "excellent response" at M12 were: gender (male better than female), predisposing event to CRPS (no event being better than any predisposing event), site of CRPS (lower limb being better than upper limb), and early response at M3 on VAS pain (2.5 times the chance of being excellent responder every 10 mm decrease). Predictors of excellent response are presented in **Table 1** (binary logistic regression analysis). **Figure 1B** shows the long-term VAS pain reduction with IV neridronate in patients with or without complete recovery from functional disability ("excellent responders").

Variable	aOR	95% CI	p value
Site of CRPS			
Lower limb vs upper limb	**12.76**	**1.65 to 199.1**	**0.0320**
Predisposing event	**71.31**	**6.511 to 176.1**	**0.0025**
None vs fracture	1.77	0.01 to 276.5	0.8329
Orthopedic surgery vs fracture	19.03	0.72 to 180.9	0.1664
Trauma w/o fracture vs fracture			
Age	0.99	0.94 to 1.05	0.9509
Sex	**14.00**	**2.75 to 104.6**	**0.0037**
Male vs Female			
BMI	0.92	0.75 to 1.11	0.4329
VAS pain at baseline	**0.91**	**0.85 to 0.96**	**0.0040**
VAS pain absolute reduction at M3	**2.51**	**1.68 to 4.18**	**<0.0001**

Conclusion: In this real-life study neridronate was associated with rapid and progressive improvement of symptoms of CRPS which was maintained up to 3 years of follow-up. The predictors of excellent response were early response, lower limb localization, absence of predisposing events and male gender.

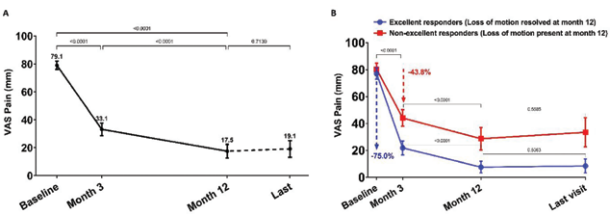


Figure 1.

REFERENCES: NIL.
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Disclosure of Interests: Giovanni Adami Speakers bureau: Theramex, Eli-Lilly, BMS, Amgen, UCB, Fresenius Kabi, Galapagos, Davide Gatti: None declared, Angelo Fassio: None declared, Vania Teresa Braga: None declared, Camilla Benini: None declared, Ombretta Viapiana: None declared, Davide Bertelle: None declared, Maurizio Rossini: None declared.
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AB1239 THE INVERTED J-SHAPED RELATIONSHIP BETWEEN SERUM URIC ACID LEVEL AND ABDOMINAL MUSCLE MASS AMONG KOREAN MALE POPULATION: A SINGLE-CENTER STUDY OF 5114 CASES

Keywords: Gout, Sarcopenia

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Background: Sarcopenia is the decline of muscle mass and strength with age. Evidence suggests that oxidative stress and molecular inflammation play important roles in muscle atrophy by interfering with the balance between protein synthesis and breakdown. Uric acid (UA) may be related to sarcopenia through its role as either an antioxidant or pro-oxidant properties. Although the association of serum UA level with sarcopenia has been investigated in previous studies, the results are conflicting.
Objectives: The purpose of this study was to investigate the association of serum UA with abdominal muscle mass using abdominopelvic computed tomography (apCT) among Korean adult men.
Methods: We evaluated 5114 men aged above 20 years, who voluntarily underwent laboratory tests and apCT as a part of general health examination from May 2014 to June 2019. The participants were stratified into quartiles according to their serum UA levels. The low-attenuation abdominal muscle area (LAMA), normal-attenuation abdominal muscle area (NAMA) and total abdominal muscle area (TAMA) were measured using cross-sectional apCT data of the L3 lumbar vertebrae. Between-group comparisons were performed using Pearson's chi-square test for categorical variables, and the ANOVA for numerical variables, as appropriate. The trends between serum UA quartiles and each AMA were analyzed by univariate (ANOVA) and multivariate analysis (ANCOVA).
Results: The mean age of individuals was 52.5 ± 9.37 years and the mean body mass index (BMI) was 24.6 ± 2.92 kg/m^2. In univariate analysis LAMA, NAMA and TAMA were increased continuously across quartiles of serum UA. However, serum UA levels (quartiles) showed an inverted J-shaped curve with NAMA and TAMA, after adjustment for confounding factors including age, BMI, smoking status, hypertension, diabetes, dyslipidemia, glomerular filtration rate, and c-reactive protein (Table 1).
Conclusion: The results suggest that a specific range of serum UA levels may be associated with better abdominal muscle mass in Korean adult men.

Table 1. Adjusted mean value of abdominal muscle mass by serum uric acid quartiles

variables	Uric acid				
	quartile 1 < 5.00 mg/dl (n = 1228)	quartile 2 5.01 ~ 5.80 mg/dl (n = 1328)	quartile 3 5.81 ~ 6.70 mg/dl (n = 1251)	quartile 4 > 6.70 mg/dl (n = 1247)	p-value
LAMA, cm^2	26.7 [a] (26.29-27.20)	26.7 [b] (26.29-27.20)	27.1 (26.65-27.56)	27.9 [a,b] (27.44-28.37)	0.003
NAMA, cm^2	133.2 [a] (132.18-134.27)	133.9 [b] (132.93-134.93)	132.9 [c] (131.89-133.95)	130.9 [a,b,c] (129.80-131.92)	< 0.001
TAMA, cm^2	158.4 (157.41-159.30)	159.2 [a] (158.28-160.09)	158.4 (157.49-159.36)	157.0 [a] (156.03-157.96)	0.015

Values are expressed as means (95% confidence interval). Multivariate analysis was performed with adjustment for age, body mass index, smoking status, hypertension, diabetes, dyslipidemia, glomerular filtration rate, and c-reactive protein. a,b,c: same letters indicate statistically significant based on Bonferroni multiple comparsion Abbreviations: LAMA low-attenuation abdominal muscle area, NAMA normal-attenuation abdominal muscle area, TAMA total abdominal muscle area

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1240 PERCEPTIONS OF GOUT AND ITS MANAGEMENT PATTERNS: FINDINGS FROM SURVEY AND STRUCTURED INTERVIEWS WITH PRIMARY CARE PHYSICIANS AND RHEUMATOLOGISTS

Keywords: Quality of care, Gout

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Background: Despite the high prevalence of gout worldwide,[1] there is widespread undertreatment of this painful, debilitating inflammatory arthritis.[2,3] Gout patients who maintain serum urate (SU) <6 mg/dL have fewer flares, less joint involvement, and overall better quality of life.[3] However, gout management guidelines differ substantially between the American College of Physicians (ACP)[4] and the American College of Rheumatology (ACR),[5] most notably with ACP recommending oral urate-lowering therapy (ULT; allopurinol, febuxostat, probenicid) use only in patients with frequent gout attacks with no clear SU-target and ACR recommending oral urate-lowering therapy use in all gout patients with tophi, flares, or gout-related bone damage with a treat-to-target approach to an SU <6 mg/dL. Because primary care physicians (PCPs) are often a first point-of-contact for patients suffering from gout, understanding their perceptions and management strategies of gout is of importance.
Objectives: To better understand how PCPs perceive and manage gout.
Methods: An online survey was administered to PCPs regarding perceptions of gout patients, gout severity grading, gout treatment strategies, and gout patient referral patterns. A 5-point Likert scale was used to gauge perceptions and patterns. Additionally, structured 30-60 minute interviews of similar focus were conducted with PCPs and rheumatologists (all interviews conducted by a single interviewer [RL]). These interviews provided further insight into PCP perceptions of gout and allowed similarities and differences between physician types to be examined. A 10-point Likert scale was used to quantify select interview responses.
Results: A total of 56 PCPs completed the online survey, with most practicing in a metropolitan area (84%) and seeing >50 patients/week (66%). 98% of participating PCPs reported seeing <10 known gout cases/week, with 82% having high or very high confidence in their ability to manage gout. Anti-inflammatory treatments (89%), oral ULTs (88%), diet (70%), and biologic therapies (59%) were viewed by most as being highly effective or very highly effective. Further, 63% of PCPs viewed gout patients as always or almost always compliant with medication and 66% of PCPs reported that gout patients never or almost never ask for referral to a gout specialist. However, when PCPs did make a referral, it was most often for severe gout. The low referral rate coincided with the observation that the majority of PCPs (79%) reported most-commonly seeing gout of "medium" severity. Further insight was gained from 5 PCP and 5 rheumatologist interviews conducted. PCPs and rheumatologists viewed gout patient compliance differently, with PCPs perceiving a higher rate of compliance (7.3 vs. 5.7). Both PCPs and specialists expressed that gout flare data collection and gout severity determinant tools would be useful for patient management, including therapy efficacy evaluation.
Conclusion: These findings suggest that, despite widespread undertreatment of gout outside of specialty care,[2] PCPs reported high comfort in managing gout, high compliance of gout patients, and little need for specialty referral except when gout is severe and refractory. Both PCPs and rheumatologists expressed that tools for determining gout severity and tracking gout flares would be helpful. We suggest that such tools could serve as guides for PCPs when monitoring for success of therapy and when to make a rheumatology referral.
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AB1241 FACTORS ASSOCIATED TO LOSS FOR FOLLOW-UP IN A PROSPECTIVE GOUT COHORT

Keywords: Gout, Crystal arthritis

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Background: Adherence to treatment has been widely studied, but not adherence to follow-up visits.
Objectives: To analyze factors associated to loss for follow-up in patients with gout and with a programmed follow-up visit to the rheumatology office.
Methods: Analysis of data from an inception cohort of patients with gout prospectively followed-up in a university hospital setting. Variables include general data, along with clinical characteristics of gout, comorbidities, treatment and adherence to prescribed urate-lowering therapy (ULT). Those variables associated (p<0.20) in bivariate analysis were included in a multivariate analysis. Patients who did not attend to a visit because they passed were not considered as lost for follow-up.
Results: From a series of 1,442 consecutive patients, 354 (24.5%) were lost for follow-up; 219 (15.2%) did not attended because they died between programmed visits. Mean follow-up until lost for follow-up was 32 months vs. 49 months for patients who still remained in active follow-up. Age (older), gender (women), pooled comorbidity (higher), severity of gout (monoarticular), alcohol intake (<15 g/day), adherence (MPR> 80%), previous treatment (none), and consultation (primary care), were associated to higher rates of loss for follow-up in bivariate analysis. No association was found between persistence on follow-up and time from onset of gout, presence of tophi, number of flares per year, previous and prescribed ULT.

	B	Sig.	Exp(B)	95% C.I.L. for EXP(B)	
				Lower	Upper
Age (year)	**-,029**	**,001**	**,972**	**,955**	**,989**
Primary care consultation	**-1,651**	**,008**	**,192**	**,057**	**,647**
Adherence (MPR > 0.8)	**-1,120**	**,000**	**,326**	**,186**	**,572**
Severity (polyarticular)	***-,358***	***,107***	***,699***	***,416***	***1,17***
Highest comorbidity (Kaiser 3-4)	,199	,519	1,220	,666	2,234
Previous ULT (none)	-,196	,477	1,217	,709	2,089
Gender (male)	,256	,566	1,292	,539	,988
Ethanol >15g/day	,005	,987	,995	,543	1,823

In multivariate analysis (Table 1), only higher age, higher adherence to prescribed, and consultation from primary care were independently associated to persistence on follow-up. Severity of gout (polyarticular disease) seemed to be also associated to persistence, but lacked statistical significance.
Conclusion: In our clinical setting, the profile of patients at higher risk of abandoning prescribed follow-up is that of a younger, poorly adherent, with lower burden of disease and consulting through a assistance "short-cut".
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AB1242 GOUT AND VENOUS THROMBOEMBOLISM IN THE US: A NATIONAL PERSPECTIVE

Keywords: Gout, Epidemiology, Cardiovascular disease

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Background: Venous thromboembolism (VTE) is a leading cause of preventable death in the USA [1]. Gout has been associated with higher risk of venous thromboembolism [2]. However, there is little nationwide data in the United States (US) on the clinical and economic consequences of of VTE in persons with gout.
Objectives: To study venous thromboembolism (VTE) hospitalizations in patients with gout in the United States (US) and estimate their clinical and economic impact.
Methods: The National Inpatient Sample (NIS) is a stratified random sample of all US community hospitals designed to produce national estimates of inpatient utilization, cost and outcomes. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. Unweighted it contains data from around 7 million hospitalizations a year, weighted it estimates around 35 million hospitalizations nationally. We examined all inpatient hospitalizations in the NIS in 2020, the most recent year of available data, with a primary or secondary diagnosis of gout and venous thromboembolism.
Results: In 2020, there were 32.4 million all-cause hospitalizations in the US, with 19.7 million occurring in persons 45 years or older. Of these, 785,905 hospitalizations occurred in people aged 45 years and over with a diagnosis of gout. These people had a mean age of 71.8 years (95% confidence limits 71.7 - 71.9 years) and were more likely to be men (68.4%). Of these, 79,260 hospitalizations (10.1%) also had concomitant diagnosis of venous thromboembolism. As a comparison, only 8.2% of hospitalizations in the general population 45 years or older had a concomitant diagnosis of VTE (p<0.001 compared to persons with gout). Persons with gout and VTE had a mean age of 71.6 years (95% confidence limit 71.4 - 71.8 years) and were mostly men (62.4%). However, hospitalizations in women with gout were more likely to have VTE (11.0%) compared to men (9.7%). The average cost of each hospitalization was $76,373 (95% confidence limit $73,343 -$ 79,403), with a total annual national cost of $6.1 billion.

Table 1. Percentage of VTE hospitalizations in Gout versus General population

	General population			Gout		
	Total Hospitalizations	Hospitalizations with primary or secondary diagnosis of VTE	Percentage VTE Hospitalizations	Total Hospitalizations	Hospitalizations with primary or secondary diagnosis of VTE	Percentage VTE Hospitalizations
People 45 years and over	19741256	1626055	8.20%	785905	79260	10%
Men 45 years and over	9,919,915	797530	8.04%	541010	52310	9.7%
Women 45 years and over	9,820,250	828450	8.44%	244855	26950	11.0%
Age 45-64 years	7683856	604550	7.9%	210530	21860	10.4%
Age 65 years and older	12057400	1021505	8.5%	575375	57400	10.0%

Conclusion: One out of 10 hospitalizations in persons with gout have a concomitant diagnosis of VTE, significantly higher than the VTE rate in the general population. This calls for increased awareness and steps to prevent the development of VTE in patients with gout.
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AB1243 WHICH IS THE MOST APPROPRIATE SONOGRAPHIC DEFINITION FOR ASYMPTOMATIC HYPERURICEMIA WITH MSU CRYSTAL DEPOSITION?

Keywords: Imaging, Gout, Ultrasound

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Background: Cumulative data indicates that 20-30% of subjects with asymptomatic hyperuricemia (AH) have silent monosodium urate (MSU) crystal deposition[1]. For its evaluation, several sonographic examination schemes have been used[2], and the scanning of the 1st metatarsophalangeal (MTP) joint and femoral condyle for double contour (DC) sign, plus 1st MTP for tophi, shows the highest prevalence and discrimination compared to subjects with normouricemia. However, how we should sonographically classify AH with crystal deposits remains to be defined.

Objectives: To compare the variations in prevalence of sonographic deposits in AH across different classification schemes.

Methods: Observational, cross-sectional study. Patients with AH were consecutively recruited from clinics and wards of internal medicine, cardiology, nephrology, endocrinology, rheumatology and primary care units in an academic center. Subjects with a recent serum urate level ≥7mg/dL were included, excluding those under urate-lowering therapy and/or colchicine or with gout or other inflammatory rheumatic disease. Ultrasound was performed by an expert rheumatologist sonographer, blinded to clinical and laboratory data, following 2021 OMERACT definitions for elementary gout lesions (DC sign, tophi, aggregates) and 0-3 grading[3]. The locations scanned bilaterally were knees with patellar tendons, ankles with Achilles' tendons, and 1st and 2nd MTP joints. We applied different definitions for AH with deposits, varying in relation to deposits (any deposits; only DC sign and/or tophi; only grade 2-3 deposits; only grade 2-3 DC sign and/or tophi) or locations (10 locations; reduced 4-joint scheme including knees and 1MTPs; more than 1 location with deposits). Comparisons were performed by Chi2 test.

Results: Seventy-seven participants with AH were studied, 55 males (71.4%) and a mean age of 59.8 years (SD 17.3). Mean body mass index was 31.2 kg/m2 (SD 5.2), and 37.66% and 29.9% suffered from cardiovascular and chronic kidney disease, respectively. Mean uricemia was 7.6 mg/dL (SD 1.6) with a fractional excretion of uric acid of 5.6% (DS 2.2). Regarding the elementary lesions, the median (p25-75) number of locations with DC sign, tophi or aggregates was 0 (0-1), 1 (0-2) and 1 (1-2), respectively. For grade 2-3 lesions, numbers were 0 (0-0), 1 (0-1) and 1 (0-2), respectively. As shown in **Figure 1**, the proportions of sonographic deposits largely varied according to the different classifications considered to define AH with deposits, ranging from 23.38% up to 87.01%, in a significant manner (p<0.050).

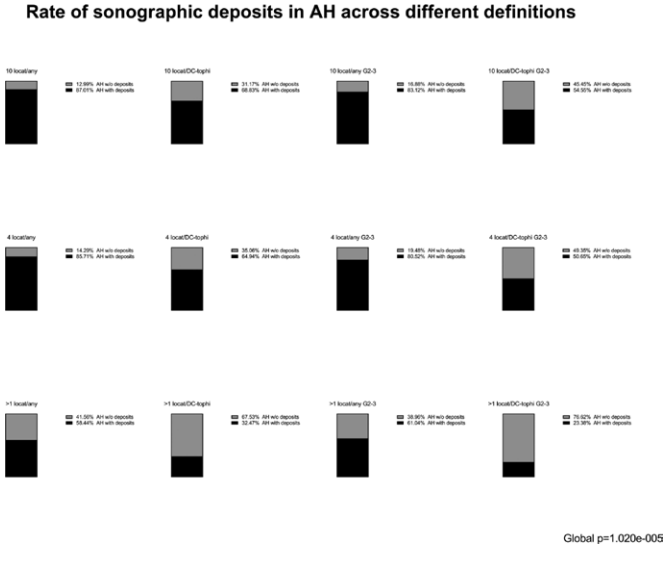


Figure 1. Rate of sonographic deposits in AH across different definitions.

Conclusion: In a multidisciplinary sample of AH, the rates of sonographic deposits dramatically varied across the different classifications used, highlighting the need for an agreed and validated definition that facilitates further research in this setting.

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AB1244 CHANGES IN THE GUT MICROBIOTA OF GOUT PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Gout

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Background: Gout is a crystal-related joint disease caused by the deposition of monosodium urate crystals in or around the joints[1][2]. Structural changes or imbalances in the gut microbiota could cause metabolic disorders and participate in the synthesis of purine-metabolizing enzymes and the release of inflammatory cytokines, which is closely related to the occurrence and development of metabolic, immune disease and gout.

Objectives: This study aimed to explore the disorders of intestinal microflora alpha diversity and microbial community composition in patients with gout through meta-analysis.

Methods: According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), we comprehensively searched the databases of PubMed, Web of Science, Embase, Cochrane Library, CNKI, VIP, CBM, and Wanfang database without language restrictions. We obtained data related to the alpha diversity index(Shannon index, Simpson index, ACE, Chao1, Observed species) and analyzed phylum and genus composition.

Results: Nine studies, including 423 gout patients and 458 healthy controls(HCs), were included in our analysis. The Simpson index of gout was significantly lower than that of HCs (SMD=-1.037, 95%CI:-1.959~-0.115). There was no significant difference in other alpha diversity indexes between the two groups(Shannon index: SMD=-0.429, 95%CI:-0.900~0.041; ACE: SMD=0.102, 95%CI:-0.918~1.122; Chao1: SMD=0.863, 95%CI:-0.267~1.993; Observed species: SMD= -1.962, 95%CI:-5.011~1.088). We collected the relative abundance of 30 genera of gout and classified them according to the species affiliation. The results showed that the relative abundance of microflora in *proteobacteria* was significantly lower than that of HCs(SMD= -0.498, 95%CI:-0.911~-0.086). However, the relative abundance of microflora in *Fusobacteria*(SMD=0.589, 95%CI:0.249~0.929), *Actinobacteria*(SMD=0.546, 95%CI:0.207~0.885), and *Bacteroides*(SMD=0.395, 95%CI:0.035~0.755) increased in gout patients. We did not observe significant changes in the gut microbes of *Firmicutes*(SMD=-0.210, 95%CI:-0.456~0.036).

Conclusion: This systematic evaluation and meta-analysis showed that the impact of gout microbiota was mainly observed at the level of phylum and genus, but limited to microbial diversity. It is necessary to further study the role and function of specific bacteria and their influence on the physiology and pathology of gout.

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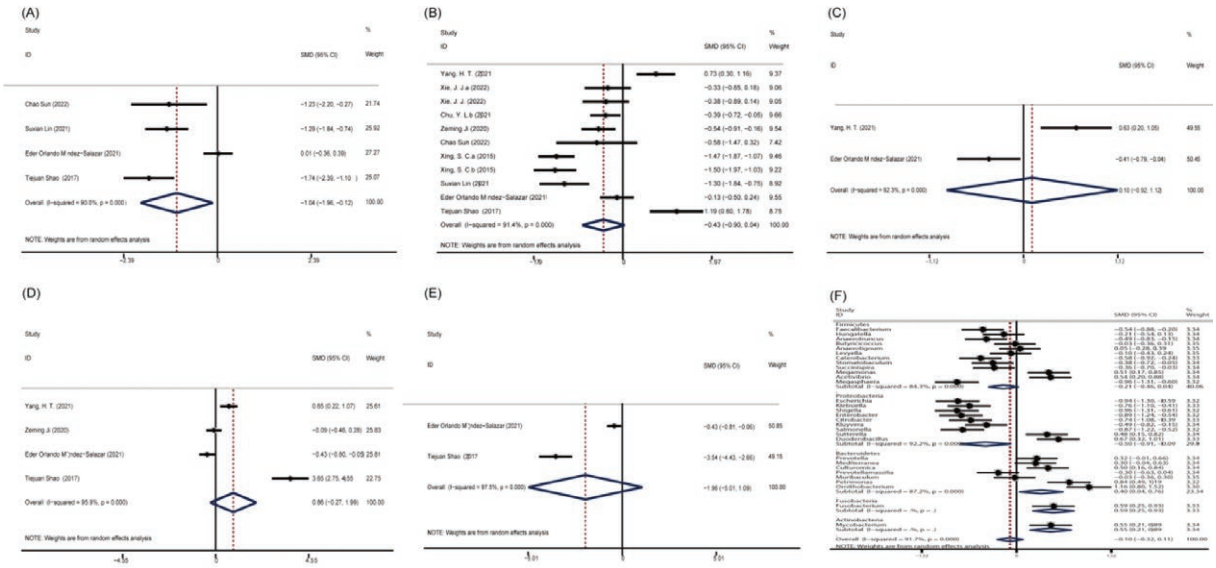


Figure 1: Forest map of intestinal flora alpha diversity in osteoporosis patients compared with healthy controls. (A)Simpson index; (B)Shannon index; (C)ACE; (D)Chao1; (E)Observed species; (F)Phylum composition of intestinal microorganisms.

AB1245

OSTEOMALACIA RELATED TO BARIATRIC SURGERY: HOW FREQUENT IS IT?

Keywords: Vitamin D, Bone diseases, Descriptive studies

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Background: The development of osteoporosis and fractures is a well-documented complication of bariatric surgery (BS), especially with procedures associated with malabsorption. Due to the gradual increase of BS performed worldwide, several national and international societies have developed clinical guidelines for managing these patients, with special attention to osteoporosis prevention and treatment. Nevertheless, these subjects can also develop osteomalacia, which can easily be misdiagnosed as osteoporosis. It is crucial to differentiate osteoporosis and osteomalacia in BS patients since different therapeutic approaches are necessary.
Objectives: To analyse the prevalence of osteomalacia and the main clinical characteristics of subjects with previous BS referred to the Rheumatology Department for osteoporosis treatment.
Methods: This was a retrospective study of a cohort of 46 subjects (aged 42-77 years) referred to the Metabolic Bone Diseases Unit of the Rheumatology Department for evaluating osteoporosis treatment. Clinical data were obtained from an in-depth review of medical records, including the type of BS (restrictive: gastric banding, and sleeve gastrectomy, or malabsorptive surgery: Roux-en-Y gastric bypass [RYGB], biliopancreatic diversion with duodenal switch), time since surgery, previous treatment with calcium and/or vitamin D, anthropometric data, clinical, laboratory, radiologic and densitometric findings. Osteomalacia was diagnosed by compatible bone biopsy and/or by Bingham and Fitzpatrick criteria[1] (two of the following: low calcium, low phosphate, elevated total alkaline phosphatase [TAP] or suggestive radiology).
Results: Five of the 46 patients (10.8%) presented criteria compatible with osteomalacia, two being confirmed by bone biopsy. All subjects with osteomalacia were Caucasian and most were women (4/5) treated with malabsorptive surgery (mainly RYGB) from 4 to 23 years prior to the visit. All presented increased serum TAP values (some presenting a progressive increase 1-3 years prior to the visit). Most subjects showed low serum calcium (4/5) and vitamin D serum levels; the latter were markedly decreased in 4 individuals (with only one presenting values >20 ng/ml). Parathyroid hormone (PTH) levels were increased in all subjects. Bone scan showed a pattern compatible with osteomalacia in all evaluated subjects (4/4) and bone densitometry showed values compatible with densitometric osteoporosis in most (4/5), with four individuals developing fractures/pseudofractures after BS. Three of these subjects were poorly adherent to calcium and vitamin D supplements and in 2 cases higher doses of calcium (3 g/day) and/or parenteral vitamin D administration were necessary to achieve serum vitamin D levels >30 ng/ml and decrease serum PTH levels in the posterior follow-up. Of note, no subject was referred to the Rheumatology Department with clinical suspicion of osteomalacia. Among the remaining 41 subjects, 28 (68%) presented densitometric osteoporosis and 18 (45%) developed fractures (mainly vertebral) after BS; one subject developed primary hyperparathyroidism (treated with surgery). Again, malabsorptive surgery was the most frequent surgical procedure in these subjects.
Conclusion: Nearly 10% of subjects with previous BS referred for osteoporosis treatment may have osteomalacia. Increased serum TAP values should alert clinicians to this diagnosis since it requires a differential treatment approach with some of these patients needing high doses of calcium or even parenteral vitamin D supplementation.

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AB1246

SOCIOECONOMIC STATUS, WORK IMPAIRMENT, DISABILITY AND SEVERITY OF GOUT IN LATIN AMERICA (LAT)

Keywords: Education, Crystal arthritis, Gout

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Background: Previous reports suspected that gout patients from Latin-América (LAT) are different to those from developed countries and similar to Asian.
Objectives: We aimed to characterize patients with gout attending to Rheumatologists at Health public institutions and private practices in LAT and its association with socioeconomic status and clinical severity.
Methods: This cross-over, multi-centric, multinational and descriptive study was performed between 2019 and 2022. We invited to participate ≈150 certified rheumatologists from 14 countries in LAT. The project was authorized by IRB. Gout (ACR-EULAR 2015) patients signed informed consent. During face to face and on-line interviews, we discussed clinical variables (≈200), questionnaires and CRFs in Spanish and Portuguese. Demographics, socioeconomic status: (AMAI <111= low socioeconomic status), clinical gout, associated diseases and treatment related variables were included. We defined severe gout (SG) if ≥5 tophi

and/or intradermal tophi. Metabolic syndrome (MS: ≥ 3, ATP3 definitions and criteria). HAQ score, VAS for pain and general health and EuroQoL: EQ5D were obtained during regular visit to Rheumatologist. Data was sent and analyzed at GRESGO (Gout study group) coordination centre). Statistical analysis included mean SD, median, IQR, t test, x2, ANOVA.

Results: Fifty two rheumatologists from 11 countries in LAT sent the data of 500 gout patients. Males (95%), mean (SD): age 57(14), age at onset 41(13), educational level 10(4) and duration of the disease 14 (12) years. The clinical spectrum of gout was evaluated first in 3 groups: 1) **SG** (SG+MS-, n=78, 16%); 2) **MS** (MS+SG1-, n=218, 44%) and 3) **others** (gout: SG- and metabolic data ≤ 2 ATP criteria, n=204, 41%). Second analysis included comparison of extreme groups (SG VS MS) (Table 1).

Conclusion: LAT SG patients were different compared to MS gout ant others. SG are younger males from low educational and socioeconomic status, >familial history of gout. As a consequence, SG patients also had aggressive and active poor controlled disease: >flares, tophi number and size, more hospitalizations and lower quality of life: >HAQ scores and more frequent alterations in the 5 EQ5D domains: (mobility, self-care, daily activities, pain, anxiety and depression) and disability consequences as work impairment. In the other hand, MS group had clearly more data associated to metabolic syndrome and higher cardiovascular risks.

Gout in LAT: SG vs MS comparison of demographics and clinical characteristics.

	SG+ MS- n=78	MS+ SG- n=218	Total ∞ SG+/MS+ and others n=500	p
Age at onset <30 years	38	17	24	0.001
Relatives with gout	45	33	36	0.047
Educational level <9 years	47	35	37	0.032
ACR/EULAR criteria for gout	99	70	79	0.001
Flares ≥ 2/year	57	39	44	0.004
Hospitalizations due to gout ¥	0.4 (0.8)	0.2 (0.5)	0.2 (0.4)	0.001
Urate level ≥ 10	56	29	37	0.001
HAQ >0.50	58	25	34	0.001
Work impairment.	28	8	13	0.001
MS/ATP criteria ≥3	20	62	41	0.001
Obesity	52	90	76	0.001
Hypertriglyceridemia	27	42	36	0.015
Hypertension atp	30	57	49	0.001
Hyperglycemia/Diabetes	41	57	49	0.011
Low HDL	45	42	39	0.427
KDIGO ≤3	30	15	21	0.006
Low socioeconomic level (AMAI <111)	62	38	42	0.001
Public health institution	91	77.5	85	0.01
Private practice	9	22.5	15	0.011

Values represent percentages unless specified, ¥= mean (SD)

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AB1247

RATIONALE AND DESIGN FOR PODAGRA II: A MULTICENTER RANDOMIZED PHASE 2/3 STUDY ASSESSING THE EFFICACY AND SAFETY OF DAPANSUTRILE, AN ORALLY ADMINISTERED SPECIFIC INHIBITOR OF THE NLRP3 INFLAMMASOME IN SUBJECTS WITH AN ACUTE GOUT FLARE

Keywords: Gout, Randomized control trial, Targeted synthetic drugs

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Background: The formation of the NOD-, LRR-, and pyrin-containing 3 (NLRP3) inflammasome plays a critical role in the initiation of the inflammatory reaction induced by the monosodium urate (MSU) crystals in an acute gout flare. Once assembled, the NLRP3 inflammasome converts pro-interleukin-1β into its active form and initiates IL-1β-dependent inflammation. NLRP3 activation, therefore, occurs upstream of IL-1β, the pivotal cytokine in gouty inflammation and the causative agent mediating symptoms of acute gout flares, including joint pain. Monoclonal antibodies against IL-1β can decrease inflammation and gout flares by neutralizing cicrulating IL-1β and shutting down the IL-1β-mediated inflammatory cascade. However, they must be injected and are associated with immune suppression and increased risk of infection. There remains an unmet need for an orally administered treatment for acute gout flare to safely reduce IL-1β-mediated inflammatory pain without the risk of immunosuppression. In an initial dose-range finding study, PODAGRA I, we reported preliminary evidence of efficacy and safety in this setting with dapansutrile, an orally administered specific inhibitor of the NLRP3 inflammasome.

Objectives: PODAGRA II study is designed to further evaluate the effects of dapansutrile on reducing joint pain and IL-1β-dependent inflammation during acute gout flare.

Methods: The study (NCT05658575/EudraCT 2019-002717-19) is a multicenter, placebo-controlled, prospective, randomized, double-blind trial conducted in the Netherlands, Spain, France, and the USA. A total of 300 patients with acute symptomatic gout flare are being randomized centrally to receive either dapansutrile (2000mg loading dose followed by 1000mg BID) or matching placebo tablets for 7 days (2:1 ratio dapansutrile: placebo). The study is designed to determine the superiority of dapansutrile compared to placebo on the symptoms and signs of an acute gout flare. The primary endpoint is the subject-reported pain intensity score in the target joint (evaluated on a 100-mm visual analogue scale) at 72 hours. Secondary endpoints include patient- and investigator-assessment of response to treatment and the investigator-assessed scores for joint tenderness, swelling, erythema, warmth, and range of motion. A subject-assessed quality-of-life questionnaire will be collected, and biomarkers associated with acute gout inflammation (IL-1 β, IL-6 and CRP) will be evaluated. In order to demonstrate both statistical and clinical significance, approximately 170 and 85 evaluable subjects are needed in the dapansutrile and placebo arms, respectively. This assumes a one-sided significance level of $\alpha = 0.025$, 85% power (1-β), a standard deviation of 25 points, an expected mean difference (Δ=10 points) plus an additional clinical significance of (δ=10 points). To account for dropouts and non-evaluable subjects, up to 200 subjects in the dapansutrile arm, and up to 100 in the placebo arm will be randomized.

	Group Size		
Power (%)	**Dapansutrile**	**Placebo**	**Study Size**
80	150	75	225
85	**170**	**85**	**255**
90	200	100	300
	Group Size		
Std deviation at 85% power	**Dapansutrile**	**Placebo**	**Study Size**
20	110	55	165
25	**170**	**85**	**255**
30	244	122	366

Results: The trial has launched and is currently enrolling subjects.

Conclusion: There is a need for an orally administered, safe, and well-tolerated treatment for acute gout flares. PODAGRA II will be the first placebo-controlled, adequately powered, large, multi-center study with an oral NLRP3-specific inhibitor. As gout is a prototypical disease of NLRP3 activation, this trial will provide important new data on NLRP3 inhibition leading to a reduction in joint pain and associated inflammatory biomarkers in acute gout flare.

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AB1248 LESSONS TO BE LEARNED FROM REAL LIFE DATA FROM 98 GOUT PATIENTS USING A URICOSURIC: BENZBROMARONE

Keywords: Crystal arthritis, Treat to target

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Background: Decreased renal urate excretion is the predominant driver of attracting gout, an auto-inflammatory disease secondary to hyperuricemia. Therefore there is an interest in effective urate lowering therapies with a uricosuric mode of action.
Objectives: The objective of this study was to analyses the efficacy and safety of uricosuric treatment i.e., benzbromarone in a real-life clinical setting.
Methods: data from gout patients was collected retrospectively from the digital hospital dossiers. Inclusion criterium was a diagnosis of gout (ICD10 code M10). Demographics, clinical variables and laboratory parameters at baseline and 6 months were collected. Efficacy was measured from reaching a serum urate target at 6 months, and/or increase in Fractional Urate Exctretion (FeUA).
Results: We analyzed data from 98 gout patients with an indication of benzbromarone treatment. Patients were 70 (±12) years of age, and 90% was male. After 6 months of treatment 90 out of 98 patients (91%) reached a sUA level <0.36 mmol/l (6mg/dL); We found that efficacy appeared to be best in low excretor type gout defined as FeUA<4.5%, as their FeUA increased from the initial mean value FeUA 3.2% (SD±1.0%) to reach in 6 months with benzbromarone mean FeUA of 12.1% (SD±6.9%). A considerable percentage (38%) is using benzbromarone on average for 3.8 (SD 3.4) years. 4 patients stopped benzbromarone treatment due to decrease renal function, condition that was already present prior to uricosuric initiation.
Conclusion: Using available benzbromarone in a real-life context proved to be efficient in lowering sUA levels in 6 months. Renal function must be considered before indicating benzbromarone. Determining FeUA in gout patients can further help better characterize the patient profile from whom is this the best treatment option.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1249 ASSOCIATION OF SERUM URIC ACID LEVEL WITH HAND OSTEOARTHRITIS

Keywords: Osteoarthritis, Crystal arthritis, Gout

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Background: Asymptomatic hyperuricemia is often considered as a biological anomaly, when the appearance of the gouty disease rather represents the evolution towards an inflammatory disease. In this case, the inflammation is usually due to a response to crystal deposits in the tissues, associated with cartilage damage, as seen in osteoarthritis. Although we know that neglected gout can lead to osteoarthritis, we still don't know if there is a link between hyperuricemia and osteoarthritis.
Objectives: The aim of this study is to assess the link between asymptomatic hyperuricemia (AH) and hand osteoarthritis (HO).
Methods: It's a cross-sectional study included 46 patients (28 in the HO group and 18 in a group without HO) with mean age of 67.23 ± 4.67 years, 32 women for 14 men. We collected demographic, clinical, biological (uricemia) and radiographic data. The association between AH and digital osteoarthritis was assessed by logistic regression.
Results: The mean serum uric acid level in patients with osteoarthritis was higher than that of patients without osteoarthritis (6.71 ± 1.13 mg/dl versus 6.26 ± 1.26 mg/dl, p=0.021). Hyperuricemia was more common in older patients with osteoarthritis than in those without osteoarthritis (45% vs. 23%, p=0.001). After adjusting for age, gender, body mass index and other variables, the association between asymptomatic hyperuricemia and osteoarthritis remained significant with an odds ratio [OR] of 2.28, for a 95% confidence interval [CI] (1.18-4.80), p=0.023. Subgroup analyzes were performed by sex where significant associations between asymptomatic hyperuricemia and osteoarthritis were obtained in women (p=0.027).
Conclusion: AH is a common comorbidity in elderly patients with hand osteoarthritis. A significant link has been found between AH and hand osteoarthritis in elderly subjects, especially females.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1250 OUTPATIENT FOLLOW-UP AFTER AN EMERGENCY DEPARTMENT VISIT FOR ACUTE GOUT FLARE

Keywords: Health services research, Gout, Crystal arthritis

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Background: Patients with acute gout are frequently treated in the emergency department (ED). Appropriate outpatient follow-up for an acute flare after an ED visit is variable and has not been systematically examined.
Objectives: We aimed to determine the characteristics of patients with gout treated in EDs, the nature of their ED visits, and to determine the types and rates of outpatient follow-up after an ED visit for an acute gout flare.
Methods: This study was conducted at one academic medical center that serves patients at 3 EDs (2 urban, 1 suburban) and 1 urban urgent care center. Patients were identified as having a possible acute gout flare upon initial triage in the ED using a previously developed electronic medical record (EMR) gout flare alert. We validated the presence/ absence of an acute gout flare through manual EMR review using adjudicated expert consensus assessed with kappa coefficient as the gold standard. Among those patients identified with an acute gout flare, we abstracted their medical records to determine the presence/ absence of an outpatient visit for gout care within 6 months of the index ED visit. This was defined as having had a documented outpatient visit with any provider (e.g., primary care, rheumatology) with a mention of 'gout' in the free text portion of history of present illness or assessment and plan. We used descriptive statistics to characterize patients with gout and reported the proportion of patients with an acute gout flare that followed up in the outpatient setting after an ED visit.
Results: From September 1, 2021 to February 28, 2022, there were 458 patients identified by the gout flare alert as possibly having an acute gout flare. Of these, 33 patients were excluded from this analysis due to participation in an ongoing randomized clinical trial testing a behavioral intervention to improve gout care. The remaining 425 patients included 72 patients (16.9%) who were determined to have a true gout flare at 85 unique ED visits by manual EMR review by 2 assessors. The kappa coefficient for agreement between the consensus expert determinations of acute gout flare was 0.8. Of those with an acute gout flare, 53 (74%) were men and 49 (68%) were Black or African American. At ED discharge, a majority of patients (64%) were prescribed corticosteroids, while 63% were prescribed opioids. A majority (54%) of ED visits for acute gout occurred between 8am and 5pm, with another 27% occurring between 5pm and midnight. The proportion of patients with an acute gout flare who followed up with an outpatient clinician in our healthcare system was 46% (**Table 1**), with 29% of patients having an outpatient visit within 30 days of the index ED encounter. Only 26 patients (36%) had an outpatient visit addressing gout, and of these, 17 (24%) occurred within 3 months of the index ED visit.
Conclusion: More than half of patients received opioids at discharge among patients with gout treated in the ED, who were mostly Black. Follow-up was ~46% among patients that received gout care in an acute setting, yet only a third saw a clinician who addressed gout. This data will inform sample size calculation for interventional studies testing behavioral interventions focused on promoting improved outpatient follow-up for gout flares.

Table 1. Healthcare utilization among participants following an emergency department visit for acute gout.

Healthcare Outcome	Total, N=72
Hospitalized, N (%)	13 (18)
Received care at Emergency Department or Urgent Care, N (%)	34 (47)
Any Outpatient Follow-up Service (N=33), N(%)*	
Internal Medicine Subspecialties†	24 (33)
Rheumatology	*4 (6)*
Surgical Subspecialty	20 (28)
General Internal Medicine	15 (21)
Family Medicine	4 (6)
Neurology	3 (4)
Palliative Care and Geriatrics	3 (4)
Dermatology	3 (4)

* Categories are not mutually exclusive.† Internal medicine subspecialties included cardiology, endocrinology, nephrology, oncology, pulmonology, and rheumatology.

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AB1251 SERUM URIC ACID LEVEL IN INTRACEREBRAL HEMORRHAGE PATIENTS

Keywords: Crystal arthritis, Gout, Cardiovascular disease

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Background: Intracerebral hemorrhage (ICH) is a life-threatening type of stroke caused by a rupture of a blood vessel into the brain's parenchyma, accounting for 10~15% of all stroke. Uric acid (UA) is the end product of purine metabolism; it is catalyzed by xanthine oxidase. UA may be related to cerebrovascular diseases through its role as either an antioxidant or pro-oxidant properties. Although the association of serum UA level with ICH has been investigated in previous studies, the results are controversial.
Objectives: In this study, we determined serum UA levels in patients with ICH and assessed its relationship with cerebrovascular risk factors.
Methods: We evaluated 721 patients with ICH who were admitted ton emergent department in tertiary hospital from July 2008 to December 2017 in South Korea. Demographics, laboratory data, neurological course, and brain magnetic resonance imaging (MRI) findings were collected using electrical medical records and picture archiving and communication systems. The participants were stratified into quartiles according to their serum UA levels. Between-group comparisons were performed using Pearson's chi-square test for categorical variables, and the ANOVA for numerical variables, as appropriate.
Results: Among 721 patients with ICH acute stroke. 413 (57.3%) were male. The mean age of patients was 58.9±14.03 and mean value of body mass index was 23.9±6.84 kg/m^2. Mean serum UA levels in the patients studied 5.94±1.70 mg/dl and there was a significant negative correlation between age of patients and their serum UA level ($p < 0.001$, $R = -0.212$). Serum UA level was significantly higher in men (5.82 ± 1.87 mg/dl) than women (4.43 ± 1.33 mg/dl) ($p = 0.03$). Concomitant intraventricular hemorrhage consistently decreased continuously across quartiles of serum UA. However, ICH recurrence and mortality rate did not differ according to serum UA level.
Conclusion: The results suggest that serum UA may be the predictor of intraventricular hemorrhage in ICH patients.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1252 BONE CHANGES EVALUATION DURING PREGNANCY BY MEANS OF RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY (REMS) TECHNOLOGY

Keywords: Ultrasound, Pregnancy and reproduction, Bone diseases

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Background: Degennaro, Cagninelli*, Casciaro*, Conversano*, Di Pasquo*, Lombardi*, Pisani*, Ghi.
***Equal contributors in alphabetical order.**
Typically, pregnancy and lactation greatly expose women to develop osteoporosis due to the high demand of calcium from the foetus or neonate. In some cases, especially in the first pregnancies or in the early breastfeeding period, women with persistent lower back pain, are suspected to be at risk for fragility fractures, mostly involving vertebral fractures[1]. Therefore, there is an urgent need to perform an accurate monitoring of the maternal bone health status in order to prevent complications of pregnancy and lactation-associated osteoporosis.
Objectives: Through a longitudinal study, the present work aims to determine the changes of bone status in pregnant women from the first to the third trimester of gestation by means of the non-ionizing Radiofrequency Echographic Multi Spectrometry (REMS) technology.
Methods: A cohort of 43 pregnant women were enrolled in the study. Longitudinal measurement of bone mineral density (BMD) was carried out at the femur during the first (baseline) and third (follow-up) trimesters of pregnancy using the REMS technology. A paired t-test was performed to assess the difference in femoral neck BMD between baseline and follow-up.
Results: Compared to the baseline (first trimester), a significant femoral neck BMD reduction was observed at the follow-up of the third trimester, (0.762 ± 0.075 g/ cm^2 *versus* 0.711 ± 0.074 g/ cm^2, respectively with $p<0.0001$). As a result, an overall BMD decrease of 2.07% has be measured.
Conclusion: As previously demonstrated with this technology, pregnant women have a significant decline of BMD compared with the non-pregnant counterpart[2]. With this study, for the first time, bone changes throughout pregnancy could be determined by means of this technology: a marked bone reduction was demonstrated in the pregnant group during the last trimester of pregnancy. In conclusion, REMS represents an appropriate method for BMD assessment which can be safely employed to monitor the bone status across gestation and lactation.
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AB1253 FEBUXOSTAT DOSE ADJUSTMENT ACCORDING TO RENAL FUNCTION TO ATTAIN TARGET SERUM URATE LEVEL: A RETROSPECTIVE COHORT STUDY

Keywords: Gout

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Background: Current guideline for gout recommends the use of allopurinol or febuxostat in moderate-to-severe chronic kidney disease (CKD). However, the appropriate febuxostat dosage required to attain the target serum urate (SU) level remains unclear, especially in patients with renal impairment.
Objectives: We aim to investigate the different febuxostat dosages stratified by renal function to achieve the target SU level.
Methods: We collected the clinical and laboratory information of patients using the Clinical Research Data Warehouse system of Asan Medical Center, Seoul, South Korea. Of the 3153 patients with gout and a prescription for febuxostat at a tertiary-care referral center, 731 with initial SU levels >6 mg/dL were collected and categorized, according to their eGFR levels at febuxostat therapy initiation, into three groups based on CKD stage: 1, 2–3, and 4–5. We defined the cumulative febuxostat as the total dose of febuxostat used from the initiation of febuxostat to the moment patient reached the SU target (SU<6 mg/dL).
Results: This cohort of 731 gout patients, with a median age of 52 (IQR, 41-63) years, included 64 (8.8%) women. Compared with the other groups, in the CKD 4–5 group, the mean SU value at febuxostat initiation was significantly higher (9.6 [SD, 3.1] mg/dL; CKD 2–3, 8.6 [SD, 1.6] mg/dL; CKD 1, 8.8 [SD, 1.8] mg/dL; $p<0.001$) and significantly fewer patients achieved the SU target during the follow-up period, median 31 (IQR, 13-55) months. In the subgroup analysis of patients who achieved target SU levels, the cumulative dose of febuxostat was significantly lower in CKD 4-5 patients compared to those with other groups (CKD 4–5, 5.9 (IQR, 2.5–12.0) g; CKD 2–3, 7.1 (IQR, 3.5–15.7) g; CKD 1, 7.0 (IQR, 2.7–20.1) g; p=0.010 for CKD 4–5 and CKD 1, p=0.006 for CKD 4–5 and CKD 2–3). The average febuxostat dose used during 4 months to reach the SU target was 50.0 (IQR, 21.0–101.0) mg in the CKD 4-5 group, which was significantly lower than in other groups (CKD 2–3, 59.3 (IQR, 29.4–130.7) mg; CKD 1, 58.5 (IQR, 22.7–167.8) mg; p=0.006 for CKD 4–5 and CKD 1, p=0.003 for CKD 4–5 and CKD 2–3). In addition, when we examined the clinical factors associated with the required dose of febuxostat to achieve SU target, CKD 4-5 group showed a significant negative correlation with cumulative febuxostat dosage to reach target SU compared with CKD 1 (rho -2.334, p=0.02).

Conclusion: The febuxostat dose required to reach the target SU level was significantly lower in patients with markedly decreased renal function (CKD stage 4–5).

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Table 1. Febuxostat acquirement to reach target SU

	Total (n=731)	CKD 1 (n=204)	CKD 2-3 (n=388)	CKD 4-5 (n=139)	p-value	CKD 1 vs 4-5	CKD 2-3 vs 4-5
SU target achievement, n (%)	626 (85.6)	176 (86.3)	336 (86.6)	114 (82.0)	0.25	**0.043**	**0.045**
Patients achieving SU target							
Mean SU at 4 months, mg/dL	6.2 (5.1, 7.2)	6.2 (5.1, 7.3)	6.0 (5.1, 7.1)	6.3 (5.1, 7.2)	0.49	0.27	0.05
Duration to achieve SU target, months	4.0 (1.9, 9.6)	3.3 (1.8, 11.7)	4.1 (2.1, 9.2)	3.2 (1.4, 7.4)	0.22	**0.038**	0.08
Cumulative febuxostat dose, g	7.0 (3.0, 15.7)	7.0 (2.7, 20.1)	7.1 (3.5, 15.7)	5.9 (2.5, 12.0)	0.12	**0.010**	**0.006**
Average dose of febuxostat, mg	58.3 (25.7, 130.7)	58.5 (22.7, 167.8)	59.3 (29.4, 130.7)	50.0 (21.0, 101.0)	0.09	**0.006**	**0.003**
Percentage change in SU	-41.4 (-51.3, -30.1)	-39.4 (-49.2, -31.1)	-40.2 (-50.0, -29.7)	-47.2 (-58.3, -35.6)	**<0.001**	**<0.001**	**<0.001**
Delta SU, mg/dL	-3.4 (-5.0, -2.4)	-3.3 (-4.8, -2.3)	-3.4 (-4.8, -2.3)	-4.2 (-6.4, -3.0)	**<0.001**	**<0.001**	**<0.001**

[a]p-value was obtained using ANOVA statistical analysis

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AB1254 ECTOPIC ARTICULAR CALCIFICATIONS AND ARTERIAL OCCLUSIVE DISEASE DUE TO 5-NUCLEOTIDASE DEFICIENCY

Keywords: Inflammatory arthritides, Rare/orphan diseases, Crystal arthritis

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Background: Calcification of Joints and Arteries (CALJA) is a rare disease presenting with recurrent/chronic arthritis and *claudicatio intermittens* of the lower limbs. Since the discovery of specific mutations of the *5'-nucleotidase* (*NT5E*) gene responsible for the disease, only few cases have been reported.
Objectives: To collect available information about CALJA to better characterize the disease and to raise awareness of this often unrecognized rheumatologic condition.
Methods: All available publications regarding CALJA since its first description in 2011 were included and a case report is described.
Results: A 65-year-old woman, affected by seronegative oligoarthritis since 2007, reported lower limb claudication. In 2021 past medical history consisted of migratory, non-erosive arthritis with asymmetrical involvement of peripheral joints since the age of 30, poorly responsive to glucocorticoids and immunosuppressive therapy. She had never presented any clinical sign of connective tissue disease or microcrystalline arthritis, as shown in X-rays performed in 2007/2010. In November 2021, because of the worsening of the claudication, an arterial color Doppler ultrasound of the lower limbs was performed, which revealed bilateral obliteration of superficial femoral artery, of posterior and anterior tibial arteries, and of lateral plantar arteries. X-rays showed extensive calcifications of the femoral and popliteal arteries as well as widespread articular and periarticular calcific deposits, with the appearance of hydroxyapatite deposits. Laboratory findings included inflammatory markers elevation, whereas calcium-phosphorus metabolism, lipid and glucose profile, blood count, and renal/hepatic function were normal. She had never smoked and had no significant cardiovascular risk factors. Based on the knowledge of a very rare genetic condition called **CAL**cification of **J**oints and **A**rteries (*CALJA,* MIM 211800), *ecto-5'-nucleotidase (NT5E)* gene analysis was performed, which resulted positive for the homozygous inactivating variant NM_002526.3:c.751(1G>A). NT5E activity leads to adenosine production, which in turn inhibits Tissue Non-specific Alkaline Phosphatase (TNAP) synthesis. TNAP degrades PPi into inorganic phosphate, an activator of calcification; therefore, inactivation of NT5E leads to vascular (lower limbs) and periarticular calcification in CALJA patients, with the clinical features of progressive arterial disease and microcrystalline arthritis. To date, 23 patients with CALJA had been reported (*Table 1*). Seventeen patients are female (74%), mean age at diagnosis is 59-year-old and the most common symptoms are intermittent claudication (87%) and joint pain due to periarticular calcification (70%); upper extremities arterial calcifications (9%) and calcific aortic valve stenosis (17%) are less commonly described.
Conclusion: To our knowledge, this patient is the first case of CALJA with variant NM_002526.3:c.751(1G>A) of *NT5E*. Patients presenting with CALJA are often treated with immunosuppressive agents in the suspicion of inflammatory rheumatologic diseases. Thus, it is important for the Rheumatologist to recognize the features of this disease and to keep it in mind in the differential diagnosis of patients suffering from arthritis and/or early osteoarthritis along with lower limb arterial insufficiency.

Table 1. Demographics and clinical characteristics of described patients with CALJA. AVS: aortic valve stenosis, AC: articular calcifications, IC: claudicatio intermittens, UEAC: upper extremities arteries calcifications, RP: Raynaud Phenomenon.

Case report	Year	Country	Patients	Age	Male sex	Female sex	Exon	NT5E variant	Symptoms
St. Hilaire	2011	USA	5	44 - 54	2	3	3	c.662>A homozygous	IC, AC
St. Hilaire	2011	USA	3	68 - 73	0	3	5	c.1073G>A homozygous	AC, IC
St. Hilaire	2011	USA	1	44	0	1	9, 3	c.1609dupA, c.662C>A heterozygous	IC
Ichikawa	2015	Japan	1	54	0	1	1, 2	c.3G>C heterozygous, c.373G>C heterozygous	IC, AC
Zhang	2015	China	2	26 - 30	1	1	7, 8	c.1360G>A, c.1387C>T heterozygous	AC, UEAC
De Nijs	2016	Netherlands	1	42	1	0	intron 3	c.751+2T>C homozygous	IC, AC
Yoshioka	2017	Japan	1	66	1	0	1	c.3G>C homozygous (speculated)	IC, AC, UEAC
Azuma	2020	Japan	3	70 - 80	1	2	1	c.3G>C homozygous	IC, AC, none
Azuma	2020	Japan	2	74 - 81	0	2	1	c.3G>C homozygous	IC, AVS, AC
Avruscio	2020	Italy	1	47	0	1	9	c.1608dupA homozygous	IC, AC, RP
Uchida	2022	Japan	2	71-77	0	2	1	c.3G>C homozygous	IC, AC, AVS
Maffi	2023	Italy	1	65	0	1	intron 3	c.751+1G>A homozygous	IC, AC

REFERENCES: NIL.
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AB1255 PEGLOTICASE + METHOTREXATE COTHERAPY IN UNCONTROLLED GOUT PATIENTS WITH PRIOR PEGLOTICASE MONOTHERAPY FAILURE: FINDINGS OF THE ADVANCE OPEN-LABEL TRIAL

Keywords: Gout, Clinical trials

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Background: Pegloticase is often the last treatment option for patients (pts) with uncontrolled/refractory gout but anti-drug antibodies (ADAs) cause loss of serum urate [SU] lowering response and infusion reactions (IRs).[1] MIRROR RCT showed higher response rate (71% vs 39% during month 6) and lower IR risk (4% vs 31%) with methotrexate (MTX) cotherapy, which attenuated ADAs in pegloticase-naïve pts.[2] Therefore, retreating pts who previously developed ADAs with pegloticase monotherapy is clinically relevant. The ADVANCE trial examined pegloticase+MTX cotherapy safety and efficacy in pts with prior monotherapy failure.
Objectives: To report interim efficacy and safety findings of the ADVANCE open-label trial.
Methods: Pts with uncontrolled gout (SU ≥6 mg/dL, ULT failure/intolerance, and ≥1 symptom [≥1 tophus, ≥2 flares in past yr, or chronic gouty arthritis) who did not maintain SU-lowering during prior pegloticase monotherapy were included. Key exclusion criteria were prior moderate/severe IR or anaphylaxis to pegloticase, MTX contraindication, current immunosuppressant use, G6PD deficiency, and eGFR<30 mL/min/1.73 m^2. After a 6 wk MTX Run-in (subQ MTX titrated to 25 mg/wk [15 mg/wk if eGFR <45]), pts began pegloticase (8 mg biweekly) + MTX Treatment for 24 wks (option to extend to 48 wks). Pts took 1 mg/d folic acid, gout flare prophylaxis, and pre-infusion IR prophylaxis (included 125 mg IV methylprednisolone). The primary endpoint was proportion with SU-lowering response during Month 6 (SU <6 mg/dL for ≥80% of Wks 20-24). Other key endpoints were response rate during Month 3 (SU <6 mg/dL for ≥80% of Wks 10-14) and IR rate. Safety was evaluated via AEs and laboratory monitoring.
Results: 13 pts began the MTX Run-in; 11 met study criteria and entered pegloticase+MTX Treatment (intent-to-treat population; 91% male, mean [±SD] age: 58.6±11.3 yrs, BMI: 31.8±5.4 kg/m^2, eGFR: 70.2±15.8 [all ≥45]). SU before pegloticase exposure (Day 1) was 8.5±3.2 mg/dL and gout burden was high (gout history: 25.2±8.4 yrs, 91% had tophi, 4.5±3.8 flares in prior 6 months). Prior pegloticase

course range was 2-27 infusions, with last infusion 3.7±2.4 yrs prior (range: 0.7—9.2 yrs). One pt (9%) was a responder during Month 3 and during Month 6 (ongoing treatment through Wk 30 at analysis). 8 pts (73%) met SU-discontinuation criteria (first SU >6mg/dL: 20.8±18.3 days after infusion 1), and 2 (18%) had moderate IRs. 7/13 pts (54%) had ≥1 AE during Run-in (1 SAE); 8/11 (73%) had ≥1 AE during Treatment (0 SAE, all Rheum CTC[3] grade 1 or 2), most commonly gout flare (**Table 1**).

Table 1. Key findings of pegloticase+MTX treatment in pts with prior loss of urate-lowering efficacy during pegloticase monotherapy. AEs reported in >1 pt are listed, along with all SAEs and AEs of special interest.

	MTX Run-in (N=13)	Pegloticase+MTX Treatment (N=11)
Efficacy endpoints		
SU response during Month 6, n (%)	---	1 (9%)
SU response during Month 3, n (%)	---	1 (9%)
Treatment-emergent AEs		
≥1 AE, n (%)	7 (54%)	8 (73%)
Gout flare	6 (46%)	7 (64%)
Arthralgia	1 (8%)	2 (18%)
Infusion reaction*†	0	2 (18%)
Pain in extremity	0	2 (18%)
Fatigue	2 (15%)	0
Anaphylaxis*	0	0
Cardiovascular event*‡	0	0
Serious AEs		
≥1 serious AE, n (%)	1 (8%)	0
Perineal abscess§	1 (8%)	0

*AE of special interest. †throat tightness, erythema, itching, urticaria in 1 pt; back pain in 1 pt. ‡included non-fatal stroke, non-fatal MI, cardiovascular death, CHF. §2 days before first pegloticase infusion, deemed unrelated to MTX.

Conclusion: Treatment response rate with pegloticase+MTX following failed monotherapy was 9%, markedly lower than in pegloticase-naïve pts (71%).[2] IR rate was 18%, higher than in pegloticase-naïve pts (4%),[2] but all were moderate (no anaphylaxis). These findings demonstrate the challenge of overcoming established ADAs against pegloticase and emphasize the importance of initiating immunomodulation before pegloticase therapy.

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AB1256 WORTH'S DISEASE (LRP5 HIGH-BONE-MASS): CASE REPORT AND REVIEW OF THE LITERATURE

Keywords: Rare/orphan diseases, Genetics/Epigenetics, Bone diseases

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Background: Worth's disease is a rare autosomal dominant sclerosing bone dysplasia determining high bone mass. It is caused by mutations of the *low-density lipoprotein receptor-related protein 5 (LRP5)* gene. Clinical findings include torus palatinus and craniofacial changes, such as increased gonial angle [1]. The absence of neurological involvement has long been considered a key aspect to discriminate between Worth's disease and Van Buchem's disease, in which cranial nerve deficits and intracranial hypertension are frequent [2]. Alternative names have been employed to describe Worth's disease, such as "autosomal dominant osteosclerosis", "Van Buchem's disease, type 2", and "LRP5 high-bone-mass (HBM)". The rarity of the disorder, the use of several denominations and the lack of reviews have rendered research of information on Worth's disease complicated and confusing.

Objectives: To gather all case reports of Worth's disease and provide comprehensive data on the condition, and to describe a patient with neurological involvement.

Methods: After collecting all case reports, we assessed the prevalence of neurological involvement and other relevant clinical and laboratory findings. A thorough clinical, radiological, and genetic assessment was performed on an affected patient.

Results: A 44-year-old Caucasian woman was referred to us in 2009 for chronic and debilitating dorsolumbar pain (Visual Analogue Scale 8/10). Since her twenties, she has been affected by chronic and disabling low back pain, frontoparietal headache, hypo-/anosmia, and numbness and tingling of arms, face, and oral cavity. She noticed the early appearance of facial changes that became more evident with time. In 1999, external hearing aids were placed due to complete mixed hearing loss caused by the narrowing of internal and external acoustic meati. At presentation, clinical examination revealed prominent jaw, frontal bossing, and torus palatinus. She denied previous bone fractures. Family history was unremarkable. A complete skeletal survey revealed endosteal hyperostosis of the limbs and severe osteosclerosis of clavicles, ribs, vertebrae, hip, and cranium, in the absence of deformities except for a deepened and widened jaw. Bone scintigraphy with technetium-99m was normal. Dual-energy X-ray absorptiometry (*DEXA*) scan revealed T-score +10.8 (Z-score +11.1) and bone mineral density (BMD) of 2.5 g/cm^2 for L1-L4 spine, T-score +6.5 (Z-score +6.2) and BMD of 1.8 g/cm^2 for femoral neck, and T-score +8.5 (Z-score +8.1) and BMD of 2 g/cm^2 for total hip. Markers of bone turnover and calcium metabolism were normal. The ophthalmologic evaluation revealed bilateral papilledema. Head MRI showed mild cerebellar tonsillar herniation through the foramen magnum. Neither pyramidal tract signs nor cerebellar disturbances were present. Genetic analysis detected the A242T mutation in exon 4 of the *LRP5* gene. To date, 169 patients with Worth's disease have been reported since its first description in 1966, including the present case (Table 1). Neurological involvement and increased serum alkaline phosphatase were present in 33 (19.5%) and 14 (8.2%) cases, respectively. Facial changes and torus palatinus were observed in 96 (56.8%) and 63 (37.4%) cases, respectively.

Table 1. Cases of Worth's disease grouped by decade.

Decade	Number of case reports	Cumulative number of cases	High serum alkaline phosphatase	Facial changes	Torus palatinus	Neurological involvement
1960s	2	15	0	9	3	0
1970s	8	42	2	29	20	7
1980s	4	19	1	2	1	4
1990s	4	19	1	7	5	4
2000s	9	48	8	33	20	8
2010s	6	25	2	15	13	9
2020s	Present case	1	0	1	1	1
Total	34	169	14	96	63	33

Conclusion: For the first time, we collected all known case reports of Worth's disease. Neurological involvement is present in one-fifth of the patients, and facial changes are not a consistent finding. Thus, Worth's disease may be asymptomatic and is often incidentally detected in routine radiographs showing generalized osteosclerosis. Our case is the first report of hypo-/anosmia in Worth's disease.

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Disclosure of Interests: None Declared.

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AB1257 EVALUATION OF ADHERENCE TO AND AGREEMENT WITH THE 2020 AMERICAN COLLEGE OF RHEUMATOLOGY GUIDELINE FOR THE MANAGEMENT OF GOUT BY US RHEUMATOLOGISTS

Keywords: Inflammatory arthritides, Gout, Crystal arthritis

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Background: In 2020, the American College of Rheumatology (ACR) presented an updated gout treatment guideline.[1]

Objectives: In this report, we evaluated US rheumatologists' stated adherence to and agreement with the 2020 ACR Guideline for the Management of Gout.

Methods: A 57-item questionnaire was administered to US rheumatologists, surveying their adherence to and agreement with the 2020 ACR Guideline for the Management of Gout. Stated adherence scores were based on the number of Guideline recommendations reported to be followed by rheumatologists in practice, whereas stated agreement scores were based on degree of agreement with the recommendations.

Results: All 201 rheumatologists approached completed the questionnaire. Mean age of participants was 50 years, 54% had >15 years of practice experience, and ~70% were in private practice (**Table 1**). Mean overall stated adherence score was 11.5, with a possible maximum of 15, whereas the mean overall stated agreement score was 7.7, with a possible maximum of 14. Rheumatologists with less experience (≤8years; n=49) were likely to claim adherence with more individual ACR recommendations than those with more experience (>8years; n=152) (mean stated adherence score: 12.3 vs 11.3; p<0.05), whereas those who claimed to see

≤75 patients with gout in 6 months (n=66) had a mean stated adherence score of 12.1 vs 11.2 for rheumatologists who claimed to have seen >75 patients ($p<0.05$). Approximately 78% of rheumatologists claimed to follow the guideline for initiating urate lowering therapy (ULT) and 89% were likely to prescribe allopurinol as a first line ULT for all patient types (**Figure 1**). Claimed adherence to recommendations for dosing was lower (43% and 39%, for febuxostat and allopurinol, respectively). Approximately, 92% of the rheumatologists claimed adherence on first-line therapy for gout flares (**Figure 1**). Rheumatologists from academic settings were more likely to prescribe an interleukin-1 inhibitor for gout flares than those in other settings.

Conclusion: The self-reported practice of the surveyed US rheumatologists was generally concordant with the 2020 ACR Guideline for the Management of Gout. However, there were gaps in guideline knowledge and stated adherence among rheumatologists, mainly concerning the dosing of treatment regimens.

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Table 1. Demographics of rheumatologists participating in the survey

Characteristic	Respondents (N=201)
Age, mean (SD), years	50.2 (10.9)
Gender, male, n (%)	135 (67.2)
Practice setting, n (%)	
Academic medical center/academic-affiliated teaching hospital	47 (23.4)
Community hospital (non-teaching)	14 (7.0)
Private practice (solo/group)	140 (69.7)
Years of practice, n (%)	
≤8	49 (24.4)
9–15	44 (21.9)
16–25	61 (30.4)
≥26	47 (23.4)
Patients with gout seen per 6 months, n (%)	
1–75	66 (32.8)
76–150	79 (39.3)
151–225	25 (12.4)
≥226	31 (15.4)

Figure: Stated adherence versus stated agreement to the strong recommendations of 2020 American College of Rheumatology Guideline for the Management of Gout

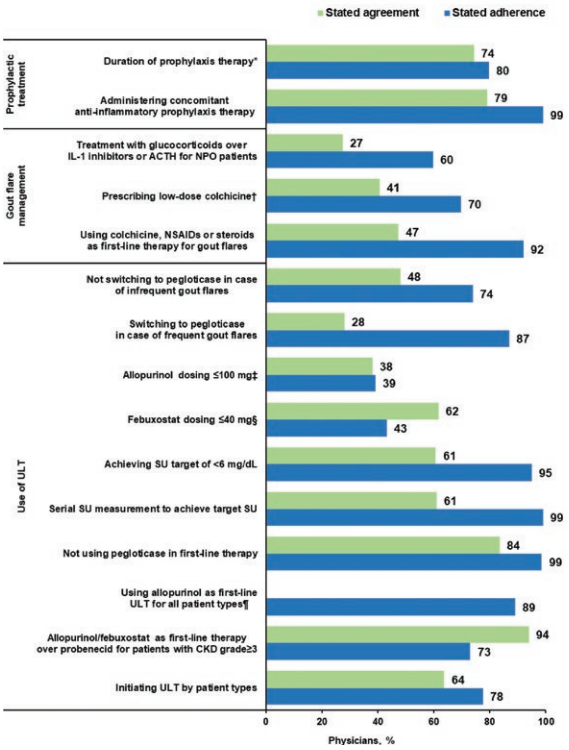


Figure 1. Stated adherence versus stated agreement to the strong recommendations of 2020 American College of Rheumatology Guideline for the Management of Gout *n=187; respondents who did not administer concomitant anti-inflammatory prophylaxis therapy were not asked about the duration of prophylaxis. †n=155; respondents who did not select oral colchicine as first-line or standard of care for gout flare management for any patient types were not asked about the prescribed colchicine dosage. Respondents who did not state high agreement with the use of prophylaxis were not asked about the duration of treatment. ‡n=197; respondents who did not select allopurinol as first-line ULT for any patient types were not asked about daily dosing of allopurinol. §n=81; respondents who did not select febuxostat as first-line ULT for any patient types were not asked about daily dosing of febuxostat. ¶Not tested for stated agreement. ACTH, adrenocorticotropic hormone; CKD, chronic kidney disease; IL, interleukin; NPO, nothing by mouth; NSAID, non-steroidal anti-inflammatory drug; SU, serum urate; ULT, urate-lowering therapy.

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AB1258 CAMURATI-ENGELMANN DISEASE: EFFICACY OF ANTI-TNFALFA TREATMENT

Keywords: Rare/orphan diseases, Bone diseases, bDMARD

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Background: Camurati-Engelmann disease (CED) is a rare osteosclerotic autosomal dominant condition responsible for chronic diaphyseal pain. It is caused by mutations of *Tumor Growth Factor β1 (TGFβ1)* gene. Currently there are no validated therapies for this condition.

Objectives: To test the efficacy of anti-TNFα antibody in a patient affected by CED.

Methods: Etanercept 50 mg per week was administered in a patient with CED. Data regarding pain and assumption of glucocorticoids and non-steroidal anti-inflammatory drugs were collected. Technetium-99m bone scintigraphy was performed at baseline, and after six months of treatment.

Results: A 34-year-old woman came to our attention in 2011 due to chronic pain of lower and upper limbs, especially localized at the diaphyses of long bones. The symptoms began in adolescence, but independently resolved during pregnancy. Two sisters and her 16-year-old son presented with a similar clinical picture. She had no clinical features or laboratory findings compatible with a systemic autoimmune disease. In the same year, along with relevant imaging exams, a genetic evaluation of all family members was performed, with the aim to find a hereditary disease. Compatibly with CED, the mutation *c.505G>A* of exon 2 of TGF*β1* gene was confirmed. Treatment with daily glucocorticoids, losartan and zoledronic acid 5 mg per year was administered, with little benefit for the patient. During an evaluation in 2022 she complained severe pain (visual analogue scale 8/10) unresponsive to 6-methylprednisolone 8 mg and indomethacin 100 mg daily. Technetium-99m bone scintigraphy showed abnormal accumulation in the skull, humeral and femoral diaphysis (Figure 1). Based on a single case report in on a patient with CED and Chron's disease successfully treated with success with an anti-TNFα drug, we decided to administer etanercept 50 mg per week. After 3 months we observed a clear subjective and objective improvement in pain (VAS 4/10) and a reduction in the assumption of indomethacin (150 mg weekly) and 6-methyl prednisolone (4 mg daily). However, technetium-99m bone scintigraphy carried out six months later did not reveal document a reduction in uptake of the tracer.

Conclusion: A patient with CED experienced a significative improvement in symptoms after treatment with anti-TNFα antibody. Our experience opens a window on a possibly new therapeutic option which could be implemented in the treatment of CED unresponsive to traditional drugs.

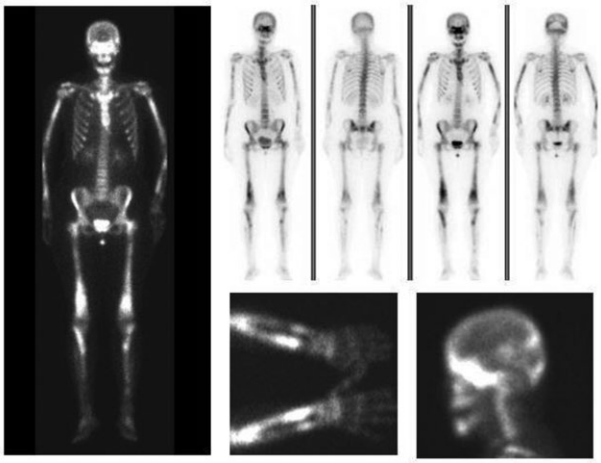


Figure 1. Technetium-99m bone scintigraphy with abnormal tracer accumulation in skull and long bones diaphyses.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.3731

AB1259 SERUM IRON LEVELS WERE POSITIVELY ASSOCIATED WITH THE RISK OF HYPERURICEMIA: NHANES 1999-2014

Keywords: Gout, Gender/diversity issues

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Background: Increasing evidence proofs that serum ferritin plays an important role in the development of hyperuricemia (HUA), however, few studies focus on the relationship between serum iron and serum urate (sUA).
Objectives: To examine the relationship between serum iron and serum urate as well as the risk of HUA classified by gender in the US adult population.
Methods: The present cross-sectional study pooled data from 1999 to 2014 National Health and Nutrition Examination Survey (NHANES). The association between serum iron quartiles and hyperuricemia was evaluated by logistic regression. The restricted cubic spline regression was performed to analyze the association between continuous serum iron and sUA.
Results: The study enrolled 25757 participants in total from 1999-2014 annual NHANES cycles. The crude prevalence of hyperuricemia was 11.9%. Serum iron was significantly higher in those with HUA than in those without HUA (16.6μg/dl vs 15.6μg/dl, p<0.0001). Logistic regression showed that serum iron levels were positively associated with the risk of HUA in the whole participants and male participants after adjusting for age, BMI and eGFR (Table 1). A dose-response association was observed in the whole participants (P for trend < 0.05). The restricted cubic spline regression analysis showed that the association between continuous serum iron and sUA was different in male participants and female participants (Figure 1). The curve of male participants showed an increasing trend (folding point 13.3μg/dl, P=0.033), while for women, sUA first increased linearly, but after the folding point (6.6μg/dl, P<0.001) the curve flattened out and the increasing trend was not significant.
Conclusion: Serum iron levels were positively associated with the risk of HUA in men. The correlation between serum iron and serum uric acid was influenced by gender. More studies are needed to confirm this relationship and to find out the mechanisms behind as well as the reasons for the gender differences.

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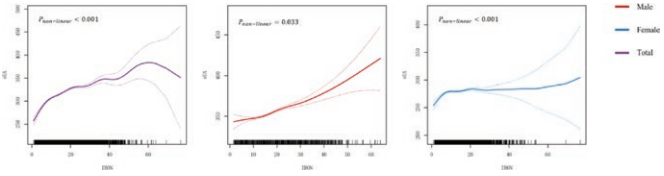


Figure 1. Associations of Serum Iron and Serum Urate in the US adult populationIRON, serum iron; sUA, serum urate. The restricted cubic spline regression analyses were adjusted for age, BMI and eGFR.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1260 EPIDEMIOLOGICAL, CLINICAL AND CHRONOLOGICAL PROFILE OF HOSPITALIZATIONS FOR CRYSTALLINE ARTHROPATHIES IN SOUTHERN TUNISIA: A DECLINE OF 14 YEARS

Keywords: Gout, Nursing, Crystal arthritis

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Background: Crystalline arthropathies (CA) are a group of joint disorders caused by deposits of crystals in joints and the soft tissues around them. The most common type is gout. Over time, CA could lead to joint damage and even for other serious complications that could require hospitalization.
Objectives: This study aimed to determine the epidemiological, clinical and chronological profile of hospitalizations for CA in southern Tunisia for 14 years.
Methods: This was an observational retrospective study that included patients hospitalized for CA in the Hedi Chaker University Hospital Southern Tunisia, during the period 2003-2016. Data collection was done as part of the continuous survey of hospital morbidity and mortality.
Results: Among 148596 admissions, 187 cases were hospitalized for CA (0.12%), of which 122 subjects (64.9%) were males. The median age of hospitalized patients was 66 years (IQR=[54-75]) years. There were 96 patients (51.3%) aged>65 years. The most frequent type of CA noted was gout with a global frequency of hospitalizations about 72.2% (n=135). Complications were noted among 11 patients (5.9%). They were essentially cardiovascular diseases in 5 cases (2.6%). The mean total cost of hospitalizations for CA was about 507 Tunisian Dinars (IQR=[355-718])Tunisian Dinars. The median length of hospital stay was 10 days (IQR=[6.25-15]) days. A duration>10 days was statistically more frequent among patients with CA other than gout (Odds Ratio (OR)=2.12; p=0.026). Moreover, gout was statistically more frequent among patients aged less than 65 years old (OR=2.8; p=0.002). The study of the evolution profile of hospitalizations for CA showed a global trend statistically constant across the years (Rho=0.17; p=0.54). As well, there were no statistical variability of hospitalizations trends according to CA type specifically gout (Rho=0.28; p=0.32) and other CA types (Rho=0.08; p=0.77) during the survey period.
Conclusion: CA notably gout continue to be a relatively frequent source of hospitalizations in southern Tunisia with a stable chronological trend over the years. Thus, an adequate and a continuous management must be maintained for patients in order to control the complicated forms of these pathologies.

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Disclosure of Interests: None Declared.
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AB1261 DEVELOPMENT AND VALIDATION OF GOUT "TREAT-TO-TARGET" BOOKLET

Keywords: Education, Gout

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Background: Gout is a treatable disease but often sub-optimally managed. The main gaps identified in gout management are sub-optimal urate lowering therapy (ULT) adherence and lack of adequate ULT dosage.[1] Nurse-led care by providing individualized information led to a reduction in gout flares and tophi,[2] while a structured gout management programme led by pharmacists[3] resulted in a higher rate of reaching serum uric acid (SUA) compared to usual care. Most patients with gout are being managed in primary care setting where nurse-led or pharmacists-led care may not be realistic, especially in developing countries where human resources are limited. Furthermore, clinic visits for every ULT increment can be burdensome to the healthcare system and even patients. Would a booklet on gout be helpful to improve patients' education and ultimately care of patients with gout?
Objectives: This study was conducted to validate our newly developed Gout 'Treat-to-Target' Booklet, which was intended to document individual patient's data relevant to gout and to provide basic written information on gout, for patients' reference.
Methods: This methodological research was conducted following three stages; stage 1 involved the review of the Malaysian Clinical Practice (CPG) for the

Table 1. Associations of Serum Iron levels with the Prevalence of HU in the US adult population. Weighted

		Total(n=25757)				Male(n=12582)				Female (n=13175)			
		OR	95%CI low	95%CI upp	P.value	OR	95%CI low	95%CI upp	P.value	OR	95%CI low	95%CI upp	P.value
Iron	Q1		Ref.	Ref.			Ref.	Ref.			Ref.	Ref.	
	Q2	1.28038	1.10223	1.48733	0.001590	0.91762	0.77062	1.09266	0.336445	0.97520	0.68184	1.39477	0.890840
	Q3	1.52865	1.32013	1.77010	<0.000001	1.01387	0.86415	1.18952	0.866144	1.30254	0.95108	1.78387	0.102158
	Q4	2.18591	1.89460	2.52201	<0.000001	1.42917	1.19726	1.70599	0.000133	1.16573	0.78260	1.73643	0.452212

CI, confidence interval; Ref., reference; OR, odd ratio. The model was constructed by using logistic regression.

management of gout[4] and the EULAR evidence-based recommendations for gout management,[1] stage 2 involved adoption of the content which was written into a booklet called Gout 'Treat-to-Target' Booklet, and stage 3 was the evaluation of the booklet for content and face validity. The content validity index (I-CVI) was assessed by 11 healthcare providers who were involved in managing gout patients (four consultant rheumatologists, two general physicians and five medical officers) using a four-point Likert scale regarding relevancy, clarity, simplicity and ambiguity of each item in the booklet. A scale with excellent content validity composed of I-CVI of 0.79. The face validity index (FVI) was performed by 10 patients with gout who were asked to rate each content item independently (rating 1 and 2 represent invalid comprehensiveness and rating 3 and 4 represent valid comprehensiveness). An FVI for each item of >0.79 was considered relevant.

Results: The size of the booklet was 148 x 120 mm, which fits into pockets of trousers. (Figure 1) It consisted of 15 printed pages (excluding the front page) and divided into two segments. The first segment would contain items related to individual patient's data related to gout such as onset of the first symptoms, onset of tophi, cardiovascular co-morbidities, the SUA target, ULT used (including the dates for dose increment), colchicine dose and SUA level at each visit. The second segment consisted of four appendices which contained basic information on gout (appendix 1: treatment options in gout, appendix 2: medication information, appendix 3: gout diet and appendix 4: recommended gout lifestyle). The I-CVI assessed by the 11 experts for all items were >0.79 (minimum 0.9, maximum 1.0), while the FVI evaluated by 10 gout patients for all items were 1.0.

Conclusion: The development and validation process of our Gout 'Treat-to-Target' Booklet was described. This booklet achieved excellent I-CVI and FVI, and thus would be applicable in clinical practice.

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Figure 1. The front page of Gout 'Treat-to-Target' Booklet in Malay (sized 148 x 120 mm)

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AB1262

AMORPHOUS MINERALIZATION, CHONDROID AND/OR OSTEOID FORMATION IN CRYSTAL INDUCED METABOLIC DISORDERS – A COMPARATIVE STUDY OF APATITE RHEUMATISM, CHONDROCALCINOSIS AND PRIMARY SYNOVIAL CHONDROMATOSIS APATITE RHEUMATISM, CHONDROCALCINOSIS, PRIMARY SYNOVIAL CHONDROMATOSIS

Keywords: Synovium, Crystal arthritis

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Background: Apatite rheumatism (**AR**), chondrocalcinosis (**Ch-C**) and primary synovialis chondromatosis (**prSynCh**) are calcium hydroxyapatite (**HA**) and calcium pyrophosphate dihydrate (**CPPD**) crystal induced progressive metabolic diseases, accompanied by more or less amorphous calcium phosphate [$CaPO_4$], calcium carbonate [$CaCO_3$]) deposits, chondroid and/or bone formation [1 – 5].

Objectives: The **aim** of this study was.

(1)to assess the mineralization, chondroid and/or bone formation of **AR**, **Ch-C** and **prSynCh** with conventional histologic stains and histochemical reactions,

(2)to identify **HA** [$Ca_5(PO_4)_3(OH)$] and **CPPD** [$Ca_2P_2O_7.2H_2O$] crystal deposits in conventionally fixed and stained tissue sections in comparison with unstained sections (Bély and Apáthy 2013) [6].

Methods: Ten joints (6 knees, 1 hip, 3 shoulders) of **5** patients with **AR**, **16** joints (8 knees, 4 hips, 1 shoulder, 1 elbow, 2 wrists) of **16** patients with **Ch-C**, and **21** joints (14 knees, 5 hips, 2 elbows) of **20** patients with **prSynCh** were studied histologically. The amount of amorphous calcium phosphate and/or calcium carbonate deposits, furthermore chondroid and/or bone formation were evaluated by a semiobjective score system in conventionally stained tissue sections (**0** - no mineral deposits, chondroid and/or bone formation, **1** – minimal, **2** – moderate, and **3** – abundant). Standard stained and unstained tissue sections were examined with the light microscope and under polarized light, respectively.

Results: Summary of Patients' Demographics.

Table 1.

Clinical diagnosis	Total n of patients (n=41)	Mean age in years at surgery ± SD	Range of age (In years)
Apatite rheumatism (n=5)	**5 of 41**	**74.80±6.91**	**66 – 82**
Female	4	77.00±5.60	69 – 82
Male	1	66.00	66.00
Chondrocalcinosis (n=16)	**16 of 41**	**63.67±21.17**	**39 – 81**
Female	14	62.00±21.93	39 – 81
Male	2	74.00±1.41	73 – 74
Primary synovial chondromatosis – (n=20)	**20 of 41**	**50.20±12.51**	**30 – 76**
Female	13	53.15±10.49	40 – 74
Male	7	44.71±14.90	30 – 76

The amount of amorphous calcium phosphate and/or calcium carbonate deposits was different in all patient groups; the average value of scores in tissue samples of patients with clinical diagnosis of **AR** was (1.80), with **Ch-C** (2.60), and with **prSynCh** (0.556). Chondroid formation in synovial membranes was minimal in tissue samples of patients with the clinical diagnosis of **AR** (0.058) or **Ch-C** (0.050); osteoid or bone formation was not detected (0.0). Massive chondroid formation (with or without osteoid or bone formation) was characteristic for **prSynCh** (2.1351). In tissue sections stained with **HE**, **HA** crystals were found only in **3** (**4.054** %), and **CPPD** in **15** (**20.27** %) of 74 tissue sections of **28** patients with the clinical diagnosis of **AR**, **Ch-C**, or with **prSynCh**. Using Bély and Apáthy's non-staining technique (2013), different amounts of **HA** and **CPPD** crystals were demonstrated in all **28** patients (**100** %) with the clinical diagnosis of **AR**, **Ch-C** and **prSynCh**. In unstained sections **HA** crystals were found in **49**, (**66.216** %), and **CPPD** in **44** (**59.459** %) of 74 tissue samples. The unstained sections were more efficient to demonstrate **HA** or **CPPD** crystals than conventionally stained ones.

Conclusion: Our study indicates that **AR**, **Ch-C** and **prSynCh** are crystal induced maladies and belong to the same group of metabolic diseases. All of these diseases start with **HA** and **CPPD** crystal deposition which provokes an inflammatory reaction. The inflammatory reaction is inhibited or moderated by calcium carbonate [CaCO3] and/or calcium phosphate [CaPO4] deposition in case of **AR** or **Ch**, and is inhibited or moderated by chondroid and/or osteoid formation in case of **prSynCh**. In our view **prSynCh** is a defect variant of metabolic

disorders, characterized by diminished calcium phosphate and/or carbonate production.

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AB1263 REGIONAL VARIATIONS OF CARDIOVASCULAR RISK IN GOUT PATIENTS: A NATIONWIDE COHORT STUDY IN KOREA

Keywords: Cardiovascular disease, Gout

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Background: Gout is also closely associated with systemic disorders and cardiovascular (CV) risk profiles, such as hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease, alcohol consumption, and obesity.[1] In addition, gout has been suggested as a cause of CV diseases via pathogenic mechanisms such as endothelial dysfunction, oxidative metabolism, platelet adhesiveness, and aggregation. [2-4] Accordingly, several epidemiological studies reported that patients with gout had an increased risk for CV events. [3, 4] In particular, differences in population characteristics between urban regions and other regions are getting more significant owing to recent rapid industrialization. Accordingly, a study on regional differences should be conducted; however, there are still few studies on it.

Objectives: We aimed to investigate the risk of major cardiovascular events in gout patients in different regions.

Methods: This was a nationwide cohort study based on the claims database of the Korean National Health Insurance and the National Health Screening Program. Patients aged 20 to 90 years newly diagnosed with gout after January 2012 were included. After cardiovascular risk profiles before gout diagnosis were adjusted, the relative risks of incident cardiovascular events (myocardial infarction, cerebral infarction, and cerebral hemorrhage) in gout patients in different regions were assessed.

Results: In total, 231,668 patients with gout were studied. Regional differences in cardiovascular risk profiles before the diagnosis were observed. Multivariable analysis showed that patients with gout in Jeolla/Gwangju had a significantly high risk of myocardial infarction (adjusted hazard ratio [aHR] 1.27 [95% confidence interval [CI], 1.02–1.56], P = 0.03). In addition, patients with gout in Gangwon (aHR 1.38 [95% CI, 1.09–1.74], P = 0.01), Jeolla/Gwangju (aHR 1.41 [95% CI, 1.19–1.67], P < 0.01), and Gyeongsang/Busan/Daegu/Ulsan (aHR 1.37 [95% CI, 1.19–1.59], P < 0.01) had a significantly high risk of cerebral infarction.

Conclusion: We found there were regional differences in cardiovascular risk and associated risk factors in gout patients. Physicians should screen gout patients for cardiovascular risk profiles in order to facilitate prompt diagnosis and treatment.

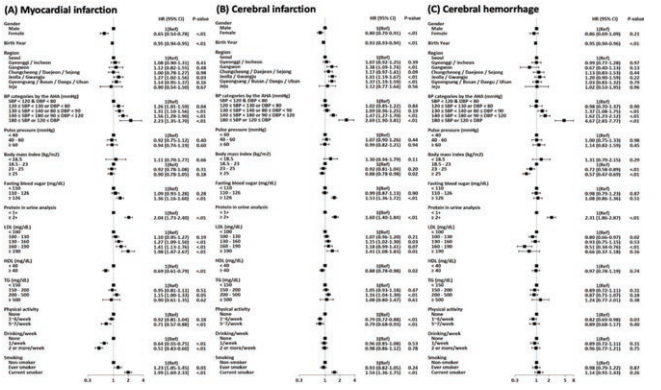


Figure 1. Forest plot of the risk of myocardial infarction (A), cerebral infarction (B), and cerebral hemorrhage (C). BP: blood pressure, DBP: diastolic blood pressure, HDL: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, SBP: Systoric blood pressure, TG: Triglyceride

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AB1264 RHEUMATOLOGISTS BEWARE OF LOW ALP: A CASE OF HYPOPHOSPHATASIA MISDIAGNOSED AS FIBROMYALGIA, CAUSING LONG DIAGNOSTIC DELAY

Keywords: Quality of life, Patient information and education, Rare/orphan diseases

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Background: Hypophosphatasia(HPP), a rare, inherited metabolic disease featuring low serum alkaline phosphatase (ALP) activity due to ALPL (encoding tissue non-specific alkaline phosphatase) gene mutation[1,2]. A wide-ranging clinical spectrum is often seen due to defective mineralisation affecting teeth, bones, joints and muscles[1]. This disease has a prevalence of 1/6370 in Europe and is often misdiagnosed and underdiagnosed with a diagnostic delay of more than ten years[1] The treatment is often supportive for milder cases and enzyme replacement therapy in severe cases.

Objectives: To share this case to raise awareness among Rheumatologists.

Methods: This 58-year-old Caucasian female had her first HPP symptom as early eruption of deciduous teeth, along with recurrent dental infections and gum problems. She was diagnosed with flat feet at age five, had a big toe fracture at sixteen, followed by a metatarsal fracture. She experienced leg muscle cramps and aches, affecting her performance in sport during school life. At the age of thirty she began noticing weakness in arms and legs, which progressed over the years. She faced significant early morning stiffness along with painful ribs, hips, knees, shoulders, and small joints of feet when walking. She was diagnosed with Fibromyalgia at the age of forty-four. The following ten years she met numerous specialists including rheumatologist, pain specialist and physiotherapists. She was also diagnosed with early osteoarthritis, pernicious anaemia, hyperlipidemia, functional neurological syndrome, and central sensitization syndrome. She had multiple trials of steroids and opioids, all of which were stopped either due to side effects or inefficiency. A major flare of symptoms five years ago rendered her bedbound for three months, following which a chemical pathologist noticed a persistent low ALP levels and decided to investigate for HPP. It took another four years to complete these investigations due to the coronavirus pandemic. Currently, she is unable to weight bear or climb stairs and must stay indoors or in bed during flareup. She moved into a ground floor flat at the age of 54 and use a walking stick occasionally. By 58, she is unable to work and had given up her own business due to pain, weakness, and disability.

Results: On clinical assessment, her height is 160 cm, faced difficulty getting up from chair, has an antalgic waddling gait, with a 6-minute walking distance of 60 metre, stopped after three minutes, and had a Brief Pain Inventory pain severity score of 7/10. Her ALP level is 24 U/L and PLP/PA ratio is 18.8 (ref < 5), and genetic testing showed heterozygous missense variant of ALPL gene mutation.

Conclusion: It took more than forty years to reach a conclusive diagnosis of childhood onset HPP. Low ALP level is a signature of HPP and warrants investigations. Diagnosis can be challenging due to the rareness and variable presentation, however recognition of HPP features is crucial for timely referral, optimal disease management and potential improvement in quality of life.

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AB1265 THE INCIDENCE OF ACUTE CORONARY SYNDROME IN GOUT AND ASSOCIATED FACTORS

Keywords: Gout, Heart

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Background: The Gout is a metabolic arthropathy including monosodium urate crystal deposition associated with an increased risk of cardiovascular morbidity and mortality, particularly related to coronary heart disease.
Objectives: The purpose of our work was to determine the frequency of heart attack in our gouty patients and the factors associated with its incidence.
Methods: A retrospective observational study was conducted. The inclusion period was from January 2011 to March 2022.
Results: Our sample included 138 patients. The mean age was 58±13 years and the sex ratio was 1.46 M/W. The mean duration of evolution was 20±28 months. The prevalence of patients with metabolic syndrome including diabetes, hypertension and dyslipidemia was 25.4%, 43.5% and 16.7% of cases respectively. Smoking was present in 9.5% of cases. Medication was found in 31.2% of cases. The disease was mono-articular in 64.5% of cases and poly-articular in 35.5% of cases, with tophus present in 11 patients. Monosodium urate crystals were found in the synovial fluid in 9.4% of cases. The mean uric acid level, C - reactive protein and creatinine were 78.35±22 mg/l; 55.9±86 mg/l and 15±19 mg/l respectively. The number of patients with heart attack in our sample was 22 or 15.9% of cases. In bi-variate analysis, the presence of heart attack in our patients was associated with five factors, age (p=0.007), smoking (p=0.021), drugs including antiplatelet agents (p=0.0001) and loop diuretics (p=0.002), dyslipidemia (p=0.038) and uric acid level (p=0.028). In multivariate analysis, the risk of developing an acute coronary syndrome in our patients followed for gout was increased sevenfold in the presence of smoking (OR=7.591; CI95% [1.474; 39.098]; p=0.015), and fivefold in the presence of dyslipidemia (OR=5.744; CI95% [1.323; 24.947]; p=0.020).
Conclusion: In addition to our work, several previous studies confirm the increased cardiovascular risk of gout but few investigate the predictive factors [1]. Biological studies have indicated that the systemic inflammation induced by the crystals characteristic of gout leads to atherogenesis through endothelial dysfunction [2]. In our sample, the incidence of acute coronary syndrome is associated with smoking and dyslipidemia. The vital prognosis is at stake, hence the need for adequate and early management of this rheumatism as well as the prevention of associated factors.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1266 REVIEW OF THE MANAGEMENT OF GOUT BY THE GENERAL PRACTITIONER

Keywords: Gout, Crystal arthritis

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Background: Gout is the most common microcrystalline arthritis. It is a life-threatening disease due to joint damage, but also due to renal complications, which depends on adequate management of the disease. Unlike other inflammatory arthritides, gout is largely managed in primary care.
Objectives: The objective of this study is to compare the general practitioners management with international recommendations.
Methods: For this we conducted a survey among 117 general practitioners during 1 month. The questionnaire was established in the form of 7 clinical cases.
Results: Oral colchicine is prescribed as first-line therapy in acute access by 85.3% of physicians. In 69% of the physicians, colchicine is combined with analgesics, prednisone or allopurinol. Allopurinol was prescribed alone by 31.9% of physicians. In case of side effects of colchicine, 49.6% of general practitioners recommend reducing the dose of colchicine, 35% of doctors proposed to stop it, 13.7% and 11.1% proposed to replace it by allopurinol and an analgesic respectively. For the initial assessment to be requested before starting allopurinol, 69.8% of the doctors indicated that the renal assessment is systematic before starting the treatment, while no assessment is necessary is noted by 23.3% of the doctors. Thirty-one physicians have a therapeutic goal of lowering uricemia below 50mg/l in case of tophaceous gout versus 45.7% recommending a level below 60mg/l and 4.3% suggesting a level below 70mg/l. The maximum dose of allopurinol not to be exceeded was 900mg noted by 47% of general practitioners, 300mg, 600mg and 1200mg by 21.4%, 17.1% and 15.4% respectively. Hypo-uricemic treatment is indicated in patients with recurrent attacks, arthropathies, tophus or radiological signs of gout. Thus, 8.5% of the physicians recommend disease-modifying therapy for the recommended indications. Among other things, 36.8% of patients recommend starting hypouricemic treatment in the event of asymptomatic hyperuricemia. Regarding patient education, the majority of doctors advise for weight loss (77.6%) and a low purine diet by (75%).
Conclusion: This work has objectified that gout is often poorly managed by general practitioners suggesting the need for continuing medical education of general practitioners which will certainly help improve practices.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1267 THE CORRELATION BETWEEN URIC ACID AND BONE MINERAL DENSITY OF TOTAL HIP WITH BONE MICROARCHITECTURE ANALYSIS IN TOPHACEOUS GOUT PATIENTS

Keywords: Imaging, Bone diseases, Gout

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Background: Gout is the most common inflammatory arthropathy[1]. It is related to elevated uric acid levels and often associated with bone loss[2]. Furthermore, chronic inflammation has been associated with fragility fractures despite normal bone mass by dual-energy X-ray absorptiometry (DXA). However, the evaluation of bone microstructure in patients with tophaceous gout and its association with bone mineral density (BMD) has not been studied yet.
Objectives: The present study aimed to investigate the correlation between densitometric parameters and bone microstructure using high-resolution peripheral quantitative computed tomography (HR-pQCT) in patients with tophaceous gout.
Methods: Eleven male tophaceous gout (Figure 1) patients were enrolled in this cross-sectional study. Patients using drugs that can affect bone metabolism (e.g bisphosphonates, teriparatide and denosumab), corticosteroid use for more than 3 months and those with end-stage chronic kidney disease were excluded. Demographics and clinicals data were obtained through interviews and medical records. Laboratory tests were performed using standard automated methods. DXA was performed to evaluate the BMD. HR-pQCT at the distal radius and tibia was performed to assess trabecular and cortical volumetric BMD (Tb.vBMD= trabecular volumetric BMD; Ct.vBMD= cortical volumetric BMD), microstructure (Tb.N= trabecular number, Tb.Th= trabecular thickness, Tb.Sp= trabecular separation, Ct.Th= cortical thickness, Co.Po= cortical porosity) and strength (S= stiffness, F.Load= failure load) bone parameters. Pearson's correlation (r) tests were performed.
Results: Demographic data are described in Table 1. Uric acid levels were negatively correlated with HR-pQCT microstructure data, such as Ct.Th tibia (r= -0.720, p= 0.029) and S tibia (r= -0.810, p= 0.008) as well as DXA data, such as lumbar spine BMD (r= -0.685, p=0.02).On the other hand, it

was found a positive correlation between BMD of total hip and Tb.N tibia (r= 0.743, p= 0.035), Ct.Th tibia (r= 0.902, p= 0.005) and S tibia (r= 0.938, p= 0,001).

Conclusion: The results of this study showed that uric acid levels were negatively correlated with tibia bone microarchitecture parameters. However, total hip BMD was positively correlated with these tibia bone microstructure data.

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Table 1. Clinical and demographic characteristics of patients.

	Tophaceous Gout (n = 11)
Age (years)	62.5 ± 11.5
BMI	31.1 ± 7.9
Number of tophi	8.0 ± 10.5
Years of disease	16.4 ± 7.6
Calcium (mg/dL)	9.4 ± 0.3
Vitamin D (ng/mL)	26.2 ± 8.3
HDL (mg/dl)	39.6 ± 10.4
LDL (mg/dl)	112.2 ± 45.0
Triglycerides (mg/dl)	235.1 ± 117.0
ESR (mm/h)	21 ± 39
CRP (mg/L)	5.3 ± 6.1
Nephrolithiasis	(4) 36.4
Diabetes	(5) 45.5
Hypertension	(8) 72.7
Gout crises in the last 3 years	(7) 63.6

Results are expressed in mean ± SD (standard deviation), or n (%).ESR: erythrocyte sedimentation rate; CRP: c-reactive protein; LDL: low-density lipoprotein; HDL: High-density lipoprotein; BMI: Body mass index.



Figure 1.

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AB1268

FIRST DIAGNOSIS OF MONOSODIUM URATE CRYSTAL FROM CEREBROSPINAL FLUID IN PATIENT WITH NECK PAIN

Keywords: Spondyloarthritis, Crystal arthritis, Gout

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Background: Gout is a common arthritis caused by the deposition of monosodium urate (MSU) crystals within joints after chronic hyperuricemia. Deposition of MSU in the spine as a rare manifestation of gout, but the actual prevalence of spinal involvement is unknown.

Objectives: We present a vertebral osteomyelitis and spinal meningitis misdiagnosed cervical spinal gout.

Results: An 85-year-old man was admitted due to a 5-day history of fever and neck pain. On admission, physical examination revealed neck pain and stiffness. He had a blood pressure of 140/102 mmHg, pulse rate of 95/min, respiration rate of 18 breaths/min, and body temperature of 38.0°C. Laboratory results revealed a white blood cell count (WBC) of 11,200/mm^3 (reference: 4,000–10,000) and C-reactive protein level of 12.26 mg/dL (reference: 0.0–0.3). Magnetic resonance imaging findings suggested cervical osteomyelitis and meningitis (Figure 1A). Cervical spine computed tomography (CT) revealed curvilinear calcifications of the transverse ligament of the atlas (Figure 1B). After assessing blood cultures, an empirical antibiotics were administered intravenously. On the second day of admission, cerebrospinal fluid (CSF) analysis did not reveal meningitis (WBC 8/μL; glucose and protein levels 79 and 168 mg/dL, respectively), and CSF culture and molecular tests were negative for bacteria and mycobacteria. The patient was diagnosed with crowned dens syndrome and administered with 20 mg prednisolone, and his symptoms dramatically improved. However, CSF examination under polarising microscopy revealed monosodium urate (MSU) crystals (Figure 1C), and dual-energy CT confirmed the calcifications to be MSU crystals (Figure 1D).

Conclusion: Crowned dens syndrome is a rare finding in calcium pyrophosphate deposition disease and may be clinically similar to meningitis, so it should be suspected when the evidence for infection is unclear. Our patient had gout history, and MSU crystals were confirmed by CSF analysis and dual-energy CT, suggesting that the symptoms were caused by gout flare in the cervical spine. Thus, physicians should consider that intrathecal MSU crystal formation can cause meningitis-like symptoms in patients with gout history.

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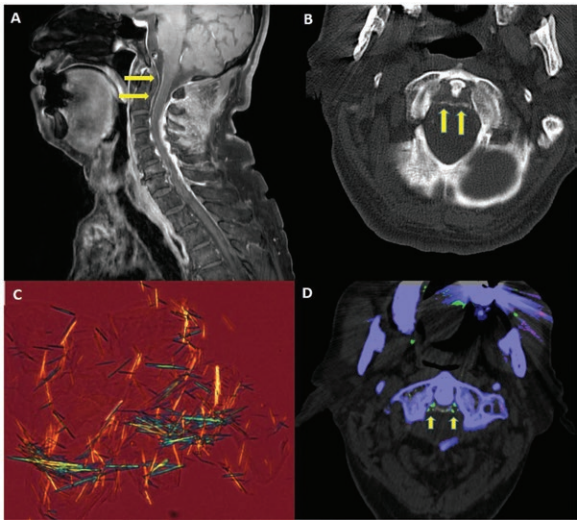


Figure 1. Images and monosodium urate crystal from cerebrospinal fluid in patient with cervical spinal gout

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1269 HEARING LOSS – A RARE MANIFESTATION OF THE CALCIUM PYROPHOSPHATE DIHYDRATE DEPOSITION DISEASE

Keywords: Descriptive studies, Crystal arthritis

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Background: Calcium pyrophosphate dihydrate (CaPPD) deposition disease is a illness with a wide range of manifestations from acute gout-like episodic arthritis to an accentuated osteoarthritis picture. A common feature is the deposition of CaPPD crystals in tissues. Middle ear involvement is a rare manifestation of the disease, described in a few case reports.
Objectives: Middle ear involvement is a rare manifestation of the disease, described in a few case reports.
Methods: Histological examination of operating specimen.
HRCT.
Results: 71-year-old man, athlete (tennis, cycling) underwent a partial menisectomy in 2008 for acute knee blockade, in October 2022 he suffered polytrauma after a traffic injury. Het is treated for arterial hypertension. He has never had inflammatory arthritis, joint problems he had only in connection with sports injuries. Last 12 months he has observed a gradually progressing hearing loss, mild dizziness and tinnitus. HRCT of a scull base demonstrated a left-sided osteoma with fixation to the malleus. Tumor mass was removed by surgery. Histology proved calcium pyrophosphate dihydrate crystals in the operating material. We have not demonstrated hyperparathyroidism, hypomagnesemia, or any other primary disease associated with CaPPD deposition. During subsequent X-ray examination, we found the chondrocalcinosis of the menisci of both knees.
Conclusion: Deposits of calcium pyrophosphate in the middle ear region are a rare manifestation of the calcium pyrophosphate dihydrate deposition disease. Clinically, progressive hearing loss may occur, morphologically resemble osteoma and may not be associated with other clinical signs of the underlying disease.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1270 ANALYSIS OF PREVALENCE AND RELATED RISK FACTORS OF HYPERURICEMIA IN BOZDUN AKSU PREFECTURE OF XINJIANG

Keywords: Gout

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Objectives: To investigate the prevalence of Hyperuricemia (HUA) in Bozidun Kirghiz Township, Aksu region, Xinjiang, and to explore the risk factors for the occurrence of HUA in the local area.
Methods: A cross-sectional survey study was conducted by randomly selecting 9 villages in Bozidun Kirgiz Township by the whole-group sampling method and using a questionnaire distributed to households. The questionnaire included: general information, history of previous diseases, personal history, and all subjects were measured for he-ight, weight, blood pressure, abdominal circumference, etc. The diagnostic of HUA: serum uric acid (SUA) >420μmol/L in men or >360μmol/L in women.
Results: ①A total of 2138 subjects were surveyed, among which 68 patients with HUA, the prevalence of HUA in Bozidun Kirghiz Township, Aksu regionrate general population was 3.2% (68/2138); the prevalence rate of men was 4.6%, with 45 patients; and the prevalence rate of women was 2.0%, with 23 patients. The peak age of male and female patients was 51~60 years old. ②The prevalence of HUA was lower in those who consumed dairy products, nuts and eggs, and lower in those who consumed more. Different intake of cereals, meat, vegetables and fruits had no effect on the prevalence of HUA.③In terms of different life behaviors, the prevalence of HUA in men who had been smoking was higher than those who had never smoked (57.78%, 28.89%, 13.33%, P=0.017). In the relationship between drinking and HUA, the prevalence rates of male always drinking, ever drinking and never drinking were 80.00%, 11.11% and 3.89%, respectively, showing significant differences(P=0.038);④Multi-factor logistic regression analysis showed that BMI, age, TG, Cr and WBC were risk factors for the occurrence of HUA.
Conclusion: The prevalence of HUA in Bozidun Kirgiz township in Aksu prefecture of Xinjiang is lower than that in other areas with continental climate. High body mass index, old age, high triglyceride, increased creatinine and increased white blood cell count are the risk factors for the development of HUA.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1271 FACTORS ASSOCIATED TO FRAGILITY FRACTURES IN RA PATIENTS: IS URIC ACID INCRIMINATED?

Keywords: Osteoporosis, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) has been reported to be associated with low bone mineral density (BMD) and increased risk of fractures. Recently, several observational studies have revealed that a higher serum uric acid level was associated with higher bone mineral density (BMD), and therefore, a reduced risk of osteoporosis and fragility fractures in men, post- and perimenopausal women. Although the relationship between serum UA levels and BMD has been evaluated in the general population, data regarding the effect of UA levels on bone loss in patients with RA was lack [1].
Objectives: To evaluate the relationship between UA levels, BMD and fragility fractures (FF) and the different factors associated with the occurrence of FF in RA patients.
Methods: We conducted a cross-sectional study in a single rheumatology hospital in Morocco. All patients satisfied the ACR-EULAR 2010 RA classification criteria. All the patients underwent BMD examination by dual energy x-ray absorptiometry and serum UA levels measurement. Osteoporosis was diagnosed when the T-score was - 2.5 or less. Socio-demographic data, comorbidities, disease-related variables (duration, characteristics, and drugs) were also collected. Statistical analysis were performed with SPSS 22.
Results: We included 88 (85.44%) women and 15 (14.56%) men with a mean age of 52.59 ± 14.77 years old. They had a mean disease duration of 14.27±10.84 years, a mean DAS 28 CRP of 2.59 ±1.35. Their mean lumbar spine, femoral neck and total proximal femur were 0.843 ± 0.134, 0.694 ± 0.111, and 0.826 ± 0.119 respectively. The UA levels were elevated in 10.8 % of patients, dyslipidemia was found in 19.3 % of patients and 38.9 % of the patients had osteoporosis. There was no correlation between UA concentrations and BMD, whether at the lumbar spine femoral neck and total proximal femur, and UA and fragility fractures. However, the occurrence of fragility fractures was significantly associated to BMD at the femoral neck (0.606 ± 0.126 vs 0.705 ± 0.104; p=0.027), to high concentrations of LDLc (3.69 ± 0.38 vs 2.71 ± 0.77 mmol/L; p=0.004), Total cholesterol (5.84 ± 0.74 vs 4.55 ± 0.85 mmol/L; p=0.001), ACPA antibodies titres (364.25 ± 101.35. vs 167.96 ± 120.30; p=0.047), cumulative corticosteroid dose (11057.64 ± 4653.35 vs 1330.20 ± 211.80 mg; p=0.008), to BMI (22.41 ± 4.41 vs 27.24 ± 4.94; p=0.018) and to the glomerular filtration rate (87.43 ± 12.11 vs 103.50 ± 15.38; p=0.018).
Conclusion: Although there was no relation between UA levels, BMD and FF in our population. FF were related to ACPA antibodies, BMD, kidney fonction and corticosteroid use.
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Infection-related rheumatic diseases

AB1272 **SHOULD RHEUMATOLOGISTS ROUTINELY REQUEST PARASITE SEROLOGY IN CANDIDATES FOR IMMUNOSUPPRESSIVE TREATMENT? PREVALENCE OF STRONGYLOIDES STERCORALIS IN A NON-ENDEMICAL AREA (CATALONIA, SPAIN)**

Keywords: Inflammatory arthritides, Epidemiology, Infection-related RMDs

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Background: Infection is one of the main causes of morbidity and mortality in patients with autoimmune and immune-mediated diseases (AI/IMID). Multiples recommendations exist for prevention of bacterial and viral infections, however, there are no specific recommendations for parasitosis. Strongyloidiasis is an infection caused by *Strongyloides stercoralis.* This parasite is distributed globally throughout tropical and subtropical areas. The majority of cases in Spain are imported. Often this infection is asymptomatic, however, in immunosuppression situation, severe presentations, hyperinfestation syndrome or disseminated strongyloidosis can occur.
Objectives: To determine the prevalence of positive *S. stercolaris* serology and describe the epidemiological, clinical and analytical characteristics of this subjects.
Methods: Cross-sectional study. Subjects: patients with AI/IMID candidates for immunosuppressive treatment. Study period: patients attended in the Rheumatology Service between June 2018 and December 2022. Main outcome: Prevalence of *positive S. stercoralis* serology. Independent variables: demographic, clinical manifestations and travels to endemic countries. Statistical analysis: descriptive and bivariate analysis.
Results: Three hundred and ten patients were included. The majority were women (63.2%) with a mean age of 55.9 years (SD 14.7) and 9.3% were not born in Spain. Our patients had and inflammatory arthritis (81.2%) or an autoimmune disease (8.1%). At the moment of serology determination, 41.9% received disease-modifying antirheumatic drug and 54.9% prednisone. Positive serology was found in 10 patients (3.2%; 95%CI: 1.6-5.9) and 4 (1.3%; 95%CI: 0.4-3.3) were indeterminate. No patient developed symptomatic infection nor hypereosinophilia. Every positive patient received prophylactic therapy with ivermectin. The 60% of patients didn't referred any epidemiological risk, 10% were born in endemic country but have never returned, 10% were born in endemic country and have visited this country subsequently, and 20% were born in non-endemic country and had travelled to an endemic zone. No differences were observed in the prevalence of *S. stercolaris* according to sex, disease, treatments nor epidemiologic contacts. Patients with positive serology were younger (48.4 years vs 56.2; p=0,048). The highest prevalence of infection was observed in workers of the quinary sector (12%; p=0.072).
Conclusion: Prevalence of *S. stercolaris* infection in rheumatic patients in our area is 3.2%. Increasing migration and international travelling was suspected the most probable cause of this prevalence. Surprisingly no epidemiological risk was referred in 60%. Although none of our patients presented active infection, serological determination and prophylactic treatment should be routinely assessed in candidates for immunosuppressive therapy due to the potential lethality of *S. stercolaris.*
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1273 **RARE INFECTION RELATED ARTHROPATHIES IN RHEUMATOLOGY: A MULTI-CENTRIC STUDY**

Keywords: Rheumatoid arthritis, Infection-related RMDs, Inflammatory arthritides

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Background: Various infections can mimick inflammatory arthropathies and misdiagnosed as rheumatoid arthritis, Spondyloarthritis or lupus. Occasionally, rare infections prevalent in a specific geographical region may present with arthritis as their first and only symptom which may confuse the clinician leading to incorrect diagnosis and management. Many a times, such patients land up in a rheumatology clinic prior to the diagnosis. Hence, Rheumatologists practicing worldwide should be aware of such manifestations of infectious diseases.
Objectives: Main objective of this multi-centric study was to appraise the clinical features and demographics of various rare infectious diseases (newly or previously diagnosed) that presented with arthritis.
Methods: This retrospective study (January 2022- December 2022) was carried out at 3 tertiary care centres, two in central India (city Indore and Bilaspur) and 1 in northern India (city Saharangpur). Patients who were previously diagnosed with an infectious disease and presented with arthritis were included. Patients with arthritis who were diagnosed as infectious disease were also included. Their details regarding demographics and clinical presentations were collected. Pearson chi-square test was applied and cases were studied according to their Age, Sex, distribution of joints, rheumatoid arthritis (RA) factor and anti cyclic citrullinated peptide (anti-ccp) antibodies positivity,presence of myalgias, rashes, extra-articular manifestations and cutaneous manifestations.
Results: Seventy- nine patients (39 male) were identified. Out of these,34 (43%) patients had chikungunya arthritis, 12 (15.2%) leprosy, 11 (13.9%) Covid-19, 10 (12.9%) Dengue, 4 (5.1%),Hepatitis C, 4 (5.1%) HIV, 3 (3.8%) HCV and 1 (1.3%) Poncet's disease. No significant association was seen among rheumatoid factor (p=0.494) or anti-ccp antibodies positivity (p=0.987) with these diseases. Patients with chikungunya had oligoarthritis (14.7%) or polyarthritis (85.3%). Patients with Covid-19 had oligoarthritis (18.2%), polyarthralgia (27.3%) and polyarthritis (54.5%). Patients with dengue, HCV and Poncet's disease had only polyarthritis. Majority of the patients with hepatitis C and leprosy had polyarthritis. Patients with HIV showed enthesitis (25%), oligoarthritis (25%) and polyarthritis (50%). There was a statistically significant association between presence/ absence of myalgia and infectious diseases (P=0.001). It was absent in patients with hepatitis C. Only about one-third of the patients with leprosy had myalgia; while most of the patients with other infectious diseases had myalgia. 20% of the dengue patients and 41.7% of the leprosy patients had rashes, while rashes were absent in patients with other infectious diseases. Erythema nodosum was seen in only 25% patients with leprosy; while it was absent in the patients with other infectious diseases. Extra-articular manifestations were seen in 35.3% patients with chikungunya, 9.1% with Covid-19, 20% with dengue, 25% with hepatitis C, 33.3% with leprosy and 100% patients with Poncet's disease; while extra-articular manifestations were not seen in patients with HCV and HIV infection. 9.1% patients with Covid-19, 25% with hepatitis C, 25% with HIV, 83.3% with leprosy had cutaneous manifestations, while cutaneous manifestations were not seen in patients with chikungunya arthritis, dengue, HCV and Poncet's disease.
Conclusion: Rheumatological manifestations of various infections can mimic various inflammatory arthritis and can be a diagnostic challenge. Apart from the joint involvement, these infections can also have various extraarticular manifestations as well. One should be aware of such manifestations as increased awareness can prevent diagnostic delay and complications.
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Disclosure of Interests: None Declared.
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AB1274 **RISK FACTORS FOR ACTIVE TUBERCULOSIS DURING FOLLOW-UP IN PATIENTS WITH RHEUMATIC IMMUNE DISEASE**

Keywords: Infection-related RMDs, bDMARD

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Background: Rheumatic immune disease is a group of diseases caused by the strong immune response to self-antigens, leading to tissue and cell damage, affecting bone, joints, bursa, muscle and its surrounding soft tissues (tendons, ligaments and fascia). The risk of tuberculosis infection in rheumatic immune patients is 2 to 5 times [1-3] than that of the general population. Patients with rheumatic immune diseases require long-term treatment with glucocorticoids and immunosuppressants, and the risk of complicated tuberculosis infection significantly increases in [4]. When active tuberculosis infection occurs in rheumatic immune patients, quite a number of patients have atypical clinical manifestations, severe disease, difficult to cure, long infection time, high fatality rate, which seriously endanger people's health. Therefore, this study intends to explore the risk of active tuberculosis infection using immunosuppression agents and biological agents in patients with rheumatic immune diseases.
Objectives: The risk factors of active TB in rheumatic immune disease patients were explored.
Methods: The confirmed patients who went to the Rheumatology and Immunology Department of Xinjiang Uygur Autonomous Region from December 2014 to June 2015 were included. The clinical data and treatment plan were collected, followed up to December 2021 and the prognosis were collected. The risk factors of active tuberculosis were analyzed by K-M survival curve method.
Results: Data of 499 patients collected in this study, Including: In 213 cases of rheumatoid arthritis, In 79 cases of ankylosing spondylitis, In 84 cases of systemic lupus erythematosus, In 58 cases of Sjogren's syndrome, And 65 patients with other rheumatic diseases; Of them, 62 patients were lost to follow-up, Ten patients have died, Four patients were diagnosed with active TB infection when enrolled; Thus, 423 patients were included in the study, Among these, 109 males (25.8%), In 314 women (74.2%), Mean age was 48.2 ± 13.7 years, The mean follow-up was 80.2 ±7.7 months, Six cases of active tuberculosis (one case was bone tuberculosis, One case had a pleural tuberculosis, The remaining four cases were pulmonary tuberculosis). Survival analysis showed that patients with rheumatic immune diseases had an increased risk of using immunosuppressive agents compared with active TB infection (p=0.039) and an increased risk of using biologics compared with active TB infection (p=0.004). Multivariate COX regression analysis showed that the use of biologics was an independent risk factor in rheumatic immune disease patients with active TB (P=0.011).
Conclusion: Patients with rheumatic diseases have an increased risk of active TB using immunosuppressants or biologic agents , Use of biologic agents is an independent risk factor for the emergence of active TB.
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AB1275 **NEISSERIA GONORRHOEAE ARTHRITIS: A GROWING PROBLEM**

Keywords: COVID, Infection-related RMDs, Epidemiology

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Background: *Neisseria Gonorrhoeae* infection (commonly gonococcus) have increased in recent years. Additionally, an increase in the antibiotic-resistance of the bacteria has been detected, including broad-spectrum cephalosporins, which could lead to untreatable complications like arthritis.
Objectives: The goal of this study is to describe the gonococcal arthritis events identified in a Rheumatology service between 2008 and 2022.
Methods: Retrospective longitudinal observational study based on the review of the medical records of patients diagnosed with gonococcal arthritis in the Rheumatology Department of the Doctor Peset University Hospital in Valencia (Spain) since 2008 to 2022. Sociodemographic and clinical variables, antibiotic sensitivity profile and antibiotic therapy used were studied. Evolution of infections were also analyzed.
Results: Eight cases of gonococcal arthritis were recorded in the period analyzed, all of them diagnosed between the years 2021-2022. All patients except one were male. Half of the patients had sexual transmitted infection history, 75% of which were syphilis infected and 25% had previous hepatitis B infection. The most common form of presentation was oligoarthritis. In three cases a component of tenosynovitis was also observed. Diagnostic arthrocentesis was performed in seven of eight cases and a high profitability of synovial fluid culture was observed (only in one patient bacteria was not isolated). All infections showed cephalosporin and azithromycin sensitivity, all of them displayed a favorable evolution (Table 1).

Table 1. Antibiotic sensitivity profile, treatment regimens administered and duration of treatment, need for surgery and evolution of the infection.

CASE	ANTIBIOTIC SENSITIVITY PROFILE	HOSPITAL TREATMENT	OUTPATIENT TREATMENT	NEED FOR SURGERY	EVOLUTION
CASE 1	Ceftriaxone, cefotaxime, cefixime, gentamicin, azithromycin, doxycycline.	Ceftriaxone (6 days).	Cefixime (14 days).	No.	Resolution.
CASE 2	Ceftriaxone, ceftazidime, cefixime, ciprofloxacin, levofloxacin, azithromycin.	Gentamicin + azithromycin (Three days).	Ciprofloxacin (10 days).	No.	Resolution.
CASE 3	Ceftriaxone, cefotaxime, cefixime, azithromycin.	Ceftriaxone (7 days).	Cefixime + Azithromycin (14 days).	No.	Resolution.
CASE 4	Penicillin, ceftriaxone, cefotaxime, aztreonam, rifampicin, azithromycin, chloramphenicol.	Cloxacillin + ceftriaxone (2 days). After ceftriaxone (4 days).	Amoxicillin-clavulanic acid (1 month).	Yes (elbow arthrotomy and debridement).	Resolution.
CASE 5	Ceftriaxone, cefotaxime, rifampicin, ciprofloxacin, clindamycin, azithromycin.	Ceftriaxone (7 days).	Ciprofloxacin (7 days).	No.	Resolution.
CASE 6	Unrealized.	Not hospitalized.	Azithromycin + cefixime (single dose).	No.	Resolution.
CASE 7	Penicillin, ceftriaxone, cefotaxime, cefixime, azithromycin.	Ceftriaxone + cloxacillin + doxycycline (2 days). After ceftriaxone (7 days).	Intravenous ceftriaxone by Home Hospitalization Unit (21 days).	No.	Resolution.
CASE 8	Ceftriaxone, cefotaxime, cefixime, azithromycin.	Patient refuses hospitalization.	Levofloxacin (14 days).	No.	Lost to follow up.

Conclusion: An increase in gonococcal arthritis cases has been detected in the Rheumatology Department of the Doctor Peset University Hospital in the last two years, overlapping with the end of the social restrictions caused by the COVID-19 pandemic. Despite having described in recent years a growing increase antibiotic resistance, in our study the antibiotic sensitivity profiles were favorable without isolating strains resistant to cephalosporins or azithromycin.
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AB1276 SCREENING FOR LATENT TUBERCULOSIS INFECTION BEFORE BIOLOGICS IN ALGERIAN PATIENTS WITH RHEUMATIC DISEASES

Keywords: Infection-related RMDs, bDMARD

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Background: The use of biological agents has significantly improved the management of chronic rheumatic diseases (CRD). However, these treatments increase the risk of tuberculosis due to the reactivation of a previous latent tuberculosis infection (LTBI), making its diagnosis and treatment very important prior to initiating therapy.
Objectives: To identify the prevalence of LTBI in Algerian patients with CRD before the initiation of biotherapy.
Methods: We conducted a multicenter, retrospective study over a period of 10 years including patients with CRD receiving biological therapy for at least 6 months. LTBI diagnosis was based on a positive tuberculin skin test (TST) or QuantiFERON-TB Gold In-Tube test (QFT-GIT) without clinical symptoms, and bacteriological and radiographic signs of disease.
Results: 271 (154 men/117 women) were included, and the mean age of patients was 40.6± 12.9 years. The most common CRD was ankylosing spondylitis (57.9%) followed by rheumatoid arthritis (22.1%), psoriatic arthritis (12.2%), and spondyloarthritis associated with inflammatory bowel disease (4.8%). Patients received adalimumab in 117 (43.2%) cases, etanercept in 89 (32.8%) cases, infliximab in 40 (14.8%) cases, tocilizumab in 24 (8.9%) cases and anakinra in 1 case. Medical history of tuberculosis was noted in 3 cases and 4 patients have a history of household contact with tuberculosis. TST was performed in 186 cases and was positive in 13.2%. 261 patients underwent a QFT-GIT, which was positive in 16.9%. The diagnosis of active pulmonary tuberculosis was made in one patient who had positive TST and images of active tuberculosis in the chest X-ray. Quadruple therapy including rifampicin (10mg/kg/day), isoniazid (5mg/kg/day), pyrazinamide (25mg/kg/d) and ethambutol (15mg/kg/d) was prescribed for this patient. However, LTBI was diagnosed in 54 cases (19.9%), 29 had negative TST with positive QFT-GIT. 34 patients received a combination of rifampicin and isoniazid for three months and 20 received the isoniazid monotherapy for six months without developing active disease. Hepatotoxicity was observed in 5.6% of cases. The biological therapy was initiated 10.34±9.96 weeks after chemoprophylaxis, and 55.5% were treated with etanercept. After a follow-up of 23.5±15.7 months 4 cases of active tuberculosis infection were reported (2 lymph nodes, 1 pleural, and 1 intestinal tuberculosis) in patients with initially negative TST and QFT-GIT. One patient had TST conversion and received antibiotic prophylaxis.
Conclusion: Our study showed that the screening and chemoprophylaxis recommendations for LTBI improve the safety of biological treatments. However, because tuberculosis infection remains a potential complication, especially in endemic countries like Algeria, we suggest that annual screening of patients on biotherapy could reduce the risk of active tuberculosis.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1277 FACTORS ASSOCIATED WITH THE PRESENCE OF SPINAL EPIDURAL ABSCESS IN SPONDYLODISCITIS

Keywords: Infection-related RMDs

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Background: Spondylodiscitis (SD) is a severe infectious disease that affects the intervertebral disc and adjacent vertebral bodies, but may also extend to adjacent neural structures and cause a spinal epidural abscess (SEA). The clinical picture of SD is not very specific, but there are clinical and radiological differences that may point to an epidural extension.
Objectives: This study aimed to compare the clinical, biological, and radiological features of spondylodiscitis (SD) with and without spinal epidural abscess (SEA).
Methods: We conducted a retrospective monocentric study involving 90 cases of SD admitted between January 2009 and August 2022 at our rheumatology department. Clinical, laboratory, and radiological data of the patients were collected.
Results: Among the 90 patients with SD, 54 (60%) had a spinal epidural abscess. The mean age of the SEA group was 54 ± 13.52 years [23-82]. A female predominance was observed with a sex ratio (M/F) of 0.92. Thirty-seven patients or 68.5% had at least one comorbidity. Diabetes was the most frequent comorbidity (33.3%). All our patients had back pain on admission. Motor deficits were reported in 48% of the patients with the heaviness of the limbs. Fever was reported in 46.3% of cases. Physical examination revealed spinal stiffness in 23.3% of the patients, motor deficit in 37%, sharp osteotendinous reflexes in 18.5% of the patients, and abolished in 9.25%. The blood tests showed hyperleukocytosis in 18 patients (36%). An erythrocyte sedimentation rate greater (ESR) than 100mm at the first hour was found in 17 patients. C-reactive protein (CRP) greater than 100mg/ml was found in 14 patients. 64.8% had pyogenic spondylodiscitis (mainly Staphylococcus aureus), 11.1% had brucella spondylodiscitis and 24.1% had tubercular spondylodiscitis. MRI confirmed the diagnosis of SEA in all cases. The lesions were located at the cervical level in 9.2% of cases, at the dorsal level in 24 %, and at the lumbar level in 48.1% of cases. The lesions were anterior in 64.8% of cases and anterolateral in 35.2% of cases. The involvement was uni-focal in 63% of cases and extensive in 37% of cases. SEA was significantly more frequent in elderly patients (51.4% vs 48.6% p=0.038). The presence of a neurological deficit (80% vs 20% p=0.016), spinal cord compression (71.4% vs 28.6% p=0.04), and Multifocal involvement (82.6% vs 17.4% p=0.01) were significantly associated with SEA. There was no significant association between the types of germs and the presence of SEA.
Conclusion: In our study, a little more than half of patients with spondylodiscitis had a spinal epidural abscess. This entity was associated with advanced age, multifocal involvement, and neurological deficit. Therefore, a high index of suspicion is warranted when a patient presents these signs.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1278 ANALYSIS OF THE DIFFERENCES BETWEEN TUBERCULOSIS PROPHYLAXIS REGIMENS IN BIOLOGIC CANDIDATE PATIENTS

Keywords: Descriptive studies, bDMARD, Safety

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Background: Patients with systemic rheumatic disease present alterations in the regulation of the immune system, which may contribute to the reactivation of latent tuberculosis. That risk increases significantly in patients receiving biological treatment (approximately 10%, especially with infliximab). The detection and treatment of latent tuberculosis infection constitutes a fundamental pillar to prevent the evolution of the pathology in patients receiving biological therapy protocolized in the US in the year 2000 by the FDA. Multiple studies have shown that diagnosis and treatment of latent tuberculosis infection is the best method of preventing progression to active tuberculosis.
To prevent that condition que have two types of treatment schemes:
-The short chemoprophylaxis regimen,consisting of the administration of isoniazid together with rifampicin for 3 months
-The long chemoprophylaxis regimen consisting of the administration of isoniazid for a period of 6 months without interruption.
Objectives: To analyze the efficacy,safety and to difference the treatment adherence between the two regimens of chemoprophylaxis in patients who are candidates to start biologic therapy with latent tuberculosis.
Methods: Retrospective descriptive study of a cohort of patients who start biological therapy between (January-December 2021), in the Rheumatology Service of Virgen del Rocio Hospital. Latent tuberculosis screening protocol was performed by Mantoux/Booster and IGRA tests.
Results: We included a total of 223 patients in the study who started treatment with biological therapy, during a period of 12 months, 125 (58,13%) of those where men, 90 patients (41,8%) were women with a mean age of 51.4 years. We started chemoprophylaxis in 32 patients, of whom 15 (46.8%) received short therapy with

isoniazid/rifampicin daily for 3 months, only 1 patient he had to discontinue treatment due to hepatotoxicity. The rest of the patients 17 (53.2%) underwent long therapy for 6 months with isoniazid 300 mg every 24 hours, completing it in 94.2% of the cases. Only one patient had to discontinue due to persistent nausea.

Conclusion: After analyzing the data of our cohort of patients candidates to start biological therapy and after having performed the screening for latent tuberculosis infection(as can be seen in the Table 1 below) a homogeneous group (46.8% in the case of short regime) and (53.2% in the case of long regime) were treated with chemoprophylaxis, without significant differences in terms of adverse effects or adherence in the two therapies performed. The most common cause of discontinuation in both groups was hypertrasaminasaemia and nausea. No tuberculosis reactivation has occurred in any of the groups. Therefore, we conclude that short term therapy is as safe as long therapy and with similar patient adherence. However, long-term studies with a larger number of patients are required to evaluate the two treatment regimens.

Table 1.

N (TOTAL)	223
MEN %	125(59.6%)
WOMEN %	90(49.4%)
MEAN AGE	51.4
MANTOUX	
+	23(10.3%)
-	200(89.7%)
BOOSTER	
+	16(7.2%)
-	207(92.8%)
IGRA	
+	29(13%)
-	197(87%)
CHEMOPROPHYLAXIS	32(14.3%)
ISONIAZID TOGETHER WITH RIFAMPICIN FOR 3 MONTHS	15 (46.8%)
SUSPENSION	1(6.6%)
HEPATOTOXICITY	1(6.6%)
REACTIVATION TBC	0(0%)
ISONIAZID FOR 6 MONTHS	17(53.2%)
SUSPENSION	1(5.8%)
NAUSEA	1(5.8%)
REACTIVATION TBC	0(0%)

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1279 CLINICAL FEATURES AND FUNCTIONAL OUTCOME OF SURGICALLY TREATED TUBERCULOUS AND BRUCELLAR SPONDYLODISCITIS IN TUNISIA

Keywords: Infection-related RMDs, Motor function

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Background: Tuberculous and brucellar spondylodiscitis are still a frequent condition in the Mediterranean countries [1]. Management of spondylodiscitis may require surgical procedures in case of spinal cord or root compression, bone destructions and deformities, unsuccessful medical treatment or large abscesses.

Objectives: To study characteristics and outcome of surgically treated tuberculous and brucellar spondylodiscitis.

Methods: Medical records of patients who presented to the physical therapy and rehabilitation ward or outpatient clinics after spine surgery for spondylodiscitis were retrospectively studied. The study included records from January 2010 to December 2022.

Results: Thirty-two patients were diagnosed with spondylodiscitis for which they underwent surgery. Mean age of diagnosis was 44,6 ± 10.4 years. The sex ratio was 1:1. Atypical presentations caused diagnosis to be delayed in 37,5% of the patients. Back pain was the most frequent symptom seen in 78,12% of the cases, radicular pain was seen in 46,7% of the cases, fever in 37,5% of the patients and abnormal gait in 68,7% of the cases. Tuberculosis caused 71,8% of cases and brucellar infection 28,1% of the cases. On biology, elevated inflammatory markers were noted in 68,7% of the cases. Intradermal reaction for tuberculosis was positive in 11 patients while cultures allowed the diagnosis of tuberculosis in 1 patient. Wright serology test confirmed the diagnosis of brucellar infection in all 9 cases. Vertebral biopsy or intraoperative samples allowed the diagnosis of the tuberculous spondylodiscitis in the remaining cases. Cervical spine location was involved in 9,3% of cases, lumbar spine in 43,75% and dorsal spine in 34,3% of the cases. All patients have been prescribed antibiotics and spinal immobilization. Surgery was indicated in 71.8% of cases for spinal cord decompression and in 28.1% of the cases for voluminous abcesses. Anterior approach was used in 9,3% of the cases and posterior approach in 90.6% of cases. 37.5% of the patients benifited concomitantly with spinal fusion surgery. Post-operative complications were reported in 43,75% of the cases. They consisted in spinal instability in 71,4% of the cases, abcesses in 14,28% of the cases and the emergence of secondary articular localizations in 28,57% of the cases. 25% of the patients underwent a second surgery mainly to stabalize the spine. Before surgery, walking was impossible for 68,7 % of the patients and 12 months after surgery only 37,5% of the patients couldn't walk.

Conclusion: Spinal surgery in tuberculous or brucellar spondylitis are indicated if medical treatment is insufficient and especially in the occurrence of neurological complications. Surgery may be invasive with various complications but sometimes it could be the only option to treat a neurological deficit.

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AB1280 PREVALENCE OF LEISHMANIASIS IN A SAMPLE OF PATIENTS TREATED WITH BIOLOGIC THERAPIES

Keywords: Infection-related RMDs, Spondyloarthritis, bDMARD

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Background: Leishmaniasis is an infectious disease caused by an intracellular parasite of the genus Leishmania. According to the clinical expression, it can be identified: subclinical, cutaneous (CL) and visceral leishmaniasis (VL). The immune response triggered in this type of infections is based in the activation of the TH1 pathway, in which molecules such as TNF α and interleukins such as IL 12 and IL1 are involved [1,2]. In recent years, an increase in the incidence of opportunistic infectious diseases, such as leishmaniasis, has been observed in patients with rheumatological diseases under treatment with anti-TNFα drugs, such as Psoriatic Arthritis (PsA), Ankylosing Spondylitis (AS) or Rheumatoid Arthritis (RA) [1,3,4].

Objectives: Evaluate the prevalence of Leishmaniasis in a sample of patients in a hospital center in treatment with biologic therapies. As secondary objective, study the characteristics of the patients with Leishmania.

Methods: It can been carried out an observational, descriptive, retrospective, and single-center study. The sample consisted of patients followed in a rheumatology department between January 1, 2022 and January 1, 2023, whose only inclusion criteria was to be in treatment with biologic therapies, including a total of 720 subjects, and, only five patients were found with de diagnosis of leishmaniasis.

Results: Five patients were found diagnosed with leishmaniasis in the 720 subjects on biological treatment included in the sample, which represents a prevalence of 0.69%. Three patients were male (60%) and two were female (30%). The mean age was 52.164 ± 10.38 years with a mean duration of rheumatic disease of 13.2 ± 7.8 years. All the subjets were diagnosed with spondyloarthritis: 3 with AS (60%), 1 with PsA (20%) and another with spondyloarthritis associated with inflammatory instetinal

disease (20%). About the forms of leishmaniasis, four subjects were diagnosed with CL (80%) and only one patient was diagnosed with LV (20%). The 100% of the patients diagnosed with LC were on treatment or had been on treatment before with an antiTNFα (75% with adalimumab and 25% with infliximab). The only case diagnosed with LV, was in treatment with an anti-IL 17, although the patient had been on adalimumab up to 3 months prior to diagnosis. It can be stated that 100% of the patients diagnosed with leishmaniasis had received treatment with an anti-TNFα, with a mean duration of the treatment of 6.94 ± 4.7 years.

Table 1. Subjects diagnosed with leishmaniasis included in the study.

Gender/Age	Disease	Current biological	CL/VL	Localization
M43	AS	ADALIMUMAB	LC	thigh
M48	Spondyloarthritis	ADALIMUMAB	LC	elbows
M62	AS	INFLIXIMAB	LC	elbow
W40	PsA	SECUKINUMAB	LV	
W66	AS	ADALIMUMAB	LC	elbow

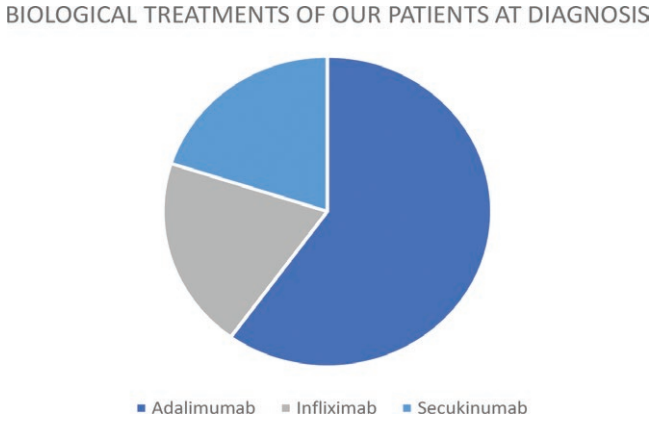


Figure 1. Biological treatment administered at the time of diagnosis of leishmaniasis.

Conclusion: In the present study, 100% of the subjects suffering from Leishmaniasis were on treatment with an anti-TNF α molecule, being adalimumab the most frequent, which coincides with other case series published in the literature.

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AB1281

PREDICTIVE FACTORS FOR FAILURE OF NON-OPERATIVE TREATMENT OF SPONDYLODISCITIS ASSOCIATED WITH SPINAL EPIDURAL ABSCESS

Keywords: Infection-related RMDs

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Background: Spinal epidural abscess (SEA) associated with infectious spondylodiscitis is a rare but serious pathology. It is a serious complication and difficult to diagnose at an early stage. With enough knowledge of risk factors and clinical features, it may be possible to reduce diagnostic delay and treatment failure.

Objectives: The objective of our work was to describe the clinical, radiological, therapeutic, and evolutionary particularities of SEA during infectious spondylodiscitis and to determine factors associated with the failure of conservative treatment.

Methods: We conducted a retrospective study of 54 cases of SEA associated with infectious spondylodiscitis over a period of 13 years [January 2009-April 2022] in the rheumatology department of the Fattouma Bourguiba University Hospital of Monastir. The diagnosis of SEA was retained in clinical, biological, and radiological data.

Results: The mean age was 54 ± 13.52 years [23-82]. A female predominance was observed with a sex ratio (M/F) of 0.92. Thirty-seven patients or 68.5% had at least one comorbidity. Diabetes was the most frequent comorbidity (33.3%). All our patients had back pain on admission. Motor deficits were reported in 48% of the patients with the heaviness of the limbs. Fever was reported in 46.3% of cases. Physical examination revealed spinal stiffness in 23.3% of the patients, motor deficit in 37%, sharp osteotendinous reflexes in 18.5% of the patients, and abolished in 9.25%. The blood tests showed hyperleukocytosis in 18 patients (36%). An erythrocyte sedimentation rate greater (ESR) than 100 mm at the first hour was found in 17 patients. C-reactive protein (CRP) greater than 100 mg/ml was found in 14 patients. 64.8% had pyogenic spondylodiscitis (mainly Staphylococcus aureus), 11.1% had brucella spondylodiscitis and 24.1% had tubercular spondylodiscitis. MRI confirmed the diagnosis of SEA in all cases. The lesions were located at the cervical level in 9.25% of cases, at the dorsal level in 24.07%, and at the lumbar level in 48.14% of cases. The lesions were anterior in 64.8% of cases and anterolateral in 35.2% of cases. The involvement was uni-focal in 63% of cases and extensive in 37% of cases. All our patients had received antibiotic therapy, initially probabilistic and then adapted to the bacteriological results. Immobilization of the spine was indicated in all our patients. Six patients had undergone decompressive surgery after failure of conservative treatment and worsening of the neurological deficit. This treatment consisted of a decompressive laminectomy with debridement of infected tissues. SEA was more frequent in elderly patients (p=0.038), those with a neurological deficit (p=0.016), the presence of spinal cord compression (p=0.04), and in multifocal involvement (p=0.01). When comparing the spinal epidural abscess groups according to the isolated germ, only the diagnostic delay was significantly more important in the course of the brucella SEA (p <0.004). Factors associated with poor evolution under conservative treatment were: diagnostic delay with OR = 0.324 [IC à 95%:0.135-0.777] (p=0.01), neurological deficit with OR = 2.418 [1.187-4.926] (p<0.001), spinal cord compression with OR = 2.77 [1.5-5.07] (p<0.001), and alteration of the general state with OR = 1.41 [1.05-1.87] (p=0.041).

Conclusion: The classical clinical triad of the infectious SEA (back pain + fever + neurological deficit) is not specific enough, hence the delay in diagnosis which has a negative influence on the prognosis. MRI and bacteriological investigation confirms the diagnosis. Early surgical intervention with intravenous antibiotic therapy may be the best choice, especially in patients with progressive neurological deficits. Conservative treatment may be indicated for some patients.

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Disclosure of Interests: None Declared.

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Infection-related rheumatic diseases

AB1282 CLINICAL AND RADIOLOGICAL FEATURES IN BRUCELLA SPONDYLODISCITIS: A DESCRIPTIVE STUDY

Keywords: Epidemiology, Pain

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Background: Spondylodiscitis is an infectious inflammation that affects the vertebrae, vertebral discs and adjacent structures. Vertebral involvement during brucellosis is considered not only as the most frequent localization but also as the most severe one.
Objectives: The aim of the present study was to describe the clinical and the magnetic resonance imaging features of brucella spondylodiscitis.
Methods: We conducted a retrospective study including 11 patients who have presented in the outpatient clinics of physical medicine and rehabilitation for spinal brucellosis with or without neurological disorders from 2016 to 2021. The diagnosis of brucellosis was based on clinical symptoms, MRI findings and isolation of brucella species in blood or tissue specimens and/or a positive Wright agglutination test.
Results: Eleven patients were included. The mean age was 52.5 years [33-74] (6 males and 5 female). The consumption of unpasteurized dairy was found in 4 patients. The main symptom was an inflammatory back pain and it was found in all patients. It was associated with radiculopathy in 8 cases. The other clinical symptoms were fever in 10 patients, sweats in 4 cases, weight loss in 4 cases and hepatomegaly in 1 patient. The median delay before diagnosis was 5,2 months [1-7]. On examination, we revealed tenderness on palpation in 10 cases and muscular weakness of lower limbs in 5 cases. Brucella agglutination test was ≥1/160 in all cases. Blood cultures were negative in all cases. Median erythrocyte sedimentation rate (ESR) and serum C-reactive protein level were 42 mm and 15 mg/dl respectively. Spondylodiscitis was located in the lumbar dorsal and cervical spine in respectively 8, 2 and 1 cases. The involvement of more than 2 vertebrae was found in 2 cases. The most affected level were the L4-L5 level in 3 cases followed by the T10-T11 level in 2 cases. Associated sacroiliitis was found in one patient. All MRI images of the affected vertebrae showed hypo intense signal on T1 weighted image and hyper intense signal on T2 weighted image. Disc space narrowing was documented in 8 cases. Vertebral body osteolysis was found in 5 cases. Epidural collection was found in 3 cases with a size up to 5cm. Paravertebral and peri-vertebral abscesses were detected in 3 cases. Intradiscal abscesses were observed in 2 cases. Cord compression and involvement of root nerve were noted in respectively 5 and 1 cases. Biopsy was performed in 5 cases, but bacteriological examination was contributory to the diagnosis in 1 case. All patients received antibiotic treatment with a combination of two or three drugs, corticosteroids were prescribed in 5 patients and four patient underwent a surgical intervention.
Conclusion: Although not always specific, MRI findings associated with clinical symptoms may help establish the diagnosis of brucella spondylodiscitis even if bacteriological examinations are negatives [1].
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COVID-19

AB1283 COVID-19 WAS NOT TRIGGER FOR RHEUMATIC DISEASE ACTIVITY AFTER 6 MONTHS FOLLOW-UP: RESULTS FROM REUMACOV BRASIL REGISTER

Keywords: COVID

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Background: The COVID-19 pandemic has brought uncertainties to rheumatology practice, mainly related to the possibility of triggering disease activity after infection in immune mediated rheumatic diseases (IMRD). To date, there are few data in the literature specifically evaluating this issue.
Objectives: Evaluate the disease activity in IMRD patients after 6 months of the infection, compared to pre infection status.
Methods: ReumaCoV Brasil is a longitudinal study performed at 35 study centers designed to follow-up IMRD patients for 6 months after clinical or laboratorial COVID-19 diagnosis (cases), comparing with patients with IMRD who had not had the infection at the time of inclusion (controls). Demographic data such as age, sex, comorbidities, clinical characteristics, treatment, evolution of COVID-19 and disease activity status were collected using a Research Eletronic Data Capture (REDCap) database on three consecutive visits (inclusion and 6 months). The analysis was carried out on the four diseases with the highest inclusion number in the study: systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA). In addition to specific disease activity assessment metrics, we used patient's global assessment of disease activity (PGA), ranging from 0 to 10, at all visits, with 0 being no activity and 10 being intense activity. All conclusions were drawn considering the significance level of 5%. This study was registered at the Brazilian Registry of Clinical Trials—REBEC, RBR-33YTQC. All patients read and signed the informed consent form before inclusion.
Results: Between May 2020 and January 2021, 2032 patients were included in the registry, and of these, 1322 patients (721 cases and 601 controls), completed 6 months of follow-up, being 550 SLE (42.0%), 497 RA (37.6%) and 176 SpA (13.3%) and 99 (7.4%) PsA. Most patients were female (82.0%); the median age was 46.7 (13.8). Disease activity at the time of enrollment, according to the PGA, was similar between cases and controls, except for patients with RA and AS, where it was higher in controls. After the follow up time, no worsening of activity was observed in any of the diseases evaluated in the case group (Table 1). Despite this, worsening of disease symptoms after COVID-19 was reported by 23.3%, 24.6%, 25.0% and 25.8% of patients with SLE, RA, AS and PsA respectively, not related with disease activity.
Conclusion: In patients with IMRD, no worsening of disease activity was observed after COVID-19 in this cohort of Brazilian patients. Despite this, many patients noticed worsening of symptoms, possibly associated not with the triggering of the activity, but with the so-called long COVID syndrome.

Table 1. Comparison of disease activity, according to PGA, comparing disease activity status at inclusion and after 6 months of follow up, in cases and controls

	INCLUSION			AFTER 6 MONTHS		
	Cases	*Controls*	p-value	*Cases*	*Controls*	p-value
SLE	2 (0-4,5)	2 (0-4)	0,810	2 (0-5)	2 (0-4)	0,172
RA	3 (1-5)	4 (2-6)	0.001	3 (1-5)	3 (1-5,5)	0,731
AS	2 (0-5)	4 (1-6)	0,002	2 (0-5)	3,5 (1-6)	0,044
PsA	2 (0-4)	2 (0-5)	0,816	2 (0-5)	2 (0-5)	0,939

**Median and interquatile range; Student t test; CI 95%*

Acknowledgements: ReumaCoV Brasil researchers, Brazilian Society of Rheumatology and National Council for Ccientific and Technological Development.
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AB1284 COMPARISON OF THE EFFECTS OF COVID-19 AND INFLUENZA VACCINATION ON RHEUMATIC DISEASES: ANALYSES OF PATIENT SURVEY DATA AFTER VACCINATION

Keywords: Patient reported outcomes, Real-world evidence, Vaccination/immunization

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Background: As the coronavirus disease 2019 (COVID-19) pandemic continues worldwide, vaccination has been considered an essential medical care to protect people from the COVID-19 and end the pandemic. While vaccine development programs and reported epidemiological data are reassuring us, concerns about the risks and adverse events associated with vaccination in patients with rheumatic diseases.
Objectives: The purpose of this study was to analyse the incidence of adverse events and disease flares after vaccination against COVID-19 and influenza in patients with rheumatic diseases.
Methods: From November 2021 to March 2022, a survey was conducted on those who received COVID-19 and influenza vaccinations among patients with rheumatic diseases at Ajou University Hospital. The questionnaire contained questions about medical history, immunization history, type of injected vaccines, patient-reported adverse events and flare-up of the underlying disease after vaccination, and confirmed diagnosis of COVID-19 or influenza. Based on the results of the survey, we compared the incidence of vaccine-related adverse reactions between the COVID-19 and influenza vaccine and identified the factors affecting adverse events or disease flare.
Results: A total 601 valid questionnaires were obtained. The mean age of patients who participated in the survey was 49.6 years and 80.5% of female. Two hundred fifty-five participants (42.4%) received the complete course of primary vaccination, 342 (56.9%) participants completed the booster dose, and 132 (38.6%) of them received mixing vaccine. The frequency of adverse events (188 [52.2%] vs. 21 [5.8%]; p <0.001) and disease flare (58 [16.2%] vs. 5 [1.4%]; p<0.001) after the COVID -19 vaccination was significantly higher than that of the influenza vaccination. In the risk factor analysis, previous allergic reaction to other vaccination (OR 1.95, CI 1.07-3.70; p=0.034) was the only factors associated with the occurrence of adverse events. Female sex (OR 2.64, CI 1.29-6.17; p=0.014) was associated with higher odds of rheumatic disease flare relative to the male. There was no difference in the post-vaccine response between the mixing and matching vaccine.
Conclusion: In a real-world survey conducted on patients with rheumatic diseases, patient-reported adverse events and underlying disease flares after the COVID-19 vaccine was significantly higher than that of the influenza vaccine.
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AB1285 MODELING OF ANTIBODY RESPONSE TO COVID-19 VACCINATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, COVID, Vaccination/immunization

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Background: Understanding the dynamics of humoral immunity after COVID-19 vaccination is crucial in developing vaccination strategies. Antibody response patterns are more complex in patients with rheumatoid arthritis (RA) because of their underlying autoimmunity and immunosuppressive medications. The kinetics of vaccine response in RA patients are not well understood.
Objectives: To construct a model of antibody response to COVID-19 vaccination in patients with RA.
Methods: Two patient groups were included for the study. The first group was composed of RA patients who were enrolled for influenza vaccination study between Oct 6, 2021 and November 3, 2021, in whom serial serum samples were obtained 0, 4, 16 weeks after vaccination. The second group was consecutively enrolled from outpatient clinic between October 6, 2021 and June 3, 2022, in whom serum sample was obtained once. After collecting data on demographics, vaccination and infection history of COVID-19 were obtained by self-report via questionnaire and data from Korean center for disease control. We then measured antibody titers against receptor binding domain of spike protein (anti-RBD) and nucleocapsid (anti-N), using Chemiluminescence microparticle immunosaasy (Abbott, USA) and Electrochemiluminescence immunoassay (Roche, Germany) respectively. The anti-RBD titer was log-transformed to improve normality. Time from vaccination and log of anti-RBD titer was modeled using fractional polynomial. Covariates including age, sex, BMI, underlying disease and immunosuppressive drugs were analyzed using Generalized Estimating Equations to account for repeated measured from a subject.
Results: A total of 736 patients (1042 samples) were enrolled. After excluding patients who experienced COVID-19 infection before sampling (n=84), those unvaccinated (n=44) and uncertain COVID-19 infection history (n=59), the data on 778 samples from 549 patients were analyzed (Group 1: 125, Group 2: 424). Antibody titer reached peak at 12 days after vaccination and decreased exponentially (Figure 1) which fell to 36.5% from peak after 2 months. Compared to the first vaccination, the 3rd and 4th vaccination significantly shifted anti-RBD antibody response curve (28 times, 95% CI 4~195; 32 times 95% CI 4~234, respectively). However, there was no significant shift after the 4th vaccination from the 3rd vaccination (p=0.6405). Multivariable analysis showed that number of vaccinations and sulfasalazine (coefficient: 0.40, 95% CI 0.12~0.68) increased vaccine response but age (coefficient: -0.03, 95% CI -0.04~-0.02), abatacept (coefficient: -2.07, 95% CI -3.30~-0.84) and, JAK inhibitor (coefficient: -0.82, 95% CI -1.34~-0.31) decreased vaccine response.
Conclusion: Anti-RBD response to COVID-19 vaccination showed a peak at 12 days after vaccination and then exponentially decreased in patient with RA. The antibody response is affected by age and medications used for the treatment of RA.

Table 1.

ln[RBD (U/ml)]		coefficient (univariable)	95% CI	p-value	coefficient (multivariable)	95% CI	p-value
sex (female)		0.17	-0.22, 0.55	0.393	-	-	-
age		-0.02	-0.03, -0.01	<.001**	-0.03	-0.04, -0.02	<.001**
DM		0.11	-0.27, 0.50	0.568	-	-	-
HTN		-0.38	-0.69, -0.07	0.018*	-	-	-
CKD		0.68	0.07, 1.29	0.030*	-	-	-
RA duration (yr)		-0.04	-0.06, -0.01	0.001**	-	-	-
Pd (mg/d)		-0.06	-0.11, 0.00	0.035*	-	-	-
MTX use		-0.23	-0.52, 0.05	0.105	-	-	-
HCQ use		0.01	-0.28, 0.29	0.965	-	-	-
SSZ use		0.45	0.07, 0.84	0.022*	0.40	0.12,0.68	0.005**
LEF use		0.00	-0.37, 0.37	0.988	-	-	-
TNF inhibitors use		0.29	-0.16, 0.73	0.208	-	-	-
Abatacept use		-2.07	-3.14, -0.99	<.001**	-2.07	-3.30, -0.84	0.001**
JAK inhibitors use		-0.88	-1.52, -0.24	0.007**	-0.82	-1.34, -0.31	0.002**
Time (months)	log(t)	-1.96	-2.37, -1.54	<.001**	-1.90	-2.29, -1.50	<.001**
	t^(-0.5)	-2.45	-3.30, -1.60	<.001**	-2.40	-3.21, -1.60	<.001**
Vaccination dose	2	1.95	-0.26, 4.15	0.084	1.77	-0.16, 3.71	0.072
	3	3.47	1.26, 5.68	0.002**	3.33	1.40, 5.27	0.001**
	4	3.47	1.20, 5.74	0.003**	3.46	1.48, 5.45	0.001**

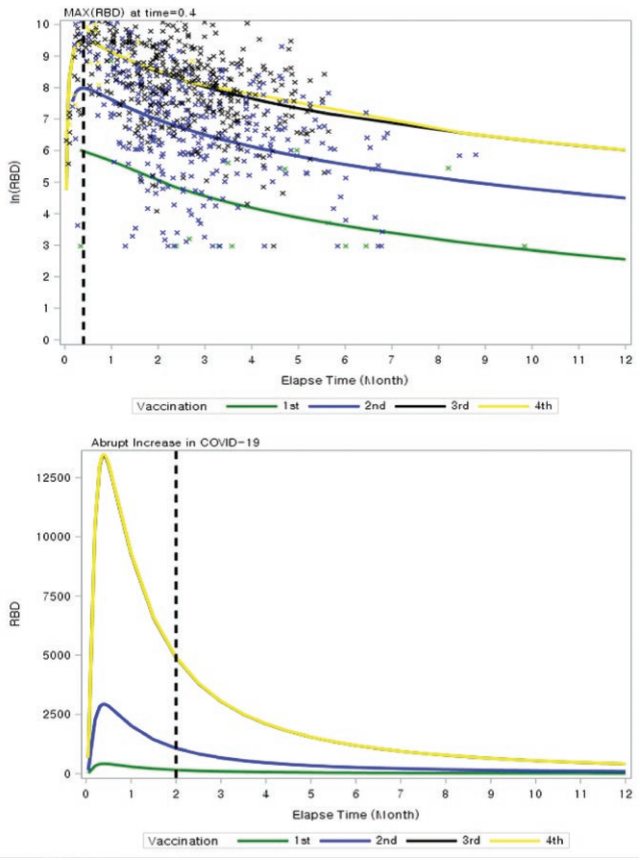


Figure 1.

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Disclosure of Interests: None Declared.
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AB1286 HUMORAL AND CELLULAR IMMUNOGENICITY INDUCED BY THIRD BOOSTER OF SARS-COV-2 VACCINES IN PATIENTS WITH RHEUMATIC MUSCULOSKELETAL DISEASES

Keywords: Vaccination/immunization, COVID

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Background: Amid the coronavirus disease 2019 (COVID-19) crisis, two messenger RNA (mRNA) vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have benefited most people worldwide. While healthy people can acquire sufficient humoral immunity against COVID-19 even in the elderly by vaccination with three doses of vaccine., recent studies have shown that complex factors other than age, including the type of vaccines and immunosuppressive drugs, are associated with immunogenicity in patients with rheumatic musculoskeletal disease (RMD). Identifying factors that contribute to the vulnerability of those patients to acquire not only humoral but also cellular immunity to SARS-CoV-2 despite multiple vaccinations is crucial for establishing an appropriate booster vaccine strategy.
Objectives: To assess humoral,and T cell immune responses after third doses of mRNA vaccines against SARS-CoV-2.
Methods: This prospective observational study included consecutive RMD patients treated with immunosuppressant who received three doses of mRNA vaccines including BNT162b2 and mRNA-1273. Blood samples were obtained 2-6 weeks after second and third dose of mRNA vaccines. We measured neutralizing antibody titres, which against the receptor-binding domain (RBD) of the spike protein of SARS-CoV-2 and seroconversion rates to evaluate the humoral responses. We also assessed T-cell immunity responses using interferon releasing assay against SARS-CoV-2.
Results: A total of 586 patients with RMD treated with mmunosuppressive treatments were enrolled. The mean age was 54 years, and 70% of the patients were female. Seroconversion rates and neutralizing antibody titres after third vaccination of SARS-CoV-2 were significantly higher compared to those after second vaccination (seroconversion rate, 94.5% vs 83.6%, p<0.001; titres of neutralizing antibody, 48.2 IU/mL vs 11.0 IU/mL, p<0.001, respectively). Interferon releasing assay after third vaccinations demonstrated that T cell reaction against SARS-CoV-2 was also increased from that of second vaccination (interferon for antigen 1, 1.11.9 vs 0.61.9, p=0.004,interferon for antigen 2, 1.72.6 vs 0.82.3, p=0.004). Humoral and cellular immunogenicity did not differ between the types of third vaccination including full dose of BNT162 and half dose of mRNA1273.(neutralizing antibody titers, 47.8±76.1 IU/mL vs 49.0±60.1 IU/mL, p<0.001; interferon for antigen 1, 1.12.0 vs 1.01.5, p=0.004, respectively). Attenuated humoral response to third vaccination was associated with BNT162b2 as second vaccination age (>60 years old), glucocorticoid (equivalent to prednisolone > 7.5 mg/day), and immunosuppressant use including mycophenolate, and rituximab. On another front, use of mycophenolate and abatacept or tacrolimus but not rituximab were identified as negative factors for T-cell reactions against SARS-CoV-2. Although 53 patients (9.0%) who had been immunised with third-vaccination contracted COVID-19 during Omicron pandemic phase, no one developed severe pulmonary disease that required corticosteroid therapy.
Conclusion: Our results demonstrated third mRNA vaccination booster of SARS-CoV-2 contributed to restore both humeral and cellular immunity in RMD patients with immunosuppressants. We also identified that certain immunosuppressive therapy with older RMD patients having BNT162b2 as a second vaccination may need additional booster vaccination.

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AB1287 FACTORS ASSOCIATED WITH ADHERENCE TO ANTI TNF-A THERAPY DURING THE COVID-19 PANDEMIC IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, bDMARD, COVID

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Background: Rheumatoid Arthritis (RA) patients are effectively treated with anti-TNF-α therapy. However, pharmacological non-adherence limits the achievement of the therapeutic objective. This is a multifactorial behavior where factors such as the route of administration, frequency, tolerance, perception of improvement, polypharmacy and social factors are involved [1,2].
Objectives: To explore the factors associated with non-adherence to anti TNF-α in RA patients during the COVID-19 pandemic.
Methods: This is a cohort of RA patients treated with anti TNF-α in Medicarte SAS, a Colombian center for Immune-Mediated Diseases, between January to December 2021. The program implements strategies such as pharmacotherapeutic support, informed dispensing, phone calls, text messages and home care services to increase adherence. Adherence was defined as dispensing at least 10/12 (>0.80) prescribed monthly doses for 1 year. Sociodemographic characteristics, time in the program, DAS28-CRP, HAQ and treatment were included as exposure variables. For continuous variables, median and interquartile range (IQR) were calculated. Adjusted Odds Ratio (AOR) with logistic regression were calculated, and a p-value <0.05 was considered as statistically significant.
Results: 565 patients were included, 85.8% (n=485) were women, median age 56 years (IQR: 49-65), disease evolution time 13.7 years (IQR: 7.7-20.8), 51% (n=288) had been in the program for more than 3 years, the median time in treatment with anti TNF-α was 3 years (IQR: 1-3) and DAS-28-CRP 2.4 (IQR: 1.6-3.4). The most frequently anti TNF-α prescribed was etanercept 46.0% (n=260), followed by adalimumab 23% (n=130), subcutaneous golimumab 13.3% (n=75), certolizumab 11.0% (n=62) and intravenous golimumab 6.7% (n=38). At the admission, 18.2% (n=103) of the patients had high activity, 38.6% (n=218) mild activity, 9.2% (n=52) low activity and 34% (n=192) were in remission. At the end of follow-up, 6.4% (n=36) of patients had high activity, 18.2% (n=103) mild activity, 14.3% (n= 81) low activity and 61.1% (n= 345) were in remission. The 51.5% (n=291) did not have pharmacological adherence. The use of etanercept (AOR 0.36 CI95% 0.23- 0.58, p < 0.001) and adequate functionality measured through

HAQ (AOR 0.64 CI95% 0.42- 0.97, p < 0.04) were associated with a lower risk of non-adherence. Higher DAS28-CRP at the end of follow up was associated with non-adherence (AOR 1.29 CI95% 1.12 - 1.48, p < 0.001).

Conclusion: During COVID-19 pandemic, the implementation of strategies in the home care patient program guaranteed adherence close to 50% in our cohort. Higher values of DAS28-CRP were associated with non-adherence, whilst etanercept use and a normal HAQ value were associated with a higher probability of adherence.

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AB1288 LONG-TERM AND BOOSTER VACCINATION RESPONSES IN PATIENTS WITH GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA

Keywords: Vaccination/immunization, Vasculitis, Disease-modifying drugs (DMARDs)

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Background: Vaccination remains essential in preventing morbidity of SARS-CoV-2 infections. We previously showed that >10mg/day prednisolone and methotrexate use were associated with reduced antibody concentrations four weeks after primary vaccination in patients with giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) [1].

Objectives: Here, we performed a follow-up study to measure the decay of antibody concentrations over time and the immunogenicity of SARS-CoV-2 booster vaccination.

Methods: GCA/PMR patients included in the primary vaccination (BNT162b2 or ChAdOx1) study were asked again to donate blood samples six months after primary vaccination (n=24) and one month after booster vaccination (n=46, BNT162b2 or mRNA1273). Data were compared to that of age-, sex-, and vaccine-matched controls (n=58 and n=42, respectively).

Results: Antibody concentrations decreased faster over time in GCA/PMR patients than in controls, but this decrease was not associated with treatment during primary vaccination. Post-booster antibody concentrations were comparable between patients and controls. Antibody concentrations post booster vaccination associated strongly with antibody concentrations post primary vaccination, but not with treatment during booster vaccination. However, the fold-change of post-booster vaccination showed a slight negative correlation with the post-primary vaccine antibodies.

Conclusion: These results indicate that patients with impaired vaccine responses after primary vaccination, have slightly stronger increases in humoral immunity after booster vaccination, but this is not enough to reach a similar protection. The decrease in humoral immunity, and subsequent increase after booster vaccination, is likely not impacted by prednisolone or methotrexate treatment. Rather, these treatments put the patients at an immunogenic disadvantage during primary SARS-CoV-2 vaccination, which is not fully repaired by a single booster vaccination. This longitudinal study in GCA/PMR patients stresses the importance of repeat booster vaccination for patients that used >10mg/day prednisolone or methotrexate during primary vaccination.

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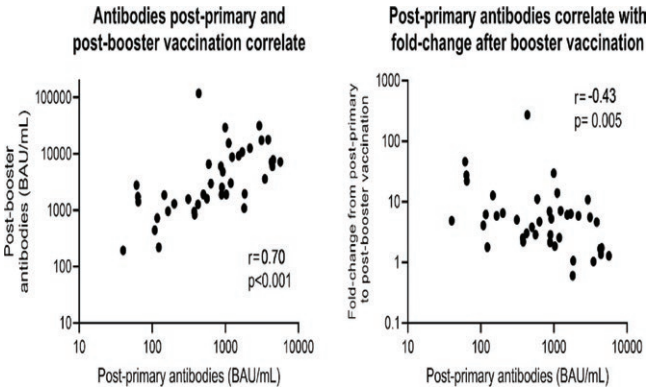


Figure 1.

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AB1289 IS THERE HIGHER RISK OF FATIGUE, DEPRESSION, ANXIETY AND STRESS AFTER COVID-19 IN PATIENTS WITH IMMUNE-MEDIATED RHEUMATIC DISEASES? DATA FROM THE REUMACOV BRASIL COHORT

Keywords: COVID

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Background: Some individuals may have persistent symptoms after COVID-19, a new condition known as long COVID-19. However, these complaints can be misunderstood with disease activity in patients with immune-mediated rheumatic diseases (IMRD), especially fatigue and mental distress.

Objectives: To evaluate fatigue, depression, anxiety, and stress in IMRD patients after 6 months of COVID-19, compared with IMRD patients without COVID-19.

Methods: The ReumaCoV Brasil is a longitudinal study designed to follow-up IMRD patients for 6 months after COVID-19 diagnosis (cases) compared with IMRD patients no COVID-19 (controls). Clinical data, such as age, sex, comorbidities, as well as disease activity measurements and current treatment regarding IMRD, and COVID-19 outcomes were evaluated in all patients. The FACIT questionnaire (Functional Assessment of Chronic Illness Therapy) and the DASS 21 (Depression, Anxiety and Stress Scale - 21 Items) were applied at 6 months after COVID in both groups.

Results: A total of 606 IMRD patients were included, of whom 322 (53.1%) cases and 284 (46.9%) controls. Most patients were female (85.3%) with mean age 46.1 (13.0) years old. Specific disease activity were similar between cases and controls. There was a significant difference between FACIT scores and 3 domains of DASS-21 comparing cases and controls (Figure 1). The factors associated with FACIT were female gender, diabetes, obesity, no comorbidities, COVID manifestations (skin, joint pain, asthenia, diarrhea, and dyspnea), and chronic oral corticosteroid use. DASS-21 Depression was associated with these same factors. Female gender, COVID manifestations as skin, joint pain, asthenia, cough, dyspnea, and chronic oral corticosteroid use were associated with DASS-21-Anxiety. DASS-21 Stress was associated with female gender, asthenia,

Table 1. Final model using binary Logistic Regression analysis to evaluate the preditive factors associated with FACIT and DASS-21 scores

FACIT *Score ≤ 37 x score > 37*[§]			**DASS-21-DEPRESSION** *Score ≤ 6 (normal/mild) x score > 6 (moderate/ severe*			**DASS-21-ANXIETY** *Score ≤ 5 (normal/mild) x score > 5 (moderate/ severe)*			**DASS-21-STRESS** Score ≤ 9 (normal/mild) x score > 9 (moderate/ severe		
Variable	P-value	OR (CI 95%)	Variable	P-value	OR (CI 95%)	Variable	P-value	OR (CI 95%)	Variable	P-value	OR (CI 95%)
Female	0.15	1.83 (1.12-2.98)	No comorbidities	0.029	0.66 (0.46-0.95)	Joint pain	0.002	2.44 (1.39-4.26)	Female	0.012	2.31 (1.20-4.46)
Diabetes	0.006	2.35 (1.28-4.32)	Joint pain**	0.001	2.58 (1.57-4.22)	Dyspnea	0.001	3.61 (2.11-6.19)	Dyspnea	0.001	3.69 (2.09-6.51)
Dyspneia	0.001	2.00 (1.23-3.26)	Dyspnea	0.001	2.82 (1.79-4.44)	Oral CE	0.014	1.55 (1.09-2.21)			
Joint pain	0.005	2.20 (1.41-3.43)	Oral CE	0.048	1.41 (1.00-1.99)						

[§]Lower scores mean worse fatigue; CE: corticosteroid; OR: odds ratio; CI: confiance interval

diarrhea, dyspnea, cough, chronic oral corticosteroid use, and hospitalization. Table 1 shows the variables that remained in the models after the univariate logistic analysis. A weak correlation between disease activity and FACIT was observed in rheumatoid arthritis (p=0.010; r^2 = 0.035) and ankylosing spondylitis patients (p=0.010; r^2 = 0.129). No other correlations were observed between the scores results and disease activity (patient's global assessment - PGA), medications or specific IMRD.

Conclusion: Fatigue and mental changes such as depression, anxiety, and stress, occurred more frequently in IMRD patients who had COVID-19 than in those who did not have COVID-19, especially in women, regardless of disease activity score. Fatigue was more related to female gender, diabetes, obesity, and current joint pain. Mental impairment was more associated with severity of COVID-19, including respiratory and non-respiratory symptoms.

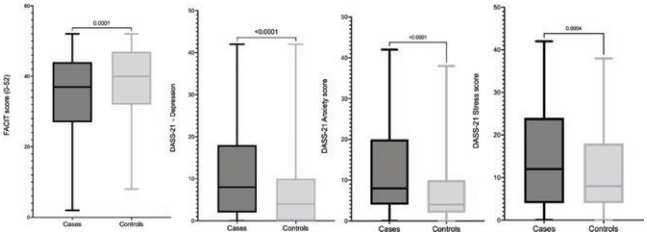


Figure 1. Comparison between cases and controls of FACIT and DASS-21 depression, anxiety, and stress scoresFACIT (Functional Assessment of Chronic Illness Therapy); DASS-21 (Depression, Anxiety and Stress Scale - 21 Items):

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Disclosure of Interests: None Declared.
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AB1290 **IMPACT OF THE COVID-19 PANDEMIC ON SEPTIC ARTHRITIS MANAGEMENT**

Keywords: Descriptive studies, COVID

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Background: Since 2020, the SARS-Cov-2 pandemic has disrupted the organization of healthcare systems worldwide.
Objectives: This study aimed to assess the impact of this pandemic on septic arthritis management in a tertiary rheumatology department.
Methods: It was a single-center descriptive case-control study, which included patients hospitalized for septic arthritis between January 2018 and December 2021, whose diagnosis was retained after positive bacterial growthor on culture on according to presumptive criteria. Our patients were divided into two groups: G1: patients hospitalized during the COVID-19 pandemic (2020-2021), and G2: patients hospitalized during a similar period before the COVID-19 pandemic (2018-2019). In both groups, septic arthritis prevalence was calculated, socio-demographic characteristics, risk factors, clinical, paraclinical, and therapeutic data were collected. COVID-19 status was reported in the G1.
Results: Twenty-two patients were enrolled: G1 (n = 15), G2 (n = 7). The prevalence of septic arthritis was 0.77% and 0.36% respectively. The median age was 54.6±12.25 and 54.29±21.81 years old respectively. Diabetes was found in 26, 7% in G1 and 28.6% in G2. During the pandemic, arthropathy and oral corticosteroids use were noted in 53.3% and 28.6% of patients versus 26.7% and 14.3% in G2. The diagnosis delay and the prior use of antibiotic therapy were more significant in G1: 14.08[7-30] d versus 6.5[3.25-19.25] d, and 46.7% versus 14.3%. The knee was the most common localization in both groups. Other joints were affected in G1: shoulder (n = 2), hip (n = 1), and sacroiliac (n = 1). The most common germ was staphylococcus aureus. The duration of hospitalization and duration of antibiotic therapy in G1 and G2 were 26.07±9.12d versus 27.43±10.87d and 50±10d versus 48±25.79d, respectively. Concerning COVID-19 status, 33.3% of patients in G1 have received their vaccination and no recent SARS-Cov2 infection was noted before hospitalization. During the pandemic, synovectomy was required in three patients, one of whom was also transferred to intensive care for septic shock (two of these three patients are being followed for rheumatoid arthritis, and only one has never been vaccinated against COVID-19).
Conclusion: During the COVID-19 pandemic, the prevalence of septic arthritis in our department was higher and the diagnosis was delayed. Duration of hospitalization was not impacted, however, atypical localisations, prior use of antibiotics, recourse to synovectomy, and transfer to intensive care were reported. These results suggest an inadequate and difficult access to healthcare services during the lockdown, as well as an impact of social distancing on the immune system [1, 2]. More studies are needed to confirm these findings.

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AB1291 **COVID-19 AND CRYOGLOBULINEMIC VASCULITIS. LONG-TERM SURVEY STUDY ON THE IMPACT OF PANDEMIC AND VACCINATION ON A LARGE PATIENT'S POPULATION**

Keywords: COVID, Infection-related RMDs, Vasculitis

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Background: Cryoglobulinemic Vasculitis (CV) is a rare autoimmune systemic disorder with multiple organ involvement. During the current COVID-19 pandemic, the patients with CV can accounted among frail populations because of the presence of multiple organ involvement, chronic steroid treatment, and more frequent old age.
Objectives: The present study aimed to investigate the prevalence and outcome of COVID-19, as well the safety and immunogenicity of COVID-19 vaccines in a wide CV cohort by a multicenter survey.
Methods: Patients with CV were consecutively recruited at 11 Italian referral centers. CV diagnosis, clinico-serological parameters, COVID-19 tests, and vaccination immunogenicity were carried out according to current methods.
Results: Four-hundred-thirty unselected CV patients (130 M; mean age 70±10.96 years) were recruited from February 2020 to October 2021. COVID-19 prevalence was significantly higher in CV patients compared to the Italian general population (11.9% vs 8.0%, p<0.005); furthermore, we observed a higher mortality in CV subjects with COVID-19 compared to those without (5.9% vs 0.5%, p<0.01). An older age (≥60 years) correlated with a worse COVID-19 outcome. Vaccine was administered in 87% of patients, and 50% received a boostering dose. Disease flares/worsening following the vaccination were significantly less frequent than those associated to COVID-19 (5% vs 14%, p=0.0012). CV patients showed an impaired vaccination immunogenicity compared to controls (p<0.05), as well an increased no-response rate after the booster.
Conclusion: CV patients have a higher risk to develop COVID-19, as well of more severe disease manifestations. Vaccines had a good safety profile in CV patients and of note, the vaccine-related side effects/disease flares were significantly lower compared to those COVID-19-related. However, a quarter of vaccinated individuals do not show detectable seroconversion; this is a major challenge for clinicians. Overall, a close monitoring of these frail patients during the ongoing pandemic is particularly advisable.

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AB1292

EFFECTS OF DMARD TREATMENT ON SARS-COV-2 MRNA VACCINATION IN PATIENTS WITH SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASE: A MATCHED, PROSPECTIVE COHORT STUDY

Keywords: Undifferentiated connective tissue disease, Vasculitis, COVID

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Background: Patients suffering from systemic autoimmune rheumatic disease (SARD) display poor antibody development after two doses of mRNA vaccinations leaving these patients with only limited humoral protection against severe SARS-CoV-2 disease courses. Of key interest is the effect of conventional synthetic (csDMARD) and biological/ targeted drugs (b/tsDMARDs) disease modifying antirheumatic drugs on the time of protection.
Objectives: To compare antibody titer development in patients with vasculitis and connective tissue disease (CTD) with healthy controls 6 months after two mRNA vaccinations and after third immunization. To analyze factors, that affect the velocity of titer decline, well as qualitative humoral response.
Methods: Patients with SARD were enrolled and matched for gender and age with healthy control subjects (HC) and the humoral response after 6 months to two doses of mRNA vaccine BNT162b2 in terms of SARS-COV-2 antibody titer was assessed. In addition to binding antibody units (BAU) we also analyzed neutralizing antibodies. Patients receiving B-cell depleting therapy and those with prior SARS-CoV-2 infection (via detection of nucleocapsid antibodies) were excluded. Differences between two groups were calculated with Wilcoxon signed-rank test.
Results: A total of 53 patients with SARD (42 patients suffering from connective tissue disease and 11 with vasculitis respectively) and 73 HC were analysed. Interestingly only patients receiving a combination therapy of different csDMARDs/ b/tsDMARDs demonstrated diminished antibody titers 6 months after two doses of mRNA vaccine (p-value p-value<0,001), whereas patients receiving only csDMARD as monotherapy displayed comparable antibody levels to healthy controls. This effect was equalized after a third booster vaccination (p-value=0,13). Concerning disease entities, patients with vasculitis seemed to have lower BAU than HC (p-value<0,05) and patients suffering from CTD. After third vaccination both patient groups had lower antibody levels than HC (vasculitis: p-value <0,0001; CTD: p-value p-value<0,01). Lower antibody levels before third vaccination correlated with lower antibodies after third immunization.
Conclusion: Patients with autoimmune rheumatic diseases undergoing combination therapy may be more vulnerable to SARS-CoV-2 infection, due to reduced antibody levels 6 months following two doses of mRNA vaccine. Our data strongly recommends antibody measurements in patients receiving combination therapy and individualized earlier booster vaccination.

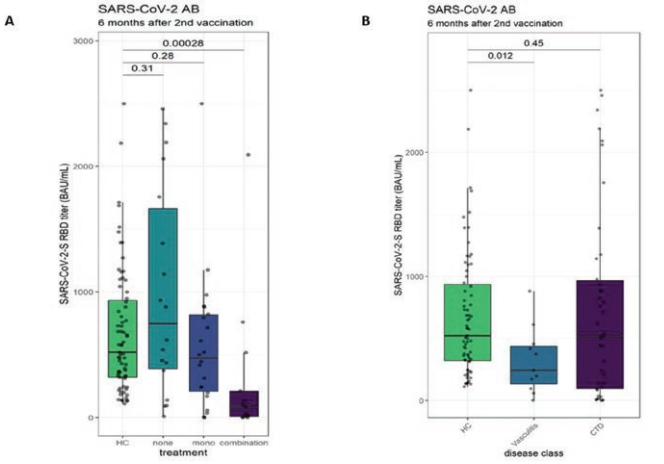


Figure 1. Anti-SARS-Cov-2 S antibody titers. **A**: Antibody titers measured 6 months after two doses of mRNA vaccination in patients with connective tissue disease, vasculitis and healthy controls. **B**, Antibody levels according to disease entity. AB: antibody; BAU: binding antibody unit; CTD: connective tissue disease; HC: healthy control; mono: disease modifying anti-rheumatic drug monotherapy; combination: combination therapy of disease modifying anti-rheumatic drugs; RBD: receptor binding domain;

Table 1. Demographic parameters and therapy of study participants.

	SARD (n=53)	HC (n=73)
Age, mean (standard deviation)	53.55 (±14.04)	51.27 (±14.07)
Female	45 (84.9%)	47 (64.4%)
Connective tissue disease	42 (79%)	
Vasculitis	11 (21%)	
csDMARD or b/tsDMARD monotherapy	22 (41%)	
csDMARD and/or b/tsDMARD combination therapy	13 (25%)	
No therapy	18 (34%)	
Methotrexate	8 (15%)	
Mycophenolate mofetil	10 (19%)	
Hydroxychloroquine	17 (32%)	
Azathioprine	8 (15%)	
Belimumab	3 (6%)	
Tocilizumab	3 (6%)	
Glucocorticoid dose 1. vaccination, mean (standard deviation)	2.8 (±10.8)	
Glucocorticoid dose 2. vaccination, mean (standard deviation)	2.6 (±10.7)	

SARD: Systemic autoimmune rheumatic disease, HC: Healthy controls, csDMARD: conventional synthetic disease modifying antirheumatic drugs and b/tsDMARD: biological/ targeted drugs disease modifying antirheumatic drugs

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AB1293 OMICRON BREAKTHROUGH INFECTIONS AMONG RITUXIMAB AND NON-RITUXIMAB TREATED PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES: A MULTICENTER CONTROLLED STUDY

Keywords: Vaccination/immunization, COVID, bDMARD

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Background: Little is known about the efficacy of booster COVID-19 vaccination in rituximab (RTX)-treated patients with autoimmune inflammatory rheumatic diseases (AIIRD).
Objectives: To estimate COVID-19 breakthrough infection rate in AIIRD patients treated with RTX compared to patients treated with other therapies and immunocompetent controls.
Methods: This observational multi-center study investigated COVID-19 infection rate and humoral response (anti-S1/S2 IgG) to the BNT162b2 mRNA vaccination in RTX-treated vs non-RTX treated AIIRD patients and immunocompetent controls for 18 months. To investigate the impact of the 3rd and 4th mRNA COVID-19 vaccine doses, a survival analysis was applied. Predictors of time-to-infection were analyzed using a multivariate Cox proportional hazard model.
Results: A total of 115 RTX-treated patients, 590 non-RTX-treated patients, and 121 immunocompetent controls were included in the analysis. AIIRD patients received more vaccine doses than controls, median 3 (range 2-4) vs 2 (2-4), respectively, p<0.0001; the rate of vaccination with the 3rd and 4th vaccine doses were 53.82% (n=402) vs 32.8% (n=41), and 3.88% (n=29) vs 2.4% (n=3), respectively, p <0.0001 for both comparisons. Patients treated with RTX within one year from the last vaccination (n=84) had the lowest anti-S1/S2 IgG level following each vaccination compared to others patients and controls. RTX-treated patients had the highest rate of COVID-19 infection since the start of the vaccination campaign compared to the AIIRD patients in general and controls, 32.26% (40/124), 27.29% (170/623), and 28.8% (36/125), respectively, p=0.2206. During the Omicron surge, time-to infection from the last booster vaccination was shorter among AIIRD patients compared to controls, irrespective of the type of anti-rheumatic therapies (Figure 1A). In a Cox-regression model, a time interval between the RTX treatment and the last vaccination was associated with a lower risk to contract COVID-19, HR 0.998 (95% CI 0.997-1), p=0.0298 (Figure 1B) For each 30-day interval between the RTX treatment and the vaccination date, the risk to contract COVID-19 declined 0.941-fold. The risk to contract COVID-19 among RTX-treated patients within the last year after adjustment to age and S1/S2 serology was HR 2.077, 95% CI 1.056-4.086, p=0.0342. Reassuringly, no cases of severe COVID-19 or COVID-19-related mortality were reported during the Omicron surge.
Conclusion: This study found comparable rates of the Omicron infection rate among vaccinated AIIRD patients treated with RTX and other immunomodulators. Recent exposure to RTX predisposed to a breakthrough COVID-19 infection.

Figure 1A. Covid-19-free survival from the last booster vaccination among rituximab-treated patients, patients treated with other medication, and immunocompetent controls.

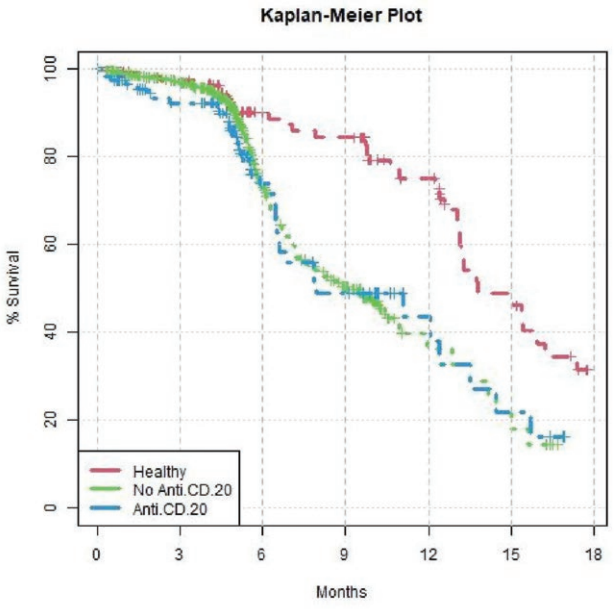
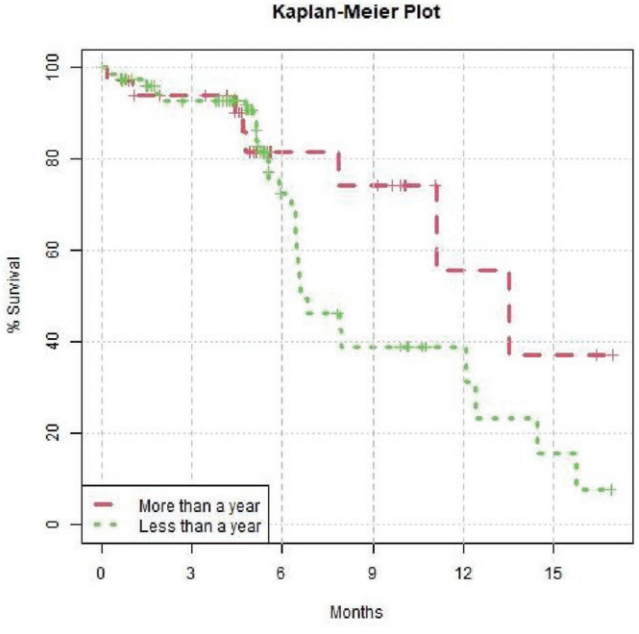


Figure 1B. Covid-19-free survival from the last booster in rituximab-treated AIIRD patients stratified by timing of rituximab administration within or after one year from the last vaccination.



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AB1294 SAFETY OF COVID-19 VACCINES AND HEALTH CARE UTILIZATION FOLLOWING VACCINATION AMONG ADULTS WITH RHEUMATOID ARTHRITIS – A POPULATION-BASED SELF-CONTROLLED CASE SERIES ANALYSIS

Keywords: Vaccination/immunization, COVID, Rheumatoid arthritis

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Background: Although adverse events of special interest (AESIs) following COVID-19 vaccination are considered to be rare, emerging reports have suggested that risk of AESIs may be higher in certain subgroups of individuals. The self-controlled case series method represents a useful approach to study adverse events whereby an individual's risk is compared between a control pre-exposure period and a risk period following vaccine exposure.
Objectives: This study assessed whether COVID-19 vaccines were associated with an increase in AESIs and health care utilization [emergency department (ED) visits, hospitalizations, and rheumatologist visits] among adults with rheumatoid arthritis (RA).
Methods: We used the Ontario RA Database, a validated Canadian population-based cohort. Among adults with an RA diagnosis, we identified those who received at least 1 COVID-19 vaccine. AESI included Bell's Palsy, Idiopathic Thrombocytopenia, Acute Disseminated Encephalomyelitis, Myocarditis, Pericarditis, Guillain-Barre syndrome, Transverse Myelitis, Acute Myocardial Infarction, Anaphylaxis, Stroke, Deep Vein Thrombosis, Pulmonary Embolism, Narcolepsy, Appendicitis, and Disseminated Intravascular Coagulation. Secondary outcomes included all-cause ED visits, hospitalizations, and rheumatology visits (a potential proxy for disease flare). The study end date was March 2022. Self-controlled case series analyses were used to determine event rates in any 21-day risk period following vaccination compared to control periods. For rheumatologist visits, the risk window was confined to a 30-day risk period. Control periods were defined as 6 months prior to the first vaccination [with a 14-day washout period before first dose, as patients may wait until they are in relatively good health before receiving a vaccine]; Control periods in between doses start on Day 22 from the last dose and ends 14 days prior to the next dose; and a final control period commencing after the final dose risk period (up to a maximum of 6 months). Relative incidence (RI) rates were estimated (using Poisson Regression) across risk windows relative to control periods. Relative incidence rate ratios (RIR) in each risk period vs control period were estimated using non-RA comparators (matched on sex, age, and region of residence).
Results: In total 123,466 RA patients and 493,864 comparators were included. 71% of individuals were female and the median age of RA patients was 65 years (IQR: 55-74), with a median RA duration of 9.3 years (IQR: 4.2-17.1). The majority received mRNA vaccines. Within RA, 8,727 (7.1%) received >3 doses, 89,583 (72.6%) received 3 doses, 23,652 (19.2%) received 2 doses, and 1,504 (1.2%) a single dose. Within the general population, 373,735 (75.7%) received 3 doses and only 7,963 (1.6%) received >3 doses. Among RA individuals, relative to control periods, event rates were not significantly increased after the first dose in terms of AESIs (RI 1.05 95% CI 0.90-1.22) or ED visits (RI 0.97 95% CI 0.94-1.01). Hospitalizations were slightly lower for RA patient in post-vaccination versus control periods (RI 0.83 95% CI 0.78-0.88). Compared to control periods, rheumatology visits slightly increased after the first dose (RI 1.08 95% CI 1.07-1.10), then decreased after doses 2-3, normalizing after dose 4. Relative to non-RA comparators, RA individuals had a higher relative incidence rate of AESIs after dose 3 (RIR 1.28 95%CI 1.05-1.56) but no differences in hospitalizations or ED visits. Potential limitations of our study include the possibility that individuals avoided additional doses if they had an adverse event after the first dose, and that access to rheumatologists likely changed over time.
Conclusion: In this self-controlled case series, we did not detect a significant increase in AESI or health care use when comparing pre-vaccine to post-vaccine periods in RA.
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Disclosure of Interests: None Declared.
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AB1295

SAFETY AND TOLERANCE OF ANTI-SARS-COV-2 VACCINES IN SJÖGREN'S SYNDROME: RESULTS FROM THE COVAD STUDY

Keywords: Vaccination/immunization, COVID, Sjögren syndrome

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Background: Despite the large number of studies on safety of anti-SARS-CoV-2 vaccines in people with rheumatic and musculoskeletal diseases (RMDs), data on Sjögren's syndrome (SS) are scarce.
Objectives: To determine anti-SARS-CoV-2 vaccine-related adverse events (AEs) in the seven-day post-vaccination period in patients with SS vs other connective tissue diseases (CTDs), non-rheumatic autoimmune diseases (nrADs), and healthy controls (HC).
Methods: Data were captured through the COVID-19 Vaccination in Autoimmune Diseases (COVAD) questionnaire (March–December 2021) and analysed to compare frequencies and identify associations with demographic, disease-specific and vaccine-specific variables.
Results: Among 9462 complete respondents having received at least one vaccine dose, 356 were patients with SS, of which 129 with primary (p) SS and 227 with SS associated (a) with other RMDs (rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and inflammatory myopathies (IM). SS patients were compared to 1586 patients with other CTDs (RA, SLE, SSc or IM) and without SS, 825 patients with nrADs and 4712 HC. SS patients mean age was 52 years, mean disease duration was 12 years; 94% of patients were females and 68% were Caucasian. Respondents were mainly based in the United Kingdom (19%), United States (15%) and Italy (14%) but in total 33 countries were represented. The BNT162b2 vaccine was the most frequently administrated (47%) and 78% of SS respondents had received 2 doses at the time of survey completion. Mild AEs were reported by 291 (82%) SS patients (p<0.0001 vs 3581 (76%) HC; vs 1296 (82) other CTD and 686 (83%) nrADs; all p=not significant (NS)) and severe AEs by 11 (3%) patients (vs 98 (2%) HC, 52 (3%) other CTDs and 36 (4) nrADs; all p=NS) (Table 1). Younger SS patients were more likely to develop mild AEs (odds ratio (OR): 0.97; 95% confidence interval (CI): 0.95-0.99) while no association with age was observed for severe AEs. Disease activity in the 4 weeks prior vaccination did not affect the development of mild/severe AEs not even when stratifying patients according to ongoing immunosuppressive (IS) and/or glucocorticoid (GC) treatment. Diffuse myalgia and fever were more frequently observed in ChAdOx1nCoV-19 recipients while rash in mRNA-1273 recipients. No differences in overall AE frequency emerged between pSS and aSS (mild AE= OR: 0.8; 95% CI: 0.5-1.4; severe AE: OR). However, while at univariate analysis fever was associated with pSS (OR: 1.95; 95% CI: 1.09-3.5), this was no longer significant when adjusting for vaccine type. The use of IS or GC in the 4 weeks prior vaccination did not affect AE frequency and no differences were observed in those withholding or not their therapy before/after vaccination.
Conclusion: Our data confirm that anti-SARS-CoV-2 vaccination is safe and well tolerated in both pSS and aSS. Data collection is ongoing to gather data about safety of subsequent vaccine doses.

Table 1. Anti-SARS-CoV-2 vaccine-related adverse events in the seven-day post-vaccination period

	pSS (N=129)		aSS (N=227)		Other CTD (N=1586)		nr-AD (N=825)		HC (N=4712)	
	N	%	N	%	N	%	N	%	N	%
Any mild AE	108	84	183	81	1296	82	686	83	3581	76
Injection site (arm) pain and soreness	95	88	156	85	1067	82	563	82	2873	80
Muscle pain in all arms and legs	18	17	40	22	230	18	124	18	715	20
Body ache	29	27	51	28	316	24	207	30	997	28
Fever	29	27	29	16	278	21	158	23	919	26
Chills	21	19	35	19	227	17	148	22	592	16
Nausea/Vomiting	7	6	16	9	100	8	68	10	224	6
Headache	41	38	69	38	407	31	238	35	1045	29
Rash	6	6	7	4	44	3	16	2	51	1
Fatigue	42	39	88	49	496	38	290	42	1282	36
Diarrhoea	4	4	9	5	49	4	40	6	129	4
Abdominal pain	0	0	6	3	37	3	28	4	65	2
High pulse rate or palpitations	7	6	8	4	53	4	48	7	114	3
Rise in blood pressure	1	1	2	1	18	1	16	2	40	1
Fainting	1	1	1	0.5	7	0.5	6	1	16	0.4
Difficulty in breathing	3	3	1	0.5	24	2	17	2	42	1
Dizziness	9	8	16	9	89	7	66	10	214	6
Chest pain	4	4	4	2	20	1	14	2	58	2
Any severe AE	6	5	5	5	52	3	36	4	98	2
Anaphylaxis (shock)	0	0	0	0	3	6	0	0	4	4
Marked difficulty in breathing	3	50	0	0	9	17	5	14	25	25
Tongue swelling or throat closure	2	33	0	0	3	6	2	6	8	8
Severe diffuse body rash (hives)	1	17	0	0	8	15	7	20	17	17
Required hospitalisation	1	17	1	20	8	15	3	8	10	10

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AB1296 EQUATED HOSPITALIZATION RATE OF PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES AS COMPARED TO GENERAL POPULATION – DATA FROM THE SECOND WAVE OF THE COVID-19 PANDEMIC

Keywords: COVID

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Background: The outbreak of COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (called SARS-CoV-2), has quickly became a global health emergency with over 660 million confirmed cases and over 6 million deaths worldwide. Over the last two years, several registries and cohort studies have collected data about the course and possible predictors of outcomes of COVID-19 infection in of inflammatory rheumatic and musculoskeletal disease (iRMD) patients. However, whether iRMD patients perform differently from the general is not clear, as most studies miss an adequate control group [1].

Objectives: To investigate the clinical manifestations and outcome of coronavirus disease (COVID-19 second wave) in patients with iRMD compared to the general population.

Methods: This is a case-control study of patients with and without an iRMD affected by COVID-19. Patients were selected in South Tyrol health trust, Italy, retrieving data from a single central database. We included patients ≥18 years of age and with a positive SARS-CoV-2 PCR test result between October 1sts 2020 and March 1st, 2021. During the study period, a whole population screening was conducted in South Tyrol with central registration of all results. Cases were identified by linking the diagnosis of a rheumatic disease with the result of the PCR test. Cases were subsequently matched in a 1:2 ratio for age, sex, and date of COVID-19 diagnosis with non iRMD patients (controls). Differences in demographics, clinical features, and outcomes of COVID-19 infection were compared between the two groups. The outcomes analyzed were hospitalization, severe course (ICU, mechanical ventilation/ECMO) and mortality.

Results: The study population consisted of 201 iRMD patients (mean age 60.4 years±14.9; 65.2**%** female) and 360 controls (mean age 59.8 years ± 5.6; 64.7**%** female). Asthenia and malaise were the most common symptoms, reported more frequently in the iRMD as compared to the control group (61.7% vs 43.1%, respectively, p<0.001). The majority of iRMD patients (88.6%) received an immunosuppressive drug at time of COVID-19 diagnosis, 36.3% were under glucocorticoids therapy. iRMD patients more frequently had three or more comorbidities than controls (34.8% vs. 6.1%, p<0.001). iRMD patients received more commonly glucocorticoids to treat COVID-19 disease [n=42 (20.9%) vs n=23 (6.4%), p=<0.001] than controls. The rate of COVID-19 related hospitalization (12.4% vs. 10.6%, p=0.49), severe course (40.0% vs. 44.7%, p=0.80) and mortality (3.5% vs. 4.2%, p=0.82) in iRMD and control group respectively, did not show significant differences. Among hospitalized patients, mechanic ventilation was significantly more common among iRMD than control group [n=5 (20.0%) vs. n=1 (2.6%), p=0.035].

Conclusion: Our study indicates similar rates of admission, severe course and mortality among iRMD and non-iRMD patients affected by COVID-19. However, iRMD patients displayed a higher number of comorbidities and were more frequently treated with glucocorticoids. Among hospitalized patients, mechanical ventilation was more frequently required among iRMD group.

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AB1297 EFFECT OF ABO AND RH BLOOD TYPE ON SARS-COV-2 INFECTION SEVERITY IN PATIENTS WITH RHEUMATIC DISEASES: DATA FROM THE NATIONAL SAR-COVID REGISTRY

Keywords: COVID

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Background: Blood group A has been associated with a higher risk of SARS-CoV-2 infection, although the effect on its severity is being discussed.

Objectives: To evaluate the association between the ABO and Rh antigens and the clinical characteristics and evolution of the SARS-CoV-2 infection in patients with rheumatic diseases.

Methods: SAR-COVID is a national, longitudinal, and observational registry. Patients ≥18 years with a diagnosis of inflammatory or degenerative rheumatic disease, and confirmed SARS-CoV-2 infection (RT-PCR or serology) were included. Data were collected from August 2020 to June 2022. Sociodemographic, clinical data, comorbidities, underlying rheumatic disease, disease activity, and its treatment at the time of SARS-Cov-2 infection diagnosis were recorded. Symptoms of the infection, complications, medical interventions and treatments received for COVID-19 were also documented. The WHO ordinal scale (WHO-OS)[1] was used and severe COVID-19 was defined as WHO-OS ≥5. Patients were categorized as follows: blood group A or non-A, and Rh factor positive or negative. *Statistical analysis:* Descriptive statistics. Chi[2] test or Fischer's exact test and Student's test or Mann-Whitney and Kruskal Wallis test or ANOVA, as appropriate. Multiple logistic regression.

Results: A total of 1356 patients were included, 547 (40,3%) had blood group A and 809 non-A (59,7%). Regarding the Rh factor, 1230 (90,7%) were positive and 126 (9,3%) negative. Age, sex and ethnicity, as well as the presence of comorbidities were comparable between both groups. In both cases, the most frequent rheumatic diseases were rheumatoid arthritis (38,9%; p=0,052), systemic lupus erythematosus (17,4%; p=0,530) and osteoarthritis (10,1%; p=0,888). Patients with non-A blood type presented a higher frequency of psoriatic arthritis (group A 5,1% vs non-A 8,7%; p= 0,015). At the time of SARS-CoV-2 infection diagnosis, the use of glucocorticoids, immunosuppressive and immunomodulatory drugs were similar in both groups. During SARS-CoV-2 infection, more than 90% of patients in both groups were symptomatic (group A 96% vs non-A 94,8%; p= 0,384). Non-A blood group patients had a significantly higher frequency of arthralgia and dysgeusia. In A blood group 18,5% of the patients required hospitalization, 41,0% of them were admitted in the intensive

care unit and 5,9% presented complications, while in the non-A blood group, were 16,7%, 31,1% and 5,5%, respectively (p>0,05 in all the cases). The most frequent complications in both groups were respiratory distress syndrome and sepsis (p>0,05). The outcome of the COVID-19 infection is detailed in Figure 1. In the multivariate analysis, adjusted for poor prognostic factors, patients with A blood type and those with negative Rh factor presented more likely severe COVID-19. (OR 1,75, 95%CI 1,20 - 2,56, p=0,003 and OR 2,63, 95%CI 1,45 - 4,55, p=0,001, respectively).

Conclusion: Blood type A and negative Rh factor were associated with worse COVID-19 outcomes in this national cohort of patients with rheumatic diseases.

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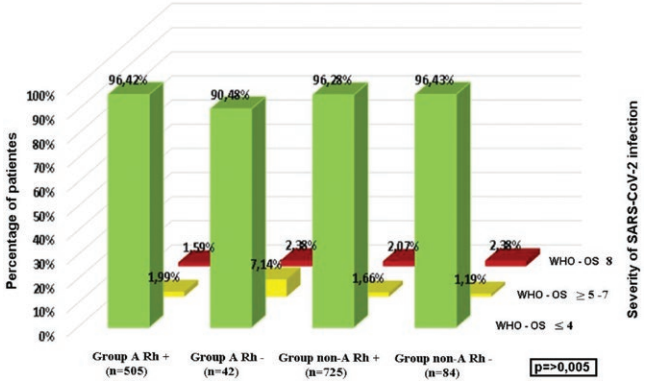


Figure 1. Severity and mortality of SARS-CoV-2 infection according to ABO and Rh blood type in patients with rheumatic diseases.

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AB1298

PATIENTS WITH AXIAL SPONDYLOARTHRITIS HAVE BETTER SARS-COV-2 OUTCOMES COMPARED WITH PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE NATIONAL SAR-COVID REGISTRY

Keywords: COVID, Spondyloarthritis

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Background: Patients with rheumatic diseases may present more severe SARS-CoV-2 infection compared to the general population. However, in some studies, hospitalization and mortality due COVID-19 were lower in patients with axial spondyloarthritis (axSpA) compared to other rheumatic diseases.

Objectives: To assess the severity of SARS-CoV-2 infection in patients with axSpA from the SAR-COVID registry, comparing them with patients with rheumatoid arthritis (RA), and to determine the factors associated with poor outcomes and death.

Methods: Patients ≥18 years old from the SAR-COVID national registry with diagnosis of AxSpA (ASAS criteria 2009) and RA (ACR/EULAR criteria 2010) who had confirmed SARS-CoV-2 infection (RT-PCR or positive serology), recruited from August 2020 to June 2022 were included. Sociodemographic and clinical data, comorbidities, treatments and outcomes of the infection were collected. Infection severity was assessed using the WHO-ordinal scale (WHO-OS)[1]: ambulatory [1], mild hospitalizations (2.3 y 4), severe hospitalizations (5.6 y 7) and death [8].

Statistical analysis: Descriptive statistics. Chi[2] or Fischer test and Student T or Mann-Whitney as appropriate. Poisson generalized linear model.

Results: A total of 1226 patients were included, 59 (4.8%) with axSpA and 1167 (95.2%) with RA. RA patients were significantly older, more frequently female, and had a longer disease duration. More than a third of the patients were in remission. 43.9 % presented comorbidities, arterial hypertension being the most frequent. At the time of SARS-Cov-2 diagnosis, patients with RA used glucocorticoids and conventional DMARDs more frequently than those with axSpA, while 74.6% of the latter were under treatment with biological DMARDs being anti-TNF the most used (61%). 94.9 % of the patients in both groups reported symptoms related to SARS-CoV-2 infection. Although the differences were not significant, patients with RA presented more frequently cough, dyspnea, and gastrointestinal symptoms, while those with axSpA reported more frequently odynophagia, anosmia, and dysgeusia. During the SARS-CoV-2 infection, 6.8% and 23.5% of the patients with axSpA and RA were hospitalized, respectively. All of the patients with axSpA were admitted to the general ward, while 26.6% of those with RA to intensive care units. No patient with axSpA had complications or severe COVID-19 (WHO-OS>=5) or died as a result of the infection while mortality in the RA group was 3.3% (Figure 1). In the multivariate analysis adjusted to poor prognosis factors, no association was found between the diagnosis of axSpA and severity of SARS-CoV-2 infection assessed with the WHO-OS (OR -0.18, IC 95%(-0.38, 0.01, p=0.074).

Conclusion: Patients with EspAax did not present complications from SARS-CoV-2 infections and none of them died due COVID-19.

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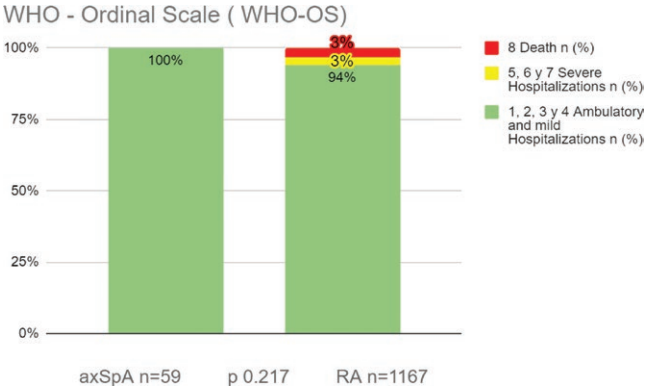


Figure 1. Outcomes and severity of SARS-CoV-2 infection in patients with axSpA and RA.

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AB1299 THE INCIDENCE OF POST-COVID SYNDROME IN PATIENTS WITH RHEUMATIC DISEASES

Keywords: Mental health, Comorbidities, COVID

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Background: Post-COVID Syndrome occurs in people after coronavirus infection with confirmed SARS-CoV-2 infection or in people with suspected coronavirus infection, usually 3 months after the onset of COVID-19, with symptoms that last at least 2 months and cannot be explained by an alternative diagnosis. Although post-COVID manifestations have been previously studied in the general population, they have not been studied in a specific population of patients with inflammatory rheumatic diseases. The list of post-covid syndromes includes arthralgia, arthritis, myalgia, vasculitis with damage to vessels of various sizes, antiphospholipid syndrome, as well as a number of immunological markers that are characteristic of a wide range of rheumatic diseases [1]
Objectives: to study the incidence of post-COVID syndrome in patients with rheumatic diseases (RD).
Methods: From March 2020 to September 2022, 271 patients with RD who had a novel coronavirus infection (NCI) with a confirmed SARS-CoV-2 PCR result and/or X-ray computed tomography (CT) of the lungs were under observation. Among the patients, 68 (25%) were males, 203 (75%) were females. The median age was 56 [46.65] years. The average duration of RD at the time of NCI was 10.9 [5.15] years. The distribution of patients was as follows: rheumatoid arthritis (RA) - 186 people (68.6%), ankylosing spondylitis (AS) - 46 people (16.9%), psoriatic arthritis (PsA) - 38 people (14%). The results of clinical and laboratory examinations for RD were assessed before the NCI and 3 and 6 months after the NCI. A survey of patients was conducted as part of an in-depth medical examination 3 and 6 months after undergoing NCI for the presence of post-COVID manifestations.
Results: 90.4% of patients noted the persistence or appearance of symptoms after undergoing NCI, and all of them had a combination of at least 3 different groups of symptoms. The most common increase/appearance of pain in the joints was 91.1%. Among the respondents, the second symptom in terms of frequency of occurrence, in 52.9% of cases, were asthenic manifestations in the form of the appearance and intensification of fatigue, muscle pain, headaches. A decrease in working capacity and quality of life was noted by 52.9%. Complaints about a significant increase in dyspnea and a decrease in exercise tolerance were noted by 35.3% of the respondents, while there was no connection with the severity of NCI, and half of the patients had a mild course of NCI. Increased chest pain and/ or palpitations - in 23.5% of people. Half of the patients noticed hair loss and skin rash at 3-6 months after NCI: significant 35.2%, insignificant 20.5%. A slight persistence of elevated temperature since recovery from NCI was recorded in 17.6% of patients. RD stage of remission before NCI was in 9 (3.3%), low degree of activity 58 (21.4%), moderate degree of activity 140 (51.6%), high degree of activity 21 (7.7%), 43 (15.8%) people - no data. Moderate and high degrees of RD activity before NCI influenced the increase in joint pain ($p<0.023$), unstable course of diabetes mellitus ($p<0.032$) by 3 after recovery.
Conclusion: In patients with RD, post-covid manifestations persist, primarily due to articular (91.1%) and general constitutional symptoms (85.3%) from 3 to 6 months after undergoing NCI. Moderate and high degrees of RD activity before NCI significantly affect the severity of the articular syndrome and the unstable course of diabetes mellitus. Therapy for post-COVID syndrome in patients with rheumatological diseases should be personalized and determined by the characteristics of this patient's condition.
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AB1300 RHEUMATOLOGICAL MANIFESTATIONS IN A COHORT OF LONG-COVID PATIENTS: SEARCHING FOR POSSIBLE BIOMARKERS

Keywords: COVID

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Background: Approximately 10-20% of patients recovered from SARS-COV-2 infection develop persistent heterogeneous symptoms and autoantibody positivity suggesting persistence of low-grade inflammation.
Objectives: To assess the prevalence of rheumatological manifestations in a cohort of convalescent SARS-CoV-2 patients and to find possible biomarkers.
Methods: Two-hundred and seventy-nine convalescent SARS-CoV-2 patients underwent multidisciplinary assessment in our Post-Covid19 outpatient service (119 females and 160 males; mean age±SD, 55.87±0.88). For each patient, demographic, clinical and immunological data were collected. Long-COVID symptoms were assessed by a questionnaire submitted to patients; IL-1β, IL-6, TNFα and e IL-8 plasma levels were assessed by ELISA (ELLA).
Results: 221 (80.7%) convalescent SARS-CoV-2 patients presented at least one Long-Covid symptom, most frequently fatigue (52.6%), dyspnea (40.7%), arthralgia (28%) and myalgia (28%). The prevalence of symptoms was significantly higher in females ($p = 0.009$) and in patients 60-75 years old ($p = 0.02$) and the presence of symptoms was independent from disease severity and care setting during acute infection. Assessing cytokines plasma levels, we observed that patients presenting Long-COVID arthralgia showed higher IL-6 plasma levels ($p = 0.006$). Moreover, the most common rheumatological symptoms, asthenia and arthralgia, in Long-COVID patients were significantly correlated with female sex ($p = 0.002$), at least one autoantibody positivity ($p = 0.003$) and IL-6 plasma level higher than 2.1 pg/ml ($p = 0.009$).
Conclusion: Rheumatological symptoms are frequent in Long-Covid patients and this study suggests that they are underpinned by persistent dysregulated inflammatory pathways after the acute infection.
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AB1301 CYCLOPHOSPHAMIDE THERAPY DURING THE COVID19 PANDEMIC

Keywords: Vasculitis, COVID, Best practices

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Background: During the Coronavirus disease (COVID-19) pandemic, one of the biggest concerns of rheumatologists and rheumatology patients has been whether the risk or severity of the disease will increase with immunosuppressive therapy. Some drugs have been reported to be associated with adverse Covid19 outcomes [1,2]. Cyclophosphamide (CYC) is a drug that has been used in rheumatology practice for many years. There is not enough data in the literature on the frequency or consequences of COVID-19 while receiving CYC therapy.
Objectives: The aim of this study is to examine the frequency and outcomes of Covid19 in patients who received CYC therapy during the Covid19 pandemic.
Methods: The files of patients who received CYC therapy protocol between March 2020 and March 2022 at Başkent University Faculty of Medicine Ankara Hospital, Rheumatology outpatient clinic were retrospectively reviewed. In our clinic, CYC therapy is administered as an intravenous treatment protocol of 500 mg three times every 10 days, then 500 mg every two weeks. Although the cumulative dose varies depending on the disease and the patient, it is usually planned to be at least three gram. The diagnosis of Covid 19 was made in the patients with clinically compatible radiology and SARS-CoV-2 PCR test results.
Results: A total of 36 patients received CYC during the specified period. CYC indications were ANCA-associated vasculitis in 12 patients, interstitial lung disease

associated with undifferentiated connective tissue disease in 5 patients, SLE in 5 patients, scleroderma in 4 patients, Sjögren's syndrome in 4 patients, Behçet's disease in 1 patient, vasculitis associated with sarcoidosis in 1 patient, rheumatoid vasculitis in 1 patient, leukocytoclastic vasculitis in 1 patient, polymyositis in 1 patient and Takayasu disease in 1 patient.The median age (q1-q3) was 62 (52-68) years. Covid19 infection was detected in only 3 patients (8%) during the CYC therapy protocol. The median cumulative CYC dose for these patients was 3.5g. One out of 3 patient was hospitalized for Covid 19 pneumonia. There was no death due to Covid19.

Conclusion: In this study, it has been shown that CYC therapy was safe during the Covid19 pandemic period.

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AB1302 IMPACT OF THE COVID-19 PANDEMIC ON TREATMENT ADHERENCE AND THE ACTIVITY OF RHEUMATOID ARTHRITIS

Keywords: Outcome measures, Rheumatoid arthritis, COVID

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Background: During the COVID-19 pandemic, repetitive lockdowns and fear of SARS-CoV-2 infection compromised the treatment adherence of immunocompromised patients, particularly those with rheumatoid arthritis (RA). These therapeutic changes have certainly affected RA activity.

Objectives: To assess the treatment adherence among RA patients during COVID-19 and the impact on disease activity.

Methods: We conducted a cross-sectional study involving patients with RA who met the ACR/EULAR 2010 criteria. To evaluate therapeutic adherence we used 2 validated scores: the Compliance Questionnaire of Rheumatology-5 (CQR-5) and the Morisky Medication Adherence Scale-4 (MMAS-4). For each patient, we compared the DAS28 score, visual analog pain scale (VAS), sedimentation rate (ESR), and C-reactive protein (CRP) before and during the pandemic.

Results: We included 190 patients, of whom 155 were women and 35 were men. The average age was 55 ± 13.16 years. During the COVID-19 pandemic, the mean DAS28 score was 4.17 ± 1.03. Poor adherence was observed in 33% of cases according to MMAS-4 and in 34.5% of cases according to CQR-5. Patients who missed at least one consultation appointment accounted for 65% of cases. Teleconsultation was used in 17% of cases. Non-renewal of the prescription was the most frequent reason for therapeutic modification (47%). Sixty patients (31.7%) had contracted COVID-19 and the minor form was the most frequent (86% of cases). Poor therapeutic adherence assessed by the CQR-5 was significantly associated with: rural origin (p<0.001), low intellectual level (p=0.006), missed consultations (p<0.001), non-use of teleconsultation (p<0.001), and high disease activity (p<0.001). Factors associated with poor adherence according to MMAS-4 were: advanced age (p=0.01), rural origin (p=0.007), low intellectual level (p=0.004), comorbidities (p=0.003), failed consultations (p=0.001), non-use of teleconsultation (p<0.001) and SARS-CoV-2 infection (p=0.043). The correlational study showed that compared to pre-pandemic values: pain (p=0.001), ESR (p=0.008), CRP (p=0.04), and DAS-28 (p=0.001) were significantly higher during the pandemic. increased disease activity was significantly associated with the presence of comorbidities (p=0.018), low therapeutic adherence (p<0.001), and missed consultations (p=0.014). There was no significant association between SARS-CoV-2 infection and disease activity.

Conclusion: Treatment adherence of RA patients during the COVID-19 era was challenged. Elderly, illiterate, and rural patients were the most likely to miss their appointments and stop their treatments. These therapeutic changes were responsible for an increase in RA activity. Hence the importance of insisting on good adherence and close medical follow-up.

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AB1303 AVASCULAR NECROSIS OF THE FEMORAL HEAD – NOT TO BE OVERLOOKED SEQUELA AFTER COVID 19 INFECTION

Keywords: Bone diseases, COVID

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Background: COVID 19 infection could lead to different sequelae in survivors, known as post-COVID or long COVID 19 syndromes. Some of them are thought to be due to the thrombophylic changes observed in COVID 19 infection, but some are thought to be caused by the administrated (especially high dose) corticosteroid treatment. Avascular necrosis of the femoral head (AVNFH) is a multifactorial disease which leads to compromised vascular supply, ischemia and finally necrosis of the femoral head. As corticosteroids usage and thrombophylic states are among the main known risk factors for the development AVNFH [1], it could be presumed that the frequency of this disease will increase with the COVID 19 pandemic. The exact corticosteroid dose needed for the development of AVNFH is not clear, but it has been stated that a higher daily dose and a larger total cumulative dose increase substantially the risk for the development of osteonecrosis [2].

Objectives: To describe in detail the characteristics of AVNFH diagnosed in patients after COVID 19 infection.

Methods: The study was done in a tertiary university rheumatological clinic. Data was extracted from the records of patients who have been referred to the clinic because of hip pain between June and December 2022. Inclusion criteria were: - a new onset of uni-or bilateral hip pain that started after a documented COVID 19 infection; and an MRI scan of the hip joints showing osteonecrosis of one or both femoral heads. Exclusion criteria were the presence of hip pain prior to the COVID 19 infection, anamnesis of traumatic injuries of the hips or pelvis, personal history of hypercoagulable states.

Results: Nine patients (4 women and 5 men) with an average age 59.1 years (range 38-72) were included in the study. Four patients had been diagnosed with bilateral and five – with unilateral AVNFH, thus 13 hip joints were analysed in total (8 left and 5 right sided). The mean time lap between the COVID 19 infection and the start of the hip pain was 26.2 weeks (range 10-48 weeks). All patients had limited and painful movement in their symptomatic hip(s), especially internal rotation and four of the patients had also elevated CRP levels (mean 11.7 mg/L). The stage of the AVNFH was evaluated according to the Ficat-Arlet classification (0-IV stage). In four hips the AVNFH was stage I, five hips were classified as stage II and the remaining four joints - as stage III. All symptomatic hip joints exhibited effusion/synovitis on both ultrasound examination and the corresponding MRI scan. It should be noted that the presence of hip effusion was found to be related with a worse prognosis in AVNFH [1]. In three patients the amount of the effusion required arthrocentesis and fluid aspiration. The analysis of the joint fluid was consistent with a degenerative disease (i.e., low WBC count with predominant lymphocytes and no crystals). All patients included in our study had received corticosteroids during their COVID19 infection, while 6 of the patients had also been hospitalized due to more severe disease. According to the patients' documentation, the mean cumulative dose of the received corticosteroids was 936.2 mg prednisolone equivalent per patient (range 187-2272 mg).

Conclusion: AVNFH must not be overlooked in a new onset hip pain after COVID 19 infection. Our results show that corticosteroids administrated during the infection and the presence of hip joint effusion on ultrasound are especially suggestive for the development of osteonecrosis, as they were registered in all of our patients. The presence of these two factors necessitates patient referral for an MRI scan of the hips, in order that AVNFH be detected timely.

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AB1304 CHRONIC CHILBLAIN-LIKE LESIONS ASSOCIATED WITH THE COVID-19 PANDEMIC

Keywords: Imaging, COVID, Skin

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Background: The term long-covid encompasses a heterogeneous spectrum of chronic symptoms following infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1].
Objectives: We report the features of chronic chilblain-like digital lesions newly presenting since the start of the covid-19 pandemic. Comparison with primary perniosis and acrocyanosis, reveals a unique phenotype which appears to be a long-covid phenomenon.
Methods: The case records of 26 patients with new onset persistent chilblain-like lesions presenting to the Rheumatology service of St George's University Hospital, London between Autumn 2020 and Spring 2022 were reviewed. Demographic and clinical features, serology, imaging, treatment response and outcome up to Summer 2022 were collated retrospectively.
Results: Chilblain-like lesions first occurred between September and March; 2019/2020 6 cases, 2020/2021 18 cases and 2021/2022 2 cases. Mean age 35.4 (17-60) years, female 88%, white 85%, all non-smokers. Median body mass index (BMI) 20.2, range 17.0 – 33.2. BMI underweight (<18.5) in 27%. All cases reported new red-purple-blue colour changes of the fingers, some with pain, swelling and pruritis, affecting both hands in 12, one hand in 6, and both hands and feet in 8 cases. There was a past history of cold sensitivity or primary Raynaud's in 54%. Covid was confirmed in 3 cases, 2 – 8 months prior to onset of chilblain-like symptoms. Possible covid, unconfirmed, was suspected in 5 cases, 1 – 11 months earlier. Affected digits appeared diffusely erythro-cyanotic in 81%, with blotchy discrete maculo-papular erythematous lesions in 42%, some with both features. Involvement was asymmetric in 54%, thumbs spared in 69%. Complement was low in 50% (8/16), ANA positive in 26% (6/23). MRI of hands showed phalangeal bone marrow oedema in keeping with osteitis in 4/7 cases, and no synovial hypertrophy or entheseal abnormalities. More severe signs and symptoms were associated with low BMI, low C3/4 and a past history of cold sensitivity or Raynauds. Cold avoidance strategies were sufficient for 58%. Pain prompted a trial of NSAIDs, aspirin, nitrates, calcium channel blockers, hydroxychloroquine, oral or topical corticosteroid or topical tacrolimus in 42%. In general, these were at best minimally effective or not tolerated. Four severe cases received sildenafil or tadalafil, effective in 2 cases. In 27% complete remission occurred during the first summer season after symptoms commenced, median duration 6 (range 2 – 10) months. In the remaining 19 cases, chilblain-like symptoms returned or worsened in the subsequent second winter period, with 6/19 entering remission the following summer. For the remaining 13 persistent cases the total duration of symptoms spans more than a year, and in four cases more than 2 years.
Conclusion: This series illustrates a distinct chronic chilblain-like condition. Features similar to primary perniosis include female predominance, middle age, pruritic painful blotchy lesions, asymmetry and low BMI. Features in keeping with acrocyanosis include chronicity, extensive diffuse erythro-cyanotic discoloration, relative improvement in warm weather and lack of association with smoking.
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AB1305 RHEUMATOID ARTHRITIS FLARE FOLLOWING COVID-19 VACCINATION IN MALAYSIAN POPULATION AND ITS ASSOCIATED RISK FACTORS

Keywords: Vaccination/immunization, Rheumatoid arthritis, COVID

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Background: Flare of Rheumatoid Arthritis (RA) following COVID-19 vaccination has been reported with a low occurrence observed in those patients with disease remission. However, no local data is available in our multi-ethnic Malaysian population.
Objectives: To evaluate the prevalence of RA flare in Malaysian patients following COVID-19 vaccination and its associated risk factors.
Methods: This was a cross-sectional study assessing RA flare based on patient-reported disease flare through self-administered questionnaires and physician-reported flare. Patient self-reported disease flare was defined as 'a sudden worsening of rheumatology condition or arthritis within 1 month post-vaccination' while physician-reported flare was defined as 'an increment of disease activity score 28-joint documented within 3 months post-vaccination' from either a scheduled or unscheduled clinic visit. A total of 186 RA patients attended the rheumatology clinic in Hospital Putrajaya from May to July 2022 who completed the primary COVID-19 vaccination under the Malaysian National Vaccination Programme were recruited. Demographic data, disease parameters including serology for rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA), cessation of disease modifying anti-rheumatic drugs (DMARDs) around vaccination, type of vaccines and adverse events were examined using descriptive and univariate analyses.
Results: Majority (93%) of RA patients enrolled were female with a mean age of 58 years old (standard deviation, SD 12.2) and mean disease duration was 12 years (SD 7.7). More than half were seropositive (66% RF, 63% ACPA) with 47.4% had double seropositivity (RF and ACPA positive). All patients received DMARDs with the majority (71%) were on methotrexate (MTX), 21.5% were on leflunomide, 17.7% on other DMARDs, with a small proportion (14%) of patients were receiving prednisolone. Only 4.8% of patients were on biologics or targeted synthetic disease modifying anti-rheumatic drugs. Half of the patients were in remission prior to vaccination. 62% of patients received Pfizer-BioNTech vaccine as the primary vaccine, followed by Sinovac-CoronaVac (24.6%) and Oxford-AstraZeneca (13.4%) vaccines. A booster dose had been administered to 80% of patients, of which 88.7% was Pfizer-BioNTech vaccine. MTX therapy were discontinued in 39.4% of patients (n=52) post-vaccination for a week duration. The prevalence of RA flare was only 12.9% (n=24) in which 14 were self-reported and 10 were physician-reported flares (4 severe flare, 6 mild-moderate flare). Flare rates were higher during the first and second dose of vaccination with 29.2% respectively, and only 12.5% were reported after booster vaccination. Common vaccine adverse effects were fever (16.8%), myalgia (8.6%) and arthralgia (6.4%). There were no significant differences in the occurrence of flare post-vaccination between age, gender, disease activity prior to vaccination, types of vaccine, usage of MTX and prednisolone, and discontinuation of MTX post-vaccination. Although seropositivity did not exhibit statistically significant flare rate post vaccination, sub-analysis revealed four times higher rate of flare in those who has double positivity compared to seronegative RA patients (12% vs 4%).
Conclusion: Prevelance of RA flare post-COVID-19 vaccination in Malaysian RA population is low. No significant associated risk factors were identified although double seropositivity appeared to have higher number of flares.
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AB1306 HOW DOES COVID-19 VACCINATION AFFECT DISEASE ACTIVITY AND SAFETY IN SECUKINUMAB TREATED PATIENTS WITH AXIAL SPONDYLOARTHRITIS? REAL WORLD DATA FROM THE GERMAN AQUILA STUDY

Keywords: Spondyloarthritis, Vaccination/immunization, COVID

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Background: Patients (pts) suffering from a chronic rheumatic condition, such as axial spondyloarthritis (axSpA), and receiving immunosuppressive treatment during the COVID-19 pandemic have been shown to be at higher risk of severe disease outcomes. The German non-interventional study AQUILA provides real-world data in pts with axSpA under secukinumab (SEC) treatment and the influence of COVID-19 vaccination on disease activity (DA) and safety [1].
Objectives: The aim of this interim analysis was to describe selected baseline (BL) characteristics and the effect of vaccination on DA and safety in axSpA pts.
Methods: AQUILA is an ongoing, multi-center study including up to 3000 pts with axSpA or psoriatic arthritis. This analysis focuses on axSpA pts included from May 2019 to Oct 2022 and their vaccination status (no vs ≥1 vaccination) for study time points from BL up to week (w) 52 according to clinical routine. DA was assessed by validated Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questionnaire and safety by documented number of (serious) adverse events (S)AEs). Only pts with available BL BASDAI were considered and characterized by selected BL parameters, such as demographics and global functioning

(measured by assessment of spondyloarthritis international society health Index, ASAS-HI). Real-world data were analyzed as observed. Vaccination was performed according to prescription and took place at any timepoint throughout observational period of 52 weeks.

Results: Totally, 273 axSpA pts were included. For 56 pts ≥1 vaccination during study was documented: number of vaccinations (75% mRNA-based): n1 = 26 pts, n2 = 20 pts, n3 = 9 pts, n4 = 1 pt.

Both pts groups were comparable regarding the BL characteristics, such as age, smoking status, BMI, physician global assessment (PhGA), and ASAS-HI. Pts with no vaccination received less pretreatments with biologics (59.9% vs 76.8%) and were less affected by comorbidities and extra-articular manifestations (EAMs) than pts with ≥1 vaccination (e.g. depression 6.5% vs 12.5%) (Table 1). There was no difference in mean BASDAI between pts with no and with ≥1 vaccination throughout observational period of 52 weeks (except for a higher mean value in pts with ≥1 vaccination at w16). In both groups, slight improvement was observed in mean BASDAI over time (no vaccination: 5.1 to 3.8, ≥1 vaccination: 5.4 to 3.7) (Figure 1). However, due to different numbers of pts with no and ≥1 vaccination, data must be interpreted carefully. The number of pts with AEs and AEs leading to interruption of SEC was lower in pts with no vs pts with ≥1 vaccination (62.7% vs 75.0% and 13.4% vs 17.9%, respectively) (Table 1), with no new and unexpected safety signals in each group.

Conclusion: In a real-world setting, no differences in DA between axSpA pts with and without vaccination were observed. DA improved similarly up to w52 in both patient groups with similar BL characteristics, though more comorbidities/EAMs were documented in pts with ≥1 vaccination. There were no new safety signals in both groups. Further progress of the AQUILA study will reveal whether this trend will be confirmed with more patients included.

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Table 1. Overview of characteristics at BL and (S)AEs during treatment

Parameters at BL	No vaccination (N=217)	≥1 vaccination (N=56)
Age* (years)	47.1 (13.5)	46.7 (13.0)
Smoking status (smoker)**	73 (33.8)	19 (33.9)
BMI* (kg/m^2)	27.4 (5.6)	27.5 (5.4)
PhGA*	5.3 (2.0)	5.0 (2.0)
ASAS-HI*	7.5 (3.4)	8.6 (3.5)
Pre-treatment with biologics**	130 (59.9)	43 (76.8)
Comorbidities/EAMs at BL**		
Coronary heart disease	10 (4.7)	3 (5.3)
Heart insufficiency	3 (1.4)	2 (3.6)
Stroke	2 (1.0)	1 (1.8)
Plaque psoriasis	20 (9.2)	7 (12.5)
Uveitis	6 (2.7)	3 (5.3)
Depression	14 (6.5)	7 (12.5)
Safety - number of pts with**		
AEs/ SAEs	136 (62.7)/ 13 (6.0)	42 (75.0)/ 5 (8.9)
AEs leading to interruption of SEC	29 (13.4)	10 (17.9)

* mean (sd), ** n (%)

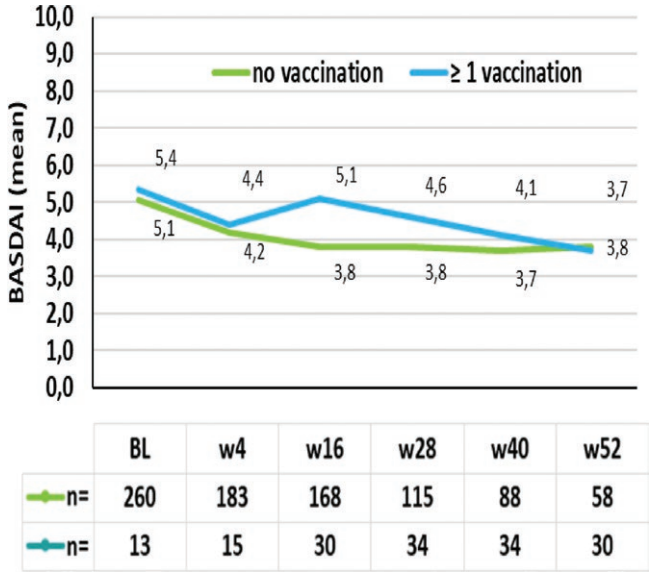


Figure 1. DA under SEC treatment in axSpA pts stratified by vaccination

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AB1307

ANALYSIS OF ANTI-SARS-COV-2 S-RBD IGG ANTIBODY LEVELS IN A COHORT OF PATIENTS RECEIVING IL-1 INHIBITORS

Keywords: Vaccination/immunization, COVID

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Background: Rheumatological patients are notoriously at increased risk of infections, since they receive immunosuppressive or immunomodulatory drugs, which may reduce the response to vaccination. However, current evidence has shown that several biologics may have little or no influence on the efficacy of COVID-19 vaccination. In this context, anti-IL-1 drugs, commonly employed for the treatment of several autoinflammatory disorders such as Familial Mediterranean Fever (FMF) and adult-onset Still's disease (AOSD), have been successfully used to treat the "hyperinflammatory syndrome", provoked by SARS-CoV-2, by contrasting the cytokine storm and avoiding the more severe consequences of the infection, although not inhibiting the recovery.

Objectives: In this study, our aim is to evaluate the antibody response after COVID-19 vaccination in a group of patients affected by systemic autoinflammatory diseases (SAID) undertaking IL-1 inhibitors, compared to a group of healthy vaccinated controls (HC). Then, we evaluated the course of COVID-19 infection in a group of vaccinated patients treated with anti-IL-1.

Methods: In 43 patients, referred to the Outpatient Autoinflammatory Clinic of the Rheumatology Unit of Padova University Hospital, the serological response after anti-SARS-CoV-2 vaccination was assessed using the CLIA MAGLUMI™ 2000 Plus test, 40 days, and six months after the first vaccination cycle and after the booster dose. Fifty-four full-vaccinated healthcare workers of equal age and sex were enrolled as HCs. Due to significant differences in antibody levels, HC and SAID patients who had COVID-19 were excluded from the analysis. *GraphPad Prism 8* software was used for statistical analysis.

Results: All SAID patients vaccinated with two or three doses developed an adequate antibody response (>33 kBAU/L). No significant differences were observed between antibody levels developed by patients receiving IL-1 inhibitors compared to those not on anti-IL-1 after the first vaccination cycle (T3, p = 0.99, T6, p = 0.99) or the booster dose (p=0.99). The mean antibody titer after booster dose was not different in SAID compared to HC (2276 ± 2653 kBAU/L of HC vs 3738 ± 3974 kBAU/L of SAID, p = 0.99). No gender differences were observed between the antibody titres. With increasing age, a physiological decrease in antibody production was assessed six months after the second vaccine shot in SAID (r = 0.67, p = 0.0003). Overall, 13/43 (30.2%) patients in our cohort had COVID-19 and 5/43 (11.6%) had it after receiving vaccination. None of them developed a severe disease, long-COVID, or experienced flares of the underlying autoinflammatory disease.

Conclusion: In patients receiving anti-IL-1 drugs, the antibody response after vaccination is comparable to the serological response observed in HC. Furthermore, no side effects were observed after vaccination and anti-IL-1 therapies were continued before and after the injections to avoid flare-up of the disease.

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COVID-19

AB1308 POLYMYALGIA RHEUMATICA FOLLOWING SARSCOV-2 VACCINATION: A SINGLE CENTER COHORT STUDY

Keywords: Descriptive studies, Vasculitis, Vaccination/immunization

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Background: Polymyalgia rheumatica (PMR) incidence peaks in individuals between 70 and 80 years of age; this same group is also at increased risk of complications and mortality related to COVID-19 infection. Vaccination against SARS-CoV2 is an essential tool in combatting COVID-19. There have been several case reports of PMR following vaccination with mRNA SARS-CoV2 vaccines.
Objectives: The aim of this study was to identify patients with temporal association between mRNA SARS-CoV2 vaccination and PMR onset and to compare characteristics and disease course to those with new onset PMR without temporal association with SARS CoV2 vaccine exposure.
Methods: We conducted a retrospective chart review of all newly diagnosed PMR patients in a single center. Using ICD-10 codes, our EMR was queried to identify patients with newly diagnosed PMR beginning in December 2020, when the first SARS-CoV-2 vaccines were available in the US. Charts were reviewed for demographic information, disease characteristics and vaccination details. Patients who developed onset of PMR symptoms within 6 weeks after vaccination were compared to those whose PMR symptoms occurred without temporal association to vaccination. When available data at 6 and 12 months following diagnosis was collected.
Results: Eighty patients with newly diagnosed PMR between 12/1/2020 and 12/31/2021 were identified. There were 60 patients with new PMR without a temporal association to vaccination who were compared to 20 patients who developed PMR symptoms within 6 weeks of vaccination. Baseline demographics did not differ between the two groups. In the 20 cases with PMR onset after vaccination, symptoms developed a mean 38 days (IQR 19.5-48) after first dose of vaccine and 11.5 days (IQR 1-22) after second dose. There were no differences in baseline demographics, glucocorticoid dosages or relapse rates at 6 and 12 months following diagnosis. There was no association between vaccine manufacturer and PMR onset after vaccination (Table 1)
Conclusion: In this cohort, patients with onset of PMR within 6 weeks following mRNA vaccination against SARS-CoV2 were similar to patients with de novo PMR at diagnosis, with no significant differences in disease course over the first 12 months. This does not support the notion that PMR following vaccination is a unique disease entity. The recognition of new PMR onset following SARS CoV2 vaccine may be coincidental in this common inflammatory disorder in a population with high rates of vaccine exposure.

Table 1.

	Entire Cohort	PMR without temporal association to vaccine	PMR within 6 weeks of vaccine	p-value
N	80	60	20	
Age, median (IQR)	74.5 (71, 80)	75.5 (71, 80)	73.5 (69, 79.5)	0.43
Sex				0.80
Male	40 (50%)	29 (48%)	11 (55%)	
Female	40 (50%)	31 (52%)	9 (45%)	
Vaccine Type				1.00
Moderna	38 (48%)	29 (48%)	9 (45%)	
Pfizer	42 (53%)	31 (52%)	11 (55%)	
Baseline ESR (mm/hr), median (IQR)	44 (24, 65)	42 (24, 63)	44.5 (23, 65)	0.89
CRP at baseline (mg/L), median (IQR)	20 (7.55, 48.5)	20 (9, 42)	14.2 (7, 60.2)	0.77
Initial steroid dose, median (IQR)	20 (15, 30)	20 (15, 24)	20 (15, 37.5)	0.96
Additional vaccine received?				0.55
No	22 (28%)	15 (25%)	7 (35%)	
Yes	43 (54%)	33 (55%)	10 (50%)	
missing	15 (19%)	12 (20%)	3 (15%)	
ESR at 6 months (mm/hr), median (IQR)	16 (5, 24)	16 (5, 30)	9.5 (4, 21.5)	0.27
Steroid dose at 6 months (mg), median (IQR)	5 (4, 8)	5 (4, 9.5)	6 (2, 8)	0.74
Relapse at 6 months				0.74
No	51 (64%)	36 (60%)	15 (75%)	
Yes	15 (19%)	12 (20%)	3 (15%)	
missing	14 (18%)	12 (20%)	2 (10%)	
ESR at 12 months (mm/hr), median (IQR)	14 (4, 29)	14 (4, 34)	13.5 (3, 24)	0.81
CRP at 12 months (mg/L), median (IQR)	7 (4, 7.5)	7 (5, 9)	7 (3, 7)	0.51
Steroid dose at 12 months (mg), median (IQR)	3 (0, 6)	3 (1.25, 6)	0 (0, 4)	0.11
Relapse at 12 months				0.65
No	27 (34%)	22 (37%)	5 (25%)	
Yes	8 (10%)	6 (10%)	2 (10%)	

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AB1309 CLINICAL CHARACTERISTICS OF NEW-ONSET IDIOPATHIC INFLAMMATORY MYOPATHIES FOLLOWING SARS-COV-2 INFECTION OR VACCINATION – ANALYSIS OF A CASE SERIES

Keywords: Vaccination/immunization, Myositis, COVID

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Background: Recent data showed that SARS-CoV-2 infection and vaccination could act as a trigger for different autoimmune diseases, including idiopathic inflammatory myopathies (IIM).
Objectives: The aim of this study was to describe the clinical characteristics of patients diagnosed with IIM following SARS-CoV-2 infection and vaccination in a tertiary rheumatology center.
Methods: We conducted a retrospective analysis on patients newly diagnosed with IIM, from 1 January 2020 to 31 December 2022, using information from the hospital database. The patients were selected according to the ICD-10 codes indicating IIM (M33.0, M33.1, M33.2, and M33.9). The cases with onset of specific IIM symptoms within 6 months after SARS-CoV-2 infection or vaccination were selected for further analysis. Clinical, biological and immunological parameters were assessed using descriptive statistics.
Results: A total of 58 patients newly diagnosed with IIM were identified, and in 10 (17.2 %) patients the onset was after SARS-CoV-2 infection (n = 6) or vaccination (n = 4). All patients diagnosed with IIM following vaccination (F:M=1:1, median age 46 years) received a mRNA vaccine and had the clinical onset within several days to a month after vaccination. Among IIM cases following SARS-CoV-2 infection (F:M=1:1, median age 60.5 years), the clinical onset of myopathy was variable, with a minimum of 14 days and a maximum of 6 months after infection. Myalgia, muscle weakness and elevated levels of creatinine kinase were reported in 9 patients. The average CK level was 2534.6 (3760.8) U/L, ranging from 43 to 11827 U/L. Skin lesions were present in all patients with IIM following vaccination and in 4 cases with IIM after SARS-CoV-2 infection. Mechanic's hands and arthralgia were noted in 5 patients each. Dyspnea and interstitial lung disease (ILD) were reported in 8 cases, with severe pulmonary involvement present in 2 cases. Myocarditis was reported in 2 patients, 1 case from each group. Myositis-specific antibodies (MSAs) and myositis-associated antibodies (MAAs) were reported in 9 patients. Anti-threonyl-tRNA synthetase antibodies (anti-PL7) were present in 5 cases (3 after vaccination and 2 after infection), anti- histidyl-tRNA synthetase antibodies (anti-Jo-1) in 2 patients (in 1 associated with anti-PL7 antibodies), and anti-isoleucyl-tRNA synthetase (anti-OJ antibodies) in 1 patient. ILD was diagnosed in all anti-PL7 antibody positive patients.
Conclusion: Anti-PL7 antibodies are frequent in newly diagnosed IIM following SARS-CoV-2 infection or vaccination. Further studies are needed to investigate the relationship between SARS-CoV-2 infection and vaccination in the occurrence of IIM.
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Disclosure of Interests: None Declared.
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AB1310 UTILIZATION AND ATTITUDES TOWARDS NAILFOLD VIDEOCAPILLAROSCOPY FOR THE ASSESSMENT OF MICROVASCULAR STATUS IN PATIENTS WITH LONG-COVID: A MULTICENTER ONLINE SURVEY

Keywords: COVID, Imaging

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Background: Human SARS-CoV-2 infection is responsible for a large variety of clinical manifestations related to Coronavirus disease-19 (COVID-19) [1]. SARS-CoV-2 can induce microvascular damage, that can be safely detected by nailfold videocapillaroscopy (NVC), as recently demonstrated [2-4]. Virus-induced endothelial dysfunction has been implicated in the pathogenesis of both active infection and long-COVID clinical manifestations (the last as persistence of disease symptoms after at least three months from onset) [5]. The study group on capillaroscopy and microcirculation in rheumatic diseases of the Italian Society of Rheumatology (CAPSIR) carried out an internal survey on the interest of the Italian Centers that perform NVC in participating in a detailed capillaroscopic and clinical data collection in long-COVID patients.
Objectives: To carry out an Italian multicenter cognitive survey on the interest in collecting NVC and clinical data of patients affected by long-COVID with or without previous rheumatological diseases.
Methods: The steering committee of the CAPSIR study group formulated a cognitive questionnaire, entitled "Study on the role of capillaroscopy in patients with long-COVID" (CAPSIR_2 Study), consisting of 27 open or multiple-choice questions. A Google Form of the questionnaire was emailed to all the member of the study group between September and October 2022. Data are reported with a descriptive analysis.
Results: The online questionnaire was completed by 41 CAPSIR members, belonging to 33 different Italian centers. Of note, 63% of participants had already experienced NVC in patients with long-COVID. The primary indication to perform the NVC was the onset of a new Raynaud's phenomenon (46% of cases) and the requests come mainly from General Practitioners (33% of cases). In 2/3 of the cases, patients with long-COVID and previous rheumatic diseases, who underwent NVC examination, represented less than 20% of the total. It should be noted that always in 2/3 of the cases there was no preferential channel for the study of the microcirculation in patients affected by long-COVID nor a NVC investigation prior to the SARS-CoV-2 infection. According to the previous experience of the participants in the interview, the most important NVC parameters considered to be evaluated in long-COVID patients were number of capillaries per linear millimeter (24% of cases), presence of hemorrhages (34% of cases) and giant capillaries (22% of capillaries). All participants (100%) therefore agreed to participate in a further collection of NVC and clinical data in this cohort of patients.
Conclusion: This survey highlighted the interest of Italian Rheumatologists in assessing by NVC the COVID-related microvascular involvement. A consensus has emerged that future research is needed. After this pilot survey, the second part of the CAPSIR_2 Study will concern the collection/analysis before and after the SARS-CoV-2 infection of NVC and clinical data in patients with primary and secondary (to rheumatic diseases) Raynaud's phenomenon and affected by long-COVID versus adequate controls. The aim is to investigate if the presence/severity of the microvascular damage might be involved in the pathogenesis of the clinical manifestations observed in COVID-19 patients after the active infection. CAPSIR_2 Study will be open to all Italian rheumatological centers that participated in the previous national CAPSIR_1 Project [6].
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AB1311

EVALUATION OF A POTENTIAL INDUCTION OF AUTOANTIBODIES IN A COHORT OF PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS, SYSTEMIC SCLEROSIS OR WITH TRIPLE POSITIVITY FOR ANTIPHOSPHOLIPID ANTIBODIES FOLLOWING ANTI-SARS-COV2 VACCINATION

Keywords: Vaccination/immunization, COVID, Autoantibodies

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Background: Vaccines anti-SARS-CoV2 showed a good efficacy in prevention of severe COVID-19 [1]. Their potential in induction of autoantibodies (abs) has not been well established [1]. One recent study demonstrated an increase of abs' titer after anti-SARS-CoV2 vaccination only in patients (pts) with already pre-existing positivity [2].
Objectives: To evaluate the potential induction of abs after SARS-CoV2 vaccination in a cohort of pts affected by Rheumatoid Arthritis (RA), Systemic Sclerosis (SSc) or with triple positivity for antiphospholipid antibodies (aPL).
Methods: Consecutive pts affected by RA, SSc or with triple positivity for aPL were enrolled from February 2021 to November 2021. Serum samples were collected before the first (T0) and at least one month after the second administration (T1) of the anti SARS-CoV-2 vaccine. A wide panel of abs were evaluated through routinely methods. Qualitative variables were compared using Chi-square test or Fisher's exact test; quantitative variables were compared using Wilcoxon signed-rank test.
Results: 52 pts were considered [F/M= 48/4; median age=58(51-61.3) years; 15 RA, 19 SSc and 18 with triple positivity for aPL]. Regarding vaccination, 27 pts were administered BNT162b2, 24 mRNA-1273 and 1 Gam-COVID-Vac. No difference regarding frequency of abs' positivity was found between T0 and T1, except for aB2GPI IgG, that showed a reduction in positivity frequency (**Table 1**) No difference was found in the titer of the following abs: anti-dsDNA (p:0.318), anti-MPO (p:0.678) ed anti-PR3 (p:0.139). ACL IgG showed a significant reduction in chemiluminescence (CL) (T0 vs T1: 9.3 CU [6.1-41.6] vs 5.1 CU [2.5-35.7]; p:0.001), but not in ELISA (p:0.480). A significant reduction was found for aCL IgM both in CL (T0 vs T1: 5.7 CU [2.4-17.1] vs 3.4 CU [2.1-13.1]; p:0.006) and ELISA (T0 vs T1: 13.1 IU/ml [11.2-30.5] vs 11.2 IU/ml [11.2-19.5]; p:0.010). A significant reduction was found for aB2GPI IgG in CL (T0 vs T1: 25 CU [9.1-210.7] vs 6.4 CU [6.3-102.2]; p:0.001), but not in ELISA (p:0.953) Titre of aB2GPI IgM remained stable in CL (p:0.078) and ELISA (p:0.211). No variation was observed in ANA positivity. No significant difference was found in anti-ENA titre (p:0.141). None of the pts developed any new symptom or sign of autoimmune disease upon vaccination.
Conclusion: Anti-SARS-CoV2 vaccination didn't induce any clinical sign of autoimmunity in this cohort of pts affected by RA, SSc or with triple positivity for aPL. Serology for abs remained stable in pts' majority; only a fluctuation of aPL titre was found, generally in terms of reduction and without clinical significance.
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Table 1. Frequency of autoantibodies positivity before (T0) and after (T1) anti-SARS-CoV2 vaccination. Chi-square test or Fisher's exact test were applied. In bold, statistically significant comparison.

Autoantibodies	Patients positive at T0	Patients positive at T1	p-value
Anti-dsDNA*	8/51 (15.7%)	10/52 (19.2%)	0.636
aCL IgG *	18/51 (35.3%)	16/52 (30.8%)	0.625
aCL IgG°	10/50 (20%)	9/52 (17.3%)	0.727
aCL IgM*	10/51 (19.6%)	9/52 (17.3%)	0.763
aCL IgM°	27/50 (54%)	20/52 (38.5%)	0.116
aβ2GPI IgG*	28/51 (54.9%)	18/52 (34.6%)	**0.038**
aβ2GPI IgG°	10/50(20%)	12/52(23.1%)	0.706
aβ2GPI IgM*	9/51 (17.6%)	8/52 (15.4%)	0.757
aβ2GPI IgM°	9/50(18%)	10/52(19.2%)	0.873
aMPO°	8/50 (16%)	8/52 (15.4%)	0.932
aPR3°	7/50 (14%)	7/52 (13.5%)	0.844

dsDNA=double-stranded DNA; aCL: anti-cardiolipin; aβ2GPI: anti-beta2-glycoprotein I; aMPO: anti-myeloperoxidase; aPR3: anti-proteinase3 *= chemiluminescence method; °= ELISA method

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AB1312 **MYOSITIS PATIENTS WITHOUT AUTOIMMUNE MULTIMORBIDITY AT LOWER RISK OF DELAYED ONSET COVID-19 VACCINE ADVERSE EVENTS THAN OTHER AUTOIMMUNE DISEASES: RESULTS FROM THE COVAD STUDY**

Keywords: Safety, Myositis, Vaccination/immunization

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Background: Limited data on the delayed onset effects of COVID-19 vaccination in patients with idiopathic inflammatory myopathies (IIMs) continues to be a significant cause of hesitancy in this vulnerable group.
Objectives: To analyze the delayed onset adverse events (ADEs) of COVID-19 vaccination in patients with IIMs, other systemic autoimmune and inflammatory disorders (SAIDs), and healthy controls (HCs), using data from the ongoing 2nd COVID-19 Vaccination in Autoimmune Diseases (COVAD) study.
Methods: A validated patient self-reporting e-survey was circulated by the international COVAD study group (157 collaborators, 106 countries) from Feb to June 2022, collecting respondent demographics, comorbidities, IIM/SAID details, COVID-19 infection history and outcomes, and vaccination details including ADEs. Delayed onset (> 7 day) ADEs (including minor and major ADEs and hospitalizations) were analyzed in patients with IIMs, SAIDs, and HCs, using various regression models.
Results: 15,165 total respondents completed the survey, of whom 8759 complete responses from vaccinated individuals [median age 46 (35-58) years, 74.4% females, 45.4% Caucasians] were included in the analysis. Of these, 1390 (15.9%) had IIMs, 50.6% other SAIDs, and 33.5% were HCs. 16.3% of IIMs patients reported minor ADEs, and 10.2% experienced major ADEs, and 2.9% required hospitalization. Patients with IIMs had a lower risk of minor ADEs than other SAIDs, though a higher risk of rashes compared to HCs [OR 4.0 (2.2-7.0), p<0.001]. In the IIMs subgroup, patients with active disease, overlap myositis, and ChadOx1 nCOV-19 (Oxford/AstraZeneca) recipients were at a higher risk of ADEs, while those with inclusion body myositis, and BNT162b2 (Pfizer) vaccine recipients were comparatively protected. Patients with IIMs with co-existing SAIDs were at a higher risk of minor [OR 5.2 (3.3-8.2), p<0.001] and major ADEs [OR 2.1 (1.2-3.8), p<0.05] compared to those with IIMs alone.
Conclusion: Patients with IIMs were at a lower risk of delayed onset COVID-19 vaccine ADEs compared to other SAIDs, though within this patient group, those with active disease, overlap myositis and autoimmune multimorbidity were vulnerable, and warrant close monitoring and long term follow up post COVID-19 vaccination.
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Disclosure of Interests: Syahrul Sazliyana Shaharir Speakers bureau: Pfizer, Novartis, Bohdana Doskaliuk: None declared, Naveen Ravichandran: None declared, Jessica Day Grant/research support from: CSL Limited, Parikshit Sen: None declared, Samuel Katsuyuki Shinjo: None declared, Mrudula Joshi: None declared, Nelly Ziade Speakers bureau: Pfizer, Roche, Abbvie, Eli Lilly, NewBridge, Sanofi-Aventis, Boehringer Ingelheim, Janssen, and Pierre Fabre, Consultant of: Pfizer, Roche, Abbvie, Eli Lilly, NewBridge, Sanofi-Aventis, Boehringer Ingelheim, Janssen, and Pierre Fabre, Grant/research support from: Pfizer, Roche, Abbvie, Eli Lilly, NewBridge, Sanofi-Aventis, Boehringer Ingelheim, Janssen, and Pierre Fabre, Tsvetelina Velikova Speakers bureau: Pfizer and AstraZeneca, Marcin Milchert: None declared, Sreoshy Saha: None declared, Johannes Knitza: None declared, Ashima Makol: None declared, Kshitij Jagtap: None declared, Vishwesh Agarwal: None declared, Dzifa Dey: None declared, Carlos Enrique Toro Gutierrez: None declared, Carlo Vinicio Caballero: None declared, Vikas Agarwal: None declared, Rohit Aggarwal Consultant of: Bristol Myers-Squibb, Pfizer, Genentech, Octapharma, CSL Behring, Mallinckrodt, AstraZeneca, Corbus, Kezar, Abbvie, Janssen, Kyverna Alexion, Argenx, Q32, EMD-Serono, Boehringer Ingelheim, Roivant, Merck, Galapagos, Actigraph, Scipher, Horizon Therapeutics, Teva, Beigene, ANI Pharmaceuticals, Biogen, Nuvig, Capella Bioscience, and CabalettaBio., Grant/research support from: Bristol Myers-Squibb, Pfizer, Genentech, Octapharma, CSL Behring, Mallinckrodt, AstraZeneca, Corbus, Kezar, Abbvie, Janssen, Kyverna Alexion, Argenx, Q32, EMD-Serono, Boehringer Ingelheim, Roivant, Merck, Galapagos, Actigraph, Scipher, Horizon Therapeutics, Teva, Beigene, ANI Pharmaceuticals, Biogen, Nuvig, Capella Bioscience, and CabalettaBio., Latika Gupta: None declared.
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AB1313 **EFFICACY AND SAFETY OF COVID-19-SPECIFIC TREATMENTS IN SLE: A MULTICENTRE CASE-CONTROL STUDY**

Keywords: Systemic lupus erythematosus, COVID, Targeted synthetic drugs

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Background: COVID-19 is associated with higher morbidity and mortality burdens in immunocompromised individuals, including patients with systemic lupus erythematosus (SLE; 1). These patients might benefit from treatment with anti-SARS-CoV-2-specific antiviral agents and monoclonal antibodies, but clinical evidence is to date limited.
Objectives: to comparatively assess the course of COVID-19 in patients with SLE treated or untreated with COVID-19-specific agents.
Methods: Patients with SLE and COVID-19 treated with antivirals and/or monoclonal antibodies from February 2020 to December 2022 were identified within a three-centre cohort of tertiary referral centres and age-, sex- SLE extension- and SLE duration-matched 1:2 with patients with a history of untreated COVID-19. Data on COVID-19 presentation, course (including time to viral clearance) and sequelae, along with SLE treatment at COVID-19 onset and SLE course after

COVID-19 were collected. COVID-19 severity at presentation was quantitated through a 0-4 analogue scale [2]. Data are expressed as median (interquartile range, IQR) unless otherwise specified.

Results: Over three years, 39% of patients with SLE had at least one COVID-19 event. Eighteen subjects (16 women) were treated with antivirals (n=12) or monoclonal antibodies (n=6) and were matched with 36 controls. There was no difference in the frequency of organ involvement between the two groups. Treated patients were receiving significantly higher prednisone daily doses at COVID-19 onset (6.25 (0-10) vs 0 (0-2.5) mg; p=0.005) and had a higher prevalence of previous high-dose steroid treatments (83% vs 47%; p=0.019) compared to controls. SLE disease activity index (3 (0-5) vs 1 (0-4)) and SLE International Collaborating Clinics Damage Index scores (1 (0-3) vs 0 (0-1)) were also numerically higher in treated patients at COVID-19 onset. Patients in the treated group had more severe COVID-19 at presentation but showed no significant differences with control subjects in terms of COVID-19 resolution, prevalence of sequelae and viral clearance (**Table 1**). There was also no difference in flare occurrence between the two groups (Log-rank=0.02, p=0.889). Two patients reported mild adverse events with monoclonal antibodies (muscle cramps and chest pain, both self-resolving).

Conclusion: These data support the safe use of COVID-19 specific treatments in patients with SLE. Patients treated with antivirals and monoclonal antibodies had a favourable COVID-19 course, despite a more severe presentation and a higher risk of deterioration due to SLE and corticosteroid treatment burden, suggesting the potential efficacy of COVID-specific treatments in preventing severe COVID-19 in patients with SLE.

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Table 1. COVID-19 presentation and course

	Treated (n=18)	Untreated (n=36)
Number of vaccine doses	3 (2-3)	3 (2-3)
Time from last vaccine administration (days)	118 (53-184)	134 (30-210)
COVID-19 features		
WHO class at presentation	1 (1-1)**	0 (0-1)
Symptoms at presentation: n(%)		
Dyspnoea	3 (17)	3 (8)
Fever	10 (56)	22 (61)
Upper Respiratory Symptoms	16 (89)	29 (81)
GI symptoms	1 (6)	2 (6)
Pneumonia	3 (17)	3 (8)
COVID-19 course		
Time to symptom resolution (days)	5 (4-8)	7 (3-8)
Time to viral clearance (days)	10 (7-14)	9 (7-14)
Any complication: n(%)	1 (6)	6 (17)
Hospitalisations: n(%)	1 (6)	0 (0)
Long COVID: n(%)	3 (17)	6 (17)
Deaths: n(%)	0 (0)	1 (3)

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AB1314 EFFICACY AND SAFETY OF ANTI-SARS-COV-2 VACCINATION IN PEOPLE WITH RMDS: RESULTS FROM A SYSTEMATIC LITERATURE REVIEW

Keywords: Vaccination/immunization, COVID, Systematic review

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Background: As the third year of the pandemic begins, over 13 billion doses of anti-SARS-CoV-2 vaccines have been administrated worldwide and growing evidence on their efficacy and safety in people with RMDs has accrued.

Objectives: To update our previous systematic literature review (SLR)[1] on efficacy and safety of anti-SARS-CoV-2 vaccination in people with rheumatic and musculoskeletal diseases (RMDs)

Methods: A literature search according to the PICO framework was conducted on July 22, 2022 to identify references in seven databases published after June 1, 2021 (end date of previous SLR). Title and abstracts were independently screened by 3 investigators (AA, AN and FK). Eligibility criteria were stricter in terms of requirement of the inclusion of control group or undertaking a multivariable analysis. However, for some outcomes (e.g., RMD flares), descriptive studies were also included due to the paucity of data. Data extraction and risk of bias (RoB) assessment were performed as in the previous SLR.

Results: Of 1583 references, 219 were included for full text assessment and 30 fulfilled the eligibility criteria. Recent studies confirmed that a full vaccination cycle was generally immunogenic, though the seroconversion rate and the anti-spike antibody (Ab) titre were lower in patients with RMDs compared to healthy controls. Vaccination was also able to induce neutralising antibodies (NAb) but the seroconversion rate and the neutralising activity were lower than in controls. Glucocorticoids, mycophenolate mofetil, rituximab and abatacept were negatively associated with Ab and NAb seroconversion. Two studies specifically investigating RTX-treated RMD patients identified an association between lower dose and longer period of time after the last RTX infusion before vaccination and higher likelihood of Ab seroconversion. The majority of breakthrough infections (B-INFs) were asymptomatic and, if symptomatic, mild to moderate. A higher number of vaccine doses was associated with a lower incidence and severity of B-INFs, although B-INF incidence rate was generally higher in the post-delta variant period. Higher disease activity was associated with higher likelihood of severe/critical B-INFs. Regarding safety, in general, patients with RMDs showed higher rates of mild AEs compared to the general population, however severe AEs were rare, if any. Disease flares have been observed in/reported by less than 10% of patients in the various cohorts and although often requiring treatment with glucocorticoids or change of the ongoing immunosuppressive therapy, hospitalization was generally not needed. Pre-vaccination colchicine prophylaxis seemed useful to prevent gout flares in the post-vaccination trimester.

Conclusion: Overall anti-SARS-CoV-2 vaccination is immunogenic and safe in patients with RMDs. However, careful and individualised assessment of the ongoing therapy and disease activity when planning the vaccination schedule is necessary to minimise the risk of reduced immunogenicity, post-vaccination disease flares and breakthrough infections.

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Disclosure of Interests: None Declared.

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AB1315 EFFECTS OF COVID-19 IN RHEUMATOLOGICAL PAIN CONDITIONS SIX MONTHS AFTER INFECTION

Keywords: Pain, Epidemiology, COVID

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Background: Up to 60% of COVID-19 survivors develop long-COVID symptoms[1,2]. Musculoskeletal pain is also a common (~11%) symptom of

long-COVID[3,4], but current evidence does not usually differentiate between muscular and joint (arthralgias) symptoms. Data on joint pain as long-COVID symptom is limited to specific populations. Additionally, studies investigating how COVID-19 affects previous rheumatological conditions experienced by the patient before the infection are also scarce.

Objectives: 1, To identify post-COVID changes in those previous joint pain conditions experienced by the patients before SARS-CoV-2 infection.

2, To compare the development of "de novo" joint pain as a long-COVID symptom between previously hospitalized and non-hospitalised COVID-19 survivors.

Methods: This nation-wide, cross-sectional exploratory study was based on a questionnaire collecting demographics, previous rheumatological pain conditions and changes in their symptoms, and the development of joint pain after SARS-CoV-2 infection from a population-based sample in Denmark.

Results: Data from 1.000 randomly previously hospitalised (51.2% males; 60.4±15.2 years; 85.6±18.5kg) and 1.000 randomly previously non-hospitalised COVID-19 survivors (43.5% males; 50.4±15.9 years; 79.2±16.6 kg) were analyzed. Distribution of gender (p<0.001), age (p<0.001), and weight (p<0.001) was different between groups. The presence of joint pain before COVID-19 infection was significantly higher (P=0.01) in hospitalised (3.5%) than in non-hospitalised (1.6%) COVID-19 survivors. No differences in the presence of previous arthritis (P=0.212) or osteoarthritis (P=0.549) were found between the two groups. Both groups experienced similar worsening of symptoms in their previous rheumatological conditions, A significant higher proportion (P<0.001) of hospitalised patients (18.9%) developed "de novo" joint pain when compared with non-hospitalised patients (5.5%).

Conclusion: This exploratory study shows that joint pain seems more likelyto occur in hospitalised patients compared to non-hospitalised patients. Experiencing COVID-19 worsened the symptoms of rheumatological pain conditions in both hospitalised and non-hospitalised COVID-19 survivors. Rheumatological pain will need attention in COVID-19 survivors independently of hospitalisation or not.

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AB1316

SAFETY AND IMMUNOGENICITY OF TWO HETEROLOGOUS VACCINE SCHEDULES AGAINST SARS-COV-2 IN PATIENTS WITH RHEUMATOID ARTHRITIS: BRAZILIAN MULTICENTER STUDY

Keywords: Rheumatoid arthritis, Vaccination/immunization, COVID

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Background: Patients with immune-mediated rheumatic diseases (IMRDs) have been prioritized for COVID-19 vaccination to mitigate the infection severity risks. Patients with rheumatoid arthritis (RA) are at a high risk of severe COVID-19 outcomes, especially those under immunosuppression or with comorbidities associated. However, few studies in the literature assessed the safety and immunogenicity of the COVID-19 heterologous vaccine schedules in patients with RA.

Objectives: Evaluate the safety and immunogenicity of two heterologous vaccine schedules against SARS-CoV-2 in patients with RA.

Methods: These data are from the study "SAFER - Safety and Efficacy on COVID-19 Vaccine in Rheumatic Diseases," a Brazilian multicentric prospective phase IV study to evaluate COVID-19 vaccine in IMRDs in Brazil. Immunogenicity and adverse events (AEs) in patients with RA of all centers were assessed after two doses of ChAdOx1 plus additional dose of BNT162b2 or after two doses of inactivated SARS-CoV-2 vaccine CoronaVac plus additional dose of BNT162b2. The titers of neutralizing antibodies against the receptor-biding domain of protein spike (S) of SARS-CoV-2 (anti-RBD) were measured by chemiluminescence test after each dose of immunizers. Proportions between groups were compared using the chi-square and Fisher's exact tests for categorical variables. Clinical Disease Activity Index (CDAI) before and after vaccination was assessed using the McNemar test.

Results: A total of 107 patients with RA were include in the study, most of them female, with a mean age of 46 years. Biological disease modifying anti-rheumatic drugs (DMARDs) were used by 50 % of the patients and conventional synthetics DMARDs in 48 %. Two doses of CoronaVac plus additional dose of BNT162b2 was used in 66 patients and two doses of ChAdOx1 plus additional dose of BNT162b2 in 41. Only mild AEs were observed, mainly after the first dose. The most common AEs after all doses, regardless of the immunizer type, were pain at the injection, headache, arthralgia and myalgia. ChAdOx1 had a higher frequency of pain at the injection (66% vs 32 %, p < 0,001) and arthralgia (68% vs 15%, p < 0,001) compared to CoronaVac. No patients had flare after the vaccination. The titers of anti-RBD after two doses of ChAdOx1 were higher compared to two doses of CoronaVac (6,03 BAU/mL vs 4,67 BAU/mL, p < 0,001). However, after the additional dose of BNT162b2, the anti-RBD titers were similar in both groups (7.28 BAU/mL vs 7.06 BAU/mL, p = 0.56). Only two cases of COVID 19, with mild symptoms, were reported, one in each group.

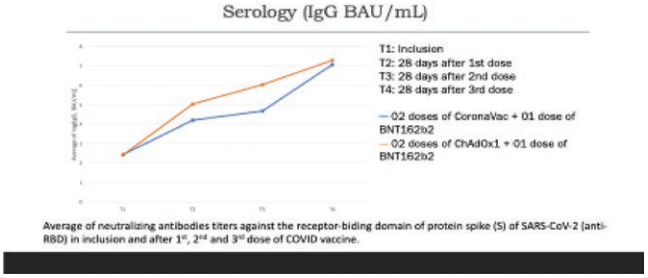


Figure 1.

Conclusion: ChAdOx1, CoronaVac, and BNT162b2 vaccines are safe in RA patients. The frequency of local adverse effects, particularly pain at the injection

site, is high. AEs are more frequent with ChAdOx1, especially after the first dose. The use of the immunizers does not change the degree of inflammatory activity of the disease. The immunogenicity of the two heterologous regimens analyzed was similar.

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AB1317 EFFICACY AND SAFETY OF COVID-19 VACCINES IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH DIFFERENT ANTI-RHEUMATIC THERAPIES

Keywords: Rheumatoid arthritis, COVID, Vaccination/immunization

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Background: The coronavirus disease (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 has led to rapid progress in vaccine development to prevent the spread of the disease. Rheumatoid arthritis (RA) is a common systemic inflammatory autoimmune disease that are vulnerable to infection due to their underlying conditions and immunomodulatory therapy.

Objectives: This study aimed to evaluate the seroconversion after SARS-CoV-2 vaccination in patients with RA and the impact of various drugs on seroconversion rates to provide information for clinicians and patients to guide decisions.

Methods: Systematic searches of the CBM, CNKI, China Science and Technology Journal Database, WanFang Data, PubMed, Embase, Web of Science, Cochrane Library, and Medline were performed. We included observational studies evaluating RA patients undergoing SARS-CoV-2 vaccination. Random effects model was used to calculate the pooled efficacy. Heterogeneity and risk of bias were examined with the I-squared index (I^2) statistic. Inconsistency was evaluated using the I^2 and Egger tests to assess potential publication bias (STATA v.12.0).

Results: A total of 5 observational studies comprising 502 RA patients were identified (Table 1).The seropositivity rate in patients with RA was 0.701 (95%CI: 0.531-0.871) after vaccination with SARS-CoV-2 vaccines. Drugs used by patients with RAs had an impact on the seropositivity rate. The seropositivity rate of RA using GC, bDMARDsS, and csDMARDs was 0.713 (95%CI: 0.544-0.982), 0.764 (95%CI: 0.593-0.935) and 0.625 (95%CI: 0.546-0.704), respectively. Patients with csDMARDs treatment had the lowest seropositivity rate while bDMARDs had a high seropositivity rate(Figure 1). The most commonly reported adverse events in RA patients vaccinated with SARS-CoV-2 vaccines were fever (0.101, 95%CI:0.036-0.165), and the lowest rates of adverse events in RA patients was diarrhea(0.053, 95%CI: 0.004-0.101).

Conclusion: After vaccination with SARS-CoV-2 vaccines, the seropositivity rates of RA patients using csDMARDs have the lowest seropositivity rate.

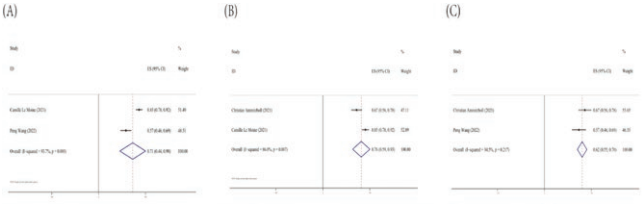


Figure 1: Forest plot of the subgroup meta-analysis of positive serum rate of RA patients who received GC(A),bDMARDs(B), and csDMARDs(C) treatment after COVID-19 vaccination.

Table 1. Characteristics of the individual studies included in the meta-analysis.

Author	Publish Year	Case number	Treatments		
			GC therapy	bDMARDs therapy	csDMARDs therapy
Christian Ammitzbøll	2021	73		73	43
Camille Le Moine	2021	104		10	
Lars Erik Bartels	2021	154	10	22	90
Peng Wang	2022	70	27		40
Clodoveo Ferri	2021	101	44	49	61

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Disclosure of Interests: None Declared.

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AB1318 CLINICAL CHARACTERISTICS & OUTCOMES AMONG PATIENTS WITH SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES AND SARS-COV-2 INFECTION: 2-YEAR DATA FROM A TERTIARY RHEUMATOLOGY CENTRE IN GREECE

Keywords: COVID, Descriptive studies

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Background: Patients with autoimmune rheumatic diseases (ARDs) under moderate/severe immunosuppression are considered a high-risk population to develop severe Covid-19 infection.

Objectives: The aim of our study was to describe the clinical characteristics and the outcome of patients with ARD who contracted a Sars-Cov-2 infection.

Methods: Among patients with ARD being followed in our tertiary outpatient rheumatology clinic, we retrospectively identified those infected with SARS-CoV-2 between the beginning of the pandemic and August 2022. Patients' medical files were reviewed for demographics (age, gender and comorbidities) and disease-related characteristics, as well as coronavirus disease (COVID-19) characteristics, including vaccination status, treatment, and outcomes (covid-19 severity, hospitalization, death).

Results: A total of 209 cases of ARD patients with confirmed Covid-19 infection were recorded. Most of them were women (62.7%), with a mean age of 52.4± 13.8 years. The most prevalent ARDs were seronegative spondyloarthropathies (28.7%), systematic lupus erythematosus (21.5%), rheumatoid arthritis (16.5%), and systemic sclerosis (11.5%). More than half of the patients received corticosteroids (57.8%), while the most frequently used immunosuppressants were hydroxychloroquine (30.9%), TNF inhibitors (26.5%), mycophenolate mofetil (24.0%), methotrexate (19.1%) and rituximab (15.2%). One hundred and fifty-eight (76%) patients were either on remission or had mild disease activity. Most of the patients (131/209) had at least one comorbidity, more commonly arterial hypertension (48.5%) and pulmonary disease (45.2%). Most of the patients were vaccinated against Sars-Cov-2 (73.7%), either with two doses (38.0%), three doses (57.0%) or four doses (5.0%) of mRNA-based vaccines. The big majority of the patients (83.3%) were asymptomatic or had mild Covid-19 disease. About half of the patients (53.1%) reported to have received Covid-19 treatment. Thirty-two of them (15.3%) needed hospitalization, and five death cases were reported overall. Among the demographic characteristics, age ($p<0.0001$ for hospitalization) and comorbidities were associated with worse covid-19 outcomes. In particular, cardiovascular disease (OR 5.37, $p=0.001$ for covid-19 severity, OR 6.89, $p=0.001$ for hospitalization), pulmonary disease (OR 3.02, $p=0.006$ for hospitalization), and obesity (OR 3.46, $p=0.044$ for hospitalization) had the stronger associations. Non-vaccination status was also associated with a higher risk for hospitalization (OR 2.68, $p=0.015$). In relation to ARD-related factors, treatment with rituximab (OR 4.11, $p=0.002$ for hospitalization), systemic sclerosis diagnosis (OR 3.45, $p=0.03$ for Covid-19 severity) and myositis diagnosis (OR 4.91, $p=0.033$ for hospitalization) were associated with worse Covid-19 outcomes. On the other hand, spondyloarthropathies appear to be negatively associated with Covid-19 severity (OR=0.27, $p=0.035$).

Conclusion: According to our study, most ARD patients recovered uneventfully from Covid-19. However, there are several indications that we should be vigilant for patients who remain unvaccinated, are older, have a systemic sclerosis or myositis diagnosis, and/or receive intense immunosuppressive regiments such as rituximab.

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Table 1.

	N=209
ARD Diagnosis	**n (%)**
Rheumatoid arthritis	34 (16.3)
Seronegative spondyloarthropathies	60 (28.7)
Systemic lupus erythematosus	45 (21.5)
Systemic sclerosis	24 (11.5)
Sjogren's syndrome	15 (7.2)
Vasculitis	19 (9.1)
Myositis	9 (4.3)
Other	3 (1.4)

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Disclosure of Interests: None Declared.

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AB1319 DYNAMIC IMMUNE FEATURES REVEALED BY SINGLE-CELL RNA AND SINGLE-CELL TCR/BCR SEQUENCING IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING SARS-COV-2 BOOSTER VACCINATION

Keywords: COVID, Vaccination/immunization, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is one of the most common autoimmune diseases and have been shown to be more vulnerable to SARS-CoV-2 infection. Numerous COVID-19 vaccines have demonstrated significant efficacy in reducing SARS-CoV-2 infection and severe cases[1]. Booster vaccinations played an imoprtant role in maintaining this protection.

Objectives: The use of COVID-19 vaccines is considered to potentially provoke autoimmunity by molecular mimicry, and subsequently trigger flare of underlying autoimmune diseases[2, 3]. Little is known about the delicate immune responses after inactived SARS-CoV-2 booster vaccination in RA.

Methods: Three RA patients who were in remission were prospectively enrolled. Peripheral blood mononuclear cell (PBMC) were collected 1 week before and after their inactivated SARS-CoV-2 booster vaccination, respectively. Single-cell RNA sequencing (scRNA-seq) combined with scTCR/BCR-seq analyses were performed using the 10x Genomics Single Cell technique.

Results: Vaccination with booster vaccination only had limited impact on the composition of peripheral immune cells in RA patients, but significantly altered the proportion in myeloid cells, B cells and plasma cells. Transcriptomic changes, which were mostly involved in antibody production as well as B cell activation and differentiation, were observed after booster vaccination. No pro-inflammatory response genes were found to be significantly upregulated in SARS-CoV-2 booster vaccinated RA individuals. Moreover, single-cell TCR/BCR analysis showed a different clone expansion and repertoire diversity after booster vaccination.

Conclusion: Our study provide a comprehensive single cell atlas of the peripheral immune response and TCR/BCR immune repertoire profiles to SARS-CoV-2 booster vaccination in RA patients, which helps us to better understand COVID-19 vaccination and immunization.

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Disclosure of Interests: None Declared.

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AB1320 COVID-19 OUTCOME IN AN ITALIAN RHEUMATOID ARTHRITIS COHORT

Keywords: Rheumatoid arthritis, COVID

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Background: It is known that rheumatologic patients often present a course of COVID-19 similar to that of the general population. Some factors are linked to a worse COVID-19 outcome, such as moderate glucocorticoid (GC) dose, high body mass index (BMI), and comorbidities.

Objectives: To describe the outcome of COVID-19 in patients with rheumatoid arthritis (RA) in terms of symptoms, therapy and need for hospitalization compared to a control group. Also, to evaluate the variation in disease activity before and after COVID-19.

Methods: In this monocentric prospective study, we recruited consecutive adult patients with RA classified according to ACR-EULAR 2010 criteria who received a diagnosis of COVID-19 through molecular or rapid antigen swab tests between September 2020 and December 2022. Demographic and clinical data, including age, BMI, smoking habit, comorbidities, treatment at the diagnosis of COVID-19, duration of COVID-19, symptoms related to the infection and therapy required, together with the vaccination status were collected through a self-administered questionnaire. We compared DAS28-CRP before the infection and at the first visit after the resolution. As controls (Cs), individuals with COVID-19 but with no referred diagnosis of rheumatic/autoimmune disease were recruited.

Results: We enrolled 111 patients affected by RA (males 15%, median age 56 years, IQR 25) and 89 Cs (males 44%, median age 47 years, IQR 43), whose demographic and clinical characteristics are reported in **Table 1**. The median RA disease duration was 108 months (IQR 201). At the COVID-19 diagnosis, 62 patients (56%) were assuming csDMARDs, 67 (60%) bDMARDs, and 18 (16%) GC with a median prednisone equivalent dose of 4 mg/day (IQR 1). DAS28-CRP was available for 62 patients, with a median value of 1.67 (IQR 2.71); 42 patients (60%) were in remission (Figure 1). Before developing COVID-19, only 35 (32%) RA patients and 42 (47%) Cs had completed the vaccinal cycle, which was performed by mRNA vaccine in all the patients and 87% of Cs. The median COVID-19 duration was 18 days (IQR 18) for RA patients and 14 days (IQR 13.5) for Cs ($p>0.7$). Cs reported a significantly higher frequency of constitutional symptoms (headache and asthenia) compared to RA patients ($p<0.00001$). When hospitalization was required, RA patients received heparin more frequently than Cs ($p<0.039$). Once COVID-19 was resolved, RA patients were evaluated after a median of 2 months (IQR 2). DAS28-CRP was available for 68 patients, with a median value of 1.61 (IQR 1.77); 42 patients (68%) were in remission (Figure 1). No differences in terms of COVID-19 duration, clinical manifestations, and therapy emerged comparing RA patients in remission (40; 58%) with patients with the active disease before COVID-19 (29; 42%). Also, in vaccinated subjects, the outcome of COVID-19 was similar in RA patients and Cs, irrespective of RA activity.

Conclusion: COVID-19's impact on patients with RA was not significantly different from the general population, even for patients with active RA. Patients did not suffer from reactivation of RA because of COVID-19. In our opinion, these positive results could be ascribed to the massive vaccination campaign.

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Table 1. Clinical characteristics, COVID-19 symptoms, and therapy of the two groups. Values in brackets are expressed as percentages unless specified. Musculoskeletal diseases: osteoarthritis and osteoporosis.

	Rheumatoid arthritis N=111	**Controls N=89**	**P value***
ACTIVE SMOKERS	13 (12)	20 (22)	
BMI (IQR)	24 (7)	23(6)	
COMORBIDITIES	64 (58)	44 (49)	
Cardiovascular	26 (23)	18 (20)	
Endocrine	24 (22)	14 (16)	
Musculoskeletal	11 (10)	6 (7)	
Neoplastic	12 (11)	3 (3)	
CLINICAL MANIFESTATIONS	96 (86)	74 (83)	
Fever	50 (45)	47 (53)	
Constitutional symptoms	52 (47)	75 (84)	***p* <0.00001**
Respiratory symptoms	100 (90)	86 (97)	
Gastrointestinal symptoms	12 (11)	13 (15)	
THERAPY	88 (79)	74 (67)	
NSAIDs	41 (37)	31 (35)	
Glucocorticoids	24 (22)	21 (30)	
Antibiotics	33 (30)	27 (24)	
Oxygen	6 (5)	5 (6)	
Heparin	8 (7)	0 (0)	***p* <0.039**
HOSPITALIZATION	10 (9)	6 (9)	

*Where not indicated, p value >0.5

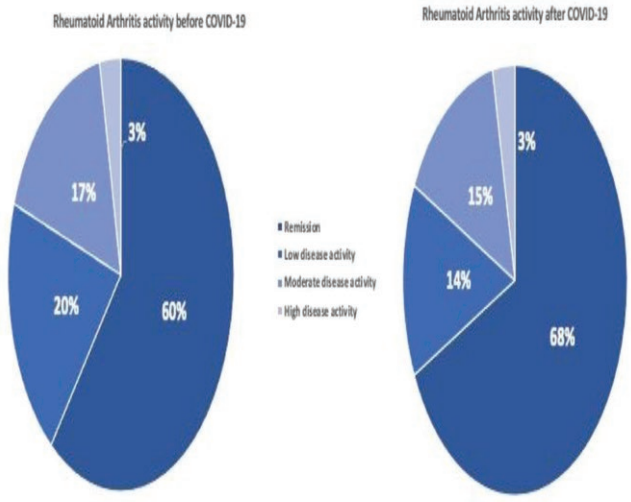


FIGURE 1. Rheumatoid arthritis disease activity before and after COVID-19.

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AB1321

CLINICAL CHARACTERISTICS AND DISEASE COURSE BEFORE AND AFTER SARS-COV-2 INFECTION IN A LARGE COHORT OF SYSTEMIC SCLEROSIS PATIENTS

Keywords: COVID, Lungs, Systemic sclerosis

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Background: Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) has diverse and wide array of clinical presentations ranging from asymptomatic to severe disease. The exact pathophysiological mechanism of severe COVID-19 is still obscure; however, unrestrained immune response, exaggerated systemic inflammation, endothelial activation, and vascular damage are implicated in its pathogenesis similar to systemic sclerosis (SSc) and autoimmune diseases [1-2].
Objectives: to assess the clinical presentation and worse outcomes of COVID-19 in SSc patients and evaluate the effects of SSc features on the clinical course of COVID-19
Methods: This multicentre, retrospective, observational study included SSc patients with COVID-19 diagnosis which was confirmed by SARS-CoV-2 RT-PCR or suggestive symptoms with typical radiologic pulmonary findings. Clinical features of SSc and detailed COVID-19 data were provided from medical records ab and patient interviews.
Results: One hundred twelve patients (age mean 51.4±12.8 years, 90.2% female) were included in the study. SSc associated interstitial lung disease (ILD) was evident in 57.1% of the patients. SSc-specific treatments were low-dose glucocorticoids and mycophenolate. We found 25.5% hospitalization, 16.3% respiratory support, 3.6% intensive care unit admission, 2.7% long-COVID, and 2.7% mortality rate in SSc patients. ILD and ≥1 comorbidity were more frequent in inpatients compared to outpatients (82.1% vs 49.4% p= 0.005; 67.9% vs 42.7% p=0.037, respectively). Risk factors for respiratory failure were ILD (OR:7.49, 95%CI:1.63-34.46, p=0.01), ≥1 comorbidity (OR:4.55, 95%CI 1.39-14.88, p=0.01), having a higher physician global assessment score at the last outpatient visit (OR 2.73, 95% CI: 1.22-6.10, p:0.01), and use of MMF at the time of getting the infection (OR: 5.16, 95 %CI: 1.79-14.99, p:0.003) by univariate analysis. Having ≥1 comorbidity was the only significant predictor of the need for respiratory support in COVID-19 (OR:5.78, 95%CI:1.14-29.23, p:0.03). In the early post-COVID-19 period, 17% of patients reported the progression of the Raynaud phenomenon, and 10.6% of patients developed new digital ulcers. Progression or new onset of dyspnea and cough were detected in 28.3% and 11.4% of patients, respectively.
Conclusion: SSc-related ILD, severe disease activity, and use of mycophenolate might be related to adverse outcomes of COVID-19, and having comorbidity is an independent risk factor for respiratory support.

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Table 1. The comparison of pre-COVID-19 characteristics of SSc patients according to need of respiratory support (n:110)

	Respiratory support No (n=92)	Respiratory support Yes (n= 18)	p
Age, years, mean±SD	51.13± 12.94	53.28±13.36	0.52
Age≥ 65 years, n (%)	12 (13)	4 (22.2)	0.29
Gender, female n (%)	83 (90.2)	16 (88.9)	1.00
Disease duration, years (median, min-max)	10.5 (1-41)	10.5 (3-23)	0.79
lSSc/dSSc, n (%)	60 (65.2)/32 (34.8)	9 (50)/9 (50)	0.34
mRSS, median (IQR)	11 (10)	12 (6)	0.30
ILD, n (%)	47 (51.6)	16 (88.9)	0.008
FVC, mean± SD	87.39± 18.99	82.85±17.09	0.42
PAH, n (%)	8 (9)	4 (22.2)	0.12
Cardiac involvement, n (%)	10 (11.2)	4 (22.2)	0.25
History of DU, n (%)	44 (44.8)	10 (55.6)	0.76
Anti-centromere positivity, n (%)	24 (27.3)	2 (11.9)	0.23
Anti-topoisomerase I positivity, n (%)	47 (54)	10 (55.6)	1.00
Comorbidity≥1, n (%)	40 (43.5)	14 (77.8)	0.01
Rituximab, n (%)	6 (6.6)	2 (11.1)	0.61
Mycophenolate, n (%)	21 (23.3)	11 (61.1)	0.003
Glucocorticoid, n (%)	45 (49.5)	13 (72.2)	0.13
Glucocorticoid ≥10 mg, n (%)	2 (4.4)	3 (23.1)	0.07
Continuation of SSc specific treatment, n (%)	46 (52.9)	5 (31.3)	0.19
Pre-COVID-19 PGA, median (IQR)	1 (0)	1 (1)	0.01

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Disclosure of Interests: None Declared.
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AB1322

COVID-19 PANDEMIC AND SYSTEMIC INFLAMMATORY RHEUMATIC DISEASES: OUR EXPERIENCE IN DAKAR, SENEGAL (SUB-SAHARAN AFRICA)

Keywords: Disease-modifying drugs (DMARDs), Inflammatory arthritides, COVID

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Background: There are paucity data regarding the Covid-19 pandemic on the management of systemic autoimmune rheumatic diseases in sub-Saharan Africa.
Objectives: The aim of our study was to assess the impact of the Covid-19 pandemic on the follow-up of patients with systemic inflammatory diseases and their adherence to vaccination against SARS-CoV-2.
Methods: We performed a multicentric cross-sectional study between August 1st and October 31, 2021. The study targeted the patients diagnosed for systemic diseases according to the international criteria. The patients were followed in the departments of Internal Medicine, Rheumatology and Nephrology of 04 hospitals in Dakar (Senegal). The survey was based on records of 13 questions (with responses collected from the patients' medical records) and was completed by a telephone interview with 38 potential questions. All responses were collected using a web-based application and then exported and analyzed using SPSS 26 software.
Results: 131 patients were included with a mean age of 41.5 years (+/-12.4) and a sex ratio of 0.08. Inflammatory rheumatic diseases included: Rheumatoid arthritis (47.3%), Systemic lupus erythematosus (22.9%), Autoimmune myositis (10.7%), Sjögren's syndrome (6.9%), Systemic sclerosis (4.6%), Spondylarthritis (2.3%), Antiphospholipid syndrome (1.5%), ANCA-associated vasculitis (1.5%),

Adult-onset Still's disease (0.8%), Systemic sarcoidosis (0.8%) and Relapsing polychondritis (0.8%). Patients reported missing one or more follow-up appointments in 45%, a drug break (33.6%) regarding particularly the methotrexate (21/44 of patients: 47.7%) and hydroxychloroquine (18/44 patients: 40.9%) with a flare-up of their disease in 31% of cases. Covid-19 infection was confirmed in 11 patients (8.4%). Our survey showed that 47 patients (35.8%) were vaccinated with: Ad.26.COV2.S (40.4%), chAdOx1 nCoV-19 (27.7%) and BBIBP-CorV (31.9%). Side effects were reported by 21 of 47 patients (45%) only after the first dose. 2 of 47 (4.25%) patients had a medically confirmed flare. 84 (64.2%) patients were not vaccinated. Fear of vaccine side effects and the effects of the vaccine on systemic disease were the main reasons for non-adherence to vaccination.

Conclusion: The covid-19 pandemic has had a significant impact on the follow-up of patients with systemic inflammatory diseases in Dakar. Vaccine hesitancy is a reality in these patients.

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AB1323 ANALYSIS OF ADVERSE EFFECTS AFTER VACCINATION AGAINST COVID-19 IN PATIENTS WITH IMMUNO-MEDIATED RHEUMATIC DISEASES IN MANAUS – AMAZONAS

Keywords: Epidemiology, Vaccination/immunization, COVID

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Background: Immune-Mediated Rheumatic Diseases (IMRD) are characterized by a chronic inflammatory response, have several clinical manifestations and are more susceptible to infections and worse prognosis. Thus, in the context of the COVID-19 pandemic, to reduce morbidity-mortality, vaccination is an effective method of prevention. However, there are not enough studies that encompass this group of patients, leaving many doubts about the adverse effects and its safety and effectiveness.

Objectives: Analyze the adverse effects observed in patients with IMRD after vaccination against COVID-19.

Methods: Observational, longitudinal, ambidirectional research, with follow-up of groups of patients with IMRD immunized with vaccines made available by the Programa Nacional de Vacinação with Coronavac (Instituto Butantan), AstraZeneca (BioManguinhos/Fiocruz), Pfizer/BioNTech and Janssen (Johnson & Johnson). Sociodemographic data and data on the adverse effects presented were collected, recorded through a diary delivered to each patient, filed on an online platform. This study was approved by the local Ethics and Research Committee.

Results: 223 patients over 18 years of age were included, the mean age is 42.79±15, 83% women. The main DRIM: Systemic Lupus Erythematosus (39%) and Rheumatoid Arthritis (33.6%). In the 1st dose, 78.3% of the vaccines applied were Coronavac, 18.9% AstraZeneca and 2.8% Pfizer/BioNTech, the adverse effects found were: Pain at the injection site (49.3%), Headache (43.3%), Tiredness (34.3%) and Nausea (21.6%). In the 2nd dose, with the same vaccines applied as the previous dose, the adverse effects: Pain at the injection site (44.6%), Headache (33.9%), Tiredness and Vertigo (21.5%). In the 3rd dose, 55.3% of AstraZeneca, 44.2% of Pfizer and 0.4% of Janssen, in relation to adverse effects: Pain at the injection site (65.2%), Headache (41.8%), Tiredness (36.2%) and Edema and hardening of the skin at the injection site (31.9%). For the 4th dose, the AstraZeneca (14.9%) and Pfizer (85.1%) vaccines were applied, the adverse effects found: Pain at the injection site (58.5%), Hardening of the skin at the injection site injection (24.4%), Headache (19.5%), Tiredness (17.1%).

Conclusion: It is observed that the adverse effects presented after each administered dose are mild to moderate, more frequent: pain at the injection site and headache without significant differences compared to the general adult population.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1324 COVID-19 CHALLENGE IN THE ANTIPHOSPHOLIPID SYNDROME – AN OBSERVATIONAL STUDY OF A SERBIAN COHORT

Keywords: Anti-phospholipid syndrome, Vaccination/immunization, COVID

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Background: Facing the outburst of the COVID-19 pandemic, we gradually comprehend its pathophysiology as a coagulopathy characterized by increased risks of arterial, venous, and microvascular thrombosis. Antiphospholipid syndrome (APS) is an autoimmune, thrombo-inflammatory disease characterized by thrombosis and/or pregnancy loss in the presence of one or more antiphospholipid antibodies (aPL).

Objectives: To evaluate the clinical scenario of COVID-19 in the APS population of patients.

Methods: This is a single-center, observational, cross-sectional study. Data regarding the severity of COVID-19 (severe COVID-19 considered if interstitial pneumonia was diagnosed), COVID-19 vaccinal status, and post-vaccinal reactions (divided into mild, consisting of fever, myalgia, nausea, and severe if thrombosis at any point occurred) were collected from 44 APS patients (21 with primary and 23 with APS associated with systemic lupus erythematosus (SLE), 90.1% female). aPL analysis included the detection of aCL (IgG/IgM), ß2GPI (IgG/IgM), and LA Results were compared to the control group consisting of 31 healthy individuals, with no APS, matched to the APS group regarding age and gender.

Results: At the moment of COVID-19 infection, 75% of the APS group was taking Aspirin, 15.9% warfarin, 2.3% non-vitamin K oral anticoagulant, 59.1% chloroquine, 31.8% corticosteroid, 2.3% methotrexate. None of the above-mentioned medications were taken from a control group. There was no difference regarding the severity of COVID-19 between APS patients and healthy controls: 84.1% of APS had mild and 15.9% severe COVID-19 (p=0.509, p=0.292 respectively). But the difference regarding the need for hospitalization was significant (none of the healthy controls compared to 11.4% APS patients, p=0.0073). Interestingly, COVID-19 occurred in 72.7% of APS patients before the COVID-19 vaccination compared to 35.5% of healthy controls, p=0.001, conversely, a significantly lower percentage of vaccinated APS patients had COVID-19 compared to healthy controls (34.1% to 71.0%, p=0.002). 27% of APS patients had mild post-vaccinal reactions, none with severe.

Conclusion: During the COVID-19 pandemic, APS patients in Serbia were at higher risk for hospitalization. However, there was no difference in the severity of clinical presentation compared to non -the APS population. We can only speculate that APS therapy consisting of Aspirin, Chloroquine, and oral anticoagulant therapy contributed to this finding. Moreover, COVID-19 vaccination in the APS population, followed by a low incidence of mild post-vaccinal reactions, had more benefits in protection than in non-APS individuals.

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AB1325

SINGLE CELL MULTIOMIC PROFILING OF DISRUPTED REGULATORY NETWORKS IN COVID19 ASSOCIATED MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN

Keywords: COVID, Rare/orphan diseases, Genetics/epigenetics

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Background: Children infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) usually present minimal symptoms or are asymptomatic. Nevertheless, a subset of children 2-6 weeks after the initial SARS-CoV-2 infection develops a postinfectious SARS-CoV-2-related multisystem inflammatory syndrome in (MIS-C). Recently, transient expansion of TRBV11-2 T cell clonotypes in MIS-C was associated with signatures of inflammation and T cell activation, however, the underlying pathophysiology of MIS-C is not fully understood [1].
Objectives: The purpose of our project is to characterize the complexity of cell populations and capture cellular heterogeneity to uncover the regulatory networks and interactions that are disrupted during MIS-C flare with simultaneous profiling of gene expression and open chromatin regions from the same nuclei.
Methods: Samples of peripheral blood mononuclear cells from patients with MIS-C diagnosed at the University Children's Hospital, University Medical Center Ljubljana, were collected during the initial presentation before any treatment and at 6-12 months in remission. The primary aim is to identify which regulatory networks are driving inflammation in MIS-C flare, for which we are performing single cell Multiome ATAC + Gene Expression Sequencing. To enable simultaneous profiling of epigenomic landscape and gene expression from the same nuclei, we are using Chromium Next GEM Single Cell Multiome ATAC + Gene Expression kit from 10X Genomics.
Results: We included 32 patients with MIS-C from whom we collected paired blood samples during the initial presentation before treatment and at 6-12 months in remission. In single cell multiomic experiment we included 10 patients with paired samples, with the most viable cell count prior cryopreservation. All samples that are included into multiomic single cell analysis have 75% - 99% viability prior cryopreservation. In the protocol the key is to remove remaining granulocytes causing high mitochondrial RNA burden and extensively optimize the dilution factor of lysis buffer and the length of cell lysis step in order to get intact nuclei with no significant blebbing. Afterward, the single cell ATAC libraries as well as single-cell gene expression libraries are constructed and sequenced. Data are undergoing pairwise analysis to compare the cell population heterogeneity, expression profile and open chromatin landscape in the time of the initial presentation of MIS-C and in the remission, with Cell ranger software as well as with R package scREG [2], and custom scripting. In the second step we will inspect if the resulting altered transcriptomic signature from single-cell experiment is present on larger cohort. In that regard, we will perform bulk transcriptomic profiling on all paired collected samples during the initial presentation of MIS-C before treatment and at 6-12 months in remission.
Conclusion: The results of this project are expected to enlighten the underlying pathophysiology of MIS-C flare and thus support clinical decision on more targeted treatment. The identified disrupted networks during MIS-C flare could lead the way to establish an early diagnosis and improve long-term outcome, including prevention of myocardial and neuropsychological impairment. Moreover, a better understanding of the disrupted regulatory networks that are driving inflammation in MIS-C, could lead to new insights into diseases with similar clinical presentations as is Kawasaki Disease.

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AB1326

DIFFERENCES IN ADVERSE EVENTS EXPERIENCED BY INDIVIDUALS WITH INFLAMMATORY RHEUMATIC DISEASES AND HEALTHY INDIVIDUALS AFTER SARS-COV-2 VACCINATION

Keywords: Vaccination/immunization, COVID, Safety

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Background: Since individuals with inflammatory rheumatic diseases (IRDs) were excluded from the SARS-CoV-2 vaccination trials (1), uncertainty on the tolerability of the vaccines in this population was high. This caused a lower willingness to be vaccinated compared to the general population. Gaining more information on vaccine reaction in this population is critical.
Objectives: The aim of the study was to improve knowledge of the tolerability of SARS-CoV-2 vaccination in patients with IRD and to identify potential specific risks of this population by comparison with a healthy cohort.
Methods: IRD patients were recruited from the outpatient clinic of the Division of Rheumatology and Clinical Immunology at the hospital of the LMU Munich. Health care workers served as healthy controls. Questionnaires were used to identify adverse effects in all study participants after each SARS-CoV-2 vaccination and to obtain information about patients' disease and therapy. Descriptive statistics and non-parametric tests were used to discern differences between IRD patients and controls.
Results: 235 IRD patients (60% female), mean (±SD) age 54 (±15) years, and 102 healthy individuals (67% female), mean age 48 (±16) years, were recruited between Jan 2021 and Sep 2022. Pain at the injection site and fatigue were the most common adverse events in both groups. (Table 1) Patients presented adverse events significantly less often after the first vaccination (59.6%) compared to healthy individuals (84.3%) (OR=0.274 [95% CI: 0.151-0.497]; P<0.0001). With 58.7% of patients and 78.4% of controls experiencing adverse events after the second vaccination the difference stayed significant (OR=0.391 [0.228-0.670]; P<0.001). Same goes for the third vaccination with 56.4% of patients and 69.3% of controls presenting adverse events (OR=0.573 [0.348-0.946]; P=0.029). No difference was seen when the occurrence of local effects were compared. However, systemic effects were experienced significantly less by patients compared to controls after the first (41.3% vs 59.8%) (P=0.002), second (38.7% vs 58.8%) (P<0.001) and third vaccination (39.0% vs 51.5%) (P=0.036). Younger age and female sex showed higher frequencies of adverse events in both groups. 2% of patients experienced an activation of their IRD. Serious adverse events did not occur.

Table 1. Adverse events experienced after SARS-CoV-2 vaccination in patients and controls

	Patients			Healthy controls		
Adverse effects	**1. vaccination**	**2. vaccination**	**3. vaccination**	**1. vaccination**	**2. vaccination**	**3. vaccination**
	n=235	**n=233**	**n=218**	**n=102**	**n=102**	**n=101**
Local reactions, % (n)						
Any	49.8 (117)	48.9 (115)	47.7 (104)	66·7 (68)	57·8 (59)	49·5 (50)
Pain at the injection site	46.4 (109)	47.2 (110)	45.0 (98)	65·7 (67)	55·9 (57)	47·5 (48)
Swelling at the injection site	12.3 (29)	9.9 (23)	13.3 (29)	10·8 (11)	10·8 (11)	9·9 (10)
Redness at the injection site	8.9 (21)	7.3 (17)	8.7 (19)	7·8 (8)	7·8 (8)	6·9 (7)
Systemic reactions, % (n)						
Any	41.2 (97)	38.7 (91)	39.0 (85)	59·8 (61)	58·8 (60)	51·5 (52)
Fatigue	29.4 (69)	27 (63)	28.0 (61)	42·2 (43)	45·1 (46)	37·6 (38)
Chills	6.8 (16)	8.2 (19)	6.4 (14)	12·7 (13)	15·7 (16)	5·9 (6)
Fever	5.5 (13)	6.4 (15)	6.0 (13)	12·7 (13)	16·7 (17)	8·9 (9)
Headache	15.3 (36)	12.9 (30)	13.3 (29)	22·5 (23)	19·6 (20)	21·8 (22)
Nausea	2.6 (6)	2.1 (5)	3.7 (8)	2·9 (3)	3·9 (4)	0 (0)
Muscle pain	13.2 (31)	12.0 (28)	13.8 (30)	26·5 (27)	25·5 (26)	22·8 (23)
Joint pain	6.8 (16)	5.2 (12)	6.4 (14)	10·8 (11)	11·8 (12)	8·9 (9)
Others	5.1 (12)	5.2 (12)	6.0 (13)	1.0 (1)	3.9 (4)	3.0 (3)

Conclusion: IRD patients are at no higher risk of experiencing adverse events than controls after SARS-CoV-2 vaccination. In fact, systemic effects seem to occur less frequently in patients compared to healthy individuals, which potentially shows an influence of IRDs or their therapies on vaccination reactions.

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AB1327

COVID-19 CUTANEOUS AND SYSTEMIC MANIFESTATIONS AMONG DIFFERENT RACIAL GROUPS: A META-ANALYSIS

Keywords: COVID, Skin

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Background: COVID-19 cutaneous manifestations were first reported in February 2020, after a rash was listed as a sign of the virus.[1] In 2020, an article emphasized the absence of images among skin of color with respect to COVID-19 skin manifestations.[2] Without detection and treatment, individuals with skin of color may experience a disproportionate incidence of morbidity and mortality.[3] Discussion of cutaneous findings in skin of color remains limited to reviews and individual studies, and although there are meta-analyses that assess systemic manifestations among different races, investigation of various symptoms among people with skin of color, and overall comparison of systemic manifestations to cutaneous manifestations remains unreported to our knowledge.[4]

Objectives: The objective of this meta-analysis was to quantify the frequency of reported cutaneous and systemic manifestations among different races.

Methods: A search for studies on dermatologic and systemic manifestations associated with COVID-19 published before February 2022 was run on PubMed and Embase. Two independent reviewers screened abstracts and full manuscripts for eligibility based on the following criteria: studies included children or adult patients diagnosed with COVID-19 or temporal association to COVID-19, studies included assessment of cutaneous and systemic manifestations of individuals, studies identified cutaneous and systemic manifestations among different races, and studies were peer-reviewed case reports, original studies, systematic reviews, meta-analyses, and letters to the editor. Race and the most common systemic and dermatologic manifestations were extracted from included studies. Event rates for each outcome by race were pooled using a single-arm meta-analysis and the random-effects model to account for heterogeneity.

Results: Seventeen studies, involving 2,525 patients, were selected. Pooled estimates for multisystem inflammatory syndrome (MIS) for Black, White, and Asian cases were 28% (95% CI, 18.8-40.7, p=0.001), 40.1% (95% CI, 23.0-60.1, p=0.332), and 20% (95% CI, 13.2-29.2, p=0.000), respectively. The most common manifestations were pyrexia, elevated inflammatory markers, cardiac dysfunction, and gastrointestinal symptoms. The frequency of elevated inflammatory markers within Black cases surpassed White and Asian cases (30.9%, 28.7%, and 19.6%). The percentage of Black cases for cardiac dysfunction exceeded White and Asian cases (38.8%, 25%, and 21.2%,). The frequency of pyrexia reported among Asian and Black cases exceeded White cases (26.7%, 24.3%, and 15.3%). The prevalence of dermatologic manifestations in Black cases was 4.2% (95% CI, 0.8-19.8, p=0.000) compared to White and Asian cases, 70.7% (95% CI, 42.9-88.6, p=0.139) and 11.7% (95% CI, 9.0-15.1, p=0.000).

Conclusion: This meta-analysis highlights the discordance in reporting systemic manifestations compared to dermatologic manifestations by race in COVID-19 patients. Further investigation is needed to determine the underlying cause.

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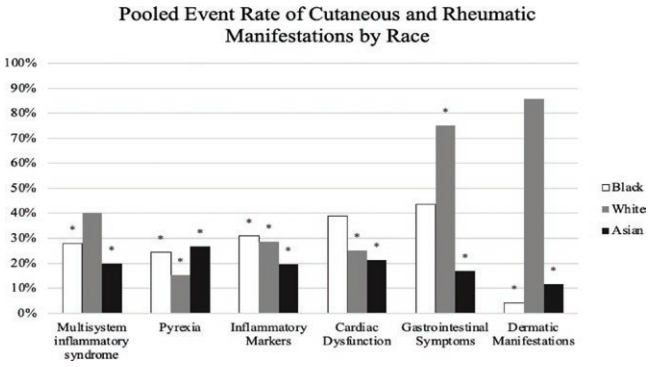


Figure 1. Meta-Analysis Pooled Event Rate of Cutaneous and Rheumatic Manifestations by Race. *Denotes a p-value less than 0.05

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AB1328

LONGITUDINAL SEROLOGICAL STUDY OF ANTI-SARS-COV-2 SPIKE PROTEIN ANTIBODIES AFTER TWO DOSES OF MRNA VACCINES IN PATIENTS WITH RHEUMATIC DISEASES: ANALYSIS OF EFFECTS OF IMMUNOSUPPRESSANT THERAPY

Keywords: COVID, Vaccination/immunization

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Background: The longitudinal efficacy and safety data of vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in patients with rheumatic disease (RD) remains unclear.

Objectives: The objective of the study was to examine changes over time in anti-SARS-CoV-2 spike protein IgG (anti-S IgG) values in RD patients compared with controls and investigate the effects of immunosuppressants on the values. Safety of vaccine was also evaluated.

Methods: RD patients receiving glucocorticoids or immunosuppressants who were scheduled to receive two doses of SARS-CoV-2 mRNA vaccines were included. Patients not receiving these drugs and were attending the hospital for diseases other than RD or malignancies served as the control group (CG). Following the guidance of the American College of Rheumatology, some immunosuppressive drugs were withheld before and after vaccinations. Blood samples were collected before and 1, 3, and 6 months (M1, M3, M6) after the vaccinations, and anti-S IgG values were measured using SARS-CoV-2 IgG II Quant Reagent Kit (Abbott Laboratories, USA).

Results: BNT162b2 mRNA vaccine-received 289 RD patients {mean age 66.9 [standard deviation (SD), 12.6] years; 241 females and 48 males} and 33 controls (mean age 70.7 [SD, 7.8] years; 22 females and 11 males) were mainly analyzed. Anti-S IgG values markedly increased in both groups at M1 [CG; 9751.5 (2385.3 – 21506.1), RD; 2300.8 (188.5 – 7671.7) AU/mL, expressed as median (25th to 75th percentiles)], subsequently decreased, and were significantly lower in the RD group than in the CG at all time points [CG; 5012.2 (2933.3 – 6628.4), RD; 1505.0 (459.0 – 3229.0) at M3, CG; 1353.6 (505.8 – 1910.3), RD; 402.0 (130.5 – 836.2) at M6]. Regarding antibody positivity, all patients in the CG tested positive at all time points. The antibody positivity rate was significantly lower in the RD group (85.0% at M1, 92% at M3, 86.4% at M6). In comparisons by disease, anti-S IgG values were significantly lower in patients with rheumatoid arthritis, systemic lupus erythematosus, vasculitis and dermatomyositis/polymyositis. In comparisons by treatment, anti-S IgG values were significantly lower in patients receiving rituximab [8.9 (5.8 – 68.2) at M1, 51.7 (26.4 – 144.0) at M3, 45.3 (23.1 – 67.4) at M6], mycophenolate mofetil [258.4 (1.1 – 713.7), 395.1 (18.0 – 2096.1), 212.3 (14.2 – 458.9)], cytotoxic T lymphocyte-associated antigen 4-immunoglobulin (CTLA4-Ig) [336.8 (33.5 – 1166.7), 324.9 (111.2 – 480.6), 84.0 (37.9 – 118.7)],

and prednisolone (PSL) [449.4 (26.3 – 2920.1), 709.6 (135.3 – 2008.5), 201.4 (44.7 – 602.5)]. A multivariate analysis with a linear mixed model indicated that there was a significant inverse association between age and the extent of changes in anti-S IgG values from M1, indicating greater decreases in antibody values at an older age from M1 [-75 (-133 – -18), expressed as regression coefficient (95% confidence interval)]. The extent of the decrease in anti-S IgG values was also significantly greater in males [-1873 (-3604 – -142)] and patients treated with PSL [-2071 (-3590 – -551)], CTLA4-Ig [-4018 (-6606 – -1429)], TNF inhibitors [-2009 (-3861 – -157)], and IL-6 inhibitors [-2422 (-4488 – -355)]. Adverse reactions were similar in both the CG and RD group.

Conclusion: These results showed that SARS-CoV-2 mRNA vaccination is effective and safe in patients with RD treated with a variety of immunosuppressants. However, even following the ACR guidance on withholding dugs, anti-S IgG values were lower and significantly decreased over time depending on disease and immunosuppressive drugs. Therefore, relative short-term repetitive vaccination might be warranted in patients with RD receiving immunosuppressive drugs.

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Disclosure of Interests: Mai Kawazoe Speakers bureau: Ayumi Pharmaceutical Corporation, Asahi Kasei Pharma Corp, AstraZeneca K.K., Gilead Sciences Inc and GlaxoSmithKline K.K., Kotaro Aoki: None declared, Wataru Hirose Speakers bureau: Pfizer Japan Inc., Asahikasei Pharma Corp., Chugai Pharmaceutical Co., AbbVie GK and Mitsubishi-Tanabe Pharma Co., Shotaro Masuoka: None declared, Kaichi Kaneko Speakers bureau: Asahi Kasei Pharma Corp, AstraZeneca K.K.,Boehringer Ingelheim Co., Ltd., Daiichi Sankyo Co., Ltd., Eli Lilly Japan K.K.,Gilead Sciences Inc, GlaxoSmithKline K.K., Janssen Pharmaceutical K.K., Novartis Pharma K.K. and Pfizer Japan Inc., Grant/research support from: Asahi Kasei Pharma Corp, Boehringer Ingelheim Co., Ltd. and Daiichi Sankyo Co., Ltd., Junko Nishio Speakers bureau: Asahi KASEI Pharma and Taisho Pharmaceutical Holdings., Grant/research support from: Asahi KASEI Pharma, CHUGAI PHARMACEUTIAL CO., LTD., ONO PHARMACEUTIAL CO., LTD., Boehringer Ingelheim, Nippon KAYAKU CO., AYUMI Pharmaceutical CO., Abbvie GK, Abbott Japan LLC and Taisho Pharmaceutical Holdings., Eri Watanabe Grant/research support from: GlaxoSmithKline K.K., Karin Furukawa: None declared, Miwa Kanaji: None declared, Toshihiro Nanki Speakers bureau: Eisai Co., Ltd., Astellas Pharma Inc., Janssen Pharmaceutical K.K., Ayumi Pharmaceutical Corporation, Pfizer Japan Inc., Asahikasei Pharma Corp., Eli Lilly Japan K.K., Takeda Pharmaceutical Co., Nippon Boehringer Ingelheim Co., Ltd., isho Pharmaceutical Co., Ltd., UCB Japan Co., Ltd., Ono Pharmaceutical Co., Ltd., AstraZeneca K.K., Mochida Pharmaceutical Co., Ltd., GlaxoSmithKline plc., and AbbVie GK., Consultant of: UCB Japan Co., Ltd., Eisai Co., Ltd., and Chugai Pharmaceutical Co., Grant/research support from: Chugai Pharmaceutical Co., Eisai Co., Ltd., Teijin Pharma Ltd., Eli Lilly Japan K.K., Bristol-Myers K.K., Ono Pharmaceutical Co., Ltd., Asahikasei Pharma Corp., Mitsubishi-Tanabe Pharma Co., Ayumi Pharmaceutical Corporation, Shionogi & Co., Ltd., Nippon Kayaku Co., Ltd., AbbVie GK, Nippon Boehringer Ingelheim Co., Ltd., Abbott Japan LLC and Taisho Pharmaceutical Co., Ltd.

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AB1329

CLINICAL CHARACTERISTICS OF SARS-COV-2 INFECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN ARGENTINA: DATA FROM THE SAR-COVID NATIONAL REGISTRY

Keywords: COVID, Systemic lupus erythematosus

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Background: Patients with systemic lupus erythematosus (SLE) present greater severity of SARS-CoV-2 infection compared to the general population, particularly those with glomerulonephritis and who are treated with glucocorticoids. Likewise, high disease activity and some immunosuppressants have been associated with worse outcomes.

Objectives: To describe the characteristics of SARS-CoV-2 infection in patients with SLE in Argentina from the SAR-COVID registry and to establish factors associated with a worse outcome.

Methods: Observational study. Patients diagnosed with SLE with confirmed SARS-CoV-2 infection (RT-PCR and/or positive serology) from the SAR-COVID registry were included. Data was collected from August 2020 to March 2022. The outcome of the infection was measured using the World Health Organization - ordinal scale (WHO-OS). Severe COVID-19 was defined as an WHO-OS value ≥5. Descriptive analysis, Student's T test, Mann Whitney U, ANOVA, Chi2 and Fisher. Multiple logistic regression.

Results: A total of 399 patients were included, 93% female, with a mean age of 40.9 years (SD 12.2), 39.6% had at least one comorbidity. At the time of infection, 54.9% were receiving glucocorticoids, 30.8% immunosuppressants, and 3.3% biological agents. SARS-CoV-2 infection was mild in most cases, while 4.6% had a severe course and/or died. The latter had comorbidities, used glucocorticoids and had antiphospholipid syndrome (APS) more frequently and higher disease activity at the time of infection. In the multivariate analysis, high blood pressure (OR 5.1, 95%CI 1.8-15.0), the diagnosis of APS (4.7, 95%CI 1.2-15.8), and the use of glucocorticoids (10 mg/day or more: OR 5.5, 95%CI 1.6-20.5) were associated with severe hospitalization and/or death from COVID-19 (WHO-EO≥5).

Conclusion: In this cohort of SLE patients with confirmed SARS-CoV-2 infection, most had a symptomatic course, 22.1% were hospitalized, and 5% required mechanical ventilation. Mortality was close to 3%. The diagnosis of APS, having high blood pressure, and the use of glucocorticoids were significantly associated with severe COVID-19.

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AB1330

FREQUENCY OF DISEASE FLARE AND ITS RISK FACTORS FOLLOWING TWO-DOSE OF COVID-19 VACCINATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Vaccination/immunization, Rheumatoid arthritis, Safety

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Background: Amid the coronavirus disease 2019 (COVID-19) crisis, two messenger RNA (mRNA) vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have benefitted most people worldwide. However, the safety of vaccine has not been established in patients with rheumatic arthritis (RA). Previous studies reported that flares of underlying RA following SARS–CoV-2 vaccination were not so frequent, and there was no report of severe flare. However, those reports did not assess patients' disease activity with validated disease activity measures and described only simple self-reported questionnaires. Hence, the effect of vaccination on disease activity in patients with RA is still unclear. Understanding the association between arthritis flare in patients in RA and vaccination is important to overcome vaccine hesitancy.

Objectives: To clarify the effect of SARS-CoV-2 vaccination on disease activity in patients with RA and identify risk factors associated with RA flares following the vaccination.

Methods: This is a prospective cohort study in patients with rheumatic musculoskeletal disease including RA who received the SARS-CoV-2 mRNA vaccines BNT162b2 or mRNA-1273 from March 16, 2021, at Keio University Hospital. The disease activity was evaluated with disease activity score for 28 joints using C-reactive protein (DAS28), simplified disease activity index (SDAI), and clinical disease activity index (CDAI) before vaccination and after second vaccination (within two months). RA flare was defined as ΔDAS28-CRP>0.6with requirement of treatment intensification. All analysis in this study was carried out with JMP.

Results: We enrolled 318 patients with RA in this analysis. The mean age was 61 years old, and 283 (89%) were female. The mean DAS28-CRP before vaccination and after 2nd dose of vaccination were 1.70±0.71 and 1.78±0.81, respectively (p=0.84). The increase in DAS28-CPR after vaccination > 0.6 was observed in 53 patients (16.7%), and among them, 23 patients (8.2%) needed treatment intensification. The types of SARS-CoV-2 vaccine, humoral immunogenicity including neutralizing antibody titer and its adverse effects including systemic reaction (fever or general fatigue) were not different between the flare and non-flare groups (9.8 vs 9.1 IU/mL, p=0.88; 31.2% vs 18.7%, p=0.32, respectively). In the flare group, swollen joint counts (SJC), hourly erythrocyte sedimentation rates, DAS28-CRP, and SDAI were significantly higher than those in the non-flare group (0.5 vs 0.0, p<0.000; 13 vs 11 mm/h, p=0.01; 1.57 vs 1.45, p<0.001; 3.9 vs 2.4, p=0.02, respectively). Multivariable logistic regression analysis revealed that the number of swollen joints before vaccination contributed RA exacerbation after SARS-CoV-2 vaccination significantly (odds ratio 1.3, 95% confidence interval 1.06-1.65, p=0.01). The receiver operating curve analysis identified that having two or more swollen joint counts predicts RA flares after vaccination with an area under the curve of 0.64, a sensitivity of 42.3%, and a specificity of 86.9%.

Conclusion: Disease flare with requirement of treatment intensification is observed in 8.2% of patients with RA. Patients with higher disease activity, especially having two or more swollen joint counts are at high risk of flare following mRNA SARS-CoV-2 vaccination.

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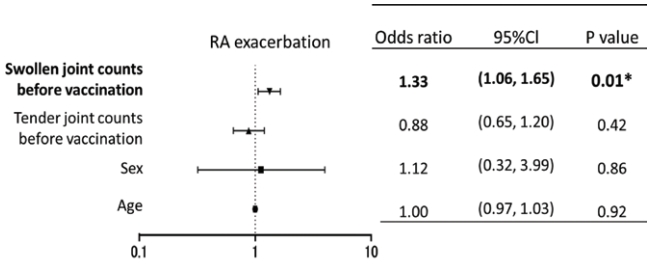


Figure 1. Risk factors associated with RA flares after vaccination

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AB1331 COVID VACCINATION AND ADVERSE REACTIONS AMONG PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: WHAT IS THE RHEUMATOLOGIST'S ROLE?

Keywords: Vaccination/immunization, Myositis, COVID

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Background: Since 2021, EULAR has advocated for the vaccination of patients with rheumatic and musculoskeletal diseases [1]. However, there is significant patient hesitancy, and it is often attributed to concern regarding vaccine adverse events (AEs) [2]. Idiopathic inflammatory myopathies (IIMs) are an example of rare rheumatic conditions in which population-specific data is limited and rheumatologists may play vital role in a vaccine discussion.
Objectives: Our aim was to evaluate COVID vaccination and AEs rates in patients with IIM and determine whether rheumatologist-initiated vaccine discussions correlated with patient vaccination rates.
Methods: The Montefiore Medical Center Myositis registry was created from patients that met 2017 EULAR/ACR classification criteria for IIM. Patients without a history of rheumatology care at our hospital or those who had died prior to COVID vaccines availability were excluded. Demographics and IIM subtype were documented. Vaccination details, including vaccination type and number, were recorded. Medical records were reviewed for minor and major vaccine AEs and documentation by a rheumatologist of COVID vaccine discussion. The presence of fever, headache, fatigue, or pain at injection site within 2 weeks of vaccine administration was considered a minor vaccine AE. The presence of anaphylaxis, Guillen Barre Syndrome, myocarditis, pericarditis, death or IIM flare within 3 months of vaccination administration was defined as a major AE. Statistical analyses included two-sample t-test, Chi-square tests or Fisher's exact tests.
Results: Of 153 within the registry, 116 met inclusion criteria. 81 of 116 (70%) of patients had received at least one COVID vaccination. Demographics (age, sex, race, ethnicity) were similar between vaccinated and unvaccinated patients. Of the vaccinated patients, all had received the primary series, 69% (56/81) had received a booster, and only 7% had received the primary, booster, and bivalent series. Overall, the rates of minor and major AEs were 17% and 2%, respectively. There were no differences in AEs based on the vaccine type (Pfizer, Moderna, or Janssen). However, it was more likely for patients to have minor AEs after receiving a booster vaccine in comparison to the primary or bivalent series, regardless of vaccine type (p=0.02). 7% (6/81) patients experienced a flare within 3 months of vaccination. In total, 38/116 (33%) of IIM patients had a documented COVID vaccine discussion with their rheumatologist. Of those patients who discussed the vaccine, 34 (89%) received at least one COVID vaccine while only 60% (47/78) of the patients who had not discussed vaccination were vaccinated (Figure 1).
Conclusion: While majority of IIM patients have received the primary series, the booster and bivalent series are much less prevalent. IIM patients whose rheumatologist discussed vaccination were more likely to be vaccinated. This signifies the importance of rheumatologist-initiated vaccine discussions. We reported less minor AEs and the same frequency of major AEs as larger, self-reported IIM studies. The low prevalence of AEs and IIM flares may be a tool in the rheumatologist-led vaccination discussion.
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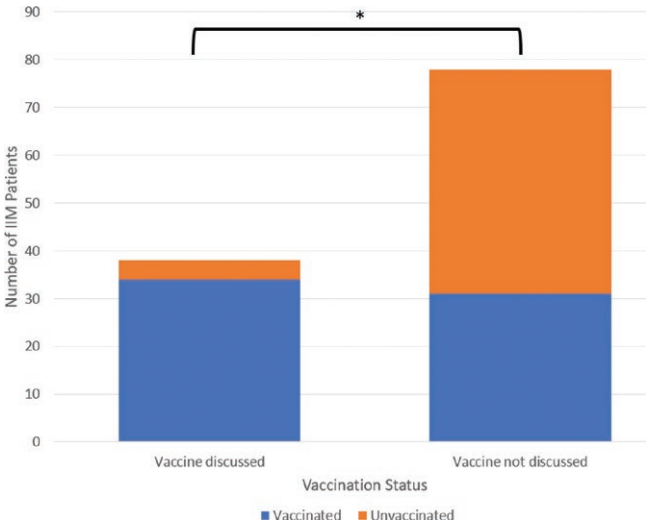


Figure 1. Comparison of vaccination status between patients who experienced a rheumatologist-led vaccination discussion and those who did not.

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Disclosure of Interests: None Declared.
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AB1332 CLINICAL OUTCOMES AND RISK FACTORS OF COVID-19 IN AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES: A LARGE REAL-WORLD SURVEY IN CHINA

Keywords: COVID, Vaccination/immunization

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Background: The impact of COVID-19 on vulnerable populations with autoimmune inflammatory rheumatic diseases (AIIRDs) has been of great concern.
Objectives: The aim is to report the clinical features, outcomes as well as risk factors of infection and hospitalization in Chinese AIIRDs patients during the big wave of infection last month.
Methods: A real-world survey was conducted during the peak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) (8 December 2022 to 13 January 2023) in China. All patients completed the survey via internet or at the rheumatology inpatient and outpatient clinic of a tertiary hospital in Beijing with a medical diagnosis of AIIRDs. Clinical features, outcomes and risk factors of COVID-19 in AIIRDs were analyzed. The main outcome were SARS-CoV2 infection and hospital admission related to COVID-19. We apply the multivariable logistic regression model to assess risk factors for the infection and hospitalization.
Results: Totally 2005 patients with AIIRDs completed the survey. The leading AIIDs were systemic lupus erythematosus (SLE) (1039, 51.8%), rheumatoid arthritis (RA) (290, 14.5%) and Behcet's disease (BD) (231, 11.5%). There were 1690 (84.3%) patients who were infected and 315 (15.7%) patients not infected. The independent factors protecting patients from COVID-19 infection were the time interval of less than 3 months from last vaccination (OR: 0.53; p=0.037) and RA as the underlying AIIRDs (OR: 0.62; p=0.041). 57 out of 1690 patients (3.4%) were hospitalized. 46 (80.7%) of them experienced severe/critical course. In multivariable logistic regression analysis, independent risk factors for hospitalisation with COVID-19 were age over 60 years (OR: 11.5; p<0.001), with comorbidity (OR: 1.83; p=0.045) and SLE as the underlying AIIRDs (OR: 2.59; p=0.036).
Conclusion: Our study suggested that time from last vaccination of less than 3 months and having RA decreased the risk of COVID-19 in AIIRDs. Among the infected patients, older age, having previous comorbidity and having SLE increased the risk of hospitalization.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2226

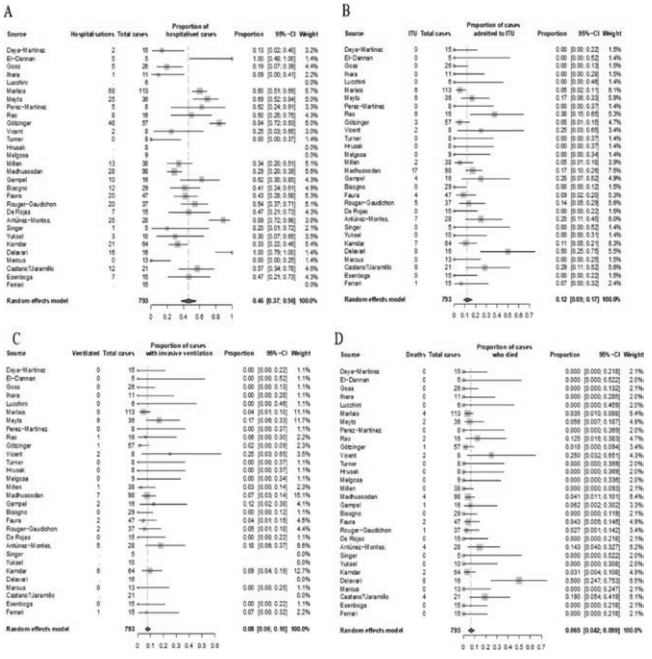
COVID-19

AB1333 **THE IMPACT OF IMMUNOCOMPROMISE ON OUTCOMES OF COVID-19 IN CHILDREN AND YOUNG PEOPLE - A SYSTEMATIC REVIEW AND META-ANALYSIS**

Keywords: Outcome measures, COVID

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Background: Despite children and young people (CYP) having a low risk for severe Coronavirus disease 2019 (COVID-19) outcomes, there is still a degree of uncertainty related to their risk in the context of immunodeficiency or immunosuppression, primarily due to significant reporting bias in most studies, as CYP characteristically experience milder or asymptomatic COVID-19 infection and the severe outcomes tend to be overestimated.
Objectives: To systematically evaluate the impact of immunosuppression on severe COVID-19 infection outcomes in CYP and perform a meta-analysis to estimate differences in outcomes compared to general population.
Methods: A comprehensive systematic review to identify globally relevant studies in immunosuppressed CYP and CYP in general population (defined as younger than 25 years of age) up to 31st October 2021 (to exclude vaccinated populations), was performed. Studies were included if they reported the two primary outcomes of our study, admission to intensive therapy unit (ITU) and mortality, while data on other outcomes, such as hospitalisation and need for mechanical ventilation were also collected. A meta-analysis estimated the pooled proportion for each severe COVID-19 outcome, using the inverse variance method. Random effects models were used to account for interstudy heterogeneity.
Results: The systematic review identified 30 eligible studies for each of the two populations investigated: immunosuppressed CYP (n=793) and CYP in general population (n=102,022). Our meta-analysis found higher estimated prevalence for hospitalization (46% vs. 16%), ITU admission (12% vs. 2%), mechanical ventilation (8% vs. 1%) and increased mortality due to severe COVID-19 infection (6.5% vs. 0.2%) in immunocompromised CYP compared to CYP in general population (Figure 1A-D depicts the pooled estimates for the above outcomes in immunocompromised CYP). This analysis shows an overall trend for more severe outcomes of COVID-19 infection in immunocompromised CYP, similar to adult studies.
Conclusion: This is the only up to date meta-analysis in immunocompromised CYP with high global relevance, which excluded reports from hospitalised cohorts alone and included 35% studies from low- and medium-income countries. Future research is required to characterise individual subgroups of immunocompromised patients, as well as impact of vaccination on severe COVID-19 outcomes.



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AB1335 **INTAKE OF ACETAMINOPHEN SUPPRESSES ANTIVIRAL HUMORAL IMMUNE RESPONSES IN PATIENTS WITH RA FOLLOWING VACCINATION WITH ANTI SARS-COV-2 MRNA BASED VACCINES**

Keywords: Disease-modifying drugs (DMARDs), Rheumatoid arthritis, Vaccination/immunization

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Background: Acetaminophen (APAP = paracetamol) may potentially impact vaccine-associated immune responses as the intake of APAP has been associated with a worse outcome in tumor patients receiving checkpoint inhibitors.[1] Different DMARD regimen have been shown to impair the humoral immune response to mRNA SARS-CoV-2 vaccines in patients with rheumatoid arthritis but the effect of paracetamol has not been explored thus far.
Objectives: To analyse whether the intake of APAP may interfere with antiviral humoral immune responses following two doses of an anti-SARS-CoV-2 mRNA based vaccine in patients with rheumatoid arthritis (RA) on DMARD therapy.
Methods: The RECOVER trial (**R**heumatoid **C**ovid-19 **V**accin**e** Immune **R**esponse) was a non-randomised, prospective observational control group trial and enrolled 77 RA patients on DMARD therapy and 21 healthy controls (HC). We performed a posthoc analysis of blood samples taken before the first vaccine dose (T0), two (T1) and three (T2) weeks after the first and second vaccine dose, and at 12 (T3) weeks. APAP intake was measured using ELISA. The antibody response (anti-S) to the receptor binding domain (RBD) within the SARS-CoV-2 S1 protein was measured with the Elecsys Anti-SARS-CoV-2-S (Roche Diagnostics GmbH) test. The neutralizing activity NT50 at week 12 was assessed using an HIV-based pseudovirus neutralization assay against Wuhan-Hu-1.
Results: Baseline characteristics of participants are detailed in Table 1. The immunogenicity analyses were based on 73 RA patients after exclusion of 4 patients with previously unnoticed SARS-CoV-2 infection (positive for anti-nucleoprotein at baseline). APAP was detected in serum samples from 34/73 (25%) RA patients and in 7/21 (33%) HC (least at one timepoint T0, T1 and/or T2). APAP intake in HC did not affect levels of anti-S at any timepoint and all HC developed potent neutralizing activity (NT50 ≥ 250) at week 12. RA patients, who tested positive for APAP at T1, showed comparable anti-S levels at T1, T2 and T3 compared to RA patients not exposed to APAP. The detection of APAP at T2 corresponded to lower anti-S levels at T2 (Figure 1 A, B). The detection of APAP at T2 was associated with a significantly lower SARS-CoV-2 neutralizing activity at week 12 compared to patients without perivaccination APAP exposure (p =0.04) (Figure 1 C).
Conclusion: A decrease of antiviral humoral immune responses was observed in RA patients (but not in HC) who were exposed to APAP at the time of the second mRNA vaccine dose compared to patients in whom APAP was not detected. Our data suggest that the use of paracetamol within the time period around vaccination may impair vaccine-induced immune responses in patients with an already higher risk for blunted immune responses.

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Table 1. Baseline characteristics: RA patients and HC with/without APAP exposure

	RA APAP – n = 37	RA APAP + n = 36	p-value	HC APAP – n = 8	HC APAP + n = 13	p-value
Age (yrs), mean (± SD)	62 (13)	67 (10)	0.07 (NS)	45 (12)	44 (14)	0.90 (NS)
Female sex, n (%)	24 (65)	19 (53)	0.29 (NS)	2 (25)	5 (38)	0.53 (NS)
Vaccination type/ schedule						
mRNA-1273, n (%)	4 (11)	8 (22.2)	0.19 (NS)	0 (0)	0 (0)	
BNT162b2, n (%)	33 (89)	28 (77.8)	0.19 (NS)	8 (100)	13 (100)	
RA disease characteristics						
ACPA ± RF, n (%)	17/37 (46)	19/36 (53)	0.56 (NS)	NA	NA	NA
RA disease duration (yrs ± SD)	9.2 (9.8)	10.2 (8.1)	0.67 (NS)	NA	NA	NA
DMARD therapy						
csDMARD-mono, n (%)	13/37 (35)	9/36 (25)	0.35 (NS)	NA	NA	NA
bDMARD-mono/ combo, n (%)	16/37 (43)	16/36 (44)	0.92 (NS)	NA	NA	NA
tsDMARDs-mono/ combo, n (%)	8/37 (22)	11/36 (31)	0.38 (NS)	NA	NA	NA
Prednisone, n (%)	15/37 (41)	12/36 (33.3)	0.52 (NS)	NA	NA	NA
Mean daily dose prednisone (mg ± SD)	4.6 ± 1.1	3.9 ± 2.3	0.39 (NS)	NA	NA	NA

* APAP = acetaminophen

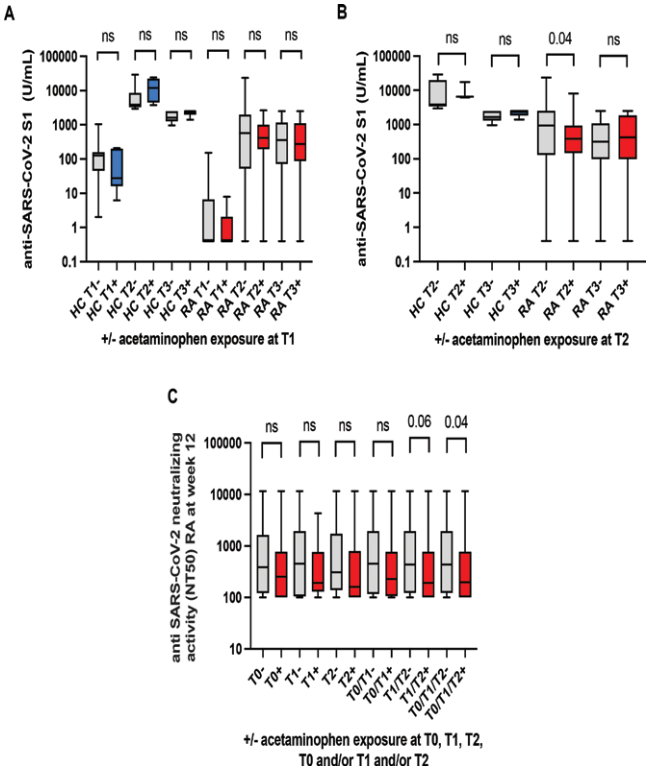


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.3264

AB1336

EVALUATION OF THE IMMUNOGENICITY AND EFFICACY OF THE SARS-COV-2 VACCINE IN PATIENTS WITH CHRONIC INFLAMMATORY DISEASES TREATED WITH BIOLOGICAL THERAPY

Keywords: COVID, Vaccination/immunization, bDMARD

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Background: Data on the immunogenicity and efficacy of vaccines against COVID-19 in patients with chronic inflammatory diseases (CID) are uncertain and possibly lower than those observed in the general population, but the potential for severe COVID-19 in this population warrants their use.
Objectives: To determine the seroconversion rate and efficacy after the complete vaccination regimen against SARSCoV-2 in patients with CID on bDMARD treatment, as well as to evaluate the infection rate after vaccination and adherence to vaccination regimens.
Methods: Single-center, prospective observational study of 114 patients with CID from the HURS of Córdoba, who have received full vaccination for SARS-CoV-2 in 2021 (without having previously suffered from COVID-19 disease) according to national guidelines with a 12-month follow-up after vaccination. All of them underwent two determinations of specific IgG antibodies against the trimeric spike protein of SARS-Cov2 (2021 and 2022). It has been established that an Ab titer of less than 260 BAU/ml can be considered indicative and indicative of a poor response to vaccination. Information was collected for each patient regarding IHD, type of bDMARD, vaccine administered, concomitant treatments, adverse effects, and infection after vaccination.
Results: 114 patients were included (mean age 50 years, 67.5% women). 36% of the patients had RA, 12.3% SpA, 9.6% PSO, 28.9% IBD, and 13.2% other CID. 16.7% were receiving treatment with Rituximab, 36.8% anti-TNF, 9.6% Tocilizumab, 7% abatacept, 4.5% anti-JAK, and 6.1% other treatments. 19.3% only with synthetic Fame. Anti-SARS-CoV-2 antibodies and neutralizing activity were detected in 80% of study participants. Rituximab-treated patients showed significantly higher non-seroconversion (73.7% vs. 5.3%, p<0.001) (Figure 1) as well as a 58-fold higher risk of non-seroconversion compared to patients without bDMARDs (OR: 58.80 CI (8.86 - 120.4) p<0.001. Interestingly, we found that methotrexate alone also decreased seroconversion significantly (mean Ab titer reduction -654.6 (95%CI -1127.7 to -181.4, p=0.007). Furthermore, we observed a significant interaction between the type of biologic and the concomitant use of methotrexate, such that the reduction in the antibody titer is enhanced by the combination of methotrexate and anti-TNF, anti-IL 6, Rituximab, and other DMARDsb (Figure 2). 18.9% presented mild adverse effects after the administration of the vaccine.17.5% presented covid-19 infection during the last year of follow-up, being more frequent in the group vaccinated with Astrazéneca, although without statistically significant differences. No patient experienced a disease flare. In relation to adherence to vaccination, slightly more than half (56.14%) have administered at least 4 doses.
Conclusion: Our results show that mRNA vaccines against SARSCoV-2 produce seroconversion in the majority of patients with CID, except in the case of patients with rituximab. No serious adverse effects or ICD reactivation were found. Despite the small number of patients included, this study suggests the need for revaccination and the use of other vaccination strategies in the group of patients treated with rituximab and in the group of patients taking methotrexate. Efforts should be made to improve adherence to covid 19 vaccination in this group of patients.

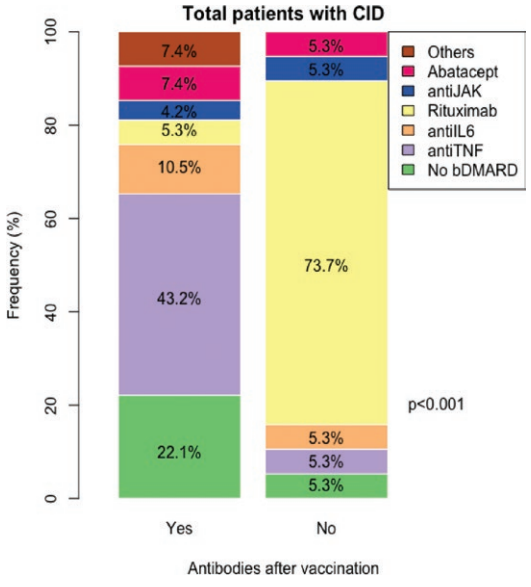


Figure 1. Shows how the use of rituximab is significantly associated with not developing antibodies.

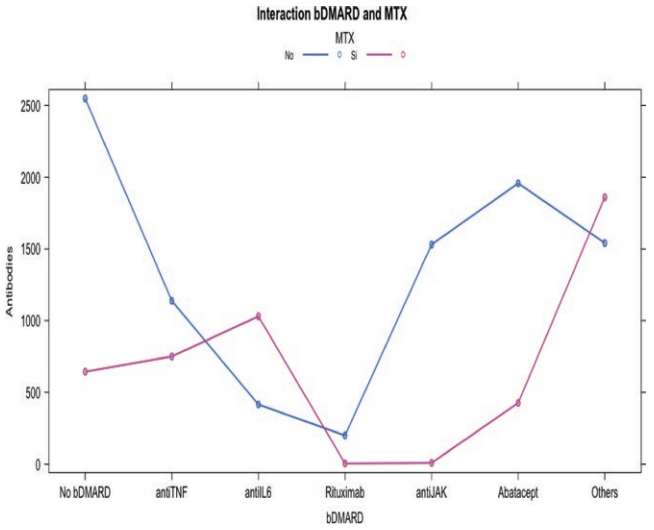


Figure 2. Represents the interaction between the biological drug and the use of methotrexate in relation to the level of Antibodies.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4060

AB1337

COVID-19 AND JAKI: ANALYSIS AFTER THREE-YEAR PANDEMIC AT A SPANISH TERTIARY CARE HOSPITAL

Keywords: Targeted synthetic drugs, COVID

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Background: The Coronavirus disease (COVID-19) is caused by the SARS-CoV-2 virus, which has led to a world revolution in many spheres, especially in the field of health, for more than three years. It is important to take into account that patients who are immunocompromised, such as those treated with JAK inhibitors (JAKi) are at higher risk to get sick with COVID-19 and have a worse prognosis.
Objectives: To analyze the impact after a three-year pandemic in those patients treated with JAKi in a Rheumatology Department at a Spanish tertiary care Hospital.
Methods: Retrospective longitudinal observational study of patients treated with JAKi from December 2019 to December 2022. Demographic and clinical variables were collected from the electronical medical record. Incidence of COVID-19 was considered as adverse event. Those infections which required hospitalization or were a threat to the patient's life were categorized as serious adverse event. The proportion of COVID-19 vaccinated patients was analyzed.
Results: 209 patients treated with JAKi were included. Rheumatoid Arthritis was the most frequent disease (n=162) and tofacitinib the most used JAKi (n=89). 193 (92,34%) patients received at least 1 dose of the vaccine against COVID-19. 17 infections were observed as adverse event. 3 of them were seriously ill and required hospitalization, none of them were vaccinated at that moment. Out of the 14 patients with minor infection, 7 were vaccinated. One death was registered but it was not caused by infection. Baricitinib (n=7) was the most related JAKi with minor infection. Upadacitinib (n=2) was the most associated JAKi with serious infection.
Conclusion: In our series of patients, we observed an incidence of 17 infections from COVID-19, 3 of them serious. The 92,34% of the patients were vaccinated. We didn't notice any infection in patients treated with Filgotinib, probably because of the short time of commercialization and few patients treated. The scarce number of infections reported is remarkable, especially in the second part of the pandemic. This is probably due to the effectivity of the vaccine, the success of vaccination campaigns and the normalization of the disease, with the consequent infradiagnosis.

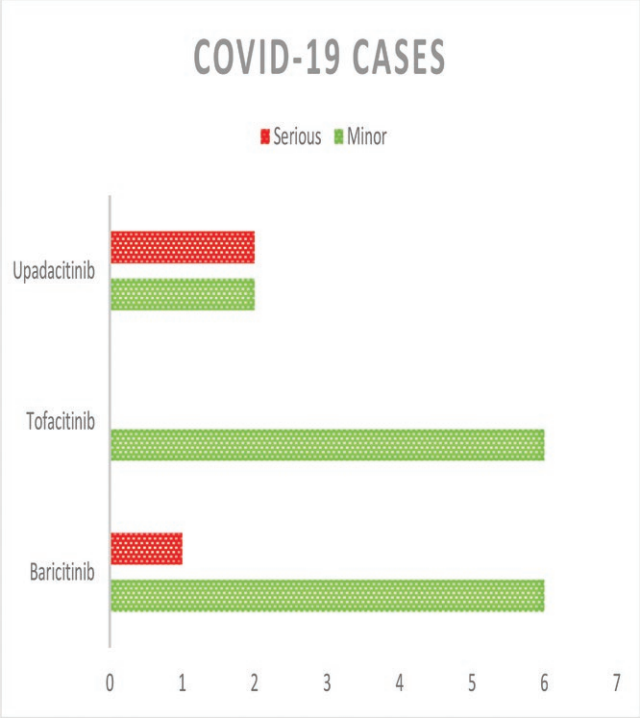


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1338

CLINICAL COURSE IN COVID 19 DISEASE IN IMMUNOSUPRESSED PATIENTS DIAGNOSED WITH RHEUMATIC DISEASES

Keywords: Comorbidities, COVID, Vaccination/immunization

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Background: Patients with pre-existing rheumatic diseases may be exacerbated during SARS-CoV-2 infection, or may develop new autoimmune features. Furthermore, immunosuppressive agents used to treat autoimmunity-inflammation as well as comorbidities can also affect the disease outcome.
Objectives: To evaluate the outcome of rheumatic diseases after Covid 19 infection in patients diagnosed with rheumatic diseases, under various immunosuppressive treatment, as well as the effects of vaccines against Covid or antiviral treatment in this sensitive population group.
Methods: During the pandemic, 1493 patients with autoimmune or autoinflammatory disease who were continuously followed up in two tertiaries hospitals in northern and northwestern Greece were included in the current study. The patients were compared with 769 controls after adjustment for age, sex, weight, vaccination status and comorbidities. Of the 1493 patients, 648 had rheumatoid arthritis, 282 psoriatic arthritis, 173 ankylosing spondylitis, 122 systemic lupus erythematosus, 98 Sjogren's syndrome, 43 polymyalgia rheumatica, 34 mixed connective tissue disease or overlapping syndromes, 31 vasculitis, 27 systemic sclerosis, 18 myositis, 10 Behcet syndrome, 5 primary antiphospholipid syndrome and 2 had Familial Mediterranean Fever. The vast majority of patients and controls were fully vaccinated (82%) and 397 patients received antiviral treatment, 94% of them were fully vaccinated.
Results: Covid 19 disease in vaccinated patients with rheumatic diseases was shown to perform the same or about the same as those in the control group after adjustment for risk factors for severe disease. 19 of our patients required admission in the intensive care unit (62% full vaccinated) while a total of 12 died (66% non vaccinated). Major risk factors for severe disease were previous respiratory failure, chronic renal impairment, obesity, and failure to receive antiviral therapy. It was also shown that infection with Covid led to an exacerbation or induction of autoimmune disorders in 25 of the participants.

Table 1.

	Total of patients n=209
Age - years (SD)	62 (8.20)
Female - n (%)	165(78.94%)
Diagnosis – n (%)	
Rheumatoid Arthritis	162 (77.51%)
Psoriatic Arthritis	23 (11%)
Axial Spondyloarthritis	12 (5.74%)
Juvenile Idiopathic Arthritis	2 (0.95%)
Others	10 (4.78%)
Comorbidities - n (%)	
Dyslipidemia	64 (30.62%)
Hypertension	56 (26.79%)
Diabetes Mellitus	20 (9.56%)
Tobacco use	38 (18.18%)
Type of JAKi - n (%)	
Tofacitinib	89 (42.58%)
Baricitinib	56 (26.79%)
Upadacitinib	60 (28.70%)
Filgotinib	4 (1.91%)
Concomitant treatment – n (%)	
DMARD	107 (51.19%)
Corticosteroids	110 (52.63%)
COVID-19 Vaccination – n (%)	193 (92.34%)
COVID-19 Infections – n	
Minor	14
Serious	3

Conclusion: In this large cohort, Covid 19 disease was shown to affect patients with autoimmune rheumatic diseases the same or approximately the same way as the general population if they are fully vaccinated and if they start timely antiviral treatment where indicated. Further research and monitoring of the results after the multiple mutations of the virus is advisable.

References: None.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1339 EFFICACY AND SAFETY OF THE SARS-COV-2 VACCINE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Vaccination/immunization, Rheumatoid arthritis, COVID

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Background: Rheumatoid arthritis (RA) and DMARDs are associated with a dysfunction of the cellular and humoral immune system that increases their susceptibility to infection, with vaccinations being one of the main infection prevention measures in these patients.

Objectives: To describe the efficacy and safety of the SARS-CoV-2 vaccine in a series of patients with RA.

Methods: Retrospective observational study of RA patients, fulfilling the ACR/EULAR 2010 classification criteria, vaccinated against the SARS-CoV-2 virus from December 2020 to October 2021, who had post-vaccination serology and subsequent follow-up for a minimum of 6 months in a university hospital. The efficacy and effectiveness of the vaccine was evaluated by analyzing the serological response (anti-SARS-CoV-2 IgG antibodies) and the incidence of post-vaccination SARS-CoV-2 infection. Vaccine safety was investigated recording adverse events and RA flares. Logistic and linear multivariate regression analyzes adjusted for age, sex, and time elapsed from vaccination to serological determination were used to identify factors associated with vaccine response. Statistical analysis was carried out with Stata® and significance was set at p<0.05.

Results: We included 118 patients with RA (87.2% women, mean age 65.4±11.6 years, mean evolution 12.0±9.6 years) vaccinated against SARS-CoV-2 (95.76% received the complete vaccination schedule). Patient characteristics regarding socio-demographic, clinical and laboratory RA related variables, as well as prior Covid infection are shown in Table 1.

Table 1.

	POPULATION CHARACTERISTICS	SEROLOGICAL RESPONSE TO VACCINE			GRADE OF SEROLOGICAL RESPONSE
		YES	NO	p	p
Age (years)	65.47±11.69	65.25±11.67	67.14±12.10	0.233	0.498
Sex (male/female)	15 (12.71)/ 103 (87.29)	12 (11.54)/ 92 (88.46)	3 (21.43)/ 11 (78.57)	0.385	**0.019**
Smoking (pack-year index)	8.79±18.55	6.87±15.23	23.01±31.83	**<0.001**	0.387
Comorbility	68 (57.63)	58 (55.77)	10 (71.43)	0.389	0.498
RA duration	12.08±9.63	11.57±8.59	15.93±15.28	0.994	0.815
Rheumatoid factor +	79 (66.95)	72 (69.23)	7 (50.00)	0.151	0.102
Anticitrullinated protein antibodies +	63 (53.39)	52 (82.54)	52 (94.55)	**0.051**	0.328
Erosive RA	32 (27.11)	26 (25.00)	6 (42.86)	0.158	0.423
Extraarticular manifestations	26 (22.03)	20 (19.23)	6 (42.86)	**0.045**	0.129
ESR	19.88±18.64	20.00±19.04	19.00±15.94	0.855	**0.020**
CRP	0.51±0.78	0.47±0.64	0.82±1.44	0.239	**0.006**
HAQ	0.575 (0.66)	0.59±0.67	0.43±0.59	0.810	0.561
DAS28	2.39±1.07	2.37±1.12	2.53±0.60	0.110	0.603
Prior COVID-19	21 (17.8)	22 (20.19)	0 (0)	0.072	**<0.001**

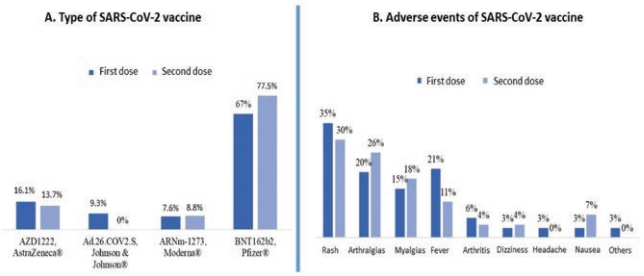


Figure 1.

57.6% of the patients had associated comorbidity, especially dyslipidemia 41.5%, arterial hypertension 31.4% and diabetes mellitus 10.2%. Almost all patients received csDMARDs, especially MTX (83.9%), and 46.6% had biologic therapy or JAK inhibitors, with a predominance of TNF antagonists (20,3%) and RTX (16,1%). Types of vaccines and schedule are shown in Figure 1A. Most patients (88.1%) developed humoral immunogenicity. Univariate analysis of factors associates with humoral response and grade of response to the vaccine are shown in Table 1. Multivariate analysis found that smoking (OR 0.96, 95%CI: 0.94-0.99, p=0.034) was the only variable significantly associated with humoral response to the vaccine. The degree of serological response was significantly related to younger age (coefficient -16.11, 95%CI: -31.84 to -0.39, p=0.045) and previous COVID-19 infection (coefficient 4.496, IC 95%: 3.604-5.388, p<0.001), which had occurred in 17.8% (5% severe) and was associated with male gender (p=0.016). After vaccination, 18.6% presented SARS-CoV-2 infection, although mild. Vaccine adverse events (19.5%) were mostly mild (Figure 1B) and associated with age (OR 0.95, 95%CI: 0.91–0.99, p=0.042). RA flares were anecdotal (1.7%), being inversely related to age (OR 0.95, 95%CI: 0.91-0.99, p=0.042).

Conclusion: Our results, with a limited sample, suggest that the SARS-CoV-2 vaccine induces adequate humoral immunogenicity, with an acceptable safety profile in RA patients, reducing the severity of SARS-CoV-2 infection.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.4560

AB1340 CRYOFIBRINOGENEMIA IN PRECOVID-19 AND COVID-19 ERA: A COMPARATIVE STUDY IN A SINGLE UNIVERSITY HOSPITAL

Keywords: Descriptive studies, Skin, COVID

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Background: Cryofibrinogenemia (CF) is an under-recognized syndrome due to the lack of definitive criteria and the rarity of disease. CF may be essential or secondary to autoimmune, neoplastic or infections conditions **[1]**. Skin manifestations, mainly ulceration, are the most common and may be a pseudovasculitic syndrome. During COVID-19 era the number of cases with skin lesions get increased. Further studies are needed to characterize this association between CF and SARS-CoV-2 **[2].**

Objectives: A) To evaluate the frequency of CF during preCOVID era and COVID era. **B)** To describe the clinical profile of CF and the mainly characteristics of patients in both study groups.

Methods: Observational single-center study in northern Spain University Hospital of 134 patients with at least one positive cryofibrinogen determination, between January 2017 and March 2020 (preCOVID era) and March 2020 and December 2022 (COVID era). CF diagnosis was confirmed accordingly to reported criteria **[3].** Clinical conditions, laboratory parameters, including immunological and serological analysis were collected from all patients. Blood was collected in citrated tubes for cryofibrinogen detection. Stadistical analysis was performed using SPSS software. Quantitative variables were expressed as mean±SD. Qualitative variables were compared using chi-squared test. Quantitative variables were compared using the student's *t*.

Results: CF was confirmed in 19/134 (14.2%) patients with at least one positive cryofibrinogen test determination (5 in preCOVID era; 14 in COVID era). Patients of COVID-19 era were more frequently male (64.3% to 40%) and younger (43.6 to 60.6 years). Main features are shown in **Table 1**. In preCOVID era most of cases were essential CF (60%) and in COVID era most of them were secondary ones (64.3%). The 33.3% of secondary CF were mainly due to COVID. Cutaneous manifestations were similar in both subgroups, especially as purpuric macules (perniosis-like) in acral distributions. Antiaggregant drugs and corticosteroids were used more frequently in preCOVID era. The comparative incidence after and before COVID is shown in **Figure 1.** From patients with positive cryofibrinogen test, a greater proportion in preCOVID had a CF.

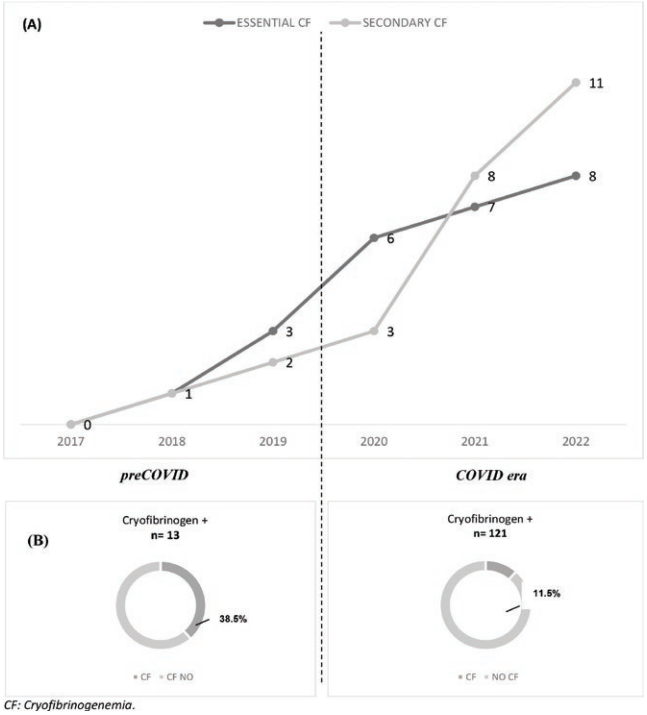
Conclusion: CF is a rare disorder with a low prevalence. This study showed the change in the trend of CF subtypes, probably due to the influence of the COVID infection. In COVID era the number of positive cryofibrinogen test had envolved due to SARS-CoV2 infection, CF cases were not increased. Clinical expression of the disease has not changed in both groups.

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[3] Grada A, Falanga V. Am J Clin Dermatol. 2017 Feb;18(1):97-104.

Table 1. Number of cases and clinical features of Cryofibrinogenemia (CF) in preCOVID era and COVID era.

	PRECOVID ERA (n= 5)	COVID ERA (n=14)	p
Cryofibrinogen test; (%positive) (N=134)	5/13 (38.5)	14/121 (11.5)	0.008
Age, years, mean±SD	60.6±11.2	43.6±21.0	0.195
Sex, n (%)			
Male	2 (40)	9 (64.3)	0.345
Female	3 (60)	5 (35.7)	
CF Essential, n (%)	3 (60)	5 (35.7)	0.345
CF Secondary, n (%)	2 (40)	9 (64.3)	0.345
COVID19	0	3 (33.3)	0.239
Connectivopathy	2 (100)	3 (33.3)	0.418
Vasculitis	0	3 (33.3)	0.259
Clinical expression			
Cutaneous manifestations			
Location			
Hands	3 (60)	7 (50)	0.701
Feet	1 (20)	2 (14.3)	0.764
Hands and feet	1 (20)	5 (35.7)	0.516
Clinical pattern, n (%)			
Purpuric macules	4 (80)	6 (42.9)	0.153
Raynaud	2 (40)	3 (31.4)	0.418
Distal ulceration	1 (20)	6 (42.9)	0.363
Others	1 (20)	2 (14.3)	0.764
General symptoms, n (%)	1 (20)	1 (7)	0.383
Gastrointestinal symptoms, n (%)	1 (20)	3 (21.4)	0.659
Rheumatologycal symtoms, n (%)	2 (40)	2 (14.3)	0.486
Treatment, n (%)			
Antiaggregant treatment	4 (80)	4 (28.6)	0.131
Corticosteroid treatment	3 (60)	4 (28.6)	0.577
Other treatments	3 (60)	4 (28.6)	NA



CF: Cryofibrinogenemia.

Figure 1. (A) Number of cases of essential CF vs secondary CF in preCOVID and COVID era. **(B)** Proportion of positive cryofibrinogen in both eras.*CF: Cryofibrinogenemia.*

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Disclosure of Interests: Carmen Lasa: None declared, Maria Enriqueta Peiró Callizo: None declared, Juan Irure-Ventura: None declared, Marcos Lopez-Hoyos: None declared, Mónica Renuncio García: None declared, Adrián Martínez Gutiérrez: None declared, Carmen Secada-Gómez: None declared, Amparo Sanchez-López: None declared, Ricardo Blanco Speakers bureau: Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, lilly, Bristol-Myers, Janssen, Galapagos and MSD, Consultant of: Abbvie, Pfizer, Roche, lilly, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD, novartis and Roche.

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AB1341

COVID-19 IN PATIENTS WITH RHEUMATIC IMMUNE-MEDIATED INFLAMMATORY DISEASES IN AMERICA: DIFFERENCES AND SIMILARITIES BETWEEN MEXICO AND ARGENTINA

Keywords: COVID, Registries, Real-world evidence

C. A. Isnardi[1,2], D. Alpizar-Rodriguez[3], M. U. Martínez-Martínez[3], R. Quintana[1,2], I. E. Petkovic[2], S. Ornella[2], V. V. Castro Coello[2], E. Velozo[2], D. Zelaya[2], M. Severina[2], A. K. Cogo[2], R. Nieto[2], D. A. Pereira[2], I. J. Colunga-Pedraza[3], F. Irazoque-Palazuelos[3], G. C. Reyes Cordero[3], T. S. Rodriguez-Reyne[3], J. A. Veloz Aranda[3], C. M. Skinner Taylor[3], I. M. Juarez Mora[3], B. E. Zazueta Montiel[3], A. Martínez[3], C. F. Pacheco Tena[3], G. Pons-Estel[1,2]. [1]*Argentina Society of Rheumatology, Research Unit, Buenos Aires, Argentina*; [2]*Argentina Society of Rheumatology, SAR-COVID Registry, Buenos Aires, Argentina*; [3]*Colegio Mexicano de Reumatologia, Mexican Study Group of COVID-19 in Rheumatic Diseases, Ciudad de México, Mexico*

Background: Patients with immune-mediated rheumatic diseases (IRD) have poorer outcomes of SARS-CoV-2 infection compared to the general population.

Objectives: To assess and compare clinical course, severity and complications of SARS-CoV-2 infection in patients with rheumatic immune-mediated inflammatory diseases (IMIDs) from Mexico and Argentina.

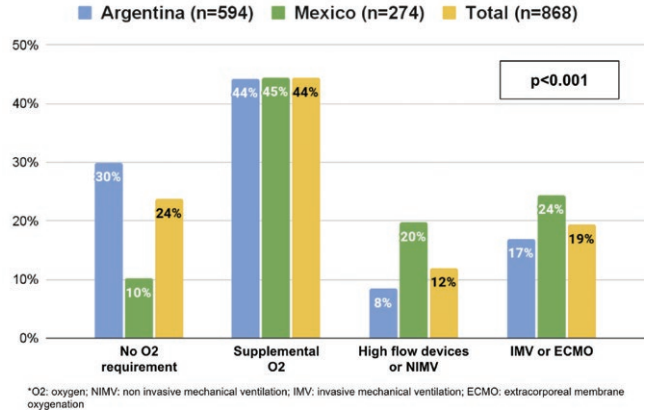
Methods: Data from both national registries, CMR-COVID (Mexico) and SAR-COVID (Argentina), were combined. Briefly, adult IRD patients with SARS-CoV-2 infection were recruited between 08.2020 and 09.2022 in SAR-COVID

and between 04.2020 and 06.2022 in CMR-COVID. Sociodemographic data, comorbidities, and DMARDs were recorded, as well as clinical characteristics, complications, and treatment for SARS-CoV-2 infection. Descriptive analysis. Chi square, Fisher, Student T, Mann Whitney U tests and multiple logistic regression analyses were performed.

Results: A total of 3709 patients were included, 1167 (31.5%) from the CMR-COVID registry and 2542 (68.5%) from the SAR-COVID registry. The majority (82.3%) were women, with a mean age of 50.4 years (SD 14.4). The most frequent IRD were rheumatoid arthritis (47.5%) and systemic lupus erythematosus (18.9%). Mexican patients were significantly older, had a higher female predominance and had higher prevalence of rheumatoid arthritis, antiphospholipid syndrome, and axial spondyloarthritis, while the Argentine patients had more frequently psoriatic arthritis and ANCA-associated vasculitis. In both cohorts, approximately 80% were in remission or low disease activity at the time of infection. Mexicans took glucocorticoids (43% vs 37%, p<0.001) and rituximab (6% vs 3%, p<0.001) more frequently. They also reported more comorbidities (48% vs 43%, p=0.012). More than 90% of patients presented symptoms related to SARS-CoV-2 infection. The frequency of hospitalization was comparable between the groups (23.4%), however, the Mexicans had more severe disease (Figure 1) and a higher mortality rate (9.4% vs 4.0%, p<0.0001). After adjusting for risk factors, Mexicans were more likely to die due to COVID-19 (OR 2.2, 95%CI 1.5-3.1).

Conclusion: In this cohort of patients with IRD from Mexico and Argentina with SARS-CoV-2 infection, the majority presented symptoms, a quarter were hospitalized and 6% died due to COVID-19. Mexicans presented more severe disease, and after considering risk factors they were two times more likely to die.

Figure 1. Oxygen requirements in hospitalized patients



*O2: oxygen; NIMV: non invasive mechanical ventilation; IMV: invasive mechanical ventilation; ECMO: extracorporeal membrane oxygenation

REFERENCES: NIL.

Acknowledgements: NIL.

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AB1342 THE EMERGENCE OF FIBROMYALGIA FOLLOWING ACUTE COVID-19 INFECTION

Keywords: Pain, COVID, Fibromyalgia

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Background: The exact pathogenesis of fibromyalgia (FM) syndrome is unclear. However, different infections including hepatitis C virus, Human immunodeficiency virus and Lyme disease have already been implicated with the development of FM after their acute phase[1]. Imbalance between pro-inflammatory and anti-inflammatory cytokines has been suggested as a possible mechanism that facilitates the neuropathic pain[2].

Objectives: To investigate the incidence of FM syndrome among convalesced individuals following hospitalization for Acute Coronavirus Disease-2019 (COVID-19) and to identify possible risk factors.

Methods: We performed a cross-sectional study on patients who were discharged after COVID-19 hospitalization from the Sheba Medical Center, Israel, between July 2020 to November 2020. A phone interview was performed consisting of the following questionnaires: the Fibromyalgia Survey Diagnostic Criteria Questionnaire, Sense of Coherence Questionnaire to evaluate resilience, and the Subjective Traumatic Outlook Questionnaire to assess the associated psychological aspects of the trauma. The incidence of post-COVID FM was calculated and regression models were performed to identify predictors.

Results: The study population consisted of 198 eligible patients who completed the phone interview. The median age was 64 (52-72) and 37% were women. The median follow-up was 5.2 months (IQR 4.4-5.8). The incidence of FM was 15% (30 patients) and 87% (172 patients) had at least one FM-related symptom. Female gender was significantly associated with post-COVID FM (OR 3.65, p=0.002). In addition, high median Subjective Traumatic Outlook scores and low median Sense of Coherence scores were both significantly associated with post-COVID FM (OR 1.19, p<0.001 and OR 0.92, p<0.001, respectively).

Conclusion: FM is highly prevalent among COVID-19 convalescent patients. Our finding suggests that a significant subjective traumatic experience and a low resilience are highly associated with post-COVID FM.

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Disclosure of Interests: None Declared.

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AB1343 PERSISTENCE OF SYMPTOMS AFTER SARS-COV-2 INFECTION IN PATIENTS WITH INFLAMMATORY ARTHRITIS: A RETROSPECTIVE STUDY

Keywords: Spondyloarthritis, COVID, Rheumatoid arthritis

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Background: The World Health Organization defined long-COVID or post-COVID-19 condition as "the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation" [1]. Data on long-COVID in patients with inflammatory arthritis are very limited. The prevalence of this condition is 45% in the general population affected by COVID-19 who still experience symptoms after 4 months from the infection [2].

Objectives: To investigate the persistence of symptoms after SARS-CoV-2 infection in a cohort of patients with inflammatory arthritis and the most common clinical manifestations.

Methods: We enrolled adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) classified according to standard criteria that received a diagnosis of COVID-19 through molecular, rapid or quantitative antigen swab tests between September 2020 and September 2022. Demographic and clinical data including age, body mass index (BMI), smoking habit, comorbidities, rheumatic treatment at diagnosis of COVID-19, date of COVID-19 diagnosis and clinical manifestations were collected through a questionnaire and recorded in a database.

Results: Thirty-eight (40%) patients with RA, 49 (51.6%) with PsA, and 8 (8.4%) with AS [total: 95 patients; F:M=65:30, median age 56 years (IQR

15), median BMI 25.54 kg/m^2 (IQR 5.58), active smokers 21 (22.1%), median rheumatic disease duration 96 months (IQR 120), median COVID-19 duration 13 days (IQR 7)] were recruited. Eighteen (19%) were only treated with csDMARDs, 38 (40%) only with bDMARDs, 29 (30.5%) with csDMARDs and bDMARDs, 8 (8.4%) were not taking any treatment and 2 (1%) were only taking glucocorticoids. Six (6.3%) patients were hospitalized (either in Day Hospital facilities for monoclonal antibodies infusion or in the emergency room). Twenty-six (27.3%) and 7 (7.3%) patients reported pre-existing cardiovascular or respiratory comorbidities, respectively. Ninety patients (94.7%) had a symptomatic SARS-CoV-2 infection. Seventy-five (79%) patients reported the persistence of symptoms after the end of the infection (negative swab), while 20 (21%) patients reported no symptoms. Among the former, 38 (50.7%) patients were symptomatic for ≤3 months and 37 (49.3%) were symptomatic for >3 months. In the hospitalized subgroup, 6 (100%) patients reported the persistence of COVID-19 symptoms, while this was reported by 69 (77.5%) patients in the non-hospitalized subgroup (p=ns). The clinical manifestations and their persistence after the infection are reported inFigure 1. The most common were cough and fatigue, which both lasted ≤3 months in 38 (42.2%) patients and >3 months in 3 (3.33%) and 21 (23.3%) patients, respectively. Headache (32 patients - 35.5%), arthralgias (28 patients - 31.1%), myalgias (27 patients - 30%) and shortness of breath (25 patients - 27.7%) were the most common symptoms that persisted in the first 3 months after the infection. Symptoms that persisted for >3 months in more than 20% of the patients were arthralgias (24 patients - 26.6%) and sleep disturbances (19 patients - 21.1%). However, it is difficult to assess whether arthralgias and myalgias were consequences of COVID-19 or secondary to the rheumatic disease. No COVID-19-related deaths were recorded.

Conclusion: Our data show the persistence of symptoms of COVID-19 after recovery in 79% of patients with chronic inflammatory arthritis. 49.3% of patients were symptomatic for >3 months. Cough, fatigue, headache, arthralgias, myalgias and shortness of breath were the most represented symptoms in the first 3 months after the infection, while arthralgias, fatigue, and sleep disturbances were the most reported after 3 months from SARS-CoV-2 infection.

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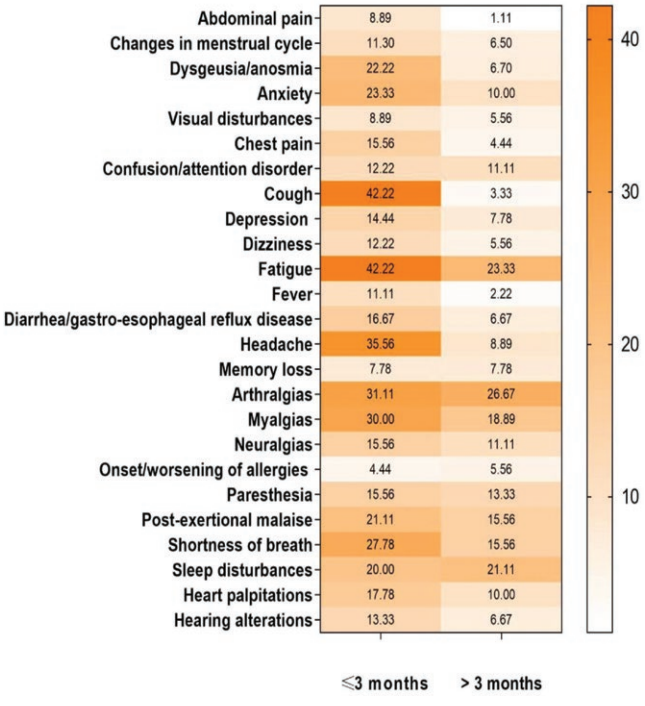


Figure 1. Persistence of symptoms and signs after the end of SARS-CoV-2 infection. Data are represented as percentages

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1344

DO PATIENTS ON SUPPRESSIVE THERAPY HAVE A DECREASED HUMORAL RESPONSE TO SARS-COV2 VACCINATION?

Keywords: bDMARD, Vaccination/immunization, COVID

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Background: SARS-Cov2 vaccination has been shown to be effective against severe forms of SARS-Cov2 infection. Several studies investigated the humoral and cellular response to SARS-Cov2 vaccines in patients followed for autoimmune and inflammatory diseases under immunosuppressive or immunomodulatory treatments. It has been shown that patients on immunosuppressive or immunomodulatory therapies have a poor humoral response to the vaccine[1]

Objectives: The aim of our study was to investigate the humoral response in patients under conventional immunosuppressive and biotherapies compared to healthy controls.

Methods: Patients followed for immuno-inflammatory diseases under immunosuppressive or immunomodulatory drugs who received at least one dose of anti-SARS-Cov2 vaccines were included. Quantitative Anti- SARS-Cov2 antibodies (IgM and IgG assay) VIDAS ® were assessed for all patients. Patients were then compared with healthy controls.

Results: We enrolled 93 blood samples (63 patients with autoimmune and inflammatory disease and 30 healthy controls), the median age was 52 years [Q1 43, Q3 56]. The immuno-inflammatory diseases were: Crohn's disease (n=28), Rheumatoid arthritis (n=9), Hemorrhagic rectocolitis (n=5), Behçet's disease (n=5), Systemic lupus erythematosus (n=4), Sjogren's syndrome (n=3), Sarcoidosis (n=2), Takayasu disease (n=1). All patients continued their treatment during and after vaccination. Nineteen patients were on biotherapies: Infliximab (n=12), Adalimumab (n=3), etanercept (n=2), Ustekinumab (n=1), tocilizimab (n=1). Forty-three patients were on conventional immunosuppressive: azathioprine (n=18), methotrexate (n=16), corticosteroids > 10 mg/d (n=12). All patients had received at least one dose of vaccine: the median number of doses in both groups was 2[1-4] with no statistically significant difference between the 2 groups (p=0.2). The vaccines received in the group of patients were mRNA vaccine (n=35) and other type of vaccine (n=28). In the healthy control group, type of vaccine were mRNA (n=13) other type vaccine (n=17). The patient had a lower mean level of Ig G against SARS-Cov2 antibodies (24.64 IU +/- 16.65) comparing to healthy controls (33.05+/-10) with statically significant difference (p= 0.014). No difference between the 2 groups was noted in Ig G levels according to the history of SARS-Cov2 infection. No difference was found between conventional immunosuppressive drugs and biotherapies regarding to the level of antibodies.

Conclusion: Our study highlights that patients with autoimmune disease and under immunosuppressive therapy displayed a decrease of humoral response comparing to healthy controls. This finding was reported in several studies, Geisen et al[2] reported that patients with chronic inflammatory condition and receiving TNF alfa blockers had a decreased protection and a low level Ig A against spike. Based on these data, patients with autoimmune and inflammatory diseases have decreased humoral immunity to SARS-Cov2 and should be encouraged to receive a booster dose of SARS-COv2 vaccine.

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AB1345

COVID-19 AND ADVERSE MENTAL HEALTH OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Mental health, COVID

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Background: The COVID-19 outbreak is known to increase the fear level of most patients with chronic diseases. Patients with rheumatoid arthritis (RA) are very vulnerable to environmental stress. During this pandemic, the psychological pressure may be further increased due to the perplexing nature of information about the risk of infection in RA patients.
Objectives: The objective of this study was to determine the impact of the COVID-19 pandemic on the mental health of RA patients and to investigate associated factors.
Methods: This is a cross-sectional study of 190 patients with RA who met the ACR/EULAR 2010 criteria. For each patient, we collected sociodemographic, clinical, and biological data. Depression and anxiety were assessed by the Hospital Anxiety and Depression scale (HADs) and disease activity by the DAS-28 score.
Results: The average age of our patients was 55 years with a female predominance (86.3%). The average duration of the disease was 8 years. The mean DAS 28 score was 4.1 ±1.03. The disease was deforming in 52.9% of cases. All of us patients were on disease-modifying therapy, 87.1% were on methotrexate and 12.9% were on biotherapy. Sixty patients (31.57%) had contracted SARS-CoV-2. During the pandemic, depression was present in 38.4% of patients. It was mild in 33.1% of cases, moderate in 4.1%, and severe in 1.2% with a mean HADs depression score of 4.4 ± 3.1. This score was significantly higher in patients with a history of SARS-COV-2 infection in a family member (p=0,002), comorbidities (p<0.001), joint deformities (p=0.008), and high disease activity (p<0.001). Anxiety was present in 55.6% of patients. It was mild in 32.6% of cases, moderate in 20.6%, and severe in 2.4% of cases with a mean HADs anxiety of 6.4 ± 3.9. The presence of anxiety was correlated with fear of COVID-19, higher disease activity, the presence of comorbidities, and the presence of deformities (p<0.001 for all cases). This score was also significantly higher in the illiterate (p<0.001) and unemployed patients (p=0.001).
Conclusion: In our study, depression and anxiety were frequent in RA patients during the COVID-19 pandemic. These psychological disorders were more common in patients with active and disabling RA associated with comorbidities. As the pandemic continues, more patients are susceptible to experience anxiety and depression. Therefore, rheumatologists must remain vigilant to these psychological alterations and provide the necessary support.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1346 ASSOCIATION OF URIC ACID LEVELS WITH COVID-19 SEVERITY DURING 2020 AND 2021 YEARS

Keywords: Prognostic factors, COVID, Lungs

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Background: The decrease in uric acid levels attracts more and more attention from clinicians every year [1]. In particular, a factor such as Covid-19 can cause a significant decrease in uric acid due to its increased excretion by the kidneys [2]. This retrospective study aimed to determine changes in the level of uric acid in different years, which allows us to assume the influence of different strains of Covid-19 on uric acid.
Objectives: To analyze the relationship between uric acid levels through admission to the hospital and Covid-19 severity during 2020 and 2021 years.
Methods: Our retrospective study includes 127 hospitalized patients with confirmed Covid-19 in 2021 and 63 patients in 2020 (only patients who didn't receive urate-lowering therapy). Most patients were over 45 years old (84,2% vs 90,5%), women and men almost equally. The severity of Covid-19 we determined by the type and presence of oxygen support ((1) without O2, (2) O2 by mask or nasal cannula, (3) continuous positive airway pressure, (4) positive bi-pressure in the airways or high-flow oxygen, (5) invasive ventilation). A chi-squared test and comparison of means were used.
Results: We cannot establish the dependence of the uric acid level on the severity of the course of the Covid-19 disease, which is determined by the type of oxygen support in both 2020 and 2021. For example, in 2021, the difference between the least severe type (without O2) and the most severe (invasive ventilation) was almost the same (246.2 vs 277.12 μmol/L), as between O2 by mask or nasal cannula and positive bi-pressure in the airways or high-flow oxygen (257 vs 239.1 μmol/L). However, it was established that in 2020, higher indicators of the level of uric acid were observed for all types of oxygen support. For example, for patients who were without O2, it is higher by 72.95 μmol/L, which is statistically significant. In addition, we analyzed the dependence of the uric acid level on such indicators as the patient's age, the level of lymphocytes, C-reactive protein, and LDH at admission to the hospital. As a result of the analysis, it was found that the dependence is present for the LDH indicator (the lower the LDH, the higher the uric acid: chi-square at the level of 0.05), and for all other indicators, it was absent in 2021. In 2020, a positive relationship between CRP, LDH, and uric acid levels was also observed.
Conclusion: Although there is a trend towards lower uric acid levels in the background of Covid-19, it is not a marker of a severe disease course. The lower uric acid levels in 2021 are likely due to a feature of the strains circulating in 2021 that caused more significant renal excretion of uric acid.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5749

AB1347 LABORATORY PARAMETERS ASSOCIATED WITH CODIV-19 CYTOKINE STORM DEVELOPMENT

Keywords: COVID, Prognostic factors

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Background: Since the end of 2019, physicians became more and more familiar with SARS-CoV-2 infection and the variety of forms in which it may present and evolve. There have been a lot of studies trying to understand and predict why some patients develop a dysregulation of the immune response, with an exaggerated release of pro-inflammatory cytokines, called cytokine storm (1–4). There is scarce evidence in Romania regarding this aspect.
Objectives: This study aims to verify the correlation between some laboratory parameters and the development of cytokine storm in SARS-CoV-2 infection in a cohort of over 200 patients admitted in a tertiary hospital from Romania, hoping that early identification of these risk factors of progression to a severe form of the disease can bring considerable benefit to patient care.
Methods: This is an analytical, observational, case-control study which includes 219 patients (all COVID-19 hospitalized patients on the Internal Medicine 3 department of Colentina Clinical Hospital, Bucharest, from 01 March 2020 to 1 April 2021). A series of data were collected, the laboratory parameters being the most important, including: albumin, lymphocyte (percentage), neutrophil (absolute value), aspartate aminotransferase, alanine aminotransferase, D-dimers, lactate dehydrogenase (LDH), anionic gap, chloremia, potassium and the BUN:creatinine ratio (BUN - blood urea nitrogen). The laboratory parameters used for the statistical analysis represent the average values of the first 7 days of hospitalization for those who did not develop cytokine storm, respectively until the day of its development, for the others. Patients were classified into these groups, those who developed cytokine storm, respectively those who did not have this complication taking into account the clinical and paraclinical criteria (impairment of respiratory function, elevations of certain markers 2-3 times above the upper limit of normal, those who died as a result of SARS-CoV-2 infection). Then Binary Univariate Logistic Regression was applied in order to verify the individual impact of every laboratory parameter on cytokine storm development. Furthermore, all laboratory parameters were subsequently included in the multivariate analysis, using the backward selection technique to achieve a model as predictive as possible.
Results: We mention that the analysis of demographic data was previously performed, showing no statistically significant relationship between patient gender, age or comorbidities (history of neoplasm, lung diseases, cardiac pathology, obesity, type II diabetes and hypertension) and their evolution to cytokine storm. After performing binary univariate logistic regression we concluded that 8 of the 13 laboratory analyzes have had a significant change between groups (ferritin, PCR, albumin, Lymphocyte, Neutrophils, TGO, LDH, BUN:creatinine ratio). Only 150 patients were then included in the multivariate analysis. After the analysis, some of the variables lost their statistical significance, the final model including C-reactive protein, neutrophilia, LDH, ferritin and the BUN:creatinine ratio. This model correctly predicts the development of cytokine storm in 88% of cases.
Conclusion: High C-reactive protein, neutrophilia, LDH, ferritin and the BUN:creatinine ratio are risk factors for cytokine storm development and should be monitored in all COVID-19 patients in order to predict their evolution.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6265

AB1348 PERICARDITIS AFTER COVID-19 VACCINATION: A CASE SERIES

Keywords: Heart, COVID, Vaccination/immunization

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Background: COVID-19 vaccination campaigns successfully impacted on viral spreading and in particular on clinical course of the disease. However, secondary to a highly extended vaccination program, several local and systemic adverse events associated with mRNA COVID-19 vaccines have been reported. Pericarditis and myocarditis are examples of cardiac complications related to these vaccines. In particular, cases of pericarditis have occurred after mRNA COVID-19 vaccination (mostly secondary to vaccination with Moderna than Pfizer-BioNTech), especially in male adolescents and young adults, more often after the second dose. The incidence is approximately of 1-2 cases/100.000.
Objectives: Aim of our study was to study the clinical profile of pericarditis occurred within 30 days after COVID-19 vaccines in our clinic.
Methods: We present a case series of patients who developed pericarditis after COVID-19 vaccination in the Department of Internal Medicine at Fatebenefratelli Hospital in Milan, followed from December 1, 2021 to April 15, 2022.
Results: Twenty-five individuals, of which 18 (72%) were women and 7 (28%) were males, had vaccine related pericarditis. Two patients were vaccinated with AstraZeneca, 2 with Moderna, the remaining with Pfizer-BioNTech. Median age was of 42 years. Of all patients, one subject was affected by constrictive effusive pericarditis, while another required treatment of pericarditis with Anakinra, switched to Canakinumab after severe skin reactions, because of failure of therapeutic response to first-line treatments. Two patients required hospital admission, in one case for a transient constrictive pericarditis. In the remaining cases clinical symptoms associated with post-vaccines pericarditis were mild and didn't require hospitalization. Chest pain was reported in 100% of cases, whereas pericardial effusion (in one case larger than 10 mm) was evidenced in 30% of subjects. Eighty percent of patients experienced tachycardia, whereas 90% reported asthenia. An increase in indices of inflammation (CRP) was documented in 50% of patients, usually mild. With regard to therapy, 90% of patients were treated with NSAIDs, 95% with colchicine, while 50% of cases required treatment with low-dose steroids.
Conclusion: COVID-19 vaccination induces a particular form of pericarditis, often insidious and very troublesome, but with good prognosis. The clinical phenotype showed less typical chest pain, often normal indices of inflammation and little or no instrumental changes, but patients often experimented tachycardia and functional limitation. With regard to therapy, we used NSAIDs at adequate dosages to control the clinical condition, or low-dose colchicine. Low doses of cortisone (e.g., prednisone 5-10 mg a day) were useful in the presence of marked asthenia or systemic symptoms. Beta-blockers or ivabradine were used in the presence of tachycardia.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6408

AB1349 D-DIMER AND FIBRINOGEN TRENDS IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES INFECTED WITH SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2: A RETROSPECTIVE COMPARATIVE STUDY

Keywords: COVID, Infection-related RMDs, Biomarkers

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Background: D-dimer and fibrinogen elevation has been observed in severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infection which is associated with higher incidence of venous thromboembolism (VTE) and higher mortality rates. [1-3]. Autoimmune Rheumatic Diseases (ARDs) are associated with higher rates of VTE compared to general population [4]. Whether patients with ARDs infected with SARS-CoV2 have similar D-dimer and fibrinogen trends compared to patients without ARDs is unknown.
Objectives: Compare D-dimer and fibrinogen levels in patients with ARDs infected with SARS-CoV2 to patients without ARDs.
Methods: Patients with ARDs infected with SARS-CoV2 were identified retrospectively from the electronic medical records (EMR) of Hamad Medical Corporation and matched (age and sex) to controls (1:3). D-dimer and fibrinogen levels were extracted electronically from EMR and stratified into six-time intervals defined in table 1. Day 0 was defined as the date of positive nasopharyngeal polymerase chain reaction swab test. 2 Independent Samples test (Mann-Whitney U) was used to compare the median (25th - 75th interquartile range [IQR]) level of D-dimer and fibrinogen between both study groups at the defined intervals.
Results: The study included 203 cases and 551 controls with a mean (SD) age of 45.3 (11.7) and 44 (12.5) years, females were (122 [60.1%] vs. 297 [53.9%], p = 0.129), respectively. Distribution of ARDs was rheumatoid arthritis 86 (42.4%), spondyloarthropathy 33 (16.1%) and systemic lupus erythematosus 31 (15.7%) cases. 67% were on conventional synthetic disease modifying anti-rheumatic drugs (Cs-DMARDs), 15.8% on biological DMARDs and 4.9% on rituximab. About 83% of the ARDs group were in remission or low disease activity and 13% were in moderate or high disease activity. The median (25^{th} - 75^{th} IQR) level of D-dimer and fibrinogen were comparable between study groups in all defined intervals with insignificant p values except at interval 4, fibrinogen was significantly higher in the cases, p 0.006. Table 1
Conclusion: There was no significant difference in the trend of D-dimer and fibrinogen levels during SARS-CoV2 infection between patients with ARDs and those without ARDs. Additional studies are needed to quantify the actual risk of VTE in patients with ARDs during SARS-CoV2 in correlation with serum markers of VTE.
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Table 1. Differences in D-dimer and fibrinogen during SARS-CoV2 infection between patients with ARDs and those without at the defined intervals.

	Case N = 203	Control N = 551	P value
Median (25th - 75th IQR), D-dimer (mg/L)			
(0 to < 3 days)	0.56 (0.34 – 1.31)	0.86 (0.54 – 1.41)	0.096
(≤ 3 to < 6 days)	0.67 (0.35 – 2.58)	1.11 (0.44 – 1.11)	0.340
(≤ 6 to < 9 days)	0.81 (0.33 – 5.12)	1.12 (0.56 – 3.28)	0.299
(≤ 9 to 12 days)	0.94 (0.72 – 5.44)	5.20 (1.0 – 15.05)	0.058
(≤ 12 to < 15 days)	2.88 (0.72 – 5.53)	4.96 (0.57 – 9.98)	0.681
(≤ 15 to 18 days)	1.81 (0.89 – 2.55)	5.56 (2.60 – 15.1)	0.086
Median (25th – 75th IQR), fibrinogen (mg/L)			
(0 to < 3 days)	6.53 (2.0 - 6.53)	5.65 (3.75 – 7.17)	1.000
(≤ 3 to < 6 days)	6.25 (3.72 – 8.3)	4.6 (4.1 – 5.6)	0.385
(≤ 6 to < 9 days)	3.53 (3.29 – 4.62)	3.4 (3.2 – 3.92)	0.328
(≤ 9 to 12 days)	4.3 (2.82 – 4.78)	2.2 (1.65 – 3.05)	0.006
(≤ 12 to < 15 days)	4.4 (2.37 – 5.13)	3.1 (1.7 – 4.45)	0.170
(≤ 15 to 18 days)	3.6 (3 – 5.7)	3.7 (2.0 – 4.88)	0.524

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1350 THE KINETICS OF HUMORAL AND CELLULAR RESPONSES AFTER THE BOOSTER DOSE OF COVID-19 VACCINE IN INFLAMMATORY ARTHRITIS PATIENTS

Keywords: COVID, Vaccination/immunization

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Background: Impaired immunogenicity of COVID-19 vaccinations in inflammatory arthritis (IA) patients results in diminished immunity. However, optimal booster vaccination regimens are still unknown, due to unstudied kinetics of the immune response after booster vaccinations.
Objectives: This study aimed to assess the kinetics of humoral and cellular responses in IA patients after the COVID-19 booster.
Methods: In 29 IA patients and 16 healthy controls (HC) humoral responses (level of IgG antibodies) and cellular responses (IFN-γ production) were assessed before (T0), after 4 weeks (T1), and after more than 6 months (T2) from the booster vaccination with BNT162b2.
Results: IA patients, but not HC, showed lower anti-S-IgG concentration and IGRA fold change at T2 compared to T1 (p=0.026 and p=0.031). Furthermore, in IA patients the level of cellular response at T2 returned to the pre-booster level (T0). All immunomodulatory drugs, except IL-6 and IL-17 inhibitors for the humoral and IL-17 inhibitors for the cellular response, impaired the immunogenicity of the booster dose at T2. However, none of the immunomodulatory drugs affected the kinetics of both humoral and cellular responses (measured as the difference between response rates at T1 and T2).
Conclusion: Our study showed impaired kinetics of both humoral and cellular responses after the booster dose of the COVID-19 vaccine in IA patients, which, in the case of cellular response, did not allow the vaccination effect to be maintained for more than 6 months. Repetitive vaccination with subsequent booster doses seems to be necessary for IA patients.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1511

AB1351 FREQUENCY OF VACCINE-RELATED ADVERSE EVENTS IN PATIENTS WITH RHEUMATIC DISEASE

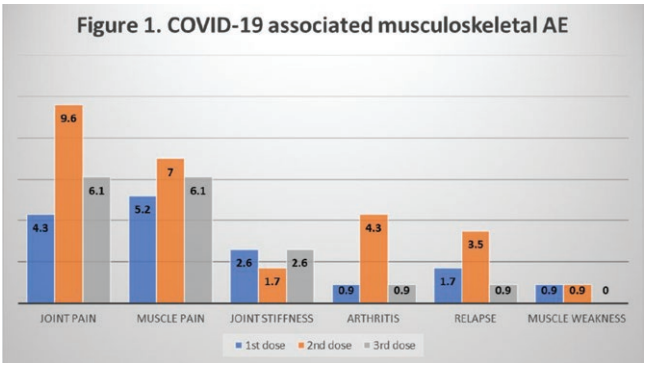
Keywords: COVID, Rheumatoid arthritis, Vaccination/immunization

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Background: Patients with rheumatic diseases are at greater risk of developing serious infections due to dysregulation of the immune system and the use of immunosuppressants1. Therefore, preventing infection is crucial, with vaccination being the most important primary prevention intervention, leading to a lower rate of hospital admissions due to infections. However, vaccine hesitancy among persons with rheumatic diseases is widespread due to concerns regarding the safety of vaccines2.
Objectives: Describe the frequency of adverse events associated with vaccination in patients with rheumatic diseases.
Methods: Observational, descriptive, cross-sectional and retrospective study was carried out in patients with rheumatic diseases from the Rheumatology Department of the Hospital Regional 1° de Octubre ISSSTE, from February to May 2022; it included patients over 18 years of age with an established diagnosis of rheumatic disease who had received a vaccine; the researcher applied the vaccine-associated adverse events survey to those patients who agreed to participate by signing the informed consent. The sample size was of 95 patients. Descriptive statistics and summary measures were employed for analysis. We used the chi-square test or Fisher's exact test (when <5) for the comparative analysis of the frequencies of nominal qualitative variables. P<0.05 was considered significant.
Results: The survey was applied to 115 patients. 85.2% were women; mean age 57.9 years; 61.7% had rheumatoid arthritis (RA), followed by systemic lupus erythematosus (SLE) in 13.9%. 55.6% of the patients were treated with steroids, 52.2% received bDMARDs and 48.7% csDMARDs. Patients received various vaccines, of which the most frequent was the one for COVID-19, with 99.1% of included patients having received at least one dose, followed by influenza in 30.4%. 78% of the patients who received at least one dose of a vaccine against COVID-19 presented ≥1 adverse events. The disease in which the highest frequency of adverse events occurred was RA, without this difference being statistically significant (Table 1). The adverse events according to the type of COVID-19 vaccine were the following: Sputnik-V 80%, Pfizer 76.6% and AstraZeneca 76.1%, without statistically significant difference between vaccine types. The most frequently occurring adverse events were injection site pain (80.1%), headache (30.7%), and fatigue (30.7%); In addition, the main vaccine-associated musculoskeletal symptoms were joint pain, myalgia, and morning joint stiffness (Figure 1), which on most cases improved after a NSAID use. Joint pain was more frequent after the second dose of certain vaccine types.

Table 1. Frequency of AE after COVID-19 vaccination in patients according to disease.

	AE (%)	p
RA	56	0.790
SLE	14	0.326
Spondyloarthritis	4	0.068
Osteoarthritis	6	0.614



Conclusion: Vaccination-associated AE occurred more frequently than reported in international studies; however, they were not more serious. Providing this information to patients is important to improve vaccine acceptance. In addition, the administration of NSAID after the application of the vaccine could be proposed to reduce the presence of side effects.
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Disclosure of Interests: Daniel Xavier Xibille Friedmann Speakers bureau: GSK, Lilly, UCB, Paid instructor for: GSK, Lilly, UCB, Consultant of: GSK, Lilly, UCB, Vanessa Balderas Reyes: None declared, María Olvera: None declared, María Alcocer León: None declared, ALFREDO ALEXANDRI REYES SALINAS Paid instructor for: Abbvie, Janssen, Novartis, Minerva Rodríguez Falcón: None

declared, Sandra Miriam Carrillo Vazquez Speakers bureau: Abbvie, Janssen, UCB, Paid instructor for: Abbvie, Janssen, UCB, Consultant of: Abbvie, Janssen, UCB.

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AB1352 IMPACT OF SYSTEMIC THERAPIES ON THE SEROPREVALENCE OF SARS-COV-2 IN PATIENTS WITH IMMUNE-MEDIATED DISEASES

Keywords: COVID, bDMARD, Disease-modifying drugs (DMARDs)

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Background: The disease modifying antirheumatic drugs (DMARD) impair the immune response of patients with immune-mediated inflammatory diseases (IMID).

Objectives: To analyze the seroprevalence of SARS-CoV-2 in patients with IMID treated with biological disease modifying antirheumatic drugs (bDMARD) or targeted synthetic (tsDMARD).

Methods: An ambispective cross-sectional study was performed in patients with IMID treated with bDMARD or tsDMARD. Seroprevalence was compared by measuring IgG against SARS-CoV-2 between October 2020 and May 2021.

Results: A total of 550 patients with IMID were studied, all of them on bDMARD or tsDMARD therapy, none of them vaccinated at that time against SARS-CoV-2. Patients receiving anti-TNFα therapy had a higher seroprevalence than other biologic and synthetic targeted therapies (OR= 1.792; 95% CI 1.088-2.951; p= 0.021). Patients with bDMARD or tsDMARD treated concomitantly with some type of conventional synthetic DMARD (csDMARD) presented a lower seroprevalence compared to patients treated in monotherapy, 10.7 vs. 19.9% (p= 0.003). When analyzing the treatments with the different csDMARD separately (methotrexate, leflunomide, sulfasalazine, azathioprine, hydroxychloroquine and the others), methotrexate was determined to influence in a lower seroprevalence, compared to those who did not receive any csDMARD, 9.8 vs 19.9% (OR= 0.439, 95% CI 0.232-0.828; p= 0.011). When evaluating the influence of methotrexate on seroprevalence among the different groups of bDMARD or tsDMARD, a lower seroprevalence was demonstrated in the group of patients receiving anti-TNFα and methotrexate in combination, versus patients on this bDMARD in monotherapy, 10.1 vs 24.1% (OR= 0.355, 95% CI 0.165 - 0.764; p=0.006). No significant differences were identified with the other bDMARD. Regarding the patients' IMIDs, no differences in seroprevalence were observed when compared by disease groups with each other.

Conclusion: Seroprevalence in the group of patients with IMID is influenced according to the therapy received, being higher in patients receiving anti-TNFα monotherapy, but significantly lower if concomitant to this drug they receive methotrexate. These differences are not seen with the other b/tsDMARD and csDMARD.

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AB1353 RHEUMATOLOGICAL PAIN CONDITIONS ARE NOT RISK FACTORS FOR THE DEVELOPMENT OF WIDESPREAD POST-COVID PAIN IN COVID-19 SURVIVORS

Keywords: COVID, Epidemiology

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Background: Up to 60% of COVID-19 survivors develop long-COVID symptoms[1]. Musculoskeletal pain is also a common (~11%) symptom of long-COVID.[2] Current theories hypothesize that post-COVID pain can be widespread as in other chronic pain conditions. The presence of previous rheumatological diseases could act as a risk factor for the development of persistent widespread post-COVID pain due to a potentiation of pro-inflammatory responses seen during the infection or due to a less robust immune response. A previous pilot study investigated if rheumatological diseases were associated with post-COVID symptoms in a specific population of hospitalised COVID-19 survivors.[3]

Objectives: The aim of this study was to identify if the presence of previous specific rheumatological diseases are risk factors for the development of widespread post-COVID pain in previously hospitalised and non-hospitalised COVID-19 survivors.

Methods: We conducted a nation-wide, cross-sectional exploratory study with a pain-related questionnaire collecting demographics, pre-existing rheumatological conditions and the development of widespread pain symptoms after SARS-CoV-2 infection from a Denmark-based population.

Results: Data from 1.000 randomly previously hospitalised (51.2% males; 60.4±15.2 years; 85.6±18.5kg) and 1.000 randomly previously non-hospitalised COVID-19 survivors (43.5% males; 50.4±15.9 years; 79.2±16.6 kg) were analyzed. Distribution of gender ($p<0.001$), age ($p<0.001$), and weight ($p<0.001$) was different between groups. The presence of widespread pain symptoms six months after infection was higher ($P<0.001$) in hospitalised survivors (20%) as compared to non-hospitalised patients (4.2%). The presence of previous rheumatological conditions such as arthritis, osteoarthritis or joint pain were not associated with the development of widespread post-COVID pain in either group (all, $P>0.1$).

Conclusion: This exploratory study shows that the presence of previous rheumatological conditions before SARS-CoV-2 infection was not a risk factor associated with development of widespread post-COVID pain symptomatology. Other risk factors e.g., female sex or the presence of musculoskeletal pain, could be more relevant for widespread post-COVID pain-related research.[4]

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AB1355 EFFECT OF COVID-19 VACCINES ON ACTIVITY OF AUTOIMMUNE RHEUMATIC DISEASES

Keywords: Vaccination/immunization

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Background: The SARS-CoV-2 pandemic has paralyzed the world, Patients with autoimmune rheumatic diseases (AIRDs) are at high risk for SARS-CoV-2 infection[1]. Worldwide vaccination campaigns, which have increasingly built up immunity in this populations. Studies on the efficacy and safety of the vaccines have shown rapid and strong development of immunity in healthy populations and AIRDs [2].
Objectives: To evaluate COVID-19 vaccination status in patients with autoimmune rheumatic diseases (AIRDs) whether receiving primary and booster vaccination and its relation to disease activity.
Methods: An observational cross section study conducted on a total number of 282 subjects divided into 2 groups: group (I): 179 vaccinated AIRD patients and group (II): 103 non-vaccinated AIRDs patients where Complete COVID-19 vaccination history. Disease activity scores of AIRDs were measured pre to post vaccination.
Results: Most of studied group 63% were vaccinated, Pfizer vaccine was the most common 33%, Asterzinca 19%, Sinpharm/Sinovac 10%, while Moderna was the least the least type of vaccine 1%, Figure 1. Pfizer vaccine 46% was the most common booster type, Asterzinc 39%, Sinopharm/Sinovac 8% and Moderna vaccine 3% and 4% of studied group not received booster vaccination, Figure 2. Most of Rheumatic disease were vaccinated; 46.4% Rheumatoid arthritis 39.7% Systemic Lupus Erythematosus, 5% Bechet's disease 3.9% Ankylosing Spondylitis and 2.8% Vasculitis. In vaccinated group, severity of disease activity was statistically significantly higher in post-vaccination than pre -vaccination, Table 1.
Conclusion: Pfizer vaccine was the most common vaccine in AIRDs.
COVID-19 vaccination may induce flare of disease activity in AIRDs.
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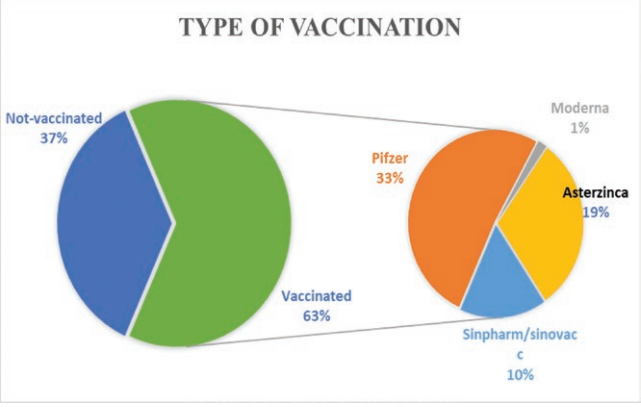


Figure 1. Percentage of status of COVID vaccination and its type.

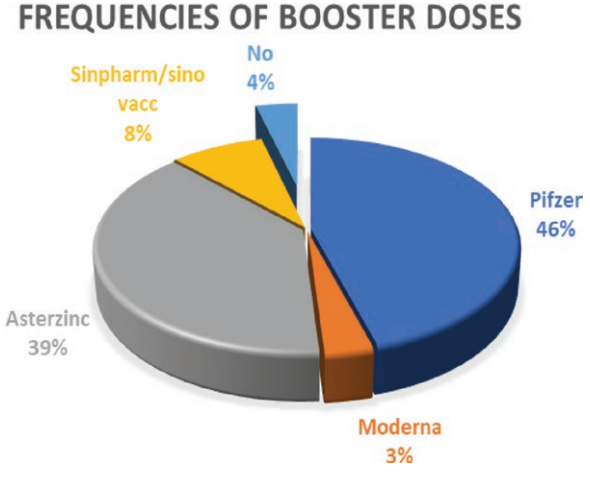


Figure 2. Frequency of booster dose of COVID vaccination.

Table 1. Correlation of disease activity in vaccinated and non-vaccinated group:

		Disease activity index				P*
Vaccination	Severity of disease activity	Pre-vaccination		Post-vaccination		
		n	%	n	%	
yes	mild	29	16.2	3	1.7	< 0.001
	moderate	113	63.1	47	26.3	
	sever	37	20.7	129	72.1	
No	mild	6	5.8	0	0%	1
	moderate	68	66.0	16	76.2	
	sever	29	28.2	5	23.8	

*P value was measured using Wilcoxon signed rank test

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1356

COVID-19 VACCINE PERCEPTION AND HESITANCY AMONG PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASE (AIRD) IN MALAYSIA

Keywords: Vaccination/immunization, COVID, Comorbidities

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Background: Patients with autoimmune rheumatic disease (AIRD) are at risk of severe COVID-19 infection and vaccine has been demonstrated to be able to reduce the severity of infection. Malaysia has a low flu vaccination coverage rate (approximately 3%) and hence it is important to assess the perception and hesitancy of COVID-19 vaccine especially among the vulnerable group.
Objectives: To study the perception of COVID-19 vaccine and to determine the prevalence of vaccine hesitancy among AIRD patients in Malaysia.
Methods: This was a cross-sectional survey using online Google Forms® that was conducted among adult AIRD patients (18 years and older) from August 2021 until February 2022. Patients were recruited from the outpatient clinics as well as distribution of the survey through social medias. The survey was in English and Malay language. The survey collected data on the socio-demographic background, prior history of other vaccination after the age of 18 and COVID-19 vaccination with reasons of hesitancy, defined as being unsure or unwilling to be vaccinated. The survey also assessed the patients' perception by specifying the level of agreement to COVID-19 vaccine statements using the Likert response scale: 1-Strongly disagree; 2- Disagree; 3-Neither agree nor disagree; 4-Agree; 5-Strongly agree.
Results: A total of 162 patients participated in the survey and majority of them were females (87.7%). Our multi-racial cohort consisted of Malay (n=103, 63.5%), followed by Chinese (n=38, 23.5%), Sabahan Bumiputra (n=12, 7.4%) and Indian (n=7, 4.3%). More than half (n=107,66.6%) have not had any history of other vaccination after the age of 18. Only 16.7% (n=27) agreed/strongly agreed that COVID-19 vaccine can be given to patients with co-morbidities and 24.1 (n=39) agreed/strongly agreed that COVID-19 vaccine can be given to patients who have history of allergy to other drugs or food. At the time of the survey, vast majority of the respondents have received at least the 1st dose of Covid-19 vaccine (n=148, 91.4%). A total of 9 (5.6%) patients were hesitant to be vaccinated (6 were unsure and 3 patients were not willing to be vaccinated). The commonest reasons of being unsure or not willing to be vaccinated was worried of the vaccine's adverse effects (66.7%), worried of the blood clot complication (33,3%), worried of disease flare post-vaccine (33,3%), worried of allergic reaction (22.2%), lack of information on the safety of the vaccine in patients with AIRD from government and media (22.2%), face mask and social distancing measures were adequate (22.2%). Statistical analysis revealed that more patients who had vaccine hesitancy were from the lower socioeconomic status (income <1066 Euro/month), 88.9% vs 11.1%, p=0.03 but no association with ethnicity, education status, marital status or place of residence (urban vs rural).
Conclusion: COVID-19 vaccine hesitancy is low in Malaysian patients with AIRD but patients with a low socioeconomic status are prone to have vaccine hesitancy. More education on the vaccine's efficacy and safety especially among patients with co-morbidities are warranted.
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AB1357 RISK OF APS AND APLS POSITIVE PATIENTS FOR THROMBOSIS WITH COVID-19

Keywords: COVID, Autoantibodies, Anti-phospholipid syndrome

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Background: Coagulopathy, thromboembolic events and DIC during COVID-19 infection has been reported. Antiphospholipid antibodies (aPLs), present in 1–5 % of healthy individuals. aPLs are associated with the risk of antiphospholipid syndrome (APS) which is associated with higher risk of thrombosis.

Objectives: We wanted to see if patients with known APS or aPLs only are at higher risk of a thrombotic event compared to control when developed COVID-19. We retrospectively review EMR for over a year for thrombotic events in patients with COVID and prior history of APS or aPLs only and matched them to control.

Methods: Patient characteristics and laboratory testing were summarized according to the following groups: APS, aPLs detected or control. The control were matched according to age and gender for each group. Continuous variable were summarized as median (range) and mean (standard deviation), while categorical variables were reported as frequency (percentage). The binary patient outcome of thrombotic event, hospitalization for COVID, death, and composite event (the combined occurrence of thrombotic events, hospitalization, death) were calculated and interpreted as the multiplicative increase in odds of the given outcome for aPL group compared to control group. Multivariable logistic regression models were adjusted for potential risk factors (immobilization, hypertension, coronary artery disease, diabetes mellitus, and smoking) one at a time due to the rare occurrences of events studied.

Results: In single variable analysis (unadjusted) the odds of the patient having a thrombotic event was approximately 27 times higher in patients with aPL only compared to Controls (P<0.001). We see similar results in multivariable analyses (adjusted) adjusting for the following variables one at a time: immobilization, hypertension, coronary artery disease, diabetes mellitus, and smoking. In each of the multivariable analyses, the adjusted odds of a thrombotic event was between approximately 24 and 29 times higher in patients with aPL Antibody Only compared to Controls (all P<0.001) indicating that association of aPL Antibody Only with thrombotic event was independent of immobilization, hypertension, coronary artery disease, diabetes, and smoking. There was no statistically significant risk of thrombosis in APS group vs control. Majority of patients with APS were on chronic anticoagulation.

Conclusion: We found a statistical significantly difference in patient with aPLs only versus control regarding risk of thrombosis when developed COVID-19. No statistically significant risk was noted in patients with APS. While chronic anticoagulation in APS patients is protective it seemed that patient with aPLs only do carry a high risk of thrombosis if any inciting factors like COVID-19.

Table 1. Patients baseline characteristics

	Patients that did not suspended bDMARD during pandemic (n = 689)	Patients that suspendedp bDMARD during pandemic (n = 143)	
Female gender, n(%)	549 (79.7)	125 (87.4)	0.02
Age, median (IQR)	55 (45 – 63)	52 (42 – 60)	0.04
Body mass index, median (IQR)	26.4 (23 – 30.4)	27.23 (24.2 – 30.46)	0.13
Social security, n(%)	589 (85.5)	128 (89.5)	0.2
Diagnosis			0.7
- Rheumatoid arthritis	444 (64.4)	97 (67.8)	
- Juvenil idiopathic athritis	29 (4.2)	2 (1.4)	
- Ankyosing sponylitis	93 (13.5)	19 (13.3)	
- Psoriasic arthritis	43 (6.2)	6 (4.2)	
- Systemic lupus erithematosus	32 (4.6)	9 (6.3)	
- Others	48 (6.9)	10 (6.9)	
Disease duration, median (IQR)	11 (7 – 19.5)	12 (6 - 18)	0.95
Comorbidities, n(%)	305 (44.3)	73 (51)	0.08
Previos biologic, n(%)	249 (36.1)	60 (42)	0.1
Treatment at pandemic iniciation, n(%)			0.8
- Etanercept [a]	34 (4.9)	5 (3.5)	
- Infliximab [a]	24 (3.5)	5 (3.5)	
- Adalimumab	130 (18.9)	22 (15.4)	
- Rituximab [a]	61 (8.9)	25 (17.5)	
- Abatacept	76 (11)	20 (14)	
- Tocilizumab	82 (11.9)	18 (12.6)	
- Certolizumab	92 (13.4)	28 (19.6)	
- Rituximab [b]	7 (1)	0	
- Golimumab	36 (5.2)	5 (3.5)	
- Tofacitinib	14 (2)	1 (0.7)	
- Infliximab [b]	4 (0.5)	2 (1.4)	
- Etanercept [b]	31 (4.5)	6 (4.2)	
- Baricitinib	12 (1.7)	1 (0.7)	
- Belimumab	5 (0.7)	1 (0.7)	
- Secukinumb	8 (1.2)	3 (2.1)	
Steroids use, n(%):	254 (36.9)	57 (39.9)	0.2
Steroids dose (mg), median (IQR)	6 (5 – 10)	6 (5 – 10)	0.47
DMARD use, n(%):	538 (78.1)	118 (82.5)	0.1
Treatment duration, median (IQR)	5.06 (4.04 – 5.78)	3.82 (3.35 – 4.95)	0.001
Suspension motive, n(%)			NA
- Inefficacy	-	54 (37.8)	
- Adverse event	-	16 (11.2)	
- Pregnancy	-	2 (1.4)	
- Loss of patient	-	15 (10.5)	
- Remission	-	7 (4.9)	
- Others	-	49 (34.2)	
Adverse events, n(%):	102 (14.8)	24 (16.8)	0.3
- Severe, n(%)	13 (1.9)	5 (3.5)	0.4

[a] original, [b] biosimilar

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AB1358 BIOLOGIC TREATMENT SUSPENSION AND ASSOCIATED FACTORS IN PATIENTS WITH RHEUMATIC DISEASES DURING THE COVID-19 PANDEMIC: DATA FROM MEXICAN ADVERSE REGISTRY (BIOBADAMEX)

Keywords: Registries, bDMARD, COVID

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Background: The COVID-19 pandemic triggered serious challenges in the treatment of chronic diseases due to the lack of access to medical attention. Patients with rheumatic diseases (RD) must have adequate treatment compliance in order to reach and maintain remission or low activity of their diseases.

Treatment suspension because of non-medical reasons might lead to disease activation and organ damage.
Objectives: Identify the frequency of biologic treatment (bDMARD) suspension in patients with RD during the COVID-19 pandemic and determine the associated factors for suspension.
Methods: In this study we included all patients registered in the Mexican Biologics Adverse Events Registry (BIOBADAMEX), that started bDMARD before March 2019 and suspended treatment during the COVID-19 pandemic. We used descriptive statistic to analyze baseline characteristics and main treatment suspension causes. We used Chi[2] and Kruskal Wallis tests to analyze differences between groups.
Results: A total of 832 patients patients registered in BIOBADAMEX were included in this study, 143 (17%) suspended bDMARD during the COVID-19 pandemic. The main causes of suspension were inefficacy in 54 (38%) patients, followed by *other* motives in 49 (34%) patients from which 7 (5%) was loss of medical coverage. Adverse events and loss of patients to follow up were the motive in 16 (11%) and 15 (11%) patients respectively. When we compared the group that suspended bDMARD with the non-suspenders (Table 1), we found statistical differences in patient gender, with 125 (87%) female patients that suspended bDMARD, with a median age of 52 (42-60) years, and a treatment duration of 3.8 years.
Conclusion: In our study we found that 17% of patients with RD suspended bDMARD treatment during the COVID-19 pandemic and that non-medical motives such as lack of patients follow up and loss of medical coverage due to unemployment were important motives. These results are related to the effect of the pandemic on other chronic diseases.
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AB1359 CLINICAL FEATURES OF COVID-19 IN PATIENTS WITH CONNECTIVE TISSUE DISEASES DURING THE RECENT PANDEMIC IN GUANGZHOU, CHINA

Keywords: Real-world evidence, Health services research, COVID

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Background: Patients with connective tissue diseases (CTD) are vulnerable to SARS-COV-2 infection, given that a proportion of CTD patients suffer from interstitial lung diseases (ILD). Moreover, the use of glucocorticoids and immunosuppressive agents could affect the outcome of lung diseases. The impact of coronavirus disease 2019 (COVID-19) infection on rheumatic diseases remains poorly investigated as the pandemic has recently occurred in Southern China.
Objectives: The study aimed to describe the clinical features and hospitalisation costs of COVID-19 in CTD patients, especially those with COVID-19 pneumonia.
Methods: It was a cross-sectional case series study. Demographic data, symptoms, signs, medical history, laboratory, radiological findings and costs were collected from 86 CTD patients from the inpatient department in a tertiary hospital during the COVID-19 pandemic in Guangzhou, China.
Results: Of all the 86 CTD patients, 67 (77.9%) were females, and 24 (27.9%) had CTD-ILD before admission. 54 (62.8%) of them had SARS-COV-2 infection dected by nucleic acid or antigen tests for SARS-COV-2. Patients with SARS-COV-2 infection had older age, higher WBC, neutrophil/lymphocyte ratio and CEA. Moreover, 325 (29.1%) of the participants had COVID-19 pneumonia confirmed by the HRCT. Noticeably, 15 CTD patients without ILD presents with COVID-19 pneumonia. Patients with COVID-19 pneumonia had older age, higher serum ferritin, CEA, and C-reactive protein ($p<0.05$). According to the rheumatologists' assessment, 6 (41.9%) of the patients had worsened CTD disease activity. 14 (16.3%) of the patients had confirmed infections involving the lung (6), skin (3), urinary tract (2), gastrointestinal tract (1), blood (1), and vagina [1]. The pathogens isolated included staphylococcus aureus, candida albicans, escherichia coli, cytomegalovirus, Epstein-Barr virus and herpes zoster virus. Among all the symptoms related to COVID-19, coughing was the most frequent symptom, followed by sputum, fatigue and fever. 27 (31.4%) of the patients required a nasal cannula for oxygen administration; 7 (8.1%) needed high-flow humidification therapy. 24 of the CTD patients were given higher doses of glucocorticoids. Five patients were given anti-virus medication, 4 were using baricitinib or tocilizumab, and 10 were taking intravenous immunoglobulin. There was no difference in the hospitalisation costs between the patients with or without SARS-COV-2 infection; however, patients with COVID-19 pneumonia had significantly higher costs with a mean of 24083 RMB (≈3318 Euros). All the patients got improved before the discharge.
Conclusion: Disease flare and COVID-19 pneumonia should be noticed in patients with CTD during the pandemic.
Acknowledgements: This work was supported by Scientific and Technological Planning Project of Guangzhou City [202102020150], Guangdong Provincial Basic and Applied Basic Research Fund Project [2021A1515111172], National Natural Science Foundation of China Youth Fund [82201998] and Third Affiliated Hospital of Sun Yat-Sen University Cultivating Special Fund Project for National Natural Science Foundation of China [2022GZRPYQN01].
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AB1360 AUTOANTIBODIES RELATED TO RHEUMATIC DISEASES AFTER COVID-19 INFECTION

Keywords: Real-world evidence, COVID, Autoantibodies

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Background: SARS-CoV-2(Severe acute respiratory syndrome coronavirus 2) has been circulating worldwide for three years. It mainly causes upper respiratory tract infection, which can manifest as pulmonary infection and even respiratory distress syndrome in severe cases. Different autoantibodies can be detected in patients infected with COVID-19.
Objectives: To explore autoantibodies related to rheumatic diseases after COVID-19 infection.
Methods: Ninety-eight inpatients were tested for antinuclear antibodies (ANA), antibodies to extractable nuclear antigens(ENA), anti-neutrophil cytoplasmic antibodies (ANCA), anticardiolipin antibodies,a-β2GPI (IgG/IgM). They were from a tertiary hospital in Guangzhou during the COVID-19 epidemic. Data were described statistically.
Results: Ninety-eight hospitalized patients were tested for relevant antibodies. The average age was 50.64±19.54; 67 (68.4%) were male, 64 (65.3%) were COVID-19 positive, 90 (90.9%) had rheumatic diseases, and 56 of them were COVID-19 positive patients with rheumatic diseases. There were 76 patients tested for antinuclear antibodies;29 (38.16%) were negative, 18 (23.68%) had a 1/80 titre, and 29 (28.16%) had a titre greater than 1:80. The 31 covid patients were positive for ANA. In the high-titer group, 19 patients with rheumatic diseases were positive for COVID-19, and 12 patients had an exacerbation of the rheumatic diseases (6 of whom had previously had pulmonary fibrosis). Of 31 covid patients, only two were non-rheumatic patients, and both were elderly, aged 85 and 100, respectively. Fifty-six patients had ENA results, and 29 for positive antibodies, 8 for ds-DNA antibodies, 2 for anti-Sm antibodies, 6 for anti-nucleosome antibodies, 12 for anti-U1RNP antibodies, 2 for anti-Scl-70 antibodies, 12 for anti-SS-A antibodies, 3 for anti-mitochondrial M2 antibodies, 2 for anti-centromere antibodies, 1 for anti-Po antibodies, and one for anti-Jo-1 antibody. All 56 patients had rheumatic diseases, and no new patients were found. There were 62 patients with ANCA data. P-ANCA was positive in 12 cases(19.35%), and MPO-ANCA was positive in 2 cases. An 85-year-old non-rheumatic COVID-19 patient was P-ANCA positive. She had a history of hypertension, colon cancer, CKD3, coronary heart disease, and atrial flutter. In the anticardiolipin antibodies group, there were 62 patients; only 6 were positive, and 2 were rheumatic patients infected with COVID-19. Antiphospholipid antibodies were detected in 33 patients, and a-β2GPI was tested in one patient, an 82-year-old COVID-19 patient with gout, diabetes, and cerebral infarction in the past. We did not find a statistical difference in the above results.
Conclusion: We have not found a correlation between SARS-CoV-2 and serum autoantibodies of rheumatic immune diseases. It needs large samples and an extended follow-up to research.
Acknowledgements: This work was supported by Scientific and Technological Planning Project of Guangzhou City [202102020150], Guangdong Provincial Basic and Applied Basic Research Fund Project [2021A1515111172], National Natural Science Foundation of China Youth Fund [82201998] and Third Affiliated Hospital of Sun Yat-Sen University Cultivating Special Fund Project for National Natural Science Foundation of China [2022GZRPYQN01].
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AB1361

COVID-19 IN PATIENTS WITH INFLAMMATORY ARTHRITIS IN THE VINSCHGAU VALLEY IN SOUTH TYROL

Keywords: COVID, Inflammatory arthritides

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Background: For patients with autoimmune rheumatic diseases, the Covid-19 pandemic carried some implications in addition to those faced by the general population. In particular, the question whether these patients are at increased risk of contracting Covid-19 or have an unfavourable disease course has been and is a matter of concern. In autumn 2020, the population of the Vinschgau valley in South Tyrol, northern Italy was still largely spared from infection with SARS-CoV-2. Accordingly, incidence of the disease in the upcoming winter was anticipated to be high.
Objectives: This prospective observational study aimed at characterizing Covid-19 infections in a population of patients with inflammatory arthritis (IA) residing in the Vinschgau valley. The study was conceived as companion project to an analogously designed prospective cohort study in the general population of the Vinschgau valley, the CHRIS Covid-19 study.
Methods: Between september and december 2020, IA patients (i.e. previously diagnosed rheumatoid arthritis [RA], psoriatic arthritis [PsA] or peripheral spondyloarthritis [SpA]) residing in the Vinschgau valley (n=394 based on national healthcare system database) were contacted. Those who consented to participate in the study underwent a clinical baseline visit including TJC, SJC, VAS and assessment of RAID, PsAID9 or BASDAI (range 0-10, respectively). In addition, a Covid-19 screening questionnaire was administered. Then, active and/or past infection with SARS-CoV-2 were determined by nasopharyneal swab (PCR) and serum antibody test. In positively tested subjects, Covid-19 disease severity was graded according to WHO criteria (range 0-8, with 0 = no evidence of infection and 8 = death). Patients were followed-up with regular telephone interviews including Covid-19 screening questionnaire and RAID/PsAID/BASDAI for up to 12 months.
Results: 111 patients (72 RA, 29 PsA, 10 SpA) were enrolled (see Table 1 for demographics and comorbidities). A total number of 19 PCR-confirmed SARS-CoV-2 infections in 17 patients (10 RA, 7 PsA) were observed. Mean ± standard deviation 7-day incidence (incident cases/study population) was 0.003 ± 0.007. Fatigue, fever, anosmia and sore throat (present in 57.9%, 47.4%, 42.1% and 36.8% of infections, respectively) were the most frequent symptoms. Median (min-max) disease severity was 2 [1-4]. Two infections led to hospitalization, in one case oxygen supply was necessary. Four infections were asymptomatic (Figure 1). One patient died during follow-up due to pre-existing non-small cell lung cancer. Median absolute difference between post- and pre-infection disease activity was 0.4 and -0.8 for RAID and PsAID, respectively (both markedly below the minimal clinically important difference of 3 and 3.6 points, respectively).
Conclusion: Incidence of Covid-19 in the analysed cohort of patients with IA was low. Symptoms and comorbidities of SARS-CoV-2-positive IA patients reflected those known from the general population. Covid-19 seemed to have no relevant impact on IA disease activity. Comparison of these preliminary data with those of the general population is planned.

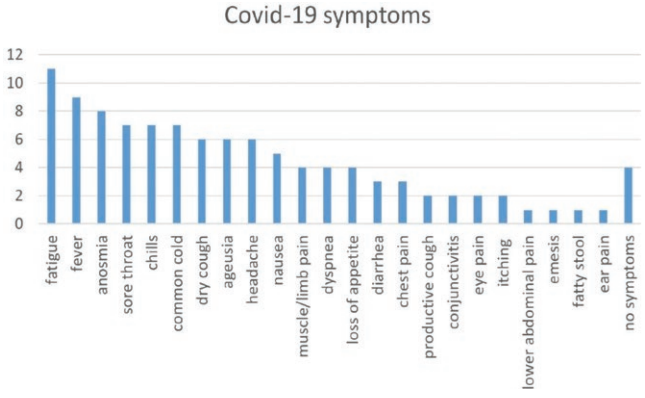


Figure 1. Spectrum of clinical symptoms reported by study patients during infection with SARS-CoV-2

Table 1. Demographic data and selected comorbidities of study patients. Age and body mass index (BMI) are given in means ± standard deviation, female sex and comorbidities are given in n (% of column totals).

	Total	SARS-CoV-2 positive	Hospitalized
	111	17	2
Age at inclusion (years)	59.7 ± 9.4	62.5 ± 10.0	76.3 ± 9.0
BMI at inclusion (kg/m^2)	27.9 ± 17.1	26.1 ± 3.3	30.5 ± 1.6
Female sex	76 (68.5)	10 (58.8)	1 (50)
Active smokers	22 (19.8)	1 (5.9)	0 (0)
Arterial hypertension	44 (39.6)	8 (47.1)	2 (50)
Diabetes mellitus	4 (3.6)	1 (5.9)	1 (50)
Hyperlipidemia	27 (24.3)	2 (11.8)	1 (50)
Cardiac arrhythmias	12 (10.8)	2 (11.8)	1 (50)
History of cancer	5 (4.5)	1 (5.9)	0 (0)
Chronic bronchitis	4 (3.6)	1 (5.9)	0 (0)
Asthma	3 (2.7%)	0 (0)	0 (0)
Hospitalized in previous 12 months	21 (18.9)	3 (17.6)	0 (0)
Surgery with general anaesthesia in previous 12 months	11 (9.9)	2 (11.8)	0 (0)

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AB1362

STUDY OF ADVERSE REACTIONS TO COVID-19 VACCINATION IN PATIENTS WITH RHEUMATIC DISEASES

Keywords: Vaccination/immunization, COVID

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Background: Vaccination has been recommended in the midst of the COVID-19 pandemic, but some patients are not vaccinated due to concerns about adverse reactions.
Objectives: The purpose of this study is to investigate the adverse reactions in rheumatic diseases and to guide the decision-making of patients and physicians.
Methods: A questionnaire was sent to patients with rheumatic diseases, and patients who could be counted as of September 2021, when they consented to this study, were surveyed.
Results: The subjects were 123 (male:female=10:113), 84 with rheumatoid arthritis and 39 with other immune diseases. The therapeutic agents used were PSL 31(25.2%), MTX 65(52.8%), NSAID/COX inhibitors 28(22.8%), bDMARDs 42(34.1%). adverse reactions after the first and second vaccination were fever 17(13.8%)/50(40.7%), joint symptoms 7(5.7%)/22(17.9%), local injection reactions (pain/irritation) 22(17.9%), local injection reactions (pain/erythema) 93(75.6)/98(79.7), systemic skin symptoms 0(0%)/2(1.6%), other symptoms (malaise, myalgia, etc.) 59(48.0%)/85(69.1%), and treatment intensification 5(4.1%)/12(9.7%). These responses differed in occurrence only for fever with and without PSL medication (22.5%: 47.3% (p=0.02)). The odds ratio for disease worsening after the first dose of vaccine and again after the second dose was 33.5 (p<0.01).
Conclusion: No specific adverse reactions other than the commonly known ones were observed, but some patients experienced worsening of symptoms after vaccination, requiring intensified treatment. Based on the results of this study, we believe that adverse reactions to vaccination are acceptable. We plan to accumulate more cases and analyze them in the future. The exacerbation of disease after the first vaccination would predict the exacerbation after the second vaccination.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1363

FIRST PRESENTATION OF AUTOIMMUNE RHEUMATIC DISEASES AFTER COVID-19 VACCINATION: A SYSTEMATIC REVIEW

Keywords: COVID, Epidemiology, Vaccination/immunization

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Background: Covid-19 vaccination prevents 52% of expected infections, 56% of expected hospitalizations, and 58% of expected deaths in adults 18 years or

older [1]. Nevertheless, some case reports and series have demonstrated the new-onset rheumatologic syndromes after vaccination.
Objectives: The aim of this systematic review is to establish the frequency, clinical features, and treatment response of new onset autoimmune rheumatic diseases after COVID-19 vaccination.
Methods: Systematic search for original research articles published between January 2021 and January 2023 was formulated. The search process was carried out following the PRISMA guidelines. Electronic searches were performed in Medline, EMBASE, Cochrane, Scopus, EBSCO, WoS and LILACS using the following key terms in all possible combinations: "Rheumatic diseases", "Systemic Vasculitis", "Myositis", "Polymyositis", "Systemic Lupus Erythematosus", "Antiphospholipid Syndrome", "Adult onset Still disease", "Rheumatoid arthritis", "ANCA-associated vasculitis", "Spondyloarthritis", "Reactive arthritis", "Sjogren's syndrome", "Systemic sclerosis", "Covid-19 vaccine" and "SARS-CoV-2 vaccine". Cohort studies, case reports or case series were included if the patients fulfilled the specific diagnostic/classification criteria and/or nomenclature for each rheumatic autoimmune disease. Publications were excluded if they did not fulfill the above criteria.
Results: The electronic search yielded 280 publications. A total of 163 articles were evaluated and 59 reports with 108 patients (GCA 10, IgA vasculitis 9, SLE 14, ANCA vasculitis 24, adult-onset Still's disease 12, reactive arthritis 2, Rheumatoid Arthritis 5, Sjögren's syndrome 3, Systemic Sclerosis 2, Takayasu's arteritis 2, cryoglobulinemic vasculitis 1, Kawasaki disease 3, Polymyalgia rheumatica 16, PAN 1, SpA 2, Overlap syndrome 1, and Antisynthetase syndrome 1) were included. 44.4% were men and 43.5% were women with a median age of 60 years (IQR 40-74 y/o), 47.2% developed rheumatic disease after the first dose and 35.2% after the second dose, with a median of 10 days (IQR 5.5-14.5 days). 67.6% received corticosteroids (16.7% High-dose and 15.7% Pulse), 31.5% received immunosuppressant (cyclophosphamide 7.4%, rituximab 2.8, hydroxychloroquine 4.6, methotrexate 6.5, tocilizumab 2.8, mycophenolate 2.8, immunoglobulin 8.3 y 4.6% others). The 55.6% had complete remission, 24.1% partial and 6.5% non-response.
Conclusion: 1. After Covid 19 vaccine, a minority of patients may develop for the first time an autoimmune rheumatic disease. Despite the increasing number of documented cases, the incidence remains low compared to the benefits of vaccination. 2. Patients present a high variability of clinical manifestations and most patients respond favorably to treatment. 3. The complex interaction between the vaccine component and the immune system must be studied.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1364 **VACCINATION AGAINST COVID-19 IN PARAGUAYAN PATIENTS WITH RHEUMATOID ARTHRITIS**

Keywords: COVID, Rheumatoid arthritis, Vaccination/immunization

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Background: In February 2021, the first doses of COVID-19 vaccines were received in Paraguay, and rheumatic patients were the preferred population to get these vaccines. Up to December 2022 the vaccination coverage in Paraguay was 59.4%, with at least one vaccine dose. 52.4% accessed the primary scheme (two doses), while 28.6% had at least one booster dose. Only 7.1% completed the COVID-19 immunization scheme.
Objectives: To describe vaccination against COVID-19 in Paraguayan patients with Rheumatoid Arthritis (RA).
Methods: Descriptive, cross sectional, observational study, in a Paraguayan cohort of RA patients meeting ACR/EULAR2010 criteria, under follow-up in two Rheumatology reference centers, from October to December 2022. A standardized questionnaire according to the variables included (clinical, vaccination, vaccine type, number of doses) was made. Quantitative variables were presented as means and qualitative as frequencies.
Results: 568 patients with RA were included, 84.1% were female, mean age 55.48±13.94 years old. 23.9% patients were from Hospital de Clínicas and 76.1% from Hospital Central del Instituto de Previsión Social. The average number of received vaccinations doses was 2.54±1.19. 88.7% of patients acquired at least one dose of COVID-19 vaccine, 85% obtained two doses; and, while 60.9% of patients received the first booster, 21.2% had the second one.
Conclusion: In this series of Paraguayan RA patients, vaccination against COVID-19 is higher than the general population, perhaps due to priority of patients with rheumatic diseases receiving immunization, and frequent access to medical care with physician's prompt to receive vaccinations. While over 80% of patients have a complete primary schedule, and more than 60% received the first booster; only 21% have a complete immunization schedule, which is still much higher than the general population in Paraguay.

Table 1. Vaccines in Paraguayan patients with Reumatoid Arthritis

Vaccines against COVID-19	First Dose n: 504	Second Dose n: 483	First booster n: 344	Second booster n: 122
Sputnik V(Gam--COVID-Vac) n (%)	149 (26.2)	137 (24.1)	10 (1.8)	0
Astrazeneca (ChAdOx1 nCoV-19) n (%)	172 (30.3)	171 (30.1)	110 (19.4)	36 (29.5)
Pfizer n (BNT162b2) (%)	81 (14.3)	80 (14.1)	198 (34.9)	68 (55.7)
Moderna (mRNA-1273) n (%)	41 (7.2)	38 (6.7)	22 (3.9)	18 (14.8)
Hayat Vax n (%)	29 (5.1)	28 (4.9)	1 (0.2)	0
Sinopharm BBIBP n (%)	2 (0.4)	1 (0.2)	0	0
Covaxin n (%)	28 (4.9)	26 (4.6)	3 (0.5)	0
CoronaVac n (%)	2 (0.4)	2 (0.4)	0	0

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Acknowledgements: NIL.
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AB1365 **COMPARISON OF HOMOLOGOUS AND HETEROLOGOUS BOOSTER SARS-COV-2 VACCINATION IN AUTOIMMUNE RHEUMATIC AND MUSCULOSKELETAL PATIENTS**

Keywords: COVID

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Background: Vaccine-induced immunity is very important for controlling the COVID-19 infection. The vaccination supports humoral and cellular immunity, and this is one of the main strategy for us. Various vaccines approved in the countries have been shown to reduce infection rates, severity, and mortality.
Objectives: We aimed to compare humoral and cellular immune responses after homologous or heterologous vaccination among patients with aiRMDs at their third vaccination with BNT162b2 or with two vaccinations followed by COVID-19 infection. We detected the anti-SARS-CoV2 antibody levels and measured the SARS-CoV-2 reactive B-, or T-cell mediated immunity in aiRMDs receiving homologous (Hom.), heterologous (Het.) vaccines or became infected (Inf.).
Methods: A single center observational study evaluated immunogenicity and safety of the third dose vaccines or after two-dose regimen of vaccine and COVID infection in patients with aiRMDs. Neutralizing anti-RBD antibodies and specific T-cell response were measured.
Results: We showed that following 4 months of the booster vaccination with the third dose of mRNA-based vaccine or after COVID infection, the positive (>21.8 BAU/mL) neutralizing anti-RBD IgG antibody response was outstanding in all three patient groups, 95.5%, 100% and 100% of the homologous and heterologous as well as the SARS-CoV-2 infected groups. Taken together booster vaccinations or SARS-CoV-2 infection after completing 2 doses of the vaccination can lead to the production of neutralizing antibodies still protective in RMD cases after 4 months of the third antigen exposition. The booster vaccination reduces the frequency of hospital admissions and mortality with ai RMDs. The vaccinations are effective independently from the type of vaccine, the SARS-CoV-2 specific memory B-cell populations showed a statistically not significant but lower frequency in the infection group. Clinical activity of aiRMDs was not increased following booster vaccination.
Conclusion: Patients, who received a heterologous booster vaccine had a higher level of peripheral memory B-cells compared to those who had COVID-19 infection. Biologic therapy decreased the level of B-cells. Patients with a disease duration of more than 10 years had higher level of CD8+TNF-α+ and CD8+IFN-γ+ T-cells compared to patients who were diagnosed less than 10 years ago. The third booster mRNA-based vaccine was as much effective as in the homologous and heterologous patients groups compared who had COVID infection.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Pain in rheumatic diseases, including fibromyalgia_

AB1366

A SYSTEMATIC REVIEW AND META-ANALYSIS OF THE PREVALENCE OF PAIN SENSITISATION AND NEUROPATHIC LIKE PAIN IN INFLAMMATORY ARTHRITIS, USING QUESTIONNAIRES

Keywords: Systematic review, Pain, Inflammatory arthritides

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Background: Targeted pain relief is a major unmet medical need for patients with inflammatory arthritis (IA), where approximately 40% of patients experience persistent pain[1]. Self-reported questionnaires which report on pain sensitivity and neuropathic like pain may provide an insight into certain pain types to guide targeted treatment.

Objectives: In this systematic review and meta-analysis we evaluated self-reported pain sensitivity and neuropathic like pain in subjects with IA, as defined by questionnaires.

Methods: MEDLINE, Embase, Web of Science, PsycINFO and google scholar were searched for publications and conference abstracts, reporting on pain sensitivity and neuropathic pain using painDETECT, DN4, LANSS, CSI, PSQ and McGill pain questionnaire in adult patients with IA. Risk of bias was assessed using National Institute of Health Quality Assessment Tool. Meta-analysis according to individual questionnaire criteria, was undertaken.

Results: 63 studies (38 full text and 25 conference abstracts) were included in the review, reporting on a total of 13,035 patients. On meta-analysis, prevalence of pain sensitivity/neuropathic pain in IA was 36% (95% CI 31-42%) according to painDETECT, 31% (95% CI 26-37%) according to the DN4, 32% (95% CI 32-49%) according to the LANSS and 42% (95% CI 34-50%) according to the CSI. On meta-regression, prevalence of pain sensitivity/neuropathic pain in RA was significantly lower than SpA (p=0.01) and PsA (p=0.002) using the painDETECT questionnaire. Across all questionnaires, pain sensitivity and neuropathic like pain were significantly associated with pain severity, disease activity, disability, quality of life and anxiety and depression measures. Studies reporting on whether neuropathic like pain is a predictor of treatment outcome were inconsistent.

Conclusion: Pain sensitivity and neuropathic like pain contributes to pain perception in up to 42% of patients with IA. Despite substantial heterogeneity between studies on meta-analysis, this review highlights the large proportion of patients with IA who may experience pain due to underlying mechanisms other than/in addition to synovial inflammation.

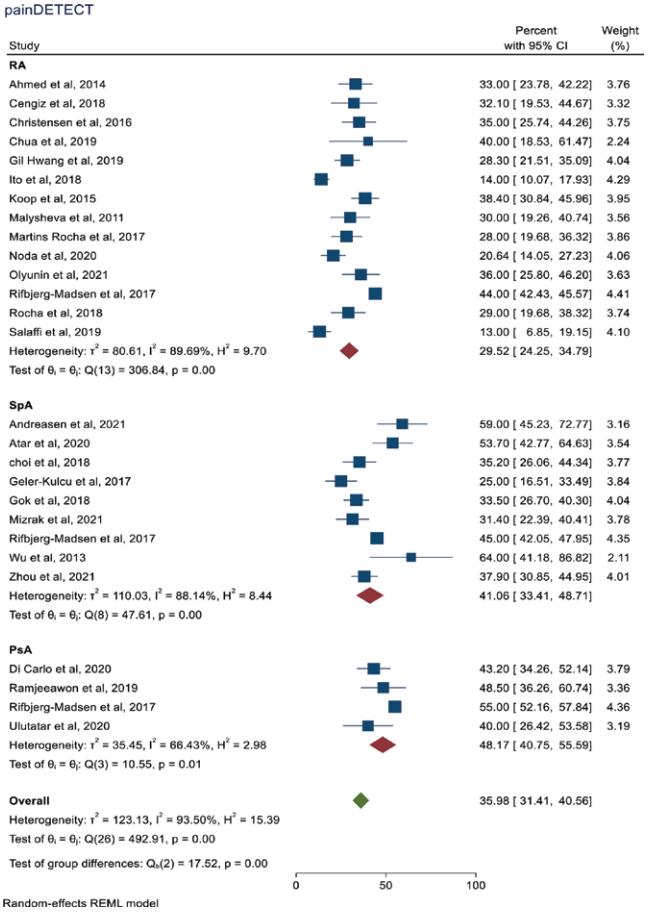


Figure 1. Prevalence of neuropathic like pain or pain sensitization according to painDETECT in RA, SpA and PsA.

Conclusion: All rehabilitation strategies were effective for pain and HRQOL, and has marginal effect on depression, sleep, and fatigue but efficacy was not maintained at the time of post-trial follow-up. However, in this review we could not

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AB1367

EFFECTIVENESS OF REHABILITATION STRATEGIES IN PRIMARY FIBROMYALGIA SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS

Keywords: Rehabilitation, Fibromyalgia, Non-pharmacological interventions

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Background: Fibromyalgia is characterized by chronic inconsistent widespread pain and tenderness. It is also associated with other comorbid symptoms like sleep disturbances, fatigue, cognitive impairments (memory and mood disturbances), and/or irritable bowel syndrome. [1] Prevalence of fibromyalgia is 2.7% globally, being slightly higher in middle aged women (4-9%). 75 to 100 % patients with fibromyalgia face depression, anxiety and/or stress. The probability of occurrence of depression is almost 40% at any stage in the course of fibromyalgia. [2] Patients usually report physical symptoms of depression (e.g. appetite, sleep, and sexual dysfunction) rather than mood-related psychological symptoms (e.g. suicidal ideation, low self-esteem), however depression is affective expression of chronic pain and neuromarkers of both cannot be isolate. [3] Reviews done till date are either oriented toward specific form of exercise or towards specific outcome. We could not come across any review which included all form of exercise with measurement of multiple outcomes.

Objectives: The aim of this review was to 1) summarize evidence on the effectiveness of rehabilitation strategies in Fibromyalgia syndrome (FMS) and 2) determine the most effective rehabilitation strategy for reducing pain and depression in people with FMS.

Methods: PubMed, Ovid (Sp), and Cochrane search engines were used for identifying the studies done till 1 July 2022. Randomized control trials (RCTs) that have passive control group and active control group were included in this review for primary and secondary aim respectively. The primary outcome measures were Pain and depression. Secondary outcome was one from the sleep or fatigue or healthy related quality of life (HRQOL).

Results: A total of 25 RCTs were included. Separate random effect model meta-analysis is performed for randomised control trial with active and passive control group. Mean difference or Standard Mean difference with 95% confidence interval used to assess the effect size. Studies with passive control group showed moderate to large positive effects on pain (SMD -0.65, 95% CI -0.93 to -0.38; I2 = 72%) and HRQOL(MD -5.40, 95% CI -10.17 to -0.62; I2 = 74%) but non-significant for sleep, fatigue, and depression. Furthermore, on subgroup analysis studies with short term protocol showed significant effect on pain only, whereas studies with long term protocols showed positive effect on pain and HRQOL only but non-significant at the time of post-trial follow-up. Studies with active control group represent non- significant results except mixed exercises which showed positive effect (MD -4.78, 95% CI -7.98 to -1.57; I2 = 0%) for HRQOL.

differentiate any rehabilitation strategies for the best among those used in the included studies.

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AB1368 PROBLEMATIC USE OF OPIOIDS IN MUSCULOSKELETAL CHRONIC NON-CANCER PAIN: A PROSPECTIVE REAL LIFE STUDY

Keywords: Descriptive studies, Epidemiology, Pain

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Background: Musculoskeletal chronic non-cancer pain (CNCP) has a multidimensional impact. Opioid treatments have a key role in their management but expose to risks of serious adverse effects and in particular to opioid use disorder and misuse. There is a lack of data on this topic in France. This work assesses the proportion of patients with problematic use of their opioid treatment in the rheumatology department and in the pain center of the University Hospital of Tours.

Objectives: This work assesses the proportion of patients with problematic use of their opioid treatment in the rheumatology department and in the pain center of the University Hospital of Tours.

Methods: We carried out a prospective monocentric observational study in routine care in patients followed for musculoskeletal CNCP and treated in this indication with weak or strong opioid treatment at the time of inclusion between January and December 2021. We collected demographic, clinical and opioid prescribing data. The primary endpoint was the percentage of problematic use of opioid treatment defined by overconsumption and/or misuse according to the Prescribed Opioid Misuse Index (POMI) and/or opioid use disorder according to DSM V criteria.

Results: 97 patients were included (68% women, median age 55 years); 37% of patients were treated with strong opioids. The median duration of opioid treatment was 4.5 years; 30% of patients had problematic use of their opioid treatment. There was overconsumption in 20% of patients, misuse in 22% and opioid use disorder in 15%. The group of patients with problematic use of opioid treatment had a higher body mass index and reported significantly more history of psychotrauma.

Conclusion: The problematic use of opioids in patients with musculoskeletal CNCP is frequent. These data are in agreement with those in the literature in other indications. The interest of therapeutic education programs or other preventive interventions remains to be defined.

Keywords: opioids, chronic non-cancer pain, opioid use disorder, misuse.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1369 FIBROMYALGIA AND INFORMATION SOURCES, THE EXAMPLE OF YOUTUBE: A CROSS-SECTIONAL ANALYSIS

Keywords: Patient information and education, Patient-led research, Fibromyalgia

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Background: Fibromyalgia is a chronic condition affecting 2 to 8% of the population. Like any chronic disease, there is a need for information. More than one in two patients use the Internet as a source of health information. YouTube is an online video-sharing website that is consulted daily by both patients and healthcare professionals. This is the second most visited website in the world after Google. Usually, users view the top 60 most relevant videos.

Objectives: The aim of our study was therefore to analyse the scientific quality of fibromyalgia videos on YouTube.

Methods: We performed an analysis by using the French version of youtube (www.youtube.fr) using the keyword "fibromyalgia". Search parameters were left as default (i.e. ranking videos by relevance as most users do). Only videos in French were included. The Global Quality Scale (GQS) was used to assess the quality of the content.

Results: 60 videos were selected. Four videos were excluded: 2 duplicates and 2 videos containing only music. The main results are presented in Table 1. 37.5% (n=21) of the videos were published by academic institutions and healthcare professionals. The mean duration of the videos was 12min34. The median GQS was 4. 75% (n=42) were scientifically relevant. 62.5% (n=35) of the videos demonstrated high quality, followed by intermediate quality (19.6% (n=11)). According to the GQS, 17.0% (n=10) of the videos were of low-quality.

Conclusion: To the best of our knowledge, we have conducted the first study examining the scientific quality of fibromyalgia-related content on YouTube. Most of the content on YouTube relating to fibromyalgia provide useful information. Nevertheless, physicians should remind their patients to be cautious about using such a source of information.

Table 1. Baseline features of the analyzed videos

Variables	Videos (n=56)
Number of comments	13 (0-227)
Number of likes	201 (0-2400)
Number of views	9676.5 (241-99618)
GQS	4 (1-5)

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.1021

AB1370 DEMOGRAPHICAL, SOCIOPROFESSIONAL FACTORS AND HABITS ASSOCIATED WITH CHRONIC WIDESPREAD PAIN IN A LARGE GENERAL POPULATION COHORT

Keywords: Epidemiology, Pain, Fibromyalgia

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Background: Clinical and demographic characteristics associated with chronic widespread pain (CWP) are well known, contrary to the social and professional characteristics in general population.

Objectives: To evaluate the set of characteristics associated with CWP.

Methods: The Constances cohort consisting of randomly selected volunteers aged 18 to 69 years, between 2013 and 2020 in France (ref). An ancillary study from this cohort aims to identify musculoskeletal pain using the Nordic Questionnaire. Chronic pain was defined as pain in at least 4 of the 6 areas, during at least 30 days during the previous year. Individuals diagnosed with a cancer were excluded. Demographic, clinical, social, and occupational data at inclusion were collected. Missing data were imputed. Multivariate analysis was performed.

Results: 193,436 people were included, of whom 7% (13,447 people) suffered from CWP. Female gender, age, higher BMI, depression, medium or high physical activity at work, current or past smoking, less sleep duration, and low socio-professional category were associated with CWP. Diploma was a protective factor, as well as leisure physical activity, while job search, household income, alcohol or cannabis were not or poorly associated with CWP.

Conclusion: CWP remains frequent in the French general population and is significantly associated with specific socioeconomic factors.

REFERENCE:

[1] Zins M et al. 2015 *Eur J Epidemiol*

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.1875

Table 1.

	Odds Ratio - Confidence interval 95%
Female sex	**1.91 [1.82 - 1.99]**
Age (reference 18-30 years)	30 to 40 years: **1.55 [1.40 - 1.72]**
	40 to 50 years: **2.35 [2.13 - 2..60]**
	50 to 60 years: **3.40 [3.07 - 3,76]**
	60 to 69 years: **2,92 [2.60 - 3.29**
BMI (reference 18.5 - 25)	< 18.5: **0.83 [0.73 - 0.95]**
	25 to 29.9: **1.19 [1.14 - 1.24]**
	30 to 34.9: **1.40 [1.32 - 1.49]**
	35 to 39.9: **1.48 [1.34 - 1.63]**
Depression (CESD score)	**2.19 [2.10 - 2.28]**
Sleep duration (Odds ratio for one hour)	**0.92 [0.91 - 0.93]**
Alcohol (reference: no misuse or dependance - Audit Score)	Misuse **0.93 [0.89 - 0.97]**
	Dependance 1.04 [0.95 - 1.13]
Smoking (reference: no smoking)	Previous smoking: **1.30 [1.24 - 1.36]**
	Actual smoking: **1.25 [1.18 - 1.32]**
Cannabis (reference: never use)	cannabis used more than a year ago 0.96 [0.91 - 1.01]
	Used in the 12 last months 0.99 [0.87 - 1.11]
	Used in the 30 last days **1.16 [1.04 - 1.28]**
Physical activity at leisure (reference: no activity)	Very low activity: 0.96 [0.85 - 1.09]
	low activity 1.01 [0.91 - 1.13]
	moderately activity 0.90 [0.81 - 1.01]
	Activity 0.92 [0.83 - 1.03]
	Quite activity **0.80 [0.71 - 0.89]**
	Important activity **0.84 [0.75 - 0.95]**
Physical activity at work (reference: sedentary)	slightly active (walking/ handling < 10 kg): **1.09 [1.03 - 1.16]**
	moderately active (handling objects between 10 and 25 kg) **1.58 [1.47 - 1.70]**
	highly active (heavy handling > 25 kg) **2.39 [2.19 - 2.62]**
Socio-professional category (reference: intermediate profession)	Farmer 1.23 [0.72 - 2.01]
	Craftsman, merchant or business owner 1.08 [0.94 - 1.23]
	Executive and higher intellectual profession **0.93 [0.87 - 1.00]**
	Employee **1.08 [1.02 - 1.14]**
	Worker **1.21 [1.12 - 1.30]**
	Never work 0.88 [0.71 - 1.08]
	Missing data 1.01 [0.93 - 1.09]
Diploma (reference: without diploma)	general certificate of secondary education 0.98 [0.88 - 1.09]
	Certificate of professional competence 0.98 [0.89 - 1.08]
	High school diploma 0.88 [0.80 - 0.97]
	2 years after high school diploma **0.76 [0.68 - 0.84]**
	Bachelor's degree **0.65 [0.57 - 0.73]**
	Master's degree **0.58 [0.51 - 0.65]**
Professional situation (reference: employed)	In formation **0.79 [0.66 - 0.95]**
	Job seeker 1.04 [0.95 - 1.14]
	Without job 0.90 [0.78 - 1.04]
	No job due to medical disease **2.46 [2.16 - 2.80]**
	Pensioner 0.94 [0.85 - 1.03]
	Missing data 0.91 [0.81 - 1.02]
Household income (reference: 1000 to 1500 euros)	Less than 45 euros: 0.89 [0.69 - 1.12]
	450 to less than 1000 euros 1.04 0.93 - 1.16]
	1500 to less than 2100 euros 0.96 [0.89 - 1.04]
	2100 to less than 2800 euros 1.05 [0.97 - 1.13]
	2800 to less than 4200 euros 1.02 [0.95 - 1.10]
	More than 4200 euros **0.89 [0.82 - 0.97]**
	Cannot answer 0.88 [0.71 - 1.09]
	Do not want answer 0.89 [0.69 - 1.12]

AB1371 CENTRAL SENSITIZATION AS A PREDICTOR OF FUNCTIONAL DISABILITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Diagnostic tests, Pain, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a common systemic inflammatory autoimmune disease. Patients with rheumatoid arthritis suffer from chronic pain, restricted function and reduction of daily activities [1]. Recent evidence reveals that central sensitization (CS) is associated with the development and maintenance of chronic pain. [2].

Objectives: The aim of this study was to determine the functional status of RA patients in the presence of CS.

Methods: The study involved patients diagnosed with RA according to the ACR/EULAR criteria (2010). The presence of the CS phenomenon was established according to the Central Sensitization Inventory (CSI) (Mayer, T. G. Et al., 2012). The Health Assessment Questionnaire-Disability Index (HAQ-DI) was used to assess the functional status of patients. RA activity was determined by DAS-28, SDAI, CDAI. Pain intensity was assessed by Visual Analog Scale (VAS). Statistical analysis was performed using MS Excel and SPSS22 software (©SPSS Inc.). Odds ratios (OR) and their corresponding 95% confidence interval (CI) were calculated. A descriptive analysis of the variables was carried out using mean and standard deviation (M±SD).

Results: A total of 168 RA patients (female 78%) were included. The median age of patients was 52.7±14.1 years, and the median duration of disease was 8.7±7.9 years. The examined patients showed mainly moderate and high activity of the disease (DAS-28 – 4.9±0.9; SDAI – 34,9±9,6; CDAI – 32,0±9,3). The presence of central sensitization (CSI≥40) was revealed in 59 (35%) of patients. The group of patients with CS had greater functional impairment compared to patients without CS: HAQ - 1.9±0.7 versus 1.0±0.6 ($p<0.05$). Also, patients with CS reported a higher intensity of pain (VAS pain - 7.8±1.2 versus 6.4±1.4; $p<0.05$). Mild functional disability (HAQ-DI value up to 1) was observed in 41% of patients with RA, moderate (HAQ-DI from 1 to 2) – in 38%, severe (HAQ-DI more than 2) – in 21%. The group of RA patients with CS had significant differences from the group without CS regarding HAQ-DI (Table 1.).

Table 1. Characteristics of the RA patients with and without CS regarding HAQ-DI.

	CSI<40 (n=109)	CSI>40 (n=59)	p
HAQ-DI (M±SD)	1.0 ± 0.6	1.9 ± 0.7	p<0.01
HAQ-DI ≤ 1, (n/ %)	61/ 55.9 %	8/ 13.6 %	
HAQ-DI 1 ≤ 2, (n/ %)	44/ 40.4 %	19/ 32.2 %	
HAQ-DI > 2, (n/ %)	4/ 3.7 %	32/ 54.2 %	

Notes: HAQ-DI - Health Assessment Questionnaire, CSI - Central Sensitization Inventory, P – the significance of differences between groups.

Finally, the strong correlation was determined between CSI and HAQ-DI (r=0,745; p≤0,01). Significant moderate correlations were also found between CSI and VAS pain (r=0,532; p≤0,01). We found that the presence of CS in patients with RA was associated with an increased risk of functional disability. Odds ratios are used to identify the risk of functional disorders in patients with CS. RA patients with CSI score ≥ 40 had an odds ratio of 6,97 [95% CI: 3,02 – 16,1] ($p < 0.0001$) for moderate functional disability and 21,3 [95% CI: 8,07 – 56,4] ($p< 0.0001$) for severe functional disability.

Conclusion: Central sensitization is common in RA patients. The phenomenon of central sensitization is associated with high level of functional disability of patients with RA and severity of pain. The phenomenon of central sensitization should be considered as a predictor of functional disability.

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Disclosure of Interests: None Declared.

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AB1372 PREDICTING ACUPUNCTURE EFFICACY IN FIBROMYALGIA: RESULTS OF A PRAGMATIC OPEN-LABEL STUDY

Keywords: Fibromyalgia

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Background: Fibromyalgia (FM) is a condition mainly characterized by the presence of chronic widespread musculoskeletal pain that affects a large proportion of the general population. Acupuncture, like other complementary and alternative medicines, is a patient-centered treatment and is generally well tolerated and appreciated by patients and the latest EUropean League Against Rheumatism (EULAR) recommendations on the management of FM made a weak recommendation for acupuncture in FM. To date, there is no study that indicates which variables predict response to acupuncture treatment in FM, either in terms of immediate response or persistence of response, and thus can enable the implementation of personalized treatment a prevention of therapeutic failure.

Objectives: The aim of this study is to identify the predictive factors of failure to acupuncture in patients with FM.
Methods: FM patients refractory to standard drug therapy (defining as standard drug theraphy the association of duloxetine and pregabalin) underwent eight weekly acupuncture sessions. Significant improvement, defined as a reduction of at least 30% of the FIQR, was assessed at the end of the eight weeks (T1) of treatment and three months after the end of treatment (T2). Univariate analysis was conducted to identify predictors of significant improvement at T1 and T2. Variables, which resulted significantly associated with clinical improvement at univariate analysis, were included in multivariate models.
Results: Analyses were conducted on 77 patients (9 males, 11.7%). At T1, significant improvement in FIQR was recorded in 44.2% of patients. At T2, significant improvement in FIQR persisted in 20.8% of patients. In multivariate analysis, predictive variables of treatment failure were tender point count (TPC) (odds ratio [OR] = 0.49, 95% confidence interval [95% CI]: 0.28 – 0.86, p = 0.01) and pain magnification (OR = 0.68, 95% CI: 0.47 – 0.99, p = 0.04) assessed with Pain Catastrophizing Scale, at T1. At T2, the only predictive variable of treatment failure was concomitant duloxetine use (OR = 0.21, 95% CI: 0.05 – 0.95, p = 0.04) (Table 1).

Table 1. Multivariate analyses considering the significant clinical improvement at the end of treatment (T1) and 3 months after the end of the treatment (T2) as dependent variable, independent variables the parameters that achieved statistical significance at univariate analyses.

T1			
Independent variables	Odds Ratio	95% CI	p
FIQR	1.00	0.96 - 1.05	0.88
PHQ15	0.95	0.83 - 1.09	0.47
PCS helplessness	0.92	0.76 - 1.13	0.43
PCS rumination	1.07	0.86 - 1.32	0.54
PCS magnification	0.68	0.47 - 0.99	0.04
PDQ VAS highest pain	0.91	0.53 - 1.55	0.72
PDQ VAS mean pain	1.06	0.64 - 1.77	0.81
TPC	0.49	0.28 - 0.86	0.01
T2			
Independent variables	Odds Ratio	95% CI	p
Duloxetin use	0.21	0.05 - 0.95	0.04
FIQR physical function	0.94	0.82 - 1.06	0.31
PCS helplessness	0.98	0.83 - 1.15	0.76
PCS magnification	0.75	0.50 - 1.12	0.16
TPC	0.69	0.40 - 1.19	0.18

Abbreviations. CI = confidence interval; BMI = Body Mass Index; FIQR = Revised Fibromyalgia Impact Questionnaire; PCS = Pain Catastrophizing Scale; PDQ = PainDetect Questionnaire; VAS = Visual Analogue Scale; TPC = Tender Point Count.

Conclusion: High TPC and a tendency for pain magnification predict immediate treatment failure, while duloxetine therapy predicts it three months after completion of the acupuncture course. The identification of clinical characteristics of unfavorable response to acupuncture could help to implement a cost-effective prevention of treatment failure in FM. The results of this study can provide a reference for the integration of a non-drug treatment such as acupuncture into the complex FM scenario.
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Acknowledgements: NIL.
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AB1373 ARE FIBROMYALGIA AND/OR DEPRESSION THE MOST COMMON DIAGNOSES SEEN IN ROUTINE RHEUMATOLOGY CARE, ALBEIT AS SECONDARY DIAGNOSES, BUT WHICH MAY COMPLICATE CLINICAL ASSESSMENT, PROGNOSIS AND MANAGEMENT?

Keywords: Outcome measures, Fibromyalgia

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Background: Fibromyalgia (FM) and depression (DEP) are common comorbidities in all primary rheumatic diagnoses, easily recognized in many patients, but often underestimated, particularly in patients who meet criteria for a primary rheumatic disease. Two screening indices to recognize FM and/or DEP are found within a 2-page multidimensional health assessment questionnaire (MDHAQ), FAST4 (fibromyalgia assessment screening tool) and MDS2 (MDHAQ depression screen) [1]. FAST4 agrees 90% with 2011 revised FM criteria, and MDS2 agrees 80% with reference HADS-D (hospital anxiety and depression scale–DEP).
Objectives: To analyze patients with different rheumatic diagnoses according to FAST4 and MDS2 as well as reference 2011 FM Criteria and HADS-D, to recognize those who screen positive for FM and/or depression.
Methods: The MDHAQ is a 2-page patient self-report questionnaire designed for routine care, completed by most patients with any diagnosis in 5-10 minutes at all visits to 2 academic rheumatology sites. The MDHAQ includes scores to calculate FAST4 and MDS2: the FM screen is positive (FAST4+) if 3/4 are present of: pain 0-10 visual numeric scale (VNS) ≥6/10, fatigue VNS ≥6/10, patient self-report 0-54 RADAI painful joint score ≥16/54, 60-symptom checklist (ROS) ≥16/60. The DEP screen is positive (MDS2+) if 0-3.3 DEP in the patient-friendly HAQ format is ≥2.2 OR DEP is + on ROS. The % of patients with various primary diagnoses, and % who screened positive or negative by FAST4, MDS2, 2011 revised FM criteria, or HADS-D was computed.
Results: Among 1,038 routine rheumatology care patients at 2 settings, 307 were FM+ by FAST4, 297 by 2011 FM criteria,295 DEP+ by MDS2, and 364 DEP+ by HADS-D. These prevalences were ≥28.0% according to FAST4 and MDS2 in all patients, as high as most prevalent primary ICD-10 diagnosis of 291 for rheumatoid arthritis (RA) (Table 1). Percentages of FM+ and DEP+ patients were within 12% for all diagnosis categories except for 6.3% of patients with primary FM (Table 1).
Conclusion: Non-somatic problems of FM and DEP are as common as any diagnosis seen in routine rheumatology care at 2 academic sites, albeit as secondary diagnoses in most patients. FM and/or DEP may complicate assessment, prognosis, and management of clinical status and explain poor responses to treatment in some patients. It is feasible to screen for FM and DEP on a single MDHAQ, completed by most patients in 5-10 minutes, as FAST4 and MDS2 indices, at any rheumatology site.
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Table 1. Number (%) of patients according to Primary ICD 10 diagnosis, and % positive by 2011 revised FM criteria fibromyalgia criteria, FAST4 (fibromyalgia assessment screening tool, HADS-D (hospital anxiety and depression scale–depression) and MDS2 (MDHAQ depression screen 2)

Primary ICD10 diagnosis	Number (%) of patients	n Percent MDHAQ FAST4 Positive	n Percent 2011 FM Criteria Positive	n Percent MDHAQ MDS2 Positive	n Percent HADS-D Positive
Total - all patients	1038 (100%)	307 (30%)	297 (29%)	295 (28%)	364 (35%)
Rheumatoid arthritis (RA)	291 (28%)	27%	22.7%	28.3%	32.5%
Osteoarthritis (OA)	131 (13%)	36.0%	32.8%	33.1%	41.7%
Fibromyalgia (FM)#	65 (6.3%)	76.6%	75.4%	52.3%	45.5%
All inflammatory diagnoses other than RA	436 (42.0%)	22.1%	22.0%	23.4%	31.2%
All non-inflammatory diagnoses other than OA and FM	115 (11.1%)	29.4%	35.7%	30.7%	47.1%

*The denominator is the total number of patients in the header of the column. The denominator for percentages in other columns is the total observations with non-missing specific variables for each row.# Fibromyalgia is according to primary physician diagnosis.

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Disclosure of Interests: None Declared.
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AB1374 ADVERSE EVENTS AFTER VACCINATION FOR SARS-COV2 IN A CASE SERIES OF FIBROMYALGIA PATIENTS VERSUS HEALTHY CONTROLS

Keywords: Fibromyalgia, Vaccination/immunization, COVID

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Background: Fibromyalgia (FM) is a chronic widespread pain syndrome of unknown origin that leads to hypersensitivity for physical, chemical and/or psychic triggers. Vaccination, as an inflammatory stimulus and as a psychologically stressful act, could represent a challenge for these patients.
Objectives: We aimed to investigate the incidence of adverse reactions after vaccination for Sars-Cov2 in a series of FM patients versus healthy controls.

Methods: We recruited 65 consecutive FM patients classified according to the 2016 ACR diagnostic criteria[1] (M/F: 5/60; mean age 53.6 +/-12.5 years), without other associated rheumatologic conditions, and 65 age/sex-matched healthy controls. All patients filled a questionnaire in order to investigate eventual adverse events occurring up to 6 months after administration of a Sars-Cov2 vaccine. The questionnaire was divided into two parts: the first part included the patient's demographic information, the vaccine type performed and the anamnestic data. In the second part, the individuals described all new symptoms or signs occurred after the first, the second or the third dose of Sars-Cov2 vaccine.
Results: Overall, FM patients reported a higher frequency of adverse events after Sars-Cov2 vaccination in comparison with healthy controls. In particular, 44/65 FM patients vs. 11/65 controls complained of exacerbation of diffuse pain ($p<0.001$). Fatigue, diarrhea, sweating, tingles, headache, dizziness, transient respiratory discomfort, and paroxysmal vision blurring were also more frequent in FM patients than controls (47/65 vs. 30/65, $p=0.004$; 6/65 vs. 0/65, $p=0.028$; 18/65 vs. 8/65, $p=0.047$; 20/65 vs. 0/65, $p<0.001$; 22/65 vs. 9/65, $p=0.013$; 21/65 vs. 5/65, $p<0.001$; 10/65 vs 1/65, $p=0.009$; 17/65 vs. 2/65, $p< 0.001$, respectively). No significant difference between FM and the control group as regards fever was reported (24/65 vs. 30/65; $p=0.7$). Interestingly, swelling at the injection vaccine site was more commonly reported in controls (9/65 vs. 20/65; $p=0.034$). Finally, one case of Bell's palsy was registered in the FM series while one case of myocarditis in the control group.
Conclusion: FM patients showed an increased frequency of adverse events to Sars-Cov2 vaccination compared to healthy controls. In particular, all the symptoms reported seemed to be associated with the functional hypersensitivity that characterizes FM.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1375 SHORT-TERM EFFECTIVENESS OF A MULTIMODAL TREATMENT PROGRAM FOR REFRACTORY CHRONIC PAIN SYNDROMES INCLUDING PRIMARY AND SECONDARY FIBROMYALGIA

Keywords: Fibromyalgia, Pain

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Background: Treatment-refractory Chronic Pain Syndromes (CPS) are highly heterogenous entities with a high socio-economic burden. Multimodal treatment programs combining physical and cognitive-behavioral interventions have shown promising results but definition of clinically relevant response remains challenging.
Objectives: To identify clinical endpoints and predictive factors for effectiveness of a multimodal CPS program.
Methods: Retrospective observational study with 201 patients (22 to 72 years old) with refractory CPS with or without concomitant inflammatory rheumatic disease participating in a 2-week inpatient program in a tertiary rheumatology center in Lausanne, Switzerland. The approach included: Intensive physiotherapy, chiropractic and osteopathy treatment, peripheral or spine infiltration (if appropriate), rheumatological assessment, occupational therapy, psychiatric assessment, group-based education, sleep assessment by actigraphy and virtual reality sessions. Patients with psychiatric or physical conditions affecting ability to follow the program were excluded. BPI (primary endpoint) plus 6 other standardized questionnaires were executed before and after program. Multivariable regression was performed between delta BPI and clinical and demographical characteristics.
Results: The descriptive analysis is compatible with patients with severe refractory CPS patients. 73.3% are women (48% > 50 years old), 33.8% are overweight, 30.6% are obese, 73.2% describe pain in childhood or adolescence, 14% have had multiple surgeries (≥ 3) related to pain, 89% report back pain (86% lumbar), 27.1% have a present or past clinical diagnosis of hyperlaxity, 78% met the 2010 ACR criteria for FM, 81% had FiRST>4, 73.8% received concomitant psychiatric diagnosis, alexithymia was diagnosed in 34%, 50.2% presented reduced sleep efficacy and 78.4% showed hyper-fragmented sleep. After the program, the majority of patients improved scores for ODI (51%), FABQ-P (57%), POAM-A (48,5%), BPI-S (51.5%), BPI-I (65.6%), HAS (55%), HDS (59%) and PCS (63.7%). 48.5% of patients improved POAM-P and 34% improved FABQ-W scores. Interesting, patients who improved in HDS often improved also in PCS and HAS (measures of affective stress). The same correlated variation did not occur between ODI and BPI impact (measures of function). TAMPA variation was slightly correlated with PCS.
Several variables associated with BPI in univariable analysis were excluded in the multivariable due to excess of missing data. Clinical and demographic variables associated with BPI-S in multivariable analysis were age ($p=0.007$), disability allowance ($p=0.062$) and post-traumatic stress disorder ($p=0.44$). For BPI-I the association were with clinically significant peripheric arthrosis ($p=0.001$), patient origin ($p=0.008$) and the diagnosis of a biomechanical disorder ($p=0.002$).
Conclusion: The present work suggests that multimodal pain programs should have other goals besides pain reduction, such as improving function, reducing fear of movement, reducing affective stress, and changing cognition and behavior associated with the persistence of pain. The above-mentioned questionnaires target these aspects and may be utilized as endpoints. Questionnaires addressing affective stress had interrelated variations so that composite scores can be proposed and should be tested in long-term. Abbreviations: 2010 American College of Rheumatology Fibromyalgia criteria (ACR-FM 2010), Brief Pain Inventory (BPI), BPI-Impact (BPI-I), BPI-Severity (BPI-S), Fear-Avoidance Beliefs Questionnaire (FABQ), FABQ-Physical (FABQ-P), FABQ-Work (FABQ-W), FM Rapid Screening Tool (FiRST), Hospital anxiety scale (HAS), Hospital depression scale (HDS), Oswestry Low Back Pain Disability Index (ODI), Pain Catastrophizing Scale (PCS), Patterns of Activity Measure (POAM), Tampa Kinesiophobia Scale (TAMPA).
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1376 CENTRAL SENSITIZATION IN AUTOIMMUNE CONNECTIVE TISSUE DISEASES: IS IT RELATED TO DISEASE ACTIVITY, COEXISTING FIBROMYALGIA, AND LABORATORY FINDINGS?

Keywords: Systemic lupus erythematosus, Sjögren syndrome, Pain

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Background: Central sensitization (CS) is a phenomenon associated with chronic pain disorders and may be seen in several rheumatic diseases with chronic musculoskeletal pain such as osteoarthritis, spondyloarthropathy, and fibromyalgia, but little is known about CS in patients with autoimmune connective tissue diseases (ACTDs).
Objectives: The purpose of the study was to investigate the role of CS in patients with ACTDs and how it relates to disease activity, coexisting fibromyalgia, and laboratory findings.
Methods: A total of 82 patients (mean age 49.2±13.1 years) with ACTDs were included and were divided into three groups in terms of their diseases: Sjögren's syndrome (SS), rheumatoid arthritis (RA), and systemic lupus erythematosus (SLE). The CS was assessed using the central sensitization inventory (CSI-A and CSI-B scores). The disease activity (using Sjögren's syndrome disease activity index, ESSDAI, for SS; Disease Activity Score-28 C-reactive protein, DAS28-CRP, for RA; and Systemic Lupus Erythematosus Disease Activity Index, SLEDAI, for SLE), pain intensity (using visual analog scale), coexisting fibromyalgia, and laboratory findings (erythrocyte sedimentation rate-ESR and C-reactive protein-CRP) of all patients were evaluated.
Results: CS were present in 39% of all ACTDs patients (57.1% in SS, 36.8% in RA, and 26.1% in SLE). No significant differences were found in the CSI-A score ($p = 0.161$) and CSI-B score ($p = 0.809$) among the groups. There was a significant correlation between disease activity and the CSI-A scores in patients with RA ($p = 0.027$, $r = 0.360$), but no significant relationship between disease activity and the CSI-A scores in SS ($p = 0.390$) or SLE patients ($p = 0.179$). CSI-A and CSI-B scores were higher in the coexisting fibromyalgia in patients with ACTDs ($p = 0.002$, $p < 0.001$, respectively). There is no significant relationship between CSI-A scores and laboratory findings (ESR, CRP) in patients with ACTDs ($p > 0.05$).
Conclusion: CS is seen as a common condition in patients with ACTDs who also have fibromyalgia and is related to the disease activity in patients with RA. In addition to specific pharmacological treatments, pain-coping strategies may reduce pain and increase the quality of life of patients with these conditions. It is essential to increase awareness about the important role played by CS pain in patients with ACTDs.
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Table 1. Comparing the central sensitization and coexisting fibromyalgia in different autoimmune connective tissue diseases

	SS group (n=21)	RA Group (n=38)	SLE group (n=23)	p value
CS positive, n (%)	12 (57.1)	14 (36.8)	6 (26.1)	0.101[a]
CSI-A, median (IQR)	41 (31-58)	28 (21-49)	31 (19-44)	0.161[b]
CSI-B, median (IQR)	0 (0-1)	0 (0-1)	0 (0-1)	0.809[b]
Coexisting fibromyalgia, n (%)	5 (23.8)	6 (15.8)	1 (4.3)	0.182[a]

SS, sjögren's syndrome; RA, rheumatoid arthritis, SLE, systemic lupus erythematosus, IQR, interquartile range[a]Chi-squared test[b]Kruskal-wallis Test

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1377 **FELDENKRAIS AWARENESS THOUGH MOVEMENT INTERVENTION FOR FIBROMYALGIA SYNDROME: A PROOF-OF-CONCEPT STUDY**

Keywords: Physical therapy/physiotherapy, Fibromyalgia, Non-pharmacological interventions

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Background: The Feldenkrais Method is a form of awareness through movement (ATM) which aims at increasing awareness about spatial and kinesthetic relationships among body segments and the environment thought verbally guided movements [1]. Fibromyalgia syndrome (FM) is a form of chronic widespread pain associated to a variety of ancillary symptoms, among which fatigue, sleep disturbances and regional pain syndromes are preponderant. Lately, increasingly more attention has been drawn on mind-body interventions and meditative movement therapies for FM treatment [2]. ATM application for chronic pain has been promising but with low quality studies [3,4].
Objectives: The aim of this study was to explore the effectiveness of ATM for FM patients after 4 months of ATM activity; in particular, the proof-of-concept design aims at determining the domains for which an ATM-based intervention may be effective for FM patients.
Methods: This is a proof-of-concept, observational, non-controlled prospective study which lasted 6 months. Participants were recruited by the Italian Fibromyalgia Syndrome Association (AISFOdv), a non-profit patient organization, through social media advertising. After signing the informed consent, they were divided into eleven groups of eleven/twelve patients each. Two Feldenkrais teachers were assigned to each group. All patients attended an ATM course lasting 15 lessons, with a lesson every week, 1.5 h long (from January to May, 2021). The sessions were entirely virtual platform- based and live. Clinimetric tests and patient-reported outcome tests were administered at baseline and at the end of the intervention.
Results: One hundred twenty-eight FM patients (mean age 54 years old, 2% males) participated in the study. A statistically significant improvement was found in FM-specific measures (Polysymptomatic Distress Scale, PDS) (p=0.003) and the Pain Catastrophization Scale (PCS) (p=0.020); coherently, the amelioration in the Revised Fibromyalgia Impact Questionnaire (FIQR) almost reached statistical significance (p=0.08). The logistic regression analysis found a correlation between PDS, fatigue and anxiety measures; PCS, years from diagnosis and anxiety.
Conclusion: In conclusion, ATM could improve FM-specific measures and pain-related catastrophizing. Improving awareness about one's one body and movements through ATM sessions may have helped FM patients to improve their cognitive attitude towards their pain condition, embracing a more positive, hence less catastrophizing attitude; furthermore, ATM could benefit FM patients because of its induction of muscular relaxation [5]. Further studies are needed to identify FM subgroups in order to find personalized targets that can be used to guide treatments.
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AB1378 **TITLE: BENEFIT OF GROUP MEDICAL VISITS IN THE MANAGEMENT OF FIBROMYALGIA**

Keywords: Fibromyalgia, Diet and nutrition, Non-pharmacological interventions

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Background: Fibromyalgia (FM) is a chronic condition characterized by widespread pain, fatigue, sleep disturbances and mood disorders (depression and anxiety)[1]. While there is no cure for Fibromyalgia, non-pharmacologic integrative modalities have been demonstrated to be effective improving clinical outcomes[3]. Group medical visits (GMV) have been used to integrate self-management skills and to deliver education to improve outcomes in patients with chronic diseases.[4-5] There are scant reports of the use of GMV in the management of patients with rheumatic diseases. The goal was to assess the benefit of GMV in patients diagnosed with Fibromyalgia (FM).
Objectives: We conducted a pilot study to assess the benefits of group medical visits (GMV) among patients with Fibromyalgia. Our primary objective was to improve outcomes by educating patients and demonstrating five integrative techniques: breath work, journaling, mindfulness, movement, and nutrition.
Methods: Patients diagnosed with Fibromyalgia participated in a series of group appointments. The four consecutive monthly sessions included: (1) an introduction to the series and demonstration of breathing techniques and journaling; (2) a presentation of the benefits of movement and participation in Tai Chi session; (3) an overview to mindfulness and guided meditation; (4) a discussion regarding the biosome, nutrition, and elimination diets. Our clinical outcome measures included: The Fibromyalgia Impact Questionnaire (FIQ score), Personal Health Questionnaire Depression Scale (PHQ8) and Multi-Dimensional Health Assessment (MDHAQ). We took measurements at baseline and following completion of the last appointment. Our analysis consisted of a paired t-test to determine whether the mean difference between the baseline and follow-up outcomes was statistically significant.
Results: The average baseline and follow up measures were as follows: FIQ 61.5 to 50.3(CI -15.8 - 4.3, p-value 0.0011), PHQ8 10.7 to 6.5 (CI -5.8 - -2.1, p-value 0.0001) and MDHAQ 16.4 to 13.59(CI -4.9 - -1.5, p-value 0.0006), respectively. All measurements were statistically significant.
Conclusion: Our findings suggest that group medical visits are a valuable, beneficial, efficacious and cost-effective way to deliver care and information to patients with fibromyalgia. GMV's facilitate education, provide social support and most importantly, improved clinical outcomes.
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Table 1.

	Number of Patients	Baseline Module 1	End Module 4	Mean change	Lower 95% CI	Upper 95% CI	P Value
FIQ	**28**	**61.5**	**50.3**	**-10.1**	**-15.8**	**-4.3**	**0.0011**
PHQ 8	**28**	**10.7**	**6.5**	**-3.9**	**-5.8**	**-2.1**	**0.0001**
MDHAQ	**28**	**16.4**	**13.59**	**-3.2**	**-4.9**	**-1.5**	**0.0006**

Measurement of the 3 outcomes measures analyzed, (FIQ, PHQ 8 and MDHAQ) at baseline and at the end of the fourth module. All the measurements were statistically significant

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Disclosure of Interests: Jose A. Pando Speakers bureau: Sanofi.
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Lilly, Catherine Welton: None declared, Susan Griffith: None declared, Oriana Pando: None declared.

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AB1379 MICROBIOTA AND MITOCHONDRIAL IMBALANCE IN FIBROMYALGIA: A PILOT STUDY

Keywords: Fibromyalgia, Biomarkers

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Background: Fibromyalgia (FM) is a widespread chronic disease characterized by chronic pain and fatigue that has a strong impact on the quality of life of patients, who represent the 6% of the world population. There is no molecular analysis FM condition, being currently diagnosed through clinical self-questionnaires. Since FM patients present a strong lack of energy and several gastrointestinal disturbances, the relationship between the microbiota-mitochondrial axis could be a relevant mechanism [1]. The intestinal microbiota has a great impact on health and energy balances. When the distribution is altered, intestinal dysbiosis appears and the majority of the dysbiosis-related conditions are strongly related to FM [2]. As a result, some authors have pointed to the intestinal microbiota as the main player in FM [3]. The intestinal microbiota works as an intermediary in the final goal of provide energy to cells through the production of ATP, the core task of mitochondria. This organelle is especially abundant in tissues such as muscle and brain, both affected by the etiology of FM [4]. In addition, many studies have highlighted the involvement of mitochondrial imbalances and oxidative stress in patients with FM [5]. Interestingly, crosstalk between mitochondria and microbiota is implicated in inflammation [6], a hallmark of FM.

Objectives: To characterize intestinal microbiota composition and mitochondrial balance in a cohort of FM patients.

Methods: A group of 26 patients (7 men and 19 women) diagnosed with primary FM according to the ACR criteria where selected. Intestinal microbiota composition was determined by qPCR of some central genera as well as secretory IgA levels. Mitochondrial mass was determined by western blot in peripheral blood mononuclear cells protein (PBMC) to detect mitochondrial mass and mitophagy biomarkers. Additionally, Total Antioxidant Capacity (TAC) was measured with e-BQC lab (Bioquochem, Asturias, Spain), an electronic device that oxidizes the samples by applying an electrochemical current.

Results: *Roseburia* spp./*Eubacterium* spp. ratio is shifted to *Roseburia* species, and *Akkermansia muciniphila* has lost its representativeness. Additionally, more than half of the patients presented sIgA values below the reference range. Lastly, the mitochondrial ratio showed a mitochondrial imbalance in most of the patients, which had higher mitochondrial mass.

Conclusion: The results suggested an imbalanced intestinal microbiota and mitochondrial ratio in FM. These results open up a wide range of possibilities, both to develop treatments and diagnostic techniques for the disease.

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AB1380 ASSESSMENT OF OPTIC NERVE AND MACULA FINDINGS WITH OPTIC COHERENCE ANGIOGRAPHY IN FEMALE PATIENTS WITH FIBROMYALGIA AND ITS RELATION WITH DISEASE SEVERITY

Keywords: Fibromyalgia

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Background: Fibromyalgia syndrome is a chronic disorder characterized by widespread pain, fatigue, sleep disturbances and cognitive dysfunction. The pathophysiology is still unknown, however, sympathetic dysfunction, central and peripheral sensitization, neuroendocrine anomalies, psychosocial factors can be counted as possible mechanisms. In recent years vascular changes and perfusion anomalies of brain, neuroretina changes have been reported.

Objectives: To evaluate the optic nerve and macula findings in female fibromyalgia patients compared with healthy controls and investigate the relations with disease severity.

Methods: Sixty-two female fibromyalgia (FMS) patients with a mean age of 43.11±7.94 years and sixty female healthy controls with a mean age of 40±12.26 years were included. Fibromyalgia was diagnosed according to the American College of Rheumatology Criteria. Schirmer and tear break up time (BUT) test were recorded. Choroidal thickness, optic nerve head blood flow area, retinal nerve fiber layer was measured with optic coherence tomography angiography (OCTA). Widespread pain index (WPI), symptom severity scale (SSS), tender point count, Fibromyalgia impact questionnaire (FIQ) were recorded.

Results: BUT test findings were lower in FMS patients compared to healthy controls and the differences were statistically significant ($p<0.0001$). There were no significant differences in Schirmer test and intraocular pressure findings between FMS patients and healthy controls ($p>0.05$). Optic disc total and peripapillary densities of FMS patients were found to be higher than healthy controls ($p<0.05$). Choroidal thickness, inner retina perifoveal thickness values of FMS patients were higher than healthy controls ($p<0.05$) but in outer retina foveal thickness values of patients were lower than healthy controls ($p<0.05$). In addition, foveal avascular zone (FAZ) and nonflow area were found to be enlarged in FMS patients compared to the healthy controls ($p<0.05$). There were weak positive correlations between fibromyalgia severity scale and choroidal thickness values, optic disc total and peripapillary densities and FAZ area. In addition, there were weak negative correlations between fibromyalgia severity scale and BUT test values.

Conclusion: Due to the known increase in inflammation in FMS patients, we found choroidal thickness and vascular density values around the optic disc to be higher than in the healthy control group. In addition, we found that FAZ and nonflow area values were enlarged compared to the control group, consistent with ischemia due to vascular damage in FMS patients. We found a significant correlation between all these values and the fibromyalgia severity scale values. In conclusion, we think that the results we evaluated with OCTA measurements are useful in detecting damage to retinal and optic disc vascular structures in FMS patients.

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AB1381 **SLEEP QUALITY AND PAIN CHARACTERISTICS IN PATIENTS WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS, AND OSTEOARTHRITIS**

Keywords: Rheumatoid arthritis, Pain, Spondyloarthritis

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Background: Pain is a cardinal symptom of chronic rheumatic conditions and can involve nociceptive and non-nociceptive (neuropathic) components that may be linked to central sensitization. Poor sleep quality has been connected to central sensitization and the appearance of neuropathic pain in patients with chronic rheumatic conditions.
Objectives: We aimed to investigate pain characteristics and sleep quality in adult patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS), and osteoarthritis (OA).
Methods: We conducted a prospective observational study including patients with RA, AS and OA who were evaluated in the Rheumatology Department of the Clinical Rehabilitation Hospital of Iasi between July-December 2022. We excluded patients with diabetes mellitus, neoplasia, and comorbid neurological conditions. We evaluated pain intensity using the visual analog scale (VAS) and pain characteristics using the PainDETECT questionnaire (PD-Q). Sleep quality was assessed using the Pittsburg Sleep Quality Index (PSQI).
Results: The final study group included 152 patients (50 RA, 52 AS, and 50 OA) with a mean age of 59 years. PD-Q scores did not differ significantly in the three subgroups. In patients with RA, PD-Q scores correlated with disease activity (DAS28 and CDAI; p=0.008 and p=0.036), whereas the relationship between BASDAI and PD-Q scores approached statistical significance (p=0.056). PD-Q scores were correlated with pain intensity in AS (p=0.037), but not RA or OA (p=0.421, p=0.393). In RA patients, nociceptive pain was significantly more prevalent compared to AS and OA (p<0.001) and was associated with a higher consumption of symptomatic medication during hospitalization. Neuropathic pain was notably more frequent in AS compared to RA (p<0.001) and OA (p<0.001). Neuropathic pain did not lead to significantly higher medication expenses in our study group. In the RA subgroup, PD-Q scores were significantly correlated to total PSQI (p<0.001), as well as the values for each of the PSQI domains. Moreover, in these patients, pain intensity was connected to poor subjective sleep quality, low sleep efficiency, and sleep disturbance. Total PSQI scores were also correlated with DAS28 (p=0.011). In AS patients, total PSQI was linked to PD-Q scores (p<0.001), but not pain intensity. PD-Q was significantly connected to subjective sleep quality, sleep latency, sleep duration, sleep efficiency, and sleep disturbance in AS. In the OA subgroup, pain intensity was associated with total PSQI (p=0.007), subjective sleep quality, sleep latency, sleep duration, and sleep efficiency. Nevertheless, poor sleep quality was not significantly linked to neuropathic pain in the OA group.
Conclusion: Non-nociceptive pain is frequent in patients with chronic rheumatic conditions. Moreover, non-nociceptive pain may impact activity score values in AS and RA. Poor sleep quality is connected to pain intensity and non-nociceptive pain in patients with RA and AS. Sleep quality was not linked to neuropathic pain in OA patients. Pain remains a key symptom in rheumatic diseases and its management remains a challenge for the clinician, especially in the context of central sensitization.
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AB1382 **IMPACT OF CENTRAL SENSITIZATION ON PAIN IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES**

Keywords: Inflammatory arthritides, Pain

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Background: Pain in chronic inflammatory rheumatism (CIR) is polymorphic; nociceptive, neuropathic and central sensitization (CS) may be involved. The International Association for the Study of Pain (IASP) defines central sensitisation as « Increased responsiveness of nociceptive neurones in the central nervous system to their normal or sub-threshold afferent input » (1) Chronic inflammation can play an important role in this CNS hyperexcitability. During CIR pain may persist, despite objective control of inflammation suggesting the involvement of SC phenomena.
Objectives: The objective of this study is to detect the impact of central hypersensitivity phenomena on pain in patients suffering from CIR. A second objectif is to look for other factors associated with this central sensitization.
Methods: This is a cross-sectional study that included all patients aged ≥ 18 years followed up for chronic inflammatory arthritis (SPA, RA, undifferentiated CIR) presenting to the rheumatology department.Patients with psychiatric or memory disorders or who refused to participate in the study were excluded. Sociodemographic data, comorbidities and treatments received were collected.Nociceptive pain was assessed by visual analogue scale (VAS),disease activity by DAS-28 and ASDAS and central sensitization by the validated Moroccan version of the Central Sensitization Inventory part A (CSI-A). This inventory has 2 parts: Part A measures a range of 25 somatic and emotional symptoms associated with central sensitization, scored from 0 (never) to 4 (always), for a possible total score of 100. Part B concerns the recording of previous diagnoses related to central sensitization (not used in our study). A CSI-A score ≥ 40 was the threshold considered for the definition of CS. The Pain catastrophizing scale (PCS) was used to assess pain-related catastrophic thoughts and the PHQ-9 (Pain Health Questionnaire) to assess the severity of depressive symptoms.
Results: We included a total of 189 patients, 107 (56.61%) had rheumatoid arthritis, 67 (35.45%) spondyloarthritis and 15 (7.94%) undifferentiated inflammatory arthritis. The median duration of the disease course was 8 years [4-17], the mean age was 47.49 ± 13.70 years [14.74], 75.7% were women. The mean pain VAS was 4.77+-2.76 and 50.8% had a strong or moderate activity. The mean central sensitization score was 37.42+- 16.75, with 44.9% having a CSI score≥40.For treatments 38.2%of patients were on corticosteroids and 6.3%were using biological treatment. In uni and multivariate analysis,the parameters associated with CS were pain severity (0.039) and depression (≤0.001) A statistically significant correlation was found between the CSI-A score and pain VAS (r=0.32 p <0.001)
Conclusion: Pain in patients with CIR has often been attributed to peripheral inflammation. However, our study suggests that central sensitization may increase pain intensity independent of disease activity. Screening for central sensitization mechanisms in patients followed for CIR seems necessary to guide management by targeting central pain in order to avoid useless therapeutic switches and escalations, sometimes even harmful for our patients.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1383 **A STUDY ON THE CLINICAL PROFILE OF PATIENTS WITH HYPERMOBILE JOINTS**

Keywords: Pain

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Background: Hypermobile joints are a common yet under-recognized cause of noninflammatory joint pains. Patients with Hypermobile joints display a range of movement that is considered excessive, considering their age, gender, and ethnic background [1]. Hypermobile joints may be asymptomatic or associated with pain, fatigue, multisystemic complaints, and significant disability. In this study, we look at the clinical profile of patients with hypermobile joints who presented to our clinic.
Objectives: To study the clinical profile of patients with Hypermobile joints.
Methods: This is a prospective observational study. Patients who presented to our clinic (from 2018 to 2022) with musculoskeletal complaints with a Beighton score of 4 without concomitant inflammatory arthritis were selected. Clinical data were collected by doctors/trained nursing professionals using a proforma, and demographic and relevant clinical data were collected and analyzed.

Results: 236 patients were studied(203 females and 33 males).The mean age of patients was 41.6 years (±12.7 SD). The median duration of symptoms was 48 months (1 540 months) Median Beighton score was 7. The mean global VAS was 4(± 2 SD). Associated clinical features were as in Table 1. Criteria for Fibromyalgia(2016 revised criteria) were satisfied by 31% of patients. Total Beighton score showed a negative correlation with age (r= 0.334, p<0.05)

Conclusion: People with joint hypermobility-related disorders present a wide range of symptoms that extend across multiple body sites. Symptomatic hypermobile joints are present across all age groups. In our study, most patients presented with pains, especially in the form of dragging pains and cramps. An increase in joint stiffness with age leads to a decrease in the Beighton score, which should be considered to not miss hypermobility in the elderly. Extraarticular features of hypermobility give a clue to diagnoses of hypermobility in those with low Beighton scores. Often these patients are labeled as having fibromyalgia. In our study, 31% of patients satisfied the criteria for fibromyalgia. Hypermobile Joint Syndrome should be considered in patients presenting with nonspecific noninflammatory pains across multiple body sites in all age groups.

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Table 1. Associated clinical features in patients with Hypermobile Joints

Signs and symptom	No of patients (Percentage of patients) N= 236
Joint pain	192 (81)
Fatigue	169 (71.6)
Clicking sensation in joints	154 (65)
Muscle cramps	144 (61)
Dragging pain	143 (60)
Early morning stiffness	101 (42.4)
Paraesthesia	87 (37)
Scoliosis	83 (35)
Striae	69 (29)
Varicose veins	65 (27)
High arched palate	61 (26)
Cutaneous laxity	44 (19)
Joint dislocation	18 (7)
Hernia	15 (6)

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Disclosure of Interests: None Declared.

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AB1384 BENEFITS OF PHYSIOTHERAPY RESOURCES IN FIBROMYALGIA

Keywords: Fibromyalgia, Non-pharmacological interventions, Physical therapy/physiotherapy

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Background: In patients with fibromyalgia, the physiotherapist is essential in the treatment. He will act throughout the patient's rehabilitation process, from the application of initial assessment instruments to full recovery.

Objectives: Check the performance and benefits of physiotherapy resources in the current scientific literature for patients with fibromyalgia.

Methods: A literature review was carried out in the databases Scientific Electronic Library Online (SciELO), Latin American and Caribbean Literature in Health Sciences (LILACS), Medical Literature Analysis and Retrieval System Online (MEDLINE), Scopus, Web of Knowledge ISI, Physiotherapy Evidence Database (PEDro), Excerpt Medical Database (Embase), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Library, and SPORTDiscus for articles dated March 2012 to March 2022. The terms fibromyalgia AND (physiotherapy OR "physiotherapy" OR rehabilitation) were used as keywords in English, Portuguese and Spanish. The searches were not limited to titles and abstracts, we chose to leave them free, appearing in all fields of the articles. In addition, some specific physiotherapy interventions were manually searched. The articles were searched in all indicated databases and then the main information was read and collected and then analyzed descriptively.

Results: Physical therapy interventions have shown positive therapeutic effects on fibromyalgia. Among the different interventions, aerobic and resisted physical exercises are the most indicated and widely used. With regard to manual therapy, myofascial release, connective tissue massage, manual lymphatic drainage and Shiatsu produce good results. Electrophysical agents are also used in the clinical practice of physiotherapists who assist individuals with this disease. The use of complementary therapies has increased and evidence shows that acupuncture, diet, herbal medicine, homeopathy, massage and supplements show promise for managing pain associated with various musculoskeletal conditions. Health education is essential and recommended for individuals with fibromyalgia. This type of intervention should promote the optimization of care through the physiotherapist's guidance to the individual, guiding him on how to control pain and deal with problems associated with his lifestyle. As such, combining multiple therapies (including exercise) to devise an optimal treatment plan for different individuals would be an important developmental step for treating fibromyalgia in the future.

Conclusion: There are several physiotherapeutic interventions that can be chosen to improve the health and quality of life of patients with fibromyalgia. Something very important is to always associate rehabilitative techniques with the patient's health education. In Brazil there is a program that was created called "Amigos de Fibro", an interdisciplinary educational program that seeks to promote the health of individuals with fibromyalgia and has shown promising results.

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AB1385 SUBOPTIMAL IDENTIFICATION AND MANAGEMENT OF NON-NOCICEPTIVE TYPES OF PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS REGARDLESS THE ACTIVITY STATUS

Keywords: Rheumatoid arthritis, Fibromyalgia, Pain

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Background: Pain represents one of the main clinical symptoms of Rheumatoid Arthritis (RA) being used as an indicator of disease activity. However, many RA patients reports clinically significant levels of pain even in the periods of remission. Recent studies [1] revealed that biological treatments are inequal in terms of how they manage inflammation and pain. The concept of Post-Remission Syndrome was defined in the context presence of residual pain in RA patients that are in clinical remission but still present clinical symptoms that impairs their quality of life [2]; the syndrome might be a reason for decreased work productivity [3,4]. Apart of the nociceptive pain previous works identified neuropathic and nociplastic pain in the composition of residual pain. In order to better understand and manage this situation is paramount important to identify and explain the exact nature of pain present during and after the periods of activity in RA.

Objectives: The present study intended to explore the quality of pain assessment and management in subjects with RA in a major tertiary clinic.

Methods: In a major tertiary clinic of rheumatology consecutive subjects with RA have been questioned about the history, evolution and management of their disease; separately the level of nociceptive, neuropathic and nociplastic (fibromyalgic) pain was evaluated by using validated instruments. For a better understanding of the differences, we included and compared subjects with osteoarthritis and other inflammatory rheumatic diseases.

Results: 43 subjects have been evaluated in a 6 months interval with a 2:1 F:M ratio; 22 of them received biological therapy (8 different molecules have been

identified). Although 32 subjects did not present any sign of inflammation 21 of them declared significant level of pain (VAS>4), 12 have identified with neuropathic pain and 11 with nociplastic pain. Both in case of neuropathic and nociplastic pain groups less than 50% have been previously actively evaluated for non-nociceptive pain. Non-nociceptive pain was poorly treated and prolonged anti-nociceptive pain treatment was used despite evident lack of effect. The variable ability of pain reduction of biological DMARDs has not been previously discussed with any subject; the subject of residual pain was also poorly covered during biological drug selection.

Conclusion: Non-nociceptive pain has the potential to be considered a major reason of residual pain in RA and non-RA subjects. Rheumatologists seems to be captured in the paradigm of nociplastic = inflammatory pain with little interest in other types of pain that results in suboptimal diagnostic and management of pain.

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AB1386 THE ROLE OF OBSESSIVE-COMPULSIVE TRAITS IN FIBROMYALGIA: ARE OBSESSIVE THOUGHTS OF PAIN CORRELATED WITH PAIN INTENSITY AND ASSOCIATED WITH FUNCTIONAL IMPAIRMENT?

Keywords: Fibromyalgia, Pain, Mental health

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Background: Fibromyalgia syndrome (FMS) is defined as a chronic pain syndrome that is characterized by widespread pain, tenderness, and diffuse stiffness. In addition, neuropsychological symptoms such as fatigue, sleep disorders, poor mood, cognitive impairment, and headaches are often reported. Many researches had demonstrated the coexistence of affective disorders and anxiety with FMS, yet few focused on its association with obsessive-compulsive disorder (OCD).

Objectives: We investigated the occurrence of classical patterns of OCD in patients with FMS and assessed their effect on pain perception and functional impairment.

Methods: The research population included 37 patients diagnosed with FMS, and treated at the Rheumatology Clinic in the Sheba Medical Center, Tel-Hashomer, Israel. We used validated questionnaires including a demographic questionnaire, assessment of average and maximal pain intensity, the Eysenck Personality Questionnaire – Revised (EPQ-R(, the Perceived Stress Scale, the Pain Catastrophizing Scale, the Pain Obsessive questionnaire, and the Yale–Brown Obsessive Compulsive Scale (Y-BOCS).

Results: Patients with FMS were found to have intrusive and obsessive thoughts regarding pain for several hours every day, causing a high degree of anxiety and high levels of pain, catastrophizing, and magnification, leading to helplessness and functional impairment. Twenty-seven percent of the patients reported severe malfunction due to pain and pain ideation, and 49% demonstrated mild obsessive-compulsive symptoms that were strongly correlated with pain intensity and functional impairment.

Conclusion: Obsessive-compulsive thinking patterns contribute to pain magnification and to the cognitive aspects of Fibromyalgia syndrome.

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AB1387 A RARE CAUSE OF PES ANSERINE BURSITIS: TIBIAL EXOSTOSIS: THREE CASE REPORTS

Keywords: Imaging, Bone diseases, Pain

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Background: Pes anserine bursitis is a syndrome causing pain at the medial knee and the proximal medial tibia [1]. Sartorius, gracilis, and semitendinous tendons attach 5 cm distal to the medial knee joint line taking a shape is called pes anserinus. It is more common obese females with knee osteoarthritis between 50-80 years of age [1]. Rarely, tibial bone spurs present as rose thorns and cause pes anserinus bursitis and knee pain [2].

Objectives: In this case report, we presented proximal tibial exostosis which randomly detected and resulting to pes anserinus syndrome in three patients.

Methods: Case 1 (NB): A 58-years-old female patient was admitted to our outpatient clinic with right knee pain. She had pain for 2 months, increasing with standing and walking. In the physical examination, she did not describe any trauma, the area where the pes anserinus tendons attached to medial proximal tibia was painful. There was no swelling and redness on the skin. A bone spur from the proximal tibial metaphysis was seen in the right knee on direct radiography (Figure 1). Case 2 (BE): A female who 22 years-old, was admitted to our outpatient clinic with left knee pain, which was for 5 months. The skin appearance above the knee was normal. There was no swelling. Medial left proximal tibia was tender with palpation. Physical examination was normal. The blood tests of the patient were completely normal. A spur like as a rose thorn forming from the proximal tibial region was observed in the left knee, similar to the first case, on the direct radiography (Figure 2). Case 3 (GB): A 64-year-old female patient was admitted to our outpatient clinic with pain in the medial left knee. Her complaint was present for 6 months. There was no history of trauma. Knee joint range of motion was normal. There was no effusion in knees. Mc-Murray test was negative. There was a minimal sweelling and tenderness on pes anserine region. A bone exostosis was observed in the left medial tibia on the direct radiography requested from the patient.

Results: The Case 1 was told to rest for two weeks and not to walk much. Non-steroidal anti-inflammatory drug therapy and 10 minutes cold application to the knee per 6 hours were recommended. At the follow-up one month later, the visual analog scale (VAS) score was regressed from 7 to 2. Non-steroidal anti-inflammatory drug was started to Case 2 and activity restriction was recommended. At the follow-up two weeks later, VAS score decreased from 6 to 4. 1 ml of methylprednisolone was injected locally to the pes anserinus region of Case 3. One month later, the patient's VAS score decreased from 7 to 1.

Conclusion: Rarely, pes anserine bursitis may be accompanied by medial tibial exostosis. The clinicians must be keep in mind proximal tibial spurs in patients presenting with knee pain and pes anserinus bursitis.

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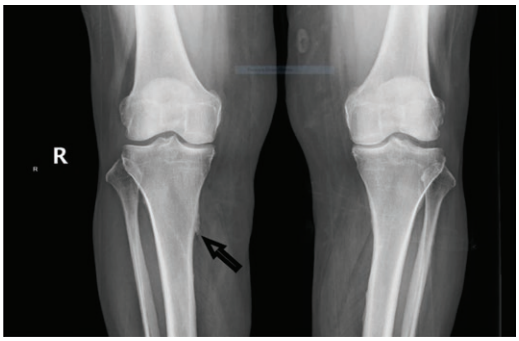


Figure 1.

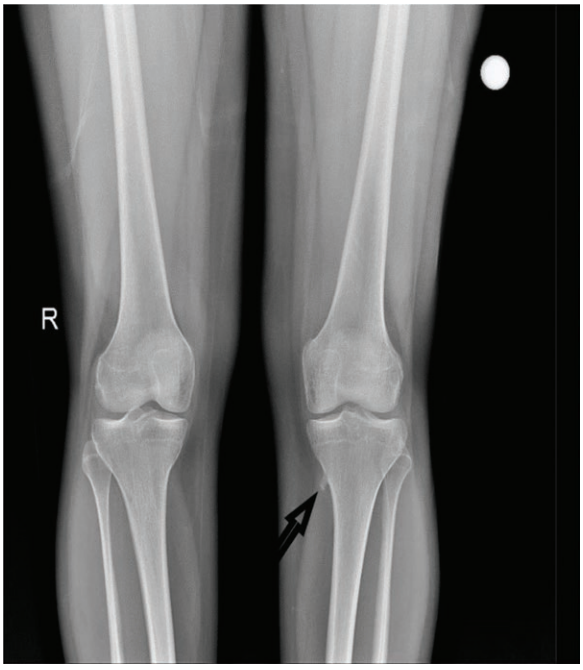


Figure 2.

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AB1388

SEVERE FIBROMYALGIA: DO CENTRAL SENSITIVITY MECHANISMS WORK TOGETHER?

Keywords: Fibromyalgia, Pain, Patient reported outcomes

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Background: Fibromyalgia (FM) is among the most common causes of diffuse chronic pain and falls into the category of central sensitivity syndrome which may be associated with other symptoms such as asthenia, sleep disturbance, bowel and memory disorders, anxiety and depression.
Objectives: We aimed at evaluating in a hospital based setting which of these symptoms were more commonly associated with disease severity.
Methods: cross-sectional evaluation of consecutive patients with a diagnosis of FM according to the ACR criteria [1] who attended the dedicated outpatient clinic between 2020 and 2022. Clinical symptoms including disease duration, demographic characteristics, education level, lifestyle, clinical and laboratory parameters and therapeutic regiment were collected for each patient as well as Pros Questionnaires-"*Italian-Fibromyalgia impact questionnaire (FIQR), Widespread Pain Index (WPI), Symptom Severity Scale (SSS)*- [2][3] Disease severity was defined as FIOR>64. Categorical and continuous variables were compared between patients with FIQR ≤ 64 and those with FIQR>64, using descriptive statistics (Chi squared test/ Fisher test and Mann-Whitney test). Thereafter, a logistic regression having as dependent variable FIQR>64 was carried out.
Results: 187 patients were included. Patients with FIQR >64 (severe disease), had a higher frequency of bowel symptoms/irritable bowel syndrome, menstrual cycle alteration or endometriosis, headache and depression, compared to those with FIQR≤ 64, (Table 1). At univariate analysis, the variables statistically associated with FIQR > 64 were: male gender (OR 0.38; 95%CI 0.13-1.08), active smoking (OR 1.97; 95%CI 0.92- 4.25), depression (OR 4.95; 95%CI 2.32-8.76), bowel symptoms (OR 1.96; 95%CI 1.09-3.53), sicca syndrome (1.71; 95%CI 0.92-3.20), and more than 4 episodes of headache each month (OR 2.22; 95%CI 1.21-4.08). In the multivariate model, the variables independently associated to FIQR >64 were depression (OR 4.95; 95%CI 2.36- 10.39) and more than 4 episodes of headache/month (OR 2.28; 95%CI 1.11-4.70).
Conclusion: Patients with severe FM more frequently present with headache, depression, irritable bowel syndrome and dysmenorrhea. All those symptoms belong to the family of central sensitivity syndromes, suggesting that some central sensitivity mechanisms play a key role in disease activity and severity.

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Table 1. Baseline characteristics of the fibromyalgia patient population

	FIQR<=64	FIQR>64	p
	81	106	
middle age	48.9(13.2)	47.78 (10.6)	0.23
males	11 (13)	6 (6)	0.06
disease time, media (SD)	7.6(8.5)	8.0(7.3)	0.20
BMI, media (SD)	26.2 (4.2)	25.7 (4.7)	0.46
WPI, media (SD)	**10.3 (4.8)**	**13.7 (4.1)**	**<0.001**
SSS, media (SD)	**7.4 (2.3)**	**10.1(1.6)**	**<0.001**
WPI-SSS, media (SD)	**17.8 (5.9)**	**23.5 (5.0)**	**<0.001**
alterations of bowel movements	**34 (42)**	**61 (59)**	**0.024**
Irritable bowel syndrome	**27 (33)**	**51 (49)**	**0.032**
Asthenia	72 (89)	54 (89)	0.89
Xerostomia o xerophthalmia	24 (30)	42 (42)	0.08
Dysmenorrhoea e/o endometriosis*	**7 (10)**	**18 (20)**	**0.006**
headache >4 episodes per month	**37 (48)**	**70 (67)**	**0.009**
Depression	**30 (42)**	**76 (77)**	**<0.001**
Antidepressants	**24 (31)**	**49 (45)**	**0.022**
Analgesic drugs	**16 (20)**	**39 (38)**	**0.012**
Pilates	**1(1)**	**8 (8)**	**0.046**
Cognitive-behavioural therapy	**1(1)**	**11 (11)**	**0.011**

Data expressed as frequency (percentage) unless otherwise specified. * Variables calculated only for female subjects

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AB1389

DO PATIENTS WITH LOW BACK PAIN AND CENTRAL SENSITIZATION SHOW DIFFERENCES IN PHYSICAL PERFORMANCE?

Keywords: Pain

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Background: Common low back pain is a common reason for rheumatology consultation. Advances in neuroscience concerning pain have advanced its understanding in chronic musculoskeletal pathologies, in particular low back pain, The role of central sensitization (CS) on physical activity remains understudied.
Objectives: The objective of our study is to investigate the role of central sensitization in patients with low back pain and its impact on their physical performance.
Methods: This is a cross-sectional study that included any patient ≥ 18 years with low back pain presenting to the rheumatology department. Patients with psychiatric or memory disorders or who refused to participate in the study were excluded. Functional capacity was assessed by the Oswestry score (Oswestry Disability Index); a 10-item self-assessing questionnaire, each item contains 6 levels of answers that can be scored from 0 to 5. A total score is calculated, percentage of disability ranges from 0% (no disability) to 100% (complete disability). The interpretation of this scale is based on the scores: from 0 to 20%: minimal disability; from 20 to 40% moderate disability; from 40 to 60%: severe disability; from 60 to 80% crippling low back pain and beyond 80% the person is confined to bed.

The physical performance of the patients was assessed by the 6-minute walk test (6MWT), catastrophizing by the PCS (Pain Catastrophizing Scale) and the CS by the validated Moroccan version of the Central Sensitization Inventory Part A (CSI-A). This inventory has 2 parts: Part A measures a range of 25 somatic and emotional symptoms associated with central sensitization, scored from 0 (never) to 4 (always), for a possible total score of 100. Part B concerns the recording of previous diagnoses related to central sensitization (not used in our study). A CSI-A score ≥ 40 was the threshold considered for the definition of CS.
Results: We included 118 patients. The average age was 53.01+-14.09, 86.4% of the patients were women and 88.7% had comorbidities. The median duration of evolution was 8 [2-10] years. The mean pain VAS was 5.75+-2.07 and 71.5% of patients had an Oswestry score >20.The average score of CS was 42.16+-17.67 while 53.4% had a CSI-A ≥ 40 The average walk test result was 377.64+-154.15 meters. There was no statistically significant difference between patients with CSI-A ≥40 and CSI-A <40 with regard to the performance of the 6MWT (362.67 Vs 394.87, p=0.094). On the other hand, there was a statistically significant difference between the two groups with regard to the pain VAS (6.00 Vs 5.47), p=0.017) and PCS score (33.03Vs 22.08, p=0.001)
Conclusion: Central sensitization does not seem to affect the physical performance of Moroccan patients with low back pain.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1390 MULTICOMPONENT NATURE OF PAIN SYNDROME IN PATIENTS WITH RHEUMATIC DISEASES AND ITS RELATIONSHIP WITH CLINICAL CHARACTERISTICS

Keywords: Spondyloarthritis, Pain, Rheumatoid arthritis

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Background: Pain is one of the leading clinical manifestations and a criterion of severity in most patients with rheumatic diseases. However, pain is not always inflammatory, and its intensity does not correlate with disease activity and dysfunction.
Objectives: To study the specifics of pain syndrome in patients with rheumatoid arthritis and ankylosing spondylitis.
Methods: 78 patients with immunoinflammatory diseases were studied, 30.8% with rheumatoid arthritis (RA) and 68.2% with ankylosing spondylitis (AS). The average age was 42 [34.5; 59.5]. Among AS patients 80.8% were men and 19.2% were women, while 100% of RA patients were women. DAS28 and ASDAS were used to rate activity in patients with RA and AS, respectively. High activity was observed in 69.3% of patients, moderate activity in 23.1%, and low activity in 7.6% of the cases; 23.1% of patients had functional class I, 34.6 – class II, 34.6% - class III, and 7.7% - class IV. The mean disease duration was 194.6±103.2 months, with a median of 192 [114;258] months. A neurological examination was performed to detect neuropathic pain (NP), and its severity was assessed using the pain DETECT questionnaire (PD); the relationship between pain and central sensitization (CS) was determined using the Central Sensitization Inventory (CSI); quality of life was assessed using the questionnaire EQ-5D. The collected data were analyzed with the IBM SPSS Statistic 26.0 program. Spearman correlation analysis was used to assess the relationship between the studied indicators; differences were considered statistically significant at p<0.05.
Results: All of the patients in the study had chronic inflammatory pain in their joints and/or back, and 69.3% of them also had non-inflammatory pain: 38.4% had NP, and 50% had pain typical of CS. There was no significant correlation between the presence and severity of NB and/or CS and the patient's age, disease duration, indices of RA and AS activity, or patient's gender. In the group of patients with RA, NB prevailed, while CS prevailed in the group of patients with AS. The PD questionnaire yielded a positive result in 53.9% of all patients, 41.2% in AS, and 87.5% in RA. A positive moderate correlation was found between the PD and laboratory indicators of inflammation (ESR and CRP) (rSp=0.445; p=0.026), pain intensity according to VAS (rSp=0.470; p=0.018), however, there was no correlation with global functional status. According to CSI, a positive result was observed in 50% of all patients, 52.9% in AS and 44.4% in RA. CSI results positively correlated to pain intensity according to VAS (rSp=0.699; p=0.001), and a negative moderate correlation was found with EQ-5D index (rSp=-0.659; p=0.001). Comorbidities were observed in 61.5% of patients: osteoporosis – in 38.5%, arterial hypertension (AH) – in 30.8%, anemia – in 38.5% of patients. Comorbidities were present in 41.7% of patients with CS and 71.4% with a positive PD index. AH occurred in 46.2% with CS and in 16.7% without CS. Anemia correlated to PD and CSI indices (rSp=-0.536; p=0.006 and rSp=-0.692; p=0.001, respectively); a negative correlation between hemoglobin levels and the VAS scale was also observed (rSp=-0.541; p=0.005). The presence of CS was found to have a negative correlation with the use of anti-inflammatory therapy (NSAIDs, DMARDS and corticosteroids).
Conclusion: The majority of patients (69.3%) with immunoinflammatory diseases have pain of mixed origin; additionally, in RA, it is more due to the neuropathic component, whereas in AS, it is CS. Pain intensity as measured by VAS was significantly higher in patients with neuropathic and central pain components, as expected. In patients with NB and CS, laboratory activity is higher, and comorbid pathology, anemia, and AH are more common. Patients with a concomitant central component of pain have a significantly lower quality of life. Thus, when examining patients with RA and AS, a detailed description of the pain syndrome is required, followed by a differentiated approach to analgesic therapy.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1391 RELATIONSHIP BETWEEN BODY MASS INDEX AND FIBROMYALGIA

Keywords: Fibromyalgia

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Background: Fibromyalgia (FM) is a clinical condition characterized by chronic widespread pain associated with symptoms such as fatigue, waking unrefreshed, depression. Several studies reported a relationship between high body mass index (BMI) and painful syndromes such as FM, but the real impact of a high BMI on clinical severity in patients with FM is still unclear. Furthermore, FM is characterized by a neuropathic component of pain. Obesity and overweight seem to get worse the intensity of neuropathic pain.
Objectives: The aim of this study was to evaluate the relationships between BMI categories and FM related symptoms, investigating fatigue, neuropathic pain, depression and sleep disorders.
Methods: We analyzed a cohort of 419 patients (M 15/ F 404, median age 56), with a diagnosis of FM according to the 2016 ACR criteria. The participants were consecutively recruited from the Fibromyalgia clinic of the University of Campania "Luigi Vanvitelli". All patients were stratified into three groups according to BMI categories: normal weight (18,5-24,9), overweight (25,0-29,9) and obesity (>30,0). We assessed fatigue by Functional Assessment of Chronic Illness Therapy-Fatigue Subscale (FACIT-F), neuropathic pain by PainDETECT Questionnaire (PDQ), depression by Patient Health Questionnaire-9 (PHQ-9) and sleep disorders by Pittsburgh Sleep Quality Index (PSQI).
Prism GraphPad software was used; the level of significance was set at $p < 0.05$.
Results: Total patient population (n=419) had a mean BMI 26,64 (SD 5,768); all patients showed fatigue (100%) with a mean FACIT-F score 23,01 (SD 10,15); we found neuropathic pain (PDQ>20) in 301 patients (71,83%) with a mean PDQ score 22,95 (SD 8,935); 52 patients (12,41%) had no depression (PHQ-9 <4), 68 patients (16,23%) showed a mild depression (PHQ-9 10-14), 121 patients (28,88%) a moderate depression (PHQ-9 15-19) and 140 patients (33,41%) a severe depression (PHQ-9 ≥20) with a mean PHQ-9 score 15,53 (SD 7,704); sleep disorders were found in 360 patients (85,91%) with a mean PSQI score 11,28 (SD 6,117). 155 (37%) normal weight patients (mean BMI 22,13) (SD 1,672) had a mean FACIT-F score 20,14 (SD 10,52), a mean PDQ score 17,93 (SD 9,740), a mean PHQ-9 score 11,62 (SD 8,266) and a mean PSQI score 8 (SD 6,330); 161 overweight patients (38,4%) (mean BMI 27,15) (SD 1,400) had a mean FACIT-F score 22,64 (SD 9,983), a mean PDQ score 24,33 (SD 7,831), a mean PHQ-9 score 15,54 (SD 6,809) and a mean PSQI score 11,57 (SD 4,978); 103 obese patients (24,6%) (mean BMI 34,80) (SD 5,320) had a mean FACIT-F score 27,96 (SD 7,808), a mean PDQ score 28,34 (SD 4,136), a mean PHQ-9 score 21,43 (SD 2,953) and a mean PSQI score 15,76 (SD 4,150). For each of the FM symptoms investigated the results were statistically significant (p *value* < 0.0001) between the category of obese and both normal weight and overweight patients, but not statistically significant (p *value* > 0,05) between the category of normal weight and overweight patients.
Conclusion: Our study suggests that obesity is a risk factor for Fibromyalgia severity. Obese patients had higher FACIT-F, PDQ, PHQ-9, PSQI scores than normal weight patients. Therefore, according to these findings, a Fibromyalgia treatment program should include weight loss strategies. Anyway further studies are needed to investigate the association between BMI and Fibromyalgia.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5356

Spine, mechanical musculoskeletal problems, local soft tissue disorders

AB1392 **GENETICALLY PREDICTED APOLIPOPROTEIN B IN RELATION TO SYSTEMIC SCLEROSIS**

Keywords: Systemic sclerosis, Diet and Nutrition, Genetics/Epigenetics

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by progressive skin and internal organ fibrosis and has significant clinical sequelae [1]. Apolipoprotein B and E are found in two major subgroups of LDL [2]. Apolipoprotein E can be used as a predictor of SSc.[3] Apolipoprotein B is involved in autoimmunity [4]. However, whether apolipoprotein B is associated with SSc remains unestablished.
Objectives: We performed a two-sample Mendelian randomization (MR) analysis to investigate the causal relationship between apolipoprotein B and SSc.
Methods: Statistics on apolipoprotein B were obtained from a genome-wide association study (GWAS) from the UK Biobank, which included 349,376 samples of European ancestry. A total of 182 single nucleotide polymorphisms (SNPs) were selected as genetic instruments, which satisfied linkage disequilibrium ($r2 < 0.001$ and clump window > 10,000 kb) and related to apolipoprotein B ($P<5\times10\text{-}8$). Summary-level data for SSc (107 cases and 218,499 controls) were derived from the FinnGen consortium. The inverse-variance weighted (IVW) method was used as the primary statistical model. The weighted median and MR-Egger regression were used as supplementary analyses to supplement the validation of IVW results. The Cochran Q-test was applied to check SNPs' statistical heterogeneity using MR-Egger estimates, with $P < 0.05$ deemed significantly heterogeneous. The leave-one-out method was used to evaluate the effect of a single SNP on the causal association by excluding each SNP in turn.
Results: Genetically predicted apolipoprotein B was inversely associated with SSc risk (odds ratio (OR):0.51, 95% confidence interval (95% CI):0.26-0.98, P=0.04). MR-Egger also confirmed that apolipoprotein B was inversely associated with SSc risk (P=0.02). No heterogeneity was detected in Cochran's Q statistic. The intercept in the MR-Egger regression indicated no pleiotropy in any analysis (all P values>0.05), suggesting this finding was reliable. Details of the results are shown in Fig. 1.

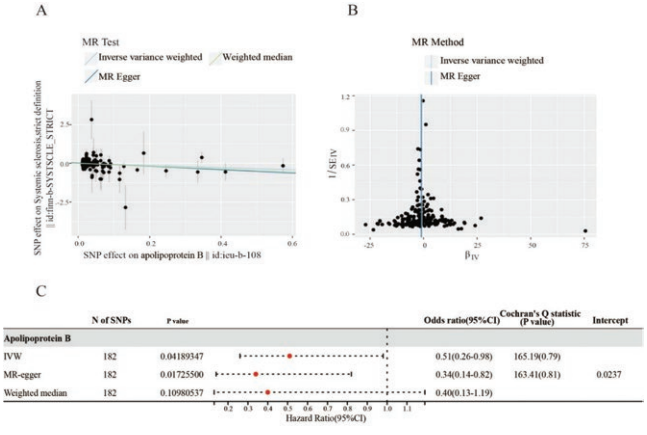


Figure 1. Scatter plots (A) and funnel plots (B) show the estimated effect of each SNP on the result. Forest plot (C) of the relationship between apolipoprotein B and SSc.

Conclusion: Apolipoprotein B is a protective factor for SSc, indicating that apolipoprotein B may be used as a component of drugs to treat SSc and slow down the development of SSc.
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AB1393 **CLINICAL AND MRI PREDICTIVE FACTORS OF SIGNIFICANT RESPONSE TO A TREATMENT COUPLING CAPSULAR DISTENSION AND INTENSIVE REHABILITATION IN PATIENTS WITH SEVERE ADHESIVE CAPSULITIS**

Keywords: Rehabilitation, Imaging, Real-world evidence

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Background: Adhesive capsulitis (AC) is a frequent shoulder affection[1] and is responsible of a significant impact on daily life. However, its management is not codified, with contradictory results in the literature on the effectiveness of capsular distension (CD), probably due to the lack of selection of patients in the studies. Furthermore, MRI has shown interest in the positive diagnosis of AC in difficult cases and to determine the stage of the disease[2].
Objectives: The aim of the study was to determine clinical and MRI predictive factors of good response to CD in patients with severe AC.
Methods: Patients addressed to physical medicine and rehabilitation unit in Cochin Hospital with a severe AC were prospectively included in the study between May 2017 and June 2021. Severe AC was defined by presence of intense shoulder pain (Numerical Analog Scale of maximal pain in daily activities ≥ 5/10) lasting for at least 3 months, with failure of first-line treatment – including NSAIDs, analgesics corticosteroid injection and physiotherapy. Participants had before treatment protocol a shoulder MRI with and without gadolinium intravenous injection. All participants then underwent 1 to 3 CD with injection of betamethasone at the same time at weekly intervals, each followed by intensive rehabilitation. Patients were evaluated 1 month after the 1st CD by a physiotherapist, who collected information on pain and range of motion and self-reported patient questionnaire. Primary outcome was the reduction of more than 50% of pain in daily activities evaluated by NAS at 1 month, by a multivariate logistic regression model. Secondary outcomes were the modification of NAS nocturnal pain, NAS incapacity, active and passive range of motion, SPADI, quick DASH, HAD and FABQ scores, and return to work at 1 month.
Results: 97 patients were included in the study. Of these, 72 (74.2%) were women, mean age was 51.2 (+/- 7.29) years, median disease duration was 8 [6-12] months and was greater than 9 months in 41 (42.3%) of patients and 62 (63.9%) had a secondary form of AC. Mean NAS pain in daily activities was 7.88 (+/- 1.47) at baseline and 4.32 (+-/ 2.68) at 1 month. 46 (47.4%) filled out the primary outcome and were considered as treatment responders. The multivariate model adjusted for age, sex, work interruption because of AC, initial shoulder traumatism, disease duration greater than 9 months, DASH score, NAS pain at baseline, and MRI thickness of the rotator interval (millimeters) found an association between response to treatment and disease duration < 9 months (OR 2.27 95% CI [1.00-5.26] p = 0.05), DASH score at baseline (OR 0.96 (per point) 95% CI [0.93-0.98] p = 0.03) and MRI thickness of the rotator interval (OR 1.65 (per millimeter) 95% CI [1.04-2.62] p = 0.04). No association was found with the injected MRI criteria.
Conclusion: This study provides original results on predictive factors of response to CD associated with intensive rehabilitation in patients with AC. It found an association of response to treatment and lower DASH score at baseline, shorter disease duration and MRI thickness of the rotator interval and offers suggestions for better patient selection to CD.
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Table 1. ***Multivariate logistic regression model: factors associated with response to treatment (CD + intensive rehabilitation)***

	Univariate analyses		Multivariate analyses	
	Crude HR 95% CI	p	Adjusted HR 95% CI	p
Age	1.07 [0.99-1.15]	0.06	1.04 [0.99-1.11]	0.14
Male gender	0.31 [0.09-1.05]	0.06	0.94 [0.37-2.35]	0.89
Currently working	1.31 [0.49-3.48]	0.60	1.62 [0.82-3.65]	0.24
Initial traumatism	0.51 [0.15-1.72]	0.28	0.86 [0.33-2.23]	0.75
Disease duration < 9 months	**3.85 [1.35-11.10]**	**0.01**	**2.27 [1.00-5.26]**	**0.05**
DASH score at baseline	**0.95 [0.92-0.98]**	**0.01**	**0.96 [0.93-0.98]**	**0.03**
NAS maximal pain in daily activities at baseline	0.98 [0.81-1.18]	0.81	0.96 [0.82-1.12]	0.63
MRI thickness of rotator interval (mm)	**1.80 [1.02-3.17]**	**0.04**	**1.65 1.04-2.62]**	**0.04**

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5125

AB1394 INTRADISCAL CUTIBACTERIUM ACNES DECIDE ON INNATE AND ADAPTIVE IMMUNE PATHWAYS IN MODIC TYPE 1 CHANGES

Keywords: Adaptive immunity, Innate immunity, -omics

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Background: Modic type 1 changes (MC1) are painful vertebral bone marrow (BM) edema of unclear etiology. Besides mechanical aspects, animal studies show the plausibility for two biological etiologies. In the bacterial etiology, *Cutibacterium acnes* (*C. acnes*) invades damaged intervertebral discs (IVDs) resulting in IVD infection and endplate damage. IVD-derived pro-inflammatory cytokines and virulence factors can consequently drain into the adjacent BM and induce an inflammatory response. In the autoimmune etiology, IVD and endplate damage expose immune privileged IVD cells and matrix to BM leukocytes, which react with an autoimmune response.
Objectives: To show that intradiscal *C. acnes* load is decisive for the pathomechnisms in MC1 bone marrow.
Methods: In a first study population, degenerated IVDs adjacent to a MC1 and not adjacent to a MC1 lesion were collected and *C. acnes* copy numbers/gram tissue (CCN) were quantified. The upper 99 % confidence interval (CI) limit in the control group was defined as threshold that distinguishes the two etiologies. From a second study population of MC1 patients, a MC1 and an intra-patient control BM aspirate, and the MC1 adjacent IVD was obtained from each patient. IVD CCN were determined, the etiology was assigned, and bulk RNA sequencing from total BM cells was performed. MC1 gene expression was normalized to intra-patient control and then compared between etiologies. Differentially expressed genes (DEGs) ($p < 0.01$, log2 fold-change > |0.5|) were identified and gene set enrichment analysis (GSEA) was performed. From a third study population, BM aspirates and IVDs were obtained. IVD CCN were quantified, ten pro- and anti-inflammatory and pro-fibrotic BM plasma proteins were quantified with ELISA, and RNA sequencing of $CD45^+CD66b^+$ sorted BM neutrophils was performed. BM plasma protein concentrations were clustered and compared between cluster with Mann-Whitney test, and overrepresentation analysis (ORA) of DEGs between MC1 and intra-patient control BM neutrophils was determined.
Results: Of the first study population, the median CCN of control IVDs (n = 10) was 388 (interquartile range (IQR): 118-685)) and the upper 99 % CI limit was 870. MC1 IVDs (n = 30) had similar median CCN overall (Mann-Whitney: p = 0.29, 464 (229-1614)), but eleven samples (36 %) had > 870 CCN (2659, (899-12900)), which was unique to MC1 IVDs and indicated a bacterial etiology (**Fig. 1a**). From a second study population, three MC1 patients from the bacterial (the three with the lowest CCN) and three from the autoimmune (the three with highest CCN) etiology were selected. Bulk RNA sequencing revealed 222 DEGs between the bacterial and the autoimmune etiology. GSEA showed enriched "neutrophil mediated immunity" and "granulocyte activation" in the bacterial and "adaptive immune response", "B- and T-cell activation" in the autoinflammatory etiology, pointing towards innate immune system contribution in the bacterial, and adaptive immunity in the autoimmune MC1 etiology (**Fig. 1b**). In the third population, MC1 to intra-patient control normalized BM plasma protein concentrations of the ten measured proteins were visualized using UMAP dimensionality reduction technique. Thereby, two patient clusters could clearly be distinguished (**Fig. 1c**). To identify whether clusters represented patients of different etiologies, CCN were compared between clusters and found to differ strongly (cluster 1: 351, (325, 387) vs. cluster 2: 2848, (1355, 3339)). Cytokine analysis between clusters showed upregulated neutrophil associated cytokines in cluster 1 vs. cluster 2 (IL-8: 16 pg/ml, (1, 54) vs. -15 pg/ml, (-21, -11), p = 0.004; ENA-78: 91 pg/ml (-5, 456) vs. -25 pg/ml, (-137, -21), p = 0.048), and a BM neutrophil "defense response to bacterium" in cluster 1, but not in cluster 2, further supporting that clusters represent different etiologies.

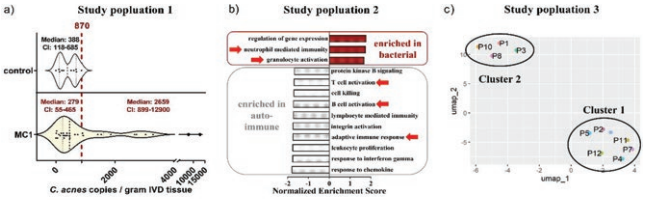


Figure 1: a) *C. acnes* copy number distribution. b) GSEA between etiologies of total cells. c) Cytokine clustering.

Conclusion: We show that IVD *C. acnes* load is decisive for the etiology-specific MC1 pathomechanisms. This has important clinical implications, as different MC1 etiologies might require different treatment strategies.
REFERENCES: NIL.
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AB1395 UROLITHIN A AND B ACCELERATE MYOCYTE FUSION INTO MYOTUBES

Keywords: -omics, Sarcopenia, Cell biology

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Background: Urolithins are intestinal bacterial metabolites of ellagic acid, from pomegranate and nuts. They modulate oxidative-regulated pathways and display anti-inflammatory, antioxidative properties. Several studies indicate that they could be inducers of muscle strengthening.
Objectives: The aim of this in vitro study was to investigate their mechanisms of action at plasma concentrations on primary human myotubes.
Methods: Urolithin A and B (UA and UB) were evaluated separately on primary human muscle CD56+ cells, isolated from the vastus lateralis of 6 men and 3 women (aged range 55 to 96-y) and differentiated in myotubes. 24h-treatment mRNA-sequencing of these 9 patients was studied by DESeq2 analysis (R software). Modulation of several target genes was then validated in several concentrations (1-5 or 10 µM) by RT-qPCR and ELISA on 4 different patients. Organelles and cell morphology changes were observed by NanoLive CX-A live cell imaging during 72h.
Results: After 24h of treatment at 5 µM, UA and UB significantly modified the expression of 1779 and 319 genes, respectively (adjusted p-value of 0.01 and Log2FoldChange |>0.32|). Among the most regulated genes, we found genes involved in myoblasts to myotubes differentiation. UA increased the expression of MYMX (+70%), PANX1 (+50%), MSTN (+64%), MYH2 (+28%) and conversely decreased FGF9 (-75%), MRLN (-33%), ICAM5 (-52%) and TGFBI (-55%). Regarding UB, it decreased IGFN1 (-75%), TGFBI (-60%) and increased MYH2 (+34%) and TGM2 (+59%). However, UA, but not UB, decreased DMD gene expression (-86%), a key factor in muscle strength, and MEF2C (-45%), a regulator of skeletal myogenesis. We also have observed the modulation of genes involved in the inflammatory process. They both induced a important decrease

of CYP1B1 expression (-95%). Further, LIF was increased by 80% by UA and PTGS1 was decreased by 41% by UA and 43% by UB. UA and UB had the opposite effect on IL17B, a cytokine involved in tissue repair but its role in muscle is still to be defined. IL17B was decreased by 49% by UA and conversely upregulated by 45% by UB. In a second step, we confirmed the modulation of MYMX, PANX1, FGF9, ICAM5, PTGS1-PGE2, IL17B and TGFBI following UA and/or UB treatment at 1, 5 and 10 µM by RT-qPCR and ELISA. Finally, we also observed with live cell imaging that UA and UB increased myocyte fusion in myotubes, already after 6h of treatment.

Conclusion: UA and UB promote the differentiation process of myoblasts to myotubes. In parallel, urolithins present anti-inflammatory properties, mainly by reducing CYP1B1 expression and the PGE2 synthesis via PTGS1, but also for UA by increasing LIF. Our data provide a better understanding of urolithin activities and highlight their potential in the treatment of muscle disorders such as sarcopenia.

References: NA.

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Disclosure of Interests: Yves Henrotin Consultant of: Artialis SA Nestlé Expanscience Tilman Allegro Immubio, Cécile Lambert: None declared, Antoine Florin: None declared, Jérémie Zappia: None declared, Prescilia Centonze: None declared, christelle sanchez: None declared.

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AB1396 FUTURE OF HIP CARTILAGE PRESERVATION: A ANGLE ENDPOINTS OPTIMIZE INDICATIONS FOR CONSERVATIVE CARE

Keywords: Cartilage, Prognostic factors, Imaging

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Background: In the context of osteoarthritis (OA) prevention, great attention is given to hip preservation surgery [1]. Patients with femoroacetabular impingement (FAI), a highly prevalent painful condition, are at increased risk of developing OA [2]. However, an undefined fraction of these patients manage to get rid of clinically significant OA with conservative care [3]. Recently, we realized that α angle can be a key to define which patients would benefit from conservative care and which of these should undergo surgery to prevent clinically significant OA.

Objectives: This meta-analysis aimed to answer: i) "does α angle predict the degree of hip chondral health in FAI?" and ii) "what are the α angle endpoints that correspond to each group of degree of chondral health?."

Methods: We followed the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA). Two independent reviewers performed the study selection and data extraction steps. Databases were screened: Embase, MEDLINE/PubMed, SCOPUS, SPORTDiscuss and The Cochrane Library. Good quality primary studies that, by using regressions and other similar statistical tests, assessed the capability of α angle values in predicting the degree of hip chondral health for patients with FAI were considered eligible. Risk of bias was assessed through the QUIPS tool. We conducted a pooled linear regression in order to establish α angle endpoints correlated to each chondral health group.

Results: Twelve studies were considered eligible for bias assessment. We found a high risk of bias due to misreporting and the presence of confounders in 2 studies, which were then excluded from analysis. A summary of the included studies' reported findings is in the Table 1. All 10 included studies demonstrated that α angle predicts the degree of chondral health, with good to excellent effect sizes. For the pooled analysis, 447 patients were enrolled. As the severity of chondral deterioration increases from 1 to 4 in an Outerbridge scale, the corresponding α angle endpoints are 56°, 61°, 65° and 72°- respectively (R^2 = 0,987; p <.001) (Figure 1).

Conclusion: The α angle is a good tool to identify FAI patients who are at higher risk of developing clinically significant OA without surgical intervention. In order to prevent clinically significant OA, we recommend that patients with an α angle greater than 65° should undergo surgery - since they are at high risk of developing significant chondral damage associated with OA progression.

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[3] DJ Hunter et al., BMC Musculoskelet Disord 22 (1), 697 (2021)

Table 1.

Author	Mean Age	N	α Angle Measurement	Chondral Health Scale	Findings
Bisciotti	39	41	45°-Dunn view (DV)	Outerbridge	**Logistic regression, ROC curve:** predictive value of the α angle for severe cartilage damage was 81° p < 0.05
Grace	36	46	DV	Beck	**Spearman:** increasing α angles correlated with less hip chondral health r: 0.61; p <.001
Heyworth	30	118	Tomography	ALAD	**Kendall Tau:** increasing α angles correlated with less hip chondral health r: 0.37; p <.001
Kapron	37	100	DV	Beck	**Logistic regression:** adjusted odds of severe chondral damage increased with greater alpha angle values OR = 1.06; p = 0.02
Ishøi	35	1511	Undefined	Beck	**Logistic regression:** OR = 2.2 between severe chondral damage and an 55°< α <78°, with an OR = 4.8 when α ≥78°
Martínez	37	155	DV	MAHORN	**Logistic regression:** Patients with severe chondral damage had greater α angle RR = 5.2; p <.001
Ortiz	37	2701	DV	Outerbridge	**2-tailed Student:** More severe chondral damage for the α angle ≥78° group 39% vs 16%; p <.001
Beaulé	38	180	DV	Beck	**Pearson:** greater α angle was independently associated with increased odds of having severe chondral damage OR = 1.04; p = 0.01
Shapira	37	1485	DV	Outerbridge	**Logistic regression:** every additional degree in α angle was associated with a 6% increase in the odds of severe chondral damage OR = 1.06; p = 0.02
Tang	33	71	AP view	MAHORN	**Logistic regression:** α angle > 70° was a significant risk factor for severe chondral damage OR = 8.84; p = 0.049

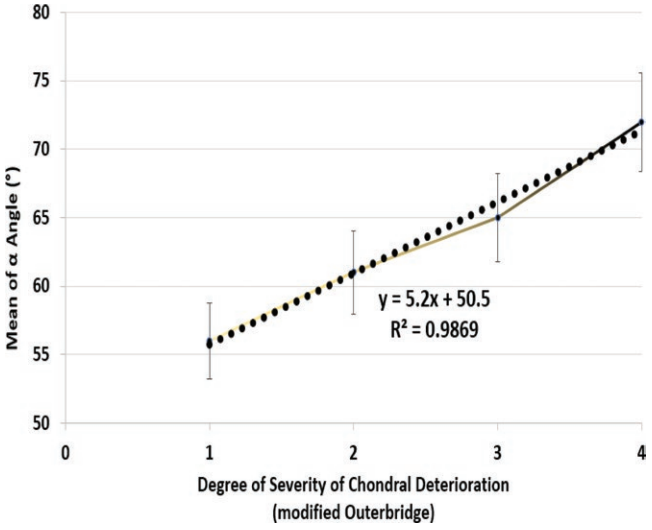


Figure 1.

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Disclosure of Interests: None Declared.

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AB1397 SERUM MASS SPECTROMETRY IDENTIFIES APOLIPOPROTEIN D AS POTENTIAL BIOMARKER FOR MODIC TYPE I CHANGES

Keywords: Pain, Diagnostic Tests, Biomarkers

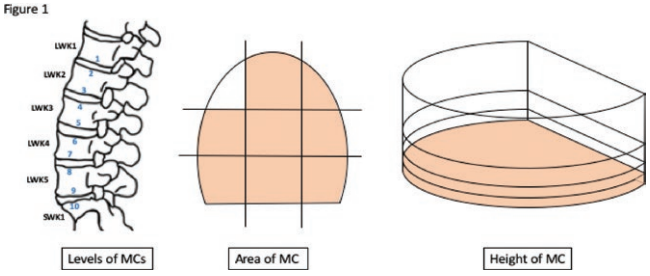
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Background: Modic changes (MC) are inflammatory vertebral bone marrow lesions adjacent to degenerative intervertebral discs [1]. On MRI, three types can be distinguished: Modic types 1 – 3 changes (MC1, MC2, MC3). Especially MC1 are associated with low back pain (LBP), and the larger the lesion, the stronger is the association with pain [3]. However, in clinics, MC is often a binary (present/absent) observation with insufficient inter-observer reliability in identifying and classifying MC.
Objectives: The aim of our study was to find potential serum biomarkers for the presence or the extent of MC using data of the Northern Finland Birth cohort of 1966 (NFBC1966) [2].
Methods: We selected 103 participants of the NFBC1966 to form 4 groups: With and without MC, and with and without LBP. For each participant with MC, we had information about the type, number, location, height, and transverse area (TA) of the MC. Height was given in 4 groups: "along the endplate", "> 25%," "25-50%" and "<50% of the height of the vertebral body". TA was measured in 1/9 parts of the vertebral endplate surface of a fictitious 3x3 grid (Fig. 1). We defined the MC load for each person and MC type as the sum of the product of height and TA of each MC. The serum samples were subjected to a sequential window acquisition of all theoretical mass spectra (SWATH-MS) analysis. To find a potential biomarker for the presence of each MC type we compared serum concentrations of proteins identified by mass spectrometry between participants with and without MC using Mann-Whitney-U tests. Performance to predict MC was calculated with Receiver Operating Characteristics (ROC). A covariate analysis for significantly different proteins was done with a ANCOVA. To find a potential biomarker for the extent of MC, we searched for associations between serum concentration and MC-load with Spearman's logistic regression. We corrected for multiple comparisons with False Discovery Rate (FDR).
Results: Of the 103 participants, 49 had MC, 54 had no MC (noMC). Of the participants with MC, 5 (10.2%) had only MC1, the others had multiple types of MC. 30 (61.2%) had MC1, 43 (87.7%) had MC2 and 40 (81.6%) had MC3. The average number of MC per person was 3.0 (1 – 9). The MC load, calculated from number, area, and height of the MC-lesions, was on average highest for MC2 (12.33, 95% CI: 9.0 – 15.6) followed by MC3 (11.26, 95% CI: 8.0 –14.5) and MC1 (7.0, 95% CI: 3.5 – 10.6). Serum Mass Spectrometry identified 1087 proteins. Of these, only the concentration of Apolipoprotein D (APOD) was significantly different between MC1 and noMC (Mann-Whitney-U-Test, FDR-adjusted p= 0.034). A covariate analysis with ANCOVA showed that this was independent of LBP. There was no significant result for MC2 or MC3 after correction for multiple comparisons. The ROC for APOD in MC1 had an Area under the curve (AUC) of 0.79. As APOD is part of lipoproteins and involved in lipid transport, we hypothesised a disturbed lipid transport in patients with MC1 and tested if adding other proteins involved in lipid transport to the model could increase the AUC of the ROC. Adding Apolipoprotein C3 (APOC3) to the linear model increased AUC of the ROC to 0.83 despite not associating with MC1. Additionally, linear regression showed a correlation between serum APOD and MC1 load (ρ=0.46, FDR adjusted p-value = 0.002).
Conclusion: The serum concentration of APOD is associated with the presence of MC1 and correlates with the load of MC1. Especially in combination with the serum concentration of APOC3, it is a potential biomarker for the presence of MC1.

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Figure 1



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AB1398 **STROMAL CELLS IN MODIC TYPE 1 CHANGE BONE MARROW PROMOTE NEURITE OUTGROWTH**

Keywords: Pain, Bone diseases

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Background: Vertebral bone marrow lesions known as Modic type 1 changes (MC1) are a major contributor to unspecific lower back pain. Pain may relate to the higher innervation of MC1 endplates. Blocking neo-innervation in MC1 could be a promising treatment approach for MC1. Bone marrow stromal cells (BMSC) can produce neurotrophic factors and are dysregulated in MC1.
Objectives: The aim of the study was to identify if BMSC in MC1 support neo-innervation through release of neurotrophic factors.
Methods: The RNA sequencing data set (ENA PRJEB39993) of MC1 BMSC vs. intra-patient control vertebral BMSC (n=3 MC1 + 3 intra-patient control) was used to investigate enriched gene sets. From additional patients, BMSC were isolated from vertebral bone marrow aspirates (n=4 MC1 + 4 intra-patient control) and were co-cultured with the neuroblastoma cell line SH-SY5Y for 8 days. Neurite outgrowth from SH-SY5Y was quantified as a measure for neurotrophic activity using microscopy. Thirty neurotrophic cytokines were analyzed in the supernatant of the co-culture using C-Series Human Neuro Discovery Array C2.
Results: Gene set enrichment analysis of MC1 vs. intra-patient control BMSC identified gene sets associated with BDNF signaling such as "BDNF TRKB signaling" (normalized enrichment score (NES) = 1.71, p<0.001) and "mBDNF and proBDNF regulation of GABA neurotransmission" (NES = 1.61, p<0.001) amongst the top enriched gene sets. SH-SY5Y cells co-cultured with MC1 BMSC compared to intra-patient control showed significantly increased neurite outgrowth after 4 days (p = 0.045), 6 days (p = 0.027), and 8 days (p = 0.031). (Fig. 1a). Cytokine array analysis revealed significantly more mature brain-derived neurotrophic factor (mBDNF) (p = 0.021) and ciliary neurotrophic factor (CNTF) (p = 0.030) in supernatant of MC1 vs. control BMSC (Fig. 1b).
Conclusion: Neurotrophic activity of MC1 BMSC is increased. This might be mediated by BDNF and CNTF. Therefore, BDNF and CNTF may represent interesting novel treatment approaches for MC1 that directly target pain mechanisms.

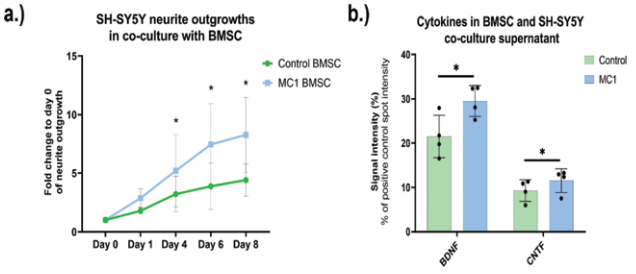


Fig. 1: a.) Effect of BMSC on neurite outgrowth of co-cultured SH-SY5Y normalized to day 0 (n=4). b.) Cytokine array spot intensities of BMSC and SH-SY5Y co-culture media (n=4) calculated as perecentage of positive control spot. Analysis for significance with paired t-tests. Asteriks indicate significance: *p < 0.05.

REFERENCES: NIL.

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Disclosure of Interests: Tamara Mengis: None declared, Irina Heggli: None declared, Nick Herger: None declared, Borbala Aradi-Vegh: None declared, Florian Brunner: None declared, Mazda Farshad: None declared, Oliver Distler Speakers bureau: Bayer, Boehringer Ingelheim, Janssen, Medscape, Consultant of: 4P-Pharma, Abbvie, Acceleron, Alcimed, Altavant Siences, Amgen, AnaMar, Arxx, AstraZeneca, Baecon, Blade, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos, Glenmark, Horizon, Inventiva, Kymera, Lupin, Miltenyi Biotec, Mitsubishi Tanabe, MSD, Novartis, Pfizer, Prometheus, Redxpharna, Roivant, Sanofi and Topadur, Grant/research support from: BI, Kymera, Mitsubishi Tanabe, Stefan Dudli: None declared.
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AB1399 **INVESTIGATING THE USE OF VERTEBRAL HEIGHT MORPHOMETRY DATA AS A PREDICTOR OF FRACTURE: AN OBSERVATIONAL COHORT STUDY**

Keywords: Bone diseases, Epidemiology

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Background: Dual energy x-ray absorptiometry (DEXA) has an established place in the diagnosis of osteoporosis and fracture risk estimation using the FRAX® tool. DEXA is also useful in producing morphometry data on bones including the vertebrae at low radiation doses during appointments. Currently there exists limited clinical use for vertebral height measurement, with no data published on the use of vertebral height as a useful clinical measurement. FRAX currently uses bone mineral density from the hip to calculate the risk of either hip fracture or major osteoporotic fracture, however, previous literature has identified that BMD as a predictor of fracture is specific but not sensitive [1]. Moreover, it may not be possible to get such value in certain patient demographics such as patients with hip replacements. Therefore, further data and predictors of fractures are needed to better allow fracture risk estimation.
Objectives: The aims of this study is to assess the use of vertebral height data measured during routine DEXA appointments as a predictor of fracture in an observational cohort.
Methods: We analysed data on 31546 patients referred to a district BMD scanner in the northwest of England between 2004-2019. Data collected at attendance include site of fragility fracture and the vertebral height at lumbar vertebrae L1-L4. Logistic models reporting odds ratio were used to examine the predictive value of vertebral height at L1-L4 in different types of fragility fracture.
Results: The mean age at the time of the first scan was 65 +/- 12.9 (SD). Our dataset comprised 26,156 (82.9%) female and 5390 (17.1%) male patients. A total of 11875 fractures occurred in our population. The mean height at L1 was 3.117 (95% CI 3.117-3.12), L2: 3.239 (95% CI 3.236-3.242), L3:3.78 (95% CI:3.75-3.381) and L4: 3.424 (95% CI: 3.420-3.428). Patients with average vertebral height at these spinal levels were less likely to experience any type of fracture. Interestingly when running the analysis individually at each fracture site, different spinal levels were associated with fractures at different sites. L1 had the highest predictive value while L2 had the least.

Table 1.

vertebral level AVG_height	L1	95 CI	L2	95 CI	L3	95 CI	L4	95 CI
tibfib fracture	1.07	(.90-1.23)	0.95	(.80-1.13)	1.04	(.89-1.23)	0.76	(.67-86)
wrist fracture	0.042	(.02-.94)	1.78	(.172-18.31)	0.68	(.0.19-25.20)	95.98	(7.35-1253.48)
spine fracture	0.32	(.27-.38)	0.52	(.44-.62)	0.83	(.70-.97)	0.92	(.80-1.05)
rib fracture	1.02	(.78-1.36)	0.85	(.65-1.12)	0.93	(.72-1.21)	1.11	(.91-1.37)
pelvis	0.5	(.32-.79)	0.81	(.51-1.29)	0.61	(.40-.94)	0.75	(.53-1.06)
humerus	0.69	(.54-.88)	0.8	(.62-1.022)	0.75	(.60-.94)	0.82	(.68-.98)
forearm	0.84	(.73-.96)	0.89	(.78-1.01)	0.77	(.68-.87)	0.78	(.71-.85)
femur	0.78	(.61-.98)	0.82	(.64-1.03)	0.72	(.56-.89)	0.79	(.66-.94)
elbow	1.4	(.36-5.5)	0.89	(.23-3.43)	0.82	(.24-2.8)	0.77	(.29-2.01)
ankle	0.02	(.00-.38)	1.7	(.05-54.3)	3.4	(.03-422.14)	2.57	(.03-249.87)
all fractures	0.45	(.42-.50)	0.49	(.45-.53)	0.52	(.48-.56)	0.57	(.54-.61)
key:								
green = p<0.05								
blue = p<0.001								

Conclusion: This study is the first to analyse the use of vertebral height data. We found that average vertebral height at spinal level L1-L4 is protective for fragility fractures however specific spinal levels were protective for certain types of fracture. While the link between BMD and fracture has been known for some time and consequently has been integrated into risk estimation tool such as FRAX®, the use of morphometry data to predict fracture is novel. Further research is needed to compare the predictive power of BMD to morphometry data as predictors of fracture, as well as understanding the role of morphometry data in future iterations of fracture risk estimation tools.

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Disclosure of Interests: Hamzah amin: None declared, Marwan Bukhari Speakers bureau: Marwan Bukhari has been sponsored to attend regional, national and international meetings by UCB celltech, Roche/Chugai, Pfizer, Abbvie, Merck, Mennarini, Janssen, Bristol-Myers Squib, Novartis and Eli-lilly He has received honoraria for speaking and attended advisory boards with Bristol-Myers Squib, UCB celltech, Roche/Chugai, Pfizer, Abbvie, Merck, Mennarini, Sanofi-aventis, Eli-Lilly, Janssen, Amgen, Novartis and Gilead. He has received honoraria from educational groups revalidaid and TREG consultants., Aqib Khan: None declared.

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AB1400

SPINE AND SACROILIAC JOINTS FINDINGS IN YOUNG MALES AND FEMALES WITH CHRONIC BACK PAIN UNDERGOING MAGNETIC RESONANCE IMAGING IN CLINICAL PRACTICE: RESULTS FROM THE SHERPAS STUDY

Keywords: Health Services Research, Spondyloarthritis, Imaging

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Background: Magnetic resonance imaging (MRI) is frequently used in patients with chronic back pain (CBP) to diagnose mechanical and inflammatory diseases, including axial spondyloarthritis (axSpA). Recent data suggest sacroiliac joints (SIJ) MRI findings in axSpA may differ according to sex[1]. Whether this holds true for spinal MRI and other causes of CBP is currently unknown.
Objectives: To analyze spinal and SIJ MRI findings in young male and female patients with CBP.
Methods: The "Strategy for a Hospital Early Referral in Patients with Axial Spondyloarthritis" (SHERPAS) is a prospective ongoing study recruiting young patients (18 to 40 years) with CBP asked to undergo an MRI of the spine by other specialists different than rheumatologists in a tertiary hospital, starting in September 2021. After inclusion, an additional MRI of the SIJ, followed by a rheumatology visit and eligible blood tests were performed. Dataset for this interim analysis was locked in October 2022. The protocol for MRI of the spine used a 1.5T scanner to acquire sagittal T1-weighted turbo spin echo (TSE) and T2-weighted TSE, both for the lateral sides of vertebral bodies, and T2-Multistack. On top of this, an MRI of the SIJ, which involved T1-TSE, T2- weighted SPAIR and short-tau inversion recovery (STIR) sequences, was performed. MRI findings were assessed according to clinical practice by one of the four musculoskeletal radiologists working in the centre, describing the presence of mechanical lesions (spondylolisthesis, spondylolysis, disc herniation, disc protrusion, facet joints abnormalities), inflammatory findings (both SIJ and spine), and SIJ structural findings. For this analysis, results were stratified by sex.
Results: Among 152 recruited patients, 85 (55.9%) were female; mean age was 34.2 (5.3) years. Spinal MRI findings were reported in 130 (87.2%) patients, with no differences between sexes (male 90.8% vs female 84.5%, p=0.3). As shown in **Table**, the most frequent diagnosis in both sexes were disc protrusion, followed by disc herniation. Inflammatory spinal findings were detected only in one male patient. No differences were found for any of the spinal lesions. SIJ MRI findings were reported in 49 (33.1%) patients, being numerically more frequently observed in males than females (41.5% vs 26.5%; p=0.08). Concurrence of both structural and inflammatory lesions was more frequently in males (9.2% vs 1.2%, p<0.05), while no differences in isolate SIJ MRI findings were found between sexes. Overall, 45 (29.6%) patients presented findings both in the spine and SIJ (**Figure 1**).
Conclusion: In young patients who are requested a spinal MRI by other specialists different than rheumatologists, spinal lesions are reported in most patients, and similarly in males and females. Remarkably, SIJ MRI findings are reported in one out of three patients in this population, being more frequently in males.

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Table 1. Findings in magnetic resonance imaging

	Total	Male	Female	p-value
Spine MRI	n=149	n= 65	n= 84	
Any finding	130 (87.2)	59 (90.8)	71 (84.5)	0.3
Structural findings	129 (86.6)	58 (89.2)	71 (84.5)	0.3
Spondylolisthesis	5 (3)	3 (4.6)	2 (2.4)	0.6
Spondylolysis	2 (1)	1 (1.5)	1 (1.2)	1
Disc herniation	34 (23)	15 (23.1)	19 (22.6)	1
Disc protrusion	64 (43)	31 (47.7)	33 (39.3)	0.3
Facet joints abnormalities	8 (5)	1 (1.5)	7 (8.2)	0.1
Other	16 (11)	7 (10.8)	9 (10.7)	1
Inflammatory findings	1 (1)	1 (1.5)	0	0.5
No findings	19 (13)	6 (9.2)	13 (15.5)	0.4
Sacroiliac Joint MRI	n=148	n= 65	n= 83	
Any finding	50 (33.5)	27 (41.5)	23 (27.4)	0.07
Structural findings	31 (20.9)	15 (23.1)	16 (19.3)	0.7
Inflammatory findings	11 (7.4)	6 (9.2)	5 (6.0)	0.5
Structural and Inflammatory findings	7 (4.7)	6 (9.2)	1 (1.2)	0.04
No findings	99 (67.8)	38 (58.5)	61 (73.5)	0.08

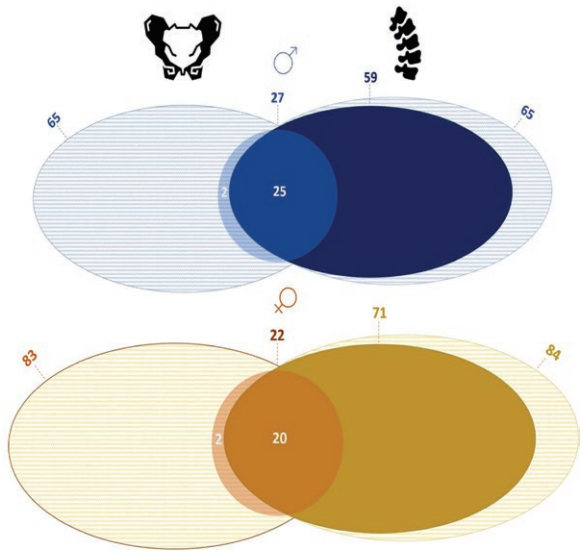


Figure 1. Patients with any reported finding in spine or sacroiliac joint magnetic resonance imaging. *Colored: any finding. Striped: no findings.*

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AB1401 HEALTH LITERACY AND OUTCOMES IN PATIENTS UNDERGOING TOTAL KNEE ARTHROPLASTY

Keywords: Outcome measures, Education

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Background: Health literacy is the ability to read and gain an understanding of health-related information, and make treatment and behavior choices accordingly. Poor health literacy is a main driver of health disparities in chronic medical conditions. Little is known about literacy in orthopedic surgery patients, which may be critical for post-surgical recovery.
Objectives: This study assessed health literacy in patients undergoing total knee arthroplasty (TKA) and its association with individual and community demographics, surgical length of stay (LOS), and discharge disposition.
Methods: The study population consisted of TKA patients at a single urban orthopedic specialty hospital from 2018-2021 who completed the health literacy screen. Health literacy, patient demographics and clinical variables were extracted from a data warehouse. Patient health literacy was defined by a validated single question tool (Morris et al. 2006) administered pre-operatively: *"How often do you have someone like a family member, friend, hospital or clinic worker or caregiver help you read health plan materials, such as written information about your health or care you are offered?"*. Answers were "Always," "Often," "Sometimes," "Occasionally" or "Never." "Always," "Often," or "Sometimes" answers reflect low health literacy and "Occasionally" or "Never" reflect adequate health literacy. Census-tract level measures of community poverty and education were obtained from the 2020 American Community Survey 5-year estimates. Variable comparisons were analyzed by $\chi 2$ and one-way analysis of variance (ANOVA), with $p < 0.05$ considered statistically significant.
Results: 7,875 TKA patients were included. 81.3% had adequate health literacy and 18.7% had poor health literacy (**Table 1**). Poor health literacy patients were older (71 vs 69, p<0.0001) and spoke a non-English preferred language (7.2% vs 1.9%, p<0.0001). These patients had more comorbidities (Charlson score 2+, 92.1% vs 11.5%, p=0.001), longer LOS (hours, 58 vs 56, p<0.001), and were less often discharged to home (84.3% vs 87.8%, p=0.002). Multiple linear regression analysis using backwards elimination showed that LOS was associated with sex, comorbidity and discharge disposition, factors themselves also shown to be linked with health literacy. There were no differences in health literacy by ethnicity, insurance, community poverty or education levels.
Conclusion: We found that patients in our population with low health literacy were older, non-English speaking, of Asian/other race, had higher comorbidity scores and a lower proportion of home discharges than those with adequate health literacy. Thus health literacy screening can identify patient groups for whom interventions during the pre-surgical process can be targeted. Based on results, further study can examine whether tools to support health literacy may lead to impact on important measures such as LOS and discharge disposition in orthopedic surgery patients.
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Table 1. Significant characteristics of patient population by health literacy levels

Variable	"Never", "Occasionally" (Adequate health literacy) (n=6400)	"Often", "Sometimes", "Always" (Low health literacy) (n=1475)	p-value
Age, years (median [IQR])	71.1 (9.6)	74.8 (9.3)	<0.0001
Sex, female %	3900 (60.9)	900 (61)	0.98
Race, %			<0.001
White	5211 (81.4)	1201 (81.4)	
Black/African American	540 (8.4)	4 (3.3)	
Asian/Other	649 (7.4)	11 (9)	
Charlson comorbidity index			0.001
0	4220 (65.9)	899 (60.9)	
1	1447 (22.6)	386 (26.2)	
2+	733 (11.5)	1358 (92.1)	
Preferred language, %			<0.0001
English	6278 (98.1)	1368 (92.7)	
Spanish	44 (0.7)	27 (1.8)	
Other	78 (1.2)	80 (5.4)	
Surgical LOS, hours (median [IQR])	56 [49, 79]	58 [51, 81]	<0.001
Discharge disposition, %			0.002
Home	687 (10.7)	161 (10.9)	
Home with physical therapy	4935 (77.1)	1082 (73.4)	
Skilled nursing facility/ Other	778 (12.1)	232 (15.7)	

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AB1402 THE EFFECTS OF SPINAL STABILIZATION EXERCISES VIA TELEREHABILITATION ON INDIVIDUALS WITH CHRONIC LOW BACK PAIN: A RANDOMIZED CONTROLLED STUDY

Keywords: Physical therapy/Physiotherapy, Telemedicine, Rehabilitation

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Background: Chronic low back pain is a very common problem worldwide. Reasons such as repetitive problems and lack of a clear treatment cause low back pain to be a serious burden for society [1]. Telerehabilitation provides remote application of rehabilitation services with the developing technology. Especially in the COVID-19 pandemic, the problems experienced in health services have increased the popularity of telerehabilitation services [2].
Objectives: Aim in this study is to investigate the effects of spinal stabilization exercises performed remotely with asynchronous video clips on pain, disability, quality of life, trunk flexion range of motion and gait parameters.
Methods: A total of 20 individuals with chronic low back pain were included in the study. After recording demographic information, pain levels were evaluated with the Visual Analogue Scale (VAS), disability levels were evaluated with the Oswestry Disability Index (ODI), and quality of life was evaluated with the Nottingham Health Profile (NHP). Trunk flexion range of motion was evaluated with

the Valedo ® system (Hocoma, Switzerland), and the spatiotemporal parameters of the gait (step time, cadance) were evaluated with the OPTOGAIT system (OPTOGait, Microgate, Italy). After the evaluation, the individuals were divided into 2 groups. One group did face-to-face progressive spinal stabilization exercises in the clinic, while the other group did the same exercise program remotely with asynchronous videos. The exercise program was 8 weeks, 3 days a week.

Results: The mean age of the telerehabilitation group (4 M, 5 F) was 41.44 ± 9.74, and their body mass index (BMI) was 26.34 ± 3.1. The mean age of the clinical group (1 M, 8 F) was 41.0 ± 13.0, and their BMI was 27.64 ± 3.55. All parameters were similar in the two groups before treatment. There was a significant difference in parameters except gait parameters in both groups after treatment ($p<0.05$). In the evaluation between the groups after treatment, the results of the two groups were similar in all parameters ($p>0.05$) (Table 1).

Table 1. Baseline and after treatment characteristics of telerehabilitation and face to face group and comparison of with-in group and between group

	Telerehabilitation			Face to Face			
	Baseline	After Treatment	p value	Baseline	After Treatment	p value	Between Group
VAS	6.51±1.61	2.41±1.17	0.00*	6.62±0.95	2.33±1.98	0.00*	0.79
ODI	20.66±9.94	13.55±10	0.00*	30.22±15.5	17.11±12	0.02*	0.54
NHP	131.51±121.29	34.0±29.61	0.01*	203.55±60.07	63.08±76.24	0.00*	0.66
Trunk Flexion Range of Motion	99.55±12.24	106.55±7.51	0.04*	88.11±15.26	94.11±15.18	0.00*	0.09
Step length (cm)	60.67±9.07	64.35±9.58	0.51	53.82±21	65.95±9.41	0.17	0.54
Step Time (sec)	0.55±0.04	0.51±0.08	0.26	0.40±0.12	0.34±0.18	0.13	0.06
Cadance	105.67±9.17	106.13±17.46	0.44	103.37±8.64	105.31±9.45	0.67	0.73

Conclusion: According to the results of our study, it is seen that both methods did not provide any change in gait parameters. However, it has similar effects in reducing pain and disability, improving quality of life, and increasing trunk range of motion. For individuals with chronic low back pain, it seems that remote exercise with asynchronous videos can be as effective a treatment as face-to-face exercise. There is a need for studies to be conducted in a larger population with longer follow-up.

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AB1403 IS MUSCLE STRENGTH ASSOCIATED WITH SPATIOTEMPORAL GAIT PARAMETERS IN PATIENTS WITH NON-SPECIFIC CHRONIC LOW BACK PAIN? THE BACKFIT PROJECT

Keywords: Pain, Motor function, Rehabilitation

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Background: Non-specific chronic low back pain (NSCLBP) is one of the most common musculoskeletal disorders globally, as approximately 10-40% of individuals experience it[1]. Chronic pain is characterized when persists more than 12 weeks, and non-specific when causes of pain are of unknown origin[2]. People with NSCLBP present weakness of multifidus, transversus abdominis, internal oblique and gluteus maximus muscles and present difficulties to maintain a coherent walking due to the lack of strength and control[3].

Objectives: To explore the association of back flexor, back extensor, lower- and upper-body muscle strength with spatiotemporal gait parameters in patients with NSCLBP.

Methods: A total of 105 patients with NSCLBP, 69 women (mean ± standard deviation= 50.9±9.9 years) participated in this cross-sectional study. Back flexor, back extensor, upper- and lower-body muscle strength were measured with reliable and valid tests (prone bridging, Biering-Sørensen, hand dynamometry (TKK 5101) and 30-second chair-stand test, respectively). Global muscle strength was calculated with normalized index (z-score) procedure from each muscle strength test. Spatiotemporal gait parameters (contact time, gait speed, stride length, stride cycle/time, double support and load respond) were obtained with an Optogait™ platform, where patients were informed to walk comfortably until 150 to 200 steps were registered in 5 meters closed circuit. Linear regression analysis was used to study the association between muscle strength and spatiotemporal gait parameters. Age, medication for pain, relaxation and depression, and fat percentage were used as covariates using the 'stepwise' method. These variables were administered via interview, except fat percentage which was measured with 8 tactile polar electrode bioimpedance system (InBody R20).

Results: In women, greater back flexor muscle strength was associated with lower contact time (β=-0.328), stride cycle/time (β=-0.382), double support (β=-0.313) and load respond (β=-0.302), higher gait speed (β=0.341), and longer stride length (β=0.272) (all $p\leq0.013$). Greater lower-body muscle strength was associated with less contact time (β=-0.160) and double support (β=-0.237), higher gait speed (β=0.365) and longer stride length (β=0.415) (all $p\leq0.031$). Greater upper-body muscle strength was associated with higher gait speed (β=0.380) and longer stride length (β=0.476) (all $p\leq0.001$). Greater global muscle strength was associated with less contact time (β=-0.370), stride cycle/time (β=-0.468), double support (β= -0.324) and lower load respond (β=-0.320), higher gait speed (β=0.431) and longer stride length (β=0.491) (all $p\leq0.03$). In men, greater back extensor muscle strength was associated with higher gait speed (β=0.353), and lower double support (β=-0.387) and load respond (β=-0.365) (all $p\leq0.038$). Greater lower-body muscle strength was associated with lower stride cycle/time (β=-0.342) ($p=0.044$). Greater global muscle strength was associated with higher gait speed (β= 0.414), longer stride length (β=0.410), and lower double support (β=-0.373) and load respond (β=-0.354) (all $p\leq0.037$).

Conclusion: Our findings suggest that greater muscle strength was consistently associated with better spatiotemporal gait parameters in females and males patients with NSCLBP. Future studies might determine whether randomized control trial focused on strengthening global musculature might contribute to improve gait abnormalities in patients with NSCLBP.

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AB1404 THE ASSOCIATION OF PAIN INTENSITY AND MUSCULOSKELETAL FACTORS, PHYSICAL ACTIVITY, AND QUALITY OF LIFE IN PREGNANT WOMEN WITH LOW BACK PAIN: A CROSS-SECTIONAL STUDY

Keywords: Pregnancy and reproduction, Quality of life, Pain

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Background: Low back pain (LBP) is one of the most common musculoskeletal problems affecting pregnant women. While the etiology/pathogenesis of pregnancy-related LBP (PR-LBP) has not been fully explained, it is thought to stem from several biological/physical factors including hormonal, vascular, and biomechanical changes, trauma, metabolic factors, insufficient muscle control, stress, weight gain, sedentary lifestyle, muscle function loss [1,2]. As such, risk factors need to be assessed comprehensively during pregnancy and those women who are at risk should be given preventive recommendations.

Objectives: The aim of this study was to determine the association between musculoskeletal factors (abdominal muscle thickness and diastasis recti), physical activity, quality of life and self-reported LBP intensity during different trimesters of pregnancy.

Methods: A total of 107 pregnant women who were between 11 and 37 weeks of gestation, without obstetric and medical complications were included in this study. Detailed, sociodemographic and obstetric characteristics were recorded. The pregnant women were shown the region of LBP on a figure and they were asked to mark the relevant average pain intensity on a 10 cm Visual Analogue Scale (VAS). Disability was evaluated using the Oswestry Disability Index (ODI) to evaluate the degree of loss of functionality. Abdominal muscle thicknesses and diastasis recti were measured by ultrasonography. Pregnancy Physical Activity Questionnaire (PPAQ) and Short Form-36 (SF-36) were used to assess physical activity and quality of life. Univariate regression was used to analyse associations between each plausible independent variable and low back pain severity.

Results: Among 107 primiparous women, 43 were in the 1st trimester (mean age: 31.18±4.58 years, mean body mass index (BMI): 24.15±4.26 kg/m^2), 33 in the 2nd trimester (mean age: 30.62±4.53 years, BMI: 25.65±3.77 kg/m^2), and 32 were in the 3rd trimester (mean age: 30.58±4.60 years, BMI: 27.08±3.70 kg/m^2).

The mean LBP intensity was 3.09±2.37 and they were 2.68±2.09, 2.73 ±1.98, 2.16± 2.01 for the 1st, 2nd and 3rd trimesters, respectively. Demographic and medical variables in pre-pregnancy and pregnancy periods were not associated with PR-LBP intensity. On the contrary, ODI score was associated with LBP intensity during pregnancy. Higher ODI score shows severe low back pain (coef=0.05, R2=0.11, p=0.03) and ODI scores explain 11%, 13% and 26% of LBP severity during 1st, 2nd and 3rd trimester, respectively. Musculoskeletal variables (abdominal muscle thickness and diastasis recti) were not associated with PR-LBP intensity. SF-36 emotional role limitation (coef=-0.03, R2=0.20, p=0.01) in the 3rd trimester and SF-36 pain in the 1st (coef=-0.04, R2=0.12, p=0.02) and 3rd (coef=-0.05, R2=0.26, p=0.004) trimesters were associated with PR-LBP intensity. Rest of the SF-36 subscales were not associated with LBP intensity during any trimester. Physical activity were not associated with PR-LBP intensity, except of the PPAQ-sedentary during the 2nd trimester (coef=0.17, R2=0.17, p=0.02).

Conclusion: Increased PR-LBP intensity can be associated with different factors in different trimesters of pregnancy. Clinicians should comprehensively assess pregnant women, taking into account the relevant risk factors according to trimester, and make preventive/therapeutic recommendations for pregnant women.

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AB1405 POSTOPERATIVE RESULTS OF JOINT-PRESERVING SURGERY WITH MITCHELL'S OSTEOTOMY FOR HALLUX VALGUS DEFORMITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Bone diseases, Rheumatoid arthritis

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Background: In recent years, joint-preserving surgery has become common surgical procedure for forefoot deformities in Japanese patients with rheumatoid arthritis (RA). Since arthritis contributes to hallux valgus deformity in patients with RA, the postoperative outcome may differ from that in patients with idiopathic hallux valgus (IHV) patients.

Objectives: In this study, we compared the postoperative results of Mitchell's osteotomy in patients with RA and IHV.

Methods: We evaluated 181 feet in 111 patients (52 feet in 34 patients with RA, 129 feet in 77 patients with IHV) who performed Mitchell's osteotomy surgery between January 2006 and September 2021 and followed-up more than one year. The hallux valgus angle (HVA) and intermetatarsal angle (IMA) were measured from standing X-ray images of the foot, before and after surgery and one year later, and the postoperative course of RA and IHV patients was compared.

Results: Preoperative HVA was 42° [20-73] in patients with RA and 40° [17-62] in patients with IHV, with no significant differences. Preoperative IMA was 14° [6-22] in patients with RA and 15° [7-23] in IHV patients, significantly smaller in the RA group (p<0.01). HVA at 1 year was 7° [-21-34] in patients with RA and 9° [-24-38] in patients with IHV, with no significant differences. IMA at 1 year was 7° [0-18] in patients with RA and 8° [1-21] in patients with IHV, with no significant differences. The recurrence rate at 1 year postoperatively was 17.3% in patients with RA and 16.3% in patients with IHV, with no difference. Traditionally, metatarsal head resection has been performed for rheumatoid forefoot deformities. However, joint-preserving surgery is recently performed due to the improvement of anti-rheumatic drugs such as biological disease modifying drugs and Janus kinase inhibitors. Mitchell's osteotomy has been recommended for IHV as a joint-preserving surgery, as has Chevron osteotomy. The results of this study showed that Mitchell's osteotomy is useful treatment method for patients with RA as well as for patients with IHV. In addition, preoperative IMA in patients with rheumatoid forefoot deformity was significantly smaller than patients with IHV, but there was no difference in HVA. This suggests joint inflammation leads to lateral dislocation of proximal phalanx without metatarsal bone medialization.

Conclusion: Joint-preserving surgery with Mitchell's osteotomy was useful method for hallux valgus deformity in patients with RA.

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AB1406 COMPARISON OF FOOT POSTURE, PAIN, FUNCTION AND QUALITY OF LIFE IN PATIENTS WITH PES PLANUS AND HALLUX VALGUS: A PILOT STUDY

Keywords: Quality of life, Pain

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Background: Hallux valgus is a common deformity characterized by abnormal rotation, lateral deviation, angulation of the great toe at the first metatarsophalangeal joint. Pes planus is known as the loss of the medial longitudinal arch. While some studies have suggested that pes planus plays an important role in the development of hallux valgus [1, 2], others reported that no correlation between these disorders [3, 4]. Thus, the differences in the problems caused by these disorders should be clarified.

Objectives: The aim of this study was to compare individuals with hallux valgus and pes planus in terms of foot posture, function, pain, and quality of life.

Methods: Thirty-one (13-hallux valgus, 18-pes planus) individuals of both sexes, who were determined to have pes planus or hallux valgus by clinical evaluation, were included in the study. The dominant foot of the patients was evaluated by the Foot Posture Index (FPI-6), Foot Function Index (FFI), The American Orthopedic Foot and Ankle Society (AOFAS), and their quality of life was evaluated by the Short Form-36 (SF-36). FPI-6 evaluates foot posture with 6 items in the range of (-12) - (+12). According to FPI-6, negative values indicate the foot is in supination, and positive values indicate that the foot is in pronation. The FFI scores for the domains of pain, disability, and activity limitations. A higher score indicates greater impairment. AOFAS, also consists of pain, function, and alignment subscales, and the total score ranges from 0-100, and higher scores indicate better outcome. SF-36 is a scale that evaluates health-related quality of life with 8 subscales, and physical function and general health subscales of SF-36 were used in this study, and higher scores also demonstrate a better quality of life. Mann Whitney-U test was used to investigate the differences between patients with hallux valgus and pes planus.

Results: Individuals with pes planus and hallux valgus were homogenous in terms of physical characteristics (p>0.05). It was determined that patients with pes planus had worse foot postures according to FPI-6 and more foot pain according to FFI and AOFAS compared to patients with hallux valgus (p<0.05). Other results were similar between patients with pes planus and hallux valgus (p>0.05) (Table 1).

Conclusion: To the best of our knowledge, this study was the first to compare between patients with hallux valgus and pes planus. Current findings revealed that pes planus caused more pain and foot posture disorders compared to hallux valgus. A comparative study on a large sample is ongoing to assess the difference between these foot disorders.

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Table 1. Summary of findings

	Hallux valgus (n=13)	Pes planus (n=18)	
Variables	**Mean±SD**	**Mean±SD**	**p**
Age (years)	33.84±16.10	29.77±13.90	0.57
Height (cm)	168.30±6.57	165.50±6.60	0.20
Weight (kg)	70.23±14.85	65.11±16.49	0.22
BMI (kg/m^2)	24.70±4.61	23.58±4.85	0.33
FPI-6	2.46±2.40	5.88±2.63	**0.00***
FFI-Pain	12.53±12.83	23.33±12.99	**0.03***
FFI-Disability	11.84±15.46	17.50±13.56	0.12
FFI-Activity Limitation	6.46±14.41	4.33±6.80	0.53
FFI-Total	30.84±37.88	45.16±27.09	**0.04***
AOFAS-Pain	32.30±5.99	27.22±6.69	**0.03***
AOFAS-Function	45.38±8.13	46.66±4.92	0.66
AOFAS-Alignment	6.15±2.19	4.55±2.43	0.11
AOFAS-Total	83.83±12.58	80.94±8.01	0.30
SF-36-Physical function	87.30±15.89	84.44±22.22	0.65
SF-36-General health	62.30±19.32	56.66±14.95	0.26

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AB1407 EFFECTIVENESS OF TREATMENT OF FACET SYNDROME BY THE METHOD OF BLOCKADE OF INTERVERTEBRAL JOINTS UNDER ULTRASOUND CONTROL

Keywords: Pain

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Background: recently there has been an increase in the prevalence of facet syndrome (spondyloarthrosis) in back pain syndromes. This is due to hypodynamia, increased body weight, and the increase in the specific gravity of the so-called "sedentary" professions. With hypertrophy of the intervertebral joints, there is chronic compression of the Lyushka nerve (return nerve), which directly causes pain, as well as constant spasm of the innervating muscles. In the treatment of facet syndromes, many methods are used - drug treatment, massage, various physical methods of influence, etc., but none of these methods provides quick relief from the pain syndrome. The blockade method has been used for a long time with considerable success, but even more works are appearing that show much better efficiency of these manipulations with high-precision introduction of drugs under ultrasound or X-ray control.
Objectives: to determine the effectiveness of blockades of intervertebral joints under ultrasound control in facet syndrome.
Methods: we conducted a study of patients in whom the clinical manifestations of the facets of the lumbosacral spine syndrome were confirmed by radiological research methods (radiographic or MRI). The level of pain syndrome was assessed according to the VAS scale before the start of treatment and after 1 and 7 days after the start of treatment. Along with traditional treatment (NSAIDs, muscle relaxants, etc.), facet blockade was performed under ultrasound control.
Results: 50 patients (22 women and 28 men) were included. The average age was 43.28 years±0.80 years. 56.42% of patients were overweight. The average body mass index was 28.18±0.43 kg/m2. 80% of patients had multilevel facet syndrome L3-S1. 20% of patients had a monofacet syndrome at the level of L4-L5 or L5-S1. Patients were divided into 2 groups of 25 people. Patients of both groups were prescribed drug therapy with NSAIDs and muscle relaxants. The patients of the first group were additionally subjected to facet blockade under ultrasound control, and a solution of corticosteroid and local anesthetic was injected into the affected areas. Depending on the number of lesion levels, a multilevel procedure was performed. Before the procedure, the average pain level according to VAS in patients of the 1st group was 84±1.7 mm, in the 2nd group - 82±2.3 mm. After 1 day, the pain level in patients of the 1st group was 31±4.2 mm, while in the 2nd - 72±2.8 mm. 7 days after the start of treatment and manipulation, the pain level was 28±2.9 mm in the 1st group and 51±3.7 mm in the second group of patients (who were not manipulated).
Conclusion: the method of facet blockade under ultrasound control is a modern, low-traumatic, highly effective method in the complex treatment of facet syndrome.
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AB1408 INVESTIGATION OF GAIT SYMMETRY, CERVICAL PROPRIOCEPTION AND FUNCTIONALITY IN INDIVIDUALS WITH CHRONIC IDIOPATHIC NECK PAIN

Keywords: Pain, Outcome measures

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Background: Previous studies have shown that persons with chronic idiopathic neck pain (CINP) have gait disturbances [1]. However, it has not been clarified whether they have gait asymmetries. Cervical proprioception is important to maintain gait function [2]. However the association between gait symmetry and cervical proprioception in CINP is not known.
Objectives: The first aim was to investigate gait symmetry, cervical proprioception, cervical range of motion, and functional disability in persons with CINP and compare them with healthy controls (HC). The second aim was to investigate the relationship between gait symmetry and cervical proprioception and functional disability in persons with CINP.
Methods: This study included 35 persons with CINP (27 females, 8 males, mean age 25.48 ± 8.69 years), and 34 HC (25 females, 9 males, mean age 25.76 ± 7.96 years). Gait symmetry was assessed with a wearable sensor device. The device, which can provide real-time data transfer in determining gait symmetry, allows the patient to move freely without laboratory conditions with its wireless sensor feature. Joint position error (JPE) was assessed for proprioceptive ability. The cervical range of motion (flexion, extension, lateral flexion, rotation) and cervical JPE (flexion, extension, lateral flexion, rotation) were evaluated with an easy-to-use device (Cervical Range of Motion; CROM) containing 3 head-mounted inclinometers. Neck Disability Index (NDI) was used to assess functional disability in the CINP group.
Results: Persons with CINP had significantly worse gait symmetry than HC ($p<0.001$). There were significant differences between the CINP and HC in all directions of cervical JPE and all directions of cervical range of motion ($p<0.01$). In the CINP group, gait symmetry was significantly correlated with the cervical JPE (flexion, extension, right lateral flexion, $r = -0.387, -0.459, -0.443$, $p<0.05$) and NDI ($r = -0.493$, $p<0.05$). There were not significant correlation between gait symmetry and cervical left lateral flexion ($r = -0.237$, $p=0.171$), and right cervical rotation ($r = -0.187$, $p=0.171$) and left cervical rotation ($r = -0.102$, $p=0.561$) JPE.
Conclusion: In our study persons with CINP had significantly more asymmetrical gait, worse cervical proprioception and worse cervical range of motion compared to the healthy controls. It has been shown that gait symmetry is related to cervical proprioception (flexion, extension, right lateral flexion) and functional disability in CINP.
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AB1409 EFFICACY AND SAFETY OF SODIUM THIOSULFATE IN CALCIFIC TENDINITIS OF THE ROTATOR CUFF – ANALYSIS OF AN ONGOING RANDOMIZED CLINICAL TRIAL

Keywords: Patient reported outcomes, Randomized control trial, Outcome measures

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Background: Calcific tendinitis of the rotator cuff is a major cause of omalgia. [1] Ultrasound guided percutaneous lavage (UGPL) is indicated when conservative treatments fail. [2] Recent reports interested the use of topical sodium thiosulfate (STS) in the treatment of other diseases with ectopic calcifications [3, 4, 5].
Objectives: To assess the efficacy and safety of UGPL with STS versus with saline solution (standard of care - SOC) in calcific tendinitis.
Methods: Double-blinded randomized clinical trial including adult patients with calcific tendinitis, omalgia ≥3 months and ≥1 positive shoulder impingement test. Only dense type A calcifications (Molé Classification) >5 mm in diameter were included. Patients were randomized in two groups: STS and SOC lavage. Informed consents were collected. Both groups were reevaluated at week 1, month 1 and 3 after UGPL. Pain Visual Analogue Scale (VAS) at rest and during activities, shoulder range of motion and strength, impingement tests, Disabilities of the Arm, Shoulder and Hand (DASH), DASH-Work, EuroQol five-dimensional (EQ5D) and University of California at Los Angeles (UCLA) scores, ultrasound (US) and radiographic evaluations were performed on all follow up visits. SPSS was used for statistical analysis with a significance level of 2-sided $p<0.05$.
Results: We included 32 patients, where 78.1% (25) were women, with a mean age of 51.0 (SD=8.5) years old. Pain's mean duration before the procedure was 16.3 months (SD=22.3). We randomized 18 patients (56.3%) to the control group (SOC) and performed a saline UGPL; the other 14 patients (43.8%) to the treatment group (STS). Baseline characteristics are shown in table 1. Since patient inclusion is dynamic, our sample met 28 patients at week 1 (SOC=15

and STS=13), 26 patients at month 1 (SOC=14 and STS=12) and 21 patients at month 3 (SOC=10 and STS=11). Both procedures numerically improved pain, range of motion, functionality and calcification size, but only SOC lavage was statistically significant for calcification size reduction (p=0.005), EQ5D, DASH work and UCLA improvements (p=0.021, 0.042 and 0.03, respectively), while both STS and SOC lavage statistically reduced the DASH score (p=0.014 and 0.06, respectively). No adverse effects/complications were reported.

Conclusion: Although well tolerated with no side effects, STS UGPL has failed to uphold the SOC benefits for calcific tendinopathy. Further studies using STS are needed to ascertain its interest in this disease. This on-going work will be reevaluated with a larger sample.

Table 1. Demographic and baseline clinical characteristics.

	STS lavage (n=14)	**Saline solution lavage** (n=18)	**p-value**
Age (years), mean (SD)	52.1 (9.7)	50.1 (7.6)	NS
Sex, female % (n/N)	78.6% (11/14)	77.8% (14/18)	NS
Number of comorbidities, median (IQR)	1 (2)	0 (1)	NS
Dominant side, right % (n/N)	92.9% (13/14)	94.4% (17/18)	NS
Nocturnal pain, yes % (n/N)	100% (14/14)	100% (18/18)	NS
Pain duration, median (IQR)	18 (31)	6 (8)	0.022
Shoulder range of motion, median (IQR)	165 (90)	180 (90)	NS
VAS at rest (0–10), mean (SD)	5.6 (1.8)	5.8 (2.1)	NS
VAS during activities (0–10), mean (SD)	7.1 (1.6)	6.1 (2.2)	NS
DASH Score, mean (SD)	56.4 (14.1)	53.5 (14.8)	NS
DASH-Work Score, mean (SD)	70.7 (10.4)	65.1 (20.8)	NS
EQ5D, mean (SD)	0.36 (0.33)	0.41 (0.20)	NS
VAS EQ5D (0–100), mean (SD)	56.4 (15.6)	60.3 (21.3)	NS
UCLA score, mean (SD)	17.7 (4.7)	14.7 (3.2)	0.041
Bursitis, yes % (n/N)	57.1% (8/14)	61.1% (11/18)	NS
Calcification morphology, % (n/N)	21.4% (3/14)	44.4% (8/18)	NS
Acr-shaped	21.4% (3/14)	27.8% (5/18)	
Fragmented	57.1% (8/14)	27.8% (5/18)	
Nodular and dense, weel-defined			
Calcification size, median (IQR)	12.6 (3.6)	12.5 (6.3)	NS

SD: Standard deviation; M: Mean; NS: non-significant; IQR: interquartile range

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AB1410

ASSOCIATION BETWEEN MUSCLE MASS PERCENTAGE WITH PAIN AND DISABILITY IN PATIENTS WITH NON-SPECIFIC CHRONIC LOW BACK PAIN: THE BACKFIT PROJECT

Keywords: Motor function, Rehabilitation, Pain

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Background: Non-specific chronic low back pain (NSCLBP) is one of the most common musculoskeletal disorders worldwide[1]. Recent studies have shown higher levels of pain[2,3] and disability[4] in patients with NSCLBP who presented higher body mass index. However, the relationship between body muscle mass and these two variables is unknown.

Objectives: To determine if there is an association of body muscle mass percentage with pain and disability in patients with NSCLBP.

Methods: 105 patients (70 women, 50.59 ± 9.95 years) participated in this cross-sectional study. Body muscle mass percentage was evaluated using portable bioimpedance of eight tactile polar electrodes (InBody R20). Pain sensitivity threshold was assessed using manual pressure algometry (FPK 20, Wagner Instruments, Greenwich, CT, USA). Pain intensity was evaluated using two instruments, on the one hand a visual analogue scale (VAS) and on the other hand the pain dimension of the Short-Form Health Survey-36 (SF-36) questionnaire. The Oswestry Low Back Pain Disability questionnaire was used to assess disability due to pain. To study the association between the main variables, a linear regression analysis was carried out, controlling for age, sex, marital and educational status, time since clinical diagnosis and waist circumference as covariates using the 'stepwise' method. As there was no interaction in terms of sex, the analyses were carried out jointly (women and men).

Results: Higher levels of body muscle mass percentage were associated with higher pain sensitivity threshold (b=0.071; 95% confidence interval (CI)= 0.017,0.130; p=0.017, lower VAS-pain (b=-0.095; 95% CI= -0.184, -0.007; p=0.03) and higher score in the SF-36 pain dimension (b=1.038; 95% CI= 0.376, 1.701 p=0.002), and lower disability due to pain (b= -1.028; 95% CI= -1.513, -0.542; p<0.001).

Conclusion: Patients with NSCLBP presenting higher body muscle mass percentage showed lower pain and disability due to pain, and higher pain sensitivity threshold. Further intervention studies are necessaries to check the effects on pain and disability of programs focused on improving muscle mass in this population.

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AB1411

THE EFFECTS OF YOGA AND AEROBIC EXERCISE ON PAIN, FUNCTION, METABOLIC CAPACITY, QUALITY OF LIFE AND COGNITIVE VARIABLES IN INDIVIDUALS WITH CHRONIC LOW BACK PAIN: PRELIMINARY RESULTS

Keywords: Rehabilitation, Cognitive Function, Pain

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Background: It is known in the literature that exercise is effective on pain and function in the treatment of chronic low back pain (CLBP). However, it is emphasized that there is insufficient evidence about which type of exercise is more effective and the effect of exercises on cognitive parameters associated with chronic pain.

Objectives: The study aims to determine the effects of yoga and aerobic exercise on pain, function, metabolic capacity, quality of life (QoL), and cognitive variables in individuals with CLBP.

Methods: Thirty individuals with LBP for 3 months or longer were included in the study. Individuals were randomly divided into 2 groups. The first group was given aerobic exercise training, and the second group was given a yoga program. Both programs were applied for 8 weeks, 2 days a week, for 1 hour, accompanied by a physiotherapist. Individuals were evaluated at baseline and after 8 weeks of treatment. Pain intensity was assessed with a visual analog scale (VAS), metabolic capacity with 6 Minute Walking Test, kinesiophobia with Fear Avoidance Beliefs Questionnaire (FABQ), pain perception with a pain catastrophizing scale (PCS), cognitive function with Montreal Cognitive Assessment Scale (MoCA), back awareness with Fremantle Back Awareness Questionnaire (FreBAQ) and QoL with the Nottingham Health Profile (NHP).

Results: In the study, it was shown that both exercises approach reduced pain and improved function, metabolic capacity, and cognitive parameters (p<0.05). The effects of both exercises on pain, function, cognitive level, metabolic capacity, and NHP total score were similar (p>0.05). However, kinesiophobia and back awareness improved only in the yoga group; pain catastrophizing, NHP-sleep, and NSP-emotional reaction sub-parameters improved only in the aerobic exercise group (p<0.05).

Conclusion: It has been shown that yoga and aerobic exercise, whose effects on pain and function are well known, are also effective on metabolic capacity, QoL, and cognitive parameters. These results may help physiotherapists to comprehensively evaluate individuals according to the multidimensional nature of CLBP and to organize the content of treatment programs for the identified needs.

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Paediatric rheumatology

AB1412 THE DAMAGE OF JUVENILE IDIOPATHIC ARTHRITIS IN ADULT PATIENTS

Keywords: Outcome measures, bDMARD, Disease-modifying Drugs (DMARDs)

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Background: Juvenile idiopathic arthritis (JIA) is the most common disease in pediatric rheumatology. After transition, chronic active JIA requires continuing treatment. Little is yet known about the JIA activity in adult patients.
Objectives: To assess disease activity, treatment and comorbidities in adult patients with JIA between 2000 and 2022 at the University Hospital of Heidelberg.
Methods: This is a monocentric, retrospective analysis of adult patients with onset as JIA. The electronic medical records were analyzed from the first to the last documented visit in our center. Prognostic factors for disease activity in adults were determined using Fisher's exact test, chi-square test and cross tables.
Results: Until March 2022, 172 JIA patients with a median age of 27.7 years (range 18.1 to 78.4) and a median disease duration of 19.4 years (range 1.3 to 68.8) at their last visit were identified. Oligoarticular (oligo-) (n=36, 20.9%), extended-oligo (ext-oligo-) (n=28, 16.3%) and polyarticular (poly-) (n=61, 35.5%) were the largest JIA subgroups. Females (n=134, 77.9%) were more prevalent than males (n=38, 22.1%) (p<0,001). The prevalence of uveitis was 27.9% (n=48). Patients with RF+ poly-JIA (n=17, p<0,001) or initiation of MTX after 2 years (n=41, p=0,006) or bDMARD after 3 years (n=44, p<0,001) of disease onset were associated with significantly more erosive joint damage. Patients with late MTX and/or bDMARD initiation (n=190) had more frequently osteoporosis (n=48, p=0,011, p=0,012) and required more frequently total joint replacement (n=41, p=0,012, p=0,04). Radiological joint damage was more prevalent in patients with a disease onset before the year 2000. At the last documented visit 51.8% of patients (n=72) were in SDAI and DAS28 remission.
Conclusion: The delay of MTX and bDMARD therapy in patients with active JIA was associated with erosive joint damage, total joint replacement and osteoporosis. The JIA onset before the year 2000 was associated with significantly more joint damage and a lower prevalence of remission.
REFERENCES: NIL.
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AB1413 ASSESSMENT OF FATIGUE IN YOUNG ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Osteoporosis, Sarcopenia, Mental health

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Background: Fatigue is a common and frustrating symptom in many chronic inflammatory diseases, including juvenile idiopathic arthritis (JIA), impacting all parts of daily life.
Objectives: This study aims to determine the prevalence of fatigue in young patients with JIA and to analyze its correlation with clinical characteristics of the disease, body mineral content (BMC), and bone mass density (BMD).
Methods: Cross-sectional study included young adults with JIA according to ILAR criteria, disease duration ≥3 years. Exclusion criteria: age<18 and >44 years, the presence of any comorbidity that could be accompanied by fatigue (diabetes, chronic kidney disease, neuropathy, obesity, chronic obstructive pulmonary disease, infections, malignancy). Demographic data and the following clinical parameters were collected: pain Visual Analog Scale (VAS) measured by patients and doctors, tender joint count (TJC), swollen joint count (SJC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Disease Activity Score 28 (DAS28), Juvenile Arthritis Disease Activity Score (JADAS27), health assessment questionnaire (HAQ), Juvenile Arthritis Damage Index-articular (JADI-A) and Juvenile Arthritis Damage Index-extra-articular (JADI-E). BMC and BMD were determined using dual photon X-ray absorptiometry (DXA). Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) short 13-item questionnaire validated in RA. Fatigue was considered mild if the FACIT-F score was ≥40, moderate if 20≤FACIT-F<40, and severe if 0≤FACIT-F<20. A p-value lower than 0.05 was considered significant.
Results: We included 40 patients with JIA (24 women and 16 men) with a mean age of 24.4±5. The mean disease duration was 13,8±8,1 years. The mean pain VAS measured by the patient was 38,8±3,4; the mean pain VAS measured by the doctor was 33,6±4,1; the mean TJC and SJC were 4,2±4,9 and 1,9±3,2, respectively. The mean levels of ESR and CRP were 20,2±2,7 mm/h and 26,1±7,0 mg/l, respectively. The mean DAS28-ESR was 3,6±1,5, the mean JADAS27 was 13,3±8,7, and the mean HAQ score was 0.60±0.6. The mean FACIT-F score was 30.1±12.4. Fatigue was mild in 37.5% (15 patients), moderate in 35% (14 patients), and severe in 27.5% (11) of patients. A significant negative correlation was noted between the FACIT-F score and the following parameters in JIA patients: disease duration (r=-0.436, p<0.001), articular and extra-articular damage obtained by JADI-A and JADI-E indices (r=-0.393, p=0.01, r=-0.440, p=0.05, respectively), pain VAS obtained by a doctor (r=-0.358, p=0.02), but not with pain VAS obtained by the patient (r=-0.167, p=0.3), ESR (r=-0.503, p<0.001), but not with CRP (r=-0.157, p=0.3), DAS28-ESR (r=-0.414, p<0.05), JADAS27 (r=-0.391, p<0.01) but not with TJC (r=-0.080, p=0.8), and SJC (r=-0.239, p=0.2). FACIT-F score was positively associated with total BMD (r=0.364, p=0.2), femoral neck BMD (r=0.519, p=0.007), appendicular lean mass (r=0.666, p<0.001), total lean mass (r=0.622, p<0.001), and skeletal mass index (r=0.703, p<0.001), but not with HAQ (r=0.035, p=0.8).
Conclusion: In our study, moderate and severe fatigue among young patients with JIA was 35% and 27.5%, respectively. The fatigue was associated with disease activity, duration of disease, articular and extra-articular damage, total and femoral neck BMD, and lean mass.
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AB1414 PREDICTIVE FACTORS OF BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (BDMARD) USE IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

Keywords: bDMARD

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Background: The advent of disease-modifying antirheumatic drugs (DMARDs), in the past two decades has been revolutionary in the treatment and prognostic outcomes of patients with Juvenile Idiopathic Arthritis (JIA). Since some patients have inadequate responses to conventional DMARDs, biologic DMARDs (bDMARDs) must be prescribed to guarantee the achievement of complete remission. Early and appropriate treatment can prevent joint destruction, loss of joint function and extraarticular manifestations, with subsequent less morbidity and mortality.
Objectives: To identify the JIA patients with a higher probability of requiring treatment with bDMARDs and to investigate the predictive factors.
Methods: A retrospective single-center study of patients with JIA followed in a tertiary Hospital was conducted. Sociodemographic, clinical, laboratory and treatment characteristics were collected from Portuguese Rheumatic Diseases Register and medical records. Statistic was performed with independent samples t-test, Mann-Whitney U test, chi-square test and Fisher's exact test. Statistical significance was set up at a p-value <0.05. A multivariate logistic regression analysis was performed to identify possible predictive factors for bDMARD use. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated.
Results: A total of 165 patients with JIA (107 females, 64.8%) were included. Seventy-five patients had oligoarthritis (45.6%, 62 had persistent oligoarthritis and 13 had extended oligoarthritis), 17 psoriatic arthritis (10.3%), 30 rheumatoid factor (RF)-negative polyarthritis (18.1%), 6 RF-positive polyarthritis (3.6%), 14 systemic arthritis (8.5%) and 23 enthesitis related arthritis-juvenile spondyloarthritis (13.9%). Fourty-five patients were treated with bDMARD (27.3%). Males were treated more frequently with bDMARDs than females (p=0.058). Regarding JIA subtype, more RF-positive polyarthritis patients needed bDMARDs to achieve remission (p=0.027). Likewise, concerning disease activity, JIA patients with higher C-reactive protein (CRP) values were more frequent treated with bDMARDs (p=0.032), which was not verified for erythrocyte sedimentation rate (ESR). Uveitis was significantly more frequent in the bDMARD group (p=0.006). Moreover, more patients with bilateral involvement were treated with bDMARDs, compared with patients with unilateral uveitis (n=0.032). Nevertheless, no differences were found concerning age and number of joints involved at onset, disease duration and ANA positivity. In a multivariate regression model adjusted for gender, the presence of uveitis (OR 4.42, 95% CI 1.43 to 13.60, p=0.010) and polyarticular involvement (OR 6.62, 95% CI 2.05-21.43, p=0.002) remained statistically significant predictive factors for bDMARD use in patients with JIA.

Conclusion: Male patients, polyarticular involvement (with negative or positive RF) and bilateral uveitis were more frequently treated with bDMARDs. In addition, CRP values at onset of JIA were higher in the bDMARD group. Thereby, the presence of uveitis and polyarticular involvement seem to predict the need of bDMARD treatment in JIA patients. Prompt treatment with these agents, early in the disease course, especially in JIA patients with more articular involvement and extraarticular manifestations like uveitis, refractory to conventional DMARDs, should be strongly recommended, in order to avoid irreversible damage and to achieve complete and long-term remission.

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AB1415 INVESTIGATION OF THE EFFECTS OF HEALTH LITERACY LEVELS OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS AND THEIR FAMILIES ON THE GENERAL HEALTH STATUS, QUALITY OF LIFE AND PHYSICAL FUNCTION CAPACITY OF THE PATIENTS

Keywords: Inflammatory arthritides, Patient information and education, Quality of life

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Background: Juvenile idiopathic arthritis is a chronic rheumatological disease characterized by persistent joint inflammation [1, 2]. This disease, which we can consider to be relatively rare, causes pediatric patients to encounter health problems at an early age and therefore struggle with more questions and problems than their peers [3]. At this point, it is important that both children and their families have access to adequate and accurate information about health and that they can use this information [4]. Access to health-related information has brought the concept of "health literacy", which has become more important in recent years, to the agenda [5].

Objectives: Our primary aim is to reveal the health literacy levels of children with JIA and their caregivers by using the Turkish Health Literacy-32 (THL-32), Adult Health Literacy Scale (AHLS) and Turkish version of the Health Literacy for School-Aged Children (HLSAC-T) the validity and reliability studies of which have been done before [6-8]. In addition, revealing the relationship between health literacy and the health status and quality of life of children with JIA is the secondary main aim of the study. Another secondary aim is to evaluate the physical limitations and functional capacity caused by JIA.

Methods: This cross-sectional study was conducted between September and December 2022 at Hacettepe University. Inclusion criteria were a confirmed JIA diagnosis according to the International League Against Rheumatism (ILAR) criteria, aged between 9–18 years. Children and one of their parents were invited to study. Demographic data, clinical findings, laboratory findings, and previous treatment information were recorded retrospectively from patient files and by asking the participants themselves. THL-32, AHLS, and HLSAC-T questionnaires were used to assess health literacy. Functional ability was assessed with the Turkish version of the Childhood Health Assessment Questionnaire (CHAQ) [9]. The Juvenile Arthritis Biopsychosocial Questionnaire (JAB-Q) was used to evaluate the problems experienced by both the child and the parent from a biopsychosocial perspective [10]. The 6-minute walk test (6MWT), 10-meter walking test (10-MWT) and 10-stair climbing test (10-SCT) were used to evaluate the physical and exercise capacity of children [11, 12].

Results: Seventy-nine patients with JIA and one of their parents were included in the study. The patients' mean age was 13.67 ± 2.80 years, and 60.8% of them were female. The mean disease duration was 6.75 ± 4.28 years. The JIA subtypes were as follows: 39 (49.4%) had oligoarticular JIA; 15 (19.0%) had polyarticular JIA; 19 (24.1%) had enthesitis-related arthritis; and 6 (7%) had systemic JIA. Following the THL-32 scale scoring, level of parents' health literacy resulted in the following percentages: inadequate, 3.8%; problematic, 22.8%; sufficient, 34.2%; and excellent, 39.2%. From a total of 79 patients with JIA, 16.5% had low HL, %55.7 had moderate HL, and 27.8% had high HL. The mean age of children with high health literacy was statistically older than the group with medium health literacy ($p < 0.017$). There was no statistically significant relationship between the children's health literacy and parent health literacy.

Conclusion: According to the results of our study, children's health literacy levels show a positive increase as they get older, and there is no significant relationship between parents' health literacy levels. Parents' health literacy levels and education levels are compatible with the AHLS, which includes objective questions. As the education level of the families increases, positive changes are observed in the CHAQ, JAB-Q parameters and 10-SCT test results. Our study shows that the education level of the families is positively related to the quality of life and physical condition of the children, but health literacy is not statistically related to other parameters other than the age of the children.

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AB1416 INTERFERON SIGNALIZATION IN CHILDREN WITH JUVENILE SCLERODERMA

Keywords: Skin, Vasculitis, Myositis

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Background:

Interferon Signalization in children with Juvenile Scleroderma: Hulya Kose[1], Abdurrahman Simsek[2], Muhammed Ali Kizmaz[2], Tugce Bozkurt, [2] Ferdi Ozturk[3], Ferah Budak [2], Hayriye Sarıcaoglu[3] Sara Sebnem Kilic [1]

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Juvenile dermatomyositis (JDM) is an inflammatory disease of the muscle, which is characterized by skin involvement, vasculitis, and progressive muscle weakness. Increased interferon signaling is thought to play a role in the pathogenesis of JDM and is associated with disease severity and activation, as well as the development of calcinosis. Juvenile scleroderma (JSc) is a heterogeneous group of diseases associated with sclerotic skin lesions, grouped together as systemic sclerosis and localized scleroderma (morphea). Although JSc has a different types of skin involvement than JDM, some similarities in their pathogenesis can be identified.

Objectives: The aim of this study is to measure the levels of cytokines and chemokines involved in interferon signaling in patients with JDM and JSc and to determine their correlation with disease severity.

Methods: Thirty-one JSc, 5 JDM, and 13 healthy controls were included in the study. Patients with morphea were scored according to the LoSCAT (activity index) and LoSDI (damage index) indices. Cytokines and chemokines involved in interferon gene signaling (IL -8, IL -1, IP-10, MCP1, TNF-α, CXCL-10, IFN-α, IFN-β, IFN-γ) and interferon signalizing genes including IFI27, IFI44, ISIG15, IFIT1, OAS1, RSAD2 were measured by ELISA and RT_PCR method respectively.

Results: The ratio of female to male patients was 24/12, the median age was 14 years (min 4, max 18), and the median follow-up time was 36 months (min 12, max 108). According to LoSCAT assessment of patients with JSc, the scores were mild 36% (n=13), moderate 25% (n=9), and severe 11% (n=4). Similarly, LoSDI assessment revealed mild 38% (n=14), moderate 22% (n=8), and severe 11% (n=4). It was found that IL-8, IFN-β, IP-10, and MCP-1 were significantly decreased in patients with JSc compared with the healthy control group. TNF-α and IFN-γ were found to tend to decrease in patients with JSc, whereas IFN-α tended to increase in patients with JDM. The correlation of LoSCAT and LoSDI indices with cytokine and chemokine levels in patients with JSc is summarized in Figure 1. In RT_PCR analysis of the interferon signaling genes, including IFI27, IFI44, ISIG15, IFIT1, OAS1, RSAD2, we found no statistically meaningful expressions of the genes compared with the healthy group. However, we identified the fold changes in RSAD2, IFI27, and IFIT1 in JDM and JSc patients compared with the healthy controls in the related genes. The fold changes of the interferon signaling genes are depicted in Figure 2.

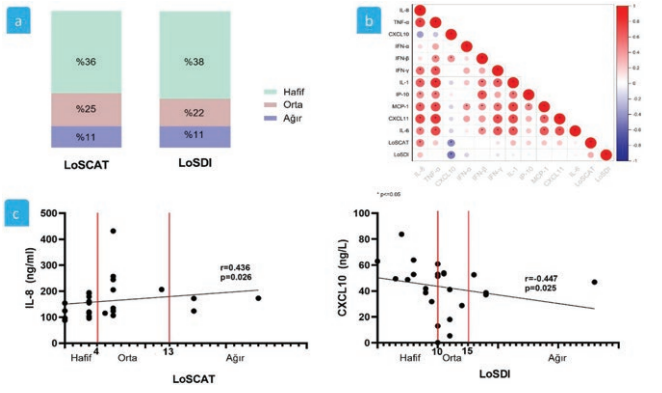


Figure 1. Correlation of LoSCAT/LoSDI Scores with cytokines and chemokines in patients with Localized Sclerodermaa. LoSCAT/LoSDI asssesment. b. Cytokine and chemokine correlation map, c. Statistically significant correlations

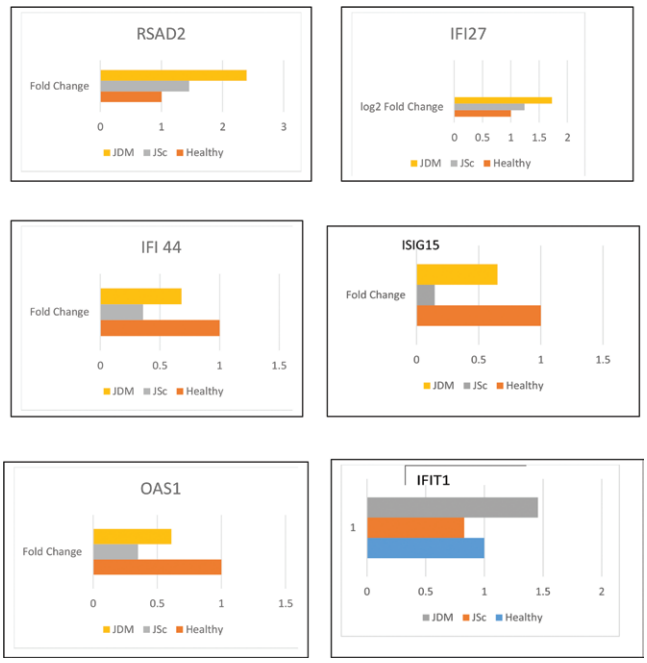


Figure 2. The diagrams of the interferon signaling genes

Conclusion: The results suggest that interferon signaling may be impaired in patients with JDM and JSc, and that cytokines and genes whose significant changes were observed in this study may play a key role in monitoring disease activity. Repeating these studies with larger numbers of patients may shed light on the clinical pathogenesis.

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Disclosure of Interests: None Declared.

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AB1417 HOW TO DIAGNOSE: JUVENILE PSORIATIC ARTHRITIS. MULTICENTER PROSPECTIVE OBSERVATIONAL STUDY IN CHILDREN WITH SUSPECTED DIAGNOSIS

Keywords: Inflammatory arthritides

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Background: Juvenile psoriatic artritis (JPSA), a subtype of juvenile idiopathic arthritis (JIA), constitutes 5% of JIA. The literature is inconsistent regarding features of JPSA, and physicians debate whether it is a distinct entity within JA. Moreover, the criteria diagnosis for JPsA is currently in debate.There are two pediatric diagnostic classifications based on clinical criteria: ILAR classification criteria and Vancouver classification criteria. Classification of JIA has been a great debate since this entity disappeared. [1] The CASPAR criteria are standard in adults. These criteria have a specificity of 91.4% and a sensitivity of 98.7%, makingdiagnostic classification easier. However, the peculiarities of childhood cause some differences to consider.

Objectives: To compare 3 diagnostic criteria for JPSA ILAR, Vancouver and CASPAR.

Methods: Multicenter, cross-sectional study of data from children with JPsA (diagnosis by prescritor physician) who consecutivelly attended in ped-rheumatology outpatient clinic and enrolled from 9 centers within the last 1.5 years. Sociodemographic, clinical characteristics and family history of Psoriasis were collected to assess compliance with diagnostic classification criteria using using the Cohen's Kappa statistic index.

Results: Forty eight children were included with the following sociodemographics characteristics;(table1) Thirty eight children who met the VANCOUVER criteria (80,9%) while thirty two children met the ILAR criteria (68.1%). As for the CASPAR criteria, thirty eight children were diagnosed (80.9%). The diagnostic agreement between the ILAR and CASPAR criteria and ILAR and Vancouver criteria (diagnosed defined) was weak (K=0.67 and K=0.67). In contrast, the agreement was total (K=1 between the CASPAR and Vancouver criteria.

Conclusion: Despite minimal changes between the Vancouver and ILAR criteria, the ILAR exclusion criteria limit the diagnosis of PsA in childhood. Given that the CASPAR and Vancouver were able to detect a significant number of patients with PsA in our series (predominantly adolescents), the application of the CASPAR criteria in the subgroup of children with late onset could be considered.

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Table 1. Clinical and demographic data of the study population

	Total (n=48)
Sex, female (%)	34(70.8)
Age at inclusion (years), mean (SD)	11.5(4)
Age at articular onset (years), mean (SD)	7.1(5)
Age at psoriasis onset (years), mean (SD)	10(3.2)
Type of onset	
Oligoarthritis n (%)	33(68.7)
Poliarthritis n (%)	12(25)
No arthritis n (%)	3(6.2)
Family with Psoriasis	39(81.2)
Extra-articular involvement	
Uveitis n (%)	(12.5)
Entesitis n (%)	7(14.6)
Onicopathy n(%)	14(29.2)
---.Skin-Psoriasis	26(54.2)
Lab	
AAN: positive n (%)	19(39.5)
RF: negative n (%)	48(100)
HLAB27: negative n (%):	43(89.6)

Acknowledgements: NIL.

Disclosure of Interests: Natalia Palmou-Fontana: None declared, Inmaculada Calvo Speakers bureau: ABVIEE, NOVARTIS, JANSEN, GSK, GISELLA DIAZ CORDOVES REGO: None declared, ADRIAN GARCIA-ROGERO: None declared, Juan Carlos Lopez Robledillo: None declared, Berta Paula Magallares López: None declared, Pablo Mesa del Castillo: None declared, ESTEFANIA MORENO RUZAFA: None declared, CARLOS REDONDO-FIGUERO: None declared, MARTINA STEINER: None declared, PAZ COLLADO: None declared.

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AB1418 SYSTEMIC JUVENILE ARTHRITIS: EPIDEMIOLOGY AND LONG-TERM OUTCOME IN WESTERN AUSTRALIA.

Keywords: Epidemiology, Registries

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Background: Systemic juvenile arthritis (S-JIA) is a rare but serious multiorgan autoinflammatory condition of childhood with an unpredictable disease course [1]. There is no data on disease frequency and outcome of S-JIA from the Pacific region.

Objectives: To investigate the epidemiological characteristics and long-term disease outcome in patients hospitalised with S-JIA in Western Australia (WA).

Methods: This population-level observational study includes children under the age of 16 with a recorded diagnosis of S-JIA (ICD-10-AM M08.20-M08.29) residing in WA between January 1999 and December 2014. Individual longitudinal health data regarding hospital admissions, ED visits, cancer and death were derived from the WA Rheumatic Disease Epidemiological Registry (WARDER) that contains routinely collected health data from public and private health care organisations for the entire state of WA.

Results: Based on 46 incident cases (71.7 % girls, median age 6.5 years) the average annual S-JIA incidence rate was 0.61/100,000 (CI 0.28-1.25), which did

not no change significantly over time. Two thirds of incident cases were diagnosed in winter/spring and point prevalence for S-JIA reached 7.15/100,000 (CI 5.29-7.45) in 2014. Disease course was monocyclic in 42% of patients with MAS findings recorded in 4.4% and no case fatality observed during median follow up of 8years. Twenty-seven patients (58%) were readmitted for S-JIA with higher rates per 100 person years in boys (58.3/100, CI 44.5-74.9 vs 14.7 CI 9.9-20.9) (p<0.001). Girls had significantly higher admissions rates for conditions not directly related to S-JIA (rate 103.3 vs 54.4, P<0.001). At last follow-up, arthroplasty had been performed in 4% of patients and there was a high rate of ED visits (72.3/100 person years) after initial s-JIA admission.

Conclusion: The epidemiology of S-JIA in Australia is not unlike other countries [2]. While s-JIA incurred no deaths in the biologic era, S-JIA admission was followed by significant morbidity and health care usage over a lengthy period suggesting the need for extended care for s-JIA patients.

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Disclosure of Interests: None Declared.

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AB1419 IS DECREASED BODY MASS INDEX -2 Z SCORE OR LESS CORRELATING WITH AN ORGAN INVOLVEMENT PATTERN? RESULTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT

Keywords: Systemic sclerosis

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Background: Juvenile systemic sclerosis (jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children. In adult patients decreased body mass index (BMI) correlates with higher mortality. We hypothesized that jSSc patients with lower BMI at presentation have more severe organ involvement.

Objectives: To compare the organ involvement pattern at inclusion into the cohort of jSSc patients with BMI ≤ -2 z score with the patients with higher BMI.

Methods: We reviewed the clinical characteristics of patients who were recruited to the juvenile jSScC till 1st of December 2022. We compared patients with BMI ≤ -2 z score with patients (lwgroup) with higher BMI (nlwgroup). jSScC is a prospective cohort of jSSc patients, who developed the first non-Raynaud´s symptom before the age of 16 years and are under the age of 18 years at the time of inclusion.

Results: At the time of the evaluation, we had 232 patients in the cohort and 217 of them had BMI data to include in the evaluation. Thirty-three patients were in the lwgroup (15%) and 88% (n=29/33) of them diffuse subtype and in the nlwgroup 64% (113/177). The median age at onset of Raynaud phenomenon in the whole group was 10.6 years and the median age at the first non-Raynaud symptom in the whole group was 11.0 years. Median disease duration in the whole group was 2.4 years at the time of inclusion. Approximately 95% of the patients were treated with a DMARD. There were no statistically significant differences between the lwgroup compared to nlwgroup regarding antibody pattern, inflammatory marker or organ involvement pattern, except higher number of patients with Gottron papules (41% lwgroup vs 25% nlwgroup; p=0.01) and sclerodactylia (84% lwgroup vs 73 % nlwgroup; p=0.049). Regarding the patient related outcomes at inclusion in the cohort, the global disease activity by VAS 0-100 was 40 in both groups (p=0.032), but the patient global disease damage by VAS 0-100 was 50 in the lwgroup which was significantly higher compared to 30 nlwgroup (p=0.014).

Table 1. Comparison of patients with different BMI z-scores at time of inclusion in the cohort

	Z-Score ≤ -2 N=33	Z-Score > -2 to < 2 N=177	P value
Gottron Papules	41% (13/32)	25% (44/175)	0.001
Puffy Fingers	13% (4/30)	38% (61/159)	0.049
Sclerodactylie	84% (27/32)	73% (121/166)	0.049
Patient global disease damage	50 (30 – 75) n=27	30 (10 – 55) n=133	0.014

Conclusion: In our jSSc cohort, currently the largest of the world, we could not find any differences regarding major internal organ involvement in patients with lower BMI at time of inclusion in the cohort. Nevertheless, there is a significant difference in patient related outcomes regarding global organ damage between the two groups. The long-term prognosis of these patients should be addressed in future studies.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1420 PAEDIATRIC PRESENTATION OF ANTIPHOSPHOLIPID SYNDROME: A REVIEW OF RECENT LITERATURE WITH ESTIMATION OF LOCAL PREVALENCE

Keywords: Anti-phospholipid syndrome, Systemic lupus erythematosus, Epidemiology

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Background: No evidence exists on any study investigating the prevalence of paediatric Antiphospholipid Syndrome (APS) in the general population (1) and most of the available recommendations on how to manage these patients come from observational studies and physicians' experience.

Objectives: We aimed to investigate the epidemiology, the clinical and laboratory characteristics of the paediatric involvement of Antiphospholipid syndrome (APS), by performing a systematic review of the current evidence and reviewing local experience in the Northwest Italy.

Methods: We performed a detailed literature search to identify articles describing clinical and laboratory characteristics of paediatric APS patients. In concomitance, we conducted a registry-study collecting data from the Piedmont and Aosta Valley Rare Disease Registry including paediatric patients diagnosed with APS in the last ten years.

Results: The systematic review included nine articles with a total of 386 paediatric patients [65% females, 50% with Systemic Lupus Erythematosus (SLE) as concomitant diagnosis]. Rate of venous and arterial thrombosis were 57% and 35% respectively. "Extra-criteria manifestations" of APS included mostly hematological and neurological involvement (91 thrombocytopenia, 32 haemolyticanaemia, 19 chorea, 8 multiple sclerosis-like lesions, 9 migraines and one transverse myelitis). Almost one quarter of patients (19%) reported recurrent events and 13% manifested as CAPS. Further details of the included studies are detailed in Table 1. A total of 17 paediatric patients (mean age 15.1 ±2.8, 76% female) developed APS in the Northwest of Italy. In 29% of cases SLE was a concomitant diagnosis. Deep vein thrombosis was the most frequent manifestation (28%) followed by Catastrophic APS (CAPS) (6%). Taking into account that the paediatric population of the Piedmont and Aosta Valley Region is around 680,000 persons, the calculated estimated prevalence of paediatric APS in Piedmont and Aosta Valley Region is 2.5 cases per 100,000 people. When analyzing the data of the register in an eleven year period (from January 2011 to December 2021), the estimated mean annual incidence was 0.2 cases per 100,000 inhabitants.

Conclusion: Clinical manifestations of paediatric APS seem to be more severe and with a high prevalence of non-criteria manifestations. International efforts are needed to better characterize this condition and to develop new specific diagnostic criteria to avoid missed/delayed diagnosis in children with APS.

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Table 1. Main characteristics of the studies included in the Systematic Review

First Author, year of publication	Design	Setting	Focus	Number of paediatric APS	Age (mean, ±SD; median, range)	PAPS (n)	SAPS (n)
M. Gattorno, 2003	Prospective	Multicenter	pPAPS prospective cohort	14	9 (3-13)	12	2
Y. Berkun, 2006	Prospective	Multicenter	pPAPS prospective cohort	28	12.9 ±3.7	23	5
T. Avcin, 2008	Registry	Multicenter	Descriptive cohort	121	10.7(1–17)	61	60
H. Berman, 2014	Registry	Multi center	CAPS	45	11,5 ±4,6	31	14
A.Nageswara Rao, 2016	Retrospective cohort	Single center	Descriptive cohort	17	15,3 (1-19)	9	8
J. Ma, 2017	Retrospective cohort	Single center	Descriptive cohort	58	14 ±3	14	44
A. G. Islabão, 2020	Retrospective cohort	Multi center	APS in pSLE	67	12 (4-18)	0	67
E. Sloan, 2021	Retrospective cohort	Single center	APS and aPL in pCTD	15	12.7 ±3.3	0	15
J. A. Madison, 2022	Retrospective cohort	Single center	pAPS	21	16 (8-18)	10	11

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1421

DOES THE SACROILIAC JOINT MAGNETIC RESONANCE IMAGING ENHANCE THE ENTHESITIS-RELATED ARTHRITIS DIAGNOSIS?

Keywords: Imaging

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Background: Magnetic Resonance Imaging (MRI) is the gold standard in the diagnosis of adult spondyloarthritis [1]. MRI sensitivity and specificity seem to be less studied in juvenile spondyloarthritis, especially in Enthsitis-related Arthritis (ERA).
Objectives: We aimed to determine the sensitivity and specificity of MRI in the diagnosis of ERA.
Methods: We conducted a retrospective study including 44 patients with Juvenile Idiopathic Arthritis (JIA) meeting the International League of Associations for Rheumatology (ILAR) 2001 criteria. For each patient, we collected the following data: age, age at the onset of JIA, JIA subtype, disease duration, C-reactive protein (CRP), HLA-B27 typing, and Erythrocyte sedimentation rate (ERS) levels. Each patient had a sacroiliac joint MRI. Sacroiliitis was defined using the OMERACT JAMARIS scoring system [1]. Disease activity was assessed using the JSpADA score for ERA and JADAS-CRP-10 for the rest of the JIA subtypes. We divided patients into two groups: Group 1 (G1) patients with ERA and Group 2 (G2) patients with non-ERA subtype. Statistical analysis was performed using SPSS software.
Results: We included 28 boys and 16 girls. The mean age was 13.65 ± 4.62 years. The mean age at the onset of the disease 9.57 was ± 3.97 years. The mean disease duration was 4.34 ± 3.09 years. There was enthesitis-related arthritis in 61% of the cases (n=27), oligoarticular JIA in 14% of the cases (n=6), polyarticular JIA in 11% of the cases (n=5), and psoriatic arthritis in 7% of the cases (n=3). JIA was undifferentiated in 7% of the cases (n=3). Sacroiliac joints were painful in 15 patients (34%). The mean CRP and ESR were 14.42 ± 19.67mg/L and 26.56 ± 20.87mm, respectively. The mean JADAS and JSpADA were 6.6 ± 4.7 and 3.09 ± 1.55, respectively. HLA-B27 was performed in 22 patients and was positive only in five patients. IRM was normal in 25 patients (57%) (G1: 11 versus G2:14) and showed bone marrow in the sacroiliac joints in 19 patients (34%) (G1=16 versus G2=3, p=0.005). The sensitivity and specificity of the sacroiliac joints MRI in the diagnosis of ERA were 61.54% and 82.35%, respectively. Positive predictive value and negative predictive value were 84.21% and 58.33%, respectively. Furthermore, sacroiliac joint pain in the clinical examination was able to predict sacroiliac bone edema in MRI with an odds ratio of 6.8 (95% confidence interval 1.68 to 28.09; p=0.006).
Conclusion: According to other studies, ours showed that MRI inflammatory lesions could be observed in JIA regardless of JIA sub-types [2]. Interestingly, we found that MRI abnormalities were not sensitive but had a good specificity in the diagnosis of ERA. Thus, MRI could guide the diagnosis of ERA but could not be the gold standard in this disease.

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Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4072

AB1422

CLINICAL MANIFESTATIONS AT THE ONSET OF PEDIATRIC MIXED CONNECTIVE TISSUE DISEASE (PMCTD): A SYSTEMATIC REVIEW.

Keywords: Systematic review, Mixed connective tissue disease, Rare/orphan diseases

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Background: pMCTD is a rare disorder that includes features of systemic lupus erythematosus, polymyositis/dermatomyositis, juvenile idiopathic arthritis, and systemic sclerosis. Fifty years have passed since Sharp identified MCTD in 1972, and diagnosis of this disorder remains challenging.
Objectives: The aim of this review is to identify any clinical features at the diagnosis of pMCTD and manifestations that are not currently part of the available diagnostic criteria.
Methods: A systematic literature review was performed in accordance with PRISMA guidelines using electronic bibliographic databases: MEDLINE via PubMed and EMBASE. Data obtained were extracted using a dedicated database containing clinical data that best categorize patient characteristics. Criteria for inclusion: studies including patients with a pMCTD diagnosis with onset before 18 years of age and reporting a description of initial clinical features.
Results: The search returned a total of 1372 results: 409 articles were excluded as duplicates and 790 based on title/abstract, 133 because of publication type (n = 4) or because the full text was not available (n = 65) or not in English (n = 64). One (n=1) eligible article resulted from manual screening of references cited in the selected publications and in the reviews. Finally, 41 articles were included: 23 case reports, 9 case series, 5 prospective, and 4 retrospective studies from 1973 to 2019, with a total number of 218 patients. They were predominantly female (81.56%, n=167), and the mean age at onset was 147 months (median 126 months, 10.5 years). When indicated, the most commonly used criteria for diagnosis were Kasukawa criteria (50%, 11 studies), then Alarcon-Segovia criteria (31%, 7 studies), then Sharp criteria (23%, 5 studies); no Khan criteria were used. Clinical features are listed in Figure 1.

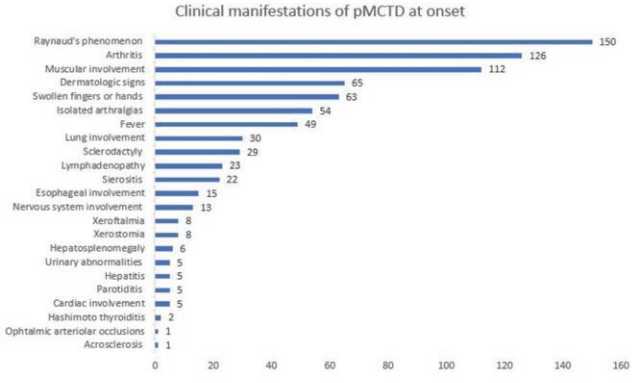


Figure 1. Number of patients for clinical feature at onset.

Joint involvement, Raynaud's phenomenon, myositis, and swollen fingers/hands are the most common clinical features at diagnosis according to the data reported in the literature, although with slightly lower percentages than in other reviews. Dermatologic signs are very heterogeneous, but were found to be a very present feature at disease onset, affecting 1/3 of patients. Fever, not covered by any of the diagnostic criteria, was noted in 1/4 of cases. Pulmonary and esophageal involvement are reported in a lower percentage at the onset of the disease, indicating a more developmental nature of these conditions.

Conclusion: The data from this systematic review suggest greater clinical heterogeneity of the disease in the pediatric population, for which there are no validated diagnostic criteria. Typical features appear to be less common when case reports are included, suggesting a less characteristic initial presentation than an advanced stage; therefore, the absence of typical features at baseline should not preclude a diagnosis of pMCTD. Fever often occurs early in the disease and is not included in the diagnostic criteria. This systematic review may provide useful insights for future research to better assess the clinical features of pMCTD and the potential development of scores/algorithms for diagnosis in the pediatric population.

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AB1423 USE OF BIOSIMILAR THERAPIES IN ADULT PATIENTS DIAGNOSED WITH JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FROM THE SPANISH REGISTRY OF ADVERSE EVENTS WITH BIOLOGIC THERAPIES (BIOBADASER)

Keywords: bDMARD

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood. The emergence of new biological drugs has changed the prognosis and therapeutic approach to these patients, and costs are reduced with the use of biosimilar disease modifying antirheumatic drugs (bsDMARD).

Objectives: Our aim was to describe the use of bsDMARD therapies in JIA.

Methods: Data was obtained from the nationwide prospective registry BIOBADASER. All patients diagnosed before age 16 in our database between 2000 and 2022 were included in the analysis. JIA is classified into 7 subgroups: systemic, persistent or extended oligoarthritis, RF positive polyarthritis, RF negative polyarthritis, enthesitis-related arthritis, psoriatic arthritis, and undifferentiated arthritis. Due to the registry design, it was not possible to identify each of the JIA subgroups; thus, we classified them into oligo/polyarticular JIA, JIA related to enthesitis, and psoriatic JIA. Proportions, means and standard deviations (SD) were used to describe our population and the utilization of treatments. Drug persistence was calculated using Kaplan-Meier survival curves until termination of treatment due to any reason.

Results: From a total of 313 patients, 130 patients (41.5%) received 151 treatments with bsDMRAD, 60.8% of which were women (n= 79). Mean age at diagnosis was 11.2 years (SD= 6.1) and mean age at the beginning of treatment was 25.1 (SD= 13.4). Patients were classified as oligo/polyarticular JIA (79.2%), JIA related to enthesitis (16.2%) and psoriatic JIA (4.6%). Methotrexate was used in combination in 39.1% of the biosimilar treatments. The most commonly used drug was Adalimumab (56.8%), followed by Etanercept (28.7%). Table 1 shows the biologic therapies used in our sample and the reasons for discontinuation. The median survival rate with the biosimilar drug and original was similar.

Conclusion: Adalimumab were the most commonly used biosimilar therapy in JIA. Ineffectiveness was the main reason for discontinuation. There were no differences on 5 years survival rates, which is a crucial endpoint in JIA.

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Table 1. Biologic therapies in JIA patients and reasons for discontinuation.

Treatment	Original	Biosimilar	Total
Adalimumab	127 (37.2)	85 (56.3)	212 (43.1)
Etanercept	104 (30.5)	44 (29.1)	148 (30.1)
Infliximab	22 (6.5)	19 (12.6)	41 (8.3)
Rituximab	6 (1.8)	3 (2.0)	9 (1.8)
Certolizumab pegol	49 (14.4)	-	49 (10.0)
Golimumab	33 (9.7)	-	33 (6.7)
Total	**341 (100)**	**151 (100)**	**492 (100)**
Reasons for discontinuation			
Inefficacy or loss of efficacy	90 (43.1)	29 (52.7)	119 (45.1)
Adverse event	42 (20.1)	10 (18.2)	52 (19.7)
Pregnancy or desire to be pregnant	14 (6.7)	0 (0.0)	14 (5.3)
Loss of patient	4 (1.9)	1 (1.8)	5 (1.9)
Remission	19 (9.1)	1 (1.8)	20 (7.6)
Change for non-medical reasons	5 (2.4)	2 (3.6)	7 (2.7)
Other	29 (13.9)	10 (18.2)	39 (14.8)
Unknown	6 (2.9)	2 (3.6)	8 (3.0)
Total	**209 (100)**	**55 (100)**	**264 (100)**

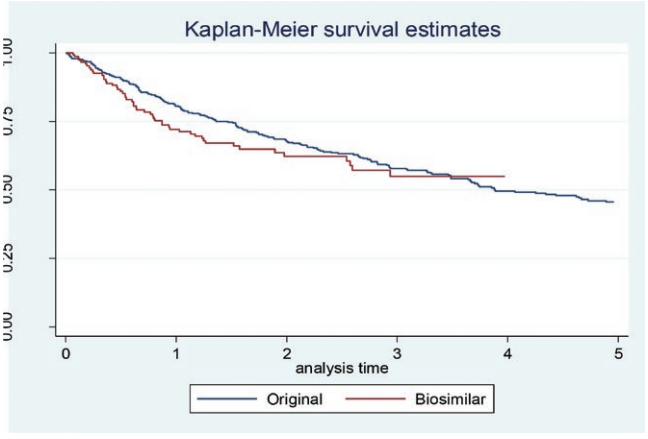


Figure 1. 5-year survival of bsDMARD vs. original bDMARD

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Disclosure of Interests: None Declared.

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AB1424 CLINICAL VARIABILITY IN PATIENTS DIAGNOSED OF JUVENILE IDIOPATHIC ARTHRITIS WITH POSITIVE AND NEGATIVE ANTINUCLEAR ANTIBODIES (ANA)

Keywords: Autoantibodies

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Background: Juvenile Idiopathic Arthritis (JIA) involves a set of chronic arthritis of onset in childhood. JIA can be splitted into 7 categories based on the classification of the International League of Associations for Rheumatology (ILAR):

systemic arthritis, oligoarthritis, rheumatoid factor (RF) negative polyarthritis, RF positive polyarthritis, enthesitis related arthritis, psoriatic arthritis, undifferentiated arthritis. In addition to this classification, some authors propose differentiating between patients who have positive (+) and negative (-) ANA in serum because there could be differences between these two subgroups, raising the possibility of homogenizing subtypes based on this [1].

Objectives: To describe the variability of extra-articular manifestations, treatment and prevalence of the different JIA subtypes between patients who have positive and negative ANA in serum.

Methods: Cross-sectional descriptive study in 68 patients with JIA according to ILAR criteria visited in the transitional consultation of a Spanish tertiary-level hospital. Clinical features, analytical and treatment data were collected, and patients were divided according to ANA+ or ANA- in serum. A >1/80 title of ANA determined by IFI on at least 2 occasions was considered positive. Subsequently, the qualitative data was analyzed using Chi-Square test, and the means were compared using ANOVA analysis.

Results: 68 patients were included in the study. 33 were grouped in ANA- and 35 in ANA+. The ANA+ group was composed with 28 women (80%) and the ANA- group was made up with 18 women (54.44%) (p= n.s.). The mean age of diagnosis was 11 years old in the ANA- group and 9 years old in the ANA+ group.

Variable (n)	*ANA-*	*ANA+*	*P-value*
	N=33	*N=35*	
	n(%)	n(%)	
Subtype			
Oligoarthritis (20)	3 (9.09%)	17 (48.57%)	<0.001
RF(-) polyarthritis (14)	8 (24.24%)	6 (17.14%)	0.6719
RF(+) polyarthritis (4)	0 (0%)	4 (11.43%)	0.1372
Enthesitis related arthritis (14)	11 (33.33%)	3 (8.57%)	0.0216
Systemic arthritis (6)	6 (18.18%)	0 (0%)	0.0268
Psoriatic arthritis (4)	2 (6.06%)	2 (5.71%)	0.9999
Undifferentiated arthritis (6)	3 (9.09%)	3 (8.57%)	0.9999
Clinical features			
Psoriasis (8)	2 (6.06%)	6 (17.14%)	0.2979
Uveitis (10)	3 (9.09%)	7 (20%)	0.354
Enthesitis (9)	3 (9.09%)	6 (17.14%)	0.5344
Oral and genital thrush (14)	7 (21.21%)	7 (20%)	0.9999
Raynaud (6)	3 (9.09%)	3 (8.57%)	0.9999
Analytical			
HLAB27+ (20)	12 (42.86%)	8 (27.59%)	0.3523
RF+ (7)	1 (3.57%)	6 (18.18%)	0.1673
CCP- antibodies+ (9)	2 (6.06%)	7 (20%)	0.1811
Treatment			
sDMARD (31)	12 (36.36%)	19 (55.88%)	0.1748
bDMARD (30)	13 (39.39%)	17 (48.57%)	0.6049
Corticosteroids (6)	5 (15.15%)	1 (2.86%)	0.1742

Oligoarticular JIA was more frequent in the ANA+ group (48.57%) than in the ANA- (9.09%), being this difference statistically significant. Enthesitis related arthritis was more frequent in the ANA- group (33.33%) than in the ANA+ (8.57%), as it was systemic arthritis (18.18% in ANA- and 0% in ANA+), both differences being statistically significant. Uveitis, psoriasis and the use of sDMARD were more frequent in the ANA+ and corticosteroid use was more frequent in ANA- patients, but without reaching statistical significance.

Conclusion: In our study, as in the literature, the oligoarticular JIA type occurred more frequently in the ANA+ group, while enthesitis related arthritis and systemic arthritis were more frequent in the ANA- group. Although the treatment patterns and the prevalence of psoriasis and uveitis appear to differ between the two groups we did not find statistically significant difference. This could be due to the small number of patients included, with the possibility that it could be corrected if the sample was expanded.

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AB1425 CLINICAL CHARACTERISTICS OF A PORTUGUESE COHORT WITH UNDEFINED AUTOINFLAMMATORY DISEASES

Keywords: Genetics/Epigenetics, Cytokines and chemokines

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Background: Systemic autoinflammatory diseases (SAIDs) are rare inherited disorders characterized by periodic or chronic multisystemic inflammation. The diagnosis is based on typical phenotypes and often supported by genetic testing. However, a distinct diagnosis cannot be met in half of these patients, being classified as undefined SAIDs (uSAIDs) [1].

Objectives: To analyse the clinical and genetic characteristics of a portuguese cohort of uSAID.

Methods: Patients followed up in 2 SAIDs clinics with recurrent or persistent episodes of systemic inflammation associated with serum acute phase reactants elevation who do not meet the PRINTO diagnosis criteria for any well-defined SAIDs [2] were classified as having uSAID. Patients who do not have any pathogenic gene mutation or have 1 variant of uncertain significance of a gene related to a well-known autosomal dominant SAID were included, as well as patients with pending genetic analysis. Categorical variables are described as frequencies and percentages and continuous variables as median (IQR1, IQR3).

Results: This study included 24 patients, of which 12 (50.0%) were female and 12 (50.0%) were male. The median age at disease onset was 2.4 (IQR: 1.4, 8.2) years old, the median age at diagnosis was 6.5 (IQR: 2.4, 9.9) years old and the median time of disease duration was 6.8 (IQR: 9, 12.4) years. The majority of the patients (n=14, 58.3%) had episodes of recurrent systemic inflammation lasting 2 to 5 days. Two patients exhibited persistent inflammation. Regarding patients with recurrent inflammation, 10 (41.7%) had more than 12 episodes per year, 7 (29.2%) had 2 to 6 episodes per year and 4 (16.6%) had 7 to 12 episodes per year. The remaining patient had an episode every 2 years. In 13 (54.2%) the intercritical interval was regular, with a median of 21 days. Besides fever, the most commonly reported clinical manifestations were mucocutaneous lesions (n=24) including mouth ulcers (n=11), abdominal pain (n=12), lymphadenopathy (n=10) and arthralgia (n=10). C-reactive protein was elevated in all patients during attacks, erythrocyte rate sedimentation in 20 (83.3%) and amyloid A protein in 10 (41.7%). In 14 (63.6%) patients, acute phase reactants normalized during the intercritical phase. Genetic analysis was performed in 22 patients of this cohort – 8 patients were found to have a variant of uncertain significance in genes associated with hereditary SAIDs or mutations in genes that are not known to be associated with SAIDs and results are pending in the remaining 4. The most frequently used therapy was oral steroids (n=18, 75.0%) and half of these patients were treated with a single dose of 1 mg/kg of oral prednisolone on demand with shortening/resolution of the episode in 8 patients. Colchicine was used in 14 patients decreasing the number of episodes in 9 (64.2%). Anakinra led to complete remission in 3 of the 5 treated patients. Two patients were treated with canakinumab achieving complete remission. Infliximab, in association with azathioprine, resulted in disease remission in the only patient in which this therapy was used. None of the 3 patients submitted to tonsillectomy achieved remission.

Conclusion: Similarly to other uSAIDs' cohorts, mucocutaneus manifestations, abdominal pain and arthralgia were frequently reported. A third exhibited acute phase reactants elevation in the intercritical phase. Most of our patients had a favourable response to colchicine and IL-1 inhibitors. It is worth noting the high frequency of mouth ulcers, lymphadenopathy and pharyngitis and the high response rate to oral steroids and colchicine. These features resemble PFAPA syndrome, highlighting the challenges in the differential diagnosis of both conditions.

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Disclosure of Interests: None Declared.

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AB1426

CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS AND BOWEL INFLAMMATION: A MONOCENTRIC COHORT

Keywords: Rare/orphan diseases, Gastrointestinal tract, Remission

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Background: Chronic recurrent multifocal osteomyelitis (CRMO) is a rare autoinflammatory disease of bone primarily affecting children and adolescents. Although CRMO can be associated with inflammatory bowel disease (IBD)[1], the prevalence of subclinical bowel inflammation and its relationship with other autoimmune bowel disorders remains uncertain.
Objectives: This study aims to evaluate the prevalence of subclinical bowel inflammation in CRMO patients and the potential association with celiac disease.
Methods: Clinical records of patients diagnosed with CRMO attending the Unit of Pediatric Rheumatology of Gaetano Pini Hospital were retrospectively reviewed. Fecal calprotectin and screening for celiac disease were performed in all patients within 2 years after diagnosis.
Results: Complete data from 24 patients were collected (83% female). The mean age at diagnosis was 10.1 (DS ± 2.7) and the median follow-up time was 68.5 months (IQR 97.5). The first symptom at onset was bone pain (100%), while only 4 patients (17%) complained of gastrointestinal symptoms (abdominal pain, weight loss, diarrhea). The patients in our cohort had no specific comorbidity, except for two patients suffering from hemophilia and pyoderma gangrenosum, respectively. 96% (23/24) of patients had polyostotic disease. During the follow-up period, 9 patients (38 %) received only non-steroidal anti-inflammatory drugs therapy, 10 patients (42%) received conventional disease-modifying antirheumatic drugs (methotrexate), 4 (17%) received anti-tumor necrosis factor (TNF) agents and 12 (50%) received intravenous bisphosphonates. Cumulative treatments are summarized in Figure 1. Two patients, both in clinical remission off medication, were lost to follow-up. Calprotectin levels were normal in 100% of patients, while 3 patients (13%) presented positive screening test for celiac disease with a positive test for IgA anti-tissue transglutaminase antibodies (Table 1). In one of these patients, the diagnosis of celiac disease was confirmed by duodenal biopsy. After a gluten-free diet, the patient, who was off medication, achieved complete clinical remission and a remarkable improvement in radiological lesions.
Conclusion: The link between autoinflammatory bone disease and intestinal inflammation should be further investigated since it might open insight into bone inflammation and new therapeutic options. In our experience, controlling bowel disease may promote a better response to CRMO treatments. On the other hand, the percentage of unexplained bone pain in celiac disease is high, and, in this scenario, a possible inflammatory bone disorder should be ruled out.

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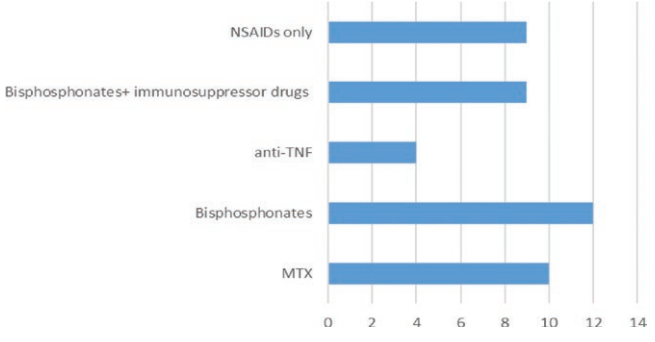


Figure 1. Cumulative treatments during the follow-up time. MTX= methotrexate; TNF= tumor necrosis factor; NSAIDs= non-steroidal anti-inflammatory drugs.

Table 1. Case series of CRMO in association with positive IgA anti-tissue transglutaminase antibodies

Case number	Sex	Age at onset	Comorbidity	Poly/monostotic disease	Duodenal biopsy	Treatment
1	F	10	No	Poly	Positive	NSAIDs
2	F	12	No	Poly	Not performed yet	NSAIDs
3	F	12	Pyoderma gangrenosum	Poly	Not performed yet	Bisphosphonates

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Disclosure of Interests: Stefania Costi: None declared, Sabino Germinario: None declared, Maria Rosa Pellico: None declared, Andrea Amati: None declared, Maurizio Gattinara: None declared, Cecilia Chighizola: None declared, Achille Marino: None declared, Roberto Caporali Speakers bureau: AbbVie, Amgen, BMS, Celltrion, Fresenius, Galapagos, Janssen, Lilly, Novartis, Pfizer, UCB, Consultant of: AbbVie, Fresenius, Galapagos, Lilly, Novartis, Pfizer, UCB.
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AB1427

HIP DAMAGE ASSESSED BY CARSH SCORE WAS MORE SEVERE IN ENTHESITIS-RELATED ARTHRITIS SUBTYPES

Keywords: Imaging, Validation

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Background: Juvenile idiopathic arthritis is a heterogeneous group of diseases characterized by unknown origin arthritis under 16 years. Compared to other juvenile idiopathic arthritis subtypes, enthesitis-related arthritis has a poor prognosis with a higher disability. Moreover, the frequency of hip involvement contributes to poorer outcomes and higher disease activity in this form. The childhood Arthritis Radiographic Score of the Hip (CARSH), a valid score of hip damage, is used to quantify and monitor hip osteochondritis changes such as space narrowing, erosions, malalignment, sclerosis, flattening of the femoral head, and growth abnormalities [1].
Objectives: This study aimed to assess hip damage using the CARSH in children suffering from different subtypes of JIA.
Methods: We conducted a cross-sectional study including patients with JIA according to the ILAR criteria with hip involvement in the rheumatology department at Kassab Institute of orthopedics. The hip involvement was defined as the presence of hip pain and/or limping and range motion limitation, and/or abnormal hip findings in pelvic radiography, ultrasound, or MRI. We collected demographic data, juvenile arthritis subtypes, hip pain and limitation, presence of antigen HLA, and extra-articular manifestations. Experimented and blinded pediatric rheumatologists read the pelvic radiograph using the Childhood Arthritis Radiographic Score of the Hip (CARSH).
Results: Twenty-two children with a median age of 13 years [5-22] were included. The gender ratio was 1.4 (13 Males/9 Females). The median age of disease onset was 9.5 years [4-14]. The frequency of each JIA subset was as follows: enthesitis-related arthritis (n=13), psoriatic arthritis (n= 3), oligoarthritis (n= 4), polyarticular with rheumatoid factor (n= 1), and polyarticular without rheumatoid factor (n=1). Antigen HLA was positive in two patients. One patient had anterior uveitis, and one patient had personal psoriasis. Eight patients had bilateral hip pain, 6 patients had unilateral hip pain and 8 patients didn't have hip pain. Six patients had limitations of both hips, 6 patients had only one limited hip and 10 patients had normal mobility of the hip. MRI showed inflammatory signal abnormality of the hip joint in 12 patients and ultrasound showed synovitis in 6 patients. Forty-four hips were assessed by the radiographic score. The median CARSH was 1.8±2.2 [0-7]. Statistical analysis showed a higher CARSH score in enthesitis-related arthritis patients compared to other JIA subtypes (p = 0.04) (Figure1).
Conclusion: This study showed that the radiographic score CARSH was higher in enthesitis-related arthritis patients. This finding prompts the escalating of the treatment approach in this JIA subtype to prevent damage and joint replacement surgery.

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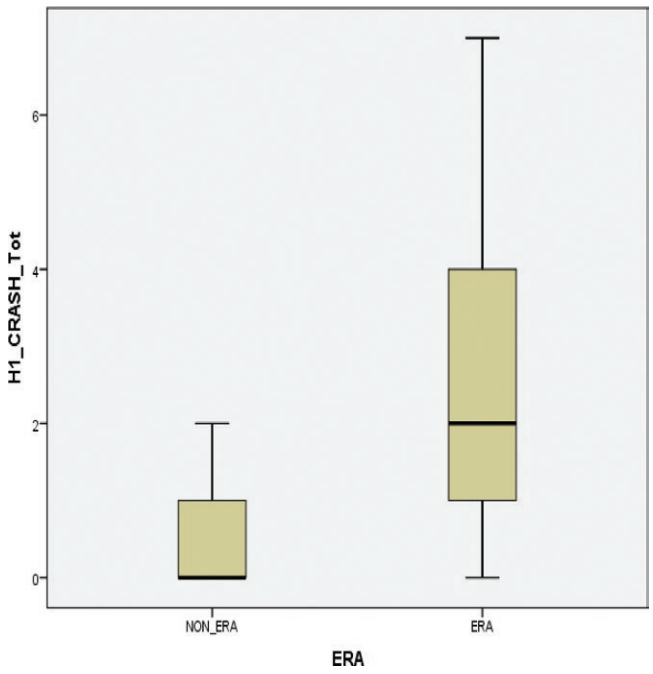


Figure 1. CARSH score in enthesitis-related arthritis (ERA) patients compared to other JIA subtypes (non ERA)

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1428

PSORIATIC ARTHRITIS: CLINICAL FEATURES IN CHILDHOOD

Keywords: Psoriatic arthritis

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Background: Diagnosis and treatment of psoriatic arthritis require attention from specialists. Clinical manifestations of psoriatic arthritis in children are variable.
Objectives: The purpose of the study: to evaluate the clinical picture of psoriatic arthritis (PsA) in children.
Methods: The case histories of 23 children with psoriatic arthritis aged 3 to 17 years who were treated by a rheumatologist from 2019 to 2022 were analyzed.
Results: Probable psoriatic arthritis was diagnosed in 7 (29%) patients, definite psoriatic arthritis was diagnosed in 16 (71%) patients. At the same time, 12 (53%) children fell ill at the age of up to 7.5 years. In 7 (29%) patients, the disease began with skin lesions, in 16 (71%) patients immediately with articular syndrome. In the group of patients with certain psoriasis, plaque psoriasis was noted, it was detected in 17 (76.3%) children, guttate psoriasis was in 3 (13.5%), isolated psoriasis of the nails in 3 (10.2%) children. In 5 (21.7%) children, lesions of the skin and nail plates were observed. It was noted that psoriatic onychodystrophy was represented by onycholysis, an "oil spot" in the area of fingers and toes in 5 (23%) patients, and thimble symptom was diagnosed in 4 (18.1%) patients. At the onset of the disease, oligoarticular or asymmetric articular syndrome was noted in 65.6% of cases, a symmetrical rheumatoid-like variant in 20.2% of cases, and psoriatic spondylitis in 14.2% of cases. The dynamics of the articular syndrome after 3 years of observation and treatment indicated the development of symmetrical rheumatoid-like arthritis in 41.2% of patients, asymmetric oligoarthritis in 24.1% of children, and spondyloarthritis in 22.1%.
Conclusion: The clinical picture of psoriatic arthritis in children is variable. Skin lesions preceded the development of arthritis in children. At the onset of the disease, asymmetric oligoarthritis predominated, followed by transformation into symmetrical rheumatoid-like arthritis.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1429

EMAPALUMAB TREATMENT FOLLOWED BY HEMATOPOIETIC STEM CELL TRANSPLANTATION IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS COMPLICATED BY RECURRENT MACROPHAGE ACTIVATION SYNDROME

Keywords: Cytokines and chemokines, Innate immunity

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Background: Macrophage activation syndrome (MAS) is a life-threatening complication of different rheumatic diseases, particularly of systemic juvenile idiopathic arthritis (sJIA).
Objectives: We report the case of 17-year-old girl with sJIA complicated by recurrent severe MAS episodes.
Methods: Patient received emapalumab (anti-IFNg antibody) in two subsequent MAS episodes, then underwent an uncomplicated hematopoietic stem cell transplantation (HSCT) from a haploidentical donor, while receiving emapalaumab and anakinra granting complete control of inflammatory activity of the underlying disease. One year after transplant she is in complete disease remission.
Results: A 13-year-old Caucasian girl presented with fever, rash and hepato-splenomegaly. Laboratory parameters were consistent with full-blown MAS (tab 1). In the absence of clear evidence of an underlining condition, a diagnosis of secondary HLH was made. Treatment with high dose of intravenous (IV) methylprednisolone (mPDN) and oral cyclosporine (CYC) was started with progressive improvement. After one year, still on CYC, she presented with fever, rash and arthritis with laboratory parameters consistent with MAS (table 1), diagnosis of sJIA complicated by MAS was made. In 24 hours, her general condition rapidly worsened and she was admitted to the ICU. High dose of IV mPDN (7 pulses of 30 mg/kg/day) as well as IV CYC (5 mg/kg/day) did not yield a response. Emapalumab was started, in the NI-0501-06 trial, (6 mg/kg initial dose followed by 3 mg/kg every 3 days) for 11 infusions. Conditions progressively improved. In order to prevent flares of the underlining sJIA, anakinra (2 mg/kg/day) was started. After 2 years in clinical remission, while she receiving anakinra every other day, she presented with fever, vomiting and diarrhea. Anakinra was immediately increased to daily dosing. Stool analysis showed Salmonella infection and antibiotic therapy was started. Her condition rapidly worsened, laboratory parameters were again consistent with full-blown MAS (tab 1). She required ICU admission for multiorgan failure. Anakinra was administered IV and the dose increased up to 12 mg/kg/day. IV MPDs (8 pulses of 30 mg/kg/day) as well as IV CYC (5 mg/kg/day) were started with partial response. Based on her previous response, emapalumab was started again (compassionate use) with marked and rapid improvement. Because of recurrent MAS episodes, particularly for their rapidly progressive evolution, the patient underwent an ex-vivo T cell-depleted haploidentical HSCT from her mother. The conditioning regimen was based on a Thiotepa-Treosulfan-Fludarabine scheme. Emapalumab was continued 1 month after HSCT together with anakinra. The patient developed mild complication, achieved full donor engraftment with complete donor-derived immune reconstitution after 3 months. One year after HSCT, the patient is in excellent clinical condition on anakinra every other day, with complete remission of sJIA/MAS, also confirmed by persistently normal levels of IL-18 and CXCL9 (tab 1).

Table 1. Laboratory parameters and cytokine levels during disease course.

Laboratory parameters	Range	First MAS	Second MAS	Third MAS	HSCT	1 year after HSCT
GB (10^3/uL)	5.5-15	10.87	8.87	3.41	1.87	8.54
PLT (10^3/uL)	150-450	80	195	147	184	327
Ferritin (ng/ml)	13-150	13.088	27.396	5.921	230	26
ALT (UI/L)	<33	50	81	505	12	13
AST (UI/L)	<32	89	125	865	24	22
LDH (UI/L)	135-225	1717	1623	941	175	234
Fibrinogen (mg/dl)	190-430	400	500	193	341	428
TGL (mg/dl)	<170	197	208	220	148	106
IL-18 (pg/ml)	<300	189764	27761	36606	995	341
CXCL9 (pg/ml)	<612	112895	22488	29403	50	50

Conclusion: This case provides further evidence of the efficacy of emapalumab in MAS [1], of the potential benefit of HSCT in difficult sJIA patients [2]. Notably, full control of inflammatory activity with emapalumab and anakinra may help to obtain a successful HSCT and reduce the risk of rejection.
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AB1430 THE EXPERIENCE OF YOUNG PEOPLE WITH RHEUMATIC DISEASES TRANSFERRING THEIR CARE FROM PAEDIATRIC TO ADULT SERVICES AND THEIR SUGGESTED AREAS FOR IMPROVEMENT

Keywords: Health Services Research, Real-world evidence, Patient information and education

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Background: Transition of care from paediatric to adult services is a critical time period for patients with rheumatic diseases. A seamless transition process can aid young people in their development to adulthood, whilst also allowing them to gain independence in managing their rheumatic condition. Young people and their caregivers often express concerns to their paediatric rheumatology teams about the transition to adult services.
Objectives: This study seeks to explore the experience of transition from the perspective of young people with rheumatic diseases, and their suggestions for areas to address in improving the transition process. The second aim of the study is to find out whether young people want to fill out information about themselves in advance of their appointment at the adult rheumatology service, in order to help staff to get to know them better, and if so, what information they felt was important to know.
Methods: Anonymised survey questionnaires were given to young people with rheumatic diseases, via a scannable QR code, to be filled in prior to their rheumatology outpatient visit. All patients surveyed had transferred their care from paediatric to adult services. Further responses were sought by sending the survey questionnaire to young people with rheumatic diseases who had consented to be on a patient and public involvement and engagement (PPIE) mailing list. Survey data were analysed in Microsoft Excel.
Results: Average age of respondents: 18 (median), range 16-26. The majority of respondents were female (76%). 52% of patients had juvenile idiopathic arthritis (JIA), 12% had juvenile dermatomyositis, 12% had juvenile systemic lupus erythematosus, and 18% did not disclose their diagnosis. Most young people were satisfied with the transition process (satisfaction score rated 8 out of 10 (mean)). Young people perceived the following aspects of transition to have been done well: "Communication about the change", having a "named transition coordinator", having a "personal tour of [the adult hospital]", and having a "smooth process". Aspects of the transition process that young people suggested could be improved included: "more transparent and understandable medical talk", "more follow-up [appointments]", "knowing how to contact [a] named transition coordinator", feeling as though the healthcare professional was "talking to my mum rather than me", and "the general feeling of… care not being as personal". Overall, 60% of young people stated that they would be willing to fill out an electronic form prior to their appointment at the adult rheumatology service to give information that would allow staff at the adult hospital to get to know them better. When stratified by age, only 50% of 16–18-year-olds would be willing to fill out a form, whereas 80% of 19–26-year-olds would. The most commonly suggested pieces of information were: hobbies, sports, favourite school subject, goals, and career aspirations.
Conclusion: Most young people were satisfied with the transition process and had helpful suggestions about how this might be improved in the future.
The majority of young people were willing to fill in a form to provide information about themselves in order to help adult rheumatology staff to get to know them better, especially those who were aged 19-26 years. At a critical time in young people's development, enabling them to provide information about themselves that they feel is important, may help to improve their perception of the transition process and reduce their anxiety about transferring care to adult services.
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AB1431 APPLICABILITY OF STANDARDIZED ULTRASOUND EXAMINATION TO ESTIMATE DISEASE ACTIVITY IN COMBINATION WITH JADAS AND INFLAMMATION MARKERS IN JIA PATIENTS – THE DAISY STUDY DESIGN

Keywords: Ultrasound, Biomarkers

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Background: New outcome measures are needed to optimize personalized tailored treatment and to predict response in patients with juvenile idiopathic arthritis (JIA).
Objectives: Aim of this multicenter, longitudinal study is to identify biomarker (clinical examination of the joints, ultrasound and inflammatory biomarkers) for the evaluation of disease activity in children with JIA.
Methods: DAISY study planned to recruit 120 patients with JIA polyarticular and at least 30 patients with JIA oligoarticular disease course according to International League of Association for Rheumatology (ILAR) classification criteria, with active disease calculated by JADAS 10 and 27 and treated according to current recommendations[1,2]. At enrollment, 3, 6 and 12 months patients were simultaneously evaluated for disease activity status (JADAS 10 and 27), examined by musculoskeletal ultrasound (MSUS) gray-scale (GS) and power-doppler (PD) in 44 joints using OMERACT synovitis scoring system by an expert in pediatric MSUS. At each visit blood samples are collected for evaluation of inflammatory biomarkers (cytokines, chemokines, S100A8, S100A9 and S100A12). In case of disease worsening, the same parameters were performed as unscheduled visit. Experienced sonographers in pediatric MSUS were blinded from clinical examination as well as pediatric rheumatologist performing clinical examination were blinded from the MSUS finding. Prior to the patient enrollment it was mandatory that all sonographers access the study educational material on DAISY web-portal and perform test for sonographers that represents calibration web-based reliability exercise on still images, presenting different grades of synovitis using OMERACT synovitis scoring in order to optimize interrater reliability.
Results: Study is conducted in 9 participating centers in 8 different countries after Ethics Committee Approvals and Informed Consents/assents were obtained. A total of 52 JIA patients were enrolled: 15 (28.8%) males and 37(71.2%) females; median age at enrollment 11.25 years, interquartile range (IQR) 8.06-14.19 years and median disease duration 1.67 years, IQR 0.97-5.26 years. Of the JIA patients, 18 (34.6%) had oligoarticular JIA, 21(40.4%) had rheumatoid factor negative polyarthritis, 5 (9.6%) had rheumatoid factor positive polyarthritis, 7 (13.5 %) had enthesitis related arthritis while only one (1.9%) had psoriatic arthritis. Two patients (3.8%) had uveitis, while eight (15.4%) of them had a family history of autoimmune diseases. In total, 42 (80.8%) were treated with synthetic disease modifying antirheumatic drugs (methotrexate) while 31(59.6%) of JIA patients were receiving biologics.
Conclusion: Study results are expected to enable definition of the new more sensitive clinical tool to predict response in JIA and achieve optimized personalized tailored treatment of our patients.
Funding: This study is supported by the Foundation for Research in Rheumatology (FOREUM) and by the Paediatric Rheumatology International Trials Organisation (PRINTO).
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for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. Arthritis Care Res (Hoboken). 2019 Jun;71(6):717-734.

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AB1432 BODY MASS INDEX AND INFLAMMATORY LESIONS IN MAGNETIC RESONANCE IMAGING IN JUVENILE IDIOPATHIC ARTHRITIS: IS THERE A LINK?

Keywords: Imaging

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Background: Obesity is usually associated with low-grade inflammation in the general population. However, several studies have noted that high body mass index (BMI) in rheumatoid arthritis patients was associated with less structural damage in X-rays and in Magnetic Resonance Imaging (MRI) [1,2]. The impact of BMI on inflammatory MRI lesions in Juvenile Idiopathic Arthritis (JIA) is less studied.

Objectives: We aimed to determine the link between BMI and inflammatory MRI lesions of sacroiliac joints in JIA.

Methods: We conducted a retrospective study including 44 patients followed for JIA meeting the International League of Associations for Rheumatology (ILAR) 2001 criteria. For each patient we collected the following data: age, age at the onset of JIA, JIA subtype, disease duration, BMI, C-reactive protein (CRP) and Erythrocyte sedimentation rate (ERS) levels, and MRI data. Disease activity was assessed using the JADAS score. Statistical analysis was performed using SPSS software.

Results: We included 28 boys and 16 girls. The mean age was 13.65 ± 4.62 years. The mean age at the onset of the disease 9.57 ± 3.97 years. The mean disease duration was 4.34 ± 3.09 years. There was enthesitis-related arthritis in 61% of the cases (n=27), oligoarticular JIA in 14% of the cases (n=6), polyarticular JIA in 11% of the cases (n=5), and psoriatic arthritis in 7% of the cases (n=3). JIA was undifferentiated in 7% of the cases (n=3). The mean BMI was 20.22 ± 5.6kg/m². Four patients had overweight (9%). The mean CRP and ESR were 14.42 ± 19.67mg/L and 26.56 ± 20.87mm, respectively. The mean JADAS was 6.6 ± 4.7. Sacroiliac joints IRM showed bone marrow edema in 43% of the cases (n=19) and irregularities in iliac edges in 9% of the cases (n=4). Inflammatory lesions in sacroiliac joints MRI was associated with lower BMI (19.15 ± 4.28 vs 21.33 ± 6.4kg/m², p=0.036). However, there were no correlations between BMI and the following parameters: CRP, ESR, or JADAS.

Conclusion: Our results are consistent with other studies conducted in rheumatoid arthritis patients, which noted that high BMI was associated with less severe synovitis and bone marrow edema, and thus less severe radiologic progression [1-3]. Baker et al. suggested that patients with greater BMI have a beneficial adipokine effect on bone remodeling [3]. In addition, it seems that JIA patients with severe disease activity suffer from early weight loss. Thus, a greater BMI may stipulate a less severe JIA phenotype.

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AB1433 FACTORS ASSOCIATED WITH DIAGNOSIS DELAY IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Descriptive Studies

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Background: The diagnosis delay is very variable in Juvenile Idiopathic Arthritis (JIA). The duration between the occurrence of symptoms, the diagnosis time, and the establishment of the treatment is very important in disease progression.

Objectives: To determine the diagnosis delay in JIA and study the factors affecting this delay.

Methods: We conducted a retrospective study including patients with Juvenile Idiopathic Arthritis (JIA) meeting the International League of Associations for Rheumatology (ILAR) 2001 criteria. For each patient, we collected the following data: age, gender, age at the onset of JIA, JIA subtype, diagnosis delay, clinical examination data, extra-articular manifestations, C-reactive protein (CRP) and Erythrocyte sedimentation rate (ERS) levels. Disease activity was assessed using the JADAS score. Statistical analysis was performed using SPSS software.

Results: We included 44 patients. They were 28 boys and 16 girls. The mean age was 13.65 ± 4.62 years. The mean age at the onset of the disease was 9.57 ± 3.97 years. The mean diagnosis delay was 4.34 ± 3.09 years. There was enthesitis-related arthritis in 61% of the cases (n=27), oligoarticular JIA in 14% of the cases (n=6), polyarticular JIA in 11% of the cases (n=5), and psoriatic arthritis in 7% of the cases (n=3). JIA was undifferentiated in 7% of the cases (n=3). The mean tender and swollen joint counts were 1.46 ± 2.33 and 0.17 ± 0.54, respectively. Fourteen patients had clinical enthesitis (32%). Sacroiliac joints were painful in 15 patients (34%). Fifteen patients had low back pain (34%). Only 4 patients had extra-articular manifestations (2 psoriasis and 2 uveitis). The mean CRP and ESR were 14.42 ± 19.67mg/L and 26.56 ± 20.87mm, respectively. The mean JADAS was 6.6 ± 4.7, respectively. The diagnosis delay was positively correlated to the patient's age ($r=0.561$, $p<10^{-3}$) and negatively correlated to the ESR level ($r=-0.331$, $p=0.037$). Besides, diagnosis delay was associated with extra-articular manifestations (4.45 ± 3.12 versus 2±0.1 years, $p<10^{-3}$). Besides, ERA patients had longer diagnosis delay compared to other JIA subtypes but the difference was not significant (p=0.061). However, diagnosis delay was not associated with low back pain, enthesitis, or sacroiliac joint pain.

Conclusion: Our results are consistent with Kurt et al. study [1]. Older age, the occurrence of extra-articular manifestations, and low ESR level could lead to diagnosis impediment.

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AB1434 CLINICAL PROFILE OF JUVENILE IDIOPATHIC ARTHRITIS: ABOUT 55 CASES

Keywords: Inflammatory arthritides, Descriptive Studies

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children with wide variety in its clinical profile.

Objectives: The aim of our study was to describe the epidemiological, clinical, paraclinical and management aspects of JIA among Tunisian children.

Methods: This is a monocentric retrospective and observational study including children who met the ILAR criteria for the diagnosis of JIA. They were collected from the rheumatology department of Farhat Hached Hospital of Sousse in Tunisia.

Results: Out of the 55 included children, 27 (49.1%) were boys and 28 (50.9%) were girls. The mean age was 13.6 years. The mean age of onset of JIA was 6.4

years [3 months-16 years]. The mean duration of JIA progression was 4.4 years. The predominant subtypes of JIA were the seronegative polyarticular form (21 cases, 38.2%), the seronegative oligoarticular form and juvenile spondyloarthritis (9 cases, 16.4% each). The other forms were: seropositive polyarthritis (7 cases, 12.7%), systemic onset JIA (SOJIA) and psoriatic arthritis (4 cases, 7.3% for each) and arthritis with enthesitis (1 case, 1.8%). Arthritis was present in all patients. Wrist followed by knee were the most affected joints in all subtypes. Fever, lymphadenopathy, hepatosplenomegaly and rash were exclusive to patients with SOJIA. Uveitis (2 cases, 3.6%) and anti-nuclear antibodies (ANA) positivity (1 case, 1.8%) were rare. Biological inflammatory syndrome was found in 65.5% of cases. The means of ESR and CRP were 42.4 mm/h and 28.8 mg/L respectively. Anemia was found in 56.4% of cases. Standard X rays revealed carpitis in 4 cases (7.2%) and bone erosions in 9 cases (16.4%). Coxitis was present in 30.9% of the patients. Concerning treatment, our patients received non steroidal anti-inflammatory drugs (61.8%), oral corticosteroids (67.3%), and pulse steroid therapy in 47.3% of cases. Methotrexate was used for 65.5% of patients. Twenty-four patients (41.8%) were treated with biologics. Delayed growth as a complication of the JIA was observed in 8 cases (14.5%). Twenty-three patients (41.8%) developed joint deformities.
Conclusion: JIA has heterogeneous presentations with a challenging diagnosis in rheumatology practice. In our study, the seronegative polyarticular form was the most common subtype of JIA. Inflammatory syndrome, coxitis and deformities were frequent whereas uveitis and ANA positivity were rare findings in our population.
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Disclosure of Interests: None Declared.
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AB1435 RELEVANCE OF AUTO-ANTIBODIES AGAINST CARBAMYLATED PROTEINS IN JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Autoantibodies, Inflammatory arthritides, Biomarkers

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Background: Auto-antibodies against carbamylated proteins (anti-CarP) are emerging biomarkers in rheumatoid arthritis with relevant prognostic value. Juvenile idiopathic arthritis (JIA) is characterized by high heterogeneity and risk-stratification could be improved.
Objectives: We aim at determining whether anti-CarP in J IA's patient, at the time of transition, could help to predict patients' outcomes.
Methods: We conducted a monocentric retrospective study at the Cochin Hospital in Paris on a cohort of JIA patients in transition to adult rheumatology for whom serum has been collected and stored in a biobank between 2011 and 2013 with the approval of research ethic committee (EUDRACT 2010-A01386-33, reference S.C.2852). Demographic data, diagnosis, biological and radiological results, and treatments were collected retrospectively thanks to computerized files. Samples of serum available in the biobank were analyzed to measure anti-CarP and anti-CCP by ELISA in the department of Immunology and Immunogenetic from the Bordeaux University Hospital.
Results: Twenty-eight (20%) patients were anti-CarP positive. The median age was 21.6 (18.6-23.1) years in anti-CarP positive as compared to 19 (17-21.1) in anti-CarP negative group (p=0.02). In anti-CarP positive group, 41% were polyarticular-JIA, 26% oligoarticular, 15% had enthesitis related arthritis and 15% were systemic, but this was not different as compared to anti-CarP negative patients. Structural radiographic damages were identified in 44% of anti-CarP positive such as in 50% in anti-CarP negative group (p=0.6). Concerning treatment, 28% of anti-CarP positive patients were treated with synthetic DMARD and 72% with biologic DMARD as compared to 44% (p=0.1) and 65% (p=0.5) for anti-CarP negative. Among anti-CarP positive patients, 10 (7.4%) were also anti-CCP positive. These double-positive patients were polyarticular-JIA for 90% and 9 (90%) received a biotherapy at the last available follow-up as compared to 16% of polyarticular-JIA (p=0.002) and 44 (46%) on biotherapy (p=0.03) for double negative.
Conclusion: Anti-CarP antibodies were observed in 20% of JIA's patients at transition but could not help for risk-stratification of the patients. The respective value of anti-CarP and anti-CCP for structural damages and treatment intensification will require larger cohort but double positive patients appeared to be the most severe polyarticular-JIA patients.
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AB1436 BIOLOGIC THERAPY IN JUVENILE IDIOPATHIC ARTHRITIS TUNISIAN PATIENTS

Keywords: bDMARD, Inflammatory arthritides

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children under the age of 16. Biologic therapy significantly improved the management and prognosis of this disease.
Objectives: We aimed to evaluate the indications, clinical efficacy and safety of biotherapy for the treatment of JIA in a tunisian population.
Methods: This is a monocentric retrospective and observational study including patients followed for JIA (ILAR criteria) in the Rheumatology department of Sousse in Tunisia.
Results: Fifty-five children (28 girls and 27 boys) were included. The mean age was 13.6 years. The predominant subtypes of JIA were the seronegative polyarticular JIA (38.2%), and the seronegative oligoarticular form and juvenile spondyloarthritis (16.4% each). Besides biologics, our patients received non steroidal anti-inflammatory drugs (61.8%), oral corticosteroids (67.3%), and pulse steroid therapy in 47.3% of cases. Methotrexate was used for 65.5% of patients. Twenty-four patients were treated with biologics, with a prevalence of 41.8%. The mean age at the beginning of biotherapy was 12 years, with a mean time for initiation of 5 years. The main indications were the first and second-line treatments failure (29.1%) and their side effects (12.7%). The most frequently used biologics were TNF alpha blockers: Etanercept (9 patients), Infliximab (6 patients), Certolizumab and Adalimumab (2 patients each). Anti-Interleukin-6 (Tocilizumab) was used in the systemic JIA form for 4 patients. The mean duration of treatment with biologics was 3.55 years. A trend towards lower disease activity was observed with steroid therapy stopped in 25%. Five patients switched biologics. The overall safety profile was good. No serious adverse drug events occurred except anaphylaxis in 2 cases: 1 with Tocilizumab and one with Infliximab. The other side effects were hepatic toxicity with elevated transaminases (2 patients) and moderate cutaneous infection (1 patient).
Conclusion: Biologics have provided interesting new therapeutic alternatives in Tunisian patients with JIA, despite the delay of their initiation. However, the long-term side effects of modulating the immune system are not yet fully understood in this young population.
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AB1437 NAILFOLD CAPILLAROSCOPY IN DEFICIENCY OF ADENOSINE DEAMINASE 2 (DADA2): A CASE-CONTROL STUDY

Keywords: Genetics/Epigenetics, Vasculitis

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Background: Deficiency of adenosine deaminase 2 (DADA2) is a rare monogenic autoinflammatory disease characterized by the presence of systemic inflammation, vasculitis, early-onset stroke, and hematologic manifestations such as cytopenia and immunodeficiency. Mucocutaneous and peripheral microvascular manifestations, such as livedo racemosa, cutaneous ulcers and Raynaud's phenomenon (RP), can occur, in up to 50%, 22% and 8 % of DADA2 patients respectively [1].
Objectives: To investigate the microvascular architecture in nailfold capillaries of DADA2 patients comparing them with adequate healthy controls (HCs) and primary RP individuals.
Methods: The data of 9 patients with DADA2 followed at Istituto Gaslini were retrospectively retrieved and compared to 11 HCs and 7 RP. Clinical and genetic data were collected for DADA2 patients. Nailfold videocapillaroscopy (NVC) findings were collected in the whole cohort, independently from their current treatment. The capillaroscopic parameters were classified according to the Fast Track Algorithm and distinguished between scleroderma-pattern (encompassing specific NVC alteration, such as the presence of giant capillaries and/or loss of capillaries combined with abnormally shaped capillaries) and non-scleroderma

patterns (non-specific NVC alterations) [2]. A validated semiquantitative scale (score 0–3 for each NVC parameter) was used to compare microvascular findings in the three groups [3]

Results: The patients with DADA2 were diagnosed according to genetic testing. The disease onset was in early infancy, while the mean age at NVC was of 18.8 years. Livedo racemosa was present in 7 patients (78%), digital ulcers in 1 patient, and an ischemic stroke was reported in 5 patients (55%). None of the patients had RP (0%). The NVC showed the presence of non-specific alterations in all DADA2 patients (capillary dilations in 100%, abnormally shaped capillaries and haemorrages in 23% of patients). The capillary density was normal (median = 9) and no scleroderma-like pattern was found. No significant differences in the rates of each microvascular finding were detected between DADA2, RP patients and HCs.

Conclusion: This is the first report investigating the NVC findings in DADA2 patients. Microvascular damage in DADA2 does not show a specific capillaroscopic alteration but the presence of non-specific findings might suggest a disease-related endothelial damage.

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AB1438 INFLAMMATORY MYOSITIS ASSOCIATED WITH GRAFT VERSUS HOST DISEASE

Keywords: Myositis

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Background: GVHD is a significant complication of allogenic stem cell transplant, mediated by donor T cell activation and proliferation and affecting 30%-70% of patients. Clinical manifestations often have overlapping features with auto-immune diseases such as scleroderma, Sjogren's syndrome, eosinophilic fasciitis, primary biliary cirrhosis and immune cytopenia. Clinical myositis with muscle tenderness and elevated muscle enzymes is recognized as a distinctive and uncommon manifestation of GVHD with estimated frequency of 3.5–7.6%. In addition to corticosteroids, various immunosuppressive agents are being used for treatment, however, the optimal therapeutic strategy has not yet been defined.

Objectives: To describe a case of GVHD related myositis in a 4 years old female, successfully treated with Rituximab and to increase awareness for this rare condition and the role of Rituximab for its treatment.

Methods: Two years old female underwent a successful bone marrow transplantation from matched unrelated donor for Juvenile myelomonocytic leukemia (JMML). Four months post BMT she developed severe GVHD, primarily involving her skin and oral mucosa, GI and liver. She was treated with mycophenolate, cyclosporine, prednisolone, ruxolitinib and tacrolimus in different combinations. Almost two years post BMT she developed fever, general weakness and severe respiratory distress which required mechanical ventilation. After a comprehensive diagnostic work-up, she was diagnosed with inflammatory myositis based on elevated CPK, characterized EMG and muscle biopsy (Fig 1, 2). She was treated with steroid pulses and IVIG with no significant improvement and therefore Rituximab was added to her regimen. Two weeks following the first dose of Rituximab, clinical and laboratory improvement were noted, and the patient could get off ventilator.

Results: Patient remained in remission with monthly IVIG and decreasing doses of prednisone.

Conclusion: Myositis is a rare complication of GVHD. High index of suspicion is recommended for early diagnosis. Rituximab should be considered as a treatment option.

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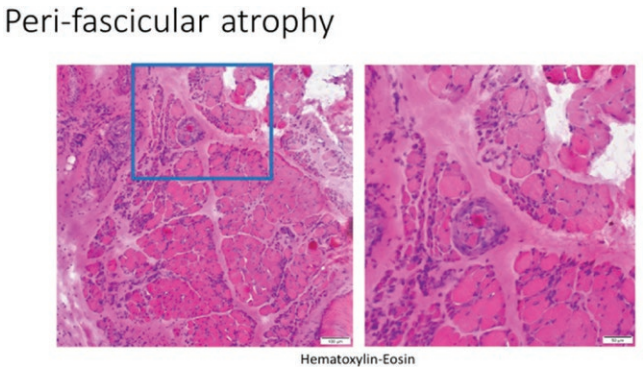


Figure 1. Muscle biopsy – Hematoxylin-Eosin – peri-fascicular atrophy

EMG Summary Table													
			Spontaneous					MUAP				Recruitment	
Muscle	Nerve	Roots	IA	Fib	PSW	Fasc	H.F.	Amp	Dur.	Poly.	Pattern	Note
L. Tibialis anterior	Deep peroneal (Fibular)	L4-L5	N	1+	1+	None	None	N	N	N	N	
L. Gastrocnemius (Medial head)	Tibial	S1-S2	N	1+	1+	None	None	N	N	N	N	
L. Vastus medialis	Femoral	L2-L4	N	None	None	None	None	N	N	N	N	
L. Deltoid	Axillary	C5-C6	N	2+	2+	None	None				No Activity	
L. Biceps brachii	Musculocutaneous	C5-C6	N	2+	3+	None	None				No Activity	
L. Triceps brachii	Radial	C6-C8	N	2+	2+	None	None	1-	1-	3+	Early	

Figure 2. EMG results: significant spontaneous muscle activity and early recruitment, both typical in inflammatory myositis.

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AB1439 ASSESSMENT OF HEALTH-RELATED QUALITY OF LIFE IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Inflammatory arthritides, Patient reported outcomes, Quality of life

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Background: Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease that causes physical and psychological disability. Considering the young age of patients and the potential long-lasting disability, the consequences of JIA on health-related quality of life (HRQoL) may be significant.

Objectives: This study aimed to measure HRQoL and identify associated factors.

Methods: This is a cross-sectional monocentric study including children with JIA diagnosed according to the International League of Associations of Rheumatology (ILAR) classification criteria. To evaluate disease activity we used the Disease activity score (DAS-28) for oligoarticular and polyarticular forms, and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score for axial forms. The Childhood Health Assessment Questionnaire (C-HAQ) was used to assess functional disability. The HRQOL was evaluated by the Pediatric Quality of Life Inventory 4.0 (PedsQL4) which is a questionnaire composed of 23 items. The higher scores indicate a better quality of life.

Results: Thirty-six patients were enrolled. The average age was 13.5 ± 5.9 with a female percentage of 55.6 %. The polyarticular form was the most frequent (52.8%) meanly seronegative, followed by the Oligoarticular form (13.9%), then the enthesitis-related form (12.4%). The mean disease duration was 5.5±4.7 years. The median of the C-HAQ was 1 (IQR=0- 2). The median of PedsQL4 was 65.8 (IQR= 43.2-90.4). The physical functioning subscale had the lowest score, with a median of 60.1 (IQR= 30.4-90.7), followed by the school functioning with a median of 63.2 (IQR=41.7-90.1), then the social functioning with a median of 69.2 (IQR=45.7-91), then the emotional functioning with a median of 70.8 (IQR=47.7-92). The impairment of HRQoL was significantly associated with higher disease activity (p=0.002), the presence of joint deformities (p=0.02), higher C-HAQ score (p=0.001), and hip involvement (p=0.003). The PedsQL4 global score and its domains had no significant correlations with age, forms of JIA, or biological abnormalities.

Conclusion: The HRQoL was impaired in our population of JIA. Physical health was the most affected. Early and effective management of disease activity could improve HRQoL in children with JIA.

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AB1440

ASSESSMENT OF THE PREVALENCE OF SARCOPENIA IN ADULT WITH JUVENILE IDIOPATHIC ARTHRITIS

Keywords: Sarcopenia, Inflammatory arthritides, Diet and Nutrition

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Background: Sarcopenia is a progressive and systemic disorder of skeletal muscles responsible for an acceleration of function impairment and loss of mass muscle [1]. It is well known associated with ageing, but a new life-course approach suggests that muscle mass and function in older people also depends on the mass muscle peak in early adulthood [2]. Prevalence increasement of sarcopenia has been well described in inflammatory rheumatic diseases, particularly in rheumatoid arthritis and spondylarthritis, but has never been studied in rheumatic diseases with a juvenile onset.
Objectives: The aim of this study was therefore to investigate the prevalence of sarcopenia in juvenile idiopathic arthritis in adult life.
Methods: We performed a monocentric cross-sectional study including patients followed up in rheumatology unit of Reims hospital for juvenile idiopathic arthritis (JIA) from November 2021 to September 2022. Each patient received a measurement of muscle quantity and quality by dual-energy X-ray absorptiometry, a measurement of muscle strength by Grip test, a screening for sarcopenia by the SCARC-F score, an assessment of physical activity by the IPAQ score and of fatigue by the FACIT-F score. The diagnosis of sarcopenia was confirmed by a decrease in appendicular muscle mass (AMM) < 20 kg in men and < 15 kg in women or an ASM/height[2] < 7 kg/m^2 in men or < 5.5 kg/m^2 in women [1].
Results: Thirty-four patients were included, aged from 18 to 45 years. The prevalence of sarcopenia was 20.6% (7/34) with a majority of women (sex ratio 0.6). Type of JIA was significantly different between the 2 groups with 57.14% oligoarticular form and 28.57% systemic form in the sarcopenic group, versus 44.4% oligoarticular form and 29.6% enthesitic form in the non-sarcopenic group (p=0.043). We did not find any significant difference in disease activity nor in treatment by biotherapy or corticosteroids between the 2 groups. Proportion of patients with a BMI <18.5 kg/m² was significantly higher in the sarcopenic population (p=0.0095). The IPAQ score showed a lower energy expenditure in the sarcopenic group, although not significantly different (p=0.099). By using a variation of -2DS of appendicular skeletal mass or <ASM/height[2] compared with age- and sex-matched reference values from a Danish cohort, we have calculated a prevalence of sarcopenia of 11.76% in our population [3]. The assessment of muscle strength defined by a -2DS decrease in grip test values compared to reference values matched for age and sex showed a decrease in muscle strength in 29.4%. By using European Working Group for Sarcopenia in Older People (EWGSOP) definition, only 11.76% of our patients presented a muscle strength decrease. Moreover, the SARC-F score established in patients over 65 years of age did not allow for the detection of sarcopenia in our population.
Conclusion: This is the first study to evaluate sarcopenia in juvenile idiopathic arthritis. JIA is associated with a risk of developing sarcopenia at an early age with an impact on peak muscle mass and, thus, on long-term muscle function prognosis. In order to prevent this risk, nutritional management and regular physical activity seem to be relevant approaches. The definition of sarcopenia by the EWGSOP does not seem to be adapted to a younger population, with a low sensitivity screening of sarcopenia in this population by the SARC-F score and an underestimation of low muscle strength by the grip test. Further studies with a larger population and a control population are needed to clarify these results.

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AB1441

CLINICAL CHARACTERISTICS OF PEDIATRIC PATIENTS WITH RHEUMATIC DISEASES UNDER TREATMENT WITH BIOLOGICAL THERAPY: INFORMATION FROM BIOBADAMEX

Keywords: bDMARD, Registries

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Background: The advent of biologic treatment (bDMARD) in childhood rheumatic diseases (RD) has changed their evolution and prognosis. Evidence is robust for diseases such as juvenile idiopathic arthritis (JIA) and systemic lupus erythematosus (SLE), but in other diseases we still have to learn which is the ideal therapy, time to discontinuation and the potential adverse events (AE) in short and long term.
Objectives: Identify the clinical and treatment characteristics of pediatric patients with rheumatic diseases with bDMARD treatment and describe the development of AE.
Methods: BIOBADAMEX is a prospective ongoing cohort of Mexican patients with RD using bDMARDs since 2016. We included all patients younger than 18 years of age registered in BIOBADAMEX. Descriptive statistics were used for the baseline characteristics and the Chi-square test to analyze the differences between the characteristics of the groups in relation to the development of AE.
Results: A total of 45 patients were included, 31 (69%) of them female, mean age of 13.3 (±3.6) years. (Table 1). The most frequent diagnosis was JIA 25 (56%), followed by SLE 9 (20%), uveitis 5 (11%), polymyositis/dermatomyositis and hidradenitis 2 (4%) respectively; systemic sclerosis and CINCA 1 patient (2%) respectively. The mean duration disease in years was 4.67 (±2.1). Nine patients (20%) used a biologic prior to the current; 23 (51%) patients had comorbidities. The most frequent bDMARDs used was Adalimumab (ADA) in 17 (38%) patients followed by Rituximab in 15 (33%) and Tocilizumab in 10 (22%), Infliximab, Abatacept and Canakinumab were used in one patient respectively. When compared by groups, ADA and Tocilizumab were the most used bDMARDs in JIA, Rituximab the only one used in SLE and PM/DM, and ADA the only one for uveitis. 15 patients discontinued biological treatment, 4 (27%) due to AE. 82% used an additional synthetic DMARD, being methotrexate the most used in 48% of patients. Steroids were

Table 1. Baseline Characteristics

Baseline characteristics (n = 45)					
	n	%			
Female, n(%)	31	68.9			
Age, media (SD)	13.3 (±3.6)				
Index Body Mass, media (SD)	19.6 (±4.9)				
Dx n(%)	n %				
- JIA	25 55.6				
- SLE	9 20				
- PM/DM	2 4.4				
- Uveitis	5 11.1				
- Hidradenitis	2 4.4				
- Systemic sclerosis	1 2.2				
- CINCA	1 2.2				
Disease duration(years) media (IQR)	4.67±2.1				
Current treatment n(%)	n %				
- Infliximab	1 2.2				
- Adalimumab	17 37.8				
- Rituximab	15 33.3				
- Abatacept	1 2.2				
- Tocilizumab	10 22.2				
- Canakinumab	1 2.2				
Treatment duration (months) median (IQR)	4.5 (0.56 – 36.9)				
Treatment suspension, n(%)	**15 (33.2)**				
Months to suspension, median (IQR)	0.66 (0.46 – 1)				
Discontinue cause, n(%)	n %				
- Inefficacy	1 6.6				
- Remission	1 6.6				
- Side effects	4 26.6				
- Others	5 33.3				
- Unknown	4 26.6				
Steroids use, n(%):	21 46.7				
Steroids dose (mg), median (IQR)	10 5 – 25				
DMARDs use n(%):	37 82.2				
AE, n(%):	**15 33.3**				
By disease:	**AE Type**				
	Infection	**Allergy**	**Neutropenia**	**Other**	**Chi^2**
JIA	**3**	**1**	**2**	**3**	**0.95**
SLE	**1**	**1**	**0**	**1**	
Uveitis	**3**	**0**	**0**	**0**	

used by 21 (47%) of the patients with a median dose of 10mg (IQR 5 - 25). Fifteen AEs were recorded: 7 (47%) were infections, 5 of these (71%) were COVID; allergies and neutropenia in 2 (13%) patients respectively. By disease infections were more frequent in patients with JIA and Uveitis; neutropenia only occurred in patients with JIA (p 0.95). 87% of the AEs were non-serious, 1 patient with JIA presented a severe AE and one patient with SLE a fatal AE associated with COVID (p 0.93), with no statistically significant difference between groups.

Conclusion: JIA is the most frequent indication to use bDMARD as worldwide reported. The AE in this analysis are similar to previous registries in terms of the prevalence of infections, in our group the most frequent infectious complication was COVID, being fatal in one patient related with rituximab in SLE. Our study did not find statistically significant differences in the development of AE between diseases; however, they will continue to be reported and the number of patients in the registry will increase.

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AB1442 OVARIAN PRESERVATION IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS: A MONOCENTRIC COHORT

Keywords: Systemic lupus erythematosus, Biomarkers, Pregnancy and reproduction

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Background: Systemic lupus erythematosus (SLE) can impact fertility outcomes and lead to ovarian premature failure. The exact mechanism is not completely understood. Anti-ovarian antibodies have been described as a possible explanation[1] but other intrinsic and extrinsic factors are involved. Cyclophosphamide (CYC) is known to have a gonadotoxic effect, but available data are derived from adult cohorts. Anti-müllerian hormone (AMH) is a surrogate biomarker of ovarian reserve in such studies.

Objectives: This study aims to evaluate the ovarian reserve in juvenile-SLE (j-SLE) using AMH and to follow the longitudinal evolution of this biomarker at diagnosis and after the start of treatment.

Methods: Patients with a diagnosis of j-SLE followed at Robert-Debré Hospital, Paris, France, were included. AMH levels were assessed before starting therapy, at 6-10, 12-18, and after 20 months from the start of immunosuppressive therapy. AMH values are expressed in pmol/L with a normal range varying from 7.1 to 51.8, according to pubertal status/age.

Results: 21 j-SLE patients were included (100% female). Patients were divided into 2 groups: i. j-SLE who received cyclophosphamide (48%) and ii. j-SLE who received anti-CD20 treatment (rituximab or obinutuzumab), mycophenolate, or hydroxychloroquine (52%). Clinical and demographical features are summarized in Table 1. 16 patients were menstruating at the initiation of immunosuppressive therapy, while 5 patients were not; however, the first menstrual period occurred between 2 to 4 months after initiation of treatment. The median cumulative dose of CYC was 4.8 grams (IQR 2.2). No statistically significant differences were found comparing pre-treatment AMH levels between the two groups (p= 0.60). The same trend was found evaluating AMH levels at 6-10, 12-18 months, and after 20 months from the start of therapy (p=0.48, p= 0.77, and p= 0.68 respectively). At 20 months the only two patients with AMH values below the normal limits had low values even before starting treatment (0.6 vs 4.9 in group 1 and 1.9 vs 7.4 in group 2 respectively). SLEDAI at the onset of the disease seems to correlate negatively with the values of AMH, nevertheless, the small sample size does not allow to reach statistical significance (S = 1550.9, p= 0.12). In addition, patients with SLEDAI score >20 have lower levels of AMH compared to patients with SLEDAI score ≤20 after 20 months from the start of therapy (p-value = 0.05) (Figure 1), independently of their treatment.

Conclusion: Fertility preservation is a key point in the management of patients with SLE. Our study shows reassuring data regarding the use of CYC in j-SLE and suggests that AMH levels, and consequently ovarian reserve, may be primarily affected by disease severity and activity rather than treatment.

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Table 1. Demographic and clinical features in j-SLE patients treated with CYC vs patients treated with other immunosuppressors.

	Group 1 CYC n=10	Group 2 Others n=11	Overall population n=21	P value
Age at diagnosis (years), median (IQR)	13 (3.5)	14 (3.2)	14 (3.4)	1
Delay diagnosis (month), median (IQR)	1.5 (3.5)	1 (3.2)	1 (4)	1
Ethnicity, % (n)				
African	50 (5)	73 (8)	62 (13)	0.214
Asia	30 (3)	27 (3)	28 (6)	1
South America	20 (2)	0 (0)	10 (2)	0.476
Clinic and serology, % (n)				
Neuropsychiatric	80 (8)	45 (5)	62 (13)	0.182
Cutaneous	100 (10)	100 (11)	100 (21)	1
Renal	90 (9)	73 (8)	81 (17)	1
Hematological	90 (9)	73 (8)	81 (17)	1
Articular	80 (8)	100 (11)	91 (19)	0.214
SLEDAI at onset, median (IQR)	31.5 (17.3)	16 (15.5)	24 (25)	0.071
ANA	100 (10)	100 (10)	95 (20)	1
Anti-dsDNA	100 (10)	100 (10)	95 (20)	1
ENA	100 (10)	100 (11)	100 (21)	1
Anti-Ribosome P	20 (2)	9 (1)	14 (3)	0.586
Menstrual abnormality, % (n)				
Amenorrhea before starting treatment	40 (4)	0 (0)	19 (4)	0.035
Amenorrhea 12 months after treatment	20 (2)	9 (1)	14 (3)	0.586

CYC= cyclophosphamide; ANA= antinuclear antibodies; AMH= anti-müllerian hormone.

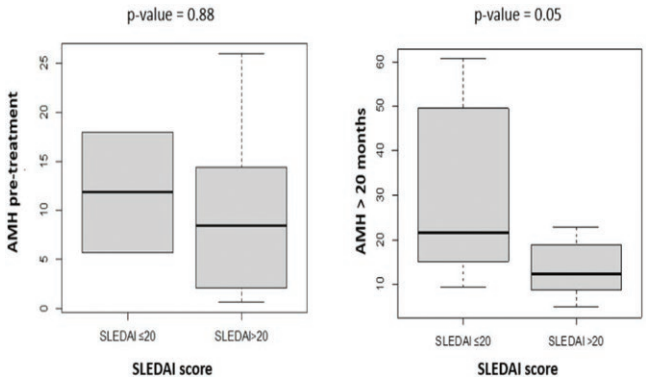


Figure 1. SLEDAI score in relation to AMH values before starting immunosuppressive therapy and after 20 months from the beginning.

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AB1443 TRIGGERING IGA VASCULITIS BY FOOD ALLERGEN EXPOSURE, VITAMIN D DEFICIENCY, AND IL-33-ACTIVATED TYPE 2 IMMUNE RESPONSES

Keywords: Vasculitis, Vitamin D

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Background: Immunoglobulin A vasculitis (IgAV) is one of the most common types of systemic vasculitis in children and usually involves the skin,

gastrointestinal tract, kidneys, and articulation[1]. The trigger of IgAV is unclear. Study elucidated that higher serum IgE levels and vitamin D deficiency existed in IgAV commonly[2, 3], while it is worth noting that T helper (Th) 2 cells increase in IgAV and are closely correlated with aberrant production of antibodies and the development of vessel vasculitis[4]. Moreover, serum IL-33 can activate many immune cell types involved in type 2 immune responses and allergic inflammatory reactions, are elevated in IgAV patients and positively correlated with the overall clinical score[5, 6]. This study aimed to further analyze their mutual relationship and reveal the mechanism underlying IgAV development.

Objectives: We investigated the levels of antigen-specific antibodies, 25-hydroxyvitamin D [25(OH)D_3], and IL-33 and the phenotypes of Th cells in the peripheral blood of IgAV patients at the early stage of disease onset. We also analyzed the correlation between each index and clinical characteristics.

Methods: Aeroallergen-specific IgE and food-specific IgE were detected by western blotting. Serum 25(OH)D_3 and total IgE levels were determined by electrochemiluminescence immunoassay. Serum IL-33 and sST2 levels were detected by enzyme-linked immunoassays. Serum IL-2, IL-4, IL-6 and IL-10 were detected using a cytometric bead array. Frequencies of T helper cell subsets were detected by flow cytometry.

Results: About half of the patients had abnormal allergic indicators and positive results in the allergen-specific IgE assay. Up to 98.25% of the patients had decreased serum 25(OH)D_3 levels, which were inversely correlated with an abnormal increase in IgE. Th2 cells were elevated and negatively correlated with the level of serum 25(OH)D_3. IL-33, a critical cytokine for the differentiation of Th2 cells, was also increased and negatively correlated with serum 25(OH)D_3 levels.

Conclusion: Food allergen exposure and 25(OH)D_3 deficiency may trigger IgAV. 25(OH)D_3 deficiency induces the activation of type 2 immune responses and a pathological increase in IgE by promoting the secretion of IL-33, which may be the underlying mechanism of IgAV pathogenesis. Monitoring vitamin D levels and administering vitamin D supplementation might play significant roles in preventing and treating IgAV.

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AB1444

BIOMARKERS IN JUVENILE IDIOPATIC ARTHRITIS: DESCRIPTION OF GROUPS WITH DIFFERENT DEGREES OF DISCREPANCY BETWEEN SERUM CALPROTECTIN AND C-REACTIVE PROTEIN.

Keywords: Inflammatory arthritides, Descriptive Studies, Biomarkers

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Background: There are no specific biomarkers of disease activity in for Juvenile Idiopathic Arthritis (JIA), and therefore it is important to identify new molecules which help us in daily practice to offer individualized treatment options. Serum Calprotectin (CLP) is an emerging biomarker of inflammation. Recent studies[1] suggest that disease activity correlates better with CLP than with classic acute phase reactants such as C-reactive Protein (CRP).

Objectives: To determine the clinical characteristics of paediatric patients with Juvenile Idiopathic Arthritis (JIA) who have discrepancy between Serum Calprotectin and C-reactive Protein.

Methods: An analytical transversal study was performed including patients with JIA from a paediatric rheumatology clinic between 2017 and 2021. A total of 25 patients were included, who had at least one measurement of CLP in daily practice. Demographic, analytical and clinical data were collected. The JADAS score by physical examination and ultrasound was collected in patients with peripheral arthritis.

Results: A total of 25 patients were included, 48% were female and the mean age was 11.5 (±4.6) years. A total of 11 (44%) patients had discrepancy between CLP and CRP. Among them, 9 (81.8%) had elevated CLP and low CRP, whereas only 2 (18.2%) had low CLP with elevated CRP. At the time of performing the analysis, 44% of the patients had an active disease. The oligoarticular JIA subtype was the one that presented a larger patient's percentage (54.5%) with discrepancy and elevated CLP. The details of clinical and analytical characteristics of the patients are shown in Table 1.

	No discrepancy. Low (n=11)	Discrepancy. Low CLP (n=2)	Discrepancy. High CLP (n=9)	No discrepancy. High (n=3)
Age (years), mean (SD)	12.2 (±4.6)	8.0 (±11.1)	10.3 (±3.5)	14.4 (±3.0)
JIA subtypes, n (%)				
- ERA + juvenile EA + APs	5 (45.4)	0 (0)	2 (22.2)	0 (0)
- Oligoarticular	3 (27.3)	1 (50)	**5 (55.6)**	2 (66.7)
- Polyarticular	2 (18.2)	1 (50)	1 (11.1)	1 (33.3)
- Systemic	1 (9.1)	0 (0)	1 (11.1)	0 (0)
Biomarkers, median (IQR)				
- CRP (mg/L)	0.5 (0.6)	8.2 (5)	1.7 (2.1)	6.3 (11.8)
- ESR (mm/h)	5 (8)	28 (32)	13 (12)	21 (56)
- Calprotectin (µg/mL)	1.4 (0.8)	0.9 (1.6)	4.3 (1.7)	4 (2.3)
JIA activity according to clinical criteria, n (%)				
- Active	4 (36.3)	2 (100)	**3 (33.3)**	2 (66.7)
- Inactive	7 (63.6)	0 (0)	6 (66.7)	1 (33.3)
JIA activity according to JADAS, n (%)				
- JADAS: activity	0 (0)	2 (100)	2 (22.2)	1 (33.3)
- JADAS US: activity	0 (0)	2 (100)	1 (11.1)	1 (33.3)
Uveitis, n (%)				
- Acute uveitis	0 (0)	0 (0)	1 (11.1)	0 (0)
Treatment, n (%)				
- PDN	2 (18.2)	1 (50)	1 (11.1)	1 (33.3)
- DMARD	6 (54.5)	1 (50)	3 (33.3)	3 (100)
- bDMARD	3 (27.3)	0 (0)	2 (22.2)	1 (33.3)

In the subgroup of patients with discrepancy and elevated CLP there were 3 (33.3%) with an active disease. Among them, 66.7% were female and all of them had an oligoarticular JIA. One of them was in a flare with both an active arthritis and uveitis at the moment of the analysis. None of them were under treatment with prednisone nor DMARD (disease-modifying antirheumatic drugs).

Conclusion: There was discrepancy between CLP and CRP in 44% of the sample. Among them, most (81.8%) had high CLP without elevation of CRP. The JIA subtype that presented discrepancy with elevated CLP was the oligoarticular one. A total of 3 (33%) patients were active in the group with discrepancy and elevated CLP, one of them being in a flare with both an active arthritis and uveitis.

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Disclosure of Interests: None Declared.

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AB1445

THE UNITED ARAB EMIRATES JUVENILE IDIOPATHIC ARTHRITIS REGISTRY PRELIMINARY RESULTS OF PATIENT DEMOGRAPHICS, SUBTYPE DISTRIBUTION, CLINICAL FEATURES, TREATMENT AND OUTCOME.

Keywords: Registries

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Background: Juvenile Idiopathic Arthritis (JIA) is a chronic inflammatory disease that affects 1 in 1000 children worldwide. Our population in the United Arab Emirates is a multiethnic diverse population. [1, 2]
Objectives: To create centralised data for JIA in the United Arab Emirates. In this abstract we describe the Demographic data, clinical features, subtype distribution as per ILAR classification, treatment received and outcome of our patients.[3]
Methods: Retrospective entry of data from all 3 participating centres (Shaikh Shakhbout Medical City, Tawam and AlJalila). Patients with the diagnosis of JIA included. Electronic clinical research form used to collect data. Data at initial diagnosis and current outcome as per Wallace and (Juvenile Arthritis Disease Activity Score) JADAS 10. Long term out come as per Juvenile Arthritis Disease Activity (JADAI) articular > 0 and extra articular JADAI > 0. All data entered and analysed through Redcap (Research Electronic Data Capture web-based application version 12.1.1 model 2022). Simple statistics used. Ethics approval obtained.
Results: 157 patients entered in to the registry so far. Male to female distribution: 39 (24.8%) to 118 (75.2%). Local Emirati patients of 107 (68.2%). Other Arabs 16 (10.2%). South Asian 12 (7.6%), Western 12 (7.6%) and African 10 6.4%). Mean age at presentation 5.3 years (1 to 15 years). Current mean age 12 (4-22 years). Family history of Rheumatoid Arthritis in 33 patients (21%). History of Consanguinity in 54 families (34.4%). Subtype distribution: Oligo articular 77 (49.4%), extended Oligo articular 5 (3.2%). Poly articular 50 (32.1%), Systemic 11 (7.1%), Enthesitis related Arthritis 1 (0.6%), Psoriatic 9 (5.8%) and other 3 (1.9%). At presentation: Joint pain in 132 patients (84.1%), Joint effusion 115 (73.2%). Affected function in 98 (63.2%). Clinical synovitis in 138 (87.9%). Joint restriction in 100 (63.7%). Uveitis in 6 (3.8%) ANA positive 35 patients (22.3%). Rheumatoid factor positive 10 (6.4%), Anti CCP positive 6 (3.8%). Low Hb less than 10 g/L in 109 (69.4%), high ESR > 20 mm/hr in 30 patients (19.1%). High CRP >5 mg/L in 48 (30.6%). Synovitis in USS 53 (33.8%). Erosions by X-ray or USS 7 patients (4.5%). Uveitis after diagnosis in 30 patients 19.1%. Dental carries at presentation in 51 patients (32.1%). COVID infection in 74 patients (47.1%). Oral systemic steroids given to 108 patients (68.8%). Intravenous methyl prednisolone to 43 patients 27.4%). Triamcinolone Acetonide/Hexa acetonide joint injections to 91 patients (58%). Synthetic Disease modifying medication methotrexate in 108 (68.8%). Biologic treatment 76 patients (49%). Etanercept 64 patients (40.8%), Adalimumab 65 patients (41.4%), Tocilizumab intra venous 32 (20.4%) and sub cut in 10 patients (6.4%). Canakinumab 9 patients (5.7%), Anakinra 8 patients (5.1%) and Infliximab in 10 patients (6.4%). Oral Tofacitinib in 2 patients (1.3%). In regards to outcome as per Wallace criteria and JADAS 10; active disease in 16 patients (10.2%). In remission 141 patients (89.8%). Out of these in remission on treatment 118 (83.7%) and in remission off treatment 23 patients (16.3%). JADAI articular >0 in 8 patients (5%) and JADAI extra articular >0 in 14 patients (8.9%)
Conclusion: We have diverse cohort and high percentage of consanguinity in our families of children with JIA (34.4%). Biologic treatment required in 49% of patients. Patients In remission 89.8%. Out of this 83.77% in remission on treatment and 8.9% in remission off treatment. Further studies needed to understand our population better with focus of effect of consanguinity.

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AB1446

TREATMENT PATTERNS IN A POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS POPULATION IN GERMANY; A RETROSPECTIVE OBSERVATIONAL HEALTH CLAIMS DATA STUDY

Keywords: Disease-modifying Drugs (DMARDs), Epidemiology, Real-world evidence

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Background: Treatment of polyarticular juvenile idiopathic arthritis (polyJIA) aims to ease symptoms and inflammation and reduce further damage and comorbidities[1]. Current treatment options however are not universally effective. With the first targeted synthetic disease modifying anti-rheumatic agent having recently been approved information on how many polyJIA patients may potentially benefit from newly accessible treatment options is needed.
Objectives: Describe current treatment patterns around incident polyJIA diagnosis and beyond, especially changes in medication regimes indicative of unsatisfactory response.
Methods: In a retrospective, observational analysis of two different non-overlapping longitudinal health claims databases (the WIG2, Scientific Institute for Health Economics and Health System Research GmbH, and InGef, Institute for Applied Health Research Berlin GmbH, databases), a representative sample in terms of age and gender of the statutory health insurance (SHI) population in Germany (about 3.5 and 4 million patients, respectively) was analysed. Two incident JIA cohorts were evaluated (2014 and 2015) in each databank, and followed up for 4 or 3 years, respectively. All incident JIA patients (without a JIA diagnosis during baseline, the 4 quarters prior to index) aged 2 to 15 years in the respective observation year (2014 and 2015), with continuous data throughout the observation year and minimum 3-year follow-up (or deceased) were included. Patients were considered to have polyJIA if they had at least one inpatient ICD-10 GM (German modification) diagnosis code, or two verified outpatient codes in two different quarters in the year, of M08.0 (juvenile chronic polyarthritis, adult type, includes rheumatoid factor (RF)+ polyJIA), or M08.3 (juvenile chronic arthritis (seronegative), polyarticular form, includes RF- polyJIA and extended oligoarthritis). We evaluated top-prescribed and pre-defined medications (by 4-digit ATC code) before, during, and following, incident polyJIA diagnosis. The pre-defined medication groups were non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids (GCs), conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), and biologic disease modifying anti-rheumatic drugs (bDMARDs).
Results: Applying the inclusion and exclusion criteria to the incident JIA populations, we identified a total of 121 and 58 polyJIA patients in both 2014 and 2015, (of which 56 and 29 belonged to the 2015 cohort) in the InGef and WIG2 databases, respectively. Among the most frequently prescribed drugs were anti-inflammatory and anti-rheumatic drugs, specific anti-rheumatic agents, and nasal decongestants, immunosuppressive agents, vitamin B12 and folic acid. Prior to diagnosis, more than half of patients of the 2015 cohort were already receiving NSAIDs, however at diagnosis the use of csDMARDs increased more than bDMARD use. From diagnosis quarter to follow-up, there was a proportionally larger increase in the use of bDMARDs than csDMARDs, however use of all medications we examined (also NSAIDs and GCs) in our population continued to increase through follow-up (fig 1). Treatment patterns were similar for both cohorts (2014 and 2015).
Conclusion: Almost all patients continued to take NSAIDs during follow-up, many had concomitant medication with glucocorticoids in addition to csDMARDs or bDMARDs. This demonstrates there was an unmet need in the past for further advanced treatment options such as targeted synthetic DMARDs.

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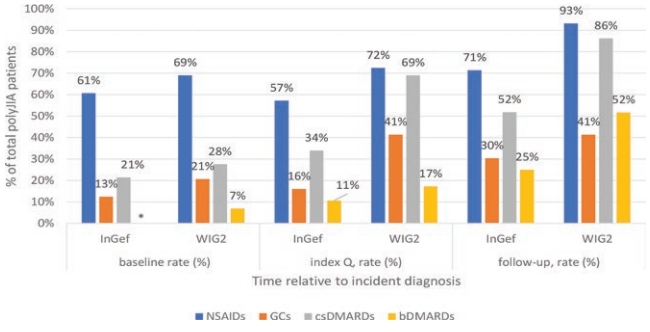


Figure 1. Pre-defined medications for patients with incident polyJIA in the 2015 cohort, for baseline (prior to year of diagnosis), index (diagnosis year) and follow-up (up to 3 years after diagnosis), *indicates n<5 and no % can be reported due to data protection

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AB1447 VALIDITY OF ULTRASONOGRAPHY IN DETECTING ENTHESITIS IN CHILDREN: A SYSTEMATIC LITERATURE REVIEW

Keywords: Ultrasound, Validation, Enthesitis

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Background: Several studies have suggested a potential role for ultrasonography (US) in detecting enthesitis in children, thus enhancing the accuracy of the classification of juvenile idiopathic arthritis (JIA) and improving the therapeutic approach. Because of no consensual definition of ultrasonographic enthesitis in children, the pediatric sub-taskforce of the OMERACT working group posed the research question of whether there are sufficient data to support the role of US in the diagnosis and follow-up of enthesitis in JIA, particularly enthesitis related arthritis (ERA).

Objectives: We performed a systematic literature review (SLR) to assess the value of US for detecting enthesitis in JIA. The main objectives were to determine: i.which elementary lesions have been evaluated by US in JIA patients; ii.which definitions and scoring systems were used; and iii.the measurement properties of US in evaluating enthesitis in JIA according to the OMERACT Filter 2.1 Instrument Selection Algorithm (OFISA).

Methods: PubMed and Embase databases were searched for articles published from January 1966 to May 2022; we selected those meeting the inclusion criteria according to the US definition of enthesitis and metric properties studied. We assessed the clinical features of the population, study design, the type and number of entheses examined, the definition and scoring system of US enthesitis and metric properties according to the OMERACT filter (truth, discrimination, feasibility). The quality of the studies was evaluated with the Quality Assessment of Diagnostic Accuracy Studies 2.

Results: Five publications met the inclusion criteria (26 to 146 patients and 1 to 10 bilaterally examined entheses)[1-5]. All studies focused on lower-limb entheses. The elementary lesions included in the definition of adult enthesitis were generally assessed. Few studies reported US reliability, and none evaluated sensitivity to change of US. US revealed entheseal abnormalities in 9.4% to 53% of JIA patients and 20% to 83% of enthesitis-related arthritis cases. No significant abnormalities were found in healthy children. US findings were poorly correlated with clinical examination. The overall quality of the studies was low, mainly because of the lack of a reference standard.

Conclusion: US could be a sensitive tool to detect entheseal abnormalities in JIA. Nevertheless, the current evidence highlights that a standardized US definition of enthesitis in children is lacking and US criteria and discriminant validity have not been established.

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AB1448 BISPHOSPHONATES IN (MONA) SPECTRUM DISORDER: TWO CASE REPORTS

Keywords: Rare/orphan diseases

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Background: Multicentric osteolysis, nodulosis and arthropathy (MONA) spectrum disorder is a rare inherited progressive skeletal disorder caused by mutations in the matrix metalloproteinase 2 (MMP2) gene. It characterized by multiple peripheral osteolysis, wide metacarpals, osteoporosis, progressive joint contractures, short stature, subcutaneous nodules as well as a coarse face, skin lesions/hirsutism and ocular and cardiac manifestations. The diagnosis is based on the typical clinical features together with normal laboratory findings, which allow this disease to be distinguished from other syndromes, including fibrotic, rheumatic and lysosomal diseases. Treatment options are limited.

Objectives: Bisphosphonates in (MONA) spectrum disorder may be an alternative therapeutic approach.

Methods: We present successful bisphosphonate therapy in two affected sisters, A.N, ten-year-old and A.I, seven-year-old, presented with history of fractures of their long bones after trivial traumas with progressive painful deformities in hands and feet with limitation motion. They were treated with bisphosphonates (intravenous zoledronate every 6 months). The following outcome variables were assessed: skeletal pain, range of motion, internal medical problems as well as neurocognitive function.

Results: Skeletal pain was reduced soon after initiation of therapy. Range of motion did not significantly improve. Neurocognitive development was normal. No further low-impact fractures occurred after starting bisphosphonate therapy. Although the nature of the disease is progressive, they are still able to walk and use their hands for writing.

Conclusion: Bisphosphonate therapy was effective especially in controlling skeletal pain and reducing fractures in MONA spectrum disorder. Early initiation of treatment seems to be particularly important in order to achieve the best possible outcome.

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Disclosure of Interests: None Declared.

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AB1449 **THE GENETIC DIVERSITY AND FEATURES OF TREATMENT OF JUVENILE IDIOPATHIC ARTHRITIS**

Keywords: Quality of life, Genetics/Epigenetics, Disease-modifying Drugs (DMARDs)

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic arthritis of childhood. Systemic JIA has many clinical features overlapping with familial Mediterranean fever, and MEFV gene mutations play a critical role in genetic background for JIA and influence the severity of the disease.
Objectives: 1.To find out associations between different immunological abnormalities, HLA-B27-positivity, carriage of familial Mediterranean fever (FMF) mutations, and clinical polymorphism of JIA. 2.To evaluate the effectiveness of treatment with DMARDs and NSAIDs.
Methods: 94 patients with confirmed JIA (100% male, mean age 14±2 years) were included in the study. All patients corresponded to ILAR criteria. 28 (29.8%) were treated with only NSAIDs, 66 (70.2%) with NSAIDs and sDMARDs (33/50%/ methotrexate, 33/50%/ sulfasalazine), 9 (13.6%) - with bDMARDs. The data is introduced as odds ratios (OR) with 95% confidence interval (CI). The results were considered significant when p<0.05.
Results: At baseline 17 (18.1%) patients were classified as a systemic, 13 (13.8%) - oligoarticular, 3 (3.2%) - polyarticular RF-positive, 8 (8.5%) - polyarticular RF-negative, 3 (3.2%) - psoriatic, 49 (52.1%) - enthesitis-related JIA. MEFV gene mutations were observed in 38 (40.4%) patients (35/92.1%/ - one heterozygous mutation, 3/7.9%/ - more than one mutation), FMF was diagnosed in 3 (3.2%) patients. We found positive significant association between MEFV carriage and systemic JIA (OR/CI95%/=10.3/2.7-39.2, p<0.01), as well as polyarticular RF-negative JIA (OR/CI95%/=5.3/1.5-10.6 p<0.05). Despite the MEFV carriage, colchicine was prescribed to only 5 (5.3%) patients. 28(29.8%) patients were HLA B27- positive and we found positive significant association between HLA B27-positivity and olygoarticular JIA (OR/CI95%/=5.6/2.3-15.7, p<0.05), as well as enthesitis-related JIA (OR/CI95%/=13.6/3.2-19.4/, p<0.01). Sacroiliitis was diagnosed in 85 (90.4%) patients, 26 (30.6%) – non-radiographic, 59 (69.4%) - radiographic. The rise in progression from non-radiographic sacroiliitis to radiographic significantly decreased in patients on methotrexate (OR/CI95%/=0.05/0.001-0.044/, p<0.01), compared to sulfasalazine (OR/CI95%/=0.78/0.36-2.79 p>0.05). For patients on DMARDs the disease had a self-limited course, without clinical manifestation in adulthood. Total remission was mostly associated with methotrexate (OR/CI95%/=13.5/1.6-95 p<0.01), in contrast to sulfasalazine (OR/CI95%/=0.69/0.28-1.72 p>0.05).
CONCLUSION:
1.The carriage of MEFV gene mutations increase the risk of manifestation of polyarticular and systemic JIA.
2.Early appointment of DMARDs together with NSAIDS makes it possible to stop the disease and prevent its transition to adult rheumatology.
3.Despite recent ACR treatment guidelines recommending NSAIDS and sulfasalazine for the treatment of sacroileitis, early administration of methotrexate also prevents the transition of nonradiographic sacroileitis to radiographic.
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Disclosure of Interests: None Declared.
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AB1450 **HIP INVOLVEMENT IN TUNISIAN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS**

Keywords: Prognostic factors, Inflammatory arthritides

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Background: Juvenile idiopathic arthritis (JIA) is characterized by widely heterogeneous clinical course and outcomes. Hips are the most commonly affected joints in severe uncontrolled JIA.
Objectives: The aim of our study was to determine the prevalence and associated factors of hip involvement in Tunisian JIA patients.
Methods: A retrospective and observational monocentric study including children with JIA according to the ILAR was conducted in the Rheumatology department of Sousse, Tunisia. We compared the disease parameters between the two groups with and without coxitis.
Results: We included 55 children (28 girls and 27 boys). The mean age was 13.6 years. The predominant subtypes of JIA were the seronegative polyarticular JIA (38.2%), and the seronegative oligoarticular form and juvenile spondyloarthritis (16.4% each). Biological inflammatory syndrome was found in 65.5% of cases. The mean ESR and CRP was 42.4mm/h and 28.8mg/l respectively. Hip involvement concerned 30.9% of the patients (n=17) and was bilateral in 64.7% of cases (n=11). Coxitis occurred on average 10 years after the JIA onset. The mean Lequesne index was 12. Hip radiographs were normal in 40% of cases. Magnetic resonance imaging was performed in 25% of cases and revealed synovitis in 70% of cases. Overall, 61.8% of patients had medical treatment combining non steroidal anti-inflammatory drugs and rehabilitation. Only two patients had local infiltration with Hexatrione. In 12.7% of cases (7 cases), a total hip replacement was necessary. Hip involvement was significantly associated with younger age at onset (p=0.02), polyarticular subtype of JIA (p=0.04) and with the presence of biological inflammatory syndrome (p=0.03). However, coxitis was not significantly associated with gender, the duration of JIA progression, extraarticular manifestations, structural damage or the different used treatments.
Conclusion: Our study showed that hip involvement is frequent among Tunisian patients with JIA. Coxitis was associated with the polyarticular subtype, with biological inflammatory syndrome and younger age at onset of JIA.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1451 **THE HIP RADIOGRAPHIC SCORE IS CORRELATED WITH THE LATE-ONSET OF JUVENILE IDIOPATHIC ARTHRITIS**

Keywords: Imaging

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Background: Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease in children affecting mobility and physical function. The hip is a load-bearing joint and its damage has a significant functional impact. An appropriate scoring system is mandatory to monitor structural progression and damage over time. The childhood Arthritis Radiographic Score of the Hip (CARSH) is a valid score covering the osteoarticular changes in the hip joint as space narrowing, erosions, malalignment, sclerosis, flattening of the femoral head, and growth abnormalities [1].
Objectives: The aim of this study was to assess radiographic changes in the hip joint using the CARSH in children suffering from JIA with hip involvement and to determine the impact of disease factors in this score.
Methods: This cross-sectional study was conducted in the pediatric rheumatology department and included patients with JIA according to the ILAR criteria. We included children with hip involvement defined as the presence of hip pain and/or limping and range motion limitation, and/or abnormal hip findings in pelvic radiography, ultrasound, or MRI. We collected from the recorded data demographics, disease characteristics [symptom duration, disease presentation, JIA subtypes], and disease activity: Juvenile arthritis disease activity (JADAS10). Experimented and blinded pediatric rheumatologists read the pelvic radiograph using the Childhood Arthritis Radiographic Score of the Hip (CARSH).
Results: Twenty-two children with a mean age of 13 years [5-22] were included in the study. The gender ratio was 1.4 (13 Males/9 Females). The median age of disease onset was 9.5 years [4-14]. The mean duration of the disease was 47 months [4-156]. The diagnostic delay median was 22 months [1-120]. The patient global assessment (PGA) median was 4 [0-8]. The visual analog scale (VAS) median was 3.6 [0-8]. The sedimentation rate (SR) and the C reactive protein (CRP) median were 25 [2-65] and 10 [1-47]; respectively. The JADAS median was 6 [0-18]. Forty-four hips were analyzed. The median score of CARSH was 1.8 [0-7]. The CARSH was positively correlated to the age of disease onset (r = 0.4; p = 0.04). No other significant correlations were found between the CARSH and the gender (p= 0.3), the duration of the disease (r = 0.7; p = 0.7), the diagnostic delay (r = 0.02; p = 0.9), the PGA (r = 0.1; p = 0.5), the VAS (r = -0.4; p = 0.8), the ESR (r = -0.08; p = 0.7), the CRP (r = -0.1; p = 0.6) and the JADAS 10 (r = 0.01; p = 0.9).
Conclusion: This study showed that the radiographic score CARSH was correlated to the age of disease onset. Our findings confirm that structural damage was more important in late-onset disease whereas early hip involvement affects growth and joint development.
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Other orphan diseases

AB1452

ABO BLOOD GROUPS AND INCREASED RISK FOR VASCULAR INVOLVEMENT IN THE PATIENTS WITH BEHÇET'S DISEASE

Keywords: Organ damage, Vasculitis, Behcet's disease

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Background: Behçet's disease (BD), a multisystem inflammatory disorder of unknown etiology, is classified as a variable vessel vasculitis affecting all types and sizes of blood vessels; and a tendency for thrombosis in association with inflammatory endothelial activation is an important characteristic of BD vasculitis. Recent studies suggest an association between ABO blood groups and vascular disease in particular in those carrying non-O (A, B, and AB) groups [1].
Objectives: We aimed to investigate the potential contribution of ABO blood groups to the risk of vascular involvement in patients with BD.
Methods: We retrospectively analyzed the records of BD patients followed between 1978 and 2022. Patients fulfilling the ISG Criteria for diagnosis of BD were screened, and those with information about ABO blood groups were included into the study. Presence or absence of vascular involvement and its features were recorded using a standard form. The chi-square test, t-test, Mann-Whitney U test, and logistic regression tests were used for statistical analyses.
Results: The study group consisted of 411 patients with available blood group data, and 143 (34.8%) were carrying O [58% men, mean age at diagnosis 31.4±10.1 years, median follow-up period 153 (98-219) months], and 268 (65.2%) were carrying non-O blood groups [60.1% men, mean age at diagnosis 30.7±8.4 years, median follow-up period 148 (92-204) months]. There was no statistical significance between O and non-O groups in regard to the potential confounding factors affecting the risk for vascular disease, including sex, age at diagnosis, family history, HLA-B51 positivity, smoking, comorbidities, and prothrombotic mutations. Vascular involvement was observed in 39 (27.3%) patients with blood group O [venous in 35 (24.5%), and arterial in 11 (7.7%)], whereas 109 patients (40.7%) with non-O blood groups had vascular involvement [venous in 95 (35.4%), and arterial in 38 (14.2%)]. The frequencies of total vascular and venous involvements between the two groups were significantly different (p=0.007, p=0.023, respectively). Unadjusted and adjusted ORs with different models in the multivariate logistic regression analyses are shown in **Table 1**. After adjustments for age, sex and comorbidities, the risk for arterial disease was also found to be increased in association with non-O blood groups.
Conclusion: Vascular involvement with a tendency for thrombosis is an important feature of BD, and inflammatory characteristics resulting in endothelial dysfunction have been considered as the main underlying pathology. The results of the preliminary study supports the previous reports revealing the potential contribution of ABO blood groups in the development of vascular disease and suggest an approximately two-fold increased risk for vascular involvement in BD patients.
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Table 1. Logistic regression analysis to estimate unadjusted and adjusted risk for vascular events comparing O with non-O blood groups. Model 1: ABO blood group, Model 2: Model 1 plus age at diagnosis and sex, Model 3: Model 2 plus comorbidities, Model 4: Model 3 plus malignancy, Model 5: Model 4 plus smoking (missing value for 84 patients).

	Total vascular involvement		Venous involvement		Arterial involvement	
	p-value	OR (CI %95)	p-value	OR (CI %95)	p-value	OR (CI %95)
Model 1	0.007	1.8 (1.2-2.8)	0.023	1.7 (1.1-2.7)	0.057	2.0 (0.9-4.0)
Model 2	0.007	1.9 (1.2-3.1)	0.024	1.7 (1.1-2.8)	0.062	2.0 (0.9-4.0)
Model 3	0.005	2.0 (1.2-3.2)	0.022	1.8 (1.1-2.9)	0.038	2.2 (1.0-4.7)
Model 4	0.006	2.0 (1.2-3.2)	0.023	1.8 (1.1-2.9)	0.046	2.2 (1.0-4.6)
Model 5	0.029	1.9 (1.1-3.2)	0.038	1.8 (1.0-3.2)	0.102	2.0 (0.9-4.5)

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Disclosure of Interests: None Declared.
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AB1453

INFLAMMATION MARKERS, SYSTEMIC INFLAMMATORY BASED SCORES (SIBS) AND CYTOKINE PROFILES IN ADULT CHRONIC NONBACTERIAL OSTEOMYELITIS (CNO)/ SAPHO SYNDROME: AN IMMUNOLOGICAL CHARACTERIZATION

Keywords: Bone diseases, Adaptive immunity, Rare/orphan diseases

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Background: Chronic non-bacterial osteomyelitis (CNO) is a rare bone disease occurring in children and adults. Adults mainly present with osteitis and hyperostosis of the anterior chest wall, sometimes occurring in the context of synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome [1]. CNO is hypothesized to be an auto-inflammatory disease, as studies on pediatric patients have shown raised erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), and elevated serum concentrations of interleukin (IL)-6, 8, 17A and TNF-a [2]. For adults, however, the suspected systemic immune activation is not consistently reflected by these generic markers, and data on cytokine expression are scarce and variable [3, 4].
Objectives: To provide broad immunological characterization of adult CNO/ SAPHO, including cytokine profiles, compared to controls.
Methods: Cross-sectional study in our CNO referral center including adult CNO/ SAPHO patients with active disease (n=172) and controls (n=82) referred between 1992-2022 not using immunomodulatory treatment (exempting NSAIDs) or bisphosphonates. Generic inflammation parameters and systemic inflammatory based scores (SIBS) were compared between patients and controls and between patients with and without concomitant arthritis/dermatitis, and with strong or moderate increase in isotope uptake on nuclear imaging. Serum levels of Th1/2 and Th17-derived cytokines were determined with electrochemiluminescent immunoassays, and receptor activator of nuclear factor kappa beta (RANKL) and osteoprotegerin (OPG) with ELISA in 33 patients and 8 controls.
Results: ESR, CRP, platelet, leucocyte and neutrophil count were higher in CNO/SAPHO patients than in controls, but generally remained within the reference range. ESR was also higher in patients with concomitant arthritis/dermatitis compared to isolated osteitis (24 versus 16, *p=0.009*), and in patients with strongly rather than moderately increased isotope uptake on nuclear imaging (20 versus 13, *p= 0.009*). Neutrophil-derived SIBS (neutrophil/lymphocyte ratio (NLR) and systemic immune inflammation index (product of NLR and platelet count)) were elevated in CNO patients compared to controls. Cytokine analyses revealed no differential expression for IL-6, -8, -10, -13, -17A, -22, -23, -27, TNF-a, IFN-γ, and MIP-3a, nor for the bone markers RANKL and osteoprotegerin.
Conclusion: In this adult CNO/SAPHO cohort, generic inflammation markers and neutrophil-derived SIBS NLR and SII were increased compared to controls. In contrast to previous studies, we found no differential expression of IL-6, -8, -17A and TNF-a to support systemic cytokine imbalance in adult CNO/SAPHO. Further studies are needed to evaluate whether the auto-inflammatory hypothesis in CNO/SAPHO applies as much to the adult as pediatric subtype, and if so, whether the local inflammasome is systemically reflected.
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AB1454 **DIAGNOSTIC AND THERAPEUTIC PRACTICES IN ADULT CHRONIC NONBACTERIAL OSTEOMYELITIS (CNO)/SAPHO SYNDROME: AN INTERNATIONAL LANDSCAPE**

Keywords: Quality of care, Bone diseases, Rare/orphan diseases

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Background: Chronic nonbacterial osteomyelitis (CNO) is a rare auto-inflammatory bone disease. CNO, especially the adult variant, may occur in the broader spectrum of Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis (SAPHO) syndrome. Adult CNO lacks diagnostic or management guidelines in contrast to pediatric disease (1, 2).
Objectives: We mapped current diagnostic and therapeutic practices for CNO/SAPHO in adults.
Methods: A primary survey was spread among global rheumatological/bone networks and 57 experts as identified from literature (May 2022), covering terminology, diagnostic tools (clinical, radiological, biochemical) and treatment steps. A secondary survey (sent to primary survey responders in August 2022) further queried diagnostic features, treatment motivations, disease activity and treatment response monitoring.
Results: 36 and 23 physicians completed the primary and secondary survey respectively. Diagnosis was mainly based on individual physician assessment, in which the combination of chronic relapsing-remitting bone pain with radiologically-proven osteitis/osteomyelitis, sclerosis, hyperostosis and increased isotope uptake on bone scintigraphy were reported indicative of CNO. Physicians appeared more likely to refer to the condition as SAPHO syndrome in the presence of joint and skin pathology. MRI was most frequently performed as imaging diagnostic, and the preferred diagnostic test for 47%. X-rays were second-most frequently used, while considered least informative. Typical imaging features reported were hyperostosis, osteitis, osteosclerosis, bone marrow edema, while degeneration, soft tissue calcification, and ankylosis were not regarded characteristic. Inflammation markers and bone markers were generally regarded unhelpful for diagnostic and monitoring purposes, and physicians infrequently performed bone biopsies. Management strategies diverged, including indications for treatment, response monitoring and declaration of remission. Step-1 treatment generally consisted of non-steroidal anti-inflammatory drugs/COX-2 inhibitors (installed by 83%). Common step 2-3 treatment were pamidronate, methotrexate, and TNF-a-inhibition (anti-TNFα), the latter two regarded especially convenient to co-target extra-skeletal inflammation as often seen in SAPHO syndrome. Pamidronate and anti-TNFα and were considered as most effective treatments overall.
Conclusion: Adult CNO appears to be a condition embedded within a broad and insufficiently characterized disease spectrum, likely including SAPHO syndrome. MRI is the favoured imaging diagnostic, while biochemical and histopathological investigations are rated less useful. Management strategies for CNO/SAPHO vary but pamidronate and anti-TNFα are commonly regarded most successful treatments. The survey results lay out current practices for adult CNO/SAPHO, which may serve as backbone for a future consensus clinical guideline.
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AB1455 **FLUORIDE UPTAKE ON QUANTITATIVE POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY (NA18F-PET/CT) AS NOVEL BIOMARKER FOR DISEASE ACTIVITY IN ADULT CHRONIC NONBACTERIAL OSTEOMYELITIS/SYNOVITIS ACNE PUSTULOSIS HYPEROSTOSIS OSTEITIS SYNDROME (CNO/SAPHO)**

Keywords: Bone diseases, Imaging, Rare/orphan diseases

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Background: Chronic nonbacterial osteomyelitis (CNO) is a rare bone disease characterized by sterile bone inflammation and locally increased bone turnover. CNO that occurs in the rheumatic spectrum of synovitis, acne, pustulosis, hyperostosis and osteitis is referred to as SAPHO syndrome [1, 2]. To date, there are no objective biomarkers for monitoring disease activity. Recommended imaging tools like technetium radiolabeled hydroxymethylene diphosphonate single positron emission computed tomography visualize the increased bone turnover, but fail to reflect the relapsing-remitting disease activity course due to an imprinting pattern [3]. Likewise, magnetic resonance imaging can track the fluctuation of bone marrow edema, but is inferior compared to computed tomography (CT) in capturing subtle inflammatory and accumulated structural changes that reflect disease duration. Sodium fluoride-18 positron emission tomography/CT($Na^{18}F$-PET/CT) is another imaging modality which produces quantitative data on the spatial distribution of bone turnover that also correlate with clinical disease activity in other metabolic bone diseases [4].
Objectives: We quantified ^{18}F-uptake in CNO/SAPHO patients to evaluate its capacities as a disease activity biomarker.
Methods: Cohort study including 43 CNO/SAPHO patients not using immunomodulatory or antiresorptive medications with $Na^{18}F$-PET/CT performed at our expert clinic between 2019-2022. Images were qualitatively assessed following a systematic reporting format. Maximal standardized uptake values (SUV_{max}) were determined in the following areas as defined by radiologic appearance on CT: osteitic areas (osseous lesions), inflamed ligaments or joint spaces (soft tissue lesions) and thoracic vertebrae 5 as reference bone (ref-bone).
Results: Qualitative assessment revealed sclerosis and hyperostosis of the manubrium as most prevalent radiologic features (present in 77% and 70%) and costae 1-2 (79% each). Calcification/ankylosis of the costoclavicular ligament was seen in 58%. Quantitative analyses showed higher SUV_{max} of osseous and soft tissue lesions compared to ref-bone (mean 22±6 and 26±9 vs. 11±3 g/mL, $p<0.001$ for paired difference). Stratified per location, highest SUV_{max} was found in soft tissue lesions of the costoclavicular ligament followed by the manubriosternal joint (mean SUV_{max} of 29±13 and 25±8 respectively). SUV_{max} in soft tissue lesions positively correlated with erythrocyte sedimentation rate (Spearman correlation coefficient 0.546, $p<0.01$).
Conclusion: CNO/SAPHO patients display distinctive qualitative imaging features that are well-captured on $Na^{18}F$-PET/CT, and also show higher SUV_{max} in osseous and soft tissue lesions compared to ref-bone. Diseased soft tissue lesions showed highest SUV_{max}. Considering $Na^{18}F$ precipitates in young osteoid, these high values may reflect the process of soft tissue ossification that is common in long-existing CNO/SAPHO, as also demonstrated in fibrodysplasia ossificans progressiva [5]. Further studies should evaluate the promising application of quantified uptake on $Na^{18}F$-PET/CT as a novel biomarker for disease activity and therapy response in CNO/SAPHO.
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AB1456 **BIOLOGICS AND JAK INHIBITORS EFFICACY IN VEXAS SYNDROME FROM FRENCH MULTICENTER CASE SERIES OF 256 PATIENTS**

Keywords: Innate immunity, Adaptive immunity, Inflammatory arthritides

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Background: A new autoinflammatory syndrome related to somatic mutations of *UBA1* was recently described and called VEXAS syndrome.
Objectives: To describe clinical characteristics, laboratory findings and outcomes of VEXAS syndrome.
Methods: Case-series. Patients referred to a French multicenter registry between November 2020 and January 2022. Frequency and median of parameters and vital status, from diagnosis to the end of the follow-up.
Results: Among 256 patients, 207/221 (94%) were males with median age at diagnosis 65 years [49-86]. Main clinical features were skin lesions (n=215; 84%), non-infectious fever (n=121; 47%), lung involvement (n=146; 57%), relapsing chondritis (n=69; 27%), venous thrombosis (n=128; 50%), lymph nodes (n=55; 21%), and arthralgia (n=65; 25%) with arthritis (n=26). Ocular inflammatory involvement was present in 119 cases (46%), mainly uveitis (n=21) and scleritis/ episcleritis (n=43). Peripheral nervous system was noted in 18 patients (7%) with peripheral neuropathy (n=11), multinevritis (n=3) and PIDC (n=5). The skin lesions were mainly neutrophilic dermatosis (n=74) and vasculitis (n=45). Hematological disease was present myelodysplastic syndrome (MDS, n= 81; 32%), monoclonal gammapathy of unknown significance (n=18), chronic myelomonocytic leukemia (n=7). AA amyloidosis was present in 2 cases. Median CRP levels were at 56 [1-423] mg/l, with abnormal somatic mutations in 44 cases (%) mostly TET2 and DNMT3. Previous immunosuppressive therapies were methotrexate (n=15; 6%), cyclophosphamide (n=6; 3%), MMF (n=5; 4%). JAK inhibitors were used in 24 cases and were stopped in 5 cases (3 for inefficacy and 2 for adverse events). IL1R inhibitors were used in 12 cases with discontinuation for inefficacy (n=7) and adverse events (n=1), and IL6R inhibitors in 12 cases with discontinuation for inefficacy in 4 cases and adverse events in 1 cases.
Conclusion: This is the largest multicenter cohort of VEXAS syndrome and which allow to compare for the first time the efficacy and tolerance of various biologics and JAK inhibitors and seem confirm the benefit of JAKi and also of tocilizumab.
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Disclosure of Interests: None Declared.
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AB1457

MULTIDISCIPLINARY PROSPECTIVE STUDY OF PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS WHO DEVELOPED RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS

Keywords: Descriptive Studies, Organ damage, Epidemiology

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Background: Immune checkpoint inhibitors (ICIs), by activating the immune system (specifically, T-cells), foster the reaction against tumor cells. However, parallelly, autoimmune phenomena, known as immune-related adverse effects (ir-AEs) (PMID 33902919, 29442540), can be triggered and manifest in any organ or tissue. The most common rheumatic manifestations are inflammatory arthritis, polymyalgia rheumatica, and myositis, but other inflammatory cases have also been described (PMID 32403289). More data on their frequency and characterization are needed.
Objectives: To prospectively evaluate the incidence of rheumatic ir-AEs during ICIs treatment, along with clinical characterization, management required, and outcomes.
Methods: An observational, prospective study was conducted at a tertiary center in Spain, led by the oncology department with the participation of several specialties, to evaluate the occurrence of ir-AEs in patients starting ICIs between January 2019 and April 2022. Participants were routinely followed at oncology clinics to detect ir-AEs through pre-specified clinical and laboratory assessments. For rheumatic symptoms, ir-AEs were studied by records review and evaluated in person at rheumatology clinics for those with a degree of involvement of ≥2, according to the ASCO guidelines [3]. The incidence - with a 95% confidence interval (CI) - and characterization of defined rheumatic ir-AEs are presented here.
Results: Of 181 patients, 21 (11.6%, 95%CI 7.7-17.1%) developed rheumatic ir-AEs, 13 men (61.9%) with a median age of 62.3 years (p25-75 51.8-75.0). The median time from the start of ICIs to the development of rheumatic ir-AEs was 85 days (p25-75 51.5-165). Blood tests for autoimmunity were positive in 69.2% of available cases (9/13), but all at a low titer **(table 1)**. According to ASCO guidelines, most patients had a toxicity grade 1-2, but 3 (14.3%) patients presented with severe manifestations (grade 3): 1 (4.8%) case of inflammatory arthritis, 1 (4.8%) of xerostomia, and 1 (4.8%) of Raynaud's phenomenon with ulcers. 9 (42.9%) patients also presented with concurrent ir-AEs of different types. Rheumatic ir-AEs were successfully settled, though infliximab and intravenous vasodilators were required for some cases. While discontinuing ICIs was mostly due to neoplasm progression (47.6%), in 3 cases (14.3%) it was due to grade-3 rheumatic manifestations. 7 (33.3%) patients died during follow-up due to the oncological disease, no case due to rheumatic toxicity.

Table 1.

Type of tumor n (%)	Drug n (%)	Clinical presentation (%)	Antibodies n (%)	Treatment n (%)	Outcome n (%)
Lung 9 (42.9)	Pembrolizumab 8 (38.1)	Inflammatory arthritis 7 (33.3)	ANA 8 (38.1)	No rheumatological treatment 10 (47.6)	Discontinuation of ICI due to progression 10 (47.6)
Melanoma 4 (19.0)	Nivolumab 7 (33.3)	Xerostomia 5 (23.8)	Anti-centromere 1 (4.8)	Glucocorticoids 8 (38.1)	Discontinuation of ICI due to severe ir-AEs 4 (19.0)
Hodgkin's lymphoma 2 (9.5)	Nivolumab + Ipilimumab 3 (14.3)	Polymyalgia-like syndrome 5 (23.8)	Rheumatoid factor 1 (4.8)	Hydroxychloroquine 3 (14.3)	ICI is currently ongoing 4 (19.0)
Kidney 2 (9.5)	Atezolizumab 3 (14.3)	Myositis 4 (19.0)	ACPA 1 (4.8)	Pilocarpine 2 (9.5)	Completed ICI regimen 2 (9.5)
Esophagus 1 (4.8)		Raynaud's phenomenon with ulcers 1 (4.8)	Anti-TIF1γ 1 (4.8)	NSAIDs 2 (9.5)	Lost to follow-up 1 (4.8)
Bladder 1 (4.8)				Infliximab 1 (4.8)	
Mesothelioma 1 (4.8)				Vasodilators 1 (4.8)	

Conclusion: Through a prospective and multidisciplinary study, we estimated an 11.6% of occurrence of rheumatic ir-AEs in patients under ICIs. Most presented with mild or moderate involvements, though severe cases were also seen. A coordinated approach with the oncologists is thus essential for patients treated with ICIs at risk of developing ir-AEs.
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Disclosure of Interests: None Declared.
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AB1458

TREATMENT UTILIZATION, SYMPTOMS, AND COMORBIDITIES IN DERMATOMYOSITIS: AN ANALYSIS OF ELECTRONIC MEDICAL RECORDS IN THE UNITED STATES

Keywords: Comorbidities, Myositis, Real-world evidence

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Background: Dermatomyositis (DM) is a rare, chronic inflammatory disease characterized by skin manifestations and/or progressive muscle weakness and other systemic manifestations. Prior analyses have reported higher morbidity, hospitalization rates, and mortality among patients with DM compared with matched controls[1-3]; however, more recent data on the disease burden and treatments for DM are warranted.
Objectives: We conducted this analysis to provide updated data on the treatment utilization, symptoms, and comorbidities recorded for patients with myopathic DM in the United States.
Methods: This was a descriptive, retrospective cohort analysis that used TriNetX US electronic medical records (EMR) of adults who had been diagnosed myopathic DM (ICD-9 codes: 710.3/ICD-10: M33.1x, M33.9x, M36.0) between 1 January 2007 and 1 September 2020. Key inclusion criteria were: age ≥18 years at index date (i.e., date of DM diagnosis), ≥6 months of baseline data before the index date, and ≥6 months of follow-up after the index date. Assessments included utilization rates for medications of interest prior to the index date, percentage of patients who received ≥2 consecutive unique non-steroidal immunosuppressive therapies within 12 months of the index date, classification and qualification of the most common post-index symptoms and comorbidities, along with their comparison to pre-index values.
Results: The TriNetX database contained 1097 patients with DM (mean age: 54.6 years; sex: 77% female). The mean observation period was 9.7 years (6.0 years pre-index; 3.7 years post-index). Prior to the DM index date, 60% of patients

were prescribed steroids and 24% were prescribed ≥1 non-steroidal immunosuppressive therapy. Within 3, 6, and 12 months of index date, 8%, 14%, and 20% of patients, respectively, received ≥2 immunosuppressive therapies (ISTs). A 2–3-fold increase in percentage was seen post-index compared with pre-index for a wide range of symptoms and comorbidities, including gastroesophageal reflux disease (43% and 22%, respectively), anxiety (25% and 13%), interstitial lung disease (26% and 10%), and osteoporosis (21% and 6%).

Conclusion: In this analysis of TriNetX EMR data, the majority of patients who were diagnosed with myopathic DM had received immunosuppressive therapies for an extended time to treat their symptoms before they received a formal DM diagnosis, which may have contributed to the delay in DM diagnosis. One fifth of patients had received ≥2 ISTs within 12 months of DM diagnosis, suggesting that even after receiving standard of care treatments, many patients experience DM symptoms that are difficult to control and/or tolerate. A wide range of symptoms and comorbidities increased post-DM diagnosis. These results highlight the remaining unmet need for earlier diagnosis and therapies that better control symptoms for patients with myopathic DM.

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AB1459 IGG4-RELATED DISEASE: 2010-2022 CASE REVISION AND PERFORMANCE OF DIAGNOSTIC CRITERIA

Keywords: Diagnostic Tests, Rare/orphan diseases, Undifferentiated connective tissue disease

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Background: IgG4 immunoglobulin-related disease (IgG4-RD) is a rare, systemic immune-mediated fibro-inflammatory process with unclear etiology and pathophysiology. Can affect multiple organs that encompass common pathophysiological, serological and clinical characteristics.

Objectives: To describe the heterogeneity of the clinical presentation, evolution, and treatment of patients diagnosed with IgG4-RD and compare the performance of the last two IgG4-RD classification and diagnostic criteria.

Methods: Single-center retrospective study in which patients with a possible diagnosis of IgG4-RD from various hospital departments are studied from January 2010 to August 2022. Some exclusion criteria were applied (patients with clinical manifestations attributable to other diseases were excluded) and to those who remained with a suspected diagnosis of IgG4-RD, the Umehara-Okazaki 2011 and ACR/EULAR 2019 criteria were applied.

Results: 182 patients with elevated IgG4 and/or a suspected diagnosis of IgG4-RD were collected. Finally, after exclusion criteria, 22 possible patients with IgG4-RD remained (Table 1). The diagnostic criteria proposed by Umehara and Okazaki in 2011 are applied to these patients, including a total of 13 patients, with a mean age of 60 years, 57% women; 5 being classified with definitive disease, 3 as probable disease and 5 as possible disease. Finally, we applied the ACR/EULAR 2019 classification criteria to those patients too, establishing diagnosis in 7 patients. The mean age was 57 years, 71% were women with a mean follow-up of 5.3 years; 85.71% of the patients had elevated IgG4, with mean levels of 176.3 mg/dL. Retroperitoneal fibrosis and aortitis was the most prevalent presentation in both groups (2011 and 2019 criteria) with 38.5% and 28.6% respectively.

Conclusion: IgG4-RD is a recently described entity that is very heterogeneous in terms of its clinical, analytical and histopathological presentation. According to our series, clinical heterogeneity is the rule, being the retroperitoneal fibrosis and aortitis the most frequent. There are differences when we use the different criteria. ACR/EULAR 2019 classification criteria are stricter criteria that allows us to classify patients more accurately. In our series 6 patients fulfilled Umehara-Okazaki criteria but not ACR/EULAR due to giving more importance to histopathology, clinical manifestations and the need to reach a minimum score in which, for example, only IgG4 levels are not enough. Therefore, on many occasions, a multidisciplinary approach with experienced teams is necessary.

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Table 1. High diagnostic IgG4-RD group, Umehara and Okazaki 2011 and ACR/EULAR 2019 IgG4-RD criteria.

	High diagnostic suspition of IgG4-RD n=22	Umehara-Okazaki criteria 2011 n=13	ACR/EULAR criteria 2019 n=7
Age, median (IQR), years	62 (34-87)	60 (34-82)	57 (34-79)
Sex, female (%)	54,54	61,54	71,42
Follow-up, median (IQR), years	5,18 (1-28)	4,4 (1-9)	5,3 (1-9)
Death, n (%)	9,09	7,69	0
IgG4 level, median (IQR), mg/dL	152 (32,6- >194)	163,71 (56,6 ->194)	176,3 (109- >194)
Elevated IgG4, n (%)	63,63	84,62	85,71
Normal IgG4, n (%)	13,63	7,69	0
No evaluated IgG4, n (%)	22,72	7,69	14,29
CRP, median (IQR), mg/dL	3,33 (0-10,7)	3 (0,1 -10,7)	6 (0,39 -7,8)
ESR, median (IQR), mm/h	32,89 (7-120)	42 (10 -120)	48,4 (16-120)
Available biopsy at IgG4 involvement site (%)	40,91	69,23	100
Clinical phenotypes			
Pancreatohepatobiliary, n (%)	18,18	15,38	14,28
Retroperitoneum and aorta, n (%)	40,91	38,46	28,57
Head and neck limited, n (%)	4,55	7,69	0
Mickulicz and systemic, n (%)	4,55	7,69	14,28
Undefined phenotype, n (%)	31,82	30,77	42,86
Initial corticotherapy, n (%)	90,91	84,61	85,71

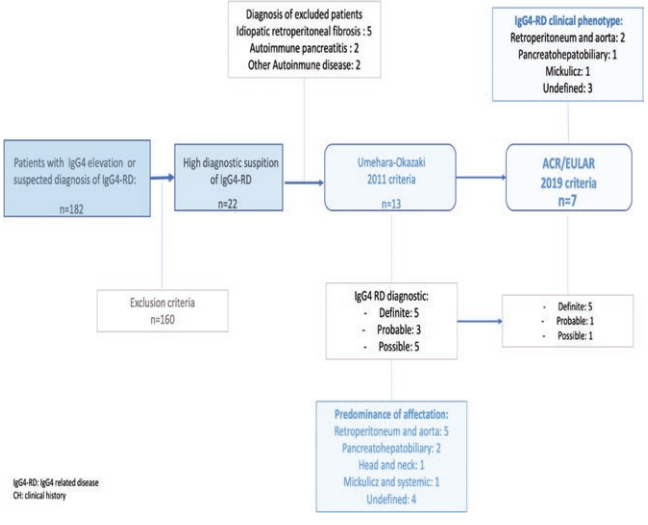


Image 1. Diagostic secuence used with IgG4-RD patients.

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AB1460

CHARACTERISTICS AND EARLY OUTCOMES OF PALINDROMIC RHEUMATISM: AN INCEPTION COHORT FROM INDIA

Keywords: Synovium, Inflammatory arthritides, Autoantibodies

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Background: The exact pathogenesis and risk factors of Palindromic Rheumatism (PR) remain uncertain, however, a subgroup of patients with PR share a close relationship with rheumatoid arthritis (RA) in terms of etiopathogenesis, clinical features, serology, and outcomes.
Objectives: We aim to describe the characteristics of patients in an inception cohort of PR along with determinants of progression to RA.
Methods: Patients with symptoms suggestive of PR were screened by a rheumatologist and after relevant exclusions, were classified into PR and included in an inception cohort at the Centre for Arthritis and Rheumatism Excellence, India. Their demographics, clinical characteristics, serology, inflammatory markers, and progression to RA or any other autoimmune rheumatic disease(AIRD) were recorded. Statistical analysis was done using GraphPad Prism v9.4.1 and results are expressed as mean ± standard deviation.
Results: Of 706 patients screened, 685 were classified into PR (age 45.5±11.9 and male-to-female ratio of 1:2.8) with a follow-up duration of 27±20.4 months. Of those with a follow-up of greater than one year, 102 of 505 (20.2%) progressed to RA at 30± 20 months and 13 to other AIRDs. Progression to RA was positively associated with a greater number of attacks per month; severe PR or >20 attacks per month; shoulder or wrist joint involvement, absence of erythema, positive rheumatoid factor, anti-CCP antibody, and ANA on univariate analysis. Additionally, they required treatment with a higher number of cDMARDs and even anti-TNFs (Table 1). On multivariate analysis, symptom duration of <5 years, wrist involvement, and anti-CCP positivity were associated with progression to RA. The RF and anti- CCP titers showed no association with progression to RA.
Conclusion: Early outcomes of the inception cohort of PR revealed progression to RA in 20% of the cohort and was associated with symptom duration of <5 years, wrist involvement, and anti-CCP positivity. The PR group was treated predominantly with colchicine and cDMARDs with a remission rate of 60%.

Table 1. Comparison of clinical presentation and treatment between persistent PR and Evolved RA

Variable	Persistent PR N=403	Evolved to RA N=102	Univariate[#]; p value, OR(95%CI)	Multivariate [##]; P value, HR(95%CI)
Age, years	46± 12	47± 11	0.4	
Sex, female	303(24.8)	78(23.5)	0.9	
Disease Duration > 5 years	186(46.1)	36(16.2)	0.06	**0.01, 0.6(0.3-0.8)**
Follow up, months	34 ± 19	34± 16	0.7	
Number of attacks per month	8.5± 9.1	11 ± 11	**0.01**	
Pain VAS	8.3 ± 1.9	8.1± 1.9	0.6	
Duration of attack, days	2.8± 1.6	2.9 ± 1.8	0.4	
Severe PR *	49 (12.2)	24 (23.5)	**0.004, 2.2(1.3-3.8)**	0.5
Joint Involvement				0.5
DIP	220 (54.6)	63 (61.7)	0.116	**0.04, 2.5(1.1-5)**
MCP/PIP	365 (90.6)	90 (89.2)	0.294	
Shoulder	326 (80.9)	92 (90.2)	**0.015, 2.8 (1.1-4.3)**	
Wrist	325 (80.6)	93 (91.2)	**0.006, 2.4 (1.2-5.1)**	
Lower Limb joints	377 (93.5)	99 (97.1)	0.382	
Presence of erythema	242 (60.0)	42 (41.2)	**<0.001, 0.4(0.2-0.7)**	0.1
Smoking	6(5.8)	7(1.7)	**0.03, 0.3(0.1-0.8)**	0.08
Baseline ESR, mm	24 ± 20	28 ± 22	0.09	0.6
RF positivity	195 (48.4)	70 (68.6)	**<0.001, 2.3(1.5-3.7)**	0.2
Anti-CCP positivity	245 (60.8)	87 (85.3)	**<0.00, 3.7(2.1-6.7)**	**0.01, 2.8(1.4-6.2)**
ANA positive	82 (40.4)	32 (31.4)	**0.014, 1.8(1.1-2.9)**	0.5
Treatment				
HCQ	24(5.9)	1(0.98)	**0.01, 0.2(0.02-0.8)**	
Colchicine	3(0.74)	0	0.9	
HCQ +Colchicine	139(34.4)	25(24.5)	0.06	
Colchicine + 2 cDMARDs	194(48)	65(63.7)	**0.01, 1.9(1.2-2.9)**	
Colchicine + 3 cDMARDs	17 (4.2)	41 (40.2)	**<0.01, 15.3(8.2-28.5)**	
Steroids	176(43.7)	50(49.0)	0.206	
Rituximab	27(6.7)	9(88.2)	0.289	
Anti TNF	0	2(1.9)	**0.04**	
Tofacitinib	4(9.9)	0	0.563	
Remission**	242(60.0)	58(56.8)	0.317	

#p value <0.05 by Chi square or unpaired t test ## cox proportional hazards test*Severe PR: attacks >20/month**Remission: asymptomatic for one month at last follow upTNF-Tumour Necrosis Factor, OR- Odds Ratio, HR- Hazards ratio, HCQ- Hydroxychloroquine, cDMARDS- Conventional Disease Modifying Anti Rheumatoid Drugs, IP- Interphalangeal Joint, P- Proximal, D- Distal, MCP- Metacarpophalangeal Joint, RF- Rheumatoid Factor, RA-Rheumatoid Arthritis

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AB1461

COLCHICINE INTOLERANT FAMILIAL MEDITERRANEAN FEVER PATIENTS RECEIVING IL-1 ANTAGONISTS: DO THEY MISS ADVANTAGE OF COMBINATION

Keywords: Rare/orphan diseases, Prognostic factors

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Background: Colchicine is the mainstay of Familial Mediterranean Fever treatment, whereas interleukin-1 antagonists (IL1A) are the treatment of choice in refractory or intolerant cases [1,2].
Objectives: Aim of the study was to evaluate clinical and laboratory processes and damage status of FMF patients who colchicine resistant and/or intolerant and compare them with FMF patients who got effective doses.
Methods: A total of 125 patients diagnosed as FMF and treated with IL-1 antagonists were enrolled to the study. Study population was divided into two group according to the use of colchicine group 1 was consisted of 96 patients treated with IL1A+colchicine combination and group 2 was 29 patients only treated with IL1A due to resistance and/or intolerance to colchicine. Demographic, clinical and laboratory features were compared between tretament groups.
Results: Clinical activity and damage scores were similar between groups. Damage parameters were also assesed seperately and showed significantly higher rate of disease related amenorrhea in those patients terated with IL1A alone (p=0,017).
Conclusion: We concluded that colchicine should be added to treatment but colchicine resistant or intolerant FMF patients may be effectively treated with IL-1 antagonists alone.

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Table 1. Demographic and baseline clinical characteristics of patients with respect to their treatments

	IL-1 inhibitor monotherapy N=29	IL-1 inhibitor + colchicine combination n=96	p value
Sex, Female/male	17/12	51/45	0,603
BMI (mean±SD)	23,9**±3,94**	24,9**±4,61**	0,177
Age, years Median (IQR)	39,7**±13,5**	36,6**±10,3**	0,130
Age at diagnosis, years,	36(25,5)	22(8-57)	0,079
Disease duration mean (SD)	13(3-28)	14,5(4-45)	0,475
Mutations*[1]			
M694V/any	26	74	0,461
M694V/M694V	17	45	0,484
Others	10	38	0,409
Inflammatory comorbidity			
Fever, n(%)	9(31,03%)	58(60,4%)	0,005
Peritonitis	13(44,8%)	55(57,2%)	0,238
Pleuritis	10(34,4%)	35(36,45%)	0,846
Arthritis	18(62,06%)	52(54,16%)	0,452
ELE	4(13,7%)	7(7,2%)	0,279
Exertional leg pain	7(24,13%)	21(21,8%)	0,798
Dominant Attack Type			0,775
1. peritonitis(50,4%)	12(41,3%)	51(53,1%)	
2. arthritis(35,2%)	10(34,4%)	34(35,4%)	
Persistent inflammation	17(58,6%)	50(52,08%)	0,450
Colchicine resistance	10(34,4%)	79(82,2%)	0,0
Colchicine intolerance	18(62%)	17(17,7%)	0,00
Anakinra treatment	18	71	0,245
Canakinumab treatment	11	25	0,157
Duration of IL-1 inhibitor treatment(s), median (IQR 25-75)	48(43)	36(24)	0,034
Background colchicine dose, mg, median (IQR 25-75)	n.a.	1,5(1)	
FMF related damage			
Proteinuria, n (%)	13(44,8%)	40(41,6%)	0,763
Amyloidosis	11(37,9%)	26(27,08%)	0,262
Dialysis	7(24,1%)	5(5,2%)	0,006
Joint restriction	1(3,44%)	4(4,16%)	0,712
Infertility	2(6,8%)	6(6,25%)	1
Amenorrhea	1	3	0,017

3. *MEFV gene mutations were available for 117 patients

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Disclosure of Interests: None Declared.

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AB1462 EFFECTIVENESS OF THE STILL ACTIVITY SCORE IN ADULT-ONSET STILL'S DISEASE

Keywords: Rare/orphan diseases

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Background: Adults Still's disease is a rare autoinflammatory disorder with an unknown etiology, characterized by fever, arthritis, and rash. There is no method to fully evaluate the disease's activity [1].

Objectives: The Still Activity Score (SAS) is a newly defined, easy-to-use disease activity assessment score for Still disease [2]. We aimed to compare the efficacy of the Modified Pouchot Activity Score (mPouchot), Systemic Feature Score (SFS), and Still Activity Score (SAS) [2-4].

Methods: The study included 45 patients diagnosed with Still between 2010 and 2022 who met the Yamaguchi criteria. The patients were assessed using the physician global assessment (PGA) by two different physicians. Still, activity levels were computed. According to the severity of the disease, patients with PGA<6 were categorized as having low disease activity, and those with PGA>6 as having high disease activity.

Results: The demographic, clinical, and laboratory data for the patients are detailed in Table 1. There was a significant difference between the two groups in terms of mPouchot and SFS disease activity scores (low and high disease activity) (Table 1). CRP level was correlated with the SAS, SFS, and mPouchot disease activity scores (respectively; p=0.43, p=0.008, and p=0.011). Ferritin level was correlated with mPouchot and SFS disease activity score (respectively; p<0.001, p=0.007) (Figure 1). There was a correlation between each score(p<0.001).

Conclusion: SAS, a new disease activity score, correlated with previous activity scores. CRP levels were correlated with SAS. There was a correlation between the three disease activity scores.

Table 1. Characteristics of patients according to Physicians Global Assessment

	All Patients (n=45)	PGA<6 (n=18)	PGA≥6 (n=27)	P
Sex, Female	29 (64.4)	12 (72.1)	16 (59,3)	0.373
Age, Year	51 [22-73]	52.5 [22-73]	49 [22-70]	0.494
Age of Diagnosis, year	42 [18-63]	43 [18-63]	42 [18-63]	0.899
Fever	42 (93.3)	16 (88.9)	26 (96.3)	0.555
Arthritis	6 (13.3)	2 (11.1)	4 (14.8)	>0.999
Rash	36 (80)	14 (77.8)	22 (81.5)	>0.999
Sore Throat	15 (33.3)	2 (11.19	13 (48.1)	**0.010**
Lymphadenopathy	22 (48.9)	6 (33.3)	16 (59.3)	0.088
Hepatomegaly	19 (42.2)	5 (27.8)	14 (51.9)	0.109
Splenomegaly	11 (24.4)	5 (27.8)	6 (22.2)	0.732
Pleural Effusion	1 (2.2)	1 (3.7)	0	>0.999
Pericarditis	4 (9.1)	1 (5.9)	3 (11.1)	>0.999
CRP	121 [20-343]	94.4 [20-191]	146 [70-343]	**0.005**
Disease Activity Scores				
SAS	6 [0-7]	6 [0-7]	6 [4-7]	0.053
MPouchot	5 [0-10]	3.5 [0-7]	6 [2-10]	**0.001**
SFS	6 [0-8]	5 [0-8]	6 [4-8]	**0.007**

(Abbreviation: PGA: physician global assessment, CRP:C-reactive protein, ESR: erythrocyte sedimentation rate, SFS:Systemic Feature Score, and SAS:Still Activity Score)

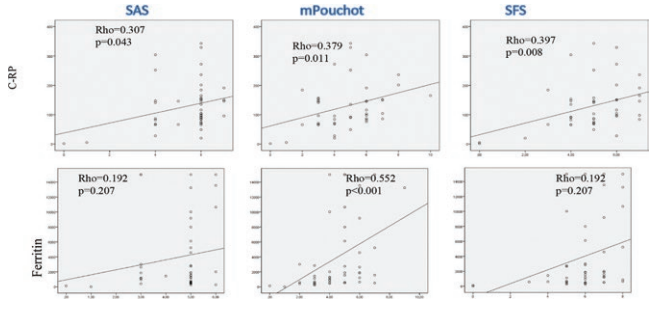


Figure 1. Correlation between CRP-Ferritin level and Disease Activity Score

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1463 AVASCULAR NECROSIS BONE IN CHRONIC GRAFT-VERSUS-HOST DISEASE POST-ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

Keywords: Pain, Bone diseases

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Background: Graft-versus-host disease (GVHD) is the most frequent complication after allogeneic hematopoietic cell transplantation (allo-HCT). The first line of treatment for moderate-severe chronic GVHD (cGVHD) is usually high and prolonged doses of corticosteroid therapy. Avascular necrosis bone (AVN) is a complication that appears after allo-HCT with an incidence of 5% to 19%. The exact mechanism by which it occurs is unkown and probably multifactorial. However, it has been associated with the presence and treatment of cGVHD.

Objectives: To describe the prevalence of AVN and its clinical characteristics in a cohort of patients with cGVHD evaluated in a multidisciplinary practice.

Methods: Descriptive and prospective observational study to describe the prevalence and characterization of AVN in a cohort of 132 patients with steroid-refractory cGVHD in multidisciplinary consultation. Variables related to baseline disease, transplantation and clinical manifestations of cGVHC are collected.

Results: 14 (10,6%) developed AVN confirmed by magnetic resonance imaging. The transplant-related characteristics and clinical features of cGVHD are detailed in Table 1. All of them had been receiving steroids. The average time from transplantation to AVN was 2,5 years (0-5,5). The mean age of AVN diagnosis was 46 years (range 17-65). Three patients had developed the AVN before the first visit.The diagnosis of AVN was during follow-up in the rest of them, with a mean onset of 23 months (1-48). 64,3% had more than one joint affected. The head of femur was the most commonly affected area (64,3%), followed by knee (35,7%). Other sites also affected were elbow, humeral head and ankle, with one case each. 64,3% needed joint replacement.

Conclusion: AVN in our cohort is a relatively common complication and it occurs in moderate-severe cGVHD. These patients present pain and limitation in range of motion and these manifestations may also appear in the context of GVHD itself. Early recognition is a challenge to avoid misdiagnosis and the risk of overtreatment with steroids that would increase the progression of the lesion.

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Table 1. BASELINE, TRANSPLANT-RELATED CHARACTERISTICS AND CLINICAL FEATURES OF CGVHD

Variables	*N (%)/ mean (range)*
Total	14
Age of transplantation,*years*	43 (16-61)
Gender (male/famale)	10 (71,4%)/4 (28,6%)
Body mass index	23,8 (17,3-41,1)
Diagnosis	
- ALL[1]/MDS[2]/AML[3]	5(35,7%)/3(21,4%)/2 (14,3%)
- CLL[4]/NHL[5]/MPS[6]/BTM[7]	1/1/1/1 (7,1%)
HCT type	
- Related *(haploidentical)*	7 (50%) (1; 7,1%)
- Unrelated	7 (50%)
Conditioning regimen:	
- Myeloablative	9 (64,3%)
- Reduced-intensity	5 (35,7%)
Stem cell graft source	
- Peripheral blood	12 (85,7%)
- Bone marrow/umbilical cord	1/1 (7,1%)
Time from allo-HCT to enrollment, *months*	18 (4-46)
Involvement site	
- ECOG[8]: 1/2/3	6 (42,9%)/ 4(28,6%)/ 1 (7,1%)
- Mouth	8 (57,1%)
- Eye	8 (57,1%)
- Genital tract	2 (14,2%)
- Gastroinestinal	4 (28,6%)
- Liver	1 (7,1%)
- Lung	4 (28,6%)
- BSA[9]: mild/moderate/severe	3/3/3 (21,4%)
- ROM[10]: mild/moderate/severe	6 (42,9%)/5 (35,7%)/1 (7,1%)
Clinical forms cGVHD:	
- Sclerotic	9 (64,3%)
- Joint	3 (21,4%)
- Lichenoid	1 (7,1%)
- Psoriasiform	1 (7,1%)
NIH[11] global score	
- Mild/moderate/severe	1 (7,1%)/4 (28,6%)/9 (64,3%)

[1]Acute lymphoblastic leukemia, [2]Myelodysplasic syndrome; [3]Acute myeloid leukemia, [4]Chronic lymphocytic leukemia, [5]Non-Hodking's lymphoma, [6]Myeloproliferative syndrome, [7]Beta-thalassemia major; [8]Eastern Cooperative Oncology Group Perfomance Status; [9]Body Surface area; [10]Range Of Mobility;[11] National Institutes of Health

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1464

COMPARATIVE STUDY OF ADALIMUMAB, INFLIXIMAB AND CERTOLIZUMAB IN THE TREATMENT OF CYSTOID MACULAR EDEMA DUE TO BEHÇET'S DISEASE

Keywords: Real-world evidence, Behcet's disease, Uveitis

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Background: the main cause of blindness in non-infectious uveitis is cystoid macular edema (CME). Behçet's disease (BD) is one of the most common diseases associated with CME [**1-3].**

Objectives: to compare efficacy and safety of Adalimumab (ADA), Infliximab (IFX) and Certolizumab (CZP) in refractory CME due to BD.

Methods: multicenter study of patients with CME secondary to BD refractory to glucocorticoids (GC) and at least 1 conventional immunosuppressant. All patients had CME (OCT>300μ) at baseline. From baseline up to 2 years, efficacy of ADA, IFX and CZP was assessed with the following ocular parameters: macular thickness (μm), visual acuity (BCVA), anterior chamber (AC) cells, vitritis and GC-sparing effect. Statistical analysis was performed with IBM SPSS Statistics v.23.

Results: a total of 50 patients (78 eyes) were considered. Twenty-five patients were treated with ADA, 15 patients with IFX and 10 patients were treated with CZP. No significant differences in demographic parameters were observed in the three groups. However, patients in the CZP group had a significantly longer time from diagnosis to drug initiation (75 [36-120] vs 30 [12-82] vs 15 [8-60] months; p=0.04) and received a greater median number of biological treatments (2 [0.75-3] vs 0 [0-0] vs 0 [0-0]) than the ADA and IFX groups. In CZP group, ADA and IFX were used previously in 7 patients. Combined therapy was used with ADA in 64%, with IFX in 66.7% and with CZP in 70% of CZP patients (p=0.94) (**TABLE 1**). Regarding efficacy outcomes, a rapid and maintained improvement in macular thickness was observed after 2 years of follow-up in three groups with no statistically significant differences between them (**FIGURE 1**). Improvement in BCVA, AC cells, vitritis and a GC-sparing effect was also noted. No serious adverse events were observed in IFX and CZP group. One case of pyelonephritis was reported in the ADA group.

Conclusion: ADA, IFX and CZP seem to be effective and safe in refractory CME due to BD. CZP appears effective even in patients with inadequate response to ADA and/or IFX.

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Table 1. Main characteristics of CME-BD patients receiving adalimumab (ADA), infliximab (IFX) or Certolizumab (CZP).

	ADA *group* **(n=25)**	**IFX** *group* **(n=15)**	**CZP** *group* **(n=10)**	**P**
Age, mean (SD) years	41 (11)	38 (9)	36 (8)	0.34
Sex, men/women, n/n	12/13	7/8	3/7	0.61
HLA-B51 positive, n(%)	19 (76)	10 (67)	4 (40)	0.13
Duration of uveitis before treatment, median	30 [12-82]	15 [8-60]	75 [36-120]	**0.04**
Unilateral, n(%)	10 (40)	9 (60)	3 (30)	0.28
Pattern of uveitis, n(%)				
Anterior	0 (0)	0 (0)	2 (20)	–
Intermediate	0 (0)	0 (0)	1 (10)	0.13
Posterior	5 (20)	5 (33.3)	3 (30)	0.62
Panuveitis	20 (80)	10 (66.7)	4 (40)	0.07
Ocular outcomes at the time of anti-TNF beginning				
AC cells (Tyndall), median [IQR]	2 [1-3]	1 [0-1]	1 [0-2]	0.15
Vitritis, median [IQR]	3 [1-3]	1 [0-2]	1 [0-2]	**0.03**
BCVA, mean (SD)	0.41±0.24	0.33±0.22	0.48±0.18	0.17
Macular thickness, mean (SD)	431.9±117.6	483.4±126.1	380.7±96.5	0.08
Previous conventional treatment, n (%)				
IV pulses of MTP	13 (52)	9 (60)	5 (50)	0.85
Cyclosporine A	22 (88)	11 (73.3)	6 (60)	0.17
Azathioprine	14 (56)	8 (53.3)	4 (40)	0.69
Methotrexate	13 (52)	8 (53.3)	2 (20)	0.18
CFM	1 (4)	2 (13.3)	0 (0)	0.33
Previous biological treatment (BT), n (%)	0 (0)	0 (0)	8 (80)	-
Number of previous BT per patient, median [IQR]	0	0	2 [1-3]	-
Combined treatment, n (%)	16 (64)	10 (66.7)	7 (70)	0.94
Cyclosporine A	10 (40)	5 (33.3)	1 (10)	0.23
Azathioprine	4 (16)	3 (20)	2 (20)	0.34
Methotrexate	2 (8)	2 (13.3)	4 (40)	0.86
Prednisone dose (baseline)	45 [30-60]	30 [20-60]	8 [6-25]	**0.04**
Follow-up, median [IQR],	24 [18-45]	24 [3-36]	30 [24-60]	0.12
Remission, n (%)	19 (76)	9 (60)	7 (70)	0.58
per 100 patient-year	28.8	30	19.4	0.20
Drug withdrawal, n (%)	8 (32)	8 (53.4)	2 (20)	-
per 100 patient-year	12.1	26.7	5.6	
Side-effects/toxicity, n (%)	1 (4)	0 (0)	0 (0)	
per 100 patient-year	3	0	0	

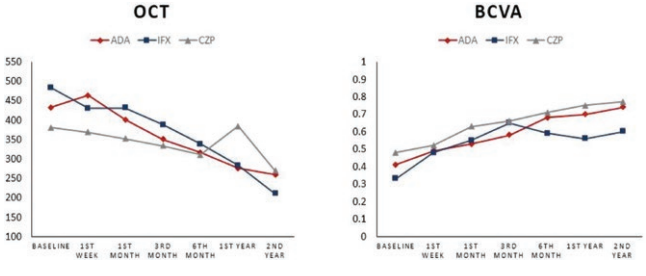


Figure 1. Evolution of OCT and BCVA after adalimumab (ADA), infliximab (IFX) or Certolizumab (CZP) initiation.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1465 CAUSAL RELATIONSHIPS BETWEEN PHYSICAL ACTIVITIES, LEISURE SEDENTARY BEHAVIORS, AND ADULT-ONSET STILL DISEASE OUTCOMES

Keywords: Rare/orphan diseases, Self-management, Genetics/Epigenetics

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Background: Adult-onset Still's disease (AOSD) is a characteristic non-familial, multi-genic systemic auto-inflammatory disorder, characterized by fever and joint pain [1]. Whether physical activities (PAs)/ leisure sedentary behaviors (LSBs) directly affect AOSD susceptibility is inconclusive.
Objectives: This study aimed to investigate the causal effects of PAs and LSBs on AOSD.
Methods: We performed a two-sample Mendelian randomization (MR) analysis to investigate the causality of 5 PAs and 4 LSBs with AOSD, of which PAs include accelerometer-base physical activity measurement (average acceleration) (n=91,084), moderate to vigorous physical activity levels (MVPA) (n=377,234), vigorous physical activity (VPA) (n=377,234), moderate physical activity 10+ minutes (n=440,266), vigorous physical exercise 10+ minutes (n=440,512) [2], and LSBs include the length of mobile phone use (n=456,972), time spent driving (n=310,555), time spent using computer (n=360,895) and time spent watching television (TV) (n=437,887). Genome-wide significant genetic instruments ($p < 5 \times 10–8$) for PAs and LSBs were extracted from European-descent genome-wide association studies (GWASs). And to satisfy the assumption that single-nucleotide polymorphisms (SNPs) were not related to outcomes, one SNP (rs2857693) was removed. The PLINK algorithm ($r2 < 0.001$) was used to clump SNPs at linkage disequilibrium (LD). AOSD data was acquired from the UK Biobank database (1,486 cases, 359,708 control samples, from Neale lab). Inverse variance weighted (IVW) was selected as the primary method for MR analysis. The MR-Egger and weighted median were considered secondarily. Moreover, sensitivity analyses were implemented with Cochran's Q test, MR-Egger intercept test, leave-one-out analysis, and the funnel plot to evaluate for heterogeneity and pleiotropy.
Results: Only spent driving time was positively correlated with AOSD in LSBs (odds ratio (OR) =1.02, 95% confidence interval (CI):0.001-0.319, p=0.0004). The Cochran's Q statistic with the IVW method revealed no heterogeneity (p=0.43), and no pleiotropy was observed (p = 0.618). However, the IVW results of PAs were not statistically significant ($p > 0.05$), so PAs were not associated with AOSD (Figure 1).

were not associated with AOSD (Figure 1).

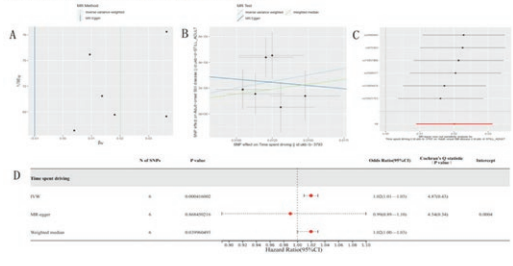


Figure 1. Mendelian randomization results for gene-level causality between physical activities (PAs), leisure sedentary behaviors (LSBs) and adult-onset Still's disease (AOSD) were evaluated by the odds ratio (OR) values of IVW, MR Egger, and Weighted median. Funnel plot (A), scatter plot (B), leave-one-out analysis (C), and forest plot (D) assessed that time spent driving increases the risk of AOSD. MR, mendelian randomization; IVW, inverse-variance weighted method; MR-Egger, Mendelian randomization-Egger; SNP, single nucleotide polymorphisms; CI, confidence interval.

Conclusion: Our findings support the hypothesis that time spent driving increases the risk of AOSD, suggesting leisurely sedentary behaviors may increase the probability of AOSD.
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AB1466 CLINICAL FEATURES OF PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER OVER 50 YEARS OF AGE

Keywords: Innate immunity, Genetics/Epigenetics, Rare/orphan diseases

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Background: Familial Mediterranean Fever (FMF) is the most common hereditary monogenic fever syndrome characterized by recurrent attacks of fever and polyserositis. Types and frquencies of attacks can change throughout the life of patients. The course of disease is affected by pathophysiological changes due to aging, increased comorbid diseases and multiple drug use.
Objectives: The objective of this study was to understand the effect of aging on clinical features and disease course in patients with Familial Mediterranean Fever.
Methods: 343 patients who were followed up with the diagnosis of FMF between 2005 to 2020 and were over 50 years old as of 2022 were included. The demographic characteristics of the patients, MEFV mutations, attack characteristics and the treatments they received were analyzed retrospectively. Attack characteristics, frequency of attacks and VAS scores of the patients were also analyzed and compared as pre-treatment, post-treatment, and most recent attacks.
Results: Female to male ratio was 1.8:1. The mean age of patients was 57.6±6.5 (50-84) years. Age of symptoms started, age at diagnosis and delay at diagnosis were compared between the female and male patients. At the age of symptoms started, no significant difference was detected between the two groups, while the age at diagnosis was later and the time of delay at diagnosis was longer in female patients (*p=0.006 and p=0.001*). Number and frequencies of attacks and VAS scores were compared as attacks before treatment, attacks after treatment and attacks in the last year, a significant decrease was found in the last attacks ($p<0.001$). The frequency of fever, abdominal pain, arthritis and chest pain was significantly lower in the most recent attacks when compared to pre-treatment and post-treatment ($p<0.001$). The last attacks of the patients were mostly in the form of abdominal pain. Patients were compared as those who did not have an attack in the last year and who had an attack, it was seen that the mean age was lower in the group that had an attack ($p<0.005$). The mean of current colchicine dose was 1.29±0.43 mg, the mean dose of colchicine at diagnosis was 1.37±0.36 mg and the mean of maximum colchicine dose was 1.6±0.43 mg.
CONCLUSION:

Demographic Status, Patients (n:343)

Male/female, n 119/224
Age of onset, mean (S.D.), years 57.6 (6.5)
Age at diagnosis, mean (S.D.), years 40.8 (10.8)
Age of symptoms started, mean (S.D), years 24 (14.4)
Delay at diagnosis, mean (S.D.), years 16.8 (14.5)

Clinical features, n (%)	Pre-Treatment n (%)	Post-Treatment n (%)	Recent Attacks n (%)	p value
Fever				
Abdominal Pain	266 (77.6)	253 (73.8)	52 (15)	**<0.001**
Arthralgia	293 (85.4)	299 (87.2)	223 (65)	**<0.001**
Arthritis	56 (16.3)	82 (23.9)	33 (9.6)	**<0.001**
Chest pain	87 (25.4)	100 (29.2)	32 (9.3)	**<0.001**
Myalgia	71 (20)	79 (23)	24 (7)	**<0.001**
Erysipelas-like	23 (6.7)	34 (9.9)	46 (13.5)	0.14
erythema	11 (3.2)	12 (3.5)	7 (2)	0.487
Number of attacks, mean (S.D.), years	15.0 (11.9)	3.04 (6.46)	2 (3.67)	**<0.001**
VAS Scores				
Pre-treatment, mean (S.D.)	8.05 (1.78)		**<0.001**	
Post-treatment, mean (S.D.)	2.91 (2.53)			
Recent, mean (S.D.)	1.75 (2.38)			

It has been shown that there is a decrease in disease activity, frequency of attacks and the dose of colchicine used in FMF with aging.
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AB1467 POTENTIAL TRIGGERS OF FAMILIAL MEDITERRANEAN FEVER ATTACKS

Keywords: Rare/orphan diseases

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Background: Familial Mediterranean Fever (FMF) is an autoinflammatory disease characterized by self-limited 1 to 4 days lasting attacks. These attacks are characterized by fever, abdominal pain, chest pain, arthritis, arthralgias, myalgia, and erysipelas-like rash that is over the affected joint. Mutations of the pyrin protein which encodes by the main mutated gene of FMF, MEFV, are responsible for the inflammasome overactivation and subsequently responsible for attacks and the main underlying occurring pathophysiology of FMF[1]. The role of the factors that can contribute to and trigger this process is on a large scale unknown.
Objectives: We aimed to search for the factors that can trigger these attacks or can increase the severity of attacks. We prepared some criteria based on our clinical observations to determine the factors that can trigger pyrin protein-associated- inflammasome mechanisms that are the underlying cause of FMF[1].
Methods: We surveyed 808 patients with FMF from our adult rheumatology outpatient clinics. We used a questionnaire assessing the following: emotional stress; use of antidepressants; consumption of tea and coffee; relationship with menses; menopause and post-menauposal alleviations; seasonal changes; long-term journeys; changes of location; starvation; sleeplessness; temperature reduction; fatigue; wind and cold weather; and humidity(Table1). We also questioned some features of the attacks of patients including fever, abdominal pain, chest pain, arthritis, arthralgia, myalgia, and erysipelas-like rash.
Results: The number of patients with FMF and their potential trigger factors are given in Table 1. We performed the questionnaire to 808 patients with FMF (354 male and 454 female). 574 patients (%71) reported worsening in severity and frequency of their attacks in relation to emotional stress. Among these 574 patients, 139 patients (%24) were using antidepressants. 443 and 474 patients reported worsening and higher frequency of their attacks in relation to seasonal changes and fatigue, respectively. Among the 454 female patients, 213 patients reported worsening during their menses cycle. 96 female patients had entered menopause and 50 of them (%52) had reported obvious improvement after their menopause. In our cohort, 530 patients had experienced fever, 642 abdominal pain, 426 chest pain, 350 arthritis, 573 arthralgias, 483 myalgias, and 152 erysipelas-like rashes during their attacks.
Conclusion: The high proportion of patients who had reported worsening in their attacks in relation to emotional stress highly suggests a correlation between emotional stress and FMF attacks. Additionally, 443 and 474 patients had reported worsening in their attacks when seasonal changes occur and in times of fatigue, respectively, which is also highly suggestive of a correlation with FMF attacks. There was also an outstanding decrease in the severity of their attacks in patients who had menopause after they entered menopause. Furthermore, there were some patients who reported miscellaneous correlations in the frequency of FMF attacks and with the use of antidepressants, consumption of tea and coffee, seasonal changes, long-term journeys, changes in location, starvation, sleeplessness, temperature reduction, fatigue, wind and cold weather, and lastly, humidity.

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Disclosure of Interests: None Declared.
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AB1468 ENTEROPATHY IN DUTCH COMMON VARIABLE IMMUNODEFICIENCY COHORT

Keywords: Disease-modifying Drugs (DMARDs), Gastrointestinal tract, Descriptive Studies

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Background: Common variable immunodeficiency (CVID) is the most common severe primary antibody deficiency. Although infections are the most prevalent clinical manifestations, a large amount of the patients also suffer from immune dysregulation. This results in significant morbidity [1]. Different manifestations of enteropathy can occur, yet little information is available regarding its optimal treatment.
Objectives: Here we describe clinical characteristics, endoscopy, histopathology and treatment response of CVID enteropathy (CVID-E) in a Dutch teaching hospital.
Methods: We included CVID patients from our hospital, that provided written informed consent. We collected, retrospectively, gender, age and start of enteropathy symptoms, and age at CVID diagnosis. Reports of endoscopies and histopathology, and clinical course of enteropathy related symptoms was recorded for each patient alongside the immunosuppressive medication (IS) used over time. Treatment response was defined as remission, response, need for step-up, and unknown. Descriptive statistics were used to study associations.
Results: 32 of 82 CVID patients at the UMC Utrecht had enteropathy. The average age of this group was 45.4 (13.5 standard deviation, SD) and the mean age of CVID diagnosis was 31.7 (16.7 SD). The age at first presentation of enteropathy was 30.9 years (14.6 SD). 16 of 32 patients were female. 28 (90.6%) of CVID-E patients had other complications: inflammatory, infectious and malignant. 26 (81.3%) patients had other inflammatory manifestations; the most common were lymphoproliferation (43.8%) splenomegaly (34.4%) and autoimmune disease (37.5%). Infectious complication bronchiectasis had a prevalence of 68.8% in this cohort. Two patients had a solid malignancy and one lymphoma. We compared CVID-E treated with IS to those who were not treated with IS. Autoimmune cytopenia, and bronchiectasis were significantly more prevalent in CVID-E treated with IS, than those without IS: 23.5% vs 0% ($P<0.05$) and 82.4% vs 46.7% ($p<0.01$) respectively. 30 patients underwent endoscopy, 29 (90.6%) coloscopy and 25 (78.1%) gastroscopy. The most common histopathologic findings consisted of inflammatory bowel disease-like colitis (n=10) and intra-epithelial lymphocytosis (n=9). Other findings of note were lymphocytic colitis(n=3), microscopic colitis (n=2), collagenic colitis (n=1) and apoptotic enteritis (n=1). 17 of the 32 (53.1%) patients received IS for CVID-E. 14 received local corticosteroids, 12 systemic corticosteroids, 15 DMARDs (methotrexate, azathioprine, mesalazine, baricitinib, mycophenolate, tacrolimus and sulfasalazine), 6 biologicals (adalimumab, infliximab and ustekinumab) and 6 had combined therapy. These 17 patients underwent 64 treatments. Local CS therapy did not result in remission. 9/17 (52.9%) of patients needed more than 2 systemic drugs. DMARD monotherapy achieved remission or response in 6 of 13 patients (46.2%). The best results concerning combined therapy in this cohort seemed to consist of combinations of DMARD(s) and systemic CS, and combinations of DMARD(s) and TNF-alpha inhibitors (TNFi).
Conclusion: CVID-E is strongly associated with other inflammatory complications and bronchiectasis, especially in CVID-E on IS. This cohort consists of the largest series reporting on treatment efficacy in CVID-E. We found combination treatment and DMARD monotherapy to be the most effective treatment. Additionally, TNFi seem to have a good clinical response in patients with CVID enteropathy, especially when combined with other treatments.

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Table 1. Potential trigger factors of FMF attacks

	Emotional stress	Consumption of tea and coffee	Relationship with menses	Menopause/ post-menauposal alleviations	Seasonal changes	Long-term journeys	Changes of location	Starvation	Sleeplessness	Temperature reduction	Fatigue	Wind and cold weather	Humidity
FMF (n:808)	574(%71)	56(%7)	213(%)	96/50	443(%55)	244(%30)	208(%26)	119(%15)	285(%35)	381(%47)	474(%59)	294(%36)	221(%27)

AB1469

HEPATITIS C IN IDIOPATHIC INFLAMMATORY MYOPATHIES: DIFFERENCES IN DISEASE PRESENTATION AND PATIENT MANAGEMENT

Keywords: Comorbidities, Myositis

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Background: It is known that Hepatitis C (HCV) can cause many extra-hepatic manifestations which overlap with rheumatic diseases. New evidence is emerging that both HCV and idiopathic inflammatory myopathies (IIMs) may have a common mechanism through B cell expansion and dysfunction [1,2].

Objectives: Our aim was to describe the prevalence of HCV in patients with IIM and to compare myositis disease course, organ involvement, and rheumatologic treatment response between IIM patients with and without HCV.

Methods: A registry was created of Montefiore Medical Center patients that met 2017 EULAR/ACR classification criteria for IIM. Demographics, IIM type, antibodies, clinical manifestations, comorbidities, and rheumatologic treatment history were documented. HCV antibody, viral load, and hepatitis treatment history were noted. Rheumatic medication failure was defined by rheumatologist, discontinuation due to adverse effects, or medication change within 3 months while medication control was defined by documented clinical improvement. Statistical analyses included two-sample t-test, Chi-square tests or Fisher's exact tests were used to compare the categorical variables as appropriate and signed rank test.

Results: Of 153 patients in the registry, 130 (85%) had been screened for Hepatitis C and 11 (8.5%) had evidence of current or past HCV infection. Comparison of demographics, myositis types, presentation, and comorbidities revealed those with HCV were more likely to be male (p = 0.03) and have inclusion body myositis (IBM) (p = 0.002, Figure 1). Despite comparable numbers of dermatomyositis (DM), those with HCV were less likely to exhibit the classic dermatologic findings of DM, including Grotton's papules (p = 0.05), heliotrope (p = 0.05), or others rashes such as holster, shawl, V sign (p = 0.02). Interstitial lung disease (ILD) was less prevalent in individuals with HCV while neoplasms were more frequent in the same group (p = 0.02, p = 0.01, respectively). There were no differences in age, race, ethnicity, or treatment between IIM patients with and without HCV. Of the 11 patients that had HCV, 6 (55%) were diagnosed with HCV within 1 year of IIM diagnosis and majority (4/6) had active HCV at that time based on viral load. The others had been diagnosed with HCV for 5-10 years prior to the IIM diagnosis. For majority of HCV cases (6/11), rheumatology evaluation prompted hepatology evaluation and/or treatment.

Conclusion: Individuals with HCV may have different disease course than individuals without HCV, specifically one with a higher frequency of neoplasms and a lower frequency of ILD and dermatologic manifestations. IIM diagnosis was usually a key time to discover a concomitant HCV infection and often led to change in HCV evaluation and treatment. These findings and their immunologic basis should be further studied in larger cohorts with more power.

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Table 1. Comparison of IIM subtype, disease manifestations, comorbidities, and treatment between HCV+ and HCV- IIM patients.

Variable	Patient Group		P-value
	HCV+ (n = 11)	HCV- (n = 119)	
IIM type, n (%)			
PM	3 (27.3)	37 (31.1)	1.00
DM	3 (27.3)	64 (53.8)	0.09
ADM	0 (0)	10 (8.4)	1.00
MCTD	0 (0)	14 (11.8)	0.61
NEC	2 (18.2)	17 (14.3)	0.66
IBM	5 (45.5)	9 (7.6)	**0.002**
Heliotrope rash, n (%)	1 (9.1)	47 (39.5)	**0.05**
Grotton's papules or sign, n (%)	1 (9.1)	47 (39.5)	**0.05**
Dysphagia, n (%)	7 (63.6)	49 (41.2)	0.21
Calcinosis, n (%)	0 (0)	10 (8.4)	1.00
Other skin manifestation, n (%)	0 (0)	45 (37.8)	**0.02**
ILD, n (%)	1 (9.1)	56 (47.1)	**0.02**
Neoplasm, n (%)	5 (45.5)	13 (10.9)	**0.01**
DVT/PE, n (%)	1 (9.1)	13 (10.9)	1.00

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AB1470

JANUS KINASE INHIBITORS IN SEVERE INFLAMMATORY OCULAR PATHOLOGY. MULTICENTER STUDY AND LITERATURE REVIEW

Keywords: Real-world evidence, Uveitis

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Table 1. Cases reports and Literature review of patients with refractory IOP treated with JAKINIB.

Study, year (Ref)	Cases	Age/Sex	Underlying Disease	JAKINIB	Ocular involvement	Previous IS treatment	Ocular Improvement
Meadow et al. 2014 (1)	1	59, F	RA	TOFA	PUK	MTX, ABA, ivMP	Partial
Bauermann et al. 2018 (2)	1	22, F	JIA	TOFA	Ant uveitis, CME	MTX, ADA, RTX, GOLI, IFX, CsA, TCZ, MMF	Complete
Paley et al. 2019 (3)	2	1.40, F 2.45, F	1.Idiopathic 2.Idiop	1.TOFA 2.TOFA	1.Scleritis 2.Ant uveitis, CME	1.MTX, MMF, AZA, CYP 2.MTX, LFN, AZA, MMF, ADA, IFX, CZP, intravitreal fluocinolone acetonide.	1.Complete 2.Complete
Liu J et al. 2020 (4)	1	30, M	Behçet s.	TOFA	Scleritis	SSZ, MTX, AZA, LFN, THD, COL, GLM	Partial
Majumder et al. 2020 (5)	1	26, F	VKH disease	TOFA	Post uveitis	ivMP	Complete
Miserocchi et al. 2020 (6)	4	1. 9, F 2. 1, F 3. 2, F 4. 10, M	JIA	1. TOFA 2. BARI 3. BARI 4. BARI	1. Panuveitis 2. Panuv 3. Panuv 4. Panuv	1. IFX, ADA, LFN, ABA, RTX, TCZ. 2. MTX, ADA, IFX, RTX, ABA. 3. MTX, AZA, IFX, ADA, TCZ. 4. ETN, MTX, CsA, IFX, ADA, ABA, TCZ, RTX.	1. Complete 2. Complete 3. Complete 4. Complete
Pyare et al. 2020 (7)	1	45, F	Idiop	TOFA	Necrot. scleritis	MMF	Complete
Kaneko et al. 2022 (8)	1	35, M	RA	BARI	Panuv	MTZ, SSZ, ADA, IFX	Complete
Xiao-Bao et al. 2022 (9)	1	18, F	Idiop	TOFA	Panuv	MTX, MMF, CsA, ADA	Complete
Present study, 2023	11	1. 25, F 2. 85, F 3. 41, F 4. 65, F 5. 59, M 6. 40, F 7. 55, M 8. 45, F 9. 49, F 10. 62, F 11. 67, M	1. Blau Syndrome 2. RA 3. Relapsing polychondritis 4. Idiop 5. AS 6. SpA and ulcerative colitis 7. AS 8. AS 9. RA 10. RA 11. RA	1. TOFA/ BARI 2. BARI 3. BARI 4. BARI 5. UPA 6. TOFA 7. UPA 8. UPA 9. UPA 10. UPA 11. BARI	1. Panuv 2. PUK 3. PUK 4. Panuv 5. Ant uveitis 6. Ant uveitis 7. Ant uveitis 8. Scleritis 9. Scleritis 10. PUK 11. PUK	1.MTX, ETN, ANA, ABA 2.MTX, LFN, CZP, ADA, iv MP. 3. MTX, CsA, SSZ, MMF, AZA, IFX, TCZ, CZP, ABA, ADA. 4. MTX, AZA 5. MTX, ADA 6. MTX, AZA, ADA 7. MTX, IFX, GOLI 8. MTX, ADA, 9. ivMP, MTX, TCZ, ADA, GOLI, CZP 10. MTX 11. MTX, LFN	1. Complete 2. Complete 3. Complete 4. Complete 5. Complete 6. Complete 7. Complete 8. Complete 9. Complete 10. Complete 11. No improvement

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Background: Inflammatory ocular pathology (IOP) includes internal (uveitis) and external (mainly ocular surface pathology) involvement. IOP may be severe ocular conditions refractory to conventional and biological immunosuppressants. Janus Kinase inhibitors (JAKINIB) had shown efficacy in refractory cases of different immune-mediated diseases (IMID).
Objectives: In patients with refractory IOP treated with JAKINIB our aims were **a)** to assess the patients of Spanish referral centers, **b)** Literature review.
Methods: Multicenter study of 11 patients with refractory IOP treated with JAKINIB. For Literature review a search was conducted in PubMed, Embase and the Cochrane library from their inception to 1st January 2023. In addition, a therapeutical approach of refractory IOP is proposed.
Results: We have identified 11 cases in eight University Hospitals and 13 cases in the literature review. These 24 patients (17 women/ 7 men) (35 affected eyes), mean age 38.9±21.9 years, had different refractory IOP (uveitis=14; scleritis=5, PUK=5). Most of IOP were associated with IMID (n=19, 79.2%). The main underlying IMID were rheumatoid arthritis (n=6, 25%) and juvenile idiopathic arthritis (n=5, 20.8%) **(TABLE 1).** In addition to systemic corticosteroids, before JAKINIB, conventional (n= 23; 95.8%) and biological immunosuppressive drugs (n=18; 75%) were required. The JAKINIB most widely used was tofacitinib (n= 11; 45.8%). In one patient with Blau Syndrome and uveitis, tofacitinib was switched to baricitinib due to severe lymphopenia. In two other patients, UPA was discontinued due to anemia and skin adverse reaction. Finally, only in one patient baricitinib was withdrawn due to lack of improvement. After starting JAKINIB, 23 patients presented clinical improvement, complete (n=21, 87.5%) or partial (n= 2; 8.3%). Based on these data a therapeutical approach of refractory IOP was proposed **(FIGURE 1).**
Conclusion: JAKINIB may be an effective and safe therapy in IOP refractory to conventional or even biological immunosuppressive therapy.
Reference: ND.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.

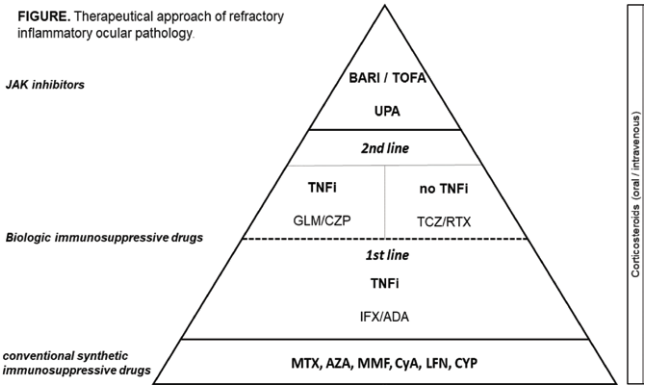


FIGURE. Therapeutical approach of refractory inflammatory ocular pathology.

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AB1471

PROSPECTIVE FOLLOW-UP OF THE POST-THROMBOTIC SYNDROME DEVELOPMENT RISK IN PATIENTS WITH VASCULAR BEHÇET'S DISEASE

Keywords: Behcet's disease

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Background: Deep vein thrombosis (DVT) is the most common form of vascular involvement in Behçet's disease (BD). Post-thrombotic syndrome (PTS) refers to the symptoms and signs of chronic venous insufficiency following DVT. It develops within the first 2 years in more than half of the patients after acute DVT [1].
Objectives: In this prospective study, we aimed to evaluate the risk of PTS development after DVT and the factors affecting the development and severity of PTS in BD patients.
Methods: BD patients (n=18) with acute DVT and were followed in 3 tertiary rheumatology centers were included in the study. Patients are evaluated for PTS presence during acute DVT, 6-12. months and then annually. Villalta scoring with a total score of >4 or presence of venous ulcer was defined as PTS. PTS was classified as mild if the score was between 5-9, moderate between 10-14, and presence of >14/venous ulcers as severe. Venous Damage Score (VDS) was used to evaluate the effect of venous disease on work productivity and Venous Clinical Severity Score (VCSS) for symptom severity.
Results: The clinical features of the 18 patients included in the study are shown in Table 1. Major-organ involvement was present in 12 patients (pulmonary involvement in 7 (39%), ocular involvement in 5 (28%), arthritis in 3 (13%), neurobehçet and enterobehçet each in 1 patient). Steroid and IS treatment was given to all patients after an acute DVT attack. Additional anticoagulant (AC) treatment was chosen in 16 of the patients. Patients were followed up for a median 23.2 (6-40) months after DVT. The number of patients followed for at least 1 year after an acute DVT attack was 15, and the median follow-up period was 26 (12-40) months. The median duration of AC use in patients who received AC treatment in the follow-up was 6 (0-12) months. PTS developed in 5 (33%) of 15 patients during follow-up. The baseline, 6th and 12th month course of Villalta, VCSS, and VDS scores are shown in figure 1.
Conclusion: In this prospective follow-up after an acute DVT attack 33% of BD patients developed PTS within 1 year. In our previous retrospective study, 62% of 205 patients, half of whom received AK, developed PTS during follow-up [2]. Despite the limitations of our study, such as the low number of patients and the short follow-up period, AC treatment in all patients (except 1) may have influenced a lower PTS development in the prospective follow-up compared to the retrospective data.
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Table 1. Characteristics of Study Patients

Clinical manifestations	SS/Std
Age, average	33.56 (9.62)
Female/male, n(%)	4/14 (%22.2)
Family history (BD)	3 (%16.7)
Oral ulcers	16 (%88.9)
Genital ulcers	9 (%50)
Papulopustular lesions	(%61.1)
erythema nodosum	6 (%33.3)
Pulmonary involvement	7 (%38.9)
Articular involvement	3 (%16.6)
Neurological involvement	1 (%5.6)
Ocular disease	5 (%27.8)
Gastrointestinal involvement	1 (%5.6)

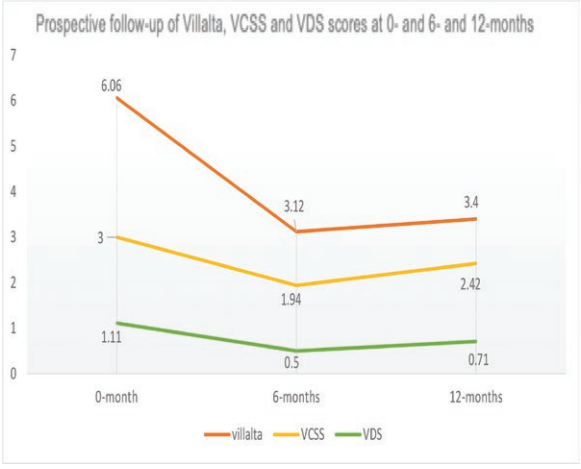


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6054

AB1472

THE PECULIARITIES OF THE CLINICAL MANIFESTATIONS OF FAMILIAL MEDITERRANEAN FEVER ACCOMPANIED WITH LUPUS-LIKE SYNDROME

Keywords: Systemic lupus erythematosus

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Background: The most common autoinflammatory disease which occurs in Armenian ethnos is familial Mediterranean fever (FMF). FMF is a hereditary disorder characterized by recurrent attacks of fever and serosal inflammation. The main clinical manifestations of FMF are recurrent fever, abdominal, chest and joint pain, erysipelas-like skin lesion but FMF also has a lot of other rare and systemic clinical manifestations. Sometimes it is difficult to distinguish if the patient has only FMF or the overlap of FMF and other rheumatological diseases: systemic lupus erythematosus (SLE), systemic vasculitis, spondyloarthropathy, etc.
Objectives: The purpose of the study is to reveal non-classic clinical manifestations of FMF, analyze and compare the course of FMF in these cases.
Methods: 100 Armenian patients with genetically confirmed FMF, who also fulfilled Tel-Hashomer classification criteria were included in this study. Molecular-genetic detection of 26 MEFV mutations which are more common among Armenians was carried out. Only 13 patients from 100 had systemic clinical manifestations like lupus, so we continued investigation and determine ANA, anti-dsDNA antibodies, which were positive. All patients with lupus-like syndrome fulfilled diagnostic criteria of SLE by ACR. Comparison of peculiarity of course of FMF was done between 13 patients - with both lupus-like syndrome and FMF (group I) and 13 patients only with FMF (group II).
Results: There were 11 female and 2 male patients in the first group. The mean age was 40,06±2,46. The 15.4% of the patients were affected with FMF and lupus-like syndrome/SLE parallelly and in 30.8% cases the onset of SLE was prior to the clinical presentation of FMF. They all had systemic clinical manifestations such as erythema (92.3%), livedo reticularis (69.2%), photosensitivity (69.2%), Raynaud's phenomenon (23.07%). Though the frequency of FMF attacks in the I group was more than in the II group, the high temperature 39-40 C° was viewed in 23% of the I group and in 46% of the II group and the duration of attack days was respectively 1-3 and 1-5. We noticed that thoracalgia and monoarthritis were viewed less frequently in the I group than in the II, 7.7% and 15.4% respectively. The difference between the clinical manifestations is presented below (Table 1). The prevalent mutation of MEFV gene in both groups was M694V- in 19 patients (73%), from which 3 (11,5%) were homozygote and 23 (88,5%) were heterozygote.

Table 1.

Clinical manifestations	I group (FMF with coexisting SLE)%	II group (only FMF)%
Abdominalgia	92,3	76,9
Thoracalgia	69,2	76,9
Arthralgia	100	100
Monoarthritis	53,8	69,2
Pleuritis	53,8	53,8
Pericarditis	15,4	7,6

Conclusion: In conclusion, both diseases FMF and SLE have common clinical manifestations: fever, arthralgia, arthritis, skin involvement, pleuritis, pericarditis. The course of FMF with coexisting SLE is milder: these patients have lower temperature, shorter duration of attack days; thoracalgia and monoarthritis also appear less frequently. Further investigations are needed to reveal the peculiarity of duration of FMF with co-exciting of systemic rheumatic diseases.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1473 HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS AMONG ADULTS

Keywords: Organ damage, Systemic lupus erythematosus

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Background: Hemophagocytic Lymphohistiocytosis (HLH) is a rare life-threatening condition resulting from an overstimulation of the immune system leading to a multi-organ damage[1]. This condition can be either primary caused by genetic mutations or secondary triggered by infections, autoimmune diseases or malignancies[1].
Objectives: We sought to examine the clinical characteristics, underling etiologies, management and outcome of adults patients diagnosed with HLH.
Methods: We performed a multi-center retrospective study in the departments of Internal Medicine and Infectious Diseases in both Fattouma Bourguiba and Taher Sfar University hospitals in Tunisia. We identified 38 patients meeting the HLH-2004 diagnostic criteria.
Results: There were 24 women and 14 men. The male/female sex ratio was 0.58. The mean age was 38 years (range 18-80 years). Eight patients (21%) had underling auto-immune disease: 6 patients had systemic lupus erythematosus, 1 patient had rheumatoid arthritis and 1 patient had idiopathic thrombocytopenic purpura. Five patients (13.5%) had underling malignancy. Among the clinical and biological variable of the HLH criteria, the most common features were fever (100%) followed by elevated ferritin level (94.7%) and cytopenia (84.2%). Triglyceride level was elevated in 76.3% of patients. Hemophgocytosis in bone marrow was found in 35 patients (92.1%). Elevated lactatdshydrogenase was found in 76.3% of cases. The most common underlying etiologies were systemic lupus erythematosus (31%) followed by infections (24%), malignancies (16%) and adult still's disease (13%). In our study, 30 patients (78.9%) underwent intravenous immunoglobulin regimen over 2 days. Twenty-three patients (60.5%) received either intravenous and/or oral steroids. Ethoposide was prescribed in 4 cases. The overall mortality in our study was 39.5%. Twenty-three patients achieved remission with 4 relapsing later. Mean cause of relapses was infections. Patients aged above 65 years and patients with systemic lupus erythematosus had poorer prognosis (p=0.013). Patients with systemic lupus erythematosus achieved remission more likely than other patients (p= 0.021).
Conclusion: HLH is an uncommon but fatal disease. The clinical symptoms are non specific leading to misdiagnosis which is associated with a dismal prognosis. Similarly to the literature a female preponderance was found in our study[1]. Systemic lupus erythematosus was found to be the commonest underling cause of HLH in our population which disagrees with the findings of similar studies who identified malignancy or infections as the principal triggers[1,2]. A combination of intravenous steroids and immunoglobulin infusions was prescribed in 47.3% of patients. This combination was proven to be effective as first line treatment [3]. Despite treatment mortality rates remained high in our populations (39.5%) especially among elderly.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1474 EFFECTIVENESS AND SAFETY OF CURRENT TREATMENT STRATEGIES FOR VEXAS SYNDROME: A SYSTEMATIC REVIEW

Keywords: Rare/orphan diseases, Systematic review

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Background: VEXAS syndrome is an adult-onset systemic autoinflammatory condition caused by an acquired deficiency of the *UBA1* gene in hematopoietic progenitor cells. Its clinical course includes relapsing and refractory inflammatory conditions with high mortality. Optimal treatment strategies remain elusive and need further investigations.
Objectives: To investigate the effectiveness and safety of treatments for VEXAS syndrome.
Methods: A systematic review of the literature in line with the PRISMA guidelines was conducted: MEDLINE, Embase and Cochrane Central Register of Controlled Trials were searched for reports on treatment strategies for VEXAS. Treatment response was recorded as complete (CR), partial (PR) or none (NR) depending on changes in clinical symptoms and laboratory parameters. Patient characteristics, safety data and previous treatments were analyzed.
Results: We identified 32 publications with a total of 83 patients. 97.6% of patients were male. Mean age at disease onset was 68 years (reported for 80/83). Mean follow up was 15.7 months (reported for 23/83). The most frequently used was azacitidine (AZA) (39.8%, 33/83): CR was reported for 9 patients (27.3%, 9/33) and PR for 11 (33.3%, 11/33) (Fig. 1). Further reports included tocilizumab (13.3%, 11/83), allogeneic stem cell transplantation (ASCT) (8.4%, 7/83), glucocorticoid

(GC) monotherapy (7.2%, 6/83), anakinra (3.6%, 3/83). Details on response are shown in **Table 1**. Data on adverse events was available for 29 patients (34.5%). Most common were infections (24.1%, 7/29), herpes zoster reactivation (6.7%, 2/29), cytopenias (13.8%, 4/29). The median number of previous treatments was 3 [IQR 2-5]. A total of 307 prior treatments were reported. In most cases (37.4%, 115/307), details on response and reasons for discontinuation were not reported. Nonresponse to therapy (30.2%, 58/192), GC dependence (22.4%, 43/192) and adverse events (11.9%, 23/192) were common triggers for therapy adjustment. Janus kinase inhibition has been reported to be beneficial in one case series (Heiblig et al., 2022). Individual patient data from this study was not available and, thus, not included in this analysis.

Conclusion: The current data on VEXAS treatment mainly stems from case reports/series and is inhomogeneous. Reporting of treatment response varies, complicating conclusions on treatment efficacy. Most patients received multiple therapies with mixed results. AZA appears promising for a subset of patients. IL-6 inhibition seems beneficial, but a risk of infections should be considered. Ciclosporine was commonly used as an add-on to IL-1 inhibitors suggesting benefits of combination therapy. In general, adverse events are scarcely reported, which hinders an objective risk-benefit assessment.

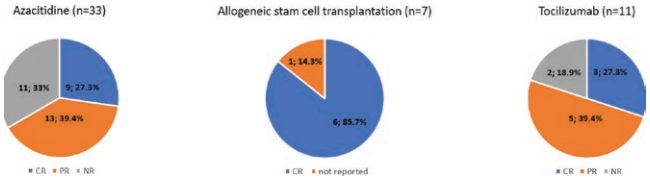


Figure 1. Summary of response

Table 1. Treatment response

Treatment (n total)	CR (n, %)	PR (n, %)	NR (n, %)	Adverse events (n)
ANA (3)	2 (66%)	-	1 (33%)	Injection site reaction (1)
ANA + CsA (2)	2 (100%)	-	-	Upper respiratory tract infection (1)
ASCT (7) *	6 (85.7%)	-		
AZA (33)	9 (27.3%)	13 (39.4%)	11 (33%)	Pneumonitis (1), diverticulitis (1)
AZA + TCZ (1)	-	-	1 (100%)	NA
AZA + CsA (1) **	-	-	-	NA
BAR (1)	-	-	1 (100%)	
CAN + CsA (1)	1 (100%)			Neutropenia (1)
COL (1)	-	-	1 (100%)	NA
CYC (1)			1 (100%)	NA
ETA (1)			1 (100%)	NA
GC monotherapy (6)	1 (16.7%)	4 (66.7%)	1 (16.7%)	NA
Infliximab (1)			1 (100%)	NA
Infliximab + MTX (1)			1 (100%)	NA
LEF (1)		1 (100%)		NA
MTX + TCZ (3)	-	2 (66%)	1 (33%)	Pancytopenia (1)
MTX + ADA + LEF (1)	-	1 (100%)	-	NA
MTX + ADA (1)	-	1 (100%)	-	NA
Rituximab (2)	1 (50%)	-	1 (50%)	NA
Siltuximab (1)	-	1 (100%)	-	NA
TCZ (11) ***	3 (27.3%)	5 (45.5%)	2 (18.9%)	Jejunum (1) and ileum perforation (1) PJP (1) Nocardia infection (1) Herpes zoster (2) neutropenia (1)
UPA (1)	-	1 (100%)	-	NA
RUX (1)	-	1 (100%)	-	NA

* death prior evaluation n=1 ** treatment just initiated *** no response reported due to discontinuation for jejunum perforation n=1**ANA** anakinra **ADA** adalimumab **CsA** ciclosporine **AZA** azacitidine **BAR** baricitinib **CAN** canakinumab **COL** colchicine **CYC** cyclophosphamide **ETA** etanercept **LEF** leflunomide **MTX** methotrexate **TCZ** tocilizumab **UPA** upadacitinib **RUX** ruxolitinib **NA** not available

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Zhivana Boyadzhieva: None declared, Nikolas Ruffer: None declared, Ina Kötter Speakers bureau: Novartis, Sobi, Martin Krusche Speakers bureau: Sobi, Novartis, Roche, Grant/research support from: Sobi, Novartis.

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AB1475 DOES VEIN WALL THICKNESS HAVE PROGNOSTIC VALUE IN BEHÇET'S DISEASE? A PROSPECTIVE FOLLOW-UP STUDY

Keywords: Ultrasound, Behcet's disease, Diagnostic Tests

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Background: We reported the first controlled doppler ultrasound study showing increased common femoral vein (CFV) thickness in Behçet's Disease (BD).[1] We also recently showed that increased CFV thickness is a distinctive feature of BD, rarely present in other inflammatory or vascular diseases with a specificity higher than 80% for the cut-off value of ≥ 0.5mm.[2] However, the association between CFV thickness and any organ involvement, disease course or treatment during disease course has not been demonstrated so far.

Objectives: This study aimed to assess the longitudinal course and prognostic value of CFV thickness measurement during a prospective follow-up BD patients.

Methods: In this study, we included 195 patients with a diagnosis of BD. The clinical, demographic, treatment data and biomarkers were recorded during routine visits. Bilateral CFV thickness was measured with ultrasonography by an experienced radiologist at the same day. Patients were started to follow up prospectively with 3-6 months intervals and in any urgent visit.

Results: At baseline, 98.6% of patients had increased CFV wall thickness above the cut-off value of ≥0.5mm. The baseline and last follow-up clinical characteristics were shown in Table 1. 139 of 195 patients had prospective clinical follow-up data with a mean of 26.5 (16.9) months. New major organ involvement or relapse leading to treatment change was seen in 39 (28%) patients. Among 22 (15.8%) patients with new major organ involvement, 12 had vascular, seven had ocular, two had neurologic and one had gastrointestinal involvement. Among 36 patients with only mucocutaneous disease at baseline, new major organ involvement developed in 9 patients during follow-up. These nine patients had higher baseline CFV thicknesses compared to patients without major organ involvement, however without reaching clinical significance (0.83mm vs 0.73mm for right CFV, 0.80mm vs 0.73mm for left CFV: p >0.05 for both) In 47 patients, the second CFV thickness measurement was done with a mean 19.8 months after the first visit. There was no statistically significant difference between the first and second CFV wall thickness measurements for both right and left CFVs (First vs. second for right CFV: 0.79 vs. 0.76mm, p=0.26; for left CFV: 0.79 vs. 0.75mm, p=0.26). We did not find any change in CFV wall thickness with the treatment modality, new organ involvement and relapses.

Conclusion: CFV wall thickness measurement with ultrasonography which is a new non-invasive diagnostic tool for BD, does not show a major change over time with treatment modality, new organ involvement or disease relapses. However, our preliminary results suggest that mucocutaneous BD patients with higher CFV thickness may have a higher risk for the development of major organ involvement during follow-up. The long term results of our prospective cohort with increased patient numbers would clarify the prognostic value of CFV thickness in BD.

Disclosures: None.

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Table 1. The baseline and follow-up clinical characteristics of patients with Behçet's Disease.

	Baseline (n=139)	Last Follow-up (n=139)	Relapses or New Involvement during follow-up
Age mean (SD)	34.85 (8.27)		
Gender F/M ratio	43/96		
Right CFV Wall Thickness mean (SD) mm	0.791 (0.253)		
Left CFV Wall Thickness mean (SD) mm	0.797 (0.207)		
Oral aftous ulcers n (%)	134 (95)	134 (95)	13 (9.4)
Genital ulcers n (%)	84 (60.4)	89 (64.5)	6 (4.3)
Eritema Nodosum n (%)	62 (44.6)	69 (49.6)	9 (6.5)
Arthritis (%)	48 (34.5)	48 (34.5)	10 (7.2)
Major Organ Involvement n (%)			
Vascular Involvement n (%)	84 (60.4)	96 (69.1)	35 (25.2)
Deep Venous Thrombosis (%)	61 (43.9)	65 (46.8)	6 (4.3)
Pulmonary trombosis n (%)	35 (25.2)	52 (37.4)	23 (16.5)
Sinus Venous Thrombosis n (%)	12 (8.6)	14 (9.9)	2 (1.4)
Trombofilebitis n (%)	4 (2.9)	6 (4.3)	5 (3.6)
Neuro-Behcet n (%)	14 (9.9)	16 (11.5)	2 (1.4)
Uveitis n (%)	33 (23.7)	40 (28.8)	7 (5)
Entero-Behcet n (%)	8 (5.8)	9 (6.5)	1 (0.7)

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1476 EVALUATION OF AUTOANTIBODIES POSITIVITY IN SARCOIDOSIS PATIENTS

Keywords: Autoantibodies, Diagnostic Tests, Imaging

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Background: Several studies reported serum positivity for anti-nuclear (ANA), extractable nuclear antigen (ENA) and antiphospholipid antibodies in sarcoidosis patients [1,2]. However, their clinical significance is still a matter of debate.
Objectives: Several studies reported serum positivity for anti-nuclear (ANA), extractable nuclear antigen (ENA) and antiphospholipid antibodies in sarcoidosis patients [1,2]. However, their clinical significance is still a matter of debate.
Methods: We enrolled 260 sarcoidosis patients (170 females and 90 males; mean age at diagnosis 46 ± 9), after giving written informed consent. We perform clinical evaluations, laboratory tests and radiology features.
Results: 89 sarcoidosis patients were ANA positive (34%, titre ≥ 1:160), 34 patients presented ENA positivity (15%) and antiphospholipid antibodies were positive in 20 patients (8%). No statistical significant correlations were observed between ANA/ENA positivity and clinical, laboratories and imaging evaluations. However, there was a statistically significant increase of the presence of antiphospholipid antibodies in sarcoidosis patients with a diagnosis of pulmonary embolism (p-value 0.04).
Conclusion: This study demonstrated an increase of antiphospholipid antibodies positivity in sarcoidosis patients with pulmonary embolism. These results may support the screening for these antibodies in all sarcoidosis patients. Further studies are underway to confirm these preliminary data and to evaluate if the positivity of autoantibody in these patients might suggest autoimmune implications in the pathogenesis of sarcoidosis.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1477 **IS HYPOPHOSPHATASIA MISDIAGNOSED IN A TERTIARY RHEUMATOLOGIC CENTRE?**

Keywords: Descriptive Studies, Rare/orphan diseases, Bone diseases

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Background: Hypophosphatasia (HPP) is a rare disease caused by mutations of the ALPL gene leading to reduced activity of tissue non-specific alkaline phosphatase (AP). HPP can mimic other diseases clinically and be overseen, misdiagnosed or in the worst-case inadequately treated.
Objectives: To identify patients with a high likelihood of HPP, explore the frequency of HPP in our rheumatologic outpatient clinic and summarize clinical presentation of HPP patients.
Methods: Patients with measured AP levels <=45 U/l between 2013 and 2022 were identified, possible HPP symptoms and lab parameters were documented.

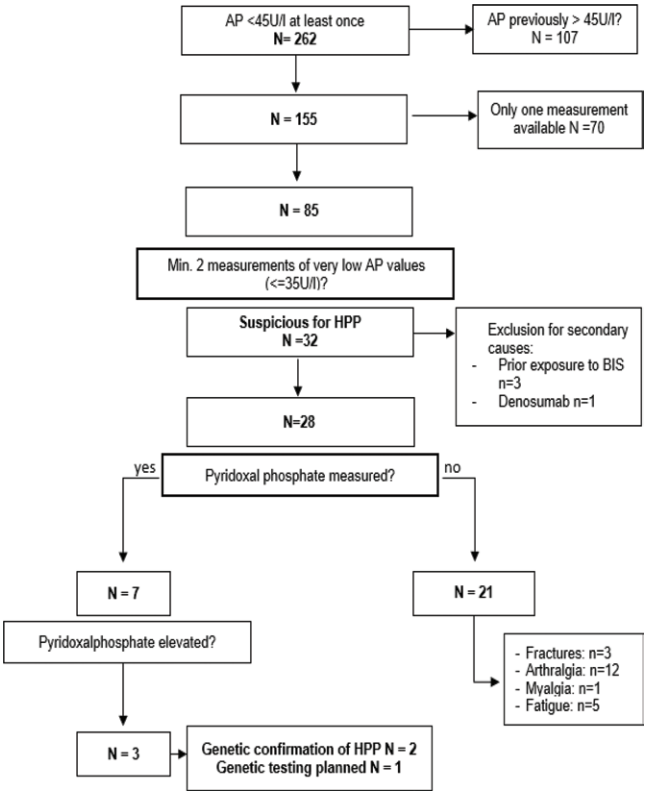


Figure 1. Workflow

Where only one measurement of AP was available, no further analysis was undertaken. All patients with AP levels>45 U/l were excluded to increase the likelihood of HPP. Those with multiple (>=2) very low AP values (<=35U/l) were defined as *suspicious for HPP*. After detailed chart review for secondary causes for low AP levels (e.g., severe hypothyroidism, exposure to bisphosphonates (BIS)) and exclusion of said cases, an analysis of the remaining ones followed. Where HPP was suspected, we aimed to initiate a measurement of pyridoxal phosphate (B6) within clinical routine. Elevated B6 levels (>50µg/l) were used as further marker suggestive of HPP.
Results: 6861 AP measurements in 3362 patients were identified. 262 (7.8%) patients had at least one low AP value. The further workflow is shown in Figure 1. 28 (10.7%) patients had AP levels <=35U/l at least twice. B6 measurements are available for 7 patients. Elevated values were seen in 3 of 7. In two cases HPP was confirmed genetically. The rest of the patients defined as *suspicious for HPP* presented unspecific symptoms (Fig. 1).

Table 1. Patient characteristics

	Age, sex	AP values	B6 value (mcg/l)	Diagnosis	ALPL mutation?	Possible HPP manifestations	Exclusion through suggested filtering strategy?
				HPP			
1	26, f	22;28	61.1	Familial mediterranean fever	No test yet	None	no
2	43, f	10;11;12	103.8	Suspected psoriatic arthritis	Heterozygous c.1343C>G	Arthralgia	no
3	74, f	33;27; 34;30;32	79	Vasculitis	Heterozygous c.1310C>T	Fracture forearm and shoulder (fall from standing height)	no
				HPP previously documented			
4	49, f	38;24;36	50 79.1	Psoriatic arthritis	Heterozygous c.526G>A	Arthralgia Myalgia Achilles tendinitis	Yes, AP>45U/l during autoimmune hepatitis
5	41, f	21;27;30; 29;36	49	Systemic sclerosis Osteoporosis	Heterozygous c.1001G>A	Calcinosis cutis universalis Arthralgia Fatigue Fracture (forearm) with delayed healing	Yes (BIS); AP values >45

During screening, 2 patients were identified with a previously confirmed HPP. However, the filtering strategy used here excluded these (for history of normal AP values and exposure to BIS). Details are shown in Table 1.

Conclusion: In our analysis of measured serum AP levels in a tertiary care centre for rheumatology we found 4 patients with definitive HPP and 1 patient with a high probability of HPP. The clinical symptoms possibly related to HPP were mild. In one case, the current diagnosis of psoriatic arthritis was documented as *suspected*; thus, the clinically leading arthralgia might be explained by HPP. All other patients had definite rheumatic diseases. Mistreatment was not found. The definitive number of patients with HPP among the cases currently defined as suspicious may be greater due to missing data on B6 in this retrospective analysis. However, only mild phenotypes were seen. Developing a universal algorithm to detect HPP remains difficult: our filtering strategy failed to identify 2 of the 4 patients with confirmed HPP. We conclude that in patients with repeatedly low serum AP levels occasionally occurring normal AP and exposure to BIS cannot rule out HPP. A further workup should include B6 levels, especially in the presence of (fragility) fractures and other symptoms not sufficiently explained by the presence of a rheumatic disease.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1478 THERAPEUTIC TACTICS OF IDIOPATHIC LOBULAR PANNICULITIS

Keywords: Disease-modifying Drugs (DMARDs)

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Background: Idiopathic lobular panniculitis (ILP) or Weber-Christian disease is a rare understudied disease, which manifests itself in recurrent *subcutaneous fat* necrosis often involving damage of the internals. Treatment of the disease is not standardized, and as a matter of fact it is provided empirically.

Objectives: to assess the efficiency of therapy in case of various forms of ILP.

Methods: We studied 34 patients (30 women, 4 men) with ILP, age 30-74, duration of disease 7.4±2.3 years. Besides general clinical examination we determined the level of *α1-antitrypsin,* amylase, lipase, *ferritin, creatine phosphokinase,* made chest CT scan *and carried out the pathomorphological study* of *skin biopsy specimen taken from the area of a node.* The following forms of the disease were identified: nodular form (NF) (14 patients), plaque form (PF) (9 patients), mesenteric form (MF) (5 patients) and infiltrative form (IF) (6 patients). In all cases the lobular panniculitis was verified by means of histopathological examination. All patients took glucocorticoids (GC), average daily dose of 12.8 ± 1.6mg, including 8.4± 1.7mg (for NF), 17.6± 3.2mg (for PF), 8,6 ± 1,6mg (for MF), 23.6 ± 5.3mg (for IF). In case of NF, we additionally prescribed Plaquenil, the dose of 600mg per day (8 patients), and Mycophenolate Mofetil 1.5-2g per day (6 patients); in case of PF – Cyclophosphamide (Cph), the dose of 200mg per week (4 patients) or Mycophenolate Mofetil (1.5-2g per day, 5 patients); in case of MF – Mycophenolate Mofetil (1.5-2g per day, 5 patients). Patients with IF took Cph (200mg per week). In case there was no effect after 3 months, we prescribed Mycophenolate Mofetil (1.5-2g per day). With an unsatisfactory effect, after 3 months, genetically engineered alpha-TNF antagonist drugs were used. On average, the observation period was 12 months.

Results: The treatment made it possible to achieve a significant positive dynamics in patients with NF, PF and MF: the body temperature got back to normal and there was regression of indurations (26 patients), joint pain intensity was reduced (16 patients), laboratory data on inflammatory intensity revealed decrease (24 patients). Average daily dose of GC was reduced to 4.5±0.7mg and 11.4±1.1mg, respectively. In general, a significant improvement was evident in all patients with NF and MF, in 75 % of patients with PF. In case of IF an average daily dose was increased to 25.4±1.7mg per day. In all patients of this group, an unsatisfactory effect was noted, which required discussion of the appointment of genetically engineered biological therapy. The tolerability of treatment was regarded as good, no adverse events were noted. After 14 weeks, 3 patients had a syndrome of "eluding" the effect and IL-1 inhibitor drugs were prescribed for the first time.

Conclusion: To work out dosages and treatment schedules for patients with ILP further studies are required.

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Disclosure of Interests: None Declared.

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AB1479 TO EACH THEIR OWN- CLASSIFICATION OF ARTHRITIS PHENOTYPE AMONG INFLAMMATORY ARTHRITIS PATIENTS WITH CANCER TREATED WITH IMMUNE CHECKPOINT INHIBITORS

Keywords: Malignancy, Inflammatory arthritides, Prognostic factors

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Background: The use of immune checkpoint inhibitors (ICIs) for the treatment of cancer can be associated with adverse events including inflammatory arthritis (ICI-IA). ICI-IA can encompass a variety of different phenotypes including: polymyalgia rheumatica (PMR)-like, spondyloarthritis-like, rheumatoid arthritis (RA)-like, and others[1]. Due to the heterogeneous clinical presentation of ICI-IA, methods are needed to find important variables and associations to describe and distinguish between clinical phenotypes.

Objectives: Use supervised machine learning techniques to find important variables associated with classification of arthritis phenotypes among patients with ICI-IA.

Methods: This study is ancillary to a retrospective observational study of patients with ICI-IA at 6 U.S sites who were treated with DMARDS (TNFi, IL6R, or methotrexate). Arthritis phenotypes was the classification target of interest. Demographics, patterns of swollen joints, medications, lab values, and concomitant irAEs were all obtained from the medical record. Descriptive statistics were computed. Classification and Regression Trees (CART) were created using the rpart and partykit packages and Random Forest (RdF) using the randomForest R package. One thousand trees were created for the forest. Variable importance scores (CART) and mean decrease in Gini scores (RdF) were created to assess the variable importance of included variables.

Results: 147 patients were included, mean age 62 years, 43% with melanoma. Arthritis phenotypes were PMR-like in 8.3%, spondylarthritis-like 19%, RA-like 48%, polyarthritis 17%, and other 8%. Two versions of the CART and RdF were performed (with and without study site) (**Table 1**). Including study site, the following were identified by both CART and RdF as important: study site was the most important variable associated with the phenotypic label, followed by cancer type, hand arthritis, age, total joint count (TJC). The CART flow diagram with study site is shown in the **Figure 1**. Excluding study site, CART and RdF identified hand arthritis, cancer type, age, TJC.

Table 1. Variable Importance (VI) from Classification and Regression Tree (CART) and mean decrease in Gini score (MDG) from Random forest (RdF) associated with Immune Checkpoint Inhibitor Inflammatory Arthritis phenotype assignment.

Characteristic	CART VI[1]	RdF MDG[2]	CART VI [1] without study site	RdF MDG[2] without study site
Study site	25	10.8	Not included	
Age	12	10.6	13	12.2
Cancer type	16	6.7	20	7.7
Maximum steroid dose of prednisone (mg)		7.3		8.7
Total Joint Count	4	5.9	6	6.2
Hand arthritis	14	3.7	25	4.0
Factors with MDG <=3		cancer stage, rash, Number of IRAEs, sex, Rheumatoid factor positive(RF+), RF+ or cyclic citrullinated peptide factor positive, arthritis affecting: shoulder, knee, ankle, hip, wrist, and knee		

[1] CART Variable importance, the higher the number the more influential the variable is in the CART[2] Mean Decrease in Gini score from RdF is a measure to rank variables; the higher the number the more important the variable.

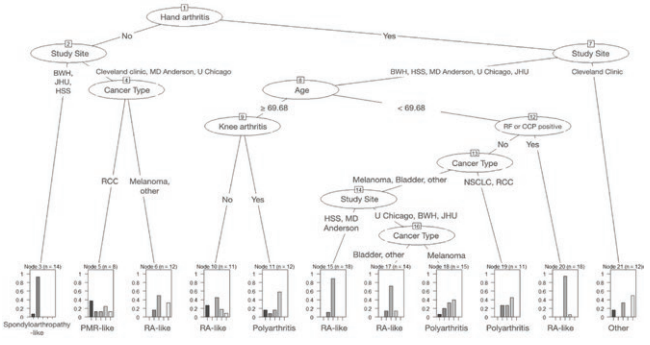


Figure 1. Classification and Regression Tree for Arthritis Phenotype with Study Site included. The bar graphs at the bottom show which arthritis phenotype is the majority for each terminal node and the y-axis shows the error rates for each group from the model.

Conclusion: We found that classification of arthritis phenotype was study site-specific in our statistical models. After excluding site, age, cancer type, TJC, maximum steroid dose, and hand arthritis were associated with phenotypic classification. The influence of study site illustrates current heterogeneity in ICI-IA phenotyping among experts and the need for formalized classification for enrollment in clinical trials. These results identify variables that could be explored by the ACR/EULAR ICI-IA classification criteria working group.

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AB1480 EXPRESSION OF JAK-STAT SIGNALING PATHWAY IN HIDRADENITIS SUPPURATIVA PATHOLOGICAL BIOPSY SPECIMENS

Keywords: Cytokines and chemokines, Skin, Cell biology

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Background: Hidradenitis suppurativa (HS) is inflammatory skin disease with an unknown etiology. JAK-STAT pathway may be implicated in its pathogenesis. Considering the unmet need in the treatment of inflammatory skin diseases, assessment of the JAK/STAT pathway could provide new understanding in the pathogenesis of these disorders. Therefore, in this study we primarily intended to investigate this pathway in patients with HS.

Objectives: Herein we aimed to investigate the JAK/STAT signaling pathway in the skin biopsies of HS patients and compared with psoriasis (PSO) and healthy subject.

Methods: This study used human tissues of healthy (n=26) and diseased skin samples obtained from the psoriatic (n=35) and HS (n=25) patients. Immunohistochemical methods were used to evaluate the expression of JAK1, JAK2, JAK3, Tyrosine Kinase 2 (TYK2), STAT1, STAT3, STAT4, STAT5, and STAT6. In the dermis, the staining intensity was recorded as 'positive' or 'negative. The epidermal part is divided into cytoplasmatic and nuclear parts and strong staining intensity recorded by staining in ≥50% of the cells.

Results: A total of 86 biopsies obtained from 25 HS (40.8 ±21.8 years, 60% male (M)), 35 PSO (46.5 ± 18.4 years, 57% M) and 26 control subjects (60.3 ± 18.3 years, 46% M) were analyzed. All JAK-STAT and TYK2 are overexpressed in dermal part of HS skin. TYK2, JAK3,STAT3 and STAT4 are strongly expressed in cytoplasmic part of epidermis in HS skin.TYK2, JAK3 and STAT1 is strongly expressed in nuclear part of epidermis in HS skin. JAK-STAT pathway is overexpressed in dermal part of psoriatic skin especially STAT2 and STAT6 but JAK1 is not expressed dermal part of psoriatic skin. All STATs and JAK1, JAK3 and TYK2 are strongly expressed in cytoplasmic part of epidermis in psoriatic skin. TYK2, JAK3 and STAT1 are strongly expressed in nuclear part of epidermis in psoriatic skin. The summary of the findings is given in Table 1. When look at the correlation analysis for TYK2 had strong correlation with HS according to control subjects in the dermal and nuclear staining. The summary of findings and the correlation analysis for HS, healty control (HC) and PSO is given in Table 1.

Conclusion: In this study, we demonstrated an increased activity in the skin biopsies of HS. When considering the unmet need in the treatment of this disease current data is significant for guiding the possible future therapies.

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Table-1. Summary of the findings and the correlation between inflammatory skin diseases and JAK/STAT pathway staining in the skin

	Hidradenitis Suppurativa (n=25)	Psoriasis (n=35)	Healthy skin (n=26)	HS vs. HC*	PSO vs. HS*
Dermal staining					
TYK2	23, (92)	34, (97.1)	0	**0.92**	
JAK1	3, (8.6)	0	0		
JAK2	14, (56)	21, (60)	2, (7.7)	**0.52**	
JAK3	23, (92)	31, (88.6)	0	**0.92**	
STAT1	16, (64)	27, (77.1)	0	**0.69**	
STAT2	25, (100)	35, (100)	14, (53.8)	**0.42**	
STAT3	23, (92)	34, (97.1)	0	**0.92**	
STAT4	4, (16)	11, (31.4)	0	**0.29**	
STAT5	17, (68)	27, (77.1)	0	**0.72**	
STAT6	14, (56)	33, (94.3)	0	**0.62**	**-0.45**
Epidermal cytoplasmic staining in ≥50% of the cells					
TYK2	2, (8)	21, (60)	8, (30.8)	**-0.69**	**-0.58**
JAK1	8, (32)	11, (31.4)	0		
JAK3	25, (100)	35, (100)	26, (100)	**0.44**	
STAT3	22, (88)	34, (97.1)	14, (53.8)	**0.37**	
STAT4	15, (60)	29, (82.9)	14, (53.8)		**-0.25**
Epidermal nuclear cells with strong staining					
TYK2	5, (20)	27, (77.1)	0	**0.76**	**-0.56**
JAK3	25, (100)	35, (100)	26, (100)		
STAT1	19, (76)	31, (88.6)	19, (73.1)		

* Note that "r" correlation coefficients were given in the cells which indicated significant correlations between the variables (p<0.05). Empty cells indicated no correlation (p>0.05) therefore "r" values were not provided.

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Disclosure of Interests: None Declared.

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AB1481 EMERALD STUDY DESIGN: A TWO-COHORT, OPEN-LABEL, SINGLE-ARM STUDY OF EMAPALUMAB, AN ANTI–INTERFERON-Γ (IFNΓ) MONOCLONAL ANTIBODY, IN PATIENTS WITH MACROPHAGE ACTIVATION SYNDROME (MAS) IN RHEUMATIC DISEASES

Keywords: Systemic lupus erythematosus, Cytokines and chemokines, Inflammatory arthritides

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Background: MAS is a severe, life-threatening form of secondary hemophagocytic lymphohistiocytosis associated with rheumatic diseases such as Still's disease (systemic juvenile idiopathic arthritis or adult-onset Still's disease) and systemic lupus erythematosus (SLE). IFNγ has been implicated in the underlying pathology of both conditions. High-dose glucocorticoids (GCs) are the standard first-line treatment for MAS; however, there is no standardized approach to treating patients who are refractory to high-dose GCs. In a pilot study of 9 patients with an inadequate response to high-dose GCs, IFNγ was rapidly neutralized, and MAS controlled, following emapalumab administration (NCT03311854). Emapalumab also had a favorable safety profile.

Objectives: To present the design of a study enrolling patients with MAS in Still's disease and SLE with the aim of evaluating the efficacy and safety of emapalumab.

Methods: EMERALD (NCT05001737) is an open-label, single-arm, multicenter, phase 2/3 interventional study enrolling pediatric and adult patients with MAS and an inadequate response to high-dose GCs into two cohorts: MAS in Still's disease (n=25) and MAS in SLE (n=16). Key eligibility criteria vary by cohort and phase (Table 1). Each cohort is a single-arm study comprising two phases: an optional run-in phase and an interventional phase. Patients are treated with high-dose GCs during the run-in phase and followed until MAS remission, inadequate response, or 12 weeks (whichever occurs first). Eligible patients enrolled in the interventional phase are treated with

emapalumab intravenously for 4 weeks (6 mg/kg on Day 1; 3 mg/kg every 3 days from Days 4–16, then 3 mg/kg twice weekly from Days 17–28) or until protocol-defined complete response (CR). Patients will be followed up for 1 year after study completion.

Key inclusion criteria	Key exclusion criteria
Run-in phase • Informed consent • Male and female patients aged 6 months to 80 years at diagnosis of MAS • MAS defined per the MAS diagnostic criteria and requiring treatment with GCs Interventional phase • Informed consent • Male and female patients aged 6 months to 80 years at diagnosis of MAS • Patients with a diagnosis of MAS having shown an inadequate response to high dose GCs as per local standard clinical practice **MAS diagnostic criteria** • Febrile patient presenting with ferritin >684 ng/mL • And any two of: – Platelet count ≤181 x10^9/L – Aspartate aminotransferase levels >48 U/L – Triglycerides >156 mg/dL – Fibrinogen levels ≤360 mg/dL	• Primary hemophagocytic lymphohistiocytosis • Confirmed malignancy • Evidence of *Leishmania* infection, clinically active mycobacteria (typical and atypical), *Histoplasma capsulatum*, salmonella infections, or latent tuberculosis • History of hypersensitivity or allergy to any component of the study drug • A bacillus Calmette-Guérin vaccine within 12 weeks prior to screening • Live or attenuated live (other than bacillus Calmette-Guérin) vaccine within 4 weeks prior to Screening • Pregnancy or lactation • At time of emapalumab initiation, treatment with: – Canakinumab, Janus kinase inhibitors, tumor necrosis factor inhibitors, tocilizumab – Anakinra at a dose >4 mg/kg • Use of etoposide for MAS within 1 month prior to treatment with emapalumab

Results: Protocol-defined CR at Week 8 after first emapalumab administration is the primary endpoint of the EMERALD study. Secondary efficacy endpoints include GC tapering, survival, time to first CR, overall response (CR and partial response), time to first overall response, MAS recurrence, pharmacokinetic/pharmacodynamic profile of emapalumab, and patient-reported outcomes. Adverse events, abnormal laboratory parameters, and anti-drug antibodies will be monitored as safety endpoints.
Conclusion: The ongoing EMERALD study is designed to address the unmet need for efficacious and safe therapies for the treatment of MAS, particularly for patients who are refractory to high-dose GCs.
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AB1482 SPECIFIC BLOOD MONOCYTE DISTRIBUTION IN HISTIOCYTOSES CORRELATES WITH VASCULAR INVOLVEMENT AND DISEASE ACTIVITY

Keywords: Innate immunity

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Background: Histiocytoses are rare clonal disorders characterized by the proliferation and accumulation of $CD68^+$ histiocytes in tissues[1]. During histiocytosis, circulating monocytes arising from bone marrow progenitors carry most MAP-kinase gene mutations, but only "classical" monocytes can differentiate into tissue histiocytes[2]. However, little is known about the circulating monocyte subset distribution in histiocytoses[3] and their differences from other myeloproliferative disorders.
Objectives: We aimed to evaluate the circulating monocyte subset distribution in patients with histiocytoses compared to patients with myeloproliferative disorders (Chronic myelomonocytic leukemia (CMML) and essential thrombocythemia (ET)) and healthy donors (HD).
Methods: Peripheral blood cells were obtained from patients diagnosed in Dijon University hospital between 2020 and 2021, with histiocytoses (n=17), CMML (n=7), ET (n=7), and from 21 HD at steady state. Monocytes were separated on a CD14/CD16 scattergram into $CD14^{++}/CD16^-$ (classical), $CD14^{++}/CD16^+$ (intermediate), and $CD14^+/CD16^{++}$ (non-classical) subsets after stained cell separation.
Results: During histiocytoses, an increase in "classical" monocytes was observed, compared to ET (p= 0.01) while "intermediate" (vs. ET; p= 0.02) and "non-classical" monocytes (vs. HD; p= 0.04) were decreased. The distribution of monocyte subsets in histiocytoses was close to that in CMML and homogenous among the different type of histiocytoses. Compared to CMML patients, clonal hematopoiesis in patients with histiocytoses was associated with a decrease in "classical" monocytes (87.50% vs. 97%; p= 0.002), with an increase in intermediate and "non-classical" monocytes: 5% vs. 2.5% (p= 0.03) and 4% vs. 0.5% (p= 0.01), excepted when MAP-kinase mutation was considered, as monocyte distribution was similar. Patients with vascular involvement (6 ECD including 5 $BRAF^{V600E}$, 1 RDD) had an increase in classical monocytes (96.00% [92.0-96.0] vs. 86.00% [82.5%-92.0%; p=0.008) and a decrease in "non-classical" monocytes (1.00% [1.0-2.0] vs. 5.00% [3.50-9.50]; p=0.007). The correlation between "non-classical" monocytes <4% and vascular involvement was confirmed by Pearson model (0.648; IC95%[0.25-0.86]; p=0.005). Histiocytoses patients achieving a metabolic response had a lower percentage of "intermediate" monocytes (3.5% [2.00-5.00] vs. 7.0% [4.00-13.00]; p= 0.04) and lower CRP levels (3.0 [1.1-8.75] vs. 33.65 [5.33-59.5] mg/L; p=0.04). The only factor influencing the monocytes subset repartition (for "classical" monocytes) was the presence of clonal hematopoiesis (ß coefficient: -10.78; 95%CI [-16.83 to -4.737]; p=0.002) in patients with histiocytoses.
Conclusion: The monocytes subset distribution is singular in histiocytoses compared to other myeloproliferative neoplasms and is influenced by clonal hematopoiesis. The decrease in the "non-classical" subset could represent a surrogate marker of vascular involvement, while the decrease of the intermediate fraction is associated with a metabolic response.
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AB1483 CLINICAL OUTCOMES OF EXTRACORPOREAL LIFE SUPPORT AND LUNG TRANSPLANTATION IN SEVERE ANTI-MELANOMA DIFFERENTIATION-ASSOCIATED GENE 5 (MDA5)-RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE: A SYSTEMATIC REVIEW

Keywords: Systematic review, Rare/orphan diseases, Lungs

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Background: Anti-melanoma-differentiation-associated gene-5 antibody (MDA5) associated dermatomyositis is associated with rapidly progressive interstitial lung disease (RP-ILD), high mortality, and progression despite aggressive immunosuppression. Extra corporeal membrane oxygenation (ECMO), as bridge to recovery or bridge to transplantation and lung transplantation offer potentially lifesaving therapy for MDA5 RP-ILD but their roles are unclear, and its use in practice is often debated[1-4].
Objectives: We systematically reviewed the clinical outcomes of patients with MDA5 RP-ILD receiving ECMO and/or lung transplantation.
Methods: Ovid Medline, Embase and CINAHL were searched (inception to Jan 2023) using keywords to identify studies of ECMO and lung transplantation in MDA5 RP-ILD. We included English language studies in adults with MDA5 RP-ILD requiring ECMO and/or lung transplantation. Review was prospectively registered on PROSPERO (CRD42022355450).
Results: The sixteen identified manuscripts reported outcomes for 33 patients with serological evidence of MDA5 (14 case reports, 2 case series). Most presented with respiratory symptoms, classic dermatomyositis cutaneous features, were amyopathic and had pulmonary radiological ground glass opacifications. Time to clinical diagnosis was usually less than 3 months from symptom onset, with rapid clinical deterioration from severe symptoms requiring hospitalisation to institution of mechanical ventilatory support within 2 weeks. Combination multi-modal aggressive induction immunosuppressants (corticosteroid, cyclophosphamide, tacrolimus, tofacitinib, rituximab and/or immunoglobulin) was used in 15/16. ECMO was used in 32 patients (Figure1): as a bridge to recovery in 16, and a bridge to transplantation in 16. ECMO used as a bridge to recovery had poor outcomes (15/16 deceased, 94%) mainly due to withdrawal of care. ECMO used as bridge to

transplantation had an 87.5% survival rate (14/16), with MDA5 disease-free remission for up to 12 years using standard induction transplant immunosuppressants.
Conclusion: In refractory MDA5 RP-ILD, early consideration of lung transplantation is essential. The findings do not support ECMO as bridge to recovery given its high mortality rate. ECMO as bridge to transplantation provided excellent patient survival and should be considered as potentially lifesaving.
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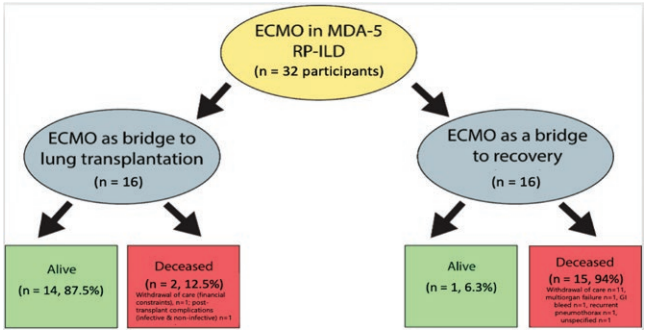


Figure 1. Key results

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AB1484

ADULT-ONSET STILL'S DISEASE AND SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: PREDICTORS OF DRUG-FREE REMISSION IN A MONOCENTRIC COHORT

Keywords: Remission, Rare/orphan diseases, Prognostic factors

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Background: Adult-onset Still's disease (AOSD) and Systemic Juvenile Idiopathic Arthritis (SJIA, formerly termed Still's Disease), are rare polygenic autoinflammatory disorders of unknown etiology. The clinical course of AOSD/SJIA has been distinguished into different phenotypes, described on the basis of the evolution of symptoms over time. In a sizeable proportion of affected patients, disease remission can be achieved with treatments, that can be progressively tapered and stopped without relapse. Not much information is available on drug-free remission predictors.
Objectives: To look for drug-free remission predictors in a retrospective monocentric cohort of AOSD/SJIA patients.
Methods: Retrospective evaluation of AOSD/SJIA patients followed up in an Italian Rheumatology Unit between January 1997 and September 2022. All patients fulfilled the Yamaguchi criteria or PRINTO preliminary criteria. Drug-free remission was defined as the absence of clinical and laboratory markers of disease activity and absence of treatment for at least 6 months. Differences between patients who achieved drug-free remission or not were assessed using the using Mann-Whitney test, Student's t-test, Chi-squared test and Fisher test when appropriate.
Results: 57 AOSD and 7 SJIA consecutive patients were included in the study. Drug-free remission was achieved in 23 patients (35.9%) after a median period of 3,62 years (IQR 1,37 – 6). Their main baseline demographic and clinical features, as well as treatment received are summarized in Table 1. Patients in the drug-free remission group more often had white blood cells count >15.000/uL at baseline (p:0.004) than other patients. On the contrary, patients who failed drug-free remission more frequently were treated with Cyclosporine A (CyA) at disease onset (p:0.042). No significant difference was observed when analyzing if treatment with csDMARDs or bDMARDs was started within 3 months of the disease onset or not.
Conclusion: Hyperleukocytosis at baseline was identified as a potential predictor of drug-free remission in our cohort of AOSD/SJIA patients, while this was more difficult to obtain in patients treated with CyA at the disease onset. Larger and collaborative studies are needed to confirm and better define these results.
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Table 1. Baseline demographic and clinical features and treatment at disease onset.

	Drug-free remission n: 23	No drug-free remission n: 41	p-value
AOSD n (%)	20 (87.0%)	37 (89.2%)	0.69
Male n (%)	12 (52.2%)	14 (34.2%)	0.16
Age at onset, years Mean±SD	30.5 ±13.6	36.6 ±15.4	0.12
Follow-up duration, years Median (IQR)	6.5 (2.7–10.7)	8.6 (3.5-15.3)	0.94
Ferritin mg/mL at onset, Median (IQR)	1766 (682-11594)	1255 (551-6620)	0.61
WBC >15000/uL at onset, n (%)	**15 (71.4%)**	**13 (32.5%)**	**0.0037**
WBC/uL at onset, Mean±SD	17337 ±8223	14562 ±5995	0.14
Hb g/dl at onset, Mean±SD	10.9 ±1.8	11.3 ± 1.8	0.37
PLTx10^3/uL at onset, Mean±SD	325.30 ±171.97	328.74 ±135.6	0.93
CRP mg/L at onset, Mean±SD	130.8 ±79.1	143.2 ±108.6	0.65
ALT U/L at onset, Median (IQR)	68 (32-122)	59 (25 -117)	0.40
AST U/L at onset, Median (IQR)	44 (22-90)	49 (27 -90)	0.26
Modified Pouchot's score, Mean±SD	6.1 ±1.46	6.6 ±1.73	0.24
MAS at disease onset, n (%)	2 (8.7%)	5 (12,2%)	1
Treatment with csDMARDs (within 3 months since disease onset), n (%)	9 (39.1%)	23 (56.1%)	0.3
Treatment with cyclosporine (within 3 months since disease onset), n (%)	**0**	**8 (19.5%)**	**0.04**
Treatment with b/tsDMARDS (within 3 months since disease onset), n (%)	3 (75%)	9 (34.6%)	0.27

Legend: WBC White Blood Cell; Hb Hemoglobin, PLT Platelets, CRP C-Reactive Protein, ALT Alanine Transaminase, AST Aspartate Transaminase, MAS Macrophage Activation Syndrome, csDMARDs conventional Disease-Modifying Antirheumatic Drugs, b/tsDMARDs biological/targeted synthetic Disease-Modifying Antirheumatic Drugs

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AB1485 **THE EVALUATION OF THE STATIC AND DYNAMIC BALANCE DISORDERS IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER**

Keywords: Rehabilitation, Enthesitis

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Background: Familial Mediterranean fever (FMF) is an autoinflammatory disease characterized by self-limiting recurrent episodes/attacks of fever, serositis, arthritis, and erysipelas-like erythema[1]. Musculoskeletal manifestations such as arthralgia, enthesitis, exertional leg pain, myalgia, sacroiliitis, and lower extremity synovitis are also common in FMF [2]. The fact that the disease progresses with lifelong persistent inflammation, as well as attacks of arthritis, synovitis, and enthesitis in the lower extremities, decreased lower extremity proprioception, muscle weakness, osteopenia, and fatigue, suggests that patients with FMF may develop a balance disorder.
Objectives: The aim of this study is to examine the relationship between static and dynamic balance in patients with Familial Mediterranean fever (FMF).
Methods: FMF patients who met the modified Tel Hashomer criteria and healthy volunteers were included in the study. The demographic data,clinical characteristics, Maastricht Ankylosing Spondylitis Enthesitis Score(MASES) and International Severity Scoring System(ISSF) of FMF patients were evaluated. The balance performance was determined by the Berg Balance Scale(BBS), Functional Reach Test(FRT),Time Up and Go(TUG) tests, and Single Leg Stance(SLS) tests.
Results: When the patient and control groups were compared in terms of BBS, FRT, TUG and SLS tests, scores in the patient group were statistically worse in all evaluations. FMF patients who were at risk of falling were older with longer disease duration($p<0.001$ and $p<0.001$, respectively). VAS scores during attack, presence of arthralgia and amyloidosis were higher in patients at risk of falling($p=0.032$, $p=0.002$, $p<0.001$, respectively). ISSF and MASES scores of patients at risk of falling were significantly higher than those of patients without($p>0.001$ and $p=0.001$,respectively).
Conclusion: Our results demonstrated that the dynamic and static balance in FMF patients was worse than the healthy subjects. Longer and more severe disease, presence of enthesitis and amyloidosis may further contribute to deteriorated balance.
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Table 2. Comparison of static and dynamic balance scores and number of patients with fall risk in the patient and control groups

	Patients (n=94)	Controls (n=90)	p
BBS, cm, median (IQR)	56 (3)	56 (0)	<0.0001
FRT, sec, median (IQR)	29 (9)	31 (5)	0.002
TUG, sec, median (IQR)	7.44 (1.21)	7.3 (0.46)	0.007
SLS, sec, median (IQR)			
Eyes open, (R)	34 (19.5)	39 (8.5)	0.003
Eyes closed, (R)	11 (5.93)	12 (4.03)	0.009
Eyes open, (L)	33 (20.48)	38.5 (9.25)	0.003
Eyes closed, (L)	11.2 (6)	11.45 (4.05)	0.020
Patients with fall risk, n (%)	27 (28.7)	5 (5.6)	<0.0001

BBS: berg balance scale, cm: centimeter, FRT: functional reach test, L: left, R: right, sec: second, SLS: single leg stance test, TUG: timed up and go test

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1486 **OCULAR MUCOUS MEMBRANE PEMPHIGOID: A RHEUMATOLOGY MULTICENTER REPORT**

Keywords: Descriptive Studies, Rare/orphan diseases

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Background: Mucous membrane pemphigoid is a systemic, chronic, cicatricial inflammatory disease of autoimmune etiology of low incidence, characterized by the appearance of subepithelial bullous and scarring lesions that detach from the mucous membranes throughout the body. Isolated ocular involvement has classically been called Ocular Cicatrizal Pemphigoid but currently guides prefer the term Ocular Mucous Membrane Pemphigoid (OMMP). This involvement can lead to irreversible blindness if not treated early. The goal of therapy is to suppress inflammation and prevent scarring and complications, and step therapy with systemic immunomodulatory/immunosuppressive drugs is often used to achieve this. The autoimmune systemic nature of this pathology and the lack of familiarity of ophthalmologists with the use of immunosuppressive drugs motivates the referral of these patients to specialists used to their management, for interdisciplinary approach and follow-up.
Objectives: To analyze the clinical/epidemiological data and the established treatments of patients with OMMP in different Argentinian rheumatology centers.
Methods: Observational and multicenter study. Medical records of patients diagnosed and re with OMMP by an ophthalmologist, from different rheumatology centers in the Argentine Republic, were reviewed from May 2006 to July 2022.
Results: One hundred forty-seven medical records of patients diagnosed with OMMP were analyzed, mostly with confirmatory biopsy. Seventy-two percent were female. The mean age at diagnosis was 64 years (SD13). The time from the first symptoms to diagnosis was 30 months (0-300). Most of the patients (72%) were diagnosed in the last 5 years. On the analysis of 120 patients who had reported Foster's stage, 73% had stage II or less. (Foster/n: 0/9; 1/43; 2/36; 3/18; 4/14). Another associated autoimmune disease was presented in 29% and the most frequent was Sjogren's Syndrome. The most widely used treatment in 80% of patients was methotrexate and 62.5% continued with this medication until the end of the observation. In 30% of the patients the treatment had to be modified to control the disease and the most used drugs were mycophenolate, azathioprine, cyclophosphamide and rituximab. When patients were discriminated by current treatments according to Foster's stage (n: 120) patients with earlier Foster's stages used methotrexate more frequently, reaching 60% considering Foster's stages 0, I and II. Mycophenolate, azathioprine, and cyclophosphamide were used in patients with Foster's stage II or higher, while rituximab was used mainly in Foster's stage 4. Systemic steroids were used in 58% of the patients and 23% continued using it at the last visit. Adverse events that led to stopping treatment were observed in 12% of all treated patients (There were: dapsone, methotrexate, azathioprine, cyclophosphamide and mycophenolate). In Addition, one death due to sepsis secondary to cyclophosphamide was recorded. Foster's stage progressed in 31% of patients despite treatment and 8.1% (n:12) finished with blindness.
Conclusion: Most of the patients were diagnosed in recent years and three quarters present initial stages (Foster II or less). Due to the inflammatory, autoimmune, progressive and scarring nature of OMMP, early initiation of immunosuppressive/immunomodulatory therapy is essential, in order to suppress inflammation and avoid scarring and sequelae. Methotrexate seems to be a good starting alternative and treatment should be escalated according to evolution. Interdisciplinary management between rheumatologists/immunologists and ophthalmologists is essential and requires fluid communication throughout the follow-up of these patients.
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Other orphan diseases

AB1487 EFFECTIVENESS OF RITUXIMAB IN IGG4-RELATED DISEASE. MULTICENTRE STUDY AND LITERATURE REVIEW

Keywords: bDMARD, Vasculitis, Organ damage

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Background: IgG4-related disease (IgG4-RD) is a systemic fibroinflammatory disease often associated with elevated serum IgG4 levels. High dose corticosteroids are the cornerstone of treatment, but relapses and side-effects are frequent, requiring synthetic and/or biologic immunosuppressants. Rituximab (RTX) seems to be useful.
Objectives: To assess the effectiveness of RTX in IgG4-RD refractory to conventional treatment.
Methods: Multicentre clinical practice study of IgG4-RD patients treated with biologic therapy. For the literature review, a search of PubMed, Embase and the Cochrane library was conducted from inception to 31 Dec 2022.
Results: We include 9 patients (5 women/4 men) (mean age±SD; 55.8±12.6 years) with refractory IgG4-RD, treated with RTX **(Table 1).** The affected organs were: aorta (n=5), lymph nodes (n=3), lung/pleura (n=2), retroperitoneum (n=2), lacrimal glands (n=1), salivary glands (n=1), orbit (n=1), subglotis (n=1), kidney (n=1), pericardium (n=1), biliary duct (n=1) and mesenterium (n=1). All patients had received oral corticosteroids, (mean±SD dose of 33.9±14.1 mg/day). Two patients also received corticosteroid boluses. Six of the patients received conventional cDMARDs. The cDMARDs received were: methotrexate (MTX) (n=4), azathioprine (n=1), and hydroxychloroquine (n=1). RTX schedule was of 1g x 2 (n=8), and 375 mg/m2 (n=1). After a median [IQR] follow-up of 27 [25-48] months, complete and partial clinical improvement was observed in 6 and 2 patients respectively. One patient died due to an acute myocardial infarction, while another patient developed a breast cancer. We found 3 series, in the literature review, showing RTX effectiveness **(Figure 1).** The most frequently used RTX regimen was 1g x 2.
Conclusion: RTX seems to be an effective and safe therapy in corticosteroid-refractory IgG4-RD.

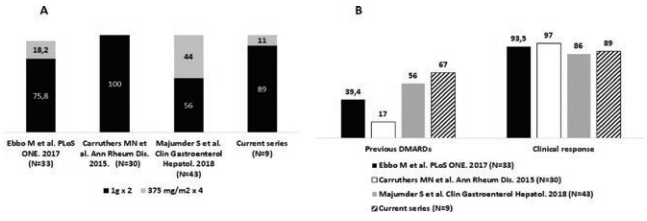


Figure 1. A) RTX regimen, **B)** previous cDMARDs and clinical response of IgG4-RD with RTX in current and other series of the literature review. All data are in %.

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AB1488 GENOTYPE-PHENOTYPE CORRELATIONS OF FAMILIAL MEDITERRANEAN FEVER IN ARMENIAN POPULATION

Keywords: Geographical differences, Genetics/Epigenetics, Descriptive Studies

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Background: Familial Mediterranean fever (FMF) is an autoinflammatory disorder that mostly affects people of Middle Eastern and Mediterranean descent, and is characterized by recurrent and self-limiting episodes of fever, serositis, arthritis and etc. Although many studies in scope of the connection of the MEFV gene variants and clinical manifestation have been carried out since the discovery of the gene, there is not yet in detail data about Armenian population peculiarities and differences in the severity of the disease between the genotypes.
Objectives: The aim of this study is to compare the severity of the disease between different FMF genotypes and propose utilization of genotype assessment as a predictor for the disease progression.
Methods: 184 Armenian patients were included in the study. All patients fulfilled Tel-Hashomer classification criteria for FMF. Patients were studied following a standard protocol. 12 most frequent mutations of MEFV gene (E148Q, P369S, F479L, M680I (G/C), M680I (G/A), I692del, M694V, M694I, K695R, V726A, A744S and R761H) were evaluated and according to the genotype patients were grouped in homozygotes, compound heterozygotes, heterozygotes and patients without mutations. Disease activity was measured by Tel-Hashomer severity score.
Results: 76,63% of examined patients were male and 23,4% -female. The mean age of the group was 41,53±18,73 years and the average duration of the disease-11,42±8,5 years. Clinical manifestation of the patients included in the study were following: episodes of fever- 124 (67,39%), abdominal pain -120 (65,2%), pleuritis - 154 (83,696%), pericarditis -11 (0,0598%) arthritis -54 (29,348%), arthralgia -101 (54,89%), erysipelas-like erythema -22(11,9565%), splenomegaly -59(32,065%), amyloidosis-6(3,26%). 118 (64,13%)of patients carried any of the MEFV examined mutations and despite the presence of clinical manifestations 66 patients (35,87%) have no mutations detected. 21 (17,8%) of patients with mutation were homozygote, 65 (55,08%)compound heterozygote and 32 (27,11 %) heterozygote. The prevalence of MEFV mutations among examined patients was 61,3%, 28,4%, 21,65%, 5,04% accordingly for M694V, M680I, V726A, E148Q exons. Patients with M694V/M694V and M694V/M680I genotype had the highest Tel-Hashomer severity score (9,8±0,6 and 8,1±1,1 accordingly). Patients with homozygote genotype have earlier onset of the disease (p=0,02), more frequent attacks (p<0,05), higher levels of ESR during the flare (P=0,009) compared with patient with other genotypes. No significant difference for the duration of the attack between different genotypes was found. Patients without any revealed mutations had the mildest disease presentations (Tel-Hashomer severity score – 3,2±1,6).
Conclusion: According to the data, age of the onset of FMF strongly correlates with the inherited genotype. Carriers of the MEFV gene mutations without any manifestations at early age should be expected to have onset years later and

Table 1. Main features of the multicentric study of 9 patients with IgG4-RD treated with rituximab.

Case	Age/ Sex	Organ involvement	Serum IgG4 (mg/ dL)/ Plasmablasts (cel/mL)	Biopsy	Diagnosis	Previous treatment	RTX regimen	Number of RTX cycles	Flollow-up (months)	Outcome
1	55/F	Aorta, Lacrimal glands, orbit,	210/ND	Negative	Umehara: probable Okazaki	GCs, MTX	1g x 2	3	56	CI
2	31/F	Salivary glands, lymph nodes, subglotis	48/ND	Positive	Umehara: possible Okazaki	GCs,	1g x 2	5	67	CI, breast cancer
3	55/M	Lung/pleura, kidney, retroperitoneum, lymph nodes	5.58/2309.07	Negative	Symptoms+imaging findings+↑PB	GCs, azathioprine	375 mg/m2	1	6	Exitus (AMI)
4	76/F	Lung/pleura, pericardium	90/954	Positive	Umehara: posible Okazaki	GCs, MTX	1g x 2	3	27	PI
5	57/F	Aorta	125/1218	Not performed	Symptoms+imaging findings+↑PB	GCs, HCQ	1g x 2	4	27	PI
6	54/F	Aorta, Biliary duct	18.5/831	Not performed	Symptoms+imaging findings+↑PB	GCs, MTX	1g x 2	4	25	CI
7	46/M	Aorta	84.7/760.6	Not performed	Symptoms+imaging findings+↑PB	GCs	1g x 2	4	41	CI
8	67/M	Aorta	11.6/ND	Positive	Umehara: posible Okazaki	GCs	1g x 2	6	48	CI
9	61/M	Retroperitoneum, lymph nodes, mesenterium	ND/ND	Positive	Umehara: posible Okazaki	GCs, MTX	1g x 2	2	9	CI

Abbreviations: F: female, GCs: glucocorticosteroids; HCQ: hydroxychloroquine, M: male, MTX: methotrexate, ND: no data, RTX: rituximab; AMI: acute myocardial infarction; CI: complete Improvement PI: Partial Improvement; ↑ PB: elevate plasmablasts counts

should be strongly monitored by clinicians. Despite the fact, that genotype is not included in Tel-Hashomer classification criteria, our study once more indicates, that not only phenotype but also genotype is very important for FMF. Further evaluation of bigger sample is required to describe the influence of the specific exons on the clinical manifestations.

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AB1489 CLINICAL COURSES AND PREGNANCY OUTCOMES OF TWELVE CASES COMPLICATED WITH BEHCET'S DISEASE IN OUR INSTITUTION

Keywords: Pregnancy and reproduction, Behcet's disease

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Background: The proportion of women with Behcet's disease (BD) has increased in recent years. BD is often diagnosed at or before the time of conception, however, its impact on the clinical courses and pregnancy outcomes is not fully understood. Previous reports showed that patients with BD had a higher rate of complications such as puerperal cerebrovascular disease and gestational diabetes [1], or pregnancy outcomes like miscarriage and fetal growth restrictions [2]. Therefore, it is important to reveal the clinical course and pregnancy outcomes in patients with BD.

Objectives: The purpose of this study was to analyze the BD pregnancy cases experienced at our facility, and to idetermine the impact of disease on the course of pregnancy.

Methods: We used the data of BD patients who had been treated at planning for pregnancy and gave birth from a single center cohort of rheumatic disease pregnancy registry in our institution. The impact of BD disease activity of BD on pregnancy outocomes was examined, including therapeutic agents such as glucocorticoid (GC) and biologics.

Results: There were 12 pregnancies complicated by BD included in this analyis. The age at conception was 32.6 ± 3.6 years old, and the disease duration was 4.4 ± 3.0 years. The mean BD current activity form (BDCAF) was 0.6 ± 0.8 in 4 oral ulcers and 2 genital ulcers in the involved domain just before conception. At conception, six cases received GC, in addition, two case received adalimumab, and one case received colchicine. There were 4 cases of exacerbation of disease activity (increase of BDCAF) during pregnancy, and the active domains during pregnancy were 3 cases of oral ulcer, 2 cases of genital ulcer, and 1 case of rash and arthritis. Two cases of them needed to increase GC dose, and mean GC dose was 5.6 ± 2.1 mg per day. **Table** showed pregnancy outcomes. All cases were live births and three cases gave birth in cesarean section, two of which were emergency cesarean section due to abnormal heart rate of the infants. Mean gestational weeks was 39.2 ± 1.5 weeks, and mean birth weight was 2724.4 ± 227.1 gram. Five of the patients had had adverse pregnancy outcomes, three of which required neonatal intensive care unit (NICU) management at birth. In the cases which had exacerbation during pregnancy, three forth had these adverse pregnancy outcomes.

Table 1. Pregnancy outcomes in patients with BD

No.	outcomes	Mode of delivery	Gestational age at delivery	Birth weight of newborn	APOs	NICU administration
1	Live birth	Transvaginal delivery	38	3160		–
2	Live birth	Transvaginal delivery	41	2736		–
3	Live birth	Transvaginal delivery	38	2405	Neonatal asphyxia, LBW	+
4	Live birth	Transvaginal delivery	41	2670		–
5	Live birth	Transvaginal delivery	40	2490	LBW, LFD	–
6	Live birth	Transvaginal delivery	39	2696		–
7	Live birth	Trans vaginal delivery	39	2598		–
8	Live birth	Transvaginal delivery	39	2880		–
9	Live birth	Transvaginal delivery	40	2676	Neonatal hypervolemia	+
10	Live birth	Cesarean section	41	3108	Meconium aspiration syndrome, neonatal asphyxia	+
11	Live birth	Cesarean section	36	2714	Preterm birth, preterm PROM	–
12	Live birth	Cesarean section	38	2560		–
Mean			39.2 ± 1.5	2724.4 ± 227.1	5 (41.7)	3 (25.0)

Conclusion: In the pregnancies with BD, the disease activity was relatively stable in many cases, however, attention should be paid to the increase in disease activity, including the subsequent pregnancy outcome. It is also necessary to consider whether to continue biologics and colchicine for controlling disease activity.

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AB1490 OVERLAPPING INFLAMMATORY DISEASES IN HIDRADENITIS SUPPURATIVA PATIENTS AND THEIR FAMILIES

Keywords: Skin, Comorbidities, Rare/orphan diseases

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Background: Hidradenitis suppurativa (HS) is an inflammatory disorder characterized by chronic deep-seated nodules, sinus tracts, and scars in the intertriginous areas. A significant decrease in quality of life accompanies chronic pain of active lesions.
Association with inflammatory bowel disease (IBD) and spondyloarthropathies suggest an inflammatory signature overlap with rheumatological disorders.

Objectives: Based on the idea that the association of HS and rheumatological disease is more important and frequent than previously thought, we aimed to evaluate the symptoms and findings of rheumatological diseases in our HS patients.

Methods: Consecutive HS patients presented to the dermatology outpatient clinic between 2021-2022 are included in the study. Among the HS patients who applied to dermatology between 2021 and 2022, patients with arthralgia and low back pain were referred to the rheumatology department for evaluation. Family history was taken in detail for inflammatory conditions. Acute phase reactants were analysed.

Results: The group comprised 55 HS patients, including sixteen Hurley stage I (27.2%), 24 Hurley stage II (41.8%), and 14 (23.6%) Hurley stage III patients. The mean age of onset for HS was 28.8 (min:14, max:56). 51% (N=28) were women. Family history for HS was present in 14 (25.4%) patients. Twenty-four (43.6%) of 55 HS patients who applied to the dermatology outpatient clinic had an autoinflammatory/autoimmune disease diagnosis or inflammatory symptom/finding other than HS (Table 1). Sixteen (29%) patients described arthralgia and were referred to the rheumatology outpatient clinic. Among the HS patients, 32.7% had a significant autoimmune or autoinflammatory condition other than HS in 1st or 2nd-degree relatives. Positive family history for inflammatory processes other than HS was present in 10 (41.6%) patients with an additional inflammatory condition and 8 (25.8%) patients without a different inflammatory disease. Family history of inflammatory disorders include (Familial Mediterranean fever, acne conglabata, inflammatory bowel disease, psoriasis, Takayasu arteritis, amyloidosis, ankylosing spondylitis, uveitis, erythema nodosum, Behçet's disease and vitiligo. Serum amyloid A levels (SAA) were calculated in 16 patients, and 62.5% had elevated SAA levels.

Conclusion: Autoinflammatory rheumatological diseases or rheumatological symptoms were present in a significant proportion of HS patients. Prominent family history of inflammatory diseases suggests common genetic pathways in this spectrum of diseases. In addition, detailed history taking, including rheumatological symptoms in HS patients, is valuable and crucial in determining the extent of inflammation.

Figure1: Inflammatory findings and risky family histories of hidradenitis suppurativa patients

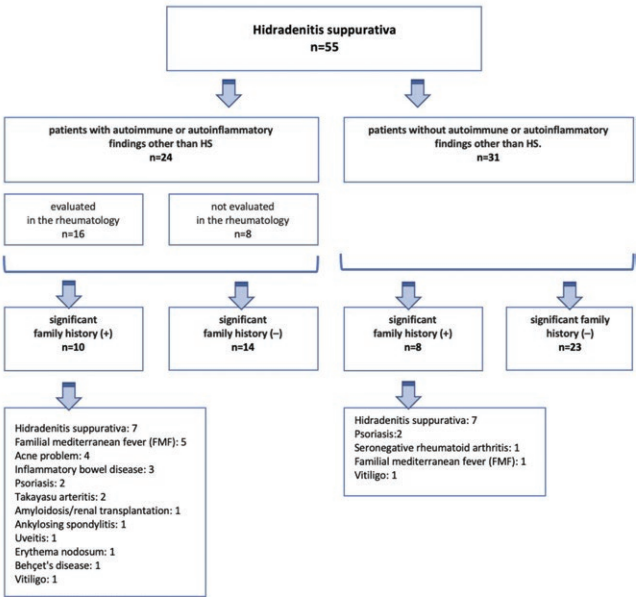


Table1: Inflammatory features of patients with autoimmune or autoinflammatory findings other than HS

Patients with autoimmune or autoinflammatory findings other than HS	n=24	%
Inflammatory joint pain or peripheral arthritis	10	41.6%
Sacroiliitis/ankylosing spondylitis	7	29.1%
Familial mediterranean fever (FMF)	5	20.8%
Oral aphtha	5	20.8%
Inflammatory low back pain	4	16.6%
Uveitis	3	12.5%
Papulopustular lesion	3	12.5%
Inflammatory bowel disease	2	8.3%
Genital aphthae	2	8.3 %
Erythema nodosum	1	4.1%
Nail psoriasis	1	4.1%
Heel pain	1	4.1%
Inflammatory neck pain	1	4.1%
Gout	1	4.1%
Sarcoidosis	1	4.1%
Autoimmune hepatitis	1	4.1%
Type1 diabetes mellitus	1	4.1%

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AB1491

CONJUNCTIVAL BIOPSY IN OCULAR CICATRICIAL PEMPHIGOID, ARE THERE PATTERNS TO PREDICT SEQUELAE?

Keywords: Rare/orphan diseases

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Background: Ocular cicatricial pemphigoid (OCP) is a chronic, immune-mediated, fibrosing disease that can lead to blindness. The diagnosis is clinical and/or based on the results of the conjunctival biopsy. There are no studies that have studied the histopathological findings and the risk of clinical sequelae in this entity.
Objectives: The describe biopsies from patients with OCP and to identify characteristics of the biopsies that may be associated with a greater risk of fibrosis and sequelae.
Methods: A retrospective, multicentre study was carried out. Patients over 18 years of age with a diagnosis of OCP by pathology were selected. Medical records were reviewed and demographic, clinical, and biopsy data were collected. To assess whether histology was associated with greater or lesser fibrosis (determined by Foster's stages), the patients were divided into two groups: early stages (0 and 1) versus stages 2, 3, and 4. The variables between the two groups were compared. groups. To determine whether immunofluorescence deposits were associated with a risk of sequelae over time, a Cox multivariate analysis was performed. Sequelae were defined as a multicomponent variable consisting of queratopia, xerophthalmia, entropion, trichiasis, cataracts, glaucoma, vitreous opacity, retinal scars, synechiae, and blindness.
Results: Fifty-seven patients with POC diagnosed by pathology were included. The mean age of presentation at diagnosis was 62.7 (SD 13.2) years and 41 (71.9%) were women. The follow-up time was 1.5 years (2.9). Patients with early Foster (stages 0 and 1) were 50.9%. The presence of rounded and spindle-shaped mast cells was associated with early stages, while the presence of eosinophils was associated with later stages at the time of diagnosis. In the immunofluorescence the presence of IgM was more frequent in early stages and IgG in the later ones, with a predominant linear pattern (92%) (Table 1). During follow-up, 15 (27.3%) patients developed sequelae. In the multivariate Cox regression analysis, the presence of IgA resulted in risk during the follow-up period for the development of sequelae; IgA positive: HR 10.8, IC 95% 1.3 a 92.9 (p-value 0.03). IgG positive; HR 0.2, IC 95% 0.02 a 1.3 (p-value 0.08); IgM positive HR 0.4, IC 95% 0.1 a 2.3 (p-value 0.29) C3 positive HR 0.2, IC 95% 0.02 a 1.7 (p-value 0.14)
Conclusion: This is one of the largest rheumatologic series that has evaluated the pathology in patients with OCP and provides information on the possible role that different antibody deposits could play in the conjunctival mucosa. The presence of IgA in the biopsy may have a role in the development of sequelae. Future larger and prospective studies could help to define the detection of different clinical patterns that give us a more accurate idea of the prognosis and treatment in these patients.

Table 1. Biopsy´s characteristics according to Foster's stage.

	Total N= 57	Early Foster (0 y 1) 29 (50.9%)	Advanced Foster (2, 3 y 4) 28 (49.1%)	P value
Hipotrofic sectors, n (%)	30 (65.2)	15 (65.2)	15 (65.2)	1
Decreased and/or absent goblet cells, n (%)	40 (76.9)	21 (80.7)	19 (73.1)	0.74
Superficial parakeratosis, n (%)	32 (58.2)	18 (64.3)	14 (51.8)	0.35
Lymphoplasmacytic infiltrates, n (%)	48 (94.1)	22 (91.7)	26 (96.3)	0.59
Infiltrates at the mucosa-submucosa or chorion-epithelial interface, n (%)	37 (88.1)	15 (88.2)	22 (88)	1
T lymphocytes, n (%)	34 (85)	12 (75)	22 (91.7)	0.19
B lymphocytes, n (%)	34 (85)	12 (75)	22 (91.7)	0.19
Rounded mast cells, n (%)	35 (67.3)	22 (81.5)	13 (52)	**0.04**
Spindle mast cells, n (%)	18 (38.3)	12 (54.5)	6 (24)	**0.03**
Degranulating mast cells, n (%)	18 (40)	9 (45)	9 (36)	0.54
Monocytes/Neutrophils, n (%)	32 (80)	11 (73.3)	21 (84)	0.44
Eosinophils, n (%)	14 (37.8)	2 (14.3)	12 (52.2)	**0.03**
Fibrosis, n (%)	27 (67.5)	9 (56.2)	18 (75)	0.3
Lymph ectasia, n (%)	43 (82.7)	23 (85.2)	20 (80)	0.72
Deposits (linear)	49 (92.4)	27 (96.4)	22 (88)	0.33
- IgG positive, n (%)	25 (43.8)	9 (31)	16 (57.1)	**0.04**
- IgM positive, n (%)	21 (36.8)	15 (51.7)	6 (21.4)	**0.02**
- IgA positive, n (%)	36 (63.2)	21 (72.4)	15 (53.6)	0.14
- C3 positive, n (%)	17 (29.8)	6 (20.7)	11 (39.3)	0.12

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AB1492

FAMILIAL MEDITERRANEAN FEVER IN GERMANY- DOES NATIONAL ORIGIN MATTER?

Keywords: Work-related issues, Rare/orphan diseases, Geographical differences

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Background: Familial Mediterranean fever (FMF) is a rare hereditary, autoinflammatory disease that is characterised by recurrent episodes of fever, increased inflammatory parameters and abdominal and thoracic pain attacks.
Germany is a low- prevalence country with approximately 5800 affected patients [1]. Due to the rarity of the disease, diagnosis is difficult and time-consuming [2]. Patients often experience a long diagnostic odyssey ensuing further physical and socioeconomic damage.
Objectives: This study aimed to investigate demographical, socioeconomic and disease-associated data, in patients with FMF in a low-incidence country like Germany.
Methods: At three German tertiary centres, adult FMF patients were included in the study. Patients were asked to report data on demographic background, disease symptoms and duration, as well as the socio-economic impact of diagnostic and surgical interventions.
Results: We included 84 adult patients (female/male 35/49), the median age was 33 years (min 18- max 94) with the confirmed diagnosis of FMF. Demographic analysis showed that 52% of FMF patients were not born in Germany (country distribution see **Figure 1).** The mean age between symptom onset and diagnosis was 4 years (0-35) for patients born in Germany and 9 years (0-65) for patients not born in Germany. Furthermore, non-German-born patients reported more disease symptoms (see **Table 1**). In both groups, the number of prior diagnostic procedures and abdominal surgeries was high (53% in German FMF patients, 56% in Non-German FMF patients). Socioeconomic effects of the disease were similar in both groups: 20% of the patients born in Germany and 22% of the non-German-born patients reported that they terminated their academic education due to the disease. Furthermore, 30% of the patients born in Germany and 27% of the patients not born in Germany reported that they lost their job due to disease related problems.
Conclusion: Our data suggest that patient care for FMF in Germany is currently not optimal. A large number of patients continue to undergo a long diagnostic odyssey with unnecessary diagnostic procedures or surgeries and also experience negative effects on their education and professional careers. Furthermore, there are differences between patients born in Germany and those not born in Germany with the latter being even more negatively affected.

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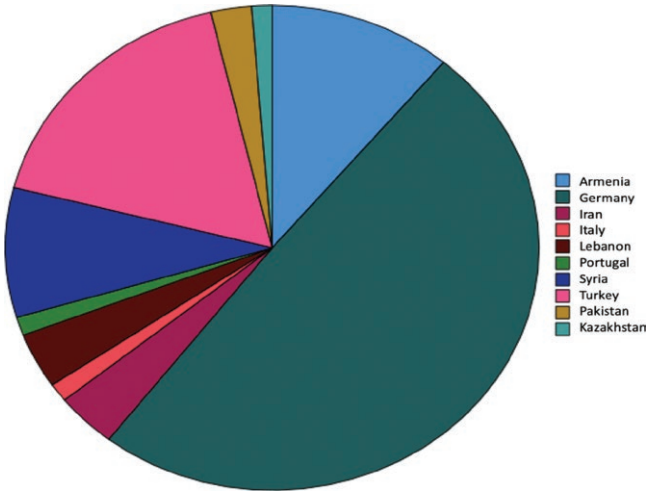


Figure 1. Country of birth in percentages: (n=84; Germany 48%, Turkey 17%, Armenia 11%, Syria 8%, Lebanon 4%, Iran 4%, Pakistan 2%, Italy 1%, Portugal 1%, Kazakhstan 1%)

Table 1. Data of patients with FMF in total and subdivided according to country of birth on demographic background, disease activity information and diagnostic and surgical interventions

	Patients with FMF		
	Total included (n=84)	Born in Germany (n=40)	Born in another country (n=41)
Age	33 (18-94)	29 (20-59)	38 (18-94)
Age at symptom onset (years)	10 (0-50)	8 (0–50)	13 (3-42)
Time to diagnosis (years)	5 (0-65)	4 (0-35)	9 (0-65)
FMF associated symptoms (%)	abdominal pain: 89 fever: 85 tiredness: 74 arthralgia: 67 fatigue: 64 chest pain: 50 joint swelling: 44 myalgia: 43 cephalgia: 40 skin inflammation: 20	abdominal pain: 83 fever: 75 tiredness: 65 arthralgia: 58 fatigue: 58 chest pain: 48 joint swelling: 40 myalgia: 25 cephalgia: 33 skin inflammation: 20	abdominal pain: 98 fever: 95 tiredness: 83 arthralgia: 78 fatigue: 73 chest pain: 49 joint swelling: 49 myalgia: 59 cephalgia: 46 skin inflammation: 22
Prior abdominal surgeries (%)	54	53	56
Appendectomy (%)	45	43	49
Diagnostic procedures before diagnosis (%)	EGD: 49 Coloscopy: 45 ERCP: 1 Laparoscopy: 10 Abdominal CT: 33 Abdominal MRI 26	EGD: 40 Coloscopy: 35 ERCP: 0 Laparoscopy: 7 Abdominal CT: 35 Abdominal MRI: 28	EGD: 59 Coloscopy: 57 ERCP: 2 Laparoscopy: 12 Abdominal CT: 32 Abdominal MRI: 27
Missed days of school due to the disease (%)	80	88	73
Missed days of work due to the disease (%)	80	70	83
Terminated education due to disease- related issues (%)	21	20	22
Lost job due to disease-related issues (%)	30	30	27

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AB1493

ADULT ONSET STILL'S DISEASE: ANALYSIS OF A MONOCENTRIC COHORT

Keywords: Rare/orphan diseases

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Background: Adult onset Still's disease (AOSD) is a systemic autoinflammatory disorder, sustained by a persistent inflammasome activation with the production of high amounts of IL-1beta and IL-18. Due to the rarity of the disorder, few multicentric cohorts of patients have been so far described.
Objectives: To analyze clinical manifestations, disease course, treatments and response to therapy in a monocentric cohort of AOSD patients.
Methods: We conducted a retrospective analysis of a cohort of consecutive patients, diagnosed as AOSD in our unit according to Yamaguchi and/or Faultrel criteria. Clinical data and therapeutic approach were analyzed; disease severity was scored by means of Pouchot score. Data were analyzed by multivariate analysis (partial least square model).
Results: We enrolled 40 patients (21 males, 19 females), mean age 63 yrs (range 21-88), age at disease onset 48 yrs. Fever and arthralgia were present in all the patients, in 77% rash, in 60% sore throat and lymphadenopathy, in 50% hepatosplenomegaly. At disease onset, 5 had intravascular disseminated coagulopathy, 4 acute respiratory distress and 2 myocarditis. In all the patients acute phase reactants were markedly increased and ferritin levels were elevated. Patients were followed for average 6,3 yrs (range 1-16 yrs): 10 patients had a monocyclic pattern, 14 polycyclic, 16 chronic articular. Mean relapses/patient

were 3,8; 26% showed >5 relapses and 7% > 25. Chronic articular pattern is the only variable that predicts the number of relapses (p=0,001). Mean Pouchot score at disease onset was 5,5 (>7 in 15 patients); it decreased to 2,2 after 6 months and was 1,2 at the last follow up visit. All the patients were treated with steroids (pulses in 18%), mean steroid dose/patient 9,6 gr. Steroids only were used in 5% of the patients, csDMARDS in 22,5% of the patients (MTX in 60%, Csa in 15%), biologicals in 72,5% (Anakinra in 62%; Tocilizumab in 28%). In 40% of the patients, steroid and one cs or bDMARD allowed to achieve disease control. In 60% one or more therapeutic switches were necessary, because of lack/loss of efficacy or adverse drug reactions. Drug retention rate was 76% at 6 months, 40% at 3 yrs and 4 yrs for Anakinra; 91% at 6 months and 36% at 5 yrs for Tocilizumab. In one patient out of 25 treated with Anakinra and in 3 out of 11 treated with Tocilizumab, the therapy was discontinued for persistent clinical remission.

Conclusion: The data we collected confirm the severity and the multisystem involvement of AOSD in a monocentric cohort with a long follow up. Among the different clinical patterns, the chronic articular one is associated with more frequent flares. Severe manifestations of the disease were present at disease onset but did not appear thereafter, suggesting the efficacy of drug therapy and close follow up. Inhibition of IL-1 and IL-6 is a safe and effective therapy. Persistent clinical remission that allows withdrawal of therapy can be obtained albeit in a small number of cases.

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AB1494 SEXUAL DYSFUNCTION IN BEHÇET'S DISEASE: IS IT AN OVERLOOKED PROBLEM, ESPECIALLY IN MALE BEHÇET'S PATIENTS?

Keywords: Behcet's disease

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Background: Behçet's disease (BD) is a chronic systemic inflammatory disease characterized by oral and urogenital ulcers, ocular, musculoskeletal, vascular, and neurological involvement. Recent evidence suggests that sexual dysfunction (SD) is prevalent in BD patients.

Objectives: We aimed to determine the frequency of SD in BD and compare the rates of SD in Behçet's patients with neurological involvement (NBD), Behçet's patients without neurological involvement (BDWONI) and healthy controls (HC).

Methods: Age matched, sexually active 59 BD (17 NBD, 42 BDWONI) patients and 36 HC were recruited. All participants were questioned with Short Form-36, Beck Depression Inventory (BDI), Golombok-Rust Inventory of Sexual Satisfaction (GRISS), Female Sexual Function Index (FSFI), International Index of Erectile Function (IIEF-5), in addition, disease activity has been assessed by Behçet Disease Current Activity Form (BDCAF) in all BD patients.

Results: The rate of SD was higher in BD patients (44.2%) compared to HC (14.2%) (p= 0.003) *(Figure 1).* Male BD patients had lower sexual function scores compared to male HC. Three parameters of GRISS (premature ejaculation, noncommunication, infrequency) were observed more frequently in male BD patients compared with male HC (6.5 vs 4.7, 3.6 vs 2.0, 3.9 vs 2.4, p< 0.05 for all). The SD rates were comparable between female BD patients and HC. SD rates were similar in BDWONI (44.2%) and NBD (42.8%) groups (p> 0.05). BDCAF score was negatively correlated with IIEF scores of male BD patients (r=-0.437) and positively correlated with GRISS scores of female BD patients (r=0.748) (p< 0.05). There was no relation between SD and depression in BD patients (p= 0.284).

Conclusion: The frequency of SD is increased in BD compared to HC and affects males more frequently than females. Premature ejaculation, infrequency and noncommunication are common sexual problems in male BD patients. In conclusion, BD has a negative effect on sexuality and BD patients should be evaluated in terms of SD during follow up.

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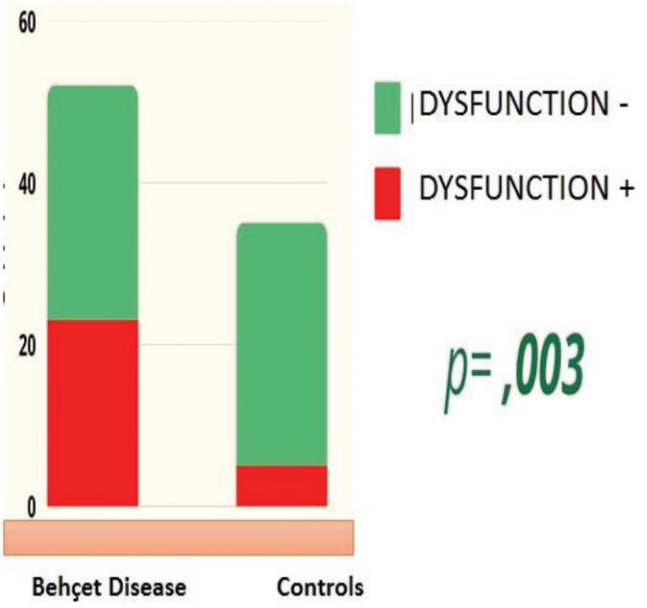


Figure 1. Numbers of patients and controls who have sexual dysfunction

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6001

AB1495 THE RELATIONSHIP BETWEEN AMYLOIDOSIS AND ATHEROSCLEROSIS IN FAMILIAL MEDITERRANEAN FEVER

Keywords: Clinical Trials, Heart, Inflammatory arthritides

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Background: Familial Mediterranean Fever (FMF) is an autosomal recessive autoinflammatory disease characterized by recurrent fever and serosal inflammation signs [1]. The most severe complication of the disease is AA amyloidosis, with increased mortality and morbidity [2].

Objectives: To determine the relationship between amyloidosis and atherosclerosis in FMF patients.

Methods: 730 FMF patients were analyzed retrospectively for the development of amyloidosis and coroner artery disease (CAD). Cut-off values of serum amyloid A (SAA), fibrinogen, c-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) variables that could predict amyloidosis and CAD were evaluated by receiver operating characteristic (ROC) analysis.

Results: The prevalences of amyloidosis and CAD were 6% and 3.7%, respectively. The incidence of CAD was higher in patients with amyloidosis (13.6%) than in patients without amyloidosis (3.1%) (p=0.004). Cut-off values that could predict amyloidosis were 44 ng/ml for SAA, 384 mg/dl for fibrinogen, 20 mm/hour for ESR, and 1.25 mg/dl for CRP (Table 1). The adjusted odds ratio for amyloidosis was 5.5-fold in patients with SSA >44 ng/ml and 3.4 in patients with ESR >20 mm/hour (Table 1). Serum AA level was significantly higher in patients with CAD (85,4±118,9) than in the group without CAD (32,4±49,5) (p=0.008). The area under the curve (AUC) values of SAA, CRP, ESR, and fibrinogen were not statistically significant for predicting CAD (Fig 1).

Conclusion: The risk of CAD is increased in amyloidosis secondary to FMF disease.

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Disclosure of Interests: None Declared.

Table 1. Cut-off SAA, fibrinogen, ESR, and CRP values for prediction of amyloidosis

	Cut-off value	AUC (%95 GA)	P value	Adjusted OR (%95 GA)	P value
SAA	44	0,788 (0,703-0,874)	**<0,001**	5,5 (2,3-12,7)	**<0,001**
Fibrinogen	384	0,728 (0,638-0,817)	**<0,001**	1,4 (0,58-3,5)	0,440
ESR	20	0,724 (0,615-0,832)	**<0,001**	3,4 (1,3-9,1)	**0,015**
CRP	1,25	0,633 (0,535-0,730)	**0,016**	0,98 (0,39-2,47)	0,964

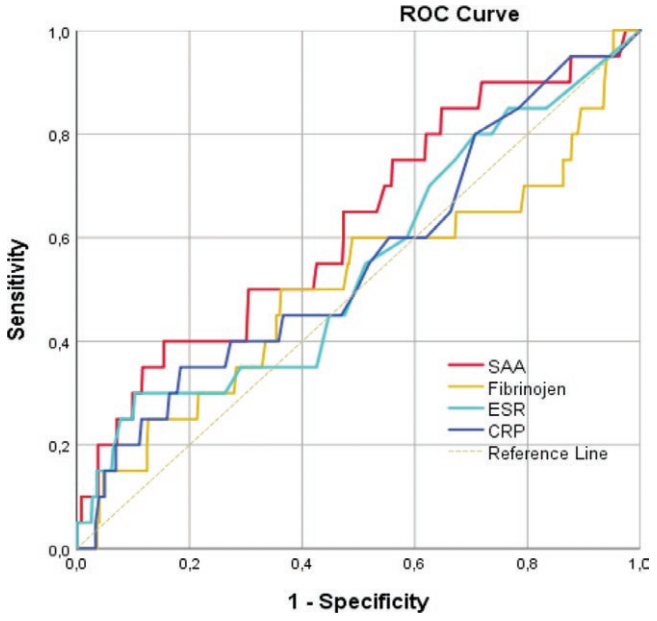


Figure 1. Receiver operating characteristic curve for acute phase markers in the prediction of coroner artery disease.

Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6217

AB1496

LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH HIDS (HYPER-IGD SYNDROME) – INTERIM ANALYSIS OF THE RELIANCE REGISTRY

Keywords: Rare/orphan diseases, Innate immunity, Real-world evidence

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Background: Hyper-IgD Syndrome/Mevalonate Kinase Deficiency (HIDS/MKD) is a rare autoinflammatory disease caused by a defect in the gene encoding mevalonate kinase. Treatment with the interleukin-1β inhibitor canakinumab (CAN, approved since 2017 for HIDS/MKD) resulted in rapid remission in most patients, both in controlled trials and in clinical practice.
Objectives: The present study investigates the long-term efficacy and safety of CAN under routine clinical conditions in pediatric (age ≥2 years) and adult patients with HIDS/MKD.
Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany. Patients with clinically confirmed HIDS/MKD diagnosis who routinely receive CAN are enrolled in the study. Disease remission, disease activity, fatigue, days absent from school/work due to study indication, and inflammatory markers are assessed at baseline and at 6-monthly intervals.
Results: The present interim analysis includes baseline (N=8) as well as preliminary 18-month (N=6) and 30-month data (N=5) from HIDS/MKD patients enrolled in the study by December 2022. Of these patients, 63% were female and median age at baseline was 8 years (2–39 years). The median duration of prior CAN treatment at study entry was 1.5 years (0–5 years). The majority of patients has been treated with greater than standard dose CAN (5/8 patients at baseline, 4/6 at month 18, 3/3 at month 30). Preliminary results indicate stable remission and disease control as assessed by physicians and patients and according to laboratory parameters (**table 1**). Even though efficacy outcomes in the HIDS cohort are based on small patient numbers, data resemble outcomes in larger cohorts within the RELIANCE registry (CAPS, TRAPS, FMF). Serious adverse events occurred in N=2 patients, but none were considered as drug related.
Conclusion: The present data from baseline and preliminary interim analysis suggest good disease control in HIDS/MKD patients participating in the RELIANCE study. In addition, data analysis at 18 and 30 months revealed no unexpected safety concerns. Further interim and end-of-study data will be analyzed to assess efficacy and safety of long-term CAN treatment in HIDS/MKD patients in the course of the study.

Table 1. Baseline characteristics and preliminary interim data of patients with HIDS/MKD.

	Baseline	18 months	30 months
Number of patients, N	8	6	5
Number of patients (consecutive patient number #1-8) in disease remission (physician assessment)	4 (#1,3,5,6)	4 (#2,5,6,7)	4 (#1,2,3,7)
Patient´s assessment of current disease activity; 0–10, median (min; max)	0.0 (0; 7)	0.0 (0; 4)	0.0 (0; 1)
Patient´s assessment of current fatigue; 0–10, median (min; max)	2.5 (0; 7)	1.0 (0; 4)	0.0 (0; 2)
Number (%*) of patients without impairment of social life by the disease	3 (50)	2 (50)	1 (50)
Number (%*) of patients with days absent from work/school during last 6 months	2 (25)	1 (17)	2 (40)
Current influence of the disease on mood; %* of patients with negative I positive I no influence	0 I 33 I 67	0 I 0 I 100	50 I 0 I 50
CRP, median (mg/dl)	0.2	0.1	0.2
SAA, median (mg/dl)	0.6	0.4	1.7
ESR, median (mm/h)	10.0	10.5	6.0
SAE	**Number of events**	**Incidence rate‡ per 100 patient-years**	
All types of SAE	2	8.95	
SADR	0	0.00	

CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; SAA, serum amyloid A; SADR, serious adverse drug reaction; SAE, serious adverse event*not reported for all patients‡ Incidence rate = number of events * 36525/ sum of observation days (=8159)

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Prasad Oommen Grant/research support from: Novartis, Tilmann Kallinich Speakers bureau: Roche, Jürgen Rech Speakers bureau: AbbVie, Biogen, BMS, Chugai, GSK, Janssen, Lilly, MSD; Mylan, Novartis, Roche, Sanofi, Sobi, UCB, Consultant of: AbbVie, Biogen, BMS, Chugai, GSK, Janssen, Lilly, MSD, Mylan, Novartis, Roche, Sanofi, Sobi, UCB, Grant/research support from: Novartis, Sobi, Norbert Blank Consultant of: Novartis, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD, Actelion, UCB, Boehringer-Ingelheim, Roche, Grant/research support from: Novartis, Sobi, Julia Weber-Arden Employee of: Novartis, J. B. Kuemmerle-Deschner Consultant of: Novartis, AbbVie, Sobi, Grant/research support from: Novartis, AbbVie, Sobi.
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AB1497

LIVER STIFFNESS IN FAMILIAR MEDITERRANEAN FEVER: ASSOCIATION WITH ENDOCAN AND PULSE WAVE VELOCITY

Keywords: Biomarkers, Imaging

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Background: Familial Mediterranean Fever (FMF) is the most common monogenic periodic fever syndrome; it is characterized by recurrent self-limited episodes of

fever, articular and serosal inflammation, and accumulation of polymorphonuclear cells into affected tissues. Recurrent inflammatory process during the attacks, and the potential chronic inflammatory status during attack-free intervals, could lead to endothelial dysfunction (ED) and atherosclerosis in FMF patients. Biomarkers could help in demonstrating ED in FMF patients. Serum endocan is a dermatan sulfate proteoglycan–structured molecule very specific for endothelium; its synthesis is stimulated by inflammatory cytokines and could be a surrogate marker of atherosclerosis.
Objectives: We designed a cross sectional study to evaluate the pulse wave velocity (PWV) as marker of arterial stiffness, carotid intima media thickness (cIMT), liver stiffness (LS, by means of FibroScan), and plasma endocan as markers of atherosclerosis process. Inflammatory markers (IM) were also evaluated.
Methods: IM, endocan plasma levels, PWV, cIMT and LS were determined in 20 FMF patients (11 men) with a median age of 36±22 years (median age at the first attack was 4 (2–7) years), and 20 matched controls (10 men) with a median age of 35±23.
Results: The body mass index 25.3±4.8 in patients was and 25.5±4.9 in controls. All subject had normal lipid profile and were not affected by diabetes or taking alcohol. All FMF patients were treated with colchicine, and 2 patients were on canakinumab. We found no differences as regards IM and cIMT in patients and controls. Endocan levels were 3-fold higher in patients as compared to controls. PWV were higher in FMF patients (8.17±2.02) with respect to controls; LS was 6.1±3.71 kPa in patients vs 5.2±2.1 kPa in controls. Hepatic Steatosis was found in 9 FMF patients (2 patients had severe steatosis, 3 moderate, and 4 mild) and 7 controls (3 moderate and 4 mild). A positive correlation was found between LS and endocan ($p<0.05$) and PWV ($p<0.05$) in FMF patients.
Conclusion: The risk of endothelial dysfunction is significantly increased in patients with FMF; moreover, a possible link between liver steatosis and CV damage could be suggested in this clinical setting.
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Acknowledgements: NIL.
Disclosure of Interests: Alberto Lo Gullo Grant/research support from: Bayer, Galapagos, Arianna Toscano: None declared, Michele Scuruchi: None declared, Carmela Morace: None declared, Maria Cinquegrani: None declared, Davide Sinicropi: None declared, Giovanni Squadrito: None declared, Michele Colaci: None declared, Giuseppe Mandraffino: None declared.
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AB1498 MANIFESTATIONS OF BONE LYMPHOMA IN A RHEUMATOLOGY DEPARTMENT

Keywords: Malignancy

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Background: Bone lymphoma is rare disease, its diagnosis is usually delayed due to the unspecefic clinical and radiological signs.
Objectives: Our objective was to describe the clinical, biological and radiological aspects of bone lymphoma to optimize diagnostic approaches.
Methods: 14 cases of bone lymphoma were collected in the Rheumatology Department of Sousse between 2001 and 2022.
Results: The mean age was 42 with a sex ratio of 1. The main symptom in 14 patients was pain associated with deterioration of general condition (10 cases), swelling of lymph glands (8 cases), fever and night sweats (6 cases), neurological signs (6 cases) with a diagnostic delay of 4 months. In biology, 13 patients had biological inflammatory syndrome, 2 of the 14 patients had hypercalcemia with a mean of 2.85, 6 patients had elevated LDH and 6 had elevated PAL. The abnormalities of the CBC were anemia in 10 cases, leukopenia in 1 case, hyperleukocytosis in 6 cases. On imaging, the lesions were single in 6 cases and multiple in 8 cases. A lytic process was found in 9 cases, osteocondensation in 3 cases and mixed lesions in 2 cases. Cortical rupture was noted in 3 cases. The soft tissues were infiltrated in 8 cases. The sites were vertebral (8 cases), sacrum (2 cases), iliac (1 case), long bone (3 cases). MRI showed a T1 hypo signal and T2 hyper signal in all cases, bone scintigraphy was performed in 6 patients and showed hyperfixation in 5 cases and a heterogeneous aspect in 1 case. A bone or lymph node biopsy was performed in all 14 patients, confirming the diagnosis and showing Hodgkin's lymphoma in 6 cases and non-Hodgkin's lymphoma in 8 cases, 7 of which were diffuse large-cell B lymphomas.
Conclusion: Due to the rarity and the various clinical and radiological presentations of bone lymphoma, the diagnosis may be difficult which is why the biopsy so important.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6443

AB1499 TWO DISTINCT SUBSETS OF IMMUNE CHECKPOINT INHIBITOR-INDUCED INFLAMMATORY ARTHRITIS DEFINED BY LATENT CLASS ANALYSIS

Keywords: Malignancy, Inflammatory arthritides

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Background: Immune checkpoint inhibitors (ICI) can lead to immune related adverse events, including inflammatory arthritis (IA). ICI-IA is heterogeneous and can be severe, even persisting after ICI cessation. Understanding the clinical heterogeneity of ICI-IA can guide future studies of pathogenesis and identify relevant groups for clinical trials.
Objectives: To define clinically relevant subgroups within ICI-IA using a data driven approach and to examine differences between subgroups.
Methods: Participants were >=18 years old, treated with anti-PD-1, anti-PD-L1, and/or anti-CTLA-4 agents alone or in combination, and had ICI-IA diagnosed by a rheumatologist. We used information from the baseline rheumatology visit (patient reported symptoms, physical exam features, physician global arthritis rating, and laboratory studies) to cluster patients with latent class analysis. The Bayesian Information Criteria (BIC) was used to select the number of phenotypes with the lowest BIC. We then compared demographics, cancer type and treatments, and IA treatments and outcomes between the estimated phenotypes. Next, we estimated the association between these features of interest and the likelihood of being in the group with the most severe IA symptoms using logistic regression.
Results: Of the 126 patients with ICI-IA, the majority of participants were female (56%) and white (92%). Most patients had a moderate or high level of disease activity by CDAI; the mean CDAI was 16.98 (SD 10.2). Eighteen variables were used to estimate latent classes. Two distinct phenotypes were indicated by the BIC; 61 patients are estimated to be the first phenotype and 65 the second phenotype. Participants in the second phenotype were more likely to have high baseline levels of patient reported pain, stiffness, and disease activity (Figure 1). There were no significant differences in age, gender, race, ethnicity or marital status between the two phenotype groups. Patients in phenotype 2 were more likely to require steroids as compared to patients in phenotype 1 and were more likely to have persistent IA (table 1). Type of ICI therapy, type of cancer, prior chemotherapy or radiation did not differ between the groups. When adjusted for age, gender, baseline steroid use, these variables remained significantly associated with the second phenotype.
Conclusion: Two separate phenotypes of ICI-IA were determined with latent class analysis. Those in the group with more severe features at baseline were more likely to need corticosteroids and to have persistent IA, but there was no association with cancer history or treatment. Future research can interrogate underlying genetic and immunologic differences between groups.

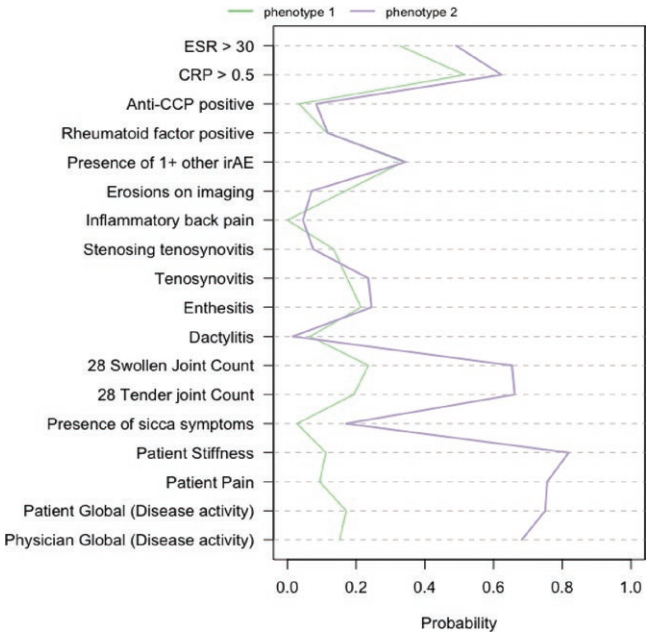


Figure 1. Predicted probabilities of features for two estimated phenotypes

Table 1. Comparison of cancer features, arthritis treatment, and outcomes between estimated phenotypes

		Phenotype 1		Phenotype 2	
Feature	**N**	**Mean (SD) or N(%)**	**N**	**Mean (SD) or N(%)**	**p**
Cancer related					
Cancer type	61		65		0.263
Melanoma		20 (33%)		21 (32%)	
Lung cancer		14 (23%)		16 (25%)	
GU cancer		3 (5%)		4 (6%)	
GI cancer		5 (8%)		12 (18%)	
Breast		3 (5%)		3 (5%)	
SCC		7 (11%)		1 (2%)	
Other		9 (15%)		8 (12%)	
Cancer Stage	59		64		0.643
2		2 (3%)		3 (5%)	
3		10 (17%)		15 (23%)	
4		47 (80%)		46 (72%)	
Prior radiation	61		65		0.850
Yes		20 (33%)		20 (31%)	
Prior chemo	57		63		1.000
Yes		30 (53%)		34 (54%)	
ICI class	61		65		0.757
Ipi		2 (3%)		2 (3%)	
Anti-PD1		38 (62%)		40 (62%)	
Anti-PD-L1		7 (11%)		4 (6%)	
Combo ipi nivo		13 (21%)		15 (23%)	
Other		0 (0%)		2 (3%)	
Nivo/relatlimab		1 (2%)		2 (3%)	
ICI duration at baseline (months)	61	9.4 (8.7)	65	9.9 (10.0)	0.767
Inflammatory arthritis related					
Symptom duration at baseline (months)	61	6.3 (7.7)	65	8.0 (10.4)	0.304
Patient on steroids at baseline	61		65		0.544
Yes		14 (23%)		19 (29%)	
Steroid (any)	61		65		**0.010**
Yes		47 (77%)		61 (94%)	
Steroid injections in the joint since starting ICI ICIIIClimmunotherapy	33		36		0.585
Yes		7 (21%)		10 (28%)	
Any csDMARd	61		65		0.135
Yes		17 (28%)		27 (42%)	
other		2 (12%)		0 (0%)	
Any biologic	61		64		0.075
Yes		8 (13%)		17 (27%)	
Erosions on imaging	19		27		0.635
Yes		3 (16%)		2 (7%)	
Persistent >6 months after ICI stop	54		60		**0.024**
Yes		37 (69%)		52 (87%)	

REFERENCES: NIL.

Acknowledgements: NIL.

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AB1500

TNF INHIBITORS ARE SAFE AND EFFECTIVE IN PATIENTS WITH SEVERE BEHÇET'S DISEASE: DATA FROM EASTERN TURKEY, INTERSECTION OF THE SILK ROAD

Keywords: Innate immunity, bDMARD, Behcet's disease

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Background: Behçet's disease(BD) is a chronic inflammatory multi-systemic disease that affect skin-mucosa, joints, eye and blood vessels. Biological disease modifying anti-rheumatic drug(b-DMARD) treatment is an emerging option into the management of severe BD.

Objectives: We aimed to evaluate the clinical features and associated factors of outcome in patients with BD receiving b-DMARD treatment.

Methods: This retrospective observational study was carried out in a tertiary referral center in Van province, Eastern of Turkey.Remission was defined as no exacerbation and/or new development of clinical manifetations attributed BD at least three months. Active disease and/or relapse was defined as inadequate response to conventional treatment and/or new development of organ or system manifestations under the treatment. Ongoing mucocutaneus manifestations did not consider as active disease or relapse.

Results: We included 80 BD patients(76.3% male) who received b-DMARD therapy into the study. Mean±standard deviation(SD) of the patients was 33.3±8.8 years and median(interquartile range [IQR]) disease duration was 10(12) years. Among those patients, recurrent oral ulcer was in 98.5%, genital ulcer in 71.3%, pseudofolliculitis in 80%, erythema nodosum-like nodular lesions in 67.5%, superficial thrombophlebitis in 37.5%, uveitis in 53.8%, pathergy positivity in 66%, arthritis in 46.3%, spondylitis in 9%, gastrointestinal(GIS) involvement in 7.5%, parenchymal central nervous system(CNS) in 11.3%, parenchymal lung in 3.8%, vascular in 44%. While 28 patients(35%) had venous and 7 patients(8.8%) had arterial involvement. Overall, nearly all patients received colchicine(98.8%) and azatiopyrine (98.8%) as a background therapy, cyclophosphamide was used in 11.3%, cyclosporin in 22.5%, mycophenolate in 3.8% and interferon in 30%.Infliximab(IFX) and adalimumab(ADA) were initiated in 54(67.5%) and 26(32.5%) patients, respectively.Overall and first line retention rate were 84.7% and 92.6% for IFX and 83.3% and 80.8% for ADA, respectively(table 1).IFX was stopped in 9 patients which were in 2 patients due to allergic reaction and tuberculosis, 3 patients for inefficacy, one patient for heart failure and one patient for orbital zona.Although, no serious advers event was observed with ADA, 5 patients were switched to IFX for inefficacy.While during the follow-up, lung lobectomy were needed in one patients, no death was observed.Overall, 72 patients(90%) resumed b-DMARD end of the study;b-DMARD was stopped in 3 patients(3.8%) due to severe advers events and in 5 patients(6.2%) prolonged remission. All those patients were retained in remission after b-DMARD cessation. GIS involvement was negatively associated with b-DMARD retention in univariate(4.2% vs 33.3%;p=0.017,OR:9.8) and multivariate analysis(p=0.01,OR: 0.09,95 % confidence interval [CI]: 0.014-0.575).Higher disease duration(p=0.007,OR:5.8,95 %CI:1.6-20.8), superficial thrombophlebitis (p=0.018,OR:1.14,95%CI:1.024-1.28) were associated with corticosteroid withdrawal in multivariate analysis.

Conclusion: During the follow-up, no case of death was observed among b-DMARD receiving BD patients.Most patients were in remission, steroid-off and also retained on b-DMARD treatment.Biological treatment was safe and effective in patients with severe Behçet's disease.

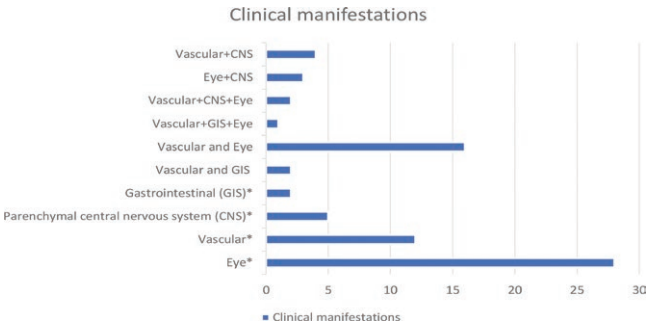


Figure 1.

Table 1. Treatment Responses of b-DMARD in patients with Behçet's Disease

Variables	**Total (n=80)**	**Infliximab (n=59)**	**Adalimumab (n=30)**	**p value**
Continuation rate, n (%)				
Overall	72 (90)	50 (84.7)	25 (83.3)	0.9
As first line	71 (88.8)	50 (92.6)	21 (80.8)	0.1
b-DMARD duration, months, median (IQR)				
Overall	49.2±30.8 (16-102)	29±22 (1-96)	26.4±17.2 (3-60)	0.6
As first line	25.5±17.8 (1-115)	25.9±19.5 (1-115)	24.3±13 (3-59)	0.7
Withdraval of steroid, n (%)				
Overall	62 (77.5)	42 (71.2)	27 (90)	***0.04 (OR:2)***
As first line	55 (88.7)	38 (70.4)	24 (92.3)	***0.03 (OR:4.8)***

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1501 **MUSCLE BIOPSY PRACTICES: AN INTERNATIONAL SURVEY**

Keywords: Diagnostic Tests, Myositis

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Background: Muscle biopsy is an important tool in assessment of idiopathic inflammatory myopathies (IIM), however the optimal approach is unknown. A variety of biopsy procedural techniques have been reported including open surgical biopsy, percutaneous needle biopsy and Conchotome forceps biopsy.
Objectives: This study aimed to describe current practices in obtaining a muscle biopsy amongst international experts who manage people with IIM.
Methods: An e-survey was designed and piloted to collect information regarding muscle biopsy practices. The e-survey was disseminated to members of the International Myositis Assessment and Clinical Studies (IMACS) group. Snowball sampling was used, whereby IMACS members were invited to forward the survey link to other clinicians involved in care of people with IIM. Information regarding respondent characteristics and their current practice in obtaining muscle tissue was collected. The e-survey was available for completion between 20th October 2022 and 20th of January 2023. Participants were included if they self-reported being a clinician or researcher with experience in IIM. Results were analysed using descriptive statistics.
Results: One hundred and one respondents completed the survey by 12th January 2023. Most respondents were from Europe (22.7%) and the United States (22.7%) followed by Asia (7.9%). The majority of respondents were rheumatologists (74.3%) and neurologists (20.8%) working in academic settings (73.3%). Open surgical biopsy was the most common method of muscle sampling (Table 1). Open surgical biopsies were often performed under local anaesthesia (55.6%) and without sedation (50.0%) or general anaesthesia (58.9%). Clinical examination was frequently used to guide muscle selection (85.4%), followed by MRI (50.0%) and EMG (43.8%). The influence of clinical and laboratory characteristics on decision to pursue muscle biopsy are presented in Figure 1. Many respondents were more likely to pursue diagnostic biopsy in the setting of seronegativity (65.6%), abnormal MRI (58.3%) and abnormal neurophysiology (56.3%). Conversely, many were less likely to pursue diagnostic biopsy in setting of positive myositis specific antibodies (53.2%) or classic dermatomyositis rash (70.8%). Low complication rates were reported for all muscle biopsy techniques. Non-diagnostic histopathology was reported as 'common' (observed rate between 1-10%) in 30.5% and 'very common' (observed rate ≥10%) in 14.8% of respondents.
Conclusion: Open surgical biopsy was the most common muscle biopsy approach reported by international experts who manage IIM. Clinical examination, MRI and EMG were frequently used to select a muscle to biopsy. Serology, radiographic and neurophysiological status and the presence of a classic dermatomyositis rash influence the decision to pursue diagnostic biopsy. Muscle biopsy is safe, although non-diagnostic histopathology was commonly reported regardless of technique.
Reference: Nil.

Table 1. Approaches and indications for muscle biopsy. Presented as frequency (%). *respondents could select >1 answer

Muscle biopsy approaches available at respondents' institution*	Frequency (%)
Needle or percutaneous biopsy	16 (13)
Conchotome forceps biopsy	12 (9.8)
Open surgical biopsy	90 (73.2)
Unsure	5 (4.1)
Most commonly used technique by respondent	
Open surgical biopsy	75 (74.3)
Needle or percutaneous biopsy	9 (8.9)
Conchotome forceps biopsy	9 (8.9)
Unsure	8 (7.9)
Indications for biopsy*	
Possible IIM	94 (42.0)
Toxin or drug induced muscle disease	32 (14.3)
Hereditary muscle disease	47 (21.0)
Degenerative muscle disease	33 (14.7)
Reaction to volatile anaesthetics	2 (0.9)
Research	16 (7.1)

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Disclosure of Interests: None Declared.
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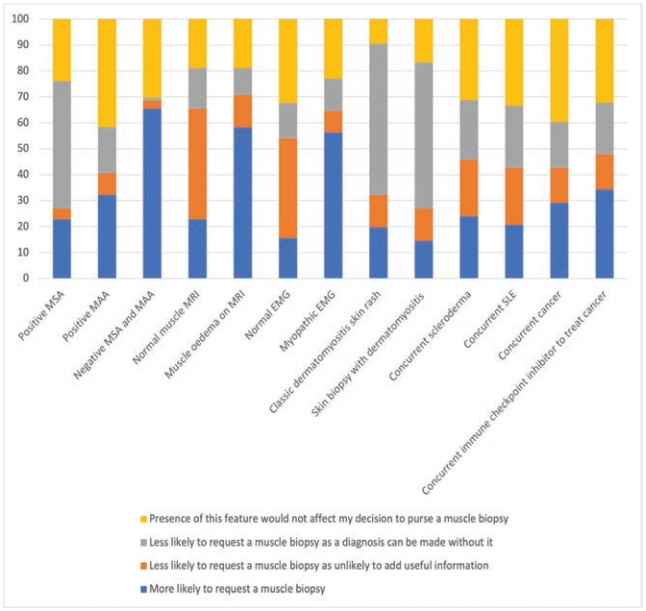


Figure 1. Influence of clinical and laboratory characteristics on decision to pursue muscle biopsy. MSA: Myositis Specific Antibody; MAA: Myositis Associated Antibody; MRI: magnetic resonance imaging; EMG: electromyography

AB1502 **FACTORS ASSOCIATED WITH VISION-RELATED QUALITY OF LIFE IN NON-INFECTIOUS UVEITIS PATIENTS: A LONGITUDINAL ANALYSIS**

Keywords: Uveitis, Quality of life, Patient reported outcomes

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Background: Non-infectious uveitis (NIU) are characterized by inflammation of the middle layer of the eye wall and have a significant impact on patients' visual-related quality of life (VRQoL). Objective measures of vision, such as visual acuity, do not fully account for the impact of these diseases on the patients' perceived QoL, as it includes other relevant and important aspects not evaluated in routine clinical practice. The assessment of the patient's QoL through standardized and validated questionnaires allows us to evaluate objectively the actual burden of the disease. Several cross-sectional studies have shown that the VRQoL of NIU patients is reduced. However, the evidence regarding how QoL evolves in real life clinical practice and what characteristics influence this evolution is scarce.
Objectives: To describe the evolution of the VRQoL in subjects with NIU and to identify factors associated with increased or decreased VRQoL during follow-up.
Methods: Prospective longitudinal observational study including consecutive NIU patients from a tertiary uveitis clinic from Madrid (Spain). Main outcome was the composite score of the Visual Functioning Questionnaire 25 (VFQ25), measured at baseline and after 1 and 2 years of follow-up. Influence of demographic, clinical, and treatment-related variables (assessed at the same time points) in repeated measures of VRQoL was analyzed using bivariable and multivariable generalized estimating equations (GEE) models nested by patient.
Results: One hundred and forty five patients were included in the analysis, with 422 visits. In the two years of follow up, no significant changes were observed in the evolution of the VFQ25 (Figure 1). In the multivariate analysis, lower best corrected visual acuity, presence of permanent work disability, being unemployed, cells in anterior chamber ≥2+, previous cataract surgery, previous glaucoma surgery, other intraocular surgeries, and prescription of synthetic immunosuppressive drugs were independently associated with lower VFQ25 (Table 1).
Conclusion: In the two years follow-up of our study, we did not identify significant changes in the evolution of the VRQoL in NIU patients. Nevertheless, we found some social factors that could contribute to a decreased VQ25 during follow-up. Essentially, work status and financial well-being. Clinical variables were also identified, such as lower visual acuity and factors that might reflect active disease (cells in anterior chamber ≥2+ and prescription of synthetic

immunosuppressive drugs). We also detected that previous ocular surgery might contribute to a lower VQ25 score. This preliminary data allows us to evaluate other variables that contribute to the burden of the disease and the extent of the patient's suffering regarding their vision and reflect the importance of identifying them to improve our patients' quality of life.

Table 1. Multivariate analysis to assess the influence of socio-demographic and clinical related variables in the VRQoL of a cohort of NIU patients.

Variable	Coef (95% IC)	p-value
Women	1.82 (-0.98 to 4.63)	0.21
BCVA (logMAR)	-8.18 (-10.93 to -5.43)	$5.68x10^{-9}$
Baseline visit	Ref.	
1 year visit	-0.18 (-1.68 to 1.32)	0.81
2 year visit	-0.9 (-1.50 to 1.11)	0.77
BCVA X 1 year visit	4.61 (2.30 to 6.93)	$9.5x10^{-5}$
BCVA X 2 year visit	4.46 (3.03 to 5.88)	$9.18x10^{-10}$
Married	1.96 (-0.34 to 4.26)	0.09
Permanent work disability	-27.42 (-36.90 to -17.93)	$1.47x10^{-8}$
Unemployed	-7.04 (-10.82 to -3.27)	$2.6x10^{-4}$
Cells in anterior chamber ≥ 2 +	-3.85 (-7.03 to -0.67)	0.02
Cataract surgery	-4.61 (-8.15 to -1.07)	0.01
Glaucoma surgery	-14.51 (-24.72 to -4.30)	0.01
Other intraocular surgery	-6.77 (-10.53 to -3.01)	$4.2x10^{-4}$
No ISD use	Ref.	
Synthetic ISDs	-5.38 (-8.19 to -2.56)	$1.9x10^{-4}$
Biological ISDs	3.11 (-0.59 to 6.81)	0.01
Synthetic and biological ISDs	-2.22 (-5.79 to 1.34)	0.22

VA: visual acuity; BCVA: best corrected visual acuity; logMAR: logarithm of the minimum angle of resolution; ISDs: immunosuppressive drugs; Coef: correlation coefficient

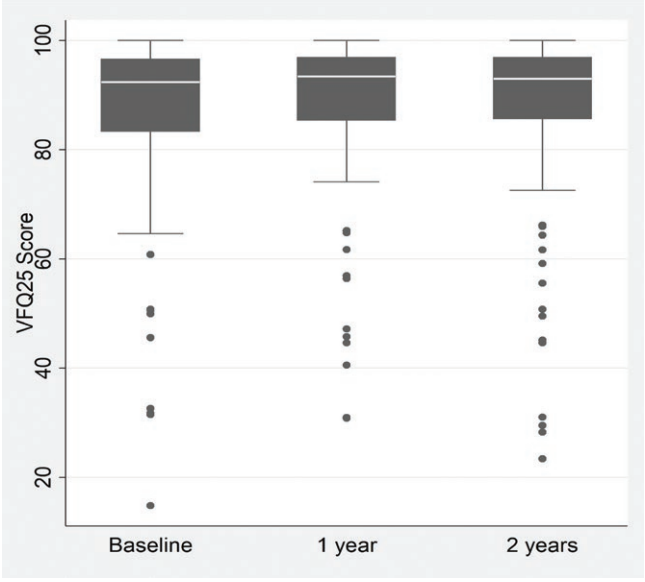


Figure 1. VFQ25 during follow-up

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1503 **THE IMPACT OF OBESITY ON CLINICAL COURSE AND BIOLOGIC DMARD FAILURE IN PATIENTS WITH ADULT ONSET STILL'S DISEASE**

Keywords: Rare/orphan diseases, Comorbidities, Prognostic factors

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Background: Adult onset Still's disease (AOSD) is a rare inflammatory disease characterised by fever, arthritis, evanescent cutaneous rash and a typical hyperferritinemia [1]. Three clinical disease courses are usually identified: i. monocyclic, characterised by a single episode; ii. polycyclic, characterised by multiple flares, alternating with remission; iii. chronic, related to a persistent active disease [1]. AOSD may be also burdened by the occurrence of life-threatening complications. The prognosis of AOSD may be affected by the presence of comorbidities; however, the impact of obesity on these patients has not fully elucidated yet. The obesity may be considered as a negative prognostic factor in patients with rheumatic diseases. In fact, it is associated with a higher disease activity, an enhanced disability, and a less probability to achieve the clinical remission [2,3].
Objectives: We assessed the impact of obesity on clinical disease course and biologic DMARD failure in patients with AOSD. We also evaluated the influence of obesity on life-threatening complication occurrence.
Methods: An assessment of obese patients with AOSD characterised by a BMI≥30 was provided among those evaluated in Gruppo Italiano di Ricerca in Reumatologia Clinica e Sperimentale (GIRRCS) cohort [4]. The presence of obesity was evaluated at the time of diagnosis and defined as BMI≥30. Cox regression analyses were performed to evaluate the predictive role of obesity on predicting different disease courses and bDMARD failure in our cohort. Multivariate analyses were adjusted for age, gender, and systemic score, which was used as marker of disease severity.
Results: In this study, 139 patients were evaluated; 26 (18.7%) had a BMI≥30 and were defined as having obesity at the time of disease diagnosis (mean age of 39.3±13.6 years, 12 male gender). Obese patients did not differ in the main clinical characteristics than non-obese [fever BMI≥30: 96.2% vs BMI<30: 99.1%, p=0.340; skin rash BMI ≥ 30: 84.6% vs BMI<30: 69.0%, p=0.147; arthritis BMI≥30: 61.5% vs BMI<30: 56.6%, p=0.826]. Furthermore, obese patients showed a higher rate of bDMARD failure in the subsequent follow-up (p=0.037). In addition, obese patients with AOSD were characterized by higher values of C-reactive protein (CRP) [BMI≥30: 109.2 mg/L (IQR 117.0) vs BMI<30: 52.0 mg/L (IQR 84.3), p=0.046] than others. Obese patients with AOSD had also higher values of CRP than 2:1 age-, gender-, and BMI-matched obese patients without immune mediated inflammatory disease (IMID) (Age: 39.8 ± 13.2 years, 24 male gender out 52 patients, BMI: 32.4 ± 3.1, CRP 33.8 mg/L [IQR 34.4], p<0.001). These obese patients without IMID were recruited to fully evaluate the impact of obesity on CRP in patients with AOSD. Additionally, obesity predicted the development of a chronic disease course in patients with AOSD in both univariate (HR: 1.72, 95%CI: 1.03-2.51, p=0.038) and multivariate analyses (HR: 1.85, 95%CI: 1.45-2.89, p=0.041). Non-significant results were obtained assessing the predictive role of obesity on monocyclic and polycyclic disease courses. Furthermore, obesity resulted to be a significant predictor of failure of at least one of biologic DMARD in patients with AOSD in both univariate (HR: 3.03, 95%CI: 1.42-6.45, p=0.004) and multivariate analyses (HR: 3.59, 95%CI: 1.55-8.27, p=0.003). Conversely, obesity did not influence the development of life-threatening complications in our cohort.
Conclusion: The presence of obesity resulted to be a predictive factor for the development of a chronic disease course and biologic DMARD failure in patients with AOSD. In addition to increase the inflammatory burden, a high BMI may be indeed associated with a more rapid clearance, a higher volume of distribution, and a consequent low concentration of biologic DMARDs and their possible clinical failure.
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AB1504 **CLINICAL SPECTRUM OF IGG4-RELATED DISEASE. SINGLE UNIVERSITY HOSPITAL EXPERIENCE AND LITERATURE REVIEW**

Keywords: Vasculitis, Systematic review, Organ damage

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Background: IgG4-related disease (IgG4-RD) is an inflammatory and fibrosing entity with very heterogeneous clinical manifestations. Its pathogenesis remains unknown, clinical features are heterogeneous and unspecific, and recently

released classification criteria are invaluable in early recognition of the disease. Therefore, regrettably IgG4 related disease continues underdiagnosed.
Objectives: a) To evaluate the clinical characteristics of patients diagnosed with IgG4-RD in a single University hospital; **b)** To compare with other large series.
Methods: Study of patients from a referral hospital and literature review of cases diagnosed with IgG4-RD. Diagnosis was made accordingly to these criteria**: a)** Okazaki; **b)** Umehara; **c)** ACR/EULAR 2020; and/or **d)** clinical, laboratory and imaging suggestive findings **(ref. 1-3)**. For the literature review, we searched PubMed and the Cochrane library from its inception until 31 December 2022, selecting the largest series.
Results: We include 11 patients (7 females/4 males) (mean±SD age; 61.2±15.6 years) diagnosed with IgG4-RD. The organs affected at diagnosis were: aorta (n=5), pleura/lung (n=4), lymph nodes (n=3), salivary glands (n=2), retroperitoneum (n=2), lacrimal glands (n=1), bile duct (n=1), kidney (n=1), orbit (n=1), subglottis (n=1), pericardium (n=1), mesentery (n=1), maxillary sinuses (n=1). IgG4 values were increase in 2 (18%) patients (median [IQR]; 250.5 [201.0-300.1] mg/dL) (normal value <135 mg/dL). Blood plasmablasts were increased in 8 (73%) patients (median; 831 [785-1218] cells/mL) (normal values <653 cells/mL). In the literature review, 6 series of more than 100 patients each were selected. The main data from the different series are listed in **table 1**. The **figure** shows the most frequently affected organs in the different series. The pancreas was one of the most frequently involved. In contrast, in our series, aortic involvement followed by lung/pleura were the most frequent.
Conclusion: IgG4-RD is a very heterogeneous disease with involvement of virtually every organ of the anatomy, usually presenting with involvement of more than one organ. Despite the name of the entity, serum IgG4 is not always elevated.
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Table 1. Main features in series of more than 100 patients and in current series

Reference	Cases	Sex Female (F)/ Male (M)	Age, median [IQR] or mean±SD	Diagnosis criteria	Number of organs affected	Level of serum IgG4 (mg/dL), median [IQR]
Lanzillotta et al. Rheumatology 2020	131	F (n=36), M (n=95)	62 [53-70]	-Umehara: possible (46%), probable (2%), definitive (52%)	-1 organ (26%) -More of 1 organ (74%)	224 [115-382]
An et al. Orphanet J Rare Dis 2022	127	F (n=35), M (n=92)	63 [55-69]	-Umehara: possible (82.6%), probable (2.3%), definitive (11.8%)	-1 organ (20%) -2-4 organs (68%) -More of 5 organs (9%)	980 [390-1520]
Zongfei et al. Clin Rheumatol 2021	102	F (n=25), M (n=77)	62 [54.1-65.8]	-Okazaki (100%)	Median [IQR]: 2 [1-3]	399 [199-776]
Wang et al. Arthritis Res Ther 2018	215	F (n=67), M (n=148)	54 [46-62]	-Umehara: possible (47.9%), probable (4.7%), definitive (47.4%)	-1-2 organs (36%) -3-4 organs (47%) -5 or more organs (17%)	896 [350-1860]
Inoue et al. Medicine (Baltimore) 2015	235	F (n=189), M(n=46)	67	-Symptoms+laboratory +image/ Compatible histology (100%)	-1 organ (41%) -2 or more organs (59%)	470 [ND]
Wallace et al. Arthritis Rheumatol 2015	125	F (n=49), M (n=76)	50.3±14.9	- Symptoms+laboratory +image/ Compatible histology (100%)	-1 organ (38%) -2 organs (24%) -3 or more organs (38%)	ND
Current series	11	F (n=7), M (n=4)	57 [54.5-73.5]	-Okazaki: 45% -Umehara: possible (18%), probable (18%), definitive (9%) -ACR/EULAR 2020 (9%) -Symptoms+laboratory +image/ Compatible histology (54%)	-1 organ (36%) -2 organs (27%) -3 or more organs (36%)	66.3 [22.2-116.3]

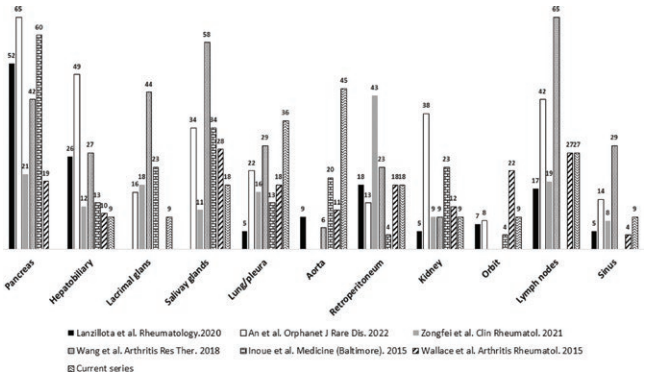


Figure 1. Involved organs in series of more than 100 patients and in current series (%)

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AB1505

THE COMPARISON OF THE EFFICACY OF INTERLEUKIN (IL)-23 TARGETED DRUGS IN THE TREATMENT OF CROHN'S DISEASE: A BAYESIAN NETWORK META-ANALYSIS

Keywords: Systematic review, Gastrointestinal tract

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Background: Crohn's disease (CD) is a chronic inflammatory disease of unknown etiology. The IL-23/IL-17 pathway plays an essential role in the pathogenesis of CD. More and more approved IL-23 inhibitors are being used for the treatment of CD. However, no studies have systematically compared and evaluated the efficacy of these IL-23 inhibitors.
Objectives: This study aims to compare the efficacy of various IL-23 inhibitors(Brazikumab, Guselkumab, Mirikizumab, Risankizumab, and Ustekinumab) for treating Crohn's disease by conducting a Bayesian network meta-analysis (NMA).
Methods: We searched the database, including PubMed, Embase, Web of Science, Cochrane Library, MEDLINE, and Web of Science, Clinical Trials. gov, (from inception until February 5, 2023). Efficacy (Clinic response, Clinic remission, Endep remission, and C-reactive protein) were compared using a Bayesian NMA. Results were presented as the pooled estimates of odds ratios (ORs) or weighted mean difference (WMD) (95% CI). The random-effects model was selected to synthesize the data. The ranking probability for each IL-23 inhibitor was evaluated using the surface under the cumulative ranking curves (SUCRA). The larger the SUCRA value, the better the rank of the intervention. The global inconsistency was evaluated by comparing the fit of consistency and inconsistency models, where $P \leq 0.05$ indicated inconsistency. All analyses were conducted using the gemtc package of R (version 4.2.2).
Results: In terms of Clinic response, a total of 40 studies were included. The NMA showed that Brazikumab combined with Guselkumab [OR=-0.98, 95% (CI, -2.9, 0.91)], PBO(PBO) combined with Risankizumab [OR=-0.54, 95% (CI, -1.16, 0.18)], PBO combined with Ustekinumab [OR=-1.38, 95% (CI, -2.77, -0.01)], Risankizumab combined with Ustekinumab [OR=-0.84, 95% (CI, -2.43, 0.63)]. According to SUCRA, Ustekinumab (78.9%), Risankizumab (52.2%), PBO(23.6%), Mirikizumab(34%), Guselkumab (87.6%), and Brazikumab (23.6%). For clinic remission, the result of NMA showed that Brazikumab combined with Guselkumab [OR=-1.59, 95% (CI, -3.78, 0.59)], Brazikumab combined with Ustekinumab [OR=-1.37, 95% (CI, -3.57, 0.83)], PBO combined with Risankizumab [OR=-0.47, 95% (CI, -1.19, 0.34)], PBO combined with Ustekinumab [OR=-1.26, 95% (CI, -2.86, 0.33)], Risankizumab combined with Ustekinumab

[OR=-0.8, 95% (CI, -2.6, 0.93)]. According to SUCRA, Ustekinumab (79.3%), Risankizumab (53.7%), PBO(22.1%), Mirikizumab(33.4%), Guselkumab (90.3%)and Brazikumab (21.7%) (Figure 1).

Conclusion: In terms of efficacy alone, Guselkumab ranked first among all IL-23 inhibitors, followed by Ustekinumab, and all had significantly different clinical remission rates than patients in the PBO group, while the remaining drugs were less effective than PBO.

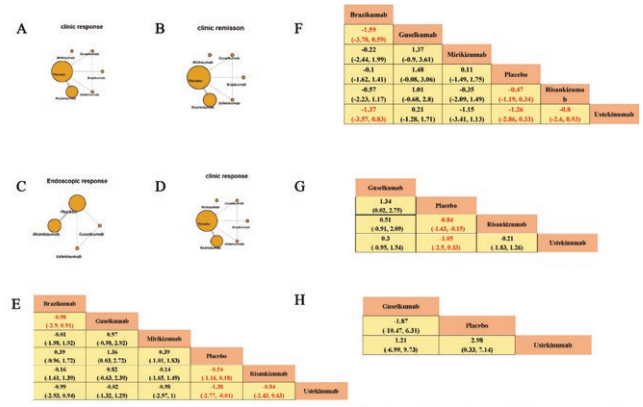


Figure 1: Network diagrams of comparisons on different outcomes of treatments of CD patients and pooled estimates of the NMA: (A, E) Clinic response; (B, F)Clinic remission; (C, G) Endep remission; (D, H)C-reactive protein. Pooled hazard ratios (95% credible intervals).

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1506 PLASMA NEUROFILAMENT LIGHT CHAIN AND GLIAL FIBRILLARY ACIDIC PROTEIN AS BIOMARKERS IN PATIENTS WITH OCULAR SARCOIDOSIS AND NEUROSARCOIDOSIS

Keywords: Biomarkers, Rare/orphan diseases, Uveitis

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Background: Sarcoidosis is a disease characterized by non-caseating granulomatous inflammation, which can affect the eyes as ocular sarcoidosis (OS) and the central nervous system (CNS) as neurosarcoidosis (NS). Neurofilament light chain (NFL) is a structural neuronal cytoskeletal protein, and glial fibrillary acidic protein (GFAP) is part of the cytoskeleton in astrocytes and retinal Müller glial cells. Inflammation would cause leakage of NFL and GFAP. It has been demonstrated that plasma NFL is highly elevated in newly diagnosed NS patients with levels over 11.4 ng/L.

Objectives: The objectives were to compare the level of NFL and GFAP in sarcoidosis patients with or without OS and NS.

Methods: This cross-sectional study included 106 biopsy-verified chronic sarcoidosis patients examined between May and November 2019. After excluding 18 patients due to systemic comorbidity, the patients were divided according to their organ involvement over time: sarcoidosis without ocular or CNS affection (non-OS/non-NS, n=44), OS (n=14), NS (n=15), and combined OS and NS (n=15). EDTA plasma was stored at -80 ◦C until analysis. NFL and GFAP were measured blinded to clinical data by single molecule array technology (Simoa, HD-1 Analyser, Quanterix©, Billerica, MA, USA), using the commercially available 2-Plex assay. Kruskal–Wallis test, Dunn test, and Fisher's exact test were used for statistical analysis.

Results: We included 88 patients with an age median (IQR) of 52 years (41 - 60). The non-OS/non-NS group was younger than the other groups (p = 0.02) but did not differ with respect to disease duration (p=0.5). Between 67-100% of the patients received immunosuppressive treatment, most frequently in the OS group (93%) and the NS group (100%) (p = 0.02). Median NFL was 5.1, 8.4, 7.0, and 7.0 ng/L in patients with non-OS/non-NS, OS, NS, and combined OS and NS, respectively (p = 0.003), although this was only statistically significant in patients with a disease duration < 5 years (p = 0.005).

The frequency of patients with an NFL level >11.4 ng/L was lower in non-OS/non-NS group compared to the three other groups (2% vs. 14% vs. 33% vs. 20%, p = 0.004). There was a trend (p = 0.06) towards a lower median GFAP in patients with non-OS/non-NS as compared to the other groups (52 vs. 72 vs. 71 vs. 69 ng/L), which became statistically significant in patients with a disease duration < 5 years (48 vs. 67 vs. 127 vs. 52 ng/L, p = 0.02).

Conclusion: In this cross-sectional study of chronic sarcoidosis patients, we generally found a low median NFL level, including in OS and NS patients. Our results suggest that neuroaxonal damage and, thereby, active inflammation decreases in treated sarcoidosis patients. However, the median NFL levels were significantly lowest in the non-OS/non-NS group, and between 14-33% of patients in OS, NS, and combined OS and NS groups had an NFL level above 11.4 ng/l, which could indicate active CNS inflammation leading to ongoing silent neuroaxonal damage.

Table 1. Baseline characteristics and clinical findings in sarcoidosis patients

	Non-OS/ non-NS (n=44)	OS (n=14)	NS (n=15)	OS and NS (n=15)	p-value
Age, years	45 (41-55)	56 (38-66)*	60 (51-65)**	52 (32-60)	0.02
Age <40, %	23	29	7	40	
Age 40-59, %	66	29	40	33	
Age ≥60, %	11	43	53	27	
Sex, % male	45	50	73	60	0.3
Duration of sarcoidosis, years	5 (3-9)	6 (3-9)	9 (4-10)	5 (3-9)	0.5
<5 years, %	50	36	27	40	0.4
Immunosuppres., %	68	93	100	67	0.02
NFL, ng/L	5.1 (4.1-6.2)	8.4** (6.6-10.3)	7.0** (5.7-14.1)	7.0[a] (4.5-10.8)	0.003
Duration <5 years	4.4 (3.2-5.5)	10.3** (8.6-10.9)	12.5** (8.1-14.6)	8.8* (3.5-10.0)	0.005
≥ 5 years	5.7 (5.0-6.9)	8.0 (6.6-8.5)	6.6 (5.2-11.8)	4.7 (4.5-10.8)	0.4
NFL > 11.4 ng/L, %	2	14	33	20	0.004
GFAP, ng/L	52 (39-71)	72(45-107)[a]	71 (43-132)*	69 (49-102)*	0.06
Duration <5 years	48 (39-60)	67 (45-107)[a]	127 (88-171)**	52 (48-58)	0.02
≥ 5 years	62 (39-93)	73 (46-83)	69 (41-120)	83 (69-110)[a]	0.4

Values are median and interquartile range (IQR), or count and percentage. * Compared to non-ocular/non-CNS group p < 0.05. ** Compared to non-ocular/non-CNS group p < 0.01. [a] Compared to non-ocular/non-CNS group p = 0.06.

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AB1507 IGG4-RELATED DISEASE – THE PORTUGUESE COHORT UNDER RHEUMATOLOGY'S CARE

Keywords: Disease-modifying Drugs (DMARDs), Geographical differences, Epidemiology

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Background: The IgG4-related disease (igG4-RD) is a rare fibro-inflammatory pseudotumoral condition, with systemic, but indolent, manifestations – pancreatic, salivary and lacrimal glands, retroperitoneal, vascular etc. It mainly occurs on middle-aged and older men[1]. It can mimic malignancies, having a complicated diagnosis. It responds favorably to corticosteroids (CCT)[2], but frequently relapses[3].

Objectives: To characterize the Portuguese sample of IgG4-RD patients followed at Rheumatology.

Methods: National multicentric observational study, including IgG4-RD patients followed on a Rheumatology consultation.

Results: Twenty-four patientes were included, with a mean present age of 59.95 years-old (SD=13.35), 56.09 (SD=14.13) at diagnosis, and 53.96 (SD=14.19) at the first symptoms. Twelve (50.0%) were men. Nine (37.5%) patients had salivary glands involvement (8 bilaterally), 6 (25.0%) had orbital, 6 (25.0%) of lacrimal glands (4 of them bilaterally), 5 (20.8%) pancreatic, 5 (20.8%) aortic, 4 (16.7%)

retroperitoneal, 4 (16.7%) of biliary ducts, 3 (12.5%) pulmonary, 3 (12.5%) renal, 2 (8.3%) of the thyroid and 1 (4.2%) of meninges. We documented a intra-ductal pancreato-biliary papillary mucinous neoplasm. Tomographically, none had a *sausage pancreas*, 3 (12.5%) had lung nodules, 1 (4.2%) a bronchovascular pattern, 1 (4.2%) an interstitial lung pattern and 4 (16.6%) had groundglass opacities. Histologically, 4 (16.6%) had *storiform* fibrosis, 20 (83.3%) lymphoplasmacytic infiltrates, and 5 (20.8%) a IgG4/IgG ratio >40%. PET scan showed inflammation in 10 (41.7%) cases. On blood analysis, 5 (20.8%) had peripheral eosinofilia, 12 (50.0%) ESR elevation and 16 (66.7%) CRP elevation, 16 (66.7%) had high levels of IgG4, 2 (8.3%) of IgG1 and 1 (4.2%) of IgE, and 4 (16.7%) had positive ANA. There was 1 (4.2%) death of unknown cause, by the age of 65. As a first line of therapy, 17 (70.8%) patients took oral CCT, with a mean dosage of 20.77mg (DP=22.98) (max=80mg/day), 1 (4.2%) took pulses of CCT, 2 (8.3%) mycophenolate mofetil (MMF), 2 (8.3%) methotrexate (MTX), and 3 (12.5%) rituximab (RTX). Presently, 1 (4.3%) patient is under pulses of CCT, due to lung and aortic disease, 16 (66.7%) are on oral CCT, with a mean dosage of 4.43mg (DP=8.59), 2 (8.3%) are on MMF, 1 (4.2%) on azathioprine, 1 (4.2%) on hydroxychloroquine, 1 (4.2%) on methotrexate, 2 (8.2%) on TNFa-inhibitor, and 7 (29.2%) on RTX. Seventeen (70.8%) patients responded well to the initial CCT; 13 (54.2%) lowered their IgG4 serum levels, and 8 (33.3%) normalized them.

Conclusion: This Portuguese cohort is heterogenous, without gender predominance, more commonly affecting middle aged people and beyond, with orbital and glandular involvement. Response to CCT was good, with a subsequent reduction in IgG4 levels, but with a frequent need to progress to other immunomodulators. Its choice relies on the affected organs – from the initial treatment, there was MTX failure, good response to MMF, and a moderate demand for RTX.

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AB1508 ANXIETY AND DEPRESSION IN PATIENTS WITH FMF

Keywords: Innate immunity, Comorbidities

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Background: Familial Mediterranean Fever (FMF) is a systemic autoinflammatory disease requiring lifelong treatment, characterized by recurrent episodes of fever, arthritis, and serositis. Recent studies denote an association between FMF and behavioral disorders such as anxiety and depression[1]. Further investigations are needed to have a better understanding of the relationship of FMF to anxiety and depression.

Objectives: In this study, we aimed to assess anxiety and depression among FMF patients and their relation to different variables such as gender, age, genotype, drug compliance, biologic treatment, family history of FMF, age of first colchicine dose, age of symptom onset, degree of education, and monthly income.

Methods: We surveyed 360 (225 F, 135 M) FMF patients in our outpatient clinic between June and October 2022. Our surveys included different inventories assessing anxiety and depression which were as follows: Beck's Depression Inventory (BDI), Beck's Anxiety Inventory (BAI), and State-Trait Anxiety Inventory (STAI). We then compared the inventory scores according to different variables.

Results: The median age for the patients was 36.4 ± 11.0 (19-64). Median scores for STAI-Y1 (state), STAI-Y2 (trait), BAI, and BDI were 42.2 ± 12.0, 45.9 ± 10.6, 24.0 ± 13.9, and 13.1 ± 8.99 respectively. There was no significant difference between male and female patients on STAI-Y1, STAI-Y2, and BDI but females scored significantly higher on BAI (25.8 ± 13.7 vs 21.0 ± 13.9, p-value: 0.001). Drug compliant patients had significantly lower scores on STAI-Y1 (41.5 ± 11.4 vs 45.2 ± 14.0, p-value:0.04) compared to non-compliant patients but their scores did not significantly differ on STAI-Y2, BAI, and BDI. M694V homozygous patients got significantly lower scores from BAI and BDI (17.0 ± 12.1 vs 25.1 ± 13.9, p-value: <.001; 12.4 ±9.37 vs 13.2 ±8.93, p-value: <.001). Exon-2 mutation positive patients scored significantly higher on BAI (29.6 ± 13.3 vs 21.6 ± 13.5, p-value: <.001) but did not get significantly different scores from STAI-Y1, STAI-Y2, and BDI compared to Exon-2 mutation negative patients. The patients with Exon-10 mutation get significantly lower scores on BAI (17.9 ± 12.3 vs 27.3 ± 13.7, p-value: <.001) but positivity of Exon-10 mutation did not affect the STAI-Y1, STAI-Y2, and BDI scores significantly. Different groups of educational levels (uneducated, elementary school, secondary school, high school, university) got significantly different scores, low level groups getting higher scores, from STAI-Y2 (56.6 ± 6.80, 48.3 ± 11.6, 43.4 ± 11.0, 45.5 ± 8.63, 45.2 ± 11.2, p-value: 0.002) but all groups scored similarly on STAI-Y1, BAI, and BDI. Different groups of monthly income (<$340, $ 340-680, $ 680-1130, $ 1130+) had significantly different scores from STAI-Y2, BAI, and BDI [(46.7 ± 10.4, 45.8 ± 10.7, 40.8 ± 12.1, 41.3 ± 6.31, p-value: 0.022), (26.1 ± 13.6, 20.9 ± 13.7, 20.1 ± 13.9, 26.2 ± 16.7, p-value: 0.004), (14.0 ± 9.16, 12.2 ± 8.64, 9.88 ± 8.55, 12.3 ± 7.89, p-value: 0.034)] whereas they all had similar scores from STAI-Y1. Having a family member with FMF, biologic agent treatment, age of onset for symptoms, and the colchicine starting age did not have a significant impact on the scores taken from all four inventories.

Conclusion: Our patients had moderate anxiety according to BAI scores, and severe state and trait anxiety according to STAI-Y1, STAI-Y2 scores all of which indicates the presence of anxiety. Medication compliant patients had lower levels of anxiety. We argue that this difference was due to better disease control because of drug compliance. Furthermore, BDI scores indicated mild depression among patients. In addition, M694V homozygous patients interestingly had lower anxiety and depression levels. Further investigations are necessary to understand the effect of different variables on anxiety and depression in FMF patients.

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Table 1.

(n:360)	n (%)
F:M	225:135 (62.5:37.5)
Age	36.4 ± 11.0 (19-64)
Median Scores	
STAI-Y1	42.2 ± 12.0
STAI-Y2	45.9 ± 10.6
BAI	24.0 ± 13.9
BDI	13.1 ± 8.99
STAI-Y1 Scores	
Compliant	41.5 ± 11.4
Non-Compliant	45.2 ± 14.0
p-value	0.04
BAI Scores	
M694V homozygous	17.0 ± 12.1
Others	25.1 ± 13.9
p-value	<.001
BDI Scores	
M694V homozygous	12.4 ±9.37
Others	13.2 ±8.93
p-value	<.001

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Disclosure of Interests: None Declared.

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AB1509 MUCOCUTANEOUS INVOLVEMENT IS THE MORE FREQUENT REASON FOR IMMUNOSUPPRESSIVE NEED COMPARED TO MAJOR ORGAN INVOLVEMENT IN AN EARLY MALE BEHÇET'S DISEASE PROSPECTIVE COHORT

Keywords: Behcet's disease

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Background: Major organ involvement is one of the main causes of mortality and morbidity in Behçet's Disease (BD) [1]. However, the prognosis and predictors of major organ involvement are insufficiently studied.
Objectives: We aimed to follow young, male BD patients with only mucocutaneous symptoms who have the highest risk for new major organ involvement prospectively.
Methods: Thirty-six male patients with BD were included in the study. Patients with BD were assessed prospectively at 3-6 months intervals and in any urgent visits. New major organ involvements and reasons for immunosuppressive (IS) need were assessed during prospective follow-up.
Results: At baseline, the mean disease duration was 3.3 years. All patients were under colchicine treatment. The mean follow-up duration was 90.7 months. Overall, 13 (36.1%) patients needed IS therapy during follow-up. The reason for IS need was major organ involvement in 5 (13.9%), refractory mucocutaneous involvement in 7 (19.4%), and articular involvement in 1 (2.8%) *(Table 1, Figure 1)*. Major organ involvement was vascular in 3 patients, ocular in 1 patient, and ocular and vascular in 1 patient. In 8 of these 13 patients, step-up treatment was needed in ISs due to refractory disease or relapse.
Conclusion: Our study demonstrated a lower incidence of major vascular events in male BD patients during prospective follow-up compared to retrospective cohorts in the literature. Our results showed that refractory mucocutaneous involvement is a more frequent reason for IS need in BD than major organ involvement during prospective follow-up.
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Table 1. Clinical characteristics of patients with immunosuppressive treatment during follow-up

	Reason for IS use	Age at Diagnosis	Disease duration when IS started	IS agent
Patient 1	Pulmonary aneurysm	35	1 year	Azathioprine
Patient 2	Refractory OU	25	5 years	Cyclosporine
Patient 3	Deep venous thrombosis	38	10 years	Azathioprine
Patient 4	Uveitis	20	5 years	Azathioprine
Patient 5	Refractory OU	28	7 years	Azathioprine
Patient 6	Refractory OU	23	6 years	Cyclosporine
Patient 7	Refractory EN	35	1 years	Azathioprine
Patient 8	Deep venous thrombosis	23	1 years	Azathioprine
Patient 9	Arthritis	28	7 years	Methotrexate
Patient 10	Refractory OU	29	13 years	Azathioprine
Patient 11	Refractory EN+ Articular Involvement	23	5 years	Azathioprine
Patient 12	Superficial Thrombophlebitis	29	2 years	Azathioprine
Patient 13	Refractory OU	28	3 years	Azathioprine

IS: Immunosuppressive, OU: Oral ulcer, EN: erythema nodosum

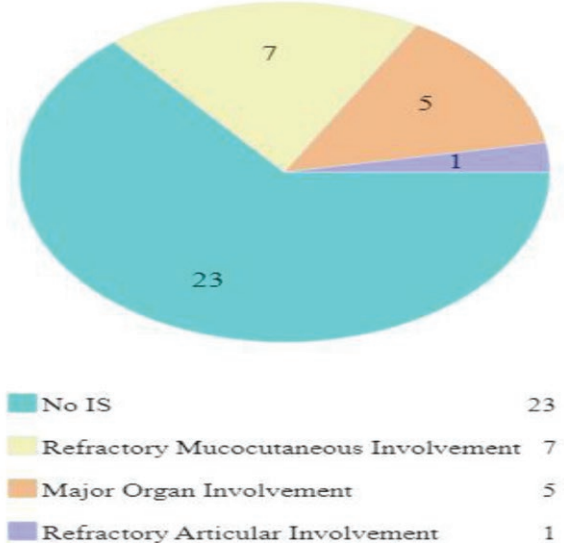


Figure 1. The reasons for immunosupressive need in Behçet patients during follow-up (n)

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Disclosure of Interests: None Declared.
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AB1510 THE RELATIONSHIP BETWEEN EMERGING NEW INFLAMMATORY MARKERS AND FAMILIAL MEDITERRANEAN FEVER SEVERITY

Keywords: Biomarkers, Rare/orphan diseases

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Background: Neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and monocyte lymphocyte ratio (MLR) are emerging inflammatory parameters. These parameters have been associated with disease activity and response to treatment in many rheumatological diseases.
Objectives: To evaluate the relation between these parameters and familial Mediterranean fever (FMF) disease severity.
Methods: We included 274 FMF patients in the study. First, we measured FMF disease severity cross-sectionally in patients with International FMF severity score (ISSF). We then divided the patients into mild disease (ISSF score ≤ 2) and moderate-severe disease (ISSF score >3) according to ISSF scores. Finally, we compared the NLR, MLR and PLR values between the two groups.
Results: Of 274 patients, 70 (25.5%) had moderate-to-severe FMF disease. More patients had amyloidosis, and the frequency of male gender was higher in the moderate-to-severe group. Other demographic and disease-related characteristics were similar between the groups. NLR, MLR, and PLR values were also similar between groups (Table 1)
Conclusion: Although emerging inflammatory markers are popular in the field of rheumatology, these parameters were unable to differentiate disease severity in patients with FMF.
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Table 1. Demographic data, disease characteristics and NLR, MLR and PLR values in FMF patients classified according to disease severity

	Mild disease n=204	Moderate-severe disease n=70	p
Age (years)	39.0 (28.2-47.7)	41.0 (30.0-51.2)	0.33
Male/Female	59/145	31/39	0.01
Disease duration (years)	10.0 (5.0-19.5)	11.0 (5.0-20.0)	0.46
Colchicine dose (mg/day)	1.5 (1.0-1.5)	1.5 (1.0-2.0)	0.51
Colchicine resistance (%)	23 (11.3)	32 (45.7)	**<0.001**
Amyloidosis (%)	7 (3.4)	18 (25.7)	**<0.001**
Exon 10 mutation (%)	98 (48.0)	25 (35.7)	0.70
NLR	1.8(1.4-2.5)	2.1 (1.5-2.8)	0.12
MLR	2.4 (1.9-3.0)	2.5 (2.0-3.3)	0.32
PLR	124.1 (98.5-154.6)	120.0 (97.3-148.7)	0.65

NLR: Neutrophil lymphocyte ratio; PLR: Platelet lymphocyte ratio; MLR: Monocyte lymphocyte ratio (MLR); p<0.05 was shown bold. Continuous variable was shown as median (Q1-Q3)

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Disclosure of Interests: None Declared.
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AB1511 HIGHER VASCULAR INVOLVEMENT IN BEHÇET'S DISEASE AMONG KURDISH ETHNICITY: DATA FROM A SINGLE CENTER AT INTERSECTION OF SILK ROAD IN EASTERN TURKEY

Keywords: Behcet's disease, Epidemiology, Uveitis

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Background: Behçet's disease (BD) is a chronic inflammatory multi-systemic disease that affect skin-mucosa, joints, eye and blood vessels. BD has some clinical differences in terms of disease manifestations and prognosis among Silk Road countries as well as various ethnicities.

Objectives: In this study, we aimed to evaluate the clinical features and course regarding cluster analysis of BD in Kurdish patients in Van provience, Eastern Turkey at the intersection of the silk road.
Methods: This retrospective observational study was carried out in a tertiarry reference center in Van province, East of Turkey. Patients data was obtained from their charts. All patients were asked about their ethnicity and patients with other ethnicities rather than Kurdish were also excluded from the study. Seven disease manifestations were included to the cluster analysis as follows; mucocutaneus findings (recurrent oral ulcer [ROU], genital ulcer [GU], pseudofolliculitis, erythema nodosum (EN)-like lesions, musculoskeletal (MSK) involvement (arthritis and spondylitis), gastrointestinal (GIS) involvement, vascular involvement (venous and/or artery), parenchymal central nervous system (CNS) involvement.
Results: We included 444 patients (of 59.2 % male) to the study. Mean±standard deviation (SD) of the patients was 35.8±10.2 years and median (Interquartile range [IQR]) disease duration was 12 [12]. Mean±SD age at initial symptom and age of diagnosis were 19.4±7 and 26.4±8.2, respectively. Fulfillment of ISG and ICBD criteria were 91.6 % and 96 %, respectively. Family history of Behçet disease and ROU were 35.4 % and 70.2 %, respectively. In cluster analysis, four clusters were observed as follow; 132 patients (31.2 %) in vascular (C1), 66 patients (15.6 %) in eye (C2), 60 patients (14.2 %) in musculoskelethal (C3) and 165 patients (39 %) in mucocutaneus (C4) clusters. Male gender (OR: 6.5, 95 % Confidence interval [CI]: 2-21.4), superficial thrombophlebitis (OR: 4.7, 95 % CI: 1.9-11.4) and uveitis (OR: 3.6, 95 % CI: 1.3-9.9) were associated with vascular involvement in multivariate analysis.
Conclusion: Among Kurdish patients with BD four disease clusters were observed. Parenchymal lung and CNS involvement were associated with vascular cluster. One third of patients had vascular involvement among Kurdish patients with BD which was quite higher compared to patients with Turkish ethnicity [1].
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Table 1. Cluster analysis of the study population

Disease manifestations	Vascular	Eye	Musculoskelethal	Mucocutaneus
	C1, n=132 (31.2 %)	C2, n=66 (15.6 %)	C3, n=60 (14.2 %)	C4, n=165 (39 %)
Mucocutaneus	Yes	Yes	Yes	Yes
Musculaskelethal	Yes	No	Yes	No
Gastrointestinal	No	No	No	No
Uveitis	No	Yes	No	No
Thrombophlebitis	Yes	No	No	No
Vascular	Yes	No	No	No
CNS paranchimal	No	No	No	No

Table 2. Univariate analysis of associated factors in disease clusters

Variables	Disease clusters				
	Vascular	Eye	Musculoskeletal	Mucocutaneus	
	C1, n=132 (31.2 %)	C2, n=66 (15.6 %)	C3, n=60 (14.2 %)	C4, n=165 (39 %)	p value (Odds ratio)
Gender, male, n (%)	111 (81)	33 (50)	34 (56.7)	69 (41.8)	***<0.001 (56.5)***
Disease manifestations, n (%)					
Recurrent oral ulcer (ROU)	130 (98.5)	65 (98.5)	59/59 (100)	164 (99.4)	0.7
Genital ulcer	112 (84.8)	46 (69.7)	52 (86.7)	132 (80)	***0.045 (8)***
Thrombophlebitis	79 (59.8)	0	0	0	***<0.001 (214)***
Pseudofolliculitis	114 (86.4)	46 (69.7)	47 (78.3)	123 (74.5)	***0.027 (9.2)***
Erythema nodosum	90 (68.2)	34 (51.5)	29 (48.3)	62 (37.6)	***<0.001 (27.7)***
Pathergy positivity	78 (75)	37 (69.8)	31 (79.5)	74 (58.3)	***0.016 (10.3)***
Arthritis	72 (54.5)	19 (28.8)	58 (96.7)	0	***<0.001 (212)***
Spondylitis	2 (1.5)	1 (1.5)	5 (8.8)	0	***0.001 (17.7)***
Gastrointestinal	6 (4.5)	2 (3)	2 (3.3)	0	0.07
CNS parenchymal	12 (9)	1 (1.5)	1 (1.7)	0	***<0.001 (20.6)***
Lung parenchymal	4 (3.1)	0	0	0	***0.03 (9)***
ISG fulfillment, n (%)	117/124 (94.4)	63/64 (98.4)	49/53 (92.5)	134/156 (86)	***0.009 (11.5)***
ICBD fulfillment, n (%)	130 (98.5)	65 (98.5)	55/57 (96.5)	147/159 (92.5)	***0.042 (8.2)***
HLAB51 positivity, n (%)	8/9 (89)	3/4 (75)	1/3 (33.3)	16/18 (89)	0.1

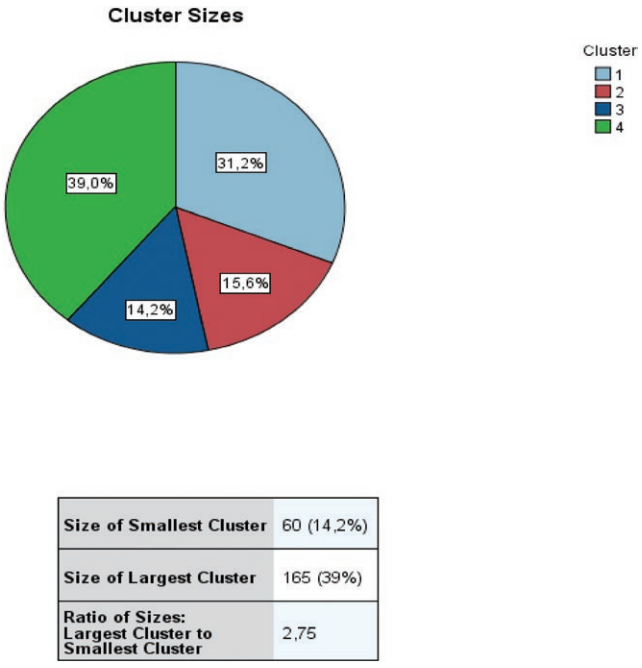


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.338

AB1512

CHARACTERISTICS OF PATIENTS WHO RECEIVED BIOLOGICAL TREATMENT AFTER KIDNEY TRANSPLANTATION AND THE INCIDENCE OF SERIOUS INFECTIONS: A MULTICENTER STUDY

Keywords: bDMARD, Kidneys

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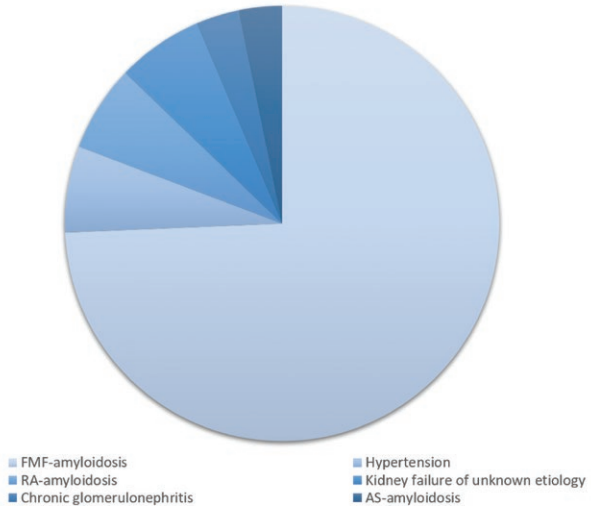
Background: Kidney transplant patients due to both primary kidney involvement of chronic/autoimmune inflammatory diseases and end-stage kidney disease related to amyloidosis are followed up in rheumatology clinics. Biological agents one of the treatment options in kidney transplant recipients with chronic/autoimmune inflammatory disease.
Objectives: However, there is insufficient data on the development of infection in kidney transplant recipients who received biological treatment. Herein, we aimed to determine the incidence of serious infections in patients with kidney transplant recipients who are received biological therapy.
Methods: Kidney transplant recipients who are received biological agents due to rheumatologic disease were included in the study. Patients' demographic features, transplantation data, biological treatment, development of infection and severity of infection were screened retrospectively. Infections that requiring hospitalization were defined as severe infections.
Results: A total of 31 patients were included in the study, 14 (45%) of whom were female and mean age was 41 ±9 years. Twenty-five patients (80%) of them were non-preemptive kidney transplant and mean duration of hemodialysis before the transplantation was 40 ±40 months. Twenty-three patients (74%) had end stage kidney failure due to FMF-amyloidosis(Figure-1-). Seventeen patients (54%) received anakinra, 11 patients (35%) received canakinumab and 3 patients (10%) received etanercept with other immunosuppressive treatment. Mean treatment duration of biological agents was 4.2±2.6 years. Two patients developed solid organ malignancy and one patient developed hematological malignancy after transplantation. Sixteen of the patients (52%) were hospitalized at least once due to infection and 4 patients (13%) died due to infection. The cause of decease in two patients was COVID-19.
Conclusion: Rheumatic diseases are an important cause of end-stage renal disease and definitive treatment is kidney transplantation. Kidney transplant recipients due to rheumatological disease also use biological agents in the post-transplantation period.

Kidney transplant recipients have higher risk for the development of infection since they receive immunosuppressive therapy and use of biologic agents may further increase the risk for development infection. Meyer et al reported that infection developed in 54 of 187 solid organ transplant recipients using biological agents.[1] Mean treatment duration of biological agents was 12 months in this study. The incidence of infection was 54% in our study. Mean treatment duration of biological agent was 4.2 year was considered main reason for higher incidence of infection in our study.

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Figure-1-Causes of end stage kidney failure in this study



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Disclosure of Interests: None Declared.
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AB1513 MANAGEMENT OF RETROPERITONEAL FIBROSIS PATIENTS: A SCOTTISH COHORT OBSERVATIONAL STUDY

Keywords: Rare/orphan diseases, Descriptive Studies, Outcome measures

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Background: Retroperitoneal fibrosis (RPF) is a rare condition characterised by the inflammation and fibrosis of tissues in the retroperitoneum. Often presenting non-specifically with a variable picture of abdominal pain, constipation, and systemic symptoms of malaise, fever, and weight loss. RPF may also present with severe obstructive uropathy. Initial response to steroids is usually good, but a significant proportion of patients relapse. Evidence for second line treatment is scarce, and a variety of immunosuppressive therapies, such as rituximab, have been used. Surgical intervention and interventional radiology may be useful in treating acute ureteric obstruction and preserving renal function.
Objectives: As an orphan disease without, traditionally, a clear home speciality, retroperitoneal disease is likely underdiagnosed and undertreated especially in those who do not have ureteric obstruction. We characterised patients with retroperitoneal fibrosis across West and South-East Scotland to better understand these patients and their outcomes.
Methods: Patients were previously identified in East Scotland by contacting rheumatologists and by searching the urological stent registry from 2019 to 2022. The method was replicated in the West of Scotland though was less successful as the urological stent register did not record diagnoses, and clinicians did not have an accessible database for this condition. A further avenue of patient identification was then pursued. All available radiological reports and their attached clinical data on the request from 2006 to September 2022 were searched for the term "RPF" and "retroperitoneal fibrosis". Patients were included if they were given a clinical diagnosis of retroperitoneal fibrosis. Patients were excluded if RPF was concurrent with metastatic malignancy, associated with infection or other secondary cause. Patient data was acquired from their electronic records.
Results: 78 patients were identified: 56 in the West of Scotland and 22 in the South-East. Patient demographics are shown in Table 1. The diagnosis was most often made by CT scan. The estimated annual incidence in the last 10 years 2.2 is per million population in the West and 1.6 per million population in the East, for catchment populations of 1.2 million and 0.9 million, respectively. Treatment was heterogenous in both groups. Renal outcomes for these patients were interrogated. Patients were classified as having lost renal function if there was either biochemical or radiological evidence.

Table 1. Summary of findings in the two cohorts across Scotland compared with literature.

	South-East Scotland	West Scotland	Literature
Number	22	56	
Age at diagnosis	60y (range 43-81y)	61.5y (range 45-83y)	54-64y[1]
Female: male ratio	1:2.7	1:1.9	1:1.2-3.4[1]
Lost renal function	73% (16)	75% (42)	
eGFR <60ml/min/1.73m^2	73% (16)	61% (34)	32%[2]
eGFR <30 ml/min/1.73m^2	27% (6)	18% (10)	

Conclusion: The literature suggests renal impairment is variable in retroperitoneal fibrosis with only 32% of patients with abnormal creatinine reported in one study which is much lower than our results. The current literature is sparce for alternative therapies. More work is required in determining efficacy for more recent therapies such as rituximab to further the treatment of this orphan disease and improve patient outcomes.

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Acknowledgements: Acknowledgements to the Rheumatology and Urology team at NHS Lothian and NHS GGC for patient identification. Acknowledgements to Greater Glasgow and Clyde Safe Haven Data Team for their assistance with accessing databases for patient identification.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1221

AB1514 EPIDEMIOLOGY OF BEHÇET'S DISEASE IN NORTHERN SPAIN

Keywords: Epidemiology, Geographical differences, Behcet's disease

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Background: The prevalence of Behçet's disease (BD) has a considerable geographical and temporal variability. Data regarding epidemiology in Spain are limited. (1,2)
Objectives: To assess the epidemiology and clinical domains of BD in a population-based cohort from northern Spain and to compare the results with other geographical areas.
Methods: We conducted a cross-sectional study of a well-defined population in Northern Spain. Cases of suspected BD between January 1980 and December 2018 were identified. The diagnosis of BD was established according to the International Study Group (ISG) for Behçet's Disease. The incidence of BD between 1999 and 2018 was estimated by sex, age, and year of diagnosis.
Results: Of 120 patients with probable BD, 59 patients met ISG criteria and were finally included in the study, with a male/female ratio of 0.97; mean age 49.7±14.7 years. Incidence during the period of study was 0.492 per 100,000 people, observing an increase from January 1999 to December 2018. Prevalence was 10.14 per 100,000 in 2018. Figure 1. Clinical manifestations were relapsing aphthous stomatitis (100%), genital ulcers (78%), skin involvement (84.7%), joint involvement (64.4%), uveitis (55.9%), central nervous system (16.9%), vascular (10.2%), and gastrointestinal manifestations (6.8%). Table 1.
Conclusion: The prevalence of BD in Cantabria is higher than in other Southern-European countries. This difference may reflect a combination of geographic, genetic, or methodological variations, as well as the free accessibility to the Spanish Public Health System. Clinical phenotypes observed are similar to those described in other world regions.

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Table 1. Epidemiological phenotypes of Behçet's disease in other geographic areas.

Author, year	Region	Oral/genital ulcers (%)	Skin lesions (%)	Ocular involvement (%)	Joint involvement (%)	Neuro-Behçet (%)	Vascular involvement (%)	Gastrointestinal tract involvement (%)
Deligny et al., 2012	Caribbean Islands (Martinique)	100/ NR	NR	25	55.6	28	30	19.4
Calamia et al., 2009	North America (Minnesota, USA)	100/ 62	85	62	46	23	23	NR
Tüzün et al., 1996	Middle East (Çamaş, Turkey)	100/ 73.7	NR	0	47.4	NR	NR	NR
Al-Rawi et al., 2003	Middle East (Saqlawia, Irak)	100/ 83.3	50	40	33.3	NR	NR	16.6
Azizlerli et al., 2003	Middle East (Istambul, Turkey)	100/ 70.2	NR	27.7	NR	NR	NR	NR
Krause et al., 2007	Middle East (Galilee, Israel)	NR/ 68	41	58	70	11.6	NR	NR
Baş et al. 2016	Middle East (Northern Anatolian, Turkey)	100/ 71	NR	28	14	NR	NR	NR
Davatchi et al., 2019	Middle East (Iran)	97.5/ 64.4	62.2	55.6	38.1	3.9	8.9	6.8
Chamberlain, 1977	Northern Europe (Yorkshire County, UK)	100/ 91	66	25	63	25	25	9
Jankowski et al., 1992	Northern Europe (Scotland, UK)	100/ 73.3	86.6	93.4	NR	20	NR	53.3
Zouboulis et al., 1997	Northern Europe (Berlin, Germany)	99/ 75	76	59	59	12.8	NR	NR
Altenburg et al., 2006	Northern Europe (Berlin, Germany)	98.5/ 63.7	62.5	58.1	53	10.9	22.7	11.6
Mohammad et al., 2019	Northern Europe (Skane County, Sweden)	100/ 80	88	53	40	0	20	NR
Ambresin et al., 2002	Central Europe (Lausanne, Switzerland)	86/ 31	60	71	60	20	20	NR
Kanecki et al., 2017	Central Europe (Poland, Nationwide)	NR	NR	NR	NR	NR	NR	NR
Mahr et al., 2014	Southern Europe (Seine-Saint-Denis County, France)	100/ 80	90	51	59	10	NR	10
Salvarani et al., 2007	Southern Europe (Reggio Emilia, Italy)	100/ 78	100	56	50	11	6	NR
Peñafiel et al., 2007	Southern Europe (Granada, Spain)	NR	86.4	65.9	68.2	10	65.9	NR
González-Gay et al., 2000	Southern Europe (Lugo-Galicia, Northwestern Spain)	100/ 87.5	87.5	43.8	62.5	31.3	43.7	18.8

Abbreviations: ISG: International Study Group; ICBD: International Criteria for Behçet's Disease; NR: Not Reported; SD: Standard Deviation.

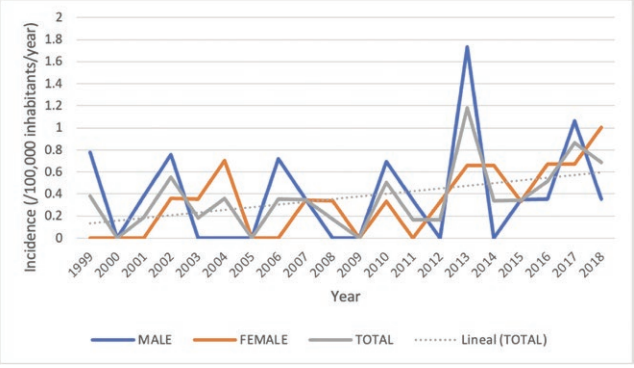


Figure 1. Annual incidence of Behçet's disease in our series.

Acknowledgements: NIL.

Disclosure of Interests: Carmen Álvarez-Reguera: None declared, Guillermo Suárez Amorín: None declared, Alba Herrero-Morant: None declared, Lara Sanchez-Bilbao: None declared, David Martínez-López: None declared, José Luis Martín-Varillas Grant/research support from: José L. Martín-Varillas received grants/research support from AbbVie, Pfizer, Lilly, Janssen, and Celgene., Raúl Fernández-Ramón: None declared, Rosalía Demetrio-Pablo: None declared, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Lilly, Janssen, and MSD, Paid instructor for: AbbVie, Pfizer, Roche, Bristol-Myers, Lilly, Janssen, and MSD., Grant/research support from: AbbVie, MSD, and Roche.

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AB1515

EPIDEMIOLOGY AND CLINICAL FEATURES OF MUCOCUTANEOUS LESIONS IN BEHÇET'S DISEASE: STUDY FROM A COHORT OF 120 PATIENTS IN A REGION IN NORTHERN SPAIN

Keywords: Behcet's disease, Epidemiology, Skin

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Background: Mucocutaneous lesions are one of the most characteristic signs of Behçet's Disease (BD) and are included in different classification criteria [**1**].
Objectives: To describe the mucocutaneous manifestations and to assess it accordingly to age and sex.
Methods: Descriptive study of a cohort of 120 patients diagnosed with BD from January 1, 1980 to December 31, 2019. Finally, we included 92 patients following the 2014 International Criteria for Behçet's Disease (ICBD) [**2**].
Results: 92 patients (45 men/ 47 women) had mucocutaneous involvement. Mean age at diagnosis was (36.3±12.6) years. 27 (29.3%) were young adults (<30 years), 61 (66.3%) middle-aged adults (30-60) and 4 (4.3%) elderly adults (>60 years). The most frequent mucocutaneous manifestations were oral ulcers (OU) (n=92, 97.9%), genital ulcers (GU) (n=69, 73.4%), pseudofolliculitis (n=47, 50%), erythema nodosum-like lesions (EN) (n=28, 29.8%) and Raynaud's phenomenon (n=2, 2%). OU, GU, EN-like lesions and Raynaud's phenomenon were more frequent in women. GU and pseudofollicullitis were more frequent in men. No statistical differences were found between sexes (χ^2 test). Pathergy test was positive in 4 patients. Histopathology of EN-like lesions was performed in 5 patients, 3 (60%) showed septal panniculitis and 2 (40%) vasculitis with neutrophil infiltration, which is a typical pathological finding of EN-like lesion in BD [2]. **Table 1**. Mucocutaneous lesions divided by age groups are represented in **Figure 1**.
Conclusion: Identifying characteristic mucocutaneous lesions of BD, as OU, GU, pseudofollicullitis and EN-like lesions may allow early diagnosis and treatment of the disease. There were no gender differences in mucocutaneous lesions.

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Table 1. Mucocutaneous manifestations in a cohort of 94 patients diagnosed of Behçet disease.

	Total	Female	Male	p
N (%)	92 (100)	47 (51.1)	45 (48.9)	-
Age (mean/ SD)	36.3±12.6	36±13	36±12.2	-
Mucocutaneous involvement	92 (100)	47 (51.1)	45 (48.9)	0.4*
Oral ulcers	92 (100)	47 (51.1)	45 (100)	0.4
Genital ulcers	69 (75)	34 (49.3)	35 (50.7)	0.5
Pseudofolliculitis	47 (51.1)	23 (48.9)	24 (51.1)	0.7
Erythema nodosum	28 (30.4)	17 (58.6)	12 (41.4)	0.3
Raynaud phenomenon	2 (2.2)	2 ()	0	0.5*
Positive pathergy test	4 (4.3)	2 (50)	2 (50)	0.9*
Skin biopsy	5 (5.4)	2 (40)	3 (60)	-

*Yates correction applied.Abbreviations: SD: Standard deviation.

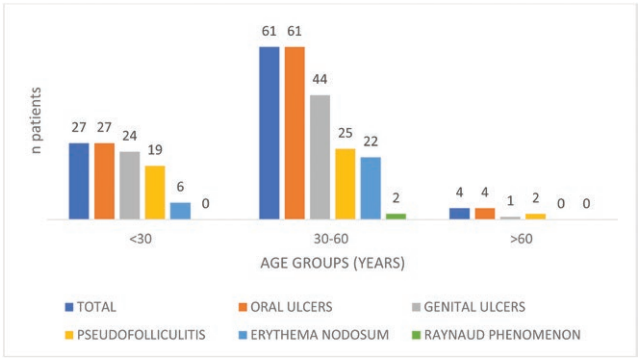


Figure 1. Mucocutaneous lesions in different age groups.

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Disclosure of Interests: Carmen Álvarez-Reguera: None declared, Alba Herrero-Morant: None declared, Lara Sanchez-Bilbao: None declared, David Martínez-López: None declared, José Luis Martín-Varillas Grant/research support from: Abbvie, Pfizer, Janssen, Lilly and Celgene., Guillermo Suárez Amorín: None declared, Rosalía Demetrio-Pablo: None declared, Ricardo Blanco Speakers bureau: AbbVie, Pfizer, Roche, Bristol-Myers, Lilly, Janssen, and MSD. Janssen, and MSD., Grant/research support from: AbbVie, MSD, and Roche.
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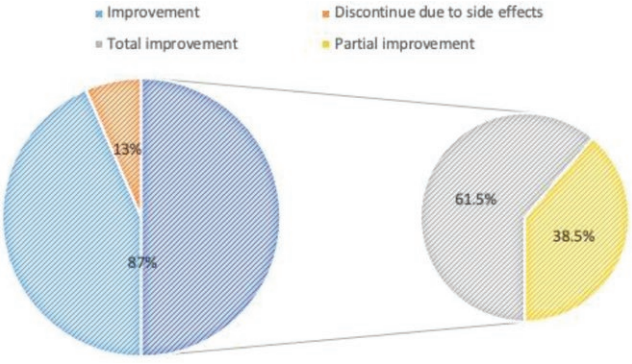
AB1516

APREMILAST FOR TREATMENT OF ORAL APHTOSIS: REAL-WORD DATA MULTICENTER STUDY

Keywords: Real-world evidence, Rare/orphan diseases

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Background: The main manifestation of Behçet's disease is oral aphthae. Treatment consists of topical corticosteroids and colchicine in recurrent cases. Drugs such as azathioprine, thalidomide, interferon-alpha, tumour necrosis factor-alpha inhibitors or apremilast should be considered in selected cases[1]. A phase 3, double-blind, placebo-controlled RELIEF study suggests that apremilast is an effective agent for the management of oral aphtae in Behçet's disease and benefits were sustained up to 64 weeks. Its onset of action occurred within 2 weeks after treatment was started. Adverse events, including nausea, vomiting, and diarrhea, occurred more frequently with apremilast than with placebo[2]. It has also been shown to be effective in the treatment of psoriasis[3].
Objectives: To assess the effectiveness of apremilast in the treatment of oral aphtosis.
Methods: Retrospective descriptive multicentre study of patients treated with apremilast for oral aphtosis associated with Behçet's disease, as well as patients with oral aphtosis who have received apremilast for another indication (psoriasis) or off-label use. Four hospitals participated in the study. The following variables were collected: age, sex, diagnosis, oral aphtosis at the time of starting apremilast, aphtosis response at 3 and 6 months (partial improvement, total improvement, lack of response, discontinuation due to side effects), ESR, CRP, ferritin, 25-OH-Vitamin D, folic acid, cyanocobalamin and concomitant treatment (none, corticosteroids, methotrexate, colchicine or anti-TNF). Descriptive statistics were performed using mean and standard deviation (SD) for continuous quantitative variables.
Results: A total of 15 patients were being treated with apremilast for oral aphtosis. Ten of them were diagnosed with Behçet's disease, one with psoriasis with oral aphtosis and four with recurrent oral aphtosis. Mean age was 47.1 ± 12.4 years, 67 % were female. All patients had active oral aphtosis at the time of starting apremilast. After 3 months of treatment, 87 % of the patients had improvement of the aphtosis (61.5 % partially and 38.5 % completely resolved); 13 % of the patients had to discontinue treatment due to side effects (diarrhea), none had to discontinue treatment due to lack of response. After 6 months, all the patients maintained improvement and only two of them discontinued apremilast after 12 months due to lack of response. Results of serological data analyzed were (mean ± SD): ESR 11.4 ± 6.7, CRP 3.7 ± 6.5, ferritin 100.8 ± 167.3, 25-OH-Vitamin D 31.4 ± 18.9, folic acid 11.7 ± 9.8, cyanocobalamin 585.8 ± 527. One patient maintained concomitant treatment with an anti-TNF drug, two with corticoids and five with colchicine.
Conclusion: Treatment with apremilast seems to improve oral aphthae in over 87% of patients.
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Graph 1. Treatment response of oral aphtae after 12 months

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Disclosure of Interests: None Declared.
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AB1517

NAILFOLD CAPILLAROSCOPIC STATUS IN HYPERMOBILE EHLERS DANLOS SYNDROME PATIENTS: PILOT INVESTIGATION

Keywords: Imaging, Diagnostic tests, Rare/orphan diseases

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Background: Hypermobile Ehlers Danlos syndrome (hEDS) is the most common subtype among the EDS syndromes and is a rare inherited connective tissue disease characterized mostly by hyperextensible skin and generalized joint hypermobility. Microvascular assessment has been documented only by one case report in the "vascular type" of EDS, despite vascular manifestations may

occur also in other EDS subtypes [1,2]. A reduced skin thickness has been previously reported in hEDS patients [3].
Objectives: To investigate, for the first time, nailfold microvascular status in hEDS patients in comparison with healthy controls (HCs). Peripheral blood perfusion (PBP) and dermal thickness (DT) were also assessed.
Methods: Twelve hEDS patients (75% females, mean age 41±16, classified with the 2017 International Classification Criteria of EDS [4]) and twelve age- and sex-matched HCs were observed from 2018 to 2022. Beighton score was calculated for both patients and HCs. Main nailfold videocapillaroscopy (NVC) parameters (dilated capillaries, giant capillaries, microhemorrhages, abnormal shapes and number of capillaries) were analysed and compared between the two groups to assess morphological features [5]. To assess the microvascular functional status, laser speckled contrast analysis (LASCA) was used to measure PBP in several region of interests. DT was also measured by cross-sectional B-mode scans obtained by a high-frequency 22 MHz ultrasound probe in 17 different areas of the body (including upper arms, lower arms, trunk and forehead).
Results: No statistically significant differences were observed in this small cohort between hEDS and HCs concerning the microvascular findings detected by NVC, even if microhemorrages were more prevalent in hEDS patients (33% vs 0 %) (see **Table 1**). Also, PBP assessed by LASCA was found similar in hEDS patients and HCs (178.12 ± 49.76 perfusional units vs 157.81 ± 67.15 at fingertips, p = 0.43). The mean DT did not significantly differ from hEDS patients and HCs in all skin areas (mean total DT of 18.44 ± 2.21 mm in hEDS patients vs 18.49 ± 2.13 mm in HCs, p = 0.96). As expected, the mean Beighton score was significantly higher in hEDS patients than in HCs (5.54±1.75 vs 1.25±1.58), but no significant correlation was detected between DT and Beighton score (r = 0.1, p = 0.76).
Conclusion: Microhemorrages seem more prevalent in hEDS patients than in ECs, suggesting a subclinical microvascular fragilility also in this subgroup of EDS patients. Skin ultrasound and PBP findings did not detect significant differences between hEDS patients and HCs, which might be due to the small sample size. These findings will be followed by further research including cases of the vascular EDS phenotype [6].
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Table 1. NVC in hEDS vs HCs. See text for abbreviations

NVC findings	hEDS (n = 12)	HCs (n = 12)	p -values
Mean capillary number	9.4±0.8	8.8±0.48	0.08
Dilations n (%)	10 (83%)	10 (83%)	0.97
Giant capillaries n (%)	0	0	1
Microhaemorrages n (%)	4 (33%)	0	0.09
Abnormal shapes n (%)	3 (25%)	4 (33%)	0.65

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Disclosure of Interests: None Declared.
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AB1518 INCIDENTALLY FOUND INTERSTITIAL LUNG DISEASE MAY NOT BE UNCOMMON IN FAMILIAL MEDITERRANEAN FEVER

Keywords: Rare/orphan diseases, Comorbidities, Imaging

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Background: Familial Mediterranean fever (FMF) is an autoinflammatory disease characterized by episodes of serositis and fever. Pleuritis is one of the common findings especially during attacks and thorax scans. However, data on other common lung findings such as interstitial lung disease (ILD) are limited in the literature.
Objectives: Here, we present the frequency of ILD and factors associated with ILD in our FMF cohort.
Methods: We included 242 patients who applied to the rheumatology outpatient clinic of a tertiary medical center within the last five years and were requested to undergo thoracic CT for any reason. The patients with a history of malignancy, active infection, active tuberculosis, or tuberculosis history, active or history of coronavirus 19 disease (COVID-19), nursing and pregnancy were excluded. An experienced radiologist blindly evaluated thoracic CT scans for ILD in accordance with relevant guidelines. We then evaluated the relationship between ILD findings and demographics and disease characteristics.
Results: Eleven (4.5%) of 242 patients had ILD. The most common ILD-related findings on thoracic CT were ground glass opacity (7/11 patients). None of the patients had honeycomb appearance. The most common reasons for requesting a thoracic CT were chest/chest pain, suspected COVID-19, and chronic cough. In addition, none of the demographic and disease-related characteristics were associated with ILD in our FMF patients (Table 1).
Conclusion: We have shown that incidentally diagnosed ILD is not uncommon in our FMF patients. In addition, FMF feature may not be associated with ILD in our patients.
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Table 1. Demographics and disease characteristics of FMF in both groups

	FMF with ILD n=11	FMF without ILD n=231	P
Age (years)	44.0 (37.0-48.0)	40.0 (30.0-48.0)	0.31
M/F	4/7	80/151	0.44
Disease duration (year)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	0.17
Smoking (%)	3 (27.1)	58 (25.1)	0.34
Pulmonary diseases (%)	3 (27.1)	35 (15.2)	0.28
Colchicine dosage (mg/day)	1.7 (1.0-2.0)	1.5 (1.0-1.5)	0.27
Amyloidosis (%)	2 (18.2)	24 (10.4)	0.33
Colchicine resistance (%)	4 (36.4)	50 (21.6)	0.31
Il-1 blocker (%)	1 (9.1)	24 (10.4)	0.89
ISSF score	1.0 (0-2.0)	1.0 (1.0-3.7)	0.25
Mild disease (%)	7 (63.6)	180 (77.9)	0.27
Moderate-severe disease (%)	4 (36.4)	51 (22.1)	
MEFV mutations (%)*			
Homozygote	3 (30.0)	36 (26.3))	0.44
Compound heterozygote	1(10.0)	48 (35.0)	
Heterozygote	5 (50.0)	42 (30.7))	
Negative	1 (10.0)	11 (8.0)	
Exon10 mutations	5 (50.0)	93 (70.5)	0.18

M: Male; F: Female; ISSF: International severity score for FMF * MEFV muations were available in 10/11 FMF patients with ILD and 147/231 FMF patients without ILD.

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Disclosure of Interests: None Declared.
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AB1519 NEUTROPHIL-TO-LYMPHOCYTE RATIO AND PLATELET-TO-LYMPHOCYTE RATIO AS POTENTIAL MARKERS FOR DISEASE ACTIVITY EVALUATION IN BEHCET'S DISEASE

Keywords: Prognostic factors, Biomarkers, Behcet's disease

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Background: Behcet's disease (BD) is an auto-inflammatory disorder, characterized by recurrent aphthous stomatitis, genital ulcers, recurrent uveitis, erythema nodosum and other numerous mucocutaneous, gastrointestinal, neurological, vascular manifestations. Despite many biomarkers (anti-lysozyme, serum endocan, serum alpha 1-acid glycoprotein (AGP)) have been investigated for evaluating disease activity and predicting disease severity, none of mentioned above have accessibility to be used in clinical routine. During recent years neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been proposed as easy countable markers for severe inflammation and endothelial injury and therefor can be used in the assessment of Behcet's disease activity.
Objectives: The aim of this study is to analyze the potential role of NLR and PLR as markers of the Behcet's disease activity.
Methods: 62 patients with Behcet's disease (76,4% male and 23,6 % female) and 56 healthy controls were included in this study. Patients with Behcet disease fulfilled The International Criteria for Behcet's disease (ICBD 2006). Disease activity was assessed with Behcet's Disease Clinical Activity Form (BDCAF). All patients at the moment of the study had active Behcet's disease. Participants from the control group didn't present any history of cardiac or endocrine disease, because mentioned above conditions can also cause high levels of NLR and PLR.
Results: The mean age of patient group was 36±11,2 years. All patients had oral ulcers at any episode of the disease, 82,26% of patients had erythema nodosum, 61,29% -genital ulcers. 40,38%- eye lesions, 0,05%-entero-Behcet, 0,032%- neuro-Behcet. According to our study, levels of NLR positively correlate with the BDCAF score (r=0.401, p<0.01) and levels of CRP (r=0,571, p<0,01),

while there was no correlation found between PLR and disease activity. Levels of NLR and PLR were both significantly higher in the patient group compare to the controls (p<0,001 and p<0,05 accordingly).

Conclusion: Taking into consideration data from our study NLR could be implemented in clinical practice as a cheap and easy accessible marker of the Behcet's disease activity. On the other hand, further studies with bigger samples are required to evaluate changes of PLR in BD. Assessment of NLR and PLR among BD patient in remission is required to find out if there are any changes compared to healthy controls.

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Disclosure of Interests: None Declared.

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AB1520 A SURVEY ON OCULAR CICATRICIAL PEMPHIGOID. WHAT DO RHEUMATOLOGISTS AND OPHTHALMOLOGISTS THINK ABOUT IT?

Keywords: Rare/orphan diseases

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Background: Mucous membrane pemphigoid is a systemic, chronic, scarring inflammatory disease of autoimmune aetiology. Isolated ocular involvement has classically been called ocular cicatricial pemphigoid (OCP). Treatment is always systemic, which is why ophthalmologists seek the support of rheumatologists and guidance on autoimmunity. Given the lack of epidemiological data by region, the seriousness of this pathology, and the possible insufficient knowledge by medical professionals, it was proposed to carry out this work.

Objectives: To know the familiarity of rheumatologists and ophthalmologists with OCP and their interdisciplinary interaction in the region.

Methods: An online survey was conducted, which was accessed through a link to a Google form. This questionnaire was addressed mainly to rheumatologists and ophthalmologists belonging to similar scientific societies in America. The link was sent by email to the rheumatology societies. The questionnaire consisted of 13 questions. Questions were asked about age, sex, country, specialty, main place of work of the respondents (public or private institution, or private practice), whether or not they are familiar with the entity, how many patients they see annually, the specialties with which they work each surveyed to address these patients, diagnostic methodology (clinical vs. biopsy), the treatments used, and the difficulties in approaching these patients in daily practice.

Results: Four hundred sixty-three surveys were received and 433 were included, excluding duplications and those surveyed that did not belong to an American country. Most of the participants were from Argentina, followed by Colombia, Chile, and Mexico. Table 1 shows that, in general, doctors who work in private institutions are more aware of the disease, and rheumatologists are the primary specialty that ophthalmologists familiarized with OCP rely on their patients for multidisciplinary management. The most used treatments in the last year were: methotrexate (54.4%), azathioprine (26.8%), mycophenolate (17.4%) and rituximab (16.1%). The main difficulties reported in diagnosing and/or treating these patients were: the lack of information, knowledge, and/or transmission of the OCP in the different scientific activities and texts of the specialties involved in treating this entity; the difficulty in accessing and performing the biopsy of the ocular conjunctiva; and the difficulties in communication between specialists in order to carry out an appropriate follow-up.

Conclusion: Due to the high percentage of insufficient knowledge of this entity by rheumatologists (70%), and the great referral of these patients to rheumatology by ophthalmologists familiar with OCP (80%), it is imperative to work to expand its knowledge, transmission and joint work between both specialties, to improve and protocolize the approach to this entity, which can produce irreversible sequelae on the ocular surface.

Table 1. General characteristics

	Total, n= 433	Familiar with OCP, n=173 (39.9%)	Not familiar with OCP, n= 260 (60.1)	P value
Female, n (%)	252 (58.6)	92 (36.5)	160 (63.4)	0.06
Age, media (DS)	46.6 (11.6)	47.8 (11.2)	45.8 (11.8)	0.08
Specialty	307 (70.9)	96 (31.3)	211 (68.7)	<0.001
- Rheumatologists, n (%)	112 (25.9)	74 (66.1)	38 (33.9)	<0.001
- Ophthalmologists, n (%)	14 (3.2)	3 (1.7)	11 (4.2)	0.17
- Other specialties, n (%)				
Workplace:	231 (53.3)	79 (45.6)	152 (58.5)	0.01
- Public institution, n (%)	269 (62.1)	121 (69.9)	148 (56.9)	0.01
- Private institution, n (%)	203 (46.9)	85 (49.1)	118 (45.4)	0.44
- Private clinic, n (%)				
Number of patients with OCP evaluated in	23 (5.4)	0	23 (8.8)	<0.001
the las year:	379 (88.7)	147 (84.9)	232 (89.2)	0.18
- Entre 0-1, n (%)	25 (5.8)	24 (13.8)	1 (0.4)	<0.001
- Entre 2-10, n (%)				
- Más de 10, n (%)				
Specialties that evaluate patients with	229 (52.8)	140 (80.9)	89 (34.2)	<0.001
OCP together with ophthalmologists:	100 (23.1)	48 (27.7)	52 (20)	0.06
- Rheumatology, n (%)	17 (3.9)	16 (9.2)	1 (0.4)	<0.001
- Dermatology, n (%)				
- Others, n (%)				
Diagnosis done by biopsy, n (%)	196 (45.5)	121 (69.9)	75 (28.8)	<0.001

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AB1521 DOES PATIENT POSITION AFFECT COMMON FEMORAL VEIN WALL THICKNESS MEASUREMENT BY DOPPLER ULTRASONOGRAPHY AS A DIAGNOSTIC TEST?

Keywords: Behcet's disease, Ultrasound

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Background: We reported the first controlled Doppler ultrasound (US) study demonstrating increased common femoral vein (CFV) thickness in Behçet's Disease (BD) [1]. We also recently showed that this is a distinctive feature of BD, rarely present in other inflammatory diseases with a specificity higher than 80% for the cut-off value of ≥ 0.5 mm [2]. Standart lower extremity venous Doppler US is performed in erect position for venous thrombosis or insufficiency [3]. However, we measured CFV thickness in supine position in our previous studies.

Objectives: In this study, we aimed to assess CFV wall thickness measurement by Doppler US both in supine and erect positions to validate the accuracy and practicability of this diagnostic method in BD.

Methods: We included 42 patients (Male/Female:27/15, mean age:39.8 (10.04) years) with a diagnosis of BD and sex and age-matched 41 healthy controls (Male/Female:21/18, mean age: 36.5 (8.4) years). The clinical data were recorded during routine visits. Bilateral CFV thickness was measured with Doppler US both in erect and supine positions by an experienced radiologist on the same day.

Results: Clinical characteristics of BD patients were given in *Table 1.* Bilateral CFV wall thickness was significantly higher in BD than in healthy controls (0.74 vs 0.18 mm, p<0.001 for right, 0.74 vs 0.19 mm, p<0.001 for left). There was no statistically significant difference between erect and supine positioned measurements of CFV wall thickness both in BD and healthy control groups *(Figure 1).*

Conclusion: CFV measurement by Doppler US is a new, accurate and non-invasive diagnostic tool for the diagnosis of BD. Although lower extremity venous Doppler US is performed in erect position for the assessment of venous thrombosis or insufficiency, our study confirmed that patient position does not affect CFV wall thickness measurement. Both erect and supine positioned CFV wall thickness measurements can be done accurately for the diagnosis of BD.

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Table 1. Clinical characteristics of patients with Behçet's Disease

	Behçet's Patients (n=42)
Age, mean (SD), years	39.8 (10.04)
Gender, male, n (%)	27 (64.3%)
Disease duration, mean (SD), years	9.1 (8.2)
Follow-up time, mean (SD), months	110.1 (98.5)
Family History, n (%)	7 (16.7%)
Pathergy positivity, n (%)	3 (7.1%)
Mucocutaneous Involvement, n(%)	16 (38.1%)
Major Organ Involvement, n (%)	26 (61.9%)
Vascular Involvement, n (%)	24 (57.1%)
Ocular Involvement, n (%)	8 (19%)
Neurological Involvement, n (%)	7 (16.7%)

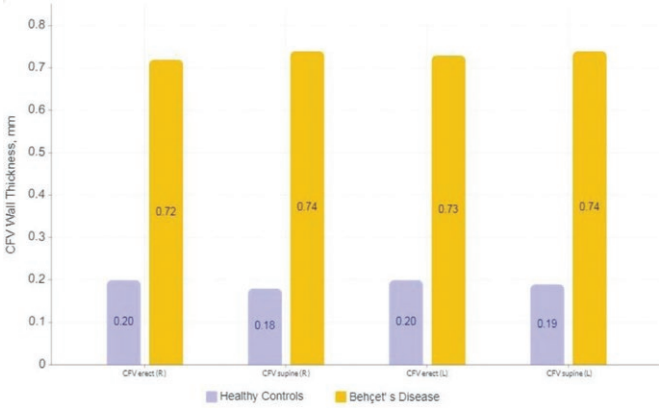


Figure 1 : Measurements of Common Femoral Vein Wall thickness of Behçet's patients and healthy controls in supine and erect positions

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1522

ROLE OF BIPHOSPHONATES IN THE MANAGEMENT OF OSTEOGENESIS IMPERFECTA

Keywords: Bone diseases

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Background: Osteogenesis imperfecta (OI), or Lobstein's disease, is a group of genetic diseases characterized by excessive bone fragility, due to a congenital defect in the elaboration of collagen fibers of the connective tissue. Bisphosphonates, with their anti-resorptive properties, are currently the reference medical treatment for this pathology, but remain a symptomatic treatment of the disease.

Objectives: This study aims to describe the addition of biphosphonates to the management of OI.

Methods: This is a retrospective descriptive study collecting patients with OI followed in the rheumatology department of the Fattouma Bourguiba Hospital of Monastir. The study period was 17 years from 2005 to 2021. We investigated the evolution of bone mineral density (BMD) under biphosphonates by evaluating the total gain in BMD with measurement of the SDD: Smallest Detectable Difference (in gr/cm2). The threshold value of the SDD in absolute value is equal to 0.030 to 0.035 g/cm2. A variation of the SDD > 0.030 g/cm2 is a significant variation whether positive or negative.

Results: We collected 16 patients. Fourteen patients had a type I of OI. Type III and type IV were found in one case each. Nine of our patients were male with a sex ratio M/F=1.3. At diagnosis, the patients were divided into 13 children and 3 adults. The mean age at diagnosis was 11 years old for children [1 year, 18 years] and 34 years old for adults [27 years, 40 years]. Fifteen patients had a history of fracture. Fractures in the lower limbs were more frequent than in the upper limbs, with a number of fractures ranging from 3 to 20. Bone deformities were found in 10 patients affecting the lower limbs in 8 cases, the spine in 4 cases, the thorax in 2 cases, and the skull in 1 case. Radiologically, all patients had bone hypertransparency. Spinal involvement was frequent and included scoliosis (2 cases), hypercyphosis (2 cases), biconcave vertebral compression (4 cases) and platyspondylia (4 cases). Osteoporosis was found in 9 cases and osteopenia in 6 cases. Therapeutically, all our patients received vitaminocalcic supplementation and biphosphonates: pamidronate, according to Glorieux's protocol: 1.5 to 3 mg/kg/cycle (i.e., 0.5 to 1 mg/kg/d 3 days in a row) for children and 90 mg (single infusion) for adults. The side effects observed with bisphosphonates were: hypocalcemia in 8 cases, flu-like syndrome in 5 cases, fever in 4 cases, and chest pain in 1 case. The evolution on biphosphonates was evaluated by the total gain in BMD. The mean SDD was: +0.105 g/cm² at the spine (significant positive change), +0.015 g/cm² at the femoral neck (non-significant positive change) and +0.014 g/cm² at the whole body (non-significant positive change).

Conclusion: The therapeutic management of patients with OI is multidisciplinary and complex. In this study, all patients were treated with pamidronate according to the protocol of Glorieux. They had a gain in bone mass that was remarkably significant in the spine.

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Diagnostics and imaging procedures

AB1523

CLINICAL SIGNS AND ACTIVITY LIMITATIONS ASSOCIATED WITH DURAL SAC ECTASIA IN INDIVIDUALS WITH MARFAN DISEASE: A CROSS-SECTIONAL CASE-CONTROL STUDY

Keywords: Cardiovascular disease, Rare/orphan diseases, Patient reported outcomes

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Background: Dural ectasia often occurs in individuals with Marfan disease. Fibrillin-1, a matrix component of microfibrils, has been hypothesized to play a role in the circulation of cerebrospinal fluid [1]. Modifications to the circulation of cerebrospinal fluid in individuals with Marfan disease may lead to an increased pressure in the lumbosacral spine and a decreased pressure in the cephalic extremity.
Objectives: We hypothesized that individuals with Marfan disease and dural ectasia, as compared to individuals with Marfan disease without dural ectasia, may display a specific pattern of painful symptoms and spine-specific activity limitations [2]. The aim of our study was to compare: the frequencies and characteristics of painful symptoms, and the intensity of back and leg pain, spine-specific activity limitations and health-related quality of life, between individuals with Marfan disease with and without dural ectasia.
Methods: We conducted a single-centred cross-sectional comparative study. All individuals with Marfan disease followed in the department of cardiology of Bichat hospital (Paris, France) and recorded in the computerized database of the department from inception to January 2022 were systematically screened. Inclusion criteria were: adults ≥ 18 and ≤ 55 years; fulfilling Ghent nosology; FBN1 mutations confirmed by genetic testing; and CT-scan or magnetic resonance imaging available. Non-inclusion criteria were: history of lumbar surgery < 1 year; specific back pain (i.e. tumor, infection, traumatism, fracture, inflammatory rheumatic disease); individuals unable to speak, read and write French. Individuals were considered to have dural ectasia or not to have dural ectasia based on CT-scan or magnetic resonance imaging, according to Ahn and colleagues' criteria [3]. All self-administered questionnaires collected between 1/28/2022 and 9/12/2022 were included in the analysis.
Results: 247 individuals were eligible to participate and were contacted by mail. 90 (36%) individuals accepted to participate and were included: 55 (61%) had dural ectasia and 45 (39%) did not **(Figure 1)**. Mean participants' age was 39.3 (9.4) years and 45 (50%) were women. 80 (89%) participants had back pain, most often located in the lower back, 65 (71%) a history of scoliosis and 8 (9%) a history of spine surgery. 15 (17%) participants had a history of high blood pressure, 84 (93%) a dilation and/or dissection of the ascending aorta, and 52 (58%) an aortic surgery. The 3 most often reported painful symptoms were increased pain in the lower back with upright posture in 53 (58%) participants, increased headache with upright posture in 36 (40%) and increased pain in the lower back when walking in 31 (34%). The frequencies of increased headache with upright posture and of increased pain in the lower back when coughing, laughing and/or sneezing were numerically higher in participants with than without dural ectasia (49% vs 26% and 13% vs 0%, respectively), without reaching statistical significance (p-value=0.030 and p-value=0.021, respectively) **(Table 1)**.
Conclusion: Individuals with Marfan disease and dural ectasia, as compared to those without dural ectasia, display a specific pattern of painful symptoms, including lower back pain and headache with upright posture. We detected too a difference in favor of a link between ectasia of the dural sac and abundance in ascending aortic surgery (64% vs 49%).

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AB1524

A NOVEL ACCELEROMETRY-BASED METHOD FOR EARLY DETECTION OF PERIPHERAL NEUROPATHY ASSOCIATED WITH SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES

Keywords: Telemedicine, Diagnostic tests, Validation

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Background: Systemic autoimmune rheumatic diseases (SARDs) such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), primary Sjögren's syndrome (SS), and systemic sclerosis (SSc) occasionally affect the peripheral nervous system. Nerve conduction studies (NCS) can almost certainly confirm the diagnosis of SARD-associated neuropathy. The NCS method is usually considered the gold standard for neuropathy assessment, although this method is based on physicians' knowledge and experience. However, it is painful for patients, long-lasting, prone to errors, and can't be used for routine follow-up. There is an urgent need for potential alternative diagnostic screening methods for implementation in everyday practice. Wearable sensor devices, such as accelerometers, are instruments that can be utilized to acquire data during different activities. Their size and wirelessness, lower cost, portability, and use in home-based and real-life situations are a few of the advantages.
Objectives: To evaluate a telemedicine wearable device with a machine learning algorithm that can be used as a screening and tracking tool for SARD-related neuropathy.
Methods: A monocentric, diagnostic study was conducted at the Institute of Rheumatology in 2020. The participants were healthy volunteers and SARD patients who had suspected neuropathy. The participant started with the NCS examination; electrodes were placed on the limbs, and amplitude, latency, and conduction velocity of n. medianus, n. ulnaris, n. peroneus, n. tibialis, and n. supraspinatus (motor and sensory fibres) were measured. The novel method consists of four wearable sensors placed over the middle of the hands and feet. The subject performed six exercises with open and closed eyes. Raw data was sent through the Bluetooth connection from the sensors to the tablet and then via WiFi connection to the central server for further analysis. A wearable device uses a specific mathematical algorithm that transforms signals from the accelerometer and gyroscope into specific values. The outcome is defined as a binary variable: whether or not neuropathy exists.
Results: The study included 23 participants (9 ♂ and 14 ♀), 11 with SARDs (45.8%). Of the total number of SARD participants, 8 (72.7%) had neuropathy confirmed with the NCS examination. The features (such as acceleration or power) obtained with signal processing were examined, and only those that can be used to discriminate SARD-related neuropathy are presented (Table 1). The model for binary classification was developed and presented in Table 2. As shown, the sensitivity and specificity are satisfactory, but the confidence intervals are still wide. Positive predictive value is significantly lower compared to negative predictive value.
Conclusion: Wearable sensors represent accurate and promising technology for the diagnosis of neuropathies related to SARDs. Further studies are needed to evaluate the true accuracy of the technology.

Table 1. The features used to discriminate neuropathy

	Neuropathy (NCS)		p value
	No (15)	Yes (8)	
EXC 1 heel-toe walk			
SDP LL Heels 10hz	0.01±0.01	0.01±0.003	0.02
SDP Acc Norm LL Heels	0.1±0.05	0.06±0.03	0.01
EXC 2 tandem walk			
SigPow Acc Norm RL Min	1.5±0.2	1.33±0.13	0.07
EXC 3 heel-knee test			
CorrSeg Acc Norm LL CIE	0.03±0.03	0.01±0.02	0.03
DiffSig Acc Norm LL_LL OpE	0.06±0.1	0.02±0.015	0.2
DiffSig Acc Norm RL_RL OpE	0.05±0.1	0.03±0.06	0.5
CorrSeg Acc Norm LL CIE Std	0.7±0.23	0.44±0.16	0.03
EXC 4 Romberg test			
Var Acc Norm LL CloseEye	0.1±0.15	0.28±0.3	0.04
EXC 5 postural tremor			
StatPos AbsDiff RA Max	0.02±0.01	0.01±0.01	0.07
Var Acc Norm LA BefAft	1.2±0.6	0.71±0.2	0.05
EXC 6 finger-nose			
DiffSig Acc Norm RA_RA OpE	1.0±0.02	0.97±0.1	0.01
Exp Acc Norm RA TotPow	0.003±0.01	-0.02±0.03	0.01

Table 2. Validation of new proposed model for neuropathy screening

Model	NCS - (n=15)	NCS + (N=8)	Sn	Sp	PPV	NPV
1 FT EXC 1 + 4 WS + FT EXC 3	3	7	0.875 (0.466-0.993)	0.800 (0.513-0.946)	0.700 (0.513–0.946)	0.923 (0.621–0.996)
WS -	12	1				

Abb. FT – feature, WS – wearable sensors, NCS – nerve condution studies

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Disclosure of Interests: Zoran Veličković: None declared, Slavica Pavlov Dolijanovic Speakers bureau: Pfizer, Novartis, Eli Lilly, Abbvie, Nina Tomonjic: None declared, Saša Janjić: None declared, Biljana Stojic: None declared, Goran Radunovic Speakers bureau: Pfizer, Novartis, Eli Lilly, Abbvie, Grant/research support from: Novartis, Abbvie.

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AB1525 THE PRESENCE OF POWER DOPPLER SIGNALS IN THE DELTOID LIGAMENT, ESPECIALLY WITH A BROAD AND DEEP DISTRIBUTION, MAY PROVIDE DIAGNOSTIC CLUES FOR SPONDYLOARTHRITIS, PARTICULARLY UNDIFFERENTIATED SPONDYLOARTHRITIS

Keywords: Ultrasound, Rheumatoid arthritis, Spondyloarthritis

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Background: Power Doppler (PD) signals are occasionally detected in the deltoid ligament on musculoskeletal ultrasound (MSUS) examination of symptomatic ankles in nontraumatic inflammatory rheumatic diseases. However, it is often neglected due to its unclear clinical significance.

Objectives: To evaluate the significance of PD signals in the deltoid ligament detected by MSUS in inflammatory rheumatic diseases.

Methods: We reviewed the record of MSUS examined in Japanese Red Cross Medical Center between April 2015 and October 2022. We examined the characteristics of medical record information and images of cases in which power Doppler signals were observed in the deltoid ligament. Patients with only a few punctate signals or less were excluded. Patients with only traumatic or degenerative disorders were also excluded.

Results: PD signals more than a few punctate signals were observed in the deltoid ligament in 31 cases. The disease categories and diagnoses of the patients were as follows: 13 spondyloarthritis (SpA) patients (9 undifferentiated SpA (USpA), 2 psoriatic arthritis, 2 reactive arthritis), 10 rheumatoid arthritis (RA) patients (6 early RA, 4 established RA), 7 crystal-induced arthritis (CIA) (6 gout, 1 CPPD), and 1 primary Sjögren's syndrome. All SpA patients met the ASAS criteria for peripheral SpA and all RA patients fulfilled the 2010 ACR/EULAR classification criteria. In SpA cases, PD signals tended to distribute widely to the deep layer of the ligament (broad distribution, 10 out of 13 cases), while they tended to be predominant on the outer surface of the ligament in RA cases (superficial distribution, 7 out of 10 cases). There was a significant difference in the PD signal distribution pattern between SpA and RA by Fisher's exact test (p=0.0397). In all CIA patients, hyperechoic materials were detected in the ligament.

Conclusion: According to literature reports, SpA is considered relatively rare in Japan, where the HLA-B27 positivity rate is < 0.3%, with an estimated population prevalence of < 0.01% [1]. The estimated prevalence of patients with RA in Japan is 0.65% [2], similar to the rest of the world. Considering the prevalence of each disease, we speculate that PD signals in the deltoid ligament are more characteristic of SpA. The presence of PD signals in the deltoid ligament, especially with a broad and deep distribution, may provide diagnostic clues for SpA, particularly USpA.

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Table 1.

Disease category & diagnosis	Number of our patients with PD signals in the deltoid ligament	Estimated prevalence in Japan reported in the literature	Distribution of PD signals in the deltoid ligament	
			superficial	broad
Spondyloarthritis	13	< 0.01% *Ref1	3	10
Undifferentiated spondyloarthritis	9			
Psoriatic arthritis	2			
Reactive arthritis	2			
Rheumatoid arthritis	10	0.65% *Ref2	7	3
Crystal-induced arthritis	7		1	6
Gout	6			
CPPD	1			

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1527 TELEDIDACTIC MUSCULOSKELETAL ULTRASOUND COURSE AND COMPARISON WITH CONVENTIONAL ON-CAMPUS TRAINING – INTERIM ANALYSIS OF THE TELMUS STUDY

Keywords: Ultrasound, Education

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Background: Musculoskeletal ultrasound (MSUS) is increasingly gaining importance as an imaging tool in rheumatology. Most training programs currently address resident doctors. However, several studies have demonstrated that teaching MSUS to medical students improves their palpation skills and understanding of musculoskeletal anatomy. With the development of portable ultrasound devices, MSUS education is lately getting more flexible and location-independent. In addition, the COVID-19 pandemic raised awareness of telemedicine training as a powerful tool to ensure the teaching of practical skills under pandemic conditions.

Objectives: The purpose of our study is to establish a telemedical MSUS course for medical students and to compare its effectiveness with a conventional on-campus course as a world-wide pilot study. In doing so, we aim to expand student educational opportunities in MSUS using innovative teaching options while ensuring quality maintenance of teaching.

Methods: Thirty medical students were randomized to either a virtual group being delivered only telemedicine instructions, or an on-campus cohort receiving the course in a conventional format. Each student was provided with a hand-held ultrasound device. Prior to the start of the course, the students' skills were assessed with an Objective Clinical Structured Examination (OSCE). During the course, a DEGUM-III-certified course instructor taught the basic physics of ultrasound and standard sections of the MUDE ultrasound protocol[1]. In order to quantify the students' learning progress, a second OSCE was carried out after completion of the course. [1].

Results: At the time of this analysis, data collection within the on-campus course has already been completed, whereas the virtual course is still ongoing. While the average score of the students in the PRE-course OSCE was 21,02% (SD ±6,78), the students were able to achieve an average of 90% (SD ±6,81) in the POST-course OSCE after the intervention.

Conclusion: With the results obtained so far, it can be shown that an innovative course concept with hand-held ultrasound devices, originally developed for dermatologists to improve the detection of psoriatic arthritis, can be used very well in student teaching without major modifications and leads to a significant increase in MSUS skills among medical students. The TELMUS study thereby offers a successful example of extending an existing course concept to student teaching and thus promoting the next generation of rheumatologists.

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Figure 1: Study design

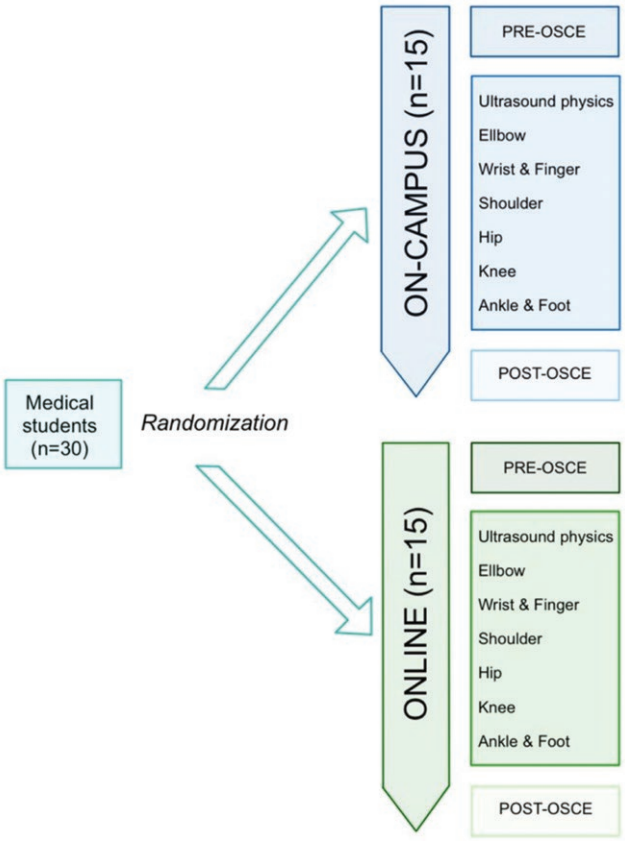


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1528

APPLICATION OF BONE MARROW EDEMA SCORING SYSTEM DERIVED ARTIFICIAL INTELLIGENCE IN RAPID RADIOGRAPHIC PROGRESSION RESCUE STUDY

Keywords: Rheumatoid arthritis, Imaging

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Background: We demonstrated new bone marrow edema (BME) scoring system in X-ray (specificity 90%, sensitivity 65-70%) using deep learning with artificial intelligence (AI) reflects MRI BME in previous EULAR meeting[1].
Objectives: In this study, to ascertain whether BME score in this system by X-ray film might reflect MRI BME in Biologics therapy, we retrospectively applied this system to the rapid. radiographic progression rescue study previously reported[2].
Methods: RA patients inadequate response with MTX who have extensive BME in single or bilateral wrist joints and DAS28-ESR>3.2 were treated by enhanced group, of conventional synthetic (cs) DMARDs (26 patients) or by biologics (23 patients). X-ray film. of two groups after 3-6 months treatment applied to BME scoringsystem (cut off:0.4) and compared with MRI BME.
Results: J-PEG file of hand Xray film were uploaded to new BME scoring system(Figure 1). BME score are expressed as Positive or Negative and index [0-1]. In biologics group, number of BME score positive rate reduced from 65.3% to 15.3% after treatment in MRI BME improvement group and reduced 78.5% to 57.1% in MRI BME unchanged group(Table 1). In csDMARDs enhanced group, number of BME score positive rate reduced from 75% to 25% after treatment in MRI BME improvement group and reduced 59.7% to 53.1% in MRI BME unchanged group. In both groups, false negative (N: Figure 1, white color back) patients were observed.
Conclusion: AI-derived bone marrow edema score may reflect bone marrow edema in MRI in biologics treatment and may help early recognition of biologics efficacy during treatment.

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Table 1. RED(P): BME score positive, Black(N):BME score negative, Before Biologics therapy (0M), after therapy (3/6M)

No	BIO	AI -L0M	AI-R0M	AI-L3/6M	AI-R3/6M	mTSS/y	ΔmTSS	MRI BE improve	BE% improve
1	TAC1.5m g +MTX4mg/w+IFX	N	P	N	N	30	0	O	82.1
2	MTX8mg/w+ADA	P	P	N	N	6.4	0	O	100
3	MTX10mg/w+ADA	N	P	N	N	8.2	0	O	79.3
4	MTX6mg+TCZ	P	P	N	N	8.4	0	O	100
5	MTX8m g /w + A D A	N	N	N	N	42	0	O	77.1
6	MTX6mg/w+ T C Z	N	P	N	P	30.8	0	O	71
7	MTX8mg/w+ADA	P	N	P	N	15.1	0	O	71.4
8	MTX12mg/w+ADA	P	N	N	N	31.2	0	O	81.5
9	MTX12mg +ADA	P	N	N	N	33	0	O	74.1
10	MTX6C,SASP1000 +CPZ	N	P	N	N	16.7	2	O	80
11	Bu100mg+ABT	N	N	N	N	10	0	O	72.7
12	TCZ	P	P	N	N	15	0	O	85.7
13	MTX6mg/w+GOL100m g	P	P	N	P	11.7	1	O	89.3
14	MTX8mg/w+ADA	P	P	N	P	8	-4.6	O	90.4
15	BU150+TAC0.5+ABT	P	P	P	P	5.4	0	X	39.3
16	MTX10mg/w+ADA	P	N	P	N	21.8	0	X	6.3
17	B u 1 0 0 m g +ADA	P	P	P	P	37.7	20.6	X	0
18	MTX8mg/w+IFX	P	P	P	P	32	8	X	-15.3
19	MTX10mg/w+ ADA	N	P	P	N	20	0	X	42.3
20	MTX12mg +ADA	P	P	P	P	14.6	0	X	-2.7
21	MTX12mg/w+ADA	N	N	N	N	8.4	10	X	29.2
22	MTX10mg+BU200mg+ADA	N	N	N	N	12	5.3	X	11.1
23	MTX6mg/w+ABT	N	P	N	P	4	12	X	-54

Figure 1



Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1529

MICROPLASTIC POLLUTION IN SYNOVIAL FLUID SAMPLES FROM SWOLLEN JOINTS ANALYZED WITH RAMAN SPECTROSCOPY

Keywords: Crystal arthritis, Diagnostic tests

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Background: Microplastics (MPs) have been identified in different types of tissue, including lung, bowel, placenta and as well in human whole blood [1]. During analysis of synovial fluid samples with Raman spectroscopy with the purpose of identification of crystals related to crystallopathies, presence of multiple types of MPS have been identified. Due to the recent interest in the effect of plastic pollution on human health, the noticed presence of these particles in synovial fluid samples is concerning and worthy of our attention.
Objectives: The objective of this study was to characterize deposited MPs in samples drawn from arthritis patients presenting to our rheumatology outpatient clinic, with the aim of calculating their prevalence and estimate the significance of their presence against blank control samples as we are using a novel and highly sensitive technique of integrated Raman spectroscopy with Polarized light microscopy in routine clinical practice.
Methods: This is an analysis of Raman spectroscopic data retrieved from 156 synovial fluid samples drawn from a consecutive series of patients visiting our outpatient clinic. Data was compared against a series of blank samples of MiliQ processed in similar fashion. The number of required blank samples was calculated with the formula of Rosner (2011, [2]), the study population was compared against the controls with a Chi-Square test.
Results: A total of 96 MPs were identified, in 4 distinct types; polyethylene (PE), polystyrene (PS), polypropylene (PP), and polyethylene terephthalate (PET). A total of 44 samples (28.2%) were positive for one or more particle (Figure 1). 19 (12.2%) samples had one identified MP, 15 (9.6%) had two identified MP, and 10 (6.4%) had three or more identified MPs (Figure 3). Combinations of MPs were present in 7 of 22 samples (31.8%) with more than one MP. Most MPs were identified extracellular, although one case of intracellular polyethylene particles was identified.

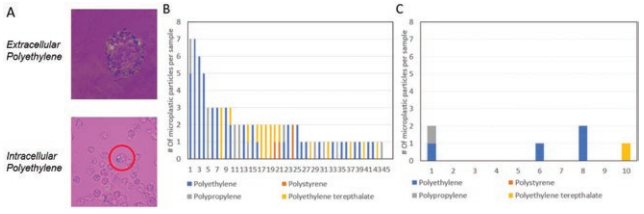


Figure 1 *: A: Compensated polarized light microscopy images of extracellularly and intracellularly found polyethylene microplastics. B: Distribution of particles over patient samples with identified microplastics. C: Microplastics found in control samples.*

The incidence in MPs in the study population was 30.8%. With an alpha (significance level) of 0.05 and a power of 90%, 10 blanks control samples would be enough to find a significant difference if in none of these samples particles are identified. However, we identified one or more microplastics in 4 (40%) of the 10 samples. Polyethylene was identified in 3 samples (30%), polypropylene in 1 (10%), and polyethylene terephthalate in 1 (10%). 1 (10%) sample had a combination of plastic types. With a threshold of 1 or more identified MPs considered positive, there is no significant difference (p = 0.542) between the blank controls and the patient sample population.
Conclusion: Due to numeric presence of extracellular microplastics in both patient material as the blank control samples we define that the presence of one or two MPs in a synovial fluid sample from a swollen joint is not significant and probably of no clinical importance. For the determination whether a higher number of extracellular MPs can be significant and of potential clinical relevance, more control samples are to be measured. The interpretation of the presence of intracellular microplastics needs further investigation.
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AB1530

USING MACHINE LEARNING TO ANALYZE THE FUNDOSCOPY OF ANKYLOSING SPONDYLITIS, PSORIATIC ARTHRITIS AND PSORIASIS

Keywords: Imaging, Artificial intelligence, Spondyloarthritis

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Background: Autoimmune diseases are associated with an increased risk of cardiovascular disease which can be preceded by microvasculature changes. The study about fundoscopy in ankylosing spondylitis is described by Bentum et al.[1] but the related study about deep learning model is insufficient.
Objectives: To validate the ability of machine learning model to verify the fundoscopy of ankylosing spondylitis, psoriatic arthritis, psoriasis and normal control.
Methods: We collected 1864 color fundus exams of 1105 patients with ankylosing spondylitis, psoriatic arthritis and psoriasis in Chang Gung Memorial Hospital in Taiwan from January 2001 to June 2022. The control group is 7122 fundoscopies of 5525 patients matched with age and gender. We separated database into training group, validation group and testing group. (7:1.5:1.5). We trained two convolutional neural networks including Vgg-11 and ResNet-18 models to perform the segmentation and capture the obscure findings of fundoscopy that human eyes cannot identify. We use the sensitivity, specificity, AUC, odds ratio and positive likelyhood ratio to evaluate the performance of machine learning to diagnose ankylosing spondylitis, psoriatic arthritis and psoriasis.
Results: The ankylosing spondylitis, psoriatic arthritis and psoriasis patients have higher body mass index, disease-modifying antirheumatic drugs and biological agent's usage, and even more comorbidities with dyslipidemia, hypertension and coronary artery disease compared with control group. In the setting of one case with solitary image of fundoscopy, the machine learning model of ResNet-18 showed AUC 0.78 with sensitivity 82% and specificity 66 %. In the setting of one case with solitary image of fundoscopy, the machine learning model of Vgg-11 showed the AUC 0.76 with sensitivity 79% and specificity 64%. The odds ratio is 8.54 and the positive likelihood ratio is 2.41 for deep learning model to predict the diagnosis of diseases.
Conclusion: The performance of machine learning model to predict the diagnosis of ankylosing spondylitis, psoriatic arthritis and psoriasis is quite acceptable. Fundoscopy analyzed with deep learning model may be a useful tool to help us to stratify the patient of ankylosing spondylitis, psoriatic arthritis and psoriasis.
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Table 1. Demographic characteristic of study population after quality control of fundoscopy

	Patients (N=537)	Control (N=2016)	p-value
Male, n(%)	350 (65.2)	1256 (62.3)	0.24
Age (years), mean±SD	55.5 ± 16.3	56.4 ± 16.1	0.272
BMI, n, mean±SD	376, 25.7 ± 4.59	792, 24.8 ± 3.92	<0.001
Systolic pressures (mmHg), n	313	667	
Mean±SD	135 ± 20.3	136 ± 21.2	0.673
Smoke, n	139	400	
Yes, n(%)	36 (25.9)	105 (26.2)	0.935
Medications			
DMARD, n(%)	167 (31.1)	9 (0.4)	<0.001
Biological agents, n(%)	86 (16.0)	0 (0.0)	<0.001
Comorbidities			
Dyslipidemia, n(%)	121 (22.5)	268 (13.3)	<0.001
Hypertension, n(%)	201 (37.4)	420 (20.8)	<0.001
CAD, n(%)	46 (8.6)	86 (4.3)	<0.001
Total cholesterol (mg/dL), n	206	464	
Mean±SD	183 ± 39.3	180 ± 41.5	0.429
HDL (mg/dL), n	177	388	
Mean±SD	48.6 ± 13.6	48.0 ± 15.1	0.629
LDL (mg/dL), n	196	420	
Mean±SD	110 ± 47.7	108 ± 52.9	0.645

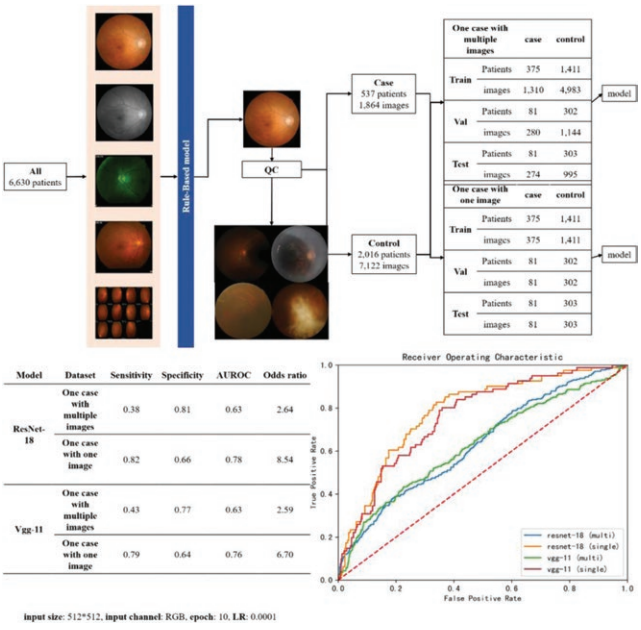


Figure 1. Flow chart and performance of machine learning models

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AB1531

HANDS-ON JOINT ASPIRATION WORKSHOP FOR INTERNAL MEDICINE RESIDENTS USING THE KNEE MODEL

Keywords: Education, Qualitative research methods, Diagnostic tests

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Background: Arthrocentesis is a procedure defined as synovial fluid aspiration that has diagnostic and therapeutic value in both the outpatient and inpatient setting. As mentioned in our prior study, joint arthrocentesis is not an Accreditation Council for Graduate Medical Education (ACGME) procedural requirement for Internal Medicine (IM) residents in the United States. Thus, we started the Phase I of our study, evaluating our in-house IM residents on their confidence level in performing intra-articular injections. This study resulted in more than half of the residents not feeling comfortable in performing arthrocentesis and nearly 100% of them reporting interest in learning arthrocentesis.[1] We later designed and implemented a resident-oriented quality improvement arthrocentesis teaching series.
Objectives: To design an arthrocentesis quality improvement (QI) teaching series for IM residents at Roger Williams Medical Center (RWMC) and evaluate their hands-on procedural skills and post procedural workshop confidence level in arthrocentesis.
Methods: Pre-workshop arthrocentesis learning material, including procedural check list and video, were compiled by IM residents at RWMC. A Rheumatology fellow demonstrated a one-to-one practice session on the knee model and the IM residents were graded based on the thoroughness of the procedural checklist. Each resident completed a post-procedure survey based on this arthrocentesis workshop.
Results: A total of 20 IM residents participated in the knee arthrocentesis workshop. As noted in Table 1, 85% of the residents believed that the pre-session information was helpful in preparing them for the workshop. (Table 1) On the post-workshop survey, 100% of the residents either agreed or strongly agreed to feeling more comfortable with the knee arthrocentesis after the practice, and all (100%) were interested in participating in future knee aspirations. The overall performance on the procedural aspect was also impressive with 40% of residents being able to complete the workshop on the knee model successfully on their first attempt and 55% on their second attempt. (Figure 1) Based on the procedure checklist score in Figure 1, residents were most proficient in the post-procedure stage with 100% score meanwhile, least successful on the aspiration of synovial fluid stage with a score of 55%.
Conclusion: Our QI project has shown that a standardized lecture series on how to perform arthrocentesis has resulted in a significant improvement in the overall confidence of internal medicine residents. This should be taken into consideration and incorporated as part of the internal medicine learning curriculum.

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Table 1. Post- workshop survey

Question	Responses
1.What post-graduate year are you?	PGY1: 35% PGY2: 40% PGY3: 25%
2. Prior to the session today, were you comfortable/confident with knee arthrocentesis/injection?	Not Comfortable/confident: 85% Somewhat comfortable/confident: 15% Quite comfortable/confident: 0%
3. The pre-session information was helpful in preparing me for the workshop	Strongly Agree: 85% Agree: 15% Undecided: 0% Disagree: 0% Strongly Disagree: 0%
4. After the first session, I feel more comfortable with knee arthrocentesis.	Strongly Agree: 75% Agree: 25% Undecided: 0% Disagree: 0% Strongly Disagree: 0%
5. Would you be interested in doing more knee aspirations/injections?	Yes: 100% No: 0%

A total of 20 Internal Medicine residents from Roger Williams Medical Center, a community hospital program, participated in this workshop.

Procedure Checklist and Overall Scores:

Patient Checklist (**Total score 6**)
- ☐ Identify correct patient
- ☐ Obtain consent (discuss risks and benefits)
- ☐ Allergy check (Lidocaine? Cleansing liquids? latex etc.)
- ☐ Is the patient on blood thinners? Have bleeding disorders?
- ☐ Any previous procedures? Adverse reactions?
- ☐ Confirm procedure site and mark pertinent landmarks

→ **Average for residents was score of 5.3 (88%)**

Aspiration Site Checklist (**Total Score 3**)
- ☐ Wash hands using sterile technique/use sterile gloves
- ☐ Clean area x3 with povidone-iodine, wipe with alcohol
- ☐ Spray site with ethyl chloride (optional)
- ☐ Inject lidocaine to form a wheal (optional)
- ☐ Insert neele, inject lidocaine along path of needle

→ **Average for residents was score of 2.9 (97%)**

Removal of Synovial Fluid (**Total Score 4**)
- ☐ Prepare aspirating syringe with 18-22 gauge needle
- ☐ Direct needle through weal into joint using technique discussed (lateral)
- ☐ Stabilize syringe with non dominant hand
- ☐ Gently aspirate as much fluid as possible

→ **Average for residents was score of 2.05 (51%)**
→ **40% (8/20) of residents were successful in 1st attempt of procedure, 55% (11/20) in 2nd attempt, 5% (1/20) in 3rd attempt**

Post Procedural Care (**Total Score 4**)
- ☐ Remove needle and dispose
- ☐ Cleanse and apply pressure to aspiration site
- ☐ Bandage +/- Ice
- ☐ Clean your area!

→ **Average for residents was score of 4 (100%)**

Figure 1: Procedure Checklist

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1532 **ULTRASOUND ASSESSMENT OF A1 AND A2 PULLEY ENTHESIS WITH ANATOMICAL AND HISTOLOGICAL CORRELATION**

Keywords: Imaging, Ultrasound, Enthesitis

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Background: Digital entheses are of particular interest in inflammatory arthritis. The annular pulleys (A) are forms of soft connective tissue organized as transverse fibers of variable width, thickness, and configuration that overlay the synovial sheath of flexor tendons. These structures prevent the flexor tendons from bowing and maintain them in constant relationship to the joint axis of motion.
Objectives: To describe and measure the ultrasonographic, anatomical, and histological characteristics of the A1 and A2 annular pulleys entheses.
Methods: A1 and A2 annular pulleys from 15 formalin-embalmed cadavers were assessed by grey-scale ultrasound (Figure 1) and then dissected. The ultrasonographic evaluations included the identification, widths, and characterization of insertion site of the annular pulleys. For the anatomical analysis, dissection was then performed, identifying the transverse fibers of the distal region of the palmar fascia as the proximal limit and the proximal interphalangeal joint as the distal limit. Measurements of the anatomical width of the pulleys were obtained with a digital caliper. For the histological study, 2x2 cm samples were received, fixed with 4% formaldehyde, and processed to obtain paraffin blocks, then cut into 4-micron sections and stained with hematoxylin-eosin. The slides were observed and measured with a Leica DMD 108 microscope. Quantitative data were expressed as mean ± standard deviation (SD) and qualitative data as n (%). Means were analyzed using Student's t-test and frequencies using the chi-square test and Fisher test when needed. Pearson's correlation coefficient (r) was used to analyze the linear correlation between the ultrasonographic and anatomical measurements. Statistical analyses will be performed using the SPSS program version 26.0.
Results: Fifteen cadaveric hands (9 males and six females) with a mean age of 79 years were included. Regarding the ultrasonographic assessment the mean ultrasound width of the A1 pulley was 0.27 ± 0.06 mm and A2 0.11 mm ± 0.04 mm in the thumb, while A1 was 0.36 ± 0.09 mm and A2 pulley 0.46 ± 0.06 mm on the other fingers. A strong correlation between the ultrasonographic and anatomical measurements was found (r=0.82). All A1 in the thumb shows sesamoid bones (SB) in the radial and ulnar sides where the annular pulley make its proximal attachment, while SB was found in just twelve hands in the second finger (80%) and two hands (13%) in the fifth finger. The histological description of the annular pulleys shows a well-vascularized outer surface and a fibrocartilaginous component in the inner surface. The insertion points at the sesamoid or the phalangeal bones demonstrate a diverse nature of the enthesis with fibrocartilaginous and fibrous areas.
Conclusion: These preliminary results show that ultrasound is a valuable tool for identifying annular pulleys' width and entheses, with good correlation with the anatomical and histological study. The annular pulleys have a mixed fibrous and fibrocartilaginous enthesis.
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Disclosure of Interests: Luis Coronel Grant/research support from: Amgen, Maribel Miguel: None declared, Joan Blasi: None declared, Sara Marsal: None declared, Maria-Antonietta D'Agostino: None declared, Ingrid Möller: None declared.
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AB1533 **DIAGNOSTIC VALUE AND BENEFITS OF PERFORMING A MINIMALLY INVASIVE TECHNIQUE FOR MINOR SALIVARY GLAND BIOPSY, A CASE SERIES**

Keywords: Sjögren syndrome, Diagnostic tests

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Background: Salivary gland biopsy plays an important role in the diagnosis of systemic diseases, especially Sjögren's Syndrome. Minimally invasive biopsy has a low risk of complications with respect to the classical technique, without losing its diagnostic capacity.
Objectives: To assess the utility and safety of minimally invasive technique in patients with suspected systemic disease and salivary gland involvement.
Methods: Retrospective analysis of 31 minor salivary gland biopsies performed by our Systemic Autoimmunity Disease Unit from November 1th 2020 to November 1th 2022, using a minimally invasive technique. Antibody profile and histopathological changes observed were recorded. Adverse events were registered immediately after the procedure and at the next medical visit.
Results: A total of 31 biopsies were reviewed. Mean age of patients was 60 years, most women (n=27, 87%). The success rate of obtaining glandular tissue was 94% (29/31). With respect to immunological data, 24 patients had positive ANAs (77,4%), 24 negative ENAs (77.4%) and 21 negative Rheumatoid Factor (67.7%). In histopathological evaluation 52% were normal salivary tissue (n=16), 23% had focal lymphocytic sialadenitis (n=7), 16% nonspecific chronic sialadenitis (n=5), 6% (n=2) non-existent or insufficient sample and 3% fatty infiltration (n=1). The only complication was a transient superficial lip ecchymosis in one patient (3,2%).
Conclusion: 23% of patients with immunonegative sicca syndrome are diagnosed with Sjögren´s Syndrome due to a minor salivary gland biopsy performed with a minimally invasive technique. This is a simple tool which saves time until diagnosis with low rate complications.
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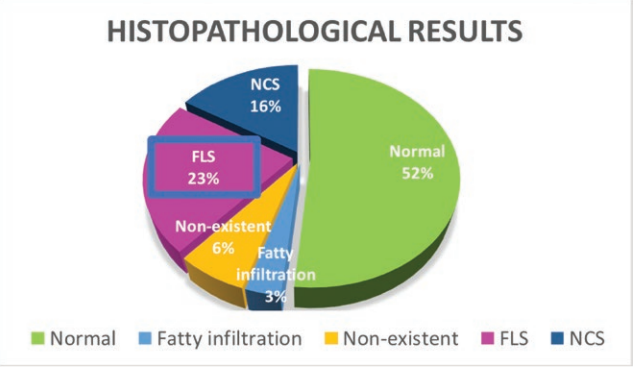


Figure 1.

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AB1534

A VALIDATION OF REGISTER DERIVED DIAGNOSES OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH INFLAMMATORY ARTHRITIS. DATA FROM NOR-DMARD

Keywords: Diagnostic tests, Comorbidities

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Background: There is a lack of knowledge concerning the validity of International classification of diseases (ICD) diagnoses extracted from health registers although this information is often used in epidemiological studies.
Objectives: To assess the validity of register derived diagnoses of interstitial lung disease (ILD) in patients with rheumatic diseases, using ILD identified on computed tomography (CT) and/or medical journal as gold standard.
Methods: The Norwegian Anti-Rheumatic Drug Register (NOR-DMARD) is a multi-centre prospective observational study that includes patients with a diagnosis of inflammatory arthritis who started treatment with disease modifying anti-rheumatic drugs. NOR-DMARD was linked to the Norwegian Patient Registry (NPR) and Cause of Death Registry. We searched both registers for ILD ICD-10 codes (J70, J84 or J99) and extracted CTs from participants at four hospitals. CTs taken three months before or within one year after the first ICD-10 diagnosis in the registries were considered relevant to the study. An expert thoracic radiologist (FA) scored all examinations according to presence of ILD and categorised the finding into; no ILD, possible ILD and confirmed ILD. Possible ILD CT images were re-examined by a second expert radiologist (TMA). In addition, medical records were searched for ILD diagnoses given by specialist clinicians on several occasions. Presence of confirmed ILD was assessed in patients with available CTs, registry ICD-code for ILD at ≥2 time points and across ILD diagnoses subgroups.
Results: We identified 80 cases with an ILD diagnosis given in a register (ICD-10 n (%); J70 10 (12.5), J84 52 (65.0) and J90 18 (22.5)). CTs were available in 72/80 (90%) patients, 60/72 (83%) within the pre-specified time-window. The ILD diagnosis was confirmed on CT in 31/80 (38.8%) and in 9/80 (11.3%) by medical records only. ILD was validated in 34 (56.7%) of 60 patients with available CT within the relevant time-period and in 28/43 (65.1%) patients who had received an ILD code at ≥2 time points and had a HRCT within the relevant time-period (Table 1). The diagnosis was confirmed in 20 (69.9%) of the 29 patients of this group who had received a J84 diagnoses. ILD diagnoses that were not validated were most frequently given under investigations for respiratory symptoms 20/38 (52.6%).
Conclusion: The validity of registry-based diagnoses of ILD must be carefully considered in epidemiological studies.

Table 1. Positive predictive value of ILD diagnoses from patient registers in cohorts with progressive selection criteria

Number of patients in cohort	Number of patients (%) with an ILD diagnosis confirmed by CT and/or medical records		
80 patients with ILD in register	42 (52.5)		
60 patients with ILD in register and available CT taken within the prespecified time-period	34 (56.7)		
43 with two or more ILD diagnoses in register and available CT taken within the prespecified time-period	28 (65.1)		
45 with two or more ILD diagnoses in register and available CT taken within the prespecified time-period across diagnoses	ICD10: J70 2 (33.3)	ICD10 J84 20 (69.0)	ICD10 J99 6 (75.0)

Footnotes: ILD: interstitial lung disease

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AB1535

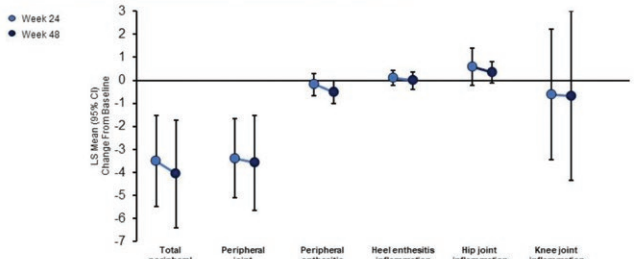
EFFICACY OF APREMILAST ON WHOLE-BODY INFLAMMATION INDICES IN PATIENTS WITH PSORIATIC ARTHRITIS: ASSESSMENTS BY WHOLE-BODY MAGNETIC RESONANCE IMAGING IN THE PHASE 4 MOSAIC STUDY

Keywords: Imaging, Psoriatic arthritis, Outcome measures

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Background: Psoriatic arthritis (PsA) is characterized by various patterns of inflammatory arthritis, enthesitis, dactylitis, and spondylitis. Apremilast is an oral immunomodulating phosphodiesterase-4 inhibitor that is indicated for treatment of PsA. Whole-body magnetic resonance imaging (WB-MRI) allows assessment of joints and entheses of the entire body in one examination when using the Outcome Measures in Rheumatology Clinical Trial (OMERACT) MRI whole-body scoring system for inflammation in peripheral joints and entheses (MRI-WIPE), which has not previously been applied in a clinical trial. Here we evaluate the efficacy of apremilast 30 mg BID (APR) on peripheral inflammation indices as measured by WB-MRI.
Objectives: To evaluate how APR affects inflammation in peripheral joints and entheses of patients with PsA as assessed by WB-MRI.
Methods: The phase 4 MOSAIC study was a multicenter, single-arm, open-label study evaluating APR (either as monotherapy or in combination with stable methotrexate) in patients with active PsA (diagnosis ≥3 months but ≤5 years, meeting the CASPAR criteria for PsA) for treatment up to 48 weeks. WB-MRI was performed at baseline, Week 24, and Week 48. Images were read and adjudicated by 2 experienced readers who were blinded to time of acquisition and clinical information. From WB-MRI, changes in the total peripheral inflammation index (83 joints and 33 entheses) were calculated using the OMERACT MRI-WIPE scoring system, as were changes in separate enthesitis and joint inflammation WB-MRI indices (WIPE-enthesitis and WIPE-joint inflammation). Changes in the heel enthesitis inflammation index (HEMRIS), the hip joint inflammation MRI index (HIMRISS), and the knee joint inflammation MRI index (KIMRISS) were explored.
Results: Overall, 122 patients were enrolled and treated with APR; 55% were women, mean age was 47 years, and patients had a mean duration of PsA of 1.9 years. The least squares mean (95% CI) change from baseline in total WIPE score based on total peripheral inflammation index (including both joint and enthesitis inflammation) as assessed by WB-MRI was -3.49 (-5.46, -1.52) at Week 24 and -4.06 (-6.39, -1.72) at Week 48, indicating significant improvement in peripheral inflammation (**Figure 1**). Significant improvements were also observed in the WIPE-joint inflammation scores at both Week 24 and 48, and in the WIPE-enthesitis scores at Week 48 (**Figure 1**). Both the heel enthesitis inflammation index (HEMRIS) and the hip joint inflammation MRI index (HIMRISS) showed little change, while the knee joint inflammation MRI index (KIMRISS) showed numerical, but not significant, improvement (**Figure 1**). No new safety signals were identified.
Conclusion: Patients with PsA treated with APR experienced a significant reduction in total peripheral inflammation, including significant improvement in peripheral joint inflammation and enthesitis, as assessed by WB-MRI. Results highlight the efficacy of APR on inflammatory manifestations of PsA as well as the benefit of using WB-MRI as a measure of inflammatory disease activity.

Figure. Inflammation Indices as Assessed by WB-MRI (FAS)[a]



	Total peripheral inflammation index[4,a]	Peripheral joint inflammation index[4,f]	Peripheral enthesitis inflammation index[4,g]	Heel enthesitis inflammation index (HEMRIS)[g]	Hip joint inflammation MRI index (HIMRISS)[g]	Knee joint inflammation MRI index (KIMRISS)[g]
Baseline Mean (SD)	28.78 (22.54)	24.06 (20.29)	4.73 (3.72)	2.22 (2.74)	0.87 (2.47)	9.93 (27.57)
Week 24[b] LS Mean Change (95% CI)	-3.49 (-5.46, -1.52)	-3.38 (-5.10, -1.66)	-0.17 (-0.65, 0.31)	0.10 (-0.21, 0.42)	0.58 (-0.23, 1.39)	-0.63 (-3.46, 2.21)
Week 48[c] LS Mean Change (95% CI)	-4.06 (-6.39, -1.72)	-3.58 (-5.66, -1.51)	-0.52 (-1.01, -0.02)	-0.01 (-0.38, 0.35)	0.34 (-0.12, 0.80)	-0.67 (-4.33, 2.99)

[a]Defined as all patients who received at least one dose of study medication.
[b]100 patients had WB-MRI assessed at Week 24.
[c]84 patients had WB-MRI assessed at Week 48.
[d]Based on mixed-effect model for repeated measures with change from baseline as the response variable and including scanner type, time as fixed effects, baseline composite score as a covariate.
[e]Sum of the peripheral joint inflammation index (BME + synovitis in 83 joints) and peripheral enthesitis inflammation index (BME and soft tissue inflammation at 33 entheses).
[f]Includes BME and synovitis in 83 joints.
[g]Includes BME and soft tissue inflammation at 33 entheses.
BME, bone marrow edema; HEMRIS, heel enthesitis MRI scoring system; HIMRISS, hip inflammation MRI scoring system; KIMRISS, knee inflammation MRI scoring system; LS, least-squares; SD, standard deviation; WB-MRI, whole-body magneticresonance imaging.

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AB1536

HOME SPIROMETRY AND OXIMETRY MONITORING IN PATIENTS WITH CONNECTIVE TISSUE DISEASE RELATED INTERSTITIAL LUNG DISEASE – A SINGLE CENTRE PROSPECTIVE STUDY

Keywords: Telemedicine, Lungs

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Background: Interstitial lung disease (ILD) is an important complication in patients with connective tissue disease causing significant impact on quality of life with a high mortality rate.
Objectives: We aim to determine the feasibility of home spirometry and oximetry reading, focusing on patients with connective tissue disease related ILD.
Methods: Patients with connective tissue disease related interstitial lung disease (CTD-ILD), idiopathic pulmonary fibrosis (IPF) and familial pulmonary fibrosis (FPF) were recruited and followed prospectively for 12 months. A handheld spirometer (MIR Spirobank Smart) and oximeter linked to a real-time electronic health journal via a smartphone app to record daily spirometry and oximetry readings were provided. Patients were asked to perform one or more spirometry manoeuvres at approximately the same time daily to reduce variability, with the best value for each day used for analysis.
Results: 62 patients with CTD-ILD, 31 IPF and 21 FPF were recruited. The median age was 66, 71 and 69 years respectively. 47.8% were males. Preliminary data on 99 patients demonstrated median forced vital capacity (FVC) predicted were 82.5% in the CTD-ILD, 84.1% in IPF and 83.7% in FPF cohorts with median follow-up of 208 days. The median oxygen saturation (SpO2) for 9501 readings was 96% in all three cohorts. 27.8% experienced Raynaud's phenomenon but only 5.6% in the CTD-ILD required an ear oximeter due to inaccurate measurement of oxygen saturation secondary to Raynaud's phenomenon.

Table 1. Forced Vital Capacity (FVC) and SpO2 readings in patients with CTD-ILD, IPF and FPF

	CTD-ILD	IPF	FPF
No. of Patients	54	28	17
Median Age (years)	66	71	69
No. of FVC Readings	5157	3384	1624
Median FVC (L)	2.35	2.66	2.06
Median FVC Predicted (%)	82.5	84.1	83.7
No. of SpO2 Readings	4475	3350	1676
Median SpO2 (%)	96	96	96

Conclusion: Home monitoring of FVC and oximetry in patients with CTD-ILD are feasible, empowers patients and generates granular data which can be useful in the detection of rapidly progressing ILD allowing early management.
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AB1537

CAN WE DIFFERENTIATE PATIENTS WITH DYSFERLINOPATHIES AND INFLAMMATORY MYOPATHIES BY MUSCLE ULTRASOUND? A DISCRIMINANT ANALYSIS STUDY

Keywords: Ultrasound, Myositis, Validation

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Background: Immune-mediated myopathies (IMM) are a heterogeneous group of diseases characterized by inflammation and muscle weakness; among their differential diagnoses are the dysferlinopathies, which are autosomal recessive neuromuscular disorders caused by mutations in the DYSF gene that present muscle weakness and significant increase of CK, just like IMM.
Objectives: Determine the sonographic differences between dysferlinopathies and immune-mediated myopathies and whether these allow their classification.
Methods: Observational, cross-sectional, and analytical study in which we evaluated 20 muscles from 11 patients with dysferlinopathies and 11 with inflammatory myopathies according to current classification criteria. They were matched for age, sex, and time of disease evolution. Clinical and laboratory variables were analyzed. GE LOGIQ™e equipment with a 4-12 MHz linear transducer was used, and the

thickness of each muscle was measured. A semiquantitative scale evaluated elementary lesions: atrophy, edema, power Doppler, and the Heckmatt scale (0-4) was calculated. Descriptive statistics were performed using measures of central tendency and dispersion according to the distribution of the variables, followed by bivariate analysis (Student's t-test and Chi[2] test). Finally, discriminant analysis was performed to determine which ultrasound variables best predicted the diagnoses.

Results: A total of 40 muscles were evaluated, finding a greater degree of atrophy and a higher Heckmatt scale in patients with dysferlinopathies compared to MII. Discriminant analysis showed that the set of 3 muscles, Right biceps/brachialis (BB), Right quadriceps (CD), and Gastrocnemius/right soleus (GC), had a diagnostic accuracy of 100% (sensitivity 100%, specificity 100%, canonical coefficient 0.733 p=.000). We present a set of 2 formulas that allow classifying with the highest score according to the measurement of the muscles in group 1 (dysferlinopathy) or group 2 (MII). Finally, a COR analysis was performed to determine the cut-off points of each muscle to classify as dysferlinopathies.

Conclusion: The study of 3 muscle groups (BB, CD, GC) presents high diagnostic accuracy to differentiate dysferlinopathies from MII, especially when there is no genetic study or antibodies available, and there is diagnostic doubt.

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Table 1. Characterization of patients with dysferlinopathies and inflammatory myopathies

	Dysferlinopathies n=11	IMM n=11	
General characteristics			*p
Women	9 (81.8%)	9 (81.8%)	
Males	2 (18.18%)	2 (18.18%)	
Ages (years)	39.54±11.24	37.36±10.62	*.971*
Evolution (years)	16±6.43	16.55±6.25	*.852*
Manual Muscle Testing Scores [MMT8 (mean)]	100 (79-112)	145 (136-147)	*.007*
Laboratories			
CK (mcg/L)	2785.50 (1052.75-4378.75)	162.00 (72.00-311.00)	*.000*
LDH (U/L)	289.00 (192.00-411.75)	170.00 (156.00-196.00)	*.001*
TGO (U/L)	52.75 (42.25-71.55)	25.30 (16.90-29.70)	*.011*
TGP (U/L)	78.30 (64.90-113.80)	20.10 (15.50-28.00)	*.016*
Muscle size			
BB (cm)	1.67±0.63	2.78±0.49	*<0.0001*
CD (cm)	2.70±0.84	3.45±0.87	*.046*
GC (cm)	1.88±0.42	3.16±0.42	***<0.001***
Discriminant analysis	Function	Function	**CP
BB	7.434	13.928	<2.44
CD	-1.117	-4.250	<2.72
GC	13.489	25.399	<2.29
Constant	-18.051	-52.935	
• Group 1: -18.051 + 7.434(B/B)-1.117(CD)+13.489(GC)			
• Group 2: -52.953 + 13.928(B/B)-4.250(CD)+25.399(GC)			

*p= <0.05; **CP: cut-off point

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AB1538 DETERMINATION OF ADENOSINE DEAMINASE (ADA) IN SYNOVIAL FLUID TO DIAGNOSE INFLAMMATORY ARTHROPATHIES

Keywords: Synovium, Inflammatory arthritides, Biomarkers

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Background: Adenosine Deaminase (ADA) determination is used to diagnose tuberculosis in several biological fluids, including synovial fluid (SF). Less known is the usefulness of ADA level in SF diagnosing other inflammatory arthropathies, and only a few reports could be found in the bibliography. In these reports ADA in SF seems higher in patients with septic arthritis, rheumatoid arthritis or crystal arthropathies compared with osteoarthritis.

Objectives: The objective is to evaluate the performance of ADA in SF in patients with joint effusion to diagnose inflammatory arthropathies.

Methods: All SF analyzed in 2022 at one center have been retrospectively reviewed. SF data have been collected (ADA levels and white blood cell) and definitive diagnosis of the treating physician -with all clinical and laboratory data- was recorded. Exclusion criteria were: bursas, prosthesis and hemarthros. Regarding the statistical analysis for the comparison of means of ADA in the different groups, the T-student test was used.

Results: There were 170 SF registered, 17 were excluded, thus finally 153 SF were included in the analysis. They were classified according to the diagnosis of the treating physician -the gold standard-: 95 inflammatory diseases (15 Spondyloarthritis, 9 Rheumatoid arthritis, 21 Gout, 10 Calcium Pyrophosphate arthropathy, 25 nonspecific arthritis, 2 Polymyalgia Rheumatica, 13 septic arthritis) and 58 non-inflammatory conditions (44 osteoarthritis, 9 meniscopathies, 2 osteonecrosis, 2 traumatic, 1 Baker cyst). ADA in SF was higher in inflammatory diseases -including septic arthritis- (mean 40.37 IU/L, SD 55.89) compared with non-inflammatory conditions (19.36, SD 12.20), and it was significant ($p<0.05$). If it is compared with inflammatory arthropathies without septic arthritis (35.28, SD 77.55) it is also statistically significant ($p<0.05$). Moreover, septic arthritis (72.43, SD 5.78) had higher levels of ADA in SF compared with other inflammatory arthritis (35.28, SD 63.66) ($p<0.05$). Furthermore, ADA in SF was higher when SF white blood cell count (WBC) was over 2000/microL – usually considered inflammatory SF- (n=104, ADA mean 40.26, SD 54.28) compared with SF WBC <2000/microL – usually considered non-inflammatory SF- (n=49, 15.72, SD 12.62) ($p<0.05$). In our center when the ADA level in SF is over 30 IU/L is considered positive. Using as gold standard the physician diagnosis, the following results were calculated to diagnose inflammatory arthropathies in patients with synovial effusion: sensitivity (Sn) 40% (30.7-50.1), Specificity (Sp) 89.7%, (79.2-95.2), positive predictive value (PPV) 86.4% (73.3-93.6) and negative predictive value 47.7% (38.6-57). And it was calculated for septic arthritis in patients with inflammatory arthropathies: Sn 69.2% (42.4-87.3), Sp 64.6% (53.8-74.1), PPV 23.75% (13-39.2%) and NPV 93% (83.3-97.2).

Conclusion: ADA in SF is higher in inflammatory arthritis -including septic or not- than non-inflammatory arthropathies. Even more, in septic arthritis SF ADA is higher than in other inflammatory arthropathies. However, comparing with the gold standard ADA test has no good results except for Sp (89.7%) and PPV (86.4%) to diagnose inflammatory arthritis and NPV (93%) to diagnose septic arthritis. The results are limited given the low number of septic arthritis (13) and the sample will be expanded to recalculate and establish a more appropriate ADA threshold for diagnosing septic arthritis and inflammatory arthropathies.

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AB1539 PREVALENCE OF ANTI-CN1A ANTIBODIES AND ITS CLINICAL SIGNIFICANCE – A RETROSPECTIVE MONOCENTRIC STUDY

Keywords: Descriptive studies, Autoantibodies, Epidemiology

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Background: Anti-cytosolic 5'-nucleotidase 1A (anti-cN1A) antibodies have recently been proposed as a biomarker for inclusion body myositis (IBM). With high specificity (87-100%), they can help differentiate IBM from other myositis.[1,2] Besides IBM, it has been detected in other inflammatory conditions. Recently, a higher prevalence of IBM has been associated with Sjogren Syndrome (SS), and anti-cN1A has been associated with myositis in SS, regardless of the subtype of myositis.[3] However, it can also be detected in healthy individuals and despite its high specificity in IBM, it may not be a useful biomarker for the diagnosis of autoimmune conditions.[4] Thus, the clinical relevance of anti-cN1A remains unknown.

Objectives: The aim of this study was to identify the clinical and laboratory manifestations associated with the presence of anti-cN1A.

Methods: A retrospective study of patients with anti-cN1A positivity (detected by immunoblot assay), observed from January 2021 to December 2022, in a tertiary hospital, was conducted. Demographic, clinical and immunological data were collected. A descriptive analysis was made.

Results: Sixty-five patients were positive for anti-cN1A: 53 women (81.5%) and the median age was 47.2±14.9 years. Rheumatic inflammatory diseases were diagnosed in 15 (22.7%) patients, of which 5 had systemic lupus erythematosus (SLE), 4 had SS, and 1 with rheumatoid arthritis, polymyalgia rheumatica, granulomatosis with polyangiitis, juvenile idiopathic arthritis, spondyloarthritis and undifferentiated connective tissue disease. Eight (12.1%) patients had autoimmune thyroiditis, without known rheumatic diseases associated. The presence

of anti-cN1A was also found in the context of infection in 7 (10.6%) patients and malignancy in 2 (3.0%) patients. Half of the patients (50.8%) patients were healthy individuals. No diagnosis of IBM or other myositis was made. Twenty-nine (44.6%) patients showed other antibodies specificities: anti-SSA/Ro52 (20%), anti-Ku (4.6%), anti-Mi-beta2 (4.6%) and anti-DSF70 (4.6%). In the SLE and SS groups, the most frequent presenting clinical features were sicca syndrome (66.7%), lymphopenia (9.2%), arthritis (6.1%) and photosensitivity (3.1%). No patient had signs or symptoms of muscular involvement.

Conclusion: Anti-cN1A was detected in diverse rheumatic conditions, but also in autoimmune thyroiditis and mostly in healthy individuals. SLE and SS were the most frequent systemic autoimmune rheumatic diseases associated with these antibodies. Contrary to expectations, no diagnosis of IBM or myositis was made. Further studies regarding the clinical significance of anti-cN1A are needed to attribute the real diagnostic value of this marker.

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AB1540 PREVALENCE AND DISTRIBUTION OF SONOGRAPHIC ELEMENTARY LESIONS IN PSA – RESULTS OF 2 COHORTS

Keywords: Imaging, Ultrasound, Psoriatic arthritis

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Background: Psoriatic arthritis (PsA) can manifest with different musculoskeletal (MSK) features. Ultrasound (US) optimizes the assessment of the different MSK features in PsA. However, there is no consensus on which MSK sonographic lesions and what locations should be evaluated by US.

Objectives: To examine the prevalence and distribution of key sonographic MSK lesions in patients with PsA.

Methods: This study included two prospectively recruited PsA cohorts. Cohort 1 included 158 consecutive PsA patients and cohort 2 included 94 patients with active PsA prior to initiation of therapy. All underwent a comprehensive US assessment, including both gray scale (GS) and power Doppler (PD) of 50 joints, 40 tendons and 14 entheses. The following sonographic lesions were assessed by two sonographers blinded to clinical data: I. Inflammatory lesions - Synovitis, tenosynovitis, peritenonitis and enthesitis and II. Structural lesions - erosions and bone proliferations. Presence/Absence of these lesions was determined based on previously suggested definitions by OMERACT (when available) or other publication and their prevalence by joint/tendon site was reported.

Results: In cohort 1, mean ± SD age was 52.7 ± 13 and 55.7% were females. In cohort 2, mean ± SD age was 47.5 ± 13.2 and 48.8% were females. The most prevalent locations of the inflammatory lesions in both cohorts were (Figure 1): Synovitis (small joints) – MCP2 (cohort 1: 11%, cohort 2: 27%), MCP 3 (cohort 1: 7%, cohort 2: 26%), IP1 (cohort 1: 5%, cohort 2: 25%) PIP 3 (cohort 1:3%, cohort 2: 16%), MTP 1 (cohort 1: 31%, cohort 2: 35%), MTP2 (cohort 1: 23%, cohort 2: 30%), MTP3 (cohort 1: 14%, cohort 2: 22%); Synovitis (medium-large joints) – wrist (cohort 1: 27%, cohort 2: 30%) and knee (cohort 1: 13%, cohort 2: 29%); tenosynovitis – 2nd finger flexors (cohort 1: 2%, cohort 2: 12%) 3rd finger flexor (cohort 1: 2%, cohort 2: 10%); extensor peritenonitis – MCP2 (cohort 1: 2%, cohort 2: 7%), MCP3 (cohort 1: 4%, cohort 2: 12%), PIP 3 (cohort 1: 3%, cohort 2: 13%), PIP4 (cohort 1: 2%, cohort 2: 12%); enthesitis – lateral epicondyle (cohort 1: 11%, cohort 2: 14%) and triceps (cohort 1: 7%, cohort 2: 20%); erosions – MCP1 (cohort 1: 4%, cohort 2: 5%), MCP2 (cohort 1: 6%, cohort 2: 7%), IP1 (cohort 1: 2%, cohort 2: 2%) PIP2 (cohort 1: 2%, cohort 2: 1%), MTP5 (cohort 2: 4%); bone proliferations – MCP1 (cohort 1: 12%, cohort 2: 7%), MCP2 (cohort 1: 10%, cohort 2: 17%), MCP3 (cohort 1: 5%, cohort 2: 17%), IP1 (cohort 1: 25%, cohort 2: 41%), PIP2 (cohort 1: 10%, cohort 2: 16%), PIP3 (cohort 1: 14%, cohort 2: 26%), DIP2 (cohort 1: 23%, cohort 2: 42%), DIP3 (cohort 1: 18%, cohort 2: 42%) and DIP5 (cohort 1: 29%, cohort 2: 49%).

Conclusion: This descriptive study provides comprehensive information on the most commonly affected sites for key inflammatory and structural domains in PsA. This information can inform efforts to develop reduced sonographic score to diagnose or monitor disease activity in PsA.

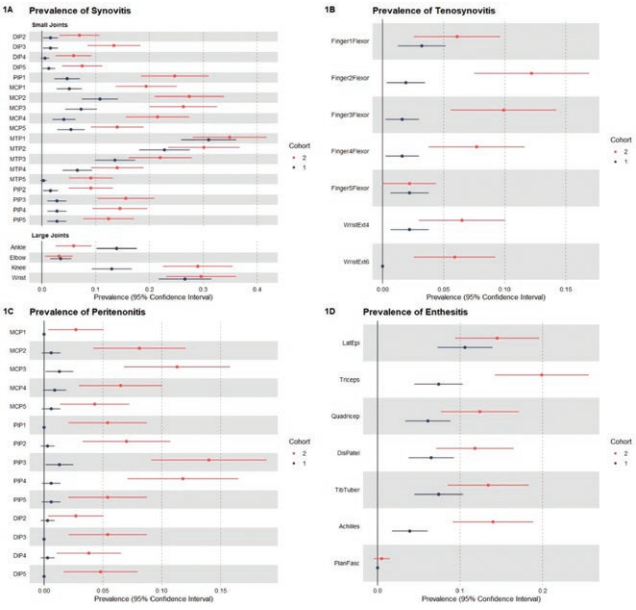


Figure 1. Prevalence and distribution of sonographic inflammatory lesions in PsA

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AB1541 THE INTENSITY OR DURATION OF INFLAMMATORY BACK PAIN HAS NO IMPACT ON THE DETECTION OF SACROILIITIS BY MAGNETIC RESONANCE IMAGING IN AXIAL SPONDYLOARTHRITIS

Keywords: Imaging, Spondyloarthritis

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Background: Sacroiliac joint (SIJ) magnetic resonance imaging (MRI) is an established tool in the evaluation of patients with axial spondyloarthritis (axSpA). In the validation study of the ASAS classification criteria for axSpA, only 63.1% of patients had sacroiliitis on the SIJ-MRI.[1] Studies that enrolled patients with axSpA based on expert opinion reported the sensitivity of MRI between 35 to 42% in detecting sacroiliitis.[2,3]

Objectives: This study aimed to evaluate the temporal relationship between ASAS defined positive MRI and the characteristics of low back pain (LBP) in axSpA.

Methods: Following axSpA groups were enrolled in the study whenever an attending physician ordered an SIJ-MRI. Patients fulfilling both the Rudwaleit criteria for inflammatory back pain (IBP) and Amor criteria, patients with a previous classification with either modified New York or ASAS classification criteria.[1] A blinded rheumatologist (GS) recorded the intensity and duration of IBP using a questionnaire before SIJ-MRI. MRI appointments were based on availability. Therefore some patients did not have IBP at acquisition. Two radiologists assessed SIJ-MRIs using the ASAS/OMERACT MRI group definition of active sacroiliitis.[4] In case of discrepant reporting, a third experienced radiologist (GE) adjudicated the SIJ-MRIs. The probability of axSpA is estimated using sum scores for SpA features excluding the SIJ-MRI.[5] The correlation between an ASAS-defined positive MRI and LBP characteristics was analyzed.

Results: Fifty-nine patients (32 F/27 M) were included. Patient characteristics are given in Table 1. Overall, 28 of 59 patients (47.5%) had a positive SIJ-MRI defined by ASAS.

The median duration of LBP was 15 (43) days and the highest intensity of LBP was felt 6.5 ± 1.2 days before the MRI appointment. At acqusition, 13 (22.0%) patients reported no LBP. There was no significant difference between the presence of LBP within 10 days prior to MRI and sacroiliitis on MRI. (p=0.6) (Sacroiliitis in 45.7% with, and 53.8% without LBP) In LBP reporting patients, pain duration and pain VAS score were 3.3 ±2.3 and 7.1 ±1.9 in patients with sacroiliitis, and 8.7 ±3.6 and 6.8 ±1.7 in patients without sacroiliitis on MRI, respectively. (p=0.48, p=0.10) Age, sex, BASDAI, CRP and calculated probability of axSpA had no correlation with the presence of sacroiliitis on MRI. Adding sacroiliitis on SIJ-MRI to axSpA probability score increased the rate of patients with a probability of >90% for axSpA from 71.2 to 83.1% but the rate of sacroiliitis on MRI was similar in all probability groups.

Conclusion: These results suggest that the presence of LBP and the duration of intense pain do not affect the detected rate of sacroiliitis on SIJ-MRI in axSPA. The low prevalence of sacroiliitis in this study population implies its value as a classification tool. Further studies with larger sample sizes are needed to clarify the factors affecting the SIJ-MRI findings in axSpA patients.

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Table 1. The characteristics of the study population

Age, years, mean ± SD	40.2 ± 10.5
BASDAI, mean ± SD	3.7 ± 2.5
Patient groups, n (%)	27 (45.8)
Classified as axSpA with Amor criteria	17 (28.8)
Previously classified as nr-axSpA with ASAS criteria	15 (25.4)
Previously classified as AS with mNY criteria	
SpA related features, n (%)	14 (23.7)
Arthritis	28 (47.5)
Enthesitis	6 (10.2)
Uveitis	24 (40.7)
Family history of SpA	57 (96.6)
Good response to NSAID	28 (47.4)
HLAB27 positivity*	26 (44.1)
CRP positivity	
Probability of axSpA using sum scores[5] (MRI not included)	42 (71.2)
>51 (Probability >90%)	7 (11.9)
44-51 (Probability >80%)	10 (16.9)
13-43	0
<13 (Probability <15%)	

AS, ankylosing spondylitis; mNY, modified New York; nr-axSpA, nonradiographic axial spondyloarthritis;*9 patients have no available HLAB27 result.

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AB1542 APPLICATION OF THE OMERACT ULTRASOUND SCORING SYSTEM FOR SALIVARY GLANDS IN PATIENTS WITH SUSPECTED SJÖGREN'S SYNDROME

Keywords: Sjögren syndrome, Imaging, Ultrasound

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Background: Primary Sjogren's Syndrome (pSS) is a connective tissue disease characterized by the presence of sicca syndrome. Confirmation of pSS requires immunological test and biopsy of the accessory salivary glands[1]. Salivary gland ultrasonography (SGUS) allows the detection of structural changes of salivary glands and is proposed as a reliable tool to assess involvement of major salivary glands in patients with pSS. Recently, a new semi- quantitative score have been validated by experts: The OMERACT US score to assess salivary gland involvement in pSS [2].

Objectives: The aim of our study was to describe salivary gland involvement in patient with suspected of pSS according to the OMERACT ultrasound scoring system for pSS.

Methods: All patients referred for a suspicion of pSS during the last period june 2022-2023 were enrolled. All underwent measurement of salivary flow, minor salivary gland biopsy, SSA antibody. SGUS was performed for all included patients. Both parotid glands and submandibular glands were exanimated using the scoring system 0-3 (OMERACT). Exact Fischer test was used to compare qualitative variables. Sensitivity, specificity and cutoffs were determined by ROC curve analysis.

Results: We enrolled 73 patients with a suspected pSS. Women represented 80 % of the cohort. Median age was 59 years [Q1 52-Q3 65]. Thirty-four patients were diagnosed with primary SS (pSS) and all fulfilled the 2016 American College of Rheumatology (ACR)/EULAR classification criteria. Thirty-one (91%) patients with pSS had a focus score > 1 in the biopsy of minor salivary gland. Twenty-one (62%) of patients with pSS had a positive SSA antibody. Of the 73 patients, 26 (35%) patients had at least one gland with an ultrasound score of 2 among them, 21 patients were diagnosed with pSS. More patients with pSS compared with non-pSS had score ≥2 in at least one gland (21 pSS vs 5 non pSS) in at least one gland. Among the 26 patients with an ultrasonographic score ≥ 2, 14 patients had positive SSA antibody (p= 0.001). When using ROC analysis, we found that an ultrasound score cutoff ≥2 in at least one gland was associated with a sensitivity at 67 % and specificity at 88%, air under the curve (AUC) was 0.83 [IC95% 0.732-0.93].

Conclusion: More patients with pSS compared with non-pSS had score ≥2 in at least one gland (21 pSS vs 5 non pSS) in at least one gland. An ultrasound cutoff > 1 is associated with a sensitivity at 67 % and Specificity at 88%. Our data supports what have been previously reported in several studies. Fana et al [3] reported in a cohort of 143 patients with suspected pSS that the best ultrasound cutoff value was ≥ 1 gland with a score ≥2 was associated to sensitivity at 72 % and specificity of 91%. Our data supports the importance of use of ultrasound as tool for diagnosing pSS. SGUS should be integrated as a criterion in ACR/EULAR score.

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AB1543 POSITIVE MRI OF THE SPINE AS IMAGING CRITERION FOR DIAGNOSIS OF AXIAL PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Spondyloarthritis, Imaging

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Background: MRI is essential for axial spondyloarthritis (axSpA) diagnosis. A positive MRI in the ASAS classification criteria of axSpA is based on inflammatory lesions in the sacroiliac joints. These lesions are defined as one bone marrow edema (BME) highly suggestive of axSpA present on ≥ 2 consecutive slices or ≥ 2 BME A on a single slice. The addition of MRI of the spine as an imaging criterion to the ASAS axSpA criteria had a low yield of newly classified patients and is therefore not recommended. Axial psoriatic arthritis (axPsA) remains poorly defined despite its high prevalence among patients with PsA. Studies comparing axPsA with other axSpA, such as Anquilosing Spondylitis (AS), have found differences in the former, including more frequent asymmetric spine and SIJ involvement, cervical involvement, and isolated spondylitis.

Objectives: Describe the presence of inflammatory and structural lesions on MRI-spine and SIJ in patients with psoriasis. Evaluate the added value of spinal inflammatory lesions on MRI-spine and structural lesions on MRI-SIJ as imaging criterion for axPsA diagnosis.

Methods: We performed a retrospective study of patients with psoriasis with at least a whole spine and sacroiliac joints (SIJ) MRI performed at Universidad de Chile Clinical Hospital between January 2015 and December 2021. MRI were performed in a 1.5 T machine, following a non-contrast protocol. Sagittal T1-weighted (T1w) and T2-weighted fat-suppressed fast spin echo sequences were available for the spine, while semi-coronal T1w and short inversion recovery sequences for the SIJ. Structural and inflammatory lesions were defined according to the ASAS/OMERACT definitions. Results are presented as mean and SD or numbers and percentages.

Results: 34 patients with psoriasis were analyzed, 17 (50%) were male, and the mean age at the time the MRI was performed was 43.7 ± 10.6 years. The

most common type of psoriasis was vulgaris (85%) and time from diagnosis was greater than ten years at least in 65% of patients. The majority of patients experienced chronic back pain (82%), and 15 (44%) patients had IBP according to ASAS criteria. MRI-SIJ showed structural and/or inflammatory changes in 16 patients. In 15 of them, BME was present. Of these 16 patients, 8 (50%) had no lesions in MRI-spine. In MRI-spine, 11 patients showed structural and/or inflammatory changes, and 5 of these 11 patients (55%) had BME suggestive of axSpA according to ASAS/OMERACT criteria. When we analyzed patients with an MRI negative for sacroiliitis (19 patients), 3 had BME on MRI-spine, with only two patients with three or more BME lesions according to ASAS/OMERACT criteria. Finally, when a chronic lesion on MRI-SIJ was considered as a possible criterion for classification, among patients without sacroiliitis, one patient could be deemed to have axSpA. The findings in this image of SIJ were erosions and fatty deposition (Romanus sign).

Conclusion: A positive MRI-spine in patients with suspected axPsA was more frequent than previously described for axSpA. Furthermore, spinal inflammation in the absence of sacroiliitis was present in 2 of the 19 patients in this cohort. Therefore, MRI-spine could be considered in the classification criterion for patients suspected of axPsA.

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AB1544

PARAVERTEBRAL MUSCLES TRIGGER POINTS ATTACHED TO FACET JOINTS ARTHROSIS ARE PREFERRED TARGETS FOR ULTRASOUND-GUIDED INTERVENTION TO TREAT LOW BACK PAIN

Keywords: Physical therapy/physiotherapy, Ultrasound, Rehabilitation

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Background: Facet joints (FJ) arthrosis can be a cause of pain and spinal instability and considered to be a potential target for injection treatment. However, FJ arthropathy is difficult for diagnosis and confirmation associations with pain syndrome, effectiveness of FJ injections is debated. Trigger points (TrPs) are major cause of pain syndromes, dry needling under ultrasound (US) guidance (DN-US) is a crucial therapeutic for treatment of myofascial pain [1], is a proven and effective method for treatment various pain conditions; can restore muscle function and motion [2], reduce fascia overload [3], and can improve movement in spine and also in FJ.

Objectives: Aim was to evaluate the relevance of US for diagnosis of FJ arthrosis as a cause of pain and evaluate the efficacy of DN-US to treat FJ-associated low back pain and improve movement in spine and facet joints.

Methods: We included 26 consecutive patients (15 females, 23-57 years old) with symptoms of LBP, suspected due to uni- and bilateral FJ arthrosis assessed at MRI and CT with three-dimensional reconstructions. Conditions of rheumatic, paresis, advanced injury background were excluded. All patients received DN-US protocol by R. Bubnov [1]: MTrP were identified according to clinical examination, referred pain pattern, US identification; single fine (28G) steel needle DN under US guidance was applied to elicit local twitch response (LTR) and/or `needle grasp`. Specific recommendations were given to preserve effect after DN-US.

Results: We diagnosed bi- and unilateral FJ arthrosis on US at the levels of Th11-S1 in all patients, assessed fluid in joints, deformation, movement restriction and revealed closely localized TrPs in paravertebral (multifidus) muscles followed by targeted DN-US. We distinguished different pain patterns (referred pain - groin pain, pelvic pain, irradiation to leg, thigh, etc.) which correlated with facet arthrosis localizations. Pain decreased in all patients VAS from 6-8 at baseline to 1-4 immediately and VAS 3-4 at one week after procedure. We noted decreasing in neuropathic pain, detected higher rates of lumbar spine motility, movements in particular segments and FJ were registered on functional US; improvement postural balance in all patients after DN-US. Additional needling sessions to FJ capsule did not induce significant LTR and effective alleviating pain compared to DN-US. All patients had postural imbalance, had multiple bilateral MTrPs: in multifidus muscles at thoracic, lumbar levels; sacroiliac joint dysfunction, shoulders impingement, other associated postural abnormalities; all MTrPs were inactivated, posture imbalance restored.

Conclusion: US is helpful to detect FJ arthrosis; DN-US has a good treatment outcome for low back pain due to FJ arthrosis. Local interventions targeting FJ in most cases not relevant approach; DN-US is not less complicated technically, however, more effective vs targeting FJ. Complex posture assessment and correction is needed.

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AB1545

A COMPARATIVE ANALYSIS BETWEEN THERMAL AND ULTRASOUND IMAGING AT THE ELBOW IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Imaging, Rheumatoid arthritis, Ultrasound

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Background: Thermal imaging (TI) is a relatively low cost, non-invasive imaging technique that offers a quick and objective measurement of joint surface temperature. However, TI data at the elbow in patients with rheumatoid arthritis (RA) is presently lacking.

Objectives: The aim of this study is to compare TI outcomes with ultrasound (US) joint inflammation findings at the elbow among patients with RA.

Methods: TI and US imaging were performed at the same study visit. TI was carried out in a draft free room following a standardized protocol. The maximum (Tmax), average (Tavg) and minimum (Tmin) temperatures at the elbow (anterior, posterior, lateral and medial aspects) were summed up to obtain the respective MAX, AVG and MIN temperatures for the right and left elbows. Ultrasound power Doppler (PD) and greyscale (GS) joint inflammation were graded semi-quantitatively (0-3) at the anterior (humeroradial) and posterior fossa recesses of the elbow joint using previously validated scoring methods; and these were summed to obtain the respective PD and GS scores at the right and left elbows per patient. Pearson's correlation coefficient was used to correlate the findings from TI and US imaging, while simple linear regression was used to describe the relationship between parameters.

Results: In this cross-sectional study, 60 elbows were evaluated by TI and US imaging among 30 adult RA patients with the following patient baseline characteristics: 76.7% female; 76.7% Chinese; mean (SD) disease duration 7.3 (6.8) months; mean (SD) DAS28 3.83 (1.19). Table 1 shows the results of the comparative analysis between the TI parameters (MAX, AVG and MIN) and the US PD and GS scores. For Pearson's correlation, the TI parameters (MAX, AVG and MIN) were all significantly correlated ($P<0.05$) with the US PD scores (Table 1) at both the right and left elbows. For US GS scores (Table 1), significant correlation ($P<0.05$) were observed with all the TI parameters (MAX, AVG and MIN) only at the right elbow but not at the left elbow (with P-values all >0.05). The simple linear regression estimates between TI and US imaging parameters at the right and left elbows are summarized in Table 1.

Conclusion: To the best of our knowledge, our study is the first to report on the correlation analysis between TI parameters and US joint inflammation outcomes at the elbow from an RA cohort. Between US PD and GS joint inflammation, TI is more consistently associated with the former at the elbow in RA. TI of the elbow in RA appears promising and will require further validation in independent RA cohorts.

Table 1. Comparative analysis between the thermal and ultrasound imaging parameters

Thermal imaging parameter	Pearson's correlation				Simple linear regression			
	vs. GS score		vs. PD score		vs. GS score		vs. PD score	
	Correlation Coefficient (95% CI)	P-value	Correlation coefficient (95% CI)	P-value	Estimates (95% CI)	P-value	Estimates (95% CI)	P-value
				Right elbow				
MAX	0.40 (0.04, 0.66)	0.029*	0.47 (0.12, 0.70)	0.009**	0.16 (0.02, 0.3)	0.030*	0.11 (0.03, 0.18)	0.009**
AVG	0.42 (0.07, 0.68)	0.020*	0.43 (0.07, 0.68)	0.017*	0.15 (0.03, 0.28)	0.020*	0.09 (0.02, 0.16)	0.018*
MIN	0.39 (0.03, 0.66)	0.032*	0.40 (0.04, 0.66)	0.028*	0.15 (0.01, 0.28)	0.033*	0.09 (0.01, 0.16)	0.029*
Left elbow								
MAX	0.32 (-0.05, 0.61)	0.086	0.55 (0.22, 0.75)	0.002**	0.11 (-0.02, 0.23)	0.086	0.08 (0.03, 0.13)	0.002**
AVG	0.26 (-0.12, 0.56)	0.174	0.52 (0.19, 0.74)	0.003**	0.08 (-0.04, 0.19)	0.172	0.07 (0.03, 0.11)	0.003**
MIN	0.15 (-0.23, 0.48)	0.433	0.45 (0.10, 0.69)	0.012*	0.04 (-0.07, 0.16)	0.430	0.06 (0.01, 0.10)	0.012*

Statistically significant: *P<0.05, **P<0.01

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AB1546

GRADING SYNOVITIS IN WRIST AND HAND USING THE MRI DERIVED APPARENT DIFFUSION COEFFICIENT FAILS TO SHOW RELIABILITY AND REPRODUCIBILITY

Keywords: Imaging, Validation

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Background: Diffusion-weighted (DWI) magnetic resonance imaging (MRI) of the hand and wrist has been suggested as an outcome measure of synovitis as an alternative to gadolinium enhanced MRI in patients with rheumatoid arthritis (RA) [1-2]. The apparent diffusion coefficient (ADC), which is a derived parameter from the DWI, may be used to grade synovitis, similar to the OMERACT Rheumatoid Arthritis MRI scoring system (RAMRIS) for synovitis [1]. In a small study criterion validity has been measured but no correlation to contrast-enhanced MRI was revealed [2].

Objectives: To test the discriminative validity of ADC in the synovium ("synovitis ADC") in a prospective cohort of patients with RA and psoriatic arthritis (PsA) and healthy controls (HC).

Methods: The right hand and wrist of all participants were imaged in a 3T MRI system with a dedicated 8 channels coil, applying a 2 mm thick coronal turbo spin echo DWI sequence with an in-plane resolution of 1.5x1.7mm. An ADC map was calculated on basis of two b-values (0;800). Assessment of ADC maps was performed in 7 regions of interest according to the same 7 areas which are assessed by the OMERACT RAMRIS (radioulnar-, radiocarpal-, and intercarpal-carpometacarpophalangeal joints and 2nd-5th metacarpophalangeal joints). Repeatability and intra-observer reproducibility were assessed using intraclass correlation coefficients (ICCs) and Bland-Altman plots.

Results: Thirty-eight participants were imaged twice within a week (median 7 days, range 3-14 days). Participant characteristics are provided in Table 1. The repeatability was moderate for RA (ICC=0.68; 95%CI: 0.45-0.83), poor for PsA (ICC=0.10; 95%CI: -0.09-0.29) and poor for HC (ICC=0.28; 95%CI: 0.07-0.47). Intra-reader reproducibility was poor for all three groups: RA (ICC=0.37; 95%CI: 0.12-0.58), PsA (ICC=0.22 95%CI: 0.02-0.40) and HC (ICC=0.34; 95%CI: 0.13-0.52). Bland-Altman plots revealed large absolute differences between 1st and 2nd MRI in all three groups of participants (Figure 1).

Table 1. Participant characteristics. RA, rheumatoid arthritis; PsA, psoriatic arthritis; HC, healthy control; VAS visual analogue scale. Values are median (range), if not otherwise indicated.

Variable	RA	PsA	HC
Age (years)	51 (31-56)	48 (46-52)	35 (30-40)
Female, n, (%)	7 (77.8%)	9 (69 %)	8 (53.33%)
Symptom duration (years)	6 (3.5-17.5)	10 (4-20.5)	-
Peripheral pain (0-100 mm VAS)	34 (30.5-57)	32 (10-65)	0 (0-1.5)
Peripheral patient global (0-100 mm VAS)	50 (23-60)	48 (15-76)	0 (0-0.75)
Number of swollen joints (0-76)	6 (4-7.5	4 (3-8)	0 (0-0)
Number of tender joints (0-78)	8 (3.5-16)	10 (5-18)	0 (0-0)
Number of tender entheses (0-31)	4 (0-8.5)	9 (1-13.5)	0 (0-2)
Serum C-reactive protein (mg/dl)	5 (1.5-7)	5 (1.5-7)	6 (4.25-8)

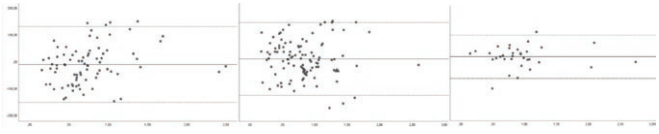


Figure 1. Figure: Bland-Altman plots of the repeatability for the three groups. Left, healthy controls; middle, psoriatic arthritis and right, rheumatoid arthritis. Full line: mean difference. Dotted lines: 95% levels of agreement. The Y-axis indicates the relative difference of apparent diffusion coefficient (ADC) between first and second scanning. The X-axis indicates the mean ADC [$x10^{-3}mm/s^2$] of the first and second MRI.

Conclusion: ADC, determined from DWI-MRI, is not a reliable outcome measure for grading synovitis in the hand and wrist of patients with inflammatory joint diseases.

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Table 1.

Variable	RA	PsA	HC
Age (years)	51 (31-56)	48 (46-52)	35 (30-40)
Female, n, (%)	7 (77.8%)	9 (69 %)	8 (53.33%)
Symptom duration (years)	6 (3.5-17.5)	10 (4-20.5)	-
Peripheral pain (0-100 mm VAS)	34 (30.5-57)	32 (10-65)	0 (0-1.5)
Peripheral patient global (0-100 mm VAS)	50 (23-60)	48 (15-76)	0 (0-0.75)
Number of swollen joints (0-76)	6 (4-7.5	4 (3-8)	0 (0-0)
Number of tender joints (0-78)	8 (3.5-16)	10 (5-18)	0 (0-0)
Number of tender entheses (0-31)	4 (0-8.5)	9 (1-13.5)	0 (0-2)
Serum C-reactive protein (mg/dl)	5 (1.5-7)	5 (1.5-7)	6 (4.25-8)

Table: Participant characteristics. RA, rheumatoid arthritis; PsA, psoriatic arthritis; HC, healthy control; VAS visual analogue scale. Values are median (range), if not otherwise indicated.

AB1547

SHEAR-WAVE ELASTOGRAPHIC ULTRASOUND OF SECOND METACARPOPHALANGEAL IN SYNOVIUM OF RHEUMATOID ARTHRITIS

Keywords: Diagnostic tests

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Background: Shear wave elastography (SWE) is a recent development in elastography ultrasound (SW-EUS). SWE allows quantitative evaluation of the elastic properties and stiffness of tissue and serves as an adjunct to conventional US techniques. There is a hypothesis that rheumatoid arthritis (RA) patients would have softer synovium than controls and this could be quantified with a slower SWV. We also assessed whether SWV varied with disease activity. The challenge in the application of SW-EUS to the synovium is that there are multiple bone tissue interfaces and fluid synovial interfaces in the joint which gave rise to increased chances of fallacious values.

Objectives: To perform a quantitative analysis of SW-EUS in second metacarpophalangeal (2MCP) synovium of RA patients and controls. Determine if there is a correlation between SW-EUS and disease activity.

Methods: A prospective case-control study. Fifteen patients with RA were consecutively recruited and matched with ten controls. Participants underwent clinical assessment, blood sampling, grey scale ultrasound (GSUS), power Doppler ultrasound and SW-EUS of MCP joints 2, on the dominant hand. Ultrasound examination was undertaken by two musculoskeletal trained sonographers. Both were blinded to patient diagnosis, clinical examination results, pathology and previous ultrasound findings. SW-EUS was performed first, followed by GSUS and PDUS. Scanning was carried out using ultrasound using linear array transducer at 6-18 mHz frequency and Virtual TouchTM software. MCP 2 of the dominant hand were scanned with joints resting at 20 degrees of flexion. The dorsal aspect of the joint was imaged in three planes; longitudinal midline (DLM), longitudinal radial (30° radial offset from midline, DLR) and longitudinal ulnar (30% ulnar offset from midline, DLU).

Results: Average age was 50. Mean RA disease activity (DAS28-ESR) was moderate at 3.85. Patients with RA (Figure 1) had lower mean SWV (5.27 m/s vs 12.00 m/s p< 0.001) than controls (figure 2); had lower maximum synovial SWV than controls (6.88 m/s vs. 12.80 m/s P <0.001). EM (RA 168.17 kPa, controls 437.81 kPa). RA low activity SWV (7.48 m/s); EM (168.17 kPa). high activity SWV (2.61 m/s); EM (25.45 kPa) Negative Pearson's correlation coefficients (PCC) were observed between mean SWV and disease activity markers including GSUS graded synovial thickness (PCC = -0.67, p = 0.03) and ESR (PCC = -0.45, p = 0.085).

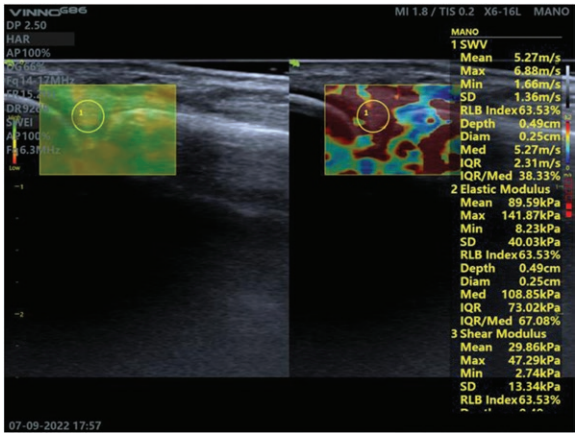


Figure 1. RA patient elastogram

Color elastogram of second metacarpophalangeal (2MCP) synovium, shows shear-wave velocity (SWV) (mean, 5.27 m/s) in RA patient. SWE data were collected using an Vinno G86 US scanner with an L16–6 MHz linear transducer

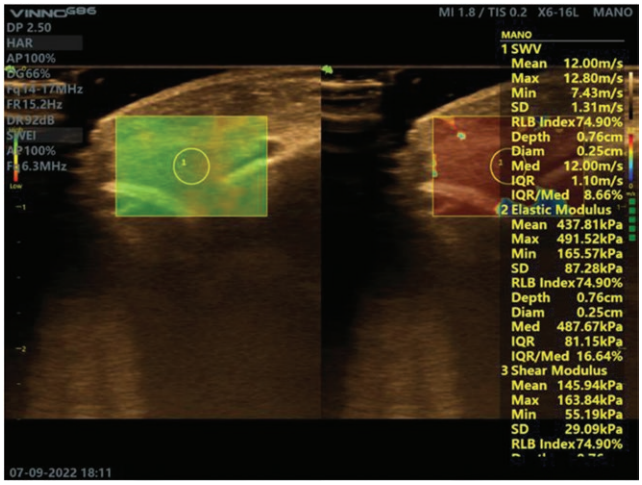


Figure 2. healthy control elastogram

Conclusion: This is the first pilot study in Latin America of SW-EUS in synovium. Mean SWV and elastic modulus was significantly lower in RA than controls. There was a negative correlation between mean and maximum SWV and GSUS synovial thickening and assessing disease activity in RA. Further study is warranted to confirm the role of SW-EUS in diagnosing and assessing disease activity in RA.

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Disclosure of Interests: None Declared.

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AB1548

ULTRASOUND ASSESSMENT OF SUB-CLINICAL NAIL INVOLVEMENT IN PSORIATIC ARTHRITIS PATIENTS

Keywords: Ultrasound, Psoriatic arthritis, Enthesitis

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Background: Several studies suggest that psoriatic nail involvement is secondary to local enthesopathy with diffusion of the inflammation to the nail.

Objectives: We aimed to compare parameters of clinically normal nail unit in patients affected by psoriatic arthritis (PsA) with healthy matched controls (HC) using ultrasonography.

Methods: This was a cross-sectional study including patients with PsA and HC. Tender joint count (TJC) (0–68) and swollen joint count (SJC) (0–66) were collected and psoriasis Area and Severity Index (PASI), Disease Activity in Psoriatic Arthritis (DAPSA), were calculated in PsA patients. All patients underwent ultrasound (US) assessment of the fingernails including the study of morphological changes and measurement of the thickness of nail bed (NBT), nail plate (NPT), and adjacent skin (ST). Significant difference was noted if p<0.05.

Results: A total of 22 PsA patients (219 nails) and 21 matched HC (210 nails) were evaluated. PsA group and HC were comparable with respect to age (53.7±12.1 vs 53±11.8, p=0.72) and male gender (13 vs 13, p=0.85). Mean disease duration of PsA was 12.7±10.9 years. The disease activity showed that mean DAPSA was 21.56±14.36 and mean PASI was 2.19 ±3.8. PsA patients had more US morphological changes than HC group (16.89% vs 3.33%,p=0.03). The comparison of NPT between each identical fingernail of PsA and HC did not reveal significant difference. However, NBT was significantly higher in the HC group than the PsA group (1.77mm vs 2.07mm, p=0.027). Additionally, ST was higher in the HC group (2.26mm vs 2.59mm, p=0.003).

Conclusion: The US morphological changes of NBT and ST were contributive to distinguish psoriatic nails from healthy nails.

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Acknowledgements: NIL.
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AB1549 VALUE OF ULTRASOUND FOR THE EARLY DETECTION OF INFLAMMATORY ABDOMINAL AORTIC ANEURYSMS

Keywords: Imaging, Rare/orphan diseases, Vasculitis

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Background: Inflammatory abdominal aortic aneurysm (iAAA), a form of chronic periaortitis, is a frequently overlooked disease, occurring in patients with abdominal aneurysms (AAA). iAAA is strongly associated with underlying systemic inflammatory diseases such as IgG4-related disease (IgG4-RD),[1] potentially leading to retroperitoneal fibrosis (RPF). Ultrasound (US) is a widely available and low-cost imaging tool that may allow the detection of iAAA at an early-stage prior development of severe complications in patients with AAA.
Objectives: This study aims to assess the feasibility of using US to detect iAAA in a small case series (exploratory cohort). And to structurally assess the diagnostic potential and overall incidence of iAAA using US in a larger retrospective cohort of patients in follow-up for AAA (validation cohort).
Methods: In the exploratory cohort, thirteen patients (median age 64 (61;72) years; 100 % male) with an established diagnosis of iAAA of whom US and CT findings were available were retrospectively included. The diagnosis of iAAA was based on a typical cuff surrounding the aneurysm on CT. Other potential causes such as infections and malignancies were ruled out by microbiological studies and when indicated by histology and/or FDG-PET scanning. Secondly, the validation cohort consisted of 191 patients (median age 74 (67;80) years; 73.3 % male) diagnosed with AAA who were in US follow-up for AAA without prior surgical intervention. In patients in whom a CT was (n=157) the diagnostic potential of US was explored using CT imaging as the golden standard. Perianeurysmal inflammation was assessed on US, as illustrated in Figure 1A, using a Siemens Acuson with 6 Mhz convex transducer in B-mode. In the validation cohort, US images were assessed by two independent observers blinded for the diagnosis.
Results: In the exploratory cohort, 62% were smokers, 77% had hypertension, 31% and were diagnosed with IgG4-RD. CRP and BSE levels were 54.5 (±66.2) mg/L and 59.8 (±51,1) mm/h. All patients showed a typical hypoechogenic cuff surrounding the aortic wall eccentric to the calcified medial layer of the aneurysm, see figure 1B). The median anteroposterior diameter of the aneurysm itself was 5.7 cm (4.8; 6.1) and 0.64 cm (0.49; 0.84) of the cuff. In the validation cohort, 180 of 191 (94.2%) patients with AAA showed no evident signs of a hypoechogenic cuff on ultrasound. Of the remaining 11 patients, 8 (4.2%) showed the cuff surrounding the aortic wall and were identified as having iAAA. In 3 (1.6%) an iAAA could not be ruled out based on US. In 149 patients with both a negative US and available CT, all CT scans were negative as well. In the 8 patients with an evident cuff on US, the median age was 66 (65;79) years; and 100% were male, definite IgG4-RD was present in 25% (n=2) of the cases. This amounts to a sensitivity of 100% and a specificity of 98%.
Conclusion: This retrospective study indicates that iAAA can be identified with US as a hypoechogenic cuff surrounding the aortic wall of the aneurysm. US could be used to rule out iAAA safely. However, in inconclusive cases, additional CT imaging is warranted. Besides a possible cost and radiation dose reduction, using US may facilitate earlier recognition and treatment of iAAA and underlying systemic inflammatory diseases such as IgG4-RD. Although this is the first study to structurally investigate US in iAAA, our results need validation in a prospective study.
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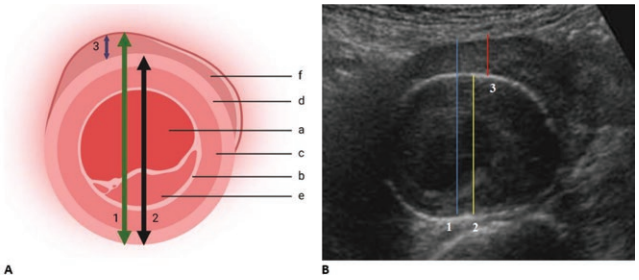


Figure 1. (a) lumen, **(b)** intima, **(c)** media, **(d)** adventitia, **(e)** thrombotic lesion, **(f)** inflammatory cuff, **(1)** The maximum anteroposterior diameter of the aorta including the hypo-echogenic cuff. **(2)** The anteroposterior diameter of the aorta excluding the hypo-echogenic cuff. **(3)** The diameter of the hypo-echogenic cuff.

AB1550 UTILITY OF WHOLE-BODY 18F-FDG PET-CT IN THE DIAGNOSIS OF NEUROSARCOIDOSIS

Keywords: Lungs, Diagnostic tests, Imaging

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Background: Neurosarcoidosis (NS) is one of the most severe manifestations of sarcoidosis [**1**]. NS diagnosis is difficult since clinical features and cranial imaging findings are often unspecific and central nervous system biopsy is unfrequently performed. Flourine-18 fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET-CT) is emerging as a powerful tool for the evaluation of sarcoidosis. Data on the role of 18F-FDG PET-CT in NS is scarce.
Objectives: To assess the utility of 18F-FDG PET-CT in patients with suspected NS.
Methods: Patients diagnosed with sarcoidosis at a University hospital in Northern Spain, between January 1999 and December 2019 were assessed. Sarcoidosis was diagnosed according to ATS/ERS/WASOG criteria as follows: compatible clinical and radiological presentation, histopathologic confirmation, and exclusion of other granulomatous diseases. NS was diagnosed according to the NS Consortium Consensus Group [**2**]. Receiver Operating Characteristic (ROC) curve for Chest Computed Tomography (CT) and 18F-FDG PET-CT were compared.
Results: NS was suspected in 30 (19 women/11 men) patients out of 384 (7.8%) (mean age; 55.0±15.8 years). The underlying neurological manifestations were chronic headache (n=13; 43.4%), peripheral neuropathy (n=6, 20%), cranial neuropathy (n=5, 16.7%), spinal cord abnormalities (n=3, 10%) and aseptic meningitis (n=3, 10%). Complementary study's findings are described in **Table 1**. 18F-FDG PET-CT was performed in 10 (33.4%) patients. 18F-FDG PET-CT were abnormal in 9 (90%) patients. Abnormalities suggestive of NS were found in 7 (70%) patients. These were located in lymph nodes (n=7, 100%), parotid gland (n=1, 14.3%) and bone (n=1, 14.3%). Other abnormalities were found in 2 (20%) patients in vocal cord (n=1, 50%) and rectum (n=1, 50%). Only 1 (10%) patient had no abnormalities in 18F-FDG PET-CT. All patients (n=2, 100%) in which chest radiography and chest CT were negative, had pathological findings suggestive of NS in 18F-FDG PET-CT. After whole-body 18F-FDG PET-CT, all patients with accessible abnormalities suggestive of sarcoidosis underwent biopsy in lymph node (n=5, 71.4%), parotid gland (n=1, 14.3%) and skin (n=1, 14.3%). In all of them non-necrotizing granulomas were found. 18F-FDG PET-CT and chest CT diagnostic ability was compared (**Figure 1**). 18F-FDG PET-CT had a higher Area Under the Curve (AUC) (0.94 [95% CI: 0.78-1]) than chest CT (0.75 [95% CI: 0.28-1]).
Conclusion: 18F-FDG PET-CT seems to be a useful tool in the evaluation of patients with suspected NS specially when the chest CT is negative or inconclusive.
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Table 1. Complementary studies in 30 patients with suspected neurosarcoidosis in the 1999-2019 period in a University hospital in Northern Spain.

Ancillary investigation	With 18F-FDG PET-CT (n=10; 33.4%)	Without 18F-FDG PET-CT (n=20; 66.6%)	Total (n=30; 100%)
• Laboratory tests, No./No. assessed (%)			
- ACE >70 U/L	3/9 (33.3)	9/13 (60)	12/24 (50)
- CRP >0.5 mg/dL	3/10 (30)	8/10 (80)	11/20 (55)
- ESR >20 mm/h	5/10 (50)	7/15 (46.7)	12/25 (48)
- CD4/CD8 >3.5	1/2 (50)	0/1 (0)	1/3 (33.4)
• Imaging studies suggestive of sarcoidosis, No./No. assessed (%)			
- Chest radiograph	8/10 (80)	16/20 (80)	24/30 (80)
- Chest CT	9/10 (90)	16/20 (80)	25/30 (83.4)
- Gammagraphy	6/9 (66.7)	10/18 (55.6)	16/27 (59.3)

Abbreviations: 18F-FDG PET-CT: Flourine-18 fluorodeoxyglucose positron emission tomography/computed tomography, ACE: Angiotensin-Converting Enzyme, CRP: C-reactive protein, CT: computerized tomography, ESR: Erythrocyte Sedimentation Rate.

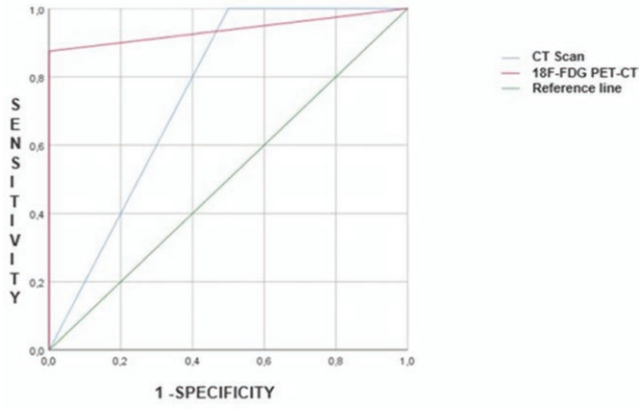


Figure 1. Receiver Operating Characteristic (ROC) curve of Chest CT and 18F-FDG PET-CT

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AB1551 IMAGING OF THE PERIPHERAL NERVOUS SYSTEM IN NOCIPLASTIC PAIN: AN ULTRASOUND STUDY IN PATIENTS WITH FIBROMYALGIA

Keywords: Ultrasound, Imaging, Pain

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Background: Fibromyalgia (FM) is a condition mainly characterized by the presence of chronic widespread musculoskeletal pain, fatigue, and sleep alterations. The pathophysiological basis of FM has not yet been clarified. It is widely recognized that FM is a condition characterized by the presence of central sensitization. The mechanisms of centralized pain have been studied mainly through functional imaging techniques. However, over the past decade, evidence of peripheral nervous system involvement has emerged alongside pathophysiological mechanisms involving the brain and spinal cord and a detailed analysis of the morphostructural abnormalities of other nerves in FM patients is still lacking.
Objectives: To investigate the sonographic changes [i.e., increased cross-sectional area (CSA)], of peripheral nerves in patients with FM compared to healthy controls and to identify potential clinical correlations associated with increased CSA in patients with fibromyalgia.
Methods: Consecutive female patients with FM included in this cross-sectional observational study underwent sonographic assessment using a standardised scanning protocol. The CSA of 7 nerves was measured bilaterally at 11 anatomic sites by an experienced sonographer. Differences in CSA of nerves were compared with those of healthy subjects by one-way analysis of variance. Patients underwent clinimetric evaluation aimed at investigating disease severity, neuropathic pain features, depression, anxiety, fatigue, and autonomic symptoms to explore the possible correlation between CSA and clinical features.
Results: 47 patients and 20 healthy controls were enrolled. Differences in terms of increased CSA between patients and healthy controls were identified at multiple levels, mainly at the level of the sural nerve, vagus nerve and 6th cervical nerve root (for all, $p < 0.001$). Sonographic findings, however, did not correlate with the clinical features explored.

Table 1. Mean cross-sectional area values (mm^2) of individual nerve scans in healthy controls and fibromyalgia patients.

	Healthy controls (n 20)		Patients (n 47)	
	Mean	SD	Mean	SD
6th cervical root right	3.95	0.75	5.91	1.52
6th cervical root left	3.90	0.64	5.78	1.36
Median distal right	8.00	0.97	8.55	1.62
Median distal left	8.10	0.96	8.36	1.84
Median proximal right	6.95	1.46	8.51	2.30
Median proximal left	7.20	1.39	8.48	2.26
Fibular right	9.10	2.44	9.95	2.27
Fibular left	9.35	2.58	10.29	2.21
Sural right	2.70	0.57	4.68	1.56
Sural left	2.85	0.58	4.42	1.09
Tibial distal right	11.35	2.47	13.89	3.49
Tibial distal left	11.40	2.70	13.76	3.44
Tibial proximal right	13.55	2.58	15.36	3.26
Tibial proximal left	13.95	2.66	15.12	4.03
Ulnar proximal right	6.15	1.34	6.55	1.80
Ulnar proximal left	6.00	1.07	6.48	1.79
Vagus right	2.75	0.78	4.08	0.85
Vagus left	2.85	0.74	3.91	0.90

Conclusion: Patients with FM show higher CSA of nerves than healthy subjects. The increased CSA is most evident at the sural nerve, vagus nerve and 6th cervical nerve root. Ultrasound, a relatively easy-to-use technique, could identify morphological changes, in peripheral nervous structures in patients with FM.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1552 PERFORMANCE OF A SOLID-PHASE PHOTOMETRIC SINGLE USE IMMUNOASSAY MICROARRAY PROTOTYPE IN THE DETECTION OF IGG ANTIBODIES AGAINST CENTROMERE PROTEIN B (CENP-B) IN HUMAN SERUM

Keywords: Systemic sclerosis, Diagnostic tests, Autoantibodies

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Background: Systemic Sclerosis (SSc) is a chronic multisystem autoimmune (AI) disease, characterized by progressive fibrosis of the skin and internal organs and vascular injury.[1] Biomarker testing plays an important part in disease classification, identification of sub-sets of SSc (e.g., CREST/ Limited SSc), prognosis and progression. Presence of antibodies against centromere proteins (CENP) weighs 3 points in the ACR/EULAR Classification Criteria.[2] Development of highly automated diagnostic tools remains a clinical need.
Objectives: To evaluate the performance of a solid-phase photometric single use immunoassay microarray prototype for the *in vitro* qualitative detection of

IgG antibodies against Extractable Nuclear Antigens (ENA) of CENP-B in human serum when tested using the MosaiQ™ System.

Methods: MosaiQ CENP-B microarray prototypes (Quotient Suisse, Eysins, CH) were prepared by printing CENP-B antigens in duplicate onto Epoxy-silane glass chips, followed by a blocking and preservative step. Microarrays consisting of 2 separate sides were assembled into Magazines (containing 250 microarrays) for processing on the MosaiQ 125 instrument. Human serum samples/buffers/reagents are loaded on the instrument and automatically the microarrays undergo sample/buffer/reagent addition to generate antigen spot signals which are read and interpreted by the instrument using a proprietary algorithm. A cohort of 26 serum samples reactive for anti-CENP-B antibodies (as defined by testing with 2 commercial assays) and 25 non-reactive serum samples from Swiss Red Cross blood donations were tested in duplicate.

Results: 25 out of 26 CENP-B antibody reactive samples were determined reactive by the MosaiQ CENP-B microarray prototype. The only discordant sample was reactive in one of the reference methods and non-reactive in the other, suggesting the potential for a false reactive by one of the reference methods. All 26 non-reactive samples were determined non-reactive by the prototype assay. Derived sensitivity (including presumptive false non-reactive) is 0.96 (95%CI 0.87 – 0.99) and specificity is 1.0 (95%CI 0.93 – 1.0).

Conclusion: These preliminary results support the performance of the investigational microarray prototype for the detection of CENP-B antibodies in human serum using the MosaiQ System. Clinical studies to confirm these observations are ongoing. Additionally, the microarray has the potential to print up to 66 spots per side, allowing for the capability to generate large multiplex panels for the detection and characterization of AI diseases.

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Disclosure of Interests: Daphne Bijlsma Employee of: Quotient Suisse SA, Ewa Lukasik Employee of: Quotient Suisse SA, Michael Hausmann Employee of: Quotient Suisse SA, Gerber Gomez Employee of: Quotient Suisse SA, Christine Ginocchio Employee of: Quotient Suisse SA, Emmanuel Moreau Employee of: Quotient Suisse SA.

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AB1553

INVESTIGATION OF FACTORS ASSOCIATED WITH PET/CT EXPERIENCE AND DIAGNOSTIC VALUE IN RHEUMATOLOGY PRACTICE

Keywords: Imaging

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Background: The use of PET/CT is becoming more common in the elucidation of inflammatory processes in which the underlying cause cannot be determined by conventional examinations. Although PET/CT is an effective method for detecting inflammatory foci, the precise diagnosis may not be obtained in all cases.

Objectives: In this study, it was aimed to examine the factors that can predict the differential diagnosis value of PET/CT by retrospectively scanning patients who underwent PET/CT for inflammation of unknown origin(IUO) in rheumatology practice.

Methods: Demographic, clinical and laboratory information of the patients followed up in our clinic and who underwent PET/CT for differential diagnosis were enrolled. Whether they were diagnosed after PET/CT and during the follow-up period, and their diagnoses were examined.

Results: A total of 132 patients were included in the study. A previous diagnosis of rheumatic disease was present in %28.8 of the patients, and a history of malignancy was present in %2.3. The patients were divided into three groups: Group 1 patients with increased FDG uptake in PET/CT and the diagnosis confirmed by PET/CT, group 2 patients with increased FDG uptake in PET/CT but the diagnosis of was not confirmed, and group 3 patients without increased FDG uptake in PET/CT. Increased FDG uptake in PET/CT was detected in %73 of the patients. While PET/CT helped the diagnosis in 47(%35.6) patients(Group 1), it did not help the diagnosis in 85(%64.4) (Group 2,3). Thirty-one (%65.9) of the diagnosed patients were diagnosed with a rheumatologic disease. When the 3 groups were compared, male gender, advanced age, CRP levels, presence of constitutional symptoms, SUVmax values and number of different organs with increased FDG uptake were higher in Group 1. %66 and %74 of the patients in groups 2 and 3 were not diagnosed during the follow-up period. No patient in group 3 was diagnosed with malignancy during follow-up.

Conclusion: PET/CT has high diagnostic value when combined with clinical and laboratory in the diagnosis of IUO. Our study revealed that various factors can affect the diagnostic value of PET/CT. Although detection of involvement in PET/CT is not always diagnostic, it was an important finding that no malignancy was detected in the follow-up in any patient without involvement.

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Table 1. Demographics, clinical, laboratory characteristics and PET findings in patient groups

	Group 1 N=47	Group 2 N=50	Group 3 N=35	p
Age, years, mean ± SD	60.0 ± 14.8	52.7 ± 14.7	50.6 ± 12.6	**0.012*** **0.027¥** **0.006¶** 0.491µ
Gender, male, n (%)	20 (42.6)	12 (24.0)	6 (17.1)	**0.027**** 0.052¥ **0.014¶** 0.446µ
CRP level, mg/L, med (IQR)	59.0 (87)	23.5 (39)	25.0 (22)	**<0.001*** **<0.001¥** **<0.001¶** 0.806µ
CRP < 10 mg/L, n (%)	2 (4.3)	9 (18.0)	3(8.6)	**<0.001****
CRP 10 - 50	18 (38.3)	29 (58.0)	25(71.4)	**0.002¥**
CRP 50 - 100	13 (27.7)	9 (18.0)	7 (20.0)	**0.001¶**
CRP > 100	14 (29.8)	3 (6.0)	0 (0.0)	0.259µ
ESR level, mm/h, med(IQR)	43.0 (49)	38.5 (41)	33.0 (29)	0.205**
Patients with constitutional symptoms, n (%)	18 (38.3)	12 (24.0)	2 (5.7)	**0.003**** 0.128¥ **0.001¶** **0.025µ**
PET findings				
Greatest SUVmax at single site, median (IQR)	8,5 (5,2) 2 (1,8)	6,4 (3,4) 1 (1.0)	- -	**0,018** **0.019**
Number of different types of organs with FDG uptake, median (IQR)				

One-way ANOVA p value,Chi-Square within three groups, ¥Comparisons between group A and B either with Student t test, Mann Whitney U test or Chi Square test, ¶Comparisons between group A and C either with Student t test, Mann Whitney U test or Chi Square test, µComparisons between group B and C either with Student t test, Mann Whitney U test or Chi Square test*

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Disclosure of Interests: None Declared.

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Diagnostics and imaging procedures

AB1554

A STUDY TO SHOW THE TOLERABILITY OF ULTRASOUND GUIDED SIJ STEROID INJECTION TO ALLOW APPROVAL OF US GUIDED SIJ SYNOVIAL TISSUE SAMPLING FOR RESEARCH

Keywords: Inflammatory arthritides, Patient reported outcomes, Safety

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Background: Sacroiliac joint (SIJ) synovial tissue analysis has the potential to improve specificity and sensitivity of spondyloarthritis (SpA) classification beyond the current Assessment for SpondyloArthritis International Society criteria allowing early diagnosis and reducing disease progression. It can aid the use of molecular biomarkers and identification of drug targets already explored in rheumatoid arthritis (RA) [1]. Furthermore, joint synovial tissue has shown histological differences in RA from psoriatic arthritis [2] and may help characterise SpA subtypes. SIJ steroid injections are used for pain management. A similar procedure, yet to be utilised, can be used to obtain synovial tissue using a co-axial needle. There is evidence of histological disease in patients experiencing sacroiliac pain without MRI features [3, 4]. Synovial biopsy offers possible earlier detection of SpA than MRI, which is limited by cost, patient weight and claustrophobia. Equally fluoroscopic or CT guided injections are limited by cost, time and radiation exposure. Early diagnosis and treatment of SpA is already linked to improved outcomes [5].

Objectives: To determine the tolerability and safety of ultrasound guided (USG) SIJ steroid injections to encourage SIJ tissue biopsies in research.

Methods: We identified 10 patients at Southend Hospital between 2010-2019. The average age was 41 years. Once verbal consent was obtained, a retrospective telephone questionnaire was completed. The USG SIJ steroid injections (Figure 1A) involved injecting Lidocaine 1% around the soft tissue using a 25G and 23G needle. Then a 22G spinal needle was guided into the SIJ and a mixture of Depomedrone 40mg and 0.5ml 0.25% bupivacaine administered. The patients were asked to indicate pain, swelling and stiffness of the injected joint pre and post procedure using a qualitative scale: none, mild, moderate or severe. They were asked to comment on side effects and how likely they were to repeat the procedure.

Results: All patients had severe pain before injection and one continued to have severe pain post procedure. None reported complications of steroid flare or back pain (Figure 1B and 1C). 70% experienced temporary numbness (Figure 1B), an expected side effect of local anaesthesia, which resolved within 24 hours. No permanent numbness was reported. 20% had peripheral arthralgia, which resolved with analgesia in 24 hours. 50% were unlikely to repeat the procedure as the steroid offered little benefit. Most importantly, all patients tolerated the procedure with only mild to moderate discomfort.

Conclusion: SIJ steroid injections are not widely offered, making it difficult to obtain large patient numbers. However, this study shows that SIJ steroid injections are tolerable for patients, an important step in convincing patients to participate in a SIJ synovial tissue biopsy research study. Tissue biopsy using a co-axial needle may be considered more invasive as it is thicker with a longer throw than a 22G spinal needle but the procedure steps and complication risks are ultimately similar. The complication risk rate has not yet be compared between the two procedures but SIJ tissue biopsy is less invasive and traumatic than the alternative SIJ trans-articular bone biopsy [6].

Whilst sample size may not be representative for a larger patient cohort and the retrospective questionnaire may have introduced time bias, the data obtained will hopefully initiate a potential study. This study could provide significant information on complication risk rate in synovial tissue biopsy of the SIJ and associated histological disease information in SpA.

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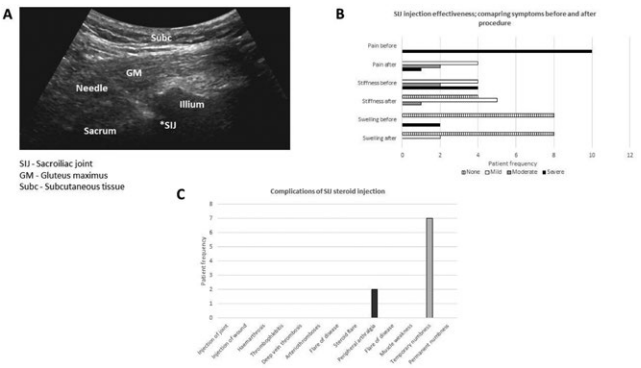


Figure 1. A: SIJ USG steroid injection and corresponding anatomy of the joint on an US longitudinal view using curvy linear probe. B: Comparing SIJ injection joint symptoms before and after injection. C: Complications post SIJ steroid injection.

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Disclosure of Interests: Jessica Bunting: None declared, Alan Tan: None declared, Nirupam Purkayastha Shareholder of: Sareum Holdings, Consultant of: Galapagos.

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AB1555

CORRELATION BETWEEN HIGH RESOLUTION CHEST TOMOGRAPHY AND CAPILLAROSCOPIC FINDINGS IN SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Lungs, Prognostic factors

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Background: Systemic sclerosis (SSc) is a chronic autoimmune multisystemic disease characterized by fibrosis and vasculopathy.[1] Mortality in patients with systemic sclerosis who present with interstitial lung disease can be up to 3x healthy population.[2] It is estimated that 70-90% have interstitial lung disease.[3] High resolution computed tomography (HRCT) of chest is recognized as a sensitive imaging method for evaluating pulmonary involvement.[4,5] Presentation patterns are also described: NSIP (non specific interstitial pneumonia), UIP (usual interstitial pneumonia), COP (cryptogenic organizing pneumonia), LIP (Lymphocytic interstitial pneumonitis). Capillaroscopy allows the study of the microcirculation. Changes are classified into “early,” “active,” and “late” scleroderma patterns.[6]

Objectives: To relate between high resolution chest tomography and capillaroscopic findings in Systemic sclerosis.

Methods: Descriptive, observational, cross-sectional study. Capillaroscopy with Optilia CapiScope 2.0/5.0MP and lung ultrasound with Siemmens Acuson X150 were performed in patients with SSc in the outpatient clinic of the rheumatology service from August-November 2021. Inclusion criteria: > 18 years old, meet criteria for classification of SSc according to ACR/EULAR 2013. Exclusion criteria: history of pre-existing lung disease.

Results: 22 patients met inclusion criteria. 80% were female. Diffuse SSc 81.8% (18), limited SSc 18.2% (4). Mean age 54±17 years, disease duration 58.1% (13) >5 years and 40.9% (9) < 5 years, mean diagnosis 15.3±9.2 years, mean mRSS 19.4 + 13.2 mRSS Mild: 22.7% (5), moderate 18.2% (4), severe 27.3% (6), terminal 31.8% (7). ANA+ 45.5% (10), Topo IA 18.2% (4). Treatment: RTX 77.3% (17), Ca+ antagonists 68.2% (15), Bosentan 36.4% (8), MMF 36.4% (8), Colchicine 31.8% (7), Sildenafil 27.3% (6). Capillaroscopy: normal pattern 59% (13), early scleroderma pattern 9.1% (2), active scleroderma pattern 4.5% (1), late scleroderma pattern 22.7% (5), nonspecific abnormalities 4.5% (1). TACAR: 54.5% (12) normal, pathological findings 45.4% (10): NSIP pattern 80% (8), UIP 20% (2). TACAR/Capillaroscopy correlation: UIP pattern and early scleroderma pattern 4.5% (1) rp=.112, NSIP pattern and active scleroderma pattern 4.5% (1) rp=.769, NSIP pattern and normal capillaroscopy 4.5% (1) rp=. 518, NSIP pattern and late scleroderma pattern 27.2% (6) rp=1, normal TACAR and capillaroscopy

with nonspecific abnormalities 4.5% (1) rp=1, UIP pattern and early pattern 4.5% (1) rp=.622, normal TACAR and normal capillaroscopy 27.2% (6).

Conclusion: We found in this study that capillaroscopic findings of active and late patterns correlated with greater pulmonary involvement. It is recommended to follow patients with early patterns and the existence or not of interstitial pattern and to evaluate response to medication.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1556 MACHINE LEARNING APPROACH FOR CLASSIFICATION OF ARTHRITIS ACTIVITY STATE, USING DATA FROM A SINGLE ACCELEROMETER

Keywords: Artificial intelligence, Rheumatoid arthritis, Validation

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Background: Machine learning (ML) potential is not fully exploited in diagnostics and follow up of autoimmune inflammatory rheumatic disease (AIIRD). It is despite the broader use of ML in, e.g. imaging diagnostics. The specific tools for AIIRD are lacking.

Objectives: This is an interim analysis of data from the first checkpoint of the proof-of-concept study on using accelerometer (ACC) data in follow up of patients with AIIRD. The main goal of the study was to investigate the value of single ACC data in the classification of arthritis activity status.

Methods: Subjects with AIIRD are enrolled in the study when they start of new treatment due to the disease activity. Several comorbidities, such as severe neurological and cardiological disorders, as wells as impaired mobility, are part of the protocol exclusion criteria. Volunteers without AIIRD who fulfil other inclusion/exclusion criteria are included as controls. The study was approved by local competent authorities and informed consent was given by all participants. We used data collected up till the first study checkpoint. This analysis covers nine patients with AIIRD (5 rheumatoid and four psoriasis arthritis) and 13 controls. Five patients had 3 study visits, 1 had 2 visits and 3 only one. Controls have only one visit per protocol. We analysed ACC data from 3 minutes of clapping using a home-brewed device based on Arduino nano 33 BLE with 6-axis MTU by Nordic Semiconductor. Data was divided into 6-second chunks that were found optimal in our prior study. We conducted binary classification between any/ no arthritis in any of the upper extremities. We used accuracy and area under curve (AUC) as an efficacy function derived from the receiver operating characteristic curve (ROC). We extracted 54 features from 3 ACC axis signal. The features encompassed, among others, Fourier's components, autoregression coefficients, median absolute deviation (MAD), variance, Fourier's entropy, etc. We built linear discriminant analysis (LDA) models on the train data that were controlled on the test data. We originally built models with all features. Then, we analysed the importance of each feature on the models. Eventually, we constructed the most effective available model formula based on 7 features: the first autoregression coefficient for the X axis, kurtosis for the Z axis, correlation between Y and Z axis, zero point cross count for the Y axis, Z axis MAD, X and Y axis skewness. As we had few subjects included, we built 210 models with all possible data combinations. To avoid model overfitting, we never used data for model training from a subject who was actually in test data. All calculation was performed with R (R Core Team, 2022 www.R-project.org), using package caret (M. Kuhn 2022, CRAN.R-project.org/package=caret).

Results: Median accuracy for all LDA models was 0.78, mean 0.72 (95%CI 0.69-0.76). Median AUC was 1.0, mean 0.82 (95%CI 0.77-0.86). Distribution of the result was skewed to upper values. However, some models showed very low efficacy in classification (Figure 1 A and B).

Conclusion: Our study shows that it is possible to predict if a patient has any arthritis activity. However, we observed some instability in the classification between models. It can be due to small amount of data but also due to other distractors, such as comorbidities or drugs. Further research on the area is required and continuation of our study is justified based on the current results.

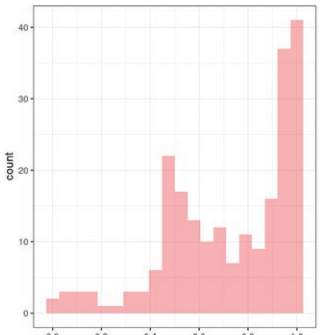


Fig. 1 A - Accuracy LDA

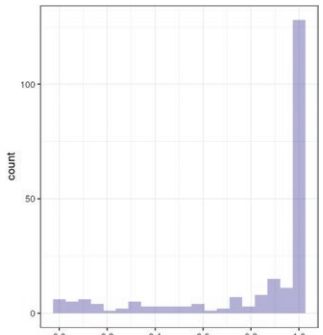


Fig. 1 B - AUC LDA

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Pawel Mielnik Consultant of: Galapagos, Anja Myhre Hjelle: None declared, Anne Traseth: None declared, Krzysztof Tokarz: None declared, Bjarte Pollen: None declared, Marcin Fojcik: None declare.d.

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AB1557 ULTRASOUND LEARNING CURVE IN INTERSTITIAL LUNG DISEASE OF AUTOIMMUNE RHEUMATIC DISORDERS: A DISEASE ORIENTED TRAINING PROGRAM

Keywords: Lungs, Ultrasound, Mixed connective tissue disease

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Background: Ultrasound (US) has elicited considerable interest among rheumatologists because of its usefulness in clinical practice. Recently, it has been demonstrated its ability to assess interstitial lung disease (ILD) in rheumatic patients. While a solid and still growing body of evidence supports its use in daily rheumatologic practice, operator dependency and the long learning curve represent the main limitations.

Objectives: To describe the learning curve of rheumatologists with limited experience using US attending an intensive disease-oriented training program focusing on the skills required to obtain and interpret US signs of ILD in patients with autoimmune rheumatic diseases.

Methods: A total of 5 investigators participated in a seven-day training program involving 15 patients with autoimmune rheumatic diseases. The expert sonographer was a Rheumatologist with >15 years of US experience, whose assessments were used as the gold standard to evaluate the US findings obtained by the remaining 4 investigators. Two beginner sonographers were fellows in rheumatology with 5 months of global US experience, whereas the other 2 beginner sonographers were fellows in rehabilitation and rheumatology with a very basic knowledge of musculoskeletal US (<3 months) and no direct US experience in ILD. The training program lasted for 7 days (at least 5 hours per day) following specific aims and activities for each day during the training program. The agreement between the expert and beginners was calculated in 4 sessions involving 15 patients (13 females and 2 males; 4 rheumatoid arthritis, 6 systemic sclerosis, 3 Sjogren syndrome, 2 dermatomyositis). The US assessment was performed according the previously proposed 14-intercostal spaces (IS) scanning protocol using the following semiquantitative scale [0 = normal (≤5 B-lines); 1 = slight (≥6 and ≤15 B-lines); 2 = moderate, (≤16 and ≥30 B-lines); 3 = severe (≥30 B-lines)] [1]. Additionally the pleural irregularity in each IS was dichotomously recorded.

Results: A total of 210 lung IS were studied. Kappa values and overall agreement percentages of qualitative and dichotomist assessments of US ILD findings

(B-lines and pleural irregularity) at the end of the exercise showed moderate to excellent agreement (between 0.769 and 0.895), while in the first session they showed poor/fair agreement (between 0.325 and 0.435). The comparison between the expert (gold standard) and beginners' examinations at the fourth and final session, including the kappa values, sensitivity, specificity, and negative and positive predictive value were also improved.

Conclusion: After 1 week of the disease-oriented training program, physicians with limited experience in US were satisfactorily able to detect and interpret the main US signs indicative of ILD in patients with autoimmune rheumatic diseases.

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Acknowledgements: To the fellows who participated in this exercise: Dr. Ana Mabel Quiroz, and Dr. Betsy Condori.

Disclosure of Interests: None Declared.

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AB1558 CLINICAL-ECOGRAPHIC OPTIMIZATION IN RHEUMATOID ARTHRITIS IN SUSTAINED REMISSION

Keywords: Tapering, Ultrasound, Rheumatoid arthritis

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Background: In recent years, the high economic impact of biologic therapies (BT) on health care systems has promoted great interest in optimizing BT in Rheumatoid Arthritis (RA) patients in sustained clinical remission (CR). A relevant percentage of those optimized patients present clinical relapses. RA patients in CR have been shown to have active synovitis detectable by ultrasound (U). U can identify synovitis in patients about to present clinical relapse. U can be a useful tool in the optimization decision.

Objectives: The main objective was to demonstrate that the optimization strategy using U is more useful than the strategy using clinical index. U used as an outcome measure, can further refine the choice of patients who are candidates for a reduction in treatment and therefore achieve lower relapse rates. To do this, we calculated the relapse rates in each of the groups and the time from the beginning in which it appears, and we compared them to assess whether they differ significantly and support our hypothesis. Secondary objective was evaluating the ultrasound remission in this group of patients.

Methods: We conducted a multicenter, randomize, prospective study in 5 tertiary centers in RA patients in sustained CR (>9 months). All signed the informed consent. Approval by the ethical committee was obtained (VDH-INF-2017-01). Two blinded and randomize arms, clinical (A) and U (B) were created to decide tapering (1/2, 1/3 or no reduction treatment) and compare flare rates (>1.2 DAS28 or >16 SDAI/CDAI increase) in 52 weeks (basal, 1, 6, 9 & 12 months). Demographic at baseline, US & clinic variables, and ESR & CRP at each visit, were registered. By using U with grayscale (GS) and power Doppler (PD) in a semiquantitative articular (A) and tendon (T) scale we studied: wrist, 1-5 MCP, 1-5 PIP, ankle, subtalar joint, 2nd, and 5th MTP, extensor tendons (Text) and flexors (Tflex) of the carpus, flexor tendons of the fingers, posterior tibial and peroneal tendons. DAS28 <2.6 was used as the clinical remission criteria, and the absence of synovitis was defined as U remission (EG and PD = 0). U activity was defined as GS≥1 and PD ≥1.

Results: 78 patients were included, 48 completed 12 moths follow up and 28 were retired (5 screening failure, 16 flare, 5 lost follow up & 4 patient decision). 33 men and 45 women, 11.92 years of disease. Group A presented a significative more flare rates than group B (10 vs 6). Using SDAI or CDAI only 7 presented a clinical flare, and for SDAI (7 vs 0) & CDAI (7 vs 0) differences were significative (p<0.005), but not for DAS28 (10 vs 6) (Table 1). In U at baseline, the main involved joint was the wrist (28.6%), and of the tendons the Text (11.2%). In 53% a pathological U (A and T) was observed, 46.9% had pathological A and in 30% pathological T was observed. Considering as remission an ultrasound score of EG + PD = 0, only 46.9% were in remission.

Conclusion: Ultrasound can improve tapering strategy when we used SDAI or CDAI score in patients in sustained clinical remission. Clinical and ultrasound remission are not equivalent. More than half of the patients do not fulfill UR and in one fifth of them a strict control should be carried out to avoid a relapse of the disease if it is decided to optimize.

Table 1. baseline clinical characteristics of the subjects included in the sample, comparing according to the treatment group and outbreaks according to clinical indices

Variable	Group		Total	p
	A	B		
Total [1]	**41** (100%)	**37** (100%)	Ns	
ESR (mm/ hr) [2]	41 **15.39** (10.07)	37 **11.27** (8.92)	78 **13.44** 9.71	Ns
CRP (mg/dl) [2]	40 **0.58** (1.32)	36 **1.18** (2.59)	76 **0.87** 2.03	Ns
RF(UI/ml) [2]	40 **96.60** (126.31)	36 **164.85** (330.84)	76 **128.93** 246.08	Ns
ACPA (UA) [2]	39 **264.29** (409.93)	36 **230.48** (601.26)	75 **248.06** 507.51	Ns
SJC [2]	41 **0.00** (0.00)	37 **0.03** (0.16)	78 **0.01** 0.11	Ns
TJC [2]	41 **0.17** (0.83)	37 **0.24** (0.60)	78 **0.21** 0.73	Ns
PtGA [2]	41 **3.10** (8.28)	37 **3.43** (9.24)	78 **3.26** 8.69	Ns
PGA [2]	41 **0.82** (3.12)	37 **1.71** (5.31)	78 **1.24** 4.29	Ns
DAS28 [2]	41 **1.85** (0.70)	36 **1.80** (0.62)	77 **1.82** 0.66	Ns
SDAI [2]	41 **1.67** (2.23)	37 **2.32** (2.59)	78 **1.98** 2.41	Ns
CDAI [2]	41 **1.59** (2.21)	37 **2.15** (2.56)	78 **1.86** 2.38	Ns
HAQ [2]	38 **0.30** (0.46)	33 **0.32** (0.38)	71 **0.31** 0.42	Ns
DAS28 flare	10	6	16	Ns
SDAI flare	7	0	7	**<0.005**
CDAI flare	7	0	7	**<0.005**

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.1438

AB1559 AUTOIMMUNE DISEASES ASSOCIATED WITH AUTOIMMUNE HEPATITIS

Keywords: Comorbidities

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Background: Autoimmune hepatitis (AIH) is a rare pathology characterized by necrotic-inflammatory hepatocyte lesions, the presence of autoantibodies, and high sensitivity to corticosteroid treatment. it is often associated with other autoimmune diseases.

Objectives: Our objective was to study the clinical aspects, associated auto-immune diseases, and response to the treatment of AIH.

Methods: We conducted a retrospective study including consecutive patients with AIH between January 2000 and December 2018.

Results: We included twenty-two patients; 21 women and one man with an average age of 46 [18-95]. Jaundice was the most frequent presenting sign (80%). Biology found cytolysis greater than ten times in 45.5% of cases. A predominant hypergammaglobulinemia on IgG was noted in 77.2% of cases. At the time of diagnosis, 59% of patients were in the stage of cirrhosis. Antinuclear antibodies, Anti-smooth muscle antibodies, and Anti-LKM1 antibodies were positive in 47.6%, 41%, and 13.3% of cases, respectively. The liver biopsy was performed in 8 patients (36.3%) with a compatible histological appearance in 7 patients. In 54.5% of cases, an associated autoimmune pathology was noted; the most common were autoimmune thyroiditis (33.3%) and autoimmune hemolytic anemia (33.3%). There were also two cases of Sjögren's syndrome, one case of systemic lupus erythematosus, and one case of rheumatoid arthritis. An overlap syndrome (AIH-PBC) was found in 22.7% of patients. The combined corticosteroid-azathioprine treatment was prescribed in 15 patients (68.1%). In overlap syndromes, ursodeoxycholic acid has been associated. The mean duration of follow-up was 94.5 months. Under treatment, biochemical remission was achieved in 23% of patients.

Conclusion: In our study, the prevalence of autoimmune diseases associated with AIH was significant, which would underline the importance of systematic screening for clinical and biological immune manifestations in those patients.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1549

AB1560 QUADRICEPS FEMORIS MUSCLE PROPERTIES IN SARCOIDOSIS: FUNCTIONAL AND CLINICAL IMPLICATIONS

Keywords: Sarcopenia, Ultrasound, Lungs

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Background: Sarcoidosis is a chronic disease which may involve muscular system subclinically at the onset of the disease. Sarcopenia is a musculoskeletal condition that may be associated with nonspecific symptoms in patients with sarcoidosis such as general weakness, arthralgia, reduced exercise capacity, and fatigue.
Objectives: This study aimed to determine the association between the functionality and the quadriceps femoris muscle (QFM) thickness measured using sonography in patients with sarcoidosis.
Methods: Thirty-one women with sarcoidosis and 27 controls were evaluated for the following outcomes: (i) handgrip strength, (ii) QFM thickness measured using ultrasound (US), and (iii) sonographic thigh adjustment ratio (STAR). The sarcoidosis group was also evaluated using the 30-second chair stand test (30s-CST) and fatigue severity scale (FSS).
Results: The QFM thickness and STAR values of the sarcoidosis group were significantly lower than those of the control group (p=0.0001). However, no statistically significant difference was observed between the handgrip strengths of the groups (p=0.581). There was no statistically significant correlation between the STAR values and handgrip strength in the sarcoidosis group (p>0.05); however, there was a statistically significant positive correlation between the STAR values and 30s-CST (r=0.467, p=0.008).
Conclusion: Probable sarcopenia is one of the musculoskeletal conditions in patients with sarcoidosis that may be associated with nonspecific symptoms, such as general weakness, exercise intolerance, and fatigue. Although the handgrip test is a frequently used test, it may not show prominent findings in the early stages of the disease. Ultrasound appears to be an innovative tool for preventing sarcopenia as it helps detect changes in muscle mass and muscle quality at an early stage.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.300

AB1561 COMPARISON OF DIAGNOSTIC PERFORMANCE OF TRUENAT™ MTB PLUS AND XPERT® ULTRA (GX) IN PATIENTS OF OSTEOARTICULAR TUBERCULOSIS (OATB): EXPERIENCE FROM NORTH INDIA

Keywords: Diagnostic tests

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Background: Diagnostic delay and drug resistance not only worsen the outcomes of tuberculosis, but are also important impediments to TB elimination efforts. Prompt and accurate diagnosis of osteoarticular tuberculosis (OATB) along with simultaneous detection of drug resistance is crucial to decrease the morbidity and associated sequelae.
Objectives: Given the need for a near point-of-care test suitable for primary healthcare centers and simultaneous detection of resistance, Truenat MTB Plus (TruPlus), a chip-based real-time polymerase chain reactionassay, was evaluated for the first time for diagnosis of OATB and detection of rifampicin resistance from pus and synovial fluid samples.
Methods: Total of 100 synovial fluid/pus samples (20 microbiologically confirmed OATB[culture-positive], 50 clinically confirmed OATB [culture-negative], and 30 control patients) were subjected to TruPlus assay and Xpert Ultra (GX Ultra) assay; and their performance was compared. Results were evaluated against both culture and composite reference standard.
Results: The overall sensitivity and specificity of TruPlus in diagnosing OATB was 77.14%(54/70) and 100%, respectively. The sensitivity was 90% (18/20) for microbiologically confirmed cases and 72% (36/50) for clinically confirmed cases. Performance of TruPlus was superior to Xpert ultra (sensitivity = 70%). Overall, sensitivity and specificity of GX ultra was 70% and 100%. However, sensitivity of GX Ultra was 85% in culture confirmed cases and 64% (32/50) in clinically suspected cases of OATB. Both TruPlus and Gx Ultra correctly reported Rifampicin resistance in four cases, when compared with phenotypic DST and rpoB gene sequencing.
Conclusion: TruPlus, with its greater portability and higher sensitivity than Xpert, could serve as an important tool for diagnosing OATB and rifampicin resistance at outreach endemic areas.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4617

AB1562 NAIL FOLD CAPILLAROSCOPY IN EVALUATING INTERSTITIAL LUNG DISEASE OF RHEUMATOID ARTHRITIS, SYSTEMIC SCLEROSIS AND IDIOPATHIC TYPE

Keywords: Rheumatoid arthritis, Systemic sclerosis

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Background: Nail fold capillaroscopy (NFC) is a non invasive diagnostic tool to detect early changes of microcirculation of different collagen diseases as rheumatoid arthritis associated interstitial lung disease (RA-ILD), systemic sclerosis interstitial lung disease (SS-ILD) and idiopathic ILD (Ting et al., 2020).
Objectives: The study aimed to evaluate role of NFC in RA-ILD, SS-ILD and idiopathic ILD, and to determine if there is a correlation of it to disease activity.
Methods: A case control study conducted on 100 patients with ILD, where 30 patients with RA-ILD, 30 patients with SS-ILD and 40 patients with idiopathic-ILD, fulfilling ACR/EULAR criteria, 2013. They were examined clinically and radiologicaly. Pulmonary function tests (PFT) and NFC were done.
Results: Pleural irregularities were found in 42% of RA-ILD, 30% of SS-ILD where subpleural irregularities were found in 31% of RA-ILD and 46.7% of SS-ILD. Ground glass opacity was in 13% of RA-ILD, 76.7% in SS-ILD and70% in idiopathic –ILD. Honeycomb appearance was in 11.5% of RA-ILD, 30% in SSILD and 65% of idiopathic ILD.SS-ILD showed the highest capillary changes especially patients with pneumonia. A significant correlation was found between NFC and PFT in idiopathic-ILD.
Conclusion: NFC is a sensitive and specific adjuvant tool in monitoring micro vascular changes in rheumatologic diseases and can be used as assessment tool in severity of the disease.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1563 CORRELATIONS BETWEEN LUNG INJURY AND PERIPHERAL VASCULAR MANIFESTATIONS IN PATIENTS WITH SYSTEMIC SCLEROSIS: A PRELIMINARY STUDY

Keywords: Lungs, Imaging, Cardiovascular disease

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Background: systemic sclerosis (SSc) is a rare autoimmune disease characterized by the presence of vascular disease and tissue fibrosis. The alteration of vascular system in SSc is due to dysfunctions of fibroblasts and endothelial cells [1-3]. This dysfunction results in excessive collagen production and vascular damage, which are associated to multiorgan damage. Lung disease in SSc is mainly characterized by interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH). Transthoracic echocardiography is the most commonly used screening tool for PAH in patients with SSc, but definitive diagnosis requires confirmation by right heart catheterization (RHC) [4]. Numerous studies have demonstrated that nail fold videocapillaroscopy (NVC) provides an accurate assessment of microvascular damage in SSc and is able to predict internal organ involvement, such as lung damage.
Objectives: This work aims to evaluate possible correlation between lung injury and peripheral microvascular involvement in SSc patients.

Methods: We enrolled, after obtaining informed consent, 16 patients affected by SSc (classification criteria EULLAR/ACR 2013) (3), who underwent cardiac catheterization for suspicion of PAH (3), in particular we paid attention to the measurement of pulmonary vascular resistance. NVC was performed in all patients, we collected information on the main capillaroscopic alterations such as number of capillaries, megacapillaries, avascular areas and microhemorrhages.
Results: After RHC evaluation, we identified 8 patients with PAH (F/M 6/2; median age 67± 7 SD years) and 8 without PAH (F/M 6/2; median age 66± 8 SD yrs). No significant differences regarding clinical and laboratoristic parameters were observed. At NVC, capillary density was significantly lower in PAH-SSc patients than in SSc patients without PAH (p = 0.04) and avascular areas were more frequent in the first group (p = 0.03). Furthermore, we evaluated a statistically significant correlation between the value of pulmonary vascular resistances at RHC and the number of capillaries at NVC (p = 0.04). We did not observe correlations with the other parameters.
Conclusion: This study confirms the correlation between peripheral microvascular alterations, evaluated by capillaroscopy and the involvement of internal organs, such as pulmonary circulation. Our findings provide additional evidence to the literature data but further studies are underway to confirm these preliminary data.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1564 PERIPHERAL BLOOD PERFUSION IN MCTD AND UCTD PATIENTS: A CROSS-SECTIONAL MONOCENTRIC STUDY

Keywords: Imaging, Mixed connective tissue disease, Undifferentiated connective tissue disease

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Background: Connective tissue diseases (CTDs) are a heterogeneous group of autoimmune disorders and, among them, mixed connective tissue disease (MCTD) and undifferentiated connective tissue disease (UCTD) show overlap symptoms with other CTDs, but share secondary Raynaud's Phenomenon (sRP) as a typical vascular symptom[1,2]. Laser speckle contrast analysis (LASCA) is a reliable tool to measure the peripheral blood perfusion (PBP) and has already demonstrated to be useful in detecting the peripheral microcirculation status of SSc patients and severe sRP[3].
Objectives: To measure hand PBP in patients with sRP in CTDs (MCTD, UCTD) and to compare it with healthy controls (HCs).
Methods: Twenty-four CTDs patients with sRP (7 with MCTD, 17 with UCTD) and 28 age- and sex-matched HCs were evaluated during standard follow-up assessments. CTDs diagnoses were set up according to the international classification criteria[4,5]. Patients had a stable therapy (mainly glucocorticoids and conventional disease modifying anti-rheumatic drugs) and had not had intravenous vasodilator treatments for the previous three months at least. All subjects underwent a LASCA registration (Laser Speckle Contrast Analysis - Pericam PSI, Perimed, Jarfalla) after acclimatization of 15 minutes at 20-22°C. After recording, PBP was quantified (perfusion units, P.U.) in the following region of interests (ROIs): fingertips (with and without thumbs) and periungual areas (with and without thumbs). Statistical analysis was performed using DATATab®, with parametric tests in case of normally distributed data and non-parametric tests in case of non-symmetrically distributed data.
Results: Although not statistically significant, a trend to a lower PBP was found when comparing MCTD LASCA values versus UCTD LASCA values, particularly for ROIs of periungual areas (see Table 1). In addition, PBP was found significantly lower in MCTD and UCTD when individually compared with HCs. This result was confirmed for all four ROIs (p<0,02; see Table 1).
Conclusion: To our knowledge, no evaluations of PBP by LASCA are available in literature in other CTDs other than SSc[6]. This preliminary study showed, using the LASCA methodology, that the PBP in MCTD and UCTD patients affected by sRP is significantly lower than in age- and sex-matched HCs. A trend with a lower PBP in MCTD patients than UCTD patients was observed but did not reach a statistical significance due to the small sample size. These results may demonstrate a potential role of LASCA in assessing the vascular involvement of CTDs other than SSc. Further investigations on a larger and more homogeneous sample size and a focus on the possible correlations between PBP and the morphological microvascular damage assessed by nailfold videocapillaroscopy have been planned.
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Table 1. Mean age and mean PBP in MCTD, UCTD and HCs, as measured by laser speckle contrast analysis (LASCA). PBP: peripheral blood perfusion; MCTD: mixed connective tissue disease; UCTD: undifferentiated connective tissue disease; HCs: healthy controls; P.U.: perfusion units.

	MCTD	UCTD	HCs	p-values
Age (years) Mean ± SD	59.8±14.2	51.2±15.9	57.6±11.7	n.s.
Mean fingertips perfusion (P.U.)	132.3±78.2	138.7±87.5	202.8±59.3	**MCTD vs HCs: p=0.013** **UCTD vs HCs: p=0.005** MCTD vs UCTD: n.s.
Mean fingertips perfusion (thumbs excluded) (P.U.)	131.5±80.1	139.2±90.7	203.9±60.9	**MCTD vs HCs: p=0.013** **UCTD vs HCs: p=0.006** MCTD vs UCTD: n.s.
Mean periungual perfusion (P.U.)	85.4±51	100±55.5	146.9±44.3	**MCTD vs HCs: p=0.003** **UCTD vs HCs: p=0.003** MCTD vs UCTD: n.s.
Mean periungual perfusion (thumbs excluded) (P.U.)	85.3±51.1	99.2±55.7	145.4±45.9	**MCTD vs HCs: p=0.005** **UCTD vs HCs: p=0.004** MCTD vs UCTD: n.s.

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AB1565 IBD AND LIGAMENTOUS LAXITY ASSOCIATION

Keywords: Diagnostic tests, Descriptive studies, Clinical trials

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Background: Inflammatory Bowel Disease (IBD) is a group of chronic relapsing-remitting diseases characterized by intestinal and extra-intestinal manifestations that unfavourably impact patients' physical and mental quality of life. Recent evidence points to a possible higher incidence of Joint Hypermobility (JH) or "ligamentous hyperlaxity" in IBD patients compared to the general population and particularly in younger and female subjects with IBD. Ligamentous hyperlaxity represents a little-known benign clinical condition characterized in its asymptomatic form by joint and ligament hypermobility.
Objectives: the aim of this study is to determine the prevalence of ligamentous hyperlaxity in a cohort of patients with IBD.
Methods: we evaluated 130 patients afferent to the joint clinic of the "Centro Regionale per le Malattie Infiammatorie Croniche Intestinali "Massimo Campieri" e MI Borghi", located at "Sant'Orsola-Malpighi" University Hospital in Bologna, in the period between June 2021 and November 2022, allocating them into 3 groups: 1) Ulcerative Colitis (UC), 2) Crohn's Disease (CD), 3) Indeterminate Colitis (IC). None of the patients was affected by hereditary collagenopathies. Out of 130 patients, 47 were affected by Ulcerative Colitis (UC), 78 by Crohn's Disease (CD) and 5 by Indeterminate Colitis (IC). The mean age at the time of the visit was 45,32 (±12,86 range 24-78) for patients with UC; 47,35 (±12,65 range 22-70) for patients with CD; 45,00 (±12,16 range 26-62) for patients with IC; in terms of sex: 47 men (20 with UC, 27 with CD, 0 with IC) and 83 women (27 with UC, 51 with CD and 5 with IC).
Results: 34 out of 130 patients presented ligamentous hyperlaxity according to Beighton's criteria (pt ≥ 4) (26,2% of total, 16 UC, 17 CD, 1 IC). Of the 47 patients with UC, 16 had ligamentous hyperlaxity (34%). Of the 78 patients with CD, 17 had ligamentous hyperlaxity (21,8%). Of the 5 patients with IC, 1 had ligamentous hyperlaxity (20%). It emerges from this analysis that the highest prevalence of ligamentous hyperlaxity occurs in patients with UC, compared with CD and IC. Chi-square test for independence was performed by comparing the variable ligamentous laxity with the variables IBD, UC, CD and IC.

The groups CD and IC did not show any statistically significant result with regards to ligamentous laxity whereas we did observe a statistically significant higher frequency of ligamentous laxity (p-value < 0,05) in the UC group.
Conclusion: a close association between Ulcerative Colitis and the presence of JH, especially compared to Crohn's disease and Indeterminate Colitis, clearly emerges from our observation, which could postulate a possible alteration of collagen development in the pathophysiology and clinical spectrum of UC only and not of IBD in general. These data, however, need to be confirmed and further investigated in the future with focused and rigorous prospective clinical studies, excluding confusing factors such as young age or inflammatory joint diseases such as spondyloarthritis.
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Acknowledgements: NIL.
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AB1566 CRYOGLOBULIN TESTING IN A TERTIARY UNIVERSITY TEACHING HOSPITAL

Keywords: Vasculitis, Diagnostic tests

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Background: Cryoglobulinaemic vasculitis is a small vessel vasculitis that is typically associated with hepatitis C viral infection (80%), however, it can also be associated with lymphoproliferative disorders and autoimmune diseases. [1] It typically presents with rheumatological, cutaneous or renal manifestations, in addition to peripheral neuropathy. [1] It is associated with significant morbidity and mortality if left undiagnosed. The detection of cryoglobulins in serum is a prerequisite for diagnosis. However, testing methods are frequently influenced by artifact, resulting from ex-vivo cryoprecipitation. Therefore, samples are often unsuitable for analysis, resulting in diagnostic delay, with associated high health care cost, utility, and burden.
Objectives: To assess cryoglobulin testing at a large tertiary hospital in Dublin, Ireland.
Methods: A retrospective analysis was performed on all cryoglobulin tests ordered at a tertiary university affiliated hospital over a five-year period from January 2017 until December 2022. We collected baseline patient demographics, location from which sample was taken (outpatient versus inpatient), suitability of sample for analysis and results of processed samples. Appropriate statistical analysis was then performed.
Results: A total of 524 consecutive samples were sent for cryoglobulin testing over the five-year period. The mean age of patients undergoing testing was 53.29 (SD 17.40). There was a total number of 360 individual patients, of which 166 (46.1%) were females. 223 (43%) samples were unsuitable for analysis and were not processed accordingly. Of those samples not processed 114 (51%) were taken on an inpatient ward, whilst 109 (49%) were taken in the outpatient setting. Of the samples unsuitable for analysis, 209 (93.7%) were received at the incorrect temperature, 11(4.9%) were duplicate samples, 2 had an incorrect serum sample sent, and in one case no sample was received. Notably, of the samples deemed unsuitable for analysis, only 117 (52%) underwent repeat testing. Unexpectedly, there was no statistically significant association between sample suitability and gender, age, date or location of testing.
Conclusion: This study demonstrates the inability to process almost half of cryoglobulin test samples received at our institution. This undoubtedly results in significant diagnostic delay, in addition to unnecessary health care costs and utility. There is a crucial unmet need to increase education and awareness on optimal sample testing, in addition to the implementation of pathways to optimize sample collection and transportation. Finally, the failure to repeat unprocessed samples in a significant proportion of cases raises the question of initial indication for testing, and the need to review criterion for diagnostic testing.
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Acknowledgements: NIL.
Disclosure of Interests: Patricia Harkins Grant/research support from: Janssen Pharmaceuticals, Sharon Cowley: None declared, Aifric Naughton: None declared, Jean Dunne: None declared, Niall Conlon: None declared, Richard Conway: None declared.
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AB1567 DIAGNOSIS OF SACROILIITIS USING LOW DOSE CT COMPARED TO MRI

Keywords: Diagnostic tests, Spondyloarthritis

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Background: Establishing a correct diagnosis of sacroiliitis is key to the early diagnosis of axial SPA. Low-dose computed tomography (LDCT) is helpful at revealing the structural changes (erosion, sclerosis and ankylosis) of sacroiliitis. How does LDCT compare with MRI for identifying sacroiliitis?
Objectives: This study compares LDCT and MRI in the diagnosis of sacroiliitis in patients with suspected axial spondyloarthritis (axSpA).
Methods: 25 patients [36 ± 7 years; female 16 (64%)] with back pain over three months and age under 45, clinically suspected of axSpA underwent radiography, LDCT and MRI of the SIJ. All imaging studies were assessed by an experienced radiologist. Radiographs and LDCT revealed erosions, bone sclerosis and ankylosis. MRI, in addition to these structural changes, also revealed osteitis and enthesitis.
Results: Out of the 25 patients, 8 (32%) had radiographic-sacroiliitis. Twelve (48%) patients had sacroiliitis on both LDCT and MRI, including 6 patients with radiographic-sacroiliitis and 6 patients with non-radiographic-sacroiliitis. There is no evidence of sacroiliitis on both LDCT and MRI for one patient, who was reported to have sacroiliitis on x-ray. No diagnosis could be made to 10 (40%) patients due to lack of evidence from imaging and 3 (12%) patients were diagnosed as osteitis condensans ilii. Agreement between MRI and LDCT was 100%, Cohen's kappa coefficient was k=1, positive predictive value was 1, and negative predictive value was 1. Using MRI as the gold standard, sensitivity and specificity of LDCT were 1 and 1 respectively. While the sensitivity and specificity of x-ray were 0.5 and 0.85 respectively.
Conclusion: Low dose CT and MRI showed comparable sensitivity in detecting sacroiliitis. If access to MRI is limited, LDCT is a good alternative to detect sacroiliitis in patients with suspected axSpA.
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Table 1. Radiography, LDCT and MRI for detecting sacroiliitis (n=25)

Radiography	LDCT			MRI		
	sacroiliitis	osteitis condensans ilii	Normal or equivocal	structural changes	osteitis condensans ilii	Normal
Sacroiliitis (n=8)	6	1	1	6	1	1
Normal or equivocal (n=17)	6	2	9	6	2	9

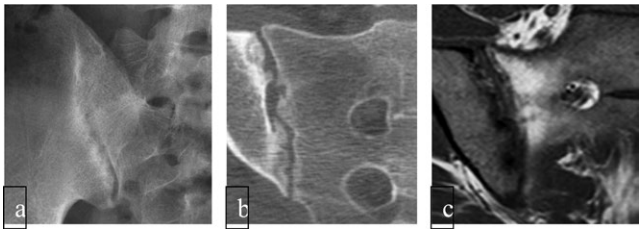


Figure 1. Radiography, LDCT, and MRI of sacroiliitis in patient with suspected axial SpA(a) Radiograph, (b) LDCT and (c) T1-weighted coronal MR image showing typical apperances of sacroiliitis.

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AB1568

ENTHESITIC INVOLVEMENT IN PATIENTS WITH SAPHO SYNDROME. ULTRASOUND EVALUATION USING THE MASEI INDEX

Keywords: Diagnostic tests, Enthesitis, Descriptive studies

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Background: SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, and osteitis) is a rare disease with a prevalence of less than 1 in 10,000 [1]. Among its musculoskeletal manifestations, enthesis involvement has been observed, which, along with the axial manifestations, has led many authors to consider it as part of the spondyloarthropathies group of diseases. Ultrasound assessment of enthesis is known to be more sensitive and specific than physical examination. The Madrid Sonographic Enthesitis Index (MASEI) is one of the most widely used tools for enthesis evaluation in spondyloarthropathies [2]. It examines six entheses (quadriceps, proximal and distal patellar, Achilles, plantar fascia, and triceps) and assesses six possible elementary lesions defined by OMERACT [3], plus Doppler. This allows the assessment of both inflammatory activity and structural damage (structure, thickness, erosions, calcifications, and bursitis) [4]. While there have been some ultrasound studies on enthesic involvement in SAPHO, demonstrating damage even in asymptomatic patients [5], there is currently no validated ultrasound index for enthesis evaluation in this disease.
Objectives: The aim of this study is to describe the ultrasound findings of SAPHO Syndrome patients' entheses using the MASEI index.
Methods: This is a descriptive, cross-sectional, single-center study, carried out in the Rheumatology Service of the Ramón y Cajal Hospital (Madrid, Spain). A convenience sampling was carried out, including all patients with SAPHO under active follow-up in our clinics.
Results: 12 patients were included (83.3% women), with a mean age of 52.41 (±9.4) years at the time of the study. 66.7% were smokers, and 25% ex-smokers. The mean BMI was 26.62 (±5.69). The average number of painful entheses was 0.92 (±1.24) and no swollen entheses were found. 25% of the patients had been diagnosed with previous clinical enthesitis. 38.5% of the patients had a positive MASEI score (>18). The mean score of the MASEI index was 20.42 (±11.02). Of this score, only a mean of 2 (±1.5) was found in the Doppler study; while a mean of 18.25 (±14.50) corresponded to structural damage. The involvement within the different explored entheses is described in Table 1. The greatest involvement was found in the distal patellar enthesis (6.58 ± 3.75) (Figure 1).

Table 1. MASEI score within the different explored entheses.

Enthesis	Triceps		Quadriceps		Proximal patellar		Distal patellar		Achilles		Plantar fascia	
Mean (±SD)	1,58 ±2,392		2,75 ±3,467		3,75 ±3,166		6,58 ±3,753		3,25 ±2,667		2,5 ±2,780	
	R	L	R	L	R	L	R	L	R	L	R	L
	0,5 ±0,52	1,08 ±2,06	1,33 ±1,83	1,42 ±1,73	2 ±1,76	1,75 ±1,91	2,17 ±1,03	4,42 ±3,09	1,50 ±1,09	1,75 ±1,76	1,25 ±1,60	1,25 ±1,60

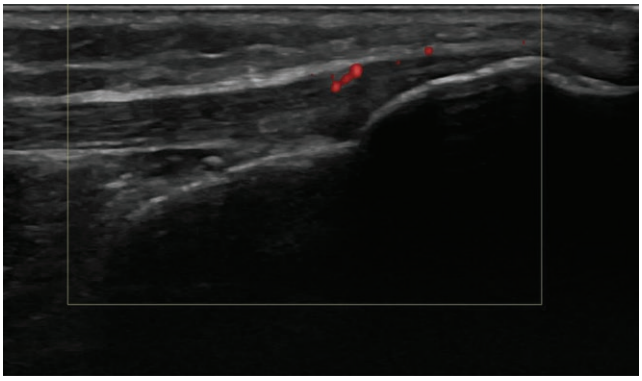


Figure 1. Ultrasound examination of the enthesis of the distal patellar tendon.

Conclusion: The patients with SAPHO Syndrome in follow-up at Ramón y Cajal hospital were found to have ultrasound entheseal abnormalities using the MASEI index. The results revealed a clear predominance of structural damage over the presence of active lesions. Further studies with larger sample size are necessary to fully comprehend the involvement of entheses in SAPHO syndrome.

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AB1569

THE USE OF MACHINE LEARNING IN DIAGNOSING AND DETECTING DAMAGE IN THE HANDS AND FEET OF PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS: A SCOPING REVIEW

Keywords: Imaging, Artificial intelligence, Psoriatic arthritis

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Background: Machine learning methods have the potential to optimise the diagnosis of inflammatory arthropathies and the quantification of damage over time.
Objectives: To summarise the literature investigating the use of machine learning methods to diagnose and detect damage in the hands and feet of patients with Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA).
Methods: A literature search was undertaken in PubMed, EMBASE, Web of Science and the Cochrane Central Register for Controlled Trials using a pre-specified search strategy. Full-text articles and conference abstracts published in English between the 1st of January 1995 and the 22nd of June 2022 that utilised machine learning (ML) in an imaging modality (X-Ray [XR], Computed Tomography [CT], Ultrasound [USS] or Magnetic Resonance Imaging [MRI]) to diagnose or assess structural damage in the hands and feet of patients with RA or PsA were included. All abstracts were reviewed by two authors (AA and AB) and all eligible full-text articles were assessed by the same authors, who subsequently independently extracted data according to the review protocol. Reference management and data extraction were conducted using Covidence. Data extracted included patient population and numbers, diagnoses, ML models and validation/testing methods, and algorithm performance.
Results: The literature review identified 851 unique references, of which 123 were eligible for full-text review; 26 references met the inclusion criteria for the review (Figure 1: PRISMA Diagram). There were 21 full-text articles and 5 conference abstracts published between 2000-2022, all of which assessed joints in the hands and/or wrists. Most studies utilised XR (n=23) rather than USS (n=1), MRI (n=1) and CT [1]. The number of patients/radiographs included used ranged from 15-5191 and most studies assessed RA only (n=23), with 2 studies assessing RA and PsA and 1 assessing PsA only. 24 studies were cross-sectional while 2 were longitudinal. ML methods were used to diagnose RA (n=9), diagnose PsA (n=2), estimate joint space score (n=5) or measure joint space width (n=3) or estimate change in joint space width (n=1), detect erosions (n=3) or estimate erosion score (n=7), estimate overall damage score (1), detect subluxation/ankylosis (n=1) and detect periarticular textural change (n=1). Additional tasks performed by ML algorithms were cropping of radiographs, localising joints and segmenting bones. Most studies utilised transfer learning on pre-trained neural networks: VGG15, VGG16, DenseNet, AlexNet, Single Shot Multibox Detector, YOLOv3, YOLOv4, LENet, Network in Network, SqueezeNet, ResNet, ResNet50, DeepTEN, U-net and EfficientNet. Some studies incorporated shape models (e.g. active shape, gaussian and local linear mapping models), multiscale gradient vector flow snakes, Graph Convolutional Networks, support vector machines, support vector regression and ridge regression. Complete model assessment with training, validation and testing cohorts were reported in 12 studies (46.2%), and of these 4 utilised n-fold cross-validation rather than hold-out validation. There was significant heterogeneity in the reporting and the performance of the models used.

Conclusion: The use of machine learning in diagnosing and detecting damage has mostly focused on plain radiography in patients with RA; there are limited data in PsA. Heterogeneity in the reporting of results limits succinct comparison of performance between ML methods.

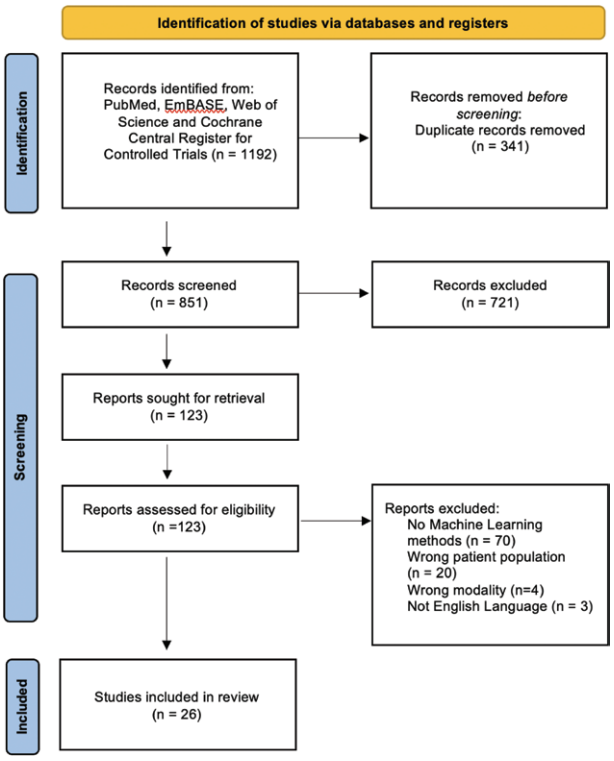


Figure 1. PRISMA Search Strategy

REFERENCES: NIL.

Acknowledgements: NIL.

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AB1570 MODERN TREATMENT OF ENTRAPMENT NEUROPATHIES, THE HYDROCHEMICAL NEUROLYSIS

Keywords: Ultrasound, Descriptive studies, Best practices

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Background: Entrapment neuropathies (E.N) are frequent and often underdiagnosed leading to significant chronic pain and functional impairment impede the quality of life. Commonly occur at the fibro-osseous tunnels through which the nerves course with various static and dynamic factors. Imaging particularly ultrasound can identify an anatomical cause, detect signs of nerve injury, assess its severity and also aid in the percutaneous treatment like our technique: "The hydrochemical neurolysis" (HCN).

Objectives: We present the US-guided hydrochemical neurolysis of E.N to relieve, in most cases, the pain caused by peripheral nerve compression and its consequences by the mechanical release and decompression of the entrapped nerves. This technique involves using US (fast, accessible, reliable, cheap and radiation-free) to find the nerve and guide a needle around the nerve to cut scat tissue and introduce fluid to mechanically push scar tissue ways from the nerve and create separation between the nerve and tissues. With **18 G needle**, a real mechanical dissection is performed and with the liquid (normal saline) we complete with a hydrodissection.

Methods: Before performing a US-guided HCN, survey imaging should be performed with low or high resolution probes, depending on the depth of the intervention. patient informed and clearly consents.

Technique: what I do.

Patient positioning: patient positioned in a supine, sitting, or prone posture according to the location of the nerve to be treated. Different positions, pillows and/or pads can be used to restrict movement during the procedure and provide comfort for patient and physician. Identification, marking the skin, disinfection and local anesthesia. The needle entry point is calculated based on the distance and inclination angle of the needle from the skin surface to the target for better and optimal visibility of the needle tip. These settings are variable depending on the superficial or deep situation of the nerve to be treated. The entry site is then marked (with skin marker) as well as the projection of the target at the level of the skin, then the skin area is cleaned and prepared for the using standard sterile technique. The US-probe is covered with a sterile semi-transparent bag and a sterile gel is used for further analysis and intervention. A 25 G needle is used to anesthetize the skin with 1% lidocaine, and is then advanced under US-guidance with an intermittent local injection for anesthesia (and hydrolocation) until the needle comes into contact with the epineurium. The in-plan approach is my favorite. Perineural Hydrolocalization, Adhesiolysis, Hydrodissection and injections. With **18 G** needle (variable length according to the site to be treated) we inject under low pressure 5-10 ml of liquid (mix of normal saline and 1% lidocaine) between the compressed nerve and the connective-fatty tissue to make the end of my needle clearly seen (**hydrolocation**), can be repeated for the duration of the procedure. Then with the same needle, we inject 20-60 ml of normal saline all around the nerve and over the entire area where it is compressed to release it completely from all surrounding structures (**hydrodissection**).

Adhesiolysis is carried out when there is scar tissue around the nerve and the hydro-dissection was not effective, in this case a real mechanical needle dissection is carried out or the needle is used like a scalpel to make needling in varying directions all the scar tissue surrounding the nerve. After hydrodissection, we **inject** corticosteroid (5-10 ml of prednisolone acetate 125 mg) for his anti-inflammatory and anti-fibrotic effect.

Results: In my practice, we have at least 70% good results at 12 months, 20 to 25% require a 2nd session of hydrochemical neurolysis and maybe 10% will resort to surgery. The results of neurolysis seem very interesting, much better than a simple US-guided infiltration and avoids surgery in many cases.

Conclusion: Success with this hydrochemical neurolysis procedure requires knowledge of anatomy, US-imaging. The HCN is a simple, safe, precise, rapid, and effective percutaneous treatment of E.N, a great alternative to surgery.

Acknowledgements: To anesthesiologist who trained me in musculoskeletal ultrasound more than 20 years ago and to all the patients who trusted me to offer them the best care.

Disclosure of Interests: None Declared.

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AB1571 IGG4-RELATED AUTOIMMUNE PANCREATITIS MIMICKING PANCREATIC CARCINOMA

Keywords: Malignancy, Undifferentiated connective tissue disease, Mixed connective tissue disease

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Background: IgG4-related disease (IgG4-RD) is a systemic fibroinflammatory disorder characterized by dense infiltration of IgG4-positive plasma cells in the affected tissue. The inflammatory infiltration along with storiform fibrosis can lead to the development of tumefactive lesions that may affect any organ. Type 1 Autoimmune pancreatitis (AIP) is a rare presentation of IgG4-RD that can present as a pancreatic mass and may mimic pancreatic carcinoma.

Objectives: The elevation of CA 19-9 is seen in autoimmune pancreatitis as well as pancreatic carcinoma. Therefore, it becomes difficult to differentiate between the two, especially in the presence of an elevated IgG4 level in the serum. We describe a rare instance of IgG4-related AIP with significantly high CA 19-9 levels.

Methods: Case report.

Results: Our patient is a 65-year-old male with past medical history of IgG-4 related retroperitoneal fibrosis, who presented with the complaint of worsening right upper quadrant abdominal pain, jaundice, and weight loss. Labs showed WBC count 13.7 (4.0-9.0 x 10*3/uL) and eosinophil count 700 (50-300/cmm). ESR 94 (0-15 mm/hr) and CRP 57.9 (0-10 mg/dL). LFTs showed elevated total bilirubin 12.5 (0.1-0.2 mg/dL), alkaline phosphatase 620 (30-115 IU/L), AST 72 (5-45 IU/L), and normal ALT 52 (5-60 IU/L). Absolute CD4 count was 1152 (332-1642 cells/cmm), CD4 percentage was 80% (28-62%), CD4 to CD8 ratio was high 8.86 (0.7-4.8). CA 19-9 was elevated to 2830 (0-35 U/ml). IgG4 was elevated 162 (2-96 mg/dL).

MRCP showed multiple biliary strictures and dilation of the main pancreatic duct. ERCP with stent placement was done to relieve biliary obstruction. EUS showed mass-like enlargement of the pancreatic head with atrophy, around the common bile duct (CBD). Biopsy of the CBD showed inflamed glandular mucosa, negative for malignancy. Pancreatic head biopsy showed normal stroma and benign mucosa, negative for malignancy. Patient had gradual improvement in bilirubin and CA 19-9 levels after ERCP and stent placement. He was started on prednisone which was followed by rituximab infusions. He followed up with rheumatology and had significant improvement in his symptoms and labs including a decrease in bilirubin to 2.8 mg/dL, alkaline phosphatase to 300 IU/L, and CA 19-9 levels to 100 U/ml within 1 month of discharge.

Conclusion: Autoimmune pancreatitis (AIP) can be difficult to distinguish from pancreatic carcinoma. High levels of CA 19-9 are usually indicative of malignancies, whereas high levels of IgG4 are characteristic of AIP. As per Van et al., the measurement of either CA 19-9 or IgG4 level alone is not accurate enough for diagnosis. However, the combination of CA 19-9 < 74 U/ml and IgG4 > 1.0 g/L distinguishes patients with AIP from patients with pancreatic carcinoma with 94 % sensitivity and 100 % specificity [1]. CA 19-9 levels can also be elevated in other GI diseases including primary sclerosing cholangitis, bacterial cholangitis, or choledocholithiasis. Differentiation between these conditions is extremely important due to the vastly different treatments and the morbidity/mortality associated with them [2,3]. IgG4-RD causing biliary obstruction with CA 19–9 elevation is a diagnostic dilemma. It can be misdiagnosed as pancreatic or cholangiocarcinoma. Our patient illustrates that IgG4-RD pseudotumors can significantly elevate CA 19-9. In these cases, further testing and biopsy should be performed to rule out malignancy.

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Disclosure of Interests: None Declared.

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AB1572 IMPACT OF MATERNAL CONNECTIVE TISSUE DISEASE ON FUNCTIONAL AND STRUCTURAL ABNORMALITIES OF THE HEART IN THE OFFSPRING

Keywords: Cardiovascular disease, Imaging, Heart

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Background: Some maternal systemic connective tissue diseases (CTD) and their associated antibodies are linked with adverse fetal outcomes, including increased risk of congenital heart diseases (CHD)[1,2]. Whether this increased risk also applies to less severe structural or functional cardiac abnormalities in the fetus is currently unknown.

Objectives: Based on a large cohort of newborns born to mothers with CTD, we aim to assess the association between maternal CTD and structural or functional cardiac abnormalities in the offspring. Data used in the study will be a combination of data collected in the Copenhagen Baby Heart Study (CBHS) and data collected via medical chart review to validate the CTD diagnosis and to obtain information about disease severity, treatment, etc.

Methods: In the CBHS we included more than 25,000 newborns between April 2016 and October 2018. All participants underwent systematic transthoracic echocardiography (TTE) within the first 60 days after birth[3,4]. The present study will include newborns from the CBHS born to mothers diagnosed with CTD, as identified through the Danish national health registries. Assuming an overall incidence of CTDs at 2% we expect to include approximately 500 newborns to mothers with CTD. Newborns born to mothers diagnosed with CTD will be matched 1:1 to newborns not exposed to maternal CTD, based on child sex; gestational age at birth; age and weight at time of TTE; and maternal age at delivery. Maternal medical charts will be reviewed to validate the CTD diagnosis and obtain information about disease severity, treatment, etc. The primary endpoint is a composite of functional and structural abnormalities in the heart of the newborns, assessed by echocardiography, including left ventricular structural and functional abnormalities, septum defects, and valve anomalies.

Results: Preliminary results are expected in spring 2023.

Conclusion: It is unclear whether children of mothers with CTD should have routine cardiac evaluation at birth, and whether certain types of maternal CTD have a higher risk of minor/subclinical CHD or less severe cardiac abnormalities in the offspring compared with children born to mothers without CTD. The size of CBHS and the comprehensive assessment of the included children provide a unique opportunity for obtaining new knowledge in this field, including better insights into whether routine TTE after birth should be considered in certain subgroups.

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Disclosure of Interests: None Declared.

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AB1573 AUTOIMMUNE HEMOLYTIC ANEMIA IN CHRONIC LIVER DISEASES

Keywords: Comorbidities, Diagnostic tests

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Background: Chronic liver diseases can be associated with autoimmune diseases. their association with autoimmune hemolytic anemia (AIHA) is poorly studied.

Objectives: Our objective was to study the prevalence and the characteristics of AIHA in chronic liver diseases.

Methods: We performed a retrospective analysis of data from consecutive patients followed in our department for chronic liver diseases recruited from January 2010 to December 2019. The diagnosis of AHAI was retained in front of regenerative anemia with a positive direct coombs test and stigmata of hemolysis (free hyperbilirubinemia, elevated lactate dehydrogenase, and low haptoglobin) in the absence of other overt causes of constitutional or acquired hemolysis.

Results: A total of 187 patients were included with an average age of 60.2 years [11-89] and a sex ratio of 1.79. Thirteen patients had an AIHA (7%). Anemia was normocytic in 77% of cases and macrocytic in 23% of cases. Five patients had a history of associated autoimmune pathologies (38.4%); autoimmune thyroiditis in two cases, one case of psoriasis, one case of Sjögren's syndrome and one case of autoimmune thrombocytopenia The AIHA was more frequent in cases of viral chronic liver diseases B and C (46.1%). Three patients had non-viral chronic liver diseases (23%): primary biliary cholangitis, autoimmune hepatitis, and alcohol.

Conclusion: In our study, AIHA was present in seven percent of cases, which would underline the importance of evoking it in the face of any anemia in the case of chronic liver diseases.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1574 DESCRIPTIVE STUDY OF CAPILLAROSCOPIES PERFORMED IN THE RHEUMATOLOGY SERVICE OF A THIRD LEVEL HOSPITAL

Keywords: Diagnostic tests, Descriptive studies

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Background: Capillaroscopy is a study technique using direct in vivo images of the skin microcirculation. It constitutes an accessible and non-invasive method to analyze microvascular abnormalities in patients with rheumatic diseases. Its usefulness has been demonstrated in diseases such as Systemic Sclerosis (ES), Sjögren's syndrome, Rheumatoid Arthritis, Dermatomyositis, Systemic lupus erythematosus (SLE) and, above all, Raynaud's phenomenon.
Objectives: To describe the clinical characteristics of a cohort of patients who underwent capillaroscopy in the Rheumatology service during the year 2022.
Methods: -Retrospective descriptive study of 100 patients who underwent capillaroscopy in the rheumatology service. The data obtained were obtained by reviewing the digital medical records and the registry of capillaroscopy images of the same service.
Results: 100 patients were included, of whom 92 were women (92%) and 8 were men (8%) with a mean age of 50 +/-17 years. Of the patients analyzed, 53 presented a normal pattern on capillaroscopy (53%) and 47 presented an abnormal pattern (47%). Of our cohort, 68 patients had Raynaud's (68%), 5 patients were diagnosed with undifferentiated connective tissue disease (5%), limited scleroderma 12 patients (12%), diffuse scleroderma 6 patients (6%), and with psoriatic arthritis, juvenile idiopathic arthritis, Sjögren's, Rheumatoid Arthritis, antiphospholipid syndrome, Bechet and Dermatomyositis, there was a patient with each named disease (7%), and finally there were 2 patients who still do not have a firm diagnosis (2%). Of the patients in our cohort with an abnormal pattern, 12 had an early scleroderma pattern (25.5%), 10 patients had a late scleroderma pattern (21.25%), 8 patients had a lupus pattern (17%), 8 patients had a nonspecific pattern (17%), 6 presented a school of fish pattern (12.75%) and 3 patients presented a pattern of mixed connective tissue disease (6.3%). Within the cohort with a pattern of early scleroderma on capillaroscopy, 4 patients were diagnosed with limited scleroderma, 5 with Raynaud's phenomenon, 1 with diffuse scleroderma, 1 with undifferentiated connective tissue disease, and 1 patient had no diagnosis. With a late-onset scleroderma pattern, there were 2 patients with Raynaud's phenomenon, 4 with diffuse scleroderma, and 4 with limited scleroderma. With a school of fish pattern, there were 3 patients with Raynaud's phenomenon, 1 with diffuse scleroderma, 1 with undifferentiated connective tissue disease, and one with Sjögren's. Of the 100 patients analyzed, 7 had lung involvement (7%), presenting late scleroderma pattern in capillaroscopy (3 patients), diffuse scleroderma pattern 1 patient, 1 patient in school of fish, early scleroderma pattern 1 patient and no alteration in capillaroscopy 1 patient.
Conclusion: The data obtained are consistent with what is reported in the medical literature. The most common abnormal capillaroscopy pattern in our environment is early scleroderma, followed by late scleroderma. Of the patients analyzed, 7 had pulmonary involvement. With the data we have collected, we can conclude that capillaroscopy is a useful, non-invasive technique that can guide us during the diagnostic process in those patients who raise doubts both in clinical judgment and in the evolution of the disease.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.2370

AB1575 A RELIABLE METHOD FOR ANNOTATING HAND AND WRIST X-RAYS FOR SUPERVISED MACHINE LEARNING ALGORITHMS

Keywords: Artificial intelligence, Psoriatic arthritis, Imaging

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Background: Machine learning (ML) algorithms could facilitate the standardisation of joint damage assessment in Psoriatic Arthritis (PsA) and improve its accessibility in clinical and research settings. ML algorithms trained on manually annotated hand and wrist radiographs have promising performance characteristics[1]. A large volume of annotated radiographs is needed, and annotation is time consuming and subject to reliability issues given X-Rays (XRs) are 2D representations.
Objectives: To develop a reliable method for the annotation of hand and wrist bones on XRs in order to facilitate the development of supervised ML algorithms for joint damage detection.
Methods: 10 bilateral hand and wrist XRs were selected at random from the Bath PsA XR database. 5 XRs were independently annotated by 3 annotators; (AA & WT (rheumatologist) and YHR (radiologist)) using the ASPAX software[2]. Annotations were visually inspected for areas of discordance and consensus annotation guidelines were developed. Annotation was repeated using the annotation guidelines on second set of 5 XRs. With annotator 1 (WT) representing ground truth, the mean error (ME; in pixels) of the annotation (deviation from ground truth) and the mean fractional error (MFE; corrects for the perimeter measurements of the bone), was estimated in pre- and post-training annotations. The ME and MFE within a single annotator (AA) were estimated in 5 radiographs after a 2-month interval.
Results: Visual inspection determined that the areas of discordance in annotation were the 1st interphalangeal joint, the metacarpal bases, the hamate and capitate bones, and the trapezium and trapezoid bones (Figure 1). The MFE between the annotators and ground truth improved for all bones following the development of annotation guidelines, with the largest improvement evident in the annotation of the metacarpal bones (Table 1). The intra-reader and inter-reader MFEs were comparable (Table 1).
Conclusion: Standardised instructions may facilitate reliable hand and wrist bone annotation and enable the acquisition of large volumes of annotated training data for supervised ML algorithms.
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Table 1. Reliability Exercise

	Exercise 1: Inter-rater error		Exercise 2: Inter-rater error		Exercise 2: Intra-rater error	
	Mean Error (±sd) Pixels	Mean Fractional Error (±sd)	Mean Error (±sd) Pixels	Mean Fractional Error (±sd)	Mean Error (±sd) Pixels	Mean Fractional Error (±sd)
Distal phalanges	201.02 (119.282)	3.97×10^{-4} (3.747×10^{-3})	550.54 (85.201)	1.66×10^{-5} (1.293×10^{-5})	1.39×10^{-2} (8.740×10^{-3})	2.40×10^{-5} (1.335×10^{-5})
Middle phalanges	218.83 (119.891)	7.43×10^{-4} (3.232×10^{-3})	544.37 (76.012)	4.33×10^{-4} (1.178×10^{-3})	7.85×10^{-3} (2.368×10^{-3})	1.02×10^{-5} (4.055×10^{-5})
Proximal phalanges	231.48 (116.095)	8.52×10^{-6} (8.113×10^{-6})	585.33 (104.098)	7.13×10^{-6} (3.119×10^{-6})	7.80×10^{-3} (3.554×10^{-3})	6.88×10^{-6} (3.972×10^{-6})
Metacarpals	184.94 (115.208)	1.74×10^{-4} (1.345×10^{-3})	571.73 (62.721)	8.65×10^{-6} (4.308×10^{-6})	9.82×10^{-3} (6.102×10^{-3})	6.07×10^{-6} (3.307×10^{-6})
Radius	232.90 (122.620)	1.75×10^{-4} (2.086×10^{-4})	552.12 (79.655)	3.25×10^{-5} (1.775×10^{-5})	1.83215×10^{-2} (9.617×10^{-3})	1.25×10^{-5} (6.534×10^{-6})
Ulna	236.60 (121.709)	3.31×10^{-4} (3.778×10^{-4})	557.25 (80.019)	2.19×10^{-5} (1.793×10^{-5})	1.68×10^{-2} (1.842×10^{-2})	1.41×10^{-5} (1.656×10^{-5})
Carpal bones[a]	197.42 (141.548)	2.75×10^{-4} (3.009×10^{-4})				
Carpal bones[b]			542.31 (77.896)	8.89×10^{-5} (1.025×10^{-4})	2.86×10^{-2} (3.285×10^{-2})	5.28×10^{-5} (7.673×10^{-5})

a. Trapezium, Trapezoid, Scaphoid, Lunate, Pisiform, Triquetrum, Hamate Capitateb. Trapezium, Hamate/Capitate, Lunate, Scaphoid

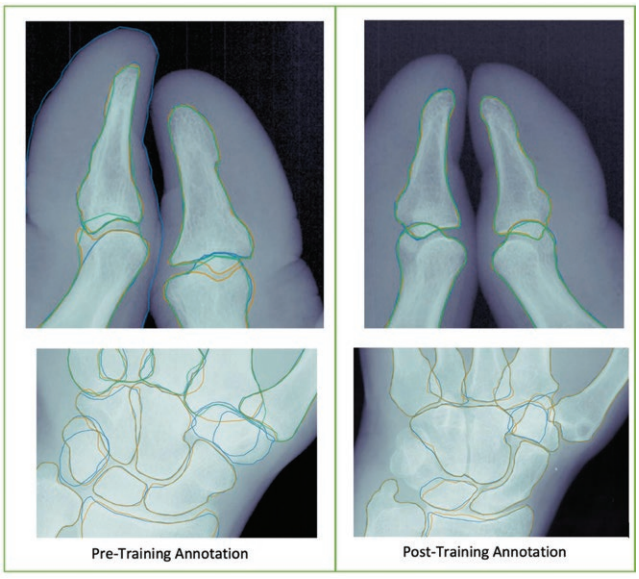


Figure 1. Pre- and Post-training annotation examples

Acknowledgements: NIL.
Disclosure of Interests: Adwaye Rambojun: None declared, Anna Antony Speakers bureau: Eli Lilly, AbbVie, Ynyr Hughes-Roberts: None declared, William Tillett Speakers bureau: Abbvie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Consultant of: Abbvie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Ono Pharma, Pfizer, UCB, Grant/research support from: Janssen, UCB, Pfizer, Eli-Lilly.
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AB1576

PERICORONARY ADIPOSE TISSUE (PCAT) ATTENUATION IS ASSOCIATED WITH INFLAMMATORY RHEUMATIC DISEASES (IMD): A RETROSPECTIVE CROSS-SECTIONAL ANALYSIS

Keywords: Heart, Imaging, Cardiovascular disease

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Background: PCAT attenuation is a non-invasive biomarker of coronary inflammation and is a poor prognostic factor in patients with coronary artery disease.
Objectives: To compare the severity of PCAT attenuation amongst patients with inflammatory rheumatic diseases (IMD) compared to patients with non-inflammatory rheumatic diseases (NIMD) in a retrospective cross-sectional study.
Methods: All patients seen in Monash Health rheumatology clinics over a 12-month period were identified. Patient records were cross-referenced with the hospital computed tomography coronary angiography (CTCA) database to identify patients who had undergone CTCAs. IMD patients who had their CTCA prior to their RMD diagnosis were excluded. Age, sex, co-morbidities, diagnoses, height, weight, and medications were extracted from the patient electronic medical records. CTCA variables were extracted (mA, DLP, contrast volume, kV, CACS, CAD-RADS) or calculated (SIS, SSS, PCAT attenuation).
Results: A total of 117 patients were included (105 with IMD and 12 with NIMD). There were no significant differences in age, sex, co-morbidities or cardiovascular medication use between groups. Patients with IMD had a lower BMI and were less likely to be smokers or have dyslipidaemia, but were more likely to have hypertension and diabetes mellitus, these were not statistically significant. The mean (±sd) PCAT was higher in IMD patients [-84.6 (±12.14) vs. -92.0 (±5.01) p<0.001) compared to non-IMD patients. There were no significant differences in any other CTCA outcomes.
Conclusion: PCAT attenuation is associated with IMD in this retrospective single-center cross-sectional study. Data from larger prospective cohorts with healthy comparator controls are needed to assess the significance of these findings.

Table 1. Baseline Demographics and CTCA Results

	IMD (n=105)	No IMD (n=12)	p-value	Missing (%)
Age (years)	56.6 (12.76)	57.6 (6.97)	0.347	0
Sex (F)	70 (66.7)	9 (75.0)	0.559	0
Co-morbidities	64 (61.0)	5 (41.7)	0.198	0
Hypertension	44 (41.9)	7 (58.3)	0.277	0
Dyslipidaemia	17 (16.2)	1 (8.3)	0.475	0
Diabetes Mellitus	40 (38.8)	6 (50.0)	0.455	2
Smoking	23.8 [27.10-31.42]	26.6 [29.20-33.20]	0.281	19
BMI	56 (65.9)	10 (76.9)	0.429	19
BMI > Normal				
Medications	40 (39.2)	3 (25.0)	0.530	3
Anti-platelet	39 (38.2)	3 (25.0)	0.531	3
Statin	70 (68.0)	6 (50.0)	0.214	2
Antihypertensive	50 (48.5)	5 (41.7)	0.652	2
ACEi/ARB	23 (22.3)	1 (8.3)	0.455	2
CC-Blocker	33 (32.0)	1 (8.3)	0.106	2
B-Blocker	26 (25.2)	2 (16.7)	0.728	2
Diuretic	5 (4.9)	0 (0)	1.000	2
GTN				
CTCA Results	**-84.6 (12.14)**	**-92.0 (5.01)**	**<0.001***	**12 (10.3)**
PCAT attenuation	0 [0.00-6.00]	0 [0.00 – 65.00]	0.240	38 (32.5)
CACS (0->400)	0 [0.00-2.00]	0 [0.00-2.00]	0.975	10 (8.5)
CAD-RADS (0-5)	1.0 [0.00-4.00]	1.0 [0.00-4.00]	0.883	9 (7.7)
SIS (0-18)	2.0 1.0 [0.00-4.00]	2.0 1.0 [0.00-4.00]	0.818	11 (9.4)
SSS (0-54)				

Abbreviations: Pericoronary Adipose Tissue (PCAT) attenuation; Coronary Artery Calcium Score (CACS), Coronary Artery Disease – Reporting and Data System (CAD-RADS), Segment Involvement Score (SIS), Segment Stenosis Score (SSS)]

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1577

EL ÍNDICE DE RESISTENCIA TIENE UNA RELACIÓN ESTRECHA CON LA DESTRUCCIÓN INTRAARTICULAR DE HUESO Y CARTÍLAGO POR DOPPLER ESPECTRAL EN LA ARTRITIS REUMATOIDE

Keywords: Ultrasound

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Background: Recent reports have shown that high-resolution ultrasound is a useful method of detecting pannus vascularization in inflamed finger joints of patients with RA and also is useful in assessing the disease activity or in monitoring therapeutic responses. Power Doppler ultrasonography (PDUS) techniques not only have the ability to detect vascularization but do also depict the flow patterns in the inflamed joints of RA patients by using spectral analysis.
Objectives: To evaluate intra-articular vascularization and flow patterns of the metacarpophalangeal (MCP) joints in rheumatoid arthritis (RA) patients by using power Doppler spectral (PDSUS) technique. The relationship between the flow patterns and bone and cartilage destruction.
Methods: Thirty-two patients (mean age 53.5 ± 13.8) with a disease duration of 7.8 ± 3.9 years were included into the study. Twenty MCP joints of five healthy subjects were also assessed as controls. Clinical activity of MCP joint inflammation was classified according to index for synovitis activity PD based on joint swelling, warmness and pain. Ultrasonography was performed using Vinno G86 unit by means of a 6–18 MHz linear array transducer. Gray-scale US and power Doppler sonography (PDUS) examination was performed. Using spectral Doppler the quality of flow was determined and the indices of pulsatility (PI) and resistance (RI) were measured in longitudinal plane. The erosive scores of the MCP joints were determined on the plain hand radiographs using Sharp/van der Heijde method.
Results: Total 128 MCP joints of 32 patients and 20 MCP joints of five healthy controls were examined in dominant hand. Flow was determined in 30 joints (10 moderately active, 20 active) in eight patients with erosions, whereas twenty-four patients had no erosions in MCP joints. MCP joints of healthy controls had quantifiable flow. Mean PI of these joints were in control (2.34 ± 0.87), in moderately

active (1.01 ± 1.1) and 0.32 ± 0.6 in active MCP joints. RI was in control 0.87 ± 0.12 in moderately active 0.61 ± 0.15 (figure 1) and 0.24 ± 0.12 in active MCP joints. There was significant difference in RI and PI of these active and moderately active MCP joints (p <0.01). There was a significant correlation between erosive scores and PI, RI of total MCP joints (r = 0.40 and r = 0.41, P < 0.05).

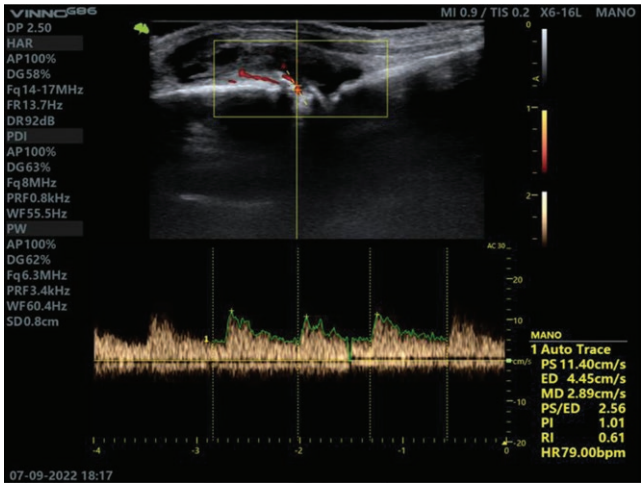


Figure 1. Moderately active

Conclusion: Spectral Power Doppler ultrasonography (PDSUS) is a useful method demonstrating synovial vascularization and flow patterns and offers new alternatives for monitoring disease activity and measurement of therapeutic response. Flow patterns had intimate correlation with intra-articular bone and cartilage destruction.

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Disclosure of Interests: None Declared.

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AB1578

HEMORRHAGIC RISK ASSOCIATED WITH SPINAL PROCEDURES AND FOCUS ON PATIENTS TREATED BY ANTICOAGULANTS OR PLATELET INHIBITORS: A SYSTEMATIC LITERATURE REVIEW AND META ANALYSIS

Keywords: Safety, Systematic review

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Background: Spinal procedures – including lumbar puncture, radiofrequency neurotomy, medial branch injection, facet joint injection, blood patch and epidural injection – are common in daily practice. Side effects can occur during these invasive procedures like hemorrhagic complications. The use of anticoagulants and platelet inhibitors can increase these risks.

Objectives: The aim of this study is to characterize the hemorrhagic risk associated with spinal procedures and to analyze if there is a sur risk of bleeding complications in patients treated with anticoagulants or platelet inhibitors.

Methods: A systematic literature review and metanalysis were made in MEDLINE, EMBASE and COCHRANE, in order to find a prevalence of hemorrhagic complications for each spinal procedure. We classify hemorrhagic risk in two categories. Bleeding and traumatic procedure were not severe complications and epidural hematoma and central nervous system bleeding were severe complications.

Results: Systematic literature analysis found 2407 articles. 75 were included in the metanalysis. The flow chart diagram, according to the PRISMA criteria is shown [Figure 1]. The global prevalence of each hemorrhagic complication according to each spinal procedure is showed in Table 1. There was no difference between patients with anticoagulants or platelet inhibitors and the others according to the epidural hematoma risk with OR of 0.95 IC95 [0.16-5.52] after a lumbar puncture and for the risk of traumatic lumbar puncture with OR of 0.78 IC95 [0.47-1.29].

Conclusion: Hemorrhagic complications during a percutaneous spinal procedure are very low. These findings are in coherence with precedents findings. In this metanalysis there was no difference between patients with anticoagulants or platelet inhibitors and the others during a lumbar puncture according to the epidural hematoma risk and the traumatic puncture risk. Strength of the study is the very important number of procedures. However studies were very heterogeneous. This metanalysis found that severe bleeding risk is very low during a spinal procedure but consequences can be severe. That is why the use of anticoagulants and platelet inhibitors has to be careful.

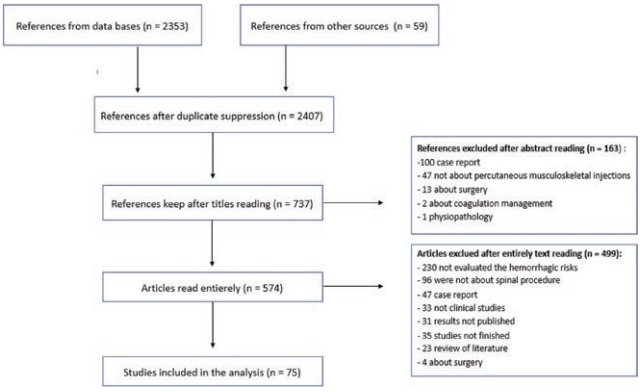


Figure 1.

Table 1.

	Local bleeding	Traumatic puncture	Epidural hematoma	Central nervous system bleeding
Lumbar puncture	**5/1 614 0% IC95% [0%-1%]**	**1820/10 961 16 % IC95 % [13%-18%]**	**169/96 524 0% IC95% [0%-1%]**	**176/6 347 2% IC95% [0%-9%]**
Epidural injection	**78/29 439 0% IC95% [0%-1%]**	**63/597 8% IC95% [0%-20%]**	**22/273 766 0% IC95 % [0%-0%]**	NA
Blood patch	NA	NA	NA	**11/684 7% IC95% [0%-33%]**
Facet joint injection	NA	NA	**0/8 162 0% IC95 % [0%-0%]**	NA
Medial block branch injection	**0/3 059 0% IC95% [0%-0%]**	NA	0/92 0%	NA
Radiofrequency neurotomy	**1/683 0% IC95% [0%-2%]**	NA	**0/162 0% IC95% [0%-0%]**	NA
Vertébroplasty/ Kyphoplasty	NA	NA	**4/365 1% IC95% [0%-3%]**	NA

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1579

ULTRASOUND JOINT ASSESSMENTS INCREASE DETECTION OF POLYARTICULAR JOINT INVOLVEMENT IN CHECKPOINT INHIBITORS-INDUCED ARTHRITIS

Keywords: Malignancy, Inflammatory arthritides, Ultrasound

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Background: CheckPoint Inhibitors (CPI) Induced arthritis (IA) is an immune related adverse event (irAEs) occurring in 0.5 to 2% of CPI-treated patients between 3 weeks up to 24 months after initiation of therapy. IA is usually described as a seronegative oligoarticular inflammatory joint disease but IA has been for long underdiagnosed and inappropriately evaluated.
Objectives: To evaluate the added value of a systematic joint ultrasound assessment in these patients by the rheumatologist.
Methods: Patients referred by their oncologist to the Rheumatology Department for suspected arthritis had a clinical swollen joint count and a joint ultrasound assessment (GE Logiq E9 Ultrasound Machine with ML6-15-D Matrix Linear Probe). Target joints were elbows, wrists, MCP 2-5, knees, ankles and MTP1-5. The swollen joint count performed by the oncologist was compared to the one made by the rheumatologist and the US assessment. A joint was considered as positive by US assessment in case of grey-scale ≥ 1 in a scale of 3.
Results: 9 patients (6 males and 3 females) were assessed. Mean age was 66.1 years (SD 11 years). 4 were treated for metastatic melanoma, 1 for renal cell carcinoma (RCC), 3 for lung cancer, 1 for uterine cancer and 1 for bladder carcinoma. They received a monotherapy with pembrozilumab (4/9), nivolumab (2/9), atezolimumab (1/9), darvalumab (1/9). None had received corticosteroids. 5 out of the 9 patients were referred for an oligoarticular (swollen joint count <5) presentation by the oncologist, 2 out of 9 for a polyarticular (swollen joint count ≥5) presentation and 2 for a PMR-like presentation. Whereas the rheumatological and the US assessments confirmed the polyarticular diagnoses made by the oncologists, the 5 oligoarticular-labelled patients had polyarticular involvement after the rheumatologist and US assessements. In the 2 patients referred for a PMR-like disease, US assessments showed one polyarticular and one oligoarticular presentation. None of the 9 patients had positive rheumatoid factors (RF) or anticitrullinated peptides antibodies (ACPAs).

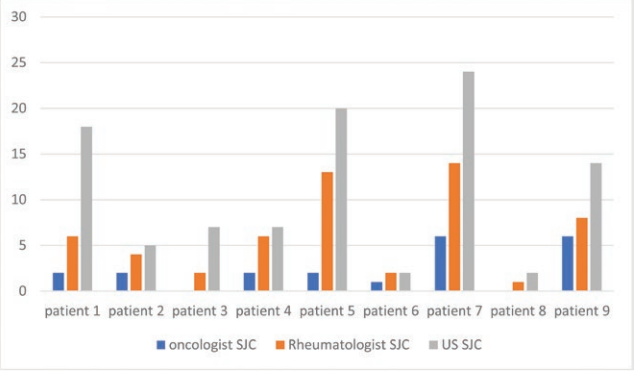


Figure 3. *Number of swollen joints (SJC) for each patient according to the oncologist, the rheumatologist and the ultrasound assessment.*

Conclusion: In this small group of patients with CPI-IA, In this small group of patients with CPI-IA, we found that US joint assessment led to a better classification of polyarticular joint involvement, present in the majority of the cases.
Our results emphasise the importance of a multidisciplinary approach of these patients and support the use of US joint assessments in CPI-IA patients.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1580

ULTRASOUND FINDINGS IN PATIENTS WITH GOUT IN A POPULATION OF THE DOMINICAN REPUBLIC

Keywords: Ultrasound, Gout, Prognostic factors

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Background: Hyperuricemia is an increase in the serum concentration of monosodium urate (MSU). Gout is secondary to the inflammatory response elicited by the deposition of UMS in the tissues. It is the most frequent inflammatory arthropathy in the general population. [1] Its prevalence has been estimated at 2-3% of the adult population. [2] The ultrasound findings observed are considered within the ACR/EULAR 2015 criteria, which derive from the presence of UMS deposits in the subcutaneous tissue and in intra- and periarticular areas (cartilage, tendons, ligaments, and bursae. [3]. There are 2 specific findings of MSU deposits: 1) enhanced echogenicity of the chondrosynovial margin (double contour sign), presence of hyperechogenic aggregates, which, in turn, can have 3 forms of presentation: hyperechogenic dots (<1 mm) within a joint effusion, (cotton-wool areas) (<1 cm) homogeneous without posterior acoustic shadow and larger tophi with calcifications and posterior acoustic shadow [4].
Objectives: To identify the ultrasound findings in patients with gouty arthritis in a population of the Dominican Republic.
Methods: Descriptive, prospective observational study. From the cohort of patients from the Rheumatology service of the Hospital Docente Padre Billini, patients from the outpatient clinic were evaluated from June to December 2022. Inclusion criteria: > 18 years, diagnosis of gouty arthritis according to ACR\EULAR 2015 criteria, presence of at least 1 attack of gouty arthritis, performance of joint ultrasound Exclusion criteria: Osteosynthesis material in areas evaluated by ultrasound and/or infiltration, traumas of less than 3 months in the evaluated joints. Elbows, wrists, 2nd metacarpophalangeal MCP, knees, and 1st metatarsophalangeal MTF were evaluated by ultrasound, recognizing positive findings of double contour sign, hyperechogenic aggregates, erosions, synovitis, and irregularities according to OMERACT definitions. Made with the Siemmens Acuson X 150 ultrasound machine, with a 13 mHz transducer. Descriptive statistics were performed with SPSS 25 V2.
Results: 52 met inclusion criteria. 100% male, mean age 59±16.1 years, mean disease duration 8.6 years, mean serum uric acid 9.5 mg/dL. BMI: overweight 32.7% (17), grade I obesity 21.2% (11), grade II obesity 40.4% (21). Diabetes mellitus 55.8% (29). Arterial hypertension 57.7% (30). Dyslipidemia 80.2% (42). Colchicine 61.5% (32), Allopurinol 48.1% (25). Febuxostat 48.1% (25), NSAIDs 48.1% (25), Prednisone 46.2% (24), Benzbromarone 3.8% (2) Ultrasound findings 55.7% (29): Elbows: irregularities 37.9% (11), Tophi 37.9% (11), erosions 20.7% (6), Carpals: Erosions 10.3% (3), aggregates 10.3% (3), power Doppler 2.69% (2), irregularities 31% (2), Knees: erosions 27.6% (8), irregularities 27.6 % (8), double contour 20.6% (6) power doppler 10.3% (3), tibiotalar: irregularities 27.6% (8), erosions 17.2% (5); 1st MTFs: erosions 48.2% (14), irregularities 27.6% (8), aggregates 3.4% (1).
Conclusion: The study demonstrated that more than half of patients with gout present structural lesions by ultrasound according to OMERACT. The elbows are the most affected joints with the presence of tophi, followed by the first metatarsophalangeal joint with the presence of erosions.
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Public health, health services research, and health economics

AB1581

HIGH PREVALENCE OF BURNOUT SYNDROME AMONG RHEUMATOLOGISTS PRACTICING IN ARAB COUNTRIES: AN ARLAR MULTINATIONAL STUDY IN 394 RHEUMATOLOGISTS

Keywords: Descriptive studies, Work-related issues, Health services research

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Background: Burnout is frequent among physicians and has significant implications for the healthcare system. However, it seems to be underestimated so far among rheumatologists, with few studies indicating a prevalence of 51-57%.
Objectives: To estimate the prevalence and predictors of burnout among rheumatologists practicing in Arab countries.
Methods: A cross-sectional study was conducted by the Arab League of Associations for Rheumatology (ArLAR) Research Group (ARCH) using an anonymous electronic survey developed and tested by a core steering committee and hosted on the Google Forms platform. All rheumatologists practicing in the Arab countries were invited in spring 2022 to participate in the e-survey by mass e-mail and via societies' WhatsApp groups and ArLAR social media accounts. In addition to demographic data, workload, practice profile, income, and specialty satisfaction (assessed indirectly through choosing another specialty if given a choice), the questionnaire included the Maslach Burnout Inventory (MBI). Rheumatologists were considered as having burnout if at least one of the three MBI domains was positive (Emotional Exhaustion (EE) ≥27, Depersonalization (DP) ≥10, or Personal Accomplishment (PA) ≤ 33). Factors associated with burnout were analyzed using a multivariable binary logistic regression.
Results: Among 3,227 rheumatologists practicing in Arab countries, 408 responded to the survey, and 394 were included in the final analysis (12.2% of all practicing rheumatologists). The mean age was 45.2 years (SD 11.5), 60.7% were females, the median practice duration was 13 years (IQR 6-22), 49% were from North Africa, 33% were from the Levant, and 18% were from the Gulf. In total, 73% worked full-time, 48% worked in the public sector, 21% in the private sector, and 31% in both; 74% worked in an urban setting only, monthly income was <1,000 USD in 31%, 1,000-1,500 USD in 41%, 5,000-10,000 USD in 9% and > 10,000 USD in 8%. The prevalence of burnout among rheumatologists was 61.3%. It was mostly driven by a low PA score (58.1%) (Figure 1). Also, 15.6% had a positive EE score, and 11.6% had a positive DP score. After adjustment for demographics, practice profile, and workload variables, burnout was independently associated with an income < 10.000 USD/ month (OR 2.26 [95% CI 1.01; 5.10), unsatisfaction with rheumatology specialty (OR 2.04 [95%CI 1.20; 3.46) and younger age (OR 1.92 (95%CI 1.20; 3.08) (Table 1).
Conclusion: The prevalence of burnout among rheumatologists in Arab countries is significantly high and driven mainly by a low personal assessment score. Associated factors were a lower income, lower satisfaction with the specialty, and younger age. Therefore, burnout among rheumatologists needs to be adequately addressed to prevent its negative impact on the healthcare system.

Table 1. Predictive factors of burnout in rheumatologists practicing in the Arab countries (multivariable analysis)

Variable	OR	95% CI	p-value
Income < 10.000 USD/month	**2.265**	**1.006 – 5.098**	**0.048**
Specialty unsatisfaction	**2.036**	**1.199 – 3.457**	**0.009**
Age < 44 years	**1.921**	**1.198 – 3.078**	**0.007**
Receiving phone calls from patients on personal phone	1.616	0.714 – 3.659	0.249
Infusion center at the rheumatology practice	0.733	0.435 – 1.236	0.733

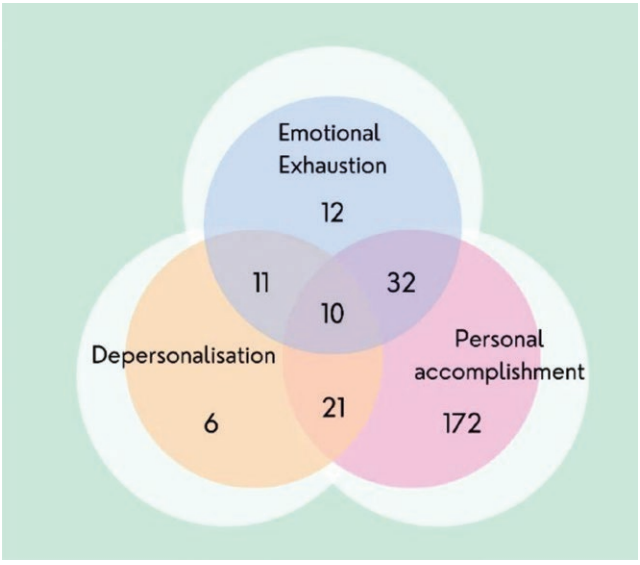


Figure 1. Venn diagram of the physicians fulfilling the domains of the MBI

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Disclosure of Interests: None Declared.
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AB1582

DEPRESSION IN RHEUMATOLOGIST FROM LATIN AMERICA

Keywords: Quality of life, Epidemiology, Quality of care

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Background: Depression, burnout, and suicide are becoming a major problem among physicians. A survey estimated that around 21% are depressed and 1 in 10 had have suicidal thoughts.[1]
Objectives: Determine the prevalence of depression in rheumatologists from Latin America and factors associated with it.
Methods: Cross-sectional study. Data was collected through an online survey distributed by PANLAR, which included demographics and work-related factors. Depression was measured with PHQ-9 questionnaire, burnout with the Maslach Burnout Inventory, happiness with the Subjective Happiness Scale and satisfaction with a 7-point Likert scale. Analysis of data was done with SPSS V 27 and included descriptive statistics and association between variables using Chi square and Student's T test.
Results: 297 rheumatologists were included from 15 countries, mainly Argentina 28.3% and Brazil 26.3%. Most were women 62%, married 65%, practiced adult rheumatology 82% and earned less than $50 K/year 74.8%. Depression

was found in 48.8%: mild 33%, moderate 8.8%, moderate severe 4%, severe 3%. The mean PHQ-9 score was 5.5±5.3. 46.1% reported anhedonia, 40.7% feeling depressed, sleep alterations 57.2%, fatigue 75.1%, appetite changes 46.1%, feelings of failure 37%, decreased concentration 50.2%, psychomotor changes 27.9%, thoughts of hurting oneself 9.8%, 8.2% suicidal thoughts and 8.4% low self-esteem. 56.6% had burnout. 14.5% were taking SSRI/SNRIs and 4% were previously diagnosed. Factors associated with depression were female sex (p=0.008), younger age (p<0.001), administrative duties (p=0.010), annual income less than $25K (p=0.002), low self-esteem (p<0.001), burnout (p<0.001), less satisfaction with career (p<0.001) and lower subjective happiness (p<0.001). Exercise (p=0.035) and practicing academics (p=0.010) were associated with less depression.

Conclusion: Depression affected almost half of the rheumatologists and was more common in females, younger population, with low self-esteem. Lower income, having burnout and less satisfaction with the career were also risk factors. Only a small proportion of the affected population was previously diagnosed and on treatment.

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Disclosure of Interests: None Declared.

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AB1583 EVALUATING THE DIRECT EFFECT OF SLE IN THE PRESENCE OF INTERMEDIATE GC ON HEALTHCARE COST

Keywords: Randomized control trial, Health services research, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is a chronic disease with a broad spectrum of autoantibodies and clinical manifestations. SLE imposes a substantial economic burden on patients and the healthcare system with the estimate of annual healthcare costs for SLE patients of $5,062 in Canada. Besides SLE, post-SLE Glucocorticoid (GC) is often associated with severe infection and mortality, hence increased healthcare costs. One recent study showed that GC users had a total of $17,232 in healthcare costs [1]. However, previous studies did not account properly for GC which acts as a mediator between SLE and healthcare costs. In addition, those studies of the costs due to SLE in Canada estimated the costs of SLE via questionnaire survey with a limited sample size. The use of questionnaires subject to selection bias can either over or underestimate the costs associated with SLE because specific groups (those who don't have access to questionnaires) are underrepresented. As a result, their conclusions may lack generalizability to all SLE patients.These limitations call for a new approach to account for post-treatment selection bias and a large dataset in the real-world setting to quantify the healthcare costs due to SLE.

Objectives: The objectives of this study are two-fold: 1) to disentangle and quantify the causal annual healthcare costs directly associated with newly diagnosed SLE accounting for GC use. 2) to identify the charactersitscs of the patients who never took GC (never-users).

Methods: Using linked administrative health data from British Columbia, Canada, we conducted an age- and gender-matched cohort study of all patients with incident SLE between 1997 and 2015. We implemented Principal stratification [2] to identify the annual healthcare costs directly attributed to SLE. Within the strata defined by post-SLE GC use: always-users, never-users, SLE-only users, and non-SLE-only users, we estimated the principal causal effects of SLE on annual healthcare cost. To face identification issues of unobserved principal stratum, estimation was performed with Bayesian Mixture Modelling.

Results: We identified 5,169 SLE patients and matched them with 25,845 non-SLE individuals from the general population. The crude incidence rate ratios for first severe infection and infection-related mortality were 2.59 (95% CI, 2.39-2.80) and 2.20 (95% CI, 1.76-2.73), respectively. The direct annual healthcare cost due to SLE was $1.01k (%95 CI, 0.94-1.10k) which was a weighted average of the cost in always and never-users strata (Figure 1). Always and never users accounted for 20.3% and 73.9% of the total population. Compared to the SLE-only users, those with older age, rural residence, higher income and more medical service visits were more likely to be in the never-user stratum.

Conclusion: This is the first study to examine the direct effect SLE on healthcare cost accounting for the GC-taking behavior using real-world data. Our findings highlighted the direct economic burden due to SLE and can be generalized to the SLE population. Recognizing the economic burden of SLE will inform future interventions for prevention, and medical management in this vulnerable patient population. What's more, when prescribing GC, the treating physicians should pay attention to the patients with with older age, rural residence, higher income and more medical service visits because they are unlikely to adhere to the treatment scheme.

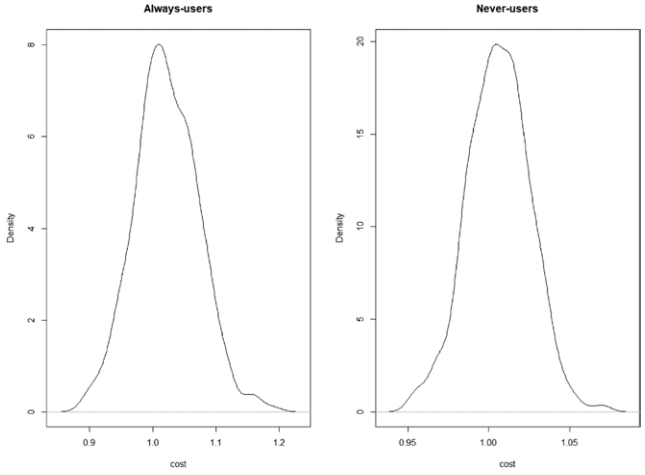


Figure 1. Annual health costs in thousand dollars

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AB1584 CONSENSUS RECOMMENDATIONS ON THE USE OF BIOSIMILARS IN THE TREATMENT OF INFLAMMATORY RHEUMATIC JOINT DISEASES

Keywords: Systematic review, bDMARD, Best practices

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Background: Biosimilars are highly similar to reference products and can help in reducing the financial burden and medication underutilization while still being comparable to reference products in treating rheumatic diseases[1].

Objectives: The objective was to develop evidence-based consensus recommendations and overarching principles aimed at standardizing best practices for the use of biosimilars in treating patients with inflammatory rheumatic joint diseases in the Gulf region.

Methods: A taskforce comprising expert rheumatologists and healthcare economists formulated specific PICO questions on key topics concerning biosimilars: comparability of efficacy, safety and immunogenicity of biosimilars to reference products; extrapolation of indications for biosimilars; switching from reference products to biosimilars or between biosimilars; cost-savings; retention rates; nocebo effect among patients, and general awareness and perceptions of biosimilars in the Gulf region. A systematic literature review was conducted to identify, select, and critically appraise the quality of published evidence that demonstrated the value proposition of biosimilars in rheumatic diseases. Meta-analyses, clinical trials, and systematic reviews of adult patients treated with biosimilars for

rheumatoid arthritis, psoriatic arthritis, spondyloarthritis, and ankylosing spondylitis were included. As the data before 2017 has been previously reviewed in another publication,1 the current review focused on data published between January 2017 and August 2022 (PROSPERO ID CRD42022364002). Consensus on each statement required a level of agreement of 70% or greater. Another group of external stakeholders comprising rheumatologists, nurses, pharmacists, payers, regulators, and patients provided external validation of the statements.

Results: Consensus was reached for all the five overarching principles and eight recommendations by both the taskforce and the external stakeholders. The recommendations are largely congruent with previously published guidelines, with adaptation for regional clinical practice considering the nuances of the healthcare systems within the Gulf region. The overarching principles emphasize the importance of improving the awareness, understanding, and perceptions of biosimilars among rheumatologists, patients, and other stakeholders. They also highlight the need for collaborative efforts to gather regional real-world data and to make affordable biosimilars a viable treatment option for all patients. The consensus recommendations advocate the need for shared treatment decisions between rheumatologists and patients when considering a switch to, or between, approved biosimilars. They further recommend that confirmation of a biosimilar's efficacy and safety in a single indication is sufficient for extrapolation to other diseases for which the reference product has been approved. Finally, they highlight the need for regulated national and regional pharmacovigilance, post-marketing surveillance, and health policies governing the adoption and prescription of biosimilars in clinical practice across the Gulf region.

Conclusion: The outcomes of this initiative represent the second international and the first regional consensus recommendations for the Gulf region based on a systematic literature review, integrating clinical evidence with clinical expertise to optimize decision-making for the use of biosimilars in patients with rheumatic diseases. While the overarching principles and consensus recommendations were developed specifically for the Gulf region, they were formulated based on predominantly international data due to the lack of robust regional data. Therefore, we suggest that these statements can be generalized to serve as recommendations for healthcare providers also in other parts of the world.

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AB1585

ASSOCIATION BETWEEN NECK CIRCUMFERENCE AND ASYMPTOMATIC HYPERURICEMIA IN NEARLY HEALTHY ADULTS

Keywords: Diagnostic tests, Gout, Comorbidities

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Background: Central obesity, a key component of metabolic syndrome, notably impacts serum uric acid levels. In previous studies, several obesity indicators (e.g., body mass index, waist circumference, and waist-to-height ratio) have been investigated as potential predictors of hyperuricemia. Meanwhile, neck circumference (NC) measurement has been recently developed as a simple and time-saving anthropometric method for predicting cardiovascular risk. Only a few studies have evaluated the relationship between hyperuricemia and NC; however, their populations have consisted only of female individuals or specific populations, or included patients with overt gout.

Objectives: This study aimed to determine the relationship of asymptomatic hyperuricemia with NC, innovative and simple anthropometric method, in the general population.

Methods: This cross-sectional study used data from the 2019–2020 Korea National Health and Nutrition Examination Survey. Among 15,469 individuals, we excluded 6,814 without available data on NC or serum uric acid, and 1,026 with critical confounders: overt cardiovascular disease; gout; chronic kidney disease; and serum creatinine > 1.2 mg/dL. Multivariate logistic regression analysis was used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) for hyperuricemia according to quartiles of NC.

Results: A total of 7,629 subjects including 6,814 with normouricemia and 815 with hyperuricemia were included. The mean age was fifty nine years in both groups. 56.1% of the hyperuricemia group and 38.7% of normouricemic group were male (p<0.001). The percentage of low income was higher in hyperuricemic than normouricemic group (50.6% vs 46.5%, P=0.027). Co-morbidities including obesity (53.0% vs. 34.8%; P<0.001) and hypertension (37.4% vs. 29.8%; P<0.001), and health-related habits including current smoking (18.8% vs. 14.7%; P=0.002) and frequent drinking (37.0% vs. 22.2%; P<0.001) were higher in hyperuricemic group than normouricemic group. The subjects with hyperuricemia displayed greater NC than normouricemia (36.5 ± 3.3 cm vs. 34.7 ± 3.3 cm; P<0.001). Multivariable regression analysis revealed that NC was significantly associated with hyperuricemia in women (OR 1.17; 95% CI 1.06-1.30), but not in men (OR 1.04; 95% CI 0.96-1.12) (Table 1).

Conclusion: NC was positively correlated with serum uric acid levels and this association was significant in women. Our finding suggests that NC can contribute to detecting asymptomatic hyperuricemia earlier and further to determining risk of metabolic syndrome in healthy adults.

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Table 1. Factors associated with hyperuricemia

	Men		Women	
	aOR† (95% CI)	*P*-value	aOR†	*P*-value
Age, per 1-year increase	0.97 (0.96–0.99)	<0.001	1.03 (1.01–1.04)	0.001
Low income‡	1.26 (0.99–1.59)	0.057	1.30 (0.97–1.74)	0.081
BMI, per 1-kg/m^2 increase	1.09 (1.03–1.15)	0.003	1.06 (1.01–1.13)	0.033
Hypertension	1.00 (0.77–1.31)	0.993	1.37 (1.00–1.89)	0.051
Type 2 diabetes	0.53 (0.36–0.78)	0.001	0.69 (0.44–1.08)	0.105
Current smoking	0.76 (0.60–0.97)	0.027	1.26 (0.70–2.29)	0.443
Frequent drinking§	1.75 (1.41–2.18)	<0.001	1.81 (1.24–2.64)	0.002
Regular aerobic exercise¶	0.96 (0.77–1.19)	0.691	1.00 (0.75–1.32)	0.974
NC, per 1-cm increase	1.04 (0.96–1.12)	0.314	1.17 (1.06–1.30)	0.002

†From the multivariable logistic regression models adjusted for all variables; ‡Less than median household income; §More than twice per week; ¶Defined as ≥2.5 hours/week of moderate-intensity activities, ≥1.25 hours/week of high-intensity activities, or a combination of both. aOR, adjusted odds ratio; CI, confidence interval; BMI, body mass index; NC, neck circumference.

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Disclosure of Interests: None Declared.

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AB1586

THE RHEUMATOLOGY WORKFORCE IN THE ARAB COUNTRIES: WHAT IS THE CURRENT STATUS AND WHAT ARE THE PROJECTED UNMET NEEDS?

Keywords: Health services research, Telemedicine

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Background: The demand for rheumatology care is consistently exceeding the workforce worldwide, which negatively impacts the care of patients with rheumatic and musculoskeletal diseases (RMDs). The number of rheumatologists per 100,000 inhabitants varies between 0.94 in Latin America to 3.44 in Spain, with a desirable number of 1-2. However, the estimation of the current and projected rheumatology workforce is lacking in Arab countries.
Objectives: To investigate the current number of practicing rheumatologists in the ArLAR countries, provide an estimate of the expected number of rheumatologists in 10 years, and evaluate the current workload, practice profile, and waiting time for a consultation.
Methods: This cross-sectional survey study was conducted by the Arab League of Associations for Rheumatology (ArLAR) Research Group (ARCH) in 16 ArLAR countries in two parts. The first survey was addressed to national societies by e-mail to estimate the current and projected workforce. The second was an anonymous e-survey addressed to all Arab rheumatologists and rheumatology fellows elaborated by the study steering committee on the Google Forms platform and distributed using social media, WhatsApp, and mass e-mails to evaluate their practice profile, workload, and waiting time for a rheumatology consultation.
Results: The mean number of rheumatologists in the ArLAR countries was 0.84 per 100,000 inhabitants (mean age 47.5 years, 55% females), ranging from 0.06 in Sudan to 1.86 in Tunisia (Table 1). The crude number of rheumatologists is expected to increase by 50% in 2032, whereas a 20% parallel increase in the population is also expected, associated with a rise in demand due to an expected increase in RMDs; thus, the percentage per 100,000 inhabitants will increase only by 22%. Data from 446 rheumatologists and rheumatology fellows (mean age 43.9 years, 60.5% females) revealed that 72% worked full-time, 53% were employed in the public sector only, and 75% worked in an urban setting. The median income was 1,000-2,000 USD/ month. There was a certified rheumatology nurse in 25%, access to musculoskeletal ultrasound in 51%, and telemedicine implemented in 29% of practices. The average waiting time for a rheumatology consultation was 19.9 days and was associated with the region, working full-time, working in the public sector, higher income, and the presence of an infusion center at the rheumatology practice.
Conclusion: Considering a desirable arbitrary level of 1-2 rheumatologists/ 100,000 inhabitants, there is a current shortage of rheumatologists in the ArLAR countries, with significant heterogeneity among countries. The projected increase in rheumatologists will probably not match the rising demand for rheumatology care. Considering local demographic disparities and healthcare system differences, national authorities are urged to implement effective intervention plans to optimize the rheumatology workforce.

Table 1. Rheumatology workforce in the Arab Countries in 2022, by country.

Region	Country	Country Population	Rheumatologists/ 100,000 inhabitants	Rheumatologists/ 1,000 physicians
Africa	Tunisia	11,820,000	**1.86**	14.3
	Egypt	102,300,000	**1.17**	2.7
	Algeria	43,850,000	**1.15**	1.2
	Morocco	36,910,000	**1.03**	14.7
	Libya	6,871,000	**0.26**	1.2
	Sudan	43,850,000	**0.06**	2.2
Levant	Lebanon	6,800,000	**0.82**	3.4
	Iraq	40,220,000	**0.61**	6.3
	Syria	17,500,000	**0.38**	1.1
	Jordan	10,200,000	**0.36**	1.3
	Palestine	4,803,000	**0.23**	1.6
Gulf	UAE	9,890,000	**1.05**	10.4
	Kuwait	4,271,000	**0.94**	36.4
	Qatar	2,881,000	**0.94**	3.7
	Saudi Arabia	34,810,000	**0.75**	26.1
	Oman	5,107,000	**0.59**	3.1
Total		**382,083,000**	**0.84**	**2.9**

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AB1587

EXPERIENCE IN REAL-WORLD CONDITIONS OF THE EFFECTIVENESS OF THE VACCINE AGAINST HERPES ZOSTER

Keywords: Targeted synthetic drugs, Infection-related RMDs

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Background: Herpes zoster infection is due to the reactivation of the varicella-zoster virus (VZV), having a high prevalence in elderly and immunocompromised patients. Since the beginning of 2022, a new vaccine that prevents herpes zoster virus reactivation has been approved and commercialized. However, there are few studies analyzing its effectiveness in real-world conditions.
Objectives: To analyze the incidence and rate of herpes zoster disease in a population at risk due to suffering from rheumatic diseases and therefore being subsidiary of receiving VZV vaccination.
Methods: A retrospective observational study of patients who started treatment with JAK inhibitors from 2013 to 2022 was performed. Demographic and clinical variables were collected from the electronic clinical history. Vaccination of patients against VZV was analyzed, as well as the incidence of herpes simplex (HSV) and herpes zoster reactivation before and after January 2022, date on which the vaccination program began. In addition, the rate of the VZV disease was calculated based on the follow-up time for both vaccinated and unvaccinated patients and was adjusted by exposure in events/100 patients-year (E/100 PY).
Results: 236 patients with an indication for vaccination against VZV due to being treated with JAK inhibitors were included, of whom the majority diagnosis was Rheumatoid Arthritis (n=179). Their characteristics are shown in the following Table 1. 30 patients were vaccinated against VZV (12.71%). An incidence of 20 herpes cases was observed in unvaccinated patients (8 HSV and 12 VZV). 3 of the VZV reactivations were of multimetameric involvement. No cases of herpes were found in the vaccinated population. The unvaccinated patients were followed up for 3500 months, remaining with a herpes rate in this population of 4.12 E/100 PY. The total follow-up of vaccinated patients was 102 months, with a herpes rate of 0 E/100 PY.

Table 1.

	Total of patients n=236
Age - years (sd)	62.45 (8.2)
Female sex - n (%)	188 (79.66%)
Diagnosis - n (%)	179 (75.84%)
RA	28 (11.86%)
PsA	14 (5.93%)
AS	10 (4.23%)
Others	5 (2.11%)
JIA	
Comorbidities - n (%)	69 (29.23%)
Dyslipidemia	65 (27.54%)
Arterial hypertension	40 (16.95)
Smoking	22 (9.32%)
Mellitus diabetes	
Vaccination	206 (87.29%)
No	30 (12.71%)
Yes	

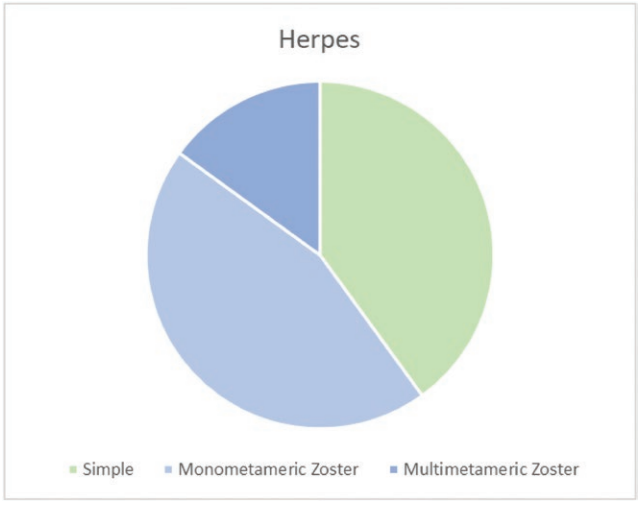


Figure 1.

Conclusion: An incidence of 12 VZV is observed in unvaccinated patients compared to an incidence of 0 in vaccinated patients. The herpes rate in non-vaccinated patients was 4.12 E/100 PY compared to 0 E/100 PY in vaccinated patients. Therefore, we conclude that the herpes zoster vaccine shows its effectiveness in our population but it would be necessary to carry out more studies in the future with a longer follow-up time.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1588 REFERRAL PATTERN FROM PRIMARY CARE TO IDENTIFY PATIENTS WITH SUSPECTED RHEUMATOID ARTHRITIS: ROOM FOR IMPROVEMENT

Keywords: Rheumatoid arthritis, Quality of care

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Background: Primary care physicians (PCPs) acknowledge the importance of early diagnosis and intensive treatment for rheumatoid arthritis (RA) patients, however the non-specific symptoms early in the disease and the long waiting list to access rheumatology clinics result in a challenge for early and adequate referral.

Objectives: To evaluate patterns for referral in an early arthritis clinic with direct access for PCPs and to explore variables that may influence an adequate referral.

Methods: An early arthritis clinic (EAC) with direct access for PCPs in our area was started in January 2022 providing direct access for patients with suspected RA or undifferentiated arthritis. Referral criteria are strictly clinical, based on previous early arthritis clinics, literature review and approved by a PCP committee. Patients can be referred if > 2 swollen joints, duration of symptoms <2 years and no previous diagnosis by a rheumatologist explaining the symptoms. A total of 180 PCPs from 11 primary care centres have direct access to the EAC. The following data was collected: distance between hospital and primary care center, number of PCP per center, and zip codes as a surrogate for patient income. A descriptive analysis of the referral pattern is presented. A multivariate logistic regression model was performed to identify variables associated with an appropriate referral.

Results: From January to October 2022, 140 patients were referred to the EAC, 66.4% female, with a mean age of 54.2 (15.3) years. A total of 38 (27%) patients fulfilled the predefined referral criteria with initial diagnosis of rheumatoid arthritis (15.8%), psoriatic arthritis (7.9%) and undifferentiated arthritis (76.3%). Patients who did not meet the referral criteria were mainly patients with osteoarthritis (36.7%), non-specific arthralgia (15.7%), gout (8.8%) and fibromyalgia (6.9%). Patients in the adequate referral group were younger (50.4 vs 55.6, p= 0.03), but have similar income and were referred from a PCP centre with similar characteristics in term of size and distance from the EAC. In the multivariate logistic regression model age was the only significant explanatory variable for an adequate referral (Table 1).

Table 1. Logistic regression model to identify variables associated with adequate referral.

	Bivariate analysis OR (95% CI)	Multivariate analysis OR (95% CI)
Age, years	0.96 (0.94 - 0.98)	0.97 (0.94 - 0.99)*
Women	0.82 (0.38 - 1.79)	0.59 (0.26 - 1.38)
Patient income	1.13 (0.73 - 1.76)	1.10 (0.67 - 1.82)
Distance to EAC in km	0.96 (0.79 - 1.16)	1.00 (0.80 - 1.25)
Number of PCPs per centre	0.96 (0.60 - 1.51)	—

*OR odds ratio, 95% CI 95% confidence interval.*Statistically significant results at the 0.05 level*

Conclusion: Only 27% of patients referred to the EAC were adequately referred. PCPs need to enhance clinical skill to detect early RA and discriminate mainly from osteoarthritis and non-specific arthralgias. Younger age was the only variable associated with adequate referral. Strategies with a special focus on PCPs are necessary to promote an early and adequate referral.

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AB1589 ESSENTIAL TREATMENT OF RHEUMATOID ARTHRITIS IN ZANZIBAR: A COST EFFECTIVENESS ANALYSIS

Keywords: Quality of life, Disease-modifying drugs (DMARDs), Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) is a major global health problem and a neglected disease in many developing countries. Health care spending is low in these countries and RA services compete with other important life-saving and effective interventions. Effective therapies for RA are now available which improve overall outcomes and prevent disability especially when initiated early and managed aggressively [1]. All these interventions are available in high-income countries but are sparse in developing countries. There are several health economic evaluations of RA treatment from high-income settings, but few are available or relevant for developing countries. More evidence is therefore needed on the benefits and costs of scaling-up RA services in resource constrained settings.

Objectives: To conduct a cost effectiveness analysis of multiple interventions in the management of RA in Zanzibar.

Methods: A cost-effectiveness analysis for a ten-year duration was conducted from a health provider perspective using a Markov model. Interventions were based on a treat to target strategy with add on therapy or switch to biologic therapy when patients did not reach target (remission or low disease activity). The model compares the efficiency of 'methotrexate monotherapy'(option1), 'methotrexate + sulfasalazine + hydroxychloroquine (triple therapy)' (option 2), methotrexate then biologic 1' (option 2b), 'option 2 then biologic 1' (option 3), 'option 3 then biologic 2' (option 4) and 'option 2b then biologic 2' (option 4b). Data on effectiveness of interventions was obtained from literature. Incremental cost-effectiveness ratios (ICERS) were calculated per quality adjusted life year (QALY) gained from treatment. Staff, building, and utility costs were obtained from the hospital administration records. Drug costs were obtained from the government supplier price list, retail pharmacies and pharmaceutical companies. Mean utility values were calculated from a Zanzibar RA- cohort based on the EuroQol-5D questionnaire responses. Willingness to pay threshold (WTP) was set at 568 USD which is two-thirds of GDP/capita for Tanzania for 2021. We conducted a base case analysis with deterministic sensitivity analysis to explore outcomes with changes in key parameters.

Results: Total costs for the treatment options were largely driven by drugs, predominantly the biologics. The lowest cost was for methotrexate therapy (option 1) at USD 1984/patient/10 years and the highest utilities were gained from treatment with methotrexate therapy + two consecutive bDMARDs (option 4b) (Table 1). Changes in drug costs resulted in significant changes in the ICERs. With variations in the WTP threshold, option 1 remained the most CE to just above USD 2500 where option 2b became the more CE option up to USD 3100 and option 3 became the more CE option. All other options were not considered CE up to 3500 USD.

Conclusion: Methotrexate was found to be the only cost-effective treatment option in our population. Other options although available may be too costly to consider feasible for clinical use unless prices drop. This may be possible via wider availability of biosimilars or via government drug price negotiation to acquire drugs at cheaper costs.

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Table 1. Ten-year costs (mean USD per treated patient), effects (mean QALY gained per patient) cost effectiveness and net-monetary benefit of six treatment scenarios for rheumatoid arthritis.

Strategy	Cost (USD)	QALYs gained	ICER (USD/ QALY)	Net Monetary benefit (USD)
Methotrexate alone (option 1)	1984	5.7	397	1273
Triple therapy (option 2)	3051	6.1	Dominated	763
Methotrexate then 1 biologic (option 2b)	2647	6	2460	406
Triple therapy then 1 biologic (option 3)	3696	6.4	2995	-88
Triple therapy then 2 consecutive biologics (option 4)	19243	6.6	61378	-15490
Methotrexate then 2 consecutive biologics (option 4b)	34509	6.8	63175	-30619

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Disclosure of Interests: None Declared.
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AB1590

RECOMMENDATIONS ON HANDLING MEDICINE SHORTAGE: LEARNING FROM HYDROXYCHLOROQUINE 2020 CRISIS FOR SLE PATIENTS

Keywords: Patient reported outcomes, Systemic lupus erythematosus, COVID

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Background: Early 2020, short supply of hydroxychloroquine sulfate (HCQ) – then claimed as effective for treatment of COVID-19 in several countries - raised significant concerns for those who use HCQ for chronic diseases including SLE. In April 2020, Lupus Europe launched a survey to quantify the access gap, as well as the anxiety expressed by patients confronted with this outage. 2422 patients responded with an average level of anxiety about access to HcQ of 6.45 on a maximum of 10. After supply issues were resolved, a follow up survey (Aug-Sept 2020 – 1854 answers) showed a significantly reduced anxiety of 4.15. A second follow up survey (Nov 2021 -Feb 2022 - 2255 answers) showed a further reduction to 3.54. Importantly, a core group of 6.2-13.7% of patients remains extremely anxious (scoring 9 or 10) about supply of their medication, substantially more than in Portugal (3.5%) and Finland (0%), where supply remained fair at the heat of the crisis.
Objectives: To provide consensus on how communication should be conducted to minimize the impact of medicine shortages on patient anxiety.
Methods: The Patient Advisory Network (PAN) of Lupus Europe established an extensive list of potential elements of a more effective communication on shortages, that could help reduce patient anxiety. 20 statements were derived from those elements and proposed to PAN members and Lupus Europe member organisations. 101 answers were collected from 17 countries. For each country, the individual ratings of all participants were averaged to assign an individual vote for each country on each statement. Consensus amongst the 17 countries was then considered as obtained if 14 or more of the 17 countries agreed or strongly agreed with statements.
Results: 9 out of the 20 statements reached consensus:
1. Lupus specialists should (a) clarify alternative medication existing and its difference versus current treatments, (b) clarify appropriate emergency procedures and (c) clarify to the patients how to handle a short supply.
2. Specialists and Hospitals should establish alternative supply mechanisms to guarantee minimum availability.
3. pharmaceutical industry should (a) provide all information to all stakeholders and (b) help create emergency supply routes to ensure that no patient is left without his/her medication for a sustained period of time.
4. National authorities should help patients with demonstrated need have priority access to limited supply quantities through a simple process.
5. Hospitals should communicate (by email or postal mail) information on the shortage, how to handle it and how to access emergency supply routes. The same number agreed with Health authorities performing that same communication.
6. pharmaceutical industry should avoid diverting products from one country to another if that would reduce supply below normal consumption level.
7. Patient organisations should stop the rumors that can quickly spread though social media.
8. pharmacists should be better equipped in terms of data (on the reasons and clear timelines for resolution as well as alternatives or recommendations for patients facing shortages)
9. *GP's should clarify alternative medication and appropriate emergency procedures.*
Conclusion: Shortages of medicine create an anxiety that can be long lasting. Even when supply is re-established, the fear remains. For this reason, establishing an effective communication system is necessary to reassure patients when short term shortages are taking place, and is key to avoid fast spreading anxiety relating to this concern. In this process, patient associations, physicians, industries and all the stakeholders should be involved.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1591

POLICY DRIVERS FOR MARKET PENETRATION OF ANTI-TNF BIOSIMILARS: MULTI-COUNTRY COMPARISONS

Keywords: bDMARD, Health services research, Disease-modifying drugs (DMARDs)

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Background: Health systems across countries have used different policy measures (e.g. price discounts, tendering, mandating switches) to encourage the introduction of biosimilars but their differential impact on market penetration is unknown.
Objectives: To evaluate the impact of policy measures on market penetration of anti-TNF biosimilars.
Methods: Quarterly IQVIA MIDAS sales data from 2012-2021 for infliximab, etanercept and adalimumab in 5 countries (Canada, France, Germany, Italy and the United Kingdom (UK)) that used different policy tools were used. Biosimilar market penetration was measured by dividing the number of defined daily dose units (DDDs) of biosimilars sold by the total number of DDDs of the originator and biosimilars sold. Market penetration since the first sale date of the biosimilars was captured by product, setting (hospital vs. retail), and country. Policy impact was examined by comparing market penetration among different policy scenarios (Table 1).
Results: Biosimilars for all three anti-TNFs had higher volume share over time (Figure 1) in the UK than Germany, suggesting that higher prescribing quotas among new and existing patients increases the market penetration of biosimilars given comparable demand-side policies. Since some anti-TNFs are dispensed only in hospitals in some countries, the settings are somewhat different. In France, infliximab biosimilars in hospital setting had faster penetration than other anti-TNF biosimilars in retail setting, indicating that tendering works better than price-links to increase biosimilar uptake. However, infliximab biosimilars in France had slower penetration than in Italy despite the higher discount price-link but absent quotas in France. Similarly, biosimilars had higher volume share over time in UK than Italy, which also suggests that higher prescribing quotas have a greater impact than price-links. Without price-link and tendering measures, Canada had the slowest penetration. By the end of our study period, the limited rollout of mandatory switching policies (3/10 provinces) for existing patients may not be sufficient in fostering market penetration, despite widespread implementation of mandatory prescribing for new patients.
Conclusion: Through comparisons between and within countries, we found that higher prescribing quotas or switching for existing patients and tendering are the key policy drivers for market penetration of anti-TNF biosimilars.
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Table 1. Policy measures in study countries as of 2020 unless noted

	Canada	France	Germany	Italy	The UK
Supply Side					
Price-link	No	–40%[1]	No[1]	–20%[1]	No[1]
Tendering	No	Mainly hospital level for inpatient sector[1]	Hospital level for inpatient sector; sickness funds for outpatient sector[1]	Regional level for inpatient sector[1]	Centralized by NHS for inpatient sector[1]
Demand Side					
Biosimilar prescribing for new patients	Mandatory[2]	No[1]	Quotas varied by sickness funds [1]	Quotas but varied[1]	90% (2017/18)[3]
Biosimilar prescribing or switching for existing patients	Mandatory switching; varied by provinces[2]	Encouraged; no quotas or targets[1]	Encouraged; quotas varied by sickness funds [1]	Encouraged; quotas but varied[1]	80% (2017/18)[3]

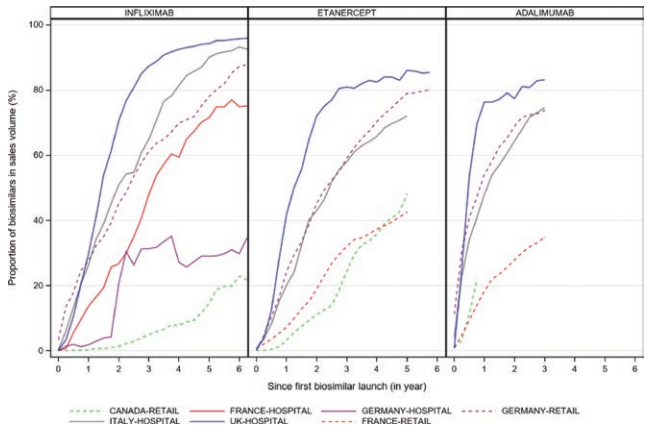


Figure 1. Biosimilar market penetration since first launch

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AB1592 WORK-RELATED IMPACT IN YOUNG PATIENTS WITH CHRONIC BACK PAIN AWAITING A MAGNETIC RESONANCE IMAGING

Keywords: Work-related issues, Health services research

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Background: Chronic back pain (CBP) is one of the major causes for medical consultation among young people. Given the limited sources, it is relevant knowing the characteristics associated with a higher burden in order to prioritize the performance of imaging exams.

Objectives: To identify factors associated with sick leave in a cohort of young patients with CBP awaiting an MRI of the spine.

Methods: The project "Strategy for a Hospital Early Referral in Patients with Axial Spondyloarthritis" (SHERPAS) is a prospective ongoing study recruiting young patients (18 to 40 years) with CBP that are requested an MRI of the spine by other specialists different than rheumatologists in a tertiary hospital. The study period started in September 2021, and the dataset for this interim analysis was locked in October 2022. Patients completed a questionnaire concerning work status, including sick leave due to CBP (at-visit or prior to this). Besides, socio-demographic and clinical characteristics were collected. Patient-reported outcomes (PROs) for fatigue, Patient Global Assessment (PGA), physical function (Bath Ankylosing Spondylitis Functional Index -BASFI), and overall health (Assessment of Spondyloarthritis international Society Health Index -ASAS HI) were also evaluated. A logistic regression analysis was performed to evaluate the association of patients' characteristics with sick leave.

Results: Of 152 recruited patients, 123 (80.9%) were actively employed, 22 (14.5%) were unemployed and 7 (4.6%) were students. Among the employed patients (52.8% female; mean age 33.8(4.8) years; 57.0 (54.0) months CBP duration), 65 (52.8%) patients had been on sick leave at some point (50 prior to visit and 15 at the study visit). Baseline characteristics are shown in **Table 1**. Night pain was more frequent in patients on sick leave (56.9 % vs 36.2%, p=0.02), and PROs on fatigue, PGA, physical function and overall health and functioning showed worse results in these patients, as compared to patients who had never been in sick leave. Additionally, patients on sick leave had more frequently pharmacological treatment. After multivariable analysis, being male (OR 2.3, 95%CI 1.0-5.6), having night pain (OR=2.4, 95%CI 1.0-5.8) and reporting higher PGA (OR=1.1, 95%CI 1.0-1.4) were associated independently with being on sick leave.

Conclusion: One out of two young patients with CBP awaiting an MRI of the spine are on sick leave at some point. These patients have poorer quality of life and use more pharmacological treatment than active patients with CBP. Male sex and night pain are associated with being on sick leave due to CBP and therefore could be used to prioritize the use of spinal MRI aiming to optimize health resources.

Table 1. Characteristics of employed patients by work status

		Total employed n=123	No sick leave n=58	Ever sick leave n=65	p-value
Demographics	Age	33.8 (4.8)	33.6 (5)	34.1 (4.8)	0.6
	Symptoms (months)	57.0 (54.0)	54.8 (54.1)	59.0 (54.3)	0.7
	BMI	25.4 (4)	25.4 (4.2)	25.4 (3.7)	0.9
	Female	65 (52.8)	33 (56.9)	32 (49.2)	0.5
	Education	66 (52.8)	27 (46.5)	38 (58.4)	0.2
	Primary/secondary	56 (45.5)	30 (51.7)	26 (40.0)	
	University				
	Type of work	33 (26.8)	19 (32.8)	14 (21.5)	0.5
	Sendentary/ not active	76 (61.8)	38 (65.5)	38 (58.5)	
	Physically active				
Characteristics of back pain	Buttock pain	42 (34.2)	17 (29.3)	25 (38.4)	0.4
	Night pain	58 (47.1)	21 (36.2)	37 (56.9)	0.02
	Inflammatory pain	29 (23.6)	14 (24.1)	15 (23.1)	1
	Flares of back pain	87 (70.7)	42 (72.4)	45 (69.2)	0.8
	Sudden onset	72 (58.5)	29 (50.0)	43 (66.1)	0.1
	Morning stiffness	76 (61.8)	32 (55.1)	44 (67.7)	0.2
PROs	Fatigue (0-10)	4.9 (3)	4 (3.1)	5.7 (2.7)	0.002
	PGA (0-10)	4.7 (2.9)	3.7 (2.9)	5.7 (2.6)	<0.001
	Physical function (BASFI)	3.2 (2.6)	2.4 (2.3)	4 (2.6)	<0.001
	Overall health (ASAS-HI)	6.7 (3.8)	5.6 (3.6)	7.8 (3.8)	0.002
Treatments	NSAIDs	109 (88.6)	52 (89.6)	57 (87.7)	0.2
	Muscular relaxants	88 (71.5)	33 (56.9)	55 (84.6)	<0.001
	Opioids	45 (36.6)	11 (18.9)	34 (52.3)	<0.001
	Antidepresants	19 (15.5)	4 (6.9)	15 (23.1)	0.01

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AB1593 SEVERE IMPACT OF THE ECONOMIC CRISIS ON TREATMENT PERSISTENCE IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES: A MULTICENTRIC CROSS-SECTIONAL STUDY IN LEBANON

Keywords: Disease-modifying drugs (DMARDs), Descriptive studies, bDMARD

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Background: Due to Lebanon's unprecedented economic crisis, access to healthcare and chronic treatments is compromised, which might affect chronic disease control.
Objectives: The primary objective of this study was to evaluate the impact of the economic crisis on chronic treatment persistence in patients with rheumatic and musculoskeletal diseases (RMDs) in Lebanon and to estimate the predictors of persistence.
Methods: A cross-sectional multicentric national study was conducted between July and October 2022 on patients with RMDs living across Lebanon (patients with chronic inflammatory rheumatic diseases (CIRDs) and controls with non-inflammatory RMDs). A questionnaire hosted on the Google Forms platform was proposed to consecutive patients during the consultation and disseminated on social media and WhatsApp lists. It included sociodemographic, disease, and treatment data, income, PHQ-9, and GAD-7 questionnaires. Treatments were categorized into corticosteroids, NSAIDs, cs-DMARDs, b-DMARDs (IV and SC), ts-DMARDs, and oral immunosuppressants. Persistence was defined quantitatively as the number of tablets or injections taken during the past month compared to prescribed and qualitatively as the percentage of patients who changed or discontinued chronic RMD treatment due to cost or nonavailability. Data were presented descriptively; factors associated with persistence were identified using multivariable linear regression.
Results: In total, 317 patients with RMDs (286 CIRDs and 31 controls) were included (207 by telephone interview and 110 by self-questionnaires); mean age 49.5 years (SD 16), 68% females, median disease duration 10 years (IQR 6-20), 58% had moderate to severe depression, and 40% had moderate to severe anxiety. Persistence was low for b-DMARDs (SC 55%, IV 63%) and ts-DMARDs (36%) and acceptable for oral immunosuppressants 85.3% and cs-DMARDs (88%) (Figure 1). Among patients with CIRDs, 55.8% discontinued or changed their chronic medication due to nonavailability (45.3%) or increased cost (21.2%). Discontinuation or change affected mainly SC b-DMARDs (66.2%), ts-DMARDs (60.0%), and IV b-DMARDs (40.0%). Notably, patients reported a decrease in their financial level in 86% of the cases, and 58% reported they were currently living in a low economic level (compared to only 6% before the crisis). Compared to controls, patients with CIRDs had a reduction in the number of visits to the doctor, more difficulty accessing chronic treatments (91% vs. 33%), and paraclinical exams (84% vs. 77%). They expressed a higher need for financial support for medication, paraclinical tests, and medical consultation. Importantly, patients could find an alternative source for getting their medication in 60% of cases (buying from abroad in 36%, depending on friends or families living abroad in 20%, and charities in 10%). Finding an alternative source for medication was independently associated with a higher persistence of cs-DMARDs, b-DMARDs, and ts-DMARDs. In addition, being unemployed and having a low financial level were associated with a low persistence of cs-DMARDs and oral immunosuppressants.
Conclusion: Chronic treatment persistence was significantly compromised for essential drugs for patients with RMDs and was rather associated with extrinsic causes related to treatment availability and cost than with classically known intrinsic factors.

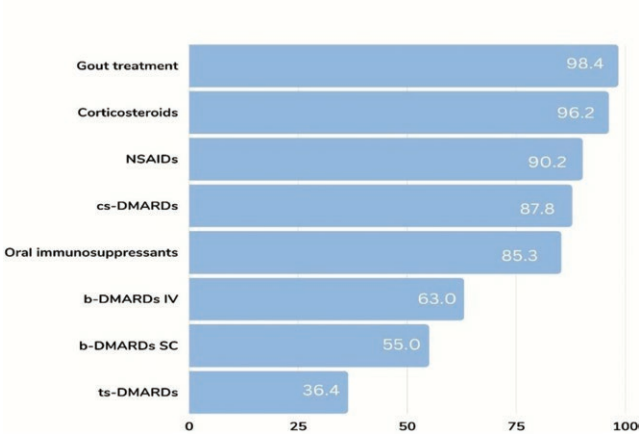


Figure 1. Chronic medication persistence in patients with chronic inflammatory rheumatic diseases

REFERENCES: NIL.
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AB1595

HOW DO WE PREVENT THE DEVELOPMENT OF MULTIMORBIDITY IN PEOPLE WITH INFLAMMATORY RHEUMATOLOGICAL DISORDERS: A QUALITATIVE INVESTIGATION

Keywords: Health services research, Qualitative research methods, Comorbidities

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Background: People with inflammatory rheumatological disorders (IRDs) are at high risk of developing multimorbidity, specifically cardiovascular disease (CVD) and mood problems. UK guidelines advocate annual reviews for people with Rheumatoid Arthritis (RA), although not other IRDs. Current healthcare reviews are often condition specific, focus on existing morbidities rather than identifying risk and preventing future illness, and may not include advice and support to change lifestyle behaviours. Before developing a healthcare review to prevent multimorbidity we sought to explore perspectives on existing healthcare reviews.
Objectives: To explore patients and healthcare professional (HCP) perspectives on healthcare reviews for people with IRDs at risk of multimorbidity.
Methods: People with IRDs were invited to take part in individual semi-structured interviews either by telephone or online platform. HCP perspectives (including primary and secondary care clinicians) were explored in online focus groups. These were transcribed verbatim. Inductive thematic analysis was undertaken (LG/LB). Data and codes were discussed, and key themes generated within the team. Ethical approval was obtained (REC Reference 22/PR/0162).
Results: 15 patients (7 male, 8 female, age 49-75) were interviewed. 3 focus groups were held with a total of 13 HCPs. Four themes were identified: content of a future review, preparing for the review, delivering a holistic review and outcomes. People with IRDs struggled to conceptualize a review which included risk of development of future conditions and wanted the review to focus on their IRD (e.g. joint assessment). People felt that current reviews felt like a 'tick-box' exercise. HCPs reported wanting to conduct a holistic review, highlighting challenges aligning patient and HCP agenda. People with IRDs also demonstrated variable attitudes to considering their risk of future conditions, ranging from whether they wanted all, some or no knowledge of their risk for other conditions influenced by whether these could be prevented. Preparation, such as written information or pre-review questionnaires were considered important to help people understand the review aims, align agendas and for the HCP to understand the patient history and context. Participants recognized the challenge of ensuring such materials consider underserved patient groups such as people with limited health literacy who may face difficulties accessing preparation materials. People with IRDs were flexible in considering whether a review should occur in primary or secondary care, whereas HCPs perceived primary care was best placed to provide a holistic approach although both groups agreed practitioner skills and expertise were more important than location. It was considered important to have outcomes from a review (including any actions to be taken by patient or HCP) clearly understood for a review to be perceived as beneficial.
Conclusion: People with IRDs are at high risk of multimorbidity and may benefit from healthcare reviews to address future risks. Such reviews need to be person-centered addressing both patient and HCP agendas to maximise utility and perceived value. Further research is needed to address how such reviews can be effectively implemented into routine care.
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Disclosure of Interests: None Declared.
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AB1596

REAL-LIFE STUDY OF IMMUNOGENECITY AND SAFETY OF THE RECOMBINANT VACCINE AGAINST VARICELLA ZOSTER VIRUS IN PATIENTS WITH RHEUMATIC DISEASES TREATED WITH JANUS KINASE INHIBITORS

Keywords: Vaccination/immunization, Real-world evidence, Targeted synthetic drugs

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Background: Adjuvanted recombinant varicella zoster virus subunit vaccine (ARZVV) has been recently approved for preventing reactivation of latent varicella zoster virus in selected groups of patients. Patients with chronic inflammatory diseases are at major risk of this reactivation, developing herpes zoster (HZ) infection (shingles). This risk is further increased under immunosuppressive treatment with janus kinase inhibitors (JAKi). ARZVV is available in Spain since March 2021 for patients treated with JAKi, among other indications. At the present, no real-life post commercialization studies have been published in patients with rheumatic diseases and JAKi vaccinated with ARZVV.

Objectives: To assess humoral immunogenicity and safety of ARZVV in patients with rheumatic diseases treated with JAKi.
Methods: Immunogenicity and short-term safety were evaluated in a cohort of patients treated with Janus Kinase inhibitors in a descriptive prospective study. Participants received two intramuscular doses of the vaccine two months apart. Blood was sampled prior to first and 2-6 weeks after the second vaccine dose. Humoral immune response was tested through a chemiluminescence immunoassay (CLIA), using varicella zoster virus glycoprotein E (gE) as the antigen to measure anti-gE levels. The cut-off for the vaccine response assessment was considered an antibody concentration four times higher in the second measure, compared with the first one, according to the results of the clinical trial NCT01165177. The influence of the different treatments on the humoral response to the vaccine was evaluated. JAKi were separated in three groups, according to their mechanism of action: inhibition of JAK 1 (Upadacitinib and Filgotinib), inhibition of JAK 1 and JAK 2 (Baricitinib) and panJAK inhibition (Tofacitinib). Concomitant treatment influence on the humoral response to the vaccine was also determined: classic disease modifying anti-rheumatic drugs (DMARDs) and corticosteroids. The data about adverse events to the vaccination, disease flare or reactivation on HZ infection were collected.
Results: We enrolled 30 patients, 23 were woman (76,7%), with a mean age of 55±12 years. Fifteen (50%) were under treatment with upadacitinib, eleven (36,7%) with baricitnib, two (6,7%) with filgotinib and two (6,7%) with tofacitinib. Six (20%) had concomitant treatment with methotrexate and 5 (16,7%) with leflunomide. Ten (33%) had low dose prednisone. Four (13%) reported clinically HZ previously. We found that 16 patients (53,3%) reached the response assessment marked initially of quadrupling their initial antibody count. Type of JAKi did not significantly influence the humoral response, neither did the concomitant treatment with disease-modifying antirheumatic drug or low dose glucocorticoid. Fiftheen patients (50%) presented mild adverse effects; 7 (23%) of them consisted in injection-side pain, and 8 (26,7%) were systemic (myalgia, fatigue or fever). One patient (3,3%) had an ischemic cerebrovascular complication 2 weeks after the first dose. None of the patients presented a disease flare in the following 4 weeks postvaccination, neither HZ infection after 7 months of follow-up.
Conclusion: Lightly more than half of the patients (53%) with rheumatic diseases treated with JAKi reached the immune response assessment stablished. In clinical trials with non-rheumatic immunosuppressed patients, the response was ranged between 65-96%. This difference could be explained due to that it is a real-life study and in the type of disease and immunosuppression. Safety and prevention of HZ infection was high. To confirm these results higher number of patients is needed.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1597

DETERMINANTS OF TELEMEDICINE ACCEPTANCE AMONG PATIENTS WITH RHEUMATOID ARTHRITIS: SECONDARY ANALYSIS OF DATA FROM A GERMAN NATIONWIDE SURVEY

Keywords: Rheumatoid arthritis, Health services research, Telemedicine

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Background: Telemedicine (TM) is an effective tool to supplement rheumatology care and address staff shortages [1]. A previous study revealed that patients' willingness to try TM is closely connected to their rheumatic and musculoskeletal disease (RMD) [2]. Yet, it is still unclear which factors are associated with patients' willingness to try TM among specific RMD groups, such as the most prevalent rheumatic arthritis (RA).
Objectives: To identify factors that determine the willingness to try TM (TM-try) among patients diagnosed with RA.
Methods: We conducted a secondary analysis of data from a German nationwide cross-sectional survey [3] among patients with RA. Bayesian univariate logistic regression analysis was applied to the data in order to determine which factors were associated with TM-try. Predictor variables (covariates) studied individually included sociodemographic factors (e.g., age, sex) and health characteristics (e.g., health status). All the variables positively and negatively associated with TM-try in the univariate analyses were then considered for Bayesian model averaging analysis (BMA) after a selection based on the variance inflation factor (≤ 2.5) to identify determinants of TM-try.
Results: A total of 22 variables/factors (22/55, 40%) were found to be positively or negatively associated (ROPE% ≤ 5%) with TM-try among 146 RA patients. A total of 9 determinant factors were identified using BMA (Figure 1). Wishing that TM services were offered by a rheumatologist, having prior TM knowledge, living in a town and considering one's health status as okay were positively associated with TM-try. By contrast, not owning an electronic device, not having internet access at home, considering to have a bad health status and being more than 60 years old were negatively associated with TM-try.
Conclusion: Our results suggest that health status, TM knowledge, age, and access to technical equipment and infrastructure influence RA patients' motivation to use telehealth in Germany. Consequently, training programs and targeted support measures in terms of equipment and infrastructure could help ensure that all patients have equal access to telehealth.
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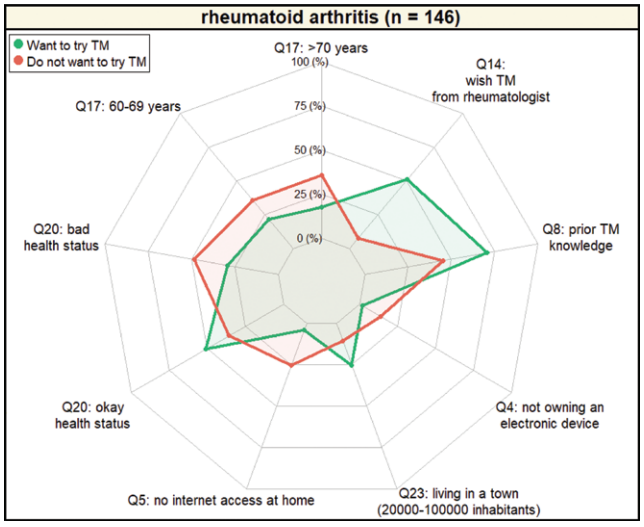


Figure 1. Determinants of TM-try in patients with rheumatoid arthritis

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Berlin Chemie, Celgene, Galapagos, Gilead, GSK, Hexal, Janssen, Medac, MSD, Mundipharma, Mylan, Novartis, Pfizer, Roche, Sanofi, SOBI, UCB, Consultant of: Abbvie, Actelion, Aescu, Amgen, Cel- gene, Hexal, Janssen, Medac, Novartis, Pfizer, Sanofi, UCB, Grant/research support from: Novartis, Abbvie, Nicolas Vuillerme: None declared.
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AB1598 TRENDS OF KNEE ARTHROPLASTY FOR PATIENTS WITH OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS IN SUPER-AGING SOCIETY IN THE LAST THIRTEEN YEARS

Keywords: Osteoarthritis, Rheumatoid arthritis

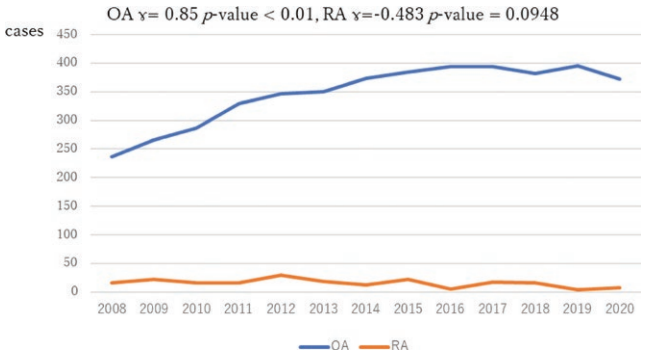
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Background: In Japan, the number of people aged 65 years or older exceeds 35 million, accounting for 28.4% of the total population. It is expected to reach 38.4% by 2065[1]. As a result, the demand for total knee arthroplasty (TKA) and unicompartmental knee arthroplasty (UKA) is increasing year by year[2].
Objectives: The purpose of this study was to investigate the number and trend of patients who underwent knee arthroplasty from 2008 to 2020.
Methods: We analyzed the age, gender, and causative disease of patients who underwent primary knee arthroplasty between January 2008 and December 2020 at two affiliated hospitals. Chi-squared test, Mann-Whitney U test and Spearman's rank correlation coefficient were utilized for statistical analysis. All p-values of 0.05 or less were considered statistically significant. All statistical analyses were conducted using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan, Version 1.55)[3].
Results: We recorded 4,199 cases of TKA (87.1%) and 623 cases of UKA (12.9%), the total of knee arthroplasty is 4,822 cases. There were 1,011 males (24.1%) and 3,811 females (75.9%). Male patients made up 18.5-23.2% of all knee arthroplasty cases, with a trend toward an increase (Spearman's rank correlation coefficient: γ= 0.633 p-value = 0.0135). The mean age at surgery was 75.0 (28-94) year-old, with no significant difference between male (75.2 year-old) and female (74.9 year-old) patients (*p*-value 0.354). The Causative diseases included 4515 cases of osteoarthritis (OA, 93.6%), 208 cases of rheumatoid arthritis (RA, 4.3%), 90 cases of osteonecrosis (ON, 1.9%), 8 cases of trauma, and 1 case of infection (Table 1). TKA/UKA for OA exhibited a significant upward trend, with an average of 346.9 cases per year, while TKA for RA showed a downward trend, with an average of 15.5 cases per year (Spearman's rank correlation coefficient: OA γ= 0.85 *p*-value < 0.01, RA γ=-0.483 *p*-value = 0.0948, Figure 1). UKA group had a significantly higher rate of osteonecrosis compared to TKA group (*p*-value < 0.01, Table 1).
Conclusion: The number of TKA/UKA for OA increased due to the growing number of elderly people affected by knee OA in a super-aging society. On the other hand, the number and rate of primary TKA/UKA due to RA decreased over time due to advances in medication therapy[4]. Osteonecrosis was the cause of a relatively high rate in the UKA group.
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Table 1.

	N (number)	Age (year-old)	Gender (cases)		Causative disease (cases)		
			Male	Female	OA	RA	ON
TKA	4,199	75.1	817	3,382	3,941 (93.9%)	208 (5.0%)	41 (1.0%)*
UKA	623	74.2	194	429	574 (92.1%)	0 (0%)	49 (7.9%)*
Total	4,822	75.3	1,011	3,811	4,515 (93.6%)	208 (4.3%)	90 (1.9%)

OA: Osteoarthritis, RA: Rheumatoid Arthritis, ON: Osteonecrosis* UKA group had a significantly higher rate of osteonecrosis compared to TKA group (*p*-value < 0.01).



Figure

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1599 EVALUATING HOW EFFECTIVELY PATIENTS WITH A NEW INFLAMMATORY ARTHRITIS ARE BEING TRIAGED INTO THE APPROPRIATE CLINIC AT A TERTIARY CARE HOSPITAL IN THE UK: A RETROSPECTIVE AUDIT

Keywords: Inflammatory arthritides

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Background: Early diagnosis and treatment of inflammatory arthritis (IA) is essential: BSR guidance states patients must be seen within three weeks and started on disease modifying anti-rheumatoid drugs (DMARDs) within six weeks.
Objectives: To evaluate how effectively people referred with a new IA are being triaged, whether national standards are met and analyse variables which may influence triage of patients with new IA.
Methods: A retrospective review was performed of all new patients seen in EIA-clinic and those with new EIA who had been seen in non-EIA clinics from 01/09/21-31/11/21. Data was collected on days' wait from referral to assessment/commencement of DMARD. We calculated the conversion rate (CR) (percentage of referrals triaged to EIA clinic that have EIA) and detection rate (DR) (percentage of new EIA patients that are seen in the EIA clinic). The standard for CR and DR was 50% and 95%, respectively. We then examined why some new EIA patients were not triaged to the EIA-clinic using information provided on the referral.
Results: Of the patients seen in the EIA-clinic 36/73 had a new diagnosis of an EIA, giving CR of 49%. Of the new diagnoses of EIA made during that time-period 36/53 were appropriately triaged to be seen in the EIA clinic, giving a DR 68%. Patients seen in the EIA clinic had an average of 5 weeks wait from referral to assessment/commencement of DMARD. In contrast, patients who had been seen in non-EIA clinics had an average of 10 weeks from referral to assessment/commencement of DMARD. A previous audit performed before COVID-19 (01/11/19- 01/01/20) showed a CR of 25% (115 patients seen in EIA-clinic, 29 new diagnoses) and a DR of 69% (29 new diagnoses, 20 seen in EIA-clinic). Of the 10 patients with new EIA who were inappropriately triaged to non-EIA clinics did not have pattern of joint involvement or ability to make a fist documented, in comparison to the 38 patients with a new EIA who were appropriately triaged to EIA-clinic.
Conclusion: Patients with EIA, seen in the EIA-clinic, do not meet guidance for review within three weeks but do meet the guidance for starting a DMARD within six weeks. Patients seen outside the EIA-clinic do not meet either of these standards. Only 68% of people with a new EIA are being triaged to be seen in the EIA clinics, highlighting the need to improve the triage process. Compared to the previous audit, the CR has improved whilst the DR has stayed steady. We have identified variables which appear to influence the triage process. Next steps include making some details from the referral compulsory, exploring using data collected from patients electronically to improve the CR/ DR rates, and artificial intelligence informed modelling.
References: N/A.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1600

TIME TO PUBLICATION AND TIME-LAG PUBLICATION BIAS FOR RANDOMIZED TRIALS ON CONNECTIVE TISSUE DISEASES

Keywords: Epidemiology, Randomized control trial

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Background: Connective tissue diseases (CTDs) are systemic autoimmune diseases, some of which rare, characterized by a dysregulated immune response and a heterogeneous clinical picture. Similarly to nonpublication, a long time from completion to publication of randomized controlled trials (RCTs) results can indirectly harm patients by allowing inefficacious or dangerous intervention being prescribed[1], or by delaying the prescription of useful treatment. We have recently shown that one-third of CTDs-RCTs registered after 2000 never reached publication[2], but we did not estimate the extent of time-lag publication bias, neither analyzed factors associated with delayed publication.

Objectives: To assess the time from completion to publication of randomized controlled trials (RCTs) on connective tissue diseases (CTDs), investigate the factors associated with, and explore the influence of significance of study results on time to publication (time-lag publication bias).

Methods: We included interventional, phase 2/3, 3 or 4 RCTs on CTDs registered in Clinicaltrials.gov from 2000 to 2016, whose results had been published in a peer-review journal less than 5 years after their completion. Two reviewers selected studies according to pre-specified criteria. Main trial features including the significance of primary outcome results were collected. Time to publication was the time from study primary completion to the earliest online publication date. Multivariable linear regression was used to identify association between time to publication and the significance of study results, adjusted for variables previously shown to impact this outcome, e.g. the funder, the size of the trial, the international status, the year of completion and the impact factor of the journal.

Results: We included 62 studies, mostly phase 3 (62%) trials on pharmacologic treatments (94%), recruiting patients with systemic lupus (55%) or systemic sclerosis (23%), and planning to enroll a median of 131 [IQR 61-288] patients. Twenty-two (35%) reported at least a statistically significant primary outcome. Median time to publication was 28 months [IQR 17-36], with more than half studies (n = 34, 55%) published 2 or more year after completion (see Table 1). In multivariable analysis, time to publication progressively improved over time (faster publication in recent years, with the time to publication begin 1.3 [0.3, 2.4] months shorter every year), and was not influenced by the significance of primary outcome results, funder, impact factor of the journal, number of recruiting countries (see Figure 1).

Conclusion: A high proportion of CTDs-RCTs is published beyond 2 years from completion. We did not find evidence of time-lag publication bias, and time to publication improved over time.

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Table 1. Factors associated with time to publication in a multivariate analysis.

Factor	Coefficient (95% CI)	P value
(Intercept)	41.3 (30.1; 52.4)	<0.001
Positive results (reference no)	-1.5 (-8.6; 5.7)	0.69
Industry-funded (ref not industry funded)	-0.2 (-9.5; 9.1)	0.97
International (ref not international)	3.3 (-8.0; 14.5)	0.57
Impact factor of journal	0.1 (-0.1; 0.3)	0.47
Number of patients (per 100 patients)	-1.2 (-2.6; 0.2)	0.09
Completion year (counting from 2000)	-1.3 (-2.3; -0.3)	0.01

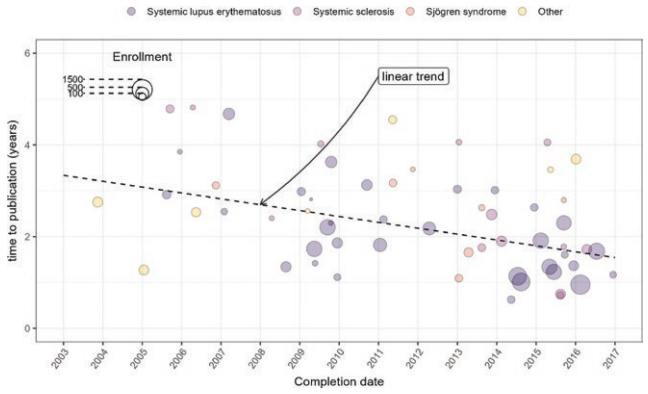


Figure 1. Time evolution of the time to publication for the 62 RCTs considered in the present study. Area of the points are proportional to RCTs enrolment size.

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AB1601

PATIENT EXPERT RECOMMENDATIONS ON WAYS TO IMPROVING THE SYSTEMIC SCLEROSIS CARE CONTINUUM ACROSS EUROPE

Keywords: Systemic sclerosis, Patient-led research, Geographical differences

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Background: Systemic sclerosis (SSc), also known as scleroderma, is a rare autoimmune disease that stiffens the skin, turning simple daily activities into real challenges for patients. It can affect all organs, and while treatments exist, there is currently no cure. The disease is relatively invisible among general practitioners and policymakers in Europe - meaning hundreds of people affected by this rare condition remain undiagnosed and untreated.

Federation of European Scleroderma Associations (FESCA) took a two-pronged approach to develop new evidence. June 2022 a Position Paper (PP) based on a literature review and a survey for healthcare providers (HCP) was published, followed by a large-scale patient and carer survey, whose results are expected in June 2023.

OBJECTIVES:

- Highlight the unmet needs of SSc patients throughout the care pathway.
- Investigate the health and socio-economic burden of the SSc
- Provide evidence to policy stakeholders on the need for policy actions to address health inequalities.

Methods: For the PP, a total of 15 publications were reviewed. To fill the knowledge gaps identified by the literature review, FESCA developed a survey questionnaire earmarked for Excellence or Reference Centers that work with FESCA member organizations and/or are part of the European Scleroderma Trials and Research group (EUSTAR). Upon validation by the authors, the survey was completed by 78 respondents from 24 countries. The upcoming survey will be distributed across 20 countries, a min. representative sample of 511 patients and 170 carers will provide new insights.

Results: The PP highlighted need for policy action in five action areas to ensure timely treatment initiation for all eligible patients and improved health outcomes and quality of life for people living with SSc, by:

1. Creating patient registries for SSc;
2. Shortening time to accurate diagnosis through expanded HCPs curricula;
3. Ensuring timelier referral of patients to specialized care;

4. Improving treatment recommendations and access to appropriate medicines through fast track pathways;
5. Delivering better quality information to SSc patients.
The survey should provide information on patients' evaluations of physical functioning and overall health as the main factors in the decision-making process and the assessment of a treatment's success, showing the inadequacy of current value attribution and appraisal frameworks. Preliminary results are expected to be published at the EULAR Congress.
Conclusion: The outcomes of the work done by FESCA aims at improving the SSc continuum of care from earlier diagnosis to better treatments as well as creating greater awareness of scleroderma so that those who suffer from it can access proper, equitable care. Most importantly, the results of both studies highlight the need for developing person-centred care pathways integrating more systematically quality-of-life considerations in healthcare and treatment decisions as well as in value attribution frameworks that are more responsive to patient needs.
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AB1602

CROSS COUNTRY DIFFERENCES IN B/TSDMARD PRESCRIPTION BEHAVIOR: ASSOCIATIONS BETWEEN SOCIOECONOMICS, REAL WORLD B/TSDMARD USE AND DISEASE OUTCOMES

Keywords: Rheumatoid arthritis, Geographical differences, Registries

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Background: The development of biologic and targeted synthetic (b/ts)DMARDs contributed to improved treatment outcomes in rheumatoid arthritis (RA). However, high medications costs may limit their use. Previously we showed that in countries with a lower socioeconomic status (SES), b/tsDMARDs were prescribed to fewer patients than in countries with higher SES. In this study we take a more detailed look at b/tsDMARD prescription behavior between countries.
Objectives: To explore cross-country relationships between Gross Domestic Product (GDP) per capita, specific indicators of b/tsDMARDs use and disease outcomes in patients with RA.
Methods: This multinational, observational study included countries that had contributed ≥100 patients using b/tsDMARDs, with available follow up, to one of 2 registries: METEOR, an international registry capturing daily clinical practice data of patients with a clinical diagnosis of RA, and JAK-POT, an investigator-initiated collaboration between national registries aiming to evaluate clinical aspects of b/tsDMARDs in RA. On a per-country basis, mean DAS28 was calculated from the last available follow-up visit per patient. b/tsDMARD usage was determined as mean time to start b/tsDMARD therapy since date of diagnosis, mean number of b/tsDMARDs tried per patient and mean duration of b/tsDMARD therapy. To calculate the time to start a first b/tsDMARD per country included from the JAK-POT registry, only bionaïve patients were included. Possible associations between GDP per capita and country-level indicators of b/tsDMARD use and DAS28 were tested in univariable linear regression models. Regression coefficients (β) are interpreted as the numerical increase in the outcome per 1 point increase in the predictor.
Results: Data from 25,832 patients living in 17 different countries showed varying b/tsDMARD prescription behavior. GDP per capita ranged from 6505 (India) to 93350 Intl$ (Ireland). Time to start b/tsDMARD therapy ranged from 0.5 (Austria) to 11.1 (Finland) years. Mean number of b/tsDMARDs tried per patient ranged from 1.0 (Turkey) to 2.4 (Switzerland). Duration of b/tsDMARD therapy ranged from 0.9 (India) to 5.5 (Portugal) years (Figure 1). Baseline DAS28 ranged between 3.7 and 6.1, but was not related to any of the indicators of b/tsDMARD use: time to start a b/tsDMARD β 0.08 (95% CI -0.7; 0.9), number of prescribed b/tsDMARDs β 0.06 (95% CI -0.03; 0.2), duration of b/tsDMARD treatment β 0.1 (95% CI -0.3; 0.5). No statistically significant associations were observed between GDP per capita and time to start b/tsDMARD therapy (Figure 1A, β 0.09 CI 95% -0.7; 0.9), the number of b/tsDMARDs tried per patient (fig 1B, β 0.07 CI 95% -0.02; 0.2) or the duration of b/tsDMARD treatment (fig 1C, β 0.1 CI 95% -0.3; 0.5). None of the indicators of b/tsDMARD prescription were significantly related to DAS28 at the end of follow up: time to start a b/tsDMARD β 0.02 (95% CI -0.05; 0.1), duration of b/tsDMARD therapy β -0.03 (95% CI -0.2; 0.1) and number of b/tsDMARDs β -0.03 (95% CI -0.6; 0.6).
Conclusion: This study showed varying b/tsDMARD prescription behavior and disease activity across 17 countries worldwide. Overall, differences in b/tsDMARD prescription behaviour did not appear to be related to socioeconomic welfare and, no significant association was observed between b/tsDMARD prescription behavior and disease activity at a country level. This seems to indicate that once patients start a b/tsDMARD, socioeconomic welfare has less impact on b/tsDMARD use.

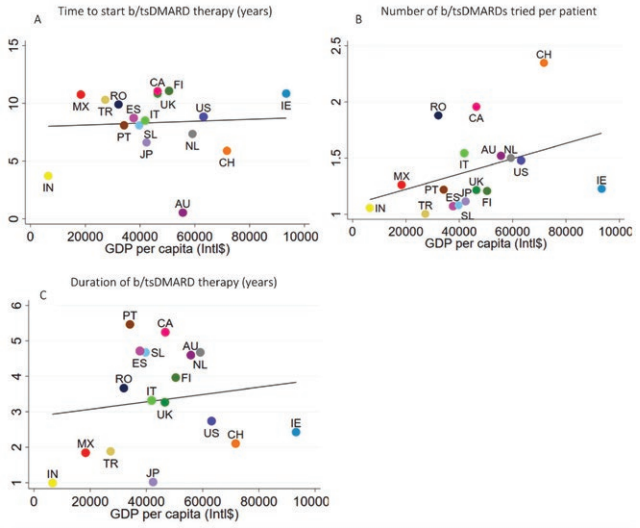


Figure 1. Associations between 'GDP per capita (Intl$)' and the 'Time to start b/tsDMARD therapy (years)' (A), 'Number of b/tsDMARDs tried per patient' (B) and 'Duration of b/tsDMARD therapy (years)' (C)

AU, Austria; CA, Canada; CH, Switzerland; ES, Spain; FI, Finland; GB, United Kingdom; IE, Ireland; IN, India; IT, Italy; JP, Japan; MX, Mexico; NL, Netherlands; PT, Portugal; RO, Romania; SL, Slovenia; TR, Turkey; US, United States

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AB1603 EVIDENTIAL REQUIREMENTS FOR DECISION-MAKING ABOUT WORKPLACE INITIATIVES TO MITIGATE THE IMPACT OF RHEUMATIC AND MUSCULOSKELETAL DISEASES: QUALITATIVE INTERVIEWS WITH REPRESENTATIVES OF UK ORGANISATIONS

Keywords: Work-related issues, Rheumatoid arthritis, Qualitative research methods

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Background: Decisions about whether to invest in RMD-related workplace initiatives/adaptations can be made by determining, from the relevant perspective, if benefits outweigh the costs of implementation. Little is known about what information organisations need to facilitate these decisions.
Objectives: This study aimed to explore motivations and evidential requirements for employers to invest in workplace health initiatives.
Methods: Semi-structured online interviews with representatives of large UK-based (not-for-profit and for-profit) organisations were audio-recorded. For each organisation, a line manager, director, and representative with workforce health remit were interviewed. Interview data were transcribed verbatim and subject to thematic analysis by two researchers trained in qualitative methods. Themes were agreed in discussion with the study team.
Results: We recruited 13 representatives (5 directors, 3 line managers, and 4 with a specific remit for workforce health). Three not-for-profit organisations (local authority, university, and National Health Service) were represented by seven participants and three for-profit organisations (restaurant chain, telecoms provider, and technology company) were represented by six individuals.
Motivations: All participants believed that investment in measures to promote employee health and well-being could positively contribute to their organisation's efficiency. *…there's loads of academic research that says… if you look after your colleagues… if you cater to their… individual needs, then that has a very positive impact on organisation performance.* (Director, not-for-profit) Attraction and retention of staff – seen as increasingly difficult - was a motivating factor to invest that was shared by employers, as was the desire to avoid litigation, promote workplace camaraderie, and to maintain organisational reputation. Low RMD prevalence rates in the young workforce in one organisation (a restaurant chain) meant that these conditions did not influence decision-making. For organisations with older workforces doing heavier manual work, higher prevalence rates of RMD were a key reason to act. *... musculoskeletal is, like, the second biggest reason for sickness within the organisation.* (Line manager, not-for-profit)
Evidential requirements: Use of checklists/assessments to reveal individual RMD-related needs was commonplace throughout organisations. Self-identified health needs, typically related to line managers, would instigate a process where occupational therapist (OT) input may be sought. Requests and OT recommendations are reportedly, without exception and irrespective of cost, met and followed. No organisation had set aside a specific budget for workplace initiatives. Decisions involving significant investments in workforce health initiatives were usually made by committees or by small teams comprising senior staff and directors. Line managers and those with a health remit would put forward a case for investment to these bodies: *…we would pull together a bit of a proposal really on what that would look like…what is the impact of it?...we support it with facts…even benchmarks of what's going on in the outside.* (Health remit representative, for-profit) Evidence from OTs/other health professionals, in-house absenteeism data, workforce survey results/informal feedback from colleagues, benchmarking data, and academic/official report findings were used to make a case for investment.
Conclusion: The demand for RMD-specific interventions varies according to needs of particular workforces. Despite diversity of organisation type, workforce factors (i.e. demographic factors, nature of work) and employer roles, common processes for informing investment decisions and typical evidence requirements have been identified. Findings can inform the development and evaluation of workplace interventions to benefit people with RMD.
Acknowledgements: This work is undertaken as part of the Centre for Musculoskeletal Health and Work, funded by Versus Arthritis and the Medical Research Council. We thank study participants.
Disclosure of Interests: None Declared.
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AB1604 PRE-EXPOSURE PROPHYLAXIS WITH TIXAGEVIMAB/CILGAVIMAB: SINGLE CENTRE EXPERIENCE IN A COHORT OF RHEUMATIC PATIENTS

Keywords: Vaccination/Immunization, Safety, COVID

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Background: Vaccination against SARS-CoV2 had a critical role in the fight against COVID19 pandemic. A weaker humoral response to COVID19 vaccine has been found in rheumatic patients treated with Rituximab (RTX) or Mycophenolate Mofetil (MMF)[1]. Despite the evidence that anti-SARS-CoV-2 mRNA vaccines can elicit a T-cell response [2], some data show that even the cellular immunity could be impaired in rheumatic patients [3] but COVID19 serology is the only parameter that is feasible to measure in daily practice. Tixagevimab+cilgavimab are two human-derived monoclonal antibodies administered parenterally and authorized by regulatory agencies in February 2022 for pre-exposure prophylaxis (PrEP) against COVID19 from different virus variants in fragile patients.
Objectives: To demonstrate safety and effectiveness of tixagevimab+cilgavimab.
Methods: Patients with autoimmune rheumatic diseases undergoing immunosuppressive treatment with RTX or MMF during the vaccination campaign were enrolled between April and June 2022. All patients must have anti-spike antibody levels below the protective threshold (defined by anti-spike IgG titre <250 BAU/ml) after receiving at least 2 vaccine doses. Patients were monitored with a questionnaire every month about COVID19 symptoms (including respiratory and gastrointestinal symptoms, anosmia and ageusia, skin rash and potential contact with COVID19+ subjects) and were checked for anti-spike and anti-nucleocapside antibodies titres every 2 months for a total of a 6 month follow-up. MMF dose was reduced at 1 g/die at the time of vaccine administration.
Results: Fifteen patients were enrolled: 9 participants had a connective tissue disease (CTD; 1 dermatomyositis, 3 anti-syntethase syndrome, 4 systemic sclerosis, 1 systemic lupus erythematosus) and 6 had vasculitis (all granulomatosis with polyangiitis). 12 of them received RTX in the preceding 12 months and 3 were taking MMF. About safety, the therapy was very well tolerated and only 4 patients (26%) reported a non-severe adverse event in the 2 weeks following drug administration (2 myalgia, 1 headache, 1 fatigue), none of them requiring hospitalization nor pharmacologic treatment. Regarding effectiveness, 3/15 patients contracted SARS-Cov2 infection (20%) with mild symptoms and no need for hospitalization nor oxygen therapy. Only 1 of them received an antiviral drug (nirmatrelvir+ritonavir). All infected patients had a CTD diagnosis. No significant correlation was observed between the type of rheumatic disease and the risk of infection or response to tixagevimab+cilgavimab.
Conclusion: None of our patients developed severe adverse events after tixagevimab+cilgavimab administration and, among the 3 SARS-CoV2 infected patients, none required hospitalization nor oxygen therapy.
We conclude that in our experience tixagevimab+cilgavimab is a safe and useful complementary immunization strategy to vaccination for COVID19 prophylaxis. These data will be implemented in a larger study, comprehending various immunocompromised patients from several departments.
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Charateristic of the cohort

Identificative	Age	Diagnosis	RTX/MMF	SARS-CoV2 Infection	Hospitalization	Antiviral drugs
1	80	SSc	MMF	-	/	/
2	70	ASSD	RTX	+	no	no
3	70	ASSD	RTX	+	no	yes
4	52	GPA	RTX	-	/	/
5	51	GPA	RTX	-	/	/
6	49	SSc+SSj	RTX	-	/	/
7	68	SSc	MMF	-	/	/
8	47	LES	RTX	-	/	/
9	64	ASSD	RTX	-	/	/
10	68	GPA	RTX	-	/	/
11	23	GPA	RTX	-	/	/
12	58	DM	RTX	+	no	no
13	61	SSc	MMF	-	/	/
14	75	GPA	RTX	-	/	/
15	69	GPA	RTX	-	/	/

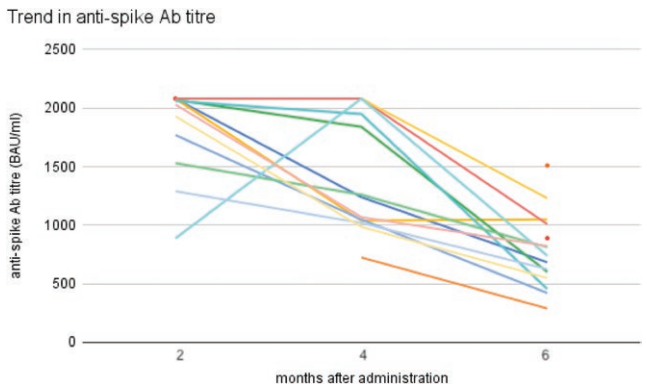


Figure 1.

Acknowledgements: NIL.
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AB1605

A PILOT RHEUMATOLOGY-INTERSTITIAL LUNG DISEASE (ILD) SERVICE - OUTCOMES AFTER 12 MONTHS

Keywords: Lungs, Organ damage

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Background: Rheumatologists have an important role in the management of interstitial lung disease (ILD). Cross-specialty collaborative working models are increasingly being used, particularly with ILD radiology MDT meetings, attended by respiratory physicians and rheumatologists, to discuss complex clinical cases. However, the infrastructure and format are not standardized) [1]. With the widespread financial and logistical pressures affecting delivery of healthcare in not only NHS setting, but worldwide; there is a need to provide robust evidence to managers and fundholders, of significant benefit to attract allocation of funding and resources towards MDT working in complex disease areas such as ILD.
Objectives: We describe the format and outcomes of a pilot rheumatology-ILD service at a large teaching hospital undertaken from January to December 2022.
Methods: Two rheumatology consultants (EB and CR) worked with the local ILD respiratory lead (JL) to plan for weekly attendance of one or both rheumatologists at a weekly ILD MDT. Prior to this, paper based referrals to general rheumatology were made if advice was felt to be required – generating paperwork, delays in the patient journey and an ad hoc approach across multiple rheumatology clinicians. This MDT is attended by respiratory clinicians, radiologists, ILD nurse specialist and respiratory trainees. Since the COVID-19 pandemic it has been conducted via Microsoft Teams and is scheduled for 1-1.5 hours weekly. Cases to be discussed are added in advance to MSTeam file on a specifically designed proforma. In addition there is a weekly ILD OPC attended by JL with a dedicated ILD nurse specialist. Rheumatology joined this clinic when other clinical commitments allowed which facilitated more focused discussion on management of complex cases.
Results: Over the course of a 12 month period rheumatology attended 24 ILD MDT meetings and 8 ILD out-patient clinics. This equated to approximately 80 hours of rheumatologist time over the pilot period.
On analysis of cases presented, 33% required rheumatology input, most often on the basis of positive antibody screening or a prior history of rheumatological disease.
The breakdown of rheumatology disease presented is detailed in Table 1 below.

Table 1. Diagnosis, Frequency and Outcome of Rheumatology-Related ILD Cases at a Pilot Cross-Specialty Clinic Over 1 Year

	NUMBER OF CASES	PRESENCE OFSIGNIFICANT ANTIBODIES	OUTCOME
ANCA	18	MPO pANCA	Watch and wait =7 cases
	3	cANCA +/- PR3	Immunosuppression (steroid, MMF*, IV cyclo*, ritux*) = 11 cases
			Death (2 cases) – despite intensive immunosuppression
			No classical GPA presented via ILD service
			2 felt to be incidental cANCA
			1 atypical case closely monitored
RA	12		Often no change to treatment, liaise with rheum treating team
Myositis (Mi2b, SAE)	7		All assessed by rheumatology, myositis confirmed in 5 – continue under rheumatology
Lupus	8		4=felt insignificant low-titre antibody 4= referred into rheumatology service
Scleroderma	9		Immunosuppression (steroid, MMF*, toc*)
IgG4	2		Referred into rheumatology
Others: shrinking lung, low titre antibodies, PMR, Sweets	13		Various: clinical advice, rheum OPC, neurology referral, derm referral

*****indicates specialist drug treatment not usually initiated by respiratory teams and requiring rheumatology advice +/- administrating and monitoring*

Conclusion: There are a large number of ILD cases within the respiratory service that require rheumatology input – 33% of all ILD cases in this real-world snapshot. The spectrum of rheumatologically associated disease is vast. ILD can have a catastrophic outcomes and therefore early and continued rheumatology input is vital. Investment is needed for formal MDT infrastructure to include rheumatology. There is a need for data collection, collaborative working and research to improve the quality of care and outcomes for this population.

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Disclosure of Interests: None Declared.
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AB1606

SYMPTOMS OF RAYNAUD'S PHENOMENON ARE NO OBSTACLE FOR BEING PHYSICALLY ACTIVE IN HEALTHY WOMEN

Keywords: Patient reported outcomes, Lifestyles, Quality of life

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Background: Women with primary Raynaud's phenomenon (RP) often experience a decreased health related quality of life (HRQoL). A physically active lifestyle could have a positive influence on vascular function and thus might improve HRQoL in women with primary RP.
Objectives: To quantify the amount and type of physical activity (PA) and sedentary behaviour, as well as HRQoL and stress, in women with primary Raynaud's phenomenon (RP), and to compare this to the behaviour of women without RP from a large population-based cohort (Lifelines).
Methods: The connective tissue disease (CTD) screening questionnaire data from the Lifelines database that was available of women ≥ 18 years old was used. This

questionnaire consists of 30 questions to detect possible CTD's. A total of 19820 women, 929 with RP and 18891 without RP, all without other comorbidities were included. By using questionnaires from the Lifelines database other patient characteristics were retrieved including physical activity and sedentary behaviour, HRQoL and stress.
Results: Women with RP reported 300 min/week minutes of moderate to vigorous physical activity (MVPA), which was more than women without RP reported (255 min/week). This difference was mainly due to a difference in vigorous activities (p<.001). 74.3% of women with RP complied to the health enhancing PA guidelines (69.5% in the group of women without RP, p=.003). Time spent sedentary by women with RP was 540 min/week, which was comparable to sedentary time of women without RP (540 min/week, p=.886). Women with RP scored lower on almost all eight domains of the QoL questionnaire (p<.05), except for physical functioning (p=.181). Regarding stress levels, the List of Threatening Experiences (LTE) showed no differences between groups (p=.226), however, the Long-term Difficulties Inventory (LDI) showed a higher stress level in the RP group (p<.001). Furthermore, women with RP were significantly younger (p<.001), had a lower Body Mass Index (BMI) (p<.001), a lower waist-hip ratio (p<.001), had a lower amount of packyears (p<.001) and a healthier diet score (p<.001) compared to the women without RP.
Conclusion: This is the first study to structurally investigate PA in a large population cohort of patients with RP. Most women with RP report they spent a sufficient amount of time on moderate to vigorous PA and thus comply to health enhancing physical activity guidelines. The PA behaviour of women with RP seems comparable to that of women without RP, showing that RP is no obstacle for being physically active. However, HRQoL was lower in women with RP; more research is needed to elucidate the relation between PA and HRQoL in this patient group, preferably using objective measurement instruments to assess PA.
Acknowledgements: The Lifelines biobank initiative has been made possible by subsidies from the Dutch Ministry of Health, Welfare and Sport, the Dutch Ministry of Economic Affairs, the University Medical Center Groningen, the University Groningen, and the Northern Provinces of the Netherlands. There was no funding for this manuscript.
Disclosure of Interests: None Declared.
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AB1607 TREATMENT OUTCOME OF RHEUMATOID ARTHRITIS IN RURAL AND URBAN POPULATION; A COMPARATIVE STUDY FROM SOUTH INDIA

Keywords: Rheumatoid arthritis

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Background: Advances in rheumatology have made the once-disfiguring rheumatoid arthritis (RA) a controllable disease. However, differences in health care delivery exist across the rural and urban populations in South India. Hence disease characteristics may be different across the two groups of patients. [1,2] Herein, we compare the disease characteristics of RA across rural and urban populations based in the state of Kerala in South India.
Objectives: The primary objective was to compare the disease characteristics of RA in rural and urban rheumatology centres in South India.
Methods: A retrospective study of patients attending rural and urban clinics of our Institute was conducted. Consecutive 100 patients who attended the clinics from April to October 2022 and who satisfied the ACR/EULAR 2010 RA criteria were selected for the study in each group. Baseline Demographics were collected, and disease activity was measured using the CDAI score. Extraarticular manifestations and comorbidities associated with RA were also considered. Treatment response was assessed at the end of 6 months.
Results: The mean age of patients was 51 years(± 12SD) and 55 years(±12SD) in urban and rural groups, respectively. Disease activity at baseline and six months was shown in Figure 1. 28% of the rural patients required triple DMARDs for disease control against 14% in the urban group (p-value 0.02). Remission at six months was attained in 47% of the urban population against 30% of the rural population (p-value 0.05). Non-alcoholic Fatty liver disease was more prevalent in the rural population (9%) than the urban population (2%)(p-value 0.05). DMARD-induced elevation of liver enzymes occurred in 15% of patients in the rural group compared to 5% of patients in the urban group(Pvalue-0.03). Even though the prevalence of uncontrolled T2DM and osteoarthritis was more in the rural population, the difference between the two groups was not statistically significant. Similarly, the use of biologicals was more in rural (8%) compared to urban (4%) without any statistical significance.
Conclusion: We observed that baseline disease characteristics and disease activity were identical across both groups. At six months, CDAI and CRP were significantly higher in the rural than urban group suggesting that response to optimal DMARD treatment was better in the urban group than in the rural group. Triple DMARD use was also significantly higher in the rural compared to the urban group. This shows that despite the advances in rheumatology, there are still unmet needs regarding awareness and access to adequate treatment in rural society.
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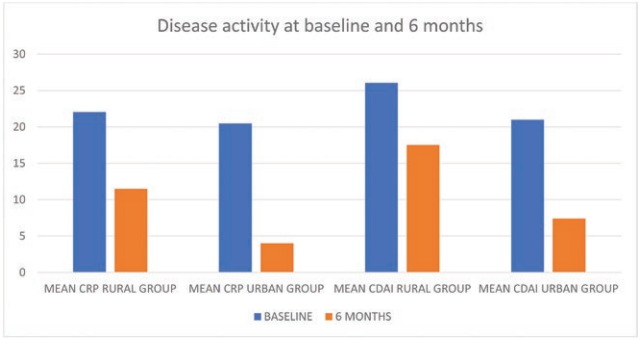


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1608 THE EFFECT OF REMOTE AND FACE-TO-FACE PREVENTIVE REHABILITATION ON THE THICKNESS OF THE MUSCLES AROUND THE SPINE

Keywords: Telemedicine, Physical therapy/physiotherapy, Ultrasound

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Background: In these days when it is extremely important to use resources efficiently, ways to reduce the cost caused by low back and neck pain are sought. Investigating the architectural features of the muscles around the spine is also an important part of this search [1]. It is a rational approach to prevent spinal problems before they occur, rather than to treat them. In addition, it is very important for the prevention of spinal health that these approaches can be offered at low cost in pandemic conditions and disadvantageous situations such as settlements in rural areas.
Objectives: This research aims to investigate the effectiveness of remote and face-to-face spinal stabilization exercises on the thickness and activation of the muscles around the spine in asymptomatic desk-based office workers.
Methods: Individuals between the ages of 18-55 who did not have chronic low back and neck pain were included in the study. While the face-to-face group exercised under the supervision of a physiotherapist, the telerehabilitation (TR) group exercised with video conferencing and asynchronous video recordings. Both groups performed progressive spinal stabilization exercises 3 days a week for 8 weeks. The thickness of the Internal Oblique, External Oblique, Sternocleidomastoideus and Upper Trapezius muscles at rest, and the thickness of the Transversus Abdominis (TrA) at rest and during contraction were measured with portable ultrasound (Sonostar, China) (Image 1). TrA activation was measured with a stabilizer. Compliance with exercise was evaluated with an exercise diary.
Results: 24 individuals, 12 in the face-to-face group and 12 in the TR group, with a mean age of 28.41(5.94) participated in the study. Age, gender distribution, and baseline values for muscles were similar between the groups (p>0.05). In both groups, right and left TrA resting and contraction, Internal Oblique thicknesses were increased (p<0.05). It was found that the level of activation of the TrA muscle, the thickness change during contraction, and the thickness of the internal oblique muscle developed more in the face-to-face group. In the TR group, on the other hand, an increase in Upper Trapezius thickness was observed (p<0.05) However, there was no significant increase in TrA activation level in this group.
Conclusion: According to preliminary results face-to-face exercise further improves the thickness, activation, and contraction amount of deep stabilizer muscles. TR, on the other hand, caused positive developments in the deep muscles, but also in the upper Trapezius muscle, which is the superficial muscle. The reason for this situation may be postural compensations that occur during remote exercise [2]. As a result, both methods cause an increase in muscle thickness around the spine. However, if possible, supervision during exercises that require intense attention, such as

stabilization exercises, can increase efficiency. In addition, further studies on compensations that may occur during exercise through TR may be instructive.

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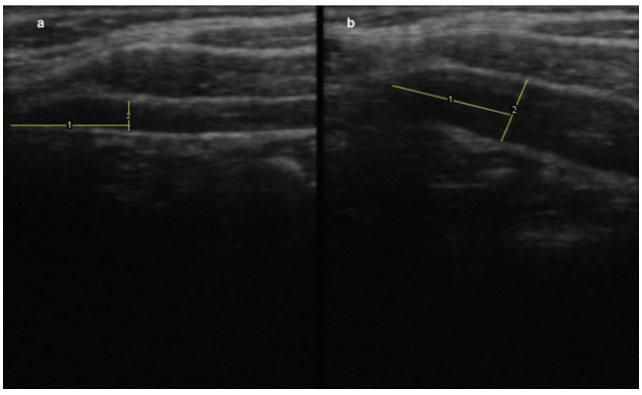


Image 1. Muscle thickness of TrA at rest (a) and contraction (b)

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Disclosure of Interests: None Declared.

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AB1609 ECONOMIC IMPACT OF HOSPITAL STAYS FOR UVEITIS PATIENTS IN THE UNITED STATES: AN ANALYSIS OF THE NATIONAL INPATIENT DATABASE

Keywords: Health services research, Uveitis, Epidemiology

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Background: Uveitis is the most common extraarticular manifestation in patients with spondyloarthritis. It may be the first presentation of spondyloarthritis. The combination of effects on vision, systemic disease and side effects of treatment have a significant impact on patient's life. Uveitis affects all age groups and results in visual impairment over a long duration of the patient's lifetime. Hence, treatment cost due to uveitis is similar to the common eye conditions such as cataract, age related macular degeneration and glaucoma.

Objectives: There is a lack of national level data regarding the medical cost of hospital stay of uveitis patients. The objective of our study is to identify health care expenses for patients hospitalized with uveitis in the United States.

Methods: The National Inpatient Sample (NIS) is used for this study. It is a de-identified, random sample data of inpatient hospitalizations in the United States. It is the largest all-payer database containing data on more than seven million hospital stays. Its large sample size is ideal for examining national estimates. We collected data from 2016 to 2020 and ICD-10 codes were used to identify uveitis cases. NIS uses the Clinical Classifications Software Refined (CCSR) categories which aggregates ICD-10 codes into 530 clinical categories. ICD-10 codes for inflammatory eye conditions are assigned to the category uveitis and ocular inflammation. Patients hospitalized with primary diagnosis of uveitis were included. Length of hospital stay; hospital charge and cost were collected. Charge is the amount hospital billed and cost represents the actual cost of hospital stay.

Results: Average charge for hospital stays for uveitis patient is approximately 60,000 US dollars and has increased from 2016-2020. Similarly, cost of hospital stays and length of stay increased during the study period. Majority of uveitis inpatients are discharged to home, smaller percentage are discharged to rehab, nursing home or to home health care. Results are shown in the Table 1.

Conclusion: Economic burden of inpatient uveitis on health care is significant and has continued to increase from 2016 to 2020. Strategy and policy for providing better outpatient care for uveitis patients would help in reducing the number of hospital admissions and costs of stay.

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Table 1. Attributes of Hospital Stay for Uveitis patients in the United States: 2016-2020: National Inpatient Sample.

	2016	2017	2018	2019	2020
	Estimate (Standard error)	Estimate (Standard error)	Estimate (Standard error)	Estimate (Standard error)	Estimate (Standard error)
Number of discharges	1270 (111)	1260 (103)	1340 (114)	1645 (116)	1290 (109)
Average Length of Stay (In days)	5.8 (0.361)	6.7 (0.451)	6.2 (0.319)	7.2 (0.57)	7.1 (0.667)
Aggregate hospital charges* (In US $)	64,574,007 (7251445)	69,891,369 (8262178)	8,4085,579 (10294805)	109,200,748 (10618923)	89,381,020 (9376801)
Aggregate hospital cost^ (In US $)	16,884,141 (1924031)	17,972,462 (2122834)	19,125,946 (2158514)	28,756,464 (3008420)	23,935,615 (2628843)
Average hospital charge per stay (In US $)	50,846 (4095)	55,469 (4611)	62,750 (5469)	66,383 (4659)	69,288 (5127)
Average hospital cost per stay (In US $)	13,295 (1064)	14,264 (1151)	14,273 (1045)	17,481 (1394)	18,555 (1488)
Number of discharges transferred to nursing home or rehab.	125 (26)	175 (34)	140 (26)	190 (32)	170 (32)
Number of discharges to home health care.	120 (24)	120 (25)	145 (30)	235 (37)	165 (29)

*Charges: Amount hospital billed. Aggregate Charges: The sum of all charges for all hospital stays in the U.S.^Costs: Actual costs of hospital stay.Charges are converted to costs using cost-to-charge ratios based on hospital accounting reports from the Centers for Medicare and Medicaid Services (CMS).

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Disclosure of Interests: None Declared.

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AB1610 NON-PHARMACOLOGICAL AND SELF-MANAGEMENT INTERVENTIONS FOR MAIN OUTCOMES IN RHEUMATOID ARTHRITIS PATIENTS: A SYSTEMATIC REVIEW

Keywords: Rheumatoid arthritis, Systematic review, Self-management

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Background: Rheumatoid arthritis (RA) is accompanied by considerable limitation of the functional abilities and a significant reduction of the patients´ quality of life (QoL).[1] Self-management has been proven to play a role in the improvement of well-being and functioning in daily life. With the help of digital tools, individualized self-management methods can become more accessible to patients.[2]

Objectives: We aimed to identify evidence on efficacy of non-pharmacological self-management interventions on core outcomes in RA. Results will inform development of self-management recommendations into the RheumaBuddy (RB) 4.0 app.

Methods: To identify evidence-based self-management interventions suitable for the inclusion in the app, a systematic literature review (SLR) was conducted. We included clinical trials or randomized controlled trials in adult (≥18years) RA patients, reported in German or English language and excluded nutritional supplements and interventional medical devices. Outcomes of interest were identified via RB4.0 as either predefined or individually used for symptom tracking in the app and agreed upon in an expert panel.

Results: Main outcomes identified and used in the SLR were pain, fatigue, mood, stiffness, and quality of life. In total, 125 studies from 644 identified articles were included for data extraction (Figure 1). Heterogeneity of the studies precluded a meta-analysis. The majority of studies used pain (n=100), mood (n=46) or fatigue (n=35) as outcome. Interventions were grouped into six main categories (Exercise, Diet, Psychosocial, Education, Multicomponent, and other). The number of studies with a significant positive effect on various outcomes per various intervention strategies are displayed in Table 1.

Conclusion: We identified a broad range of non-pharmacological, self-management interventions for RA patients which can be used to further develop self-management recommendations, for implementation into RheumaBuddy 4.0, a new generation of an algorithm-driven digital health tool, designed to support RA patients' disease self-management.

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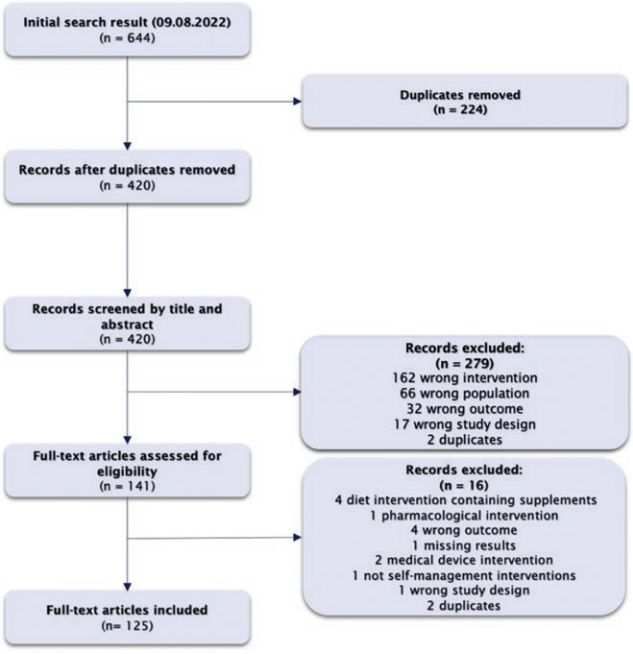


Figure 1. PRISMA Flow chart of study selection

Table 1. Overview of included studies

	Outcome					
	Pain (n=100)	**Fatigue (n=35)**	**Mood (n=46)**	**Stiffness (n=29)**	**Quality of Life (n= 29)**	**Sleep (n=6)**
Intervention	(N of studies with significant positive Outcome/ total n of studies investigating this intervention/outcome)					
Exercise (n=52)	16/40	6/17	8/17	4/11	6/14	0/3
Education (n=20)	8/15	1/7	5/15	0/3	0/4	0/0
Psychosocial (n=29)	10/21*	3/6	6/21	1/4	1/3	0/2
Diet (n=8)	5/8	½	0/0	3/5	3/4	0/0
Others (n=15)	11/13	3/3	2/2	2/7	2/7	1/1
Multicomponent (n=28)	13/22	5/10	5/9	1/6	4/6	0/0
Education + Exercise + Psychosocial + Diet (n=3/28)	2/2	1/1	1/1	0/0	1/2	0/0
Education + Exercise + Psychosocial (n=10/28)	5/9	2/5	1/3	0/1	0/0	0/0
Education + Exercise + Diet (n=2/28)	0/2	0/0	0/0	0/1	1/1	0/0
Education + Exercise + other (n=1)	1/1	0/0	0/0	0/0	0/0	0/0
Education + Exercise (n=4/28)	1/2	2/3	2/2	0/1	0/2	0/0
Education + Psychosocial (n=4/28)	3/3	0/1	1/3	1/1	0/0	0/0
Exercise + other (n=4/28)	1/3	0/0	0/0	0/2	1/1	0/0

*1/21 negative outcome

Acknowledgements: NIL.

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AB1611 INFLAMMATORY ARTHRITIS AND WORK: WHAT PROFESSIONAL ADAPTATIONS?

Keywords: Work-related issues, Inflammatory arthritides, Qualitative research methods

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Background: Despite improvements in the management of inflammatory arthritis (IA), the disease still has a significant impact on work and the support for patients with professional difficulties remains insufficient. The questionnaires currently available to us evaluate the societal impact of impact of IA on work (e.g. productivity at work) but not individual intermediate criteria such as work difficulties or possible adaptations.

Objectives: The objective of the study was to better understand the difficulties encountered at work, the coping strategies used and the motivations of patients with IA to continue working. Only the occupational adaptations are presented here.

Methods: 32 individual semi-directed interviews and 2 group interviews were conducted with patients with IA recruited in consultations or by patient associations. The participants were recruited according to a. purposive sampling with maximum variation. Inclusion criteria were: age 18 to 65 years, have IA, be professionally active, have difficulties or concerns at work due to the disease. The interviews. were conducted with an interview guide and were recorded and transcribed in full. The thematic analyses were conducted using an inductive approach.

Results: The analysis of the adaptations implemented revealed 14 main themes: adaptation of positions, tasks and mobilizations; adaptation of equipment; support from colleagues; change of working time, changing schedules and night work; taking breaks at work, splitting activities; Teleworking; reorientation, training; recognition of the status of disabled worker; occupational medicine, administrative difficulties; ergonomists; trade unions; changing position, jobs or employers.

Examples of quotes from the interviews:

Themes	Quotes
Adaptation of positions, tasks and mobilizations	There are meetings that are too long 4-5 hours. There are several of us who get up and spend the meeting standing
Change of working time	Avantages ou désavantages, possibilité et opportunité de modifier le temps de travail, dispositions psychologiques, utilisation des RTT ou des jours de congé, pérennité du travail à temps partiel
Recognition of the status of disabled worker	I've seen too many people considered disabled...put in closets. You put them in an office, doing nothing, in jobs that don't exist. You're not useful
	I went before a commission of thirty people. They ask me to explain how my handicap poses a problem to me on a daily basis.
Administrative difficulties	I don't know how it's going
	These are insane procedures, it's practically a full-time job

Conclusion: Patients discuss multiple possible adaptations, their advantages, disadvantages and difficulties encountered. These data will be useful to occupational health professionals and clinicians in helping patients to keep their jobs in good conditions and develop appropriate services.

REFERENCES: NIL.

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AB1612

EFFICACY OVER TIME OF SUBLINGUAL POLYBACTERIAL VACCINES IN PATIENTS WITH RHEUMATIC DISEASES AND ACTIVE PHARMACOLOGIC IMMUNOSUPRESSION

Keywords: Vaccination/immunization, Innate immunity, Infection-related RMDs

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Background: Synthetic and biologic disease-modifying drugs (DMARDs) have improved the prognosis of systemic autoimmune diseases (SAD). However, concerns persist about infectious complications in these patients. Previous studies of our group have shownthat sublingual polybacterial vaccines decrease the rateo of recurrent respiratory tract infections (RRTI) and recurrent urinary tract infections (RUTI).
Objectives: We aimed to evaluate the number of respiratory and urinary tract infections during 2018-2021 in patients who received sublingual polybacterial vaccines until 2018, when their administration was discontinued due to regulatory issues.
Methods: A retrospective observational study was conducted from a cohort of patients with SAD who had received sublingual polybacterial vaccines between 2014 - 2018. From 2018 onward, the incidence of UTI and incidence of RUTI and RRTI was analyzed and compared with anual incidence prior to vaccine administration and after one year post-vaccination.
Results: RRTI and RUTI were analyzed in 41 patients with SAD and active immunosuppression during the years 2018-2021. A significant increase in the number of infections was observed from 2018 to 2021, compared to the post-vaccination year, for both RUTI (1.53±2.17 vs 0.63±1.13;p=0.005) and RRTI (1.63±2.32 vs 0.67±0.92; p=0.003). When categorizing by number of infections, we observed that despite the increase in the average number of RUTI and RRTI, approximately half of the patients had no infections in the 2018-2021 period (51.2% RUTI and 43.5% RRTI). Making a comparison with the pre-vaccine year, despite the increase in the number of infections during the 2018-2021 period with respect to the immediate post-vaccination, the number of RRTI episodes was still lower (1.61±2.26 vs 2.76± 2.57; p= 0.002), as was the number of RUTI (1.56±2.12 vs 2.69±3.07; p= 0.010).
Conclusion: The effect of sublingual polybacterial vaccines was maintained up to 3 years, with a significant decrease in infections with respect to the year prior to vaccination, suggesting that these vaccines may have long-term benefit. The number of respiratory and urinary tract infections increased during the years when the vaccine administration was not available. However, an absence of infections was also observed in half of the patients.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1613

MEFV GENE TEST – WHO'S ORDERING THEM AND WHY?

Keywords: Genetics/epigenetics, Diagnostic tests

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Background: Familial Mediterranean Fever (FMF) is a rare autosomal recessive illness of periodic fever syndrome that primarily affects the Mediterranean population [1]. No single specific diagnostic test exists to accurately diagnose FMF. Testing of the MEFV gene is the primary investigation of choice to support a diagnosis of FMF [2]. Little is known regarding MEFV testing within Australian cohorts.
Objectives: We aim to describe the pattern of ordering for FMF genetic testing via the ordering of MEFV gene, and the clinical circumstances surrounding its request in a large Australian referral centre.
Methods: We retrospectively identified all MEFV genetic testing ordered within a large public referral centre over a five-year period. We collected information regarding the clinical scenario indicating genetic testing, presenting symptoms and adherence to Tel HaShomer diagnostic criteria as well as whether the genetic testing impacted the final diagnosis.
Results: 64 MEFV genetic testing were ordered through the five-year period, seven were within the paediatric population. The median age of the cohort was 37, 56.3% were male sex. There is a median of five flares of FMF prior to MEFV testing with median time from last flare being two months. 53.1% of the tests were ordered in an inpatient setting, rest were through outpatient. Rheumatology ordered the most MEFV genetic testing in 67.2% of the cohort, followed by Infectious Diseases in 10.9% and General Medicine in 7.8% of the cohort. 79.7% of the participants satisfied the Tel HaShomer criteria for clinical diagnosis of FMF prior to genetic testing. MEFV genetic testing provided a positive diagnostic result in 21.9% (14 participants), there were seven homozygotes, seven compound heterozygotes and eight heterozygotes. Only one of the 14 participants with a positive MEFV test did not satisfy the clinical diagnostic criteria. A total of 36 mutated alleles were identified and M694V was the most frequent mutation appearing in 47.2% of the mutations identified. Peritonitis was the most common presentation in 67.2% of the cohort. One participant had amyloidosis as their presentation. 43.8% of the cohort was commenced on colchicine prior to genetic testing.
Conclusion: MEFV testing is most commonly ordered by Rheumatology than other specialities. While the genetic testing can be useful in a diagnostic dilemma, it also adds further diagnostic certainty if positive in those who satisfy the clinical diagnostic criteria.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1614

THE INCREASE IN SAFETY OUTCOME TRIALS AND THE ISSUE OF INFORMED CONSENT

Keywords: Randomized control trial, Safety

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Background: The randomized controlled trial (RCT) remains a most important research as well as a tool for drug licensing. Informed consent also remains an integral component of this tool. The exact wording of this consent is not in the public domain and we had previously raised that concern and had pointed out it should [1, 2]. As we previously indicated such transparency was important from the point of an organized skepticism an essential element of scientific inquiry [3]. Moreover, we had also indicated that this transparency was even more important in safety outcome trials (SOT)s. We have the impression that such SOTs are becoming more frequent especially with the increasing popularity of pragmatic trials [4] where the safety outcome measures are not infrequently as severe as death.
Objectives: To tabulate the frequency of RCTs with the primary outcome measure of safety in mainline general medicine journals at two time points, thirty years apart.
Methods: RCTs published in 1990-1991 vs 2019-2020 in NEJM, JAMA, LANCET and BMJ were searched by 2 independent reviewers (AO and SNE). Phase 1-2 RCTs, post-hoc analyses of RCTs and RCTs reporting long term follow-up data were excluded. RCTs with an undisputable primary endpoint of efficacy were defined as an 'A trial'. Those trials with declared or obvious primary endpoints of 'safety', 'efficacy and safety' or simply as 'efficacy' in which we unanimously considered the presence of serious harm to the patients in the control arms were defined as a 'B trial'. Finally, the trials that we could not unanimously decide whether designate A or B, were designated as C. Discrepancies were resolved after discussion with the senior author (HY) and if, even then, there was no consensus the trial remained as a C. We then compared the frequencies of the types of RCTs which were published in 1990-1991 vs 2019-2020. Other salient features, like the type and the practice setting, of these patients were also tabulated.
Results: There were 309 RCTs published in 1990-1991 and 600 RCTs published in 2019-2020. Nineteen RCTs on COVID-19 infection were excluded for

fair comparisons. As seen in the Table 1 there was a significant increase in the number SOTs in the later years. Moreover, the number of intensive care unit (ICU) trials, a setting in which obtaining informed consents can often be problematic, significantly increased.

Conclusion: Recently, there is a significant increase in the number of SOTs. Moreover, they are more frequently conducted in the ICUs. We strongly re-emphasize that the informed consents of all RCTs, particularly, those related to SOTs should be public. We strongly consider that such action is necessary a. to continue receiving our patients' vital consent to enable us to continue conducting RCTs and b. for justly addressing the organized skepticism of our peers.

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Table 1.

	1990-1991 (n=309)	2019-2020 (n=581)	OR (95% CI)
Total number of RCTs	309	581	
A trial	284 (91.9%)	501 (86.2%)	0.6 (0.3-1.0)
B trial	9 (2.9%)	39 (6.7%)	2.4 (1.1-5.0)
None-A trial*	25 (8.1%)	80 (13.8%)	2.0 (1.1-2.1)
ICU trial	12 (3.8%)	52 (8.9%)	2.4 (1.3-4.6)

* All non-A trials include trials designated B and C.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1615 EVALUATION OF THE NOCEBO EFFECT WHEN SWITCHING FROM THE ORIGINATOR MOLECULE TO A BIOSIMILAR IN A NORMANDY RETROSPECTIVE COHORT OF PATIENTS WITH INFLAMMATORY RHEUMATISM TREATED WITH ETANERCEPT OR ADALIMUMAB (BIONORIC STUDY)

Keywords: Spondyloarthritis, Rheumatoid arthritis, bDMARD

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Background: The cost of treating the major inflammatory rheumatic diseases (rheumatoid arthritis and spondyloarthritis) has increased dramatically since the advent of biotherapies (bDMARD). However, the appearance of the first biosimilars has led to significant healthcare savings. However, the sometimes-negative perception of these treatments by patients and practitioners can lead to the appearance of a nocebo effect.

Objectives: To measure the prevalence of the nocebo effect after switching from an adalimumab (ADA) or etanercept (ETA) originator to one of their biosimilars.

Methods: 183 patients from 4 hospital centers in Normandy (Rouen and Caen University Hospitals, Le Havre and Evreux Hospitals) were included between January 2018 and July 2022 in this retrospective study, within the framework of the Article 51 biosimilars experiment. The subjects had an inflammatory rheumatism (RA or AS) in remission, treated with ADA or ETA originator biological treatment before being switched to a biosimilar. The occurrence of a nocebo effect was considered in patients who did not maintain treatment at 12 months and had a subjective side effect. A comparative analysis of the quantitative data collected was performed before and after the switch. The side effects that led to the discontinuation of the biosimilar were identified. During the switch, a questionnaire was distributed to 30 patients to describe the topics discussed during the consultation and their feelings about the biosimilar. Finally, a univariate and then multivariate analysis was performed to identify potential risk factors associated with the occurrence of a nocebo effect.

Results: The nocebo effect was measured in 13.1% of patients. It was also noted that 9.2% of the group study had presented a side effect objectified by the rheumatologist, and 1.6% mixed side effects. Were considered subjective side effects the sensation of rheumatic recrudescence without objective element found, as well as a certain number of complaints. There were 15.3% of patients who experienced a reactivation of their rheumatism, 8.2% an intolerance, 1.6% an infectious event, 0.5% an allergic reaction. Concerning the evolution under treatment, the comparative analysis did not show any significant difference before and after the switch for the measured parameters, except for the duration of morning stiffness duration in the AS group ($p = 0.01$). Univariate and multivariate analysis did not identify any risk factors associated with the occurrence of a nocebo effect. The responses to the questionnaire made it possible to observe the themes discussed during the consultation (mainly efficacy and cost). The majority of patients interviewed reported that the biosimilar was identical to the originator in terms of safety, efficacy, mode of use and pain at the injection site.

Conclusion: The occurrence of a nocebo effect following a switch to a biosimilar remains acceptable regarding the savings made. It appears less frequent when the switch is supervised by the practitioner, in contrast to the rare data in the literature, where the results differ when the substitution is systematic (up to 33% in some countries). The occurrence of such an effect can be explained by a bad perception of the patient. Therapeutic education as well as a shared medical decision between patient, rheumatologist and pharmacist seems to be essential in a certain population of patients which remains to be defined.

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AB1616 ADHERENCE TO THE LIFE'S ESSENTIAL 8 METRICS AND HYPERURICEMIA : A CROSS-SECTIONAL STUDY

Keywords: Lifestyles, Non-pharmacological interventions, Epidemiology

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Background: Hyperuricemia (HUA) which with a pooled prevalence of 16.4% in mainland China (1) , is a known cause of gout and is linked to chronic disorders such as myocardial infarction, stroke, type 2 diabetes, chronic renal disease, and cardiovascular morbidity (2,3) . The preventive factors against hyperuricemia are thought to be health-related behaviors and factors. As a result, suggestions for healthy habits have been incorporated into the most recent gout and HUA therapy recommendations (4) . Recently, the American Heart Association released their latest cardiovascular health metric "Life's Essential 8" (LE8M) [5]. The LE8M defined cardiovascular health with eight criteria. It contained five health behaviors (nicotine exposure, physical activity, diet, body mass index, and sleep health) and three health factors (blood lipids, blood pressure, and blood glucose). To confirm whether the LE8M could apply to HUA, these beneficial effects in cardiovascular could apply to the HUA, we looked at the connection between adherence to the LE8MScore and the likelihood of having hyperuricemia using the cross-sectional data of more than 90,000 Chinese participants from the Kailuan Study.

Objectives: Although several individual cardiovascular healths are associated with uric acid status, the association of overall cardiovascular health with hyperuricemia remains unclear. We thus examined the association between the Life's Essential 8 metrics and odds of having hyperuricemia in a Chinese adult population.

Methods: Included were 92,912 Chinese participants of the Kailuan Study (mean age: 51.32±12.45y). The Life's Essential 8 metrics were calculated based on five health behaviors (nicotine exposure, physical activity, diet, body mass index, and sleep health) and three health factors (blood lipids, blood pressure, and blood glucose). hyperuricemia was defined as serum uric acid concentrations of ≥7mg/dl for men and women. Association between the Life's Essential 8 metrics and hyperuricemia was assessed using multiple logistic regression models, adjusting for age, sex, marital status, education, income level, alcohol drinking, triglyceride and renal function.

Results: High the Life's Essential 8 metrics score was associated with low odds of having hyperuricemia (adjusted OR for quartile 4 vs. quartile 1=0.64; 95% CI, 0.59 to 0.70; P-trend, <0.001), after adjusting for potential confounders. The association between the Life's Essential 8 metrics and hyperuricemia was more

pronounced among women and younger participants (<45y), compared with their counterparts.
Conclusion: The Life's Essential 8 metrics was associated with a low likelihood of having hyperuricemia in Chinese adults.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1617 DIFFERENCES IN ACCESS TO RHEUMATOLOGICAL CARE OF PATIENTS WITH CHRONIC POLYARTHRITIS AND CONNECTIVE TISSUE DISEASES: A PILOT STUDY USING INTERACTIVE PROCESS MINING ANALYSIS

Keywords: Health services research

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Background: Process mining is a research discipline used to derive process-related knowledge from data on event occurrences at different times. In the healthcare domain, these techniques can be applied to outpatient processes to extract information regarding how they take place and identify inefficiencies or points form improvement.
Objectives: Our aim was to analyze how patients that receive a diagnosis of chronic polyarthritis (CP; including conditions such as rheumatoid arthritis and undifferentiated arthritis) or connective tissue diseases (CTD; such a Systemic Lupus Erythematosus, scleroderma or vasculitis) access a tertiary care level rheumatology outpatient clinic, using novel process mining techniques.
Methods: Retrospective study, including patients first seen at the Hospital Clínico San Carlos Rheumatology Outpatient clinic between 2016 and 2019, belonging to the Hospital Clínico San Carlos Musculoskeletal Cohort. We included those patients receiving ICD10 diagnostic codes, by their attending rheumatologists, compatible with Adult-onset Still's disease, undifferentiated polyarthritis, polymyalgia rheumatica and rheumatoid arthritis (which were later grouped under the category of "chronic polyarthritis"), and myositis, antiphospholipid syndrome, sarcoidosis, Behçet disease, polymyositis, scleroderma, mixed connective tissue disease, Sjögren syndrome, systemic lupus erythematosus, vasculitis and Raynaud's syndrome (which were later grouped under the category of "connective tissue diseases"). Information regarding outpatient activity at the Rheumatology clinic (dates of appointments, if they were a first visit in the clinic or a revision, and which department requested the appointment) was obtained from the Hospital Information System (HIS). Process Mining techniques were used to visualize the pathways followed by the patients included in both categories, and to highlight differences.
Results: 174 patients with CTDs and 341 patients diagnosed with CPs were analyzed. Regarding CPs, most patients were initially referred from Primary Care. Furthermore, most of those patients were not referred from other departments. However, we also can see that some patients undergo several referrals from different departments. Regarding CTDs, although Primary Care seems to be the most common level of referral, other origins are more likely. When the pathways of both disease classifications are compared (Figure 1), we can observe that, compared with CPs, CTDs, have a lower chance of being referred from the Orthopedic Department ("TRA-REU" node in blue) and a higher chance of being referred from "other departments" in secondary care ("REU" node in red). Furthermore, it is less likely that a patient with CTD undergo referrals from different departments and care levels during follow-up (seeing by the lines in blue color connecting the nodes "TRA-REU", "URG-REU", "PRI-REU", and "REU Rev").
Conclusion: In this pilot analysis, we have observed that the pathways followed and the referral departments of the patients diagnosed with CPs and CTDs are different. Process mining can be a very useful tool to characterize and identify the pathways that patients undergo within the healthcare system, across levels and specialties.

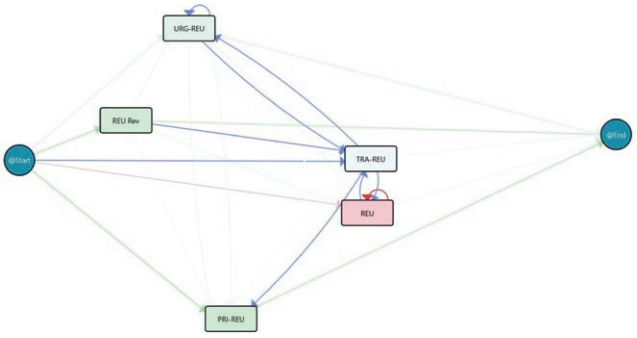


Figure 1. Differences in pathways followed by subjects with connective tissue diseases and chronic polyarthritis (Reu Rev: appointments generated by the emergency rheumatology department; URG-REU: appointments generated by the emergency department; PRI-REU: appointments generated by Primary Care; TRA-REU: appointments generated by the orthopedic department; REU: appointments generated by other departments in secondary care)

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1618 OUTCOMES OF HEPATITIS B AND TUBERCULOSIS SCREENING IN A COHORT OF PATIENTS ON BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (BDMARDS) FOR RHEUMATIC DISEASE AT A MELBOURNE PUBLIC HOSPITAL

Keywords: Vaccination/Immunization, bDMARD, Quality of care

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Background: Screening for hepatitis B and tuberculosis is recommended prior to the commencement of biologic disease modifying anti-rheumatic drugs [1]. However, in routine clinical practice this can easily be overlooked, sometimes with severe consequences.
Objectives: We aimed to identify the percentage of patients screened for hepatitis B and tuberculosis prior to the commencement of bDMARDs in our rheumatology patients. We also determined if immunisation to hepatitis B was discussed in those with no serological evidence of immunity to the disease, and whether individuals with positive quantiferon gold (QTB) serology were referred for treatment prior to commencing bDMARDs.
Methods: All current rheumatology patients on bDMARDs at the Northern Hospital in Epping, Melbourne Australia were included in this study. By retrospectively reviewing the medical records, data was collected regarding patient demographics, clinical information and pre-treatment screening results including hepatitis B and QTB serology. Ethics committee approval was sought from our institution (Reference number: ALR 63.2020).
Results: There were 138 patients on bDMARD included in this analysis. 97 (70%) were female with a mean age of 51 (SD +/-15) at the time treatment was commenced. Rheumatoid arthritis was the most common indication for biologic

therapy (67%) followed by ankylosing spondylitis (15%) and psoriatic arthritis (14%). Tumour necrosis factor inhibitors (TNFi) and Janus kinase inhibitors (JAKi) were most often utilised, prescribed to 72% and 13% of patients respectively. Prior to commencing bDMARDs, 128 (92%) patients were screened for hepatitis B infection. All of these individuals had hepatitis B surface-antigen (HBsAg) tested; 106 (76%) had Hepatitis B surface-antibody (HBsAb) tested and 92 (67%) had hepatitis B core antibody (HBcAb) tested. Among patients screened, 33 (25%) demonstrated immunity to hepatitis B either by previous infection (6%) or vaccination (19%), 1 (1%) were positive for HBsAg and 100 (75%) were susceptible to infection. Of these susceptible individuals, one (1%) was advised to have the hepatitis B vaccinations prior to commencing bDMARDs. Screening for tuberculosis with QTB serology was performed in 125 (90%) patients. Seven (5%) had a positive result and three (2%) were indeterminate. All patients with positive QTB results were referred to infectious diseases for treatment.

Conclusion: Patient demographics such as age, sex and indication for biologic therapy were similar to other bDMARD registries. Pre-treatment screening for hepatitis B was undertaken in most patients and demonstrated a significant number of non-immune individuals. Counselling on the importance of vaccination prior to commencing bDMARDs was rarely documented. There is a need for further counselling on the importance of immunisations in patients on bDMARDs and better access to vaccinations in public hospital rheumatology clinics.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1619 THE INCIDENCE, PREVALENCE AND CHARACTERISTICS OF RHEUMATOID ARTHRITIS ON ARUBA INDICATE AN UNMET NEED FOR AN EARLY ARTHRITIS CLINIC

Keywords: Rheumatoid arthritis, Qualitative research methods, Epidemiology

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Background: A long unmet need was fulfilled in January 2019 with the start of a rheumatology outpatient clinic on Aruba.

Objectives: to assess the incidence, prevalence and patient- and disease characteristics of Rheumatoid Arthritis (RA) on Aruba.

Methods: In this cross- sectional study all health records from RA patients, with an outpatient hospital visit between January 1st of 2019 and 30th of June 2022, were accessed from the hospital database Cerner. Prevalence and incidence rates were determined.

Results: The point prevalence of RA on Aruba (06/30/2022) in the insured population (n = 110.000, i.e. 96% of the total population) was 0.37% (95% C.I.: 0.34% - 0.41%) he estimate half year incidence of RA on Aruba was 0.012%. The female: male ratio within RA patients on Aruba was 4.97:1 with prevalence of 0.57% in women and 0.13% in men. Approximately 25% of RA patients on Aruba had erosions and/or bony deformations, 7% already at time of hospital diagnosis. There was a general delay of 2.5 years since start of symptoms onset until the time of diagnosis.

Conclusion: This study suggests that the prevalence of RA on Aruba is significantly lower than the global, European and North American, pooled prevalence's of 0.46%, 0.54% and 0.70%, respectively [1]. We observed a very long patient – hospital delay, with significantly more joint damage in the newly diagnosed RA patient in comparison to other clinics. Obviously, there is a clear need for an earlier referral of RA patients by primary care physicians to the hospital. Development of an Early Arthritis Clinic could facilitate this process and would ultimately decrease the joint damage of our RA patients.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1620 EMERGENCIES IN RHEUMATOLOGIC DISEASES: A REAL-LIFE EXPERIENCE FROM AN ITALIAN RHEUMATOLOGIC CENTRE

Keywords: Epidemiology, Real-world evidence, Best practices

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Background: Patients with rheumatic diseases (RDs) may present with severe and/or life-threatening conditions which might require hospitalization. RDs recognize a significant diagnostic delay because of variability of clinical features, often mimicking other systemic disorders. Accordingly, patients requiring hospitalization for new-onset emergencies should raise the suspicion of RDs also in absence of a known rheumatologic diagnosis.

Objectives: In this observational single-centre real-life study we analyse prevalence, distribution and management of RDs among patients hospitalized in a 3rd level Rheumatologic ward.

Methods: We collect demographic and clinical data from medical records of patients hospitalized in the Rheumatologic ward of "Tor Vergata" University Hospital in Rome (Italy), between 1st June 2021 to 31st December 2022. Patients are divided into two groups: known RDs at admission (Group 1) and new rheumatologic diagnoses (NRDs) at discharge (Group 2). Mean and standard deviation (SD) express normally distributed variables. Continuous variables are compared with T test, categorical variables by using Chi-square or Fisher's exact test. $P<0.05$ values are considered statistically significant.

Results: The study cohort includes 179 patients (56% women) with a mean age at hospitalization of 62 ±16 y.o. Most of patients (68%) comes from Emergency Room (E.R.), and half of them (47%) has a defined diagnosis of RD at admission (Group 1). Patients admitted for suspected RD are 47 (26% of study population): among them, most cases (n=35, 74%) has NRD at discharge (Group 2). Comparing Group 1 (n=85, 63±14 y.o.) with Group 2 (n=35, 57±19 y.o.) we observe no difference in women prevalence (63% vs 51%) and referral from E.R. (58% vs 74%). Interestingly, diagnosis of rare rheumatological diseases (RRDs) occurs in a similar prevalence in Group 1 (n=37, 43%) and Group 2 (n=14, 40%). The most common reason for hospitalization in Group 1 is disease-flare (53%), followed by acute RD-related complications (27%) and treatment failure (20%). Patients from Group 2 are mainly hospitalized for new-onset severe joint pain (71%) while myalgia (11%), neuropathy (11%) and fever of unknow origin (6%) represent rare cases. In Group 2 a significantly higher proportion of severe inflammatory arthritis ($P=0.008$) and myositis ($P<0.05$) is observed than Group 1. In the two groups we register a similar prevalence of systemic vasculitis, connective tissue diseases, systemic sclerosis, autoinflammatory diseases and primary antiphospholipid syndrome. A slightly higher proportion of patients is treated with steroids in Group 2 than in Group 1 (66% vs 55%). A quarter of patients receives csDMARDS in a similar prevalence; bDMARDs are used only in patients from Group 1 (7%). Rare cases from both groups are treated with intravenous immunoglobulin and prostanoids. In patients with non-rheumatological diseases at discharge (n=59) respiratory (51%) and renal disorders (34%) represent the main reasons for admission. Comparing them with patients with RD diagnosis (Group 1 + Group 2, n=120), a significantly higher prevalence of referral from E.R. results in the first group ($P=0.002$, Table I).

Conclusion: A relevant rate of RRDs occurs among patients requiring hospitalization in a similar prevalence between RDs and NRDs. Moreover, a new rheumatologic diagnosis is confirmed in most patients referring to E.R. in whom emergencies are suspected to be related to RDs. Accordingly, our preliminary data suggest that clinical suspicion for RDs and, thus, early referral to the Rheumatologic Unit should be adequately addressed also among patients from E.R. to improve the diagnostic delay in RD patients.

Table 1. Rheumatologic and non-rheumatologic patients from the study cohort

	Rheumatologic Diagnosis n=120	Non-Rheumatologic Diagnosis n=59
Women, n (%)	71 (59%)	29 (49%)
Age, years (mean±SD)	61±16	65±16
Caucasian, n (%)	117 (97%)	57 (97%)
Referral from E.R., n (%)	74 (62%)	49 (83%)
Duration of hospital stay, days (mean±SD)	10±11	9±7

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1621

REFERRAL BEHAVIOUR OF PRIMARY CARE DOCTORS TO RHEUMATOLOGY CLINIC IN MALAYSIA

Keywords: Quality of care, Health services research

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Background: The workload at rheumatology clinics have been growing relentlessly and an audit on new. referrals helps to identify referral behaviour of primary care doctors and improvement can be done by providing further training.
Objectives: To audit on new referral cases to rheumatology clinic from 2020-2022 and to identify new cases with misdiagnosis for future training purpose.
Methods: This was a retrospective study. The medical records of all new referral to rheumatology clinic Hospital Sultan Ismail and Hospital Pakar Sultanah Fatimah from 1st January 2020 to 31th November 2022 were reviewed. The referral diagnosis and final diagnosis were identified and analysed.
Results: There were total of 927 new cases referral throughout the 35 months during Covid-19 pandemic. Majority of them were diagnosed to have rheumatoid arthritis (217/927) followed by systemic lupus erythematosus (190/927), psoriatic arthritis (147/927), gout (62/927), osteoarthritis (58/927), systemic sclerosis (25/927), ankylosing spondylitis (25/927), soft tissue rheumatism (24/927), Sjogren syndrome (24/927), mixed connective tissue disease (14/927), vasculitis (11/927), fibromyalgia (10/927), polymyositis (7/927) and miscellaneous (39/927). 45 out of the new cases were diagnosed as unlikely rheumatic diseases. There were 29 pending cases awaiting final diagnosis. 212 of the referrals were identified as misdiagnosis with the highest as nodal osteoarthritis. (55/212) followed by unlikely rheumatic disease (43/212), soft tissue rheumatism (24/212), psoriatic arthritis (20/212), Sjogren syndrome (14/212), gout (8/212), rheumatoid arthritis (7/212), fibromyalgia (6/212), systemic lupus erythematosus (5/212), ankylosing spondylitis (4/212), mixed connective tissue disease (3/212), systemic sclerosis (2/212), polymyositis (2/212) and others (19/212): diffuse idiopathic skeletal hyperostosis, hypermobility syndrome, RS3PE syndrome, idiopathic uveitis, graft versus host disease, juvenile idiopathic arthritis, antiphospholipid syndrome, hypothyroidism, post streptococcal arthritis, prolapsed intervertebral disc, cerebrovascular disease, traumatic sternoclavicular joint subluxation, ledderhose disease, paraspinal muscle spasm and viral myalgia).
Conclusion: Nodal osteoarthritis and soft tissue rheumatism can be great mimicker for inflammatory. arthritis and if wrongly diagnosed will lead to unnecessary anxiety or wrong treatment. More training is needed to improve clinical skills amongst primary care doctors.
References: NA.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1622

ARTRO 360: NEW MANAGEMENT MODEL TO PROGRESS IN THE TREATMENT OF OSTEOARTHRITIS BY OPTIMIZING THE AVAILABLE RESOURCES

Keywords: Quality of care, Health services research, Osteoarthritis

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Background: Osteoarthritis (OA) is the most common chronic joint disease and poses a growing public health problem. In Spain, 7 million people suffer from OA [1], and only hip and knee OA represent an average annual cost of 4,738 million euros for the Spanish Health System. In 2016, more than one hundred thousand hip and knee prostheses were placed in Spain [2]. OA generates direct costs and considerable indirect costs for the National Health System, like the associated reduced productivity and labor costs. Therefore, a new OA management model is needed to reduce these expenses by optimizing the available resources.
Objectives: Design and validate a new management model that improves healthcare quality, security, and communication of OA patients.
Methods: The Osteoarthritis Foundation International (OAFI), with the collaboration of the Spanish Association of Osteoporosis and Osteoarthritis (AECOSAR), made an initial proposal with a multidisciplinary expert committee. The different proposals have been reviewed and ratified by scientific and professional organizations of physicians, pharmacists, nurses, and patients.
Results: The model is based on the needs expressed by OA patients and states how the different specialists should intervene and prescribe the most appropriate therapeutic option. The model has three levels of action: preclinical, clinical, and disabling clinical. Several Spanish scientific societies like SEAUS, SECA, SECOT, SETRADE, SER, SEMERGEN, SEMG, semFYC, SEFAC, SEIOM, and SEMDOR have supported the model. The model was presented in the Spanish Senate on September 28th, 2021, and it is being disseminated to the health departments at a regional level. Below are some of the proposals for the model:

- •Promote the participation of patients and professionals in public health policies, research, and management models.
- •Involve the patient in the decisions that affect them, making them responsible for their health and self-care.
- •Accelerate the diagnosis.
- •Facilitate access to optimal pharmacological and non-pharmacological treatment, taking into account the comorbidities and needs of the patient.
- •Raise awareness of the relevant role of patient organizations as an active resource that complements the portfolio of services, strengthens professionals, and produces significant economic savings.

Conclusion: OA is the most common chronic joint disease and poses a growing public health problem. OAFI, with the support of several scientific societies, has developed a new management model to progress in treating OA by optimizing the available resources. With this program, it will be possible to reduce the cost of OA by approximately 100 million euros while improving the quality of health care for our patients. To implement it, it is essential to take coordinated action by health authorities, scientific health authorities, scientific and professional societies, patient organizations, and other relevant organizations.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1623

INFLAMMATORY RHEUMATISM AND WORK: WHAT DIFFICULTIES IN RELATION WITH THE CHARACTERISTICS OF THE JOB?

Keywords: Inflammatory arthritides, Qualitative research methods, Work-related issues

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Background: Despite improvements in the management of inflammatory arthritis (IA), the disease still has a significant impact on work and the support for patients with professional difficulties remains insufficient. Occupational physicians and occupational health specialists are not all aware of the specific impact of IA on difficulties at work and sometimes think that all patients complaining of physical limitations are identical and require the same support.
Objectives: The objective of the study is to better understand the difficulties at work, in particular difficulties related to the employment characteristics of patients with IA.
Methods: 32 individual semi-directed interviews and 2 group interviews were conducted with patients with IA recruited in consultations or by patient associations. The participants were recruited according to a. purposive sampling with maximum variation. Inclusion criteria were: age 18 to 65 years, have IA, be professionally active, have difficulties or concerns at work due to the disease. The interviews. were conducted with an interview guide and were recorded and transcribed in full. The thematic analyses were conducted using an inductive approach.
Results: The analysis of difficulties related to the characteristics of the employment of patients with IA are numerous: physical load of the workstation; speed required by the job; simultaneous tasks; multiple tasks and flexibility; workload; working hours and schedules; routine, scheduling, commuting, job awareness, responsibilities and moral demands; cognitive characteristics; conflict of values; skills and experience; interpersonal characteristics; lack of material resources, inappropriate premises; autonomy, environment and culture of the company; productivity demands and evaluations, job insecurity or security; perceived maladjustment; isolation; lack of recognition. The difficulties are not always specific to patients with IA but are clearly aggravated by the disease for a good number of them. The patients describe the specificities of their difficulties.
Conclusion: Patients discuss multiple characteristics of employment that can be a hardship or an advantage. They explain how the disease makes these characteristics difficult for them. These data will be useful to occupational health occupational health professionals and clinicians to help patients keep their jobs in good condition and develop appropriate services.

These data will help to improve the training of occupational health occupational and to develop a questionnaire for the assessment of the work situation of patients with IA.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Anne-Christine Rat Speakers bureau: Pfizer, Lilly, Sanofi Genzyme, Abbvie, BMS, Galapagos, novartis, Isabelle Thaon: None declared, Deboreh Loyal: None declared.

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AB1624 MUSCULOSKELETAL PROBLEMS IN YOUNG DOCTORS

Keywords: Epidemiology, Pain, Work-related issues

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Background: Musculoskeletal problems (MSP) represent a major problem in the general population and also in occupational settings. Young interns and residents in medicine are exposed to different types of physical constraints (e.g., working long hours, lifting and carrying heavy objects, repetitive movements, etc.), which may lead to musculoskeletal disorders.

Objectives: Evaluate MSP in interns and residents working in the University Hospitals of Sfax, Tunisia.

Methods: We conducted a study during the month of January 2023 using the Nordic questionnaire to screen MSPs. The questionnaire was self-administrated and evaluated along with MSPs on the sociodemographic characteristics and perceived work strain measured with the borg scale.

Results: Our population consisted of 147 interns and residents. The sex ratio was 0.48 and the mean age was 25.41±2.12. Most participants were interns and 1st-year residents (53.7% and 19.7% respectively). Smokers represented 5.4% of the total population. The mean Body Mass index was 22.77± 3.7 and 20.8 % of the population presented as overweight or obese. Among the participants, 6.1% had priors of MSPs. Sixty young doctors (40.8%) reported practising a regular leisure activity with a mean of 3.76+-2.99 hours per week. The physical strain was 6.75± 2.32. Fifty-eight individuals (39.5%) reported having MSPs in the past year and twenty-four (16.3%) during the past week. Neck pain was the most frequent complaint (37.9%) in the past year followed by back pain (24.13% for the upper back and 22.4% for the lower back). The higher perceived physical strain was associated with more frequent musculoskeletal problems during the previous week ($p<0.01$) and priors of MSP were associated with more frequent complaints in the previous year($p<0.01$). BMI was not associated with the presence of MSPs. Smoking tobacco seemed to be a protective factor against neck pain ($p=0.016$).

Conclusion: Exposure to musculoskeletal constraints is frequent in interns and residents and is often underdiagnosed. More attention is needed for this young population to prevent them from developing chronic MSDs in the future.

References: NA.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1625 QUALITY OF LIFE OF PATIENTS WITH RHEUMATIC DISEASES

Keywords: Outcome measures, Quality of life, Comorbidities

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Background: Patients with rheumatic diseases (RD) have more comorbidities and worse health-related quality of life (HRQoL) than the general population. It is recommended that HRQoL be collected in medical records, but it is rarely done in routine clinical practice [1]. RD are among the most common chronic diseases in the general population, which means a large consumption of resources in Primary and Specialized Care. Therapeutic decisions in Rheumatology are usually based on levels of activity measured with disease-specific tools. However, several studies have shown differences between what is perceived by the doctor and what is declared by the patient [2].

Objectives: HRQoL is considered an important indicator to assess the state of population health and measure the impact of medical actions [3,4]. The main objective of this study is to know the HRQoL of patients with RD and compare it with the general population.

Methods: Observational, cross-sectional, single-centre study, with consecutive inclusion of outpatients over 18 years of age seen in the rheumatology hospital outpatient clinic. Sociodemographic and clinical variables were collected, as well as HRQL measured with the 5-dimensional, 5-level EuroQoL (EQ-5D-5L), which includes the EQ-Index (0-1 scale) and a visual analogue scale (VAS, 0-100 scale). A descriptive analysis and a comparison with the Spanish population according to the National Health Survey were carried out.

Results: 1,144 patients were included, 820 (71.68%) of whom were women, with a mean age of 56.1 years (range 18-95). 241 (25.44%) were new patients. In patients with RD, the HRQoL measured with the EQ-Index and with the VAS, was 0.186 and 12 points lower, respectively, than in the general population. HRQoL affected the 5 health dimensions, especially "pain/discomfort", followed by "daily activities" and "mobility". This reduction in HRQoL was maintained in both men and women, and in all age segments, although it was greater between 18 and 65 years of age. The reduction in HRQoL affected all RD subtypes, especially the "Peripheral and axial mechanical pathology" and the "Soft tissue pathology" group.

Conclusion: Patients with RD report worse HRQL compared to the general population in all HRQoL dimensions.

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Table 1. Comparation of EQ-Index of EQ-5D-5L between HURyC-RD patients and Spanish adult general population, according to sex and age.

Variable	Category	HURyC-RD Patients			Spanish adult general population (ENSE)			Difference of means	p*
		EQ-Index			EQ-Index				
		n	Median	SD	n	Median	SD		
Gender	Male	304	0,788	0,184	9.412	0,938	0,138	-0,150	0,000
	Female	755	0,703	0,236	11.175	0,892	0,159	-0,189	0,000
Age (years)	18-24	36	0,858	0,143	1.236	0,976	0,098	-0,117	0,000
	25-34	73	0,818	0,178	2.757	0,970	0,109	-0,152	0,000
	35-44	164	0,746	0,203	3.951	0,950	0,127	-0,204	0,000
	45-54	241	0,740	0,214	3.574	0,928	0,141	-0,188	0,000
	55-64	257	0,698	0,227	3.173	0,899	0,150	-0,201	0,000
	65-74	158	0,756	0,213	2.731	0,865	0,154	-0,109	0,000
	75-84	102	0,659	0,271	2.350	0,781	0,167	-0,122	0,000
	85+	28	0,473	0,233	815	0,625	0,182	-0,152	0,002
Total		1.059	0,728	0,226	20.587	0,914	0,150	-0,187	0,000

EQ-5D-5L: EuroQoL of 5 dimensions and 5 levels; HURyC-RD: Ramón y Cajal University Hospital Rheumatology Department; ENSE: National Health Survey of Spain 2011-2012; S.D.: Standard deviation. * Student's t test for independent samples. **Could not calculate statistical significance due to lack of n and S.D.

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Epidemiology, risk factors for disease or disease progression

AB1626

ASSOCIATION BETWEEN PRIOR SEVERE CUTANEOUS ADVERSE REACTIONS(SCARS) AND SUBSEQUENT AUTOIMMUNE DISEASE RISK: A NATIONWIDE POPULATION-BASED COHORT STUDY

Keywords: Epidemiology, Real-world evidence, Safety

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Background: Life-threatening severe cutaneous adverse reactions (SCARs) include Stevens-Johnson syndrome/toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and drug-induced hypersensitivity syndrome/drug reaction with eosinophilia and systemic symptoms. Previous report revealed that a gradual loss of regulatory T (Treg) cell function after resolution of SCARs may increase the risk of subsequently developing autoimmune diseases (ADs). The association between patients with SCARs and ADs remain unclear and are scarce.

Objectives: This study explored the association of SCARs with AD risk.

Methods: Individuals with SCARs between 2006 and 2015 were identified and 1:10 matched on age and sex with individuals without SCARs. We performed multivariate and stratified analysis using the Kaplan–Meier method and Cox proportional hazards models in order to estimate the association between SCAR cohort and the risk of developing ADs.

Results: A total of 26844 patients with SCAR and 268440 non-SCAR comparison subjects were selected from NHIRD. For individual organ-specific ADs, SCAR cohort as compared with non-SCAR cohort, adjusted hazard ratio (aHR) were higher for incident autoimmune hemolytic anemia (aHR 3.36, 95% CI: 1.84-6.13), Hashimoto's thyroiditis (aHR 2.26, 95% CI: 1.64-3.12), Henoch-Schonlein purpura (aHR 8.99, 95% CI:6.53-12.4) and inflammatory bowel disease were (aHR 9.78, 95% CI:5.27-18.5) (see Table 1). Furthermore, for individual systemic ADs, SCAR cohort as compared with non-SCAR cohort, aHR were higher for incident ankylosing spondylitis(aHR 1.56), psoriasis(aHR 10.39), polymyositis/dermatomyositis (aHR 10.39), rheumatoid arthritis(aHR 2.48), primary Sjogren syndorme(aHR 5.92), systemic lupus erythematosus(aHR 9.58), systemic sclerosis(aHR 7.56) and systemic vasculitis (aHR 13.54).(see Table 1)

Conclusion: Patients with SCARs have higher risk of ADs than patients with no SCARs. Further mechanistic research should be conducted.

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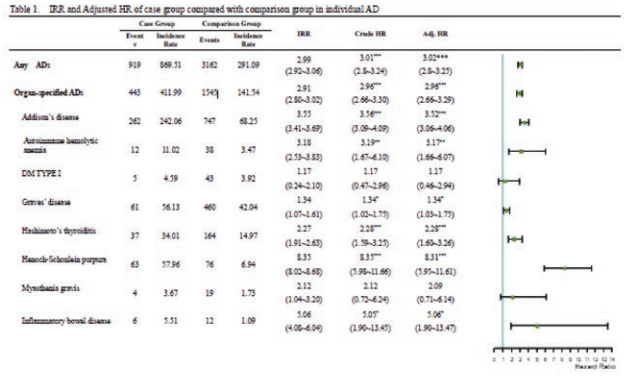
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Table 1. IRR and Adjusted HR of case group compared with comparison group in individual AD

	Case Group		Comparison Group		IRR	Crude HR	Adj. HR
	Event	Incidence Rate	Events	Incidence Rate			
Any ADs	919	869.51	3162	291.09	2.99 (2.92-3.06)	3.01*** (2.8-3.24)	3.02*** (2.8-3.25)
Organ-specified ADs	443	401.99	1543	141.54	2.91 (2.80-3.02)	2.96*** (2.66-3.30)	2.96*** (2.66-3.29)
Addison's disease	262	242.06	747	68.25	3.55 (3.41-3.69)	3.56*** (3.09-4.09)	3.52*** (3.06-4.06)
Autoimmune hemolytic anemia	12	11.02	38	3.47	3.18 (2.53-3.83)	3.19** (1.67-6.10)	3.17** (1.66-6.07)
DM TYPE I	5	4.59	43	3.92	1.17 (0.24-2.10)	1.17 (0.47-2.96)	1.17 (0.46-2.94)
Grevas' disease	61	56.13	460	42.04	1.34 (1.07-1.61)	1.34* (1.02-1.75)	1.34* (1.03-1.75)
Hashimoto's thyroiditis	37	34.01	164	14.97	2.27 (1.91-2.63)	2.28*** (1.59-3.25)	2.28*** (1.60-3.26)
Henoch-Schonlein purpura	63	57.96	76	6.94	8.35 (8.02-8.68)	8.35*** (5.96-11.66)	8.31*** (5.95-11.61)
Myasthenia gravis	4	3.67	19	1.73	2.12 (1.04-3.20)	2.12 (0.72-6.24)	2.09 (0.71-6.14)
Inflammatory bowel disease	6	5.51	12	1.09	5.06 (4.08-6.04)	5.05* (1.90-13.45)	5.06* (1.90-13.47)



Systemic ADs	506	472.93	1660	152.21	3.11 (3.01-3.21)	3.11*** (2.81-3.43)	3.12*** (2.82-3.44)
Ankylosing Spondylitis	57	52.43	403	37	1.42 (1.14-1.7)	1.42* (1.08-1.87)	1.42* (1.08-1.88)
Psoriasis	246	227.78	825	75.46	3.02 (2.88-3.16)	3.02*** (2.62-3.49)	3.03*** (2.62-3.49)
Polymyositis and dermatomyositis	14	12.86	14	1.28	10.05 (9.31-10.79)	10.09*** (4.81-21.15)	10.05*** (4.79-21.07)
Rheumatoid arthritis	44	40.46	184	16.8	2.41 (2.08-2.74)	2.41*** (1.74-3.35)	2.42*** (1.74-3.37)
Primary Sjogren's syndrome	70	64.41	156	14.24	4.52 (4.24-4.8)	4.52*** (3.41-6.00)	4.53*** (3.42-6.01)
Systemic lupus erythematosus	56	51.53	65	5.93	8.69 (8.33-9.05)	8.69*** (6.08-12.43)	8.73*** (6.11-12.48)
Systemic sclerosis	5	4.59	8	0.73	6.29 (5.17-7.41)	6.33* (2.07-19.34)	6.35* (2.08-19.4)
Systemic vasculitis	27	24.81	20	1.82	13.63 (13.05-14.21)	13.64*** (7.65-24.31)	13.54*** (7.60-24.14)

*P-value<0.05 **P-value<0.001 ***P-value<0.0001
AD: autoimmune disease
Incidence Rate per 100,000 person-year

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1627

DYNAMICS OF IMMUNOLOGICAL PARAMETERS IN PATIENTS WITH SLE DURING THE YEAR AFTER VACCINATION WITH 23-VALENT POLYSACCHARIDE PNEUMOCOCCAL VACCINE

Keywords: Systemic lupus erythematosus

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Background: Pneumococcal vaccination in systemic lupus erythematosus (SLE) is designed to reduce the risk of severe respiratory infections in this group of patients. The issues of vaccination safety remain relevant.

Objectives: to study the dynamics of immunological parameters in patients with SLE during the year after vaccination with 23-valent polysaccharide pneumococcal vaccine (PPV-23), their correlation with the clinical picture of the disease.

Methods: 78 patients with SLE were included in the study. 4 patients received monotherapy (GC-1, methotrexate-1, GC-1, anti-B-cell therapy-1), the rest received combination therapy, including 29 - anti-B-cell therapy. 3 groups of patients were identified for analysis: 1. patients (36) who received stable doses of immunosuppressive drugs. 2. patients (31) who had their medication doses reduced during the year. 3. patients (11) who received increased doses of medications during the year. The follow-up period was 12 months after vaccination.

Results: During the observation period, no new autoimmune phenomena, both clinical and laboratory, were recorded. Stable therapy group: in the first 1-3 months after vaccination, 4 out of 36 patients had a transient increase in a-DNA without an increase in ANF and without signs of exacerbation of the disease. Another 4 had an increase in ANF (1 had a transient increase), without an increase in a-DNA and without signs of deterioration. By 12 months, there was an increase in a-DNA in 4 and ANF in 5 patients. Moderate exacerbation of the disease was recorded in 3 patients (after 3.5 months, 5 months, 12 months): in the first case, persistently high immunological activity and clearly insufficient therapy were observed; in the second case, the exacerbation was not accompanied by an increase in immunological activity at all; in the third case, the exacerbation occurred after 12 months with a moderate increase in immunological activity

indicators. In all cases, the association with vaccination has not been verified. The group on the reduction of doses of therapy: 5 cases of a significant increase in a-DNA after 1-3 months were recorded: in 4-transient, in 1-with a transient increase in ANF, in all without signs of exacerbation. Moderate exacerbation was observed in 4 patients (after 4 months, 11.5 months, 12 months, 12 months), in 2 – without an increase in immunological activity, in 2 – with an increase in a-DNA and ANF by 11-12 months. The timing of the exacerbation, the cancellation of cytostatics in one case and a reduction in the dose of glucocorticoids in 3 cases did not allow the exacerbation to be associated with vaccination. Group of patients with increased therapy: no cases of significant increase in a-DNA, ANF, exacerbation of the disease was detected.

Conclusion: 1. The multidirectional dynamics of the main immunological markers observed during the year most likely reflects the immunological instability characteristic of SLE. 2. In the first 3 months after vaccination, in isolated cases, a transient increase in SLE markers is possible without symptoms of exacerbation of the disease. 3. During the year, there were no exacerbations significantly associated with vaccination. 4.There is no need for mandatory immunological monitoring 1-3 months after vaccination, clinical monitoring is necessary.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1628 THE INCIDENCE AND PREVALENCE OF RHEUMATOID ARTHRITIS IN ITALY IN THE LAST DECADE

Keywords: Registries, Epidemiology, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) prevalence is believed to be around 1% worldwide, although it varies considerably among different populations.[1] Several environmental factors such as smoking, certain infections, and diet contribute to the risk of RA and differ between populations.[2] The pooled prevalence of RA was estimated to be 0.54% (95% CI 0.50–0.59) in Europe,[1] but no studies have recently evaluated the epidemiology of RA in Italy.

Objectives: We aimed at estimating the incidence and prevalence of RA in northeastern Italy over the period 2012–2020.

Methods: A retrospective population-based study was conducted in the Veneto Region (4.9 million people) using the Population Registry, an administrative health database where all residents are recorded. The population registry was linked with healthcare co-payments exemptions, hospital discharge records, and mortality records. Between 2012 and 2020, RA prevalence was defined by a healthcare copayment exemption for RA (national registry code 006) or any hospital diagnosis of RA (ICD-9-CM 714.x), whichever came first. Incident RA was defined from 2013 to 2020 to exclude prevalent cases. Standardized incidence and prevalence rates were reported by age and gender.

Results: During the study period, we identified 37,996 prevalent RA patients, with 12,875 incident cases. Across the study period, RA standardized prevalence increased from 0.50% (95% CI 0.50; 0.51) to 0.57% (95% CI 0.57; 0.58). RA point prevalence in 2020 according to gender and age is reported in Figure 1. RA incidence corresponded to 33.1 (32.5; 33.7) per 100,000 person-years, with the lowest incidence observed in the last two years of the study: 27.4 (25.9; 28.9) in 2020 and 32.2 (30.6; 33.8) in 2019 (Table 1). The peak for both prevalence and incidence was around the eighth decade of life. Incidence was 2-times higher in females: female-to-male incidence rate ratio (IRR) 2.3 (2.2; 2.4) (p<0.0001), with a peak among people aged 20-29 years, where female-to-male IRR was 3.1 (2.4; 3.9) and the lowest value among patients aged ≥70 years, where F:M IRR was 1.6 (1.4; 1.8).

Conclusion: The prevalence of RA in Italy is 0.57%, in line with data from other European countries. Incidence was confirmed to be higher among females, especially in younger patients.

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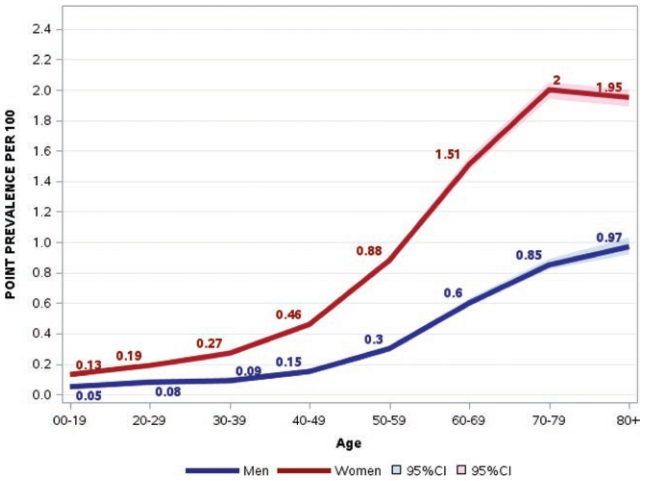


Figure 1. The point prevalence of Rheumatoid Arthritis in The Veneto Region in 2020 by age and gender.

Table 1. Incidence of Rheumatoid Arthritis in the Veneto Region between 2013 and 2020.

Year	New diagnosis, number	Population	Crude rate (95%IC) x 100,000	Standardized IR (95%IC) x100,000*	New diagnosis, number		Standardized IR (95%IC) x100,000*	
					Male	Female	Male	Female
2013	1.615	4.901.415	32.9 (31.3; 34.6)	34.2 (32.5; 35.8)	475	1140	20.8 (18.9; 22.7)	46.9 (44.1; 49.6)
2014	1.738	4.905.712	35.4 (33.8; 37.1)	36.4 (34.7; 38.1)	508	1230	21.9 (20.0; 23.9)	50.2 (47.3; 53.0)
2015	1.575	4.902.694	32.1 (30.5; 33.7)	32.7 (31.1; 34.3)	462	1113	19.8 (18.0; 21.6)	45.0 (42.4; 47.7)
2016	1.625	4.890.648	33.2 (31.6; 34.8)	33.5 (31.9; 35.2)	487	1138	20.7 (18.8; 22.5)	45.8 (43.1; 48.5)
2017	1.651	4.883.373	33.8 (32.2; 35.4)	33.8 (32.2; 35.4)	461	1190	19.4 (17.6; 21.1)	47.6 (44.9; 50.3)
2018	1.710	4.880.936	35.0 (33.4; 36.7)	34.8 (33.1; 36.4)	504	1206	20.9 (19.1; 22.7)	48.0 (45.3; 50.7)
2019	1.596	4.884.590	32.7 (31.1; 34.3)	32.2 (30.6; 33.8)	463	1133	19.0 (17.3; 20.8)	44.8 (42.2; 47.4)
2020	1.365	4.879.133	28.0 (26.5; 29.5)	27.4 (25.9; 28.9)	406	959	16.5 (14.9; 18.1)	37.8 (35.4; 40.2)
TOT**	**12.875**	**39.128.501**	**32.9 (32.3; 33.5)**	**33.1 (32.5; 33.7)**	**3766**	**9109**	**19.9 (19.2; 20.5)**	**45.7 (44.8; 46.6)**

Acknowledgements: NIL.

Disclosure of Interests: Margherita Zen Speakers bureau: Abbvie, Ely Lilly, GSK, Galapagos, AstraZeneca, Laura Salmaso: None declared, Claudio Barbiellini Amidei: None declared, Alessandro Giollo Speakers bureau: Galapagos, Abbvie, Ugo Fedeli: None declared, Stefania Bellio: None declared, Federico Arru: None declared, Ilenia Gennaio: None declared, Mario Saia: None declared, Andrea Doria Speakers bureau: GSK, AstraZeneca, UCB, Pfizer, Consultant of: GSK, AstraZeneca.

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AB1629 PREVALENCE OF MUSCULOSKELETAL AND WIDESPREAD PAIN IN A REPRESENTATIVE COHORT OF THE FRENCH GENERAL POPULATION

Keywords: Epidemiology, Pain

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Background: Few studies include a sufficient number of people to be representative of a general population and to estimate the musculoskeletal pain prevalence.
Objectives: To estimate the prevalence of musculoskeletal and widespread pain in the French popualtion using a large and representative cohort.
Methods: The Constances cohort is composed of volunteers, aged 18 to 69 years at inclusion. Eligible subjects were selected at random by stratified sampling with unequal probabilities, over-representing individuals with a higher probability of not volunteering (according to their age, sex, socioprofessional category) with adjustment coefficients weight participation bias. Individuals diagnosed with a cancer were excluded. Musculoskeletal pain was assessed by the Nordic Questionnaire. Significant pain lasted at least 30 days during the last 12 months. Widespread pain concerned at least 4 of the 6 areas. Chronic moderate to severe pain reached a pain score ≥ 4/10 in the last 7 days. Data from the entire cohort were described and then the French population prevalence was estimated, based on people included in 2017 with adjustment coefficients.
Results: 193,436 people were included in the cohort. The French population prevalence of each pain location and widespread pain were estimated among the 25,472 people included in 2017.

	Pain prevalence in the cohort (%)	Moderate to severe pain prevalence in the cohort (%)	Pain prevalence estimation in the french population (% [SD])	Moderate to severe pain prevalence estimation in the french population (% [SD])
Back	24.6	16.0	25.9 [25.4-26.5]	17.9 [17.4-18.4]
Neck	16.6	10.4	17.1 [16.7-17.6]	11.2 [10.8-11.6]
Shoulder	16.3	9.4	17.0 [16.5-17.5]	10.5 [10.1-10.8]
Knee	18.9	11.1	19.8 [19.3-20.2]	12.4 [12-12.8]
Hand	14.0	7.7	14.7 [14.2-15.1]	8.5 [8.2-8.8]
Elbow	8.5	4.3	9.2 [8.2-9.6]	4.9 [4.7-5.2]
Widespread pain	7.0	3.	8.1 [7.8-8.5]	4.2 [4-4.5]

Conclusion: The prevalence of musculoskeletal pain in the French population is high, particularly for chronic pain of moderate to severe intensity, which underlines the need to improve their detection, prevention and management.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1878

AB1630

RISK FACTORS FOR CARDIAC INVOLVEMENT IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Keywords: Cardiovascular disease, Heart, Myositis

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Background: Idiopathic inflammatory myopathies (IIMs) are heterogenous systemic autoimmune disorders that mainly affect the skin, muscles, and lungs. Whereas cardiac involvement is considered to be rare, it causes cardiac inflammation and fibrosis leading to severe morbidity and mortality. However, little is known about clinical characteristics and risk factors for cardiac involvement in patients with IIMs.
Objectives: The aim of this study was to clarify the frequency and clinical characteristics of cardiac involvement and its risk factors in patients with IIMs.
Methods: We retrospectively reviewed consecutive patients with IIMs who visited Keio University Hospital from 2002 to 2022. We divided patients into two groups according to the presence or absence of symptomatic cardiac involvement and compared their clinical characteristics and autoantibodies between the two groups. We defined symptomatic cardiac involvement as the presence of chest pain, palpitation, cardiogenic leg edema, or respiratory distress accompanied by abnormal findings of cardiac examinations such as electrocardiography, echocardiography, and/or cardiac magnetic resonance imaging (MRI).
Results: We included 145 patients with IIMs in the analysis. The mean age at IIMs diagnosis was 55 years old, and 71.7% were female. Forty patients (27.6%) were polymyositis, 53 (36.6%) were dermatomyositis, 44 (30.3%) were amyopathic dermatomyositis, and 8 (5.5%) were immune-mediated necrotizing myopathy. Among them, 52 patients (35.9%) had abnormal findings on electrocardiography, echocardiography, and/or cardiac MRI, and 17 (11.7%) were diagnosed with symptomatic cardiac involvement at the mean age of 65 years during the mean observation period of 20.0 years. Comparison of clinical characteristics identified no difference in the mean age, sex distribution, and duration from IIM diagnosis to symptomatic cardiac involvement between the two groups. Also, no significant difference was found in the positivity of anti-amynoacyl tRNA synthetase antibody, anti-MDA5 antibody, and anti-SS-A antibody, IIMs subtypes, presence of skin rash, malignancy, interstitial lung disease, history of cyclophosphamide use, and maximum levels of CK, aldolase, CK-MB, troponin T, and CRP. However, the presence of Raynaud's phenomenon and neutrophil/lymphocyte ratio at diagnosis were significantly higher in the cardiac involved group compared to the non-cardiac involved group (53.85% vs 15.24%, p=0.0009; 56.25% vs 18.25%, p=0.0006). Multivariable analysis identified Raynaud's phenomenon (odds ratio [OR] 8.42, 95% confidence interval [CI] 2.10-33.8, p=0.0026) and elevated neutrophil/lymphocyte ratio (OR 6.92, 95% CI 1.73-27.6, p=0.0061) as independent risk factors for symptomatic cardiac involvement. One patient in the cardiac involved group died of cardiac failure during the observation period.
Conclusion: Abnormal findings in cardiac examinations and symptomatic cardiac involvement are frequent in patients with IIMs. Evaluating cardiac involvement is important, especially in patients with Raynaud's phenomenon and elevated neutrophil/lymphocyte ratio at diagnosis.
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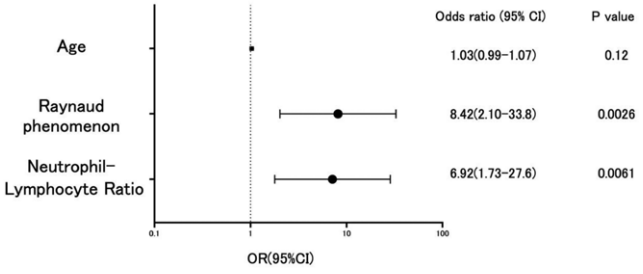


Figure 1. Risk factors for cardiac involvement in inflammatory myopathies

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1631

ASSOCIATION BETWEEN HYPERURICEMIA AND HEARING IMPAIRMENT: RESULTS FROM THE KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

Keywords: Gout

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Background: Hyperuricemia is associated with variety of comorbidities. Researchers suggest that the inflammation and increased oxidative stress produced by uric acid can impact the auditory system.
Objectives: This study investigated the association between hyperuricemia and hearing impairment in Korean adults.
Methods: Audiometric and laboratory test data from the 2019 to 2020 Korean National Health and Nutrition Examination Survey (KNHANES) were used for analysis. Hearing impairment was defined as a pure tone average (0.5,1,2,4 kHz) threshold level of ≥ 41 desibels (dB)s. Definition of hyperuricemia was different in males and females (>7 mg/dL in males and >6 mg/dL in females.
Results: A total of 4,857 (weight n = 17,990,725) subjects were analyzed. Mean age was 56.8 years old and female was 51.7%. Weighted prevalence of hyperuricemia was 12.1%. and hearing impairment was 13.4%. In univariable analysis, hyperuricemia was significantly associated with hearing impairment, but diagnosis of gout was not associated with hearing impairment. In multivariable analysis, hyperuricemia (Odds ratios [OR] 1.41, 95% confidence interval [CI] 1.03-1.92, p = 0.030) was associated with hearing impairment along with age (OR 1.12, 95% CI 1.10-1.14, p < 0.001), female (OR 0.43, 95% CI 0.34-0.64, p < 0.001), education (OR 0.43, 95% CI 0.30-0.63, p = 0.001), and occupational noise exposure (OR 1.67, 95% CI 1.25-2.22, p = 0.001). In subgroup analysis, hyperuricemia was associated with hearing impairment in female group and elderly group aged 60

years or older (OR 1.59, 95% CI 1.02-2.48, p = 0.041 and OR 1.45, 95% CI 1.05-1.99, p = 0.023, respectively).

Conclusion: Hyperuricemia was independently associated with hearing impairment especially in female and older ages.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1632 PREVALENCE OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AT THE REFERRAL CENTERS IN ITALY: A MULTICENTER STUDY

Keywords: Systemic lupus erythematosus, Epidemiology

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease mostly affecting the young women during their third-fourth decade of life. SLE is characterized by variable manifestations and, potentially, every organ can be involved. The course and the complexity of the disease, naturally appeal to manage patients with SLE at high qualified national referral centers. [1]

Despite the relevant burden associated with the disease, both from patient and physician point of view, epidemiological data on SLE in Italy are limited to isolated estimates, captured by different data sources [2-5]; however, no larger data on the prevalence of SLE at the referral centers in Italy are available to date.

Objectives: This study aimed at estimating the prevalence of SLE at tertiary referral Italian centers, representative of the Italian scenario.

Methods: We conducted an observational, cross-sectional study on SLE patients followed by referral centers in district, representative of the North, Centre, South and Isles of Italy (Brescia, Padua, Udine, Ferrara, Florence, Pisa, Rome, Bari, Naples, Cagliari). Data from patients of both sexes and any age, and fulfilling the 2019 ACR/EULAR classification criteria, were obtained from hospital medicals records. To estimate the prevalence, we reported the number of patients with SLE referring to the considered centers (numerator), over the total population resident in the included Italian districts (denominator), according to the Italian National Statistical Institute (ISTAT), responsible for the Italian general population censuses. For the analysis, we considered only complete data sent by January 13th, 2023. [7]

Results: We identified 3251 patients with SLE followed at n° 9 referral centers included in this study. 1163/3251 patients (89.3%) were female, and 1302/3251 (40%) were residing in the districts of the referral centers. The estimated overall prevalence of SLE was 21.37 cases per 100,000 individuals. As we stratified the results by geographical area (North, Centre, South and Islands) of Italy, the estimated prevalence ranged from 14.7 to 27.1 cases per 100,000 individuals. (**Table 1**)

Conclusion: Our study estimated the prevalence of SLE in multiple representative Italian referral centers. These preliminary results show for the first time the proportion of patients with SLE attending tertiary referral centers in Italy, suggesting a different distribution in diverse geographical areas of the country.

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Table 1.

	North	Center	South and Isles	Overall
Number of SLE patients followed at the referral centers involved in the study	1728	827	696	3251
Patients residing in the district of the centers (%) involved in the study	824 (47.7%)	230 (27.8%)	272 (39.1%)	1302 (40%)
Number of female (%) patients residing in the district of the centers involved in the study	734 (89.1%)	183 (88.8%)	246 (90.4%)	1163 (89.3%)
Prevalence (cases per 100,000 individuals)	27.1	16.4	16.5	21.8

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AB1633 PREVALENCE TREND OF EGPA AND ANNUAL CHANGES IN ORAL CORTICOSTEROID USE BY PATIENTS WITH EGPA FOLLOWING MEPOLIZUMAB AVAILABILITY IN JAPAN

Keywords: Real-world evidence, Epidemiology, Vasculitis

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Background: Treatment of eosinophilic granulomatosis with polyangiitis (EGPA) relies predominantly on corticosteroids which are associated with significant adverse effects when used long-term. Therefore, alternative corticosteroid-sparing therapies are needed. Mepolizumab specifically targets IL-5, a key driver of eosinophilic inflammation, and was approved in Japan for the treatment of EGPA in 2018.

Objectives: To describe the prevalence of EGPA over time and changes in OCS daily dose used by patients with EGPA in Japan.

Methods: This retrospective study used the Japanese health insurer claims database (JMDC) to describe EGPA prevalence 2005–2020. The Japanese hospital database (Medical Data Vision [MDV]) was used to describe annual mean daily doses of OCS used by patients with EGPA, comorbidities associated with OCS use, and relapse rates of EGPA 2010–2020. Patients with a record of EGPA in the year of interest and a record of allergic rhinitis, eosinophilic chronic sinusitis or asthma were included, excluding those with granulomatosis with polyangiitis and microscopic polyangiitis, before or during the year of interest. Relapse was assessed in patients who revisited the hospital and was defined as initiation of new OCS (non-OCS users), doubling of existing OCS daily dose, or use of injectable corticosteroid pulse therapy among patients who received continuous treatment from the previous year or earlier. A sub-analysis of the JMDC database assessed OCS daily dose used by patients with EGPA who initiated treatment with mepolizumab 300 mg 2018–2020.

Results: From the JMDC database, ~7.3 million subscribers were included for EGPA prevalence estimations. The reported annual crude prevalence of EGPA increased from 4.2 per million in 2005 to 58.6 per million in 2020 with a greater

prevalence in older age groups (prevalence per million in 2020: <18 years: 7.5; 18–39 years: 42.5; 40–64 years: 93.1; and 65–74 years: 181.3).
From the MDV database, 1870 patients with EGPA were included in 2020, 59.9% of whom were female, and 5.2% were aged 18–39 years, 36.4% 40–64 years, 30.6% 65–74 years, and 27.4% ≥75 years. Mepolizumab was prescribed for EGPA in <1.0% of patients before 2017 and use increased over time from 2.4% in 2017 to 20.6% in 2020. OCS remained the most prescribed treatment through 2020 (83.4%), with azathioprine used by 17.8% and injectable corticosteroids by 15.3%. Proportion of patients that used zero/low prednisolone-equivalent daily OCS doses increased from 2017 (0 mg: 13.6%; >0–≤5 mg: 41.8%) to 2020 (0 mg: 16.6%; >0–≤5 mg: 42.1%); while those who used >10 mg decreased from 2017 (11.9%) to 2020 (10.3%; Figure 1). Median OCS daily dose was 4.9–7.7 mg between 2010 and 2016, and 4.5–4.8 mg between 2017 and 2020, with the lowest dose in 2020 (4.5 mg (IQR 1.6–6.8)). Proportion of EGPA patients with comorbidities related to corticosteroids remained relatively consistent over time, except for infectious disease which showed a decrease from 94.4% in 2010 to 70.9% in 2020. Proportion of patients with other comorbidities in 2020 were dyslipidemia (37.6%), hypertension (33.6%), diabetes (23.4%), fracture (12.3%), mood disorders (10.1%), and cataract (7.2%). Of 1717 revisiting patients in 2020, 41.6% relapsed, which was 5.0–37.4% lower than in the years 2010–2019. In the subgroup of 24 patients new to mepolizumab from the JMDC database, the prednisolone-equivalent mean (SD) daily dose decreased from 11.2 mg (7.1) in the 90 days before to 4.3 mg (2.7) in the 4th quarter after mepolizumab initiation.
Conclusion: Prevalence of EGPA in Japan showed a continued increase through 2020, suggesting improved recognition of this disease. A decrease in OCS daily dosing was observed after mepolizumab was introduced in 2018, yet further improvement in EGPA management is warranted.
References: N/A.
Funding: GSK (218083/218084).

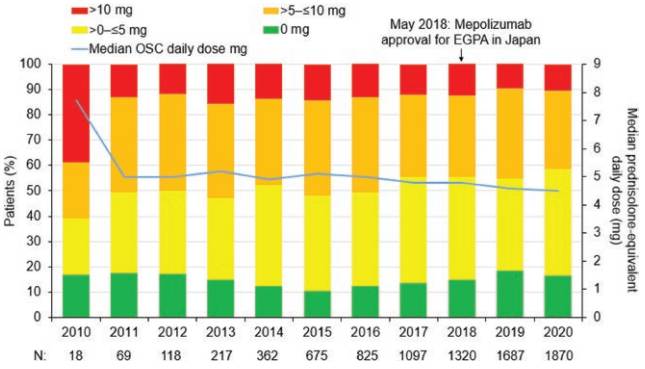


Figure 1. OCS use by daily dose category from 2010 to 2020 in Japan.

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Disclosure of Interests: KEN-EI SADA Speakers bureau: GSK, Grant/research support from: Pfizer Inc, Takeo Suzuki Employee of: GSK, Sandra Joksaite Shareholder of: GSK, Employee of: GSK, Shinyoung Ju Shareholder of: GSK, Employee of: GSK, George Mu Shareholder of: GSK, Employee of: GSK, John Logie Shareholder of: GSK, Employee of: GSK, Jeremiah Hwee Shareholder of: GSK, Employee of: GSK, Hideaki Kunishige Shareholder of: GSK, Employee of: GSK, Takeo Ishii Shareholder of: GSK, Employee of: GSK, Amit Adlak Shareholder of: GSK, Employee of: GSK, Harini Vadlamudi Employee of: GSK, Rafael Alfonso-Cristancho Shareholder of: GSK, Employee of: GSK.
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AB1634

RISK FACTORS ASSOCIATED WITH PARCIAL OR NULL REMISSION OF RENAL ACTIVITY IN PATIENTS WITH LUPUS NEPHRITIS

Keywords: Systemic lupus erythematosus, Remission, Kidneys

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Background: Systemic Lupus Erythematosus (SLE) is a multisystemic autoimmune chronic disease, the severity of organic involvement depends on factors such as sex, race and age of disease presentation. Lupus nephritis is present in up to 40% of patients with SLE. Failure to achieve complete remission at 6 months is associated with a poor long-term prognosis and implies greater use of immunosuppressants.
Objectives: To determine the factors associated with the parcial or null remission in patients with lupus nephritis.
Methods: A nested case-control study was conducted in a retrospective cohort of patients with lupus. Fifty-five patients with renal involvement were included and divided into two groups, those with partial or no remission in response to remission induction (n=30) and those with complete remission (n=25), multiple factors were analyzed and in the case of quantitative variables they were categorized into 2 groups with specific cut-off points in each case. The type of remission of each patient was taken as a factor to be analyzed and the analysis was completed in a bivariate logistic regression with a significance <0.05.
Results: The variables that showed risk of presenting a partial or null response were: not having completed the minimum time of 6 months of the remission induction scheme (Odds Ratio [OR]: 9.590; 95% Confidence Interval [95% CI]: 2.351-39.119; p=0.002), sex male (OR: 8.727; 95% CI: 1.009-75.51; p=0.049); start Renal Replacement Therapy (RRT) (OR: 8.727; 95% CI 1.009-75.513; p=0.049); family history of SLE (OR: 7.304; 95% CI: 0.832-64.098; p=0.073); have a Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) ≤60 ml/min/1.73m^2 (OR: 6.147; 95% CI: 1.577-26.110; p=0.009); Creatinine ≥1.2 mg/ dL (OR: 6.000; 95% CI: 1.767-20.369; p=0.004); C-Reactive Protein (CRP) ≥5g/dL (OR: 5.470; 95% CI: 1.680-17.811; p=0.005); age ≤30 years (OR: 4.250; 95% CI: 1.370-13.188; p=0.012); proteinuria ≥1.5 g/24 hours (OR: 3.560; IC 95%: 1.123-11.285; p=0.31).
Conclusion: The factors observed that are associated with a partial or null remission were: not completing the remission induction scheme, male sex, start with RRT, CKD-EPI ≤60ml/min/1.73m^2, creatinine ≥1.2mg/dL, CRP ≥5g/dL, age ≤30 years and proteinuria ≥1.5g/24 hours. On the other hand, factors such as a family history of SLE, BMI ≥30kg/m^2 and hemoglobin ≤10g/dl although they demonstrated an association, the values weren't statistically significant. These factors make it possible to identify areas of interest when starting remission induction therapy, demonstrating the importance of therapeutic adherence and individualized follow-up for each patient, offering timely intervention in modifiable factors and close monitoring of patients with non modifiable factors.
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Table 1. Bivariate logistic regression model for the risk of partial or null remission in patients with lupus nephritis

Variable	β	OR	IC al 95%		*p*
			Lower	Higher	
Not complete scheme	2.261	9.590	2.351	39.119	0.002
Sex male	2.166	8.727	1.009	75.51	0.049
Start Renal Replacement Therapy	2.166	8.727	1.009	75.513	0.049
Familiar antecedent of SLE	1.988	7.304	0.832	64.098	0.073
CKD-EPI ≤60 ml/min/1.73m^2	1.859	6.417	1.577	26.110	0.009
Creatinine ≥ 1.2mg/dl	1.792	6.000	1.767	20.369	0.004
BMI ≥ 30 kg/m^2	1.792	6.000	0.671	53.681	0.109
CRP ≥ 5 g/dl	1.699	5.470	1.680	17.811	0.005
Age ≤ 30 years	1.447	4.250	1.370	13.188	0.012
Proteinuria ≥ 1.5 g/24 hours	1.270	3.560	1.123	11.285	0.031
Do not give Chloroquine	1.153	3.167	0.989	10.141	0.052
Hemoglobin ≤ 10 g/dl	0.811	2.250	0.727	6.965	0.160

β: Coefficient of determination; **OR**: Odds ratio; **95% CI**: 95% confidence interval; **SLE**: Systemic Lupus Erythematosus; **CKD-EPI**: Chronic Kidney Disease Epidemiology Collaboration; **BMI**: Body Mass Index; **PCR**: C Reactive Protein.

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Disclosure of Interests: None Declared.
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AB1635

RATES OF HIGH LEVELS OF POST-PARTUM DEPRESSIVE SYMPTOMATOLOGY IN WOMEN WITH RHEUMATIC DISEASES FOLLOWED DURING PREGNANCY, AND ASSOCIATIONS WITH TYPE OF DISEASE: A STUDY BY A MULTIDISCIPLINARY TEAM

Keywords: Pregnancy and reproduction

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Background: Postpartum depression (PPD) affects 10-15% of Italian women and can lead to adverse outcomes for both mothers and children. Data on the prevalence of PPD in rheumatic diseases (RD) are limited.
Objectives: To assess the frequency of depressive symptoms in post-partum in women with RD using the Edinburgh Post-Natal Depression Scale (EPDS), and to identify potential relationships in patients with arthritis (RA, PsA, SpA, JIA) and connective tissue diseases (CTD: UCTD, SLE, SS, SSc, APS).
Methods: Patients with RD prospectively followed during pregnancy by a multidisciplinary team in an Italian rheumatology unit were included. Disease activity, patient global health (PGH), physician global assessment (PhGA), EuroQoL were collected during pregnancy. EPDS questionnaire was administered at 30-60 days, 6 and 12 months after delivery. Patients with a screen positive EPDS score (9 or more, or a positive response to question 10 -suicidal thought-) were referred to a clinical psychology specialist. Continuous variables are expressed as median (IQR).
Results: From May 2018 to June 2022, 129 patients completed at least one EPDS. Overall, 28 (22%) patients had at least one screen positive EPDS. No differences in health and demographic variables were found between patients screening positive or not, except for a higher PhGA in the 1st trimester in the first group (median VAS: 5 [0-20] vs 0 [0-0], p=0.03). Twelve out of 50 patients with arthritis had at least one screen positive EPDS (24%). These patients had a shorter disease duration (p=0.04), a lower PGH in the 1st trimester (p=0.03), and a higher frequency of anxious/depressive symptoms (evaluated with EuroQoL) during pregnancy (basal visit: p<0.001; 1st trimester: p<0.001; 2nd trimester: p=0.01), compared to patients screening negative (Table 1). Sixteen out of 69 patients with CTDs had at least one screen positive EPDS (23%). This group presented higher frequency of anxious/depressive symptoms (EuroQoL) in the 3rd trimester (p=0.004) to patients screening negative (Table 1).

Table 1. Comparison between patients positive on the EPDS on at least one occasion or never positive, among arthritis and CTDs groups.

	ARTHRITIS EPDS positive N=12	ARTHRITIS EPDS negative N=38	CTDs EPDS positive N=16	CTDs EPDS negative N=63
Age	32 (27-34)	34 (29-35)	34 (31-39)	34 (31-37)
Disease duration, years	**3 (1-9)**	**7 (4-11)***	8 (2-10)	5 (2-10)
Caucasian	8 (67%)	31 (82%)	14 (88%)	53 (84%)
Education: University/master	5 (42%)	11 (29%)	5 (31%)	33 (52%)
Employed	10 (83%)	30 (79%)	14 (88%)	57/62 (92%)
First pregnancy	7 (58%)	20 (53%)	4 (25%)	18 (%29)
Anxiety/depression at EuroQol, n. positive:	**8 (67%)**	**4 (11%)***	4 (25%)	21 (33%)
Basal visit				
1st trimester	**6/9 (67%)**	**4/31 (13%)***	4/14 (29%)	19/54 (35%)
2nd trimester	**5/11 (46%)**	**3/36 (8%)***	5/13 (38%)	11/52 (21%)
3rd trimester	4/12 (33%)	6/37 (16%)	**8 (50%)**	**10/58 (17%)***
PGH (VAS):	76 (50-90)	80 (70-91)	90 (70-90)	80 (70-93)
Basal visit				
1st trimester	**70 (50-80)**	**81 (80-95)***	90 (68-90)	85 (73-95)
2nd trimester	70 (80-90)	86 (70-95)	80 (65-95)	89 (75-90)
3rd trimester	87 (76-90)	90 (71-100)	80 (69-80)	80 (70-90)
PhGA (VAS):	5 (0-50)	2 (0-20)	0 (0-11)	0 (0-10)
Basal visit				
1st trimester	10 (0-45)	0 (0-20)	3 (0-13)	0 (0-5)
2nd trimester	0 (0-10)	0 (0-14)	0 (0-2)	0 (0-7)
3rd trimester	3 (0-28)	0 (0-3)	0 (0-8)	0 (0-7)
Breastfeeding	9 (75%)	28 (74%)	9 (56%)	45/62 (73%)

*Fisher exact test or chi-square test, p<0.05

Conclusion: More than 1 out of 5 women with RD had substantial level of depressive symptomatology on at least one occasion in the 12 months after delivery on the EPDS. Self-reported symptoms of anxiety and depression should be evaluated during pregnancy and patients could be offered a psychological interview. Our study underlines the need for a closer monitoring of mental health of pregnant women with RD and the opportunity for further studies to identify risk factors and screening procedures.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1636 **CLINICAL PHENOTYPES IN SARCOIDOSIS USING CLUSTER ANALYSIS IN A COHORT OF 342 PATIENTS**

Keywords: Epidemiology, Rare/orphan diseases

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Background: Sarcoidosis is a multi-system disease with unknown etiology characterized by the formation of granulomas in various organs. It affects people of all ethnic backgrounds and occurs at any time of life. This disease can affect any organ with a frequency varying according to ethnicity, sex and age most of the time affecting the pulmonary system with symmetrical bilateral hilar adenopathy. Extrapulmonary manifestations in skin, eyes, liver or lymphatic system can take a great morbimortality in patients.
Objectives: To **a)** indicate the phenotypes with similar characteristics with a cluster analysis and **b)** describe the principal features of those phenotypes.
Methods: A model-based clustering was performed in a cohort of 342 sarcoidosis patients, diagnosed and follow-up from 1999 to 2019 at northern Spain hospital. Four homogeneous phenotypes were proposed in our study (C1: parenchymal lung involvement with dyspnea; C2: erythema nodosum and articular involvement with asthenia; C3: isolated hilar adenopathy; C4: miscellaneous extrapulmonary sarcoidosis). Chi-square test and ANOVA were used to compare, respectively, categorical, and continuous variables among groups. Two-sample t-tests and the partition of Pearson's chi-square statistic for were used in pairwise comparisons.
Results: Cluster analysis identified four groups: C1 (n=128; 37.4%), C2 (n=75; 21.9%), C3 (n=82; 24.0%), and C4 (n=57; 16.7%) **(Table 1).** Lung involvement was predominant in all clusters, ranged from 93.3% (C2) to 100% (C3). Extrapulmonary involvement was significantly higher in C2 (97.3%) and C4 (98.2%). Systemic steroids were significantly more used in cluster 1 (75.8%) compared to the rest (C2: 57.3%; C3: 48.8%; C4: 47.4%) **(Figure 1).**
Conclusion: Sarcoidosis has a heterogenous disease, and a cluster analysis can be a useful tool to identify the clinical patterns and can be useful for the management.

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Table 1. Demographic and clinical characteristics of the study population. Data presented: n (%) or mean±SD

Characteristics	Whole cohort n=342	C1 n=128	C2 n=75	C3 n=82	C4 n=57	p-value	q-value
Gender (female)	177 (51,8)	45 (35.2) A,B,C	47 (62.7) A	46 (56.1) B	39 (68.4) C	<0.001	<0.001
Age at diagnosis (years)	47.7±15.1	46.4±14.0 A	43.4±13.1 B, C	51.7±16.8 A, B	50.5±15.5 C	0.002	<0.004
Ethnicity						0.8	0.8
Caucasian	322 (94.2)	121 (94.5)	70 (93.0)	76 (92.7)	56 (98.2)		
Hispanic	15 (4.4)	5 (3.9)	4 (5.3)	5 (6.1)	1 (1.8)		
Black	4 (1.2)	2 (1.6)	1 (1.3)	1 (1.2)	0		
Pulmonary involvement	302 (88.3)	120 (93.8) A	70 (93.3) B	82 (100) A,B	30 (52.6) A,B	<0.001	<0.001
Extrapulmonary involvement	234 (68.6)	68 (53.1) A,B	73 (97.3) A,C	37 (45.1) C,D	56 (98.2) B,D	<0.001	<0.001
Skin	117 (34.2)	26 (20.3) A	56 (74.7) A	3 (3.7) A	32 (56.1) A	<0.001	<0.001
Eye	61 (17.8)	22 (17.2) A	15 (20.0) B	21 (25.6) C	3 (5.3) A,B,C	0.02	0.04
Liver	33 (9.6)	12 (9.4)	5 (6.7)	10 (12.2)	6 (10.5)	0.7	0.8
Spleen	7 (2.0)	5 (3.9)	1 (1.3)	1 (1.2)	0	0.3	0.4
Bone	4 (1.2)	1 (0.8)	2 (2.7)	0	1 (1.8)	0.4	0.5
Joint	95 (27.8)	23 (18.0) A	49 (65.3) A	0 A	25 (43.9) A	<0.001	<0.001
Parotid	4 (2.3)	2 (1.6)	3 (4.0)	2 (2.4)	1 (1.8)	0.7	0.8
Kidney	13 (3.8)	2 (1.6) A	0 B	0 C	11 (19.3) A,B,C	<0.001	<0.001
Nervous system	29 (8.5)	6 (4.7) A	16 (21.3) A,B,C	6 (7.3) B	1 (1.8) C	<0.001	<0.001
Heart	5 (1.5)	3 (2.3)	0	0	2 (3.5)	0.2	0.3

CIS: conventional synthetic immunosuppressants; SD: standard deviation.Groups sharing the same letter (A, B, C, D) have statistically significative differences (q>0.005) in the pairwise comparison.Abbreviation in alphabetical order: n=number; SD: standard deviation.

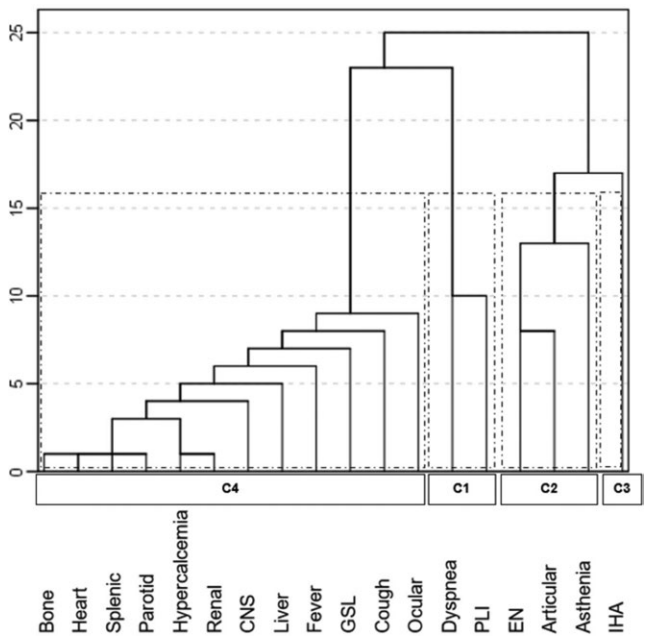


Figure 1. Dendrogram of the hierarchical clustering leading to four clusters. **C1**: parenchymal lung involvement with dyspnea; **C2**: erythema nodosum and articular involvement with asthenia; **C3**: isolated hilar adenopathy; **C4**: miscellaneous extrapulmonary sarcoidosis.

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AB1637 DO AFRO-DESCENDANT PATIENTS WITH PRIMARY SJOGREN SYNDROME SHARE CLINICAL AND BIOLOGICAL CHARACTERISTICS? EXEMPLE FROM MARTINIQUE

Keywords: Sjögren syndrome, Epidemiology, Geographical differences

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Background: Influence of geolocation and ethnicity on pSS prevalence and phenotype has been reported [1] and black pSS appear to have higher risk of unfavorable outcome[2]. In Europe, pSS prevalence ranges from 10.2 to 92.8/100 000 Inhabitants[3]. Data on primary Sjogren's disease (pSS) in populations of sub-Saharan origin are very limited and concerns mostly Europeans and Asians. Both in Africa and the African diaspora (AAD)[4,5], patients face significant healthcare limitations because of socio-economic disadvantage. In Martinique, a French island of the Caribbean where more than 90% of the population is of Sub-Saharan African descent, access to healthcare is easy and free for every citizen. pSS are treated in the Reference Center for rare systemic autoimmune diseases of the island. No other primary care facility treats pSS.
Objectives: We aim to describe pSS in an Afro-descendant population in healthcare access comparable to Europeans.
Methods: We performed a retrospective study of all patients followed for primary Sjögren's (pSS) in internal medicine and rheumatology at the University hospital of Martinique, only hospital on the island, between 2014 and 2016 included according to international criteria (AECG 2002, ACR/EULAR 2016).
Results: Among 112 patients diagnosed with pSS, 75 and 84 patients were included according to AECG 2002 and ACR/EULAR 2016 criteria respectively. Clinical and biological characteristics are presented in Table 1. In our cohort, major cumulative characteristics are a very high female proportion, young age at diagnostic and high frequency of hypergammaglobulinemia correlated with increased ESR. Considering this AECG 2002 hospital-based cohort and the retrospective aspect of the study, a minimum prevalence of pSS was calculated at 16,87/100 000 inhabitants in 2016.
Conclusion: Our data, shared by other AAD cohorts[4,5], suggest that AD pSS have specific manifestations around the world as AAD Systemic Lupus erythematosus do. A higher prevalence is reported compared to that of 7.1/100 000 inhabitants of France European pSS cohort[3].

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Table 1. Characteristics of study population

	AECG 2002 N=75	ACR EULAR 2016 N= 84
Age at diagnosis – Mean (SD) Years	49.8 (12.5)	50.2 (12.6)
Female – N (%)	74 (98.7)	81 (96.4)
Mean follow up duration – mean (SD)	9.3 (7.7)	9.3(8.2)
Classification criteria		
Subjective xerostomia – N (%)	70 (93.3)	70 (83.3)
Subjective xerophthalmia – N (%)	72 (96.0)	81 (96.4)
Positive Schirmer test – N (%)	53 (80.3)	57 (79.2)
Lymphocytic sialadenitis (focus score≥1) – N (%)	71 (95.9)	79 (96.3)
Positive SSA/Ro– N (%)	56 (74.7)	59 (70.2)
Positive SSB/La– N (%)	9 (12.0)	9 (10.7)
Biology		
Positive Antinuclear antibodies (Title≥1/320) – N (%)	66 (89.2)	73 (88.0)
Positive RNP antibodies – N (%)	9 (12.0)	10 (11.9)
Increased ESR – N (%)	36 (53.7)	42 (56.0)
Hypergammaglobulinemia – N (%)	50 (76.9)	57 (77.0)
MALT/Lymphoma – N (%)	2 (2.7)	2 (2.4)

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AB1638 RISK FACTORS FOR DEVELOPING RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS AFTER IMMUNOTHERAPY WITH IMMUNE CHECKPOINT INHIBITORS

Keywords: Malignancy

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Background: Immunotherapy with monoclonal antibodies that block specific immunological check-points has revolutionized the treatment of some forms of cancer, such as melanoma. A new group of adverse events has emerged with these new agents, called the immune-related adverse events (irAEs). Among these irAEs, rheumatic complications are relatively common, although the true frequency is still unclear.
Objectives: We aimed to assess the frequency of ir-AEs and rheumatic ir-AEs in particular, as well as identifying potential risk factors for irAEs in a cohort of patients with malignant melanoma receiving immunotherapy with immune checkpoint inhibitors (ICI).
Methods: Retrospective analysis of a cohort of patients diagnosed with malignant melanoma and starting treatment with a first-ever ICI at Karolinska University Hospital between 2012 and 2020. The type of irAEs, glucocorticoid therapy at immunotherapy start, demographics and type of ICI were collected from patient's journals.
Results: A total of 118 patients were included in the cohort, 75 male (63,6%) and 43 females (36,4%). The type of ICI was nivolumab in 54.2% of patients, ipilimumab in 13.6%, pembrolizumab in 22.9% and combination therapy with ipilimumab and nivolumab in 7.6%, ipilimumab and pembrolizumab in 0.8% and

nivolumab and pembrolizumab in 0.9%. Any irAE developed 72/118 patients (61%), while rheumatic irAEs were seen in 24 patients (20.3%) with the following clinical phenotypes; arthralgia/myalgia in 9 patients (37.5%), PMR like syndrome in 3 patients (12.5%), arthritis in 6 patients (25%), sicca syndrome in 4 patients (16%), sarcoidosis in 1 patient (4.2%) and myositis in 1 patient (4.1%). There was no significant association between the type of ICIs or combination therapy in total with the development av irAEs (OR = 1.79, 95% CI = 0.45 – 7.1, p=0.39). Neither the gender (OR 1.12, 95% CI = 0.52-2.40, p=0.76) nor the glucocorticoid use at the ICI start were associated with the development av irAEs [OR=2.0, 95% CI = 0.38 – 10.36, p=0.38]. No significant associations were observed between demographic factors (age, gender), type of ICI, glucocorticoid use at the start of ICI and rheumatic irAEs.

Conclusion: IrAEs are common and occur in more than half of patients treated with ICI. Rheumatic irAEs are also common and in this study were seen in one fifth of patients. Gender, age, type of ICI and treatment with glucocorticoids at baseline are not associated with increased (or decreased) risk for irAEs in general, or rheumatic irAEs in particular, in this cohort of patients with melanoma, with the risk of type II error due to limited power.

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AB1639

ASSOCIATION BETWEEN HYPERURICEMIA AND BONE MINERAL DENSITY WITH 8-YEAR FOLLOW-UP AMONG CHINESE ADULTS

Keywords: Osteoporosis, Epidemiology, Gout

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Background: Hyperuricemia (HUA) have been associated with bone mineral density (BMD) in recent studies, especially for elderly men and peri- or postmenopausal women[1-3]. However, this association is still unknown for the long-term follow-up observation.

Objectives: This study investigated the relationship between hyperuricemia and bone mineral density at 8-year follow-up among Chinese adults.

Methods: The cohort study was collected at Guangdong Second Provincial General Hospital in Guangzhou City, China between January 2010 and December 2018. Physical examinations and laboratory measurement variables were obtained from the medical check-up system. The physical examination population was followed up annually for 8 years. Multivariate Cox proportion models was used to explore the relationship between the hyperuricemia and bone mineral density.

Results: In total, 9017 individuals were included (2620 HUA participants (39.6% female) at baseline with an average age of 44.85 years (SD: 12.35) and average BMD of -0.83 (SD:1.24). The BMD decreased annually at the 8-year follow-up (from -0.82 to -0.93). Compared with normal participants, the Cox regression analysis showed that hyperuricemia was significant associated with lower BMD(T<-2.5) (hazards ratio (HR)=1.169, 95%CI: 1.059–1.290, P <0.05), the male (HR=2.545,95%CI: 2.389–2.710, P <0.05) and the elderly (age≥65) (HR=1.121,95%CI: 1.012–1.241, P <0.05) at follow-up.

Conclusion: Our study observed participants with hyperuricemia had significantly lower BMD, especially for males and the elderly participants. More high-quality research is needed to further support these findings.

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Disclosure of Interests:
NONE DECLARED.

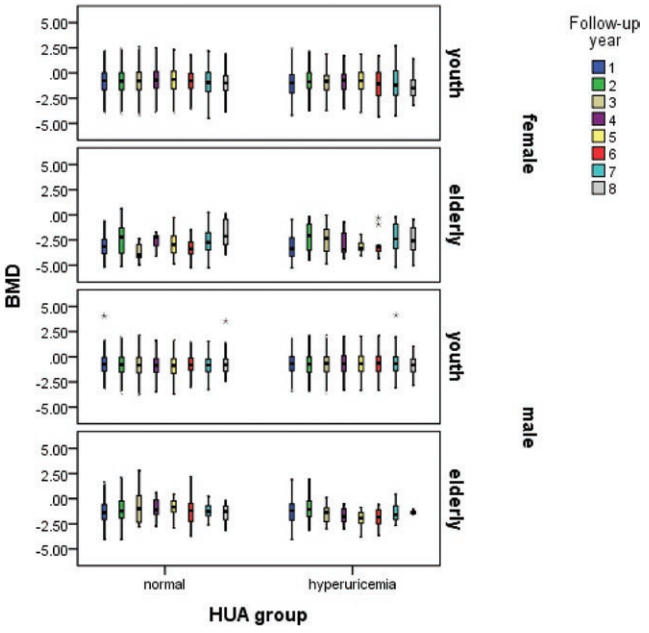


Figure 1. Distribution of hyperuricemia and BMD by gender and age group at 8-year follow up.

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Disclosure of Interests: None Declared.

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AB1640

PREVALENCE AND ASSOCIATED FACTORS OF ATLANTOAXIAL SUBLUXATION IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SINGLE-CENTER RETROSPECTIVE STUDY

Keywords: Rheumatoid arthritis, Imaging

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Background: Atlantoaxial subluxation (AAS) is a serious complication of rheumatoid arthritis (RA) that can cause severe neck pain and neurological injury.

Objectives: This study aimed to identify prevalence and associated factors of AAS in Korean RA patients.

Methods: Data of RA patients who visited an academic referral hospital in Korea between September 2007 and August 2020 were extracted. Patients who were <19 years old, had another autoimmune disease, or did not check cervical spine (C-spine) radiography were excluded. The date of the first C-spine radiography was set as the index date, and AAS was defined with anterior atlantoaxial interval (AADI) greater than 3mm. We performed multivariable logistic regression analysis to identify associated factors for AAS. The proportion of patients with AAS progression or those who received surgical treatment for AAS during observation period was investigated.

Results: There were 1,855 patients with diagnostic code of RA, and 1,115 patients with RA who checked C-spine radiography at least once were included. Among them, 156 patients had AAS at the index date with a prevalence of 14.0%, and the mean AADI in patients with AAS was 4.9±1.7 mm. In multivariable logistic regression analysis, longer duration of RA, lower body mass index (BMI), C-spine spondylosis, erosive changes on hand X-ray and higher C-reactive protein were significant associated factor for AAS. Among 156 patients with AAS, 106 patients performed C-spine radiography follow-up (mean interval 5.5±3.7 years). There were 16 patients (15.1%) with progression of AAS or surgical treatment: 12 patients who received surgery for AAS and four patients with AAS progression without surgical treatment.

Conclusion: In this study, 14.0% of patients with RA had AAS. Duration of RA, BMI, C-spine spondylosis, bone erosion at hands and RA activity were factors

associated with AAS. 15.1% of RA-AAS patients showed progression of AAS or received surgical treatment during 5.5 years of observation.

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Disclosure of Interests: Yeo-Jin Song: None declared, Sang Yoon Kim: None declared, Chaewhi Lim: None declared, Hye Won Kim: None declared, Eunwoo Nam: None declared, Soo-Kyung Cho: None declared, Yoon-Kyoung Sung Grant/research support from: YKS has received research grants from Bristol-Myers Squibb, Eisai, Pfizer, and JW Pharmaceutical.

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AB1641 TOBACCO SMOKING HAS A PREVENTIVE EFFECT ON THE INCIDENCE OF KNEE OSTEOARTHRITIS: 10-YEAR RETROSPECTIVE COHORT STUDY BASED ON KOREA NATIONAL HEALTH INSURANCE SERVICE-HEALTH SCREENING DATABASE

Keywords: Osteoarthritis, Epidemiology

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Background: Previous cross-sectional studies reported that smoking lowers the incidence of knee osteoarthritis, however, some studies show no correlation between smoking and knee osteoarthritis. Thus the relationship between the two has not been clarified [1,2]. To address this issue, we designed a retrospective cohort study to investigate the association between smoking and knee osteoarthritis, using a large-scale claim database from Korea. To the best of our knowledge, this is the first retrospective cohort study on smoking and knee osteoarthritis in Korea.

Objectives: We intended to investigate whether there was a difference in the incidence of knee osteoarthritis between patients with a history of current smoking, past smoking and those without a history of smoking.

Methods: The Korea National Health Insurance Service-Health Screening database is registered with 98% of Koreans and includes all insurance claims. From this database, a retrospective cohort observational study was conducted on 316,387 adults who had undergone the national health examination. Patients diagnosed with knee osteoarthritis prior to the examination and patients who were diagnosed with knee osteoarthritis in 2002 were excluded. The primary endpoint of this study was a diagnosis of knee osteoarthritis. The operational definition of diagnosis of knee osteoarthritis was knee osteoarthritis code (M17) or any site of osteoarthritis code (M15 to M19) along with a knee x-ray (G720, G721) [3]. The study population was followed from the day of health screening at index year to the date of incidence of knee osteoarthritis, the date of death, or December 31, 2019, whichever comes first.

Results: The patient group was classified into non-smoker, ex-smoker, and smoker groups according to the responses to the health examination questionnaire. The baseline characteristics of each group are included in Table 1. The incidence of knee osteoarthritis was 38.9%, 26%, and 23% in each group of non-smoker, ex-smoker, and smoker group with statistical significance (P-value < 0.001). When the disease-free probability for knee osteoarthritis was presented using the Kaplan-Meier curve, it was confirmed that the risk of osteoarthritis incidence was significantly different between the non-smoker group and the smoker group as time passes (Figure 1, P-value for Log-rank test < 0.001). The hazard ratio and 95% confidence intervals of ex-smoker to non-smoker were 0.95 (0.83-0.97), and those of smoker to non-smoker were 0.89 (0.87-0.91).

Conclusion: This large-scale retrospective cohort study showed a low incidence of knee osteoarthritis in smokers and ex-smokers during a follow-up period when compared to non-smokers in Korea. Additional studies on the relationship between smoking and knee osteoarthritis are required in the future.

Table 1. Baseline characteristics of study population.

All subjects (n = 316,387)	Non-smoker group (n = 187,116)	Ex-smoker group (n = 65,290)	Smoker group (n = 63,981)	P-value
Demographics				
Age (years)	58.8 ± 9.0	58.2 ± 8.5	56.5 ± 7.8	< 0.001
Health screening				
Smoking history (pack-years)	0.0	18.6 ± 15.8	24.3 ± 15.1	< 0.001
Underlying disease				
Hypertension (%)	60,840 (32.5)	20,466 (31.3)	17,488 (27.3)	< 0.001
Diabetes (%)	21,154 (11.3)	9,170 (14.0)	9,353 (14.6)	< 0.001
Dyslipidemia (%)	42,002 (22.4)	11,838 (18.1)	11,247 (17.6)	< 0.001
Outcome				
Knee osteoarthritis (%)	72,778 (38.9)	16,963 (26.0)	14,715 (23.0)	< 0.001

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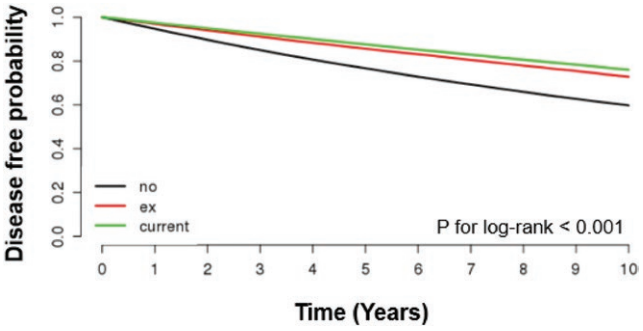


Figure 1. The K-M curve between smoking and knee osteoarthritis.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1642 A NATIONWIDE POPULATION-BASED STUDY OF EPIDEMIOLOGY, RISK FACTORS FOR CYTOMEGALOVIRUS DISEASE IN AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES

Keywords: Inflammatory arthritides, Comorbidities, Epidemiology

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Background: Human cytomegalovirus (CMV) ubiquitously distributes in general population but may cause overwhelming complications in patients with autoimmune inflammatory rheumatic diseases (AIIRDs); hence, the prevalence and associated factors of CMV disease in AIIRDs is worth investigating but the data has been limited.

Objectives: To investigate the epidemiologic data and risk factors of CMV infection in patients with AIIRDs.

Methods: The nationwide population-based cohort study was conducted by using Taiwanese National Health Insurance Database, to compare incidence rates (IR) with incidence rate ratios (IRR) of CMV disease in patients with AIIRDs and non-AIIRDs age- and sex-matched cohort; CMV disease was defined as pertinent ICD codes with concurrent anti-CMV medication administration. The individual data in various AIIRDs were analyzed and risk factors were identified by Cox proportional regression.

Results: 94,429 patients with AIIRDs and 1:1 number of matched subjects were identified; higher incidence rate of CMV disease in AIIRDs group was noted than the matched cohort. Various comorbidities and therapeutic agents including azathioprine, cyclosporin, cyclophosphamide, mycophenolate, intravenous steroid and oral daily dose > 7.5mg prednisolone or equivalence, were associated with CMV disease incidence. Comparing with RA, SLE and DM/PM posed increased risks on CMV disease.

Conclusion: Patients with AIIRDs carry higher risk of CMV disease regardless of etiologies, and attentiveness to one's health is indispensable to facilitate early detection of CMV disease in patients with AIIRDs.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1643

ONE-MONTH HOSPITALIZATION WITH HIGH-DOSE GLUCOCORTICOID THERAPY IS ASSOCIATED WITH SARCOPENIA PROGRESSION IN PATIENTS WITH RHEUMATIC MUSCULOSKELETAL DISEASES

Keywords: Diet and nutrition, Comorbidities, Best practices

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Background: Sarcopenia refers to a decrease in skeletal muscle mass and function. It is associated with daily life disability and a high risk of all-cause mortality. While sarcopenia is generally an age-related disease, it has been recently recognized to be prevalent in young patients with rheumatic musculoskeletal diseases (RMD). Especially, most patients with RMD with systemic organ manifestations are hospitalized to be treated with high-dose glucocorticoid (GC) leading to extremely low physical activity and prolonged bed rest for a long term. However, little is known about sarcopenia in patients with RMD who are administered high-dose GC in hospital.

Objectives: To clarify the incidence of sarcopenia and its risk factors in patients with RMD treated with high-dose GC therapy in more than one-month hospitalization.

Methods: We reviewed patients with RMD who had been hospitalized in Keio University Hospital from 2020 to 2021 and included those with skeletal mass indices (SMI) before and one-month after high-dose GC treatment available in the analysis. We divided them into two groups according to progression of sarcopenia. Sarcopenia was defined as less than 5.4 kg/m^2 of SMI for woman and less than 7.0 kg/m^2 of SMI for man according to definition of Asian Working Group for Sarcopenia. Progression of sarcopenia was defined as more than 10% decrease in SMI from baselines. We compared clinical characteristics between the two groups and conducted multivariable analysis identify independent risk factors associated with progression of sarcopenia.

Results: Forty-nine patients were enrolled. The mean age was 53.3 years old, and 36 patients (73.5%) were female. The most frequent disease was systemic lupus erythematosus (42.9%) followed by systemic vasculitis (18.4%) and idiopathic inflammatory myositis (14.3%). At hospital admission, 41 patients (83.7%) already met the definition of sarcopenia before high-dose GC treatment. After one-month hospitalization with high-dose GC treatment, two patients newly developed sarcopenia, and 28 (57.1%) patients were diagnosed with progression of sarcopenia. Patients in the sarcopenia progression group were male dominant (60.7 vs 90.4%, p=0.025), had a higher body weight (56.9 ± 12.9 vs 50.5 ± 7.5 kg, p=0.048), and showed higher SMI (5.5 ± 0.8 vs 5.1 ± 0.8 kg/m^2, p=0.008) than those in the non-sarcopenia progression group. Age (52.8 vs 55.8 years, p=0.755), underlying diseases, and starting dose of GC (0.98 ± 0.16 vs 0.96 ± 0.19 mg/kg/day, p=0.35) were not different between the two groups. During the mean observation period of 41.2 ± 10.4 days of hospitailization, the incidence of infection was higher in the sarcopenia progression group than the non-sarcopenia progression group (28.5 vs 5.7%, p=0.042). Multivariable regression analysis revealed body weight reduction from 0 to week 1 was associated with progression of sarcopenia (odds ratio 0.22, 95% confidence interval 0.04-0.61, p=0.007) (Figure 1). Receiver operating characteristic curve identified the reduction in body weight of -1.8 kg in one week predicted sarcopenia progression after one month in-hospital high dose GC treatment.

Conclusion: Sarcopenia is frequent in patients with RMD, and one-month hospitalization with high-dose GC therapy worsened sarcopenia in more than half of patients. Early decrease in body weight can predict significant muscle volume loss after one month in-hospital therapy.

Figure 1

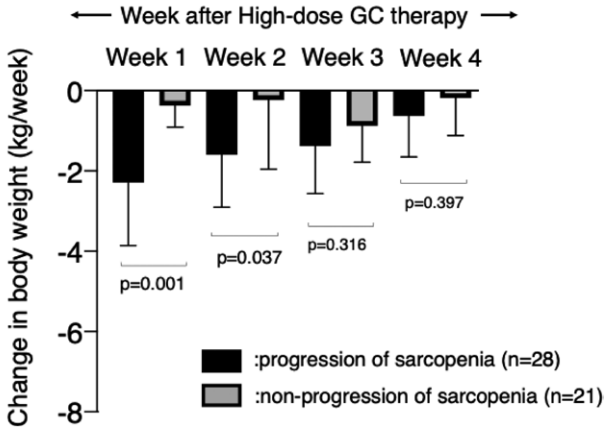


Figure 1. Change in body weight after high-dose GC treatment

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1644

INCIDENCE, PREVALENCE, AND BURDEN OF SYSTEMIC LUPUS ERYTHEMATOSUS IN URBAN CHINA, 2013-2017: A NATIONWIDE POPULATION-BASED STUDY

Keywords: Epidemiology, Systemic lupus erythematosus

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Background: Systemic lupus erythematosus (SLE) is becoming a public health concern because of increasing disease and economic burdens. However, epidemiological data on SLE, especially its incidence rate, were limited in China, the world's largest population.

Objectives: To investigate SLE incidence, prevalence, and SLE-associated cost burdens in urban Chinese, stratified by gender, age group, and region, using national administrative data from 2013 to 2017.

Methods: We conducted a population-based study using records from the national databases of Urban Employee Basic Medical Insurance and Urban Resident Basic Medical Insurance in China between 2013 and 2017. Data from over 380 million patients during the study period were analyzed, and a total of 132,258 SLE patients (mean age 43.03 years, standard deviation 15.29; 81.34% female) were identified. Incident cases were individuals with a diagnosis of SLE with a 3-year disease-free period[1]. Prevalent cases were defined as patients with at least 1 insurance claim record with the diagnosis of SLE[2]. Primary outcomes, including the overall, age-, gender-, and region-specific incidence and prevalence rates of SLE, were estimated by a two-stage approach assuming a Poisson distribution[3]. Associated annual costs and hospital visit times were also calculated in both inpatients and outpatients.

Results: The crude incidence and prevalence of SLE in China in 2017 were 14.96 (95%CI, 12.69-17.43) and 50.37 (95%CI, 44.19-56.95) per 100,000 person-years, suggesting an incident population of 0.21 million and a prevalent population of 0.71 million (Figure 1). The average annual rate of increase in prevalence was 16.86% during 2013 and 2017. Crude incidence and prevalence of SLE among females were 28.03 (95%CI, 23.20-33.30) and 99.66 (95%CI, 85.47-114.95) per 100,000 person-years, higher than those among males of 6.42 (95%CI, 4.59-8.55) and 19.31 (95%CI, 14.94-24.24) per 100,000 person-years, with a prevalent rate ratio of 5.16:1. The age-specific incidence and prevalence showed unimodal distributions, both peaked at 30-49 years old in females and at 40-49 years old in males. Estimated annual cost per-capita was US$1,599.34 in SLE patients. Female outpatients had higher costs (US$971.20 vs. US$480.76 in males) with more hospital visits (9.20 times vs. 4.85 times in males), whereas male inpatients had higher costs (US$5,095.53 vs. US$3,774.40 in females). Costs of adolescent and young adult patients were the highest among age groups. All results in sensitivity analyses showed similar trends as demonstrated by the main results aforementioned.

Conclusion: Rapidly expanding SLE population and increasing costs associated with SLE have placed considerable burdens on health systems in China. Continued and enhanced efforts are needed to make long-term care and support more accessible and cost-effective for SLE patients, especially young population.

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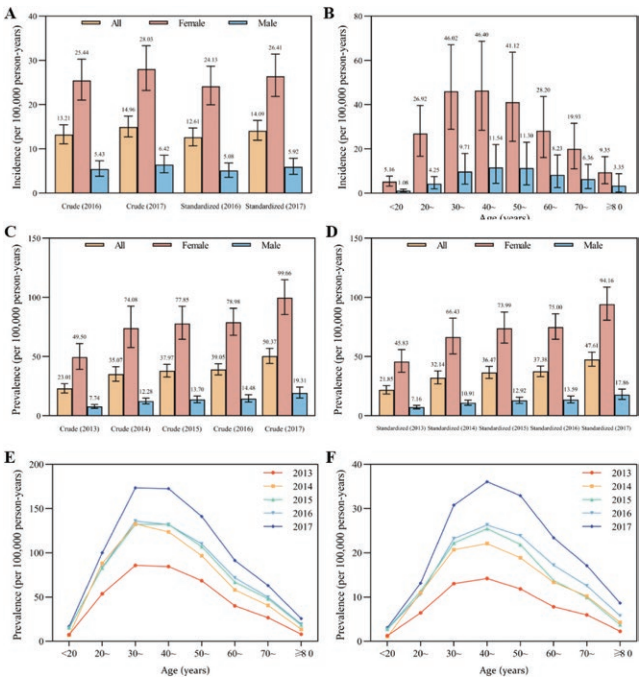


Figure 1. Incidence and prevalence of SLE in urban China from 2013 to 2017

A: Crude and standardized incidence of SLE (the standardized incidence is based on 2010 China census data) in 2016 and 2017. B: Age- and gender-stratified incidence of SLE in 2017. C: Crude prevalence of SLE from 2013 to 2017. D: Standardized prevalence of SLE (the standardized prevalence is based on 2010 China census data) from 2013 to 2017. E: Age-stratified prevalence of SLE in female from 2013 to 2017. F: Age-stratified prevalence of SLE in male from 2013 to 2017.

Acknowledgements: None.
Disclosure of Interests: None Declared.
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AB1645 CONTRACEPTION IN WOMEN WITH IMMUNE-MEDIATED INFLAMMATORY DISEASE

Keywords: Education, Patient information and education

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Background: Given that teratogenic medications prescribed to women with immune-mediated inflammatory disease (IMID) may cause significant fetal harm, the use of effective contraception is crucial in reproductive-age women receiving potentially teratogenic medications.
Objectives: To determine: Relationship between potentially teratogenic drugs and the efficacy of contraception methods. The prevalence of contraceptive methods in women of reproductive age with IMID.
Methods: Cross- sectional study (May 2021 - May 2022). All women of reproductive age with an IMID (rheumatology, dermatology and gastroenterology external consultation) were invited to participate. Patients with rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, psoriasis, Crohn's disease and ulcerative colitis were included. Patients with hysterectomy, primary or secondary amenorrhea were excluded. A self-administered questionnaire including questions on the use of contraceptive methods was administered. Medications prescribed for IMID were identified and assigned a pregnancy risk category (according FDA): Class A - B (safe to use during pregnancy), C (have not been adequately studied to assign a pregnancy classification) and D-X (potentially teratogenic, their use is relatively/ absolutely contraindicated during pregnancy). For women who were prescribed multiple drugs, we assigned their FDA risk category based on their drug with the highest potential teratogenicity. Contraceptive methods were also classified according to their relative effectiveness (based on World Health Organization (WHO)) (Table 1). When women had more than one contraceptive method we classified according to their most effective method. Our analysis categorizes drugs as either A/B/C or D/X, ("low risk" vs "high risk"). To determine the relationship between the potential teratogenic drug and the effectiveness of contraceptive method we used Chi-square tests.
Results: A total of 59 women participated (Table 2), mean age 41.2 (SD ± 6.8) years. Contraceptive use was referred by 41 (69.5%) of the patients (Table 1): 56.1% (23 patients) used a method classified as moderately effective, 31.7% (13) as highly effective and 9.8% (4) as ineffective. Of women with teratogenic drugs: 37.5% (15 patients) did not use a contraception method or it was considered as ineffective. The relationship between potentially teratogenic drugs and effectiveness of contraceptive methods has a P value of 0.668 (Table 3).
Conclusion: The prevalence of contraception methods in reproductive-age women with IMID is about 70%. In women who used a contraceptive method, contraception considered to be ineffective was the least frequent. We found no relationship between the risk of teratogenicity in drugs prescribed for IMID and the effectiveness of contraceptive method.
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Table 1. Frequency of contraceptive use (N 41)

Method	Frequency (%)	OMS classification
Condoms	15 (36.6)	Moderate
Oral contraceptive	7 (17.1)	Moderate
Surgical sterilization	6 (14.6)	High
Intrauterine device	4 (9.8)	High
Coitus interruptus	3 (7.3)	Ineffective
Vasectomy	2 (4.9)	High
Vaginal rings	2 (4.9)	Moderate
Emergency contraception	1 (2.4)	Ineffective
Subdermic implants	1 (2.4)	Moderate

Table 2. Diagnosis frequency

Diagnosis	Frequency (%)
Rheumatoid arthritis	20 (34.9)
Crohn´s disease	12 (20.3)
Psoriasis	11 (18.6)
Ankylosing spondylitis	8 (13.6)
Psoriatic arthritis	7 (11.9)
Ulcerative colitis	1 (1.7)

Table 3. Relationship between potentially teratogenic drugs and effectiveness of contraceptive methods

	High effectiveness of contraception	Moderate effectiveness of contraception	Ineffective or not use of contraception
High risk of teratogenicity (N 40)	10 (25%)	15 (37.5%)	15 (37.5%)
Low risk of teratogenicity (N 19)	3 (15.8%)	9 (47.4%)	7 (36.8%)

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1646 GENDER DIFFERENCES OF FRACTURE RISK IN PATIENTS WITH POLYMYALGIA RHEUMATICA

Keywords: Descriptive studies, Epidemiology

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Background: Polymyalgia Rheumatica (PMR) is usually treated with steroids, but long-term usage is detrimental to bone health. It is not uncommon for corticosteroid treatment to last for longer than a year [1]. No study has looked at the differential effect of steroids on either gender in this group of patients.
Objectives: To examine the effect of steroids on bone health in patients with PMR by gender.

Methods: Patients with PMR referred for BMD (Bone Mineral Density) estimation in a district hospital in the northwest of England between 2004 and 2011 were examined. Patients' demographics were recorded and Bone mineral density (BMD) were measured in both hips as well as the lumbar spine. Frax(TM) Risk factors (RF's) for osteoporosis were also ascertained at the time of DEXA. Initially RF's were compared between men and women using a students' T test for continuous variables and chi squared test for categorical variables. A logistic model was then fitted to compare RF's for fracture between men and women. Lastly a stepwise multivariate model was fitted using STATA (tm) version 12.
Results: 1051 patients with PMR were referred in the study period, mean age was 81.74 years (SD 9.58). 764 (84.7%) were females. Fractures were sustained in 26.3 % overall and there was a significant difference in males and females. Females were 2.58 times higher odds to sustain a fracture (CI 1.79 - 3.70). Using univariate logistic regression, the RF's for fracture in men were a reduced lumbar spine BMD (OR.794, CI.657 to.959) and a reduced left femur total BMD (OR.748, CI.568 -.984). In women the RF's were increasing age (OR 1.04, CI 1.020 to 1.055), reduced lumbar spine BMD (OR.841, CI.764 -.926), reduced right femur total BMD (OR.738, CI.644 -.845), reduced left femur total BMD (OR.706, CI.615 -.810) and current steroid therapy (OR.573, CI.369 -.889). In the multivariate model the RF's in men were a diagnosis of coeliac disease (OR 17.38, CI 1.746 - 173.03), and a reduced left femur total BMD (.783, CI.588 - 1.042). In women the RF's were increased age at scan (OR 1.025, CI 1.004 - 1.047), history of fracture (OR 1.891, CI 1.104 - 3.238), reduced left femur total BMD (.720, CI.611 -.849) and reduced BMI (OR 1.035, CI 1.002 - 1.068). Characteristics are shown in Table 1 below.
Conclusion: Men and women with PMR differ in their bone health, firstly in their demographics and secondly in their fracture risk with men who malabsorb having the highest fracture risk. This is the first intimation that fracture risk could be different. Limitations included not knowing the steroids' duration before scanning and only using first scan data. Strengths include the large number of subjects. Longitudinal data the collection of which is ongoing will provide further clarity.
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Table 1.

Characteristic	Males	Females	
Study	287	764	
Age, Years, mean, (SD)	81.79 (9.34)	81.72 (9.68)	P = 0.9174
Weight, KG, (mean (SD)	82.08 (12.78)	71.98 (15.91)	P = < 0.000
Height (SD)	172.74 (6.62)	158.69 (7.07)	P = < 0.000
BMI (SD)	27.50 (3.98)	28.74 (9.26)	P = 0.0278
Fracture n (%) of those in study	42 (14.63%)	234 (30.63%)	P = <0.000
Smoker current N (%)	21 (7.32 %)	59 (7.72%)	P =.825
Current Excess Alcohol Use %	27 (9.4%)	23 (3.01%)	P = < 0.000
BMD Left Femur Total	-.499 (279)	-.917 (718)	P = <0.000
BMD Right Femur Total	-.518 (271)	-.930 (705)	P = <0.000
BMD lumbar spine (mean)	.377 (287)	-.782 (762)	P = <0.000
Current steroid use %	256 (89.1%)	658 (87.4%)	P =.434

Disclosure of interest: None declared.
Disclosure of Interests: None Declared.
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AB1647

NEUROBEHÇET DISEASE INCIDENCE IN NORTHERN SPAIN 1999-2019. A POPULATION-BASED STUDY

Keywords: Vasculitis, Epidemiology, Behcet's disease

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Background: Behçet's Disease (BD) incidence varies widely worldwide. Neurobehcet's disease (NBD) is one of the most severe manifestations of BD [**1].** Data on NBD incidence is scarce and contradictory.
Objectives: To estimate NBD incidence in Northern Spain.
Methods: Population-based cohort study of 120 patients diagnosed with BD in Northern Spain, between January 1, 1999, to December 31, 2019. Finally, 92 were included according to the 2013 International Criteria for BD [**2].** NBD was diagnosed according to the International Consensus Recommendation criteria [**3].** The incidence of NBD between 1999-2019 was estimated by gender, age, and year of diagnosis. Annual incidence is expressed as cases per 100,000 people.
Results: NBD was diagnosed in 23 of 92 (25%) patients (15 women/8 men) (mean±SD age: 44±13.9 years). Ten (43.5%) patients had parenchymatous NBD, 10 (43.5%) had non-parenchymatous NBD and 3 (13%) cases had mixed NBD. Annual incidence of NBD in Northern Spain in the 1999-2019 period was 0.13 per 100,000 people [95% CI: 0.11-0.26] (0.14 [0.04-0.23] in men, 0.24 [0.12-0.37] in women). There were variations in annual incidences, with a minimum value of 0.08 in 2009-2010 and a maximum of 0.26 in 2017-2018 (**Figure 1**). The highest incidence rate was observed in men in the 20-29 years group (0.03 per 100,000 people) and in women in the 30-39 years group (0.07 per 100,000 people). On the other hand, the lowest incidence rate was observed in the 10-19 years group and 80-89 years group (0.008 per 100,000 people). When analyzed the incidence rate stratified by age, there were no statistical differences according to gender. The annual incidence studied by year showed an annual peak incidence over the last 20 years. A comparison between different geographical areas was made (**Table 1**). NBD frequency ranges from 5.6 to 38%. It is usually more frequent in male young adults.
Conclusion: NBD frequency varies widely. The epidemiological characteristics of NBD in our series are similar to other except for gender predominance. Like in other immune mediated diseases this cyclic pattern in annual incidence could possibly be related to infectious environmental factors.
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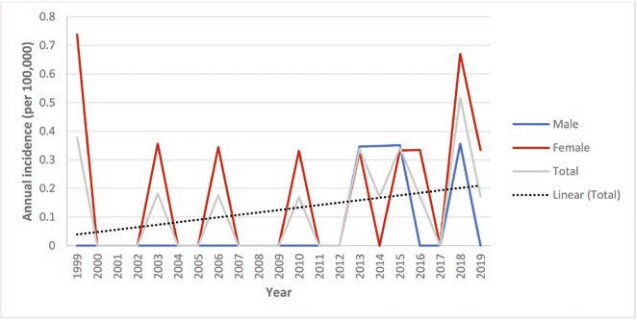


Figure 1. Incidence of neurobehçet's disease in residents in Northern Spain, in 1999-2019 according to gender.

Acknowledgements: NIL.
Disclosure of Interests: Alba Herrero-Morant: None declared, José Luis Martín-Varillas Grant/research support from: AbbVie, Pfizer, Lilly, Janssen, UCB, and Celgene, Carmen Álvarez-Reguera: None declared, Lara Sanchez-Bilbao:

Table 1. Main clinical features of neurobehçet's disease in different geographical areas.

Author, year	Country	cases			Male n (%)		Age at onset years mean ± SD		HLAB51+ n (%)	
		BD	NBD	%	BD	NBD	BD	NBD	BD	NBD
Ideguchi et al.,2010	Japan	412	54	13	33 (61)	33 (75)	36.9±11.9	35.8±10.3	123 (50)	16 (55)
E. Bolek et al., 2020	Turkey	419	26	6.2	225 (53.7)	39 (56.5)	29.2±9.0	27.4±9.2	104 (69.3)	13 (65)
Akman-Demir et al.,1999	Turkey	ND	200	ND	ND	155 (77.5)	ND±ND	31.5±ND	ND	ND
Houman et al.,2013	Tunis	430	121	28.1	295 (68.6)	78 (64.5)	29.17±ND	29.02±ND	84 (19.5)	14 (33.3)
Al-Araji et al., 2003	Iraq	140	20	14.3	105 (75)	14 (70)	34.2±ND	34.1±ND	ND	ND
Riera-Maestra et. al., 2010	Spain	360	20	5.6	ND	13 (ND)	34±ND	36.3±ND	ND	ND
Talarico et al., 2012	Italy	117	13	38	72 (61.5)	36 (50)	25±4.0	25±4.0	77 (66)	ND
Domingos et al., 2015	Portugal	138	25	18.1	45 (32.6)	10 (40)	35.8±9.2	37.5±9.4	59 (42.9)	10 (41.1)
Sbaï A et al., 2003	France	ND	109	ND	ND	78 (65.1)	ND±ND	31±ND	ND	ND
Present study, 2022	Spain	92	23	25	58 (60.4)	8 (34.8)	38±13.9	44±13.9	43 (48.3)	5 (38.4)

Abbreviations: BD: Behçet's disease, NBD: Neurobehçet's disease, ND: Non data

None declared, David Martínez-López: None declared, Guillermo Suárez-Amorín: None declared, Raúl Fernández-Ramón: None declared, Iván Ferraz-Amaro: None declared, J. Luis Hernández: None declared, Ricardo Blanco Speakers bureau: Abbvie, Lilly, Pfizer, Roche, BMS, Janssen, and MSD, Grant/research support from: Abbvie, MSD, and Roche.
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AB1648 THE USE OF DIGITAL TECHNOLOGIES BY PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A CROSS SECTIONAL MULTICENTER OBSERVATIONAL STUDY

Keywords: Patient information and education, Lifestyles, Spondyloarthritis

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Background: Digital technologies are commonly used by most patients, and the concept of e-health emerged some years ago. These tools, which include specific medical application can deliver prevention messages, allow patients to access information about their condition or treatments, and can be used in everyday life. As axial spondyloarthritis (AxSpA) is a chronic disease, such digital tools could be useful. The aim of the study was to assess digital technologies use in an AxSpA population.
Objectives: The primary objective was to describe the use of digital technologies in patients with AxSpA treated bDMARDs. A secondary objective was to identify the factors associated with digital technology use.
Methods: We conducted a prospective, cross sectional, observational study in 5 departments of rheumatology at French university hospitals. Patients were recruited from June 2021 to June 2022. Data were collected using questionnaires filled by the patient during follow-up. Medical information was collected by rheumatologists.
Results: 500 patients were included (age 49,5 ± 13,8 years, 47% women, 51% with radiograph sacro-iliitis, 71% with HLA-B27. Mean disease activity evaluated with BASDAI was 3,5 (SD ± 2,10). 429 (86%) received TNF inhibitor. 202 patients used digital technologies for their health (40%), 59 (30%) used a medical application for other chronic disease, and 54 (10,8%) had a specific application for spondyloarthritis (or rheumatic inflammatory disease). 39% used cellphone or sport-application for physical activity. Among users of digital technologies for AxSpA, most patients searched for information concerning their disease (65%) or treatment (54%). In multivariate analysis, level of study, radiograph sacro-iliitis (OR: 1,53 [1,50-2,03] p<0,01), and being membership of patient association (OR: 7,06 [1,90-26,19] p<0,01), were still associated with the use of digital technologies. Patient education program (OR: 3,00 [1,61-5,60] p<0,01) remained associated with the use of specific applications, and men used them less (OR: 0,34 [0,18-0,67 p<0,01). Only 54 patients had at least one teleconsultation with their rheumatologist during follow-up. Among them, 17 (32%) thought that teleconsultation was sufficient, as compared with a face-to-face visit.
Conclusion: To date, a significant proportion of patients use digital technologies for their AxSpA, but few a specific application for their rheumatism. The use of medical application is strongly associated with patient education program. Reliable and validated tools should be promoted by rheumatologists.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: DESPRES Jerome: None declared, Thomas Barnetche Paid instructor for: Biogen, AMORY Charlotte: None declared, Jessika BERNARD: None declared, Maxime Vandersmissen: None declared, Cédric Lukas Speakers bureau: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Consultant of: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB., Grant/research support from: Pfizer, Novartis and Roche-Chugai, Anne Tournadre Speakers bureau: Abbvie, Amgen, Janssen, Lilly, MSD, Novartis, Pfizer, Roche-Chugai, UCB, Consultant of: Abbvie, Fresenius, Lilly, Novartis, Sanofi., Grant/research support from: Fresenius, Novartis, Pfizer, UCB, Pascale Vergne-Salle Speakers bureau: Abbvie, Fresenius, Grünenthal, Janssen, Pfizer, Roche Chugai, Sanofi, Novartis, Mylan, UCB, Lilly, Consultant of: Janssen, Abbvie, UCB, Justine LANDRIN: None declared, Adeline Ruyssen-Witrand Speakers bureau: AbbVie, Amgen, Biogen, Bristol Myers Squibb, Fresenius-Kabi, Galapagos, Janssen, Lilly, MSD, Mylan, Nordic-Pharma, Novartis, Pfizer, Roche Chugai, Sanofi, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Mylan, Novartis, Pfizer Inc, Sanofi Genzyme, Grant/research support from: AbbVie, Amgen, Mylan, Pfizer Inc.
DOI: 10.1136/annrheumdis-2023-eular.4931

AB1649 2009 AND 2019-REVISED IWOS CRITERIA FOR OCULAR SARCOIDOSIS. STUDY IN A SERIES OF 384 PATIENTS FROM A SINGLE UNIVERSITY HOSPITAL.

Keywords: Uveitis

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Background: Sarcoidosis is a systemic inflammatory disorder which involves many organs, including eyes. International Workshop on Ocular Sarcoidosis (IWOS) criteria for diagnosis of ocular sarcoidosis (OS) were first published in 2009 and revised in 2019 (question-based survey and panel discussion) **[1-2]**. IWOS criteria is a remarkable tool to relate uveitis to sarcoidosis, especially when ocular is the first manifestation in the systemic disease. Due to the consequences of OS, identify and initiate appropriate therapy is essential.
Objectives: To compare the results of IWOS criteria applied in the same population.
Methods: We studied a large cohort (n=384) of all consecutive patients diagnosed with sarcoidosis from January 1, 1999, to December 31, 2019. Finally, 344 patients were included according to the ATS/ERS/WASOG criteria **[3]**. First (2009) and revised (2019) IWOS criteria were applied to patients diagnosed with Sarcoidosis and ocular symptoms and the results were compared in both groups for our population. Concordance between 2009 and 2019 IWOS criteria was evaluated by calculating Cohen´s kappa coefficient.
Results: 65 (51% men) of 344 patients had ocular involvement (18.9%), mean age 56.7±16.3 years. As for nationality, 92.3% were Spaniard and 7.7% were South American. A positive biopsy for sarcoidosis was obtained in 75.4% (n=49) and a negative biopsy in 6.2% (n=4). There was no statistically significative difference between diagnostic groups for IWOS 2009/IWOS 2019 in age (p=0.738/p=0.495), sex (p=0.534/p=0.459) nor nationality (p=0.529/p=0.393). When applied 2009 IWOS criteria, 60% (39 patients) met any of the diagnostic categories (43.1% *Definitive*, 13.8% *Presumed*, 1.5% *Probable*, 1.5% *Possible*). When 2019 IWOS criteria was applied, 53.8% (35 patients) met any of the new diagnostic categories (43.1% *Definitive*, 7.7% *Presumed*, 3.1% *Probable*). Sensitivity for IWOS 2009 was 0.6 and for IWOS 2019 was 0.53. There was statistically significative concordance between 2009 and 2019 IWOS criteria (p<0.0001) with a strong consistency level (kappa = 0.824). When analyzing IWOS categories separately, we found total concordance in the *Definitive* category. *Probable* and *Possible* categories in 2009 criteria have been merged in only probable in 2019 criteria and there is a total concordance when comparing both. *Presumed* category represent the bigger change in the revised criteria. We found statistically significative concordance (p=0.000008) with a moderate consistency level (kappa = 0,524).
Conclusion: The revised 2019 IWOS criteria is less sensitive in our population; however, the main difference is in the category *Presumed*: the requirement of at least 2 intraocular signs of uveitis led to a change of 9 patients (13,8%) in 2009 IWOS down to 5 (7.7%) in 2019. In our population IWOS criteria is still has a low sensitivity.
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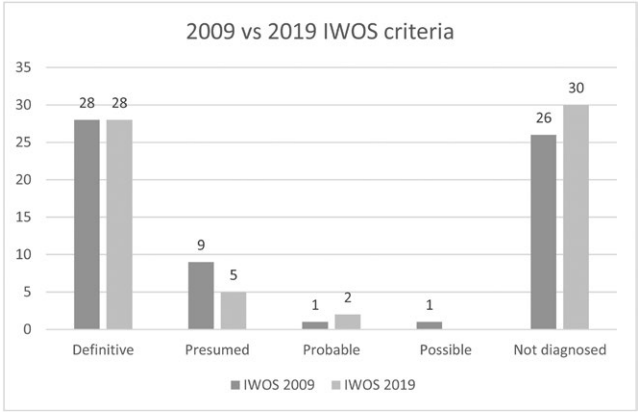


Figure 1. Results of 2009 and 2019 IWOS criteria on a defined population.

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Disclosure of Interests: Carmen Lasa: None declared, Jorge Gaitán Valdizán: None declared, Lara Sanchez-Bilbao: None declared, José Luis Martín-Varillas: None declared, David Martínez-López: None declared, Iñigo Gonzalez-Mazon: None declared, Raúl Fernández Ramón: None declared, Rosalía Demetrio-Pablo: None declared, Ricardo Blanco Speakers bureau: Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, lilly, Bristol-Myers, Janssen, Galapagos and MSD, Consultant of: Abbvie, Pfizer, Roche, lilly, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD, novartis and Roche.
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Epidemiology, risk factors for disease or disease progression

AB1650

LATENT TUBERCULOSIS INFECTION IN PATIENTS WITH RHEUMATIC IMMUNE-MEDIATED DISEASES: PREVALENCE AND SCREENING STRATEGY

Keywords: bDMARD, Geographical differences

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Background: Patients with rheumatic immune-mediated diseases (R-IMID) with latent tuberculosis infection (LTBI) requiring biologic therapy (BT) are at an increased risk of active tuberculosis (TB). The prevalence of LTBI in patients with R-IMID varies depending on geographical location. An accurate diagnosis and prophylactic treatment of LTBI is crucial to reduce the risk of developing TB. No definitive gold standard exists for diagnosing LTBI. Tuberculin skin test (TST) and interferon-γ release assays (IGRAs) are the most used tests.

Objectives: To assess: a) Prevalence of LTBI in patients with (R-IMID), b) determine the importance of using a booster test in negative TST, c) to compare TST with the IGRA test in the detection of LTBI in patients with R-IMID and d) to perform a literature review of prevalence of LTBI in different geographical areas and its relationship with R-IMID.

Methods: Cross-sectional single University hospital study including all patients diagnosed with R-IMID who underwent a TST (±booster) and/or IGRA in a period from 2016 to 2020. If TST was negative, a new TST (Booster) was performed between 1 and 2 weeks after the first TST. Patients were diagnosed with R-IMID by an expert rheumatologist according to well-established ACR/EULAR classification criteria for each R-IMID. LTBI was defined by a positive TST and/or IGRA with no evidence of active TB. Diagnosis with IGRA vs TST was compared using Cohen's kappa coefficient. We performed a literature review in search of previous prevalence studies of LTBI in patients with R-IMID. This search was performed in the month of August 2022. The aim of this review was to compare the prevalence of LTBI in patients with R-IMID in different geographical areas.

Results: We included 1117 patients (741 women/376 men), mean age 53±15 years with LTBI. Overall LTBI prevalence was 31.7 % ranging from 25% in SLE up to 33.3% in BD. Results of prevalence compared to other countries are shown in **Table 1**. Booster was positive in 66 patients (7.7%) out of 857 patients with a negative simple TST. TST (+booster) was positive in 187 patients (22.9%) out of 817 with a negative or indeterminate IGRA test. IGRA test was positive in 30 (3.8%) out of 793 patients with a negative TST(+booster), as it is represented in **Figure 1**. Cohen's Kappa coefficient between TST(+booster) and IGRA (QFT-plus), was 0.381.

Conclusion: LTBI is frequent between patients with R-IMID. LTBI screening is important in patients who need to receive BT. This assessment has to be done performing both TST and IGRA as. complementary methods to ensure the detection of all patients with LTBI, since both tests. can have false negative results, especially in patients with R-IMID receiving. immunosuppressive therapy.

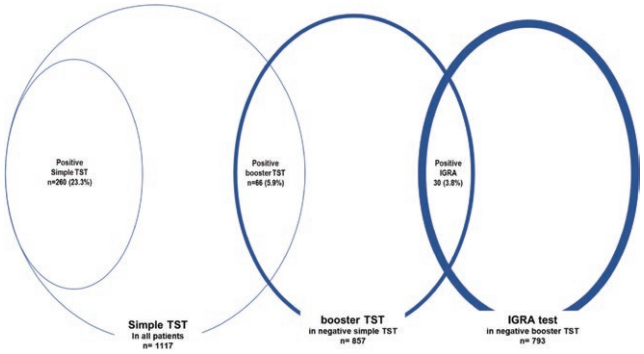


Figure 1. Proportion of positives in different test to diagnosis LTBI in R-IMID patients.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Carmen Lasa: None declared, Joy Selene Osorio Chavez: None declared, David Martínez-López: None declared, Carmen Álvarez-Reguera: None declared, Virginia Portilla: None declared, Jose Manuel Cifrián-Martínez: None declared, Iván Ferraz-Amaro: None declared, Ricardo Blanco Speakers bureau: Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, lilly, Bristol-Myers, Janssen, Galapagos and MSD, Consultant of: Abbvie, Pfizer, Roche, lilly, Bristol-Myers, Janssen and MSD, Grant/research support from: Abbvie, MSD, novartis and Roche.

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AB1651

DIFFUSE ALVEOLAR HEMORRHAGE IN RHEUMATOLOGY: CLINICAL PRESENTATION, ETIOLOGY, TREATMENT AND OUTCOME

Keywords: Lungs, Systemic lupus erythematosus, Vasculitis

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Table 1. Prevalence of LTBI in other geographic regions according to underlying R-IMID.

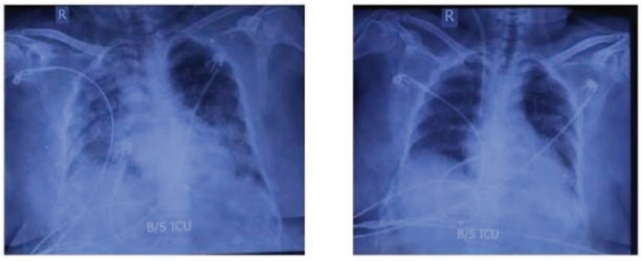
Author, year (ref. in text)	Region	Diagnostic criteria and study period	Prevalence in R-IMID (%)	Prevalence in RA (%)	Prevalence in PsA (%)	Prevalence in AS (%)	Prevalence in SLE	Prevalence in BD
Soborg, et al (2009)	Denmark	TST	19%	20%		28%		
		and IGRA	7%	9%		5%		
		2005 to March 2007						
Chang, et, al (2011)	Korea	TST or IGRA test	35%	22%		47%		
		(2007–July 2009)	30%	31%		29%		
Mínguez, S, et al. (2012)	Spain	TST, T-SPOT.TB and	13%	16%				
		QTF-plus	20%	22%				
		2008-2010	17%	22%				
Mariett X,et, al (2012)	France	TST, T-SPOT.TBand	35.2%					
		QTF-plus	15.1%					
		(2011)	9.9%					
Miras, et al. (2014)	Spain	TST and T.SPOT.TB					7%	
		August 2009 to February 2012					5%	
Carina Mori Frade Gomes et al. (2015)	Brazil	TST	20.6%	12,8%	18,8%	37.6%		
D. Perifanou, et al. (2018)	Greece	TST and IGRA test	66.7%	15%		21%		
		2008-2010	31 %					
Anton C, et al. (2019)	Brazil	TST	13 %	4%	23%	26%		
M. Sellami et al. (2019)	North of Tunisia	TST and IGRA test	45.7%					
		2015-2017	21.9%					
Lamia. Oulkadi, et, al. (2021)	Morocco	TST and IGRA test	7.7 %	15.9%	2,4%	24.8%		
		2017 – 2021	15.4 %					
Shen, et al. (2021)	China	T.SPOT.TB						29.3%
		October 2012 and June 2017.						
Present series	Spain	TST	31.7%	29.4%	32.5%	32.5%	25%	33.3%

Background: Diffuse alveolar hemorrhage (DAH) is characterized by rapid onset of pulmonary infiltrates and hypoxemia. It is a potentially life threatening complication associated with systemic autoimmune conditions.
Objectives: To describe the presentation, clinical features, etiology, treatment and outcome of DAH in rheumatological conditions.
Methods: This a retrospective, multicentre study involveing 3 rheumatology centers, wherein data about DAH cases seen over the past 5 years was collected.
Results: There were 19 patients (Female = 15). The mean age was 38 years (18 - 67). DAH was the presenting feature in 15 patients (78%). The mean duration of symptoms was 20 days (1 - 60). The symptoms of DAH were: dyspnea 16 (84%), cough 15 (78%), hemoptysis 13 (68%). Other features of DAH like hypoxemia (18 patients), fall in hemoglobin (19 patients) were common. Fever was observed in 9 (47%). Nephritis was noted in 14 (73%). Renal biopsy was done in 6 (Lupus nephritis class 3 & 5 = 1; lupus nephritis class 4 = 1; Pauci immune crescentic glomerulonephritis = 3;Anti GBM associated crescentic glomerulonephritis =1). The most common feature on chest radiograph was diffuse opacities (Image 1). The etiology of DAH was as follows (Table 1) - granulomatosis with polyangiitis (GPA = 8); Systemic lupus erythematosus (SLE =7); anti GBM disease (2); Microscopic polyangiitis (MPA=1) and undifferentiated vasculitis [1]. The treatment of DAH included - Intravenous methylprednisolone (IV MP)=18; Intravenous immunoglobulin (IVIG) = 2; Extracorporeal membrane oxygenation (ECMO) = 1; Therapeutic plasma exchange = 3; Intravenous cyclophosphamide = 11; Rituximab (RTX) = 4; Mycophenolate mofetil (MMF) = 1. Most of the patients were managed in the intensive care unit (ICU) (13/ 19) and needed ventilatory support (11/ 19). Most patients required more than 10 days of hospitalization (12/ 19 = 63%). There were a total of 5 deaths (GPA =2; SLE =2; anti-GBM disease =1).
Conclusion: DAH was the presenting feature in most of the cases. GPA and SLE were the common causes. Dyspnea, cough and Hemoptysis were the common DAH symptoms. Fever and nephritis were the common Non - DAH clinical feature. Most of the patients were treated with IV MP and required ICU care; Approximately half of the patients required ventilatory support. DAH is a potentially life threatening condition with an overall mortality rate of approximately 25%.Early recognition and appropriate treatment is needed for better outcome.
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Table 1. DAH - Causes, clinical features, treatment and outcome

Diagnosis	DAH features	Non DAH features	Treatment	Outcome
GPA (N=8) (M/ F= 4/4) DAH as presenting feature = 6	Cough - 5 Dyspnea - 6 Hemoptysis - 3	Nephritis - 5 Fever - 4 LRT - 3 Skin rash - 2 ENT - 1 Oral ulcers - 1 Scleritis – 1	IV MP - 8 TPE - 3 IV CYC - 6 RTX - 2 ICU - 5 Ventilatory support - 4	Discharge within days - 2 Discharge after 10 days - 5 Death - 2
SLE (N=7) (F = 6) DAH as presenting feature = 3	Cough - 6 Dyspnea - 6 Hemoptysis - 6	Nephritis - 6 ITP - 5 Fever - 5 Alopecia - 2 Oral ulcers - 2 AIHA - 2 CNS - 1 Serositis – 1	IV MP - 6 IVIG - 2 IV CYC - 2 RTX - 2 ICU - 5 Ventilatory support - 4	Discharge within days - 1 Discharge after 10 days - 4 Death - 2
Anti-GBM disease (N = 2; All female) DAH at presentation = 2	Cough - 2 Dyspnea - 2 Hemoptysis - 2	Nephritis - 2 Arthritis – 1	IV MP - 2 TPE - IVIG - IV CYC - 1 RTX - ECMO - 1 ICU - 2 Ventilatory support - 2	Discharge after 10 days - 1 Death - 1
MPA (N=1) (Female) DAH at presentation = Y	Cough - Y Dyspnea - Y Hemoptysis - Y	Nephritis – 1	IVMP - Y IV CYC - Y ICU - N Ventilatory support- N	Discharge after 10 days - 1
Undifferentiated vasculitis (N = 1) (Female) DAH at presentation = Y	Cough - Y Dyspnea - Y Hemoptysis - Y	Skin rash	IVMP - Y IV CYC - Y TPE - Y ICU - Y Ventilatory support - Y	Ongoing treatment > 10 days of hospitalization

LRT - lower respiratory tract; ENT - Ear, nose, throat; AIHA - Autoimmune hemolytic anemia; ITP - Idiopathic thrombocytopenic purpura; CNS - Central nervous system; M - Male; F - Female: Y = Yes;N = No.



Pre-treatment

After 5 cycles of Plasma exchange

Image 1 : Chest X ray

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1652 **THE PRESENCE OF DISEASE-SPECIFIC ANTIBODIES IN THE ABSENCE OF AN INFLAMMATORY RHEUMATIC DISEASE**

Keywords: Organ damage, Autoantibodies

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Background: Inflammatory rheumatic disease (IRD) are characterized by the appearance of a specific clinic, the presence of findings in immunological laboratory and imaging. Some patients presented specific IRD autoantibodies without a clinical manifestation of IRD.
Objectives: The objective of this study was to evaluate the frequency of disease-specific autoantibodies in patients with absence of clinical IRD manifestation.
Methods: The study included an analysis of 3793 Caucasian patients from a department of rheumatology localized at a university hospital in Europe specified for screening in IRD between 2015 and 2020. All patients revealed a standardized clinical examination and diagnostic procedure including immunological laboratory and imaging. Biopsies were performed when clinically indicated. Especially autoantibodies for rheumatoid arthritis (rheumatic factor [RF], anti-citrullinated peptide antibodies [ACPA]), connective tissue disease (antinuclear antibodies immunofluorescence test [ANA IFT] and extractable nuclear antibodies [ENA]), vasculitis (anti neutrophil cytoplasmatic antibodies [ANCA]) and myositis (myositis blot) were included.
Results: IRD was diagnosed in 1534 patients (40.4%) with the following distribution: 21.2% (n=325) rheumatoid arthritis, 22.8% (n=350) connective tissue disease, 6.5% (n=100) vasculitis and 2.3% (n=35) myositis. IRD was excluded in 762 patients (20.1%). 39.5% (n=1497) of the patients without a clinical manifestation of IRD presented a disease-specific autoantibody. 94.3% (n=1412). In detail, ANA IFT (≥1:80) with the different stages: 1:80 48.9% (n=691), 1:160 27.2% (n=384), 1:320 12.3% (n=174), 1:640 5.2% (n=73), 1:1280 4.4% (n=62), >1:1280 2.0% (n=28), extractable nuclear antibodies 14.0% (n=208), RF and/ or ACPA 16.8% (n=252), c-/p-ANCA 1.9% (n=29) and myositis autoantibodies 1.8% (n=27). The mean age of the Non-IRD patients was 52.2 ± 15.1 years, with 398 (26,6%) male and 1099 (73,4%) female patients. Both gender and age were significant different to the IRD group (p<0.001).
Conclusion: The study highlighted that in screening of IRD 40 % of the patients presented IRD associated autoantibodies without a clinical manifestation of IRD. As already known, the isolated presence of disease-specific autoantibodies cannot confirm IRD. In this case, systematic and standardized organ screening is indispensable, to evaluate the clinical significance of the autoantibody. A clinical follow-up examination should be performed, especially if there is a change in symptoms or clinical suspicion of a possible organ manifestation of IRD.
References: N/A.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1653

EPIDEMIOLOGY AND CLINICAL PRESENTATION OF GIANT CELL ARTERITIS IN A REFERRAL HOSPITAL OF NORTHERN SPAIN

Keywords: Epidemiology, Adaptive immunity, Vasculitis

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Background: Traditionally, giant cell arteritis (GCA) was described as a disease of the temporal arteries. It is now accepted that the clinical spectrum has become broader and different diagnostic tools such as PET and US have made possible to diagnose patients who have not been included in the last decades, especially in extracranial forms. Moreover, recently, new diagnosed criteria (2022 ACR/EULAR) have been proposed. This implies an evident change of the clinical epidemiology of GCA.
Objectives: To assess the clinical epidemiology of GCA accordingly to new diagnostic tools and 2022 ACR/EULAR criteria.
Methods: Observational study of patients diagnosed with GCA who underwent temporal artery biopsy (TAB) between January 2016 and December,2022. The patients were divided into 3 groups: **a)** only cranial (cGCA), **b)** only extracranial (ecGCA), and **c)** mixed affection (mixGCA). The diagnosis of GCA was made according to **a)** temporal artery biopsy, and/or **b)** EULAR/ACR2022 criteria, and/or **c)** imaging techniques. Demographic, clinical, analytical and imaging techniques characteristics were studied.
Results: We included 191 patients (120 females/71 males), with a mean±SD age of 74.9±9.6 years. The main characteristics of the patients and the differences among phenotypes are shown in **Table 1**. Only a 27.2% of the patients had a positive TAB with a mean±SD length of 16.4±6.3mm. The GCA phenotype most frequent was the cranial GCA (cGCA). Headache (79.6%) was the most common ischemic manifestations, followed by the abnormal examination of temporal artery (46.6%) and visual symptoms (including 8.4% patients with blindness), jaw or lingual claudication (26.3%), and scalp tenderness (25.1%). Polymyalgia rheumatica (PmR) was the most frequent systemic manifestations, observing in 59.2% of the patients. The values of serum CRP and ESR are shown in **Table 1**.
Conclusion: GCA is a vasculitis which has increased its clinical spectrum with extracranial involvement, affecting people with a mean age of more than 70 years and with a female predilection. PmR appears to be present in more than half of the patients, mainly in extracranial phenotype.

Table 1. Main features of the GCA patients.

	TOTAL (n=191)	cGCA (n=128)	ecGCA (n=28)	mixGCA (n=36)	p (cGCA vs ecGCA)
Age (years), mean±SD	75 ± 10	75 ± 10	74 ± 9	74 ± 9	0.55
Sex, female (% females)	120 (63)	79 (62)	16 (57)	25 (69)	0.62
TAB+, n (%)	52 (27)	39 (31)	2 (7)	11 (31)	0.010
ACR1990 Criteria, n (%)	128 (67)	95 (75)	6 (21)	27 (75)	<0.001
EULAR/ACR2022 Criteria, n (%)	155 (81)	108 (85)	14 (50)	33 (92)	<0.001
Ischemic manifestations, n (%)	152(80) 48(25)	115(91) 39(31)	7(25) 0(0)	30 (83) 9 (25)	<0.001 <0.001
-Headache	89(47)	64(50)	7(25)	18 (50)	0.015
-Scalp tenderness	76(40)	62(49)	4(14)	10 (28)	0.001
-Abnormal examination of TA	50(26)	40(32)	3(11)	7 (19)	0.034
-Visual impairment					
-Jaw/lingual claudication					
Systemic manifestations, n (%)	27 (14) 113 (59)	16 (13) 62 (49)	5 (18) 24 (86)	6 (17) 27 (75)	0.54 <0.001
-Fever					
-PmR					
Laboratory	2.5 [0.5-7.7]	2.9 [0.4-7.7]	2.2 [0.6-8.0]	2.3[0.5-6.6]	0.92
-CPR, mg/dL, median [IQR]	56 ± 35	54 ± 34	63 ± 41	56 ± 30	0.26
-ESR, mm 1ºh, mean±SD					
Predinsone therapy	40 [20-45]	40 [30-50]	30 [10-40]	40 [15-45]	0.15
- Dose (mg/day), median [IQR]	569	625	330	650	0.82
- Cumulative dose (mg), median [IQR]	[240-1875] 9 [4-21]	[285-1925] 9 [3-17]	[169-473] 8 (5-30)	[200-1875] 10 [5-25]	0.45
- Time (days) from GC onset and TAB, median [IQR]					

Abbreviations: ACR: American College of Rheumatology, cGCA: cranial giant cell arteritis, ecGCA: extracranial giant cell arteritis, EULAR: European League Against Rheumatism, GCA: giant cell arteritis, mixGCA: mixed giant cell arteritis, PmR: polymyalgia rheumatica, TA: temporal artery, TAB: temporal artery biopsy.

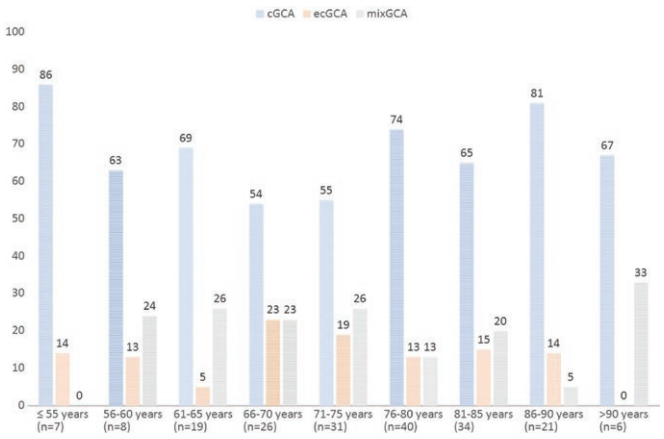


Figure 1. Distribution of GCA phenotypes in different age groups. All data are in % (n).

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AB1654

IMPACT OF WORK ORGANIZATION ON ROTATOR CUFF TENDINOPATHY

Keywords: Patient information and education

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Background: Rotator cuff tendinopathy is one of the common causes of shoulder pain. The etiology of rotator cuff tendinopathy has been reported to be multifactorial. Organizational and psychosocial work factors have also been mentioned as important contributors to work-related musculoskeletal disorders.
Objectives: The objective of this study was to assess the impact of work organization on rotator cuff tendinopathy.
Methods: A descriptive cross-sectional study was conducted at the Tahar Sfar Hospital in Mahdia, it concerned patients who consulted the occupational medicine department for shoulder tendinopathies. The information was collected using a self-questionnaire distributed during the medical visit, in order to collect the socio-professional characteristics and organizational constraints.
Results: A total of 100 patients participated in this study. The population was predominantly female (89%). Sixty-five percent of the patients worked in the manufacturing sector and working as a machine operator was the most common occupation (48%). the average job tenure was 22±9 years. The weekly working hours were 45±7 hours on average. All cases had pain in one or both shoulders. On clinical examination, subacromial impingement maneuvers were positive in 94% of the cases and ultrasound revealed rotator cuff tendinopathy in 69% of the cases. In terms of organization, the most common constraints were the need to respect production standards and deadlines (76.9%), to work at a fast pace in 78% of cases, and to carry out their work under continuous supervision (73.4%). On univariate analysis, ultrasound-diagnosed shoulder tendinopathy was significantly associated with female gender (p=0.003), working according to an imposed rhythm (p=0.008), the need to follow directions in order to perform their tasks (p=0.035), and finally, continuous supervision by the work manager (p=0.001).
Conclusion: This study examined factors that were associated with increased risk of rotator cuff tendinopathy. In conclusion, it is essential to identify these factors in order to develop prevention interventions and further high-quality prospective studies are required to identify the exact risk factors for rotator cuff tendinopathy.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6360

AB1655

PREVALENCE OF COMORBIDITIES IN RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND AXIAL SPONDYLARTHRITIS: RESULTS OF AN INTERNATIONAL, REAL WORLD PANLAR´S REGISTER

Keywords: Registries, Rheumatoid arthritis, Real-world evidence

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Background: Rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) are diseases where inflammation plays a key role in their development and have an increased risk of developing comorbid conditions. It is important to evaluate the comorbidities associated with these diseases.
Objectives: Our objective was to evaluate the prevalence of comorbidities in RA, PsA and axSpA patients from the PANLAR´s register of rheumatic diseases (PANRED).

Table 1. Prevalence of comorbidities.

	Total (N=708)	RA (N= 632) (89.3%)	PsA (N= 32) (4.5%)	axSpA (N = 38) (5.4%)	Other (N = 6) (0.8%)
Hypertension	39.5%	40.6%	34.4%	27%	33.3%
Stroke	1%	1.1%	0	0	0
Acute myocardial infarction	2.3%	2.6%	0	0	0
Dyslipidemia	35.3%	36.5%	34.4%	18.9%	16.7%
Smoking	23.5% CS: 41.4% EX: 58.6%	23.7% CS:39% Ex: 61%	34.4% CS: 63.6% Ex: 36.4%	15.3% CS: 60% Ex: 40%	0
Diabetes	13.6% Tipe II: 95.8%	14.52% Tipe II: 13.86%	15.6% Tipe II: 100%	5.4% Tipe II: 100%	0
Non-cutaneous cancers plus melanomas	2.4%	2.4%	3.1%	2.7%	0
Non-melanoma skin cancers	0.7%	0.6%	0	2.7%	0
Inflammatory bowel disease	0.6%	0.5%	0	2.7%	0
Nonalcoholic steatohepatitis	35.6%	5.5%	12.9%	2.7%	0
Uveitis	2.3%	1%	0	27%	0
Deep venous thrombosis (DVT or PT)	2.3% DVT: 68.75% TVP + PT: 31.25%	2.6% DVT: 68.75% DVT+PT:31.25%	0	0	0
Herpes Zoster	3.7% MC: 100%	3.9% MC: 100%	3.1% MC: 100%	2.7% MC: 100%	0
COPD	3.3%	3.4%	3.1%	2.7%	0
Interstitial lung disease	5.48% UIP:47.4% NSIP:34.2%	5.98% UIP: 48.6% NSIP: 35.1%	3.1%	0	0
Tuberculosis	13.3% Latent: 79.34% AP: 16.3% A-ExP: 4.36%	13.3% Latent:78% AP: 17.1% A-ExP: 4.9%	12.5% Latent:75%% AP: 25%% A-ExP: 0%	16.2% Latent: 100% AP: 0% A-ExP: 0%	0
Hepatitis B	2%	1.9%	3.1%	2.7%	0
Hepatitis C	0.7%	0.6%	3.1%	0	0
HIV	0.3%	0.3%	0	0	0
Chagas	0.7%	0.6%	3.1%	0	0

Current smoking: CS; pulmonary throboembolism: PT; deep venous thrombosis: DVT; monometameric cutaneous: MC; chronic obstructive pulmonary disease: COPD; active pulmonary: AP; A-ExP: Active Extrapulmonary.

Methods: PANRED includes real world data from Latin American consecutive patients diagnosed with RA, PsA and axSpA (ACR-EULAR 2010/CASPAR 2006-ASAS 2009) from Dec 2021 to Dec 2022. We collected: demographics, disease characteristics (activity, severity, treatment), basal comorbidities (cardiovascular, infections, cancer, gastrointestinal, pulmonary, and others) data. Data were extracted from patients initiating treatment with cDMARDS, TNF alpha inhibitors (TNFi) and Jakinasas inhibitors (JAKi). Categorical variables were expressed as percentage and tables of contingency were analyzed with $\chi 2$ or Fisher test. A p value less than 0.05 was considered significant.
Results: 708 patients were included. RA was the most frequent disease. The most prevalent comorbidities expressed as overall frequency were: hypertension: 39.5%, nonalcoholic steatohepatitis: 35.6%, dyslipidemia: 35.3%, tuberculosis 13.3%. Details of comorbidities are shown in the Table 1. Uveitis was more frequent in axSpA vs RA, RR: 2.5 (95%CI 1.35-4.8), p<0.001. Herpes zoster was present in 3.3%, 3.6% and 0.8% and tuberculosis in 15.85%, 15.1% and 3.8% in Jaki, TNFi and cDMARD groups respectively. Steatohepatitis was significantly higher in the cDMARD group compared Jaki and TNFi (p=0.01) and tuberculosis in the JAKi group (p=0.002) compared bDMARD and cDMARD, as basal characteristics, probably reflecting therapeutic decisions.
Conclusion: Cardiovascular comorbidities and tuberculosis are frequent in Latin American patients and should be considered in treatment selection.
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AB1656

THE USE OF MACHINE LEARNING METHODS IN OPIOID-ASSOCIATED OUTCOMES RESEARCH: A SYSTEMATIC REVIEW

Keywords: Artificial intelligence, Systematic review, Prognostic factors

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Background: Prescription opioids have been a considerable contributor towards the opioid epidemic, a major public health concern with profound economic repercussions and mortality. In order to address the opioid crisis, a need exists to improve understanding on how to personalise prescribing incorporating individual factors to estimate the risk of opioid-related harms. Machine learning (ML) techniques, both supervised and unsupervised, have potential identify patients at risk through the development of risk prediction models and a data-driven redefinition of patient classes. This might be particularly relevant when addressing the changing dynamics of the opioid epidemic, due to its ability to ascertain non-linear relationships between various risk factors and the risk of opioid-related harms.
Objectives: To perform a systematic review of the use of ML methods in prescription opioid-related harms research.
Methods: A systematic literature search was conducted using the databases Ovid MEDLINE, PubMed and SCOPUS databases to identify relevant articles that were published from inception to October 2022. Articles were eligible for review if they described studies that applied ML techniques with a primary outcome that was related to prescription opioid harms and using electronic health records as a main data source for the research. We excuded studies that focused patients with cancer or younger than 18 years old.
Results: A total of 760 abstracts were reviewed, yielding 75 articles for full text review. Four main categories were identified in this area: development of ML algorithms for prediction (n=81, 81%), identification of risk factors n=7, 9%),

patient subtype clustering (n=5, 7%) and the application of natural language processing to understand user-generated text for pharmacovigilance (n=2, 3%). Within the studies that developed ML models for prediction, most of them (n=16, 21%) had prolonged postoperative opioid use as their main outcome (the majority looking at arthroplasty, arthroscopy and spine surgery patient populations). All these studies had skewed outcome proportions but only three studies (4%) addressed it (with either oversampling techniques or reporting the area under the precision-recall curve). Only one study had been externally validated. Other primary outcomes of prediction models developed included opioid use disorder (n=12, 16%), opioid overdose prediction (n=9, 12%), opioid administration and prescribing (n=6, 8%) and chronic opioid use (n=3, 4%). For risk factor identification, ML techniques were limited to understanding the drivers of opioid-overdose (n=2, 3%), opioid dependency (n=2, 3%) and opioid administration and prescribing (n=3, 4%). A very limited number of studies used unsupervised and semi-supervised ML algorithms to address opioid-associated outcomes (n=8, 11%).

Conclusion: To date, application of ML techniques besides logistic regression to classify patients who experience opioid-related harms has been limited, with most publications using electronic health records from the United States in the last 5 years. The majority focused on prediction algorithms for postoperative opioid use and have limited implementation in clinical practice. The current literature lacks external validation studies for developed prediction models using ML. This is especially important if implemented outside of the United States, since the use of opioids is affected by a diverse set of individual and contextual factors that can substantially vary across countries.

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AB1657 TIME-DEPENDENT CSDMARDS USE AND INFLAMMATORY BURDEN CAN PREDICT CARDIOVASCULAR RISK IN PATIENTS WITH ANKYLOSING SPONDYLITIS:A POPULATION-BASED STUDY

Keywords: Cardiovascular disease, Prognostic factors, Disease-modifying drugs (DMARDs)

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Background: It is well established that AS patients had a higher risk of cardiovascular disease (CVD) than the general population [1,2]. To date, there is no primary studies directly addressing the relationship between risk factors and MACE in population-level study.

Objectives: To examine whether inflammatory burden and drug use over time increase major adverse cardiovascular events (MACE) independent of traditional cardiovascular (CV) risk factors in ankylosing spondylitis (AS) patients.

Methods: Patients who had been diagnosed with AS (ICD-9: 720.0) from 2006 to 2015 were recruited in a retrospective cohort study. They were followed until the end of 2018. The primary outcome was a first incidence of MACE. Time-varying Cox proportional hazard models were used to assess whether inflammatory burden (c-reactive protein [CRP] and erythrocyte sedimentation rate [ESR]), and drug use (non-steroidal anti-inflammatory drugs [NSAIDs] and disease modifying anti-rheumatic drugs [DMARDs]) can predict the development of first MACE.

Results: Totally 3827 patients (age: 45.2 ± 15.0 years, male: 2911 [76.1%]) were recruited. 135 patients (13.2%) developed a first MACE. ESR level (including ESR≥20 mm/h and ESR≥30mm/h, HR: 2.07-2.41), CRP level (including CRP>3 mg/dl, HR: 1.20-8.77) and use of steroid (HR: 3.48) were associated with a significantly higher risk of MACE during follow-up. Whereas the use of sulfasalazine (SLZ), bDMARDs and non-COXII inhibitor were associated with reduced risk of MACE. After adjusting for time-fixed CV risk scores in the multivariable models, only ESR level (including ESR≥30 mm/h, HR: 1.02-1.94) and CRP level (including CRP>3 mg/dl, HR: 1.14-5.43) remained significant predictor for increased risk of MACE, while SLZ (HR: 0.41-0.52) was protective against MACE.

Conclusion: Increased inflammatory burden was associated with increased risk of MACE, while the use of SLZ may reduce risk of future MACE in patients with AS.

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AB1658 COMPARISON OF STERNOCLEIDOMASTOIDEUS FLEXIBILITY, VAGUS NERVE FUNCTION, AND GASTROINTESTINAL SYMPTOMS IN CHRONIC NECK PAIN AND HEALTHY INDIVIDUALS

Keywords: Gastrointestinal tract, Prognostic factors, Non-pharmacological interventions

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Background: The vagus nerve emerges from the jugular foramen and continues through the carotid sheath in the cervical region. The carotid sheath is in contact with the SCM muscle. It has been hypothesized that Sternokleidomastoideus (SCM) muscle tension may affect the carotid sheath and the function of the vagus nerve passing through it. It is known that there is an increase in activation of the SCM muscle in individuals with chronic neck pain (CNP), which may change the passive mechanical properties of the muscle [1]. It has been shown that vagus nerve dysfunction can cause pathologies in the organs it innervates. Although the relationship between vagal dysfunction and gastrointestinal system symptoms is clear, the mechanisms that may affect vagus nerve function have not yet been clarified.

Objectives: This study aims to compare the passive mechanical properties of the SCM muscle, vagus nerve function, and gastrointestinal symptoms in healthy individuals with neck pain.

Methods: Tone, stiffness and elasticity, which are the passive mechanical properties of the SCM muscle, were measured with the Myoton-3 myotonometric medical device (Muomeetria AS, Estonia, EU). Vagus nerve function was evaluated with the Vagus Neurodynamic Test (VAGUS-NDT)[2]. The test was performed bilaterally. Gastrointestinal symptoms were evaluated with the Gastrointestinal Symptom Rating Scale (GSRS).

Results: 29 individuals, 15 healthy, 14 with CNP, who were not diagnosed with gastrointestinal or any systemic disease were included in the study. In individuals with CNP, the positivity of VAGUS-NDI test and GSRS all sub-scores (reflux, indigestion, diarrhea, constipation and abdominal pain) and total score were higher than healthy individuals ($p<0.05$). In addition, right and left elasticity scores for the SCM muscle were lower in these individuals than in healthy individuals ($p<0.05$) while tone and stiffness were similar($p>0.05$).

Conclusion: According to our preliminary results, SCM elasticity was lower and the incidence of vagal dysfunction and gastrointestinal symptoms were higher in individuals with CNP than in healthy. This may be due to compression of the vagus nerve passing through the carotid sheath as a result of decreased SCM muscle elasticity. The increase in the tension of the soft tissues around a nerve in the body restricts the movement of the nerve, affecting its function and making it susceptible to entrapment. Even this slight nerve compression can cause entrapment and lead to neuroinflammation[3]. This research is a preliminary conclusion that neck pain and decreased SCM elasticity may be an important factor that may affect vagal function. This relationship needs to be investigated with a larger sample group and advanced statistical methods.

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AB1659 MOROCCAN SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTER IN RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS (RBSMR): 3 YEAR-FOLLOW UP ANALYSIS

Keywords: Rheumatoid arthritis, Spondyloarthritis, bDMARD

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Background: Limited data have been published on tolerance and efficacy of biotherapy in moroccan patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA).
Objectives: To assess in real life the safety and efficacy of biological treatments in moroccan patients with RA and SpA.
Methods: The RBSMR is a registry of biological therapies in rheumatic diseases from the Moroccan Society of Rheumatology. The patients recruited were over the age of 18 years, diagnosed with RA or SpA, fulfilled ACR/EULAR 2010 criteria and ASAS 2009 criteria respectively and treated with biologics (initiation or ongoing biotherapy) in 10 Moroccan university medical centers. The inclusion period was from May 2017 to January 2019. Follow-up data were collected every 6 months for 3 years. The details of the data collected have been published previously. [1] Statistical analysis was performed using Jamovi software, 1.6.
Results: A total of 225 RA and 194 SpA including 170 ankylosing spondylitis were treated with biologics (bDMARDs). Overall median age at inclusion was 53 and 39 years. The median disease duration was 146 and 131 months for RA and SpA respectively.163 (72.4%) RA and 137(70.6%) SpA received a first line bDMARDs.10.7 % RA and 55.2 % SpA were prescribed bDMARDs in combination with csDMARDs. After 3 years of follow-up, median DAS28 CRP was 2.6 [0.9-4] (p<0.001) and median ASDAS CRP was 1.8 [1-2.4] (p=0.66). The most commonly used drug was rituximab (60%) in RA and etanercept (33%) in SpA. At 3 years-follow up, 18.3% and 17.4% adverse events were reported in RA and SpA patients respectively. The most common adverse events reported in RA and SpA were infections, mainly nonspecific infections, in both diseases (5.8%, 5.2%). One lymph node tuberculosis in an RA patient taking infliximab and 6 cases of tuberculosis in SpA patients taking anti-TNFs were reported in our registry. Malignancy was observed in 3 patients with RA (1 non-Hodgkin lymphoma, 1 bladder cancer and 1 breast cancer) and 2 SpA patients (1 vocal cord carcinoma and 1 multiple myeloma). During follow-up, 38bDMARDs switchers were reported in RA patients (10 at 1 year, 9 at 2 years and 9 at 3 years), while 41 switchers were reported in SpA patients (23 at 1 year, 14 at 2 years and 4 at 3 years).
Conclusion: In this real-world analysis of data from the RBSMR registry, a considerable proportion of patients with RA and Spa had an adequate response to bDMARDs at 36 months. Infections, mainly nonspecific infections, were the main adverse events in both RA and SpA of our registry.

Table 1. Adverse events of bDMARDs in RA and SpA patients during 3 years of follow up

	RA N=225			SpA N=194		
Adverse events	**1 year**	**2 years**	**3 years**	**1 year**	**2 years**	**3 years**
	87 (38.4)	53 (22.9)	42 (18.3)	74 (38.1)	41 (20.8)	34 (17.4)
Infection [a]	37 (16.5)	16 (7)	17 (7.6)	43 (22.3)	23 (11.8)	16 (8.2)
Non specific infection	31 (13.8)	14 (6.2)	13 (5.8)	30 (15.5)	18 (9.3)	10 (5.2)
Tuberculosis	6 (2.7)	1 (0.4)	1 (0.4)	1 (0.5)	1 (0.5)	1 (0.5)
Atypical mycobacteria		1 (0.4)	3 (1.3)	4 (2.1)	3 (1.5)	3 (1.5)
Fungal infection				5 (2.6)		
Viral infection				4 (2.1)		
Cancer [a]	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.5)		1 (0.5)
Solid tumor	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.5)		1 (0.5)
Skin cancer						
Lymphoma						
Other hematological malignancies						
Paradoxical effects [a]	2 (0.8)	1 (0.4)	4 (1.7)	7 (3.6)	2 (1)	7 (3.6)
Skin reaction	1 (0.4)	1 (0.4)	2 (0.8)	1 (0.5)	2 (1)	1 (0.5)
Uveitis	1 (0.4)		2 (0.8)	6 (3.1)		5 (2.6)
Inflammatory bowel disease						1 (0.5)
Auto-immune diseases (LEAD)	1 (0.4)					1 (0.5)
Hypersensitivity reaction [a]	4 (1.6)		2 (0.8)	7 (3.6)	2 (1)	
Hematological disorders [a]	19 (8.5)	11 (4.8)	4 (1.7)	2 (1)	1 (0.5)	1 (0.5)
Leucopenia	5 (2.2)	1 (0.4)	2 (0.8)	1 (0.5)	1 (0.5)	1 (0.5)
Neutropenia	8 (3.6)	8 (3.6)	2 (0.8)	1 (0.5)		
Thrombocytopenia	6 (2.7)	2 (0.8)				
Hypercholesterolemia [a]	8 (3.6)	9 (4)	4 (1.7)	2 (1)	2 (1)	1 (0.5)

[a] Number and percentage

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AB1660

ASSOCIATION OF COMMON COMORBIDITIES WITH ASEPTIC OSTEONECROSIS: EXPERIENCE OF RHEUMATOLOGY DEPARTMENT

Keywords: Bone diseases, Comorbidities

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Background: Osteonecrosis (ON) (avascular necrosis, aseptic necrosis or subchondral avascular necrosis) is not a specific disease entity but the final common pathway of a number of conditions leading to bone death [1].
Objectives: To examine the frequency of ON and to investigate different common comorbidities association with ON in a rheumatology department.
Methods: All patients with a first-time hospital diagnosis of ON in rheumatology department during 1995–2022 were included. We obtained a complete hospital history of comorbidities preceding the diagnosis of ON.
Results: 43 ON cases were included with an average of 1.6 cases/year. The mean age of our patients was 53 years (27-82). The sex-ratio male to female was 1,75 (12 females and 21 males). The different sites of osteonecrosis were distributed as follows: femoral head, femoral condyle, semilunar and humeral head. The diagnosis of ON was confirmed by simple radiography in15 cases, bone scan in 14 cases and with magnetic resonance imagery in 14 cases. Dyslipidemia was the most common comorbidity (13.9 % of patients), followed by high blood pressure, hypothyroidism, allergic asthma, obesity, alcohol abuse, renal failure, rheumatoid arthritis, diabetes, gout, hemopathy, trauma, and coronary artery disease. Among these chronic conditions, the most common recognized risk factor of ON in our series was medications (corticosteroids) followed by dyslipidemia, alcohol abuse, hemopathy (sickle cell anemia, Hodgkin's lymphoma and beta thalassemia) and trauma (fractures and dislocation of the hip). All patients received medical treatment based on painkillers and functional rehabilitation. 12 patients had surgical treatment: 8 total hip prosthesis, 3 Core decompression and bone marrow aspirate concentrate injection for Avascular Necrosis of the femoral head and 1 Proximal row carpectomy for semilunar osteonecrosis.
Conclusion: This monocentric study provides evidence for an increasing ON incidence associated to systemic steroid administration. Hence the need for early and adequate management of this factor to prevent possible complications such as aseptic osteonecrosis.

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AB1661

INCREASED RISK OF TOTAL HIP ARTHROPLASTY IN RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS OVERLAP SYNDROME

Keywords: Rheumatoid arthritis, Comorbidities, Systemic lupus erythematosus

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Background: Patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) have increased risk of total hip arthroplasty (THA).[1,2] Patients with RA and SLE overlap syndrome (RA+SLE) may have a more common articular involvement than each disease does. However, the risk of THA in RA+SLE patients is not fully investigated.
Objectives: To identify the risk and outcome of THA in RA+SLE patients in a longitudinal cohort.
Methods: We analyzed datasets derived from Taiwan National Health Insurance Research Database from 2000 to 2018. Patients with RA, SLE, and RA+SLE were selected and matched according to the age and gender. Risk and outcome of THA was compared, and multivariable Cox proportional hazards models were used to analyze the risk factors.
Results: 2270 RA+SLE patients were matched with 9080 RA and 9080 SLE patients. RA+SLE patients had the highest rate of THA than RA or SLE patients did (2.16% vs 1.22% or 1.76%, respectively; p=0.0008). Avascular necrosis (1.45%) followed by osteoarthritis (1.28%) were the most common reasons for THA in RA+SLE patients. The rate of THA revision was the highest in RA patients than in RA+SLE or SLE patients (9.91% vs. 4.08% or 6.25%, respectively; p<0.0001). Chronic kidney disease (HR: 4.94, 95% CI: 2.51–9.71, p<0.0001), use of prednisolone or equivalence >10 mg/day (HR: 2.1, 95% CI: 1.53–2.88, p<0.0001), azathioprine (HR: 2.15, 95% CI: 1.68–2.74, p<0.0001), and biologic agents (HR: 2.03, 95% CI: 1.46–2.81, p<0.0001) increases the risk of THA independently.
Conclusion: RA+SLE patients had the highest rate of THA than patients with individual disease alone, however, the rate of THA revision was the highest in RA patients than in the other groups. Comorbidities, treatment with a higher daily dose of steroid, and immunosuppressants may contribute to the risk of THA.
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AB1662 IMPACT OF COMORBIDITIES AND FREQUENCY OF ADMISSIONS ON MORTALITY IN PATIENTS WITH SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES

Keywords: Comorbidities, Prognostic factors, Behcet's disease

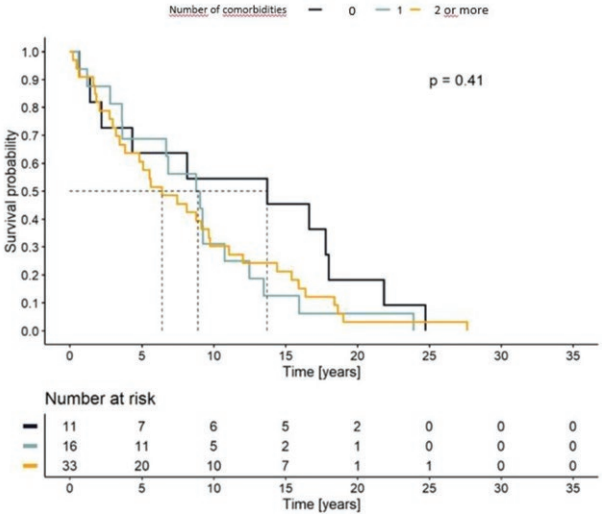
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Background: Data on mortality in patients with systemic autoimmune rheumatic diseases (SARDs) is limited. Most evidence is restricted to patients with systemic lupus erythematosus and ANCA vasculitis [1-2]. In recent years, mortality has been more closely associated with cardiovascular pathologies and infections and less with disease activity.
Objectives: To assess the impact of comorbidities and hospital admissions on mortality in patients with SARDs in a tertiary referral hospital.
Methods: We conducted a retrospective observational study including adult patients with SARDs (Table 1) followed up in our Multidisciplinary Unit of Systemic Autoimmune Diseases between January 2017 and December 2019. In this cohort, patients were under similar follow-up and treatment protocols. Gathered data includes epidemiological, hospitalization (number of admissions, hospital stay and reasons for admission) and exitus information. In hospitalized patients, associated comorbidities were also reviewed. A comparison was made between patients who required at least one admission during the study period and those who did not, in addition to a description of mortality. Kaplan Meier curves are presented by number of comorbidities and number of admissions.
Results: Of the 1749 patients with SARDs included in our cohort, 432 (24.7%) required hospitalization during the study period. Of those hospitalized, mean age was 64 years and 315 (73%) were women. A total of 61 (14%) deaths occurred among patients admitted to the hospital vs 77 (5.9%) among non-hospitalized, within the study period. Behcet's disease and IgG4-related disease presented highest mortality rate (29%) in our cohort of hospitalized patients, closely followed by antiphospholipid syndrome (23%) and Sjögren's syndrome (20%) (Table 1). No statistically significant differences were observed in mortality according to the number of admissions (p=0.56) or comorbidities (p=0.41), although in the latter, an increasing trend was observed as the number of comorbidities increased (survival according to the number of comorbidities: no comorbidities =14 years, one comorbidity =8.9 years, two or more comorbidities =6.4 years) (Graph 1).
Conclusion: We have found no impact of comorbidities or hospital admissions in mortality in patients with SARDs. Among hospitalized patients, higher mortalities were observed in Behcet's disease, IgG4-related disease, antiphospholipid syndrome and Sjögren's syndrome. In addition, a trend towards greater mortality was observed in relation to the number of comorbidities.
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Table 1. Frequencies of exitus by diagnosis and hospitalization

	HOSPITALIZED SUB-POPULATION N = 432 (25%)		NON-HOSPITALIZED SUB-POPULATION N = 1317 (75%)	
	Exitus N = 61 (14%)	No exitus N=371 (86%)	Exitus N = 77 (5,9%)	No exitus N = 1218 (94%)
RHEUMATOLOGIC DIAGNOSIS				
Systemic lupus erythematous	17 / 113 (15%)	96 / 113 (85%)	26 / 374 (7%)	348 / 374 (93%)
Polymyalgia rheumatica	8 / 92 (8,7%)	84 / 92 (91%)	15 / 258 (5,8%)	243 / 258 (94%)
Sjögren's syndrome	9 / 46 (20 %)	37 / 46 (80%)	11 / 174 (6,3%)	163 / 174 (94%)
Systemic sclerosis	5 /43 (12%)	38 / 43 (88%)	3 / 83 (3,6%)	80 / 83 (96%)
Small-vessel vasculitis	7 /36 (19%)	29 / 36 (81%)	4 / 81 (4,9%)	77 / 81 (95%)
Idiopathic inflammatory myopathies	3/ 30 (10%)	27 / 30 (90%)	7 / 79 (8,9%)	72 / 79 (91%)
Undifferentiated connective tissue disease	2 / 17 (12%)	15 / 17 (88%)	3 / 66 (4,5%)	63 / 66 (95%)
Large-vessel vasculitis	1 / 13 (7,7%)	12 / 13 (92%)	3 / 53 (5,7%)	50 / 53 (94%)
Antiphospholipid syndrome	3 / 13 (23%)	10 / 13 (92%)	2 / 51(3,9%)	49 / 51 (96%)
Behçet's disease	4 / 14 (29%)	10 / 14 (71%)	2 / 34 (5,9%)	32 / 34 (94%)
IgG4-Related disease	2 / 7 (29%)	5 / 7 (71%)	0 / 15 (0%)	15 / 15 (100%)
Polyarteritis nodosa	0 / 1 (0%)	1 / 1 (100%)	1 / 14 (7,1%)	13 / 14 (93%)
Mixed connective tissue disease	0 / 1 (0%)	1 / 1 (100%)	0 / 13 (0%)	13 / 13 (100%)



Graph 1. Survival according to the number of comorbidities

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1663 MUSCULOSKELETAL (MSK) PAIN IN VILLAGE BHIGWAN (INDIA) IN 2022- CHANGE OVER 25 YEARS: WHO COMMUNITY ORIENTED PROGRAM FOR CONTROL OF RHEUMATIC DISEASES (COPCORD) 1996-2022

Keywords: Epidemiology, Gender/diversity issues, Descriptive studies

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Background: COPCORD population surveys (Stage I) have reported the prevalence of MSK pain and rheumatic disorders in several countries. A crude point prevalence rate of 18.2% for MSK pain (adult) was reported by the maiden COPCORD India survey (1996) in rural Bhigwan (Pune) and was continued to date with a free-of-cost local rheumatology clinic and a health education program. Several other factors (development, environment, Chikungunya epidemic 2006, Covid pandemic 2019) are likely to impact the epidemiology of MSK disorders and thus we carried out a resurvey in Bhigwan from April to July 2022. We present early results of MSK pain and related factors.
Objectives: To describe and measure the current MSK pain and rheumatic disorders in Bhigwan rural population and further assess the transformation over time (1996 to 2022).

Methods: The resurvey (Stage I) was carried out using the methods of the previous survey (Bhigwan COPCORD model 1996). Trained voluntary health workers (HW) completed a house-to-house cross-sectional survey (Phase 1) of the adult population(≥ 18 years) and identified current and/or past MSK pain respondents. Pain due to recent trauma (< 3 months) was excluded. Concurrently, the respondents were also evaluated (Phase 2) for pain descriptors and other relevant issues. Rheumatologists examined (Phase 3) the respondents to make a clinical diagnosis, order relevant investigations, and begin treatment. A follow-up was scheduled. The target population was estimated at 8117 (Government records). The database was created using an indigenous software program. Standard population analysis was carried out. Crude point prevalence rates (95% confidence intervals) are presented. Further analysis is being done.
Results: 6970 population (85.9% response, 50% males) was surveyed. The age-gender distribution pattern was comparable with the India rural census 2011; 63% in 18-44 years age groups (Bhigwan). Paradoxically, only 7.6% current population in sharp contrast to about 55% in 1996 admitted working (physically) in fields; now dependent upon temporary migrant labor (not in the survey). 32% population possessed mobile phones. Five hundred eighty-six pain respondents (women 69%) were identified; 46% belonged to the 45-64 years age group. The MSK pain prevalence was 8.2% (7.5%, 8.8 %); male 2.5 (2.2 %,2.9%). female 5.6% (5.1, 6.2). 14.2% population used tobacco in some form, mostly oral; 36.3% of MSK pain respondents (58% women). Hypertension in 7.9%, diabetes in 4.7%, thyroid disorders in 1.6%, and rectal hemorrhoids in 1% was self-reported in the population; correspondingly 25%, 12%, 2.5%, and 3% were reported by the MSK pain cohort. Past history of Chikungunya in 5.7% and COVID-19 in 7.4% of the total population was reported. On univariate analysis, MSK pain was significantly associated ($p < 0.0001$, Chi-square) with Chikungunya, COVID-19, tobacco use, fieldwork, and low education status. Prevalence rates for disease groups were 1.38% (1.12. 1.68) for inflammatory arthritis, 3.66% (3.23, 4.13) for degenerative arthritis and 2.87 % (2.49, 3.29) for non-specific rheumatism/arthritis. Self-reported data, subject recall, and limited investigations were important concerns.
Conclusion: The current COPCORD survey shows that despite a substantial reduction from 1996, MSK pain continues to be a predominant and important self-reported illness in the Bhigwan rural community. Undoubtedly, the lives and livelihoods of the Bhigwan people and their MSK landscape have been transformed substantially. Interestingly, the burden of other non-communicable diseases seems increased. Further research studies will be required to unravel the role of Chikungunya and COVID-19, and other risk factors in MSK disorders.
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Disclosure of Interests: None Declared.
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AB1664 INFLUENZA, PNEUMOCOCCAL, AND TETANUS VACCINE COVERAGE AMONG PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES ON BIOLOGICAL OR TARGETED SYNTHETIC DMARDS AND THE ROLE OF THE RHEUMATOLOGIST

Keywords: Vaccination/immunization

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Background: Vaccines are one of the most efficient tools to prevent infectious diseases at a population level. Their importance is even greater in immunocompromised patients providing efficient and safe protection against common viral and bacterial infections. According to the current EULAR recommendations based on solid evidence over the recent years, non-live vaccines such as influenza, pneumococcal, tetanus toxoid, and others are safe and can be administered to patients with inflammatory rheumatic diseases during the glucocorticoid and/or disease-modifying antirheumatic drug (DMARD) therapy. Furthermore, influenza and pneumococcal vaccines "should be strongly considered" and the tetanus toxoid vaccination should be received in accordance with the recommendations of the general population[1].
Objectives: We aimed to investigate the coverage for influenza, pneumococcal, and tetanus toxoid vaccination in a cohort of patients with inflammatory rheumatic diseases on biological or targeted synthetic DMARDs.
Methods: Two hundred and one patients, aged 18 or older, were included in this single-center cross-sectional study after signing an informed consent form. They suffered from rheumatoid arthritis (RA), psoriatic arthritis (PsA), or ankylosing spondylitis (AS) and were on biological or targeted synthetic DMARDs. Individuals with psychiatric or neurological diseases preventing understanding or responding to the questions were excluded from the study. Patients' anthropometric, clinical, and demographic characteristics were collected via detailed anamnesis and clinical examination. Disease activity was evaluated using DAS28-CRP for patients with RA and peripheral PsA and ASDAS for those with axial disease (AS and axial PsA). All patients were asked to fill in a survey determining their immunization status for influenza, pneumococcal, and tetanus toxoid vaccines and whether they had a preceeding discussion with their rheumatologist about recommended vaccines during their routine medical visits.
Results: Of the 201 included patients, 40.3% (n=81) were females. Patient distribution according to their disease was as follows: 30.3% (n=61) RA patients, 51.7% (n=104) AS patients, and 17.9% PsA patients (n=36). Mean age, disease duration, and body mass index values were 54.62 (14.4) years, 11.04 (8.6) years and 28.2 (5.3), respectively. 27.4% of patients were on concomitant glucocorticoid treatment. Only 13.9% (n=28) and 1.5% (n=3) were vaccinated against seasonal influenza and pneumococcal infections, respectively. Patients who had a preceeding discussion about seasonal influenza and pneumococcal immunization with their rheumatologist had approximately 13 and 32 times higher probability to get vaccinated than people who did not (OR=12.9, $p < 0.001$ and OR 32.5, $p = 0.01$, respectively). Regular reimmunizations against diphtheria and tetanus according to the Immunization Calendar of the Republic of Bulgaria were carried out by only 44.8% (n=90) of the studied population.
Conclusion: Coverage of recommended vaccines in our group of Bulgarian patients on biological or targeted synthetic DMARDs is very low. Discussion about the potential benefits and safety profile of the recommended vaccines may increase patients' willingness to vaccinate and prevent common infectious diseases in immunocompromised rheumatic patients.
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Disclosure of Interests: None Declared.
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AB1665 NON-IMPAIRED KIDNEY FUNCTION INCREASES HYPERURICAEMIA-ASSOCIATED MORTALITY RISK EFFECT

Keywords: Epidemiology, Kidneys, Gout

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Background: Both hyperuricaemia and reduced kidney function are known mortality risk factors.[1-3] Also, hyperfiltration is associated with elevated mortality risk.[3] It has not yet been studied if renal function has a modifying effect on hyperuricaemia-associated mortality risk.
Objectives: To detect if renal function has a modifying effect on hyperuricaemia-associated mortality risk.
Methods: Data from GOAL (Good Ageing in Lahti region) study was used. It is a large, prospective, population-based study of elderly people (52–76 years) in the Lahti region. Data of serum uric acid (SUA) levels, creatinine, cystatin C as well as several other laboratory variables, comorbidities, lifestyle habits and socioeconomic factors was collected. To estimate glomerular filtration rate, we used CKD-EPI creatinine-cystatin C equation (ml/min/1.73 m^2). Persons with SUA values of >410 µmol/L (75^{th} percentile) are represented as clearly hyperuricaemic. Persons with eGFR of ≤67 ml/min (25^{th} percentile) are represented as having reduced kidney function. The results were adjusted for age, gender, education, smoking status, alcohol consumption, body mass index, hypertension and dyslipidaemia.
Results: Mortality was higher in individuals with reduced kidney function compared to those with eGFR of >67 ml/min both in the group of clearly hyperuricaemic persons and in the group of persons with SUA ≤410 µmol/L. The hazard ratio (HR) for all-cause mortality was 1.53 (95% CI: 1.26 to 1.84) in clearly hyperuricaemic persons with reduced kidney function, 1.26 (95% CI: 1.02 to 1.55) in clearly hyperuricaemic persons with eGFR of >67 ml/min, 1.26 (95% CI: 1.03 to 1.55) in persons with SUA ≤410 µmol/L and reduced kidney function, while the group of

SUA ≤410 µmol/L and eGFR >67 ml/min was used as a reference (Table 1). HR for hyperuricaemia-related premature death however was lowest in individuals with reduced eGFR, and it rises strikingly as the eGFR increases above 80ml/min (Figure 1).

Conclusion: Reduced kidney function is an important risk factor for mortality both in individuals with lower and higher SUA. The mortality risk associated with hyperuricaemia is remarkably higher in individuals with normal or only slightly reduced kidney function. This finding makes it reasonable to speculate that hyperuricaemia caused by overproduction of uric acid (metabolic hyperuricaemia) might be a separate and more deleterious entity than hyperuricaemia that has resulted from renal underexcretion of uric acid (renal hyperuricaemia).

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Table 1. Adjusted hazard ratio (HR) for all-cause mortality in persons with preserved or reduced estimated glomerular filtration rate (eGFR) and clearly elevated serum uric acid (SUA) level or slightly elevated/normal SUA level

	SUA ≤410	SUA >410
eGFR >67	1.00 (Reference)	1.26 (1.02 to 1.55)
eGFR ≤67	1.26 (1.03 to 1.55)	1.53 (1.26 to 1.84)

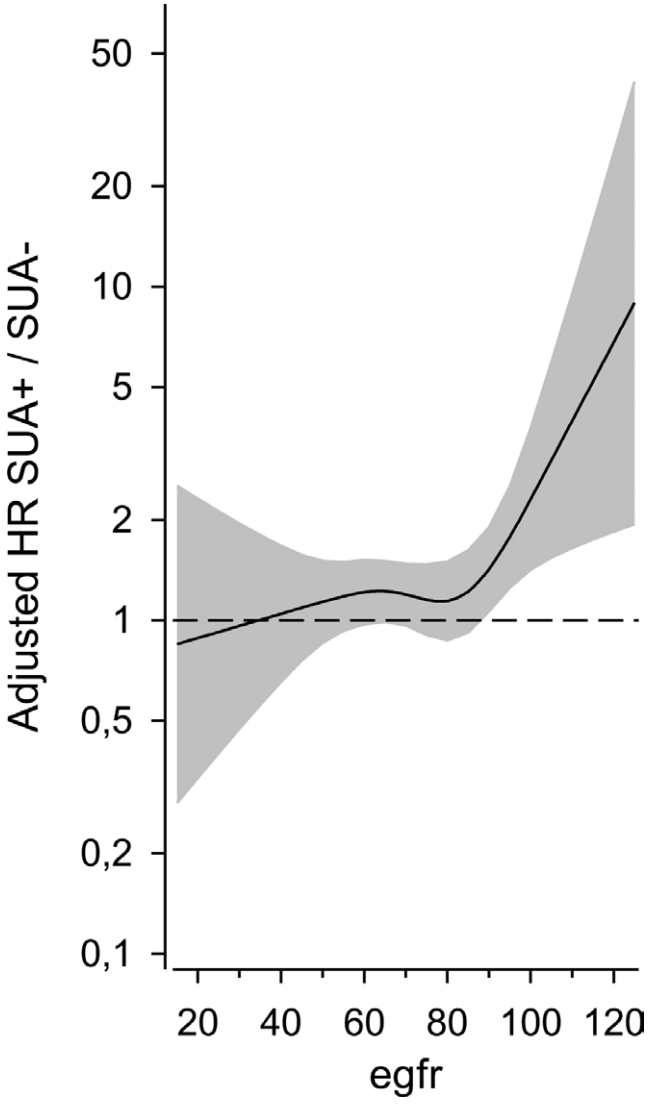


Figure 1. The impact of estimated glomerular filtration rate on hyperuricaemia-associated mortality risk effect

Acknowledgements: We thank all the participants in the GOAL (Good Ageing in Lahti region) project.

Disclosure of Interests: None Declared.

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AB1666

CLUSTER ANALYSIS TO IDENTIFY PATIENT GROUPS AND ASSESS THE PRESENCE OF ADVERSE EVENTS. REAL WORLD EVIDENCE FROM THE BIOBADASAR 3.0 REGISTRY

Keywords: Registries, Safety, Real-world evidence

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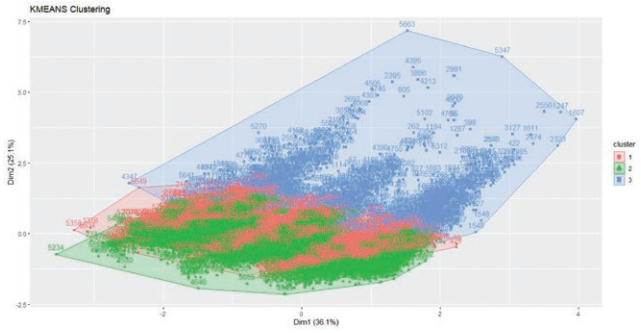
Background: The clinical manifestations of patients with rheumatic diseases are highly heterogeneous. The appearance of adverse events (AEs) related to the treatments received for these diseases considerably increases the morbidity and mortality of these patients. This is why obtaining real-world data on these AEs and analyzing their causes is paramount. The BIOBADASAR registry has data from 5,676 patients over ten years of follow-up. Classifying patients in treatment with biological drugs into subgroups with different phenotypes through unsupervised grouping could provide valuable information on the characteristics associated with specific AE.

Objectives: Through cluster analysis, this study aimed to identify different clinical phenotypes related to Adverse events in patients treated with biological drugs.

Methods: Retrospective, multicenter study of patients with rheumatic diseases treated with original biological drugs, biosimilars, or original and generic targeted therapies in Argentina; follow-up from August 2010 to July 2021. Demographic and clinical data, time of initiation and completion of treatments, data on disease activity, and the AEs presented were collected. Patients were unbiasedly matched based on their clinical and phenotypic profiles using a k-means pooling method. The initiation of biological disease-modifying antirheumatic drugs (b-DMARD) was evaluated in the segregated groups to investigate each group's clinical course and differential characteristics.

Results: A total of 5676 patients were analyzed. Three different clusters were obtained:

Cluster 1: 1041 patients. Was observed an evolution time of the disease of 30.5 years (Q1 25.8; Q3 35.6) longer than other clusters and a longer delay in starting treatment at 18.3 years (Q114.4; Q3 24) p < 0.0001.
Cluster 2: 2136 patients. We observed a higher frequency of patients with Systemic Lupus Erythematosus: 156 (7.3%) p<0.0001 and a lower frequency of AEs 190 (8.9%) p <0.0001
Cluster 3: 2499 patients. We observed a higher mean age than in the other two clusters, 57.3 (SD 8.3) p < 0.001.
The use of systemic corticosteroids was evenly distributed among the 3 clusters.
Conclusion: The unsupervised grouping of patients from the BIOBADASAR registry demonstrated the existence of clusters based on clinical and demographic characteristics. Identifying high-risk patients through a combination of these parameters may be helpful for the early identification of risk factors and their association with adverse events. Based on our hierarchical cluster analysis, we identified different patient phenotypes. Our results show that within the heterogeneity of patient characteristics, common elements provide a basis for future analyses of these variables and their relationship with certain AEs.



Graphics 1. K-means cluster analysis graph. Distribution of patients according to the cluster they belong to. Dim1: Principal component 1; Dim2: Principal component 2.

REFERENCES: NIL.

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AB1667

UNDERSTANDING THE ROLE AND ADOPTION OF ARTIFICIAL INTELLIGENCE TECHNIQUES IN RHEUMATOLOGY RESEARCH: AN IN-DEPTH REVIEW OF THE LITERATURE

Keywords: Systematic review, Artificial intelligence

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Background: Artificial intelligence (AI) is rapidly gaining adoption in the medical field [1]. We review, the original research articles that combine AI and Rheumatic and Musculoskeletal diseases (RMDs) in a five-year period (2017-2021) and classify them into one of the following categories: disease classification, disease prediction, predictors identification, patient stratification and disease subtype identification, disease progression and activity, and treatment response.
Objectives: The present review arises with the aim of characterizing how rheumatology researchers are employing AI techniques and to study to what extent these techniques have been adopted by rheumatologists.
Methods: A literature search was conducted to identify publications related to RMDs in which AI techniques played a relevant role in four different sources: PubMed, Web of Science, Scopus and in the search engines of rheumatology journals classified as Q1 and Q2 according to Journal Citation Reports 2019. The keywords employed were artificial intelligence, supervised learning, unsupervised learning, deep learning, big data, data mining, machine learning, rheumatology, musculoskeletal diseases, rheumatic. Only original research articles related to RMDs with a PubMed identification number (PMID), not duplicated, written in English, in which there was not animal involvement and in which at least one AI technique was employed, fulfilled the inclusion criteria. Later, an abstract and title filtering followed by a full text review of selected articles was performed.
Results: After applying the inclusion and exclusion criteria (see Figure 1) and performing the full text review, 91 articles remained. From those, the article title, the identifiers (DOI, PMID), the journal, the publication year, the disease, the algorithms/techniques, the programming language, the number of patients, the validation type, the objective, and the authorship information were collected. In addition, an illustrative table with more than twenty different RMDs, including arthritis, vasculitis, fibromyalgia, gout, spondylitis, sarcopenia, Sjögren, systemic sclerosis, and back and neck pain was obtained. The publication trend has increased each year, from 20% to 48%, in relation to the previous year. The techniques employed are variable, including supervised and unsupervised learning, and traditional machine learning and deep learning approaches. Some of the topics addressed are classification, regression, clustering, dimensionality reduction, topic modelling, computer vision, reinforcement learning, few-shot learning, and trajectory analyses. Osteoarthritis, rheumatoid arthritis, systemic lupus erythematosus and osteoporosis are the RMDs that accounts for most of the research studies in which AI techniques are used more assiduously. However, AI is also playing a key role in rare diseases research, such as vasculitis, with approaches such as topic modelling. The amount of data in the studies reviewed is variable, from just hundreds of observations to hundreds of thousands, showing that "big data" cohorts are not mandatory to take advantage of such techniques.
Conclusion: The outstanding and upward trend in the number of published research related to rheumatic and musculoskeletal diseases, in which AI plays a key role, has exhibited the interest of rheumatology researchers in using these techniques to answer their research questions. We can conclude that the rheumatology research community is increasingly adopting novel AI techniques.

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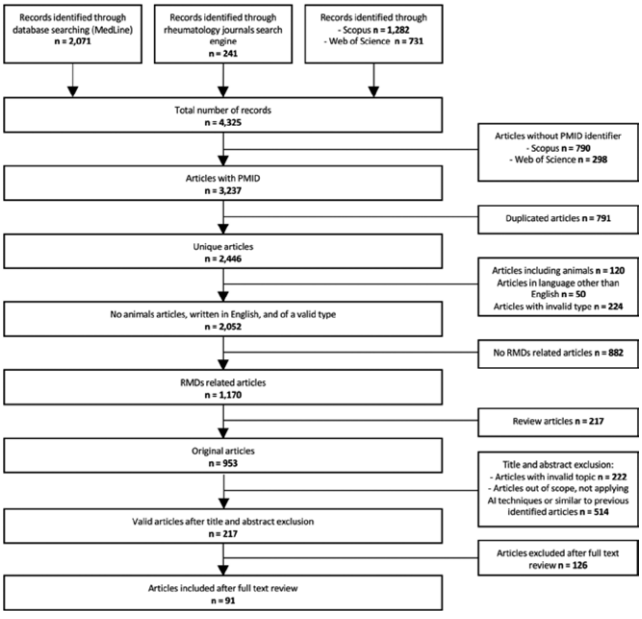


Figure 1. Inclusion and exclusion criteria

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AB1668

RESPIRATORY INFECTIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS, PRIMARY AND SECONDARY AFS BEFORE AND AFTER VACCINATION WITH 23-VALENT POLYSACCHARIDE PNEUMOCOCCAL VACCINE

Keywords: Vaccination/immunization

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Background: Infections are one of the main causes of morbidity and mortality in patients with autoimmune inflammatory rheumatic diseases (AIIRD). Pneumococcal vaccination can significantly reduce the number of serious respiratory infections in this group of patients.
Objectives: To analyze the frequency of respiratory infections in systemic lupus erythematosus (SLE), secondary and primary antiphospholipid syndrome (AFS) before and after vaccination with 23-valent polysaccharide pneumococcal vaccine (PPV-23).
Methods: 91 patients were included in the study, 78 of them with SLE, including 18 with secondary AFS; 13 patients with primary AFS. The follow-up period was 12 months. All patients with SLE and secondary AFS received immunosuppressive therapy, including 29 anti-B-cell therapy. With primary AFS, 6 patients received immunosuppressive therapy, including 1- rituximab.
Results: All LRTI were more common in SLE (48.3%, 27.8%, 11.8%, respectively), mainly due to the more frequent development of pneumonia (Pn) (20%, 11%, 7.7%, respectively). After vaccination, the number of pneumonias decreased from 15 (16.5%) to 4 (4.4%) and were registered only in patients with SLE, p=0.01. These were not severe pneumonia, did not require hospitalization; in all cases there were predisposing factors (anti-B-cell therapy with the absence of an adequate vaccine response - 3, interstitial lung disease (ISL) - 1). Before vaccination, among ENT infections, sinusitis was more common with SLE than with SLE + secondary APS (16.7%, 8.3%, respectively), with primary APS it was not detected.After vaccination, infections of ENT organs in patients with primary and secondary AFS were absent, with SLE there was a significant decrease (from 30% to 10%). With primary AFS, respiratory diseases have not been registered after vaccination.

Table 1. The frequency of respiratory infections in patients with SLE, secondary and primary AFS, n=91.

	SLE		SLE + secondary AFS		primary AFS	
	Before vaccination **n=60**	After vaccination **n=60**	Before vaccination **n=18**	After vaccination **n=17**	Before vaccination **n=13**	After vaccination **n=13**
LRTI:	**29 (48,3%)**	9 (15%)	5 (27,8%)	2 (11,8%)	3 (23%)	**-**
Pneumonia	**12 (20%)**	**4 (6,7%)**	2 (11%)	-	1 (7,7%)	**-**
Acute bronchitis	**10 (16,7%)**	3 (5%)	**3 (16,7%)**	2 (11,8%)	1 (7,7%)	**-**
Exacerbation of chronic bronchitis	**7 (11,7%)**	2 (3,3%)	-	-	1 (7,7%)	-
ENT infections:	**18 (30%)**	**6 (10%)**	3 (16,7%)	-	3 (23%)	**-**
Sinusitis	**10 (16,7%)**	**5 (8,3%)**	1 (5,5%)	-	-	-
Pharyngitis	4 (6,6%)	-	1 (5,5%)	-	1 (7,7%)	-
Exacerbation of chronic tonsillitis	3 (5%)	-	1 (5,5%)	-	1 (7,7%)	-
Otitis media	1 (1,7%)	1 (1,7%)	-	-	1 (7,7%)	-

Notes: LRTI - Lower Respiratory Tract Infections; ENT infections - otorhinolaryngological infections.

Conclusion: The clear clinical efficacy of PPV-23 in patients with SLE and AFS has been demonstrated. In primary AFS, fewer respiratory infections and their absence after vaccination are naturally explained by less aggressive immunosuppressive therapy. A possible reason for the lower number of INDO in secondary AFS, in comparison with SLE without AFS, may be the absence of ISL in these patients.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1669

CLINICAL, HISTOLOGICAL FEATURES AND PREDICTORS OF RELAPSE IN PATIENTS WITH IDIOPATHIC GRANULOMATOUS MASTITIS

Keywords: Disease-modifying drugs (DMARDs), Rare/orphan diseases, Epidemiology

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Background: Idiopathic Granulomatous mastitis (IGM) is a chronic benign inflammatory breast disease characterized by non-caseating granuloma with multinucleate giant cells and micro-abscesses[1]. It presents as painful breast lump, with axillary lymphadenopathy, nipple retraction, and peau d'orange appearance of the skin mimicking inflammatory breast cancer [1]. Till date, there are no consensus guidelines of managing IGM and it is increasingly being treated with steroids and steroid-sparing agents as it now considered to be driven by inflammatory process [2]. Since the relapse rate varies from 5-50% [3], identification of risk factors that predict relapse can help clinicians triage patients who might need close monitoring and prolonged treatment with immunosuppressive therapy.
Objectives: The objective of our study is to describe clinical, laboratory and histopathological features of IGM from a single center and identify distinguishing features of relapsing disease compared to remission.
Methods: We queried databases at our institution December 1990- January 2021 to include females ≥ 18 years with biopsy-proven diagnosis of IGM, excluding patients with breast cancer, lymphoproliferative disorders, solid organ malignancy, foreign body reaction in breast, plasma cell mastitis, and ductal ectasia. Remission was defined as three-month period without recurrence of symptoms or imaging findings. Relapse was defined as recurrence after three months of remission. Clinical and histopathological features were compared using two-sample t-tests (continuous variables) and chi-squared tests (categorical variables).
Results: 27 patients met our inclusion criteria and were included in the final analyses. The mean age at diagnosis was 35.8 years (± SD 9.4 years) with a mean body mass index of 31.7 kg/m2 (± SD 6.7 kg/m2). 11 (41%) were Hispanic, 25 (93%) had at least one previous full-term pregnancy prior to diagnosis and 8 (30%) were on oral contraceptives. 18 patients (66%) had remission and 9 (33%) had relapse. Six of these patients received steroid after antibiotics, while 5 patients were received methotrexate. Three (33%) patients with relapse and 14 (77%) with remission, had abscess formation confirmed on histopathology (p=0.04).
Conclusion: We did not identify any differences in clinical or laboratory features of patients with relapse and remission. Patients with remission had a higher number of abscesses on histopathology and history of oral contraceptive use was associated with more relapse. By identifying key histopathological findings in this population may guide prognosis and treatment of these patients.
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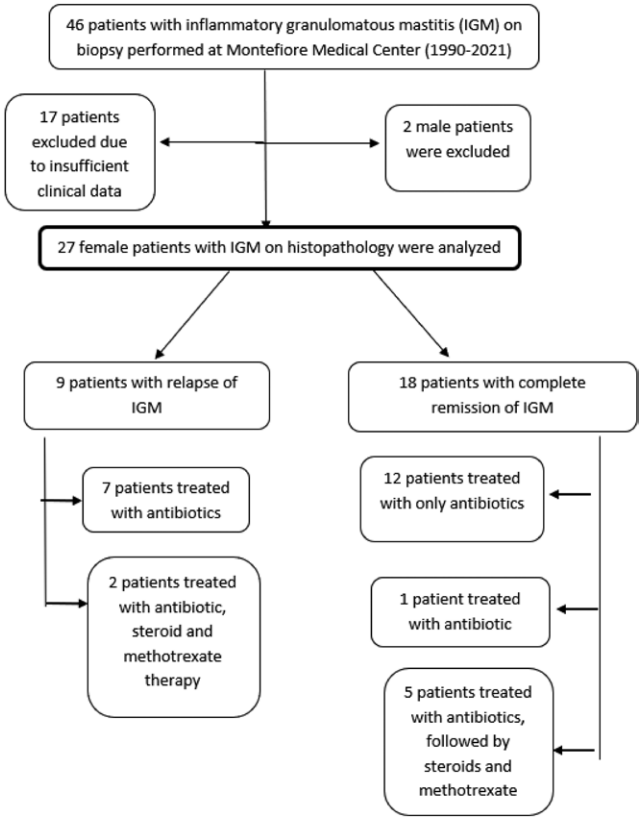


Figure 1. Flow chart depicting treatment provided in remission and relapse group

Table 1. Baseline characteristic and histopathological features of IGM patients with relapse and remission

Characteristic	IGM relapse (N = 9)	IGM remission (N = 18)	p-value
Age at diagnosis (years)	32	38	0.10
BMI ≥25 kg/m^2	5	16	0.67
Hispanic	4 (44%)	7 (39%)	0.94
first clinical symptom at diagnosis	4 (44%)	7 (39%)	1.00
pain	3 (33%)	7 (39%)	
mass	2 (22%)	4 (22%)	
ulcer/abscess			
History of smoking	4 (44%)	5 (28%)	0.69
History of OCP use at diagnosis	5 (56%)	4 (22%)	**0.01**
History of breastfeeding	2 (22%)	5 (28%)	0.89
History of previous pregnancy	7 (78%)	18 (100%)	0.23
Histopathological feature	3 (33%)	14 (78%)	**0.04**
Abscess formation			
Lobulocentric pathology	3 (33%)	9 (50%)	0.37

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AB1670

PREVALENCE OF PNEUMOCYSTIS JIROVECI PNEUMONIA(PJP)IN PATIENTS WITH RHEUMATOLOGICAL CONDITIONS ON IMMUNOSUPPRESSIVE MEDICATIONS AND THE NEED FOR PROPHYLAXIS

Keywords: Infection-related RMDs, Disease-modifying drugs (DMARDs)

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Background: Pneumocystis jirovicii pneumonia (PJP) is a life-threatening opportunistic fungal infection with a high mortality rate (30-50%) among non-HIV immunosuppressed patients. According to previous studies cotrimoxazole prophylaxis is given for patients when their risk of PJP is greater than 3.5%[1] however these guidelines were established for patients with malignancies, stem cell and solid organ transplantations[2].The data from British registries showed a slightly higher risk in patients treated with Rituximab than Anti TNF therapies. The ACR recommends PJP prophylaxis in their recently published guidelines on ANCA associated vasculitis (AAV) and studies have shown higher PJP infection in patients with GPA than other vasculitis. The benefit for prophylaxis treatment is not clearly established in inflammatory conditions like RA and other autoimmune Rheumatological conditions(ARDs)
Objectives: To investigate the incidence of PJP infection in patients with ARDs and explore the potential common risk factors.
Methods: Using our, electronic health record (EHR) cohort, we investigated the prevalence of PJP infections in Rheumatic patients on immunosuppressants over a period of one year.
Results: We identified 6 non HIV patients with a confirmed diagnoses of PJP infection over a period of one year. All patients were diagnosed following bronchial lavage looking for PJP DNA in the aspirate. Only 2 out of six patients were identified to have ARDs on immunosuppressant drugs. Case1: 68 yr old gentleman, was on longstanding methotrexate for RA, presented with breathlessness and dry cough. The blood showed CRP of 200 and CT thorax revealed features consistent with RA-ILD with superimposed ground-glass changes keeping with an acute infection. He did not respond to IV antibiotics and went on to have a bronchial lavage which tested positive for PJP and was started on high dose of steroids and intravenous cotrimoxazole followed subsequently by Vancomycin and Clindamycin after not improving on cotrimoxazole. Despite ongoing medical treatment, patient deteriorated and passed away. Case 2: 77 yr old lady on rituximab for AAV(with positive MPO >129) with an established ILD secondary to the vasculitis for 7years. She presented with breathlessness and cough. Rituximab was started 7 years ago for the AAV and due to its relapsing nature, rituximab was continued with a maintenance dose of prednisolone 5- 10mg. Blood tests showed low IgM levels with normal IgG and A levels. There was no evidence of active vasculitis and she was commenced on antibiotics which made no difference to her symptoms. A HRCT thorax was done which revealed Interval progression of ILD (UIP) bilateral ground-glass changes. Bronchoscopy and lavage showed evidence of PJP DNA on PCR and the patient was commenced on IV cotrimoxazole. Patient made a slow recovery.
Conclusion: Our survey did not identify a high incidence of PJP in the ARD cohort however, the common denominator for PJP in the two patients we have identified seem to be an underlying ILD. The commonest CT findings noted was ground glass shadowing in addition to ILD in both cases. A strong index of suspicion, early HRCT and bronchial lavage is crucial for the diagnosis.Failure to respond to conventional treatment should alert the clinician to cotrimoxazole resistant PJP.There are case reports of emerging resistance to cotrimoxazole trin in the non-HIV immunosuppressed group, increasing the mortality. We could not make any firm recommendation based on this observational study as the numbers were very small but the clinician should consider PJP prophylaxis in RA ILD patients and patient with AAVs on long term Rituximab therapy. There is a need to incorporate prophylaxis treatment in to the guidelines.

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AB1671

COMORBIDITIES AND CARDIOVASCULAR RISK FACTORS IN A MEXICAN MESTIZO COHORT OF RHEUMATOID ARTHRITIS PATIENTS

Keywords: Comorbidities, Epidemiology, Rheumatoid arthritis

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Background: Rheumatoid arthritis (RA) has been associated with a 3 to 10 years life expectancy reduction as compared to general population, with atherosclerotic disease being the leading cause of death [1].
Objectives: To determine the prevalence of comorbidities and associated cardiovascular risk factors in Mexican patients with rheumatoid arthritis.
Methods: Observational, prospective, cross-sectional, and analytic study. Patients aged 40 to 75 years who met the ACR/EULAR 2010 Classification Criteria for the diagnosis of Rheumatoid Arthritis in a period from August 2014 to December 2022 were included. Patients with a history of cardiovascular disease (myocardial infarction, cerebrovascular event, or peripheral arterial disease) were excluded. The distribution was evaluated with the Kolmogorov-Smirnov test. Normally distributed variables were described with mean and standard deviation (SD) and the 25th and 75th percentiles (p25-p75) were used to report variables without normal distribution.
Results: A total of 487 patients were included. The mean age was 55.3 ±8.9 years, women 92.2%. The median for disease duration was 7.0 (2.8-14.5) years. In this cohort, 163 (33.3%) of patients were in remission, 67 (13.8%) had low, 198 (40.7%) moderate and 60 (12.3%) high disease activity according to DAS28-CRP. Of these patients, 401 (82.3%) were on methotrexate, 296 (60.8%) were on prednisone (median dose of 5.0 mg per day), and 260 (53.4%) were in both. The cardiovascular risk factors with the highest prevalence were overweight in 208 (42.9%) and obesity in 153 (31.4%). The most prevalent comorbidity was dyslipidemia in 150 (30.9%), the rest are shown in Table 1.
Conclusion: Although patients with rheumatoid arthritis have a lower prevalence of traditional cardiovascular risk factors and comorbidities compared to the general Mexican population, they continue to have a higher cardiovascular risk and increased mortality at 3 – 10 years, which raises the question: should RA be included as a cardiovascular risk factor?

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Table 1. Patients' characteristics.

Characteristic	RA patients (*n* = 487)
Cardiovascular risk factors	
High blood pressure[a], n (%)	74.0 (15.2)
FH of premature CAD[b], n (%)	46 (9.4)
Overweight[c], n (%)	208 (42.9)
Obesity, n (%)	153 (31.5)
Active smoking, n (%)	48 (9.9)
Comorbidities	
Hypertension, n (%)	148 (30.4)
Dyslipidemia, n (%)	150 (30.9)
Diabetes, n (%)	76 (15.6)
Kidney disease, n (%)	0 (0.0)

RA, rheumatoid arthritis; FH, family history; CAD, cardiovascular disease; [a]Systolic blood pressure ≥140 and/or diastolic blood pressure ≥90; [b]BMI ≥25 and <30; [c]BMI ≥30.

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Disclosure of Interests: None Declared.
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AB1672

SCREENING OF SYMPTOMS IN THE AT-RISK OF RHEUMATOID ARTHRITIS CZECH COHORT USING SYMPTOMS IN PERSONS AT RISK OF RHEUMATOID ARTHRITIS (SPARRA) QUESTIONNAIRE

Keywords: Autoantibodies, Rheumatoid arthritis

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Background: With growing knowledge about the course of rheumatoid arthritis (RA), the focus shifts to the pre-clinical phase. The presence of RA-associated autoantibodies e.g., anti-citrullinated protein antibodies (ACPA) and rheumatoid factors (RF) increases up to 10 times the risk of developing RA in comparison to the common population. The positivity of these autoantibodies and multiple symptoms without clinical arthritis enable the characterization of individuals who are considered at risk for progression to RA. The "Symptoms in Persons at Risk of RA" (SPARRA) questionnaire was created to screen symptoms occurring in at-risk individuals. This questionnaire comprises 13 symptoms (joint pain, swelling and stiffness, burning and tingling sensations, numbness, changes in skin color over joints, muscle cramps, weakness, fatigue, emotional distress, concentration and sleep difficulties) and explores their duration, location, intensity and impact on daily activities.

Objectives: To explore the symptoms in our prospective observational cohort of individuals with arthralgia at-risk of RA (ARRA cohort) using the SPARRA questionnaire.

Methods: Individuals at-risk of RA, defined as having arthralgia without arthritis on the examination of 66/68 joints at baseline and being either ACPA+ and/or meeting the European Alliance of Associations for Rheumatology (EULAR) definition of clinically suspect arthralgia (CSA, having at least 3 out of 7 parameters), cross-sectionally filled out the SPARRA questionnaire. All individuals signed informed consent before study enrolment. Differences between ACPA+ and ACPA- individuals were analysed using Fisher's exact test.

Results: The study included **77** at-risk individuals (75% were females) with a mean age of 48,08±12,62 years, symptom duration of 34,66±35,56 months with CRP 3,17±4,24 mg/l and 5,43±7,32 tender joints on examination, out of which 61% were ACPA+, 59% met the CSA definition, and 20% were both ACPA+ and met the CSA definition. The most frequent symptoms at the time of SPARRA completion were joint pain (97%), joint stiffness (83%), fatigue (82%), emotional distress (70%), sleep problems (66%), and joint swelling reported by the patient (65%). Joint stiffness (100% vs. 71%, p=0,0005), sleep problems (84% vs. 53%, p=0,0067), and concentration difficulties (69% vs. 29%, p=0,0010) were more prevalent in ACPA- individuals than in ACPA+ group. Similarly, the intensity (none/mild vs. moderate/severe) of fatigue (p=0,0197), emotional distress (p=0,0270), and sleep problems (p=0,0054) was higher in ACPA- group; along with emotional distress (p=0,0136) and sleep problems (p=0,0407) being of higher impact on daily activities in ACPA- individuals. Joint pain was most frequently described as aching, and localized in fingers with up to mild severity and with none to a small impact on daily activities in both groups. The pain was intermittent, typically with periods without any symptoms in the ACPA+ group and always with some residual symptoms in the ACPA- group (p=0,0015). When assessing the most prevalent symptoms in ACPA+ individuals, joint stiffness appeared more frequently in ACPA+ individuals meeting the CSA definition compared to ACPA+ individuals not fulfilling the CSA criteria.

Conclusion: Symptoms of the at-risk individuals appeared more frequently and with higher intensity and impact on daily activities in ACPA- individuals, who as per the inclusion criteria, met the CSA definition, with joint pain being the most prevalent. The value of the SPARRA questionnaire in the assessment of the risk of arthritis development in at-risk individuals needs to be determined in further prospective studies.

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AB1673

THE USE OF DIGITAL FOOT SCANNING (PELMATOGRAPHY) FOR IDENTIFICATION OF STANCE ABNORMALITIES IN A YOUNG HEALTHY POPULATION

Keywords: Work-related issues, Epidemiology, Health services research

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Background: Clinical evaluation of pes anatomy and abnormalities are rarely reported in rheumatology literature. Often deviations from normal are not evaluated, unless subsequent pathology and symptoms are overt. Foot symptoms may occasionally lead to overdiagnosis of seronegative arthropathies.

Objectives: This study aims to identify any foot abnormalities in a healthy young population of army recruits, using clinical and digital foot scanning – pelmatographic (PLM) examination.

Methods: One hundred and ten (M/F:65/54) of a total of 129 new army recruits of a Military Academy in Greece participated voluntarily in the study. Subjects' informed consent and proper ethical approvals were obtained. The study conducted according to Declaration of Helsinki. A small percentage (1.12 %) reported short-term lower leg symptoms during vigorous athletic activities, the past five years. We used clinical evaluation of pes morphology on stance and compared to data obtained during the stance phase of examination using a 3400-sensors plantar pressure foot scan machine. Descriptive statistics were used for the statistical analyses.

Results: Agreement between clinical and pelmatographic observation was noted in 59.1% of subjects. In particular, clinical and pelmatographic normal pes was observed in 48.2% and 68.8% of subjects, respectively. High arched foot was observed in 23.6% and 17.2%, while flat foot in 23.6% and 9.7% respectively. There was no statistical difference between clinical and pelmatographic evaluation of high arched foot (chi-square test, p=0,815). Discrepancy between clinical and pelmatographic evaluation of flat feet was noted (p=0.04, OR:0.47, 95%CI:0.165-0.730). Finally, 37.3% of the participants presented foot pronation while in 60.8% subjects [M:41 (60.2%), F:27 (39.3%)] brachymetatarsia of the 1st toe (Morton's toe) was observed.

Conclusion: Prevalence of pes abnormalities are high and unattended in an otherwise healthy young population. These variations may predispose to future foot symptoms under specific circumstances. Digital foot pressure scanning may facilitate diagnosis and contribute to solution with foot orthotics.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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Validation of outcome measures and biomarkers___

AB1674

TOWARDS A GUIDE FOR EVIDENCE-BASED TELEMONITORING: SENSITIVITY OF PATIENT REPORTED OUTCOMES TO CHANGE IN DISEASE ACTIVITY STATUS IN EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS

Keywords: Patient reported outcomes, Rheumatoid arthritis, Telemedicine

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Background: In the treatment and follow up of rheumatoid arthritis (RA) patients, it has become more desirable to detect changes in disease activity through telemonitoring, for which patient reported outcomes (PROs) might be useful. So far associations between PROs and changes in disease activity have been mostly investigated on a continuous scale. However, in daily practice and in line with the EULAR recommendations, treatment decisions are mainly based on the patient's disease activity status. Earlier literature has shown that functionality, joint pain, morning stiffness, general health (GH), health-related quality of life and fatigue change with the development and resolution of a disease flare.
Objectives: Therefore, our aim is to determine if PROs that cover functionality, joint pain, morning stiffness, health-related quality of life and fatigue are sensitive to disease activity status alterations (from active to low disease activity to remission, and vice versa) in patients with early and established RA.
Methods: Early RA patients from the tREACH-trial and established RA patients from the TARA-trial were included. Both studies were multicentre, single blinded trials with a treat-to-target design. Treatment alterations were based on the disease activity score (DAS44) and PROs were collected at 3-montly fixed intervals. The following PROs were studied: (1) the Health Assessment Questionnaire Disability Index (HAQ-DI), (2) joint pain (numeric rating scale, NRS 0-10), (3) morning stiffness severity (NRS 0-10), (4) GH (visual analogue scale, VAS 0-100mm), (5) health-related quality of life (EQ-5D) and (6) fatigue (VAS 0-100mm).

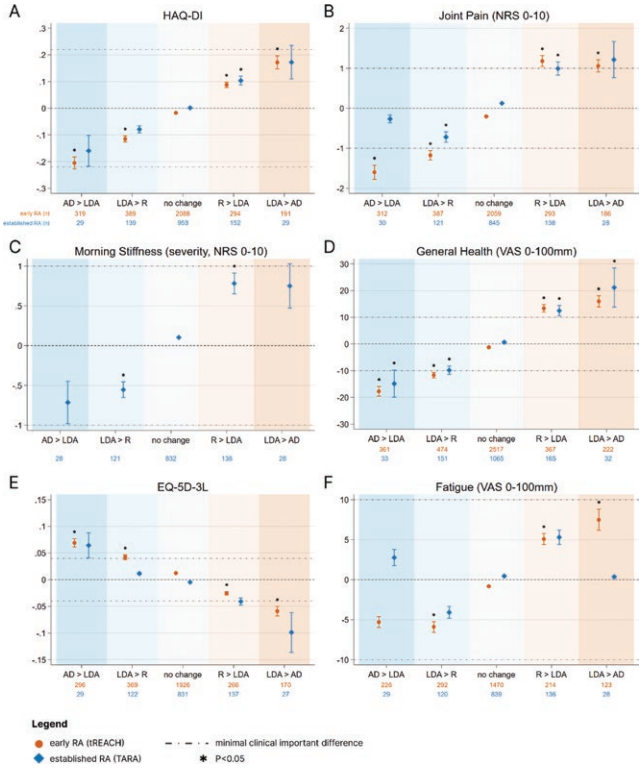


Figure 1. Mean changes in patient reported outcome per disease activity status alteration

Figure 1A-F show the mean change (95%CI) in PRO per disease activity status alteration for early and established RA patients. * indicates that the change in PRO is significantly (p<0.05) different compared to stable disease activity status.

Abbreviations: AD, active disease; HAQ-DI, Health Assessment Questionnaire Disability Index; LDA, low disease activity; NRS, numeric rating scale; R, remission; VAS, visual analogue scale.

Disease activity statuses were defined as: (1) active disease (DAS≥2.4), (2) low disease activity (LDA, DAS<2.4 and ≥1.6) and (3) remission (DAS<1.6). Differences in disease activity status between two consecutive visits were compared to changes in PROs. Mean changes in PROs per disease activity status alteration were compared to stable disease activity status, using generalized estimated equation-models.
Results: Respectively 587 and 189 early and established RA patients were included. The median symptom duration (IQR) was 0.4 (0.2-1.8) and 6.2 (4.1-8.9) years, respectively. The mean DAS (95%CI) at baseline was 3.0 (3.0-3.1) in the early and 1.0 (0.9-1.1) in the established RA group. **Figure 1** shows the mean change (with 95%CI and significance) in PROs per change in disease activity status. HAQ-DI, joint pain, morning stiffness, GH, EQ-5D and fatigue (in early RA) were in concordance with improvement or worsening of disease activity status. Change from active disease to LDA or vice versa had a larger effect on HAQ-DI, GH, and EQ-5D compared to change from and to remission to LDA. Respectively, change in HAQ-DI was 1.9 and 1.8 times greater going from active disease to LDA compared to a shift from LDA to remission and vice versa. For GH this was 1.6 and 1.2 and for EQ-5D 2.1 and 2.0 respectively.
Conclusion: Changes in HAQ-DI, morning stiffness, joint pain, GH and EQ-5D correspond to changes in disease activity status. These results suggest that changes in aforementioned PROs may be helpful in telemonitoring of RA.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1675

DEEP PHENOTYPING OF IMMUNE MICROENVIRONMENT IN ULCERATIVE COLITIS BY INTEGRATIVE SYSTEMS ANALYSIS

Keywords: Adaptive immunity

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Background: Ulcerative colitis (UC) is an inflammatory bowel disease characterized by idiopathic and recurrent mucosal inflammation [1]. The pathogenesis is multifactorial, involving genetic susceptibility, epithelial barrier defects, dysregulation of the immune response, and environmental factors. UC is a highly heterogeneous disease [2]. Despite efforts to characterize disease subgroups and predict differential outcomes in UC patients, disease heterogeneity is not adequately translated into current clinical subclassifications.
Objectives: This study seeks to unravel this complexity by using an integrated systems approach that classifies UC patients into different phenotypes based on the immune microenvironment, capable of providing new insights into the development of stratified therapies.
Methods: RNA sequencing datasets of 602 colon tissue samples from 455 patients with UC and 147 healthy controls (HC) was imported from GEO database. The microarray datasets were transformed into immune cell components by CIBERSORT, and patients were stratified by a consensus clustering algorithm. Then, the cellular characteristics of the subtypes and the overall role of specific pathways were determined by immune cell infiltration and pathway enrichment. The clinical characteristics of the different subtypes were also analyzed to clarify the characteristics of these classifications.
Results: Patients can be classified into two distinct immune phenotypes (Subtype A, B) based on their specific RIME, which have different cellular and pathway characteristics. (Figure A, B) The results show that Subtype A is mainly enriched in immune cells such as B cells, CD8+ T cells, CD4+ memory T cells, DC cells, macrophages, mast cells and plasma cells. Acidic granulocytes and neutrophils were more active in Subtype B. It was also significantly enriched in the peroxisome proliferator-activated receptor (PPAR) signaling pathway in Subtype B. In contrast, Subtype A showed a strong enrichment for most inflammatory pathways B cell and T cell receptor signaling, IL-17 signaling pathway, TNF, and interleukin 4 and interleukin 13 signaling pathway. (Figure 1 D, E) In addition, there was a significant difference between molecular subclassification and disease status, with Subtype A being more active in patients (69.3% of Subtype A vs.30.6% of Subtype B subtypes in 137 cases), while inactive patients, Subtype B were more prevalent (44.8% of Subtype A vs. 55.2% of Subtype B in 105 cases). (Figure 1C)
Conclusion: Analysis of the immune microenvironment of colonic mucosal tissue provides good insight into the pathophysiological characteristics of UC. These results can be used as a model for future studies. the response and clinical outcomes of patients with different classification need to be further investigated.

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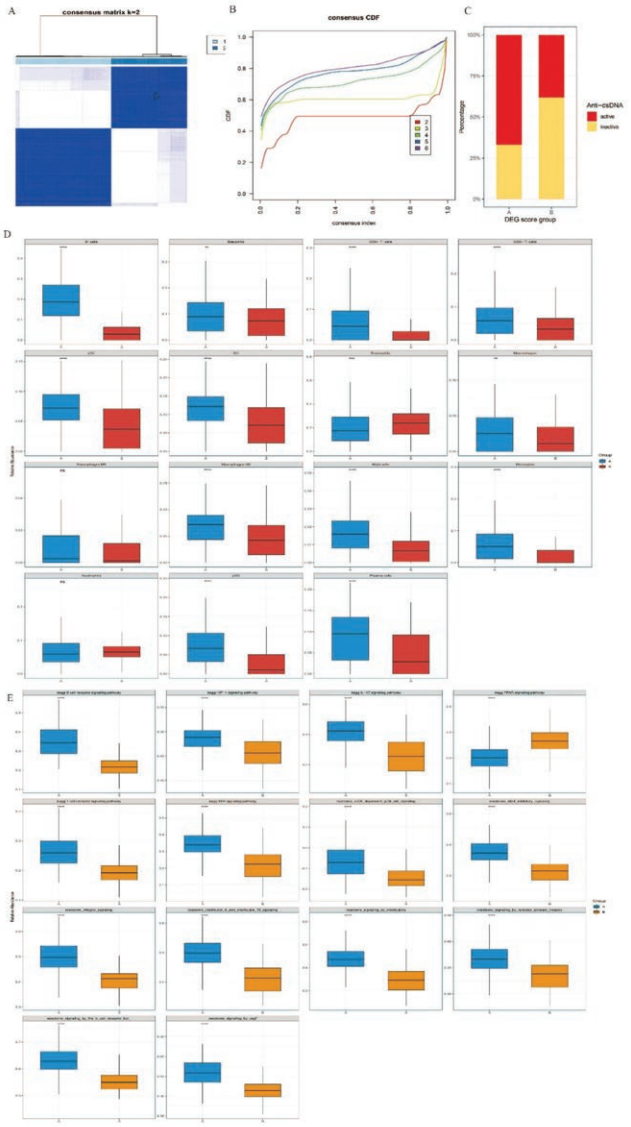


Figure (A) The consensus score matrix for Ulcerative colitis (UC) samples when k = 2. The samples were clustered using the km cluster algorithm, ward. D linkage and Euclidean distances. (B) Cumulative distribution function (CDF) curve of the consistency score for different subtype numbers (k = 2–6). (C) The disease activity in the two different subtypes are presented using the boxplot. (D) Cell subset enrichment scores according to UC subgroups. (E) Pathway enrichment scores according to UC subgroups.

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AB1676

REASSESSMENT OF THE SIGNIFICANCE OF PATIENT GLOBAL ASSESSMENT IN REMISSION CRITERIA FOR RHEUMATOID ARTHRITIS IN TERMS OF 68/66 JOINT COUNTS

Keywords: Rheumatoid arthritis, Registries, Patient reported outcomes

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Background: One rationale for including patient global assessment (PtGA) in Boolean remission is that PtGA ≤1 reduces the probability of joint findings outside the 28 joints and complements the limitations of 28-joint count assessment [1]. Meanwhile, the criterion of PtGA ≤1 has been questioned, leading to establishment of Boolean2.0 or proposal of 3V-remission [2-3]. However, the significance of PtGA as a complement to the limitations of the 28-joint assessment has been forgotten.

Objectives: This study aimed to evaluate the discriminative power of PtGA for the presence of joint findings outside the 28 joints within the framework of Boolean2.0 and 3V-remission in the real-world setting.

Methods: We analyzed 8,684 patients with rheumatoid arthritis who achieved 3V-remission (28-tender joint count (TJC), 28-swollen joint count (SJC) and C-reactive protein (mg/dL) all ≤1) registered in the National Database of Rheumatic Diseases in Japan (NinJa) in 2020, a large observational database. Based on TJC68 and SJC66, patients were divided into two groups of patients with and without joint findings outside the 28 joints (JFO28). The values and distributions of PtGA were compared between the two groups, and the positive likelihood ratio for no findings outside the 28 joints was calculated, varying cut-off values of PtGA. Receiver Operating Characteristic (ROC) analysis was performed to assess the discriminative power of PtGA for the presence of JFO28 and optimal cut-off value.

Results: Among 8,684 patients, 6,901 were patients without JFO28 and 1,783 were patients with JFO28. The values of PtGA were significantly higher in patients with JFO28 (the difference of 25% trimmed mean, 1.12 [95% CI, 1.01 to 1.24]). However, the distribution of PtGA was largely overlapping (Figure 1). About 12%, 15%, and 21% of patients had JFO28 when the cutoff values for PtGA were 1.0, 2.0 (Boolean2.0), and none (3V-remission), respectively. The positive likelihood ratios were 1.90 and 1.44 when the cutoff values of PtGA were 1.0 and 2.0, respectively. The area under the ROC curve was 0.68 [95% CI, 0.66 to 0.69], indicating low discriminative power. The optimal cut-off value was 1.0 based on Youden index.

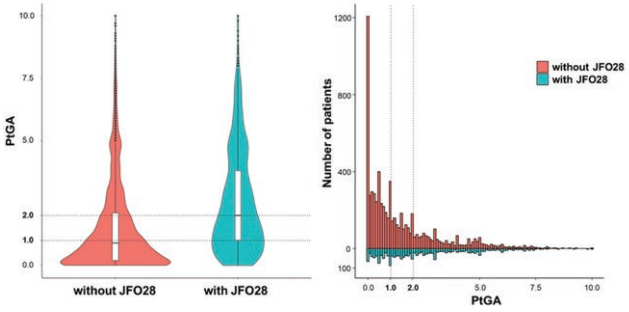


Figure 1. The distribution of PtGA in patients with and without JFO28

Conclusion: A cutoff value of 1.0 for PtGA seems reasonable in terms of 68/66 joint findings. It may be pragmatic to evaluate PtGA and joint findings separately in accordance with the concept of dual target therapy because PtGA has low discriminative power for the presence of JFO28 in patients achieving 3V-remission. However, our results suggested that there is a need to extend the criteria for joint assessment in 3V-remission to 68/66 joints, considering not a few patients had JFO28 even if they had reached 3V-remission.

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Disclosure of Interests: Takahiro Nishino: None declared, Shigeto Tohma Speakers bureau: Pfizer Japan inc., Abbie Japan Co., Ltd., Eisai Co., LTD., Janssen Pharmaceutical K. K., Celltrion healthcare Japan Co., Ltd., Consultant of: Mitsubishi-Tanabe Pharma Co., Grant/research support from: Chugai Pharmaceutical Co., LTD., Mitsubishi-Tanabe Pharma Co., Abbie Japan Co., Ltd., Toshihiro Matsui Speakers bureau: AbbVie, Asahikasei Pharma Corp., Astellas, Chugai Pharmaceutical Co, Ltd., Eisai Co., Ltd. Eli Lilly Japan, Ono Pharmaceutical Co., Ltd., Pfizer Japan Inc., Grant/research support from: Asahikasei Pharma Corp., Chugai Pharmaceutical Co, Ltd.
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AB1677

VALIDATION ANALYSIS OF THE PHYSICIAN GLOBAL ASSESSMENT (PGA) SCALE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS INCLUDED IN RELESSER-PROS REGISTRY

Keywords: Outcome measures, Systemic lupus erythematosus, Validation

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Background: There is currently no agreement on which scale should be used to evaluate systemic lupus erythematosus (SLE) disease activity. PGA describes an instrument for a global assessment of the degree of disease activity by the clinician and it is generally regarded as the gold standard. Despite its wide use and some degree of validation, the psychometric properties of this scale have not been formally evaluated and it is unclear whether more commonly used analogue scales for global assessment of rheumatic disease activity by the clinician, such as a VAS from 0 to 10, would be more appropriate.
Objectives: The aim of this study was to assess the construct and criterion validity of the physician global assessment (PGA), from 0 to 10, in a wide sample of SLE patients from Spain, analyzing the correlation with SLEDAI, health-related quality of life (QoL) and its ability to predict damage in order to promote its more widespread use.
Methods: An observational, longitudinal and prospective design was carried out. A total of 1821 patients from the RELESSER-PROS registry and data from 5 annual consecutive visits were tested. Activity was estimated using PGA from 0 to 10 transformed to AM-PGA (mean-adjusted PGA)(AMP), and AM-SLEDAI (mean-adjusted SLEDAI)(AMS); damage through SLICC/ACR Damage Index (SDI) and QoL by means of EuroQoL 5D y Lupus Impact Tracker (LIT) tools. The correlation between indices and their ability to predict damage progression (defined as any increase of 1 unit in SDI from baseline) and QoL was calculated. Pearson's or Spearman's correlation coefficients were calculated for each variable in comparison.
Results: The correlation between PGA and SLEDAI was higher for lower PGA values and there was a correlation between AMP and AMS, ranging 0.4 and 0.5. AMS explains a percentage of AMP variation that rises to 27% when introducing the number of domains affected by SLEDAI, in non-parametric model. AMS and AMP values are discrepant, especially for patients with low AMS and high AMP values and differs significantly in 3 domains: serological, neuropsychiatric, and renal. Excluding patients from the model, who were marked as discrepant, a significant linear relationship between AMS and AMP, around 0.5 shown up. Regarding damage, the correlation between AMP, AMS and SLICC/ACR (SDI) explained only 13% of SDI variance. SLEDAI accounts for a higher percentage of SDI variance than PGA (10.18% vs. 5.65% in smoothed model), but both do it independently. Analysis the discrepant and non-discrepant patients showed a fairly discrete linear relationship, less than 3%, between the AMS and AMP with the LIT and the EQ5D6 only for the non-discrepant patients.
Conclusion: The correlation between PGA and SLEDAI is low and both should be used together. PGA could improve the assessment of disease activity and its use adds the possibility to improve damage prediction.
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AB1678

CONSTRUCTION OF A COMPOSITE SCORE FOR PATIENT SELF-REPORT OF FLARE IN OSTEOARTHRITIS: A COMPARISON OF METHODS WITH THE FLARE-OA-16 QUESTIONNAIRE

Keywords: Pain, Patient reported outcomes, Outcome measures

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Background: Having a score to assess the occurrence and severity of flares of knee or hip osteoarthritis (OA) to guide interventions is essential.
Objectives: To compare different methods of constructing a composite score for the Flare-OA-16 self-reported questionnaire for measuring knee and hip OA flare, defined as a cluster of symptoms of sufficient duration and intensity to require initiation, change or increase in therapy [1].
Methods: Participants with a physician diagnosis of knee and hip OA completed a validated 16-item questionnaire [2,3] assessing five dimensions of flare in OA: pain, swelling, stiffness, psychological aspects, and consequences of symptoms, endorsed by OMERACT. Three estimation methods were compared: the score obtained i) by second-order confirmatory factor analysis (CFA) weighting the factor loadings in a linear combination of the five dimensions; ii) by logistic regression, modeling the probability of having a flare according to the participant's self-report (yes/no); and iii) by Rasch method, using the average of the weighted scores from a Rasch model in each dimension. For the scores obtained by the three methods, the disordered items were modified, and then the scores were standardized on a scale from 0 to 10. The distribution (floor effect without flare (FF) and ceiling effect with flare (CF)) of the scores in each model was compared. The similarity between the scores was analyzed by intraclass correlation coefficient (ICC) and their performance were compared by areas under the ROC curves (AUC) and 95% confidence interval. The intra-score test-retest reliability at 15 days was assessed by ICC.
Results: In a sample of 381 participants with complete questionnaires, 247 reported having a flare. With CFA, good fit indices (CFI=0.94; RMSEA=.08) justified the estimation of an overall score mean=3.90 (SD=2.79), with FF effect 27.6% and CF 2.0%. For the logistic regression estimation, the overall score was mean=6.48 (SD=3.13), with FF 0% and CF 34.0% effect. With the Rasch model, the composite score was mean=4.15 (SD=2.45), with FF 18.7% and CF 0% effect. Similarity analysis indicated a greater concordance between the CFA and Rasch scores (ICC=.99) than between the logistic regression score and the two others (ICC=.87 for each). The ROC curve indicated similar performance of the overall scores estimated by logistic model (AUC=.88 [.85-.92]), by CFA

(AUC=.86 [.82-.90]) and by Rasch model (AUC=.86 [.82-.90]). The performance in terms of reproducibility was ICC=.84[.95-.90] for Rasch and CFA scores and ICC=.78[.66-86] for logistic model.

Conclusion: This comparison of methods for constructing a global score for knee and hip OA flare explored three satisfactory alternatives. The second-order CFA confirmed the uniqueness of the flare construct measure, the logistic model had a slight superiority explained by the anchor variable used (patient-reported flare), and the Rasch model ensured that an interval scale was obtained for each dimension. The distribution of scores with the lowest combination of floor and ceiling effects was in favor of the Rasch model. The next step will be to document their respective performance in terms of sensitivity to change. A score obtained from the patient's point of view can help increase the adherence to the prescribed treatment and help physicians to optimize the scheduling and delivery of medical consultation.

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Disclosure of Interests: None Declared.

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AB1679 VASCULITIS DISEASE ACTIVITY SCORES BEFORE AND DURING THE COVID-19 PANDEMIC: A COMPARISON OF FACE-TO-FACE CLINICIAN SCORING AND PROMS COLLECTED USING REMOTE MONITORING IN A SINGLE-CENTRE COHORT

Keywords: Telemedicine, Vasculitis, Patient reported outcomes

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Background: During the COVID-19 pandemic, asynchronous consultations were introduced for patients with vasculitis. To assess disease activity without of face-to-face clinical reviews and blood testing, patients submitted patient reported outcome measures (PROMs) via electronic survey forms, which were subsequently triaged by clinicians.

Objectives: 1. To investigate how patients' vasculitis disease activity was affected by the COVID-19 pandemic through retrospective comparison of clinician-assessed scores recorded pre-pandemic with intra-pandemic self-reported patient reported outcome measures (PROMs) and disease scores submitted by patients remotely.

2. To assess patients' clinical outcomes, including allocation of follow-up and further management/treatment escalation during this period.

3. To validate self-reported BVAS scores against an existing PROM.

Methods: This is a retrospectively study of patients with a known diagnosis of vasculitis under the care of the Nuffield Orthopaedic Centre, Oxford. For the purposes of this study, we included patients with all vasculitis diagnoses. Clinician-reported scores (Bristol Vasculitis Activity score v.3, BVAS) were recorded during in-person clinics pre-pandemic (defined as 01/01/2019-31/12/2019) [1]. Patients' self-reported BVAS (SR-BVAS) and AAV-PRO (ANCA-associated vasculitis patient-reported outcomes) scores were submitted by patients via electronic forms containing the requisite questionnaires sent out during-pandemic (defined as 01/12/2020-31/03/22) [2]. SR-BVAS has not been validated but was collected to allow clinical comparison to disease activity scores completed by clinicians. Response were stored and analysed in a secure database. Score comparison was performed using Wilcoxon Sign Rank testing. Clinical outcome data was collected from the local Electronic Patient Record. Data analysis was performed in Microsoft Excel and R (version 4.2.1).

Results: We noted a significantly higher overall level of patient-reported disease activity during the pandemic than was recorded in clinics prior. In the total cohort of all vasculitis patients for whom we had data, the median BVAS increased from 2 pre-pandemic (N = 335, range 0-21) to 6 intra-pandemic (N = 143, range 0-42) (p <0.001). The overall proportion of patients with severe/active disease (defined as BVAS ≥4) increased from 27% to 36% during the pandemic period. In a smaller cohort of 64 patients for whom we had paired pre- and during-pandemic scores, increased disease activity was reported (p<0.01). Notably, the number with a BVAS consistent with severe disease increased from 7 (11%) to 19 (30%). There was a significant positive correlation between SR-BVAS and AAV-PRO (r=0.61, p< 0.001) submitted by patients during-pandemic; however, at low BVAS (≤3), the AAV-PRO ranged widely (28-87) Follow-up data was available for all 64 patients in this cohort: 8/19 (42%) with a during-pandemic SR-BVAS ≥4 were seen in clinic within 3 months (telemedicine or face-to-face).

Conclusion: Patients reported worsening of vasculitis disease activity during the COVID-19 pandemic. This may be attributable to impacts on well-being or access to healthcare services. We note that disease activity scores in vasculitis may be limited in their ability to capture the whole picture disease activity in the absence of clinical assessment [3]. 42% of patients with self-reported high disease activity were seen within 3 months. There was a significant positive correlation between AAV-PRO and SR-BVAS, suggesting it has some use as a PROM.

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AB1680 BIOMARKERS IN PATIENTS WITH VIBRATION INDUCED RAYNAUD'S PHENOMENON AND IN REFERENTS

Keywords: Biomarkers, Comorbidities, Work-related issues

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Background: Secondary Raynaud's phenomenon (RP) due to occupational exposure to hand-held vibrating tools is a well-recognized part of the Hand arm vibration syndrome (HAVS) [1]. Different pathophysiological mechanisms for HAVS-induced RP have been proposed, e.g., localized structural vascular and neuronal injuries as well as systemic inflammatory processes by increased oxidative stress [2-5]. Elevated plasma levels of thrombomodulin (TM), a marker for endothelial damage, have been shown in vibration-exposed workers [6, 7] with equal levels as in collagen diseases [7]. Von Willebrand factor (vWF) has been suggested as biomarkers for vibration induced RP [8]. Elevated levels of vWF have been found in RP patients who subsequently develop scleroderma or other connective tissue diseases, even in the absence of capillaroscopic abnormalities [9]. It is however still not clear whether the mechanisms for vibration related RP are similar to those for other forms of RP. Biomarkers for vascular injuries may shed light on this.

Objectives: To investigate serum levels of TM and vWF in patients with HAVS, with or without RP.

Methods: Blood samples were collected in the morning from 92 patients with HAVS. Forty-five (49%) of these had RP, 47 (51%) did not. Serum was removed and stored at -80 °C until analysis. TM and vWF were measured by using commercially available ELISA assays. Distributions were compared with Mann-Whitney U tests.

Results: Higher values of TM were found in HAVS patients with RP (median 6.1 ng/ml; range 2.7 – 30), compared to those without RP (5.2 ng/ml; 2.3 – 39; p = 0.02). Further higher levels of vWF were found in HAVS patients with RP (18 µg/ml; 6.2 – 33) compared to without RP (14 µg/ml; 6.9 – 34; p = 0.008).

Conclusion: As in patients with RP due to connective tissue disorders higher levels of biomarkers for endothelial damage were shown in HAVS patients with RP. Increased serum levels of TM have been shown in previous studies on vibration injured patients [8, 9] but in one of the studies, no significant difference was shown between patients with RP and those without RP [9]. Our data indicates that RP symptoms is required to detect a significant change in the biomarker TM in vibration injured patients. Our data strengthen earlier findings that biomarkers of endothelial damage could be a useful tool in the assessment of vibrational induced injuries.

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AB1681 ARE PR3 ANTIBODY TITERS REALLY IMPORTANT FOR ROUTINE CLINICAL PRACTICE?. STUDY FROM A SINGLE UNIVERSITY HOSPITAL

Keywords: Vasculitis, Autoantibodies

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Background: Anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) includes granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA). Anti-proteinase 3 are one of the main ANCA subtypes. There are contradictory studies on the relation between ANCA levels and the severity of the disease and its prognosis [1].

Objectives: In patients with positive anti-PR3 antibodies from a university hospital we assess: **a)** associated diseases, **b)** specificity in diagnosing AAV and, **c)** determine if there is a cut-off point that allows to correlate the levels of anti-PR3 antibodies with the severity and prognosis of AAV.

Methods: Observational study of patients with positive anti-PR3 from a University Hospital, from 2003 to 2022. ANCA was determined by chemiluminescence. The specificity of anti-PR3 for AAV diagnosis, predictive value of severity and prognosis were determined with Receiver Operating Characteristic (ROC) curves. At diagnosis, AAV with renal disease (hematuria and/or proteinuria) and lung involvement (hemoptysis, asthma and/or respiratory failure) were considered severe. During follow-up, the prognosis was considered worse if the patient needed dialysis, a transplant, or died.

Results: We study 54 patients with positive PR3. Most of them (81.5%) had an underlying AAV being the most frequent GPA (61.1%). The non vasculitic disease more frequent was Ulcerative colitis (11.1%). **Table** 1 summarizes the prevalence of these antibodies in different diseases. The frequencies are equivalent to those previously described and it is noteworthy the presence of anti-PR3 in drug-induced vasculitis, mainly by cocaine. Anti-PR3 antibodies for a diagnosis of vasculitis (n=44), an area under the curve (AUC) was calculated (AUC=0.7318), and a cut-off point of 20.5 IU/ml was determined **(Figure 1).** Significant differences in anti-PR3 levels were observed between those patients with renal or pulmonary dysfunction (n=30) and those without them (n=24) (p=0.0048), and a cut-off threshold of 41.5 IU/ml was established. Finally, after examining the illness's prognosis an AUC= 0.5643 was obtained, being no significant differences between those patients who had a worse disease progression (n=14) and those who did not (n=40) (p=0.4847).

Conclusion: The presence of anti-PR3 is mainly associated with AAV, although in up to a fifth of cases it can be associated with other diseases. Anti-PR3 antibodies levels, at the moment of AAV diagnosis, correlates with disease diagnosis (specificity) and with severity but not with disease outcome.

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Table 1. Diseases associated with positive anti-PR3 antibodies (n=54).

Group	Disease	Number (n)	Frequency (%)
Vasculitis (n=44; 81.5%)	Granulomatosis with polyangeiitis	33	61.1
	Drug-induced vasculitis	5	9.2
	Pauci-immune glomerulonephritis	2	3.7
	Microscopic polyangeiitis	2	3.7
	Large vessel vasculitis	1	1.9
	Unclassified vasculitis	1	1.9
No vasculitis (n=10; 18.5%)	Ulcerative colitis	6	11.1
	Chron's disease	1	1.9
	Infection	1	1.9
	Diffuse interstitial lung disease	1	1.9
	Hypereosinophil syndrome	1	1.9

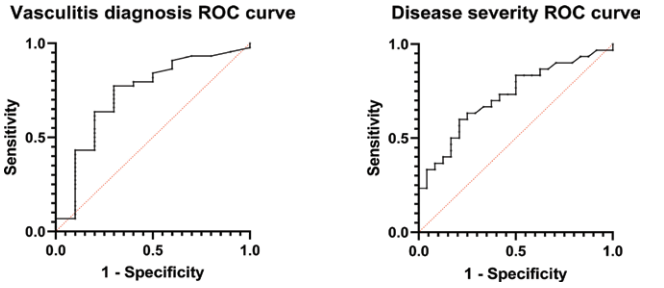


Figure 1. Receiver Operating Characteristic (ROC) plots for AAV and positive MPO-antibodies (AUC=0.7318) and disease severity at diagnosis (AUC=0.7222)

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AB1682 ARE CHANGES IN SELF-REPORTED NSAID DOSE ASSOCIATED WITH MEANINGFUL CHANGES IN PAIN OR OTHER HEALTH OUTCOMES IN RHEUMATIC DISEASES?

Keywords: Patient reported outcomes, Osteoarthritis, Pain

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Background: Rheumatic disease primary treatment effectiveness research inconsistently addresses confounding effects of nonsteroidal anti-inflammatory drugs (NSAIDs) on pain and inflammation. Further, NSAID comedication use is often captured either as a simplified binary measure (eg, yes/no) or with a more burdensome high level of detail (eg, daily pill dose).

Objectives: Evaluate if moderate complexity items measuring changes in monthly NSAID dose are associated with changes in pain.

Methods: Patient-reported data from 1998-2021 were analyzed from the Forward Databank, a US-based longitudinal rheumatic disease registry, with questionnaires completed every 6 months. Eligible participants with RA or OA reported NSAID use on ≥1 questionnaire and had ≥1 follow-up (FU) questionnaire. NSAID use recorded type of drug, initiation, discontinuation, dose, and

frequency by 0-10, 11-20, or >20 days a month. Primary exposure was change in NSAID dose from baseline (increase, no change, decrease). Increase was defined as initiation, increase in frequency, increase in dose, or any combination of the 3; decreases were similarly defined directionally. Primary outcome was change in the pain visual analog scale (VAS, 0-10). Gaussian generalized estimating equations (GEE) models with robust standard errors [SE] were used to assess the association between pain and NSAID change or type of change (increase, decrease). Models were adjusted for demographics, rheumatic disease comorbidity index (RDCI), total joint replacement, other treatments (eg, opioids, disease-modifying antirheumatic drugs), and NSAID type.

Results: A total of 22,445 RA and 5,278 OA patients initiated ≥1 NSAID. Median (IQR) FU time of NSAID exposure was 4.5 (2–9) years for RA and 2.5 (1–5) for OA. Patients with RA vs OA were younger (59 vs 64 years [y]), but similar on other characteristics (male 20% vs 15%, White 96% vs 94%, disease duration 14 vs 16y, and RDCI [1.5 ±1.5 vs 1.7±1.5]). Overall, 24% of RA 6-month observations (~160700 observations) included an NSAID increase and 18% a decrease; in OA (~39800 observations), 30% increased and 18% decreased. 70% of RA patients (OA 77%) had an NSAID increase during FU and 69% (OA 67%) decrease. Starting or stopping an NSAID was the most common change (Figure 1). In RA, any NSAID increase was significantly associated with increased pain of 0.15 units (and for any NSAID decrease, decreased pain of 0.06) (Table 1), supported by the statistically significant directional changes in pain for any individual category of NSAID increase or decrease. In OA, any NSAID increase was significantly associated with increased pain of 0.06 units but were not significant for any decrease; only the individual categories of NSAID initiation and increased dose were significantly associated with increased pain and decreased NSAID dose associated with decreased pain.

Conclusion: We quantified the change in pain associated with change in NSAID dose generally, directionally, and by change type. All types were important for an increase in pain, but a decrease in NSAID frequency was more significant than other types for RA. Further work is needed to extend the definition of change by including other confounding treatments, eg. analgesics and opioids, and to understand optimal collection of concomitant medications that may influence trial results, especially in OA.

Table 1. Pain VAS Change (95% CI) GEE Models in RA and OA Cohorts

	RA	OA
	N=22,429 β	N=5,274 β
Change in NSAID (ref. no change)		
Increase	**0.15* (0.12; 0.17)**	**0.07* (0.03; 0.12)**
Decrease	**-0.06* (-0.09; -0.03)**	-0.03 (-0.08; 0.03)
Increase type (ref. no change/decrease)		
Start an NSAID	**0.15* (0.12; 0.17)**	**0.08* (0.03; 0.13)**
Time frequency	**0.18* (0.10; 0.26)**	0.04 (-0.10; 0.18)
Dose	**0.16* (0.12; 0.20)**	**0.08* (0.00; 0.16)**
Decrease type (ref. no change/increase)		
Stop an NSAID	**-0.06* (-0.10; -0.03)**	-0.02 (-0.09; 0.05)
Time frequency	**-0.25* (-0.32; -0.18)**	-0.13 (-0.27; 0.02)
Dose	**-0.17* (-0.21; -0.12)**	**-0.10* (-0.19; -0.01)**

*P<0.05 (bolded)

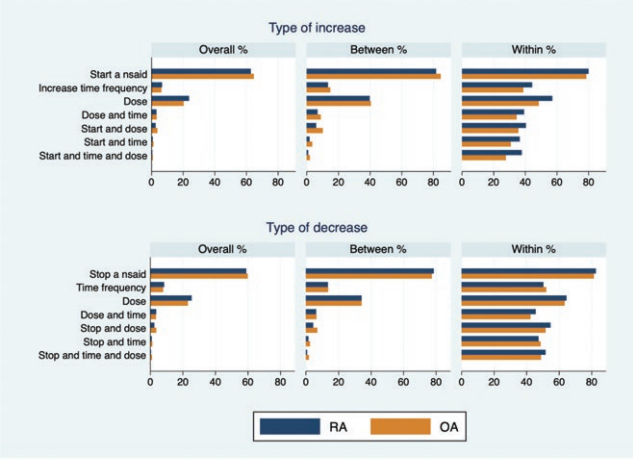


Figure – Type of increase or decrease characterizing NSAID change: overall %; between %; within%. (Overall % = % over the observations; Between % = % of patients with ≥1 change type during FU; Within % = % of time for each change within the FU per patient)

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AB1683

VALIDITY AND PSYCHOMETRIC CHARACTERISTICS OF THE DURUÖZ HAND INDEX IN PATIENTS WITH PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Outcome measures

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Background: The Duruöz Hand Index (DHI) is a valuable scale developed for evaluating hand functions of patients with rheumatoid arthritis and has subsequently proven to be valid and reliable in various diseases.

Objectives: This study aims to investigate the validity and reliability of DHI in patients with psoriatic arthritis (PsA).

Methods: Patients diagnosed with PsA according to CASPAR criteria were enrolled. The demographic, clinical, and functional characteristics of patients were evaluated. Functional assessment was performed with DHI, Hand Functional Index (HFI), Health Assessment Questionnaire (HAQ), and VAS-disability scale. C-reactive protein level, patients' and physicians' global VAS, swelling and tenderness of the hand joints, gross grip strength and thumb strength, and disease activity assessments were recorded as non-functional parameters related to active disease status. The reliability of DHI was assessed by internal consistency (Cronbach's alpha coefficient). Face, content, and construct validity (convergent and divergent) were evaluated. Face and content validities were assessed via cognitive debriefing interviews with the patients. The correlations of the DHI with HAQ, HFI, and VAS disability were assessed for convergent validity. The correlations of the DHI with DAPSA, BASDAI, MDA, PSAQoL, Jenkins index, PASI, and grip strength were evaluated for divergent validity.

Results: One hundred and forty-four patients (74.3% female) with a mean age of 45.33 (SD: 11.58) years were included in this study. Cognitive debriefing showed the DHI to be clear, understandable, and relevant. It was easy to complete and calculate, with the 4 minutes and 30 seconds, respectively. The Cronbach's alpha coefficient was 0.963, and for the test–retest reliability of the DHI, the intraclass correlation coefficient was 0.904 (p<0.001). DHI showed good correlations with the functional disability scales (HAQ, HFI, VAS-disability), indicating its convergent validity and moderate to non-significant correlations with the non-functional parameters supporting its divergent validity (Table 1).

Conclusion: The DHI is a valid and reliable scale to evaluate the functional disability of hands in patients with PsA.

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Table 1. Spearman's correlation coefficients of the Duruöz Hand Index with the other parameters for construct validity

Functional Parameters	Rho	Non-functional Parameters	Rho
VAS Disability	0.599**	Age	-0.033
Hand Function Index	0.484**	Disease duration	0.041
Health Assessment Questionnaire	0.779**	Tender joint count	0.396**
		Swollen joint count	0.341**
		Leeds enthesitis index	0.256*
		PASI	0.292**
		DAPSA	0.312**
		MDA total score	-0.257*
		Tenderness hand index	0.388**
		Swelling hand index	0.335**
		Jamar strength, right	-0.277*
		Jamar's strength left	-0.305**
		Pinch strength, right	-0.338**
		Pinch strength left	-0.394**
		CRP	0.151
		BASDAI	0.448**
		VAS-p Pain	0.359**
		VAS-p Elbow/shoulder/neck pain	0.391**
		VAS-p Morning stiffness	0.590**
		VAS-p General health	0.327**
		VAS-d General health	0.431**
		VAS-d Hand disease activity	0.503**
		Jenkins Sleep Scale	0.386**
		PsAQoL	0.585**

** p<0.001, *p: 0.001-0.049.HAQ=Health Assessment Questionnaire, VAS=Visual Analogue Scale, HFI=Hand Functional Index, PASI= Psoriasis Area Severity Index, DAPSA= Disease Activity in Psoriatic Arthritis Score, CRP= C-reactive protein, MDA= Minimal Disease Activity, BASDAI= Bath Ankylosing Spondylitis Disease Activity Index, VAS-p= Visual analog scale of patient, VAS-d= Visual analog scale for doctor's opinion, PsAQoL= Psoriatic Arthritis Quality of Life Questionnaire

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Disclosure of Interests: None Declared.
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AB1684

DIFFERENCES BETWEEN DISEASE ACTIVITY MEASURED BY ULTRASOUND VERSUS THE STANDARDIZED CLINICAL ACTIVITY INDEX (DAS28 AND DAPSA) FOR RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS BEFORE STARTING BIOLOGICAL THERAPY: A RETROSPECTIVE STUDY

Keywords: Psoriatic arthritis, Rheumatoid arthritis, Ultrasound

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Background: Numerous studies have been written about the role of ultrasound as an objective tool for measuring damage and to predict subsequent progression of inflammatory joint diseases, as well as to detect low-grade synovitis, even in patients with low disease activity.[1] It has been suggested that some patients with subclinical inflammation may experience radiological progression and joint damage despite being in clinical remission.[2]
Objectives: The main objective of this study is to analyze the differences between the disease activity measured by ultrasound versus the standardized clinical activity index (DAS28 and DAPSA) for Rheumatoid Arthritis (RA) and Psoriatic Arthritis (APS) before the start date treatment with biological therapies.
Methods: A retrospective, non-interventional study was performed by reviewing the databases of RA and APS patients from the Hospital Universitario Virgen Macarena's Rheumatology department as well as an inferential study comparing the disease activity measure by ultrasound to the standardized clinical activity index.
Results: 85 ultrasounds of patients with RA (N=54) and APS (N=31) have been included and correlated with the baseline ultrasound activity before the start date treatment with biological therapies. The contrast of the baseline DAS28 and DAPSA means for the different ultrasound findings did not show significant differences (Table 1).
Conclusion: In our daily clinical practice, an adequate correlation is found between the finding data. However, approximately 24% of patients with moderate/high clinical activity by DAS28/DAPSA had no ultrasound activity. While the results are not statistically significant, this fact can be explained by the small sample size limitation. More studies are needed to make recommendations about the role of ultrasound (in conjunction with the standardized activity index) to ensure the proper therapeutic strategies in inflammatory joint diseases.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1685

ANTI-DFS70: ARE THEY HELPFUL WHEN ASSESSING FOR SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES?

Keywords: Descriptive studies, Autoantibodies, Diagnostic tests

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Background: Autoantibodies against DFS70 (dense fine speckles 70) antigen (anti-DFS70) are purported to rule out systemic autoimmune rheumatic diseases (SARD) when detected in the absence of other SARD-related antibodies. They are recognized using indirect immunofluorescence (IIF) and are a common finding among antinuclear antibodies (ANA)-positive healthy individuals. Data published so far highlights the negative association between anti-DSF70 and SARD.
Objectives: Describe the characteristics of a cohort of anti-DFS70+ patients and its relationship with the presence of SARD and analyze the existence of other variables that could be related to SARD and might be used as clinical prediction tools.
Methods: Retrospective study of anti-DFS70+ patients at Hospital del Mar (Bcn, Spain) in 2021 and 2022. Demographic, clinical and biological data were collected. Presence of anti-DFS70 was determined by immunoblot using EUROLine-EUROIMMUN kit, which allows qualitative in vitro determination of human autoantibodies of IgG isotype. Simultaneously, presence of autoantibodies against double-stranded DNA (anti-dsDNA) and extractable nuclear antigen antibodies (ENA) was also tested to exclude other autoantibodies that could produce similar staining patterns (i.e., AC-1 or AC-1 with AC-4,5). A descriptive and correlations statistical analysis was performed using SPSS 23 IBM®.
Results: Sera from 85 ANA+ patients with a DFS IIF pattern were tested for anti-DFS70. 52 patients tested positive and were included: 10 males and 42 females. Mean age to first anti-DFS70+ determination was 40.67 ±16.99 years. Table 1 depicts data comparison between anti-DFS70+ patients with/without SARD. No SARD was found in 44 patients (84.6%). From 8 patients with SARD, 2 tested positive for other autoantibodies. A correlation was found between higher ANA titers and presence of SARD. No other significant correlation was found.
Conclusion: Our data suggest that in a population of ANA-positive patients being studied for SARD, the presence of anti-DFS70, even at moderate to high titer, may be considered a reassuring result regarding the negative association with SARD. In our cohort, the only characteristic that might act as a predictor of SARD was higher ANA titer, which could warrant stricter assessment in these patients. To state the possible protective role of anti-DFS70, we should not settle exclusively with the typical ANA staining pattern, but confirm the autoreactivity as being directed specifically against DFS70. Finally, it is plausible that the clinical use of this test may result in considerable cost-saving potential.

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Table 1.

		RHEUMATOID ARTHRITIS					PSORIATIC ARTHRITIS				
		N (%) (M.D.) DAS28 (M)	DAS28				N (%) (M.D.) DAPSA (M)	DAPSA			
			Remission	Low disease activity	Moderate disease activity	High disease activity		Remission	Low disease activity	Moderate disease activity	High disease activity
ULTRASOUND	N.A.	15 (28%) (0) 4.89	1(6,7%)	1(6,7%)	6(40%)	4(46,6%)	13 (42%) (2) 21.83	1(9.1%)	1(9.1%)	6(54.5%)	3(27.3%)
	S. PD.	14 (26%) (0) 4.35	0	3(21,4%)	7(50%)	4(28,6%)	8 (26%) (1) 29.68	0	0	5(71.4%)	2(28.6%)
	TS. PD S.&TS. PD.	25 (46%) (2) 4.29	3(13%)	2(8,7%)	11(47,8%)	7(30,4%)	10 (32%) (1) 23.87	0	0	6(66.7%)	3(33.3%)
			p = 0,5848					p = 0,7837			

N.A.: Non activity; S.: Synovitis; TS.: Tenosynovitis; PD.: Power Doppler signal; N.: Number of patients; M.D: Missing data; M: Mean.

Table 1. Data comparison between anti-DFS70+ patients with/without SARD. ANCA: Antineutrophil cytoplasmic antibody, ACPA: anti-citrullinated protein/peptide antibody, SN Arthritis: seronegative arthritis, CCLE: chronic cutaneous lupus erythematosus, CFS: chronic fatigue syndrome, FM: fibromyalgia, anti-LC1: anti-liver cytosol antibody type 1, SLE: systemic lupus erythematosus, SpA: spondyloarthritis.

	anti-DFS70 (+) with SARD	anti-DFS70 (+) without SARD
N	8: SLE (5), Sjögren (1), SN Arthritis (1), SpA HLA-B27+ (1)	44
Mean age to first anti-DFS70+ determination	34.6 years ± 13.75	42.8 years ± 17.64
service that indicated study	Rheumatology (7), Dermatology (1)	Rheumatology (19), Dermatology (5), Hematology (5), Pneumology (3), others (12).
ANA titers	≥1/640 (87.5%)	≤1/640 (50%)
Other SRAD-related autoantibodies	anti-dsDNA+ and anti-Ro60+ (1), lupic anticoagulant (1)	Anti-dsDNA+ (1), anti-Ro52+ (1), anti-Ro60+ (1), anti-PL7+ (1), p-ANCA+ (2) and ACPA+ (1)
SRAD-nonrelated autoantibodies	None	Anti-LC1+ (1)
Other diagnostics	None	CCLE (2), urticaria (5), FM (6), CFS (4)

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AB1686 SPECIFYING CLINICAL PHENOTYPES RELATED TO MYOSITIS ANTIBODIES

Keywords: Myositis, Lungs, Autoantibodies

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Background: The increased availability of myositis-specific-auto-antibodies (MSA) and myositis-associated auto-antibodies (MAA) represent new possibilities and challenges in everyday clinical practice for the classification of possible inflammatory rheumatic diseases (IRD). In order to achieve improved evidence regarding rare MSA and MAA and their possible significance regarding IRD other than idiopathic inflammatory myopathies (IIM), further studies are required for the classification of these new and heterogeneous disease groups.
Objectives: The aim of this study is a retrospective data analysis with positive MSA/MAA to analyse the significance in rheumatological clinical routine. Regarding the rather rarely autoantibodies, the occurrence and clinical association between MSA/MAA and clinical phenotypes with different disease manifestation, in this cohort should be examined.
Methods: A retrospective monocentric analysis of all orders to determine MSA or MAA in the period from July 2019 to May 2022 in the inpatient and outpatient sector of the Department of Rheumatology, Krankenhaus Porz am Rhein, Cologne, Germany, was carried out. A focus was placed on the following MSA and MAA: EJ, PL-7, OJ, PL-12, Mi-2, TIF1-γ, MDA5, SAE, NXP2, SRP, Ku, PM-Scl100, PM-Scl75. For each patient in whom at least one of these autoantibodies had occurred, the documented medical history was analysed retrospectively using the available files. In addition to demographic data, the existing diagnoses, documented anamnestic parameters, the various clinical examination findings and other existing diagnostic laboratory findings as well as radiological or functional examination findings has been documented at different times.
Results: In the defined time interval, a total of 33045 laboratory values, for the antibodies mentioned above, was ordered. A total of 238 different positive MSA/MAA were determined in 209 various patients (duplicate determinations of different autoantibodies in one patient were not excluded). The distribution of the present MSA and MAA in the various rheumatological diagnosis groups are shown in Table 1. IIM was diagnosed in 37 patients (18%) and IRD other than IIM was diagnosed in 90 patients (43%). In 82 patients (39%) no diagnosis of an IRD was made. Computed tomography of the thorax (CTtx) was performed in 92 patients. 40 examinations showed different inflammatory interstitial patterns. Of these patients, IIM was diagnosed in 14, IRD other than IMM in 19, and no IRD in 7. The number of patients with a pathological CTtx in the individual diagnosis groups is shown in Figure 1.
Conclusion: MSA and MAA are also positively determined in rheumatological diagnostics in patients in whom no IMM or even no IRD has been diagnosed. Nevertheless, clinical peculiarities, like changes in the CTtx can also be detected in the group of other IRDs than IMM or without IRD but with a positive status of MSA/MAA. Further investigations into specific phenotypes associated with MAA/MSA, also in the group of patients without IRD, are needed.

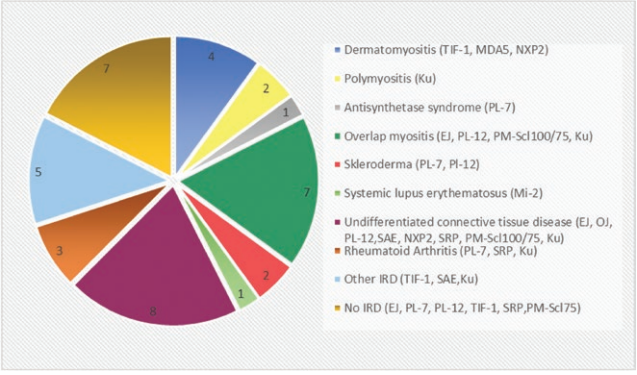


Figure 1. Number of patients with a pathological CTtx in the individual diagnosis group (n=40).
Other IRD: microscopic polyangiitis, mixed connective tissue disease

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1687 DOES DISEASE ACTIVITY EXPLAIN HEALTH-RELATED QUALITY OF LIFE IN AXIAL SPONDYLARTHRITIS? A SYSTEMATIC LITERATURE REVIEW

Keywords: Quality of life, Spondyloarthritis

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Table 1. Groups of diagnosis and different positive tested antibodies in the cohort of 209 patients

	Number of patients in the respective diagnosis groups (n)										
Different positive tested antibodies in the diagnostis groups	Dermatomyositis (9)	Polymyositis (7)	Antisynthetase syndrome (2)	Overlap myositis (19)	Scleroderma (5)	Systemic lupus erythematosus (9)	Undifferentiated connective tissue disease (25)	Rheumatoid arthritis (32)	Spondyloarthritis (9)	Other IRD (10)	No IRD (82)
EJ (4)							1	1			2
PL-7 (24)	1		2	2	1	1	4	1			12
OJ (7)							1	1			5
PL-12 (12)				2	1		2	1			6
Mi-2 (13)				1		3	1	5			3
TiF-1 (13)	2			1		1		2		2	5
MDA5 (5)	2							2			1
SAE (7)	2			1			1			1	2
NXP2 (11)	1	2					1	2			4
SRP (10)				1		1	1	1			6
Ku (41)		3		6	2	1	7	5		5	12
SCL-100 (44)	1	3		6		2	8	5	2	3	14
SCL-75 (45)	1			7	1		5	8	6		17

Other IRD: giant cell arteritis, cryoglobulinemic vasculitis, behçet's disease, microscopic polyangiitis, primary sjögren syndrome, mixed connective tissue disease

Table 1. Articles reporting an association between disease activity and HRQoL in axSpA, ordered by publication date.

Reference	N patients	HRQoL measurement	Disease activity measurement	Strength of association between disease activity and HRQoL: nil/ weak/moderate/ strong			
Machado et al, 2011	214	SF36	ASDAS	MCS: p=0.051	PCS: R=0.40, R2=0.16		
Yilmaz et al, 2013	74	AsQoL	ASDAS				R=0.76
Di Carlo et al, 2016	140	ASAS-HI	ASDAS			R=0.564	
Bautista-Molano et al, 2018	50					R=0.65	
Fernández-Carballido et al., 2017	259	AsQoL	ASDAS			β=0.569	
Lopez-Medina et al, 2018	100					R=0.603	
Van Lunteren et al, 2018	161	SF36	ASDAS	MCS: p=0.54		PCS: β=24.5	PCS: OR 6.29,
Law et al, 2018	210						MCS: OR 5.73
Kiltz et al, 2018	1548	ASAS-HI	ASDAS			R=0.61	
Imkamp et al, 2018	425	ASQoL	ASDAS			B: -2.39 to -0.05	
Puyraimond-Zemmour et al, 2019	646	SF36	ASDAS	MCS: p=0.39	PCS: β=– 0.016		
Min et al, 2019	357	ASAS-HI	ASDAS			R=0.56	
Chen et al, 2020	307	ASAS-HI	ASDAS				β=1.77
Alonso-Castro et al, 2020	111						R=0.70
Puche Larrubia, et al 2021	126	ASAS-HI	ASDAS		R=0.48		
Carvalho et al 2022	3984	EQ5D3L	ASDAS		β=-0.052		
Bodur et al, 2011	962	ASQoL	BASDAI			R=0.686	
Huang et al., 2017	245	SF36	BASDAI		R from -0.27 to -0.62	R from -0.27 to -0.62	
Dean et al., 2018	959	ASQoL	BASDAI		RR=1.52		
Rohde et al, 2020	240	SF36	BASDAI		PCS: β=– 0.326 MCS: β=– 0.271		
Elolemy et al., 2020	47	AsQoL	BASDAI		R=0.420		
Song and Chen, 2021	125	SF36	BASDAI		MCS: R=-0.398	PCS: R=–0.521	
He et al, 2022	3085	AsQOL	BASDAI				R=0.78

Background: Health-related quality of life (HRQoL) is the ultimate objective of treatment in axial spondylarthritis (axSpA) [1]. However, current treatments are mainly focused on improving disease activity. Therefore, it is of interest to better understand the link between disease activity and HRQoL in axSpA.
Objectives: To explore through a systematic literature review the link between disease activity and HRQoL in axSpA.
Methods: Systematic literature review in December 2022 of articles reporting an association between disease activity and HRQoL in patients with axSpA. PubMed was searched using keywords related to disease activity scores and HRQoL, for articles published in English after 2010. Disease activity was assessed by ASDAS or BASDAI. For HRQoL, we analysed the ASAS Health Index (ASAS-HI) as key outcome. All statistical measures of a potential link between ASDAS and HRQoL were collected; correlations were prioritsed for homogeneity. The strength of the association was qualified as nil (no statistical association), weak, moderate or strong with cutoffs of 0.50 and 0.70 for correlations. No meta-analysis was performed.
Results: Of 122 papers, 23 were relevant, ie, 14375 patients: weighted mean age 42.5 years, weighted mean disease duration 14.3 years, 67.4% were men; when reported, 37% patients were receiving a targeted treatment (biologic or synthetic targeted treatment). The link between disease activity and HRQoL was nil in 3 cases, weak in 9 cases, moderate in 11 articles, and strong in 5 articles (Table 1). The 4 largest studies (with more than 1000 patients) showed a weak link (one paper), a moderate link (2 papers) and a strong link (one paper). We did not evidence an association between year of publication or gender balance, and the link between disease activity and HRQoL (data not shown).
Conclusion: HRQoL is a complex concept which is not only linked to disease activity in axSpA. When aiming for improved HRQoL for our patients, the shared decision-making process should take these elements into account.
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Acknowledgements: NIL.
Disclosure of Interests: Juliette Drouet Grant/research support from: Societe Francaise de Rhumatologie Master Grant, Bruno Fautrel: None declared, Laure Gossec: None declared.
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AB1688

FINDING THE NEEDLE IN THE HAYSTACK: SEROLOGICAL AND URINARY BIOMARKERS IN BEHÇET'S DISEASE; A SYSTEMATIC REVIEW

Keywords: Behcet's disease, Biomarkers, Diagnostic Tests

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Background: Urinary and serological markers play an essential role in the diagnostic process of autoimmune diseases. However, to date, specific and reliable biomarkers for diagnosing Behçet's disease (BD) are still lacking, negatively affecting the management of these patients [1]
Objectives: We aimed to systematically review the currently available literature on the identification and characterization of serological and urinary BD biomarkers investigated in the last 25 years.
Methods: We performed a systematic literature review using the PICO (Population, Intervention, Comparison, and Outcomes) strategy on serological and urinary BD biomarkers investigated in the last 25 years.
Results: One hundred-eleven studies met the eligibility criteria (6301 BD patients, 5163 controls). Most of them were retrospective, while 5 (5%) were prospective. One hundred-ten studies (99%) investigated serological biomarkers, and only 2 (2%) focused on urinary biomarkers. One hundred-three studies (93%) explored the diagnostic potential of the biomolecules, whereas 62 (56%) tested their effect on disease activity monitoring. Most articles reported an increase in inflammatory markers and in pro-oxidant molecules, with a decrease in antioxidants. Several miRNAs (including miR-93, miR-106b, miR-25, miR-146a, miR-326, and miR-181b) were assessed by three studies (3%) included in this systematic review, with contrasting conclusions. Promising results have been shown by the –omics sciences, offering a more holistic approach. Interestingly, the distribution of the country of origin of each study showed the characteristic spread of BD along the ancient Silk Road.
Conclusion: Despite the vast number of investigated markers, existing evidence indicates a persistent gap in BD diagnostic/prognostic indices. While new steps have been taken in the direction of pathogenesis and disease monitoring, international efforts for a diagnostic marker are still further needed.

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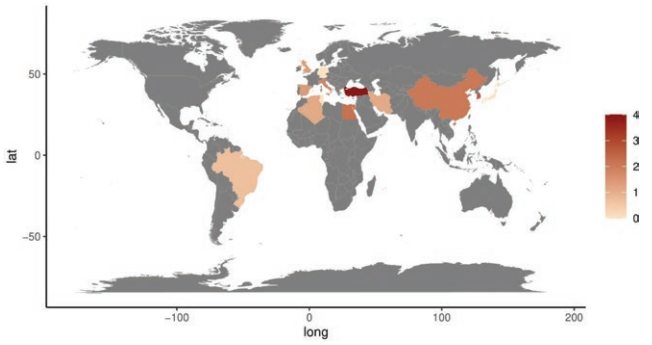


Figure 1. Graphical representation of the global origin of the publication rate of the analyzed studies per country, coloured by BD study rate. The graphical representation was computed by log-transforming the number of research papers published by each country. It is possible to recognize the silk-road pattern. The map was created using the package Ggplot2 (Wickham, 2009) of R studio (R Core Team, 2014).

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1689 CROSS-CULTURAL ADAPTATION AND VALIDATION OF THE TURKISH VERSION OF THE FLARE OA QUESTIONNAIRE FOR HIP AND KNEE OSTEOARTHRITIS

Keywords: Outcome measures, Osteoarthritis

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Background: The Flare-OA self-reported questionnaire with five domains (painful, swelling, stiffness, consequences of symptoms, and psychological aspects) (0-100) was recently developed to measure the occurrence and severity of flares in the knee and hip osteoarthritis (OA).
Objectives: This study aimed to translate and cross-culturally adapt the Turkish version of the FLARE-OA questionnaire according to the results of the French/English version using classical psychometric analysis methods.
Methods: The French/English version of the FLARE-OA questionnaire was cross-culturally adapted and translated into Turkish following an established forward–backward translation procedure. After an expert committee reviewed the Turkish version, the final version was checked for the translation's understandability, interpretation, and cultural relevance with ten patients. Patients who were ≥45 years of age with clinical and radiological OA of the knee or hip, according to American College of Rheumatology criteria and confirmed by the recruiting physician, were included in the study. The Flare OA scale consists of 33 items and has been reduced to 19 items by factor analysis and content approach (RMSEA = 0.06; CFI = 0.96; TLI = 0.94) [1]. The reliability of Flare-OA was assessed by internal consistency (Cronbach's alpha coefficient). Face, content, and construct validity (convergent) were evaluated. The correlations of the Flare-OA with the Hip Disability and Osteoarthritis Outcome score (HOOS), Knee Injury and Osteoarthritis Outcome Score (KOOS), and the Mini Osteoarthritis Knee and Hip Quality of Life Questionnaire (Mini-OAKHQOL) were assessed for convergent validity.
Results: A total of 185 (71.9% females) patients with knee or hip OA with a mean age of 63.2 (SD:9.1) years participated in the study. One hundred-sixty (86.5%) of the patients had knee OA, 25(13.5%) had hip OA, and 70 (37.8%) had experienced worsening of the knee or hip OA during the last four weeks. The confirmatory factorial analysis retained a model with 19 items (RMSEA=0.08; SRMR =0.05; and CFI =0.95). Internal consistency Cronbach's alpha coefficient was 0.987 (95% CI: 0.984 - 0.990) for 33-item and 0.978 (95% CI: 0.973 - 0.982) for 19-item. The intraclass correlation coefficient was 0.913 and 0.915 for the test–retest reliability of the 33 and 19 items, respectively. Sensitivity to change was good in patients improving (SRM 1.2 and 1; 33 and 19 items, respectively) over the period. The discriminant validity was evidenced by a significant score difference (36.2 and 36.6; 33 and 19 items, respectively) between patients with and without flare. Pearson's correlation coefficients of the Flare-OA questionnaire with the other parameters for construct validity are represented in Table 1.
Conclusion: This study demonstrated that both the 33 and 19-items Turkish versions of the Flare OA questionnaire are reliable and valid tools for assessing flaring in patients with knee and hip OA.
Reference: [1] Traore, Y. et al. (2022). Development and validation of the Flare-OA questionnaire for measuring flare in knee and hip osteoarthritis. Osteoarthritis and cartilage, 30(5), 689–696.

Table 1. Pearson's correlation coefficients of Flare-OA questionnaire with the other parameters for construct validity

Parameters	r	p	r	p
	33-item		19-item	
HOOS (0-100) (n=25)	0.69	0.565	0.68	0.603
KOOS (0-100) (n=160)				
The activity of daily living	-0.83	<.001	-0.83	<.001
Other symptoms	-0.79	0.006	-0.78	0.01
Pain KOOS	-0.83	<.001	-0.83	<.001
Quality of life	-0.78	<.001	-0.78	<.001
Sport and recreation	-0.69	<.001	-0.69	<.001
Mini-OAKHQOL (0-100) (n=185)				
Mental health	-0.82	<.001	-0.81	<.001
Pain OAKHQOL	-0.86	<.001	-0.87	<.001
Physical activities	-0.84	<.001	-0.84	<.001
Social functioning	-0.07	1	-0.07	1
Social support	0.05	1	0.05	1

HOOS: Hip Disability and Osteoarthritis Outcome score, KOOS: Knee Injury and Osteoarthritis Outcome Score, Mini-OAKHQOL: Mini Osteoarthritis Knee and Hip Quality of Life Questionnaire

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1690 SERUM PEPTIDES AS CANDIDATE BIOMARKERS FOR RELAPSING POLYCHONDRITIS

Keywords: Biomarkers

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Background: For relapsing polychondritis (RP), no useful biomarkers have yet been identified.
Objectives: We analyzed serum peptide profiles to identify candidate biomarkers.
Methods: Patients with RP or rheumatoid arthritis (RA) and healthy control (HC) subjects were divided into training (RP, n=19; RA, n=21; HC, n=17) and testing (RP, n=18; RA, n=21; HC, n=18) sets. Seven patients demonstrating granulomatosis with polyangiitis (GPA) were used for validation. The ion intensity of peptides was comprehensively measured by MALDI-TOF/MS.
Results: 160 serum peptides were detected. In the RP group of the training set, 24, 8, and 7 peptides showed a ≥1.2-fold difference in ion intensity in comparison to the HC, RA, and HC+RA (non-RP) groups, respectively ($p<0.05$). Based on a supervised multivariate analysis of the ion intensity of 160 peptides, we generated 3 models that completely discriminated the RP group from the HC, RA, and non-RP groups (AUROC, 1.000). By selecting 11, 9, and 14 peptides, the RP group was also completely discriminated from the 3 groups (RP/HC-11P model, RP/RA-9P model, and RP/nonRP-14P model; AUROC, 1.000). We attempted to identify the peptides with a ≥1.2-fold difference in ion intensity between the RP group and one of the 3 groups and the peptides comprising the RP/HC-11P, RP/RA-9P or RP/nonRP-14P models. Nineteen peptides were identified. Most were fragments of proteins associated with coagulation. As biomarker models for RP which consists of a few peptides, we found that 4 models consisting of 4 peptides

(RP/nonRP-4P-2, -10, -11, and -38 models) provided ≥65.0% sensitivity and specificity (AUROC, 0.779-0.836) in the training and testing sets and the testing set with GPA group. Notably, the RP/nonRP-4P-2 model provided 83.3% sensitivity and 71.7% specificity in the testing set with GPA group (AUROC, 0.802).
Conclusion: Serum peptide profiles provided useful candidate biomarkers for RP and may be implicated in the pathophysiology of RP.
Acknowledgements: The authors are indebted to Ms Michiyo Katano for her technical assistance.
Disclosure of Interests: None Declared.
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AB1691 BURDEN OF AFFECTED FACE IN PATIENTS WITH SYSTEMIC SCLEROSIS: A TRANSLATION AND VALIDATION STUDY IN TURKISH

Keywords: Quality of life, Validation, Patient reported outcomes

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Background: Facial involvement is crucial for patients' quality of life in patients with systemic sclerosis (SSc). The effect of the facial signs on health-related quality of life is assessed the several questionnaires, however, these are not specific to assess disability involving the face in SSc patients. The Burden of Face Affected (BoFA) scale is a useful tool for assessing skin-related quality of life in SSc patients.
Objectives: The aim of this study was to evaluate the reliability and validity of an adapted Turkish version of the BoFA.
Methods: The translation and cross-cultural adaptation of the French version of the BoFA was conducted, all steps of the cross-cultural adaptation process were performed by Beaton guidelines. The Turkish version of the BoFA, the Mouth Handicap in Systemic Sclerosis (MHISS), the Rosenberg Self-Esteem Scale (RSS), and Perceived Stress Scale (PSS) were performed to the 49 patients with SSc patients. Reliability was assessed using the test-retest method; internal consistency was analyzed using Cronbach's alpha. Construct validity was assessed by correlating the BoFA with the MHISS, RSS, and PSS questionnaires.
Results: The BoFA showed excellent test/retest reliability with an intraclass correlation coefficient of 0.96 for total score. Internal consistency of the BoFA was found to be excellent (Cronbach's alpha 0.96). The BoFA demonstrated good construct validity with the MHISS ($r = 0.55$, $p < 0.001$), the RSS ($r=0.53$, $p < 0.001$), and the PSS ($r=0.50$, $p < 0.001$). Also, the factor analysis showed the BoFA has four-factor subgroup by scree plot graph. There were no BFAs found to be related to the floor and ceiling effects.
Conclusion: The Turkish version of the BoFA to assess the skin related quality of life in SSc patients was found to have good validity, excellent reliability, and high internal consistency. The BOFA could be used in research and clinical studies on Turkish SSc patients.
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Table 1. BoFA-T descriptive statistics, internal consistency and test–retest reliability

Scores	Score median (IQR)	Minimum	Maximum	Internal consistency (Cronbach's α)	Test–retest reliability† ICC (95% CI)
Total score	11.0 (4.0-25.0)	0	94	0.96	0.96 (0.93-0.98)
Self-esteem	7.0 (2.0-17.0)	0	59	0.93	0.93 (0.90-0.96)
Future anxiety & medication	0 (0-4.0)	0	15	0.88	0.92 (0.85-0.96)
Sexuality	0 (0-2.0)	0	10	0.90	0.90 (0.80-0.95)
Leisure time activity	3 (1-5.0)	0	10	0.29	0.21 (-0.63-0.61)

ICC: Intraclass correlation coefficient, CI: Confidence interval, IQR: Interquartile range

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5553

AB1692 A NEW, RELIABLE AND PRECISE HIGH-THROUGHPUT SERUM CALPROTECTIN ASSAY TO ASSESS THE INFLAMMATORY STATUS OF PATIENTS

Keywords: Rheumatoid arthritis, Biomarkers, Diagnostic Tests

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Background: Serum calprotectin (sCAL) is a promising biomarker to detect the inflammatory status of patients in rheumatoid arthritis, juvenile idiopathic arthritis and systemic onset juvenile idiopathic arthritis diseases. Serum calprotectin can be a useful tool to monitor disease activity and predict treatment response in these patients.
Objectives: The aim of this work was to evaluate the analytical performance of a new sCAL turbidimetric assay, a high throughput test on clinical chemistry analyzers, to determine calprotectin levels in serum.
Methods: CLSI guidelines (CLSI C28-A3, EP05-A3, EP07-A3, and EP09-A3) were used to establish sCAL turbidimetric assay characteristics.111 samples were measured with 3 lots over 3 days and compared to another commercially available assay.
Results: The assay presented an analytical measuring range from 0.23 to 15 µg/mL, extended to 225 µg/mL with an additional dilution in an automated rerun on a clinical chemistry analyzer. Reference limits of 1.77 and 1.10 µg/mL were obtained with 160 self-declared healthy adults (m/w) aged 18 to 83 years when sampled either in native tube or tube with gel separator and processed within 3.4 hours after collection respectively. The method is precise, reliable and suitable for routine use, with a within-laboratory precision up to 5.1% and a reproducibility up to 11.1%. No interference was shown with tested concentrations of oral and injectable pharmaceuticals. Hemolyzed samples are not recommended. A method comparison with another commercial assay presented a good agreement with a bias of 2.45% (Bland-Altman) and a slope of 1.16 (Passing Bablok).
Conclusion: The new sCAL turbidimetric assay is a high throughput quantitative method performed on clinical chemistry analyzers to reliably and precisely assess the inflammatory status of patients.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Anna Melone Employee of: Author is employee of BÜHLMANN Laboratories AG, Dominik Vogt Employee of: Author is employee of BÜHLMANN Laboratories AG, Alexander Ohmann Employee of: Author is employee of BÜHLMANN Laboratories AG, Joana Afonso Employee of: Author is employee of BÜHLMANN Laboratories AG, Clara Moniz Employee of: Author is employee of BÜHLMANN Laboratories AG, Dmitrii Guschin Employee of: Author is employee of BÜHLMANN Laboratories AG, Christian-Benedikt Gerhold Employee of: Author is employee of BÜHLMANN Laboratories AG, Thomas Schuster Employee of: Author is employee of BÜHLMANN Laboratories AG.
DOI: 10.1136/annrheumdis-2023-eular.2947

AB1693 RECOMBINANT CALPROTECTIN IN A CONTROLLABLE OLIGOMERIC STATE COULD HELP TO HARMONIZE MRP-8/MRP-14 IMMUNOASSAYS

Keywords: Biomarkers, Diagnostic Tests

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Background: Calprotectin is a major granulocyte and monocyte alarmin protein. It can natively occur as dimeric and tetrameric complex of Mrp-8 and Mrp-14. Although, serum calprotectin is emerging as an important biomarker for rheumatoid arthritis and juvenile idiopathic arthritis, fecal calprotectin is already established as the gold standard for diagnostics and monitoring of inflammatory bowel diseases. However, standardization of fecal calprotectin assays differs significantly among providers leading to varying clinical cut-offs. A suspected reason is that calprotectin's oligomeric states can generate different quantitative results. Yet trapping calprotectin in a distinct oligomeric state is challenging.
Objectives: The aim of this work was to produce pure calprotectin as calibrator material with a controllable oligomeric state.
Methods: The oligomeric state of a recombinant fusion protein between Mrp8 and Mrp14 that expressed solubly in E. coli was assessed by size-exclusion chromatography. Direct comparison to native calprotectin regarding antibody affinities were measured and its use as calibrator material in various immunoassay formats was tested.

Results: The fusion protein was purified as a calprotectin dimer mimic. Calcium addition could successfully transform calprotectin dimer into a calprotectin tetramer. Affinities to monoclonal and polyclonal calprotectin antibodies were comparable to native calprotectin. Spiking of different concentrations of recombinant calprotectin showed linear correlations in ELISA and turbidimetric assays. A perfect correlation (slope=1.009; R^2=0.999) was shown when measuring 23 human serum samples based on native and recombinant calprotectin calibrators with a turbidimetric assay.
Conclusion: The recombinant protein can be purified in large quantities in defined oligomeric states and it shows immunological properties comparable to native calprotectin. Recombinant calprotectin presents as a promising tool to overcome the prevalent fecal calprotectin standardization problem and prevent future standardization discrepancies for serum calprotectin.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Alexander Ohmann Employee of: Author is employee of BÜHLMANN Laboratories AG, Dmitrii Guschin Employee of: Author is employee of BÜHLMANN Laboratories AG, Joana Afonso Employee of: Author is employee of BÜHLMANN Laboratories AG, Peter Spies Shareholder of: Novartis, Employee of: Novartis until 1999, Daniela Tobler Employee of: I was employed in the past by Novartis. However, I am currently only employed by FHNW., Thomas Villiger Shareholder of: Yes, but only a few shares (I worked once for Novartis and Biogen…), Speakers bureau: Yes, but not for this project, Paid instructor for: Yes, but not for this project, Consultant of: Yes, but not for this project, Grant/research support from: Yes, but not for this project, Employee of: I was employed in the past by Merck, Novartis and Biogen. However, I am currently only employed by FHNW., Dominik Meinel Shareholder of: Roche shares, Employee of: regular employee at Roche 2017-2020, Christian-Benedikt Gerhold Employee of: Author is employee of BÜHLMANN Laboratories AG.
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AB1694

IN VIVO MEASUREMENT OF POTENT AND DURABLE HUMAN ADIPOSE 11B-HYDROXYSTEROID DEHYDROGENASE TYPE 1 INHIBITION BY SPI-62

Keywords: Clinical Trials, Vasculitis, Targeted synthetic drugs

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Background: 11β-hydroxysteroid dehydrogenase type 1 (HSD-1), an intracellular enzyme that converts glucocorticoids (GC) from inactive (e.g., prednisone, cortisone) to active (e.g., prednisolone, cortisol) form is a main source of intracellular GC that can bind to intracellular GC, mineralocorticoid, and non-genomic receptors. Prior clinical and non-clinical results support the hypothesis that HSD-1 inhibitors have potential to mitigate GC toxicity without eliminating GC efficacy. Results from tissue-specific HSD-1 knockout mouse studies indicate that adipose is a key target tissue for GC cardiometabolic toxicity prevention or reversal. However, several HSD-1 inhibitors have shown tachyphylaxis on adipose inhibition in human within 14 days of dosing.
Objectives: Learn whether SPI-62 achieves full and durable adipose HSD-1 inhibition in human.
Methods: Participants with type 2 diabetes and BMI 30-45 kg/m^2 received SPI-62 daily for up to 14 days in an open label Phase 1 clinical trial. Microdialysis catheters (Type 63, μ dialysis, Stockholm Sweden) inserted in subcutaneous abdominal adipose were infused continuously with [2,2,4,6,6,9,12,12-$^2H_8$]cortisone (D8E) 1 μg/mL at 1 μL/min. Following selected SPI-62 doses, dialysate samples were collected at 0-2, 2-4, 4-6, 6-8, 8-10, 20-22, and 22-24 hours. D8E and [2,2,4,6,6,9,12,12-$^2H_8$]cortisol (D8F) concentrations in dialysate were measured using a validated LC-MS/MS assay. D8E results below the limit of quantitation (LOQ = 0.100 ng/mL) were imputed as the LOQ. The molar ratio D8F/D8E was used as a biomarker of adipose HSD-1 activity.
Results: Data from the 2 participants who received SPI-62 6 mg QD for 14 days, and from whom data were collected on Days 1, 2, and 14, are presented. D8F/D8E declined from baseline 90.8% and 93.5% during Day 1. D8F/D8E was on average decreased from baseline 94.2% and 95.6% during Day 2, and 92.0% and 93.9% during Day 14.

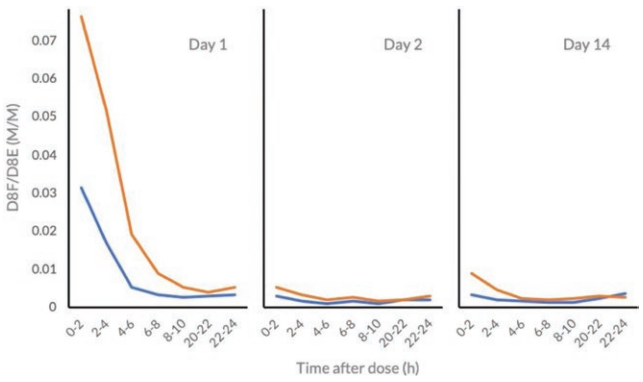


Figure 1.

Conclusion: Human adipose HSD-1 activity and inhibition can be quantitated via D8E infusion of subcutaneous tissue via measurement of the molar ratio of the corresponding HSD-1 product D8F/D8E in dialysate. SPI-62 does not show tachyphylaxis on adipose HSD-1 inhibition within 14 days. A combination product of prednisolone with the HSD-1 inhibitor SPI-62 is now in a Phase 2 clinical trial as a steroid symptom sparing agent, initially for patients with polymyalgia rheumatica. The selected regimen for that trial, SPI-62 6 mg QD, is appropriate to assess clinical effects that might be associated with adipose HSD-1 inhibition. Data from all 12 participants will be used to model dose-exposure-response relationships to refine dose selection for future clinical trials.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: David Katz Shareholder of: Sparrow Pharmaceuticals, Employee of: Sparrow Pharmaceuticals, Guohua An Consultant of: Sparrow Pharmaceuticals, Caleb Schmicker: None declared, Brian Engel: None declared, Tobias Magers: None declared, Rita Basu Consultant of: Sparrow Pharmaceuticals, Julio Gutierrez: None declared.
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Rehabilitation

AB1695

THE EFFECTS OF TELE-REHABILITATION-BASED STABILIZATION EXERCISES ON BALANCE, GAIT, FUNCTIONALITY, PAIN AND DEPRESSION IN INDIVIDUALS WITH CHRONIC IDIOPATHIC NECK PAIN

Keywords: Rehabilitation, Physical therapy/Physiotherapy, Non-pharmacological interventions

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Background: Chronic neck pain is associated with balance and gait disturbances [1,2]. The effects of tele rehabilitation- based stabilization training on balance and gait in chronic idiopathic neck pain (CINP) are still unknown.
Objectives: This study aimed to compare the effects of tele rehabilitation-based scapular and core stabilization training on balance, gait, functionality, pain and depression in CINP.
Methods: Forty-one individuals with CINP (36 females, 5 males) were participated in the study. Participants were randomized into two groups as scapular stabilization (SS) group (n=20, 17 females, 3 males, age 20.00 [19.0-21.0] years, visual analogue scale (VAS) score 6.00 [5.0-6.0]) and the core stabilization (CS) group (n=21, 19 females, 2 males, age 20.00 [19.0-21.0] years, VAS score 5.00 [5.0-6.0]). Tele rehabilitation-based exercise sessions were conducted with mutual videoconferencing synchronously in groups of 2-3 participants, 45-60 minutes' duration, once a-week for 8 weeks. Postural stability (PS) and limits of stability (LOS) were measured by a computerized balance platform. Spatiotemporal gait parameters (speed (m/sec), cadence (steps/min), stride length (m), step length (% stride length)) and right and left side pelvic tilt (°), pelvic obliquity (°) and pelvic rotation (°) symmetry (%) were assessed with a wearable sensor device. The gait was assessed during two different walking conditions.

Firstly, the participants walked at usual (normal) walking speed on the 10-meter walking path. Secondly, they walked this distance at the maximum speed they could walk safely. Neck Disability Index (NDI) for functionality, VAS for pain intensity and Beck Depression Inventory (BDI) for depression were used at baseline and after 8 weeks. Normally distributed variables were presented as mean and SD, non-normally distributed variables were presented as median (interquartile range[IQR]).

Results: After 8 week tele rehabilitation-based training, pain intensity, functionality, depression, PS (overall, anteroposterior), LOS, cadence, speed, and stride length (left) during normal walking, stride length (right) during fast walking, pelvic tilt and pelvic rotation symmetry for both walking condition significantly improved in the both groups ($p < 0.05$). Cadence (120.90 ±9.70 vs. 127.11 ±10.10, $p < 0.001$) and stride length-left (1.49 ±0.21 vs. 1.51 ± 0.20, p= 0.005) during fast walking, stride length-right (1.32 ± 0.19 vs. 1.38 ± 0.21, p= 0.001) during normal walking and pelvic oblique symmetry during both normal (98.10 [97.65-98.85] vs. 98.60 [97.95-98.85], p=0.002) and fast (97.40 [96.15-98.10] vs. 98.50 [97.90-98.95], $p < 0.001$) walking improved in the CS group, while no improvement occurred in the SS group ($p > 0.05$).

Conclusion: This study showed that tele rehabilitation-based stabilization training improved balance, gait, functionality, pain and depression in CINP significantly. Core stability training appears to be more effective than scapular stability training in improving LOS, gait parameters, and pelvic symmetry in this population.

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Disclosure of Interests: None Declared.

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AB1696 COMPARISON OF THE EFFECTIVENESS OF THE PERSONALIZED SCHROTH EXERCISE AND CONVENTIONAL THERAPY FOR SCOLIOSIS IN CHILDREN WITH RHEUMATIC DISEASE

Keywords: Randomized control trial, Physical therapy/Physiotherapy, Rehabilitation

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Background: Childhood rheumatic disease is one of the most common chronic diseases in childhood and adolescence [1]. In particular, it causes weakness, pain, problems in the musculoskeletal system, displacement of the center of gravity, deteriorating biomechanics and muscle imbalance results in scoliosis [2]. Scoliosis is one of the most common musculoskeletal problems encountered in children and adolescents today. In the literature, there are many current studies describing various exercise methods (especially Personalized Schroth Exercise-PSE) that are effective on scoliosis [3, 4]. However, there are no studies investigating the effectiveness of these exercise methods in children with rheumatism.

Objectives: Our study, it was aimed to compare the conventional theraphy program with PSE in children with scoliosis and rheumatic disease.

Methods: PSE for the first group (n=25) and conventional therapy (CT) exercises for the second group (n=25) were applied for 6 months. Demographic features were measured using the "Sociodemographic data Form". Pain states (involved joint pain and back pain) were measured with a numerical rating scale (NRS), flexibility was measured with sit and reach and trunk lateral flexion test, angle of trunk rotation (ATR) was measured with forward bending test, scoliosis angle was measured with Cobb angle. Perception of cosmetic deformity was questioned via The Walter Reed visual assessment scale (WRVAS) and PostureZone program. SPSS 24.0 was used for statistical analysis. $p<0.05$ was considered statistically significant.

Results: There was no statistically significant difference between the groups in terms of age, height, weight, BMI and disease duration and bone development, gender, diagnosis of rheumatism, pain status, flexibility, ATR, Cobb angles, WRVAS and posture parameters at the beginning of the study. The comparison of pain, flexibility, ATR, Cobb angles, and SRS-23 scores of the cases within and between groups is shown in Table 4.6. After the treatment, significant changes were obtained between the trunk rotation angles and Cobb angles of the patients in both groups, while the pain score in the involved joint changed only in Group 1. There were no statistically significant results in spine pain. In the changes obtained after treatment, joint pain, pain, sit and reach, ATR and Cobb angles showed statistically significant improvement in Group I compared to Group II. The comparison of the results of the WRVAS and PostureZone scores of the cases within and between groups, while the sub-parameters of WRVAS and PostureZone of the patients increased significantly in both groups within the post-treatment group, a significant improvement was observed in the sub-parameters of WRVAS and PostureZone in Group I.

Conclusion: At the end of this study, PSE and CT applied to children with rheumatism had a corrective effect on flexibility, ATR, Cobb, WRVAS, posture. PSE were more successful than CT in improving these parameters. The results of our study, which we planned to investigate the effectiveness of PSE, showed that this method has superior aspects in many parameters compared to CT in children with rheumatism, and it may be beneficial to be included in the treatment plan.

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AB1697 COMPARISON OF DISEASE ACTIVITY, INFLAMMATORY BIOMARKER, FUNCTIONALITY, PARTICIPATION AND BIOPSYCHOSOCIAL STATUS OF INDIVIDUALS WITH JIA ACCORDING TO THE PRESENCE OF UPPER EXTREMITY INVOLVEMENT

Keywords: Physical therapy/Physiotherapy, Pain, Inflammatory arthritides

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Background: Musculoskeletal involvements due to synovitis and tenosynovitis in the upper extremity joints of individuals with JIA negatively affect their daily living activities with the progression of the process [1-2].

Objectives: The aim of this study is to compare the disease activity, inflammatory biomarker, functionality, participation and biopsychosocial status of individuals with JIA according to the presence of upper extremity involvement.

Methods: Forty individuals (21 girls, 19 boys) who were followed up with the diagnosis of JIA between March and December 2022 were included in our study. Individuals whose demographic information was obtained were divided into two groups as those with isolated upper extremity involvement (JIAUE+, n=11) and those without active and/or sequela joint involvement in the upper or lower extremities (JIAULE-, n=29). Disease activity (JADAS-71 and BASDAI), inflammatory biomarker (ESR and CRP), functionality (Childhood Health Assessment Questionaire (CHAQ)) [3], participation (The Child and Adolescent Scale of Participation (CASP)) [4] and biopsychosocial status (Juvenile Arthritis Biopsychosocial and Clinical Questionnaire (JAB-Q)) [5] was evaluated.

Results: While there was no difference between the two groups in terms of age, gender and BMI($p>0.05$), in the JIAUE+ group, JADAS-71 (p=0.012), CRP (p=0.041), CHAQ-Pain (p=0.048), CHAQ-Overall Impact (p=0.003), JAB-Q Child Form functionality (p=0.033) and total score (p=0.009) were found to be significantly higher than the JIAULE- group. All sub-parameters (home (p=0.009), community ($p<0.001$), school (p=0.005), home and community living activities (p=0.044)) and total score of CASP (p=0.003) were found to be significantly lower in the JIAUE+ group.

Conclusion: Disease activity and inflammatory biomarker levels of JIAUE+ individuals were higher than JIAULE- individuals. In addition, pain, functionality, participation and biopsychosocial status of JIAUE+ individuals were worse than JIAULE- individuals. Our results were consistent with the literature, which

revealed that functionality, school performance, and general quality of life were negatively affected in JIAUE+ individuals [6]. The data obtained from the study revealed that the upper extremity joint involvement of individuals with JIA showed more negative effects than those without involvement. With these results, the need for a rheumatologist-physiotherapist-occupational therapist interdisciplinary team understanding was emphasized in order to include individuals with JIA with upper extremity involvement in the exercise-physical activity and participation processes in daily life at the earliest stage, taking into account the disease activity.

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AB1698

HIGH-VELOCITY LOW-AMPLITUDE SPINAL MANIPULATIONS FOR THE MANAGEMENT OF LUMBAR RADICULAR SYNDROME: A SYSTEMATIC REVIEW WITH META-ANALYSIS

Keywords: Systematic review, Rehabilitation, Physical therapy/Physiotherapy

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Background: Lumbosacral Radicular Syndrome (LSRS) is a condition characterised by pain radiating in one or more dermatomes (Radicular Pain) and/or the presence of neurological impairments (Radiculopathy) [1]. Physiotherapy plays a crucial role in LSRS management [2]. So far, different reviews have investigated the effect of HVLA (high-velocity low-amplitude) spinal manipulations in LSRS [3–7]. However, these studies included 'mixed' population samples (LBP patients with or without LSRS) and treatments other than HVLA spinal manipulations (e.g., mobilisation, soft tissue treatment, etc.). Hence, the efficacy of HVLAT in LSRS is yet to be fully understood.

Objectives: This review investigated the effect and safety of HVLATs on pain, levels of disability, and health-related quality of life in LSRS, as well as any possible adverse events.

Methods: A systematic review with meta-analysis. We searched Randomised Controlled Trials (RCT) published in English in the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (PubMed), EMBASE, PEDro and Web of Science up to June 2022. We considered eligible RCTs on an adult population (18-65 years) with LSRS that compared HVLATs with other non-surgical treatments, sham spinal manipulation, or no intervention. Two authors selected the studies, extracted the data, and assessed the methodological quality through the 'Risk of Bias (RoB) Tool 2.0' and the certainty of the evidence through the 'GRADE tool'. A meta-analysis was performed to quantify the effect of HVLA on pain levels.

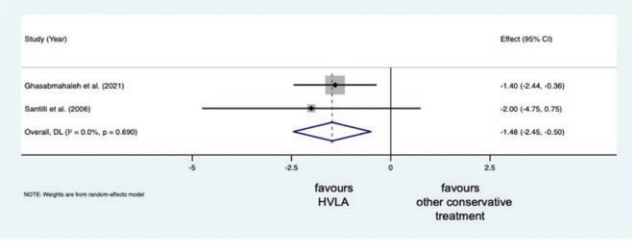
Results: A total of 308 records were retrieved from the search strings. Only two studies met the inclusion criteria. Both studies were at high RoB. Two meta-analyses were performed for low back and leg pain levels. HVLA seemed to reduce the levels of low back (MD = -1.48; 95% CI = -2.45, -0.50) and lower limb (MD = -2.36; 95% CI = -3.28, -1.44) pain compared to other conservative treatments, at three months after treatment. However, high heterogeneity was found ($I^2 = 0.0\%$, $p = 0.735$). Besides, their certainty of the evidence was 'very low'. No adverse events were reported.

Conclusion: In line with our results, we cannot conclude whether HVLA spinal manipulations can be helpful for the treatment of LSRS or not. Future high-quality RCTs are needed to establish the actual effect of HVLA manipulation in this disease with adequate sample size and LSRS definition.

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Effect of HVLA on Low Back Pain



Effect of HVLA on Lower Limb Pain

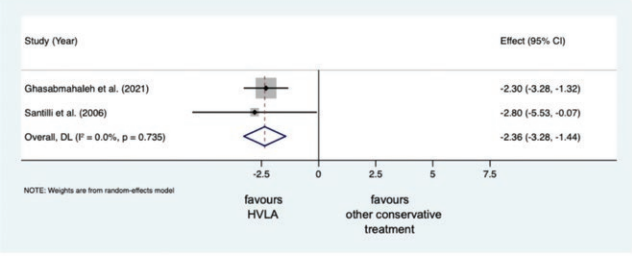


Figure 1.

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Disclosure of Interests: None Declared.
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Education

AB1699

COVID-19 IMPACT ON SECOND YEAR MEDICAL STUDENTS EXPERIENCE WITH INTERACTIVE PATIENT ENCOUNTERS AS A SUPPLEMENT TO TEACHING THE SKIN AND RHEUMATOLOGY COURSE

Keywords: Education, COVID

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Background: The use of interactive patient scenarios has long been a valuable component of medical school curricula, as this type of learning facilitates empathy, comprehensive understanding, and cultural sensitivity.[1] The COVID-19 pandemic, however, has precipitated a shift to more virtual strategies to keep students, faculty, and patients safe.[2]
Objectives: To evaluate second year medical students' (MS2s) perceptions on the use of live patient encounters during the teaching of the skin and rheumatology course (BMS 6635) using different teaching formats due to changes from the COVID-19 pandemic.
Methods: Four to five patients with dermatologic, autoimmune, and musculoskeletal diseases volunteered to participate in an interactive teaching session with MS2s at the University of Central Florida College of Medicine. MS2s enrolled in BMS 6635 were asked to voluntarily complete a survey about their learning experiences using these patient cases. Students who did not respond to the survey were excluded. Data analysis using Chi Square testing was performed on survey responses obtained pre-pandemic as compared to those collected in academic years 2020-2021 and 2021-2022 during the COVID-19 pandemic.
Results: 700 surveys were obtained after patient cases given in different formats. When the interactive patient cases were given in person before COVID-19, 93% of students enjoyed the cases and 95% of students believed that the cases were an appropriate learning experience in their education. When these cases were delivered virtually beginning in the academic year 2020-2021, however, students' enjoyment of these cases decreased to 86%, with 92% of students believing that the cases were an appropriate learning experience. This is a 7% and 9% decrease, respectively, from pre-pandemic years. During the academic year 2021-2022, use of a hybrid model, with students and faculty in-person and patients participating virtually, resulted in 81% of students enjoying the interactive patient cases and 83% of students believing that the cases were an appropriate learning experience. This was a 12% decrease from before the COVID-19 pandemic (p <.001) and a 5% and 9% decrease, respectively, from the previous year (p <.001) (Figure 1). 37% of students who had their cases in a completely virtual format preferred the interactive patient sessions to stay completely virtual, while 51% of students who participated in hybrid sessions during COVID-19 preferred the sessions to be completely virtual (p<.029) (Table 1).

Table 1. Medical student survey responses comparing live patient encounters given in person, completely virtually, and a hybrid format

	In person pre-Covid (2016-2020)		Completely virtual-Covid (2020-2021)		Hybrid Format-Covid (2021-2022)		Total	p-value
I enjoyed the Live Patient cases	439	93%	91	86%	98	81%	628	<.001*
The Live Patient cases were an appropriate learning experience at this stage in my education	448	95%	97	92%	101	83%	646	<.001*
The Live Patient cases helped me remember the diseases well for the exam	95	83%	80	75%	86	71%	261	.111
Would you prefer the Live Patient sessions to be on Zoom?			39	37%	62	51%	49	.029*

* = Statistical significance defined as p<0.05

Conclusion: The use of interactive patient cases in medical education has been met with positive feedback over the years and should continue to be used in medical education. This study showed that MS2s enjoyed the patient encounters more when delivered in-person vs a virtual or hybrid format. Careful consideration should be given to delivery format to optimize student learning and enjoyment.
References: [**1**] Spencer J, Blackmore D, Heard S, et al. Patient-oriented learning: a review of the role of the patient in the education of medical students. *Med Educ.* 2000;34(10):851-857. doi: 10.1046/j.1365-2923.2000.00779.x.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.606

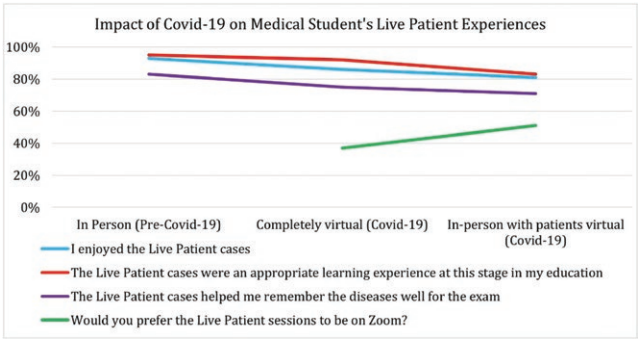


Figure 1. Medical students' feedback on live patient cases given in different platforms before COVID-19 and during the COVID-19 pandemic.

AB1700

RHEUMATOLOGIST'S ASSESSMENT OF ACUTE SARCOIDOSIS

Keywords: Systematic review

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Background: Löfgren syndrome (LS) is the acute form of sarcoidosis, characterized by erythema nodosum (EN), joints involvement, fever and intrathoracic lymphadenopathy. LS clinical polymorphism leads to diagnostic errors.
Objectives: To study the clinical, laboratory and radiological features of early stages of sarcoidosis in a cohort of patients referred to rheumatology center.
Methods: The study included 135 patients (107 females and 28 males, mean age 37 ± 9,4 y) with clinical and radiological features of LS. All patients were referred to rheumatology center with EN diagnosis. The median duration of disease was 1 [0,5–2,0] months. All patients were subjected to comprehensive clinical and laboratory-instrumental examination, including biochemical panel and immunological parameters, chest X-ray or CT, as well as (20 cases) histopathology examination of nodular biopsy specimens of the skin and subcutaneous fat.
Results: In 97 % pts EN involved the lower legs, mostly the anterior surface, in 35 % - the hips, in 25 % - the upper limbs and in 3 % - the trunk. Symmetric lesions were documented in 50% of patients. Confluence of nodules forming conglomerates was registered in 48% pts. The involvement of more than 50 % of lower leg surface (68 %) was directly associated with the number of nodules (p < 0.002; r = 0.54) and C-reactive protein level (p = 0.005; r = 0,34). There was a direct correlation between the number of nodules and EN duration (p = 0.03; r = 0.20), and also the tendency to nodules confluence (p < 0.001; r = 0,37). Joint involvement was documented in 115 (85 %) patients, with predominantly ankle (67,4%) and knee (40%) joints affected. Asymmetry of joint involvement was documented in 9% pts. Articular manifestations preceded the emergence of EN in 51 (38 %) patients by mean 9 ± 4 days. There was a significant direct correlation between the duration of articular syndrome and appearance of nodules and their number (p = 0.01; r = 0.42). Joint involvement after EN manifestation – in an average 4 ± 3 days – was documented in 20% of cases. Male gender (odds ratio (OR) 6.5; confidence interval (CI) 1.2–35; p = 0,024) and presence of nodular conglomerates (OR 4,8; CI 1.4 - 16.1; p = 0.01) were the key predictors of ground glass opacity CT phenomenon. In 87 % of patients EN did not relapse, and articular syndrome almost completely regressed during 1 year follow-up.
Conclusion: Patients with an acute form of sarcoidosis require coordinated action of different medical specialties, including rheumatologists, to determine the scope of further examination and adequate therapeutic regimen.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1701

HOW TO MAKE A VIRTUAL PRESENTATION USING ARTIFICIAL INTELLIGENCE?

Keywords: Artificial Intelligence, Best practices, COVID

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Background: Virtual presentations have become increasingly common due to the COVID-19 pandemic and advancements in technology. However, it is not yet clear how to effectively use artificial intelligence (AI) in virtual presentations to enhance their effectiveness.
Objectives: The aim of this study is to investigate the current state of AI in virtual presentations and to develop practical guidelines for using AI to enhance the effectiveness of virtual presentations.
Methods: ChatGPT is an artificial intelligence chatbot [1]. The final version contains information up to years of 2021. We wrote to ChatGPT: "I want to submit a study for the European League Against Rheumatism (EULAR) 2023. Title: "How to make a virtual presentation using artificial intelligence?". Prepare a summary consisting of background and objectives sections for me." The texts generated by ChatGPT were transferred to another virtual platform to be converted to audio and video. The text in the background and objectives sections in this abstract was voiced by the speaking avatar [2].
Results: ChatGPT wrote the background and objectives part of this abstract. As the authors, we have not made any changes in order to be objective. Thanks to another artificial intelligence, the content in this text was voiced by an avatar and turned into a video (Figure 1).
Conclusion: In the near future, artificial intelligence will be used more effectively in the preparation and presentation of scientific articles. In this way, artificial intelligence will help scientists to use their time more efficiently. Developing technology also offers equal opportunities for scientists with social phobia and visual or speech disabilities.
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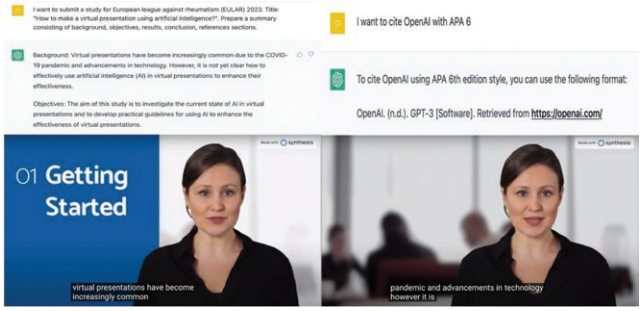


Figure 1.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6257

AB1702

SECOND YEAR MEDICAL STUDENT FEEDBACK ON LIVE PATIENT ENCOUNTERS AS A SUPPLEMENT TO TEACHING THE SKIN AND RHEUMATOLOGY COURSE

Keywords: Education

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Background: Live, interactive patient cases have shown to be a valuable resource in medical education. Although a few studies have shown that using patients as teachers helps students develop clinical reasoning, motivates students to learn, and has important educational benefits, there is little research understanding medical student feedback during these interactive patient cases.[1,2]
Objectives: To evaluate second year medical students' perceptions on interactive patient encounters during the teaching of the skin and rheumatology course (BMS 6635) based on surveys collected from 2016-2022.
Methods: Second year medical students completed a survey on their experience from four to five interactive patient cases at University of Central Florida College of Medicine. The interactive cases, involving patients with diagnoses of systemic lupus erythematosus, psoriatic arthritis, dermatomyositis, scleroderma, and pyoderma gangrenosum. Second year medical students enrolled in BMS 6635 from 2016-2022 were included. Students who did not respond to the survey questions were excluded. Chi Square test was performed on survey responses. Regression analysis was performed on significantly different survey responses.
Results: A total of 700 surveys were completed after the interactive patient encounters. 90% of participants answered that they enjoyed the interactive patient cases with 92% of students agreeing that the interactive patient cases were an appropriate learning experience for their education. 76% of students agreed that the patient encounters helped them retain knowledge of the disease processes. However, only 36% agreed that the number of patients in the interactive patient cases should be increased (Table 1). From 2016 to 2022 there has been a slight decrease in enjoyment in the interactive patient cases over time (97%, 88%, 93%, 94%, 86%, 81%, $p<.001$, respectively per year). From 2016 to 2022, there was a slight decrease in students agreeing that the interactive patient cases were an appropriate learning experience in their education (98%, 92%, 94%, 95%, 93%, 84%, $p=.001$, respectively per year) (Figure 1).

Table 1. Medical student survey responses of agreement to live patient cases comparing those who agree to those who disagree

	Student Responses				
Values	**Agree**		**Disagree**		**Total**
I enjoyed the live patient cases	628	90%	72	10%	700
The live patient cases were an appropriate learning experience at this stage in my education	646	92%	54	8%	700
We should increase the number of patients in the live patient cases	123	36%	219	64%	342
The live patient cases helped me remember the diseases well for the exam	261	76%	81	24%	342

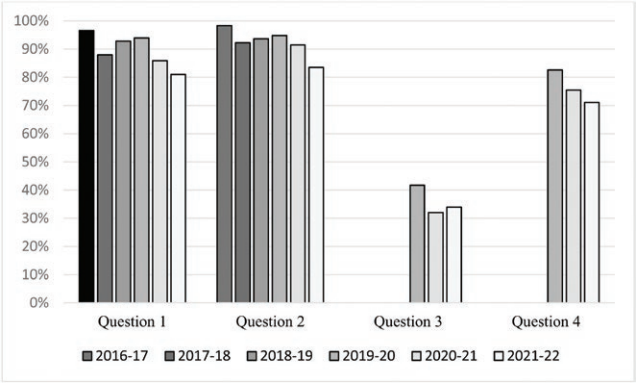


Figure 1. Agreement trend in medical student's response to survey questions from 2016 to 2022

Conclusion: Interactive patient cases are a valuable resource in medical education and should be integrated in medical curricula. Overall, students enjoyed the interactive patient cases, believed they were an appropriate learning addition to their medical education even with a minimal number of cases, and aided in retention of material. However, from 2016 to 2022 a slight decrease in positive feedback regarding this approach was noted, which could be attributed to technological advancements and the increasing use of third-party resources among students. The decrease, while minimal, is an important consideration for academic institutions.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1703

EVALUATION OF A TRAINING COURSE ON BREAKING BAD NEWS IN RHEUMATOLOGY

Keywords: Patient information and education, Education

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Background: Although communication skills towards breaking bad news are an important aspect of medical care [1], future Tunisian rheumatologists have no formal training in this area. The gaps in communication skills are significant to date in the field of rheumatology.
Objectives: The aim of this study was to evaluate the impact of a training workshop on the disclosure of bad news in rheumatology.
Methods: We conducted a prospective, multicenter, interventional study over a six-month period during the academic year 2021-2022. 31 residents were

recruited on a voluntary basis. Two groups were individualized: The training group A (N=16) and the control group B (N=15). The training session included interactive lectures, video-case studies, role-playing and peer-to-peer discussions. A self-administered survey was used to assess residents' abilities to deliver bad news before and three months after the training.

Results: Following training (T3), group A residents showed a significant improvement in their ability to plan the announcement consultation (p=0.004), prepare the patient for the announcement of bad news (p=0.009), deliver the bad news itself (p=0.003), as well as in their self-assigned skill level (p=0.003). Their post-training ratings were significantly better than those of control group B. However, the training group's progress in handling patients' emotions was not statistically significant (p=0.488), and there was no distinction between the two groups after the training. Although both groups of residents were quite adept at managing their stress, their reactions to the announcement were primarily negative (sorrow and sadness). The inclusion of this training in the rheumatology curriculum received "extremely important" or "important" ratings from all residents (100%). when looking at the determinants of a successful announcement, the year of residency was the only factor that showed a statistically significant association with enhanced theoretical knowledge (p = 0.049).

Conclusion: This study highlighted the improvement of the residents' competencies as well as their self-assigned skill level related to the use of role-play in the acquisition of competencies related to a particular situation such as the announcement of bad news. The training seminar on breaking bad news was beneficial and had a positive impact on the residents' performance. It enabled them to pick up several new abilities.

Reference: [**1]** Kurer MA, Zekri JM. Breaking bad news: can we get it right? Libyan J Med. 2008 Dec;3(4):200-3.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.3543

AB1704 CORRELATION BETWEEN LUNG ULTRASOUND AND HIGH-RESOLUTION CHEST CT IN SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Ultrasound, Validation

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Background: Systemic sclerosis (SSc) is a chronic, autoimmune, multisystemic disease characterized by fibrosis and vasculopathy. Mortality in patients with systemic sclerosis who present with interstitial lung disease can be multiplied up to 3 times in comparison with subjects who do not present it. It is estimated that 70-90% of patients with SSc have interstitial lung involvement, mainly of the diffuse type. It has been proposed that high-resolution chest tomography (HRCT) may have a role in the evaluation of interstitial lung disease in patients with autoimmune inflammatory rheumatologic diseases, with involvement of more than 20% of the lung parenchyma being a sign of poor prognosis and increased mortality. Its evaluation is determined by the detection and quantification of B lines.

Objectives: To correlate findings between lung ultrasound and high-resolution chest CT in patients with systemic sclerosis.

Methods: Descriptive, observational, cross-sectional study. Lung ultrasound was performed with a Siemmens Acuson X150 equipment, with 13mHz transducer and CT high-resolution (HRCT) in the rheumatology service of the Hospital Docente Padre Billini between August to November 2021. Inclusion criteria: ≥ 18 years, diagnosis of SSc according to ACR/EULAR 2013 criteria. Exclusion criteria: history of pre-existing lung disease.

Results: Descriptive, observational, cross-sectional study. Lung ultrasound was performed with a Siemmens Acuson X150 equipment, with 13mHz transducer and CT high-resolution (HRCT) in the rheumatology service of the Hospital Docente Padre Billini between August to November 2021. Inclusion criteria: ≥ 18 years, diagnosis of SSc according to ACR/EULAR 2013 criteria. Exclusion criteria: history of pre-existing lung disease.

Conclusion: Our study showed a positive correlation between lung ultrasound findings and HRCT. The most frequent pattern in HRCT was NSIP, while the most frequent ultrasound finding was the.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.3886

AB1705 KNOWLEDGE ABOUT CORTICOSTEROID THERAPY AMONG PATIENTS FOLLOWED FOR RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Patient information and education

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Background: Rheumatoid arthritis is a frequent chronic inflammatory rheumatic disease requiring a global management of the patient and his disease, for this, the evaluation of the level and sources of information among RA patients concerning their treatments is necessary.

Objectives: The objective of our study is to evaluate the level and sources of information regarding corticosteroid therapy among patients with RA.

Methods: This is a prospective cross-sectional study of RA patients undergoing corticosteroid therapy. Data collection was done by means of a questionnaire to which patients responded after informed consent. The patients' level of knowledge about corticosteroid therapy was assessed by 4 criteria: the purpose of the treatment, the methods of taking corticosteroids, the need for good compliance with the treatment and the action to be taken in case of forgetfulness. Good knowledge of the treatment was defined by citing of at least three criteria of the four criteria assessed.

Results: A total of 94 patients were included in this study, 83.2% were women with a mean age of 50.7 years. RA was immunopositive in 73.7% of patients, deforming in 59.6% and active (DAS28>3.2) in 82.1% of the subjects. 76.8 % of the patients were on methotrexate and 14.1% on salazopyrine. All patients were on prednisone-based corticosteroids with an average dose of 10 mg/day and an average duration of 3 years. Concerning the educational level of the patients, 57.6% were illiterate, 35.78% had received primary or secondary education. 61.6% of the patients were of low socioeconomic level. Among our patients, 73.7% were informed about the modalities of taking and weaning the treatment, 5.2% had no information and 69.4% of the patients were informed about the side effects of corticosteroids, 23.2% knew that they can induce osteoporosis, 21.2% were aware of the hyperglycemic effect, 11.1% were informed about the hypertensive effect and 44.4% of the patients linked corticosteroids to weight gain. 76.8% of patients admitted having received therapeutic education about corticosteroid therapy from a doctor, 6.1% from pharmacists, 7.1% from internet research and 3% from relatives. The level of knowledge about corticosteroid therapy was good in 47.5% and was correlated with young age, education level and a medical source of information (p at 0.0001,0.0005 and 0.0002 respectively).

Conclusion: The level of information of the patients included in this study on corticosteroid therapy seems insufficient, hence the need to reinforce therapeutic education in these patients.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1706 THE USE OF SELF-MEDICATION BY PATIENTS ADMITTED TO RHEUMATOLOGY

Keywords: Education, Safety

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Background: Self-medication is a frequent practice, especially in patients with painful and chronic pathologies. This is favored by the easy access to medication.

Objectives: The objective of this study was to evaluate the different aspects of self-medication among patients admitted in rheumatology departmen.t.

Methods: We realized a monocentric transversal study including 88 patients. The data were collected by a questionnaire including sociodemographic conditions, background pathology, drugs used, and resulting risk attitudes. Data processing was done with SPSS version 2021.

Results: A total of 88 patients were included, 54 women and 34 men. The mean age was 43.1 ± 10.1 years. Rheumatoid arthritis (RA) was found in 39%. Spondyloarthritis (SpA) in 19%, gonarthrosis in 20%, chronic mechanical low back pain in 9%, cervicobrachial neuralgia in 7%, gout in 3%, degenerative shoulder pathology in 5% and mechanical talalgia in 2%. The average duration of the disease was 6 ± 3 years. Self-medication was reported in 63% of patients. Concerning the type of self-medication, 88% of the patients used a treatment not prescribed in the initial prescription, 9% increased the doses of treatments already prescribed and 3% prolonged the duration. The most frequently used self-medication drugs were level 1 analgesics (66.7%), level 2 analgesics (6.1%), general non-steroidal anti-inflammatory drugs (NSAIDs) (39.4%), topical NSAIDs (30.3%), proton pump inhibitors (PPI) (12.1%) and corticosteroids (36%). Risk attitudes were detected in 32% of patients, of whom 6% exceeded 4 g per day of paracetamol, 15% combined 2 systemic NSAIDs, 2% took long-term NSAIDs, and 9% used PPIs for a long time without indication. The use of self-medication was not associated with sex (p = 0.5), level of education (p = 0.6) or professional activity (p = 0.58). Only one significant association was found with the duration of the disease (p 0.025).
Conclusion: Self-medication is practiced by the majority of our patients, motivated by various reasons and concerns the various analgesic drugs. The objective would be to rationalize the easy access to medication, to include therapeutic education in our medical practice in order to avoid the potential risks incurred.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5938

AB1707 FACTORS ASSOCIATED WITH SEDENTARY BEHAVIOR IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASE

Keywords: Non-pharmacological interventions, Education

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Background:
Objectives: To determine factors related to sedentary behavior in patients with a chronic inflammatory rheumatic disease(CIRD).
Methods: We conducted a cross-sectional study of 140 patients (mean age of 47.1 years, 68% females) affected by CIRD (Rheumatoid arthritis 56.4%, ankylosing spondylarthritis 32.1%, psoriatic arthritis 8.6% and juvenile idiopathic arthritis 2.9%). information on patients and disease characteristics were collected. Physical activity was measured objectively using the short version of the IPAQ questionnaire (International Physical Activity Questionnaire) for 7 consecutive days. Activity levels were subdivided into low physical activity and moderate to vigorous physical activity. We analyzed factors associated with sedentary behaviors.
Results: IPAQ Average was 413 (0.760) MET-min/week. The sedentary behavior was noted in 75.2% of patients. Table 1 summarizes factors associated with sedentary behavior in patients with chronic inflammatory rheumatic disease.

Table 1. Analysis of factors associated with sedentary behavior in patients with chronic inflammatory rheumatic disease.

Factors related to sedentary behavior	P
female gender	0,001
Lack of regular physical activity before the disease	0,03
professional inactivity	0.04
Functional disability caused by CIRD	0,01

Conclusion: Sedentary behavior is very prevalent among CIRD patients. Awareness-raising actions on the importance of physical activity in CIRDs should be a priority for women and people with reduced mobility.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6314

AB1708 SOCIAL MEDIA AS A SOURCE OF INFORMATION AMONG MOROCCAN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES

Keywords: Education, Inflammatory arthritides

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Background: Little research has been conducted on the use of different type of social media as a source information by Moroccan patients with chronic inflammatory rheumatic diseases and on the evaluation of the quality of this information that give an impact on the quality of life which that still poorly known in our context.
Objectives: The objective of our study is to evaluate the use of different type of social media by our patients and to identify the factors that may be associated with them.
Methods: This is a cross-sectional study that included any patient followed in our rheumatology department for chronic inflammatory rheumatic diseases. Sociodemographic data, comorbidities, chronic inflammatory rheumatic diseases related findings (type, pain assessment, disease activity and treatment) were collected. Patient's beliefs and attitudes regarding the various social media were assessed by a questionnaire. A list of 7 type of social media was provided, for which patients were asked to indicate the type of social media used and their confidence in them, followed by their experience with the usefulness of the sources used. Catastrophizing, trust in physician, and concerns about medicines were assessed by the validated Moroccan versions of the pain catastrophizing scale (PCS), trust in physician scale (TPS), and beliefs about medicines questionnaire (BMQ specific concerns).
Results: we included 189 patients. The average age was 47.49 ±13.7, 75.7% of patients were women, 52.4% had comorbidities, and 49.2% were illiterate. The median duration of the disease was 8 [3-16.75]. Mean pain VAS was 4.77 ±2.76. 37.6% of patients were in remission. 56.1% of the patients declared to look for information related to their chronic inflammatory rheumatic diseases on social media as a source of information. The 3 main sources were: Youtube (30.7%), Google (25.9%) and Facebook (16.9%). 19% have already applied some of this information. Only 20.1% discussed the information they found with their treating physicians and 67.2% would like to have health professionals in their virtual spaces to answer their questions. In univariate and multivariate analysis (Table1), age, education level, comorbidity, and concerns about medication were statistically significantly associated with the use of social media.

Table 1. Univariate and multivariate analysis of social media use in patients with chronic inflammatory rheumatic diseases

	Univariate analysis		Multivariate analysis	
	OR(IC 95%)	p	OR(IC 95%)	p
Gender	0,86 (0,44-0,17)	0,682		
Age	0,93(0,91-0,95)	**0,000**	0,96(0,93-0,99)	**0,028**
Level of education	4,04(2,75-5,91)	**0,000**	3,59(2,39-5,38)	**0,000**
Habitat	0,21(0,05-0,75)	**0,016**	0,25(0,04-1,5)	0,131
Comorbidity	0,58(0,39-0,86)	0,007	0,52(0,29-0,95)	**0,035**
Disease duration in years	1(0,97-1,03)	0,72		
Pain VAS	0,9 (0,81-1,01)	0,076		
Disease activity	0,76(0,6-0,97)	**0,032**	0,99(0,7-1,4)	0,993
PCS	0,98(0,54-1,76)	0,948		
TPS	0,98(0,94-1,02)	0,40		
BMQ-Concerns	1,058(1-1,11)	**0,029**	1,08(1-1,16)	**0,034**

Conclusion: Our study showed that Moroccan patients with chronic inflammatory rheumatic diseases especially are actively seeking information about their disease in social media. Moroccan rheumatologists need to be more involved, especially in virtual spaces, to meet these demands.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1709 AWARENESS OF EDUCATIONAL AND RESEARCH OFFERINGS OF EULAR AND EMEUNET AMONG YOUNG RHEUMATOLOGISTS WORKING IN TURKEY

Keywords: Education

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Background: EULAR (European Alliance of Associations for Rheumatology) has various educational and research offerings for physicians working in rheumatology. Emerging EULAR Network (EMEUNET) aims to address educational

needs and promote the research interests of aspiring young academics. A considerable number of young physician work or train in rheumatology in Turkey.
Objectives: To assess the awareness of the educational and research offerings of EULAR and EMEUNET among young rheumatologists working in Turkey.
Methods: We sent an e-mail to rheumatology trainees and consultant rheumatologists below the age of 40 years. We surveyed the general information about the offerings of the EULAR School of Rheumatology and EMEUNET. Data were analyzed descriptively.
Results: The response rate of 61% (116/190) was obtained. A slightly over half of the respondents were female (n=62,53.5%). Most of the respondents (n=75, 65%) were rheumatology fellows in training, and the remaining respondents were consultant rheumatologists. EULAR School of Rheumatology courses and EULAR research webinar series were well known (74% and 59%, respectively) among the participants (Table 1). However, less than half of the respondents who were aware of these events attended to a course or a research webinar previously (37.5% and 43%, respectively). The major obstacles to participation in these events were lack of enough time due to the clinical duties (50%) and language barrier (35%). Only 14% and 25% of the respondents were aware of the EULAR research consultation service and the EULAR scientific grant. 76 (65%) participants were aware of EMEUNET while only 13 (17%) of them were attended an EMEUNET event previously.
Conclusion: Educational offerings of EULAR and EMEUNET were well known by the young rheumatologists in Turkey. However, participation rate was not satisfactory. Majority of the respondents were unaware of the EULAR research offerings. Conducting a survey across Europe could show the main obstacles in a larger scale, thereby it helps to disseminate further offerings among young rheumatologists.

Table 1. Participants' responses to each question

Variable	n(%)
Have you ever heard about EULAR School of rheumatology courses?	116
Yes	86 (74)
No	30 (26)
Have you ever attended a EULAR School of rheumatology course?	80
Yes	30 (37.5)
No	50 (62.5)
Have you ever heard about the EULAR research webinar series?	116
Yes	68 (59)
No	48 (41)
Have you ever attended a EULAR research webinar?	68
Yes	29 (43)
No	39 (57)
Have you ever heard about the EULAR research consultation service?	116
Yes	16 (14)
No	100 (86)
Have you ever heard about the EULAR scientific grant for young fellows?	116
Yes	29 (25)
No	87 (75)
Have you ever heard about the EMEUNET organization?	116
Yes	76 (65)
No	40 (35)
Have you ever attended an EMEUNET event before?	76
Yes	13 (17)
No	63 (83)

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1710 LEARNING TO CARE FOR OLDER ADULTS WITH RHEUMATIC DISEASES: A NATIONAL SURVEY TO ASSESS CANADIAN RHEUMATOLOGY RESIDENTS' KNOWLEDGE AND INTEREST IN GERIATRIC-RHEUMATOLOGY

Keywords: Comorbidities, Education, Qualitative research methods

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Background: As the global population ages, the number of older adults with musculoskeletal and rheumatologic disorders is expected to rise.[1] This presents a challenge for rheumatologists, as the evaluation and management of older adults often requires understanding the unique considerations of multi-morbidity, polypharmacy, and geriatric syndromes.[2] Despite this growing need, it is currently unknown if rheumatology trainees receive sufficient education in geriatric-rheumatology during their training.
Objectives: To understand the perspectives and needs of rheumatology residents regarding geriatric-rheumatology education during their training in Canada.
Methods: The study conducted a cross-sectional needs assessment of rheumatology trainees in Canada who were enrolled in a residency or advanced fellowship training program within rheumatology. The survey underwent a pilot phase to ensure user-friendliness prior to its distribution. The survey was distributed to program directors of rheumatology training programs across Canada from December 2022 to January 2023, which was then forwarded to the residents within the respective rheumatology programs. The survey included multiple choice and open-ended questions exploring the residents' demographic data, exposure to geriatric-rheumatology education, knowledge gaps in managing older adults with rheumatic diseases and attitudes towards learning about geriatric-rheumatology. Data was analyzed using descriptive statistics.
Results: Fourteen rheumatology residents participated in the study, with an estimated response rate of 31.1%. Most residents (79%) had not received formal geriatric-rheumatology training during their rheumatology training. Residents (85%) were also unaware of any clinical tools or educational resources to help assess and manage older adults with rheumatic diseases. Most residents (71%) reported that geriatric-rheumatology training would be useful for their future practice and for taking care of older adults. Additionally, 65% of residents felt that formal rheumatology training curriculum should include geriatric-rheumatology contents. Areas where residents reported least confidence were applying the geriatric 5M framework, managing frailty, and providing end-of-life care to older adults with rheumatic diseases. They were most interested in learning how presentations and management of vasculitis, systemic lupus erythematosus and inflammatory arthritis differ in older adults and recognizing the indications of and risks associated with the use of DMARDs and biologics in this age group.
Conclusion: Our research revealed that rheumatology residents do not receive sufficient training in geriatric-rheumatology, indicating the need for a specialized curriculum in this field. Additionally, we discovered specific areas of interest among residents that can inform the development of future training initiatives. Overall, our study emphasizes the significance of incorporating geriatric-rheumatology education into rheumatology training programs.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1711 EVALUATION OF KNOWLEDGE AND OBSERVANCE OF PRESCRIBED TREATMENTS FOR HOSPITALIZED PATIENTS IN A RHEUMATOLOGY DEPARTMENT

Keywords: Education, Safety

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Background: Patients' knowledge of their treatment is part of therapeutic education programs.
Objectives: We studied this knowledge in patients hospitalized in a rheumatology department and the impact on therapeutic compliance.
Methods: We conducted a monocentric prospective observational study. 104 Patients of the rheumatology department who were major and autonomous with their treatments had to answer a questionnaire in 2 parts: the first part concerned the global knowledge of their medication formalized in 4 criteria (name, indication, dosage, specificity), a global knowledge score on 4 points was elaborated with the 4 previous criteria. The second part evaluated therapeutic compliance with the Morisky test.
Results: 104 patients were included. Women represented 71% and men 29%. The middle socioeconomic statut was found in 33% of cases. Chronic pathologies represented 72%. The most prescribed drug classes were: synthetic conventional drugs or csDMARDs (methotrexate, sulfasalazine) in 51% of cases, corticosteroid therapy in 69%, proton pump inhibitors in 20%, anti-hypertensives in 19%, and anti-arthritis drugs in 13%, non-steroidal anti-inflammatory drugs in 23%, topical treatments in 45%, oral antidiabetics in (17%), insulin in 6%, analgesics level 1 in (60%) and level 2 in (5%), bisphosphonates in (5%), pregabalin in (13%). Patients who had completed a maximum global knowledge score (score = 4) represented 16%. The mean compliance score (measured by Morisky test) was 6.48 ± 1.41. A significant association was found between global

knowledge score and male gender (p=0.001). The compliance score was negatively correlated with age (0.01; rs -0.65) and number of prescription drugs (0.01 rs -0.65) (p 0.014; rs -0.57), and positively correlated with the duration of disease progression (p 0.001; rs 0.87). No relationship was found between knowledge and compliance (p = 0.15).

Conclusion: The utilization of a score could be a method to evaluate knowledge and to adapt the content of educational actions to increase adherence to treatments.

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Disclosure of Interests: None Declared.

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AB1712 THE BELIEFS OF MOROCCAN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES REGARDING MEDICATION AND THEIR IMPACT ON THERAPEUTIC ADHERENCE

Keywords: Self-management, Education, Inflammatory arthritides

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Background: Adherence is one of the key elements of management in patients with chronic inflammatory rheumatic diseases, and it is likely to be influenced by beliefs about medications, which will influence the management and quality of life of patients.

Objectives: Objective is to assess chronic inflammatory rheumatic diseases patient's beliefs about medications, the factors associated with them, and their impact on therapeutic adherence.

Methods: This was a cross-sectional study that included any patient followed for chronic inflammatory rheumatic diseases. Sociodemographic data, comorbidities, information on inflammatory rheumatism ds (type, pain and activity assessment and and treatments) were collected. Beliefs about medication were assessed by the validated Moroccan version of the Belief on Medicine Questionnaire (BMQ). Catastrophizing, trust in physician and adherence to therapy were assessed by the validated Arabic versions of the pain catastrophizing scale (PCS), trust in physician scale (TPS) and Compliance Questionnaire Rheumatolgy (CQR)

Results: 189 patients were included. The average age was 47.49 ±13.7, 75.7% of the patients were women, 52.4% had comorbidities, 49.2% were illiterate, 56.6% were followed for rheumatoid arthritis, 35.4% for spondyloarthritis and 7.9% for undifferentiated chronic inflammatory rheumatic. The median duration of evolution of chronic inflammatory rheumatic diseases was 8 [3-16.75]. 41.3% of patients were on synthetic DMARDs and 4.2% on biotherapy. The mean VAS pan was 4.77 ± 2.76. 37.6% of patients were in remission. The average CQR was 55.16±8.14 The mean BMQ specific necessity was 20.75±4.77. 67.4% of the patients strongly believed that medication is essential to maintain their health. The mean of the specific BMQ concerns was 14.47±5.8. The main concerns of the patients were the fear of being dependent on the medication they were taking (36.2%) and the potentially harmful consequences of their treatment in the long term (35.5%). The median necessity-concern differential was 6[1-12] suggesting a positive benefit-risk ratio perceived by the patients. In multivariate analysis (Table1), there was a statistically significant association between education level, catastrophizing, trust in the physician. and the necessity-concern differential. There was also a signification correlation between the therapeutic compliance score and the BMQ necessity score and the BMQ differential necessity-concerns.

Table 1. Uni- and multivariate analysis for patient's beliefs about medications

	Univariate analysis		Multivariate analysis	
	OR(IC 95%)	p	OR(IC 95%)	p
Gender	0,74 (-1,55 -3,41)	0,46		
Age	3 (0,04 -0,19)	**0,003**	0,89(-0,05- 0,13)	0,373
Level of education	-2,83 (-2,2 - -0,39)	**0,005**	-2,49(-2,51- -0,28)	**0,04**
Comorbidity	0,05(-1,3 -1,4)	0,96		
Disease duration in years	0,35(-0,09-0,15)	0,725		
VAS pain	0,62(-0,26-0,51)	0,535		
Disease activity	2,22 (0,11 – 1,86)	**0,027**	0,8 (-0,61-1,44)	0,423
Corticotherapy	0,14 (-0,06-4,11)	**0,05**		
Methotrexate	0,22(1,18-5,38)	**0,002**		
bDmards	0,11(-0,88-7,95)	0,117		
PCS	-2,39 (-4,83 - -0,46)	**0,018**	-1,8 (-4,82- 0,14)	**0,03**
TPS	3,768 (0,13 – 0,439)	**0,000**	1,9 (-0,005- 0,33)	**0,05**

Conclusion: Moroccan patients followed for chronic inflammatory rheumatic diseases have a rather positive perception of their medication. This perception seems to influence their adherence to treatment.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1713 EVALUATION OF A TRAINING COURSE ON EMOTIONAL MANAGEMENT WHEN BREAKING BAD NEWS IN RHEUMATOLOGY

Keywords: Education, Patient information and education

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Background: In recent years, attitudes towards breaking bad news have changed dramatically to emphasize patient autonomy and avoid psychological harm [1]. As a result, learning how to deliver bad news efficiently became a fundamental clinical skill in professional practice. [2]. In the field of rheumatology, with learning focused on technical skills, gaps in communication skills are to date significant.

Objectives: The aim of this study was to evaluate the impact of a training workshop on the disclosure of bad news in rheumatology.

Methods: We conducted a prospective, multicenter, interventional study over a six-month period during the academic year 2021-2022. 31 residents were recruited on a voluntary basis. Two groups were individualized: The training group A (N=16) and the control group B (N=15). The training session included interactive lectures, video-case studies, role-playing and peer-to-peer discussions. A self-administered survey was used to assess residents' abilities to deliver bad news before and three months after the training.

Results: The comparison of the patient emotion management scores between the two groups in the post-training period showed no significant difference (p=0.115). And although there was a slight improvement in the scores in post-training, no significance was found either in the training group (p=0.488) or in the control group (p=0.523).

In terms of managing residents' emotions, most residents in both groups experienced neutral feelings during the periods of silence during the announcement consultation, and there was no discernible difference between the two groups at either time. The percentage of residents in group A who felt negatively during the times of silence significantly decreased by 38% after the training (T3) (p=0.013), while the percentage of residents who felt positively increased by 25% (p=0.033). In Group B, no significant difference was found between the two time periods in terms of feelings during quiet time. Although the basic skills of the residents in dealing with stressful moments were quite good as more than 50% of the residents in both groups were able to maintain their neutrality during these difficult moments, it was shown that the training had a positive impact on the residents' feelings during stressful moments such as the silent moments. At the end of the announcement, most residents in both groups unanimously had negative feelings (desolation and sadness) with no significant difference between the two groups at either time.

Conclusion: Emotional skills training requires a lot of practice and review, which was not possible during our one-day training intervention. However, our training workshop, although short in duration, had partially improved residents' ability to respond to emotional cues.

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AB1714 GOUT TREATMENT: ARE TUNISIAN INTERNS FOLLOWING INTERNATIONAL RECOMMENDATIONS?

Keywords: Gout

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Background: Gout is a common metabolic disease affecting at least 1% of the population. Its therapeutic management was recently redefined by the recommendations of the French society of rheumatology (SFR) 2020 [1,2].
Objectives: We aimed to determine the level of adherence of Tunisian rheumatology interns to these recommendations.
Methods: We conducted a 26-item online questionnaire via Google Drive Forms destined to rheumatology interns. The questionnaire intended to assess the degree of application of the French recommendations for the treatment of gout.
Results: The online questionnaire was sent to 50 rheumatology interns, 19 of whom (38%) responded. Thirty-one percent of participants were in first year, 15.7% in second year, 16% in third year and 31.5% in fourth year. The mean age was 28.3 ±8.7 years [26-33]. All participants were female. The average number of rheumatology internships performed was 3.9 ±0,2 [1-6]. All of the participants declared informing their patients of their pathology. The information given concerned the disease (94.7%), the aim of treatment (78.9%), the need for long-term adherence to treatment (94.7%), the risk of onset of gout symptoms at initiation of treatment (84.7%) and necessary adaptations to lifestyle (94.7%). Eighteen interns (94.7%) advised their patients to avoid certain foods: soda (84.2%), beer (89.4%), wine (36.8%), red meat (84.2%), fish (63.1%), chicken (26.3%) and seafood (73.6%). Almost all physicians screened for comorbidities (94.7%): hypertension (73.6%), dyslipidemia (78.9%), obesity (63.1%) and renal failure (78.9%). The therapeutic means that can be used in gout flares according to the doctors questioned were the following: non-steroidal anti-inflammatory drugs (NSAIDs) (94.7%), colchicine (100%), corticosteroid therapy (94.7%) and anti-interleukin1 (36.8%). Faced with a gout flare, 17 interns (89.4%) prescribed colchicine within 12 hours after the symptoms' onset. Eleven interns (57.8%) followed the therapeutic regimen recommended by the SFR for flare treatment with colchicine. In the event of the onset of diarrhoea under colchicine, 8 interns (42.1%) stopped the treatment. Regarding corticosteroid therapy, the recommended dose of 30 to 35 mg/day was prescribed in 42.1% of cases. In case of kidney failure, doctors avoided prescribing NSAIDs in 89.4% of cases and colchicine in 63.1% of cases. Eighteen physicians (94.7%) prescribed allopurinol from the first gout flare. Colchicine was prescribed simultaneously with allopurinol in 47.3% of cases. Sixteen interns prescribed colchicine for six months in combination with urate-lowering treatment. Interns were aiming for a therapeutic uricemia target of 50mg/L in 15.7% of cases and 60mg/L in 73.6% of cases. The urate-lowering treatment was maintained for life by 57.8% of the interns, while it was stopped as soon as the therapeutic target was reached in 26.3% with retreatment if recurrence in 21% of the cases. Faced with a decrease in renal clearance, no intern stopped allopurinol and 78.9% of doctors prescribed it subject to monitoring. Once the therapeutic target had been reached, 84.2% of participants recommended monitoring uricemia every 6 to 12 months.
Conclusion: Tunisian rheumatology interns do not fully follow the new French recommendations for the treatment of gout. Thus, medical training on the subject seems necessary in order to optimize the treatment of this pathology in Tunisian hospitals.
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Disclosure of Interests: None Declared.
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AB1715 ASSESSING KNOWLEDGE AND PRACTICES OF MOROCCAN RHEUMATOLOGISTS ON PNEUMOCOCCAL VACCINATION IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES(CIRD)

Keywords: Vaccination/Immunization, Education, Inflammatory arthritides

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Background:
Objectives: To assess rheumatologists' knowledge and practice about pneumococcal vaccination in patients with CIRD.
Methods: This is a cross-sectional study conducted by the vaccination working group of the Moroccan Society of Rheumatology. The survey collected data on the knowledge and practice of pneumococcal vaccination by rheumatologists.
Results: Out of 350 questionnaires sent, 125 valid responses were received (35%).The mean age of rheumatologists was 42.4+/-12.1 years and the average duration of practicing in rheumatology was 13.1+/-11.1 years. The sector of practice was respectively 31.2 %,34.4 %,34.4 % for the public, private and Univesity Hospital sectors. Knowledge accurency about the nature of vaccine and vaccination protocol was noted in respectively 62.4% and 46.4% of rheumatologists. Figure 1 illustrates situations of pneumococcal vaccine prescription by Moroccan rheumatologists.

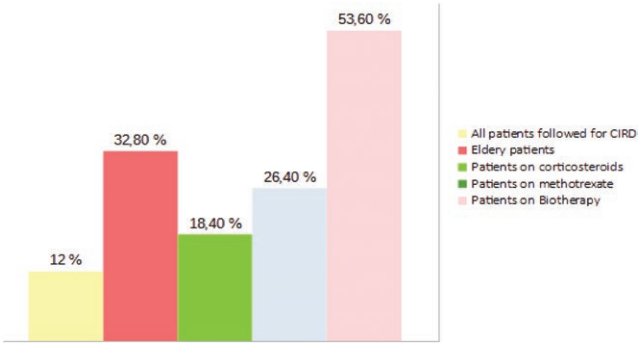


Figure 1. Situations of pneumococcal vaccine prescription by Moroccan rheumatologists.

Regarding Medication management of patients during vaccination, rheumatologists recommended reducing corticosteroid dose, holding methotrexate for 2 weeks after vaccination, postponing corticosteroid bolus and stopping the biotherapy in respectively 5.6, 20.8,16.8 and 20 % of cases. The lack of knowledge about pneumococcal vaccination was associated with rheumatology practice duration (p=0.03) and practice in the public sector (45% p=0.008).

Conclusion: This survey illustrates a lack of pneumococcal vaccinal prescription by Rheumatologists and suggests the necessity to improve rheumatologists' knowledge concerning pneumococcal vaccination.
REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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NEW TOPIC: Clinical cases

AB1716 TREATMENT MODALITIES IN ANTI-MDA5 DERMATOMYOSITIS: A CASE SERIES FROM SOUTH INDIA

Keywords: Myositis

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Background: Anti-MDA 5 antibody – associated DM presents with rapidly progressive interstitial lung disease (RP-ILD), and is known to have poor prognosis. Early detection of ILD,given the risk of rapid deterioration and best treatment guidelines are of extreme importance due to high disease burden and mortality. As we encountered different cases of DM in our OPD at a renowned tertiary care centre in Hyderabad, India, we too had tailor-made diverse treatment regime based on patients' condition and their circumstances, and henceforth we present 10 of such cases wherein the customized treatment plan brought about significant relief in their condition.
Objectives: To study and report 10 cases of Anti -MDA5 ILD and treatment outcomes.
Methods: Among 10 patients newly diagnosed with Anti- MDA5 ILD at our hospital, 5 patients had RP-ILD, out of which 3 suffered with refractory ILD. Among the varied treatments given 2 patients required IVIG and Plasma Exchange was used as an adjunct to standard treatment in 1 refractory ILD patient as salvage therapy. All patients were followed at least for six months post management and 7 patients reported significant improvement with maximum reversal of HRCT findings.

RESULTS:

Pt.	Age/Sex	Symptoms and Signs Common symptoms : Constitutional + Dyspnoea	Laboratory Parameters (Raised levels)	Antibodies Positive	HRCT Chest Findings
1	60/M	Skin darkening and thickening , Mechanic's hands, Healed papular lesions over fingers.	ESR, CEA, Ferritin	Anti-Ro 52, Anti-MDA 5	Ill-defined GGO's Dense sub-pleural consolidation Multifocal traction bronchiectasis Subcutaneous soft tissue emphysema Pneumomediastinum
2	40/M	Non scarring alopecia, Heliotrope rash, Gottron's papules , Erythematous tender palmar papules, Mechanic's hands	CPK, Ferritin	Anti-Sm, Anti -RNP/Sm , Anti-MDA 5	Subpleural GGO's bilaterally with early fibrotic changes.
3	38/M	Constitutional symptoms, Erythematous scaly rash (face, scalp, shoulders), Shawl sign, Gottron's papules.	ESR, SGOT, SGPT, CPK, CRP, Ferritin, D-dimer	ANA IF :1+ (Speckled) Anti-MDA 5	Sub-pleural GGO's and reticulations bilaterally Pneumomediastinum Loss of volume
4	42/M	Polyarthritis , facial skin thickening, Erythematous tender palmar papules, Inverse Gottron's sign.	Ferritin	Anti-Ro 52, Anti-MDA 5	Early ILD changes
5	33/F	Malar rash sparing nasolabial folds, Shawl sign, Polyarthritis, Painful oral ulcers	ESR, CRP		Sub-pleural patchy ground-glass opacities
6	44/M	Skin darkening, Polyarthritis with progressive fixity of both shoulders and knee joints, Alopecia., Ulcers in both axillae with necrotic base.	ESR, CRP, Ferritin	Anti-Mi 2, Anti-MDA 5	Subclinical ILD
7	22/M	Polyarthritis of both wrist joints and ankle joints, Heliotrope rash, facial hyperpigmentation, alopecia, symmetric b/l muscle weakness of upper as well lower limbs.	ESR, CRP, CPK	ANA IF : 4+(Homogenous) Anti-MDA 5	Early ILD changes
8	16/F	Pruritic rashes over the arms, shoulders , upper chest , back , Polyarthritis of both elbows and PIP joints of hands, Painful ulcers over b/l extensor surface of elbows.	ESR, CRP	Anti-MDA 5	Early ILD changes
9	55/F	Erythematous rashes over face , neck , Gottron's papules , ulcers over elbows and fingers, auricular papulo-pustular lesions with necrotic base.	CRP, Ferritin, D-dimer, CEA	Anti-MDA 5	B/L GGO's with mild traction bronchiectasis
10	56/F	Heliotrope rash , Progressive muscle weakness .	ESR, CPK,	ANA IF : 3+ (Cytoplasmic) Anti-SSA, Anti-Ro 52, Anti-SSB, Anti-MDA 5	B/L lower lobe ground glass opacities Traction bronchiectasis Sub-pleural consolidations

Figure 1.

Pt.	Treatment Regime				
	Corticosteroids	Immunomodulators	JAK Inhibitor	Anti-fibrotics	Others
1	Oral	-	Oral Tofacitinib	-	-
2	Injectable pulse steroids (IV Methyl Prednisolone 500mg x 3days) Followed by oral 0.5 mg/kg.bwt	Inj Cyclophosphamide Inj. Rituximab Hydroxychloroquine Mycophenolate mofetil	-	-	-
3	Injectable pulse steroids (IV Methyl Prednisolone 500mg x 3days) Followed by Oral 0.5 mg/ kg/bwt.	Oral Methotrexate Inj Cyclophosphamide Tacrolimus Inj. Rituximab Mycophenolate mofetil	-	Pirfenidone Nintedanib	-
4	Injectable pulse steroids (IV Methyl Prednisolone 250 mg x 3days)	Inj Cyclophosphamide Oral Methotrexate	-	-	-
5	Injectable pulse steroids (IV Methyl Prednisolone 250mg x 3days)	Inj Cyclophosphamide Oral Methotrexate	-	-	-
6	Injectable pulse steroids (IV Methyl Prednisolone 250mg x 3days)	Inj Cyclophosphamide	-	-	-
7	Oral (later tapered)	Methotrexate	-	-	Anti-tubercular treatment
8	Oral	-	Oral Tofacitinib	-	-
9	Injectable pulse steroids (IV Methyl Prednisolone 500mg x 3days) Followed by Oral 0.5 mg/ kg/bwt.	Inj Cyclophosphamide Tacrolimus Mycophenolate mofetil	-	Nintedanib	IVIG Plasma exchange therapy
10	Oral	Hydroxychloroquine Methotrexate Inj Cyclophosphamide Mycophenolate mofetil Rituximab	-	-	NSAIDs IV Antibiotics IVIG

Figure 2.

Conclusion: Taking into account the clinical features with which patients presented to our OPD as well as our personal experience in managing such troublesome cases, we also had to custom-make the therapeutic regimes and include different therapeutic modalities, so as to not only relieve them of their symptoms but to also ameliorate their quality of life as well as afford them with an early and sustained period of remission.

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Patient information and education

AB1717-PARE

DERMATOMYOSITIS BURDEN OF DISEASE MANIFESTATIONS AND QOL IMPACT: PATIENT-REPORTED SURVEY RESULTS

Keywords: Patient reported outcomes, Myositis

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Background: Dermatomyositis (DM) is a rare, multi-system idiopathic inflammatory myopathy characterized by skin rash and muscle weakness that is often accompanied by pain and fatigue. Other manifestations include interstitial lung disease and calcinosis. Malignancy is also highly associated with DM. The profound negative clinical impacts of DM on patients' quality of life (QoL) are not yet well-characterized in the literature.[1]

Objectives: To capture patient perspectives on the impact of DM on QoL (physical function, mental health, personal relationships, and work productivity), most bothersome symptoms (MBS), and severity of symptom burden in adults.

Methods: A 60-question survey was developed via sponsor-conducted focus groups and adaptions from existing patient-reported outcome (PRO) tools (e.g., WPAI-GH, SLE-FAMILY, and PROMIS). After IRB approval, members of The Myositis Association (~4000 individuals with DM) were invited to complete the online survey (eligibility criteria: 18 – 75 years of age, self-reported DM diagnosis, and current DM symptoms persistent for ≥ 1 year). Responses were collected per the following Likert scales: DM severity rated from "mild" to "very severe" (4-point scale), overall health rated from "poor" to "excellent" (5-point scale), life impact questions rated from "never" to "always" or "not at all" to "a great deal" (5-point scales), and severity of symptoms rated from "never experienced" to "very severe" (6-point scale).

Results: Of 195 respondents (97% from US), the median age was 57 years, 88% female, and 82% White. 53% and 35% had experienced DM symptoms for 3 to 10 years or > 10 years, respectively. 92% were currently receiving medication(s) to manage DM symptoms. The 5 MBS reported were muscle weakness (44%, n = 86), fatigue (43%, n = 84), muscle pain (30%, n = 59), itchy skin (24%, n = 46), and skin rash (19%, n = 37). A majority of respondents indicated DM had at least a "moderate" negative impact on the following domains: ability "to do the things they enjoy" (83%, n = 162), ability to engage in social activities (75%, n = 146), sexual desire and ability to engage in physically intimate relationships (64%, n = 125), relationships outside of family (57%, n = 112), and relationships with family (51%, n = 100). A majority reported negative impacts on mental health (83%, n = 162), defined as having felt "anxious or nervous" or "down, depressed or hopeless" at least "sometimes" due to DM. Almost half reported being "usually" or "always" worried about symptom flares (49%, n = 96) and about their ability to carry out daily activities (42%, n = 82). DM symptom severity was associated with negative impact on overall health. "Fair" or "poor" health was reported by 50% (n = 98) of those experiencing "moderate" DM symptoms, by 85% (n = 27) of those with "severe" symptoms, and by 100% (n = 7) of those with "very severe" symptoms. All with "very severe" DM responded "usually" or "always" to questions about DM limiting their ability to "do the things they enjoy", concern about symptoms "getting worse", and ability to "carry out daily activities." DM symptoms hindered physical functioning, with 63% and 65% of respondents, overall, reporting that DM limited their ability to climb stairs and perform usual daily activities. DM also affected respondents' ability to work; nearly half were unemployed (47%, n = 92) and had to change their employment status due to DM (49%, n = 95), while 24% (n = 47) were receiving disability assistance. Of respondents who were working, 69% (n = 77) reported that DM negatively impacted their career/career choices.

Conclusion: The survey results highlight the marked physical and psychosocial burden of DM in adults and the impact of disease severity on the ability to perform daily activities, mental health, interpersonal relationships, and work productivity. These results underscore the unmet need for new treatment options to ameliorate the progressive and debilitating consequences of DM and further inform PRO-focused research in DM.

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AB1718-PARE

DISEASE AWARENESS, MANAGEMENT PERCEPTIONS AND CARE SATISFACTION AMONG PATIENTS WITH PSORIATIC ARTHRITIS: A PROSPECTIVE MULTI-CENTRE SURVEY FROM INDIA

Keywords: Psoriatic arthritis, Patient information and education, Quality of life

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Background: Psoriatic arthritis (PsA) is a disease with heterogenous manifestations, which affects personal and professional aspects of patients' lives. Perception of disease state in PsA affects patients significantly. However, studies examining PsA patients' outlook about their disease are scarce and there are no studies from India examining PsA patients' viewpoints about their disease.
Objectives: The main objective of this multi-centric multiple domain survey was to study the PsA patients' perspectives.
Methods: A survey questionnaire with items on PsA patients' demographics, knowledge, awareness and perception of disease, its treatment, physical therapy, quality of life and the care they received was designed. After internal and external validation, a pilot survey was conducted, and survey modified. The final survey was (with translations in local languages) administered by the participating 16 centres across India.
Results: There were 262 respondents with mean age of 45.14±12.89 years (56% male). Forty percent of the patients had first consultation more than a year after the onset of joint pain and in a majority their current diagnosis was made by a rheumatologist. Most of the patients had psoriasis (92%) and arthralgia (78%) for more than one year, however, only 60% respondents took a doctor's opinion for joint symptoms within one year. For two third of the patients', a rheumatologist made the diagnosis of PsA followed by a dermatologist (15%) and general physicians (8%). Over 83% of patients were consulting their rheumatologist once every three months or earlier and were fully compliant with the treatment. Busy schedules and cost of therapy were the most common reasons for non-adherence to therapy (Table 1). Eighty-eight patients (34%) were not fully satisfied with their current treatment. Twenty-one. % of the survey respondents were still unaware of the term PsA and 10% were unaware of their current diagnosis. Over two-third of patients had never seen a physiotherapist and listed lack of time, pain, and lethargy as the main barriers to exercising. PsA had affected social and employment status of about half of the survey patients. Fatigue, busy work schedule, not able to lift weights, not able to travel without pain were elucidated by patients as main reason for this effect. Most of the patients were satisfied with disease information provided by rheumatologist and dermatologists. Eighty five % patients in this survey reported not taking any form of complementary alternative medicine therapy. The unmet needs of patients identified in this survey were better provision of remote or online consultation, reduction in pill load, better patient education on disease and drugs and financial help for biological therapies.
Conclusion: This survey informs that although survey participants are satisfied with care given by rheumatologist and dermatologists, the disease is influencing their quality of life significantly by affecting socialization and occupation.

Table 1. Common themes identified in open ended responses

Themes of open ended questions	Patient Responses
Common side effects with medications	Dyspepsia and nausea after medications (most common), fatigue, hair loss
If you are not taking the medications regularly, what are the reasons for the same?	Busy work schedule and high cost of medications (most common cause), intolerance to medications, fear of injections, high pill load, high cost of medications, lack of proper guidance
What, if any, would you say are the barriers to exercising for you?	Lack of time, pain during exercises, feeling of lethargy/tiredness so not able to do exercises
Has PsA affected your employment status? If yes, in what way?	Not able to lift weights, not able to sit for long time, lack of energy
Has PsA affected your ability to do your regular daily activities (housework, shopping, childcare, socializing) other than work at a job? If yes, in what way?	Can`t travel to socialize, can't socialize due to constant pain, getting tired quickly, need assistance, lethargy, fatigue

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Arthritis research

AB1719-PARE

MAPPING THE JOURNEY OF PEOPLE WITH RHEUMATIC DISEASES TO DIAGNOSIS IN GREECE

Keywords: Gout, Patient-led research, Real-world evidence

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Background: Rheumatic diseases (RD) are chronic mostly autoimmune diseases, multi- dimensionally affecting the musculoskeletal system and possibly other organs. Additionally, they impact the patient and family quality of life in respect to health, work, socialization and future perspectives. Previous data indicate that early diagnosis of inflammatory and other RDs is important in order to improve long-term outcome.
Objectives: To capture the journey of RD Greek patients from disease onset to diagnosis aiming to define gaps regarding the early management and uneventful outcome of these potentially debilitating chronic diseases.
Methods: An online questionnaire survey of patients with several types of RDs was uploaded by the Greek Federation REUMAZEIN, an acronym meaning co-living with an RD. 463 patients - all members of the Federation- responded to the call and were enrolled in the study.
Results: The majority were females (81%), mostly under 60yrs old (73%) and were residents of urban/suburban areas (65%). In respect to education, they were mainly graduate or postgraduate degree holders (56%). The prevailing RDs were RA (178) 38%, SLE (105) 23%, AS (61) 13% and PsA (58) 13%, respectively. The total lag time (mo) was 10.3. In respect to RD kind, it ranged from 5.9 for JIA to 19.7 for AS, respectively. The delay from disease onset to diagnosis was mainly attributed to patient underassessment of symptoms (53%) or ignorance of the proper MD specialist for these conditions (45%). Only a minority of participants (36%), reported that the diagnosis was made by the first specialty they had initially visited. The initial physician's (MD) specialist for all but SLE patients, was an orthopedic surgeon (33-60%), whereas for SLE ones, an internist (32%). The initial MD failed to establish the diagnosis in 64% pts, principally in AS ones (82%). Alternatively, rheumatologists as the primer reached MD, established the diagnosis in 60% of patients. Lag time to first visit in non-Rheumatology specialists and the corresponding diagnosis was 26mo; for AS pts it reached 50.9mo, respectively. The average lag time from symptom appearance to the first MD visit was 21.3mo and from the 1st visit to final diagnosis 72.2 mo. All patients reported as the most important problem until the final diagnosis, the lag time to diagnosis (36%), followed by a misdiagnosis (33%). Interestingly, those who looked for a second assessment pre-diagnosis, reported higher percentage either of delay or misdiagnosis (49%, 44%, respectively). The degree of satisfaction regarding information received by the MD who established the final diagnosis was totally high (3.5/5) and was irrespective of the RD type. At final diagnosis, patients were highly satisfied regarding information received by the MD for their most important problem, too. In respect of satisfaction to final diagnosis by rheumatologists vs. non-rheumatologists, the rates did not significantly differ.
Conclusion: Findings of this study indicate that the initial patient visit with an RD to the proper MD specialty, is highly important. A visit to a trained Specialist for RD as a Rheumatologist, significantly reduces lag time to diagnosis and leads to an early management and optimal prognosis. Most of the patients expressed a high rate of satisfaction at the establishment of final diagnosis in respect to the MD and his/her skill in problem solving. Therefore, informing and educating the public regarding the early recognition of initial symptoms and early guiding to

an experienced MD specialty, would effectively improves the management and co-living with RDs.

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AB1720-PARE NEGATIVE ILLNESS BELIEF ASSOCIATED WITH MORE ACTIVE DISEASE ACTIVITY AND POORER FUNCTION IN THAI PATIENTS WITH ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS

Keywords: Spondyloarthritis, Patient reported outcomes, Mental health

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Background: Regarding the common sense self-regulatory model[1], illness beliefs plays an essential role in both physical and psychological adjustment to illness. There were few studies about the value of illness representations in the outcome of spondyloarthritis[2] and no study in Thailand.

Objectives: To explore the illness perception and their associated factors in AS and PsA patients.

Methods: This was a cross-sectional study. Spondyloarthritis patients visiting at Siriraj Hospital for treatment were recruited between 27 April 2021 and 31 October 2022. They were invited to fill out the Thai version of brief Illness Perception Questionnaire(BIPQ) [total range 0 (no or best)-80(worst)], the medication taking behavior measure for Thai patients(MTB) [range 4(low adherence)-24 (high adherence)], demographic data, Ankylosing Spondylitis Disease Activity Score(ASDAS), and Bath Ankylosing Spondylitis Disease Activity Index(BASFI) were collected. The variables were associated with total BIPQ were computed by linear regression.

Results: A total of 132 patients with 73(55%) male, mean(SD) age of 49(12) years, median(IQR) disease duration of 11(14) years, median ASDAS of 1.7(1.2), median BASFI of 0.9(2.2), median BIPQ of 26(12), and mean MTB of 23.2(1.0) were recruited. The BIPQ was significantly positive associated with ASDAS and BASFI in multivariate analysis. Consequences, timeline, identity, illness concern, and emotional representation were positively associated with ASDAS while identity and emotional representation were positively associated with BASFI (Table 1). Positive emotional representative in BIPQ was associated with higher MTB ($p<0.05$).

Conclusion: The patients with positive illness perception were associated with better function, lower disease activity, and higher medication adherence. The goal of treatment should be inactive or low disease activity and normalized function as soon as possible may lead to positive illness belief and psychological strength, or vice versa. The positive illness belief may maintain the good health outcome. A longitudinal study is needed to support this association.

Table 1. The association of the brief illness perception and disease activity, and function

		Unstandardized B coefficient	
Item	Total	ASDAS[1]	BASFI[2]
1.Consequences	2(3)	0.233#	0.126*
2.Timeline	8(5)	0.071#	0.037*
3. Personal control	5(4)	-0.056	0.008*
4. Treatment control	1(2)	0.014	0.019*
5. Identity	1(2)	0.123#	0.164*
6. Illness concern	2(2)	0.097#	0.055*
7. Coherence	2(3)	-0.008	0.008*
8. Emotional representation	2 (2)	0.101#	0.154# *
Total score	26 (12)	0.047#	0.033# *

Abbreviations = ASDAS, Ankylosing Spondylitis Disease Activity Score; BASFI, Bath Ankylosing Spondylitis Functional Index; B,[1] adjusted for disease duration; [2] adjusted for disease duration and ASDAS; * ASDAS was significantly associated with BASFI with p-value <0.0001; # p<0.05Total values are in median (IQR) unless otherwise stated.

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AB1721-PARE PATIENT REVIEWERS OF APPLICATIONS FOR RESEARCH FUNDING - A PILOT STUDY

Keywords: Patient-led research

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Background: Each year the Danish Rheumatism Association supports research in the field of rheumatology with approx. 1.5-2 Million EUR to strengthen the basis for developing better prevention strategies and treatment and thus increase the quality of life for many people.

Since 2014 it has been mandatory for researchers applying for funding from the research committee of The Danish Rheumatism Association to indicated whether and how they involve patient representatives in their research. Our annual measurements show that involvement of patient representatives by researchers receiving a grant from The Danish Rheumatism Association has increased from 14 % in 2015 up to 65 % in 2021. To strengthen the patient involvement in research further The Danish Rheumatism Association would like patients to have a say in the research funding decisions by reviewing applications for research funding to the research committee of the Danish Rheumatism Association.

Objectives: To carry out a pilot study with patients as reviewers of applications for research funding to The Danish Rheumatism Association.

Methods: Three patients, one man and two women, with different RMDs participated in the pilot study and were requested to try to represent all patients with RMDs. The study was carried out from August to December 2022. The Danish Rheumatism Association provided the patients with an online introduction to the work as patient reviewer, they were provided with information material and The Danish Rheumatism Association supported them throughout their time with us. The patients reviewed a summary of 6-26 research funding applications in plain language at home individually. The applications were scored from zero to five, where zero was the lowest score and five the highest. The research committee of The Danish Rheumatism Association was presented the patients mean score of the applications and comments from one or more patients before their meetings and oral on the meetings in September 2022 and December 2022 respectively.

Results: When the research committee met to decide which research should receive funding, they took the patients mean score and comments for each application reviewed into their decision as with other parameters like methodology, research outcome, involvement of patient representatives in the research etc.

Conclusion: The patients in the pilot study represented patients with RMDs. They reviewed the applications for the research committee of The Danish Rheumatism Association based on their experience of being a patient and had a say in research funding decisions. In spring 2023 the pilot study will be evaluated and it is expected that patients with RMDs will be involved in the future research funding decisions in The Danish Rheumatism Associations and maybe in a larger scale than in the pilot study.

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AB1722-PARE LINKING PATIENT PERCEIVED TREATMENT GOALS OF PEOPLE WITH RHEUMATOID ARTHRITIS (RA) AND SEVERE LIMITATIONS IN FUNCTION TO THE INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH (ICF)

Keywords: Patient reported outcomes, Treat to target, Rheumatoid arthritis

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Background: There is a lack of knowledge about the nature and frequency of the main limitations in activities and participation experienced by a subgroup of people with rheumatoid arthritis (RA) and severe limitations in physical functioning. More insight is essential to optimize treatment for this subgroup and can be obtained by linking the treatment goals perceived by the patient to the International Classification of Functioning, Disability and Health (ICF) as a frame of reference. Goal setting is widely recognized for tailoring and optimizing treatment, and for this purpose the Patient Specific Complaint (PSC) instrument is recommended in physiotherapy practices in the Netherlands [1]
Objectives: To describe the nature and frequency of limitations in activities and participation of people with RA and severe limitations. Limitations will be derived from the PSC [1] and linked to the ICF and the comprehensive and brief ICF Core Sets for RA.
Methods: Baseline data from a randomized controlled trial on the effect of long-term exercise therapy in people with RA and severe limitations in functioning were used. For each participant, the three most limited activities were identified and prioritized using the PSC. Two researchers independently identified meaningful concepts within each PSC activity and linked them to the most specific ICF category within the "Activities and Participation" component, following standardized ICF linking rules [2]. In case of disagreement, this was discussed with a third researcher until consensus was reached. The frequencies of ICF categories were calculated overall and for PCS activities ranked 1, 2 and 3. Finally, the uniquely identified ICF categories were compared to the content of the comprehensive and brief RA ICF core sets for the component "Activities and Participation".
Results: From 206 RA patients (90.8% female, 58.7 (12.9) years of age, 1.5 (0.5) HAQ-DI score), 618 PSC activities were recorded, including 911 meaningful concepts. These concepts were subsequently linked to 909 ICF categories, with 72 unique ICF codes. Overall, the most prevalent ICF categories were: 1) d4501 walking long distances (n=121; 59%); 2) d4502 walking on different surfaces (n=79; 38%); 3), d451 stairclimbing (n=62; 30%) 4) d4103 changing body position from sitting (n=60; 29%) and 5) d4401 grasping (n=51, 25%). The categories for the ranked PSC activities differed slightly, and manipulating, d4502, often proved limited too (see Table 1). The uniquely identified ICF codes covered 21 of 32 items (66%) of the comprehensive and 4 of 6 items (67%) of the brief ICF core set for RA patients. Performing daily routine, d230 and rewarding work, d850, were limitations included in both core sets that were not identified in this subpopulation. However, stair climbing limitations were prevalent in this population, but are not part of the RA core sets.
Conclusion: The most prevalent limited activities involved walking (long distances, on different surfaces and climbing stairs), changing body position from sitting and hand use (grasping and manipulating). To optimize treatment for this specific subgroup, clinicians should be aware that not all RA core set items are prevalent in practice and that some frequent problems are not included in the core sets.
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Table 1. Most prevalent limitations within the ICF component activities and participation of people with RA and severe limitations

PSC activity 1	N, %	PSC activity 2	N, %	PSC activity 3	N, %
d4501 Walking long distances	75 36%	d4501 walking long distances	28 14%	d4103 Changing body position from sitting	28 14%
d4502 Walking on different surfaces	47 23%	d451 stair climbing	25 12%	d451 Stair climbing	27 13%
d4500 Walking short distances	33 16%	d4103 changing body position from sitting	20 10%	d4502 Manipulating	20 10%

PSC: Patient specific complaints

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AB1723-PARE **A CANADIAN PATIENT-DRIVEN SURVEY TO HIGHLIGHT WHICH PREDNISONE-RELATED SIDE EFFECTS MATTER THE MOST**

Keywords: Patient-led research, Vasculitis

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Background: Management of vasculitis has evolved for the last two decades; however, glucocorticoids (GC) remain the cornerstone of the treatment. Although the side effects (SE) of prednisone are well recognized by the clinicians, their importance for vasculitis patients has not been investigated extensively.
Objectives: We conducted a patient centered survey to identify the relative importance of GC-associated SE among patients with vasculitis.
Methods: An online questionnaire surveyed patients registered with the Vasculitis Foundation Canada about their experience and SE of GC. The questionnaire consisted of demographics and diagnosis, 5 questions about GC dose and duration, 21 about specific SE (with a rating of some pre-specified SE), 4 about knowledge and perception about possible alternatives to prednisone.
Results: 97 patients (53 GPA/MPA,44 other vasculitides) completed the survey. The mean age was 56.9 years, and disease duration was 10.6 years. Mean duration of GC use was 62.7±83.7months, and 49.5% of patients were still on GC (daily dose, 8.4±6.2mg). All the patients reported ≥1GC-related SE, with 67.1% of them reporting having had ≥11/19 SE of interest. The SE reported most frequently included mood change in 93 (95.8%) patients, insomnia and weight gain in 91 (93.8%), and body disfiguration in 89 (91.7%) patients (Table 1). Among ranked SEs, acne was ranked with the lowest score, whereas moon face/torso hump had the highest ranking, just above weight gain, insomnia and impaired quality of life (Figure 1). Half of the GPA/MPA patients and one-third of the others have heard about avacopan, and 68% of patients (similarly in both groups) stated they would prefer being the first to take a very new medication, such as avacopan, instead of prednisone.
Conclusion: This patient-driven survey emphasizes the patient experience and perspectives on GC-related SE, with weights given to some SE that may differ from those given by physicians. GC toxicity indexes should reflect this, and alternative treatment options should be developed.

Table 1. Demographics, prednisone dose and duration, and prednisone-related side effects of the patients

	GPA/MPA patients n: 53	Other Vasculitis patients n: 44	P value
Age (years), Mean (SD)	56.7 (14.5)	57.2 (15.9)	0.932
Female (%)	39 (73.6)	36 (81.8)	0.335
Disease duration (years), Mean (SD)	9.9 (7.3)	11.3 (11.2)	0.735
Total prednisone time (months), Mean (SD)	52.5 (59.4)	74.6 (104.5)	0.635
Still receiving prednisone (%)	22 (41.5)	26 (59.1)	0.085
Current dose of prednisone (mg), Mean (SD)	7.4 (5.5)	9.2 (6.7)	0.100
Prednisone related side effects, n (%)			
Impaired quality of life	51 (96.2)	43 (97.7)	0.570
Acne	21 (39.6)	21 (47.7)	0.423
Skin bruising or thinning	**42 (79.2)**	**41 (93.2)**	**0.050**
Gastrointestinal symptoms	40 (75.5)	37 (84.1)	0.296
Weight gain	51 (96.2)	40 (90.9)	0.255
Insomnia	49 (92.5)	42 (95.5)	0.431
Mood change	52 (98.1)	41 (93.2)	0.242
Anxiety or depression	46 (86.8)	40 (90.9)	0.380
Lower self-esteem	41 (77.4)	40 (90.9)	0.073
Night sweats	43 (81.1)	39 (86.6)	0.309
Body disfiguration (moon face or torso hump etc.)	51 (96.2)	38 (86.4)	0.083
Hip bone AVN requiring hip replacement	0 (0)	1 (2.3)	0.454
Diabetes requiring medication	8 (15.1)	10 (22.7)	0.241
High blood pressure requiring medication	21 (39.6)	14 (31.8)	0.280
Infections requiring antibiotics	28 (52.8)	22 (50.0)	0.471
Severe infection requiring hospitalization	8 (15.1)	6 (13.6)	0.537
Bone fracture	6 (11.3)	6 (13.6)	0.483
Osteoporosis requiring treatment	12 (22.6)	12 (27.3)	0.385
Osteoporosis	15 (28.3)	14 (31.8)	0.438
Cataracts	15 (28.3)	18 (40.9)	0.138
Loss of tooth mass or teeth	12 (22.6)	14 (31.8)	0.216
Patients' knowledge and perception about possible alternatives to prednisone			
Ever heard about avacopan, n (%)	**30 (56.5)**	**13 (29.5)**	**0.008**
Ever taken avacopan, n (%)	1 (1.8)	0 (0)	-
Would you prefer to go back on prednisone or be one of the first patients, outside of any study, to take a very new medication such as avacopan, instead of, or with less, prednisone?, n (%) New medication (avacopan) Back on prednisone Not sure.	33 (62.3) 6 (11.3) 14 (26.4)	33 (75.0) 5 (11.4) 6 (13.6)	0.290

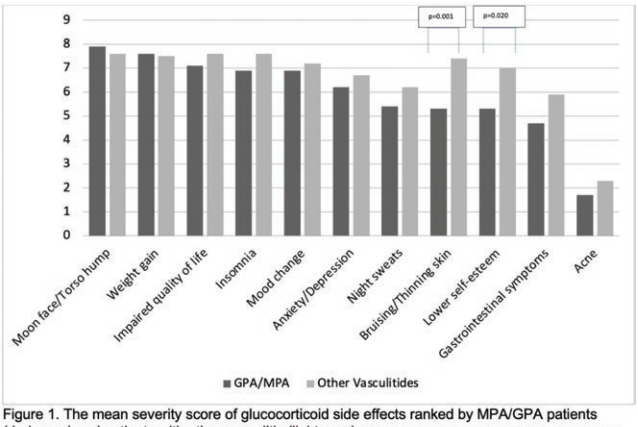


Figure 1. The mean severity score of glucocorticoid side effects ranked by MPA/GPA patients (dark grey) and patients with other vasculitis (light grey). *GPA: Granulomatosis Polyangiitis; MPA: Microscopic Polyangiitis*

Acknowledgements: The authors would like to thank the network of Vasculitis Foundation Canada patients who participated in this survey.
Disclosure of Interests: None Declared.
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AB1724-PARE

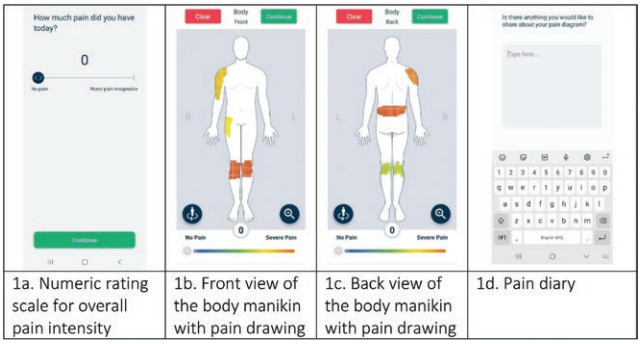
WHAT DO PEOPLE LIVING WITH MUSCULOSKELETAL PAIN CONDITIONS DESCRIBE ABOUT THEIR PAIN? AN EXPLORATORY ANALYSIS OF ELECTRONIC FREE TEXT PAIN DIARIES

Keywords: Qualitative research methods, Self-management, Pain

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Background: People living with musculoskeletal pain conditions prefer pain self-reporting for better pain management [1]. In a recent feasibility study, 104 people living with musculoskeletal pain conditions completed daily pain manikin reports, along with an optional free text pain diary using their own smartphone [2]. People shared their motivation to daily self-report their pain if that could improve their self-management [3]. There is a potential of electronic pain diaries to improve pain management [4], while it is unknown what people would describe in an optional pain diary to improve thier pain managment.
Objectives: The objective was to explore what people have described in their free text electronic pain diaries, which could be useful for improving their pain management.
Methods: In a recent study, we assessed the feasibility of daily pain self-reports for 30 days. A daily pain self-report included a single overall pain intensity question, a two-sided two-dimensional pain diagram, and a free text pain diary (see figure 1). For the latter, people could provide additional information in response to the question: Is there anything you would like to share about your pain diagram? We conducted a secondary thematic content analysis of the free text pain diary entries and identified key domains and ideas described by people. We presented themes descriptively.
Results: Out of 104 people, 94 completed 957 unique pain diary entries. We have presented key domains, ideas and illustrative quotes in the table 1. People described how medication and self-management practices (e.g., heat therpy, physical activity) helped them in managing their pain. They also described different aspects of their pain, including pain descriptors (e.g., pain location, quality, radiation), perceived causes (e.g., physical activity, cold weather) and consequences of pain (e.g., limited mobility, lack of sleep). People perceived some factors, such as medication, and level of physical activity, as both cause and consequence of their pain.
Conclusion: Electronic free text pain diaries provide useful information about people's pain management practices. However, how best to track pain and self-management practices for effective pain management requires research.
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1a. Numeric rating scale for overall pain intensity | 1b. Front view of the body manikin with pain drawing | 1c. Back view of the body manikin with pain drawing | 1d. Pain diary

Figure 1. Different components of a pain self-report

Table 1. Key domains and ideas captured in free text electronic pain diaries

Sr. No.	Domains captured in pain diaries	Key ideas	Illustrative quotes
1	Descriptions of pain	Pain location Quality of pain (e.g., numbness) Depth of pain Radiation	Crumbling pain in my back and numbness down right leg.
2	Factors associated with (self) management of pain	Medication Resting Physical activity Heat therapy Warm weather or clothing	Again my medication is keeping the pain at bay. Because it has been very hot today, I have experienced very little pain today.
3	Perceived cause of pain or factors influencing pain	Lack of physical activity Active day before Stress Weather conditions Delay or no medication Lack of sleep Comorbidity	Had a very active day before, so in higher pain today.
4	Consequences of pain	Functional limitations (e.g., mobility) Change in medication Lack of sleep Longer sleeps	The leg pain in restricting my daily movement.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1725-PARE

SEQUENCE PATIENT SURVEY: PERCEPTION OF THE USE OF ADVANCED THERAPIES FOR PSORIATIC ARTHRITIS IN THE UNITED KINGDOM

Keywords: Psoriatic arthritis, Patient-led research, bDMARD

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Background: Due to the chronic nature of psoriatic arthritis (PsA) and the increase in therapeutic options, many people are receiving multiple sequential lines of biologic and targeted synthetic disease modifying anti-rheumatic drugs (b/tsDMARDs). There is limited data on treatment response to advanced lines of therapy and therefore in the rationed UK National Health Service, some regions are limited in the number of sequential b/tsDMARD per patient. Patients have higher levels of treatment satisfaction with biologics compared to conventional DMARDs[1] but little is known about patient satisfaction with access to b/tsDMARDS in the UK.
Objectives: To assess the perceptions of people treated with b/tsDMARDS in the UK for PsA, focusing on the experience of access to advanced treatments.

Methods: The cross-sectional SEQUENCE patient survey was developed as an anonymous online questionnaire on the SurveyMonkey platform, available to be completed by people with self-reported PsA and current or previous b/tsDMARD treatment. The freely available online survey was promoted through PsA support groups via websites and social media. Descriptive analysis of the results was performed, with categorical variables summarised with frequencies and percentages.
Results: 67 people from England, Wales and Scotland responded (male 8, female 59), mean age 54.5 years, mean psoriasis duration 22 years (range 0-55) and PsA 14 years (range 1-50). The number of lines of previous b/tsDMARD treatment per respondent is outlined in Fig 1. The most common first line treatments were adalimumab (33/60) or etanercept (12/60) with secukinumab the most common second line drug (15/42). Switching treatments was most commonly due to primary or secondary failure. 46.7% (28/60) of people felt that a decision to switch treatment had been a joint decision between patient and physician. Only 9% (6/67) had been advised that there was a maximum number of biologics permitted in their region. 24% (16/66) had been advised that a particular b/tsDMARD had to be prescribed first line for PsA in their region, 76% (13/17) of whom reported this was a TNF inhibitor. One respondent had to move hospital or region to obtain access to further biologics. 32% (21/65) had been told that an individual funding request had been applied for to fund their next b/tsDMARD (likely due to limited funded treatment options), and this was successful for 90% (20/23). Qualitative responses highlighted the significant improvement that b/tsDMARDs make to people with PsA e.g. 'They have given me my life back'. However, there was frustration towards perceived delays in access: 'We should not need to suffer cDMARDS and fail, losing months of our lives, to get to a biologic.'
Conclusion: Within this UK PsA population, a minority reported limitations on the class or line of b/tsDMARD available in their region. There was an overall positive response to treatment with biologics, and perception of access generally. However, when patients have difficulty accessing later lines of treatment, it has an adverse effect on their lives. The small proportion of respondents who have had difficulty with access suggests that the overall cost of creating equitable access to b/tsDMARDs in the UK may be relatively low but would have a meaningful impact.
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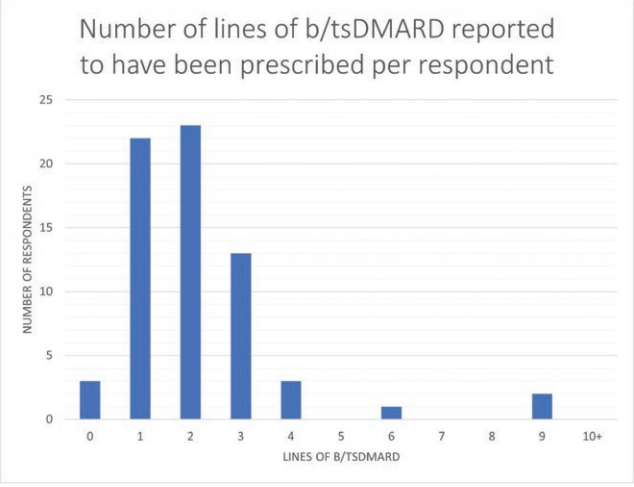


Figure 1.

Acknowledgements: Thank you to the British Psoriatic Arthritis Consortium (Brit-PACT) for help with development of the survey and to Brit-PACT, the Psoriasis Association and Andrea Jack for promotion of the online survey.
Disclosure of Interests: Charlotte Gollins: None declared, Arani Vivekanantham: None declared, Mel Brooke: None declared, Laura Coates Speakers bureau: has been paid as a speaker for AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Medac, Novartis, Pfizer and UCB., Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Galapagos, Janssen, Moonlake, Novartis, Pfizer and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB, William Tillett Speakers bureau: Abbvie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Consultant of: Abbvie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Ono Pharma, Pfizer, UCB, Grant/research support from: Janssen, UCB, Pfizer, Eli-Lilly.
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AB1726-PARE

IN WHAT EXTENT DO RHEUMATOLOGISTS DISCUSS PHYSICAL ACTIVITY WITH THEIR PATIENTS AFFECTED BY CHRONIC INFLAMMATORY RHEUMATIC DISEASE AND WHAT ARE THE PATIENTS' EXPECTATIONS?

Keywords: Non-pharmacological interventions, Patient information and education

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Background:
Objectives: To assess the level of communication about physical activity (PA) between rheumatologists and their patients and to identify patients' needs in this topic.
Methods: This is a cross-sectional study conducted on 140 patients (mean age of 47.1 ± 14.6 years, 68% females) followed for CIRD (Rheumatoid arthritis 56.4%, ankylosing spondylarthritis 32.1%, psoriatic arthritis 8.6% and juvenile idiopathic arthritis 2.9%). Physical activity was measured using the IPAQ-SF (the international physical activity questionnaire - short form). We asked patients if their rheumatologist has ever discussed or encouraged them or even explained how to do adapted physical activity. Patients ' preferences for physical activity practice were collected by specifying if patients preferred to practice it at home or outside, single or in groups. Finally, we also asked them about their needs for both audiovisual support on adapted physical activity and participation in an educational workshop.
Results: The physical activity level was low with a mean IPAQ-SF score of 413 (0,760) MET-min/week. The topic of PA was discussed by rheumatologists with 37.1% of patients. Rheumatologists advised patients to practice adapted PA and show them how to practice it, in respectively 38 and 21.4% of cases. Figure 1 illustrated patients' expectations of PA.

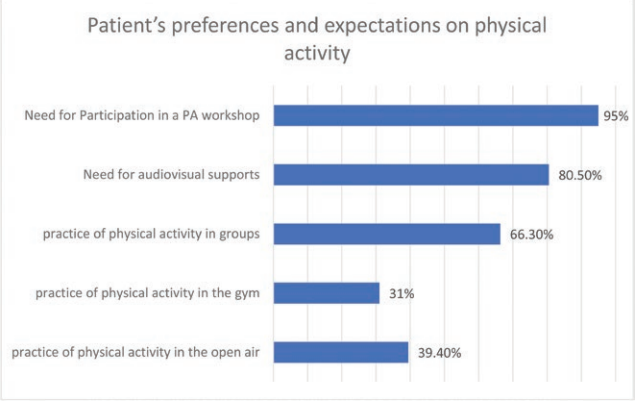


Figure 1. Patient's preferences and expectations on physical activity.

Conclusion: This study shows the lack of rheumatologist-patient communication on PA and the significant need for PA education. Hence there should be greater involvement of rheumatologists in patient education about physical activity to fight against sedentary behavior in CIRD patients.
Disclosure of Interests:
NONE DECLARED
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Psychosocial support

AB1727-PARE OPTIMISM AND PESSIMISM ARE ASSOCIATED WITH SELF-REPORTED DISEASE ACTIVITY AND PSYCHOSOCIAL FACTORS IN PATIENTS WITH RHEUMATIC DISEASES

Keywords: Prognostic factors, Patient reported outcomes, Quality of life

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Background: The primary goal in patients (pts) with rheumatic diseases is to control disease activity, prevent irreversible damage and reduce disease burden. Despite a broad armamentarium of effective treatments in most rheumatic diseases, a substantial number of pts does not achieve disease control.
Objectives: As psychosocial factors and mindset might influence the treatment response of pts with rheumatoid arthritis (RA)[1], the EXPERD (Expectations in Rheumatic Diseases) study aimed to assess these factors and their association with disease activity in pts with various rheumatic diseases.
Methods: For this cross-sectional analysis, pts with diagnoses of RA, systemic lupus erythematosus (SLE), spondyloarthropathy (SpA) and inflammatory vasculitis treated in the outpatient clinic of the university hospital Duesseldorf were included. In all pts the following psychosocial factors were assessed by patient reported questionnaires: health related quality of life (HRQoL) (Short Form-12), depressive symptoms (Patients-Health-Questionnaire-9), anxiety symptoms (Generalized-Anxiety-Disorder-Scale-7), disease duration (in years) and trustworthy relationship with the treating physician (Numeric-Rating-Scale 0-10). Pts´ optimism and pessimism was assessed by the Life-Orientation-Test. Pts´ reported disease activity was captured on a numeric rating scale from 0 (no disease activity) to 10 (high disease activity). Statistical analysis was performed using linear regression models with a significance level of 5%.
Results: A total of 158 pts completed the questionnaires: 51 pts with RA, 32 pts with SLE, 43 pts with SpA and 32 pts with inflammatory vasculitis. Univariate analyses adjusted for sex, age and number of comorbidities found higher pessimism associated with higher disease activity (est. 0.14, CI 0.008-0.27, p 0.04). Further, lower HRQoL was correlated with higher pessimism (physical component (PCS): est. -0.05, CI -0.08 - -0.02, p 0.003; mental component (MCS): est. -0.05, CI -0.09 - -0.01, p 0.02) and lower optimism (PCS: est. 0.04, CI 0.01 – 0.07, p 0.01; MCS: est. 0.05, CI 0.01 – 0.08, p 0.007). Referring to this, pts´ depressive symptoms and pronounced anxiety symptoms manifested the strongest association with lower optimism (depression: est. -0.28, CI -0.34 - -0.22, p <0.001; anxiety: est. -0.36, CI -0.42 - -0.29, p <0.001) and higher pessimism values (depression: est. 0.22, CI 0.14 – 0.3, p <0.001; anxiety: est. 0.26, CI 0.17 – 0.35, p <0.001). In contrast, a longer disease duration and a trustworthy doctor-patient relationship showed primarily lower pessimism values (est. -0.07, CI -0.11 - -0.02, p 0.002; est. -0.26, CI -0.47 - -0.06, p 0.01).
Conclusion: Mindset in terms of optimism and pessimism was associated with several psychosocial factors and self-reported disease activity in pts with rheumatic diseases. While pessimistic pts tended to have higher self-reported disease activity and considered their physicians less trustworthy, optimism was associated with higher HRQoL. Our results emphasize the relevance of encouraging psychological support to improve a pessimistic mindset. A longitudinal analysis of this investigation is currently ongoing.
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Table 1. Baseline characteristics

Feature	Total	RA	SLE	SpA	Vasculitis
Number of pts, n (%)	158	51 (32.3)	32 (20.3)	43 (27.2)	32 (20.3)
Female, n (%)	107 (67.7)	38 (74.5)	25 (78.1)	25 (58.1)	19 (54.4)
Age in years, mean (SD)	52.97 (15.49)	56.16 (15.43)	42.66 (13.75)	50.33 (12.77)	61.78 (14.32)
HRQoL, PCS, mean (SD)	39.9 (15.89)	40.29 (16.83)	42.47 (15.54)	41.90 (12.51)	33.63 (17.83)
HRQoL, MCS, mean (SD)	39.36 (13.1)	41.96 (14.56)	37.43 (12.69)	42.20 (6.71)	33.11 (15.45)
Self-reported disease activity, mean (SD)	1.8 (1.8)	2.14 (2.17)	1.39 (1.23)	1.76 (1.81)	1.69 (1.57)

HRQoL: Health related Quality of Life, MCS: mental component, PCS: physical component, pts: patients, RA: Rheumatoid Arthritis, SLE: Systemic Lupus Erythematosus, SpA: Spondyloarthropathy

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1728-PARE CASE OF PERIODIC FEVER SYNDROME IN PEDIATRIC PATIENT FROM PARENTS' AND DOCTORS' PERSPECTIVES

Keywords: Best practices, Prognostic factors

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Background: every patient experiment own disease differently as well as their families. Even modern medicine sometimes can't address all explanation to each clinical question, cover all needs and cure all diseases. Rheumatology is one of medical filed with more question than answer sometimes. And this uncertainty usually is difficult for patient. What if doctor can't answer your question? What if treatment patient is asking for is not the best option or even harmful?
Objectives: show through our case different prospective and expectation between parents and doctors view on pediatric patient medical care based on past family experience, standards of medical care and possible future health outcomes.
Methods: analysis of own experience managing patient with periodic fever syndrome.
Results: L., 3 yo boy, originally from country in South America, with past medical history of periodic fever, myelodysplastic syndrome associated with pathologic polymorphism of gene SRP72 (C1384C>T), multiple café au lait spots and autism spectrum disorder was admitted to our hospital due to fever. Fever episodes occurred since 6-month-old (up to 40C), every 3 months and lasted 5-15 days. The episodes associated with rash, conjunctivitis, arthralgias, reactive lymphadenopathy, oral and duodenal ulcers, Raynaud syndrome and elevation of C-reactive protein level. The initially managed the fever with Prednisone due to concerns for an autoimmune condition or PFAPA. The fever responded to steroid in the early course of disorder but haven't had effect with following episodes. Extensive work up has been done. Autoimmune, immunology, oncology was negative, but genetic testing was positive for pathologic polymorphism of gene SRP72. At 18-months of age, he was diagnosed with neutropenia first time. Family history was significant for periodic fever and lupus-like symptoms in his mother and rheumatoid arthritis in maternal uncle. Tests results were inconclusive for possible reason of his symptoms. So, his parents moved to the USA with hope to find some answers. Next comprehensive evaluation has been performed at National Institute of Health in June 2022 and unfortunately studies were still inconclusive and without a certain diagnosis. Only pending test that might shed light on the cause was full genome sequencing. During admission to our hospital with taking into account results of previous evaluations and clinical symptoms that did not completely coincide with any of the common or rare periodic fever disorders, diagnosis of syndrome of undifferentiated recurrent fever was made. A few possible treatments were discussed. Recommendations were against using prednisolone for treatment. Continue treatment at home country or US after establishing care with local medical house were discussed. Excessive discussions with family took place multiple times. However, parents have continued expressed extreme frustration with requests for definitive diagnosis and appropriate treatment.
Discussion: There is no doubt that parent and medical team have the same goals and try to find answers to the same questions. And there is no doubt that understanding and parents' perspectives are different from medical team ones often. Different previous medical experience, no clear answers make waiting without any treatment extremally hard for family. However, modern medicine is matter of tries and hope sometimes. This bring us as doctors to ethical dilemma: *what can and what should we do?*
Conclusion: it is difficult for parent to make right decision due to numerous biases and expectations. The effort of medical team should be directed to work together with patient family and shared decision making with parents in order to provide the best care to a child.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1729-PARE BEING "THE HEALTHY ONE": THE HARD LIVING WITH A SICK BROTHER/SISTER

Keywords: Real-world evidence, Patient information and education, Lifestyles

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Background: In 2019 our project "A paw? Yes, thank you", in which even healthy brothers and sisters of patients with JIA (Juvenile Idiopathic Arthritis) could benefit from playing with dogs and cats and live the same experience, highlighted their (more or less disguised) discomfort. All attention, even by the patients' associations, is focused on the needs of the sick people and nobody take care of brothers, sisters and relatives who feel neglected.
Objectives: AMaR Piemonte (Rheumatic Patients Association of Piedmont) would like to know exactly the unmet needs of these young people to help them to overcome their condition and have the best possible quality of life.
Methods: A Psychologist developed two different questionnaires - one for children (easier and more intuitive) and one for the teenagers - to assess the discomfort and the unmet needs of healthy brothers and sisters living with a sick one. The questionnaires will be administered online on the websites and social media of the association (www.amarpiemonte.org – Facebook: @amarpiemonte – Instagram: amarpiemonte) since February 2023 for 6 months to reach as many contacts as possible. Teenagers will be asked also to share posts, videos, papers, podcast on an dedicated platform, created to preserve their anonymity.
Results: Preliminary results will be available in September 2023 and the final report will be ready in October.
Conclusion: Healthy brothers and sisters are nearly always neglected by their parents, whose attention is mostly focused on the specific needs of their sick sons/daughters. The quality of life of these children and teenagers is poor and they are ashamed to show their discomfort, often ending up feeling negative feelings towards their sick brother/sister and their family. With this survey we expect to have a broad and clear picture of the discomfort and poor quality of life of these people, to design specific projects in order to help their families to overcome this unintentional discrimination and to help them to restrict it and to speak about it with their parents without fear of creating further problems for them.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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Arthritis research

AB1730-PARE **CAVIPA, THE SURVEY EXPLORING PATIENTS' QUALITY OF LIFE WITH OSTEOARTHRITIS DESIGNED BY PATIENTS FOR PATIENTS**

Keywords: Quality of life, Quality of care, Osteoarthritis

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Background: Osteoarthritis (OA) is the most common chronic joint disease and poses a growing public health problem. In Spain, 7 million people suffer from OA [1], and only hip and knee OA represent an average annual cost of 4,738 million euros for the Spanish Health System. In 2016, more than one hundred thousand hip and knee prostheses were placed in Spain [2]. In the Spanish population, errors in the quality of care and a deterioration in OA patient care have been described from the perspective of health professionals [3]. However, a comprehensive analysis of the OA patients' profile, experience, and needs is still missing.
Objectives: The objective is to determine the perception of the quality of life (QoL) of patients with knee and/or hip OA in Spain, focusing on critical factors associated, such as knowledge of the disease, satisfaction with their treatment plan, diagnosis, symptoms, functional disability, and limitations on daily activities.
Methods: Cross-sectional observational study including data collection through a telephone survey of 200 patients living through the Spanish territory. The survey was prepared by a group of patients, clinical experts, and methodologists and validated by a pilot with 10 patients. The final version, approved by the CEIC of the Hospital la Paz in Madrid, was divided into 8 parts that investigate socio-demographic, diagnostic, therapeutic, assistance, and joint functionality, focusing on patient satisfaction and perception of health and QoL.
Results: Patients reported that pain is the first word that comes into their minds when they think about OA. Although pain contributes to the loss of QoL and health, our results show that pain is a multidimensional affection since comorbidities such as depression and anxiety profoundly influence their QoL. Another factor that negatively affects the perception of QoL is the diagnostic delay, where the mean delay obtained in our results was 3.12 years. Regarding their pharmacological treatment, only half of the patients are satisfied, and only a fifth of the respondents believe it can alleviate their pain. Despite this lack of satisfaction, patients take a very long time to make it known to their doctors since they think their doctor will not listen to them or believe another therapeutic option does not exist. Moreover, only half of the patients received non-pharmacological recommendations from their doctors, of which only 20% received professional support for their implementation. Moreover, they reported the need for more treatments to improve their condition and advocated for more information, empathy, and comprehension since they feel their situation is poorly understood by their family, friends, and healthcare providers.
Conclusion: The Osteoarthritis Foundation International (OAFI) designed and conducted the first Spanish survey on QoL of OA patients: the CAVIPA study, to analyze the perception of QoL by patients. Our results show that OA severely impacts patients' QoL due to associated functional limitations, comorbidities, diagnostic delay, and treatment satisfaction. These results provide a portrait of patients' perceptions of OA to give a baseline to take better quality performance in the future. Also, it was a proof-of-concept study designed to prove the strength and capacity of patients and their organizations to contribute to the scientific community. Empowering patients to have a more active role in their health and engaging them in research are key aspects to ensure the effective implementation of interventions aimed at improving the QoL of patients and, consequentially, the current OA management strategies.
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Acknowledgements: We want to acknowledge the volunteers from OAFI who conducted the telephone interviews and the data analysts from SERMES that helped us with the statistical analysis. Also, we want to thank M. Bernad, M. Santiñà, A. Sanchez, and M. Reyes, who supervised the development of the study.
Disclosure of Interests: None Declared.
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Patient information and education

AB1731-PARE **INFLUENCE OF A MULTICOMPONENT EDUCATIONAL PROGRAM ON PATIENT REPORTED OUTCOMES MEASUREMENTS IN A GROUP OF PATIENTS WITH RHEUMATOID ARTHRITIS**

Keywords: Patient information and education, Rheumatoid arthritis

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Background: Educational strategies in patients with rheumatoid arthritis (RA) are a fundamental tool for the objective measurement of clinimetry by patients (Patient Reported Outcomes Measurements- PROMs).
Objectives: The objective of this study is to evaluate whether there are differences in the measurement of clinimetry when performed by a medical group (MG) with PROMs in an educational context.
Methods: Cross-sectional study. A group of adult patients with RA who participated in a multicomponent RA education program (EMRA) and another who did not participate in this program (NEMRA) were included. The multicomponent educational program is responsible for educating the patient for self-management and management of their health condition, providing different knowledge regarding the disease, including clinimetry, with a duration of 14 months (divided into three levels, mixed face-to-face and virtual). The group of EMRA and NEMRA patients performed the PROMs, through a form designed in "Google forms". Clinimetry measurements were performed by a medical group, MG (blind to the type of patient group) with a difference of 1 week. Clinical, sociodemographic, and clinimetry variables were included in the RedCap platform. The MDHAQ, RAPID3, PAS, EQ5 and Fatigue scales were evaluated by the MG and the two groups of patients. Univariate and bivariate analysis was performed. A comparison of the medians of the variables evaluated by PROMs and by the MG (Wilcoxon for paired data) was made. The ethics committee approved the study design.

Results: 91 women were included. The median duration of the disease was 10.9 years (12.1). 30.8% had polyautoimmunity. The EMRA group had a higher proportion of education above secondary school (p=0.013). In the EMRA group, there were no significant differences between the clinimetry evaluated by the MG and the PROMs. In the NEMRA group, significant differences were found in 4 of the 6 variables evaluated (Table 1).

Table 1. Comparison of clinimetry and autoclinimetry according to the two groups

	Total Group n=91			EMRA Group n=28			NEMRA Group n=63		
Variable*	PROMs	C-MG	P-value **	PROMs	C-MG	P-value**	PROMs	C-MG	P-value **
Fatigue	5 (4)	5(7.5)	***0.05***	4.1 (4)	4 (5.8)	0.778	5.3 (6)	5 (8)	***0.021***
MDHAQ	2 (2.7)	2.7 (3)	***0.013***	1.5 (2.5)	1.7 (2.7)	0.329	2.3 (3)	3 (2.6)	***0.018***
RAPID3	15.3 (7.6)	13.7 (7.7)	0.350	12.8 (7.3)	11.8 (7.6)	0.927	15.7 (7)	14.7 (8.7)	0.251
PAS	5 (2.6)	4.5 (2.5)	0.352	4.2 (2.4)	3.9 (2.5)	0.927	5.2 (2.4)	4.8 (2.8)	0.259
EQ-5D-3L TTO score	0.640 (0.306)	0.710 (0.240)	***0.014***	0.695 (0.250)	0.812 (0.198)	0.151	0.640 (0.460)	0.710 (0.267)	***0.038***
EQ-5D-3L VAS score	0.590 (0.240)	0.645 (0.191)	***0.008***	0.635 (0.195)	0.722 (0.153)	0.130	0.590 (0.270)	0.645 (0.298)	***0.027***

*Median (Interquartile range) ** Wilcoxon test for paired samples.PROMs: Patient reported outcomes measurements. C: Clinimetry.EMAR: Multi-component educational program in RA. MG: Medical Group.NEMAR: Non-participation in a multi-component education program in RA

Conclusion: PROMs measurements have a value comparable to the clinimetry performed by the MG in those patients who are under an educational program with emphasis on self-management of their disease. This can be valuable to have an objective measurement by the patient with RA that can be useful at the time of the consultation, save time in its development and facilitate the adoption of therapeutic behaviors. It is suggested that for a good development of PROMs, patients have prior educational training so that these measurements are similar to those performed by the MG.

REFERENCES: NIL.

Acknowledgements: NIL.

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AB1732-PARE "FLARE, DID YOU SAY FLARE?" FLARES IN SJÖGREN'S DISEASE: THE PATIENT PERSPECTIVE

Keywords: Sjögren syndrome, Outcome measures, Patient information and education

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Background: "Flare" is a word often used by Sjögren's patients and medical professionals, without any official definition or consensus on what it means. In addition, the heterogeneous nature of Sjögren's symptoms means that the definition of a "flare" will vary greatly from patient to patient. As part of the European Necessity project, www.necessity-h2020.eu, 7 Sjögren's patients from the Patient Advisory Group (PAG) addressed this issue and hereby present our definition of a Sjögren's flare from the patient perspective.

Objectives: To provide a common definition of a flare in Sjögren's despite the heterogeneity and subjectivity of symptoms and provide patients and medical professionals with a mutual, basic understanding of flares.

Methods: The Necessity PAG Members discussed which symptoms should be included in the definition of a flare. Flares are as heterogeneous and variable as the disease, but some symptoms appear more prominent than others. The symptoms selected by the PAG were compared with findings from the 2021 U.S. Sjögren's Foundation survey. The 9 symptoms determined as the most commonly reported by patients were: dryness, fatigue, morning stiffness, global pain (joints, muscles, nerves, headache), forgetfulness and brain fog, depression and anxiety and sleep disorders. It was agreed that these are among the symptoms most likely to worsen the patient's condition from the patient's perspective. Not all of these symptoms are included in the usual assessment indices, such as the ESSDAI* or ESSPRI*. However, the different impairments experienced by patients should be taken into account when defining and assessing a flare. In addition, it is also important to clarify and mention that a flare is not necessarily systemic. It may relate to only one of the symptoms, e.g. the dryness, without necessarily leading to a worsening of the other symptoms.

Results: The PAG agreed on the following definition: "A flare is the temporary and sudden onset of symptoms that become significantly worse before resolving and, on average, last at least 3 days."

Conclusion: The PAG considers agreement on how the term "flare" is used to be important for clinical trials as well as for patients and clinical management. For trials, use of a tool to measure flares as a patient reported outcome (PRO) would add value in gauging the patient experience in a global way and provide another potential index for evaluating treatments. Further discussion and validation is needed, however, as the high variability and subjectivity of symptoms makes establishing such a tool especially difficult. Nevertheless, patients need to be aware of flares so they can identify potential organ damage and obtain the best care possible. A flare assessment tool can allow the patient to be better informed, to better monitor their condition and to facilitate communication with their doctor.

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[2] EULAR Sjögren's syndrome disease activity index (ESSDAI)
[3] EULAR Sjögren's Syndrome patient reported index (ESSPRI)

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1733-PARE SHARED DECISION MAKING ABOUT RMD TREATMENT: WHICH VALUES MATTER TO PEOPLE WITH A MIGRATION BACKGROUND?

Keywords: Outcome measures, Patient reported outcomes, Treat to target

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Background: In the Netherlands, Shared Decision Making (SDM) between healthcare professionals and patients with a migration background stays behind, when compared to SDM with patients with a Dutch background. This can be due to the fact that patients with a migration background might hold different values when deciding on treatment. Values they find difficult to express. Values that health care professionals find difficult to talk about or understand.[1] Research into the values of inflammatory arthritis patients (IA) with a migration background will help health care professionals to better take these values into account, when deciding together on a best fitting treatment.

Objectives: In the Netherlands:

• Which values are important to people with IA and a 1st or 2nd generation migration background when deciding on the best fitting IA treatment?

• Do these values differ from those of the general Dutch population with IA?

Methods: To get an idea of the values that play a role in the choice of treatment, the National Association ReumaZorg Nederland (RZN) conducted research in 2020 amongst people with IA. It resulted in a list of most important values that was published[2]. People with a migration background were underrepresented in the group of respondents. That is why RZN organized a focus group session in 2021 together with the Erasmus Medical Center (MC) in Rotterdam amongst 6 people with IA and a 1st or 2nd generation migration background. The focus group gave an insight into the values that play an important role, when choosing IA treatment. In order to verify these values within the broader migrant community of people with IA, RZN set out a questionnaire based on outcomes from the focus

group and previous research[2] in June 2022. The questionnaire consisted of 56 values that could be scored on a 6-point Likert scale. Patient research partners of RZN provided feedback on the questionnaire. The approved questionnaire was then translated into Polish, Arabic, Turkish, English and Spanish. After translation, the questionnaire was made available through a unique online link. Adult patients, treated at the Erasmus MC with IA and a migration background, were invited to complete the questionnaire during their visit with their rheumatology nurse. Twenty-four patients completed the questionnaire.

Results: • Values that were scored as (very) important by most respondents focused on the effectiveness of IA treatment (on pain, fatigue, inflammation and on physical functioning). Respondents also placed great importance on clear information about IA treatment. Values with regards to the healthcare professional (someone: who helps to make a decision about treatment, who is involved, who has time and who listens) were also perceived as important. Finally, respondents placed great value on their wish not to depend on other people for their daily activities.

• Values amongst people with IA and a migration background were ranked very similarly to the values amongst people with IA in the general study in 2020[2]. Due to differences in the way values were scored in both studies, no statistical conclusion can be drawn from this.

Conclusion: Values with regard to the effectiveness of treatment and the supporting role of the healthcare professional are experienced as very important by patients with IA and a 1st and 2nd generation migration background. Healthcare providers should be aware of this and adapt their communication, if necessary.

A safe environment is key for the willingness of people with IA and a migration background to participate in research. The question is if this safe environment is possible in a hospital setting.

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AB1734-PARE THE JOURNEY TOWARD DISEASE MANAGEMENT: A NATIONAL SURVEY OF GOUT PATIENTS SEEN BY A RHEUMATOLOGIST

Keywords: Patient information and education, Quality of care, Gout

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Background: The purpose of this survey is to assess the multifaceted impact of gout patients' physical and emotional wellbeing prior to their seeking treatment from a rheumatologist.

Objectives: The objective of the survey is to better understand patients' experience related to obtaining a gout diagnosis and care seeking for their symptoms. This information is helpful in that it can improve rheumatologists' understanding of their patients' experience and provide better patient-centered care.

Methods: An online survey of self-reported, physician-diagnosed individuals with gout was conducted between May and July 2022. The 30-question survey collected responses pertaining to frequency of gout flares, point of care location(s), point of care provider(s), comorbidities, and a 4-point Likert-scale (strongly agree, agree, disagree, strongly disagree) on experiences living with gout. Sociodemographic data was also collected.

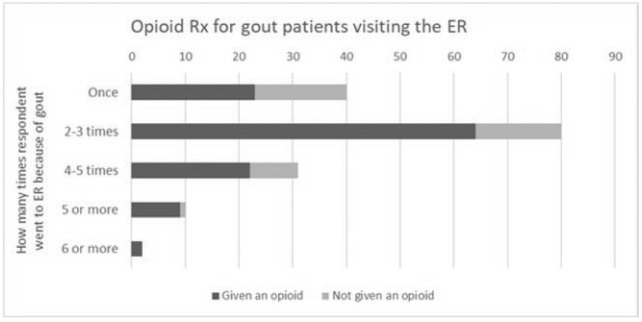
Results: At total of 355 self-reported, physician diagnosed individuals participated in the survey; results presented are unweighted. Among respondents, 88% reported a gout flare has negatively impacted their ability to do their job, care for loved ones, participate in activities, remain socially active, and/or enjoy their life (Table 1). Just four in 10 participants saw a rheumatologist within a year of first suffering with symptoms of gout. It took 37% of patients 2-5 years, 13% 6-10 years, and 6% more than 10 years to see a rheumatologist for their gout. Moreover, 56% of respondents reported to have visited multiple health care providers without getting a clear answer about their gout, and 46% saw multiple health care providers without getting an effective treatment plan. Close to half of respondents reported having gone to the emergency department because of a gout flare, and of those, about three-quarters were prescribed an opioid for pain relief (Graph 1). Additionally, 58% reported anxiety, depression or hopelessness because of gout pain. However, after seeing a rheumatologist, 82% reported their gout is getting better, and they are learning how to manage it – even with other co-morbid conditions. A full 84% of respondents reported living with at least one co-morbid condition, the most common being high blood pressure (48%), cardiovascular conditions (30%), diabetes (28%), obesity (27%), kidney disease 20% and kidney stones (19%). The male to female distribution of gout patient respondents is 64% male, 36% female. Most respondents (58%) identified as white, 16% as Black and 15% as Hispanic with the remaining 11% representing other racial/ethnic groups. The mean age was 43, and 42% are employed full-time. Roughly six in 10 are married and 43% have children under the age of 18.

Conclusion: Survey results demonstrate a substantial burden of disease has been placed on those suffering with undiagnosed, misdiagnosed or undertreated gout. The survey results confirm that many of those suffering with gout spend years searching for a diagnosis. Results also elucidate patients' struggle to connect with a health care provider who is knowledgeable about gout and to receive an effective treatment plan for managing their gout. Without appropriate care, patients continue to live with the pain and receive opioids to urgently mask symptoms. As opioids do not actually treat gout, these patients are not receiving appropriate care. This is unfortunate as gout can be successfully managed by working with knowledgeable health care providers and adhering to a plan of care.

Table 1.

Gout flares have impacted my ability to…	Percentage affected
Do my job	41%
Care for my children, spouse, or other family members	30%
Participate in hobbies or community activities	50%
Maintain friendships and stay socially active	28%
Enjoy my life	56%
Other	6%
None of the above	12%

Note: Respondents could select multiple categories.



Graph 1.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1735-PARE DIETARY PRACTICE AND CHRONIC INFLAMMATORY RHEUMATIC DISEASES. WHAT DO OUR PATIENTS?

Keywords: Diet and Nutrition, Inflammatory arthritides

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Background:

Objectives: Patients show interest in non-drug approaches in particular by the mode of feeding. The objectives of this study are to evaluate the prevalence of dietary changes among patients with.

chronic inflammatory rheumatism, describe their practices and food designs, to compare them between the different subgroups of patients as well as describe the potential impact on care and well-being of the patients.

Methods: Questionnaire survey of patients followed in the Rheumatology department of Poitiers University Hospital, France, for rheumatoid arthritis or spondyloarthritis, including psoriatic arthritis.
Results: Two hundred and three patients were included (112 rheumatoid arthritis, 91 spondyloarthritis, including 25 psoriatic arthritis). They are 45.3% to have been informed of beneficial dietary practices, and 34.5% to have discussed the subject with a professional (13.3% with a rheumatologist). The prevalence of dietary changes is 42.9% (IC95%: [36% - 50%]), and 14.77% of patients were on a diet or taking a dietary supplement at the time of the survey. Diets mainly tested are the reduction in the consumption of dairy products, Seignalet-type diets, fasting, the gluten-free diet and the reduction in meat consumption. For the majority of patients, there was no improvement in pain, fatigue, general condition or reduction in drug intake, except with fasting (n=9) for which a decrease in drug intake was reported at 66.7% (n=7). The discussion on the subject with a health professional is a factor associated with the modification of dietary practices (p=0.001).
Conclusion: Changes in dietary practices concern nearly half of patients, but are only slightly in line with recent recommendations. The information by the physician is often absent and deserves to be improved.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1736-PARE CHALLENGES FOR PATIENTS WITH RMD'S IN BULGARIA DURING THE COVID-19 PANDEMIC

Keywords: COVID, Rheumatoid arthritis, Spondyloarthritis

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Background: The Covid-19 pandemic has put patients with rheumatic diseases in front of a number of obstacles that had to be solved together with Bulgarian rheumatologists. The lockdowns and restrictive measures have made it difficult for people with rheumatic diseases to have access to timely hospital and pre-hospital care. A number of digital solutions have been implemented to address these issues.
Objectives: To highlight the problems that patients with rheumatic diseases had during the Covid-19 pandemic; access to rheumatologists and the effectiveness of hospital and pre-hospital care during the pandemic, access to treatment, changes of treatment; communication between physicians and patients, the impact of the pandemic on work, social contacts, hobbies.
Methods: An anonymous survey was conducted online and by telephone. The survey was developed by Medical university, Plovdiv, University hospital "Kaspela":, Plovdiv, Bulgarian Association for Musculoskeletal Ultrasound, Bulgarian organization for people with rheumatic diseases; Association for patients with autoimmune diseases. Number of participants: 1205 patients with RMD's. Age range: 18-82
Results: Face to face meetings with doctors have been limited during the pandemic. Visits to the rheumatologist's office are significantly reduced and phone, email, text messaging, online consultations were preferred as communication channels. Before the pandemic, 76% of respondents most often communicated with their physicians by visiting their practice, during the pandemic their relative share decreased to 46%, with a significant difference of 30% Phone consultations: patients using this type of communication increasing from 38% before the pandemic to 56% during the pandemic, a significant difference of 18% The percentage of patients who communicated via text or email rises from 10% to 17 %. It has become apparent that Digital transformation is needed and patients and physicians should work together to achieve it and to be established in Bulgaria. 245 patients reported a change in their treatment. Of these: (30%) reduced the dose of their medications, 119 (49%) increased the dose and the remaining 55 (21%) stopped their therapy. From the responses of the respondents, it is clear that 71% have not experienced a change in their work during the COVID-19 pandemic, 17% have worked from home. From the responses of the respondents, it is clear that 71% have not experienced a change in their work during the COVID-19 pandemic, 17% have worked from home, 4% have been fired, 3% have left their jobs due to the risk of their health and 5% left their jobs for other reasons.
Conclusion: The Covid-19 pandemic has shown that the digital transformation in rheumatology care can be an efficient alternative to some of the services offered to patients with rheumatic diseases in Bulgaria (especially secondary examinations and therapy monitoring examinations). The results of the conducted survey could be used to support digitization in healthcare in Bulgaria. Very important was the collaboration between the patient organizations and the Bulgarian Association for Musculoskeletal Ultrasound, Medical University, Plovdiv and the rheumatologists from University hospital "Kaspela" Plovdiv.
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Bulgarian Association for Musculoskeletal Ultrasound.
Disclosure of Interests: None Declared.
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AB1737-PARE IN WHAT EXTENT DO RHEUMATOLOGISTS DISCUSS PHYSICAL ACTIVITY (PA) WITH THEIR PATIENTS AFFECTED BY KNEE OSTEOARTHRITIS AND WHAT ARE THE PATIENTS' EXPECTATIONS?

Keywords: Patient information and education

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Background:
Objectives: To Assess the level of communication between patient and rheumatologist and to identify patients' expectations and needs in terms of PA.
Methods: This is a cross-sectional study conducted on 130 Knee osteoarthritis patients. Physical activity was measured using the IPAQ-SF (the international physical activity questionnaire - short form). We asked patients if their rheumatologist has ever discussed or encouraged them or even explained how to do adapted PA. Patients' preferences for PA practice were collected by specifying if patients preferred to practice it at home or outside, single or in groups. Finally, we also asked them about their needs for both audiovisual supports on adapted physical activity and participation in educational workshop.
Results: The mean age of the patients included was 59.9+/-10 years with 110 (84.6%) females. The PA level was low with a mean IPAQ-SF score of 130 (0.500) MET.Min/week. The topic of PA was discussed by rheumatologists with 49.2% of patients. Rheumatologists advised patients to practice adapted PA and show them how to practise it, in respectively 40 and 39.8% of cases. Figure 1 illustrated patients' expectations on PA.

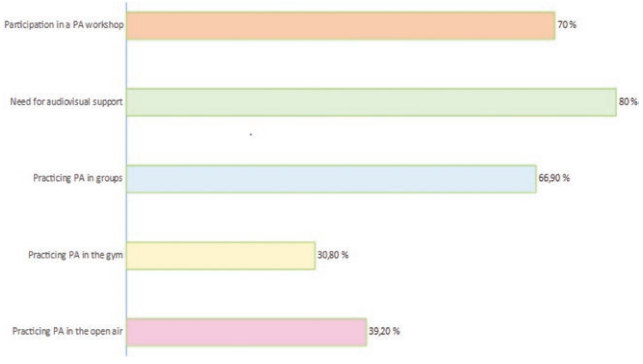


Figure 1. Patients' preferences and expectations on physical activity.

Conclusion: This study shows a lack of rheumatologist-patient communication on PA and a significant need for PA education. Hence there shoud be greater involvement of rheumatologists in patient education about physical activity to fight against sedentary behavior in Knee Osteoarthritis patients.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1738-PARE RELATIONSHIP BETWEEN DEPRESSION, ANXIETY, AND STIGMATIZATION IN RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Mental health, Cognitive Function

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Background: Depression and anxiety are common comorbidities associated with rheumatoid arthritis (RA). Despite their impact on patients' quality of life, their detection is often neglected.

Objectives: We aimed to assess the anxiety state in patients with RA and to search for associated factors.

Methods: We conducted a cross-sectional study that included patients followed for RA. Patient and disease data were recorded. Patients completed the Hospital Anxiety and Depression Scale (HAD) [1] and the Stigma Scale for Chronic Illnesses-Short Form (SSCI-8) [2] during their day hospital visit or consultation. Disease activity by DAS28-CRP and functional impairment by the HAQ score were calculated.

Results: There were 100 patients. They were mostly women (81%) with a mean age of 55.33±10.08 years [25-76]. Concerning professional status, 61.8% were unemployed, 26.5% were employed, and 11.6% were retired. The mean disease duration was 14.21±10.10 years [1-46]. The mean DAS28-CRP was 3.81±1.56 [0.12-6.90]. The mean HAQ score was 0.91±0.64 [0-2.4]. The mean anxiety score was 7.6±3.2 [1-15]. A definite anxiety state was noted in 21% of patients. The mean depression score was 10.1±3.1 [3-16]. A definite depressive state was noted in 56% of patients. The mean SSCI-8 score was 17.85±6.02 [8-32]. None of the parameters related to the patient, disease activity and functional impairment were correlated with anxiety and depression. The presence of anxiety was influenced by the number of swollen joints (p=0.037). The stigma score was statistically significantly greater in the presence of depression (19.3±6.2 vs 16±5.2, p=0.006). It was also correlated with disease activity (p=0.034, r=0.244). There was no association between stigma scale/HAQ (p=0.754) and stigma scale/anxiety (p=0.137).

Conclusion: According to the results of our study, depression was frequently present in patients followed for RA (56%). Moreover, the stigma is finely related to this comorbidity. This encourages the systematic psychological management of chronic pathologies such as RA.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1739-PARE COVID-19 PANDEMIC: THE IMPACT ON PSORIATIC DISEASE PATIENTS' LIFE

Keywords: Real-world evidence, COVID, Psoriatic arthritis

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Background: In last years, "psoriatic disease" identifies a complex pathology, characterized by the involvement not only of the joints but also of other organs and systems such as skin, eyes, bowl, cardiovascular system. About 30% of patients with psoriasis may manifest involvement of the musculoskeletal system, involving joints in its various anatomical components and enthesis. Psoriatic arthritis and psoriasis have certainly been – during the pandemic - among the most neglected pathologies from the care perspective.

Objectives: AMaR Piemonte (Rheumatic Patients Association of Piedmont) and ANAP (National Association "Friends for the skin") due to the number of phone calls received during the first stages of pandemic and interacting with rheumatologists, dermatologists and psychologists made a specific survey to assess the impact of the pandemic both on people suffering from psoriatic disease and by their caregivers. In this abstract we focus our attention to the "caregivers world".

Methods: A specific questionnaire for caregivers, developed by a dermatologist and a psychologist and aimed to assess the experience during the pandemic (feelings, changes in care, interpersonal relationships, possible recourse to the intake of "comfort goods" such as smoking, alcohol, food, substances, etc.) was administered in parallel with that for patients online on the websites and social media of the two associations from mid-October to mid-December 2020 and from mid-January to mid-March 2021.

Results: 251 were the complete answers, mainly (84%) provided women who cared for family members (75%) suffering from Psoriatic Arthritis (37%). The average age was 46 years and people reported dealing with people with moderate (46%) or severe (41%) disease, whose symptoms worsened in 69% Impotence, anxiety, stress, sadness and frustration are the emotions most often reported by the caregiver who, moreover, believes they are also experienced by the assisted person. The assistance is worsened in 59% of cases, especially due to the inability to contact the doctor (16%) and undergo examinations/ checks (35%).

Conclusion: The COVID-19 pandemic has deeply changed the life of caregivers, mainly women of working age and patient's relatives or partners. Caregivers and patients, however, developed a full agreement, manifesting the same emotions and resorting to refuge substances in overlapping percentages. The need not to suffer interruptions or changes in care by the attending physician is felt with greater intensity by caregivers, perhaps due to they have no specific preparation to assist their loved ones.

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Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1741-PARE THE IMPACT OF THE DISEASE'S ANNOUNCEMENT ON RHEUMATOID ARTHRITIS PATIENTS

Keywords: Rheumatoid arthritis, Patient information and education

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Background: Rheumatoid arthritis is a chronic disease that can cause irreversible joint damage and significant disability [1]. The announcement of this diagnosis remains one of the most unpleasant moments in the medical practice for both patients and caregivers. For the physician, whose primary mission is to provide relief, knowing that it may cause psychological distress is a challenging task.

Objectives: We aimed to study the impact of the disease's announcement on rheumatoid arthritis patients.

Methods: We conducted a cross-sectional study including patients fulfilling the American Congress Of Rheumatology/ European League Against Rheumatism (ACR EULAR) 2010 criteria. We collected epidemiological, clinical, biological (C-reactive protein: CRP, erythrocyte sedimentation rate (ESR), immunological status (rheumatoid factor RF and anti-citrullinated protein/peptide antibody ACPA), disease activity index (The Disease Activity Score 28 DAS 28). Patient's experience during the announcement of diagnosis was assessed using a questionnaire.

Results: Thirty patients were enrolled. There were 25 women and five men. The mean age was 67.10 ± [29-75]. The mean duration of the disease was 10.41 ± [2.5-38] years. The mean DAS 28 VS was 4.5 ± [1.36-6.27]. Among 30 patients, 66.67 % received the news with anxiety, particularly because of the chronic nature of the disease and possible multi-organ involvement. Nine patients were reassured and felt less anxious for having understood the cause of their pain. Seventy patients (56.67 %) found that the doctor was empathetic and tried to explain the therapeutic alternatives reducing their stress. However, 30% of patients (n=9) found the announcement shocking and would have preferred a gradual approach.

Conclusion: Our study showed stress and anxiety are common feelings for most patients, highlighting the importance of a patient-centered approach to improve initial acceptability of. their disease.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1742-PARE **HEALTH INFORMATION UTILIZATION IN RHEUMATOID AND PSORIATIC ARTHRITIS**

Keywords: Patient information and education, Psoriatic arthritis, Rheumatoid arthritis

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Background: Technology has facilitated widespread general access to health information publicly. However not all health information available for consumption is accurate, reliable, updated, and of equal value to people seeking to be informed advocates of their own health. This cross-sectional study sought to establish the preferred resources patients with rheumatologic conditions seek out for health information. This study provides recent evidence to inform patient education, open dialogue, with the hope to improve clinical practice and patient outcomes.
Objectives: To describe utilization of health information preferences to inform physician-patient shared decision-making and best clinical practice.
Methods: From December 2019 to March 2020, 236 Rheumatoid Arthritis (RA) and 43 Psoriatic Arthritis (PsA) patients receiving care at an academic rheumatology practice in the USA were enrolled in this study. Subjects were provided with a brief, voluntary, and anonymous Qualtrics survey which gathered data on health information utilization, willingness to discuss information gathered with physicians, and desire for resources to be provided.
Results: Modern technology has provided multiple ways for patients to gather additional health information of variable accuracy. This information impacts patient willingness to adhere to clinical recommendations. These data show that patients seek open and honest discussion of health information gathered from other sources. A substantial percentage of patients also desire guidance towards reliable online health resources from their physicians.
Conclusion: Modern technology has provided multiple ways for patients to gather additional health information of variable accuracy. This information impacts patient willingness to adhere to clinical recommendations. These data show that patients seek open and honest discussion of health information gathered from other sources. A substantial percentage of patients also desire guidance towards reliable online health resources from their physicians.

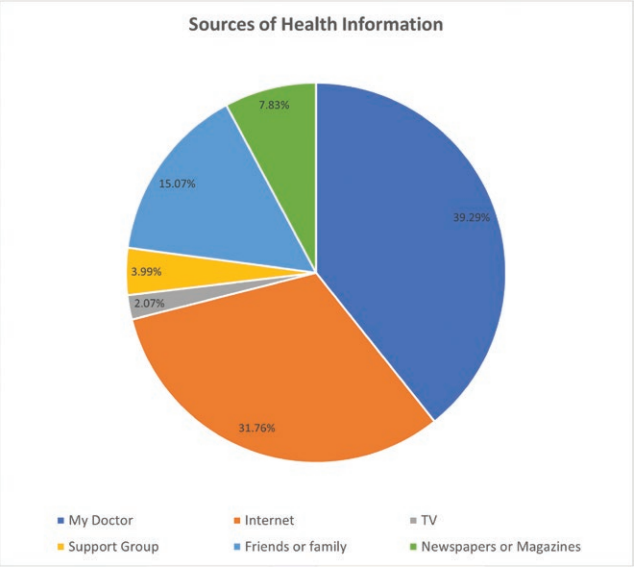


Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6527

AB1743-PARE **PUBLIC INTEREST IN LUPUS IN AFRICA**

Keywords: Systemic lupus erythematosus, Patient information and education

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Background: Accessibility to internet has allowed people to have a better knowledge of Systemic lupus erythematosus (SLE), however, this interest in doing research is influenced by several factors, including socio-economic conditions. Google Trends (GT) is the most popular tool for examining online behavior because it provides information regarding trends and changes in online interest at certain times during a particular period.
Objectives: The aim of this study was to use the Google Trends data to evaluate the public interest in Systemic lupus erythematosus (SLE) in different African countries and to assess people's interest in Africa comparing to worldwide.
Methods: Google Trends provides the relative interest of Google Searches (RSV), on a range of 0–100. We analysed a large amount of data generated by Google Trends concerning the search of the word 'lupus' in a 7-year web-based research (2016-2022) in Africans' countries. Student's t-test was used to compare means. Analyses were performed with SPSS 21.0. P values less than 0.05 were considered statistically significant.
Results: Googling "lupus" was variable depending on the country. The mean annually research volume (RSV) in Africain countries was 18.20±3.92. Annual RSV was more important in Morocco50.89±16.52, Algeria 49.19±23.84. There was a significant difference in the mean annually research volume between African countries and all over the word (versus 50.86± 14.58, p<10-3). (Figure1)

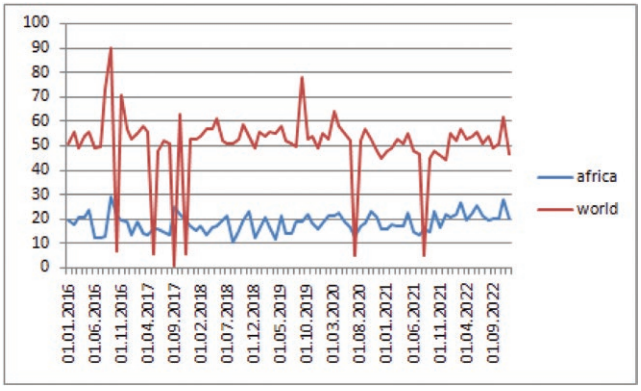


Figure 1. Search volume of lupus variation in African Countries Versus all over the world s from 01.01.2016 to 01.09.2022

Conclusion: Google Trends allows us to find useful information about SLE on the internet. However lack of internet coverage, low socio-economic level and low education level can explain this difference between African countries and the rest of the world.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6096

AB1744-PARE **TREATMENT ADHERENCE IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) DURING THE COVID-19 PANDEMIC**

Keywords: COVID, Rheumatoid arthritis, Patient reported outcomes

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Background: During the last 2 years, the SAR COV2 pandemic has impacted the lifestyle, health care, physical and psychological health status of people with rheumatic diseases. In the REUMAVID study, almost half of the respondents stated that their state of health had worsened during the pandemic[1]. It's known that aspects such as fear, job loss, social isolation, uncertainty about their treatments, worsening of symptoms due to the interruption of treatment and hospital visits, increased his fatigue and pain[2]. Treatment adherence estimates in patients with RA are usually low (Between 30 and 80%)[3]. Adherence lack has been associated with worsening symptoms and increased disability[4].

Objectives: The aim of this work is to evaluate SARS COV2 pandemic impact on the adherence perception in a cohort of patients with RA and their clinical associations.

Methods: Descriptive cross-sectional study; included patients ≥18 years old with RA (ACR/EULAR 2010 criteria), between June 1 and July 31, 2022 who gave their written consent to perform the questionnaire. Data sociodemographic, socioeconomic level (Graffar modified), clinical, laboratory, treatments, previous COVID-19 infection and vaccination status were consigned. Activity was evaluated by DAS28-PCR and functional ability with HAQ-II. Questions about the perception of the impact of the pandemic on adherence, follow-up, health status deterioration or fear of continuing treatment were included. They were measured by a visual analogue scale, with 0 being no impact and 10 being the maximum. These answers were compared with adherence measured by the Compliance Questionnaire for Rheumatology (CQR5).

Results: Sixty nine outpatients with RA were included. 45 patients (65%) did not perceive adherence changes during the pandemic while 24 (35%) perceive some degree of adherence disturbances. Sociodemographic characteristics are detailed in Table 1. Having an independent laboral status and the modification or suspension of work activity was statistically associated with the perception of impaired adherence (p=0.04 and 0.01 respectively). Patients with a perception of impaired adherence had significantly higher means in the VAS of affected follow-up, deterioration in their health status, and fear of infection (p= <0.001, <0.001 and 0.04 respectively). DAS28-PCR, HAQ-II, ERS and CRP were also significantly higher in this group (p= 0.002, 0.005, 0.01 and 0.04 respectively). No association was found between the perception of adherence disturbance and adherence measured by CQR5 (p= 0.20).

Conclusion: The SARS COV2 pandemic has a great impact on adherence, rheumatological follow-up and quality of life of patients with RA. Although the perception of adherence disturbance during the pandemic period is a subjective parameter, we found a significant association between this perception and higher rates of suspension or modification of work activity, greater disease activity, functional impairment, and higher acute phase reactants. Studies with a larger number of patients are needed to corroborate these findings.

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Table 1. Baseline characteristics. Adherence perception during pandemic

	Disturb n = 24	Not change n=45	OR	CI	p
Women n (%)	18 (75)	32 (71.11)	1.21	0.35-4.60	0.73
Age x̄ (SD)	53.58 (10.45)	55.31 (12.10)	n/a	n/a	0.55
Marital status (%)					
Single	5 (20.83)	6 (13.33)	1.71	0.36 - 7.66	0.41
Married	12 (50)	26 (57.78)	0.73	0.24-2.22	0.53
Concubinage	2 (8.33)	5 (11.11)	0.72	0.06-4.92	0.71
Widowed	2 (8.33)	5 (11.11)	0.72	0.06-4.92	0.71
Divorced	3 (12.50)	3 (6.67)	2	0.24-16	0.41
Graffar modified scale n (%)					
Strata 2	2 (8.33)	4 (8.89)	0.93	0.07-7.11	0.93
Strata 3	10 (41.67)	15 (33.33)	1.42	0.45-4.44	0.49
Strata 4	12 (50)	26 (57.78)	0.73	0.24-2.22	0.53
Place of residence n (%)					
CABA	9 (37.50)	16 (35.56)	1.08	0.33-3.39	0.87
BsAs	15 (62.50)	28 (62.22)	1.01	0.32-3.23	0.98
Other provinces	NA	1 (2.22)	n/a	n/a	n/a
Laboral status n (%)					
Employee	10 (41.67)	16 (35.56)	1.29	0.41-3.99	0.61
Independent	**6 (25)**	**3 (6.67)**	**4.66**	**1.05-20.74**	**0.04**
Student	NA	1 (2.22)	n/a	n/a	n/a
Housewife	6 (25)	13 (28.89)	0.82	0.21-2.83	0.73
Retired	1 (4.17)	9 (20.00)	1.33	0.33-4.97	0.07
Pensioner	1 (4.17)	3 (6.67)	0.60	0.01-8.14	0.67
Current smoker n (%)	8 (33.33)	9 (20.00)	2	0.55-7.04	0.22
Smoker previously n (%)	5 (20.83)	14 (31.11)	0.58	0.14-2.09	0.36
BMI x̄ (SD)	30.15 (7.81)	28 (4.99)	n/a	n/a	0.16
Disease duration in years Me (ICR)	8 (12.5)	11 (11)	n/a	n/a	0.30
ERS Me (ICR)	**24,5 (32)**	**19 (13)**	**n/a**	**n/a**	**0,01**
CRP Me (ICR)	**6,47 (10,77)**	**3,91 (7,2)**	**n/a**	**n/a**	**0.04**
DAS 28- PCR x̄ (SD)	**3.72 (1.60)**	**2.58 (1.30)**	**n/a**	**n/a**	**0.002**
HAQ x̄ (SD)	**1.6 (0.85)**	**0.99 (0.84)**	**n/a**	**n/a**	**0.005**
Suspended or modified work activity due to pandemic n (%)	**17 (70.83)**	**18 (40)**	**3.64**	**1.12-12.41**	**0.01**

Table 1. Baseline characteristics. Adherence perception during pandemic

	Disturb n = 24	Not change n=45	OR	CI	p
Perception of impact by the COVID-19 pandemic (VAS)					
Follow-up disturbance x̄ (SD)	**5.83 (3.27)**	**2.48 (2.38)**	**n/a**	**n/a**	**<0.001**
Health decline x̄ (SD)	**4.91 (3.51)**	**1.37 (1.21)**	**n/a**	**n/a**	**<0.001**
Fear of getting infected x̄ (SD)	**6.08 (4.04)**	**4.04 (3.81)**	**n/a**	**n/a**	**0.04**
CQR5 x̄ (SD)	18.70 (3.09)	19.37 (1.26)	n/a	n/a	0.20
Current treatment n (%)					
MTX monotherapy	9 (37.50)	12 (33.33)	1.61	0.49-5.35	0.35
MTX ≠ monotherapy	1 (4.17)	2 (4.44)	0.93	0.01-18.87	0.95
csDMARD plus MTX	3 (12.50)	12 (26.67)	0.39	0.06-1.72	0.17
csDMARD plus (without MTX)	1 (4.17)	1 (2.22)	1.91	0.02-153.51	0.64
bDMARD monotherapy	1 (4.17)	NA	n/a	n/a	n/a
bDMARD plus MTX	8 (33.33)	7 (15.56)	2.71	0.71-10.33	0.08
bDMARD plus ≠ MTX	NA	1 (2.22)	n/a	n/a	n/a
tsDMARD monotherapy	1 (4.17)	1 (2.22)	1.91	0.02-153.51	0.64
No treatment	NA	6 (13.33)	n/a	n/a	n/a
Current glucocorticoids n (%)	13 (54.17)	26 (57.78)	0.86	0.28-2.64	0.77
COVID 19 infection n(%)					
Mild	9 (37.50)	15 (33.33)	1.2	0.37-3.76	0.72
Moderate	3 (12.50)	1 (2.22)	6.28	0.45-337.23	0.08
Severe	NA	NA	n/a	n/a	n/a
Never	11 (45.83)	26 (57.78)	0.61	0.20-1.87	0.34
Unknown	1 (4.17)	3 (6.67)	0.60	0.01-8.14	0.67
Treatment suspension for COVID-19	7 (29.17)	6 (13.33)	2.67	0.65-11.09	0.10
Vaccination status for SARS COV 2 n (%)					
4 dose	8 (33.33)	18 (40)	0.75	0.22-2.35	0.58
3 dose	15 (62.50)	23 (51.11)	1.59	0.51-5.02	0.36
2 dose	n/a	3 (6.67)	n/a	n/a	n/a
1 dose	n/a	n/a	n/a	n/a	n/a
No vaccination	1 (4.17)	1 (2.22)	1.91	0.02-153.51	0.64

bDMARD: Biological disease-modifying antirheumatic drugs; BMI: Body Mass Index; BsAs: Buenos Aires; CABA: city of buenos aires; CI: Confidence interval; CRP: C reactive protein; CQR5: Compliance Questionnaire for Rheumatology; COVID-19: coronavirus disease 2019; csDMARD: conventional synthetic disease-modifying antirheumatic drugs; DAS28: disease activity score; ERS: erythrocyte sedimentation rate, HAQ: Health Assessment Questionnaire; IRC: interquartile range; Me: median, MTX: methotrexate; SARS COV2: severe acute respiratory syndrome coronavirus 2; SD: standard deviation; tsDMARD: targeted synthetic disease-modifying antirheumatic drugs; VAS: visual analog scale.

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Disclosure of Interests: None Declared.

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AB1745-PARE **ROLE OF DIET IN INFLUENCING RHEUMATIC DISEASE ACTIVITY: A TUNISIAN PATIENTS SURVEY**

Keywords: Spondyloarthritis, Diet and Nutrition, Rheumatoid arthritis

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Background: The possible influence of diet on rheumatic disease (RD) is a controversial issue. However, rheumatic patients often ask for specific diet because they experience change in joint symptoms after taken some food. Few studies have been conducted regarding patients' perceptions of the influence of diet and fasting on their RD. None of such studies have been conducted so far in countries.
Objectives: The main purpose of this study is to survey patients regarding diet and RD symptoms.
Methods: This is a survey based on a questionnaire that included patients followed for rheumatoid arthritis (RA) (ACR/EULAR 2010 criteria) and spondyloarthritis (SA) (ASAS 2009 criteria), in remission or low disease activity, who presented to the rheumatology department. We didn't include patients with inflammatory bowel or malabsoption diseases or current smokers. Socio-demographic data, co-morbidities, and data of RD (disease duration, disease activity (Disease Activity Score (DAS28) and Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) and medication (Disease-modifying antirheumatic drugs (DMARDs)) were recorded. The questionnaire consisted of 7 major questions with variety of sub-questions. Patients were asked whether they believe diet had a major role on the RD onset, if they have experienced aggravation or improvement of their symptoms with food intake, and if the answer was yes, then they were asked to name the food item. The patients were also asked if they have changed their dietary habits since the diagnosis of RD, if they believe that healthy dietary habit may improve their disease, and if fasting relieve their disease.
Results: We enrolled 39 RA (34 female) and 22 SA (2 female) patients with respective mean age of 52.74±11.31 years and 54.54±11.2 years. Among patients with RA, 53.8% and 22.7% had primary school level, 45.5% of SA patients had secondary educational level. Half of RA and SA patients had comorbidities: 56.4% and 54.5% respectively. The mean disease duration was 8.68±6.6 years and 14.77±9.1 in RA and SA respectively. Half of patients (53%) with RA had obesity and overweight and 40.9 % of SA. The mean DAS28 was 2.06±0.71 and the mean ASDAS-CRP was 1.28±0.41. The majority of RA patients were on conventional synthetic DMARDs (82.1%) and SA patients on biologic (72.7%). Among RA patients, 64% believed that diet have some role in the onset of their RD and 68 % of SA. The main food incriminated were red meat in 64 % and 68%, fried food in 31% and 27% and pasta in 23% and 32% of RA and SA respectively. In addition, 84% of RA and 91 % of SA patients reported improvement of their joint disorder by consuming certain food and 90 % of RA and 91 % of SA reported aggravation of their disease. Most often the positive influence was assigned to green leavy vegetables in 74% and 86%, citrus in 67% and 77%, olive oil in 26% and 32% of RA and SA patients respectively. In our study, red meat was the major constituent of diet which aggravated the symptoms in RD as 87% and 91 % of RA and SA patients respectively, reported aggravation of symptoms with red meat. Modifying in dietary habit occurred in 12.8% of RA and 4.5% of SA to improve their disease activity. The majority of patients thought that healthy dietary habit could be a disease therapy: 94.9% of RA and 95.5 % of SA. Only 5.1% of RA patients reported receiving dietary advice from their rheumatologist and none of the SA patients, while an average of 80% of RA and SA patients showed interest in such discussion. All patients reported relief of joint symptoms after fasting Ramadan.
Conclusion: In this real-life population, there is an ultimate need to investigate the nutritional states in patients with RD, since certains food may improve or aggravate joint symptoms. Red meat release alert signals on RD health patients. Studies of the molecular mechanisms behind these phenomena attract increasing attention.
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AB1746-PARE THE CORRELATION OF FUNCTIONAL DISABILITY AND MENTAL DISORDERS IN PATIENTS TREATED FOR SPONDYLODISCITIS

Keywords: Patient reported outcomes, Infection-related RMDs, Quality of life

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Background: Although it still remains a rare disease, spondylodiscitis has been on the rise in the past decades. Early diagnosis can be difficult, but Improved diagnostic techniques and modern treatments have reduced patient mortality. However, studies reporting the outcome of spondylodiscitis are scarce.
Objectives: To assess the influence of functional impairment on mental health in patients surgically treated for spondylodiscitis.
Methods: A prospective study was carried out on patients treated for spondylodiscitis over a two-year period at a single spine center. The socio-demographic data, clinical, radiological, biological and therapeutic parameters were collected. A questionnaire was conducted on all eligible patients with the hospital anxiety and depression scale: HAD and the Oswestry disability index: ODI. All data was collected after patient consent and was analyzed using the SPSS statistical package.
Results: Thirty –six patients were selected for the study, with a sex ratio (M/ F) of 1.57. The average age was 56 [18_73]. 22% had comorbidities: 16% diabetes, 6% psychiatric illnesses. 22% were smokers. 72% had a sedentary lifestyle. Mycobacterium tuberculosis was the predominant pathogen(33%) followed by Staphylococcus aureus (22%). Culture was negative in 5 % of patients. Of these, 33% patients received antituberculosis medical treatment. The lumbar spine was the most frequent level of spinal focus (55%). 22% of patients had more than one focus in the spine. 54% of patients had neurological impairment: paraplegia 33%, sensory deficit 11% and confusion 6%. All patients were treated surgically: 32% internal corset, 31% fixation, 20% arthrodesis, 11% corporectomy, 6% laminectomy. The mortality rate was 6%. Average HAD score was 13.3[0-40]: depressive dimension: 6.6[0-20], anxiety dimension 6.8[0-20], with scores indicating very likely depression and anxiety in 22% and 25 % of patients, respectively. Mild, moderate and severe functional disability was noted in 44%, 18% and 6%, respectively, according to the ODI score. In our series, there were positive correlations between gender, VAS (visual analog scale) spinal pain and ODI score: p=0.025 and p=0.007, respectively. In the same way, there were positive correlations between the ODI score and the HAD depression dimension (p=0.001) and the anxiety one (p=0.001).
Conclusion: Two years after surgery, patients treated for spondylodiscitis have significant functional disability. Anxiety and depression, mainly due to interaction with the disability level, are two comorbidities to consider in spondylodiscitis. Screening and psychological support is then necessary.
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Disclosure of Interests: None Declared.
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AB1748-PARE CYLPER'S SUPPORT GROUPS: STRUCTURE AND BENEFITS

Keywords: Pain, Mental health, Self-management

The GPSD (Groups of People with the same disease of CYLPER) are subordinated and report to the Board of CYLPER and operate within the framework of its goals and programs. The role of the Groups is particularly important for the organisation of events and activities of information/ education/ self-management. The contribution of the groups to events of wider information/ public awareness is equally important.

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Background: When someone is first diagnosed, he/she is faced with a number of feelings and changes in their life. Such feelings are usually shock, anger, sadness, fear, the feeling of being judged, the feeling of a sense of loss of control. Usually, the supportive environment like family members, friends and colleagues cannot understand exactly how the person feels unless they have received a rheumatic diagnosis themselves. Doctors and health professionals may sometimes offer minor emotional support, but their primary focus is always medical. This may cause feelings of loneliness, misunderstanding or isolation. And here is where the role of support groups finds its place.
OBJECTIVES:
Methods: The general coordination of the Groups is done by the Vice President of CYLPER and the Psychosocial Support Officer, in collaboration with the Social Officer of CYLPER. Members of each Group can become Registered Rheumatism Members of CYLPER. The coordination of the operation of each Group is done by the coordinator who is elected by the members of the committee. The GPSD will be responsible for organising their events through their volunteers, and for this purpose an amount will be approved that will be available to the team to carry out its work.
Results: Finding a support group is a way for people with rheumatism to interact with other people who have similar, first-hand experiences with rheumatism. People can talk about their experiences and share their own. This can help reduce stress. In a support group, members can feel more comfortable sharing feelings and experiences that may be too difficult or too awkward to share with their family and friends. Being part of a group often creates a sense of belonging that helps each person feel more understood and less isolated. They can also discuss practical information in a support group such as: What to expect during treatment; How to manage specific side effects; How to find support services; How to communicate with health care providers and family members. Talking about these topics within the support group could provide a sense of control and reduce feelings of helplessness. Many studies have shown that support groups help people with a chronic disease cope with anxiety and depression.
Conclusion: Running a support group is a good way to reach out and get people interested in the other things your organisation or initiative does. With relatively little effort and cost, a support group can make a significant impact in the lives of people dealing with a problem.

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AB1749-PARE IMPACT OF FACIAL SIGNS OF SYSTEMIC SCLEROSIS ON PATIENTS' SELF-ESTEEM

Keywords: Systemic sclerosis, Mental health

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Background: The dimensions of self-concept and body image are essential for assessing the quality of life of individuals with chronic diseases. Systemic sclerosis (SSc) is characterized by facial involvement that can lead to aesthetic changes, functional disability as well as psychological impact.
Objectives: To assess the influence of face involvement on self-esteem in SSc patients.
Methods: A cross- sectional study was carried out on patients followed for Systemic sclerosis at a rheumatology department. Included patients completed the Burden of Face Affected (BoFA) questionnaire as well as the Rosenberg self-esteem scale (RSES). All data was collected after patient consent and was analyzed using the SPSS statistical package.
Results: Forty patients who fulfilled the 2013 ACR/EULAR Classification Criteria for Systemic Sclerosis were included. There were 8 male and 32 female with a sex ratio female to male of 4. The median age was 45 years old [19-71] and median disease duration 1 year. The majority of our patients (85%, n=34) suffered from diffuse form of SSc. 15%(n=6) had a limited form. Fingertip ulcers were observed in 13 patients (32.5%) and telangiectasia in 16 patients (40%). Raynaud's phenomenon was found in 34 patients (85%). Severe organ involvements were detected as interstitial lung disease in 17 patients (42,5%), pulmonary hypertension in 7 patients (17.5%) and renal involvement in 2 patients (5%). Mean (±SD) Rodnan score was 19.6 ± 6.2 and 70% (28 patients) had a limited mouth opening. Mean(±SD) BoFA score was 68±10.3; 0 implying no impact and 100 for major impact of face affection. Mean Rosenberg self-esteem scale was 26.6±3.3 reflecting low self-esteem. Rosenberg self-esteem correlated negatively with BoFA scores r = -0,36; p=0,02 with low levels of self-esteem associated with more face affection symptoms and no significant correlation between RSES and gender, age or Rodnan score.
Conclusion: Patients' perception of their face affection in SSc is poor and can be considered as an important component of patients' self-esteem. Effective interventions need to be directed during follow-up to improve function and satisfaction with body image.
REFERENCE:
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AB1750-PARE PATIENT-DOCTOR COMMUNICATION FROM PERSPECTIVE OF STENE PRIZE TOPIC 2023

Keywords: Patient information and education, Self-management, Quality of care

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Background: Poland participates in European Edgar Stene Prize Competition from early eighties 20th century. Three times our participants won this Prize – last time in 2018. Every competition on national level starts from appropriate translation of topic into Polish and invitation to participate in this using different channels of information to reach as many as possible potential participants. This year topic: "How better communication with my doctor improved my life with an RMD" gave an opportunity for every person living with rheumatic and musculoskeletal disease to present his/her experiences in building good cooperation with his/her physician. Patient-doctor communication was a topic of many educational events for people with RMDs including 2 perspectives: of patient and doctor. It was used Polish version of PART (prepare, ask, repeat, take action) from "Challenging arthritis" by Kate Lorig and James Fries to be more aware and responsible for his/her own health. This important topic didn't find interest among patients with RMDs and national jury received no entry for this year competition.
Objectives: Lack of entry on topic of patient-doctor communication among rheumatic patients was surprised and identifying the causes of this situation can be important in two areas: future Stene Prize competition and personal cooperation with health professionals including physicians.
Methods: Invitation for participation in competition was shared using the same channels how always. There were: websites of associations, social media (facebook and Twitter), e-mailing to leaders of associations, online meeting on occasion of World Arthritis Day, personal contacts with potential authors. Before deadline of submitting entries reminders were sent and put in social media. Reasons of lack of entries were discussed with active members of our associations.
Results: In opinion of people living with RMDs reality is different than model of good practice in communication patient-doctor. Asking potential authors of essays there were responses like: "what I can write – true?", "what communication?", "it will be some day in future but not today". Patients note the lack of time during medical consultation for open discussion. Physician during 15-20 minutes should examine patient, check results of tests, issue a prescription and referral using electronic system what can be added stress for some doctors and takes time devoted for talk with patient for technical issue. If discuss is started it's from initiative of patient mostly, but patient should be aware and active in process of treatment not only passive participant of consultation. Appropriate sources of information and knowledge help patient to take responsibility for his/her own health and life.
Conclusion: Pandemic COVID-19 accelerated involving e-prescriptions and e-referrals in health care system. Pandemic involved remote consultation on place of consultation in-person. This new form of consultation needed concrete and short exchange of information between doctor and patient. Return to consultations in-person didn't change form of consultation to more friendly for patient. Remote consultation stays like an alternative to consultation in-person.
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AB1751-PARE MUSCULOSKELETAL DISORDERS IN THE ERA OF THE COVID-19 PANDEMIC

Keywords: Work-related issues, Descriptive Studies

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Background: In Tunisia, during the last decade, the number of MSDs declared as compensable occupational diseases has been increasing. So, what is the impact of the COVID-19 pandemic on the MSD reporting rate.
Objectives: To describe the socio-professional characteristics of workers with musculoskeletal disorders (MSDs) and to determine the reporting rate of MSDs as occupational diseases.
Methods: A descriptive cross-sectional study among workers with work-related MSDs who consulted the occupational medicine department of the Charles Nicolle Hospital for medical advice between January 2021 and September 2022.
Results: A total of 109 workers with MSDs were included in this study. The workers were 64.2% female. The average age was 46 ± [21-61 years]. The sectors most prone to MSDs were the health sector (27.5%), food processing (16.5%) and textiles (15.6%). The workers reported MSDs of the upper limb in 31.2%, MSDs of the lower limb in 33.9% and of the spine in 69.7%. These MSDs reported included 5/13 cases of rotator cuff tendinopathy, 6/13 cases of carpal tunnel syndrome, one case of achilles tendonitis and one case of Dequervain's tenosynovitis.

Conclusion: During the COVID-19 pandemic, the reporting of MSDs as occupational diseases has declined considerably. This decline can be explained by the difficult access to hospital facilities.

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AB1752-PARE THE RATE OF COVID-19 VACCINATION IN PATIENTS WITH RHEUMATOID ARTHRITIS. SINGLE-CENTER CROSS-SECTIONAL PILOT STUDY

Keywords: Rheumatoid arthritis, COVID, Vaccination/Immunization

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Background: The rate of COVID-19 vaccination in patients with rheumatoid arthritis. Single-center cross-sectional pilot study.

Objectives: Morocco was the first country in Africa to launch the COVID19 vaccination campaign. Vaccination of immunocompromised subjects was recommended from the beginning by the Moroccan Society of Rheumatology. The primary objective of this study was to assess the vaccination rate of patients with rheumatoid arthritis two years after the start of the pandemic. The secondary objective was to investigate factors associated with vaccination.

Methods: This was a 3-month monocentric cross-sectional study from 31.05.22 to 31.08.22, including patients whose age was greater than 18 years, who have rheumatoid arthritis according to ACR/EULAR 2009 criteria. Socio-demographic data, comorbidities and disease characteristics were collected by the attending physician at the time of the consultation using a questionnaire. Statistical analysis was performed using JAMOVI software.

Results: The study included 73 patients, 82.2% of whom were women. The mean age was 57±11years, with a median disease progression of 8 years. 58 patients (80.6%) were vaccinated against COVID19. Among the vaccinated patients, 30 (51.7%) were illiterate, 8 patients (13.8%) had primary education, 11 (19%) had secondary education and 9 (15.5%) had higher education 53 (91.4%) patients were previously on or on corticosteroids, 8 patients (14, 3%) had a history of tuberculosis, 10 patients (17.5%) had diffuse interstitial lung disease routinely detected on computed Tomography (CT) Scan of the Chest, 26 patients (45.6%) had received a pneumococcal vaccination (p=0.24), and 21 (36.2%) had received an influenza vaccination. 15 patients (25.8%) were on Tumor necrosis factor-alpha inhibitors, 25 patients (43.1%) were on Rituximab, 6 patients (10.3%) were on Tocilizumab, 4 patients (6.9%) were on Methotrexate, 1 patient (1.7%) was on Leflunomide, 1 patient (1.7%) was on Salazopyrine, 2 patients (3.4%) were on csDMARD combinations, and 4 patients (6.9%) were not on any disease-modifying treatment.Only the level of education was statistically significantly different between vaccinated and non-vaccinated patients (p=0.06).

Conclusion: In this study, almost 80% of patients were vaccinated. Further studies are needed to develop population-specific education programs.

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AB1753-PARE APPLICATION OF THE THEORY OF PLANNED BEHAVIOR: THE ROLE OF FAMILY AND PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Self-management, Rheumatoid arthritis, Education

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Background: The TPB suggests that patient attitudes, subjective norms, and perceived behavioral control predict behavioral intentions and behaviors regarding health behavior (Yaoyao et al., 2021). Behavioral theories aid in improving the behavioral changes in the self-management of diabetes (Damayanti et al., 2018) and other lifestyles changes such as healthy eating (Rahmati-najarkolaei et al., 2017). Most recently, Jormand et al. (2022) uses TPB for the self-care behaviors of knee osteoarthritis patients in which TPB aided educational intervention, by examining variables such as their attitudes and perceived behavioral control. Saffari et al. (2018) explains that although they are not as popularly researched and surgical interventions, the benefits of non-medical approaches endorsing healthy lifestyles can improve symptoms and reduce the need for other treatments.

Objectives: This study will use three variables in the TPB model, namely, attitude, PBC (self-efficacy) and family support to examine the intention of self-management behaviors on a sample of patients with rheumatoid within a developing country and collectivist society.

Methods: The model proposed for this research includes independent variables; support from family (novel variable), attitude and perceived behavioral control. Dependent variables include intention and total self-management (cognitive, physical and communication with a health professional). Adult patients who meet the criteria of the American College of Rheumatology (ACR) and live with family will be asked to complete a self-administered questionnaire. This cross-section study proposes a model that will be tested using regression analyses and structural equation model.

Results: Data is still under analysis and will be available at the time of the conference. However, based on previous studies it is hypothesized that TPB variables and relative support will be reported as significant.

Conclusion: Insights through the model proposed could aid healthcare professionals in understanding elements that support or hinder rheumatoid patients from initiating or maintaining self-management behavior.

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AB1754-PARE INFLAMMATORY RHEUMATIC DISEASES AND RELIGIOUS RITUALS: WHICH IMPACT?

Keywords: Descriptive Studies, Quality of life, Patient reported outcomes

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Background: Religious events are privileged occasions for sharing and conviviality. In a joyful atmosphere, festive meals are shared with family, neighbors, and friends, and gifts are exchanged. Little is known about the impact of chronic inflammatory rheumatic diseases on patients' celebrations of religious events.

Objectives: To study the satisfaction of patients with their religious rituals during Islamic holidays.

Methods: We conducted a transversal study, including patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA). Patients were invited to answer to a satisfaction scale (SS) composed of four domains: prayer practice, religious food preparation, family visits, and satisfaction with spiritual fulfillment. For each domain, there were 6 degrees of satisfaction (extremely satisfied, satisfied, slightly satisfied, slightly dissatisfied, dissatisfied, extremely dissatisfied) rated from 1 to 6 from best to worst satisfaction. The sub-SS for each domain ranged from 1 to 6, and the global SS ranged from 4 to 24.

Results: Seventy-one patients (45 females) answered the SS with a median age of 48±13 [20-81] years. Thirty-three patients had RA and thirty-eight SpA with a mean disease duration of 8±7.3 [0.04-36] years. The RA and SpA were active according to DAS28 and BASDAI in, respectively, 78% and 47% of cases. The mean global SS was 13.2±3.1 [6-23] and the mean sub-SS for prayer practice was 3.3±1.3 [1-6], for religious food preparation was 4±1.4 [1-6], for family visits was 3±1.3 [2-6] and for satisfaction for spiritual fulfillment was 3.3±1.4 [1-6]. A better satisfaction with prayer practice and religious food preparation was correlated with age (p=0.04, p=0.043, respectively) and married marital status (p=0.021, p=0.008, respectively). SpA patients reported less satisfaction with prayer practice than RA patients (sub-SS means 3.44 versus 3.13), but this did not reach a statistically significant level (p=0.337). Patients with inactive disease reported better satisfaction with family visits than those with active disease (sub-SS means 2.46 versus 3.04) but without statistically significant difference (p=0.178). The satisfaction with spiritual fulfillment correlated with age (p=0.001), whereas there were no associations with gender (p=0.216), type of the rheumatism (p=0.653) and disease activity (0.516). There was no correlation between the global SS and the type of rheumatism, disease activity, and gender (p=0.631, p=0.403, p=0.569, respectively).
Conclusion: Our study showed that RA and SpA affect negatively patients' religious practices, especially prayer practice, religious food preparation, and spiritual fulfillment. Therefore, the impact on religious rituals should be taken into account when assessing the quality of life of patients with rheumatic diseases.
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AB1755-PARE EVALUATION OF THE FRAGILITY OF ELDERLY PATIENTS HOSPITALIZED IN THE RHEUMATOLOGY DEPARTMENT

Keywords: Quality of life

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Background: Fragility is defined by a clinical syndrome that reflects a decrease in physiological capacities altering the mechanisms of adaptation to stress[1]. Elderly patients hospitalized in the rheumatology department are at risk of significant fragility.
Objectives: The aim of our study is to evaluate the fragility of elderly patients considering the bio-psycho-social parameters.
Methods: Prospective study started in July 2022 in the rheumatology department including 40 patients who were subject to questionnaires assessing their fragility and quality of life.
Results: 40 patients were collected including 27 women (67.5%) and 13 men (32.5%). 15 (37.5%) patients were hospitalized for chronic inflammatory rheumatism, 19 (47.5%) for a degenerative disease and 6 (15%) for a tumoral disease. The mean age of the patients was 72.6 ± 5.4 years. The social context of each patient was assessed: 30 (90%) patients lived with their family and 10 (25%) lived alone. 19 (47.5%) patients reported having financial difficulties and 17 (42.5%) patients needed daily help with household chores. We studied the level of frailty of our patients using the Tilbourg Fraility Indicator (TFI): 29 (72.5%) patients had a score ≥ 5 indicating significant frailty. 21 (52.5%) patients presented a risk of depression evaluated at 5 according to the geriatric depression scale (GDS15). A nutrition assessment was made using the Mini Nutritional Assessment (MNA) test, concluding with poor nutritional status in 10 (25%) patients. Finally, five (12.5%) patients had a dependency score ≤ 3 according to the Activities of Daily Living (ADL) scale.
Conclusion: Elderly patients with rheumatological disease hospitalized in our department show an alteration in their quality of life and a significant level of fragility which should motivate us to adapt care programs for the elderly concerned.
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AB1756-PARE FACTORS ASSOCIATED WITH QUALITY OF LIFE AMONG SCLERODERMA PATIENTS

Keywords: Quality of life, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is an autoimmune multi-systemic disease with predominant affection of connective tissue resulting in progressive fibrosis of the skin and internal organs. Monitoring measures of functioning and disability is crucial during follow up to identify quality of life impairment.
Objectives: To assess the influence of functional impairment on quality of life in SSc patients.
Methods: A cross- sectional study was carried out on patients followed for systemic sclerosis at a rheumatology department. Included patients completed the Hospital Anxiety Depression scale in its Arabic validated version. The SF-36 short form questionnaire score with its domains (general health, physical function, role physical function, emotional role function, vitality, mental health, social function, body pain, general health) in its arabic Tunisian version was used to assess quality of life. All data was collected after patient consent and was analyzed using the SPSS statistical package.
Results: Forty patients who fulfilled the 2013 ACR/EULAR Classification Criteria for Systemic Sclerosis ACR criteria for SSc were were included. 80% of the patients were female, the median age was 45 years old and median disease duration 1 year. 15%(n=6) had a limited form, and 85% (n=34) had a diffuse form of SSc. Fingertip ulcers were observed in 13 patients (32.5%) and Raynaud's phenomenon was found in 34 patients (85%). Severe organ involvements were detected as interstitial lung disease in 17 (42,5%), pulmonary hypertension in 7 patients (17.5%) and renal involvement in 2 patients (5%). 38 % patients had an HAD scoring rate for "possible clinical anxiety" and for 42% for "possible clinical depression". The SF-36 questionnaire score of each domain was significantly lower in patients with diffuse than in limited form, especially the score in the dimension of Role Physical function and Body Pain, p=0.04 and p=0.02 respectively. Skin involvement and organ damage were also significantly associated with lower SF36-PF (physical function) (p=0.001) and SF36-MH (mental health) p=0.0025 with no significant association with the other score components.
Conclusion: Systemic Sclerosis has a significant effect on patient quality of life. Body image, fatigue, pain, and psychological morbidity should be screened in patients with SSc to promote quality of life.
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Disclosure of Interests: None Declared.
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AB1757-PARE PATIENTS WITH SPONDYLOARTHRITIS SUFFER IN SILENCE: THE IMPACT OF THE DISEASE ON THEIR QUALITY OF LIFE

Keywords: Quality of life, Spondyloarthritis, Patient reported outcomes

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Background: Spondyloarthritis (SpA) is a chronic disease that often causes functional impairment, resulting in a negative impact on patients' quality of life (QoL).
Objectives: We aimed to assess QoL of patients with SpA using a validating tool.
Methods: We conducted a cross-sectional study including patients with SpA. Sociodemographic, clinical, and therapeutic data were collected. Patients' QoL was assessed using the validated Tunisian version of the EQ-D5 questionnaire, which is a standardized measuring instrument that assesses the state of health according to five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The answers were converted into EQ-5D index.
Results: There were 100 SpA patients with a mean age of 43.68±10.3 years [20-76]. Regarding mobility, 2 patients reported extreme problems, 61 patients had some problems, and 37 patients had no problems. Six patients were totally non-autonomous, 55 were partially autonomous, and 39 patients had no problems in the self-care domain. Thirty-five patients had no problems in their usual activities, 60 patients had some problems, and 5 patients had extreme problems. Twenty-six patients had significant pain or discomfort at the time of the study, 61 patients had moderate pain or discomfort, and 13 patients had no pain. A significant level of anxiety/depression was observed in 12 patients, 46 patients had moderate depression or anxiety, and 42 patients had no psychological problems. The global VAS of health status had a mean value of 59± 25% [7-100]. The mean EQ-5D index was 0.485±0.378 [-0.448-1]. In 12 cases the index was negative, defining an extremely large effect of the disease on QoL, while 7 patients had an index equal to 1, showing that the disease had no effect on their QoL.
Conclusion: Despite therapeutic advances, patients with SpA still suffer in their daily living. So, an early and appropriate management is necessary.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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HPR Measuring health (development and measurement properties of PROs, tests, devices)

AB1758-HPR IDENTIFYING THE RISK OF STEROID INDUCED ADRENAL INSUFFICIENCY IN RHEUMATOLOGY PATIENTS WEANING FROM PROLONGED STEROID THERAPY

Keywords: Tapering, Diagnostic Tests, Inflammatory arthritides

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Background: Rheumatologists often prescribe steroids, and long-term use can lead to suppression of the hypothalamic-pituitary-adrenal (HPA) axis, leading to Steroid Induced Adrenal Insufficiency (SIAI). Our departmental guidelines suggest patients on steroid weaning regimes should have morning serum cortisol levels once weaned to 3mg.
Objectives: We aimed to identify what proportion of cortisol levels were abnormal in patients weaning from steroids in various Rheumatological conditions. There are currently no established guidelines to identify patients for possible SIAI, which is usually only assessed if a patient develops steroid withdrawal symptoms at low doses. We wanted to investigate if SIAI was seen commonly and analyse whether patients who had abnormal cortisol levels went on to have a Short Synacthen Test (SST), Endocrinology input and SIAI diagnosis.
Methods: Retrospective review of Rheumatology patients who had morning serum cortisol levels whilst weaning from oral prednisolone at Sheffield Teaching Hospitals. Patients identified via the Clinical Laboratory Database.
Results: Data collected Sept'19 – Oct'22, only samples taken pre-9AM assessed (n=58). 33 Female, 25 Male. Age 21-83 years; mean 65 years. Starting dose prednisolone 5mg-60mg (IQR 15-40mg). Treatment length 6-96 months (IQR 14-48). Samples taken when 84.5% (n=49) taking 3mg, 10.3% (n=6) 2mg and 5.2% (n=3) 2.5mg, (IQR 3mg). Cortisol levels <300 nmol/L in 43.1% (n=25), 300-350 nmol/L in 15.5% (n=9) and >350 nmol/L in 41.4% (n=24). 68% (n=17) of <300 nmol/L (n=25) referred for a SST. SST results were <430 nmol/L in 35.3% (n=6) and >430 nmol/L in 64.7% (n=11). All patients with SST <430 nmol/L (n=6) referred to Endocrinology. 33.3% (n=2) had "borderline" SST results (421nmol/L, 415nmol/L) and advised to wean steroids by 1mg every 4 weeks and discharged. 66.7% (n=4) diagnosed with SIAI, with only one (25%, n=1) having documented symptoms. All (n=4) had further Endocrinology investigation; 100% (n=4) had a repeat SST and pituitary function tests and 75% (n=3) had or awaiting Waking Salivary Cortisol (WSC). 75% (n=3) showed recovery of HPA axis on repeat testing and so advised to slowly wean steroids. 25% (n=1) had persistently abnormal results suggesting ongoing SIAI and advised to remain on 3mg prednisolone. All patients with an abnormal SST (n=6) remained on prednisolone and did not change to hydrocortisone. 90.1% (n=10) of patients with an SST of >430 nmol/L referred to Endocrinology concurrently with SST request and outcome for all patients was to continue slowly weaning steroids. 32% (n=8) patients with a cortisol <300 nmol/L did not have an SST. 37.5% (n=3) had alternative WSC testing; 33.3% (n=1) discharged after normal WSC, 33.3% (n=1) awaiting WSC and 33.3% (n=1) require ongoing Endocrine input as WSC indicated SIAI. This patient awaits steroid clinic and remains on 3mg prednisolone. 62.5% (n=5) had no further investigations. Outcomes: steroids continued by Rheumatology (n=3), steroids weaned by Rheumatology (n=1), too early for further tests (n=1). 15.5% of patients (n=9) had a cortisol between 300-350 nmol/L. None had an SST due to not having symptoms, in line with our guidelines. 33.3% (n=3) had a repeat cortisol, all repeats >350 nmol/L. Outcomes: Rheumatology weaned steroids (n=5), dose increase due to flair (n=2), no further documentation (n=1), moved away (n=1).
Conclusion: 10.3% (n=6) of all patients who had a serum cortisol measurement had an abnormal SST and 8.6% (n=5) of all patients were diagnosed with SIAI. Only one patient had documented symptoms of SIAI. Given the introduction of the more sensitive WSC as an alternative to the SST we aim to modify our department guidelines in collaboration with the Endocrinologists. In line with the 2020 National Patient Safety Association alert and 2022 British Society for Rheumatology guidance the focus is to recognise adrenal insufficiency, which our guidelines are designed to do. Adrenal insufficiency is unpredictable and rare but adrenal crisis can be fatal, so Rheumatologists must be aware of it.
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AB1759-HPR THE USE OF PROMIS MEASURES IN CLINICAL STUDIES IN PATIENTS WITH INFLAMMATORY ARTHRITIS: A SYSTEMATIC REVIEW

Keywords: Inflammatory arthritides, Patient reported outcomes, Systematic review

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Background: Patient-reported outcome measures (PROMs) are of vital importance to evaluate the outcomes of inflammatory arthritis and its management, but limitations of conventional PROMs include a lack of precision and/or comparability across conditions. Patient Reported Outcomes Measurement Information System (PROMIS) measures [1-2] were developed since 2007 to overcome these disadvantages. They use a standardized metric (T-score), centered around the general population (score 50), enhancing their interpretability. The use of PROMIS measures in patients with inflammatory arthritis was recommended by the International Consortium for Health Outcomes Measurement (ICHOM) [3], but little is known about the extent and nature of their actual use in clinical research.
Objectives: We aimed to describe the use and outcomes of PROMIS measures in clinical studies involving people with rheumatoid arthritis (RA) or axial spondyloarthritis (axSpA).
Methods: We conducted a systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A search of nine electronic data bases on July 29th, 2022 was conducted to identify clinical studies in patients with RA or axSpA, reporting the use of PROMIS measures and written in English, Dutch or German. Study characteristics, details of PROMIS measures and, if available, their outcomes, were extracted. Both the selection and the data extraction were performed independently by two researchers and disagreements were resolved by consensus, either or not with a third researcher.
Results: In total, 714 records were retrieved (272 unique references), of which 29 studies met the inclusion criteria (25 RA, 3 axSpA and one both RA and axSpA). In total, 15 different PROMIS measures were used, 13 of which were domain-specific and 2 pertained to general health (PROMIS Global Health, PROMIS-29). The five most frequently used domain specific measures were the PROMIS Pain Interference (n=17), Physical Function (n=14), Fatigue (n=13), Depression (n=12) and Anxiety (n=7) measures. The general PROMIS Global Health and PROMIS-29 were both reported in 3 studies. The PROMIS measures that were used varied considerably, with a total of 74 unique identified measures, as a result of differences in their typology into Item Banks, Computer Adaptive Tests, Short Forms, the described name or the version number. In total, 21 studies reported on 98 PROMIS results in terms of T-scores, of which 91 were worse than the general population mean (score 50), indicating impaired health status. The other 8 studies did not report actual T-scores but psychometric properties of PROMIS measures (e.g. the validity, reliability, correlations with other questionnaires, responsiveness, meaningful change).
Conclusion: Given the availability of PROMIS measures since 2007 and the vast amount of clinical studies in RA and axSpA, PROMIS measures seem to be relatively underused. Among the studies there was considerable variety regarding the PROMIS measures that were used as well as their versions. The reported PROMIS outcomes overall reflected the impaired health status of patients with in RA and axSpA as compared to the general population. Apart from the promotion of the use of PROMIS measures, more standardization regarding the type of measures and their versions is needed to facilitate comparisons across studies.
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AB1760-HPR THE RELATIONSHIP BETWEEN DISEASE ACTIVITY LEVEL AND WRIST JOINT POSITION SENSE, GRIP STRENGTH AND DYNAMIC GRIP ENDURANCE IN PSORIATIC ARTHRITIS

Keywords: Psoriatic arthritis, Physical therapy/Physiotherapy

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Background: Dynamic grip endurance in psoriatic arthritis is one of the affected functional parameters during the disease process. However, there are limited studies about dynamic grip endurance related factors.
Objectives: To investigate the relationship between disease activity level and joint position sense and dynamic grip endurance in psoriatic arthritis.
Methods: A total of 27 PsA patients (age:53.33 ±11.85 years, women/men:16/5) who were classified by the Classification Criteria for Psoriatic Arthritis (CASPAR) criteria and followed in outpatient clinic were included in our study. The socio-demographic characteristic of all patients recorded. Disease activity level was assessed with the DAPSA score. Wrist joint position sense was evaluated by a goniometric re-position error test. Grip strength and endurance were examined by a hand dynamometer (Lafayette Professional Hand Dynamometer, USA). Data analysis was performed with Spearman Correlation Coefficient.
Results: Patients' diagnosis year, tender joint on hand, and swollen joint on hand were 4.50 years, 23, and 18, respectively. DAPSA scores were 28.67 ±14.85 and moderate-high level. There was no relationship between DAPSA scores and joint position error and dynamic grip endurance on both sides (p>0.05). A moderate level correlation was found between the DAPSA score and grip strength on both sides (p<0.05, r=-0.516 and -0.570 dominant and non-dominant side, respectively).
Conclusion: Our study showed that PsA patients had lower grip strength during the exacerbation period. Since joint position sense and grip endurance were low independents of disease activity, they may not are associated with disease activity in this study. We think that in cases where disease activity increases, approaches that protect grip strength can be added to the disease management process.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1761-HPR A TELE-MONITORING PROGRAM FOR TIGHT CONTROL OF TREATMENT SAFETY IN PATIENTS WITH RHEUMATIC DISEASES

Keywords: Health Services Research

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Background: Initiation of an immuno-modulatory treatment is a vulnerable part of the patient journey. Distance monitoring via patient reported outcomes (PROs) and wearables are used to assess treatment efficacy. In combination with remote vital sign measurement and tele-nursing, remote care may also increase safety and save resources. However, it is unclear how such telemedicine services integrate into the clinical workflow.
Objectives: Feasibility and User Experience (UX) study of a combined app-based and nurse-assisted tele-monitoring program in rheumatic patients with different risk profiles starting a new biologic treatment.
Methods: In this quantitative and qualitative study, we explored a distance monitoring service including contactless optical vital sign measurement and tele-nursing in ambulatory rheumatic patients in Switzerland. System Usability Scores (SUS) and semi-structured interviews were performed with patients, tele-nurses, and rheumatologists. Patients collected weekly PROs and vital signs via an app (Vtuls, Switzerland) after instruction by tele-nurses. Vital sign deterioration triggered automated notification (categorized in yellow, green, and red) allowing corrective actions. Rheumatologists received monthly summaries of PRO and vital signs in PDF form.
Results: 15 patients with rheumatoid arthritis or spondylarthritis with a mean age of 43.9 years (32-79) were included and monitored up to three months with the app and phone calls of the tele-nurse. 15/15 patients found the program useful, mainly for staying in contact with their rheumatologist after therapy start or switch. 13/15 patients measured their vital signs regularly, the adherence to PRO questionnaires was significantly lower. 6 patients had technical problems with the contactless blood pressure measurement. The app generated in average 16 vital sign alarms per patient, of those 7.1 green, 1.1 yellow and 2.2 red alarms. The rheumatologists considered the program as useful, especially in one patient with high-level comorbidity who experienced infection and in another patient after dosing error of the new treatment. The number of consultations (e.g. routine control 1-2 months after starting the new treatment) were significantly lower in this cohort compared to patients without remote care. PDF reports via email were considered as suboptimal and digital integration into the workflow needs to be implemented in future versions of the care program. Tele-nurses considered patients with high comorbidity, shorter disease duration and younger age as most suitable for remote control. False alarms initially increased the workload of the nurses, but this later reduced through technical advice and adjustment of the thresholds. SUS scores were slightly higher in patients (median 97.5) compared to tele-nurses (median 77.5). One patient outlier (17.5) had higher expectations in the responsiveness of tele-nursing, based on entered PROs.
Conclusion: Tight remote control of safety and efficacy through a combined app, biosensor and tele-nursing program was appreciated by all stakeholders, especially in patients with high comorbidity. A better integration of data and communication in the clinical workflow is required, ideally through the electronic medical record. A reduced workload in the rheumatology clinic was observed, but a complete reorganization of the processes was necessary.
REFERENCES: NIL.
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Disclosure of Interests: Marco Fedeli: None declared, Jas Saini Shareholder of: Board of directors at Vtuls, Henrik Ibsen Shareholder of: Board of director Opentelehealth, Miriam James Employee of: Mediservice AG, Thomas Hügle Shareholder of: Scientific board member at Vtuls, Consultant of: GSK, Novartis, Medac., Grant/research support from: Fresenius Kabi, Eli Lilly, Abbvie.
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AB1762-HPR CAN PATIENT-REPORTED OUTCOMES BE USED TO TRIAGE PATIENTS WITH ANKYLOSING SPONDYLITIS TO MOBILITY MEASUREMENTS OR TESTING OF C-REACTIVE PROTEIN?

Keywords: Spondyloarthritis, Patient reported outcomes, Outcome measures

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Background: Patients with Ankylosing Spondylitis are assessed by healthcare with regular controls of mobility and disease activity. If these controls can be replaced by valid patient-reported index, it would unburden both patients and healthcare.
Objectives: In this study we analysed associations between healthcare measured mobility and disease activity and patient-reported disease activity, physical function and well-being in patients with AS.
Methods: This register-based cross-sectional study used data from 1541 visits (of which 1093 visits were men and 448 women) in the Swedish Rheumatology Quality Register. Variables for healthcare measured spinal mobility and disease activity were Ankylosing Spondylitis Metrology Index (BASMI) and C-Reactive Protein (CRP). Variables for patient-reported disease activity, physical function and well-being were Bath Ankylosing Spondylitis Disease Activity Index (BAS-DAI), Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Global Score (BAS-G). First, associations were tested with Pearsons correlation. Secondly, discriminative ability to identify subnormal BASMI, or CRP [defined as below the 2.5th percentile of healthy individuals, and >3, respectively [1,2], was determined by means of receiver operating characteristic (ROC) curve analysis for variables with coefficients r >0.4.
Results: Associations with r >0.4 was found only between BASMI and BASFI (r=0.49), resulting with an area under the curve (AUC) of 0.74 (95% CI; 0.72-0.76) in the ROC analyses. Among the subquestions of BASMI/BASFI, the highest association was seen between measured cervical rotation and the self-assessed ability to look over shoulder (r=-0.69), resulting in AUC of 0.85 (95% CI; 0.83-0.88) in the corresponding ROC analyses, using cervical rotation below 2.5th percentile of healthy individuals as discrimination value.
Conclusion: A significant association with r >0.4 was seen between BASMI and BASFI. The resulting AUC of 0.74 between BASMI and BASFI, and 0.85 between measured cervical rotation and self-assessed ability to look over shoulder, can be deemed as acceptable and excellent, respectively [3]. BASFI and its sub-questions may therefore be of interest for further evaluation if they could be used for screening and triaging patients to spinal mobility measurements with BASMI. Neither of the self-reported indices associated with CRP to any higher degree (r <0.4).
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AB1763-HPR RELIABILITY AND VALIDITY OF THE TURKISH VERSION OF SCLERODERMA SKIN PATIENT-REPORTED OUTCOME IN PATIENTS WITH SYSTEMIC SCLEROSIS

Keywords: Systemic sclerosis, Patient reported outcomes, Validation

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Background: Systemic sclerosis (SSc), which is characterized by fibrosis of the skin and, internal organs and vasculopathy, is an autoimmune rheumatic disease. Skin fibrosis is the most seen feature of SSc patients and affects nearly all patients with SSc at different levels and severity. Skin involvement is generally evaluated with the modified Rodnan skin score (mRSS). However, several studies have indicated that there is no relation between mRSS and appearance self-esteem. Based on evidence from previous studies that it is significant to comprehensively evaluate the effects of skin fibrosis on QoL in SSc patients. There is a need for an instrument to assess the effects of skin involvement on the quality of life of the Turkish population in SSc patients.

Objectives: Scleroderma Skin Patient-Reported Outcome (SSPRO) is useful scale to evaluate the skin related quality of life in SSc patients. This study purposed to translate the SSPRO questionnaire to Turkish (SSPRO-T) language and to assess its validity and reliability.

Methods: Fifthy-four SSc patients (female:male, 51:3) participated in the reliability and validity analysis. The translation and cross-cultural adaptation of the original version of the SSPRO were applied in accordance with the procedure described by Beaton guidelines. The SSPRO-T, the Scleroderma Health Assessment Questionnaire (SHAQ), the Health Assessment Questionnaire Disability Index (HAQ-DI), Skindex-29 and patient global skin severity were conducted to 54 patients with SSc for construct validity. The SSPRO-T was re-tested to assess its reliability after seven days.

Results: The SSPRO-T had a four-factor structure. The total SSPRO-T score and its subgroups correlated positively with SHAQ, HAQ, Skindex-29 and patient global skin severity. The internal consistency and reliability were excellent the SSPRO-T and physical effects subgroup, emotional effect subgroup, physical limitation subgroup and social effect (Cronbach's α = 0.94, 0.80, 0.95, 0.93 and 0.84, respectively) (Table 1). The SSPRO-T had excellent test-retest reliability (r=0.91, p<0.001). In addition; it was not seen floor effect and ceiling effect related SSPRO-T.

Conclusion: The SSPRO-T questionnaire is an excellent a reliable and valid tool. It could be used in research and clinical studies in the Turkish patients with SSc.

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Table 1. SSPRO-T descriptive statistics, internal consistency and test-retest reliability

Scores	Number of items	Score median (IQR25th-75th)	Minimum	Maximum	Floor effect (%)	Ceiling effect (%)	Internal consistency (Cronbach'sα)	Test-retest reliability ICC (95% CI (Lower-upper bound))
Total score	18	29.0 (12.0-56.0)	0	96	1.85	1.85	0.94	0.91 (0.82-0.95)
PE	5	12.0 (6.0-19.0)	0	30	1.85	1.85	0.80	0.88 (0.77-0.93)
EE	6	5.5 (0-20.0)	0	36	9.72	1.85	0.95	0.90 (0.81-0.94)
PL	4	6.0 (0-14.0)	0	24	7.56	1.08	0.93	0.81 (0.62-0.90)
SE	3	0 (0-3.2)	0	17	16.74	1.85	0.84	0.68 (0.46-0.82)

SSPRO-T: Scleroderma skin patient-reported outcome Turkish, PE: Physical effects, EE: Emotional effects, PL: Physical limitations, SE: Social effects ICC: Intraclass correlation coefficient, CI: Confidence interval

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AB1764-HPR

EXPRESSION OF CYTOKINES RELATED TO "INFLAMMAGING" AND ARTERIAL STIFFNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS: A GENE ONTOLOGY AND PATHWAY ENRICHMENT ANALYSIS

Keywords: Rheumatoid arthritis, Cytokines and chemokines

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Background: Cardiovascular disease is the leading cause of premature death among patients with rheumatoid arthritis (RA). Inflammatory cytokines play a pivotal role in this process, leading to impaired artery elasticity by priming endothelial dysfunction and enhanced arterial stiffness.

Objectives: To assess the expression of inflammatory cytokines associated to cardiovascular alterations such as arterial stiffness among patients with RA and osteoarthritis (OA) through Gene Ontology and Pathway Enrichment analysis.

Methods: Inclusion criteria for this analytical cross-sectional study were patients with RA and OA between 40 and 70 years old. Sociodemographic and clinical characteristics as well as inflammatory, metabolic markers, acute phase reactants, autoantibodies were analyzed. Levels of 18 cytokine: including VCAM1 (CD106), ICAM1(CD54), CCL7 (MARC), MCP1, SPP1 (OPN), PDGF, CXCL10 and inflammaging related cytokines: INF-γ (IFNG), IL-10, IL-1RA, IL-1β, IL-6, TNF-α, MMP1, MMP2, MMP9, TIMP-1, TIMP2, were measured using a Luminex Assay (Invitrogen, Carlsbad, CA, United States). Cardiovascular measurements (Including Pulse Wave Velocity -PWV and aortic augmentation index – Aix) were performed within one month after blood sampling using the TensioMed Arteriography. A protein-protein interaction network (PPI) was built using the string App plugin from Cytoscape v3.9.1. Gene Ontology and pathway analysis were carried out using ClueGO (v2.8.9) + Cluepedia (v1.5.9) Cytoscape plugin for the proteins that showed a significant overexpression against GO biological processes, KEGG, and Reactome pathways databases (*Homo sapiens*).

Results: A total of eighty patients were included (71.3% women). The average age was 57 years, interquartile range (IQR) 10. OA patients had higher waist circumference, weight, and body mass index values than RA patients. There were no differences in lipid profile or glucose levels. CRP levels were higher in RA patients. Levels of disease activity in RA patients was low according to the measurement of the DAS-28-PCR. 12.5% of patients with RA had polyautoimmunity. There were no significant differences in the measurement of cardiovascular variables between the two groups except for Brachial diastolic blood pressure, which was higher in the RA group (p=0,049). Plasma levels of VCAM1 (CD106;), MARC (CCL7; p=0.000), OPN (SPP1; 0.040), IL-1RA; p=0.015) and IL-1β (p=0.031) were significantly higher in the group of RA patients. ICAM1 (CD54), MARC, and INF-γ levels were correlated with Aix in the RA group. In the OA group, IL-10 levels positively correlated with Brachial pulse pressure and other central and peripheral pressure measurements (mild or moderate). The merged network between upregulated cytokines (VCAM1, SPP1, PDGF1, IFNG, ICAM1 and CCL7), RA query in DISESASE database and "Arterial stiffness" query (PubMed) resulted in a PPI network with 26 nodes and 88 interactions. (Figure 1.) The nodes with BC above 0.05 (VCAM1, TNF, JAK1, ICAM1, IL-10, CD4, PTK2B, FN1, ITGB1) represents the key genes. Ten *GO* terms and twelve pathways were significantly enriched (Figure 2). The principal GO terms were as follows: "membrane to membrane docking" (34% genes), "response to type II interferon" (7.89% genes), and "regulation of lipid biosynthetic process" (5.26% genes). KEGG and REACTOME included: signaling by PDGF (7.89%), integrin cell surface interaction (2.63%), extracellular matrix organization (2.63%).

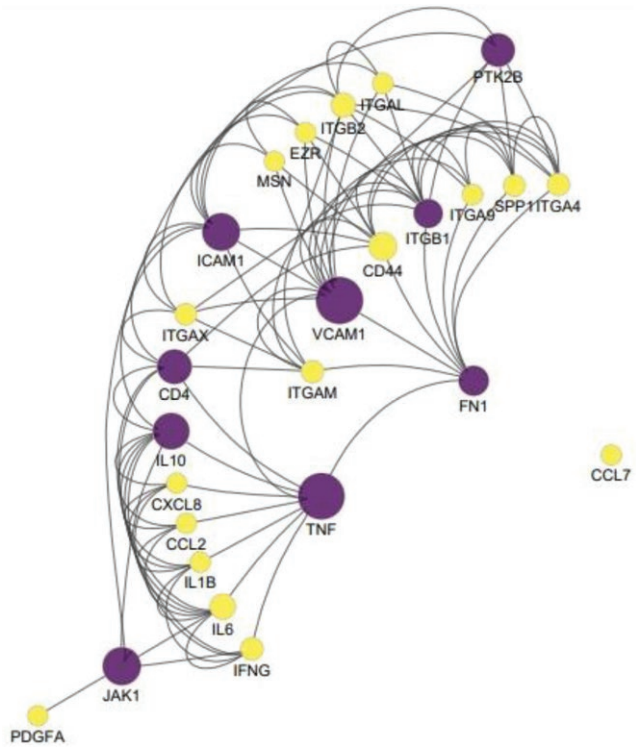


Figure 1. Protein-protein interaction network (PPI)

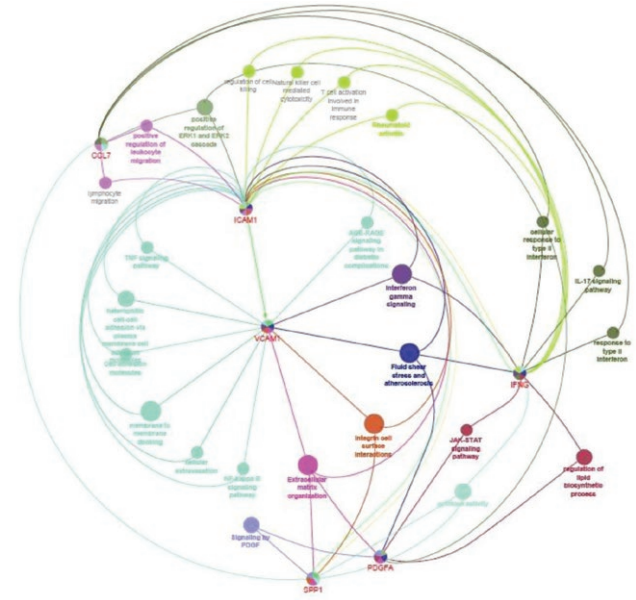


Figure 2. Molecular function and Pathway analysis

Conclusion: Cytokines related to "Inflammaging" shown significant relationship with arterial stiffness parameters measured in RA patients and IL-10 in OA group. These representative nodes/proteins were related with cellular adhesion, MAPK activation pathway and proinflammatory responses showing that those are key processes in arterial stiffness and rheumatoid arthritis.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: Jonathan Carvajal-Veloza: None declared, Jaime-Andrés Rubio-Rubio: None declared, Gustavo Salguero: None declared, Luz-Dary Gutiérrez-Castañeda: None declared, Gabriel-Santiago Rodríguez-Vargas: None declared, Pedro Santos-Moreno Speakers bureau: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi, Grant/research support from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi, Dario Echeverri: None declared, Paula-Katherine Bautista-Niño: None declared, Luis Saenz: None declared, Adriana Rojas-Villarraga: None declared.

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AB1765-HPR

APPLICATION OF THE EULAR SYSTEMIC SCLEROSIS IMPACT OF DISEASE (SCLEROID) QUESTIONNAIRE IN AN ITALIAN COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS: ANALYSIS OF PATIENT-REPORTED OUTCOMES AND THEIR ASSOCIATION WITH MAIN DISEASE FEATURES

Keywords: Patient reported outcomes, Outcome measures, Systemic sclerosis

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Background: Systemic sclerosis (SSc) is characterized by a chronic and frequently progressive course and by a high patient-to-patient variability. Due to the lack of disease-specific, patient-reported outcome measures for use in clinical trials and in clinical practice, EULAR recently validated the Systemic Sclerosis Impact of Disease (ScleroID) questionnaire, calculated as a composite score of 10 different health dimensions with Numeric Rating Scales (NRS) from 0 to 10 (from best to worst)(Figure 1). For each dimension, the NRS score is multiplied by the specific weight for its item and the weighted scores are summed up.

Objectives: The aim of this study was to apply ScleroID questionnaire to an Italian cohort of patients affected by SSc and to find any possible association with their main demographical, clinical and serological features.

Methods: 55 consecutive patients with SSc (defined by 2013 ACR/EULAR criteria) were enrolled, ScleroID was administered. Socio-demographic variables and clinical features were recorded. Data were analyzed using GraphPad Prism 8 software. Wilcoxon nonparametric test was used to compare data. Spearman's rank correlation coefficient was used and Linear regression analysis (r correlation coefficient) was employed to identify significant correlations, defined by a p value <0.05.

Results: The main demographic, clinical and serological features of the study population are shown in table 1. ScleroID total score median value of our patients was 42 (IQR 21-57). Significant associations were found among the presence of DU and higher values in the domains of Raynaud's phenomenon (p 0.03), impaired hand function (IHF)(p 0.005), pain (p 0.013), life choices (LC)(p 0.03) and body mobility (BM)(p 0.01). Anti-SCL70 positivity was associated with higher DU domain score (p 0.01). Diffuse SSc form was associated with higher values of IHF (p 0.006), pain (p 0.02), LC (p 0.002), BM (p 0.0005) and DU domains (p 0.003). Moreover, a positive correlation was found between mRSS and IHF (p 0.02), LC (p 0.006), BM (p 0.02) and DU (p 0.04), as well as between lower gastrointestinal symptoms domain and age (p 0.02). A higher ScleroID global score was associated with the diffuse SSc form (p 0.002), the use of immunosuppressive therapy (p 0.01) and the presence of DU (p>0.0001). Finally, this last result was confirmed on multivariate analysis (p0.007).

Conclusion: Our results confirm the reliability of ScleroID questionnaire in the real life of ScS patients, highlighting the impact of an extensive cutaneous involvement and the presence of DU in several health quality dimensions. Thus ScleroID appears to be a valid and easy to perform tool, able to assess the disease activity by a patient reported outcome.

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Table 1. Main features of n55 patients

AGE (median-IQR)	57 (49-56)
Female (n%)	54 (98)
disease duration in years (median-IQR)	8 (4-14)
Scl70+	20 (36)
dcSSc (n%)	19 (34)
mRSS (median-IQR)	4 (0-10)
NVC Scleroderma pattern	45 (81)
Digital Ulcers (n%)	30 (55)
Calcinosis (n%)	7 (12)
ILD (n%)	11 (20)
GI involvement (n%)	33 (60)
CV involvement (n%)	5 (9)
Arthritis (n%)	19 (34)

Figure 1. The EULAR Scleroderma Impact of Disease Score (SclerolD)

How much have the different aspects of systemic sclerosis affected you during the last week? Please mark your responses on the scale by choosing the appropriate number for each of the following dimensions:

Raynaud's phenomenon:
Circle the number that best describes the severity of your Raynaud's phenomenon during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Hand function:
Circle the number that best describes your hand function limitations due to your systemic sclerosis during the last week:
No limitation 0 1 2 3 4 5 6 7 8 9 10 Extreme limitation

Upper gastrointestinal tract symptoms (e.g. swallowing difficulties, reflux, vomiting):
Circle the number that best describes the severity of your upper gastrointestinal tract symptoms due to your systemic sclerosis during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Pain:
Circle the number that best describes the pain you felt due to your systemic sclerosis during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Fatigue:
Circle the number that best describes the impact of overall fatigue due to your systemic sclerosis during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Lower gastrointestinal tract symptoms (e.g. bloating, diarrhea, constipation, anal incontinence):
Circle the number that best describes the severity of lower gastrointestinal tract symptoms during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Limitations of life choices and activities (e.g. social life, personal care, work):
Circle the number that best describes how severe the limitations of life choices and activities due to your systemic sclerosis were during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Body mobility:
Circle the number that best describes how much your body mobility was affected due to your systemic sclerosis during the last week:
Not affected 0 1 2 3 4 5 6 7 8 9 10 Extremely affected

Breathlessness:
Circle the number that best describes how severe your breathlessness due to systemic sclerosis was during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Digital ulcers:
Circle the number that best describes how much your digital ulcers affected you overall during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Becker MO *et al*, Development and validation of a patient-reported outcome measure for systemic sclerosis: the EULAR Systemic Sclerosis Impact of Disease (SclerolD) questionnaire. Ann Rheum Dis. 2022 Apr; 81(4):507-515. doi: 10.1136/annrheumdis-2021-220702. Epub 2021 Nov 25. PMID: 34824049.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1766-HPR

THE IMPACT OF FASTER DIAGNOSIS THROUGH ARTIFICIAL INTELLIGENCE ON THE QUALITY OF LIFE OF PATIENTS WITH RARE DISEASES

Keywords: Quality of life, Descriptive Studies, Artificial Intelligence

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Background: Diseases that affect fewer than 2000 people in the general population are defined as rare diseases [1]. The rarity and the associated limited experience with these diseases, but also the large number of about 8000 rare diseases [2], pose a major diagnostic challenge for physicians. On average, affected patients need 5.6 to 7.6 years until they receive a diagnosis and thus the correct therapy [3]. These diagnostic odysseys place a heavy financial, health, and psychological burden both on patients and their families. Diagnostic decision support systems (DDSS) have great potential to assist physicians in diagnostic decision-making and can indicate the presence of a rare disease much earlier. An exploratory study conducted at the Outpatient Clinic for Rare Inflammatory Systemic Diseases with Renal Involvement at Hannover Medical School showed that the diagnostic process can be shortened by a DDSS. The median lead between diagnosis and the hypothetical time of diagnosis by a DDSS was three months [4]. A follow-up study showed that health economic savings were also possible by making the diagnosis so early [5].
Objectives: Measured against the hypothetical diagnosis time points determined in the previous study [4], this study aimed to investigate, in the same patient population, the extent to which earlier diagnosis using a DDSS would have influenced patients' quality of life (QOL).
Methods: To determine the potential for improving QOL through artificial intelligence (AI), 71 patients from the patient cohort of the previous studies were surveyed [4][5]. The questionnaire was composed of established questionnaires such as the WHO HPQ and the SF-36. In five interview sessions from the onset of the disease, the time of professional diagnosis, to the current time, the development of QOL was retrospectively recorded. To analyze the development of QOL during the disease, but also to show the influence of the DDSS on QOL, data were also collected for the time points at which the DDSS would have indicated the correct diagnosis as the first suggestion or among the first five suggestions.
Statistical analysis, graphical presentation and interpretation of the questionnaires were performed using statistical software.
Results: The study showed that the QOL of most patients improved with a correct diagnosis. The graphically depicted progression of the patients' health perception are shown in **Figure 1**: with the onset of the first symptoms, 65% of the patients found their state of health to be less good or bad, in course of disease, this number increased to 70%. At the current time, the time of the interviews, the number declined to 28%. Originally, no patient was in excellent health, but at the current condition after the diagnostic odyssey, 10% were able to describe their state of health as excellent. The interviews show an overall decline in well-being during the diagnostic odyssey, which slowly increases with the correct diagnosis.
Conclusion: The study showed how much a correct diagnosis affects the patients' QOL. The use of a DDSS would have significantly shortened the diagnostic odysseys and thus improved patients' QOL at an earlier stage.

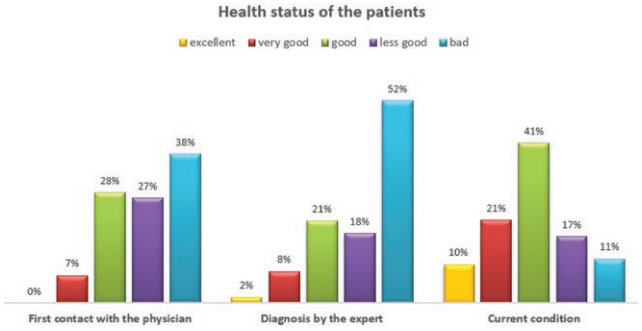


Figure 1. Retrospective development of health perception over the course of the disease among the study participants (n=71). Displayed are the results as an extract of the SF-36.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6357

HPR Epidemiology and public health (including prevention)

AB1767-HPR

DOCUMENT SEARCH IN LARGE RHEUMATOLOGY DATABASES: ADVANCED KEYWORD QUERIES TO SELECT HOMOGENEOUS PHENOTYPES

Keywords: Artificial Intelligence, Systemic lupus erythematosus, Systemic sclerosis

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Background: Natural language processing tools are powerful for mining rheumatology databases, extracting patient information directly from clinical notes. However, these algorithms come with a high computational cost and are often not applicable at the scale of very large databases in the temporality of clinical practice.

Objectives: The objective of our study is the automatic detection of clinical documents of interest for a specific clinical question, with low computational cost, to be applied on a database of millions of documents. These sets of documents of interest constitute a pre-screening to allow the development of more complex algorithms.
Methods: The task was considered as an information retrieval task in French clinical texts. Two different methods were compared. For the first method, we used several state-of-the-art document vector representations: TF-IDF, doc2vec, docBERT and tested if the closest documents are relevant. The second method consists in building a powerful query expansion from a key term entered, its French synonyms from the UMLS and the synonyms found by similarity with the embeddings of the CODER algorithm. These methods are developed and evaluated on a set of 8 and on 20 phenotypes respectively (e.g. "pericarditis in lupus", etc.). Our database corresponds to 2 million documents from a cohort of patients suffering from four autoimmune diseases: systemic lupus erythematosus, scleroderma, antiphospholipid syndrome, and Takayasu's disease, coming from the AP-HP's data warehouse.
Results: Our experience does not support the vector representation model of clinical notes for searching similar patients. However, searching with an advanced synonym search method can lead to very good results without additional burden for the clinician: we achieved a precision (or positive predictive value) of 0.93 [0.90; 0.96] evaluated manually by a physician and a recall (or sensitivity) of 0.78 [0.71; 0.85] evaluated on the basis of the ICD10 codes of the retrieved patients.
Conclusion: We propose a new advanced keyword search method with automatic synonym search with very good accuracy and recall performance.
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Table 1. Accuracy and recall results for 13 over 20 queries.

	Query	Accuracy (on 50 manually-annotated document per query)	Recall (comparison with respective CIM10)	Number of corresponding documents
1	"Rheumatoid Arthritis"	0.98	0.73	15189
2	"Takayasu"	1	0.94	2459
3	"Pericarditis in lupus"	0.92	0.93	7490
4	"Kidney transplantation"	0.92	0.98	10716
5	"Autoimmune hepatitis"	0.8	0.85	2797
6	"Dermatomyositis"	1.0	0.77	3510
7	"Idiopathic thrombocytopenic purpura"	0.98	0.81	3749
8	"Acute kidney injury"	0.86	0.81	15775
9	"Raynaud syndrome"	0.98	0.98	31900
10	"HIV"	0.90	0.98	43582
11	"Scleroderma"	1.0	0.92	24199
12	"Diabetes"	0.96	0.96	51224
13	"Stroke"	0.64	0.63	28162
…	…			
	Overall	**0.93 [0.90; 0.96]**	**0.78 [0.71; 0.85]**	

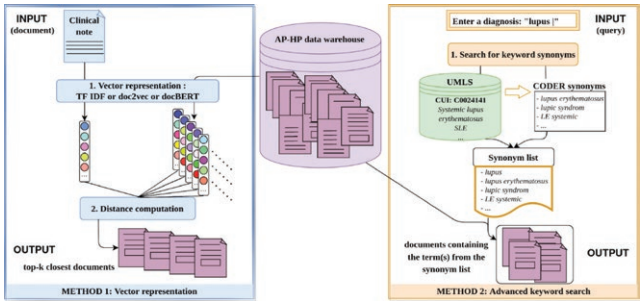


Figure 1. Overview of the two methods of searching for documents in our data warehouse. Method 1 is document oriented and method 2 is keyword oriented.

Acknowledgements: The authors would like to thank the AP-HP data warehouse, which provided the data and the computing power to carry out this study under good conditions. We would like to thank all the medical colleges, including internal medicine, rheumatology, dermatology, nephrology, pneumology, hepato-gastroenterology, hematology, endocrinology, gynecology, infectiology, cardiology, oncology, emergency and intensive care units, that gave their agreements for the use of the clinical data.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6231

AB1768-HPR SAFETY AND EFFICACY OF IMMUNE CHECKPOINT INHIBITORS IN PATIENTS WITH RHEUMATIC AUTOIMMUNE DISEASE: EXPERIENCE FROM THE CANADIAN RESEARCH GROUP OF RHEUMATOLOGY IN IMMUNO-ONCOLOGY (CANRIO)

Keywords: Safety, Epidemiology

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Background: Immune checkpoint inhibitors (ICI) have changed the landscape of treatment for many cancers. However, most cancer clinical trials for ICI excluded patients with pre-existing autoimmune disease (PAD). Efficacy and safety data on the use of ICI in patients with rheumatic PAD (Rh-PAD) is limited to retrospective case series and reports, and many do not differentiate between Rh-PAD and non-rheumatic PAD. In addition, little is known about optimal use of concurrent immunosuppression and its impact on PAD flares and development of de novo irAE. There is some data that patients on immunosuppression at baseline are at risk for poorer tumor outcomes [1].
Objectives: To explore the safety and efficacy of ICI in patients with Rh-PAD and to determine if immunosuppression at baseline impacts risk of PAD flare, de-novo irAE and early tumor outcomes using data from the CanRIO prospective cohort.
Methods: The CanRIO cohort includes adult patients with Rh-PAD treated with immune checkpoint inhibitors (ICI, including CTLA-4, PD-1 or PDL-1 inhibitors), recruited across 9 Canadian academic sites and followed prospectively at regular intervals as per a standardized study protocol. In this study, we evaluated patients with Rh-PAD who received at least one dose of ICI.
Results: Forty patients with Rh-PADs were recruited into the CanRIO prospective cohort between Jan 2020 and Nov 2022, including 14 (35%) with rheumatoid arthritis, 11 (27.5%) psoriatic arthritis, 7 (17.5%) polymyalgia rheumatica, 5 (12.5%) ankylosing spondylitis and 7 (17.5%) other. The most frequently observed cancers were melanoma 14 (35%) and lung cancer 10 (25%), with stage 3 and stage 4 disease each making up 37.5% of all cases. 25 patients (62.5%) were on baseline immunosuppression prior to ICI start. Anti-PD-1 therapy was most common (45%), followed by combination ICI therapy (22.5%), with a median exposure of 2 months (IQR: 0.5-3.0). Over a median (IQR) follow-up of 3.0 (1.0–6.0) months, 55% experienced a de-novo irAE (68.2% with rh-irAE; of which 46.7% were on baseline immunosuppression), 25% had Rh-PAD flare, of which 60% were on baseline immunosuppression. Of these, 40% were severe (of which 50% on baseline immunosuppression); 70% required corticosteroid treatment; and 40% required a change in immunosuppression. ICI was continued in 50%, transiently held or delayed in 40% and stopped in only 10%. Of the 9 patients on baseline immunosuppression who had been re-staged, 8 had a favorable tumor response (i.e., stabilization, partial or complete response) and only 1 had disease progression.
Conclusion: Early data from patients with Rh-PAD in the CanRIO multi-center prospective cohort suggests that (1) ICI can be effective for cancer treatment in patients with Rh-PAD and should be offered as indicated; (2) flares of Rh-PAD are common but can be managed with corticosteroids or escalation of immunosuppression; (3) baseline immunosuppression did not significantly change rate of de-novo irAE or rate/severity of PAD flare (3) most patients with Rh-PADs had good tumour response despite baseline immunosuppression.
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Disclosure of Interests: Lourdes Gonzalez Arreola: None declared, Jeremiah Tan: None declared, Alexandra Ladouceur: None declared, Marie Hudson Consultant of: Consulting fees: Boehringer Ingelheim, Grant/research support from: Unrestricted research grants: Bristol-Myers Squibb, Boehringer Ingelheim; Clinical studies: Astra-Zeneca, Carrie Ye: None declared, Janet Roberts: None declared, Aurore Fifi-Mah: None declared, May Choi: None declared, Sabrina Hoa: None declared, C. Thomas Appleton: None declared, Janet Pope: None declared, Nancy Maltez: None declared, Shahin Jamal: None declared.
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HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

AB1769-HPR **HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH SEPTAL PANNICULITIS**

Keywords: Quality of life

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Background: Idiopathic lobular panniculitis (ILP) or Weber-Christian disease is a rare understudied disease, which manifests itself in recurrent *subcutaneous fat* necrosis often involving damage of the internals. Treatment of the disease is not standardized, and as a matter of fact it is provided empirically.
Objectives: to assess the efficiency of therapy in case of various forms of ILP.
Methods: We studied 34 patients (30 women, 4 men) with ILP, age 30-74, duration of disease 7.4±2.3 years. Besides general clinical examination we determined the level of *α1-antitrypsin,* amylase, lipase, *ferritin, creatine phosphokinase,* made chest CT scan *and carried out the pathomorphological study* of *skin biopsy specimen taken from the area of a node*. The following forms of the disease were identified: nodular form (NF) (14 patients), plaque form (PF) (9 patients), mesenteric form (MF) (5 patients) and infiltrative form (IF) (6 patients). In all cases the lobular panniculitis was verified by means of histopathological examination. All patients took glucocorticoids (GC), average daily dose of 12.8 ± 1.6 mg, including 8.4± 1.7 mg (for NF), 17.6± 3.2 mg (for PF), 8,6 ± 1,6 mg (for MF), 23.6 ± 5.3 mg (for IF). In case of NF, we additionally prescribed Plaquenil, the dose of 600 mg per day (8 patients), and Mycophenolate Mofetil 1.5-2 g per day (6 patients); in case of PF – Cyclophosphamide (Cph), the dose of 200 mg per week (4 patients) or Mycophenolate Mofetil (1.5-2 g per day, 5 patients); in case of MF – Mycophenolate Mofetil (1.5-2 g per day, 5 patients). Patients with IF took Cph (200 mg per week). In case there was no effect after 3 months, we prescribed Mycophenolate Mofetil (1.5-2 g per day). With an unsatisfactory effect, after 3 months, genetically engineered alpha-TNF antagonist drugs were used. On average, the observation period was 12 months.
Results: The treatment made it possible to achieve a significant positive dynamics in patients with NF, PF and MF: the body temperature got back to normal and there was regression of indurations (26 patients), joint pain intensity was reduced (16 patients), laboratory data on inflammatory intensity revealed decrease (24 patients). Average daily dose of GC was reduced to 4.5±0.7 mg and 11.4±1.1 mg, respectively. In general, a significant improvement was evident in all patients with NF and MF, in 75 % of patients with PF. In case of IF an average daily dose was increased to 25.4±1.7 mg per day. In all patients of this group, an unsatisfactory effect was noted, which required discussion of the appointment of genetically engineered biological therapy. The tolerability of treatment was regarded as good, no adverse events were noted. After 14 weeks, 3 patients had a syndrome of "eluding" the effect and IL-1 inhibitor drugs were prescribed for the first time.
Conclusion: To work out dosages and treatment schedules for patients with ILP further studies are required.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1770-HPR **WITHDRAWN**

AB1771-HPR **COMPARISON OF FLARES IN 85 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS, WHO DISCONTINUED, REDUCED DOSE OR MAINTAINED HYDROXYCHLOROQUINE DURING A PROSPECTIVE STUDY OF OPHTHALMOLOGICAL SCREENING FOR RETINOPATHY**

Keywords: Remission, Systemic lupus erythematosus

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Background: Hydroxychloroquine (HCQ) remains one of the most valuable therapies in SLE, and its use is supported by every recent international guideline regardless of the severity of the disease. It is however associated with long term side effects, mainly ophthalmologic whereby is recommended ophthalmologic screening. Little is known on the risk of systemic lupus erythematosus (SLE) flares associated with hydroxychloroquine (HCQ) reduction or cessation, especially following ophthalmologic screening.
Objectives: We analyzed the risk of SLE flares after HCQ reduction or cessation in the context of detection of early signs of ophthalmological toxicity.
Methods: Among 109 patients included in the prospective PERFOCTAPS study and treated with HCQ for at least 5 years, we included all patients with SLE. Patients were divided in three groups: group maintenance corresponding to patients with no ophthalmological alterations maintaining their treatment at the same dose, group reduction corresponding to patients with mild ophthalmological alterations that led to reduction of HCQ dose, and group discontinuation corresponding to patients with retinal abnormalities that led to stopping HCQ. Occurrence of flares (SELENA-SLEDAI flare index) was assessed in the two years following HCQ reduction or discontinuation or following inclusion in PERFOCTAPS study for the maintenance group.
Results: 85 patients were included (98% female, mean age 40.0 years, mean duration of SLE 14.4±7.7 years and of HCQ treatment 12.9±7.2 years, mean dose per kilogram of HCQ was 5.6±1.8 mg/kg/day). PERFOCTAPS study identified ophthalmological abnormalities in 25 patients (29.4%) that led to dose reduction in 20 patients and discontinuation in 5. At inclusion groups maintenance and reduction were very similar; patients in group discontinuation were significantly older with a longer SLE and HCQ treatment duration. There was no significant difference in HCQ dose (mg/kg/day) between the three groups. After reduction, the proportion of patients with a dose of HCQ <5 mg/kg/day became significantly higher in the reduction group than in the maintenance group (85% vs. 35% P<0.001). Flares occurred in 29 patients (34.1%): 17 (28.3%) in the maintenance group, 10 (50%) in the reduction group, and 2 (40%) in the discontinuation group. Flares were severe in 6 patients (10%) in the maintenance group, 4 (20%) in the reduction group and none (0%) in the discontinuation group. After adjustments on potential confounders, HCQ reduction was independently associated with the risk of flare (adjusted HR 2.57; 95% CI 1.14-5.75). The same trend was observed in the discontinuation group but without reaching statistical significance (adjusted HR 3.03; 95% CI 0.66–13.87).
Conclusion: In this prospective study, HCQ reduction due to an early suspicion of retinal toxicity was associated with a statistically significant increased risk of disease flare. This adds data to the growing pendulum return regarding HCQ dose reduction and we should always balance the potential benefits of tapering or discontinuing HCQ with the risk of SLE flare and subsequent need to increase or start other drugs, especially corticoids or immunosuppressors that have well-known adverse effects.
Acknowledgements: JEBRANE Hajar; LAFOLIE Justine; ALONSO Anne Sophie; AUGE Emmanuel; GUILLAUME Jessica.
Disclosure of Interests: None Declared.
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HPR Professional education, training and competencies

AB1772-HPR **PNEUMOCOCCAL VACCINATION IN CHRONIC INFLAMMATORY DISEASE(CIRD) PATIENTS: REASONS FOR NON-PRESCRIPTION AND SOLUTIONS**

Keywords: Vaccination/Immunization, Inflammatory arthritides

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Background:
Objectives: To explore rheumatologists' reasons for non prescription of pneumococcal vaccination in CIRD patients and to collect solutions proposed by rheumatologists.
Methods: This is a cross-sectional study carried out by the vaccination working group of the Moroccan Society of Rheumatology. The survey collected data on reasons of pneumococcal vaccination abstinence in rheumatology practice, and solutions proposed to improve pneumococcal vaccination in CIRD patients.
Results: This survey included 125 rheumatologists (mean age 42.4 +/-12.1 years). The sector of practice was respectively 31.2 %,34.4 %,34.4 % for the public sector, private sector and University Hospital. 36.9% of rheumatologists have never prescribed pneumococcal vaccination for their CIRD patients. Table 1 illustrate reasons given by rheumatologists for non vaccination of their CIRD patients against pneumococcal infection.

Table 1. Reasons for not prescribing the pneumococcal vaccine

I don't vaccine my CIRD patients because	%
The pneumococcal vaccine is not recommended for CIRD patients	2,4
The pneumococcal vaccine is expensive	30,4
I don't master enough the protocol	40,8
I forget to prescribe it	57,6
Patients refuse the pneumococcal vaccination	10,4

Concerning proposed solutions, rheumatologists recommended reinforcing pneumococcal vaccination awareness among rheumatologists, Integrating the vaccine into the social security reimbursement protocol, and including the pneumococcal vaccination for CIRD patients in respectively 92 %,71.2 %,60 % of cases.

Conclusion: The main obstacles to the pneumococcal vaccination prescription by rheumatologists are related to the lack of knowledge of vaccination protocol and the forgetfulness. Therefore, the Optimization of pneumococcal vaccination would necessarily focus on combating the obstacles to this preventive practice in CIRD patients.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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HPR Interdisciplinary research

AB1773-HPR CONNECTIVE TISSUE DISEASE-RELATED INTERSTITIAL LUNG DISEASE: AN EXPERIENCE OF A MULTIDISCIPLINARY TEAM IN COLOMBIAA

Keywords: Lungs, Descriptive Studies, Imaging

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Background: Interstitial lung disease (ILD) occurring in a person with a known or classifiable connective tissue disease (CTD) is referred as CTD-ILD. Approximately 15% of ILDs will have a background CTD. The presence of ILD is the primary determinant of prognosis. High-resolution CT (HRCT) is the diagnostic image of choice. Interstitial involvement can have different patterns, with nonspecific interstitial pneumonia (NSIP) being the most frequent. CTD-ILD is a challenging entity and its approach requires multidisciplinary teams (MDT).
Objectives: To describe clinical, serological, and radiological characteristics of patients who present with CTD-ILD at a reference ILD center in Colombia between 2021 and 2022
Methods: A descriptive study of patients with ILD diagnosed by HCTR who have a confirmed autoimmune disease or at least one autoimmune feature, clinical or serological. Every case was evaluated by our MDT composed by pulmonologists, radiologists, rheumatologists, and pathologists. We developed an ILD registry from our inpatient and outpatient ILD-clinic between 2021 and 2022. The continuous variables were described as the mean and standard deviation, and nominal variables were evaluated based on frecuencies and percentages. All analysis were done in statistical package for the social sciences (SPSS) v. 21.0.
Results: Forty patients with ILD were included; 57% were hospitalized, and 65% were women. The majority of patients with ILD were diagnosed as interstitial pneumonia with autoimmune features (IPAF, 30%), followed by multiple autoimmune syndromes (22,5%), rheumatoid arthritis (15%) and primary Sjogren's syndrome (12,5%). The most common radiologic pattern was usual interstitial pneumonia (40%), followed by fibrotic NSIP (22.5%). The most common clinical finding where lung crackles (61,5%), sicca symptoms (57,5%) and arthritis (30%). Mean CVF in L(%) was 173 ± 89,8(72,6±27,2) and mean DLCO(%)52,6 ± 21. Progressive pulmonary fibrosis was frequent (20%), and 12.5% received antifibrotic therapy. Our mortality rate related to ILD was 21.7%.

Table 1. General characteristic of patients with CTD-ILD

Characteristic	N= 40
Age - yr	65 ± 11.6
Female sex – no. (%)	26 (65)
Inpatient – no (%)	23 (57,5)
Mortality – no. (%)	5 (21,7)
Diagnosis confirmed by biopsy	9 (22,5)
Autoimmune disease no. (%)	N= 40
SLE¥	1 (2,5)
SSp ¥	5 (12,5)
RA¥	6 (15)
SSc¥	3 (7,5)
AAV ¥	1 (2,5)
IPAF¥	12 (30)
Poliautoimmunity & multiple autoimmune syndrome	9 (22,5)
Radiologic pattern no. (%)	
NSIP¥	5 (12,5)
Fibrotic NSIP¥	9 (22,5)
NSIP & OP ¥	1 (2,5)
UIP ¥	16 (40)
UIP & OP¥	2 (5)
Indeterminate UIP ¥	3 (7,5)
Probable UIP¥	2 (5)
OP¥	2 (5)

¥SLE systemic lupus erythematosus, SSp: Sjogren syndrome, RA: rheumatoid arthritis, SSc: systemic sclerosis,AAV: anti-neutrophil cytoplasmic antibody-associated vasculitis, IPAF: Interstitial pneumonia with autoimmune feature,NSIP: non-specific interstitial pneumonia, OP: organizing pneumonia, UIP: usual interstitial pneumonia

Conclusion: In our 1-year cohort, we found that IPAF was the most prevalent CTD-ILD, followed by multiple autoimmune syndromes. The most common radiologic pattern overall was UIP, followed by fibrotic NSIP. CTD-ILD had a high mortality rate. Most of these cases were related to ILD. Our results highlight the importance of early disease detection and early therapeutic interventions. Treatment decisions must be individualized, and the risk of disease progression must be considered.
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Acknowledgements: Hospital Universitario San Ignacio - Interstitial lung disease multidisciplinary team.
Disclosure of Interests: Camila Borda Samper: None declared, Juan Sebastian Sierra: None declared, Daniel G. Fernández-Ávila Speakers bureau: yes, Carlos Celis Preciado: None declared, Maria Díaz Speakers bureau: yes.
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AB1774-HPR SAFETY OF THE RECOMBINANT HERPES ZOSTER VACCINE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH JAKI DRUGS

Keywords: Epidemiology, Vaccination/Immunization, Health Services Research

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Background: Patients receiving JAK inhibitor drugs (JAKi) have an increased risk of herpes zoster (HZ). A new recombinant vaccine effective against HZ (Shingrix-RV) is currently recommended for patients treated with JAKi.
Objectives: To evaluate the safety of first and second dose of the recombinant vaccine against HZ (HZ-RV) in patients with RA, in treatment with JAKi.
Methods: Retrospective study of the safety after receiving the first and after 2 months, second dose of the HZ-RV in patients with RA treated with JAKi.
The following variables were collected: general information of the patients, type of JAKi and time in treatment; use and dosage of DMARDcs drugs and/or corticosteroids. Regarding HZ: infection prior to HZ-RV and time elapsed; occurrence and type of side effects after vaccination.
Results: Of 138 patients treated with JAKi, 9 (7%) refused vaccination, 129 (93%) received the first dose on HZ-RV, but 38 (28%) patients received it before starting JAKi and 98 (72%) being a mean of 36 months in treatment with JAKi. The second dose was administered in 113 (82%) patientes, 21 (15%) patients had suffered HZ, before vaccination. One hundred and eight (84%) are female (mean age: 64 [SD: 3] years), on JAKi treatment a mean of: 2.4 (SD: 1.6) years: 89 (69%) baricitinib (2 mg/day: 29 [33%] patients; 4 mg/day: 60 [67%]), upadacitinib: 48 (44%) and 3 (3%) patients with tofacitinib. Eighty seven (67%) patients were receiving DMARDcs: methotrexate: 55 (63%), mean weekly dose: 17.5 mg (SD: 3.5), leflunomide: 22 (25%), hydroxychloroquine: 8 (9%), sulfasalazine: 2 (2%). Fity six (40%) patients received prednisone: mean daily dose: 5.2 mg (SD: 1.8). During one month after first dose of vaccine, 97 (75%) and 62 (55%) after second dose had side effects (p=0.68): local pain: 95 (74%) vs 62 (55%) patients, p=0.014; fatigue: 27 (21%) vs 15 (13%), p=0.17; arthralgia-myalgia: 21 (19%), p=0.17; fever < 38ºC: 10 (8%) vs 15 (13%), p=0.69; headache: 9 (7%) vs 3 (3%), p=0.72; local itching: 3 (2%) vs 2 (2%), gastrointestinal symptoms: 2 (2%) vs 2 (3%), p=0.943; and after first dose, others in 4 (4%) patients: urinary tract infection, oral ulcer, dizziness, injection site erythema. Lymphadenopathy, hospital admission, flare of RA or serious secondary effects were not detected. After 90 days of second vaccine, a 58-year-old woman (0.8%) undergoing 5-month treatment with baricitinib 4 mg/day and methotrexate, without corticosteroids, presented a slight facial HZ reactivation dose.
Conclusion: 1. Vaccination with HZ-RV was safe. 2. Although a great percentage of pacients have experienced any side effect, especially after the first dose of vaccine, these were mild. 3. No flare of RA has been detected in this period. 4. Less than 1% of patients suffered HZ reactivation after vaccination.
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Disclosure of Interests: None Declared.
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AB1775-HPR

ECONOMIC BURDEN OF PRENATAL CARE FOR WOMEN WITH RHEUMATIC DISEASES

Keywords: Health Services Research, Pregnancy and reproduction, Quality of life

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Background: Autoimmune rheumatic diseases (ARDs) affect childbearing women. To prevent adverse maternal and fetal outcomes, multidisciplinary attention is needed, leading to increased costs of pregnancy attention [1].The financial burden that pregnant women with ARDs have,lacksprofound research.
Objectives: This study aims to estimate the total cost of prenatal care in pregnant women with ARDs in northeast Mexico.
Methods: A cross-sectional and descriptive study was carried out at the University Hospital "Dr. Jose E. Gonzalez", offering affordable care to uninsured patients. We estimatedthe direct costs of prenatal care for women with rheumatoid arthritis(RA), systemic lupus erythematosus (SLE), and Sjögren's syndrome(SS) from the ACR/ EULAR perspective[2, 3]. National standardswere used to determine the regular prenatal care requirements [4].To calculate the total expense, prices declared by the University Hospital in 2021 were used. The used currency is USD, considering an equivalence of USD 1 = 20.28 MXN. Calculating indirect costs, such as transportation, medication, or other interventions, was not performed. No sociodemographic data from patients was used.
Results: The itemized costs for medical appointments, ultrasounds, laboratory tests and vaginal delivery or cesarean section for women without ARDs, with SS, RA andSLE are in **Table 1.**Prenatal care total costs for women without ARDs, with SS, RA and SLE are exposed in **Figure 1.** Our findings reported an average cost of pregnancy per trimester was up to 102.76% in women with ARDscompared to women without ARDs (USD 386.52 vs 783.72) Limitations include the variability of service prices and the absence of indirect cost calculations.
Conclusion: In conclusion, ARD-affected women had a high economic burden secondary to prenatal costs. In this vulnerable population, creating programs for prenatal care that consider the patient's financial statusshould be a priority for public health officials and institutions.

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Table 1. Prenatal care costs by unit and mean total expenditure for women with ARDs

Clinical assessment and laboratory tests	Cost (USD)	Frequency	Total (USD)		Cost per trimester	Total cost
*Rheumatology **	12.32	Per trimester	36.96	Women without ARD	142.15 - 173.37	426.44 - 520.11
Obstetrics	23.00	At least 5	69.00			
Ultrasound	53.74	Per trimester	161.22			
Genetics	49.30	If necessary	49.30			
Psychology	39.44	If necessary	39.44			
Nutrition	4.93	If necessary	4.93			
Complete blood count	8.87	Per trimester	26.61			
Blood chemistry	38.46	Per trimester	115.38			
25-hydroxy vitamin D*	59.17	Per trimester	177.51			
Thyroid profile*	16.27	Per trimester	48.81			
PT, TTP*	36.40	Per trimester	109.20			
CRP and ESR*	25.11	Per trimester	75.33			
Urinalysis	5.92	Per trimester	14.79			
HIV and VDRL test	29.09	Once	29.09			
Blood type with Rh factor	10.35	Once	10.35			
Immunological tests for SS			38.94	Women with SS		913.19 - 1,006.86
Immunological tests for RA			97.12	Women with RA		971.37 - 1,065.04
Immunological Tests for SLE			454.60	Women with SLE		1,328.85 - 1,422.52

PT: Prothrombin time, PTT: Partial thromboplastin time, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

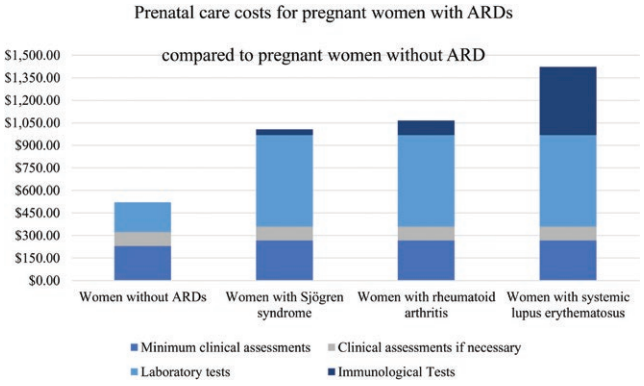


Figure 1.

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HPR Interventions (educational, physical, social and psychological)

AB1776-HPR

REVMAMAS – A PODCAST FOR PEOPLE WITH RHEUMATIC DISEASE WHO ARE PLANNING A PREGNANCY OR ARE PREGNANT

Keywords: Patient information and education, Pregnancy and reproduction

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Background: A survey distributed by patient organisations in rheumatology in 2019 have uncovered an unmet need for high quality and accessible patient information on pregnancy and rheumatic diseases. Previous publications have presented the same results (1, 2). During the pandemic, we have seen a shift from healthcare with physical consultations to digital follow-up of the inflammatory rheumatic disease. The Norwegian National Advisory Unit on Pregnancy and Rheumatic Diseases (NKSR) primary task is to spread updated knowledge, including patient information, regarding different aspects of pregnancy and rheumatic diseases. To reach out to the target population in this digital era, NKSR have started using social media, such as Facebook and Instagram, in addition to YouTube to spread patient information. As a natural next step we wanted to establish a podcast on different topics related to pregnancy and rheumatic diseases so patients and partners could have easy access to high quality reliable information at all times and for all of Norway.
Objectives: To develop a podcast with different topics related to pregnancy and rheumatic diseases. The podcast is primary aimed at people with inflammatory rheumatic disease and their partners, but is also relevant for healthcare professionals.
Methods: Based on webinars published on YouTube from NKSR during the pandemic, we edited and published six podcast episodes. We had help from the department of communications to adjust the podcast for publication. We chose a platform for podcasts without fees and easy access to make sure it was available for everyone.
Results: We published six podcast episodes as season one. A multidisciplinary team with rheumatologist, nurse, midwife, patient representatives, partner and occupational therapist participated in the podcast. The episodes have the following topics: Planning a pregnancy, preparing for birth, patient experience, fatigue and everyday activities with small children, partners perspective and men and anti-rheumatic medications. The episodes lasts from 16 to 27 minutes. The podcast is available on the most used platforms for podcast listeners in Norway. We used NKSR platforms in social media to spread the word about the podcast.
Conclusion: Using podcast as a platform to spread high quality and knowledge based patient information can be effective to increase accessibility of patient information. The episodes are available on demand, regardless of where you live. People with rheumatism can stream the short episodes whenever convenient, for example in the car, one the buss to work, when walking the dog or when doing chores. Planning of season two has already begun.

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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1777-HPR

INVESTIGATION OF THE EFFECT OF HAND EXERCISES ON GRIP STRENGTH, FUNCTIONALITY, DISEASE ACTIVITY AND QUALITY OF LIFE IN INDIVIDUALS WITH PSORIATIC ARTHRITIS: A RANDOMIZED CONTROLLED TRIAL

Keywords: Randomized control trial, Psoriatic arthritis, Physical therapy/ Physiotherapy

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease accompanied by psoriasis in the spondyloarthritis group and often progresses with peripheral arthritis, dactylitis, enthesitis and spondylitis [1]. Majority of PsA patients have peripheral arthritis involvement [2]. In addition to peripheral arthritis in PsA patients, structural damage occurs in the joints as the process is chronic and progressive. This structural damage causes worsening of the functional status of the patients [3]. Worsening functionality reduces patients' quality of life. Also EULAR (Recent European League Against Rheumatism) recommends physical therapy in inflammatory arthritis including PsA [4]. It is known that individuals with PsA have lower hand strength, dexterity, coordination and functionality compared to their healthy peers [5]. There is no scientific study that applies a hand-focused home exercise program to improve the grip strength and functionality of the hand in individuals with PsA.
Objectives: The aim of this study was to examine the effect of hand exercises on grip strength, functionality, disease activity, and quality of life in patients with PsA.
Methods: 37 PsA patients (29female, 8 male) with an average age of 50.32± 9.12 were included in this study. Patients were randomized into intervention (group 1) and control (group 2) groups. Group 1 received hand home exercises for 4 days a week for 8 weeks. Group 2 was on the waiting-list and they received the same exercises when the study was finished. The Disease Activity Index for Psoriatic Arthritis (DAPSA) was used to evaluate the disease activity. Hand Dynamometer and pinchmeter was used to evaluate the hand grip and pinch strength. Duruoz Hand Index (DHI), Michigan Hand Outcomes Questionnaire (MHQ), Hand Functional Index (HFI), Nine Peg Hole Test (NPHT) were used to evaluate the hand functionality. Psoriatic Arthritis Quality of Life was used to evaluate the quality life. All evaluations were performed at baseline and at the end of the 8th week.
Results: When the groups were compared before training, there was no significant difference (p> 0.05). In post-training comparisons, there was a significant difference in MHQ, hand grip and pinch strength in hand exrecises group. (p:0.02-0.00). In addition, after post-training, hand exercises group was found to be superior in terms of MHQ and NPHT compared with control group.
Conclusion: According to this study, hand exercises have a positive effect on grip strength and functionality in patients with PsA. Hand exercises should be included in rehabilitation programs as a home exercise to improve grip strength, functionality and daily living activities for patients with PsA.
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AB1779-HPR

ASSESSING THE INTERNAL VALIDITY OF THE BSR PAIN MANAGEMENT FOR INFLAMMATORY ARTHRITIS QIP TOOL

Keywords: Patient reported outcomes, Inflammatory arthritides, Pain

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Background: Pain management is an important component of many Inflammatory Arthritis consultations. The BSR Pain Management for Inflammatory Arthritis Quality Improvement Tool uses 11 questions and 38 sub questions that assess three domains; background information (3 questions), pain management in the consultation (5 questions) and pain management in previous consultations (3 questions) [1]. The questions are based on the EULAR Guidelines for Pain Management in Inflammatory and Osteoarthritis [2]. The tool is free to use, produces results in real time in anonymised PDF form. The project is sponsored by Cambridge University Hospitals NHS Foundation Trust Audit Department (Number 2200).
Objectives: To assess the internal validity of the Pain Management for Inflammatory Arthritis Quality Improvement (QIP) tool 2020.
Methods: Two independent researchers (A & B) reviewed appointment/clinic notes from 33 patients who had attended Rheumatology appointments at Addenbrooke's Hospital. 20 of these patients were found to experience pain during the consultation and the QIP tool questionnaire was used to assess their pain management. To assess the internal validity of the QIP tool; results from each reviewer were compared to generate a Cohen's Kappa Score for each question.
Results: The overall Kappa Score for the QIP tool was 0.75, with 570 congruent results and 190 incongruent results. The congruence was found to be high across the majority of questions. 87/190 (46%) of the incongruent scores were from just 6/38 questions. The QIP tool questions can be modified to improve clarity. There was systematic bias in the questions with lower kappa scores (A answering "Yes" and B answering "No").
Conclusion: The Pain Management for Inflammatory Arthritis QIP Tool has a high internal validity as shown by the Kappa scores generated by results from two independent reviewers. To overcome the low Kappa scores on individual questions; additional guidance on how to answer specific questions may need to be provided to those filling out the questionnaire.
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AB1780-HPR

FIBROMYALGIA PATIENTS' EXPERIENCES AFTER ONE-WEEK SELF-MANAGEMENT PROGRAMME FOUR TO TEN MONTHS AFTER DISCHARGE: A QUALITATIVE STUDY

Keywords: Fibromyalgia, Qualitative research methods, Self-management

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Background: The European League Against Rheumatism (EULAR) emphasizes in its guidelines for the treatment of fibromyalgia (FM) that Health professional should aim to improve health-related quality of life, which often requires a combination of non-pharmacological and pharmacological treatment methods. Non-pharmacological approaches have been shown to be effective In this study, a multidisciplinary self-management programme (SMP) was used to treat patients with (FM).
Objectives: To investigate and understand the experiences of individuals with FM who participated in a one-week SMP.
Methods: A qualitative study using semi-structured interviews was used to investigate the participants' experiences. A total of 22 women and 2 men with

FM were interviewed 4 to 10 months after participating in a one-week SMP. The participants' goals and action plans after the SMP were used together with an interview guide. All the interviews were audio-recorded, transcribed verbatim and analysed using thematic analyses. The large body of material is divided into three sub-studies. The first sub-study is presented here.

Results: The mean age of the participants was 54.7 years (range 32–68). The participants' experiences were categorized into four main themes: recognition of the diagnosis, a turning point for a better life, changing one's way of thinking and having control over one's own life. Giving up the past was one description that the participants used as a way of changing their mindset. They could then focus more on the present and the future. To have control over their own lives, it became important to accept the opportunities and limitations they had in everyday life.

Conclusion: Four to ten months after completing the SMP, the participants in this study experienced that they were taken seriously with their FM diagnosis. The participants had attained a heightened awareness of what they could do to take control and manage their disease and daily life.

Acknowledgements: The author would like to thank all the informants who shared their experiences.

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AB1781-HPR PERFORMANCE OF A NURSE-LED INTERVIEW FOR MALIGNANCY SCREENING AND ALERTING PHYSICIAN PROGRAM

Keywords: Malignancy, Rheumatoid arthritis, Nursing

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Background: Malignancy is one of the leading causes of death in patients with rheumatoid arthritis (RA). While there has been a debate about whether or not biological disease-modifying antirheumatic drugs (bDMARDs) increase cancer development in RA patients, these patients should be screened appropriately for their malignancies. However, there has been limited data about the method to increase malignancy screening.

Objectives: We implemented a nurse-led malignancy screening and alerting physician program into our daily clinical practice. The aim of this study is to evaluate the performance of this program.

Methods: Our program included patients with RA treated with intravenous biological DMARDs between September 2015 and October 2020. We first created a list of the required malignancy screening based on the patient's gender and age (Figure 1). Nurses interviewed the patients during the administration of bDMARDs to assess if they were appropriately screened for malignancies as required and thereafter provided education about the importance of malignancy screening. Nurses recorded the patient's malignancy screening status and alerted physicians by sharing the results if the patient needed additional screenings. This program was periodically repeated once a year. We assessed the difference in the proportions of completed per required screening between repeated assessment time points.

Results: A total of 154 patients were included in the analyses. The mean (standard deviation) age was 64.6 (13.2) at the first screening, and 113 (73.4%) were female. Ninety-three, forty-five, and fourteen patients underwent 2nd, 3rd, and 4th interviews, respectively. Repeating this program numerically increased the proportion of conducted malignancy screenings per required screening. (58.6%, 66.5%, 60.6%, and 73.1% at the 1st, 2nd, 3rd, and 4th interview, respectively) (Table 1). In addition, several patients understood, for the first time, the importance of malignancy screening during this interview with nurses.

Conclusion: Implementing a nurse-led interview for malignancy screening and alerting physician program numerically increased the screening of malignancy in RA patients treated with bDMARDs. This multi-disciplinary cooperation can potentially improve the quality of healthcare for patients with RA.

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Table 1. Result of malignancy screening at each time point of repeated-interview

	1st screening (n=154)	2nd screening (n=93)	3rd screening (n=45)	4th screening (n=14)
The proportion of conducted per required malignancy screening	58.6 (36.4) %	66.5 (34.1) %	60.6 (30.8) %	73.1 (25.2) %
P value (vs 1st screening)	Ref	0.095	0.89	0.17
For each examination (Conducted/Required)				
MMG or Breast US	50/107	39/68	23/38	8/11
Uterine examination	30/46	29/24	12/15	5/5
EGD	94/148	57/92	30/45	11/14
Occult fecal blood test	65/132	49/83	23/44	9/13
Colonoscopy	84/132	59/83	25/44	8/13

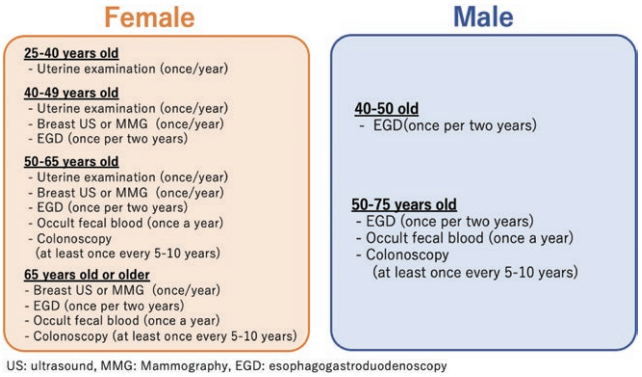


Figure 1. The list of recommended malignancy screenings

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Disclosure of Interests: None Declared.

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AB1782-HPR USABILITY AND ACCEPTABILITY OF A NEW AUTOINJECTOR DEVICE AND ITS ASSOCIATED APP IN RHEUMATOLOGY PATIENTS

Keywords: Self-management, bDMARD, Inflammatory arthritides

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Background: SMARTCLIC is a new reusable autoinjector with a dose-dispensing cartridge for subcutaneous self-administration of biotherapeutics for patients. The device can connect to the optional SmartClic mobile app to aid in tracking injections and other treatment or symptom data.

Objectives: The aim of this study was to assess patient opinion data on ease of use and usability of the SmartClic injector and app.

Methods: This study presents final data of all patients (N=264) from a global study. Patients from Argentina (n=50), Australia (n=15), Germany (n=46), France (n=28), Japan (n=75), and Spain (n=50), were included. After completing a patient profiling questionnaire, adult patients (≥18 years old) with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or juvenile idiopathic arthritis (JIA), and prescribed an injectable biologic, each received training to use the device and cartridge and performed simulated injections. Participants completed a device evaluation questionnaire with including the following categories: 'ease of use' (14 questions), 'usability effectiveness' (11 questions), 'benefit of device features' (8 questions) and 'form factor' (7 questions). Participants also received a storyboard presentation summarizing key features of the optional app, which they could test on an Android/or iOS device,

before completing up to 16 questions on connectivity and the app. Responses to device/and app questions were recorded as Likert scale ratings from 1 (extremely negative) to 7 (extremely positive). Estimates of patient training time for the device were also provided. Hand function based on the Functional Index of Hand Osteoarthritis Arthropathies (FIHOA) score, hand pain in the injection hand due to arthritis and grip strength were also recorded. Mean values are reported. The percentage of negative (Likert scale rating 1-2), neutral (3-5) and positive (6-7) responses for each category were determined.

Results: A total of 264 patients (mean age [range], 50 [18-85] years; 76% female) participated in the study. Patient diagnosis was, RA (71%), PsA (24%) and JIA (5%). The majority of patients (90%) were right-handed. While most patients (73%) always self-injected their medication, 19% of patients reported that they were mostly assisted with their injections or never self-inject. Most patients performed injection simulations using the dominant hand (77%) and chose the abdomen (54%), thigh (36%) or both (10%) abdomen and thigh as the injection site. Hand function based on the mean FIHOA score was 5.6 (range 0-24), and hand pain in the injection hand due to arthritis was 2.8 (range 1-7). Mean grip strength (range) was 19 (0-60) kg and 18 (2-54) kg in the dominant and non-dominant hand, respectively. Patients reported being “extremely comfortable” (58%) or “slightly comfortable” (35%) with digital equipment. Mean device evaluation scores (% positive responses) were: device ease of use 6.4 (87%), usability effectiveness 6.4 (87%), benefit of device features 6.6 (92%), form factor 6.2 (80%) and connectivity and app 6.2 (79%). The mean time (range) estimate for training a patient to effectively use the device and cartridge was 9.6 minutes (range 0-30 minutes).

Conclusion: Patients with RA, PsA or JIA, and experienced at receiving biologic treatment for their conditions, responded positively to the new autoinjector device and app across all categories. These features will contribute to a better experience of self-injection.

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AB1783-HPR VALIDATION OF AN ELECTRONIC VISUAL ANALOG SCALE APP FOR PAIN EVALUATION IN CHILDREN AND ADOLESCENTS WITH SYMPTOMATIC HYPERMOBILITY: CROSS-SECTIONAL STUDY

Keywords: Mixed connective tissue disease, Patient information and education, Pain

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Background: Rapid advances in mobile apps for clinical data collection for pain evaluation have resulted in more efficient data handling and analysis than traditional paper-based approaches. As paper-based visual analogue scale (p-VAS) scores are commonly used to assess pain levels, new emerging apps need to be validated prior to clinical application with symptomatic children and adolescents.

Objectives: This study aimed to assess the validity and reliability of an electronic visual analogue scale (e-VAS) method via a mobile health (mHealth) App in children and adolescents diagnosed with hypermobility spectrum disorder/hypermobile Ehlers-Danlos syndrome (HSD/HEDS) in comparison with the traditional p-VAS.

Methods: Children diagnosed with HSD/HEDS aged 5-18 years were recruited from a sports medicine center in Sydney (New South Wales, Australia). Consenting participants assigned in random order to the e-VAS and p-VAS platforms were asked to indicate their current lower limb pain level and completed pain assessment e-VAS or p-VAS at one time point. Instrument agreement between the 2 methods was determined from the intraclass correlation coefficient (ICC) and through Bland-Altman analysis.

Results: In total, 43 children with HSD/HEDS aged 11 (SD 3.8) years were recruited and completed this study. The difference between the 2 VAS platforms of median values was 0.20. Bland-Altman analysis revealed a difference of 0.19 (SD 0.95) with limits of agreement ranging -1.67 to 2.04. An ICC of 0.87 (95% CI 0.78-0.93) indicated good reliability.

Conclusion: These findings suggest that the e-VAS mHealth App is a validated tool and a feasible method of collecting pain recording scores when compared with the traditional paper format in children and adolescents with HSD/HEDS. The e-VAS App can be reliably used for pediatric pain evaluation, and it could potentially be introduced into daily clinical practice to improve real-time symptom monitoring. Further research is warranted to investigate the usage of the app for remote support in real clinical settings.

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AB1784-HPR COMPARISON OF POSTURAL CHANGES AND FUNCTIONAL LEVELS AMONG DIFFERENT SUB-TYPES OF AXIAL SPONDYLOARTHRITIS PATIENTS

Keywords: Physical therapy/Physiotherapy, Patient reported outcomes, Outcome measures

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Background: Axial Spondyloarthritis (axSpA) is divided into two sub-types as radiographic axSpA which is commonly known as ankylosing spondylitis, and non-radiographic axSpA which defines no structural radiographic damage in sacroiliac joints. The systemic, inflammatory nature of axSpA, chronic pain, inflammatory cytokines, changes in the bone and ligaments of the spine may affect spine posture and functional level.

Objectives: The aim was to compare spine posture and functional levels differences among radiographic axSpA, non-radiographic axSpA patients and healthy controls.

Methods: Twenty patients with radiographic axSpA (mean age; 39.95± 9.75, 15 female), 20 patients with non-radiographic axSpA (mean age; 38.55± 2.74, 15 female), and 20 age and sex-matched healthy controls (15 female) were included in the study. The patients were evaluated with Bath Ankylosing Spondylitis Metrology Index, Bath Ankylosing Spondylitis Disease Activity Index, Bath Ankylosing Spondylitis Functional Index, Ankylosing Spondylitis Quality of Life Questionnaire. Thoracic and lumbar curvature tests were measured with a digital inclinometer (Acumar, Dual Digital Inclinometer, Lafayette Instrument Company, IN, USA).

Results: No differences were detected in disease activity level, disease-related functional status, disease-related quality of life between radiographic and non-radiographic axSpA patients ($p>0.05$). However, time since onset of symptoms, spinal mobility were higher in radiographic axSpA patients ($p<0.05$, Table 1). Radiographic axSpA patients showed higher thoracic curvature degree compared to non-radiographic axSpA patients and healthy controls ($p<0.05$, Table 1). Radiographic and non-radiographic axSpA patients presented lower lumbal lordosis degree compared to healthy controls ($p<0.001$, Table 1).

Conclusion: The results of the present study suggest that disease sub-types of axSpA may affect the spine posture, in particular thoracic curvature degree. Every effort should be taken to impove spine postüre in axSpA patients; however, sub-type specific considerations should be kept in mind for planning exercise/physical activity programs.

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Table 1. Comparison of groups

	Radiographic axSpA (n: 20) X±SS	Non-radiographic axSpA (n: 20) X±SS	Healthy Controls (n:20) X±SS	p
Disease-Related Characteristics				
Time Since Onset of Symptoms (months)	167.50±101.05	103.83±49.16	NA	**0.009***
BASMI	3.27±1.25	1.95±0.52	NA	**<0.001***
BASDAI	4.43±1.86	3.62±1.48	NA	0.104*
BASFI	3.25±1.47	3.08±1.66	NA	0.721*
ASQoL	9.87±3.35	10.70±3.81	NA	0.438*
Spine Posture				
Thoracic curvature (°)	44.64±6.86	39.40±4.55	33.78±2.32	**<0.001****
Lumbar curvature (°)	39.48±8.26	38.94±9.15	47.83±4.02	**<0.001****

*Student's T Test, **One-way ANOVA Test, BASMI: Bath Ankylosing Spondylitis Metrology Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, ASQoL: Ankylosing Spondylitis Quality of Life Questionnaire, NA: Not Applicable, p<0.05.

AB1785-HPR RELIABILITY, AND VALIDITY OF THE TURKISH VERSION OF THE EXERCISE THERAPY BURDEN QUESTIONNAIRE

Keywords: Outcome measures, Patient reported outcomes, Validation

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Background: Chronic diseases, as demonstrated by the 36 million deaths they caused in 2008, are the most common cause of death worldwide. Exercise is one of the non-pharmacological treatment methods. The main objectives of exercise, one of the treatment methods, is to reduce pain, prevent loss of function in daily activities and work, and increase the quality of life, exercise capacity, and muscle strength. Although exercise benefits are known, more than half of the population does not exercise due to some exercise burden. However; there are no measurement methods assessing exercise burden patients with chronic disease.

Objectives: The objectives of the current study were to evaluate the Turkish validation of the Exercise Therapy Burden Questionnaire into Turkish (ETBQ-T) and to investigate its reliability and validity.

Methods: 100 participants (69 female and 31 male) who were diagnosed with at least 1 chronic disease participated in the translation validity, and reliability analysis of the study. Cross-culturally adaptation of the ETBQ-T was performed according to Beaton's guideline. The ETBQ-T, the European Quality of Life 5 Dimensions (EQ-5D), pain, satisfaction, and self-efficacy were applied for convergent validity. The ETBQ-T was retested to examine its reliability after seven days.

Results: The internal consistency and reliability were excellent (Intraclass correlation coefficient= 0.959; Cronbach's alpha= 0.919) (Table 1). The ETBQ-T had a good correlation with pain (r = 0.564, p <.001), satisfaction (r = 485, p <.001), and self-efficacy (r = 0.582, p <.001). However; The correlation of the ETBQ-T with EQ-5D (r = 0.364, p <.001) was weak. A factor was extracted, accounting for 58.289% of the total variation. There were no floor and ceiling effects.

Conclusion: The ETBQ-T is a reliable and valid tool to evaluate the exercise burden in the Turkish population with chronic disease.

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Table 1. ICC and Cronbach's alpha if item deleted results for the ETBQ-T

ETBQ-T	ICC (95% confidence interval) Lower-Upper Bound	Cronbach's alpha if item deleted	
Item 1	0.842 (0.725-0.909)	Except for item 1	0.909
Item 2	0.926 (0.871-0.958)	Except for item 2	0.910
Item 3	0.861 (0.757-0.920)	Except for item 3	0.910
Item 4	0.898 (0.822-0.941)	Except for item 4	0.909
Item 5	0.876 (0.784-0.929)	Except for item 5	0.913
Item 6	0.946 (0.906-0.969)	Except for item 6	0.913
Item 7	0.932 (0.881-0.961)	Except for item 7	0.910
Item 8	0.861 (0.759-0.920)	Except for item 8	0.915
Item 9	0.855 (0.747-0.917)	Except for item 9	0.911
Item 10	0.855 (0.748-0.917)	Except for item 10	0.915
Total score	0.959 (0.929-0.977)	Total score	0.919

ICC: Intraclass Correlation Coefficient, ETBQ-T: Exercise Therapy Burden Questionnaire turkish

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Disclosure of Interests: None Declared.
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AB1786-HPR ASYNCHRONOUS TELECONSULTATION BY WHATSAPP CHATBOT IN CONTROLLED AXIAL SPONDYLOARTHRITIS (SPA) PATIENTS UNDER BIOLOGICAL THERAPY: CLINICAL RESULTS OF A SINGLE CENTER

Keywords: Spondyloarthritis, bDMARD, Telemedicine

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Background: The use of telehealth in the control of rheumatic diseases had been scarce, but COVID pandemic forced to try alternatives to classic face-to-face consultation, and an overflow of telehealth consultations appeared, mainly synchronous (phone, video calls), and finally asynchronous. We try to demonstrate that asynchronous WhatsApp teleconsultation is a good alternative, at least for followup of patients that find it difficult to attend face-to-face visits. We chose axial spondyloarthritis (AxSPA) patients under biological therapy with controlled disease and we proposed teleconsultation with a WhatsApp platform chatbot created for this purpose. The chatbot sends PROMS (BASDAI, VAS for patient global disease assessment, ASDAs, and 3 questions for extraarticular disease), and receive feedback and schedule for the following visits.

Objectives: To prove that teleconsultation through WhatsApp platform is not inferior to face-to-face consultation in terms of maintaining axial SPA patients disease controlled.

Methods: Prospective study with retrospective control of patients diagnosed of Axial SPA, fulfilling ASAS criteria and with stable disease under biological therapy for the previous year, recruited from 01 jan to 30 nov 2021. We recruited 62 patients, but two of them gave up (personal reasons, one moved to other region), so we finally include 60 patients. We offer them two teleconsultation visits with their personal mobile device, every four months, and a face-to-face final visit one year after inclusion. In the case of lab test or PROMs deviation or when the patient asks for contact (possible via WhatsApp) he/she is called up by the person in charge (nurse/doctor) that solves the question and arranges an additional presential visit if needed. We consider disease controlled if BASDAI <4, ASDAS < 2,1 or if in rheumatologist´s opinion there is no need to change treatment. We collect patient and disease information (age, gender, employment, characteristics of the disease, previous and actual treatment), activity (BASDAI, PCR, ASDAS), physical function (BASFI), and Quality of life (AsQol).

Results: 60 patients (50 men, 83,3%) were included, mean aged 48,22 years (SD 12,128), 36% were under 45 years at the time of inclusion. They were mostly Ankylosing Spondylitis (AS) (90%; only 6 non radiographic SPA), positive HLA B27 (85%) and with longstanding disease (mean 23 years, SD 12,8), and only 6 patients less than five years. 25% had peripheral impairment (arthritis/dactylitis/enthesitis), and more than 40% presented extraarticular manifestations, mainly psoriasis (26,7%) and uveitis (21%)

71,7% were under their first biological (TNF inhibitor, mostly adalimumab), 23,3% were refractory to the first, and 3 patients to at least two biologicals. 51,7% of patients were treated with tapered dose of TNF inhibitors. At inclusion 93,3 %

presented remission/LDA by ASDAS/BASDAI-RCP. Only 4 patients included presented higher activity scores but were considered clinically controlled.

Table 1.

	BASAL MEAN	FINAL MEAN	MEAN DIFFERENCE
BASDAI	1,725 (SD 1,496)	2,268 (SD 1,3420)	0,5434 (SD 1,1483)
BASFI	2,108 (SD 1,619)	1,943 (SD 1,6228)	0,1492 (SD 1,3420)
ASDAS-RCP	1,288 (SD 1,496)	1,608 (SD 0,6297)	0,3198 (SD 0,6005)
AsQOL	2,53 (SD 3,311)	2,35 (SD 2,906)	0,2456 (SD 1,7856)

We did not find meaningful clinical differences between basal to final visits in BASDAI, BASFI, ASDAS-RCP or AsQOL.
3 patients with reduced dose of biological drug needed to increase to standard dose with no other need to treatment adjustment.
Conclusion: We consider asynchronous teleconsultation is promising, and not inferior to face to face consultation in terms of keeping disease control and quality of life, especially for follow-up in patients with stable rheumatic disease, The clinical results presented here are consistent with this considerations.
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Disclosure of Interests: None Declared.
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AB1787-HPR A REAL-LIFE OF EXPERT PATIENT WITH RHEUMATOID ARTHRITIS. AN EVALUATION OF THE PATIENT ACTIVATION MEASURE PAM-13

Keywords: Rheumatoid arthritis, Patient reported outcomes

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Background: In 2021, a group of rheumatoid arthritis (RA) patients were certified as an expert patients. These were trained for the care and management of their disease. During their training, they answered the Patient Activation Measure PAM-13 questionnaire, which measures people's knowledge, skills and confidence in self-managing their health and medical care.
Objectives: The aim of this study is to know the activation and empowerment levels of the patients in their daily life and in their exercise as expert patients in RA, determining the self-management they have of their disease and the perspective they have developed towards their health and towards their health care team.
Methods: A group of expert patients with a diagnosis of RA were included. A sociodemographic characterization was carried out and variables such as age in years, marital status, educational level and support networks, among others, were measured. Patients filled out the PAM-13 questionnaire. This tool contains some phrases that people use to talk about their health. Each sentence contains response options that include: "strongly agree", "agree", "disagree" and "strongly disagree". This exercise seeks to find out what patients think about aspects related to the care of their health condition and medical care. Descriptive statistics were done and the responses of the first two options were totalized ("strongly agree" and "agree").
Results: A total of 91 patients were evaluated with the PAM-13 tool. General sociodemographic and clinical characteristics are shown in table 1. With respect to the responses of the 13 variables of the PAM-13 questionnaire, the patients state [n(%)] that they have developed a high level of awareness in the care management of their disease [83 (91)], they have developed a high therapeutic adherence [83 (91)], understand that lifestyles are essential to avoid complications [83 (91)], adopted an effective and clear communication language with their medical team [82 (90)], developed self-care lifestyles [80 (88)], understand the importance of using prescribed medications [80 (88)], developed habits oriented towards a healthy and active life [78 (85)], understand the nature and symptoms of their disease [78 (85)], are aware that they are the main co-managers of their condition [78 (85)], frequently assist their medical team and use emergency services [79 (87)], act in crisis situations [80 (88)), follow instructions of their medical team [73 (80)] and make shared decisions as [65 (71)] (see Figure 1).

Table 1. Demographic characterization of the participating patients.

Participant´s characteristics		n= 91
Gender (n %)	Male	6 (7)
	Female	85 (93)
Age in years, mean		61
Age in years, group (n %)	<65	62 (68)
	≥65	29 (32)
Marital status (n %)	Married	46 (51)
	Divorced	11 (12)
	Single	29 (32)
	Widowed	5 (5)
Education (n %)	Primary School	8 (9)
	High School	34 (37)
	Vocational training	26 (29)
	University or more	22 (24)
	None	1 (1)
Duration of disease in years (n %)	≤20	52 (57)
	>20	39 (43)
Support and family (n %)	Direct support	81 (89)
	No support	10 (11)

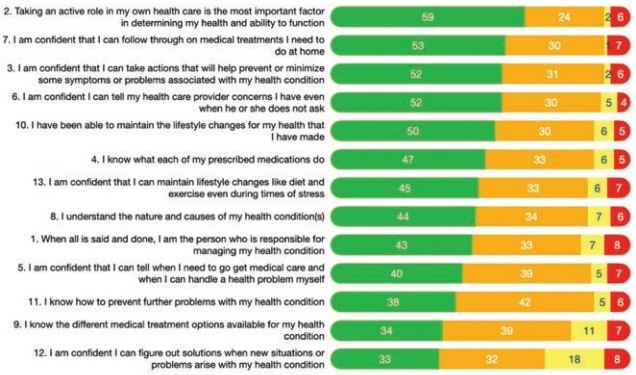


Figure 1: Results of the PAM-13 tool in expert patients with RA

Conclusion: In general, expert RA patients are proactive with their health and have developed strong self-management skills evaluated through PAM-13. The use of these tools is important to assess the role of the patient in their treatment. This allows generating strategies that increase the commitment of patients during their therapy.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: Fernando Rodriguez: None declared, Gabriel-Santiago Rodríguez-Vargas: None declared, Adriana Rojas-Villarraga: None declared, Pedro Santos-Moreno Speakers bureau: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi, Grant/research support from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi.
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AB1788-HPR ASYNCHRONOUS TELECONSULTATION BY WHATSAPP CHATBOT IN CONTROLLED AXIAL SPONDYLOARTHRITIS PATIENTS UNDER BIOLOGICAL THERAPY: PATIENTS' PERSPECTIVE

Keywords: Telemedicine, Spondyloarthritis, Quality of life

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Background: Before COVID pandemic, rheumatologists were not confident with telehealth for the need to adquire new technology, need of specific training and poorer reimbursement [1]. Two groups of rheumatoid arthritis (RA) patients have been identified in a study of PROMS-based telehealth use (2): the keen and the reluctant. We proposed teleconsultation followup with a whatsapp platform chatbot to our axial spondyloarthritis (AxSPA) patients with controlled disease and we asked them for preferences at the end of the study.

Objectives: To explore the degree of acceptance of asynchronous telehealth followup with whatsapp platform chatbot among our controlled AxSPA patients under biological therapy, and to search for a patient profile more prone to telehealth consultation.
Methods: A prospective study with retrospective control was performed, chosing AxSPA patients under biological therapy with stable disease, visited in our centre from 01/01 to 30/11/2021. We recruited 62 patients, but finally include 60 (2 quit for home moving or personal reasons). We offered them two teleconsultation visits (using their personal mobile), every four months, and a presential final visit one year after inclusion. The chatbot sends PROMS (BASDAI, VAS for patient global disease assessment, ASDAS, and 3 questions for extraarticular disease), and feedback and schedule for the following visits. In the case of lab test or PROMs deviation or when the patient asks for contact, he/she is phoned by nurse/doctor who solves the question and/or arranges an additional presential visit. We collect patient and disease characteristics (age, gender, educational level, employment, disease activity, duration and treatments), and patient´s satisfation and preferences in the final visit.
Results: We included 60 patients (83,3% men), mean aged 48,22 years (SD 12,128), 36% under 45 years at inclusion. 27% had received primary, 33.9% secondary and 39% tertiary education. 83.3% were active working and only 10 patients were jobless or retired. They were Ankylosing Spondylitis (AS) (90%), HLA B27 positive (85%) with longstanding disease (mean 23 years, SD 12,8), and were receiving the first (71%), or the second (23%) biological therapy (51,7% tapered anti-TNF). 50% were never smokers and 70% presented no remarkable comorbidity; 25% presented peripheral impairment, and over 40% extraarticular manifestations. At inclusion 93,3% were at remission/LDA by ASDAS/BASDAI-RCP and 4 patients were considered clinically controlled in spite of higher scores. At followup 3 patients with reduced dose needed to increase to standard dose of biological drug, with no other need of treatment change. There was no worsening from basal to final visits according BASDAI, BASFI, ASDAS-RCP or AsQOL. Patients final VAS score (1-10) assessment of telehealth consultation was very high: mean 9,14 (DS 1,498); 91.7% ≥ 8 and 76.7% ≥ 9. 83,3% preferred telehealth followup. There was a trend towards telehealth preferences in higher educational levels, and active working (86% vs 70%) but not statistically significant. We found no correlation with gender, age and disease characteristics tested.
Conclusion: Asynchronous teleconsultation seems promising, not inferior to presential consultation and preferred for follow-up by our AxSpa patients with stable disease with biological drugs. We met some "reluctant patients", that were more inactive working and with lower educational levels, but the differences were not significant. Further reserarch is needed with this telehealth model in other age and disease populations (RA), in order to characterize the reluctant and keen patients.
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AB1789-HPR

30 SECONDS CHAIR STAND TEST - FEASIBLE AS SELF-ASSESSMENT TEST FOR KNEE OSTEOARTHRITIS?

Keywords: Self-management, Diagnostic Tests, Outcome measures

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Background: A reliable self-assessment test to evaluate physical performance could be useful for patients with knee osteoarthritis to monitor physical function over time. However, studies comparing a self-assessment test with standardized testing in the clinic supervised by a physiotherapist is lacking. The 30 seconds chair stand test is part of a test battery which is recommended both in research and in clinical settings for patients with osteoarthritis [1]. The chair stand test is a reliable physical performance test for patients with knee osteoarthritis [2, 3].
Objectives: The purpose is to evaluate the 30 seconds chair stands test as self-assessment test for patients with knee osteoarthritis and when it is supervised by a physiotherapist.
Methods: A sample size of 147 patients with knee osteoarthritis will be recruited. Each patient will perform two self-assessment tests with two days in between. Another test supervised by physiotherapist will be conducted within a week after the second self-test. Demographic data, knee-related quality of life using knee injury and osteoarthritis score – short version (KOOS-PS) [3], pain duration, pain intensity using numeric rating scale (NRS) 0-10 [4]; pain sites, experienced intermittent and constant knee pain (ICOAP) [5], will be collected. Data collection is ongoing and preliminary data will be presented descriptively.
Results: So far, 91 patients have been recruited, whereas 60 patients (58% females) with a mean age of 69 years, and mean body mass index of 30 (SD 5) have been included in the preliminary analysis. Patients reported mean pain duration of 46 months (SD 52), rating mean pain intensity 3/10 (SD 2), and 83% had pain in more than one joint. Patients reported mild to moderate pain (total mean ICOAP-score 44/100, SD 21). KOOS-PS score was 60/100 (SD 14) showing moderate difficulties in knee-related daily activities. Mean number of chair stands for self-assessment tests 1 and 2 were 13.7 (SD 5.6) and 14.7 (SD 6.0) respectively and mean number supervised by physiotherapists were 13.3 (SD 4.8).
Conclusion: Preliminary results of this study indicate that 30 seconds chair stand test as self-assessment test might be an option for patients with knee osteoarthritis to monitor their own physical performance. Yet, to ensure the agreement between self-assessment and physiotherapist assessment, a reliability study is needed.
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Acknowledgements: NIL.
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HPR Epidemiology and public health (including prevention)

AB1790-HPR COVID-19: AFTER TWO YEARS OF IATROGENIC AND BIOLOGIC IMMUNIZATION/ VACCINATION DO WE ACTUALLY NEED FURTHER BOOSTER IMMUNIZATION/ VACCINATION?

Keywords: COVID, Vaccination/Immunization, Epidemiology

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Background: The Covid19 pandemic started in late 2019 and went through different phases by spreading from China around the whole globe. During the pandemic different mutation types got predominant from original Wuhan type through Alpha, Delta and Omicron variate BA 1/2 to BA 4/5 with different infectiousity and different potential to harm people´s health status. Immunization/ vaccination program started late 2020, first booster phase started midst of 2021, second booster phase in late 2021/ beginning of 2022 and Omicron specific booster phase midst of 2022.
Objectives: Is there a need of further iatrogenic (booster) immunization/ vaccination after 2 years of immunization/ vaccination program from efficacy driven analysis and safety issues standpoint?
Methods: Analysis of Covid-19 antibody development every three months since August 2021 with comparison of infection rates and assessment of safety parameters by assessing D-Dimers as potential endothelium damage marker in 725 patients (600 female, 125 male, age mean: 62,2 years) of a German rheumatological practice to improve the medical care.
Results: In 99 % of the patients longstanding immune memory could be shown by analyzing the antibody curves in different exemplary shown biologic and iatrogenic immunization pathways after 2 years of immunization/ vaccination program and biologic immunization, mainly by Delta variate since late 2021 and Omicron variate since beginning of 2022. In 38.5 % of the patients the safety concerns of potential endothelium damage by analysing D-Dimers every 3 months showed a side effect potential of at least 8 months after every MRNA/ Vector immunization, but not after protein based vaccination and even not after infections in that amount.
Conclusion: Out of the obligation “nil nocere” no further iatrogenic Covid-19 immunization/ vaccination is of need in nearly all (99 %) already immunized people. At present only adult people with very low antibody levels (at least below 64 BAU/ml) (considering the infection or iatrogenic immunization/ vaccination status and time since last spike protein contact) and not yet immunized adult people should be forseen for iatrogenic immunization/ vaccination with protein based or attenuated viral vaccines or in rare cases one Omicron specific MRNA immunization drug. In that case D-Dimer controls for up to 8 months should be obligatory to detect endothelial damage side effect of MRNA (or Vector) technique. Intense cardiovascular monitoring (small vessels) of MRNA/ Vector immunized people in the next 10 – 20 years is necessary.

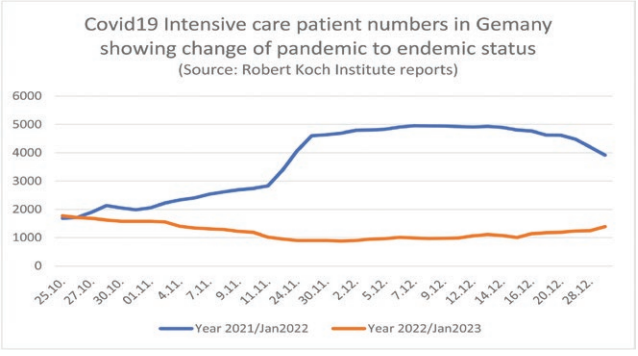


Figure 1.

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AB1791-HPR EVALUATION OF DIAGNOSTIC AND THERAPEUTIC DELAY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

Keywords: Education, Inflammatory arthritides, Health Services Research

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Background: Inflammatory arthritis, such as Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA), are diseases that require timely therapeutic intervention to reduce or stop the progression of joint damage and diseases flares. Early diagnosis and rapid accessibility to care lead to a better patient management.
Objectives: We conducted a monocentric study in a cohort of patients affected by RA and PsA to assess factors related to diagnostic delay and accessibility to treatments, in order to improve patients management.
Methods: Between June and September 2022, clinical and serological characteristics, time (months-years) between symptoms onset and the diagnosis and the initiation on csDMARDs-ts/bDMARDs therapy, of RA patients - according to EULAR/ACR 2010 criteria - and PsA patients - according to CASPAR criteria - were collected. In addition we evaluated place of residence (small/big city (>200.000)), who made referral to the rheumatology center, physician who made the diagnosis (rheumatologist/other specialist/family doctor), possible wrong diagnosis previously made. Statistical analysis was conducted using Student T-test/ Mann-Whitney U Test/one-way ANOVA when appropriate, via GraphPad Prism version 8.0.2. *P* values <.05 were considered significant.
Results: 100 RA patients and 100 PsA patients were included *(table I)*. Statistical significant differences were observed concerning: diagnostic delay (PsA patients 5.2±7.6 yrs vs versus RA patients 2.5±4.6 yrs, *p=0.003*), time passed between symptoms onset and initiation of csDMARDs therapy (PsA 5.3±7.6 vs RA 2.7±5.1, *p=0.006*), and between diagnosis and initiation of ts/bDMARDs therapy (PsA 3.5±5.5 vs RA 7.1±8.6, *p=0.0007*). In the two groups: **-** In the residents of small and medium sized cities compared to the big cities residents, in the diagnostic delay (6.1±10.2 vs 2±1.8, *p=0.02*), in the time between symptoms onset and the start of first line therapy with csDMARDs (6.4±10.7 years vs 2.3±1.9 years, *p=0.02*). **-** In patients who have been diagnosed by another physician rather than rheumatologist, in the diagnostic delay (4.7±11.1 vs 3.9±6.2, *p=0.034*) and in the start of I-line therapy (4.7±11 vs 4.2±6.7, *p=0.019*) In RA: - In the group of patients who had a previous diagnosis - mostly osteoarthritis (35.5%) and UCTD (16.1%) - in diagnostic delay (3.7±6.7 vs 1.9±3.1, *p=0.03*) and in the time between symptoms onset and initiation of a csDMARD (4±6.8 vs 2.1±4, *p=0.05*). In seronegative RA: - Delay in diagnosis (4.2±4.7 vs 1.8±4.6, *p=0.02*) and starting of I-line therapy (4.5±5.3 vs 2±5.1, *p=0.03*) and II-line therapy from symptoms onset (11.6±9.6 years vs 7.9±7.8 years, *p=0.04*) compared with the seropositive ones. In PsA: - In patients with previous diagnosis - mostly osteoarthritis (34.1%) and fibromyalgia (19.1%) - in the diagnostic delay (8.1±10 vs 3±4.1, p=*0.003)*, in the time passed between symptoms onset and initiation of csDMARDs (8.1±10 vs 3.1±4.2, *p=0.001*) and ts/bDMARDs therapy (12±11.1 vs 6±6.5, *p=0.0004*).
Conclusion: Diagnostic delay is greater in PsA than in RA, in both groups of patients living in small-medium cities and in those who have been diagnosed by another specialist. Major diagnostic delay is present in both groups of patients who

have previously been misdiagnosed and in the seronegative RA patients. Consequence is a delayed starting of therapies, with possible permanent joint damage.

Table 1. Clinical, serological and demographic features of the study population.

	PsA	RA	Total
Sex			
Male (n/%)	35 (35)	23 (23)	58 (29)
Female (n/%)	65 (65)	77 (77)	142 (71)
Age (±SD)	55±139	61.3±12	58. 1±13.3
RF (n/%)	-	66 (66)	-
ACPA (n/%)	-	63 (63)	-
PsO (n/%)	68 (68)	-	-
Previous diagnosis (n/%)	44 (44)	32 (32)	76 (38)
Big city (n/%)	46 (46)	47 (47)	93 (46.5)
Small/medium city (n/%)	54 (54)	53 (53)	107 (53.3)
Diagnosed by rheumatologist (n/%)	85 (85)	81 (81)	166 (83)
Referral			
Spontaneous (n/%)	43 (43)	36 (36)	79 (39.5)
Family doctor (n/%)	17 (17)	36 (36)	53 (26.5)
Another specialist (n/%)	40 (40)	28 (28)	68 (34)

REFERENCES: NIL.
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Disclosure of Interests: None Declared.
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HPR Interventions (educational, physical, social and psychological)

AB1793-HPR SPINAL INVOLVEMENT IN PAGET'S DISEASE OF BONE

Keywords: Bone diseases

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Background: Paget's disease of bone (PDB) is a benign acquired osteodystrophy characterized by excessive and disorderly bone remodeling that may affect one or more bones. The spine is the second site affected by Paget's disease (53%) after the pelvis (70%). Vertebral involvement is therefore likely to lead to complications which are fortunately relatively rare.
Objectives: to describe the clinical, biological and radiological aspects of the of PDB with spinal involvement, to highlight certain complications and to describe the management of patients with spinal localization.
Methods: This is a retrospective and descriptive study of the files of patients hospitalized for Paget's disease of bone with spinal involvement over a period of 20 years (Year 2000- Year 2020).
Results: Twenty-six patients (12 women and 14 men) were included. The average age of our patients was 66,8 years. The discovery of the PDB was fortuitous on standard radiographs and an elevation of PAL in 7,6% of cases. PDB was symptomatic in 92,4% of cases. Spinal pain was mechanical in 95,2% of cases. Three of our patients had spinal cord compression: Two patients had cervical compression and one patient had lumbar compression with Brown Sequard syndrome. Phosphocalcium balance was normal according to laboratory standards in all cases. An increase in PAL was found in 73% of cases. Standard X-ray of the dorsal spine showed condensation with widening affecting the vertebral bodies of D4, D8 and D11 in 43% of cases. Vertebral compression at levels D4, D8, D10 and D11 was found in 28.5% of cases. The radiograph of the lumbar spine showed condensation with hypertrophy of the vertebrae L1, L2, L3, L4, L5 in 37.5% of cases. A vertebral compression of L1, L2 and L4 was found in 31.25% of cases and an aspect of ivory vertebra in L3 and L4 in 12.5% of cases. A fibrillar aspect of the vertebral bodies of L1, L2 and L3 was objectified in 18.75% of cases. An aspect of vertebra in frame of L2 was observed in 6.25% of cases. Hypertrophy of the posterior L4 joints was reported in 6.25% of cases. Technetium 99m bone scintigraphy showed hyperfixation of a single seat in 9% of cases and multiple in 91% of cases. It had highlighted asymptomatic localizations in 9% of cases. Spinal CT was performed when there was doubt about the metastatic origin of the bone lesions in 5 cases, when there was low back pain or lumbo-radiculalgia in 5 cases. It showed signs in favor of PDB with corticomedullary dedifferentiation type in 6 cases, lytic bone lesions in 1 case and condensing lesions in 1 case, hypertrophy of the cortex and vertebral bodies in 1 case and vertebral collapse in 1 case. Spinal magnetic resonance imaging (MRI) was performed in 7 patients (27% of cases) when in doubt about the secondary metastatic origin of bone lesions in 3 cases (42.8%) or in search of a spinal cord compression in 4 cases (58.2%). It showed hypertrophy of the vertebral bodies, vertebral compression with recoil of the posterior wall in 4 cases and intramedullary hypersignal in 1 case. Sensorineural complications such as sensorineural hearing loss and occipital headache in 1 of our patients. Sarcomatous degeneration was observed in 1 of our patients. Drug treatment based on calcitonin or bisphosnate was administered in 77% of patients. The general evolution was good in 77.3% of cases (17 cases) with disappearance of pain in 95.3% of cases and normalization or maintenance of a normal level of ALP in 71.5% of cases.
Conclusion: Paget's disease of bone with spinal involvement is a serious disease that can compromise the functional and sometimes life-threatening prognosis of our patients. Diagnosis, early management and close monitoring of our patients are necessary to prevent its complications.
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HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

AB1794-HPR SPONDYLOARTHRITIS: IS THERE A GENDER DIFFERENCE?

Keywords: Gender/diversity issues, Spondyloarthritis

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Background: Spondylarthritis (SpA) affects men more frequently than women. Few studies have analysed gender differences in clinical and biological characteristics of SpA, hence the purpose of this study.
Objectives: We aimed to analyse gender differences in SpA manifestations and disease activity.
Methods: We conducted a cross-sectional study including 30 men and 30 women with SpA meeting the 2009 ASAS criteria. The comparison between men and women included the following data: age at onset, disease duration, clinical and biological characteristics, activity scores (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS)), and functional impact (Bath Ankylosing Spondylitis Functional Index (BASFI)).
Results: Compared to women, male patients had a younger age at disease onset (male (M)= 24.7 ±7.7 vs female (F)= 28.9 ±5.8, p= 0.00), a longer disease duration (M= 14.3 ±6.1 vs F= 11.9 ±4.2, p= 0.05), a longer morning stiffness (p=0.01) and a greater number of nocturnal awakenings (p=0.01). Similarly, SpA was more active in male patients compared to female patients: CRP (M= 22 ±3.5 vs F= 14 ±2, p=0.00) and ASDAS (M= 3.7 ±0.7 vs F= 2.9 ±0.2, p= 0.01). Coxitis was more common among male patients: M= 28.3% vs F= 13.3%, p= 0.00. However, no gender differences were observed for VS, BASDAI, BASFI and therapeutic strategy. Comorbidities were predominant in male patients: cardiovascular disease (M= 18.3% vs F= 8.3%, p=0.00), osteoporosis (M= 16% vs F= 13.3, p=0.05), hypertension (M= 15% vs F= 6.6%, p=0.01) and dyslipidemia (M= 11.6% vs F= 6.6%, p=0.00). However, depression was more common among female patients (p= 0.01).
Conclusion: Our study showed that SpA was more active in male patients. Comorbidities were more common among men compared to women. Further studies should be conducted to better illuminate gender differences in SpA.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1795-HPR COXITIS IN RHEUMATOID ARTHRITIS: IS THERE ANY CORRELATION BETWEEN CATASTROPHIZING AND FUNCTIONAL DISABILITY?

Keywords: Rheumatoid arthritis

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Background: Coxitis is a marker of severity in rheumatoid arthritis (RA) since it is associated with a functional disability. Therefore, it leads to a loss of autonomy with a significant psychological impact.
Objectives: We aimed to assess the correlation between catastrophizing and functional disability associated with rheumatoid coxitis.
Methods: We conducted a cross-sectional study including patients with RA (2010 ACR/EULAR criteria). Clinical, biological and radiological data were collected. RA activity was assessed using the Disease Activity Score (DAS_{28} ESR). The quality of life was assessed using the Health Assessment Questionnaire (HAQ). Hip function was assessed using the Lequesne algofunctional index (IAF). Catastrophizing was evaluated by the Pain Catastrophizing Scale (PCS), which is composed of 13 items. PCS total score varies from 0 (no catastrophizing) to 52 (significant tendency to catastrophizing). The correlation between Lequesne IAF and PCS was evaluated using the Spearman test.
Results: We included 80 patients (76 women and 4 men) with an average age of 47±12 years [37-77]. The average age at diagnosis was 29±7.5 years. The mean disease duration was 11±6.2 years. RA was erosive in 90% of cases. Rheumatoid factor and anti-citrullinated peptides antibodies were positive in 83% and 85% of cases, respectively. Seventy-five percent of patients were on corticosteroids with an average dose of 10 mg per day of Prednisone equivalent. All patients were on DMARDs: methotrexate (85%), leflunomide (11.2%), and bDMARDs (37.5%). The mean pain Visual Analog Scale was 5.5 cm. The mean overall patient assessment was 4 cm. The mean number of nocturnal awakenings was 1.5. The mean duration of morning stiffness was 45±7.5 minutes. The mean ESR was 29.4±6. The mean CRP was 19.5± 4.4. The mean DAS_{28} ESR was 4.5±2.2. The mean HAQ was 1.2±0.4. The mean PCS was 34±3. Coxitis was noted in 28.7% of patients. It was inaugural in 52.1% of cases and bilateral in 14 cases. The mean coxitis duration was 6.8 years. The mean Lequesne IAF was 10.5±3.2. A statistically significant correlation was noted between Lequesne IAF and PCS (r=0.41; p=0.01).
Conclusion: Our study showed that functional disability associated with rheumatoid coxitis was moderately correlated with catastrophizing. Comprehensive management, taking into account the cognitive behavioural sphere, is thus recommended in RA patients with coxitis.
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Disclosure of Interests: None Declared.
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AB1796-HPR ALTERED ANKLE AND KNEE MUSCLE ARCHITECTURE AND FOOT PRESSURE DISTRIBUTION IN KNEE OSTEOARTHRITIS PATIENTS: A COMPARATIVE CROSS SECTIONAL STUDY

Keywords: Ultrasound, Osteoarthritis, Physical therapy/Physiotherapy

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Background: Osteoarthritis (OA) of the knee is a common degenerative and chronic disease as well as a major cause of knee pain and functional disability. Alterations in lower extremity biomechanics may lead adaptive changes in walking, foot pressure distribution, lower extremity muscle strength as well as the architectural characteristics of the knee and ankle muscles in patients with knee OA.
Objectives: The aim of this study was to compare the knee and ankle muscle architecture and foot pressure distribution differences in knee OA patients with healthy individuals.
Methods: Twenty patients with knee OA (mean age= 53.35±1.21 years, mean BMI=31.69±0.93 kg/m2) and twenty healthy controls (mean age= 51.05±0.63 years, mean BMI=29.28±1.15 kg/m2) were included in the study. Rectus Femoris (RF), Vastus Medialis (VM), Peronalis Longus (PL) and Medial Gastrocnemius (MG) muscles thickness, pennation angle and fat thickness were evaluated using B-Mode ultrasonography (Esaote MyLab X8 eXP Ultrasound System, Florence, Italy). Ultrasound images were analyzed offline using an image analysis software (Image J, National Institutes of Health, Bethesda, MD, USA) program. Plantar pressure distribution was evaluated using the Digital Biometry Scanning System and Milletrix software (DIASU, Italy). Mann-Whitney U test was used to compare knee OA patients with the healthy individuals.
Results: The age (p=0.189) and BMI (p=0.367) were comparable between groups. The muscle architectural characteristics of RF, VM, PL and MG were different between groups (Table1). The distribution of foot pressure parameters were altered in knee OA patients compared to healthy controls (Table1).
Conclusion: The fat thickness of ankle and knee muscles were higher in knee OA patients compared to healthy controls. Clinicians should consider adding aerobic and resistance exercises to their treatment programs that will increase muscle thickness and decrease fat thickness. The medial load of the foot increased while the lateral load decrease in these patients. Medial supported insoles may be recommended to reduce the medial load on the foot.
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Table 1. Muscle architectural characteristics and foot pressure distribution among the groups

	Parameters	OA Group (n=20) median (IQR)	Healthy Group (n=20) median (IQR)	p
RF	Fat thickness (cm)	1.4 (1-2.2)	1.05 (0,6-1.5)	**0.001***
	Muscle thickness (cm)	1.8 (1.3-2.8)	2 (1.5-2.9)	0.211
	Pennation angle (°)	12 (8.7-18.2)	12.8 (10.3-17.5)	0.341
VM	Fat thickness (cm)	1.4 (0.8-2.1)	0.9 (0.6-1.8)	**0.001***
	Muscle thickness (cm)	1.7 (1.4-2.8)	1.9 (1.3-2.6)	**0.048***
	Pennation angle (°)	11.6 (7.2-16.9)	13.4 (10.1-19.6)	**0.046***
PL	Muscle thickness (cm)	0.8 (0.6-1.1)	1 (0.6-1.3)	**0.007***
	Pennation angle (°)	11.1(7.2-15.7)	10.6 (8.6-16.6)	0.296
MG	Fat thickness (cm)	1 (0.7-1.6)	0.8 (0.6-1.6)	**0.005***
	Muscle thickness (cm)	1.8 (1.3-2.5)	1.9 (1.2-2.4)	0.398
	Pennation angle (°)	20.6 (15.2-23.3)	21.6 (17.8-28.2)	0.221
Foot Pressure Distribution	Total surface area (cm^2)	265.2 (186-331.2)	224.1 (143.2-350)	0.050
	Total load (kg)	39.7 (25.2-52)	32.2 (22.4-62)	**0.009***
	Medial load (kg)	18.3 (12.8-25.8)	15.6 (11.3-31.5)	**0.009***
	Lateral load (kg)	16.6 (12.3-28)	20.6 (11.1-30.5)	**0.008***
	Foot angle (°)	8.1 (2.6-16.7)	10.5 (4.9-14.6)	**0.043***
	Foot progression angle(°)	9.3 (0.7-27.9)	11 (1.5-17.9)	0.134

OA: Osteoarthritis, RF: Rektus Femoris, VM: Vastus Medialis, PL: Peronalis longus, MG: Medial Gastrocnemius, IQR: interquartile range*p<0.05 Mann-Whitney U test

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AB1797-HPR HIGH AWARENESS AMONG NURSES OF THE SYMPTOM BURDEN PATIENTS WITH SSC-PAH IS IMPORTANT TO PROVIDE THE BEST POSSIBLE PATIENT CARE

Keywords: Systemic sclerosis, Qualitative research methods, Nursing

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Background: Systemic sclerosis (SSc) is a severe disease with significant increased morbidity and mortality. A feared organ manifestation is pulmonary arterial hypertension (PAH). Little is known how the development of PAH affects SSc patients in their symptom burden. It is therefore important to explore the health-related quality of life (HRQoL) in patients with SSc-PAH. A major purpose of care is to reduce symptoms and disability, and be able to improve the HRQoL.
Objectives: 1) To explore SSc patients perceived HRQoL.
2) The nurses role to influence the patients to improve their HRQoL for the best possible care in the clinical practice.
Methods: Six SSc patients diagnosed with PAH from the Oslo University Hospital were assessed by in-depth interviews conducted in the period June to August 2022. The interview guide contained 21 questions. The results were coded into ten subthemes and five main themes. The study had a qualitative phenomenological-hermeneutical design, based on individual semi-structured interviews. This means we focused on the patients` subjective opinions to gain insight of each patient about their individual experiences of HRQoL based on their meeting with nurses within the special health care. We assessed symptom burden using VAS-scale based on patients` pain, general health and fatigue, and wanted to see if there was an association between the symptoms and what was told in the interviews. The patients experience in the meeting with nurses

was one of the questions in the interview, where the patients themselves elaborated on their answers.

Results: Of the included six SSc patients with PAH, 4 (67%) were female and 2 (33%) men with mean disease duration of 5 years since PAH diagnosis (Table 1). NYHA functional class varied from 1 (mild) to 4 (severe) with a median of 3. Patients reported fatigue (VAS) was the most prominent symptom (Figure 1), confirmed by the results from the interviews. This also lead to physical and psychological challenges in everyday life, and reduced HRQoL. The patients` were mostly satisfied with the nurses, but felt some nurses had not the time when the patients needed it the most. The patients also highlighted that they felt that some of the nurses did not have enough knowledge about the diagnosis. This led to patients` repetition and explanation why their oxygen level was reduced, why they had heavy breathing or why it was not possible to measure pulse or oxygen level on the fingers, due to reduces peripheral circulation. The patients` wish was also to be seen and understood by their caregivers and friends.

Conclusion: Our study revealed that fatigue was the main symptom causing reduced HRQoL. Moreover, we show the importance of educated expert nurses in the management of PAH in SSc and the inclusion of information to caregivers, patients and next of kin. Nurse's awareness about the symptom burden and unmet needs of patients with SSc-PAH is important to give the best possible patient care.

Table 1. Patient characteristics.

PATIENT	1	2	3	4	5	6
Gender	K	M	M	K	K	K
Age	32	77	73	67	59	63
SSc duration (y)	11	2	18	3	12	17
PAH duration (y)	6	2	12	2	4	10
PAH treatment	ERA PDE5 PGI2	ERA PDE5	ERA PDE5	ERA PDE5	ERA PDE5	ERA PDE5 PGI2
RHC – mPAP (mmHg)	52	40	60	75	35	61
NYHA Class	3	3	3 to 4	4	1	2 to 3

F: female; M: male; SSc: systemic sclerosis; PAH: pulmonary arterial hypertension; ERA: endothelin receptor antagonist; PDE5: Phosphodiesterase 5 inhibitor; PGI2: Prostacyclin pathway agonist; RHC: right heart catheterization at the time of PH diagnosis; mPAP: mean pulmonary arterial pressure; NYHA: New York Heart Association.

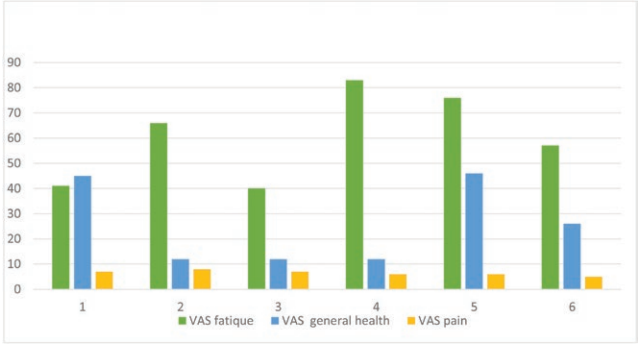


Figure 1. Overview of VAS-Scale, fatigue, general health and pain.

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AB1798-HPR FOOT ALTERATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A 1-YEAR LONGITUDINAL STUDY

Keywords: Systemic lupus erythematosus, Patient reported outcomes

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease mediated by autoantibodies, with involvement of various organs[1,2]. El 95% of patients with SLE have musculoskeletal involvement[1], most often in the form of arthralgias or non-erosive arthritis affecting mainly the hands and knees. Although the feet are equally affected and can result in significant disability, they have been little studied.

Objectives: To determine changes in foot involvement in patients with SLE after 12 months of follow-up.

Methods: Longitudinal case series. Thirty-six subjects with a diagnosis of SLE were consecutively recruited in the Rheumatology Unit between March and June 2021 and followed up at 12 months. Inclusion criteria were: patients with a diagnosis of SLE according to EULAR/ACR 2019 criteria, with at least one year of evolution and age equal to or older than 18 years. A Rheumatology nurse collected information on socio-demographic data and the questionnaires at baseline and at 12 months. The questionnaires were: SLEDAI (Systemic Lupus Erythematosus Disease Activity Index) and SLICC (Damage Index for Systemic Lupus Erythematosus), quality of life: EQ-5D, foot function: FFI (Foot Function Index), FAAM (Foot and Ankle Ability Measures Questionnaire), FAAM-Sport, FPI (Foot Posture Index). A descriptive analysis of the main variables, and a paired t-test or Wicoxon t-test, as appropriate, were performed between the baseline and 12-month follow-up visits.

Results: Thirty-six patients with SLE (97.2% women) with a mean (SD) age of 49.31 (11.4) years with a range 23-66 years participated. Regarding treatment a total of 22/36 patients (66.2%) had immunosuppressive treatment, 4/36 (11.1%) biological therapy and 26/36 (72.2%) hydroxychloroquine treatment. After 12 months of follow-up, the disease remained stable and there were no significant differences in the SLICC and SLEDAI indices of SLE. There were also no significant differences in the different foot questionnaires administered: FAAM, FAAM-Sport, FPI, FFI after 12 months of evolution. There was only a worsening in VAS EQ5D (p=0.028) although there was no significant change in EQ5D (p=0.773) (Table 1).

Conclusion: In SLE patients with stable disease over one year of follow-up, assessments of foot function and ability remain unchanged. It is important to integrate foot assessment into the joint evaluation because of the high impact on the patient's quality of life and patient functionality.

Table 1.

	Baseline (Mean± SD)	12 months (Mean± SD)	P value
EQ5D	0,54±0,25	0,55±0,23	0,773
EVAEQ5D	66,43±21,61	57,36±24,77	0,028
FFI	37,52±25,23	36,24±25,29	0,965
FAAM	0,65±0,23	1,05±2,57	0,322
FAAM-Sport	0,51±0,28	0,57±0,28	0,779
FPI rigth	2,33±2,19	2,37±2,21	0,324
FPI left	1,36±1,85	1,37±1,88	0,248
SLICC	0,86±1,45	0,72±1,16	0,257
SLEDAI	1,44±1,94	1,02±1,87	0,117

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AB1799-HPR COMPARISON OF EXERCISE CAPACITY, PHYSICAL ACTIVITY LEVEL, AND PERIPHERAL MUSCLE STRENGTH IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH HEALTHY INDIVIDUALS

Keywords: Systemic lupus erythematosus, Physical therapy/Physiotherapy, Quality of life

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Background: Systemic lupus erythematosus (SLE) is a chronic, autoimmune, inflammatory rheumatic disease that causes tissue damage through autoantibodies and immune complexes. Patients with chronic diseases such as SLE fall into a vicious circle. Fatigue and depression can negatively affect the quality of life and cause patients to stay at home and hence, be physical inactivity. As a result of physical inactivity; the exercise capacity and muscle strength of SLE patients can decrease.

Objectives: The aim of this study is to investigate the physical activity, peripheral muscle strength, exercise capacity, sleep, fatigue, anxiety, and depression levels between patients with SLE and healthy individuals.
Methods: Twenty-six patients with SLE (32.5 (24.75/43.25) years) and 29 healthy individuals (30 (23/32) years) were compared. Exercise capacity (6-minute walk test (6MWT)), peripheral muscle strength (dynamometer), physical activity (the Xiaomi Mi Band 4 smart bracelet device), fatigue (Fatigue Severity Scale (FSS)), anxiety and depression (Hospital Anxiety Depression scale (HAD)), quality of life (SLE-specific QOL scale (SLEQoL)), and sleep (Pittsburgh Sleep Quality Index (PSQI)) were assessed.
Results: Demographic characteristics were similar in both groups except for cigarette consumption (pack*years) ($p>0.05$). 6MWT distance, peripheral muscle strength, physical activity level, SLEQoL, and PSQI scores were significantly lower; FSS and HAD scores were higher in patients with SLE ($p<0.05$). Moreover; the difference between post and pretest values of heart rate, dyspnea, fatigue, and quadriceps femoris muscle fatigue was higher in patients with SLE compared to healthy individuals.
Conclusion: Patients with SLE had lower exercise capacity, muscle strength, quality of life, and sleep quality, and higher fatigue, anxiety, and depression. In addition; These patients were physically inactive. Further studies are needed to investigate the effects and efficiency of these symptoms on patients with SLE.
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AB1800-HPR EVALUATION OF KNOWLEDGE AND PRACTICES OF PATIENTS WITH SPONDYLOARTHRITIS

Keywords: Spondyloarthritis, Patient information and education, Best practices

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Background: Spondyloarthritis is a chronic inflammatory rheumatic disease mostly affecting young adults, causing functional disability and impaired quality of life. Thus, patient education is a major component to improve their knowledge of the disease, therapeutic compliance and quality of life.
Objectives: The aim of this study is to evaluate the knowledge and practices of patients with spondyloarthritis and determine the factors associated with them.
Methods: This is an observational, descriptive, analytical and monocentric study, in patients followed up at Al Ayachi University Hospital in the Rabat-Sale region of Morocco. The study duration was from the beginning of May 2022 to the beginning of July 2022. The consent of the study population was free and informed. The participants were interviewed and voluntarily responded to a questionnaire drawn up by a team of rheumatologists, which includs socio-demographic information, prior knowledge and practices of patients with spondyloarthritis.We calculated a score of correct answers ranging between 0 and 10 for each patient.
Results: We recruited 100 patients with a mean age of 39.3 years ± 12.9, 59% were men and 17% were illiterate. 85% of the population came from an urban environment, and 79% were unemployed. 68% of the patients suffered from ankylosing spondylitis, 17% had psoriatic arthritis, 13% were affected by inflammatory bowel disease associated arthropathy and 2% had juvenile spondylarthritis. 31% of patients considered that the disease can affect young adults, wherein 43% reported a male predominance. 47% reported that the cause of the disease is genetic, 34% declared that it is related to immunity whereas entheses affection was known by 52% of patients. 81% find that therapeutic management helps prevent deformities and 97% see that it improves the quality of life. Furthermore, only 4% of patients knew that NSAIDs are a disease-modifying treatment and 7% were aware that pneumopathy could be a potential complication of Methotrexate. 73% of patients knew what a biologic drugs is, when biosimilar was only known by 10% of them, yet 45% knew that tuberculosis is one of the infections that can occur under biologic drugs. This study revealed that 63% of patients had a total score of correct answers superior to 5 (for a max score of 10) and 37% had a total score between 0-5.
Conclusion: Althought this study showed decent knowledge and good practices among the Moroccan patients with spondyloarthritis. The doctor-patient contact and the multimedia information as well as patients' associations remain as useful means to improve this knowledge.
REFERENCES: NIL.

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Disclosure of Interests: None Declared.
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AB1802-HPR PAIN IN AXIAL SPONDYLARTHRITIS MAY NOT BE ALWAYS INFLAMMATORY

Keywords: Pain, Spondyloarthritis, Inflammatory arthritides

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Background: Many patients with axial spondyloarthritis (axSpA) report persistent pain even when treated with anti-inflammatory agents. Therefore, it can be hypothesized that this persistent pain may not be always entirely of inflammatory origin and additional pain mechanisms may play a role (1)
Objectives: To evaluate the frequency of central sensitization (CS) and neuropathic pain (NP) in patients with axial spondylarthritis (axSpA) and its relationship with disease activity and functional status.
Methods: Patients classified as axSpA according to ASAS 2009 criteria were included in this cross-sectional study. Presence of CS was evaluated with the CS inventory (CSI; a 25-item questionnaire that a score of ≥40 point scored out of 100 is positive for CS. Presence of depression and anxiety were evaluated with Hospital Anxiety and Depression questionnaire (HADS), and fibromyalgia syndrome (FMS) by ACR 2016 criteria. Neuropathic pain (NP) was assessed with DN4 (Douleur Neuropathique en 4 questions) questionnaire. In addition, the patients' BASDAI, ASDAS-CRP, BASFI, ASQoL, ASAS-HI/environmental scores were also calculated.
Results: 121 axSpA patients[102 (84.3%) radiographic axSpA, 74 (61.2%) male, mean age: 43.9 ± 10.6 years] were included in the study. Of our patients 84% were receiving biological therapy. Other characteristics of the patients are summarized in **Table 1**. CS was detected in 35 (28.9%), NP in 12 (10.1%) and FMS in 9 (7.7%) patients. Age and advanced treatment usage rates were similar between the groups. Among patients with CS the percentage of female was higher, there was no sex difference for patients with NP and FMS. Duration of the disease was shorter in the CS group. Pateints and physician global assessment of disease activity (PGA and PhGA recpectively), BASDAI, Leeds enthesitis *index* (LEI), ASQoL, ASAS-HI were found to be significantly higher in patients with CS and NP. In addition, BASFI and ASAS-HI environmental scores were worse in those with CS. While anxiety was higher in those patients with CS and NP according to the HADS questionnaire, the rates of depression were similar. Six (17.1%) patients with CS also had NP and 6 (50%) patients with NP had also CS. While all 9 patients with FMS had CS, only 2 had NP. CS severity and disease activity and quality of life scores showed a strong positive correlation **(Figure 1)**.
Conclusion: Approximately one-third of axSpA patients, most of which received advanced therapy, have CS and %10 of them have NP. Both quality of life and activity measures were found to be higher in patients who have CS. Therefore it should be kept in mind that in axSpA patients pain may not be always due to inflammatory origin of the disease, but may be due to non-inflammatory causes of pain.
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Table 1. Clinical and sociodemographic characteristics of axSpA patient group

Variables	n=121	Patients with CS n:35	Patients without CS n:86	p value
Age,year+	43.9 (10.6)	41 (11)	44 (19)	0.109
Gender, female*	47 (38.8)	22 (62.9)	25 (29.1)	0.001
Disease duration,year&	4.5 (9)	10 (11)	13.9 (8.2)	0.022
Peripheral arthritis,ever*	54 (45.1)	10 (28.6)	25 (71.4)	0.049
Joint limitation,ever*	40 (33.6)	6 (15.4)	33 (84.6)	0.028
LEI&	0 (0)	7 (20.6)	4 (4.7)	0.012
BASDAI&	2 (2.1)	3.9 (2.9)	1.5 (1.4)	<0.001
BASFI&	1.9 (3.1)	3.8 (3.9)	1.5 (2.4)	<0.001
ASDASCRP &	1.8 (1.2)	2.7 (1.8)	1.6 (0.9)	<0.001
ASQOL&	4 (8)	11 (7)	1 (5)	<0.001
ASASHI&	5 (6)	9 (5)	3.5 (4)	<0.001
ASASHI_env&	0 (1)	4 (2)	3 (2)	0.010
HADS depression*n:117	9 (7.6)	5 (14.3)	4 (4.9)	**0.125**
FMS * n:117	9 (7.6)	9 (27.3)	0 (0)	**<0.001**
HADS anxiety+ * n:117	21 (17.9)	15 (42.9)	6 (7.3)	<0.001

*:n(%) +:mean(SD) &:median (IQR)

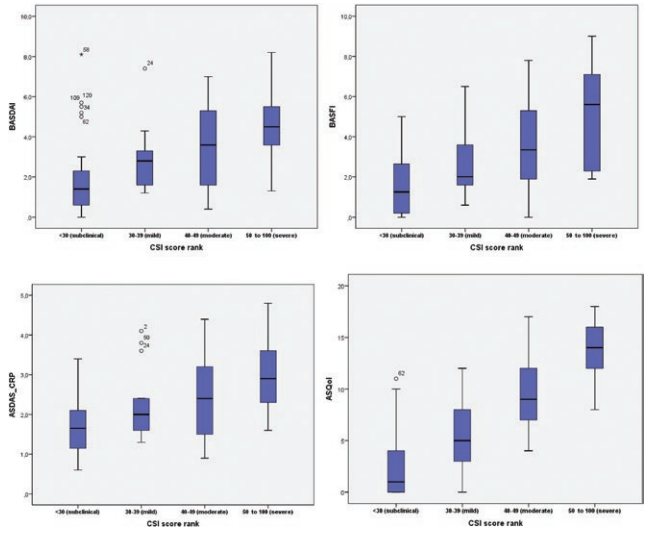


Figure 1. CS severity and disease activity and quality of life scores correlation

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AB1803-HPR

EVALUATION OF THE FACTORS ASSOCIATED WITH THE BIOPSYCHOSOCIAL STATUS OF PATIENTS WITH AS WHO WERE DECIDED TO BE TREATED WITH ANTI-TNF THERAPY FOR THE FIRST TIME

Keywords: Spondyloarthritis, Patient reported outcomes, Cognitive Function

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Background: Ankylosing spondylitis (AS) is a rheumatic disease that affects patients in a biopsychosocial framework due to its chronic inflammatory nature. It is known that anti-TNF therapy is given to patients with persistently high disease activity despite conventional treatments according to the ASAS recommendations [1].
Objectives: The aim of this study was to examine the factors associated with the biopsychosocial status of patients with AS who were decided to be treated with anti-TNF therapy for the first time.
Methods: 76 AS patients who were decided to treated with anti-TNF therapy included in the study. Socio-demographic informations of patients were collected. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) values were recorded for disease activity levels. Biopsychosocial status of the patients was evaluated by the BETY-Biopsychosocial Questionnaire (BETY-BQ). The Bath Ankylosing Spondylitis Functional Index (BASFI) and Health Assessment Questionnaire (HAQ) were used to assess functional and and daily living activities. The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression levels.
Results: The mean age of the patients was 39.99 ± 10.0 years. The mean BASDAI scores indicated active disease and were 5.98 ± 1.78. There was a statistically significant moderate correlation between the BETY and the anxiety and depression subscales of HADS and BASDAI, in the positive direction (r= 0.692, p <0.001 and r= 0.685, p <0.001 and r= 0.552, p <0.001). A statistically significant, strong correlation was found between the BETY, HAQ and BASFI scores in the positive direction (r= 0.834, p <0.001 and r= 0.747, p <0.001) (Table 1). It was observed that patients showed anxiety and depression characteristics according to HADS cut-off values (>10 and >7).
Conclusion: It was concluded that the biopsychosocial status of anti-TNF naive patients with AS was affected by anxiety-depression levels, functionality, and disease activity score. In addition to anti-TNF therapy, it was interpreted that the treatment of biopsychosocial characteristics of patients should also be taken into consideration in disease management.

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Table 1. Patients characteristics and correlation of outcome measures

Patients Characteristics (n=76)	
Age (year)	39.99 ± 10.0
BMI (kg/m^2)	27.81 ± 5.51
Duration of disease (year)	4.21 ± 5.65
BETY-BQ (0-120)	60.0 ±23.7
BASDAI (0-10)	5.98 ± 1.78
BASFI (0-10)	5.16 ± 2.31
HADS	
anxiety	10.43 ± 4.92
depression	8.53 ± 4.34
HAQ	15.70 ± 9.48

Correlations						
		BASDAI	BASFI	HAQ	HADS-a	HADS-d
BETY-BQ	r	0.552*	0.747*	0.834*	0.692*	0.685*
	p*	0.000	0.000	0.000	0.000	0.000

* Pearson test

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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HPR Service developments, innovation and economics in healthcare

AB1804-HPR

IMPROVING PATIENT SAFETY THROUGH THE ESTABLISHMENT OF A PHARMACIST-LED BLOOD MONITORING CLINIC FOR JAK INHIBITORS IN RHEUMATOLOGY

Keywords: Safety

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Background: Janus kinase inhibitors drugs (JAKi) are novel small molecule medications known to cause abnormalities such as elevations in hepatic transaminases, decreases in neutrophil and lymphocyte counts and elevations in cholesterol and creatinine kinase. Blood monitoring is recommended and dose adjustments are advised if abnormalities arise. Recent warnings by the EMA and MHRA have highlighted the importance of monitoring these medications. Timely review and management of patients on JAKi drugs is difficult to maintain with increasing workload amongst the rheumatology team. A baseline audit (2020) demonstrated that hospital blood monitoring guidelines for JAKi drugs were not being followed. The rheumatology multidisciplinary team met and utilised Quality Improvement methodology including fish and driver diagrams to address this. This led to the creation of a pharmacist-led JAKi blood monitoring clinic.

Objectives: To establish a pharmacist-led rheumatology blood monitoring clinic for the JAKi drug class in order to: increase patient safety with increased compliance to blood monitoring, save consultant/nurse time, improve communication with primary care on the frequency of blood testing required, increase patient understanding of the importance of blood monitoring with JAKi drugs, reinforce counselling advice such as risk of infections, shingles and thrombosis and promote medication adherence.
Methods: The clinic was established in March 2021. Patients commencing JAKi drugs are referred to the pharmacist-led clinic by the medical team. The pharmacist contacts the patient by phone following delivery of their medication. The patient is counselled on their new medication and dates for blood checks are agreed. A letter is sent to the patient and their GP providing this information. The patient is booked into virtual telephone appointments and bloods are monitored every month for the first 3 months and every 3 months thereafter. Any change or abnormality in blood results are flagged early in the patient's treatment and if necessary, discussed with the consultant. Adjustments are made to the patient's dose if appropriate.
Results: In order to evaluate the benefit of the pharmacist clinic a re-audit of compliance with blood monitoring (March 2021- September 2022) was carried out alongside a patient satisfaction postal survey (August 2022). A total of 58 patients were sampled in the re-audit. The re-audit found an increase in compliance in blood monitoring since the introduction of the pharmacist clinic. 98% of patients had their full blood count performed at 3 months compared to 56% in audit 1 and 95% of patients had their lipid profile completed at 3 months compared to 15% in audit 1 (Table 1). A patient satisfaction survey (N=62, response rate 48%) found that 28 (93%) patients either agreed or strongly agreed that they were more aware of the importance of attending for regular blood monitoring when prescribed JAKi therapy as a result of the clinic. The pharmacy team made several significant interventions (self-graded Eadon grade 4 and 5). For example by improving medication adherence, detecting haematological abnormalities that required JAKi dose reduction, identifying patients suffering from infection requiring intervention including shingles and Covid-19.

Table 1. Comparison of audit results pre (Audit 1) and post (Audit 2) clinic establishment

	Audit 1 (N=48)	*Audit 2 (N=58)*
Number of patients with full blood count completed at weeks 4, 8 & 12	27 (56%)	57 (98%)
Number of patients with lipid profile completed at week 12	7 (15%)	55 (95%)
Number of patients LFTs completed at weeks 4, 8 & 12	26 (54%)	54 (93%)

Conclusion: Introduction of the pharmacist-led clinic has increased patient safety by ensuring compliance with blood monitoring as per hospital guidelines. The clinic has paved the way for improved communication with primary care teams and has provided patients with extra support during their first months on treatment with their JAKi. It has also expanded the role of the rheumatology pharmacy team and saved nursing and medical time.
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AB1805-HPR

SERVICE EVALUATION OF COMBINED RHEUMATOLOGY/ OBSTETRIC CLINIC, SOUTH TEES NHS FOUNDATION TRUST, UNITED KINGDOM''

Keywords: Pregnancy and reproduction, Patient information and education, Quality of care

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Background: Multidisciplinary management in a combined clinic improves patient experience and outcomes for pregnant women with inflammatory rheumatic diseases (IRD). Achieving better IRD control pre, during, and post-pregnancy with pregnancy-compatible disease-modifying anti-rheumatic therapies (DMARDs) reduces maternal and foetal mortality/ morbidity minimising complications. EULAR published recommendations for core data sets around maternal, pregnancy, and treatment information for pregnancy registries in Inflammatory rheumatic diseases.
Objectives: Service evaluation of the Combined Rheumatology Obstetrics clinic held in our hospital to evaluate pregnant patients with Inflammatory rheumatoid diseases against the EULAR recommendations.
To improve Patient and disease outcome in terms of maternal health and fetal health.
Methods: Retrospective data was collected on interventions and outcomes of pregnancies in 40 women with Inflammatory rheumatic diseases seen in the-Combined Rheumatology/ Obstetric Clinic from November 2020 to February 2022 reviewing clinic letters and medical notes.
Results: 77% of patients had inflammatory arthritis including rheumatoid, psoriatic, juvenile idiopathic, and axial spondylo-arthritis.15% had connective tissue disease (CTD) including lupus with anti-phospholipid syndrome, Bechet's and undifferentiated CTD. 2%patients did not have a formal IRD diagnosis. 12.5% of patients had only pre-pregnancy counselling, 2.5% had miscarriages. Of the remaining 85% of pregnant patients' 10% had obstetric care/ delivery in other trusts. Treatment received by patients 12 months prior to conception included DMARDs (37%), biologics (24%), combination (8%), and steroids (10%). 25% were on no treatment.During pregnancy 29% received oral DMARDs, 11% biologics and 16% needed steroids. 50% of patients did not require any treatment. Interventions done in the clinic included medication review (100%), VTE assessments (100%), commenced VTE prophylaxis (7.5%), change in DMARD dosage (10%), additional medication added (10%), intramuscular/ intra-articular steroid injections (16%) and physiotherapy referrals (10%). Maternal adverse outcomes include 5% preeclampsia, 0.07% gestational diabetes and 0.02% pregnancy-induced hypertension and foetal growth restriction. 93.3% were full-term deliveries. Only 10% had adverse neonatal outcomes including 6.6% preterm births. None had congenital heart block. 3.3% had congenital malformations unrelated to IRD/ DMARD therapy.Patient satisfaction surveys were sent out to 40 patients with a 30% response rate. The patient satisfaction questionnaire revealed all patients had their consultation with rheumatology and obstetric consultants with 100%satisfaction. 100% felt the staff was supportive and they would recommend our service to friends and family. Of 66.7% of patients receiving pre-pregnancy counselling, 50% were in the combined clinic. Of the 33.3% of patients not receiving counselling 22.2% felt they would have benefitted from it.
Conclusion: Our service evaluation of the combined rheumatology/ obstetric clinic revealed favourable outcomes for the mother and baby with high patient satisfaction rates. The clinic offered appropriate timely interventions to control IRD improving pregnancy outcomes. The future aim is to deliver this high-quality service to all pregnant patients with IRD through robust referral pathways to improve the patient experience.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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HPR Professional education, training and competencies

AB1806-HPR

EXPECTED FEATURES OF THE COURSE LEADER IN THE REHABILITATION HEALTHCARE PROFESSIONALS' HIGHER EDUCATION: A QUALITATIVE STUDY ON STUDENTS' PERSPECTIVES

Keywords: Education, Qualitative research methods, Rehabilitation

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Background: Previous evidence showed that Healthcare Professionals (HPs) working with rheumatic and musculoskeletal diseases (RMD) from Mediterranean countries have higher educational needs than Northern-European ones [1]. Hence, it is necessary to find new strategies to improve their training. Course leaders (CLs) are the responsible of the quality and delivery of the training of rehabilitation HPs, since they oversee designing and directing degree courses that are experienced by students first-hand [2]. To better understand their leadership role, it is helpful to focus on the people with whom the leader interacts daily [3–5]. Therefore, students become an essential source on that matter [2].

However, little attention has been given to the expected features that course leaders should hold, starting from students' perspectives.
Objectives: This study explored students' expected features of a course leader.
Methods: A qualitative study was carried out based on semi-structured interviews. A panel of recent graduates and students of the Master of Science in 'Healthcare Professionals Rehabilitation Sciences' (University of Verona, Verona, Italy) was recruited using purposive sampling. Data were analysed using the 'Reflexive Thematic Analysis' by Braun&Clarke [6].
Results: Ten HPs in training agreed to partake in the study (age 30 ± 9; men N=2; women N=8). Five themes were generated from the analysis: 1) 'A Collaborative Manager', as students perceived the CL as a non-authoritarian manager who involved all the stakeholders in the decision-making process; 2) 'A Diplomatic yet Honest Communicator', as students needed someone capable of communicating with them transparently; 3) 'A Flexible Mediator', as the CL should actively listen to all their stakeholders and mitigate conflicts; 4) 'An Empathic and Available Guide', as students need someone available and ready to help or guide them; 5) 'An Experienced Healthcare Professional', since students felt that the CL should have a clinical background related to the course they lead.
Conclusion: The results of this study suggest that students expect CL to have a wide range of qualities and attitudes more related to soft (i.e., adaptation, communication, organisation skills, teamwork) rather than hard skills (i.e., clinical experience). They expect a CL that considers all stakeholders' needs and preferences to guarantee course harmony and satisfaction.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4425

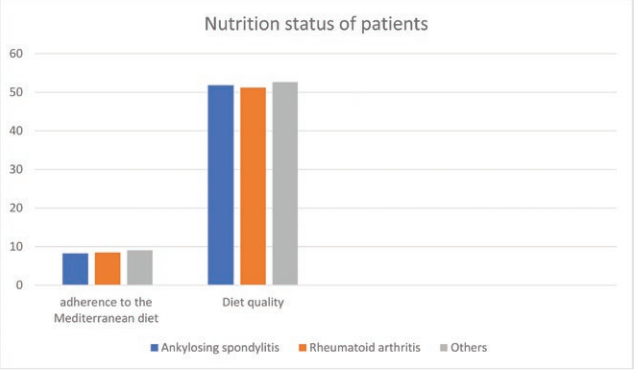
HPR Interdisciplinary research

AB1807-HPR INVESTIGATION OF RELATIONSHIP BETWEEN NUTRITIONAL STATUS AND PHYSICAL ACTIVITY LEVEL IN RHEUMATIC DISEASES

Keywords: Diet and Nutrition, Patient reported outcomes, Physical therapy/ Physiotherapy

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Background: Rheumatic diseases are chronic diseases that negatively affect the quality of life. Ankylosing spondylitis (AS) and rheumatoid arthritis (RA) are the most common clinical manifestations. Non-pharmacological treatments include exercise, healthy and balanced diet recommendations [1,2].
Objectives: The aim of this study was to investigate nutritional status and the physical activity level and relationship between those in patients with rheumatic diseases.
Methods: 108 patients (64 AS, 22 RA and 22 others (Sjogren, scleroderma, psoriatic arthritis)) with rheumatic diseases (47.92±12.26 years) were included in the study. The International Physical Activity Questionnaire (IPAQ) was used to assess physical activity. Food consumption records of the patients included in the study were recorded using a 24-hour retrospective reminder method. The adherence of the patients to the Mediterranean diet was evaluated using the 'Mediterranean Diet Scale' and their diet quality was evaluated with the Healthy Eating Index.
Results: The majority of patients (67.6%) were adapting to the Mediterranean diet and 56.5% had poor overall diet quality. Patients with AS had the worst adherence to the Mediterranean diet 8.21±1.99), while patients with RA had the worst overall diet quality (51.19±14.47, Graph 1). The physical activity level of the patients was inactive (n:49, 39.8%) and there was no significant relationship between nutritional status and physical activity level (p<0.05).
Conclusion: According to the results of the study, although the majority of patients had adherence to the Mediterranean diet, the overall diet quality was poor and the level of physical activity was low. These results show that patients cannot be fed adequately and in moderation. Since these patients live in the Mediterranean region, although the consumption rate of vegetables and fruits is high, they cannot be fed with high quality. It is recommended that future studies be conducted in different regions with larger numbers of patients with rheumatic diseases. These results show that patients should also be evaluated in terms of balanced and healthy nutrition.
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Graph 1. Nutrition status of patients according to diseases

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Disclosure of Interests: None Declared.
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AB1808-HPR VIOLENCE: A REALITY IN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES?

Keywords: Pregnancy and reproduction, Quality of life, Mental health

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Background: Intimate partner violence (IPV) is defined as any aggression that includes physical, psychological and sexual harm by a current or former intimate partner. In Mexico, 39.9% of women aged 15 years or over have experienced IPV throughout their romantic relationships [1]. IPV in pregnancy and postpartum can lead to mood disorders, obstetric comorbidities, and low birth weight. Pregnant women with autoimmune rheumatic diseases (ARD) are a high-risk population. Using screening tools to detect women experiencing abuse and explore its severity helps us to intervene appropriately and prevent complications [2].
Objectives: The aim of this study is to describe the frequency of IPV in patients with ARD.
Methods: A descriptive, cross-sectional, exploratory study at the Hospital Universitario "Dr. José Eleuterio González" in Mexico. We included women from the pregnancy and rheumatic diseases clinic (CEER) with a screening of IVP with the HITS scale and categorized them as reproductive-age women and pregnant-postpartum women. We defined reproductive age as the age range of 18-45 years and postpartum up to 1 year after the birth of the last child. The demographic characteristics and ARD data were obtained from the clinical record. Women without ARD were matched (1:1) by age and condition (reproductive age and pregnant-postpartum. A virtual survey was applied including sociodemographic data and the Spanish version of HITS. The Kolmogorov-Smirnov test was used to determine normality. To analyze the differences between groups Mann–Whitney U test, Chi-square or Kruskal–Wallis test were employed. A $p < 0.05$ was considered statistically significant. The statistical analysis was performed with the statistical program SPSS version 25.

Results: 96 women were included: 48 with ARD and 48 without ARD. The median age was 27 (IQR 24 – 32). In both groups, 24 were reproductive-age women and 24 were pregnant-postpartum women (18/ 75% postpartum and 6/ 25% pregnant). In the ARD group, the most frequent diagnoses were rheumatoid arthritis (22/ 46%) and systemic lupus erythematosus (20/ 42%). The sociodemographic characteristics and HITS results are in **table 1**. 18 (19%) women suffered IVP: 11 (23%) women without ARD and 7 (15%) women with ARD **(figure 1)**; in both the most reported item was being insulted (10 without ARD vs 7 ARD) followed by being screamed (6 without ARD vs 6 ARD). Threatened with harm was reported in 3 ARD women while physical hurt was reported in 3 women without ARD. We found significant differences between the HITS scores of ARD women and women without ARD (p= 0.007). No differences in IVP frequency in women without ARD and in the ARD group were found (p= 0.433). Overall, more pregnant-postpartum women were identified as IPV victims than reproductive-age women (p= 0.433).
Conclusion: Pregnant and postpartum women are prone to report IPV than women of reproductive age. The current rise in IPV requires us to actively participate in research to prevent complications in pregnant and postpartum patients with ARD.
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Figure 1. Women with ARD and women without ARD categorized as reproductive-age women and pregnant-postpartum women that reported intimate partnet violence (IPV).

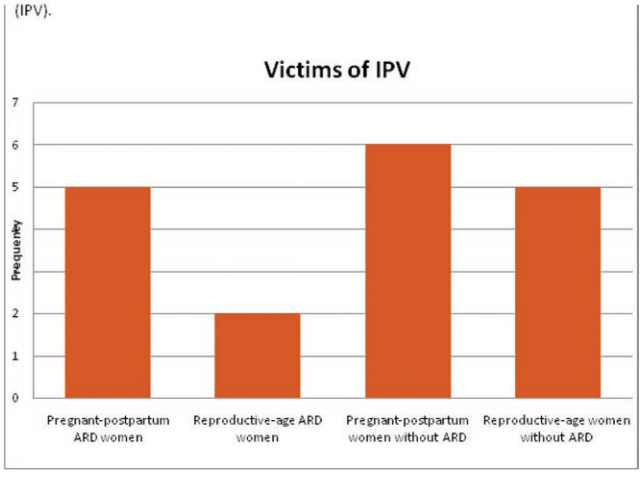


Table 1. Sociodemographic characteristics and HITS results

	Pregnant-postpartum ARD women n= 24	Reproductive-age ARD women n= 24	Pregnant-postpartum without ARD women n= 24	Reproductive-age without ARD women n= 24	
Age, median, (IQR), years	28.5 (23.3 – 35.0)	27.0 (23.0 – 32.0)	28.5 (22.3 – 35.0)	27.0 (26.0 – 29.0)	
Marital status, n (%)					
Single	4 (17)	20 (83)	3 (13)	18 (75)	
Common law marriage	9 (38)	1 (4)	11 (46)	2 (8)	
Married	11 (46)	3 (13)	10 (42)	4 (17)	
Occupation, n (%)					
Employee	7 (29)	21 (88)	7 (29)	21 (88)	
Housewife	14 (58)	2 (8)	16 (67)	-	
Student	3 (13)	1 (4)	1 (4)	3 (13)	
Years of education, n (%)					
<9 years	10 (42)	5 (21)	9 (38)	-	
>9 years	14 (58)	19 (33)	15 (63)	24 (100)	
HITS score, median, (IQR)	4 (4.0 – 4.8)	4 (4.0 – 4.0)	5 (4.0 – 5.8)	4 (4.0 – 5.0)	***p*=0.027**

IQR: Interquartile range, IPV: Intimate Partner Violence

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1809-HPR

DETERMINATION OF PRE-SARCOPENIA IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Quality of life, Sarcopenia, Inflammatory arthritides

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Background: Sarcopenia is described as the decline in muscle mass and strength that generally occurs with increased age which may cause increased fall risk, mortality, disability, and adverse health outcomes. Patients with axial spondyloarthritis (axSpA) may be more prone to sarcopenia due to the presence of chronic inflammation.
Objectives: This study aims to determine the presence of sarcopenia or pre-sarcopenia and to clarify the associated factors with pre-sarcopenia.
Methods: This cross-sectional study recruited 39 patients with axSpA. Sarcopenia was assessed according to the European Working Group on Sarcopenia in Older People in 2018 (EGSWOP2) criteria by evaluating muscle mass, gait speed, and grip strength. Muscle mass was measured using a bioimpedance body analyzer. Physical performance was assessed with the five times sit-to-stand (FTSTS) test and Short Physical Performance Battery (SPPB). Quality of life (QoL) and physical activity level were evaluated using Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire and the International Physical Activity Questionnaire – Short Form (IPAQ-SF) respectively. Between-group comparison and correlation analysis were performed.
Results: The mean age of the patients was 47.58±6.78 with (64.1 % women), the mean disease duration was 8.17±7.33 years, and the mean body mass index was 28.05±4.74 kg/m2. Pre-sarcopenia was detected in 43.6% of all patients which was defined by low grip strength and no patients had sarcopenia. Patients with pre-sarcopenia were more physically inactive, had worse quality of life, and had lower physical performance compared with those without pre-sarcopenia ($p < 0.05$). The grip strength as the indicator of pre-sarcopenia was significantly moderately correlated with the SPPB ($r = -0.48$, $p = 0.002$), FSST ($r = -0.43$, $p = 0.006$), ASQoL ($r = -0.45$, $p = 0.003$), and IPAQ-SF ($r = 0.48$, $p = 0.002$).
Conclusion: Pre-sarcopenia is commonly detected in axSpA patients and physical performance is impaired which may result in a further decline in functional status. Maintaining adequate muscle strength and muscle function in patients with axSpA may contribute toward improving QoL. Patients with axSpA should be assessed in terms of sarcopenia-related findings.
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Table 1. Comparison of patients according to their frailty status

	No-sarcopenia (n =22)	Pre-sarcopenia (n = 17)	P value
Age (years), mean (SD)	46.13 (5.49)	49.47 (7.93)	0.13
Sex, women/men	12/10	13/4	0.19
BMI (kg/m^2), mean (SD)	27.32 (3.38)	29.01 (6.06)	0.28
SPPB, mean (SD)	10.22 (1.37)	9.05 (1.29)	**0.012**
FSST, sec, mean (SD)	14.56 (4.58)	19.19 (6.31)	**0.010**
ASQoL,mean (SD)	6.90 (5.39)	11.35 (3.46)	**0.005**
IPAQ-SF (MET), mean (SD)	15.20.77 (1365.42)	726.29 (573.13)	**0.020**

Bold values indicate significancy.BMI; body mass index, SPPB; Short Physical Performance Battery, FSST; Five Times Sit to Stand Test, ASQoL; Ankylosing Spondylitis Quality of Life Questionnaire, IPAQ-SF; International Physical Activity Questionnaire – Short Form, MET; Metabolic Equivalent.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1810-HPR

RESILIENCE AND PERINATAL LOSS IN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES

Keywords: Quality of life, Mental health, Pregnancy and reproduction

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Background: Resilience has been defined as the capacity of individuals to successfully maintain or regain their mental health in the face of significant adversity or risk. [1]. The Wagnild and Young Resilience Scale (RS) from 1993 is one of the most widely used instruments in the evaluation of resilience [2]. Having an autoimmune rheumatic diseases (ARDs) and perinatal losses (PL) have been considered traumatic events [3,4]. Identifying women at risk is important for developing psychological support strategies.
Objectives: Evaluate the resilience capacity in patients with and without ARDs with PL.
Methods: Descriptive, cross-sectional, comparative study at the Hospital Universitario "Dr. José Eleuterio González" in México. We included women from the Pregnancy and Rheumatic Diseases Clinic (CEER) that answer a virtual survey with the RS. The demographic, ARD and PL data were obtained from the clinical records. The women without ARD were invited to fill a virtual survey with the RS, sociodemographic and PL data. The RS is a Likert-type scale that consists of 25 items with seven response options. The responses are summed to produce a total score that ranges from 25 to 175; the greater the score the greater the resilience capacity. The Kolmogorov-Smirnov test was used to determine normality. To analyze the differences between groups Mann–Whitney U test, Chi-square, T- test were employed. A $p < 0.05$ was considered statistically significant. The statistical analysis was performed with the statistical program SPSS version 25.
Results: A total of 50 women were included: 25 with ARD and 25 without ARD. The median age for the group with ARD was 42 (38.5-51) and 34 (26-42.5) for the without ARD group. In the ARD group the most frequent diagnosis were systemic lupus erythematosus (7/28%), rheumatoid arthritis (6/24%) and Antiphospholipid Syndrome (4/16%). For the RS scores, women without ARD have a greater median 137.56 (SD =22.14) than the group with ARD 132.72 (SD =31.03). No statistically differences were found in other variables between groups. The sociodemographic and PL data and the RS score for both groups are included in **table 1.**
Conclusion: Even though there were no significant differences between groups, our results suggest that higher education (> 9 years) and suffering only 1 PL can be variables that enhance the resilience capacity of women with PL. Our limitation was the sample size for both groups.
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Table 1. Clinical characterization

	Patients with ARD N=25	Patients without ARD N=25	P=0.05
Resilience Scale score, mean (SD)	132.72 (31.03)	137.56 (22.14)	0.529
Years of education			0.114
>9 years	21 (84%)	15 (60%)	
<9 years	4 (16%)	10 (40%)	
Marital Status			0.225
Single	2 (8%)	2 (8%)	
Married/Common law	20 (80%)	15 (60%)	
Divorced	3 (12%)	8 (32%)	
Perinatal Losses			0.387
1	13 (52%)	17 (68%)	
>1	12 (48%)	3 (32%)	
Living children			0.725
Yes	21 (84%)	19 (76%)	
No	4 (16%)	6 (24%)	
Number of living children, median (IQR)	2 (1-3)	1 (0.5-2)	0.123

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4654

AB1811-HPR **CATASTROPHIC HEALTH EXPENSES IN PREGNANT WOMEN WITH RHEUMATIC DISEASE**

Keywords: Quality of life, Pregnancy and reproduction, Health Services Research

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Background: Rheumatic diseases (RD) have an impaired quality of life and a high cost of healthcare. Out-of-pocket health expenses are those expenditures that households make to acquire medicines and associated services that come from family income [1]. A disease with catastrophic health expenses is a condition that, due to its high cost and the expenses derived from treatment and medications, exceeds 30% of the family income [1]. Such catastrophic expenses can negatively influence the therapeutic adherence of patients and the prognosis [2]. A policy challenge has been the achievement of universal coverage of health services. A key was the implementation of "Seguro Popular" (SP) in 2003; however, the abolition of the SP in 2020and the foundation of "Instituto de Salud para el Bienestar" (INSABI) by the current government, created uncertainty due to some omissions detected regarding the clarity of its performance [1].
Objectives: To estimate the frequency of pregnant patients with RD who experienced catastrophic health expenses when using medical services.
Methods: An observational cross-sectional, retrospective study was carried out at the Pregnancy and Reproductive Health Clinic for Rheumatic Diseases (CEER) from the University Hospital "Dr. José Eleuterio González", in Mexico. The data of all pregnant patients was collected from the clinical record. From the socioeconomic study, sociodemographic data, family nucleus, family's monthly income, monthly health expenditures, as well as the type of health insurance they had, were obtained. The percentage of out-of-pocket health expenses (medication) of each patient was calculated, and if this exceeded 30%, it was defined as a catastrophic expense. For statistical analysis, the sociodemographic and clinical characteristics of the population are presented as frequencies, percentages, or standard deviations.
Results: A total of 54 patients were included in the period from 2019 to 2022 with a mean age of 28.02 (±6.45) years. The rheumatic diagnoses were rheumatoid arthritis with 24 (44.4%), systemic lupus erythematosus with 13 (24.1%), antiphospholipid syndrome with 5 (9.3%), dermatomyositis with 3 (5.6%),juvenile idiopathic arthritis with 2 (3.7%),Sjögren's syndrome with1 (1.8) and others with 6 (11.1%).The sociodemographic characteristics are described in **Table 1**. Most of the patients had health insurance coverage with 43 (79.6%), where SP stood out as the main one with 24 (55.8%). Of the 43 patients who had health insurance coverage, 5 (11.6%) experienced catastrophic health expenses, which we can see in **Figure 1**. Of the 11 (20.4%) patients who did not have health insurance coverage, 1 (9.1%) experienced catastrophic health expenses.
Conclusion: The 11.6% of the patients who had health insurance coverage reported having catastrophic health expenses, in which they spent more than 30% of the family's monthly income. 9.1% of those who did health insurance coverage presented catastrophic health expenses. It is of vital importance that rheumatic diseases should be recognized as catastrophic illnesses to ensure quality patient-tailored care.
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Figure 1. Out-of-pocket health expenses in pregnant patients with rheumatic disease. When the percentage exceeds 30% of the family's monthly income, patients experienced catastrophic health expenses.

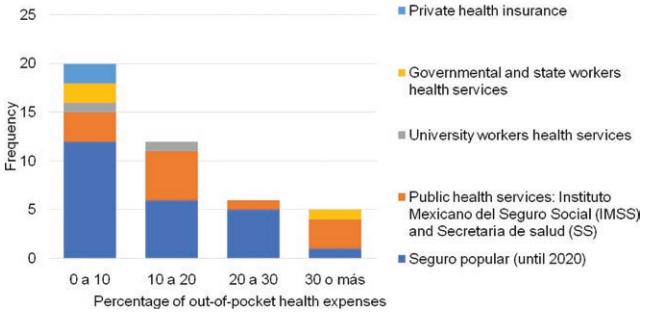


Table 1. Sociodemographic characteristics

	n= 54
Age, media ±SD	28.02±6.45
MaritalStatus, n (%)	
Single	12 (22.2)
Married/ Cohabitating	42 (77.8)
Education, n (%)	
< 9 years	20 (37.0)
> 9 years	34 (63.0)
Occupation, n (%)	
Housewife	28 (51.9)
Employed and self-employed	8 (14.8)
Student	18 (33.3)
Typeoffamily, n (%)	
Nuclear	34 (63)
Extense	20 (37)
Healthinsurancecoverage, n (%)	
Yes	43 (79.6)
No	11 (20.4)

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1812-HPR VACCINATION UPTAKE IN A COHORT OF PATIENTS ON BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (BDMARDS) AT A MELBOURNE PUBLIC HOSPITAL

Keywords: COVID, bDMARD, Vaccination/Immunization

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Background: As a result of immunosuppression, rheumatology patients (particularly those on bDMARDs) are at a greater risk of infections. However, little is known about the number of rheumatology patients who have are vaccinated for influenza, COVID-19, Hepatitis B and Pneumococcal vaccinations.
Objectives: To ascertain the number of patients on bDMARDs who received the COVID-19, Influenza, Hepatitis B, Pneumococcal and Shingles Vaccines. With regards to the Influenza vaccine information was obtained over the years 2018 – 2022 to determine if rates of influenza vaccination increased during the COVID-19 pandemic.
Methods: All rheumatology patients on bDMARDs at the Northern Hospital in Epping, Melbourne Australia were included in this study. By retrospectively reviewing the medical records, data was collected regarding patient demographics, clinical information and vaccination to COVID-19, Hepatitis B, Pneumococcal and Influenza. Information for influenzae was obtained over the period from 2018 to 2022. Ethics committee approval was sought from our institution (Reference number: ALR 75.2022).
Results: There were 201 patients on bDMARDs included in this analysis. 139 (69%) were female with a mean age of 54 (SD +/-15.0). Rheumatoid arthritis was the most common indication for biologic therapy (55%) followed by psoriatic arthritis (19%) and ankylosing spondylitis (18%). Tumour necrosis factor inhibitors (TNFi) and Janus kinase inhibitors (JAKi) were most often utilised, prescribed to 62% and 18% of patients respectively. With regards to the influenza vaccine 99 patients (49%) were vaccinated in 2022, compared to 49 patients (24% in 2018). Women were more likely to be vaccinated than men (54% versus 38% using Chi-squared test (p=0.05). No significant difference was seen by disease category or class of bDMARD. Older patients were more likely to be vaccinated (57, SD = 15) versus younger patients (50, SD = 14) p <0.001. In terms of COVID-19 vaccinations 7% were unvaccinated, 24% received 2 vaccinations, 42% received 3 vaccinations and 25% received 4 or more vaccinations (the recommended number of vaccinations as per current health advice). Finally, regarding the other vaccines 15% received the hepatitis B vaccine, 15% the Pneumococcal vaccine, and 8% received the shingles vaccine.
Conclusion: In this cohort of bDMARD patients there was a significant increase in the proportion of patients who received the influenza vaccine during the pandemic. This finding is novel in a rheumatology cohort. Despite this there remains under-utilisation of COVID-19, hepatitis B, Pneumococcal and Shingles vaccinations. Further work looking at the reasons for the low vaccinations rates in immunosuppressed populations is needed to address this public health issue.
References: Nil.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1813-HPR PREVALENCE AND EVOLUTION OF OCCUPATIONAL SHOULDER TENDINITIS OVER A PERIOD OF 10 YEARS IN THE TUNISIAN CENTER REGION

Keywords: Epidemiology, Work-related issues, Descriptive Studies

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Background: Shoulder pain is one of the most common regional pain syndromes. Shoulder tendinitis is the second recognized cause of musculoskeletal disorders of the upper limbs after carpal tunnel syndrome. Symptoms can be persistent and disabling in terms of an individual's ability to carry out daily activities both at home and in the workplace with significant and socio-economic costs.
Objectives: To assess the prevalence of occupational tendinitis of the shoulder and its evolution during the study period, and to describe the socioprofessional characteristics of the workers.
Methods: This is a retrospective cross-sectional study of all cases of tendonitis of the rotator cuff, working in the private sector, recognized by the competent medical commission of the National Medical Care Fund of the region of Tunisian center over a period of 10 years.
Results: During the study period, we identified 635 cases of shoulder tendinitis, i.e. 29.5% of all musculoskeletal disorders of the upper limbs. The average age of the population was 44.56 years ± 7.7 years. Our study population was mainly women (82.5%) with a sex ratio of 0.21. The majority of patients worked in the textile sector (76.2% i.e. n= 487) and the electronic sector (4.5% i.e. n= 28). Average seniority of workers in their jobs was ranging from 1 to 36 years. Seamstress (63.4%) and workman (17.7%) were the most affected jobs. The cases of shoulder tendinitis were in continuous rise over the 10 years (p=0.001, r=0.86).
Conclusion: Our study add an evidence to suggest that shoulder disorders may be increased among some workers, particularly those with jobs involving combinations of exposure to: overhead work and repetition. Most of the research on management of shoulder disorders has rarely included occupational outcomes. Adequate and rigorous prevention is essential to reduce the prevalence of this with painful consequences.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1814-HPR RHEUMATOLOGY NURSING OUTPATIENT CLINIC IN PORTUGAL

Keywords: Patient information and education, Inflammatory arthritides, Nursing

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Background: Systemic inflammatory rheumatic diseases are characterized by being chronic diseases. These diseases affect the person, in their various dimensions and are often associated with pain, loss of mobility and function, fatigue, anxiety and depression (Matcham, Norton, Scott, Steer & Hotopf, 2016; Primdhal & Esbensen, 2020; Ryan, 2020). The complex needs of these patients require and benefit of an advanced nursing practice and a guided and specialized attention that can be provided in a nursing clinic. The awareness of rheumatic patient needs and lack of this type of care led, to our knowledge, to the development of the first rheumatology nurse clinic in Portugal.
Objectives: Characterize a guided nursing clinic with the aim to support patients with systemic inflammatory rheumatic diseases, mainly initiating subcutaneous (sc) classic and biological DMARDs.
Methods: Summarized description of first guided rheumatology nurse clinic in Portugal.

Results: This nurse clinic was created and developed during the pandemic period of SARS-CoV 2 (starting February 2020). For the last three years a total of 556 appointments was performed. The targeted patients had systemic inflammatory rheumatic diseases, mainly rheumatoid arthritis, psoriatic arthritis and spondylarthritis treated with sc classic and biological DMARDs. Appointments are scheduled at week 0 and 4 of starting these therapeutics and also whenever needed, at the request of the patient or the treating physician, in order to ensure a good nurse availability to clarify doubts at the beginning of these treatments. In the specific case of sc methotrexate, a protocol was created by the Rheumatology multidisciplinary team, defining the parameters eligible for evaluation, and the respective procedures of care. During appointments nurses also assess specific disease implications in the person's daily life, both physical, emotional and social domains. Additionally, this is an opportunity to reinforce reliable information on disease management, coping strategies, including information how to manage medication side effects.

Conclusion: The rheumatology nursing outpatient clinic provides key additional care and monitorization to patients with systemic inflammatory rheumatic diseases, treated with sc classic and biological DMARDs. Nurses improve the management of chronic diseases, namely by promoting autonomy of the patient in self-administration of sc therapies at home, counselling and informing about possible adverse effects and respective management strategies, constituting a valid contribution to disease control and patient engagement and education.

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AB1816-HPR

RELIABILITY AND VALIDITY OF THE LIE-TO-SIT-TO-STAND-TO-WALK TRANSFER TEST IN TOTAL KNEE ARTHROPLASTY

Keywords: Osteoarthritis, Outcome measures, Comorbidities

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Background: Total knee arthroplasty (TKA) is the gold-standard procedure for end-stage knee osteoarthritis, however, some residual problems may still continue and cause a variety of dysfunctions, such as pain, impaired strength, proprioception, postural instability, dynamic balance, and gait deficiencies [1]. Falls are the most frequent cause of injuries in elderly people, accounting for 90% of hip and wrist fractures and 60% of head injuries [2] requiring expensive and difficult procedures such as fracture surgeries and arthroplasties [3]. The most frequent cause of falling was transfer activities while shifting body weight which accounted for 41% of falls [2] especially getting up from bed and walking to the bathroom [2,4,5]. Additionally, the three major classes of activities—walking, sitting down, and standing—were the most common precipitants of falls. These findings emphasize the need to target each of these activities in fall risk assessment and prevention strategies [2,5]. The Lie-to-Sit-to-Stand-to-Walk Transfer Test (LSSWT) incorporates a multitask approach to measure complicated transfer abilities in older people. However, there is no study investigating the reliability and validity of the LSSWT in TKA patients.

Objectives: The aim of the study is to determine the reliability, validity, and minimal clinically important difference (MCID) of the LSSWT in patients with TKA.

Methods: Twenty-one patients with TKA were included in the study. The LSSWT, the Timed Up and Go Test (TUG), and the Hospital for Special Surgery (HSS) were administered to the patients. Patients rested between the tests for an hour to prevent fatigue.

Results: The mean age was 68.1 ± 2.59 years and the mean HSS Knee Score was 85.43± 3.47. The relative (ICC coefficient) and absolute (SEM and SRD95) reliability values were 0.88, 1.21, and 3.33 respectively. The Spearman correlation coefficient of the LSSWT with the TUG was 0.63.

Conclusion: The LSSWT has excellent reliability and high validity in evaluating fall risk and complex dynamic balance and mobility for the activities of daily living in patients with TKA. The low MCID value (3.33) shows that it is sensitive and identifies little alterations in a patient's condition over time or management strategies. Therefore, it is advisable to use the LSSWT for assessing the fall risk, dynamic balance, and mobility for living in the community, discharging, or admitting to a facility.

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Disclosure of Interests: None Declared.

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HPR Measuring health (development and measurement properties of PROs, tests, devices)

AB1817-HPR

CROSS-CULTURAL ADAPTATION AND VALIDATION OF THE TURKISH VERSION OF THE NORWICH PATELLAR INSTABILITY SCORE IN PATIENTS WITH PATELLAR INSTABILITY

Keywords: Patient reported outcomes, Outcome measures, Validation

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Background: The Norwich Patellar Instability Score (NPIs) score is a tool for evaluating the impact of patellofemoral instability on joint function. It has not been translated or culturally adapted for the Turkish population before.

Objectives: The aim of this study was to translate and validate the NPIs in Turkish patients with patellar instability.

Methods: Sixty-four individuals with patellar instability were included in this cross-sectional study. Test-retest reliability of the Turkish version of NPIs was assessed by the intraclass correlation coefficient (ICC) and Cronbach's alpha for internal consistency. For construct validity, correlation coefficients between the Turkish version of NPIs developed by the translation-back translation method, Kujala patellofemoral disorder score, and Lysholm knee score were analyzed.

Results: The Turkish version of the NPI score showed high internal consistency (Cronbach's alpha = 0.97) and excellent test-retest reliability ($ICC_{2,1}$ = 0.90). The Turkish version of the NPI score had a strong correlation with Kujala patellofemoral disorder score (Rp = -0.85, p< 0.001) and the Lysholm knee score (Rp = -0.89, p< 0.001). A floor effect was observed in the present study and there was no ceiling effect.

Conclusion: The Turkish version of the NPIs is a reliable and valid tool in patients with patellar instability. The Turkish version of the NPIs will be a guide for clinicians and researchers to understand the functional status of patients with patellar instability.

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AB1818-HPR QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Keywords: Systemic lupus erythematosus, Quality of life

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Background: According to the Treat to Target strategy, in addition to monitoring the activity of the process and monitoring the formation of irreversible organ damage, it is necessary to recognize the Health-Related Quality of Life, which allows a full assessment of the patient's condition. Quality of life is defined as an integral characteristic of the patient's physical, psychological, emotional and social functioning, based on his subjective perception. Often, changes in quality-of-life indicators precede the dynamics of clinical manifestations of the disease, so they can be used as auxiliary criteria for the effectiveness of treatment already in the early stages of the course of the disease.
Objectives: To evaluate the quality of life of children and adolescent patients with systemic lupus erythematosus (SLE) depending on the activity and duration of the disease.
Methods: 18 children and adolescents with SLE aged from 8.5 to 18.6 years (14.3 ± 0.7) were examined. The average duration of SLE was 3.1 ± 0.7 years, the age of onset was 11.4 ± 0.8 years. Most of the examined were girls (94.4%). The diagnosis was established according to the classification criteria EULAR/ASR 2019 for SLE[1] with at least 10 points. High activity of SLE was found in 5.56% of patients, moderate in 33.33%, minimal in 61.11%. The patients' quality of life was assessed using the Lupus QoL questionnaire, which is a questionnaire with 34 questions, combined for 2–8 questions in 8 separate blocks: physical health, pain, planning, intimate relationships, dependence on other people, emotional health I, body image (the patient's assessment of his body), fatigue. The questionnaire was filled out by the patients themselves, the answers to the questions were modeled on a five-point Likert scale (0 – constantly, 1 – almost always, 2 – quite often, 3 – occasionally, 4 – never). Zero points corresponded to the worst quality of life, 100 points to the best state of quality of life for each domain (scale) of the questionnaire.
Results: Hhe quality of life related to health was worsened in all persons. The average total score for all domains was 65.51 ± 2.09 points and ranged from 38.41 to 89.45 points. The spheres "intimate relations" and "body image" were the most disturbed, which had the lowest score according to the test data (35.58 ± 4.87 and 62.08 ± 6.89, respectively). The best the quality-of-life indicator was recorded in the "pain" domain, which scored the highest number of points (82.41 ± 4.99 points). According to other scales of Lupus QoL, the quality of life was equal: in the domain "physical health" 77.60 ± 4.17 points, "planning" - 79.63 ± 5.52 points, "dependence on other people" - 66.21 ± 5.74 points, "emotional health" and "fatigue" - 76.15 ± 4.24 and 75.00 ± 4.46 points, respectively. Correlation analysis revealed inverse correlations between the degree of disease activity and the domains "pain" ($r = -0.530$; $p < 0.05$), "planning" ($r = -0.529$; $p < 0.05$), "intimate relationships" ($r = -0.720$; $p < 0.05$), "emotional health" ($r = -0.728$; $p < 0.01$). Direct correlations were found between the age of patients and indicators of the domain "pain" ($r = 0.647$; $p < 0.01$) and "planning" ($r = 0.642$; $p < 0.01$, respectively), the age of patients at the onset of the disease and the indicator the "body image" scale ($r = 0.611$; $p < 0.01$), the duration of the disease and the "fatigue" scale ($r = 0.638$; $p < 0.05$).
Conclusion: In all patients with SLE, a violation of the health-related quality of life was established. Its deterioration was recorded in all domains and was due to the activity of the disease. Monitoring the quality of life of adolescents with SLE in combination with disease activity monitoring will allow for a better assessment of the health status of patients and timely identification of the need for correction of therapy and the selection of the most effective treatment program.
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AB1819-HPR INTRA-RATER RELIABILITY OF SHEAR WAVE ELASTOGRAPHY FOR THE QUANTIFICATION OF THUMB MUSCLE ELASTICITY

Keywords: Ultrasound

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Background: Shear wave elastography (SWE) is a technique that evaluates tissue elasticity by applying an acoustic radiation force impulse [1]. It is undetermined how reliable this modality is in assessing thumb muscles. Quantitative evaluation of muscle stiffness in conditions such as trapeziometacarpal osteoarthritis where increased fibrosis, muscle tone, spasm, and contractures can be seen can provide important information about the pathophysiology and prognosis of the diseases [2].
Objectives: This study aimed to assess the intra-rater reliability of thumb muscle elasticity and thickness in healthy people.
Methods: Ten healthy participants (20 hands) enrolled in the study. Thickness and shear wave velocity (SWV) of adductor pollicis (AdP) and first dorsal interosseous (FDI) muscles were obtained using an ACUSON S3000 Ultrasonography System and a 9L4 probe (4-9 MHz) (Siemens Medical Solutions, Mountain View, California). Ultrasound data (SWV, thickness) were collected and analyzed by an experienced radiologist. Three repeated SWV and thickness measurements were recorded in the resting position and an average was taken. Two sessions were performed at a 15-minutes interval.
Results: Ten healthy participants (20 hands; 5 female; 5 male; mean age: 25.9±2.68 years; BMI: 22.4±1.39 kg/m2) were included in this study. Nine subjects had right-hand dominancy and 1 had left-hand dominancy. The mean (±SEM) shear wave velocity for the AdP was 1.86 ± 0.6 m/s (=10.86 kPa), and for the FDI was 1.76 ± 0.5 m/s (=9.72 kPa). The intra-rater trial agreement was excellent, with intraclass correlation coefficients of 0.887 and 0.828 respectively. The mean (±SEM) muscle thickness for the AdP was 12.4 ± 3.93 mm, and for the FDI was 12.0 ± 3.68 mm. The intra-rater trial agreement was excellent, with intraclass correlation coefficients of 0.953 and 0.984 respectively.
Conclusion: SWE ultrasound was a reliable imaging technique to assess the stiffness and thickness of thumb muscles.
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AB1820-HPR BIOELECTRICAL IMPEDANCE ANALYSIS SHOWED HIGH AGREEMENT AND SPECIFICITY TO ASSESSMENT OF LOW APPENDICULAR SKELETAL MUSCLE MASS IN WOMEN WITH SYSTEMIC SCLEROSIS: PRELIMINARY DATA

Keywords: Validation, Sarcopenia, Systemic sclerosis

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Background: Patients with systemic sclerosis (SSc) are particularly prone to skeletal muscle wasting, affecting nearly one-third of patients, increasing the risk of disability[1,2]. To assess muscle mass, there are direct methods, such as magnetic resonance imaging, computed tomography and dual-energy X-ray absorptiometry (DXA), considered the gold standard[3]. DXA is widely used in clinical practice and in population studies, but it has some disadvantages, such as specific technical skills and higher costs[3]. Bioelectrical impedance analysis (BIA) is a validated method in healthy individuals of body composition assessment with greater affordability and minimum requirements[4]. To our knowledge, in patients with SSc only one study compared DXA with BIA. Soanjer et al found agreement between these two techniques only for fat-free mass, without evaluating appendicular skeletal muscle mass (ASM)[5].
Objectives: (1) Our objective was to compare ASM measured by BIA versus DXA and (2) to verify the associations with clinical features in women with SSc.
Methods: Women with SSc according to ACR/EULAR 2013 criteria were consecutively included at a tertiary public hospital in Rio Grande do Sul, Brazil (Hospital de Clínicas de Porto Alegre, HCPA) in 2022. Modified Rodnan's skin score (mRSS), EUSTAR activity index were calculated. The ASM by BIA (In Body 370s) and DXA (GE FamBeam 4500A) were calculated from sum lean mass of arm and legs (kg). Low muscle mass (BIA or DXA) was defined according to the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) less than 15 kg. Pearson's and intraclass correlation coefficients, dependent samples t-test and simple linear regression for Bland–Altman plot were performed. The significance level was set at $p<0.05$.
Results: Until this moment, 62 women with SSc were included. The mean age was 62.0 ± 10.1 years-old and median disease duration was 15.0 (7.0–21.0) years. Forty-one patients (66.1%) had limited cutaneous disease, 14 (22.6%) diffuse-cutaneous and 7 (11.3%) *sine scleroderma*. The median mRSS was 4.0

(2.0–8.0) and the EUSTAR index was 1.5 (0.6 - 2.4). The mean appendicular skeletal muscle mass measured by DXA was 16.0 ± 2.2 kg while by BIA was 15.5 ± 2.3 kg (Δ = 0.5 kg; p = 0.005), underestimating the ASM. On other hand, the mean differences between DXA and BIA showed within the confidence interval (p= 0.358; CI 95%: -2.8 – 1.8; Figure 1). ASM by BIA was strongly correlated (r= 0.866, p < 0.001) and had a high agreement (Intraclass Correlation Coefficient = 0.919, p < 0.001) with ASM by DXA. We found only weak association between ASM by BIA and age (r= -0.282; p= 0.026). Low muscle mass in women with SSc was found in 18 patients (29%) by DXA and in 26 patients (42%) by BIA with a sensitivity of 80% and specificity of 94%.

Conclusion: BIA and DXA show high correlation and agreement in ASM assessment of women with SSc. Our findings suggest BIA as a useful tool due to its high specificity with DXA for the early assessment of low ASM in women with SSc. Furthermore, completion of this study is needed to confirm these results.

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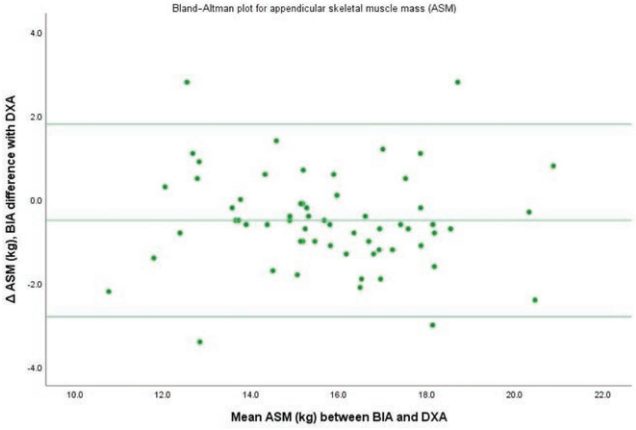
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Figure 1. Agreement between DXA and BIA



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AB1821-HPR FUNCTIONAL CAPACITY AND WORK ABILITY IN PATIENTS WITH COMMON SCIATICA

Keywords: Work-related issues, Quality of life, Pain

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Background: Spinal radicular syndromes are a serious healthcare issue in the society nowadays. A common form of ailments related to the syndromes is sciatica, manifesting with severe pain radiating along the course of the sciatic. In many patients the pain limits the ability to perform daily routine at work and at home [1].

Objectives: The aim of study was to assess the functional capacity in patients with sciatica and its influence on their quality of life, their ability to function in daily life and at work.

Methods: We conducted a cross-sectional study including patients suffering from documented common sciatica evolving for more than 3 months collected in a rheumatology department over a period of 3 years. The Quality-of-life SF-36 questionnaire - Short Form Health Survey was used in the study, along with a supplement specifying the study group, with an indication of the pain location and the patients' occupations. Additionally, the Oswestry Disability Index, the work ability index (WAI) -and the Visual Analogue Scale (VAS) were applied.

Results: The study covered 104 patients, both male and female (71 women and 33 men with sex ratio male/female of 0.46). The mean age of our patients was 55.4 years-old (23-74). The most common etiology of sciatica was herniated disc, followed by lumbar spinal stenosis and spondylolisthesis. The root path was L5 in 74 cases and S1 in 30 cases. the average duration of sciatica was 6.4 months. The mean oswestry score was 25(15-38). The mean of the VAS was 7.4(4-9). The mean of WAI was 25.2(15-38). The Quality-of-Life index, at a statistically significant level ($\alpha < 0,05$), is higher (hence the quality of life is lower) in females suffering from sciatica. The duration of sciatica was a factor strongly correlated with the intensity of pain - the Oswesty score and the WAI were negatively correlated with age ($p<0.05$, r= -0.6 and r=-0.4 respectively).

Conclusion: In our series sciatica affects the quality of life of the female patients studied in this research to a greater extent than the male patients. The intensity of pain associated with sciatica duration. WAI and Oswestry were negatively associated with age.

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AB1822-HPR EXPERIENCE AND PRELIMINARY DATA IN IMPLEMENTATION OF PRO (PATIENT REPORTED OUTCOME) IN THE DAILY ROUTINE IN INFLAMMATORY ARTHRITIS PATIENTS BASED IN ICHOM-ARTHRITIS MODEL AND A NEW ELECTRONIC PLATFORM (QÜESTCLINIC)

Keywords: Outcome measures, Quality of life, Patient reported outcomes

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Background: In clinical practice of patients with chronic rheumatic inflammatory disease: rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA) it is not used to assess quality of life issues in relation to the disease. Patient Reported Outcomes (PROs) can inform about these symptoms suffered by patients using questionnaires or patient reported outcome measures (PROMs). International Consortium Health Outcomes Measures has the main purpose to recognize the crucial role of patients in outcome measures in value-based health, providing a specific ICHOM-arthritis model [1].

Objectives: To describe the pilot study and some very initial data of the implementation of PROs in an Arthritis Unit of a tertiary hospital based on ICHOM-arthritis through an electronic platform.

Methods: Rheumatologists, nurses, and quality management staff have worked for a period of 2 years in two aspects based on the ICHOM-arthritis model: 1. the use of the "standard set" described that includes the main clinical, and demographic data and a list of generic and specific questionnaires or PROMs to collect for RA, PsA, and axSpA patients. 2. the typology and frequency of visits to establish. MyClinic is an electronic bidirectional platform provided for the Hospital to connect patients and doctors. We designed the Qüestclinic, a space where place questionnaires to send to patients and where patients could answer them. Patients with the 3 diagnoses of adult inflammatory arthritis (RA, PsA, and axSpA) are invited to participate in their visit to outpatient clinics, accepting and signing their informed consent.

Results: We selected 4 generic questionnaires sent to patients to answer in the QuestClinic: MDHAQ (VAS_pain, PGA, VAS_fatigue), EuroQoL, HADS anxiety and depression, and FACIT(FS), and also a disease-specific one: RAID for RA, PsAID for PsA, and BASDAI and BASFI for axAspA. The 12-month visits set at baseline (Vb), 6 months (V6), and 12 months (V12) were performed in a double integrated format (Figure 1). In Vb, 3 tasks are performed: 1. Check questionnaire completion. 2. Initial characteristics (only in Vb): Demographic data (level of studies) and pathological history: smoking, hypertension, heart disease, stroke, COPD, diabetes mellitus, neoplasms, depression, bone fracture, gastric ulcer, other gastric problems, obesity. 3. Monitoring: vital signs and calculation of BMI; adherence to oral or parenteral treatment. Then, in the standard visit the rheumatologist reviews the PROM scores met by the patients in the QüestClinic. Preliminary data in V6 were: A total of 74 records belonging to 55 patients, 40 (54%) female, 39 (53%) RA, 20 (27%) axSpA, and 15 (20%) PsA were collected from February to December 2022. 54 (73%) patients have only visited in baseline and 20 (27.03%) had already 2 visits (V6). The first "snapshot" of the median of generic PROMs (VAS-pain, PGA, VAS-fatigue, HADS-anxiety, and depression) for the diseases were around a median of 4 for pain, PGA, fatigue, and depression, but higher for anxiety in an unselected group of inflammatory chronic rheumatic disease patients (Table 1).

Conclusion: We describe the functional model proposed to implement PROMs in clinical routine to cover the most important PRO dimensions of quality of life of disease and we present here the first picture of preliminary data.

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Table 1. median results of the most important generic PROMs studied.

PROM	RA patients	PsA Patients	axSpA patients
VAS-Pain	4,61	4,00	4,10
PGA	4,22	4,27	3,95
VAS-Fatigue	4,11	3,89	4,11
HAS anxiety	7,38	6,08	7,00
HADS depression	5,30	5,54	5,00

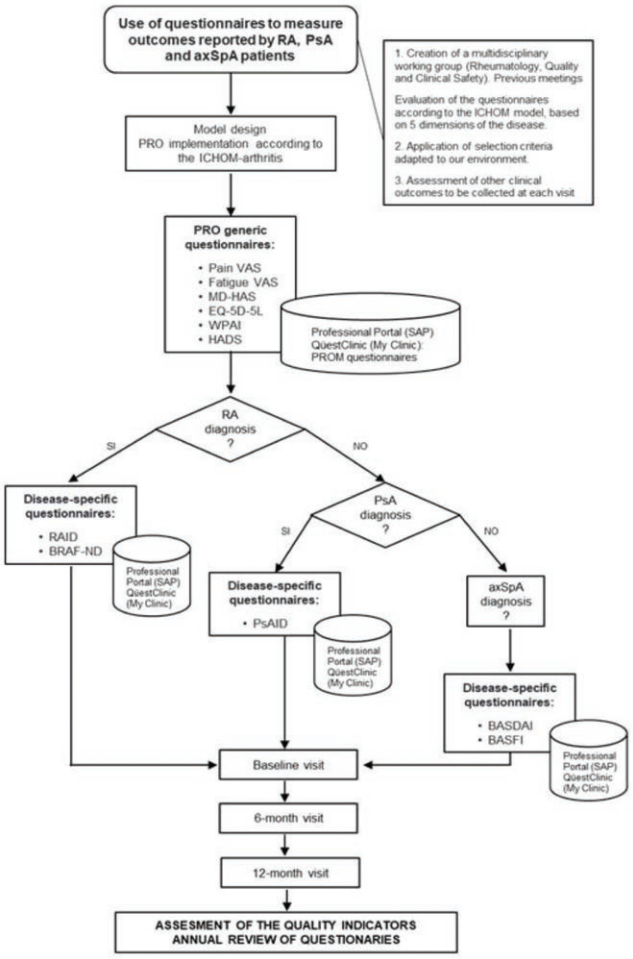


Figure 1. Algorithm of the PRO pilot study implementation.

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AB1823-HPR

VALIDATION OF THE LUPUS IMPACT TRACKER IN ARGENTINA

Keywords: Validation, Patient reported outcomes, Systemic lupus erythematosus

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Background: The Lupus Impact Tracker (LIT) is a patient reported outcome (PRO) questionnaire. The results demonstrated their reliability in clinical practice for evaluation and follow-up.

Objectives: To validate the LIT and the degree of correlation with other scores in SLE patients in Argentina.

Methods: Observational, analytical and multicenter study. Patients older than 18 years with SLE (2019 ACR/EULAR criteria) were included. In the first stage, we evaluated the reproducibility in a period of 7 days measured by intraclass correlation (ICC) as well as the time to answer the questionnaire. In a second stage, the scores LIT, LupusQoL, PGA, SLEDAI and SLICC SDI were calculated for each patient and the Spearman correlation coefficient between scores was analyzed.

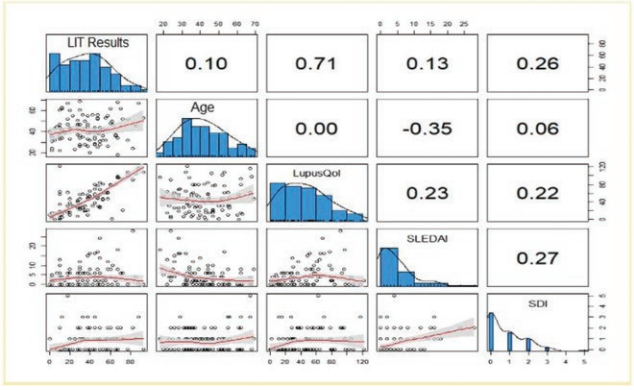
Results: Initially the LIT was performed in 10 patients. The average time to complete the questionnaire was 2,1 minutes. The mean of LIT (T0) was 57,1 (SD 24,2) and 51,5 (SD 25,5) seven days later. The ICC was 0,808 (95% CI 0,431 – 0,948). In the second stage, 100 SLE patients were included consecutively. Table 1 shows the main characteristics of the patients. The Spearman correlation coefficient between LIT/ LupusQol was 0.71, LIT/ SLEDAI was 0.13, and LIT/ SLICC was 0.26 (Graphic 1).

Conclusion: The median of the LIT questionnaire was 37 points. LIT demonstrated test-retest reliability and linear correlation with LupusQol. There was no correlation with SLE activity. LIT is a practical, quick and easy tool to evaluate he patient's perspective in relation to the disease in daily practice.

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Variable	Category	Total	LIT Median	Q1	Q3	p-value
Age	≤40 years	50 (50.0)	37.50	13.12	50.00	0.3941
	>40 years	50 (50.0)	36.25	20.0	56.8	
Sex	Female	91 (91.0)	37.50	20.00	51.25	0.9232
	Male	9 (9.00)	32.50	12.50	65.00	
Attention of the patient	Outpatient	97 (97.0)	37.50	20.00	52.50	0.9436
	Hospitalized	3 (3.00)	45.00	28.75	46.25	
GRAFFAR scale (socioeconomic level)	I Upper class	4 (4.0)	16.25	10.00	29.38	0.0610
	II Upper middle class	10 (10.0)	32.50	15.00	37.50	
	III Middle class	32 (32.0)	26.25	10.00	50.00	
	IV Middle-low class	43 (43.0)	45.00	30.00	57.50	
	V Lower class	11 (11.0)	37.50	28.75	54.75	
Physician global assessment (PGA)	Mild	41 (41.0%)	32.50	17.50	55.00	0.1096
	Moderate	18 (18.0)	46.25	38.13	55.63	
	Normal	38 (38.0)	28.75	12.13	50.00	
	Severe	3 (3.0)	45.00	41.25	47.50	
SLEDAI	Mild or moderate activity	34 (34.0)	31.25	18.13	47.50	0.1386
	Severe activity	9 (9.0)	47.50	45.00	50.00	
	Without activity	57 (57.0)	37.50	15.00	52.50	



Graphic 1. Spearman correlation coefficient

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HPR Patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

AB1824-HPR MULTIPLE TNFI TREATMENT CYCLES AND THE FAILURE OF TRIAL-AND-ERROR CARE FOR PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: bDMARD, Patient reported outcomes, Rheumatoid arthritis

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Background: Inhibitors of tumor necrosis factor-alpha (TNFi) are central to management of rheumatoid arthritis (RA) though continued use beyond initial failure is negatively associated with response to subsequent TNFi treatment.
Objectives: To assess the patterns of recurrent TNFi use relative to reasons for switch as observed in community rheumatology care in the US.
Methods: Data: PIONEER-Rheumatology, an EMR and open text-extracted database specific to care given by the American Rheumatology Network (ARN). Study population: Adult (18+ years old) patients with RA, TNFi-treated in 2018 to 2021. Full histories were assessed for each patient and index was set as the initiation date of the last TNFi observed for each patient prior to 2022. Reasons for discontinuation were extracted from chart notes and broadly classified (and subclassified) as attrition (death, moved/left practice, non-clinical reasons), lost to follow up (LTFU, patient disengaged), or clinical (treatment goal achieved, lack/loss of efficacy, or condition resulting from disease, treatment, or patient burden).
Results: 13994 patients and 19925 episodes (defined as distinct patient & TNFi drug) were examined. Of 13944 patients, 9399 (67%) received 1 TNFi, 3527 (25%) 2 TNFi, 1068 (8%) ≥3 TNFi; treatment patterns may have included intervening non-TNFi treatment cycles. [TABLE]

Table 1.

No. (% row, % column) patients by years history (rows) and # of distinct TNFi drugs (columns)

Years History	1 TNFi	2 TNFi	≥3 TNFi	Total
<1 year	4262 (89%, 45%)	477 (10%, 14%)	37 (1%, 3%)	4776 (100%, 34%)
1<2 years	1476 (65%, 16%)	680 (30%, 19%)	118 (5%, 11%)	2274 (100%, 16%)
2<3 years	957 (59%, 10%)	530 (33%, 15%)	139 (9%, 13%)	1626 (100%, 12%)
3<4 years	634 (53%, 7%)	410 (35%, 12%)	144 (12%, 13%)	1188 (100%, 8%)
4<5 years	606 (55%, 6%)	352 (32%, 10%)	135 (12%, 13%)	1093 (100%, 8%)
≥5 years	1464 (48%, 16%)	1078 (35%, 31%)	495 (16%, 46%)	3037 (100%, 22%)
Total	9399 (67%, 100%)	3527 (25%, 100%)	1068 (8%, 100%)	13994 (100%, 100%)

Reasons for discontinuation/switch were available for 4254/4595 (93%) and 998/1068 (93%) patients treated with 2+ or 3+ distinct TNFi, respectively. Lack/loss of efficacy was the reason for 1 or more TNFi discontinuations prior to the last TNFi received for 2689/4254 (63%) and 829/998 (83%) of patients with 2+ or 3+ TNFi, respectively. For a patient subset with ≥1 year history pre-index, prior failure of 1+ TNFi was observed for 2690/3765 (71%) and 814/936 (87%) patients who received 2+ or 3+ TNFi, respectively.
Conclusion: A third of TNFi-treated study patients received >1 TNFi with most discontinuing prior TNFi due to lack/loss of efficacy. Though trial-and-error care is seemingly standard to RA management, this study suggests that some patients do not benefit from this approach.

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AB1825-HPR DECISION TO INITIATE A TUMOR NECROSIS FACTOR INHIBITOR IN RHEUMATOID ARTHRITIS UNCOUPLED FROM DISEASE ACTIVITY MEASURES

Keywords: bDMARD, Real-world evidence, Rheumatoid arthritis

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Background: Previous studies have demonstrated discordance between patient-based (e.g. RAPID3) and predominantly physician-based (e.g. CDAI) disease activity measures (DAMs).
Objectives: To examine the relationship between DAMs and decision to initiate TNFi following csDMARDs.
Methods: Data: PIONEER-Rheumatology, an EMR and open text-extracted database specific to care given by the American Rheumatology Network. Study population: Adult RA patients who received TNFi as initial targeted synthetic or biologic DMARD treatment between Jan 2014 to Apr 2022 after csDMARDs. Assessments: CDAI, RAPID3, DAS28 (includes DAS28-CRP, DAS28-ESR), tender/swollen joints (TSJ), pain score, and HAQII closest to but within -180 days of TNFi initiation. Paired (+/- 30 days) CDAI, RAPID3, and DAS28 assessed via Pearson correlation.
Results: 2811/3682 (76%) patients had 1+ DAM prior to TNFi initiation; 2332/3682 (63%) pain score, 2047/3682 (56%) TSJ, 1570/3682 (43%) DAS28, 1442/3682 (39%) RAPID3, 1430/3682 (39%) CDAI, and 143 (4%) HAQII. Of the 2331/3682 patients with RAPID3, DAS28, or CDAI, 982/2331 (42%) had near-remission/low disease by at least 1 DAM prior to index. 582 patients had paired CDAI and RAPID3 scores; moderate/severe disease was indicated for 474/582 (81%) by CDAI and 395/582 (68%) by RAPID3 ($p<0.001$) and 163/582 (28%) of patients were indicated as near-remission/low by one DAM but as moderate/severe by the other. Correlations between paired DAMs: strong for CDAI:DAS28 (n=1063, r=0.788) and moderate for CDAI:RAPID3 (n=582, r=0.399) and for RAPID3:DAS28 (n=637, r=0.225).
Conclusion: DAMs were not present for 24% of study patients at initiation of TNFi. Of patients with RAPID3, DAS28, or CDAI, 42% patients started TNFi despite near-remission/low disease activity. Where conducted, paired DAS28:RAPID3 and CDAI:RAPID3 scores were moderately correlated though severity categories for CDAI:RAPID3 were discordant for 28% of evaluated patients. These results suggest that clinical decision-making to initiate TNFi does not rely solely on standard DAMs.

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Disclosure of Interests: Jasvinder Singh Consultant of: Scipher, Crealta/Horizon, Medisys, Fidia, PK Med, Two Labs Inc., Adept Field Solutions, Clinical Care Options, Clearview Healthcare Partners, Putnam Associates, Focus Forward, Navigant Consulting, Spherix, MedIQ, Jupiter Life Science, UBM LLC, Trio Health, Medscape, WebMD, Practice Point Communications, National Institutes of Health, American College of Rheumatology, Zimmer Biomet Holdings, Intuitive Surgical Inc./Philips Electronics North America, TPT Global Tech, Vaxart Pharmaceuticals, Atyu Biopharma, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix Pharmaceuticals Holding Corp, Charlotte's Web Holdings, Inc., Amarin, Viking, Moderna Pharmaceuticals, Simply Speaking, Outcomes Measures in Rheumatology (OMERACT), FDA Arthritis Advisory Committee, Veterans Affairs Rheumatology Field Advisory Board (FAB), Christopher Adams: None declared, Andrew Frick Grant/research support from: GSK, ViiV, AbbVie, AstraZeneca, Scipher, UCB, Takeda, JNJ, Horizon, Gilead, Merck, Simon Helfgott: None declared, Kent Huston: None declared, Scott Milligan Grant/research support from: GSK, AbbVie, AstraZeneca, Scipher, UCB, Takeda, JNJ, Horizon, Gilead, Nehad Soloman Speakers bureau: AbbVie/Abbott, Horizon, Janssen, Amgen, GlaxoSmithKline (GSK), Exagen, UCB, Consultant of: Novartis, Grant/research support from: AbbVie/Abbott, Horizon, Janssen, Amgen, Colin Edgerton Consultant of: Novartis, Boehringer Ingelheim.

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AB1826-HPR HOW TO ASSESS THE SATISFACTION OF PATIENTS WITH CHRONIC INFLAMMATORY DISEASES AFTER SWITCHING TO A BIOSIMILAR? INSIGHTS FROM AN EXPLORATORY QUALITATIVE STUDY PRELIMINARY TO AN OBSERVATIONAL STUDY

Keywords: Patient reported outcomes, Quality of life, bDMARD

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Background: Patients experience may be negatively impacted when starting biosimilar due to a poorly executed switch which could result in poor adherence and nocebo effect.

Objectives: This study aims to identify suitable patient satisfaction dimensions to design an observational study on real-life switches.

Methods: A qualitative exploratory study was performed. In-depth, semi-structured interviews were conducted by a sociologist with patients with inflammatory diseases treated by anti-TNF biosimilar to determine patient switching experiences and expectations, identify dimensions for the observational study's questionnaire (ePRO). Patients were recruited with the help of patients' associations.

Results: Four patients (3 females) were included: 2 with rheumatoid arthritis and 2 with Crohn's disease. Two patients had adalimumab biosimilar, 1 etanercept biosimilar and 1 adalimumab originator (switch-back). The following dimensions were identified:

● **Information transparency:** patients were unfamiliar with biosimilars and some did not know they were using them. Some reported distrusting biosimilars but accepted them because they trust their physician.

● **Patient Involvement:** physicians decide whether to offer a biosimilar, but patient acceptance is determined by their interpretation of the situation. Patients found it difficult to express their treatment preferences and reported that physicians didn't always prompt these discussions.

● **The time of injection:** patients had to learn the injection procedures but received relatively little support during the switch in handling the new device. Some experienced greater pain, differences in comfort or reported errors in use.

● **Transition:** the sustainability of the switch may have been constrained by delays in supply in the city. In some cases, the pharmacy dispensed the originator drug as a replacement.

These led to the following ePRO composition: BMQ, HLSEU-Q16 (health literacy), ad hoc items on shared decision making, expectations, patient training, satisfaction with provided information and injection. All 4 patients understood the final questionnaire. The study design is an open label multicentric study of 300 patients in 30 sites (rheumatology and gastroenterology, hospital, and private practice) when offered a switch. The primary objective is to assess patients' overall satisfaction with injections 3 months post-initiation compared to the previous adalimumab. The first patient was included in June 2022.

Conclusion: This work proposes an original methodology for the selection and design of criteria for an observational study. An exploratory qualitative study highlighted different factors of patient satisfaction during the switch to adalimumab biosimilar. It guided the choice of e-PROs and the construction of specific items.

REFERENCES: NIL.

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Disclosure of Interests: Guillaume BOUGUEN Speakers bureau: AbbVie, Takeda, MSD, Janssen, Celltrion, Consultant of: AbbVie, Takeda, Mylan, Pfizer, Sandoz, Amgen, Ferring, Janssen, Celltrion, Grant/research support from: AbbVie, Takeda, Fresenius, Laurent Peyrin-Biroulet Speakers bureau: Galapagos, AbbVie, Janssen, Genentech, Ferring, Tillotts, Pharmacosmos, Celltrion Healthcare, Takeda, Boerhinger Ingelheim, Pfizer, Index Pharmaceuticals, Sandoz, Celgene, Biogen, Samsung Bioepis, Alma, Sterna, Nestle, Inotrem, Enterome, Allergan, MSD, Roche, Arena, Gilead, Hikma, Amgen, BMS, Vifor, Norgine, Mylan, Lilly, Fresenius Kabi, Oppilan Pharma, Sublimity Therapeutics, Applied Molecular Transport, OSE Immunotherapeutics, Enthera, Theravance, Anne BUISSON: None declared, Delphine LAFARGE: None declared, Sonia Tropé: None declared, Guillaume Montagu: None declared, Alice DENIS Shareholder of: Celltrion Healthcare France, Employee of: Celltrion Healthcare France, Caroline HABAUZIT Shareholder of: Celltrion Healthcare France, Employee of: Celltrion Healthcare France, salim benkhalifa Shareholder of: Celltrion Healthcare France, Employee of: Celltrion Healthcare France, Hubert MAROTTE Shareholder of: AbbVie, Amgen, Bristol Myers Squibb, Celltrion HealthCare, Galapagos, Lilly France, Merck Sharp & Dohme, Novartis, Nordic Pharma, Pfizer, and Sanofi Aventis, Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celltrion HealthCare, Galapagos, Lilly France, Merck Sharp & Dohme, Novartis, Nordic Pharma, Pfizer, and Sanofi Aventis, Grant/research support from: Bristol Myers Squibb, Celltrion HealthCare, Galapagos, Lilly France, Novartis, Nordic Pharma, Pfizer, and Sanofi Aventis.

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AB1827-HPR PAIN MANAGEMENT IN OLDER POPULATION FROM GERMANY AND SWEDEN: SUB-GROUP ANALYSIS FROM A TOPICAL DICLOFENAC PROSPECTIVE REAL-WORLD EVIDENCE STUDY

Keywords: Pain, Quality of life, Patient reported outcomes

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Background: Adequate pain management in older individuals is essential to support functional lifestyle and enable robust quality of life (QoL). Topical non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac gel, with limited systemic exposure, provide a better pharmacological alternative to oral NSAIDs for musculoskeletal pain management especially in elderly due to favorable benefit-risk profile[1].

Objectives: To evaluate impact of over the counter (OTC) topical diclofenac (1.16% & 2.32%) use in an older German and Swedish population on different aspects related to QoL such as pain, functional status, and treatment satisfaction.

Methods: A subgroup analyses of older participants (≥65 years) from a prospective real-world evidence study conducted among 731 adult (≥18 years) consumers (467 in Germany and 264 in Sweden) of OTC topical diclofenac (1.16% & 2.32%). Treatment satisfaction, functional status and pain relief were assessed using electronic surveys (baseline, Week 4, and Week 12) via personalized link. Numerical Rating Scale (NRS-11) and Likert scale were used for questionnaire-based response collection.

Results: Data from 279 (72.3%) older participants, 203 German and 76 Swedish, were included. Baseline characteristics of participants and reported outcomes are shown in Table 1. Majority purchased 2.32% strength, were repeat users and reported having previously identified cardiovascular conditions. Improvement in pain score ≥ 1 point was observed in >57% of users at Week 12. Participants reported reduction of pain interference in different functional activities at Week 4 and 12. >70% of participants were satisfied with the treatment at Week 4 and >75% at Week 12.

Conclusion: Older participants reported reduction in pain over time, improvements in their ability to participate in daily life activities, treatment satisfaction with the use of OTC topical diclofenac and thus improved QoL.

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Table 1. Baseline characteristics and Outcomes for older German and Swedish participants

	Germany 203 (43.5%)	Sweden 76 (28.8%)
Baseline characteristics		
Mean age (years)	74.3	72.1
Repeat users of OTC topical diclofenac (2.32%)	87.7%	70%
Quality of pain	43.3%	47.4%
Transient pain ('My pain comes and goes')	38.4%	44.7%
Persistent pain ('My pain never really goes away')	18.2%	7.9%
Inconsistent pain ('My pain usually occurs unexpectedly and infrequently')		
Cardiovascular disease[#]	65.5%	59.2%
Gastrointestinal disorders[^]	3.0%	6.6%
Outcomes		
Mean (SD) worst pain on NRS	6.1 (1.9)	5.8 (2)
7 days prior to baseline	5.2 (2.2)	4.9 (2)
7 days prior to Week 4	4.8 (2.5)	4.2 (2.4)
7 days prior to Week 12		
Improvement in pain score ≥ 1 point	57.1%	56.8%
At Week 4	57.7%	61.6%
At Week 12		
Reports of severe pain	46.3%	38.2%
- At Baseline	28.0%	23.0%
- At Week 4	26.9%	21.9%
- At Week 12		
Reports of pain interference ('Quite a bit') with daily activities	47.3%	39.5%
- At Baseline	34.1%	33.8%
- At Week 4	32.7%	17.8%
- At Week 12		
Reports of pain interfering with errands and chores around and outside the home	41.4% 31.3%	27.6% 29.7%
- At Baseline	24.2%	13.7%
- At Week 4		
- At Week 12		
Reports of pain interfering with physical activities	50.2%	48.7%
- At Baseline	37.9%	41.9%
- At Week 4	32.1%	27.4%
- At Week 12		
Reports of pain interfering with social activities	26.6%	21.1%
- At Baseline	20.3%	9.5%
- At Week 4	15.4%	12.3%
- At Week 12		
Satisfied with OTC topical diclofenac	71.4%	78.4%
- At Week 4	75.0%	86.3%
- At Week 12		
Social independence among participants satisfied with OTC topical diclofenac	90.0% 93.2%	84.5% 95.2%
- At Week 4		
- At Week 12		

OTC = Over the counter; NRS = Numerical Rating Scale; SD = Standard deviation[#]heart problems, high blood pressure;^stomach or intestinal ulcers, bleeding from stomach, or blood in stool

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AB1828-HPR ASSOCIATION BETWEEN COMPLEMENTARY AND ALTERNATIVE MEDICINE USE AND TRUST IN THE PHYSICIAN IN PATIENTS WITH INFLAMMATORY RHEUMATISM?

Keywords: Diet and Nutrition, Rheumatoid arthritis, Spondyloarthritis

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Background: Generally, patients with chronic rheumatic diseases use complementary and alternative medicine (CAM) in addition to their conventional treatments to manage their health. Discussing these treatments with their physician is still rare, which might be directly related to patients' trust toward them.

Objectives: The primary objective of this study was to assess the association between patients' trust in their physician and the use of complementary and alternative medicine. As a secondary objective, to estimate the prevalence of complementary and alternative therapy use among patients with chronic inflammatory rheumatism.

Methods: This is a cross-sectional study, which included patients with established chronic inflammatory rheumatism, followed at the University Hospital Center in Tangier. The questionnaire included demographic and clinical information, use of conventional therapy, complementary and alternative therapy, as well as the interpersonal trust in patient-physician relationships using the Trust in Physician Scale (TPS).

Results: The study included 189 patients. 57.14% of patients reported using complementary medicine at least once, most patients were women (77.78%), mean age was 46.67±13.25 years with an average course of the disease 11.11±9.23 years. The most frequent used complementary and alternative treatments were cupping therapy (45.90%), massage (40.40%) and the ingestion of a mixture of plants (27%). Mean±SD Trust in Physician Scale was 47.64 ±7.2, and there were no significant differences between CAM users vs. non-users (48.08±6.9 vs. 47.04±7,4; p=0,35).

Conclusion: More than half of patients with inflammatory rheumatism reported the use of complementary and alternative medicine. However, the association between their use and trust in the physician assessed with TPS was not established.

REFERENCES: NIL.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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AB1829-HPR FACTORS ASSOCIATED WITH SEDENTARY BEHAVIOR IN PATIENTS WITH KNEE OSTEOARTHRITIS

Keywords: Education, Pain

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Background:

Objectives: To determine factors related to sedentary behavior in patients with Knee Osteoarthritis.

Methods: we conductued a cross-sectional study of 130 patients affected by knee osteoarthritis. Information on patients and disease characteristics were collacted. Physical activity was measured objectively using the short version of IPAQ questionnaire (International Physical Activity Questionnaire) for 7 consecutive days. Activity levels were subdivided into low physical activity and moderate to vigorous physical activity. We analysed factors associated with sedentary behaviour.

Results: The mean age of the patients included was 59.9+/-10 years with 110 (84.6%) females. The median IPAQ was 260 (0.500) MET-min/week. The sedentary behaviour was noted in 69.2% of patients. Table 1 summuriezed factors associated with sedentary behaviour in knee osteoarthritis patients.

Table 1. Analysis of factors associated with sedentary behavior in knnee osteoarthritis patients.

Factors related to sedentary behavior	P
Age	0,005
Lack of regular PA before the disease	0,01
Socio-cultural and/or economic barriers	0,01
Pain caused by knee ostoarthritis	0,02
Functional disability caused by knee ostoarthritis	0,01

Conclusion: Sedentary behaviour is prevalent among knee osteoarthritis patients. It is important to overcome this unhealthy lifestyle and to encourage practice of physical activity in this population by combating the barriers reported by patients.

REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1830-HPR **MUSCULOSKELETAL DISORDERS DURING COVID-19 INFECTION: A SURVEY OF HEALTHCARE WORKERS**

Keywords: COVID, Health Services Research, Epidemiology

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Background: COVID-19 infection has revealed a considerable number of extra-pulmonary manifestations, especially rheumatological. The detection of these manifestations, which herald the infection, is of great value in the early diagnosis of the disease, especially in health care workers (HCWs) who are at considerable risk of infection. Although myalgia is a common clinical feature of COVID-19, other musculoskeletal disorders (MSDs) have been rarely described.
Objectives: To describe MSDs during SARS-COV2 infection in HCWs.
Methods: Prospective descriptive study conducted at the department of occupational pathology and fitness for work of Charles Nicolle Hospital in Tunis, having included the HCWs affected by COVID-19 during the period from 01 September 2020 to 28 February 2021. Data collection was carried out by regular telephone follow-up during the containment period using a pre-established form.
Results: During the study period, 656 HCWs were infected with SARS COV 2, of whom 134 (20.4%) had at least one musculoskeletal event. The mean age was 42±9 years with a sex ratio (M/F) of 0.2. The most represented occupational category was nurses (33.6%) followed by health technicians (23.1%). The median professional length of service was 12 [7; 20] years. The presence of comorbidity was noted in 58.2% of HCWs. A pre-existing osteoarticular disease was found in 8.2% of cases. Obesity was noted in 25.4% of the population. Active smoking was reported by 14.3% of respondents. A known vitamin D deficiency was noted in 16.5% of patients. Spinal pain was the most reported MSD, present in 87.3% of cases. Low back pain was the most frequent spinal pain (56.7%) followed by back pain (37.4%) and neck pain (5.9%). MSDs of the lower limbs were found in 12.7% of patients. They were represented by gonalgia in 11.9% of cases, ankle pain in 5.2% of cases and hip pain in 4.3% of cases. MSDs of the upper limbs were described by 7.5% of the patients, 92.5% of whom presented with shoulder pain. The median duration of MSDs during COVID-19 was 5 [3; 8] days. These manifestations were persistent on return to work in 21.1% of cases.
Conclusion: Knowledge of the frequency and consequences of musculoskeletal manifestations related to COVID-19 infection is of great importance, particularly in HCWs, in order to optimise management and ensure a rapid return to work.

REFERENCES: NIL.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6467

HPR Service developments, innovation and economics in healthcare

AB1831-HPR **SYSTEMATIC REVIEW OF LABORATORY MONITORING GUIDELINES OF CONVENTIONAL SYNTHETIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS**

Keywords: Systematic review, Best practices, Disease-modifying Drugs (DMARDs)

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Background: Conventional synthetic disease modifying anti-rheumatic agents (csDMARDS) have a significant role in the management of multiple rheumatological disorders. Several clinical practice guidelines (CPG) exist to guide practitioners in the appropriate frequency and type of laboratory monitoring during csDMARD use, however few appraisals of the quality of these guidelines have been performed.
Objectives: The purpose of this study was to summarise the content and appraise the quality of CPGs for laboratory monitoring during csDMARD use.
Methods: A systematic search of electronic databases, online guideline repositories and the websites of professional societies was conducted to identify CPGs for the frequency and type of laboratory monitoring in csDMARD use. A pair of reviewers screened CPGs using predetermined selection criteria and reported according to the PRISMA-P statement. Recommendations from included CPGs were extracted and compared across guidelines. The list of csDMARDS this study reviewed includes methotrexate, leflunomide, hydroxychloroquine, mycophenolate, sulfasalazine and azathioprine.

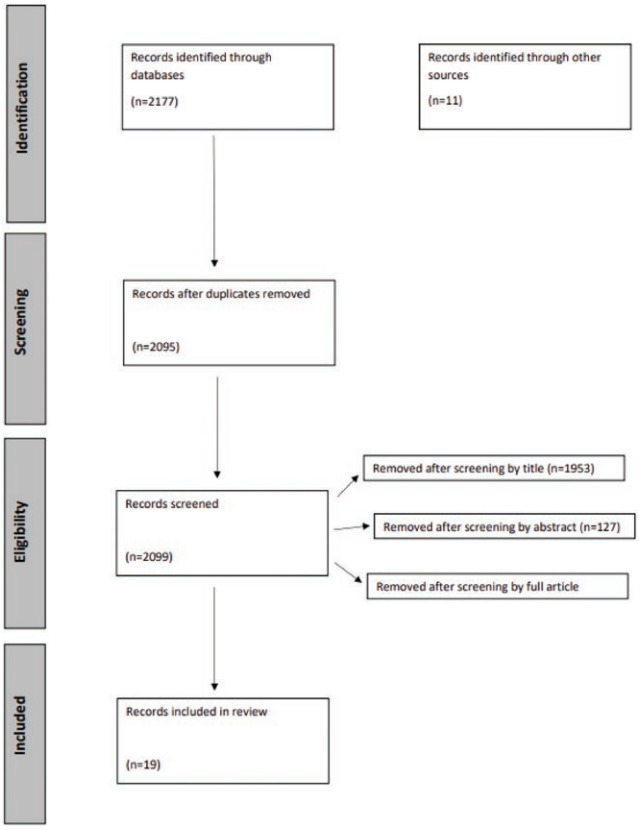


Figure 1.

Results: The review identified 19 sources, resulting in 33 guidelines for laboratory monitoring of conventional synthetic DMARDS (see table 1) Within the 33 guidelines seen there were 10 for methotrexate, 7 for sulfasalazine, 6 for leflunomide, 5 for hydroxychloroquine, 3 for azathioprine and 2 for mycophenolate. There was a notable variation in terms of detail, specifics and monitoring intervals.
Conclusion: In summary, this review identified several possible recommendations going forward. There is an argument to be made for a more uniform international guideline of laboratory monitoring to be synthesised, as there could be an element of uncertainty for those noting and comparing the variation between recommendations. A role for a more extensive review of the incidence of treatment complications and implications as a result of the laboratory monitoring would be of benefit. This poses an additional role for a cost-effective analysis, as was commented on within the discussion and literature reviews.

REFERENCE:
[1] Abstract not cited or published to date.

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Disclosure of Interests: None Declared.
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Table 1. Example of extracted laboratory monitoring guidelines for methotrexate (other csDMARDS not included for purposes of word count)

DMARD	Liver enzymes	Full blood count	Renal function	Additional recommendation	Source
Methotrexate	Baseline, every 2-4 weeks for first 3 months, then every 8-12 weeks for following 3-6 months, every 12 weeks thereafter. More frequent monitoring in those at risk for complications.	Baseline, every 2-4 weeks for first 3 months, every 8-12 weeks for 3-6 months after initiation, every 12 weeks thereafter.	Baseline, every 2-4 weeks for first 3 months, every 8-12 weeks for following 3-6 months, every 12 weeks thereafter.		*American College Rheumatology (ACR) America 2008*
Methotrexate	Every 2 weeks until stable dose for 6 weeks, then monthly for 3 months, every 12 weeks thereafter	Every 2 weeks until stable dose for 6 weeks, then monthly for 3 months, at least every 12 weeks thereafter	Every 2 weeks until stable dose for 6 weeks, then monthly for 3 months, at least every 12 weeks thereafter		*British Society Rheumatology (BSR) 2017 England*

AB1832-HPR

REMOTE SCREENING OF SELF-REFERRALS FOR JOINT INJECTION CLINIC

Keywords: Telemedicine

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Background: Intra-articular steroid injections are a valuable option in the management of inflammatory joint flare-ups.[1] The Gartnavel General Hospital (GGH), Glasgow operates a joint injection clinic for rheumatological patients via a self-referral system. This allows patients to book clinics directly and enables prompt access to an appointment. This system was modified in July 2022 to include remote screening, allowing for the evaluation of self-referrals prior to booking appointments. Waiting times have decreased significantly from 3 months to 1 week since the use of remote screening.
Objectives: To determine the efficacy of remote screening on self-referrals and identify self-referring patient groups where joint injections are not indicated.
Methods: Retrospective analysis was conducted on patient self-referrals to the joint injection clinic from 07/07/2022 to 07/12/2022. Patient demographics, diagnoses, reasons for rejection and outcomes were analysed.
Results: 108 patients self-referred for a joint injection during this period. There was a 41.7% (n=45) decrease in clinic bookings with remote screening. 50.9% (n=55) were refused on screening; 81.8% (n=45) of these patients were not indicated for a joint injection. 35.2% (n=38) of patients were not under rheumatology review. 25.9% (n= 28) of patients had solely osteoarthritis; 71.4% (n=20) of these patients were rejected and directed to outpatient physiotherapy services.
Conclusion: Remote screening was effective in reducing the patient waiting list for joint injections. The self-referral system used in isolation has significant limitations and has led to clinic booking beyond its capacity. This issue is also exacerbated by self-referrals from non-rheumatological patients.
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Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6196

HPR Professional education, training and competencies

AB1833-HPR

STUDY OF THE DEMAND FOR REFERRALS FROM PRIMARY CARE TO THE RHEUMATOLOGY DEPARTMENT OF A TERTIARY HOSPITAL

Keywords: Descriptive Studies

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Background: EPISER study has confirmed the great burden of rheumatic diseases, which represent almost 30% of primary care medical consultations in Spain[1,2]. Electronic consultation could be an alternative response[3] as well as rheumatologist-led update programmes and joint case discussion with primary care physicians have shown to reduce the burden of care and waiting times in rheumatology units[4].
Objectives: To analyze the demand from primary care to the rheumatology service of a tertiary hospital.
Methods: Retrospective descriptive study of the data consecutively collected from 15 to 30 May 2022 from new rheumatology consultations at the reference hospital requested from primary care (PC) health centers in the area. The following variables were collected: waiting time (median and range in days), referral route (ordinary, preferential or e-consultation), reason for derivation, type of visit (discharge or follow-up), suspicion of inflammatory disease by the specialist in Family and Community Medicine (Yes/No), confirmation diagnosis of inflammatory disease by the specialist in Rheumatology (Yes/No), time from onset of inflammatory symptoms to rheumatology consultation (median and range in months), referral with analytical tests (Yes/No/With acute phase reactants) and with musculoskeletal image requested by the PC physician (Yes/No); those provided by patients in private centers were excluded. Descriptive statistics were used for the presentation of results and Cohen's Kappa coefficient was calculated to quantify the degree of agreement in the diagnosis of inflammatory disease between primary care physicians and rheumatologists.
Results: A total of 116 new consultations were registered in the system referring to 100 patients, 16 did not attend their appointment. Results are shown in *Table 1*. The degree of agreement according to Cohen's Kappa index was 0.53, representing 80% of agreement (moderate degree). No differences were found between health care centers in the referral rate according to the population assisted by each health care center.
Conclusion: Main reasons for consultation were 'osteoporosis assessment' and 'polyarthralgias'. Ordinary route was the most frequently used with a median waiting time of 80 days and 50 days for preferential route. Thirty percent of patients were referred with analysis and 75% with some musculoskeletal image. The degree of agreement was moderate in the diagnosis of inflammatory disease between primary care physicians and rheumatologists.
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Table 1. Description of variables

Waiting time in days (median (range))	79 (159)
Ordinary	50 (150)
Preferential	35 (58)
e-consultation	
Referral route (%)	73
Ordinary	23
Preferential	4
e-consultation	
Reason for derivation (%)	22
Osteoporosis	17
Polyarthralgia	9
Arthrosis	8
Rheumatoid arthritis	8
Spondyloarthritis	5
Fibromyalgia	4
Gout	4
Low back pain	3
Polymyalgia rheumatica	2
Psoriatic arthritis	1
Raynaud's phenomenon	19
Other	
Type of visit (%)	18
Dsicharge	82
Follow-up	
Suspicion of inflammatory disease by the specialist in Family and Community Medicine (%)	38
Confirmation diagnosis of inflammatory disease by the specialist in Rheumatology (%)	20
Time from onset of inflammatory symptoms to Rheumatology consultation in months (median (range))	13 (44)
Additional tests (%)	31
Analysis (with PCR and VSG)	75
Musculoskeletal image	

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Disclosure of Interests: None Declared.
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AB1834-HPR A SURVEY OF OPHTHALMOLOGISTS REGARDING CLINICAL PRACTICE FOR DRY EYE AND RHEUMATIC DISEASES

Keywords: Education

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Background: Diagnostic delay is a major problem in rheumatic diseases that can present with symptoms often underestimated by patients. Often, the rheumatologist is not the first specialist to encounter these patients, and the lack of referral can lead to a significant delay in diagnosis.[1] Dry eye disease is a condition seen frequently by ophthalmologists that can be one of the first signs of a serious rheumatic condition such as Sjögren's Syndrome.[2] Thus, collaboration is needed between specialists for the diagnosis and treatment of these diseases. One study addressed this issue in the United States, showing a significant under-referral to rheumatologists.[2] To date, no such investigations have been done in Italy.
Objectives: The aim of our study was to evaluate the use of functional tests and validated scores among ophthalmologists in the work-up of patients with dry eye to investigate the possible presence of a rheumatic condition.
Methods: A multiple-choice questionnaire was submitted to participants of the Ocular Surface Inflammation course held in Bologna in September-October 2022. The questionnaire was administered to all the participants before the start of the course. The questions were designed to assess the knowledge of specialists in ophthalmology regarding signs and symptoms of rheumatic diseases associated with dry eye, their preferences regarding the use of functional tests to investigate dry eye in their clinical practice, and whether or not they used validated ocular scores. Functional tests investigated included were fluorescein staining of the cornea, tear break-up time, lissamine green staining of the conjunctiva, rose bengal staining of the conjunctiva, and Schirmer's test. Ocular scores considered were the National Eye Institute Visual Function Questionnaire (NEI-VFQ), Ocular Staining Score (OSS), and Dry Eye Disease (DED) severity grading scale.
Results: Twenty ophthalmologists participated in the survey. The estimated prevalence of dry eye among the participants' patients is summarized in Table 1. Ten ophthalmologists reported rheumatology referrals in <5% of cases, four in 5-20% of cases, three in 20-50% of cases, and three in >50% of cases. When presented with patients with dry eye, other signs and symptoms investigated by the ophthalmologists during the patient history and clinical examination were: arthritis or arthralgia (95%, n=19), xerostomia (85%, n=17), dry skin or cutaneous rash (65%, n=13), and periodontitis or cavities (30%, n=6). When asked to rank the most frequent functional tests performed in patients with dry eye, 55% (n=11) reported that the fluorescein test was their top choice, followed by Schirmer's test (35%, n=7) and tear break-up time (10%, n=2). More than half of the participants reported not using clinical scores in the management of patients with dry eye, while 15% (n=3) used the DED severity grading scale, 10% (n=2) used NEI-VFQ, and 10% (n=2) used both NEI-VFQ and OSS.
Conclusion: This preliminary data suggests that dry eye is a very frequent condition encountered by ophthalmologists that is often underestimated, and patients are not always properly screened for associated rheumatological conditions using validated scores and functional tests or referred to a rheumatologist. Large studies to further investigate awareness of potential rheumatological diseases in the field of ophthalmology are needed, and the creation of "dry-eye teams" comprised of ophthalmologists and rheumatologists may be useful to avoid diagnostic delay.
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Table 1. Estimated prevalence of dry eye according to ophthalmologists

Estimated prevalence of dry eye among patients in clinical practice	Ophthalmologists' response to the questionnaire
>80%	1 (5%)
60-80%	3 (15%)
40-60%	8 (40%)
20-40%	6 (30%)
<20%	2 (10%)

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.4666

AB1835-HPR WHAT IS THE ROLE OF RHEUMATOLOGY NURSES IN THE MANAGEMENT OF GOUT PATIENTS IN PRACTICE? A MULTICENTRIC MOROCCAN STUDY

Keywords: Nursing, Gout

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Background:
Objectives: The aim of this study was to assess nurses' skill level and educational needs on gout disease.
Methods: This is a multicenter cross-sectional study carried out in 10 rheumatology departments in different university hospitals in Morocco. We invited nurses working in those departments to participate in the study. Nurses answered to a questionnaire provided data on their professional activity and socio-demographic status. The questionnaire collected also nurses' management skills on gout disease including systematic measurement of the different clinical parameters of patients, visual pain analogic scale (VAS) pain, collecting comorbidities, identification and verification of adherence to the treatment, therapeutic education of patients and treatment side effects notification.
Results: Our study has included 45 nurses (mean age of 34.2 years, 77.8% females). The mean work duration at a rheumatology department was 7.2 ± 4.6. Table 1 summarized assessment results of the competencies which are required for the management of patients suffering from gout.

Table 1.

Acquired skills	(%)
Systematic measuring of clinical parameters:	**97.8**
Arterial tension	**97.8**
Waistline	**100**
Weight	**71.1**
BMI	
Systematic assessment of pain by VPAS: visual pain analogic scale	**62.2**
Collecting comorbidities	**42.2**
Identifying gout treatments	**71.1**
Differentiating symptomatic treatments from background Gout treatments	**42.2**

Conclusion: Gout is the prototype of chronic diseases where the nurse plays a central role in the multidisciplinary care of patients.
We realize through our study the urgent need to remedy to alarming shortcomings in nurses management of patients suffering from gout.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.5154

HPR Interdisciplinary research

AB1836-HPR SERUM LEVEL OF VITAMIN D IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CORRELATION WITH BONE MINERAL DENSITY AND THE DISEASE ACTIVITY

Keywords: Vitamin D, Systemic lupus erythematosus, Osteoporosis

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Pirogov Memorial Medical University, Vinnytsia, Internal Medicine #2, Vinnytsia, Ukraine

Background: Decrease in vitamin D levels in patients with systemic lupus erythematosus (SLE) arouses particular interest. Vitamin D levels and their correlation with bone mineral density (BMD) loss are still seen as contradictory.
Objectives: To study serum vitamin D levels in SLE women and to estimate their correlation with BMD and disease activity.
Methods: 101 SLE women and 30 individuals in a control group participated in the study. The activity of SLE was evaluated by SLEDAI. The average age of patients was 47.12 ± 0.14 years, in the control group it was 46.17 ± 0.12. Serum levels of C-reactive protein (CRP) and 25-hydroxyvitamin D (25(OH)D) were measured in all participants. Changes in BMD of the lumbar spine and hip were determined by dual-energy X-ray densitometry.
Results: In patients with SLE, the average level of 25(OH)D equalled 14.6 ± 1.19 ng/ml, and in the individuals from the control group, it was 1.9 times higher, constituting 24.7 ± 1.32 ng/ml. In SLE women with normal BMD (T score > -1.0 SD) vitamin D deficiency (< 20 ng/ml) was detected in 18.3%. In the group with osteopenia (T-score from -1.0 to -2.5 SD), the proportion of individuals with vitamin D deficiency has increased to 26.7%. In women with osteoporosis (T-score ≤ -2.5 SD), vitamin D deficiency was found in 63.9%. In the group of patients with the maximum CRP level there were only 10% of persons with the optimal (> 30 ng/ml) 25(OH)D level, 40% had insufficiency (20-30 ng/ml), while deficiency (< 20 ng/ml) was detected in every second patient. Among patients with optimal CRP levels, only every fourth person was diagnosed with vitamin D deficiency, 10% of the individuals had vitamin D insufficiency, while 65% had optimal vitamin D levels. Decrease in vitamin D level was closely associated with SLE activity revealed by SLEDAI ($r = -0.44$; $p < 0.05$).
Conclusion: The average vitamin D level in SLE women is likely to be lower than that in the control group. Decrease in vitamin D levels was associated with BMD loss and high inflammatory process as well as the disease activity according to CRP and SLEDAI.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1272

AB1837-HPR THE NON-INFLAMMATORY RHEUMATIC DISEASES AND CARDIOVASCULAR RISK: THE UNKNOWN COMORBIDITY

Keywords: Cardiovascular disease, Osteoarthritis, Ultrasound

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Background: Several factors were associated with non-inflammatory rheumatic diseases such as diabetes and overweight. As far as we know, no previous research has studied cardiovascular risk in this population. For this goal, we used the carotid intima-media thickness (cIMT) screening as a relevant tool for CV risk assessment.
Objectives: This study mainly aimed to determine the importance of CV risk in non-inflammatory rheumatic diseases.
Methods: The present study is a study conducted on Tunisian non-inflammatory rheumatism patients in the rheumatology department. We collected the characteristics of the patients and those of the disease. The CV risk was assessed using the measurement of cIMT. According to the American Society of Echocardiography guidelines, the cIMT thickness was measured using high-resolution B-mode carotid US with a Philips machine with the patient in the supine position. The cIMT was measured using the two inner layers of the common carotid artery and an increased IMT was defined as ≥0.09 cm.
Results: Fifty patients were collected, of which 82% were women. 64% of them were followed for knee osteoarthritis, the rest were chronic low back pain patients. The mean age was 53 ± 11.08 years. 10% of patients were active smokers. Two percent were hypertensive and 4% were diabetics. The average BMI was 28,1±4,5 kg/m2. It was greater than 25 kg/m2 in 76% of them. [cholesterol] was 4,9±0,9 mmol/l. 48,9% had a high rate. [Cholesterol HDL] was1,1±0,2 mmol/l. The mean [cholesterol LDL] was 3,3 ±0,8 mmol/l. [triglyceride] was 1,3±0,6 mmol/l. The mean IMT in the left common carotid (LCC) was 0,06±0,02, in the left internal carotid (LIC) was 0,06±0,01, in the left external carotid (LEC) was 0,05±0,01. The mean IMT was 0,05±0,018 in the right common carotid (RCC), 0,06±0,01 in the right internal carotid (RIC), and 0,05±0,01 in the right external carotid (REC). Thirty six percent had an atheroma plaque. Twenty six percent had a high CV risk according to the IMT. There was no correlation in our series between diabetes, high blood pressure, smoking, BMI, and high CV risk p=1; p=1; p=1, and p=0.5, respectively.
Conclusion: While the absence of systemic inflammation in non-inflammatory osteoarticular diseases, the cardiovascular risk is higher in our study. Therefore, cardiovascular risk screening should not be limited to chronic inflammatory rheumatism.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.6076

HPR Epidemiology and public health (including prevention)

AB1838-HPR THE TYPE AND THE EFFECT OF PHYSICAL ACTIVITY ON QUALITY OF LIFE AND FATIQUE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN GREECE: A CROSS-SECTIONAL STUDY

Keywords: Systemic lupus erythematosus, Quality of life, Epidemiology

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease with sever symptoms, such as fatigue and has a high impact on patient's quality of life.
Objectives: The aim of this study was to determine the rate, the type, and the effect of physical activity (P.A.), and exercise in patients with SLE on quality of life and fatigue in Greece.
Methods: Three questionnaires were used to measure quality of life (SF-36), fatigue (FSS), and P.A. (mIPAQ). 101 patients with SLE from Greece answered about their personal choices. For statistics the IBM SPSS 25 was used for the statistical analysis. Descriptive analysis conducted to describe quantitative variables of interests. Data normality was verified from Kolmogorov-Smirnov test, and Pearson Correlation test was performed to determine the relationship between P.A. and QoL and Fatigue.
Results: The results showed that the sample average for QoL was 48.3(±19,3), for Fatigue 41,73(±7,2). The total score of P.A. was 1603,79(±1695.8) METs. Furthermore, for vigorous P.A. was 557,79(±987,6) METs, for moderate P.A. 824,65(±811,6) METs, and for low P.A. 239,87(±405) METs. The most common type of P.A. was housekeeping and cleaning for 74% of the sample, and even thought it is not considered as P.A. activity there was an option. A high average (50,5%) of the sample was presented by patients who chose to remain seated during the day. Positive correlation between P.A. and QoL was found (R=,385, P<,01). Negative correlation between P.A. and Fatigue was also found (R=-,384, P<,01).
Conclusion: The conclusions were that the patients with SLE in Greece do not perform high level of P.A. and exercise. The moderate level of P.A. was more likely activities of day living, that are classed as P.A., than exercise. Furthermore, the sample choose a sedentary lifestyle, although correlation between P.A. and QoL and Fatigue in patients with S.L.E. was found.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1839-HPR PERINATAL GRIEF IN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES

Keywords: Mental health, Quality of life, Pregnancy and reproduction

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Background: Perinatal loss (PL), defined as a loss from any gestational age or in the neonatal period [1] lead women to the process of grieving. Perinatal Grief (PG) involves suffering and reaction such as sadness, disbelief and anger [2]. PL and PG symptoms affect many women around the world; women with autoimmune rheumatic diseases (ARDs) have greater risk of PL. The Perinatal Grief Scale (PGS) can help health providers prevent complicated grief in their patients [3].
Objectives: Determine which PL and sociodemographic variables are associated factors to a complicated grief in women with ARDs.
Methods: Descriptive, cross-sectional, comparative study at the Hospital Universitario "Dr. José Eleuterio González" in México. We included women from the Pregnancy and Rheumatic Diseases Clinic (CEER) that answer a virtual survey with the PGS. The demographic, ARD and PL data were obtained from the clinical records. For the control group, women without ARD were invited to fill a virtual survey with the PGS, sociodemographic and PL data. The PGS is a Likert-type scale that consists of 27 items with four response options. The questions are distributed in four subscales: active grief (10 items), guilt (8 items), depression (6 items), acceptance (3 items). Scores greater than 50 points suggests a complicated grief comorbidity.

The Kolmogorov-Smirnov test was used to determine normality; to analyze the differences between groups, Mann–Whitney U, Chi-square tests and T-test were employed. A $p < 0.05$ was considered statistically significant. The statistical analysis was performed with the statistical program SPSS version 25.

Results: A total of 50 women were included: 25 with ARD and 25 without ARD. The median age for the group with ARD was 42 (38.5-51) and 34 (26-42.5) for the without ARD group. In the ARD group the most frequent diagnosis were systemic lupus erythematosus (7/14%), rheumatoid arthritis (6/12%) and Antiphospholipid Syndrome (4/8%). For the PGS, twenty (40%) of the 50 women got a score >50; 11 (55%) were women without ARD and 9(45%) have ARD. The PL, suffered by these 20 women were 18 during the pregnancy (17/85% on the first trimester and 1/5% on the second trimester) and 2 (10%) after birth. No statistically differences were found in the total score and subscales of the PGS between groups. The sociodemographic and PL data and the PGS score for both groups are included in **table 1.**

Conclusion: Even though there were no significant differences between groups; we hypothesize that the greater number of PL in women with ARD serves as a protective factor and prevents that the PG evolve to a complicated grief. On the other hand, having the PL during the first trimester of the pregnancy can be a risk factor for complicated grief. Our limitation was the sample size for both groups.

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Table 1. Clinical characterization

	Patients with ARD N=25	Patients without ARD N=25	P=0.05
Years of education			0.114
>9 years	21 (84%)	15 (60%)	
<9 years	4 (16%)	10 (40%)	
Marital Status			0.225
Single	2 (8%)	2 (8%)	
Married/Common law	20 (80%)	15 (60%)	
Divorced	3 (12%)	8 (32%)	
Perinatal Losses			0.387
1	13 (52%)	17 (68%)	
>1	12 (48%)	3 (32%)	
Number of pregnancies, median (IQR)	4 (2.5-5)	3 (2-3.5)	0.38
Number of living children, median (IQR)	2 (1-3)	1 (0.5-2)	0.123
PGS score, median (IQR)	43(37.5-60.0)	46 (39.5-62.5)	0.587
PGS active grief subscale	13 (10-18)	14 (12-18.5)	0.355
PGS depression subscale	12 (10-19)	12 (10-22)	0.782
PGS guilt subscale	12 (9-18.5)	12 (8-17)	0.815
PGS acceptance subscale	6 (6-8)	7 (6-8)	0.347

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Clinical cases

AB1847

ANTI-MYELOPEROXIDASE ANTIBODY-POSITIVE GRANULOMATOSIS WITH POLYANGIITIS MIMICKING MUCOSAL LEISHMANIASIS: A RARE CASE REPORT

Keywords: Autoantibodies, Descriptive Studies, Vasculitis

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Background: Granulomatosis with polyangiitis (GPA) features necrotizing granulomatous inflammation of the upper and lower respiratory tracts, with vasculitis of small- and medium-sized vessels [1]. Anti-proteinase 3 antibodies (PR3-ANCA) are found in the majority of cases, yet anti-myeloperoxidase (MPO-ANCA) may be identified in approximately 10% of patients with GPA [2, 3]. One of the differential diagnoses is mucosal leishmaniasis, especially in patients from endemic regions. Atypical presentations of GPA may delay diagnosis.

Objectives: To report a case of a female patient previously diagnosed with and treated for mucosal leishmaniasis due to upper respiratory tract lesions. As the symptoms returned alongside arthritis, further investigation concluded to a diagnosis of anti-myeloperoxidase-positive GPA.

Methods: Case report and discussion.

Results: A 51-year-old woman from Brazil presented in 2021 with epistaxis and joint pain. The patient reported a prior history of recurring bilateral epistaxis and maxillary pain since 2008. At that time, she had a wide nasal septal perforation. CT scan of the sinuses showed maxillary and ethmoidal sinusopathy. A nasal biopsy showed epithelioid granulomas without amastigotes, but the patient had a 25mm Montenegro skin test (strongly positive). Syphilis, hepatitis B, hepatitis C and HIV screenings and acid-fast bacilli smear were negatives. As Brazil is an endemic region for leishmaniasis, a presumptive diagnosis of mucosal leishmaniasis was made and the patient was appropriately treated. In 2016, she was lost to follow-up. In 2021, she returned with fever, epistaxis, important unspecified weight loss and arthralgia with edema in ankles, distal interphalangeal joints, metacarpophalangeal joints and wrists. Blood screening revealed an RCP of 9.5 and an ESR of 28. Urine tests were normal. A thoracic CT scan showed multiple lung nodular formations, including a subpleural nodule in the anterior lower right lobe, with a size of 3.8 x 3.1 x 2.9 cm. Lung histopathology revealed foci of poorly formed, non-necrotic granulomas in centrilobular parenchyma and angiitis in small-caliber arteries (image 1). Autoimmune screening revealed positive MPO-ANCA superior to 1/80 and negative c-ANCA, rheumatoid factor and anti-CCP. Thus, a diagnosis of GPA was made, and oral methotrexate 20mg weekly was started. Improvement of arthritis could be observed in four weeks.

Conclusion: GPA may present upper respiratory tract symptoms, and is considered a differential diagnosis for mucosal leishmaniasis [4]. Recurrence of the symptoms in a patient treated for mucosal leishmaniasis should prone further investigation for other conditions. The renal system was spared in our patient, however nasal septal involvement, prominent sinusopathy, joint symptoms and pulmonary typical findings strongly favored the hypothesis of GPA. A positive MPO-ANCA and good therapeutic response following methotrexate strengthened the certainty of the diagnosis. Physicians should be aware of GPA as a differential diagnosis for mucosal leishmaniasis and recognize its MPO-ANCA-positive presentation.

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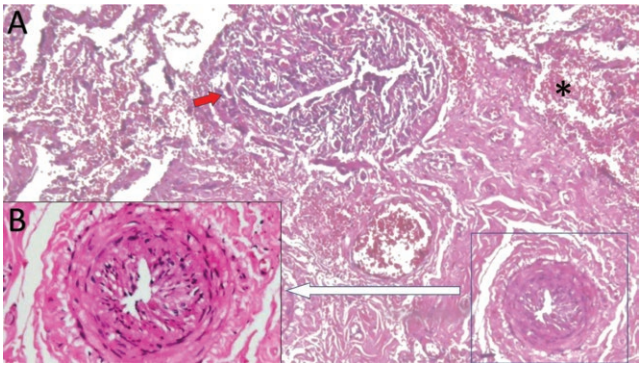


Image 1: H&E 100x (A) and 200x (B) section of pulmonary nodule showing lymphocytic bronchiolitis (A, red arrow) and angiitis, featuring sub-intimal thickening with neutrophilic exudate, edema and segmental destruction of internal elastic lamina (B – 200x, white arrow). Alveolar hemorrhage is seen in (*).

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AB1848

ARTIFICIAL INTELLIGENCE IN THE CLINICAL SETTING OF THE RHEUMATIC DISEASES; A SYSTEMATIC REVIEW OF THE LITERATURE

Keywords: Systematic review, Artificial Intelligence

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Background: Autoimmune Rheumatic Diseases (AIRD) are chronic multifactorial diseases that present with a variety of pathologic findings due to immune abnormalities. The pathogenesis is a complex interplay of genetic and environmental factors, and there are usually large individual differences in phenotype, imaging and blood findings, treatment response, and prognosis. As a result, clear algorithms for diagnosis and treatment are scarce, and clinicians must interpret complex disease images from a variety of data to make analogies between diagnosis, prognosis prediction, and treatment effects. Artificial intelligence, encompasses concepts such as machine learning and deep learning neural networks, is a substitute for these complex tasks, and attempts are gradually beginning to replace it in the clinical practice of AIRD. Accountability is often required for decisions in medicine that directly affect human lives, and the same is true for the black box of models used by AI. Therefore, in recent years, emphasis has been placed on the explainability of AI, and a method called explainable AI (XAI) has emerged to explain decisions made by AI models. Research in this area is still in its infancy, and it would be of significance to present an overall picture.
Objectives: To clarify the overall picture of AI/machine learning in the clinical application or research in AIRD by the systematic review of the literature.
Methods: A systematic literature review was conducted using the Pubmed and Web of Science according to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses"(PRISMA) guidelines. The search formula used Artificial Intelligence, Machine learning, Deep learning, Neural Network, AIRD and connective tissue diseases as main keywords, and selected references went through a primary/secondary screening. After screening, the literature was reviewed to validate the diseases studied, published years, the object of the study, type of training data, the algorithms, and, for XAI, the methods for algorithms explanation.
Results: The literature search yielded 1483 articles, that were published before June, 2022 and resulted in 164 articles after primary and secondary screenings. Among them, 153/163(93.9%) were published in or after 2017. The main target diseases of the articles were rheumatoid arthritis(RA) 72, systemic lupus erythematosus(SLE) 42, spondyloarthritis 11, inflammatory myositis 7, systemic vasculitis syndrome 5, systemic sclerosis 5 and others 21. The main objects of the studies were diagnosis or classification of the disease in 98, followed by the prognosis prediction in 49 and analysis of the therapeutic reagent in 19. The most common types of data used as training were demographic data in 114 articles followed by physical data 101, clinical test data 92, genomics data 40, image data 30 and pathological data 28. The most commonly used algorithms were tree-based algorithm(random forest etc.) followed by support vector machine and neural network. XAI were performed in 8 studies (3 studies with RA, 3 with SLE one with SLE/RA and 1 with AIRD in general) in which Shapley Additive exPlanations (SHAP) was the most frequently used tool (5/8; 62.5%).
Conclusion: The clinical application of AI in AIRD is mainly used as a tool for diagnosis or the prognostic prediction in RA and SLE. On the other hand, only a very small number of the study have examined the explainability of AI. The review indicates that research on the clinical implementation of AI applications is still at an early stage despite the great potential.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1849 AUTOIMMUNE MANIFESTATIONS OF CTLA-4 HAPLOINSUFFICIENCY IN TWO PATIENTS OF SOUTHEAST ASIAN ETHNICITY

Keywords: Rare/orphan diseases, Skin, Adaptive immunity

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Background: Cytotoxic T- lymphocyte antigen 4 haploinsufficiency (CTLA4-H) is an autosomal dominant monogenetic disorder caused by heterozygous CTLA4 germline mutation.[1] Its diagnosis is complicated by a highly variable clinical phenotype including an immune dysregulation syndrome with autoimmunity, lymphoproliferation, atopy and malignancy; as well as immunodeficiency with hypogammaglobulinemia and recurrent infections.[2] CTLA4-H has been reported mainly in North America and Western Europe, whilst lipopolysaccharide-responsive beige-like anchor (LRBA) deficiency (LATAIE) mainly in East Asia.[3]
Objectives: To raise awareness of adults with CTLA4-H presenting with varied autoimmune end-organ manifestations to rheumatologists.
Methods: Case reports.
Results: A 53-year-old Malay male first developed violaceous papules and nodules on both legs and arms at the age of 44 years old. He later developed widespread lymphadenopathy, maxillary sinusitis, lung nodules, cholestatic hepatitis, splenomegaly and thrombocytopenia over the course of the next 6 years. Biopsy of the skin, lymph nodes and liver all demonstrated non necrotizing granulomas and returned negative for mycobacterial studies and malignancy. He was diagnosed with sarcoidosis and started on moderate dose corticosteroids and azathioprine. He later developed hypogammaglobulinemia, listeria meningoencephalitis and two episodes of disseminated zoster, prompting further evaluation. Genetic analysis identified a missense variant of uncertain significance (VUS) c.506C>A (p.Ala169Glu) in the CTLA-4 gene. Functional testing showed reduced expression of CTLA-4 on both unstimulated and stimulated Foxp3+T cells by flowcytometry. He is treated with regular replacement intravenous immunoglobulin (IVIg), prednisolone and ciclosporin. The second patient is a 28-year-old Chinese male with a prior history of endogenous eczema diagnosed at 13 years old. He developed recurrent sinusitis at 18 years old, followed by 3 episodes of pneumonia over a course of 2 years. He was found to have chronic rhinosinusitis, bronchiectasis, hypogammaglobulinemia, blunted post-vaccination responses to pneumococcus and tetanus. He was initially treated for Common Variable Immunodeficiency with regular IVIg while continuing to require regular prednisolone for control of eczema. 2 years later, he developed immune-mediated thrombocytopenia. He later developed photosensitive eczematous patches over his face, chest, legs and the diagnosis was revised to chronic actinic dermatitis. He was eventually found to have a novel deletion on his CTLA4 gene c.522del (p.Leu174Phefs*13) on genetic analysis, reduced CTLA4 expression on resting Treg cells by flowcytometry, with levels returning to normal with stimulation. He is treated with regular IVIg, prednisolone and methotrexate.
Conclusion: Diagnosis of adult-onset primary immunodeficiency syndromes can be a challenge when these present with autoimmune phenomena rather than recurrent infections. Genetic testing in this era of rapidly expanding knowledge of inborn errors of immunity and detection of VUS may have potential clinical and therapeutic implications.
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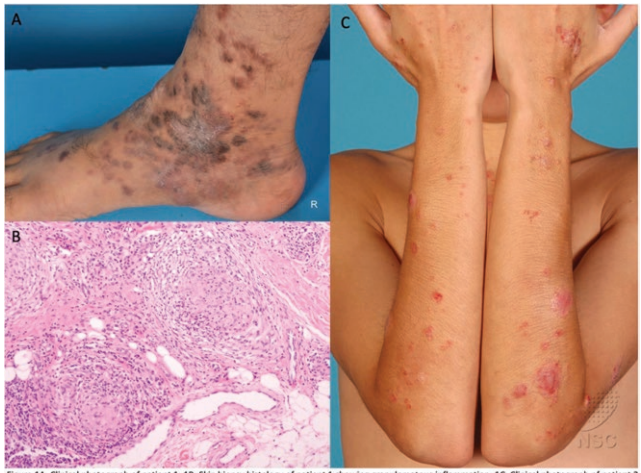


Figure 1A: Clinical photograph of patient 1; 1B: Skin biopsy histology of patient 1 showing granulomatous inflammation; 1C: Clinical photograph of patient 2

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Disclosure of Interests: None Declared.
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AB1850 MICROSCOPIC POLYANGIITIS WITH CONCURRENT THROMBOTIC THROMBOCYTOPENIC PURPURA: A CASE REPORT

Keywords: Vasculitis

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Background: Thrombotic thrombocytopenic purpura (TTP) and Microscopic polyangiitis (MPA) rarely occur in conjunction. Autoimmune TTP is caused by autoantibodies to the ADAMTS13 protein that cleaves von Willebrand factor. MPA is a small-vessel vasculitis that typically affects the small blood vessels of the lung and kidney [1]. We present a case of concurrent TTP and MPA which we believe could highlight a pathogenetic correlation and treatment overlap between the two diseases.
Objectives: To report a rare case of concurrent TTP and MPA and to educate physicians on optimal treatment strategies.
Methods: Case report and literature review.
Results: A 67-year-old patient with history of stroke and sickle cell trait presented to the emergency department due to altered mental status and fever. Serology on admission was notable for marked acute kidney injury and anemia requiring transfusions. Urinalysis showed hematuria and proteinuria. Autoimmune serology was remarkable for p-ANCA positivity at 1:80 with myeloperoxidase antibody > 30 pmol/L; a diagnosis of MPA was made. Patient's serology was also remarkable for thrombocytopenia with a nadir under 60 and evidence of thrombotic microangiopathy on peripheral blood smear and hemolysis labs. ADAMTS13 autoantibodies were reduced with less than 3% functionality and an inhibitor of 1/0 BU, confirming a concurrent diagnosis of TTP. Patient was initiated on high-dose steroids and therapeutic plasma exchange (TPE) with resultant normalization of platelets and improvement in renal function. TPE was discontinued, and the patient was transitioned to rituximab with continuation of high-dose steroids. The patient was ultimately discharged home with a steroid taper and maintenance rituximab dosing.
Conclusion: Per literature review, three other cases of concurrent TTP and MPA have been reported [2-4]. Further investigation into pathogenetic and treatment overlap of MPA and TTP may be warranted. Although rare, when occurring together the presentation is often severe, and urgent initiation of treatment is critical. TPE is the mainstay of treatment in TTP but is usually only recommended in MPA patients with anti-GBM antibodies, those at high risk of progression to end stage renal disease, or those unresponsive to first-line therapies [1,5,6]. Rituximab, which acts to decrease B cell activity and overall antibody production, has been shown to reduce disease activity in both conditions [1,5]. This case report suggests that, in the rare event that TTP and MPA are concurrently diagnosed, the combined use of rituximab and TPE in conjunction with steroids may induce remission more efficiently than either treatment alone.
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Disclosure of Interests: None Declared.
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AB1851 TERMINATION OF PREGNANCY IN LUPUS NEPHRITIS: A BIOETHICAL ANALYSIS WITH THE INTEGRATIVE METHOD

Keywords: Best practices, Pregnancy and reproduction, Systemic lupus erythematosus

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Background: Termination of pregnancy in patients with rheumatic diseases is controversial due to current lack of evidence. Around one fourth of pregnancies in patients with rheumatic diseases are terminated due to medical reasons. Only 0.026% of articles in Rheumatology relate to bioethics despite the high frequency of ethical dilemmas in the treatment of pregnant patients with autoimmune diseases. [1]
Objectives: To analyze from a bioethical perspective the case of a pregnant patient with lupus nephritis unresponsive to treatment, for whom termination of pregnancy is considered as a therapeutic measure.
Methods: The integrative model was applied combining different normative ethical theories. The central moral dilemma and main stakeholders were identified. The case was analyzed from utilitarian, deontological and virtue ethics perspectives, followed by integration to establish a global conclusion.
Results: *Case presentation.* A 30-year-old woman was diagnosed with systemic lupus erythematosus in 2019 in Mexico. Induction therapy for lupus nephritis was started; however, it was interrupted due to COVID-19 pandemic. When she returned for follow-up, despite treatment was reinstated, she persisted with proteinuria without achieving complete remission criteria. Multi-target therapy was started; however, patient stopped treatment for economic reasons and became pregnant shortly after. She presented for prenatal control follow-up at 20 gestational weeks with edema in the lower extremities and hypertension, for which she was hospitalized in intensive care. Renal replacement therapy was initiated without further response to treatment. A multidisciplinary team suggested pregnancy termination as a therapeutic option, which the patient refused. *Bioethics analysis.* Figure 1 shows the background factors and initial steps for defining and analyzing the bioethical dilemma. Three different normative ethical theories were used. *Utilitarianism*. The consequences of the action are the central component, and the decisions made must be profitable and effective for the majority. Terminating the pregnancy would seek to protect the mother's life, since saving one life represents a greater benefit than losing two. For the patient's family, the costs of continuing with the pregnancy would be unsustainable. For the institution, the termination of the pregnancy would lead to a more efficient use of human and material resources. Therefore, interrupting the pregnancy is justifiable. *Deontology*. Duty-based ethics center the action itself regardless of consequences, as well as valuing autonomy. Seeking all therapeutic alternatives, including termination of pregnancy, is a good action itself. However, considering the patient's autonomy, her desire to continue pregnancy must be taken into account. Therefore, both terminating and continuing the pregnancy are justifiable. *Virtue ethics.* Aretology centers the importance of decisions in the person who performs the action. Core values involve enabling flourishing and personal growth. For both the family and the institution, flourishing would imply preserving the life of the patient. Therefore, the termination of pregnancy is justifiable.
Conclusion: Using the integrative method, we conclude that termination of the pregnancy is justifiable from the three ethical theories and is an appropriate resolution to the ethical dilemma. However, considering the patient's desire to continue pregnancy, health professionals should offer psycho-emotional support. The lack of recommendations about medically indicated termination of pregnancy in rheumatology leads to complex moral decisions, making the bioethical analysis of paradigmatic cases essential to ensure the best possible action and as a precedent for future similar situations.
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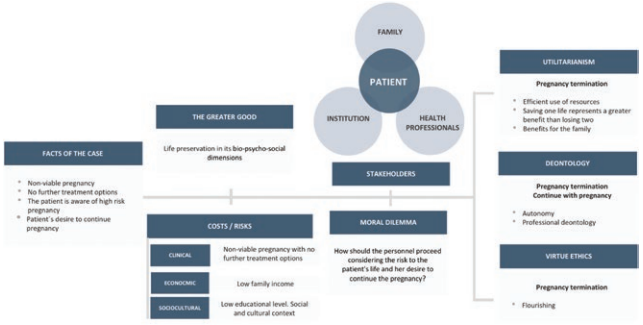


Figure 1. Integrative method and analysis based on normative ethical theories

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Disclosure of Interests: None Declared.
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AB1852 DERMATO-NEURO SYNDROME PRECIPITATED BY COVID-19 INFECTION IN THE SETTING OF SCLEROMYXEDEMA

Keywords: Skin, COVID

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Background: A black female in her 40s presented with a nonpruritic rash for 10 months consisting of bumps on the face, hands, forearms, and thighs. She had no prior treatment. Past medical history was significant for pulmonary embolism (PE) 6 years prior. She had no personal or family history of autoimmune disease. Physical exam revealed numerous smooth 2-3 mm skin-colored papules over the bilateral forearm dorsa, hands, anterior thighs, and face. Serum protein electrophoresis revealed monoclonal IgG lambda gammopathy. Skin biopsy of her left elbow showed dermal fibroplasia with mucin deposition. IgG was less than 1.5 grams/deciliter; bloodwork was otherwise stable. The diagnosis of scleromyxedema was rendered.
Objectives: The objective of this clinical case was to evaluate a neurologic sequela of COVID-19 infection in a patient with scleromyxedema.
Methods: One month following diagnosis of scleromyxedema, our patient was diagnosed with COVID-19 five days before admission to the emergency department with altered mental status and aphasia. Rheumatology was consulted due to malignant hypertension and acute kidney injury with question of scleroderma-like renal crisis in the setting of recently diagnosed COVID-19 infection, although she had no other features of systemic sclerosis. The infectious disease team was consulted due to COVID-19-induced inflammatory reaction.
Results: The patient's creatinine kinase and brain natriuretic peptide were elevated. Creatinine and potassium trended upwards. She developed seizures and became hemodynamically unstable with rapidly declining clinical status. She was transferred to the intensive care unit, where she developed respiratory arrest, shock, hyperkalemia, and acidemia. She received escalating doses of pressors but experienced frequent arrhythmic disturbances and developed asystole. Resuscitation efforts were unsuccessful; she expired within 24 hours of consultation.
Conclusion: Dermato-neuro syndrome (DNS) is a potential complication of scleromyxedema associated with confusion, dysarthria, seizures, and coma. The patient's clinical presentation is consistent with DNS in the setting of scleromyxedema likely precipitated by COVID-19. Intravenous immunoglobulins are first-line treatment for scleromyxedema; however, it is associated with risk of venous thromboembolism. The patient was considered for treatment as an outpatient but deferred due to history of PE. She was reevaluated for treatment upon presentation to the hospital, but given the severity and rapidity of her condition, it was already too late. This is the second reported case of COVID-19 induced DNS in a patient with scleromyxedema. Given the severity, we recommend early initiation of treatment in patients with scleromyxedema and aggressive treatment for those contracting COVID-19.

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Disclosure of Interests: None Declared.
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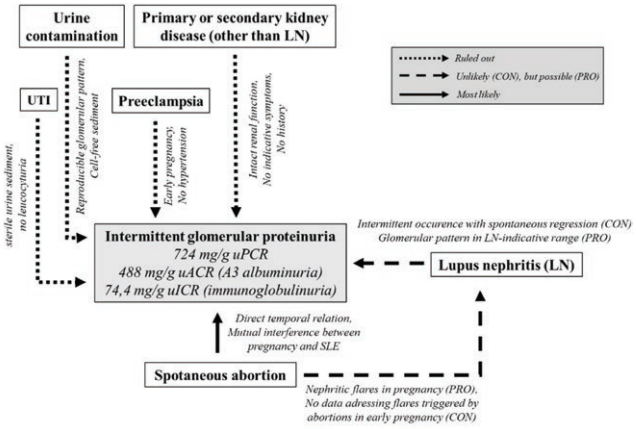
AB1853

SPONTANEOUS ABORTION AS DIFFERENTIAL DIAGNOSIS OF INTERMITTENT GLOMERULAR PROTEINURIA IN CLINICALLY AND SEROLOGICALLY INACTIVE SLE

Keywords: Systemic lupus erythematosus, Pregnancy and reproduction, Kidneys

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Background: In SLE, new-onset proteinuria and albuminuria raise concern for renal involvement, even when isolated and subnephrotic. In women of childbearing age, pregnancy-related complications are other causes of renal protein loss. Distinguishing renal disease from pregnancy-related complications of SLE is difficult because SLE is associated with adverse maternal and fetal events, while pregnancy is also a cause of disease relapses. Common to all causes of pathologic proteinuria in SLE is that they are related to disease activity and/or the need for intervention, as proteinuria does not normalize on its own.
Objectives: We report a case of a patient with inactive SLE who intermittently developed significant isolated proteinuria and albuminuria of glomerular origin that was directly related to spontaneous abortion in early (possibly twin-) pregnancy.
Methods: A 39-year-old female with SLE on hydroxychloroquine presented at our clinic for a routine check-up. Physical examination and laboratory tests were performed. To that date, SLEDAI-2K during most visits had a score of 0, indicating inactive disease.
Results: The patient reported feeling well, and the physical examination was unremarkable. Stable low-grade thrombocytopenia was the only relevant abnormality in recent years. On the current examination, the urine showed significant proteinuria and A3 albuminuria in the protein/albumin to creatinine ratio (uPCR 724 mg/g, uACR 488 mg/g). IgG/creatinine was markedly elevated (74.4 mg/g), and α1-microglobulin was normal, indicating nonselective glomerular proteinuria without tubular impairment. There were no other abnormalities suggestive of SLE activity. After she recalled having vaginal spotting a week earlier, a pregnancy test was performed and was positive. Subsequently, the βHCG level increased insufficiently, and ultrasound detection of a live embryo was not successful, but the presence of two amniotic cavities was suspected. An early incomplete miscarriage was diagnosed, and the gestational age was calculated to be 6+5 weeks. Shortly thereafter, a planned suckling curettage was performed. One week later, she had a final vaginal bleed. At this time, the urine showed a decrease in proteinuria of over 50% (uPCR 317 mg/g, uACR 210 mg/g, IgG 26.9 mg/g). Three weeks later, urine protein was completely normalized, which proved stable 12 weeks after initial diagnosis. Throughout the follow-up period, she did not show any SLE relapse.
Conclusion: After exclusion of differential diagnoses (chart), causality of the miscarriage with the urinary findings seems evident. To date, there have been no reports of the concomitant occurrence of early pregnancy miscarriage, possibly LN-indicative glomerular proteinuria, and its spontaneous regression in a clinically and serologically inactive SLE patient. Recently, observations were confirmed that a large proportion of patients with a uPCR <1g/g had LN histology, whereas a relevant proportion had inactive sediment or normal serology like our patient. As the kidney is the organ most affected in SLE pregnancy, it is important to be aware of intermittent proteinuria, as the consequences may be very different from persistent proteinuria as would be expected in nephritis.



Diagnostic algorithm of intermittent glomerular proteinuria. *Clustering in probability of etiology. Arrow labeling indicates diagnostic steps leading to "rule-out" or "rule-in" of diagnosis.*

Figure 1.

REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1854

CORRELATION OF THE OUTCOMES MEASURED BY THE PATIENTS AND BY THE MEDICAL TEAM ACCORDING TO THE LEVEL OF ADHERENCE AND AN EDUCATIONAL TOOL FOR PATIENTS

Keywords: Outcome measures, Patient reported outcomes

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Table 1. Impact of education in patients with RA on clinical outcomes and the level of adherence

		Total group					Adherents only				
		MM					MM				
PM		Global VAS	Fatigue	MDHAQ	RAPID-3	EQ5	Global VAS	Fatigue	MDHAQ	RAPID-3	EQ5
Global VAS	Group A	**0,591****	0,339	0,651**	0,706**	-0,595**	**0,459***	0,369	0,537**	0,598**	-0,514*
	Group B	**0,498****	0,255*	0,397**	0,493**	-0,447**	**0,325**	0,236	0,432*	0,345	-0,517**
Fatigue	Group A	0,370**	**0,578****	0,363	0,409*	-0,253	0,391	**0,661****	0,542**	0,469*	-0,407
	Group B	0,483**	**0,457****	0,327**	0,451**	-0,415**	0,440*	**0,510****	0,480*	0,425*	-0,535**
MDHAQ	Group A	0,330	0,581**	**0,660****	0,398*	-0,525**	0,268	0,588**	**0,653****	0,364	-0,527*
	Group B	0,372**	0,330**	**0,679****	0,514**	-0,581**	0,395*	0,399*	**0,745****	0,514**	-0,744**
RAPID-3	Group A	0,581**	0,477*	0,736**	**0,693****	-0,658**	0,457*	0,518*	0,659**	**0,602****	-0,593**
	Group B	0,581**	0,370**	0,614**	**0,658****	-0,614**	0,477*	0,335	0,631**	**0,549****	-0,705**
EQ5	Group A	-,634**	-,575**	-0,756**	-0,705**	**0,865****	-0,644**	-0,665**	-0,769**	-0,761**	**0,791****
	Group B	-,440**	-,463**	-0,593**	-0,543**	**0,662****	-0,506**	-0,501**	-0,728**	-0,617**	**0,742****

MM: Medic measures; PM: Patient measures. Group A: Patients with educational training in RA. Group B: Patients without training.**. The correlation is significant at the 0.01 level (bilateral). *. The correlation is significant at the 0.05 level (bilateral).

Colombia; [4]*Fundación Universitaria de Ciencias de la Salud FUCS, Research Institute, Bogotá, Colombia*

Background: The level of adherence to treatment in patients with rheumatoid arthritis (RA) is important to achieve control of the disease. In turn, educational strategies in self-care and knowledge of RA help improve adherence and promote knowledge for self-measurement of clinimetry.

Objectives: The purpose of this work was to evaluate the correlation of the clinimetry measurements made by the doctor (MM) with those made by the patient (PM) in a group of patients with education in their disease and to compare it with another group of patients without specific education, according to the level of adherence.

Methods: A cross-sectional study was carried out that included adult patients with RA. Two groups were included, Group A: Patients with educational training in RA (12-14 months, face-to-face and virtual modules developed by an expert health group), Group B: Patients without training. Both groups measured their PM by means of a digital form and after one week they were evaluated (blind MM). Both PM and MM included global VAS, Fatigue, MDHAQ, RAPID 3 and EQ5, additionally the physician evaluated the DAS28, CDAI and the Morisky Green Levine Medication Adherence Scale. Correlations were made using the Pearson coefficient. The project was approved by the ethics committee.

Results: All the participants were women (Group A: 28, Group B: 63). Group A had a significantly higher proportion of higher than secondary schooling, erosivity, nodularity, polyautoimmunity, anti-CCP positivity, treatment with biologics, older age, and disease duration. The total group had a low level of disease activity (DAS28). A significant correlation (Table 1) was found in all the MM variables with corresponding ones PM, with the highest coefficients in group A (except in MDHAQ). There was a significantly higher proportion of adherent patients in group A (78.5%) than in group B (42.8). When analyzing the correlations in the subgroup of adherent patients, all the coefficients increased (except global VAS), maintaining the same ratio of superiority of correlation coefficients in group A compared to group B.

Conclusion: MM has a higher correlation with PM in patients with educational training in RA. These correlations are even greater in the group that is adherent to the treatment, persisting higher in the group with training. The results deserve to be replicated in patients with different levels of severity to those studied here.

REFERENCES: NIL.

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AB1855

SUSAC SYNDROME: CASE SERIES FROM ADULT & PEDIATRIC TERTIARY ACADEMIC MEDICAL CENTERS

Keywords: Vasculitis, Rare/orphan diseases

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Background: Susac Syndrome (SS) is a rare autoimmune endotheliopathy that affects the brain, retina, and inner ear, characterized by a clinical triad of encephalopathy, branch retinal artery occlusion (BRAO), and sensorineural hearing loss (SNHL)[1]. Brain MRI, fluorescein angiogram (FA), and audiometry help to establish a diagnosis[2]. The clinical presentation of SS is often variable leading to a delay in the diagnosis.

Objectives: This study aims to compare clinical features and therapeutic strategies in adult and pediatric populations with Susac Syndrome.

Methods: This was a retrospective chart review of cases with a diagnosis of SS from December 2010 to December 2020 at The Ohio State University Wexner Medical Center (OSUWMC) and Nationwide Children's Hospital in Columbus, Ohio, USA (tertiary care centers). We analyzed the following: age, gender, ethnicity, symptoms at the time of presentation, diagnostic studies, autoimmune serologies, brain MRI, FA, audiometry, treatment approaches, and outcomes.

Results: All the patients (seven adult- patients and two pediatric-onset patients) identified as females, and the majority (78%) were Caucasian. The age at presentation ranged from 10 to 45 years old with a mean age of 38 years. The time to diagnosis ranged from 3 to 17 months with a mean of 7.8 months. The most common symptoms at onset included dizziness, hearing loss, and visual change. ESR was elevated in 50% with a range of 23 to 52 mm/hr (normal<30 mm/hr). CRP was elevated in 22% of patients with a range of 11 to 22 mg/dl (normal <10 mg/dL). Low to medium titer ANA was positive in 30%. FA detected unilateral or bilateral BRAO in seven patients (78%). Sensorineural hearing loss was confirmed on audiogram testing in 7 of 9 patients, and 44% of patients had bilateral hearing loss. 88% of our patient population had evidence of corpus callosal involvement ("snowball lesions") in the brain MRI. CSF study was done in 5 patients - 4/5 had elevated CSF protein at 77 mg/dL (range 15-45 mg/dL) and the mean cell count was <3 (normal), without any oligoclonal bands. One patient had a brain biopsy. The most common initial treatment was high-dose steroids followed by a taper. Oral immunosuppressive therapy with mycophenolate mofetil (MMF) was initiated in 78% and was maintained in 56% of patients, who remained stable. Intravenous immunoglobulin (IVIG) was initially used in 56% of patients. Two patients transitioned from MMF to azathioprine due to pregnancy. Due to the severity of the disease, one patient transitioned from MMF to tacrolimus and Rituximab. 20% had a disease flare after the initial therapy requiring additional immunosuppression.

Conclusion: Our series highlights the rarity of SS. A neurologic exam, brain MRI, fluorescein angiogram, and audiogram should be performed in every case. A brain biopsy is not necessary for the diagnosis, unless for exclusion. BRAO was detected in 75% of our patients, highlighting the importance of an ophthalmology evaluation with FA, even in the absence of visual symptoms. In our series, only 20% presented with the full clinical triad of visual, auditory, and central nervous system symptoms, indicating that presentation of SS is often incomplete and diagnosis relies on a high index of suspicion[3]. Treatment depends on the severity of the presentation and involves the use of high-dose corticosteroids along with immunosuppression including mycophenolate, IVIG, tacrolimus, rituximab, and cyclophosphamide[4].

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Disclosure of Interests: None Declared.
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AB1856 IDENTIFYING THE ADULT-ONSET FAMILIAL COLD-ASSOCIATED AUTOINFLAMMATORY SYNDROME TYPE 2

Keywords: Genetics/Epigenetics, Innate immunity

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Background: Autoinflammatory syndromes encompass a group of diseases caused by dysregulation of the innate immune system that classically present with periodic fevers and usually debut in childhood.
Objectives: An unusual case of an autoinflammatory syndrome with adult onset is presented.
METHODS:
Results: This is a 57-year-old adult woman, ex-smoker, and ex-alcoholic, with no other personal history of interest. She was referred to internal medicine in 2017 for weight loss of 10-15 kg for two months, without other symptoms. Complementary test ruled out autoimmune aetiology and viral infections (hepatotropic and HIV), and a thoracoabdominal-pelvic CT scan identified micronodular millimetric liver lesions and sclerosing lesions in the vertebral and in the iliopubic bones, with no pathological data in a subsequent bone scan. The follow-up showed new symptoms, such as Raynaud's phenomenon, right carpitis (calcium pyrophosphate crystals in synovial fluid), and once again weight loss, and episodes of profuse sweating, predominantly in the evening, without thermometric fever. Studies at that time highlighted massive splenomegaly, retroperitoneal and mesenteric lymphadenopathy. Serologies HBV, HCV, HIV, Leishmaniasis, Rose Bengal, LUES and Mantoux were negative. Acute phase reactants changed from normal to sustained elevation: erythrocyte sedimentation rate (ESR) up to 120 mm/h, C-reactive protein (CRP) up to 136 mg/L and ferritin to 1380 ng/ml. In addition, she began to present progressive cytopenia (red and white series), with normocellular bone marrow biopsy. Given the suspicion of probable tumour origin, a liver biopsy was indicated, splenectomy with excision of abdominal lymphadenopathy with corresponding anatomopathological studies that ruled out tumours such as splenic lymphoma, tricholeukaemia and lymphoproliferative syndromes. After splenectomy, she presented clinical improvement interrupted by febrile episodes lasting a week with self-limited peaks (4-5 hours/day). Coinciding with one of the episodes, she presented with diffuse abdominal pain, vomiting and diarrhoea for which she was admitted. Gastrointestinal examination revealed evidence of hypertensive gastropathy and oesophageal varices, as well as liver fibrosis grade F4 (possible enolic origin). In the current year, an urticarial rash appeared on her legs, arms, trunk, and face, with a biopsy compatible with vasculitis-urticaria, which required treatment (prednisone 30 mg/day and colchicine 0.5 mg/day) getting remission but maintaining the febrile peaks and elevated ESR y CRP. A next-generation sequencing (NGS) genetic study was requested, which detected a c.753C>G p. (Asn251Lys) variant in the NLRP12 gene, a missense-type change. This mutation is associated with familial cold-associated autoinflammatory syndrome type 2.
Conclusion: Although the diagnosis of autoinflammatory syndrome is strongly linked to paediatric age, we should not forget to include this diagnosis in the study of an adult patient with recurrent febrile episodes after ruling out infectious processes before performing invasive techniques.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1857 A FIRST CASE REPORT OF SCHNITZLER SYNDROME PRESENTING WITH ACROPACHY AND LITERATURE REVIEW

Keywords: bDMARD, Imaging, Inflammatory arthritides

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Background: Schnitzler syndrome (SchS) is a rare and easily misdiagnosed autoinflammatory disease. The misdiagnosis not only delays proper treatment, but also leads to the unreasonable use of immunosuppressants or even chemotherapeutic agents which results in needless financial and physical burdens.
Objectives: The objective of this study was to summarize the clinical features and help physicians to avoid more misdiagnosis.
Methods: Here we report a 52-year-old female with SchS, who suffered from chronic pruritic urticaria, fever, and arthralgia for over 10 years. Then we systemically reviewed 471 patients, 470 from 138 previous case reports and 1 from our case report.
Results: Most of the patients were middle-aged or elderly women from European and American countries. There were limited number of cases coming from Asia, and no cases from Africa had yet been identified. The main clinical manifestations included chronic urticaria with or without pruritus, fever, arthralgia, ostealgia/myalgia, fatigue, and weight loss. Some cases also presented with lymphadenopathy, hepatomegaly, and splenomegaly. The presence of monoclonal immunoglobulin was the main diagnostic criteria, and the most common was IgMκ. Laboratory examinations also showed elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Neutrophil infiltration was the most common pathological results in the skin tissue of SchS patients. Currently, anti-IL-1 therapy seems to be the best choice, followed by anti-IL-6 therapy. Glucocorticoid and traditional immunosuppressants seemed to be ineffective to SchS.
Conclusion: As the diversity and variability of clinical symptoms, clinicians should pay more attention to the features of SchS to avoid misdiagnosis. Nearly half a century has passed since the first case of SchS was reported. Exploring its pathogenesis is still on the way. More Research is warranted for individualized therapy.
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Figure 1. Abnormalities in appearance. A: Urticaria on the face and thigh; B: Acropachy of both hands and feet.



Figure 2. A: X-ray showed bony hyperplasia "burr sign" at the acral areas of fingers (A) and toes (B).

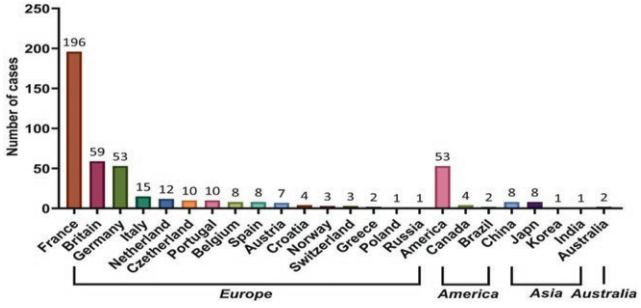


Figure 3. Number of reported cases sorted by country. Most of the patients with Schnitzler syndrome were from the reports of European and American countries, while limited cased were from Asia and none from Africa.

Acknowledgements: NIL.
Disclosure of Interests: None Declared.
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AB1858

RHEUMATOID MENINGITIS - A RARE PRESENTATION OF RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Diagnostic Tests

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Background: Rheumatoid arthritis (RA) is a multisystem autoimmune disease mainly affecting the joints. Rarely it can present with extra articular manifestations without any joint symptoms. Rheumatoid meningitis (RM) is an uncommon extra articular manifestation of the disease and can be the first presentation of RA very rarely.
Objectives: A 76 year old Caucasian lady was presented with aphasia of 10 minutes duration with frontal headache. Furthermore she complained of gradual onset difficulty in walking for the last 10 months and jerky legs. She was on treatment for hypothyroidism, hypertension, anxiety and denied any joint pains. Examination showed normal cranial nerves and spastic quadriparesis with limb power of 4/5, global hyperreflexia and extensor plantar reflexes. She was also observed to have focal clonic seizures of the left lower limb. Lungs were clear. 10 days later she developed painful left wrist and metacarpophalangeal joints with swelling and tenderness.
Methods: MRI of the brain with contrast showed right fronto-parietal leptomeningeal enhancement. Cerebrospinal fluid (CSF) tested repeatedly showed lymphocytic pleocytosis, normal glucose, mildly elevated proteins (0.6g/l). CSF was negative for flow cytometry, TB PCR, TB culture, antineuronal antibodies, cryptococcal antigen, viral PCR, fungal cultures, fungal studies and beta D glucan. Rheumatoid factor (141 iu/ml) and anti CCP antibodies (447u/ml) were strongly positive. CSF anti CCP antibody titre was 8 u/l. Rest of the autoimmune serology was negative. ACE level was normal. Inflammatory markers were raised. X ray of the hands showed degenerative changes only. CT chest abdomen and pelvis and FDG PET scan showed left sided axillary lymphadenopathy of which the biopsy showed reactive changes. CT also showed possible early interstitial lung disease (ILD).
Results: Patient was managed with the collaboration of the neurology team, rheumatology team and input from a tertiary care center. Meningeal biopsy was not done due to the risks involved and delay in starting treatment. RM was diagnosed after exclusion of other differential diagnosis. Patient was treated with IV methyl prednisolone 1g 3 pulses and started on a tailing off regime of oral prednisolone. Hydroxychloroquine and sulfasalazine were started as disease modifying treatment. Methotrexate was avoided due to the suspicion of ILD. Patient had good recovery clinically and radiologically in 6 months.
Conclusion: RM can be the first presentation of RA rarely. Hence it is important for rheumatologists to be aware of this rare manifestation. Usually patients develop joint symptoms within a year of presentation of RM [1]. Most of the patients are strongly sero positive [2]. Clinical symptoms can be diverse with focal neurological deficit, focal seizures, neuropsychiatric symptoms, stroke like episodes and headache. MRI characteristically shows meningeal enhancement. It can be confirmed with a meningeal biopsy. However RM can be diagnosed with confidence as in patient by thorough exclusion of other inflammatory, infective and paraneoplastic causes of chronic meningitis. It is postulated that anti CCP antibody levels in CSF is raised in patients with RM. Direct measurement of these values and calculation of intrathecal anti CCP antibody production based on these values are useful in diagnosing RM in patients, unable to go ahead with a meningeal biopsy [3]. Acute treatment of RM is immunosuppression with steroids that can be combined with cyclophosphamide or rituximab.

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AB1859

CERVICAL INVOLVEMENT IN CALCIUM PYROPHOSPHATE DEPOSITION DISEASE - DISEASE SPECTRUM

Keywords: Education, Imaging, Crystal Arthritis

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Background: Calcium pyrophosphate deposition disease (CPPD) is microcrystalline arthropathy that affect space joints and fibrocartilage, leading to inflammation and structural damage. CPPD affects predominantly the appendicular skeleton. For this reason, CPPD has several pseudonyms such as pseudogout, pseudo-rheumatoid arthritis, and pseudo-osteoarthritis. The involvement of the axial skeleton is less common or recognized but may have a broad spectrum of clinical presentations.
Objectives: To describe the clinical spectrum of axial manifestations of CPPD.
Methods: Case report and discussion.
Results: 1–Asymptomatic deposition of calcium pyrophosphate (CPP) in C1-C2: 68-year-old woman, diagnosed with CPPD with a pseudogout-like presentation. Previously, a knee arthrocentesis has been performed during an episode of monoarthritis. Blunt crystals with weak birefringence and positive elongation were identified in the synovial fluid analysis by polarized light microscope, compatible with CPP crystals. Later, the patient underwent a brain computed tomography (CT), after a head trauma, and it was observed the presence of calcification of the atlas transverse ligament (figure A), without associated symptoms.
2–Crowned Dens Syndrome: A 59-year-old woman, with a definitive diagnosis of CPPD secondary to iatrogenic hypomagnesemia by proton pump inhibitor, requested urgent evaluation due to inflammatory neck pain with 2 days of evolution. She reported sudden onset during the night, limitation of cervical mobility, and fever (38.1ºC). Moreover, the patient had suspended her medication (colchicine and oral magnesium) 1 month before the onset of complaints, without

medical advice. Analytically, she presented acute phase reactants elevation. Cervical spine CT showed mineralization of the transverse atlas and alar ligaments (figure B). The patient completed a low-dose corticosteroid regimen and restarted the usual medication, with rapid and complete recovery.

3–Retro-odontoid pseudotumor: An 85-year-old woman followed by neurosurgery for clinical signs suggestive of cervical myelopathy was referred to rheumatology. From the imaging study carried out, she had CT and MRI of the cervical spine and skull, where calcification and marked thickening of the atlantoaxial ligament complex and peri odontoid soft tissues were identified, with anterior dislocation of the odontoid and stenosis of the vertebral canal at the medullary bulb transition (figure C). Clinically, she reported longstanding episodes characterized by mixed rhythm cervicalgia. She denied a previous history of peripheral arthritis. Radiographic and ultrasound studies evidenced triangular fibrocartilage of the carpus and knee menisci chondrocalcinosis, and intracartilaginous hyperechoic images in multiple locations, suggestive of CPP deposition. The patient started therapy with colchicine 1mg/day and cervical orthosis for symptomatic control.

4–Inflammatory discitis: 78-year-old male, hospitalized for inflammatory neck pain, wrist and metacarpophalangeal joints arthritis, dysphagia, dyspnea, urinary incontinence, and fever. The laboratory analysis showed acute phase reactants elevation, without leukocytosis. After an exhaustive investigation of infectious etiology and refractoriness to multiple antibiotics, the patient started high-dose corticosteroid therapy with rapid resolution of complaints. The CT image showed C4-C5 and C5-C6 discitis with osteophytosis leading to pharyngeal anatomical distortion and periodontal and posterior longitudinal ligament calcification (figure D).

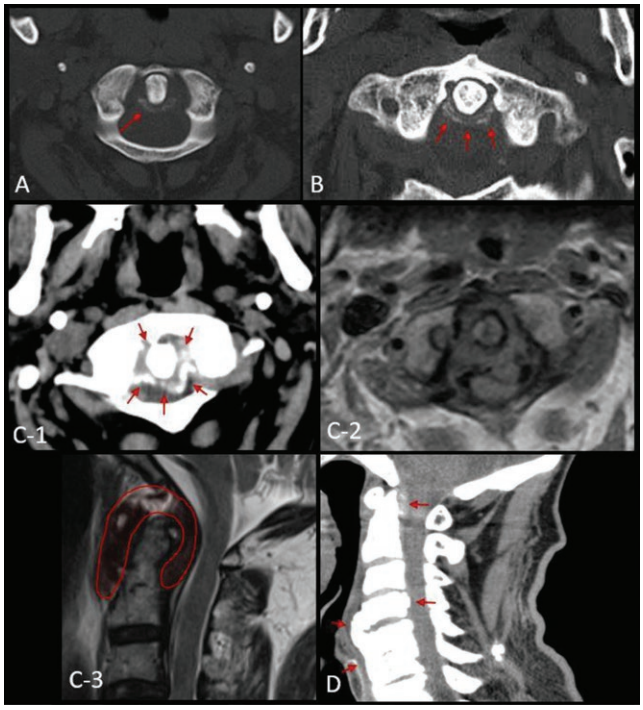


Figure 1.

Conclusion: The axial involvement of CPPD can have several clinical presentations, from asymptomatic to acute presentation with manifestations of other organ systems. The imaging findings of axial involvement are distinctive and can be crucial in the diagnosis. The differential diagnosis with other etiologies in situations of acute presentations, namely infectious, is imperative. Recognition of this potential clinical manifestation is essential to avoid underdiagnosis.

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AB1860 **CHARACTERISTICS OF IMMUNE CHECKPOINT INHIBITOR INDUCED SICCA SYNDROME**

Keywords: Sjögren syndrome, Real-world evidence

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Background: Immune checkpoint inhibitors (ICIs) have revolutionised management of certain cancers and significantly improved mortality. They work by blocking specific checkpoint proteins or ligands: CTLA-4 (ipilimumab), PD-1 (pembrolizumab and nivolumab) and PDL-1 (durvalumab and atezolizumab). This augments anti-tumour immunity through improved T cell function. Unfortunately the augmented immune function can lead to immune related adverse events (irAEs). One of these irAEs is sicca syndrome, which is a discrete entity from Sjogren's syndrome and was first reported by Cappelli in 2017[1].

Objectives: To report on a supra-regional cohort of patients with immune checkpoint inhibitor induced sicca syndrome, exploring clinical and pathological features.

Methods: We evaluated data from patients who were referred with new onset sicca symptoms to Queen Elizabeth Hospital Birmingham's Sjogren's service, between 2017 and 2022.

Results: 22 patients were identified (male =12, median age = 66) with underlying cancers (metastatic melanoma =16, renal cell carcinoma = 4, small cell lung cancer =1, hepatocellular carcinoma =1) who were being treated with various ICIs (atezolizumab =2, durvalumab =3, pembrolizumab = 5, nivolumab and ipilimumab combination = 11 and monotherapy nivolumab =1). 4 patients had pre-existing autoimmune disease (autoimmune thyroiditis =2, coeliac disease =1, type 1 diabetes mellitus =1). 21 patients reported xerostomia, with 15 of the 16 patients who performed salivary flow tests having very low unstimulated flow rates. Xeropthalmia was reported by 10 patients; interestingly 4 patients did not report dry eye symptoms but had significantly reduced tear production on Schirmer's testing. Glandular swelling was only seen in 2 patients. ANA was positive in 3 patients, none had a positive ENA. One patient was rheumatoid factor positive (38.8 IU/ml). 4 had IgG levels >16 g/L. No cases of hypocomplementaemia were seen. The median time to symptom onset, after ICI initiation, was 3 months, with varied intensity of onset. The mean oral dryness score, on initial assessment, was 6.5 out of 10 (SD ±2.5). ICI Therapy was stopped in 5 patients due to severity of symptoms. 3 required temporary discontinuation, due to sicca syndrome with an average pause of 9.3 weeks. 13 of the 22 patients had a history of additional irAEs, most commonly arthritis, colitis and endocrine issues (new onset diabetes, hypothyroidism, hypercalcaemia). Systemic steroids were required in 12 patients to alleviate their symptoms (starting doses 10-30mg), and 6 of these subsequently started hydroxychloroquine. Mean oral dryness score, following treatment (ICI cessation or aforementioned treatments) had reduced by over half, to a mean of 3.1 (SD ±2.9) at last clinical assessments. Labial salivary gland biopsy was performed in 15 patients; 4 showed focal lymphocytic sialadenitis (FLS; a biopsy finding also associated with Sjogren's syndrome). None of the patients with FLS had autoimmune disease or dryness symptoms predating ICI. The other 12 samples showed nonspecific chronic sialadenitis, with characteristic atrophy and fibrotic changes. Immunohistochemistry typically showed lightly dispersed CD3+ T cells with an even mixture of CD4+ and CD8+ cells.

Conclusion: We have presented the clinicopathological features of a supra-regional ICI induced sicca syndrome cohort. Our findings mirror those from the US cohort described by Warner et al[2] with significant oral symptoms which occur soon after treatment initiation and may respond to withholding or stopping ICI, steroids and hydroxychloroquine. ICI induced sicca syndrome significantly impacts quality of life and should be recognised as an irAE that in certain cases requires treatment.

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POS0759

MONOGENIC DISORDERS IN THE MAIDEN COHORT OF PEDIATRIC RHEUMATOLOGICAL DISEASES OF NEPAL- A SPECK OF IMPRINT ON EVEREST

Keywords: Real-world evidence, Genetics/epigenetics, Descriptive studies

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Background: Monogenic causes are increasingly being detected in pediatric rheumatological diseases (PRDs).[1] Monogenic disorders are inborn errors of immunity resulting into innate immune disturbance and autoinflammation. With increasing awareness and diagnostics, PRDs are diagnosed with increasing frequency and accuracy in Nepal.

Objectives: To describe the profile of children diagnosed with PRDs and monogenic causes explored on them at a tertiary care center in Nepal during 2020-2022.

Methods: Case records of patients diagnosed with PRDs during Aug 2020-November 2022 were analysed. The lead author (DB) collated data from all patients. Diagnosis and treatments were based on internationally acclaimed guidelines. Genotyping was done by whole exome sequencing and/or sanger sequencing.

Results: The availability of subspecialists, diagnostics, and therapeutics has shifted the paradigm of PRDs in developing countries. A total of 454 patients with PRDs were diagnosed. Mean duration from initial presentation to diagnosis was 12.5 months. Juvenile idiopathic arthritis (JIA) (including systemic JIA) (n = 131), connective tissue disorders (n = 113) and vasculitides (n = 104) constituted the largest proportion of PRDs. Arthritis related to infection was observed in 42 cases whereas autoinflammatory disorders were diagnosed in 29. Monogenic causes were detected in 19 patients (**Table 1**). Majority were of non-inflammosome related conditions. Causative genes were *CECR1, ARPC1B, TNFAIP3, NLRP3, TNFRSF1A, MVK, PSTPIP1, NOD2, NLRP3, STX11, TNFRSF6, XIAP, BMPR2, PIK3CD, CTLA4, GATA2* and *C1QA*. Clinical features included recurrent fever, rashes, edema, lymphadenopathy, arthritis, vasculitis, ear and ocular issues, organomegaly, and various multisystemic symptoms. Treatment of polyarteritis nodosa with mycophenolate mofetil and idiopathic calcinosis with methotrexate and pamidronate were notable reports from our cohort. Oligoarthritis in X-linked agammaglobulinemia was a peculiar finding. One child with the monogenic PRD has undergone hematopoietic stem cell transplantation.

Conclusion: We present first and largest cohort of PRDs from Nepal. Noticeable number of unique monogenic causes of PRDs were diagnosed for the first time in the country. There are significant challenges in diagnosis and treatment of PRDs in resource-limited settings. Various socioeconomic and environmental factors coupled with lack of awareness, fewer referrals, and inexpedient treatment accounted for a late presentation, missed diagnosis, increased morbidity, disability, and mortality.

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Table 1. Details of monogenic causes of pediatric rheumatological diseases from Nepal (2020-2022)

Diagnosis	Number of patients	Gene affected
Deficiency of Adenosine deaminase 2 (DADA2)	2	*CECR1*
ARP2/3-mediated filament branching defect	2	*ARPC1B*
Haploinsufficiency of A20	1	*TNFAIP3*
Familial cold autoinflammatory syndrome	1	*NLRP3*
Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)	1	*TNFRSF1A*
Hyperimmunoglobinemia D with periodic fever syndrome	1	*MVK*
Pyogenic sterile arthritis, pyoderma gangrenosum, and acne syndrome (PAPA) syndrome	1	*PSTPIP1*
Juvenile systemic granulomatosis (Blau syndrome)	1	*NOD2*
Neonatal-onset multisystem autoinflammatory disease	1	*NLRP3*
Familial hemophagocytic lymphohistiocytosis	1	*STX11*
Autoimmune lymphoproliferative syndrome	1	*TNFRSF6*
X-linked inhibitor of apoptosis protein deficiency	1	*XIAP*
Primary pulmonary hypertension	1	*BMPR2*
Activated Phosphoinositide 3-kinase δ syndrome (APDS)	1	*PIK3CD GOF*
CTLA4 haploinsufficiency (ALPS-V)	1	*CTLA4*
GATA2 deficiency	1	*GATA2*
C1Q deficiency (early complement defect lupus)	1	*C1QA*

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